Home-Based Exercise Program for Recovery After Transcatheter Aortic Valve Replacement:

A Pilot and Feasibility Study Protocol

Clinical Trial Registration: NCT02805309

Update History

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Version 2 (01/09/2017)

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Version 6 (06/08/2017)

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Version 9 (09/23/2019)

Version 10 (03/09/2021)

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0. UPDATE HISTORY

12/14/2016: The initial protocol was written for the Boston Claude D. Pepper Older American Independence Center Pilot Award.

01/09/2017: The protocol was modified to include several cognitive-behavioral interventions to maximize the adherence to the exercise intervention. Additional measures – self-efficacy and outcome expectation about exercise – were added. The target enrollment was increased to 30 patients per each group. After discussion with co-investigators and collaborators, the primary endpoint was changed from Short Physical Performance Battery (which measures specific functional tasks) to the patient-reported measure of Late Life Function Disability Instrument (which measures the actual performance of daily activities). These modifications were made in preparation for the Boston Roybal Center Pilot Award Program.

02/14/2017: The protocol was modified to have a 3-group comparison, home exercise with cognitive behavioral intervention, home exercise alone, and attention control education groups. The sample size was changed to 20 participants in each group. The aims and study interventions were modified accordingly. Data and Safety Monitoring Plan has been expanded. These changes were made in response to the comments from the Boston Roybal Center Pilot Award Program Review Committee.

03/27/2017: Minor updates were made to the data safety monitoring plan in response to the Boston Roybal Center Pilot Award Program Committee.

05/01/2017: Modifications were made per IRB request.

06/08/2017: Minor updates were made to include details of interventions (e.g., individualized goal setting, weekly plan, and progression schedule) and the related forms (**Appendices 1 and 2**) based on the physical therapists' input. Pre-specified subgroup analysis was added. The Clock drawing test was added to the baseline assessment for measurement of executive function.

08/21/2017: New safety officer was designated per NIA requirement. The intervention details were modified to allow flexible visit schedule to accommodate the participant's medical appointments and personal preference; a RPE scale copy will be provided. Time on study will be counted from the date of first intervention visit. Before the intervention 1, 15 to 20-minute introduction was added to review the study intervention schedule with the participant.

08/31/2017: Additional refinement in the intervention protocols and outcome assessment schedule was made.

09/23/2019: Addition of BWH as a site for recruitment. In July 2019, a problem occurred with the assessment of the primary endpoint, LLFDI score. The LLFDI-CAT software, which was originally developed in 2008, was no longer compatible with the latest version of the operating system. LLFDI paper version was used instead, but the items and assessment domains were not consistent between the two versions. In addition, these changes were not immediately implemented by the outcome assessors, which resulted in missing measurements.

03/09/2021: Since LLFDI-CAT scores were unavailable for most of the participants at 8 weeks, a post-hoc outcome measure, disability score, was analyzed. Analysis plan was revised for the disability score.

1. OVERVIEW

With the increasing number of transcatheter aortic valve replacement (TAVR) procedures in multi-morbid frail older adults with aortic stenosis (AS), more high-quality evidence is needed to improve the postoperative care of high-risk patients after TAVR. Under the current model of care, TAVR patients continue to experience functional decline and disability despite symptomatic improvement. Currently, there is no established exercise intervention targeting both frailty and cardiac rehabilitation in older adults treated with transcatheter procedure.

A pilot randomized controlled trial (RCT) of a home-based exercise intervention with or without cognitive behavioral interventions vs. attention control educational intervention will be conducted to evaluate its feasibility in improving functional status and disability over 8 weeks in 60 older patients who are discharged home after TAVR from Beth Israel Deaconess Medical Center (BIDMC) or Brigham and Women's Hospital (BWH).

Following informed consent and baseline testing, the participants will be randomized in a 1:1:1 fashion (20 patients per group) to receive either an individualized home-based exercise intervention with or without cognitive behavioral interventions or attention control educational intervention for 8 weeks. The intervention will target balance, flexibility, strength, and endurance. Exercises for the intervention group will be adopted from the National Institute of Aging (NIA) *Go4Life* exercise guide and modified to the participant's need and home environment. The interventions will be conducted by a physical therapist at the participant's home. Upon discharge after TAVR, the participant will have 2 sessions per week for Weeks 1-2, 1 session per week for Weeks 3-4, and 1 session every other week for Weeks 5-8. Cognitive-behavioral strategies will target self-efficacy, self-control, and positive outcome expectations of exercise to maximize adherence to the exercise program. Participants in the attention-control arm will receive weekly telephone calls for 8 weeks to learn general information about exercise and lifestyle tips. Physical therapy outside the study is allowed per the participant's physician.

Participants will undergo measurements of physical function and disability at baseline, 4- and 8-weeks. The primary outcome is the Late Life Function and Disability Instrument – Computer Adaptive Test (LLFDI-CAT), or the paper version (LLFDI). As secondary outcomes, the change in physical function will be assessed using the Short Physical Performance Battery (SPPB) and other performance measurements [revised 1/9/2017]. Adverse events and adherence will be monitored during the intervention phase.

The proposed research will provide essential information to design a larger clinical trial of a home-based exercise intervention that promotes independence and improves functional status and quality of life in multi-morbid frail older adults undergoing TAVR through individualized risk assessment and interventions.

2. STUDY OBJECTIVES

The objective of this study is to determine the feasibility of an RCT comparing a home-based exercise intervention with or without cognitive behavioral interventions in older patients after undergoing TAVR. We will evaluate the feasibility based on a) proportions of enrollment, refusal, and retention; b) adherence and potential barriers to exercise intervention; c) correlation of self-reported physical function and disability, LLFDI-CAT or LLFDI, vs. an objectively measurement of physical function, SPPB; and d) resources and costs of home visits and data management. The information that we learn from this pilot study will inform

design of a larger, definitive RCT.

2.1. PRIMARY OBJECTIVE

The objective of this study is to conduct a pilot RCT of an 8-week, home-based exercise intervention with or without cognitive behavioral interventions vs. attention control educational intervention to evaluate its feasibility in improving physical function and disability over the 8-week period after TAVR. We hypothesize that a home-based exercise program with cognitive behavioral intervention is more effective than home-based exercise alone; home-based exercise program with and without cognitive behavioral intervention is more effective than attention control educational intervention in preventing decline in physical function and disability after TAVR, as measured by LLFDI-CAT or LLFDI.

2.2. SECONDARY OBJECTIVES

To examine the effect of the intervention on the following endpoints at 8 weeks after discharge:

- Change in SPPB score
- Change in 2-minute walk distance
- Change in dominant hand grip strength
- Adherence to exercise
- Adverse events

2.3. OTHER OBJECTIVES

- To assess the correlation between the change in SPPB vs. the change in LLFDI-CAT or LLFDI score over 8 weeks after discharge.

3. BACKGROUND

Over 2 million older Americans are affected by AS and over 50% die within 2 years of symptom onset without treatment. TAVR, a catheter-based surgical procedure, provides symptomatic and survival benefits in older adults who are considered high risk for surgical aortic valve replacement (SAVR).[1-3] Symptomatic improvement has been reported in 80-90% of patients after TAVR,[2,3] but it is unclear whether their functional status also improves. Despite the high burden of frailty and disability in older adults undergoing TAVR, we found that functional status was infrequently measured in previous research; in the few studies that measured functional status, clinically important improvement was not consistently seen.[4]

According to our unpublished data from an ongoing prospective study of older adults with AS who underwent TAVR (N=59) or SAVR (N=47) between 2/2014-1/2015 at BIDMC and were followed for 6 months, we observed a modest correlation between the change in the New York Heart Association (NYHA) functional class and the change in ADL (correlation: 0.33). TAVR patients had higher prevalence of frailty phenotype (85% vs. 36%) and lower mean SPPB score (5.6 vs. 8.8) than SAVR patients. Compared with SAVR patients whose ADL improved over 6 months, TAVR patients had ADL decline (**Figure 1**). Our preliminary data highlights an urgent need for an intervention that promotes independence in TAVR patients.

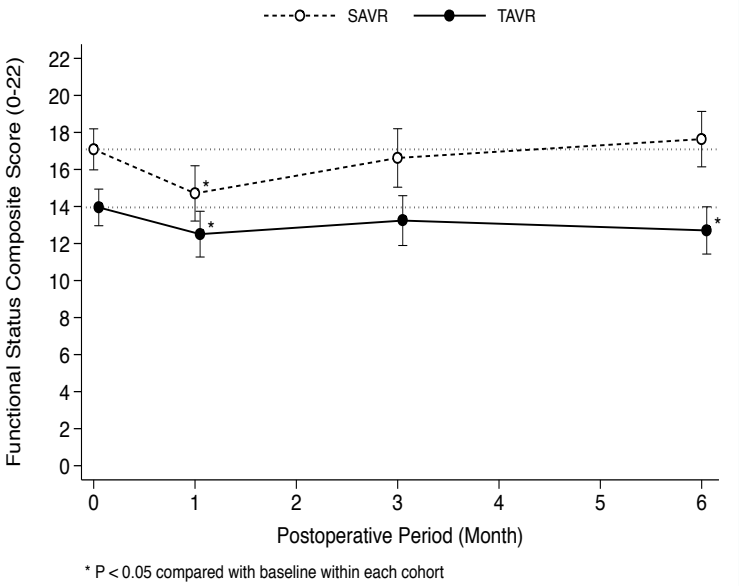

Figure 1. Functional status, measured in number of 22 daily activities (higher number indicating better function), seems to improve after SAVR but to decline after TAVR below their baseline. The data were derived from our ongoing prospective study of older adults with AS undergoing TAVR (N=59) or SAVR (N=47) in 2/2014-1/2015 at BIDMC. *p<0.05

The accumulating evidence suggests that multi-component exercise programs targeting balance, gait, strength, and endurance can improve mobility and physical function in frail older adults.[5,6] Exercise is a core component of cardiac rehabilitation that reduces mortality and hospitalization and also improves the quality of life in younger patients with myocardial infarction or heart failure.[7-10] Although most studies required on-site training, a home-based program appears to be as effective, with better adherence.[11] The following studies (**Table 1**) provide supporting evidence.

Table 1. Selected Studies of Home-Based Exercise Programs in Frail Older Adults

Study	Participants	Intervention	Outcome
Jette (1998)[12]	215 sedentary, functionally limited older adults (107 intervention group and 108 control group)	• **Intervention:** 6-month home-based exercise program ○ 35-min video-taped program of 10 exercise routines x 3 times a week ○ 2 home visits by PT ○ Cognitive behavioral interventions: bimonthly exercise calendars, enhance positive attitudes and beliefs, discuss potential barriers, and review benefits of exercise ○ Bimonthly telephone monitoring • **Control:** continue normal routines	• Follow-up: 6 months • 6-12% increased lower extremity strength • 20% improved tandem gait • 15-18% reduction in physical and overall disability
Gill (2002)[13]	188 frail older adults in the community (94 intervention group and 94 control group)	• **Intervention:** 6-month home-based exercise program ○ 16 PT visits over 6 months ○ Exercise sessions ○ Removal of home safety hazards ○ Education on safety techniques • **Control:** health education	• Follow-up: 12 months • Slower progression of ADL disability

Study	Participants	Intervention	Outcome
Matsuda (2010)[14]	72 frail older adults (no control group)	• **Intervention:** 6-week home-based exercise program on strength, flexibility, gait, balance, and cardiovascular fitness ○ 1-hour weekly session ○ Graduate PT students ○ Cognitive behavioral interventions: weekly review of exercise log, discussion of barriers, goal-setting • **No control group**	• Follow-up: 6 weeks • Increased 3 reps on the biceps curl • Increased 2.4 reps on the chair stand • Increased 0.17 m/s in gait speed • Decreased 5.7 s on Timed-Up-and-Go • Increased 7 points on Self Efficacy Scale
Molino-Lova (2013)[15]	140 frail older adults with SPPB score <9 after cardiac rehab (70 intervention group and 70 control group)	• **Intervention:** 1-year home-exercise program on strength, flexibility, balance, coordination, and aerobic endurance ○ 2 classes by PT before discharge from cardiac rehab ○ Provided a booklet (no face-to-face contact) ○ 30-min session x 3/week • **Control:** aerobic exercise	• Follow-up: 1 year • Intervention: SPPB improved from 7.7 ± 1.4 to 9.0 ± 1.1 • Control: no changes
Latham (2014)[16]	232 older adults who completed rehab after hip fracture (120 intervention group and 112 control group)	• **Intervention:** 6-month home-based exercise program ○ Initial 3 home visits by PT for teaching, followed by 3/week independent exercise ○ Monthly telephone calls, DVD ○ Cognitive-behavioral interventions: overcoming fear of falls, setting specific goals, self-monitoring of progress • **Control:** attention control	• Follow-up: 9 months • Intervention: SPPB improved from 6.2 ± 2.7 to 7.2 ± 3.0 • Improved the Activity Measure for Post-Acute Care (AM-PAC) score • Control: no change
Abizanda (2015)[17]	91 frail older adults in nursing homes (no control group)	• **Intervention:** 12-week exercise and nutritional supplement program ○ PT sessions 5 days a week ○ Nutritional supplement 2 cans/day • **No control group**	• Follow-up: 12 weeks • 48% improved at least 1 point on SPPB at 12 weeks

Despite the benefit of exercise, the proportion of older adults who are participating in regular exercise and physical activity is small.[18] Barriers to participation include health problems, pain, fear of falling and injury, and negative expectations that exercise will not help their aging process.[12,19-21] Previous research indicates that self-efficacy (i.e., one's ability to engage in exercise) and self-control (i.e., one's ability to regulate one's emotions and behaviors) about exercise as well as positive expectation (i.e., belief that exercise will lead to desired outcomes) mediates the long-term adherence and beneficial response to an exercise program.[22-24] Therefore, cognitive-behavioral interventions to correct negative beliefs, promote self-efficacy, and enhance positive expectations are essential for success of an exercise program.

The accumulating evidence provides a strong rationale to conduct a pilot study to develop and test the

feasibility of a home-based exercise intervention combined with cognitive behavioral interventions in older adults undergoing TAVR.

4. STUDY POPULATION

4.1. INCLUSION CRITERIA

Patients must meet all the following criteria to be included in the study:

1) Age ≥65 years old
2) Underwent TAVR
3) Live within a 20-mile radius of the recruiting site
4) Plan to be discharged home
5) Able to provide informed consent

4.2. EXCLUSION CRITERIA

Patients will be excluded if they meet any of the following criteria:

1) Stroke or any other medical disease that precludes participation in the exercise program
2) Severe cognitive impairment, defined as Mini-Mental Status Exam score <15
3) Concurrent enrollment in another clinical trial
4) Lack of confirmation from the patient's health care provider that the patient is medically safe to participate in the exercise program

If the patient's clinical condition changes after signing the consent form, and the patient is going to a rehabilitation or skilled nursing facility instead of home, we will dis-enroll these patients; outcomes and adverse events will not be collected from these patients.

5. ENROLLMENT

5.1. SCREENING

We will contact the clinical team to obtain a list of patients who are planned for home discharge. One day before the planned discharge date or on the day of discharge, patients will be approached in the hospital for eligibility and informed consent. The screening process will continue until we enroll 60 patients. Based on our experience at BIDMC, approximately 50% of TAVR patients are discharged home.

5.2. BASELINE ASSESSMENT OF FUNCTIONAL STATUS

Once the informed consent is signed, the participant will undergo geriatric assessment before hospital discharge. A trained research personnel will administer the following measures:

- Mini-Mental State Examination (MMSE) or Telephone Interview for Cognitive Status (TICS) (10

minutes) (range: 0-30) (if in-person MMSE is not feasible)

- LLFDI-CAT or LLFDI (5 minutes): LLFDI (range: 0-100) is a self-reported measure of activity limitation and participation restriction for community-dwelling older adults.[25-27] A shorter computerized adaptive version has shown comparable performance to the full version of LLFDI.
- Dominant hand grip strength (2 minutes): average of 3 measurements (kg)
- SPPB (5 minutes): A measure of lower extremity performance (range: 0-12) that includes the following components[28-31]:
    - Balance: side-by-side, semi-tandem, and tandem stand
    - Gait: 4-meter walk time (average of 2 measurements)
    - Strength: 5-chair stand
- Two-minute walk test (3 minutes): a measure of endurance (meters walked)

Based on validated cut-points,[28-32] physical functional capacity will be categorized as very low, low, intermediate, or high level of functioning (**Table 2**). Based on the baseline functioning, an individualized home-based exercise program will be designed (see the Study Intervention Section below).

Table 2. Physical Functioning Levels for Balance, Gait, Strength, and Endurance

		Very Low	Low	Intermediate	High
Balance	Side-by-side	<10.00 s	≥10.00 s	≥10.00 s	≥10.00 s
	Semi-tandem	<10.00 s	<10.00 s	≥10.00 s	≥10.00 s
	Tandem	<3.00 s	<3.00 s	3.00-9.99 s	≥10.00 s
Gait	4-meter walk	>8.70 s	6.21-8.70 s	4.82-6.20 s	<4.82 s
Strength	Chair stand	16.70-60.00 s	13.70-16.69 s	11.20-13.69 s	<11.20 s
Endurance	2-minute walk	<212 ft	212-427 ft	428-495 ft	≥496 ft

5.3. BASELINE INTERVIEW AND MEDICAL RECORD REVIEW

Trained research personnel will interview the participant to obtain the following health information using the standardized case report form (see **Appendix 1**).

- Demographic information: date of birth, gender, race, ethnicity
- Social support: living status, support at home
- Physical activity level: miles walked in the past week; stairs climbed in the past week
- History of falls and use of assistive device
- Pre-procedure NYHA class
- Geriatric problems: hearing, vision, fatigue, insomnia, incontinence
- ADL disability
- Mini-Nutritional Assessment
- Depression
- Clock drawing test
- Self-Efficacy for Exercise (SEE) scale (9 items)[33]
- Outcome Expectation for Exercise (OEE) scale (9 items)[34]
- The following information will be obtained from medical records (see **Appendix 1**).
- Vital signs: blood pressure, heart rate, oxygen saturation, weight, height (at baseline assessment)
- Dates of admission, surgery, discharge
- Pre-procedure tests: echocardiogram, cardiac catheterization, laboratory test results

- Procedure characteristics: Society of Thoracic Surgeons predictive risk of mortality and of mortality or major morbidity, TAVR type, access route, VARC-2 complications[35]
- Pre-procedure tests: echocardiogram, laboratory test results (last values before discharge)
- Comorbid conditions and medications from discharge summary

5.4. RANDOMIZATION

The participant will undergo TAVR prior to randomization. At the time of discharge, those who are being discharged home will be randomized in 1:1:1 ratio to home-based exercise with cognitive behavioral interventions vs. home-based exercise alone vs. attention-control education group using a computer-generated randomization sequence.

6. STUDY INTERVENTION

6.1. HOME-BASED EXERCISE WITH COGNITIVE BEHAVIORAL INTERVENTIONS

6.1.1. Schedule and contents of individualized exercise program

A study physical therapist will make a home visit 10-14 days after discharge to allow patients to adjust to their home environment and make follow-up doctors' appointments. When scheduling the first visit, the physical therapist will ask about the interim history (between discharge and the day of the scheduling call) to identify any medical condition changes. At first visit, the physical therapist will spend 15-20 minutes reviewing the study goal; orienting the participant to the intervention and outcome assessment schedule; as well as the study staff they will interact with during the study period. This time is not considered part of the study intervention.

During the visit, the physical therapist (PT) will set individual goals and teach exercises designed to improve balance, flexibility, strength, and endurance. Over an 8-week period, a PT will visit twice a week for Weeks 1 and 2; once a week for Weeks 3 and 4; and every other week for Weeks 5 through 8 (on Weeks 6 and 8, respectively). While adhering to this visit schedule is ideal, modification of the schedule is allowed to accommodate the participant's competing needs for doctor's appointments and personal preferences, as long as the first 6 visits are in 4 weeks, the 7th visit in week 6, and the 8th visit in week 8. [Revised 08/31/2017] The visits that did not happen within 4 weeks will not roll over to the second half of the intervention period. If the study physical therapist is unable to schedule/confirm the visit with the participant, they will call one more time during the week. No more than 2 scheduling calls will be placed.

Exercises targeting balance, flexibility, strength, and endurance will be adopted mainly, though not exclusively, from the NIA *Go4Life* exercise guide booklet (source: https://go4life.nia.nih.gov/) and then modified based on the participant's baseline physical function (**Table 2**) and home environment. Sample exercises are shown in **Table 3**.

Table 3. Sample exercises adapted from the NIA *Go4Life Guide*

Balance	Flexibility (stretching)	Strength	Endurance
• Stand on one foot • Heel-to-toe walk • Balance walk	• Neck rotation • Shoulder • Shoulder and upper arm towel stretch • Upper body • Chest • Back • Ankle-modified to focus on hamstring stretch • Back of leg • Thigh • Hip, performed on the bed • Calf • Diaphragmatic breathing	• Hand grip • Wrist curl • Front arm raise-seated • Side arm raise • Arm curl-seated • Seated row • Wall push-up • Elbow extension • Chair dip • Back leg raise • Side leg raise • Knee curl • Leg straightening • Chair stand • Toe stand	• Walking

At each home visit, the physical therapist will work with the participant to set and adjust daily exercise goals to improve balance, flexibility, strength, and endurance. Exercise sessions will be 40 minutes in duration. The progression of exercise will be individualized as following:

- Balance: based on baseline function as tested by SPPB and use of the Borg Rating of Perceived Exertion (RPE) scale, (as well as cardiac monitoring), the goal would be for patients to rate the exercise intensity between 11 and 13. Progression would be adjusted based on this rating scale making the exercise either easier or harder. The ability to perform the exercise with appropriate form and length would also determine the progression (i.e., stand on one foot with good form and without loss of balance with incremental time without touch support until the participant is able to reach norms for age).
- Strength: based on manual muscle test and baseline chair stand reps, initiate an appropriate weight where 8 reps would likely cause an RPE of 13-15 with appropriate cardiac response. Progress to 10-15 reps at 13-15 RPE, then progress to 2 sets of 10-15 reps at RPE 13-15, before increasing the weight.
- Endurance: based on cardiac measures and baseline 2-minute walk test, adjust exercise intensity to maintain the goal of RPE of 11-13.
- Flexibility: start with 10 second hold of each exercise and 3 reps, progress holding of stretch to 30 seconds based on the goal RPE of 11-13 and cardiac status.

The participants will be provided a copy of the RPE scale and instructed to exercise for at least 30 minutes daily focusing on upper and lower body exercises on alternating days, exercises for flexibility and balance daily, and walking daily. By the end of the 8-week intervention period, the participant will receive the following exercises:

- 4 upper body strengthening exercises
- 4 lower body strengthening exercises
- 2-3 flexibility exercises, based on impairment
- 1 balance exercise, based on impairment and safety
- Walking program
- Diaphragmatic breathing

The study physical therapist will keep track of the participant's progress, identified barriers, complaints, or any adverse events in a paper chart for each home visit. Participants may receive physical therapy for medical needs outside the study if deemed necessary by their treating physician. We will continue to weekly monitor use of outside physical therapy. While the participant is receiving physical therapy outside the study, the study intervention will not be administered. Once the outside physical therapy is complete, the study intervention will resume. The study intervention will conclude after Week 8 according to the original schedule.

6.1.2. Cognitive behavioral interventions to improve adherence

A written exercise plan will be provided weekly. Exercise images in the *Go4Life* guide booklet will be used, whenever appropriate. Participants are instructed to do prescribed exercises for 30 minutes daily. A diary will be given to track exercises (see **Appendix 2**). The diary will include sections of 1) individualized goals; 2) weekly plan; 3) weekly progress; 4) daily exercise tracking; and 5) adverse events. The physical therapist will review the participant's progress during each home visit, while also assessing for possible adverse events and offering specific safety tips for the future prevention of adverse events. When necessary, exercise intensity or progression will be modified. To improve adherence, the following cognitive-behavioral strategies will be employed to improve self-efficacy, self-control, and outcome expectation for 20 minutes of each session:

<u>Week 1</u>

- Enhance positive attitudes and beliefs about exercise through discussion of benefits of exercise: Refer to the following sources:
    - NIA Go4Life guide page 6-7 (Why is physical activity such a big deal?)
    - NIA Go4Life guide page 11 (Benefits of exercise and physical activity)
    - NIA Go4Life guide page 13 (Specific types of exercise and their benefit)
    - NIA Go4Life guide page 31 (Building up the benefits)
- Discussion of barriers to exercise:
    - Individualize to each participant
- Individualized goal setting:
    - Complete the study form "Your Goals" sheet (Appendix 2 – Diary – Exercise-CBT Group)
- Develop a detailed exercise plan on what, when, and where to conduct exercise:
    - NIA Go4Life guide page 20 (Write a plan to add exercise and physical activity to your life)
    - Complete the study form "Your Weekly Plan" sheet (Appendix 2 – Diary – Exercise-CBT Group)

<u>Week 2 through 8</u>

- Revise "Your Weekly Plan" every week
- Self-monitor progress using exercise calendar
    - Review "Your Progress" sheet (Appendix 2 – Diary – Exercise-CBT Group)
- Receive $10 rewards for achieving 30 mins of exercise daily for at least 5 of 7 days (or equivalent to 70% of days for the week)

Prior to the intervention, physical therapists will be trained by an expert in Boston Roybal Center For Active Lifestyle Interventions (PI: Margie Lachman) who has developed and implemented a cognitive behavioral intervention protocol for exercise intervention for use by PTs without formal cognitive behavioral therapy

training.

6.1.3. Preventing and monitoring adverse events

Prior to each session, the physical therapist will review the health status of the participant, evaluate their home environment to identify safe areas for exercise, and teach safety tips and warning symptoms (e.g., chest pain or pressure, severe dyspnea, left shoulder or arm pain, indigestion, palpitations, lightheadedness, dizziness, and headache). Participants will be instructed to begin slowly at a low level of effort and gradually increase the intensity according to the therapist's guidance. Whenever available, we will engage caregivers or family members in supervising self-exercise. Blood pressure, heart rate, and pulse oximetry will be monitored during the physical therapy sessions to assess the appropriateness of exercise.

A research assistant who is unaware of the treatment assignment will monitor adverse events weekly using a standardized checklist (section 9; see **Appendix 3**). Nonetheless, the participants may volunteer adverse events. In addition, adverse events may occur during the exercise session. In the case of adverse events, the physical therapist will evaluate the seriousness of the event and recommend the best course of action, in consultation with the PI or other licensed physician in the research team. Participants and their caregivers will be instructed to activate the emergency medical service for serious adverse events that require immediate medical attention. All adverse events will be reported to the PI. If the severity of adverse events is high enough to require medical attention, we will obtain medical clearance from the participant's physician. Cardiac-related issues will require clearance from the participant's cardiologist and non-cardiac issues will require clearance from the participant's primary care physician.

6.1.4. Summary of tasks at each home visit

A study physical therapist will be responsible for the following tasks at each home visit:

- Reviewing the participant's diary for progress since the last session and provide feedback.
- Before exercise, checking vital signs (blood pressure, pulse, oxygen saturation) and checking for any change in health status (contraindication for exercise).
- Providing an individualized exercise training session for 40 minutes
- Providing a cognitive behavioral session for 20 minutes
- Revising the individualized exercise plan, if necessary.
- Reinforcing safety precautions and the procedure for emergency study contact.
- Scheduling the next session

6.2. HOME-BASED EXERCISE ALONE

6.2.1. Schedule and contents of individualized exercise program

The home visit schedule, exercises, and individualized progression protocol will be identical to those outlined in the home-based exercise with cognitive behavioral interventions in section 6.1.1. Participants will be provided with daily exercise tracking sheet and adverse event reporting log. However, the participants will not receive any cognitive behavioral interventions. The duration of exercise session will be 40 minutes.

6.2.2. Preventing and monitoring adverse events

Physical therapists will implement the same precautionary and monitoring actions to prevent adverse events during exercise as outlined in section 6.1.3. Similarly, a research assistant who is unaware of the treatment assignment, will monitor adverse events weekly using a standardized checklist via telephone.

6.2.3. Summary of tasks at each home visit

A study physical therapist will be responsible for the following tasks at each home visit:

- Reviewing the participant's diary for progress since the last session and provide feedback.
- Before exercise, checking vital signs (blood pressure, pulse, oxygen saturation) and checking for any change in health status (contraindication for exercise).
- Providing Individualized exercise training session for 40 minutes
- Revising the individualized exercise plan, if necessary.
- Reinforcing safety precautions and the procedure for emergency study contact.
- Scheduling the next session

6.3. ATTENTION CONTROL EDUCATION INTERVENTION

6.3.1. Schedule and contents of attention control educational intervention

Participants randomized to the attention control group will receive written instruction on general exercise at the time of discharge from the hospital after TAVR as part of usual care (this information is given to all cardiac patients). After discharge, a health care professional (MD investigator or physical therapist) will call the participant weekly for a period of 8 weeks to teach general tips about exercise and diet (**Table 4** and **Appendix 4**) (source: https://go4life.nia.nih.gov/). No recommendations for a specific exercise program will be made, except for walking 30 minutes daily or as tolerated. Each telephone session will last approximately 30 minutes and will cover the following 8 topics (4 exercise tips alternating with 4 healthy eating tips). However, they may receive physical therapy outside the study if deemed appropriate by their treating physician. This will be recorded.

Table 4. Education Topics for Attention Control Group

Schedule	Topic
Week 1	Walking for Your Health
Week 2	What Does Healthy Eating Mean?
Week 3	Preventing Falls
Week 4	Overcoming Roadblocks to Healthy Eating
Week 5	Do Exercise and Physical Activity Protect the Brain?
Week 6	Making Smart Food Choices
Week 7	Exercising with Pain
Week 8	Choosing Healthy Restaurant Meals

6.3.2. Preventing and monitoring adverse events

Although the educational intervention for the attention control group does not recommend a specific exercise program, it is possible that education on the beneficial effects of exercise and lifestyle may increase participants' physical activity level. Therefore, adverse events can occur in the participants in the attention

control group. Although a research assistant who is unaware of the treatment assignment monitors adverse events weekly using a standardized checklist (section 9; see **Appendix 3**), the participants may volunteer adverse events during the educational intervention. In this situation, the study physician or health care professional who makes the call will determine the seriousness of the event and recommend the best course of action, in consultation with the PI or a licensed physician in the research team. Participants and their caregivers will be instructed to contact the emergency medical services for serious adverse events that require immediate medical attention. All adverse events will be reported to the PI.

6.3.3. Summary of tasks at each telephone call

A health care professional will be responsible for the following tasks at each telephone call:

- Deliver education intervention (30 minutes).
- Reinforce safety precautions and knowledge about emergency study contact.

7. FOLLOW-UP ASSESSMENT

7.1. ASSESSMENT SCHEDULE

Patients who were dis-enrolled due to rehabilitation discharge (this is an exclusion criterion) will no longer be included in the outcome follow-up. After 4 weeks and 8 weeks of discharge (beginning of week 5 and week 9), all participants will be evaluated at home by a physical therapist (see **Study Endpoint** section below) (**Table 5**). Time on study will be counted from the date of first intervention visit or call. This will be used to schedule the subsequent visit schedule and outcome assessment schedule.

Table 5. Overview of Study Assessment BIDMC

Study Procedures	Research Personnel	Place
Recruitment	NP (Cardiology)	BIDMC
Consent	MD investigators	BIDMC
Baseline assessment	RA 1	BIDMC
Medical record review	RA 1 (review by an MD)	BIDMC
Randomization	RA 2	BIDMC
Intervention	• Intervention group 1: Physical therapist 1 (HSL) • Intervention group 2: Physical therapist 2 (HSL) • Attention control group: Physical therapist 3 (HSL)	Home Home Telephone
Outcome assessment	• Performance Measures: Physical therapist 3 (HSL) • Self-Reported Measures and adverse events: Physical therapist 3 (HSL)	Home Home

Table 6. Overview of Study Assessment at BWH

Study Procedures	Research Personnel	Place

Recruitment	MD/RN investigators	BWH
Consent	MD/RN investigators	BWH
Baseline assessment	RA 1	BWH
Medical record review	RA 1 (review by an MD)	BWH
Randomization	RA 2	BWH
Intervention	• Intervention group 1: Physical therapist 1 (HSL) • Intervention group 2: Physical therapist 2 (HSL) • Attention control group: Physical therapist 3 (HSL)	Home Home Telephone
Outcome assessment	• Performance Measures: Physical therapist 3 (HSL) • Self-Reported Measures and adverse events: Physical therapist 3 (HSL)	Home Home

7.2. BLINDING OF OUTCOME ASSESSORS

A physical therapist who is unaware of the treatment assignment will perform the outcome assessment. In the intervention group, this physical therapist will be different from the therapist delivering the intervention. Before the assessment, we will remind the participants not to reveal their group assignment to maintain blinding. We will also keep track of blinding efficacy by adding a data element for the maintenance of blinding status in the Outcome Assessment form (**Appendix 1**).

7.3. MAXIMIZING RETENTION

To maximize retention, we will accommodate the participant's personal preference in scheduling home visits and telephone calls. We will provide a schedule and reminders for the next home visit (intervention group) and subsequent telephone calls (attention control group).

8. STUDY ENDPOINTS

8.1. PRIMARY ENDPOINT

The primary endpoint is the change in the LLFDI-CAT or LLFDI score, a self-reported measure of physical functioning and disability. The LLFDI-CAT has 2 domains: activity limitation domain and participation restriction domain. The score ranges from 0 to 100, with higher values indicating better functioning or low disability. This will be measured at 4 weeks and 8 weeks. We will determine the effect of the intervention based on the change from baseline to 8 weeks. In older adults at risk for mobility impairment, LLFDI was shown to have comparable psychometric properties and ability to predict meaningful changes in adverse health outcomes compared to performance-based measures.[26] This will be measured at baseline and 4 and 8 weeks after discharge.

In July 2019, a problem occurred with the assessment of the primary endpoint, LLFDI score. The LLFDI-CAT software, which was originally developed in 2008, was no longer compatible with the latest version of the operating system. LLFDI paper version was used instead, but the items and assessment domains were not consistent between the two versions. In addition, these changes were not immediately implemented

by the outcome assessors, which resulted in missing measurements. As a result, a disability score was calculated as an alternative post-hoc outcome measure (section 8.2.3).

8.2. SECONDARY ENDPOINTS

The following secondary endpoints will be measured at baseline and at 4 weeks and 8 weeks after discharge. We will calculate the change from the baseline to 8 weeks to determine the efficacy of the intervention.

1) Change in the SPPB: The SPPB is a simple, standardized, objective assessment of lower extremity function, which is highly correlated with frailty.[28-31]
    - Measurement: balance (0-4), gait speed (0-4), and chair stand score (0-4) (**Table 6**)
    - Range: 0-12 points
    - Interpretation: higher values indicate better function.
    - Clinically important change: 1 point[36,37]

Table 6. Scoring of Short Physical Performance Battery

Component	Measurement	0	1	2	3	4
Balance	Side-by-side	<10.00 s	≥10.00 s	≥10.00 s	≥10.00 s	≥10.00 s
	Semi-tandem	<10.00 s	<10.00 s	≥10.00 s	≥10.00 s	≥10.00 s
	Tandem	<3.00 s	<3.00 s	<3.00 s	3.00-9.99 s	≥10.00 s
Gait	4-meter walk	>30.0 s (unable)	8.70-30.00 s	6.21-8.70 s	4.82-6.20 s	<4.82 s
Strength	Chair stand	>60.0 s (unable)	16.70-60.00 s	13.70-16.69 s	11.20-13.69 s	<11.20 s

2) Change in 2-minute walk distance (meters): a test of endurance
    - Measurement: distance walked in 2 minutes
    - Range: >0 meters; 0-4 category (Table 2)
    - Interpretation: higher values indicate better endurance.
    - Clinically important change: 1 category increase
3) Change in dominant hand grip strength (kg): a test of upper extremity strength
    - Measurement: use hydraulic hand dynamometer in dominant hand (average of 3 trials)
    - Range: >0 kg
    - Interpretation: higher values indicate better strength.
    - Clinically important change: 3 kg[38]
4) Adverse events: see section 9.1.
5) Adherence to the exercise program
    - Measurement: Proportion of days with completed daily task during the study period
    - Range: 0-1 (proportion)
    - Interpretation: higher values indicate better adherence.
    - Clinically important change: NA

8.3. EXPLORATORY ENDPOINTS

The following exploratory endpoints will be measured at baseline and at 4 weeks and 8 weeks after discharge. We will calculate the change from baseline to 8 weeks to determine the efficacy of the intervention.

1) Change in MMSE or TICS: a measure of global cognitive function
    - Measurement: MMSE or TICS standard form (purchased from PAR, Inc)

- Range: 0-30
- Interpretation: higher values indicate better cognitive function.
- Clinically important change: ≥2 points based on reliable change index[39]

2) Change in NYHA functional class (range: 1-4)
   - Measurement: a questionnaire to assess the extent of physical activity limitation due to heart failure
   - Range: 1-4
   - Interpretation: higher values indicate more severe limitations.
   - Clinically important change: ≥1 class
3) Change in SEE
   - Measurement: Self-Efficacy Scale for Exercise[33]
   - Range: 0-90
   - Interpretation: higher values indicate higher self-efficacy.
   - Clinically important change: NA
4) Change in OEE
   - Measurement: Outcome Expectation for Exercise[34]
   - Range: 1-5
   - Interpretation: higher values indicate stronger outcome expectations.
   - Clinically important change: NA

8.3. POST-HOC ENDPOINT

Because the primary outcome measure, LLFDI-CAT score, could not be analyzed, we calculated a disability score from 7 activities of daily living, 7 instrumental activities of daily living, and 8 Rosow-Breslaw and Nagi physical tasks. The score indicates the number of activities that a person requires help from another person to perform. It ranges from 0 (no disability) to 22 (total dependence), with a clinically important change of 1 activity. This measure has been used in previous studies.[40] We will examine the correlation between the LLFDI baseline scores and the disability score (see section 10.1).

8.4. TIMING OF OUTCOME ASSESSMENT

The 4-week outcome assessment will take place during Week 5. The 8-week outcome assessment will take place during Weeks 9-10. Time on study will be counted from the date of first visit.

9. SAFETY MONITORING AND ADVERSE EFFECTS

9.1. ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

For this study, the following standard adverse event definitions are used:

- **Adverse events:** Any unfavorable and unintended sign, symptom, or disease temporally associated with the use of the study intervention, regardless of whether it is considered related to the study intervention.
- **Serious adverse event:** Any adverse event that results in death, life-threatening experiences, hospitalization or prolonged hospitalization, persistent or significant disability or incapacity.

- **Unanticipated problems:** Any experience that 1) is unexpected in terms of nature, severity, or frequency, given the research procedures described in the protocol document and the characteristics of the study population; 2) is related or possibly related to participation in the research; 3) suggests that the research places participants or others at a greater risk of harm than was previously recognized.

Adverse events are graded according to the following scale:

- **Mild:** An experience that is transient, and requires no special treatment. The experience does not generally interfere with usual daily activities.
- **Moderate:** An experience that is alleviated with simple therapeutic treatments. The experience impacts usual daily activities.
- **Severe:** An experience that requires therapeutic intervention. The experience interrupts usual daily activities. If hospitalization (or prolongation of hospitalization) is required for treatment, it becomes a severe adverse event.

The study uses the following adverse event attribution scale:

- **Not related:** The adverse event is clearly not related to the study procedures (i.e., another cause of the event is most plausible and/or a clinically plausible temporal sequence is inconsistent with the onset of the event).
- **Possibly related:** An event that follows a reasonable temporal sequence from the initiation of study procedures, but that could readily have been produced by a number of other factors.
- **Related:** The adverse event is clearly related to study procedures.

A research assistant who is unaware of treatment assignment will interview participants via telephone *weekly* to assess adverse events using a standardized checklist (see **Appendix 3**). If a participant reports adverse events during the intervention session (to a physical therapist or a health care professional), these adverse events will be reported to the PI *on a weekly basis*.

Severe adverse events and unanticipated problems will be reported to the IRB, safety officer, and NIA *within 24 hours*. In addition, all adverse events will be reported according to the IRB guidelines.

9.2. DATA SAFETY MONITORING PLAN

Patients who were dis-enrolled due to rehabilitation discharge (per exclusion criterion), will no longer be included in adverse event data collection.

A. PARTICIPANT SAFETY

A1. Potential Risks and Benefits for Participants

The potential risks to study participants include a modest risk of physical harm, such as musculoskeletal pain, falls, or cardiac events from low-intensity exercise intervention. Loss of confidentiality is another potential risk. We do not anticipate any psychological, financial, or legal risks.

The potential benefits to study participants include improvement in their physical function in response to our study intervention. In addition, participants in the intervention group will receive a weekly incentive of $10 for achieving high adherence for 8 weeks. All participants will be paid for $20 per outcome assessment at 4 and 8 weeks.

A2. Adverse Event and Serious Adverse Event Collection and Reporting

Refer to the section 9.1 above.

A3. Protection against Study Risks

Informed consent process: A study team member will screen inpatient list of the cardiology service daily to identify eligible patients. Age, home address, and procedure note will be reviewed for assessment of eligibility. Potentially eligible patients will be approached 1-2 days prior to or on the day of discharge. After explaining the study objectives, interventions, procedures, and potential risks and benefits, MD investigators will obtain a written informed consent. Any questions from the participant or their proxy will be answered. This process will be documented in the patient's medical record.

Expected adverse events: The following adverse events can occur during study procedures or interventions.

- Fall and fall-related injury: the expected risk is low to moderate.
- Musculoskeletal pain (new or worsening): the expected risk is moderate.
- Cardiovascular events including angina, arrhythmia, myocardial infarction, heart failure, or stroke: the expected risk is very low.
- Other symptoms including chest pain, dizziness/lightheadedness, dyspnea, palpitations, or syncope: the expected risk is low.

Protection against risk: Before obtaining consent, the research team will contact the patient's attending physician to obtain medical clearance for the patient to participate in exercise. To minimize physical harm, the physical therapist will adapt the exercise program according to the participant's physical function, level of confidence, and home environment. Prior to each exercise session, the therapist will encourage participants to express any concerns about exercise and teach them safe exercise techniques. In the case of adverse events, the physical therapist or the participant (or caregiver) will be instructed to contact a study physician for any adverse events and emergency medical services (EMS) for serious adverse events. These procedures will prevent or mitigate the consequences of adverse events. If the participants are evaluated in the emergency department or hospitalized for any reason during the study period, the research team will contact the participant's treating physician to obtain permission before resuming our study intervention.

B. INTERIM ANALYSIS

Since this is a pilot study, no interim analysis will be performed. Data analysis will be performed after study enrollment is complete.

C. DATA AND SAFETY MONITORING

The PI assures that informed consent is obtained prior to performing any research procedures, that all participants meet eligibility criteria, and that the study is conducted according to the IRB-approved research plan. Because this is a pilot study, a formal Data and Safety Monitoring Board will not be formed; instead, a safety officer will be designated.

Per NIA guideline, Dr. Houman Javedan, a geriatrician at Brigham and Women's Hospital, will be a new safety officer who will be responsible for study oversight.

C1. Frequency of Data and Safety Monitoring

Study data are always accessible for the PI to review. The PI will review study conduct (number of potential patients screened, number of patients who provided informed consent, number of drop-out, and potential protocol deviations) on a *weekly* basis. The PI reviews adverse events individually real-time and in aggregate on a *weekly* basis. The PI reviews serious adverse events in real-time. The PI ensures that all protocol deviations, adverse events, serious adverse events, and unanticipated problems are reported to the IRB; serious adverse events and unanticipated problems that are likely to be related to the study intervention are reported to the safety officer and NIA. The safety officer will review the study progress and status and adjudicate adverse events every 3 months. The PI will annually prepare a report to NIA. Other Sites, BWH, will have all study conduct reviewed by the lead MD at their site. BWH is responsible to report all AEs to the PI at BIDMC. The PI will be responsible to ensure that all BWH protocol deviations, adverse events, serious adverse events, and unanticipated problems are reported to the IRB; serious adverse events and unanticipated problems are reported to the safety officer and NIA.

C2. Content of Data and Safety Monitoring Report

The content of the data and safety monitoring report will include accrual, baseline characteristics, efficacy data on primary and secondary outcomes, and adverse events.

C3. DSMB/Safety Officer

A formal Data Safety Monitoring Board will not be formed for this multi-center pilot study of behavioral interventions. Instead, a physician who is not directly involved in this study will be identified for the safety officer role.

C4. Conflict of Interest for DSMB/Safety Officer

The safety officer should have no direct involvement with the study investigators or intervention. The safety officer will declare any affiliations with pharmaceutical and biotechnology companies, and any other relationship that could be perceived as a conflict of interest related to the study and/or associated with commercial interests pertinent to study objectives.

C5. Protection of Confidentiality

To protect confidentiality, data will be recorded in paper forms or using tablet computers. Data at all sites will be entered into the secure REDCap database for data management and tracking purpose. Paper records from all sites will be stored in a locked cabinet within the investigator's office. Only IRB-approved study personnel will have access to individually identifiable private information for the purpose of data collection, contact of participants for home visits and telephone calls. All research personnel will have up-to-date training on human subject research.

C6. DSMB/Safety Officer Responsibility

- Review the research protocol, informed consent documents and plans for data safety and monitoring
- Recommend subject recruitment be initiated after receipt of a satisfactory protocol
- Evaluate the progress of the trial, including periodic assessments of data quality and timeliness, recruitment, accrual and retention, participant risk versus benefit, performance of the trial sites, and other factors that can affect study outcome

- Consider factors external to the study when relevant information becomes available, such as scientific or therapeutic developments that may have an impact on the safety of the participants or the ethics of the trial
- Review study performance, make recommendations and assist in the resolution of problems reported by PI
- Protect the safety of the study participants
- Report to NIA on the safety and progress of the trial
- Make recommendations to the NIA and PI concerning continuation, termination or other modifications of the trial based on the observed beneficial or adverse effects of the treatment under study; and
- Ensure the confidentiality of the study data and the results of monitoring

10. STATISTICAL CONSIDERATIONS

10.1. STATISTICAL ANALYSIS PLAN

The analyst who will conduct statistical analysis will be blinded to the group assignment. To ensure that randomization is properly conducted, we will check the balance in health status, including the measures of physical performance and functional status between the 3 treatment groups using analysis of variance, Kruskal-Wallis test, or Fisher's chi-square tests.

We will assess the Spearman correlation coefficient between the disability score and the LLFDI-CAT score from baseline. High correlation supports that the disability score can be a reasonable alternative post-hoc outcome measure.

Aim 1 (home-based exercise combined vs. education): In analyses for primary endpoint (LLFDI-CAT or LLFDI score), secondary endpoints (SPPB score, 2-minute walk test distance, and dominant handgrip strength), and exploratory endpoints (MMSE or TICS score, NYHA class, SEE, and OEE), we will use a linear mixed effects model that models the outcomes as a function of time indicators (at 4 weeks and 8 weeks) and treatment-by-time interaction terms, with a random intercept. The treatment indicator is not included in the model because the baseline value of the outcome is assumed to be equal in an RCT. The main treatment effect will be determined based on the treatment-by-time interaction term for 8 weeks (β_4). The analysis will be performed according to the intention-to-treat principle.

$$E[Y_i] = \alpha_i + \beta_1 time_{week\,4} + \beta_2 time_{week\,8} + \beta_3 treatment * time_{week\,4} + \beta_4 treatment * time_{week\,8}$$

As a secondary analysis, we will include baseline variables that were not adequately balanced (standardized difference >0.1) in the regression model. As exploratory analysis, the Spearman correlation between the LLFDI-CAT or LLFDI change and the SPPB score change over 8 weeks will be examined. [Revised 06/08/2017] As a pre-specified subgroup analysis, we will examine whether the effect of the home-based exercise program combined is different by the baseline SPPB performance (median value to define the subgroup).

Aim 2 (home-based exercise with cognitive behavioral intervention vs. home-based exercise alone): We will use a linear mixed effects model that models the outcomes as a function of time indicators (at 4 weeks and 8 weeks) and treatment-by-time interaction terms, with a random intercept. The treatment indicator is not included in the model because the baseline value of the outcome is assumed to be equal in an

RCT. The main treatment effect will be determined based on the treatment-by-time interaction term for 8 weeks. The analysis will be performed according to the intention-to-treat principle. As a secondary analysis, we will include baseline variables that were not adequately balanced (standardized difference >0.1) in the model. We will assess the effect of cognitive behavioral intervention on the change in self-efficacy and outcome expectation over the 8-week period by using a linear mixed effects model that includes time indicators (at 4 weeks and 8 weeks) and treatment-by-time interaction terms, with a random intercept.

10.2. SAMPLE SIZE JUSTIFICATION

Since a pilot study is designed to test the feasibility of recruitment and conduct of study procedures, this study is not powered to test a minimal clinically meaningful effect of an intervention. Nonetheless, we provide power calculations under the assumption that the primary endpoint, LLFDI-CAT or LLFDI, has a standard deviation of 10 at a given time,[26,41] low to moderate within-individual correlation ranging from 0.10 to 0.40, and dropout rate of 20% in each group. Type 1 error rate is set to 0.05. The aim 1 of our study (home-based exercise vs. education) will have 66-83% power to detect an effect size of 10 (equivalent of 1 standard deviation). The aim 2 (home-based exercise with cognitive behavioral intervention vs. home-based exercise alone) will have 53-71% power to detect an effect size of 10. The estimation was done using GLIMMPSE (glimmpse.samplesizeshop.org).[42] As this is a small exploratory study, we will not perform any interim analysis.

Table 7. Power calculation

SD of LLFDI-CAT/ LLFDI score		Aim 1 (sample size: 40:20)			Aim 2 (sample size: 20:20)		
Within-individual correlation		0.10	0.20	0.40	0.10	0.20	0.40
Effect size*	10.0 (equivalent to 1-SD)	0.66	0.72	0.83	0.53	0.58	0.71

*Effect size is estimated using the difference of (LLFDI-CAT/ LLFDI) / MMSE or TICS score between the groups at 8 weeks.

11. HUMAN SUBJECT PROTECTION AND PROTECTION OF CONFIDENTIALITY

11.1. RISKS TO HUMAN SUBJECTS

Because the study intervention involves low-intensity exercise, there is a modest risk of physical harm, such as musculoskeletal pain, falls, or cardiac events. Alternative options to a home-based exercise program include center-based exercise programs or no exercise. Center-based exercise programs may have an advantage of having professional supervision, but 2-3 weekly visits to the center are not practical in this frail population. As we presented in our unpublished preliminary data (**Figure 1**), patients show decline in physical function and disability. Low adherence to center-based exercise programs or no exercise will result in more progressive functional decline. Loss of confidentiality is another potential risk. We do not anticipate any psychological, financial, or legal risks.

11.2. ADEQUACY OF PROTECTION AGAINST RISKS

The physical therapist will adapt the exercise program according to the participant's physical function, the level of confidence, and home environment. Prior to each exercise session, the therapist will encourage participants to express any concerns about exercise and teach them safe exercise techniques. In the case

of adverse events, the therapist or the participant (or caregiver) will be instructed to contact a study physician for any adverse events and emergency medical services for serious adverse events. These procedures will prevent or mitigate the consequences of adverse events.

We will collect information on health status based on in-person and telephone assessments and review of medical records. This information will be recorded on paper forms or using tablet computers. Data at all sites will be entered into the secure REDCap database for data management and tracking purposes. Paper records at all sites will be stored in a locked cabinet within the investigator's office. Only IRB-approved study personnel will have access to individually identifiable private information for the purpose of data collection, contact of participants for home visits and telephone calls. All research personnel will have up-to-date training on human subject research.

11.3. POTENTIAL BENEFITS OF THE PROPOSED RESEARCH TO HUMAN SUBJECTS AND OTHERS

The proposed research will provide essential information for the future design of a large clinical trial that examines the effect of a home-based exercise intervention on the functional status and quality of life in multimorbid frail older patients undergoing TAVR. Under the current standard of care, TAVR patients continue to experience functional decline and disability. Thus far, there is a paucity of rehabilitation interventions that have proven effective. As such, patients may benefit from our study intervention. The potential benefit is likely to outweigh the modest risk of physical harms from exercise. In addition, participants in the intervention group will receive a weekly incentive of $10 for achieving high compliance for 8 weeks. All participants will be paid for $20 per outcome assessment at 4 and 8 weeks.

11.4. IMPORTANCE OF THE KNOWLEDGE TO BE GAINED

With the increasing number of TAVR procedures in multimorbid frail older adults, more high-quality evidence is needed to improve the postoperative care of high-risk patients after TAVR. Currently, there is no established rehabilitation intervention for these high-risk patients. Our proposed intervention, once confirmed in a large clinical trial, has great potential to influence the standard of care for future TAVR patients. We believe that this anticipated benefit outweighs the modest risk of physical harm to participants.

12. MULTI-CENTER PLAN

BIDMC will serve as a coordinating center. Currently, Brigham and Women's Hospital is the only other site involved in this study. They will be recruiting patients from their center, consenting, and conducting baseline visits at BWH. Their physical therapy interventions will occur through HSL.BWH Research assistants will also conduct the follow-up phone calls for their enrolled participants.

The plan for monitoring the research activities at the BWH site is as follows:

1. Both BWH and BIDMC sites will have regular conference calls to review progress and enrollment, database entries, and AE reporting for the BWH site. As the overseeing site, BIDMC is responsible for maintaining protocols and study procedures, as well as informing BWH of new procedures as they occur. This will be done through monthly conference calls, as well as emails, to notify BWH of all study changes.

2. BWH personnel will be required to complete training in the study procedure and REDcap per BIDMC protocol. BWH will be required to enter all patient screens, participant's data and other pertinent documentation for all study visits into REDcap. The overseeing PI has access to all information that will be entered at the BWH site.
3. AE reporting at BWH will follow the same rules as those outlined for BIDMC . For mild, moderate events and severe AEs, the PI will be informed of deviations, unanticipated problems and adverse events, that occur at BWH by email as well as at a bi-weekly meeting with both BIDMC and BWH study teams in attendance. All reportable events occurring at BWH will be reported to the CCI in accordance with reporting requirements. All AEs that are recorded by the physical therapist from patients enrolled at BWH will be reported to the BIDMC PI by the physical therapist.
4. The study monitors will be a research assistant and nurse from BIDMC. They will conduct on-site monitoring visits as indicated below and will also periodically review the BWH data in REDcap after 10 patients are enrolled. Monitoring visits will verify that study protocols are followed (including adherence to inclusion and exclusion criteria and proper execution of study procedures), that proper consenting processes are used, verify all entries in REDcap by reviewing source documentation and review records to ensure that all adverse events are reported in a timely manner to the study PI and the BIDMC IRB,as appropriate.

Monitoring visits will occur at the following time points:

- An on-site monitoring visit will be performed after the first participant is enrolled
- An on-site monitoring visit will be performed after the subsequent 2-3 participants are enrolled.
- Monitoring after initial enrollment will occur quarterly unless more frequent monitoring is warranted due to non-compliance with protocol.

A written monitoring report will be provided to BWH and BIDMC CCI sites.

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13. LIST OF APPENDIX MATERIALS

- **Appendix 1:** Study Assessment Forms
- **Appendix 2:** Diary to Record Weekly Exercise Plan and Progress Report
- **Appendix 3:** Adverse Events Checklist

Appendix 1. Study Assessment Forms

BASELINE ASSESSMENT (updated: 06/16/2017) **ID: _____**

Interviewer		Date	MM / DD / YYYY

I. SOCIODEMOGRAPHIC INFORMATION

Name		DOB	MM / DD / YYYY
MRN		Gender	Male / Female
Race	☐ American Indian/Alaska Native	Marital status	☐ Married
	☐ African American		☐ Divorced
	☐ Asian		☐ Widowed
	☐ Native Hawaiian or other Pacific Islander		☐ Single
			☐ Unknown
		Lives in	☐ Home
	☐ White		☐ Assistive living facility
	☐ More than one race		☐ Nursing home
	☐ Unknown		☐ Others:
			☐ Unknown
Ethnicity	☐ Not Hispanic/Latino	Support	☐ Informal support
	☐ Hispanic/Latino		☐ Formal support (eg, VNA)
	☐ Unknown		☐ No support
			☐ Unknown

II. HEALTH STATUS

BP	_____ mmHg	HR	_____ bpm
O2 sat	_____ %	Height	_____ inch
Weight	_____ lbs	BMI	_____ kg/m2

In general, how would you rate your health?	☐ Excellent
	☐ Good
	☐ Fair
	☐ Poor
	☐ Unknown
During the last week, about how many miles did you walk outside your home?	☐ # of miles:_____
	☐ Did not walk outside
	☐ Unknown
During the last week, about how many flights of stairs did you climb? (1 flight = 10 steps)	☐ # of flights:_____
	☐ Did not climb stairs

☐ Unknown

Did you have any falls in the past year? ☐ Yes, # of falls:_____

☐ No

☐ Unknown

Do you use an assistive device for walking? ☐ Cane

☐ Walker

☐ None

☐ Unknown

Do you have SOB or fatigue when you … ? ☐ Class I

☐ do ordinary physical activity (class II) ☐ Class II

☐ do less than ordinary activity (class III) ☐ Class III

☐ are at rest (class IV) ☐ Class IV

☐ Unknown

Do you have (condition)? ☐ Poor eyesight ☐ Poor hearing

☐ Lack of energy ☐ Sleeping difficulty

☐ Loss of bladder control ☐ None of the above

III-1. LATE LIFE FUNCTION AND DISABILITY INSTRUMENT

Administer LLFDI-CAT Record scores

☐ Activity Limitation domain __ __ . __ __

☐ Basic mobility and handling __ __ . __ __

☐ Daily activities __ __ . __ __

☐ Participation Restriction domain __ __ . __ __

☐ Social roles __ __ . __ __

☐ Instrumental roles __ __ . __ __

III-2. DISABILITY

Taking bath or shower	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Using a toilet	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Getting in/out bed	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Walking inside house	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Dressing/undressing	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Grooming	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Eating	☐ No difficulty	☐ Difficulty, no help	☐ Need help

Using the telephone	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Doing light housework	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Doing heavy housework	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Preparing own meals	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Taking own medications	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Handling own money	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Shopping for groceries	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Transportation	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Walking a flight of stairs	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Walking half a mile	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Pushing a large object	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Lifting 10 lbs	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Crouching or kneeling	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Reaching above shoulder	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Handling small objects	☐ No difficulty	☐ Difficulty, no help	☐ Need help

IV. NUTRITION (MNA SCORING IN PARENTHESIS)

Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing problems?	☐ Severe decrease (0) ☐ Moderate decrease (1) ☐ No decrease (2) ☐ Unknown
Did you lose weight in the last 3 months?	☐ Lost >6.6 lbs (0) ☐ Does not know (1) ☐ Lost 2.2-6.6 lbs (2) ☐ No weight loss (3) ☐ Unknown
Mobility	☐ Bed or chair bound (0) ☐ Able to get out of bed but does not go out (1) ☐ Goes out (2) ☐ Unknown
Has suffered psychological stress or acute disease in the past 3 months?	☐ Yes (0) ☐ No (2)

	☐ Unknown
Neuropsychological problems	☐ Severe dementia or depression (0)
	☐ Mild dementia (1)
	☐ No problems (2)
	☐ Unknown
Body mass index (kg/m2)	☐ <19 (0)
	☐ 19 to <21 (1)
	☐ 21 to <23 (2)
	☐ ≥23 (3)
	☐ Unknown

V. SELF-EFFICACY SCALE FOR EXERCISE

How confident are you right now that you could exercise three times per week for 20 minutes if:

	Not confident										Confident
1. The weather was bothering you	0	1	2	3	4	5	6	7	8	9	10
2. You were bored by the program or activity	0	1	2	3	4	5	6	7	8	9	10
3. You felt pain when exercising	0	1	2	3	4	5	6	7	8	9	10
4. You had to exercise alone	0	1	2	3	4	5	6	7	8	9	10
5. You did not enjoy it	0	1	2	3	4	5	6	7	8	9	10
6. You were too busy with other activities	0	1	2	3	4	5	6	7	8	9	10
7. You felt tired	0	1	2	3	4	5	6	7	8	9	10
8. You felt stressed	0	1	2	3	4	5	6	7	8	9	10
9. You felt depressed	0	1	2	3	4	5	6	7	8	9	10

VI. OUTCOME EXPECTATION SCALE FOR EXERCISE

Do you agree or disagree that exercise:

	Strongly agree	Agree	Neither	Disagree	Strongly disagree
1. Makes me feel better physically	1	2	3	4	5
2. Makes my mood better in general	1	2	3	4	5
3. Helps me feel less tired	1	2	3	4	5
4. Makes my muscles stronger	1	2	3	4	5

5. Is an activity I enjoy doing	1	2	3	4	5
6. Gives me a sense of personal accomplishment	1	2	3	4	5
7. Makes me more alert mentally	1	2	3	4	5
8. Improves my endurance with my daily activities	1	2	3	4	5
9. Helps to strengthen my bones	1	2	3	4	5

VII. PSYCHOLOGICAL

Over the past 2 weeks, how often have you been bothered by little interest or pleasure in doing things?

- ☐ Not at all
- ☐ Several days
- ☐ More than half the days
- ☐ Nearly every day
- ☐ Unknown

Over the past 2 weeks, how often have you been bothered by feeling down, depressed or hopeless?

- ☐ Not at all
- ☐ Several days
- ☐ More than half the days
- ☐ Nearly every day
- ☐ Unknown

MMSE score

- ☐ Not performed
  - ☐ Patient refused
  - ☐ Patient unable
  - ☐ Other:
- ☐ Performed

  Score:

  Total score (if <30):

Clock drawing test (1 point for each component):

1) Draw the outline of a clock face
2) Put in all the numbers
3) Set the hadns at ten past eleven

- ☐ Not performed
  - ☐ Patient refused
  - ☐ Patient unable
  - ☐ Other:
- ☐ Performed
  - ☐ Clock circle
  - ☐ Numbers in the correct order
  - ☐ Numbers in the

		correct spatial position
		☐ Insert two hands of the clock
		☐ Correct time

VIII. PHYSICAL

Dominant handgrip strength:	☐ Not performed	☐ Left hand
	☐ Patient refused	☐ Right hand
	☐ Patient unable	1st: __ __ . __ kg
	☐ Other:	2nd: __ __ . __ kg
	☐ Performed	
Chair stands 5 times	☐ Not performed	__ __ . __ sec
	☐ Patient refused	
	☐ Patient unable	
	☐ Other:	
	☐ Performed	
Standing balance	☐ Not performed	side-by-side: __ __ . __ sec
	☐ Patient refused	semi tandem: __ __ . __ sec
	☐ Patient unable	full tandem: __ __ . __ sec
	☐ Other:	
	☐ Performed	
4-meter walk speed	☐ Not performed	1st: __ __ . __ sec
	☐ Patient refused	2nd: __ __ . __ sec
	☐ Patient unable	
	☐ Other:	
	☐ Performed	
2-min walk distance (feet)	☐ Not performed	__ __ __ feet
	☐ Patient refused	
	☐ Patient unable	
	☐ Other:	
	☐ Performed	

II. MEDICATIONS (FROM DISCHARGE SUMMARY)

- ☐ Alpha-blocker
- ☐ Angiotensin-converting enzyme inhibitor
- ☐ Angiotensin-receptor blocker
- ☐ Antianxiety
- ☐ Antiarrhythmic
- ☐ Anticoagulant
- ☐ Anticonvulsant
- ☐ Antidepressant – SSRI or SNRI
- ☐ Antidepressant – TCA
- ☐ Antidepressant – Others
- ☐ Antiplatelet
- ☐ Antipsychotic
- ☐ Antihypertensive – others (hydralazine, etc)
- ☐ Beta-blocker
- ☐ Bronchodilators (beta-2 agonists)
- ☐ Calcium-channel blocker
- ☐ Cholinesterase inhibitor
- ☐ Digoxin
- ☐ Diuretic
- ☐ Incontinence drugs
- ☐ Inhaled corticosteroid
- ☐ Inhaled anticholinergic
- ☐ Inotrope
- ☐ Insulin
- ☐ Lipid-lowering – Statin
- ☐ Lipid-lowering – Non-statin
- ☐ Memantine
- ☐ Nitrate
- ☐ NSAIDs
- ☐ Opioids
- ☐ Oral hypoglycemic – sulfonylurea
- ☐ Oral hypoglycemic – metformin
- ☐ Oral hypoglycemic – others
- ☐ Sedative - Benzodiazepine
- ☐ Sedative – Non benzodiazepine

III. PREOPERATIVE TEST RESULTS (LATEST RESULTS)

Test date	MM / DD / YYYY	Hemoglobin	___ . ___ g/L
Creatinine	___ . ___ mg/dL	EGFR	_____ ml/min/1.73m^2
Albumin	___ . ___ g/L	HBA1C	___ . ___ %
Echo date	MM / DD / YYYY	LVEF	_____ %
Aortic valve	Area: __ . __ cm^2	Aortic regurgitation	☐ None ☐ Trace ☐ Mild ☐ Mild-moderate ☐ Moderate ☐ Moderate-severe ☐ Severe ☐ Unknown
	Peak velocity: __ . __ cm/s		
	Mean gradient: _____ mmHg		
Mitral	☐ None	Tricuspid	☐ None

regurgitation	☐ Trace	regurgitation	☐ Trace
	☐ Mild		☐ Mild
	☐ Mild-moderate		☐ Mild-moderate
	☐ Moderate		☐ Moderate
	☐ Moderate-severe		☐ Moderate-severe
	☐ Severe		☐ Severe
	☐ Unknown		☐ Unknown
Severe	☐ Yes	Right	☐ Yes
diastolic	☐ No	ventricular	☐ No
dysfunction	☐ Unknown	dysfunction	☐ Unknown
Cath date	MM / DD / YYYY	LVEF	_____ %
Significant	☐ No significant stenosis	Significant	☐ N/A (no graft)
stenosis in	☐ LM ≥50%	stenosis in	☐ No significant stenosis
native	☐ LAD ≥70%	grafts	☐ IMA graft ≥70%
vessels	☐ LCX/OM ≥70%		☐ Radial graft ≥70%
	☐ RCA/PDA/PL ≥70%		☐ Vein graft ≥70%
Risk score		ACC TAVR	___ ___ . ___ %
STS PROM	___ ___ . ___ %	STS PROMM	___ ___ . ___ %

IV. POSTOPERATIVE TEST RESULTS (LATEST RESULTS)

Test date	☐ MM / DD / YYYY	Hemoglobin	☐ ___ . ___ g/L
Creatinine	☐ ___ . ___ mg/dL	EGFR	☐ _____ ml/min/1.73m^2
Albumin	☐ ___ . ___ g/L	HBA1C	☐ ___ . ___ %
Echo date	☐ MM / DD / YYYY	LVEF	☐ _____ %
Central	☐ None	Paravalvular	☐ None
aortic	☐ Trace	aortic	☐ Trace
regurgitation	☐ Mild	regurgitation	☐ Mild
	☐ Mild-moderate		☐ Mild-moderate
	☐ Moderate		☐ Moderate
	☐ Moderate-severe		☐ Moderate-severe
	☐ Severe		☐ Severe
	☐ Unknown		☐ Unknown

V. POSTOPERATIVE COMPLICATIONS (VARC-2 DEFINITION)

- ☐ Myocardial infarction (MI)
  - ☐ Peri-procedural MI (≤72 hr after the index procedure)
  - ☐ Spontaneous MI (>72 hr after the index procedure)
- ☐ Stroke
  - ☐ Ischemic
  - ☐ Hemorrhagic
  - ☐ TIA
- ☐ Bleeding
  - ☐ Life-threatening or disabling bleeding
  - ☐ Major bleeding
  - ☐ Minor bleeding
- ☐ Acute kidney injury (AKIN classification)
  - ☐ Stage 1
  - ☐ Stage 2
  - ☐ Stage 3
- ☐ Vascular access site and access-related complications
  - ☐ Major vascular complications
  - ☐ Minor vascular complications
  - ☐ Percutaneous closure device failure
- ☐ Conduction disturbances and arrhythmia
  - ☐ Implant-related new or worsened cardiac conduction disturbance
  - ☐ Persistent or transient high-degree AV block
  - ☐ New permanent pacer implantation
  - ☐ New-onset A fib or flutter
  - ☐ New arrhythmia resulting in hemodynamic instability or requiring therapy
- ☐ Conversion to open surgery
- ☐ Unplanned CPB use
- ☐ Coronary obstruction
- ☐ Ventricular septal perforation
- ☐ Mitral valve damage or dysfunction
- ☐ Cardiac tamponade
- ☐ Endocarditis
- ☐ Valve thrombosis
- ☐ Valve malpositioning
- ☐ TAV-in-TAV deployment
- ☐ Prosthetic valve dysfunction
  - ☐ Prosthetic aortic valve stenosis
  - ☐ Prothesis-patient mismatch
  - ☐ Prosthetic aortic valve regurgitation

OUTCOME ASSESSMENT (updated: 06/08/2017) **ID: _____**

Interviewer Date MM / DD / YYYY

I. IDENTIFYING INFORMATION

Name Assessment schedule
- ☐ 4 Week
- ☐ 8 Week

Accidental un-blinding of the group assignment
- ☐ Yes
- ☐ No

II. HEALTH STATUS

In general, how would you rate your health?
- ☐ Excellent
- ☐ Good
- ☐ Fair
- ☐ Poor
- ☐ Unknown

During the last week, about how many miles did you walk outside your home?
- ☐ # of miles:_____
- ☐ Did not walk outside
- ☐ Unknown

During the last week, about how many flights of stairs did you climb? (1 flight = 10 steps)
- ☐ # of flights:_____
- ☐ Did not climb stairs
- ☐ Unknown

Do you use an assistive device for walking?
- ☐ Cane
- ☐ Walker
- ☐ None
- ☐ Unknown

Do you have SOB or fatigue when you … ?
- ☐ do ordinary physical activity (class II)
- ☐ do less than ordinary activity (class III)
- ☐ are at rest (class IV)

- ☐ Class I
- ☐ Class II
- ☐ Class III
- ☐ Class IV
- ☐ Unknown

III-1. LATE LIFE FUNCTION AND DISABILITY INSTRUMENT

Administer LLFDI-CAT Record scores
- ☐ Activity Limitation domain __ __ . __ __
  - ☐ Basic mobility and handling __ __ . __ __
  - ☐ Daily activities __ __ . __ __

☐ Participation Restriction domain __ __ . __ __

☐ Social roles __ __ . __ __

☐ Instrumental roles __ __ . __ __

III-2. DISABILITY

Taking bath or shower	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Using a toilet	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Getting in/out bed	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Walking inside house	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Dressing/undressing	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Grooming	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Eating	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Using the telephone	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Doing light housework	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Doing heavy housework	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Preparing own meals	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Taking own medications	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Handling own money	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Shopping for groceries	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Transportation	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Walking a flight of stairs	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Walking half a mile	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Pushing a large object	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Lifting 10 lbs	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Crouching or kneeling	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Reaching above shoulder	☐ No difficulty	☐ Difficulty, no help	☐ Need help
Handling small objects	☐ No difficulty	☐ Difficulty, no help	☐ Need help

IV. SELF-EFFICACY SCALE FOR EXERCISE

How confident are you right now that you could exercise three times per week for 20 minutes if:

	Not confident										Confident
1. The weather was bothering you	0	1	2	3	4	5	6	7	8	9	10
2. You were bored by the program or activity	0	1	2	3	4	5	6	7	8	9	10

3. You felt pain when exercising	0	1	2	3	4	5	6	7	8	9	10
4. You had to exercise alone	0	1	2	3	4	5	6	7	8	9	10
5. You did not enjoy it	0	1	2	3	4	5	6	7	8	9	10
6. You were too busy with other activities	0	1	2	3	4	5	6	7	8	9	10
7. You felt tired	0	1	2	3	4	5	6	7	8	9	10
8. You felt stressed	0	1	2	3	4	5	6	7	8	9	10
9. You felt depressed	0	1	2	3	4	5	6	7	8	9	10

V. OUTCOME EXPECTATION SCALE FOR EXERCISE

Do you agree or disagree that exercise:	Strongly agree	Agree	Neither	Disagree	Strongly disagree
1. Makes me feel better physically	1	2	3	4	5
2. Makes my mood better in general	1	2	3	4	5
3. Helps me feel less tired	1	2	3	4	5
4. Makes my muscles stronger	1	2	3	4	5
5. Is an activity I enjoy doing	1	2	3	4	5
6. Gives me a sense of personal accomplishment	1	2	3	4	5
7. Makes me more alert mentally	1	2	3	4	5
8. Improves my endurance with my daily activities	1	2	3	4	5
9. Helps to strengthen my bones	1	2	3	4	5

VI. PSYCHOLOGICAL

Over the past 2 weeks, how often have you been bothered by little interest or pleasure in doing things?

- ☐ Not at all
- ☐ Several days
- ☐ More than half the days
- ☐ Nearly every day
- ☐ Unknown

Over the past 2 weeks, how often have you been bothered by feeling down, depressed or hopeless?

- ☐ Not at all
- ☐ Several days
- ☐ More than half the days
- ☐ Nearly every day
- ☐ Unknown

MMSE score

- ☐ Not performed

	☐ Patient refused	
	☐ Patient unable	
	☐ Other:	
	☐ Performed	Score:
		Total score (if <30):

VII. PHYSICAL

Dominant handgrip strength:	☐ Not performed	☐ Left hand
	☐ Patient refused	☐ Right hand
	☐ Patient unable	1st: __ __ . __ kg
	☐ Other:	2nd: __ __ . __ kg
	☐ Performed	
Chair stands 5 times	☐ Not performed	__ __ . __ sec
	☐ Patient refused	
	☐ Patient unable	
	☐ Other:	
	☐ Performed	
Standing balance	☐ Not performed	side-by-side: __ __ . __ sec
	☐ Patient refused	semi tandem: __ __ . __ sec
	☐ Patient unable	full tandem: __ __ . __ sec
	☐ Other:	
	☐ Performed	
4-meter walk speed	☐ Not performed	1st: __ __ . __ sec
	☐ Patient refused	2nd: __ __ . __ sec
	☐ Patient unable	
	☐ Other:	
	☐ Performed	
2-min walk distance (feet)	☐ Not performed	__ __ __ feet
	☐ Patient refused	
	☐ Patient unable	
	☐ Other:	
	☐ Performed	

Appendix 2. Diary

Your Goals

ID:
Name:

Short-term	What will you do over the next week or two that will help you make physical activity a regular part of your life?
1	
2	
3	

Long-term	Write down at least two long-term goals. Focus on where you want to be in a year.
1	
2	
3	

Your Weekly Plan

ID:
Name:

Week 1	Mon	Tue	Wed	Thur	Fri	Sat	Sun
Endurance (where:)							
Upper body strength (where:)							
Lower body strength (where:)							
Balance (where:)							
Flexibility (where:)							

Your Progress

ID:
Name:

	Week 1	Week 2	Week 3	Week 4	Week 6	Week 8
Upper Body Strength Count number of arm curls you can do in 1 minute						
Lower Body Strength Count number of chair stands you can do in 1 minute						
Balance Time you can stand on one foot without support for as long as possible						
Flexibility Note how far you can reach toward your toes until you feel a stretch						
Endurance Pick a fixed course and see how long it takes you to walk that far						

Track Your Activities

ID:
Name:

Week 1	**Mon**	**Tue**	**Wed**	**Thur**	**Fri**	**Sat**	**Sun**
What activity did you do?							
How long did you do it? Report in minutes							
What activity did you do?							
How long did you do it? Report in minutes							
Did you have a fall? Answer yes or no							

Appendix 3. Adverse Events Checklist

Participant ID:	**Interview Date:** MM/DD/YY
Participant Name:	**Interviewer Name:**
Fall	[ ] No [ ] Yes (provide the details below) ***Was there an injury?*** [ ] No [ ] Yes (provide the details below) ***Was medical attention (e.g. ED or office visit) sought?*** [ ] No [ ] Yes (provide the details below)
Musculoskeletal pain (new or worsening)	[ ] No [ ] Yes ***Location(s):*** ***Intensity (0 to 10):*** ***Was medical attention (e.g. ED or office visit) sought?*** [ ] No [ ] Yes (provide the details below)
Cardiovascular events (new or worsening existing condition)	[ ] No [ ] Yes (provide the details below) ***What was the diagnosis made by your doctor?*** [ ] Angina [ ] Arrhythmia (e.g., atrial fibrillation) [ ] Myocardial infarction [ ] Heart failure [ ] Stroke
Other symptoms (new or worsening symptoms – without physician diagnosis)	[ ] No other symptoms [ ] Chest pain [ ] Dizziness/lightheadedness [ ] Dyspnea – [ ] at rest or [ ] on exertion [ ] Palpitation [ ] Syncope (loss of consciousness) [ ] Other: _____
Details of the event	***Event date:*** MM/DD/YY ***Describe the event (e.g., location, duration, intensity, outcome).***
Action taken	[ ] N/A – No adverse events [ ] PI notified – Date & time: MM/DD/YY HH:MM (Initial:) [ ] Clinical team notified – Date & time: MM/DD/YY HH:MM (Initial:)

ADJUDICATION OF ADVERSE EVENTS

Date and time	MM/DD/YY HH:MM
Adjudication team	**Study physician:** **Independent non-study physician:**
Adjudication	***Is this event serious?*** (Adverse events that lead to death, life-threatening experience, hospitalization or prolonged hospitalization, persistent disability or incapacity, or receipt of medical or surgical treatment to prevent any of the listed outcomes) [ ] No [ ] Yes ***Is this event unexpected?*** (Adverse events that are not consistent with the risk information described in the investigational plan, in terms of nature, severity, or frequency) [ ] No [ ] Yes ***Is this event related to participation in the research?*** (Adverse events that are consequences of a) the intervention or interactions used in the research or b) the collection of identifiable private information in the research) [ ] No [ ] Unlikely [ ] Possibly [ ] Probably [ ] Yes
Study participation	***Was the participant suspended from participation in the study?*** [ ] No [ ] Yes – Date: MM/DD/YY (provide the details below) ***Was the participant medically cleared to resume the study?*** [ ] No [ ] Yes – Date: MM/DD/YY (provide the details below)
IRB notified	[ ] Not immediately (reported in progress report) [ ] Immediately – Date & time: MM/DD/YY HH:MM (Initial:)
Comments	