What’s new in HF in 2021

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Faculty/Presenter Disclosure

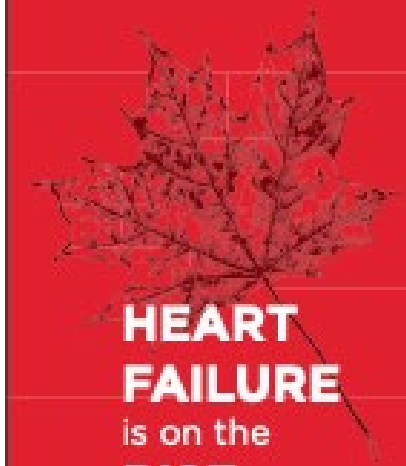
- **Faculty:** Kiran Sidhu

- **Relationships with commercial interests:**
  - **Grants/Research Support: N/A**
  - **Speakers Bureau/Honoraria: HF update, CV update**
  - **Consulting Fees:** N/A
  - **Other:** N/A

Objectives

- What to consider in your differential of a new onset HFrEF or HFpEF patient?
- What new therapies are available in the treatment of HF?
- Review changes in the 2021 CCS HF guidelines
- When to refer and clues to identify a sliding patient?

HEART FAILURE IS A GROWING EPIDEMIC



HEART FAILURE is on the **RISE** in **CANADA.**

600,000 CANADIANS are living with **HEART FAILURE.**

50,000 CANADIANS are diagnosed each year with **HEART FAILURE.**

1 in 2 CANADIANS has been touched by **HEART FAILURE.**

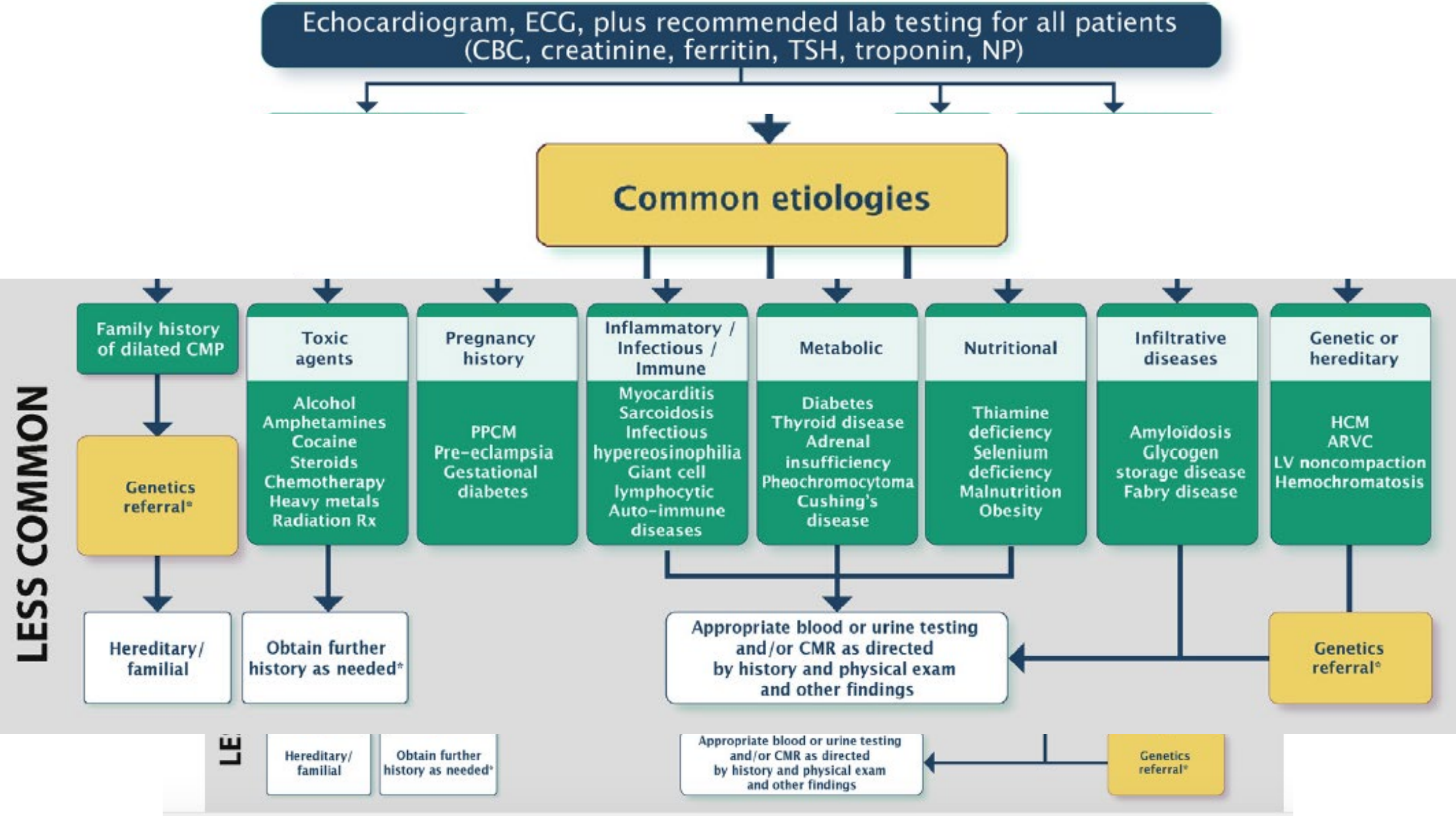
HEART FAILURE costs more than **$2.8 BILLION** per year.

ESC 2016 definition

Ponikowski P, et al. EHJ 2016;37:2129-200

Table 3.1 Definition of heart failure with preserved (HFpEF), mid-range (HFmrEF) and reduced ejection fraction (HFrEF)

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF <40%	LVEF 40–49%	LVEF ≥50%
	3	–	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).


Echocardiogram, ECG, plus recommended lab testing for all patients
(CBC, creatinine, ferritin, TSH, troponin, NP)
Common etiologies
LESS COMMON
Family history of dilated CMP
Genetics referral*
Hereditary/ familial
Toxic agents
Alcohol
Amphetamines
Cocaine
Steroids
Chemotherapy
Heavy metals
Radiation Rx
Obtain further history as needed*
Pregnancy history
PPCM
Pre-eclampsia
Gestational diabetes
Inflammatory / Infectious / Immune
Myocarditis
Sarcoidosis
Infectious hypereosinophilia
Giant cell lymphocytic
Auto-immune diseases
Metabolic
Diabetes
Thyroid disease
Adrenal insufficiency
Pheochromocytoma
Cushing's disease
Nutritional
Thiamine deficiency
Selenium deficiency
Malnutrition
Obesity
Infiltrative diseases
Amyloïdosis
Glycogen storage disease
Fabry disease
Genetic or hereditary
HCM
ARVC
LV noncompaction
Hemochromatosis
Appropriate blood or urine testing and/or CMR as directed by history and physical exam and other findings
Genetics referral*

Precipitants

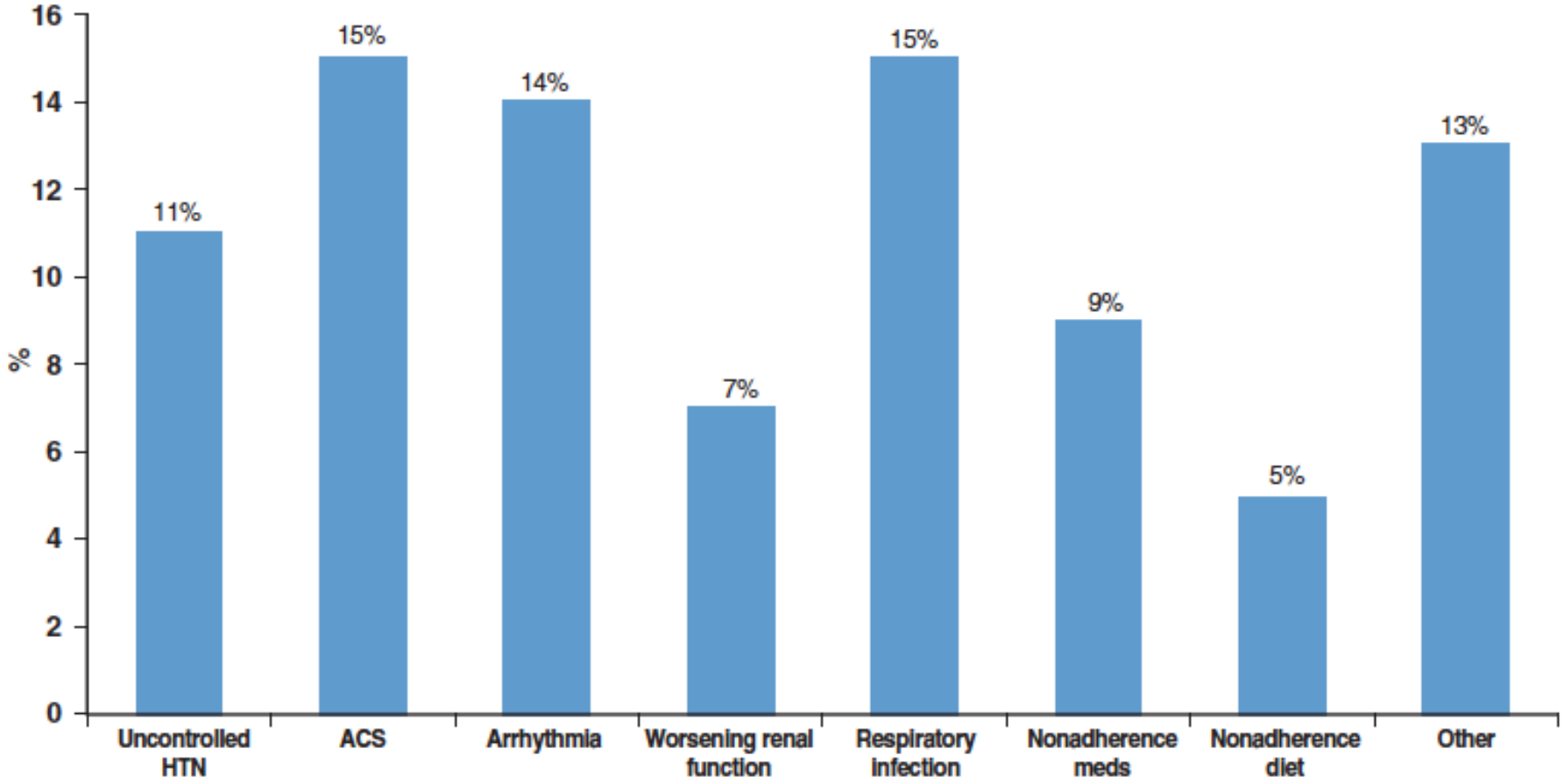
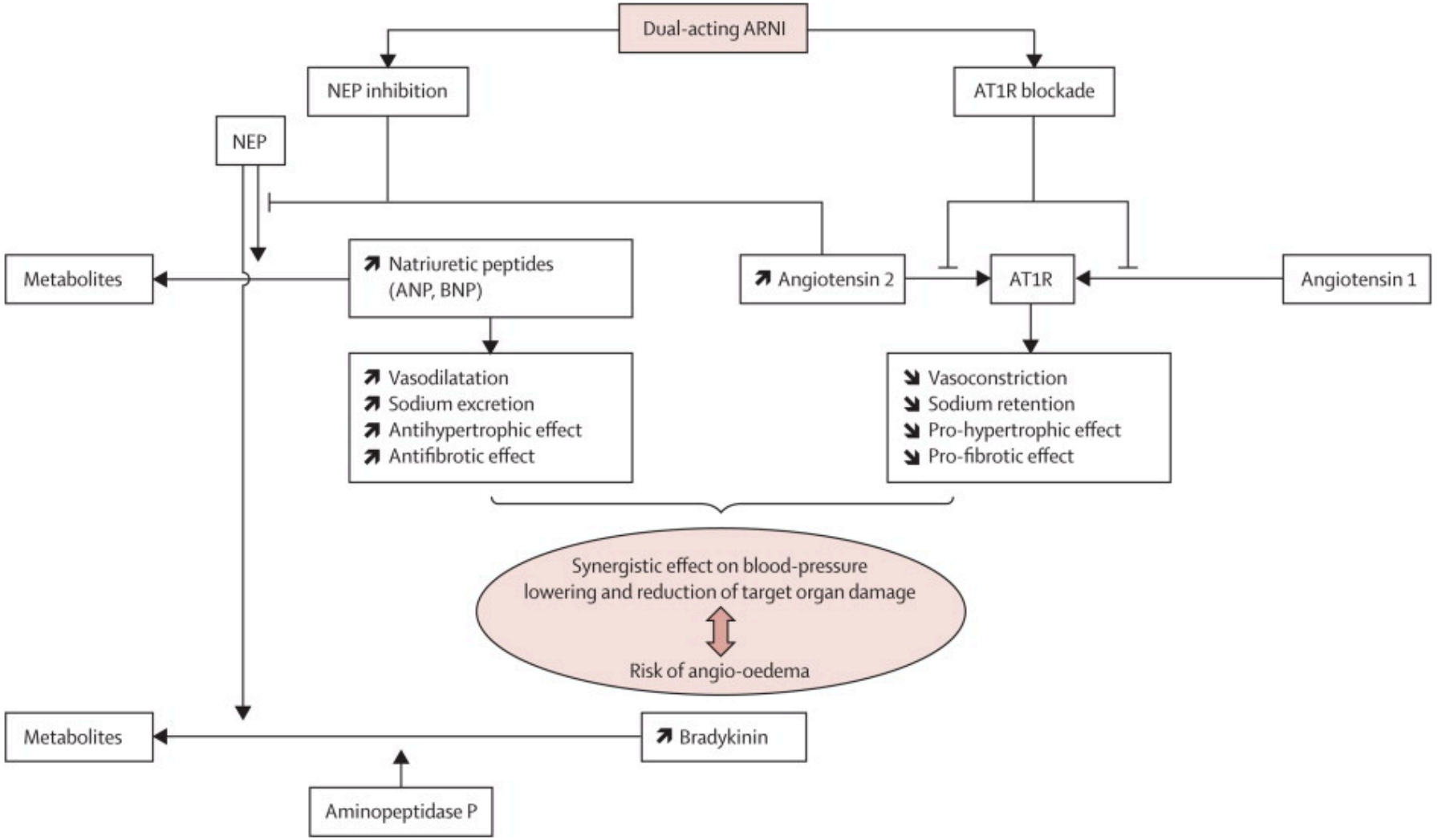


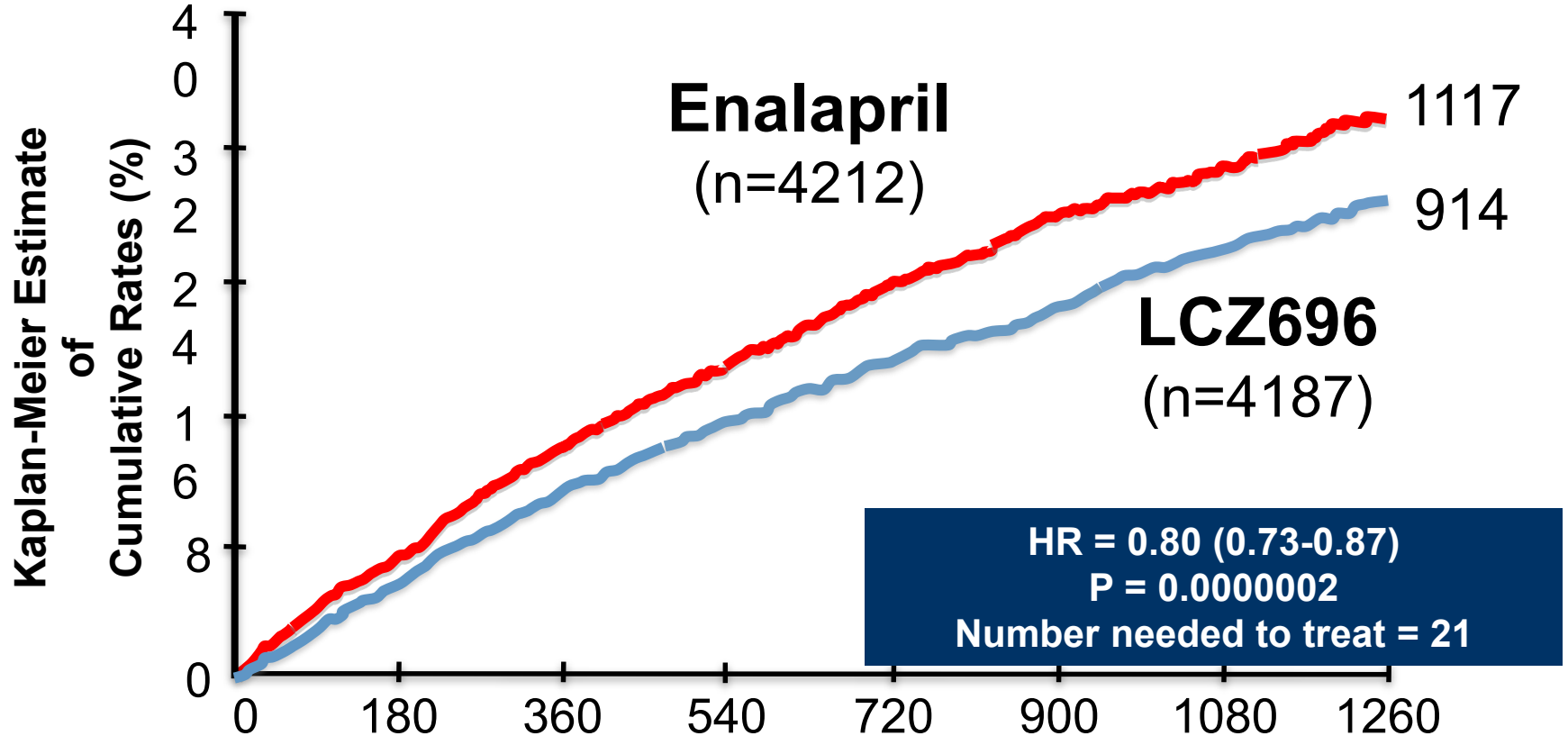
FIGURE 24-5 Identified triggers for acute heart failure hospitalization in the OPTIMIZE-HF Registry. HTN = hypertension. *(From Fonarow GC, Abraham WT, Albert NM, et al: Factors identified as precipitating hospital admissions for heart failure and clinical outcomes: Findings from OPTIMIZE-HF. Arch Intern Med 168:847, 2008.)*

Entresto

Vitally important to do a 36 hour washout when going from ACEi to Entresto



PARADIGM-HF: Primary endpoint

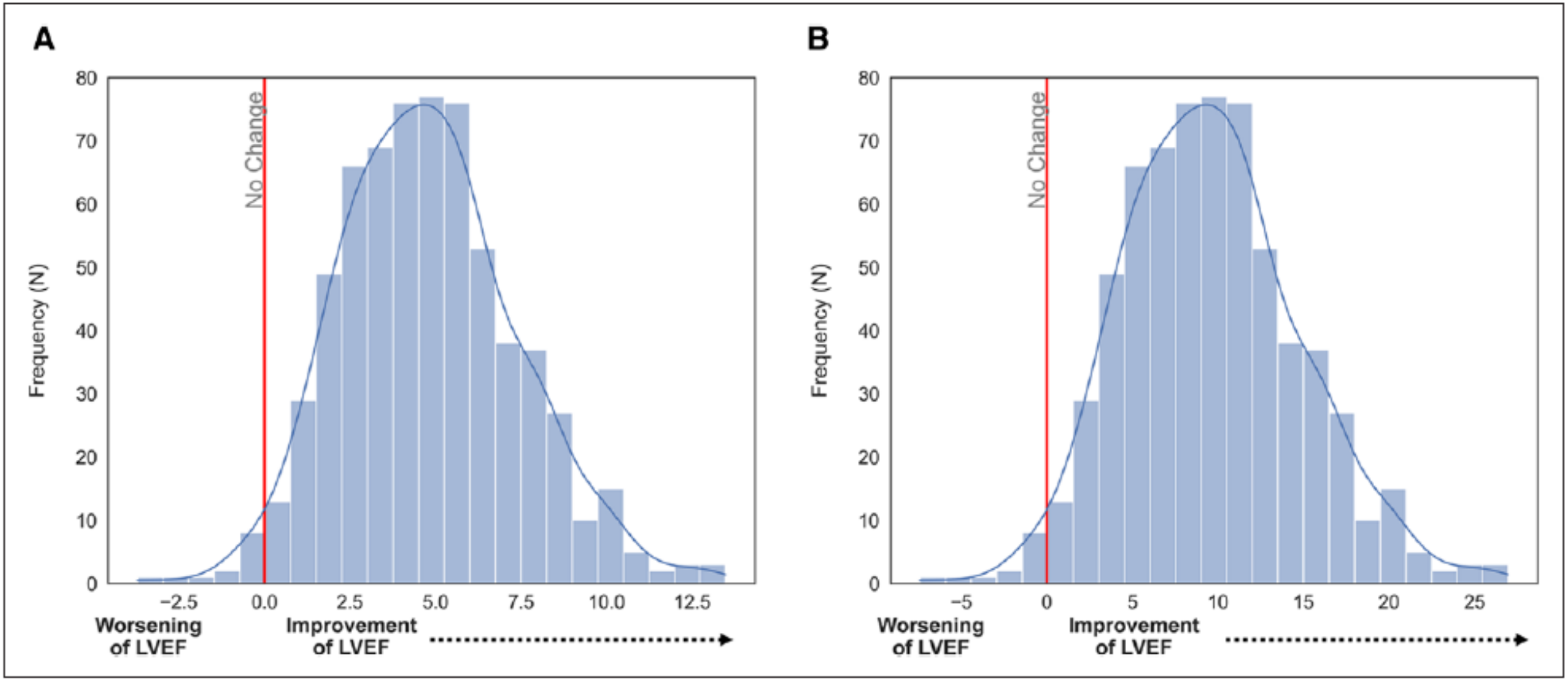


Patients at Risk

LCZ696	4187	3922	3663	3018	2257	1544	896	249
Enalapril	4212	3883	3579	2922	2123	1488	853	236

McMurray *NEJM* 2014

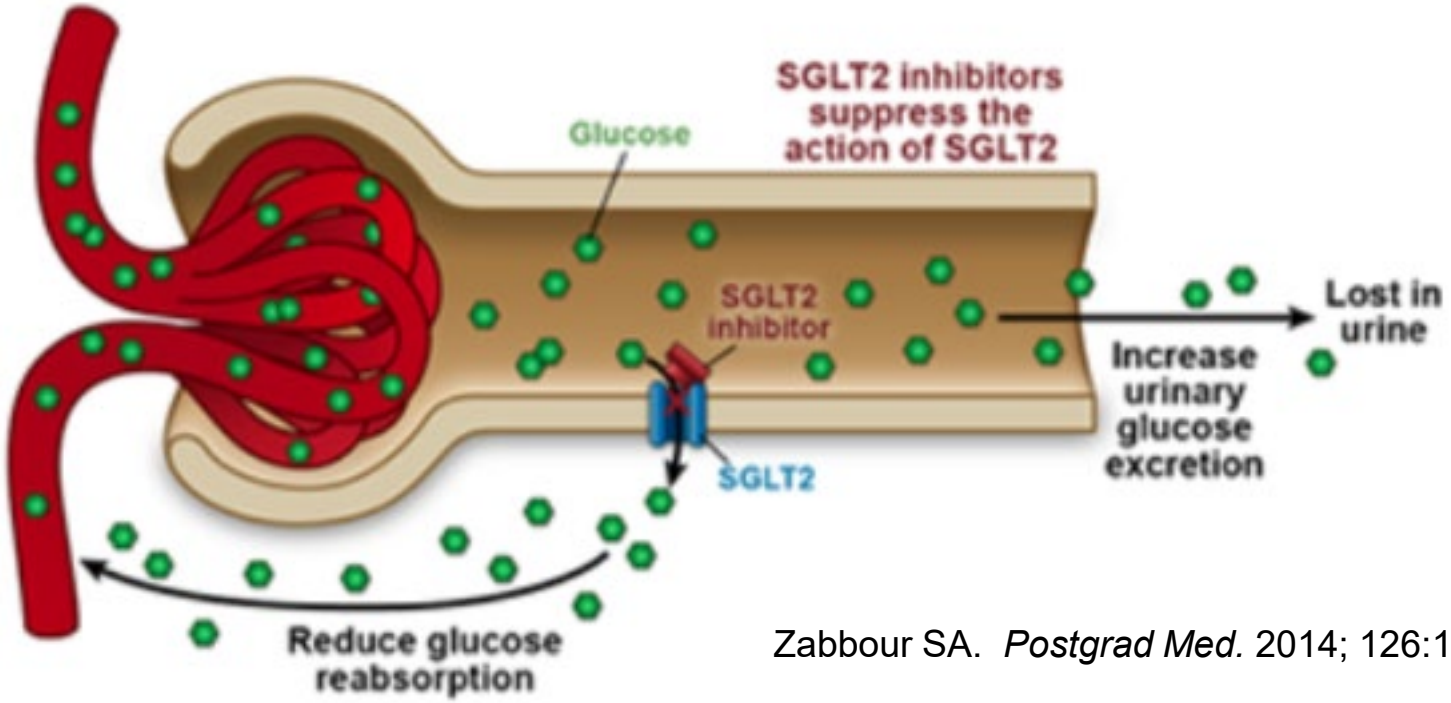
ICD eligibility after Entresto initiation in PROVE HF



Felker GM et al. Circulation. 2021;144:180–182

New kid on the block: SGLT2 inhibitors

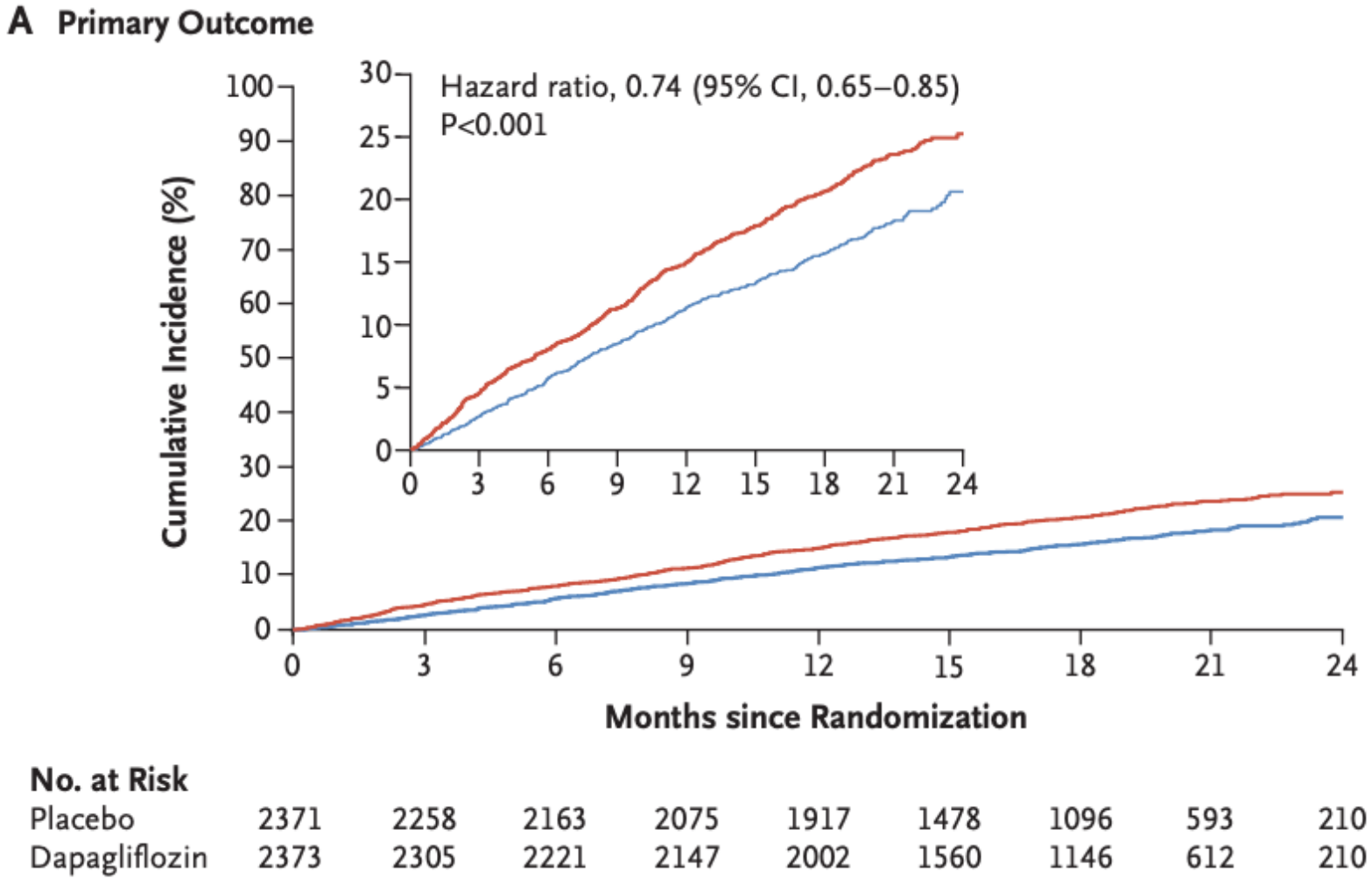
- Work in the proximal tubule to block the reabsorption of glucose back into the bloodstream



Zabbour SA. *Postgrad Med.* 2014; 126:111-117.

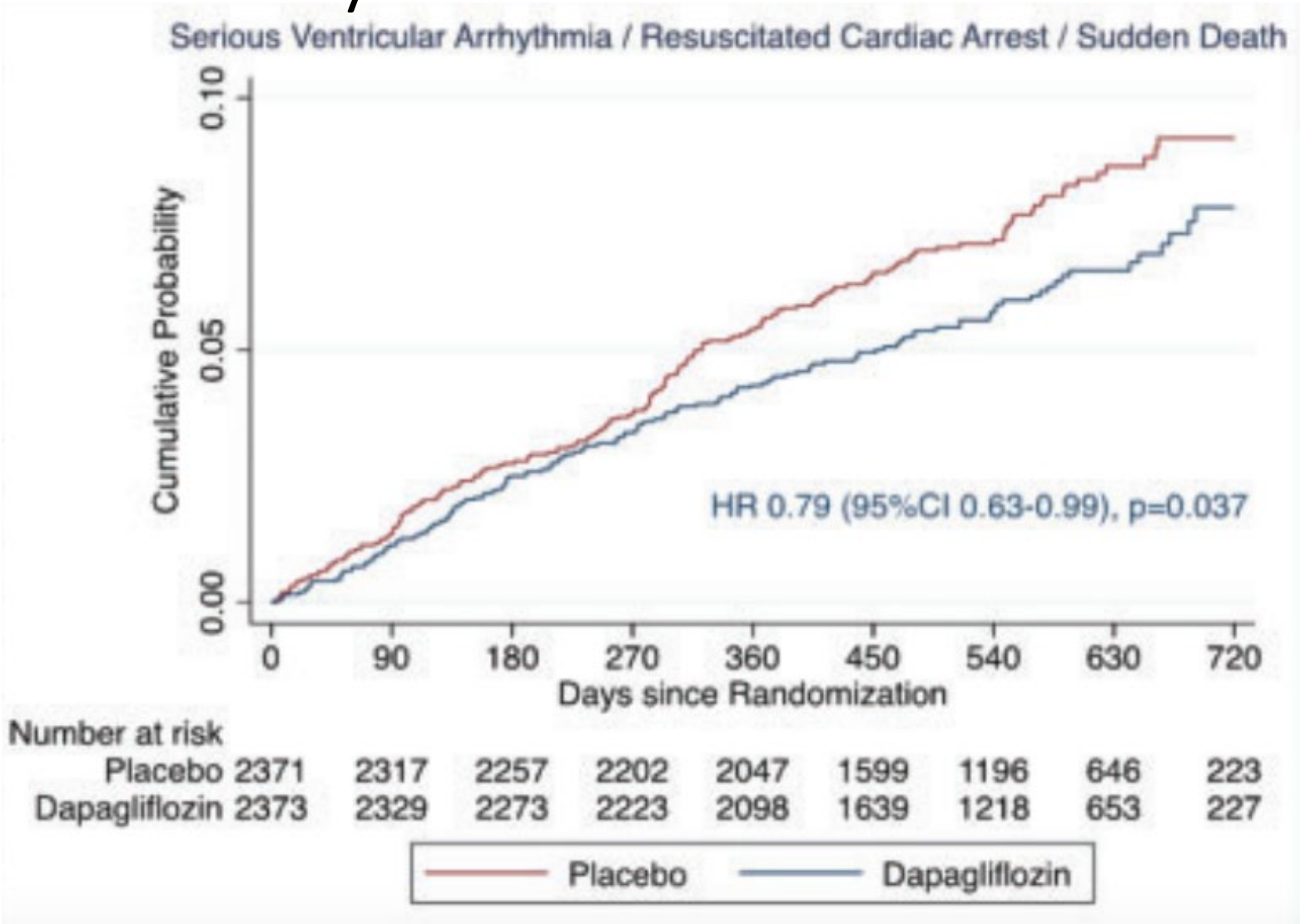
SGLT2 inhibitors

** Counsel around sick day management**

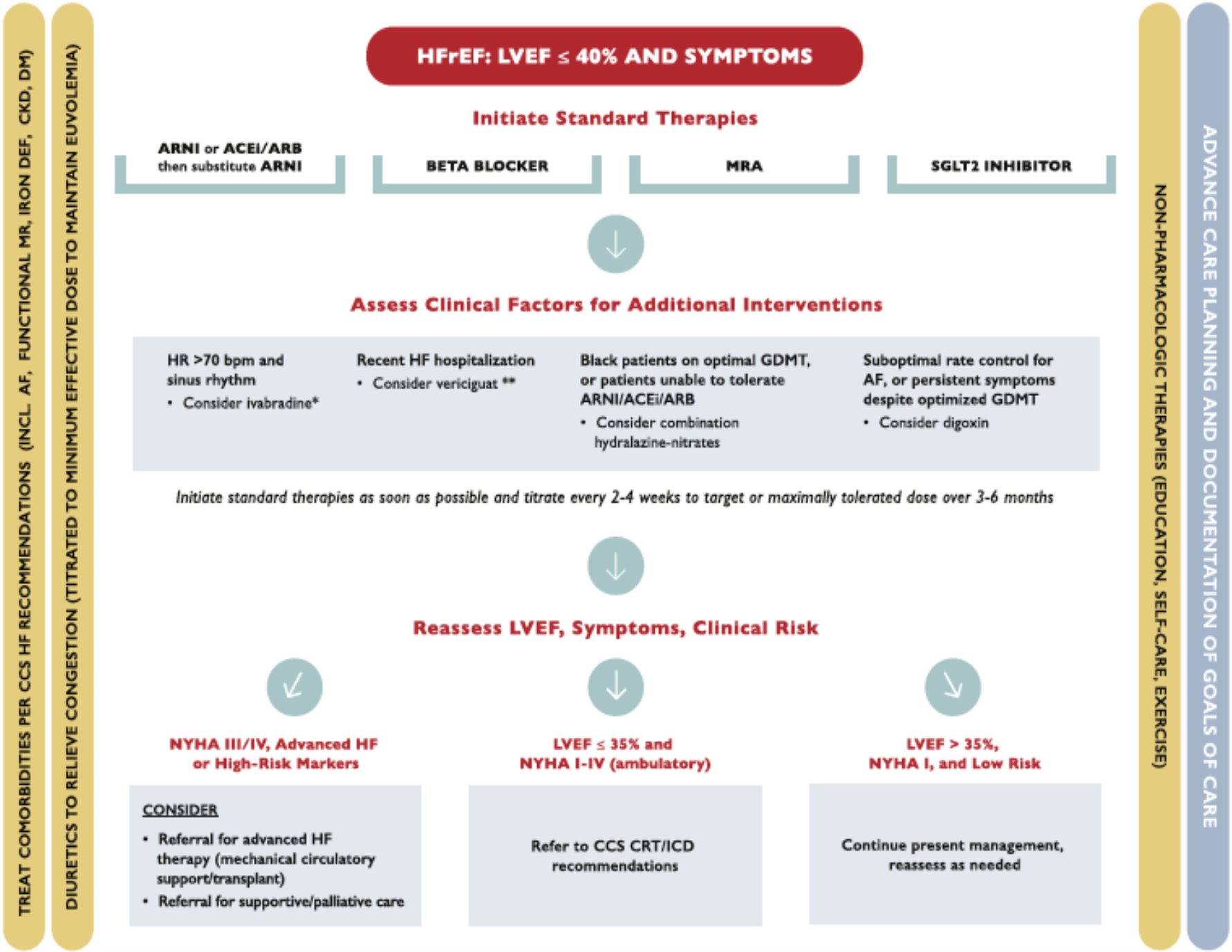


McMurray JJV et al. NEJM 2019. 381(21): 1995-2008.

Post hoc analysis of DAPA HF



Curtain JP et al. Eur Heart J 2021 Aug 27



2021 CCS HF guidelines

Cumulative Impact of Evidence-Based Heart Failure with Reduced EF Medical Therapies

	Relative-risk	2 yr Mortality
None	- -	35%
ACEI or ARB	↓ 23%	27%
Beta Blocker	↓ 35%	18%
Aldosterone Ant	↓ 30%	13%
ARNI (replacing ACEI/ARB)	↓ 16%	10.9%
SGLT2 inhibitor	↓ 17%	9.1%

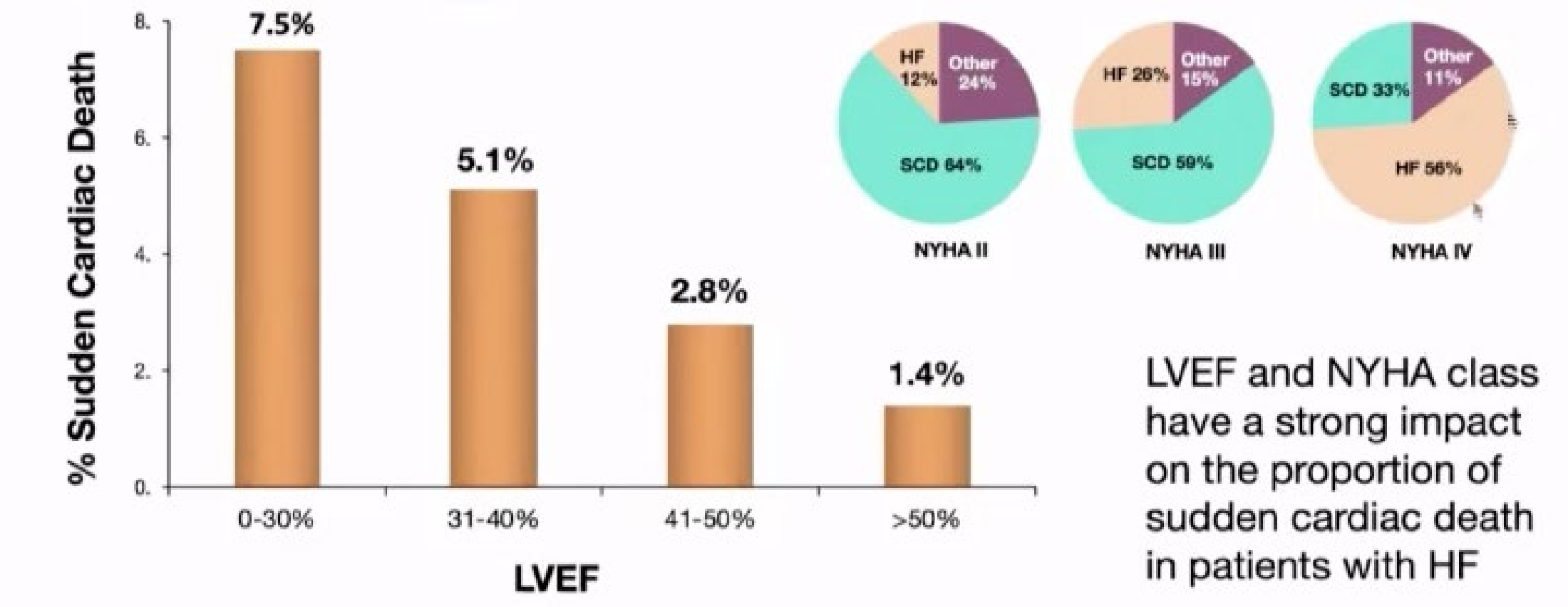
Cumulative risk reduction if all evidence-based medical therapies are used:
Relative risk reduction 74.0%, Absolute risk reduction: 25.9%, NNT = 3.9

Updated from Fonarow GC, et al. Am Heart J 2011;161:1024-1030 and Lancet 2008;372:1195-1196.

Dealing with comorbidities

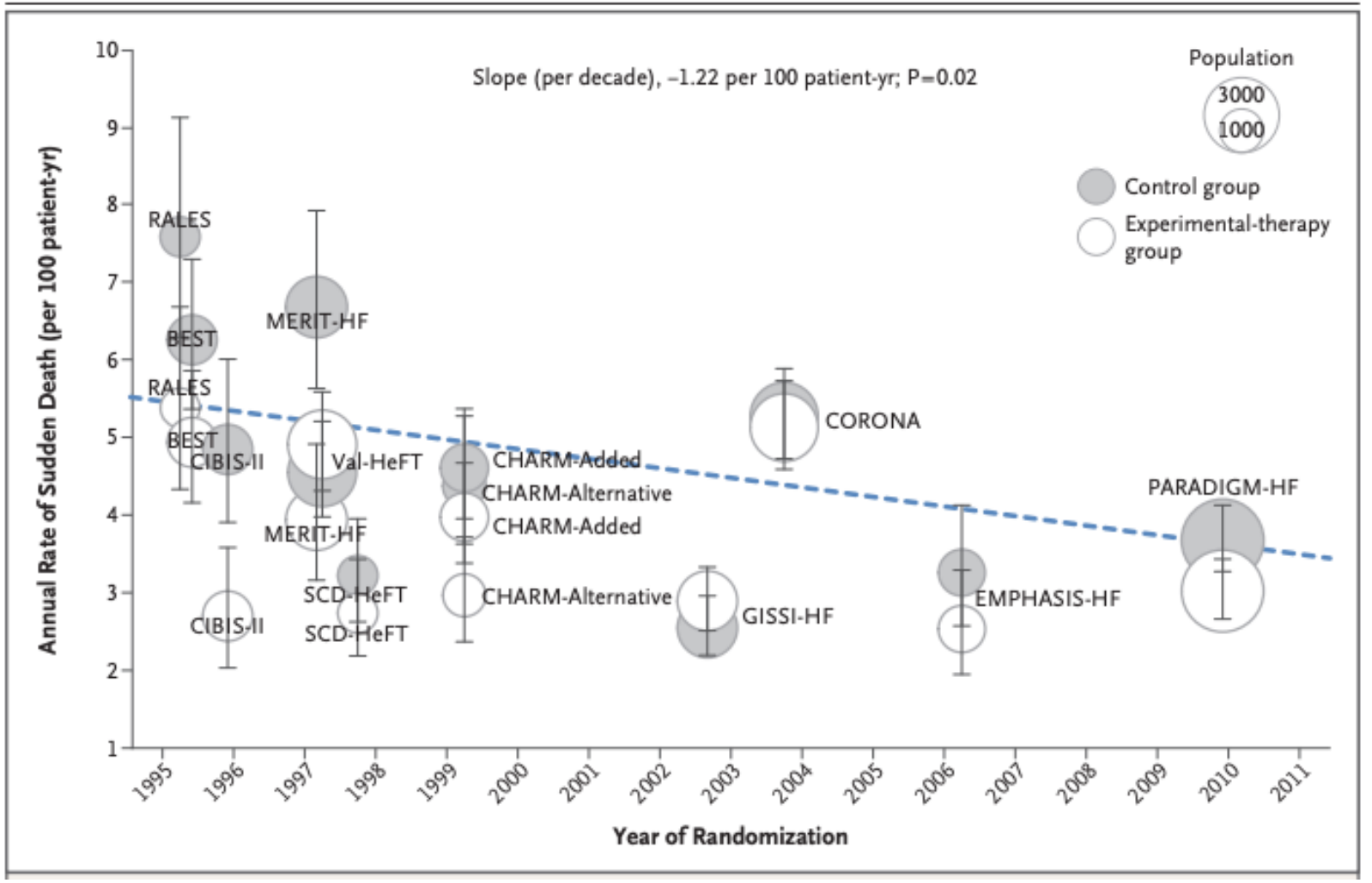
- AF – rate control, some will require rhythm control
- CAD – revascularization when appropriate
- OSA – weight loss, CPAP → will also help with AF if they co-exist
- Fe-deficiency – role for IV iron if iron sats < 20%
- Cardiac rehab
- Encouraging dietary and medication compliance

Causes of death in HF patients



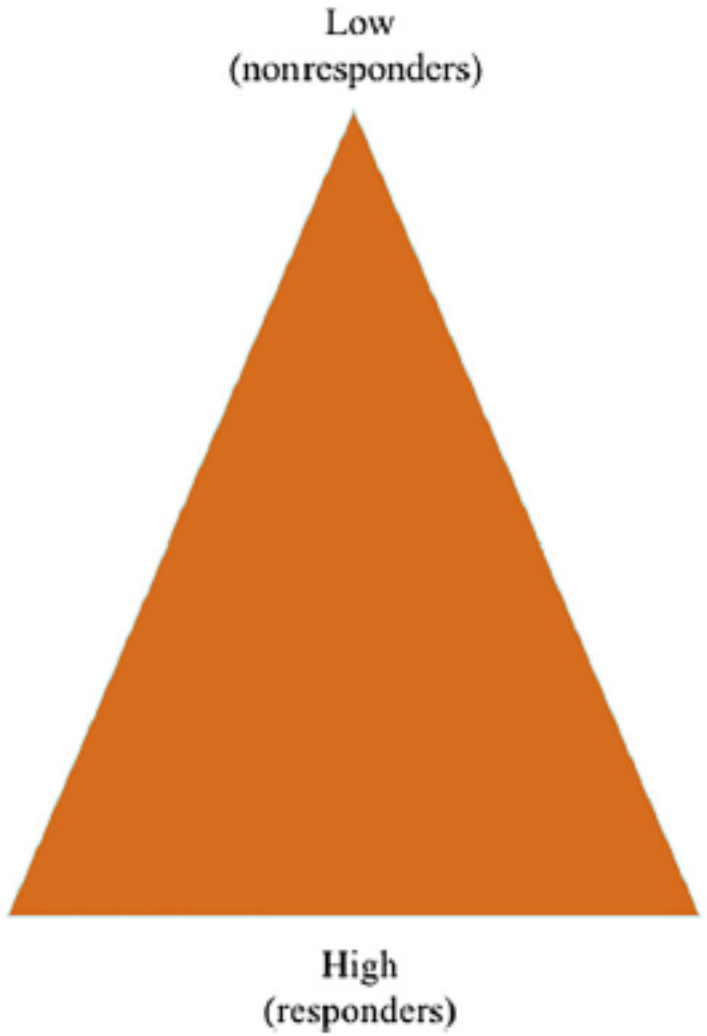
Adapted from HFSA review course
Gorgels AP et al. Eur Heart J. 2003;24:1204-1209.

Risk of SCD has decreased with GDMT



Shen L et al. N Engl J Med 2017;377(1):41-51.

CRT: Appropriate patient selection



QRS (120–130 ms)
non-LBBB morphology

Ischemic cardiomyopathy
males

QRS >150 ms
LBBB morphology
nonischemic
cardiomyopathy
females

Tolosana JM et al. Heart Failure Clin 13 (2017): 233-240.

Who to refer and other clues

- Worsening renal function with increasing diuretics in someone who is clearly volume overloaded is a sign of either low CO or RV failure
- ESHF pts may have clear lungs and no edema, they may present just with a grossly elevated JVP and abdominal symptoms (increased LFTs, ascites, nausea, low appetite)
- Asymptomatic hypotension (SBP in the 90's) is often seen in advanced HF and is not an indication to d/c GDMT

Remember acronym to assist in decision making for referral to advanced heart failure specialist:

I-NEED-HELP (also see *Table 6*)

I: IV inotropes

N: NYHA IIIB/IV or persistently elevated natriuretic peptides

E: End-organ dysfunction

E: Ejection fraction ≤35%

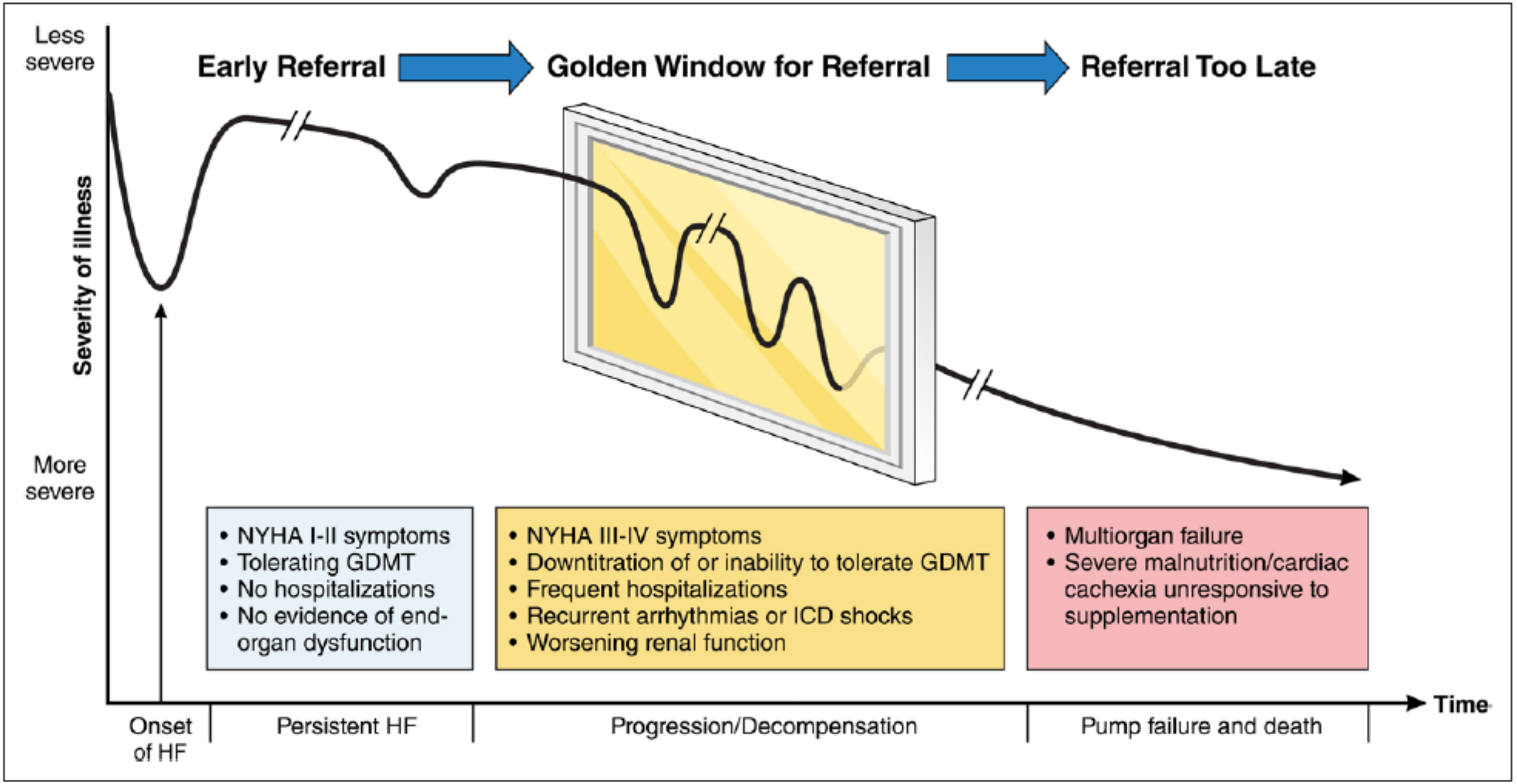
D: Defibrillator shocks

H: Hospitalizations >1

E: Edema despite escalating diuretics

L: Low blood pressure, high heart rate

P: Prognostic medication – progressive intolerance or down-titration of GDMT

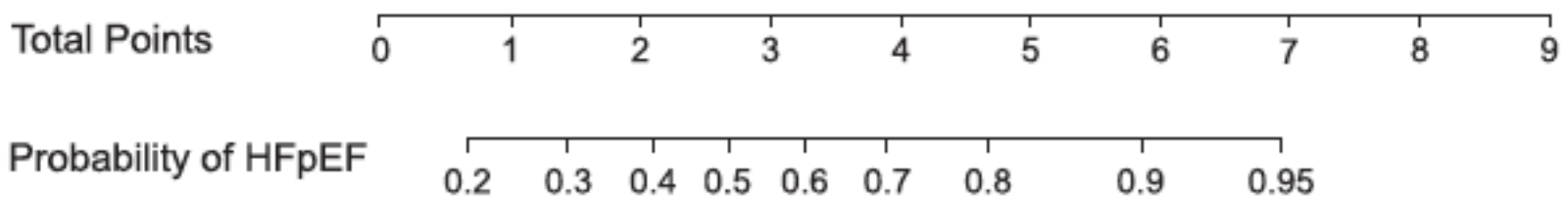


Morris AA et al. Circulation 2021 Sep 10

What’s new in HFpEF?

HFPEF score

	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)

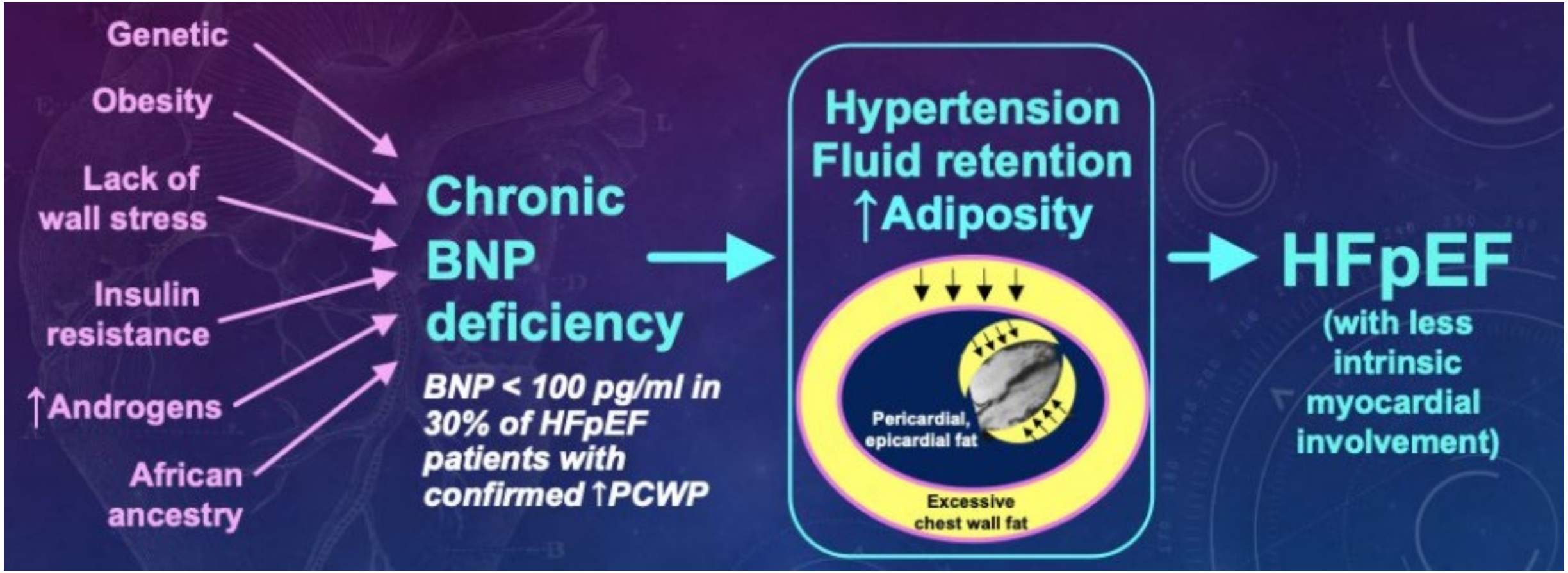


Reddy Y et al. Circulation 2018; 138(9): 861-70.

Etiologies of HFpEF

- Hypertensive/diabetic heart disease
- Myocardial ischemia/infarction
- Aortic stenosis, other valvular disease
- HOCM
- Infiltrative disorders (amyloidosis, sarcoidosis, hemochromatosis)
- Pericardial disease
- Early presentation of cardiomyopathy that may progress to HFrEF

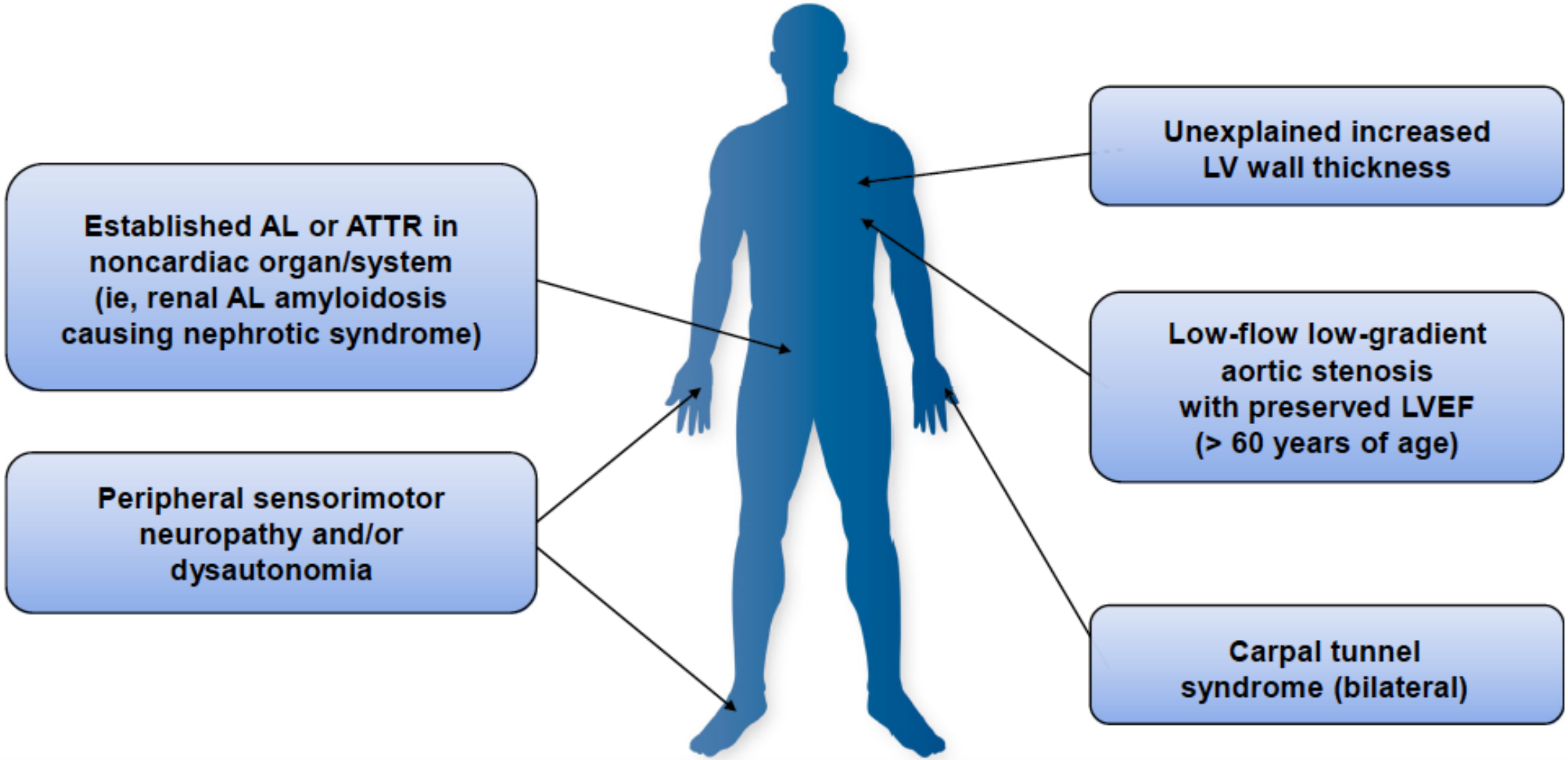
Some may be BNP deficient



Courtesy of Dr. Sanjiv Shah

Don’t miss cardiac amyloidosis – we have treatments available now!

SUSPECT CARDIAC AMYLOIDOSIS WHEN NEW ONSET HEART FAILURE WITH ≥ 1 OF THE FOLLOWING



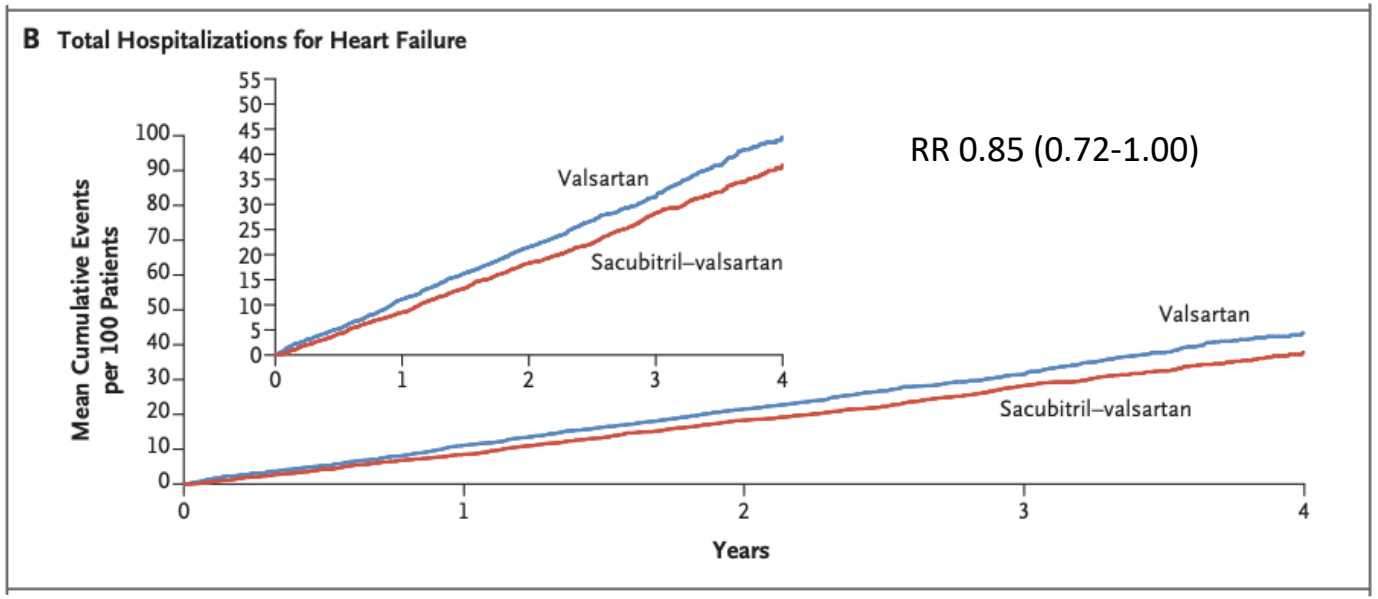
RECOMMENDATION

46. We suggest candesartan be considered to reduce HF hospitalizations in patients with HFpEF (Weak Recommendation; Moderate-Quality Evidence).
47. We recommend systolic/diastolic hypertension be controlled according to current Canadian Hypertension Education Program hypertension guidelines (2017) (http://www.onlinecjc.ca/article/S0828-282X(17)30110-1/abstract) to prevent and treat HFpEF (Strong Recommendation; High-Quality Evidence).
48. We recommend loop diuretics be used to control symptoms of congestion and peripheral edema (Strong Recommendation; Moderate-Quality Evidence).
49. We suggest that in individuals with HFpEF, serum potassium < 5.0 mmol/L, and an eGFR > 30 mL/min, an MRA like spironolactone should be considered, with close surveillance of serum potassium and creatinine (Weak Recommendation; Moderate-Quality Evidence).

Values and preferences. These recommendations place a high value on the known etiologic factors for HFpEF and less on known outcome-modifying treatments which, unlike in HFrEF, are still limited.

The MRA recommendation is on the basis of post hoc geographic subgroup analyses of the TOPCAT trial conducted within North and South America mentioned previously.

Drugs used in idiopathic HFpEF



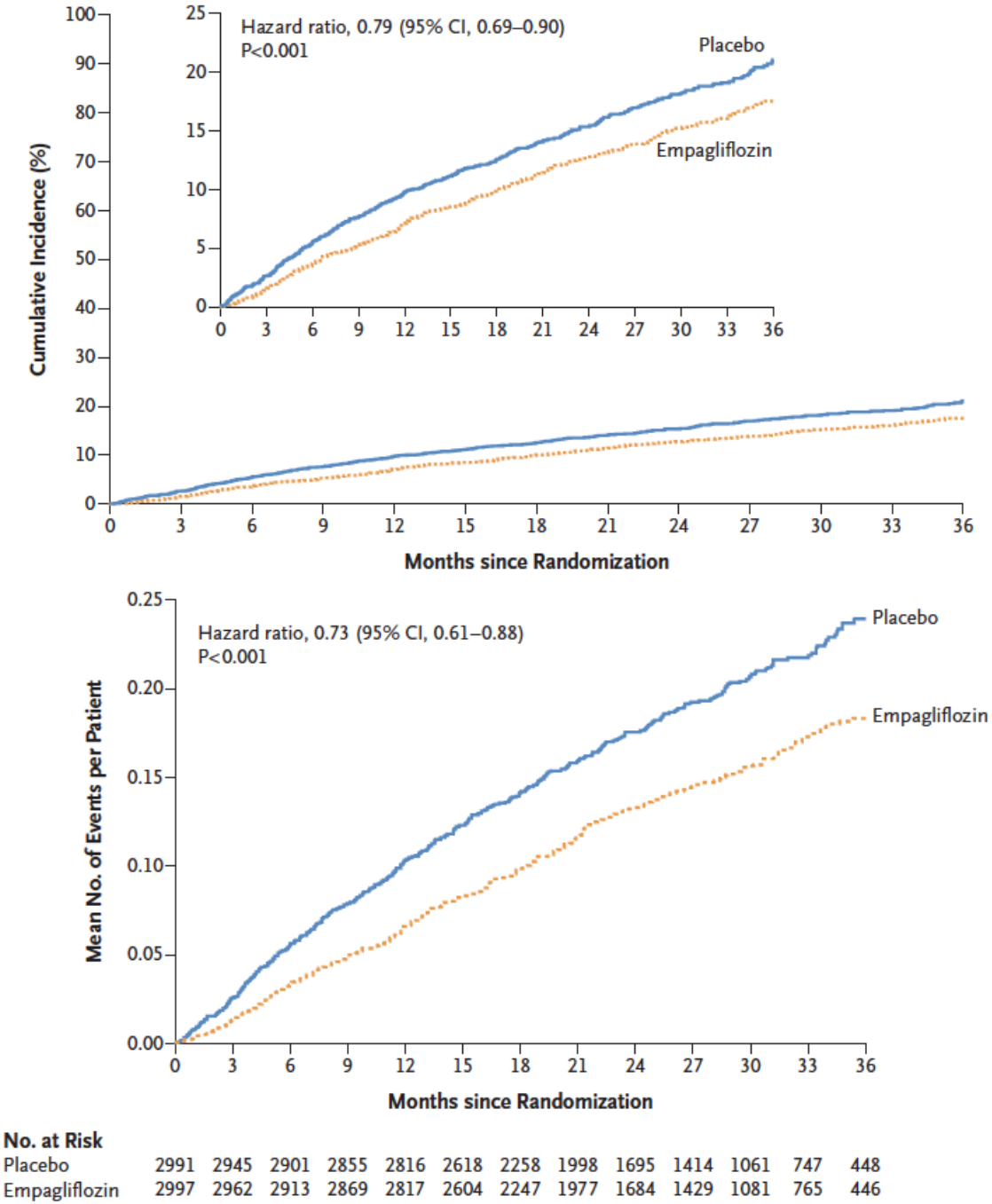
RR 0.85 (0.72-1.00)

Solomon S.D et al. N Engl J Med. 2019;381(17):1609-20.

EMPEROR PRESERVED

- 5988 pts with symptomatic HFpEF randomized, DB trial comparing Empa 10 vs. placebo

- Primary endpoint: Composite of CV death/HFH

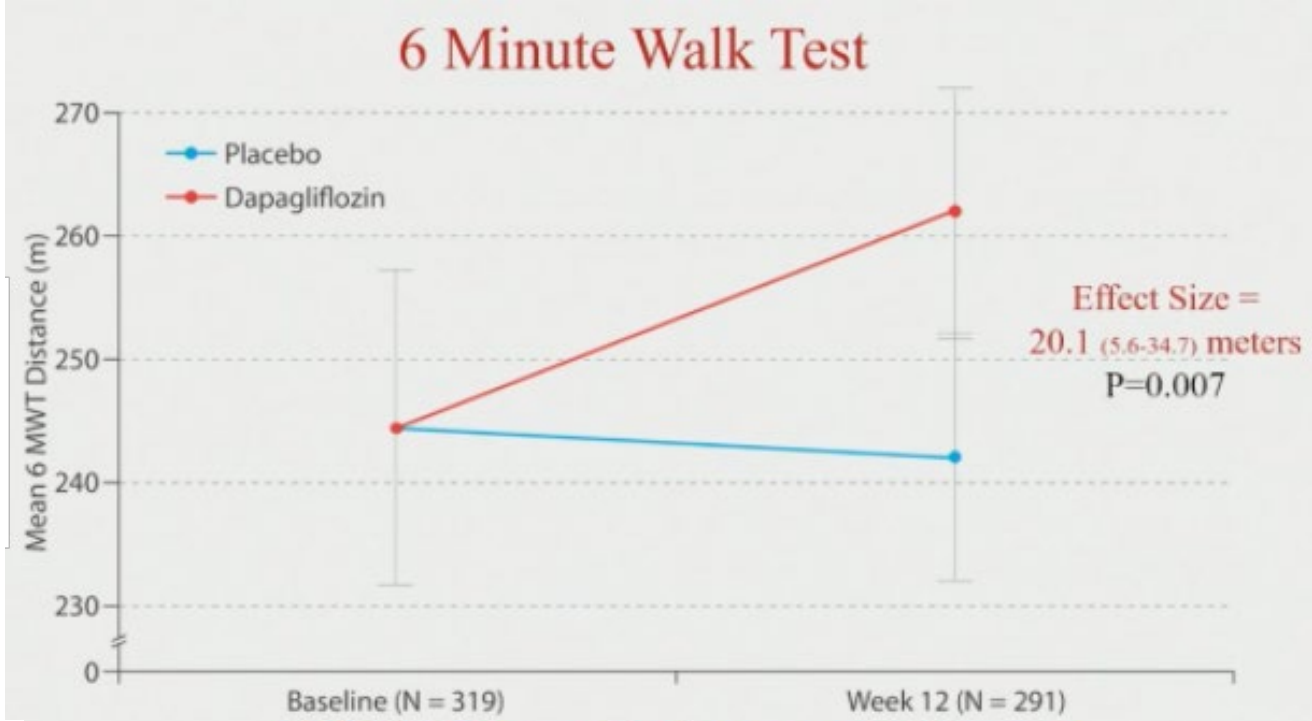


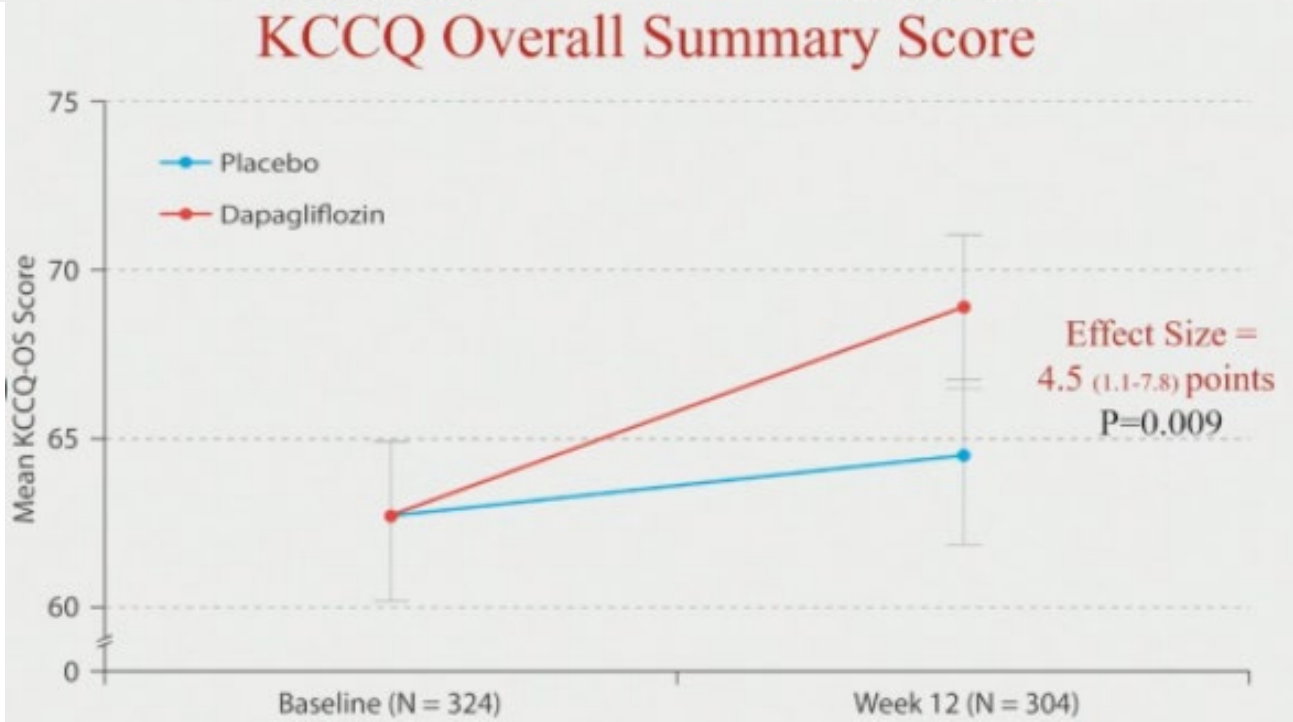
Anker SD et al. N Engl J Med 2021 Aug 27.

PRESERVED-HF

- 324 patients with HFpEF (EF>45%) randomized to Dapa 10 vs. placebo
- 12 week trial
- Outcomes:
  - QOL
  - 6MWT
  - NTproBNP

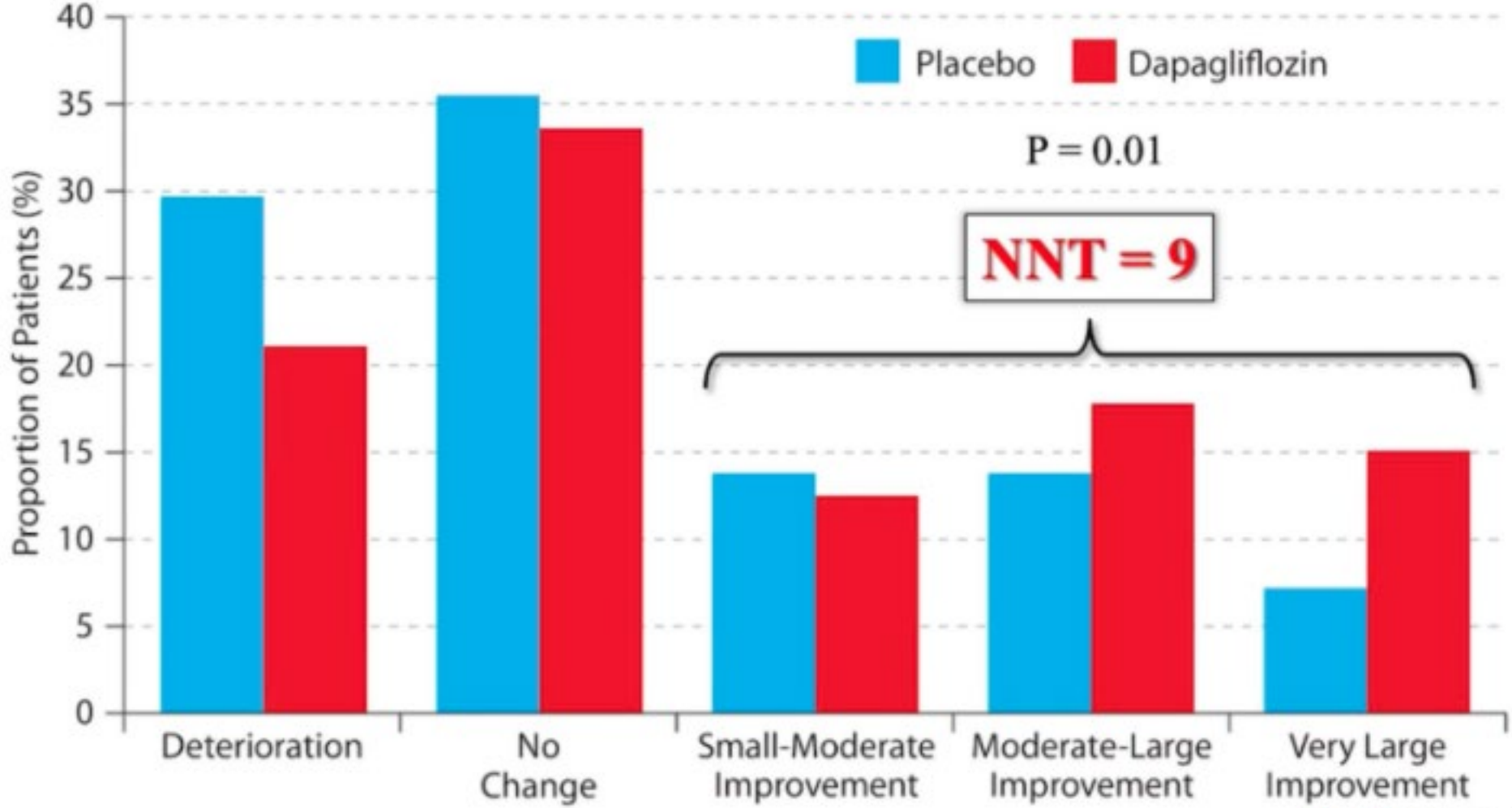
Presented at HFSA 2021



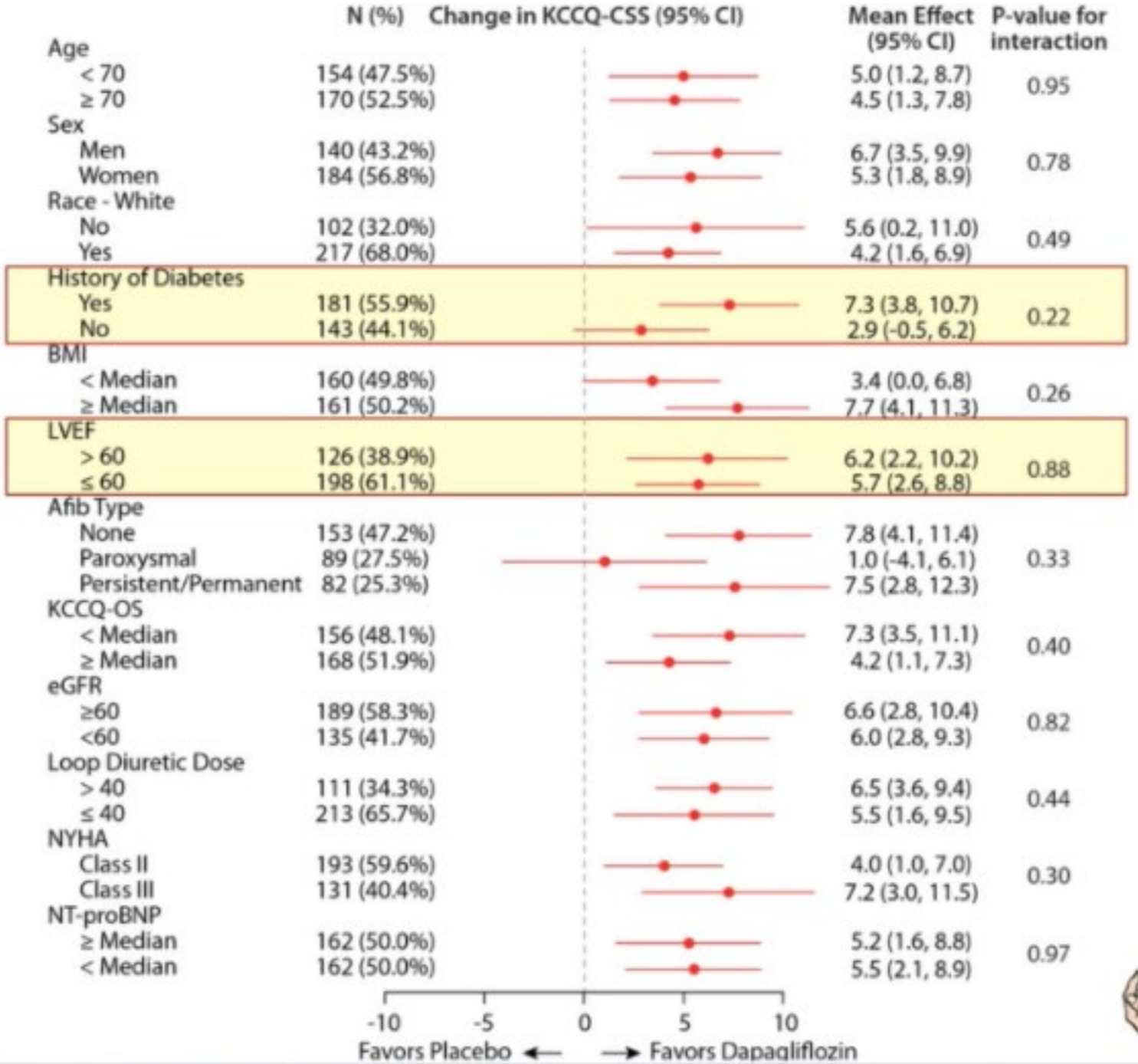


KCCQ Clinical Summary Score

Proportion of Patients with Clinically Meaningful Change at 12 weeks



PRESERVED-HF
Effects of Dapagliflozin on Biomarkers, Symptoms and Functional Status in Patients with PRESERVED Ejection Fraction Heart Failure



Subgroup Analyses

PRESERVED-HF
Effects of Dapagliflozin on Biomarkers, Symptoms and Functional Status in Patients with PRESERVED Ejection Fraction Heart Failure

Baseline Characteristics	Dapagliflozin (n = 162)	Placebo (n = 162)	P-Value
Physical Exam			
Body Mass Index (median IQR)	35 (30 – 42)	35 (30 – 40)	0.50
Heart Rate	70 (61, 77)	68 (62, 75)	0.28
Systolic Blood Pressure	134 (120, 152)	132 (118, 148)	0.14
Baseline Laboratory Studies			
NTproBNP (pg/mL)	641 (373, 1210)	710 (329, 1449)	0.83
eGFR (mL/min)	56 (42, 69)	54 (41, 68)	0.99
Hemoglobin A1c (%)	6.0 (5.6, 7.3)	6.2 (5.6, 7.1)	0.67
Functional Measures			
NYHA Class II	96 (59%)	90 (56%)	0.50
NYHA Class III-IV	65 (40%)	72 (44%)	
KCCQ-OS	63.2 ± 20.4	62.3 ± 20.6	0.68
KCCQ-CS	63.4 ± 19.7	61.8 ± 20.3	0.47
6-Minute Walk (m), Median (IQR)	244 (165, 329)	244 (154, 317)	0.65

PRESERVED-HF
Effects of Dapagliflozin on Biomarkers, Symptoms and Functional Status in Patients with PRESERVED Ejection Fraction Heart Failure

What's next?

- DELIVER – Dapagliflozin in 6100 HFpEF patients, primary endpoint is CV death/HFH/urgent HF visit – due to complete in November 2021

- PARAGLIDE – Entresto vs. Valsartan in 800 acute decompensated HFpEF patients, enrolled before d/c or within 30 days, primary endpoint is change in BNP at 4 and 8 weeks – enrolling currently

- FINEARTS HF – Finerenone in 5500 HFpEF patients, primary endpoint is CV mortality/HF events – enrolling currently

Phenotype based treatment approach in HFpEF

HFpEF Predisposition Phenotypes	HFpEF Clinical Presentation Phenotypes: Lung Congestion	+Chronotropic Incompetence	+Pulmonary Hypertension (CpcPH)	+Skeletal muscle weakness	+Atrial Fibrillation
Overweight/obesity/ metabolic syndrome/ type 2 DM	• **Diuretics (loop diuretic in DM)** • **Caloric restriction** • Statins • Inorganic nitrite/nitrate • Sacubitril • Spironolactone	+Rate adaptive atrial pacing	+Pulmonary vasodilators (e.g. PDE5I)	**+Exercise training program**	+Cardioversion + Rate Control **+Anticoagulation**
+Arterial hypertension	+ACEI/ARB	+ACEI/ARB +Rate adaptive atrial pacing	+ACEI/ARB +Pulmonary vasodilators (e.g. PDE5I)	+ACEI/ARB **+Exercise training program**	+ACEI/ARB +Cardioversion + Rate Control **+Anticoagulation**
+Renal dysfunction	+Ultrafiltration if needed	+Ultrafiltration if needed +Rate adaptive atrial pacing	+Ultrafiltration if needed +Pulmonary vasodilators (e.g. PDE5I)	+Ultrafiltration if needed **+Exercise training program**	+Ultrafiltration if needed +Cardioversion + Rate Control **+Anticoagulation**
+CAD	+ACEI +Revascularization	+ACEI +Revascularization +Rate adaptive atrial pacing	+ACEI +Revascularization +Pulmonary vasodilators (e.g. PDE5I)	+ACEI +Revascularization **+Exercise training program**	+ACEI +Revascularization +Cardioversion + Rate Control **+Anticoagulation**

Shah S, Paulus W et al. *Circulation* 2016

Summary points

- New four pillar approach to the treatment of HFrEF – start all 4 therapies within 4-6 weeks and then uptitrate
- Identify and treat co-morbidities such as OSA and iron deficiency
- Identify patients who are sliding and need an early referral to an advanced HF specialist (I NEED HELP acronym)
- HFpEF is a heterogeneous group of conditions that may need more tailored care

Questions/comments