Yale SCHOOL OF MEDICINE

The Yale New Haven Health System as an Evidence Generation Ecosystem for Heart Failure

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Friday December 4th, 2020
NIH Collaboratory Grand Rounds

Disclosures

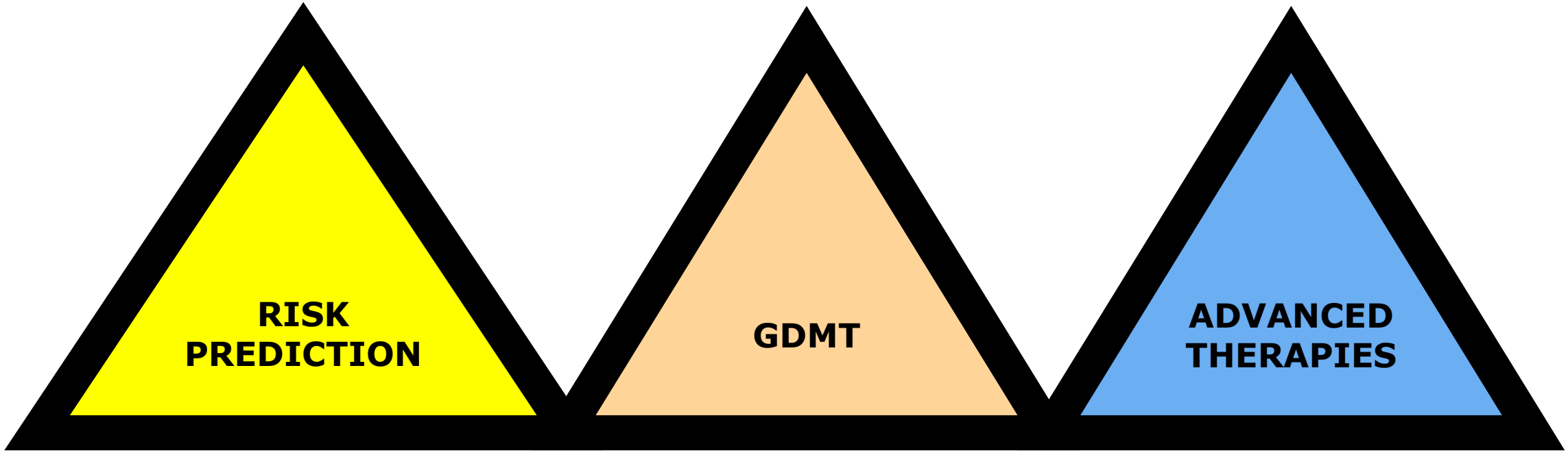
Advisory boards for Amgen, AstraZeneca, Boehringer Ingelheim, Cytokinetics, Novartis, and Relypsa.

Research Funding from PeraHealth, AstraZeneca, Boehringer Ingelheim, Amgen, and Cytokinetics.

Alumnus of the K12 AHRQ Program.

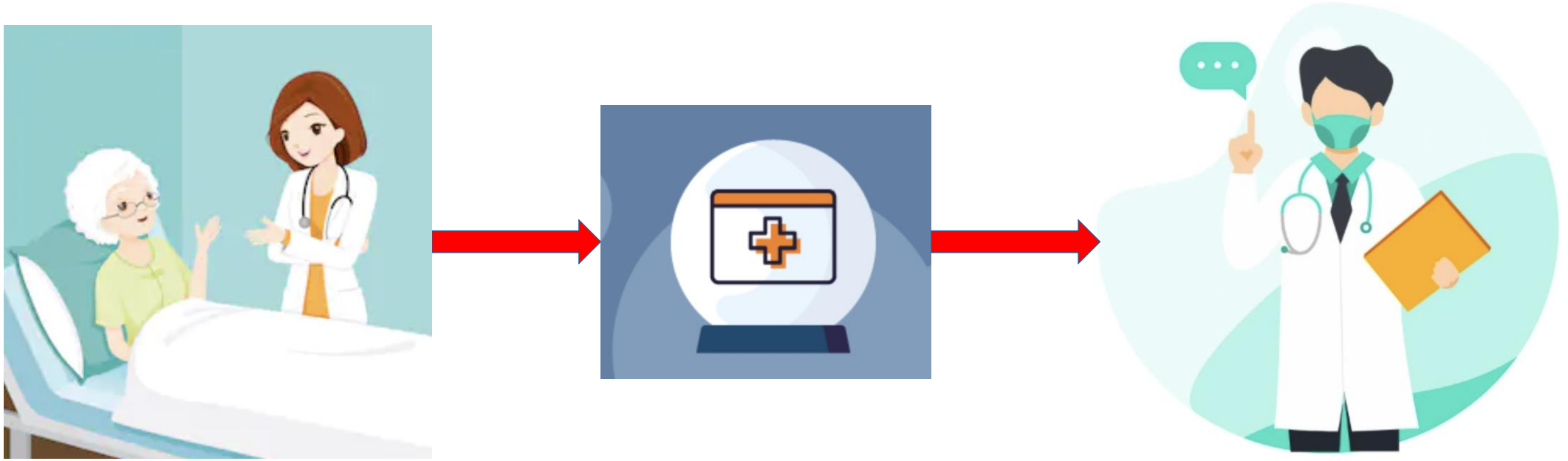
Evolution of These Ideas

The Three Challenges in Heart Failure

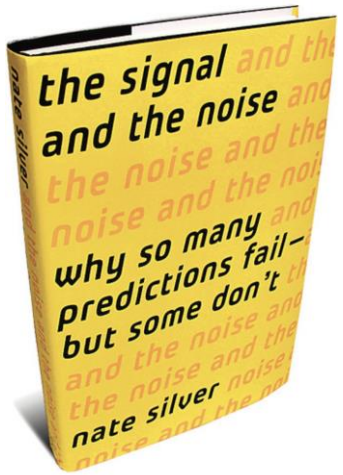


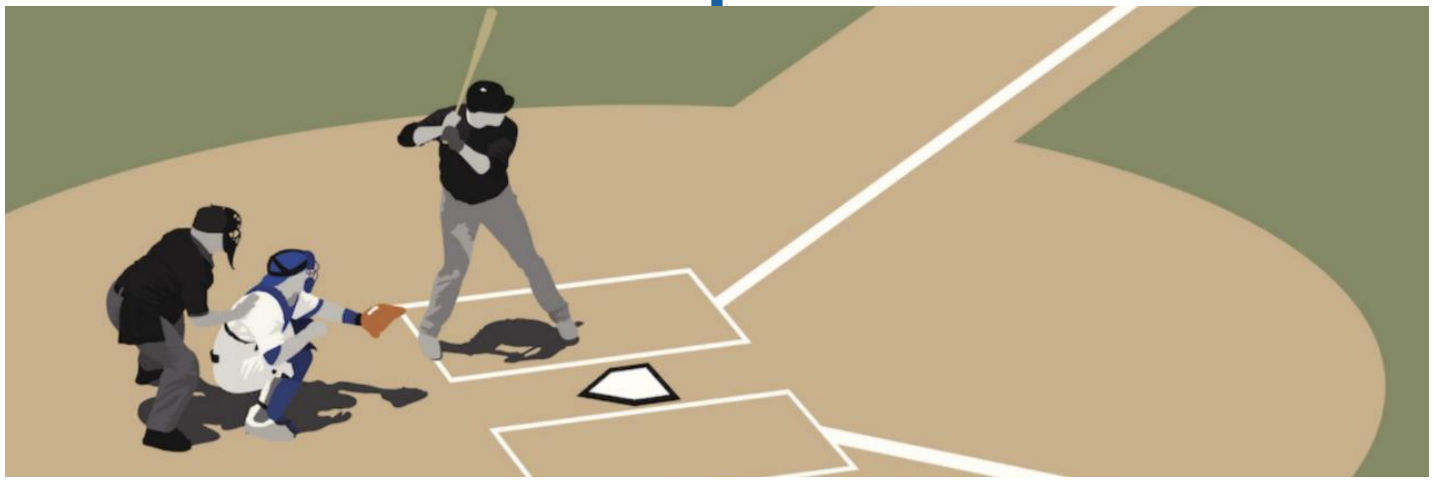

RISK
PREDICTION

The Best-Case Scenario (That Patients Expect)

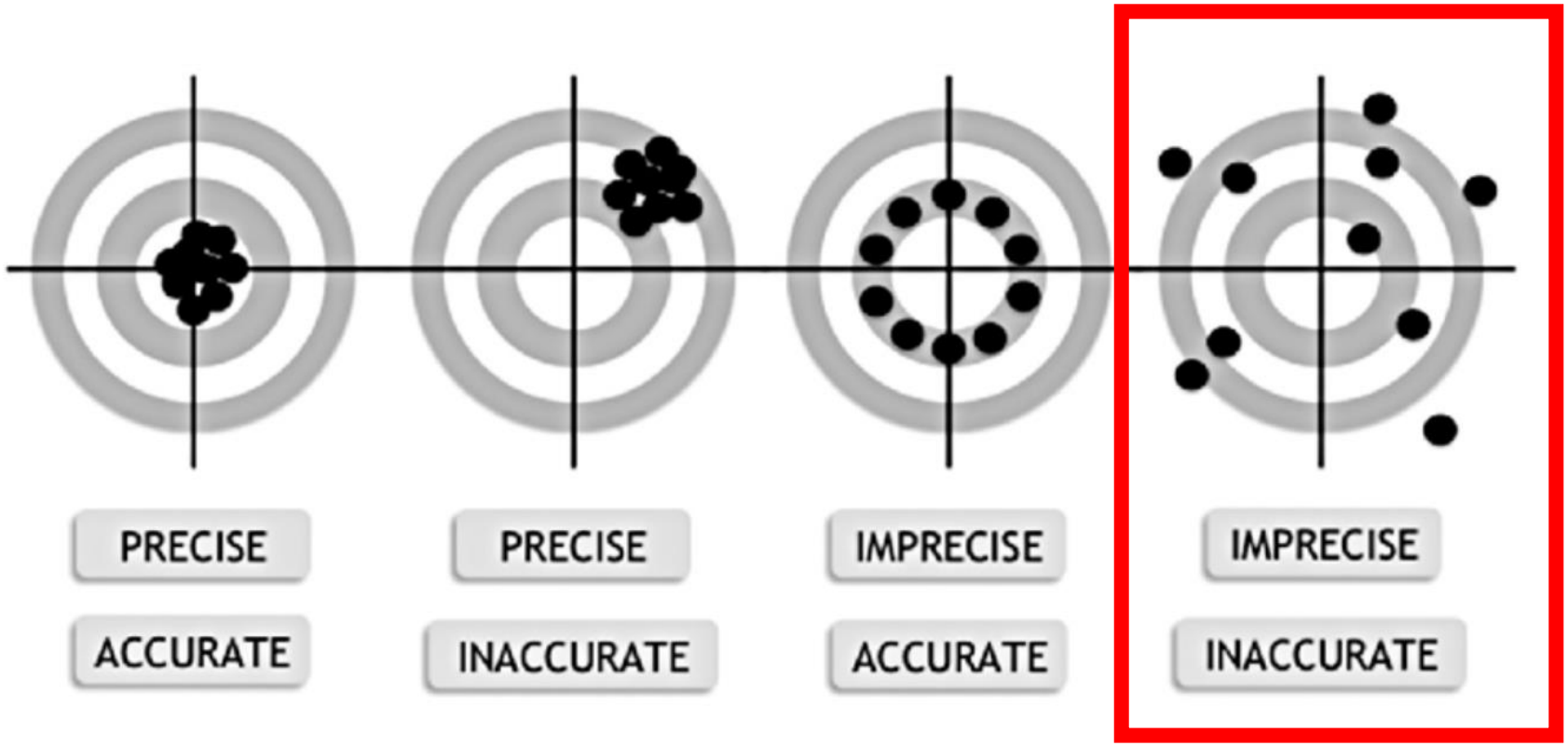


Moneyball as it Applies to Heart Failure





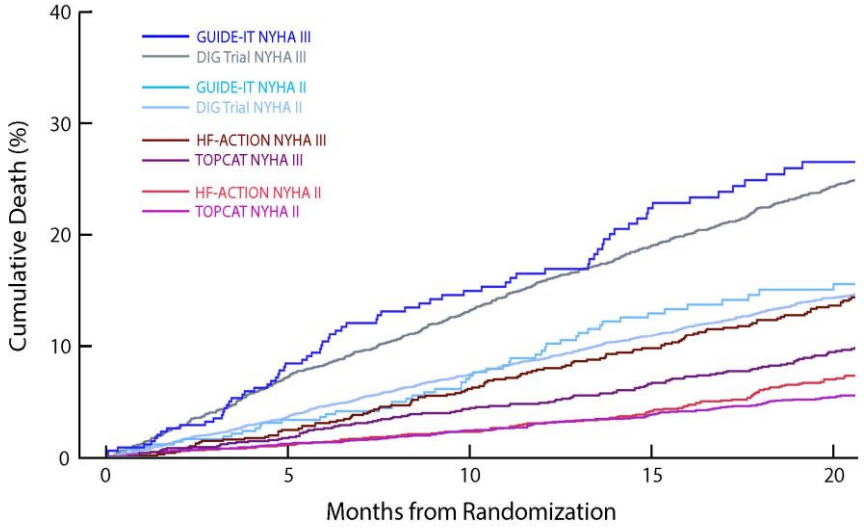
Limitations of Current Methodologies

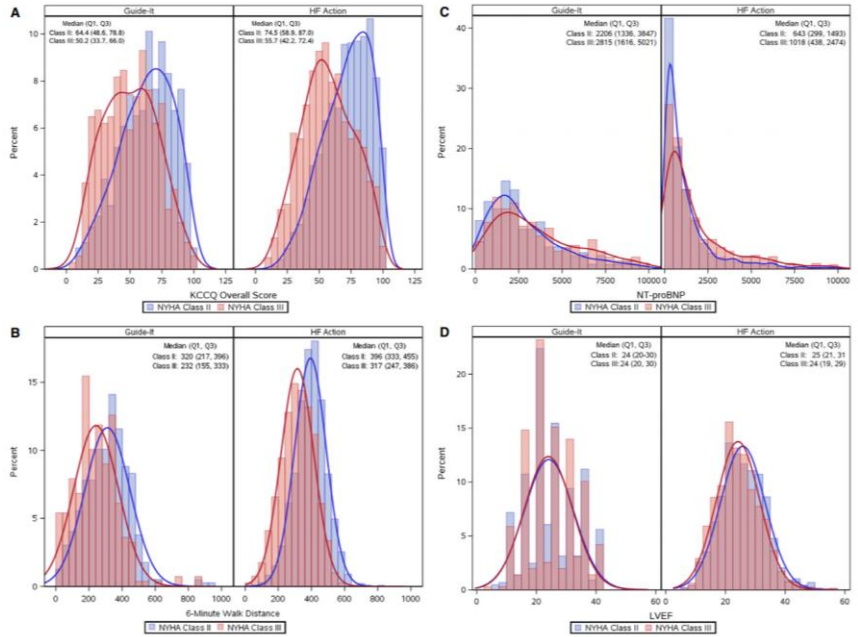


The NYHA Classification System

Clinical Implications of the New York Heart Association Classification

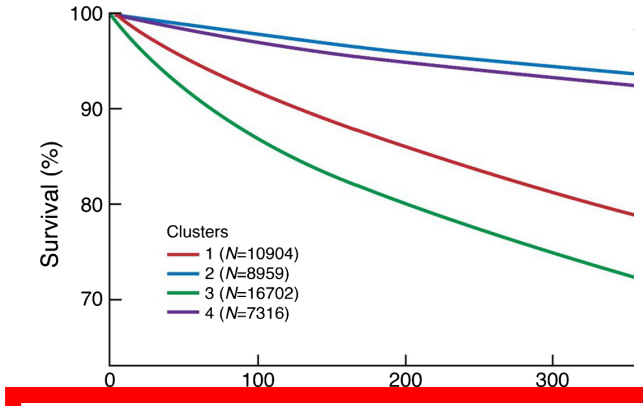
César Caraballo, MD; Nihar R. Desai, MD, MPH; Hillary Mulder, MS; Brooke Alhanti, PhD; F. Perry Wilson, MD, MS; Mona Fiuzat, PharmD; G. Michael Felker, MD; Ileana L. Piña, MD, MPH; Christopher M. O'Connor, MD; Joanne Lindenfeld, MD; James L. Januzzi, MD; Lawrence S. Cohen, MD; Tariq Ahmad, MD, MPH

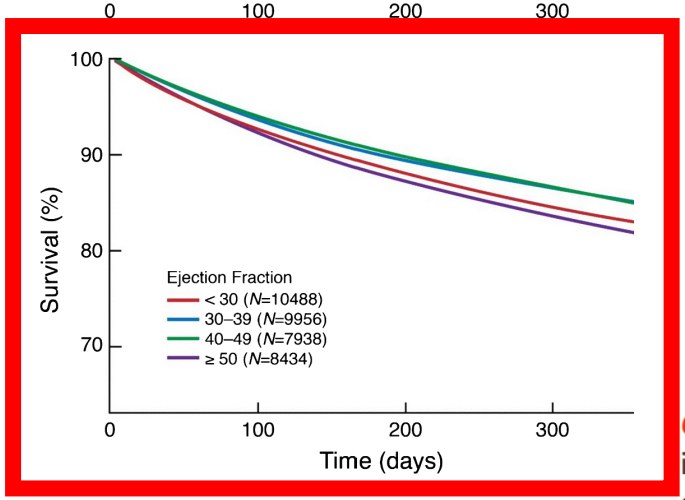




Conclusions—The NYHA system poorly discriminates HF patients across the spectrum of functional impairment. These findings raise important questions about the need for improved phenotyping of these patients to facilitate risk stratification and response to interventions. **(*J Am Heart Assoc*. 2019;8:e014240. DOI: 10.1161/JAHA.119.014240.)**

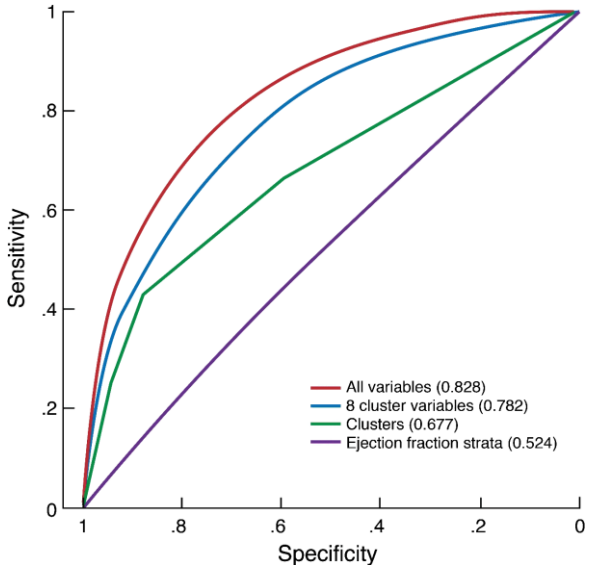
Ejection Fraction as a Predictor of Outcomes





Machine Learning Methods Improve Prognostication, Identify Clinically Distinct Phenotypes, and Detect Heterogeneity in Response to Therapy in a Large Cohort of Heart Failure Patients

Tariq Ahmad, MD, MPH; Lars H. Lund, MD, PhD; Pooja Rao, MBBS, PhD; Rohit Ghosh, MSc; Prashant Warier, PhD; Benjamin Vaccaro, MD; Ulf Dahlström, MD, PhD; Christopher M. O'Connor, MD; G. Michael Felker, MD, MHS; Nihar R. Desai, MD, MPH

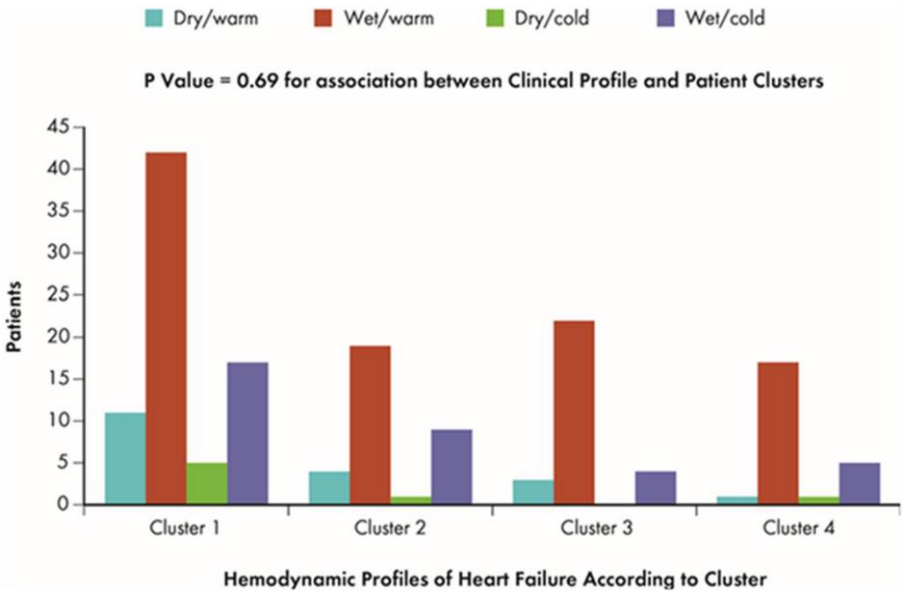


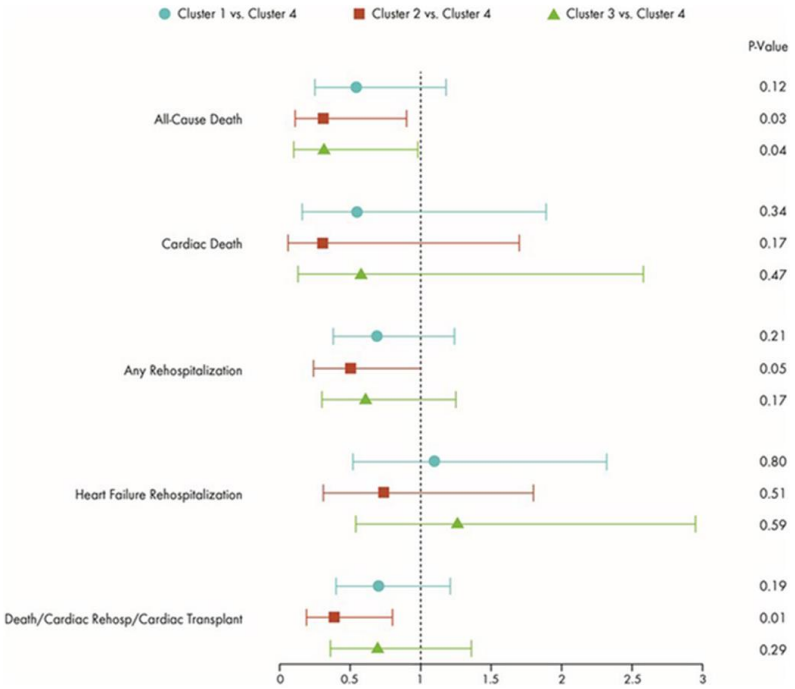
Conclusions—Machine learning algorithms accurately predicted outcomes in a large data set of HF patients. Cluster analysis identified 4 distinct phenotypes that differed significantly in outcomes and in response to therapeutics. Use of these novel analytic approaches has the potential to enhance effectiveness of current therapies and transform future HF clinical trials. **(*J Am Heart Assoc*. 2018;7:e008081. DOI: 10.1161/JAHA.117.008081.)**

Hemodynamic Profiles vs. Data Driven Prediction

Clinical Implications of Cluster Analysis-Based Classification of Acute Decompensated Heart Failure and Correlation with Bedside Hemodynamic Profiles

Tariq Ahmad[1]*, Nihar Desai[1], Francis Wilson[2], Phillip Schulte[3], Allison Dunning[4], Daniel Jacoby[1], Larry Allen[5], Mona Fiuzat[4], Joseph Rogers[4,6], G. Michael Felker[4,6], Christopher O'Connor[7], Chetan B. Patel[4,6]





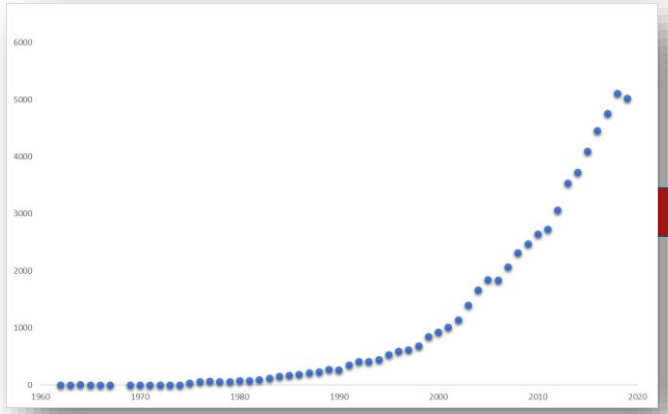
Conclusions

By clustering patients with similar objective variables, we identified four clinically relevant phenotypes of ADHF patients, with no discernable relationship to hemodynamic profiles, but distinct associations with adverse outcomes. Our analysis suggests that ADHF classification using simultaneous considerations of etiology, comorbid conditions, and biomarker levels, may be superior to bedside classifications.

What About Heart Failure "Risk Scores"?

Factors Related to Morbidity and Mortality in Patients With Chronic Heart Failure With Systolic Dysfunction
The HF-ACTION Predictive Risk Score Model

An Administrative Claims Measure Suitable for Profiling Hospital Performance on the Basis of 30-Day All-Cause Readmission Rates Among Patients With Heart Failure



Predicting survival in heart failure: a risk score based on 39 372 patients from 30 studies

The Seattle Heart Failure Model
Prediction of Survival in Heart Failure

A Validated Risk Score for In-Hospital Mortality in Patients With Heart Failure From the American Heart Association Get With the Guidelines Program

Predictors of clinical outcomes in acute decompensated heart failure: Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure outcome models

REVeAL-HF Study: https://www.reveal-hf.com

R**isk **EV**aluation *a*nd its Impact on Clinic**AL** Decision Making and Outcomes in **H**eart **F**ailure: **REVeAL:HF

REVeAL-HF is a **pragmatic randomized controlled trial** testing an **electronic alert system** that informs practitioners about their heart failure patient's **1-year predicted mortality** using validated data from the **EHR**

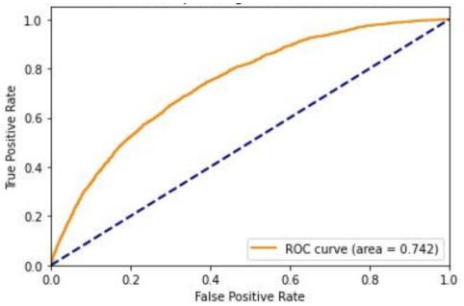
Our primary hypothesis is that electronic alerting about prognostic information on heart failure patients will lead to reductions in hospitalizations and 1-year mortality via improved use of therapies and appropriate referral to subspecialties

REVeAL-HF Study: https://www.reveal-hf.com

EHR Data: Heart Failure Patients Meeting I/E N=7376 (2014-2018)

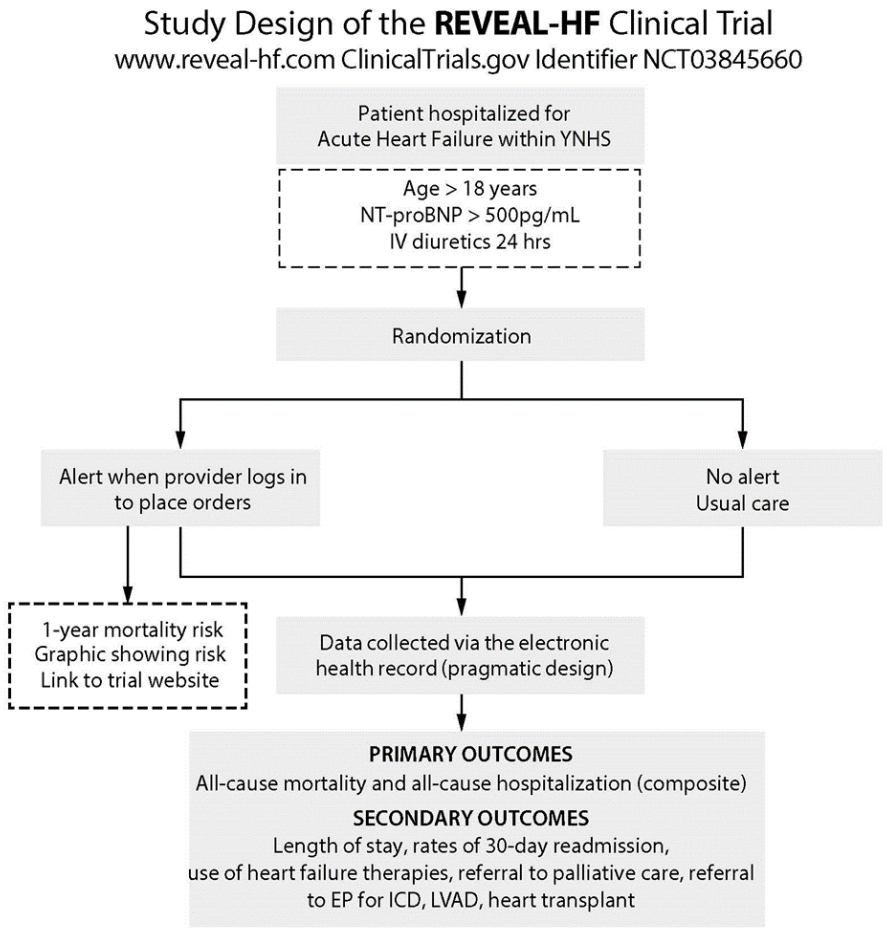
Validation and Derivation Cohort, Compare with Current Models

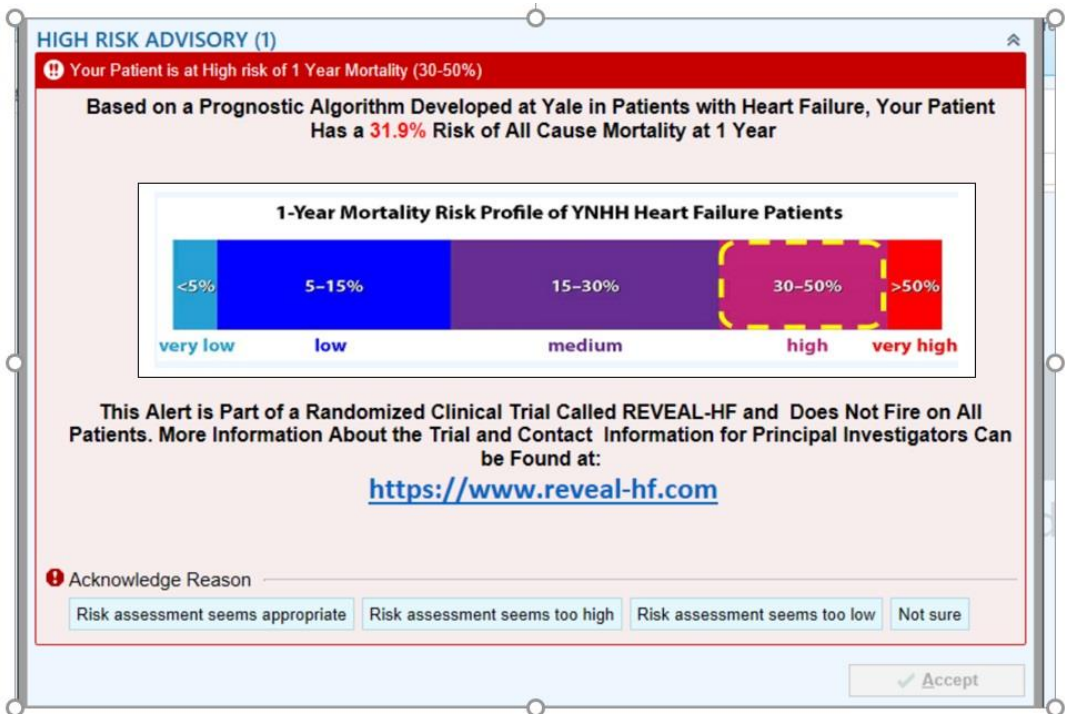
Age
Weight
ACE/ARB
SBP
RDW
BUN
BUN/Cr
NTproBNP
Troponin
MCV
Lymph%
***AMC**
ICU
pH ABG



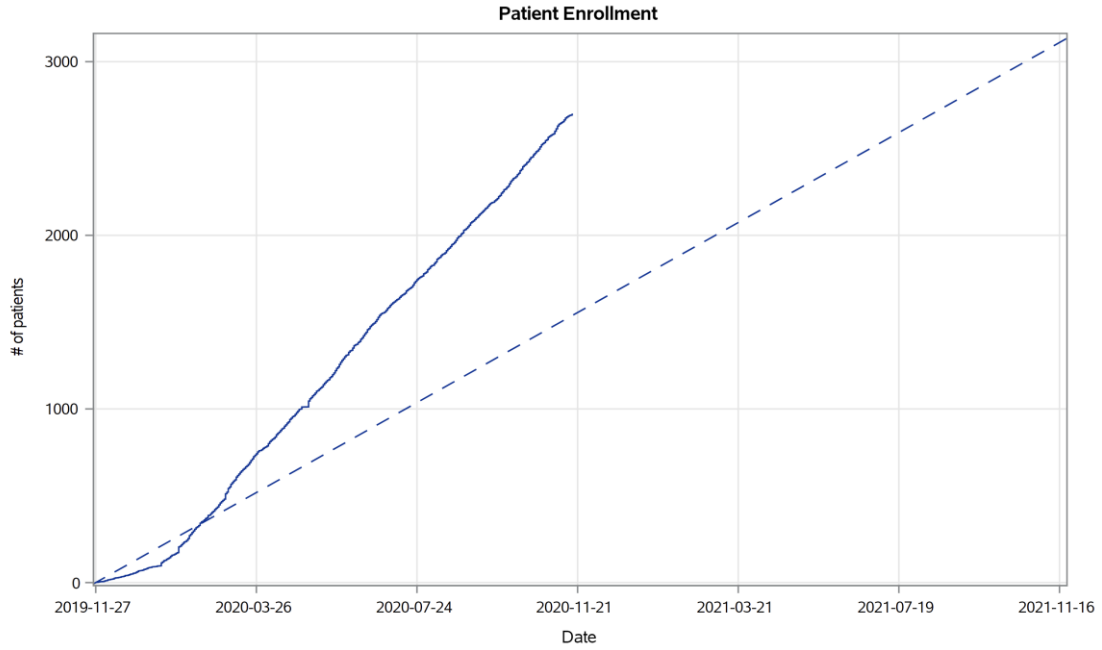
1 Year Mortality: AUC=0.74

Study Design and Alert

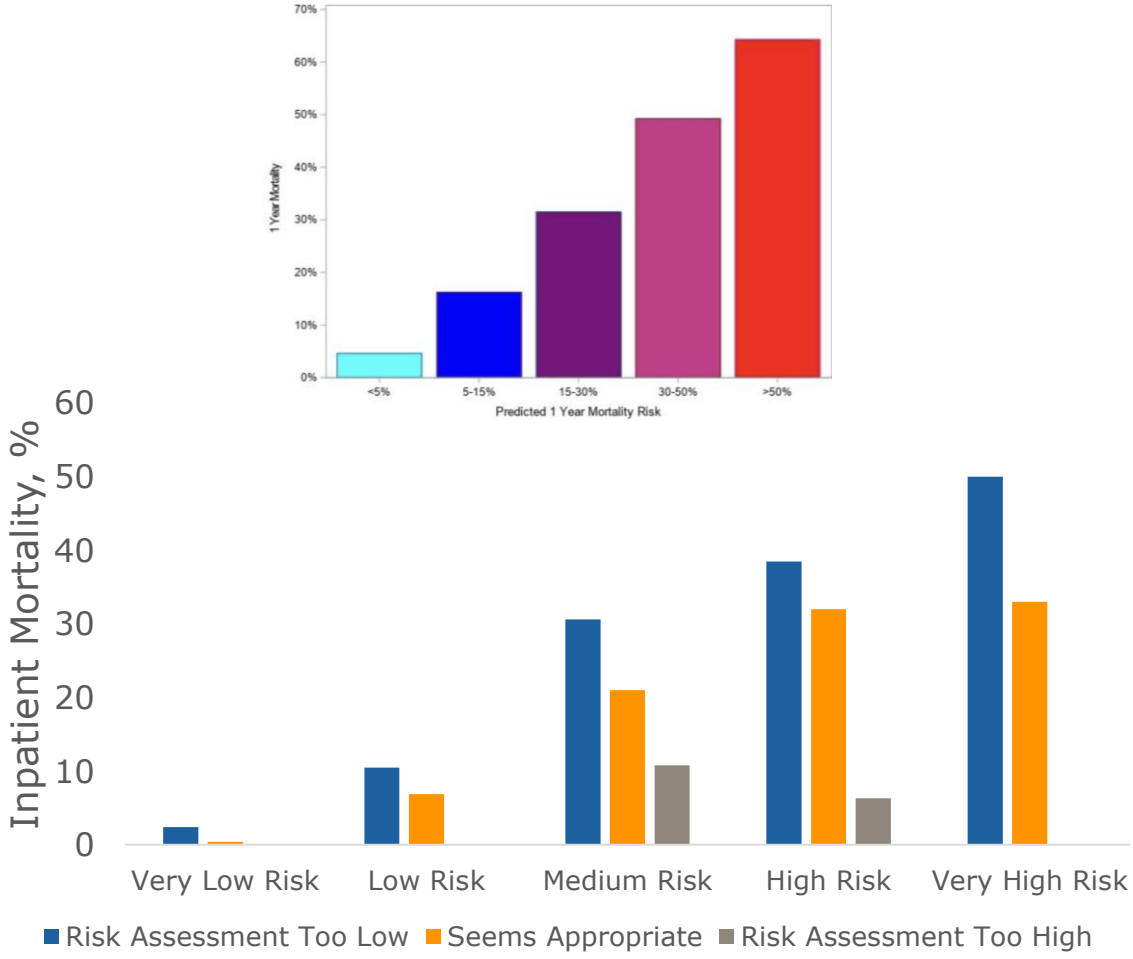


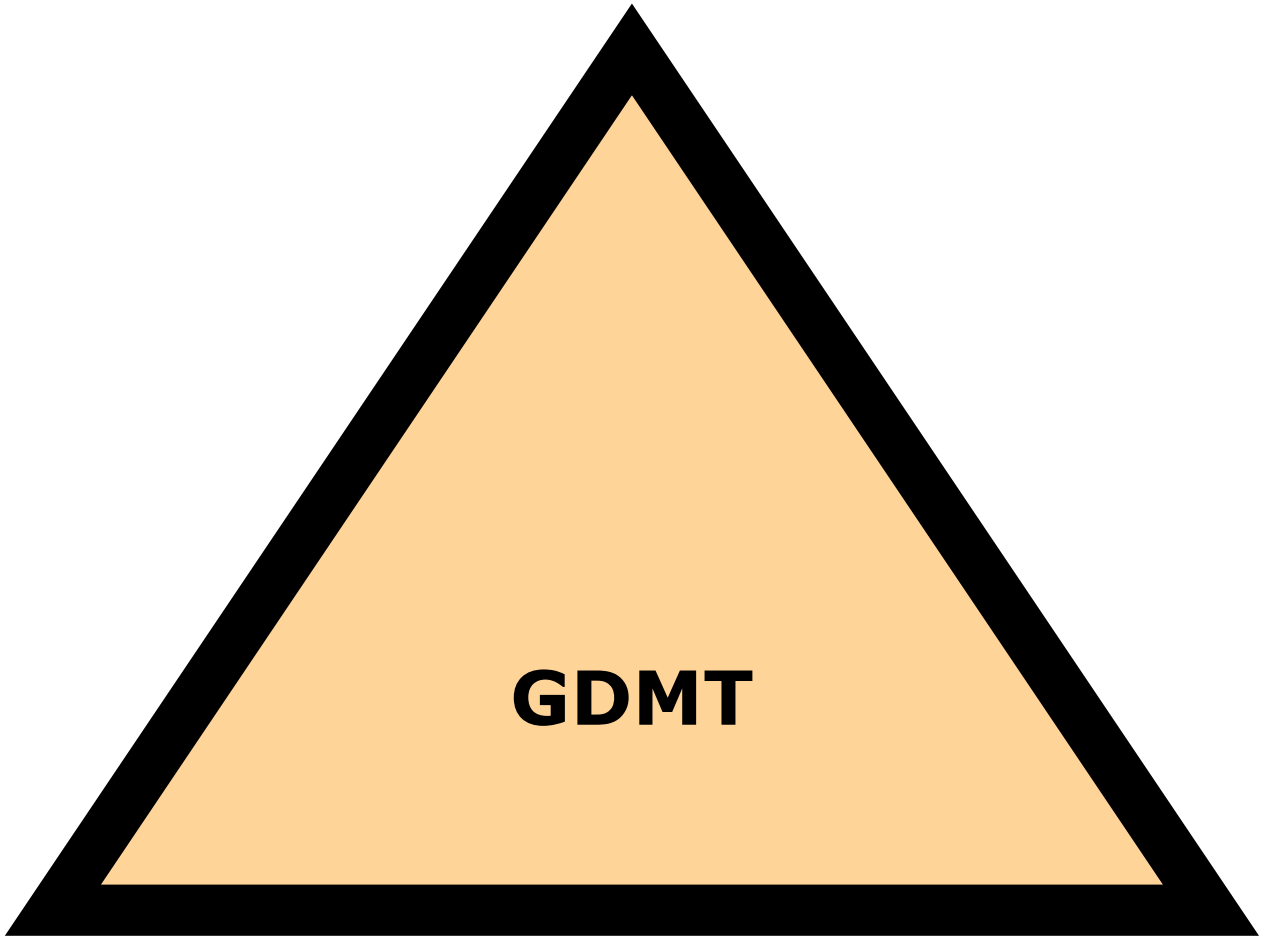


State of Recruitment and Preliminary Findings



N=2788/3120




GDMT

Patients with Heart Failure and Reduced Ejection Fraction

Guideline Directed Medical Therapy Saves Lives

Estimating lifetime benefits of comprehensive disease-modifying pharmacological therapies in patients with heart failure with reduced ejection fraction: a comparative analysis of three randomised controlled trials

Muthiah Vaduganathan, Brian L Claggett, Pardeep S Jhund, Jonathan W Cunningham, João Pedro Ferreira, Faiez Zannad, Milton Packer, Gregg C Fonarow, John J V McMurray, Scott D Solomon

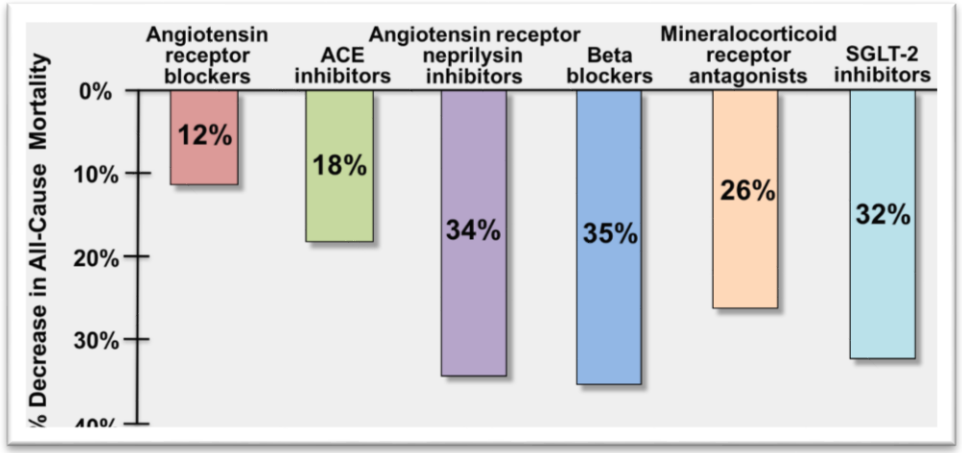
Background Three drug classes (mineralocorticoid receptor antagonists [MRAs], angiotensin receptor–neprilysin inhibitors [ARNIs], and sodium/glucose cotransporter 2 [SGLT2] inhibitors) reduce mortality in patients with heart failure with reduced ejection fraction (HFrEF) beyond conventional therapy consisting of angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) and β blockers. Each class was previously studied with different background therapies and the expected treatment benefits with their combined use are not known. Here, we used data from three previously reported randomised controlled trials to estimate lifetime gains in event-free survival and overall survival with comprehensive therapy versus conventional therapy in patients with chronic HFrEF.

Findings The hazard ratio (HR) for the imputed aggregate treatment effects of comprehensive disease-modifying therapy versus conventional therapy on the primary endpoint of cardiovascular death or hospital admission for heart failure was 0·38 (95% CI 0·30–0·47). HRs were also favourable for cardiovascular death alone (HR 0·50 [95% CI 0·37–0·67]), hospital admission for heart failure alone (0·32 [0·24–0·43]), and all-cause mortality (0·53 [0·40–0·70]). Treatment with comprehensive disease-modifying pharmacological therapy was estimated to afford 2·7 additional years (for an 80-year-old) to 8·3 additional years (for a 55-year-old) free from cardiovascular death or first hospital admission for heart failure and 1·4 additional years (for an 80-year-old) to 6·3 additional years (for a 55-year-old) of survival compared with conventional therapy.

EDITORIAL COMMENT

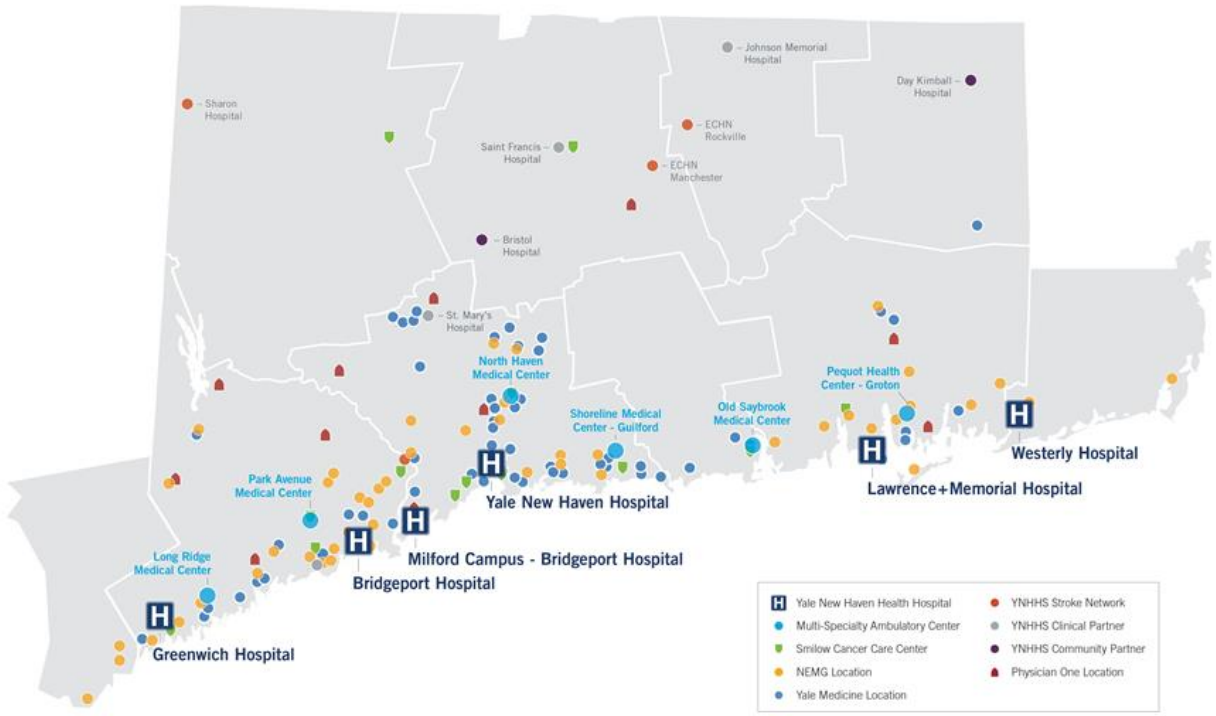
Quadruple Therapy Is the New Standard of Care for HFrEF

Tariq Ahmad, MD, MPH, Nihar R. Desai, MD, MPH



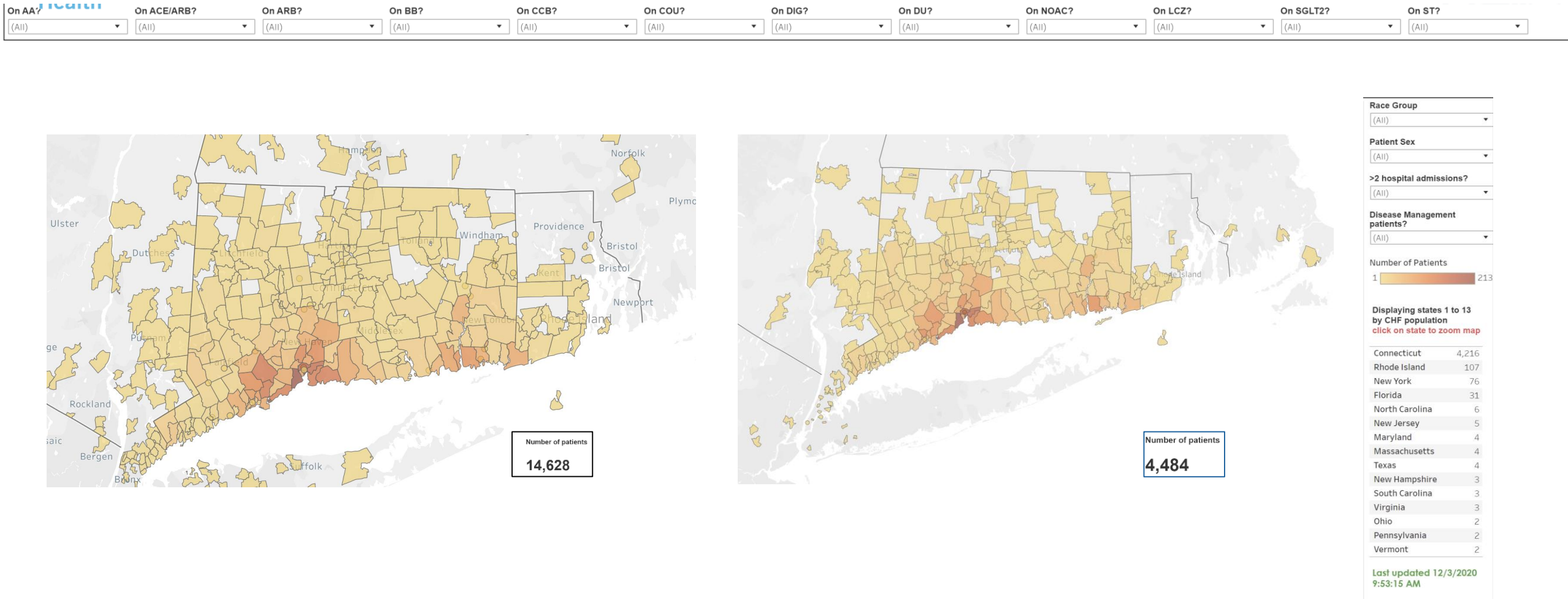
"Now comes the hard part. How we do get these therapies to patients who would benefit? **With current approaches, our success has been dismal**. In the era of "triple therapy," **<1% of eligible patients are receiving appropriate medications at the right dose.** However, reimbursement for care of heart failure is **increasingly focusing on value**, and health care systems will soon be held more **accountable for adverse outcomes** in this patient population. With the pressure to increase value, getting patients on the best available medical therapy will take on a new kind of urgency."

Care within the Yale Health System is Generalizable



2010 US Census Demographics	2019 Yale Patient Demographics
72.4% White	66.0% White
16.3% Hispanic	14.3% Hispanic
12.6% Black	12.0% Black
4.8% Asian	2.7% Asian
9.1% Other	11.4% Other

The Live Yale Heart Failure Dashboard



The COVID-19 Example: A Learning Health Care System

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COVID-19 Infections and Outcomes in a Live Registry of Heart Failure Patients Across an Integrated Health Care System

Cesar Caraballo, Megan McCullough, Michael Fuery, Fouad Chouairi, Craig Keating, Neal Ravindra, Elliott Miller, Maricar Malinis, Nitu Kashyap, Allen Hsiao, Francis Perry Wilson, Jeptha Curtis, Matthew Grant, Eric J Velazquez, Nihar Desai, Tariq Ahmad

doi: https://doi.org/10.1101/2020.04.27.20082016

This article is a preprint and has not been peer-reviewed [what does this mean?]. It reports new medical research that has yet to be evaluated and so should *not* be used to guide clinical practice.

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Posted May 03, 2020.

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COVID-19 SARS-CoV-2 preprints from medRxiv and bioRxiv

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Citation: Caraballo C, McCullough M, Fuery MA, Chouairi F, Keating C, Ravindra NG, et al. (2020) COVID-19 infections and outcomes in a live registry of heart failure patients across an integrated health care system. PLoS ONE 15(9): e0238829. https://doi.org/10.1371/journal.pone.0238829

Editor: Chiara Lazzeri, Azienda Ospedaliero Universitaria Careggi, ITALY

Received: May 7, 2020

Accepted: August 25, 2020

Published: September 30, 2020

Peer Review History: PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: https://doi.org/10.1371/journal.pone.0238829

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Data Availability Statement: Data are available from the Yale Institutional Data Access / Ethics Committee (contact via teshia.johnson@yale.edu)

RESEARCH ARTICLE

COVID-19 infections and outcomes in a live registry of heart failure patients across an integrated health care system

César Caraballo[1,2☯], Megan McCullough[3☯], Michael A. Fuery[3☯], Fouad Chouairi[4☯], Craig Keating[5], Neal G. Ravindra[1], P. Elliott Miller[1], Maricar Malinis[6], Nitu Kashyap[5], Allen Hsiao[5], F. Perry Wilson[7], Jeptha P. Curtis[1,2], Matthew Grant[3], Eric J. Velazquez[1], Nihar R. Desai[1,2], Tariq Ahmad[1,2]*

1 Department of Internal Medicine, Section of Cardiovascular Medicine, Yale School of Medicine, New Haven, CT, United States of America, **2** Center for Outcomes Research & Evaluation (CORE), Yale New Haven Hospital, New Haven, CT, United States of America, **3** Department of Internal Medicine, Yale School of Medicine, New Haven, CT, United States of America, **4** Yale University School of Medicine, New Haven, CT, United States of America, **5** Joint Data Analytics Team, Yale New Haven Hospital, New Haven, CT, United States of America, **6** Department of Internal Medicine, Section of Infectious Diseases, Yale School of Medicine, New Haven, CT, United States of America, **7** Department of Internal Medicine, Section of Nephrology, Yale School of Medicine, New Haven, CT, United States of America

☯ These authors contributed equally to this work.
* tariq.ahmad@yale.edu

Abstract

Background

Patients with comorbid conditions have a higher risk of mortality with SARS-CoV-2 (COVID-19) infection, but the impact on heart failure patients living near a disease hotspot is unknown. Therefore, we sought to characterize the prevalence and outcomes of COVID-19 in a live registry of heart failure patients across an integrated health care system in Connecticut.

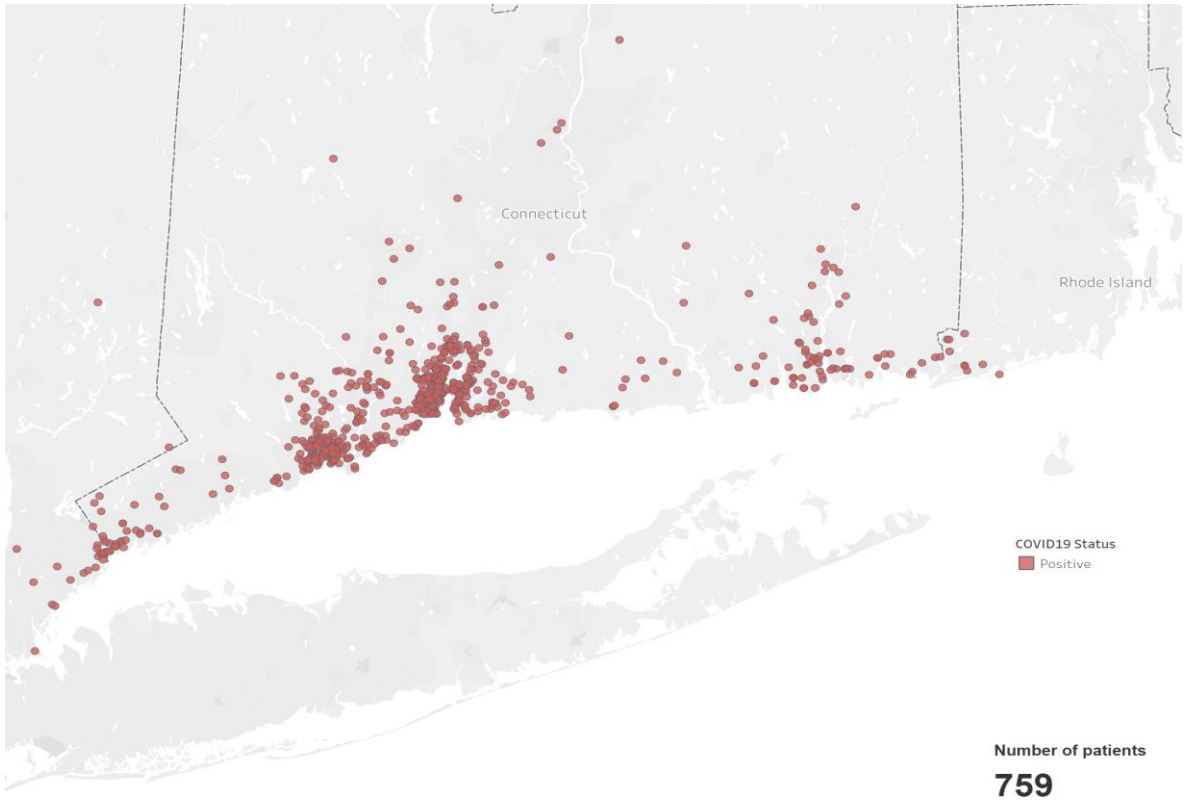
Methods

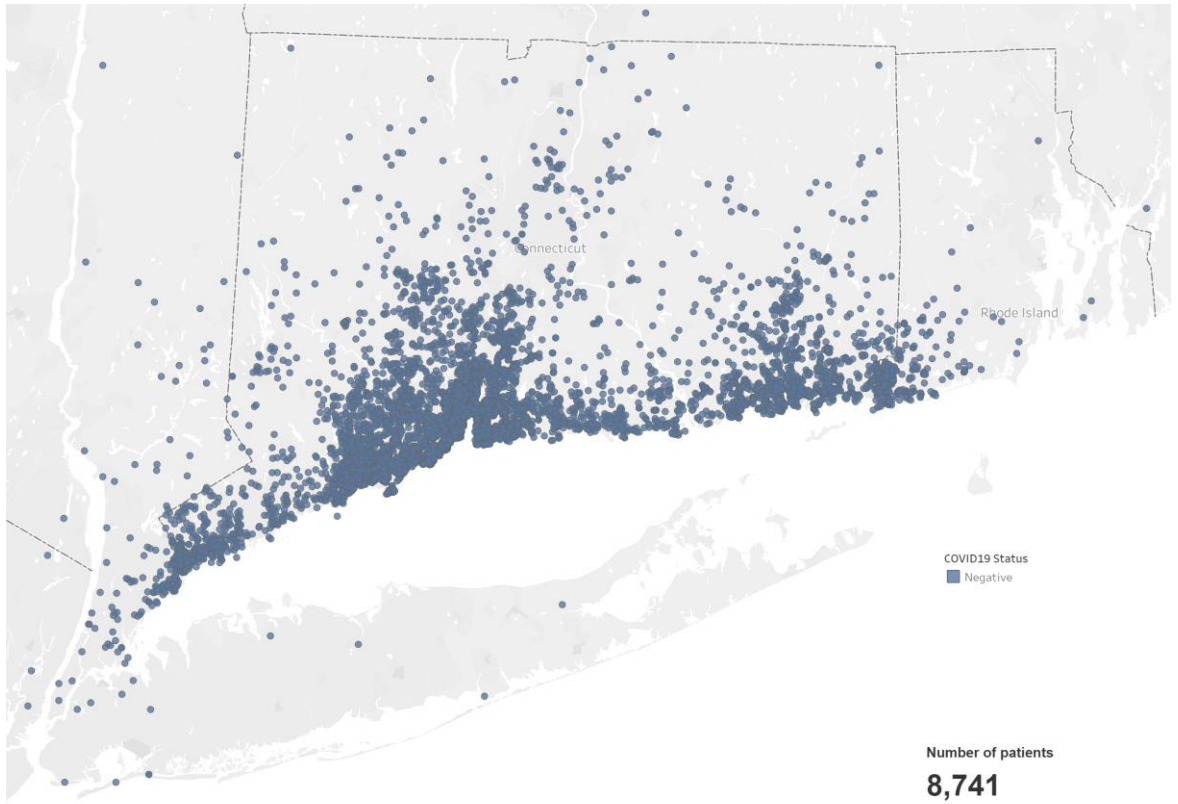
In this retrospective analysis, the Yale Heart Failure Registry (NCT04237701) that includes 26,703 patients with heart failure across a 6-hospital integrated health care system in Connecticut was queried on April 16th, 2020 for all patients tested for COVID-19. Sociodemographic and geospatial data as well as, clinical management, respiratory failure, and patient mortality were obtained via the real-time registry. Data on COVID-19 specific care was extracted by retrospective chart review.

Results

COVID-19 testing was performed on 900 symptomatic patients, comprising 3.4% of the Yale Heart Failure Registry (N = 26,703). Overall, 206 (23%) were COVID- 19+. As compared to COVID-19-, these patients were more likely to be older, black, have hypertension, coronary artery disease, and were less likely to be on renin angiotensin blockers (P<0.05, all). COVID-19- patients tended to be more diffusely spread across the state whereas

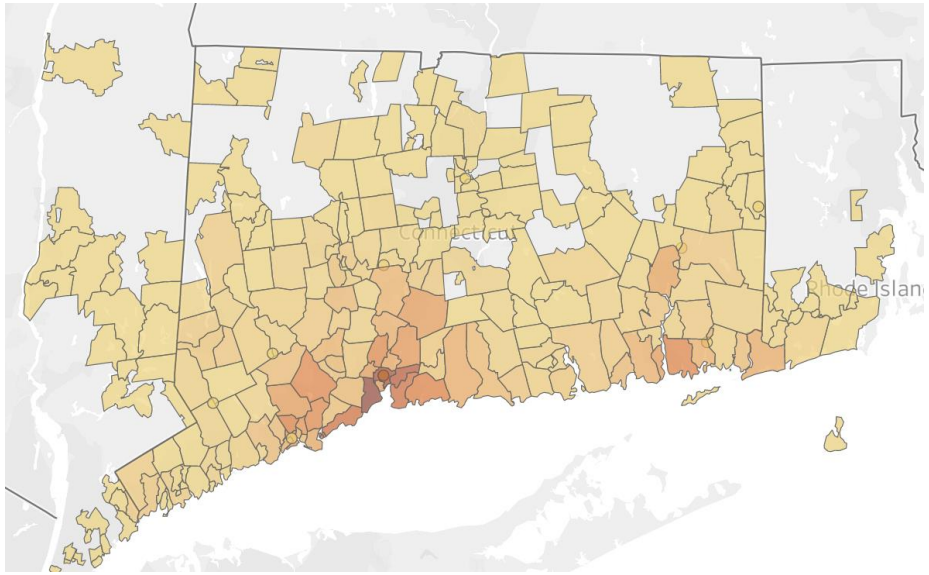
Allows for a Live Look at Heart Failure (e.g. COVID)





Treatment of HFrEF Across YNHH

All Patients with HFrEF



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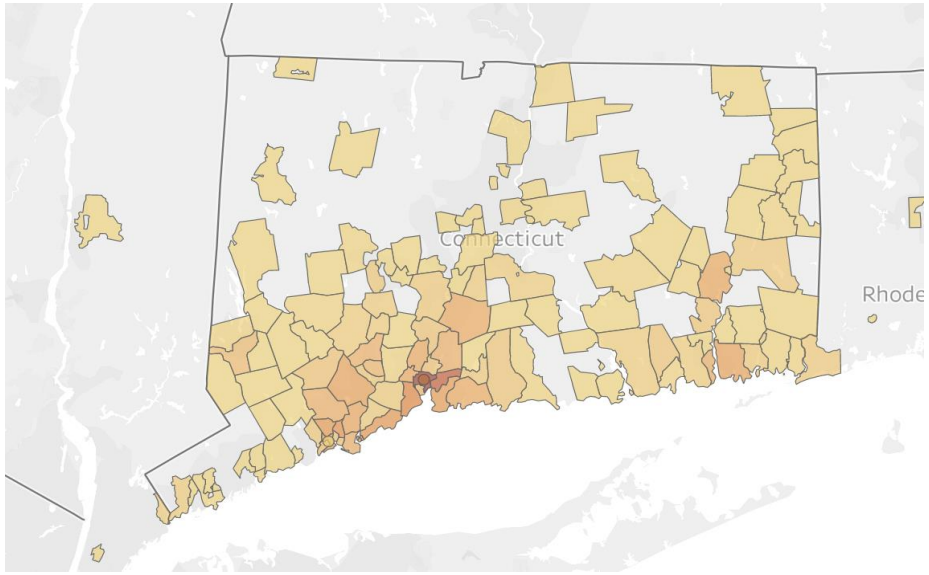
All Patients with HFrEF on Triple Rx



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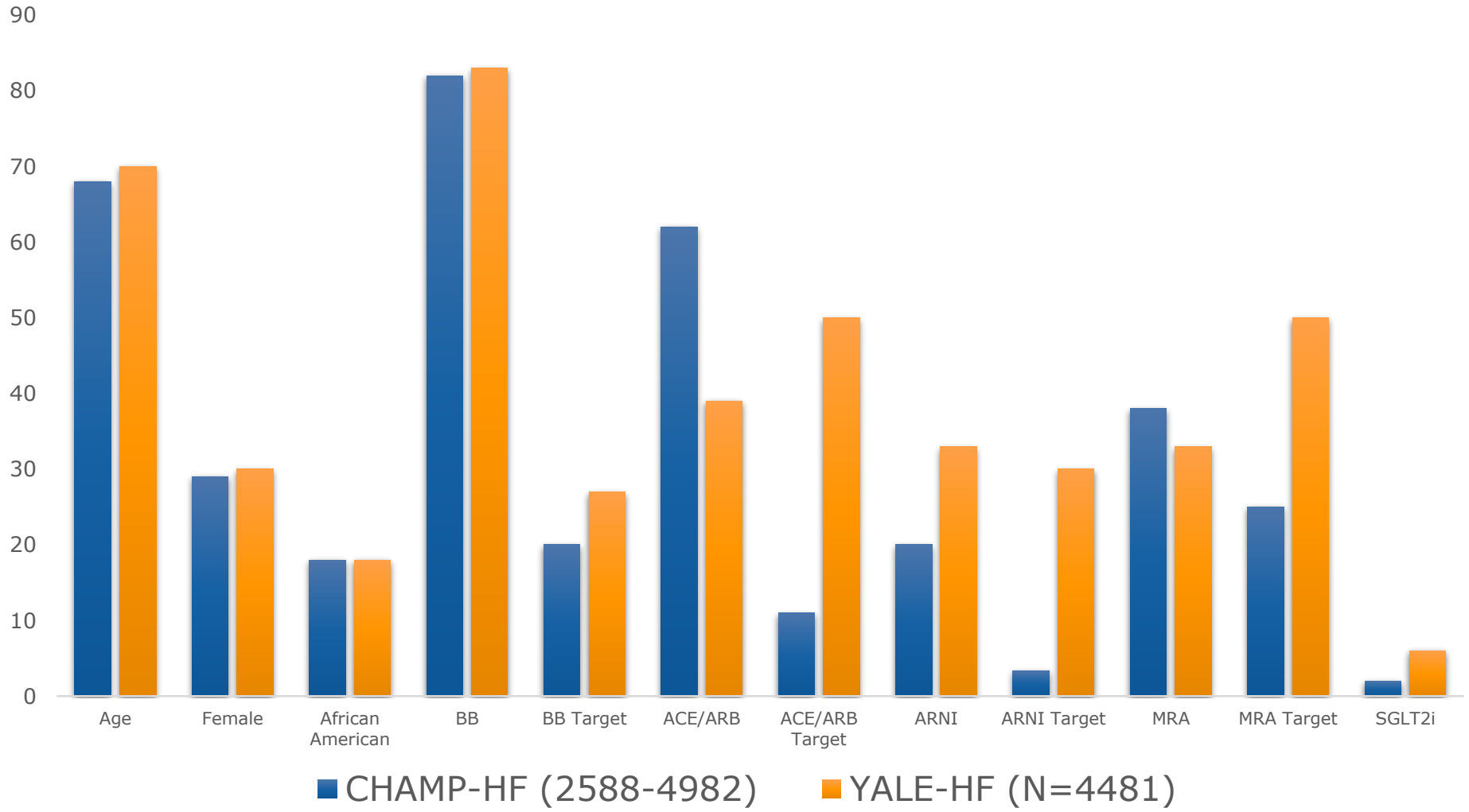
Our Registry Mirrors National Data



PROMPT-HF https://www.theprompttrials.org

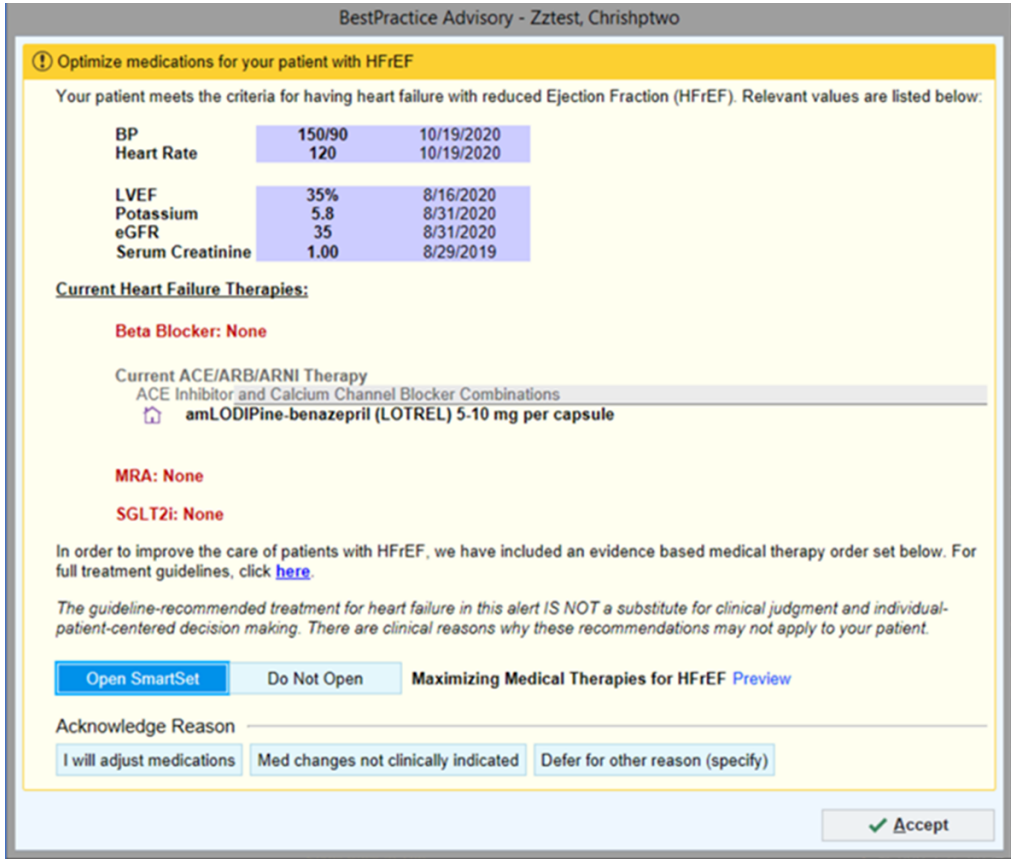
PRagmatic **T**rial *Of* **M**essaging to ***P***roviders about ***T***reatment of ***H***eart ***F***ailure (**PROMPT-HF**)

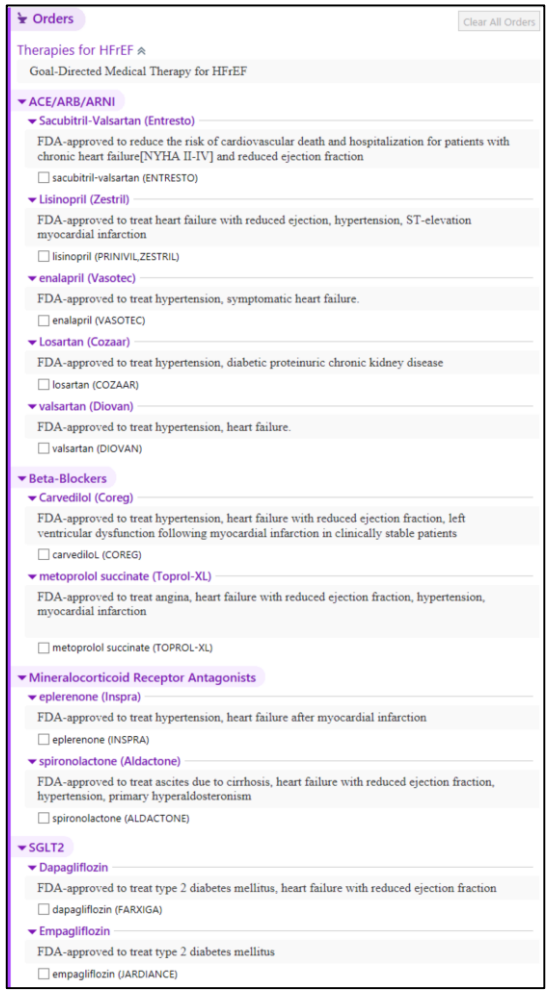
PROMPT-HF will be two **parallel pragmatic randomized controlled trials (outpatient and inpatient)** that will test the impact of **an electronic alert system** that **informs** practitioners about **evidence-based therapies** for their patients with heart failure and reduced ejection fraction and **facilitates prescription** of these therapies

Our primary hypothesis is that electronic alerting about evidence-based medications in HFrEF will lead to an increase in the use of appropriate pharmacotherapies

PROMPT-HF

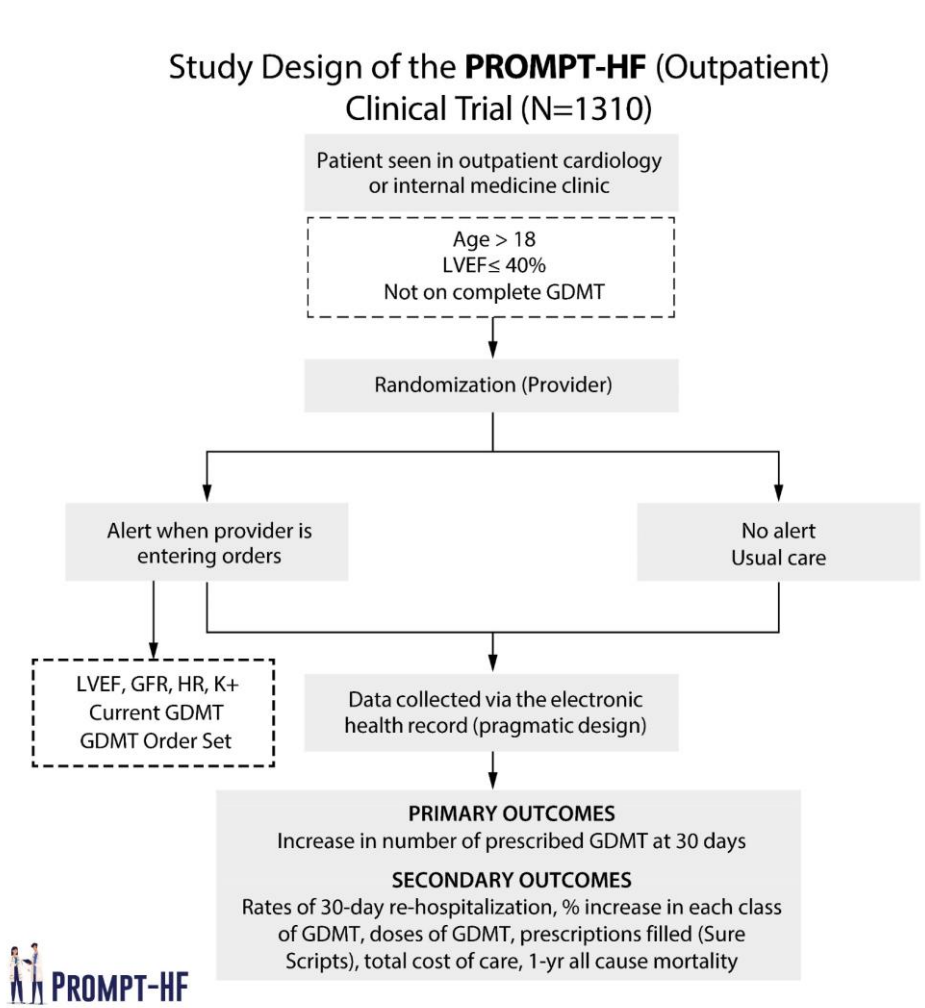
PRagmatic Trial ***O***f ***M***essaging to ***P***roviders about ***T***reatment of ***H***eart ***F***ailure

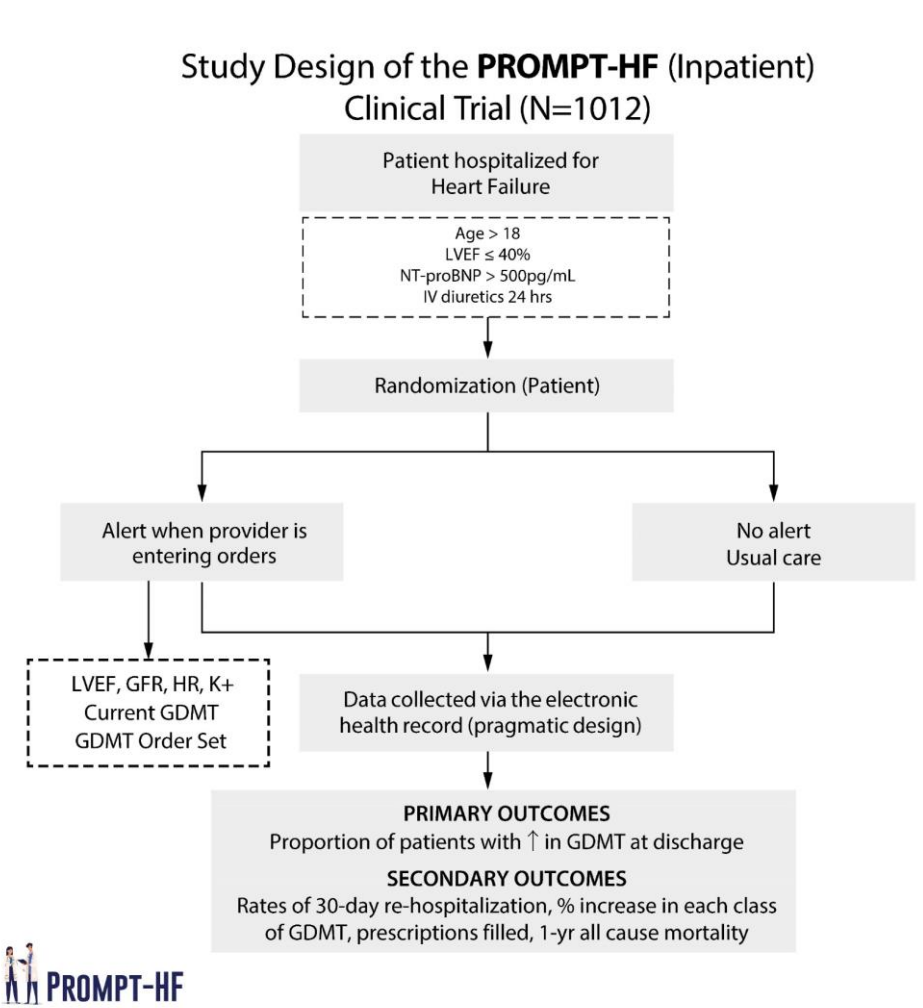


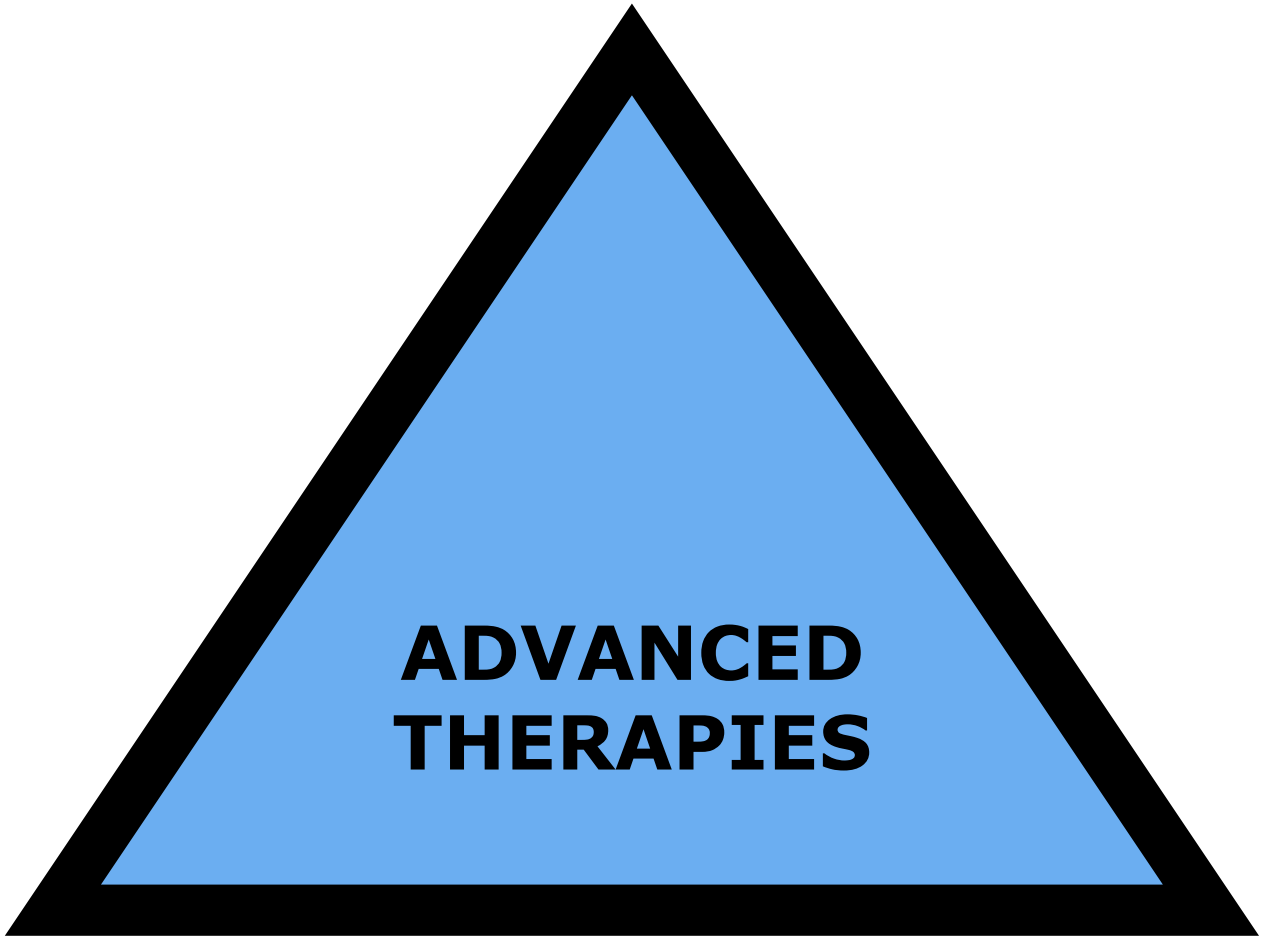


PROMPT-HF

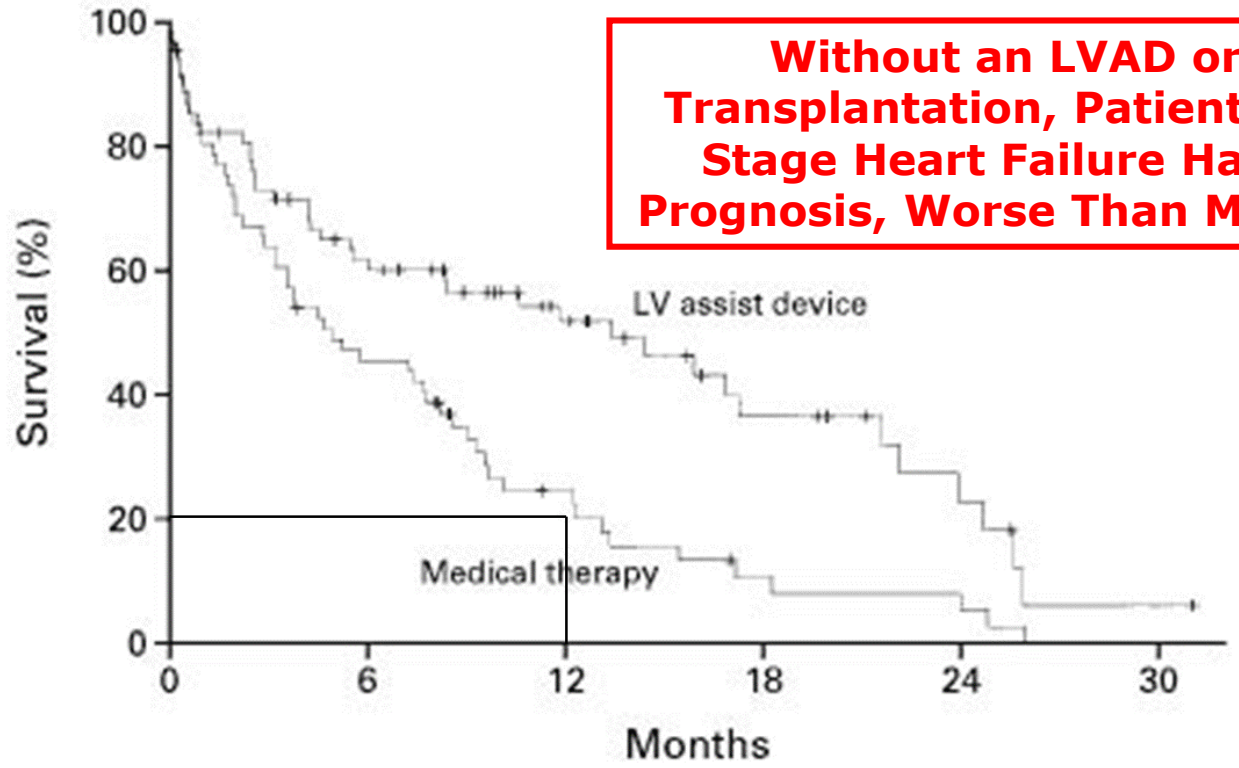
*PR*agmatic Trial *O*f *M*essaging to *P*roviders about *T*reatment of *H*eart *F*ailure






ADVANCED
THERAPIES

Stage D Heart Failure Has a Dire Prognosis



No. at Risk						
LV assist device	68	38	22	11	5	1
Medical therapy	61	27	11	4	3	0

Without an LVAD or Heart Transplantation, Patients with End Stage Heart Failure Have a Dire Prognosis, Worse Than Most Cancers

N Engl J Med 2001; 345:1435-1443

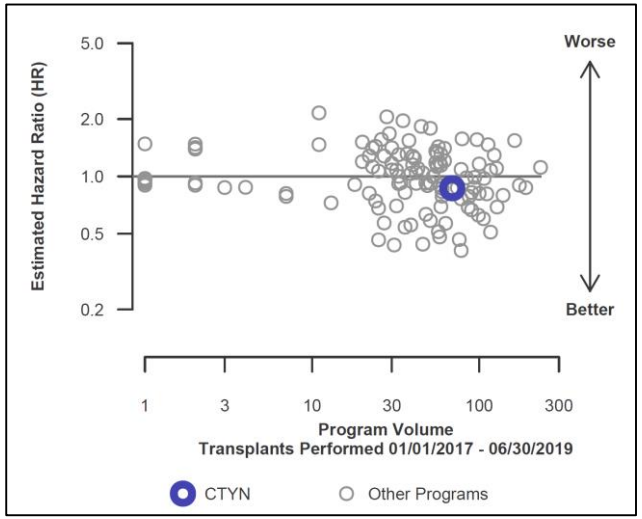
Heart Transplantation at Yale

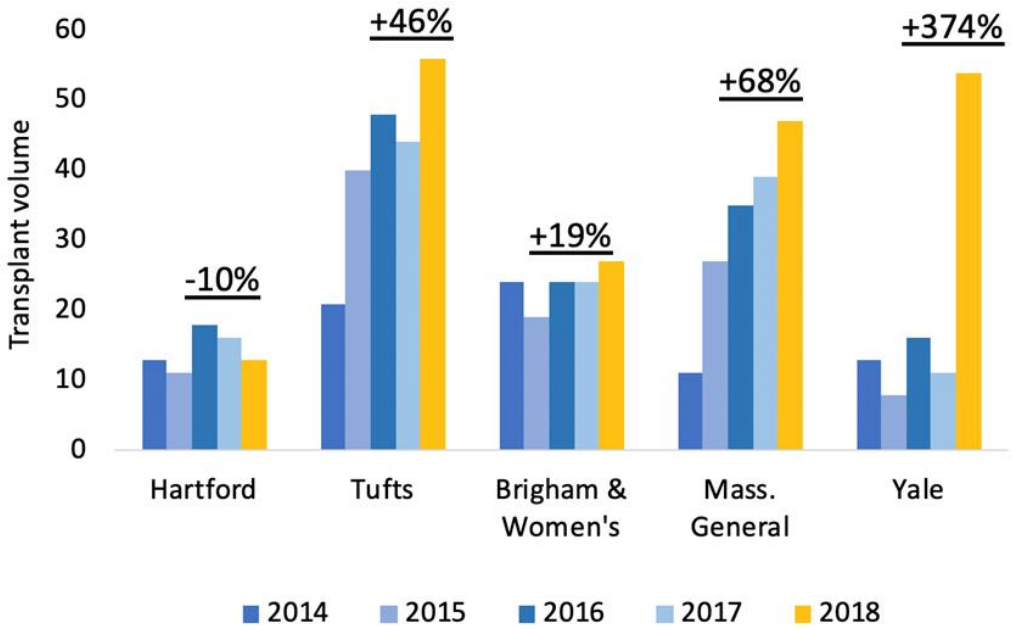
Original Investigation | Cardiology

Evaluation of Case Volumes of a Heart Transplant Program and Short-term Outcomes After Changes in the United Network for Organ Sharing Donor Heart Allocation System

Makoto Mori, MD; Lynn Wilson, RN; Ayyaz Ali, MD, PhD; Tariq Ahmad, MD, MPH; Muhammad Anwer, MD; Daniel Jacoby, MD; Arnar Geirsson, MD; Harlan M. Krumholz, MD, SM

CONCLUSIONS AND RELEVANCE This study suggests that strategic changes in donor heart and recipient selection may significantly increase the number of heart transplants while maintaining short-term outcomes comparable with more conservative patient selection. Such an approach may augment the allocation of currently unused donor hearts.





Academic Medical Centers Should be Leading Implementation

Geographical affiliation with top 10 NIH-funded academic medical centers and differences between mortality from cardiovascular disease and cancer

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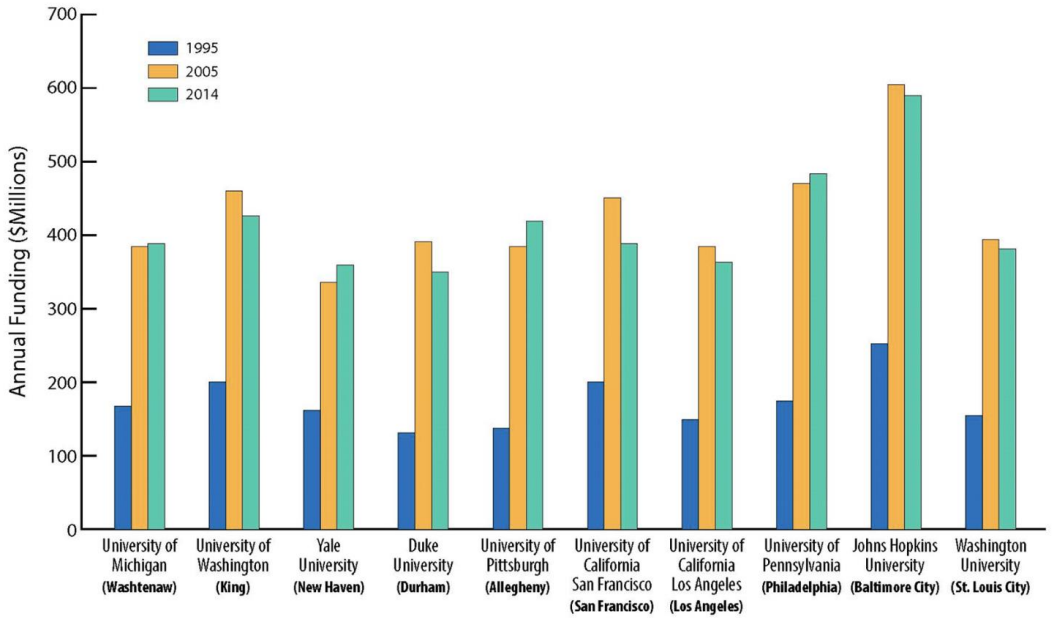

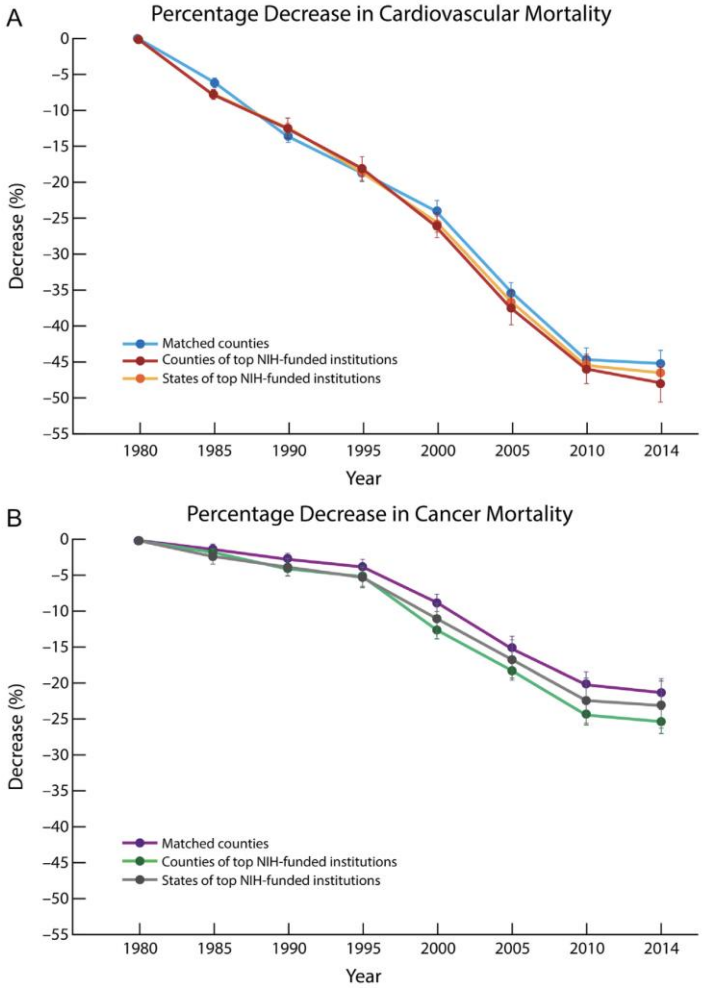

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Thank You!

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