Cardiac Resynchronization in the Elderly: Piloting Pacemaker vs. Defibrillator Therapy (Randomized Trial and Observational)

CRT-P vs. CRT - D

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Funded by: National Heart, Lung, and Blood Institute (NHLBI)

Protocol A Version 6

24 May 2018

NCT # 03031847

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LIST OF ABBREVIATIONS

AE	Adverse Event
BioLINCC	Biologic Specimen and Data Repository Information Coordinating Center
BMI	Body Mass Index
BNP	Brain Natriuretic Peptide
CFR	Code of Federal Regulations
CMS	Centers for Medicare and Medicaid Services
CRF	Case Report Form
CRT	Cardiac Resynchronization therapy
CRT-D	Cardiac Resynchronization therapy-Defibrillator
CRT-P	Cardiac Resynchronization therapy- Pacemaker
DCC	Data Coordinating Center
DSMB	Data Safety Monitoring Board
eCRF	Electronic Case Report Forms
EKG	Electrocardiogram
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HF	Heart Failure
HIPAA	Health Insurance Portability and Accountability Act
ICH	International Conference on Harmonisation
ICH E6	International Conference on Harmonisation Guidance for Industry, Good Clinical Practice: Consolidated Guidance
ICMJE	International Committee of Medical Journal Editors
IRB	Investigational Review Board
LVEF	Left Ventricular Ejection Fraction
NIH	National Institutes of Health
NHLBI	National Heart, Lung, and Blood Institute
NYHA	New York Heart Association
OSUMC	Ohio State University Medical Center
PI	Principal Investigator
QC	Quality Control
QOL	Quality of Life
RCT	Randomized Clinical Trial
REDCap	Research Electronic Data Capture
SAE	Serious Adverse Event
SD	Standard Deviation
SMC	Safety Monitoring Committee
SOC	System Organ Class
SOP	Standard Operating Procedure
UPMC	University of Pittsburgh Medical Center
US	United States
VaPITT	Veterans Hospital of Pittsburgh

STATEMENT OF COMPLIANCE

This trial will be conducted in accordance with all applicable US Federal regulations regarding the protection of hum subjects and the Declaration of Helsinki. All sites will maintain compliance to this protocol as well as any additional regulations imposed by their IRB. All personal who participate in the study related activities must have undergone Human Subjects Protection Training.

I agree to ensure that all staff members involved in the conduct of this study are informed about their obligations in meeting the above commitments.

Principal Investigator: _____
Print/Type Name

Signature _____ Date:_____.

PROTOCOL SUMMARY

Title: Cardiac Resynchronization in the Elderly: Piloting Pacemaker vs. Defibrillator Therapy (Randomized Trial and Observational). CRT – P vs. CRT – D.

Précis: Pilot trial designed with a two part aim at enrollment. Aim 1 is designed as a randomized, controlled trial for older patients (≥75 years) who are indicated for CRT device implantation to receive a CRT-P or CRT-D. Information collected will help to assess the ability to enroll and retain older patients is a randomized controlled trial of CRT-P versus CRT-D in preparation for a large pivotal trial. Aim 2 is a non-randomized, observational study of patients who were offered inclusion into Aim 1 but refused to participate. Aim 2 subjects present an opportunity to understand the reasons why older patients may refuse enrollment into a randomized trial as well as still allowing for collection of data regarding their chosen CRT device.

Objectives: **Primary Objective**: Feasibility of enrolling and maintaining elderly heart failure patient in CRT-P vs CRT-D randomized trial.
Secondary Objectives: Examine predictors of refusing randomization and of choosing CRT-P vs. CRT-D device implantation in elderly patients.

Endpoint **Primary Endpoint**: The ability to enroll in the randomized controlled trial of CRT-P versus CRT-D patients.
Secondary Endpoints: Determinants of refusing participation in CRT-P versus CRT-D clinical trial.

Population: Patients 75 years or older who are clinically indicated for CRT device implantation based on published guidelines[6] will be considered for this trial. The racial, gender, and ethnic characteristics of the proposed subject population represent the populations cared for at the participating institutions. Subjects meeting all inclusion and none of the exclusion criteria for Aims 1 and 2 will be enrolled in this research. No exclusion criteria shall be based on race, gender, or HIV status. Patients younger than75 years of age are excluded based on study rationale and design.

Study Type: Pilot trial with two clinical Aims. Aim 1 is a randomized clinical trial and Aim 2 is an Observational clinical trial.

Number of Sites Enrolling Participants: Total of four participating sites

Study Duration: Approximately 24 months

Participant Duration: Up to 18 months from enrollment

1 KEY ROLES

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2 INTRODUCTION: BACKGROUND INFORMATION AND SCIENTIFIC RATIONALE

2.1 BACKGROUND INFORMATION

Heart failure (HF)[1-5] is a disease of epidemic proportions in the United States affecting over 5 million individuals. While the incidence of many diseases in the U.S. is decreasing, HF represents one of only two human diseases that are increasing in frequency. It is estimated that nearly 400,000 new cases of HF will be diagnosed in the next year, one million patients will be hospitalized, and 300,000 patients will die from HF in the U.S. Although the development of new medications has substantially broadened the therapeutic armamentarium over the past decades, the long-term prognosis for patients with HF remains poor with less than 50% of patients surviving five years after the initial diagnosis. A characteristic feature of HF is that it is a progressive disease with patients having repeated and progressively more frequent hospitalizations for worsening symptoms. HF puts an overwhelming burden on patients as evidenced by dramatically diminished quality of life (QOL). It also has a marked impact on the economics of our health system accounting for over 50 billion dollars in annual national healthcare expenditure.

Cardiac resynchronization therapy (CRT) is an established therapy in HF[6]. HF patients with severe cardiomyopathy and ventricular conduction abnormalities, as demonstrated by a wide QRS waveform on surface electrocardiogram (>120 ms), who continue to suffer from HF symptoms (New York Heart Association Classes II, III, and ambulatory IV) despite optimal pharmacological therapy

including angiotensin converting enzyme inhibitors/angiotensin receptor blockers, β-blockers, and potassium-sparing diuretics can benefit from CRT with improved maximum oxygen consumption, exercise tolerance, and improved QOL[7,8]. Results of large, multicenter, randomized controlled trials such as *Companion*[9] and *Care-HF*[10] demonstrate, in addition, a significant decrease in the composite endpoint of death or HF hospitalization with CRT over optimal pharmacological therapy. Studies also suggest a benefit of CRT on reducing the burden of ventricular arrhythmias[11]. It is estimated that about 40% of patients who have systolic HF are CRT candidates by current guideline criteria[6].

CRT-P versus CRT-D

CRT can be delivered through a pacemaker (CRT-P) or a defibrillator (CRT-D). CRT-P devices are smaller (i.e. require a smaller surgical incision at implantation) and cost a fraction of the price of CRT-D devices. Both CRT-P and CRT-D provide resynchronization to the failing heart through low energy pacing impulses, but CRT-D can additionally deliver high-energy shock therapy to terminate life-threatening ventricular arrhythmias. Compared to optimal pharmacological treatment, both CRT-P and CRT-D have been shown in randomized controlled trials[9,10] to reduce all-cause mortality and improve patient symptoms and cardiac function. In one study comparing them to each other[9], CRT-P and CRT-D had equivalent benefits in reducing the composite endpoint of death or HF hospitalization[9]. For the endpoint of all-cause mortality however, CRT-D exhibited a non-significant trend towards lower mortality compared to CRT-P when considering HF patients of all ages[9]. Published guidelines do not distinguish between the clinical indications for CRT-P and CRT-D[6].

High Energy Defibrillator Therapy is Non-Specific

High energy defibrillator shocks are non-specific i.e. most defibrillator recipients never receive shock treatments. Of 100 patients implanted with a defibrillator for primary prevention, ~23% receive appropriate shocks in response to life-threatening ventricular arrhythmias over long term follow-up[12]. In addition, it is estimated that about 4 appropriate defibrillator shocks account for one life saved[13, 14]. Moreover, defibrillators may deliver inappropriate therapy[15] and may have significant short and long term complications[16] thus negatively impacting QOL. Shocks are painful, drain device battery, and add significantly to the cost of care for patients because of a higher burden of visits to the emergency department or outpatient clinics as well as admissions to the hospital and surgical procedures for replacement of depleted device batteries. In addition, the number of defibrillators and defibrillator lead malfunctions resulting in advisories and recalls by the Food and Drug Administration have increased significantly over the past decade[17] out of proportion to those seen with the simpler pacemaker devices, thus adding to the morbidity and mortality of defibrillator recipients and to the overall cost of health care.

CRT in the Elderly

The U.S. and Europe populations are getting older. For instance, in the United States, the population aged 80-84 years increased by 16.1%, and those aged 85-89 years increased by 29.8% from 2000 to 2010[18]. Although not excluded from the large CRT randomized trials[9, 10], older patients (≥75 years) have been largely underrepresented in these trials but still receive up to 40% of all CRT-D's in the United States[19,38]. Moreover, older patients have a higher risk of death than younger patients based on competing causes of death and comorbid conditions, thus stirring controversy regarding the role of defibrillator therapy in the elderly[20-24]. In addition, data from large CRT-D registries show that the odds of receiving appropriate defibrillator shocks decrease significantly with every decade of age[25].

Potential Impact

A large, randomized, non-inferiority trial comparing mortality and QOL in older HF patients receiving CRT-P versus CRT-D therapy addresses a critical clinical practice area. Uncertainty about the comparative outcomes of older patients with these two therapies leads to suboptimal and costly management of HF: Older CRT recipients often receive the larger and more expensive CRT-D device that can deliver painful shocks, in the absence of any proof for incremental survival benefit with CRT-D over CRT-P. The pilot randomized trial of this proposal (Aim 1) will be essential to the design of a large pivotal trial. This project will also have significant scientific impact because it will evaluate the clinical and demographic predictors of choosing CRT-P or CRT-D therapy as well as patients' change in their satisfaction with their decision 6 months after enrollment. The results of this research will ultimately effect clinical change in the management of elderly CRT recipients driven by changes to the CRT published guidelines. This research is likely to impact clinical practice and will be important to many stakeholders, including elderly patients and their families, physicians, hospitals, and third party payers, especially Medicare.

2.2 RATIONALE

Since the initial introduction of the defibrillator as a life-saving therapy almost 30 years ago, most large scale clinical trials[9, 10, 12-16] have focused on expanding its clinical indications by identifying newer patient groups at increased risk of sudden cardiac death that may benefit from this therapy. From the original surgically-implanted single-chamber 'shock box' devices used in survivors of cardiac arrest, the field moved steadily in the direction of expanding the indications to larger patient groups. Today, defibrillators are implanted mainly for primary prevention of sudden cardiac death in patients with low left ventricular ejection fraction (≤35%) who have never experienced a life-threatening arrhythmia[13, 14]. They are also implanted in HF patients, a significant proportion of whom requires CRT devices[9, 10]. Driven by industry sponsors, on-going trials are now investigating the role of the implantable defibrillator in patients with relatively preserved ventricular function (ejection fraction between 36% and 50%)[26] who never had ventricular arrhythmias. Yet, despite the established benefits of defibrillator therapy on survival, few patients implanted with these devices receive electrical treatment from them[19].

The proposed research is innovative because it takes a perspective that goes in the opposite direction to most studies of the past 3 decades that have aimed to expand the indications for defibrillator therapy. Instead, our project investigates whether in a subset of patients (age ≥ 75 years) who are currently indicated for CRT device implantation, the smaller, simpler, and cheaper CRT-P is equivalent to the CRT-D in decreasing mortality and improving QOL. Of note, the proposed patient population overwhelmingly receives CRT-D therapy in the U.S. today (>80% of cases)[27], presumably because of an overinflated estimate of the protective role of defibrillator therapy in these patients, which is based on results extrapolated from other non-CRT trials, which were performed in different patient populations[13-15]. As opposed to studying the eligibility of non-indicated patients to receive an available therapy with the goal of expanding its clinical indications, we propose to study a subgroup of patients that is currently indicated for CRT-D therapy according to the published national guidelines[6] and CMS reimbursement policies[28] but is poorly represented in large randomized trials[14] and is least likely to benefit from defibrillator therapy.

Our proposal is also important because it focuses exclusively on elderly patients who although not excluded from randomized trials of cardiac implantable electronic devices, have been grossly underrepresented in these trials[9, 10, 12-16]. Elderly patients constitute a fast-growing stratum of the United Sates population and an important one given that the burden of cardiac disease and the cost of health care increase dramatically in the later years of life. To our knowledge, the proposed trial would be the first cardiac implantable electronic device trial to be performed exclusively in

patients 75years of age or older, thus focusing on this large stratum of the population that is neglected in clinical cardiac research.

Finally, our research will create a cohort of patients who declined enrollment into the pilot randomized controlled trial. This observational cohort will provide an opportunity to examine the clinical and demographic determinants of choosing CRT-P versus CRT-D in older HF patients. These decisions are typically made by the patients with help from caregivers and other family members, after discussing the pros and cons with the treating physician. We will also assess the patients' satisfaction with their decision to receive CRT-P versus CRT-D, at baseline and 6 months after enrollment. Examining the factors that predict patients' choice of CRT-P versus CRT-D in HF management and the level of satisfaction of patients is novel in the field of cardiac implantable electronic device management.

2.3 POTENTIAL RISKS AND BENEFITS

2.3.1 KNOWN POTENTIAL RISKS

For the Aim 1 randomized trial subjects, they will be screened for appropriateness of the trial before being randomized. If there is any indication that the patient should receive a CRT-D over a CRT-P then the patient will not be considered for the trial. Once the patient is enrolled in the Aim 1 the choice to have a randomized decision will not increase any health risks to the patient. Both the CRT-P and CRT-D device implantations are part of the standard medical care for HF patients. The risks involved with the implantation of either device are comparable to those of patients not enrolled in this research study. The risks include, but are not limited to, death, stroke, heart attack, damage to the heart or lungs or veins, infections, bleeding, arrhythmias, or the need for emergent open-heart surgery. These risks are the same in patients undergoing the CRT-P or CRT-D implantation procedures but who are not enrolled in this research study. Defibrillator devices include additional risk of shocks that can occur when there is an abnormal heart rhythm detected by the device. Occasionally, the device may deliver a shock for unintended reasons (a benign heart rhythm or noise).

For the observational Aim there is no additional health risk to the patients as only the patients' health information will be collected. There is a risk that the patients personal or health information may become exposed outside of the observational trial. This risk will be minimized by using all possible safeguards to help reduce risk of exposure. This risk also applies to the Aim 1 subjects.

2.3.2 KNOWN POTENTIAL BENEFITS

There may be no direct benefits to the subjects as a result of their participation in this study. The possible benefits of this procedure, using the pacemaker or the defibrillator, would be to help the subjects heart function in a more synchronized manner. By participating in this study, subjects may contribute valuable information to medical science that may benefit future patients with their same condition. The sponsor cannot guarantee any benefit to the subjects for their participation in this study.

3 OBJECTIVES AND PURPOSE

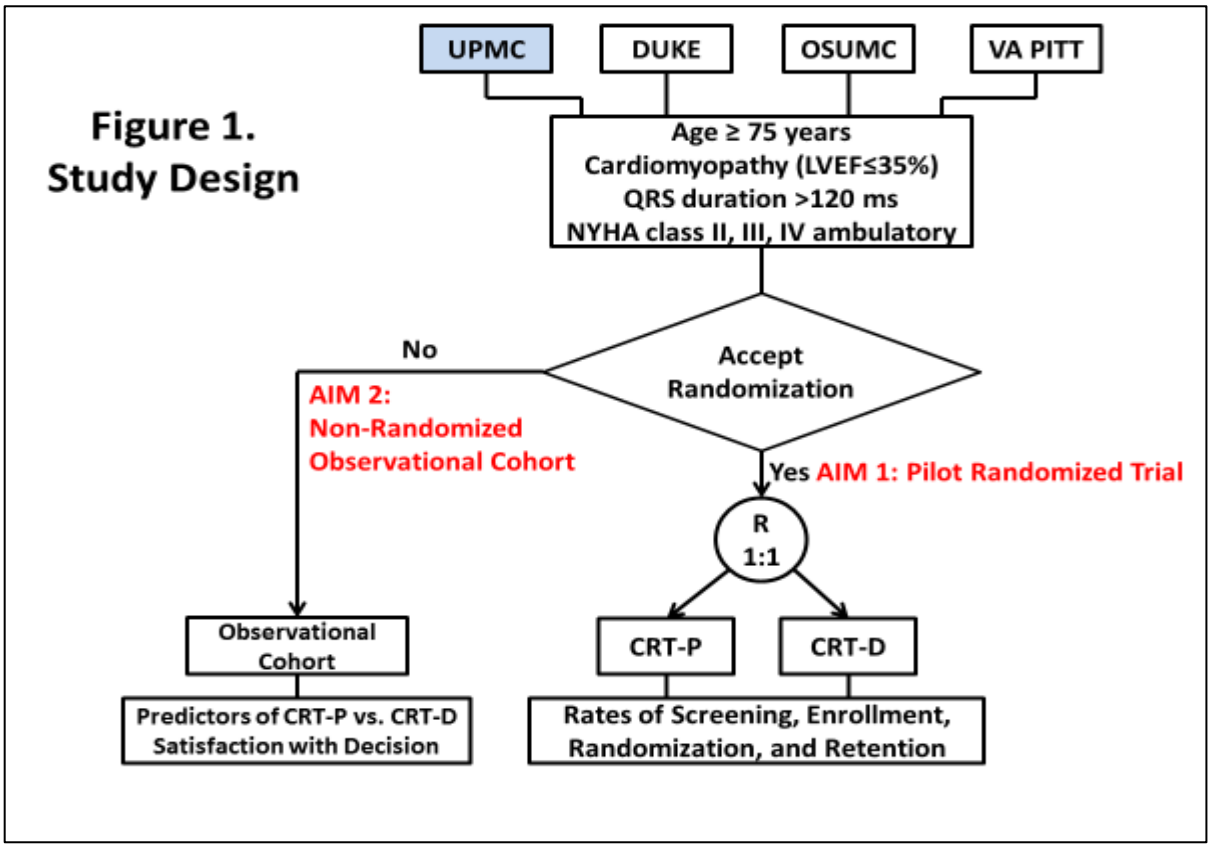
The primary objective is to evaluate and determine the feasibility of enrolling and maintaining elderly heart failure patients in the CRT-P versus CRT-D randomized trial. Additionally, for Aim 2, the observational arm will also maintain the same objective. Secondary objective is to examine the predictors of undergoing Pacemaker versus Defibrillator device implantation in elderly patients (≥75b years).

4 STUDY DESIGN AND ENDPOINTS

4.1 DESCRIPTION OF THE STUDY DESIGN

The design of this pilot study is in two parts corresponding to Aims 1 and 2 (Figure 1). Aim 1 is designed as a pilot randomized, controlled trial to be conducted at 4 institutions in the United States. It will randomize older patients (≥75 years) who are indicated for CRT device implantation to receive a CRT-P or a CRT-D. The choice of the design of Aim 1 was intended to mimic the design of a future large, multicenter, non-inferiority trial which would provide definitive answers regarding the relative impact of CRT-P versus CRT-D on total mortality and QOL in older patients. This specific design is necessary to allow the gathering of hard data on rates of screening of patients, acceptance of enrollment, randomization, device implantation, and patient retention during follow-up. Any design variations are likely to introduce biases which would increase the chances of flawed design of the pivotal trial.

Aim 2 is a non-randomized, observational study of patients who were offered inclusion into Aim 1 but refused to participate. We speculate that a majority of those patients who refuse participation in the randomized pilot trial do so because of a strong preference for CRT-P or CRT-D. This cohort complements Aim 1 and presents an opportunity to understand the reasons why older patients may refuse enrollment into a randomized trial of CRT-P versus CRT-D and to examine the demographic and clinical determinants associated with choosing a CRT-P versus a CRT-D device. It also provides the means to measure patients' QOL and satisfaction[32-34] with decision (CRT-P or CRT-D), at baseline and 6 months after enrollment into this observational cohort.



4.2 STUDY ENDPOINTS

4.2.1 PRIMARY ENDPOINT

With the Aim 1 randomized subjects the primary endpoint is the ability to enroll in the randomized controlled trial of CRT-P versus CRT-D patients. The subjects enrolled with aid in determining and assessing feasibility of screening, enrolling, randomizing, and retaining participants in this pilot trial.

4.2.2 SECONDARY ENDPOINTS

The subjects enrolled in Aim 2 will help to determine the clinical and demographic characteristics of subjects who refused participation in the pilot randomized trial and to compare them to those in Aim 1. Therefore the secondary endpoint is the determination of predictors of refusing participation in CRT-P versus CRT-D clinical trial.

5 STUDY ENROLLMENT AND WITHDRAWAL

5.1 PARTICIPANT INCLUSION CRITERIA

1. Age ≥ 75 years
2. LVEF≤ 35% by cardiac imaging including echocardiogram, nuclear imaging, cardiac catheterization, or cardiac magnetic resonance imaging
3. QRS width >120 ms on surface electrocardiogram
4. New York Heart Association class II, III, or ambulatory IV for HF
5. Patient undergoing de novo CRT device implantation or CRT-D device change-out for battery depletion

5.2 PARTICIPANT EXCLUSION CRITERIA

1. Patient within 40 days of acute myocardial infarction
2. Patient within 3 months of cardiac revascularization (percutaneous coronary intervention or bypass surgery)
3. Patient with prior history of cardiac arrest or documented sustained ventricular arrhythmia
4. Patient with expected longevity < 1 year
5. Patient not on optimal medical therapy for HF management including when tolerated β-blockers, angiotensin converting enzyme inhibitors or angiotensin receptor blockers
6. Patient unable or unwilling to sign a written informed consent
7. Patient's with dementia that are unable to consent for themselves
8. Participating in any other clinical trials (observational/registries allowed)

5.3 OBSERVATIONAL SUBJECT ENROLLMENT

Patients identified in Aim 1 who refuse to participate will be offered to enroll in the observational cohort of Aim 2. Patients are eligible to enroll in the observational cohort at the time of implant through fourteen days' post procedure. There is a separate written, informed consent designed specifically for the prospective observational study. Sites are to collect, from all patients enrolled in Aim 2, their reason(s) why they refused enrollment in Aim 1. It is anticipated that a majority of these patients will accept participating in the observational study of Aim 2 that allows them to retain control over their decision.

The research coordinator at each site will maintain a detailed log of all patients who were offered participation in the non-randomized observational cohort, whether they signed a consent form or not. Reasons for declining participation in the research protocol of Aim 2 will be recorded. The inclusion and exclusion criteria for Aim 2 are identical to Aim 1.

5.4 STRATEGIES FOR RECRUITMENT AND RETENTION

Patients presenting to the outpatient cardiology clinics or inpatient services of the 4 participating institutions and who are prescribed CRT device implantation or CRT-D device change-out for battery depletion will be considered for participation in this pilot randomized trial. The main investigator at each site will identify prospective patients who may require CRT device implantation. This will be achieved by screening the inpatient services and outpatient clinics of the cardiac electrophysiology services at each site. Research coordinators will verify that the prospective subjects meet all the inclusion and none of the exclusion criteria for the study. Once this information is ascertained, the investigator, research coordinator, or both will approach the patient to explain the rationale of the study and its requirements. After signing written informed consent, patients will be randomized to receive a CRT-P or a CRT-D device. Block randomization by enrolling site will be adopted. The randomization status of the patient will be communicated to the treating cardiologist. Of note, the surgical procedure for CRT-P or CRT-D implantation is similar with respect to duration and risk of the procedure, with the exception that CRT-D implantations require a larger skin incision (~1.5 inches versus 0.75 inches).

The research coordinator at each site will maintain a log of all patients who were screened for this pilot trial. The log should include reasons for why the patient did not meet either the inclusion or the exclusion criteria. Additionally, the log would also include the patient's reason for not wanting to enroll in the Aim 1 clinical trial. This log will be maintained at each individual site and redacted of identifiable information in order to send to the sponsor upon request. Use of patient initials and age will be used in place of patient's full name and date of birth.

5.5 PARTICIPANT WITHDRAWAL OR TERMINATION

During the consenting process subjects will be informed of their rights to withdraw from the study at any time without prejudice. Subjects who no longer attend their required in-office follow-up or are unable to be reached by telephone after 2 documented attempts by investigator, will be considered lost to follow-up. These subjects will not undergo any additional study activities once they have been withdrawn. The Social Security Death Index[37] will only be used as an adjunctive method of confirming death if no contact at all could be established with the patient or family during follow-up. Any identifiable research or medical record information recorded for, or resulting from, the subject's participation in this research study prior to the date that they formally withdraw consent may continue to be used and disclosed by the investigators for research purposes.

A patient may be discontinued from participating in this research if their device implantation procedure is not successful or is complicated by death or if they fail to follow-up after device implantation according to the research protocol requirements.

5.6 PREMATURE TERMINATION OR SUSPENSION OF STUDY

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to each of the individual sites. It is the responsibility of each individual site to then notify their respective IRB. If the study is prematurely terminated or suspended, the PI will promptly inform the sponsors IRB and will provide the reason(s) for the termination or suspension to each site. The study may resume once concerns about safety, protocol compliance, data quality are addressed and satisfy the sponsor and IRB. Before resuming any study enrollments each individual site must first receive notification from the sponsor.

6 STUDY PROCEDURES AND SCHEDULE

Randomization Aim

Table 1 details the baseline data collected for every enrolled patient. Baseline demographics (e.g. age, gender, and race) and clinical information (e.g. cardiac condition, comorbid conditions, echocardiographic parameters, EKG parameters) will be abstracted from the electronic medical records of each participating institution. QOL questionnaires will be obtained at enrollment and at the 6-month follow-up visit using both the RAND-36 health Status Inventory[35] and the Minnesota Living with Heart Failure Questionnaire[36]. A paper and pencil option will be provided unless the patient is unable to read or write in which case the questionnaires will be administered verbally by a research coordinator.

Patients will be followed in the pilot randomized trial from the date of enrollment until study closure. During follow-up, information will be collected on procedural details and complications, as well as clinical events including death, hospitalizations, and emergency room visits. The events will be ascertained by asking the patient or their caregiver. Data pertaining to hospitalizations and emergency room visits will be readily available if they occurred at the enrolling institution. If at another institution, these data will be collected by asking the patient to sign a release of medical records form and by obtaining relevant clinical information from the other institution. The cause of death and primary reason for hospitalization will be adjudicated as cardiac (arrhythmic or non-arrhythmic) or non-cardiac by an adjudication committee that is independent from the research team. For the CRT-D arm of the study, information about appropriate and inappropriate device shocks and anti-tachycardia pacing therapies will be collected. Importantly, rates of patient screening, enrollment, randomization, and retention in the study will also be collected.

Table 1. Baseline Data	**Variables Collected**
Demographic variables	Age, Gender, Ethnic background, type of insurance (primary and secondary), Zip code
Clinical variables	Type of heart disease (ischemic/non-ischemic), New York Heart Association class of heart failure, atrial fibrillation, BMI, tobacco and alcohol use, comorbidities that affect survival (19 conditions included in the modified Charlson comorbidity index, which include: myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, peptic ulcer disease, mild liver disease, Diabetes, hemiplegia, renal disease, end-organ damage from diabetes, any tumor, leukemia, lymphoma, metastatic solid tumor, moderate to severe liver disease, acquired immune deficiency syndrome)

Laboratory variables	Serum sodium, creatinine, calculated glomerular filtration rates, BNP
EKG variables	HR, PR, QRS, QT, QTc, Rhythm, QRS axis, QRS morphology
Medications	B-adrenergic blocking agents, Angiotensin converting enzyme inhibitors, Angiotensin receptor blockers, aldosterone, Class I and class III antiarrhythmic medications, statins, nitrates
Imaging variables	LVEF assessment with imaging modality used. Left ventricular systolic and diastolic dimensions, any other abnormality
Quality of Life	RAND-36 Health Status Inventory[34] (Appendix 1) Minnesota Living with heart Failure Questionnaire[35] (Appendix 2)

The milestones of data collection are detailed in Table 2. Patients enrolled in the randomized pilot trial will have baseline demographic, clinical, and pharmacological information collected after they sign written informed consent. QOL questionnaires and patient satisfaction will also be obtained at baseline. At the scheduled date of device implantation, which will be within 30 days of enrollment, procedural details will be collected including total and fluoroscopic durations of the procedure, device and lead models, and any acute major or minor procedural complications. Patients whose device implantation procedure is scheduled > 30 days from the date of enrollment have to be re-consented for participation in this trial. In follow-up, each patient will be contacted by phone at 30 days, 3 months, and 6 months post enrollment and every 6 months thereafter until the end of the study. The phone calls will be used to collect interim information from patients or next of kin regarding non-acute procedural complications or clinical events (e.g. death, hospitalization). Original medical records will be obtained for all clinical events and will be reviewed by an independent adjudication committee. Each scheduled phone visit will also be associated with a remote device interrogation to assess device function and obtain information about stored arrhythmic events.

Observational Aim

Patients enrolled in the observational cohort of Aim 2 will have demographic and clinical data collected at baseline similarly to patients enrolled in the randomized trial of Aim 1. Table 1 details the clinical variables collected at enrollment. Table 2 details the follow-up milestones. Also, patients enrolled in Aim 2 of this proposal will undergo QOL assessment using the RAND-36 Health Status Inventory[35] and the Minnesota Living with heart Failure Questionnaire[36] (Appendices 1 and 2) at baseline and at the 6-month follow-up visit which could be conducted by phone. Procedural information and complications as well as clinical events will be collected on patients enrolled in the non-randomized observational cohort, similarly to patients enrolled in Aim 1. Data on cost of care will also be collected for all patients enrolled in Aim 2.

In addition, patients enrolled in the observational cohort will be asked about their decision to receive a CRT-P or CRT-D device and will be probed for the reason (s) behind their decision and their answers will be recorded. The actual type of device implanted (CRT-P versus CRT-D) will be ascertained at the time of the implantation procedure. At baseline and at the 6-month research call, they will be assessed for their level of satisfaction with their decision about device therapy (CRT-P or CRT-D) using the Satisfaction with Decision Scale[32-34] (Appendix 3), which assigns a score of 1 to 5 to the answer of each of 6 questions pertaining to the patient's level of satisfaction with their medical decision (lowest satisfaction score is 6 and highest is 30).

6.1 Schedule of Events

Table 2. Schedule of Events	Enrollment visit	Device implant	30-day phone call	3-month phone call	6-month visit or phone call	Every 6 months phone call	End of Study
Demographic Information	X						
Baseline Clinical Characteristics	X						
Medications	X				X	X	X
Procedural Complications		X	X				
Clinical Events (survival, hospitalizations, arrhythmias)		X	X	X	X	X	X
The Satisfaction with Decision Scale	X				X		
Quality of Life Questionnaires	X				X		
Device complications		X		X	X	X	X
Device Interrogation		X			X	X	X
Economic Data							X

7 ASSESSMENT OF SAFETY

7.1 ADVERSE EVENT (AE) AND SERIOUS ADVERSE EVENT (SAE) REPORTING

The main investigator at each of the participating institutions will be responsible daily for the appropriate implementation of study protocols and for patient safety. All adverse events will be reported to the DSMB, to the local IRB of the participating institution where the adverse event occurred per their respective reporting guidelines, and if required, to the NHLBI. Each adverse event will be classified by the site investigator as 'study-related' or 'not study related' and reviewed by the DSMB for adjudication. Serious adverse events (death, procedural complications, or hospitalizations for any reason) will be reported to the coordinating center and the local IRB (per their reporting guidelines) within 48 hours of adverse event awareness.

7.2 REPORTING PROCEDURES

The study clinician will have oversite of completed SAE Forms. Reporting of the forms should occur within the following timelines:

- All deaths and immediately life-threatening events, whether related or unrelated to the clinical trial, will be recorded on the SAE Form and submitted to the study sponsor within 48 hours of site awareness.
- Other SAEs regardless of relationship will be submitted to the study sponsor within 72 hours of site awareness.

All SAEs will be followed until resolution or until the site investigator deems the event to be chronic or stable. Other supporting documentation of the event may be requested by the study sponsor and should be provided as soon as possible.

7.3 SAFETY OVERSIGHT

Safety oversight will be under the direction of a DSMB composed of individuals with the appropriate expertise, including cardiologists. The DSMB will meet at least quarterly to assess safety and efficacy data on each arm of the study. The DMSB will operate under the rules of an approved charter that will be written and reviewed at the organizational meeting of the DSMB. At this time, each data element that the DSMB needs to assess will be clearly defined. The DSMB will provide its input to the NHLBI.

8 CLINICAL MONITORING

The primary responsibility of the DSMB, an independent group of experts that advises the study investigators, is to oversee the progress of the study and review adverse events. All adverse events in both arms of the clinical trial will be reviewed and adjudicated as 'research-related' or not. Stoppage rules of the clinical trial will be mandated by the DSMB if examination of the adverse events revealed that one treatment arm is clearly superior to the other treatment for the primary endpoint of all-cause mortality. The DSMB will also review the overall progress of the trial, the quality of data collection, the safety and confidentiality of data storage, and the overall management of the trial. A Data and Safety Monitoring report will be generated including information on study status and enrollment milestones, quality of data collected, and safety data.

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL AND ANALYTICAL PLANS

Randomized Aim

Descriptive patient characteristics will be presented as mean (SD) for continuous variables and n (%) for categorical variables. Baseline comparisons of patients assigned to CRT-P vs. CRT-D will be performed using t-tests for continuous variables (Wilcoxon rank-sum test if non-normally distributed) and chi-squared tests for categorical variables (Fisher's Exact Test in case of small sample sizes within cells) to confirm that the randomized treatment arms are balanced in key demographics and potential confounders. The proportion of patients experiencing major/minor procedural complications within 30 days will be reported as n (%) within each treatment arm. These complication rates will be ascertained through review of pertinent medical records following the device implantation. Mortality [as n (%)] and the 6-month QOL outcomes [as mean (SD)] within each treatment arm will be reported as well. Cost of care for the index hospitalization for CRT device implantation and for the follow-up period will be measured at the conclusion of the study and compared between the 2 cohorts using a 2-sample t-test (or Wilcoxon test if the data are non-normally distributed). Retention will be presented as n (%) completing at least 6-month of follow-up. In addition to the retention, in order to document the recruitment success, we will report the number of patients approached in order to successfully enroll n=50 patients, which will be useful information in planning a large scale trial.

Observational Aim

All patients who do not enroll in the trial, but consent to be followed, will be enrolled in a parallel observational cohort. Patients' clinical and demographic characteristics will be examined and compared between CRT-P and CRT-D recipients using t-tests, Wilcoxon rank-sum tests, chi-squared tests, or Fisher's Exact tests, as appropriate. Patient satisfaction among CRT-P vs. CRT-D recipients will be assessed at baseline and 6 months after enrollment using the Satisfaction with Decision Scale. The scores will be presented as mean (SD) and tested using a 2-sample t-test (or Wilcoxon test if the data are non-normally distributed). Deceased patients will be included in the analysis (assigned the lowest possible satisfaction score of 6) to avoid survival bias in the event of differential mortality in CRT-P vs. CRT-D. Cost of care will also be presented as mean (SD) and compared between the two cohorts using a 2-sample t-test (or Wilcoxon test if the data are non-normally distributed). Multivariate modeling with adjustment for selected patient factors will be considered if there are differences in CRT-P vs. CRT-D patients on key demographics, but the power to test this difference while accounting for multiple confounders may be limited.

9.2 SAMPLE SIZE

Randomized Aim

It will be of interest to estimate the recruitment success rate and the retention rate in this population, as that will be useful knowledge for designing a pivotal non-inferiority trial. The proposed sample size of 50 patients guarantees a maximum sample standard deviation = √(.5*(1-.5)/50) = 7%, meaning that a 95% confidence interval will have a maximum margin of error ± 13% in estimating true retention rate. However, this margin-of-error may be lower (the further the sample retention is from 50%). For example, if 40/50=80% participants enrolled complete at least the 6-month visit, a 95% CI estimating the true 6-month retention in this population would range from 68.9-91.1%, information that can be used to guide recruitment estimates for the large scale trial. The recruitment success rate can be estimated with even more precision, as there will be a larger N approached than N enrolled (and thus a smaller standard deviation of the sample proportion).

Observational Aim

It is anticipated based on the physician and patient surveys that approximately 40% of patients offered the opportunity to enroll in the pilot randomized controlled trial of Aim 1 will do so. Therefore, 125 patients will need to be screen to enroll 50 in the pilot randomized trial. It is assumed that 80% of those who decline participation in Aim 1 will agree to be followed in the observational cohort, the cohort will consist of 60 non-randomized patients. A comparison will be scored on the Satisfaction with Decision Scale using a t-test (or Wilcoxon rank-sum test, if non-normally distributed). Assuming roughly equal numbers select CRT-D vs. CRT-P, enrollment of 60 cohort participants will have 80% power to detect a difference in Satisfaction with Decision scores if one treatment group's average score is at least 0.75 standard deviations higher than the other group.

9.3 STUDY PITFALLS AND SUGGESTED SOLUTIONS

Randomized Aim

Based on the total volume of CRT recipients at the 4 enrolling institutions and the estimated percentage of acceptance of patients to enroll in a randomized CRT-P versus CRT-D trial provided by the physician (Appendix 1) and patient (Appendix 2) surveys, it is anticipated that the actual enrollment rate will exceed the rate needed to reach the target sample size of 50 patients in Aim 1 over a 1.25-year enrollment period. The required threshold for the rate of enrollment is 0.83 patients per institution per month. If the actual enrollment rate turns out to be slower than expected, then more institutions may be added to the pilot trial. The data gathered from this pilot trial will be necessary to inform the design of a future large, non-inferiority, randomized trial of CRT-P versus CRT-D with respect to number of sites needed and duration of the enrollment phase.

The present pilot randomized trial is by necessity un-blinded, i.e. patients and physicians know whether the implanted device is a CRT-P or CRT-D. In order to better understand if there are biases in the type of patients who accept randomization, the research is to be conducted as described in Aim 2 by doing so this will provide insight into the determinants of accepting participation in the randomized trial (compare patients in Aim 1 versus Aim 2) as well as insights into the determinants of choosing a CRT-P versus CRT-D device (compare patients in Aim 2 who received CRT-P versus CRT-D).

Observational Aim

The sample size needed for Aim 2 is likely to be easily achieved as we will offer enrollment to all patients screened but not enrolled into Aim 1. We expect the patient acceptance to enroll in an observational study where no clinical decisions are imposed by the research protocol to be very high. If our estimates of enrollment turn out to be too optimistic however, we would consider adding another institution to the research protocol to mitigate this issue.

The main purpose of Aim 2 is to provide insight into which patients refuse to enroll in the large RCT and why in order to inform the design of the pivotal RCT. Since all investigators on this proposal are electrophysiologists, if the pilot proposal were to reveal that a major reason for patients' refusal to participate in a randomized study of CRT-P vs. CRT-D is because of the opinion of their referring cardiologist about the relative merits of these devices, then the pivotal RCT could be designed to include referring cardiologists as primary site investigators, which would likely mitigate this problem. This is one example for how the results of Aim 2 may inform the design of the large scale trial.

10 SOURCE DOCUMENTS AND ACCESS TO SOURCE DATA/DOCUMENTS

The individual study sites will maintain a patient binder to include all source documents that correlate with the information that is obtained with this trial. The sponsor has the right to request redacted source documents to aid in verification of information provided for the sole purpose of the trial. With each adverse event that is reported, the sites will submit all source documents pertaining to that event. These records will also be redacted of any patient identifiable information and marked with the corresponding patient identification number and correlating case report form. Each site is responsible for maintaining a patient log that indicates the patient that corresponds with their study identification number.

11 QUALITY ASSURANCE AND QUALITY CONTROL

QC procedures will be implemented beginning with the data entry system and data QC checks will be run on the database for reports to be generated. Any missing data or data anomalies will be communicated to the site(s) for clarification/resolution. Each site is responsible for conducting the clinical trial and that the data is generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirements. The investigational sites will provide access to all trial related information, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor.

12 ETHICS/PROTECTION OF HUMAN SUBJECTS

12.1 ETHICAL STANDARD

The investigator at each site will ensure that this study is conducted in full conformity with Regulations for the Protection of Human Subjects of Research. All personal planning to be involved must ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with GCP and the applicable regulatory requirement(s).

12.2 INSTITUTIONAL REVIEW BOARD

The protocol, informed consent form(s), and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form will also need IRB approval; a determination will be made regarding whether previously consented participants need to be re-consented. Any changes to the consent by the individual sites will first be required to obtain approval from the sponsor prior to submitting changes to the IRB.

12.3 INFORMED CONSENT PROCESS

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Participants and their families should be informed of risks and possible benefits of participation. Consent forms will be IRB-approved and the participant will be asked to read and review the document. The investigator will explain the research study to the participant and answer any questions that may arise. All participants will receive a verbal explanation in terms suited to their comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing.

The participants should have the opportunity to discuss the study with their family members or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to any procedures being done specifically for the study. The participants may withdraw consent at any time throughout the course of the trial. A copy of the informed consent document will be given to the participants for their records. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study. Additionally, each informed consent process will be documented and maintained with the original copy of the consent at each study site according their institutional SOP.

12.4 PARTICIPANT AND DATA CONFIDENTIALITY

Participant confidentiality is strictly held in trust by the participating investigators, their staff, and the sponsor. This confidentiality is extended to cover clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor. The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by local IRB and Institutional regulations.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at UPMC. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by clinical sites and by UPMC research staff will be secured and password protected. At the end of the study, all study databases will be de-identified and archived at the UPMC.

13 DATA HANDLING AND RECORD KEEPING

13.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site PI. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data. Black ink is required to ensure clarity of reproduced copies. When making changes or corrections, cross out the original entry with a single line, and initial and date the change. DO NOT ERASE, OVERWRITE, OR USE CORRECTION FLUID OR TAPE ON THE ORIGINAL.

Copies of the electronic CRF (eCRF) will be provided for use as source documents and maintained for recording data for each participant enrolled in the study. Data reported in the eCRF derived from source documents should be consistent with the source documents or the discrepancies

should be explained and captured in a progress note and maintained in the participant's official electronic study record.

All clinical data will be entered into REDcap by the individual sites, the data system will be provided by UPMC. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data will be entered directly from the source documents.

13.2 STUDY RECORDS RETENTION

Each individual site is required to maintain research records for a period of no less than seven years after the study ends. The sponsor may continue to use and disclose study records which may contain subject identifiable information related to this research study for a minimum of 10 years and for as long (indefinite) as it may take to complete this research study.

13.3 PROTOCOL DEVIATIONS

A protocol deviation is any noncompliance with the clinical trial protocol or GCP requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. It is the responsibility of the site to use continuous vigilance to identify and report deviations within 7-14 working days of identification of the protocol deviation, or within 7-14 working days of the scheduled protocol-required activity. All deviations must be addressed in study source documents and reported the sponsor. Protocol deviations must be sent to the local IRB per their guidelines. The site PI/study staff is responsible for knowing and adhering to their IRB requirements.

13.4 PUBLICATION AND DATA SHARING POLICY

The sponsor plans to make the dataset generated by this research available to other investigators in the field. To that end, the sponsor will make the data available through the NHLBI data repository managed by BioLINCC, within 2 years of the end of the clinical activities and the publication of the main findings. The sponsor will also provide full description of variable definitions, format, forms used in data collection as well as study procedures and protocols. A summary documentation file, providing a brief description of the study's general orientation, its components, and its examination and follow-up timeline, will also be made available in appropriate format in order to facilitate the use of these data by other researchers and institutions.

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APPENDIX 1

RAND-36 HEALTH STATUS INVENTORY

This section includes a wide variety of questions about your health and your life. We are interested in how you feel about each of these issues.

1. In general, would you say your health is: [Mark an ☒ in the one box that best describes your answer.]
   - ☐ Excellent
   - ☐ Very good
   - ☐ Good
   - ☐ Fair
   - ☐ Poor
2. Compared to one year ago, how would you rate your health in general now?
   - ☐ Much better now than one year ago
   - ☐ Somewhat better now than one year ago
   - ☐ About the same as one year ago
   - ☐ Somewhat worse now than one year ago
   - ☐ Much worse now than one year ago

The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much? [Mark an ☒ in a box on each line.]

	Yes, limited a lot	Yes, limited a little	No, not limited at all
3. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports.	☐	☐	☐
4. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf.	☐	☐	☐
5. Lifting or carrying groceries.	☐	☐	☐
6. Climbing several flights of stairs.	☐	☐	☐
7. Climbing one flight of stairs.	☐	☐	☐
8. Bending, kneeling, or stooping.	☐	☐	☐
9. Walking more than a mile.	☐	☐	☐
10. Walking several blocks.	☐	☐	☐
11. Walking one block.	☐	☐	☐
12. Bathing or dressing yourself.	☐	☐	☐

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	YES	NO
13. Cut down the amount of time you spent on work or other activities.	☐	☐
14. Accomplished less than you would like.	☐	☐
15. Were limited in the kind of work or other activities.	☐	☐
16. Had difficulty performing the work or other activities (for	☐	☐

example, it took extra effort)

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

		YES	NO
17.	Cut down the amount of time you spent on work or other activities.	☐	☐
18.	Accomplished less than you would like.	☐	☐
19.	Didn't do work or other activities as carefully as usual.	☐	☐

20. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?
    - ☐ Not at all
    - ☐ Slightly
    - ☐ Moderately
    - ☐ Quite a bit
    - ☐ Extremely

21. How much bodily pain have you had during the past 4 weeks?
    - ☐ None
    - ☐ Very mild
    - ☐ Mild
    - ☐ Moderate
    - ☐ Severe
    - ☐ Very severe

22. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?
    - ☐ Not at all
    - ☐ Slightly
    - ☐ Moderately
    - ☐ Quite a bit
    - ☐ Extremely

These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks…

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
23. Did you feel full of pep?	☐	☐	☐	☐	☐	☐
24. Have you been a very nervous person?	☐	☐	☐	☐	☐	☐

25. Have you felt so down in the dumps that nothing could cheer you up?	☐	☐	☐	☐	☐	☐
26. Have you felt calm and peaceful?	☐	☐	☐	☐	☐	☐
27. Did you have a lot of energy?	☐	☐	☐	☐	☐	☐
28. Have you felt downhearted and blue?	☐	☐	☐	☐	☐	☐
29. Did you feel worn out?	☐	☐	☐	☐	☐	☐
30. Have you been a happy person?	☐	☐	☐	☐	☐	☐
31. Did you feel tired?	☐	☐	☐	☐	☐	☐

32. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ None of the time

Please choose the answer that best describes how true or false each of the following statements is for you.

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
33. I seem to get sick a little easier than other people.	☐	☐	☐	☐	☐
34. I am as healthy as anybody I know.	☐	☐	☐	☐	☐
35. I expect my health to get worse.	☐	☐	☐	☐	☐
36. My health is excellent.	☐	☐	☐	☐	☐

APPENDIX 2

MINNESOTA LIVING WITH HEART FAILURE QUESTIONNAIRE

The following questions ask how much your heart failure (heart condition) affected your life during the past month (4 weeks). After each question, circle the 0, 1, 2, 3, 4 or 5 to show how much your life was affected. If a question does not apply to you, circle the 0 after that question.

Did your heart failure prevent you from living as you wanted during the past month (4 weeks) by -	**No**	**Very Little**				**Very Much**
1. causing swelling in your ankles or legs?	0	1	2	3	4	5
2. making you sit or lie down to rest during the day?	0	1	2	3	4	5
3. making your walking about or climbing stairs difficult?	0	1	2	3	4	5
4. making your working around the house or yard difficult?	0	1	2	3	4	5
5. making your going places away from home difficult?	0	1	2	3	4	5
6. making your sleeping well at night difficult?	0	1	2	3	4	5
7. making your relating to or doing things with your friends or family difficult?	0	1	2	3	4	5
8. making your working to earn a living difficult?	0	1	2	3	4	5
9. making your recreational pastimes, sports or hobbies difficult?	0	1	2	3	4	5
10. making your sexual activities difficult?	0	1	2	3	4	5
11. making you eat less of the foods you like?	0	1	2	3	4	5
12. making you short of breath?	0	1	2	3	4	5
13. making you tired, fatigued, or low on energy?	0	1	2	3	4	5
14. making you stay in a hospital?	0	1	2	3	4	5
15. costing you money for medical care?	0	1	2	3	4	5
16. giving you side effects from treatments?	0	1	2	3	4	5
17. making you feel you are a burden to your family or friends?	0	1	2	3	4	5
18. making you feel a loss of self-control in your life?	0	1	2	3	4	5
19. making you worry?	0	1	2	3	4	5
20. making it difficult for you to concentrate or remember things?	0	1	2	3	4	5
21. making you feel depressed?	0	1	2	3	4	5

APPENDIX 3

THE SATISFACTION WITH DECISION SCALE

	Strongly Disagree [1]	Disagree [2]	Neither Agree nor Disagree [3]	Agree [4]	Strongly Agree [5]
I am satisfied that I am adequately informed about the issues important to my decision	☐	☐	☐	☐	☐
The decision I made was the best decision possible for me personally	☐	☐	☐	☐	☐
I am satisfied that my decision was consistent with my personal values	☐	☐	☐	☐	☐
I expect to successfully carry out (or continue to carry out) the decision I made	☐	☐	☐	☐	☐
I am satisfied that this was my decision to make	☐	☐	☐	☐	☐
I am satisfied with my decision	☐	☐	☐	☐	☐