What's new in HF?

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Medical Director Mechanical Circulatory/Heart Failure Program

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Learning Objectives

- Classification of Heart Failure
- Review some key points from 2022 HF Guidelines
- What's in HFrEF? HFmrEF? HFpEF?
- Who is an Advanced Heart Failure Patient?

Heart Failure Statistics

- Increasing prevalence (6.5 million in US)
- Mean age of diagnosis: mid 70’s
- High symptom burden (average KCCQ 55)
- Overall mortality remains high, 40% @ 5 years after diagnosis
- High Hospitalization rates (20% at 30 days;60% at 12 months)

Virani SS et al. Circulation. 2020; 141: e139-e596.

Heart Success not Heart Failure

So why am I optimistic?

Reference

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Journal of Cardiac Failure

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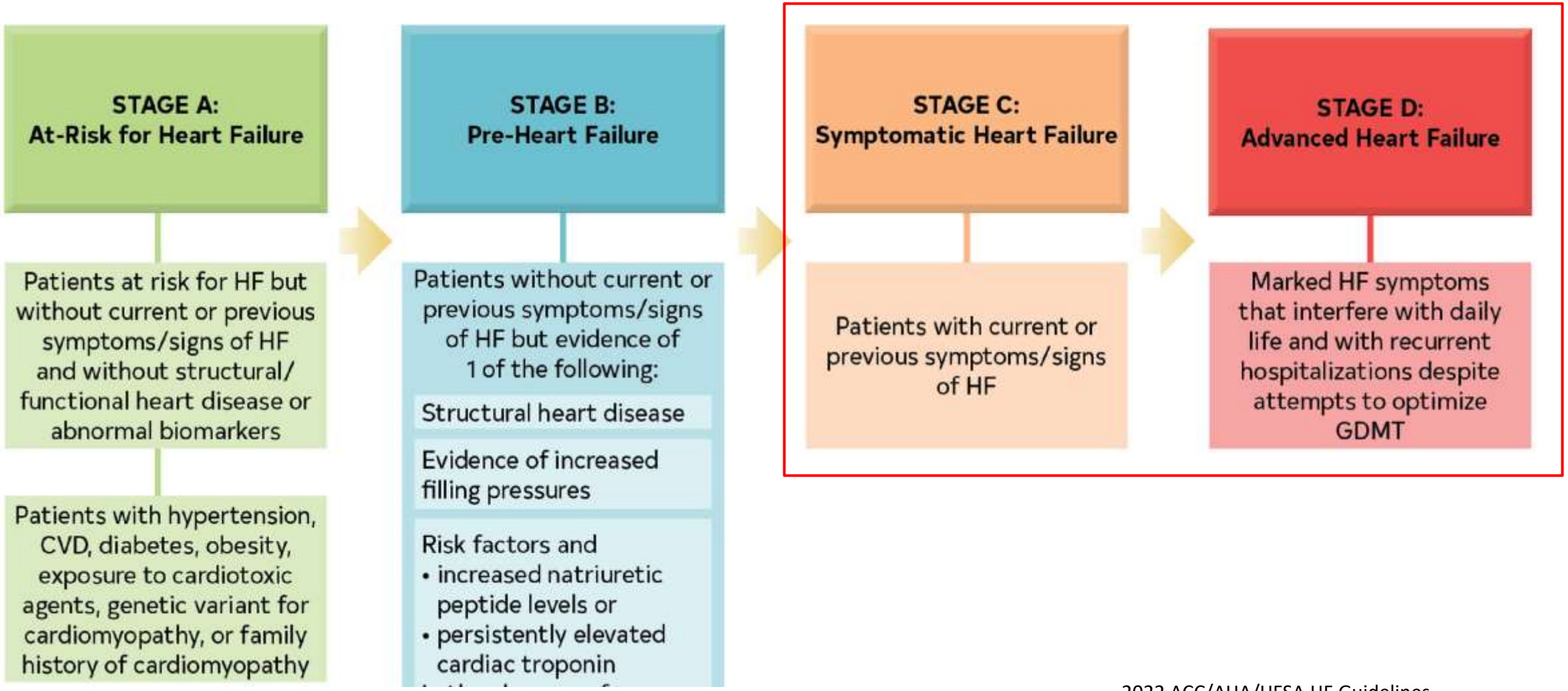
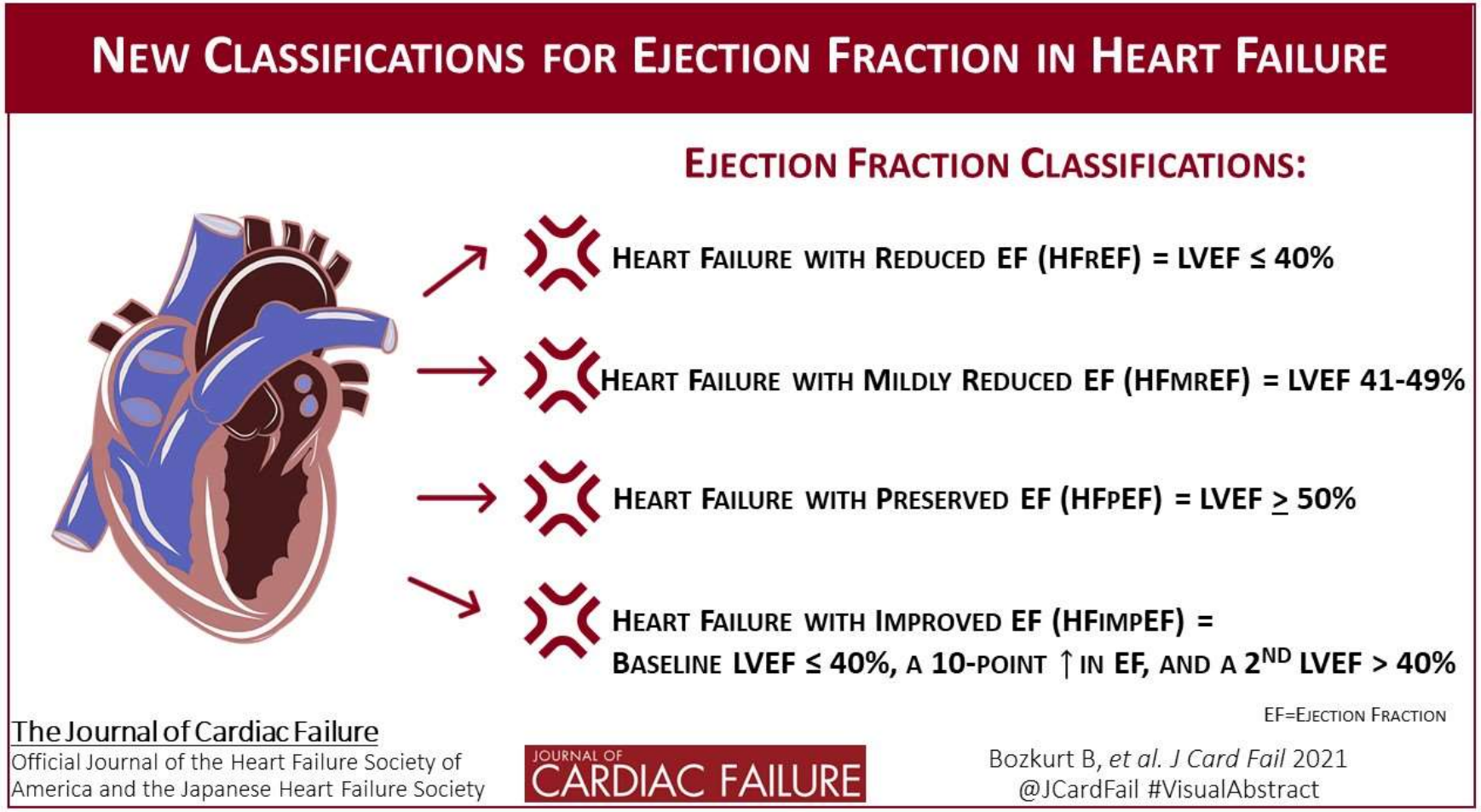
Staging of Heart Failure

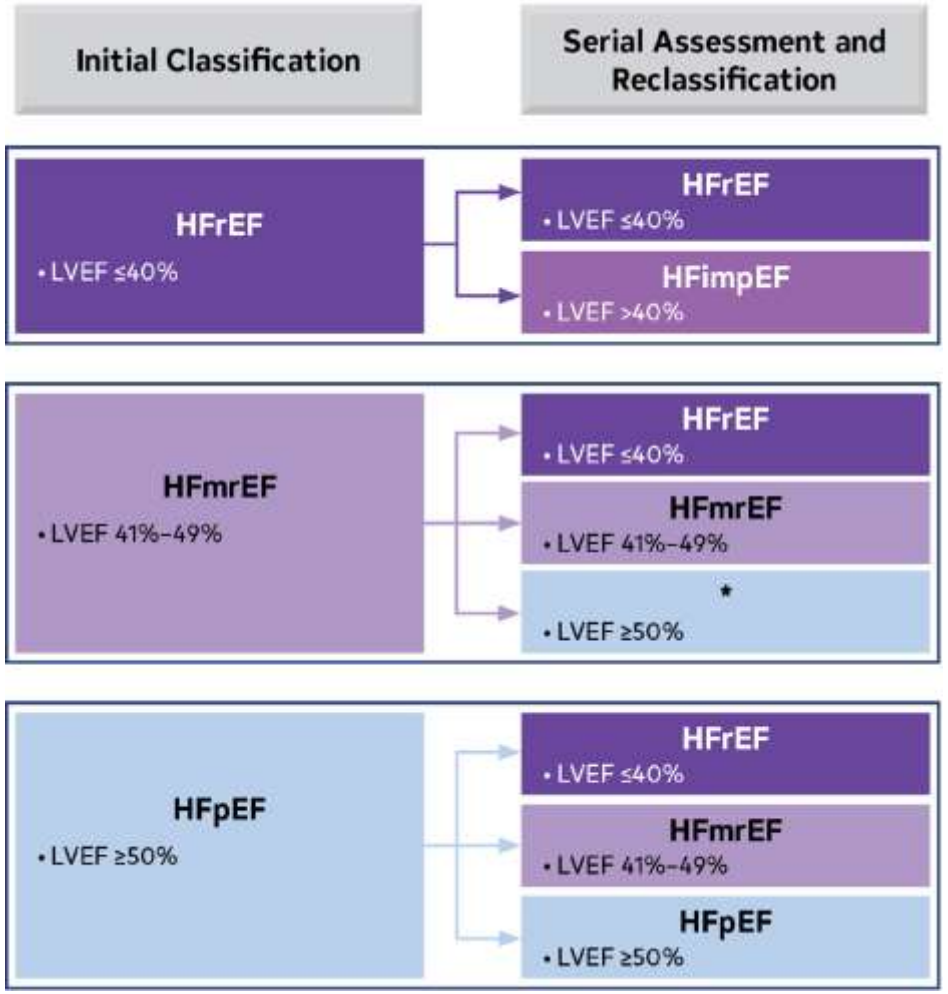


2022 ACC/AHA/HFSA HF Guidelines
Journal of Cardiac Failure
4.1.2022

Classification of Heart Failure



Classification of Heart Failure



2022 ACC/AHA/HFSA HF Guidelines
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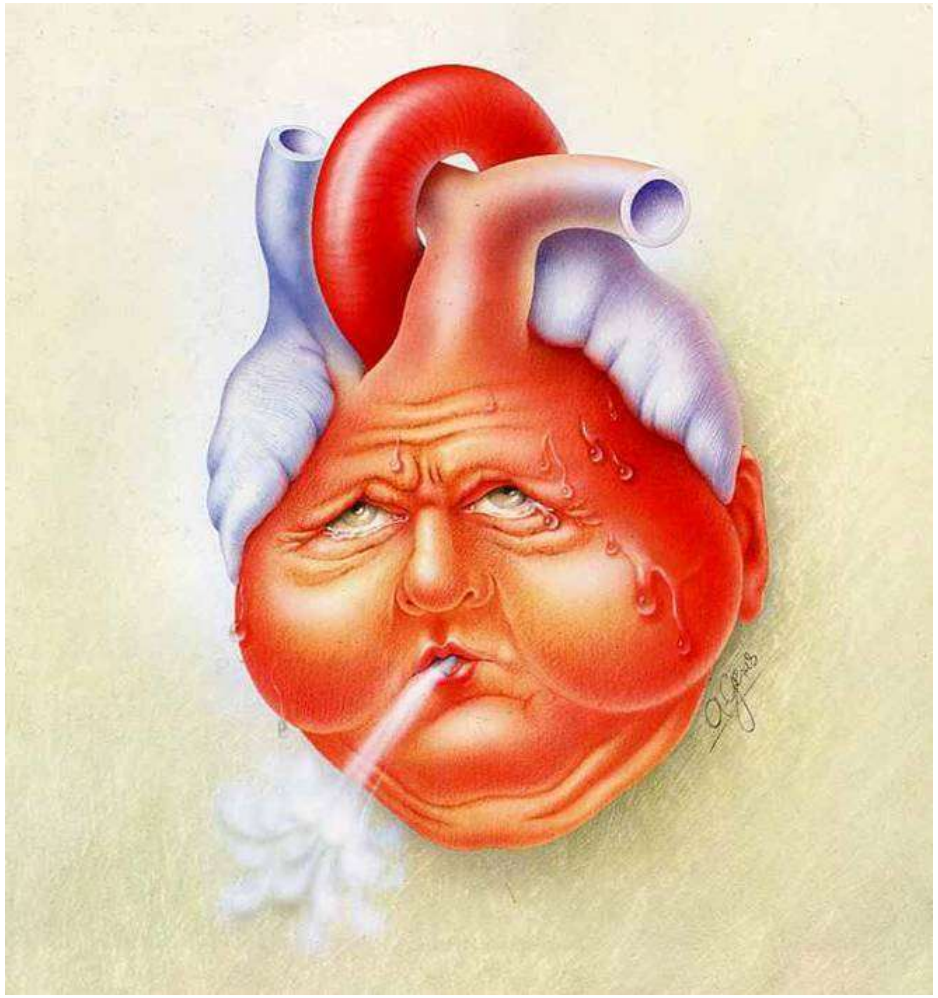
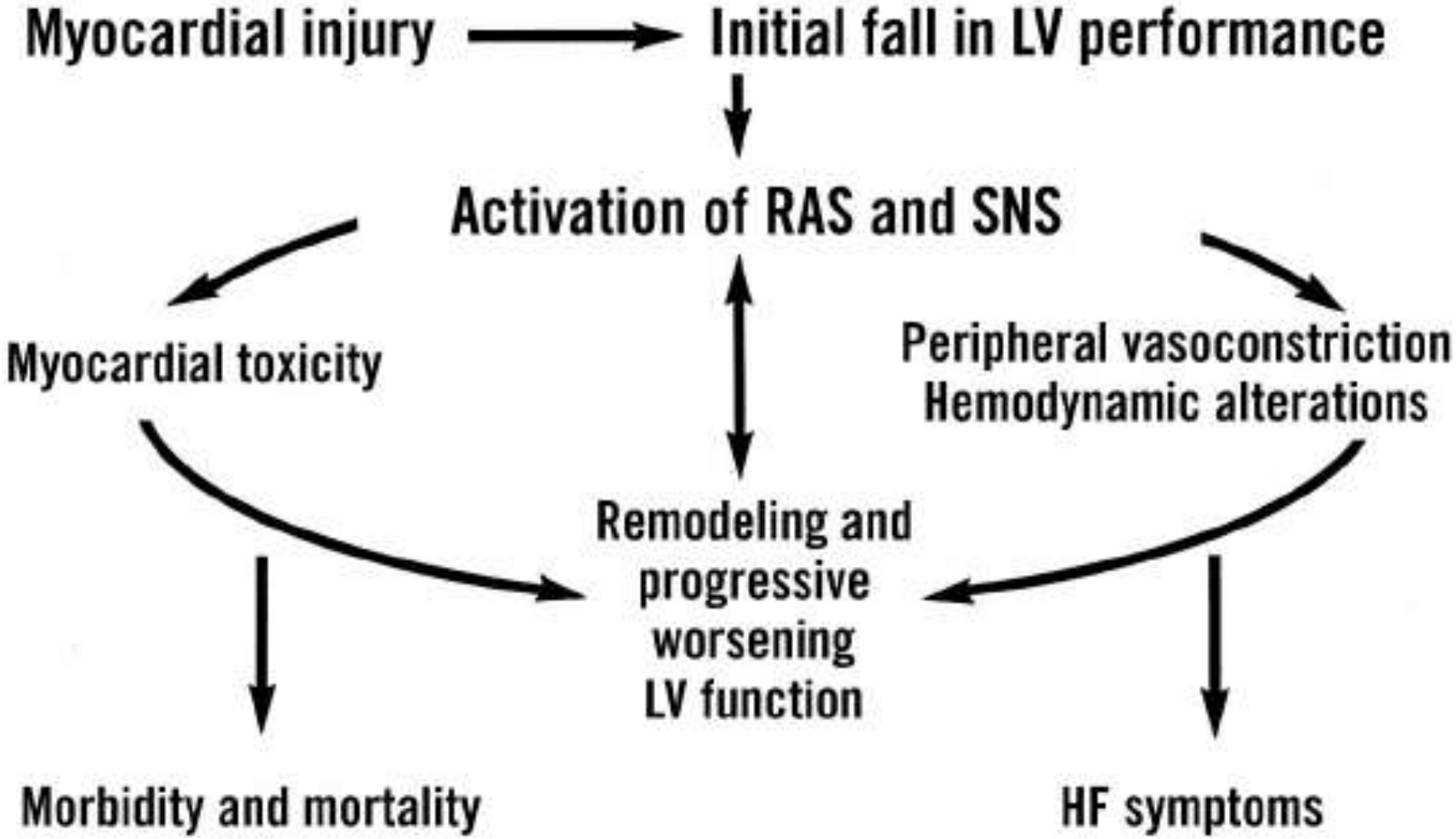
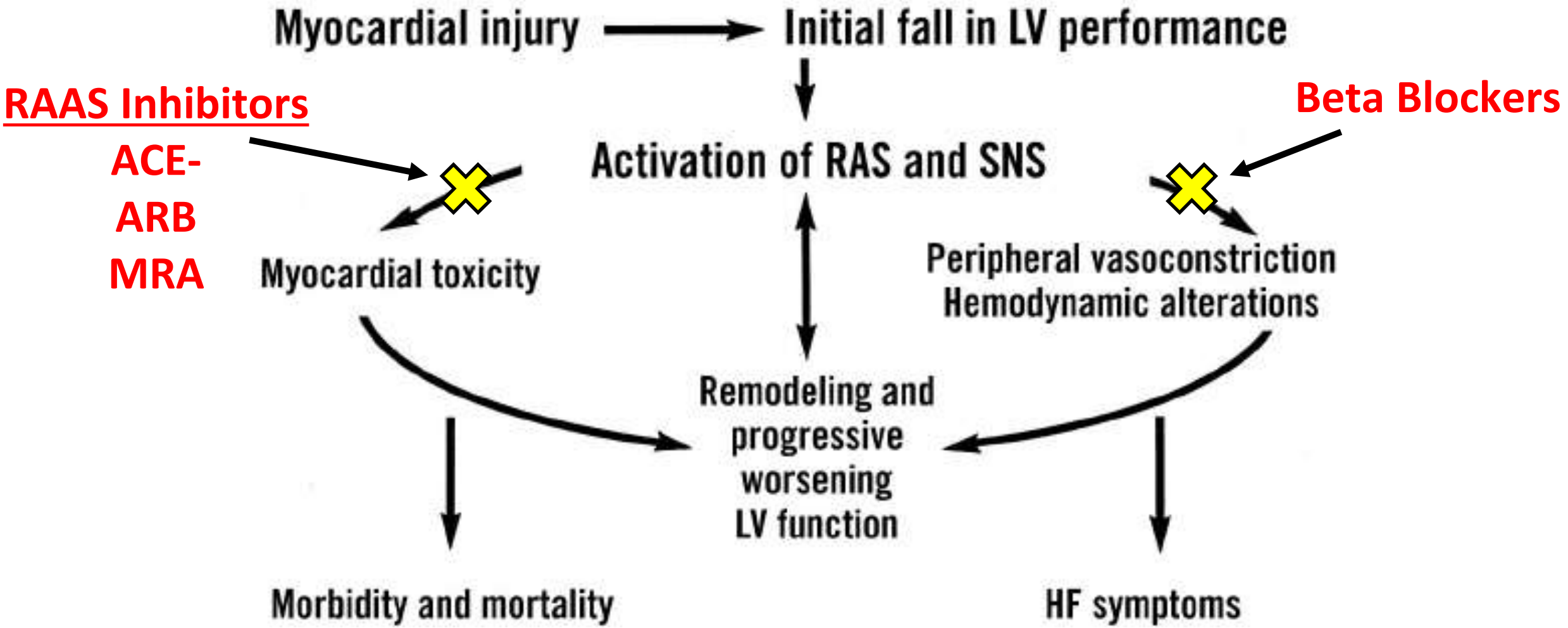
Heart Failure with Reduced Ejection Fraction



Pathophysiology of Heart Failure

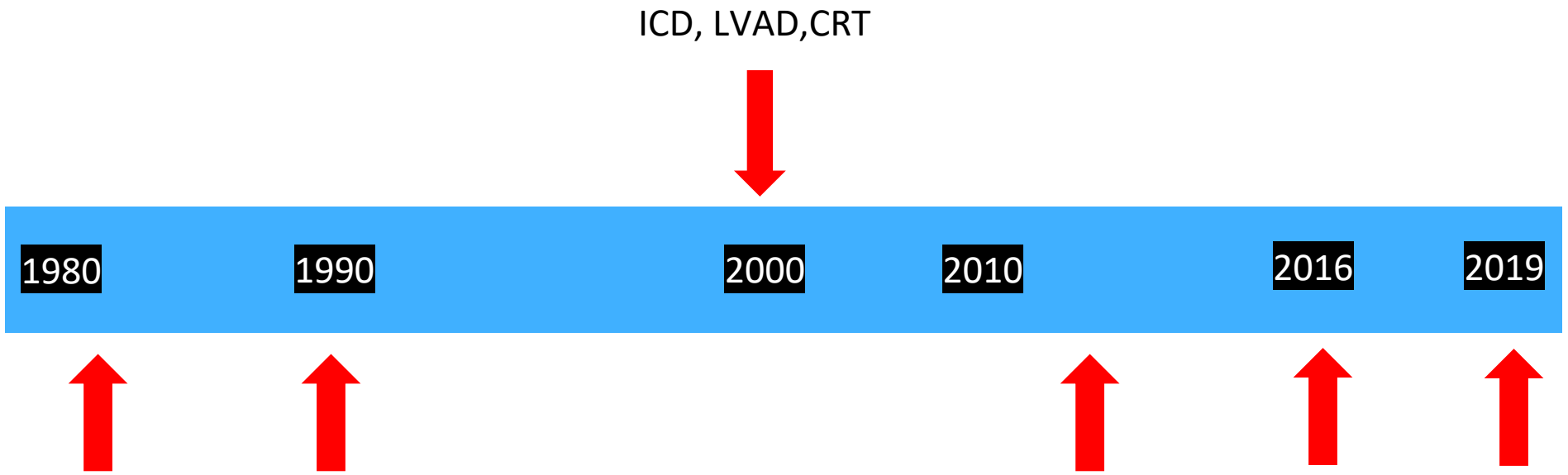


Pathophysiology of Heart Failure



Advancements in Medical Therapy for HFrEF

Device Advances



Pharmaceutical Advances

Digitalis
Diuretics

Beta Blockers
ACE-
ARB
Aldosterone Antagonists
Isosorbide + hydralazine

Ivabradine

ARNI

SGLT2-

In Last 15 years, we have 2 novel new pathways in HFrEF

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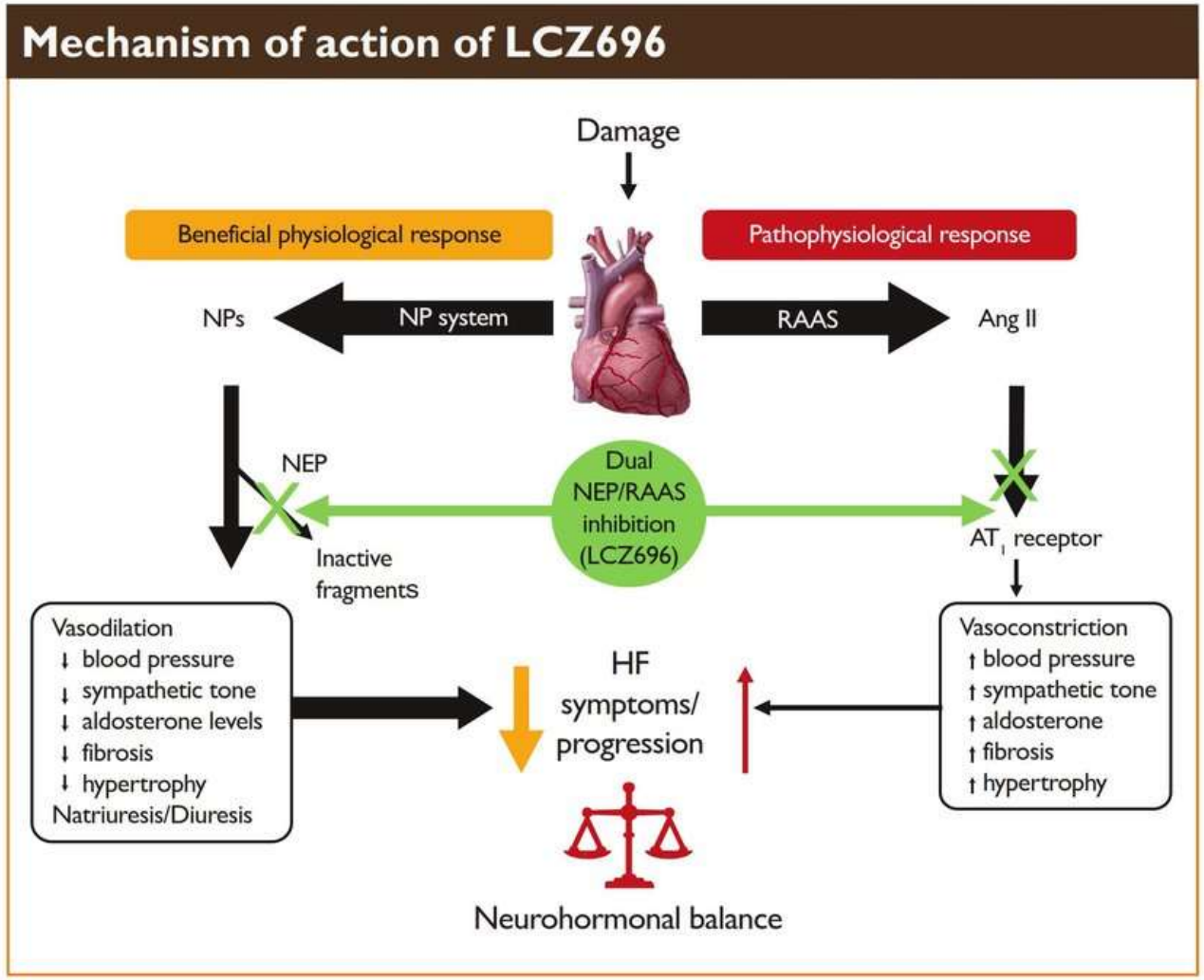
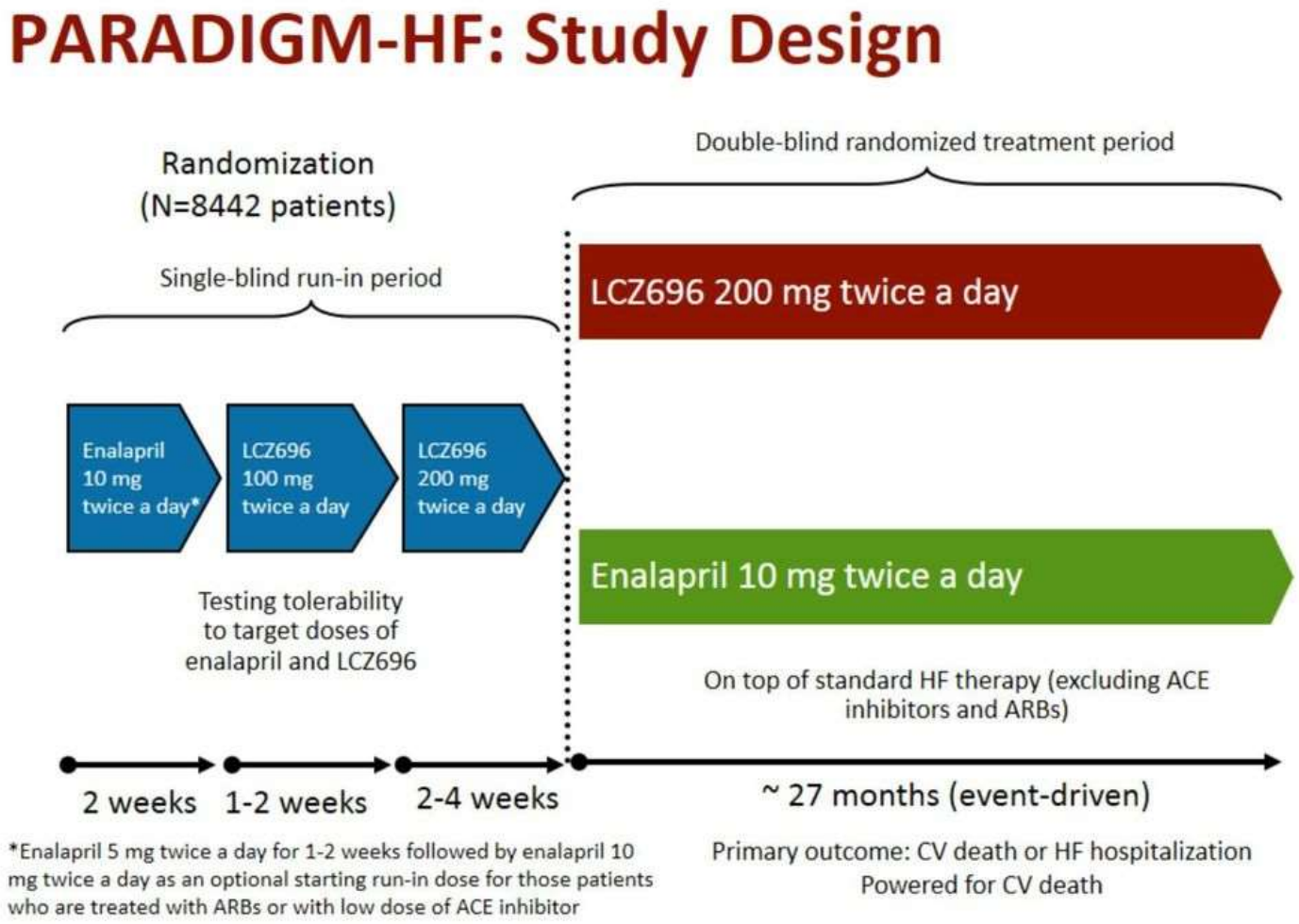
ARNI (sacubitril/valsartan): Heart Failure Mechanism



Angiotensin-converting enzyme (**ACE)**
Angiotensin receptor blockers (**ARBs**)
Mineralocorticoid receptor antagonists (**MRAs**)

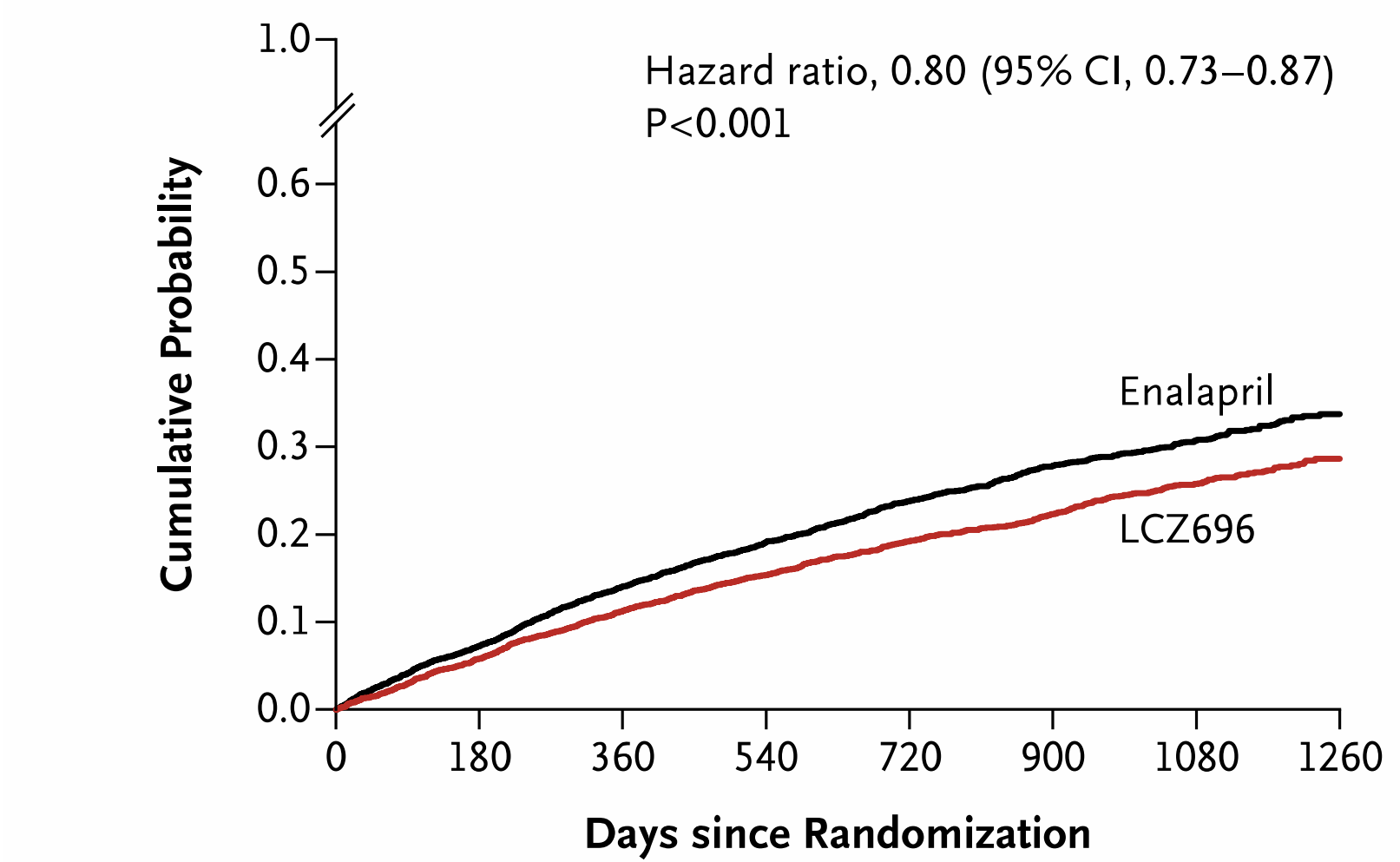
Beta Blockers

PARADIGM-HF Study Design: ARNI (sacubitril/valsartan):



McMurray JJ, et al. *N Engl J Med.* 2014;371:993-1004.

PARADIGM-HF: CV Death or Hospitalization



20% RRR

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McMurray JJV et al, N Engl J Med 2014

PROVE-HF

Prospective Study of Biomarkers, Symptom Improvement and Ventricular Remodeling During Entresto Therapy for Heart Failure *(PROVE-HF; NCT02887183)*

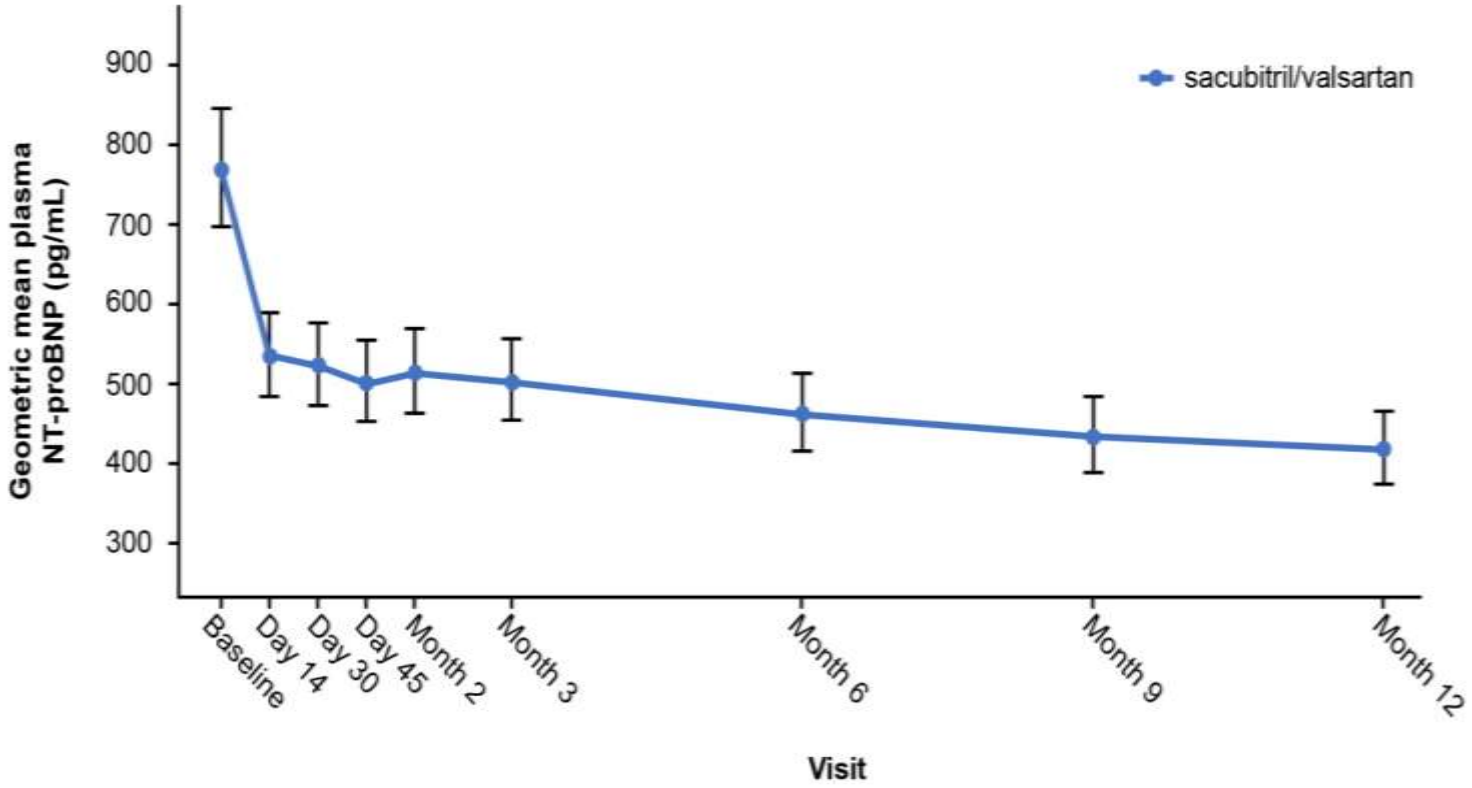
James L. Januzzi MD[1,2], Margaret F. Prescott PhD[3], Javed Butler MD MPH MBA[4], G. Michael Felker MD MHS[5], Alan S. Maisel MD[6], Kevin McCague MA[3], Alexander Camacho PhD[1], Ileana L. Piña MD MPH[7], Ricardo A. Rocha MD[3], Amil M. Shah MD MPH[8], Kristin M. Williamson PharmD[3], and Scott D. Solomon MD[8] on behalf of the PROVE-HF Investigators

[1]Massachusetts General Hospital, [2]Baim Institute for Clinical Research, Boston, MA, USA; [3]Novartis Pharmaceuticals, East Hanover, NJ, USA; [4]University of Mississippi Medical Center, Jackson, MS, USA; [5]Duke University Medical Center and Duke Clinical Research Institute, Durham, NC, USA; [6]University of California, San Diego School of Medicine, San Diego, CA, USA; [7]Detroit Medical Center, Detroit, MI, USA; [8]Brigham and Women's Hospital, Boston, MA, USA

ESC Congress Paris 2019 Together with World Congress of Cardiology

NT-proBNP concentrations

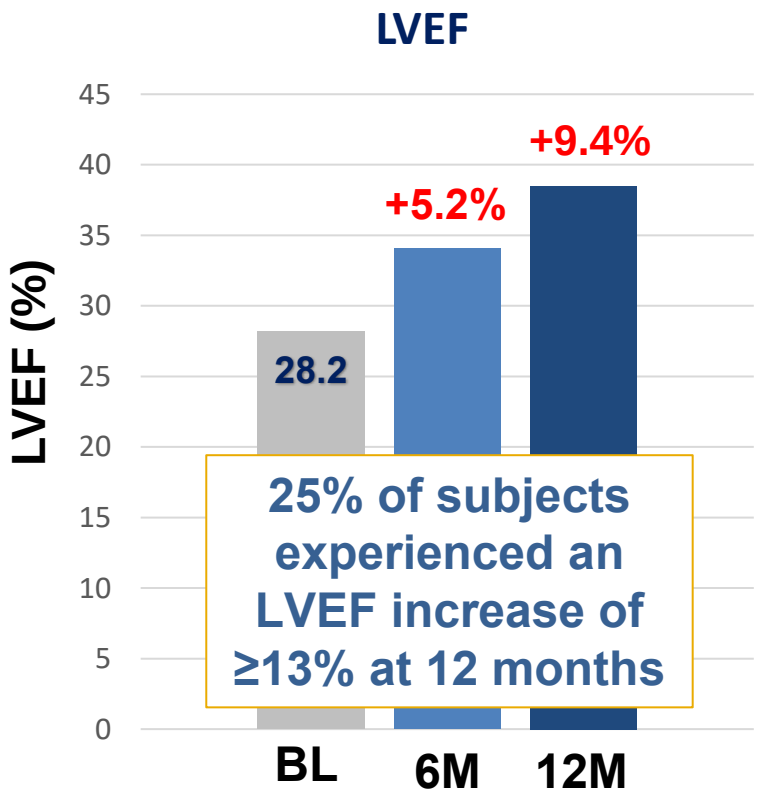
Rapid and significant reduction of NT-proBNP was observed, with majority of reduction within the first 2 weeks

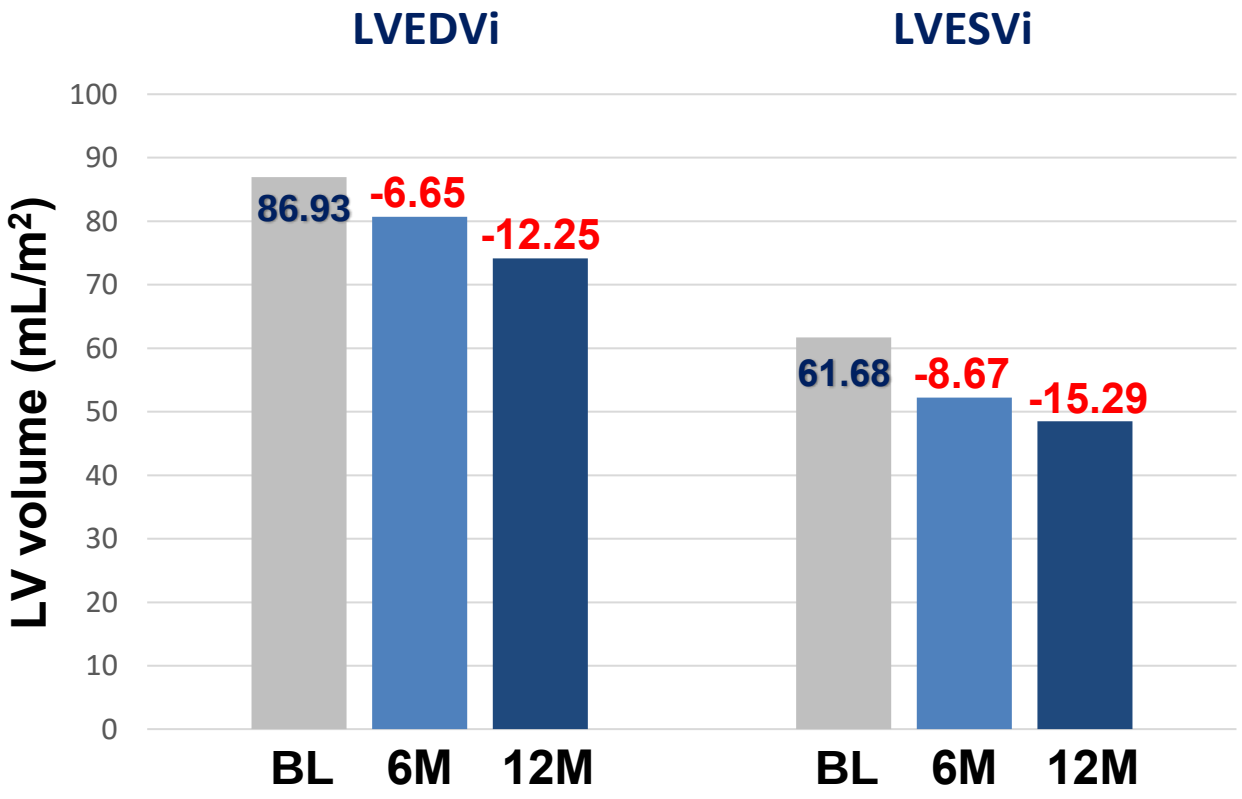


Time point	N	Median NT-proBNP (25th, 75th percentile), pg/mL
Baseline	760	816 (332, 1822)
Day 14	754	528 (226, 1378)
Day 30	740	546 (211, 1321)
Day 45	734	514 (192, 1297)
Month 2	721	535 (210, 1299)
Month 3	719	488 (211, 1315)
Month 6	699	473 (179, 1163)
Month 9	659	444 (170, 1153)
Month 12	638	455 (153, 1090)

Reverse cardiac remodeling

Baseline to 12 months: all P <.001

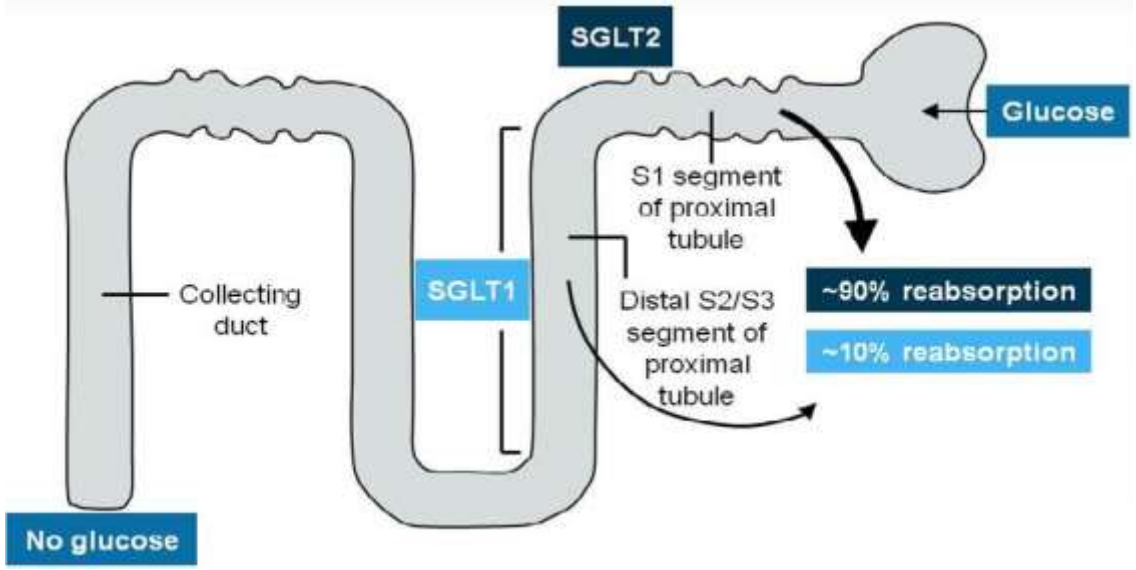




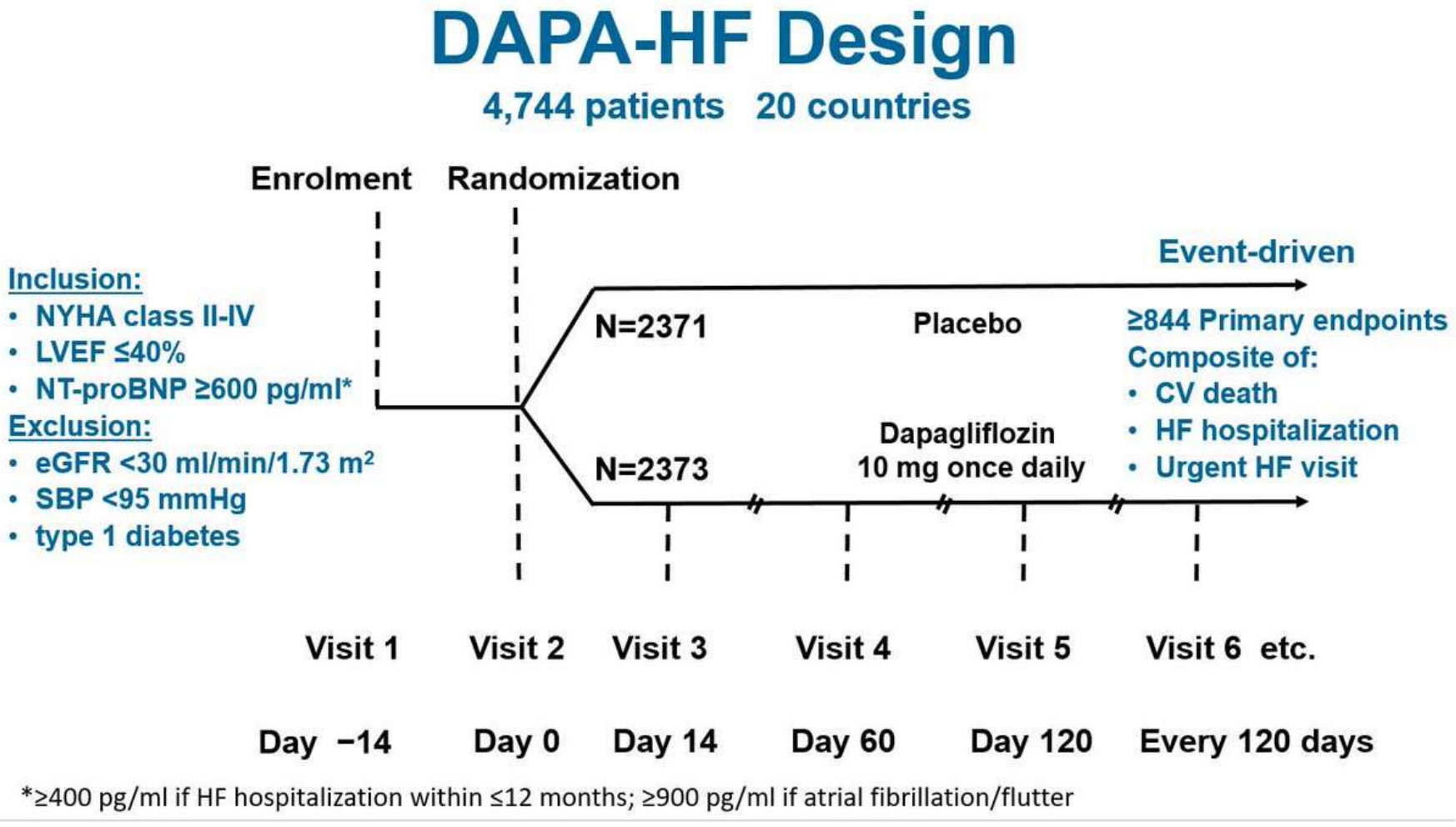
BL, baseline; LVEF, left ventricular ejection fraction; LVEDVi, left ventricular end-diastolic volume index; LVESVi, left ventricular end-systolic volume index

SGLT2- in Heart Failure

- 2008, FDA required that any approved therapy for type 2 diabetes demonstrate cardiovascular safety.
- Multiple SGLT2i were deemed not only safe, but also effective in reducing atherosclerotic and HF events.



DAPA HF Trial

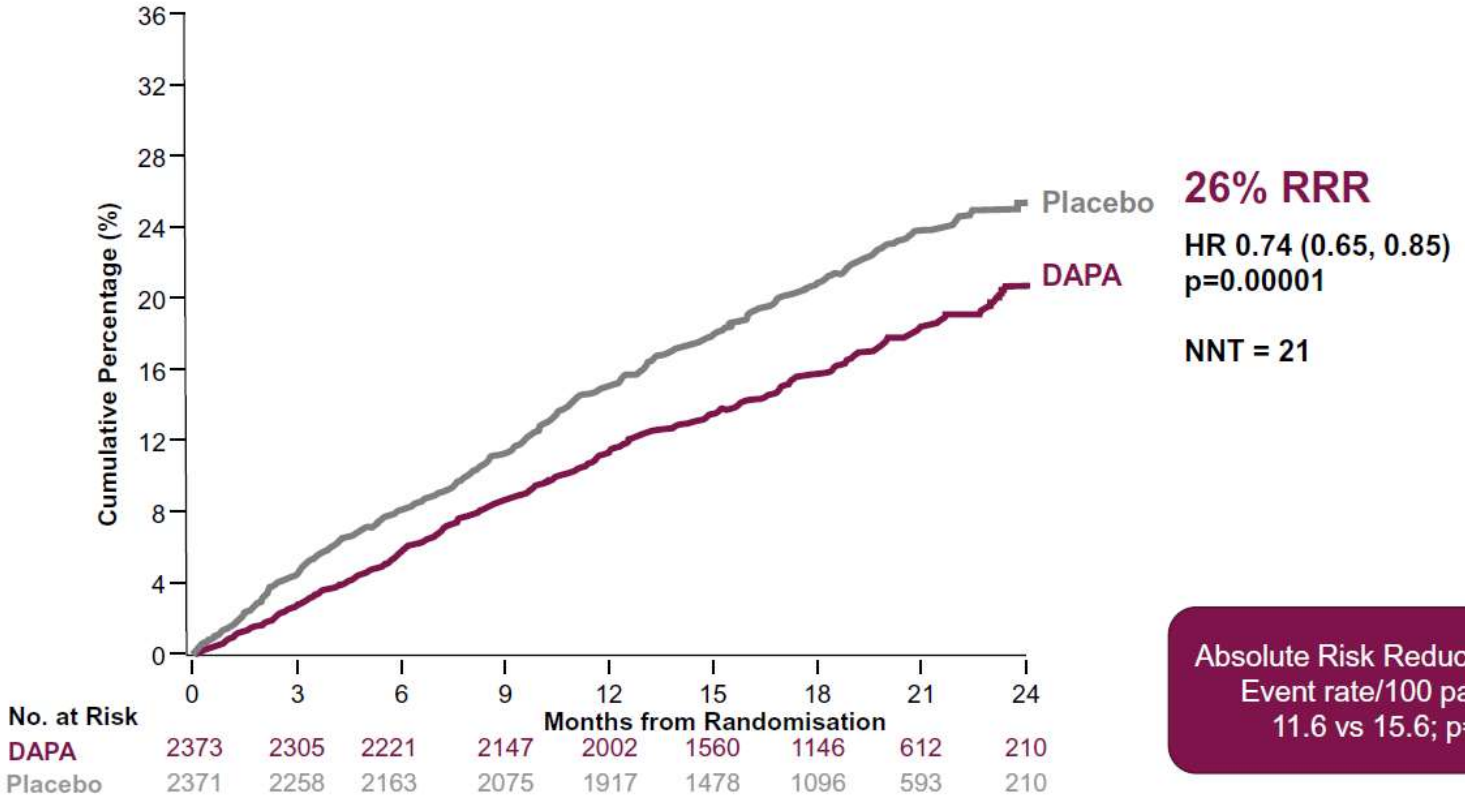


*≥400 pg/ml if HF hospitalization within ≤12 months; ≥900 pg/ml if atrial fibrillation/flutter

NEJM 11.21.19

DAPA-HF

Primary Endpoint: CV Death or hHF or an Urgent HF Visit



26% RRR

HR 0.74 (0.65, 0.85)
p=0.00001

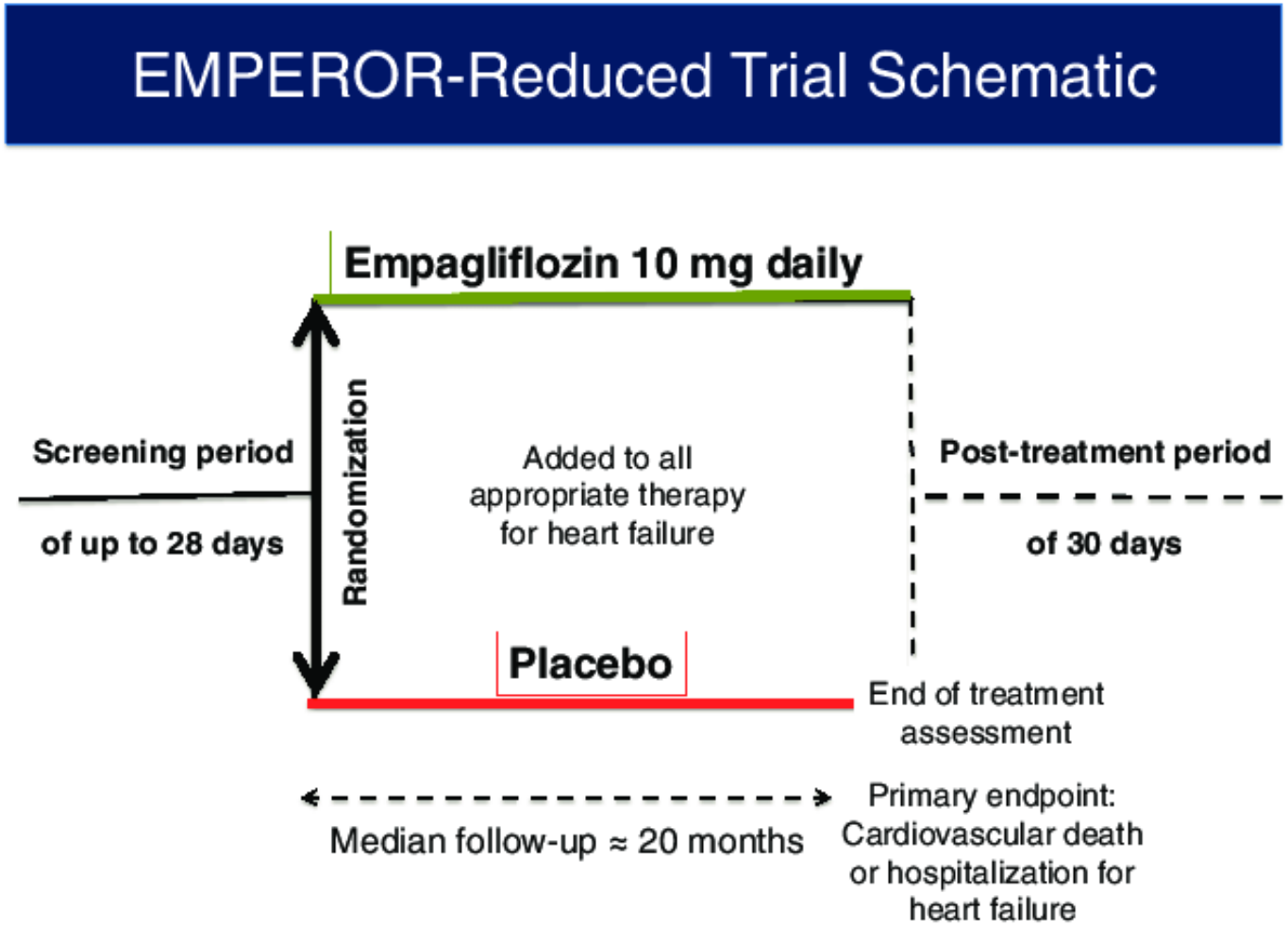
NNT = 21

Absolute Risk Reduction [ARR]=4%
Event rate/100 patient years:
11.6 vs 15.6; p=0.00001

DAPA = dapagliflozin; HF = heart failure; hHF = hospitalisation for heart failure; HR = hazard ratio; NNT = number needed to treat.

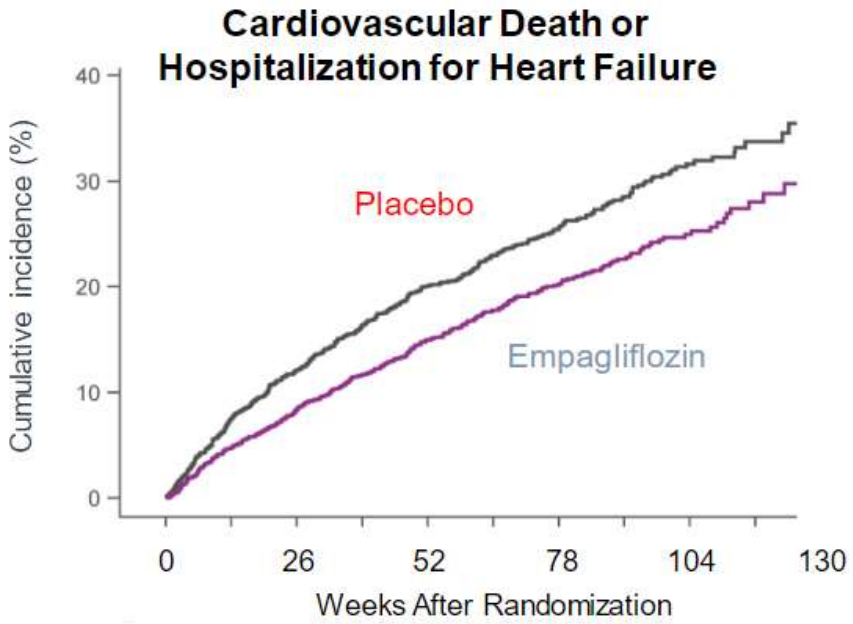
NEJM 11.21.19

EMPEROR-Reduced Trial

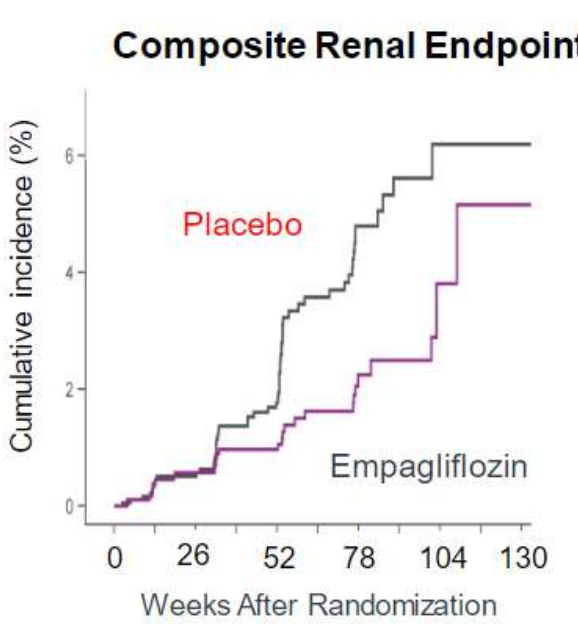


EMPEROR-Reduced Trial

Empagliflozin Prevented Both Serious Heart Failure and Serious Kidney Failure Events



Hazard ratio 0.75 (25% reduction in risk)
(95% CI 0.65, 0.86), P < 0.0001



Hazard ratio 0.50 (50% reduction in risk)
(95% CI 0.32, 0.77), P = 0.0019

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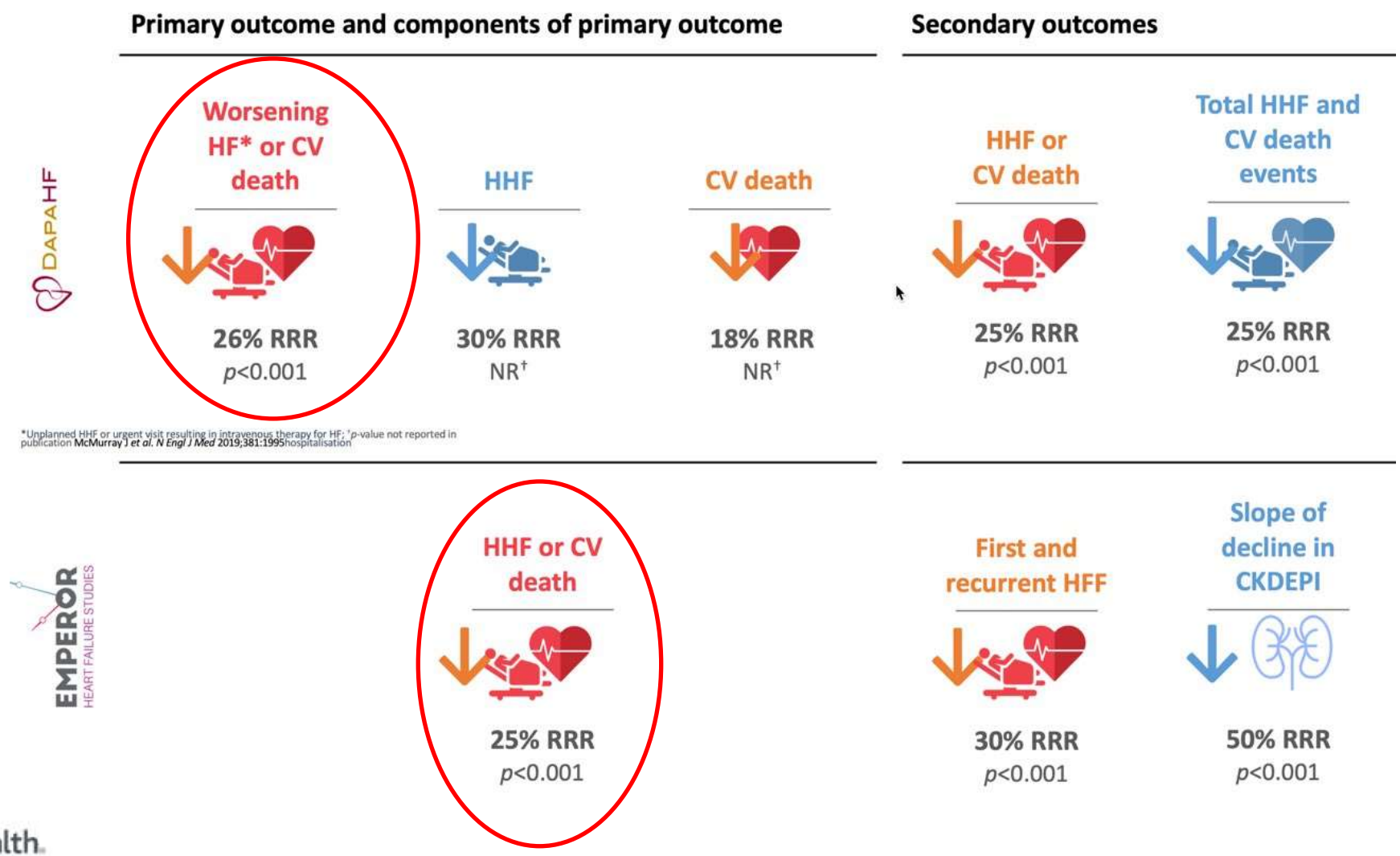
NEM 10.8.2020

SGLT2- in HFrEF



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Reference

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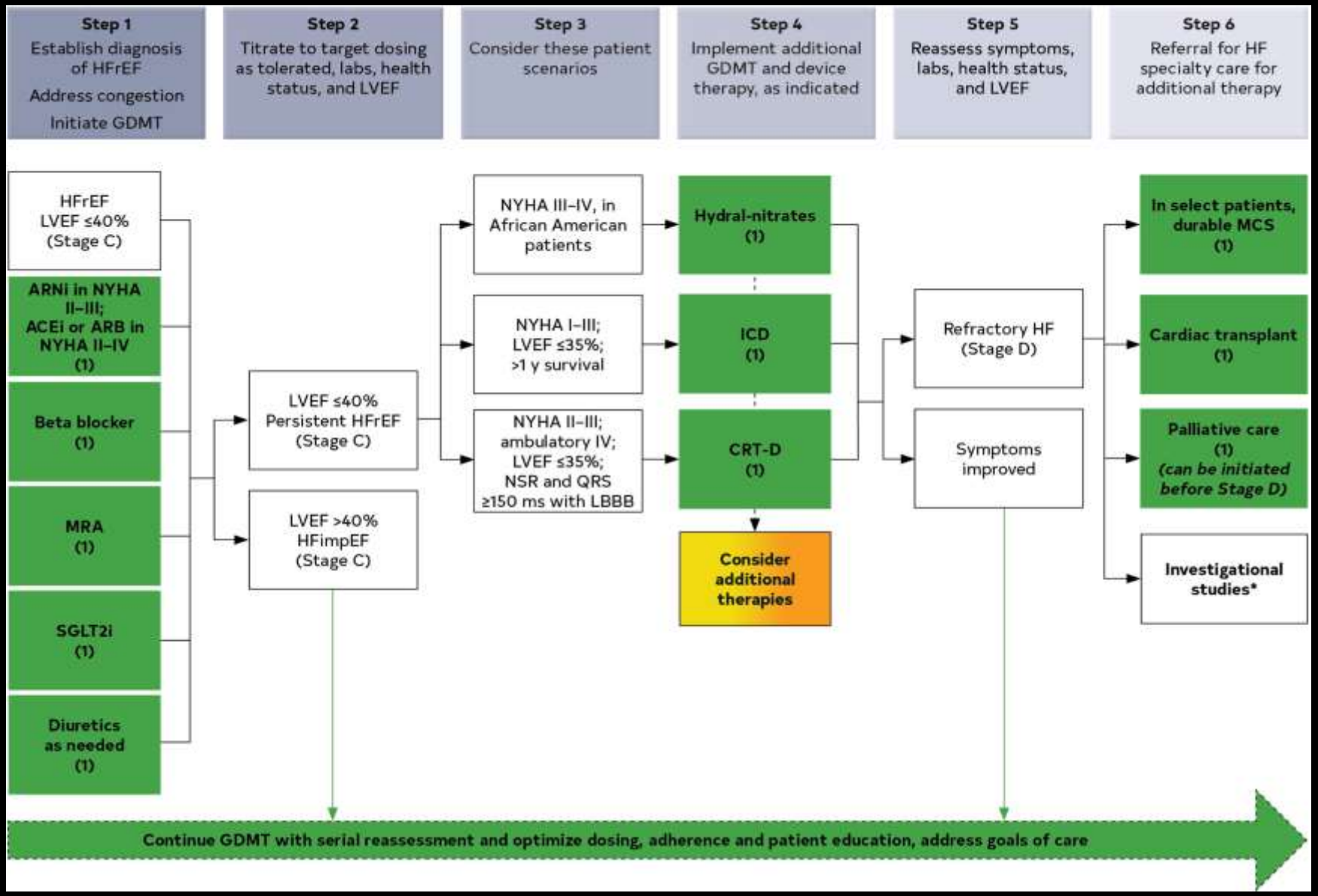
Figure 6



Journal of Cardiac Failure DOI: (10.1016/j.cardfail.2022.02.010)

4 Pillars or GOATS of HFrEF

ARNI

BB

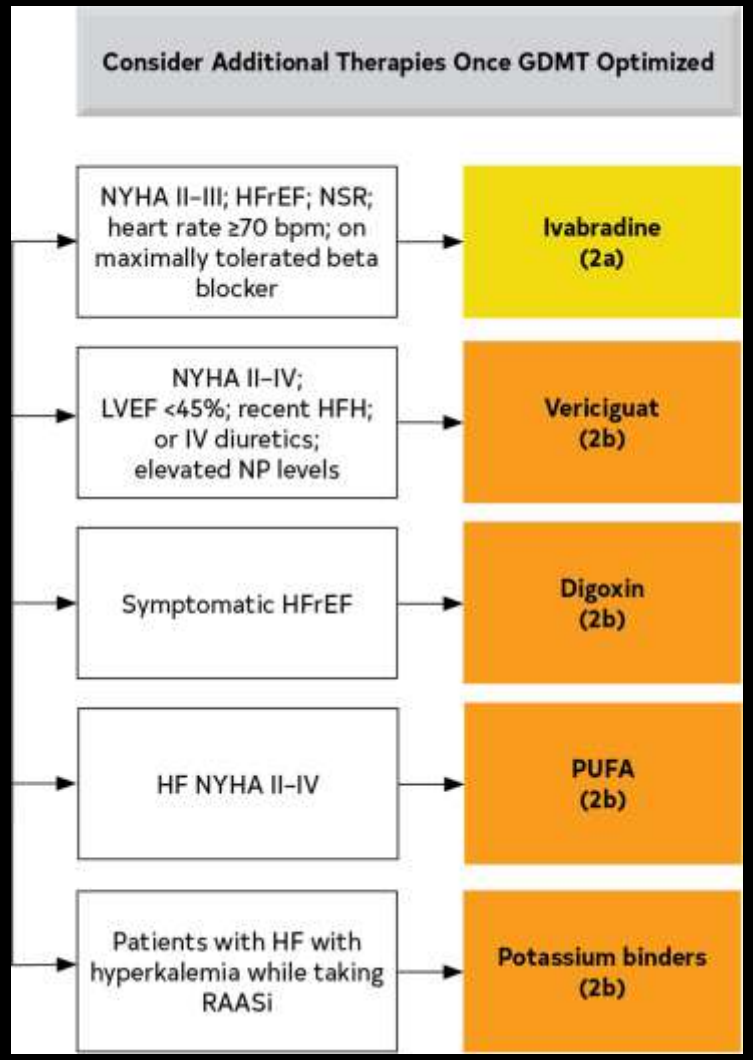
MRA

SGLT2-

@DrMunirJanmohamed

Figure 7

Additional Therapies



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MR and HFrEF

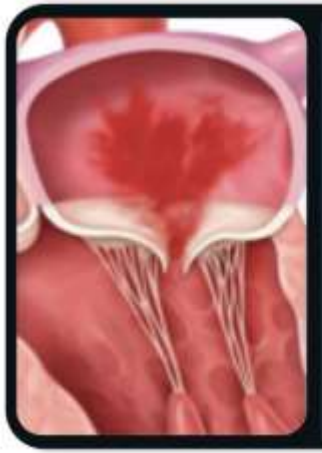
Two Types of Mitral Regurgitation

Incompetent mitral valve closure

Systolic retrograde blood flow from the LV into the LA

Primary:
Anatomic abnormality of the mitral valve

- Leaflets
- Subvalvular apparatus
- Chordae and papillary muscles

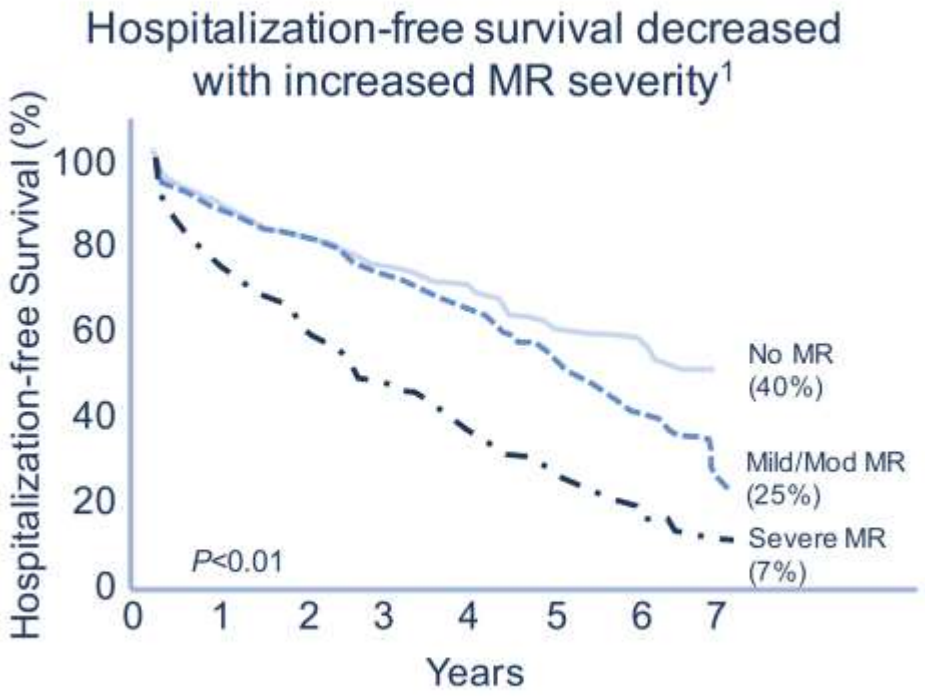


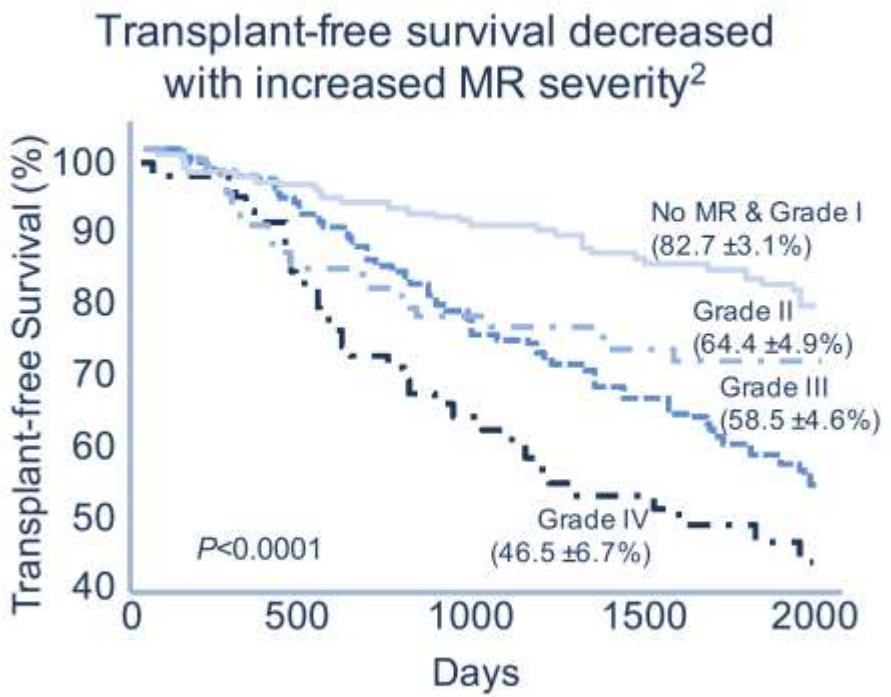
Secondary:
LV dilation; secondary to ischemic and non-ischemic heart disease

- Leads to mitral annular dilation
- Incomplete coaptation of the mitral valve

MR and Heart Failure

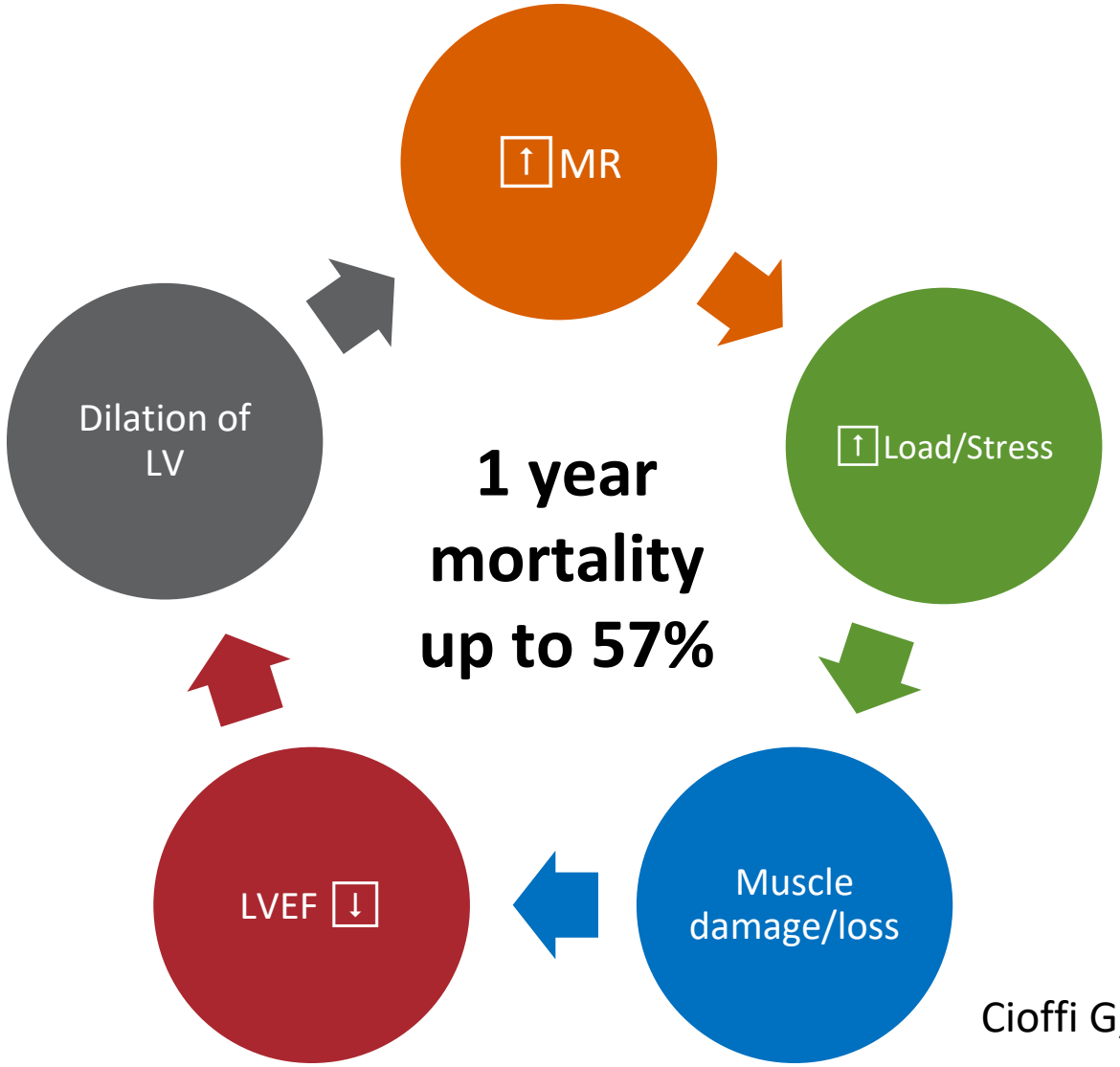
Secondary MR Worsens Heart Failure Outcomes





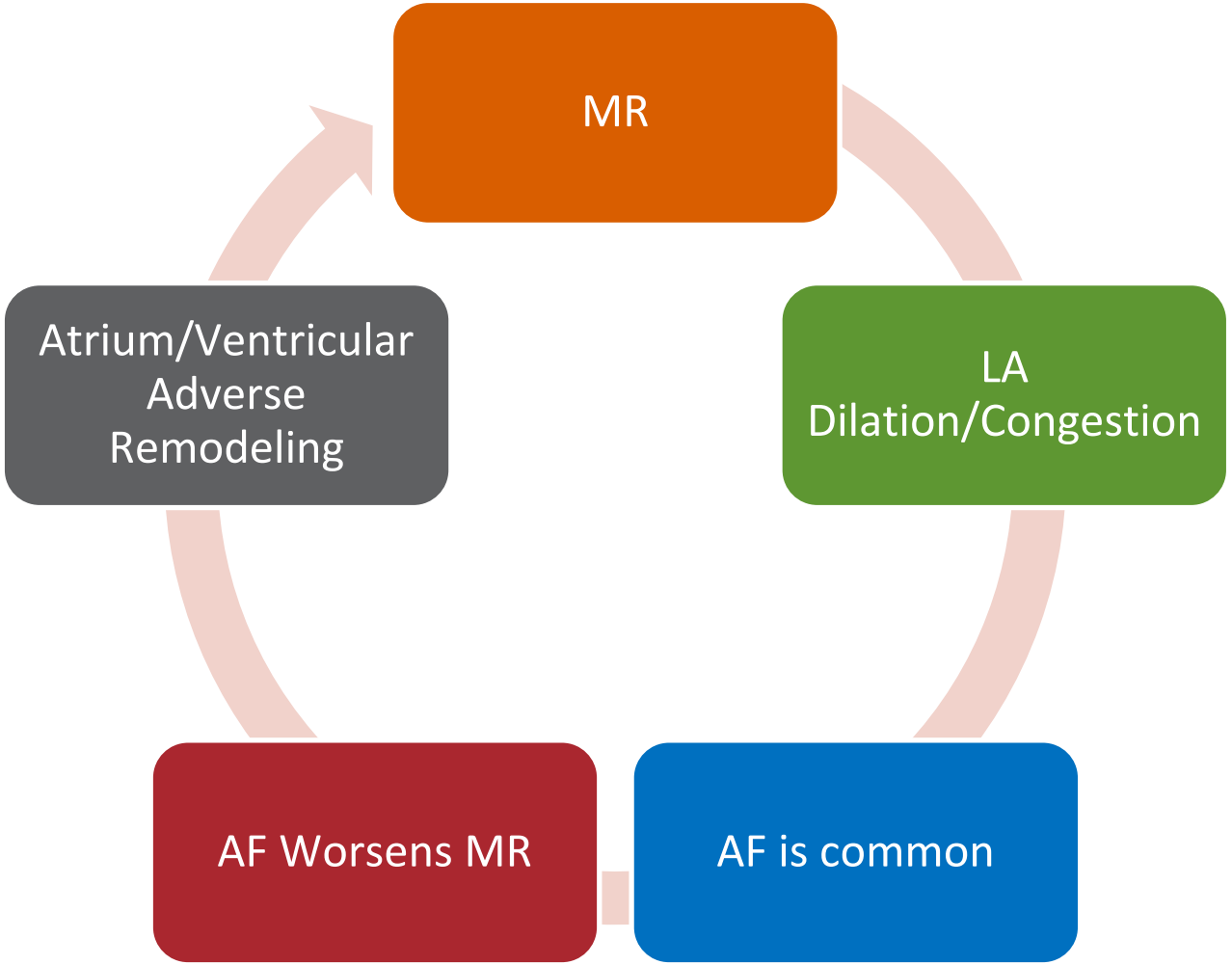
1.Rossi A, et al. Heart 2011; 97:1675-1680; 2. Bursi F, et al. Eur J Heart Fail 2010; 12:382-388

MR and HF: Vicious Cycle of LV Dilation/Dysfunction



Cioffi G, et al. Eur J Heart Failure 2005

MR and AF


MR
LA Dilation/Congestion
AF is common
AF Worsens MR
Atrium/Ventricular Adverse Remodeling

History of Mitral Clip

Ottavio Alfieri M.D. .

Mehmet Oz M.D.

1996, Dr Alfieri proposed to Dr Oz MV only needed one suture to close a leak

Dr Oz developed the idea to use a catheter, submitted patent in 1987

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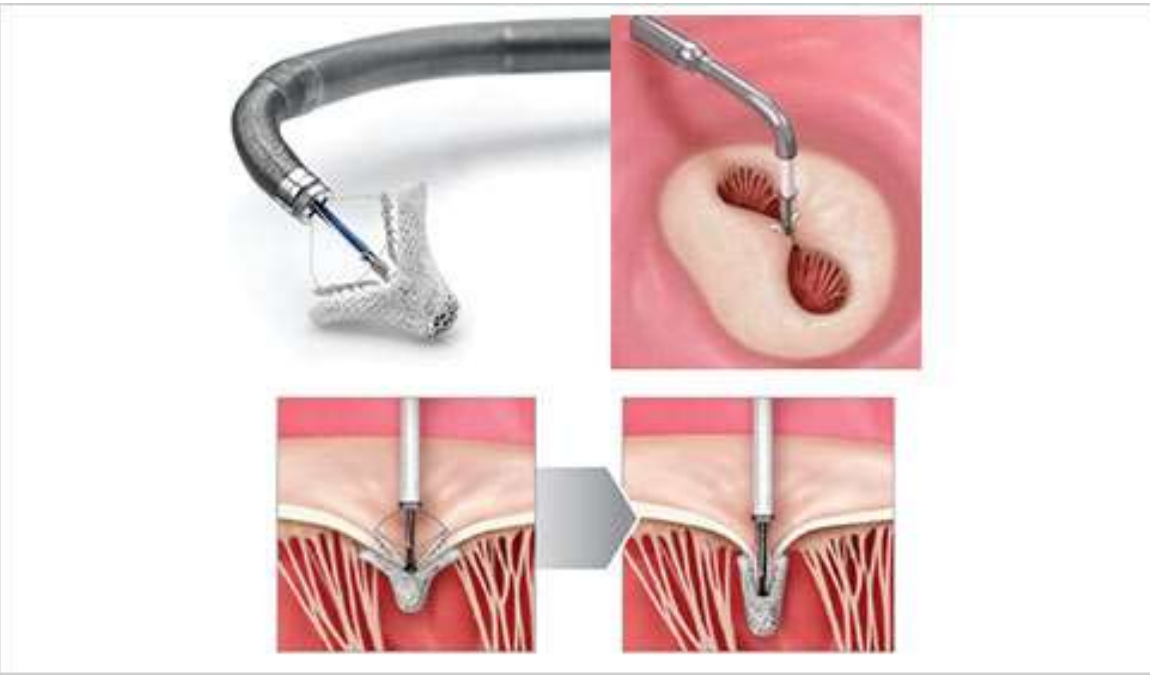
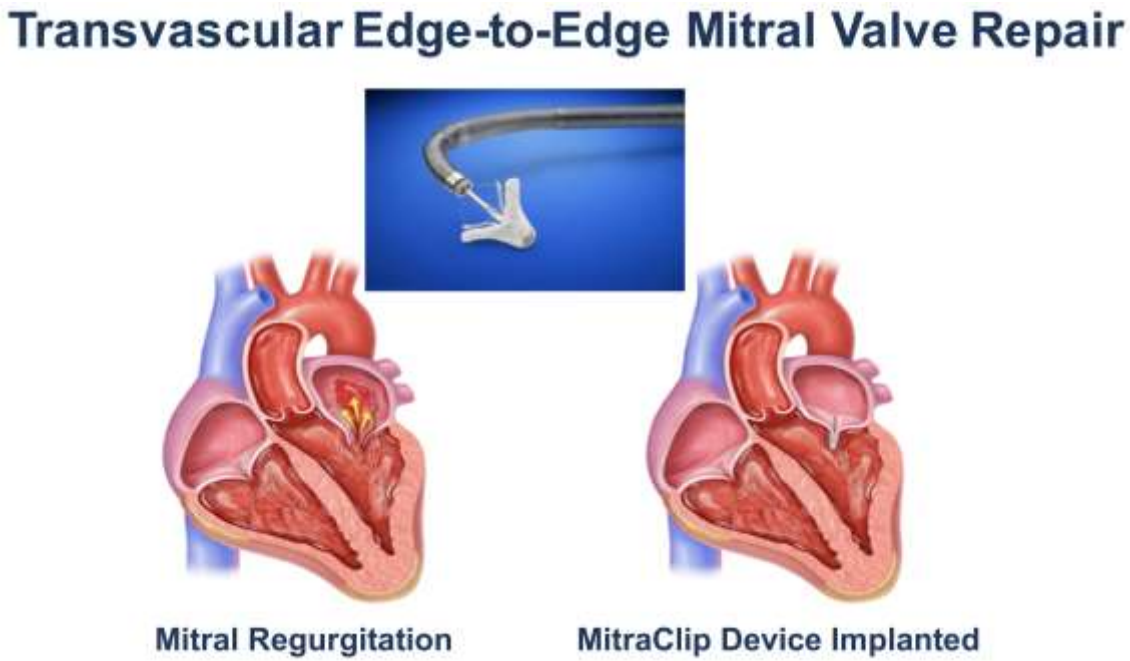
What is Mitral-Clip

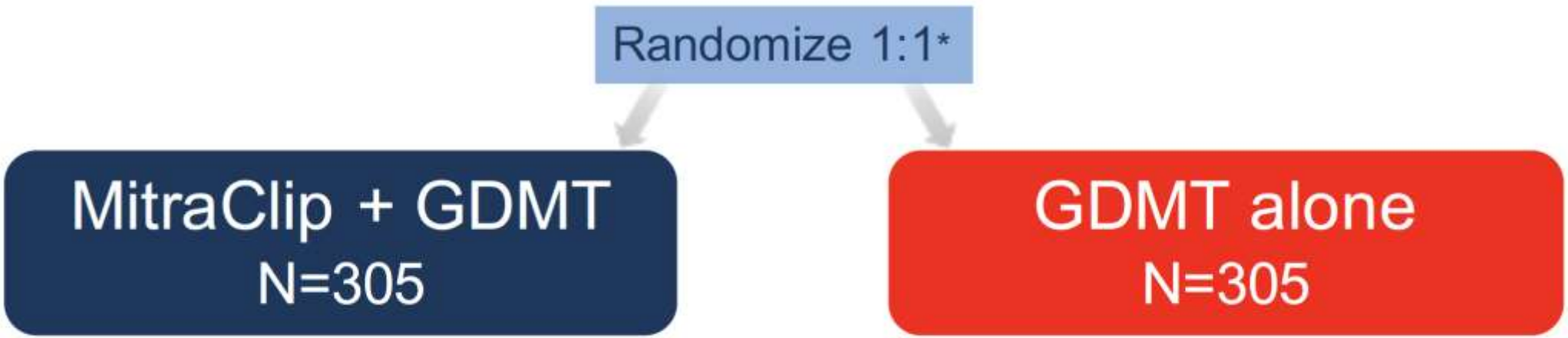




The COAPT Trial Design

Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation

A parallel-controlled, open-label, multicenter trial in ~610 patients with heart failure and moderate-to-severe (3+) or severe (4+) secondary MR who remained symptomatic despite maximally-tolerated GDMT

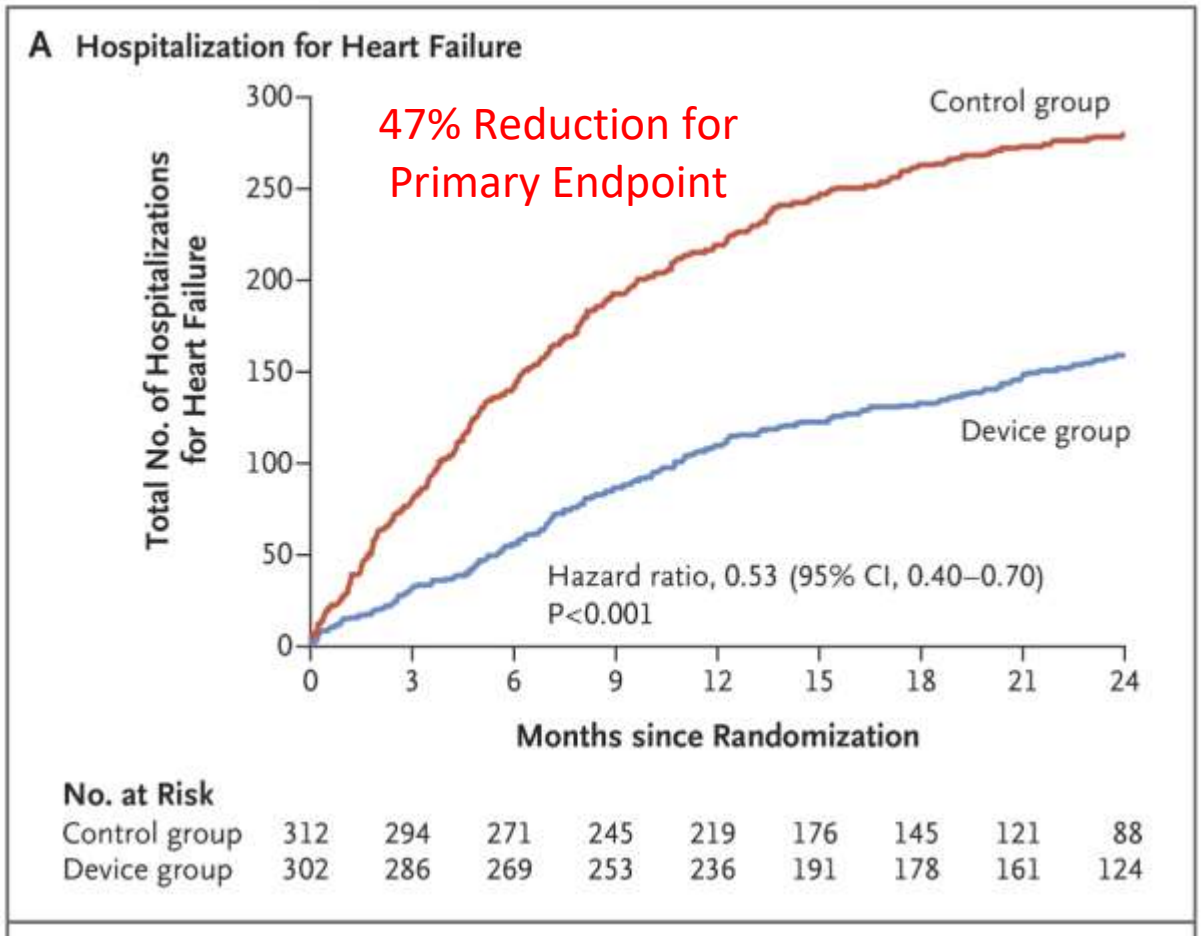


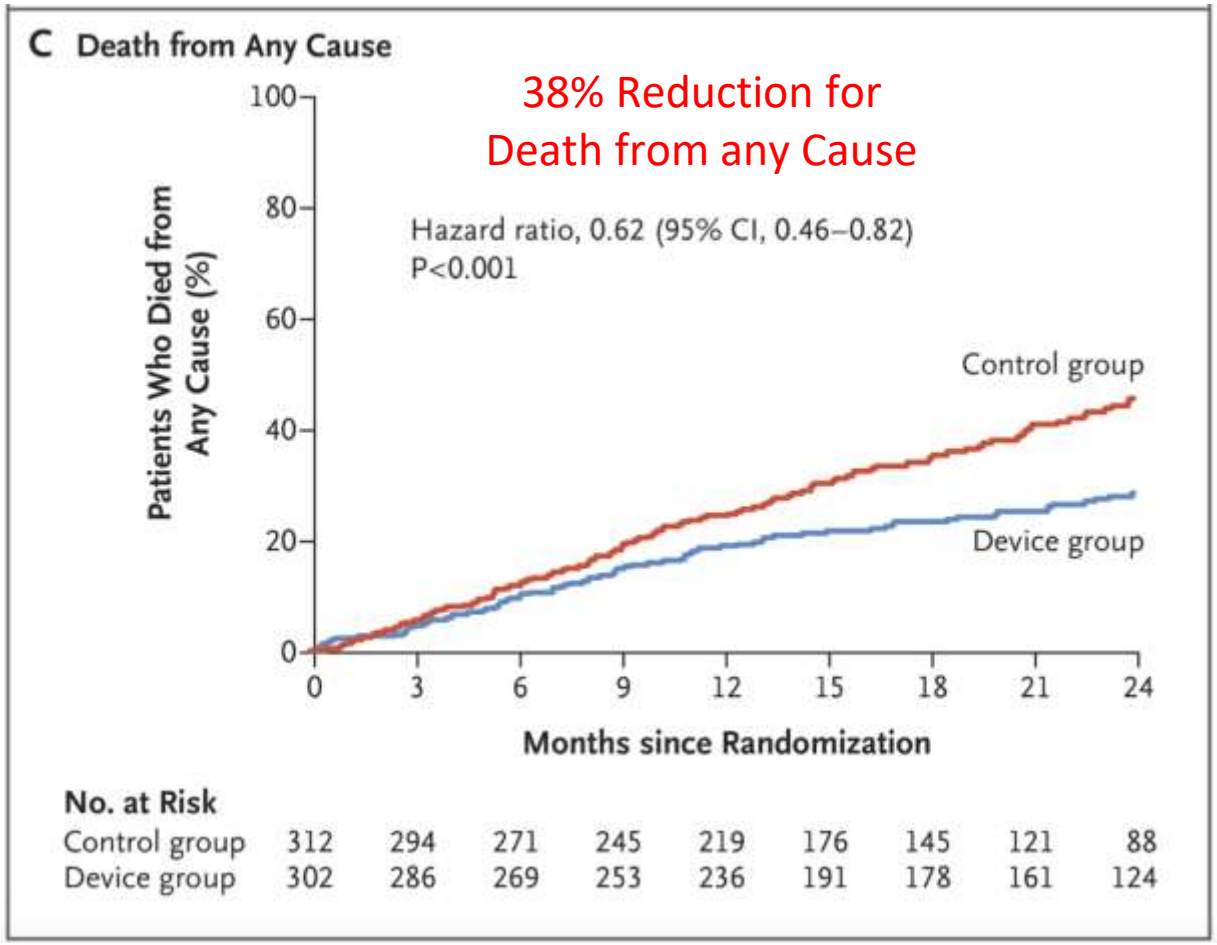
*Stratified by cardiomyopathy etiology (ischemic vs. non-ischemic) and site

Principal Investigators: Gregg Stone, Michael Mack, William Abraham, Joann Lindenfeld,

NEJM Dec 23, 2018

COAPT Trial Results





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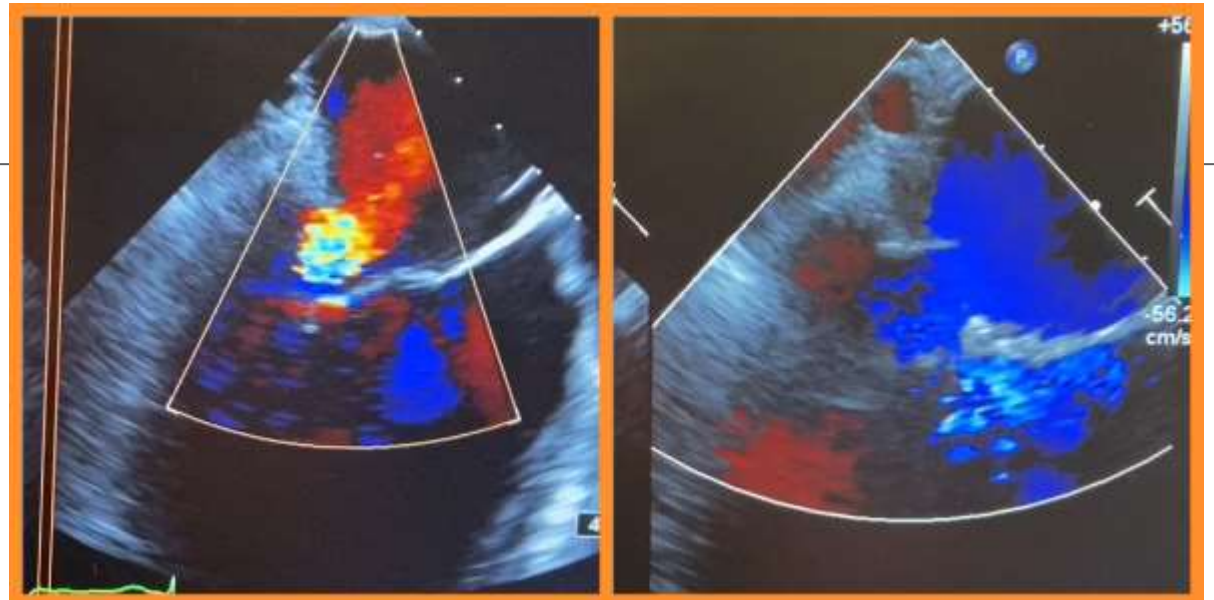
NEJM Dec 23, 2018



MitraClip
Pre MR 3+
Post MR <1
1 NTR at A2/P2

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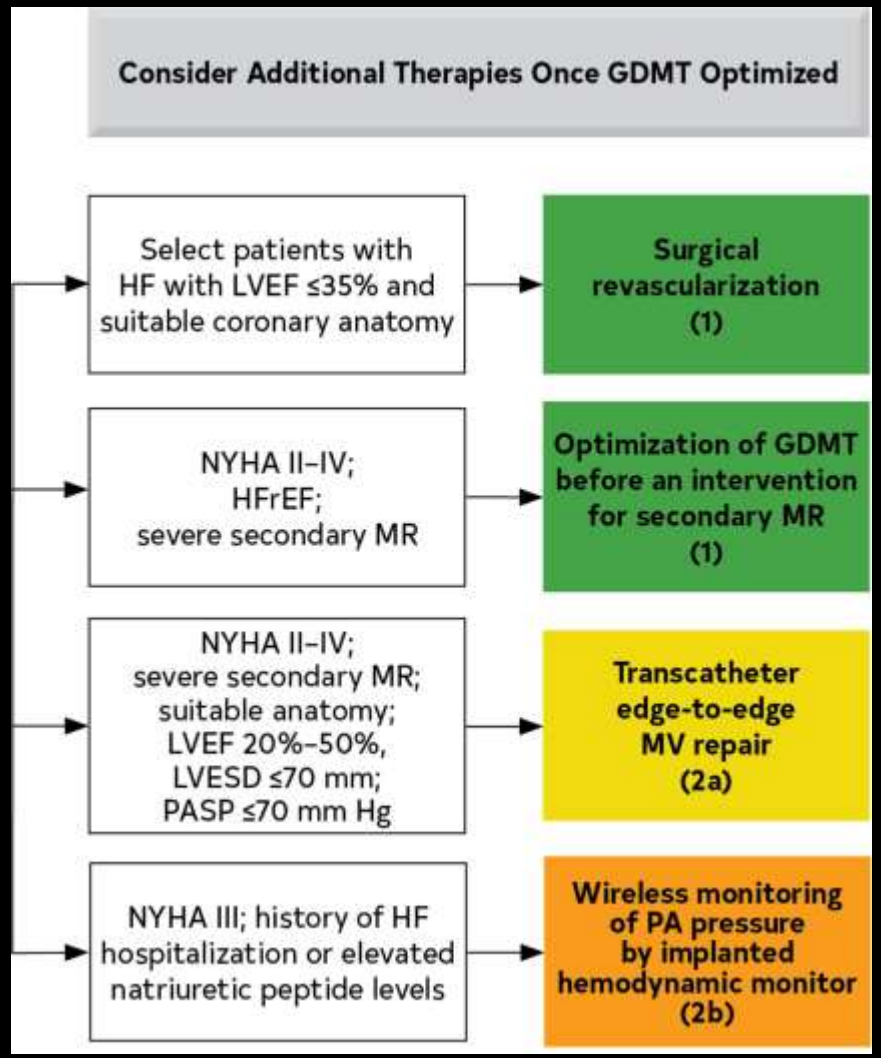
Courtesy of Dr Sharma

Figure 9



Journal of Cardiac Failure DOI: (10.1016/j.cardfail.2022.02.010)

Acute Decompensated Heart Failure

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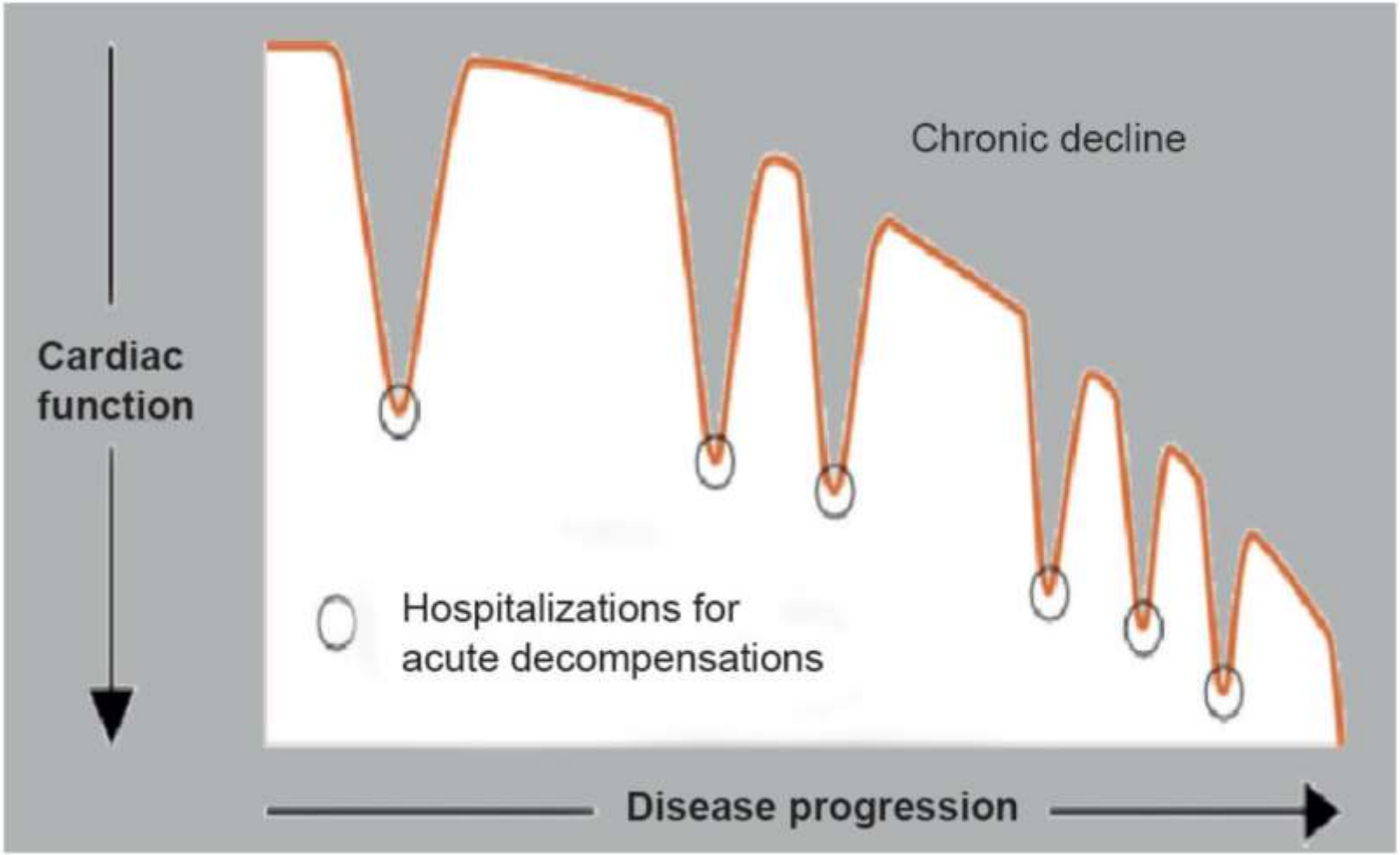
Hospitalization for HF is a Sentinel Event



Patients admitted with Acute Decompensated HF

Recommendations for Assessment of Patients Hospitalized With Decompensated HF		
COR	**LOE**	**Recommendations**
1	**C-LD**	1. In patients hospitalized with HF, severity of congestion and adequacy of perfusion should be assessed to guide triage and initial therapy.[1–5]
1	**C-LD**	2. In patients hospitalized with HF, the common precipitating factors and the overall patient trajectory should be assessed to guide appropriate therapy.[5,6]
Goals for Optimization and Continuation of GDMT		
1	**C-LD**	3. For patients admitted with HF, treatment should address reversible factors, establish optimal volume status, and advance GDMT toward targets for outpatient therapy.[6]

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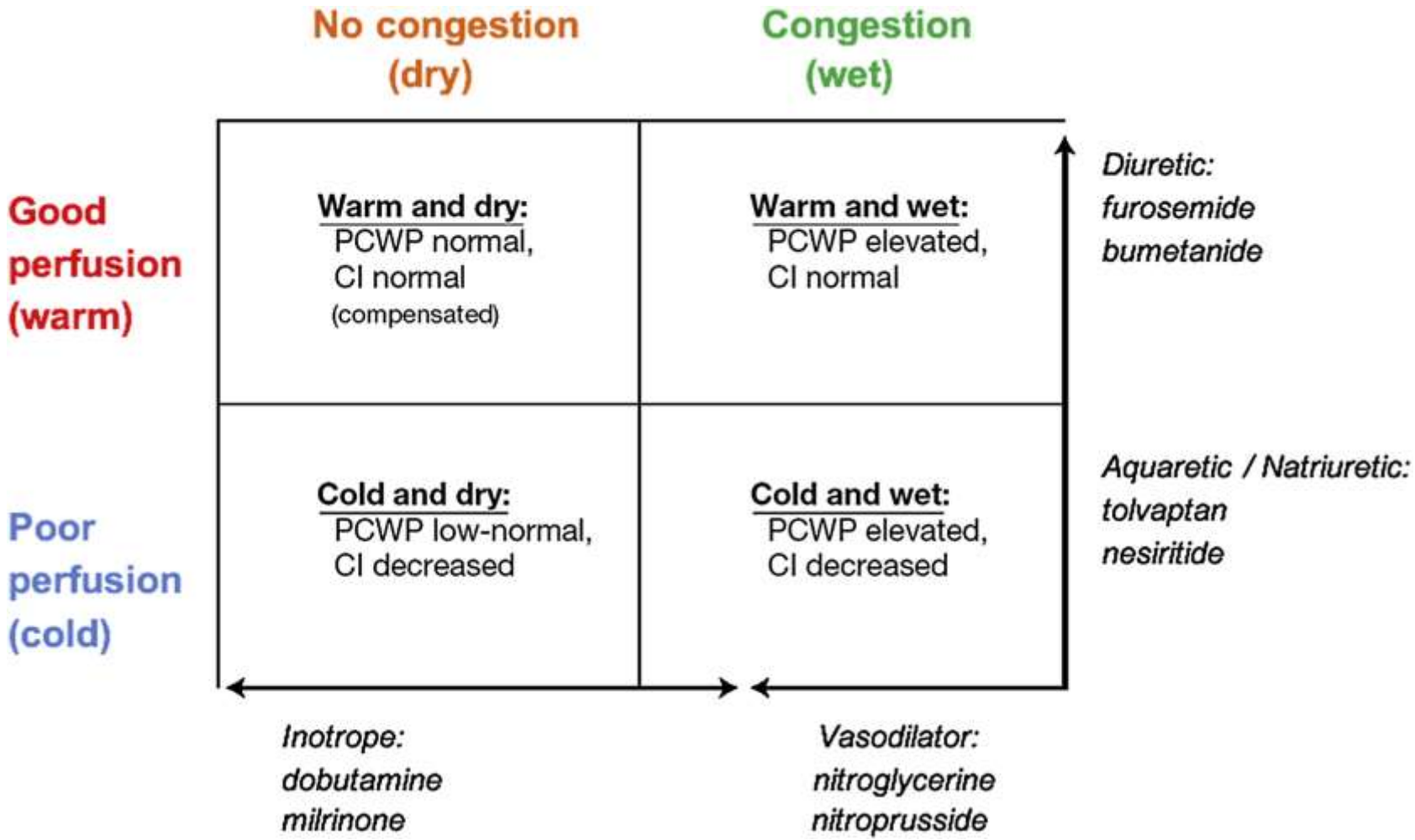

No congestion (dry)
Congestion (wet)
Good perfusion (warm)
Poor perfusion (cold)
Warm and dry:
PCWP normal,
CI normal
(compensated)
Warm and wet:
PCWP elevated,
CI normal
Cold and dry:
PCWP low-normal,
CI decreased
Cold and wet:
PCWP elevated,
CI decreased
Diuretic:
furosemide
bumetanide
Aquaretic / Natriuretic:
tolvaptan
nesiritide
Inotrope:
dobutamine
milrinone
Vasodilator:
nitroglycerine
nitroprusside

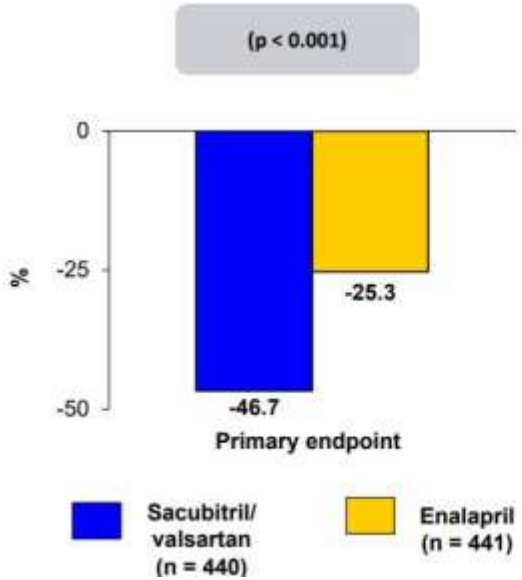
Inpatient use of ARNI

PIONEER-HF

#AHA18

AMERICAN COLLEGE of CARDIOLOGY

Trial description: Patients hospitalized with acute decompensated heart failure (ADHF) were randomized in a 1:1 fashion to either sacubitril/valsartan or enalapril. Patients were followed for 8 weeks.



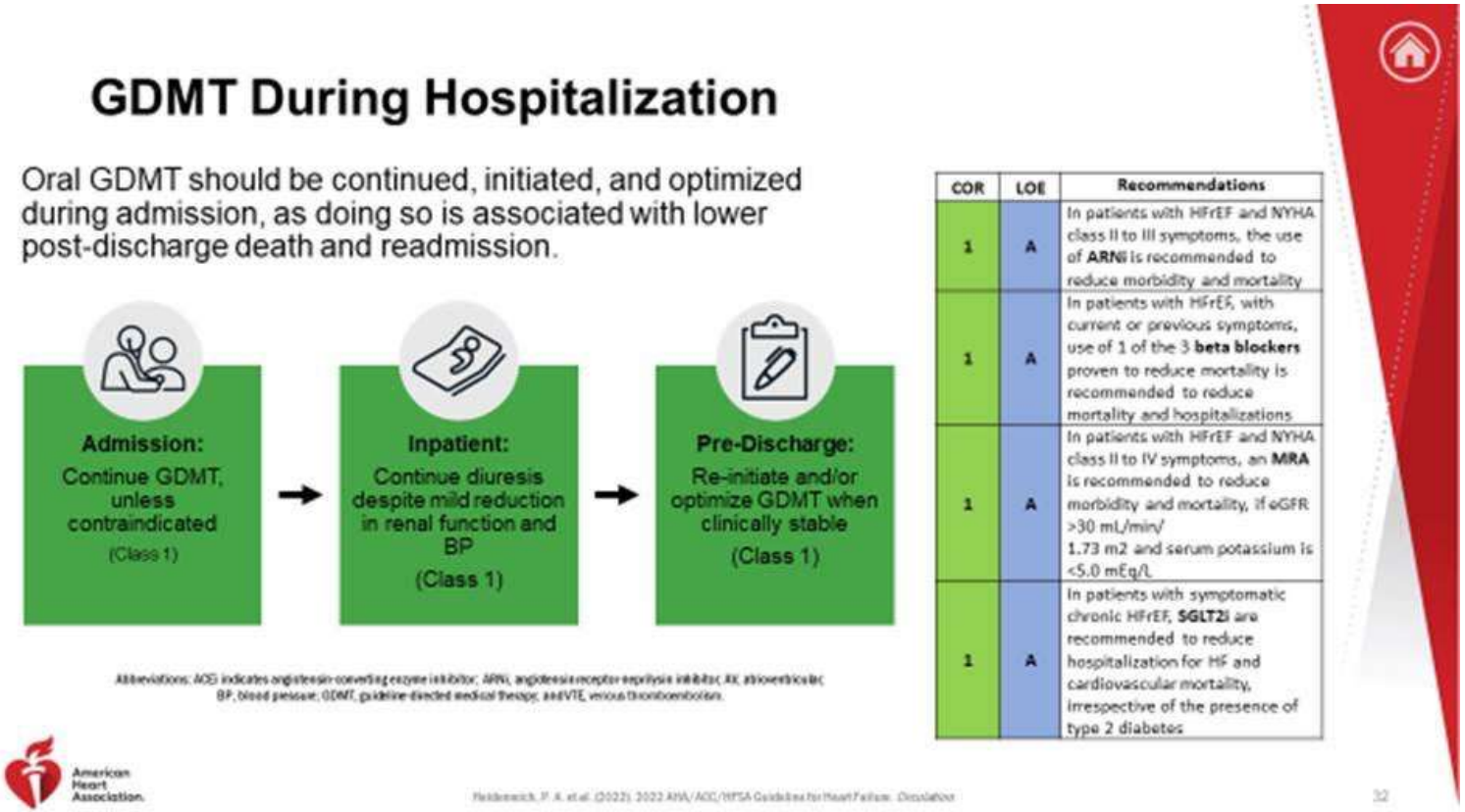
RESULTS

- Primary endpoint, time-averaged reduction in NT-proBNP: sacubitril/valsartan vs. enalapril: -46.7% vs. -25.3%, $p < 0.001$
- Worsening renal function: 13.6% vs. 14.7%, $p > 0.05$, symptomatic hypotension: 15.0% vs. 12.7%, $p > 0.05$
- Rehospitalization for HF: 8.0% vs. 13.8%, $p < 0.05$

CONCLUSIONS

- Sacubitril/valsartan reduced NT-proBNP more than enalapril among patients with ADHF; noted as early as 1 week after drug initiation
- Although not powered for clinical endpoints, a reduction in rehospitalization for HF was noted

Velazquez EJ, et al. N Engl J Med 2018;Nov 11:[Epub]



- ARNI + BB + MRA + SGLT2-
- ↓ ↓ ↓ Post Discharge HF Hospitalization and Survival
- How to Implement?
  - Changing our goals in a patient with ADHF
  - Transition of Care Pharmacist

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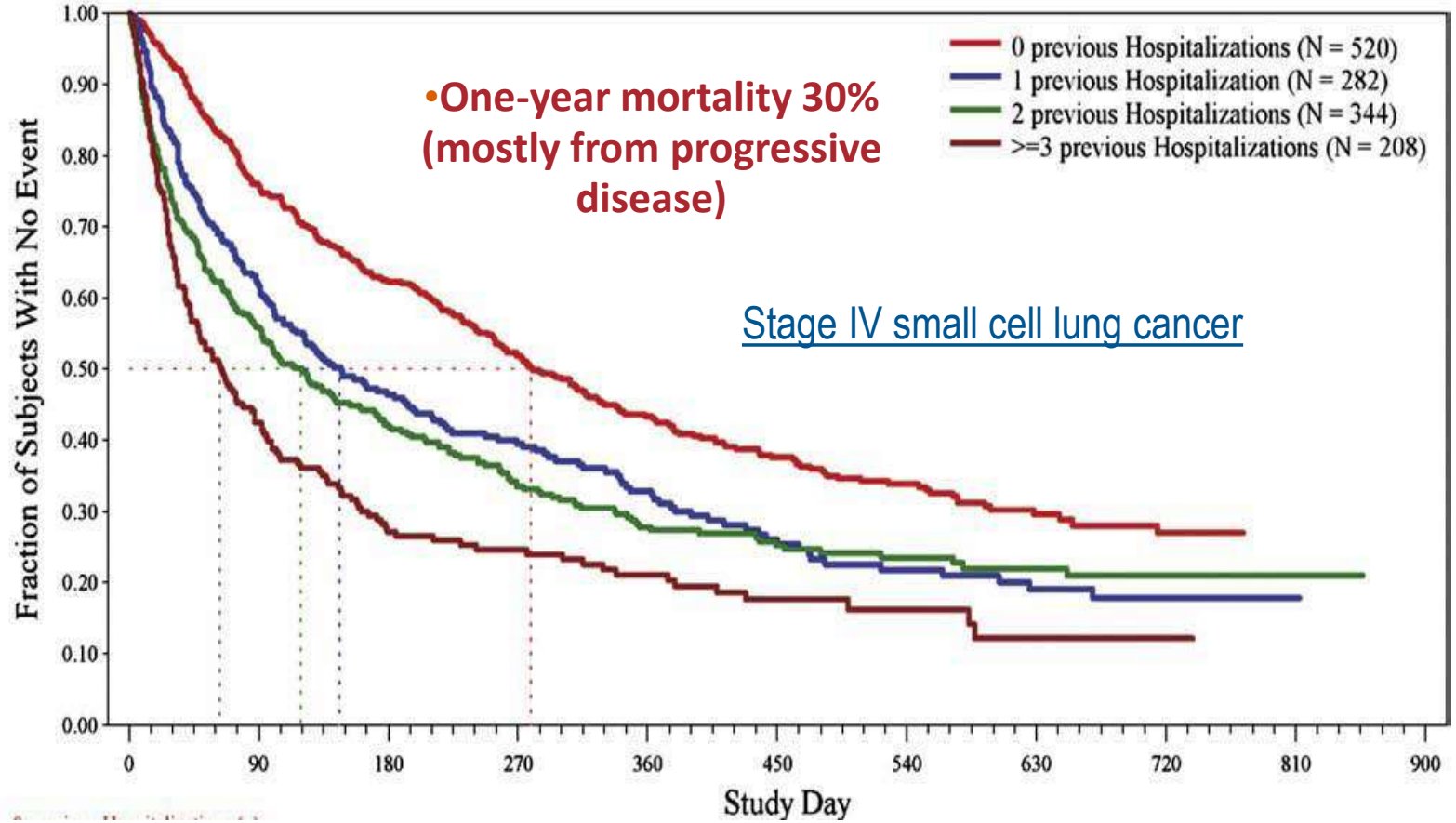
Advanced Heart Failure

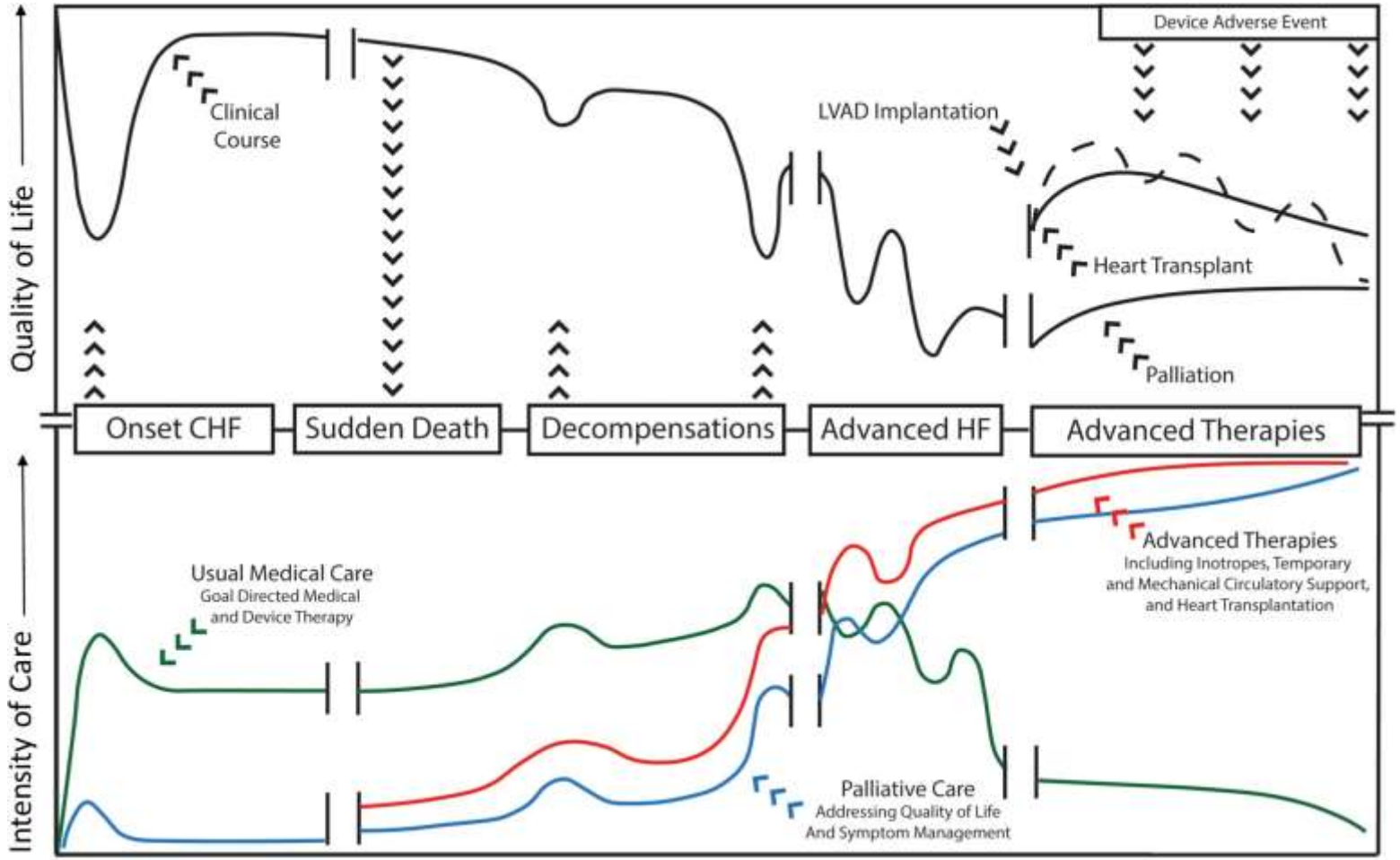
Advanced Heart Failure Outcomes



- **One-year hospitalization: 60% (2/3 > than once)**

Constanzo MR et al. Am Heart J. 2008; 155: 341-349

HF is a Progressive Condition

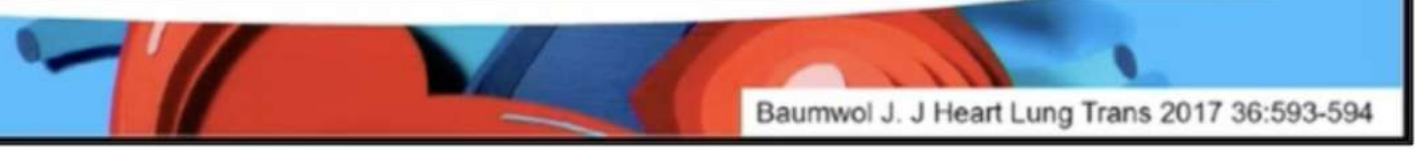


JACC 2020.July, 8 (7) 523-536

Markers of Advanced Heart Failure

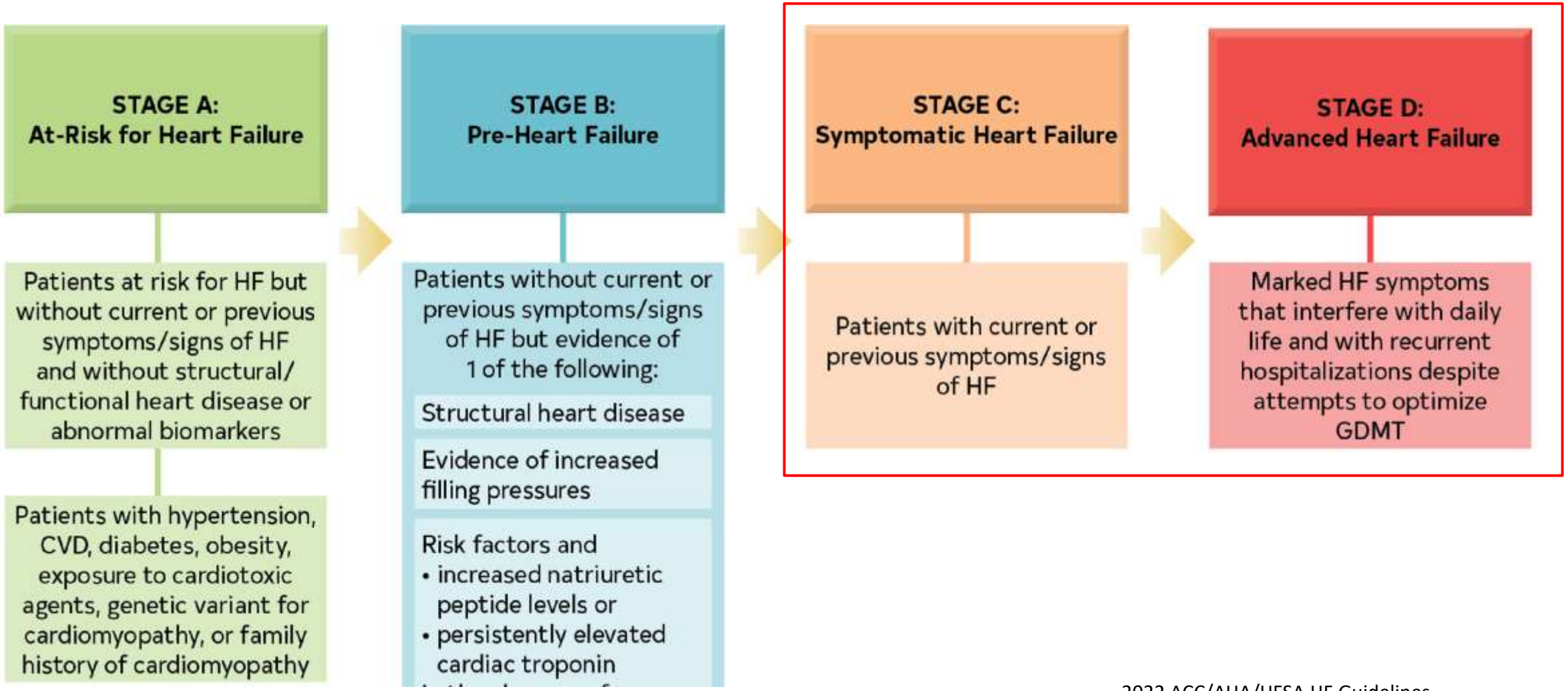
I	Inotropes	Previous or ongoing
N	NYHA class/Natriuretic peptides	NYHA III/IV or high NT-pBNP
E	End-organ dysfunction	Worsening renal/liver function
E	Ejection fraction	EF <20%
D	Defibrillator shocks	Appropriate shocks
H	Hospitalizations	≥1 HF hospitalizations in 12 months
E	Edema/Escalating diuretics	Persistent overload, diuretic resistance
L	Low blood pressure	<90mmHg
P	Prognostic medication	Inability to titrate (or decrease) GDMT

ACC.21



Baumwol J. J Heart Lung Trans 2017 36:593-594

Staging of Heart Failure



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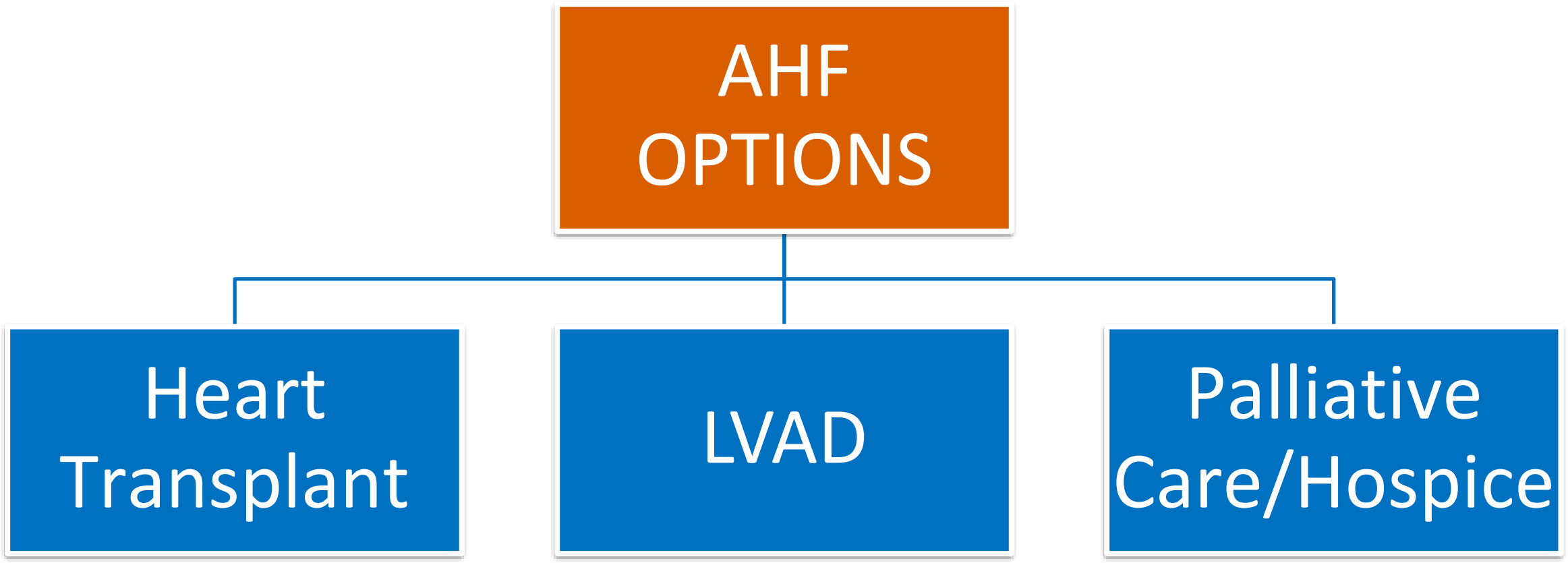
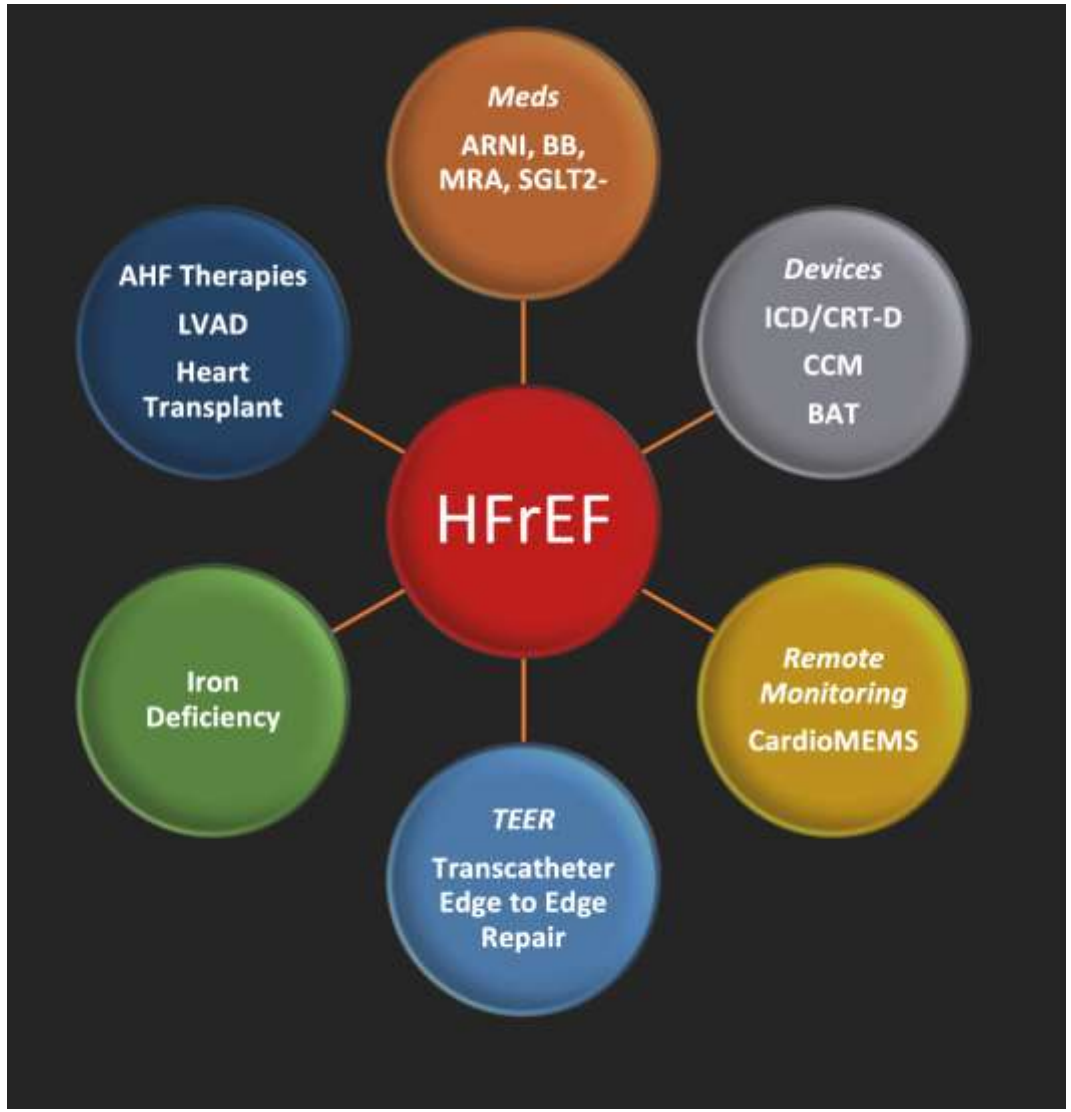
4.1.2022

AHF Management



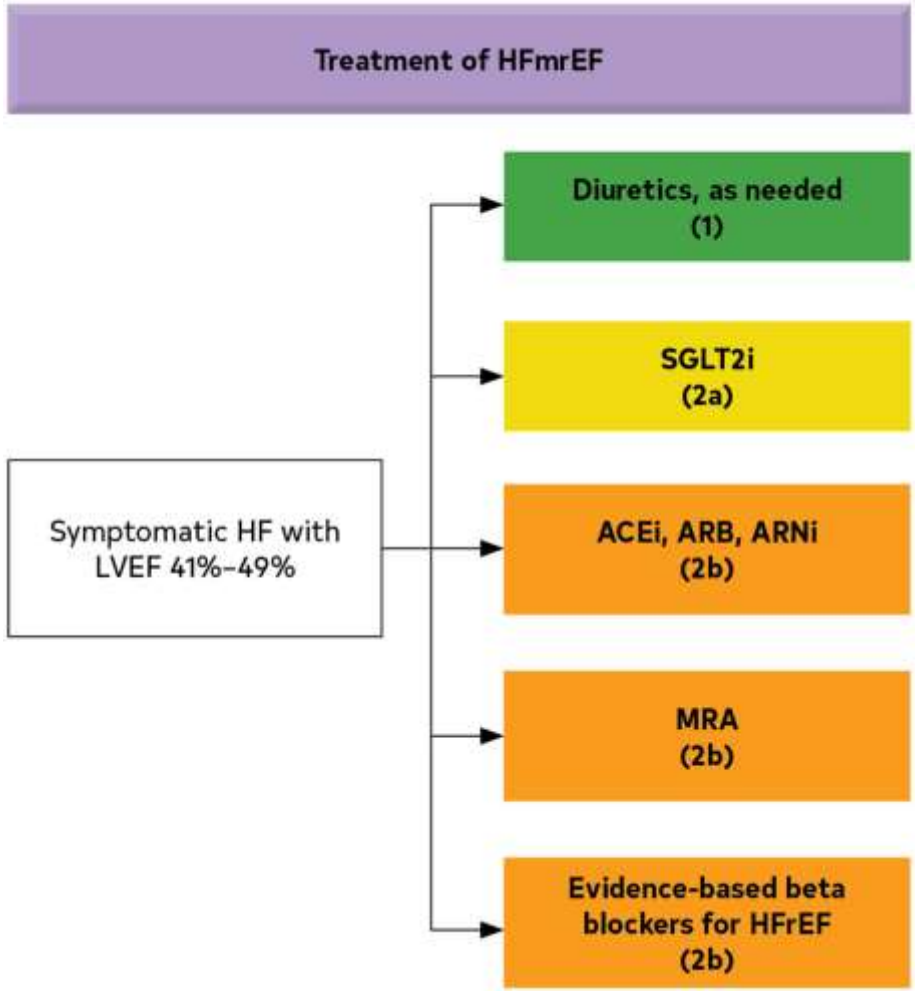
HFrEF: Heart Success, Not Failure



Dignity Health
Heart and Vascular Institute of Greater Sacramento

Heart Failure with Mild Reduced EF (41-49%)

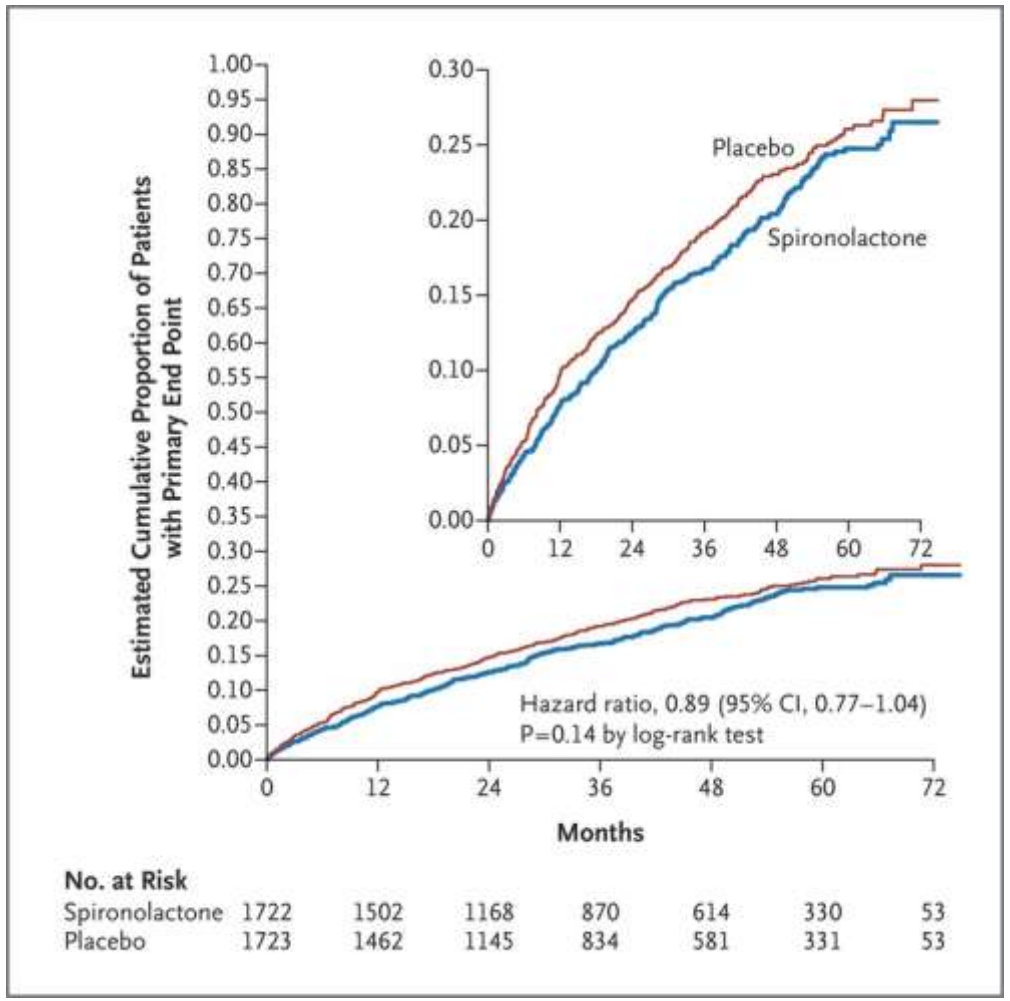
Heart Failure with Mildly Reduced Ejection Fraction (41-49%)



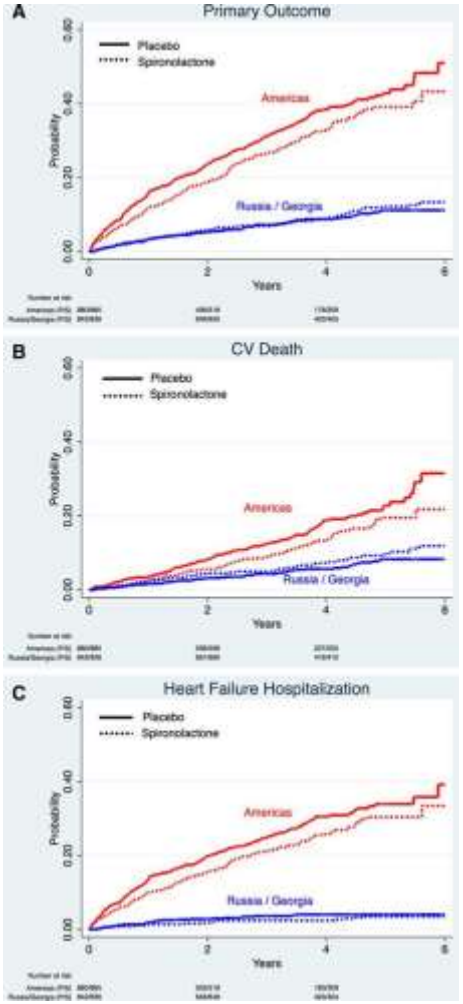
Published 4.1.2022
Journal of Cardiac Failure

Heart Failure with Preserved EF (>50%)

TOPCAT Study (Post Hoc Analysis)



NEJM 4.10.14



Circulation 11.18.14

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Heart and Vascular Institute
of Greater Sacramento

ORIGINAL ARTICLE FREE PREVIEW

Empagliflozin in Heart Failure with a Preserved Ejection Fraction

Stefan D. Anker, M.D., Ph.D., Javed Butler, M.D., Gerasimos Filippatos, M.D., Ph.D., João P. Ferreira, M.D., et al., for the EMPEROR-Preserved Trial Investigators*

October 14, 2021

N Engl J Med 2021; 385:1451-1461

DOI: 10.1056/NEJMoa2107038

EMPEROR-PRESERVED

Empagliflozin in Heart Failure with a Preserved Ejection Fraction

Anker et al, Aug 27, 2021. NEJM.

QUESTION

In patients with heart failure and a preserved ejection fraction, does Empagliflozin improve outcomes?

INCLUDED

- 18 and older
- NYHA II-IV
- LVEF > 40%
- ntProBNP>300; or>900 if AFib
- Evidence of LAE or LVH
- Stable diuretic use
- BMI <45 kg/m2

5988 PATIENTS

EMPAGLIFLOZIN 10MG
(SGLT-2 INHIBITOR)

vs

PLACEBO

Stratified by region, diabetes status, eGFR of 50, and LVEF 50%

PRIMARY OUTCOME

CV Death*
HF Hospitalization

13.8%

17.1%

HR 0.79; 95%CI 0.69-0.90; P<0.001

*Mostly driven by HF hospitalizations

SECONDARY OUTCOMES

HF Hospitalization

↓ WITH EMPAGLIFLOZIN

HR 0.73; 95% CI, 0.61-0.88; P<0.001

Rate of GFR decline

E -1.25 vs. -2.62 P

ml/min/1.73m2/year; P<0.001

CONCLUSION

Empagliflozin reduced the combined risk of cardiovascular death or heart failure hospitalization in patients with heart failure with preserved ejection fraction, regardless of the presence or absence of diabetes.

@IsaMathiasMD

2022 ACC/AHA/HFSA Guidelines for HFpEF

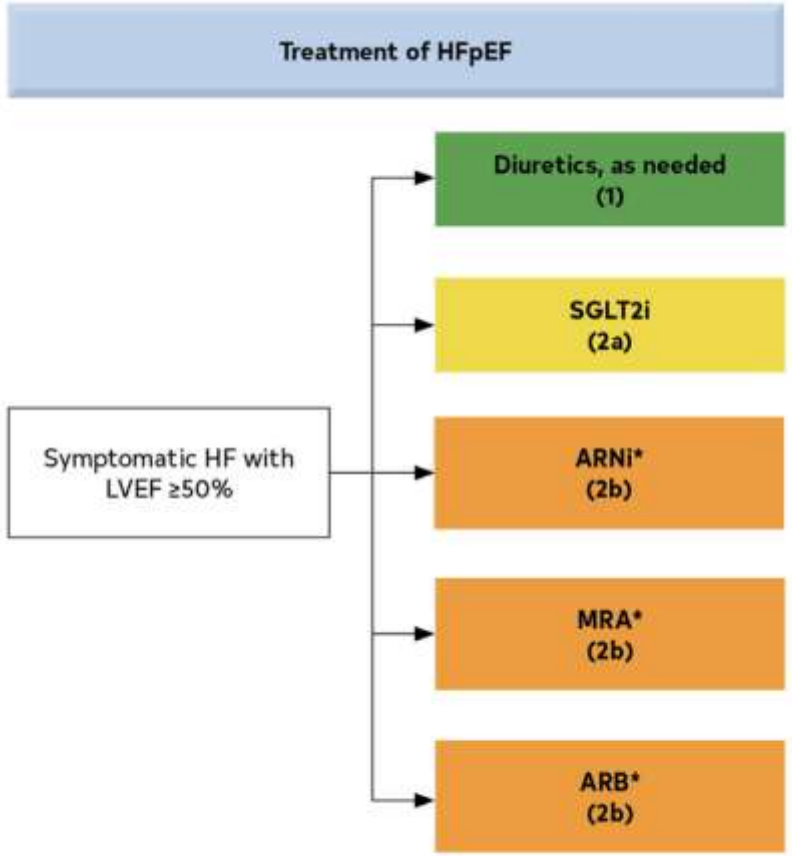

Figure 12. Recommendations for Patients With Preserved LVEF (≥50%)

Summary

- Updated 2022 ACC/AHA/HFSA Guidelines on HF
- Classification of Heart Failure (HFrEF, HFmrEF, HFpEF)
- QUAD Therapy for HFrEF (ARNI, BB, MRA, SGLT2-)
- Recognition of AHF
- Guidelines on management of HFmrEF (41-49%)
- Guidelines on management of HFpEF

Thank You

Munir S Janmohamed M.D. FACC, FHFSA

@DrMunirJanmohamed