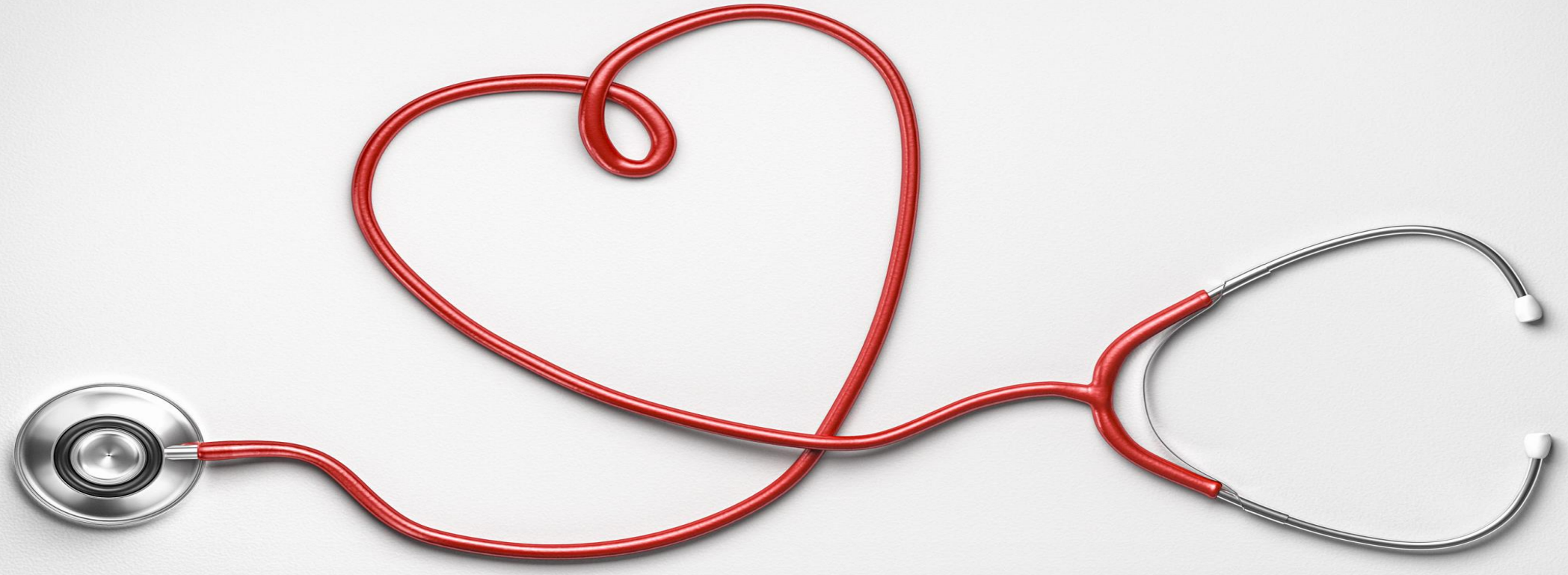


IMPLEMENT-EF: Clinical Perspectives – Foundations of HFpEF/HFmrEF

Webinar will begin shortly

American Heart Association.
IMPLEMENT-EF

The American Heart Association's IMPLEMENT-EF initiative is supported by Bayer

Initiative **Overview**

Scan the QR code to see a map of participating sites, stay informed about upcoming educational opportunities, and insights from the initiative.

heart.org/IMPLEMENTEF

GOALS:

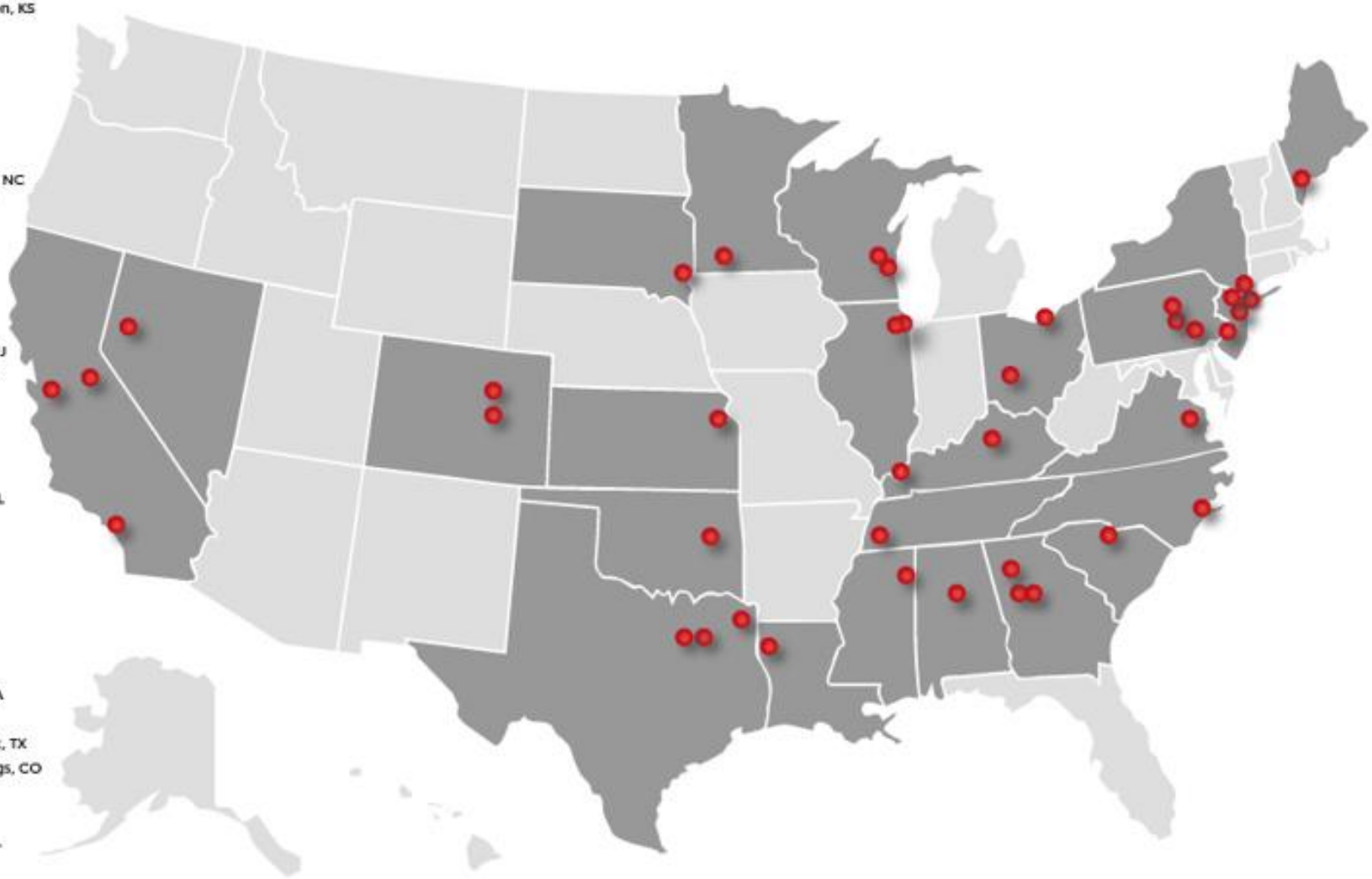
- In 2025, the American Heart Association, launched a quality improvement initiative.
- Discover current gaps and identify ideal care models in the HFpEF/HFmrEF patient journey
- Build a network of multidisciplinary team members focused on improving HFpEF/HFmrEF care
- Amplify HFpEF/HFmrEF awareness with providers and monitoring adherence to evidence-based therapies for HFpEF/HFmrEF patients in hospitals

https://www.heart.org/en/professional/quality-improvement/implement-ef

American Heart Association.
IMPLEMENT-EF

IMPLEMENT-EF Participating Sites

1.	AdventHealth Redmond	Rome, GA
2.	AdventHealth Shawnee Mission	Shawnee Mission, KS
3.	Avera McKennan Hospital & University Health Center	Sioux Falls, SD
4.	Baptist Health Paducah	Paducah, KY
5.	Baptist Health Lexington	Lexington, KY
6.	Baptist Memorial Hospital - Memphis	Memphis, TN
7.	Bon Secours St. Mary's Hospital	Richmond, VA
8.	Carolina Pines Regional Medical Center	Hartsville, SC
9.	Carteret Health Care	Morehead City, NC
10.	Cleveland Clinic	Cleveland, OH
11.	Dayton Veterans Affairs Medical Center	Dayton, OH
12.	Froedtert Hospital	Milwaukee, WI
13.	Froedtert West Bend Hospital	West Bend, WI
14.	Geisinger Medical Center	Danville, PA
15.	Hackensack Meridian JFK University Medical Center	Edision, NJ
16.	Hackensack Meridian Southern Ocean Medical Center	Manahawkin, NJ
17.	Hackensack University Medical Center	Hackensack, NJ
18.	MaineHealth Maine Medical Center Biddeford	Biddeford, ME
19.	Mount Sinai Health System	New York, NY
20.	Murray County Medical Center	Slayton, MN
21.	North Mississippi Medical Center	Tupelo, MS
22.	Northwestern Medicine Palos Hospital	Palos Heights, IL
23.	NYC Health + Hospitals / Elmhurst	Elmhurst, NY
24.	Ochsner LSU Health Shreveport	Shreveport, LA
25.	Penn Medicine Lancaster General Health	Lancaster, PA
26.	Penn State Health Milton S. Hershey Medical Center	Hershey, PA
27.	Renown Regional Medical Center	Reno, NV
28.	Saint Francis Hospital Muskogee	Muskogee, OK
29.	Stanford Health Care	Stanford, CA
30.	Sutter Medical Center, Sacramento	Sacramento, CA
31.	Texas Health Fort Worth	Fort Worth, TX
32.	Titus Regional Medical Center	Mount Pleasant, TX
33.	UCHealth - Memorial Hospital Central	Colorado Springs, CO
34.	UCHealth University of Colorado Hospital	Aurora, CO
35.	UI Health	Chicago, IL
36.	University of Alabama at Birmingham Hospital	Birmingham, AL
37.	University of California Irvine Medical Center	Orange, CA
38.	University of Texas Southwestern Medical Center	Dallas, TX
39.	WellStar Kennestone Regional Hospital	Marrieta, GA
40.	WellStar Paulding Hospital	Hiram, GA



heart.org/IMPLEMENTEF

Clinical Perspectives: Foundations of HFpEF/HFmrEF

Georges Chahoud, MD, FACC, FAHA, FHFSA,
FASE Regional Director, Heart Failure Clinical Program-SSM Health, St. Louis & Southern IL

American Heart Association.

Disclosures

I have these relevant financial relationships. I don not intend to present any off-label indications for medications or devices.

Type of Relationship: Speaker Bureau

- Zoll, Astra Zeneca, Boehringer Ingelheim Pharmaceuticals, Merck, SCpharma, Abiomed, Abbott, Impulse Dynamics, CVRx, Bayer

Type of Relationship: Research

- Zoll, Impulse Dynamics

Type of Relationship: Advisory Board

- Astra Zeneca, Zoll, Bayer, Abiomed

Disclaimer

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Universal Definition of Heart Failure

HF is a Clinical Syndrome

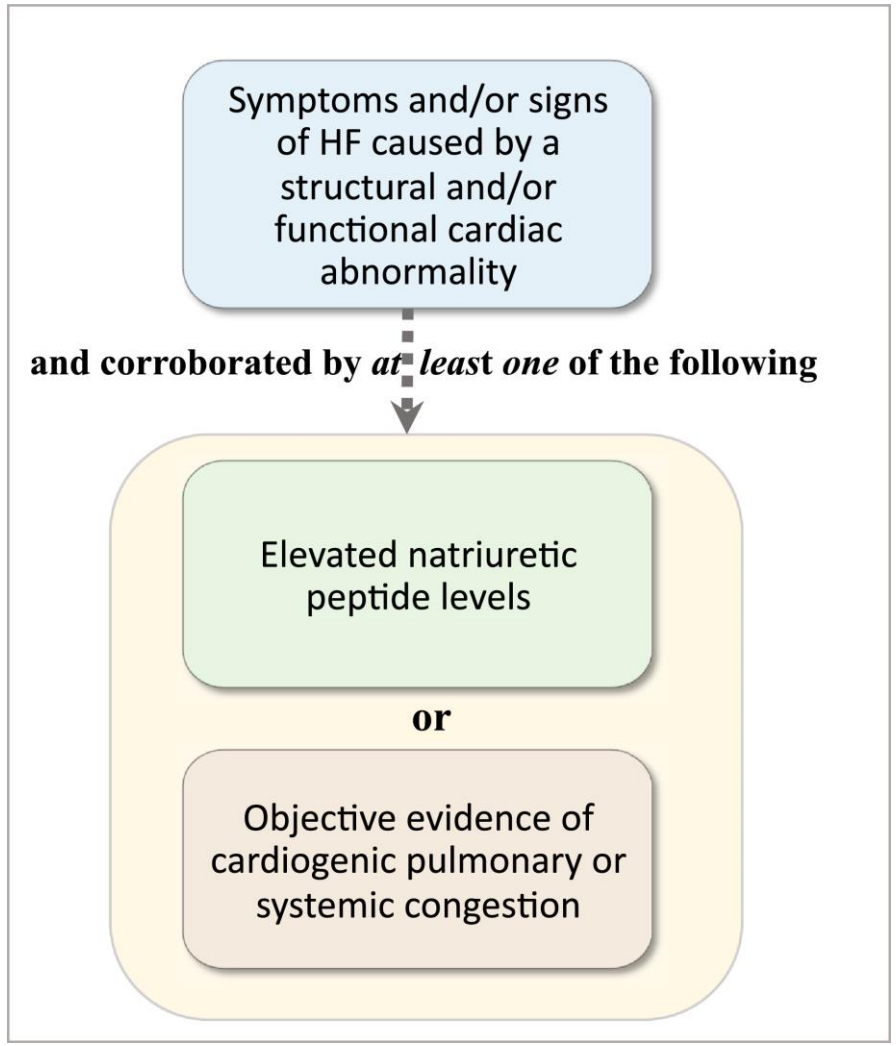
- HF is a clinical syndrome with current or prior ***Symptoms and or signs caused by a structural and/or functional cardiac abnormality***, as determined by
  - Abnormal cardiac chamber enlargement
  - E/E' of >15
  - Moderate/severe ventricular hypertrophy
  - or moderate/severe valvular obstructive or regurgitant lesion

- And corroborated by at least one of the following:
  - ***Elevated natriuretic peptide levels***

Natriuretic Peptide Levels Supporting Definition of HF		
	Ambulatory	Hospitalized/Decompensated
BNP, pg/mL	≥35	≥100
NT-ProBNP, pg/mL	≥125	≥300

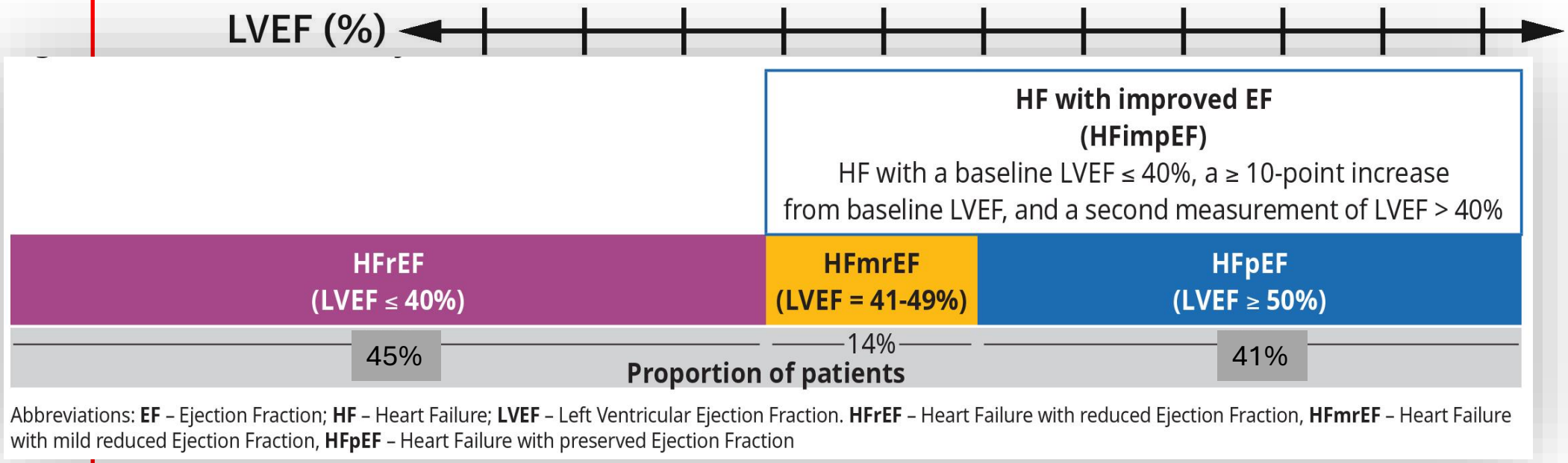
* Reduced specificity in older patients, CKD, A.fib

  - Objective evidence of ***Cardiogenic Pulmonary or Systemic Congestion*** by diagnostic modalities, such as imaging (eg, by chest radiograph or elevated filling pressures by echocardiography) or hemodynamic measurement (eg, right heart catheterization, pulmonary artery catheter) at rest or with provocation (eg, exercise)



Universal definition and classification of Heart Failure: Published March 01, 2021. https://doi.org/10.1016/j.cardfail.2021.01.022

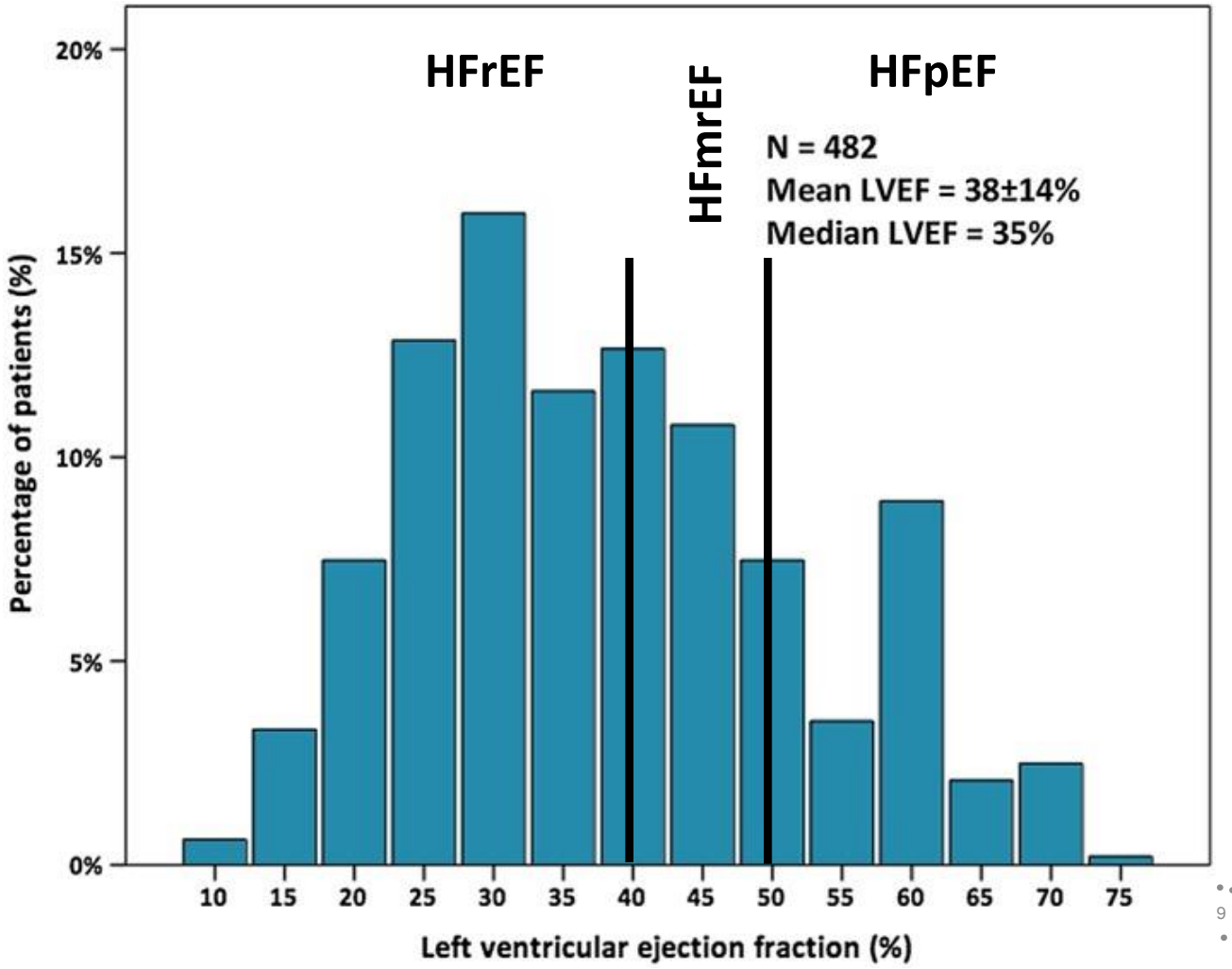
Classification of Heart Failure According to Ejection Fraction



1. Bozkurt B, et al. *J Card Fail*. 2025;31(1):66-116.

Distribution of EF in Heart Failure Patients

- Patients with HFrEF, HFmrEF, and HFpEF share the same cardiovascular risk factors, medical history, and prognosis.
- Patients with HFmrEF have a different clinical profile, which is nearly the same as patients with HFpEF, except for sex.
- Between 13-24% of HF patients have EF below 50% but above 40%, suggesting that there are ~ 1.6 million HFmrEF in the US along.
- These patients have been largely excluded from clinical trials that have focused on patients with HFrEF (usually defined as < 35%) or HFpEF (usually defined as EF > 50%).



Delepaul et al. ESH HF 2017 May;4(2):99-104

What is HFpEF?

How do we make the diagnosis?

- **Classical Definition: Inability of the heart to pump blood adequately *at normal filling pressures* in patient with EF≥50%**
  - New "Universal" Definition: Clinical syndrome with symptoms and or signs caused by a structural and/or functional cardiac abnormality and corroborated by elevated natriuretic peptide levels and/or objective evidence of pulmonary or systemic congestion

- ***Diagnosis relies on finding objective evidence of congestion*:**
  - Physical exam
  - Natriuretic peptides & radiography
  - Echocardiography: left atrial (LA) enlargement, LA dysfunction
  - Catheterization: ↑PCWP (≥15 mmHg at rest, ≥25 mmHg with exercise)

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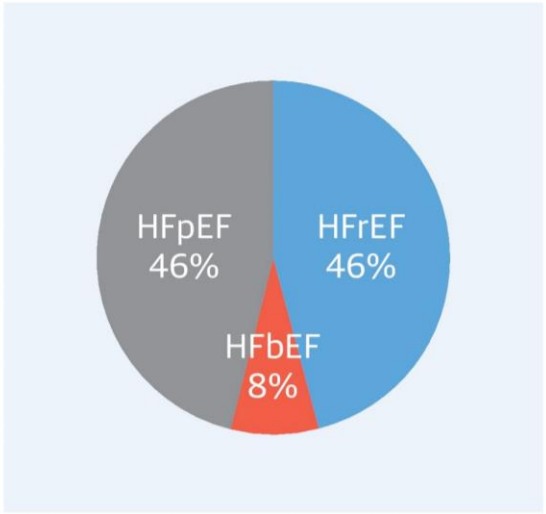
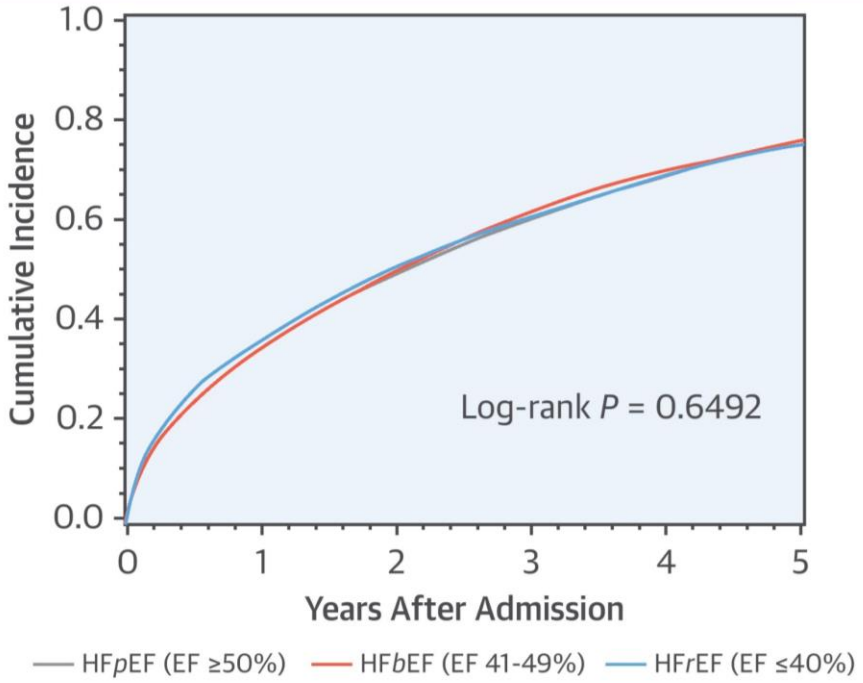
Epidemiology of HFpEF

	HFpEF Incidence	HFpEF Prevalence	HFpEF Clinical Outcomes
	• 27 cases per 10,000 person-years • Lifetime risk: 1 in 10 at age 45 years	• 1.0%-1.5% of population • Highly age dependent	• 5-year mortality: 75.3% (GWTG registry) • 30-day all-cause readmission rate: 21%
Secular trends	↑ incidence over time	↑ prevalence over time	?
Sex differences			
HFpEF vs HFrEF	HFpEF incidence rising relative to HFrEF	HFpEF prevalence rising relative to HFrEF	Similarly poor survival ↓ CV death in HFpEF vs HFrEF

Borlaug BA, et al. J Am Coll Cardiol. 2023;81(18):1810-1834

5-Year Outcome in Patients With HF With Preserved, Borderline, and Reduced EF



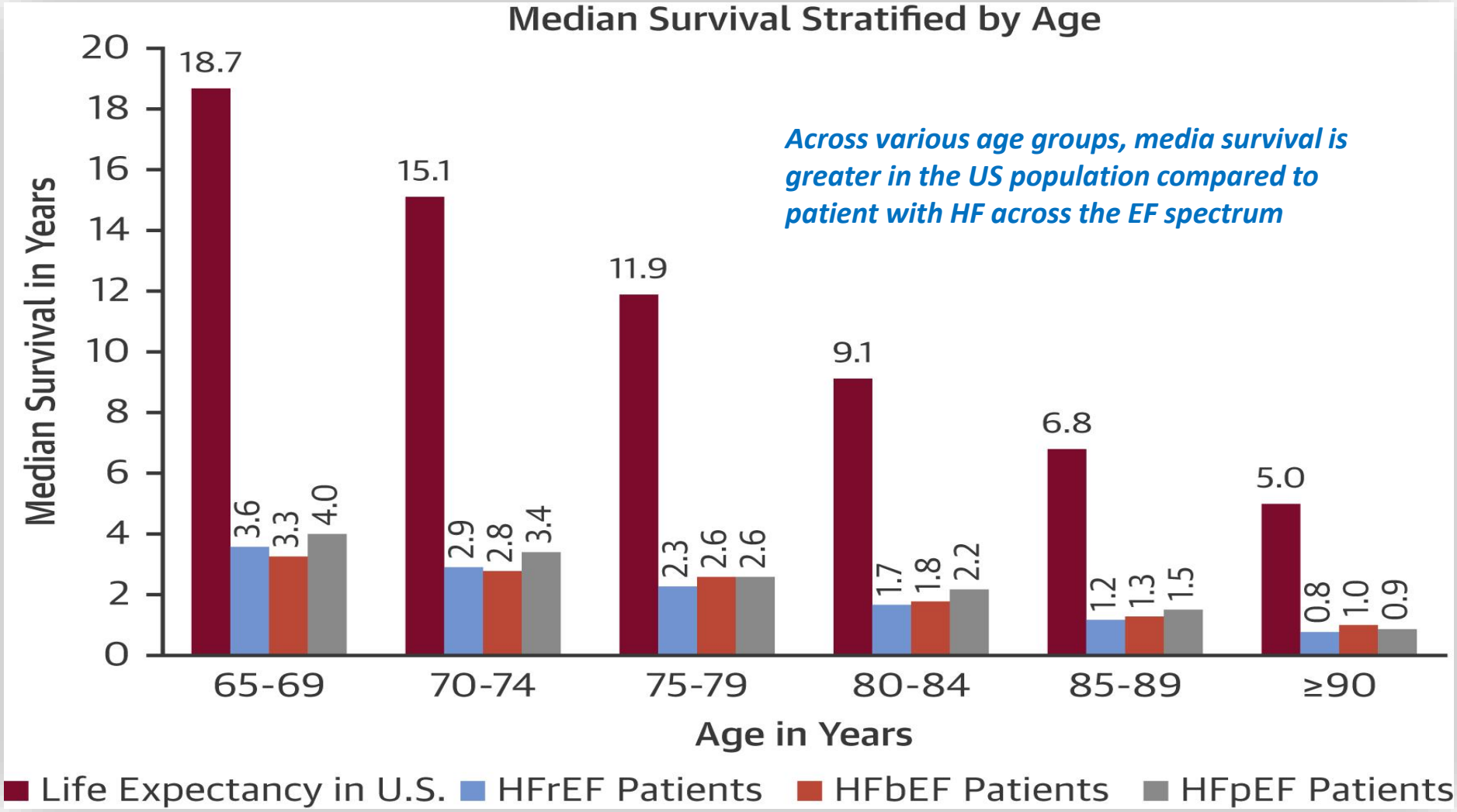


Outcomes – 5-Year Event Rates (%)					
	Mortality	Readmission	CV Readmission	HF Readmission	Mortality/Readmission
HFrEF	75.3	82.2	63.9	48.5	96.4
HFbEF	75.7	85.7	63.3	45.2	97.2
HFpEF	75.7	84.0	58.9	40.5	97.3

Shah, K.S. et al. J Am Coll Cardiol. 2017;70(20):2476-86

Outcomes with HF Hospitalization

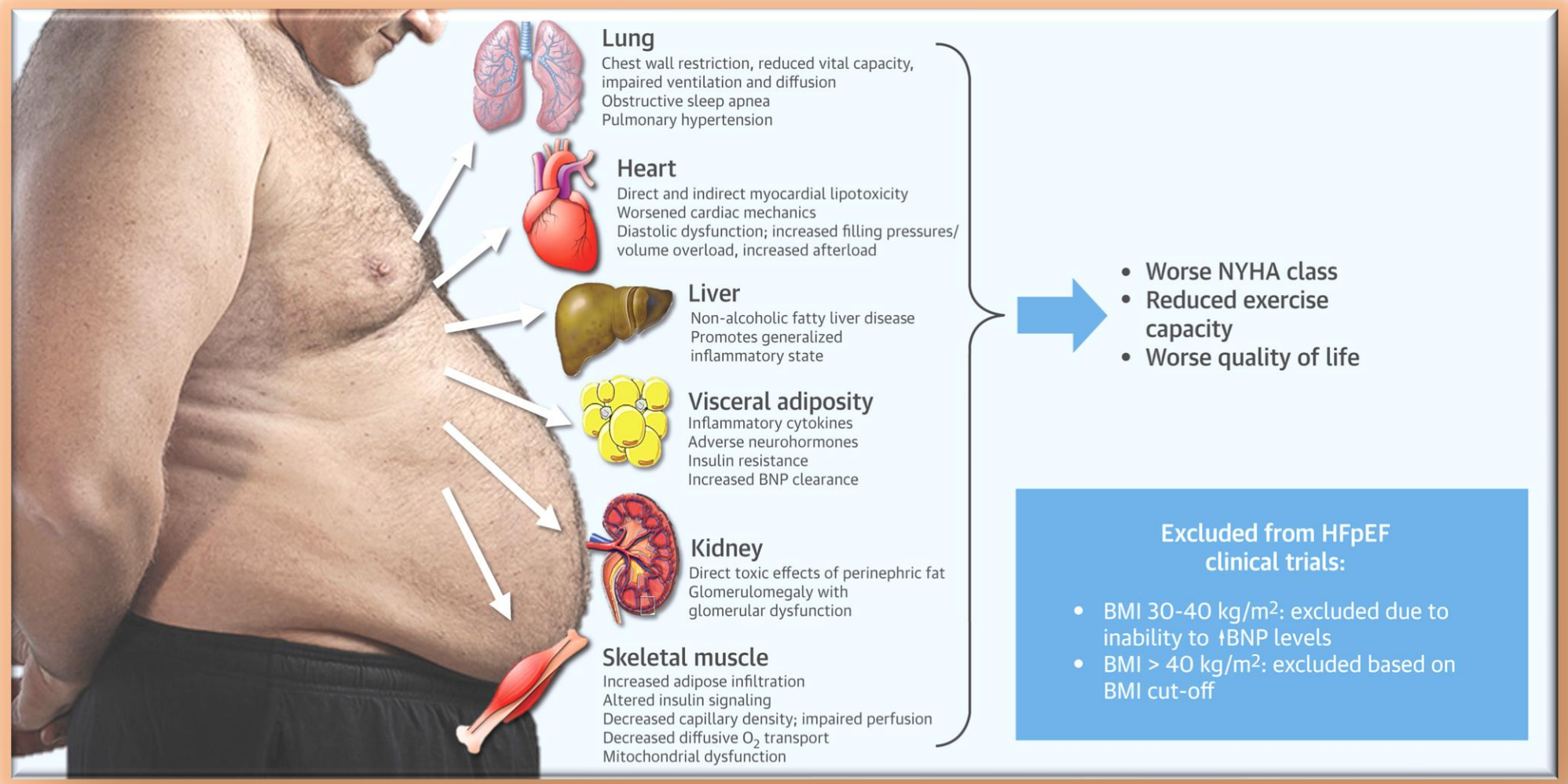
5-year Outcomes Compared with the General US Population



Across various age groups, media survival is greater in the US population compared to patient with HF across the EF spectrum

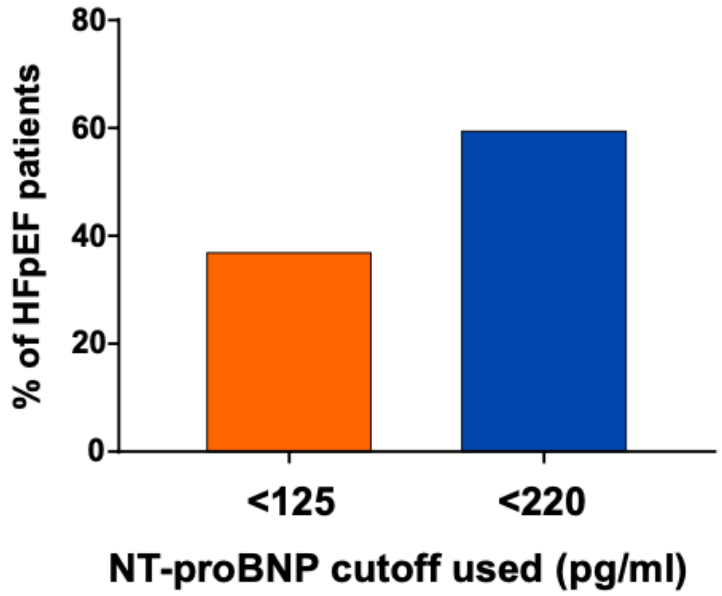
Shah KS, Fonarow, GC et al. J Am Coll Cardiol 2017;70:2476–86

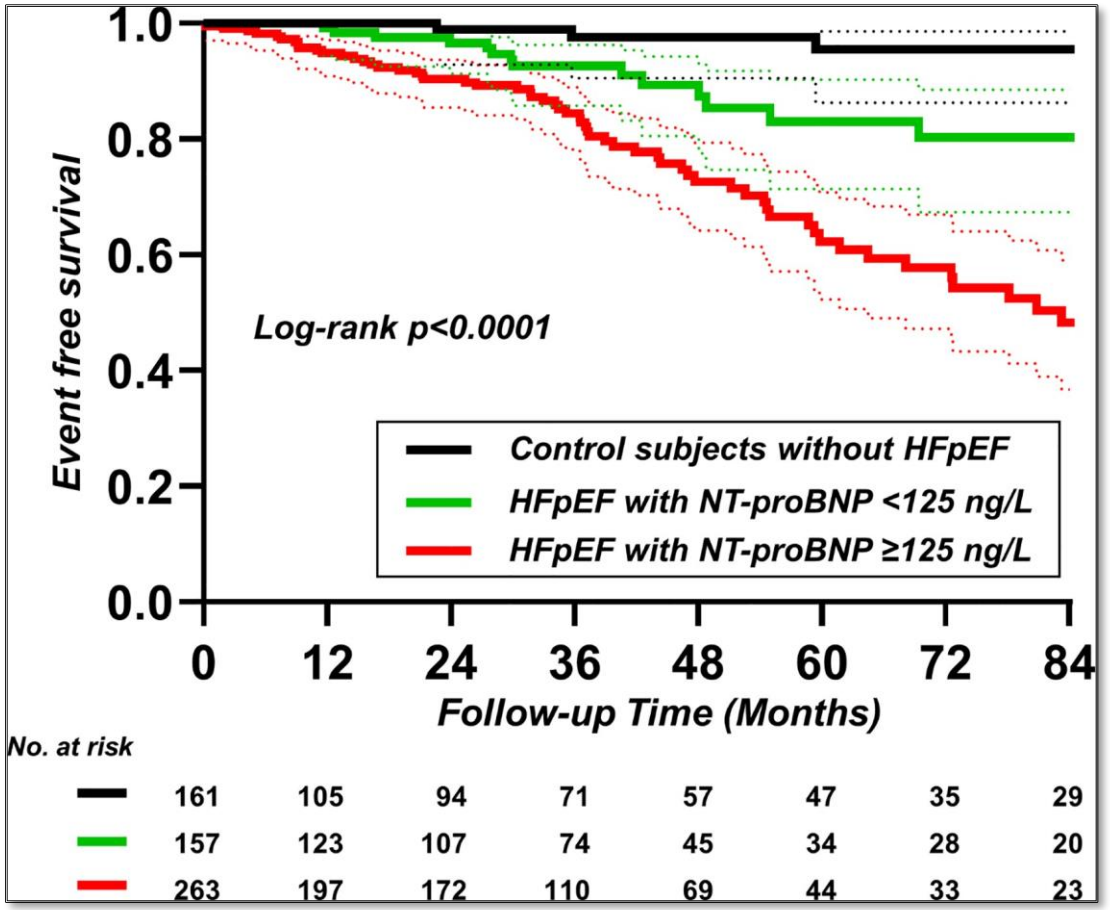
HFpEF: A heterogeneous, systemic syndrome



Kitzman D, Shah SJ. JACC 2016; Borlaug B. Nat Rev Cardiol 2014

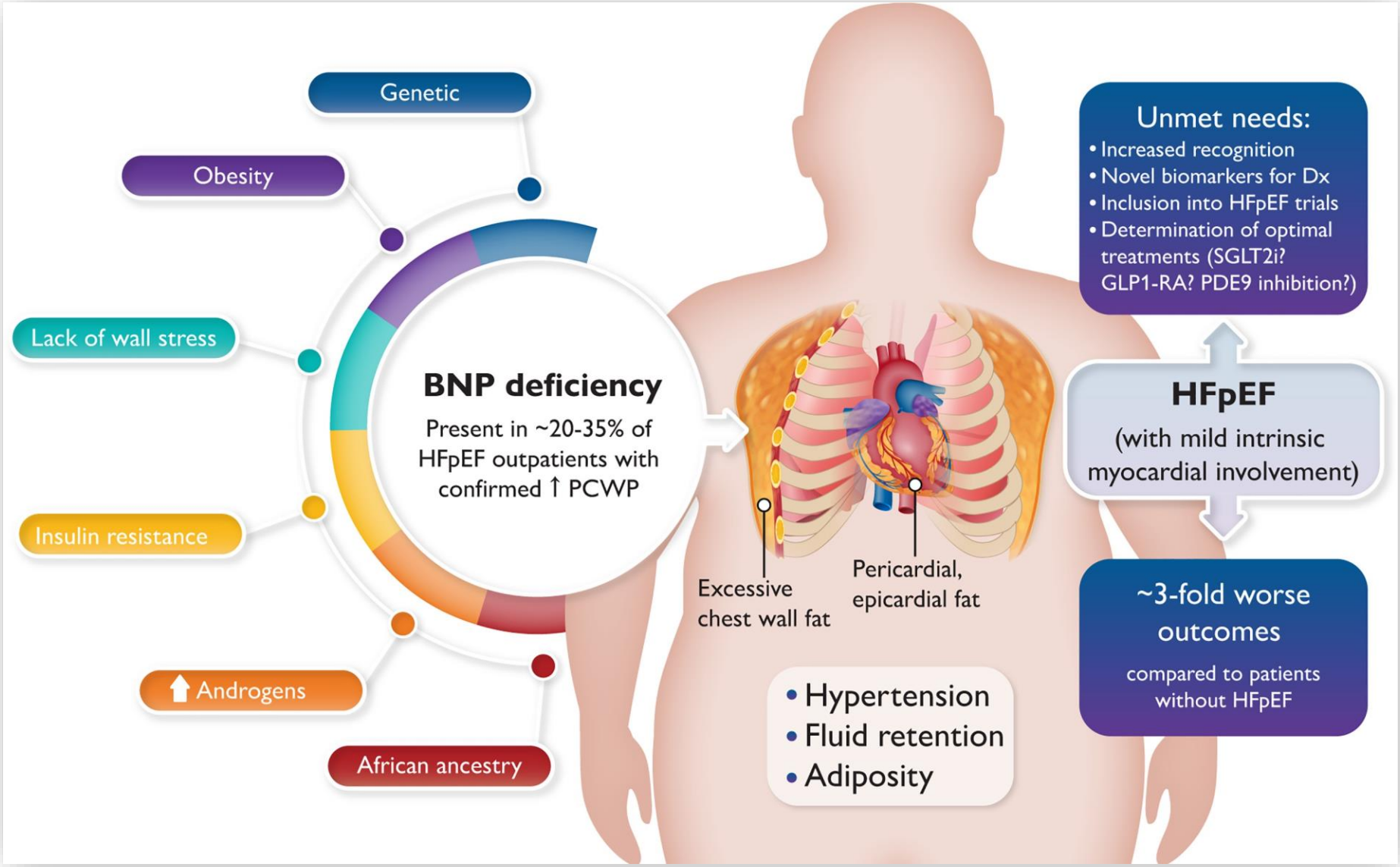
Normal NT-proBNP does NOT exclude HFpEF





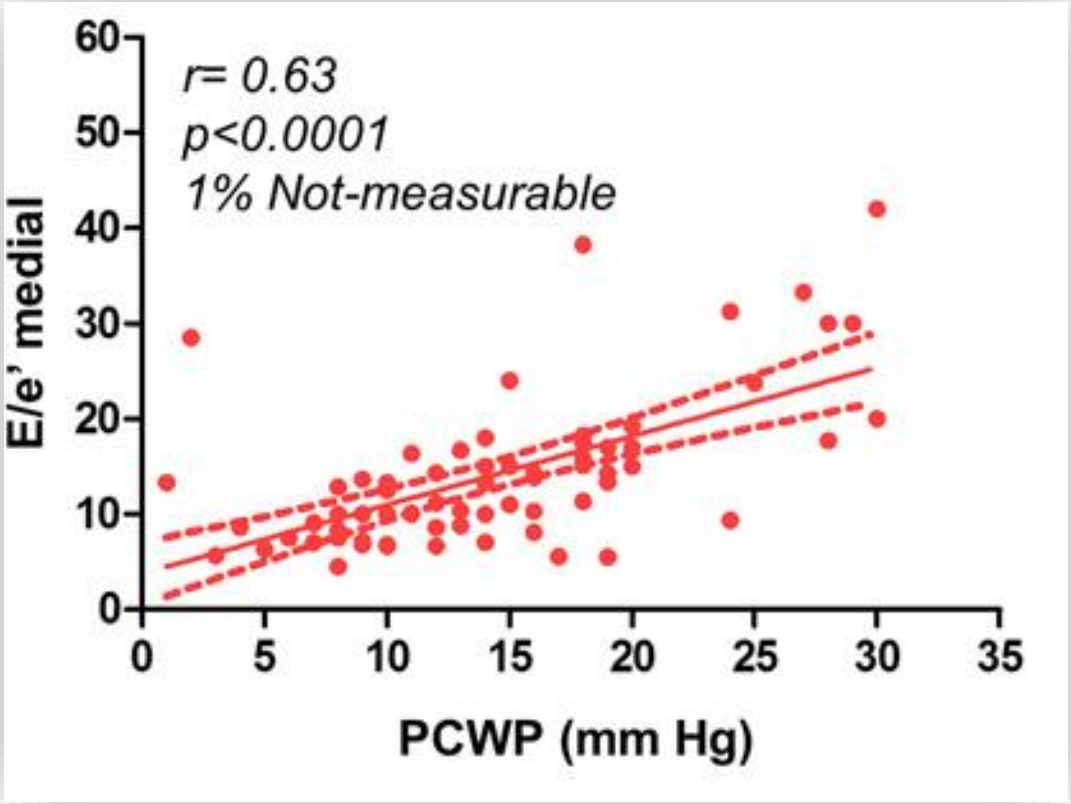
Verbrugge, Borlaug *Eur Heart J* 2022

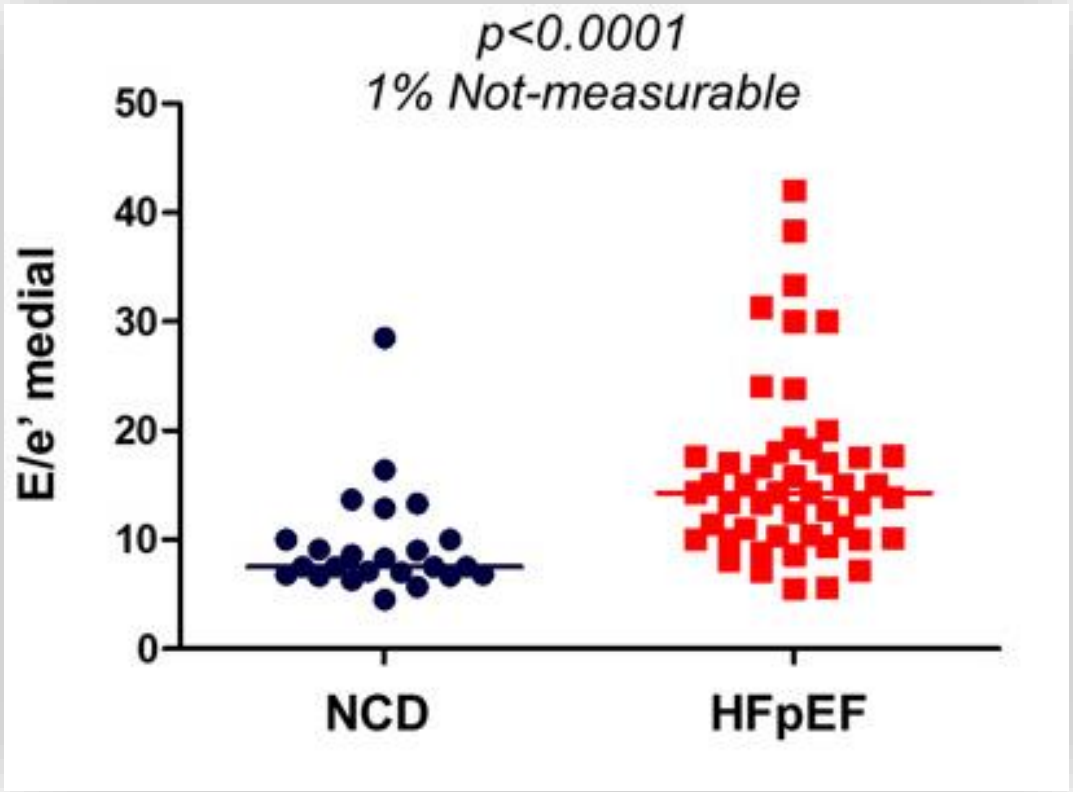
BNP DEFICIENCY SYNDROME IN HFpEF



Shah SJ. Eur Heart J 2022

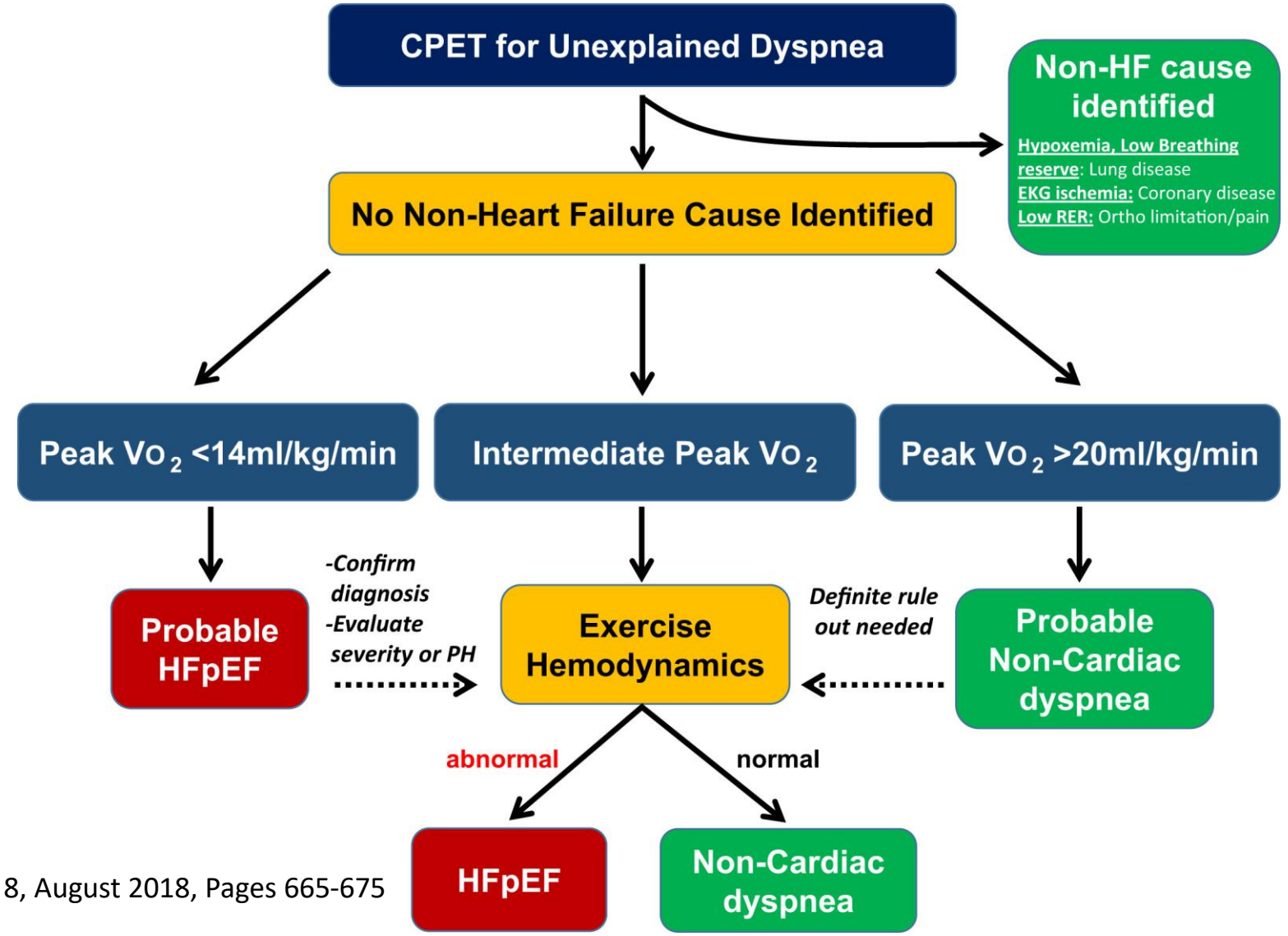
E/e' ratio: Useful when high only





Obokata, Borlaug *Circulation* 2017

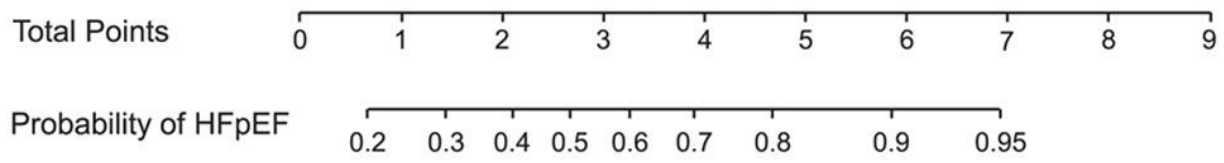
Utilization of CPET in the Evaluation of Unexplained Dyspnea



Barry Borlaug et al. JACC: HF: Volume 6, Issue 8, August 2018, Pages 665-675

H2FpEF Score and Probability of HFpEF

	Clinical Variable	Values	Points
H_2	**H**eavy	Body mass index > 30 kg/m^2	2
	Hypertensive	2 or more antihypertensive medicines	1
F	Atrial **F**ibrillation	Paroxysmal or Persistent	3
P	**P**ulmonary Hypertension	Doppler Echocardiographic estimated Pulmonary Artery Systolic Pressure > 35 mmHg	1
E	**E**lder	Age > 60 years	1
F	**F**illing Pressure	Doppler Echocardiographic E/e' > 9	1
H_2FPEF score			Sum (0-9)



DOE, normal EF ≥50%:

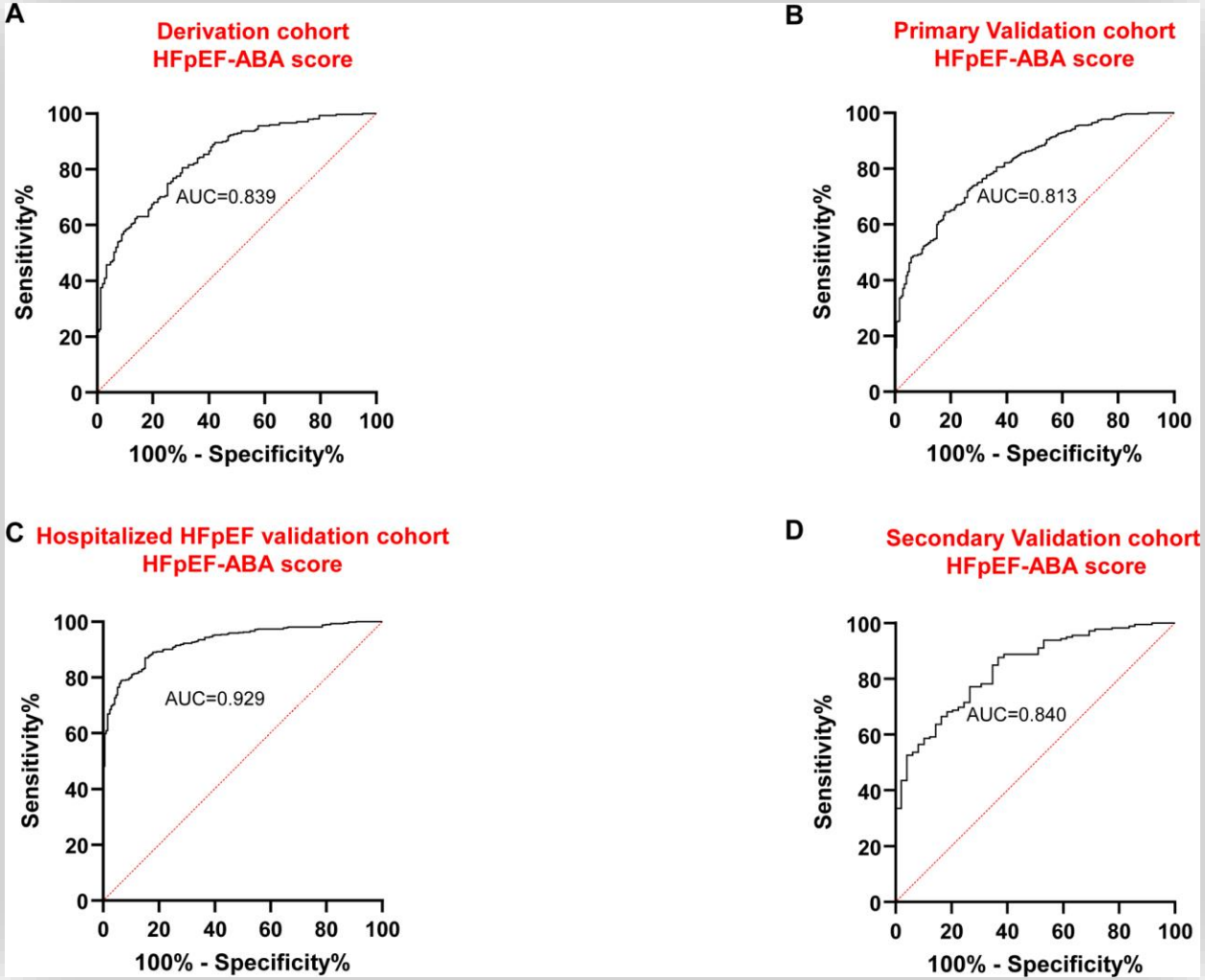
- HFpEF vs. non-cardiac dyspnea?
- Intermediate pre-test probability

Probability of HFpEF based on H2FPEF score:

- Score 0-2 ⇢ Unlikely HFpEF
- Score 2-4 ⇢ Exercise testing
- Score 5-9 ⇢ Likely HFpEF (> 80% probability)

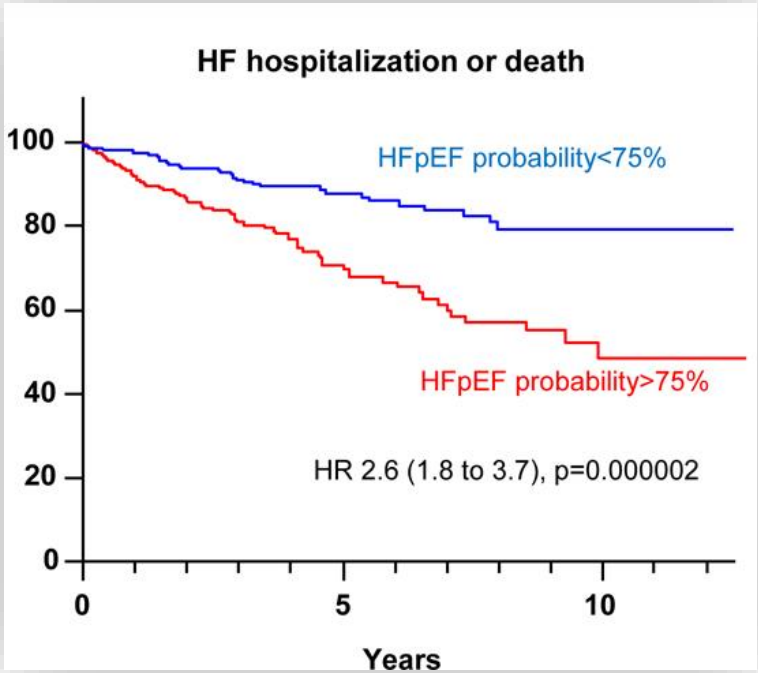
Reddy YN, et al. Circulation 2018

Evidence-based screening tool for HFpEF: the HFpEF-ABA Score



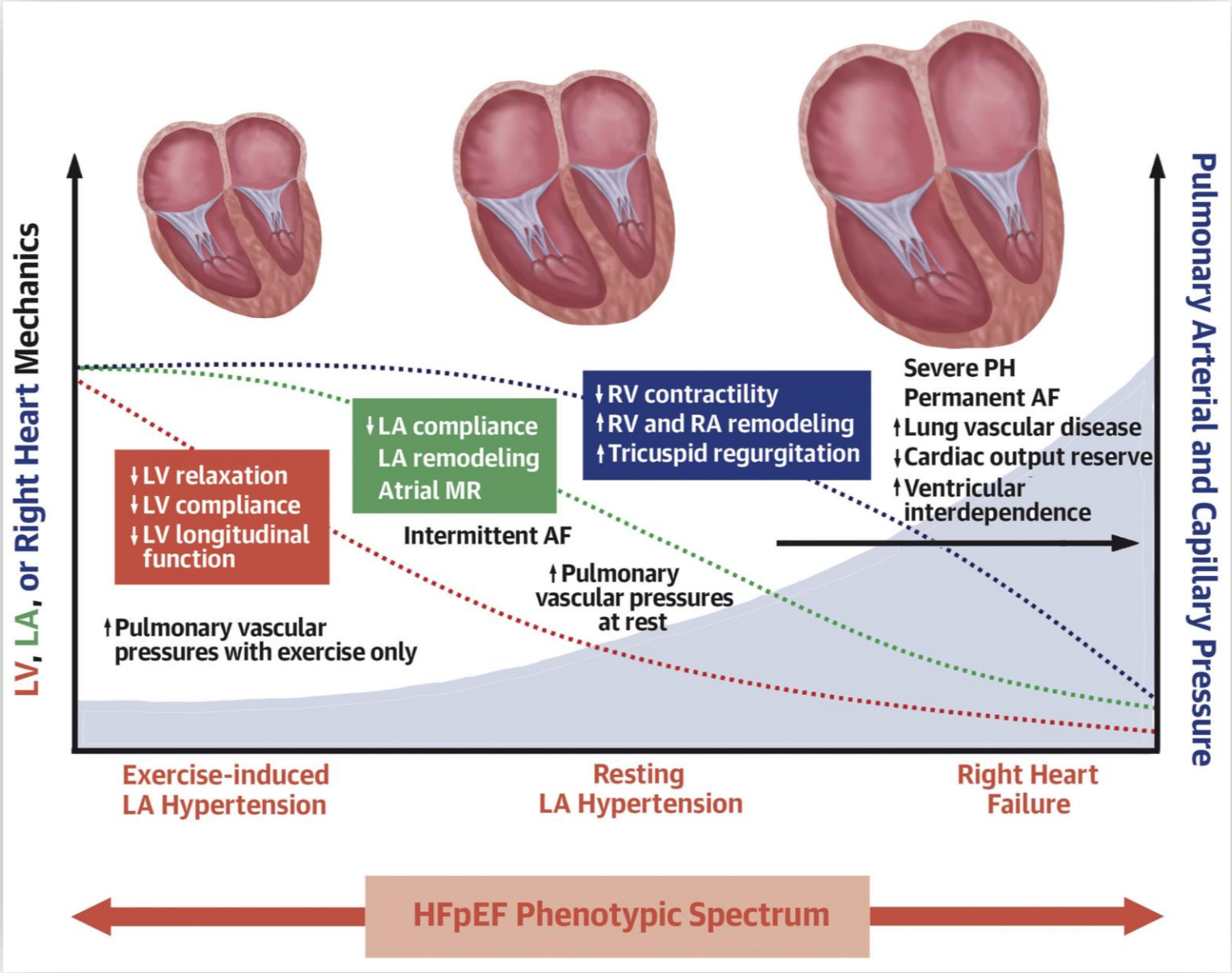
HFpEF screening model that is based exclusively on clinical variables:

1. Age
2. Body mass index
3. and history of atrial fibrillation



From Reddy, Borlaug *Nature Medicine* 2024

Temporal Disease Progression in Heart failure with Preserved EF

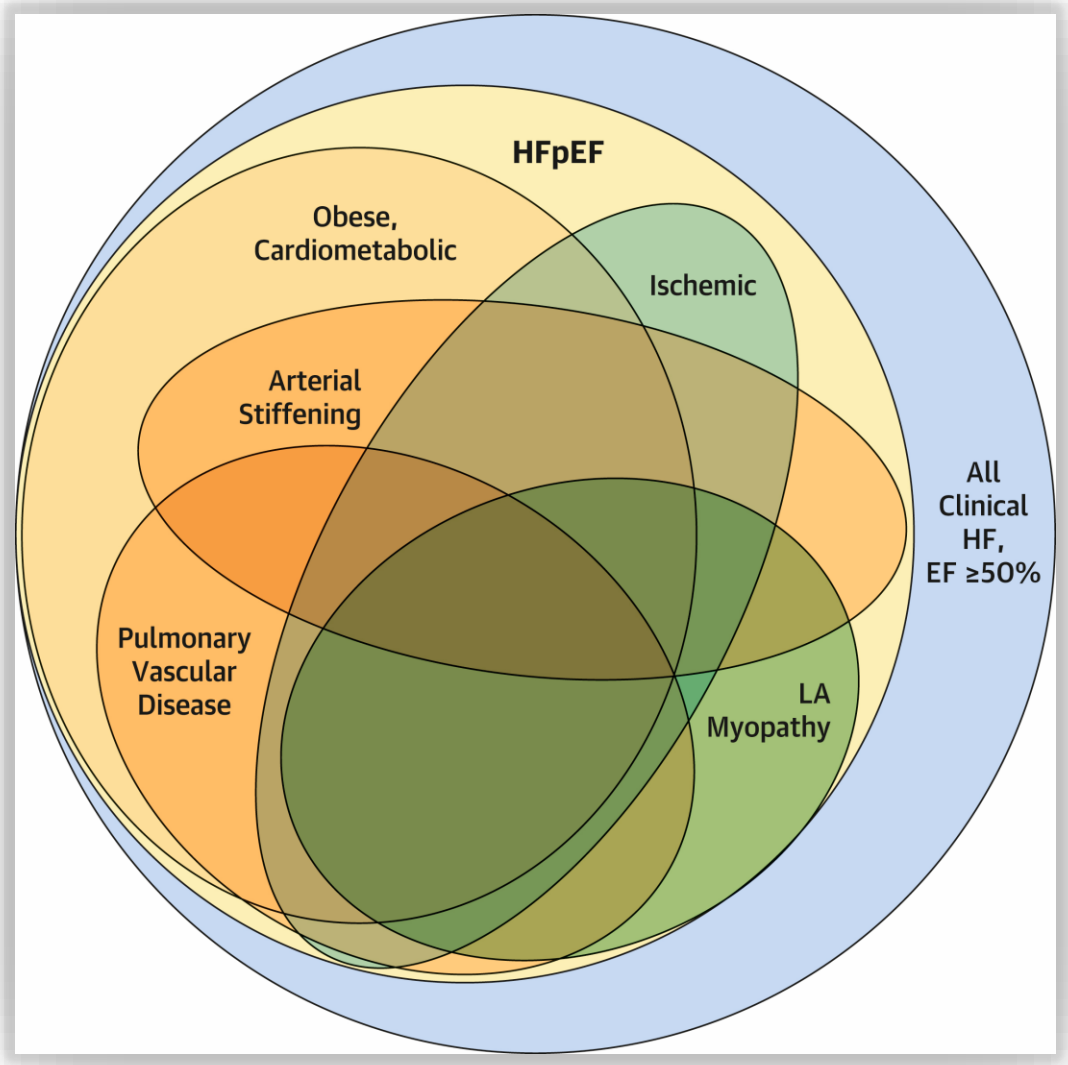


Borlaug BA, et al. J Am Coll Cardiol. 2023;81(18):1810-1834

Phenotypic Spectrum of HF With Normal EF

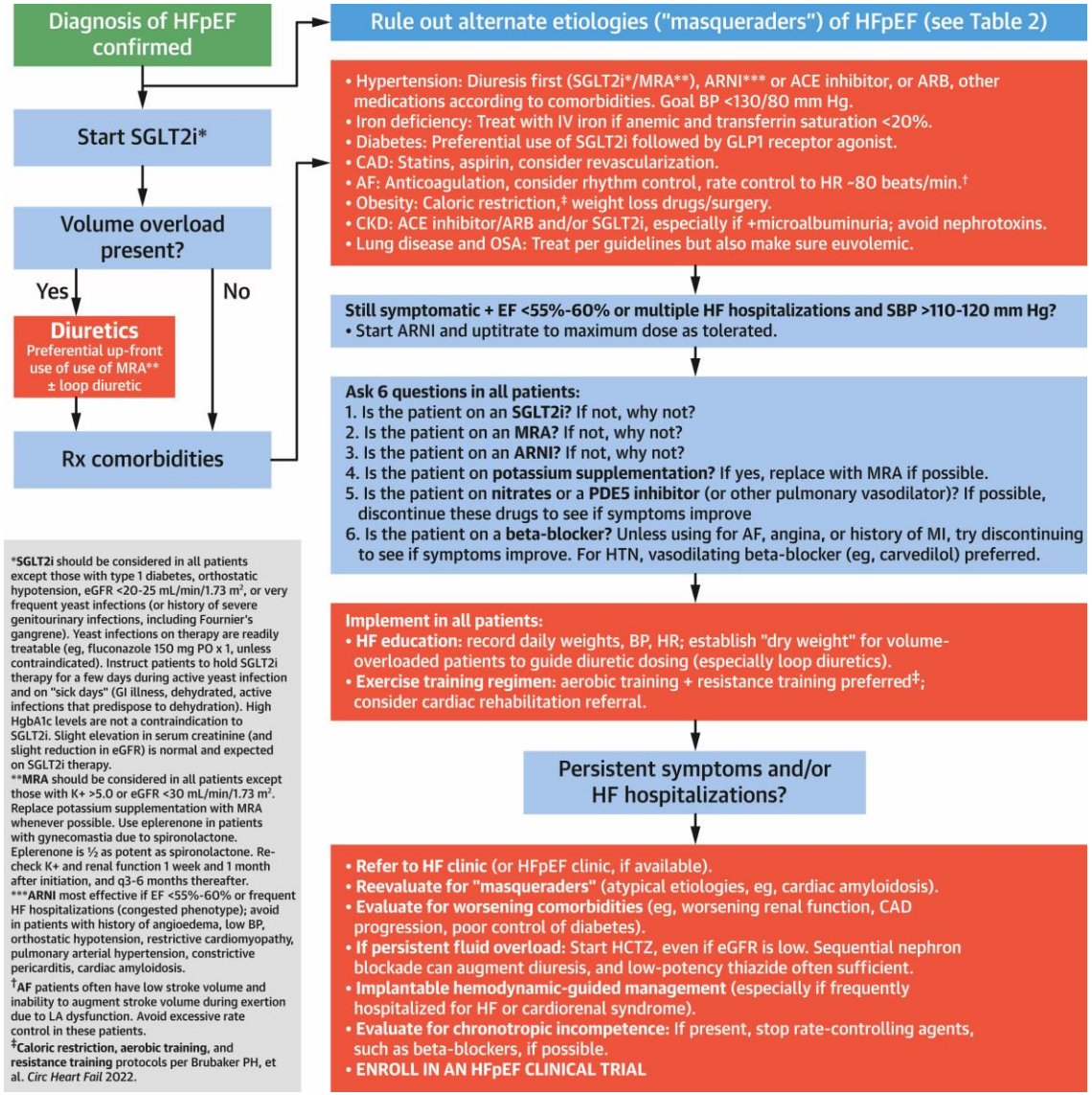
Even after excluding non-HFpEF "masqueraders", shown here by the **shaded blue area**, multiple pathophysiologically distinct phenogroups exist within the broader spectrum of HFpEF **(yellow circle)**

These individual phenogroups are sometimes singular but typically display considerable overlap with one another, complicating schemes to separate them into discrete cohorts



Borlaug BA, et al. J Am Coll Cardiol. 2023;81(18):1810-1834

Summary of Key Points for Treatment of HFpEF



*SGLT2i should be considered in all patients except those with type 1 diabetes, orthostatic hypotension, eGFR <20-25 mL/min/1.73 m^2, or very frequent yeast infections (or history of severe genitourinary infections, including Fournier's gangrene). Yeast infections on therapy are readily treatable (eg, fluconazole 150 mg PO x 1, unless contraindicated). Instruct patients to hold SGLT2i therapy for a few days during active yeast infection and on "sick days" (GI illness, dehydrated, active infections that predispose to dehydration). High HgbA1c levels are not a contraindication to SGLT2i. Slight elevation in serum creatinine (and slight reduction in eGFR) is normal and expected on SGLT2i therapy.

**MRA should be considered in all patients except those with K+ >5.0 or eGFR <30 mL/min/1.73 m^2. Replace potassium supplementation with MRA whenever possible. Use eplerenone in patients with gynecomastia due to spironolactone. Eplerenone is ½ as potent as spironolactone. Re-check K+ and renal function 1 week and 1 month after initiation, and q3-6 months thereafter.

***ARNI most effective if EF <55%-60% or frequent HF hospitalizations (congested phenotype); avoid in patients with history of angioedema, low BP, orthostatic hypotension, restrictive cardiomyopathy, pulmonary arterial hypertension, constrictive pericarditis, cardiac amyloidosis.

†AF patients often have low stroke volume and inability to augment stroke volume during exertion due to LA dysfunction. Avoid excessive rate control in these patients.

‡Caloric restriction, aerobic training, and resistance training protocols per Brubaker PH, et al. *Circ Heart Fail* 2022.

Borlaug BA, et al. J Am Coll Cardiol. 2023;81(18):1810-1834

Thank You.

Current Evidence – Based Therapies and Treatments

Pardeep S Jhund BSc(Hons), MBChB, MSc, PhD

Disclosures

Speakers fees: AstraZeneca, ProAdWise Communications;

Advisory board fees: AstraZeneca, Bayer AG

Research funding: AstraZeneca, Boehringer Ingelheim, Analog Devices Inc, Roche Diagnostics

My employer the University of Glasgow has been remunerated for clinical trial work from AstraZeneca, Bayer AG, Novartis, and Novo Nordisk

Director at GCTP Ltd

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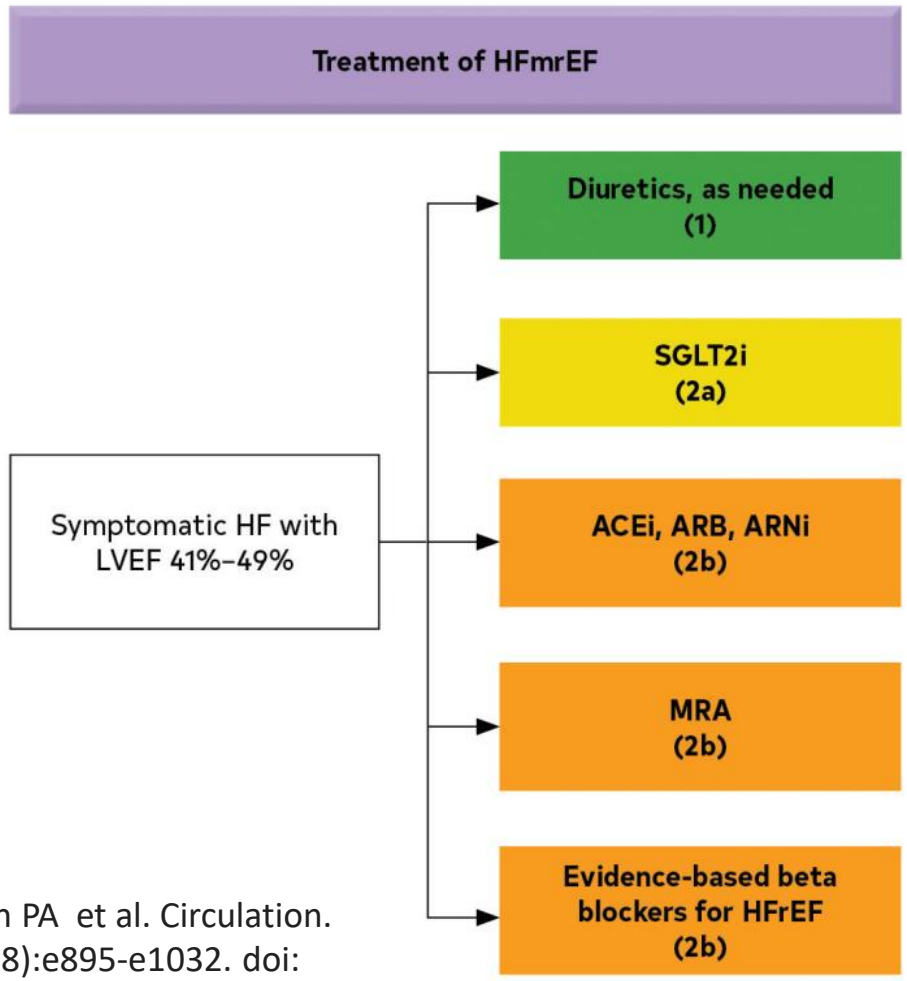
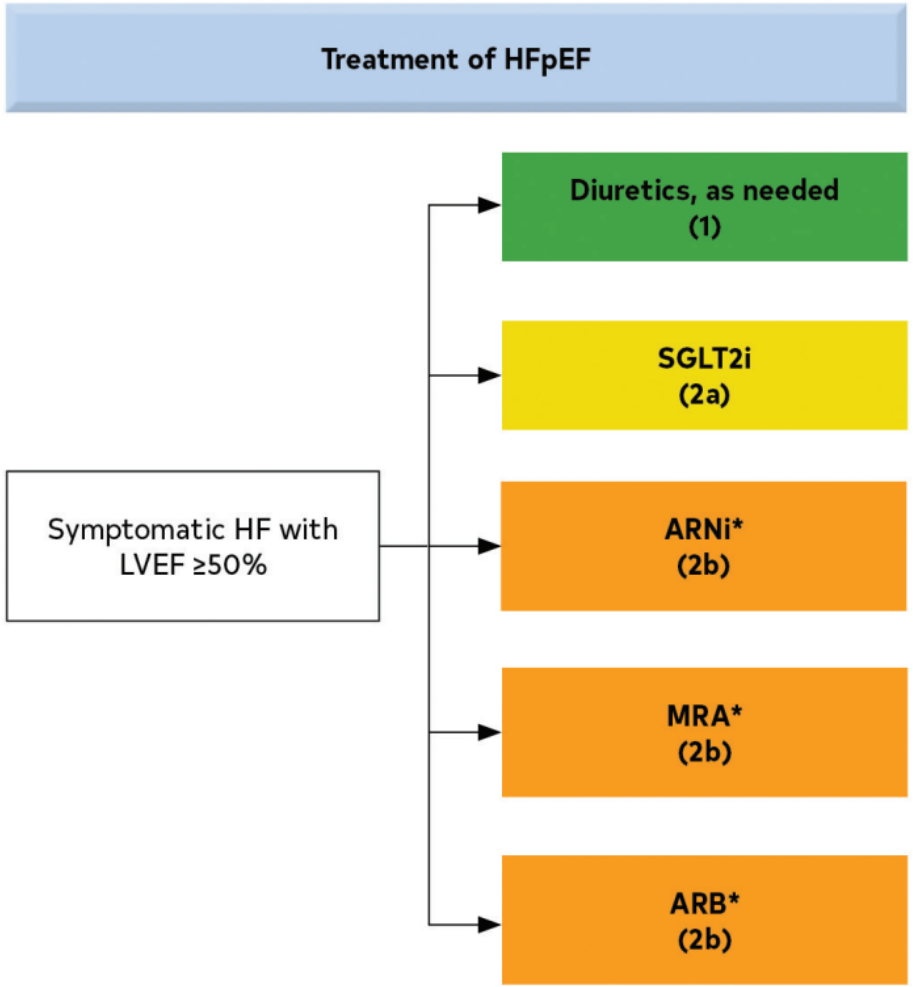
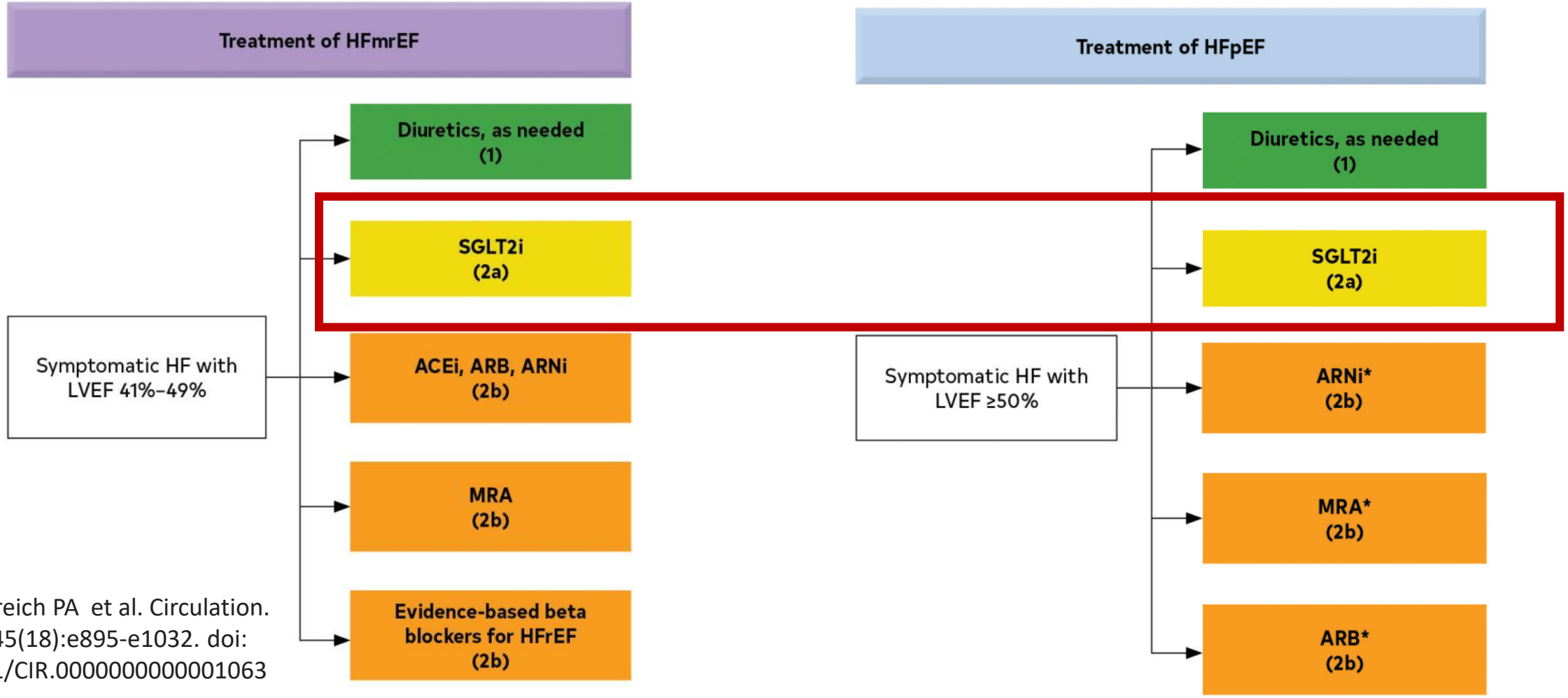
Management of HFmrEF/HFpEF 2022 AHA/ACC/HFSA Guideline





Heidenreich PA et al. Circulation. 2022;145(18):e895-e1032. doi: 10.1161/CIR.0000000000001063

Management of HFmrEF/HFpEF 2022 AHA/ACC/HFSA Guideline



Heidenreich PA et al. Circulation. 2022;145(18):e895-e1032. doi: 10.1161/CIR.0000000000001063

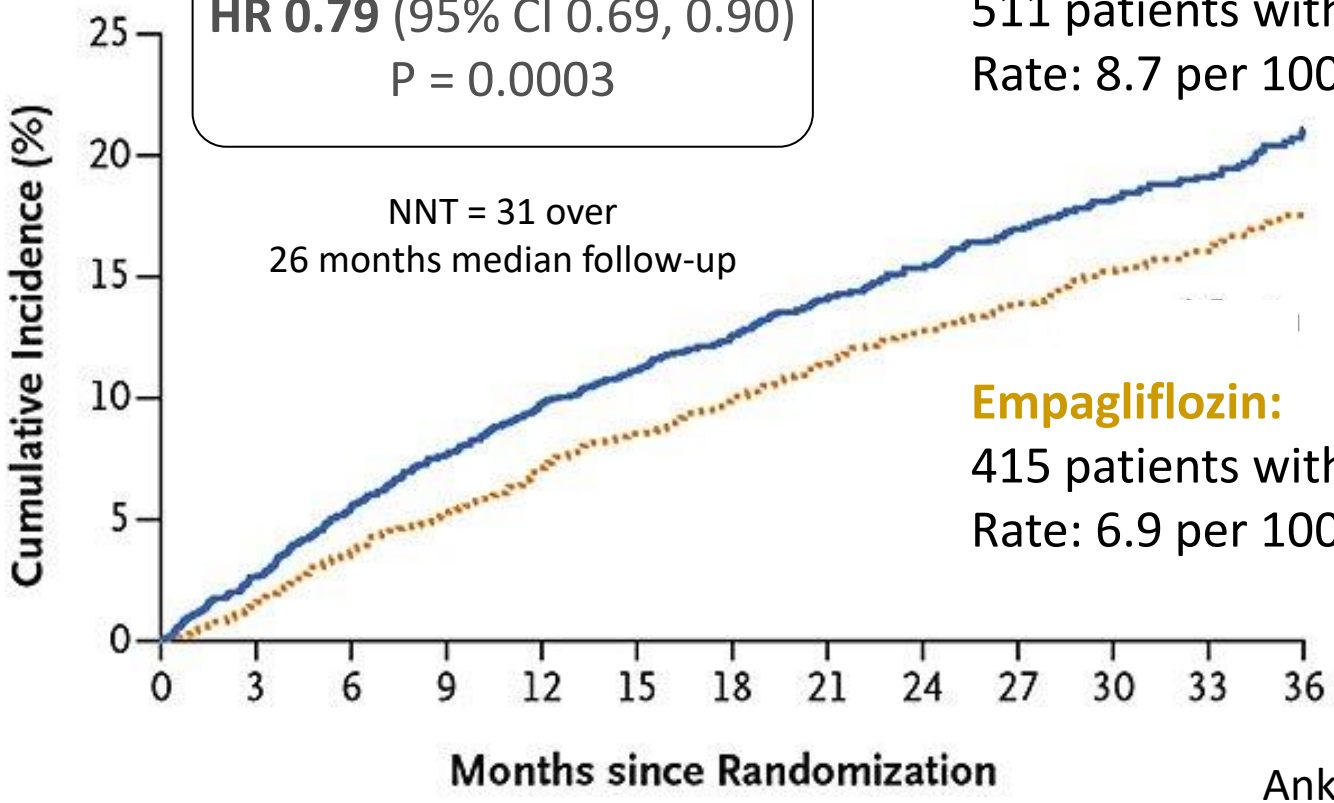
EMPEROR-Preserved

Empagliflozin Outcome Trial in Patients with Chronic Heart Failure with Preserved Ejection Fraction

Primary composite endpoint:
Cardiovascular death or heart failure hospitalization

HR 0.79 (95% CI 0.69, 0.90)
P = 0.0003

NNT = 31 over
26 months median follow-up



Placebo:
511 patients with event
Rate: 8.7 per 100 patient-years

Empagliflozin:
415 patients with event
Rate: 6.9 per 100 patient-years

HF hospitalization
HR 0.71 (0.60, 0.83)

CV death
HR 0.91 (0.76, 1.09)

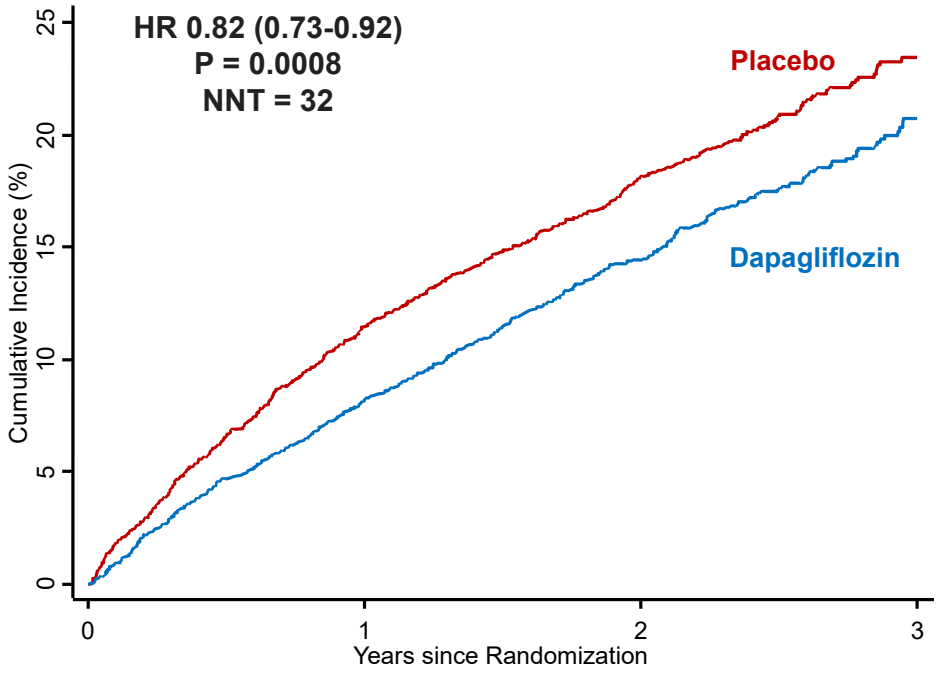
Anker et al. N Engl J Med. 2021;385(16):1451-1461.

SGLT2 inhibitors in patients with HFmrEF and HFpEF

Patients with and without type 2 diabetes

DELIVER

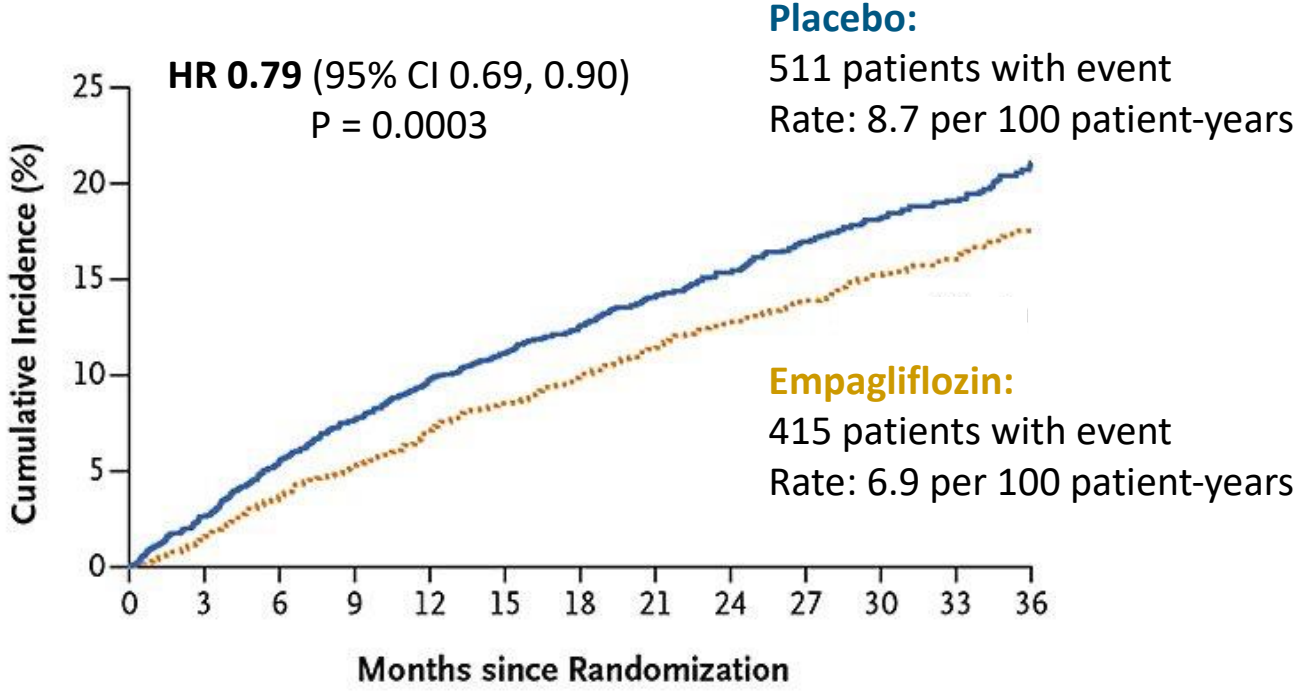
CV Death/worsening HF event



Solomon SD et al, N Engl J Med. 2022;387:1089-1098

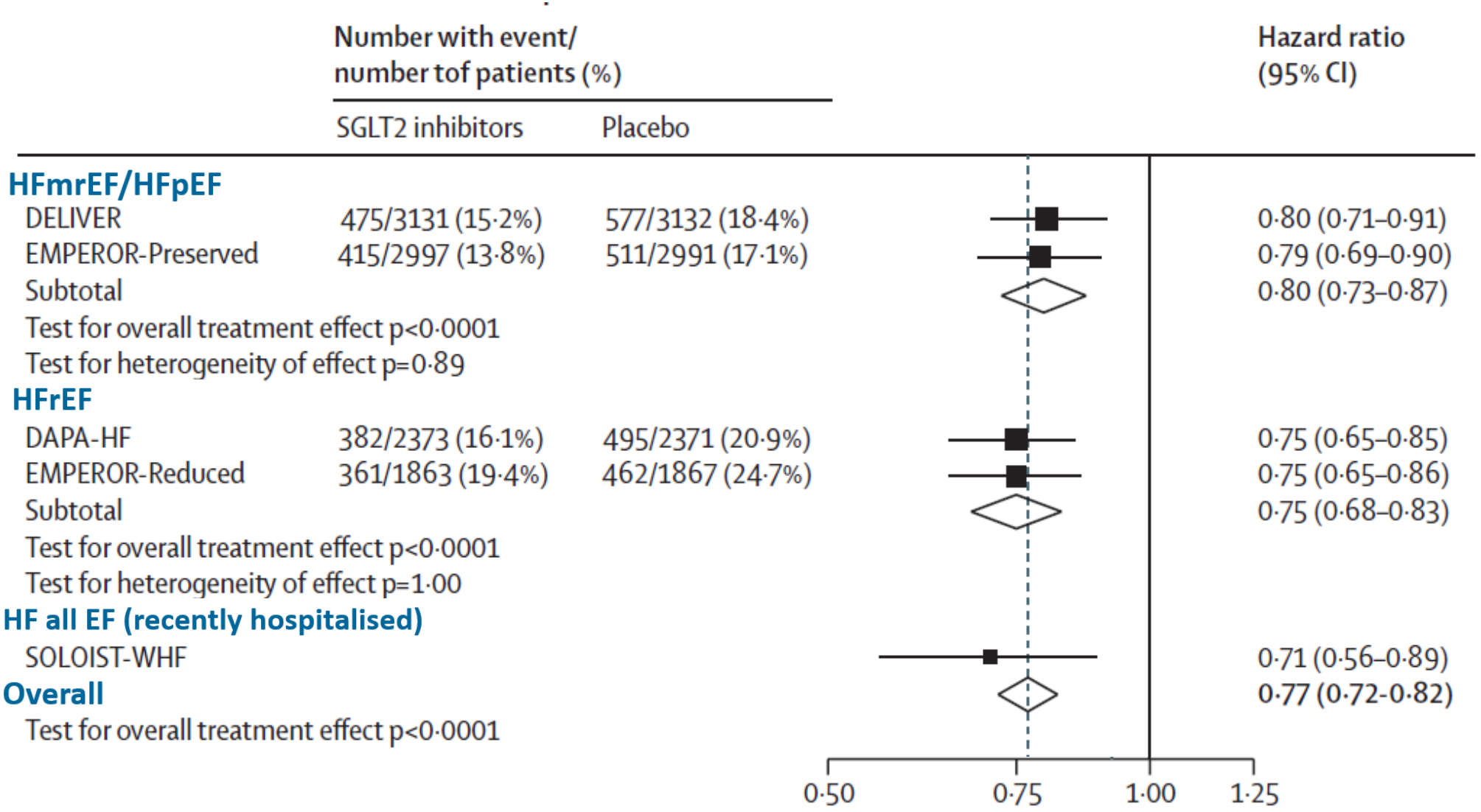
EMPEROR-Preserved

CV Death/ HF hospitalization



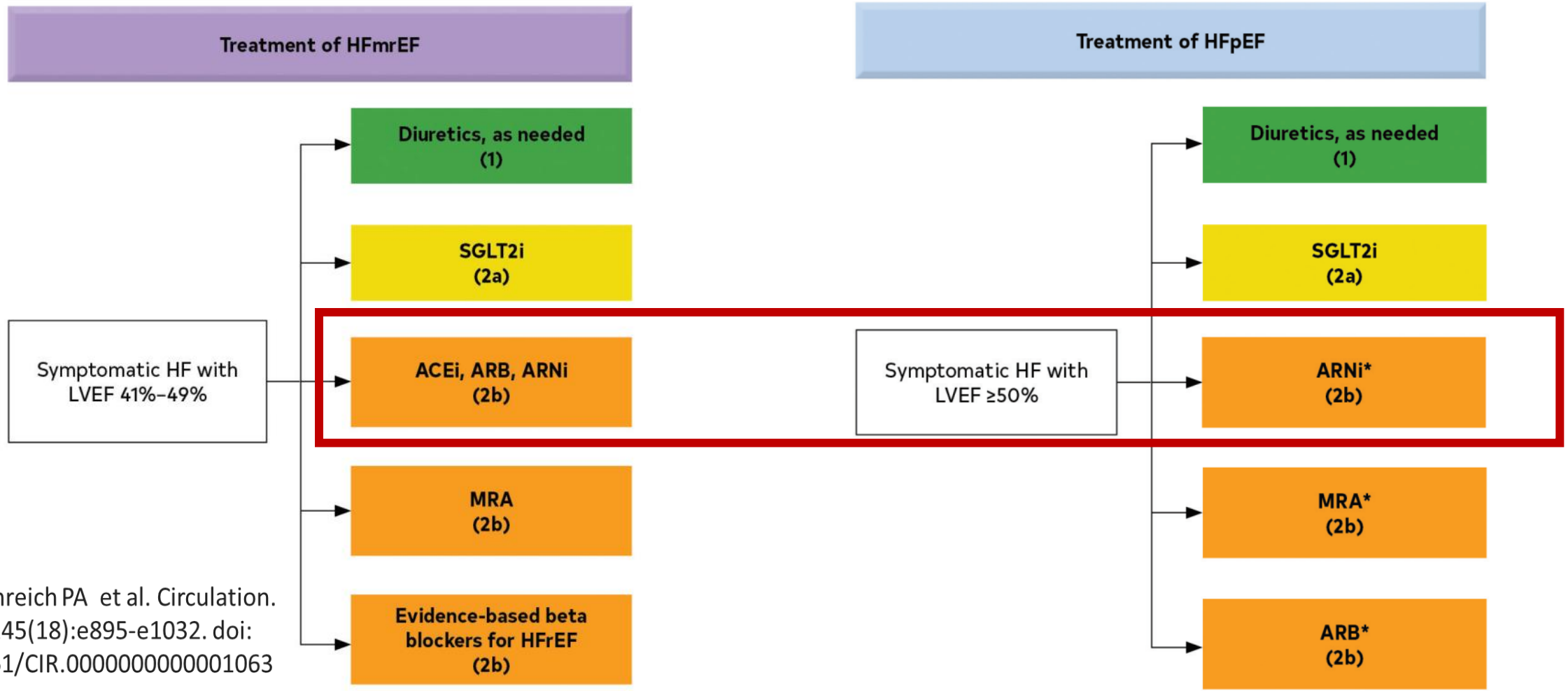
Anker S et al N Engl J Med. 2021;385:1451-1461

Meta-analysis of 5 large RCTs with SGLT2i in patients with HF (CV death/ HF hospitalisation)



Vaduganathan, Docherty et al Lancet. 2022;400(10354):757-767

Management of HFmrEF/HFpEF 2022 AHA/ACC/HFSA Guideline



Heidenreich PA et al. Circulation. 2022;145(18):e895-e1032. doi: 10.1161/CIR.0000000000001063

PARAGON-HF

Prospective comparison of ARni with Arb Global Outcomes in heart failure with preserved ejectioN fraction

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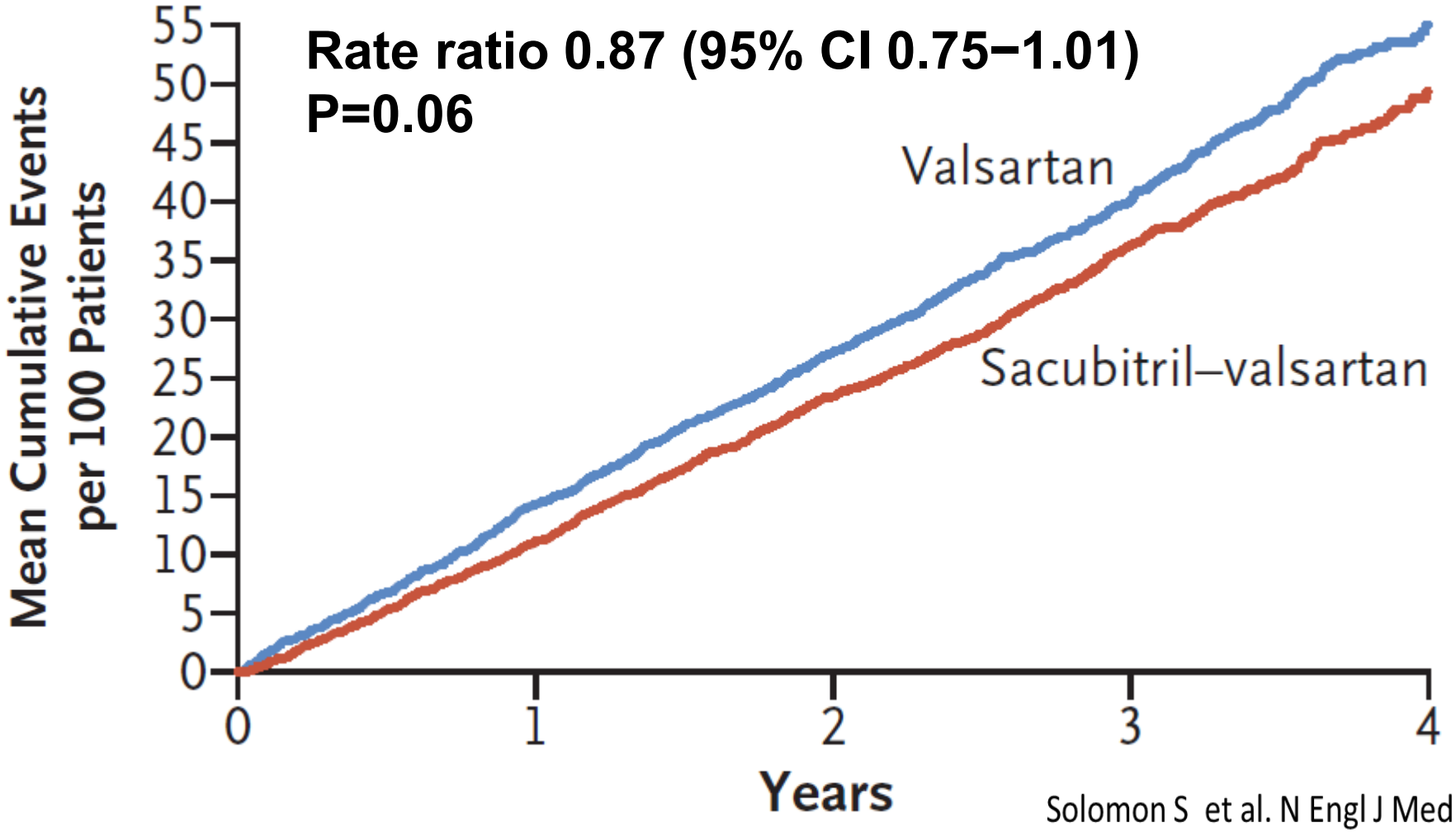
Angiotensin–Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction

S.D. Solomon, J.J.V. McMurray, I.S. Anand, J. Ge, C.S.P. Lam, A.P. Maggioni, F. Martinez, M. Packer, M.A. Pfeffer, B. Pieske, M.M. Redfield, J.L. Rouleau, D.J. van Veldhuisen, F. Zannad, M.R. Zile, A.S. Desai, B. Claggett, P.S. Jhund, S.A. Boytsov, J. Comin-Colet, J. Cleland, H.-D. Düngen, E. Goncalvesova, T. Katova, J.F. Kerr Saraiva, M. Lelonek, B. Merkely, M. Senni, S.J. Shah, J. Zhou, A.R. Rizkala, J. Gong, V.C. Shi, and M.P. Lefkowitz, for the PARAGON-HF Investigators and Committees*

PARAGON-HF

Prospective comparison of ARni with Arb Global Outcomes in heart failure with preserved ejection fraction

Primary Outcome – CV death / Total HF hospitalizations

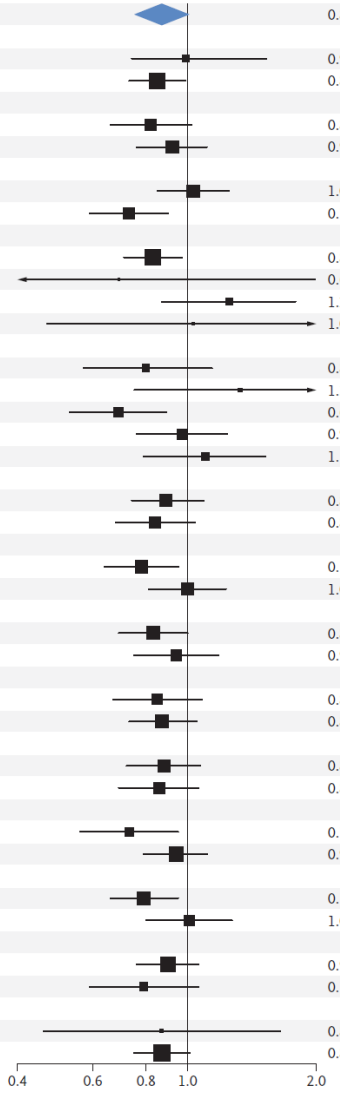


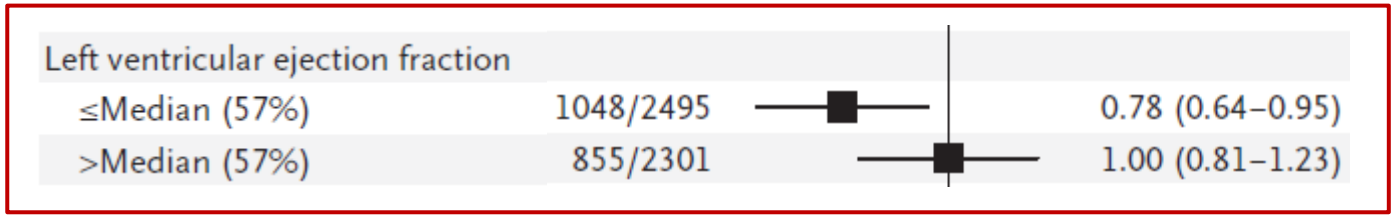
Solomon S et al. N Engl J Med. 2019;381(17):1609-1620

PARAGON-HF

Subgroups– CV death / Total HF hospitalizations

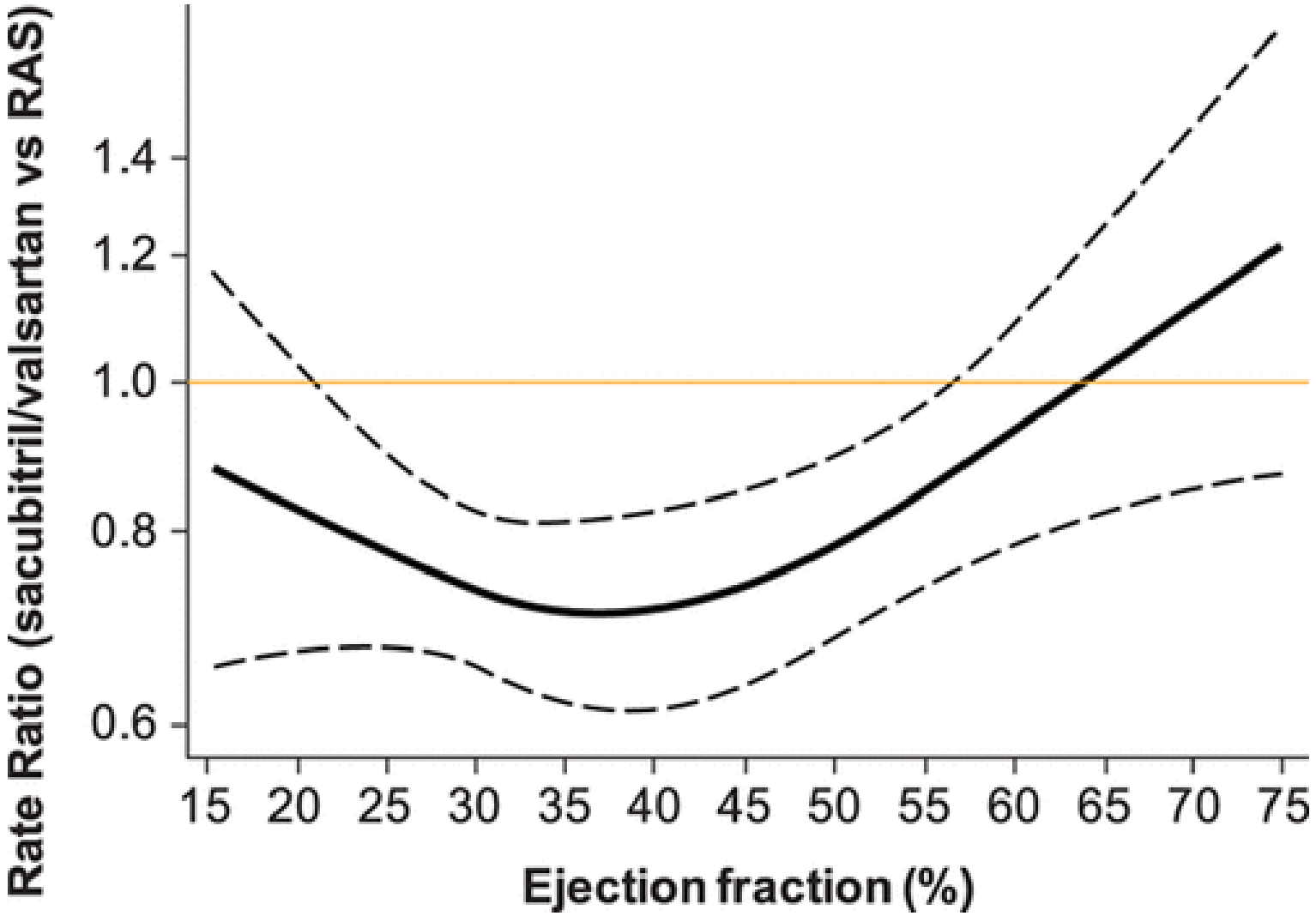
Subgroup	No. of Events/No. of Patients	Hazard Ratio (95% CI)
Overall	1903/4796	0.87 (0.75–1.01)
Age		
<65 yr	276/825	0.99 (0.64–1.53)
≥65 yr	1627/3971	0.85 (0.73–0.99)
Age		
<75 yr	938/2597	0.82 (0.66–1.02)
≥75 yr	965/2199	0.92 (0.76–1.11)
Sex		
Male	980/2317	1.03 (0.85–1.25)
Female	923/2479	0.73 (0.59–0.90)
Race		
White	1542/3907	0.83 (0.71–0.97)
Black	89/102	0.69 (0.24–1.99)
Asian	237/607	1.25 (0.87–1.79)
Other	35/180	1.03 (0.47–2.28)
Geographic region		
North America	478/559	0.80 (0.57–1.14)
Latin America	83/370	1.33 (0.75–2.36)
Western Europe	544/1390	0.69 (0.53–0.89)
Central Europe	466/1715	0.97 (0.76–1.24)
Asia–Pacific or other	332/762	1.10 (0.79–1.52)
History of diabetes		
Yes	1041/2069	0.89 (0.74–1.09)
No	862/2727	0.84 (0.68–1.04)
Left ventricular ejection fraction		
≤Median (57%)	1048/2495	0.78 (0.64–0.95)
>Median (57%)	855/2301	1.00 (0.81–1.23)
History of atrial fibrillation		
Yes	1140/2521	0.83 (0.69–1.00)
No	763/2275	0.94 (0.75–1.18)
NT-proBNP at screening		
≤Median (911 pg/ml)	708/2379	0.85 (0.67–1.08)
>Median (911 pg/ml)	1183/2378	0.87 (0.73–1.05)
Systolic blood pressure at screening		
≤Median (137 mm Hg)	984/2450	0.88 (0.72–1.07)
>Median (137 mm Hg)	919/2344	0.86 (0.69–1.06)
Mineralocorticoid-receptor antagonist use		
Yes	545/1239	0.73 (0.56–0.95)
No	1358/3557	0.94 (0.79–1.11)
Baseline estimated GFR		
<60 ml/min/1.73 m^2	1115/2341	0.79 (0.66–0.95)
≥60 ml/min/1.73 m^2	787/2454	1.01 (0.80–1.27)
NYHA class		
I or II	1402/3843	0.90 (0.76–1.06)
III or IV	499/951	0.79 (0.59–1.06)
Unable to take ACE inhibitor		
Yes	86/262	0.87 (0.46–1.65)
No	1817/4534	0.87 (0.75–1.01)





Solomon S et al. N Engl J Med. 2019;381(17):1609-1620

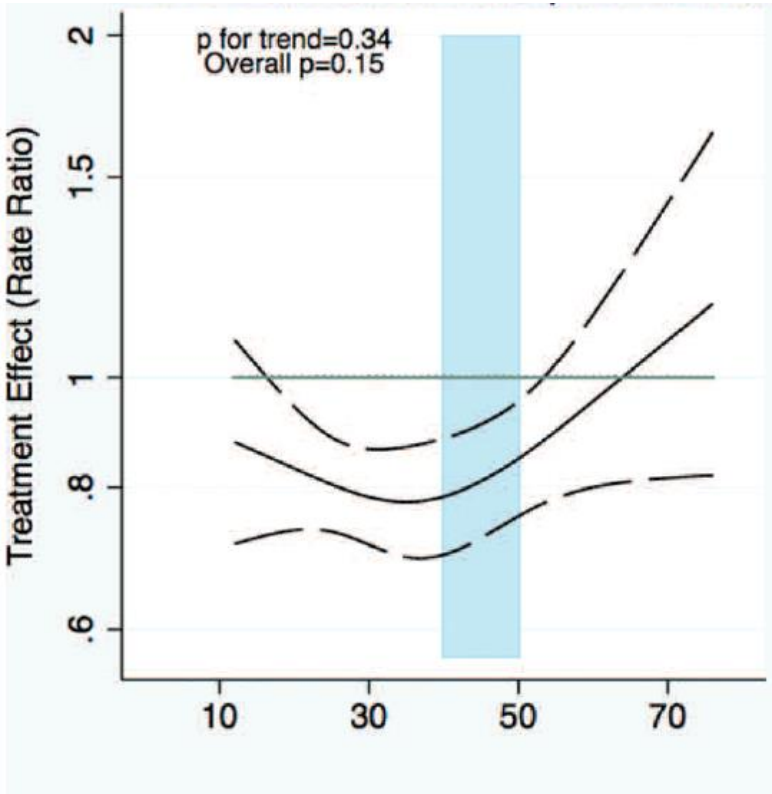
PARAGON-HF & PARADIGM-HF
Total HF hospitalization or CV death



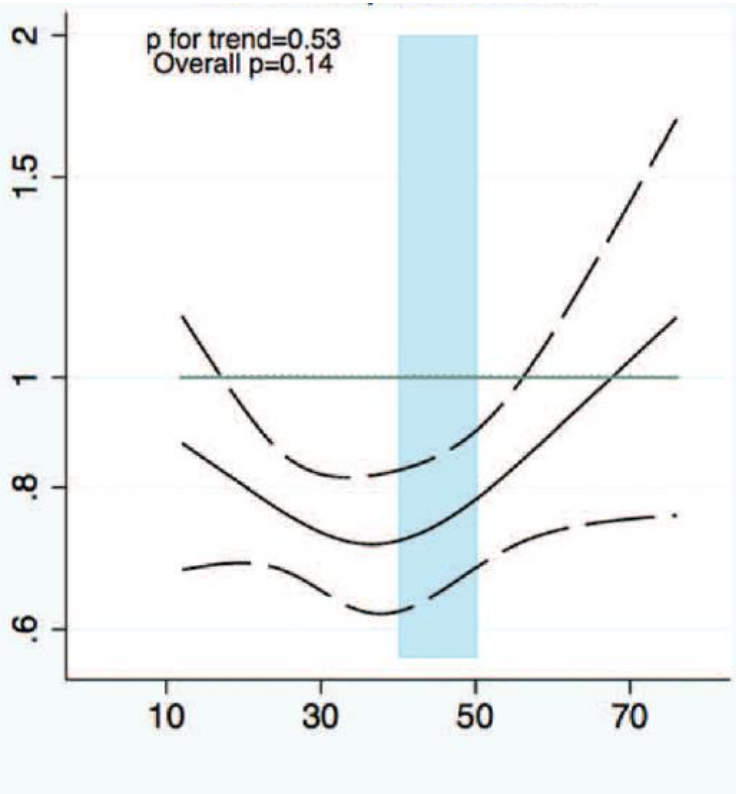
Solomon et al Circulation. 2020;141:352–361

CHARM-Programme: Effect of candesartan across the LVEF spectrum

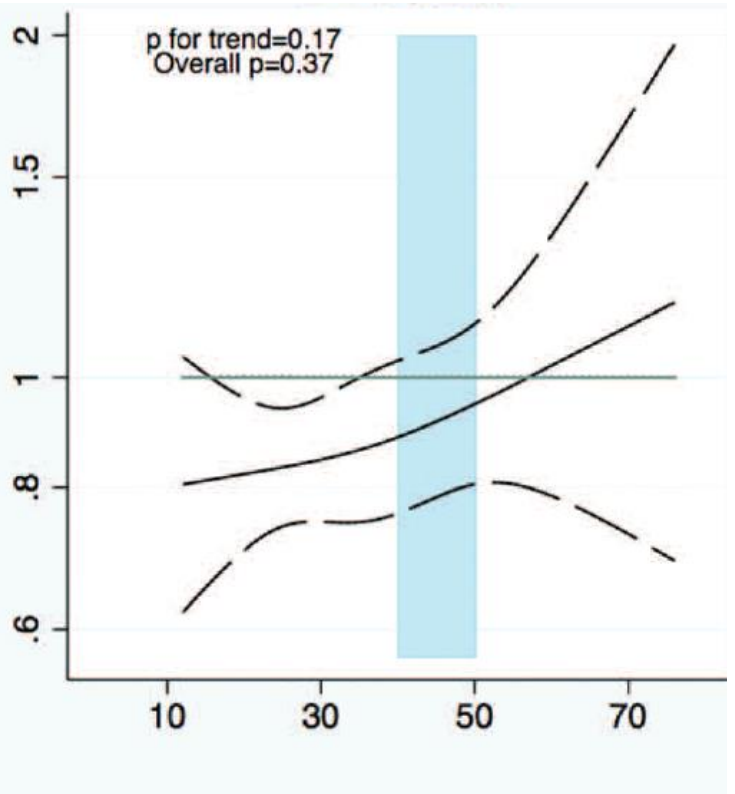
CV death or HF hospitalization



HF hospitalization

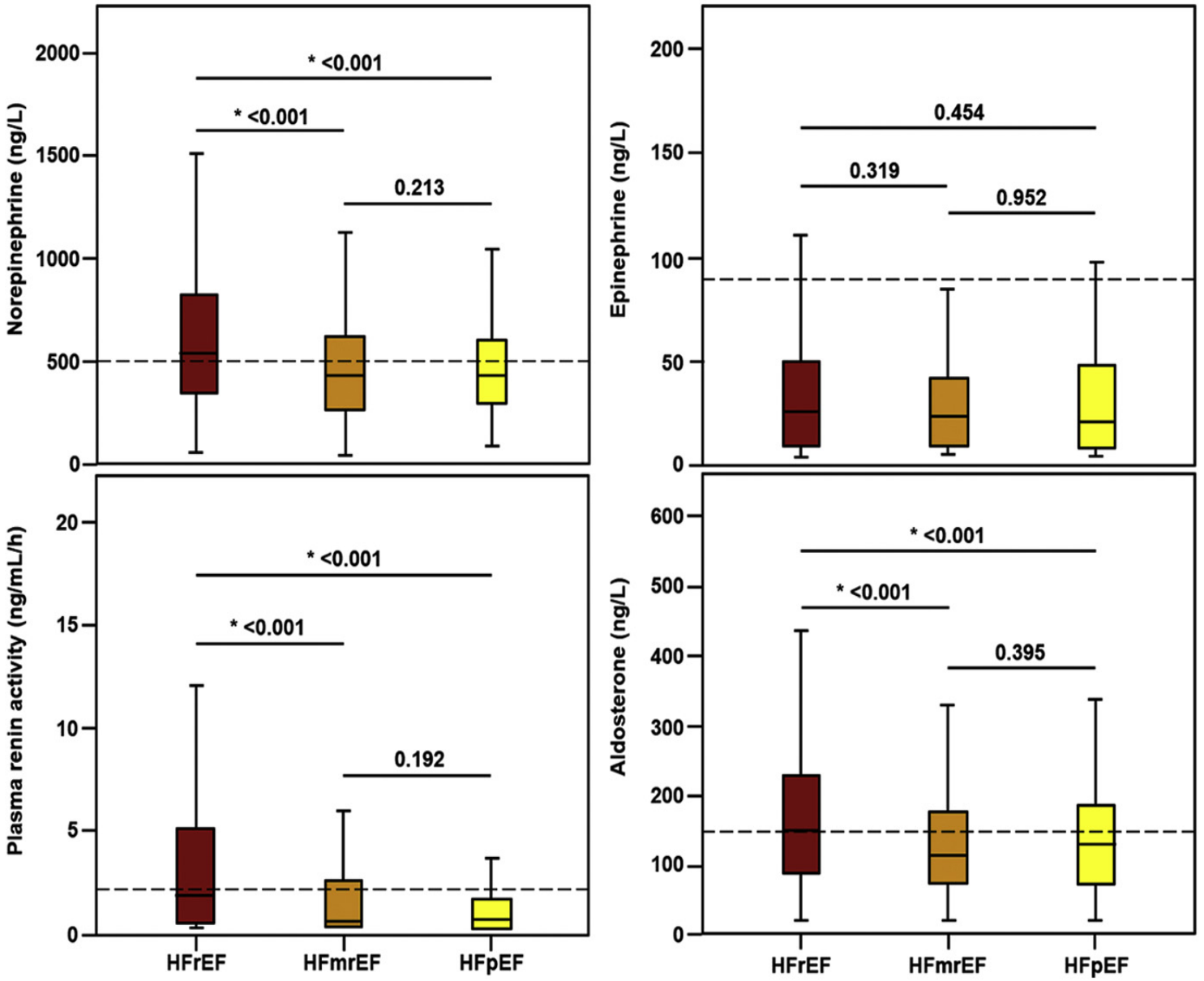


CV death



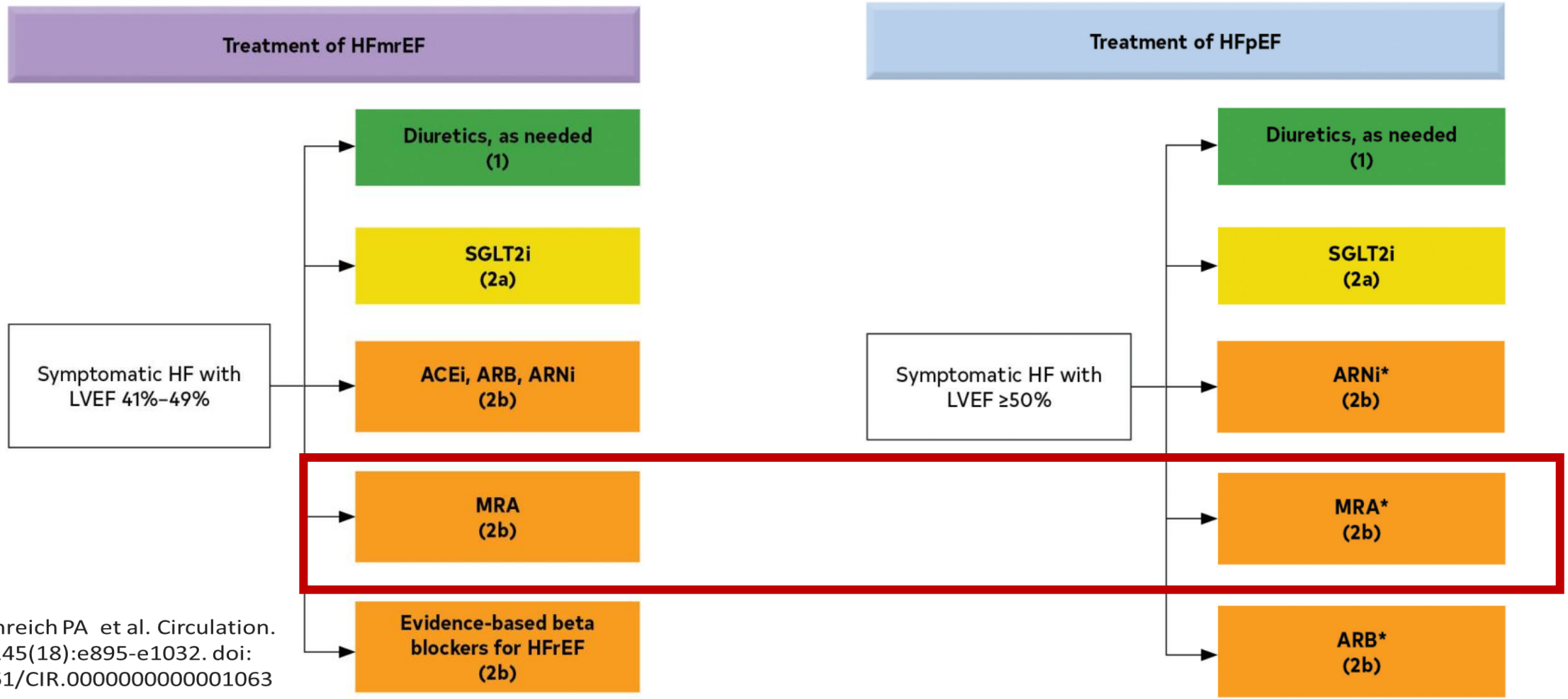
Lund et al European Journal of Heart Failure 2018;20:1230–1239

Less neurohormonal activation in HFpEF



Vergaro G et al *Int J Cardiol.* 2019;296:91–97

Management of HFmrEF/HFpEF 2022 AHA/ACC/HFSA Guideline

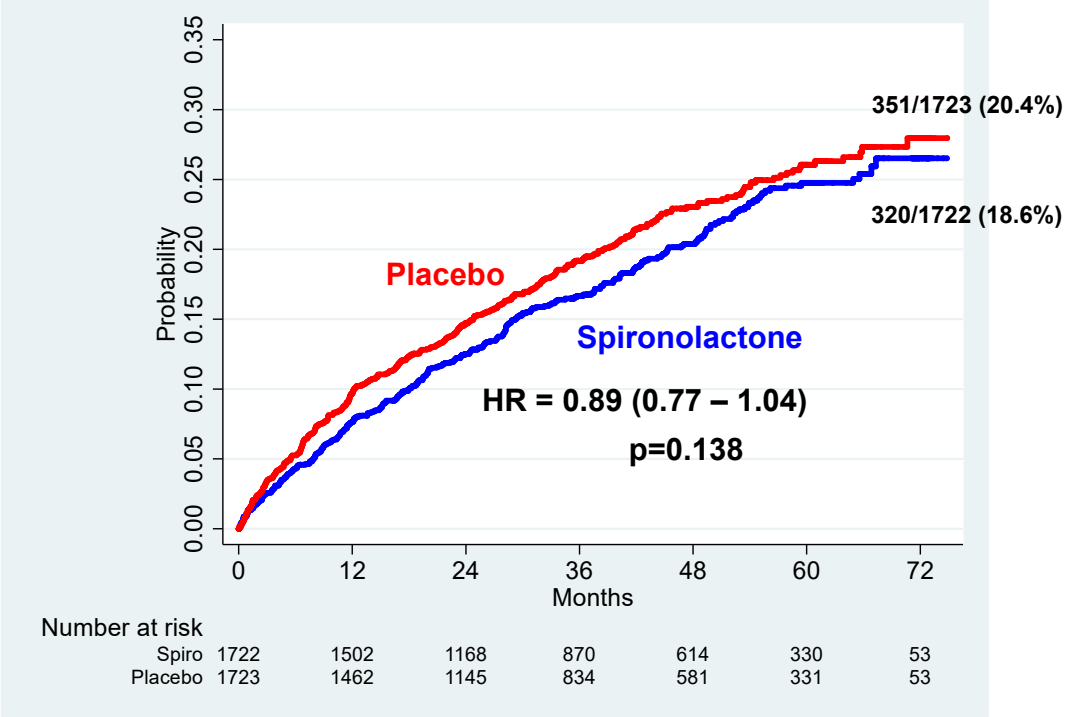


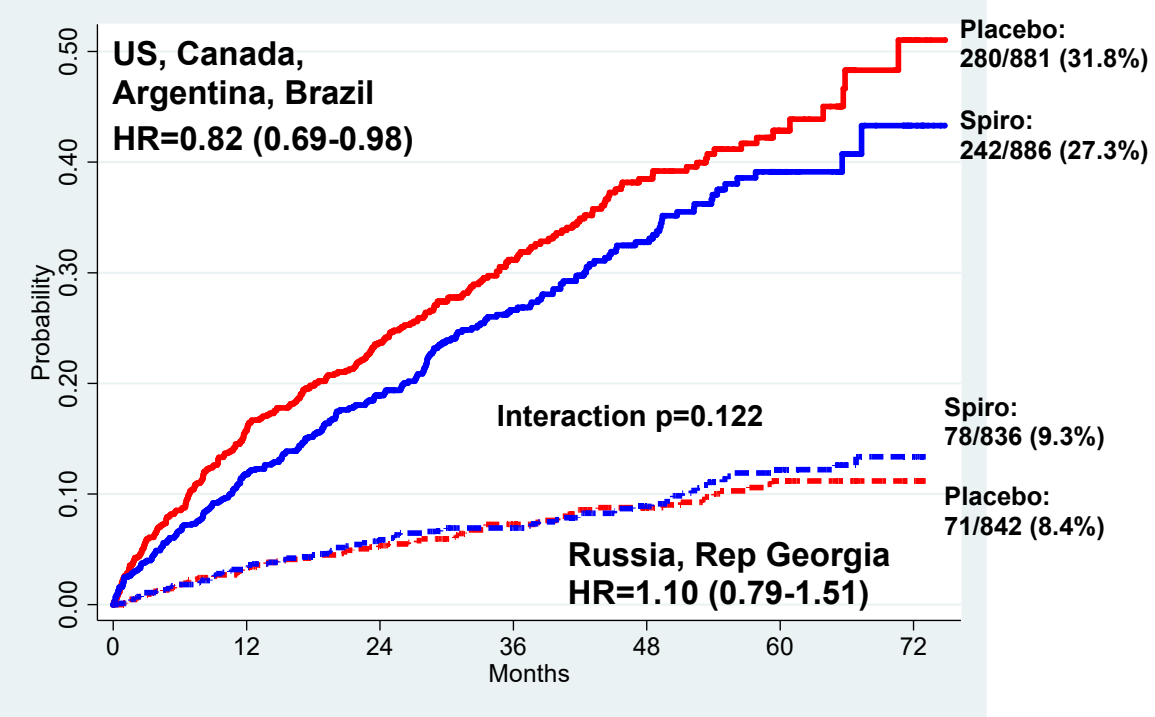
Heidenreich PA et al. Circulation. 2022;145(18):e895-e1032. doi: 10.1161/CIR.0000000000001063

MRAs in HFpEF

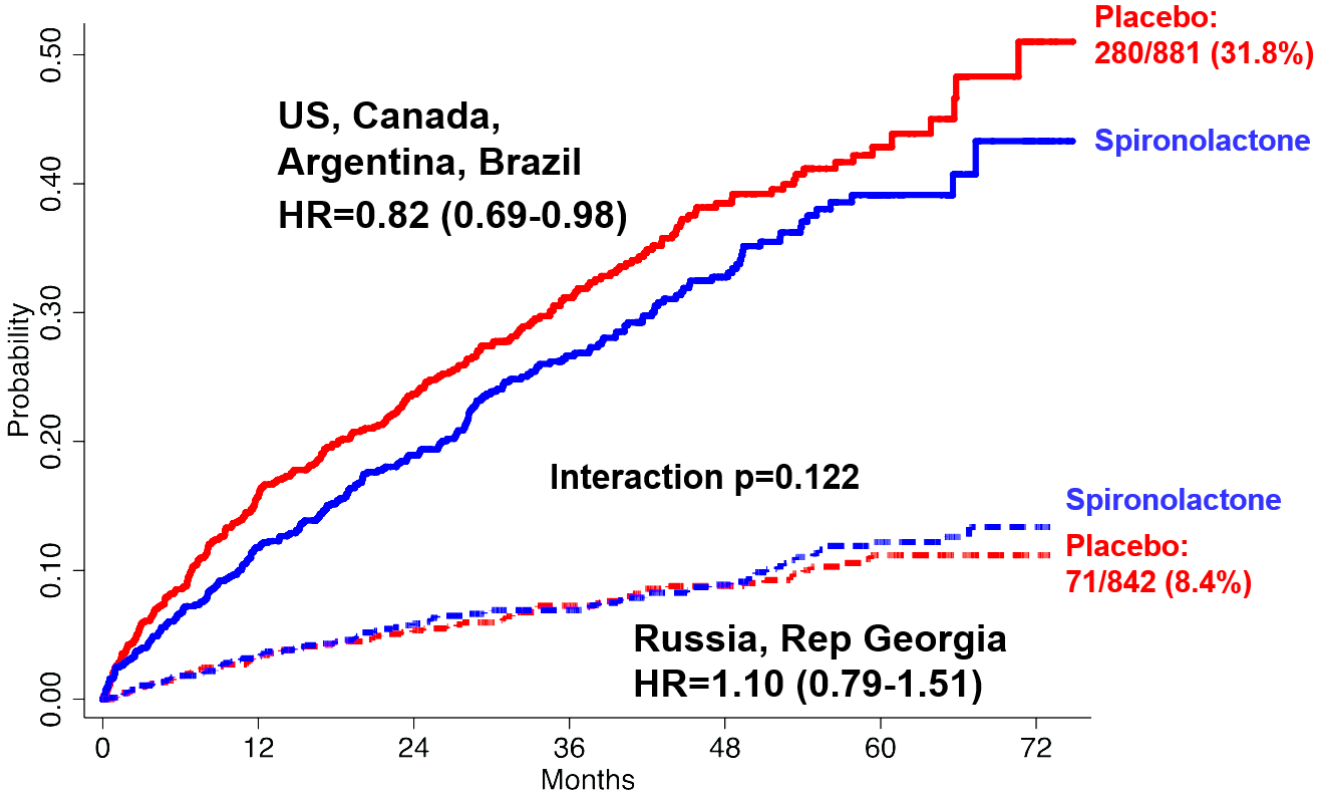
- Mineralocorticoid receptor antagonists (MRAs) have a IA recommendation in guidelines for HFrEF but not HFpEF
- Based on interpretation of TOPCAT

Pfeffer et al. *N Engl J Med* 2017; 376:1690-1692

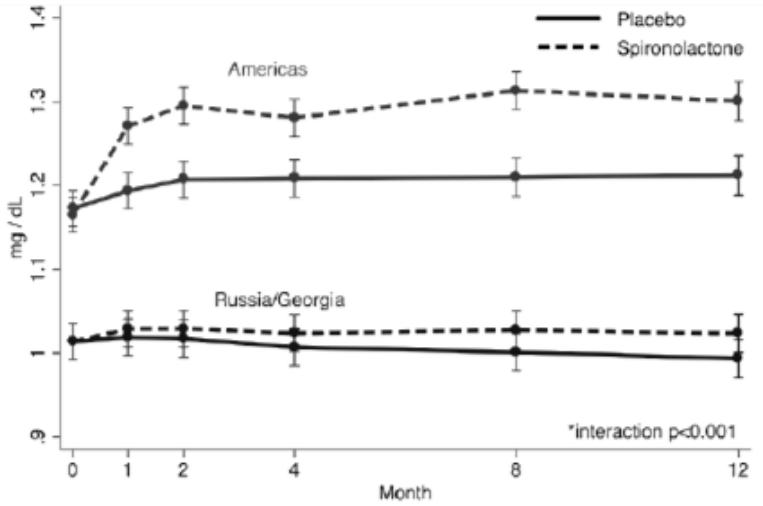




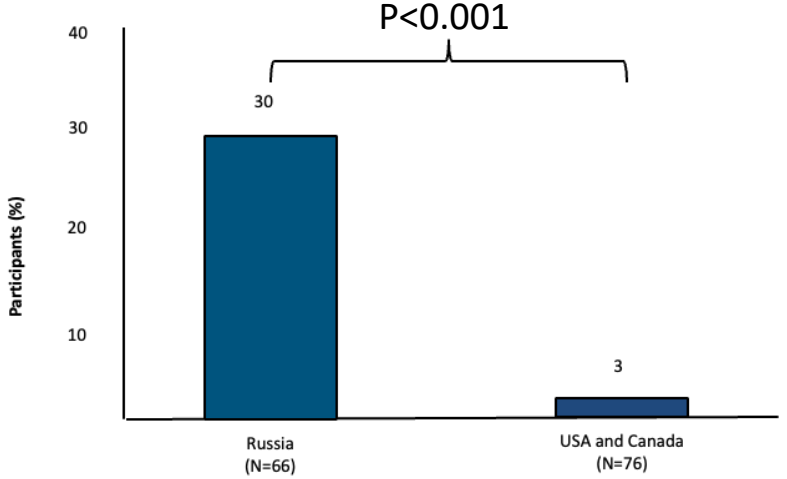
TOPCAT: Forensic analysis by Marc Pfeffer et al



Change in creatinine



Reported use with no detectable canrenone



Pfeffer MA et al Circulation. 2015;131:34-42. de Denus S et al N Engl J Med. 2017;376:1690-1692. Pfeffer et al. *N Engl J Med* 2017; 376:1690-1692

Management of HFmrEF/HFpEF 2022 AHA/ACC/HFSA Guideline

IIb B-R

A post hoc analysis6 showed efficacy in the Americas (HR 0.83) but not in Russia-Georgia (HR 1.10). A sample of the Russia-Georgia population in the active treatment arm had nondetectable levels of a spironolactone metabolite. Post hoc analyses have limitations, but they suggest a possibility of benefit in appropriately selected patients with symptomatic HFpEF (LVEF ≥45%, elevated BNP level or HF admission within 1 year, eGFR >30 mL/min/1.73 m2, creatinine <2.5 mg/dL, and potassium <5.0 mEq/L).

Heidenreich PA et al. Circulation. 2022;145(18):e895-e1032. doi: 10.1161/CIR.0000000000001063

FINEARTS-HF: Trial design

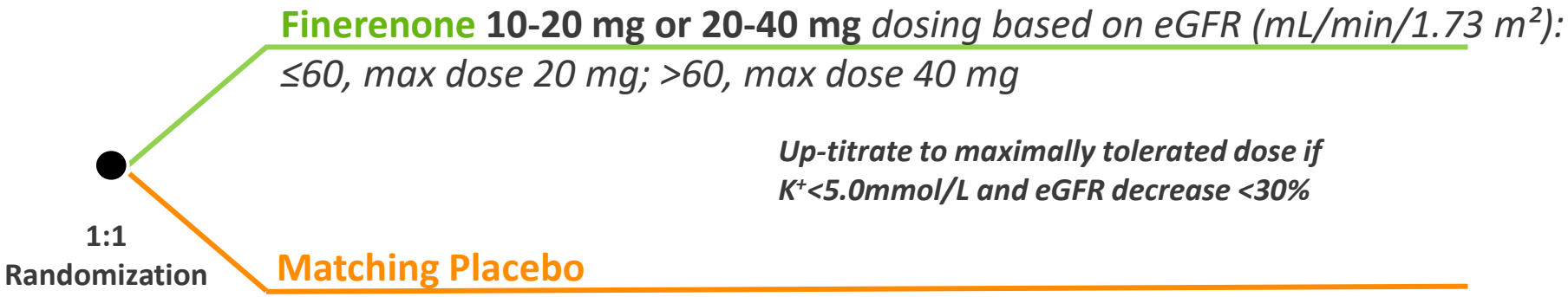
Randomized, double-blind, placebo-controlled trial testing the hypothesis that finerenone would reduce cardiovascular death and total worsening heart failure events in patients with heart failure and mildly reduced or preserved ejection fraction

Key inclusion criteria

- Symptomatic HF (NYHA class II-V) with LVEF ≥40%
- Hospitalized, recently hospitalized, or ambulatory
- Elevated natriuretic peptide levels
- Structural heart disease (LA Enlargement or LVH)
- Diuretics in the 30 days prior to randomization

Key exclusion criteria

- Potassium >5.0 mmol/L; eGFR <25 mL/min/1.73 m^2
- MRA use 30 days prior to randomization
- History of peripartum, chemotherapy induced, or infiltrative cardiomyopathy (e.g., amyloidosis)
- Alternative causes of signs or symptoms



Visits: Month 1, then 3-monthly for first 12 months, 4-monthly visits thereafter with telephone contact in between

Trial endpoints

Primary Endpoint

- CV death and total HF events (hospitalizations/urgent visits)

Secondary Endpoints

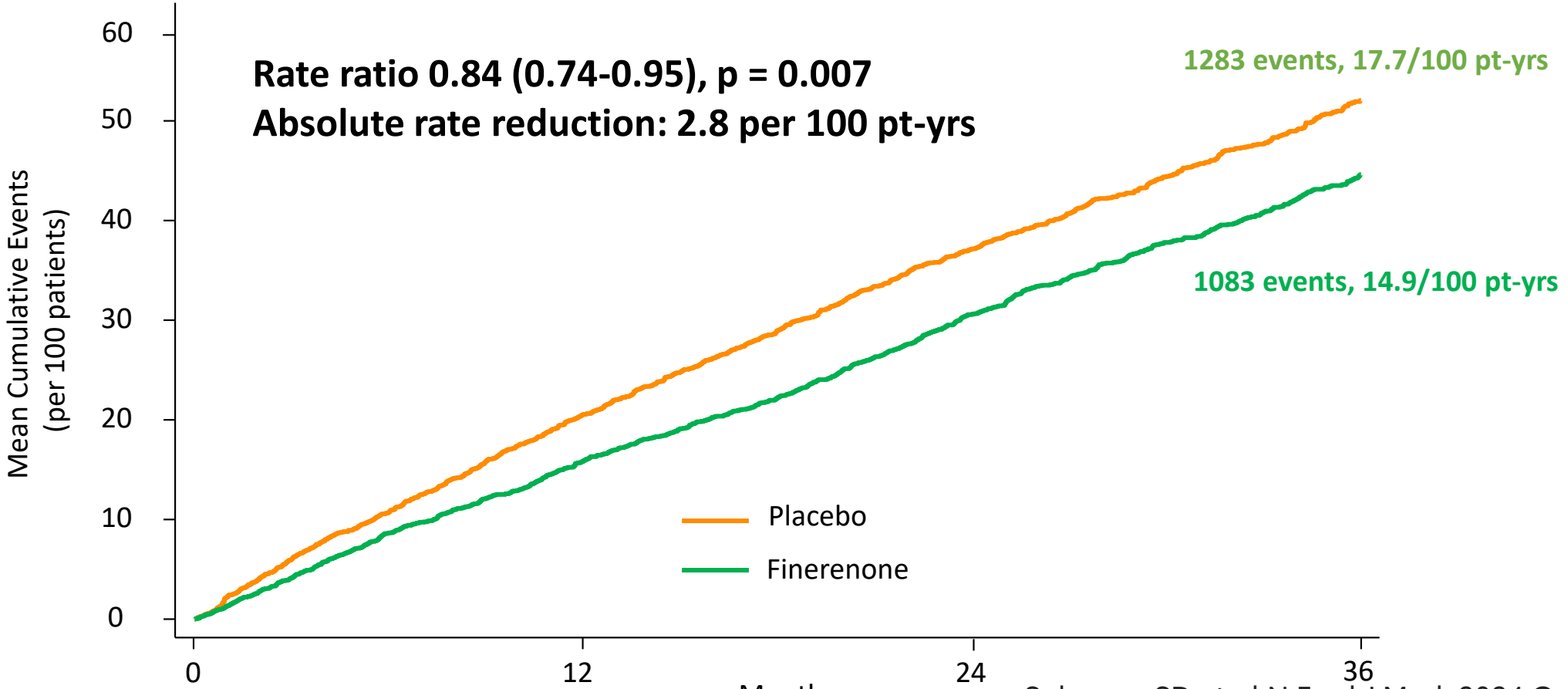
- Total HF events
- KCCQ-TSS at 6,9, and 12 months
- NYHA class at 12 months
- Renal composite endpoint
- All-cause mortality

Solomon SD et al N Engl J Med. 2024 Oct 24;391(16):1475-1485.

FINEARTS-HF: Primary endpoint

CV Death and total HF events

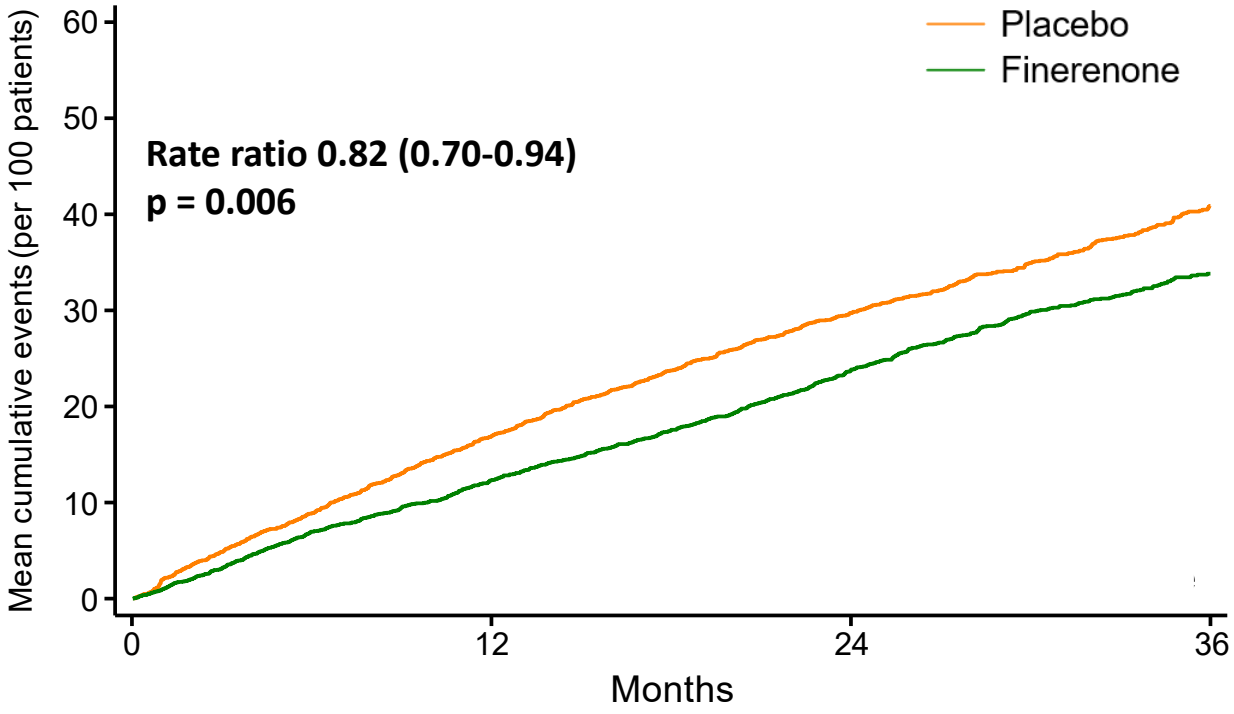
Median follow-up of 32 months



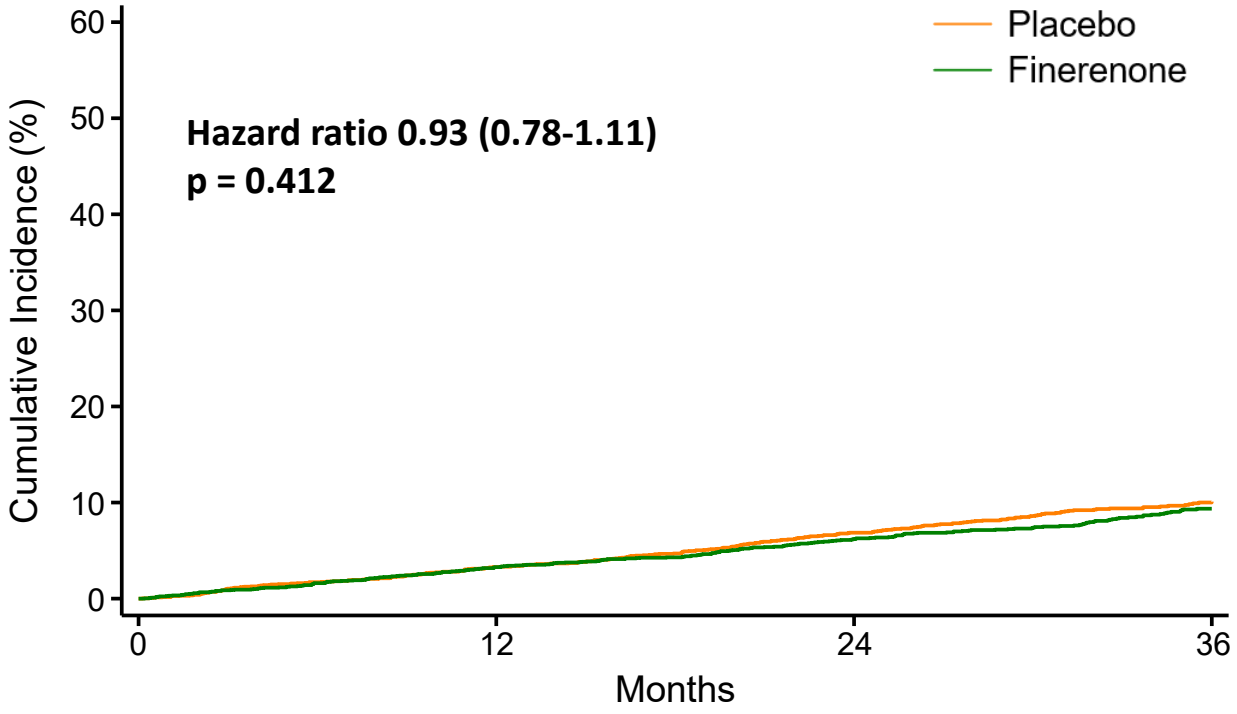
Solomon SD et al N Engl J Med. 2024 Oct 24;391(16):1475-1485.

FINEARTS-HF: Components of primary endpoint

Total HF events



CV death



Solomon SD et al N Engl J Med. 2024 Oct 24;391(16):1475-1485.

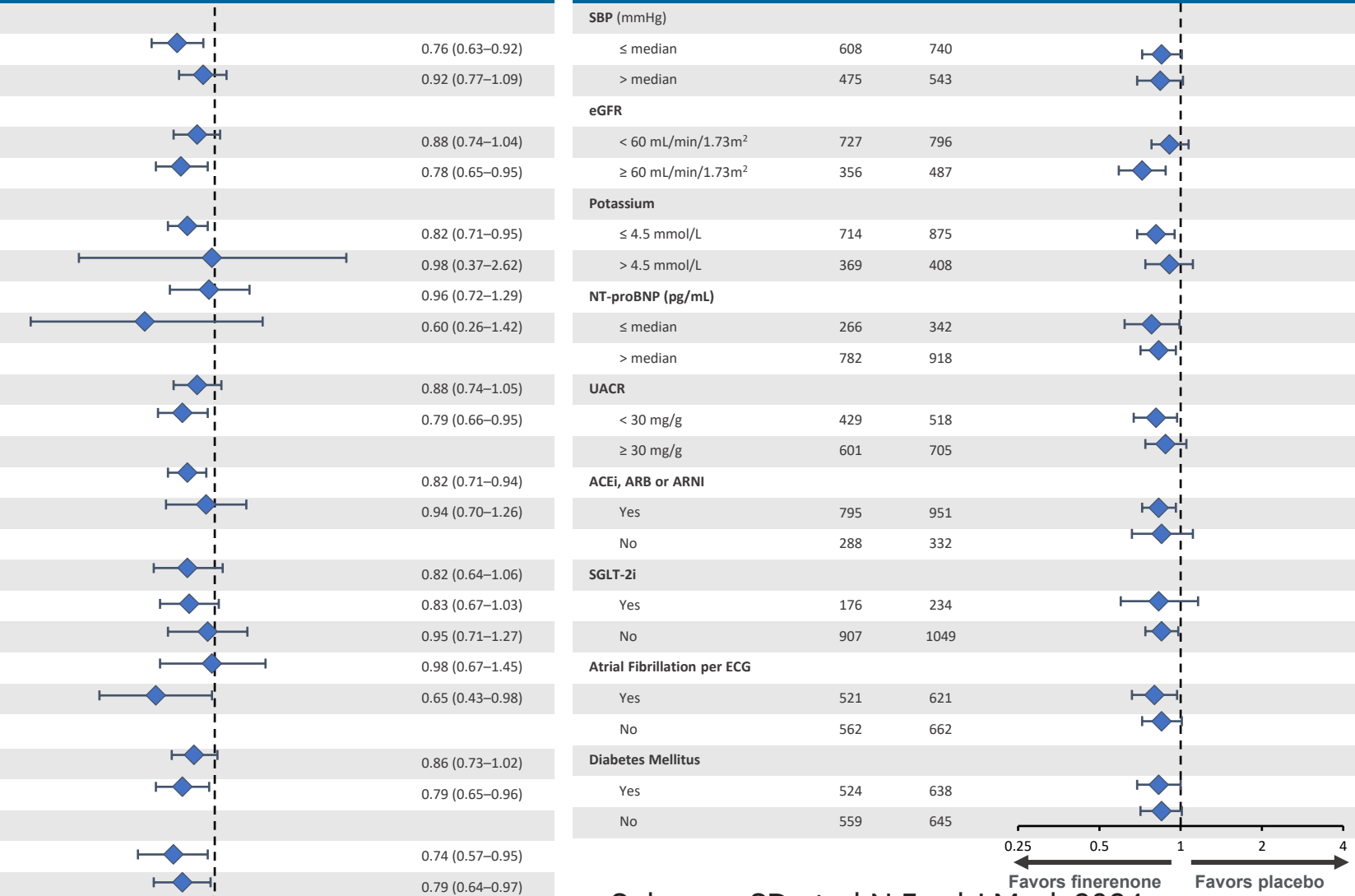
FINEARTS-HF: Prespecified subgroups (Primary outcome)

Consistent treatment effects across all pre-specified subgroups, including ejection fraction and SGLT2-inhibitor use

American Heart Association.

Category	Finerenone Events	Placebo Events	RR (95% CI)
Age (years)			
≤ median	468	623	0.76 (0.63–0.92)
> median	615	660	0.92 (0.77–1.09)
Gender			
Male	632	691	0.88 (0.74–1.04)
Female	451	592	0.78 (0.65–0.95)
Race			
White	809	986	0.82 (0.71–0.95)
Black	29	22	0.98 (0.37–2.62)
Asian	211	218	0.96 (0.72–1.29)
Other	34	57	0.60 (0.26–1.42)
BMI			
< 30 kg/m^2	586	648	0.88 (0.74–1.05)
≥ 30 kg/m^2	486	632	0.79 (0.66–0.95)
LVEF			
< 60%	877	1061	0.82 (0.71–0.94)
≥ 60%	206	222	0.94 (0.70–1.26)
Region			
W Eur, Oce & Others	322	395	0.82 (0.64–1.06)
Eastern Europe	322	389	0.83 (0.67–1.03)
Asia	211	218	0.95 (0.71–1.27)
North America	122	118	0.98 (0.67–1.45)
Latin America	106	163	0.65 (0.43–0.98)
NYHA Class			
II	646	741	0.86 (0.73–1.02)
III/IV	437	542	0.79 (0.65–0.96)
Index HF Events			
≤ 7 days	270	372	0.74 (0.57–0.95)
> 7 days to ≤ 3 months	404	492	0.79 (0.64–0.97)
> 3 months or no prior HFE	409	419	0.99 (0.81–1.21)

Category	Finerenone Events	Placebo Events	RR (95% CI)
SBP (mmHg)			
≤ median	608	740	0.85 (0.72–1.01)
> median	475	543	0.84 (0.69–1.02)
eGFR			
< 60 mL/min/1.73m^2	727	796	0.91 (0.78–1.07)
≥ 60 mL/min/1.73m^2	356	487	0.72 (0.59–0.88)
Potassium			
≤ 4.5 mmol/L	714	875	0.81 (0.69–0.95)
> 4.5 mmol/L	369	408	0.91 (0.74–1.11)
NT-proBNP (pg/mL)			
≤ median	266	342	0.78 (0.62–0.99)
> median	782	918	0.83 (0.71–0.96)
UACR			
< 30 mg/g	429	518	0.81 (0.67–0.97)
≥ 30 mg/g	601	705	0.88 (0.74–1.05)
ACEi, ARB or ARNI			
Yes	795	951	0.83 (0.72–0.96)
No	288	332	0.85 (0.66–1.11)
SGLT-2i			
Yes	176	234	0.83 (0.60–1.16)
No	907	1049	0.85 (0.74–0.98)
Atrial Fibrillation per ECG			
Yes	521	621	0.80 (0.66–0.97)
No	562	662	0.85 (0.72–1.01)
Diabetes Mellitus			
Yes	524	638	0.83 (0.69–1.00)
No	559	645	0.85 (0.71–1.01)



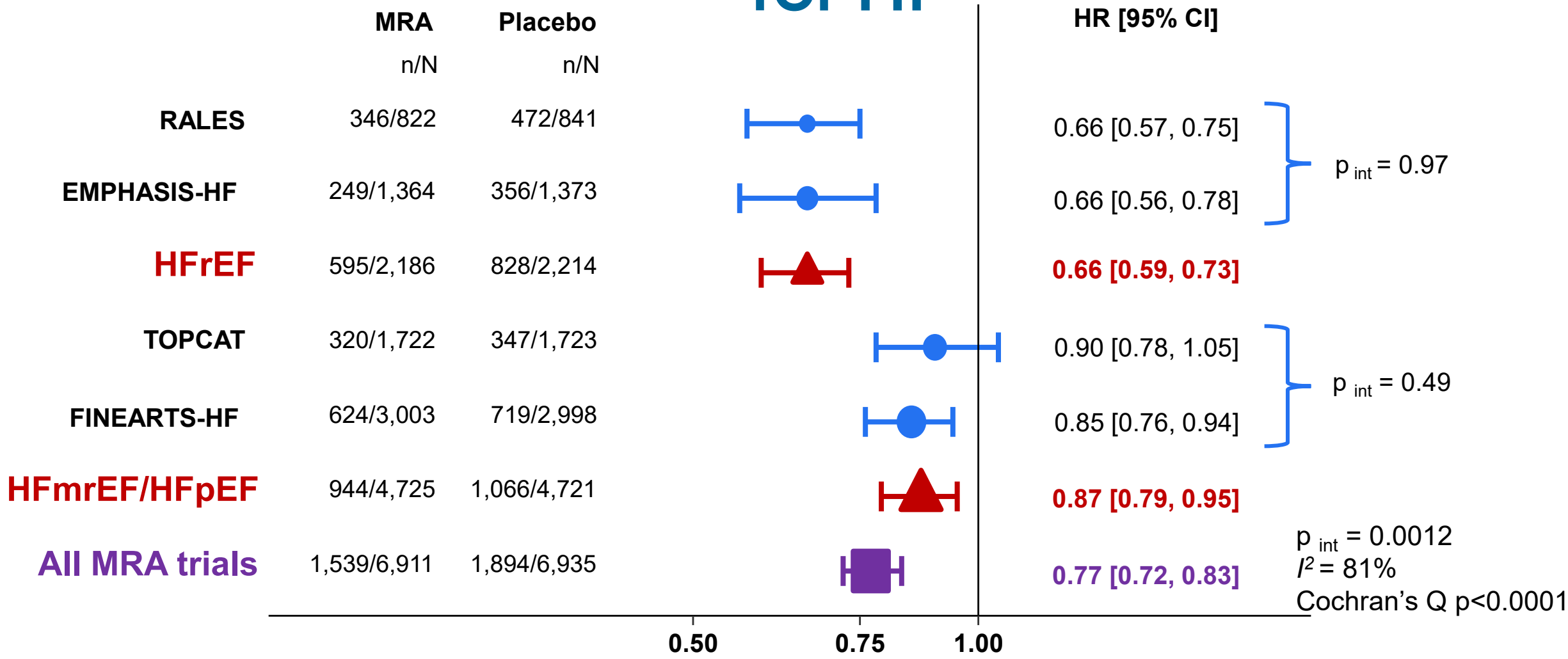
Solomon SD et al N Engl J Med. 2024 Oct 24;391(16):1475-1485.

FINEARTS-HF: Prespecified safety and tolerability

Treatment emergent safety outcome	Finerenone (N=2993)	Placebo (N=2993)
Any Serious Adverse Event (SAE)	38.7%	40.5%
Serum creatinine ≥3.0 mg/dl	2.0%	1.2%
Serum potassium		
>5.5 mmol/l	14.3%	6.9 %
>6.0 mmol/l	3.0 %	1.4 %
<3.5 mmol/l	4.4 %	9.7 %
Investigator-reported hyperkalaemia	9.7%	4.2%
Leading to hospitalization	0.5%	0.2%
Leading to death	0%	0%
Systolic blood pressure <100 mmHg	18.5%	12.4%

Solomon SD et al N Engl J Med. 2024 Oct 24;391(16):1475-1485.

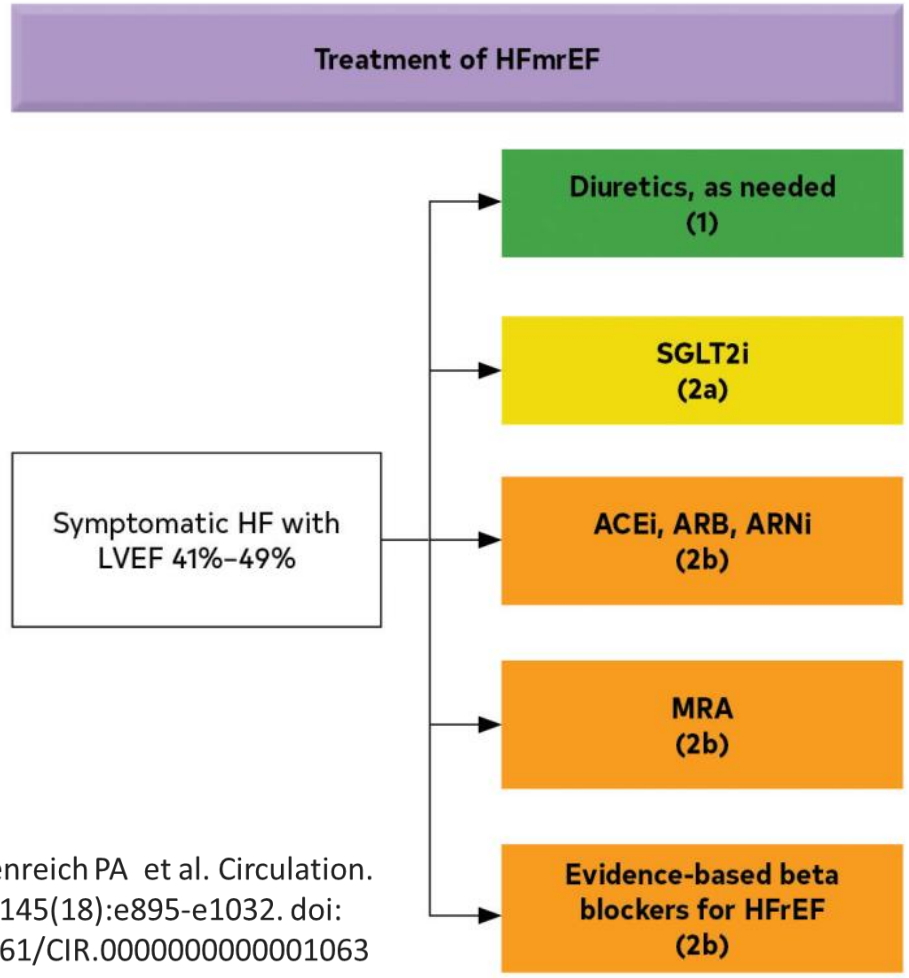
MRAs in HF: CV Death or hospitalisation for HF

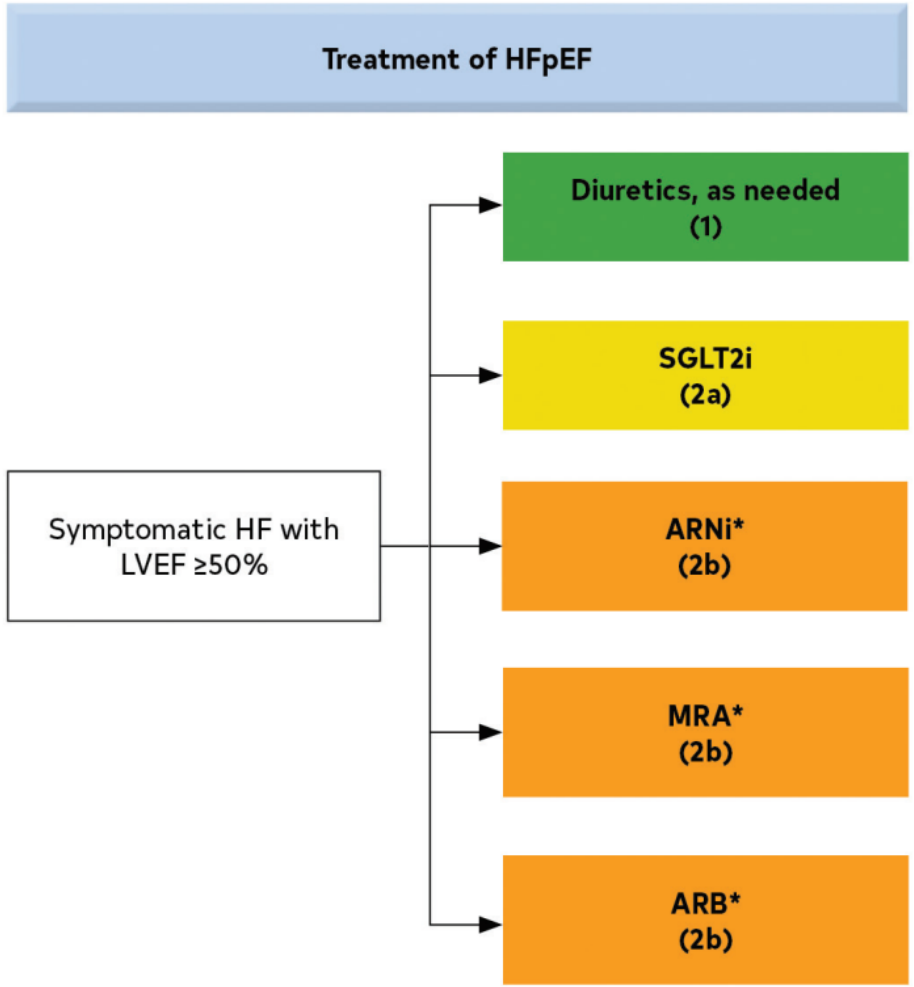


HR, hazard ratio; p int, p value for interaction ; I^2, Higgins and Thompson's I^2

Jhund PS *et al Lancet*. 2024;404(10458):1119-1131

Management of HFmrEF/HFpEF 2022 AHA/ACC/HFSA Guideline





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Summary

- Patients with HFmrEF and HFpEF now have multiple therapies that improve outcomes
- SGLT2is have data to support their use across the ejection fraction spectrum
- MRAs look to also be effective across the ejection fraction spectrum
- ARNis are indicated in patients with lower than normal ejection fraction
- There is a role for beta blockers in HFmrEF and angiotensin receptor blockers in HFpEF

Summary

- Patients with HFmrEF and HFpEF now have multiple therapies that improve outcomes
- SGLT2is have data to support their use across the ejection fraction spectrum
- MRAs look to also be effective across the ejection fraction spectrum
- ARNis are indicated in patients with lower than normal ejection fraction
- There is a role for beta blockers in HFmrEF and angiotensin receptor blockers in HFpEF

All these data are fantastic but are only valuable if we use them to treat our patients!

Thank You.

Questions?

Upcoming Event

American Heart Association. IMPLEMENT-EF

Virtual Event

Bridging Gaps in HFpEF/HFmrEF Care: Diagnosis, Treatment, and Addressing Social Needs

Wednesday, December 10th 10:00am – 1:30 pm CT

This half-day summit brings together innovative models and practices to improve the identification, diagnosis, and treatment of HFpEF and HFmrEF. Through four focused sessions, participants will explore strategies for recognizing these conditions at admission, leveraging AI for diagnosis, implementing evidence-based therapies, and addressing health-related social needs from both clinical and patient perspectives. Join us to learn effective implementation strategies in caring for HFpEF/HFmrEF patients

- AI in Action: Enhancing HFpEF/HFmrEF Diagnosis Through Site-Based Model
- Spotlight on Admission: Models for Identifying HFpEF/HFmrEF at Admission
- Putting Evidence into Action: Real-World HFpEF/HFmrEF Treatment Model
- Barriers to Better Care: Tackling Health-Related Social Needs in HFpEF/HFmrEF Management

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