



**HEART
FAILURE
IN 2019**

**WHAT DO WE KNOW?
WHERE CAN WE GO?**



Welcome and Introductions

Serge Lepage
MD, FRCPC, CSPQ



Faculty

Serge Lepage, MD, FRCPC, CSPQ (Chair)

Full Professor

Director, Heart Function Clinic, Department of cardiology, Université de Sherbrooke

Past President, Quebec Heart Failure Society
Sherbrooke, QC

Douglas Lee, MD, PhD, FRCPC

Cardiovascular Program Lead & Senior Scientist,
ICES

Ted Rogers Chair in Heart Function Outcomes
Division of Cardiology, Peter Munk Cardiac Centre,
University Health Network

Professor of Medicine, University of Toronto
Toronto, ON

Nadia Giannetti, MDCM, FRCPC

Associate Professor, Department of Medicine
Medical Director, Heart Failure and Heart
Transplant Program

Chief, Division of Cardiology
McGill University Health Centre
Montreal, QC

Mark Liskowski, MD, FRCPC

Cardiologist in advanced heart failure
Cardiac intensivist

Director cardiac intensive care unit
President of the Clinical Ethics committee
Medical coordinator for organ and tissue donation
Montreal, QC

Conflict of Interest

Serge Lepage, MD, FRCPC, CSPQ

- **Consulting Fees/Honoraria:** Novartis, AstraZeneca, Jenssen, Servier, Bayer, Amgen, Sanofi
- **Clinical Trials:** Novartis, Amgen

Conflict of Interest

Douglas Lee, MD, PhD, FRCPC

- **Consulting Fees/Honoraria:** N/A
- **Clinical Trials:** COACH Trial funded by the Ontario SPOR Support Unit

Conflict of Interest

Nadia Giannetti, MDCM, FRCPC

- **Funding/Honoraria/Research:** Novartis, Servier, Amgen, Pfizer, Boehringer Ingelheim, Astra, Merck

Conflict of Interest

Mark Liskowski, MD, FRCPC

- **Consulting Fees/Honoraria:** Servier, Bayer, Novartis, CardiacAssist, Abbott medical, Boehringer, Mallinkrodt, BMS, Otsuka
- **Clinical Trials:** Bayer

Disclosure of Commercial Support

Specific details of relationship:

- This program has received financial support from Novartis Pharmaceuticals Canada in the form of an educational grant

Potential for conflict(s) of interest:

- Speakers have received honoraria from Novartis Pharmaceuticals Canada
- Novartis is the manufacturer and benefits from the sale of Entresto

Mitigating Potential Bias

Potential biases are acknowledged and are mitigated by presenting data supported by national and international guidelines, and as follows:

- Information presented is evidence-based
- Material has been developed and reviewed by a Planning Committee

Off-label uses of drugs will be discussed and identified as such by the speaker

Learning Objectives

After attending the symposium, participants will be able to:

- Discuss the burden of heart failure (HF) in Canada with an emphasis on the burden of disease and societal impact of HF hospitalizations
- Recognize the high risk of recurrent events and deterioration after hospitalization for acute HF decompensation and the need to optimize treatment before discharge
- Translate current clinical data into daily practice and evaluate the impact on patient outcomes

Agenda

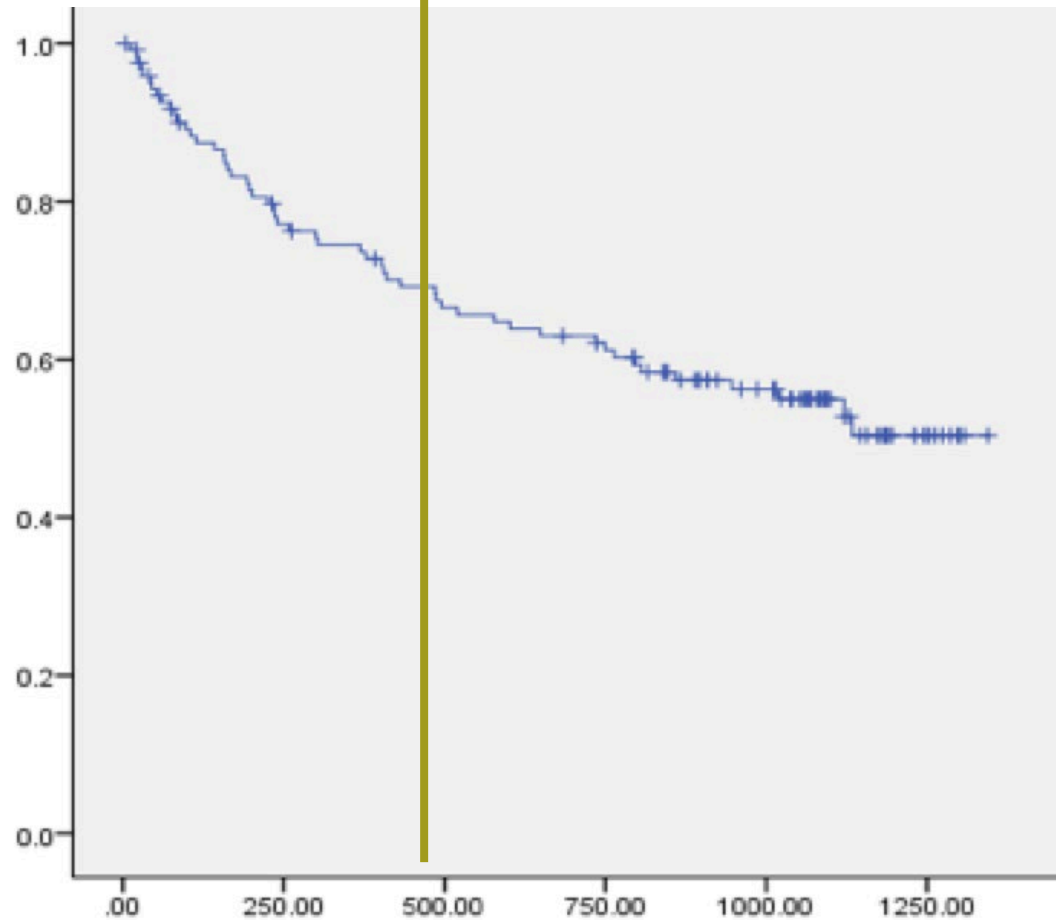
| TIME | TOPIC | SPEAKER |
|------------|---|---------------------|
| 9:55 a.m. | Welcome and Introductions | Serge Lepage, MD |
| 10:00 a.m. | Burden of the Disease: Health Expenditure, Costs of Hospitalization, Diagnosis, and Management of HF | Douglas S. Lee, MD |
| 10:15 a.m. | Question and Answer Period | All |
| 10:20 a.m. | Optimizing HF Therapies During Hospitalization: Time Matters | Nadia Giannetti, MD |
| 10:40 a.m. | Question and Answer Period | All |
| 10:45 a.m. | Best Practices and Practical Tips for Optimizing HF Patient Care in Hospital | Mark Liszkowski, MD |
| 11:00 a.m. | Question and Answer Period | All |
| 11:05 a.m. | Closing Remarks and Evaluations | Serge Lepage, MD |

Situation At My Hospital

- Consecutive patients with ADHF
- EF 40% and below
- Mean stay 10 days

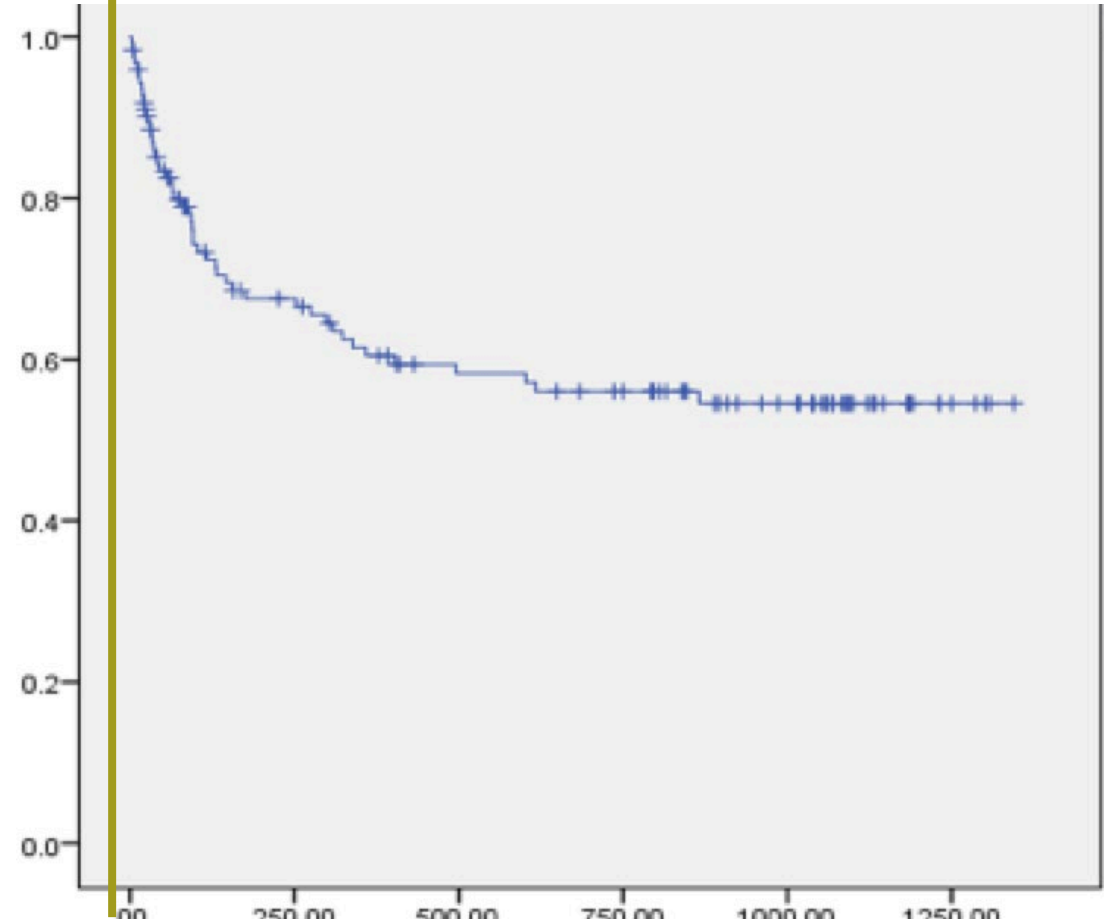
Mortality

- 1 month
➤ 3%
- 3 month
➤ 10%
- 6 month
➤ 17%
- 1 year
➤ 25%



HF Re-hospitalization

- 1 month
➤ 11%
- 3 month
➤ 21%
- 6 month
➤ 32%
- 1 year
➤ 40%



Burden of the Disease: Health Expenditure, Costs of Hospitalization, Diagnosis, and Management of HF

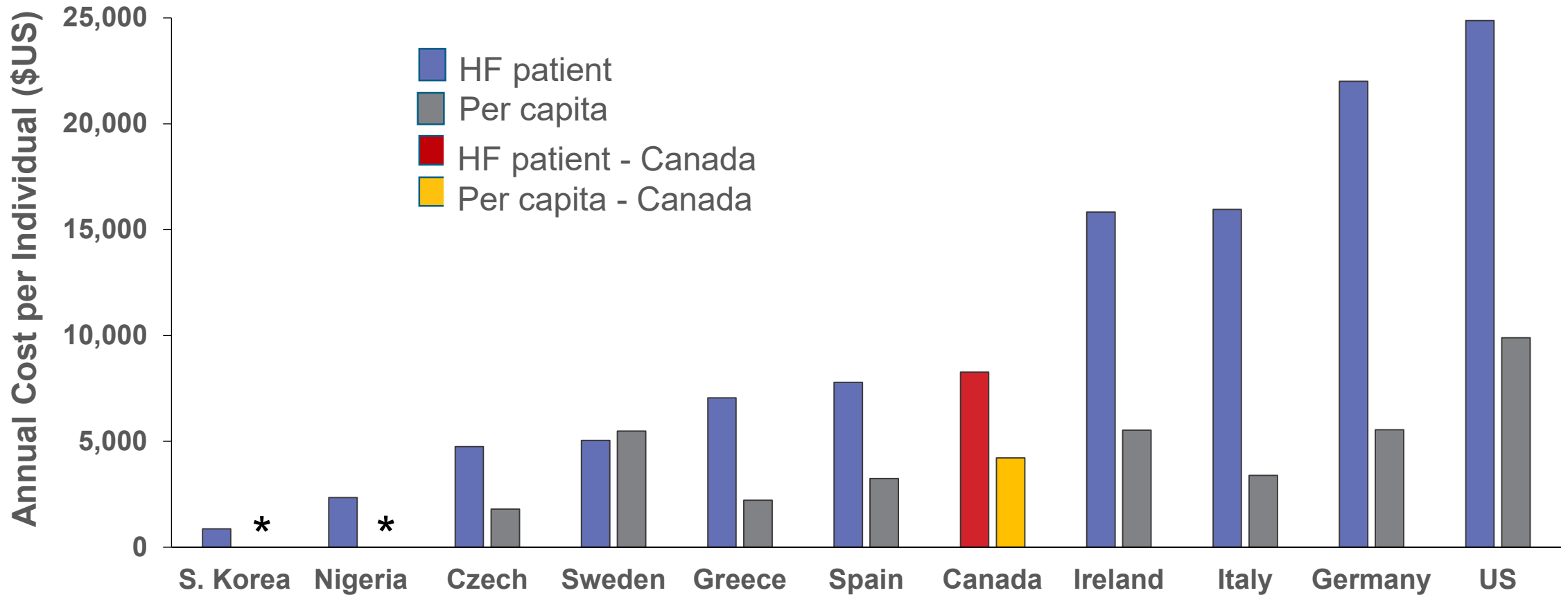
Douglas S. Lee
MD, FRCPC



Objectives:

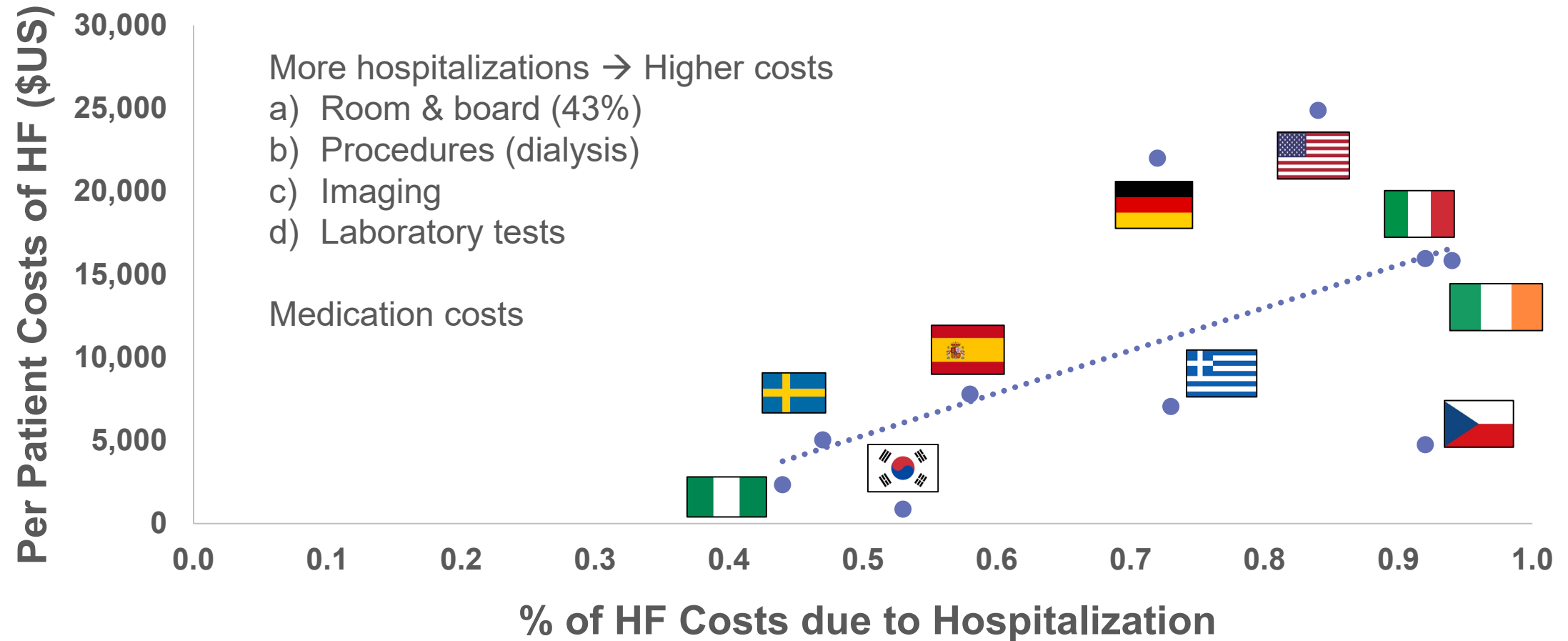
1. To examine potential strategies to improve earlier diagnosis of heart failure
2. To explore the importance of coronary artery disease in heart failure
3. To understand the challenges in preventing heart failure readmissions and potential solutions

Cost of HF Care: International Comparison

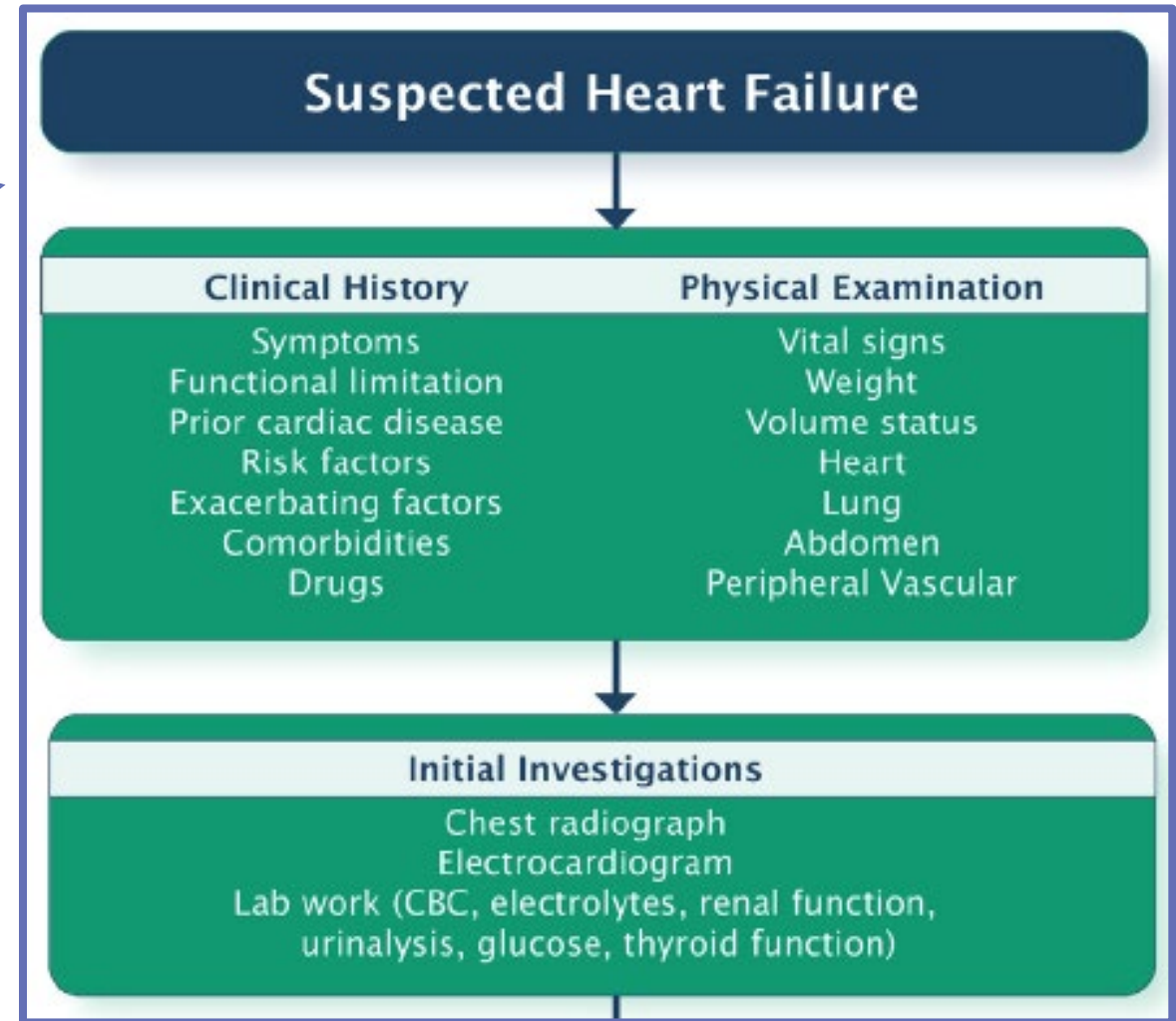
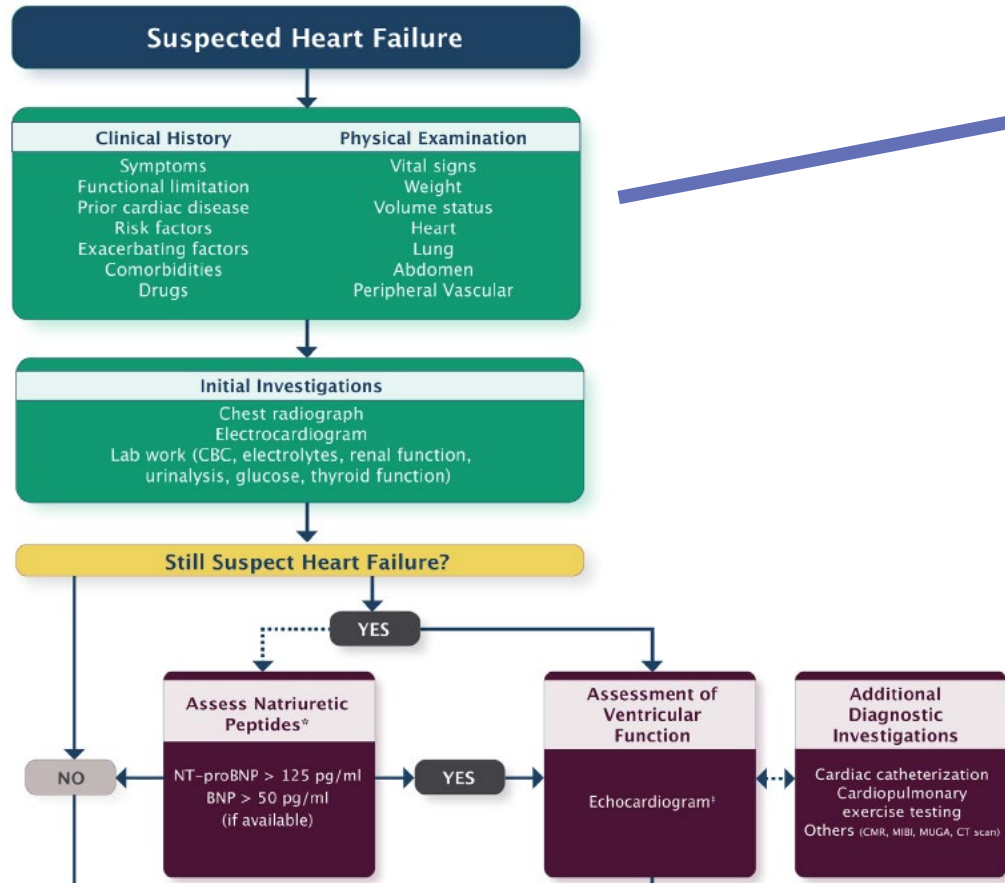


* N/A

Spending on HF Patients Correlate with More Spent on HF Hospitalization



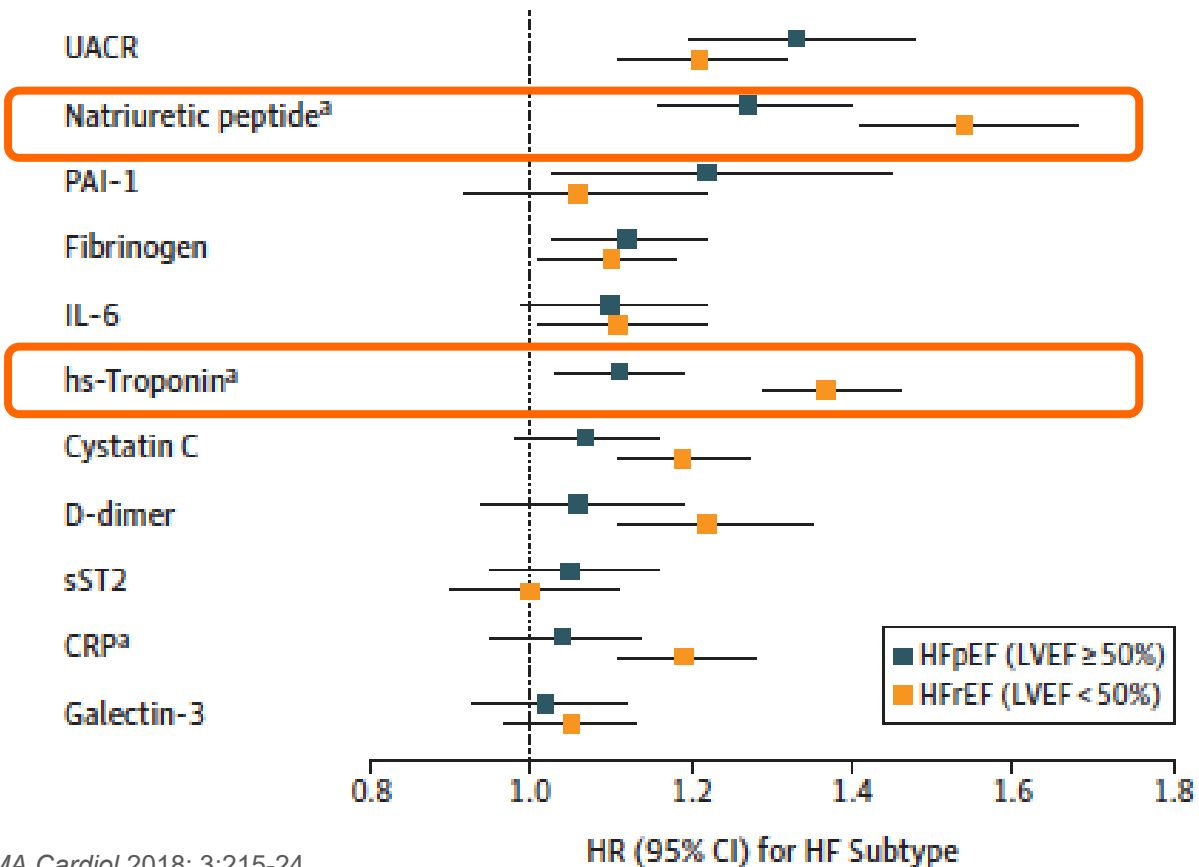
Improving Diagnosis of HF



Association of Cardiovascular Biomarkers With Incident Heart Failure With Preserved and Reduced Ejection Fraction

Rudolf A. de Boer, MD, PhD; Matthew Nayor, MD, MPH; Christopher R. deFilippi, MD; Danielle Enserro, PhD; Vijeta Bhambhani, MS, MPH; Jorge R. Kizer, MD, MSc; Michael J. Blaha, MD, MPH; Frank P. Brouwers, MD, PhD; Mary Cushman, MD; Joao A. C. Lima, MD; Hossein Bahrami, MD, PhD, MPH; Pim van der Harst, MD, PhD; Thomas J. Wang, MD; Ron T. Gansevoort, MD, PhD; Caroline S. Fox, MD, MPH; Hanna K Gaggin, MD, MPH; Willem J. Kop, PhD; Kiang Liu, PhD; Ramachandran S. Vasan, MD; Bruce M. Psaty, MD, PhD; Douglas S. Lee, MD, PhD; Hans L. Hillege, MD, PhD; Traci M. Bartz, MS; Emelia J. Benjamin, MD, ScM; Cheeling Chan, MS; Matthew Allison, MD, MPH; Julius M. Gardin, MD, MBA; James L. Januzzi Jr, MD; Sanjiv J. Shah, MD; Daniel Levy, MD; David M. Herrington, MD; Martin G. Larson, ScD; Wiek H. van Gilst, PhD; John S. Gottdiener, MD; Alain G. Bertoni, MD, MPH; Jennifer E. Ho, MD

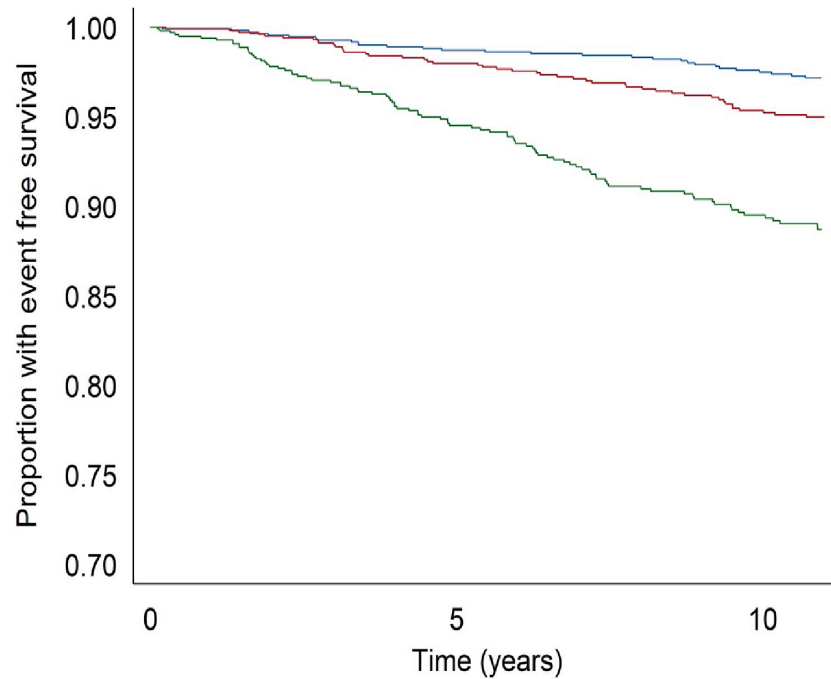
Association of Cardiovascular Biomarkers With Incident Heart Failure With Preserved and Reduced Ejection Fraction



Only BNP and hs-Troponin improved the c-statistic and NRI compared with clinical, echocardiographic and ECG variables

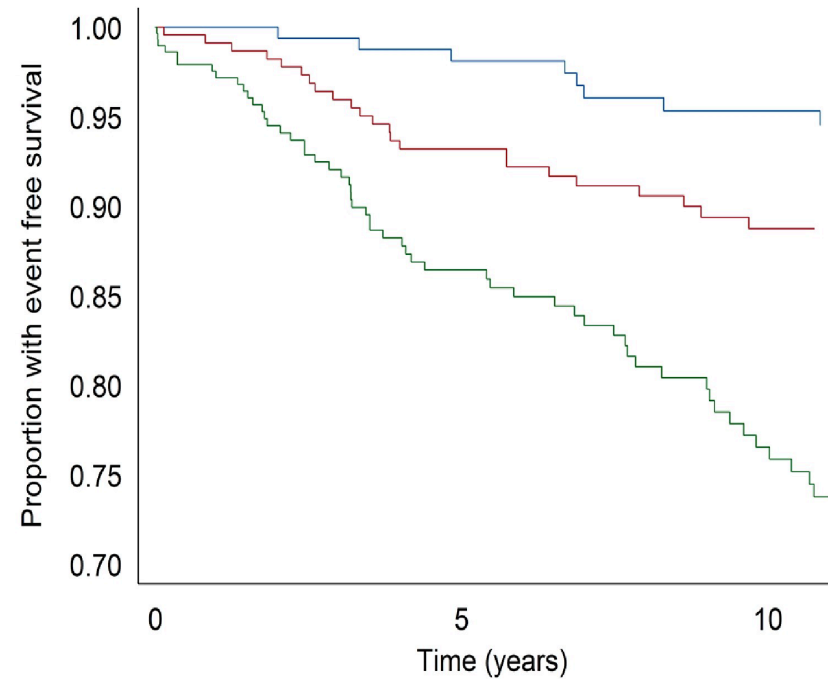
HS-Troponin and Incident HF: British Regional Heart Study (7735 men, 40-59 yrs)

Free of Coronary Artery Disease



| Number at risk | 0 | 5 | 10 |
|-----------------|------|------|-----|
| TnT_tertile = 1 | 1125 | 1043 | 922 |
| TnT_tertile = 2 | 1048 | 928 | 771 |
| TnT_tertile = 3 | 992 | 775 | 577 |

History of Coronary Artery Disease



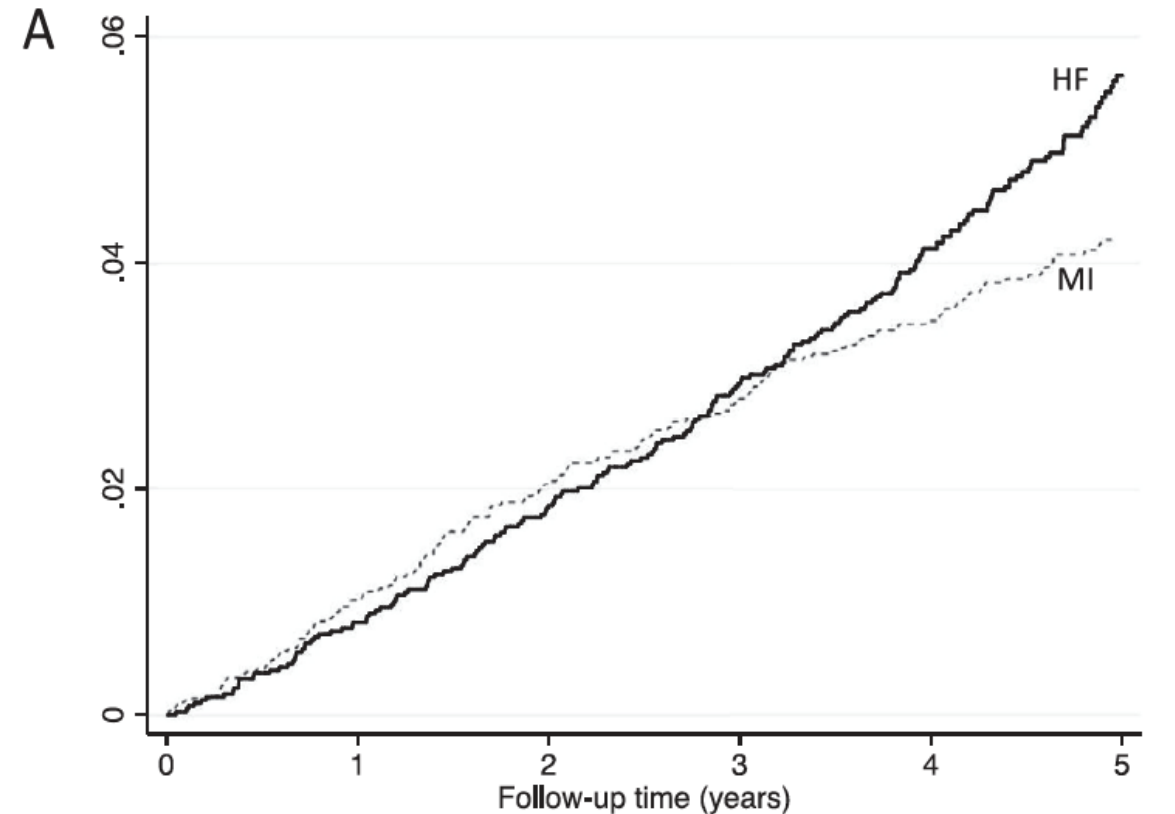
| Number at risk | 0 | 5 | 10 |
|-----------------|-----|-----|-----|
| TnT_tertile = 1 | 165 | 152 | 127 |
| TnT_tertile = 2 | 231 | 194 | 142 |
| TnT_tertile = 3 | 291 | 182 | 114 |

TnT Tertiles:

- Lowest: ≤ 9.7 ng/L
- Middle: 9.8-14.2 ng/L
- Highest: ≥ 14.3 ng/L

Ischemic Heart Disease and HF

- CORONOR study (Nord-Pas-de-Calais, France)
- Registry of 4184 outpatients with stable CAD:
 - Prior MI (> 1 year)
 - Prior coronary revascularization
 - $\geq 50\%$ obstruction of at least 1 V
- Baseline LVEF categorized as $\geq 50\%$ vs. $< 50\%$



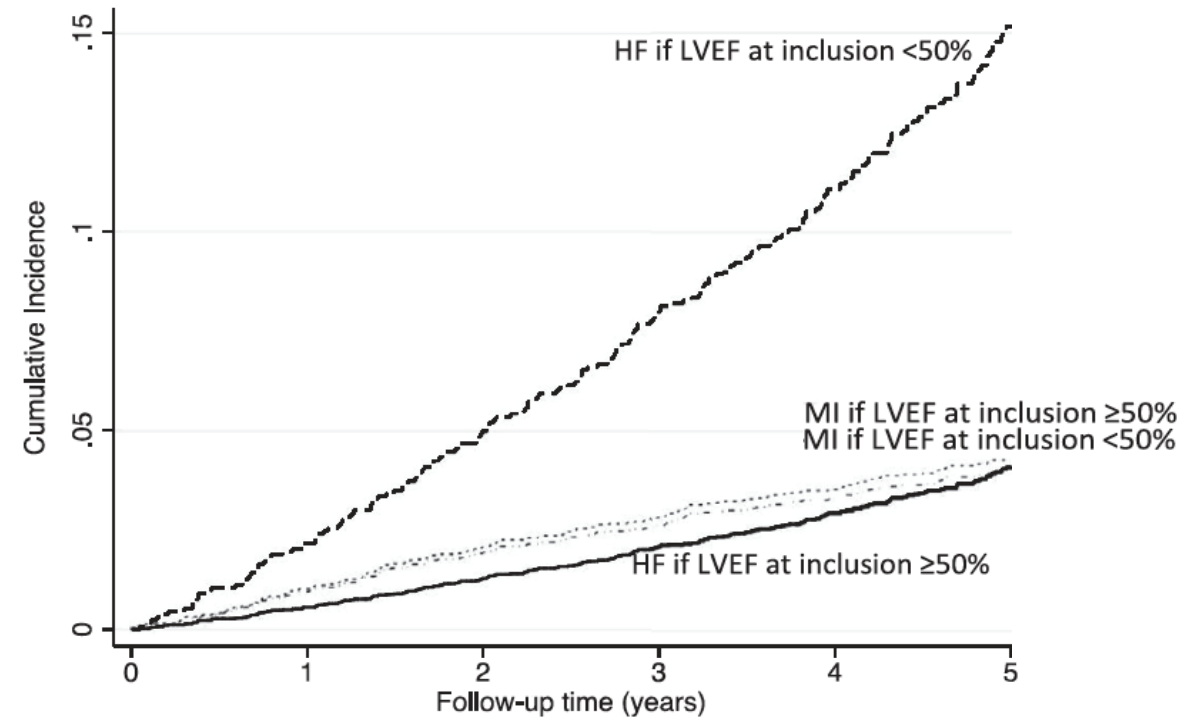
Number at

| | | | | | |
|------|------|------|------|------|------|
| 3785 | 3670 | 3541 | 3399 | 3204 | 1554 |
| 3785 | 3666 | 3530 | 3385 | 3190 | 1549 |

Ischemic Heart Disease and HF

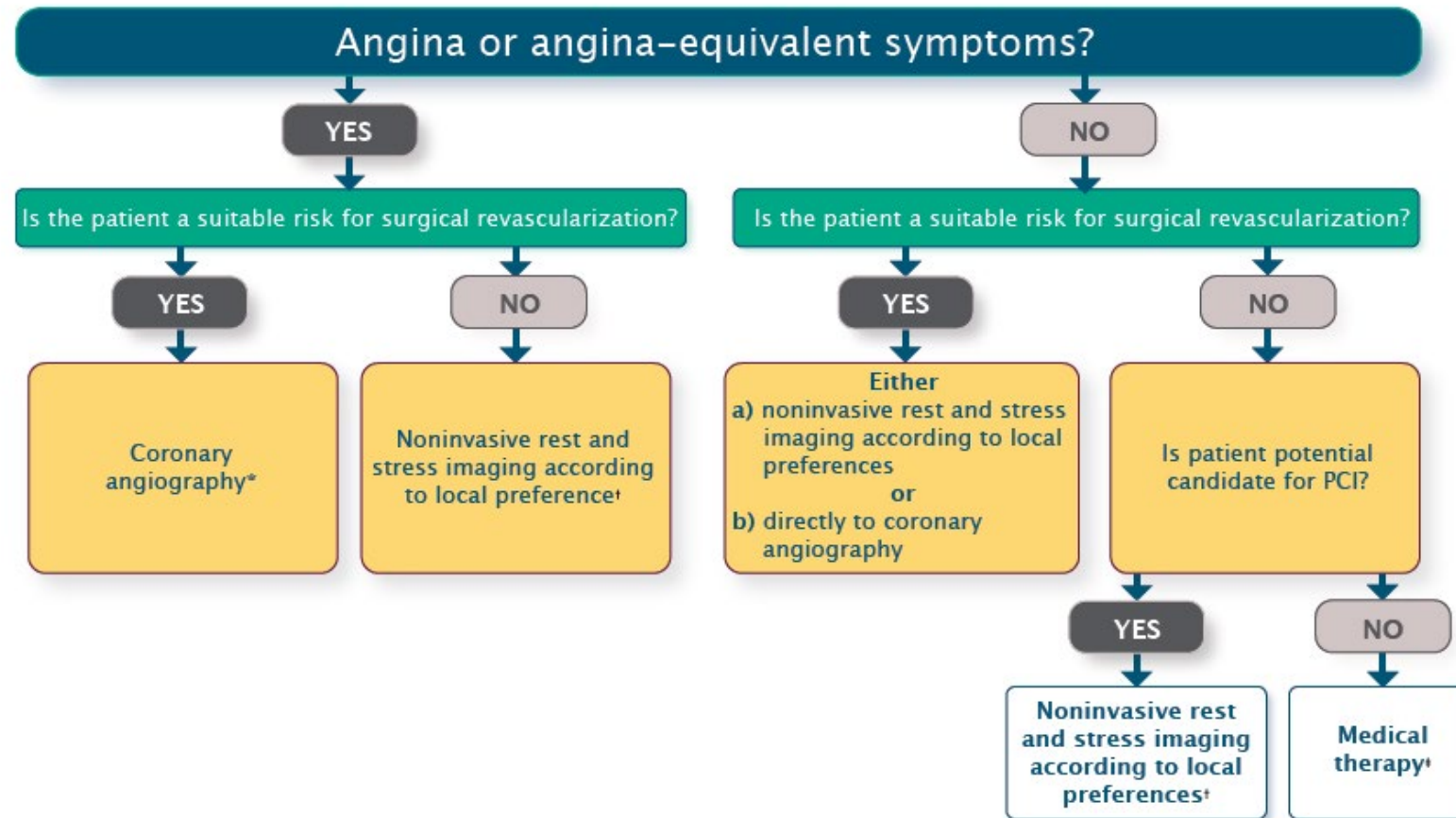
- CORONOR study (Nord-Pas-de-Calais, France)
- Registry of 4184 outpatients with stable CAD:
 - Prior MI (> 1 year)
 - Prior coronary revascularization
 - $\geq 50\%$ obstruction of at least 1 V
- Baseline LVEF categorized as $\geq 50\%$ vs. $< 50\%$

B

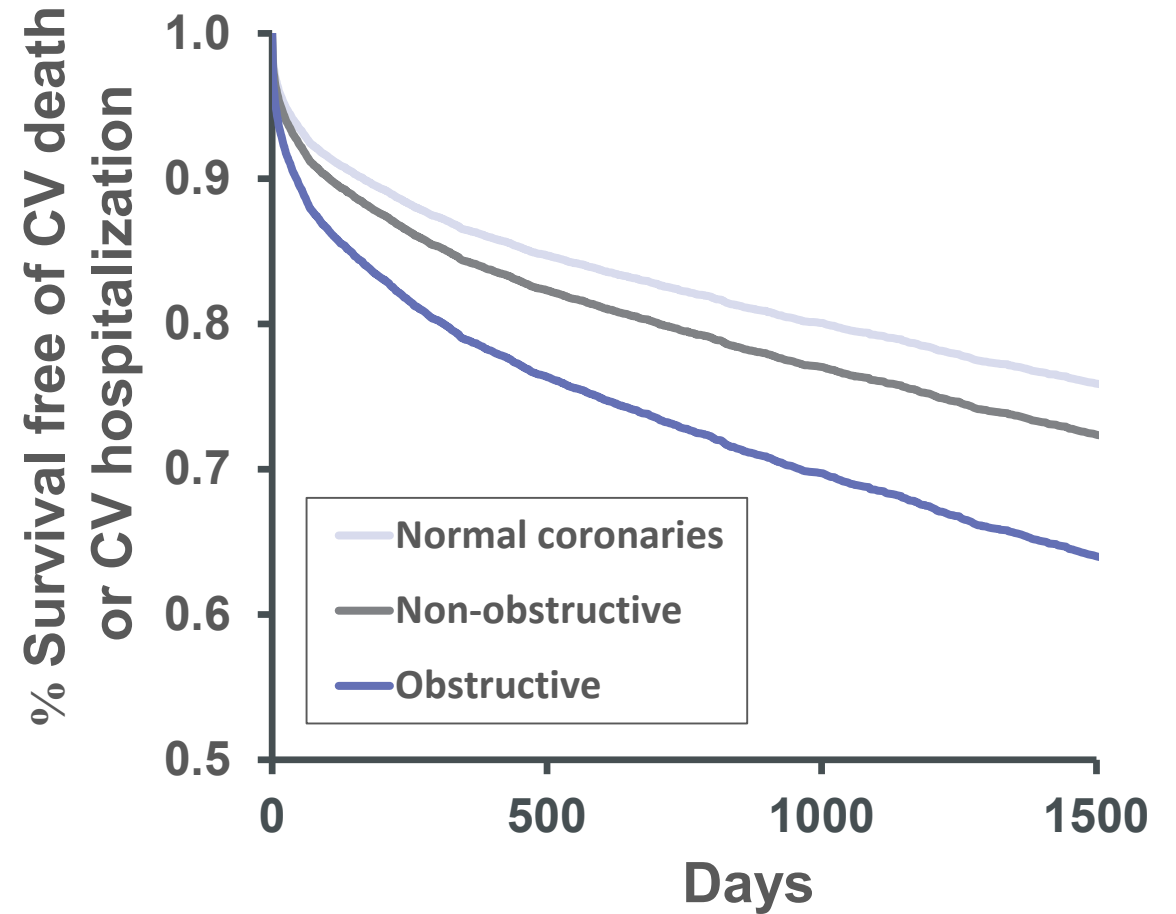
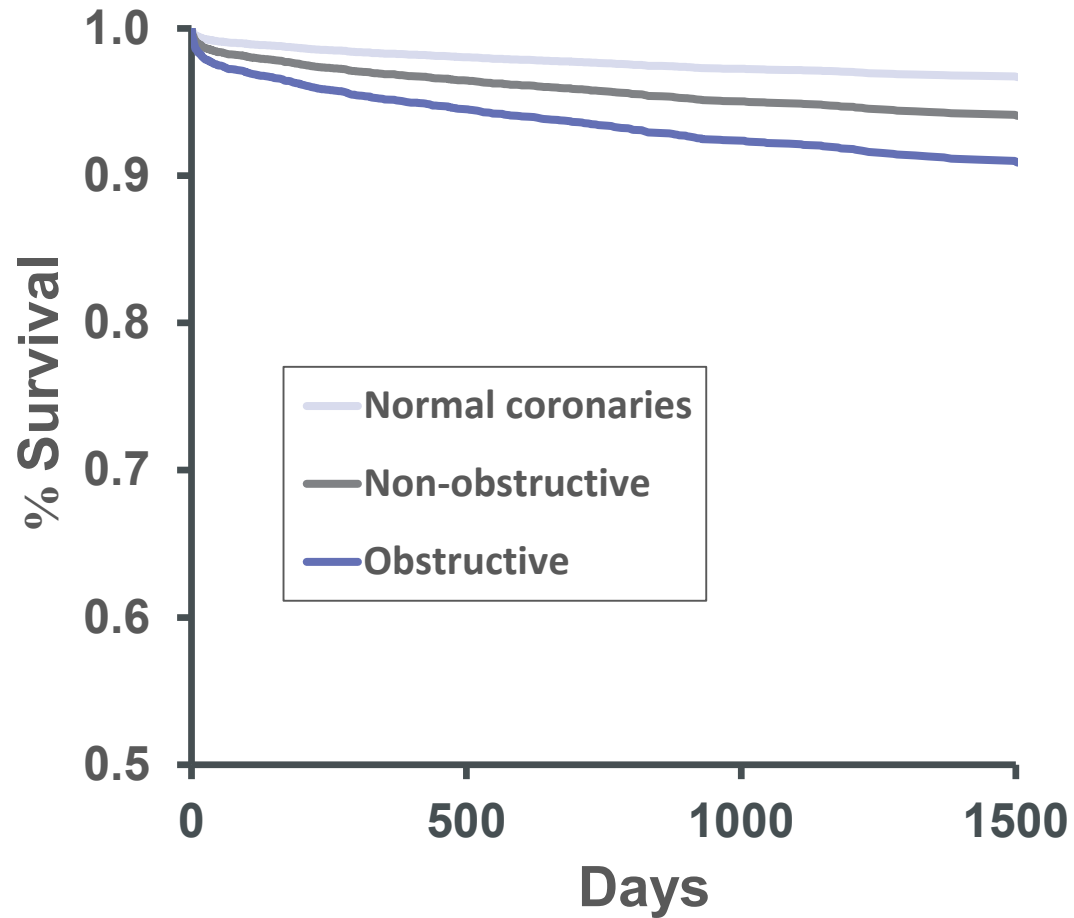


| Number at risk | 0 | 1 | 2 | 3 | 4 | 5 |
|------------------------|------|------|------|------|------|------|
| HF if LVEF $\geq 50\%$ | 3206 | 3128 | 3037 | 2931 | 2774 | 1353 |
| HF if LVEF $< 50\%$ | 523 | 491 | 455 | 419 | 387 | 177 |
| MI if LVEF $\geq 50\%$ | 3206 | 3113 | 3010 | 2899 | 2738 | 1336 |
| MI if LVEF $< 50\%$ | 523 | 501 | 470 | 436 | 407 | 188 |

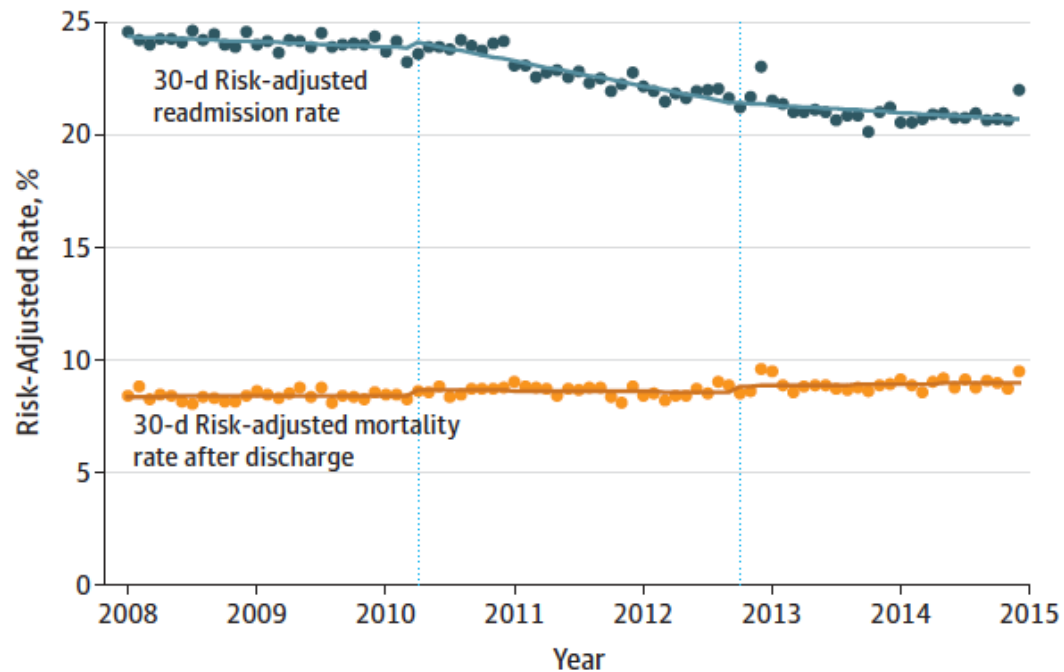
Assessment for CAD



Outcomes of Normal, Non-obstructive or Obstructive Lesions on Coronary Angiography in HFrEF

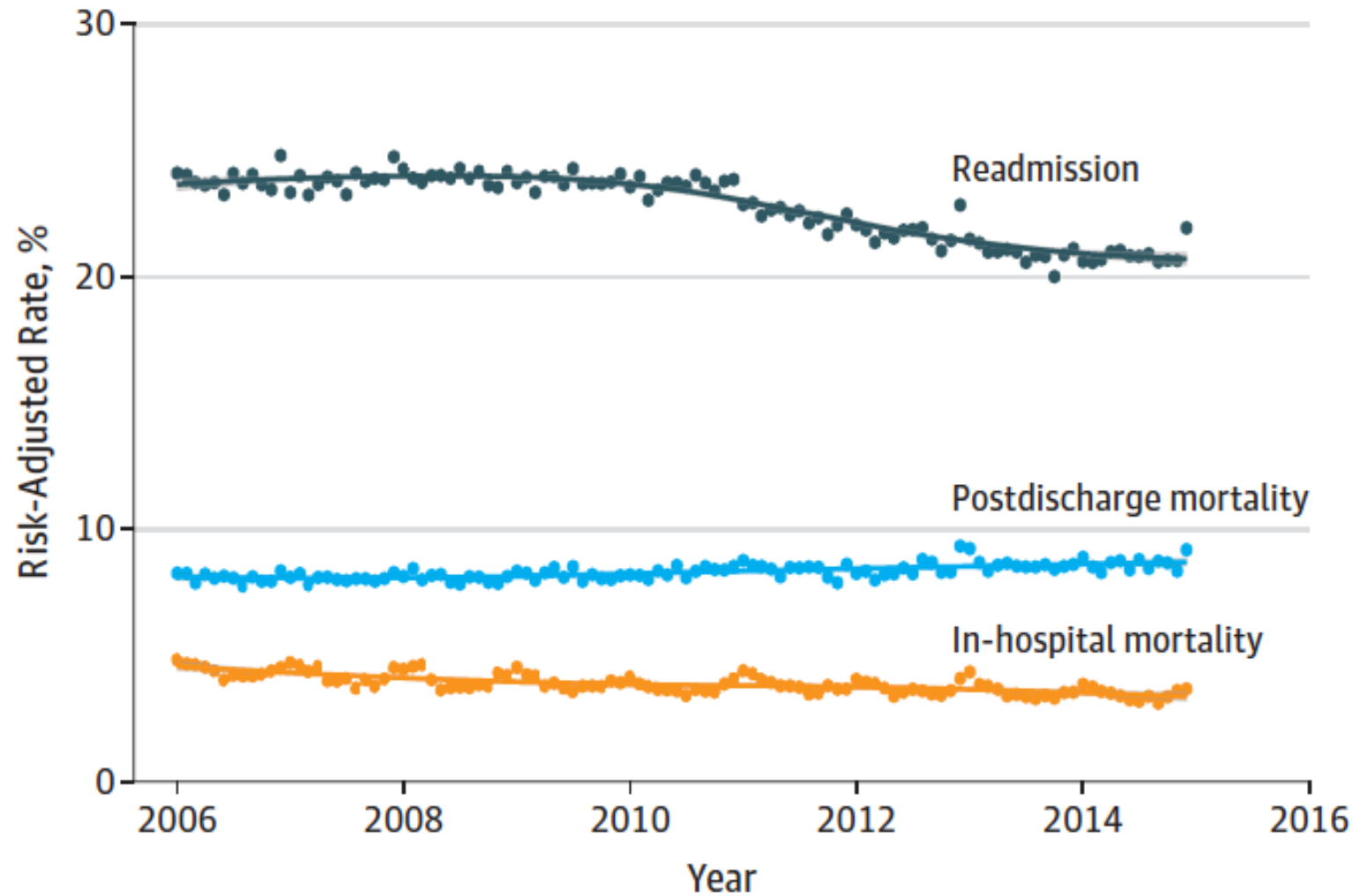


Association of Changing Hospital Readmission Rates With Mortality Rates After Hospital Discharge



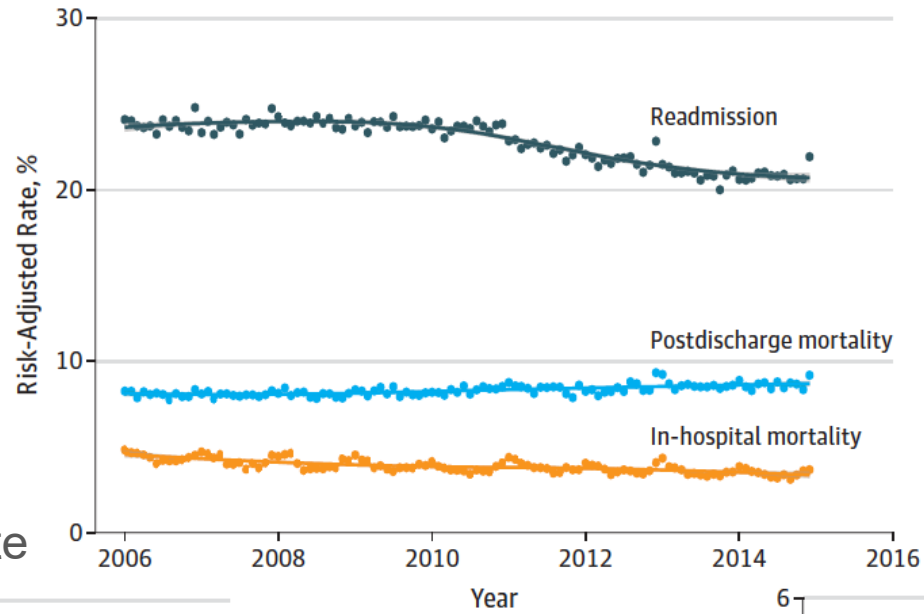
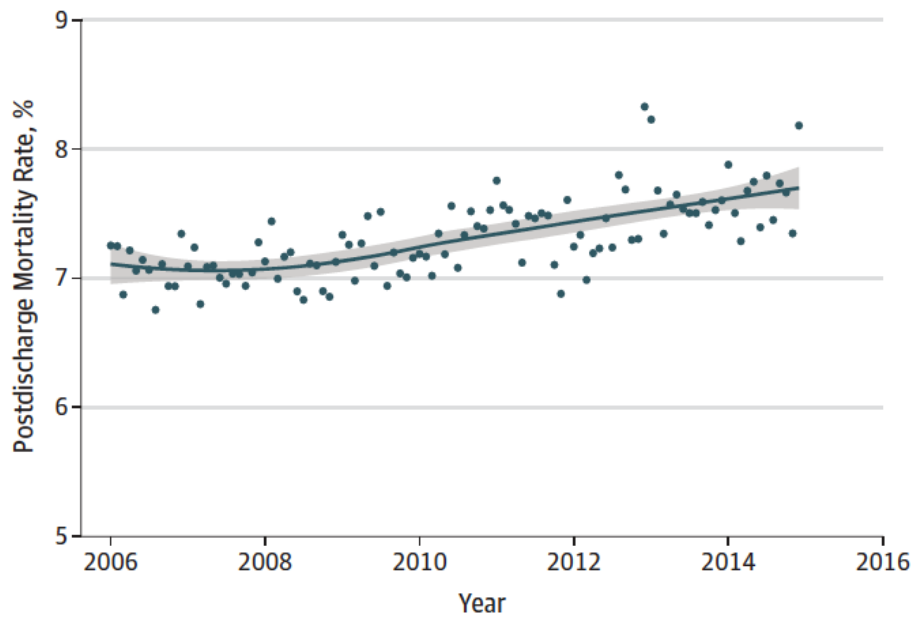
- 2,962,554 hospitalizations for HF
- U.S. Medicare beneficiaries
- 2009: readmission performance provided
- 2012: financial penalties applied
- **For HF:**
- - 0.05% change in risk-adjusted readmission rates per month after HF hospitalization
- 0.008% change in risk-adjusted mortality rates per month after discharge

Readmission vs. Mortality

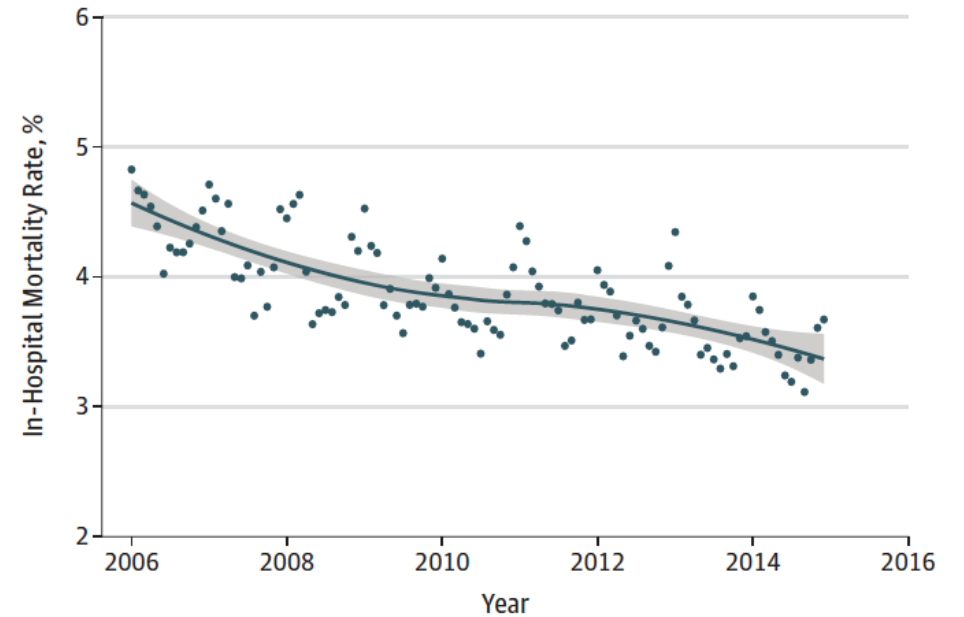


- 4,000,000 HF patients
- U.S. Medicare

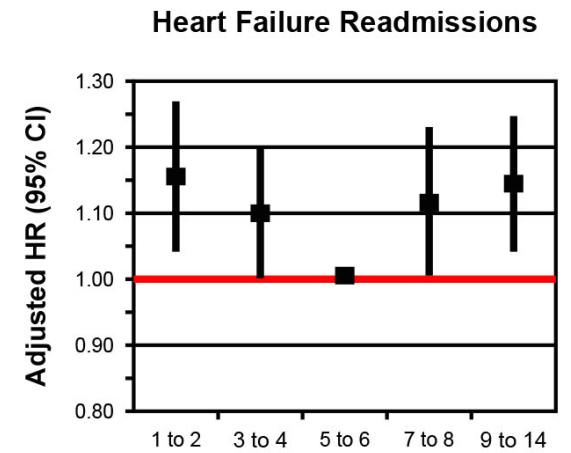
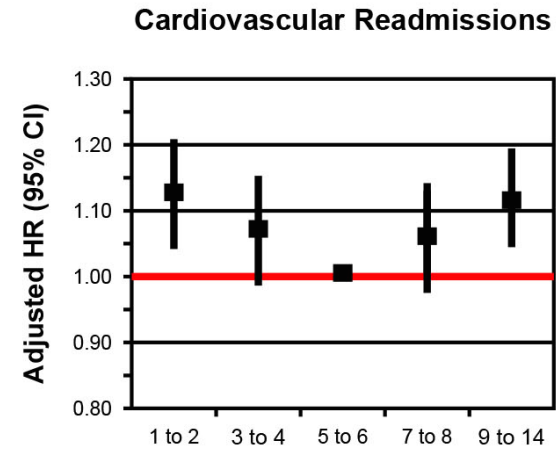
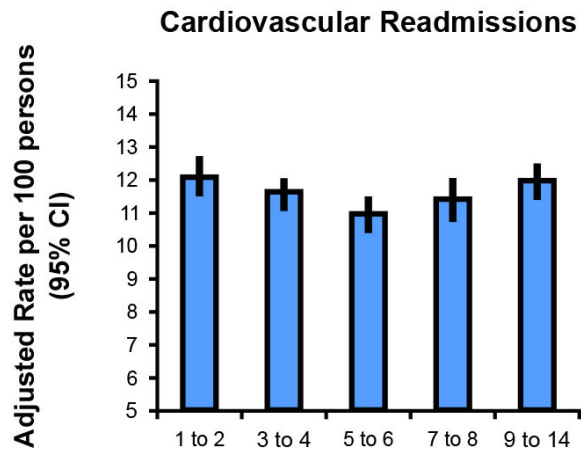
Risk-adjusted post-discharge mortality rate



Risk-adjusted In-hospital mortality rate



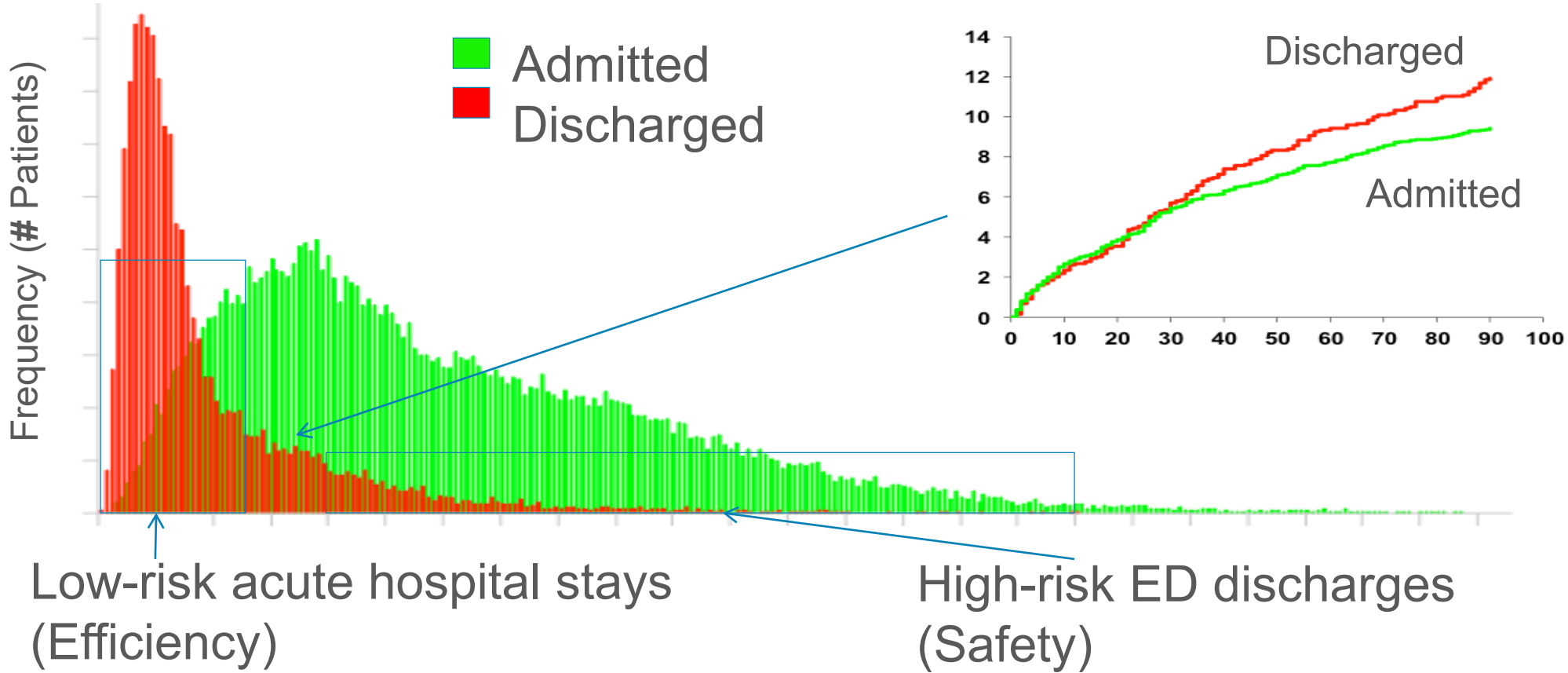
Length of Stay and Readmission Risk



Strategies to Reduce Readmissions



Need for Improved Safety and Efficiency of Acute HF Decision-Making in the ED



From: Prediction of Heart Failure Mortality in Emergent Care: A Cohort Study

Ann Intern Med. 2012;156(11):767-775. doi:10.7326/0003-4819-156-11-201206050-00003

EHMRG

Emergency Heart failure Mortality Risk Grade

Derivation Cohort (n=7433)

5254 Admitted

2179 Discharged

Validation Cohort (n=5158)

3560 Admitted

1598 Discharged

Table 3. EHMRG 7-Day Mortality Risk Score

| Variable | Units | Additive or Multiplicative Component |
|--------------------|-------------------|--------------------------------------|
| Age | y | $2 \times \text{age}$ |
| Transported by EMS | If "yes" | +60 |
| SBP | mm Hg* | $-1 \times \text{SBP}$ |
| Heart rate | beats/min† | $1 \times \text{heart rate}$ |
| Oxygen saturation | %‡ | $-2 \times \text{oxygen saturation}$ |
| Creatinine | mg/dL§ | $20 \times \text{creatinine}$ |
| Potassium | 4.0 to 4.5 mmol/L | 0 |
| | ≥4.6 mmol/L | +30 |
| | ≤3.9 mmol/L | +5 |
| Troponin | >ULN | +60 |
| Active cancer | If "yes" | +45 |
| Metolazone at home | If "yes" | +60 |
| Adjustment factor | | +12 |
| Total | | EHMRG score¶ |

EHMRG = Emergency Heart Failure Mortality Risk Grade; EMS = emergency medical services; SBP = systolic blood pressure; ULN = upper limit of normal.

* Initial/triage SBP, maximum of 160 mm Hg.

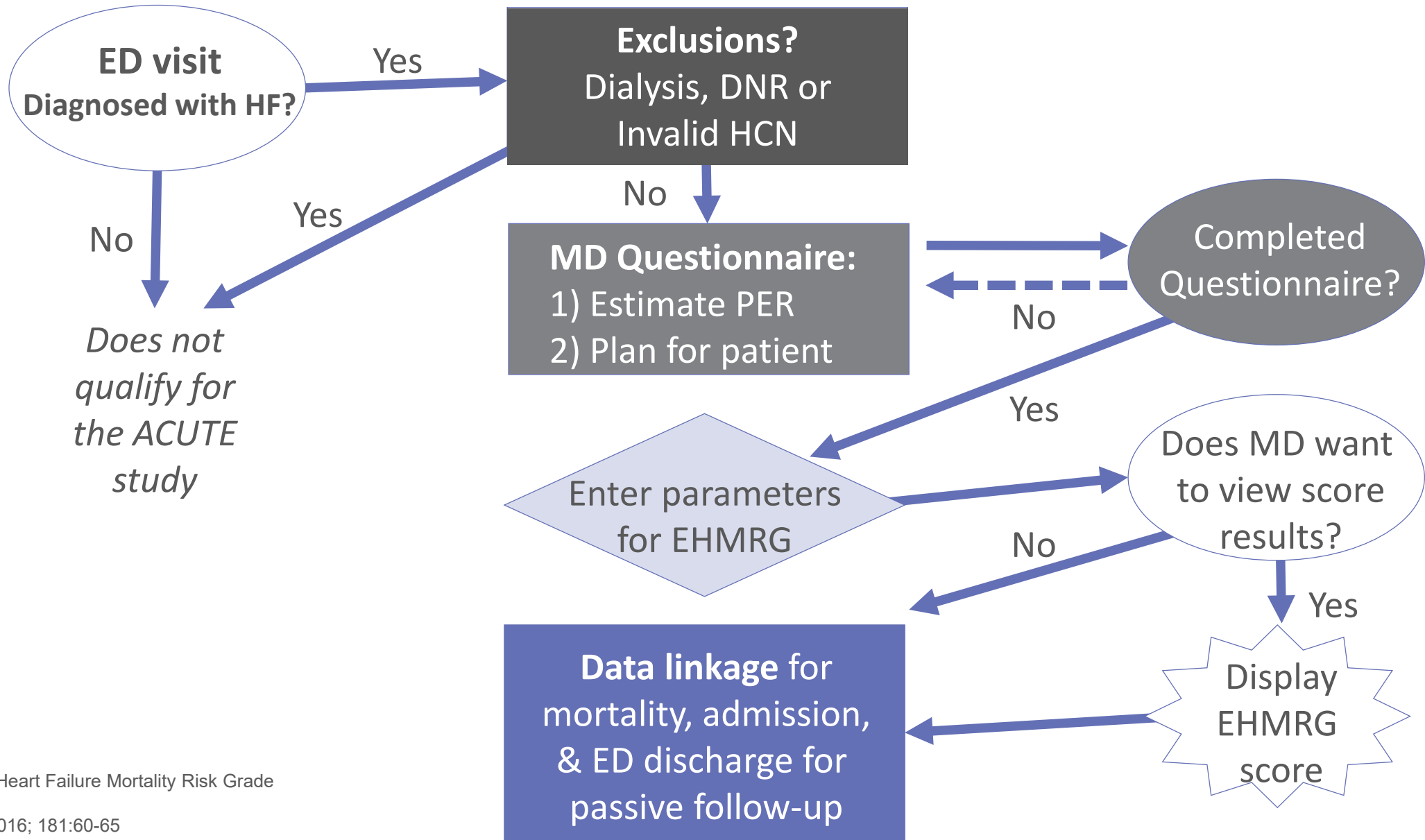
† Initial/triage heart rate, minimum of 80 beats/min and maximum of 120 beats/min.

‡ Lowest initial/triage oxygen saturation, maximum of 92%.

§ If creatinine concentration is in $\mu\text{mol/L}$, divide by 88.4 to convert to mg/dL.

|| Adjustment factor of +12 added to allow for an approximate 0 median score.

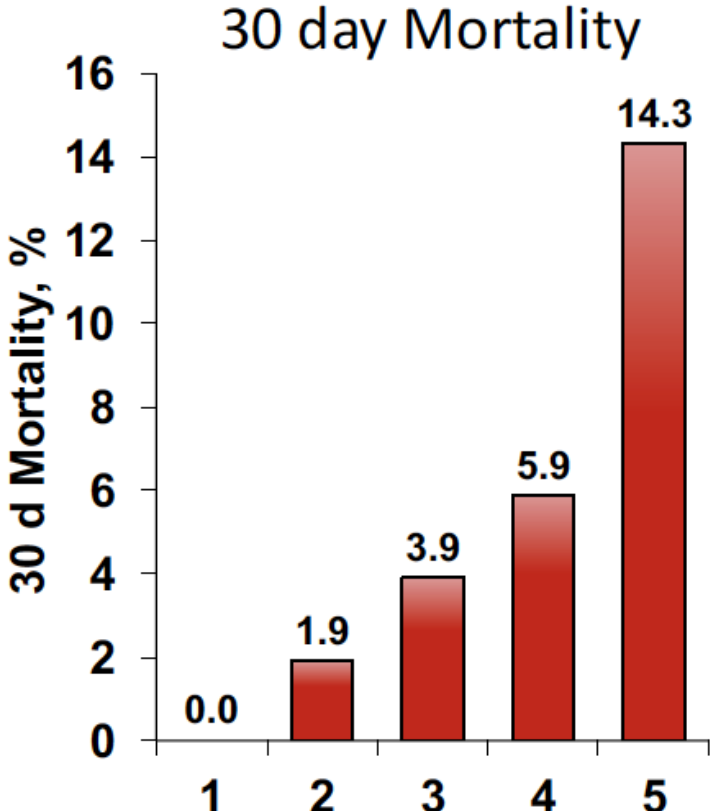
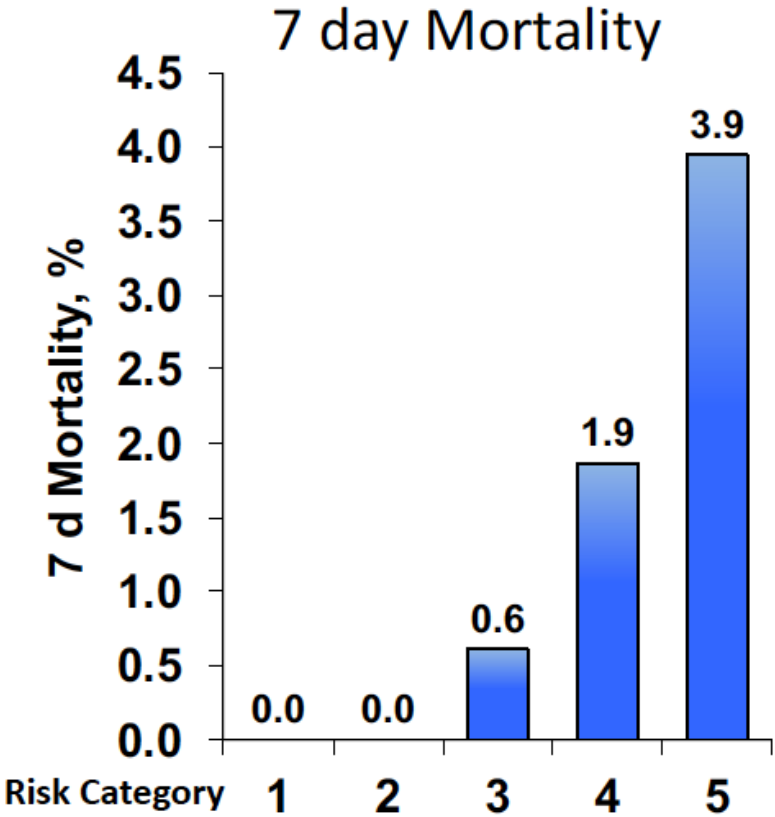
¶ All variables are required to calculate the score; users are cautioned against estimating component values. The EHMRG is not for use in patients who are dialysis-dependent.



EHMURG: Emergency Heart Failure Mortality Risk Grade

Lee DS, *Am Heart J* 2016; 181:60-65

ACUTE: Acute Congestive heart failure Urgent and Transitional care Evaluation



| Risk Category | 1 | 2 | 3 | 4 | 5 |
|----------------|--------|--------|--------|-------|-------|
| High threshold | -49.05 | -15.91 | 17.97 | 56.55 | -- |
| Low threshold | -- | -49.04 | -15.90 | 17.98 | 56.56 |

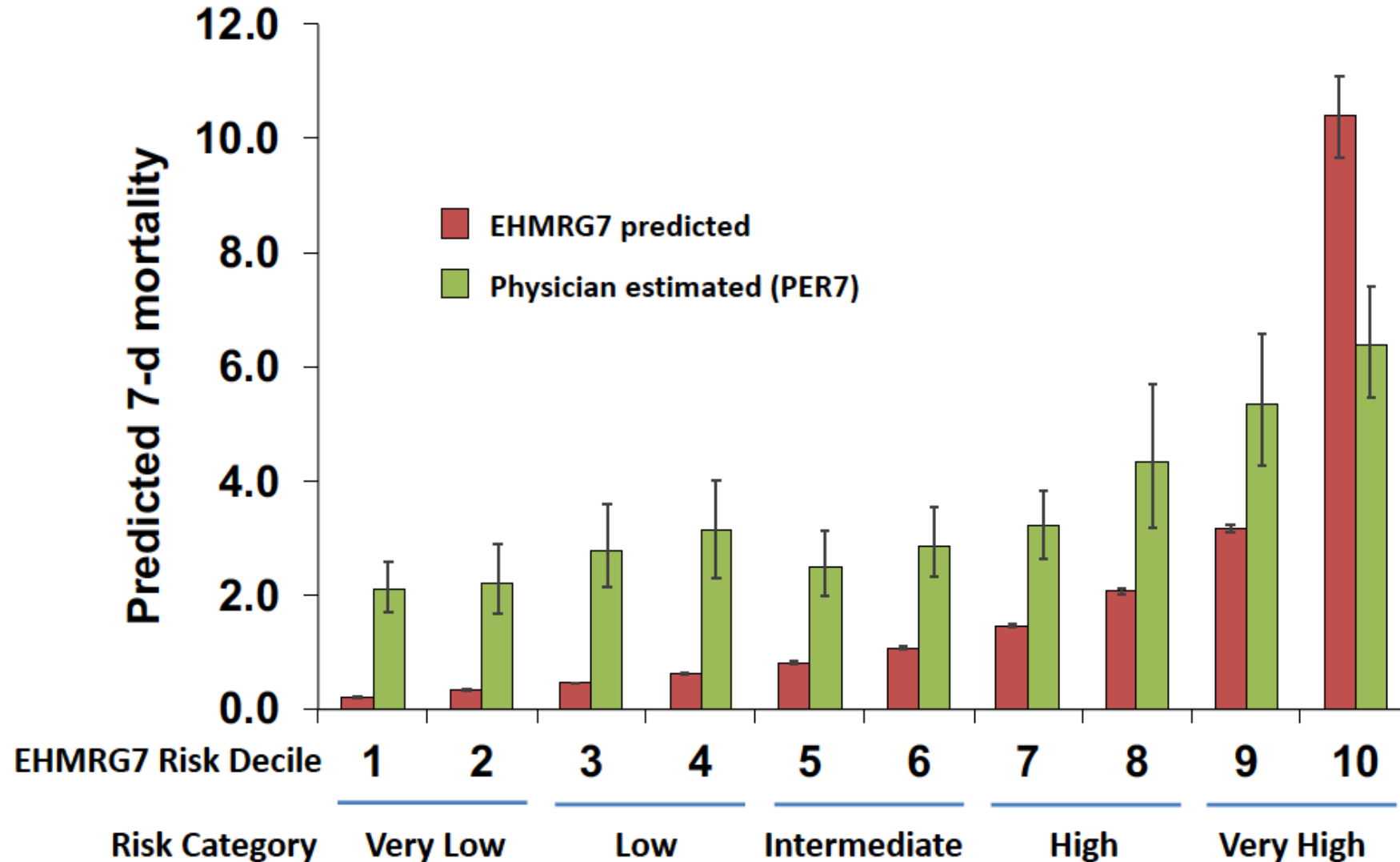
| Risk Category | 1 | 2 | 3 | 4 | 5 |
|----------------|-------|-------|-------|--------|--------|
| High threshold | 1.86% | 3.55% | 6.47% | 12.19% | -- |
| Low threshold | -- | 1.87% | 3.56% | 6.48% | 12.20% |

Prospective validation of Emergency HF Mortality Risk Grade (EHMRG):

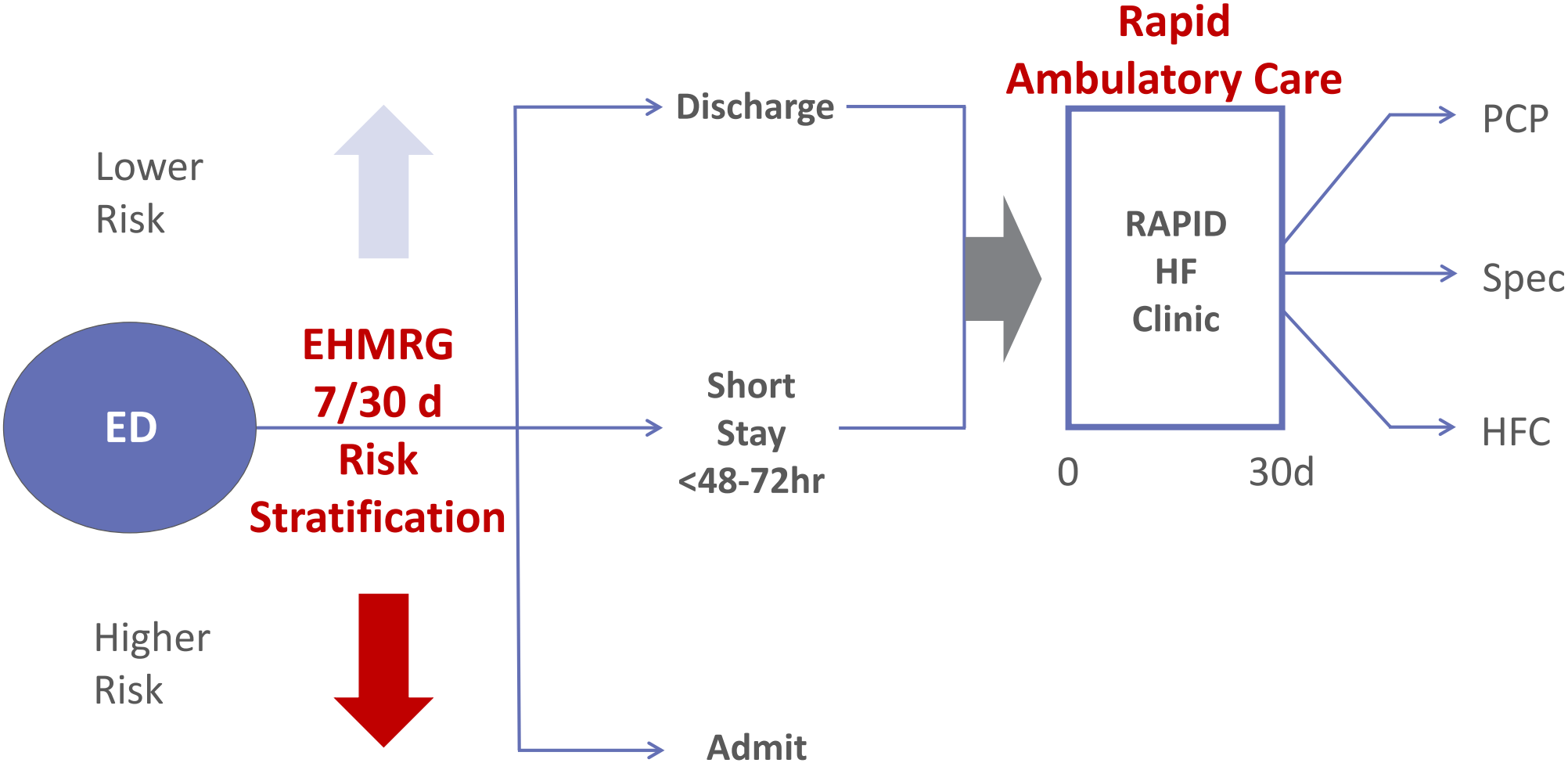
- 1983 acute HF pts
- 9 hospitals

7-day risk score available at: <https://ehmrg.ices.on.ca>

Physician Estimated vs Model-Predicted Mortality



Comparison of Outcomes and Access to Care for HF (COACH trial)



Conclusions

- The economic burden of HF is high and correlates with higher rates of hospital admission
- Strategies to improve early diagnosis of HF:
 - Reduce the need for acute emergency department presentation:
 - May be improved with BNP and hs-Troponin
- Coronary artery disease:
 - Important antecedent for HF → prevention target
 - Even minimal CAD is associated with higher risk of readmissions and CV death

Conclusions

- Readmissions:
 - Global problem
 - Highest rates of readmission are in North America
- Better risk stratification strategies may reduce readmissions and hospitalizations by improving efficiency and safety of acute decision-making for HF



**TED ROGERS CENTRE
FOR HEART RESEARCH**

Peter Munk
Cardiac Centre  **UHN**

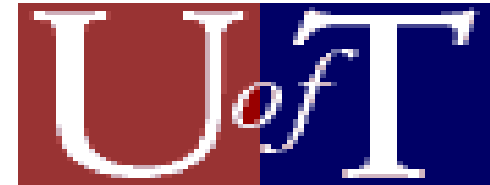


ONTARIO
SPOR SUPPORT
UNIT



University Health Network

Toronto General Hospital Toronto Western Hospital Princess Margaret Hospital



Question and Answer



Optimizing HF Therapies During Hospitalization: Time Matters

Nadia Giannetti

MD, FRCPC



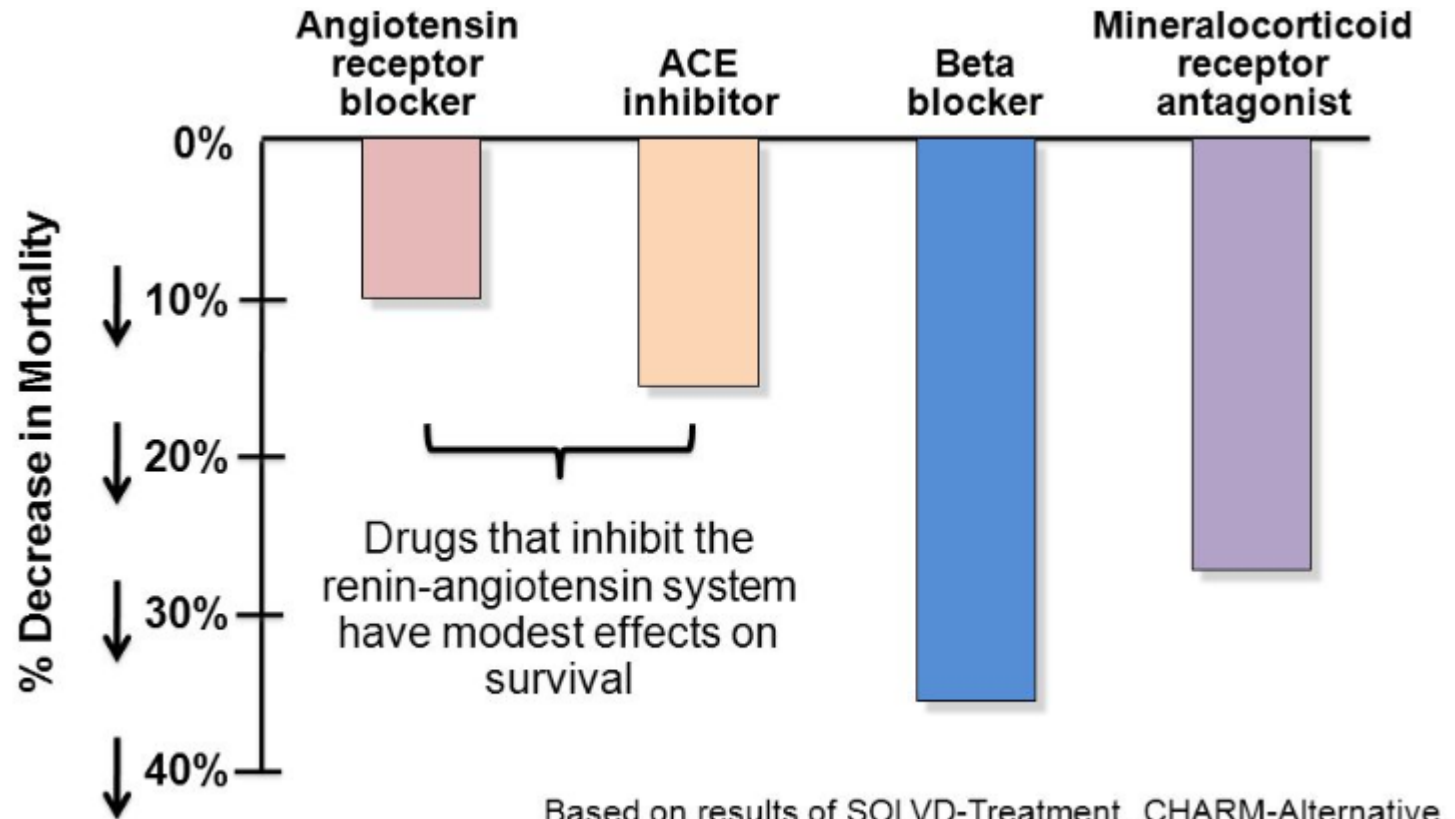
Overview

- What is our goal for therapy?
- Are we achieving this goal?
- How quickly we need to get there?
- How can we do better?

What is Our Goal for Therapy?



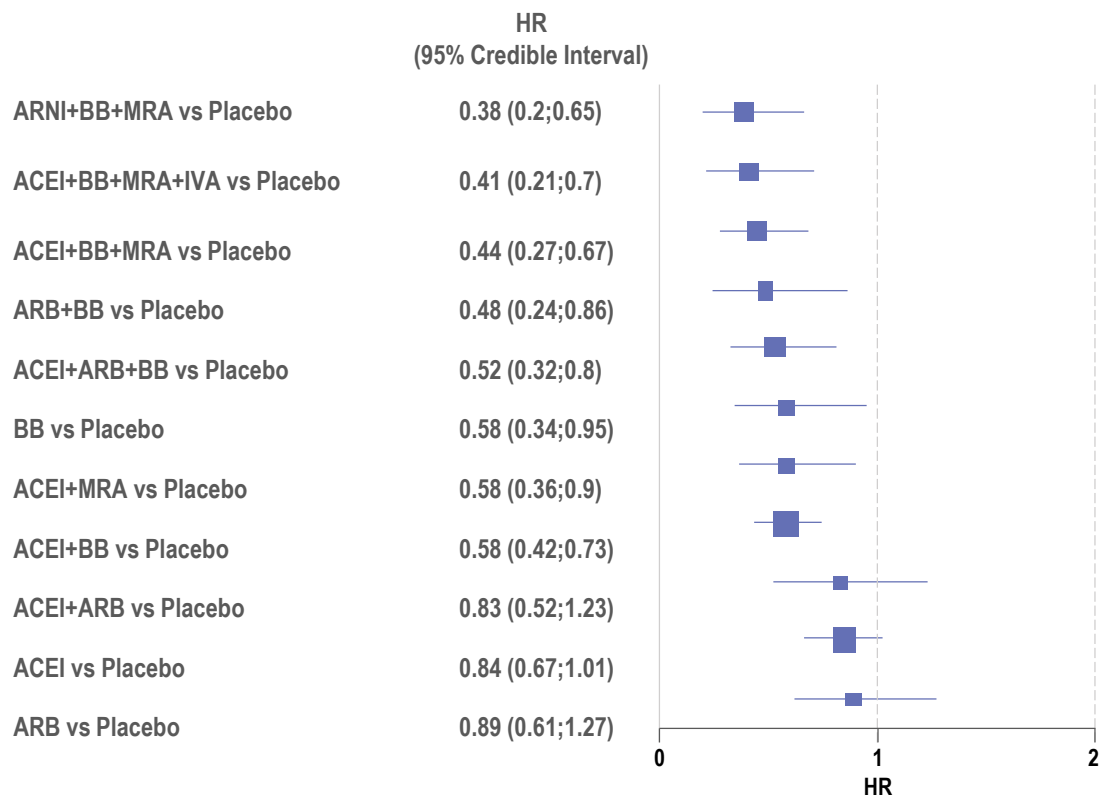
Medical Therapy Benefits



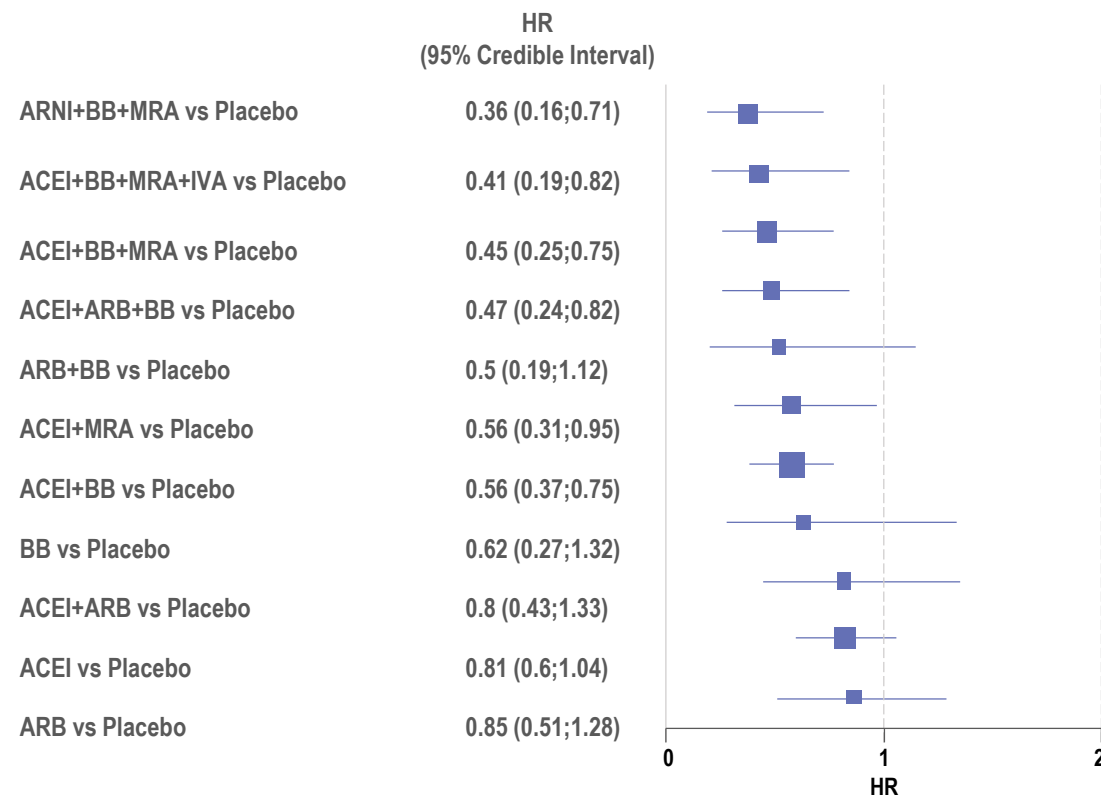
Based on results of SOLVD-Treatment, CHARM-Alternative, COPERNICUS, MERIT-HF, CIBIS II, RALES and EMPHASIS-HF

Incremental Benefit of Drug Therapies for Heart Failure

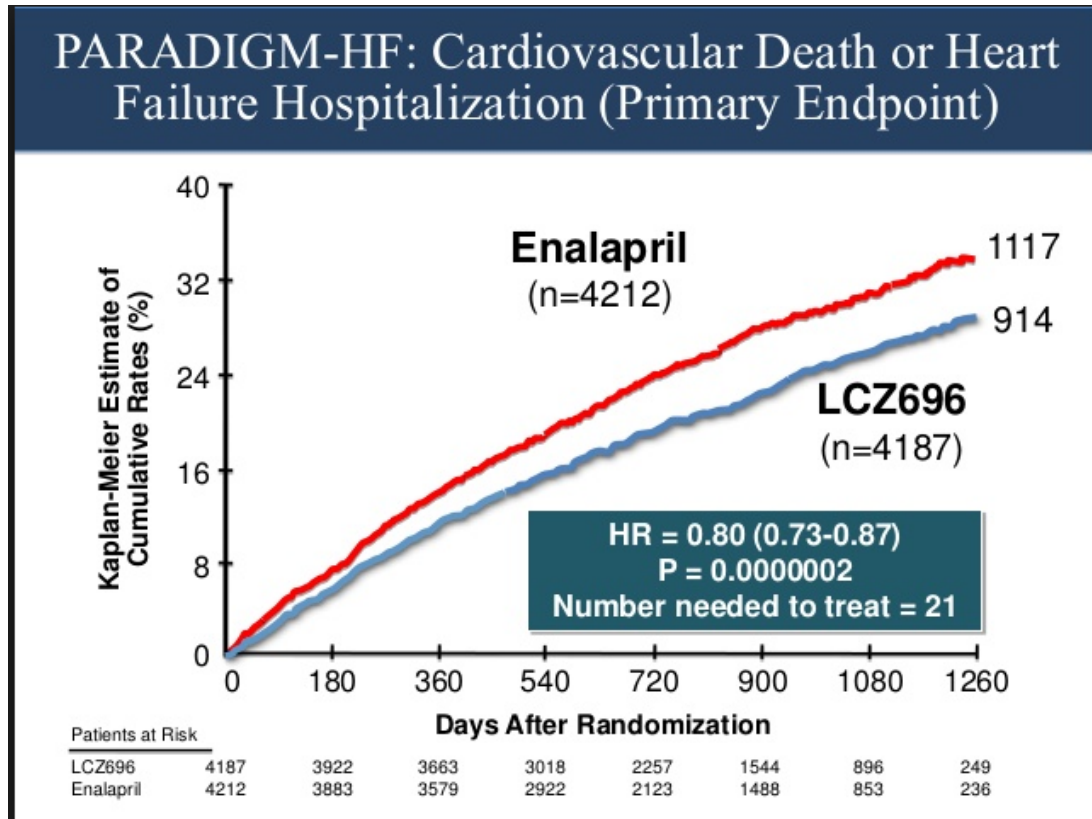
All-cause Mortality



Cardiovascular Mortality

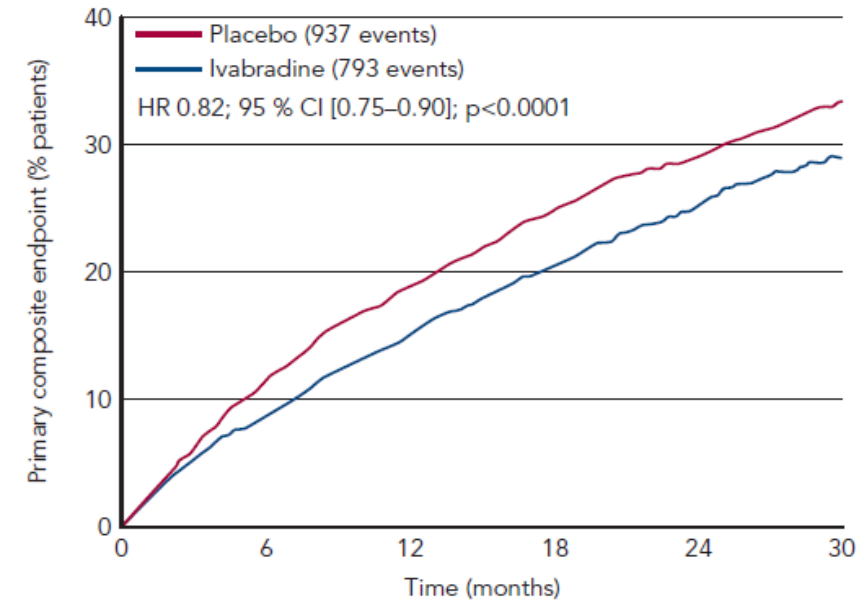


Medical Therapy Benefits



McMurray NEJM 2014

Figure 1: Patients From the SHIFT Trial Reaching the Composite Primary Endpoint (Cardiovascular Death or Hospitalisation For Worsening Heart Failure) in Placebo and Ivabradine Groups

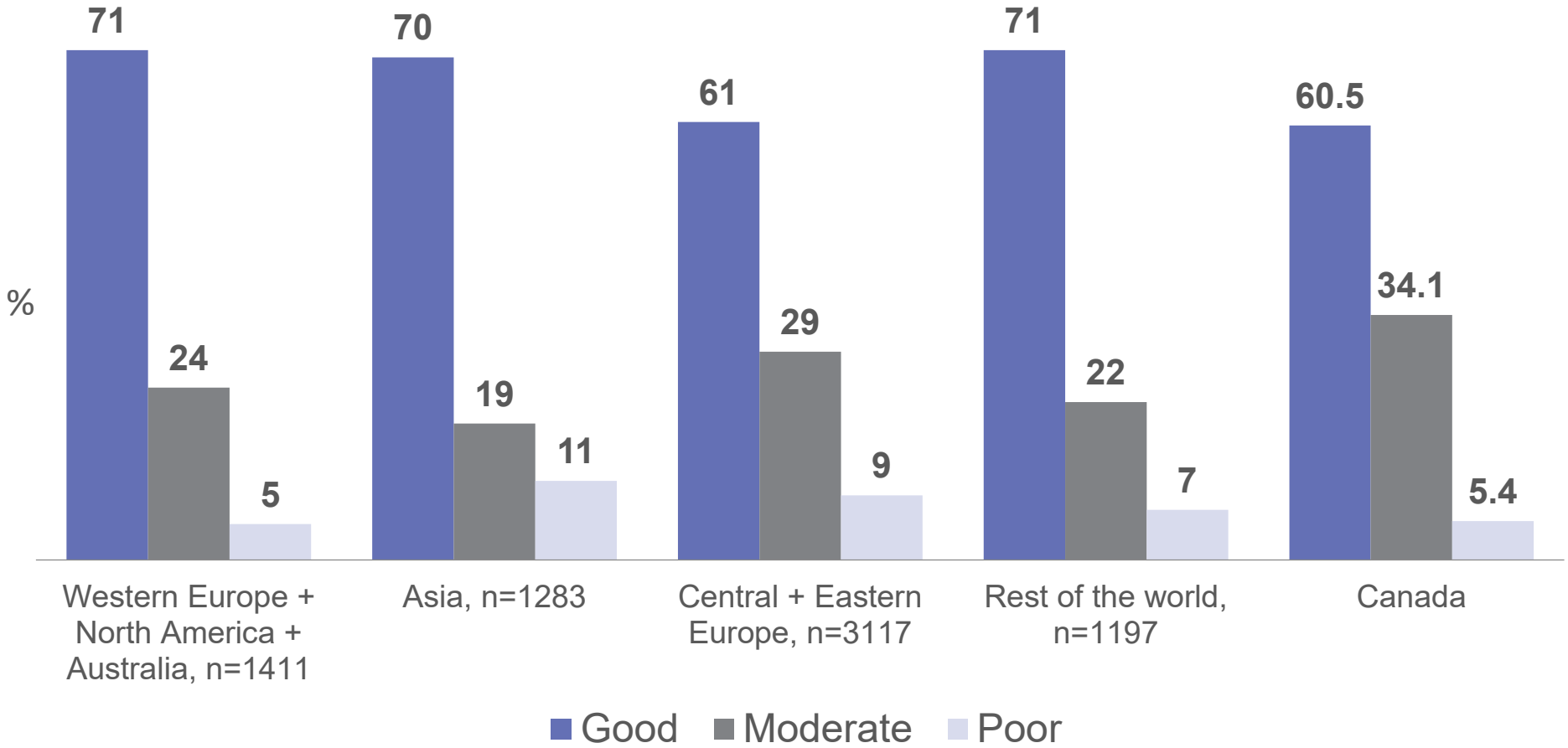


Swedberg Lancet 2010

Are We Achieving This Goal?



Adherence to Guidelines Score by Geographic Zone



CHAMP-HF Registry: Use of Therapy

A



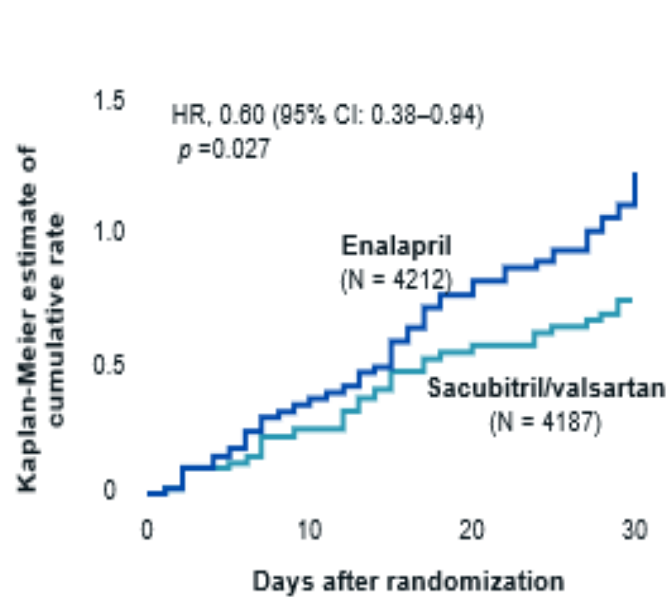
| | ACEI/ARB | ARNI | ACEI/ARB/ ARNI | Beta- Blocker | MRA |
|--|----------|------|-------------------|------------------|------|
| Without Contraindication and Not Treated | 1374 | 3029 | 920 | 1159 | 2317 |
| Treated | 2107 | 452 | 2536 | 2351 | 1163 |
| With Contraindication | 37 | 37 | 62 | 8 | 38 |

How Quickly Do We Need To Get There?

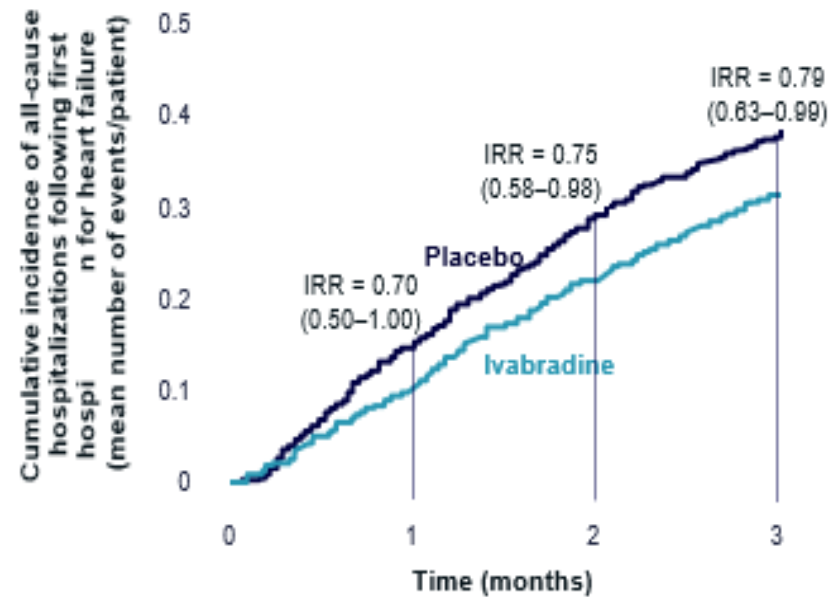


Hospitalization For HF

Endpoint – hospitalization for HF



The curves begin to diverge at 3 months, and the difference is statistically significant at 6 months.



Early treatment with IVA reduces readmission for HF in SHIFT trial.

The curves begin to diverge at 2 weeks for those hospitalized for HF.

19

Initiation, Continuation, or Withdrawal of Angiotensin-Converting Enzyme Inhibitors/Angiotensin Receptor Blockers and Outcomes in Patients Hospitalized With Heart Failure With Reduced Ejection Fraction

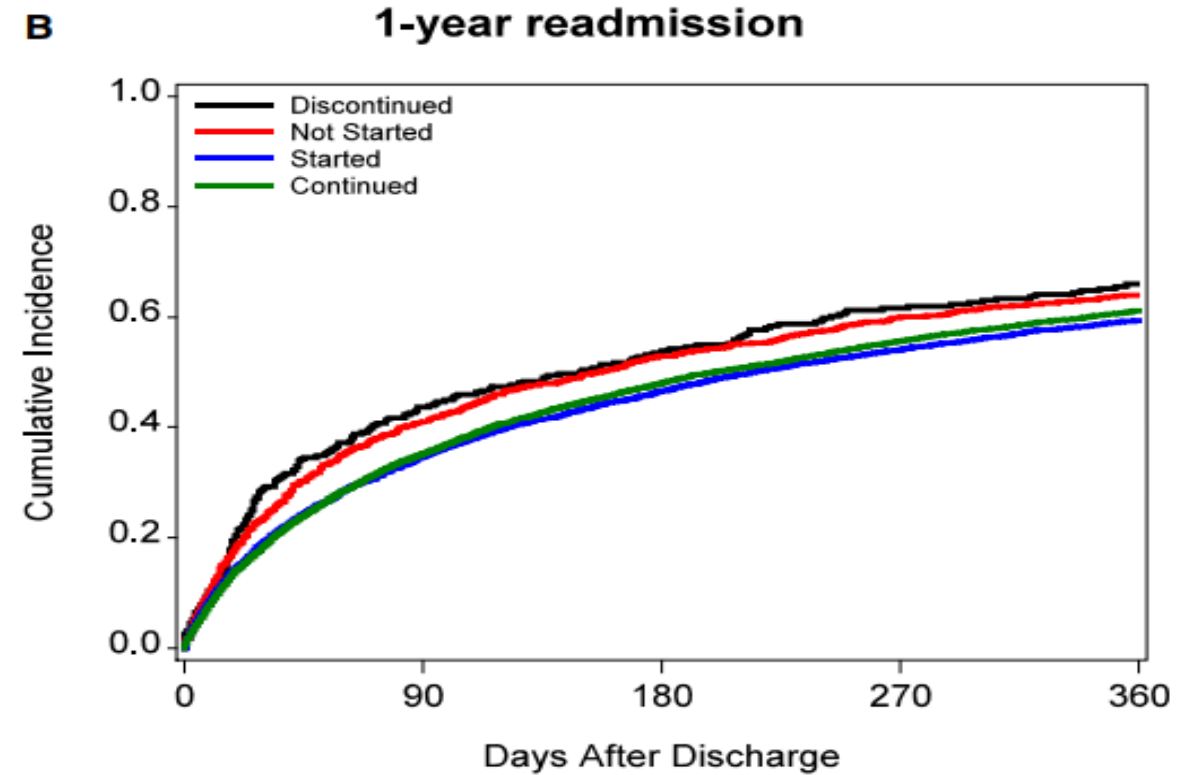
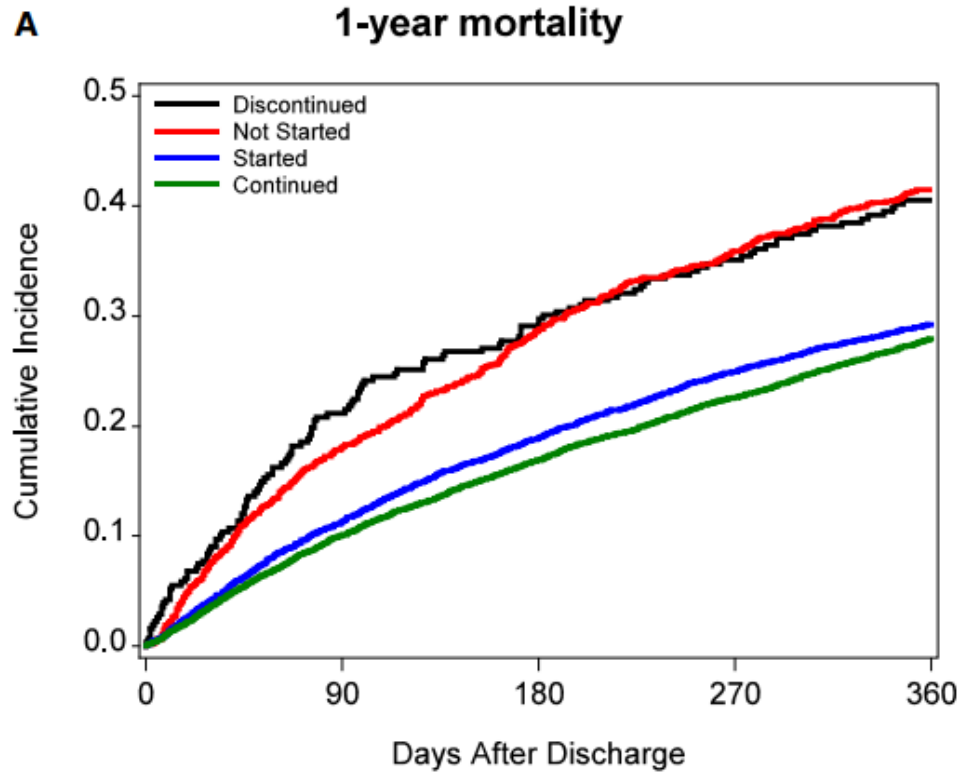
Lauren G. Gilstrap, MD; Gregg C. Fonarow, MD; Akshay S. Desai, MD, MPH; Li Liang, PhD; Roland Matsouaka, PhD; Adam D. DeVore, MD, MHS; Eric E. Smith, MD, MPH; Paul Heidenreich, MD, MS; Adrian F. Hernandez, MD, MHS; Clyde W. Yancy, MD; Deepak L. Bhatt, MD, MPH

Background—Guidelines recommend continuation or initiation of guideline-directed medical therapy, including angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers (ACEi/ARB), in hospitalized patients with heart failure with reduced ejection fraction.

Methods and Results—Using the Get With The Guidelines-Heart Failure Registry, we linked clinical data from 16 052 heart failure with reduced ejection fraction (ejection fraction $\leq 40\%$) patients with Medicare claims data. We divided ACEi/ARB-eligible patients into 4 categories based on admission and discharge ACEi/ARB use: continued (reference group), started, discontinued, or not started on therapy. A multivariable Cox proportional hazard model was used to determine the association between ACEi/ARB category and outcomes. Most, 90.5%, were discharged on ACEi/ARB (59.6% continued and 30.9% newly started). Of those discharged without ACEi/ARB, 1.9% were discontinued, and 7.5% were eligible but not started. Thirty-day mortality was 3.5% for patients continued and 4.1% for patients started on ACEi/ARB. In contrast, 30-day mortality was 8.8% for patients discontinued (adjusted hazard ratio [HR_{adj}] 1.92; 95% CI 1.32-2.81; $P < 0.001$) and 7.5% for patients not started (HR_{adj} 1.50; 95% CI 1.12-2.00; $P = 0.006$). The 30-day readmission rate was lowest among patients continued or started on therapy. One-year mortality was 28.2% for patients continued and 29.7% for patients started on ACEi/ARB compared to 41.6% for patients discontinued (HR_{adj} 1.35; 95% CI 1.13-1.61; $P < 0.001$) and 41.7% (HR_{adj} 1.28; 95% CI 1.14-1.43; $P < 0.001$) for patients not started on therapy.

Conclusions—Compared with continuation, withdrawal of ACEi/ARB during heart failure hospitalization is associated with higher rates of postdischarge mortality and readmission, even after adjustment for severity of illness. (*J Am Heart Assoc.* 2017;6:e004675. DOI: 10.1161/JAHA.116.004675.)

Medical Therapy During Hospitalization



How Can We Do Better?



Angiotensin–Neprilysin Inhibition in Acute Decompensated Heart Failure

Eric J. Velazquez, M.D., David A. Morrow, M.D., M.P.H., Adam D. DeVore, M.D., M.H.S., Carol I. Duffy, D.O., Andrew P. Ambrosy, M.D., Kevin McCague, M.A., Ricardo Rocha, M.D., and Eugene Braunwald, M.D. for the PIONEER-HF Investigators*

PIONEER-HF

Study Design

Hospitalized with Acute Decompensated HF with Reduced EF

While hospitalized

Sacubitril/valsartan
97/103 mg twice daily*

vs

Enalapril
10 mg twice daily*

In-hospital initiation

Study Drug for 8 weeks

- Evaluate biomarker surrogates of efficacy
- Evaluate safety and tolerability
- Explore clinical outcomes

*Target Dose
HF, Heart Failure. EF, Ejection Fraction

Velazquez EJ et al. [nejm.org/doi/full/10.1056/NEJMoa1812851](https://doi.org/10.1056/NEJMoa1812851)

PIONEER-HF

Key Entry Criteria

- Hospitalized for Acute Decompensated Heart Failure (ADHF)
- LVEF $\leq 40\%$ within the last 6 months
- NT-proBNP ≥ 1600 pg/mL or BNP ≥ 400 pg/mL*
- While hospitalized:
 - SBP ≥ 100 mmHg in prior 6h; no symptomatic hypotension
 - No increase in IV diuretics in prior 6h
 - No IV vasodilators in prior 6h
 - No IV inotropes in prior 24h

*At screening
A complete list of inclusion and exclusion criteria has been previously published at Velazquez et al. Am Heart J 198 (2018) 145-151
LVEF, Left Ventricular Ejection Fraction. NT-proBNP N-terminal pro-Brain Natriuretic Peptide. BNP, Brain Natriuretic Peptide. SBP, Systolic Blood Pressure.
IV, Intravenous

PIONEER-HF

*Study Endpoints**

Primary endpoint:

- Time-averaged proportional change in NT-proBNP from baseline at 4 and 8 weeks

Safety

- Worsening renal function
- Hyperkalemia
- Symptomatic hypotension
- Angioedema

Exploratory Clinical Outcomes

- Serious Clinical Composite: Death, Hospitalization for HF, LVAD or listing for cardiac transplant

*A more complete list of PIONEER study endpoints has been previously published at Velazquez et al. *Am Heart J* 198 (2018) 145-151
NT-proBNP N-terminal pro–Brain Natriuretic Peptide. HF, Heart Failure. LVAD, Left Ventricular Assist Device. HF, Heart Failure
Data on File: PIONEER-HF Protocol, Novartis Pharmaceutical Corp; October 2018

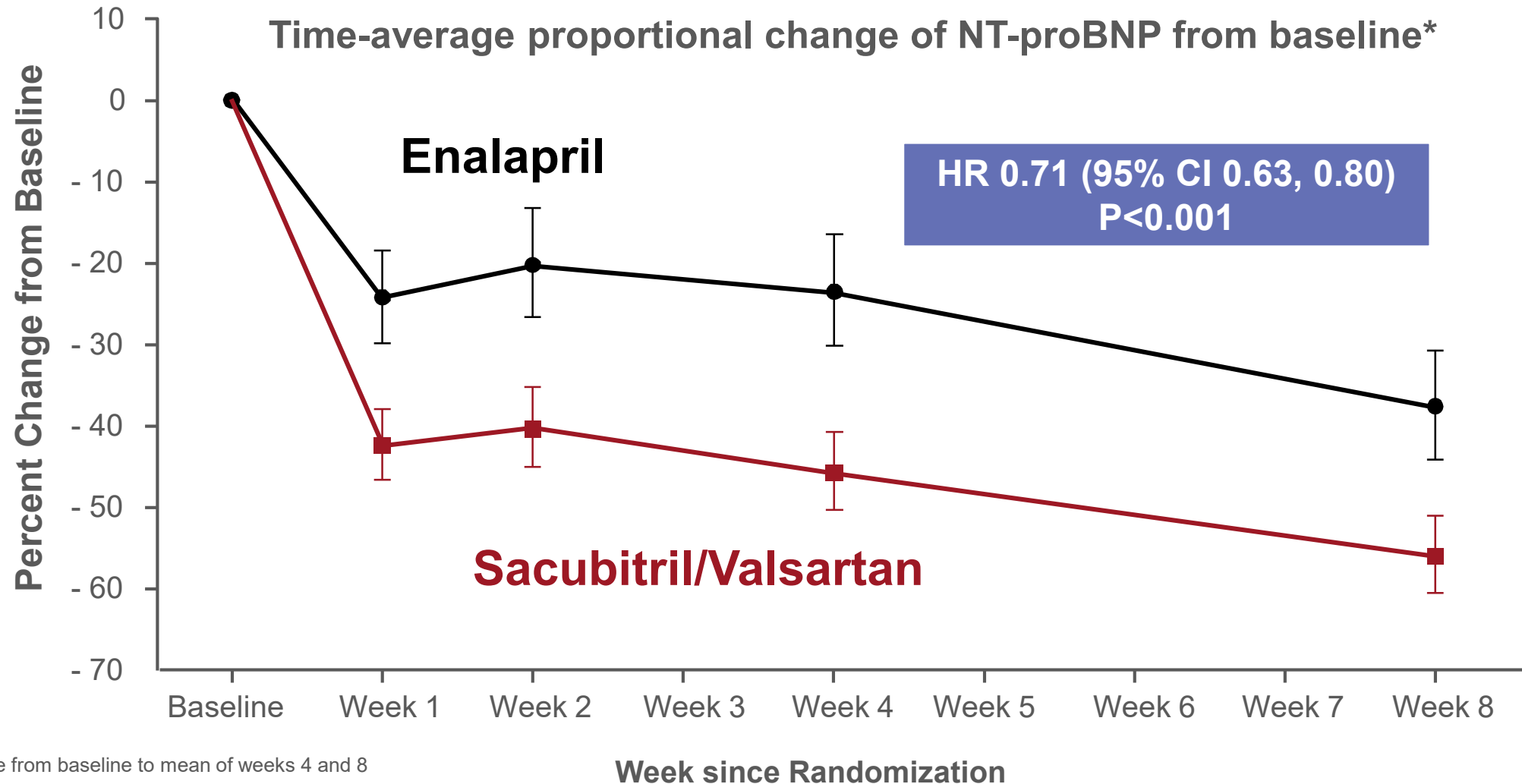
PIONEER-HF

Baseline Characteristics

| | Sacubitril/Valsartan (n=440) | Enalapril (n=441) |
|--|---------------------------------|----------------------|
| Age (years) | 61 (50.5, 71) | 63 (54, 72) |
| Women (%) | 25.7 | 30.2 |
| Black (%) | 35.9 | 35.8 |
| Prior HF diagnosis (%) | 67.7 | 63.0 |
| LVEF, median (25th, 75th) | 0.24 (0.18, 0.30) | 0.25 (0.20, 0.30) |
| Systolic pressure, median (25th, 75th) mm Hg | 118 (110, 133) | 118 (109, 132) |
| NT-proBNP median (25th, 75th) pg/mL at randomization | 2883 (1610, 5403) | 2536 (1363, 4917) |
| ACEi/ARB therapy (%) | 47.3 | 48.5 |
| Beta-adrenergic blockers (%) | 59.6 | 59.6 |

PIONEER-HF

Primary Endpoint



*Percentage (%) change from baseline to mean of weeks 4 and 8

PIONEER-HF

Exploratory Clinical Endpoints

| Endpoint Nr. (%) | Sacubitril/ Valsartan (n=440) | Enalapril (n=441) | RR Sac/Val vs Enalapril (95% CI) |
|---|----------------------------------|----------------------|--|
| Composite of serious clinical events * | 41 (9.3) | 74 (16.8) | 0.54 (0.37 to 0.79) |
| Death | 10 (2.3) | 15 (3.4) | 0.66 (0.30 to 1.48) |
| Re-hospitalization for HF | 35 (8.0) | 61 (13.8) | 0.56 (0.37 to 0.84) |
| Requirement of LVAD | 1 (0.2) | 1 (0.2) | 0.99 (0.06 to 15.97) |
| Inclusion on list for heart transplantation | 0 | 0 | n/a |

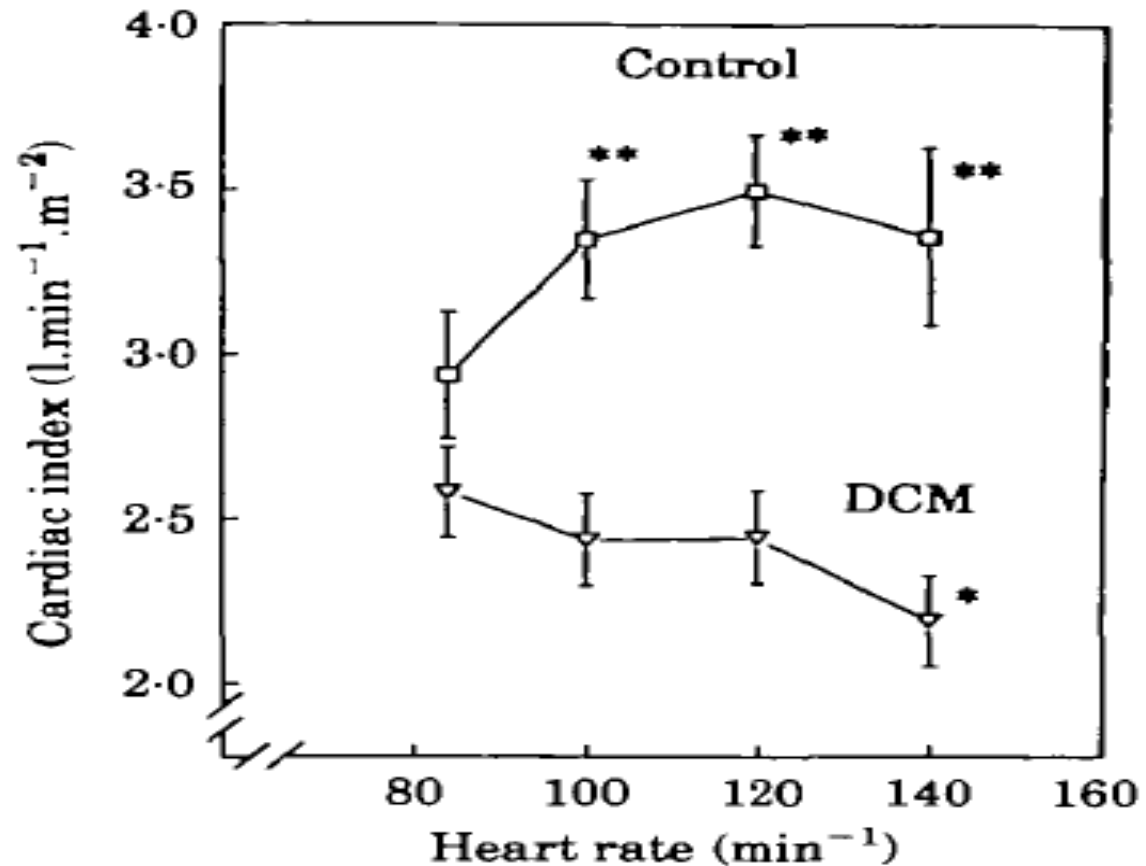
*Exploratory Serious Clinical Composite endpoint consisted of death, rehospitalization for heart failure, implantation of a left ventricular device, and inclusion on the list of patients eligible for heart transplantation

PIONEER-HF

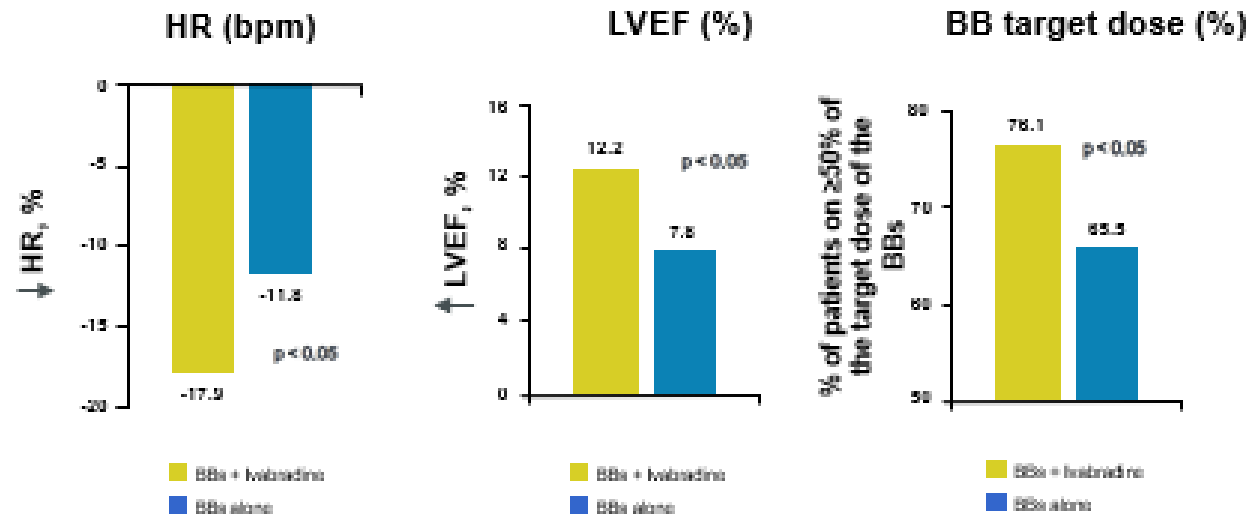
Study Limitations

- The study was powered for changes in NTproBNP and interpretation of secondary and exploratory endpoints should be viewed with caution
- Safety data were collected for only 12 weeks, therefore adverse events that take longer to transpire may not have appeared in this study. Safety information should be interpreted in the context of prior trials with longer duration
- In-hospital initiation included 2 placebo doses in the sacubitril/valsartan group and 6 hours of mandatory observation after the 3rd dose of study medication in both arms, which may have prolonged length of stay
- The 8 week double-blind study duration could limit the ability to fully assess long-term outcomes such as death, cardiac transplantation, and LVAD implantation

Effect of HR Upon Normal and Failing LV



Early Co-administration of Ivabradine and β -blockers During Hospitalization is Safe and May Improve HF Parameters (effects at 12 months)

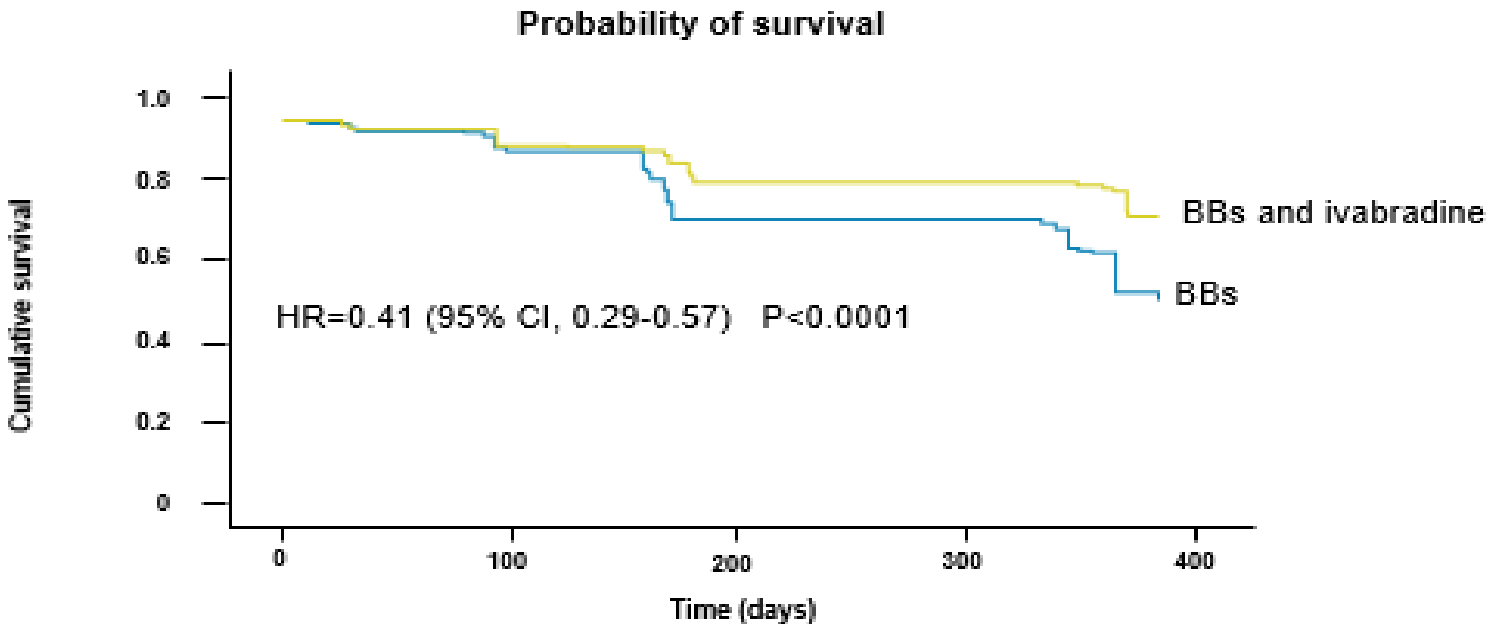


N=414 patients hospitalized due to worsening HF who were in sinus rhythm, NYHA Class II-IV, and LVEF <40%. Physicians were free to choose the strategy of co-administration of BBs and ivabradine (37.2%) or with BBs alone (62.8%).

Lopatin et al. *AHA* 2017 (Abstract 12310).

Early co-administration of ivabradine and β -blockers During Hospitalization May Reduce Mortality

A retrospective analysis on 370 hospitalized HF patients with heart rate ≥ 70 bpm (150 BB + ivabradine, 220 BB alone) in the Optimize Heart Failure Care Program from 8 countries (2015-2016)



Summary

- Heart failure has a high morbidity and mortality, with a high re-admission rate
- Medical therapy can reduce all of the above with **benefits achieved early on**
- Medical therapy is under-utilized
- There is a better way to approach these patients
- In well selected patients, can initiate therapy and titration in hospital

Question and Answer



Best Practices and Practical Tips for Optimizing HF Patient Care in Hospital

Mark Liskowski

MD, FRCPC



Conflict of Interest

Mark Liszkowski, MD, FRCPC

- **Consulting Fees/Honoraria:** Servier, Bayer, Novartis, CardiacAssist, Abbott medical, Boehringer, Mallinckrodt, BMS, Otsuka.
- **Clinical Trials:** Bayer, Boehringer

Tips and tricks to optimize CHF patients

- What the guidelines say
- Heart failure hospitalization: time to act!
- In-hospital medical optimization
- In-hospital risk identification
 - CVP, optimal medical therapy, HR, ntBNP
- Post-discharge early surveillance and follow up

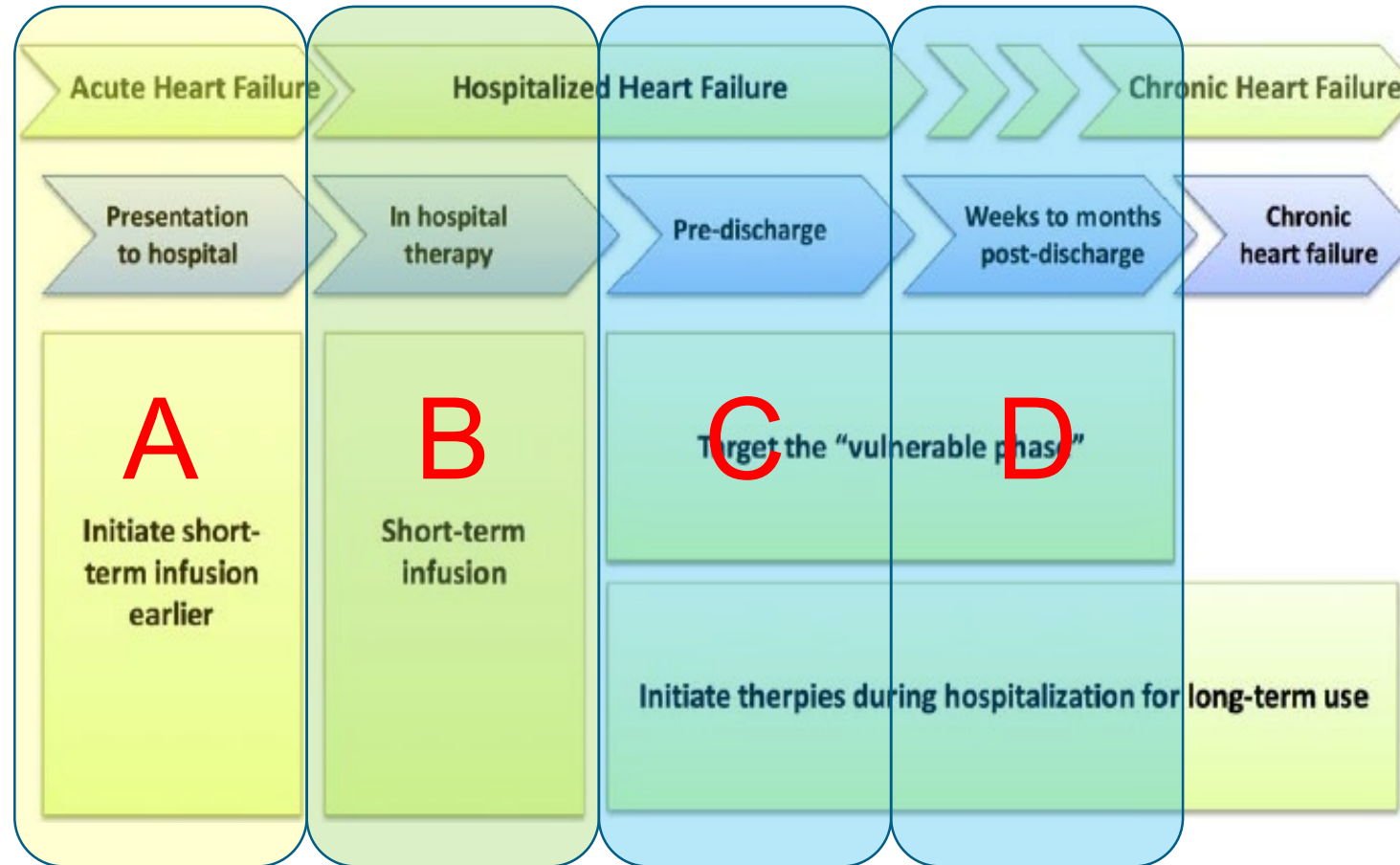
Reality of treating heart failure in hospital

- 1- Older frail patients
- 2- Multiples co-morbidities
- 3- Acute renal failure
- 4- **Hypotension**
- 5- Complex polypharmacy
- 6- **Often maximally treated CHF patients**
- 6- Multiple possible precipitants of decompensation
 - Non-compliance to Rx or follow-up
 - Rx stopped by other healthcare professionals
 - ER visit or off-service hospitalization
 - Septic precipitants

CHF medications
not-tolerated
not started
decreased
Stopped
Cannot be increased

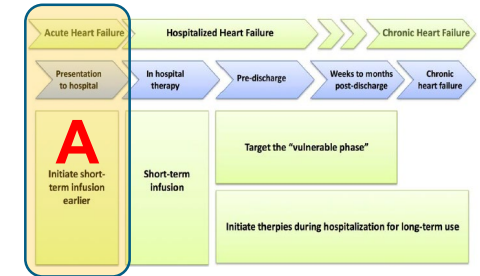
-Not your standard CHF trial patient
-May explain why some patients not on Full/maximal CHF triple therapy

CHF hospitalization is the time to act!



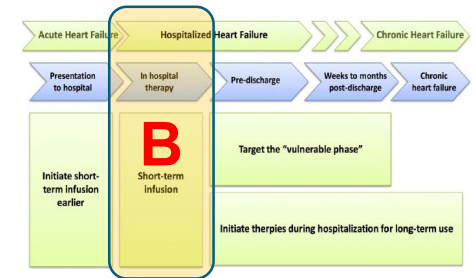
A- Treat CHF

- **First phase** (acute hypervolemia and neuro-hormonal activation)
- **Hospitalize (10-15% mortality)**
 - Volume control (IV diuretics)
 - Vasodilatation
 - Inotropic support (rare)
 - Rhythm control (AF, AV block, VT, PVCs)
- Search for ischemia/valvular disease
- Myocardial dysfunction (review LVEF - <40%?)
- Search for precipitants
- Review complete list of medications
- Realize that current therapy might be ineffective!



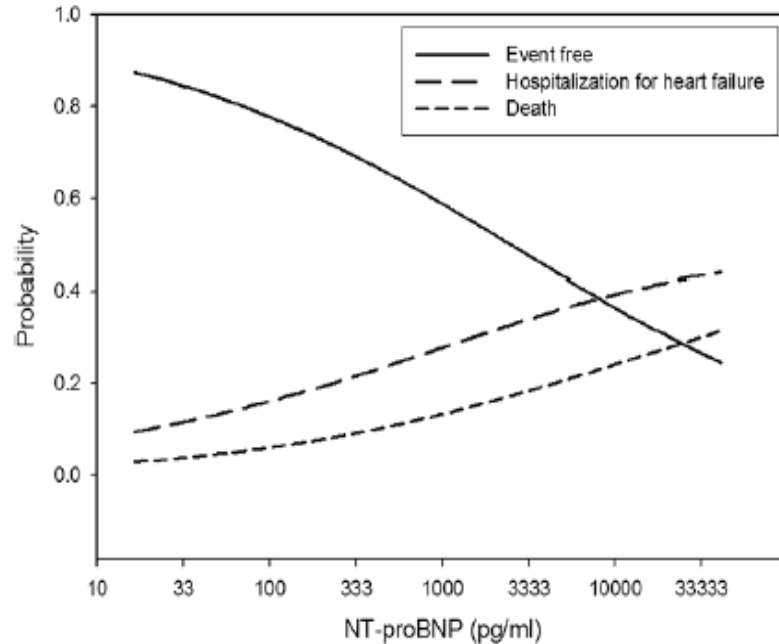
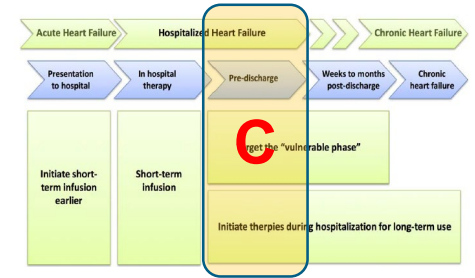
B- Stabilize CHF

- Identify and manage precipitants
 - Ischemia (revascularize)
 - Valvular heart disease (repair/replace)
 - Rhythm (rate or rhythm control)
 - Non-compliance (understand/teach)
 - Infection
 - Harmful medications (DPP4, glitazones, NSAIDS, steroids, alpha-blockers, CCB)
- Was current medical therapy adequate to improve prognosis?
 - **Triple therapy**? (BB, ACEi/ARB, and MRA)
 - **Quadruple therapy** (BB, Ivabradine, ACEi/ARB/ARNi, and MRA)
 - **Restart / Switch / Up titrate doses** with daily monitoring of vital signs and biochemistry



C- Optimize CHF therapy

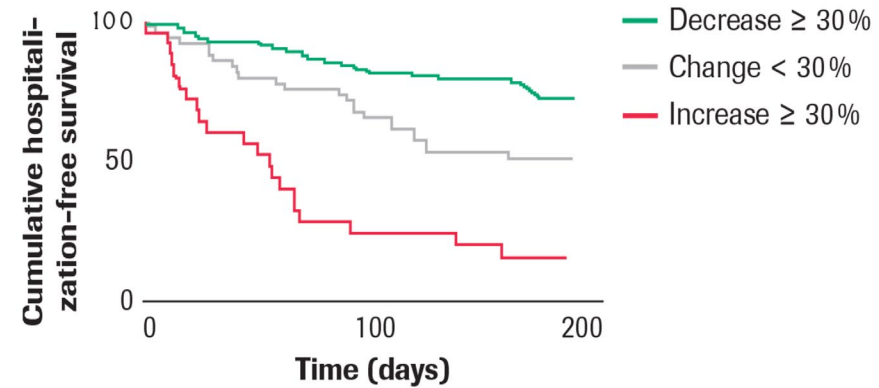
ntBNP as a modifiable predictor of outcome



Neth Heart J (2018) 26:486-492

N-Terminal-Pro-Brain Natriuretic Peptide Predicts Outcome After Hospital Discharge in Heart Failure Patients

Paulo Bettencourt, PhD; Ana Azevedo, MD; Joana Pimenta, MD; Fernando Friões, MD;

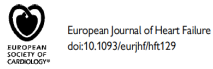
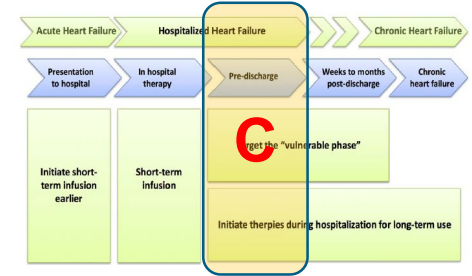


Cumulative hospitalization-free survival according to patterns of response of Roche NT-proBNP³

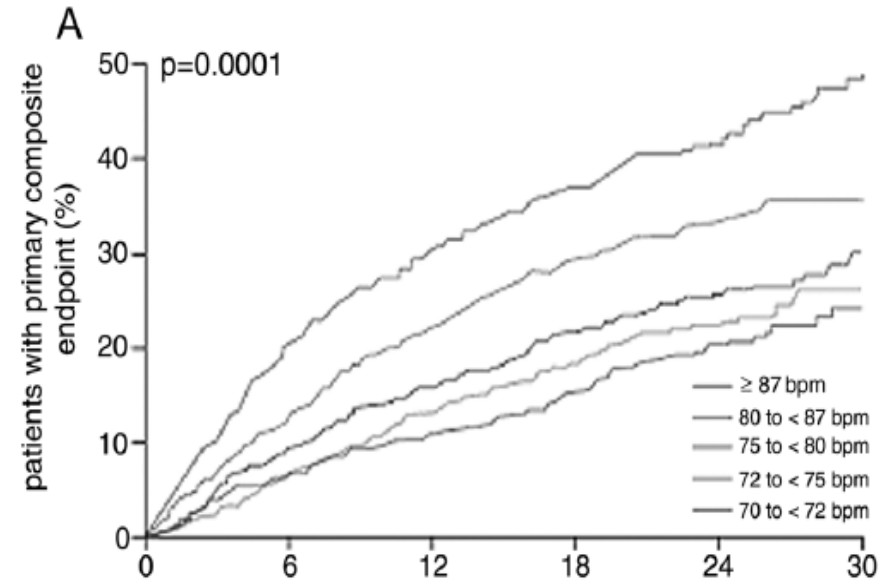
(Circulation. 2004;110:2168-2174

C- Optimize CHF therapy

Heart rate as a modifiable predictor of outcome

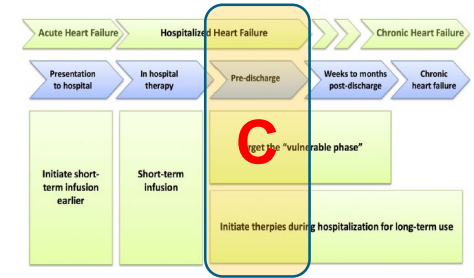


Heart rate: a prognostic factor and therapeutic target in chronic heart failure. The distinct roles of drugs with heart rate-lowering properties



| Number at risk | 0 | 6 | 12 | 18 | 24 | 30 |
|----------------|-----|-----|-----|-----|-----|-----|
| ≥ 87 bpm | 682 | 534 | 441 | 351 | 185 | 66 |
| 80 to < 87 bpm | 639 | 552 | 464 | 375 | 202 | 81 |
| 75 to < 80 bpm | 777 | 699 | 616 | 501 | 270 | 110 |
| 72 to < 75 bpm | 702 | 650 | 580 | 497 | 254 | 111 |
| 70 to < 72 bpm | 461 | 430 | 385 | 334 | 176 | 69 |

C- Optimize CHF therapy

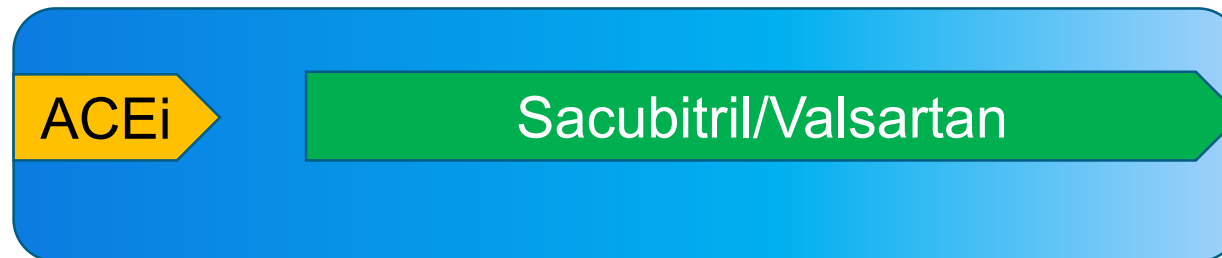


- How can I improve current CHF therapy?
- Switch/Add therapies proven to further reduce mortality and rehospitalizations
- 1- Monitor nt-BNP at admission and near discharge
- 2- Follow resting heart rate
- 3- Diabetes control
- **Switch** ACEi/ARB for Sacubitril/Valsartan (ARNI)
- **Add** Ivabradine to lower HR a goal of 50-60/min if >77/min
- Consider adding an SGLT2i to oral Db therapy

C- Optimize CHF Therapy

Sacubitril/Valsartan

- ADCHF: volume overload and neuro-hormonally activated state
- Hold ACEi x48h and restart ARNi at equivalent dose
- Stop ARB and immediately start ARNi at equivalent dose
- Do this while the patient is still congested
- Within 48-72 hours of stopping IV diuretics (before PO)

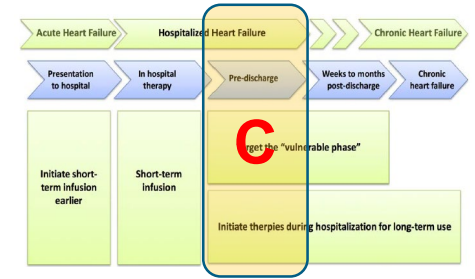


C- Optimize CHF Therapy

Heart rate: a marker of risk

- During ADCHF: **continue same Beta Blocker dose** unless hypotensive/in shock
- **Look at heart rate as prognostic indicator**
 - If already on maximal beta blocker dose
 - If not tolerating beta blocker dose (hypotension/low output)
 - Clinical profiles:
 - Hypotensive female
 - Symptomatic low cardiac output patient
 - Older patient needing reduction of dose due to excessive fatigue
- HR >77 beats/min
- **Add** starting dose of 2.5 mg po bid of Ivabradine atop beta blocker dose
- **Uptitrate** Ivabradine to 5 mg po bid then 7.5 mg po bid is needed
- **Combination therapy** to lower resting HR 60/min
- Goal to lower heart rate <70 beats/min at discharge

C- Optimize CHF therapy

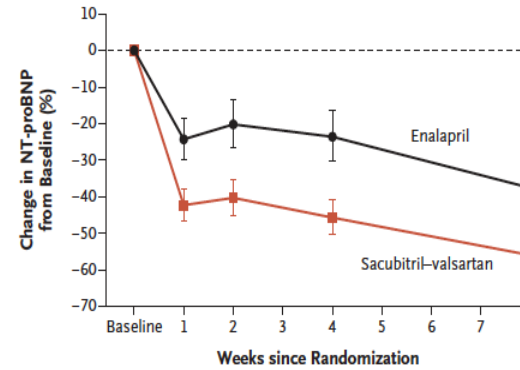


The NEW ENGLAND JOURNAL of MEDICINE

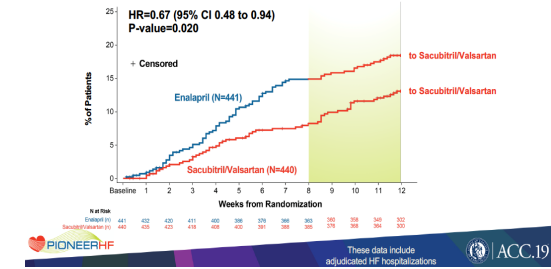
ORIGINAL ARTICLE

Angiotensin–Neprilysin Inhibition in Acute Decompensated Heart Failure

Eric J. Velazquez, M.D., David A. Morrow, M.D., M.P.H.,

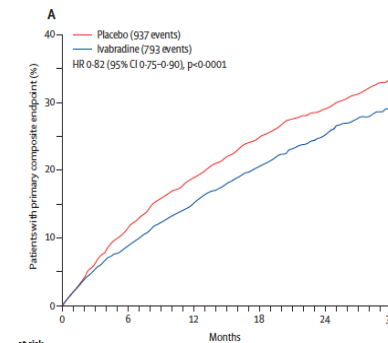
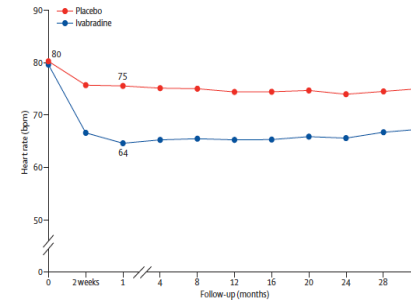


Death, HF Hospitalization, or LVAD Implantation



Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study

Karl Swedberg, Michel Komajda, Michael Böhm, Jeffrey S Borer, Ian Ford, Ariane Dubost-Brama, Guy Lerebours, Luigi Tavazzi, on behalf of the SHIFT Investigators*





C- Optimize CHF therapy

Management of diabetes in CHF



European Journal of Heart Failure (2018) 20, 853–872
doi:10.1002/ehf.1170

HFA POSITION STATEMENT

**Type 2 diabetes mellitus and heart failure:
a position statement from the Heart Failure
Association of the European Society of
Cardiology**

| Study | Antidiabetic drug | Comparator | Results |
|--------------------------------|-------------------|------------|---|
| DPP4 inhibitors | | | |
| SAVOR-TIMI 53 ^{16,17} | Saxagliptin | Placebo | Increase in HF hospitalization |
| EXAMINE ^{19,184} | Alogliptin | Placebo | No statistically significant increase in HF hospitalization |
| TECOS ^{18,185} | Sitagliptin | Placebo | No effect on HF hospitalization |
| GLP-1 receptor agonists | | | |
| ELIXA ²³ | Lixisenatide | Placebo | No effect on HF hospitalization |
| LEADER ²² | Liraglutide | Placebo | No effect on HF hospitalization |
| SUSTAIN-6 ¹⁸⁶ | Semaglutide | Placebo | No effect on HF hospitalization |
| EXSCEL ²⁴ | Exenatide | Placebo | No effect on HF hospitalization |
| SGLT2 inhibitors | | | |
| EMPA-REG OUTCOME ²⁰ | Empagliflozin | Placebo | Reduced HF hospitalization |
| CANVAS ²¹ | Canagliflozin | Placebo | Reduced HF hospitalization |
| Declare TIMI 58 | Dapagliflozin | Placebo | Reduced HF Hospit |

Thiazolidinediones (glitazones) – contra-indicated in CHF

C- Optimize CHF therapy

complete care with a checklist

Implementation of a mandatory checklist of protocols and objectives improves compliance with a wide range of evidence-based intensive care unit practices

Matthew C. Byrnes, MD; Douglas J. E. Schuerer, MD; Marilyn E. Schallom, MSN; Carrie S. Sona, MSN;
(Crit Care Med 2009; 37:2775-2781)

International Journal for Quality in Health Care 2008; Volume 20, Number 1: pp. 22-30
Advance Access Publication: 11 December 2007

Development of medical checklists for improved quality of patient care

BRIGETTE HALES¹, MARIUS TERBLANCHE², ROBERT FOWLER¹ AND WILLIAM SIBBALD¹

- Baseline discharge parameters
- Teaching
- Reminder for full medical therapy
- Standardized approach

Pre- and post-hospital discharge checklist

| | | | |
|-----------------|--|--|--|
| Patient's name: | <input type="text"/> | Gender: <input type="checkbox"/> Male <input type="checkbox"/> Female | Age: <input type="text"/> / <input type="text"/> / <input type="text"/> |
| | PRE-DISCHARGE VISIT | EARLY POST-DISCHARGE VISIT 1 | EARLY POST-DISCHARGE VISIT 2 |
| | Hospital specialist: | Doctor/Nurse: | Doctor/Nurse: |
| | Date of discharge: <input type="text"/> / <input type="text"/> / 20 <input type="text"/> | Date of visit: <input type="text"/> / <input type="text"/> / 20 <input type="text"/> | Date of visit: <input type="text"/> / <input type="text"/> / 20 <input type="text"/> |

CLINICAL ASSESSMENT

| | PRE-DISCHARGE VISIT | EARLY POST-DISCHARGE VISIT 1 | EARLY POST-DISCHARGE VISIT 2 |
|---|---|---|---|
| Weight | <input type="text"/> kg | <input type="text"/> kg | <input type="text"/> kg |
| Resting heart rate | <input type="text"/> bpm Rhythm: <input type="checkbox"/> sinus <input type="checkbox"/> atrial fibrillation <input type="checkbox"/> not available | <input type="text"/> bpm Rhythm: <input type="checkbox"/> sinus <input type="checkbox"/> atrial fibrillation <input type="checkbox"/> not available | <input type="text"/> bpm Rhythm: <input type="checkbox"/> sinus <input type="checkbox"/> atrial fibrillation <input type="checkbox"/> not available |
| Blood pressure | Systolic/diastolic: <input type="text"/> / <input type="text"/> mm Hg | Systolic/diastolic: <input type="text"/> / <input type="text"/> mm Hg | Systolic/diastolic: <input type="text"/> / <input type="text"/> mm Hg |
| Clinical symptoms of volume overload | <input type="checkbox"/> Signs of congestions: pulmonary rales, jugular venous congestion, hepatomegaly, peripheral edema <input type="checkbox"/> Breathlessness <input type="checkbox"/> Orthopnea | <input type="checkbox"/> Signs of congestions: pulmonary rales, jugular venous congestion, hepatomegaly, peripheral edema <input type="checkbox"/> Breathlessness <input type="checkbox"/> Orthopnea | <input type="checkbox"/> Signs of congestions: pulmonary rales, jugular venous congestion, hepatomegaly, peripheral edema <input type="checkbox"/> Breathlessness <input type="checkbox"/> Orthopnea |
| NYHA class | <input type="checkbox"/> Class I <input type="checkbox"/> Class II <input type="checkbox"/> Class III <input type="checkbox"/> Class IV | <input type="checkbox"/> Class I <input type="checkbox"/> Class II <input type="checkbox"/> Class III <input type="checkbox"/> Class IV | <input type="checkbox"/> Class I <input type="checkbox"/> Class II <input type="checkbox"/> Class III <input type="checkbox"/> Class IV |
| Other measurements | LV ejection fraction <input type="text"/> % Serum creatinine <input type="text"/> Potassium <input type="text"/> mmol/L | LV ejection fraction <input type="text"/> % Serum creatinine <input type="text"/> Potassium <input type="text"/> mmol/L | LV ejection fraction <input type="text"/> % Serum creatinine <input type="text"/> Potassium <input type="text"/> mmol/L |

C- Optimize CHF therapy

complete care with a checklist

Implementation of a mandatory checklist of protocols and objectives improves compliance with a wide range of evidence-based intensive care unit practices

Matthew C. Byrnes, MD; Douglas J. E. Schuerer, MD; Marilyn E. Schallom, MSN; Carrie S. Sona, MSN;
(Crit Care Med 2009; 37:2775–2781)

International Journal for Quality in Health Care 2008; Volume 20, Number 1: pp. 22–30
Advance Access Publication: 11 December 2007

Development of medical checklists for improved quality of patient care

BRIGETTE HALES¹, MARIUS TERBLANCHE², ROBERT FOWLER¹ AND WILLIAM SIBBALD¹

- Baseline discharge parameters
- Teaching
- Reminder for full medical therapy
- Standardized approach

Pre- and post-hospital discharge checklist

PATIENT EDUCATION

| | | | |
|--------------------------------|--|--|--|
| Nonpharmacological measurement | <input type="checkbox"/> Diet <input type="checkbox"/> Exercise <input type="checkbox"/> Weight monitoring <input type="checkbox"/> Detection of worsening symptoms | <input type="checkbox"/> Diet <input type="checkbox"/> Exercise <input type="checkbox"/> Weight monitoring <input type="checkbox"/> Detection of worsening symptoms | <input type="checkbox"/> Diet <input type="checkbox"/> Exercise <input type="checkbox"/> Weight monitoring <input type="checkbox"/> Detection of worsening symptoms |
|--------------------------------|--|--|--|

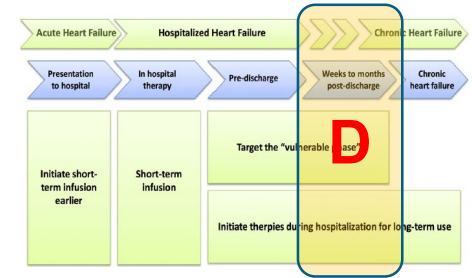
OPTIMIZATION OF MEDICAL THERAPY

| | | | |
|---------------|--|--|--|
| ACEIs or ARBs | <input type="checkbox"/> Prescribed <input type="checkbox"/> Not prescribed (CI or intolerance) <input type="checkbox"/> Not prescribed (patient refused) | <input type="checkbox"/> Prescribed <input type="checkbox"/> Not prescribed (CI or intolerance) <input type="checkbox"/> Not prescribed (patient refused) | <input type="checkbox"/> Prescribed <input type="checkbox"/> Not prescribed (CI or intolerance) <input type="checkbox"/> Not prescribed (patient refused) |
| Beta-blockers | <input type="checkbox"/> Prescribed <input type="checkbox"/> Not prescribed (CI or intolerance) <input type="checkbox"/> Not prescribed (patient refused) | <input type="checkbox"/> Prescribed <input type="checkbox"/> Not prescribed (CI or intolerance) <input type="checkbox"/> Not prescribed (patient refused) | <input type="checkbox"/> Prescribed <input type="checkbox"/> Not prescribed (CI or intolerance) <input type="checkbox"/> Not prescribed (patient refused) |
| MRAs | <input type="checkbox"/> Prescribed <input type="checkbox"/> Not prescribed (CI or intolerance) <input type="checkbox"/> Not prescribed (not indicated) <input type="checkbox"/> Not prescribed (patient refused) | <input type="checkbox"/> Prescribed <input type="checkbox"/> Not prescribed (CI or intolerance) <input type="checkbox"/> Not prescribed (not indicated) <input type="checkbox"/> Not prescribed (patient refused) | <input type="checkbox"/> Prescribed <input type="checkbox"/> Not prescribed (CI or intolerance) <input type="checkbox"/> Not prescribed (not indicated) <input type="checkbox"/> Not prescribed (patient refused) |
| Ivabradine | <input type="checkbox"/> Prescribed <input type="checkbox"/> Not prescribed (CI or intolerance) <input type="checkbox"/> Not prescribed (not indicated) <input type="checkbox"/> Not prescribed (patient refused) | <input type="checkbox"/> Prescribed <input type="checkbox"/> Not prescribed (CI or intolerance) <input type="checkbox"/> Not prescribed (not indicated) <input type="checkbox"/> Not prescribed (patient refused) | <input type="checkbox"/> Prescribed <input type="checkbox"/> Not prescribed (CI or intolerance) <input type="checkbox"/> Not prescribed (not indicated) <input type="checkbox"/> Not prescribed (patient refused) |

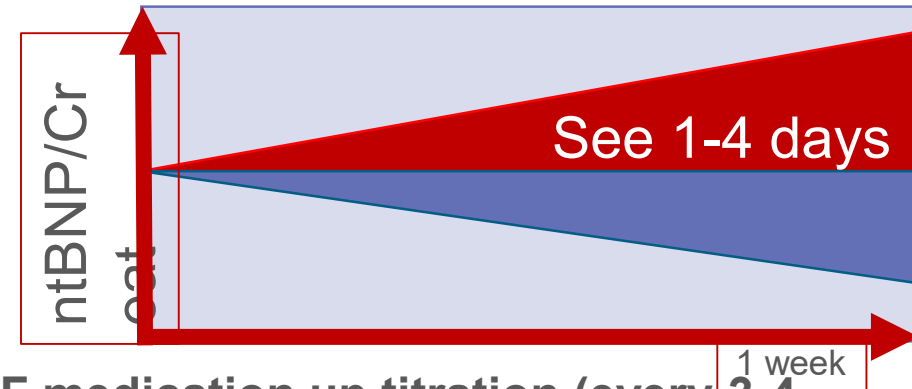
PLANNING OF VISITS

| | | |
|--|--|--|
| Date of next follow-up visit: <input type="text"/> / <input type="text"/> / 20 <input type="text"/> | Date of next follow-up visit: <input type="text"/> / <input type="text"/> / 20 <input type="text"/> | Date of next follow-up visit: <input type="text"/> / <input type="text"/> / 20 <input type="text"/> |
|--|--|--|

D- Predict and prevent



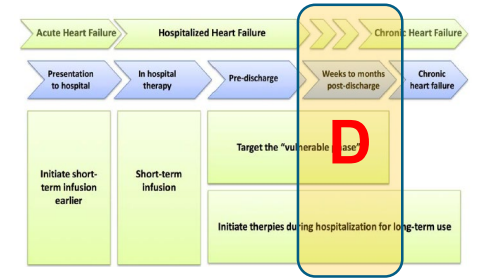
- How to identify and follow up the vulnerable population after discharge?
- 1- Biomarkers of risk at discharge (ntBNP, CVP, HR)
- 2- Biomarkers of risk at 1 week post-discharge
 - If **nt BNP** and/**creatinine** increase → needs **FASTER** follow up
- 3- Patient self surveillance
 - Document daily symptoms/weight/HR
- 3- Outpatient rapid follow up → 2-4 weeks
 - CHF clinic
 - Nurse led rapid reassessment clinic
- 4- Pharmacist or nurse driven protocolized CHF medication up titration (every 3-4 wks)
 - tends to be faster and more complete than if MD driven
- 5- Refer to CHF specialist if needed or if not improving with standard therapy



D- Predict and prevent

What do patients want?

- Improved symptoms
- Fewer pills
- Fewer hospitalizations
- Do not want to die/suffer
- Contact person in case of questions or concerns



Take home points

- In-hospital CHF optimization is practical
- Assure at least standard triple CHF therapy is started (BB, ACEi/ARB and MRA)
- If worsening CHF on standard therapy
 - Identify precipitants
 - **Consider ADCHF as a failure of current therapy**
 - Switch/add more aggressive evidence based therapy
 - Sacubitril/Valsartan
 - Ivabradine
 - SGLT2i

Take home points

- Identify vulnerable patients that you can improve
 - **ntBNP remains elevated** (less than 30% decrease from admission)
 - **Remains with HR >77/min** in spite of maximally tolerated BB
 - **Sub-optimal Db control**
- Required clinical follow-up within 2-4 weeks post-discharge
- Faster follow-up if ntBNP and/or creatinine increase within 7 days post-discharge

Question and Answer



Closing Remarks and Evaluations

Serge Lepage
MD, FRCPC, CSPQ



Question #1

Heart Failure Management in Canada

Compared to other countries...

- a. Canada is a leader in acute decompensated heart failure (ADHF) = 15%
- b. Canada is in the middle of the pack for management of ADHF = 75%
- c. Canada is doing poorly in ADHF management = 10%

Question #2:

The US Has Established a Policy to Decrease 30 Day Readmission

They have in fact

- a. Decreased 30 day readmission = 45%
- b. Increased 30 day readmission = 16%
- c. Increased 30 day death = 25%
- d. Reduced 30 day death = 14%

Question #3: Regarding In-hospital Stay...

- a. All our interventions are evidence-based medicine (EBM) = 4%
- b. Our efforts are aimed at relieving symptoms = 16%
- c. As long as the patient is not in acute kidney injury (AKI) = 2%
- d. We all should do better = 78%



**HEART
FAILURE
IN 2019**

**WHAT DO WE KNOW?
WHERE CAN WE GO?**

