

A Cluster Randomized **PR**agmatic Trial Aimed At Impr**O**ving Use Of Guideline Directed **M**edical Therapy In Out**P**atien**T**s With **H**ear**T** **F**ailure: **PROMPT-HF**

Lama Ghazi MD PhD, Yu Yamamoto MS, Ralph Riello PharmD, Claudia Coronel-Moreno MPH,
Melissa Martin MA, Kyle O'Connor MS, Michael Simonov MD, Joanna Huang PharmD, Temitope
Olufade PhD MPH, James McDermott PhD, Ravi Dhar PhD, Silvio Inzucchi MD, Eric Velazquez MD,
F Perry Wilson MD MSCE, Nihar Desai MD MPH, Tariq Ahmad MD MPH

Yale SCHOOL OF MEDICINE



Funding Information and Disclosures

JH, TO, JM are employees of AstraZeneca. RJR is a consultant for Alexion, AstraZeneca, Boehringer Ingelheim, Janssen, Johnson & Johnson, PhaseBio, and Portola. RD does executive teaching for Sanofi Consumer Healthcare. SEI has served on clinical trial committees and advisory boards for Boehringer Ingelheim, AstraZeneca, and Novo Nordisk. He has served as a consultant to Merck, Pfizer, Lexicon, vTv Therapeutics, Esperion and Abbott and has delivered lectures supported by Boehringer Ingelheim and AstraZeneca. TA is consultant for Sanofi-Aventis, Amgen, Cytokinetics. He has research funding from Boehringer Ingelheim, AstraZeneca, Cytokinetics, and Relypsa. NRD works under contract with the Centers for Medicare and Medicaid Services to develop and maintain performance measures used for public reporting and pay for performance programs. He reports research grants and consulting for Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Cytokinetics, Novartis, SCPharmaceuticals, and Vifor. The remaining authors have nothing to disclose.

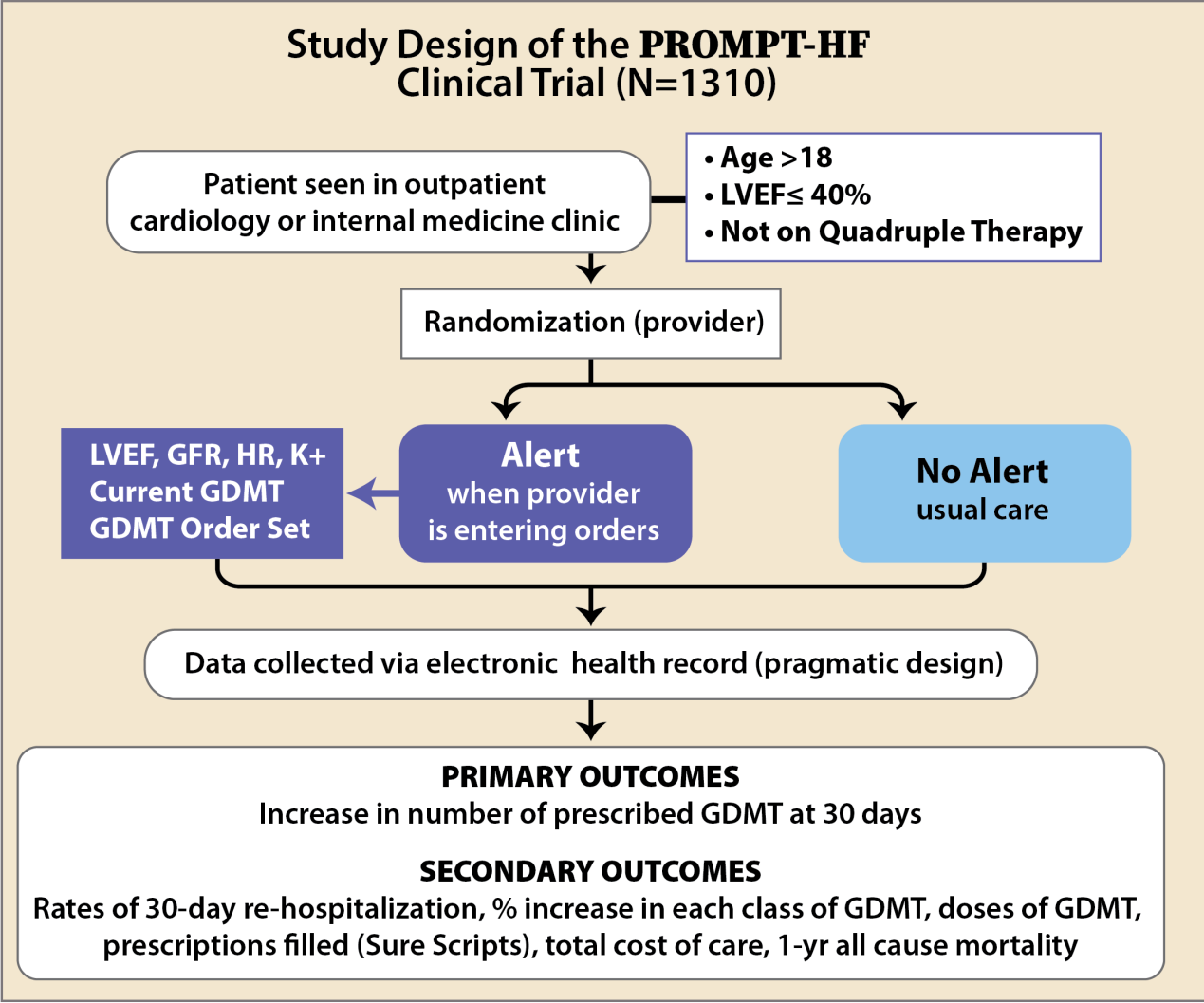
Background

- GDMT improves clinical outcomes in HFrEF but remains pervasively under-prescribed
- Efforts to optimize GDMT are abundant and resource intensive but limited evidence supports their use
- The electronic health record (EHR) may be used to target and individualize GDMT recommendations
- This approach is easily scalable and a low-cost way to accelerate high value care

Study Hypothesis

The ***PR***agmatic Trial ***Of M***essaging to ***P***roviders about outpatient ***T***reatment of ***H***eart ***F***ailure (***PROMPT-HF***) was designed to test the hypothesis that **timely** and **targeted** alerting of recommendations about medical treatment of HFrEF tailored to the patient would lead to **higher** rates of GDMT prescription compared to usual care

Study Design



Alert Arm

BestPractice Advisory - Zztest, Chrishtwo

⚠️ Optimize medications for your patient with HFrEF

Your patient meets the criteria for having heart failure with reduced Ejection Fraction (HFrEF). Relevant values are listed below:

BP	150/90	10/19/2020
Heart Rate	120	10/19/2020
LVEF	35%	8/16/2020
Potassium	5.8	8/31/2020
eGFR	35	8/31/2020
Serum Creatinine	1.00	8/29/2019

Current Heart Failure Therapies:

Beta Blocker: None

Current ACE/ARB/ARNI Therapy
ACE Inhibitor and Calcium Channel Blocker Combinations
🏠 amLODIPine-benazepril (LOTREL) 5-10 mg per capsule

MRA: None

SGLT2i: None

In order to improve the care of patients with HFrEF, we have included an evidence based medical therapy order set below. For full treatment guidelines, click [here](#).

The guideline-recommended treatment for heart failure in this alert IS NOT a substitute for clinical judgment and individual-patient-centered decision making. There are clinical reasons why these recommendations may not apply to your patient.

Open SmartSet

Do Not Open

Maximizing Medical Therapies for HFrEF [Preview](#)

Acknowledge Reason

I will adjust medications

Med changes not clinically indicated

Defer for other reason (specify)

✓ Accept

Orders Clear All Orders

Therapies for HFrEF ⌵

Goal-Directed Medical Therapy for HFrEF

▼ ACE/ARB/ARNI

▼ Sacubitril-Valsartan (Entresto)

FDA-approved to reduce the risk of cardiovascular death and hospitalization for patients with chronic heart failure[NYHA II-IV] and reduced ejection fraction

☐ sacubitril-valsartan (ENTRESTO)

▼ Lisinopril (Zestril)

FDA-approved to treat heart failure with reduced ejection, hypertension, ST-elevation myocardial infarction

☐ lisinopril (PRINIVIL,ZESTRIL)

▼ enalapril (Vasotec)

FDA-approved to treat hypertension, symptomatic heart failure.

☐ enalapril (VASOTEC)

▼ Losartan (Cozaar)

FDA-approved to treat hypertension, diabetic proteinuric chronic kidney disease

☐ losartan (COZAAR)

▼ valsartan (Diovan)

FDA-approved to treat hypertension, heart failure.

☐ valsartan (DIOVAN)

▼ Beta-Blockers

▼ Carvedilol (Coreg)

FDA-approved to treat hypertension, heart failure with reduced ejection fraction, left ventricular dysfunction following myocardial infarction in clinically stable patients

☐ carvedilol (COREG)

▼ metoprolol succinate (Toprol-XL)

FDA-approved to treat angina, heart failure with reduced ejection fraction, hypertension, myocardial infarction

☐ metoprolol succinate (TOPROL-XL)

▼ Mineralocorticoid Receptor Antagonists

▼ eplerenone (Inspra)

FDA-approved to treat hypertension, heart failure after myocardial infarction

☐ eplerenone (INSPIRA)

▼ spironolactone (Aldactone)

FDA-approved to treat ascites due to cirrhosis, heart failure with reduced ejection fraction, hypertension, primary hyperaldosteronism

☐ spironolactone (ALDACTONE)

▼ SGLT2

▼ Dapagliflozin

FDA-approved to treat type 2 diabetes mellitus, heart failure with reduced ejection fraction

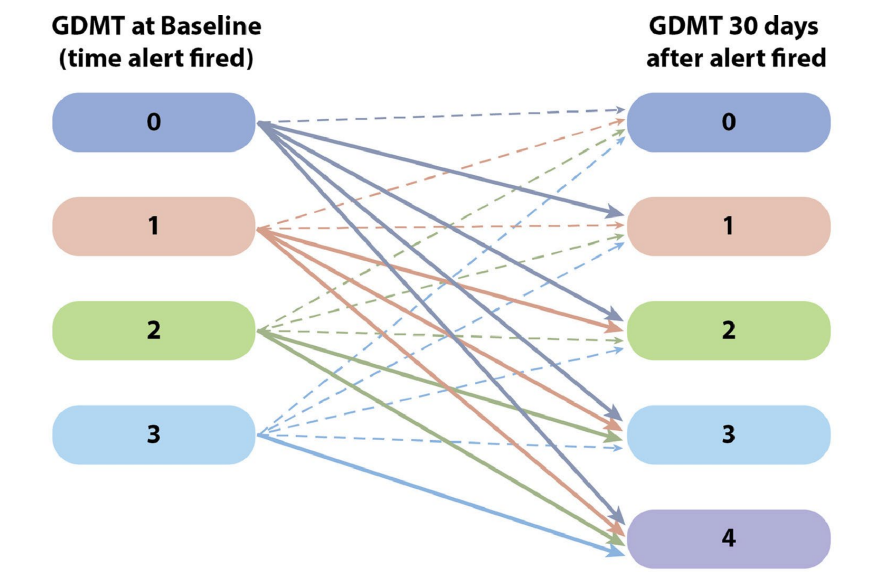
☐ dapagliflozin (FARXIGA)

▼ Empagliflozin

FDA-approved to treat type 2 diabetes mellitus

☐ empagliflozin (JARDIANCE)

Primary Outcome: Addition of GDMT Class

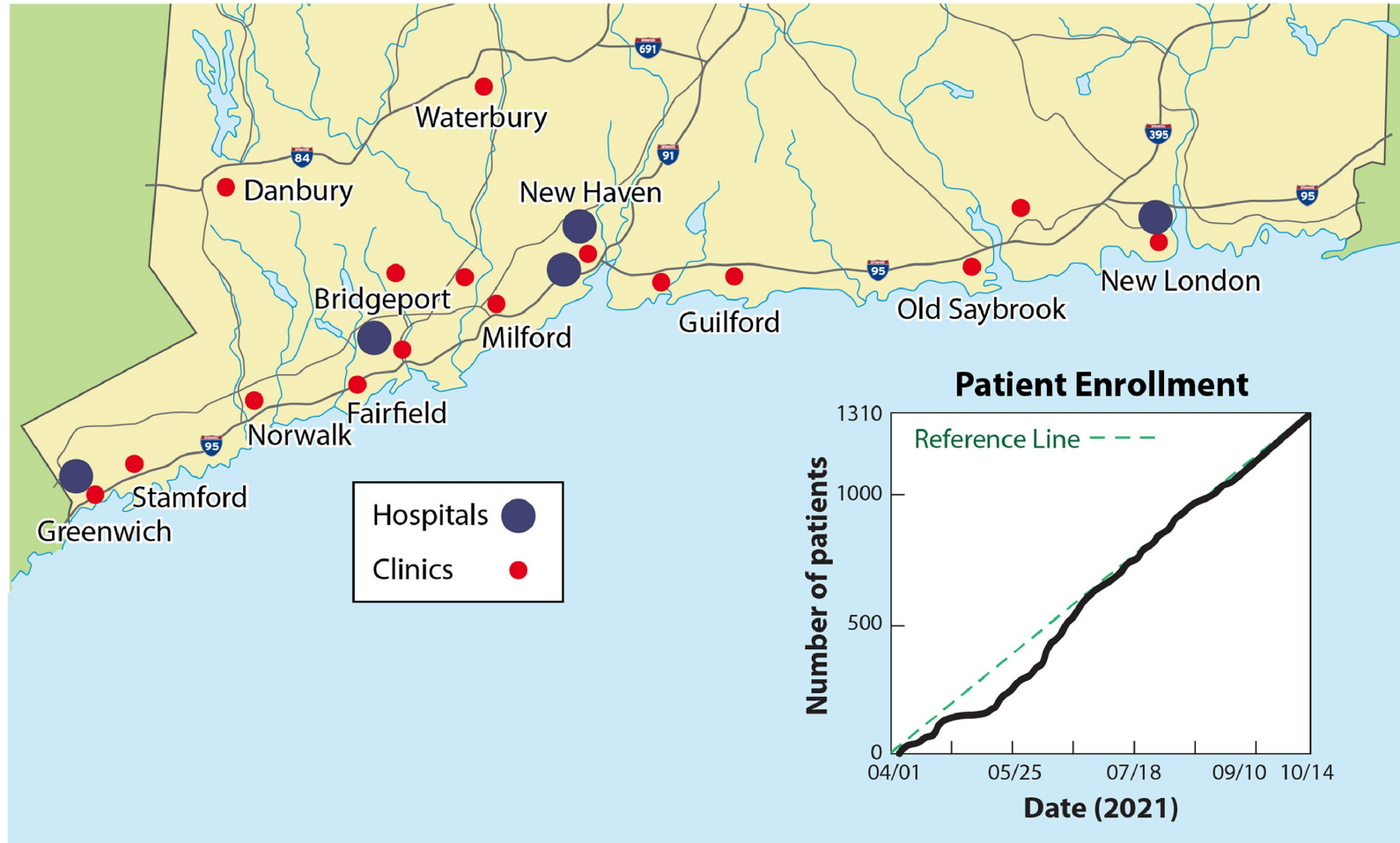


Scenario	Evidence-based medications at randomization	Evidence-based medications 30 days post-randomization	Outcome present (increase evidence-based medications)
1	ACEi + beta blocker	ARB + beta blocker	No
2	ARB + MRA	ARB + SGLT2i	No
3	ACEi	ACEi + SGLT2i + beta blocker	Yes
4	ACEi + MRA	ARNi	No
5	ARB + MRA + SGLT2i	ARB + MRA + SGLT2i + beta blocker	Yes
6	ACEi	ARNi	No

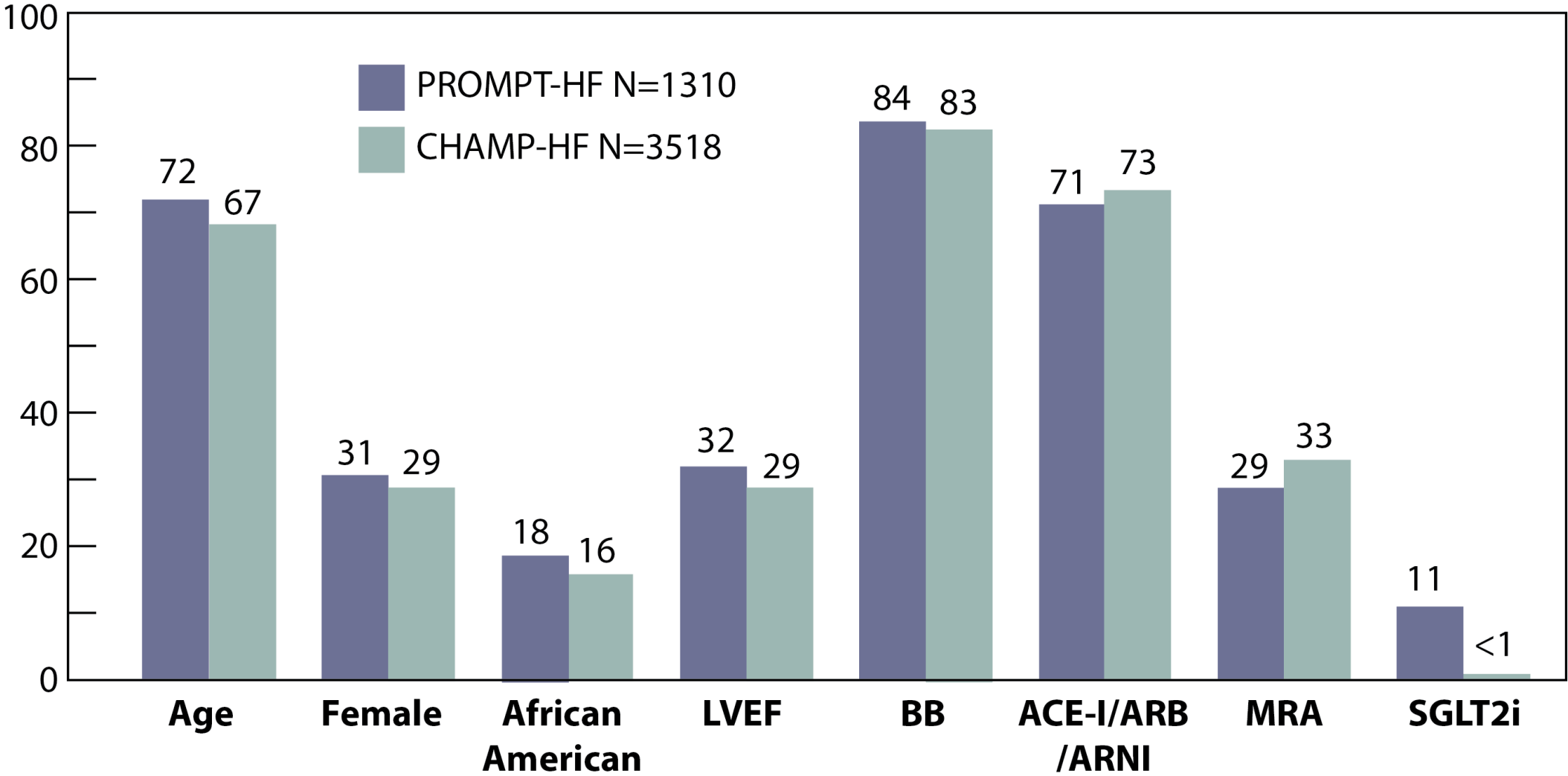
Sample Size and Power Calculations

- Absolute increase of 10% in proportion of patients on an additional class of GDMT at 30 days
- Sample size of 1310 achieved 91% power to detect a 10% difference between study arms at $\alpha=0.05$ and ICC of 0.05
- Primary outcome examined association between intervention and outcomes using generalized linear models adjusting for prespecified baseline characteristics and accounting for clustering at provider level

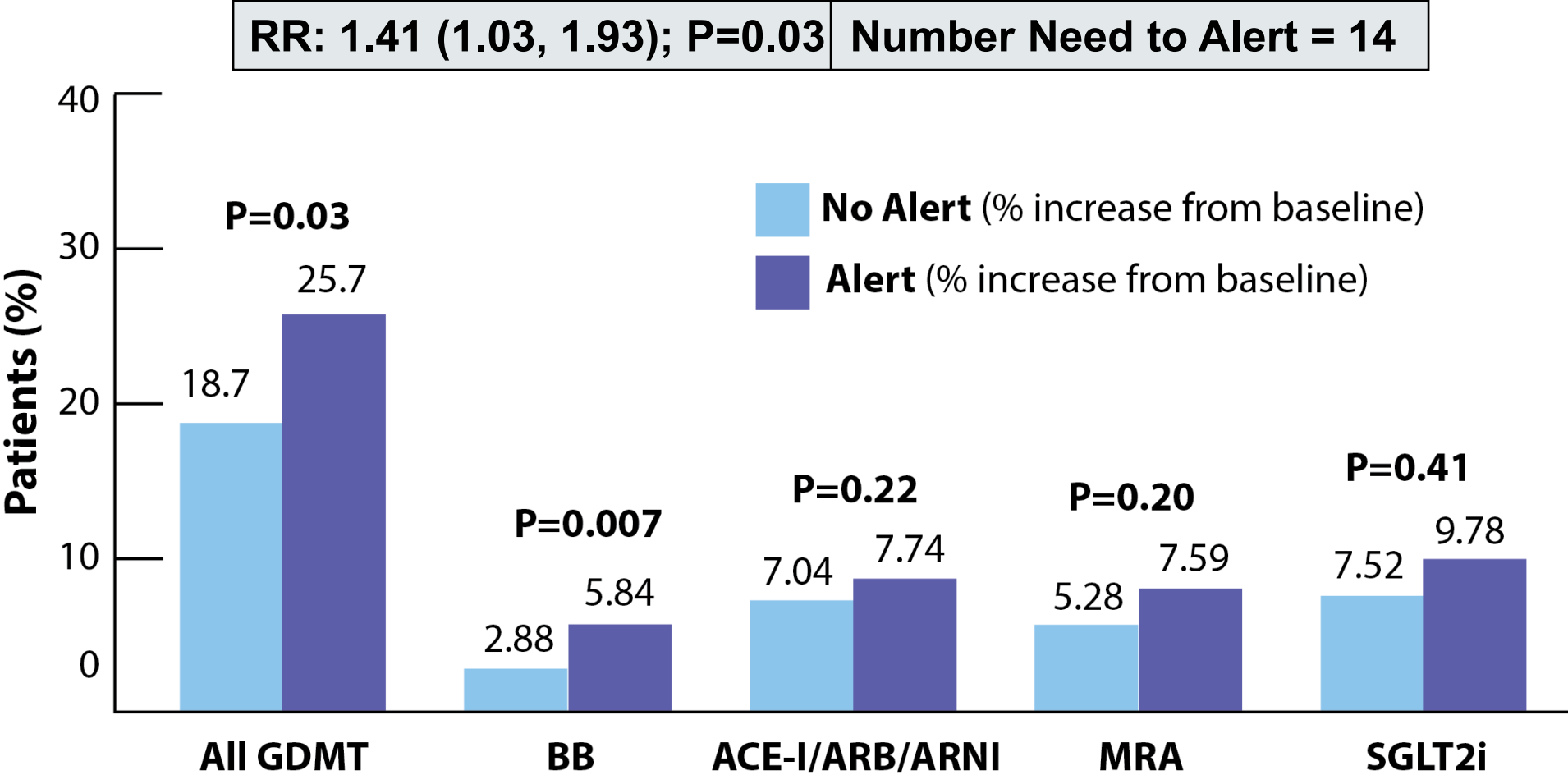
Embedded EHR-Based Pragmatic Clinical Trial



Baseline Characteristics



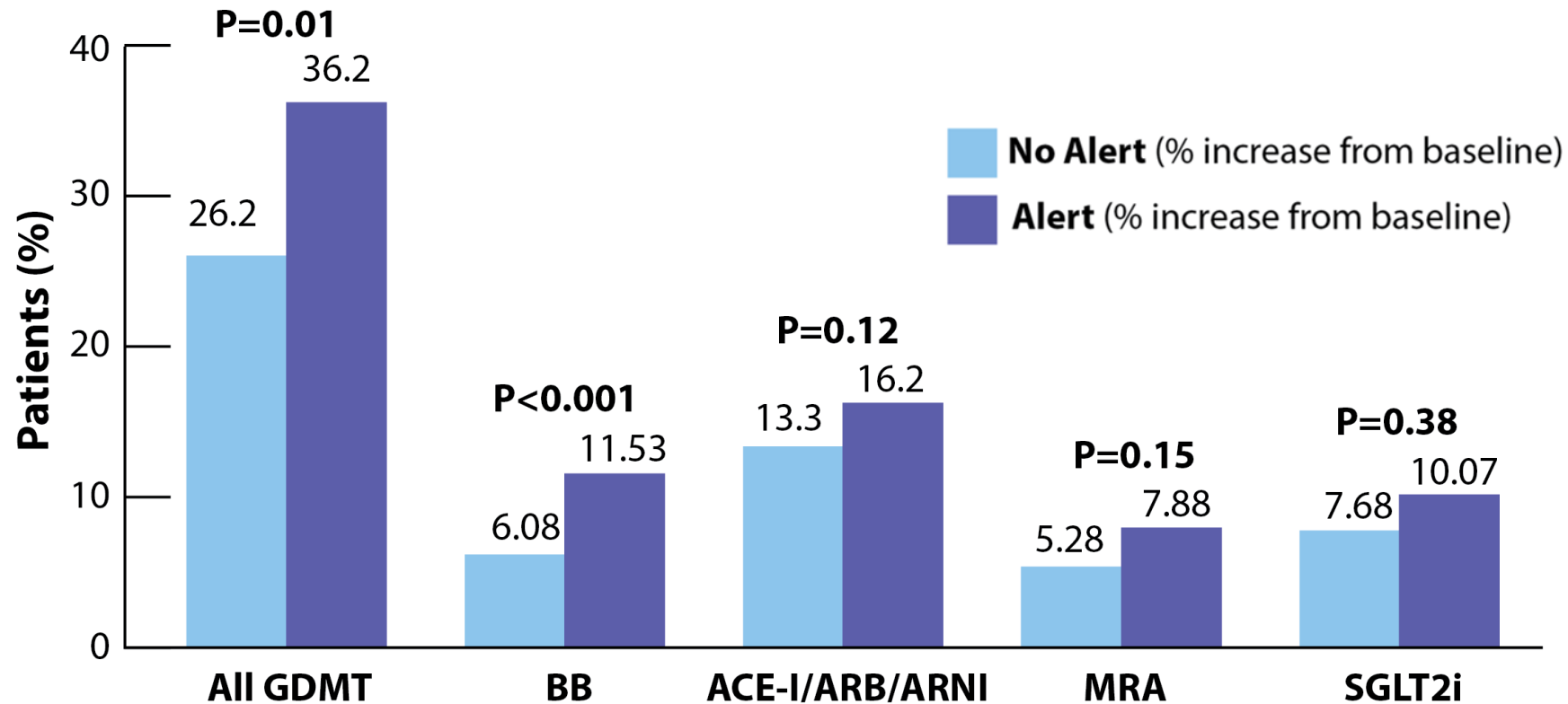
Primary Clinical Endpoint: Additional GDMT Class









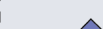

Secondary Clinical Endpoint: +GDMT Class/↑Dose

RR: 1.39 (1.08, 1.79); P=0.01

Number Need to Alert= 10



Pre-Specified Subgroups

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]		

Limitations

- Results from Single Health Care System
- Only Included High Volume Clinicians
- Tested in Outpatient Setting; Inpatient Trial Ongoing
- Tested within the Epic® EHR
- Increase in Dose was Secondary Outcome
- Impact Beyond 30 Days Subject of Future Study

Conclusions

A personalized alert triggered via the EHR during office visits led to significantly higher number of HFrEF patients on appropriate 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

Full Results Now Available Online



JACC
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

We Thank The Participants of PROMPT-HF

Questions or Comments

tariq.ahmad@yale.edu

 [@YaleHFdoc](https://twitter.com/YaleHFdoc)