Randomized Evaluation of Audit and Feedback and Referral Nudges to Increase Heart Failure Medication Optimization Among Primary Care Pharmacists in the Veterans Affairs Healthcare System (PHARM-HF-2)

Protocol V-1.1

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PROJECT SUMMARY

Title	Randomized Evaluation of Audit and Feedback and Referral Nudges to Increase Heart Failure Medication Optimization Among Primary Care Pharmacists in the Veterans Affairs Healthcare System (PHARM-HF-2)
Study Objectives	The co-primary objectives are to determine whether either (1) a education and feedback (E+F) intervention providing pharmacists with HF education and feedback of their heart failure (HF) medication titration encounter rates or (2) primary care referral nudges increase the frequency of primary care pharmacist heart failure medication management encounters.
Study Design	The PHARM-HF-2 is a multi-site pragmatic randomized quality improvement project that evaluates two different interventions. First, the education and feedback intervention will be randomized at the level of the clinical site in a stepped wedge design. A total of 22 VHA sites will be randomized to different time points at which they begin receiving the intervention. In the initial phase, all sites will receive education only. At intervals of 2 months, 4 sites will transition from education only to education and feedback in a randomized order. By the end of the project, all sites will be receiving the education and feedback intervention. Second, primary care referral nudges will studied with a two-arm parallel design with randomization at the level of the primary care team (PACT team) with 1:1 allocation stratified by site. This nested evaluation will start four months into the study.
Number of Participants	N ~22 sites with ~400 pharmacists and ~400 PACT teams
Trial Location	United States: Veterans Health Administration VISN 6 sites (n=7), VISN 10 sites (n=7), and VISN 19 sites (n=8)
Inclusion Criteria	Pharmacists and primary care clinicians employed within the VHA VISN and providing Patient Aligned Care Team (PACT) care
Exclusion Criteria	Lack of site alignment with this quality improvement initiative
Intervention 1: Audit and Feedback + Education vs. Education Only	VHA Sites will be randomly assigned to Education + Feedback vs. Education Only groups. At sites randomized to the Education+Feedback group, PACT pharmacists with prior HF actions will receive data monthly via email including their total medication titration encounters. They will also receive invitations to monthly educational sessions and access to shared resources on HF medication management. At sites randomized to Education only, PACT pharmacists will receive access to the monthly educational sessions and access to

	shared resources on HF medication management. They will not receive monthly emails or other reminders.
Intervention 2: Primary Care Pharmacy Referral Nudges vs. Usual Care	VHA sites will be randomly assigned to primary care pharmacy referral nudges (Referral Nudges) vs. Usual Care. For sites randomized to primary care pharmacy referral nudges, primary care clinician will receive a weekly Teams message with Veterans being seen that week with HF that are on suboptimal medication therapy with a suggestion to consider discussing PACT pharmacy referral. For PACT teams randomized to usual care, there will be no referral nudges.
Randomization	For the education and feedback intervention, we will randomize PACT teams via a stepped wedge design stratified by VISN using 2-month intervals. There will be 4 sites that transition from Education Only to Education and Feedback every 2 months. For the primary care pharmacy referral nudges, we will use permuted block 1:1 randomization with block sizes of 2 to primary care pharmacy referral nudges vs. usual care.
Co-Primary Endpoint	Number of monthly heart failure medication adjustment encounters for pharmacists in the Education+Feedback vs. Education Only arms.
Co-Primary Endpoint	Number of monthly heart failure medication adjustment encounters for pharmacists in PACT teams with Referral Nudges vs. Usual Care.
Secondary Endpoints	• Number of HF encounters with pharmacists • For the primary care referral intervention, the rate of GDMT utilization (beta-blocker, ACE-I/ARB/ARNI, MRA, SGLT-2) among patients without documented contraindications based on vitals, allergies, and laboratory values. • For the primary care referral intervention, the percentage of HF patients at greater than 50% target dose of each GDMT category among patients without documented contraindications based on vitals, allergies, and laboratory values
Study Timeline	• Sites and PACT teams will be randomized at the study start for each VISN.

	• Following randomization, monthly educational sessions will start, and educational resources will be available. • Starting month 5, primary care clinicians will receive weekly messages regarding patients with upcoming visits on suboptimal GDMT.
Assessment	Heart failure medication actions and heart failure medications will be assessed via the VHA Corporate Data Warehouse at the end of the study.
Duration	The overall study duration will be 12 months. This will include 6 study intervals.
Statistical Considerations	For the education and feedback intervention, we assumed there are at 4 sites randomized during each of 5 steps with a mean number of pharmacists of 21 per site. With a moderate coefficient of variation of 0.3 for sites, a mean number of HF medication adjustment encounters of 0.4 and a standard deviation of 0.8, we have 90% power for identifying a change in HF medication adjustment encounters of 0.2. For the primary care pharmacist referral intervention, we assumed there will be 11 sites randomized to referral nudges and 11 to usual care. With a mean number of 0.8 monthly pharmacist HF medication adjustment encounters in the usual care arm and a standard deviation of 0.8, we have 90% power for identifying a change in HF medication adjustment encounters of 0.8.

1. BACKGROUND AND RATIONALE

HF causes >1.2 million hospitalizations and 300 thousand deaths annually. This occurs despite effective GDMT for HFrEF.[1] With SGLT2i, there is now also therapy for improving quality of life and reducing hospitalizations for HF with preserved ejection fraction (HFpEF).[2] While prior quality improvement efforts have focused on inpatient care, there is a critical need to improve outpatient care. GDMT escalation in the outpatient setting is rare.[3] This inertia leads to persistent GDMT gaps with <2% of outpatients on optimal therapy.[3,4]

Nurse or pharmacist led GDMT management programs have been shown to effectively increase GDMT rates.[5] The VHA has a pharmacist-based HF remote management program that uses an online, real-time, patient dashboard to optimize HF therapy. However, only 10% of VHA patients with recent-onset HF received HF care from pharmacists, with many of the encounters being limited to monitoring and education. Expanding the pharmacist program is a national VHA goal, but how to successfully implement this is unclear. Prior studies at single-center academic VAs have shown that utilization of the VHA pharmacist management program significantly increases GDMT rates.[6–11]

The PHARM-HF 2 study is testing an implementation strategy for pharmacist HF care across three VHA regions to evaluate if combined pharmacist education and monthly feedback messages increases VHA pharmacist HF management. Simultaneously, the project will evaluate if primary care nudges for pharmacist referral increase pharmacist HF management.

2. HYPOTHESIS

Our primary hypotheses are the following: (1) Education with feedback messages increase the frequency of pharmacist HF medication management compared with education alone and (2) Primary care pharmacist referral nudges increase the frequency of pharmacist HF medication management compared with usual care.

3. PROJECT DESIGN

This is a multisite randomized quality improvement project. The project evalues two separate interventions to increase pharmacist HF medication adjustment. First, in a stepped wedge randomized design, we will compare education and feedback messages with education versus education alone. The education and feedback intervention will be randomized at the level of the clinical site. A total of 22 VHA sites will be randomized to different time points at which they begin receiving the intervention. In the initial phase, all sites will receive education only. At intervals of 2 months, 4 sites will transition from education only to education and feedback in a randomized order. By the end of the project, all sites will be receiving the monthly education and feedback intervention. The figure below displays the randomization. The figure below displays the site randomization over time.

All pharmacists will receive access to educational material. The educational material will include monthly Teams webinars and sharepoint resources with titration protocols, frequently asked questions documents, and other HF educational information. Following randomization to the education and feedback arm, the pharmacists will receive a monthly Teams message containing the intervention. Data for the intervention will be obtained from the VHA national HF dashboards. The frequency of pharmacist HF medication actions will be assessed at the end of the 12-month study.

Site 1	Education	Education	E&F	E&F	E&F	E&F	E&F	E&F	E&F	E&F	E&F	E&F
Site 2	Education	Education	E&F	E&F	E&F	E&F	E&F	E&F	E&F	E&F	E&F	E&F
Site 3	Education	Education	E&F	E&F	E&F	E&F	E&F	E&F	E&F	E&F	E&F	E&F
Site 4	Education	Education	E&F	E&F	E&F	E&F	E&F	E&F	E&F	E&F	E&F	E&F
Site 5	Education	Education	Education	Education	E&F	E&F	E&F	E&F	E&F	E&F	E&F	E&F
Site 6	Education	Education	Education	Education	E&F	E&F	E&F	E&F	E&F	E&F	E&F	E&F
Site 7	Education	Education	Education	Education	E&F	E&F	E&F	E&F	E&F	E&F	E&F	E&F
Site 8	Education	Education	Education	Education	E&F	E&F	E&F	E&F	E&F	E&F	E&F	E&F
Site 9	Education	Education	Education	Education	E&F	E&F	E&F	E&F	E&F	E&F	E&F	E&F
Site 10	Education	Education	Education	Education	Education	Education	E&F	E&F	E&F	E&F	E&F	E&F
Site 11	Education	Education	Education	Education	Education	Education	E&F	E&F	E&F	E&F	E&F	E&F
Site 12	Education	Education	Education	Education	Education	Education	E&F	E&F	E&F	E&F	E&F	E&F
Site 13	Education	Education	Education	Education	Education	Education	E&F	E&F	E&F	E&F	E&F	E&F
Site 14	Education	Education	Education	Education	Education	Education	Education	Education	E&F	E&F	E&F	E&F
Site 15	Education	Education	Education	Education	Education	Education	Education	Education	E&F	E&F	E&F	E&F
Site 16	Education	Education	Education	Education	Education	Education	Education	Education	E&F	E&F	E&F	E&F
Site 17	Education	Education	Education	Education	Education	Education	Education	Education	E&F	E&F	E&F	E&F
Site 18	Education	Education	Education	Education	Education	Education	Education	Education	E&F	E&F	E&F	E&F
Site 19	Education	Education	Education	Education	Education	Education	Education	Education	Education	Education	E&F	E&F
Site 20	Education	Education	Education	Education	Education	Education	Education	Education	Education	Education	E&F	E&F
Site 21	Education	Education	Education	Education	Education	Education	Education	Education	Education	Education	E&F	E&F
Site 22	Education	Education	Education	Education	Education	Education	Education	Education	Education	Education	E&F	E&F
	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 7	Month 8	Month 9	Month 10	Month 11	Month 12
	7/16-8/15	8/16-9/15	9/16-10/15	10/16-11/15	11/16-12/15	12/16-1/15	1/16-2/15	2/16-3/15	3/16-4/15	4/16-5/15	5/16-6/15	6/16-7/15

The second component of the project will be a parallel randomized project comparing primary care pharmacist referral nudges with usual care. This second project will be nested within sites randomized to education and feedback above in months 5 and later. Sites will be block randomized 1:1 with block sizes of 2.

4. PROJECT PROCEDURES

Randomization

The sequence generation process will be performed using a secure password-protected computerized randomization algorithm on REDCap. Site randomization for education and feedback intervention crossover will occur at the start of the study for all sites.

Randomization of PACT teams will occur at the time each site crosses over to the education and feedback arm. Sites will be randomized with block sizes of 2.

5. TREATMENT ARMS

5.1 Educational Only

All pharmacists will be informed regarding the educational material on a VHA Sharepoint site. The educational information will include suggested titration protocols, education about heart failure medications, a frequently asked questions document, guideline documents, patient educational material, and recordings of Teams webinars on heart failure management. The pharmacists will be invited to a regular webinar regarding heart failure medication management.

5.2 Education and Feedback (E+F)

For sites randomized to education and feedback, all PACT pharmacists with a heart failure action within the last year will receive a monthly Teams message. The monthly Teams message will contain information including their heart failure medication actions over the prior 3 month period. This data will be obtained from VHA pharmacy data. The message will also include reminders regarding the monthly educational sessions and access to the educational sharepoint. They will also receive a Teams calendar hold for the monthly educational meeting.

5.3 Primary Care Pharmacist Referral Nudges

For sites randomized to the referral nudges, primary care clinicians will receive a weekly email that lists potential patients with HF with reduced ejection fraction with upcoming clinic visits that are not on optimal medication therapy. These patients will be eligible for, but not prescribed, at least 50% of the target dose of one of four classes of guideline-recommended heart failure therapy: beta-blockers, renin angiotensin system inhibitors, mineralocorticoid receptor antagonists, or sodium glucose cotransporter 2 inhibitors. The message will suggest referral to PACT pharmacists for medication optimization.

6. STATISTICAL CONSIDERATIONS AND ANALYSIS PLAN

6.1 Sample Size Assumptions

For the education and feedback intervention, we assumed there are 4 sites randomized during each of 5 steps with a mean number of pharmacists of 21 per site. With a moderate coefficient of variation of 0.3 for sites, a mean number of HF medication adjustment encounters of 0.4 and a standard deviation of 0.8, we have 90% power for identifying a change in HF medication adjustment encounters of 0.2.

For the primary care pharmacist referral intervention, we assumed there will be 22 sites with 400 PACT teams randomized to referral nudges or usual care. With a mean number of 0.8 monthly pharmacist HF medication adjustment encounters in the usual care arm and a standard deviation of 0.8, we have over 90% power for identifying a change in HF medication adjustment encounters of 0.8.

6.2 Statistical Analysis Plan

To be finalized.