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Electronic Alerts to Improve Heart Failure Therapy in Outpatient Practice: A Cluster Randomized Trial

Brief title: The PROMPT-HF Clinical Trial

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Abstract

Background

Use of GDMT is under-prescribed in patients with HFrEF.

Objectives

To examine whether targeted and tailored EHR alerts recommending GDMT in eligible patients with HFrEF improves utilization.

Methods

PROMPT-HF was a pragmatic, EHR-based, cluster-randomized comparative effectiveness trial. 100 providers caring for patients with HFrEF were randomized to either an alert or usual care. The alert notified providers of individualized GDMT recommendations along with patient characteristics. The primary outcome was an increase in the number of GDMT classes prescribed at 30 days post-randomization. Providers were surveyed on knowledge of guidelines and user experience.

Results

We enrolled 1,310 ambulatory HFrEF patients April-October 2021. Median age was 72 years; 31% were female; 18% were black; median LVEF was 32%. At baseline, 84% were receiving β-blockers, 71% RAASi, 29% MRA, and 11% SGLTi. The primary outcome occurred in 176/685 (26%) participants in the alert arm versus 117/625 (19%) in the usual care arm, increasing GDMT class prescription by >40% after alert exposure [adjusted RR: 1.41 (1.03, 1.93); P=0.03]. The number of patients needed to alert to result in an increase in addition of GDMT class was 14. 79% of alerted providers agreed that the alert was effective at enabling improved prescription of medical therapy for HF.

Conclusions

A real-time, targeted, and tailored EHR-based alerting system for outpatients with HFrEF led to significantly higher rates of GDMT at 30 days when compared with usual care. This low-cost intervention can be rapidly integrated into clinical care and accelerate adoption of high-value therapies in heart failure.

Condensed Abstract: PROMPT-HF examined whether an alert providing personalized recommendations for outpatients with heart failure would increase use of guideline directed medical therapies. This cluster randomized trial included 1310 patients and found significantly greater increases in addition of GDMT classes added to the alert arm (26% in the alert arm versus 19% in the usual care arm; P=0.03). The number of patients for which an alert was needed to result in an additional GDMT class was 14. This low-cost alert can be embedded into the electronic health record at integrated health care systems and lead to widespread improvements in the care of heart failure patients.

Keywords: Heart Failure with Reduced Ejection Fraction, Randomized Controlled Trial, Electronic Health Record

Abbreviations and Acronyms

HFrEF = Heart Failure with reduced Ejection Fraction

GDMT = Guideline Directed Medical Therapy

EHR = Electronic Health Record

BPA = Best Practice Alert

Trial Registration: Clinicaltrials.gov NCT04514458

Introduction

Pharmacotherapy for heart failure with reduced ejection fraction (HFrEF) comprises four medication classes proven to reduce hospitalizations and mortality, and are therefore afforded the highest level of professional society guideline recommendation.[1-3] The medication classes are β-blockers (BB), Renin-Angiotensin-Aldosterone System (RAAS) inhibitors [angiotensin converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), or angiotensin receptor-neprilysin inhibitors (ARNI)], mineralocorticoid receptor antagonists (MRA), and the newer sodium-glucose cotransporter-2 inhibitors (SGLT2i). Together, these are referred to as guideline-directed medical therapy (GDMT) for HFrEF.[4] Despite compelling evidence supporting their clinical use, real-world data shows persistent suboptimal adoption of these treatments, demonstrating an unmet need to identify and overcome barriers to implementation.[5-7]

Efforts aimed at optimizing GDMT in patients with HFrEF are abundant across hospitals and healthcare systems, but there is limited evidence to support whether such resource-intensive interventions have any demonstrable benefit. Recently, 2 large randomized controlled trials showed no discernible impact of intensive quality improvement initiatives or patient-centered transitional care services on either use of GDMT or clinical outcomes.[8,9]

Electronic health record (EHR) embedded clinical decision support via best practice alerts (BPA) are cost-effective interventions that can be targeted, individualized, and rapidly scalable if found to be impactful.[10] The PRagmatic Trial Of Messaging to Providers about outpatient Treatment of Heart Failure (PROMPT-HF) was designed to test the hypothesis that timely alerting of recommendations about medical treatment of HFrEF tailored to the patient's circumstance would lead to higher rates of prescription of these therapies when compared with usual care.

Methods

Trial Oversight and Study Population

The full study protocol is accessible at www.theprompttrials.org (NCT04514458) and the design manuscript was previously published.[11] The trial was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Yale School of Medicine Institutional Review Board which deemed it minimal risk, thus allowing for a waiver of informed consent at the patient level. Randomization was clustered at the provider level (physicians or advanced practice providers) to intervention (alert) or usual care (no alert) and all providers consented to be part of the study.[12] All providers utilized a single EHR (Epic Systems, Verona, WI). Inclusion criteria for patients were age ≥18, left ventricular ejection fraction (LVEF) ≤ 40%, and not already on all four classes of GDMT for HFrEF (**Central Figure and Figure 1**). GDMT was defined as the following classes of medications: BB, ACEI/ARB/ARNI, MRA, and SGLT2i.[3] Patients who opted out of EHR-based research (<1% of patients), or who were in hospice care were excluded. The study was funded by AstraZeneca but the study design, conduct, all analyses, and manuscript preparation and writing were performed independently. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper and its final contents. The study began on 4/1/2021 and completed enrollment on 10/14/21.

Trial Procedures

Enrollment

We retrospectively identified the top 100 providers caring for HFrEF patients in outpatient internal medicine and cardiology practices and clinics affiliated with Yale-New Haven Health System in 2020. Eligible providers included nurse practitioners, physician assistants, and

physicians. Trainees (residents/fellows) were not included in this study. Eligible providers were contacted by the study team via email and Epic (Verona, WI) "In Basket" messaging with an overview of the study along with a consent hyperlink based out of REDCap (Research Electronic Data Capture) that is hosted by Yale School of Medicine. Consenting providers were asked to complete a pre- and post-study survey assessing knowledge and comfort levels with the treatment guidelines for HFrEF. The post-study survey also included questions that assessed provider opinions on user experience with the alert.

Randomization

Randomization occurred at the level of the provider. All consented physicians were randomized within the EHR system to either the intervention group (Alert) or usual care (No Alert) group via a permutated block randomization scheme to ensure an equal number of providers in each study arm and to minimize contamination across study arms. This created 100 clusters (providers) to which eligible patient participants were assigned upon their first eligible clinic visit. Patients who initially saw a "no alert" provider would never generate an alert even if they saw an alert provider in the future. Similarly, patients who initially saw an alert provider would not generate alerts if they subsequently saw a no alert provider to avoid contamination of the control arm. Finally, we limited the number of enrolled patients linked to a single provider to 33 (5% of the number per study arm) to avoid providers with a high proportion of patients with HFrEF from skewing the results.

Intervention

The intervention was an EHR-embedded best practice alert that triggered for eligible patients upon provider opening of the order entry module in the patient's medical record. The alert was created and modified after targeted sessions with virtual focus groups comprised of

providers to solicit feedback on its design, user friendliness, and hindrance to workflow. The alert informed the provider as to the patient's current LVEF along with the most recent blood pressure, heart rate, serum potassium and creatinine levels, and estimated glomerular filtration rate—patient-specific clinical data commonly taken into consideration at time of heart failure medication adjustments (**Supplementary Figure 1**). The alert displayed all four recommended GDMT classes: BB, ACEI/ARB/ARNI, MRA, and SGLT2i. If the patient was not currently being prescribed a recommended medication class, that class was bolded in red with "none" displayed. If the patient was already prescribed a recommended class, the specific drug would be displayed. Allergies to recommended drugs or drug categories were specifically noted. The alert also contained a direct link to an order set that was customized to the patient and displayed all available medications within the classes not currently prescribed listed alphabetically along with their FDA indication (**Supplementary Figure 2)**. Finally, we included a hyperlink to the study webpage that contained informational documents expanding upon evidence-based medical therapy recommended by current guidelines for patients with HFrEF. The provider could acknowledge the alert by simply selecting 1 of 3 responses: (a) "I will adjust medications", (b) "Med changes not clinically indicated", and (c) "Defer for other reason". The last option generated a free text field in which the provider could (but was not obligated to) enter the reasoning for the decision. Finally, there was the option to skip prior questions and either "agree" with or "dismiss" the alert.

Outcome Measures

The primary outcome was the proportion of patients with HFrEF who had an increase in the number of prescribed GDMT classes at 30 days after randomization. Any increase in GDMT class number was considered a positive outcome and a decrease or no change in GDMT number

was a "null" outcome. Any increase in dose of currently prescribed GDMT was a secondary outcome. Additional secondary outcomes included: filling of prescriptions, total health care costs, hospitalizations, emergency department visits, and death. Safety outcomes included the proportion of patients with potassium >5.5 mEq/L, heart rate <60 beats/minute, or a 50% increase in creatinine at 30 days after randomization. Additionally, we measured provider opinions on user experience with the alert along with knowledge and comfort level with HFrEF guidelines via surveys completed before and after the study.

Statistical Analysis

We compared categorical variables using χ^2 and continuous variables using the Wilcoxon rank sum test between patients randomized to the alert compared to usual care, accounting for clustering at the provider level. We considered an absolute increase of 10% in the proportion of patients on an additional class of GDMT at 30 days to be considered clinically significant. Consequently, a sample size of 1,310 patients (655 patients in each arm) achieved a 91% power to detect a 10% difference between the study arms at a two-sided alpha of 0.05 and an intraclass correlation coefficient of 0.05. To ensure the safety of participants, we undertook two interim analyses at 25% to 50% recruitment, using the O'Brien and Fleming stopping rule, with pre-specified discontinuation of study for efficacy of $P \leq 0.00007$ at the 25% and $P < 0.005$ at the 50% analysis, respectively.[13] The primary analysis utilized the intention to treat principle: we examined the association between our intervention and outcomes using generalized linear models (binomial distribution, log link) while adjusting for prespecified baseline characteristics (age, sex, LVEF, Elixhauser Comorbidity Index, cardiology versus non-cardiology provider, and number of GDMT classes at baseline) and accounting for clustering at the provider level. Statistical significance was based on a $P<0.048$ for the primary outcome. Secondary outcomes

were evaluated at $P<0.05$ and considered hypothesis generating. All the analyses were performed with the use of Stata software, version 15 (StataCorp) and R, version 3.5.1 (R Foundation for Statistical Computing).

Results

Patients and Providers

From April 2021 through October 2021, the trial enrolled 100 providers (69 % physicians, 31% advanced practice providers) who cared for 1,310 patients. Characteristics for patients were well balanced between trial groups at baseline (**Table 1**). At baseline, 84% of patients were receiving BB, 71% were receiving an ACEI/ARB/ARNI, 29% were receiving an MRA, and 11% were receiving an SGLT2i. At 30 days post intervention 98.9% of the patients were alive. 75% of patients triggered 1 alert, 17% of patients triggered 2 alerts, and 8% of patients triggered 3 or more alerts.

Outcomes

The primary outcome was observed in 25.7% of the alert arm and 18.7% of the no alert arm [adjusted RR: 1.41, 95% CI (1.03, 1.93), P=0.03]. The intra-cluster correlation coefficient was 0.13. As shown in **Figure 2**, there were numerical increases in prescription of each GDMT class in both study arms: 5.8 vs. 2.9% in BB (P=0.007), 7.7% vs. 7.0% in ACE-I/ARB/ARNI (P=0.22), 7.6 vs. 5.3% in MRA (P= 0.20), and 9.8% vs. 7.5% in SGLT2i (P= 0.41). The number of patients for which an alert was needed to result in an increase in addition of GDMT class was 14. Subgroup analysis showed consistent increase in GDMT utilization of the alert across sex, race, LVEF, provider type, insurance coverage, and baseline GDMT (**Figure 3**). The secondary outcome of an increase in dose or addition of a class of GDMT was observed in 36.2% of the alert arm and 26.2% of the no alert arm [adjusted RR: 1.39, 95% CI (1.08, 1.79), P=0.01]. The

number of patients for which an alert was needed to result in an increase in dosing or addition of GDMT class was 10. There were no significant differences in the rate of emergency department visits or hospitalization at 30-days in the alert versus usual no alert arm (**Table 2**). There were also no significant differences in safety outcomes between alert and no alert (**Table 3**). **Figures 4a and 4b** demonstrates the changes in GDMT that were considered a "win" versus a "loss" outcome according to the alert versus no alert arms. Changes according to the number of GDMT classes at baseline are shown in **Supplemental Table 1**.

Provider Feedback

Of those receiving the alert, 79% agreed or strongly agreed that it was effective at enabling improved prescription of GDMT for patients HFrEF. Of these, 25% accepted the recommendations, 48% indicated they will address suggested interventions in the future, 14% indicated that the patients do not meet the criteria, and the rest did not acknowledge the alert. The main reasons given for not accepting recommendations were as follows: (a) hypotension, (b) renal failure/decompensation, (c) medication not tolerated, and (d) refused by patient.

Discussion

Appropriate use of medical therapy reduces morbidity and mortality in patients with heart failure. Despite this, the proportion of eligible patients treated with guideline recommended medications remains suboptimal. In this pragmatic randomized controlled trial involving outpatients with HFrEF, a personalized alert triggered via the EHR during office visits led to significantly higher number of patients on appropriate GDMT. The majority of clinicians exposed to the alert found to it to be helpful in optimizing medical treatment of their patients. These results suggest that this low-cost and widely scalable intervention can be part of a multi-faceted program that rapidly improves the quality of care in patients with heart failure.

Data from national registries shows a conspicuous gap between professional society guidelines and clinical utilization of medical therapies shown to improve outcomes in patients with HFrEF.[14] In particular, due to public attention and penalties associated with gaps in heart failure care, healthcare systems have placed considerable investments into programs aimed at improving care delivery in HF. Nevertheless, two recent large multicenter randomized controlled trials showed that neither extensive efforts aimed at quality improvement nor intensive transitional care services led to improvements in clinical outcomes.[8,9] Patient-facing interventions such as those tested in EPIC-HF that consisted of a patient activation tool consisting of a 3-minute video with a 1-page medication checklist delivered electronically before a cardiology visit may have a modest impact, but these are difficult to implement on a large scale.[15] Our approach of using an easily customizable alert that is delivered at time of clinical decision-making has benefits beyond prior interventions as it can be applied easily to the EHR and scaled much more easily than a patient-facing intervention or a remote team-based program. Most importantly, it can lead to significant improvements in the prescription of guideline directed medications, with only 10 patients needed to alert in order to see a positive change.

These results contrast with prior trials that have failed to show an impact of informational EHR-based alerts on provider behavior.[16,17] This is likely because the current study provided specific guidance based on information rather than information alone, a distinction that has been noted in the behavioral economics literature.[18,19] Furthermore, the alert was developed in concert with practicing clinicians, whose input was used in its design and timing during clinical workflow.[20] We believe that these factors led to most providers finding that it added value to the care of their patients and should be considered in future iterations of EHR alerting in heart failure.[21] Importantly, given the time pressures of modern medical care, these must be

streamlined to optimize therapies but also to minimize any interruption in the flow of the outpatient visit.

This trial has several limitations. First, it was done entirely at a single academic health system. However, Yale-New Haven Health System is one of the largest integrated delivery networks in the country and patient demographics very closely matched with those across the United States. For example, the characteristics of our patient population was very similar to those of in Change the Management of Patients with Heart Failure (CHAMP-HF), a contemporary registry of HFrEF patients from 150 primary care and cardiology practices across the United States.[11,22] Second, our trial primarily examined an increase in medication initiation rather than up-titration of dosing even though we found an impact on the latter outcome. This will need to be examined in future study as increases in dosing of heart failure medications are apt to confer a clinical benefit. Third, the alert was created and tested within the Epic EHR ecosphere and might need significant modifications for other systems. Fourth, this intervention was testing during a time when there were coordinated and intensive efforts across the Yale New Haven Health System to improve medical therapy for heart failure, a fact reflected in medication increases in the non-BPA arm of the study. This likely biased our results towards the null and underestimated the true impact of the PROMPT-HF intervention.

An alert that provided personalized recommendations for outpatients with HFrEF led to rapid and substantial increases in the use of GDMT. This low-cost tool can be rapidly embedded into the EHR at integrated health care systems and lead to widespread improvements in the care of heart failure patients.

Clinical Perspectives

Competency in Practice-Based Learning and Improvement: Targeted and tailored clinical decision support prompts in the electronic health record can accelerate adoption of underutilized therapies for patients with heart failure.

Translational Outlook: Further research is needed to compare the improvements in care achieved through electronic record alerts in various patient populations based on socioeconomic, racial and ethnic demographics, types and severity of heart failure, and other relevant clinical variables.

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Figure Legends

Figure 1: Study Design and Consort Diagram of the PROMPT-HF Trial. The PROMPT-HF trial was entirely automated with study enrollment done via the electronic health record and providers randomized to an informational risk alert versus usual care. The trial examined whether tailored EHR based alerting for outpatients with HFrEF led to higher rates of GDMT at 30 days post randomization when compared with usual care.

Figure 2: Primary and Secondary Outcomes According to Alert vs. No Alert. The primary and secondary outcome of the PROMPT-HF trial. As shown, there was a significant improvement in number and doses of GDMT in the alert arm.

Figure 3: Changes in primary outcome according to prespecified patient characteristics. This prespecified subgroup analysis showed consistent increase in GDMT utilization of the alert across sex, race, LVEF, provider type, insurance coverage, and baseline GDMT.

Figure 4: Wins and Losses According to Alert and No Alert Arm. PROMPT-HF counted any increase in GDMT number as a positive outcome (win) and a decrease or no change in GDMT number as a "null" outcome (loss).

Central Figure: EHR-based alerting led to significantly higher rates of GDMT. PROMPT-HF was a pragmatic, multicenter, EHR-based, cluster-randomized comparative effectiveness trial. 100 providers caring for 1310 patients with HFrEF were randomized to either a best practice alert exposure or usual care. The alert notified providers of GDMT recommendations individualized to their HFrEF patients who were not receiving all recommended medication classes and displayed key patient characteristics. The study found significantly greater increases in addition of GDMT medication classes added to the alert arm (26% in the alert arm versus 19% in the usual care arm; P=0.03). This low-cost alert can be embedded into the electronic health

record at integrated health care systems and lead to widespread improvements in the care of heart failure patients.

Table 1. Baseline Characteristics of Study Population.

	Overall N=1310	**Alert N=685**	**No Alert N=625**
Age	72 [63, 81]	72 [64, 81]	72 [62, 80.8]
Sex, Female	402 (30.7)	207 (30.2)	195 (31.2)
Black	237 (18.1)	119 (17.4)	118 (18.9)
White	939 (71.7)	492 (71.8)	447 (71.5)
Asian	20 (1.5)	9 (1.3)	11 (1.8)
Hispanic or Latino	125 (9.5)	67 (9.8)	58 (9.3)
Medicaid/Medicare	1,117 (85.3)	535 (85.6)	582 (85.0)
Medical History			
Atrial Arrhythmias	691 (52.8)	349 (51.0)	342 (54.7)
CAD	470 (35.6)	262 (38.3)	208 (33.3)
CKD	453 (34.6)	241 (35.2)	212 (33.9)
Depression	223 (17.0)	124 (18.1)	99 (15.8)
Diabetes	495 (37.8)	260 (38)	235 (37.6)
Dyslipidemia	1024 (78.2)	524 (76.5)	500 (80.0)
Hypertension	1,114 (85)	583 (85.1)	531 (85)
Obesity	275 (21.0)	145 (21.2)	130 (20.8)
Chronic Pulmonary Disorders	401 (30.6)	202 (29.5)	199 (31.8)
Peripheral Vascular Disease	778 (59.4)	386 (56.4)	392 (62.7)
Baseline Vital Signs			
Systolic BP (mmHg)	120 [108, 130]	120 [108, 130]	118 [108, 130]
Diastolic BP (mmHg)	70 [62, 78]	70 [62, 78]	70 [62, 78]
Heart Rate (beats/minute)	74 [65, 84]	74 [65, 84]	74 [65, 83]
Baseline Laboratory findings (at time of randomization)			
Potassium (mEq/L)	4.3 [4, 4.6]	4.2 [3.9, 4.6]	4.3 [4, 4.68]
Creatinine (mg/dL)	1.2 [0.95, 1.5]	1.2 [0.95, 1.6]	1.2 [0.94, 1.5]
eGFR (ml/min/1.73m^2)	57.8 [40.7, 77.5]	56.9 [40.1, 76.9]	58.4 [41.2, 78.1]
LVEF	32 [25, 37]	32 [24, 36]	32 [25, 37]
Provider Types			
Physicians	905 (69.1)	467 (68.2)	438 (70.1)
Advanced Practice Providers	405 (30.9)	218 (31.8)	187 (29.9)
Baseline GDMT classes			
BB	1,098 (83.8)	581 (84.8)	517 (82.7)
ACE-I/ARB/ARNI	926 (70.7)	489 (71.4)	437 (69.9)
ACE-I	189 (14.4)	93 (13.6)	96 (15.4)
ARB	193 (14.7)	102 (14.9)	91 (14.6)
ARNI	544 (41.5)	294 (42.9)	250 (40.0)
MRA	379 (28.9)	193 (28.2)	186 (29.8)
SGLT2i	145 (11.1)	83 (12.1)	62 (9.9)

Data are % (n) or median (interquartile range). BP: blood pressure, eGFR: estimated glomerular filtration rate, LVEF: left ventricular ejection fraction, GDMT: guideline directed medical therapy, BB: beta-blockers, ACE-I/ARB/ARNI: angiotensin converting enzyme inhibitors/angiotensin receptor blockers/ angiotensin receptor-neprilysin inhibitors, MRA: mineralocorticoid antagonist, SGLT2i: sodium-glucose cotransporter-2 inhibitors

Table 2. Clinical Outcomes at 30 Days According to Alert vs. No Alert.

Outcome	Alert N= 685	No Alert N= 625	Unadjusted RR [95%CI]	Adjusted RR* [95% CI]
Emergency Department Visits not resulting in Hospitalization	45 (6.6%)	30 (4.8%)	1.37 [0.87, 2.14]	1.45 [0.92, 2.29]
Emergency Department Visits resulting in Hospitalizations	41 (6.0%)	47 (7.5%)	0.81 [0.52, 1.26]	0.85 [0.58, 1.25]
Direct Hospitalization	6 (0.9%)	16 (2.6%)	0.35 [0.14, 0.87]	0.36 [0.15, 0.87]
Death	7 (1%)	7 (1.1%)	0.89 [0.35, 2.28]	0.98 [0.36, 2.63]

*Adjusted for age, sex, LVEF, elixhauser comorbidity score, provider type, and number of GDMT classes at baseline.

Table 3. Safety Outcomes at 30 Days According to Alert vs. No Alert.

Outcome	Alert N=685	No Alert N=625	*P*
% Potassium >5.5 mEq/L	10 (1.5)	15 (2.4)	0.22
% Heart Rate <60 bpm	5 (0.7)	10 (1.6)	0.11
% Creatinine increased by ≥50%	19 (2.8)	21 (3.4)	0.65

Data is in count (percent). P-values reflect risk adjusted for age, sex, LVEF, elixhauser comorbidity score, provider type, and number of GDMT classes at baseline.

Study Design of the PROMPTHF Clinical Trial (N=1310)

Patient seen in outpatient cardiology or internal medicine clinic

- Age >18
- LVEF≤ 40%
- Not on Quadruple Therapy

Randomization (provider)

Alert when provider is entering orders

LVEF, GFR, HR, K+
Current GDMT
GDMT Order Set

No Alert usual care

Data collected via electronic health record (pragmatic design)

PRIMARY OUTCOMES

Increase in number of prescribed GDMT at 30 days

SECONDARY OUTCOMES

Rates of 30-day re-hospitalization, % increase in each class of GDMT, doses of GDMT, prescriptions filled (Sure Scripts), total cost of care, 1-yr all cause mortality

Consort Diagram

Enrollment

Assessed for eligibilty (n= 100 clusters of providers)

Excluded (n=7)*

Randomized (n=93 clusters)

Allocation

Alert
(46 providers, n=685 participants)
Received allocated intervention with median number of participants/clusters:12.5 [7, 21]

No Alert
(47 providers, n=625 participants)
Received allocated intervention with average number of participants/clusters:11 [7, 18]

Patients excluded from analysis/lost to follow-up (n=0)

Follow-up

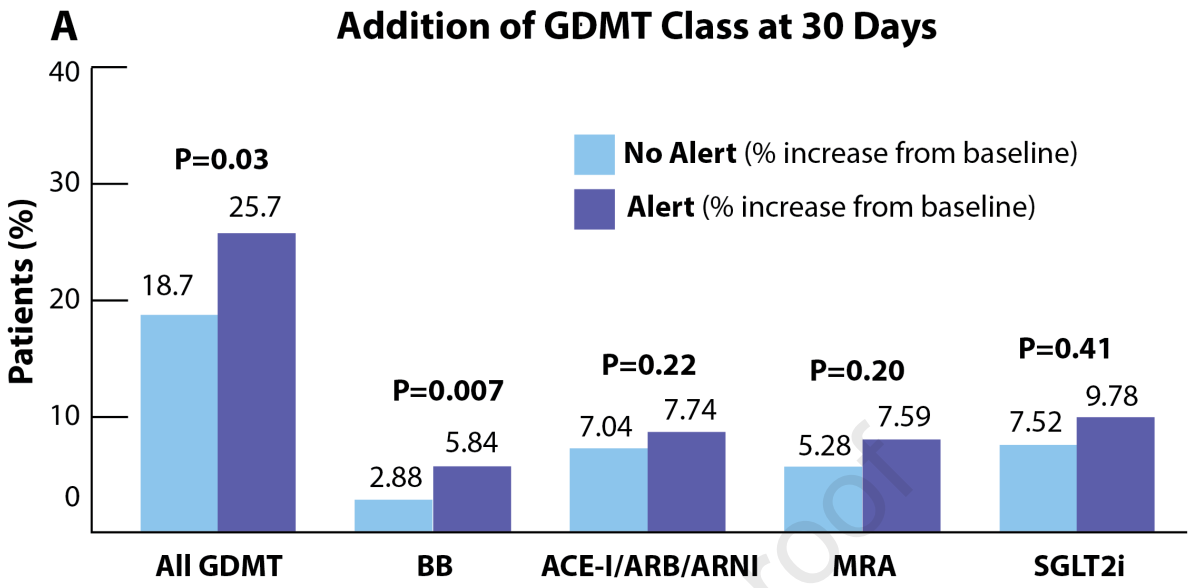
Patients excluded from analysis/lost to follow-up (n=0)

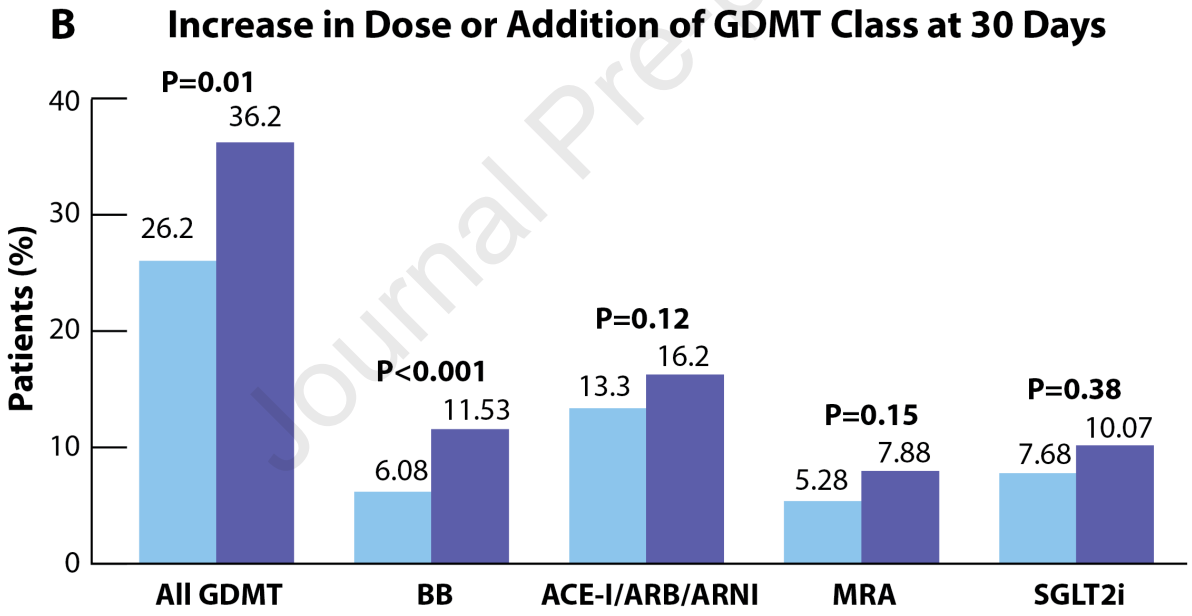
Analysed
(46 providers, n=685 participants)
Excluded from analysis (n= 0)

Analysis

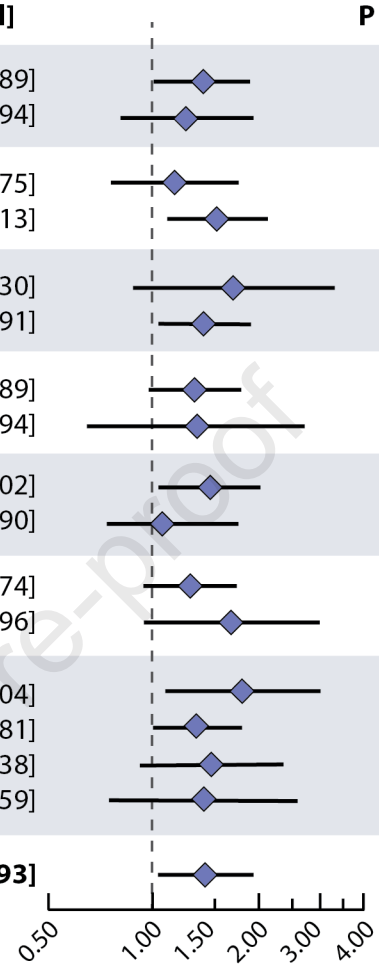
Analysed
(47 providers, n=625 participants)
Excluded from analysis (n= 0)

*Finished recruitment before provider saw eligible patients

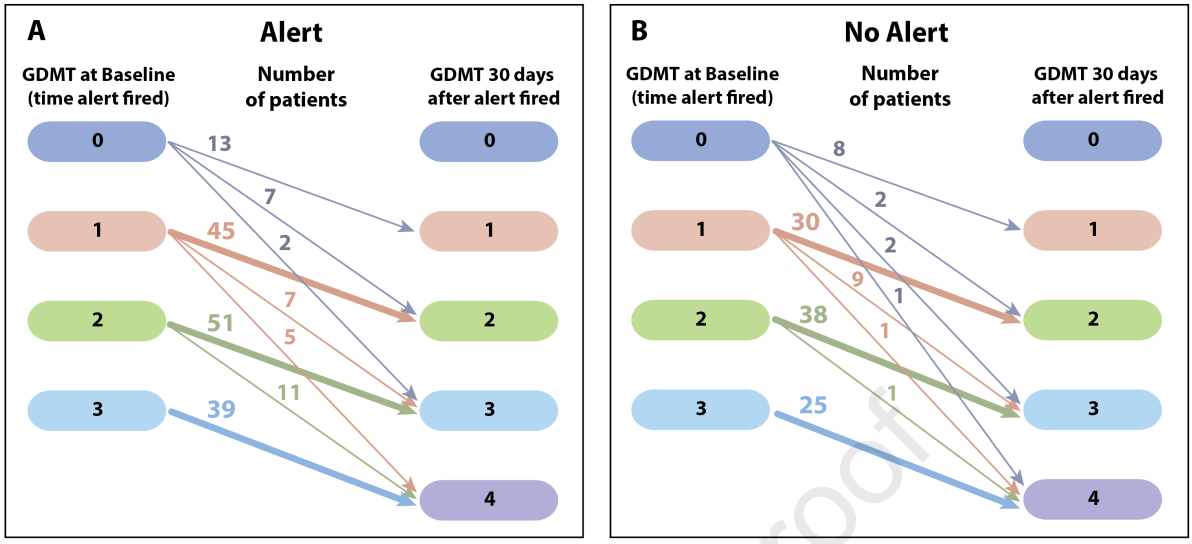




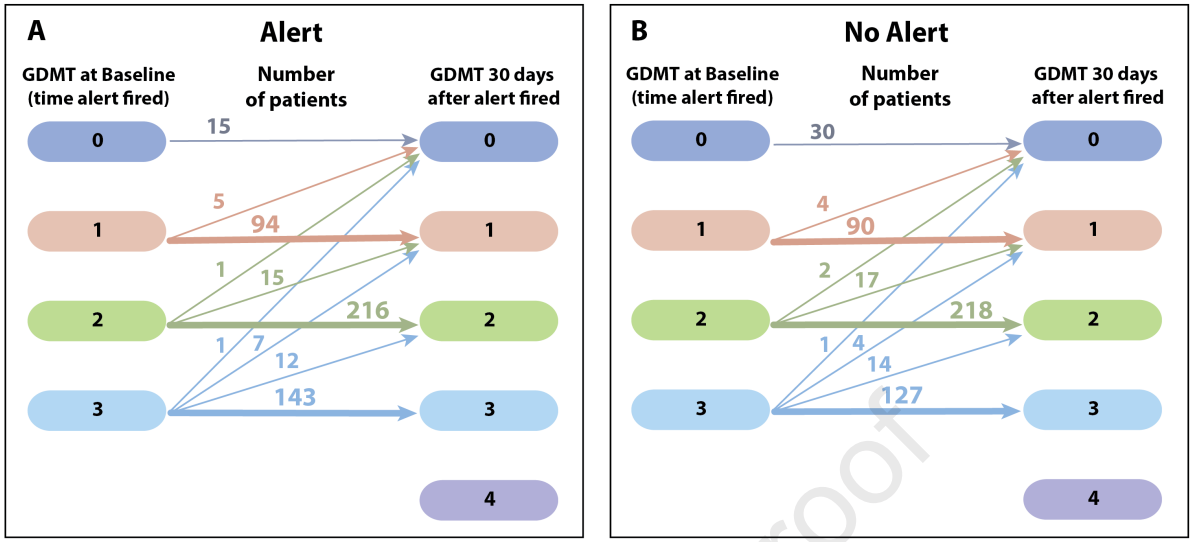
Subgroup	No. of Patients	RR [95%CI]	Interaction P Value
Age ≥ 65 yr	937	1.39 [1.01, 1.89]	0.86
Age < 65 yr	373	1.24 [0.79, 1.94]	
Female	402	1.15 [0.75, 1.75]	0.09
Male	908	1.53 [1.09, 2.13]	
Black	237	1.70 [0.87, 3.30]	0.67
Non-black	1073	1.40 [1.03, 1.91]	
LVEF ≥ 20%	1157	1.31 [1.01, 1.89]	0.41
LVEF < 20%	139	1.24 [0.79, 1.94]	
Cardiology	981	1.45 [1.04, 2.02]	0.65
Non-cardiology	329	1.05 [0.58, 1.90]	
Medicare/Medicaid	1117	1.27 [0.93, 1.74]	0.20
Other	193	1.57 [0.94, 2.96]	
GDMT: 0	80	1.81 [1.08, 3.04]	0.71
GDMT: 1	286	1.34 [0.99, 1.81]	
GDMT: 2	570	1.47 [0.91, 2.38]	
GDMT: 3	374	1.39 [0.75, 2.59]	
Overall	**1310**	**1.41 [1.03, 1.93]**	



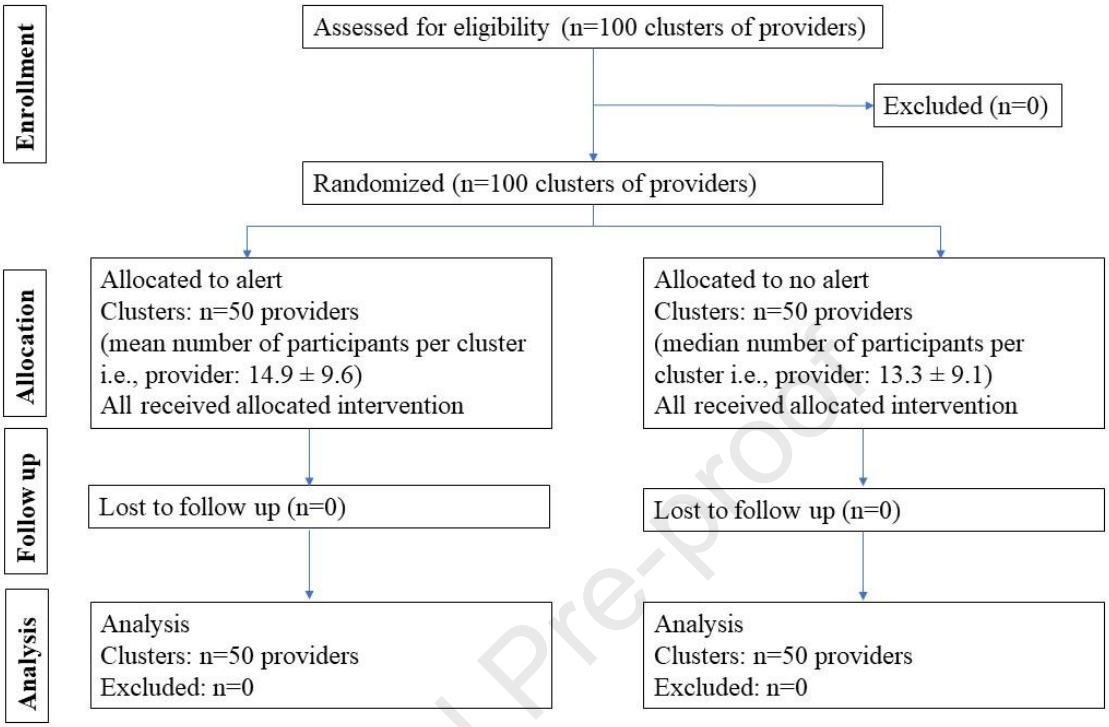
"Wins" – Increase in GDMT



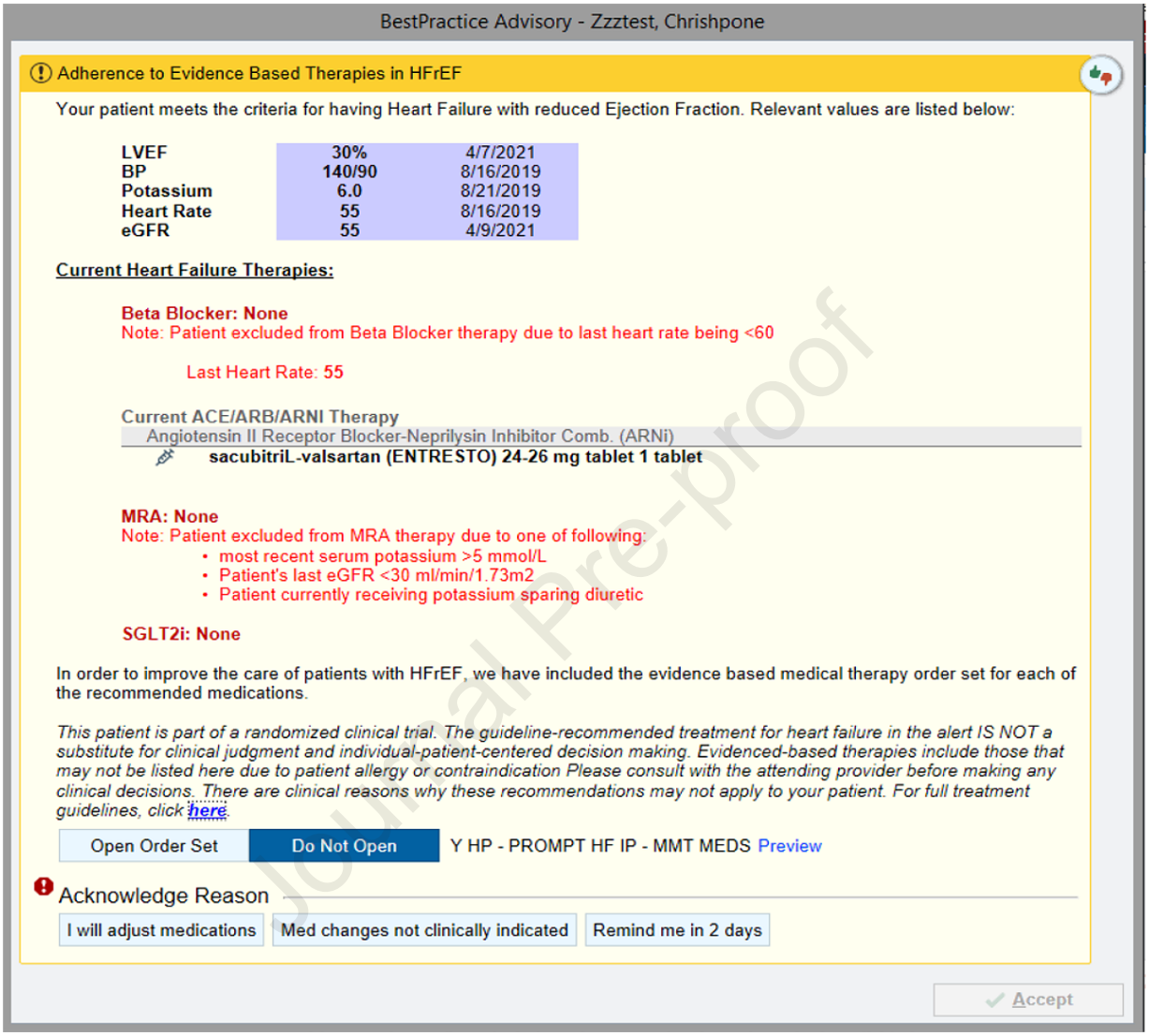
"Losses"- No Change or Decrease in GDMT



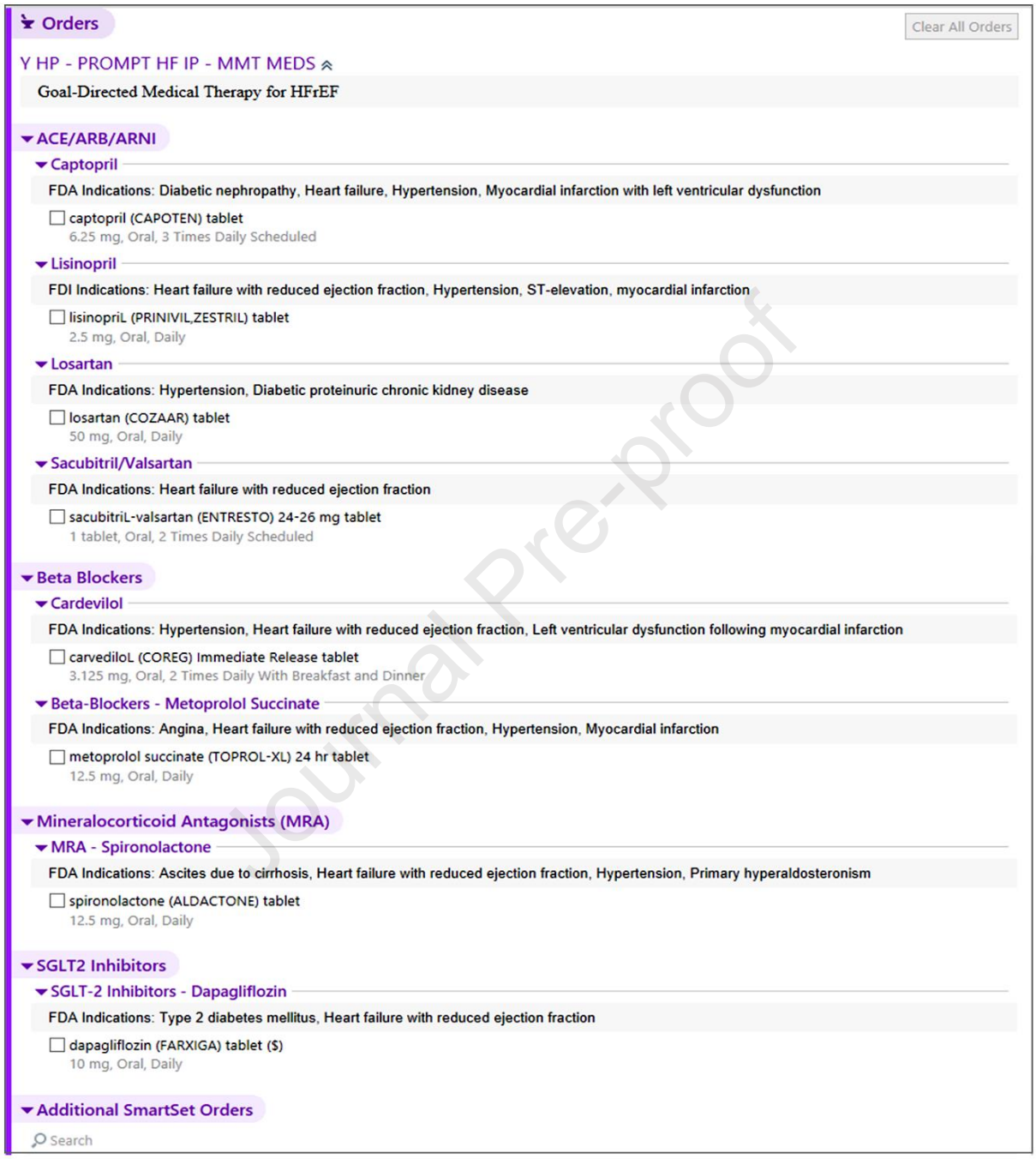
Supplementary Figure 1. Consort Diagram of Trial.



Supplementary Figure 2. The Best Practice Alert Seen by Providers Randomized to the Alert Arm.



Supplementary Figure 3. Display of Medications Tailored for Specific Patients.



Supplemental Table 1. Change in GDMT According to Alert Group.

Changes in GDMT	Alert N=685	No Alert N=625	*P*
Baseline at 0 GDMT			
Stay at 0	15 (2.2)	30 (4.8)	0.16
Increase to 1	13 (1.9)	8 (1.3)	
Increase to 2	7 (1)	2 (0.3)	
Increase to 3	2 (0.3)	2 (0.3)	
Increase to 4	0 (0)	1 (0.2)	
Baseline at 1 GDMT			
Decrease to 0	5 (0.7)	4 (0.6)	0.67
Stay at 1	94 (13.7)	90 (14.4)	
Increase to 2	45 (6.6)	30 (4.8)	
Increase to 3	7 (1)	9 (1.4)	
Increase to 4	1 (0.2)	1 (0.2)	
Baseline at 2 GDMT			
Decrease to 0	1 (0.1)	2 (0.3)	0.11
Decrease to 1	15 (2.2)	17 (2.7)	
Stay at 2	216 (31.5)	218 (34.9)	
Increase to 3	51 (7.4)	38 (6.1)	
Increase to 4	11 (1.6)	1 (0.2)	
Baseline at 3 GDMT			
Decrease to 0	1 (0.1)	2 (0.3)	0.57
Decrease to 1	7 (1)	4 (0.6)	
Decrease to 2	12 (1.8)	14 (2.2)	
Stay at 3	143 (20.9)	127 (20.3)	
Increase to 4	39 (5.7)	25 (4)	

Data are % (n) or median (interquartile range) Any increase is considered a "win" i.e., primary outcome observed. No change or decrease in number of GDMT is considered a "null" outcome i.e., primary outcome not observed. P-values reflect clustered chi-square without adjustment for baseline factors (given small sample sizes).