1. Study Objective

We propose a multicenter randomized trial of patient-centered CHF disease management that includes case-finding, a collaborative care intervention with telemonitoring, and evidence-based CHF and depression management. The study is designed as an ‘effectiveness’ intervention to enhance broad implementation. It is a study of a care delivery strategy and involves no investigational drugs or devices.

The primary aim of the proposed project is to:

1. Determine whether a patient-centered CHF disease management intervention in the VA results in better patient health status (i.e. symptom burden, functional status, and quality of life) than usual care;

The secondary aims of the proposed project are to:

1. Determine whether the disease management intervention results in reduced hospitalizations and mortality.
2. Determine whether the disease management intervention reduces depression and increases patient self-efficacy in the management of CHF, and medication adherence.
3. Determine whether the care of patients assigned to the disease management intervention is more consistent with national clinical practice guidelines than patients receiving routine care.
4. Evaluate the cost and incremental cost-effectiveness of the disease management intervention.

2. Background

Chronic heart failure (CHF) is a leading cause of disability, hospitalization, and death in the VA and in the United States.\(^1\)\(^-\)\(^3\) Despite advances in available therapies for patients with CHF, population-based outcomes such as mortality and hospitalization rates have not improved substantially over the past decade.\(^4\) In addition, CHF has a major impact on patients’ health status, including their symptom burden (e.g. dyspnea), functional status, and health-related quality of life, and yet few CHF interventions have targeted these critical ‘patient-centered’ outcomes.\(^5\)\(^-\)\(^8\)

Disease management has emerged as a promising strategy to improve the outcomes of patients with CHF. Some previous studies have reported that CHF disease management can reduce rates of hospitalization, and a few have demonstrated reductions in mortality, reductions in cost, or improvements in quality of life.\(^9\)\(^-\)\(^21\) However, many of these studies have been small, single-center, and of short duration, and the association between disease management and improved outcomes has been inconsistent.\(^20\)\(^-\)\(^25\) Many CHF disease-management studies to date have relied solely on nurse case management rather than multidisciplinary collaborative care, have not leveraged health information technology, and have had a limited focus on patient self-care. In general, these programs have failed to empower patients in their care, providing inadequate
attention to health status and self-care support, and failing to address key barriers such as comorbid depression. The effectiveness of disease management for CHF has not been evaluated in the VA.

3. Methods

We plan a 3-year, multi-site randomized study to evaluate the effectiveness of a Patient-Centered Disease Management (PCDM) intervention for CHF. An overview of study design is in Appendix A. First, we will identify CHF patients from 4 VA Medical Centers and their affiliated clinics. Then, we will screen these patients with the KCCQ and invite eligible patients with diminished CHF-specific health status (i.e. KCCQ summary scores <60) to an enrollment visit. Enrolled patients will be randomized to a PCDM intervention versus usual care, and will be followed for 12 months.

The PCDM intervention will include:

- Evaluation of CHF care by the collaborative care team, with diagnostic and therapeutic treatment recommendations based on current ACC/AHA national clinical practice guidelines.26
- Daily telemonitoring and patient self-care support utilizing the VA telemonitoring system (Health Buddy system).
- Screening and treatment for comorbid depression.

The Collaborative Care (CC) team at each site will consist of a primary care provider, cardiologist, and psychiatrist, who are local opinion leaders, as well as a nurse site coordinator and pharmacist.

The primary outcome will be change in overall CHF-specific health status between baseline and 12-months, as reflected in the KCCQ Summary Score.

Secondary outcomes will include: hospitalization and mortality, depressive symptoms, patients’ self-efficacy in management of CHF, adherence to prescribed medications, the proportion of patients with guideline-concordant care, and cost-effectiveness of the intervention.

Patient Identification

The project will be conducted at the Denver, Palo Alto, Richmond, and Seattle VAMC’s and their affiliated community-based outpatient clinics (CBOC’s), representing 4 Veterans Integrated Service Networks (VISNs 6, 19, 20, and 21). Active VA enrollment will be defined as having an assigned primary care provider in the Primary Care Provider Management Application of the Veteran’s health information system and technology architecture (ViSTA) and at least one appointment during the prior 12 months. The presence of CHF will be defined as an in- or outpatient diagnosis for CHF (ICD-9 code 402.01, 402.11, 402.91, 404.01, 404.11, 404.91, or any 428.x) within the past 18 months. We will obtain this information directly from ViSTA as we have done in several previous studies. This is a validated methodology developed by Ischemic Heart Disease Quality Enhancement Research Initiative (IHD-QUERI) for case finding for that has been used in similar projects (ACQUIP and C3P).
Appendix B demonstrates the estimated flow of patients from the number of eligible patients through randomization. Based on preliminary evaluations of ViSTA at the study sites in preparation for this proposal, 8,574 veterans have a diagnosis of CHF and are actively enrolled in primary care across the 4 sites. Target enrollment will be 600 patients, as this will provide adequate power for primary and secondary outcomes.

**Eligibility Screening**

To ascertain patients’ interest in participation, we will conduct a mail survey of all actively enrolled patients identified as having CHF who are not currently followed by a cardiac subspecialty or care coordination. This approach was developed and validated as part of the ACQUIP study (SDR-96-002) and has been successfully employed in the C3P study (COMIRB 03-1024; IHI 02-062-1). We will employ standard techniques to maximize survey response including follow-up surveys. Based on previous studies, we anticipate a response rate of 60% to the screening mailing. Additionally, we will recruit patients in the hospital, either clinic or inpatient. At this time we will explain the study and conduct the KCCQ survey. If the patients are eligible we will schedule a baseline visit for a later date. The baseline survey will include a brief eligibility screening and the KCCQ, so we can identify those patients with diminished health status (KCCQ summary scores <60) that will be the principal focus for the study (Appendix S1). Patients with KCCQ scores <60 are at significantly elevated risk of subsequent hospitalization and mortality. Based on prior work, approximately 33% of CHF outpatients will have a KCCQ score <60. The mailed survey packet will include: Cover letter (Appendix2), Information Sheet (Appendix 3), Eligibility survey (Appendix 4) and refusal card with stamped/addressed envelope (Appendix 5) or phone number to call to refuse participation. We are requesting a waiver of authorization for the identification of patients and eligibility screening steps. This request is based on prior work with C3P (COMIRB #03-1024). Initially, the C3P protocol included one consent for screening and one consent for participation. Because of the low response rate (14% with correctly signed consents) leading to selection bias and statistical power concerns, a request to replace the screening consent with an information letter was submitted. An amendment approval was received to waive the initial screening consent (approval PAM 004) and replace it with a patient information sheet similar to the information sheet we have included in this study. Importantly, the waiver and use of primary identifiers to conduct the screening will not adversely affect privacy rights and the welfare of any individual. Subjects will be identified for research purposes only, and the data obtained from administrative databases or electronic medical records will not be used for any other purpose. For the screening stage of this study, we believe that a waiver actually protects the privacy of patients and reduces burden. Most of the patients screened by mail (65-75%) will not report KCCQ scores <60 to make them eligible for the full study. Therefore, if consent is required for screening, we would actually be creating documents with names and signatures for patients who will ultimately not be eligible for participating in the full study. The information sheet that will be sent with the screening questionnaire includes the elements of consent and the investigator’s signature (Appendix 3).

Standard survey methodology will be used (mailing, reminder letter, phone call follow-up, repeat mailing to non-respondents). Additionally, patients are also provided with a postage paid refusal card/addressed/stamped envelope and a phone number to call if they do not wish to participate (Appendix 5). If patients decline by letter or phone call, they will not be contacted. If
they do not respond within 2 weeks, we will send a letter reminder (Appendix 6). If they do not respond within 4 weeks, we will call them and send another package. If there is no response in 6 weeks, we will consider this a refusal to participate. All mailings will be organized in Denver, but sent from each local site to the patients. Data entry will be centralized in Denver.

**Consent and Authorization Procedures for Full Study**

Ineligible patients will be mailed a thank you letter that will explain the results of their survey to them. For example, the majority of ineligible patients will have CHF that does not interfere with their daily activities and quality of life. (Appendix 7)

**Inclusion Criteria**

Patients who report having a KCCQ<60 will be the focus of the intervention. Ability in home to connect to telehealth.

**Exclusion Criteria**

1) Cognitive or psychiatric impairment that precludes completion of questionnaires; 2) Nursing home resident; 3) Irreversible, non-cardiac medical conditions (e.g. metastatic cancer) likely to affect 6-month survival or ability to execute the study protocol; 4) AUDIT-C – if score>=7 then exclude; 7) Inability to read English at a fifth-grade level (unless there is presence, on a daily basis, of someone who can read at this level for the purposes of telemonitoring); and 8) Prior heart transplantation, since their care is focused more on anti-rejection regimens.

**Enrollment Visit Invitation**

Providers of eligible patients will be mailed a cover letter and list of potentially eligible patients (Appendix 1) and asked if there is any reason the patient should not be included. They will return the form if they want any of their patients excluded. If the form is not mailed back within 2 weeks, the patients will be contacted. If the patient is not excluded by their PCP, the patient will be phoned with an invitation to a baseline visit:

**Recruitment Call script (Appendix 10)**

**Research Nurse Training on Consent Procedure**

Prior to the start of the study, all research nurses will attend training in Denver. The training will include the process of fully explaining the study and consent procedures, explaining the possible risks and inconveniences, answering patient questions and assessment of the patient’s understanding of the study and consent process.

**Consent and Enrollment Visit**

Appendix C displays the timing of study measures. The enrollment visit will take place in an established clinic space at the VA hospital. At the enrollment visit, the site coordinator will confirm the patient’s eligibility and provide a verbal explanation of the study. If the patient remains eligible and wishes to proceed, the site coordinator will review the informed consent document, answer any questions, and obtain written consent (Appendix 19) and HIPAA authorization (Appendix 20). The consent form will be explained to the patient and the following questions will be asked of the patient:

_We have gone over the study, but before you sign I’d like to ask you a few questions to ensure you properly understand what you are enrolling in._

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Can you describe your health condition for which this study cares for?
[Criteria]: Heart Failure, Congestive Heart Failure, weak heart (doesn’t pump as well as it used to)

What is your understanding of the process of the usual care group and the intervention care group?
[Criteria]: Usual care will be no different than my regular care now. Intervention care involves a team reviewing my care and they may make recommendations about my care. Patients and their primary care provider will still make all final decisions regarding care.

What do you understand are the risks of the study? Do you understand them?
[Criteria]: Patient understands that there are no physical risks. Risk is loss of privacy and they verbalize understanding of safeguards.

What do you understand to be the benefits of the study?
[Criteria]: Patient understands they may not benefit personally, but that they will contribute to information that may potentially improve the quality of care for other veterans with heart failure.

**If the subject gives acceptable responses to the questions that demonstrate that they understand the study say:**
Great. It sounds like you fully understand the study and we are ready for you to sign the consent to participate. You are not required to participate, it is totally voluntary. If you choose not to participate you will receive your usual care.

**If it sounds as if the subject does not fully understand say:**
Ok, let’s review a few things from the consent.

**If after reviewing the consent twice, the subject still does not understand or seems confused say:**
Based on your answers to these questions, it doesn’t seem like this study is a good fit for you. Thank you for your time.

If the patient answers the questions correctly, a signature will be obtained. If the patient does not answer the questions correctly, the consent will be explained again and the questions will be asked again to assure the patient understands the consent correctly. A copy of the consent will be given to the patient. If the patient declines participation in the study or is not eligible based on data obtained at this visit, the site coordinator will thank the patient for his/her consideration and explain that care will be provided in the usual manner by their current VA providers. The patients will be reimbursed for travel by offering them $20 payment for each the baseline and final visit.

For enrolled patients, the site coordinator will complete baseline study forms and surveys (Appendices), administer a 6-minute walk test and order labs and EKG’s to be completed during the visit. Upon completion of these items, the patient will be randomized to either...
usual care or the PCDM intervention based on the Coordinating Center defined computer
randomization scheme. Patients assigned to usual care will receive the packet of educational
materials about CHF and self-care. Patients assigned to the PCDM intervention will receive
the telemonitoring appliance and training on how to set up and use the appliance. Scales will
be provided to patients in both groups, if needed. All patients will be informed that study
personnel will be contacting them at 3 and 6 months to ask them how they are doing and to
complete a survey by phone similar to the baseline surveys, and that there will be a final 12-
month study visit. Finally, for intervention patients who score equal to or over 10 (significant
depressive symptoms) on the PHQ survey a depression educational video will be shown to
them. If an intervention patient scores greater to or equal to 1 on question 9 of the PHQ
(suicide question) survey, the nurse will call the collaborative care team psychiatrist for
intervention. For control patients who score equal to or over 10 on the PHQ survey, the
nurse will notify the patient’s PCP of their score. For control patients who score greater or
equal to 1 on question 9 of the PHQ (suicide question), the nurse will call the patient’s PCP
or the patient’s mental health provider to notify them of the patient’s depression status.
Additionally, the research nurse will enter a progress note into CPRS noting the contact with
the provider and the provider’s plan for follow-up. In the situation where the patient (control
or intervention) expresses imminent suicidal thoughts, the research nurse will actively
transfer the patient to the emergency or mental health department.

KCCQ (Appendix S1) (eligibility)
AUDIT-C (Appendix S2) (eligibility)
PHQ + Prime MD (Appendix S3)
GAD-7(Appendix S4)
Symptoms/spirituality (Appendix S5)
EQ-5D (Appendix S6)
SCL-20(Appendix S7)
Mini-cog(Appendix S8)
Medication Adherence(Appendix S9)
Cardiac Self-efficacy (Appendix S10)
RSQ (Appendix S11)

Labs
ECG
6-minute walk test
Educational Materials Distributed (Appendix 22)
Depression Video (for patients scoring >=10 on the PHQ who are in the intervention arm)
Telemonitoring Demonstration/Distribution
Contact/Notification to PCP/MH (for control patients scoring >=10 on the PHQ)

Telephone Surveys at 3 months and 6 months include KCCQ and PHQ. For patients who score
equal to or over 10 on the PHQ survey during the 3 or 6 month telephone surveys, the PCP will
be notified of the patient’s depression status. If the patient scores greater to or equal to 1 on
question 9 of the PHQ survey, the patient will be given the phone number to the VA national
suicide prevention hotline.
**Autonomy**
Patients will be assigned a study identifier, a number unrelated to any personal identifying information. All identifying information will be kept in a database separated from the study data. These data will be kept on a secured server in a locked room. At the end of the study follow up period, all personal identifiers will be stripped from the database. All surveys will NOT be labeled with the subject’s name or identifying information. The surveys will be coded with the patient’s study identification number.

**Final Visit**
A 12-month study visit will be planned for all patients to complete final study forms, surveys, and 6-minute walk test. In cases where a final study visit cannot be executed (e.g. due to patient logistic constraints), we will complete 12-month study forms and surveys by phone to maximize complete data through 12-months on as many participants as possible. Travel expenses will be covered for study participants

KCCQ (Appendix S1)
PHQ + Prime MD (Appendix S3)
GAD-7(Appendix S4)
Symptoms/spirituality (Appendix S5)
EQ-5D (Appendix S6)
SCL-20(Appendix S7)
Medication Adherence(Appendix S9)
Cardiac Self-efficacy (Appendix S10)
6-minute walk test
Final Visit Survey (Appendix 16)

**Description of the Intervention**
Collaborative Care: As noted earlier, the CC team at each site will consist of a local opinion-leading primary care provider (PCP), cardiologist, psychiatrist, pharmacist and nurse site coordinator. Additionally, the study PI’s (Dr. Heidenreich, Dr. Rumsfeld and Dr. Sullivan) will participate in the CC team meetings at each site to maintain consistency across sites.

The CC team is designed to function as an efficient consultative team to PCPs for intervention patients. Following the approach successfully employed in the C3P study (03-1024), CC team recommendations will be put into a progress note for co-signature by PCPs, and unsigned orders will be placed for PCPs to review and sign at their discretion. As in the C3P study, the CC teams will meet weekly during the study period to develop treatment plans and conduct progress evaluations for intervention patients. The nurse coordinator will stay in close/daily contact with the site PI to review patient progress, telemonitoring data (including detection of deterioration), etc., with input from other CC team members as indicated.

For a given intervention patient, there will be an initial assessment of care by the CC team following the enrollment visit. Each intervention patient will be re-reviewed by the CC team a minimum of 3 additional times (at 6-weeks, 6 months and 12 months). In addition, patients will have daily telemonitoring, and their care will be reviewed by the CC team if the telemonitoring
data suggests clinical deterioration. Patient data for the CC team review will be collected and, if recommendations are made, a progress note will be generated for PCP co-signature.

The CC team will recommend care changes for a given patient in accordance with current ACC/AHA Guidelines for the Management of Chronic Heart Failure. The ACC/AHA guidelines are fully consistent with current VA CHF Performance Measures (which are overseen by Dr. Jesse, Co-Investigator for this project). For example, a given patient may require titration of diuretics for symptom / weight management, initiation or titration of medications (e.g. ACE-inhibitors for mortality benefit and/or blood pressure control), referral for stress testing to evaluate for ischemia as a cause of decompensation, addition or titration of secondary prevention medications such as statins for patients with underlying coronary artery disease, and/or referral for ICD implantation in patients with systolic dysfunction.

As noted earlier, in cohorts of CHF outpatients, ~30% have moderate-severe depressive symptoms. Since we are targeting CHF outpatients with reduced health status, we expect an even higher prevalence, closer to 50%. In support of this estimate, in the C3P Study of VA outpatients with stable angina (analogous to symptomatic CHF), the prevalence of moderate-severe depressive symptoms at baseline was 49%. Thus, the study cohort will be an ‘enriched sample’ with regard to depressed patients.

The intervention will incorporate management of comorbid depression, adapted from the successful IMPACT and Pathways depression interventions. In brief, patients will be screened for depressive symptoms at the enrollment visit using the PHQ, a validated and reliable short version of the widely-used PRIME-MD. Patients with PHQ scores ≥ 10 will complete the remainder of the PRIME-MD to establish whether a diagnosis of Major Depression or Dysthymia is present, because these are the patients for whom it has been shown that collaborative treatment is superior to usual care. If so, patients will enter a stepped depression management module with the following components:

- Patients will be offered behavioral activation, delivered by the nurse site coordinator, and anti-depressant pharmacotherapy. First-line recommended pharmacotherapy will be selective serotonin reuptake inhibitors (SSRI’s), which are safe and effective in cardiac patients. Behavioral activation will include both physical activity, ‘pleasant activity’ scheduling, targeting avoidance behaviors, and problem solving around CHF self-care behaviors. Some patients will already be taking antidepressants (chronic depression that is not adequately treated) and their medication may be adjusted and/or behavioral activation initiated. Patients will receive a follow-up call 1 week later to reinforce behavioral activation principles, assess for side effects, and answer questions.

- Patients will be given an educational video that has been an important part of the IMPACT and Pathways interventions, as it de-stigmatizes depression treatment and engages patients by providing educational content about depression in relation to comorbid disease.

- Patients will return in 2 weeks to review behavioral activation treatment and to evaluate tolerance and efficacy of anti-depressants. Treatment will be re-offered to those patients who initially declined treatment. Patients will receive a follow-up phone call 1 week after this visit to reinforce behavioral activation principals, assess for side effects, and answer questions.

- Patients will return 4-6 weeks later to review behavioral activation treatment and evaluate tolerance and efficacy of anti-depressants. Patients who are responding will be monitored for
continued improvement and to avoid relapse. Patients who are not responding will have their anti-depressants augmented or switched. Patients will receive a follow-up phone call 1 week after this visit, and will have a return visit in 4-6 weeks to re-evaluate response to therapy. Subsequent calls/visits will be tailored by response to therapy.

- For patients who are refractory to the intervention outlined above, a facilitated referral to specialty VA mental health services will be made with ongoing monitoring of care processes and depression outcomes by the study team.
- Through the study period, patients’ depressive symptoms will be monitored via the telemonitoring system.

We will use the VA-contract telemonitoring system, the Health Buddy. It is an in-home communication appliance that allows patients to transmit information to clinicians and provides patient education and self-care support. The premise is that: 1) because the CC team will have access to the telemonitoring data, the team will be able to detect decompensated CHF early and will be able to intervene to correct the problem; and 2) patient self-care will be enhanced via promotion of adherence to medications, lifestyle activation (e.g. exercise and salt restriction), and self-monitoring for detection of early decompensation (e.g. daily weights, symptom monitoring). In addition, depression symptoms will be monitored, as depression is a barrier to medication adherence and self-care.

Patients randomized to the intervention group will receive daily telemonitoring for 12 months. During the enrollment visit, the nurse site coordinator will instruct the patient on how to connect the telemonitoring system to the telephone and how to use the appliance. The Health Buddy appliance measures 12” x 8” x 4” and consists of an LCD screen and 4 large buttons (Figure 6). It shares the conventional telephone line with the existing telephone handset, and does not interfere with telephone function. Patients will be clearly instructed that the appliance is for daily monitoring and NOT to be used for urgent care needs. All enrolled patients (usual care and intervention arms) will be instructed to contact their PCP directly with any concerns about their health or call 911 for emergent situations.

The Health Buddy has modules for both CHF and depression monitoring. Patients are asked a pre-programmed series of questions in English or Spanish at a fifth-grade reading level. A typical session will last 1-3 minutes. Examples of questions in the CHF module are: “Are you more short of breath than usual today?”; “Do you have any new or any more swelling than usual in your feet or ankles today?”; and “What is/was your weight this morning?” Examples of questions in the depression module are: ‘Are you feeling depressed or hopeless?’; ‘Do you have less interest in your usual activities today?’ Patients respond using the buttons on the appliance. Depending on the response, follow-up questions may be generated using branching-chain logic. For instance, a patient responds that he/she is experiencing shortness of breath is then asked to rate the symptoms. In addition, advice is given to continue to take medications and call the CC team (with phone number provided).

Moreover, there is a program designed to educate patients and promote self-care. The program includes medication reminders to promote adherence, an educational curriculum about CHF and medication effects/side effects, and lifestyle activation (e.g. exercise and dietary guidelines). Patients are also taught signs and symptoms to report and ways to manage CHF and cardiovascular risk factors. Examples of self-care skills that patients will be instructed about...
include proper technique and importance of daily self-weighing, adherence to a low sodium diet and medication regimens, the importance of physical and pleasant activities, and recognition of early signs and symptoms of CHF decompensation.

After patients complete a session, the appliance automatically dials out during the night to a toll-free number where responses are uploaded to a secure data center and the questions for the next day are downloaded into the appliance. The delay in transmission and review is consistent with the premise that clinicians are responding to gradual changes in the patients’ status, not acute changes, and patients will be instructed about timing of review. Past experience with the appliance has demonstrated that patients are able to understand this issue and use the appliance appropriately.

The nurse site coordinators will log onto a secure VA Intranet site to review the patients’ responses on a daily basis, except weekends and holidays. All responses are color-coded and flagged according to pre-determined criteria to facilitate rapid interpretation (e.g. a ‘yellow flag’ for weight gain ≥3 lbs; a ‘red flag’ for worsening shortness of breath). Since all responses for a given patient are summarized, the site coordinator can determine at a glance whether or not a patient is experiencing significant problems. When deterioration in clinical status is detected, the site coordinator will contact the patient to verify the accuracy of responses to questions and acquire further information. Depending on the responses, the site coordinator can then either provide counseling to the patient or present the patient to the CC team for recommendations such as adjustment in medications, referral for further diagnostic testing (e.g. lab tests), an outpatient appointment, or more urgent evaluation in the emergency department or urgent care. In a situation where the patient needs immediate care, the nurse will immediately contact at least one of the physicians on the collaborative care team. A recommendation for treatment will be made and implemented immediately. The patient’s PCP will be informed of the treatment decision through a progress note in the patient’s medical chart. Information regarding patients’ compliance with the intervention is also provided. Patients who miss several sessions in a row will be contacted by the site coordinator (unless the patient has indicated they will be away from home for vacation or other reason) to troubleshoot the cause for missed sessions, e.g., problem with the telemonitoring system or signal of decompensation.

**Comparison group: Usual care**

Patients randomized to the usual care arm will continue to receive care at the discretion of their regular VA providers (for a given patient, this could include cardiology specialty care in addition to PCP care, participation in site-specific CHF programs such as CHF patient education classes, etc.), in direct continuity with the care they were receiving prior to enrollment. Patients in the usual care group will also be given information sheets that outline self-care for CHF, and will be provided with a scale, if needed, at the enrollment visit. Patients in the usual care group will have the same amount of interaction with the study team as the intervention patients (i.e. complete questionnaires at the same frequency; have the same study visits). PCPs of usual care patients will be notified of the results of all screening studies (patient survey results, lab tests) as we have done in previous studies. Therefore, the usual care patients will receive current standard of care for VA CHF patients, and may additionally benefit from the education and feedback of screening study results to their PCPs. This sets a high but appropriate standard by which to judge the
effectiveness of our intervention. As in previous depression effectiveness trials, PCPs of patients in the usual care arm found to have significant depressive symptoms (including scores of >=1 on question 9 of the PHQ survey) will be immediately notified of such. The PCPs will thereafter assume responsibility for depression care with no constraints on the treatment or referral (to Mental Health). The research nurse will write a note in CPRS to indicate that he/she has contacted the PCP and include the PCP’s plan for follow-up. Usual care patients are not denied any depression care and may benefit from the case-finding apparatus of the trial. Drs. Rumsfeld, Heidenreich, and Fihn are using this approach in the ongoing C3P trial, and it is consistent with current IRB standards.

**Nurse Training/Education**

Research nurses will attend training in Denver prior to the start of the study. Training will include patient enrollment, consent procedures, and specific study procedures with the goal of consistency across all study sites. A training manual will be given to each nurse researcher and weekly multi-site conference calls will be set up to answer any questions the nurses might have regarding the study protocol to ensure consistency across all study sites.

**Exclusion criteria**

1) Cognitive or psychiatric impairment that precludes completion of questionnaires; 2) Nursing home resident; 3) Irreversible, non-cardiac medical conditions (e.g. metastatic cancer) likely to affect 6-month survival or ability to execute the study protocol; 4) AUDIT-C – if score>=7; 5) Inability to read English at a fifth-grade level (unless there is presence, on a daily basis, of someone who can read at this level for the purposes of telemonitoring); and 8) Prior heart transplantation, since their care is focused more on anti-rejection regimens.

**Selection of Study Population**

Age: All ages included. Veteran population ranges in age from approximately 18-100. Gender: All eligible females will be included. However, VHA population is predominantly male. Ethnic and racial minority populations: All ethnic categories and racial minorities will be included.

**Patient Accrual**

Patients: Denver VHA’s Eastern Colorado Health Care System (ECHCS): 175 consented. All 4 sites: 600 consented.

**Estimated Duration of Study**

Study duration: 01 January 2008 through 30 June 2011
Patient participation: 1 year

**Drugs, devices or instruments to be used**
The proposed intervention is expected to pose minimal safety risks for patients. No experimental devices or drugs will be used, and there have been no reported adverse events with use of the VA’s Health Buddy system, nor with telemonitoring or collaborative care interventions in general (rather, the increased surveillance may be a patient safety measure). Nevertheless, this is a randomized trial and we will monitor the patients closely to detect any problems posed by the intervention, and all standards of IRB and privacy (HIPAA) review and monitoring will be in effect (including full IRB review for the 4 sites, employment of approved informed consent and HIPAA authorization, reporting of serious adverse events, etc.).

Protected Health Information

The computerized records of approximately 8,500 patients seen in Denver, Palo Alto, Seattle and Richmond’s VHA General Internal Medicine Clinics in the past year will be screened using the VHA computerized medical record system. All patients actively enrolled in primary care with CHF will be screened for eligibility to participate. Active VA enrollment will be defined as having an assigned primary care provider in the Primary Care Provider Management Application of ViSTA and at least one appointment during the prior 12 months. The presence of CHF will be defined as an in- or outpatient diagnosis for CHF (ICD-9 code 402.01, 402.11, 402.91, 404.01, 404.11, 404.91, or any 428.x) within the past 18 months. In addition, we will extract name, address, phone number, SSN, provider, scheduled clinic visits, and demographics (dob, race, income, marital status, employment status, presence/absence of other chronic conditions). This information will be used for the purpose of describing the characteristics of our study population and to contact patients by letter for recruitment/follow-up. The data will also be used in aggregate to compare the characteristics of patients who consent with those who do not consent to be in the study. All data will be de-identified for those patients who do not ultimately consent to be in the study as described in this application. We will obtain this information directly from ViSTA as we have done in several previous studies. The randomization form will serve as a cross-reference master, linking the patient’s name to his/her randomization number. Both the randomization and tracking forms will be kept separate from other research material. Only members of the VHA research team will have access to the data. Electronic data files will be encrypted/password-protected on computers maintained in a secure environment per VA security regulations. All paper records will be maintained in locked file cabinets within locked offices. There are no other other government agencies or sponsors involved with the study. All study results will be presented as aggregate data only and will be presented in a way that does not permit any individual provider or patient to be identified.

Data and Safety Monitoring Plan

Data Analysis Proposed

Data analysis will be conducted at the Denver VHA Medical Center. As described above, our primary outcome measure will be the change in CHF health status. Secondary outcomes will include hospitalization, mortality, depressive symptoms, patients’ self-efficacy in management of CHF, adherence to prescribed medications, the proportion of patients with guideline-concordant care, and cost-effectiveness of the intervention. The unit of randomization and analysis will be
Monitoring and Reporting Adverse Events
The proposed study consists of an administrative intervention with the main risk being loss of confidentiality for patients and providers. Mechanisms as described in this application will be in place to protect the privacy of all participants and the security of data collected. The Research Assistant at each site will also maintain a record of any patient or provider comments/complaints. Authority for monitoring data and safety will reside with the VA-mandated Combined Monitoring Board (CoMB) for multi-site interventional health services studies/randomized trials.\textsuperscript{38} CoMB will review the study annually. They will assess the participation of each participating center and make recommendations regarding continuation. COMB will assess adverse effects and patient safety, intervention effectiveness and proper monitoring/reporting by the study team. The COMB will prepare a detailed report for the study chairman and a short report for distribution to the IRB’s of all participating sites informing them of any safety issues. The CoMB will hold the PI, co-PI, and other investigators responsible for data quality and completeness, and for ensuring the safety of all study participants. The investigator group has experience with CoMB regulations based on studies such as C3P. To ensure a rapid and systematic approach to adverse events, an Internal Safety Committee will be established to evaluate all suspected adverse events, however mild or severe. An important function of the Committee will be to classify severe adverse events and forward them immediately to the CoMB, IRB and other study sites. Investigators will notify the IRB with 5 days of the occurrence of the serious adverse event. A serious adverse event (SAE) includes death, life-threatening, hospitalization or prolongation of hospitalization, congenital anomaly/birth defects, and persistent/significant disability. SAE’s that occur at an off-site study site should be report to the Denver IRB at least quarterly using safety reports. All deaths must be reported to the IRB, whether or not the death was related to the research study. Death due to disease must be reported immediately if the death occurs within 30 days of the study treatment. All deaths that might be related to the study, but occur more than 30 days after the treatment must be reported immediately. All other deaths that are due to disease (therefore expected) and unrelated to the treatment, should be reported at continuing review.

Interim analysis
This study has a fixed enrollment period at the beginning, and all patients are followed concurrently. Evaluations of the efficacy of the intervention will occur after the patients have completed the study.

Data Safety Monitoring Board
The COMB described above will perform the function of a Data Safety Monitoring Board.

Monitoring Study Conduct
The COMB will assess patient accrual and study progress. Specifically, the following will be evaluated:
Enrollment – number of patients entered into the study (by time and site) in comparison with the projected number.
Baseline comparison of relevant characteristics of intervention groups
Patient Retention – deaths, losses to follow-up, withdrawals, etc., by site
Patient Safety – Adverse Events and Serious Adverse Events
Effectiveness - Aggregated outcome data, and a comparison of the overall event rates with the rate predicted in the original protocol.
Reconsideration of the power/sample size issues

Confidentiality of Data
Paper questionnaires will not include the patient’s name or other direct identifiers such as SSN. Physical copies of questionnaires will be kept in locked files in a locked office. Consenting patients will be assigned a confidential study ID number, which will be used on paper copies of questionnaires. The crosswalk for this ID number will be accessible only by restricted study staff and investigators. Two layers of password protection, one to get into our department network, and a second to access our study server and database servers, will protect it. The crosswalk will be maintained on a separate database server than the study data files. RAs will need to have access to identifiers for the purpose of telephoning and scheduling appointments with patients. Logs of these contacts will be maintained on the computer with the multiple levels of security described above. Because this study involves feedback to clinicians, these documents will necessarily include patient identifiers. Copies will be maintained in locked files in a locked office.

The privacy of patients who 1) do not return the screening questionnaires, 2) return screening questionnaires and are found to be ineligible, or 3) are eligible and do not consent to participate will be protected. For these patients, we will de-identify their records at the end of the projected study recruitment period. The confidential study ID number will be replaced with an anonymous, random study ID number and all linkages to their identity will be destroyed.

Statistical Analysis

Primary Hypothesis: The primary hypothesis of this study is that, compared with those receiving usual care, CHF outpatients receiving a Patient-Centered Disease Management intervention will have improved health status (fewer CHF symptoms, better physical function, and better quality of life) over a 12-month follow-up period that begins at randomization.

All analyses will be conducted using the intention-to-treat principle. We will summarize the baseline characteristics of patients by study group and test for differences in age, CHF severity, depressive symptoms, and other patient attributes. In the event that there are significant differences, these will be accounted for in the analyses. We will test the primary hypothesis by comparing a continuous variable, change in KCCQ summary scores, between baseline and 12 months across the two study arms using Student’s t-tests, stratified by site. Then, to account for any imbalance in baseline characteristics and to improve the precision of estimates, we will test the primary hypothesis using a linear regression model. This model will use the primary outcome as the dependent variable and include baseline characteristics, site, and study group as independent variables. We will employ current methods of regression modeling as we have in previous studies, following the principals of Frank Harrell, and use standard model diagnostics (e.g. adjusted R² as a measure of global goodness of fit, residuals and DF-FIT tests for...
outliers). Area under the curve (AUC) analysis will also be performed to incorporate the 3- and 6-month KCCQ measurements in the comparison of KCCQ summary scores across the study period.

Secondary hypotheses to be tested are whether the intervention reduces the rate of hospitalization and mortality, leads to care that is more consistent with national clinical practice guidelines, improves depressive symptoms, improves self-efficacy in the management of CHF and medication adherence, is associated with higher patient treatment satisfaction, and is cost-effective. Additional hypotheses to be tested for completeness include whether the intervention is associated with a lower rate of all-cause hospitalization, lower rate of cardiac hospitalization, and improved survival (measured in number of days alive after randomization) as separate outcomes, but the study is not specifically powered to test these hypotheses. As noted earlier, other measures such as number of ambulatory care and ED visits, will also be captured for descriptive comparison.

We will follow all patients for 12 months starting on the day of randomization, and analyses will be intention-to-treat.

Hospitalization and mortality: Rates of all-cause hospitalization and mortality will be compared between study arms using Chi-Square tests, stratified by site. Then, to improve the precision of estimates, we will use logistic regression with hospitalization or mortality as the dependent variable and include baseline characteristics and study group as independent variables. Survival analysis (Kaplan Meier curves for unadjusted time to event, Cox Proportional Hazards regression for multivariable time to event) will also be used to compare time to hospitalization or mortality. Depressive symptoms, self-efficacy, and 6-minute walk distance are all continuous variables and analysis will directly mirror the analysis of the primary outcome variable.

Guideline-concordant care: We will compare the proportion of patients in each study arm receiving guideline-concordant care at 12-months using a Chi-Square test. For a given patient, the proportion of guideline-concordant care will be determined using criteria mapping. Criteria mapping estimates the overall proportion of guideline-concordant care for a given patient by employing sequential judgments to guideline-indicated therapies based upon the specific clinical data for that patient, allowing for sequential logic within each indicator (e.g. first and then second-line recommendations if the first-line therapy is contraindicated), and then summing the proportion of adherence.

Medication adherence: Following established methodology, the proportion of days covered (PDC) will be calculated for each patient, based on the total number of days supplied for filled prescriptions over the observation time interval (minimum 180 days to ensure stable estimates). Primary medications to be evaluated will be ACE/ARB’s, beta-blockers, aldosterone antagonists, and statins. The PDC for each study group will be compared as a continuous measure (t-test) and as the proportion of patients achieving a PDC>0.80 (Chi-Square), a cut-off used in multiple medication adherence studies.

Sample size: As noted earlier, target enrollment will be 600 patients (300 per study arm). In estimating the sample size required for the trial, we wanted to ensure that the study has sufficient power to detect a clinically meaningful difference in change in KCCQ summary scores between the 2 study arms. Key data used in the sample size calculations included: 1) The minimal clinically meaningful difference in KCCQ summary scores is 5 points, and changes in KCCQ scores between baseline and follow-up of up to 20 points have been seen in observational studies.
of CHF outpatients.\textsuperscript{8,49,50} We therefore considered the sample size range for score differences (effect size) ranging from 5 to 20; and 2) The standard deviation (SD) of change in KCCQ scores was assumed to be in the range of 15-20, based on previous work including the KCCQ Interpretability Study.\textsuperscript{50,51} The table below displays the power to detect a range of effect sizes in the primary outcome with different numbers of participants per study group with SD = 18. The figure below displays power curves to detect the minimal clinically important difference in change in KCCQ scores of 5 points for a range of sample sizes, varying the SD between 15 and 20.

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The estimates above are relevant to the analytic cohort of the study, and thus not the enrollment cohort as there will be loss to follow-up. We conservatively estimated needs for enrollment sample size based on a loss to follow-up of 30%. Under this scenario, enrollment of 600 patients will lead to an analytic cohort of approximately 420, or 210 per group. As noted in Table 3 and Figure 8, under the reasonable assumption of SD=18, the study will have >80% power to detect the clinically important difference in change in KCCQ scores of ≥5 points with >200 patients per group, and have 99% power to detect differences ≥7.5 points. Even under the more extreme situation of SD=20, the study will have 96% power to detect differences in change in KCCQ scores of ≥7.5 points with >200 patients per group.

Secondary outcomes are, by definition, exploratory and supportive of the primary outcome. However, it is useful to have a sense of the power for these pre-specified outcomes:

Rate of hospitalization and mortality: Previous studies have reported combined annual admission and mortality rates of 45-60%. In the KCCQ Interpretability study (CHF outpatients), the 12-month combined admission and mortality rate was 40%. Using this estimate for the usual care group, this study will have >80% power to detect an 11% reduction in the combined outcome.

Depressive symptoms: Based on previous literature and our previous studies, a clinically meaningful change in PHQ scores is ~3-5 points, and SD of change is ~5. Even with a conservative estimate of baseline prevalence of moderate-severe depressive symptoms of 30% in the study population, we will have >90% power to detect a difference in change in PHQ scores between the two arms.

Self efficacy / generic health status: Score ranges and SD of change for the Cardiac-SELF is similar to the KCCQ; thus, power will be similar (if anything, KCCQ estimates are conservative).
Guideline-concordant care and medication adherence: This study will have >80% power to detect a ≥11% difference in proportion of patients with guideline-concordant care and differences in proportion of medication adherence.

Cost: We will have 80% power to detect a cost difference of $1370 (90% power to detect difference of $1585), and even higher power for the incremental cost-effectiveness analysis.

Cost Determination and Cost Effectiveness Analyses: For the base case analysis, we will determine the cost of care for each subject by multiplying resources consumed by cost per resource. For patients in the intervention arm, the cost of the intervention will be added. In a separate VA-specific cost analysis, we will determine the cost of VA care from Average Cost Files created by the VA’s Health Economics Resource Center (HERC). These files assign a cost to each admission and outpatient encounter. These cost estimates were created using non-VA costs for different Diagnostic Related Groups (DRG) and Current Procedural Terminology (CPT) codes and applying these to the VA. Indirect costs are also included. It is expected that these data will not be available until one year after the trial is complete and for that reason we will not rely on them for our primary analysis.

Resource data: We will collect data from the medical record and patient (for non-VA care) on hospitalizations including length of stay and diagnosis (DRG), medications, outpatient visits, ER visits and major outpatient procedures (coronary angiography, stress testing). The cost per resource will be obtained from Medicare reimbursement for hospitalization (based on DRG from Medicare), outpatient visits, and ER visits. A separate cost will be applied to all outpatient (mid-level established patient visit-CPT 99213) and all ER visits (med level CPT 99283) using averages from Medicare’s Resource Based Relative Value System (RBRVS). Although more detailed coding of outpatient visits could be performed, we believe this is not worth the expense given that the majority of cost differences will come from differences in hospitalization. We use Medicare data because they are a standard for measuring costs and are applicable to the U.S. population. Medication cost will be obtained from an average of U.S. wholesale costs (Redbook survey) and online pharmacy prices (usually lower than reported wholesale costs). In the VA specific analysis, we will use VA specific drug costs.

Intervention Cost: The cost of the intervention will be determined by tracking personnel (staff and physician) time for patient identification, patient enrollment and maintenance. Time spent on research specific tasks will be excluded. Personnel cost will be calculated as wages per hour*hours devoted to the program. Equipment, supplies, and patient time costs will also be included.

Estimation of Long-term Health and Economic Outcomes: We will use data following the end of the study to estimate the impact of discontinuing the program on subsequent cost of care and quality of life. If the benefit of the intervention rapidly dissipates, we will use a time-horizon equal to the trial duration. However, if a persistence of effect is noted, then different time horizons for the program’s effect will be modeled (1-5 years). We will discount cost and outcomes at 3% per year.

Quality of Life: The primary analysis will be of cost per quality-adjusted life-year (QALY) gained. We will use an average of the EQ-5D utility measures obtained at 3, 6, and 12 months. QALY are obtained by multiplying patient survival during the trial by the patient utility (range 0-1) during the trial.

Calculation of Cost-Effectiveness: Each intervention and usual care patient will be assigned a cost of care and quality adjusted survival (QALYs) for the duration of the trial. The incremental
cost-effectiveness ratio (ICER) is calculated by dividing the difference (intervention vs. usual care) in mean cost by the difference in mean QALYs. Standard errors for this ratio will be determined by bootstrap analysis, which is performed by randomly selecting N patients with replacement from the original dataset where N is the number of patients in the original dataset. An ICER is then calculated based on this new sample. This process will be repeated 5000 times to create a distribution of ICER’s whose standard deviation will equal the standard error of the mean. ICER’s and associated 95% confidence limits will be determined in this fashion for the different sensitivity analyses.

Pre-specified subgroup analyses: Exploratory subgroup analyses will be performed to assess any differential effects of the intervention. We will compare primary outcomes between study groups by categories of age, sex, race/ethnicity, baseline health status, baseline depressive symptom status, and baseline left ventricular systolic function. Finally, the incidence of adverse events will be calculated and compared among the study arms using statistics appropriate for discrete or count data.

**Missing data:** We will report rates of missing data for each outcome by study group and known reasons for missing data. Missing follow-up surveys are a potential source of bias in the analysis of study results. Every attempt will be made to obtain follow-up surveys on survivors, but some loss to follow-up is expected, as in all studies. To minimize this, we will be as flexible as possible in scheduling the final study visit for all enrolled patients, including looking for opportunities to have the final study visit coincide with scheduled visits to the Medical Center/CBOC, and will reimburse travel expenses. If logistics of the study visit remain a barrier, we will administer the 12-month surveys by phone (sensitivity analysis can be employed to evaluate whether difference in mode of administration influenced results, but this has not had a significant effect in previous studies). We will do our best to ensure equal follow-up of patients across study arms, which has not been a problem in previous IHD-QUERI studies. In the event that the rate of missing data is not independent of study group, we will conduct sensitivity analyses under a range of assumptions about the missing values and assess consistency of results across those scenarios. To address missing data in analysis, we will employ well-validated, advanced statistical methods. These include multiple imputation (for missing clinical data), and, to address the possibility of follow-up survey data not missing at random (NMAR), pattern mixture models (to assess across multiple time points, i.e. 3, 6, and 12 months) and the Heckman two-step method for the primary 12-month survey outcome analysis. The study team has extensive experience with each of these methods, including prior publication on the Heckman method by Drs. Rumsfeld and Plomondon. Importantly, in previous studies in which we have employed these statistical methods (including randomized trials), the results of these analyses have directly supported the primary analysis. In addition, we have chosen secondary outcomes as a ‘safety net’, including clinical events (hospitalization/mortality) and assessment of guideline-concordant care, where little to no missing data is expected. We are also collecting 3 and 6 month outcomes, where missing data should be lower than 12 months, and such data can inform multiple imputation and AUC (area under the curve) analyses.

4. **Risks**

The risks to patients participating in this study are minimal. Patients are randomized to either ‘usual care’ or to receive the collaborative care intervention, which involves no experimental drugs or devices. Information provided in reports to the collaborative care team consists of
questionnaire data and other data routinely available to the providers who see these patients. Patients and their primary care provider will still make all final decisions regarding care.

A potential risk is a loss of confidentiality due to researchers and chart auditors having access to medical records. This is standard for such research, this risk is minimal, and confidentiality will be protected by locking up all paper records, password protecting all computer files and keeping computers in a locked office. Confidential study ID numbers will be used in the analyses, and the data analysts will not have the key.

To protect the privacy of non-respondents to the first mailing, ineligible respondents to the initial screening questionnaires based on their responses, and eligible patients who do not consent, will have their records de-identified at the end of the projected study recruitment period (December 30, 2011). The confidential study ID number will be replaced with an anonymous, random study ID number and all linkages to their identity will be destroyed. Data and results from the study will be presented in a way so that no individual patient can be identified. Patients are also free to withdraw from the study at any time.

5. Benefits

Although there may be no direct benefit to a patient from participating in this study, they will contribute to information that may potentially improve the quality of care for other veterans with heart failure. In addition, this study will also give patients access to up-to-date educational materials regarding disease management. For patients who indicate on their questionnaires that they are very symptomatic or have depressive symptoms, this study provides a communication mechanism so that providers can further evaluate these conditions. It is likely that the PHQ questionnaire may reveal that some patients are suffering from depressive symptoms (indicated by a score of 10 or greater). If this occurs, the information will be relayed to the patient’s primary care provider for follow-up evaluation.

If one of these systems of care works better than the other, we hope that it will be implemented in other VHA’s so that all patients with heart failure will receive better care. The model developed may also be applicable to other serious, chronic medical conditions.

6. Funding

Funding is provided by the Department of Veterans Affairs, Health Service R&D. There will be no costs to participants, or third party payers.
REFERENCES


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Post-PCDM Interviews to Inform a Quality of Life Program

Introduction
The purpose of this amendment is to interview patients who have completed the Patient-Centered Disease Management (PCDM) trial (COMIRB 07-0588) to learn about unmet health care needs related to quality of life. We will also describe a new quality of life intervention to subjects and their family caregivers and ask them what they think of this intervention. This information will help us to modify the intervention prior to pilot testing.

Methods and Procedures
1. Study Population
   a. Inclusion Criteria: (1) Subjects who enrolled in the PCDM trial, were randomized to the intervention arm; (2) Family caregivers of subjects, identified by the subjects
   b. Exclusion Criteria: None

2. Procedures
   a. Recruitment: Subjects enrolled in the PCDM trial will be recruited by phone or in person at or within 3 months prior to their final PCDM study visit. We will recruit a convenience sample of 20-30 subjects. We will ask subjects to identify a family member or person who helps them the most with their medical condition (“family caregiver”). We will ask the subject to give the family caregiver our contact information or sign a HIPAA A form and return it to us.
   b. Informed Consent: Informed consent will be obtained either in writing or by phone. Many veterans/caregivers do not have the ability to make an in person visit either because they are functionally impaired or they do not have financial means. We are providing Attachments M and O to request a partial waiver of consent and HIPAA authorization (waivers of documentation) for those who consent over the phone.
   c. Interviews: Please see the Interview Guides below for a description of what will be asked to patients and caregivers. The purpose of the interview is to ask subjects about (1) what we can do over and above the PCDM trial to improve quality of life, and (2) for feedback on a new intervention named Collaborative Care to Alleviate Symptoms and Adjust to Illness (CASA) to improve quality of life. Interviews will be done in person or on the phone according to the subject’s preference. Interviews will be digitally audiotaped. The interviewer will label each audiotape with the subject’s PCDM study ID. No PHI will be on the audiotape.
   d. Questionnaires: Please see the Questionnaires below for the questionnaires that will be given to patients only.

3. Description, Risks, and Justification of Procedures and Data Collection Tools
   a. Interviews: These pose minimal risks. We are asking how subjects felt about the PCDM intervention and what they think of a new program for heart failure patients. We do not anticipate any significant physical, social, psychological or legal risks.
b. Data storage: There is a possible risk of loss of confidentiality if the digital recorder is lost or stolen. However, no PHI will be stored on the recorder; subjects will be identified by PCDM study id.

c. Surveys: There is a theoretical risk that patients may experience stress when answering quality of life surveys. However, none of the veterans in the PCDM study (who are filling out similar quality of life surveys) have had any trouble doing so.

4. Privacy

Interviews will be conducted in the subject’s preferred setting. The following options will be made available to subjects: the research assistant’s private VA office (Carolyn Nowels, 4495 Hale Parkway, room 209), a private VA clinic room in the VA outpatient clinic, or by phone.

5. Confidentiality

We will not collect any additional personal information for these interviews.

6. HIPAA

We will obtain HIPAA authorization to allow us to access PCDM records.

7. Data Management & Security

Digital audio files will not contain PHI or PII. They will be transferred from the recorder and stored on a secure server that is located on the internet and password protected. After the files are transferred, they will be deleted from the audio recorder. The transcriptionist will transcribe the audio files into MS Word files on the same server.

8. Data Analysis

Transcribed interviews will be loaded into the qualitative research software ATLAS.ti for analysis. Responses to the same question will be analyzed side-by-side to inform changes to the proposed program. We will group the responses under more general categories (e.g., process of care, symptom intervention) and then count the number of times a particular change is suggested.

9. Summary of Knowledge to be Gained

By asking subjects about what we can do over and above the PCDM trial to improve quality of life, and for feedback on a new intervention to improve quality of life, we will be able to modify the intervention prior to pilot testing.

INTERVIEW GUIDES: Post-PCDM Interviews to Inform a Quality of Life Intervention

Patient Interview guide
**INTRODUCTION:** Thank you for agreeing to this interview. We really appreciate your time. I’m going to ask you some questions about your experience with the PCDM project and then your opinions about a new and different program for people with heart failure. In asking these questions, we are hoping to learn more about how we can develop a program to better meet the needs for people like you with a heart condition. So, I encourage you to tell me as much as you can – we hope to learn from specific experiences like yours. As you read in the consent form, we would like to tape this interview if you are comfortable – so we have a good record of exactly what you say. You will never be identified, either on the recording or in any summary or report. The digital recording will be kept on a secure password-protected drive where no one except the research team will have access to it. My most important goal is that you feel comfortable. Are you ok with the tape recording?

Before we start, I want to make sure you are aware that your participation is voluntary, you do not have to answer any question that makes you uncomfortable, and you may stop at anytime. If you have any concerns about this study, you may contact the Primary Investigator – Dr. David Bekelman (303-724-2242) or COMIRB (303-724-0155).

**Evaluation of PCDM**

1. If you had to choose one thing, what would you say was most helpful/least helpful about PCDM? Why? How? In what way?
   a. If you could change one thing about the program, what would that be/why?

2. Did PCDM affect your quality of life (QOL)? In what way?
   a. We see you marked xxx on QOL scale. What would it take (or how would things be different) for that to be a xxx?
   b. Can you think of specific things a VA health care program could provide to help?

**Reaction to CASA**

Thanks for sharing your experience with the PCDM project. Now we’re going to “switch gears” and talk about a different heart failure program that we’re planning to start at the VA. We’d really like your opinion about some of our ideas and how we could improve this new program.

We’re calling this program Collaborative Care to Alleviate Symptoms and Adjust to Illness, or CASA for short. The goal of CASA is to improve your quality of life by: (1) improving several symptoms, such as fatigue, shortness of breath, feeling down or worried, and pain; and (2) helping you adjust to your heart condition, (3) involving family caregivers. Many adjust well to having heart problems and we will build on what you have done so far. Also, we will only try to help symptoms that are bothersome or distressing that you would like help with. This program consists of a nurse who will work collaboratively with your primary doctor, cardiologist (if you have one), and a social worker. The nurse will be in touch with you regularly about your heart condition. The nurse will also meet weekly with a care team who will review your care and provide recommendations. The nurse will give these recommendations to you and your doctor.

**CASA: Process & Symptoms**

- So let me tell you briefly a little more about how the FIRST part of the program would work, improving symptoms:
a) You would meet with the CASA nurse to talk about your heart condition; s/he will ask about your symptoms
b) You would choose which symptom you’d like to work on first
c) The nurse will work with the team I mentioned previously to come up with other ideas for helping with the symptom as well as to help with your heart condition.
d) The nurse will check in with you regularly to see if we’re making progress

Reaction to CASA: Process & Symptoms
1. So, after hearing a little bit about this program, what do you think about this approach?
2. How likely is it that you would participate in this program if you were asked? On a scale of 1-10, with 1 being “Not at all likely” and 10 being “Definitely likely.” (If less than 10, ask “what would it take for you to be a 10?” “What would you need to rate it higher?” “Anything else you’d need to know before rating it?”)
3. What do you think about the team composition? Any one you think should be added/deleted? If yes, “can you tell me about that?” (Explore reasons.)
4. If you were going to pick a symptom, what would you pick first (fatigue, shortness of breath, feeling down or worried, pain)?

CASA: Adjusting to illness

- Now, let me tell you a little more about how the SECOND part of the program would work, adjusting to illness. Based on our prior work, we think this part of the program could help with symptoms also:
  a) The team social worker would meet with you and describe how s/he will be working with you to help you adjust to illness. This will involve around 8 visits, most of which will be by phone.
  b) The visits will focus on these topics:
     a. Adapting to change in illness: loss, grief, and acceptance
     b. Changing circumstances, changing roles
     c. Getting active
     d. Pacing myself
     e. Where am I going? (coping with uncertainty in the future of illness)
     f. What’s important to me? (what are my goals for my health care)

Reaction to CASA: adjusting to illness component
1. What do you think about this part of the program?
   a. What do you like/not like about it? Can you tell me more about that (reasons)?
2. How willing would you be to participate in this part of the program (scale of 1-10 with 1 being “extremely unwilling” to 10 being “extremely willing”? What would it take for you to be a 10?

CASA: Caregivers
Let me tell you about the final part of the program, involving family caregivers. Many of our veterans have a person who helps them with their medical conditions such as heart failure. Do you have somebody like this?

IF NO: Sounds like this part of the program wouldn’t be applicable to you [GO TO “Final Questions”]

IF YES: The social worker would contact your caregiver to see if they have any questions or concerns about your condition. S/he would see how your caregiver is doing caring for you. Also, we would see if we could provide any help with financial issues, practical needs, or community resources.

1. What do you think about this part of the program?
   a. What do you like/not like about it? Can you tell me more about that (reasons)?

We’d like to get your caregiver’s perspective on this part of the program. Would you please tell your caregiver and ask him/her to call us so we could speak with him/her? Alternatively, you could give him/her this form so we could contact them. [Give HIPAA A form].

Final Questions
Thanks for your help so far. I have a few final questions:

1. Most of the program will be delivered over the phone, but some visits would need to be in person. Let me ask you: How many times would you be willing to come in in-person for this program? (1-2 visits, 3-4 visits, 5 or more visits)

2. Is there something missing from this program you think we should include?

Thank you so much for taking the time to talk with me today. We’ll be using this information to help improve the CASA program. Would you be willing to review our results after we’ve completed all the interviews? (If yes, get email address if available.) Thanks so much.
Caregiver Interview guide

INTRODUCTION: Thank you for agreeing to this interview. We really appreciate your time. I’m going to ask you some questions about your experience of living with someone who has been diagnosed with heart failure, and then I’d like to get your opinions about a new and different program (CASA) for people with heart failure. In asking these questions, we are hoping to learn more about how we can develop a program to better meet the needs of people with heart failure as well as the people who care for them. So, I encourage you to tell me as much as you can – we hope to learn from specific experiences like yours.

As you read in the consent form, we would like to tape this interview if you are comfortable – so we have a good record of exactly what you say. You will never be identified, either on the recording or in any summary or report. The digital recording will be kept on a secure, password-protected drive where no one except the research team will have access to it. My most important goal is that you feel comfortable. Are you ok with the tape recording?

Before we start, I need to make sure you are aware of the following:

- Your participation is voluntary, you do not have to answer any question that makes you uncomfortable, and you may stop at anytime.
- As mentioned in the consent form, if you have any concerns about this study, you may contact the Primary Investigator – Dr. David Bekelman (303-724-2242) or COMIRB (303-724-0155).

**General Experience with Caregiving for HF**

1) Please tell me: in what ways do you help the person you care for?

**Reaction to CASA**

Thanks for sharing something about how you help the person you care for. Now I’d like to tell you about a new program we’re considering for veterans with HF. This program will be called CASA, Collaborative Care to Alleviate Symptoms and Adjust to Illness. The main purpose of the CASA program is to improve veterans’ quality of life. To improve quality of life, the program will do three things: (1) improve several symptoms, such as fatigue, shortness of breath, feeling down or worried, and pain; and (2) help veterans’ adjust to having a heart condition, (3) involve family caregivers.

1) What do you think about this approach? What do you like about it/not like about it?

I’d like to hear what you think about the part of the program that involves family caregivers, like you. In this part of the program, a social worker or nurse will contact you to ask you some questions and offer assistance in the following areas:

- a. Your understanding of HF and HF treatments
- b. How you the caregiver and the person you care for are coping with and adjusting to HF
- c. What kind of support you have, such as who helps you when you need help?
- d. How you’re doing financially to see if the VA or community could help
- e. Practical issues such as getting to appointments

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2) What do you think about this approach? What do you like about it/not like about it? If you could add something to this list, what would it be?

3) How do you feel about working with a social worker or nurse on these issues?

4) How likely is it that you would talk with a social worker about these issues, on a scale of 1-10, with 1 meaning not at all, 10 meaning absolutely? What would it take to get it to a 10?

5) Is there anything else that you think is important for us to know about CASA as we develop this program? Is there anything we haven’t included that you think should definitely be included to help improve quality of life in veterans with HF?

Thank you so much for taking the time to talk with me today. We’ll be using this information to modify the CASA program before we test it. Would you be willing to review our results after we’ve completed all the interviews? Thanks so much. (If yes, get email address if available.)
QUESTIONNAIRE: FOR PATIENTS ONLY

I'd like you to think back over the last month. Please tell me the three physical symptoms or problems that have bothered you the most during that time. Some examples are pain, nausea, lack of energy, confusion, depression, anxiety, and shortness of breath.

Symptom #1 ___________________________  Symptom #3 ___________________________
Symptom #2 ___________________________

• If no symptoms were elicited, then state the following:
  So, just to be sure, over the last month, you have had no physical or emotional symptoms that bothered you.
  If correct, skip to question #5.

Which of these symptoms or problems has bothered you the most this past week?

1. During the last week, how often have you experienced ________________?
   Rarely 1  A few times 2  Fairly often 3  Very often 4  Most of the time 5

2. During the last week, on average, how severe has ________________ been?
   1. Very mild 1  Mild 2  Moderate 3  Severe 4  Very severe 5

3. During the last week, how much has ________________ interfered with your ability to enjoy your life?
   Not at all 1  A little bit 2  A moderate amount 3  Quite a bit 4  Completely 5

4. How worried are you about ________________ occurring in the future?
   Not at all 1  A little bit 2  A moderate amount 3  Quite a bit 4  Completely 5

5. In general, how important are your PHYSICAL SYMPTOMS OR PROBLEMS to your overall quality of life?
   Not at all 1  A little bit 2  A moderate amount 3  Quite a bit 4  Completely 5

Below is a list of statements that other people with a serious illness have said may be important. Please tell me how true each statement is for you.
6. Although I cannot control certain aspects of my illness, I have a sense of control about my treatment decisions.

   Not at all    A little bit    A moderate amount    Quite a bit    Completely
   1             2                   3                   4               5

7. I participate as much as I want in the decisions about my care.

   Not at all    A little bit    A moderate amount    Quite a bit    Completely
   1             2                   3                   4               5

8. Beyond my illness, my doctor has a sense of who I am as a person.

   Not at all    A little bit    A moderate amount    Quite a bit    Completely
   1             2                   3                   4               5

9. In general, I know what to expect about the course of my illness.

   Not at all    A little bit    A moderate amount    Quite a bit    Completely
   1             2                   3                   4               5

10. As my illness progresses, I know where to go to get answers to my questions.

    Not at all    A little bit    A moderate amount    Quite a bit    Completely
    1             2                   3                   4               5

11. In general, how important is feeling like an ACTIVE PARTICIPANT in your HEALTH CARE to your overall quality of life?

    Not at all    A little bit    A moderate amount    Quite a bit    Completely
    1             2                   3                   4               5

12. I worry that my family is not prepared to cope with the future.

    Not at all    A little bit    A moderate amount    Quite a bit    Completely
    1             2                   3                   4               5

13. I have regrets about the way I have lived my life.
14. At times, I worry that I will be a burden to my family.

15. Thoughts of dying frighten me.

16. I worry about the financial strain caused by my illness.

17. In general, how important are CONCERNS ABOUT THE FUTURE to your overall quality of life?

18. I have been able to say important things to those close to me.

19. I make a positive difference in the lives of others.

20. I have been able to help others through time together, gifts, or wisdom.
21. I have been able to share important things with my family.

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22. Despite my illness, I have a sense of meaning in my life.

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23. I feel at peace.

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24. There is someone in my life with whom I can share my deepest thoughts.

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25. In general, how important is the feeling that your LIFE IS COMPLETE to your overall quality of life?

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26. How would you rate your OVERALL QUALITY OF LIFE?

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<th>Very Poor</th>
<th>Poor</th>
<th>Fair</th>
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