Randomized Trial of Patient-Reported Outcome Measurement in Heart Failure Clinic (PRO-HF Trial)

Version 5

June 30, 2023

CLINICAL TRIAL SUMMARY

Title	Randomized Trial of Patient-Reported Outcome Measurement in Heart Failure Clinic
Study Objectives	Primary objective is to evaluate the impact of routine assessment of patient-reported heath status among outpatients with heart failure on heart failure health status one year later. Secondary objectives include evaluating the following: - Changes in heart failure therapy patterns - Changes in healthcare utilization (testing, clinic visits, acute care visits) - Patient experience - Concordance between clinician and patient perception of patient health status
Study Design	This randomized clinical trial evaluates the routine assessment of patient-reported heath status, using the Kansas City Cardiomyopathy Questionnaire-12 (KCCQ-12) among adult outpatients with heart failure. Any patients being seen in the heart failure clinics are eligible for enrollment. Patients will be enrolled via secure email or telephone call. They will be randomized in a 1:1 fashion to KCCQ-12 assessment or usual care with permuted block randomization stratified by clinician. Participants randomized to KCCQ-12 assessment will complete the KCCQ-12 at every heart failure clinic visit. Their results will be available to clinicians to assist with clinical management. Heath status surveys will not be integrated into clinical care for patients in the usual care arm. In a subset of the total study, we will compare clinician perception of patient health status and patient experience across the two arms.
Number of Participants	Minimum of 1,200 participants will be randomized; 600 patients in sub-study
Trial Location	Stanford Hospital & Clinics adult heart failure clinic
Inclusion Criteria	Adult heart failure clinic visit
Exclusion Criteria	None
Intervention	Participants randomized to KCCQ assessment will complete a KCCQ-12 survey with each heart failure clinic visit. These responses will be shared with their heart failure clinician. Treating clinicians will continue to make all diagnostic and treatment decisions at their discretions.

Primary Endpoint	KCCQ-12 score at least 1 year post-randomization
Secondary Endpoints	Treatment patterns at 12 months: • Rates of guideline-directed therapy use • Dose of guideline-directed medical therapy • Advanced heart failure therapy evaluation • Cardiovascular testing Healthcare resource use at 12 months: • Heart failure clinic visits (in-person and televisits) • Heart failure telephone encounters (other than visits) • Emergency department visits • Hospitalizations (heart failure and non-heart failure)
Other Outcomes of Interest in Sub-Study	• Clinician perception of health status • Patient experience
Assessment Schedule	• Baseline KCCQ-12 at time of first clinic visit • Repeat KCCQ-12 within 12-15 months post-randomization *Sub-study:* • Patient experience survey • Clinician evaluation of patient health status
Study Duration	Patients will be enrolled for 12 months. Expected follow-up will be 12-15 months post-randomization. Patients will be followed until their first clinic visit after one year. Patients without a follow-up visit within 15 months, will be contacted for final outcome ascertainment at that time.
Statistical Considerations	A sample size of 1,200 randomized participants has 95% power to detect a mean difference in KCCQ-12 of 5 between arms (72 in KCCQ arm versus 67 in usual care; SD ~24) and an 80% power to detect a mean difference in KCCQ-12 of 4 without covariate adjustment.

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1. LIST OF ABBREVIATIONS AND DEFINITIONS

EHR	Electronic health record
KCCQ-12	Kansas City Cardiomyopathy Questionnaire-12
PHI	Protected health information
PRO	Patient-reported outcome
STARR	Stanford Research Repository

2. BACKGROUND AND RATIONALE

Patient-reported outcome (PRO) measures are being increasingly emphasized by quality measurement programs and healthcare payers. The Centers for Medicare & Medicaid Services now include the measurement of patient-reported health status as a quality measure. While these measures capture patient symptoms accurately and have been shown to be highly prognostic, the feasibility and impact of PRO assessment among heart failure patients is unknown. There are no prior studies evaluating the effect of collecting this data on patient experience or quality of care. This study aims to fill those gaps.

Understanding the effect of PRO assessment on patient outcomes will determine the overall utility of the data collection. Although PRO assessment is low-cost and low-risk for a given patient, a systematic collection of PRO data and reporting is costly and shifts resources away from other potentially important interventions. There is currently a large gap in the evidence whether routine assessment of heart failure PROs improves clinical care. Determining whether PRO collection improves health-related quality of life or increases the use of guideline-recommended therapies will fill this gap. This knowledge will help weigh the benefits and costs of integrating PRO collection into clinical practice. Finding that PRO assessment leads to a significant improvement in quality of life will promote broader adoption of PRO assessment in clinical care. This could lead to an important reduction in the morbidity and mortality of heart failure. Finally, the trial will provide critical preliminary data for a multicenter trial that will verify these findings in a larger, broader sample.

3. HYPOTHESIS

Routinely assessing heart failure health status during outpatient clinic visits leads to differences in treatment patterns and better health status at one year.

4. STUDY OBJECTIVES

PRIMARY AIM

The primary aim of this study is to estimate the impact on heart failure health status in 1 year among outpatients with heart failure who are randomized to routine KCCQ-12 assessment vs. usual care.

SECONDARY AIMS

The secondary aims of this trial are to compare the following outcomes at 1 year in participants randomized to KCCQ-12 or usual care:

- Rates of guideline-directed therapy use
- Dose of guideline-directed medical therapy
- Advanced heart failure therapy evaluation
- Cardiovascular testing
- Heart failure clinic visits (in-person and televisits)
- Heart failure telephone encounters (other than visits)
- Emergency department visits
- Hospitalizations (heart failure and non-heart failure)

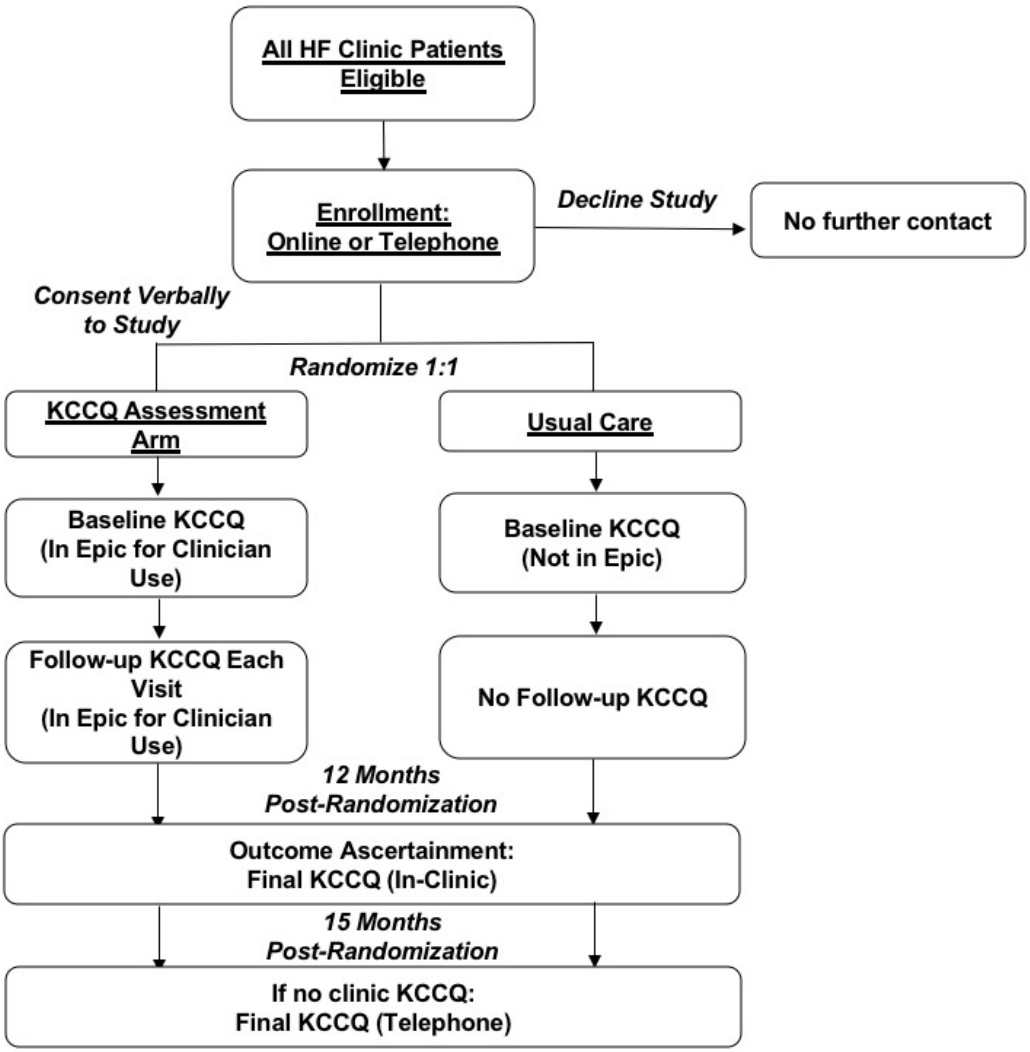
Additional aims include comparing the following outcomes between participants randomized to KCCQ-12 or usual care:

- Patient experience
- Clinician perception of patients' heart failure heath status

5. STUDY DESIGN

This randomized trial will prospectively evaluate the effectiveness of patient-reported health status assessment among patients with heart failure seen in the Stanford Heart Failure Clinic. Any adult patients with heart failure who have a clinic visit during the 6-month enrollment period will be potentially enrolled. Before the appointment, patients will be contacted via either secure email or via telephone. Patients who consent will undergo stratified permuted block randomization to routine KCCQ assessment or usual care with stratification by treating clinician. Patients randomized to KCCQ assessment will undergo KCCQ-12 assessment at each clinic visit. The results of these assessments will be available in Epic to the clinical heart failure team. Those randomized to usual care will only undergo KCCQ-12 assessment at baseline and again at the conclusion of the study. For usual care patients, the baseline KCCQ-12 will not be displayed on Epic.

5.1 Study Flow



5.2 Study Population

Patients with an outpatient visit in Stanford adult heart failure clinic.

5.3 Inclusion/Exclusion Criteria

5.3.1 Inclusion

- Clinic visit in Stanford adult heart failure clinic
    - In-person
    - Telehealth

5.3.2 Exclusion

Patients may be excluded at the discretion of their treating cardiologist if already enrolled in an alternate clinical trial. There are no other clinical exclusions.

6. STUDY PROCEDURES

6.1 Clinic Training

Before trial enrollment, all heart failure clinic staff will receive educational material regarding patient-reported health status and the KCCQ-12. These materials will summarize data regarding the survey, its interpretation, and prognostic significance. Examples of how patient-reported health status has impacted disease management in other health conditions will also be included. The information will also be presented during an interactive educational session with heart failure clinicians and clinic staff.

6.1 Screening

All patients with a clinic visit in adult heart failure are eligible for the study. Heart failure clinicians have agreed to enroll any of their patients. Select patients may be excluded due to enrollment in alternate clinical trials.

6.2 Enrollment and Enrollment

Patients with a heart failure clinic appointment during the 6-month enrollment period will be contacted regarding potential enrollment approximately one week before their visit via secure email. The email will include information regarding the study and consent. There will also be contact information for additional information. Patients who consent will be randomized to KCCQ assessment or usual care. Patients who decline enrollment will receive no further contact from the study team.

Patients without an email response (confirming or declining participation) will be contacted via postal letter approximately two weeks before their clinic visit with information about the study and the opportunity to either enroll in the trial or decline further communication. Patients who neither decline or enroll will be contacted by telephone a few days before the visit. They have the ability to consent or decline further communication during the telephone encounter. Individuals who do not respond via telephone may also be contacted via text message.

We aim to enroll at least 1,200 patients over the 6 month enrollment period. If we enroll 1,200 patients prior to 6 months, we will still complete the 6-month enrollment period with a potential enrollment exceeding 1,200 patients given the minimal-risk nature of the study and ability to provide more precise effect estimates. If the trial fails to enroll 1,200 patients by 6 months, we will discuss reducing the trial enrollment versus extending enrollment with the IRB and the National Institute of Health (the trial sponsor).

6.3 Randomization

We will randomize patients using a secure online randomization module on REDCap. Randomization will be stratified by treating clinician with a block sizes of 2 and 4. Randomization occurs automatically via the online platform after a patient consents. Following randomization, the patient either receives the usual care KCCQ survey via REDCap or notification of an upcoming KCCQ survey via MyHealth for those in the KCCQ arm.

6.4 KCCQ-12 Completion: KCCQ Assessment Arm

6.4.1 Index Visit

For the KCCQ assessment arm, the KCCQ-12 will be collected before each heart failure clinic visit (in person and tele-visit). For patients who consent online, the KCCQ-12 will be available for online completion. For patients who do not complete the survey pre-visit, the survey can be completed during check-in. Patients who did not complete their assigned KCCQ-12 survey before the visit will be able to use their personal device or an office computer to complete the survey.

For patients who are consented via telephone, patients will be given the option of completing the survey during the call or via the online site. If completed over the phone, survey responses will be entered directly into the online database without any additional paper records.

6.4.2 Follow-up Visits

Patients in the KCCQ-12 assessment arm will complete the questionnaire prior to each follow-up clinic visit. They will be automatically messaged regarding questionnaire completion via Epic MyHealth message. Those who do not complete the questionnaire in advance will be able to complete it during check-in as described above. Patients can voluntarily select to not complete the questionnaire at any time.

6.4.3 Clinician Accessibility of KCCQ-12 Data

The KCCQ-12 is either entered by patients onto MyHealth app that is linked to Epic or by a research team member during a telephone call. For patients in the KCCQ arm, the KCCQ-12 will be printed out for clinicians at the time of the visit. The KCCQ-12 results, in addition to prior results, are also available in Epic. However, clinicians will not need to access the results or use them in any way if they select not to.

6.4 KCCQ-12 Completion: Usual Care

6.4.1 Index Visit

Patients in usual care will undergo baseline assessment of KCCQ-12. This data will be used to understand the change in KCCQ-12 between arms at follow-up. The data will be captured in the same way as the KCCQ arm using a secure website, REDCap. This data will not be available on Epic.

Patients who have not completed the KCCQ-12 questionnaire before their clinic visit will receive an email to notify them to complete the questionnaire. If they have received the notification email and the questionnaire remains unanswered, the participant will receive a phone call from the study team to help them complete the KCCQ-12.

6.4.2 Follow-up Visits

Patients in the usual care are will not be assigned any KCCQ-12 surveys during the 12-month follow-up period after their first clinic visit.

6.5 KCCQ-12 Assessment at Trial Completion

This study will compare KCCQ-12 across trial arms at least one year after randomization. All patients with clinic visits between 12-15 months after their initial visit will be assigned the KCCQ-12. The data will be collected similar to the manner described above. Patients will be messaged regarding KCCQ-12 completion one week before their clinic visit. Patients who do not complete the

KCCQ-12 will be able to complete the survey in clinic during the check-in process. Patients who do not complete the survey within 15 months (either due to not having a clinic visit between 12-15 months or not completing the survey in clinic) will be contacted via telephone to complete the survey. Among patients without clinic visits, we will ask additional questions regarding their medications and other heart failure therapies.

6.6 Sub-study: Clinic Experience Surveys

Approximately 600-patient subset will also be enrolled in a sub-study. This will involve one brief survey, conducted either in-person, via telephone or online, regarding their overall experience during clinic.

The substudy participants will be selected based on the month of enrollment. Three of the six enrollment months will automatically enroll patients in the substudy. After each clinic visit during the sub-study months, participants will receive an email notification to complete their Clinic Experience Survey if they have not already completed the survey in-person. They will receive a subsequent phone call following the email if the survey remains incomplete.

6.7 Sub-study: Clinician Perception of Health Status

A related sub-study will ask clinicians regarding their perception of patient health status. All heart failure clinicians will undergo informed consent and enrollment. Clinicians who are caring for the 600-patient sample described above (section 6.6) will be asked a brief set of questions regarding their perception of their patient's health status. Each treating clinician will also be consented given their involvement in the sub-study.

6.8 **Data Storage**

For the KCCQ assessment arm, the KCCQ-12 responses will be stored in REDCap, a secure research database. For patient responses collected via telephone, those responses will be transcribed directly to the database. At the end of the study, all trial data will be stored on a secure hospital server (Stanford Medicine Box) that is HIPAA-compliant and approved for patient-level data including personalized health information and personally identifiable information. Patient identifiable information and personalized health information, however, will not be stored. Each patient will be given a non-identifiable study code, and all dates will be coded based on an index date.

7. TREATMENT ARMS

7.1 KCCQ Assessment

Participants randomized to KCCQ assessment will complete the KCCQ-12 each clinic visit. Their results will be made visible to their treating clinician in Epic. The treating clinicians will be able to incorporate these results in their assessment as they see fit.

7.2 Usual Care

Patients in usual care will only undergo KCCQ assessment at the start of the trial and one-year follow-up. Their results will not be made visible to their treating clinicians. Their treating clinicians can continue to assess their quality of life and health status via clinical interview, which is the current standard of care.

8. STUDY ASSESSMENTS AND SCHEDULE

8.1 Baseline Clinical Eligibility

Any patients with a clinic visit scheduled for Stanford's adult heart failure clinic will be eligible. Eligibility will be based on the clinic schedule.

8.2 Surveys

8.2.1 KCCQ-12

The KCCQ assessment is described in detail above in Section 6.4. The KCCQ-12 is shown in Appendix A.

8.2.2 Clinic Experience Survey

The clinic experience survey will be distributed to patients in the sub-study following their first heart failure clinic visit post-randomization. The survey will be emailed to patients. Patients who do not complete the survey online will be contacted via telephone. The clinic experience survey is shown in Appendix B.

8.2.3 Clinician Perception of Health Status

The clinician perception of health status survey will be completed by the treating clinician for each patient in the sub-study following their first heart failure clinic visit post-randomization. The survey will be distributed on paper but also be available online. The clinician perception of health status survey is shown in Appendix C.

8.3 Other Baseline Clinical Data

Baseline clinical values of the following will be extracted from the EHR using structured data elements:

- Demographic characteristics (age, sex, race, ZIP)
- Vital signs, average over prior 3 months
    - Systolic/diastolic blood pressure over previous 3 months
    - Heart rate over previous 3 months
    - Respiratory rate
    - Oxygen saturation
- Most recent BMI
- Comorbidities using diagnosis coding
    - Diabetes mellitus
    - Hypertension

    - Hyperlipidemia
    - Chronic kidney disease
    - Cerebrovascular disease
    - Liver disease
    - Atherosclerotic cardiovascular disease
    - Peripheral vascular disease
    - Chronic lung disease
    - Major psychiatric disease
    - Cognitive dysfunction
    - Smoking status
    - Cancer
- Prior procedures
    - Implantable cardiac defibrillator
    - Cardiac resynchronization therapy
    - Valve repair/replacement
    - Coronary artery bypass surgery
    - Percutaneous coronary intervention
    - Right heart catheterization
- Lab Results
    - NT-Brain natriuretic peptide
    - Creatinine
    - Hemoglobin
    - Hemoglobin A1c
    - White blood count
    - Blood urea nitrogen
- Echocardiography results
    - Left ventricular ejection fraction
    - Right ventricular systolic pressure
    - Left ventricular internal diameter during diastole
    - Right ventricular systolic function, qualitative
    - Left atrial volume
    - Average E/e’
    - Mitral regurgitation, qualitative
    - Tricuspid regurgitation, qualitative
    - Tricuspid regurgitation peak velocity
    - Estimated right ventricular systolic pressure
    - Left ventricle posterior wall thickness
    - Left ventricle septal thickness
- Medications (specific drug and dose)
    - Beta-blocker
    - Angiotensin-converting enzyme inhibitor

    - Angiotensin receptor blocker
    - Angiotensin-receptor neprilysin inhibitor
    - Sodium-glucose co-transporter 2 inhibitor
    - Mineralocorticoid antagonist
    - Long-acting nitrates
    - Hydralazine
    - Loop diuretics
    - Other diuretics
    - Digoxin
    - Statin
    - Aspirin
    - Other antiarrhythmic agents
    - Other blood pressure medications
    - NSAIDs
    - Bronchodilators
    - Inhaled steroids
    - Oral steroids
- Prior Stanford Cardiology Clinic (specific to the affiliated clinician's clinic)
    - Date of last clinic visit
    - Number of clinic visits since 2018
- Other Healthcare utilization
    - Number of total Stanford clinic visits since 2018 (tele-health and in-person)
    - Prior cardiovascular diagnostic tests
        - Electrocardiogram
        - Echocardiogram
        - Stress test
        - CT Coronary Angiogram
        - Invasive coronary angiography)
    - Number of health system ED visits since 2018
        - Heart failure related
        - Non-heart failure related
    - Number of health system hospitalizations since 2018
        - Heart failure related
        - Non-heart failure related

8.4 Endpoint Assessments

Primary and secondary endpoints will be assessed using direct assessment (KCCQ-12 assessment) or EHR structured data elements. The following will be assessed between 12-18 months post-randomization:

- KCCQ-12
- Medications, as listed above

- Procedures, as listed above in addition to the following:
    - Left ventricular assist device
    - Cardiac transplant
- Transplant or LVAD workup initiation
- Hospitalizations
    - Heart-failure
    - Non-heart failure
- ED Visits
    - Heart-failure
    - Non-heart failure
- Clinic Visits
    - Heart failure clinic (tele-visit and in-person)
    - Non heart failure
- Telephone Encounters
    - Heart failure clinic
- Referrals
    - Palliative medicine
    - Psychiatry
    - Other referrals

9. STATISTICAL CONSIDERATIONS AND ANALYSIS PLAN

9.1 Primary Analysis and Statistical Power

The primary effectiveness outcome is the difference in KCCQ-12 overall summary score after one year of follow-up. Scores will be compared using mixed effects linear regression with adjustment for baseline KCCQ-12 score and a random intercept for the treating clinician. The primary analysis will be limited to patients with follow-up scores. Baseline covariate adjustment can substantially improve the precision of the statistical estimate. This has been previously shown to improve statistical power even in randomized trials with baseline covariate balance (as modeled below in the statistical power analysis).[1-3] The covariate used for adjustment of the primary analysis (baseline KCCQ) has been selected due to the moderate association with follow-up health status. As a secondary analysis, we will repeat the analysis with adjustment for other baseline characteristics (age and left ventricular ejection fraction) that have also been previously shown to be associated with health status.[4-6] As an additional secondary analysis, the unadjusted KCCQ-12 scores will be compared using a two-sample t-test.

Prior work has suggested a 6 point increase in the KCCQ represents a small improvement and 11 a moderate improvement, with a standard deviation of 24.[7-9] However, these estimates represent a significant change for an individual. A smaller mean change across a population may be clinically meaningful. The sample size calculations are based on prior Stanford Heart Failure clinic data. Prior studies of populations with heart failure have found an average KCCQ score of approximately 67. With 1,200 patients, with 20% loss to follow-up, we estimate a 97% power to detect a difference of 6, a 90% power of a mean difference of 5 in the KCCQ-12, and 73% power for a mean difference of 4 in the KCCQ-12.

As discussed above, the statistical power should be amplified with baseline covariate adjustment. We assumed baseline KCCQ-12 would explain approximately 35% of the variance in the final KCCQ-12. With baseline adjustment, we estimate approximately 55% power for a mean difference of 3 in the KCCQ-12 and 81% power for a mean difference of 4. This was estimated by simulating trial results.

Multiple sensitivity analyses to account for missing data will be conducted. First, potential assumptions around mortality will be explored. The primary analysis assumes the collection of KCCQ-12 data is independent of mortality over a 1-year follow-up. If KCCQ-12 assessment is associated with a reduction in mortality, the primary analysis will underestimate the effect of KCCQ assessment on health status. If KCCQ-12 assessment is associated with increased mortality, it will overestimate the effect of KCCQ assessment. In a secondary analysis, a KCCQ-12 score of 0 will be used for all patients who die during follow-up. This secondary analysis will test if the primary findings are consistent after placing a negative weight on mortality. Second, sensitivity analyses will account for living patients with missing data. This is important given loss to follow-up may be differential between treatment arms. This will be addressed with two different imputation techniques. The first will predict follow-up KCCQ-12 score using observed patient characteristics (including baseline KCCQ) via multiple imputation. This assumes the data is missing at random. The second approach conservatively assumes patients with missing data have worse outcomes by using the minimum observed KCCQ-12 value in the trial. These sensitivity analyses will assess the robustness of the findings.

As secondary analyses, we will compare domain scores (physical limitation, social limitation, quality of life) and the clinical summary score across arms. For these models, we will adjust for baseline domain score and include random intercepts for the treating clinician.

9.2 Primary Analysis Subgroup Analyses

We will evaluate the primary effectiveness outcome across multiple subgroups. We identified these subgroups as having potential heterogeneity of treatment effect based on likely differences in symptom reporting or treatment patterns:

- Age
- Sex
- Left ventricular ejection fraction
- Charlson comorbidity index (marker of disease comorbidity)
- Baseline KCCQ-12 score
- Prior heart failure/cardiomyopathy diagnosis
- Baseline use of recommended therapies

Each of the continuous covariates will be analyzed by modeling the interaction between the continuous covariate and the randomization allocation (KCCQ assessment) along with stratification at the median value. Binary characteristics (e.g. sex) will also be interacted with the randomization allocation.

We will also evaluate the primary analysis among the subgroup with a history of heart failure/cardiomyopathy and a baseline KCCQ-12 score of <100.

Secondary Outcomes

Secondary outcomes will include evaluating the effect of KCCQ assessment on heart failure therapy use and healthcare resource utilization. Details regarding each outcomes are listed above in the “Study Outcomes” section. Each secondary outcome will be evaluated using multivariable regression with adjustment for prespecified patient characteristics: age, left ventricular ejection fraction, baseline therapy/utilization, and Charlson Comorbidity Index. A standard regression model will be selected based on the distribution of the outcome. Therapy use (a binary outcome) will be evaluated using multivariable logistic regression. Therapy doses (ordinal outcome) will be evaluated using an ordinal regression model (including no therapy as the base category). The number of medication changes each visit (a count outcome with a high frequency of no medication changes) will be evaluated using a zero-inflated negative binomial model. Hospitalizations and telephone encounters will also be evaluated using a zero-inflated negative binomial model. Clinic visits (count outcomes without a high frequency of zero events) will be evaluated using a standard negative binomial model. For each model, an indicator variable for allocation to the KCCQ assessment arm will be included. The coefficient on this variable represents the effect of PRO collection. Each model will be adjusted for the baseline rate (e.g. hospitalizations or telephone encounters in the prior year) or baseline treatment (e.g. baseline therapies and doses) to improve model precision. Each of the secondary outcomes will be analyzed for the subgroup with a history of heart failure/cardiomyopathy and a baseline KCCQ-12 score of <100. For secondary outcomes of treatment intensity (clinic visits, therapy rates, and testing), we will also evaluate if the association between baseline KCCQ-12 and the secondary outcome is significantly larger in the KCCQ arm than the usual care arm.

9.3 Sub-Study Analyses

9.3.1 Clinic Experience

Clinic experience will be compared across the two arms of the study. Each question will receive an ordinal score from worst to best response. For each question, the score across trial arms will be compared using an mixed effects ordinal logistic regression model with a random intercept for the

treating clinician. We will perform subgroup analyses based on patient characteristics as described above for the primary analysis.

9.3.2 Concordance Between Clinician and Patient Perception of Health Status

We will compare the concordance of health status assessment between patients and their treating clinician across the two arms. First, we will evaluate the proportion of explained variation of KCCQ-OSS via the clinician's NYHA score in each arm using linear regression.

Second, we will define concordance by linking the ordinal responses in the clinician survey to ordinal responses in the KCCQ-12 or the patient experience survey.

For question 1 of the clinician survey (NYHA Class), we will approximate patient estimation of NYHA category using their KCCQ-OSS score: KCCQ-OSS ≥80 – NYHA Class I, ≥60 to < 80 – NYHA Class II, ≥30 to <60 – NYHA Class III, and <30 – NYHA Class IV.

Question 2 of the clinician survey (quality of life) will be linked to the quality of life domain score. We will classify the response "none" as equivalent to a domain score>80, "mildly" as a score of ≥60 to <80, "moderately" as a score of ≥30 to <60 and <30 as "severely."

Question 3 of the clinician survey evaluates symptom frequency of edema, dyspnea, orthopnea, and fatigue on a 4-point ordinal scale with a 5th option of "I don't know." The following is the mapping between the KCCQ-12 responses and the clinician survey:

Edema	KCCQ	Never over past 2 weeks	Less than once per week	1-2 times per week	3 or more times per week but not every day	Every morning		
	Clinician Perception	None	Once	More than once, but not daily	More than once, but not daily	Daily		
Fatigue	KCCQ	Never over past 2 weeks	Less than once per week	1-2 times per week	3 or more times per week but not every day	At least once per day	Several times per day	All the time
	Clinician Perception	None	Once	More than once, but not daily	More than once, but not daily	Daily	Daily	Daily
Shortness of breath	KCCQ	Never over past 2 weeks	Less than once per week	1-2 times per week	3 or more times per week but not every day	At least once per day	Several times per day	All the time
	Clinician Perception	None	Once	More than once, but not daily	More than once, but not daily	Daily	Daily	Daily
Orthopnea	KCCQ	Never over past 2 weeks	Less than once per week	1-2 times per week	3 or more times per week but	Every night		

				not every day	
Clinician Perception	None	Once	More than once, but not daily	More than once, but not daily	Daily

Questions 4 and 5 in the clinician survey will be mapped directly to questions 10 and 9 in the patient experience surveys.

Questions 1-4 have ordinal responses with linked questions as described above. For these questions, we will classify concordance as “concordant” if the categories match, “neither concordant or discordant” if the response categories differ by 1, and “discordant” if the response categories differ by >1. For question 5, we will classify as concordant or discordant. We will compare concordance between arms for each of these questions using mixed effects ordinal logistic regression with random intercepts for the treating clinician.

10. DATA HANDLING AND RECORD KEEPING

10.1 Electronic Data Capture (EDC) System

EHR data will be extracted via the STARR registry and kept on the REDCap system. After data extraction, patients will be de-identified and labeled with a study ID number. Linkage between the medical record number and study ID will be kept separately as a locked file and only be available to the data analyst.

10.2 Data Confidentiality and Security

Computerized data will be accessible only by password. The Stanford University computer network is protected by a firewall. Participants will be identified by study number only, to ensure participant anonymity. No participant identifiers will be used in the presentation of data. Study records that might identify participants will be kept confidential as required by law. Except when required by law, participants will not be identified by name, personal identification number (e.g. social security number, social insurance number), address, telephone number, or any other direct personal identifier in study records.

10.3 Training

All investigational site staff authorized to enter the study data will receive training on the EDC system.

10.4 Records Retention

Study records will be maintained by the site investigators for a period of six (6) years following the expiration of the grant or length of time as required by local regulations, whichever is longer.

11. DATA AND SAFETY

11.1 OVERALL PLAN

As per NHLBI requirements, there is a data and safety monitoring plan commensurate with the risk of the trial, The planned study is minimal risk and non-blinded given the intervention solely consists on an additional patient survey of health status at the time of clinic visits. The heart failure clinician will continue to make all treatment decisions.

The data and safety monitoring plan will screen for any concerns, unanticipated problems, or adverse events related to KCCQ assessment. Both heart failure clinic staff and enrolled patients will be given contact information for the study team to report concerns related to assessment.

The independent safety monitors will be Kelsey Flint, MD, Assistant Professor (Cardiovascular Medicine) at University of Colorado and Dr. Lee Chang at Swedish Hospital in Seattle, Washington. Dr. Flint is an advanced heart failure specialist. She is also a health services researcher with experience evaluating heart failure health status. Dr. Chang is also an advanced heart failure specialist with experience in clinical research. He also has detailed experience with the Stanford cardiology clinics, having completed his cardiology fellowship at Stanford. They will review issues raised by clinic staff or heart failure patients as they arise and will advise the research study team regarding the need to adjust the collection protocol or terminate the study prematurely.

Adverse events or serious adverse events related to KCCQ assessment are very unlikely. Potential adverse events detected by heart failure clinic staff or patients will be reported to the study principal investigator on a continuous basis. Potential adverse events will also be reported to the Stanford University IRB committee and the NIH Program Officer. As a second step, the PI, IRB committees, and the independent safety monitors will review adverse events to evaluate if the events were caused by the intervention.

12. PROTOCOL AMENDMENTS

12.1 Protocol Amendments

Any change or addition to the protocol can only be made in a written protocol amendment that must be approved by the IRB. Notwithstanding the need for approval of formal protocol amendments, the investigator is expected to take any immediate action required for the safety of any participant included in this study, even if this action represents a deviation from the protocol. In such cases, the IRB will be informed.

13. REFERENCES

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Appendices

Appendix A: Kansas City Cardiomyopathy Questionnaire-12

Kansas City Cardiomyopathy Questionnaire (KCCQ-12)

The following questions refer to your **heart failure** and how it may affect your life. Please read and complete the following questions. There are no right or wrong answers. Please mark the answer that best applies to you.

1. **Heart failure** affects different people in different ways. Some feel shortness of breath while others feel fatigue. Please indicate how much you are limited by **heart failure** (shortness of breath or fatigue) in your ability to do the following activities over the past 2 weeks.

Activity	**Extremely** Limited	**Quite a bit** Limited	**Moderately** Limited	**Slightly** Limited	**Not at all** Limited	Limited for other reasons or did not do the activity
a. Showering/bathing	O	O	O	O	O	O
b. Walking 1 block on level ground	O	O	O	O	O	O
c. Hurrying or jogging (as if to catch a bus)	O	O	O	O	O	O
	1	2	3	4	5	6

2. Over the past 2 weeks, how many times did you have **swelling** in your feet, ankles or legs when you woke up in the morning?

Every morning	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
O	O	O	O	O
1	2	3	4	5

3. Over the past 2 weeks, on average, how many times has **fatigue** limited your ability to do what you wanted?

All of the time	Several times per day	At least once a day	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
O	O	O	O	O	O	O
1	2	3	4	5	6	7

4. Over the past 2 weeks, on average, how many times has **shortness of breath** limited your ability to do what you wanted?

All of the time	Several times per day	At least once a day	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
O	O	O	O	O	O	O
1	2	3	4	5	6	7

5. Over the past 2 weeks, on average, how many times have you been forced to sleep sitting up in a chair or with at least 3 pillows to prop you up because of **shortness of breath**?

Every night	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
O	O	O	O	O
1	2	3	4	5

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6. Over the past 2 weeks, how much has your **heart failure** limited your enjoyment of life?

It has **extremely** limited my enjoyment of life	It has limited my enjoyment of life **quite a bit**	It has **moderately** limited my enjoyment of life	It has **slightly** limited my enjoyment of life	It has **not limited** my enjoyment of life at all
O	O	O	O	O
1	2	3	4	5

7. If you had to spend the rest of your life with your **heart failure** the way it is right now, how would you feel about this?

Not at all satisfied	Mostly dissatisfied	Somewhat satisfied	Mostly satisfied	Completely satisfied
O	O	O	O	O
1	2	3	4	5

8. How much does your **heart failure** affect your lifestyle? Please indicate how your **heart failure** may have limited your participation in the following activities over the past 2 weeks.

Activity	**Severely** Limited	Limited **quite a bit**	**Moderately** limited	**Slightly** limited	**Did not** limit at all	Does not apply or did not do for other reasons
a. Hobbies, recreational activities	O	O	O	O	O	O
b. Working or doing household chores	O	O	O	O	O	O
c. Visiting family or friends out of your home	O	O	O	O	O	O
	1	2	3	4	5	6

Appendix B: Clinic Experience Survey

This survey is to evaluate your experience at your recent cardiology clinic visit. Using the 5-item scale below each question, please indicate how much you agree with the following statements by **marking the answer that best applies** to you :

1.) My clinician **listened to me** carefully:

O Completely agree	O Somewhat agree	O Neither agree nor disagree	O Somewhat disagree	O Completely disagree

2.) My clinician **understood symptoms** related to my heart:

O Completely agree	O Somewhat agree	O Neither agree nor disagree	O Somewhat disagree	O Completely disagree

3.) My clinician **showed respect** for what I had to say:

O Completely agree	O Somewhat agree	O Neither agree nor disagree	O Somewhat disagree	O Completely disagree

4.) My clinician and I **agreed on how I was doing overall**:

O Completely agree	O Somewhat agree	O Neither agree nor disagree	O Somewhat disagree	O Completely disagree

5.) My clinician **spent enough time** with me:

O Completely agree	O Somewhat agree	O Neither agree nor disagree	O Somewhat disagree	O Completely disagree

6.) My clinician explained things in a way that was easy to understand:

O Completely agree	O Somewhat agree	O Neither agree nor disagree	O Somewhat disagree	O Completely disagree

7.) I understand the **importance of taking the treatments** recommended by my clinician:

O Completely agree	O Somewhat agree	O Neither agree nor disagree	O Somewhat disagree	O Completely disagree

8.) My goals regarding treatment and those of my clinician are aligned:

O	O	O	O	O
Completely agree	Somewhat agree	Neither agree nor disagree	Somewhat disagree	Completely disagree

9.) What has the biggest impact on your quality of life?

O	O	O	O	O	O
Heart Failure	Other Cardiovascular Problems	Other Medical Problems	Heart Failure and Other Medical Problems Equally	Non-medical Reasons	None of the Above

10.) In terms of your overall quality of life, how do you expect your heart failure health status to change over the following year:

O	O	O	O	O
Significant Improvement	Mild Improvement	Remain Stable	Mild Worsening	Significant Worsening

Appendix C: Clinician Perception of Health Status Survey

You saw _____ in clinic today. We have five questions regarding your perception of their heart failure health status (please circle all answers).

1.) What is their current New York Heart Association functional class?

○	○	○	○
NYHA Class I	NYHA Class II	NYHA Class III	NYHA Class IV

2.) How much does heart failure impact their overall quality of life?

○	○	○	○
None	Mildly	Moderately	Severely

3.) How frequently did they have the following symptoms in the last two weeks?

Edema	○ None	○ Once	○ More than once, but not daily	○ Daily	○ I Don't Know
Orthopnea	○ None	○ Once	○ More than once, but not daily	○ Nightly	○ I Don't Know
Fatigue	○ None or once	○ More than once, less than daily	○ Daily	○ Frequently each day	○ I Don't Know
Shortness of breath	○ None or once	○ More than once, less than daily	○ Daily	○ Frequently each day	○ I Don't Know

4.) In terms of their overall quality of life, how do you expect their heart failure health status to change over the following year:

O	O	O	O	O
Significant Improvement	Mild Improvement	Remain Stable	Mild Worsening	Significant Worsening

5.) What has the biggest impact on your patient's quality of life?

O	O	O	O	O	O
Heart Failure	Other Cardiovascular Problems	Other Medical Problems	Heart Failure and Other Medical Problems Equally	Non-medical Reasons	None of the Above