BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-065032
Article Type:	Protocol
Date Submitted by the Author:	10-Jul-2022
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Keywords:	COVID-19, Rehabilitation medicine < INTERNAL MEDICINE, Neurology < INTERNAL MEDICINE

Home based tele-exercise for people with Chronic Neurological Impairments, COVID-19 and beyond: Protocol for a randomized control trial (RCT)

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Word count: 3910

Keywords: Tele-exercise, chronic neurological impairments, home-based, virtual training.

Abstract

Introduction: Exercise is vital to staying well and preventing secondary complications in people with Chronic Neurological Impairments (CNI). Appropriate exercise is often inaccessible to this population and effectiveness of virtual programs has seldom been studied. The purpose of the study is to investigate the effects of a 12-week seated virtual exercise program on heart rate, recovery, fatigue, pain, motivation, enjoyment, and quality of life in people with CNI. **Methods and Analysis:** Individuals with CNI will be screened for eligibility, and a total of 60 participants will be randomized into either a live or pre-recorded group. The live group will exercise with an instructor via Zoom while the pre-recorded group will exercise at their chosen time using pre-recorded videos. Heart rate during exercise/recovery, fatigue, motivation, level of pain and exertion will be assessed before and after each session. Physical well-being, enjoyment of physical activity, motivation, and quality of life will be assessed at baseline, midpoint, end of study, and one-month post-study. Adverse events, medication changes, and physical activity will be tracked throughout. Within-group and between-group comparisons will be performed using Wilcoxon Rank-Sum and Kruskal Wallis tests, respectively. **Ethics and Dissemination:** NCT04564495. Registered on September 25, 2020. Protocol version 1, dated May 15, 2022. Funded by Sabrina Cohen Foundation, the Burke Foundation, and grant number UL1 TR 002384 from the National Center for Advancing Translational Sciences (NCATS) of the National Institutes of Health (NIH).

Strengths and Limitations

Strengths

1. This is the first study to evaluate the impact of virtual adaptive seated exercises on cardiovascular function in individuals with chronic neurological impairments during COVID-19.
2. If objectives are met, individuals may be able to participate in virtual exercise programs without any expenditure of cost, travel, or time for community and fitness centers.
3. This study will use a comprehensive set of physiological and behavioral assessment measures to correlate effects of moderate intensity exercises on personal engagement and wellness.

Limitations

1. For those participants with limited technological experience, difficulty using blood pressure devices and heart rate monitors will cause missing data values.
2. The study population includes participants with any neurological diagnosis; thus, it is possible that the findings will not be generalizable to a specific sub-population.

Introduction

Exercise is a vital component to staying well and preventing secondary impairments. Exercise is known to positively influence a range of factors including cardiovascular health, cognition, mental health, bone health, sleep, and quality of life, among many others[1-8]. The benefits of exercise are further amplified in the estimated one billion people worldwide with Chronic (> 6 months) Neurological Impairments (CNI), as the injuries often lead to sedentary lifestyles and thus higher rates of obesity and cardiovascular disease. Incorporating an exercise regimen is vital to preventing secondary complications such as muscular weakness, fatigue, limited mobility, pain, spasticity, bone loss, and increased risk of fractures, falls, diabetes, depression, and obesity[7-10]. Exercise can be neuroprotective and neuro-regenerative by increasing neurotrophic factors, which are involved in neuroprotection, neuroplasticity, and maintenance of neuronal health[2, 11-15]. Exercise can also improve muscle strength and bone integrity in people with CNI[16-18].

People with CNI often cannot access community exercise centers, as mobility can be more difficult, insurance payments sparse, centers not welcoming or accessible, and assistive exercise equipment too costly for most facilities[19-32]. The COVID-19 pandemic has further reduced exercise options for people with disabilities, since many of these individuals are at increased risk of COVID-19 complications and therefore often cannot return to fitness centers.

Another key barrier to exercise for people with CNI is transportation[33]. Although COVID-19 introduced many new barriers to community participation, it also had some silver

linings for people with CNI. COVID-19 resulted in the emergence of many new Zoom or online classes tailored to people with CNI, which removed the barrier of transportation.

This study will examine the cardiovascular benefits, as well as differences in compliance, motivation and feelings of socialization and exertion between synchronous and asynchronous classes. The classes will be held for 12 weeks, 3 times/week using seated exercise via Zoom. The instructor will remain the same and alternate between boxing, high intensity interval training (HIIT) and power posture classes. We will examine the potential benefits of an accessible form of exercise for a population that is in urgent need, during times of COVID-19 and beyond. Additionally, by comparing live group synchronous and solo pre-recorded asynchronous classes, we will compare user compliance, motivation, enjoyment, and socialization.

We hypothesize that individuals in the synchronous class will have better attendance, more robust exertion as measured by heart rate, and better enjoyment than people in the asynchronous class, due to the social component of the synchronous classes. We hypothesize that participants in both groups will show improvement in heart rate recovery, physical wellness, quality of life, enjoyment, and motivation/engagement, and that changes will be greater in the synchronous class due to consistent supervision and contact.

Methods and Analysis

Study Design

This study is a parallel randomized controlled trial to investigate the effects of a 12-week, 3 times/week, seated tele-exercise program for adults with chronic neurological impairments (Figure 1). All 36 exercise sessions will be completed online via Zoom with the physical exercise instructor (live, synchronous group) or offline using recorded videos (pre-recorded, asynchronous group). Participants will be in their own homes as they complete the exercise classes. Participants can continue their medications, physical, occupational, speech therapies, and existing exercise routines (2 times/week or fewer).

Eligibility Criteria and Participants

The eligibility criteria will be kept broad to accommodate all neurological impairments.

Inclusion Criteria:

1. Participants diagnosed with Chronic (>6 months) Neurological Impairments
2. Ages 18 to 75 years
3. Able to sit for at least 1 hour
4. Stable Heart rate (HR) and Blood Pressure (BP)
5. Medical clearance to participate in moderate intensity exercises
6. Can don and doff a wrist HR monitor with or without assistance
7. Can maintain daily exercise and physical activity during the study
8. No other neurological, medical or cognitive impairments
9. Able to access the internet and use the cloud-based Zoom conference platform
10. Ability to speak and understand English
11. Currently exercising 2 days or less per week

12. Presence of caregiver or supervisor during exercise, for safety

Exclusion Criteria:

1. Unstable or uncontrolled medical conditions
2. Medical issues preventing safe participation
3. Unable to follow simple 2-step commands

Number of Participants

We plan to conduct multiple cohorts of participants, each with different participant populations, e.g., multiple sclerosis, cerebral palsy, stroke, spinal cord injury.

For each cohort, with 25 participants in the synchronous and asynchronous groups, we will have 80% power to detect a change in mean heart rate from about 80 bpm to 100 bpm (or greater) at 12 weeks (final session) (in each group, separately), using a paired t-test with a 0.05 two-sided significance level. This calculation assumes a conservative standard deviation of the pre/post differences in heart rate of 35 bpm at 12 weeks (final session). We plan for a 20% dropout rate, which means that we will recruit 30 participants per group to achieve 80% power.

Recruitment

Participants will be recruited via the Sabrina Cohen Foundation, which has a network of people with chronic neurological disabilities, and by BNI who has a database of potential participants from prior studies or programs. We will also post our recruitment

flier on our website, social media, and will mail it to neurological patient advocacy groups. If we cannot recruit appropriate numbers using these methods, we will pursue paid advertising in our community.

Randomization

One study team member will generate a series of permuted randomized blocks in a computerized spreadsheet with a defined block size of 4. Participants will be allocated to either the live (synchronous) or pre-recorded (asynchronous) group, with a 1:1 ratio between groups. Due to the nature of the intervention, it is not possible to conceal allocation from the participants or the study team. However, the two groups will never interact with one another.

Blinding and Rigor of Data

Due to the nature of the study, blinding of participants and study team members to group allocation will not be possible. All participants will complete the outcome surveys directly online, without input or assistance from the study team. Heart rate data will be collected through a heart rate monitor that collects quantitative data without input or filtering by the study team.

Intervention

The exercise intervention will be delivered by a trained professional who specializes in adaptive exercise for individuals with CNI. The instructor will structure each class to ensure standardization in terms of class structure, including warm-up, cool-down, cues for recording heart rate during class, use of additional equipment, and adherence to the general study protocol.

All participants, regardless of allocation to live or pre-recorded groups, will participate in 45 minutes of aerobic exercise intervention, three times a week, for a period of 12 weeks. The overall exercise session will be up to one hour long to include measuring vitals, answering questions before/after sessions, and rest breaks (if any). Two additional weeks will be provided for making up missed sessions, if applicable. Each intervention will be preceded by a warm-up and followed by a cool-down period. All participants will be asked to document any adverse events and changes in medications before each session. The order of classes will be rotated. Individual aerobic interventions for the first cohort are described below.

High intensity interval training (HIIT): HIIT involves repetitive bouts of high intensity exercises with intermittent periods of rest or active recovery. Exercise intensity could be as high as 80-100 percent of maximal heart rate during the intense circuits, but the duration of each bout of high intensity is about 10-30 seconds. Since this study will include participants with variable neurological impairments, the upper limit of exercise intensity in HIIT will be dependent on instructor's judgement, participant feedback, and rate of perceived exertion.

Boxing: Boxing involves a circuit of individual and combinations of moves like 'jabs', 'hooks', and 'uppercuts.' Boxing is a moderate to high intensity aerobic activity by

nature. Traditionally, bouts of upper body punching moves are planned around 'shuffling' to promote active recovery. All interventions will be done in a seated position to ensure participants' safety in their home environments. Active recovery will include upper body shuffling motions, relaxed upper body movements, etc. The exercise intensity for boxing, as in HIIT, will be subjective for participants based on level of perceived exertion as well as exercise heart rate restrictions, if any.

Power posture: Power posture is a HIIT-style strength and endurance class that promotes postural awareness. The warm-up period will be 5-10 minutes and focused on education of movement with slow, gentle repetitions to prepare the trapezius and other supporting scapular muscles for movement. This HIIT workout will target form, with fast paced targeted movements for 10-12 minutes. The cool-down will focus on gentle deep neck flexor/extensor chin tuck exercises, range of motion, and stretching.

Virtual Nature of the Study

Each aspect of this study will be performed virtually. Screenings will be performed on the telephone, with a standard list of criteria asked of each person. If deemed eligible, the potential participant will be sent a Zoom link to go through the informed consent on a one-to-one basis. The informed consent will be uploaded to REDCap, a secure web application for building and managing online surveys and databases. REDCap is 21 CFR Part 11-ready and HIPAA compliant and is specifically geared to support online and offline data capture for research studies and operations.

To obtain informed consent directly from participants, a study team member will arrange a Zoom call with each participant. The informed consent will be signed virtually by sharing a virtual remote with the participant during the call. If anyone has difficulty, they can be sent the informed consent from REDCap via email and return it to REDCap just as easily. Each participant will be sent a copy of their signed consent form via the same REDCap email system.

Each participant will be mailed a home exercise kit, which will contain a Polar optical heart rate monitor (OH1), yellow and green resistance TheraBands and wrist weights.

All questionnaires and questions to be answered before and after each class will be sent from and stored on REDCap. All heart rate data will be transmitted to the Polar website, which can be accessed only by the participant or the researchers. Then, the data will be analyzed in MATLAB using custom scripts written by the study team.

Study Safety

We will monitor side effects before and after each session by having participants complete surveys on REDCap. If pain or blood pressure are higher than usual, we will ask the participant if they wish to continue. If blood pressure rises near limitations prescribed by a participant's doctor, we will discontinue the participant. If any injury occurs during or outside of study sessions that may increase the risk of further injury, we will discontinue the participant.

Patient and Public Involvement

Persons with disabilities were involved in the design of this study, and will be involved in the conduct, reporting, and dissemination plans of this research.

Strategies to improve adherence

The study team will take attendance at each synchronous session and will monitor session completions for the asynchronous group. If a participant misses a class, we will reach out and inquire about their ability to attend future sessions. We have *a priori* set a minimum number of 30 of 36 classes that a participant must attend to be included in the main analyses of the study. We will offer 2 weeks of makeup sessions at the end of the 12 weeks. If a participant drops out before completing 30 sessions, we will encourage them to complete the post-study outcome measures and the satisfaction survey. We will use the number of sessions completed as a covariate in the analyses.

Outcome Measures

Session-specific Measures

Session-specific outcomes will capture changes before, during, and after each exercise session for both groups.

Heart rate tracking

Continuous heart rate tracking is the primary outcome measure for the study. All participants will receive the OH1 Polar HR monitor as part of their exercise kit for the study (Figure 2). Scheduled virtual training sessions will be held to train participants for

donning/doffing the heart rate monitor, using the Polar app, using their Polar accounts, syncing the Polar devices with their smartphones and starting/ending their heart rate tracking during exercise sessions. Heart rate (HR) tracking for exercise sessions begins at the start of the session and ends at 10 minutes after completion of session to capture heart rate during exercise (at 10Hz) as well as HR recovery after the end of exercise sessions. The live group will be supervised by the research team for each session. The pre-recorded groups will have the research team available for assistance and troubleshooting. Data are stored on the Polar Coach website, where study staff can export sessions as CSV files that are then processed in MATLAB (MathWorks). In MATLAB, baseline HR, peak HR, HR at end of session, and HR at 30s intervals for 5min after the end of the session will be analyzed, to measure heart rate recovery.

Secondary session-specific measures

On the day of the intervention, participants will complete an online assessment to rate the level of pain and perceived exertion (RPE), BP, HR, and adverse events before and after the exercise session. After the session is over, participants will complete a lab-developed survey to rate their experience on a 10-point scale from 1 (not a good experience) to 10 (very good experience) on questions related to motivation, energy, satisfaction, and performance. In addition, participants will provide information on changes related to health, falls, or other adverse events.

Timepoint Measures

A comprehensive set of outcome measures will be completed by participants at baseline, mid-study (6 weeks), end of study (12 weeks) and follow-up after one month. On study completion, participants will complete a study feedback form. The feedback will be based on study acceptance, ease of using HR and BP devices and exercise equipment, and support from the research team. Participants who do not complete the study will also provide their final timepoint measure at the end of their final exercise session.

Physiological Measure

Polar OH1 Heart Rate (HR) monitor: the Polar OH1 (Polar Electro Inc., Bethpage, NY, USA) is an optical heart rate sensor on an armband that records HR activity. It has 6 LED sensors that record at 1-second intervals[34]. HR activity is recorded via Bluetooth to a phone compatible with the Polar Flow or Polar Beat app. It has validity in moderate to vigorous intensity exercises and high endurance sports activities[34-36].

Surveys and Questionnaires

All questionnaires will be self-administered or administered by a trained researcher virtually using REDCap.

Perceived Wellness Survey (PWS): the PWS is a 36-item instrument used to measure an individual's perceived health status in physical, psychological, emotional, intellectual, spiritual, and social wellness constructs. Items under each construct are scored on a scale of 1 (very strongly disagree) to 6 (very strongly agree). Higher scores indicate better perceived wellness. The PWS has good reliability and validity in healthy and neurological populations[37-39].

Physical Activity Enjoyment Scale (PACES): the PACES is a self-assessment measure of enjoyment with their current physical activity. It is an 18-item scale with scoring from 1 (I enjoy it) to 7 (I hate it). Scores on the bipolar rating scale are summed with higher scores indicative of more enjoyment. It is reliable and valid in neurological populations[40-43].

Short Form-36 Health Survey (SF-36): the SF-36 measures physical health and mental health. There are eight scales - Physical Functioning, Physical Role Limitations, Bodily Pain, General Health, Vitality, Social Functioning, Emotional Role Limitations, and Mental Health. It is easy to use with good validity and reliability in neurological populations[44-47].

Numerical pain rating (NPR) scale: the NPR is a standardized instrument for pain assessment in clinical and research practice. It is an 11-point scale from 0 (no pain) to 10 (the most intense pain) at rest and during movement. It is simple to use with high sensitivity to changes in chronic pain in adult populations[48, 49]. It is reliable and valid for pain assessments of neurological populations[50].

Borg's Rating Scale of Perceived Exertion (RPE): the Borg RPE is a widely used standardized measure to evaluate perceived intensity of exertion, effort, and fatigue during physical exercise. The scale ranges from 6 (no exertion at all) to 20 (absolute maximum). Higher ratings on the scale indicate greater overall body exertion. It is a reliable and valid measure in neurological populations[51-58].

Reason for exercise inventory (REI): the REI is a 24-item scale to assess the reason that motivates a person to exercise. The modified version has 4 subscales:

Weight/appearance management, fitness/health management, stress/emotion management, and socialization. A 7-point scale ranges from 1 (not at all important) to 7 (extremely important). Higher scores represent greater motivation to exercise[59].

Statistical Methods

Descriptive statistics (including mean, standard deviation, median, interquartile range, frequency, and percent) will be calculated for demographic and clinical characteristics of the study participants. For the primary endpoint, heart rate, the two-sample t-test or nonparametric Wilcoxon Rank-Sum test will be used, as appropriate, to compare the mean (median) heart rate between the live and pre-recorded groups at 12 weeks (final session). The paired t-test or Wilcoxon Rank-Sum test will be used, as appropriate, to compare mean (median) heart rate before and after the final session (at 12 weeks) for the live and pre-recorded groups, separately. Similar analyses for heart rate (i.e., between and within groups) will also be performed after each session. Analysis of Covariance (ANCOVA) will be used to evaluate the independent effect of live versus pre-recorded group status on heart rate (at 12 weeks, final session), after controlling for baseline heart rate and any other factors that may remain imbalanced between groups after randomization. Adjusted mean differences in heart rate (at 12 weeks, final session) between the live and pre-recorded groups and 95% confidence intervals for these differences will be estimated from the multivariable ANCOVA model. Similar analyses as described above will be performed for other continuous outcomes (primary and secondary), including blood pressure, Borg's RPE scale, mood, motivation, and pain scales, Perceived Wellness Survey, SF-36v2 score, etc., at 12 weeks (final session)

and other time points of interest. Categorical variables (e.g., safety questions, adverse events, medication changes, etc.) will be compared between the live and pre-recorded groups (at baseline, 6 weeks, and 12 weeks) by the chi-square test or Fisher's exact test, as appropriate. Generalized estimating equations (GEE) modeling will also be explored to evaluate between-group differences over repeated assessments, and to account for potential missing data in some of the outcome variables at one or more of the evaluation time points. All estimates from the multivariable models will serve as preliminary data (i.e., hypothesis-generating) for future studies. All p-values will be two-sided with statistical significance evaluated at the 0.05 alpha level. Ninety-five percent confidence intervals for all parameters of interest will be calculated to assess the precision of the obtained estimates. All analyses will be performed in R and SPSS.

Data Management

Participant identifying information will be kept confidential by providing a unique identification number (ID number) for the course of the study. To maintain privacy, only authorized research investigators involved in the study will have access to participant information. Password protected laptops, online documents, and access to cloud-based servers will prevent leaks in data privacy. All records including informed consent, screening tools, medical records, and participant surveys will be completed, and documented on REDCap, a HIPAA-compliant online research database.

Privacy on Zoom platform: Our institutional Zoom account (through Weill Cornell Medicine) is compliant with HIPAA guidelines. Participant profile names will be updated

to display their ID. After each session, the recorded video will be uploaded to the password protected WCM cloud-based server. Respective group participants will be given the live Zoom links (synchronous) or passwords to access the asynchronous Zoom sessions.

Polar OH1 HR monitor (Optical HR sensor): Participants' profiles using allotted ID's will be created in the Polar Beat App and the Flow for Coach cloud-based online platform. All information uploaded to the platform will be accessible by the investigators using a secured login ID and password.

Adverse events, change in medications, and protocol deviation will be documented and updated before and after each class on REDCap. The study team will perform weekly self-audits to ensure data quality and completeness.

Procedure for handling missing data

This study is an intention-to-treat trial. If data are missing, we will use a mixed linear regression model that accounts for uneven numbers of data points across participants.

Data Monitoring and Stopping Rules

Since this is a low-risk study, our IRB determined that a data monitoring committee is not necessary. We will audit our data weekly and assess safety data at each session. If we find an increase in pain by 25% or a decrease in quality of life measures by 25% across participants in a cohort, we will pause the trial and evaluate how to improve the safety of the study.

Resource Sharing Plan

We plan to use the concept, methods and analysis as a framework to develop evidence-based protocols for future cohorts and studies. We have made a commitment to publish all relevant scientific information in a timely manner. Unpublished information may be available to interested individuals or organizations by request to the Principal Investigator.

Ethics and Dissemination

The study has been approved by the BRANY Institutional Review Board 20-08-388-512. All protocol deviations, adverse events, and protocol modifications will be reported to the IRB immediately. The results of the study will be disseminated to the academic community via publications and presentations. The deidentified study data will be shared on our laboratory website.

Trial Registration: Clinicaltrials.gov NCT04564495.

Acknowledgements: We thank the Sabrina Cohen Foundation for funding and for commitment to assist with study development and recruitment. We thank Devon Palermo at DPI Adaptive Fitness who will serve as the adaptive fitness instructor for this study.

Contributors: KMF is the Principal Investigator. KMF, AAD and AB were responsible for ethics applications and reporting. AAD, AB, DSK, RMG, LC and KMF drafted the final version of this manuscript. All authors have contributed to the writing and critical review of the manuscript and have approved the final version.

Funding: This work is supported by funding from the Sabrina Cohen Foundation and the Burke Foundation. This work is supported by grant number UL1 TR 002384 from the National Center for Advancing Translational Sciences (NCATS) of the National Institutes of Health (NIH).

Role of Funder in Study: The Sabrina Cohen Foundation has established the tele-exercise classes we are studying and will assist with recruitment. The Sabrina Cohen Foundation and Burke Foundation will have no role in data collection, analyses, interpretation, or publication of the work.

Competing Interests: None to declare

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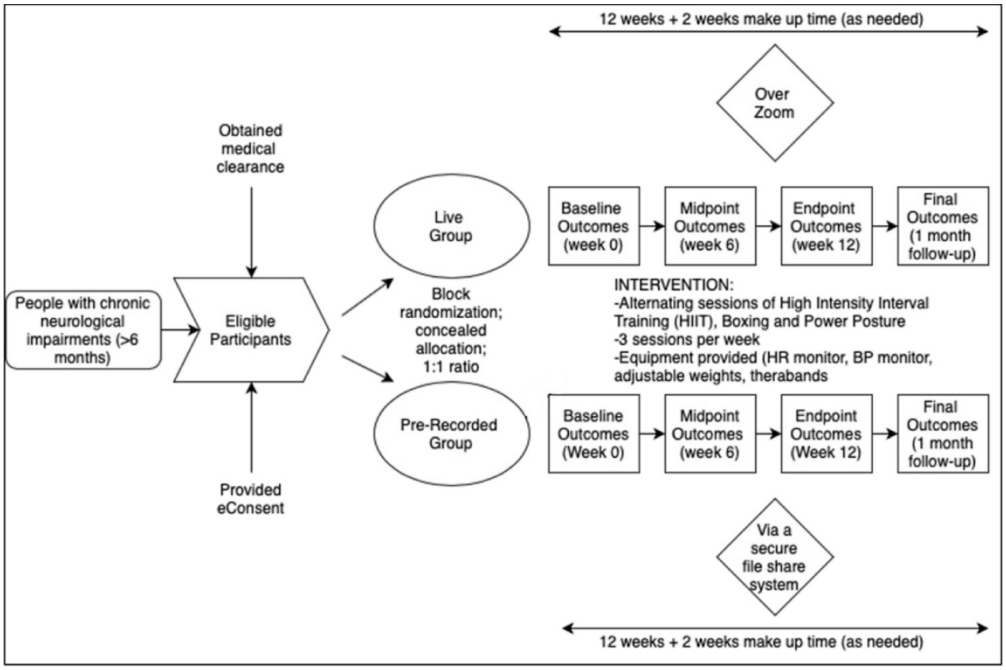
Figure Legends

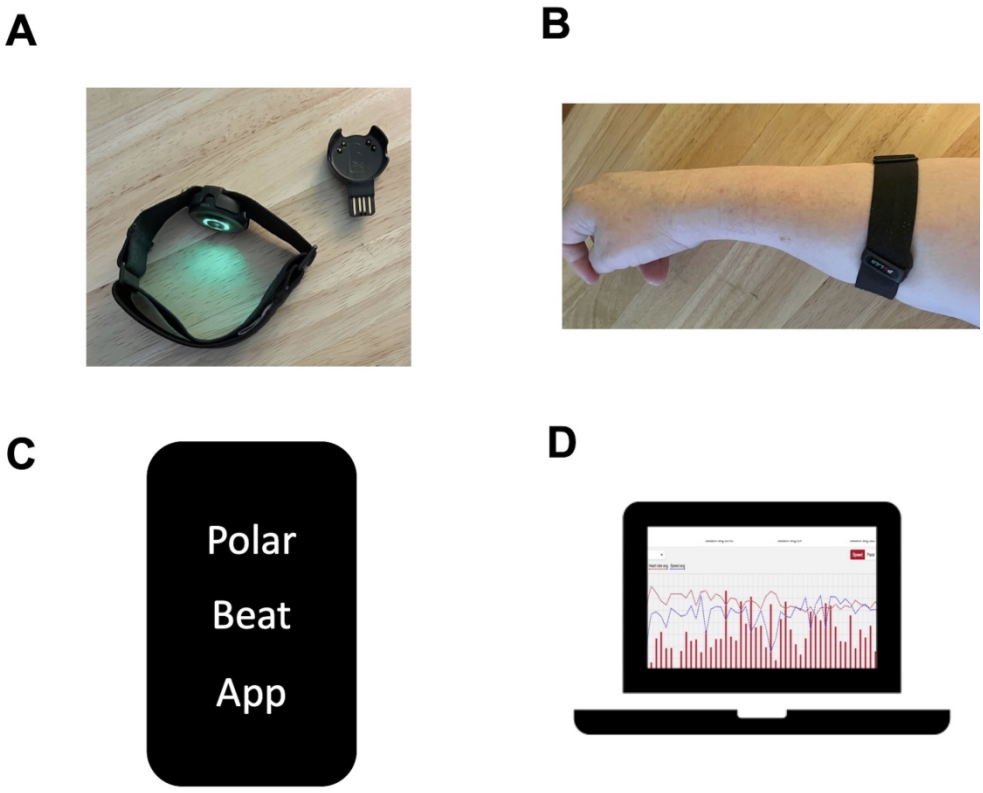
Figure 1: Study flow diagram.

Figure 2: Polar OH1 Heart Rate monitor. A. Picture of the monitor and charger. B. Proper placement of the monitor, with the device on the forearm. C. The Polar Beat app on a smart phone streams data in real time from the OH1 monitor via Bluetooth. D. After a session, data are retrievable from the Polar Coach website, where it is exported to a CSV file and processed in MATLAB.



Study flow diagram.

254x168mm (300 x 300 DPI)



Polar OH1 Heart Rate monitor. A. Picture of the monitor and charger. B. Proper placement of the monitor, with the device on the forearm. C. The Polar Beat app on a smart phone streams data in real time from the OH1 monitor via Bluetooth. D. After a session, data are retrievable from the Polar Coach website, where it is exported to a CSV file and processed in MATLAB.

254x212mm (300 x 300 DPI)

Informed Consent Form

This form explains our study and asks you to agree to partiicpate. Please read the form carefully. A member of our study team will talk with you over Zoom to explain the study. Thank you so much for your interest in our study!

BIOMEDICAL RESEARCH ALLIANCE OF NEW YORK
THE BURKE NEUROLOGICAL INSTITUTE

SUBJECT INFORMATION AND INFORMED CONSENT

Project Title: Home-Based Exercise for People with Chronic Neurological Impairments
Principal Investigator: Kathleen Friel, PhD
Institution Name: Burke Neurological Institute
Institution Address: 785 Mamaroneck Ave, White Plains, NY 10605
Telephone: 914-368-3116, 646-351-9063 (24 hour)
Protocol # TELEX

ABOUT VOLUNTEERING FOR THIS RESEARCH STUDY
You are invited to participate in a research study. The purpose of the study is to determine the effect of a home-based exercise program on cardiovascular fitness and your quality of life. We will assess your motivation, enjoyment and compliance to either a live or pre recorded exercise class on Zoom.

You are eligible for this study because you have a neurological impairment that you've had for at least six months. A neurological impairment is weakness in your arms and/or legs that was caused by a stroke, brain injury, spinal cord injury, or any other condition that affects your brain or spinal cord.

WHY IS THIS STUDY BEING DONE?
Scientists at The Burke Neurological Institute (BNI) are partnering with the Sabrina Cohen Foundation (SCF) to test whether a home-based exercise program can improve cardiovascular health and quality of life in people who have had a chronic neurological impairment. We designed this study after the onset of COVID-19 in the United States. Since COVID-19 limits accessibility to gyms and other types of exercise venues, we hope to learn and understand the physiological and behavioral aspects of this rehabilitation strategy to optimize wellness after a neurological injury. You were selected as a possible participant in this study because you've had a neurological impairment for at least six months.

WHAT WILL I DO IF I AGREE TO BE IN THIS STUDY?
If you agree to be in the study, you will participate in 36 at-home, Zoom-based exercise classes. Classes will be held three times a week, for twelve weeks. You will be randomized to either a live class with other video participants, or a pre-recorded class that you will take on your own.

Before the first class, we will review your medical history with you to be sure it is safe for you to be in the study. If you qualify for the study, we will send you a kit that contains items you will need for the study, including a heart rate monitor, blood pressure cuff and adjustable wrist weights. We will also send you some surveys that ask about your ability to do everyday activities, such as dressing and cooking.

After you receive your home exercise kit, we will have an orientation Zoom class. You will meet the other people in the exercise class. During the orientation, the study team will teach you how to use the heart rate monitor. If you cannot put on the heart rate monitor, we will ask that a caregiver be present to assist you during each class.

You will download one applications onto your phone or computer that will allow us to access the information from your heart rate monitor. No one but the research team will be able to see this information aside from you.

Each exercise class will take approximately one hour. Each session will begin with instructions and questions from the study team regarding your pain level, level of motivation, and blood pressure. The exercise portion of the class will take 45 minutes. At the end of the class, the study team will ask you additional questions, such as how hard you worked, pain level, level of motivation and blood pressure.

The class instructor will tailor exercises to different abilities, so everyone can be active and safe. The entire class will be done in a seated position.

Approximately 100 people will be enrolled in the live class, and 100 in the pre-recorded class.

After the 18th class, which is midway through the study, we will send you another set of the same surveys you completed before the first class. We will send you a third set of surveys after the final class.

RISKS AND INCONVENIENCES OF THE STUDY
Your participation in the project might involve the following risks:

The largest risk in this study is the risk of fatigue and muscle aches. These symptoms are common with exercise. The instructor will offer modifications of each exercise, to offer easier or more difficult options. You will always be welcome to use a modification, request an additional modification, or rest.

The risk of fall in this study is small, since you will be seated. If you normally have trouble with stability of your torso while you are seated, we will ask that a caregiver be present in case a fall occurs.

There is a risk that your personal health information be disclosed in error. For this study, we are using secure Zoom settings from an academic medical center, and we will require a password for each class, to mitigate this risk. The app containing your heart rate information will also be secure.

PERMISSION FOR PHOTOGRAPHY
We will record each live class, video and audio. Since we are not together in one space, we need to record each class for purposes of data collection. Therefore, we require each participant to agree to being recorded. We want to make sure that you understand this.

Do you agree to be photographed in this study?
◯ Yes
◯ No

Please initial here to confirm your choice about being photographed during the study:

_____

NEW INFORMATION
You will be told about any new significant findings developed during the course of the study that might affect your willingness to continue in the research.

COST OF STUDY TO PARTICIPANTS
There is no cost to you for participating in the research study.

BENEFITS OF THIS STUDY
Participation in this study is not guaranteed to benefit you. This study is only for the purpose of research. You may feel stronger by the end of the study, but there is no guarantee that this will occur. However, the information learned from this study may help other people in the future.

ALTERNATIVES TO STUDY PARTICIPATION
You do not have to participate in this research study to receive treatment for your condition. Your participation in this study is voluntary. If you decide to participate, you are free to discontinue participation at any time. Your participation in this study may be terminated without your consent by the study team or regulatory authorities, in certain circumstances, such as, if the investigator determines it is in your best interest, you cannot adhere to the study procedures, or in the event the study is terminated.

IN CASE OF INJURY
In accordance with Federal regulation, we are obligated to inform you about our policy in the event injury occurs. For medical emergencies, call 911. If, as a result of your participation, you experience injury from known or unknown risks of the research procedures as described, emergency medical care and treatment will be provided on our premises to the extent possible. We will assist you in obtaining additional medical care, as needed, but you will be responsible for the costs of such further medical treatment, either directly or through your medical insurance and/or other forms of medical coverage. No other compensation will be offered by or Burke Neurological Institute or the Biomedical Research Alliance of New York. Further information can be obtained from Dr Kathleen Friel (914 368-3116). You are not waiving any legal right to seek additional compensation through the courts by signing this form.

CONFIDENTIALITY
To the extent allowed by law, every effort will be made to keep your personal information confidential. However, information from this study will be submitted to the study sponsor and to the U.S. Food and Drug Administration. It may be submitted to governmental agencies in other countries where the study product may be considered for approval. Medical records, which identify you and the consent form signed by you, will be looked at by the sponsor or the sponsor's representatives and may be looked at by the FDA and other regulatory agencies, the Institutional Review Board, and the Biomedical Research Alliance of New York. While these parties are aware of the need to keep your information confidential, total confidentiality cannot be guaranteed. The results of this research project may be presented at meetings or in publications; however, you will not be identified in these presentations and/ or publications.

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study doctor must get your authorization (permission) to use or give out any health information that might identify you. If you choose to be in this study, the study doctor will get personal information about you. This may include information that might identify you. The study doctor may also get information about your health, including:

• Past and present medical records
• Research records
• Records about phone calls made as part of this research
• Records about your study visits
• Information obtained during this research about laboratory test results
• Results from diagnostic and medical procedures including but not limited to X-rays, physical examinations and medical history
• Billing records

Information about your health may be used and given to others by the study doctor and staff. They might see the research information during and after the study. Your information may be given to the sponsor of this research. "Sponsor" includes any persons or companies that are working for or with the sponsor, or are owned by the sponsor. Information about you and your health which might identify you may be given to:

• The U.S. Food and Drug Administration
• Department of Health and Human Services agencies
• Governmental agencies in other countries
• Biomedical Research Alliance of New York (BRANY)
• The Institutional Review Board
• Accrediting agencies

Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the U.S. federal privacy laws. However, these groups are committed to keeping your personal health information confidential. If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others without your permission.

Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study. In addition, people from the sponsor and its consultants will be visiting the research site. They will follow how the study is done, and they will be reviewing your information for this purpose. The information may be given to the FDA. It may also be given to governmental agencies in other countries. This is done so the sponsor can receive marketing approval for new products resulting from this research. The information may also be used to meet the reporting requirements of governmental agencies.

This authorization does not have an expiration date. If you do not withdraw this authorization in writing, it will remain in effect indefinitely.

By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. You do not have to sign this consent form. If you choose not to sign this consent form, you will not be able to be in this research study. Your decision not to sign this consent form will not have any effect on your medical care and you will not lose any benefits or legal rights to which you are entitled. You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you may not be allowed to look at or copy your information until after the research is completed.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor at the address on the front of this informed consent form. If you withdraw your permission, you will not be able to continue being in this study, but you will not have any penalty or loss of access to treatment or other benefits to which you are entitled. When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Notice Concerning HIV-Related Information: HIV-related information that either is collected as part of the research or that may already exist in your medical record might be accessed for the research by the research staff and the study sponsor, but will not be shared with others without your authorization, unless federal or state law requires the disclosure. You have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights or New York City Commission on Human Rights. These agencies are responsible for protecting your rights.

QUESTIONS ABOUT THIS STUDY
If you have any questions or requests for information relating to this research study or your participation in it, or if you want to voice a complaint or concern about this research, or if you have a study related injury, you may contact Dr. Friel at 914-368-3116, 646-351-9063 (24 hour).

If you have any questions about your rights as a research subject or complaints regarding this research study, or you are unable to reach the research staff, you may contact a person independent of the research team at the Biomedical Research Alliance of New York Institutional Review Board at 516-318-6877. Questions, concerns or complaints about research can also be registered with the Biomedical Research Alliance of New York Institutional Review Board at www.branyirb.com/concerns-about-research.

You will be given a copy of this form to keep.

A description of this clinical trial will be available on http://www.Clinical Trials.gov as required by U.S. Law This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can research this Web site at any time.

You are making a decision as to whether or not to participate. Your signature indicates that the above information has been reviewed with you and that you have decided to participate. You may withdraw at any time without prejudice after signing this form should you choose to discontinue participation in this study.

Signature:

_____

Date:

_____

Time:

_____

Upload a copy of informed consent here, if the participant chose to provide consent on paper

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
	2b	All items from the World Health Organization Trial Registration Data Set	1, 2, 3, 7, 8-10, 12-15-18, 20
Protocol version	3	Date and version identifier	2
Funding	4	Sources and types of financial, material, and other support	2
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1, 19
	5b	Name and contact information for the trial sponsor	N/A
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	20
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
	6b	Explanation for choice of comparators	4-5
Objectives	7	Specific objectives or hypotheses	5
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	5-6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6-7
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8-10
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	11
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	11-12
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	6
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	12-15
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	13 and Fig 1

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	7
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	7
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	8
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	8
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	8
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	9
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	9
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	12-15
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	11-12

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	17-18
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	15-17
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	15-17
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	18
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	18
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	18
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	18
	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	18
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	19
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	19

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	10-11
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	17-18
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	20
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	17
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	no plans for post-trial care, compensation plan due to injury listed in ICF p2 “In Case of Injury”
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	19
	31b	Authorship eligibility guidelines and any intended use of professional writers	19
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	19
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	supplemental
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

BMJ Open

Effects of a 12-week, seated virtual home-based tele-exercise program compared with a pre-recorded video-based exercise program in people with chronic neurological impairments: protocol for a randomized control trial (RCT)

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-065032.R1
Article Type:	Protocol
Date Submitted by the Author:	14-Nov-2022
Complete List of Authors:	Divecha, Ayushi A.; Burke Neurological Institute Bialek, Amy; Burke Neurological Institute Kumar, Devina S.; Burke Neurological Institute Garn, Rachel; Burke Neurological Institute Currie, Lydia; Burke Neurological Institute Campos, Talita; Burke Neurological Institute Friel, Kathleen M.; Burke Neurological Institute; Weill Cornell Medicine
Primary Subject Heading:	Sports and exercise medicine
Secondary Subject Heading:	Rehabilitation medicine
Keywords:	Rehabilitation medicine < INTERNAL MEDICINE, Neurology < INTERNAL MEDICINE, Telemedicine < BIOTECHNOLOGY & BIOINFORMATICS

Effects of a 12-week, seated virtual home-based tele-exercise program compared with a pre-recorded video-based exercise program in people with chronic neurological impairments: protocol for a randomized control trial (RCT)

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Word count: 4676

Keywords: Tele-exercise, chronic neurological impairments, home-based, virtual training.

Abstract

Introduction: Exercise is vital to staying well and preventing secondary complications in people with Chronic Neurological Impairments (CNI). Appropriate exercise is often inaccessible to this population. The purpose of the study is to investigate the effects of a seated virtual exercise program on heart rate, recovery, fatigue, pain, motivation, enjoyment, and quality of life in people with CNI. **Methods and Analysis:** Individuals with CNI will be screened for eligibility, and 60 participants will be randomized 1:1 into either a live or pre-recorded group. There is no geographic limitation to where participants reside, since participation is virtual. The study will be coordinated by one site in White Plains, NY, USA. The live group will exercise with an instructor via Zoom while the pre-recorded group will exercise at their chosen time using pre-recorded videos, 3x/week for 12 weeks. Primary outcome measure: change in heart rate during exercise/recovery. Secondary outcome measures: fatigue, motivation, level of pain and exertion, physical well-being, enjoyment of physical activity, motivation, and quality of life. Outcomes will be assessed at baseline, midpoint, end of study, and one-month post-study. Adverse events, medication changes, and physical activity will be tracked throughout. Within-group and between-group comparisons will be performed using Analysis of Covariance and regression. **Ethics and Dissemination:** BRANY IRB approval: 09/22/2020. All participants will provide written informed consent. Results will be disseminated through presentations, publications, and clinicaltrials.gov. Trial registration number: ClinicalTrials.gov, NCT04564495.

Strengths and Limitations of This Study

1. This study will use a comprehensive set of physiological and behavioral assessments to assess effects of exercise.
2. The virtual design of the study enables people to participate without commuting to our institute.
3. For those participants with limited technological experience, difficulty using blood pressure devices and heart rate monitors will cause missing data values.
4. The virtual design of the study prohibits hands-on evaluations.

Introduction

Exercise is a vital component to staying well and preventing secondary impairments. Exercise is known to positively influence a range of factors including cardiovascular health, cognition, mental health, bone health, sleep, and quality of life, among many others[1-8]. The benefits of exercise are further amplified in the estimated one billion people worldwide with Chronic (> 6 months) Neurological Impairments (CNI), as the injuries often lead to sedentary lifestyles and thus higher rates of obesity and cardiovascular disease[9-11]. Incorporating an exercise regimen is vital to preventing secondary complications such as muscular weakness, fatigue, limited mobility, pain, spasticity, bone loss, and increased risk of fractures, falls, diabetes, depression, and obesity[7, 8, 12, 13]. Exercise can be neuroprotective and neuro-regenerative by increasing neurotrophic factors, which are involved in neuroprotection, neuroplasticity, and maintenance of neuronal health[2, 14-18]. Exercise can also improve muscle strength and bone integrity in people with CNI[19-21].

People with CNI often cannot access community exercise centers, as mobility can be more difficult, insurance payments sparse, centers not welcoming or accessible, and assistive exercise equipment too costly for most facilities[22-35].

Another key barrier to exercise for people with CNI is transportation[36]. Although COVID-19 introduced many new barriers to community participation, it also had some silver linings for people with CNI. COVID-19 resulted in the emergence of many new Zoom or online classes tailored to people with CNI, which removed the barrier of transportation.

Although there has been an explosion of virtual-based exercise opportunities since 2020, much is unknown regarding optimal delivery models to bring exercise to people

with CNI. Two general types of virtual exercise delivery models exist. In synchronous exercise, one or more participants join a virtual space via videoconferencing, and interact with the trainer in real time. Synchronous exercise enables the trainer to provide feedback as participants exercise. In contrast, in asynchronous exercise, trainers record instructional videos, which participants complete on their own time, without being in the same virtual space with the trainer at the same time. Asynchronous exercise provides scheduling flexibility to participants but does not allow for real time interaction and feedback from the trainer. There has only been one study directly comparing synchronous versus asynchronous exercise training in people with CNI.

In a recent study, forty adults with spinal cord injury were randomized to either synchronous or asynchronous tele-exercise. While there was no significant difference in average daily workload between the interventions, the synchronous tele-exercise found significantly higher values for adherence and successful data recording of the exercise, resulting in greater weekly training loads[37]. Virtual exercise platforms are part of society even as the pandemic wanes. Thus, it is important to determine optimal delivery models for specific groups of participants.

This study will examine the cardiovascular benefits, as well as differences in compliance, motivation and feelings of socialization and exertion between synchronous and asynchronous classes. The classes will be held for 12 weeks, 3 times/week using seated exercise via Zoom. The instructor will remain the same and alternate between boxing, high intensity interval training (HIIT) and power posture classes. We will examine the potential benefits of an accessible form of exercise for a population that is

in urgent need. Additionally, by comparing synchronous and asynchronous classes, we will compare user compliance, motivation, enjoyment, and socialization.

We hypothesize that individuals in the synchronous class will have better attendance, more robust exertion as measured by heart rate, and better enjoyment than people in the asynchronous class, due to the social component of the synchronous classes. We hypothesize that participants in both groups will show improvement in heart rate recovery, physical wellness, quality of life, enjoyment, and motivation/engagement, and that changes will be greater in the synchronous class due to consistent supervision and contact.

Methods and Analysis

Study Design

This study is a parallel randomized controlled trial to investigate the effects of a 12-week, 3 times/week, seated tele-exercise program for adults with CNI (Figure 1). All 36 exercise sessions will be completed online via Zoom with the physical exercise instructor (live, synchronous group) or offline using recorded videos (pre-recorded, asynchronous group). Participants will be in their own homes as they complete the exercise classes. Participants can continue their medications, physical, occupational, speech therapies, and existing exercise routines (2 times/week or fewer).

Eligibility Criteria and Participants

The eligibility criteria will be kept broad to accommodate all neurological impairments.

Inclusion Criteria:

1. Participants diagnosed with Chronic (>6 months) Neurological Impairments
2. Ages 18 to 75 years
3. Able to sit for at least 1 hour
4. Stable Heart rate (HR) and Blood Pressure (BP)
5. Medical clearance to participate in moderate intensity exercises
6. Can don and doff a wrist HR monitor with or without assistance
7. Can maintain daily exercise and physical activity during the study
8. No other neurological, medical or cognitive impairments
9. Able to access the internet and use the cloud-based Zoom conference platform
10. Ability to speak and understand English
11. Currently exercising 2 days or less per week
12. Presence of caregiver or supervisor during exercise, for safety

Exclusion Criteria:

1. Unstable or uncontrolled medical conditions
2. Medical issues preventing safe participation
3. Unable to follow simple 2-step commands

Number of Participants

We plan to conduct multiple cohorts of participants, each with different participant populations, e.g., multiple sclerosis, cerebral palsy, stroke, spinal cord injury.

For each cohort, with 27 participants in the synchronous and asynchronous groups, we will have 80% power to detect a change in maximum heart rate during exercise from about 80 bpm to 100 bpm (or greater), from the first session to the last session of the intervention. This calculation assumes a conservative standard deviation of the pre/post differences in heart rate of 35 bpm. We plan for a 30% dropout rate, which is an estimate based on our feasibility pilot study (see below), which means that we will recruit 35 participants per group to achieve 80% power.

Recruitment

Participants will be recruited via the Sabrina Cohen Foundation, which has a network of people with CNI, and by the Burke Neurological Institute, who has a database of potential participants from prior studies or programs. We will also post our recruitment flier on our website, social media, and will mail it to neurological patient advocacy groups. If we cannot recruit appropriate numbers using these methods, we will pursue paid advertising in our community.

Randomization

A person not affiliated with the study will generate a series of permuted randomized blocks in a computerized spreadsheet with a defined block size of 4. Participants will be allocated to either the live (synchronous) or pre-recorded (asynchronous) group, with a 1:1 ratio between groups. Due to the nature of the intervention, it is not possible to

conceal allocation from the participants or the study team. However, the two groups will never interact with one another.

Blinding and Rigor of Data

Due to the nature of the study, blinding of participants and study team members to group allocation will not be possible. All participants will complete the outcome surveys directly online, without input or assistance from the study team. Heart rate data will be collected through a heart rate monitor that collects quantitative data without input or filtering by the study team.

Intervention

The exercise intervention will be delivered by a trained professional who specializes in adaptive exercise for individuals with CNI. The instructor will structure each class to ensure standardization in terms of class structure, including warm-up, cool-down, cues for recording heart rate during class, use of additional equipment, and adherence to the general study protocol. The instructor has extensive experience in offering adaptations to exercises in a virtual setting. He offers alternative ways to perform the exercises, such that everyone in class will be able to fully participate safely.

All participants, regardless of allocation to live or pre-recorded groups, will participate in 45 minutes of aerobic exercise intervention, three times a week, for a period of 12 weeks. The overall exercise session will be up to one hour long to include measuring vitals, answering questions before/after sessions, and rest breaks (if any). Two

additional weeks will be provided for making up missed sessions, if applicable. Each intervention will be preceded by a warm-up and followed by a cool-down period. All participants will be asked to document any adverse events and changes in medications before each session. The order of classes will be rotated. Individual aerobic interventions for the first cohort are described below and summarized in Table 1.

Table 1: Summary of Exercise Sessions

Minutes into Session	HIIT	Boxing	Power Posture
5	Warm up	Warm up	Warm up
10	Intervals of 30 sec high intensity movements, 1-2 min lower intensity	Intervals of 30 sec high intensity boxing movements, 1-2 min lower intensity	Stretching
15			Fast paced movements targeting trunk, posture
20			
25			
30			Stretching
35			
40	Cool down	Cool down	Cool down
45	End	End	End

High intensity interval training (HIIT): In HIIT sessions, participants will do repetitive bouts of high intensity exercises, with intermittent periods of rest or active recovery. Examples of high intensity movements used in these sessions include fast punching movements, repeatedly rapidly lifting one's arms overhead (with or without weights, as tolerated by each participant), and abdominal crunches. The duration of each bout of high intensity is about 10-30 seconds. Since this study will include participants with variable neurological impairments, the upper limit of exercise intensity in HIIT will be

dependent on instructor's judgement, participant feedback, rate of perceived exertion, and any exercise heart rate restrictions given by their doctor in the medical screening.

Boxing: In boxing sessions, participants will do a circuit of individual and combinations of various arm strikes and punches. Boxing is a moderate to high intensity aerobic activity by nature. During the session, participants will do bouts of high intensity movements, similar to HIIT, along with periods of lower intensity arm movements such as practicing defensive blocks of punches from an imaginary boxing opponent. The exercise intensity for boxing, as in HIIT, will be subjective for participants based on level of perceived exertion as well as exercise heart rate restrictions, if any.

Power posture: Power posture is a HIIT-style strength and endurance class in which participants will move in ways that train trunk stability and control of sitting with correct posture. In these sessions, there will be a warm-up period of 5-10 minutes, focused on slow, gentle repetitions to prepare the trapezius and other supporting scapular muscles for movement. This workout will target postural form, with fast paced targeted movements for 10-15 minutes. After the fast paced movements, a cool-down period will focus on gentle deep neck flexor/extensor chin tuck exercises, range of motion, and stretching.

Virtual Nature of the Study

Each aspect of this study will be performed virtually. Screenings will be performed on the telephone, with a standard list of criteria asked of each person. If deemed eligible, the potential participant will be sent a Zoom link to go through the informed consent on

a one-to-one basis. The informed consent will be uploaded to REDCap, a secure web application for building and managing online surveys and databases. REDCap is 21 CFR Part 11-ready and HIPAA compliant and is specifically geared to support online and offline data capture for research studies and operations.

To obtain informed consent directly from participants, a study team member will arrange a Zoom call with each participant. The informed consent will be signed virtually by sharing a virtual remote with the participant during the call. If anyone has difficulty, they can be sent the informed consent from REDCap via email and return it to REDCap just as easily. Each participant will be sent a copy of their signed consent form via the same REDCap email system (see Supplemental Material for a sample consent form).

Each participant will be mailed a home exercise kit, which will contain a Polar optical heart rate monitor (OH1), blood pressure monitor, yellow and green resistance TheraBands and wrist weights.

After the home kits have been received by the participants and before the intervention begins, we will hold a series or training videoconferencing calls to acquaint participants with the study procedures and the use of all devices.

Polar OH1 heart rate monitor: we will train participants in donning/doffing the heart rate monitor, using the Polar app, using their Polar accounts, syncing the Polar devices with their smartphones and starting/ending their heart rate tracking during exercise sessions.

Blood pressure monitor: we will send each participant a commercially available automatic blood pressure (BP) monitor. We will train each person to use it, and we have

embedded an instructional video into the REDCap data entry form on which participants will input their BP.

Checking compliance: after each session, a study team member will review each participant's data entry forms and synching of their heart rate data with the Polar app. For the synchronous group, this will occur before the participant leaves the session. For the asynchronous group, this will occur within one day of when the participant completes the session.

All questionnaires and questions to be answered before and after each class will be sent from and stored on REDCap. All heart rate data will be transmitted to the Polar website, which can be accessed only by the participant or the researchers. Then, the data will be analyzed in MATLAB using custom scripts written by the study team.

Study Safety

We will monitor side effects before and after each session by having participants complete surveys on REDCap. If pain or blood pressure are higher than usual, we will ask the participant if they wish to continue. If blood pressure rises near limitations prescribed by a participant's doctor, we will discontinue the participant. If any injury occurs during or outside of study sessions that may increase the risk of further injury, we will discontinue the participant.

Patient and Public Involvement

Persons with disabilities were involved in the design of this study, and will be involved in the conduct, reporting, and dissemination plans of this research.

Strategies to improve adherence

In this study, adherence is defined as the number of sessions a participant completed. The study team will take attendance at each synchronous session and will monitor session completions for the asynchronous group. Completion for the asynchronous group will be monitored via REDCap. Each time a person completes a data entry form before and after the session, it will be automatically saved and time stamped in REDCap.

If a participant misses a class, we will reach out and inquire about their ability to attend future sessions. We have *a priori* set a minimum number of 30 of 36 classes that a participant must attend to be included in the main analyses of the study. We will offer 2 weeks of makeup sessions at the end of the 12 weeks. If a participant drops out before completing 30 sessions, we will encourage them to complete the post-study outcome measures and the satisfaction survey. We will use the number of sessions completed as a covariate in the analyses.

Outcome Measures

All outcome measures are summarized in Table 2.

Table 2: Outcome Measures

PRIMARY OUTCOME MEASURE			
Measure	**Modality Assessed**	**Method of Ascertainment**	**Timepoints**
Peak heart rate	Cardiovascular function	Polar OH1/Polar Beat app	Each session
SECONDARY OUTCOME MEASURES			
Measure	**Modality Assessed**	**Method of Ascertainment**	**Timepoints**
Demographics	--	REDCap survey	Before first session
Attendance	Adherence	REDCap time stamps	Each session
Baseline heart rate	Cardiovascular function	Polar OH1/Polar Beat app	Each session
Heart rate at end of session	Cardiovascular function	Polar OH1/Polar Beat app	Each session
Heart rate recovery	Cardiovascular function	Polar OH1/Polar Beat app	Each session
Blood pressure	Cardiovascular function	Automatic BP device	Before and after each session
Rate of Perceived Exertion	Cardiopulmonary fitness	REDCap survey	Before and after each session
Perceived Wellness Survey	Wellness	REDCap survey	Baseline, weeks 6, 12, 16
Physical Activity Enjoyment Scale	Enjoyment of exercise	REDCap survey	Baseline, weeks 6, 12, 16
Short Form-36	Physical and mental health	REDCap survey	Baseline, weeks 6, 12, 16
Numerical Pain Rating Scale	Pain	REDCap survey	Baseline, weeks 6, 12, 16
Reason for Exercise Inventory	Motivation to exercise	REDCap survey	Baseline, weeks 6, 12, 16
Participant Feedback Survey	Participant satisfaction	REDCap survey	End of study or at dropout

Demographics

We will collect the following demographics by having each participant complete a demographics data entry form on REDCap: age, gender, neurological diagnosis, time of diagnosis, and comorbid health issues (e.g., diabetes, high blood pressure, etc.). We will also document whether a person needs assistance with walking or transfers. In addition, we will require each participant to receive written medical clearance by their doctor to participate in the study, and if any exercise restrictions need to be followed.

Primary outcome measure: Peak heart rate during exercise

Continuous heart rate tracking is the primary outcome measure for the study. All participants will receive the OH1 Polar HR monitor as part of their exercise kit for the study (Figure 2). The Polar OH1 (Polar Electro Inc., Bethpage, NY, USA) is an optical heart rate sensor on an armband that records HR activity. It has 6 LED sensors that record at 1-second intervals[38]. HR activity is recorded via Bluetooth to a phone compatible with the Polar Flow or Polar Beat app. It has validity in moderate to vigorous intensity exercises and high endurance sports activities [38-40].

Immediately before each exercise session, participants will turn on their OH1 monitor. Then, the participant will open the Polar Beat app on their smart phone and hit “start” when the exercise session begins. The Polar OH1 continuously records heart rate (HR) at 10Hz when the device is powered on and the Polar Beat app recording has been started. Participants will record HR through the entire exercise session and for 10 minutes after completion of the session to capture HR during exercise as well as HR

recovery for 10 minutes after the end of exercise sessions. The live group will be supervised by the research team for each session. The pre-recorded groups will have the research team available for assistance and troubleshooting. Data are stored on the Polar Coach website, where study staff can export sessions as CSV files that are then processed in MATLAB (MathWorks). In MATLAB, peak HR (primary measure) will be calculated.

Secondary outcome measures

Measures acquired at each exercise session

We will calculate secondary measures of HR in MATLAB using the same Polar CSV files mentioned above: baseline HR, HR at end of session, and HR at 30s intervals for 10min after the end of the session will be analyzed, to measure heart rate recovery.

At each session, participants will complete an online assessment to rate the level of pain and perceived exertion (RPE), BP, HR, and adverse events before and after the exercise session. Additionally, as described above, attendance will be taken at each session as a measure of adherence. After the session is over, participants will complete a lab-developed survey to rate their experience on a 10-point scale from 1 (not a good experience) to 10 (very good experience) on questions related to motivation, energy, satisfaction, and performance. In addition, participants will provide information on changes related to health, falls, or other adverse events.

Measures acquired at specified times during the intervention

A comprehensive set of secondary outcome measures will be completed by participants at baseline, mid-study (6 weeks), end of study (12 weeks) and follow-up after one

month. All questionnaires will be self-administered or administered by a trained researcher virtually using REDCap.

Perceived Wellness Survey (PWS): Participants will quantify their perceived health status by completing the PWS. The PWS is a 36-item instrument used to measure an individual's perceived health status in physical, psychological, emotional, intellectual, spiritual, and social wellness constructs. Items under each construct are scored on a scale of 1 (very strongly disagree) to 6 (very strongly agree). Higher scores indicate better perceived wellness. The PWS has good reliability and validity in healthy and neurological populations[41-43].

Physical Activity Enjoyment Scale (PACES): the PACES is a self-assessment measure of enjoyment with their current physical activity. It is an 18-item scale with scoring from 1 (I enjoy it) to 7 (I hate it). Scores on the bipolar rating scale are summed with higher scores indicative of more enjoyment. It is reliable and valid in neurological populations[44-47].

Short Form-36 Health Survey (SF-36): the SF-36 measures physical health and mental health. There are eight scales - Physical Functioning, Physical Role Limitations, Bodily Pain, General Health, Vitality, Social Functioning, Emotional Role Limitations, and Mental Health. It is easy to use with good validity and reliability in neurological populations[48-51].

Numerical pain rating (NPR) scale: the NPR is a standardized instrument for pain assessment in clinical and research practice. It is an 11-point scale from 0 (no pain) to 10 (the most intense pain) at rest and during movement. It is simple to use with high

sensitivity to changes in chronic pain in adult populations[52, 53]. It is reliable and valid for pain assessments of neurological populations[54].

Borg's Rating Scale of Perceived Exertion (RPE): the Borg RPE is a widely used standardized measure to evaluate perceived intensity of exertion, effort, and fatigue during physical exercise. The scale ranges from 6 (no exertion at all) to 20 (absolute maximum). Higher ratings on the scale indicate greater overall body exertion. It is a reliable and valid measure in neurological populations[55-62].

Reason for exercise inventory (REI): the REI is a 24-item scale to assess the reason that motivates a person to exercise. The modified version has 4 subscales: Weight/appearance management, fitness/health management, stress/emotion management, and socialization. A 7-point scale ranges from 1 (not at all important) to 7 (extremely important). Higher scores represent greater motivation to exercise[63].

Participant feedback: on study completion, or when withdrawn/dropped out from the study, participants will complete a study feedback form. The feedback will be based on study acceptance, ease of using HR and BP devices and exercise equipment, and support from the research team. Participants who do not complete the study will also provide their final timepoint measure at the end of their final exercise session.

Statistical Methods

Descriptive statistics (including mean, standard deviation, median, interquartile range, frequency, and percent) will be calculated for demographic and clinical characteristics of the study participants.. Analysis of Covariance (ANCOVA) will be used to evaluate the

independent effect of synchronous versus asynchronous group status on change in peak heart rate (first session versus final session), after controlling for baseline heart rate and any other factors that may remain imbalanced between groups after randomization. Adjusted mean differences in peak heart rate (first session versus final session) between the synchronous and asynchronous groups and 95% confidence intervals for these differences will be estimated from the multivariable ANCOVA model. Similar analyses as described above will be performed for other continuous outcomes (primary and secondary), including Borg's RPE scale, mood, motivation, and pain scales, Perceived Wellness Survey, SF-36v2 score, and PACES score. Categorical variables (e.g., safety questions, adverse events, medication changes, etc.) will be compared between the synchronous and asynchronous groups (at baseline, 6 weeks, and 12 weeks) by the chi-square test or Fisher's exact test, as appropriate. Generalized estimating equations (GEE) modeling will also be explored to evaluate between-group differences over repeated assessments, and to account for potential missing data in some of the outcome variables at one or more of the evaluation time points. All estimates from the multivariable models will serve as preliminary data (i.e., hypothesis-generating) for future studies. All p-values will be two-sided with statistical significance evaluated at the 0.05 alpha level. Ninety-five percent confidence intervals for all parameters of interest will be calculated to assess the precision of the obtained estimates. All analyses will be performed in R and SPSS by a person blinded to treatment allocation.

Data Management

Participant identifying information will be kept confidential by providing a unique identification number (ID number) for the course of the study. To maintain privacy, only authorized research investigators involved in the study will have access to participant information. Password protected laptops, online documents, and access to cloud-based servers will prevent leaks in data privacy. All records including informed consent, screening tools, medical records, and participant surveys will be completed, and documented on REDCap, a HIPAA-compliant online research database.

Privacy on Zoom platform: Our institutional Zoom account (through Weill Cornell Medicine) is compliant with HIPAA guidelines. Participant profile names will be updated to display their ID. After each session, the recorded video will be uploaded to the password protected WCM cloud-based server. Respective group participants will be given the live Zoom links (synchronous) or passwords to access the asynchronous Zoom sessions.

Polar OH1 HR monitor (Optical HR sensor): Participants' profiles using allotted ID's will be created in the Polar Beat App and the Flow for Coach cloud-based online platform. All information uploaded to the platform will be accessible by the investigators using a secured login ID and password.

Adverse events, change in medications, and protocol deviation will be documented and updated before and after each class on REDCap. The study team will perform weekly self-audits to ensure data quality and completeness.

Procedure for handling missing data

This study is an intention-to-treat trial. If data are missing, we will use a mixed linear regression model that accounts for uneven numbers of data points across participants.

Data Monitoring and Stopping Rules

Since this is a low-risk study, our IRB determined that a data monitoring committee is not necessary. We will audit our data weekly and assess safety data at each session. If we find an increase in pain by 25% or a decrease in quality of life measures by 25% across participants in a cohort, we will pause the trial and evaluate how to improve the safety of the study.

Current Status of Study

We have performed a feasibility cohort, with people with a range of abilities and diagnoses. The first participant was consented on 01/22/2021, for an intervention that began on 03/24/2021 and ended on 06/28/2021. In this feasibility study, we determined that participants could readily complete the online assessments, exercise sessions, and could effectively use Zoom, the Polar OH1 sensor and Polar Beat app, and the blood pressure measurement device. Our next step will be to enroll separate cohorts of people with specific neurological diagnoses, such as cerebral palsy, stroke, and multiple sclerosis. This will begin in 2023.

Resource Sharing Plan

We plan to use the concept, methods and analysis as a framework to develop evidence-based protocols for future cohorts and studies. We have made a commitment to publish all relevant scientific information in a timely manner. Unpublished information may be available to interested individuals or organizations by request to the Principal Investigator.

Ethics and Dissemination

The study was approved by the BRANY Institutional Review Board on 9/22/2020, protocol #20-08-388-512. All study participants will provide written informed consent before participation. All protocol deviations, adverse events, and protocol modifications will be reported to the IRB immediately. The results of the study will be disseminated to the academic community via publications and presentations. The deidentified study data will be shared on our laboratory website.

Trial Registration: Clinicaltrials.gov NCT04564495.

Acknowledgements: We thank the Sabrina Cohen Foundation for funding and for commitment to assist with study development and recruitment. We thank Devon Palermo at DPI Adaptive Fitness who will serve as the adaptive fitness instructor for this study.

Contributors: KMF is the Principal Investigator. KMF, AAD and AB were responsible for ethics applications and reporting. AAD, AB, DSK, RMG, LEJC, TAC and KMF

drafted the final version of this manuscript. All authors have contributed to the writing and critical review of the manuscript and have approved the final version.

Funding: This work is supported by funding from the Sabrina Cohen Foundation and the Burke Foundation. This work is supported by grant number UL1 TR 002384 from the National Center for Advancing Translational Sciences (NCATS) of the National Institutes of Health (NIH).

Role of Funder in Study: The Sabrina Cohen Foundation has established the tele-exercise classes we are studying and will assist with recruitment. The Sabrina Cohen Foundation and Burke Foundation will have no role in data collection, analyses, interpretation, or publication of the work.

Competing Interests: None to declare

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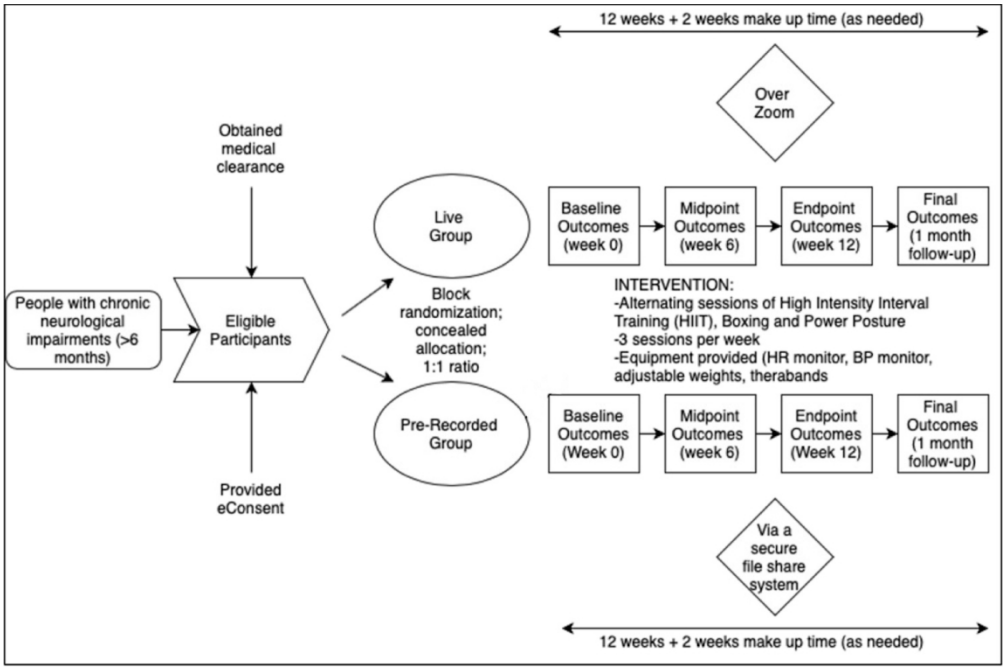
Figure Legends

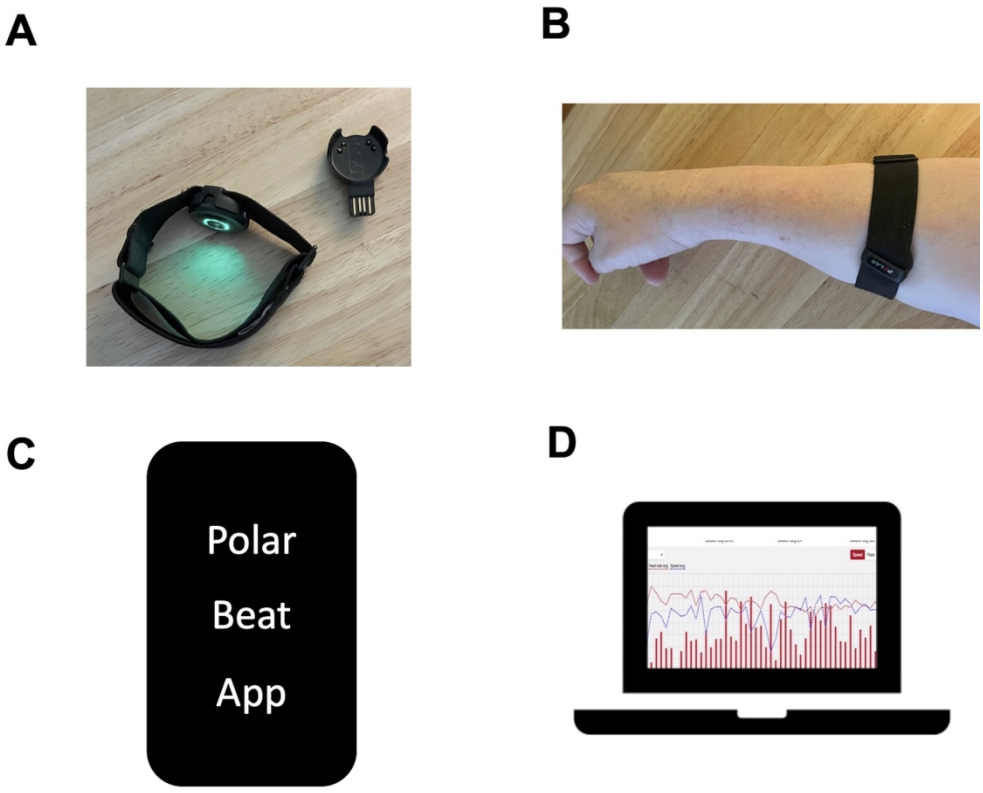
Figure 1: Study flow diagram.

Figure 2: Polar OH1 Heart Rate monitor. A. Picture of the monitor and charger. B. Proper placement of the monitor, with the device on the forearm. C. The Polar Beat app on a smart phone streams data in real time from the OH1 monitor via Bluetooth. D. After a session, data are retrievable from the Polar Coach website, where it is exported to a CSV file and processed in MATLAB.



Study flow diagram.

254x168mm (300 x 300 DPI)



Polar OH1 Heart Rate monitor. A. Picture of the monitor and charger. B. Proper placement of the monitor, with the device on the forearm. C. The Polar Beat app on a smart phone streams data in real time from the OH1 monitor via Bluetooth. D. After a session, data are retrievable from the Polar Coach website, where it is exported to a CSV file and processed in MATLAB.

254x212mm (300 x 300 DPI)

Informed Consent Form

This form explains our study and asks you to agree to partiicpate. Please read the form carefully. A member of our study team will talk with you over Zoom to explain the study. Thank you so much for your interest in our study!

BIOMEDICAL RESEARCH ALLIANCE OF NEW YORK
THE BURKE NEUROLOGICAL INSTITUTE

SUBJECT INFORMATION AND INFORMED CONSENT

Project Title: Home-Based Exercise for People with Chronic Neurological Impairments
Principal Investigator: Kathleen Friel, PhD
Institution Name: Burke Neurological Institute
Institution Address: 785 Mamaroneck Ave, White Plains, NY 10605
Telephone: 914-368-3116, 646-351-9063 (24 hour)
Protocol # TELEX

ABOUT VOLUNTEERING FOR THIS RESEARCH STUDY
You are invited to participate in a research study. The purpose of the study is to determine the effect of a home-based exercise program on cardiovascular fitness and your quality of life. We will assess your motivation, enjoyment and compliance to either a live or pre recorded exercise class on Zoom.

You are eligible for this study because you have a neurological impairment that you've had for at least six months. A neurological impairment is weakness in your arms and/or legs that was caused by a stroke, brain injury, spinal cord injury, or any other condition that affects your brain or spinal cord.

WHY IS THIS STUDY BEING DONE?
Scientists at The Burke Neurological Institute (BNI) are partnering with the Sabrina Cohen Foundation (SCF) to test whether a home-based exercise program can improve cardiovascular health and quality of life in people who have had a chronic neurological impairment. We designed this study after the onset of COVID-19 in the United States. Since COVID-19 limits accessibility to gyms and other types of exercise venues, we hope to learn and understand the physiological and behavioral aspects of this rehabilitation strategy to optimize wellness after a neurological injury. You were selected as a possible participant in this study because you've had a neurological impairment for at least six months.

WHAT WILL I DO IF I AGREE TO BE IN THIS STUDY?
If you agree to be in the study, you will participate in 36 at-home, Zoom-based exercise classes. Classes will be held three times a week, for twelve weeks. You will be randomized to either a live class with other video participants, or a pre-recorded class that you will take on your own.

Before the first class, we will review your medical history with you to be sure it is safe for you to be in the study. If you qualify for the study, we will send you a kit that contains items you will need for the study, including a heart rate monitor, blood pressure cuff and adjustable wrist weights. We will also send you some surveys that ask about your ability to do everyday activities, such as dressing and cooking.

After you receive your home exercise kit, we will have an orientation Zoom class. You will meet the other people in the exercise class. During the orientation, the study team will teach you how to use the heart rate monitor. If you cannot put on the heart rate monitor, we will ask that a caregiver be present to assist you during each class.

You will download one applications onto your phone or computer that will allow us to access the information from your heart rate monitor. No one but the research team will be able to see this information aside from you.

Each exercise class will take approximately one hour. Each session will begin with instructions and questions from the study team regarding your pain level, level of motivation, and blood pressure. The exercise portion of the class will take 45 minutes. At the end of the class, the study team will ask you additional questions, such as how hard you worked, pain level, level of motivation and blood pressure.

The class instructor will tailor exercises to different abilities, so everyone can be active and safe. The entire class will be done in a seated position.

Approximately 100 people will be enrolled in the live class, and 100 in the pre-recorded class.

After the 18th class, which is midway through the study, we will send you another set of the same surveys you completed before the first class. We will send you a third set of surveys after the final class.

RISKS AND INCONVENIENCES OF THE STUDY
Your participation in the project might involve the following risks:

The largest risk in this study is the risk of fatigue and muscle aches. These symptoms are common with exercise. The instructor will offer modifications of each exercise, to offer easier or more difficult options. You will always be welcome to use a modification, request an additional modification, or rest.

The risk of fall in this study is small, since you will be seated. If you normally have trouble with stability of your torso while you are seated, we will ask that a caregiver be present in case a fall occurs.

There is a risk that your personal health information be disclosed in error. For this study, we are using secure Zoom settings from an academic medical center, and we will require a password for each class, to mitigate this risk. The app containing your heart rate information will also be secure.

PERMISSION FOR PHOTOGRAPHY
We will record each live class, video and audio. Since we are not together in one space, we need to record each class for purposes of data collection. Therefore, we require each participant to agree to being recorded. We want to make sure that you understand this.

Do you agree to be photographed in this study?
◯ Yes
◯ No

Please initial here to confirm your choice about being photographed during the study:

_____

NEW INFORMATION
You will be told about any new significant findings developed during the course of the study that might affect your willingness to continue in the research.

COST OF STUDY TO PARTICIPANTS
There is no cost to you for participating in the research study.

BENEFITS OF THIS STUDY
Participation in this study is not guaranteed to benefit you. This study is only for the purpose of research. You may feel stronger by the end of the study, but there is no guarantee that this will occur. However, the information learned from this study may help other people in the future.

ALTERNATIVES TO STUDY PARTICIPATION
You do not have to participate in this research study to receive treatment for your condition. Your participation in this study is voluntary. If you decide to participate, you are free to discontinue participation at any time. Your participation in this study may be terminated without your consent by the study team or regulatory authorities, in certain circumstances, such as, if the investigator determines it is in your best interest, you cannot adhere to the study procedures, or in the event the study is terminated.

IN CASE OF INJURY
In accordance with Federal regulation, we are obligated to inform you about our policy in the event injury occurs. For medical emergencies, call 911. If, as a result of your participation, you experience injury from known or unknown risks of the research procedures as described, emergency medical care and treatment will be provided on our premises to the extent possible. We will assist you in obtaining additional medical care, as needed, but you will be responsible for the costs of such further medical treatment, either directly or through your medical insurance and/or other forms of medical coverage. No other compensation will be offered by or Burke Neurological Institute or the Biomedical Research Alliance of New York. Further information can be obtained from Dr Kathleen Friel (914 368-3116). You are not waiving any legal right to seek additional compensation through the courts by signing this form.

CONFIDENTIALITY
To the extent allowed by law, every effort will be made to keep your personal information confidential. However, information from this study will be submitted to the study sponsor and to the U.S. Food and Drug Administration. It may be submitted to governmental agencies in other countries where the study product may be considered for approval. Medical records, which identify you and the consent form signed by you, will be looked at by the sponsor or the sponsor's representatives and may be looked at by the FDA and other regulatory agencies, the Institutional Review Board, and the Biomedical Research Alliance of New York. While these parties are aware of the need to keep your information confidential, total confidentiality cannot be guaranteed. The results of this research project may be presented at meetings or in publications; however, you will not be identified in these presentations and/ or publications.

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study doctor must get your authorization (permission) to use or give out any health information that might identify you. If you choose to be in this study, the study doctor will get personal information about you. This may include information that might identify you. The study doctor may also get information about your health, including:

• Past and present medical records
• Research records
• Records about phone calls made as part of this research
• Records about your study visits
• Information obtained during this research about laboratory test results
• Results from diagnostic and medical procedures including but not limited to X-rays, physical examinations and medical history
• Billing records

Information about your health may be used and given to others by the study doctor and staff. They might see the research information during and after the study. Your information may be given to the sponsor of this research. "Sponsor" includes any persons or companies that are working for or with the sponsor, or are owned by the sponsor. Information about you and your health which might identify you may be given to:

• The U.S. Food and Drug Administration
• Department of Health and Human Services agencies
• Governmental agencies in other countries
• Biomedical Research Alliance of New York (BRANY)
• The Institutional Review Board
• Accrediting agencies

Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the U.S. federal privacy laws. However, these groups are committed to keeping your personal health information confidential. If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others without your permission.

Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study. In addition, people from the sponsor and its consultants will be visiting the research site. They will follow how the study is done, and they will be reviewing your information for this purpose. The information may be given to the FDA. It may also be given to governmental agencies in other countries. This is done so the sponsor can receive marketing approval for new products resulting from this research. The information may also be used to meet the reporting requirements of governmental agencies.

This authorization does not have an expiration date. If you do not withdraw this authorization in writing, it will remain in effect indefinitely.

By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. You do not have to sign this consent form. If you choose not to sign this consent form, you will not be able to be in this research study. Your decision not to sign this consent form will not have any effect on your medical care and you will not lose any benefits or legal rights to which you are entitled. You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you may not be allowed to look at or copy your information until after the research is completed.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor at the address on the front of this informed consent form. If you withdraw your permission, you will not be able to continue being in this study, but you will not have any penalty or loss of access to treatment or other benefits to which you are entitled. When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Notice Concerning HIV-Related Information: HIV-related information that either is collected as part of the research or that may already exist in your medical record might be accessed for the research by the research staff and the study sponsor, but will not be shared with others without your authorization, unless federal or state law requires the disclosure. You have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights or New York City Commission on Human Rights. These agencies are responsible for protecting your rights.

QUESTIONS ABOUT THIS STUDY
If you have any questions or requests for information relating to this research study or your participation in it, or if you want to voice a complaint or concern about this research, or if you have a study related injury, you may contact Dr. Friel at 914-368-3116, 646-351-9063 (24 hour).

If you have any questions about your rights as a research subject or complaints regarding this research study, or you are unable to reach the research staff, you may contact a person independent of the research team at the Biomedical Research Alliance of New York Institutional Review Board at 516-318-6877. Questions, concerns or complaints about research can also be registered with the Biomedical Research Alliance of New York Institutional Review Board at www.branyirb.com/concerns-about-research.

You will be given a copy of this form to keep.

A description of this clinical trial will be available on http://www.Clinical Trials.gov as required by U.S. Law This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can research this Web site at any time.

You are making a decision as to whether or not to participate. Your signature indicates that the above information has been reviewed with you and that you have decided to participate. You may withdraw at any time without prejudice after signing this form should you choose to discontinue participation in this study.

Signature:

_____

Date:

_____

Time:

_____

Upload a copy of informed consent here, if the participant chose to provide consent on paper

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
	2b	All items from the World Health Organization Trial Registration Data Set	1, 2, 3, 7, 8-10, 12-15-18, 20
Protocol version	3	Date and version identifier	2
Funding	4	Sources and types of financial, material, and other support	2
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1, 19
	5b	Name and contact information for the trial sponsor	N/A
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	20
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
	6b	Explanation for choice of comparators	4-5
Objectives	7	Specific objectives or hypotheses	5
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	5-6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6-7
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8-10
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	11
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	11-12
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	6
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	12-15
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	13 and Fig 1

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	7
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	7
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	8
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	8
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	8
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	9
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	9
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	12-15
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	11-12

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	17-18
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	15-17
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	15-17
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	18
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	18
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	18
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	18
	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	18
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	19
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	19

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	10-11
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	17-18
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	20
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	17
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	no plans for post-trial care, compensation plan due to injury listed in ICF p2 “In Case of Injury”
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	19
	31b	Authorship eligibility guidelines and any intended use of professional writers	19
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	19
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	supplemental
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

BMJ Open

Effects of a 12-week, seated, virtual, home-based tele-exercise program compared with a pre-recorded video-based exercise program in people with chronic neurological impairments: protocol for a randomized controlled trial

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-065032.R2
Article Type:	Protocol
Date Submitted by the Author:	14-Dec-2022
Complete List of Authors:	Divecha, Ayushi A.; Burke Neurological Institute Bialek, Amy; Burke Neurological Institute Kumar, Devina S.; Burke Neurological Institute Garn, Rachel; Burke Neurological Institute Currie, Lydia; Burke Neurological Institute Campos, Talita; Burke Neurological Institute Friel, Kathleen M.; Burke Neurological Institute; Weill Cornell Medicine
Primary Subject Heading:	Sports and exercise medicine
Secondary Subject Heading:	Rehabilitation medicine
Keywords:	Rehabilitation medicine < INTERNAL MEDICINE, Neurology < INTERNAL MEDICINE, Telemedicine < BIOTECHNOLOGY & BIOINFORMATICS

Effects of a 12-week, seated, virtual, home-based tele-exercise program compared with a pre-recorded video-based exercise program in people with chronic neurological impairments: protocol for a randomized controlled trial

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Word count: 4676

Keywords: Tele-exercise, chronic neurological impairments, home-based, virtual training.

Abstract

Introduction: Exercise is vital to staying well and preventing secondary complications in people with Chronic Neurological Impairments (CNI). Appropriate exercise is often inaccessible to this population. The purpose of the study is to investigate the effects of a seated, virtual exercise program on heart rate, recovery, fatigue, pain, motivation, enjoyment, and quality of life in people with CNI.

Methods and analysis: Individuals with CNI will be screened for eligibility, and 60 participants will be randomized 1:1 into either a live or pre-recorded group. There is no geographic limitation to where participants reside, since participation is virtual. The study will be coordinated by one site in White Plains, NY, USA. The live group will exercise with an instructor via Zoom while the pre-recorded group will exercise at their chosen time using pre-recorded videos, 3x/week for 12 weeks. Primary outcome measure: change in heart rate during exercise/recovery. Secondary outcome measures: fatigue, motivation, level of pain and exertion, physical well-being, enjoyment of physical activity, motivation, and quality of life. Outcomes will be assessed at baseline, midpoint, end of study, and one-month post-study. Adverse events, medication changes, and physical activity will be tracked throughout. Within-group and between-group comparisons will be performed using Analysis of Covariance and regression.

Ethics and dissemination: BRANY IRB approval: 09/22/2020, protocol #20-08-388-512. All participants will provide written informed consent. Results will be disseminated through presentations, publications, and clinicaltrials.gov.

Trial registration number: ClinicalTrials.gov, NCT04564495.

Strengths and limitations of this study

- This study will use a comprehensive set of physiological and behavioral assessments to assess effects of exercise.
- The virtual design of the study enables people to participate without commuting to our institute.
- For those participants with limited technological experience, difficulty using blood pressure devices and heart rate monitors will cause missing data values.
- The virtual design of the study prohibits hands-on evaluations.

Introduction

Exercise is a vital component to staying well and preventing secondary impairments. Exercise is known to positively influence a range of factors including cardiovascular health, cognition, mental health, bone health, sleep, and quality of life, among many others[1-8]. The benefits of exercise are further amplified in the estimated one billion people worldwide with Chronic (> 6 months) Neurological Impairments (CNI), as the injuries often lead to sedentary lifestyles and thus higher rates of obesity and cardiovascular disease[9-11]. Incorporating an exercise regimen is vital to preventing secondary complications such as muscular weakness, fatigue, limited mobility, pain, spasticity, bone loss, and increased risk of fractures, falls, diabetes, depression, and obesity[7, 8, 12, 13]. Exercise can be neuroprotective and neuro-regenerative by increasing neurotrophic factors, which are involved in neuroprotection, neuroplasticity, and maintenance of neuronal health[2, 14-18]. Exercise can also improve muscle strength and bone integrity in people with CNI[19-21].

People with CNI often cannot access community exercise centers, as mobility can be more difficult, insurance payments sparse, centers not welcoming or accessible, and assistive exercise equipment too costly for most facilities[22-35].

Another key barrier to exercise for people with CNI is transportation[36]. Although COVID-19 introduced many new barriers to community participation, it also had some silver linings for people with CNI. COVID-19 resulted in the emergence of many new Zoom or online classes tailored to people with CNI, which removed the barrier of transportation.

Although there has been an explosion of virtual-based exercise opportunities since 2020, much is unknown regarding optimal delivery models to bring exercise to people

with CNI. Two general types of virtual exercise delivery models exist. In synchronous exercise, one or more participants join a virtual space via videoconferencing, and interact with the trainer in real time. Synchronous exercise enables the trainer to provide feedback as participants exercise. In contrast, in asynchronous exercise, trainers record instructional videos, which participants complete on their own time, without being in the same virtual space with the trainer at the same time. Asynchronous exercise provides scheduling flexibility to participants but does not allow for real time interaction and feedback from the trainer. There has only been one study directly comparing synchronous versus asynchronous exercise training in people with CNI.

In a recent study, forty adults with spinal cord injury were randomized to either synchronous or asynchronous tele-exercise. While there was no significant difference in average daily workload between the interventions, the synchronous tele-exercise found significantly higher values for adherence and successful data recording of the exercise, resulting in greater weekly training loads[37]. Virtual exercise platforms are part of society even as the pandemic wanes. Thus, it is important to determine optimal delivery models for specific groups of participants.

This study will examine the cardiovascular benefits, as well as differences in compliance, motivation and feelings of socialization and exertion between synchronous and asynchronous classes. The classes will be held for 12 weeks, 3 times/week using seated exercise via Zoom. The instructor will remain the same and alternate between boxing, high intensity interval training (HIIT) and power posture classes. We will examine the potential benefits of an accessible form of exercise for a population that is

in urgent need. Additionally, by comparing synchronous and asynchronous classes, we will compare user compliance, motivation, enjoyment, and socialization.

We hypothesize that individuals in the synchronous class will have better attendance, more robust exertion as measured by heart rate, and better enjoyment than people in the asynchronous class, due to the social component of the synchronous classes. We hypothesize that participants in both groups will show improvement in heart rate recovery, physical wellness, quality of life, enjoyment, and motivation/engagement, and that changes will be greater in the synchronous class due to consistent supervision and contact.

Methods and analysis

Study design

This study is a parallel randomized controlled trial to investigate the effects of a 12-week, 3 times/week, seated tele-exercise program for adults with CNI (Figure 1). All 36 exercise sessions will be completed online via Zoom with the physical exercise instructor (live, synchronous group) or offline using recorded videos (pre-recorded, asynchronous group). Participants will be in their own homes as they complete the exercise classes. Participants can continue their medications, physical, occupational, speech therapies, and existing exercise routines (2 times/week or fewer).

Eligibility criteria and participants

The eligibility criteria will be kept broad to accommodate all neurological impairments.

Inclusion criteria:

1. Participants diagnosed with Chronic (>6 months) Neurological Impairments
2. Ages 18 to 75 years
3. Able to sit for at least 1 hour
4. Stable Heart rate (HR) and Blood Pressure (BP)
5. Medical clearance to participate in moderate intensity exercises
6. Can don and doff a wrist HR monitor with or without assistance
7. Can maintain daily exercise and physical activity during the study
8. No other neurological, medical or cognitive impairments
9. Able to access the internet and use the cloud-based Zoom conference platform
10. Ability to speak and understand English
11. Currently exercising 2 days or less per week
12. Presence of caregiver or supervisor during exercise, for safety

Exclusion criteria:

1. Unstable or uncontrolled medical conditions
2. Medical issues preventing safe participation
3. Unable to follow simple 2-step commands

Number of participants

We plan to conduct multiple cohorts of participants, each with different participant populations, e.g., multiple sclerosis, cerebral palsy, stroke, spinal cord injury.

For each cohort, with 27 participants in the synchronous and asynchronous groups, we will have 80% power to detect a change in maximum heart rate during exercise from about 80 bpm to 100 bpm (or greater), from the first session to the last session of the intervention. This calculation assumes a conservative standard deviation of the pre/post differences in heart rate of 35 bpm. We plan for a 30% dropout rate, which is an estimate based on our feasibility pilot study (see below), which means that we will recruit 35 participants per group to achieve 80% power.

Recruitment

Participants will be recruited via the Sabrina Cohen Foundation (SCF), which has a network of people with CNI, and by the Burke Neurological Institute (BNI), who has a database of potential participants from prior studies or programs. We will also post our recruitment flier on our website, social media, and will mail it to neurological patient advocacy groups. We will send the study flier to all above mentioned entities, without prioritizing any database or group over another. If we cannot recruit appropriate numbers using these methods, we will pursue paid advertising in our community.

Randomization

A person not affiliated with the study will generate a series of permuted randomized blocks in a computerized spreadsheet with a defined block size of 4. Participants will be allocated to either the live (synchronous) or pre-recorded (asynchronous) group, with a 1:1 ratio between groups. Due to the nature of the intervention, it is not possible to

conceal allocation from the participants or the study team. However, the two groups will never interact with one another.

Blinding and rigor of data

Due to the nature of the study, blinding of participants and study team members to group allocation will not be possible. All participants will complete the outcome surveys directly online, without input or assistance from the study team. Heart rate data will be collected through a heart rate monitor that collects quantitative data without input or filtering by the study team.

Intervention

The exercise intervention will be delivered by a trained professional who specializes in adaptive exercise for individuals with CNI. The instructor will structure each class to ensure standardization in terms of class structure, including warm-up, cool-down, cues for recording heart rate during class, use of additional equipment, and adherence to the general study protocol. The instructor has extensive experience in offering adaptations to exercises in a virtual setting. He offers alternative ways to perform the exercises, such that everyone in class will be able to fully participate safely.

All participants, regardless of allocation to live or pre-recorded groups, will participate in 45 minutes of aerobic exercise intervention, three times a week, for a period of 12 weeks. The overall exercise session will be up to one hour long to include measuring vitals, answering questions before/after sessions, and rest breaks (if any). Two

additional weeks will be provided for making up missed sessions, if applicable. Each intervention will be preceded by a warm-up and followed by a cool-down period. All participants will be asked to document any adverse events and changes in medications before each session. The order of classes will be rotated. Individual aerobic interventions for the first cohort are described below and summarized in Table 1.

Table 1: Summary of exercise sessions

Minutes into Session	HIIT	Boxing	Power Posture
5	Warm up	Warm up	Warm up
10	Intervals of 30 sec high intensity movements, 1-2 min lower intensity	Intervals of 30 sec high intensity boxing movements, 1-2 min lower intensity	Stretching
15			Fast paced movements targeting trunk, posture
20			
25			
30			Stretching
35			
40	Cool down	Cool down	Cool down
45	End	End	End

High intensity interval training (HIIT): In HIIT sessions, participants will do repetitive bouts of high intensity exercises, with intermittent periods of rest or active recovery. Examples of high intensity movements used in these sessions include fast punching movements, repeatedly rapidly lifting one's arms overhead (with or without weights, as tolerated by each participant), and abdominal crunches. The duration of each bout of high intensity is about 10-30 seconds. Since this study will include participants with variable neurological impairments, the upper limit of exercise intensity in HIIT will be

dependent on instructor's judgement, participant feedback, rate of perceived exertion, and any exercise heart rate restrictions given by their doctor in the medical screening.

Boxing: In boxing sessions, participants will do a circuit of individual and combinations of various arm strikes and punches. Boxing is a moderate to high intensity aerobic activity by nature. During the session, participants will do bouts of high intensity movements, similar to HIIT, along with periods of lower intensity arm movements such as practicing defensive blocks of punches from an imaginary boxing opponent. The exercise intensity for boxing, as in HIIT, will be subjective for participants based on level of perceived exertion as well as exercise heart rate restrictions, if any.

Power posture: Power posture is a HIIT-style strength and endurance class in which participants will move in ways that train trunk stability and control of sitting with correct posture. In these sessions, there will be a warm-up period of 5-10 minutes, focused on slow, gentle repetitions to prepare the trapezius and other supporting scapular muscles for movement. This workout will target postural form, with fast paced targeted movements for 10-15 minutes. After the fast-paced movements, a cool-down period will focus on gentle deep neck flexor/extensor chin tuck exercises, range of motion, and stretching.

Virtual nature of the study

Each aspect of this study will be performed virtually. Screenings will be performed on the telephone, with a standard list of criteria asked of each person. If deemed eligible, the potential participant will be sent a Zoom link to go through the informed consent on

a one-to-one basis. The informed consent will be uploaded to REDCap, a secure web application for building and managing online surveys and databases. REDCap is 21 CFR Part 11-ready and HIPAA compliant and is specifically geared to support online and offline data capture for research studies and operations.

To obtain informed consent directly from participants, a study team member will arrange a Zoom call with each participant. The informed consent will be signed virtually by sharing a virtual remote with the participant during the call. If anyone has difficulty, they can be sent the informed consent from REDCap via email and return it to REDCap just as easily. Each participant will be sent a copy of their signed consent form via the same REDCap email system (see Supplemental Material for a sample consent form).

Each participant will be mailed a home exercise kit, which will contain a Polar optical heart rate monitor (OH1), blood pressure monitor, yellow and green resistance TheraBands and wrist weights.

After the home kits have been received by the participants and before the intervention begins, we will hold a series or training videoconferencing calls to acquaint participants with the study procedures and the use of all devices.

Polar OH1 heart rate monitor: we will train participants in donning/doffing the heart rate monitor, using the Polar app, using their Polar accounts, syncing the Polar devices with their smartphones and starting/ending their heart rate tracking during exercise sessions.

Blood pressure monitor: we will send each participant a commercially available automatic blood pressure (BP) monitor. We will train each person to use it, and we have

embedded an instructional video into the REDCap data entry form on which participants will input their BP.

Checking compliance: after each session, a study team member will review each participant's data entry forms and synching of their heart rate data with the Polar app. For the synchronous group, this will occur before the participant leaves the session. For the asynchronous group, this will occur within one day of when the participant completes the session.

All questionnaires and questions to be answered before and after each class will be sent from and stored on REDCap. All heart rate data will be transmitted to the Polar website, which can be accessed only by the participant or the researchers. Then, the data will be analyzed in MATLAB using custom scripts written by the study team.

Study safety

We will monitor side effects before and after each session by having participants complete surveys on REDCap. If pain or blood pressure are higher than usual, we will ask the participant if they wish to continue. If blood pressure rises near limitations prescribed by a participant's doctor, we will discontinue the participant. If any injury occurs during or outside of study sessions that may increase the risk of further injury, we will discontinue the participant.

Patient and public involvement

Persons with disabilities were involved in the design of this study, and will be involved in the conduct, reporting, and dissemination plans of this research. Our pilot study participants provided constructive feedback on the study, in surveys and in a zoom discussion group after they completed the study. Our class instructor owns and operated an adaptive gym for people with disabilities, and received feedback from his clients when designing the exercise classes. We will continue to involve these people as we complete the study, through regular meetings and surveys.

Strategies to improve adherence

In this study, adherence is defined as the number of sessions a participant completed. The study team will take attendance at each synchronous session and will monitor session completions for the asynchronous group. Completion for the asynchronous group will be monitored via REDCap. Each time a person completes a data entry form before and after the session, it will be automatically saved and time stamped in REDCap.

If a participant misses a class, we will reach out and inquire about their ability to attend future sessions. We have *a priori* set a minimum number of 30 of 36 classes that a participant must attend to be included in the main analyses of the study. We will offer 2 weeks of makeup sessions at the end of the 12 weeks. If a participant drops out before completing 30 sessions, we will encourage them to complete the post-study outcome measures and the satisfaction survey. We will use the number of sessions completed as a covariate in the analyses.

Outcome measures

All outcome measures are summarized in Table 2.

Table 2: Outcome measures

PRIMARY OUTCOME MEASURE			
Measure	**Modality Assessed**	**Method of Ascertainment**	**Timepoints**
Peak heart rate	Cardiovascular function	Polar OH1/Polar Beat app	Each session
SECONDARY OUTCOME MEASURES			
Measure	**Modality Assessed**	**Method of Ascertainment**	**Timepoints**
Demographics	--	REDCap survey	Before first session
Attendance	Adherence	REDCap time stamps	Each session
Baseline heart rate	Cardiovascular function	Polar OH1/Polar Beat app	Each session
Heart rate at end of session	Cardiovascular function	Polar OH1/Polar Beat app	Each session
Heart rate recovery	Cardiovascular function	Polar OH1/Polar Beat app	Each session
Blood pressure	Cardiovascular function	Automatic BP device	Before and after each session
Rate of Perceived Exertion	Cardiopulmonary fitness	REDCap survey	Before and after each session
Perceived Wellness Survey	Wellness	REDCap survey	Baseline, weeks 6, 12, 16
Physical Activity Enjoyment Scale	Enjoyment of exercise	REDCap survey	Baseline, weeks 6, 12, 16
Short Form-36	Physical and mental health	REDCap survey	Baseline, weeks 6, 12, 16
Numerical Pain Rating Scale	Pain	REDCap survey	Baseline, weeks 6, 12, 16

Reason for Exercise Inventory	Motivation to exercise	REDCap survey	Baseline, weeks 6, 12, 16
Participant Feedback Survey	Participant satisfaction	REDCap survey	End of study or at dropout

Demographics

We will collect the following demographics by having each participant complete a demographics data entry form on REDCap: age, gender, neurological diagnosis, time of diagnosis, and comorbid health issues (e.g., diabetes, high blood pressure, etc.). We will also document whether a person needs assistance with walking or transfers. In addition, we will require each participant to receive written medical clearance by their doctor to participate in the study, and if any exercise restrictions need to be followed.

Primary outcome measure: peak heart rate during exercise

Continuous heart rate tracking is the primary outcome measure for the study. All participants will receive the OH1 Polar HR monitor as part of their exercise kit for the study (Figure 2). The Polar OH1 (Polar Electro Inc., Bethpage, NY, USA) is an optical heart rate sensor on an armband that records HR activity. It has 6 LED sensors that record at 1-second intervals[38]. HR activity is recorded via Bluetooth to a phone compatible with the Polar Flow or Polar Beat app. It has validity in moderate to vigorous intensity exercises and high endurance sports activities [38-40].

Immediately before each exercise session, participants will turn on their OH1 monitor. Then, the participant will open the Polar Beat app on their smart phone and hit “start” when the exercise session begins. The Polar OH1 continuously records heart rate (HR) at 10Hz when the device is powered on and the Polar Beat app recording has been started. Participants will record HR through the entire exercise session and for 10 minutes after completion of the session to capture HR during exercise as well as HR recovery for 10 minutes after the end of exercise sessions. The live group will be supervised by the research team for each session. The pre-recorded groups will have the research team available for assistance and troubleshooting. Data are stored on the Polar Coach website, where study staff can export sessions as CSV files that are then processed in MATLAB (MathWorks). In MATLAB, peak HR (primary measure) will be calculated.

Secondary outcome measures

Measures acquired at each exercise session

We will calculate secondary measures of HR in MATLAB using the same Polar CSV files mentioned above: baseline HR, HR at end of session, and HR at 30s intervals for 10min after the end of the session will be analyzed, to measure heart rate recovery.

At each session, participants will complete an online assessment to rate the level of pain and perceived exertion (RPE), BP, HR, and adverse events before and after the exercise session. Additionally, as described above, attendance will be taken at each session as a measure of adherence. After the session is over, participants will complete a lab-developed survey to rate their experience on a 10-point scale from 1 (not a good experience) to 10 (very good experience) on questions related to motivation, energy,

satisfaction, and performance. In addition, participants will provide information on changes related to health, falls, or other adverse events.

Measures acquired at specified times during the intervention

A comprehensive set of secondary outcome measures will be completed by participants at baseline, mid-study (6 weeks), end of study (12 weeks) and follow-up after one month. All questionnaires will be self-administered or administered by a trained researcher virtually using REDCap.

Perceived Wellness Survey (PWS): Participants will quantify their perceived health status by completing the PWS. The PWS is a 36-item instrument used to measure an individual's perceived health status in physical, psychological, emotional, intellectual, spiritual, and social wellness constructs. Items under each construct are scored on a scale of 1 (very strongly disagree) to 6 (very strongly agree). Higher scores indicate better perceived wellness. The PWS has good reliability and validity in healthy and neurological populations[41-43].

Physical Activity Enjoyment Scale (PACES): the PACES is a self-assessment measure of enjoyment with their current physical activity. It is an 18-item scale with scoring from 1 (I enjoy it) to 7 (I hate it). Scores on the bipolar rating scale are summed with higher scores indicative of more enjoyment. It is reliable and valid in neurological populations[44-47].

Short Form-36 Health Survey (SF-36): the SF-36 measures physical health and mental health. There are eight scales - Physical Functioning, Physical Role Limitations, Bodily Pain, General Health, Vitality, Social Functioning, Emotional Role Limitations, and

Mental Health. It is easy to use with good validity and reliability in neurological populations[48-51].

Numerical pain rating (NPR) scale: the NPR is a standardized instrument for pain assessment in clinical and research practice. It is an 11-point scale from 0 (no pain) to 10 (the most intense pain) at rest and during movement. It is simple to use with high sensitivity to changes in chronic pain in adult populations[52, 53]. It is reliable and valid for pain assessments of neurological populations[54].

Borg's Rating Scale of Perceived Exertion (RPE): the Borg RPE is a widely used standardized measure to evaluate perceived intensity of exertion, effort, and fatigue during physical exercise. The scale ranges from 6 (no exertion at all) to 20 (absolute maximum). Higher ratings on the scale indicate greater overall body exertion. It is a reliable and valid measure in neurological populations[55-62].

Reason for exercise inventory (REI): the REI is a 24-item scale to assess the reason that motivates a person to exercise. The modified version has 4 subscales: Weight/appearance management, fitness/health management, stress/emotion management, and socialization. A 7-point scale ranges from 1 (not at all important) to 7 (extremely important). Higher scores represent greater motivation to exercise[63].

Participant feedback: on study completion, or when withdrawn/dropped out from the study, participants will complete a study feedback form. The feedback will be based on study acceptance, ease of using HR and BP devices and exercise equipment, and support from the research team. Participants who do not complete the study will also provide their final timepoint measure at the end of their final exercise session.

Statistical methods

Descriptive statistics (including mean, standard deviation, median, interquartile range, frequency, and percent) will be calculated for demographic and clinical characteristics of the study participants.. Analysis of Covariance (ANCOVA) will be used to evaluate the independent effect of synchronous versus asynchronous group status on change in peak heart rate (first session versus final session), after controlling for baseline heart rate and any other factors that may remain imbalanced between groups after randomization. Adjusted mean differences in peak heart rate (first session versus final session) between the synchronous and asynchronous groups and 95% confidence intervals for these differences will be estimated from the multivariable ANCOVA model. Similar analyses as described above will be performed for other continuous outcomes (primary and secondary), including Borg's RPE scale, mood, motivation, and pain scales, Perceived Wellness Survey, SF-36v2 score, and PACES score. Categorical variables (e.g., safety questions, adverse events, medication changes, etc.) will be compared between the synchronous and asynchronous groups (at baseline, 6 weeks, and 12 weeks) by the chi-square test or Fisher's exact test, as appropriate. Generalized estimating equations (GEE) modeling will also be explored to evaluate between-group differences over repeated assessments, and to account for potential missing data in some of the outcome variables at one or more of the evaluation time points. All estimates from the multivariable models will serve as preliminary data (i.e., hypothesis-generating) for future studies. All p-values will be two-sided with statistical significance evaluated at the 0.05 alpha level. Ninety-five percent confidence intervals for all

parameters of interest will be calculated to assess the precision of the obtained estimates. All analyses will be performed in R and SPSS by a person blinded to treatment allocation.

Data management

Participant identifying information will be kept confidential by providing a unique identification number (ID number) for the course of the study. To maintain privacy, only authorized research investigators involved in the study will have access to participant information. Password protected laptops, online documents, and access to cloud-based servers will prevent leaks in data privacy. All records including informed consent, screening tools, medical records, and participant surveys will be completed, and documented on REDCap, a HIPAA-compliant online research database.

Privacy on Zoom platform: Our institutional Zoom account (through Weill Cornell Medicine) is compliant with HIPAA guidelines. Participant profile names will be updated to display their ID. After each session, the recorded video will be uploaded to the password protected WCM cloud-based server. Respective group participants will be given the live Zoom links (synchronous) or passwords to access the asynchronous Zoom sessions.

Polar OH1 HR monitor (Optical HR sensor): Participants' profiles using allotted ID's will be created in the Polar Beat App and the Flow for Coach cloud-based online platform. All information uploaded to the platform will be accessible by the investigators using a secured login ID and password.

Adverse events, change in medications, and protocol deviation will be documented and updated before and after each class on REDCap. The study team will perform weekly self-audits to ensure data quality and completeness.

Procedure for handling missing data

This study is an intention-to-treat trial. If data are missing, we will use a mixed linear regression model that accounts for uneven numbers of data points across participants.

Data monitoring and stopping rules

Since this is a low-risk study, our IRB determined that a data monitoring committee is not necessary. We will audit our data weekly and assess safety data at each session. If we find an increase in pain by 25% or a decrease in quality of life measures by 25% across participants in a cohort, we will pause the trial and evaluate how to improve the safety of the study.

Current status of the study

We have performed a feasibility cohort, with people with a range of abilities and diagnoses. The first participant was consented on 01/22/2021, for an intervention that began on 03/24/2021 and ended on 06/28/2021. In this feasibility study, we determined that participants could readily complete the online assessments, exercise sessions, and could effectively use Zoom, the Polar OH1 sensor and Polar Beat app, and the blood pressure measurement device. Our next step will be to enroll separate cohorts of

people with specific neurological diagnoses, such as cerebral palsy, stroke, and multiple sclerosis. This will begin in 2023.

Resource sharing plan

We plan to use the concept, methods and analysis as a framework to develop evidence-based protocols for future cohorts and studies. We have made a commitment to publish all relevant scientific information in a timely manner. Unpublished information may be available to interested individuals or organizations by request to the Principal Investigator.

Ethics and dissemination

The study was approved by the BRANY Institutional Review Board on 9/22/2020, protocol #20-08-388-512. All study participants will provide written informed consent before participation. All protocol deviations, adverse events, and protocol modifications will be reported to the IRB immediately. The results of the study will be disseminated to the academic community via publications and presentations. The deidentified study data will be shared on our laboratory website. The trial is registered at Clinicaltrials.gov, number NCT04564495.

Acknowledgements: We thank the Sabrina Cohen Foundation for funding and for commitment to assist with study development and recruitment. We thank Devon Palermo at DPI Adaptive Fitness who will serve as the adaptive fitness instructor for this study.

Contributors: KMF is the Principal Investigator. KMF, AAD and AB were responsible for ethics applications and reporting. AAD, AB, DSK, RMG, LEJC, TAC and KMF drafted the final version of this manuscript. All authors have contributed to the writing and critical review of the manuscript and have approved the final version.

Funding: This work is supported by funding from the Sabrina Cohen Foundation and the Burke Foundation. This work is supported by grant number UL1 TR 002384 from the National Center for Advancing Translational Sciences (NCATS) of the National Institutes of Health (NIH). The Sabrina Cohen Foundation has established the tele-exercise classes we are studying and will assist with recruitment. The Sabrina Cohen Foundation and Burke Foundation will have no role in data collection, analyses, interpretation, or publication of the work.

Competing interests: None to declare.

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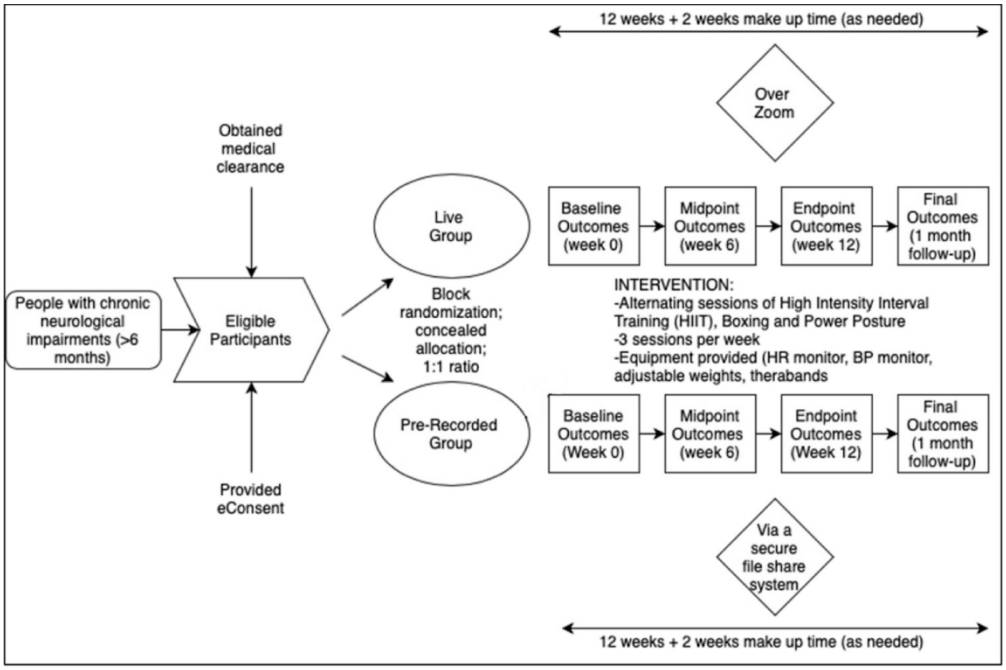
Figure legends

Figure 1: Study flow diagram

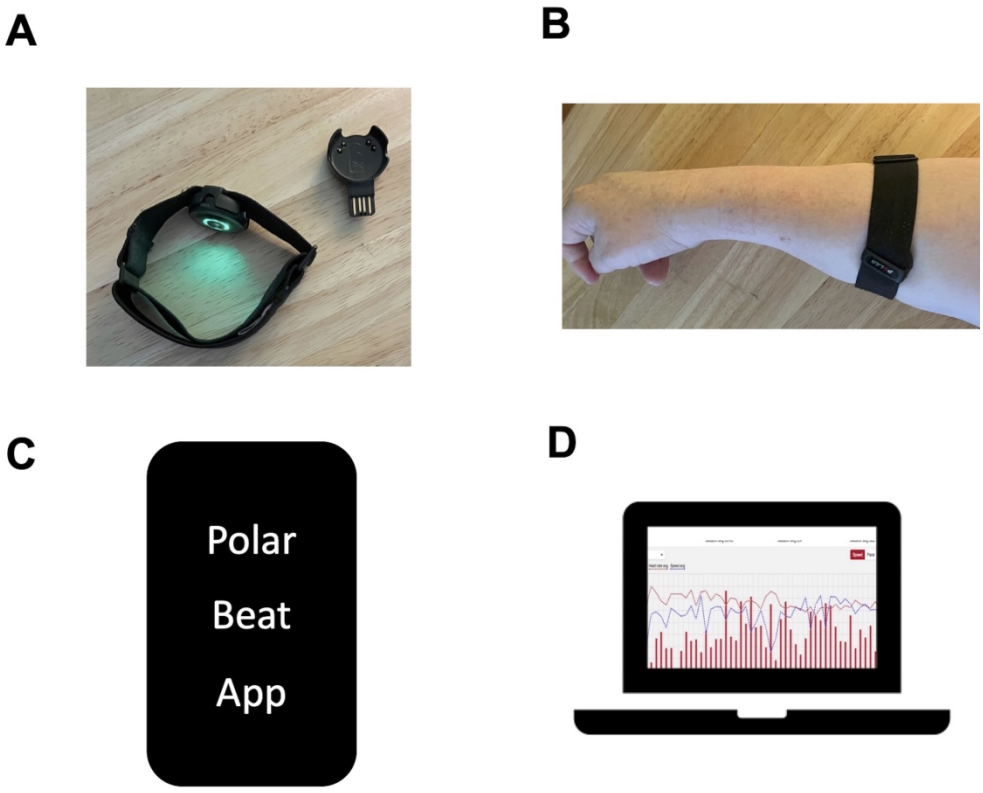
Figure 2: Polar OH1 heart rate monitor

A. Picture of the monitor and charger. B. Proper placement of the monitor, with the device on the forearm. C. The Polar Beat app on a smart phone streams data in real time from the OH1 monitor via Bluetooth. D. After a session, data are retrievable from the Polar Coach website, where it is exported to a CSV file and processed in MATLAB.



Study flow diagram.

254x168mm (300 x 300 DPI)



Polar OH1 Heart Rate monitor. A. Picture of the monitor and charger. B. Proper placement of the monitor, with the device on the forearm. C. The Polar Beat app on a smart phone streams data in real time from the OH1 monitor via Bluetooth. D. After a session, data are retrievable from the Polar Coach website, where it is exported to a CSV file and processed in MATLAB.

254x212mm (300 x 300 DPI)

Informed Consent Form

This form explains our study and asks you to agree to partiicpate. Please read the form carefully. A member of our study team will talk with you over Zoom to explain the study. Thank you so much for your interest in our study!

BIOMEDICAL RESEARCH ALLIANCE OF NEW YORK
THE BURKE NEUROLOGICAL INSTITUTE

SUBJECT INFORMATION AND INFORMED CONSENT

Project Title: Home-Based Exercise for People with Chronic Neurological Impairments
Principal Investigator: Kathleen Friel, PhD
Institution Name: Burke Neurological Institute
Institution Address: 785 Mamaroneck Ave, White Plains, NY 10605
Telephone: 914-368-3116, 646-351-9063 (24 hour)
Protocol # TELEX

ABOUT VOLUNTEERING FOR THIS RESEARCH STUDY
You are invited to participate in a research study. The purpose of the study is to determine the effect of a home-based exercise program on cardiovascular fitness and your quality of life. We will assess your motivation, enjoyment and compliance to either a live or pre recorded exercise class on Zoom.

You are eligible for this study because you have a neurological impairment that you've had for at least six months. A neurological impairment is weakness in your arms and/or legs that was caused by a stroke, brain injury, spinal cord injury, or any other condition that affects your brain or spinal cord.

WHY IS THIS STUDY BEING DONE?
Scientists at The Burke Neurological Institute (BNI) are partnering with the Sabrina Cohen Foundation (SCF) to test whether a home-based exercise program can improve cardiovascular health and quality of life in people who have had a chronic neurological impairment. We designed this study after the onset of COVID-19 in the United States. Since COVID-19 limits accessibility to gyms and other types of exercise venues, we hope to learn and understand the physiological and behavioral aspects of this rehabilitation strategy to optimize wellness after a neurological injury. You were selected as a possible participant in this study because you've had a neurological impairment for at least six months.

WHAT WILL I DO IF I AGREE TO BE IN THIS STUDY?
If you agree to be in the study, you will participate in 36 at-home, Zoom-based exercise classes. Classes will be held three times a week, for twelve weeks. You will be randomized to either a live class with other video participants, or a pre-recorded class that you will take on your own.

Before the first class, we will review your medical history with you to be sure it is safe for you to be in the study. If you qualify for the study, we will send you a kit that contains items you will need for the study, including a heart rate monitor, blood pressure cuff and adjustable wrist weights. We will also send you some surveys that ask about your ability to do everyday activities, such as dressing and cooking.

After you receive your home exercise kit, we will have an orientation Zoom class. You will meet the other people in the exercise class. During the orientation, the study team will teach you how to use the heart rate monitor. If you cannot put on the heart rate monitor, we will ask that a caregiver be present to assist you during each class.

You will download one applications onto your phone or computer that will allow us to access the information from your heart rate monitor. No one but the research team will be able to see this information aside from you.

Each exercise class will take approximately one hour. Each session will begin with instructions and questions from the study team regarding your pain level, level of motivation, and blood pressure. The exercise portion of the class will take 45 minutes. At the end of the class, the study team will ask you additional questions, such as how hard you worked, pain level, level of motivation and blood pressure.

The class instructor will tailor exercises to different abilities, so everyone can be active and safe. The entire class will be done in a seated position.

Approximately 100 people will be enrolled in the live class, and 100 in the pre-recorded class.

After the 18th class, which is midway through the study, we will send you another set of the same surveys you completed before the first class. We will send you a third set of surveys after the final class.

RISKS AND INCONVENIENCES OF THE STUDY
Your participation in the project might involve the following risks:

The largest risk in this study is the risk of fatigue and muscle aches. These symptoms are common with exercise. The instructor will offer modifications of each exercise, to offer easier or more difficult options. You will always be welcome to use a modification, request an additional modification, or rest.

The risk of fall in this study is small, since you will be seated. If you normally have trouble with stability of your torso while you are seated, we will ask that a caregiver be present in case a fall occurs.

There is a risk that your personal health information be disclosed in error. For this study, we are using secure Zoom settings from an academic medical center, and we will require a password for each class, to mitigate this risk. The app containing your heart rate information will also be secure.

PERMISSION FOR PHOTOGRAPHY
We will record each live class, video and audio. Since we are not together in one space, we need to record each class for purposes of data collection. Therefore, we require each participant to agree to being recorded. We want to make sure that you understand this.

Do you agree to be photographed in this study?
◯ Yes
◯ No

Please initial here to confirm your choice about being photographed during the study:

_____

NEW INFORMATION
You will be told about any new significant findings developed during the course of the study that might affect your willingness to continue in the research.

COST OF STUDY TO PARTICIPANTS
There is no cost to you for participating in the research study.

BENEFITS OF THIS STUDY
Participation in this study is not guaranteed to benefit you. This study is only for the purpose of research. You may feel stronger by the end of the study, but there is no guarantee that this will occur. However, the information learned from this study may help other people in the future.

ALTERNATIVES TO STUDY PARTICIPATION
You do not have to participate in this research study to receive treatment for your condition. Your participation in this study is voluntary. If you decide to participate, you are free to discontinue participation at any time. Your participation in this study may be terminated without your consent by the study team or regulatory authorities, in certain circumstances, such as, if the investigator determines it is in your best interest, you cannot adhere to the study procedures, or in the event the study is terminated.

IN CASE OF INJURY
In accordance with Federal regulation, we are obligated to inform you about our policy in the event injury occurs. For medical emergencies, call 911. If, as a result of your participation, you experience injury from known or unknown risks of the research procedures as described, emergency medical care and treatment will be provided on our premises to the extent possible. We will assist you in obtaining additional medical care, as needed, but you will be responsible for the costs of such further medical treatment, either directly or through your medical insurance and/or other forms of medical coverage. No other compensation will be offered by or Burke Neurological Institute or the Biomedical Research Alliance of New York. Further information can be obtained from Dr Kathleen Friel (914 368-3116). You are not waiving any legal right to seek additional compensation through the courts by signing this form.

CONFIDENTIALITY
To the extent allowed by law, every effort will be made to keep your personal information confidential. However, information from this study will be submitted to the study sponsor and to the U.S. Food and Drug Administration. It may be submitted to governmental agencies in other countries where the study product may be considered for approval. Medical records, which identify you and the consent form signed by you, will be looked at by the sponsor or the sponsor's representatives and may be looked at by the FDA and other regulatory agencies, the Institutional Review Board, and the Biomedical Research Alliance of New York. While these parties are aware of the need to keep your information confidential, total confidentiality cannot be guaranteed. The results of this research project may be presented at meetings or in publications; however, you will not be identified in these presentations and/ or publications.

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study doctor must get your authorization (permission) to use or give out any health information that might identify you. If you choose to be in this study, the study doctor will get personal information about you. This may include information that might identify you. The study doctor may also get information about your health, including:

• Past and present medical records
• Research records
• Records about phone calls made as part of this research
• Records about your study visits
• Information obtained during this research about laboratory test results
• Results from diagnostic and medical procedures including but not limited to X-rays, physical examinations and medical history
• Billing records

Information about your health may be used and given to others by the study doctor and staff. They might see the research information during and after the study. Your information may be given to the sponsor of this research. "Sponsor" includes any persons or companies that are working for or with the sponsor, or are owned by the sponsor. Information about you and your health which might identify you may be given to:

• The U.S. Food and Drug Administration
• Department of Health and Human Services agencies
• Governmental agencies in other countries
• Biomedical Research Alliance of New York (BRANY)
• The Institutional Review Board
• Accrediting agencies

Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the U.S. federal privacy laws. However, these groups are committed to keeping your personal health information confidential. If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others without your permission.

Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study. In addition, people from the sponsor and its consultants will be visiting the research site. They will follow how the study is done, and they will be reviewing your information for this purpose. The information may be given to the FDA. It may also be given to governmental agencies in other countries. This is done so the sponsor can receive marketing approval for new products resulting from this research. The information may also be used to meet the reporting requirements of governmental agencies.

This authorization does not have an expiration date. If you do not withdraw this authorization in writing, it will remain in effect indefinitely.

By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. You do not have to sign this consent form. If you choose not to sign this consent form, you will not be able to be in this research study. Your decision not to sign this consent form will not have any effect on your medical care and you will not lose any benefits or legal rights to which you are entitled. You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you may not be allowed to look at or copy your information until after the research is completed.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor at the address on the front of this informed consent form. If you withdraw your permission, you will not be able to continue being in this study, but you will not have any penalty or loss of access to treatment or other benefits to which you are entitled. When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Notice Concerning HIV-Related Information: HIV-related information that either is collected as part of the research or that may already exist in your medical record might be accessed for the research by the research staff and the study sponsor, but will not be shared with others without your authorization, unless federal or state law requires the disclosure. You have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights or New York City Commission on Human Rights. These agencies are responsible for protecting your rights.

QUESTIONS ABOUT THIS STUDY
If you have any questions or requests for information relating to this research study or your participation in it, or if you want to voice a complaint or concern about this research, or if you have a study related injury, you may contact Dr. Friel at 914-368-3116, 646-351-9063 (24 hour).

If you have any questions about your rights as a research subject or complaints regarding this research study, or you are unable to reach the research staff, you may contact a person independent of the research team at the Biomedical Research Alliance of New York Institutional Review Board at 516-318-6877. Questions, concerns or complaints about research can also be registered with the Biomedical Research Alliance of New York Institutional Review Board at www.branyirb.com/concerns-about-research.

You will be given a copy of this form to keep.

A description of this clinical trial will be available on http://www.Clinical Trials.gov as required by U.S. Law This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can research this Web site at any time.

You are making a decision as to whether or not to participate. Your signature indicates that the above information has been reviewed with you and that you have decided to participate. You may withdraw at any time without prejudice after signing this form should you choose to discontinue participation in this study.

Signature:

_____

Date:

_____

Time:

_____

Upload a copy of informed consent here, if the participant chose to provide consent on paper

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
	2b	All items from the World Health Organization Trial Registration Data Set	1, 2, 3, 7, 8-10, 12-15-18, 20
Protocol version	3	Date and version identifier	2
Funding	4	Sources and types of financial, material, and other support	2
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1, 19
	5b	Name and contact information for the trial sponsor	N/A
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	20
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
	6b	Explanation for choice of comparators	4-5
Objectives	7	Specific objectives or hypotheses	5
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	5-6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6-7
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8-10
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	11
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	11-12
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	6
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	12-15
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	13 and Fig 1

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	7
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	7
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	8
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	8
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	8
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	9
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	9
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	12-15
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	11-12

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	17-18
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	15-17
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	15-17
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	18
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	18
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	18
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	18
	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	18
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	19
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	19

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	10-11
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	17-18
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	20
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	17
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	no plans for post-trial care, compensation plan due to injury listed in ICF p2 “In Case of Injury”
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	19
	31b	Authorship eligibility guidelines and any intended use of professional writers	19
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	19
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	supplemental
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.