

Official Title: Vivo Heart: Home-Based Virtual Exercise Program for Older Adults with Cardiovascular Disease
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Study Title: Vivo Heart: Home-based Virtual Exercise Program for Older Adults with Cardiovascular Disease

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Background, Rationale and Context

Exercise-based cardiac rehabilitation (CR) is integral to recovery among patients with cardiovascular disease (CVD); yet enrollment and completion rates are low (<20%), especially among underserved communities (e.g., rural, lower socioeconomic conditions) and older adults. Multiple barriers disproportionately affect these underrepresented groups, including lack of transportation, accessibility, and cost. The COVID-19 pandemic heightened disparities and reinforced the need for proven alternatives to center-based CR programs. Home-based CR has the potential to expand reach and utilization, thereby enhancing long-term benefits and improving cost-effectiveness.¹⁻³ To date, few studies have investigated the feasibility and efficacy of home-based CR designed for older adults who may have unique physical and cognitive challenges.^{4,5} Digital health technologies could enhance home-based CR programs with remote supervision, support, monitoring, and education;⁶ but data on the use of **digital CR delivery strategies tailored for older adults are lacking**. Our work has advanced the understanding of underlying pathways altered by exercise,⁷ social-cognitive theories used to promote lifestyle changes,⁸ and mobile health technologies that enhance and support behavior change.⁹ We **hypothesize** that a digital approach would be feasible and acceptable to underserved communities of older adults with CVD, leading to improved strength and physical function.

Objectives

This pilot will assess the feasibility and generate preliminary efficacy data of a novel, synchronous, home-based exercise training program for underserved communities of older adults with CVD using Vivo, an online, live, small group fitness program developed for older adults. It uses individually tailored dual-task (i.e., cognitive-motor) exercises to improve strength, endurance, balance, and cognition and incorporates social engagement. Certified trainers deliver instruction and coaching through an interactive session (45 min, 2-3 times/week) delivered over 12 weeks. Vivo Heart adapts this unique program to meet the exercise needs of older adults with CVD. The pilot study will enroll 40 **older adults** (60-80 years) **with a history of CVD** (prior myocardial infarction, angina, or coronary procedure) who live in a rural area or a socioeconomically disadvantaged neighborhood. A sample size of 40 provides sufficient precision to inform subsequent trial planning.⁹ The **Specific Aims** are as follows:

Aim 1: Evaluate feasibility, acceptability, and uptake of Vivo assessed by completion rates, recruitment yields, attendance and satisfaction;

Aim 2: Obtain pre- and post-intervention measures of exercise capacity, strength, lower-extremity physical function, cognition, quality of life, stress, fatigability, physical activity, and aging biomarkers to provide trial design benchmarks for planning a larger trial.

Impact: This pilot will provide data and experience to expand the reach of our interventions and improve accessibility for underserved communities of older adults.

Sources of Materials

Participants will self-report demographic, behavioral, and medical information using questionnaires. Data will also be obtained from review of medical records and performance of specific tests. Participants will be asked to answer questions about their medical history, health habits, socioeconomic status, physical function, and psychological well-being. Participants will also complete exercise tests to assess maximal and submaximal exercise capacity and fatigability. Data will primarily be recorded on paper forms and then entered into an electronic database on a computer workstation. All material and data will be obtained specifically for research purposes.

Design

This is a prospective, single-arm non-randomized trial.

Setting

The intervention will take place virtually in the participant's place of residence using a virtual class format with Zoom calls. The study assessments will take place at Atrium Health Wake Forest Baptist facilities in Winston-Salem, NC.

Sample Size

Our sample size calls for the recruitment of 40 community-dwelling older adults with CVD who live in rural areas or socioeconomically disadvantaged neighborhoods who will be identified through the Atrium Health Wake Forest Baptist electronic health record (EHR). Patients who meet the inclusion/exclusion criteria listed in **Table 1** will be asked to participate. These criteria are in place to identify an underserved community at high risk for non-participation in a center-based CR program and who are also at increased risk of functional decline and loss of independence. These criteria also help to ensure the safety of all enrolled participants. We expect to enroll a study population that consists of approximately 50% women and 25% racial/ethnic minorities.

Table 1. Inclusion/Exclusion Criteria			
Criterion	Inclusion	Exclusion	Assessment
Older age	60 – 80 years	<60 years or >80 years	Self-report
Underserved community	Lives in a rural area based on established urban-rural definitions (e.g., RUCA codes, RUCC, UIC) OR Lives in a neighborhood with medium-to-high socioeconomic disadvantage (ADI score: 5-10)	Lives in a non-rural area Lives in a neighborhood with low socioeconomic disadvantage (ADI score: 1-4)	Objective urban-rural classification systems Area Deprivation Index (ADI) scores
History of CVD	A prior qualifying CVD event or procedure	No CVD; Congestive heart failure, heart transplant, or ICD	Self-report and review of ICD-10 codes in EHR
Cognitive status	Cognitively unimpaired (TICS-m ≥ 32)	Dementia or severe cognitive impairment (TICS-m <32)	Questionnaire
Depression status	No major depressive symptoms (PHQ-8 <10)	Clinical depression (PHQ-8 ≥ 10)	Questionnaire
Functional status	Ambulatory and community-dwelling	Non-ambulatory, institutionalized, or requires walker	Self-report
Sedentary status	Less than 150 min per week of moderate-to-intensive aerobic	Regular aerobic or resistance exercise (including current	Self-report

	or resistance exercise in the past month	participation in a cardiac rehab program)	
Medical clearance	Medically cleared for exercise (only if most recent event or procedure was in the last 3 months)	Not medically cleared for exercise	Participation approved by treating cardiologist
Exercise tolerance	Normal exercise stress test	Positive exercise stress test (i.e., evidence of ischemia)	CPET
Co-morbidities/health status	Approved for participation by cardiologist	(1) advanced kidney disease requiring dialysis or dialysis anticipated within 6 months; (2) insulin-dependent diabetes; (3) use of any supplemental oxygen for COPD (CPAP ok); (4) significant impairment from a prior stroke; (5) progressive neurologic disease (Parkinson's, ALS, MS, Alzheimer's/Dementia); (6) severe arthritis, fracture, chronic injury, or other musculoskeletal disorder that prevents walking independently (straight cane ok; walker is not); (7) cancer (not including non-melanoma skin cancers) requiring treatment with the past year; (8) excessive alcohol consumption (>7/wk alcoholic beverages for women and >14/wk for men) in the past month; (9) joint replacement or other orthopedic surgery in past 12 months or planned in next 6 months	Self-report and review of EHR
Internet & Smartphone access	Access to a smartphone AND tablet or computer and internet/Wi-Fi in defined exercise space	No smartphone, computer, tablet or internet access	Self-report
Reliable transportation	Able to provide own transportation to study visits	No access to transportation for travel to study visits*	Self-report
Current research participation	Not participating in a clinical trial	Current participation in a clinical trial	Self-report
Likelihood of adherence	Willing to provide informed consent	Inability or unwillingness to comply with the study requirements	Self-report

*Depending on participant location and our need, we may offer transportation when able.

Interventions and Interactions

Participation in this study will last for approximately five months and will involve phone interviews, online assessments, two visits to the Sticht Center for testing, weekly virtual group exercise and health education classes for 12 weeks, remote health monitoring, and two individual meetings with a registered dietitian (RD). Table 2 summarizes the timeline for all study assessments.

Phone Screening

Individuals who express interest in the study will be contacted by telephone by trained staff who will explain the purpose of the study and assess eligibility to the extent possible over the telephone (e.g., age, presence of contraindicated health conditions, access to internet, etc.). The following will also be administered via the phone to further establish eligibility:

- The Telephone Interview for Cognitive Status-modified (TICS-m) is a brief, 13-item standardized test of cognitive functioning that is designed to be administered over the telephone. Scores range from 0-50, with higher scores indicating better cognitive function.¹¹
- The 8-Item Patient Health Questionnaire (PHQ-8) measures current depression in the general population, with higher scores indicating greater depressive symptoms.¹²

Baseline Visit

Participants will be asked to come to the Sticht Center at Atrium Health Wake Forest Baptist to complete the following:

Cardiopulmonary Exercise Test (CPET)

- Peak aerobic capacity (VO₂ peak): VO₂ peak will be measured during a progressive exercise test on a motorized treadmill.¹³ The test will begin with participants walking on the flat treadmill surface at their usual pace (determined by an 80-m walk test) for five minutes. As the test progresses, the treadmill will gradually steepen to mimic walking up a hill. Throughout the treadmill test, ventilatory and gas exchange responses will be measured on a breath-by-breath basis using a computerized system (MGC Diagnostics Ultima system, Minneapolis, MN). Heart rate (via ECG), pulse oximetry, and blood pressure will also be monitored. Participants will be asked to give a maximal, exhaustive effort confirmed objectively by a respiratory exchange ratio >1.05, a rating of perceived exertion (RPE) >17, or a >90% age-predicted maximal heart rate.¹⁴ Participants who do not meet two of these criteria will be re-tested; however, in our experience this typically occurs in less than 5% of tests.
- Energy costs of walking: After a ~20-minute rest period following the VO₂ peak test, participants will be asked to walk on the treadmill for 5 minutes at a standard slow pace of 1.5 miles per hour and a zero percent grade. Oxygen consumption, RPE, and vitals will be measured as described above.

Inter-muscular and Cardio-muscular Coordination

- Myoelectrical activity will be assessed during the treadmill test using surface electromyography (sEMG) electrodes placed bilaterally on the rectus femoris muscle on the front of the thigh, the biceps femoris muscle on the back of the thigh, and on each kneecap (ground). A standard 3-lead ECG will also be used to obtain the recording for lead II with ECG electrodes placed on the right shoulder (-), left shoulder (ground), and lower left abdomen (+). A Biopac MP150 unit (Biopac Systems Inc, Goleta, CA, USA) will be used to collect synchronized ECG and EMG signals throughout the test. Skin preparation, electrode placement, and signal processing will follow standard guidelines.¹⁵

Table 2: Timeline of Study Assessments						
Phase	Phone Screening	Baseline Clinic Visit	Baseline Virtual Assessment	Intervention	Follow-up Clinic Visit	Follow-up Virtual Assessment
Week(s)	-1	0	0	1-12	12-13	12-13
Outcomes						
Peak aerobic capacity (CPET)		X			X	
80-m walk test		X			X	
Lower extremity function (eSPPB)		X			X	
Grip strength		X			X	
Dynamic balance (FSST)		X			X	
Leg power (4SCT)		X			X	
Arm strength (Arm curl test)			X			X
Leg strength (Chair stand test)		X	X		X	X
Balance (Balance test)		X	X		X	X
Submaximal step test			X			X
Agility (8-ft TUG)		X	X		X	X
Cognitive status (TICS-m)	X					
Global cognition (MoCA)		X			X	
Psychomotor speed (DSC)		X			X	
Additional measures						
Height		X			X	
Body weight		X	X		X	X
Demographics		X				
Medication and Medical History		X				
Waist / hip circumference		X	X		X	X
Vitals (blood pressure, heart rate)		X		X	X	
Fatigability (PFS)		X			X	
Myoelectrical activity (sEMG)		X			X	
Depression (PHQ-8)	X					
Quality of life (SF-36)		X			X	
PAT-D		X			X	
Health Status*				X	X	
Stress (PSS)		X			X	
UCLA Loneliness Scale		X			X	
Life Space		X			X	
Self-efficacy (SEE, EXSE)		X			X	
Remote monitoring				X		
Program satisfaction					X	

CPET: Cardiopulmonary exercise test; DSC: Digit Symbol Coding; eSPPB: expanded Short Physical Performance Battery; EXSE: Exercise Self-efficacy; FSST: Four Square Step Test; MoCA: Montreal Cognitive Assessment; PAT-D: Pepper Assessment Tool for Disability; PFS: Pittsburgh Fatigability Scale; PHQ-8: 8-item Patient Health Questionnaire; PSS: Perceived Stress Scale; SEE: Self-efficacy for Exercise; sEMG: surface electromyography; SF-36: 36-item short form health survey; TICS-m: Telephone Interview of Cognitive Status modified; TUG: timed up and go; 4SCT: 4-step Stair Climbing Test;

* Assessed via monthly phone calls (1mo, 2mo) by clinic staff and again at follow-up

Physical Function Tests

- An 80-m walk will be used to determine usual walking speed. Participants will be asked to walk at their usual pace for 80 meters.
- The Timed Up and Go (TUG) measures the time for a person to rise from a chair, walk 3 meters, turn, walk back to the chair, and sit.¹⁶ The TUG has been shown to have good specificity and sensitivity for identifying older adults at risk of falling. TUG is reported as the time in seconds to complete the task (faster time is better). We will use an 8-ft course to mirror what Vivo is doing virtually.
- The Expanded Short Physical Performance Battery (eSPPB) will be used to assess lower extremity function. The SPPB¹⁷ is a brief test of global mobility function with excellent test-retest and inter-examiner reliability.¹⁸ It is sensitive to change,¹⁹ safe, and a robust predictor of future physical disability and death.¹⁷ To avoid ceiling effects, we will use an expanded version (eSPPB).²⁰ The resulting score is normally distributed, continuous, and shows greater sensitivity to change than the SPPB.²¹
- The Four Square Step Test (FSST) is a test of dynamic standing balance where participants are asked to step over 4 canes arranged in a 'plus sign' configuration in a specific pattern.²² The FSST is scored as the time in seconds to complete the sequence forward (squares 1-2-3-4) and then backward (squares 4-3-2-1) where a faster time is better.
- The 4-step Stair Climb Test (4SCT) is a test of functional leg power where participants are asked to climb up 4 stairs as fast as possible.²³ The 4SCT is scored as the time in seconds to complete the test. Power (in watts) can be calculated using body weight (in kilograms), stair height (in meters), and time.²⁴
- Grip strength will be measured twice in each hand using an isometric hydraulic hand dynamometer (Jamar, Bolingbrook, IL). Participants will be excluded from performing the test if they report hand pain or recent hand or wrist surgery.

Cognitive Function Tests

- The Montreal Cognitive Assessment (MoCA) is a 30-item test of global cognition that has been validated as a highly sensitive tool for early detection of mild cognitive impairment.²⁵
- Digit Symbol Coding (DSC) is contained in the Wechsler Adult Intelligence Scale-III and is a timed pencil and paper test measuring perceptive-motor processing speed.²⁶

Questionnaires

- The Perceived Stress Scale assesses how uncontrollable and stressful life has been over the past week or month.²⁷
- The Short Form-36 Health Survey (SF-36) is a 36-item questionnaire that assesses overall health status and quality of life.²⁸
- The UCLA Loneliness Scale v3 is a 20-item scale designed to measure subjective feelings of loneliness and social isolation.²⁹

- The Life Space questionnaire is a measure of the extent of mobility of older adults and assesses how far people travel outside of their home.³⁰
- The Pittsburgh Fatigability Scale (PFS) is a 10-item self-administered questionnaire that assesses self-reported whole-body physical and mental tiredness related to activities of fixed intensity and duration in adults age ≥60.³¹
- The Pepper Assessment Tool for Disability (PAT-D) consists of 19 items that yield three subscales and a total score. The three subscales include activities of daily living (ADL) disability, instrumental activities of daily living (IADL) disability, and mobility disability. Responses are made on a five-point Likert scale ranging from 1 (“usually did with no difficulty”) to 5 (“unable to do”) or a box can be checked that reads “usually did not do for other reasons”.³²
- The Self-Efficacy for Exercise (SEE) scale is a 9-item questionnaire that assesses potential barriers to exercise.³³ The total score is calculated by summing the responses to each question and ranges from 0-90. A higher score indicates greater self-efficacy for exercise.
- The Exercise Self-Efficacy (EXSE) scale is an 8-item questionnaire designed to assess self-efficacy for continued exercise participation in the future.³⁴ Respondents are asked to indicate how confident they are in their ability to continue exercising three times per week at a moderate intensity for 40 or more minutes per session, with responses ranging from 0% (not at all confident) to 100% (highly confident). Self-efficacy is then calculated by summing the confidence ratings and dividing by the total number of items in the scale, resulting in a maximum possible efficacy score of 100.

Vitals

- Resting blood pressure and heart rate will be measured in the seated position two times and the average will be used. If blood pressure values are not within 5mmHG or exceed 180/100 then a third value will be taken.

Anthropometric Measurements

- Height and weight will be determined using a stadiometer and digital scale. BMI will be calculated from measured height and weight.
- Waist and hip circumference will be determined using a tape measure. Waist-to-hip ratio will be calculated from measured waist and hip circumference.

Medication Inventory and Medical History

- The participant’s medical record will be reviewed to confirm medications and medical history for eligibility as well as through self-report.

If the participant is deemed eligible, they will receive a welcome kit that includes resistance bands, a blood pressure cuff, and a smartwatch, along with a tape measure and written instructions about the assessments. The participant will be asked to complete an online Vivo registration form (using the link: https://8469861.hs-sites.com/navigation_at_home) so that a Vivo team member can contact them to schedule an online assessment. They will also be asked to download two apps

(Garmin Connect app and Labfront Companion app) on their smartphone to use with the smartwatch. The study coordinator will assist them with this process and orient them to the procedures necessary to collect study data and sync their devices with the apps.

Vivo Virtual Assessment

This visit will be conducted virtually in the individual's home by Vivo staff using Zoom. Participants will receive information about the class format and expectations. Vivo staff will assess the physical space to ensure the safety of the surroundings and will also complete an online assessment to confirm functional status. This will include a chair stand test, TUG test, step test, arm curl test, and balance tests. The baseline assessment will be used by the trainer to develop an exercise plan that meets the individual needs of the participant and will be challenging enough to elicit measurable changes in physical function. Following the online assessment, participants may have to wait until a group is formed before they can start intervention. This assessment will be completed again at the end of the study to assess changes in functional status.

Study Intervention

All study participants will complete the 12-week Vivo Heart program. Participants will be enrolled in cohorts of 4-6 and will meet virtually with a certified trainer for 45 minutes twice a week. Vivo's comprehensive training program currently encompasses five unique components to provide an individualized experience that will be challenging. Each class incorporates stretching, balance, and dual-task exercises in addition to resistance training. As part of the Vivo Heart program, participants will also be asked to complete a third exercise session on their own that incorporates moderate-intensity aerobic activity (e.g., walking, biking) for at least 30 minutes each week. In addition, group health education classes will be taught each week by an RD, who will also meet individually with participants to provide personalized dietary counseling.

- **Functional Training:** Total body resistance training will be the primary exercise focus. The American College of Sports Medicine (ACSM) recommends that activity intensity for older adults be defined relative to an individual's fitness within the context of perceived physical exertion. As such, program intensity will be set using a 10-point Borg scale, on which 0 = "no exertion at all/sitting" and 10 = "maximal effort." Participants will be instructed to exercise between 3 (light to moderate) and 7 (moderate to hard); these levels will be reinforced by advising participants to exercise at a level that is close to their "conversational limit" (i.e., talk test), which is associated with more labored breathing. This method of specifying intensity is easily understood, easily observable via Zoom, can be readily applied to individual activities, and will increase as an individual's fitness level improves. Individual limitations such as musculoskeletal conditions and balance will also be considered when prescribing the exercises. With an emphasis on serving the needs of older adults, Vivo also incorporates elements of cognitive training through dual-task cognitive-motor exercises (e.g., doing squats while counting backwards from 100 by 7 aloud) that have been shown to improve balance, walking speed, and cognition. The exercise component will be overseen by Vivo.
- **Personalized Dietary Counseling:** Participants will meet with the RD at the beginning of the study (weeks 0-1) and at the conclusion of the study (weeks 12-13). The RD will discuss with the participants their typical eating habits and advise on healthy eating recommendations. The dietary counseling component will be overseen by Vivo.
- **Health Education:** Weekly educational classes will be incorporated to provide support and general information on healthy lifestyle behaviors. Topics may include risk factor control, diabetes, hypertension, lipids, medications, aerobic exercise, strength training and flexibility, weight control, reading food nutrition labels, eating out, holiday eating, intimacy, stress,

relaxation, cardiac symptoms, and cardiac interventions. The health education component will be led by Vivo staff.

Blood Pressure Monitoring

Participants will be asked to monitor their blood pressure before and after exercise using a Garmin blood pressure cuff provided by the study. Participants will also be asked to record their blood pressure weekly in written exercise logs.

Heart Rate and Activity Monitoring

Participants will be given a Garmin smartwatch to wear continuously throughout the study to track their heart rate, physical activity, and other health metrics. Participants will be asked to record their heart rate before and after exercise using weekly logs as described above. They will also be instructed to download two apps (the Garmin Connect and Labfront Companion Apps) on their iOS or Android device which connect directly to the smartwatch via Bluetooth technology. Data is then securely transmitted to the encrypted Labfront cloud through an internet connection. Data travelling between Labfront users and the system is encrypted with the use of the Secure Socket Layer (SSL) and Transport Layer Security (TLS) technologies. This keeps data secure while in transit and ensures it can only be interpreted by the intended parties.

Monthly Phone Calls

Clinic staff will call each active participant every 4 weeks (at 1mo, 2mo) to see if they have had any health or medication changes utilizing the Health Status questionnaire.

Follow-up Visit

Participants will be asked to come back to the Sticht Center at Atrium Health Wake Forest Baptist to repeat the same study assessments as completed at the baseline visit. In addition, participants will be asked to complete a program satisfaction survey, and they will be asked again about any health or medication changes. This is the final visit and completes participation in the study. Participants can opt to continue with the Vivo program at a discounted rate that they would be responsible for. This is optional and does not impact their eligibility for Vivo Heart.

Outcome Measures

Primary Outcome: The primary outcome in this study is completion rate which will be determined by the percentage of enrolled participants who complete the study with $\geq 80\%$ compliance.

Secondary Outcomes: Secondary outcomes will include additional measures of feasibility, as well as acceptability and uptake as described below:

- Recruitment rate will be determined by the total number of enrolled participants divided by the number of months recruitment occurred.
- Recruitment yield will be determined based on the number of participants randomized relative to the total number of volunteers screened.
- Compliance will be determined based on adherence to the prescribed intervention. Compliance metrics will include attendance at the exercise sessions, health education classes, and dietary counseling sessions.

- Retention will be determined by the percentage of enrolled participations who complete follow-up testing.
- Acceptability will be assessed at the end of the study using a program satisfaction survey.
- Uptake will be determined by the number of participants who continue in the Vivo program after the study is over.

Tertiary Outcomes: Tertiary outcomes will include a number of physiologic, cognitive, and behavioral outcomes as described above and in Table 2. Healthcare utilization will also be assessed at the baseline and follow-up visits and by telephone at 1-month intervals.

Analytical Plan

Sample Size and Power Calculation

Assuming that at least 50% of eligible patients will be interested in participating in the study and meet the full inclusion/exclusion criteria, we anticipate enrolling 1-2 participants per week. Based on a conservative dropout rate of 20%, we expect a final sample size of 32. While this pilot study is not designed to provide sufficient statistical power to detect differences in the measured outcomes, we will obtain estimates of treatment efficacy and estimate the variability of outcome measures in this population to use in the design of a larger, more definitive trial.

Data Cleaning

We will examine the distributions of the outcome variables and the need for any transformations to approximate conditional normality for further analysis. Summary statistics will be calculated, including means, standard deviations, quartiles, and ranges for continuous variables, and counts and percentages for categorical variables. Range and validation checks will be performed on all variables in collaboration with study personnel. We will examine the distributions of all the variables, identify the potential outliers and influential points, and clean any unreasonable data.

Statistical Analyses

This study will test the feasibility and efficacy of a novel, synchronous, home-based virtual exercise training program (Vivo Heart) in underserved communities of older adults with CVD. The aims are to evaluate the feasibility, acceptability, and uptake of Vivo Heart (Aim 1) and examine changes in physiologic, cognitive, and behavioral outcomes in response to the intervention (Aim 2). To address Aim 1, descriptive statistics will be calculated for the outcomes of interest. As mentioned previously, we anticipate a recruitment rate of 1-2 participants per week. We also anticipate that <20% of enrolled participants will drop out prior to the end of the study and expect to achieve a compliance rate of ≥80%. In addition, we expect >80% of participants will be satisfied with the program and that approximately half will continue with Vivo after the 12-week study. To address Aim 2, paired t-tests or Wilcoxon matched-pairs signed rank test will be used to compare physiologic, cognitive, and behavioral outcomes before and after the intervention. We anticipate that the Vivo Heart program will have favorable effects on the outcomes of interest.

Subject Recruitment Methods

We plan to recruit older adults with CVD who live in a rural area or a socioeconomically disadvantaged neighborhood. Potential participants will be identified through the Atrium Health Wake Forest Baptist EHR. Individuals identified through the EHR who express interest in the study will be contacted by telephone to assess initial eligibility. Individuals who pass the initial telephone screening will be scheduled for a baseline visit.

Recruitment will be supported by the Clinical Research Core of the Wake Forest Older Americans Independence Center. We will employ our well-developed retention strategies to maximize participation including utilizing well-trained and experienced staff who will provide a positive experience and defraying participant costs for travel or parking, as needed. Our retention plan also includes regular communication with participants and offering extended participation in the Vivo program at a reduced rate after the study.

Human Subjects Protection

Informed Consent

Signed informed consent will be obtained from each participant. The informed consent process will follow the procedures of the Wake Forest Institutional Review Board (IRB). The study team will explain the purpose, methods and extent of the study to prospective participants. The potential participant will be asked to read the informed consent form and ask questions. The form will be written in simple easy to understand language. We require study staff to review all of the key aspects of the study verbally with the potential participants. Staff is then required to question potential participants to ascertain whether s/he has understood the information. Potential participants who are illiterate or have impaired vision must have the consent read to them, followed by review of the checklist, opportunity for questions, and discussion. This process will take place in a quiet, private room. A copy of the signed and dated consent form will be given to participants, and the original document will be placed in each participant's individual study file, which will be stored in a secure location. In compliance with the Health Insurance Portability and Accountability Act (HIPAA) and the Standards for Privacy of Individually Identifiable Health Information of the Department of Health and Human Services, we will access personal health information only after obtaining informed consent.

Potential Risks

There are potential risks associated with some aspects of this research study. The nature, purpose, and risks of all procedures and protocols will be explained to each participant before obtaining written consent. All examiners will be trained in the standardized conduct of all assessments before data collection. Participants will be instructed to wear appropriate and comfortable clothing, and standardized written instructions will be provided prior to each study visit. The intervention procedures have been designed to minimize the danger of major complications, and all tests are performed by trained, experienced research staff who will be supervised by qualified medical personnel as needed. A Data Safety and Monitoring Committee, an independent group of experts, will be reviewing safety and other data from this research throughout the study. Risks associated with specific procedures and the intervention are discussed below.

- ***Functional Training:*** The risks associated with the prescribed aerobic and resistance exercises are minimal and include loss of balance, risk of injury from falls, fatigue, and muscle strains or sprains. Other potential risks from exercise, such as an abnormal heart rhythm, a heart attack, a stroke, or even death, are rare (less than 1 in 50,000 patient hours of exercise). To minimize the risk of injury and ensure the safety of study participants, standard procedures for exercise progression will be followed in accordance with ACSM recommendations. Vivo training is done in the virtual presence of a certified trainer who has expertise in risk management for training older adults, and safety measures are integrated throughout the session.
- ***Tests of Physical Function:*** There is a small risk of injury during the physical function tests, such as muscle strains or pulls, falls, or joint injury. Risks will be minimized by having experienced and trained staff conduct these assessments. If a participant reports pain, dizziness, or other medical problem, the test will be terminated.

- **Surface Electromyography:** There is a very small risk of skin irritation from the surface electrodes. Risks will be minimized by thoroughly cleaning the skin prior to electrode placement and using caution when taking them off.
- **Tests of Cognitive Function:** Cognitive testing may produce frustration in some participants. If the participant appears distressed during cognitive testing, they will be comforted and encouraged. If the distress persists, testing may be discontinued.
- **Peak Exercise Test:** Graded exercise stress tests on a treadmill are common clinical procedures with minimal risks, including muscle strains or pulls, falls, or joint injury. There is also a small (1 in 10,000) risk of sudden death or serious cardiac event. To minimize these risks, patients will be screened prior to testing to identify any safety concerns and to verify that the participant is able to safely exercise. During testing, blood pressure, heart rate and rhythm, and breathing will be continuously monitored by an exercise physiologist and physician trained in advanced cardiac life support. Tests will be stopped if the following problems occur: fainting, dizziness, chest pain, irregular heartbeat, or a heart attack. In case of an adverse event, a fully equipped code card is available on the unit. We have performed exercise testing in over 750 study participants without incident.
- **Questionnaires:** The interviews and questionnaires participants complete in this study are of minimal risk. Care will be taken to ensure participant privacy and confidentiality while discussing personal and health information. It is possible that some patients with previously undiagnosed cognitive impairment or major depressive symptoms will be found to have these problems. Patients with moderate-to-severe cognitive impairment and major depression will be excluded from further participation and referred for appropriate medical follow-up.

Protections Against Risk

We will take several steps to minimize the potential risks described above. Only trained and certified staff will conduct the exercise intervention and outcome assessments. All research staff will be trained to recognize any signs of distress or discomfort in study participants and will be reminded to inform all participants that participation is voluntary, can be stopped at any time, and will not affect their clinical care. In addition, participants with a cardiac event or procedure in the past 6 months must be medically cleared to exercise by their cardiologist. The study physician may review the relevant medical records and communicate with the participant's doctor as needed to ensure inclusion/exclusion criteria are met and that it is safe for the individual to participate. If a participant discontinues the intervention for safety reasons, participation may only be resumed after consultation with the participant's doctor.

Confidentiality and Privacy

All data are obtained for research purposes only. Confidentiality of data is maintained by using research identification numbers which uniquely identify each individual. Data will only be used in aggregate and no identifying characteristics of individuals will be published or presented. Confidentiality will be protected by collecting only information needed to assess study outcomes, minimizing to the fullest extent possible the collection of any information that could directly identify participants, and maintaining all study information in a secure manner. To help ensure participant privacy and confidentiality, only a unique study identifier will appear on the data collection form. Any collected patient identifying information corresponding to the unique study identifier will be maintained on a linkage file, stored separately from the data. The linkage file will be kept secure, with access limited to designated study personnel. Data access will be limited to study staff. Data and records will be kept locked and secured, with any computer data password protected. No

reference to any individual participant will appear in reports, presentations, or publications that may arise from the study.

Our internet-based data entry system protects confidentiality and data security by using state-of-the-art https transmission protocols which are the same as those used by banks and financial institutions to protect customer transactions. Our network/server infrastructure employs the most up-to-date controls and protection from hackers and malicious software programs. Security access levels are established so that staff performing statistical analyses and reporting have retrieval access to the database but cannot add or modify information in it. The database administrator has separate security access to make modifications to the database and to its structure. Use of identifying information is scrutinized and minimized where possible. Access to any forms or data is protected by user ids and passwords that meet our institutional policies for length, composition and renewal. Disaster recovery incorporates industry best practices, including frequent off-site backup of our data systems. The backups are regularly tested to verify recoverability in the event of equipment failure or other business interruption events.

Heart rate, activity, and other health-related data will be collected remotely using devices produced and managed by Garmin Ltd. Data will be synchronized with the Garmin Connect and Labfront apps via a smartphone, tablet, or computer and then stored on the Garmin Connect and Labfront cloud services. To enhance privacy, anonymized participant accounts will be created. Participants will receive a personalized code that enables them to anonymously log into the Labfront App without having to enter any personally-identifying information. Data travelling between Labfront users and the system will be encrypted with the use of the Secure Socket Layer (SSL) and Transport Layer Security (TLS) technologies. Only the PI and approved study team members will have access to the study data. Select Labfront employees will also be able to access the secure server network in order to provide the remote monitoring service. However, in accordance with Labfront's privacy policy, they do not share personal information with third parties without participant consent, except in specific circumstances outlined in the Privacy Policy. As with any use of such technology there is the possibility of data breach or that Garmin or Labfront employees may be able to associate the individual with their data. Therefore, all participants will be educated about these risks prior to providing consent to participate in this study.

Data and Safety Monitoring

A Data and Safety Monitoring Plan (DSMP) will be implemented as described below to ensure the safety of all participants involved in the study and to ensure the validity and integrity of the data. The PI, co-investigators and the biostatistician will meet regularly to review study progress and to examine reports of adverse incidents as well as participant recruitment and follow-up. This study will also be reviewed by the Wake Forest Pepper Center DSMB every 6 months. The PI and the study physician will meet as needed to review all reported events.

Adverse events include any event that occurs during the course of the study and results in a participant suffering physical or mental injury, pain or suffering. Adverse events can be major, such as a participant who suffers cardiac arrest during testing, or minor such as a participant pulling a muscle during neuromuscular function testing. This includes any events occurring while a participant is enrolled in the study, even if the event did not occur while s/he was actively participating in the activities called for in the research protocol. Deviations from the study's protocol are also considered an adverse, unexpected, or notable event and will be reported to the PI.

Reporting of Unanticipated Problems, Adverse Events or Deviations

Any unanticipated problems, serious and unexpected adverse events, deviations or protocol changes will be promptly reported by the PI or designated member of the research team to the IRB

and sponsor or appropriate government agency if appropriate. In addition, an amendment will be made to the consent form if necessary and the PI will request new IRB approval.

Potential Benefits of the Proposed Research to Research Participants and Others

It is possible that research participants may benefit from taking part in this study., Participation in this study involves more than minimal risk however the benefits, such as improved strength, aerobic capacity, and physical function, outweigh the risks.

Importance of the Knowledge to be Gained

The knowledge gained by determining the feasibility and potential efficacy of Vivo Heart may help identify novel models of care for older adults with CVD and promote greater accessibility and utilization of CR programs for underserved communities. Ultimately this research may contribute robust evidence to support refinement of clinical guidelines and approval for insurance reimbursement.

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