Study Protocol and Statistical Analysis Plan

Project Title:	Version Date:
Transitional rehabilitation in CABG patients	4-17-17

NCT number:	NCT03892460
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Grant Sponsor:	University of Vermont, College of Medicine, Department of Medicine

Summary:

Coronary artery bypass graft (CABG) surgery is a common surgical procedures and an important treatment option for coronary artery disease. As with any major surgical or medical procedure, the period of rest and recovery that follows is associated with cardiorespiratory and skeletal muscle deconditioning that can leave patients feeling weak and fatigued. Cardiac rehabilitation exercise training is recommended to recover lost strength and fitness. However, patients typically do not begin cardiac rehabilitation until 4-6 weeks following CABG surgery. Rehabilitative interventions to bridge the period between discharge following CABG surgery and the start of cardiac rehabilitation could improve patient cardiorespiratory and their ability to perform daily activities.

The goal of this research study is to understand whether an at-home exercise program started soon after CABG surgery, and continuing for 4 weeks following discharge from the hospital, can serve as a bridge between surgery and the start of cardiac rehabilitation to preserve physical function. Volunteers will be randomly assigned to receive neuromuscular electrical stimulation (NMES) of their quadriceps muscles or not to receive NMES (control group). Volunteers will be evaluated prior to CABG (Pre-surgery testing), upon discharge and 4 weeks Post-CABG surgery. Assessments will include measurements of physical function by the Short Physical Performance Battery and 6 min walk tests, as well as assessment of subjective physical functional capacity and quality of life using the Medical Outcomes Short form 36. Additionally, accelerometry will be used to monitor weight-bearing physical activity during the 4 week treatment phase.

If successful, results from these studies will advance knowledge by providing proof-of-principle evidence for the utility of NMES to counter physical functional deterioration in the early, post-surgical period following CABG. Additionally, our findings may advance postoperative care of CABG patients by providing a clinical intervention to bridge a gap in rehabilitation services prior to entry into formal CR. Maintaining functional capacity in patients post-discharge may reduce the risk for re-hospitalization and progression towards disability. Greater functionality upon entry into CR may permit greater functional and health benefits from exercise during CR.

Purpose:

CR programs were initially developed to counter the deconditioning effects of medical and surgical interventions in cardiac patients and they have well-accepted health and survival benefits (1). Although CR is an important part of the care continuum (2), CABG patients typically do not start CR until ~4-6 wks after discharge (3). During this period, patients can experience further deterioration in physiological reserve, with increased risk for post-operative complications, readmission and development of physical disability (4-6). Whereas a large number of studies have focused on transitional care initiatives in medical and surgical cardiac populations to improve clinical outcomes and minimize costs (7), very few have focused on bridging this gap in physical rehabilitation care.

One reason for the absence of transitional rehabilitative care services in cardiac surgical patients is the inherent difficulty of intervening in a post-surgical population, as pain and limited mobility from surgical wounds diminishes motivation towards classical exercise. Moreover, reduced physical function related to surgery and hospitalization may render patients unable to perform basic activities of daily living at home, much less exercise. *These hurdles represent a significant barrier to bridging the gap in rehabilitative care of cardiac surgical patients*. Alternative exercise modalities that confer a training effect, but that do not have the physical requirements of classical aerobic or resistance training, could bridge this gap. Optimal candidates should induce an exercise training response, integrate easily into outpatient and home environments and be easy to use and inexpensive.

NMES is an intervention that fulfills many of these criteria. An inexpensive (~$500), FDA-approved, portable, hand-held NMES unit permits non-volitional initiation of muscle contractions that can mimic resistance- or aerobic-type exercise (8), producing a training response that is near comparable to classical aerobic training (9, 10). NMES improves muscle size, strength and performance in older adults with chronic disease (11), and counteracts muscle atrophy coincident with pathophysiologic catabolic stimuli (12-14) and muscle disuse (15), both of which occur in the post-operative period following CABG. Although NMES has been studied in stable heart failure patients (16), to our knowledge, it has never been employed in CABG or other cardiac surgical populations as a potential bridge therapy from post-

operative discharge to the start of CR.

Transitional care following hospitalization has been recognized as a national priority (17, 18) and efforts to implement new services were incentivized by the Affordable Care Act (19). Numerous studies have shown the utility of transitional care services to improve outcomes, reduce unnecessary use of health services and decrease costs (20, 21), but few of these studies have focused on ways to extend rehabilitation services (22) and fewer still have focused on these services following CABG surgery.

CR is an important part of the rehabilitative care of cardiac medical and surgical patients that restores physiological reserve lost during the acute disease event and subsequent hospitalization and convalescence, as well as conferring long-term health benefits (23). Although this deterioration in physiological reserve is well-accepted, our current knowledge of such adaptations in CABG patients is limited and there are currently no evidence-based interventions that bridge rehabilitative care between discharge and the start of CR, aside from acute, in-patient rehabilitation facilities in cases of substantial frailty. Successful completion of our studies would impact the field of transitional care of CABG patients in several ways:

Fill an important knowledge gap. Our results will provide the first characterization of early, post-surgical functional and physiological adaptations to CABG (in patients randomized to control). Studies have noted that CABG patients have reduced self-reported or objectively-measured physical function post-surgery compared to non-surgically-treated patients. However, no study has systematically tracked the erosion of physical functional capacity from CABG surgery to the start of CR. Knowledge of the extent of the reduction in functional capacity due to CABG can spur the development of new transitional care services aimed at improving outcomes/costs.

Define the utility of NMES to prevent early, post-surgical erosion in physiological capacity. Based on studies in other post-surgical populations, we anticipate uncovering novel effects of NMES to prevent the loss of physiological function, providing an important evidence base upon which to build support for further studies evaluating the utility of NMES in CABG recipients. Maintenance of physiological function in the post-CABG period may improve the response to CR, particularly in those with low baseline functionality (24). Because NMES is FDA-approved, inexpensive, portable to the outpatient and home environments and there are clinicians already trained in its use (PTs/OTs), barriers to its broader clinical application to the CABG population are minimal.

Relevance to other surgical populations. Demonstration of the utility of NMES in the post-surgical CABG population has direct relevance to other older adult surgical populations beyond cardiac populations, where follow-up rehabilitative care, such as CR, is not available, as well as other non-surgical populations (eg, heart failure, COPD patients). NMES may serve as an inexpensive, transitional care service that allows these patients to maintain/regain functional reserve.

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Objectives:

The *goal of this application* is to explore the utility of neuromuscular electrical stimulation (NMES) to counter the early, post-surgical deterioration in physical functional capacity. We chose NMES because it permits non-volitional initiation of muscle contractions that can produce an exercise training response similar to classical exercise training, with near comparable effects. We will test the ability of NMES to preserve physical function, as measured by the Short Physical Performance Battery (SPPB), a metric whose change in the first month post-hospitalization has been shown to predict re-hospitalization and death and that is validated for use in physically compromised elderly populations. We will also asses 6-minute walk (6MW) performance as a secondary outcome, a metric that is commonly used for FDA approval of various interventions that seek to improve physical function/fitness. Our *rationale* for the proposed studies is that interventions directed towards preventing deleterious skeletal muscle changes during this period and maintaining functional capacity will enhance the effects of CR to improve functionality and future cardiovascular risk. We will *accomplish these goals* using a randomized, controlled design. Based on our preliminary data, we *hypothesize* that NMES will prevent deleterious reductions in physical function by preserving skeletal muscle size function. To address this hypothesis, we propose a single aim:

***Aim:* Define the utility of NMES to preserve or increase physical functional capacity in patients during the period following CABG and prior to entry into CR.**

Primary Clinical Outcome: NMES will diminish CABG-induced erosion of physical functional capacity, as assessed by the SPPB.

Secondary Clinical Outcome: NMES will diminish CABG-induced erosion of physical functional capacity, as assessed by the 6MW.

METHODS AND PROCEDURES

Study Design:

We will use a prospective design, in which patients scheduled for elective CABG will be *recruited* and evaluated prior to CABG (Pre-surgery) and upon discharge (Discharge) for physical function (*SPPB Testing and 6 min walk*). Patients will be recruited for this study during the normal process of clinical recruitment for cardiac rehabilitation. This includes patients from cardiothoracic consultation lists and/or those scheduled for elective CABG. In some instances, we will identify patients from cardiothoracic consultation lists who are or will be scheduled for CABG, but are not on the surgical unit. We will contact these patients by phone regarding participation in cardiac rehabilitation and, at that time, introduce this research study. Patients will be randomized (1:1) to NMES or control intervention (n=18/group; *Treatment Phase*), with stratification for age and sex. Following completion of the 4 wk intervention,

volunteers will undergo *Post- Testing*, which will be identical to Pre-surgery and Discharge testing. Each protocol phase is described below.

Pre-surgery testing Baseline testing will occur prior to CABG surgery and at discharge and consist of functional assessment by the SPPB and a quality of life (QOL) questionnaire (MOS-SF36). Tests are described below.

Discharge testing will repeat Pre-surgery testing and include a 6MW. At this time, volunteers will receive an accelerometer, which will be worn during three (3) 5-day periods during the Treatment phase.

Treatment Phase

Patients will be randomized (1:1) to NMES or control intervention and will continue in this Treatment phase until 4 weeks post-CABG surgery.

4 wk Post-surgery testing will be identical to Discharge testing.

Procedures:

All of the procedures and interventions on volunteers recruited for these studies are carried out solely for research purposes, as none are part of standard therapy in CABG patients.

Physiological Testing (during Pre-surgery (excluding 6 MW), Discharge and 4 wk Post-surgery testing)

SPPB will be measured, as described by us (1), as this assessment is prognostic for functional competence and mortality in cardiac surgical patients (2). This measure takes ~5 min to perform and is comprised of: 5 repeated chair stands, balance testing (3 tasks each 10 s long) and a 4 meter walk. As increasing SPPB score in the first month post-discharge in a sample of elderly patients with diverse clinical backgrounds was associated with lower risk for rehospitalization and death (3), improvements in, or maintenance of, this metric would provide strong evidence for the clinical utility of NMES. We have experience with this measure in cardiac populations (4).

6 MW was developed to assess cardiopulmonary fitness in patients with lung and cardiac disease (5), but has been used widely to assess disability in older adults (6) and is the most common metric used when seeking FDA approval for interventions to improve physical function. We have experience with this measure in heart failure patients (7).

Medical outcome survey short form 36 is a commonly used questionnaire to assess subjective quality of life and physical function.

Accelerometry (Lifecorder Plus) will be used to monitor steps taken, caloric cost and minutes in activity and will be performed for three (3) 5-day periods during the Treatment phase of the study.

Treatment phase

NMES will be carried out bilaterally on the quadriceps using a portable stimulator (EMPI Continuum). Two adhesive electrodes will be affixed to the anterior surface of each thigh: ~1 cm distal to the inguinal crease and ~5 cm proximal to the patella, just lateral to the midline of the thigh to assure that it does not interfere with incisions for vein harvest. Symmetrical, biphasic pulses (400 μs duration at 25 Hz) will be used, with a duty cycle of 25% (10 s on, 30 s off). Patients will be trained to conduct NMES sessions and will select stimulation intensities sufficient to cause visible muscle contractions below their pain threshold. Training in the use of the NMES device will begin within 96 hrs of transfer to the surgical step down unit. This training will consist of one session per day of ~15 min to familiarize the volunteer with the unit and the exercise/contraction stimulus. Upon discharge, NMES sessions will occur 5 d/wk once per day for 45 min per occasion (5 min low-intensity warm-up, 40 min higher-intensity stimulation) for 4 wks. This program is meant to mimic an aerobic-type exercise stimulus (8) and has been shown in heart failure patients to have functional benefits over a similar treatment period (9, 10). The 4 wk duration reflects the approximate average time that most CABG patients take to enter CR at our center. We acknowledge that the NMES training load is substantial, but have modeled this program on others that have shown morphological and functional effects in heart failure patients (11). At this exploratory stage, we feel that it is essential to use a stimulus that affects muscle size and function, with future studies modifying the NMES dose to establish a threshold that elicits a training effect with the highest subject

compliance rate. Daily logs and weekly phone contacts will be used to track compliance, and compliance will be covertly monitored using the device software.

Control patients will not receive an NMES device. We chose not to utilize a control NMES intervention (eg, stimulation below threshold to elicit contraction) to mitigate the possibility that patients may increase stimulation to produce muscle contractions if there is perceived benefit. Rigorous control over the NMES stimulus is preferable to controlling for any effects of sub-threshold, cutaneous electrical stimulation. Patients will be contacted weekly to assess their recovery and discuss issues related to general health to equate the degree of interaction with study personnel to that of the NMES intervention group.

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Questionnaires:

We will assess physical functionality/quality of life with the MOS-SF36 questionnaire. This questionnaire takes about ~10 min to complete and will be completed at Pre-surgery and Discharge and 4 wk Post-surgery testing.

Risks/Benefits:

Potential risks: Below we have highlighted those procedures/measurements that have anything greater than negligible risk to the volunteers' health for each phase of the study.

Pre-surgery, Discharge and 4 wk Post-surgery Testing: Risks associated with functional testing are minimal. All of the activities are similar to those performed during the conduct of normal daily activities. If volunteers are unable to do any of the activities because of limitations of their heart condition, they will not be required to perform them and testing will be monitored by trained personnel.

NMES intervention: NMES is a generally safe procedure, delivered in the proposed study by an FDA approved device. Although evidence is limited, some have suggested that NMES could increase the risk of DVT, which may have serious health consequences. However, several published reports show that NMES significantly reduces the risk of developing deep vein thromboses (DVT) (1) and we will actively exclude any individual with a known coagulopathy. Because of the location of the stimulating electrodes (upper leg), the risk of NMES dislodging a DVT is likely minimal. We will also exclude any volunteers that currently have an implanted cardiac defibrillator or pacemaker, as this is contraindicated for NMES

use (1). Patients may experience some painful muscle contractions as they first adjust the stimulus to a tolerable level, which can be quickly corrected by reducing the stimulation intensity. After treatment, muscles soreness may occur. The level of fatigue and/or soreness, however, will be similar to that which occurs following a standard exercise training session and should dissipate over time as the volunteer's muscles become accustomed to the electrically-stimulated contractions (ie, they become trained).

Benefits: The direct benefit of the research to volunteers is minimal. NMES may improve skeletal muscle structure or function and, in turn, improve physical functional capacity. Because of this, patients may experience improved physiological capacity, which could reduce disability post-surgery and potentially enhance the beneficial effects of CR. If we find that NMES has beneficial effects on physical function, further research and application of the technique to CABG patients post-surgery may assist in the development of more effective transitional rehabilitative care approaches to mitigate long-term functional morbidity.

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Therapeutic Alternatives:

There are no alternative rehabilitation regimens during the early, post-operative period in CABG patients.

Data Safety and Monitoring:

Drs. Toth and Ades will monitor the safety of the research procedures for this study. We have not set up a formal safety committee for several reasons. First, the PIs and the investigative team have a long history of performing the measurements proposed in this proposal. The procedures carry relatively low risk to the volunteers. Second, because of the small number of patients and track record of performing these procedures, it is highly unlikely that we will need to "stop" the study or significantly alter the procedures. If any problems/unanticipated events arise related to the NMES intervention, Dr. Ades will determine the nature of the problem and its relatedness to the NMES intervention and decide whether continued participation in the study is in the best interest of the patient. As detailed above, however, NMES is FDA-approved for this indication and we have taken precautions to minimize the potential for adverse effects.

Adverse Event and Unanticipated Problem (UAP) Reporting:

The PIs or the study coordinator (Jason Rengo) will monitor the safety of the research procedures/interventions for this study. Mr. Rengo or Dr. Toth will be available on-site for all assessments that may pose safety concerns for volunteers. In this context, study personnel will be readily available to monitor volunteer safety throughout the study. If an event occurs that affects participant safety, Dr. Toth or Mr. Rengo will alert Dr. Ades, who will adjudicate the event with respect to its severity, expectedness and relatedness to participation in the study. Because numerous studies in our laboratories and others have demonstrated the safety of this regimen of testing in patients from with a broad range of clinical backgrounds (eg, heart failure patients, cancer patients, advanced-stage, knee OA patients; healthy elderly), we expect minimal problems related to testing or the intervention. Considering the low risk nature of these studies, we have not incorporated "stoppage criteria" for the overall study. Instead, Dr. Ades will decide whether an individual participant should continue with the study following occurrence of any adverse events or unanticipated problems, taking into consideration what is in the best interest of each individual patient.

Adverse events will be reported by one of 3 mechanisms. First, the joint University of Vermont/University of Vermont Medical Center (UVMMC) Committee for Human Subject Research Adverse Event Reporting Document. These reports will be sent to the office of the Committee for Human Research in the Medical Science (CHRMS) within 2 days of the event. Reporting any adverse events will be the responsibility of the PIs. The CHRMS will make a determination as to whether additional reporting requirements are indicated. Additionally, the UVMMC Patient Safety Reporting system (SAFE), which may be initiated by health care center staff or study personnel. These forms will be forwarded within 3 days to the PI, UVMMC Risk Management Office, CHRMS and other appropriate agencies, as indicated by the nature of the report. Reviews of protocol specific adverse events will be

performed no less than annually. Additionally, any adverse event that occurs will be forwarded to the PIs for reporting to the Human Subject Research Protection Office within 1 week of occurrence. Of note, these protections against risk include both physical risks to the volunteers, as well as risks associated with any breach in confidentiality.

On an annual basis, Drs. Toth and Ades will assess data being gathered and safety of volunteers to assess the pattern or frequency of events to identify occurrence of any event or problem that alters the safety profile of the procedures being performed. The exception would be occurrence of a serious adverse event or unanticipated problem that necessitates re-evaluation of the expected risk of the study procedures at an earlier time point. Additionally, they will evaluate data collection and storage to ensure the confidentiality of data and quality. Each of these evaluations will be followed by reports of study progress and patient safety to the University of Vermont CHRMS via yearly progress reports.

Withdrawal Procedures:

Volunteers will be withdrawn if the research team, clinician and/or safety officer feels that further participation in the study or performance of any procedure associated with this study would, in any way, put the volunteer at undue risk or not be in their best interest. Moreover, volunteers may be withdrawn if s/he fails to attend scheduled visits or do not comply with instructions from research staff.

Sources of Materials:

An individual research record will be kept on each volunteer in compliance with HIPAA standards. This record will contain identifying data, demographic information and results from all clinical research measurements and evaluations. The results of all testing will be kept confidential. All materials gathered in conjunction with the proposed studies will be used for research purposes only and will be available only to research personnel working on these studies, who have obtained proper training in human subjects research and privacy protection.

Statistical Analysis Plan:

Our primary goal is to assess changes in SPPB score and 6 MW between study groups to test whether NMES prevents the erosion of functionality from admission to 4 wk post-discharge (approximate time for starting CR). A general linear mixed model will be used, with group and time as fixed effects. The primary comparison will be between measures at admission and 4 wks post-discharge, as changes over this time period will reflect the effects of the surgery, post-op recovery and post-discharge/pre-CR periods. Because function may be impaired pre-surgery due to angina/dyspnea/etc, post-surgery measures may be a better indicator of functional capacity and we have the ability to calculate the changes in these measures from Discharge to 4 wks post-surgery. We will assess QOL by questionnaire and activity by accelerometry as secondary outcomes to determine if NMES improves patient-reported QOL and free-living daily activity, respectively, vs. usual care. Covariates (eg, length of stay, time to start of CR, admission SPPB, etc) can be included in the models to control for potential confounders that might differ by group in the event that randomization fails to equate groups for these variables.

DRUG AND DEVICE INFORMATION

Drug (s) [X] ***Not applicable***

Device (s) [ ] ***Not applicable***

The interventional device used in this study: EMPI Continuum complete electrotherapy system has received FDA approval (501K: K093324) for retarding disuse-related atrophy, which we believe is one of the primary mechanisms whereby CABG patients become more functional disabled in the early, post-surgical period. That is, muscle disuse secondary to pain, limited range of motion and muscle weakness causes skeletal muscle fiber atrophy and weakness, as well as mitochondrial rarefaction and dysfunction that further impair physical fitness.

Is it FDA approved:

Yes. It is approved to mitigate muscle atrophy/dysfunction associated with muscle disuse (501K: K093324).

Risk assessment:

The device (and similar devices) has been used extensively in the orthopedic and neural rehabilitation settings by physical and occupational therapists and in numerous disease states (heart failure, chronic obstructive pulmonary disease, knee replacement) to improve muscle size and function in clinical trial settings. Thus, NMES is generally a safe modality, with a long safety record. Although evidence is limited, some have suggested that NMES could increase the risk of dislodging a DVT because of the rhythmic muscle contractions induced by the electrical stimulation. However, several published reports show that NMES significantly reduces the risk of developing DVTs. In fact, the device we are using is FDA-approved for prevention of DVT of the calf muscles immediately following surgery, as it would function similar to intermittent pneumatic compression. Moreover, we will actively exclude any individual with a known coagulopathy or DVT. Because of the location of the stimulating electrodes (upper leg), the risk of NMES dislodging a DVT is likely minimal. There are also several case reports that NMES may be sensed by cardiac defibrillators as an arrhythmia, causing the device to discharge inappropriately. However, interference with ICDs mostly involved low frequency stimulation of the upper or lower back. In contrast, a more recent study has shown that higher frequency stimulation of the leg muscles does not cause electromagnetic interference with the device (1). Regardless, consistent with current clinical practice guidelines (2), we will exclude any volunteers that currently have an implanted cardiac defibrillator or pacemaker. Finally, during the first couple of NMES sessions, muscle soreness may occur, but this is comparable to what might occur with classical exercise training and dissipates over time.

Literature cited

1. Kamiya, K., Satoh, A., Niwano, S., Tanaka, S., Miida, K., Hamazaki, N., Maekawa, E., Matsuzawa, R., Nozaki, K., Masuda, T., and Ako, J. Safety of neuromuscular electrical stimulation in patients implanted with cardioverter defibrillators. *Journal of Electrocardiology* **49**, 99-101
2. Houghton, P. E., Nussbaum, E. L., and Hoens, A. M. (2010) Electrophysical agents. Contraindications and precautions: an evidence-based approach to clinical decision making in physical therapy. *Physiother Can* **62**, 1-80

SUBJECT CHARACTERISTICS, IDENTIFICATION AND RECRUITMENT

Prior to our rationale for subject selection, we provide a brief accounting of inclusion/exclusion criteria. Ambulatory patients (50-80 yrs of age) scheduled for elective CABG and able to give informed consent will be recruited. Patients will be excluded if they have: 1) rheumatoid arthritis or other inflammatory/autoimmune diseases; 2) cancer, excluding non-melanoma skin cancer; 3) exercise-limiting peripheral vascular disease, neuromuscular disease or lower extremity neuromuscular dysfunction related to prior cerebrovascular event; 4) body mass index $\geq$38 kg/m^2 or 5) significant (moderate or greater) valvular heart disease that was not corrected surgically. We will also exclude patients with an existing lower blood clot or an implanted pacemaker or ICD, as both are contraindications for NMES (1). Patients will be excluded from further study post-operatively if they have serious complications that prolong hospitalization beyond 7 d post-surgery (eg, stroke, prolonged intubation, infection, etc), although this will likely be a small proportion of the population.

These criteria were chosen to obtain a cohort of CABG patients who are free of other clinical conditions that may complicate our ability to detect an effect of NMES on physical function (eg, cancer w/ its accompanying treatments or motor deficits due to CVA, etc) and who may have difficulty conducting the NMES (eg, very obese individuals may have difficulty obtaining muscle contractions with the NMES device because fat in their legs serves as an electrical insulator). Finally, we exclude those volunteers with contraindications for NMES use.

Literature cited:

1. Houghton, P. E., Nussbaum, E. L., and Hoens, A. M. (2010) Electrophysical agents. Contraindications and precautions: an evidence-based approach to clinical decision making in physical therapy. *Physiother Can* **62**, 1-80

Number of Subjects:

We intend to enroll 48 volunteers. This will allow for n=36 to complete the study, conservatively assuming 25% total attrition rate: 15% dropout, 10% non-compliance, based on prior studies of NMES use in post-surgical populations (1) and compliance data in our prior training studies (85-95% compliance).

Literature cited:

1. Stevens-Lapsley, J. E., Balter, J. E., Wolfe, P., Eckhoff, D. G., and Kohrt, W. M. (2012) Early neuromuscular electrical stimulation to improve quadriceps muscle strength after total knee arthroplasty: a randomized controlled trial. *Phys Ther* **92**, 210-226

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Inclusion of Minorities and Women:

Inclusion of Women

This study will seek to include equal numbers of men and women.

Inclusion of Minorities

Every effort will be made to recruit minorities for the proposed studies. The contribution of minorities to the total population of Vermont is 3.2%, with a similar minority profile in Chittenden County (3.6%), where the University of Vermont (UVM) is located.

Inclusion of Children:.

The proposed studies will not include children because elective CABG surgery is confined to the adult/ older adult population.

Recruitment:

Patients will be recruited through the Cardiothoracic Surgery Clinic and local clinical practices.