Prehabilitation of Veterans with Exercise and Nutrition (PREVENT)

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List of Abbreviations

PREVENT	Prehabilitation of Veterans with Exercise and Nutrition
RR&D	Rehabilitation Research and Development Service
KDIGO	Kidney Disease Improving Global Outcomes
GFR	Glomerular Filtration Rate
PAEC	Pre-Anesthesia Evaluation Clinic
POSH	Preoperative Optimization of Senior Health (Clinic)
5RSTS	Five Repetition Sit-to-Stand
TMST	Treadmill Stress Testing
MoCA	Montreal Cognitive Assessment
ASA	American Society of Anesthesiologists
VCM	Virtual Care Management
RPE	Rate of Perceived Exertion

1.0 Purpose

The goal of VA's RR&D office is to maximize functional recovery. Considering that goal, our proposal allows us to test an intervention that combines the fundamentals of Physical Medicine and Rehabilitation with state-of-the-art nutritional support and innovations in care such as telehealth to optimize patients before high-risk surgery. This intervention has the potential not only to reduce complications and hospital readmissions, but also to maximize functional recovery and quality of life for thousands of veterans undergoing high-risk surgery every year. Furthermore, the proposal is the first step in the design and implementation of prehabilitative services for veterans living in rural areas and those with inadequate support or transportation.

2.0 Background and Significance

Approximately half a million operations are performed each year in VA hospitals across the country[4]. Veterans undergoing high-risk surgery have a 1 in 5 chance of suffering complications, a 1 in 10 chance of being readmitted to the hospital within 30 days, and a 1 in 50 chance of dying within 30 days[4]. Long-term survival is significantly reduced for those patients who have perioperative complications, even if they survive to leave the hospital[5].

Low fitness and poor functional status are among the strongest predictors of postsurgical complications[1,2]. Prehabilitation takes advantage of the weeks leading up to surgery in order to improve fitness, mobility and nutrition in preparation for the upcoming surgical stress[13]. Indeed, prehabilitation has been shown to improve fitness, reduce complications, and improve quality of life in high-risk surgical patients[7,9,12]. The most effective prehabilitation programs combine exercise with nutritional support (are multimodal). They provide exercise that is supervised and individualized and ensure that exercise intensity is appropriate and escalated according to improvements in fitness and strength. Most supervised prehabilitation programs are facility-based, with participation limited by travel time, distance, and transportation[10]. Unfortunately, home-based prehabilitation programs have shown small effect sizes and low compliance rates, likely because the intensity required in programs of such short duration is often not achieved with such unsupervised programs[14-16].

The goal of prehabilitation is to enhance fitness and physical function in anticipation of a forthcoming physiological stress[9]. One of the main components of prehabilitation is a structured exercise protocol that typically includes aerobic and resistance exercise. By repeatedly exposing the body to physiologic stress, physical activity stimulates muscle protein synthesis resulting in improved objective markers of physical fitness and improved strength[10-13]. Nutrition is another key component of prehabilitation because it works synergistically with exercise[14]. It is generally accepted that exercise provides the primary anabolic stimulus and nutrition potentiates the muscle protein response[15]. Indeed, studies using stable isotopes have shown that exercise without provision of adequate protein does not result in optimal gains in muscle accretion[16,17]. After a single session of resistance exercise in healthy individuals, muscle protein breakdown and synthesis are both stimulated[16]. Net protein balance in the muscle (protein synthesis minus breakdown)remains negative after exercise until exogenous amino acids are administered[16]. Amino acids stimulate both the synthesis of structural (myofibrillar) muscle protein as well as the synthesis of mitochondrial proteins, required for aerobic metabolism and maintenance of functional exercise capacity[18].

Compliance with prehabilitation programs is extremely variable, with reported rates that vary between 16 and 100%[13,19-22]. Hospital-based prehabilitation programs delivered under direct

supervision have the highest compliance rates, yet barriers such as travel time, distance, and transportation limit participation [21,23]. Previously, we found that rural veterans lack access to exercise programs[20,22,23]. Home-based interventions are attractive but are typically unsupervised and associated with reduced compliance rates[13,19,21]. If applied to prehabilitation, new telehealth technologies could address the shortcomings of home-based approaches because they combine accessibility with supervision, encouraging compliance while ensuring adequate training intensity. However, this mode of prehabilitation care delivery has not yet been studied in a veteran population.

The proposed "tele-supervised" exercise program may allow Veterans living in rural areas and lack transportation or are otherwise unable to travel to participate in prehabilitation in preparation for an upcoming high-risk operation. These findings are expected to inform the design of a larger multicenter trial on the effects of multimodal prehabilitation on surgical outcomes and healthcare resource utilization and to foster the widespread adoption of multimodal prehabilitation in preoperative optimization of high-risk patients at the Durham VAHCS and other VA Health Care Systems. It represents an important step towards providing optimal perioperative care for veterans by identifying and improving fitness, physical function, and nutrition before surgery in a manner that is not geographically constrained. These improvements will contribute to the reduction in health care costs due to decreased complications and fewer readmissions following surgery in high-risk patients.

3.0 Design

The objective of this protocol is to determine the feasibility, acceptability, and safety and estimate the effect size of a multimodal prehabilitation program that incorporates exercise training and nutritional support. The central hypothesis is that a short-duration, individualized multimodal prehabilitation intervention administered prior to high-risk surgery is feasible and safe at a tertiary VA hospital. The intervention will consist of individualized exercise training delivered remotely using VA telehealth technology, combined with nutritional support consisting of tailored nutritional advice, protein supplementation, and multivitamin and vitamin D supplements. Based on local surgical volume, local expertise in the Gerofit and telehealth exercise programs in non-surgical populations, and published participation numbers and attrition rates, we anticipate that 24 patients can be enroll and safely participate in a home-based telehealth exercise program plus nutritional support. Adherence to the intervention will be encouraged by use of automated text messages.

This is a pilot intervention that combines the most promising elements of prehabilitation along with innovations in telehealth delivery to develop a VA patient-centered multimodal prehabilitation program with the following specific aims:

- To determine the feasibility, acceptability, and safety of a short-term (3-4 week) multimodal prehabilitation intervention followed by a 4-6 week period of rehabilitation in a cohort of veterans undergoing high-risk surgery.
- To estimate the effect size of a multimodal prehabilitation program for important postoperative outcomes (improvements in functional capacity and physical function, anxiety/depression, and quality of life).

While aspects of the intervention are novel and the work exploratory, based on available evidence, we expect the Cohen's effect sizes for functional capacity and quality of life to be approximately 1.6 and 0.4, respectively.[11]

4.0 Risk/Benefit Assessment

4.1 Risk Assessment

There are minimal risks associated with the proposed prehabilitation program. Generally, nutrition and exercise are known to improve health. Physical injury or discomfort are potential risks and are inherent in any exercise, rehabilitation or prehabilitation program. Patients invited to participate will be screened by qualified physical therapists as part of the screening evaluation and the inability to complete the physical functional assessment will be cause for exclusion. Also, patients for whom physical activity is inappropriate or cognitive impairment affects their ability to consent for participation or to successful participate in the exercise program will not be enrolled. The team has extensive experience with tele-exercise therapies, including strategies for optimizing safety during individual, independent, home-based exercise. Examples of home-based exercises include marching in place, standing (potentially supported) while tapping a heel or toes, performing chair stands, and moving a leg or arm against a resistance band. It is entirely self-regulated, and any advancement will be based on self-reported levels of exertion.

Similarly, the nutrition and vitamin supplementation will be closely monitored by nutrition experts and adjusted based on personal telephone check-ins. Patients with advanced kidney disease are excluded from the study and those with renal impairment (KDIGO 3a and 3b) will receive reduced protein supplement in accord with ESPEN and 2012 KDIGO Guidelines. Renal function will be regularly monitored to ensure there is no adverse effect from the nutritional intervention.

Participation in our study poses no additional cost and every effort will be made to preserve the privacy and confidentiality of participants.

The similarity of the study interventions to conditions potentially encountered in daily life coupled with the measures taken to protect participants from adverse impact create a total risk that is minimal. The types of exercise resemble activities of daily living, especially in that they are self-regulated, and no patient will, or could be forced to do something they choose not to do.

4.2 Benefit Assessment

The benefit of participation in this study is available to both current enrollees and future patients. If a monitored prehabilitation program paired with nutrition support is found to be feasible, acceptable, and safe, and in the future, adequately powered clinical trials found to be effective, significant improvement to perioperative care is possible. Furthermore, the telehealth component of this program would facilitate delivery of prehabilitation to rural populations and those with limited support or access to transportation.

5.0 Selection of Subjects

5.1 Study Population

The study population includes frail veterans scheduled to undergo high-risk surgical procedures. Veterans scheduled for surgery are evaluated in either the Pre-Anesthesia Evaluation Clinic (PAEC) or the Preoperative Optimization of Senior Health (POSH) Clinic. We plan to screen veterans who are seen in either clinic and enroll a total of 24 patients over 2 years.

5.2 Inclusion and Exclusion Criteria

5.2.1 Inclusion Criteria

- Scheduled for high-risk surgery (colorectal, major urologic, hepatibiliary, esophageal, thoracic).
- Time from assessment to surgery ≥ 21 days
- Age ≥ 50 years
- English speaking
- 5RSTS time ≥ 11 sec and/or TMST score ≤ 25% percentile for gender/age

5.2.2 Exclusion Criteria

- Montreal Cognitive Assessment (MoCA) score of <21 (high school education) or 20 (< high school education) or Saint Louis University Mental Status (SLUMS) score ≤20
- Dementia diagnosis documented in electronic health record
- Inability to complete physical function assessment
- ASA PS categories 4 or 5
- Currently residing in skilled nursing facility
- Lack of access to a telephone
- Advanced chronic kidney disease (KDIGO stage 4 and 5)
- Pregnant at the time of preoperative assessment
- Inability to receive SMS text messages (i.e. does not own a text-enabled cellular telephone or tablet)

5.3 Inclusion of Women and Minorities

It is the policy of our institution (Durham VAHCS) not to discriminate against any patient because of sex, age, ethnicity, race, sexual orientation, or any other attribute. Therefore, all patients, including those who are lactating or otherwise of childbearing potential (excluding those who are pregnant), who present for surgery at DVHCS and meet inclusion/exclusion criteria would be eligible for inclusion in this study. Given that the small size of the cohort, and the focus of this study (feasibility, acceptability, safety, and effect size estimation), we do not plan to analyze racial, ethnic or gender groups separately.

6.0 Subject Recruitment

For the purposes of screening, recruiting, and determining eligibility, information will be obtained by accessing medical records—a HIPAA Waiver to screen and recruit will be requested. Once eligibility is determined, patients will be approached for interest and enrollment during their preoperative visit, typically 3-4 weeks prior to surgery. At that time, they will have adequate time to consider the study and its benefits and risks, ask questions, and decide if they wish to take part. Written informed consent will be obtained by study personnel.

7.0 Consent Process

7.1 Screening

Patients will be identified in 3 ways:

(a) Information about this new prehabilitation pilot program will be disseminated among our surgical colleagues. Surgeons will be encouraged to alert the PREVENT team to any patients being evaluated in the Surgery clinic who may be good prehabilitation candidates (frail, undergoing high-risk surgery).
(b) Additionally, a list of proposed cases is currently available in our Perioperative Scheduling Software (DSS) and in the VA's Corporate Data warehouse (CDW). This list will be screened periodically to identify potential candidates.
(c) Finally, the list of patients scheduled for evaluation in the PAEC and POSH clinics will be reviewed for potential prehabilitation candidates (review of Anesthesiology E-Consult or POSH Consult requests).

A HIPAA Waiver for screening purposes will be requested so that eligible participants can be identified prior to their PAEC or POSH clinic appointment, if possible ~4 weeks or more before their proposed operation.

7.2 Eligible Patients

When an eligible patient is identified, the day of the PAEC/POSH appointment will be determined. On the day of the clinic visit, the MoCA or SLUMS score, and physical function assessments (routinely performed by nursing staff during the clinic visit) will be reviewed to establish final eligibility for inclusion in the study, and the research coordinator or an investigator will be notified. A study coordinator or investigator will review the ICF with each eligible patient, answering all questions or concerns. After a review of the ICF, the patient will sign under the supervision of the study personnel and a full copy provided to the patient and/or family member. Study personnel may discuss the project with their other physicians or family members as needed.

All study personnel have completed the VA Human Subjects Protections and Good Clinical Practices training requirement and have experience with the process of obtaining and documenting informed consent for research. Any new study personnel who have not had such experience will be trained in several stages, including verbal instruction, shadowing consenting visits, VA training modules, and observation by qualified personnel.

No study procedures will be performed until after the ICF and HIPAA Authorization have been signed and received. Patients with impaired decision-making capability will

not be included in this study. Original signed copies of the informed consent form and HIPAA Authorization will be kept in our research office (C3011A) while photocopies will be provided to patients for their use.

8.0 Study Interventions

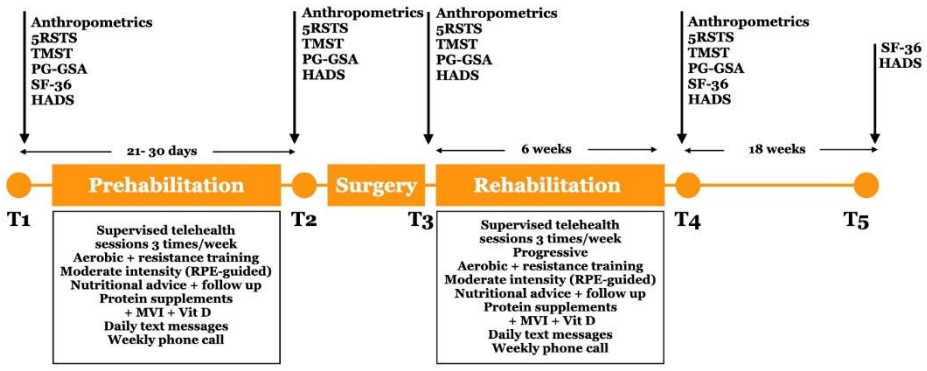
8.1 Screening Procedures

Patient screening will begin with a review of the proposed surgical cases list in DSS and CDW, review of Anesthesiology e-consults (PAEC or POSH) and direct surgical referrals (as described above in Section 7.1, Screening). A review of the patient's medical record via CPRS on the day of the PAEC/POSH clinic visit will verify that they meet inclusion/exclusion criteria.

Patients meeting all inclusion criteria by chart review will then undergo a baseline physical function assessment at the time of their PAEC or POSH in-person visit using the TMST and 5RSTS tests (as above, part of standard clinic evaluation). Eligible patients who consent to participate will then complete a baseline assessment that includes anthropometrics, assessment of handgrip strength (HGS), and the PG-GSA, SF-36 and HADS questionnaires.

8.2 Study Procedures

Eligible veterans who consent will enroll in a program of individualized exercise training combined with nutritional support during intervening time before and after surgery.



Study procedures and assessments are outlined in Figure 1 below.

Figure 1. Study milestones and assessments

Subjects who do not have a smart phone or tablet or who prefer not to use their own devices will receive a *VA-issued tablet* device that they will use to interact with their exercise trainer. They will be asked to download the Annie texting app and aa teleconference platform app on either their personal device or the VA-issued device. The VA issued tablets are then the property of the participant and no VA data will be stored on them. Automated text messaging via de VA Annie App will supplement our patients' exercise and nutritional support efforts.

8.2.1 Exercise Program

The exercise program will consist of a progressive function-based exercise program that includes 3 days per week of supervised exercise delivered directly to the home using telehealth technology. Exercise prescriptions will be individualized to baseline fitness and functional capacity.

Supervised exercise will consist of progressive, rotating, low-impact training interspersed with brief rest periods aimed at progressing to 30-minutes of moderate intensity aerobic training. Intensity of effort will be titrated to rate-of-perceived-exertion (RPE), with a target of 4-6 out of a maximum of 10 per national guidelines for older adults[36,37]. Resistance and functional training will be included and focus on strengthening the large muscle groups of the core, upper and lower extremities, and on maximizing mobility using body weight or resistance bands when the participant reaches higher levels of RPE (6-7).

Activities will be constantly monitored and adjusted to increase difficulty but stay below the target ceiling of 6-7 RPE. Due to the limited time window, each participant will be challenged daily to increase some element of the exercise program. A detailed description of the proposed exercise routine is included in Appendix 2. Post-operative aerobic and strength exercise will follow similar progression beginning as early as 1 week postoperatively. Exercise staff will work closely with surgical staff to safely provide exercise progressions given some surgeries may contraindicate specific exercises and intensities.

8.2.2 Nutritional Support Program

The nutrition intervention will be directed by a Registered Dietitian Nutritionist and will consist of tailored nutritional advice at the time of enrollment, followed by high quality protein supplementation individualized for kidney function (1.5 gm/kg/day for patients with normal kidney function, 1.2 gm/kg per day for patients with KDIGO GFR categories G3a and G3b). Patients with KDIGO GFR category G4 or G5 will be excluded (see Appendix 3). These recommendations are in accordance with current clinical guidelines for nutrition in the perioperative period [39,40].

Multivitamin and vitamin D supplementation will be provided (50% of RDA) during prehabilitation and recovery. Preoperatively, a 3-4-week supply of supplements will be provided at the PAEC or POSH clinic visits (T1). At the time of hospital discharge, participants will be given an additional six-week supply.

8.2.3 Assessments and Supplemental Interventions

Objective physical function assessments will be performed at baseline (T1), before surgery (T2), immediately prior to hospital discharge (T3), and then again 6 weeks postoperatively (T4) by administering the **2MST,5RSTS and HGS tests**[1] either in-person or remotely using telehealth technology (see Table 1 for details).

The nutritional support intervention will be assessed at baseline (T1), before surgery (T2), immediately prior to hospital discharge (T3)and then again 6 weeks postoperatively (T4) using **anthropometrics**, a weekly **24-hour dietary recall** (via telephone or videoconference, see Appendix 6), and the administration of the **PG-GSA**, a validated nutritional assessment instrument (see Table 1 for details).

Both the exercise and nutritional support programs will be supplemented with **text messages** on veterans who own text message-enabled cellphones. Messages will be sent daily using the VA Annie App during the prehabilitation period (T1 - T2). The purpose of these messages is as a reminder about the timing of training sessions, to prompt independent exercise on days between formal sessions, to take protein supplement following exercise, and to maintain a nutritional diary (see above).

Text messages and weekly telephone or videoconference calls will resume upon hospital discharge and extend until the 6-week follow-up visit (T4).

Anxiety, depression, and health-related quality of life will be assessed using the HADS and SF-36 questionnaires at baseline (T1), before surgery (T2), immediately prior to hospital discharge (T3), and 6 and 24 weeks postoperatively (T4 and T5, respectively). These questionnaires will be administered either in person or via telephone or videoconference.

Details and timelines for each of these assessment instruments are described in Table 1.

Table 1. Assessments of physical function & mobility, nutrition, anxiety/depression, and health-related quality of life

Domain	Measure	Details	When Collected
Screening Measures			
Medical History		A chart review will be conducted for every potential participant to assess eligibility (see criteria above) and to document surgery type.	Baseline (T1)

[1] The HGS test will only be administered when the assessment is conducted in person

Cognition		Participants must have a score of ≥20 (< high school education) or ≥21 (high school or more) on the MoCA or a score of ≥21 on the SLUMS test and able to do ADLs to qualify for participation in this study.[41]	T1
Outcome Measures			
Demographics		Standard demographic information will be gathered via self-report and physical examination at baseline to describe the study sample.	T1
Physical Function & Mobility	5RSTS	The five repetition sit-to-stand test (5RSTS) is widely used as an indicator of lower limb strength among older adults.[31] The test is easy to administer and has good to high test-retest reliability.[42] In a meta-analysis conducted to generate normative values for this test, patients older than 60 years of age exceeding 11.4 sec were considered to have worse than average performance.[31]	T1, T2, T3, T4
	TMST	The two-minute step test (TMST) requires that individuals march in place as fast as possible for 2 minutes while lifting the knees to a height midway between their patella and iliac crest when standing. The performance on the test is defined as the number of right-side steps of the criterion height completed in 2 minutes.[35]	T1, T2, T3, T4
	HGS	Handgrip strength can be quantified by measuring the amount of static force that the hand can squeeze around a dynamometer. Low handgrip strength is a clinical marker of poor mobility and a better predictor of clinical outcomes than low muscle mass. Grip strength may also be used as a reliable surrogate for more complicated measures of muscle strength in the lower arms or legs.	T1, T2, T3, T4
Nutrition	Anthropo-metrics	Anthropometric measurements, including body mass index (BMI, weight in kilograms over the square of height in meters), mid-upper arm circumference, upper thigh circumference, waist circumference, hip circumference, and waist-to-hip ratio.	T1, T2, T3, T4
	PG-SGA	The PG-SGA includes assessments of weight, food intake, and nutrition impact symptoms.[43] The PG-SGA provides a global rating nutritional diagnosis (A, B, or C) and a continuous numerical score (1 to 30) for intervention triage. The Subjective Global Assessment (SGA), included in the PG-SGA, has also been applied and validated in predicting length of stay, postoperative complications, and mortality.[44]	T1, T2, T3, T4
	24-hour recall	Under the guidance of the Registered Dietitian Nutritionist, the study Physiologist will administer 24-hour dietary recalls once a week to assess compliance. This will be done using the USDA 5-step Multiple Pass Method (Conway et al 2003) to capture detailed information about all foods and beverages consumed by the participant in the past 24 hours. The USDA multiple-pass method for dietary recall consists of five steps: (a) the quick list, which is an uninterrupted listing by the subject of foods and beverages consumed; (b) the forgotten foods list, which queries the subject on categories of foods that have been documented as frequently forgotten; (c) a time and occasion at which foods were consumed; (d) the detail cycle, which elicits descriptions of foods and amounts eaten aided by the interactive use of the USDA	Weekly phone calls

		Food Model Booklet and measuring guides; and finally (e) the final probe review. The USDA Food Model Booklet (9) was used to assist in portion-size estimation of consumed foods. It has eight sections: (a) the forgotten foods list, (b) glasses and mugs, (c) bowls, (d) mounds, (e) circles, (f) grid and thickness blocks, (g) wedges, and (h) shapes and chicken pieces.	
Health-related Quality of Life	SF-36	The 36-Item Short-Form Health Survey (SF-36) contains 36 items that are scored as 8 multi-item scales, namely vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, and mental health.[45]	T1, T4, T5
Anxiety and Depression	HADS	Hospital Anxiety and Depression Scale (HADS) is a questionnaire involving statements relevant to generalized anxiety and depression.[46] Each item is answered on a four-point (0–3) response category, and the possible scores range from 0 to 21 for anxiety and 0 to 21 for depression.	T1, T2, T3, T4, T5

9.0 Adverse Events

Because the intervention closely resembles daily activities and is so closely monitored, we expect a low rate of adverse events. All adverse events will be reported per Durham VAMC requirements. All Serious, Unanticipated and Related Adverse Events will be reported to IRB within five business days of a member of the study team learning of the event. All other adverse events will be reported at the time of continuing review. Should any incident such as theft or loss of data, unauthorized access of sensitive data, or non-compliance with security controls occur, it will be immediately reported according to VA policy. All incidents regarding information security/privacy incidents will be reported to the ISO and PO within one hour of report.

10.0 Costs and/or Payments to Subjects

Participants will be reimbursed $50 for each in-person clinic visit they make for purposes of study procedures (range $100-$200). The initial preoperative visit and the 6-week postoperative visit for all participants with an optional second preop visit immediately prior to surgery if the T2 assessment cannot be performed on the day of surgery and at T5 if the assessments cannot be performed over the telephone.

11.0 Data and Safety Monitoring

Hardcopy documents, including those containing PHI, will be stored in folders and binders and kept inside a locked cabinet in the Anesthesia Research Office (C3011A), and are accessible to research personnel only. Electronic data will be stored on secure VA servers accessible only to study personnel [S:\Anesthesia Research\Atilio Barbeito\PREVENT\Data]. Study data will be reviewed as patients are enrolled and any member of the study team may review source documents or data at any time. Protocol deviations, data discrepancies, errors, or missing information will be resolved and/or reported per DVAHCS and IRB policy.

12.0 Withdrawal of Participants

Participants will be withdrawn from the study if any of the following occur:

- Withdrawal of study consent
- Inability to continue with the exercise or nutritional support program for any reason
- At the Principal Investigator's discretion

If a participant is withdrawn, follow-up for the purposes of research is not anticipated. The subject will continue to see their respective health care providers during scheduled clinic visits.

13.0 Data Analysis and Statistical Considerations

Feasibility will be assessed by calculating the acceptance rate, measured as the number of patients enrolled divided by the number eligible. In addition, we will evaluate veterans' reasons for enrollment or non-enrollment in the program using patient interviews and semi-structured questionnaire (see Appendix 4). No PHI will be recorded in questionnaires obtained from eligible but non-recruited veterans.

Acceptability will be measured by rate of compliance with the exercise/nutrition programs. For the exercise intervention, the percentage of patients completing ≥75% of sessions divided by the number of enrolled patients will be calculated. For the nutritional intervention, compliance will be measured by the percentage of patients with ≥75% adherence to protein intake goal, as assessed using the text message-based nutrition diary, lids returned, and 24-hour recall administered during the weekly telephone call.

Safety will be evaluated by the number of adverse events (significant injury or medical event) during exercise. A significant injury or medical event is defined as an event that causes the participant to seek attention from a health professional or limits their activities of daily living for at least two days.

Effect size will be estimated by comparing physical function before and after the prehabilitation intervention, as measured by the 5RSTS and the 2-minute step tests using Cohen's D. Changes in health-related quality of life (SF-36) and anxiety and depression (HADS) before surgery and at the 6-week and 24-week study periods following surgery will be calculated.

14.0 Privacy, Confidentiality, and Information Security

14.1 Lists of Data Reviewed and/or Collected for Screening/Recruitment and Conduction of Study:

The Personal Health Information that will be obtained, used, and/or shared for this study includes:

Identifier(s)	Source(s) of Health Information
☒ Names	☒ Medical history & physical exam information

Identifier(s)	Source(s) of Health Information
☒ All geographic subdivisions smaller than a State, including street address, city, county, precinct, and zip code. Describe: street address, city, state, zip code for mailing participant payments	☐ Photographs, videotapes, audiotapes, or digital or other images
☒ All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, visit or treatment dates, etc.; and all ages over 89, Describe: *Date of preop evaluation/POSH appt.; dates of postop appointments; date of surgery; dates of laboratory test results; date of birth*	☐ Biologic specimens (e.g., blood, tissue, urine, saliva). Describe:
☒ Telephone numbers	☒ Progress notes
☐ Fax numbers	☒ Diagnostic / Laboratory test results
☒ Electronic mail addresses	☒ Operative reports
☒ Social Security Numbers	☐ Imaging (x-ray, CT, MRI, etc.)
☒ Medical record numbers	☒ Discharge summaries
☐ Health plan beneficiary numbers	☒ Survey / Questionnaire responses
☐ Account numbers	☒ Billing records
☐ Certificate and/or license numbers	☐ HIV testing or infection records
☐ Vehicle identifiers and serial numbers, including license plate numbers	☐ Sickle cell anemia information
☐ Device identifiers and serial numbers	☐ Alcoholism or alcohol use information
☐ Web Universal Resource Locators (URLs)	☐ Drug abuse information
☐ Internet Protocol (IP) address numbers	☐ Mental health (not psychotherapy) notes
☐ Biometric identifiers, including finger & voice prints	☐ Psychological test results
☐ Full-face photographic images and any comparable images	☐ Genetic testing
☒ Any other unique identifying number, characteristic, or code, describe: Patient address including latitude/longitude and rural/suburban/urban designation. **Note: This is not the unique code assigned to otherwise de-identified health information for re-identification purposes.*	☐ Other, describe:

All non-Veterans enrolled in this study will receive the VA Notice of Privacy Practices (NOPP) and are requested to sign the acknowledgment form. The signed acknowledgment form will be maintained with the research records.

14.2 Data and/or Specimen Acquisition:

Data for this study will be collected through (*check all that apply*):

☒ Prospective data and/or specimen collection obtained from participants. Provide description of processes: Assessments of physical function, mobility, nutrition,

anxiety/depression, and health-related quality of life will be collected. Data from the medical record will also be accessed and used.

iPad devices will be issued to relevant participants and become their property. There will be no research data stored on these devices – they are used solely for communicating with study team members regarding appointments and food diaries, as well as participating in exercise sessions.

☐ Retrospective data collection and/or specimens obtained from medical chart review/data access. Describe how data will be obtained (e.g., fileman, CDW, etc.):
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☐ Retrospective data collection and/or specimens obtained from an IRB-approved data and/or specimen repository. Indicate the repository source including name, VA location, and IRB number: .

Note: for data and/or specimens obtained from a VA approved data repository, a Data Use Agreement (DUA) must be executed prior to obtaining data and/or specimens. See VHA Handbook 1200.12 for further information.

14.3 Level of Data:

The following level(s) of data will be acquired/maintained for this study (*check all that apply*):

☒ Identifiable—Data contains direct identifiers.
☒ Coded—Data linked to a specific by a code rather than a direct identifier for re-identification purposes. Only someone possessing the key to the code can link the data to a particular participant.
☐ De-Identified (all 18 HIPAA identifiers removed
- ☐ Verified Statistically
  OR
- ☐ Verified by Absence or Removal of 18 HIPAA identifiers

☐ Limited Data Set
☐ Other: Describe:

14.4 Location of Data and/or Specimens, and Data Retention Plan

14.4.1 Data and/or Specimen Location

Hardcopy documents, including surveys, ICFs and HIPAA Forms, will be stored in folders and binders and kept inside a locked cabinet in our Anesthesia Research Office (C3011A).

Data will be stored electronically on secure VA servers accessible only to study personnel through VA workstations—file path S:\Anesthesia Research\Atilio Barbeito\PREVENT\Data. Data that will be stored electronically include screening and enrollment logs, adverse events log, and data sets related to functional and nutritional assessments.

There will be no research-related data stored on the iPad tablet devices.

Paper records of data include ICFs, HIPAA Forms, and assessments on function and nutrition and will be stored inside locked cabinets in our research office.

Specimens will not be collected for this research project.

☐ Data will be also be placed at the VA Informatics and Computing Interface (VINCI; http://vaww.vinci.med.va.gov/vincicentral/VINCIWorkspace.aspx). The VA Informatics and Computing Infrastructure is a partnership between the VA Office of Information Technology and the Veterans' Health Administration Office of Research and Development. Researchers and operations staff can use VINCI to access data and statistical analysis tools in a virtual working environment through a certified VHA network computer using the VA Intranet or Virtual Private Network (VPN).

14.4.2 Data Retention Plan

☒ Research records will be maintained and destroyed according to the National Archives and Records Administration, Records Schedule Number: DAA-0015-2015-0004. Records destruction, when authorized, will be accomplished using the then current requirements for the secure disposal of paper and electronic records. Currently, destruction of research records (see DAA-0015-2015-0004, section 7.6 "Research Investigator Files" for materials included in research records) is scheduled for 6 years after the cut-off (the cut-off is the completion of the research project) and may be retained longer if required by other federal agencies. Records will not be destroyed without pre-notification to the facility records manager.

☐ Other data retention plan, describe:

14.4.3 Data Access and Data Recipients

Only members of our DVAMC research team will have access to identifiers and coded data. Coded data with direct identifiers removed (i.e., name, address, telephone numbers, SSN, DOB) will be placed on secure VA servers accessible only to study personnel through VA workstations. Hardcopy documents, kept inside a locked cabinet in our Anesthesia Research Office (C3011A), will be accessible to research personnel only.

All VA research personnel who have access to VHA records are instructed, in accordance with VA policy, on the requirements of Federal privacy and information laws and regulations, VA regulations and policies, and VHA policy. All study personnel who are VA employees working within the VA system have fulfilled all required HIPAA and other VA security and privacy policy training requirements and have agreed to follow guidelines pertaining to the protection of patient data. All research staff sign VA Rules of Behavior, and all study staff are up to date with VHA Privacy Policy Training and the VA Office of Cyber and Information Security Awareness Training Course. The data security and privacy procedures summarized in that course include logging off or locking the computer when walking away from it; no sharing of access codes, verify codes or passwords; not allowing anyone else to use the computer under one's password; and disposing of sensitive information using VA-approved methods (e.g., shredder bins).

Access to study data will be removed for all study personnel when they are no longer part of the research team.

14.5 Data and/or Specimen Transportation and/or Transmission for all data and/or specimens involved in the study

☒ Data and/or specimens will not be transported or transmitted outside of Durham VAMC environment.

☐ Data and/or specimens will be transported BETWEEN sites that are under the auspices of the Durham VA Medical Center.

☐ Data and/or specimens will be transmitted to other VA sites using the following method(s):

☐ Data and/or specimens will be transported to non-VA/VHA sites (e.g., academic affiliates, laboratories, etc.) using the following method(s):

A. Data

☐ Data are de-identified and thus will be sent via unencrypted e-mail or unencrypted CD.

☐ Data are coded or-contain identifiers and thus will be sent via <choose method of transfer such as FIPS 140-2 encrypted CD or FIPS 140-2 encrypted hard drive/flash drive> using VA—approved carrier with tracking.

☐ Data are coded or identified and will be sent via the Safe Access File Exchange (SAFE) at https://safe.amrdec.army.mil/safe/. SAFE is a secure method of exchanging files <2GB to and from individuals with a valid .gov, .mil, .com, or .edu email address. <insert information including collaborator name.>

☐ Data are coded or identified and will be uploaded to sponsor website using electronic case report form (eCRF) <insert information including sponsor name and URL and the encryption the site uses.>

☐ Other, describe:

B. Specimens

☐ Specimens are de-identified and thus will be sent via standard carrier (tracking is optional) or will be hand-delivered by research study personnel. Specify method of delivery:

☐ Specimens are coded and thus will be sent via VA-approved carrier with tracking or will be hand-delivered by research study personnel. Specify method of delivery:

In accordance with the HIPAA and the Privacy Act, for any coded or identifiable data or specimens released from the Durham VAMC (with the exception of Limited Data Sets), an Accounting of Disclosure (AOD) will be maintained (e.g., in a database or spreadsheet) that includes the participant's name, date of the disclosure, description of the nature of the Individually Identifiable Information (III) disclosed, purpose of each disclosure, and the name and address of the person/agency to whom the disclosure was made.

C. ☐ Local DVAMC memorandum "Authorization to Use, Process, Store, or Transmit VA Sensitive Information Outside VA Owned or Managed Facilities" has been pre-filled out for each study team member who may transport the data and/or specimens off-site. This (these) forms are included with the IRB materials.

D. ☐ Containers (e.g., briefcase, bin) are labeled with the following notice (label placed on the outside of container) in accordance with VHA Directive 6609:
NOTICE!!!

Access to these records is limited to: AUTHORIZED PERSONS ONLY.
Information may not be disclosed from this file unless permitted by all applicable legal authorities, which may include the Privacy Act; 38 U.S.C. §§ 5701, 5705, 7332; the Health Insurance Portability and Accountability Act; and regulations implementing those provisions, at 38 C.F.R. §§ 1.460 – 1.599 and 45 C.F.R. Parts 160 and 164. Anyone who discloses information in violation of the above provisions may subject to civil and criminal penalties.

☐ We will communicate with veterans enrolled as participants in this research study through MyHealtheVet.

14.7 Risk Mitigation Strategies

All VA research personnel who have access to VHA records are instructed, in accordance with VA policy, on the requirements of Federal privacy and information laws and regulations, VA regulations and policies, and VHA policy. All study personnel who are VA employees working within the VA system have fulfilled all required HIPAA and other VA security and privacy policy training requirements and have agreed to follow guidelines pertaining to the protection of patient data. All research staff sign VA Rules of Behavior, and all study staff are up to date with VHA Privacy Policy Training and the VA Office of Cyber and Information Security Awareness Training Course. The data security and privacy procedures summarized in that course include logging off or locking the computer when walking away from it; no sharing of access codes, verify codes or passwords; not allowing anyone else to use the computer under one's password; and disposing of sensitive information using VA-approved methods (e.g., shredder bins). Access to study data will be removed for all study personnel when they are no longer part of the research team.

☐ Data are fully de-identified (stripped of HIPAA 18 and study ID/code) before being shared outside of Durham VAMC.

☐ Specimens are fully de-identified (stripped of HIPAA 18 and study ID/code before being shared outside of Durham VAMC.

☒ Data or specimens are coded, and the code is not related to, or derived from, information about the individual and that code is not otherwise capable of being translated as to the identify the individual. Only someone possessing the key to code can link the data to a particular participant.

☐ Other, specify:

14.8 Suspected Loss of VA Information

Should any incident such as theft or loss of data, unauthorized access of sensitive data or non-compliance with security controls occur it will be immediately reported according to VA policy. All incidents regarding information security/privacy incidents will be reported to the ISO and PO within 1 hour of acknowledgement of issue and done so using the VHADUR Research Events Report e-mail group (VHADURResearchEventReport@va.gov).

14.9 Reporting of Results

☒ Reporting of results, such as in scientific papers and presentations, will never identify individual subjects. Data will be presented in aggregate and individual-level data will not be published.

☐ Other results reporting plan, describe:

14.10 Future Use of Data

☐ Data will be retained for future use. This is described elsewhere in the protocol and is noted in the HIPAA authorization.

☐ Future Use of data is optional (i.e., not required by the research subject).

☐ Future Use of data is required for participation in the study.

☒ No future use of data is currently planned.

14.11 Use of Mail Merge Technology

☐ Mail merge programs will be used to generate letters and/or address labels for mailings to potential or already enrolled research subjects. The study team is aware that to reduce risk of mail merge related privacy incidents, use of mail merge programs requires a 25% accuracy check to verify that (potential) research subject name and mailing address are properly "matched". If discrepancies are found, a 100% accuracy check is required before letters may be mailed.

14.12 Use of Non-Standard Software

☐ I do NOT intend to use any new specialized software (i.e. Software that's not already approved OR installed) in this study.

☒ I intend to use specialized software that has not already been installed and it has been approved for use by the VA Technical Reference Model (TRM) Group.
(Note: All new software must be approved by TRM before it can be installed on VA systems.)
☒ I intend to use previously installed software on my VA computer.

14.13 Use of Cloud Computing Services

☒ Cloud computing services will NOT be used in this study.

☐ Cloud computing services WILL be used in this study as described below and have been approved nationally by the VA Chief Information Officer (CIO). (Note: ONLY cloud computing services that have been approved nationally may be used.)

15.0 References

1. Massarweh NN, Legner VJ, Symons RG, McCormick WC, Flum DR. Impact of advancing age on abdominal surgical outcomes. *Arch Surg*. 2009;144(12):1108-1114.

2. Balentine CJ, Naik AD, Berger DH, Chen H, Anaya DA, Kennedy GD. Postacute Care After Major Abdominal Surgery in Elderly Patients: Intersection of Age, Functional Status, and Postoperative Complications. *JAMA Surg*. 2016;151(8):759-766.

3. Older P, Hall A, Hader R. Cardiopulmonary exercise testing as a screening test for perioperative management of major surgery in the elderly. *Chest*. 1999;116(2):355-362.

4. Moran J, Wilson F, Guinan E, McCormick P, Hussey J, Moriarty J. Role of cardiopulmonary exercise testing as a risk-assessment method in patients undergoing intra-abdominal surgery: a systematic review. *Br J Anaesth*. 2016;116(2):177-191.

5. Smith TB, Stonell C, Purkayastha S, Paraskevas P. Cardiopulmonary exercise testing as a risk assessment method in non cardio-pulmonary surgery: a systematic review. *Anaesthesia*. 2009;64(8):883-893.

6. Lai CW, Minto G, Challand CP, et al. Patients' inability to perform a preoperative cardiopulmonary exercise test or demonstrate an anaerobic threshold is associated with inferior outcomes after major colorectal surgery. *Br J Anaesth*. 2013;111(4):607-611.

7. Kaibori M, Ishizaki M, Matsui K, et al. Assessment of preoperative exercise capacity in hepatocellular carcinoma patients with chronic liver injury undergoing hepatectomy. *BMC Gastroenterol*. 2013;13:119.

8. Robinson TN, Wallace JI, Wu DS, et al. Accumulated frailty characteristics predict postoperative discharge institutionalization in the geriatric patient. *J Am Coll Surg*. 2011;213(1):37-42; discussion 42-34.

9. Carli F, Zavorsky GS. Optimizing functional exercise capacity in the elderly surgical population. *Curr Opin Clin Nutr Metab Care*. 2005;8(1):23-32.

10. West MA, Wischmeyer PE, Grocott MPW. Prehabilitation and Nutritional Support to Improve Perioperative Outcomes. *Curr Anesthesiol Rep*. 2017;7(4):340-349.

11. Wilkinson SB, Phillips SM, Atherton PJ, et al. Differential effects of resistance and endurance exercise in the fed state on signalling molecule phosphorylation and protein synthesis in human muscle. *J Physiol*. 2008;586(15):3701-3717.

12. Barberan-Garcia A, Ubre M, Roca J, et al. Personalised Prehabilitation in High-risk Patients Undergoing Elective Major Abdominal Surgery: A Randomized Blinded Controlled Trial. *Ann Surg*. 2018;267(1):50-56.

13. Kim DJ, Mayo NE, Carli F, Montgomery DL, Zavorsky GS. Responsive measures to prehabilitation in patients undergoing bowel resection surgery. *Tohoku J Exp Med*. 2009;217(2):109-115.

14. Biolo G, Tipton KD, Klein S, Wolfe RR. An abundant supply of amino acids enhances the metabolic effect of exercise on muscle protein. *Am J Physiol*. 1997;273(1 Pt 1):E122-129.

15. Glover EI, Oates BR, Tang JE, Moore DR, Tarnopolsky MA, Phillips SM. Resistance exercise decreases eIF2Bepsilon phosphorylation and potentiates the feeding-induced stimulation of p70S6K1 and rpS6 in young men. *Am J Physiol Regul Integr Comp Physiol*. 2008;295(2):R604-610.

16. Phillips SM, Tipton KD, Aarsland A, Wolf SE, Wolfe RR. Mixed muscle protein synthesis and breakdown after resistance exercise in humans. *Am J Physiol*. 1997;273(1 Pt 1):E99-107.

17. Tipton KD, Ferrando AA, Phillips SM, Doyle D, Jr., Wolfe RR. Postexercise net protein synthesis in human muscle from orally administered amino acids. *Am J Physiol*. 1999;276(4):E628-634.

18. Wolfe RR. The underappreciated role of muscle in health and disease. *Am J Clin Nutr*. 2006;84(3):475-482.

19. Carli F, Charlebois P, Stein B, et al. Randomized clinical trial of prehabilitation in colorectal surgery. *Br J Surg*. 2010;97(8):1187-1197.

20. Dronkers JJ, Lamberts H, Reutelingsperger IM, et al. Preoperative therapeutic programme for elderly patients scheduled for elective abdominal oncological surgery: a randomized controlled pilot study. *Clin Rehabil*. 2010;24(7):614-622.

21. Gillis C, Li C, Lee L, et al. Prehabilitation versus rehabilitation: a randomized control trial in patients undergoing colorectal resection for cancer. *Anesthesiology*. 2014;121(5):937-947.

22. West MA, Loughney L, Lythgoe D, et al. Effect of prehabilitation on objectively measured physical fitness after neoadjuvant treatment in preoperative rectal cancer patients: a blinded interventional pilot study. *Br J Anaesth*. 2015;114(2):244-251.

23. Valencia WM, Botros D, Pendlebury D, et al. Proactive reach and telehealth monitoring (Gerofit) enhance resistance exercise at rural setting. *Innovat Aging*. 2017;1:225.

24. McDonald SR, Heflin MT, Whitson HE, et al. Association of Integrated Care Coordination With Postsurgical Outcomes in High-Risk Older Adults: The Perioperative Optimization of Senior Health (POSH) Initiative. *JAMA Surg*. 2018;153(5):454-462.

25. Morey MC, Crowley GM, Robbins MS, Cowper PA, Sullivan RJ, Jr. The Gerofit Program: a VA innovation. *South Med J*. 1994;87(5):S83-87.

26. Morey MC, Lee CC, Castle S, et al. Should Structured Exercise Be Promoted As a Model of Care? Dissemination of the Department of Veterans Affairs Gerofit Program. *J Am Geriatr Soc*. 2018;66(5):1009-1016.

27. Morey MC, Pieper CF, Crowley GM, Sullivan RJ, Puglisi CM. Exercise adherence and 10-year mortality in chronically ill older adults. *J Am Geriatr Soc*. 2002;50(12):1929-1933.

28. McDonald SR, Porter Starr KN, Mauceri L, et al. Meal-based enhancement of protein quality and quantity during weight loss in obese older adults with mobility limitations: Rationale and design for the MEASUR-UP trial. *Contemp Clin Trials*. 2015;40:112-123.

29. Porter Starr KN, Pierper CR, Orenduff M, et al. Improved function with enhanced protein intake per meal: A pilot study of weight reduction in frail, obese older adults. *J Gerontol A Biol Sci Med Sci*. 2016;71(10):1369-1375.

30. Morey MC, Manning KM, Guo Y, et al. Physical Activity Trackers: Promising Tools to Promote Resilience in Older Surgical Patients. *J Surg (Lisle)*. 2018;9(12).

31. Bohannon RW. Reference values for the five-repetition sit-to-stand test: a descriptive meta-analysis of data from elders. *Percept Mot Skills*. 2006;103(1):215-222.

32. Pahor M, Guralnik JM, Ambrosius WT, et al. Effect of structured physical activity on prevention of major mobility disability in older adults: the LIFE study randomized clinical trial. *JAMA*. 2014;311(23):2387-2396.

33. Guralnik JM, Ferrucci L, Pieper CF, et al. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. *J Gerontol A Biol Sci Med Sci*. 2000;55(4):M221-231.

34. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol*. 1994;49(2):M85-94.

35. Rikli RE, Jones CJ. Development and validation of criterion-referenced clinically relevant fitness standards for maintaining physical independence in later years. *Gerontologist*. 2013;53(2):255-267.

36. 2018 Physical Activity Guidelines Advisory Committee Scientific Report. 2018; https://health.gov/paguidelines/second-edition/report/pdf/PAG_Advisory_Committee_Report.pdf.

37. Lee PG, Jackson EA, Richardson CR. Exercise Prescriptions in Older Adults. *Am Fam Physician*. 2017;95(7):425-432.

38. Waite I, Deshpande R, Baghai M, Massey T, Wendler O, Greenwood S. Home-based preoperative rehabilitation (prehab) to improve physical function and reduce hospital length of stay for frail patients undergoing coronary artery bypass graft and valve surgery. *J Cardiothorac Surg*. 2017;12(1):91.

39. Andrassy KM. Comments on 'KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease'. *Kidney Int*. 2013;84(3):622-623.

40. Weimann A, Braga M, Carli F, et al. ESPEN guideline: Clinical nutrition in surgery. *Clin Nutr*. 201 7;36(3):623-650.

41. Tariq SH, Tumosa N, Chibnall JT, Perry Iii MH, Morley JE. Comparison of the Saint Louis University Mental Status Examination and the Mini-Mental State Examination for Detecting

Dementia and Mild Neurocognitive Disorder—A Pilot Study. *The American Journal of Geriatric Psychiatry*. 2006;14(11):900-910.

42. Bohannon RW. Test-retest reliability of the five-repetition sit-to-stand test: a systematic review of the literature involving adults. *J Strength Cond Res*. 2011;25(11):3205-3207.

43. Bauer J, Capra S, Ferguson M. Use of the scored Patient-Generated Subjective Global Assessment (PG-SGA) as a nutrition assessment tool in patients with cancer. *Eur J Clin Nutr*. 2002;56(8):779-785.

44. Mueller C, Compher C, Ellen DM. A.S.P.E.N. clinical guidelines: Nutrition screening, assessment, and intervention in adults. *JPEN Journal of parenteral and enteral nutrition*. 2011;35(1):16-24.

45. Jenkinson C, Coulter A, Wright L. Short form 36 (SF36) health survey questionnaire: normative data for adults of working age. *BMJ*. 1993;306(6890):1437-1440.

46. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983;67(6):361-370.

Appendix 1. Expedited Review of Research

The categories of research that may be reviewed by the IRB through the expedited review procedure include research activities that present no more than minimal risk to human subjects **AND** involve procedures listed in one or more of the specific categories listed below.

The expedited review procedure is not to be used when identification of the subjects or their responses would reasonably place them at risk of criminal or civil liability; be damaging to the subjects' financial standing, employability, insurability, or reputation; or be stigmatizing, unless reasonable and appropriate protections are implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal. The IRB must apply the standard requirements for informed consent (or its waiver, alteration, or exception) to all studies that undergo expedited review.

EXPEDITE CATEGORIES
1-Drugs and Devices: One of the following must be met: (1) The research is on drugs for which an IND application is not required. (2) The research is on medical devices for which an investigational device exemption (IDE) application is not required; or the medical device is cleared or approved for marketing, and the medical device is being used in accordance with its cleared or approved labeling.
2-Blood Samples: Collected by finger / heel / ear stick or venipuncture: (1) From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 milliliters (ml) in an 8-week period, and collection may not occur more frequently than two times per week; or (2) From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kilogram (kg) in an 8-week period, and collection may not occur more frequently than two times per week.
3-Noninvasive Collection of Biological Specimens: Collected prospectively for research purposes by noninvasive means: (1) Hair and nail clippings in a non-disfiguring manner. (2) Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction. (3) Permanent teeth if routine patient care indicates a need for extraction. (4) Excreta and external secretions (including sweat). (5) Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue. (6) Placenta removed at delivery. (7) Amniotic fluid obtained at the time of rupture of the membrane prior to, or during, labor. (8) Supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques. (9) Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings. (10) Sputum collected after saline mist nebulization.
4-Noninvasive Collection of Data: Data must be collected through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves.

EXPEDITE CATEGORIES
(1) Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy. (2) Weighing the subject. (3) Testing sensory acuity. (4) Magnetic resonance imaging (MRI). (5) Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography. (6) Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing, where appropriate, given the age, weight, and health of the individual.
5-Collected Material: Research involves: (1) Materials (data, documents, records, or specimens) that have been collected for any purpose, including previous research; or (2) Materials (data, documents, records, or specimens) that will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).
6-Collection of Data From Voice, Video, or Photographs: Research involves collection of data from voice, video, or photographs.
7-Group Characteristics, Surveys, Interviews, and Quality Assurance: Research must be on individual or group characteristics or behavior (including, but not limited to: research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior), or will employ survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. ***NOTE**: Some research in this category may be exempt from the VA regulations for the protection of human subjects (38 CFR 16.101(b)(2) and (b)(3)). This listing refers only to research that is not exempt.*

Appendix 2. Progressive Functional Exercise Routine for Home-Based Prehabilitation

General Principles

Home-based exercise requires adaptations for the lack of equipment typically available in facility-based programs and for widely varying functional states of program participants. Building on known evidence-based progressive programs such as the Otago program and substantial work developed by our Gerofit team, we deploy a continuous cardio and strength circuit training program using increased cadence, body weight, and resistive bands to increase intensity of effort. The program follows recommended guidelines for older adults, with four levels of intensity based on the baseline functional status of participants, as described in the tables below.

The exercise intervention of this multimodal prehabilitation program will consist of *moderate intensity* cardio and strength training exercises performed in succession to warrant continuous cardiovascular benefit. The number of rounds of aerobic and functional exercises will be progressed as fitness improves, with an entire sequence being completed in 30 minutes (Table 1). The RPE will be assessed after each round to help patients keep intensity within moderate levels. Exercise sessions will also include 5-minute warm up and cool down sections at light intensity (RPE 2-3) to ensure safety and recovery of all participants.

As patients progress, up to 4-6 rounds of aerobic circuits (Table 2) and 2-3 rounds of functional resistance exercises (Table 3) may be completed. Given the limited timeline of prehabilitation, participants will be encouraged to increase at least one or more levels where possible at each session. In addition to the supervised exercise sessions, Veterans be asked to monitor and increase daily step counts, allowing for one day of rest each week.

Table 1. General Structure of the Exercise Program

	Duration	Intensity
Warm-up	5 min	2-3 RPE
Aerobic and Resistance Exercise Circuit	30 min[2]	Aerobic: 4-6 RPE Resistance: 6-7 RPE
Cool down	5 min	

[2] The duration of the circuit will be progressed towards the 30 minute goal

Table 2. Aerobic Exercise Circuit

One circuit of aerobic exercises features 30 seconds per exercise, for a total of aprox. 5 minutes. All exercises are adapted for different levels of ability. Exertion will be assessed after each circuit level and adjusted to keep intensity within the moderate range (RPE 4-6).

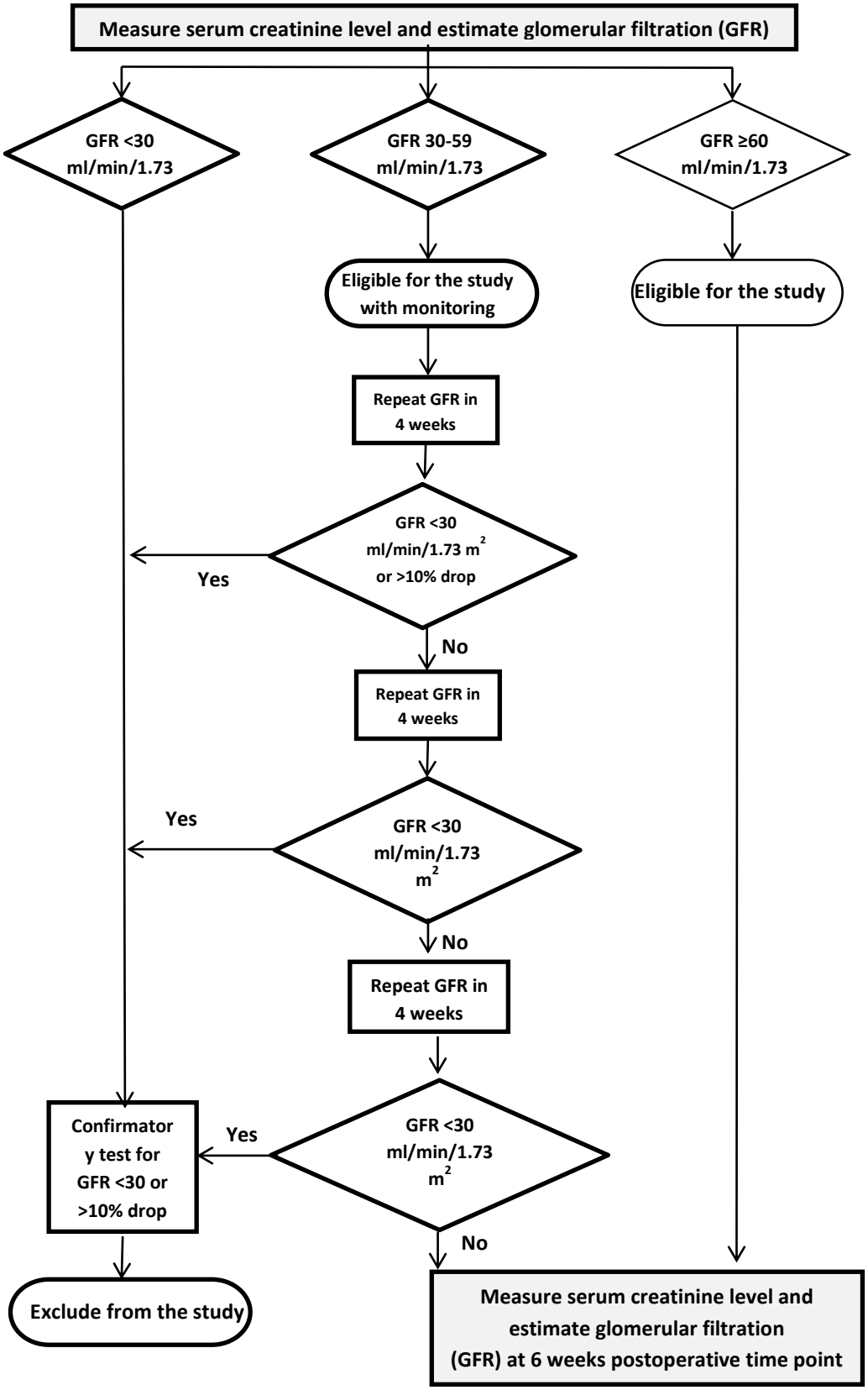
Aerobic Exercise Circuit	**Level 1** **Most Deconditioned**	**Level 2**	**Level 3**	**Level 4** **Least Deconditioned**
Marching	Seated	1 arm support	Unsupported	Higher step march
Forward/ Backward March	Seated	1 arm support	Unsupported	Unsupported increased speed
March w/ arm swing	Seated	1 arm support	Unsupported	Higher swings/speed to sustain RPE
Step both feet out, step in	Seated	1 arm support	Unsupported	Wider step
Single leg toe taps (R)	Seated	Standing two arm support	Standing two arm support	Standing two arm support
Single leg toe taps (L)	Seated	w/ toe tap to shoulder width	w/ toe tap wider than shoulder	w/ wide step with increased speed
Step Jacks	Seated	Standing w/ 1 hand support	Standing no support	Standing increased speed to sustain RPE
Mini-Squat and cross punch	Seated	Standing w/ 1 hand support	Standing no support	Standing increased speed to sustain RPE
Walking with hand claps	Seated	Standing arm claps only	Standing arm claps + stepping	Standing arm claps + stepping increased speed
Heel Taps	Seated	Standing 1 arm support	Standing unsupported	Standing increased speed to sustain RPE

Table 3. Functional Resistance Training Exercises

One set of functional resistance training exercises will be performed following two rounds of aerobic circuits. Between 8 and 12 repetitions of the training exercises will be performed as indicated and tolerated by the patient. Exertion will be measured following one set of the strength exercises to best determine resistance and intensity levels, with the goal RPE being 6-7.

Functional Exercise Circuit	**Level 1** **Most Deconditioned**	**Level 2**	**Level 3**	**Level 4** **Least Deconditioned**
Chair stands	Use Arms	Arms in front	Arms across chest	Arms across chest
Mid back row	Yellow	Red	Green	Blue
Hip Abduction	Seated w/ band	Standing straight leg arm supported, no band	Lateral band walk Yellow/Red	Lateral band walk Green/Blue
Hip Extension	Standing straight leg	Standing straight leg	Standing bent knee ext.	Standing bent knee ext.
Bicep Curls	Seated, yellow	Standing yellow/red	Standing red/green	Standing green/blue
Abdominal hold	Seated, bent knee off floor	Seated straight leg off floor	Seated straight leg off floor, arms overhead	Seated straight leg off floor, Arms overhead
Chest Press	Yellow	Red	Green	Blue
Tricep Dips	Dip w/knees bent feet flat	Dip w/ knees bent feet flat	Dip with legs extended	Dip with legs extended

Appendix 3. Patient Eligibility and Monitoring Based on Kidney Function



Appendix 4. PREVENT Acceptance/ Non-acceptance Questionnaire

1. Are you willing to enroll in this exercise and nutrition program?
    a. Yes
    b. No

    If **YES**, then please answer questions 2 and 3. If **NO**, then answer question 4.

2. If **YES**, what are you seeking to accomplish with this program?
    a. I want to improve my overall fitness and/or nutrition in general, and this is a great opportunity to do it
    b. I want to do well in surgery
    c. Other

3. If **YES**, which ONE element is MOST attractive to you about this program?
    a. The physical exercise routine
    b. The nutritional support component
    c. The phycological support and close monitoring I will receive
    d. Other

4. In **NO**, what is the MAIN reason for not enrolling in this program?
    a. I don't think I have the physical energy to participate in this program
    b. I don't like or want to take any nutritional supplements
    c. I don't want to receive text messages
    d. I don't want to wear an activity tracker
    e. I am not in the mood to participate in this program
    f. I don't have internet access at home
    g. I am not comfortable with technology
    h. Other

Appendix 5: For dropouts:

1. Why did you stop participating in this program?
    a. I don't see the utility of this
    b. The exercise routine is too hard
    c. The exercise routine is boring
    d. I don't like the trainer
    e. I don't like the nutritional supplements
    f. I don't like the text messages and/or phone calls
    g. I can't figure out how to use the device
    h. I don't have the time
    i. Other

2. How many sessions did you participate in?

Appendix 6: USDA 5-Step Multiple Pass Method**

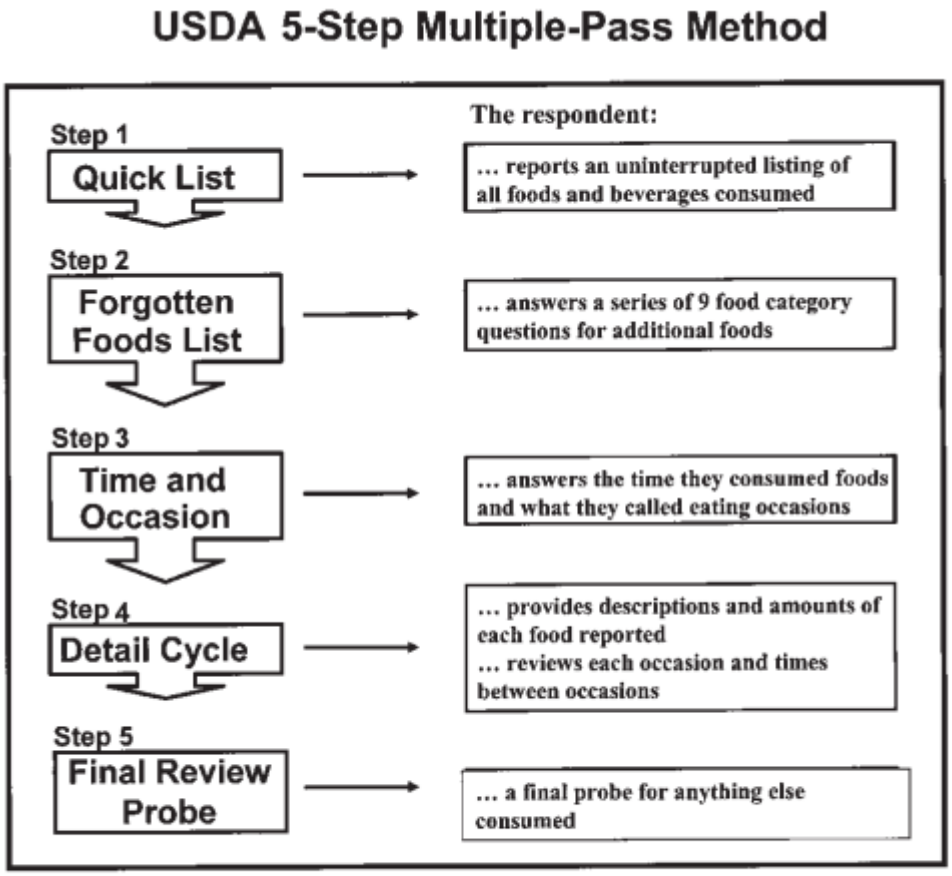


FIGURE 1. Outline of the US Department of Agriculture (USDA) 5-step multiple-pass method for dietary recall.

Effectiveness of the US Department of Agriculture 5-step multiple-pass method in assessing food intake in obese and nonobese women.

Conway JM, Ingwersen LA, Vinyard BT, Moshfegh AJ.

Am J Clin Nutr. 2003 May;77(5):1171-8. doi: 10.1093/ajcn/77.5.1171.

PMID: 12716668