Incorporating Heart Failure Titration Guidelines into the TCU/Outpatient Care Setting

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Chronic Heart Failure (CHF) is a disabling condition that affects over six million adults in the United States and is characterized by the inability of the heart to pump enough blood to support the body's organs (CDC, 2020). Twenty percent of Americans over 40 years old will develop HF in their lifetime (Djoussé et al., 2009). The incidence of CHF increases with age, affecting 2.1% of the population over 65 years, with slightly more new onsets occurring in females than in males (Virani et al., 2021). CHF develops over time and is associated with many different factors, including coronary artery disease, insufficiency of blood flow supply to the heart, heart inflammation, high blood pressure, and cardiomyopathy; damage to the heart muscle (NHLBI, 2021). Heart failure has significant symptoms, including the buildup of fluid around the lungs and kidneys, and can lead to liver damage and other heart conditions. The significance of heart failure is high. Heart failure is a major cause of mortality, with only half of all HF patients surviving five years after diagnosis (Levy et al., 2002). Heart failure has been associated with frequent hospital readmission (Shah et al., 2017) and is the primary diagnosis in over one million hospitalizations annually (Go et al., 2013).

Heart failure has two clinical subsets relating to the underlying cause of cardiac insufficiency. *Diastolic heart failure* occurs when the heart's chamber walls become too stiff and prevent the chamber from being fully filled with blood, thus limiting its effective volume, while *Systolic heart failure* occurs when the heart can no longer squeeze with sufficient force (Chatterjee & Massie, 2007). Systolic heart failure is the focus of this project and is further categorized based on the quantitative measurement of the fraction of the blood that is pumped out with each contraction, known as the *ejection fraction* (EF), measured via echocardiography. Healthy individuals have ejection fractions greater than 55%, while heart failure patients with EF

below 40% are termed *heart failure with reduced ejection fraction* (HFrEF), and heart failure patients with EF above 50% are termed *heart failure with preserved ejection fraction* (HFpEF) (Vedin et al., 2017). Although there are effective pharmaceutical interventions have been proven to reduce mortality and morbidity for systolic heart failure, there remains a gap in their utilization. Closing this gap is the focus of this project.

Optimal treatment for HFrEF includes therapies common to all heart failure modalities together with systolic heart failure-specific treatments that will be described next. Generalized heart failure therapies seek to reduce fluid volume and control the factors associated with the progression of the disease. Generalized treatments include both nonpharmacologic and pharmaceutical interventions. Evidence-based nonpharmacologic treatments include dietary measures such as the restriction of sodium to less than 2 grams per day (Lenihan & Uretsky, 2000) and the elimination of tobacco and alcohol. Moderate exercise is also recommended for patients with stable heart failure (Belardinelli et al., 1999). Pharmaceutical treatments include the use of diuretics to reduce fluid volume.

Pharmaceutical treatment options for HFrEF include the use of three first-line medications that seek to relax the ventricle wall and reduce blood pressure. Angiotensin-converting enzyme (ACE-i) inhibitors prevent the production of angiotensin II, a substance that causes vasoconstriction. ACE inhibitors reduce blood pressure and relax veins and arteries (Bœuf-Gibot et al., 2021). Angiotensin-receptor blockers (ARBs) block the pathways to vasoconstriction, similar to ACE inhibitors but using a different mechanism (Barreras & Gurk-Turner, 2003). Beta-blockers target the beta-androgenic receptor and block the effects of adrenaline. Beta-blockers lower blood pressure, reduce the patient's heartbeat rate, and improve blood flow (Sin & McAlister, 2002). The efficacy of these therapies is well supported by the

evidence. The review articles by (Oliver-McNeil et al., 2020) and (Espinoza et al., 2021) provide an overview of the evidence for these medications and the landmark trials that led to their current use guidelines. Despite the demonstrated efficacy of these therapies, there are pervasive gaps in their utilization, with fewer than 25% of eligible patients being prescribed the target doses of these medical therapies.

This project seeks to improve outcomes for heart failure patients' utilization of pharmacological therapy, focusing on the transitional care unit (TCU)/out-patient setting. The PICOT question for this project is, how would the provision of an educational session to out-patient providers (**P**), focusing on GDMT for Heart Failure (**I**), impact the utilization of GDMT Heart Failure medications among heart failure patients (**O**) by the time of discharge from a Transitional Care Unit (**T**) compared to current practice (**C**).

The education intervention would teach about the importance of optimal titration to the guideline targets for heart failure medications. A secondary focus of this project is a parallel educational intervention for heart failure patients in the transitional care system with the goal of training them to be better self-advocates of their medical therapies.

This review will outline the scope and significance of the problem and will evaluate the existing evidence related to this research. A synthesis of the literature will be provided, and its support for the proposed approach will be ascertained.

Problem Statement

Pharmacological therapies have been demonstrated to reduce morbidity, mortality, and hospital readmissions for patients with heart failure with reduced ejection fraction. The proper use and dosing of these drugs are covered by Guideline-directed medical therapy (GDMT). Yet many patients remain on sub-optimal doses of these life-saving medications. This gap in care has

multifold causes, including significant gaps in provider knowledge and adherence to the GDMT targets.

Background to the Problem

Congestive Heart Failure (CHF) is a disabling progressive chronic medical condition that affects 6.5 million adults in the United States and contributes to over 300,000 deaths each year (CDC, 2020). Management of heart failure patients after discharge has proven to be challenging, with an approximate 20% readmission rate within 30-days of discharge (Blecker et al., 2019). For the 50% of heart failure patients with reduced ejection fraction (HFrEF) (Dunlay et al., 2017), pharmaceutical interventions have been shown to reduce readmission and mortality (Loop et al., 2020). However, fewer than 25% of eligible HFrEF patients are currently receiving guideline-directed medical therapy doses (Balakumaran et al., 2019). In a longitudinal study of the CHAMP-HF registry, for example, less than 1% of patients were simultaneously titrated to target doses on their HF therapies (Greene et al., 2019).

Multiple factors are associated with the sub-optimal use of these pharmaceuticals. Guidelines recommend initiation at low dosage, followed by up-titration to the optimal target dosage based on patient tolerance. In an out-patient setting, the optimization of therapy is performed by cardiologists or primary care providers, who monitor for known side effects. Intensification of dosage is often delayed due to the difficulty associated with scheduling the routine clinic visits currently required for each up-titration. This problem has been further exacerbated by the COVID-19 pandemic, with access to clinicians reduced and some patients more reluctant to seek care. Furthermore, despite clear guidance from the GDMT, adherence to GDMT dosing among providers is low (Cornelio & Di Palo, 2018).

The burden of therapy optimization intersects negatively with the myriad patient-related issues that influence medication compliance and health management. The World Health Organization estimates that the long-term compliance for chronic therapies is only 50% (Sabaté & Sabaté, 2003). Medication nonadherence rates for heart failure patients are estimated to range from 40% to 60% (Wu et al., 2008). Riegel et al. (2012) stratified their medication adherence results, finding *taking adherence* averaged 81-87%, *dosing adherence* was 73-80%, and *timing adherence* averaged 59-66%. Common reasons for nonadherence are multifaceted and include socioeconomic factors, marital status, health illiteracy, trust in healthcare providers, and symptom severity, among many others.

Problem Scope

Patients with heart failure experience fatigue, dyspnea, and fluid retention that leads to weight gain and edema in the lower extremities and abdomen and may result in chronic cough or wheezing. The heart may increase its heart rate to compensate for its failure to adequately pump blood. The reduced blood flow may impact the liver and digestive system, resulting in a loss of appetite, and can impact the brain, causing memory loss and confusion. Heart failure symptoms lead to a loss of independence and degrade the quality of life (Dunlay et al., 2015). Heart failure patients report increased difficulty in walking and climbing stairs and reduced social and family interaction. Heart failure management for HFrEF patients seeks to control these symptoms and reduce rehospitalization and mortality through the use of well-established usage of beta-blockers and ACEI/ARBs as directed by guideline-directed-medical-therapy together with diuretics for fluid overload.

Heart failure, due to its prevalence and its association with frequent rehospitalization, is one of the leading contributors to healthcare costs in the US. Increases in rehospitalization rates

associated with the failure to achieve GDMT targets directly impact the system. This problem also involves cardiologists and primary providers that fail to adhere to GDMT guidelines. Overall, however, the negative consequences of sub-optimal therapy most directly impact the patient and their families. Patients who are not optimally managed on GDMT have increased healthcare utilization, including hospital days and emergency room visits, and higher mortality risk. Inadequate utilization of medications for patients with heart failure affects the healthcare system through increased healthcare utilization and increased costs (McCullough et al., 2021). This research will focus on transitional care unit (TCU)/out-patient clinics, for which there is evidence for a larger gap in medication titration compared to specialized heart failure clinics.

Problem Consequences

Guideline Directed Medical Therapy in heart failure with reduced ejection fraction directs the use of several pharmaceutical interventions that have been shown to have clinical benefits in large randomized controlled trials (Balakumaran et al., 2019). Despite clear evidence-based guidelines regarding targets, few HFrEF patients are titrated to optimal dosages. The impact of suboptimal medical therapy is an increased risk for rehospitalization, morbidity, and mortality (McCullough et al., 2021) and the risk of the increased financial burden associated with disease severity (Lesyuk et al., 2018).

Knowledge Gaps

The evidence presented in this review has multiple limitations. Despite the strong evidence for the benefits of beta-blockers and ACE-i/ARBs and the well-established guidelines for their use and CMS penalties for excessive 30-day HF readmissions, there remains a significant gap in their optimal usage. A complete understanding of the policy, health systems,

and provider-related issues that underlie this gap remains incompletely understood, together with our knowledge of the full impacts of this gap.

The multivariate study of the impact of suboptimal therapy on HFrEF patients taking one or more pharmaceuticals has not yet been studied with the detail needed to provide guidance that would identify which patients are most in need of up-titration, what the relative risk of sub-optimal dose for each pharmaceutical is to the patient, and how this problem interrelates with ejection fraction. The evidence for an educational intervention is also incomplete due to the novel nature of this proposed intervention.

Proposed Solution

The proposed solution is an educational intervention that will target the TCU/out-patient providers. Providers will be educated on the importance of up-titration of heart failure medications within their patient population and on the guideline directives on optimal dosing, the identification of potential side effects, and laboratory testing required to monitor these patients. Provider education will be delivered during a regular provider group meeting in a short 10-minute presentation and reinforced by email communication with the providers. Prior to the presentation, we propose to assess the current attitudes and practices of the TCU providers with a short email survey to measure the baseline of knowledge of GDMT, quantify the current standards of care regarding HF medication titration with the TCUs, and identify any reservations or barriers to implementation that can be addressed in the presentation.

A secondary component of this intervention is the education of heart failure patients, with the goal of increasing their understanding of the importance of these medications and why it is in their self-interest to hold their providers accountable. Patient education will leverage the EPIC-HF patient education tool (Allen et al., 2021). EPIC-HF provides a 3-minute instructional video

teaching about the importance of HF medications and gives the patient a 1-page checklist (see Appendix A) that helps patients understand their current medication dosages in relation to GDMT goals. EPIC-HF was developed to help patients work collaboratively with their clinicians and to help them understand the importance of reaching GDMT targets. In this project, we propose to present newly admitted HF patients in the TCU with a copy of the worksheet, together with a QR-code link to the instructional video. For patients without access to personal electronics, the video would be played for the patient on the clinic's iPad or similar tablet computer. The provider will review the worksheet with the patient and mark changes in dosages reflecting titration changes during routine weekly visits. By following this two-pronged educational intervention, targeting the providers and patients, it is hypothesized that patients will successfully up-titrate their medications before discharge from TCU.

Project Setting, Sponsor, Stakeholders, and Participants

Project Setting: The setting of this DNP project will be a Midwest Transitional Care Unit (TCU) in Plymouth, MN. It is a well-known 50-bed facility in MN. The project will be implemented through in-person contact with patients and virtual provider education.

Stakeholders: Key stakeholders of this project are TCU clinicians, members of the heart failure team, patients with heart failure, and clinical site management.

Participants: Participants of the study will include 1) patients with a new or existing diagnosis of heart failure with reduced ejection fraction [EF<50%] who are discharged from the hospital to TCU and 2) a group of TCU clinicians consisting of 25 Nurse Practitioners and 9 MDs.

Organizational Needs Assessment/SWOT Analysis

An organizational needs assessment and a SWOT (strengths, weaknesses, opportunities, threats) analysis was undertaken to evaluate the project site. The published values statement of the participating research site is well aligned with the proposed project, and its mission statement (Allina, 2021) is consistent with the goals of this project.

SWOT analysis

Strengths:

- This intervention has the potential to improve health outcomes and well-being for HF patients and potentially reduce HF readmissions.
- This project encourages the patient to be involved and better understand their therapies.
- This project supports the desire of clinicians to improve outcomes for their patients

Weaknesses**:**

- The impact of the proposed intervention will be evaluated in a small pilot study with a convenience sample lacking sufficient statistical power to demonstrate the effectiveness
- The practical limitations of the project will limit the longitudinal surveillance of patients required to monitor for rehospitalization and other long-term outcomes
- Budget limitations will make participation incentives for the pilot study impossible, potentially making recruitment more difficult and subject attrition more likely
- The impact on provider and nurse workflow is unclear

Opportunities**:**

- The Centers for Medicare & Medicaid Services' Hospital Readmission Reduction program incentives hospitals to reduce 30-day CHF readmission rates
- The challenges of COVID-19 have made scheduling specialty (cardiology) appointments less available. The proposed project would provide guidance to out-patient providers to share responsibility for achieving optimal medication regimens for HF patients
- The proposed project will leverage the EPIC-HF patient education intervention successfully developed at the University of Colorado (Allen et al., 2021), creating the opportunity for partnership and co-learning

Threats**:**

- Reluctance by prescribing providers to adopt a change to current behavior
- Provider noncompliance
- Adverse reactions and intolerance to medication
- Lack of provider time
- Institutional inertia

Literature Matrix Table

For clarity, the literature matrix has been broken into separate sections based on the themes of the literature search for this project. The organization of evidence is intended to support the project rationale that there is a gap in heart failure care in the out-patient setting that can be closed by an educational intervention with out-patient providers. The evidence will show that (1) a gap in care exists, (2) that the gap is worse in out-patient settings, (3) that the reasons for this include provider-related factors, (4) that the gap in heart failure medication is associated with significantly worse outcomes, and finally (5) that related interventions to the approach proposed here have shown success at closing the gap in care. Table 1 lists evidence to support the assertion that a significant gap in medication titration exists.

Citation	Purpose/Design	Subjects	Interventions Measures	Results Level of Evidence
Atherton, J. J., & Hickey, A. (2017). Expert comment: Is medication titration in heart failure too complex? Cardiac Failure Review, 3(1), 25.	This review article looks at strategies to improve medication titration in HF, reviewing 19 studies with a cumulative enrollment of 52,355 subjects	19	The primary endpoint was the percentage of GDMT target for ACEIs/ARBs and beta-blockers achieved	**Level** III **(review article)** Only 29 % of patients were on target doses of ACEIs, and 18 % were on target doses of beta-blockers, compared to 50-60% in RCTs
Fiuzat, M., Ezekowitz, J., Alemayehu, W., Westerhout, C. M., Sbolli, M., Cani, D., Whellan, D. J., Ahmad, T., Adams, K., & Pina, I. L. (2020). Assessment of limitations to optimization of guideline-directed medical therapy in heart failure from the GUIDE-IT trial: A secondary analysis of a randomized clinical trial. JAMA Cardiology, 5(7), 757–764.	This is a secondary analysis of RCT results seeking to examine medical therapy for HF in GUIDE-IT and potential reasons why the intervention did not produce improvements in medical therapy	838	The primary endpoint was time to rehospitalization, reasons for not-titrating and HR med doses at 6-months	**Level** II **(quasi-experimental study)** Despite a protocol-driven approach, many patients in GUIDE-IT (84.5%) did not receive medication adjustments and did not achieve optimal GDMT
Fuery, M. A., Chouairi, F., Januzzi, J. L., Moe, G. W., Caraballo, C., McCullough, M., Miller, P. E., Reinhardt, S. W., Clark, K., Oseran, A., Milner, A., Pacor, J., Kahn, P. A., Singh, A., Ravindra, N., Guha, A., Vadlamani, L., Kulkarni, N. S., Fiuzat, M., … Desai, N. R. (2021). Intercountry Differences in Guideline-Directed Medical Therapy and Outcomes Among Patients with Heart Failure. JACC. Heart Failure, 9(7), 497–505.	This multi-center randomized trial examined patterns of care and clinical outcomes among patients with heart failure with reduced ejection fraction (HFrEF) in the United States and Canada. The focus of this study was a controlled trial of an N-terminal pro–B-type natriuretic peptide treatment strategy compared to usual care. This secondary analysis of the trial compares treatment and	894	The primary measures of this analysis were the clinical outcomes, implementation of GDMT, and the impact of natriuretic-guided therapy.	**Level** II **(secondary analysis of RCT study)** At the completion of the study period (6 months), few patients in the US cohort were at GDMT target dosing. The fraction of patients at target dose for ACE inhibitors or ARBs was 17%, and the fraction that was at target for Beta Blocker was 11%

Citation	Purpose/Design	Subjects	Interventions Measures	Results Level of Evidence
	clinical outcomes in the US and Canada			
Greene, S. J., Fonarow, G. C., DeVore, A. D., Sharma, P. P., Vaduganathan, M., Albert, N. M., Duffy, C. I., Hill, C. L., McCague, K., & Patterson, J. H. (2019). Titration of medical therapy for heart failure with reduced ejection fraction. Journal of the American College of Cardiology, 73(19), 2365–2383.	This prospective, observational study sought to characterize longitudinal titration of HFrEF medical therapy in clinical practice and to identify associated factors and reasons for medication changes	2588	Four medication classes were examined: ACEI/ARB, ARNI, beta-blocker, and MRA. For each patient and each medication, available dosing information was reviewed in reference to guideline-recommended target doses at baseline and 12-months	**Level** II **(quasi-experimental study)** In this contemporary U.S. out-patient HFrEF registry, most eligible patients did not receive target doses of medical therapy at any point during longitudinal follow-up, and few patients had doses increased over time

Table 1: Literature matrix supporting the assertion of gaps in HF medication titration

The next table presents evidence that a larger gap in medication titration is seen in the out-patient setting when compared to heart failure clinics.

Citation	Purpose/Design	Subjects	Interventions Measures	Results Level of Evidence
Gouya, G., Hammer, A., Elhenicky, M., Neuhold, S., Wolzt, M., Hülsmann, M., & Pacher, R. (2011). Benefit of specialized clinics for the treatment of patients with heart failure. European Journal of Internal Medicine, 22(4), 428–431.	This observational cohort study seeks to determine whether an equivalent benefit is achieved in all HF patients treated in specialized heart failure clinics	474	The primary endpoint was the enhancement of pharmacotherapy	**Level** II **(quasi-experimental study)** This study demonstrated increased medication optimization in an HF clinic compared to standard care
Greene, Stephen J., Javed Butler, Nancy M. Albert, Adam D. DeVore, Puza P. Sharma, Carol I. Duffy, C. Larry Hill, et al. 2018. "Medical Therapy for Heart Failure With Reduced Ejection Fraction: The CHAMP-HF Registry." Journal of the American College of Cardiology 72 (4): 351–66. https://doi.org/10.1016/j.jacc.2018.04.070.	This retrospective study sought to characterize patterns and factors associated with the use and dose of HFrEF medications in contemporary U.S. out-patient practice	3518	usage and dose ACEI, ARB ARNI, beta-blocker, and MRA. Patient-level factors associated with medication use were examined.	**Level** II **(quasi-experimental study)** This study found 17.4% of patients in an out-patient setting at target for ACEI/ARB and 27.5% of patients at target for beta-blockers

Table 2: Literature matrix supporting the assertion that gaps in HF titration are worse in out-patient settings

The reasons for the low proportion of patients on GDMT target doses are addressed by the following references,

Citation	Purpose/Design	Subjects	Interventions Measures	Results Level of Evidence
Bozkurt, B. (2019). Reasons for Lack of Improvement in Treatment With Evidence-Based Therapies in Heart Failure∗. Journal of the American College of Cardiology, 73(19), 2384–2387.	Expert editorial seeking to identify the causes for the continuing low proportion of HF patients on GDMT target dosages	n/a		**Level** IV **(expert opinion)** Overall, patient-related factors such as the severity of illness; system, payer, and coverage issues; provider-related issues such as provider inertia/aversion and lack of knowledge; and practice-level variation with differences in expertise and care coordination, all appear to play a role in the care gap.
Cornelio, C., & Di Palo, K. E. (2018). Guideline-Directed Medical Therapy in Hospitalized Heart Failure Patients: Still Underprescribed Despite Updated Guidelines and Over 20 Years of Evidence. Journal of Cardiac Failure, 24(8), S100.	This is a retrospective study to evaluate the rates of prescriber adherence to GDMT guidelines. This study enrolled patients hospitalized with acute decompensated heart failure (ADHF) at the time of discharge after the publication of the guideline update.	50	percent of eligible patients receiving GDMT therapy (broken down into five drug classes) at discharge	**Level** II **(quasi-experimental study)** Guideline adherence among the internal medicine service was 33.3% (12/36) compared to 28.5% (4/14) among the cardiology service. Overall, 32% of patients were discharged on appropriate GDMT dosages.
Jarjour, M., Henri, C., de Denus, S., Fortier, A., Bouabdallaoui, N., Nigam, A., O'Meara, E., Ahnadi, C., White, M., Garceau, P., Racine, N., Parent, M.-C., Liszkowski, M., Giraldeau, G., Rouleau, J.-L., & Ducharme, A. (2020). Care Gaps in Adherence to Heart Failure Guidelines: Clinical Inertia or Physiological Limitations? JACC: Heart Failure, 8(9), 725–738. https://doi.org/10.1016/j.jchf.2020.04.019	A retrospective study evaluated the impact of clinical and physiological factors limiting treatment optimization toward recommended medical therapy in heart failure	511	The primary endpoint was adherence to GDMT for pharmaco-therapies.	**Level** II **(quasi-experimental study)** This study found 30% nonadherence in an academic hospital-based multidisciplinary HF clinic with a clinical pharmacist leading up-titration clinics. nonuse/non-intensification of pharmacotherapy was associated with older age, more severe symptoms, and a history of stroke/TIA, suggesting that perceived frailty may influence our willingness/capacity to up-titrate the pharmacological regimen

Table 3: Literature matrix supporting the assertion that gaps in HF titration are multifold and include provider aversion and inertia

Evidence that the failure to follow the GDMT targets is associated with negative outcomes is summarized in the following table,

Citation	Purpose/Design	Subjects	Interventions Measures	Results Level of Evidence
Fitzgerald, A. A., Powers, J. D., Ho, P. M., Maddox, T. M., Peterson, P. N., Allen, L. A., Masoudi, F. A., Magid, D. J., & Havranek, E. P. (2011). Impact of Medication Nonadherence on Hospitalizations and Mortality in Heart Failure. Journal of Cardiac Failure, 17(8), 664–669. https://doi.org/10.1016/j.cardfail.2011.04.011	A retrospective longitudinal cohort study of 557 patients with heart failure with reduced ejection fraction (HFrEF) sought to assess the association between adherence and outcomes among patients with heart failure	557	The primary measures were multivariable Cox proportional hazards models to assess the relationship between adherence (with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, b-blockers, and aldosterone antagonists) and the primary outcome of all-cause mortality plus cardiovascular hospitalizations.	**Level** II **(quasi-experimental study)** Medication nonadherence was associated with an increased risk of all-cause mortality and cardiovascular hospitalizations in a community heart failure population. Nonadherence (defined as <80% adherence) was associated with a statistically significant increase in the primary outcome in the cohort overall (hazard ratio 2.07, 95% confidence interval 1.62e2.64; P < .0001).
Gathright, E. C., Dolansky, M. A., Gunstad, J., Redle, J. D., Josephson, R., Moore, S. M., & Hughes, J. W. (2017). The Impact of Medication Nonadherence on the Relationship Between Mortality Risk and Depression in Heart Failure. *Health Psychology: Official Journal of the Division of Health Psychology, American Psychological Association*, *36*(9), 839–847. https://doi.org/10.1037/hea0000529	In this secondary analysis of the HeartABC study, depressive symptoms electronically monitored medication adherence, and mortality was measured in a sample of 308 patients with heart failure participating in a study of self-management behavior. Cardiovascular and all-cause mortality data were obtained from the CDC's National Death Index (median 2.9-year follow-up). Cox proportional hazards were used to assess the relationship between depression, mortality, and medication nonadherence.	372	The primary measures in this study were all-cause and cardiovascular mortality, depressive symptoms assessed with the Patient Health Questionnaire-9, and medication nonadherence assessed through 28-days of monitoring with the Medsignal's pillbox.	**Level** II **(quasi-experimental study)** This study found that mild depressive symptoms were associated with lower medication adherence and increased all-cause and cardiovascular mortality. The relation between medication nonadherence and mortality was found to be significant; a 10% increase in nonadherence was associated with a 12% increase in the 2.7-year mortality risk.
McCullough, P. A., Mehta, H. S., Barker, C. M., Houten, J. V., Mollenkopf, S., Gunnarsson, C., Ryan, M., & Cork, D. P. (2021). Healthcare utilization and guideline-directed medical therapy in heart failure patients with reduced ejection fraction. Journal of Comparative Effectiveness Research, 10(14), 1055–1063.	This is a retrospective study examining the uptake and effect of GDMT among real-world HFrEF patients in the USA. The purpose of our study is to assess the impact of GDMT (and the lack thereof) on healthcare utilization.	28426	The primary endpoint was all-cause hospitalizations, cardiovascular (CV) related hospitalizations, hospital days, emergency department (ED) visits, out-patient visits, and office visits. All outcomes were measured up to 2 years from the end of the landmark period (6 months after a patient's diagnosis of HFrEF in which drug regimens were assessed)	**Level** II **(quasi-experimental study)** In a real-world population setting, a sizeable amount of HFrEF patients (31–44%) were not optimally managed on GDMT. The absence of GDMT was independently associated with increased annual healthcare utilization, in particular annualized hospitalizations, hospital days, and emergency room visits.

Citation	Purpose/Design	Subjects	Interventions Measures	Results Level of Evidence
McCullough, P. A., Mehta, H. S., Barker, C. M., Van Houten, J., Mollenkopf, S., Gunnarsson, C., Ryan, M., & Cork, D. P. (2021). Mortality and guideline-directed medical therapy in real-world heart failure patients with reduced ejection fraction. Clinical Cardiology, 44(9), 1192–1198. https://doi.org/10.1002/clc.23664	Retrospective study seeking to estimate the prevalence of guideline-directed medical therapy (GDMT) in commercially insured US patients with heart failure with reduced ejection fraction (HFrEF) and examine the effect of GDMT on all-cause mortality.	14880	The primary endpoint was the two-year mortality risk to HFrEF patients.	**Level** II **(quasi-experimental study)** Patients in the not-on-GDMT cohort had a 29% increased risk of mortality versus GDMT (hazard ratio 1.29; 95% CI (1.19–1.40); p < .0001). As a sensitivity analysis, the effect of patients not-on-GDMT compared to GDMT with concurrent medication fills was more pronounced, with a 37% increased mortality risk.
Wu, J.-R., Lennie, T. A., Dekker, R. L., Biddle, M. J., & Moser, D. K. (2013). Medication Adherence, Depressive Symptoms, and Cardiac Event-Free Survival in Patients with Heart Failure. *Journal of Cardiac Failure*, *19*(5), 317–324. https://doi.org/10.1016/j.cardfail.2013.03.010	This was a secondary data analysis of two prospective studies in which patients with HF were enrolled to measure medication adherence seeking to explore the combined influence of medication adherence and depressive symptoms on cardiac event-free survival	216	The primary endpoints were medication adherence measured objectively with the Medication Event Monitoring System, depressive symptoms measured with the PHQ-9 at baseline, and cardiac events occurring during a 3.5 year surveillance period	**Level** II **(quasi-experimental study)** The risk of experiencing a cardiac event for patients with medication nonadherence *and* depressive symptoms was five times higher compared to those who were medication adherent without depressive symptoms. Medication nonadherence alone found the time to the first cardiac event was significantly shorter (p=0.005), and the cardiac event-free survival hazard ratio was 1.8
Wu, J.-R., & Moser, D. K. (2018). Medication Adherence Mediates the Relationship Between Heart Failure Symptoms and Cardiac Event-Free Survival in Patients with Heart Failure. *The Journal of Cardiovascular Nursing*, *33*(1), 40–46. https://doi.org/10.1097/JCN.0000000000000427	This was a secondary data analysis of two prospective studies in which patients with HF were enrolled to measure medication adherence seeking to explore the relationships between HF symptoms, medication adherence, and cardiac event-free survival	219	The primary endpoints were heart failure symptoms assessed using a portion of the Self-Care of Heart Failure Index, medication adherence measured objectively with the Medication Event Monitoring System, and cardiac events occurring during a 3.5 year surveillance period	**Level** II **(quasi-experimental study)** Patients reporting dyspnea or ankle swelling were more likely to have poor medication adherence (p=.05). Poor medication adherence was associated with worse cardiac event-free survival (p=.006). In Cox regression, patients with HF symptoms had two times greater risk for a cardiac event than patients without HF symptoms (p=.042).

Table 4: Literature Matrix supporting the assertion that sub-GDMT dosing for HF has a significant risk to patients

And finally, evidence to support the proposed project is summarized in the final table.

Citation	Purpose/Design	Subjects	Interventions Measures	Results Level of Evidence	Relevance to This Project
Allen, L. A., Venechuk, G., McIlvennan, C. K., Page, R. L., Knoepke, C. E., Helmkamp, L. J., Khazanie, P., Peterson, P. N., Pierce, K., Harger, G., Thompson, J. S., Dow, T. J., Richards, L., Huang, J., Strader, J. R., Trinkley, K. E., Kao, D. P., Magid, D. J., Buttrick, P. M., & Matlock, D. D. (2021). An Electronically Delivered Patient-Activation Tool for Intensification of Medications for Chronic Heart Failure with Reduced Ejection Fraction. Circulation, 143(5), 427–437.	Compare the efficacy of an intervention, EPIC-HF, seeking to intensify medication regimen for patients with HFrEF through the use of an electronically delivered patient tool before cardiology clinic visit to standard care. The study design was RCT	306	The intervention was an electronically delivered tool vs. standard care. The primary endpoint was the percent of patients with GDMT intensification from immediately preceding the study qualifying cardiology clinic visit to 30 days later	**Level I (RCT)** 49.0% of the patients in the intervention group and 29.7% of the patients in the control group experienced an intensification of their GDMT (P=0.001; risk ratio,1.6 [95%CI, 1.2-2.2])	This study is directly relevant to this study. The authors of this study have authorized the use of the EPIC-HF in this study
Driscoll, A., Currey, J., & Tonkin, A. M. (2016). 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 Cardiology, 1(7), 842–843.	Review article seeking to evaluate strategies facilitating HF medication titration, specifically Nurse-Led Titration clinic	n/a	The primary endpoint was the level of beta-blocker therapy compared to GDMT and readmission r and therefore decreased readmissions rates	**Level** II **(quasi-experimental study)** patients in the NLT group had significantly improved outcomes, including lower hospital readmission rates. The NLT group also achieved higher proportions of patients reaching GDMT targets	This study describes alternatives to up-titration centered around nurse-led initiatives
Hickey, A., Suna, J., Marquart, L., Denaro, C., Javorsky, G., Munns, A., Mudge, A., & Atherton, J. J. (2016). Improving medication titration in heart failure by embedding a structured medication titration plan. International Journal of Cardiology, 224, 99–106.	To assess if improvements to heart failure disease management (HFDM) programs, using awareness-raising and education, audit and feedback, integration into existing work practice, and incentive payments would increase patients reaching target doses. The study design was retrospective and prospective audits.	280	The intervention was improved HFDM programs in development at one year and two years. The primary endpoint was the proportion of patients who were on target doses at six months following discharge from the hospital	**Level** II **(quasi-experimental study)** Results: Baseline cohort A: 38 %, Intervention cohort B: 33 % Intervention cohort C: 51 %	This study describes multiple approaches to medication intensification relevant to the proposed project
Kommuri, N. V., Johnson, M. L., & Koelling, T. M. (2012). Relationship between improvements in heart failure patient disease-specific knowledge and clinical events as part of a randomized controlled trial. Patient Education and Counseling, 86(2), 233–238.	A randomized controlled study comparing the effects of a 1-hour HF education intervention at discharge versus standard discharge in heart failure patients	265	The primary endpoints were patient knowledge assessed with the HFKQ and clinical event, death, or rehospitalization within 6-months	**Level I (RCT)** The intervention group had fewer readmissions compared to the standard care group (136 vs. 146, p = 0.02) and improved knowledge of their disease and its management.	This experimental study highlights the power of patient education, a secondary component of this research

Citation	Purpose/Design	Subjects	Interventions Measures	Results Level of Evidence	Relevance to This Project
McLachlan, A., Aldridge, C., Morgan, M., Lund, M., Gabriel, R., & Malez, V. (2021). An NP-led pilot telehealth programme to facilitate guideline-directed medical therapy for heart failure with reduced ejection fraction during the COVID-19 pandemic. The New Zealand Medical Journal (Online), 134(1538), 77-6.	This prospective, observational study assessed an NP-led pilot telehealth programme seeking to facilitate guideline-directed medical therapy for heart failure with reduced ejection fraction during the COVID-19 pandemic	50	The primary outcome of this study was the patient's titration success. Physiological variables, including BP and Pulse rate, were also measured	**Level** II **(quasi-experimental study)** Patients found the process acceptable and experienced rapid titration with less need for clinic review.75% were optimally titrated within two months	This study describes a successful up-titration strategy coupling patient education and NP-led telehealth follow-up

Table 5: Literature Matrix reviewing evidence for patient-focused and provider-focused interventions to close the GDMT gap

Literature Search Process

A literature review was undertaken to identify evidence to support the proposed project. The literature review sought evidence to address the prevalence of sub-optimal heart failure medication and provider nonadherence to the guidelines, the risk associated with sub-optimal medication, and evidence supporting the proposed solution.

Twenty-one articles have been reviewed and categorized using the Johns Hopkins Nursing EBP Levels of Evidence (Dang & Dearholt, 2018). The inclusion criteria included journal articles written in the last ten years (between 2011 and 2021) in English. Searches were conducted using Google Scholar, and PubMed searches on the search terms "*heart failure*," "*HFrEF*," "*GDMT*," "*up-titration*," alone and with the additional search term "*out-patient*." The resulting articles were reviewed, and if they contained evidence related to the topic of GDMT dosing for HFrEF relevant to the research questions, they were included in this review. The evidence supporting the current GDMT guidelines was not itself a focus of this review but is well documented in the review articles by (Oliver-McNeil et al., 2020) and (Espinoza et al., 2021). These articles both review the landmark trials that led to the GDMT and highlight the need for providers to recognize the importance of titrating medications to these targets and the special role NPs can play in the optimization of these medications.

Literature Synthesis

The focus of this literature search was to find evidence to support the rationale for the proposed project and evidence that the proposed intervention will have an immediate impact on closing the gap in medication optimization in heart failure patients in the TCU/out-patient setting. The evidence presented in this review can be broken into several thematic categories, (1) evidence for widespread sub-optimal titration to GDMT targets for HFrEF patients, (2) evidence that out-patient clinics have lower rates of provider adherence to GDMT and lower rates of optimal titration to GDMT when compared to in-patient and HF clinics, and (3) evidence that the causes in this gap in care include gaps in provider knowledge, inertia, and aversion, (4) evidence that the sub-optimal medication doses have negative outcomes for HF patients, and finally (5) evidence that an educational intervention will help to close the gap and improve outcomes for HF patients in the transitional care and out-patient settings. A discussion of the literature in each thematic category is presented below.

The evidence for the widespread sub-optimal titration of angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARBs), and beta-blockers is strong, despite their demonstrated ability to lower mortality and hospitalization risks in heart failure patients with reduced ejection fraction (HFrEF.) In one review by (Atherton & Hickey, 2017), it was noted that over 90% of patients on a large registry were on ACEI or ARB therapy and beta-blockers, yet less than a third were titrated to target doses. Similar findings were reported by Greene et al. (2019). In their observational study, it was observed that most eligible patients enrolled in a U.S. out-patient HFrEF registry did not achieve their GDMT targets at any point during longitudinal follow-up, and even more revealing, they noted that few patients had doses increased over time, providing evidence that their providers were not up-titrating them. Fuery et

al. (2021) performed a secondary analysis of data collected in a large multi-center trial of 45 clinics in the U.S. and Canada. The focus of this study was to contrast care in the two healthcare systems, but the relevant evidence for this project was the large gap in HF medication dosing in the U.S. cohort at the end of the study period. Only 17% of the subjects were at GDMT targets of ACE inhibitors or ARBs, and 11% were at GDMT targets for beta-blockers. The gap in titration for these medications is widely acknowledged and is further supported by each cited paper in the remaining review themes.

Table 2 provides evidence that there are gaps in HF care in the out-patient setting. This contention is established by two studies. (Greene et al., 2018) utilized the large CHAMP-HF registry to undertake a large retrospective study of therapy for HFrEF patients in contemporary U.S. out-patient practices. The use of GDMT medications was studied, and each patient's therapy was reviewed to determine if there were contraindications. The study found nearly 40% of patients with no contraindications were *not* treated with ACEI/ARB, and 33% were similarly not treated with beta-blockers. Among those using these medications, their dosing showed significant gaps with the GDMT targets. Only 17.4% of patients reached GDMT targets for ACEI/ARB, and only 27.5% of patients achieved targets for beta-blockers. In an observational study, (Gouya et al., 2011) compared up-titration rates between specialized heart failure clinics and standard care and found the standard care clinics showed inferior medication optimization rates compared to HF clinics. This evidence supports the goal of this project, to focus on improvements to care in the TCU/out-patient setting.

To affect a meaningful solution, it is important to gain a deeper understanding of the current low proportion of patients on GDMT target doses. Table 3 presents studies that sought evidence for the underlying reasons for the gap. (Jarjour et al., 2020) focused on clinical and

psychological factors limiting treatment optimization in an academic hospital-based HF clinic. In this setting, provider adherence was relatively high, at 70%. Reasons for nonadherence were associated with the perceived frailty of patients. Similarly, (Cornelio & Di Palo, 2018) focused their study on adherence rates in the in-patient setting. They found low GDMT adherence among both internal medicine providers (33%) and cardiology (29%). The most revealing article is the editorial by Bozkurt (2019). Bozkurt investigated this problem using the CHARM-HF registry database and categorized the reasons for the lack of target dosing into three domains, *patient-related, provider-related*, and *system/payer-related* issues. Overall, the patient-related factors, including illness severity, payer coverage, provider aversion/inertia, and variation in practice, all provided a role in the gap. This project seeks to focus on the provider-related factors and, as a novel addition – to educate and equip patients to become better advocates during routine visits with their providers.

The next thematic goal of the review was to assess the evidence that sub-optimal dosing is associated with increased patient mortality and worse outcomes. Table 4 highlights two very large retrospective studies. In (McCullough, Mehta, Barker, Van Houten, et al., 2021), the two-year mortality hazard was estimated using insurance data for HFrEF patients in the U.S. It was shown that the not-on-GDMT cohort had a significantly high risk of mortality compared to the GDMT group. The second article by (McCullough, Mehta, Barker, Houten, et al., 2021) examines the usage of HF medications and their association with all-cause hospitalizations. The proportion of the population of the patients with optimal medications was low, between 31-44%, reinforcing the evidence for the gap in GDMT therapy provided above. The key finding was the absence of GDMT was associated with increased healthcare utilization, rehospitalization, and ER visits.

Fitzgerald et al. (2011) conducted a retrospective longitudinal cohort study to assess the association between adherence and outcomes for HF patients and found that nonadherence was associated with a doubling in the hazard ratio for all-cause mortality. A similar result, a doubling in the mortality hazard ratio, was seen in the secondary data analysis of Wu & Moser (2018). They also reported a statistically significant ($p < 0.05$) association between poor medication adherence in HF symptoms, dyspnea or ankle swelling, and a worse cardiac event-free survival rate. In related work, Wu et al. (2013) found that the combination of medication nonadherence *and* depressive symptoms was associated with a five-fold increased likelihood of cardiac events raising the question of the potential cause-and-effect relationship between medication nonadherence, the worsening of symptoms, and the psychological impact of the consequences of the symptoms leading to depression. Gathright et al. (2017) studied this association between depressive symptoms and medication adherence in a different secondary data analysis and confirmed the association, finding depressive symptoms were associated with lower medication adherence and reinforcing the finding that increases in medication nonadherence are associated with increases in mortality for HF patients.

Finally, Table 5 presents evidence for the potential impact of the proposed educational intervention. (Allen et al., 2021) describe a patient-focused educational intervention called EPIC-HF. This intervention supported the goal of increasing patients' understanding of the importance of these medications and aimed at helping them to make their providers accountable. In this RCT, patients in the EPIC-HF group had significantly higher rates of medication intensification compared to controls. The authors of this study have communicated their support for this DNP project and have granted the use of their educational materials. (Hickey et al., 2016) assessed the potential of a provider-focused intervention consisting of an iteratively developed structured

titration plan is demonstrated. The final iteration of the plan demonstrated improved numbers of patients at GDMT targets compared to baseline (51% vs. 38%.) Kommuri et al. (2012) conducted a randomized controlled trial comparing the effects of additional education versus standard discharge for patients with heart failure. They found a short 1-hour education session with a nurse educator led to fewer readmissions compared to the standard care discharge group ($p=0.02$) as well as higher scores on a 30-point heart failure questionnaire at one, three and six months after discharge. Finally, both (Driscoll et al., 2014) and McLachlan et al. (2021) describe a nurse-led initiative to titrate patients that led to increases in the proportion of patients reaching GDMT targets and a decrease in hospital readmissions. Taken together, these papers illustrate the potential for an out-patient titration initiative, combining education and medication guidance for providers together with patient education. We hypothesize that the combination of these two approaches (provider- and patient-focused) will reinforce each other and have the potential to achieve more dramatic improvements than were demonstrated for the individual interventions.

This synthesis has provided evidence to support the central narrative of this project, that there exists a significant gap in medication up-titration for HF patients and that an initiative targeting provider and patient education within an out-patient setting can lead to improved outcomes for patients and a reduced burden on the healthcare system.

Theory Overview

Lewin's Three-Step change model was selected as a theoretical framework for this project. Lewin's model is frequently used by healthcare professionals seeking to improve outcomes by establishing new guidelines for patient care. It consists of three steps: unfreezing, change, and refreezing.

Theory Application/Relationship

The up-titration protocol implemented aimed to change the current process of HF medication management in the TCU environment. As was shown in the above literature review, one of the underlying causes of the current gap in care is provider aversion and inertia. This model is especially well suited to this project, as we're seeking to break the current *status quo*, unfreeze the inertia responsible for gaps in HF care, and establish a new *status quo*.

The first step in this project will be to develop an educational intervention to initiate the *unfreezing* process. At the outset of the project, we will assess the current practices within the TCU system to fully understand the challenges that will be required to implement a new process for heart failure patients. To initiate the unfreezing process, we will engage clinicians by presenting an educational session emphasizing the importance of GDMT for managing heart failure patients and highlighting the potential benefit to patients and the burden of rehospitalizations for the system if the gap in care were to be closed. Finally, a practical approach to up-titration in the TCU/out-patient setting to meet GDMT goals will be presented. These efforts may increase providers' knowledge and lessen the gap between current practice and guideline recommendations. Gaining management support and cardiology department support is a necessary step in the unfreezing process. Once the environment is unfrozen, an opportunity to improve the *status quo* has been created. The objective of this project is to provide leadership by implementing an evidence-based approach to HF medication management. If the outcome of this study is successful, it will establish a new standard for HF management in the TCU setting. Finally, a "refreezing" of the new process will occur, a final stage that is described as the consolidation of gains achieved in the change process into the new status quo. Standardizing medication up-titration for heart failure patients will benefit the healthcare teams' professional

practice, improve patient health, and improve future organizational outcomes for HF readmission rates.

Project Goal: Overall Goal/Mission

The mission of this project is to improve outcomes for heart failure patients' by optimizing their utilization of pharmacological therapy in the TCU/out-patient settings. We hypothesize that the use of an educational intervention targeting providers will lead to improved titration of the patients' medication targets during their stay in the transitional care facility. We will achieve this goal by pursuing the following objectives.

Goals and SMART Objectives

Three objectives have been developed for this project, (1) development and delivery of an educational intervention, (2) implement a medication optimization program for heart failure patients in the TCU/outpatient setting, and (3) the success goal of up-titration of 70% of the enrolled heart failure patients by the time of discharge. Each of these objectives is described in detail below.

Development and delivery of an educational intervention to TCU providers

The primary objective of this project is the development and delivery of an educational intervention to providers within the participating midwestern TCU clinics. The educational intervention will take the form of a virtual presentation to be delivered during a routine provider meeting. The educational intervention will discuss the importance of successfully up-titrating patients to GDMT targets or the maximum tolerable dosages. An overview of the GDMT targets and the steps to successfully up-titrating patients will be provided. The goal will be to make this presentation before 5/1/2022 and reach more than 50% of TCU providers. If that goal is not

achieved, a second presentation will be scheduled to reach any providers who were absent during the regular meeting.

Implement a medication optimization program for heart failure patients with 50% provider adherence by 8/31/2021

The target population will be newly diagnosed heart failure with reduced ejection fraction patients (HFrEF) within the participating TCU clinics. Patients with newly prescribed HF medications (beta-blockers and ACEI/ARB's) will be enrolled in this study between 6/1/2021 and 8/1/2021. To assess utilization of therapies, enrolled patients will receive weekly visits from their provider to check the current medications, assess patient status and medication tolerance and plan medication changes for the following week. At the conclusion of the study, the final titration rate will be used to determine if the intervention was successful at optimizing to GDMT or maximum tolerable dosage, and the overall change from baseline will be used to assess the overall intensification of therapy. The intermediate deadline is 8/31/2021 when the preparations for the human study will be completed, and 9/31/2021, when the study will be concluded.

Successful up-titration of 70% of the enrolled heart failure patients

To assess the impact of the provider educational intervention, the final objective of this project is to monitor the titration of HF meds in at least one TCU. The goal of the guideline will be for providers to titrate their patients towards GDMT or to a maximum tolerable dosage. The mean duration of stay for HF patients in the participating TCUs has been estimated at 21-days. This duration is anticipated to be too short an interval to successfully reach GDMT targets but offers ample time for medication intensification. Titration will be assessed by the clinical pharmacologist at the TCU. The success goal for this objective will be the medication intensification of 70% of the enrolled patients during their stay at a TCU.

GANTT Chart

To plan the execution of this project, a GANTT chart was created to outline the project timeline (see Appendix B), covering the period between September 2021 and September 2022. The initial project conception, planning, and research began in the fall 2021 semester and was refined with a literature search that identified gaps in current practice for heart failure patients. The selection of the clinical study site and initial coordination with the site's DNP project manager and principal investigator began in October 2021. An outcome of this coordination was the development of a research proposal and a request for authorization to execute this project within their regional transitional care clinics. The future execution of this project is outlined in detail and highlights the development and delivery of the research tools (pre- and post-intervention surveys) and the design and delivery of the educational intervention. The baseline survey results will provide insights on current practice in the site TCU system and will help refine the educational presentation. Following the study period, the survey will be repeated to assess potential changes in self-reported provider practices and attitudes regarding up-titration in their TCU setting. Descriptive and inferential statistics will be developed to describe the study population and to infer the efficacy of the intervention. The final DNP project paper and its dissemination are anticipated in August 2023.

Work Breakdown Structure

The project structure is outlined in the work breakdown shown in Appendix C, and the work items are categorized into five phases describing the project design and planning, the execution of the intervention, the analysis of the results, and the final evaluation and dissemination of the results. The project design was begun in the fall of 2021 and included the initial project conceptualization and the refinement of the concept through the literature review

and SWOT analysis. Project planning began with the identification of the project team at the participating Midwest TCU. Feedback from the project chair, the TCU PI, and the program manager was used to align the project with the clinical needs and research interests of the TCU, as well as to keep it on track within the CSS DNP program. The planning stage is nearing the submission of a formal research proposal for review by the TCU research council at the time of writing, and the final step in the project plan will be the grant of approval by the IRB.

The proposed intervention consists of a preliminary survey to be electronically delivered to all the providers within the Midwest TCU system. The survey will be used to assess baseline practices and attitudes regarding the optimization of medication for heart failure patients in their care. The survey will provide this DNP student with insights into why providers are not up-titrating their patients. This knowledge will help to shape the educational intervention, which will be given to the providers during a routine periodic provider meeting. At the conclusion of the intervention period, a follow-up survey will re-assess the providers' attitudes and practices. Inferential statistics will be developed comparing changes in survey scores from baseline and will be used to infer the efficacy of the educational intervention. These results will be summarized, and the final report for the project will be completed and disseminated.

Communication Matrix

The intent and frequency of communication between the project members and stakeholders have been classified in a communication matrix shown in Appendix D. The DNP student managed the project via communication with the clinical site team, including the site program manager and the principal investigator who manages the DNP research within their TCU system. Frequent communication with the CSS project chair was essential to keep the project on track and aligned with the CSS DNP requirements. Communication with the clinical

site principal investigator was needed to align the project with the sites' clinical interests, as well as to navigate through the institutional requirements needed for human studies conducted within their system. Communication with the site's program manager was critical to developing the timeline and logistics for the project. Collaboration with the clinical site team was also critical to finalizing the study endpoints and designing the methods to collect the study data.

Logic Model

A logic model for the proposed project was developed and is shown in Appendix E. The model illustrates the purpose of the project, the inputs and actions that will be used during the execution of the project, and the anticipated results. The results have been grouped into three categories relating to the short-term, intermediate-term, and long-term outcomes of the project. Short-term outcomes are the anticipated changes in provider practices and the associated changes in patient medication. The intermediate-term outcomes are the anticipated organizational changes that will occur as the result of a successful project, including institutional support to sustain the project beyond the period of performance for this project. Long-term outcomes are the beneficial impact of medication optimization for the patients, which has been associated with improved outcomes and lower morbidity and mortality. The desired long-term outcome for the institution will be a reduction in the readmission rates for their heart failure patient population.

Methodology and Analysis

The aim of this project is to improve outcomes for heart failure patients within the transitional care/out-patient environment through the optimization of their medications to the GDMT goals. To achieve this goal, an educational intervention highlighting the importance of medication optimization and outlining the steps to safely titrate patients will be developed and

delivered to the providers within the participating system's transitional care facilities. To measure the impact of the proposed intervention, data will be collected from two main sources.

Data Sources

To assess the impact on provider attitudes and practices, data will be collected via a survey questionnaire (see Appendix F) given to providers at two separate time points, before and after the intervention. A second data source will assess provider practices via the electronic health records of their patients. To support this quality improvement project, the participating healthcare system made heart failure management one of its 2022 quality goals. As part of this effort, they have added a new requirement for providers writing patient notes for heart failure patients. An EPIC smart phrase, `.TCUHFSTATUS` has been defined to automate the reporting on medication titration and status changes into the electronic records for each heart failure patient in the TCU. After adding the required keyword, EPIC presents the provider with a menu of text phrases that can automatically be added to their note. This menu will include phrases for *(1) increased HF medication, (2) decreased HF medications, (3) patient tolerates current regiment based on HR, BP, symptoms, and kidney, and (4) patient is not tolerating current regimen*. This new requirement will enable a more objective measurement of provider practices than the self-reported survey results, and these data will be created with every patient visit and will be summarized monthly by the administrators within the medical system to support this project.

In addition to the survey data and electronic health record data, the DNP student will monitor the attendance of the educational session to measure attendance, monitor the subsequent medication adherence and attitudes of the education group, and potentially contrast it with the performance of the non-education group of providers. In this quasi-experimental research design, we will compare the post-education measures to their pre-education baseline values to determine

if there were significant changes that could be attributed to the intervention. Additional stratifications contrasting the changes in pre-/post- measures between the education and non-education providers will also be made. The convenience sample of providers and HF patients may not be adequate to power this study, and no a priori significance level will be established.

Project Measures

The project measures have been summarized in the measure's worksheet shown in Appendix F. The outcome and balancing measures are derived from EPIC database queries and attempt to identify the proportion of heart failure patients that have been titrated or who have shown signs of medication intolerance. These measures offer an independent and objective view of provider adherence, but they present a challenge due to the varying number of heart failure patients in the system at any time, the potential of any single patient to have their medication titrated more than once, and potentially over more than a single month. To solve this challenge, a patient's records will only be analyzed at the time of discharge. This means that one patient will not contribute to the summary results more than once, eliminating the potential for unwanted correlations that would occur if some patients fell into more than two or more monthly summaries. This approach also simplifies the measurement by looking at the entire record of the patient at the TCU rather than potentially breaking it into shorter intervals separated by month boundaries. By having the entire TCU record, the determination of titration or no-titration is less prone to error. An additional set of EPIC queries will stratify the data by provider group, separating providers that attended the educational intervention from those who did not.

The process measures described in Appendix F will be formed from the survey results compiled by the DNP student (see Appendix E.) and from the presentation attendance determined by the list of providers logged in to the video conference tool during the presentation.

Data Analysis Plan

Provider survey results will be analyzed in paired tests comparing the changes in the post-education responses to baseline. Providers who complete both surveys will be included in the results. Provider self-assessment of GDMT knowledge and titration practice provide ordinal data that will be analyzed with paired-samples Wilcoxon Signed-Rank test. This test is appropriate for ordinal data and compares the hypothesis that the mean value will increase in response to the educational intervention as compared to the null hypothesis of no change.

Provider practice from the EPIC database will provide monthly data on the numbers of heart failure patients, the number of patients who had their heart failure medications up-titrated, or changed, and whether they showed symptoms of intolerance. Data will be divided into pre-education baseline data and post-intervention data. The attendance roster for the educational intervention will be provided to the clinical data manager enabling them to stratify the data into a provider education group and a non-education group. These two groups and data collected at two time points (baseline and post-intervention) will be analyzed with a two-way repeated-measures ANOVA. The convenience sample of providers and HF patients may not be adequate to power this study, and no a priori significance level will be set for this pilot study; instead, p-values and confidence intervals will be reported.

IRB/Ethical Considerations

Research involving human participants conducted by students of the College of St. Scholastica must comply with the ethical requirements of the U.S. Code of Federal Regulations (CFR), Title 45 Part 46, and 21 CFR part 50 and 56, and the following core historical reports: Nuremberg Code, Declaration of Helsinki, and the Belmont Report. CFR Title 21, part 50 outlines the requirements for informed consent and additional safeguards for children in clinical

investigations, and part 56 describes the requirements of institutional review boards. CFR Title 45 Part 46 describes the additional protections required for vulnerable subjects, including pregnant women, neonates, human fetuses, and prisoners. St. Scholastica has established its own Institutional Review Board (IRB) to review all research activities conducted by students, faculty, and staff involving human subjects to comply with this obligation. The college also requires all researchers to complete training through the Collaborative Institutional Training Initiative (CITI) program. The CITI program educates researchers on ethics, responsible conduct, and regulatory oversight relevant to their research activities. The ethical aspects of the proposed intervention are chiefly associated with informed consent, subject confidentiality, and recruitment.

To assure informed consent in this project, interested participants will be provided with a written description of the study and instructed they may schedule a telephone call with the principal investigator to ask questions before giving consent. Informed written consent will be obtained from the subject using the document attached in Appendix G. Subjects will be informed that study participation is voluntary, and subjects retain their right to withdraw their consent at any time without any adverse effects. Study subjects will be told that participation in this study may help improve outcomes and quality of life for their heart failure patients and that sub-optimal use of heart failure drugs has been associated with significantly higher hospitalizations and mortality hazards.

To ensure subject confidentiality, Study participants will be assigned a study number that will be used instead of any identifying information. To minimize potential breach of confidentiality, completed survey data will be identified by a study number only in a filing system separate from any identifying information about the subjects. Only the principal investigator and the clinical study coordinator will have the need and necessary access to the

collected data. Study documents will be stored in locked file cabinets. All computerized data will be protected by password access. Email correspondence with participants will be retained for the duration of the study, then deleted.

The participants will be a convenience sample of providers from the Minnesota regional TCU system. Participation will be solicited via an email invitation sent to all TCU providers within the system. Any providers who respond to the email and sign the informed consent document will be included in this study. We anticipate twenty (N=20) providers will be recruited. It is expected that a population of medical providers may include disabled and elderly individuals. The inclusion criteria are that participants must be healthcare providers within the regional TCU system, defined as Medical Doctors, Nurse Practitioners, and Physicians' Assistants. No exclusion criteria are defined, and all eligible volunteers will be accepted into the study.

All clinical activities performed as part of this quality improvement project will be compliant with the established guidelines of the College of St. Scholastica. This DNP student has completed the required CITI training program for Social-Behavioral-Educational Researchers (see documentation in Appendix I.) This course presented the key ethical concepts associated with research on human subjects through case studies and described the IRB review process. An application for review by the College of St. Scholastica Institutional Review Board was completed by the DNP student and submitted on 3/30/2022. The project received an expedited review, and the board determined that the proposed activity does not meet the definition of research under the relevant federal regulations and does not require ongoing review or approval from The College of St. Scholastica Institutional Review Board (see Appendix H.)

This project will also abide by the Health Insurance Portability and Accountability Act (HIPAA) standards. No personal health information will be extracted from the patient charts by the hospital administrators in their monthly summaries of provider EPIC keyphrase responses. Finally, this research project will adhere to the American Nurses Association (ANA) Code of Ethics by,

- Respecting the inherent dignity and worth of each person (Provision 1)
- Advocating for the health and safety of heart failure patients (Provision 3)
- Supporting the accountability and responsibility of providers in the care of their patients (Provision 4)
- Promoting health, safety, personal and professional growth (Provision 5)
- Improving the work setting to make it more conducive to quality healthcare (Provision 6)
- Advancing the profession through scholarly inquiry and professional standards development (Provision 7)
- Collaborating with other health professionals to reduce health disparities (Provision 8)

Implementation

Project implementation was begun following IRB approval from the College of St. Scholatica IRB and the IRB of the regional TCU system. Implementation began with the recruitment phase of the project. All providers within the regional TCU system were contacted via email on May 26, 2022. The initial email described the quality improvement project, outlined its purpose, and highlighted the responsibilities of participation. Those responsibilities were described as (1) the completion of the baseline Attitudes and Practices survey (See Appendix F),

(2) attendance in the upcoming educational intervention to be presented at the next provider meeting, and (3) the completion of the follow-up survey.

An electronic version of the Attitudes and Practices questionnaire was created to facilitate the collection of survey data using the website freeonlinesurveys.com. This electronic survey made the collection of the data simple and anonymous, ensuring that no personally identifying information was collected and had to be managed. Eleven (11) providers responded to the email, and ten (10) completed the baseline survey. After studying the provider baseline feedback regarding reasons for not up-titrating, an educational intervention was developed consisting of an 18-slide PowerPoint presentation (see Appendix J.). The goal of the presentation was to communicate the rationale and potential benefits of up-titrating in the TCU environment in a brief 15-20 minute presentation. On June 23rd, 2022, the DNP student presented at the monthly providers meeting. Two weeks later, on July 11th, 2022, the follow-up survey was sent to providers. Due to the anonymity of the baseline survey, two additional questions were included to ascertain whether the respondent had completed the baseline survey and if they had attended the presentation. The follow-up survey received eleven (11) responses.

In parallel with this activity, the regional TCU implemented the EPIC smartphrase .TCUHFSTATUS. in April 2022. This dataset is anticipated to be summarized by the TCU site administrator in the August 2022 timeframe and is not available in time to complete this document. These data will be summarized and integrated into the project to justify its value and further the goal of sustaining its impact on the TCU system.

Results from Data Collection

The recruitment email was sent to twenty-seven (27) providers in the regional TCU system. Eleven (11) providers were recruited for the study, giving the recruitment phase a 41%

(11/27) success rate. The baseline survey received ten responses. Table 6 shows the summary of the results of the three survey questions. The baseline showed that 100% percent of the responding providers had recently cared for HF patients, highlighting the importance of provider knowledge and the opportunity for optimizing care within the TCU system. The self-reported knowledge of GDMT targets and up-titration was only 6.30 on a scale of zero to ten, with a standard deviation of 1.38. This result suggests an opportunity to impact provider knowledge through educational intervention. It may not only highlight the importance of medication optimization for patients but may serve as a brief refresher to the providers on heart failure care. More optimistically, 80% of the providers responded that they currently up-titrate their patients, and 100% reported at least sometimes up-titrating patients. The low rate of responses in the categories of "sometimes" resulted in meager feedback on the providers' rationale. Only one respondent answered the final question. They reasoned that they would potentially defer to cardiology due to patient frailty or complexity. This feedback and the baseline results were considered while constructing the presentation. The slides shown in Appendix J reflect this feedback and show an emphasis on GDMT/HF knowledge.

	Baseline	Follow-up
Knowledge Level (0-10)	6.30 +/- 1.38	7.55 +/- 1.28
Percent of providers with HF patients in the previous eight weeks	100% (10/10)	100% (11/11)
Percent of providers attempting up-titration (yes, sometimes, no)	80%/20%/0% (out of ten)	70%/30%/0% (out of 10)

Table 6: Attitudes and Practices numerical, binary and ordinal results

Following the educational intervention, the follow-up survey was delivered via emailed links to the electronic Attitudes and Practices questionnaire. Since the follow-up survey was sent

to all 27 providers, additional questions were included asking if the respondent had completed the baseline survey and if they had attended the presentation. Eleven responses were received, with 100% of the respondents reporting that they had responded to the baseline survey, and 64% (7/11) reported attendance at the presentation. The results of the follow-up survey are shown in Table 6. The knowledge score increased to 7.55 on a 0-10 scale with a standard deviation of 1.28. Again, all respondents reported having recently cared for HF patients, and of the ten respondents to the question about up-titrating, the results were 70% reported they up-titrated their eligible patients, and 100% reported that they up-titrate at least sometimes. The three respondents that answered only up-titrating "sometimes" gave their rationale,

- RESPONDENT #1: *If they are being closely followed by cardiology then I might focus more on keeping them euvolemic. If they were "my" patients as PCP rather than TCU, I certainly would. Alternatively, when I increase or decrease meds I try to in-basket message the CHF team.*
- RESPONDENT #4*: [I] rarely have [a] patient under my care long enough to follow up of changes made, manage acute issues but leave long-term management[t] to PCP*
- RESPONDENT #11: *Patients are typically not in a stable situation in TCU, weights and VS in all facilities are notoriously inaccurate, I tend to treat each patient individually according to their symptoms when I see them(mostly only one time during their TCU stay) as there is no ongoing relationship or follow up of patients while they are in my care, their stay is typically short with the goal of discharge as soon as possible. Of course, any acute decompensation is treated*

more aggressively, but for most of my TCU population heart failure is a secondary issue and is relatively stable.

Discussion of Data/Outcomes Interpretation

The follow-up survey dataset had 100% yes responses to the question "Did you participate in the Baseline survey." The follow-up data did, however, contain four respondents who did not attend the educational presentation. The DNP student ran both independent t-tests and two-way ANOVAs and found comparable answers to the main questions considered. For simplicity, only the simpler statistical tests are presented.

Hypothesis #1, The intervention will result in an increase in provider self-reported knowledge

Two-Tailed Independent Samples *t*-Test

Introduction

A two-tailed independent samples *t*-test was conducted to examine whether the mean Knowledge score was significantly different between the categories of Baseline/Follow-up.

Assumptions

Normality. Shapiro-Wilk tests were conducted to determine whether the Knowledge score could have been produced by a normal distribution for each category of Baseline/Follow-up (Razali & Wah, 2011). The result of the Shapiro-Wilk test for Knowledge score in the Baseline data category was significant based on an alpha value of .05, $W = 0.83$, $p = .034$. This result suggests that the Knowledge score in the Baseline data is unlikely to have been produced by a normal distribution. The result of the Shapiro-Wilk test Knowledge score in the Follow-up data category was not significant based on an alpha value of .05, $W = 0.91$, $p = .429$. This result suggests that a normal distribution cannot be ruled out as the underlying distribution for the

Knowledge score in the Follow-up data category. The Shapiro-Wilk test was significant for the Baseline category, indicating the normality assumption is violated.

Homogeneity of Variance. Levene's test was conducted to assess whether the variance of Knowledge score was equal between the categories of Baseline and Follow-up surveys. The result of Levene's test for Knowledge score was not significant based on an alpha value of .05, $F(1, 15) = 0.50$, $p = .490$. This result suggests it is possible that the variance of Knowledge score is equal for each category of Baseline and Follow-up, indicating the assumption of homogeneity of variance was met.

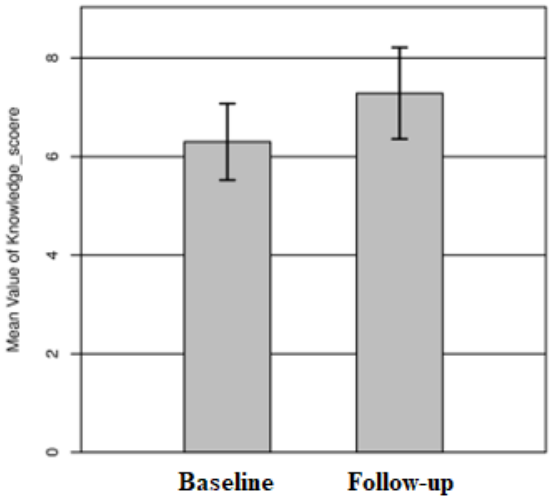


Figure 1: *The mean Knowledge score by levels of Baseline/Follow-up with 95.00% CI Error Bars*

Results

The result of the two-tailed independent samples *t*-test was not significant based on an alpha value of .05, $t(15) = -1.60$, $p = .131$, indicating that the null hypothesis cannot be rejected. This finding suggests the mean of the Knowledge score was not significantly different between the Baseline and Follow-up surveys. The results are presented in Table 7. A bar plot of the means is presented in Figure 1.

Table 7: *Two-Tailed Independent Samples t-Test for Knowledge score by Baseline/Follow-up*

	Baseline		Follow-up				
Variable	*M*	*SD*	*M*	*SD*	*t*	*p*	*d*
Knowledge score	6.30	1.25	7.29	1.25	-1.60	.131	0.79

Note. N = 17. Degrees of Freedom for the *t*-statistic = 15. *d* represents Cohen's *d.*

Two-Tailed Mann-Whitney *U* Test

Introduction

A two-tailed Mann-Whitney two-sample rank-sum test was conducted to examine whether there were significant differences in the Knowledge score between the levels of Baseline and Follow-up. The two-tailed Mann-Whitney two-sample rank-sum test is an alternative to the independent samples *t*-test but does not share the same assumptions (Conover & Iman, 1981). There were ten observations in the Baseline group and seven in the Follow-up group.

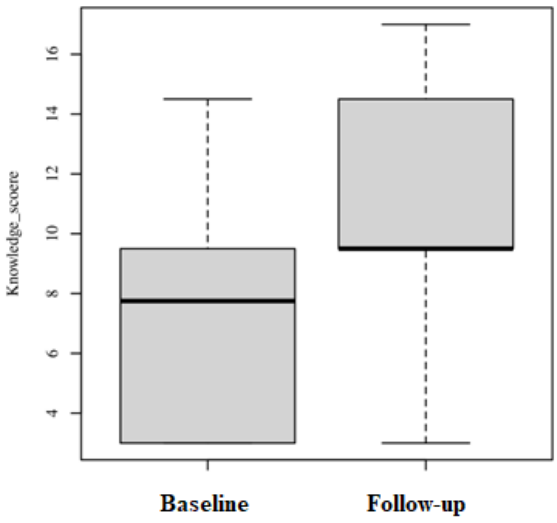


Figure 2: Ranks of Knowledge score by Survey_Nominal

Results

The result of the two-tailed Mann-Whitney *U* test was not significant based on an alpha value of .05, $U = 20.5$, $z = -1.48$, $p = .140$. The mean rank for the Baseline data was 7.55, and the mean rank for the Follow-up data was 11.07. This suggests that the distribution of the Knowledge score for the Baseline data ($Mdn = 6.50$) was not significantly different from the distribution of the Knowledge score for the Follow-up data ($Mdn = 7.00$) category. Table 8 presents the result of the two-tailed Mann-Whitney *U* test. Figure 2 presents a boxplot of the ranks of Knowledge score by Survey_Nominal.

Table 8: *Two-Tailed Mann-Whitney Test for Knowledge score by Survey_Nominal*

	Mean Rank				
Variable	Baseine	Follow-up	*U*	*z*	*p*
Knowledge score	7.55	11.07	20.50	-1.48	.140

Hypothesis #2: The intervention will increase provider self-reported up-titration practices

The response to the question "Do you currently attempt to up-titrate your eligible heart failure patients?" consisted of three potential responses, "yes," "sometimes," and "no." This data was interpreted as ordinal for the following significance test.

Two-Tailed Mann-Whitney *U* Test

Introduction

A two-tailed Mann-Whitney two-sample rank-sum test was conducted to examine whether there were significant differences in Titrating_patients between the levels of Baseline and Follow-up. The two-tailed Mann-Whitney two-sample rank-sum test is an alternative to the independent samples *t*-test but does not share the same assumptions (Conover & Iman, 1981). There were ten observations in the Baseline data and six observations in Follow-up data.

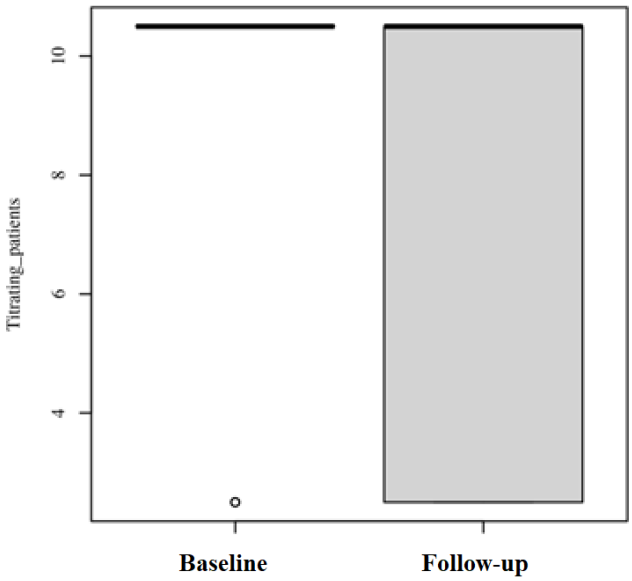


Figure 3: *Ranks of Titrating_patients by Survey*

Results

The result of the two-tailed Mann-Whitney *U* test was not significant based on an alpha value of .05, $U = 34$, $z = -0.58$, $p = .564$. The mean rank for the Baseline data was 8.90, and the mean rank for the Follow-up data was 7.83. This suggests that the distribution of results for the Titrating_patients data for the Baseline group (*Mdn* = 10.50) was not significantly different from the distribution of Titrating_patients data for the Follow-up (*Mdn* = 10.50) group. Table 9 presents the result of the two-tailed Mann-Whitney *U* test. Figure 3 presents a boxplot of the ranks of Titrating_patients by Survey.

Table 9: *Two-Tailed Mann-Whitney Test for Titrating_patients by Survey*

	Mean Rank				
Variable	Baseline	Follow-up	*U*	*z*	*p*
Titrating_patients	8.90	7.83	34.00	-0.58	.564

Discussion

The descriptive statistics of the knowledge scores show a tantalizing increase in knowledge scores in the follow-up dataset. Unfortunately, these results and the titration question were inconclusive, failing to achieve statistical significance at the alpha = 0.05 level. This result was anticipated owing to the convenience sample that included only six participants that completed both surveys and attended the educational presentation.

Dissemination

The presentation has been disseminated within the regional TCU system, and the DNP student anticipates that this project will be presented at the poster session at a future nursing conference. The abstract for the conference submission is presented in Appendix K.

Conclusion

The effectiveness of guideline-directed medication therapy in controlling the symptoms and reducing rehospitalization and mortality for patients with systolic heart failure is well established. Yet, a significant number of patients remain at sub-optimal dosages of these life-saving therapies. The reasons for this gap are complex and include patient-related factors together with system, payer, and coverage issues. In addition, provider-related issues such as provider inertia/aversion and lack of knowledge also appear to play a role in the care gap. The proposed project seeks to address this gap in care within the transitional care/out-patient setting by providing an educational intervention to providers, together with a patient education video. This literature review provides compelling evidence to support the proposed project. Evidence

has been marshaled to support the following logical argument that there is widespread sub-optimal titration for HFrEF patients and that this gap is associated with provider inertia and gaps in knowledge and is more likely to occur in out-patient clinics. The evidence showed that sub-optimal medication titration is associated with negative outcomes, including significant increases in mortality hazards, and that educational interventions have been shown to improve outcomes and increase the numbers of patients with appropriate medication dosages. Taken together, this provides strong support for the proposed intervention and suggests a strong likelihood that the project will have a positive impact.

References

Allen, L. A., Venechuk, G., McIlvennan, C. K., Page, R. L., Knoepke, C. E., Helmkamp, L. J., Khazanie, P., Peterson, P. N., Pierce, K., Harger, G., Thompson, J. S., Dow, T. J., Richards, L., Huang, J., Strader, J. R., Trinkley, K. E., Kao, D. P., Magid, D. J., Buttrick, P. M., & Matlock, D. D. (2021). An Electronically Delivered Patient-Activation Tool for Intensification of Medications for Chronic Heart Failure With Reduced Ejection Fraction. *Circulation*, *143*(5), 427–437. https://doi.org/10.1161/CIRCULATIONAHA.120.051863

Allina. (2021). *Allina Health Values Statement*. https://www.allinahealth.org/-/media/allina-health/files/allina-health-mission-vision-values-promise.pdf

Atherton, J. J., & Hickey, A. (2017). Expert comment: Is medication titration in heart failure too complex? *Cardiac Failure Review*, *3*(1), 25.

Balakumaran, K., Patil, A., Marsh, S., Ingrassia, J., Kuo, C.-L., Jacoby, D. L., Arora, S., & Soucier, R. (2019). Evaluation of a guideline directed medical therapy titration program in patients with heart failure with reduced ejection fraction. *IJC Heart & Vasculature*, *22*, 1–5.

Barreras, A., & Gurk-Turner, C. (2003). Angiotensin II receptor blockers. *Proceedings (Baylor University. Medical Center)*, *16*(1), 123–126.

Belardinelli, R., Georgiou, D., Cianci, G., & Purcaro, A. (1999). Randomized, controlled trial of long-term moderate exercise training in chronic heart failure: Effects on functional capacity, quality of life, and clinical outcome. *Circulation*, *99*(9), 1173–1182.

Blecker, S., Herrin, J., Li, L., Yu, H., Grady, J. N., & Horwitz, L. I. (2019). Trends in Hospital Readmission of Medicare-Covered Patients With Heart Failure. *Journal of the American College of Cardiology*, *73*(9), 1004–1012. https://doi.org/10.1016/j.jacc.2018.12.040

Bœuf-Gibot, S., Pereira, B., Imbert, J., Kerroum, H., Menini, T., Lafarge, E., De Carvalho, M., Vorilhon, P., Boussageon, R., & Vaillant-Roussel, H. (2021). Benefits and adverse effects of ACE inhibitors in patients with heart failure with reduced ejection fraction: A systematic review and meta-analysis. *European Journal of Clinical Pharmacology*, *77*(3), 321–329. https://doi.org/10.1007/s00228-020-03018-4

Bozkurt, B. (2019). Reasons for Lack of Improvement in Treatment With Evidence-Based Therapies in Heart Failure∗. *Journal of the American College of Cardiology*, *73*(19), 2384–2387. https://doi.org/10.1016/j.jacc.2019.03.464

CDC. (2020, September 8). *Heart Failure | cdc.gov*. Centers for Disease Control and Prevention. https://www.cdc.gov/heartdisease/heart_failure.htm

Chatterjee, K., & Massie, B. (2007). Systolic and diastolic heart failure: Differences and similarities. *Journal of Cardiac Failure*, *13*(7), 569–576. https://doi.org/10.1016/j.cardfail.2007.04.006

Conover, W. J., & Iman, R. L. (1981). Rank transformations as a bridge between parametric and nonparametric statistics. *The American Statistician*, *35*(3), 124–129.

Cornelio, C., & Di Palo, K. E. (2018). Guideline-Directed Medical Therapy in Hospitalized Heart Failure Patients: Still Underprescribed Despite Updated Guidelines and Over 20 Years of Evidence. *Journal of Cardiac Failure*, *24*(8), S100.

Dang, D., & Dearholt, S. (2018). *Supplemental materials for Johns Hopkins Nursing Evidence-Based Practice: Model and Guidelines*. Sigma Theta Tau International.

Djoussé, L., Driver, J. A., & Gaziano, J. M. (2009). Relation between modifiable lifestyle factors and lifetime risk of heart failure. *Jama*, *302*(4), 394–400.

Driscoll, A., Srivastava, P., Toia, D., Gibcus, J., & Hare, D. L. (2014). A nurse-led up-titration clinic improves chronic heart failure optimization of beta-adrenergic receptor blocking therapy—A randomized controlled trial. *BMC Research Notes*, *7*(1), 668. https://doi.org/10.1186/1756-0500-7-668

Dunlay, S. M., Manemann, S. M., Chamberlain, A. M., Cheville, A. L., Jiang, R., Weston, S. A., & Roger, V. L. (2015). Activities of Daily Living and Outcomes in Heart Failure. *Circulation. Heart Failure*, *8*(2), 261–267. https://doi.org/10.1161/CIRCHEARTFAILURE.114.001542

Dunlay, S. M., Roger, V. L., & Redfield, M. M. (2017). Epidemiology of heart failure with preserved ejection fraction. *Nature Reviews Cardiology*, *14*(10), 591–602. https://doi.org/10.1038/nrcardio.2017.65

Espinoza, C., Alkhateeb, H., & Siddiqui, T. (2021). Updates in pharmacotherapy of heart failure with reduced ejection fraction. *Annals of Translational Medicine*, *9*(6), 516. https://doi.org/10.21037/atm-20-4640

Fitzgerald, A. A., Powers, J. D., Ho, P. M., Maddox, T. M., Peterson, P. N., Allen, L. A., Masoudi, F. A., Magid, D. J., & Havranek, E. P. (2011). Impact of Medication Nonadherence on Hospitalizations and Mortality in Heart Failure. *Journal of Cardiac Failure*, *17*(8), 664–669. https://doi.org/10.1016/j.cardfail.2011.04.011

Fuery, M. A., Chouairi, F., Januzzi, J. L., Moe, G. W., Caraballo, C., McCullough, M., Miller, P. E., Reinhardt, S. W., Clark, K., Oseran, A., Milner, A., Pacor, J., Kahn, P. A., Singh, A., Ravindra, N., Guha, A., Vadlamani, L., Kulkarni, N. S., Fiuzat, M., … Desai, N. R. (2021). Intercountry Differences in Guideline-Directed Medical Therapy and Outcomes

Among Patients With Heart Failure. *JACC. Heart Failure*, *9*(7), 497–505. https://doi.org/10.1016/j.jchf.2021.02.011

Gathright, E. C., Dolansky, M. A., Gunstad, J., Redle, J. D., Josephson, R., Moore, S. M., & Hughes, J. W. (2017). The Impact of Medication Non-Adherence on the Relationship Between Mortality Risk and Depression in Heart Failure. *Health Psychology : Official Journal of the Division of Health Psychology, American Psychological Association*, *36*(9), 839–847. https://doi.org/10.1037/hea0000529

Go, A. S., Mozaffarian, D., Roger, V. L., Benjamin, E. J., Berry, J. D., Borden, W. B., Bravata, D. M., Dai, S., Ford, E. S., & Fox, C. S. (2013). Heart disease and stroke statistics—2013 update: A report from the American Heart Association. *Circulation*, *127*(1), e6–e245.

Gouya, G., Hammer, A., Elhenicky, M., Neuhold, S., Wolzt, M., Hülsmann, M., & Pacher, R. (2011). Benefit of specialized clinics for the treatment of patients with heart failure. *European Journal of Internal Medicine*, *22*(4), 428–431.

Greene, S. J., Butler, J., Albert, N. M., DeVore, A. D., Sharma, P. P., Duffy, C. I., Hill, C. L., McCague, K., Mi, X., Patterson, J. H., Spertus, J. A., Thomas, L., Williams, F. B., Hernandez, A. F., & Fonarow, G. C. (2018). Medical Therapy for Heart Failure With Reduced Ejection Fraction: The CHAMP-HF Registry. *Journal of the American College of Cardiology*, *72*(4), 351–366. https://doi.org/10.1016/j.jacc.2018.04.070

Greene, S. J., Fonarow, G. C., DeVore, A. D., Sharma, P. P., Vaduganathan, M., Albert, N. M., Duffy, C. I., Hill, C. L., McCague, K., & Patterson, J. H. (2019). Titration of medical therapy for heart failure with reduced ejection fraction. *Journal of the American College of Cardiology*, *73*(19), 2365–2383.

Hickey, A., Suna, J., Marquart, L., Denaro, C., Javorsky, G., Munns, A., Mudge, A., & Atherton, J. J. (2016). Improving medication titration in heart failure by embedding a structured medication titration plan. *International Journal of Cardiology*, *224*, 99–106.

Jarjour, M., Henri, C., de Denus, S., Fortier, A., Bouabdallaoui, N., Nigam, A., O'Meara, E., Ahnadi, C., White, M., Garceau, P., Racine, N., Parent, M.-C., Liszkowski, M., Giraldeau, G., Rouleau, J.-L., & Ducharme, A. (2020). Care Gaps in Adherence to Heart Failure Guidelines: Clinical Inertia or Physiological Limitations? *JACC: Heart Failure*, *8*(9), 725–738. https://doi.org/10.1016/j.jchf.2020.04.019

Kommuri, N. V., Johnson, M. L., & Koelling, T. M. (2012). Relationship between improvements in heart failure patient disease specific knowledge and clinical events as part of a randomized controlled trial. *Patient Education and Counseling*, *86*(2), 233–238.

Lenihan, D. J., & Uretsky, B. F. (2000). Nonpharmacologic treatment of heart failure in the elderly. *Clinics in Geriatric Medicine*, *16*(3), 477–487.

Lesyuk, W., Kriza, C., & Kolominsky-Rabas, P. (2018). Cost-of-illness studies in heart failure: A systematic review 2004–2016. *BMC Cardiovascular Disorders*, *18*(1), 74. https://doi.org/10.1186/s12872-018-0815-3

Levy, D., Kenchaiah, S., Larson, M. G., Benjamin, E. J., Kupka, M. J., Ho, K. K., Murabito, J. M., & Vasan, R. S. (2002). Long-term trends in the incidence of and survival with heart failure. *New England Journal of Medicine*, *347*(18), 1397–1402.

Loop, M. S., Van Dyke, M. K., Chen, L., Brown, T. M., Durant, R. W., Safford, M. M., & Levitan, E. B. (2020). Evidence-based beta blocker use associated with lower heart failure readmission and mortality, but not all-cause readmission, among Medicare

beneficiaries hospitalized for heart failure with reduced ejection fraction. *PLoS ONE*, *15*(7), e0233161. https://doi.org/10.1371/journal.pone.0233161

McCullough, P. A., Mehta, H. S., Barker, C. M., Houten, J. V., Mollenkopf, S., Gunnarsson, C., Ryan, M., & Cork, D. P. (2021). Healthcare utilization and guideline-directed medical therapy in heart failure patients with reduced ejection fraction. *Journal of Comparative Effectiveness Research*, *10*(14), 1055–1063.

McCullough, P. A., Mehta, H. S., Barker, C. M., Van Houten, J., Mollenkopf, S., Gunnarsson, C., Ryan, M., & Cork, D. P. (2021). Mortality and guideline-directed medical therapy in real-world heart failure patients with reduced ejection fraction. *Clinical Cardiology*, *44*(9), 1192–1198. https://doi.org/10.1002/clc.23664

McLachlan, A., Aldridge, C., Morgan, M., Lund, M., Gabriel, R., & Malez, V. (2021). An NP-led pilot telehealth programme to facilitate guideline-directed medical therapy for heart failure with reduced ejection fraction during the COVID-19 pandemic. *The New Zealand Medical Journal (Online)*, *134*(1538), 77–6.

NHLBI. (2021). *Heart Failure | NHLBI, NIH*. https://www.nhlbi.nih.gov/health-topics/heart-failure

Oliver-McNeil, S., Bowers, M., LaRue, S. J., Vader, J., DeVore, A. D., & Granger, B. B. (2020). Benefits of Optimizing Heart Failure Medication Dosage. *The Journal for Nurse Practitioners*, *16*(7), 498–503.

Razali, N. M., & Wah, Y. B. (2011). Power comparisons of shapiro-wilk, kolmogorov-smirnov, lilliefors and anderson-darling tests. *Journal of Statistical Modeling and Analytics*, *2*(1), 21–33.

Riegel, B., Lee, C. S., Ratcliffe, S. J., De Geest, S., Potashnik, S., Patey, M., Sayers, S. L., Goldberg, L. R., & Weintraub, W. S. (2012). Predictors of Objectively Measured Medication Nonadherence in Adults With Heart Failure. *Circulation: Heart Failure*, *5*(4), 430–436. https://doi.org/10.1161/CIRCHEARTFAILURE.111.965152

Sabaté, E., & Sabaté, E. (2003). *Adherence to long-term therapies: Evidence for action*. World Health Organization.

Shah, K. S., Xu, H., Matsouaka, R. A., Bhatt, D. L., Heidenreich, P. A., Hernandez, A. F., Devore, A. D., Yancy, C. W., & Fonarow, G. C. (2017). Heart Failure With Preserved, Borderline, and Reduced Ejection Fraction: 5-Year Outcomes. *Journal of the American College of Cardiology*, *70*(20), 2476–2486. https://doi.org/10.1016/j.jacc.2017.08.074

Sin, D. D., & McAlister, F. A. (2002). The effects of beta-blockers on morbidity and mortality in a population-based cohort of 11,942 elderly patients with heart failure. *The American Journal of Medicine*, *113*(8), 650–656. https://doi.org/10.1016/S0002-9343(02)01346-3

Vedin, O., Lam, C. S. P., Koh, A. S., Benson, L., Teng, T. H. K., Tay, W. T., Braun, O. Ö., Savarese, G., Dahlström, U., & Lund, L. H. (2017). Significance of Ischemic Heart Disease in Patients With Heart Failure and Preserved, Midrange, and Reduced Ejection Fraction. *Circulation: Heart Failure*, *10*(6), e003875. https://doi.org/10.1161/CIRCHEARTFAILURE.117.003875

Virani, S. S., Alonso, A., Aparicio, H. J., Benjamin, E. J., Bittencourt, M. S., Callaway, C. W., Carson, A. P., Chamberlain, A. M., Cheng, S., & Delling, F. N. (2021). Heart disease and stroke statistics—2021 update: A report from the American Heart Association. *Circulation*, *143*(8), e254–e743.

Wu, J.-R., Lennie, T. A., Dekker, R. L., Biddle, M. J., & Moser, D. K. (2013). Medication Adherence, Depressive Symptoms, and Cardiac Event-Free Survival in Patients with Heart Failure. *Journal of Cardiac Failure*, *19*(5), 317–324. https://doi.org/10.1016/j.cardfail.2013.03.010

Wu, J.-R., & Moser, D. K. (2018). Medication Adherence Mediates the Relationship Between Heart Failure Symptoms and Cardiac Event-Free Survival in Patients with Heart Failure. *The Journal of Cardiovascular Nursing*, *33*(1), 40–46. https://doi.org/10.1097/JCN.0000000000000427

Wu, J.-R., Moser, D. K., Lennie, T. A., & Burkhart, P. V. (2008). Medication Adherence in Patients Who Have Heart Failure: A Review of the Literature. *Nursing Clinics of North America*, *43*(1), 133–153. https://doi.org/10.1016/j.cnur.2007.10.006

Appendix A: Patient Checklist

Your Heart Failure Medicines Checklist:

*Work with your doctor for **ONE Positive Change!***

Below is a chart that shows the different heart failure medications. Please:
1) Check off which medicines you take in the "common names of medicine" column.
2) Fill in the dose of medicine that you take each day in the "my current dose" column.

Bring this chart to your next clinic appointment and discuss your medicines with your medical provider or doctor. **Aim to make one positive change.**

Medicine Family	Common Names of Medicine (Brand name)	My Current Dose	Target Dose	Your Cost
Water Pill (diuretic)	❒ *Furosemide (Lasix)*		As much as you need to feel better	
	❒ *Bumetanide (Bumex)*			
	❒ *Torsemide (Demadex)*			
Adrenaline Blocking (beta blocker)	❒ *Carvedilol (Coreg)*		25-50 mg 2x per day	
	❒ *Metoprolol Succinate (Toprol XL)*		200 mg daily	
	❒ *Bisoprolol (Zebeta)*		10 mg daily	
Blood Vessel Relaxing (ACE/ARB)	❒ *Sacubutril/Valsartan (Entresto)* [recommended medicine]		97/103 mg 2x per day	
	❒ *Lisinopril (Prinivil or Zestril)*		20-40 mg daily	
	❒ *Enalapril (Vasotec)*		10-20 mg 2x per day	
	❒ *Captopril (Capoten)*		50 mg 2x per day	
	❒ *Ramipril (Altace)*		10 mg daily	
	❒ *Losartan (Cozaar)*		100-150 mg daily	
	❒ *Candesartan (Atacand)*		32 mg daily	
	❒ *Valsartan (Diovan)*		160 mg 2x per day	
Potassium Raising	❒ *Spironolactone (Aldactone)*		50 mg daily	
	❒ *Eplerenone (Inspra)*		50 mg daily	
Sodium Glucose Eliminating	❒ *Canagliflozin (Invokana)*		100 mg daily	
	❒ *Dapagliflozin (Farxiga)*		10 mg daily	
	❒ *Empagliflozin (Jardiance)*		10 mg daily	
	❒ *Ertugliflozin (Steglatro)*		5 mg or 15 mg daily	
OTHERS to consider	❒ *Hydralazine/Isosorbide*		100 mg/40 mg 3x per day	
	❒ *Ivabradine (Corlanor)*		7.5 mg 2x per day	
	❒ *Digoxin (Lanoxin or Digoxin)*		Depends on kidney function (0.0625-0.25 mg daily or every other day)	

Remember: YOU are the person who knows you best. YOU have the most to gain by being on the best treatments possible. YOU have a right to ask questions about your own care!

Appendix B: GANTT Chart

Task	Owner	2021				2022							
		9	10	11	12	1	2	3	4	5	6	7	8
		NSG8201				NSG8206				NSG8207			
Project Design	AH, RF												
Develop project scope	AH, RF												
Develop objectives	AH, RF												
Identify Stakeholders	AH, RF, PI												
Research	AH, PI												
Project Planning	AH, PI, PM, RF												
Identify project team	AH, RF, PI												
Develop project plan	AH, PI, PM, RF												
Council Approval	AH, PI												
IRB Approval	AH, PI, RF												
Intervention	AH, PM, PI												
Baseline Survey	AH, PM												
Survey Design	AH, PI												
Survey Delivery	AH, PM												
Survey Analysis	AH												
Provider Presentation	AH, PM												
Presentation Design	AH, PI, PM												
Presentation Delivery	AH, PM, PI												
Provider attendance	AH, PM												
Follow-up Survey	AH, PM												
Results	AH												
Analyze Survey Data	AH												
Gather prescribing data	AH, PI, PM												
Inferential Statistics	AH												
Summarize Findings	AH												
Evaluation													
Write Final Report	AH												
Results Dissemination	AH, PI, PM, RF												

AH = Anastasiya Huberty, PI = Study site Principal Investigator, PM = Study site Provider Manager, RF = Dr. Rhea Ferry

Appendix C: Work Breakdown Structure

1.0 Design

- 1.1 Develop Project Scope
- 1.2 Develop Project Objectives
- 1.3 Identify Stakeholders
- 1.4 Research, Literature Review, SWOT

2.0 Plan

- 2.1 Identify Project Team
- 2.2 Develop Project Plan
- 2.3 Obtain Council Approval
- 2.4 Obtain IRB approval

3.0 Intervention

- 3.1 Baseline Provider Survey
  - 3.1.1 Survey Design
  - 3.1.2 Survey Delivery
  - 3.1.3 Survey Results Analysis
- 3.2 Provider Presentation
  - 3.2.1 Presentation Design
  - 3.2.2 Presentation Delivery
- 3.3 Follow-up Survey

4.0 Results

- 4.1 Analyze Survey Data
- 4.2 Collect and analyze provider prescribing data
- 4.3 Develop inferential statistics
- 4.4 Summarize Findings

5.0 Evaluation

- 5.1 Write final report
- 5.2 Results dissemination
  - 5.2.1 DNP paper
  - 5.2.2 DNP presentation

Appendix D: Communication Matrix

Project Title: Incorporating Heart Failure Titration Guidelines into the TCU/Outpatient Care Setting

Project Chair: Dr. Rhea Ferry

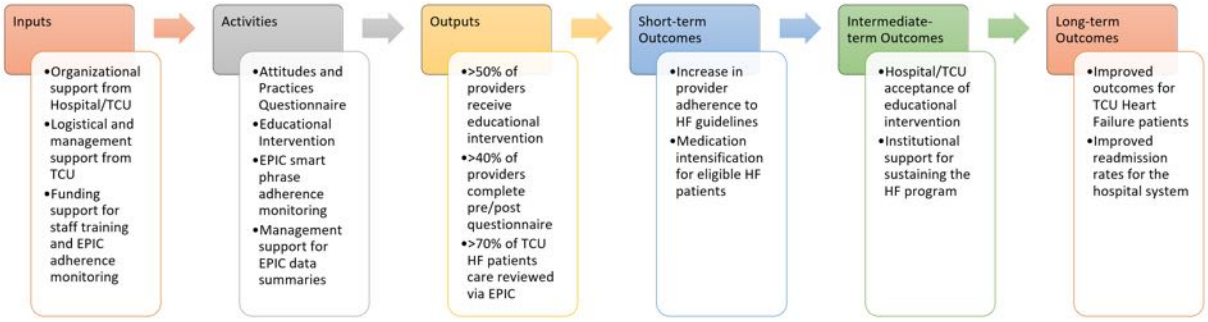
Project Stakeholders: TCU providers, TCU patients, Clinical Site Principal Investigator, Clinical Site Provider Manager

ID#	Purpose/Objectives	Method of Communication	Frequency	Recipient	Person Responsible	Notes
1	Meet with the Heart Failure program director to validate the project's significance	email	once	HF specialist	AH	a few emails were exchanged, and support and encouragement for the project were earned
2	Meet with site research coordinator to finalize research plan and review research council form	email/zoom	weekly	PI	AH	Ongoing communication with the Clinical Site PI to develop and complete the applications for human research within their clinical system
3	Meet with the provider manager to coordinate the survey email and plan the educational meeting	email/zoom	bi-weekly	PM	AH	Ongoing discussions about organizing the logistics of the project
4	Meet with Dr. Ferry for project status review and planning	email/zoom	monthly	RF	AH	These meetings are essential to keep this project on track
5	Communication with providers involved in the project	email/zoom/in-person	As needed	AH	AH	To obtain feedback from the TCU providers

AH = Anastasiya Huberty, PI = Study site Principal Investigator, PM = Study site Provider Manager, RF = Dr. Rhea Ferry

Appendix E: Logic Model

Logic Model: Incorporating Heart Failure Titration Guidelines into the TCU/Outpatient Care Setting



Appendix F: Attitudes and Practices Questionnaire

1. How would you score your level of knowledge concerning guideline-directed medical therapies (GDMT) for heart failure patients and the process of properly titrating dosages to GDMT targets? <0-no knowledge – 10-expert>

2. Have you had a heart failure patient with reduced ejection fraction under your care within the last eight weeks? <yes/no>

3. Do you currently attempt to up-titrate your eligible heart failure patients? <yes/sometimes/no>

4. If you did not answer yes to question 3, can you give your reasons for not doing so? <open-ended>

Appendix F: Project Measures

Outcome measures		
percent of HF patients titrated at TCU	This measure indicates the number of HF patients receiving medication increases or decreases as identified by EPIC keywords, divided by the total number of HF patients. This measure will be accumulated monthly	Queries of the EPIC database will be run by the clinical staff in support of this project. Monthly queries will identify HF patients discharged during the previous period (forming the denominator) and will query their notes to identify EPIC keywords for increases or decreases in heart failure medication. If either is found at least once, the patient will be added to the numerator.
percent of HF patients up titrated at TCU	This measure indicates the number of HF patients receiving medication increases as identified by EPIC keywords, divided by the total number of HF patients. This measure will be accumulated monthly	Queries of the EPIC database will be run by the clinical staff in support of this project. Monthly queries will identify HF patients discharged during the previous period (forming the denominator) and will query their notes to identify EPIC keywords for increases in heart failure medication. If found at least once, the patient will be added to the numerator.
Process measures		
provider level of GDMT knowledge	This self-reported quantitative score will be measured via a Likert scale (0-no knowledge, 10-expert)	The survey results will be collected by the DNP student
provider titration practice	This self-reported measure will assess provider practice regarding the up-titration of HF patients. The response will have three ordinal response values, yes (titrates), sometimes (titrates), and no (doesn't titrate)	The survey results will be collected by the DNP student
percent of providers attending educational intervention	This measure indicates the number of providers who attend the educational session divided by the total number of providers within the TCU system	Attendance will be monitored by the DNP student during the presentation

Balancing Measures		
percent of patients experiencing intolerance to titration	This measure indicates the number of HF patients receiving medication increases or decreases as identified by EPIC keywords, divided by the total number of HF patients. This measure will be accumulated monthly	Queries of the EPIC database will be run by the clinical staff in support of this project. Monthly queries will identify HF patients discharged during the previous period (forming the denominator) and will query their notes to identify EPIC keywords for symptoms of medication intolerance. If found at least once, the patient will be added to the numerator.

Appendix G: Informed Consent Document

The College of St. Scholastica

Incorporating Heart Failure Titration Guidelines into the TCU/Outpatient Care Setting

Informed Consent

You are invited to participate in a quality improvement project investigating the effectiveness of an educational intervention for healthcare providers of heart failure patients in the TCU/outpatient setting. The educational intervention will take the form of a virtual presentation to be delivered during a routine provider meeting. The educational intervention will discuss the importance of successfully up-titrating patients to Guideline-directed medical therapy (GDMT) targets or the maximum tolerable dosages. An overview of the GDMT targets and the steps to successfully up-titrating patients will be provided. This study is being conducted by Anastasiya Huberty, a graduate student in the Department of Nursing under the supervision of Dr. Rhea Ferry. You were selected as a possible participant because you are a provider within the Allina TCU system. We ask that you read this form and ask any questions you may have before agreeing to be in the study.

Study Purpose

The purpose of this study is to explore the impact of a short educational intervention on the delivery of care to heart failure patients within the TCU system.

Study Procedure

If you agree to participate in this study, we will ask you to make complete a short survey at the very beginning of the study and again at the completion of the study. The survey consists of four questions, and we expect you will easily complete it within five minutes. At a monthly Allina TCU provider meeting following the completion of the first survey, the principal investigator will deliver a short ten-minute educational presentation about the optimization of care for heart failure patients at Allina TCUs. If you agree to be in this study, your time commitment will be minimal, approximately twenty minutes.

Risk of Study Participation

This is considered a minimal-risk study. Privacy will be protected by the Principal Investigator. Study participants will be assigned a study number, and all study data (surveys) will be stored with the de-identified subject identification number. The document linking study numbers to participants' identities will be stored in a password-protected research folder only accessible to IRB-approved study members.

Benefits of Study Participation

You will not directly benefit from your participation in this study. The information you will

receive about guideline-directed medication therapy for heart failure may be useful to you in your practice.

Alternative to Participation

Alternatives to study participation include consultation with the cardiology clinic and continuing medical education (CME) focusing on heart failure care.

Research Related Injury

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment, and follow-up care as needed. Care for such injuries will be billed in the ordinary manner to you or your insurance company. If you think that you have suffered a research-related injury, let the researcher know right away.

Confidentiality

The records of this study will be kept private. In any publications or presentations, we will not include any information that will make it possible to identify you as a subject. Your record for the study may, however, be reviewed by individuals at CSS with appropriate regulatory oversight. All data collected will be stored in a locked filing cabinet and/or on a password-protected computer. To these extents, confidentiality is not absolute. Your consent form and data will be retained securely for five years, after which time they will be destroyed.

Voluntary Nature of the Study

Participation in this study is voluntary. Your decision on whether or not to participate in this study will not affect your current or future relations with Allina. If you decide to participate, you are free to withdraw at any time without affecting those relationships.

Contact and Questions

The researcher conducting this study is Anastasiya Huberty. You may ask any questions you have now, or if you have questions later, you are encouraged to contact the principal investigator at 651-955-7537 or ahuberty1@css.edu

If you have any questions or concerns regarding the study and would like to talk to someone other than the researcher, you are encouraged to contact the following individuals:

- Research Advisor: RHEA Ferry, DNP, APRN, FNP-C, NE rferry@css.edu
  Phone: 218.791.5052
- Department Chair: JULIE HONEY, DNP, APRN, CPNP, C-FNP jhoney@css.edu
- School Dean: Dr. Sheryl Sandahl, Dean of the School of Nursing
- Nicole Nowak-Saenz, Ph.D., Chair of the Institutional Review Board at nnowaksaenz@css.edu

You may also contact any of the above-named individuals in writing or in person at The College of St. Scholastica, 1200 Kenwood Ave, Duluth, MN 55811.

You will be given a copy of this form to keep for your records.

Your signature below indicates that you have read and understood the information in this consent form. Your signature indicates that you want to participate in this study.

_____
Printed Name of Participant

_____ _____
Signature of Participant Date Signed

_____ _____
Signature of Investigator Date Signed

Appendix H: Institutional Review Board Review Board Action

The College of St. Scholastica

Institutional Review Board

DATE:	March 30, 2022
TO:	Anastasiya Huberty and [Dr. Rhea Ferry]
FROM:	The College of St. Scholastica, Institutional Review Board
RE:	Incorporating Heart Failure Titration Guidelines into the TCU/ Outpatient Care Setting
SUBMISSION TYPE:	New Project
ACTION:	NOT RESEARCH
REVIEW TYPE:	Expedited Review

Thank you for your submission of materials for your project. The College of St. Scholastica Institutional Review Board has reviewed your application and determined that the proposed activity does not meet the definition of research under the Code of Federal Regulations 45 Part 46.102 provided by the Department of Health and Human Services. As such, your project does not require ongoing review or approval from The College of St. Scholastica Institutional Review Board. We will retain a copy of this correspondence within our records.

Any modification to your project procedures that could change the determination of "not research" must be submitted to the IRB before implementation.

When your project is complete, submit a protocol closure form by following these steps: (1) log in to your project in IRBNet, then create a new package (not project), (2) download the protocol closure form from the Forms and Templates menu, (3) complete, sign and submit the protocol closure form.

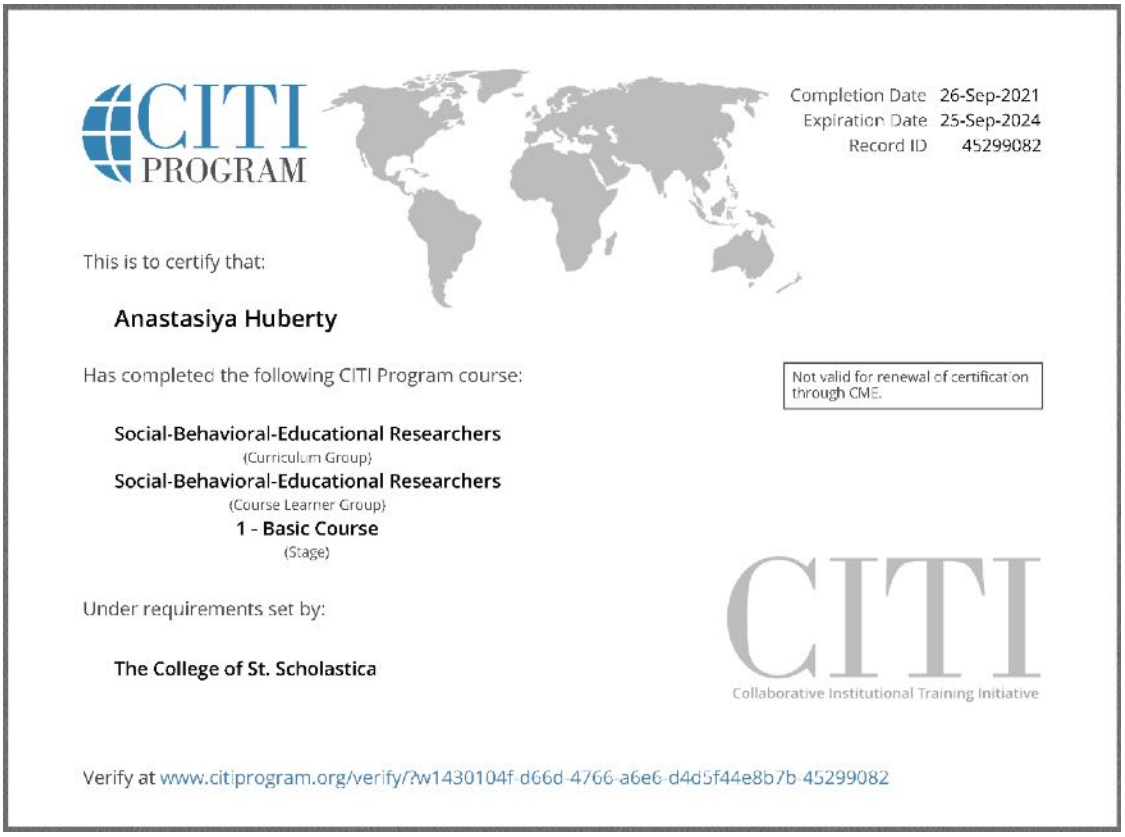
If you have any questions, please contact Nicole Nowak through the project email function in IRBNet or nnowaksaenz@css.edu. Please include your study title and reference number in all correspondence with the IRB office.

Best regards,

Nicole T. Nowak, Ph.D.
Chair, Institutional Review Board

The College of St. Scholastica
Duluth, MN 55811

Appendix I: CITI Training Documentation



CITI PROGRAM

Completion Date 26-Sep-2021
Expiration Date 25-Sep-2024
Record ID 45299082

This is to certify that:

Anastasiya Huberty

Has completed the following CITI Program course:

Not valid for renewal of certification through CME.

Social-Behavioral-Educational Researchers
(Curriculum Group)
Social-Behavioral-Educational Researchers
(Course Learner Group)
1 - Basic Course
(Stage)

Under requirements set by:

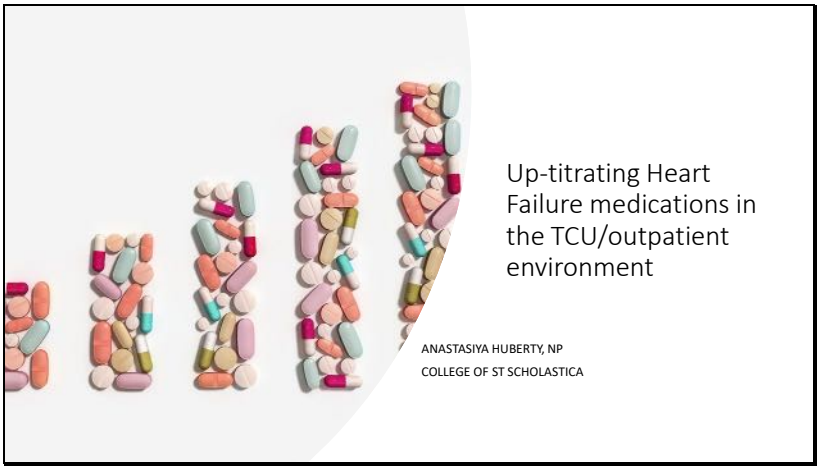
The College of St. Scholastica

CITI
Collaborative Institutional Training Initiative

Verify at www.citiprogram.org/verify/?w1430104f-d66d-4766-a6e6-d4d5f44e8b7b-45299082

Appendix J: Educational Intervention

Slide 1



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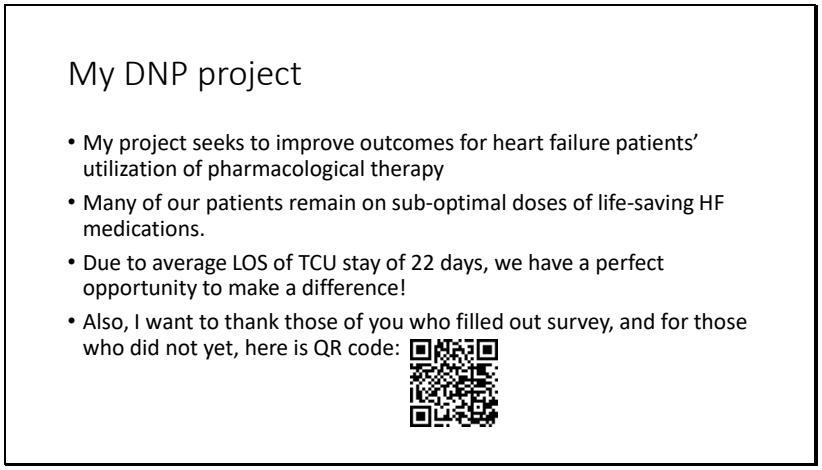

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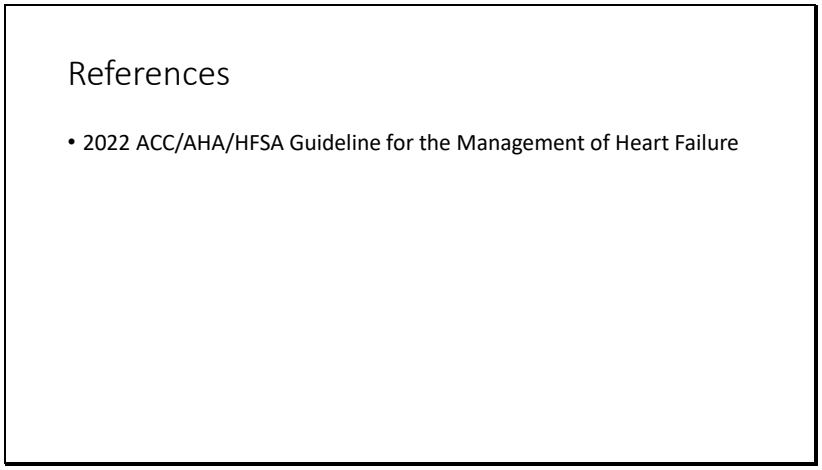


Slide 4

Heart Failure

clinical syndrome resulting from any structural or functional impairment of ventricular filling or ejection of blood

Slide 5

HF epidemiology

HF is a growing health and economic burden for the US, in large part because of the aging population

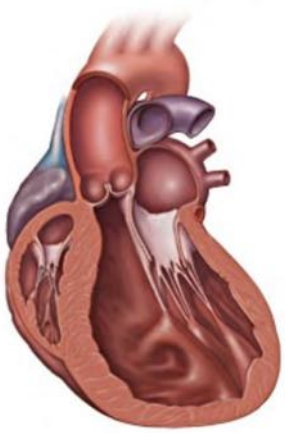
- 650,000 new cases annually
- Annually > 1 million HF hospitalizations in the US
- 6 million Americans with symptomatic HF
- More prevalent in our patient population [age 65 and older]

Slide 6

HF subtypes

- Heart failure with preserved ejection fraction (HFpEF) with EF > 45-50%
- Heart failure with reduced ejection fraction (HFrEF) with EF < 40-45%
- Roughly equal proportions among Americans

Slide 7



HF with reduced EF

- multiple disease-modifying therapies
- **guideline-directed medical therapy (GDMT)**

titrated to target dose or limiting side effect

- GDMT improves cardiac function, decreases morbidity and mortality, reduces readmissions
- Despite overwhelming evidence of medications effectiveness and clear clinical guidelines on their use, fewer than 25% of eligible patients are on the appropriate doses of medical therapy .

Slide 8

AHA GDMT recommendations for HFrEF

- **beta-blocker** and angiotensin-converting enzyme inhibitor (**ACEI**)/angiotensin receptor blocker (**ARB**)/angiotensin receptor-neprilysin inhibitor (**ARNI**)
  - Each agent should be up-titrated to maximally tolerated or target dose.
  - Initiation of a beta-blocker is better tolerated when patients are dry and an ACEI/ARB/ARNI when patients are wet.
  - Only guideline-recommended beta-blockers (i.e., carvedilol, metoprolol succinate, or bisoprolol) should be used in patients with HFrEF.
  - Among angiotensin antagonists, ARNIs are preferred agents. Renal function and potassium should be checked within 1 week of initiation or dose up-titration of ACEI/ARB/ARNI.

Slide 9

ACE-I/ARB in NYHA I-IV

- improve symptoms and survival
- ACEi first line
- careful w/ SBP < 95, K >5, Cr > 3
- Goal:
  - lisinopril 40 mg/d, start at 2.5 – 5mg QD
  - losartan 150 mg/d, start 25-50 mg QD
- watch BP, K, Cr (check 1-2 wks p. adjustment)
- cough (10-20% -> switch to ARB)
- angioedema (↑in blacks, can recur w/ARB)

Slide 10

Beta Blockers in NYHA I-IV

- improve Sxs and survival
- careful w/ acute HF, SBP <95, bradycardia, reactive airways (most can tolerate)
- goal
  - carvedilol 25mg BID, start at 3.125 mg BID
  - metoprolol XL 200 mg QD, start at 12.5- 25 mg QD
- watch BP, increased fluid retention in short term, bradycardia, fatigue

Slide 11

Combined angiotensin receptor & neprilysin inhibitors (ARNIs)

- ARNI should not be used within 36 hrs of ACEi
- ARNI should not be used in pts with h/o angioedema
- in patients on ACEi/ARB with chronic symptomatic HFrEF (NYHA II-III), switching to ARNI is recommended to reduce morbidity & mortality
  - Entresto [sacubitril/valsartan] – goal 97/103 mg BID.
    Start at 24mg sacubitril – 26 mg valsartan "50"
  - check K, Cr

Slide 12

Loop Diuretics to control congestion

- furosemide 20-80 mg QD up to 160 mg BID
- torsemide up to 80 mg BID (better absorption)
- bumetanide up to 4 mg BID (better absorption)
  - 1 bumetanide = 20 torsemide = 40 furosemide
- when on max dose loop, metolazone at 1.25 or 2.5, generally not more than 1-2x/week
- Frequent K, Cr checks and supplementation

Slide 13

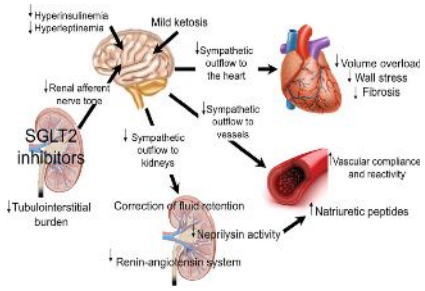
Aldosterone (mineralocorticoid receptor) antagonists

- NYHA II-IV -> improve Sxs/survival, ↓SCD
- not with K > 5, eGFR < 30
  - spironolactone 12.5-25/d to start, goal 25-50 mg
  - gynecomastia/tenderness -> switch to eplerenone 25mg/d to start
- watch K, Cr, may need to lower loop diuretic, KCl doses

Slide 14

SGLT-2 inhibitors

- Sodium-glucose cotransporter-2 (SGLT-2) inhibitors should also be considered for HFrEF with New York Heart Association (NYHA) class II-IV patients
- No titration
- 10 mg daily for empa/dapa
- Do not use in DM1
- Monitor for genital yeast



Slide 15

hydralazine + isosorbide

- NYHA III-IV w/cont'd symptoms on ACEi/BB/MRA
- proven in African Americans (AHEFT trial) -> improved Sxs/survival
- alternative to ACEi/ARB with renal insufficiency

  Goal hydralazine 75 mg TID, start at 25 mg TID

  Goal Isosorbide 40 mg TID, start at 20 mg TID

Slide 16

- The best approach is one that is individualized to your patients and works for your resources to follow up and monitor

Slide 17

Thank you

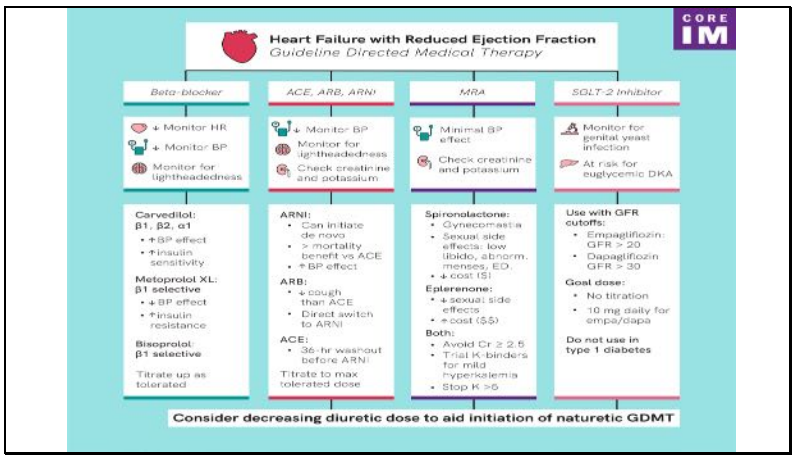
- For taking a survey
  Please contact me if you need a link
- For adding Epic HF phrase
.tcuheartfailure

Slide 18

Table 18. Medical Therapy for Stage C HF*r*EF: Magnitude of Benefit Demonstrated in RCTs

GDMT	RR Reduction in Mortality (%)	NNT for Mortality Reduction (Standardized to 36 mo)	RR Reduction in HF Hospitalizations (%)
ACE inhibitor or ARB	17	26	31
Beta blocker	34	9	41
Aldosterone antagonist	30	6	35
Hydralazine/nitrate	43	7	33

Slide 19


CORE IM
Heart Failure with Reduced Ejection Fraction
Guideline Directed Medical Therapy
Beta-blocker
ACE, ARB, ARNI
MRA
SGLT-2 Inhibitor
↓ Monitor HR
↓ Monitor BP
Monitor for lightheadedness
↓ Monitor BP
Monitor for lightheadedness
Check creatinine and potassium
Minimal BP effect
Check creatinine and potassium
Monitor for genital yeast infection
At risk for euglycemic DKA
Carvedilol:
β1, β2, α1
• ↑BP effect
• ↑insulin sensitivity
Metoprolol XL:
β1 selective
• ↓BP effect
• ↑insulin resistance
Bisoprolol:
β1 selective
Titrate up as tolerated
ARNI:
• Can initiate de novo
• > mortality benefit vs ACE
• ↑BP effect
ARB:
• ↓cough than ACE
• Direct switch to ARNI
ACE:
• 36-hr washout before ARNI
Titrate to max tolerated dose
Spironolactone:
• Gynecomastia
• Sexual side effects: low libido, abnorm. menses, ED.
• ↓cost ($)
Eplerenone:
• ↓sexual side effects
• ↑cost ($$)
Both:
• Avoid Cr ≥ 2.5
• Trial K-binders for mild hyperkalemia
• Stop K >6
Use with GFR cutoffs:
• Empagliflozin: GFR > 20
• Dapagliflozin GFR > 30
Goal dose:
• No titration
• 10 mg daily for empa/dapa
Do not use in type 1 diabetes
Consider decreasing diuretic dose to aid initiation of naturetic GDMT

Appendix K: Abstract

Background: Persistent gaps exist in the routine up-titration of pharmacological therapies for heart failure patients with reduced ejection fraction (HFrEF.) Despite improved survival and reduced hospital readmissions when HFrEF patients are up-titrated to evidence-based guideline-directed medical therapy (GDMT) targets, fewer than 25% of eligible patients are currently at GDMT target dosages. This project aims to improve the medication optimization of heart failure patients within the Transitional Care Unit (TCU) setting via an educational intervention targeting TCU/outpatient providers.

Methods: The educational intervention took the form of a virtual presentation delivered during a routine provider meeting. The educational intervention discussed the importance of successfully up-titrating patients to GDMT targets or the maximum tolerable dosages. An overview of the GDMT targets and the steps to successfully up-titrating patients were also provided. A survey questionnaire asking providers about their knowledge of GDMT and current practices was completed prior to the intervention (baseline) and again six weeks later (follow-up). The participating clinics have also implemented a mandatory EPIC smart-phrase automating the titration monitoring in provider notes. This approach provides an objective measurement of provider practices and enables monitoring of the percentage of TCU patients up-titrated monthly.

Results: 27 providers were recruited for this study. The baseline survey received a response rate of 37% (10/27), and the follow-up survey received a response rate of 41% (11/27). These data were analyzed with independent-sample t-tests and the Wilcoxon Signed-Rank test to evaluate the hypothesis that the mean value of knowledge would increase in response to the educational intervention compared to the null hypothesis of no change. The increase in knowledge scores, from 6.30 ± 1.25 to 7.29 ± 1.25, was not significant at the alpha=0.05 level.

Recommendations: Based on the positive outcome of this study, Institutional support will be sought to sustain this project by making the educational intervention part of the new hire process.