ACC Middle East Conference 2018

In partnership with:

جمعية القلب السعودية
Saudi Heart Association

A NEW CLASS OF HEART FAILURE THERAPY- LESSONS LEARNED

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Heart Failure Therapy in 1950's

- Digitalis
- Diuretics (NH_4Cl, Organic Mercurials)
- Strict bed rest, sedation, O_2
- Low calorie, low Na diet (200-400 mg/day)

Harrison TR. HPIM 1st ed., 1950 (Courtesy: Eugene Braunwald)

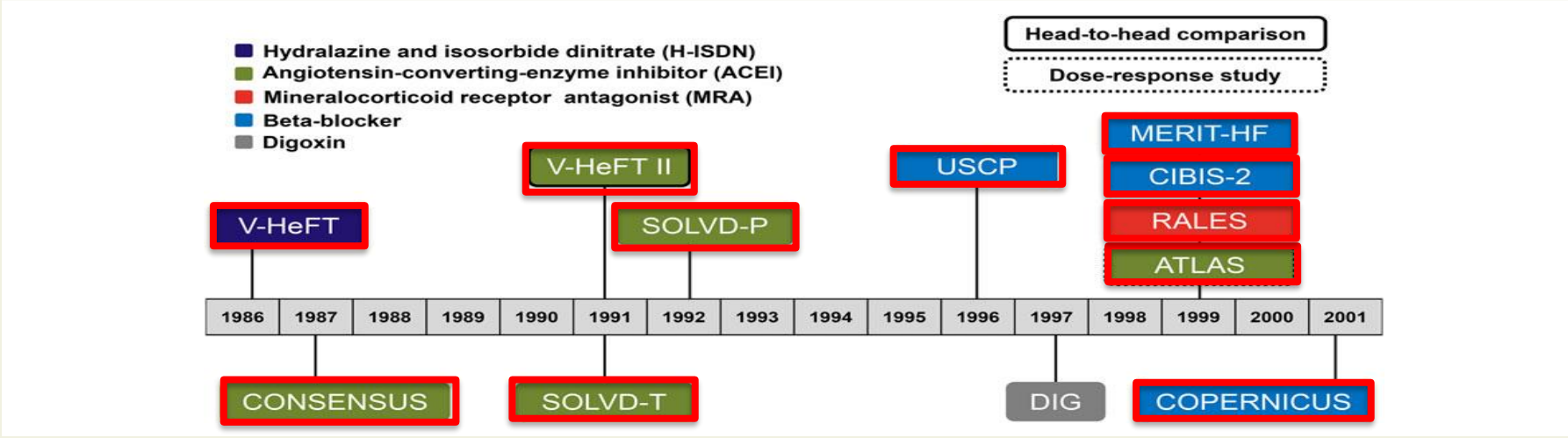


Figure 1 Heart failure-reduced ejection fraction: thirty years of progress - positivedrug trials 1986–2001.

McMurray J. European Heart Journal (2015) 36, 3467–3470

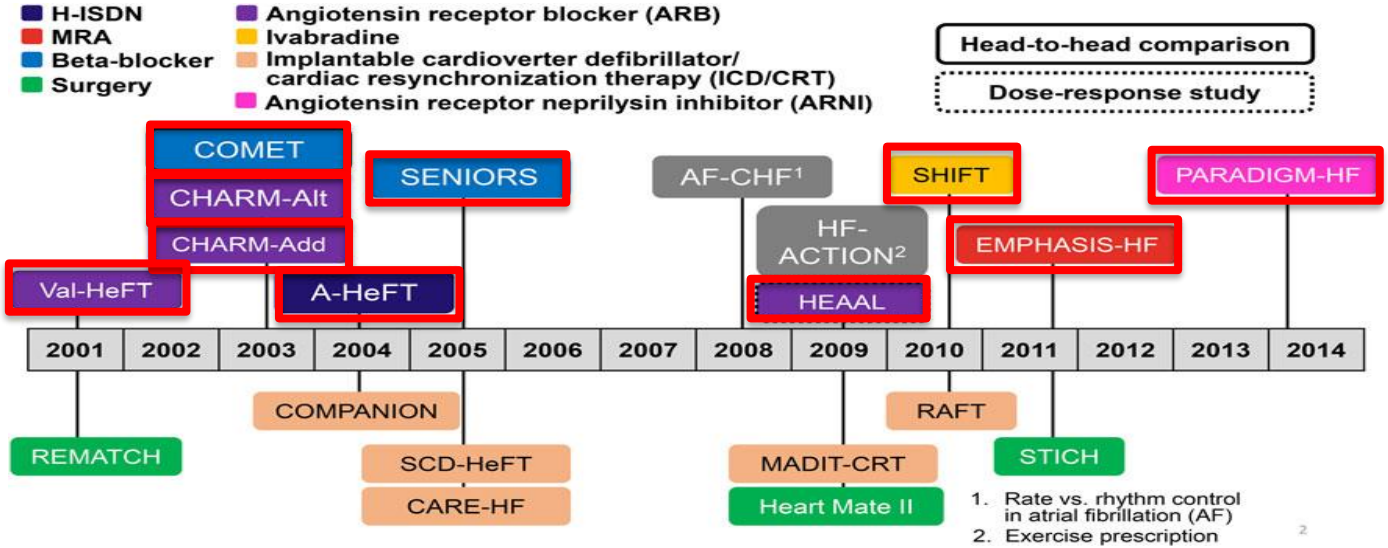


Figure 2 Heart failure-reduced ejection fraction: thirty years of progress - positive drug, device and other trials 2001–2014.

McMurray J. European Heart Journal (2015) 36, 3467–3470

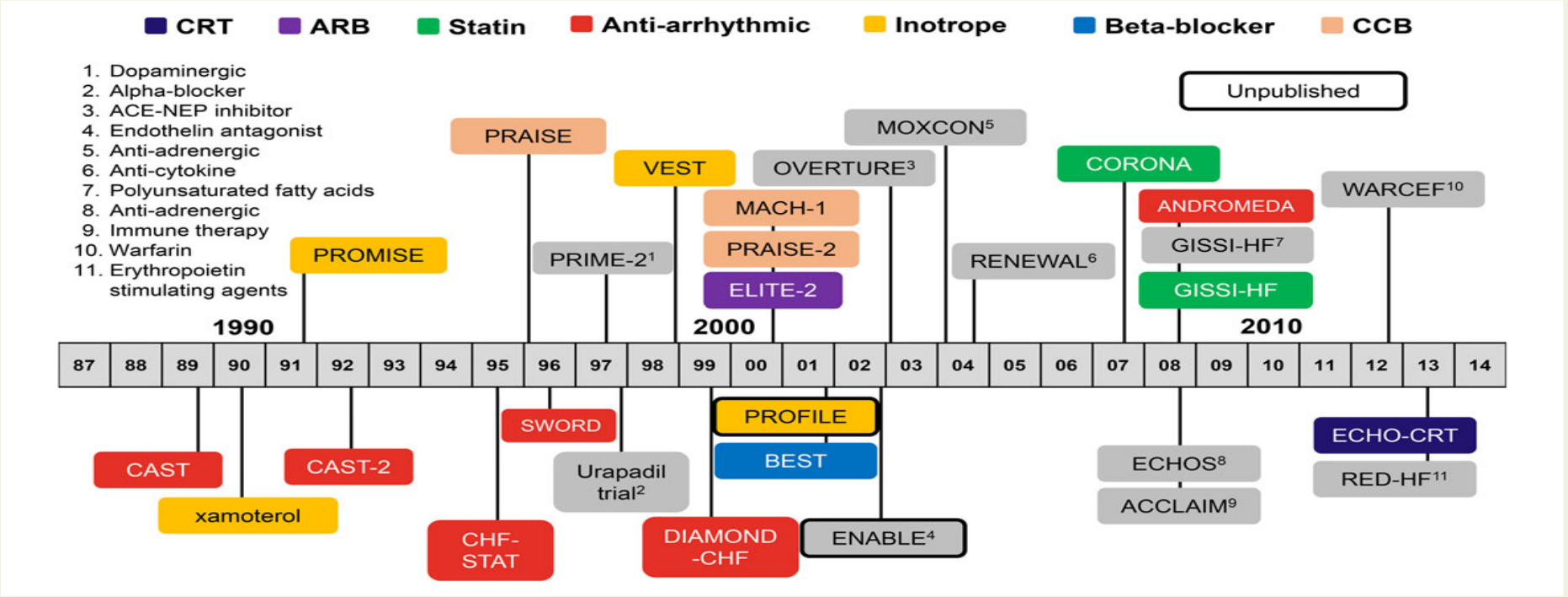


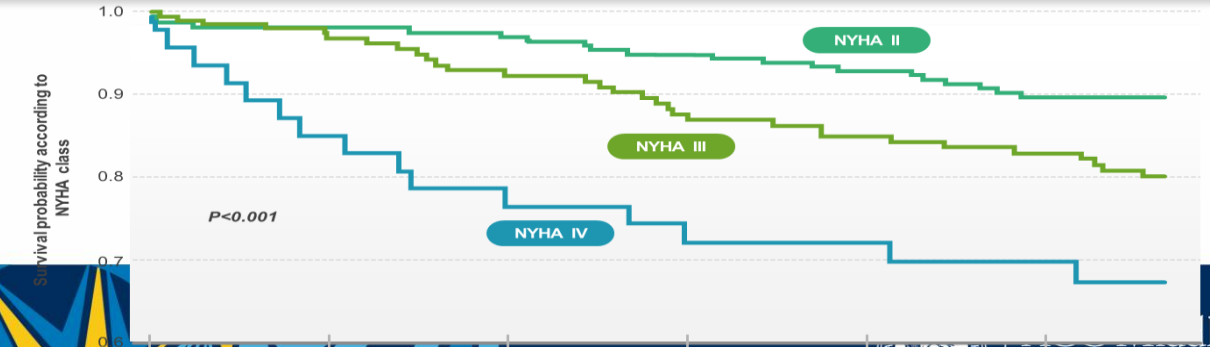
Figure 3 Heart failure trials: the disappointments: 1987–2013.

McMurray J. European Heart Journal (2015) 36, 3467–3470

ACCF/AHA Stage of HF and NYHA Functional Classification

	ACC/AHA stage of HF		NYHA classification
A	High HF risk No structural heart disease or HF symptom	N/A	
B	Structural heart disease No signs or HF symptoms	I	No symptoms related to heart disease
C	Structural heart disease Prior or current HF symptoms	I	No symptoms related to heart disease
		II	Mild symptoms
D	Refractory HF requiring specialized intervention	III	Moderate symptoms
		IV	Severe symptoms

NYHA functional classes are linked to outcome



NYHA: New York Heart Association. Adapted from Muntwyler et al. Eur Heart J 2002;23:1861–6.

Why is the NYHA class limited?

- It is subjective! *The more information you obtain, the more precise it will be.*
- It is momentary! *Patients have variable NYHA classes depending on their state of compensation. Labeling someone as a specific NYHA means that most of the time is lived in it.*
- It is collective! *Patients under one class can have many profiles of physical exam, laboratory, imaging, and hemodynamic findings.*

Therefore, it is critical that more parameters are used to verify, confirm, or perhaps revise our NYHA designation.

In Cleveland Clinic Abu Dhabi, For the First 400 Patients:

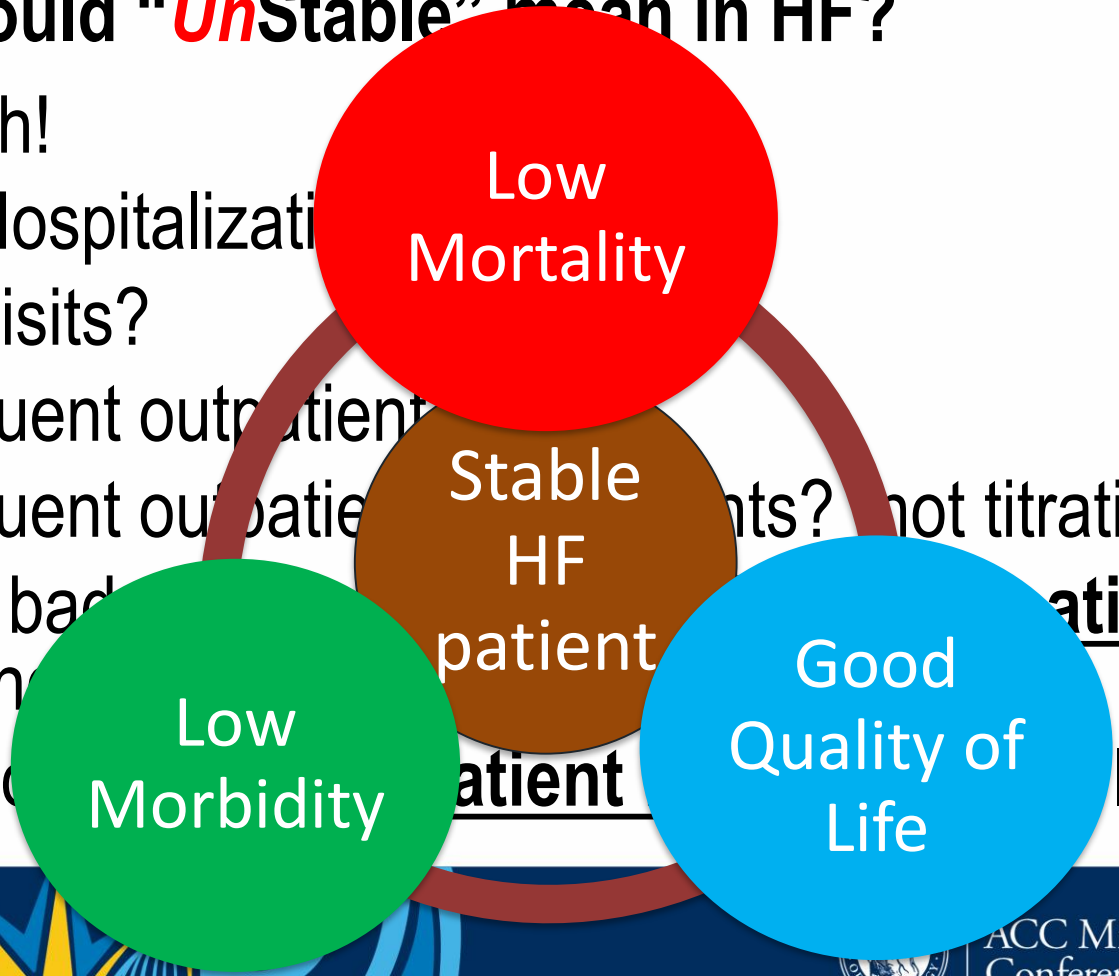
- NYHA I: 10%
- NYHA II: 57.5%
- NYHA III: 30%
- NYHA IV: 2.5%

In Cleveland Clinic Ohio, for almost 10,000 patients:

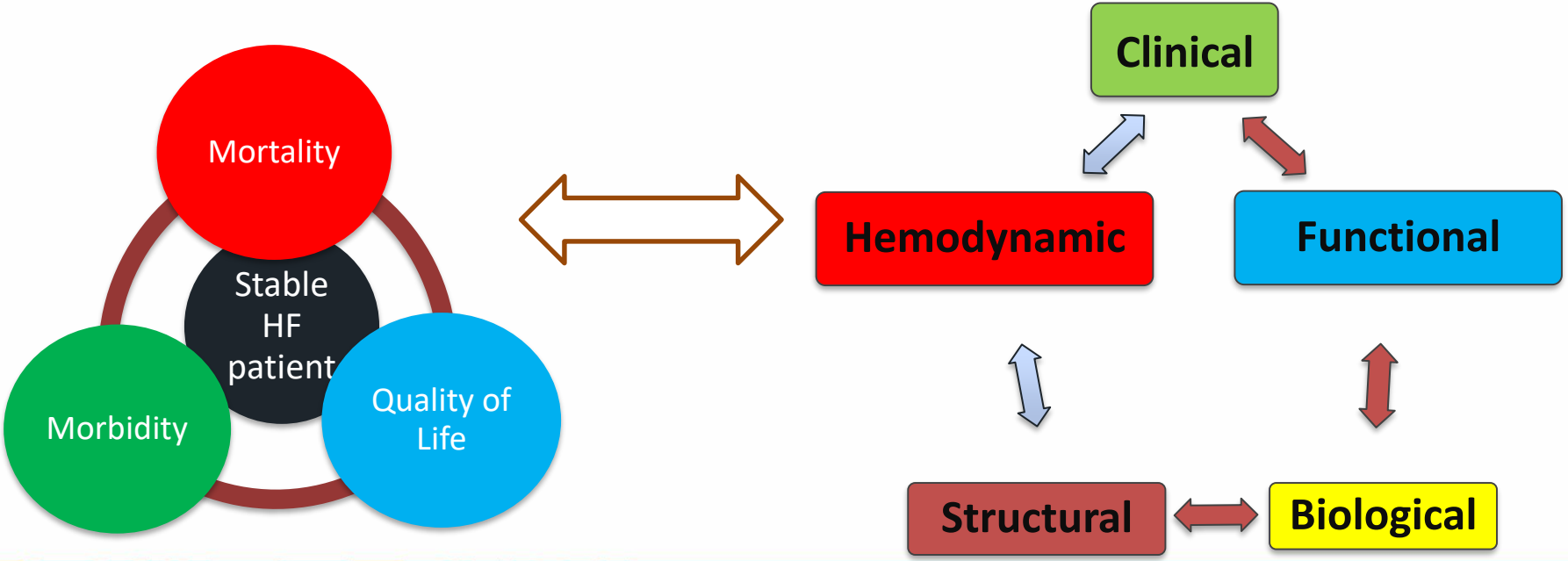
- NYHA I: 10%
- NYHA II:
- NYHA III: } 75%
- NYHA IV: 15%

What should "*Un*Stable" mean in HF?

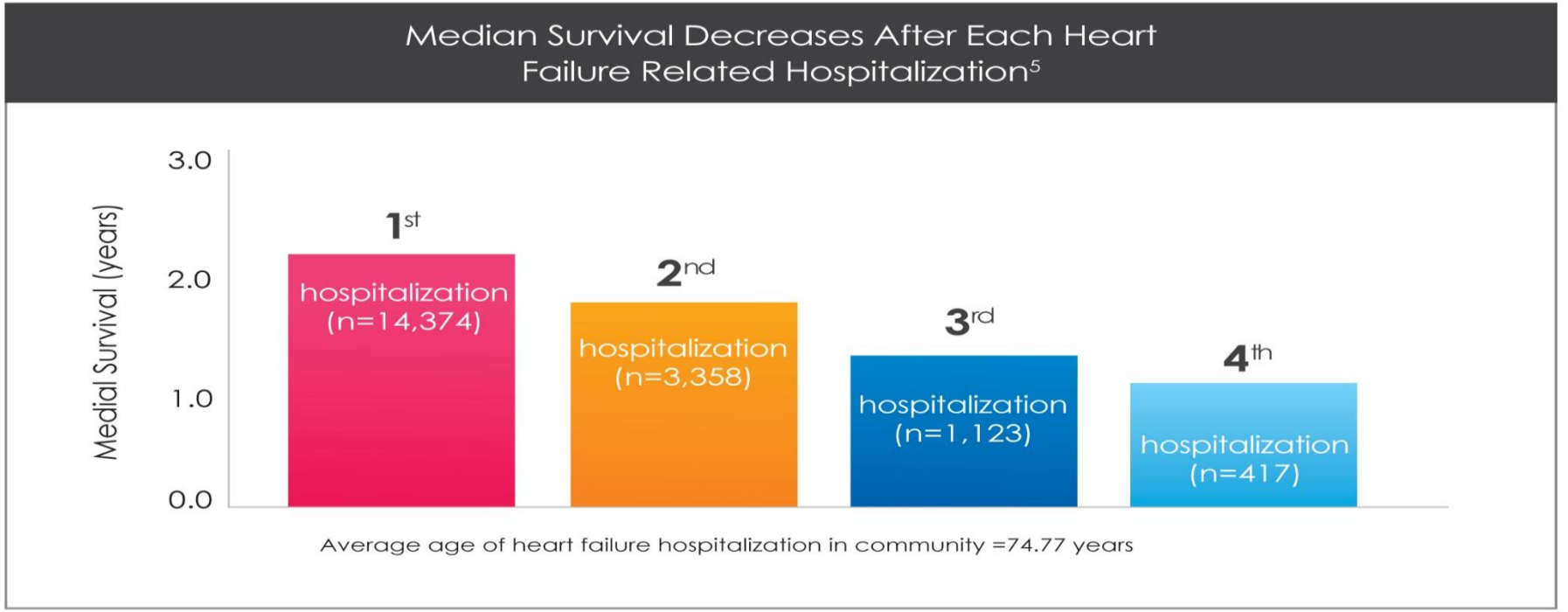
- Death!
- HF Hospitalizati
- ED visits?
- Frequent outp tient
- Frequent ou batie nts? not titrations).
- How bad atient (abun
- Or, h atient life).



How do we evaluate "*stability*"?
How do we predict "*instability*"?



Hospitalizations



[5] Miller L, Guglin M. Patient selection for ventricular assist devices: A moving target. J Am Coll Cardiol. 2013;61:1209-21.

So hospitalizations are bad, but it is certainly not the end of the story, especially in an era where everyone wants to reduce the burden of hospitalizations.

Association of the Hospital Readmissions Reduction Program Implementation With Readmission and Mortality Outcomes in Heart Failure

Ankur Gupta, MD, PhD; Larry A. Allen, MD, MHS; Deepak L. Bhatt, MD, MPH; Margueritte Cox, MS, MGIST; Adam D. DeVore, MD, MHS; Paul A. Heidenreich, MD, MS; Adrian F. Hernandez, MD, MHS; Eric D. Peterson, MD, MPH; Roland A. Matsouaka, PhD; Clyde W. Yancy, MD, MSc; Gregg C. Fonarow, MD

- *This is an analysis of 115,245 Medicare patients comparing those admitted with HF before the HRRP (2006-2010) and after the penalty phase (2012-2014); at 416 US hospitals enrolled in the "Get with the Guidelines HF Registry.*
- *It examined the association between the HRRP and outcomes (readmissions and mortality) at 30 days and 1 year.*

JAMA Cardiol. 2018;3(1):44-53.

Table 3. Hazards of Risk-Adjusted Readmissions and Mortality by the Hospital Readmissions Reduction Program Periods[a]

Outcome	Pre-HRRP Implementation Phase	HRRP Implementation Phase (95% CI)	*P* Value[b]	HRRP Penalties Phase (95% CI)	*P* Value[c]
30 d					
Readmissions, HR	1 [Reference]	1.00 (0.95-1.06)	.88	0.91 (0.87-0.95)	<.001
Mortality, HR	1 [Reference]	1.15 (1.08-1.24)	<.001	1.18 (1.10-1.27)	<.001
1 y					
Readmissions, HR	1 [Reference]	1.01 (0.98-1.05)	.45	0.92 (0.89-0.96)	<.001
Mortality, HR	1 [Reference]	1.10 (1.07-1.14)	<.001	1.10 (1.06-1.14)	<.001

- The 30-day risk-adjusted readmission rate declined from 20.0% before the HRRP implementation to 18.4%in the HRRP penalties phase (p<0.001)
- The 30-day risk-adjusted mortality rate increased from 7.2%before the HRRP implementation to 8.6%in the HRRP penalties phase (p<0.001)
- The 1-year risk-adjusted readmission rate declined from 57.2%to 56.3% (p<0.001)
- The 1-year risk-adjusted mortality rate increased from 31.3%to 36.3% (p<0.001)

A Few Lessons from PARADIGM-HF

- When stratified by previous hospitalizations (< 3months, 3-6 months, 6-12 months, >12 months, never); more recently hospitalized patients had a higher risk.

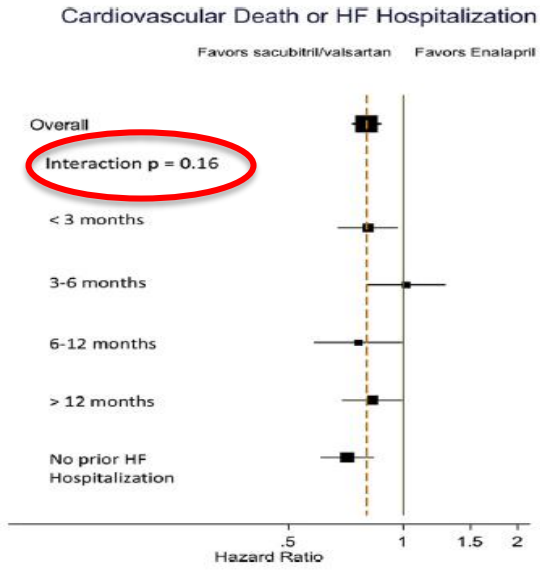
- In the most "stable" patients "without prior HF hospitalization", 20% experienced a primary endpoint of CV death or heart failure (HF) hospitalization, and 17% died during the trial. About 30% of those were SCD.

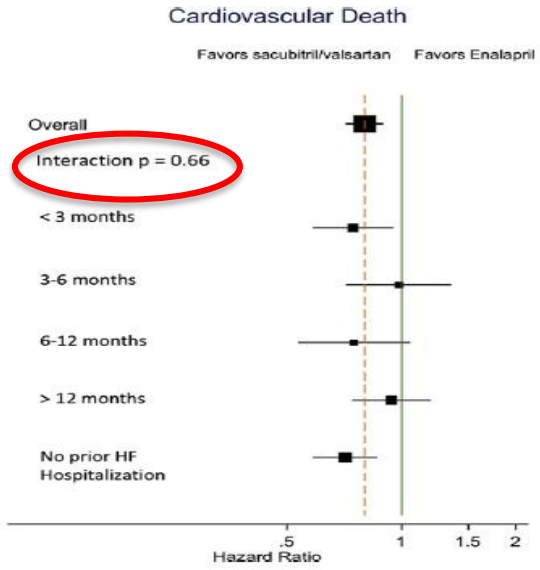
- In the least "stable" patients "hospitalization within 3 months", 29% experienced a primary end point, and 19% died during the trial.

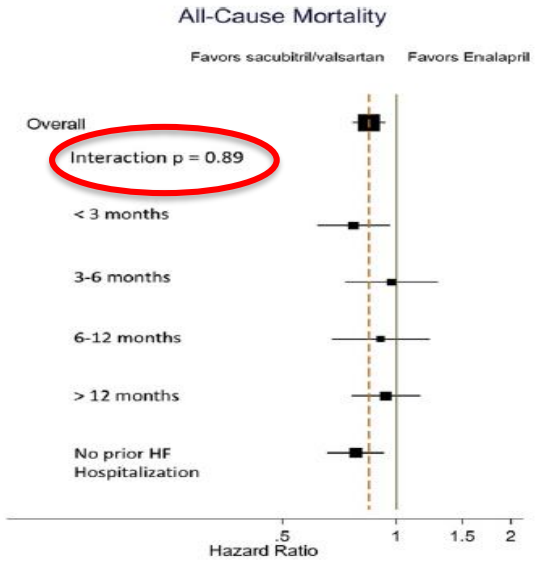
- Efficacy of sacubitril-valsartan didn't differ according to history of hospitalization.

A Few Lessons from PARADIGM-HF

FIGURE 2 Treatment Effect of Sacubitril/Valsartan Therapy







JACC HF 2016; 4(10): 816-22

Importance of Clinical Worsening of Heart Failure Treated in the Outpatient Setting

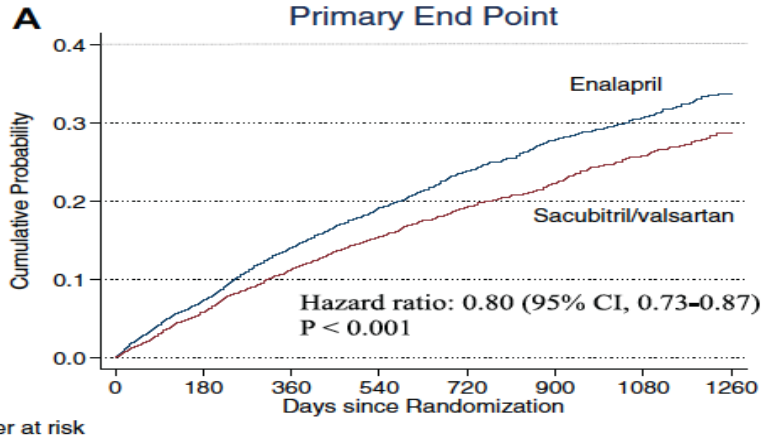
Evidence From the Prospective Comparison of ARNI With ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure Trial (PARADIGM-HF)

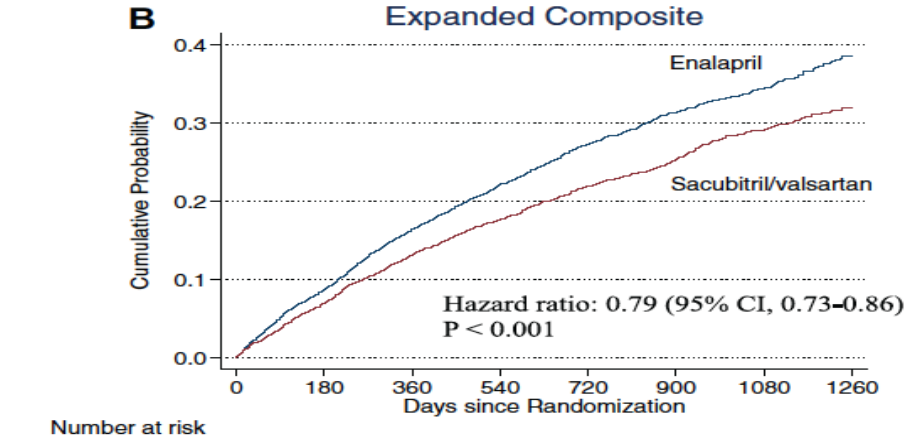
Naoki Okumura, MD, PhD; Pardeep S. Jhund, MBChB, MSc, PhD; Jianjian Gong, MD; Martin P. Lefkowitz, MD; Adel R. Rizkala, PharmD; Jean L. Rouleau, MD; Victor C. Shi, MD; Karl Swedberg, MD; Michael R. Zile, MD; Scott D. Solomon, MD; Milton Packer, MD; John J.V. McMurray, MD; PARADIGM-HF Investigators and Committees*

- **Intensification of outpatient HF therapy was included in an expanded composite outcome with ED visits, HF hospitalizations, and CV deaths.**
- There was a total of 4.3% with OP intensification of therapy and no subsequent event, 1% with ED visits and no subsequent event, and 13.2% with HF hospitalization and no preceding event (out of a total of 8399)

Okumura N, et al. Circulation 2016;133:2254-2262

	None of the Events	Hospitalization for HF	Emergency Department Visit for HF	Intensification of HF Therapy
Each event as the first event experienced in a time-updated model, hazard ratio (95% CI)				
Adjusted for randomized treatment and region	1	6.1 (5.4–6.8)	4.5 (3.0–6.7)	5.2 (4.2–6.3)
Adjusted for randomized treatment, region, and baseline covariates*	1	5.3 (4.7–6.0)	3.3 (2.2–5.0)	4.6 (3.7–5.6)
Each event as the only event experienced in a time updated model, hazard ratio (95% CI)				

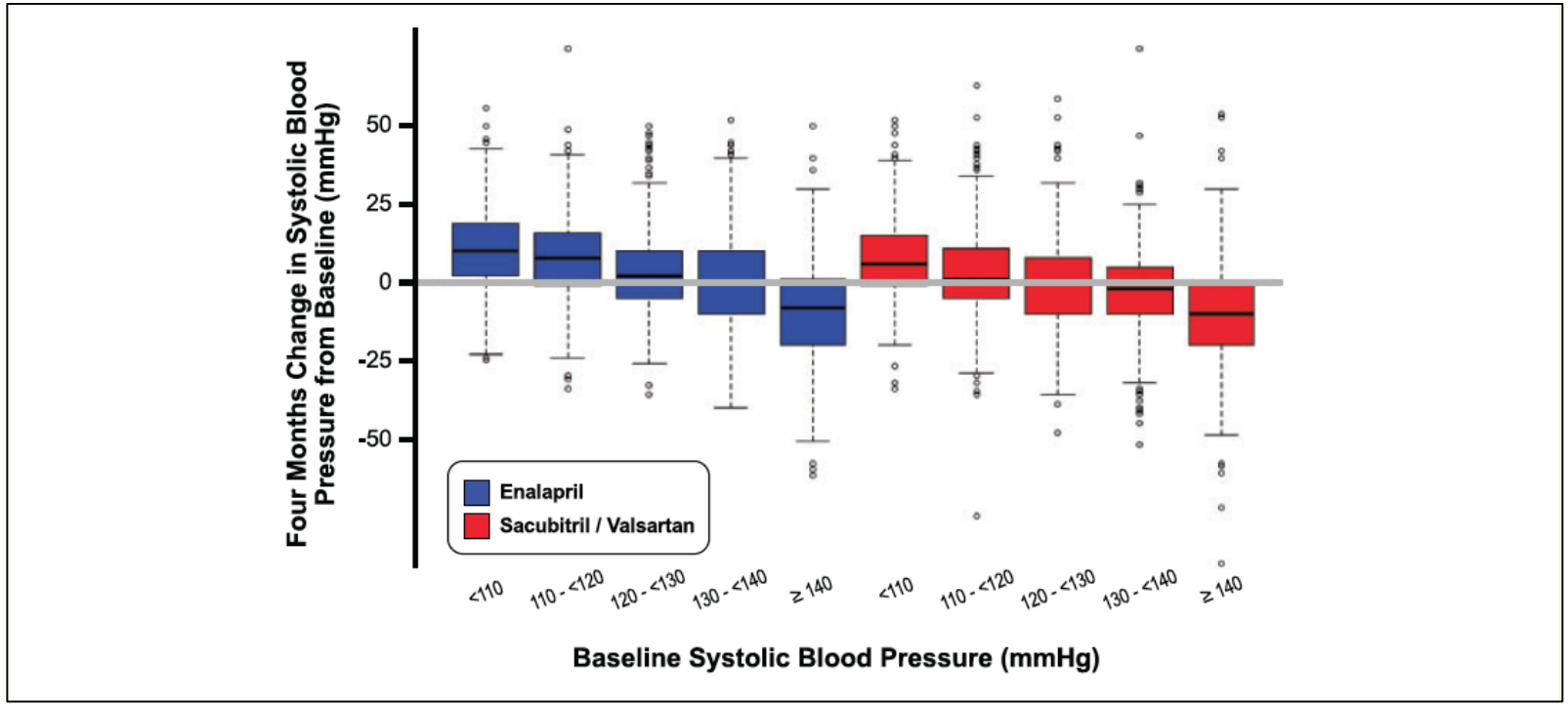




Systolic blood pressure, cardiovascular outcomes and efficacy and safety of sacubitril/valsartan (LCZ696) in patients with chronic heart failure and reduced ejection fraction: results from PARADIGM-HF

Michael Böhm[1]*, Robin Young[2], Pardeep S. Jhund[3], Scott D. Solomon[4], Jianjian Gong[5], Martin P. Lefkowitz[5], Adel R. Rizkala[5], Jean L. Rouleau[6], Victor C. Shi[5], Karl Swedberg[7], Michael R. Zile[8], Milton Packer[9], and John J.V. McMurray[3]

European Heart Journal (2017) **38**, 1132–1143



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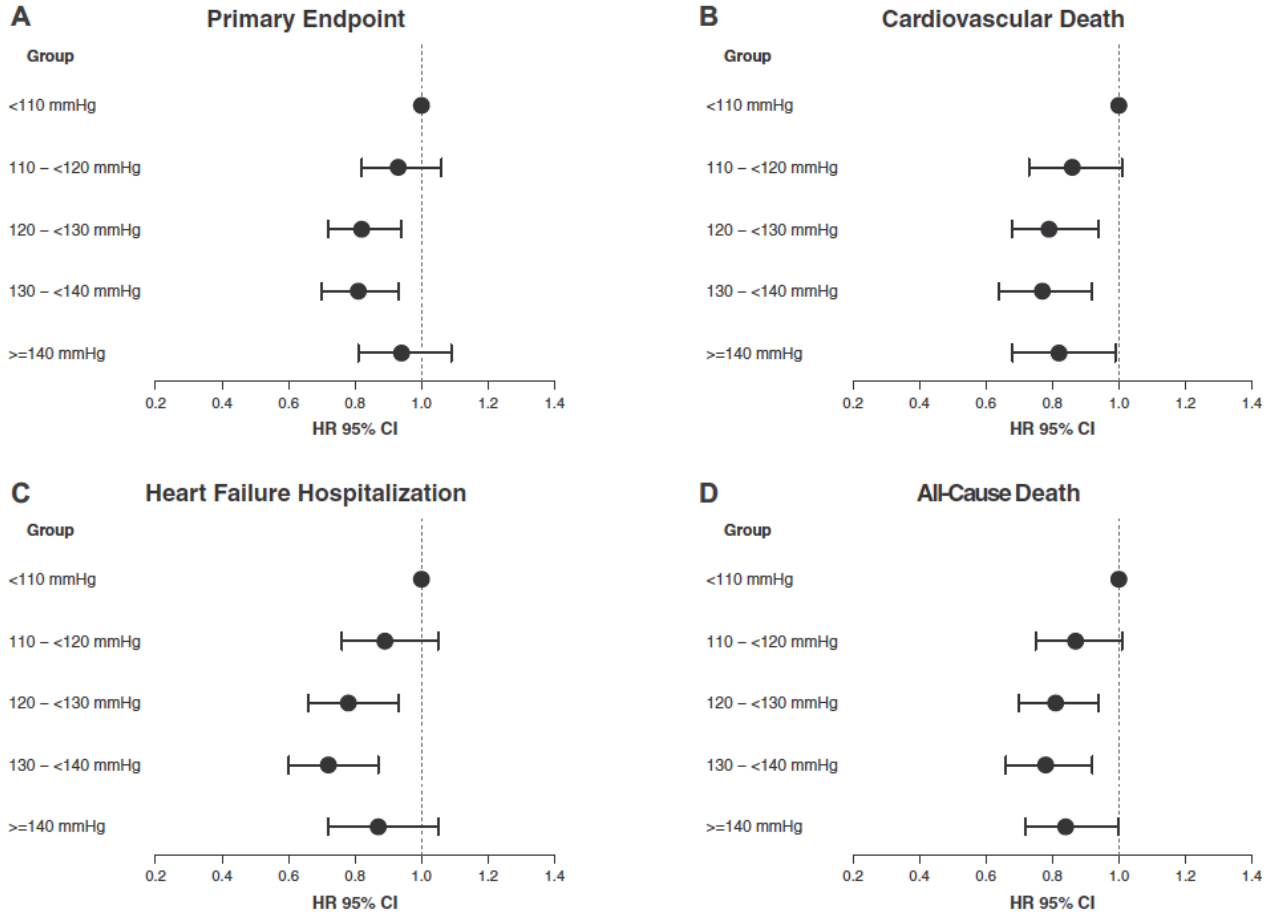

Figure 2 Adjusted hazard ratios for the (*A*) primary endpoint, (*B*) cardiovascular death, (*C*) heart failure hospitalization and (*D*) all-cause death according to systolic blood pressure at baseline in all patients. The group with systolic blood pressure < 110 mmHg is given as a reference (=1).

Benefits of Sacubitril-Valsartan vs. Enalapril According to Baseline BP

- Those with a SBP ≤100 mmHg had worse outcomes, although there was no clear objective evidence of worse disease (EF, eGFR, NPs,..etc).
- Despite worse outcomes with low BP, rates were lower using sacubitril-valsartan compared to enalapril. The benefit was seen across all BP subgroups.
- The “absolute” benefit was greater in patients with lower (compared to higher) baseline BP.

Summary

- Heart failure is associated with significant mortality, morbidity, and poor quality of life.
- Stability in HF is relative. There is no absolutely “stable” HF patient.
- It is critical that objective parameters are used to follow patients. These parameters have to be diverse and comprehensive.
- Hospitalizations are very important. However, by the time they occur during the course of therapy, it is already a very “unstable” course!
- Seemingly “sick” HF patients can still benefit from appropriate medical therapy.

Thank you