general anesthesia, allergies to local anesthesia, incarceration or bowel strangulation, or evidence of an active infection.

means/medians and dispersion) for these key outcomes.

2 BACKGROUND AND RATIONALE

2.1 Background on Condition, Disease, or Other Primary Study Focus

Inguinal hernia repair - the most common general surgery operation in the U.S. - provides a unique opportunity to improve outcomes for older patients by changing surgical practice.[1] Nearly 80% of inguinal hernia operations are performed under general anesthesia versus 15%-20% using local anesthesia, despite the absence of evidence for superiority. [2,3] The choice of anesthesia has particular implications for older adults because they face substantial short- and long-term risk of cognitive and physical decline after exposure to general anesthesia. [4,5] Consequently, the American College of Surgeons and the American Geriatrics Society have identified a critical need in surgery: determining which operations have better outcomes when performed under local rather than general anesthesia.[4]

Currently, the evidence for choosing an anesthesia technique for inguinal hernia repair in older adults is inconclusive. Several small randomized trials and cohort studies have suggested that using local anesthesia for hernia repair reduces morbidity by one-third, unplanned admissions by 20%, and operative time and costs by 15%, while other studies showed no significant differences. [2,6-8] However, there are significant flaws in these studies that severely limit their applicability to older adults: (1) They mainly focused on younger patients with limited comorbidity burden, largely ignoring individuals aged 65 years and older, (2) They did not adequately examine the effects of general anesthesia on cognitive function and quality of life for older adults and their caregivers. In particular, the only randomized trial that evaluated neurocognitive recovery evaluated a mostly younger population and did not look specifically at outcomes for older adults where the largest benefit is expected to occur.[8] (3) They did not consult with stakeholders (patients, caregivers, physicians, hospitals, or health systems) to identify outcomes relevant to those groups. There is an urgent need to evaluate benefits of local anesthesia for inguinal hernia repair in older adults because the proportion of Americans age 65 and older is rapidly growing and will reach 20% of the population in the next 10 years. [9] Improving postoperative recovery for patients having the most common general surgery operation in our country will have a tremendous effect on patient and caregiver quality of life.

2.2 Study Rationale

The study rationale is that prior to conducting a multisite randomized trial, it is necessary to identify relevant outcomes, understand barriers to greater use of local anesthesia, test study procedures, and confirm our ability to adequately recruit and randomly assign participants. Additionally, the proposed study will provide the applicant with critical training in the design, conduct, and analysis of clinical trials. This will uniquely position the applicant to change surgical care for older adults.

There have been two prior randomized clinical trials that compared local versus general anesthesia for inguinal hernia repair. Nordin et al. randomized 616 patients in Sweden to local,

hernia surgery under local versus general anesthesia for adults aged 65 years and older. This will demonstrate feasibility of conducting a multisite randomized trial and will optimize study procedures prior to conducting the multisite trial. The secondary objective is to generate preliminary comparisons between the two study arms, to inform design of a larger multisite trial.

The study design is illustrated in Figure 1.

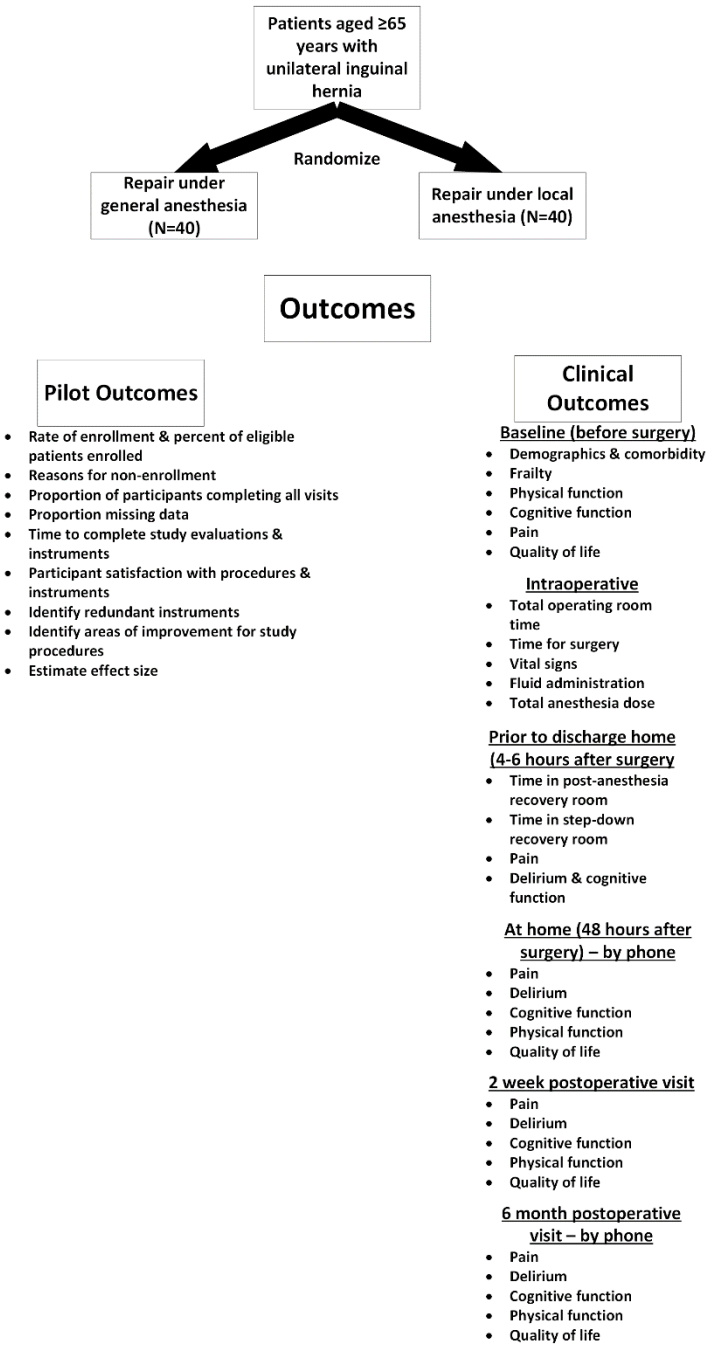

Figure 1. Overview of study design. Patients will be randomized to inguinal hernia surgery under either local or general anesthesia. We will collect baseline characteristics prior to surgery. Intraoperative and immediate postoperative outcomes include time, pain, and cognitive recovery. Post-discharge outcomes include pain, cognitive & physical function, and quality of life. All outcomes collected in-person unless otherwise noted

3.2 Study population

The target population is patients aged 65 years and older who are having elective, open inguinal hernia surgery for initial, non-incarcerated, unilateral inguinal hernias.

3.3 Study location

The study will be conducted at general surgery clinics for 2 sites:

(1) VA North Texas Healthcare System in Dallas, TX
(2) Michael E DeBakey VA in Houston, TX

3.4 Duration of enrollment and follow up

Participants will be followed for a total of 6 months after surgery. For total study duration, recruitment will start 18 months after funding begins and will conclude after a total of 24 months of recruitment. Data collection will terminate 6 months after the last patient is enrolled.

3.5 Randomization and stratification

We will randomly assign older patients having inguinal hernia surgery to one of the two study arms: (1) local anesthesia or (2) general anesthesia. Our goal for enrollment will be 40 patients in

Assessment	Screening: Visit-1 (Initial Surgery Clinic Visit)	Baseline, Enrollment, Randomization: Visit 1 (Day 0: Initial Clinic Visit)	Treatment Visit 2 (During Surgery)	Treatment Visit 3 (After Surgery & Before Same Day Discharge)	Treatment Visit 4 (48 Hours After Surgery)	Treatment Visit 5 (2-Week Postoperative Visit)	Follow-Up: Final Visit (6-Month Postoperative Visit)
Informed Consent Form	X						
Demographics	X						
Medical & Surgical History	X						
General Physical Examination	X						
Current Medications	X						
Inclusion/Exclusion Criteria	X						
Blood Chemistries		X					
Hematology		X					
Urine Analysis		X					
Vital Signs		X	X	X		X	
Enrollment/Randomization		X					
Physical Function Assessment: Katz Index		X			X	X	X
Delirium & Cognitive Assessment: (1) Confusion Assessment Method short form, (2) Montreal Cognitive Assessment (5 minute version), (3) Trail Making Tests Parts A & B,		X		X	X	X	X
Frailty Assessment: Fatigue, Resistance, Ambulation, Illness and Loss of Weight Scale		X					
Pain Assessment: Visual Analog		X		X	X	X	X
Quality of Life: Carolinas Comfort Scale		X			X	X	X

- Demographics: if patient age is <65 years old, they will not be eligible
- Medical & surgical history:
    - if the patient had prior hernia surgery on the affected side, then they will not be eligible
    - if the patient has a known allergy to local anesthesia or general anesthesia (or a reaction such as malignant hyperthermia), then they will not be eligible
    - If the patient has medical conditions that are relative or absolute contraindications to the use of general anesthesia or to surgery (heart failure with ejection fraction <20%, chronic obstructive pulmonary disease with a significant oxygen requirement, Child's C cirrhosis, any terminal disease with life expectancy < 6 months), then they will not be eligible
    - If the patient is taking any medication that might adversely interact with anesthesia and cannot be discontinued, then they will not be eligible

Specify allowable range of time prior to study entry during which all screening evaluations to determine eligibility must be completed. List and briefly describe all screening evaluations in bulleted format.

Include only those evaluations that are necessary to assess whether an individual meets enrollment criteria. Discuss the sequence of events that should occur during screening and the decision points regarding eligibility. List the time frame prior to enrollment within which screening tests and evaluations must be done. For example, DXA must be measured within 30 days of study enrollment.

Consenting Procedure

Potential participants will be identified by study research assistants 24-48 hours prior to their initial visit to the surgeon to discuss whether they will undergo hernia repair. We have obtained a waiver of informed consent from the IRB to review upcoming clinic records for this purpose. Once the consulting surgeon has determined that the patient needs surgery and the patient agrees to proceed with the operation, our research assistants will approach the patient to obtain consent for screening and study procedures (as a single consent form). At that time, the research assistant will explain the study purpose and discuss the potential risks/benefits of local anesthesia and general anesthesia, including the possibility of allergic reactions, heart attacks, stroke, blood clots, low blood pressure, pain, nausea, vomiting, and cognitive changes.

Patients who are not enrolled at the initial clinic visit may still be enrolled at subsequent preoperative visits as long as they occur at least 24 hours prior to surgery.

We will maintain records of informed consent as follows: a hard copy will be given to the patient and also stored in a secured filing cabinet in the PI's research office. We will also scan a copy

anesthesiologist automatically records data on the below information as part of the routine anesthesia record.

- Vital signs: maximum, minimum, and median values for systolic and diastolic blood pressure and heart rate
- Total operating room time: the difference between the time the patient enters the operating room and the time the patient leaves the operating room
- Time for surgery: the time from the start of the operation (skin incision) and the end of the operation (skin closure)
- Adverse events, serious adverse events, and intraoperative complications
- Volume of fluids administered
- Minimum alveolar concentration of volatile anesthetic
- Dose of local anesthesia used

- Visit 3 (After Surgery & Before Same Day Discharge)
  - Inguinal hernia repair is typically an outpatient procedure where the patient is observed for several hours to ensure that there are no immediate complications of surgery or anesthesia and that patients are able to ambulate, tolerate oral intake, and manage basic self-care with assistance from family or other caregivers. From the time the patient leaves the operating room until the time the patient leaves the hospital, we will assess the following:
    - Vital signs: We will record any episodes of hypotension (mean arterial pressure <60) or hypertension (systolic blood pressure >180 or diastolic > 110), fever (temperature >101.6 F), tachycardia (heart rate >120), or poor oxygenation (oxygen saturation on pulse oximetry <85%). This information will be obtained from the post-anesthesia care unit and stepdown unit records.
    - Delirium and cognitive assessment: we will administer a battery of tests to assess (1) cognitive function (overall and particular domains including processing, visual scanning, attention, mental set-shifting, executive function, and verbal memory) and (2) delirium risk
      - Confusion Assessment Method (short form)
      - Montreal Cognitive Assessment (5-minute version)
      - Trail Making Tests Parts A and B
    - Time in post-anesthesia care unit: after surgery, all patients who had their operations performed under general anesthesia are observed in a unit with a nurse:patient ratio of ≤2:1, similar to intensive care units. This level of nursing care is required to quickly detect immediate complications of anesthesia, including respiratory failure and hypotension. Our research assistants will use the nursing records to determine what time the patient entered the unit and what time they were transferred to the next phase in care: the step-down unit. Patients having

7.1.1 Definition of adverse events (AE)

Adverse event means any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention-related (21 CFR 312.32(a)).

7.1.2 Definition of serious adverse events (SAE)

A SAE is any event that results in death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when appropriate medical judgement indicates they may jeopardize the patient and may require medical or surgical interventions to prevent outcomes listed in this definition.

7.1.3 Definition of unanticipated problems (UP)

Unanticipated problems involving risks to participants or others include any incident, experience, or outcome that meets all of the following criteria:

- Unexpected in terms of nature, severity, or frequency, given (1) the research procedures that are described in the protocol-related documents (IRB protocol or informed consent), and (2) the characteristics of the patients being studied
- Related or possibly related to participation in the research, where "possibly related" means there is a reasonable probability that the incident, experience, or outcome may have been caused by the research procedures
- Suggests the research places participants (or others) at a greater risk of physical, psychological, economic, social, or other harm than was previously known or recognized

7.1.4 SAE/AE potentially occurring with either local or general anesthesia

- Allergic reaction: if patients develop hives (raised red lesions) or a significant and persistent rash after administration of local or general anesthesia, this will be managed per the usual hospital protocol. Patients will receive a combination of epinephrine, corticosteroids, and antihistamines. Any patient with an allergic reaction will also be admitted for 24 hour observation that includes monitoring of vital signs, and blood pressure support with intravenous fluids. If the allergic reaction occurs during the operation, then the surgery will be canceled along with all assessments and will be rescheduled after it is determined that the operation can be performed safely without the allergic reaction.
- Hematoma or seroma: a collection of fluid in the tissues over the incision site or in the scrotum that is detected on physical exam constitutes either a seroma or hematoma. If minimal symptoms present, this will be managed by observation. If persistent and significant symptoms occur, the seroma/hematoma will initially be managed by aspiration under local anesthesia up to two times. If the symptoms persist after aspiration, then the patient can be taken back to the operating room for surgical evacuation.
- Infection: we define postoperative infections according to the National Surgical Quality Improvement Program definitions of superficial, deep, or organ space.[16] Infections will be managed by obtaining source control via opening the wound

and providing 10 days of oral antibiotics for infections not involving surgical mesh. If infections involve the mesh, then oral or intravenous antibiotics and may be attempted at the discretion of the attending surgeon versus mesh explantation.

- Injury to vessel: during dissection and/or mesh placement, there is the possibility of injury to the femoral or inferior epigastric vessels. If bleeding occurs at these vessels that cannot be resolved by applying pressure, this will be categorized as vascular injury. The inferior epigastric vessel is typically ligated without consequence if injured. Injury to femoral vessels will result in consult to vascular surgery for repair.
- Neuralgia/chronic pain: if patients experience pain at/near the site of surgery for >3 months after the operation, they are considered to have neuralgia. This will be managed initially by consultation with the pain service for injection of steroids and local anesthetic at the site for up to 3 times. If this proves unsuccessful, the patient will be considered for surgical neurectomy.
- Spermatic cord injury or orchitis: during surgical repair, the spermatic cord (including vas deferens, spermatic artery, venous plexus) are mobilized away from the hernia sac. If the surgeon identifies injury (division of the vas deferens, bleeding from artery or veins that requires intervention beyond holding pressure) or if there is involution of the testicle on the side of the surgery (identified by pain beyond the ordinary, swelling in the groin, ultrasound showing no flow) then we will categorize as a spermatic cord injury. Intraoperatively, a vas deferens injury will result in consultation of urology for repair. Arterial and venous injuries are generally too small to repair intraoperatively, but vascular surgery service can be consulted for evaluation. Postoperatively, there is no treatment for cord injury other than pain control, urologic evaluation, and possible removal of testicle on the injured side.
- Thromboembolic event: if patients develop deep venous thrombosis or pulmonary embolism from surgery, the diagnosis will be confirmed by the appropriate imaging tests (typically lower extremity ultrasound and CT of the chest) and treatment with anticoagulation (therapeutic heparin or Lovenox) will be immediately started. Patients will be admitted until they are clinically stable, and we will transition the patient to oral anticoagulation as soon as clinically feasible and arrange for evaluation by the hematology service for long-term follow-up and treatment. Additionally, any supportive care (oxygen, intravenous fluids, medications to support blood pressure) will be provided at the discretion of the treating team. Similarly, myocardial infarction and cerebrovascular accident will be treated by consulting specialists (cardiology or neurology) per the usual hospital protocol. These include anticoagulation and antiplatelet agents along with supportive care. Unless the patient becomes unable to complete study assessments, these complications would not result in changing the study schedule. If patients are unable to complete assessments during the specified time points, then that information would be missing for their records.

7.1.5 SAE/AE occurring only with general anesthesia

- Malignant hyperthermia: some patients can have a severe reaction to general anesthesia that includes a substantial increase in body temperature (sometimes as

benefits of your research may be different than initially presented to the IRB.
- A breach of confidentiality.
- Incarceration of a participant in a protocol not approved to enroll prisoners.
- Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a research participant.
- Complaint of a participant when the complaint indicates unexpected risks or cannot be resolved by the research team.
- Protocol violation (accidental or unintentional change to the IRB approved protocol) that harmed participants or others or that indicates participants or others may be at increased risk of harm.
- Any other event that indicates participant or others might be at risk of serious, unanticipated harms that are reasonably related to the research.

7.4 Follow-up for Adverse Events

AEs will be followed until resolution even if this extends beyond the study-reporting period. Resolution of an AE is defined as the return to pretreatment status or stabilization of the condition with the expectation that it will remain chronic.

Describe how AEs will be followed until resolved or considered stable. Specify duration of follow-up.

7.5 Safety Monitoring

The NIA Guidelines on Data and Safety Monitoring generally require that a NIA-appointed Data and Safety Monitoring Board or Safety Officer monitor clinical trials. Please see the Safety Monitoring Guidelines (a link will be inserted here).

Inguinal hernia repair is generally considered a safe procedure with very few (<1% risk of SAE).[3,7,8] Both local and general anesthesia are considered reasonable standard of care for the operation, and there are generally few AE or SAE resulting directly from the anesthesia modality. Most complications, AE, SAE, or UP result from the surgery rather than anesthesia, and the surgical technique is the same for both study arms. Consequently, we will convene our data safety and monitoring board to review all AE, SAE, and UP once 50% of expected enrollment is obtained. The UT Southwestern Department of Surgery maintains a standing DSMB for monitoring of all trials in our department. Given that all published studies of local versus general anesthesia have been completed without significant rates of adverse events or early termination, it is highly unlikely that the use of stopping rules will be required.

8 INTERVENTION DISCONTINUATION

The study will be halted if three grade 3 AEs are identified and determined to be probably related or definitely related to the study interventions (distinct from surgical complications). The PI will notify NIA and the IRB immediately when the third grade 3 event is reported, and enrollment screens will stop accepting new study participants.

Participants may voluntarily withdraw/stop participation at any time and for any reason (noted on consent form). If participants withdraw, we will make every effort to obtain permission and convince them to complete planned evaluations and will try counseling patients to re-enroll in the study if possible. We will also make every effort to continue monitoring and treating AE/SAE for participants who withdraw.
There will be no replacement of participants who withdraw early. Additionally, we will continue to follow participants, with their permission, even if the study intervention is discontinued.

List criteria for discontinuing the study intervention/product (e.g., development of toxicities, study closure by institute) for a participant and methods for determining when criteria are met.

If relevant, include criteria for temporary discontinuation of treatment and define its length.

Also note that subjects may withdraw voluntarily from participation in the study at any time and for any reason. Participants should continue to be followed, with their permission, even if the study intervention is discontinued. Discuss any modifications to the schedule and duration of continued follow-up and indicate the evaluations to be completed while the participant is either temporarily or permanently discontinued from study intervention but followed for outcomes, if applicable.

This section should also include a discussion of replacement of subjects who discontinue early, if replacement is allowed.

Note: It is vital to collect safety data on any subject discontinued due to an AE or SAE. In any case, every effort must be made to undertake protocol-specified safety follow-up procedures. If voluntary withdrawal occurs, the subject should be asked to continue scheduled evaluations, complete an end-of-study evaluation, and be given appropriate care under medical supervision until the symptoms of any AE resolve or the subject's condition becomes stable.

9 STATISTICAL CONSIDERATIONS

9.1 General Design Issues

9.1.1 General approach

This is a two-arm (parallel) pilot randomized trial where adults aged 65 years and older are assigned to have their inguinal hernias repaired under either local (arm 1) or general anesthesia (arm 2).

9.1.2 Central hypothesis

The overarching hypothesis driving design of this study is that performing inguinal hernia surgery under local rather than general anesthesia for patients aged 65 years and older will

significantly reduce operative and recovery time, will lead to fewer complications, and will lead to better cognitive and physical recovery from surgery. This hypothesis will eventually be tested in a multisite randomized trial whose design will be informed by this pilot randomized trial.

The hypothesis for this pilot study is that we will be able to successfully recruit, randomize, and retain enough patients for a fully powered multisite randomized trial. Additionally, we plan to test study procedures for screening, enrollment, randomization, outcome measurement, and retention while also evaluating whether we can reduce the study burden by eliminating some of the study instruments. We also hypothesize that, although the pilot study (by definition) is not powered to detect differences between groups, that the local anesthesia group will have fewer complications and better physical and cognitive function (though the difference may not be statistically significant).

9.1.3 Justification for pilot design

The chances of completing a successful multisite randomized clinical trial are increased by testing study procedures and processes on a smaller scale prior to conducting a fully powered trial.[18,19] This will enable us to identify and address problems prior to initiating the fully powered study. Conducting a pilot study also allows us to test study instruments and potentially reduce the time burden at each evaluation visit by determining whether study measures are statistically redundant (the other measures explain a substantial portion of one measure's variance). Reducing the time burden for participants is an important step to enhance the completeness of data collection by minimizing missing data and reducing withdrawals from the study.

As outlined below and in the attached grant proposal, data from the pilot study will also be used for preliminary estimation of effect sizes for the future randomized trial. As the pilot is, by definition, not fully powered to detect all relevant differences between groups, this analysis is entirely exploratory.

9.1.4 Primary outcomes and hypotheses

1) Outcome: Rates of enrollment
    a. Hypothesis: Based on our preliminary data, at least 75% of eligible patients will agree to be randomized.
2) Outcome: Proportion of participants completing all study visits
    a. Hypothesis: We will be able to follow 100% of patients up to their 2 week postoperative visit (as essentially all patients keep this appointment in our clinical practice), and we will be able to follow at least 90% of patients at the six month time point.
3) Outcome: Proportion of missing data
    a. Hypothesis: Missing data on study instruments will be <5%
4) Outcome: Time to complete study evaluations and instruments
    a. Hypothesis: Total time to complete each study evaluation will be acceptable to patients and <30 minutes.
5) Outcome: Participant satisfaction with study procedures and instruments
    a. Hypothesis: Overall time burden for instrument completion will be acceptable to patients

6) Outcome: Whether survey instruments can be eliminated due to redundancy
    b. Hypothesis: One or more study instruments can be eliminated (thus reducing the time burden) because the other instruments may predict a substantial portion of variance
(7) Outcome: Estimate sample size for fully powered randomized trial.
    a. Hypothesis 1: Using data from the pilot study, we will be able to establish stable estimates of the necessary sample size for a randomized trial.
    b. Hypothesis 2: We will be able to identify the optimal primary outcome for a multisite randomized trial by balancing the necessary sample size needed to adequately power the study versus the clinical significance of each outcome.

9.1.5 Secondary outcomes and hypotheses

Again note that this pilot trial is not powered to detect differences in the secondary (clinical) outcomes described below. Our hypotheses reflect expected findings for a larger, multisite randomized clinical trial that will follow this pilot study.

1) Outcome: Quality of life
    a. Hypothesis: quality of life will be significantly improved when older adults have their inguinal hernias repaired under local rather than general anesthesia.
2) Outcome: Physical function
3) Hypothesis: physical function (activities of daily living) will be significantly improved when older adults have their inguinal hernias repaired under local rather than general anesthesia.
4) Outcome: Cognitive function
    a. Hypothesis: Cognitive function will be significantly improved when older adults have their inguinal hernias repaired under local rather than general anesthesia.
5) Outcome: Pain
    a. Hypothesis: Pain will be similar for older adults having hernia surgery regardless of anesthesia modality.
6) Outcome: Postoperative complications
    a. Hypothesis: The overall incidence of postoperative complications will be significantly reduced when older adults have their inguinal hernias repaired under local rather than general anesthesia. This will mostly be due to decreased rates of urinary retention (a common complication of general anesthesia).
7) Outcome: Operative and anesthesia times
    a. Hypothesis: Time for surgery (incision to closure) and anesthesia (enter to exit operating room) will be significantly decreased when older adults have their inguinal hernias repaired under local rather than general anesthesia.
8) Outcome: Recovery time (time spent in the post-anesthesia care and stepdown units)
    a. Hypothesis: Time spent in the post-anesthesia care and stepdown units after surgery will be significantly decreased when older adults have their inguinal hernias repaired under local rather than general anesthesia.

State the statistical hypotheses.

Describe the reasons for choice of study design (e.g., parallel groups, crossover, immediate versus deferred intervention, factorial, large simple trial, equivalency or non-inferiority trial); why certain design features were chosen (e.g., for a crossover trial, how the length of the washout period was chosen).

Describe the primary and secondary hypotheses and the primary and secondary outcome measures as well as their validity and reliability.

9.2 Sample Size and Randomization

Describe sample size calculation and effect size with respect to power. Specify the test statistic; Type I and Type II error rates; assumed event rate event rate for dichotomous outcome (mean and / or variance for continuous outcome) for each study arm; assumed rates of drop-out, withdrawal, cross-over to other study arms, missing data, etc.; and approach to handling withdrawals and protocol violations, in terms of an "intent to treat" approach.

9.2.1 Treatment Assignment Procedures

We will randomly assign older patients having inguinal hernia surgery to one of the two study arms: (1) local anesthesia or (2) general anesthesia. Our goal for enrollment will be a total of 80 participants with 40 participants in each arm and a total of 40 participants from each site. We will use a stratified randomization scheme with blocking within strata. Stratification factors include hospital location (Dallas or Houston) and age (65-75 or 75+ years). Equal allocation by strata will be used so that differences among hospitals and age groups will be balanced. Randomized assignments will be generated ahead of time for each combination of strata and placed within stored and numbered envelopes kept at each hospital location. We will generate 20% more assignments than necessary to allow for potential withdrawals. Before patients are enrolled, physicians, patients, and research coordinators will not know which anesthesia modality will be assigned. Once patients are enrolled, the next envelope that applies to that participant (based on stratification factors) will be selected and labeled with the date and time of enrollment, the patient's name, and the research team member responsible for enrollment. The labeled and unopened envelope will be photographed for our records and the envelope number will be recorded in the participant's record.

9.2.1 Masking treatment assignment

Although the patient and operating team (surgeon, anesthesiologists, nurses) will unavoidably be aware of which study arm participants are assigned to, the investigative team will remain blinded to treatment assignment at all times. Research assistants collecting baseline, peri-, and postoperative outcomes will be blinded to study assignment when conducting their assessments. For the baseline assessment, the research assistant will not open the envelope containing the treatment assignment until the baseline assessment is complete. For subsequent assessments, a different research assistant will interact with the patient. The investigator and study team will also be blinded to treatment assignment until after data analysis is complete, with the exception of the statistician (Dr. Reisch) who will be analyzing the data. All study results will be presented to the investigator and DSMB with patients identified as belonging to "group A" or "group B"

99) to facilitate easy counting of missing items vs total items to complete. Research assistants will generate a report showing overall percentage of missing data (number of missing items/current number of possible items for each patient) and the percent of missing data for each patient.

b. Timing: Each bi-weekly team meeting will involve a review of missing data at the overall study and patient level.

4) Outcome: Time to complete study evaluations and instruments
    a. Measurement: Research assistants will time participants while completing each study research form and will also time the entire encounter at each study visit.
    b. Timing: Data will be collected at each visit and will be reviewed by the study team at the last team meeting of each month to establish reasonably stable estimates of time.
5) Outcome: Participant satisfaction with study procedures and instruments
    a. Measurement: At each visit, after completing all other study forms and procedures, participants will be asked to complete a brief 10-item Likert-type score to measure overall satisfaction with the study visit and a similar item assessing satisfaction with the time burden of the instruments. Additionally, we will conduct a brief interview with open-ended questions at the end of each visit asking patients to provide any feedback on the study procedures or instruments. These will not be recorded but field notes by the research assistant will be taken.
    b. Timing: Assessments will occur at each study visit and will be reviewed at the last team meeting of each month.
6) Outcome: Whether survey instruments can be eliminated due to redundancy
    a. Measurement: To determine whether we can reduce the survey burden by eliminating redundant measures, we will employ methods outlined by Harrell for data reduction.[22] Each survey instrument will be evaluated as the dependent variable in a separate linear regression with the scores of all other instruments used as predictors, along with demographic information. The adjusted R^2 (explained variance) for each regression will be estimated. Any instrument where the R^2 exceeds 40% will be eliminated based on the idea that little additional information is provided by including that instrument (i.e. the other surveys explain a substantial portion of the information contained within that instrument).
    b. Timing: We will assess survey redundancy once 25% of planned enrollment is achieved and we will measure again at 75% enrollment. This will provide reasonable data stability for estimation and also provide time for us to test study procedures after eliminating any instruments that are found to be redundant.
7) Outcome: Estimating sample size for fully powered trial
    a. Measurement: For continuous variables, we will estimate means and standard deviations. For categorical variables, we will estimate proportions and 95% confidence intervals.
    b. Timing: Final sample size estimate will be performed after data collection for the last patient is complete.

1) Outcome: Quality of life
    a. Measurement: The Carolinas Comfort Scale (CCS) was developed specifically to measure quality of life in patients having hernia repair.[23] The instrument consists of 8 items on a 6-point Likert-type scale. The Cronbach's alpha was 0.979 in the original development paper and 0.95 on a subsequent international validation study.[21] The CCS demonstrates superior discrimination when compared to generic quality of life instruments (SF-36), with reasonable test-retest reliability (kappa coefficients for questions range from 0.40-0.60 for all but 1 item. Additionally, the CCS is used as the primary quality of life instrument for the International Hernia Mesh Registry because it can be rapidly administered, is well accepted by patients, is highly reliable, and typically has only 10-15% missing data when used for the international registry.[21] The CCS can be scored as a summary of all items and as a binary score for the presence or absence of symptoms. We will use a 0.5 standard deviation difference on the continuous scale as the minimal clinically important difference.[24]
    b. Timing: The CCS will be measured at baseline, 48 hours after surgery, at 2 weeks after surgery, and at 6 months after surgery.
2) Outcome: Physical function
    a. Measurement: We will measure independence in activities of daily living with the 6-item Katz Index, a long-established measure for physical/functional status for individuals expected to have at least some degree of disability.[25] Prior work demonstrates coefficients of scalability ranging from 0.74-0.88, indicating the Katz Index offers a useful cumulative scale.[25] We will score the instrument on a 0-6 scale, indicating the number of activities where the participant is partially or fully dependent. A 0.5 standard deviation difference will again represent the minimal clinically important difference.[24]
    b. Timing: Measurement will occur at baseline, at 2 weeks after surgery, and at 6 months after surgery.
3) Outcome: Cognitive function and delirium
    a. Measurement
        i. Confusion Assessment Method (CAM) short form: The CAM is the most widely used instrument for detection of delirium, with typical sensitivity of 94% and specificity of 89% across multiple studies.[26] The instrument is scored on a 7-point scale and we will consider a 0.5 standard deviation difference as the minimal clinically significant difference.[24] Items include evaluation of attention, disorganized thinking, and altered levels of consciousness.
        ii. Montreal Cognitive Assessment (MoCA) 5-minute form: The MoCA is a widely used tool for detection of dementia and other cognitive impairment, and is sensitive when used as a global cognitive screening tool.[27] The 5-minute form was developed to (1) reduce the significant time burden of the longer version which typically takes 15 minutes to complete, while (2) maintaining the psychometric advantages of the longer form, and (3) facilitating assessment by

9.5.2 Analysis of secondary/clinical outcomes

For comparison of secondary/clinical outcomes we will use the Wilcoxon rank-sum test to compare continuous variables and the likelihood ratio chi-square to compare proportions of categorical variables. Our prior work suggests that there are no significant differences in effects by subgroups categorized by comorbidity or gender. Consequently, we do not plan any subgroup analysis.

Describe the descriptive and inferential statistical methods that will be used to analyze the outcomes and other study data. Specify any confounding variables for which it is anticipated adjustment will be made.

In accordance with NIH policy, unless data from prior studies strongly support no significant differences of clinical or public health importance in the intervention effect between gender and racial/ethnic subgroups, investigators should include a statement noting that a valid analysis of the intervention effect will be performed in these subgroups. If data from prior studies do not strongly support the existence of significant differences in the intervention effect between subgroups, then the analyses need not have high statistical power for detecting clinically meaningful differences.

9.5.3 Missing data

A complete-case analysis will be performed for the primary analysis of survey and other data. To test sensitivity of the survey results to missing data, we will use multiple imputation with either Poisson or negative binomial regression (depending on overdispersion). For instruments scored by time to completion, we will employ multiple imputation with chained equations. Analysis will then proceed using post-imputation methods that take into account the variance of imputed values across samples (i.e. "pooling rules").

10 DATA COLLECTION AND QUALITY ASSURANCE

10.1 Data Collection Forms

Data will be collected for each participant by a research assistant blinded to the treatment assignment. For the baseline assessment, all forms will be completed after verifying eligibility but before opening the envelope with the treatment assignment. For subsequent assessments, another research assistant not familiar with the patient's assignment will complete all case report forms. Every case report form will be reviewed, approved, and signed by the site principal investigator and by the project principal investigator.

Case report forms will be provided for each patient and instructions for completion maintained in our Manual of Procedures, which will be given to study staff at each participating site.

Data will be entered into an online, secure REDCap database to help maintain participant confidentiality. Additionally, separate databases will be maintained with (1) participant identifying information and (2) data from case report forms, which will be labeled with the participant's study number. After entering data into the database, the participant can only be

identified by combining the two datasets. Otherwise, all data entry is guided by the participant's study identification number.

Indicate how information will be collected for each participant and by whom. For example if a blinded observer will perform outcome assessments, state who this person will be. Describe methods for maintaining confidentiality of participant records. Refer to Manual of Procedures (MOP) for description of study forms (also called Case Report Forms).

10.2 Data Management

The principal investigator will monitor data for both sites. The principal investigator will design and modify the study data and the REDCap database storing research data. The principal investigator will also be responsible for performing quality control checks, preparing data quality reports, and preparing progress reports. In consult with the biostatistician (Dr. Reisch), the principal investigator will be responsible for design and analysis of research questions.

The site principal investigator in Houston will assist with data monitoring at that site.

There will not be a data coordinating or management center.

Data collection forms will be maintained in paper and electronic forms.

The principal investigator will maintain records in accordance with good clinical practice guidelines that include:

1. IRB correspondence related to the clinical protocol, including but not limited to approval notifications, adverse event reports, and interim reports.
2. Current and past versions of IRB-approved protocols, consent forms, and subject recruitment pamphlets
3. Signed investigator agreements and certification of financial conflicts of interest
4. Bio sketches for all study staff
5. Certificates of required research training for all study staff
6. Master randomization list
7. Signed consent forms
8. Complete Case Report Forms signed and dated by the investigator
9. Source documents or certified copies of source documents
10. Copies of correspondence to site investigator
11. Subject screening and enrollment logs
12. Subject identification code list
13. Final clinical study report

The investigator will retain the above records and reports for up to two years after the study is complete.

Briefly describe clinical site responsibilities in data collection and management.

STUDY TEAM ROSTER

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regional, or general anesthesia.[10] They did not specifically look at older patients but the mean age in each group was 56 years old. They found that the total operative time was five minutes faster for the local anesthesia group (90 versus 95 minutes) the incidence of postoperative pain requiring opioids and catheterization for urinary retention was decreased by 29% for the local compared to general anesthesia group and the rate of unplanned admission was decreased by 19%. A cost-effectiveness analysis conducted by the same group indicated that hospital costs were lower in the local anesthesia group (a difference of €311/$378) and total healthcare costs were also lower (€316/$384). A second trial from Scotland randomized 279 patients to local or general anesthesia, with a mean age of 55 years for both groups.[8] This study did not find a significant difference in operative time, complications, length of stay, pain, or neurocognitive recovery as measured by a battery of tests. However, like the paper by Nordin et al., they did not specifically analyze outcomes in older patients which would tend to dilute the potential benefits of local anesthesia. Equally important, this study focused almost exclusively on healthy patients with smaller hernias, as evidenced by >90% of patients having an American Society of Anesthesiology score of 1 or 2 and a mean total surgical time of 48 minutes for each group (nearly 50% of operative time in the Nordin study).

There are several observational studies that compare outcomes from hernia repair under local or general anesthesia, and these mostly suggest that local anesthesia is associated with shorter operative time (5-10 minutes), fewer complications (1-3% reduction), and enhanced quality of life. [2,11-15] However, only two of these studies look specifically at outcomes for older adults and both suffer from a poor approach to risk adjustment.[11,12] Additionally, all the observational studies have a limited assessment of complications and failed to effectively evaluate rates of urinary retention and catheterization after surgery. Urinary retention is the most common complication of general anesthesia after hernia repair and results in considerable discomfort for patients who are catheterized to relieve it. Additionally, when patients do not resolve retention in a timely fashion, it results in the need for unplanned admission which increases hospital costs.[6]

The intervention chosen for testing in this study is the choice of anesthesia (local or general) for unilateral inguinal hernia repair. These are the primary methods of anesthesia for inguinal hernia surgery by most surgeons (though some perform the operation under spinal or regional anesthesia, this is rare). Both approaches are used in clinical practice with acceptable known risks and complications. General anesthesia is associated with risks of hypotension, venous thromboembolism, heart attack, stroke, pulmonary dysfunction, cognitive dysfunction, allergic reaction, and malignant hyperthermia. The main risks of local anesthesia include allergic reaction and hypotension (when the anesthetic is improperly injected into a blood vessel).

3 STUDY DESIGN

3.1 Summary & objectives

This will be a pilot randomized trial with two arms for patients having open unilateral inguinal hernia repair: (arm 1) local anesthesia versus (arm 2) general anesthesia. Each arm will recruit 40 patients.

The primary objective is to conduct a pilot randomized trial comparing outcomes of inguinal

each arm, equally distributed by site. We will use a stratified randomization scheme with blocking within strata. Stratification factors include hospital location (Dallas or Houston) and age (65-75 or 75+ years). Equal allocation by strata will be used so that differences among hospitals and age groups will be balanced.

3.6 Blinding

Research assistants will be blinded to study assignment when conducting all assessments.

A description of the trial design should include:

- *Type/design of trial (e.g., placebo-controlled, double-mask, parallel design, open-label, dose escalation, dose-ranging)*
- *Specific statement of the primary and secondary outcomes (must be consistent with Study Objectives)*
- *Study population and groups/arms including sample size (including a table, if appropriate)*
- *Study location (e.g., in-patient or out-patient, clinic, community)*
- *Approximate duration of enrollment period and follow-up (specify individual participant vs. entire trial)*
- *Description of intervention and administration*
- *Randomization, blinding and any stratification*
- *Other protocol specific details, such as centralization of evaluations (e.g., central laboratory or central reading center for clinical scans)*

3.7 Study timeline

Table 1 (next page) outlines the study timeline. This includes completion of proposal aims 1 and 2, which will identify and prioritize study outcomes to supplement the list of measurements shown in section 6. Pre-trial data collection and analysis of interviews and focus groups will be completed by 18 months. We will then begin recruiting participants for the pilot randomized trial over a period of 24 months, allowing an additional 6 months for follow up of the last enrolled participant. In year 3, we anticipate beginning to write manuscripts and our R01 application based on the data from our pilot study. This will leave sufficient time to revise the grant in year 4 if the initial submission is not funded.

Total Operating Room Time			X				
Time for Surgery			X				
Time in Post-Anesthesia Recovery Room				X			
Time in Step-Down Recovery Room				X			
Urinary Function/Unplanned Catheterization				X			
Unplanned Admission				X			
Adverse Events			X	X	X	X	X

into the electronic medical record and store another scanned copy on our secure electronic research server. All informed consent forms will have a date and version number on the top right corner of all pages. The consent will include permission to contact participants by phone if needed to discuss any changes to the study protocol or other issues that occur during the trial.

Before any screening procedure is performed, informed consent must be obtained. Indicate whether there will be two consenting processes or a single informed consent form that describes both the screening and study procedures.

State which study staff will conduct the consent process and how it will be implemented.

Describe individual's education and informed consent process; any plan for review of consent document in case changes may be required; and how documentation of signed consent will be maintained by the study.

6.2.2 Enrollment, Baseline, and/or Randomization

Enrollment

Enrollment is defined as the date that screening criteria are met and the individual agrees to participate and be randomized to either local or general anesthesia. The enrollment date will be recorded on the participant's case report form.

The act of enrolling a study participant should be defined. Since informed consent must be obtained if screening procedures are not a part of routine care, some studies use two informed consents: one for screening and one for enrollment. In this case the enrollment date is day the individual has met all the screening criteria and signs the second informed consent form.

Some studies utilize a single informed consent form that describes both screening and study procedures. In these studies enrollment is defined as the randomization date or as the date all of the screening criteria are met and the individual agrees to participate

In any case the enrollment date should be defined and recorded on a case report form along with the allowable window between screening and randomization.

Baseline Assessments

In addition to the information obtained as part of the screening evaluation, our research assistants will also obtain the following information:

- Laboratory evaluations: as part of the routine preoperative evaluation at our hospital sites, the following labs are obtained: blood chemistry, hematology/complete blood count, urine analysis. None of these labs will be ordered as part of our study, but we will record the information from this

surgery under local anesthesia are sent directly from the operating room to the step-down unit.
        - Time in step-down unit: Once general anesthesia patients meet criteria in the post-anesthesia care unit (awake, normal respiratory drive and blood pressure), they are transferred to the step-down unit. All local anesthesia patients are transferred directly to the step-down unit once their operation is complete. In this unit, patients are provided food and liquids to test their ability to tolerate oral intake. Patients also are asked to ambulate and void to ensure that they are capable of self-care and have not developed urinary retention. Our research assistants will use nursing records to identify the time of entry and departure from the step-down unit.
        - Urinary function/unplanned catheterization: research assistants will review nursing notes to determine whether patients were able to void or whether they required assistance. Our standard clinical protocol is that if patients have not urinated by 4 hours after surgery, they will undergo a bladder scan. If >200cc of urine is found in the bladder, the patients undergo in-and-out catheterization and are observed until they void again. If still unable to void, the patient has a foley catheter placed, is started on medication for prostatic hypertrophy, and arrangements are made with the urology service to undergo outpatient voiding studies and removal of the catheter within 1-2 weeks.
        - Unplanned admission: since most inguinal hernia surgeries are outpatient procedures, our nursing assistants will check the medical record the day after surgery to see if the patient was able to leave or was admitted. If admitted, we will contact the team to determine the reason for admission.
        - Adverse events and serious adverse events
- <u>Visit 4 (48 Hours After Surgery)</u>
    - Research assistants will contact the patient by phone to complete assessments. This may be completed at any time from 48 hours to 1 week after surgery.
    - Physical function assessment: we will administer the 6-item Katz index to measure independence in activities of daily living
    - Delirium and cognitive assessment: we will administer a battery of tests to assess (1) cognitive function (overall and particular domains including processing, visual scanning, attention, mental set-shifting, executive function, and verbal memory) and (2) delirium risk
        - Confusion Assessment Method (short form)
        - Montreal Cognitive Assessment (5-minute version)
        - Trail Making Tests Parts A and B
    - Pain assessment: we will administer a 10-point visual analog scale to quantify pain levels related to the hernia
    - Quality of life: we will use the 8-item Carolinas Comfort Scale to

high as 113° F) and rigid/painful muscles. If this occurs during surgery, the operation will immediately be stopped and patients will receive intravenous dantrolene. Patients will be admitted to the intensive care unit where they will continue to receive care including cooling blankets and fluids, oxygen, correction of electrolyte abnormalities, and standard medications to manage tachycardia and hypotension. We will also monitor kidney function and changes in creatinine kinase. The occurrence of this complication will not change the study intervention regimen or the schedule of participant assessments.

- Urinary retention: per our standard hospital protocol, if patients are unable to urinate by four hours after surgery, we will perform a bladder scan. If >200 mL of urine is seen, the patient will receive an in-and-out catheterization followed by observation for up to an additional four hours. If the patient is still unable to urinate, they will have a Foley catheter placed, be admitted for overnight observation, and be evaluated by urology. Typically, the patient goes home with a Foley leg bag and undergoes urodynamic testing 1 to 2 weeks later after being discharged with medication for benign prostatic hypertrophy. The occurrence of urinary retention will not change the study intervention regimen or the schedule of participant assessments.

7.2 Methods and Timing for Assessing, Recording, and Analyzing Safety Parameters

7.2.1 Assessing and recording

At each study visit, research assistants will actively elicit evidence of SAE and AE by asking questions related to symptoms and conducting physical exam in conjunction with the clinical team (which should be examining for these complications as well up to the 2 week postoperative time point). For the 6 month visit, symptoms will be elicited by asking questions via phone. At each time point, after reviewing the list of SAE and UE, an open-ended question will be asked regarding whether the patient is having any other additional problems or concerns. Any SAE/AE will be conveyed to the clinical team if not already identified, documented in the research record, and referred to the data safety and monitoring board immediately upon ascertainment. Information to be collected includes event description, time of onset, severity, relationship to study arm, and time of resolution/stabilization. All AE occurring during the study will be documented regardless of relationship to study assignment and all will be followed to adequate resolution

Any medical condition present at the time of screening will be considered as patient baseline and will not be reported as an AE. If the condition deteriorates during the study, it will be recorded as an AE. UP will be recorded in the research record throughout the study. Changes in severity of an AE will be recorded to allow an assessment of duration at each level of severity to be performed. AE found to be intermittent will have documentation of each episode onset and duration. We will record all events with start dates occurring after informed consent until 30 days after the last date of study participation.

and the assignment will remain masked until the final analysis is complete and the findings are ready for publication.

9.2.2 Sample Size

There is no widely accepted method for estimating statistical power for a pilot study since, by definition, it is not powered to detect significant differences between groups. Instead, the goal is to demonstrate feasibility of conducting a fully powered trial and to provide some baseline information that can assist with estimation of the final sample size for the multisite trial. However, our sample size of 80 patients over 2 years (20 patients per site per year) does provide 80% power at $\alpha < 0.05$ for a 30 minute difference in operative and recovery time, assuming a common standard deviation of 45 minutes and a total operating + post-anesthesia unit time of 180 minutes for the general anesthesia group (consistent with our preliminary data). We would also have 80% power to detect a 5-point difference in quality of life on the Carolinas Comfort Scale, given prior published data on this instrument.[20,21] Additionally, we generated 1000 bootstrap samples using data from our prior retrospective study comparing local versus general anesthesia for hernia repair. Each sample contained 40 patients who had surgery under local anesthesia and 40 under general anesthesia. We then evaluated the range of estimated mean and standard deviation for total operative and recovery time across all 1000 samples and found that the mean range (156-205 minutes) and standard deviation (42-113) provided reasonable and stable estimates for the actual values in the original sample. This provides further evidence that a sample size of 80 patients would provide reasonable data for estimating sample size for a fully powered multisite randomized trial.

Describe the treatment assignment procedures (randomization, minimization, relevant criteria, etc). If such procedures are proposed describe rationale as well as the procedure.

Plans for the maintenance of trial randomization codes and maintaining appropriate masking for the study should be discussed, including the timing and procedures for planned and unplanned breaking of randomization codes should be included. Include a statement regarding when unmasking may occur and who may unmask.

If the randomization will be stratified, indicate whether (and why) there is a sample size goal for each stratum. Identify what factors (if any) will be used to stratify the randomization.

9.3 Interim analyses and Stopping Rules

Since the overall safety of both general and local anesthesia have long been established and both techniques are considered reasonable standard of care, we plan for a single interim analysis once 50% enrollment is reached. We will not employ formal stopping rules, given the incredibly low likelihood of this necessity. However, as outlined above, we will temporarily halt enrollment if 3 AE occur so that we can identify potential causes before proceeding.

If an interim analysis is planned, describe the rationale, effect on "spending" the Type I error, and method for adjusting calculations. As relevant, provide guidelines for stopping the study for reasons of efficacy, safety, futility, or poor study performance (e.g., slow accrual, high losses-to-follow-up, and poor quality control).

Table 2. Analysis of primary (pilot) outcomes		
Outcome	**Measurement**	**Timing**
Rate of enrollment and percent of eligible patients enrolled	• Running count and graph of planned versus actual enrollment	Team meeting (every other week)
Reasons for non-enrollment	• Running count and graph	Team meeting (every other week)
Proportion of participants completing all visits	• Running count and graph	Team meeting (every other week)
Proportion missing data	• Running count and graph	Team meeting (every other week)
Time to complete study evaluations and instruments	• Research assistant uses timer during visit	Once per month at team meeting
Participant satisfaction with procedures and instruments	• 10-point Likert-type scale • Short interview at end of each visit	Once per month at team meeting
Identify redundant instruments	• Predict explained variance (R-squared) of each instrument from scores of other instruments	At 25% and 75% enrollment
Identify areas of improvement for study procedures	• Short patient interview at end of each visit • Study team discussions at weekly meeting	Team meeting (every other week)
Estimate sample size	• Measures of dispersion (mean and standard deviation) • Proportions and 95% confidence intervals	After data collection for final patient is complete

State and define the primary outcome measure and specify at which study visit the outcome assessments will be performed.

9.4.2 Secondary outcomes

Timing of measurements for secondary outcomes is outlined in the schedule of evaluations (section 6.1). Instruments are briefly summarized in Table 3 below.

telephone rather than in-person interviews. The instrument evaluates memory/attention, language fluency, orientation, and recall. The 5-minute MoCA has strong correlation with the full version (r=0.87), maintains the discrimination of the full version (area under the curve 0.78 versus 0.75 for full version, p>0.05), and has strong test-retest validity (intraclass correlation coefficient 0.89).[27] Since the 5-minute MoCA was also developed for testing by phone or in person, it meshes with our protocol plans to conduct immediate and long-term follow up by phone. A difference of 3 points is typically considered clinically significant.[27]

iii. Trail Making Tests Parts A and B: The Trail Making Test is one of the most popular neuropsychological tests for detecting processing speed, attention, and visual scanning.[28] Part A requires participants to draw a line between circles containing numbers, and the circles must be connected in numerical order. Part B is similar, but alternates letters and numbers (1, A, 2, B, et). Both items are scored as time to completion and then normalized to population data based on age and education.[28] To address ceiling effects on Part B, we will use the efficiency score for individuals who do not complete the instrument in <300 seconds.[29] A 0.5 standard deviation difference in time is considered clinically significant.[28]

b. Timing: All measures will be administered at baseline, prior to discharge, at 48 hours after discharge, at 2 weeks after surgery, and at 6 months after surgery

4) Outcome: Pain
   a. Measurement: We will use a 10-point visual analog scale to measure overall pain levels. A 0.5 standard deviation will be considered a clinically significant difference.
   b. Timing: Overall pain will be measured at baseline, prior to discharge, at 48 hours after surgery, at 2 weeks from surgery, and at 6 months from surgery.
5) Outcome: Postoperative complications
   a. Measurement: All complications will be recorded based on VA Surgical Quality Improvement Program definitions.[30] For complications not defined in VASQIP, definitions are also provided below.
      i. Allergic reaction: if patients develop hives (raised red lesions) or a significant and persistent rash after administration of local or general anesthesia, this will be managed per the usual hospital protocol. Patients will receive a combination of epinephrine, corticosteroids, and antihistamines. Any patient with an allergic reaction will also be admitted for 24 hour observation that includes monitoring of vital signs, and blood pressure support with intravenous fluids. If the allergic reaction occurs during the operation, then the surgery will be canceled along with all assessments and will be rescheduled after it is determined that the operation can be performed safely without the allergic reaction.
      ii. Hematoma or seroma: a collection of fluid in the tissues over the

Briefly describe Coordinating Center (or Data Management/Statistical Center) responsibilities in data management.

Briefly describe data collection forms.

10.3 Quality Assurance

10.3.1 Training

10.3.1.1 Surgeon training in use of local anesthesia

All participating surgeons will undergo training in the injection of local anesthesia for inguinal hernia repair. The training will consist of either in person or video training with the principal investigator serving as instructor. Instruction will consist of two parts: a slideshow demonstrating pictures of the technique and practice performing the injection. For the practice session, a chicken breast purchased from a local grocery store will serve as the practice site for injection. Under supervision of the principal investigator, the participant and surgeon will first mark a practice "incision" on the chicken and inject the "skin" with 10 mL of the local anesthesia mix, using a 10cc syringe. The surgeon will then hub the syringe to practice injecting the deep tissue and fascia along the length of the incision. To verify application of the above training and practice, the principal investigator will observe (either in person or by video) the first operation under local anesthesia by each surgeon.

A brief training session will be repeated after the first six months to reinforce study protocols.

10.3.1.2 Training of research assistants

All research assistants at both sites will undergo in person or video training for all study protocols. The training will include thoroughly reviewing the study manual of procedures. Training will also include administration of all study instruments to mock participants, with feedback from the principal investigator on performance.

Training of research assistants will be repeated every six months to reinforce study protocols. If new research assistants are hired as the study progresses, they will undergo training prior to first approaching patients.

Describe types and mechanisms of training of staff for the study.

10.3.2 Quality Control Committee

There will not be a quality control committee. The principal investigator will be responsible for quality control.

10.3.3 Metrics

Metrics for quality control include the following:

- Successful completion of all training activities for surgeons and research assistants