# Older Adult Safety in Surgery (OASIS) IV

## Study Protocol with Statistical Analysis Plan

March 7, 2019

# INVESTIGATOR STUDY PLAN - REQUIRED

## 1. TITLE
Older Adult Safety in Surgery (OASIS) IV

## 2. EXTERNAL IRB REVIEW HISTORY*
N/A

## 3. PRIOR APPROVALS:
N/A

## 4. OBJECTIVES*
Surgery is a life-saving procedure for patients with cancer and can enhance quality of life for patients with intractable abdominal or thoracic disease. Although most patients tolerate the procedure well, frail older adults have as much as a threefold increase in the risk of adverse outcomes after surgery.[1] In response to this risk, some investigators[2-4] have studied preoperative exercise interventions (a.k.a. pre-habilitation).

So far, pre-habilitation studies[2,4] have shown improvement in endurance but not a reduction in adverse outcomes such as medical complications, discharge to nursing home, or readmission. Potential explanations are that these studies were too small to show a difference but also they did not focus on frail older adults who could benefit most from prehabilitation. A final explanation is that they relied on clinic visits with physical therapists or kinesiologists which can add to the stress and cost of surgery for patients already burdened with appointments in the short preoperative period.

A home walking prescription self-monitored with a modern pedometer (e.g. Fitbit type wristband) provides a convenient and cost-effective method for prehabilitation. Despite the apparent advantages of a home walking program, no one has demonstrated that such a program can reduce the incidence of adverse outcomes or improve physical status assessments such as endurance, balance, gait speed, strength, and self-reported function. If our investigative group establishes that a walking prescription supported by pedometer improves these assessments, we would be in a favorable position to embark on a larger study to demonstrate a reduction in adverse clinical outcomes.

There are other data that would be helpful to collect prior to embarking on the larger study. These include the role of varying duration of the walking regimen. Given the rush to proceed with surgery in anxious patients, it would be important to know how well the intervention works over the range of times available and if there exists a threshold of duration (e.g. 1-2 weeks) below which a walking prescription would have no effect. Additionally, it would be important to analyze step counts from the pedometer and the percentage of days in which individual patients achieved prescribed targets. This would permit assessing whether any improvements in physical status resulted from the walking intervention. Conversely, if there is no improvement in physical status assessments, we could diagnose if nonadherence with the walking prescription was the reason. Finally, it would be helpful in guiding future research to calculate the time and cost required to recruit eligible patients as well as to assess patient satisfaction with the walking prescription.

We therefore propose a study of 400 older adults scheduled for surgery with the following aims which will prepare us to conduct a larger trial focused on clinical outcomes.

**Aim 1:** To assess the impact of a walking prescription intervention on outcomes of endurance, balance, gait speed, strength, and self-reported function in patients with frailty.

**Aim 1a:** To estimate improvement in outcomes as a function of duration of the walking intervention.

**Aim 1b:** To re-estimate the effect of the intervention adjusting for the percentage of days each patient met his/her walking goal.

**Aim 1c:** To measure patient satisfaction with the walking intervention.

**Aim 2:** To measure the average time and cost required to recruit and follow up each patient.

**Aim 3:** Postoperative outcomes: we may also measure several postoperative outcomes

Change in six-minute walk distance from baseline
The number of steps per day in the hospital
Time to 100 steps at the day of discharge.
Discharge to skilled nursing facility
Length of stay
Thirty-day outcomes including serious complication, readmission, and death

Aim 4: Measure the performance of Edmonton frailty score for predicting 30 day outcomes including serious complication, readmission, death.

**5. BACKGROUND***

Frail older adults are at elevated risk for adverse postoperative outcomes. With aging, impairments underlying physical function emerge, such as muscular weakness, decreased lower extremity proprioception/balance, and visual deficits. These impairments limit walking ability which in-turn limits participation in daily life activities. A more sedentary lifestyle ensues leading to further lower extremity weakness which becomes manifest in slow gait speed.[5] These sedentary individuals also undergo significant loss of endurance/exercise capacity as their bodies becomes less efficient at using oxygen.[6] This is significant given the stress on the body during surgery. Frail older adults are also at risk for delayed mobilization which can lead to multiple other medical complications. Afilalo et al.[1] found that cardiac surgery patients with slow gait speed, a good single marker of frailty, had more than a threefold increase in morbidity and mortality (odds ratio= 3.05 95% CI 1.23-7.54)

In that study, the authors used gait speed < 0.83 m/s which is a relatively stringent criterion for slow speed. Using a more liberal gait speed criterion (≤ 1.0 m/s), our research group still found a 1.7 fold increased risk (hazard ratio=1.71 95% CI 0.67-4.31) of developing an adverse postoperative course for older adults.[7]

A pure walking intervention (without resistance or other exercise components) can lead to improved physical status in frail older adults but it has not been tested previously in the surgical setting. Investigators have shown that long term care residents (typically frail) can participate and benefit from regular walking.[8] Similarly, investigators with the COPD Seat study[9] have

proposed looking at whether a two-week movement intervention (i.e. essentially a walking program) titrated to step count can improve balance, gait speed, and strength in patients discharged after hospitalization for COPD.

Our proposal will assess the role of a walking intervention in the surgical context assessed over multiple dimensions of physical status-endurance, balance, gait speed, strength, and self-reported function.

The gains we achieve with the walking intervention will pay dividends in terms of clinical endpoints. We hypothesize that a preoperative walking intervention will lead to improvement in physical status by the time of surgery.

Prior studies did not use pedometers and also did not isolate the most vulnerable participants like frail older adults. Gillis et al.[2] studied 77 patients of varying physical status (i.e. all comers) scheduled in a randomized control trial. In this trial the authors compared a tri-modal intervention administered 4 weeks preoperatively and 8 weeks postoperatively for improving endurance, nutrition, and anxiety compared with a group that received this only postoperatively. At the end of the preoperative phase, patients receiving pre-habilitation walked on average 41.6m more during six minute walk distance (6MWD) testing than controls. However, the rate of postoperative complications did not differ significantly between groups and the cost and convenience of that intervention were unfavorable.

Dronkers et al.[4] had both clinic-based and home-based exercise components in their preoperative intervention (with multiple trainers enlisted at presumed great cost). As part of their intervention they tracked patients with traditional pedometers. Despite these comprehensive efforts, they did not find any significant differences in endurance or clinical complications. One explanation for the lack of effect may be that the investigators did not use the pedometer for goal setting. Goal setting has proven itself when it comes to pedometers increasing physical activity / number of steps.[10] In addition, neither the Dronkers nor Gillis study isolated frail older adults whose elevated baseline risk provides an increased opportunity for preventing adverse events.

## Impact

**We target frail older adults.** Unlike prior prehabilitation studies, we focus on frail older adults. Working with this group provides a unique opportunity to make big gains in endurance and other aspects of physical status (relative to baseline status). In future work we can assess whether these relative gains translate into significant clinical outcome reduction.

**Our intervention is low-cost and convenient.** The convenience to patients of a home walking intervention will pay dividends in terms of adherence. Given the low baseline physical status of the patients we are recruiting, walking is the intervention that makes the most sense.

**We are goal setting with a modern pedometer**. Goal setting with a modern pedometer will

overcome the shortcomings of the prior studies[2,4] that either did not use a pedometer or only used it for research staff tracking steps. By having the user pay close attention to the steps being walked, we anticipate they will walk more than other patients not using a pedometer, consistent with the literature.[10]

**We are collecting more comprehensive physical status data than prior studies.** Prior studies collected endurance but other dimensions of physical status are also important to consider. Improvements in balance and strength can lead to better and earlier postoperative mobilization. Similarly, improved function can predict increased independence with activities of daily living reducing the need for skilled nursing.

## 6. INCLUSION AND EXCLUSION CRITERIA*

**Inclusion criteria for screening -** We will enroll participants age 50 and older undergoing any abdominal or thoracic surgery.

**Inclusion criteria for randomized controlled trial -** We will enroll participants age 50 and older undergoing any abdominal or thoracic surgery.

**Exclusions for screening – non-adults, prisoners, Non-English language speaker for whom short form consent is not available.**

**Exclusions for randomized controlled trial -** The exclusions we will apply pertain mainly to the measurement of 6MWD – (1) unstable angina or stable angina with minimal exertion or at rest (2) visual impairment such that walking impairs safety (3) fall within previous three months, (4) resting heart rate of more than 120, a systolic blood pressure of more than 180 mm Hg, or a diastolic blood pressure of more than 100 mm Hg (5) patient who does not walk independently (e.g. wheel chair; cane walking is ok)

**Individuals who are not yet adults (infants, children, teenagers)**
This study excludes anyone who is less than 50 years old; no children will be included in this study.

**Pregnant women**
Pregnant women will not be included.

**Prisoners**
Prisoners will not be included in the study.

**Non-English language speaking subjects**

Non-English language speaking subjects for which an IRB approved short form is available will be included; patients speaking a language for which the UMass IRB does not have a short form consents available will not be included.

**Adults unable to consent (adults lacking capacity)**
*Adults who are deemed cognitively impaired or unable to consent will be included; given the topic of study and the inclusion/exclusion criteria, it is possible that potential participants with impaired decisional competency will be identified for this study. If substantial cognitive impairment is indicated through the use of the MiniCog test, we will implement consent procedures consistent with those recommended for patients with cognitive impairment. This includes reviewing consent with a legally authorized representative and close monitoring of patients. If patients appear unduly distressed, they will be withdrawn from the study. Please see section # 30. Consent Process for additional details.*
*See also section #18.

**7. STUDY-WIDE NUMBER OF SUBJECTS***
N/A; this is not a multi-site study.

**8. STUDY-WIDE RECRUITMENT METHODS***
N/A; this is not a multi-site study.

**9. STUDY TIMELINES***

The overall study timeline is two years from start of recruitment. The first year will focus on preparation (training on frailty measurement, scripting interviews, and testing the questions we ask) and recruitment of study subjects. Individual subjects will be actively involved for 30 minutes during their first appointment (not including time spent in clinic appointment), approximately 15 minutes during the day of their surgery, and potentially approximately ten additional minutes on their day of discharge from the hospital, though patient data collection will continue for up to one year after the day of surgery.

**10. STUDY ENDPOINTS***

**Aim 1a: Endurance:** For endurance, we will measure 6MWD following the American Thoracic Society (ATS) guideline.[15] Briefly, we will establish an unimpeded 20m course within the colorectal surgery office. Studies have varied with the length of course but a multicenter study mentioned in the guideline statement[15] suggested lengths ranging from 20 to 50m did not significantly change patient walking distance results. Every effort will be made to control for variation, including the amount of encouragement provided by project staff member and stopping conditions. We will follow the ATS guideline providing encouragement at one minute intervals.

Patients may stop by leaning against the wall before resuming. At the end of six minutes, we

will record patient-perceived exertion using the Borg scale. We will also ask the patient for a reason for stopping. Recording the perceived exertion and reason for stopping will allow us to interpret outlier values and other potential variation among patients who otherwise have similar predicted walk distance. Although a research staff member will record the walk distance, we will require that a RN or another more senior clinician be present during the examination to monitor for patient fatigue or angina. Reasons for immediately stopping a 6MWD include the following:(1) chest pain, (2) intolerable dyspnea, (3) leg cramps, (4) staggering, (5) diaphoresis, and (6) pale or ashen appearance. If space is not available, we will conduct the test on a treadmill with guard rails which should provide adequate safety. An RN or another more senior clinician will be present during the examination to monitor for patient fatigue or angina for subjects completing the assessment on a treadmill as well.

**Aim 1a: Balance, strength and gait speed:** We will follow the short performance physical battery (SPPB) protocol by Guralnik.[11] A research staff member will measure the patient's ability to balance in three separate positions: side-by-side stand, semi-tandem stand, and tandem stand. Scores range from 0 for someone unable to balance in any of the positions to 4 for someone able to stand in each position for 10 seconds. Given we have already measured gait speed during the screening process we will move on to patient's ability to perform five chair sit-to-stand maneuvers with scoring based on the time required.

**Aim 1a: Self-reported function:** We will administer the 12 items of the Veteran Rand (VR-12) in order to measure self-reported function.[16] We will then calculate the summary physical component score (PCS) using a published algorithm.[16] The algorithm norms PCS to range between 0 and 100, with 50 as a mean, and 10 as the standard deviation for the US population.

**Aim 1b:** Adherence with exercise: We will measure the percentage of days in which the participant meets his/her step count target for intervention patients and activity journals for both groups of patients

**Aim 1b:** Patient satisfaction: We will design a custom instrument to assess patient satisfaction with our intervention.

**Aim 2:** Time and cost to recruit 400 frail older adults: We will calculate the time and cost to recruit 400 patients. We will assess time in multiple ways: number of calendar days and number of working clinic days. For cost, we will assign an hourly wage for research staff member and RN efforts and then multiply by the number of hours required to perform recruitment, follow-up telephone calls, and follow-up assessments.

**Aim 3:** Postoperative outcomes: we may also measure several postoperative outcomes, including:

Change in six-minute walk distance from baseline

The number of steps per day in the hospital

Time to 100 steps at the day of discharge.

Discharge to skilled nursing facility

Length of stay
Postoperative Recovery (measured via quality of recovery scale, abdominal surgery impact scale)
Thirty-day outcomes including serious complication, readmission, and death

**Aim 4:** Thirty-day outcomes including serious complication, readmission, and death

**Descriptive variables / covariates.** We will collect basic demographic information (age, race, and gender), comorbidity, body mass index information, and surgical information including principal CPT code for surgical procedure and anesthesia type. We will also assess exercise self-efficacy using a modified version of the exercise self-efficacy scale.[1] Exercise self-efficacy is the belief that a patient can exercise targeted amounts without additional assistance from others. Assessing for this will allow us to control for baseline difference in the intervention and control patients that might impact on our interpretation of the efficacy of the intervention. The instrument is a simple inventory of items questioning if a patient can accomplish exercise target under various circumstances. A copy of the instrument has been included with the protocol submission.

**11. PROCEDURES INVOLVED***

Recruitment and screening phase:
Using HIPAA waiver, we will review the charts of potential patients prior to scheduled visit in the colorectal surgery office. Typically, we will review charts the day before scheduled visits but up to four weeks prior. In terms of the variables we will collect, we are specifically interested in information about age, sex, race, ethnicity, functional status, height, weight, type of surgery, surgeon, and date and time of appointment in colorectal surgery office These variables will allow us to compare patients who agree to participate with those that decline for the purpose of reporting generalizability in future scholarship originating from this work. The appointment time and provider involved will help with cueing clinic staff members to broach the subject of participation in the research as described further in the next paragraph. We are also reviewing charts for evidence of guardianship or significant cognitive impairment. Specifically, we will look evidence of guardianship established or prior consent documents signed by somebody other than the patient.

Using the information gathered above, we will request clinic staff members (surgeon, surgical resident, nurse practitioner, nurse, or medical assistant) working in the colorectal surgery office to ask if any patient undergoing intestinal surgery would be willing to speak to a research staff member about our research study. For those agreeing, the research staff member will discuss participation in the frailty screening phase of the study through an informed consent process as described further in section 30. The research staff member will also obtain hipaa authorization to collect postoperative outcomes (aim 3) to all adults aged 50 and above scheduled for colectomy or other intestinal surgery not including hemorrhoid surgery. Investigators have previously demonstrated that the Edmonton frailty scale can predict outcomes of surgery including postsurgical complications and length of stay.[2] For patients scoring 4 or above (out

of 17) which has been linked with frailty, we will invite to participate in this study to assess preoperative walking as described further below. For those with score of 4 or below, we will not require any further participation apart from the six-month interview. For patients for whom consent can be obtained at the same visit as patient surgical consultation, we will proceed with the baseline assessment as described below. For patients for whom consent cannot be obtained right away or who prefer to come back at another time, we will schedule a follow-up visit within two weeks of initial visit.

**Baseline assessment:** The RA will record baseline physical status assessments to establish baseline values. We anticipate this will take approximately 30 minutes in addition to the regular office visit. Included in the baseline assessments will be the 6MWD, the SPPB (See attachment), and the Veteran Rand (VR-12) (see attachment).

We will follow the guidelines set in place by the American Thoracic Society (ATS) for administration of the 6MWD. We will utilize safety precautions such as keeping a chair with wheels at the ready nearby at all times for any patient who becomes dizzy or needs to sit for any reason. The baseline 6MWD will be completed in the hallway of the colorectal surgery office at 67 Belmont Street. This is a very low traffic area but we will also do as much as we can to prevent anyone from walking on the course during use. For later assessments administered in the hospital we will set up temporary cones to ensure that no one walks on the course as the patient is walking. Also per the ATS guidelines, the RA will walk the course prior to the patient, so they can ensure that there are no obstructions on the course that may hinder the patient.

We will also follow the ATS guidelines in regards to instructing and encouraging the patient during the walking test. These instructions are stated as follows:
"After the first minute, tell the patient the following (in even tones): "You are doing well. You have 5 minutes to go." When the timer shows 4 minutes remaining, tell the patient the following: "Keep up the good work. You have 4 minutes to go." When the timer shows 3 minutes remaining, tell the patient the following: "You are doing well. You are halfway done." When the timer shows 2 minutes remaining, tell the patient the following: "Keep up the good work. You have only 2 minutes left." When the timer shows only 1 minute remaining, tell the patient: "You are doing well. You have only 1 minute to go." Do not use other words of encouragement (or body language to speed up). If the patient stops walking during the test and needs a rest, say this: "You can lean against the wall if you would like; then continue walking whenever you feel able." Do not stop the timer. If the patient stops before the 6 minutes are up and refuses to continue (or you decide that they should not continue), wheel the chair over for the patient to sit on, discontinue the walk, and note on the worksheet the distance, the time stopped, and the reason for stopping prematurely. When the timer is 15 seconds from completion, say this: "In a moment I'm going to tell you to stop. When I do, just stop right where you are and I will come to you." When the timer rings (or buzzes), say this: "Stop!" Walk over to the patient. Consider taking the chair if they look exhausted. Mark the spot where they stopped."

**Randomization:** we will randomize patients in a 1:1 fashion into intervention and control groups using a prespecified table generated by our study statistician. More specifically we will use REDCap software to assign a study arm assignment using randomly permutated blocks of sizes 4 and 6.

**Intervention patients: intervention patients will receive a walking prescription weekly calls from a study staff member as described below**

**Walking prescription:** A study staff member in consultation with study physician (PI or co-I) will then provide the initial walking prescription based on the participants' baseline performance on the 6MWD following a published example [12,13] and will focus the participant on walking at a moderate intensity (level of approximately 3 on the modified Borg Perceived Exertional Scale;[14] laminated Borg scales will be distributed to participants).

Participants may walk steps over the course of a day or in one session. The initial walking prescription will also provide instructions to the participant to increase his/her number of steps each week by 10 to 20%.

A research staff member will then orient the participant to the pedometer

**Weekly calls:** During the interim between the day of consultation until the day of surgery, a study staff member will make weekly calls to each patient. The calls will provide participants an opportunity to report any symptoms which could warrant stopping the walking regimen and/or seeking urgent medical attention. In addition, we will train the study staff member to troubleshoot any problems setting step count targets or other problems with the pedometer. In cases in which the pedometer fails, we will budget to have additional pedometers available to mail to the patient.

**Activity log:** we will ask participants to log all of their physical activities-date, activity type, number of minutes. We will submit a copy of the activity log to the irb for approval prior to recruiting randomized participants to complete it.

Control subjects: a study staff member will provide general walking advice with typical warnings about when to stop (e.g., chest pain, breathing difficulty, or fall). Control subjects will receive no other intervention. We will also ask control subjects to log their physical activities.

**Preoperative assessment:** On the day of preoperative testing, which will usually occur three to five weeks after the baseline measurement, a research staff member or other project staff member will collect the pedometer and record the repeat physical status assessments (6MWD and SPPB). On the day of surgery, we may also place a research grade monitor on patients so as to track their steps while in the hospital.

**Hospital period assessment:**. By the day of discharge, we will collect the research grade monitors and repeat our physical status measurements.

In order to test the above procedures in the randomized individuals, we will enroll up to 15 patients as test patients. All these patients will undergo screening, baseline assessment/interview, follow-up assessment on day of preoperative testing, in-hospital step tracking and Hospital period assessment.

**30 day assessment:** Approximately 30 days from day of surgery, at office of surgery clinic, we will repeat our physical status measurements

During the 6MWD measurement issued during the baseline assessment, day of surgery, hospital period, and 30-day assessment, a nurse or more senior clinician will be available during the examination to monitor for patient fatigue or angina.

6 month assessment: We will attempt to make contact by phone, mail, or email with enrolled patients no more than five times total (regardless of the method of contact). For patients not picking up the phone, we will leave a voicemail message up to three times following a script that we will forward to the IRB prior to implementation of this procedure. We will make these attempts over 2 months (i.e. months 7 and 8) and not contact patients after 8 months have elapsed from the day of surgery). During our conversation with patients, we will request information about the occurrence of any serious complication since surgery and also will re-administer VR-12. Our prior experience with contacting patients (Pfizer - Anticoagulation Medical Home study) demonstrated the growing difficulties in reaching patients, particularly older vulnerable adults, often who are shifting location between children and rehabilitation facilities making follow-up more challenging. We will use a mailer or post card (depending on availability/prevailing pricing) for the purpose of this correspondence. (See attached)

NSQIP data download
In order to capture information about patient comorbidities and outcomes, study staff will download information already collected on surgical patients at UMass for the purposes of quality control as organized by the National Surgical Quality Improvement Program. Specifically, the study staff member will search for all records relating to the operation. These records will be stored in a password-protected server, same as for the information collected directly from the patient. A programmer assigned to the project will then link data we collected directly with NSQIP using the medical record number and date of surgery. The project programmer/analysts will assemble a limited dataset with no direct personal identifiers to support merger and creation of a common analytic file.

The analytic dataset will be a limited dataset, containing at a minimum dates and a unique artificial Study ID number that is linked through separate coding to the patient's health record number. This linkage coding will be stored separately from the analysis coding. Analyses will be performed using only limited datasets and only aggregate data will be reported.

We will create the interview scripts and data collection forms as one of our first tasks of the study and will upload for approval. We will not commence with any data collection until the tools have been reviewed and approved by the IRB.

**12. DATA AND SPECIMEN BANKING***

No specimens are being collected as part of the research. Data will not be banked for use in future research outside of the scope of this study.

**13. Data Analysis and Management**

***Analysis*** As a first step, we will examine the distributions of all variables using histograms and summary statistics for continuous variables, and frequencies for categorical variables. We will consider transformations to enhance normality where continuous variables demonstrate substantial skew or outliers.

Aim 1: We will calculate the distribution of within-participant change for each of the five physical status measures and assess the average and median change against the minimal clinically important difference (MCID) for each assessment, as well as the percentage of patients with a minimal clinically important difference. In cases where a MCID is not available we will decide among our expert advisory team members the threshold values that indicate some important improvement. In our analysis we will also examine the role of baseline assessment on the amount of improvement by using a generalized linear model for the outcome of change in physical status controlling for baseline assessment.

Aim 1a: In this aim, we will examine the association of duration of time available for the intervention with within-participant change in physical status outcomes, using nonparametric locally-weighted scatterplot smoothing (LOESS) regression.[17] We will rerun our generalized linear model controlling for duration of time available for the intervention, transforming the duration variable if indicated by the LOESS plots, e.g., piecewise linear if a threshold effect is seen.

Aim 1b: Similar to Aim 1a analyses, we will examine the association of percentage of days (of the 30 days available in pedometer memory), the step count target was met with within-participant change in physical status outcomes, again using LOESS plots. We will rerun our generalized linear model controlling for the percentage of days in which the patient met their step count target, transforming the percentage of days if indicated by the LOESS plots.

Aim 1c: We will calculate the distribution of patient satisfaction with the intervention, using descriptive statistics, e.g., mean, percentiles, as well as a histogram. Using generalized linear modeling, we will measure patient satisfaction adjusted for changes in physical status. Given the possibility of co-linearity of physical status assessments, we will construct five separate models, one for each of the five physical status assessments.

Aim 2: We will calculate the average time and cost required to recruit each patient by taking the total time and cost divided by the number of patients we eventually enroll (i.e. 200 patients).

Aim 3: In patients for whom we have recorded postoperative six minute walk distance and step counts, we will calculate change in six minute walk distance from baseline to day of discharge. We will also calculate steps per day and time to first 100 steps. We will calculate the average steps per day using postoperative days 1 and 2 given variation in the start time of surgery for the surgical day and time of transportation availability on the discharge date. For the rare patient leaving the hospital on postoperative day 2, we will only use postoperative day 1. For patients with serious complications requiring ICU stay, we anticipate no steps will be taken and will adjust for this in our analysis. We will measure time to walking at least 100 steps in a single bout, defined as continuous minutes walking at least 1 step/minute following example in the literature. Being able to walk 100 steps in a single bout approximates criteria used to predict successful discharge home from acute hospitalization. We recognize that some patients will not walk 100 steps and so we will adjust for this in our analysis (i.e. we will censor their data in survival analysis).

In terms of the other outcomes, we will compute length of stay in hours from the time of surgery until time of discharge. We will also perform chart review between 30 and 120 days after surgery to tabulate number of patients discharged to nursing home, readmitted at 30 days, dead at 30 days, or having a serious complication of 30 days.

Interim Analyses: Given the possibility that our walking intervention does not improve our physical status measures, we will perform the Aim 1 analysis after recruitment of each batch of 10 patients. More specifically, we will assess the average and median change against the MCID for each of the five measures. If we have not achieved the MCID for any of the measures after any one batch, we will work with our advisors, particularly Roger Fielding, to revise our intervention (e.g. intensifying the walking regimen) with the goal of improving physical status more than the MCID of one or more measures by the time of the next interim analysis.

**14. PROVISIONS TO MONITOR THE DATA TO ENSURE THE SAFETY OF SUBJECTS***
The proposed study involves no more than minimal risk to participants. Therefore, we believe that an intensive data and safety monitoring plan is not needed. However, we will take steps to ensure the integrity of the data and to detect any adverse effects of the study on participants.

See also #27 Provisions to Protect the Privacy Interests of Subjects.

**15. WITHDRAWAL OF SUBJECTS WITHOUT THEIR CONSENT***
We do not anticipate the need to withdraw patients unless it is at their request. However, we will remove patients who appear unduly distressed during the research interview.

**16. RISKS TO SUBJECTS***
**Potential Risks**

The proposed study poses minimal risks to the participants. There is a slight risk that research records (interview forms, interview notes, audio-recordings, transcripts, and electronic data) might be obtained by persons not authorized to do so. There is a slight risk that research data files might be compromised, and obtained or viewed by unauthorized persons. There is also a risk that the patient may feel uncomfortable answering some of the questions in the interviews. We will inform all patients during the informed consent process that they do not have to answer any questions that they do not want to. There is also a risk that the patient may fall. We screen patients initially based on prior falls to minimize this risk. In addition, there is screening for cognitive impairment for patients who may not fully appreciate risks of walking. The same screening process protects patients against development of chest pain or shortness of breath. We exclude patients with existing angina is such that small amount of walking or being at rest (i.e. class III or IV angina). We also have a physician or nurse on the premises at all times responsible for the patient if he or she were to develop shortness of breath, chest pain, or fall.

See also #14 Provisions to Monitor the Data to Ensure the Safety of Subjects, and #27 Provisions to Protect the Privacy Interests of Subjects.

**17. POTENTIAL DIRECT BENEFITS TO SUBJECTS***

The walking intervention has the potential to decrease adverse post-surgical outcomes for patients involved in our study, but cannot be guaranteed.

**18. VULNERABLE POPULATIONS***

**Adults unable to consent (adults lacking capacity)**

Given the topic of study and the inclusion/exclusion criteria, it is possible that potential participants with impaired decisional competency will be identified for this study. However, this study has anticipated direct benefits to subjects, and we will therefore enroll cognitively impaired patients. We will implement consent procedures consistent with those recommended for patients with cognitive impairment. This includes reviewing consent with a legally authorized representative and close monitoring of patients. If patients appear unduly distressed, they will be withdrawn from the study. Please see section # 30. Consent Process for additional details.

**Individuals who are not yet adults (infants, children, teenagers)**

This study excludes anyone who is less than 65 years old; no children will be included in this study.

**Pregnant women**

Pregnant women will not be included.

**Prisoners**

Prisoners will not be included in the study.

**Non-English speaking subjects**

Patients speaking a language for which the UMass IRB does not have a short form consents available will not be included. For non-English speaking patients, we will utilize an interpretive

service referred to us by UMass Memorial Interpretive Services. The interpretive service will not be given any information about the patients we enroll. They are only notified of the department from which we are calling from.

We will use the telephone interpretive services or a family member who is conversant in English and the language understood by the subject to conduct the interview. We will use the short forms provided by the UMass IRB. We will have the interpreter or family member act as the witness. If the interpreter is the only witness, we will send the consent form for his/her signature and keep a copy of the version signed by the interpreter. Because the involvement of each patient does not extend beyond one interview study session, we will not reassess consent with the research participant.

**19. MULTI-SITE RESEARCH***
N/A; this is not a multi-site study.

**20. COMMUNITY-BASED PARTICIPATORY RESEARCH***
*N/A*

**21. SHARING OF RESEARCH RESULTS WITH SUBJECTS***
There are no specific plans to share results with study subjects; study procedures do not include any type of diagnostic testing.

All results shared in published research will be in aggregate or summary format and will not include identifiable information about participants. Published results are available to the greater community at large, including study subjects.

**22. SETTING**
We will recruit patients from the surgery clinics of UMass Memorial Medical Center - strewn between University and Memorial campuses.

**23. RESOURCES AVAILABLE**
All research personnel listed on this study will read the protocol and receive the appropriate supervision and possess the appropriate experience (both higher education and related work experience) needed to fulfill their roles and complete their responsibilities for this study. All investigators and project staff are required to receive and complete IRB and HIPAA training.

The Principal Investigators will oversee all personnel and all research activities conducted within this study.

The Principal Investigator will have responsibility for the overall conduct of the project at this study site. They will have primary oversight of all study personnel. They will participate in the

design and the execution of the respective study analyses and will be responsible for the reporting of study results. The Principal Investigators have extensive experience and expertise in surgical outcomes research and perioperative medicine.

The Programmer will perform a range of programming and data management activities essential to conduct of the project. S/he will develop study data bases, and perform analyses under the direction of the PI. Programmers at the Meyers Primary Care Institute all hold graduate level degrees and have vast experience working with administrative claims data for research purposes.

The Project Manager will assist the Principal Investigator and the Co-Investigators in implementing all aspects of the project. Under the direction of Principal Investigator, the Project Manager will be responsible for day-to-day coordination and oversight of the project, including: developing timelines, work allocation, workflow plans, monitoring project progress and task completion, monitoring spending and effort allocation, and managing correspondence and administrative tasks. S/he will monitor/manage ethics and regulatory approvals (IRB, HIPAA/DUA). The Project Manager will attend and plan for all project-related meetings as needed. S/he will work under the direction of the Principal Investigator to assist with all study activities, preparing IRB submissions and reports, and developing study materials such as development of data collection instruments and intervention-related tools. S/he will be responsible for maintaining communications with all parties participating in the project. She will maintain project documentation and will assist in developing and filing required project reports. Project Managers at the Meyers Primary Care Institute all hold graduate level degrees and have vast experience working on healthcare services research projects.

A research staff member will work under the direction of Principal Investigator, Project Manager and Research Manager to assist with all study activities. S/he will assist the PI and other project staff in managing the administrative activities of the project. S/he will prepare materials for team meetings, and will facilitate communication between all project staff through written correspondence, telephone, fax, and email. A research staff member will be trained to formulate walking prescriptions (with oversight from the PI) as well as conduct the 6MWD measurement. A nurse or senior clinician will be available during the time when a research staff member is conducting the 6MWD measurement.

The REDCap Administrator will be the contact with UMass for all REDCap administrative needs throughout the study. As the appointed REDCap administrator for the Meyers Primary Care Institute site, s/he will have access to all study data collected within REDCap.

All study personnel are required to undergo Human Subjects Training and hold a current CITI Human Subjects Training Certificate and will familiarize themselves with the study protocol and IRB documents.

Individuals have not yet been identified to fill the roles of programmer and research staff member. Once the staff has been identified they will be added into the eIRB system. No study staff will begin any study activities until they have been added into the eIRB.

## 24. LOCAL RECRUITMENT METHODS

We will attempt to recruit 200 subjects from the surgery clinics affiliated with UMass Memorial Medical Center. We believe 200 subjects is the requisite number we need to successfully answer our research question. We believe the annual pool of eligible patients is more than 400. This accounts for a reasonable amount of refusal, surgery cancellation, and also loss to follow-up.

Typically, consultation with colorectal surgeon occurs after colonoscopy has detected a significant lesion. Once the surgeon and participant have agreed to a surgical plan, the surgeon will invite the participant to speak to our project staff member about the study.

For those participants agreeing, the research staff member (already on site based on having reviewed the appointment lists the day before) will obtain informed consent and conduct initial interview.

The research staff member will then ask the patient about falls, visual impairment, and chest pain to elicit any exclusion to eligibility.

We do not intend to provide stipends.

## 25. LOCAL NUMBER OF SUBJECTS

We will attempt to recruit 400 subjects who contribute to the ultimate analysis of this work.

## 26. CONFIDENTIALITY

All persons accessing patient records must adhere to the following guidelines:

- The information in a patient's record cannot be disclosed without the patient's knowledge and consent; however, there are occasions when there is a legal obligation or duty to disclose information. Requests for patient information from external sources must be directed to the Medical Records Department.
- Paper medical records must be signed out by an authorized person whenever they are removed from the department.
- All paper records must be returned to the Medical Records Department.
- Medical records must not be left unattended where unauthorized persons might read them Access to business information, including billing information, is also granted on a need-to-know basis.
- No patient records will be left open on a computer unless actively in use.
- Patient records will be closed as soon as the necessary information has been retrieved.
- Computers with access to patient medical records will be locked unless actively attended.

All computerized data will be kept on secured computers or network servers. These data will be accessible only by approved research staff, using confidential usernames and passwords. Direct

patient identifiers will be removed from study data files as soon as possible in the data processing steps. Statistical analyses will be performed using a limited dataset. All information linking identifiable data to analysis files will be kept separate from analysis files. All data will be used only for research purposes only; published data will not contain any individual identifiers, only aggregate-level data will be reported.

Only study personnel included in IRB applications have access to project-specific data. All persons collecting or handling data are trained in human subjects' procedures, confidentiality and privacy protection. All investigators and project staff are required to receive and complete IRB and HIPAA training.

In addition, risks to confidentiality of the data collected throughout the proposed study will be addressed as follows: Assurance and confidentiality of information will be made to all participants. Data will be handled with the same confidentiality accorded to patient's medical records. Specific procedures protecting participant confidentiality will be as follows:

- ID number, as well as full name, medical record number, and dates of service will be placed on electronic study forms or records on which data are collected and/or stored (specifically medical record abstraction forms in RedCap).
- Access to data files will be secured with a password-filing system (that logs entry) and is restricted to authorized staff only
- Necessary hard-copy records containing study data of any type will be kept in locked files. Master lists linking participant information with ID number will be numbered consecutively and prepared before data collection to ensure accurate accounting. These lists will be kept locked, in duplicate, with access only by the PI and other investigators.
- All project staff will sign an oath of confidentiality to ensure their understanding of the terms of confidentiality required. They will be trained in specific procedures to ensure confidentiality.
- Sign-out procedures for all access to data files will be strictly enforced.
- All reports and publications will preserve the subjects' anonymity.

Any breach of confidentiality will be subject to a root cause analysis and preventive measures taken as appropriate. We will report any breach of confidentiality as required.

## 27. PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF SUBJECTS

**Protection for Risks Associated with Potential Loss of Confidentiality**

The organizations proposing this study have systems, oversight, experienced personnel, and an organizational culture that supports the appropriate use, access and storage of confidential information. All persons collecting or handling data will be trained in human subjects' procedures, confidentiality and privacy protection. All investigators and project staff are required to receive and complete IRB and HIPAA training.

Data for all participants will be kept strictly confidential. All research files will be kept in locked file cabinets or a locked file room. Participants will be assigned a numerical code (Study ID) for identification in the files. Names and other identifiers will be kept in separate locked files.

Individual identifier information will be removed from study data files as soon as possible in the data processing steps. All computerized data will be kept on secured computers or networks at each site. These data will be accessible only to research staff, using confidential usernames and passwords. Analysis files of de-identified data will be created at each site and will be transferred between sites using password-protected files and secure encrypted web transfer procedures. Statistical analyses will be performed using only de-identified datasets and only de-identified data will be reported. All data will be used only for research purposes only; published data will not contain any individual identifiers.

We are requesting a HIPAA waiver for the purposes of recruitment, for which we need to access patient medical record and contact information.

We will ask study participants to sign a HIPPA authorization form.

**28. COMPENSATION FOR RESEARCH-RELATED INJURY**

None; there are no resources available. We do not anticipate any research-related injuries. We believe the research poses no more than minimal risk to subjects.

**29. ECONOMIC BURDEN TO SUBJECTS**

We anticipate no economic burden to subjects in this study.

**30. CONSENT PROCESS**

During the patient's scheduled surgery clinic appointment, a surgery clinic staff member will then introduce the study and ask if the patient is willing to discuss the study with a study staff member after his/her surgery clinic appointment. If a patient expresses interest, the surgery clinic staff member will notify study staff member.

For patients who agree to speak, the study staff member will find a private room and discuss enrollment and informed consent. Prior to documenting written consent, the study staff member will determine if a patient needs to undergo cognitive testing. Criteria for this determination include presence in the electronic medical record of prior consent document such as for undergoing medical procedures signed by a person other than the patient, patient report of having somebody else sign for him or herself, mention of legal guardian in electronic medical record, or study staff members belief that the patient may be cognitively impaired. If legal guardian documentation in the electronic medical record indicates that medical decision-making requires guardian to sign consent, we will omit cognitive testing and proceed to obtain consent from the guardian and assent from the patient. Otherwise, to execute cognitive testing, the study staff member will administer the MiniCog test. We are waiving written documentation of consent, as the MiniCog presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is

normally required outside of the research context. If the patient passes the MiniCog assessment, the patient will sign a consent form to participate in the study. If the patient does not pass, we will obtain informed consent from a caregiver or surrogate and will ask the patient to indicate their assent. At the time of consent, the recruiter will also ask the participant and/or caregiver to sign a HIPAA authorization form for the purposes of chart review.

In order to facilitate organization/storage of informed consent and HIPAA authorization documentation and to permit participation in the research in the case of legal guardian who is not available in person to sign hardcopy of consent document, we will permit written or electronic signature. For electronic signature when guardian is not available in person we will send a link through redcap to sign the informed consent. We will then print a hard copy of signed consent form to subject and send a secure email with signed consent and HIPAA authorization to any legal guardian signing remotely. For those patients and/or guardians who are consenting in person, we will allow for electronic or written signature, and will print a hard copy for them to keep. We will then maintain all documents in REDCap system including uploading of written consent and HIPAA forms for ease of storage and IRB audit.
Note: For those who sign consents electronically, the printed hard copy will not contain the IRB stamp.

For non-English speaking patients, we will utilize an interpretive service referred to us by UMass Memorial /University Of Massachusetts Medical School interpretive services. The interpreting service is not given any information about the patients we enroll. They are only notified of the department from which we are calling from.

We will use the telephone interpretive services or a family member who is conversant in English and the language understood by the subject to conduct the interview. We will use the short forms provided by the UMass IRB. We will have the interpreter or family member act as the witness. If the interpreter is the only witness, we will send the consent form for his/her signature and keep a copy of the version signed by the interpreter. Because the involvement of each patient does not extend beyond one interview study session, we will not reassess consent with the research participant.

For test patients who will not be randomized, we will administer a separate consent that explicitly mentions that they will not be randomized but that their data will still be useful and that the intervention will still be useful to them in terms of improving their physical condition prior to undergoing surgery.

For the consent process, we will follow SOP: Informed Consent Process for Research (HRP-802) in obtaining and documenting consent.

### 31. PROCESS TO DOCUMENT CONSENT IN WRITING

Please see #30 above.

**32. DRUGS OR DEVICES**
N/A

## LITERATURE CITED


1. Afilalo J, Eisenberg MJ, Morin JF, et al. Gait speed as an incremental predictor of mortality and major morbidity in elderly patients undergoing cardiac surgery. *Journal of the American College of Cardiology.* 2010;56(20):1668-1676.
2. 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.
3. Li C, Carli F, Lee L, et al. Impact of a trimodal prehabilitation program on functional recovery after colorectal cancer surgery: a pilot study. *Surgical endoscopy.* 2013;27(4):1072-1082.
4. 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. *Clinical rehabilitation.* 2010;24(7):614-622.
5. Jette AM. Toward a common language for function, disability, and health. *Physical therapy.*

   2006;86(5):726-734.
6. Carli F, Scheede-Bergdahl C. Prehabilitation to enhance perioperative care. *Anesthesiology clinics.*

   2015;33(1):17-33.
7. Kapoor A, Shaffer NS, McDonough CM, et al. Examining New Preoperative Assessment Tools. *Journal of the American Geriatrics Society.* 2016. Sep 2. doi: 10.1111/jgs.14349. [Epub ahead of print]
8. Forster A, Lambley R, Young JB. Is physical rehabilitation for older people in long-term care effective? Findings from a systematic review. *Age and ageing.* 2010;39(2):169-175.
9. Orme M, Singh S, Esliger D, et al. The feasibility of a home-based sedentary behaviour intervention for hospitalised chronic obstructive pulmonary disease (COPD) patients: Sitting and ExacerbAtions Trial (COPD-SEAT). http://www.frontiersin.org/10.3389/conf.fpubh.2016.01.00024/event_abstract. Accessed September 30, 2016.
10. Bravata DM, Smith-Spangler C, Sundaram V, et al. Using pedometers to increase physical activity and improve health: a systematic review. *JAMA.* 2007;298(19):2296-2304.
11. Guralnik JM. Assessing Physical Performance in the Older Patient. National Institutes of Health, National Institute on Aging.
12. Bittner V. Role of the 6-Minute Walk Test in Cardiac Rehabilitation. In: Kraus WE, Keteyian SJ, eds. *Cardiac Rehabilitation* 2007:131-139.
13. The Australian Lung Foundation Pulmonary Rehabilitation Toolkit. http://www.pulmonaryrehab.com.au/index.asp?page=67. Accessed October 4, 2015.

14. Kendrick KR, Baxi SC, Smith RM. Usefulness of the modified 0-10 Borg scale in assessing the degree of dyspnea in patients with COPD and asthma. *Journal of emergency nursing: JEN : official publication of the Emergency Department Nurses Association.* 2000;26(3):216-222.
15. American Thoracic Society. ATS statement: guidelines for the six-minute walk test. American Journal of Respiratory and Critical Care Medicine. 2002; 166(1):111-117.
16. Iqbal SU, Rogers W, Selim A, et al. The Veterans Rand 12 Item Health Survey (VR-12): What It is and How It Is Used. 2009; http://www.chqoer.research.va.gov/docs/VR12.pdf. Accessed May 27, 2009.
17. Cleveland WS, Devlin SJ. Locally Weighted Regression: An Approach to Regression Analysis by Local Fitting. *Journal of the American Statistical Association.* 1988;83(403):596-610.

1. Resnick B, Jenkins LS. Testing the reliability and validity of the Self-Efficacy for Exercise scale. *Nursing research.* 2000;49(3):154-159.
2. Shephard JM, Kosslyn SM. The minicog rapid assessment battery: developing a "blood pressure cuff for the mind". *Aviation, space, and environmental medicine.* 2005;76(6 Suppl):B192-197.