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Study Title:	BETTER CARE - HF: Building Electronic Tools To Enhance and Reinforce CArdiovascular REcommendations – Heart Failure
NYULH Study Number:	S21-00644
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Statement of Compliance

This study will be conducted in accordance with the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46), any other applicable US government research regulations, and institutional research policies and procedures. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the sponsor and documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the study participants. All personnel involved in the conduct of this study have completed Human Subjects Protection Training.

Table of Contents

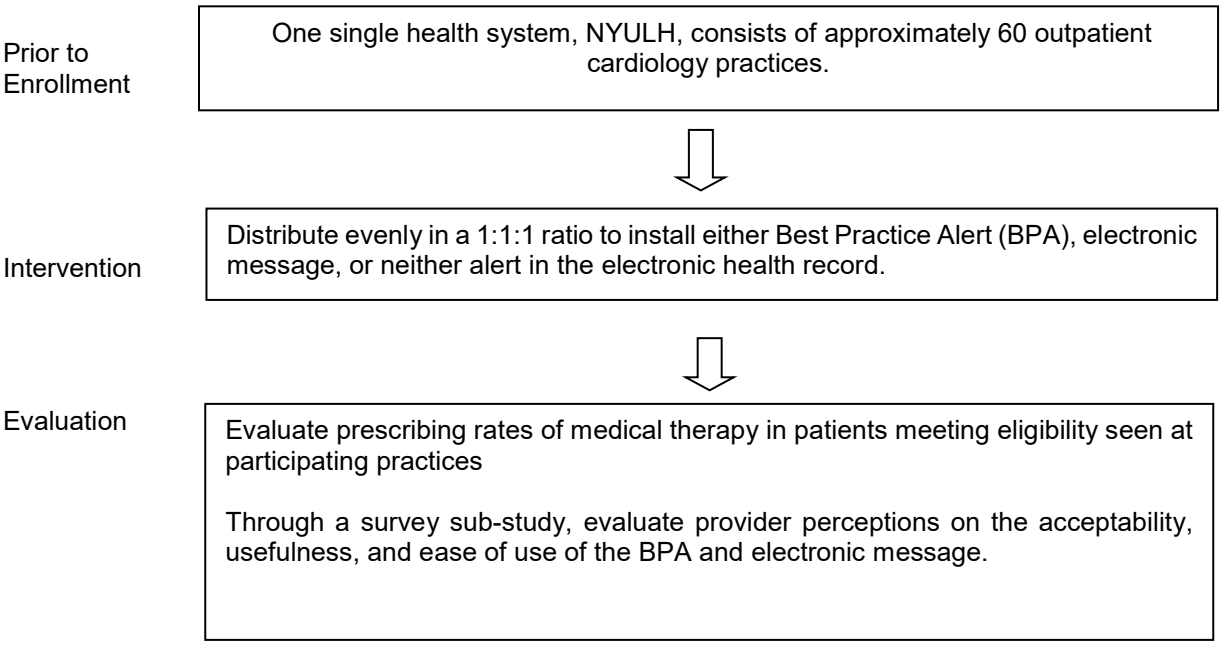
List of Abbreviations

ACE-I	Angiotensin converting enzyme-inhibitor
AE	Adverse event
ARB	Angiotensin receptor blocker
BB	Beta-blocker
BPA	Best Practice Alert
CFR	Code of Federal Regulations
CRF	Case Report Form
CSOC	Clinical Study Oversight Committee
DCC	Data Coordinating Center
DHHS	Department of Health and Human Services
EF	Ejection Fraction
EHR	Electronic Health Record
FFR	Federal Financial Report
FWA	Federalwide Assurance
HIPAA	Health Insurance Portability and Accountability Act
HFrEF	Heart Failure with Reduced Ejection Fraction
ICF	Informed Consent Form
IRB	Institutional Review Board
MOP	Manual of Procedures
MRA	Mineralocorticoid Receptor Antagonist
N	Number (typically refers to participants)
NIH	National Institutes of Health
NYULH	New York University Langone Health
OHRP	Office for Human Research Protections
OHSR	Office of Human Subjects Research
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event/Serious Adverse Experience
SOP	Standard Operating Procedure
US	United States

Protocol Summary

Title	BETTER CARE – HF: Building Electronic Tools To Enhance and Reinforce CArdiovascular REcommendations – Heart Failure
Short Title	BETTER CARE – HF: Building Electronic Tools To Enhance and Reinforce CArdiovascular REcommendations – Heart Failure
Brief Summary	This study will test two types of electronic health record (EHR)-based alerts to improve guideline-adherent care for patients with heart failure and reduced ejection fraction (HFrEF). Alerts will be triggered for patients with ejection fraction (EF) $\leq$ 40% who are not on guideline-recommended medical therapy. The two types of alerts tested will be a Best Practice Alert (BPA) and an electronic message.
Objectives	To test two types of EHR-based alerts that promote appropriate medical therapy for patients with HFrEF.
Methodology	Prospective cohort study
Endpoints	Primary endpoint: medication prescribing patterns Secondary endpoint: hospitalization and mortality
Study Duration	Eighteen months
Participant Duration	Eighteen months
Population	Patients with EF $\leq$ 40%
Study Sites	One single health system, NYULH, consists of approximately 60 outpatient cardiology practices.
Number of participants	Up to 2000 participants
Statistical Analysis	We will begin all analyses with descriptive summary statistics and graphical displays of all variables. Primary analyses will utilize McNemar's tests for medication prescriptions and patient outcomes of hospitalization and mortality. We will adjust for patient demographics and clinical characteristics, as well as provider-level characteristics, such as demographics, panel size, insurance mix, and sub-specialty training.

Schematic of Study Design



1 Introduction, Background Information and Scientific Rationale

1.1 Background Information and Relevant Literature

For patients with heart failure and reduced ejection fraction (HFrEF), the cornerstone of evidence-based care includes several medications that have been found to significantly reduce morbidity and mortality, which include: 1) mineralocorticoid antagonists (MRA), 2) angiotensin converting enzyme inhibitors, angiotensin receptor blockers, angiotensin receptor neprilysin inhibitors (ACE-I/ARB/ARNI), and 3) beta-blockers (BB). Current guidelines give these medications a class I recommendation,[1] and recently published performance measures[2] also strongly recommend these agents. However, despite their well-accepted benefits, several prior studies have revealed significant gaps in medical therapy for HFrEF patients.[3-5] Using number-needed-to-treat estimates based on data from randomized trials, these gaps in medical therapy account for an estimated 68,000 deaths per year nationwide, with the largest proportion being from lack of appropriate MRA therapy.[6]

In prior studies, successful interventions for improvement have often included multidisciplinary approaches with nurses, pharmacists, or other trained individuals.[7-9] However, the need for dedicated staff can be costly, and electronic health record (EHR)-based interventions could be a potential cost-effective solution. Prior studies assessing the efficacy of EHR-based interventions to improve medical therapy for HFrEF have mainly been conducted in the inpatient setting.[10-12] Inpatient algorithms may be limited as they reflect one instance in time. Additionally, acute hospitalization may restrict the ability to add multiple agents due to renal dysfunction or hypotension. Therefore, we propose the development of an outpatient EHR-based system to target patients with HFrEF who are not on the appropriate therapy.

Outpatient provider-facing EHR-based interventions could include best practice alerts (BPA) or electronic messages. While limited data exist for both types of interventions, some studies have observed significant improvements in health outcomes.[13-15] Potential adverse effects have also been described, such as increased alert frequency with BPAs[14] and physician burnout with electronic messages.[16] Given the potential for benefit and/or harm, it is imperative to study such interventions with rigor. Currently, no study directly compares different types of EHR-based alerts.

In this study, we aim to test a BPA and an electronic message for HFrEF patients who are not on guideline-recommended therapy. This work is significant because it aims to reduce gaps in medical therapy for HFrEF patients, which we hope will reduce mortality, decrease hospitalizations, and improve symptoms.

We will not be directly recruiting or enrolling patients. However, we will be monitoring patients for clinical outcomes using EHR data and are requesting a waiver of authorization and consent.

We will also conduct a survey to assess provider acceptability and perceived usefulness and ease of use of the BPA and electronic messages. This survey will be sent to the cardiologists at NYULH who received the BPA and electronic messages.

1.2 Rationale

This study aims to evaluate EHR-based alerts to improve adherence to guideline-recommended medical therapy among patients with HFrEF.

Understanding provider feedback on the BPA and electronic messages is necessary to understanding why these EHR tools may or may not work to improve care. For example, the BPA may be more effective at improving prescribing, and the surveys could help us understand if this was because cardiologists thought that they were easier to use. Moreover, there may be drawbacks, such as increased time needed during visits due to the BPAs or electronic messages. The only way to obtain this type of information is from the cardiologists at NYULH who received the BPAs and electronic messages, as they are the only ones who can comment on the acceptability, usefulness, and ease of use of the EHR tools.

1.3 Potential Risks & Benefits

1.3.1 Known Potential Risks

The risk is not greater than minimal risk (i.e., risk encountered in daily life or in the course of usual clinical practice). Individual case determinations of potential safety gaps will never be released to supervisors of any clinicians whose charts are being reviewed.

The principal risk of the study, as for any medical record review, is inadvertent release of confidential patient information. We will avoid such inadvertent disclosure by storing all identifiable information on a secure server and restricting access to the data to authorized study personnel.

For provider surveys, we expect the level of risk due to this study to be minimal. Potential risks to providers may include the following issues listed.

- Coercion/Undue Influence: The study will include NYULH employees. Participants may feel coerced or under pressure to participate in the survey or provide positive remarks about their work activities. Staff will be informed that participation is solely voluntary and has no bearing on their employment status or salary. Additionally, employee's will be informed that their decision to participate in the research study may not affect (favorably or unfavorably) performance evaluations, career advancement, or other employment-related decisions made by peers or supervisors.
- Discomfort: Participants may feel uncomfortable answering some of the study questions. They will be informed that they can refuse to answer any questions they wish. The information that we are retrieving is not sensitive in nature and we do not expect it to be of concern to the participant.

1.3.2 Known Potential Benefits

There may be benefit to individual patients for whom alerts may be triggered in this pilot study if their care is improved to comport with guidelines. The research will contribute critically to our knowledge of EHR-based alerts.

For the provider surveys, the information gained will put the effectiveness results into context (for example, help explain why one type worked better than another). Additionally, from an institutional quality improvement perspective, this will allow us to inform plans for next steps. The information gained from these surveys may also be beneficial to the providers themselves, as the feedback from this could impact next steps for the institution and future workflow within the EHR.

2 Objectives and Purpose

2.1 Primary Objective

The primary objective of the study is to evaluate EHR-based alerts to promote appropriate medical therapy for patients with HFrEF.

3 Study Design and Endpoints

3.1 Description of Study Design

NYU Langone Health has ambulatory care sites in the five boroughs of New York City (NYC) as well as in suburbs of New York and New Jersey. All have the NYU Epic EHR.

3.2 Intervention

The two types of EHR-based alerts include: 1) BPA and 2) electronic message.

Best Practice Alert (BPA) – BPAs are alerts that appear at the time of the visit, allowing for real-time intervention while the provider is with a patient, but also potentially interrupting provider workflow. The BPA appears at the beginning of a visit/encounter and includes 1) a tailored advisory, 2) educational link to guidelines, 3) medication information, 4) vital sign and pertinent lab results, and 5) options for next steps (i.e. ordering medication, providing reasons for not prescribing).

Electronic Message – Unlike the BPA, the electronic message is not necessarily seen at the time of the visit, and is more likely to be seen between visits. The electronic message is similar to the BPA in terms of information provided, but can include information on multiple patients in the same message, and overall prescribing metrics.

3.3 Study Endpoints

Outcomes measured at the prescription encounter level include whether there is a prescription for BB, ACE-I/ARB/ARNI, and/or MRA. Secondary patient outcomes include hospitalization, hospitalization for HF, and mortality.

3.4 Provider Surveys

We will conduct surveys of cardiology providers after the implementation of the EHR-based alerts across all NYULH Cardiology locations. The survey will aim to obtain further understanding of provider real-world experiences with, and perception of the clinical decision support tools. We will use a mix of likert-scale, multiple-choice, and open-ended questions to assess the alerts based on previously reported implementation science frameworks, specifically focusing on acceptability, usefulness, and ease of use of the two EHR-based alerts.

The goal for this survey is to obtain an overall assessment of the EHR-based alerts' usefulness as a long-term strategy for health system-wide quality improvement. Past evidence suggests that physicians dislike clinical decision support tools, believing they have minimal utility and result in general inefficiency, increased time required for care, and contribute to a sense of alert fatigue. We seek to determine whether these perceived downsides of EHR-based alerts were a factor in providers' impressions of the alerts used in this study. . The final survey is attached.

4 Study Population

4.1 Total Number of Participants and Sites

This is a single site study involving NYULH outpatient cardiology clinics serving a total of approximately 2000 participants.

4.2 Inclusion Criteria

- Patient with an encounter visit at NYULH cardiology practice during the study period
- Patient with EF $\leq$ 40% on most recent echocardiogram
- Patient ages 18-100

4.3 Exclusion Criteria

- Pregnancy
- Ventricular assist device
- In order to give providers time to add and up-titrate medications, we will exclude patients who had a newly reduced EF in the last 3 months.
- Medication-specific exclusion for MRA: most recent systolic blood pressure less than 105 mm Hg, most recent potassium < 5.1, any potassium > 5.5, most recent glomerular filtration rate < 30 (using MDRD equation), or a documented MRA allergy.

4.4 Vulnerable Subjects

No vulnerable patients will be enrolled.

For the survey, we will recruit NYULH cardiologists who received the BPAs or messages. The only way to obtain feedback on the BPAs and electronic messages is from the cardiologists at NYULH who received the BPAs and electronic messages, as they are the only ones who can comment on the acceptability, usefulness, and ease of use of these EHR tools. Cardiologists will be informed that their decision to participate or not, and their responses, will in no way affect their employment, salary, or performance evaluations and they will be reminded that they can stop participating whenever they want. Their information will be de-identified and completely anonymous. No identifiable PII or health information will be collected.

5 Strategies for Recruitment

Eligible patients from the chosen practice sites will be identified electronically within EPIC using an algorithm developed by the study team and NYULH's DataCore. This algorithm reviews patient records for EF $\leq$ 40% on most recent echocardiogram, and exclusion criteria listed above. Patients meeting eligibility will be automatically included, and all data collection will take place passively via the NYULH EHR system, EPIC. An EPIC reporting analyst will extract the relevant parameters from EPIC into a report. Patients from the selected practice sites will undergo their usual interactions with their providers and no study-specific activities will take place.

5.1 Duration of Study Participation

Patients' clinical outcomes will be monitored through EHR data for 18 months.

5.2 Participant Withdrawal or Termination

Not applicable as the subjects are recruited at the clinic level.

5.3 Provider Survey Recruitment

For the provider survey, we will recruit cardiologists who received the BPA or electronic message through emails (see attachment). They will be made aware that completing the survey is completely anonymous and will in no way impact their employment. The recruitment emails will be sent via listservs of cardiologist who received the BPAs and electronic messages. These listservs are specific for those cardiologists who received BPAs or electronic messages and the survey does not require cardiologists to self-select whether they received a BPA or a message. Only cardiologists who received a BPA or electronic message will be contacted. We will send an initial recruitment email and a subsequent follow up email.

The consent form will be attached to the email. It will also be available via link within the first question in Qaltrix. The first question in Qaltrix asks the provider to review the consent document and requires the provider to click a button stating that they are consenting to participate before being shown the remaining survey questions. If the provider does not click this button, they will not be able to move forward or complete the survey.

6 Study Schedule

Participants will be included in this study by virtue of meeting eligibility criteria and having a patient encounter during the study period. <u>There are no study-specific visits.</u> Any patient meeting criteria who has one or more patient encounters during the study period will be included. <u>Therefore, no study-specific visits are relevant for this study, so there is no schedule of visits.</u>

7 Study Procedures / Evaluations

There are no study-specific procedures that patients will undergo. They will receive care as usual by their outpatient providers. The EHR algorithm developed by the study team identifies eligible patients with EF ≤ 40% on most recent echocardiogram, and exclusion criteria listed above. The EHR algorithm will also capture information on demographics, diagnoses in the patient's problem list, prescription history, allergies, EF, and relevant lab results.

For patients meeting the eligibility criteria, a message in the EHR will automatically be sent to the provider. The provider will receive either a Best Practice Alert (BPA) or electronic message indicating that their heart failure patient is not on guideline-recommended therapy. The message will offer guidance for physician decision-making regarding HFrEF care. The study team presented the proposed project to the NYULH MCIT Project Portfolio Review Committee on February 11, 2021 and was approved to work with MCIT to build the electronic messages. Providers will be notified through the Weekly Epic Update and in presentations to medical directors that they may see the alert prior to the start of the study.

Patients' clinical outcomes will be monitored through EHR data collection for 18 months. Data collection will include elements of protected health information including patient name, medical record number, address zip code, and service dates. These will be necessary for data linkages and in order to track patients for receipt of intervention and clinical outcomes. All PHI data will be kept on a secure NYULH server and destroyed at the earliest possible point. Data on the patient's medication prescription, hospitalization, hospitalization for HF, and mortality will be recorded as study outcomes. The study team members will not collect this information directly; data will be collected in NYULH's EHR system, EPIC, and an EPIC Reporting analyst from DataCore will extract the relevant parameters from the EHR into a report.

Data points that will be collected for research purposes
Medication prescription
Hospitalization
Hospitalization for HF
Mortality
Name
Medical record number
Address zip code
Service dates

Provider survey data will be anonymously collected via Qaltrix. No identifiable information, PII, or health information will be collected. The URLs for the survey are below:

BPA version = https://nyumc.yul1.qualtrics.com/jfe/preview/previewId/f42fb1cb-b997-4fb8-8f60-9e311e6b6320/SV_7P3UhfvSH6KgpuK?Q_CHL=preview&Q_SurveyVersionID=current

IBM version = https://nyumc.yul1.qualtrics.com/jfe/preview/previewId/c97ab951-3feb-478a-8af8-a53e9abbe02d/SV_7PQoQunPLM8l8ZU?Q_CHL=preview&Q_SurveyVersionID=current

8 Safety and Adverse Events

8.1 Definitions

Unanticipated Problems Involving Risk to Subjects or Others
Any incident, experience, or outcome that meets all of the following criteria:

- Unexpected in nature, severity, or frequency (i.e., not described in study-related documents such as the IRB-approved protocol or consent form, the investigators brochure, etc)

- Related or possibly related to participation in the research (i.e., possibly related means there is a reasonable possibility that the incident experience, or outcome may have been caused by the procedures involved in the research)
- Suggests that the research places subjects or others at greater risk of harm (including physical, psychological, economic, or social harm).

Adverse Event
An ***adverse event*** (AE) is any symptom, sign, illness or experience that develops or worsens in severity during the course of the study. Intercurrent illnesses or injuries should be regarded as adverse events. Abnormal results of diagnostic procedures are considered to be adverse events if the abnormality:

- results in study withdrawal
- is associated with a serious adverse event
- is associated with clinical signs or symptoms
- leads to additional treatment or to further diagnostic tests
- is considered by the investigator to be of clinical significance

Serious Adverse Event
Adverse events are classified as serious or non-serious. A ***serious adverse event*** is any AE that is:

- fatal
- life-threatening
- requires or prolongs hospital stay
- results in persistent or significant disability or incapacity
- a congenital anomaly or birth defect
- an important medical event

All adverse events that do not meet any of the criteria for serious should be regarded as ***non-serious adverse events***.

8.1.1 Investigator reporting: notifying the IRB

Federal regulations require timely reporting by investigators to their local IRB of unanticipated problems posing risks to subjects or others. The following describes the NYULMC IRB reporting requirements, though Investigators at participating sites are responsible for meeting the specific requirements of their IRB of record.

Report Promptly, but no later than 5 working days:
Researchers are required to submit reports of the following problems promptly but no later than 5 working days from the time the investigator becomes aware of the event:

- ***Unanticipated problems including adverse events*** **that are unexpected and related**
  - *Unexpected: An event is "unexpected" when its specificity and severity are not accurately reflected in the protocol-related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document and other relevant sources of information, such as product labeling and package inserts.*
  - *Related to the research procedures: An event is related to the research procedures if in the opinion of the principal investigator or sponsor, the event was more likely than not to be caused by the research procedures.*
  - *Harmful: either caused harm to subjects or others, or placed them at increased risk*

Other Reportable events:
The following events also require prompt reporting to the IRB, though ***no later than 5 working days***:

- ***Complaint of a research subject*** when the complaint indicates unexpected risks or the complaint cannot be resolved by the research team.

- ***Protocol deviations or violations*** (includes intentional and accidental/unintentional deviations from the IRB approved protocol) for any of the following situations:
  - *one or more participants were placed at increased risk of harm*
  - *the event has the potential to occur again*
  - *the deviation was necessary to protect a subject from immediate harm*
- ***Breach of confidentiality***
- ***Incarceration of a participant*** when the research was not previously approved under Subpart C and the investigator believes it is in the best interest of the subject to remain on the study.
- ***New Information indicating a change to the risks or potential benefits*** of the research, in terms of severity or frequency. (e.g. analysis indicates lower-than-expected response rate or a more severe or frequent side effect; Other research finds arm of study has no therapeutic value; FDA labeling change or withdrawal from market)

Reporting Process
The reportable events noted above will be reported to the IRB using a Reportable New Information submission and will include a description of the event with information regarding its fulfillment of the above criteria, follow-up/resolution, and need for revision to consent form and/or other study documentation. Copies of each report and documentation of IRB notification and receipt will be kept in the Clinical Investigator's study file.

9 Statistical Considerations

9.1 Study Hypotheses

Patient in clinics receiving the EHR-based alerts will have higher rates of adherence to guideline recommended medical therapy.

Providers will like the EHR-based alerts and will want to continue to use them in their practice.

9.2 Sample Size Determination

In order to have 80% power to detect a 10% improvement in prescribing for each intervention arm vs. control, we will require a total of at least 1503 patients (501 per arm). Based on prior data, we estimate that alerts will trigger for a sample between 1500-2000 patients, but are unable to accurately control the specific number of patients due to fluctuating clinical volume at practices.

9.3 Statistical Methods

We will begin all analyses with descriptive summary statistics and graphical displays of all variables. Primary analyses will utilize McNemar's tests for medication prescriptions and patient outcomes of hospitalization and mortality. We will adjust for patient demographics and clinical characteristics, as well as provider-level characteristics, such as demographics, panel size, insurance mix, and sub-specialty training.

9.4 Provider Survey Assessment

Answers from surveys will be tabulated with descriptive statistics.

10 Source Documents and Access to Source Data/Documents

The EPIC electronic health record is the primary data collection instrument for the study. Study-specific case report forms will not be used.

Access to study records will be limited to IRB-approved members of the study team. The investigator will permit study-related monitoring, audits, and inspections by the IRB/EC, the sponsor, government regulatory bodies, and University compliance and quality assurance groups of all study related documents (e.g., source documents, regulatory documents, data collection instruments, study data etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g., pharmacy, diagnostic laboratory, etc.).

11 Ethics/Protection of Human Subjects

11.1 Ethical Standard

The investigator will ensure that this study is conducted in full conformity with Regulations for the Protection of Human Subjects of Research codified in 45 CFR Part 46.

11.2 Institutional Review Board

A request for waiver of informed consent, and request for waiver of HIPAA authorization will be submitted to the IRB for review and approval. Approval of the protocol, the waiver of consent, and the waiver of HIPAA authorization must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study.

11.3 Informed Consent Process

We will obtain a waiver of informed consent and a waiver of HIPAA authorization for patients seen in the participating clinics to acknowledge their participation at a clinic level. The risks to subjects are exactly equivalent to the risks experienced in the standard setting of patient care. The new module to be activated in EPIC relates only to guidance for physician decision-making regarding HFrEF care, and has no impact on disclosure or treatment of PHI. Patients will receive care from their providers in the usual way. The only difference is the interface with the electronic health record that is used by the physician during the course of the patient encounter. The autonomy of the provider to make decisions about patient care will not be affected. It is impracticable to obtain consent from patients for receipt of standard medical care by their usual providers. It is unclear what they would be providing consent for, since they will receive care as usual from their providers. Patients will not be provided with additional information. They will be treated as usual by their providers and the providers' experience with the module is irrelevant to their patient experience.

For provider surveys, we are requesting a waiver of documentation of consent. These surveys present no more than minimal risk to providers. Prior to beginning survey questions, providers will be given consent form that contains all pertinent study and contact information. The consent form will be attached to the recruitment email and also will be available via link in Qaltrix prior to the survey. The providers will be asked to acknowledge consent through clicking a button within Qaltrixbefore they are able to participate in the survey questions. Providers will be informed that they may agree not to participate and that this will have no bearing on their employment status.

11.3.1 Research Use of Stored Data

- Intended Use: Data collected under this protocol may be used to study the effectiveness of the EHR-based alerts.
- Tracking: Data will be tracked using Epic reports generated by study team members.
    - Disposition at the completion of the study. Data will be retained in de-identified electronic form on secure, password-protected digital storage media in the NYULH MCIT-managed shared network drive, under the supervision of Drs. Blecker and Mukhopadhyay.
- Storage: Data with identifiable information will be stored on an MCIT-shared network drive, a secure, firewall-protected university server in a location with restricted access. Anti-virus software

is installed and current. Electronic access to the server will be through unique ID and complex password login and will only be granted to authorized researchers approved through this proposal. Login sessions can be individually monitored and tracked. All computer workstations require password login and have up-to-date virus software. Identifiable data will never be stored on moveable electronic media. Identifiable data will never be transmitted outside NYU. Only group-level information without personal identifiers will be included when presenting results or submitting manuscripts for publication.

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If any information is shared with external interested site(s), dataset agreements with NYU LANGONE will be established.

11.4 Future Use of Stored Data

Access to the dataset for any future research will require separate IRB approval.

12 Data Handling and Record Keeping

12.1 Data Collection and Management Responsibilities

Data collection is the responsibility of the study staff at NYULH under the supervision of Dr. Blecker. The investigator is responsible for ensuring the accuracy, completeness, and timeliness of the data reported.

12.2 Study Records Retention

Study documents and data will be retained for the longer of 3 years after close out or 5 years after final reporting/publication. These documents should be retained for a longer period, however, if required by local regulations. No records will be destroyed without the written consent of the sponsor, if applicable. It is the responsibility of the sponsor to inform the investigator when these documents no longer need to be retained.

12.3 Publication and Data Sharing Policy

This study will comply with the NIH Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

13 Study Finances

13.1 Funding Source

This study is financed through a grant from the NYU CTSI (Clinical and Translational Sciences Institute) Pilot Project Award.

13.2 Costs to the Participant

There are no costs to participants in this study.

13.3 Participant Reimbursements or Payments

There are no participant reimbursements or payments.

14 Study Administration

14.1 Study Leadership

Not applicable

15 Conflict of Interest Policy

The independence of this study from any actual or perceived influence, such as by the pharmaceutical industry, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this study will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the study. The study has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

Any investigator who has a conflict of interest with this study (patent ownership, royalties, or financial gain greater than the minimum allowable by their institution, etc.) must have the conflict reviewed by the NYU Langone Conflict of Interest Committee with a Committee-sanctioned conflict management plan that has been reviewed and approved by the study sponsor prior to participation in this study. All NYULH investigators will follow the applicable conflict of interest policies.

16 References

1. Yancy, C.W., et al., *2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America.* Circulation, 2017. **136**(6): p. e137-e161.
2. Heidenreich, P.A., et al., *2020 ACC/AHA Clinical Performance and Quality Measures for Adults With Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Performance Measures.* J Am Coll Cardiol, 2020. **76**(21): p. 2527-2564.
3. Fonarow, G.C., et al., *Improving evidence-based care for heart failure in outpatient cardiology practices: primary results of the Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting (IMPROVE HF).* Circulation, 2010. **122**(6): p. 585-96.
4. Greene, S.J., et al., *Medical Therapy for Heart Failure With Reduced Ejection Fraction: The CHAMP-HF Registry.* J Am Coll Cardiol, 2018. **72**(4): p. 351-366.
5. Chin, K.L., et al., *The treatment gap in patients with chronic systolic heart failure: a systematic review of evidence-based prescribing in practice.* Heart Fail Rev, 2016. **21**(6): p. 675-697.
6. Fonarow, G.C., et al., *Potential impact of optimal implementation of evidence-based heart failure therapies on mortality.* Am Heart J, 2011. **161**(6): p. 1024-30.e3.
7. Desai, A.S., et al., *Remote Optimization of Guideline-Directed Medical Therapy in Patients With Heart Failure With Reduced Ejection Fraction.* JAMA Cardiol, 2020. **5**(12): p. 1-5.
8. Driscoll, A., J. Currey, and A.M. Tonkin, *Nurse-Led Titration of Angiotensin-Converting Enzyme Inhibitors, β-Adrenergic Blocking Agents, and Angiotensin Receptor Blockers in Patients With Heart Failure With Reduced Ejection Fraction.* JAMA Cardiol, 2016. **1**(7): p. 842-843.
9. Lowrie, R., et al., *Pharmacist intervention in primary care to improve outcomes in patients with left ventricular systolic dysfunction.* Eur Heart J, 2012. **33**(3): p. 314-24.
10. Blecker, S., et al., *Interrupting providers with clinical decision support to improve care for heart failure.* Int J Med Inform, 2019. **131**: p. 103956.
11. Riggio, J.M., et al., *Effectiveness of a clinical-decision-support system in improving compliance with cardiac-care quality measures and supporting resident training.* Acad Med, 2009. **84**(12): p. 1719-26.
12. Qian, Q., et al., *ACEi/ARB for systolic heart failure: closing the quality gap with a sustainable intervention at an academic medical center.* J Hosp Med, 2011. **6**(3): p. 156-60.
13. Lee, J., et al., *Cluster Randomized Trial Examining the Impact of Automated Best Practice Alert on Rates of Implantable Defibrillator Therapy.* Circ Cardiovasc Qual Outcomes, 2019. **12**(6): p. e005024.
14. Powers, E.M., et al., *Efficacy and unintended consequences of hard-stop alerts in electronic health record systems: a systematic review.* J Am Med Inform Assoc, 2018. **25**(11): p. 1556-1566.
15. Kirby, A.M., et al., *Using Clinical Decision Support to Improve Referral Rates in Severe Symptomatic Aortic Stenosis: A Quality Improvement Initiative.* Comput Inform Nurs, 2018. **36**(11): p. 525-529.
16. Tai-Seale, M., et al., *Physicians' Well-Being Linked To In-Basket Messages Generated By Algorithms In Electronic Health Records.* Health Aff (Millwood), 2019. **38**(7): p. 1073-1078.

17 Attachments

These documents are relevant to the protocol, but they are not considered part of the protocol. They are stored and modified separately. As such, modifications to these documents do not require protocol amendment.