Human Subjects Research Protocol

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PROTOCOL SUMMARY

Project Title:	Protocol Version Date:
Incentives and Case Management to Improve Cardiac Care	2-12-21

Principal Investigator:	Diann Gaalema, PhD

Grant Sponsor:	NIH	Grant Number:	32796

(For grants routed through UVM, indicate the OSP Proposal ID # located at the top of the OSP Routing Form)

Lay Language Summary: *(Please use non-technical language that would be understood by nonscientific IRB members to summarize the proposed research project. The information must include: (1) a brief statement of the problem and related theory supporting the intent of the study, and (2) a brief but specific description of the procedure(s) involving the human subjects. Please do not exceed one single-spaced 8 ½ X 11" page.)*

Participation in outpatient cardiac rehabilitation (CR) decreases morbidity and mortality for patients hospitalized with myocardial infarction, coronary bypass surgery or percutaneous revascularization. Unfortunately, only 10-35% of patients for whom CR is indicated choose to participate. Lower socioeconomic status (SES) and Medicaid coverage are robust predictors of CR non-participation. There is growing recognition of the need to increase CR among economically disadvantaged patients, but there are no evidence-based interventions available for doing so. In the present study we propose to examine the efficacy of using financial incentives and case management, alone and in combination, for increasing CR participation among low-income patients. Financial incentives and case management have both been shown to be highly effective in altering other health behaviors among disadvantaged populations (e.g., smoking during pregnancy, weight loss). Additionally, case management and final incentives have properties that might compensate for executive function deficits, which often impede healthy behavior change and are overrepresented in lower-socioeconomic status populations. For this study we will randomize 200 CR-eligible lower-socioeconomic status patients to a usual care control

condition or to an experimental condition where they receive financial incentives contingent on initiation of and continued attendance at CR sessions, a case-manager assigned at the hospital, or to a combination of these two interventions. Participants in all conditions will complete, and be compensated for, pre- and post-treatment assessments. Treatment conditions will be compared on attendance at CR and end-of-intervention improvements in fitness, decision making and health-related quality of life. Cost effectiveness of the treatment conditions will also be examined by comparing the costs of the intervention and usual care conditions with their effects on increasing CR initiation and adherence. Furthermore, we will model the value of the intervention based on increases in participation rates, intervention costs, long-term medical costs and health outcomes after a coronary event.

PURPOSE AND OBJECTIVES

Purpose: *The importance of the research and the potential knowledge to be gained should be explained in detail. Give background information.*

1. SIGNIFICANCE

1.A. Cardiovascular Disease is the Deadliest and Most Costly Disease in the US

Cardiovascular disease continues to be the number one killer in the US, responsible for 800,000 deaths per year, more than all types of cancer combined.[1,2] One in three deaths in the US is attributable to cardiovascular disease.[2] Decreases in quality of life and disability as a result of cardiovascular disease are also concerning, with disability adjusted life years increasing steadily over the last 10 years.[3] Heart disease is also costly, dominating all other diagnoses in direct health expenditures, estimated at $116 billion a year.[2] If indirect costs are included, costs attributed to cardiovascular disease are estimated at over $200 billion a year. Costs are projected to keep increasing with costs attributable to cardiovascular disease expected to more than double over the next 20 years. The vast majority of that increase will be due to costs associated with initial and subsequent hospitalizations.[2] Rehospitalizations after an cardiac event are a major concern, as there are more than 305,000 recurrent myocardial infarctions (MI) each year.[2] In one study, 30% of those hospitalized for an MI were readmitted within 90 days.[4] These hospitalizations are extremely costly. A recent study estimated the average cost of the first rehospitalization after a myocardial infarction (MI) at $20,000.[5] If a vascular or cardiac surgery procedure is needed, the costs are even higher, ranging in 2012 from $70,027 to $149,480.[2] Interventions that successfully prevented rehospitalizations could significantly reduce health-care costs.

1.B. Lower-SES Patients Suffer a Disproportionate Burden of Cardiovascular Morbidity and Mortality

The burden of cardiovascular disease is not spread evenly across the population. Certain groups, such as those of lower-socioeconomic status (SES) shoulder a higher proportion of the morbidity and mortality resulting from this disease.[6] These disparities can be seen both in the development of cardiovascular disease and in outcomes after serious cardiac events. First, cardiovascular disease is significantly more prevalent among persons of lower-SES.[7] Second, lower-SES patients also have higher rates of MI that are also more severe at presentation.[8,9] Third, outcomes after a cardiac event also differ by SES. Lower-SES patients have worse outcomes after MI, with in-hospital mortality rates of those on Medicaid nearly double those with commercial insurance[10] and 1-year death rate following discharge of 5% compared to 2% among more affluent patients.[8,9,11]

However, these disparities by SES are largely accounted for by modifiable behaviors, including smoking, diet, physical activity, and adherence to medication. Disparities by SES in developing coronary heart disease as well as disparities in outcomes following a serious cardiac event are significantly attenuated or become non-significant when controlling for these risk-factor behaviors.[8,9,11-15] Thus, the increased morbidity and mortality following a serious cardiac event in lower-SES individuals should be modifiable by promoting behavior change. A promising platform for cardiac-related behavior change is cardiac rehabilitation (CR).

1.D. Cardiac Rehabilitation Reduces Morbidity and Mortality

Cardiac rehabilitation, a structured secondary prevention program consisting of supervised exercise and risk-factor control interventions, is standard of care following a major cardiac event such as MI or coronary revascularization.[16] Attendance at CR following a major cardiac event results in a 26% reduction in cardiovascular mortality and a 31% reduction in one-year hospital readmissions.[17,18] Consequently, attendance at CR is given the highest level of recommendation and strength of evidence in the secondary prevention guidelines established by the American Heart Association and the American College of Cardiology (AHA/ACC). Yet, despite proven benefits of CR, attendance rates for appropriate patients has been disappointingly low ranging from only 18–34%.[19,20] Leaders in the field, as part of the Million Hearts CR Collaborative, have called for programs to employ strategies to increase rates of attendance at CR in an effort to prevent one million cardiac events over the next five years.[21]
Attendance at CR is also commonly associated with improvements in fitness and other health-related behaviors. Patients who participate in CR experience significant improvements in exercise capacity,[22] lipid control,[23] medication compliance,[24,25] body composition,[23] as well as improvements in quality of life.[26,27] It is likely that the increased fitness and adherence to other health-related behaviors accounts for the demonstrated reductions in morbidity and mortality. It has been shown that increases in fitness garnered during CR reduces future mortality, especially among those who have low levels of fitness at intake.[22,28]
In the general population, CR has repeatedly been shown to be cost-effective. One comprehensive economic analysis in Sweden estimated that over 5 years decreased hospitalization rates and associated averted health costs, as well as higher employment rates of those who attended CR actually saved 5 times as much to the Swedish system as the cost of CR.[29] In general, however, cost effectiveness is expressed as dollars per quality-adjusted year of life saved. In more recent reviews of that subject, cost effectiveness for CR has been estimated at $7,517 - $14,458 (in 2011 dollars) per year of life saved.[30-33] These returns on cost are better than most other post-MI treatment interventions, including thrombolytic therapy and coronary bypass surgery.[31]

1.E. Lower-SES Patients Have Low Rates of CR Attendance and High Risk for Cardiovascular Events

Despite the significant health gains associated with CR, lower-SES patients have extremely low rates of attendance. Several studies have demonstrated this association, using education or insurance type to define SES. Looking in detail on the state level, Oberg et al tracked the Medicaid claims of all patients who were enrolled in the Washington State Medicaid system during 2004 and were discharged alive following an MI.[34] Of the 322 patients eligible to attend CR, only two (< 1%) did so within the year following their MI. In a national study of Medicare data, while overall 18% of older adults (≥65 years) attended CR as recommended, only 3-5% of those with dual Medicare/Medicaid status (i.e., lower-SES) did so.[19,35] A recent meta-analysis concluded that those with limited educational attainment were a third less likely to attend CR.[36] Additionally, in the most recent comprehensive data on the subject, a national survey demonstrated that those with less than a high-school education were half as likely to attend CR compared to college graduates (23 vs. 46%).[20] Overall these studies paint a bleak picture of lower-SES CR attendance.
The lack of attendance at CR is troubling especially as lower-SES patients are higher-risk for subsequent cardiovascular events, entering CR with low fitness levels and higher rates of smoking, obesity, and diabetes.[8,37] Given the relatively high-risk profiles of lower-SES patients, and their increased risk of morbidity and mortality from cardiovascular disease,[8,9,11] they stand to benefit greatly from CR. The few studies examining gains from CR participation by SES support this idea, demonstrating that lower-SES patients who complete CR make similar gains in fitness and risk factor reduction as higher-SES patients.[38-40] Indeed, increasing CR participation among lower-SES patients has the potential for an even greater return than among more affluent populations given the high-risk profiles of lower-SES patients. We note these high-risk profiles locally as well. Lower-SES patients from our prior studies had higher-risk profiles such as lower fitness and rates of smoking as high as 40% vs. ~7% in higher-SES patients (Preliminary data) and high rates of morbidity, being hospitalized as many as 6 times and visiting the ED up to 16 times within a year (Preliminary data).

1.E.1 SES is Associated with Executive Function which Predicts Adherence to Medical Regimes

CR attendance can be challenging for lower-SES patients. Attending requires creating time in your schedule to attend, remembering to attend, organizing coverage for responsibilities you may have elsewhere as well as obtaining transportation to attend, a set of behaviors that require complex

planning. Additionally, attending entails engaging in behaviors (exercise) or inhibiting others (smoking) that, while beneficial in the long term, may be unpleasant in the short term. These sets of behavior (planning and execution of complex behaviors and behaving or inhibiting behavior for long-term benefit) can be considered aspects of a construct known as executive function (EF) which has shown to be useful in understanding health-related behaviors.[41] EF has been demonstrated to predict adherence to a variety of medical regimes including appropriate medication dosing and exercise interventions in older adults.[42,43] Especially relevant, EF was shown to predict success in heart failure management, which included a variety of complex tasks including taking medications appropriately, keeping medical appointments, and adhering to recommendations for diet and exercise.[44] Additionally, in our prior trial, two measures of executive function were significant predictors of completing the CR program (Preliminary data). Executive function has also been shown to be correlated with SES[45] and in our prior trial, lower-SES patients reported significant EF challenges during CR (Preliminary data).

1.F. Interventions Needed for Lower-SES Patients to Attend CR

While there appears to be broad agreement that CR participation rates need to be increased, the literature on interventions to improve CR participation is limited.[21] One area where interventions have been successful is in improving CR *referral* rates. Automatically referring eligible patients and providing in-hospital liaisons to meet with patients can double referral rates and increase enrollment.[46] Other approaches, such as providing more flexible hours, having a nurse call the patient after discharge, having patients sign participation contracts, and allowing patients to exercise at home have also led to enrollment improvements of 10-25%.[47-51] However, the most challenging aspect of improving CR utilization appears to be increasing longer-term adherence. Considering that the health benefits of CR increase with number of sessions attended[35,52] adherence is critical. In a Cochrane review of interventions designed to improve CR uptake and adherence, none of the three studies examining interventions to improve adherence to CR sessions demonstrated a significant improvement.[53] As such, strategies to increase CR adherence rates are sorely needed. Also, as lower-SES populations are at increased cardiac risk and have significantly lower adherence to CR than higher-SES populations, interventions targeting them are especially needed. However, to our knowledge, not a single study, other than the trial on financial incentives reported in our preliminary data, has focused on increasing CR participation in lower-SES patients. Ideally, interventions to improve attendance in CR among low-SES patients would promote attendance while addressing the specific challenges this population faces. Two interventions have these qualities: case management (CM) and financial incentives (FI).

1.G. Case Management is a Promising Approach for Supporting CR Attendance and Improving Outcomes among Lower-SES Patients

Case management involves an individual, often a nurse, who is assigned to a patient with the goal of improving health outcomes through coordinated care. CM programs involve several activities including individual-based assessment, planning and coordination of care, coordination of other services, and patient monitoring and evaluation. Outside of cardiac populations, a series of studies conducted by our research group has demonstrated that case management is efficacious for promoting adherence to medical treatment (abstinence from cocaine) when offered as a single treatment or when combined with incentives.[54-58] Supporting its use within the cardiac population, case management has been demonstrated to be successful at reducing cardiovascular risk, and reducing rehospitalizations in cardiac patients,[59-62] even in lower-SES patients,[63] with improvements sustaining even after the intervention was completed.[64] CM has also been successful in reducing psychological distress, which is common in lower-SES patients as well as being a barrier to participation.[65] CM has been efficacious in other aspects of cardiac care, such as precipitating clinically significant reductions in depression in patients who have undergone bypass surgery.[66] Indeed, there is evidence that CM can be helpful in CR specifically, increasing referral rates as well as improving health outcomes.[59]

CM is considered a promising strategy to improve rates of CR enrollment and participation, especially among those from particularly vulnerable subgroups. Specifically, approaches using strength-based case management, which focus on helping patients identify individual strengths and how they might be used to overcome obstacles, has had good success engaging traditionally disenfranchised medical populations in on-going care.[67] Through its multifaceted approach tailored towards patients' individual needs, CM can overcome a wide array of barriers that impede lower-SES patients' participation in CR such as psychological stressors, difficulties in managing appointments, and transportation issues.[68,69] After a comprehensive individual-based assessment of health- and social-related needs of the patient,

the designated case manager can assist by facilitating entry into the CR program, connecting patients to available resources in the community, collaborating with the patient's health care team, and scheduling subsidized transportation services. Case managers can also help sustain participation by providing timely information about recommended care for the cardiac condition, emphasizing the importance of CR in recovery from a cardiac event and managing appointments and transportation needs.[66,70,71] Finally, case managers can help prevent unnecessary ED visits and hospitalizations[59] by serving as a first line review of patient symptoms, determining which can be managed outside of the ED setting.

1.G.1 Case Management Supports those with Executive Function Deficits

One of the aspects of EF is the ability to plan and execute complex patterns of behavior. Given the challenges of coordinating appointments, taking new medications, and executing other areas of risk factor control (e.g. changes in diet, smoking and physical activity) it is not surprising that patients with EF challenges would struggle with post-cardiac event care. Addressing EF challenges can take two general forms, a remedial approach, which seeks to improve EF directly, or a compensatory approach, which seeks to create environmental supports that improve quality of life by reducing cognitive burdens and stress.[72] Case management is an example of the latter. In comprehensive case-management a case manager performs a functional needs assessment to characterize a patient's ability to initiate and perform necessary self-care activities. Armed with this information, the case manager can work with the patient to identify the patient's strengths and create an individualized plan of environmental supports, while providing timely education about the patient's illness and regularly interacting with the health-care providers, to maximize the patient's engagement with care and quality of life.[66,67,72]

1.H. Incentives are also a Promising Avenue for Promoting CR Attendance in Lower-SES Patients

Incentive-based interventions can also be highly effective in altering health-related behaviors among disadvantaged populations. One treatment approach, termed contingency management, involves providing financial incentives contingent on objective evidence of behavior change, and was originally developed here at the University of Vermont as a method to encourage abstinence from cocaine use among cocaine-dependent outpatients.[57] This incentives-based model was subsequently shown to be effective at increasing abstinence from a wide variety of substances, regularly resulting in treatment effect sizes of 0.32-0.42.[73,74] In a specific example from meta-analyses of treatments for smoking during pregnancy, a problem almost exclusive to lower-SES women, patients treated with this incentive-based model had 3.79 (95% CI: 2.74-5.25) greater odds of quitting smoking than those treated without incentives[75] and this treatment is significantly more effective at promoting smoking abstinence (RR 0.76) than any other behavioral or pharmacological treatments (RR 0.92-0.99).[76,77] Similar positive findings have been observed with other health-related behaviors in predominantly lower-SES groups.[78,79] Overall, financial incentives are one of the most promising approaches for motivating behavior change in lower-SES populations. Additionally, the use of incentives to promote health-related behaviors has become widely accepted in the private sector with the majority of large private employers include financial incentives as part of their employee wellness programs.[80]

More recently, financial incentives to promote behavior change has been adapted to increase a broader variety of health-related behaviors. Incentives have been used for increasing physical activity, medication adherence,[81] and weight loss,[82,83] including weight loss in economically disadvantaged populations.[84] Financial incentives are also highly efficacious at increasing treatment completion and adherence rates. For example, in a notoriously challenging population (cocaine dependent outpatients), adding incentives to a comprehensive treatment program approximately doubled treatment completion rates.[85] In CR, where health effects are dose-dependent,[35,52] this ability to sustain participation could be of considerable benefit. Indeed, our prior work suggests that incentives can increase CR adherence and may also be improving health (Preliminary Data).[86]

1.H.1 Incentives Help Overcome Executive Function Challenges

In line with the challenges faced by lower-SES populations, the use of incentives can help overcome EF challenges. One aspect of executive function, often referred to as delay discounting, is the weighing of future outcomes when considering current behaviors.[87] Those with EF challenges may overvalue the immediate (continued smoking, not exercising) and devalue the future (improved health) consequences when engaging in health-related behaviors.[88] Incentives can harness this bias towards the immediate outcome by providing an immediate positive outcome (earning an incentive) following the desired behavior (completing CR session).[89,90]

1.I. Summary and Conclusions

Lower-SES cardiac patients are at disproportionate risk for increased morbidity and mortality after a cardiac event. Much of this risk is attributable to lack of adherence to secondary prevention behaviors which are addressed at CR. Lower-SES patients who attend CR show significant improvement in health-related outcomes and subsequent reductions in risk. However, the number of lower-SES patients who attend CR is remarkably low.[19,34] Interventions to increase participation rates among lower-SES patients could have a particularly high return, as these patients, along with dismal CR participation rates, also have remarkably high levels of ED visits and rehospitalizations. This study has the potential to make a substantial contribution to reducing health disparities by improving health outcomes among those who are the most at risk but also with the most to gain. Additionally, this randomized, controlled study will add important data on the cost effectiveness of increasing CR attendance in lower-SES populations, which may differ in important ways from the analyses based on the general population. Given their high rate of costly rehospitalizations and the greater potential for health gains, the cost and benefits may differ even more favorably than those observed in more affluent populations. Accordingly, improved CR attendance could also have a substantial positive impact on health care costs by preventing costly rehospitalizations[17] which, during an interim analysis, averaged over $26,000 each in our prior trial. Preliminary data suggests that financial incentives are an efficacious approach to increase adherence to CR. Additionally our supporting data from trials of treatment for cocaine dependence, as well as evidence from the literature, suggests that case management should also be an efficacious intervention for promoting CR attendance and that these two interventions combined could promote attendance in an additive manner. Identifying efficacious treatments will significantly reduce cardiovascular disease disparities and costs in lower-SES cardiac patients.

***References**. Include references to prior human or animal research and references that are relevant to the design and conduct of the study.*

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Objectives: *Clearly state the primary and secondary objective(s) of the study.*

The primary objective of this study is to determine whether providing financial incentives or case management alone or in combination increases participation in, and continued attendance at, a cardiac rehabilitation program. Secondary objectives are: 1) Determine if differences in attendance affect health or other quality of life measures. 2) Quantify the costs of the incentive intervention and compare to expected reductions in health care costs.

METHODS AND PROCEDURES

Study Design: *Describe the research design, including a description of any new methodology and its advantage over existing methodologies.*

The proposed project is a four parallel-condition, randomized controlled trial to assess the efficacy of the use of incentives and case management for increasing CR participation in a lower-SES cardiac population. The study population will be comprised of 200 lower-SES patients with a recent CR-qualifying coronary event (including congestive heart failure). The experimental conditions will be: 1) an intervention where patients are assigned a case manager (CM) to coordinate their care 2), an intervention wherein patients earn financial incentives (FI) contingent on participating in CR, or 3) a combination of these two interventions (FI+CM). These intervention conditions will be compared to a usual care control (i.e., referral to CR). The main outcome measure for this project will be CR participation and adherence (% who complete 30+ sessions, # of sessions completed). Secondary outcomes will include improvements in executive function, fitness (PVO2), and quality of life over four months and at one-year follow-up, as well as rehospitalizations and emergency department visits through one-year follow-up. A comprehensive cost effectiveness analysis of the interventions will be conducted, incorporating rehospitalization rates and the cost of both delivering and receiving the treatment.

Procedures: *Describe all procedures (sequentially) to which human participants will be subjected. Identify all procedures that are considered experimental and/or procedures performed exclusively for research purposes. Describe the types, frequency and duration of tests, study visits, interviews, questionnaires, etc. Include required screening procedures performed before enrollment and while on study. Please provide in table, list or outline format for ease of review. (describe and attach all instruments)*

Note: A clinical research protocol may involve interventions that are strictly experimental or it may involve some aspect of research (e.g., randomization among standard treatments for collection and analysis of routine clinical data for research purposes). It is important for this section to distinguish between interventions that are experimental and/or carried out for research purposes versus those procedures that are considered standard therapy. In addition, routine procedures performed solely for research purposes (e.g., additional diagnostic/follow-up tests) should be identified.

All procedures are being undertaken for research purposes.

Study Measures: Study measures are taken by clinical staff blinded to treatment condition at three timepoints: baseline, end of treatment (four months) and one-year follow-up.

Demographic Information: We will collect the following sociodemographic data: age, gender, educational attainment, race/ethnicity, smoking status, marital status, and health insurance status at baseline. These demographic measures will allow us to characterize the population.

CO level: Carbon Monoxide level (CO) will be collected using a coVita carbon monoxide measuring device. The participant will be required to breathe slowly through a cardboard tube to obtain this measurement. This measurement will quantify recent exposure to carbon monoxide (e.g. smoke/secondhand smoke/car exhaust/heater emissions).

Maximal Exercise Capacity: Maximal exercise capacity will be assessed on a treadmill using measurements of peak oxygen uptake, duration of treadmill exercise and maximal exercise intensity in METS. A continuous modified-Balke protocol will be used, with exercise increasing gradually at 1 MET increments at 2-minute intervals. Exercise is EKG monitored and stopped prior to exhaustion if the patient develops progressive angina, > 2mm ST segment depression, exercise induced hypertension (230 systolic, 105 diastolic), severe arrhythmias, dizziness or symptomatic hypotension. The occurrence of any concerning responses, other than high threshold angina, excludes a patient from the training protocol unless effective therapy is instituted. Patients will perform the maximal stress test taking their usual medications at a standardized time of day. The clinical staff at UVMMC have extensive experience

measuring peak exercise capacity in patients in the CR setting.[127] In lieu of a maximal stress test at CR exit, estimated METS while exercising on the treadmill may be used at the final CR session as a clinical measure of fitness at exit.

Socio-Cognitive Measures: We will assess current depressive symptoms (Beck Depression Inventory, BDI, Patient Health Questionnaire (PHQ-2) [128129] as well self-reported adaptive functioning and problems (ASEBA - Achenbach System of Empirically Based Assessment.[130] We will also assess self-reported social support (ISEL - Interpersonal support evaluation list).[147]

Quality of Life: The General Health Status M.O.S. SF-36 questionnaire will be administered with special attention to the physical function component score).[131,132] Quality of life measures incorporate the EuroQual[133] and the disease specific MacNew Cardiac Health Status Questionnaire.[134,135] These measures are all standardized and have adequate test-retest reliability.[136,137]

Executive Function (EF): Several assessments will be administered to measure executive function, which has been shown to be important in characterizing how likely populations are to engage in various health behaviors.[138,139] For initial characterization we will administer the Wechsler Abbreviated Scale of Intelligence (WASI),[140] and the Delis-Kaplan Executive Function System (D-KEFS).[141] In addition, programmatic exercise has been shown to improve measures of executive function.[142] To measure changes in these characteristics we will administer the following instruments/tasks at each assessment: Behavior Rating Inventory of Executive Function (BRIEF),[143] discounting of delayed hypothetical monetary rewards (Delay discounting, DD),[144] Time Perspective Questionnaire (TPQ),[139] digit span test (subset of the WASI), and Stop Signal Task (SST).[145,146]

Treatment Access and Cost: To assess costs to participants (e.g. travel expenses, time spent, and out-of-pocket expenses), we will use a tool created for our prior study that adapted the Client Drug Abuse Treatment Cost Analysis Program (DATCAP; www.datcap.com/client.htm) for use in cardiac rehabilitation. Direct nonmedical and indirect costs include the value of time of participants attending the program, waiting, traveling, or exercising, as well as transportation expenses.

Physical Activity: We will be utilizing a portion of the IPAQ (International Physical Activity Questionnaire) at one-year follow up.

Procedures by condition:

Usual care: Participants in usual care will come in for the scheduled assessments but will not receive other interventions.

Case Management Intervention: In the CM condition patients will receive the usual care program described above but will also receive case management, initiated after consent. The case manager will subsequently be available by phone daily between the hours of 0900 and 1900 during the week and 0900 and 1200 on Saturday. The case manager will work with the patient to identify the patient's strengths and create an individualized management plan. The designated case manager will support CR attendance by facilitating entry into the program, connecting patients to available resources in the community, collaborating with the patient's health care team, and scheduling subsidized transportation services as needed. Case managers will also sustain participation by emphasizing the importance of CR in recovery from a cardiac event, and managing appointments and transportation needs. To maximize benefits from case management, supporting patient's engagement with care and quality of life, the case manager will also provide timely education about the patient's illness, answer questions on cardiac self-management, regularly interact with health-care providers, and provide plans of environmental supports. Finally, case managers will serve as a first line review of patient symptoms, preventing unnecessary ED visits and hospitalizations by determining which can be managed outside of the ED setting.

Financial Incentive Intervention: In the incentives condition, participants will receive financial incentives (FI) for participation in cardiac rehabilitation sessions, paid upon completion of each of the 36 sessions. Participation will be defined as attending the scheduled session and completing the recommended exercise and other activities scheduled for that day. Participation will be verified by a program staff person. Visits will be scheduled 2-3 times a week over a period of 4 months to comprise the 36 visits commonly prescribed. Participation in an introductory group meeting will earn the participant $20. Participation in subsequent exercise sessions will be compensated on an escalating schedule. Participation in the first exercise session earns a participant $10 with each subsequent session increasing the amount earned by $2 per session up to a maximum of $40 per session. Failure to attend a session (unless advanced notice is given) results in no earnings for that session and the amount possible to be earned in the next scheduled session is reset to $10. If the participant successfully participates in two consecutive sessions following a reset, the amount earned is returned to the amount it was prior to the reset. This schedule of escalating value incentives combined with a reset contingency for failure to meet the targeted goal has been experimentally demonstrated to sustain continuous periods of adherence for other health-related behaviors. The total possible incentive earnings is $1220, however, some participants assigned to the incentives condition will fail to adhere to the recommended 36 sessions. Based on our prior studies using financial incentives, we estimate that mean earnings in the intervention condition will be approximately 70% of maximal, or $854. Incentives will be earned in the form of vouchers exchangeable for retail goods (e.g. gift cards) which has been shown to be a form of incentives can be clinically useful, as incentives earned can be used to purchase goods that further prevention goals or help overcome barriers (e.g. healthy food, new shoes, transportation costs).

Financial Incentive and Case Management Intervention: In the combined condition (FI + CM), participants will receive both the case management and financial incentives program described above.

Data Collection: CR Session and Exercise Amidst Contact Restrictions (e.g. COVID-19)

If the CR clinics (UVMMC, Copley Hospital, Northwestern Medical Center) cease in-person visits, session completion will be calculated by tracking remote participation. Study participants across arms will be expected to complete two CR sessions per week. One session will consist of completing the weekly telemedicine call conducted by CR staff and one session will consist of completing a recommended step goal for that day, as confirmed by an Omron pedometer. A session will be coded as missed (excused or unexcused, depending on the situation) if a participant fails to send a step count or fails to complete the telemedicine call from the CR case manager.

For research involving survey, questionnaires, etc.: *Describe the setting and the mode of administering the instrument and the provisions for maintaining privacy and confidentiality. Include the duration, intervals of administration, and overall length of participation. (describe and attach all instruments)*

☐ ***Not applicable***

Questionnaires will be administered at intake, after 4 months, and at one year. All questionnaires will be administered in a private setting at the Cardiac Rehabilitation Facility. Questionnaires should take approximately one hour to complete.

As listed above the following questionnaires will be administered (and are attached):

Beck Depression Inventory. Note: the BDI includes a question about suicidal thoughts. If a subject endorses this item research staff will follow the attached suicidality protocol.
MacNew Cardiac Health Status Questionnaire
TCAP
Interpersonal Support Evaluation List
International Physical Activity Questionnaire (IPAQ, brief form)

Executive Function Battery Questionnaires:
The Time Perspective Questionnaire – Exercise (TPQ)
Euroqol (Quality of Life)
Achenbach System of Empirically Based Assessments (ASEBA) – Adult Self Report or Older Adult Self Report
Behavior Rating Inventory of Executive Function (BRIEF)

Data Collection: Questionnaire Administration Amidst Contact Restrictions (e.g. COVID-19)

Whenever possible, paper questionnaires will be completed remotely, either by mail (completed and returned by the study participant) or with the researcher over the phone. If in-person research visits are not allowed the following assessments will not be collected: IQ test (WASI), Stop Signal Task (SST), Delay Discounting Task (DD), Trail Making Task (TMT), Digit Span Task. If in-person research visits are allowable these assessments will be completed using appropriate distancing measures and PPE as is outlined in our approved lab safety reopening plan (attached).

Statistical Considerations: *Delineate the precise outcomes to be measured and analyzed. Describe how these results will be measured and statistically analyzed. Delineate methods used to estimate the required number of subjects. Describe power calculations if the study involves comparisons. Perform this analysis on each of the primary and secondary objectives, if possible.*

Power: Sample sizes were calculated to provide sufficient power to calculate differences in our primary outcome (CR adherence, as measured by % completing 30+ sessions) between the control condition and any of the three intervention conditions as well as between the combined intervention and either of the interventions delivered alone. Of most relevance, preliminary data from a previous trial on the use of incentives to increase CR rates among lower-SES individuals show that 54% of those receiving incentives completed the 30+ sessions compared to 28% of those receiving usual care. Using these proportions and the likelihood ratio test for two proportions in SAS POWER, 56 individuals per condition would be needed to detect a significant difference between conditions with 80% power. A seminal set of studies, conducted by Co-I Higgins, that systematically determined the efficacy of case management and incentives, alone and in combination, on cocaine abstinence, provided additional data for the power estimates.[54-58] Using effect sizes from these five studies, the maximum estimated number of participants needed per condition is 50 to detect a significant difference in treatment adherence in combined intervention vs. single intervention with 80% power. Comparing any of the interventions singly or combined to usual care at four months post-treatment is estimated to require at most 25 participants per condition. Supporting these estimates, additional studies on the use of case management or incentives for adherence to other health-related behaviors have demonstrated effect sizes comparable to the studies referenced above.[66,67,73,106,107] As such, the proposed sample size of 200 randomized subjects (56/intervention condition, 32 control) will allow us to conduct all pre-planned pairwise comparisons of the primary outcome measure (program adherence) with 80% power.

Data Analysis: Treatment conditions will be compared for differences in baseline demographic characteristics using one-way Analysis of Variance (ANOVA) (or a nonparametric alternative, such as the Kruskal-Wallis Test) for continuous measures and chi-square tests (or Fisher's Exact Test) for categorical variables. If specific characteristics differ significantly across treatment conditions and are predictive of treatment outcomes, they will be considered as covariates in subsequent analyses. Primary analyses will include all subjects randomized to treatment conditions independent of early dropout or non-adherence, consistent with an intent-to-treat approach for randomized clinical trials.[147]
The primary outcome measure in this trial will be CR adherence (% completing 30+ sessions) compared between the control condition and any of the three intervention conditions as well as between the combined intervention and either of the interventions delivered alone. Proportions completing all CR sessions will be examined across conditions using the test for differences between two population proportions (z), with 95% confidence intervals on effect sizes. To look at other measures of attendance, Cox proportional hazard models will be used to test differences in number of CR sessions completed

(i.e., time to dropout) between conditions. Purposeful selection of covariates will be used to build models.[164] Once final models have been derived, we will generate estimated hazard ratios with 95% confidence intervals and graphs of covariate-adjusted survival functions. Across all tests, statistical significance will be defined as $p < 0.05$ (2-tailed).

Although this study is powered for our primary outcome of adherence to CR, we will also carefully examine improvements in fitness, and other health outcomes (quality of life, maximal exercise capacity, weight, waist measurements) between conditions, using the pre-planned comparisons outlined for the primary outcome. Additionally, we will examine changes in executive function measures and socio-cognitive status at 4 and 12 months. Changes in these scores will also be examined for possible gender interactions. Since multiple observations for each participant will be obtained, the general analytic approach will consist of analysis of covariance (ANCOVA) at 4 months and repeated measures analysis of variance (ANOVA) at 12 months. Formal testing will examine the condition by time interaction term to assess differential time changes between treatment conditions. Post-hoc comparisons between conditions will be made if significant interactions are observed.

Risks/Benefits: *Describe any potential or known risks. This includes physical, psychological, social, legal or other risks. Estimate the probability that given risk may occur, its severity and potential reversibility. If the study involves a placebo or washout period, the risks related to these must be addressed in both the protocol and consent. Describe the planned procedures for protecting against or minimizing potential risks and assess their likely effectiveness. Where appropriate, discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Discuss the potential benefits of the research to the subjects and others. Discuss why the risks to the subjects are reasonable in relation to the anticipated benefits to subjects and others. Discuss the importance of the knowledge gained or to be gained as a result of the proposed research and why the risks are reasonable in relation to the knowledge that reasonably may result. If there are no benefits state so.*

Risks: Exercise testing is a common procedure with minimal risks, but the test is monitored by a physician and will be stopped if problems occur. These include fainting, dizziness, chest pain, irregular heartbeats, or a heart attack, although the latter is extremely rare. The risks of this test are roughly 1 death in every 10,000 tests performed and serious adverse effects such as a heart attack or serious irregular heart beat (arrhythmias) requiring hospitalization occur in less than 1 in 1,000 tests. Blood pressure, heart rate and rhythm and breathing are closely and constantly monitored by a physician and exercise technician trained in CPR, exercise testing and emergency treatment of cardiac arrhythmias. This team has a specific, well-practiced protocol that includes contacting emergency services and providing interim medical support if needed.

- The participant may feel uncomfortable answering some of the questions. We will work with them to minimize this discomfort and no one has to answer any question that they do not wish to answer.
- There is a risk that participants will express suicidal thoughts or actions as we will be using the Beck Depression Inventory which queries suicidality. A suicidality protocol (attached) will be used in the case of a participant endorsing a suicidality item.
- There is a risk that confidential information might accidentally be disclosed. Professional standards for protecting confidential information will be used to minimize this risk.

Benefits: It is likely that those who complete CR will be healthier and have a higher quality of life than those who do not. However, just being in this study does not guarantee benefits.

This study will benefit society as a whole, however. Low-income patients are not recovering from cardiac events as well as higher-income patients. If we can find an effective way to engage them in appropriate post-cardiac care they will have better recovery and a higher quality of life. Improving outcomes in this vulnerable population could help narrow the gap in health outcomes between high and low income patients.

Therapeutic Alternatives: *List the therapeutic alternatives that are reasonably available that may be of benefit to the potential subject and include in the consent form as well.*

X ***Not Applicable***

Cardiac rehabilitation through the aforementioned facility is the only formal recovery program for these patients in the area. Patients will be told they can attend CR without being in the study. The other

alternative would be for a patient to recover on one's own at home without the supervised exercise training, education and counseling.

Data Safety and Monitoring: *The specific design of a Data and Safety Monitoring Plan (DSMP) for a protocol may vary extensively depending on the potential risks, size, and complexity of the research study. For a minimal risk study, a DSMP could be as simple as a description of the Principal Investigator's plan for monitoring the data and performance of safety reviews or it could be as complex as the initiation of an external, independent Data Safety and Monitoring Board (DSMB). The UVM/UVM Medical Center process for review of adverse events should be included in the DSMP.*

What is Monitored

All research procedures will be monitored to ensure that they conform to the approved protocol. In addition, monitoring will be done of all adverse events that might arise and affect safety. This will include all reports of serious adverse events (SAE) as defined by FDA. An SAE is defined as any adverse experience occurring that results in any of the following outcomes: life-threatening, death, new or prolonged hospitalization, persistent or significant disability/incapacity, or congenital anomaly/birth defect. Additionally, other significant adverse events (adverse events that lead to drop out by the participant or termination by the investigator) and other expected and unexpected adverse events resulting from the study will be monitored.

Frequency of Monitoring

Cardiac-related symptoms will be rated at baseline and monitored during each participant contact (in person and by telephone) using scales that are operationally-defined, have good-to-excellent inter-rater reliability and are widely used in clinical and research settings. In addition, participants will be asked about their general health, symptoms and adverse events weekly during the study. Any clinically-significant symptom exacerbations noted during the study (i.e., changes in severity of existing symptoms, presentation of new symptoms) will trigger review and contact with the participant by the Medical Director Dr. Ades. Any serious adverse event and any unexpected and apparently related adverse event will trigger immediate review and contact with the participant by Medical Director Ades and will be reported by the PIs to the IRBs. Participants will be given study contact cards so that they can inform us of events that occur in between study visits. Monitoring by the PI is conducted on an ongoing basis and monitoring by the IRB is conducted at the continuing reviews as scheduled by the IRB and upon receiving reports of adverse events from the PIs.

Charge of DSMB. The DSMB will be charged with monitoring and evaluating two aspects of the clinical trial. These include: a) monitoring study progress; i.e., screening, recruitment, and retention data, to assure that the study can be completed in the time proposed, and b) reviewing safety data, especially serious adverse events (SAEs). SAEs, study or non-study related, will be reported to the DSMB, as well as to NIH, by the PI within 72 hours of the PI learning of the event. The DSMB will review all adverse events.

DSMB Members: Our DSMB will consisting of four individuals. The DSMB will include members with experience in cardiac rehabilitation, lower-SES patients, conduct of clinical trials, and data analysis. It will include at least one physician and one researcher. The chair will have served on prior DSMBs.

Meetings: The DSMB will meet approximately every 6 months either in-person or by teleconference call. Meetings of the DSMB will be coordinated by the PI (Gaalema) and Lead Statistician (Priest). Three members will constitute a quorum. Members who are unable to attend will be contacted and given an opportunity to provide input on the issues at hand. Interim data reports will be supplied to the DSMB by the PI at least two weeks prior to each meeting. Data will be supplied in tabular and electronic forms per request of the DSMB. Examples of acceptable interim reports will be made available to investigators to facilitate their interaction with the DSMB. In addition, any new information from external sources that could alter the DSMB's perception of the trial, for example, relevant findings published from other trials on improving CR participation in lower-SES patients, will be assembled and summarized with respect to the PI's perception of its importance.

Meeting Procedure: Prior to each formal meeting, it is the responsibility of the chair of the DSMB to assure that the required data have been submitted with appropriate explanations. This material will be sent to Board members at least two weeks prior to the DSMB meeting. The formal meeting of the DSMB for the trial shall consist of three parts. The first part is an open session in which members of the research team, including the Principal Investigator and the study statistician, will attend. Outcome results must not be discussed during this open session. Minutes from the open session will be taken by project staff. Following the open session, the DSMB will hold a closed session. The study statistician will be available to discuss the results with the DSMB during the closed session. Minutes from the closed session will be taken by the chair or her/his designate. The third phase of each meeting is a final executive session involving only voting DSMB members and may be held to allow the DSMB to discuss general conduct of the trial and all outcome results, including adverse events, to develop recommendations, and to take votes as necessary. Following the meeting, the DSMB Chair will provide a summary of the DSMB's recommendations to the PI. Study investigators will also have the opportunity to ask questions to clarify the recommendations.

Reports of DSMB Deliberations: Clerical support will be provided by research staff as requested by the chair of the DSMB. Following each DSMB review, the chair shall prepare a written report to be finalized within 20 working days following the formal meeting and be sent to the PI. The report will review the two main aspects of the trial for which the DSMB is responsible as noted in section 2 above (i.e., study progress and safety). In addition, following each study review, the DSMB will recommend either: a) continuation of the trial using the current protocol and statistical plan, b) Continuation of the project with modifications as outlined by the Board, c) Immediate suspension of the trial for safety reasons with a recommended plan of follow-up to minimize subject harm (requires unanimous vote), d) placing a clinical hold on the trial. This should include freezing further accrual. Subjects may continue on their assigned treatments until clarifications requested by the Board are resolved (requires unanimous vote), e) Termination of the trial because of: 1) treatment effectiveness demonstrated earlier than expected ("early stopping"); 2) futility of further accrual to meet the trial's goal; 3) discovery of new information that precludes completion of the trial; and/or 4) structural problems in trial execution that are not amenable to correction (requires unanimous vote).

Adverse Event and Unanticipated Problem (UAP) Reporting: *Describe how events and UAPs will be evaluated and reported to the IRB. All protocols should specify that, in the absence of more stringent reporting requirements, the guidelines established in the Committees on Human Research "Adverse Event and Unanticipated Problems Reporting Policy" will be followed. The UVM/UVM Medical Center process for review of adverse events and UAPs to subjects or others should be included in the DSMP.*

Reporting Plan
Serious and unexpected adverse events that are related to the study will be reported to the IRB and to NIH. Any actions taken by the IRB other than acceptance will be reported to the sponsor along with any changes or amendments to the protocol requested by the IRB in response to these reports. Proposed changes or amendments to the protocol in general must first be requested in writing to the IRB, which will then grant or deny permission to make the requested change in protocol. The NIH will be informed of any changes or amendments in the approved protocol.

Withdrawal Procedures: *Define the precise criteria for withdrawing subjects from the study. Include a description of study requirements for when a subject withdraws him or herself from the study (if applicable).*

There are no predefined criteria for withdrawal from the study. However, participants may be withdrawn if the medical director (Phillip Ades, MD) determines it is not advisable that they continue on in the program. Participants may withdraw themselves at any time, for any reason. Research data gathered from such participants will be not be retained.

Sources of Materials: *Identify sources of research material obtained from individually identifiable human subjects in the form of specimens, records or data. Indicate whether the material or data will be obtained specifically for research purposes or whether use will be made of existing specimens, records or data.*

Data for this project will come from clinical records (number of cardiac rehabilitation sessions completed, cause and cost of hospitalizations) or from research procedures: demographics, physical exams, CO measurements, exercise tolerance testing, administered questionnaires, executive function/decision making measures.

To track CR attendance and monitor adverse events among NMC patients, UVMMC research staff will obtain a secure research login to access the electronic medical record at NMC.

DRUG AND DEVICE INFORMATION

Investigators are encouraged to consult the UVM Medical Center Investigational Pharmacy Drug Service (847-4863) prior to finalizing study drug/substance procedures.

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

Drug name – generic followed by brand name and common abbreviations. Availability – Source and pharmacology; vial or product sizes and supplier. If a placebo will be used, identify its contents and source. (attach investigational drug brochure)

Preparation: Reconstitution instructions; preparation of a sterile product, compounded dosage form; mixing guidelines, including fluid and volume required. Identify who will prepare.

Storage and stability – for both intact and mixed products.

Administration – Describe acceptable routes and methods of administration and any associated risks of administration.

Toxicity – Accurate but concise listings of major toxicities. Rare toxicities, which may be severe, should be included by indicated incidence. Also adverse interactions with other drugs used in the protocol regimen as well as specific foods should be noted. Address significant drug or drug/food interactions in the consent form as well. List all with above details.

Is it FDA approved: (include FDA IND Number)

1. in the dosage form specified? If no, provide justification for proposed use and source of the study drug in that form.

2. for the route of administration specified? If no, provide justification for route and describe the method to accomplish.

3. for the intended action?

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

Device name and indications (attach investigational device brochure)

Is it FDA approved: (include FDA IDE Number)

1. for indication specified? If no, provide justification for proposed use and source of the device.

Risk assessment (non-significant/significant risk) - PI or sponsor needs to assess risk of a device based upon the use of the device with human subjects in a research environment.

SUBJECT CHARACTERISTICS, IDENTIFICATION AND RECRUITMENT

Subject Selection: *Provide rationale for subject selection in terms of the scientific objectives and proposed study design.*

Participants will include individuals hospitalized at UVMMC, or receiving outpatient care at UVMMC or Copley Hospital, due to a recent MI, coronary revascularization, diagnosis of congestive heart failure, or heart valve replacement or repair who are also enrolled in Medicaid, receiving other income-based state support, or have a less than high school educational attainment. Low-income individuals are being targeted as historically this population has had extremely low participation rates in cardiac rehabilitation. This study will be testing methods of increasing cardiac rehabilitation participation in low-income individuals.

Vulnerable Populations: *Explain the rationale for involvement of special classes of subjects, if any. Discuss what procedures or practices will be used in the protocol to minimize their susceptibility to undue influences and unnecessary risk (physical, psychological, etc.).*

X ***Not applicable***

Number of Subjects: *What is the anticipated number of subjects to be enrolled at UVM/UVM Medical Center and in the case of a multi-center study, with UVM/UVM Medical Center as the lead, the total number of subjects for the entire study.*

We will screen 240 with the goal of enrolling 200.

Inclusion/Exclusion Criteria: *Eligibility and ineligibility criteria should be specific. Describe how eligibility will be determined and by whom. Changes to the eligibility criteria at a later phase of the research have the potential to invalidate the research.*

Inclusion Criteria:

- A recent MI, coronary revascularization, diagnosis of congestive heart failure or heart valve replacement or repair
- Enrolled in a state-supported insurance plan for low income individuals or receiving other state benefits that are based on financial need (housing subsidy, food stamps, etc.) or received less than a high school education
- Lives in and plans to remain in:
  1. the greater Burlington, VT area (Chittenden county, UVMMC catchment area)
  2. Morrisville, VT (Copley catchment area) or
  3. St Albans, VT (Northwestern Medical Center catchment area) for the next 12 mos.

Exclusion criteria:

- Dementia (MMSE<20) or current untreated Axis 1 psychiatric disorder other than nicotine dependence as determined by medical history
- Advanced cancer, advanced frailty, or other longevity-limiting systemic disease that would preclude CR participation
- Rest angina or very low threshold angina (<2 METS) until adequate therapy is instituted
- Severe life threatening ventricular arrhythmias unless adequately controlled (e.g. intracardiac defibrillator)
- Class 4 chronic heart failure (symptoms at rest)
- Exercise-limiting non-cardiac disease such as severe arthritis, past stroke, severe lung disease

- Previous successful attendance at cardiac rehabilitation (defined as completing 6+ sessions in the past year)

Eligibility will be determined by the PI in concert with the medical director (Philip Ades, MD).

Inclusion of Minorities and Women: *Describe efforts to include minorities and women. If either minorities or women are excluded, include a justification for the exclusion.*

Neither women nor minorities will be excluded from this study. As eligible candidates will be identified based purely on diagnosis code and insurance type potential bias should be minimized.

Inclusion of Children: *Describe efforts to include children. Inclusion is required unless a clear and compelling rationale shows that inclusion is inappropriate with respect to the health of the subjects or that inclusion is inappropriate for the purpose of the study. If children are included, the description of the plan should include a rationale for selecting or excluding a specific age range of children. When included, the plan must also describe the expertise of the investigative team in working with children, the appropriateness of the available facilities to accommodate children, and the inclusion of a sufficient number of children to contribute to a meaningful analysis relative to the purpose of the study.* ***If children are excluded*** *then provide appropriate justification. Provide target accrual for this population.*

Children will not be included in this study. This project aims to develop an efficacious intervention to increase cardiac rehabilitation among those who have experienced a recent cardiac event. As such events are exceedingly rare in children no children will be enrolled.

For protocols including the use of an investigational drug, indicate whether women of childbearing potential have been included and, if not, include appropriate justification.

n/a

If HIV testing is included specifically for research purposes explain how the test results will be protected against unauthorized disclosure. Include if the subjects are to be informed of the test results. If yes, include the process and provision for counseling. If no, a rationale for not informing the subjects should be included.

X ***Not applicable***

Recruitment: *Describe plans for identifying and recruitment of subjects. All recruitment materials (flyers, ads, letters, etc) need to be IRB approved prior to use.*

For UVMMC and NMC patients, research staff will review the census of the two floors of the UVMMC hospital that handle acute cardiac-related cases (Miller 3 and Miller 4). Additionally for UVMMC, staff will review the outpatient heart failure clinic schedule (UVMMC Outpatient Cardiology). A list of eligible patients will be created based on patients who have had a qualifying condition (MI, coronary revascularization, congestive heart failure or heart valve replacement or repair), who are receiving financial assistance (as seen by having Medicaid insurance or receiving other financial assistance, information available in the medical record), or who have less than a high school education. This list of patients will be taken to the treating team who will introduce the study to the patients as appropriate. If the patient agrees to hear more about the study research staff will explain the study in detail and obtain written consent from willing participants.

For Copley patients, a UVM research staff member, under Dr. Kunin's supervision, will use a research-specific login to screen Copley's outpatient cardiology electronic record. Potentially eligible patients (those who have had a qualifying condition (MI, coronary revascularization, congestive heart failure or heart valve replacement or repair), and who are receiving financial assistance (Medicaid insurance or receiving other financial assistance) will be introduced to the study by Dr. Kunin (see info sheet). Patients who are interested will be referred to UVM staff for consenting.

NMC patients will only be screened for and approached by research staff while inpatient at UVMMC. Screening and consent procedures will not take place at NMC.

FINANCIAL CONSIDERATIONS

Expense to Subject: *If the investigation involves the possibility of added expense to the subject (longer hospitalization, extra studies, etc.) indicate in detail how this will be handled. In cases where the FDA has authorized the drug or device company to charge the patient for the experimental drug or device,* ***a copy of the authorization letter from the FDA or sponsor must accompany the application. Final approval will not be granted until the IRB receives this documentation.***
There are very limited circumstances under which study participants may be responsible (either directly or via their insurance) for covering some study-related expenses. If the study participant or their insurer(s) will be billed for any portion of the research study, provide a justification as to why this is appropriate and acceptable. For example, if the study involves treatment that is documented standard of care and not investigational, state so. In these cases, the protocol and the consent should clearly define what is standard of care and what is research.

There are no expenses to the participant.

Payment for participation: *Describe all plans to pay subjects, either in cash, a gift or gift certificate. Please note that all payments must be prorated throughout the life of the study. The IRB will not approve a study where there is only a lump sum payment at the end of the study because this can be considered coercive. The amount of payment must be justified. Clarify if subjects will be reimbursed for travel or other expenses.*

☐ ***Not applicable***

Participants will receive payment for participating in this study. All participants will receive $100 in compensation for their time for attending each assessment ($300 total). Reimbursement for travel costs for transportation to assessments will also be offered (up to $150 total). In addition, participants in incentive conditions will receive gift cards for attending cardiac rehabilitation sessions totaling up to $1220. Once incentives are earned they can be requested by the participant at any time.

Collaborating Sites*. When research involving human subjects will take place at collaborating sites or other performance sites when UVM/UVM Medical Center is the lead site, the principal investigator must provide in this section a list of the collaborating sites and their Federalwide Assurance numbers when applicable. (agreements may be necessary)*

☒ ***Not applicable***

INFORMED CONSENT

Consent Procedures*: Describe the consent procedures to be followed, including the circumstances under which consent will be obtained, who will seek it, and the methods of documenting consent. Specify the form(s) that will be used e.g. consent (if multiple forms explain and place identifier on each form), assent form and/or HIPAA authorization (if PHI is included). These form(s) must accompany the protocol as an appendix or attachment.*

Note: Only those individuals authorized to solicit consent may sign the consent form confirming that the prospective subject was provided the necessary information and that any questions asked were answered.

Patients who are hospitalized, or being cared for, due to a recent cardiac event and are enrolled in Medicaid, or have less than a high school education will be approached for possible inclusion by the PI or a trained representative. Patients will be given an unlimited amount of time to decide about participating in the study. A consent form with appropriate HIPAA language will be used for this study.

Information Withheld From Subjects: *Will any information about the research purpose and design be withheld from potential or participating subjects? If so, explain and justify the non-disclosure and describe plans for post-study debriefing.*

☒ ***Not applicable***