

Heart Failure Management

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Heart failure prevalence is expected to continue to increase¹

21 MILLION

ADULTS WORLDWIDE ARE LIVING WITH HEART FAILURE AND THIS NUMBER IS EXPECTED TO RISE^{1,2}



AGING POPULATION²



INCREASING PREVALENCE OF RISK FACTORS²



IMPROVED POST-MI SURVIVAL²

A person at age 40 has a 1 in 5 lifetime risk of developing HF, and more than 1 million hospitalizations due to HF are reported annually in Europe^{1,4}

HF=heart failure; MI=myocardial infarction

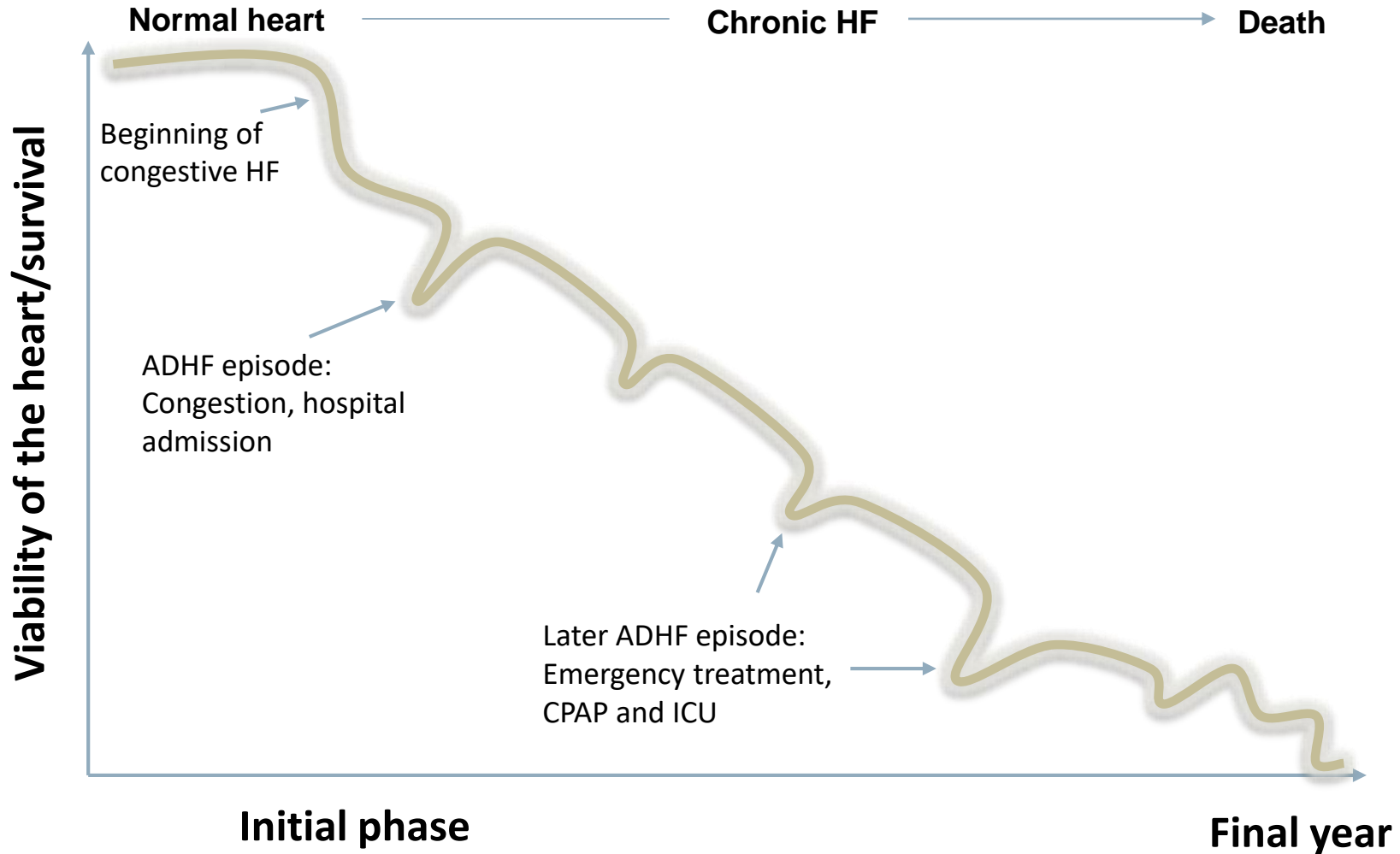
1. Mozaffarian et al. *Circulation* 2015;131:e29–e322. 2. Mosterd and Hoes. *Heart* 2007;93:1137–46. 3. Velagaleti and Vasan. Epidemiology of heart failure. In: Mann, ed. *Heart Failure: A Companion to Braunwald's Heart Disease*. 2nd ed. St Louis: Saunders; 2011. 4. Ponikowski et al. *ESC Heart Failure* 2014;1:4–25

HF is associated with high mortality rates

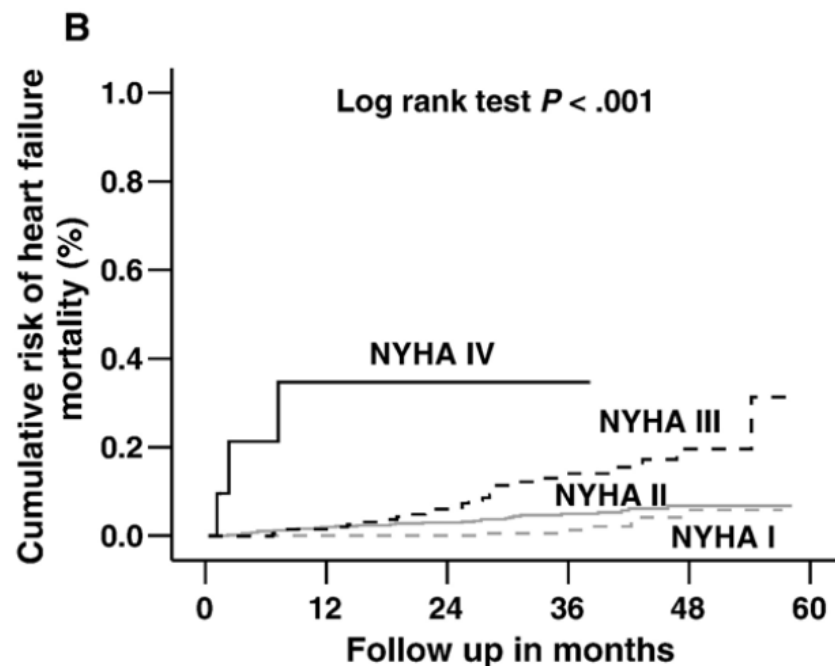
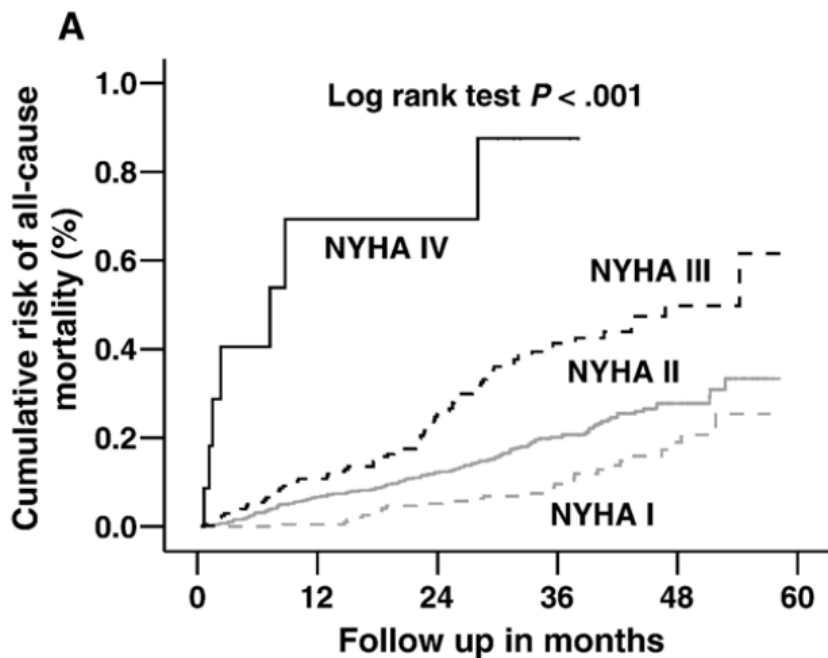
~50% OF PATIENTS DIE WITHIN
5 YEARS OF DIAGNOSIS¹

~1 IN 4 HF PATIENTS DIE WITHIN
1 YEAR OF DIAGNOSIS²

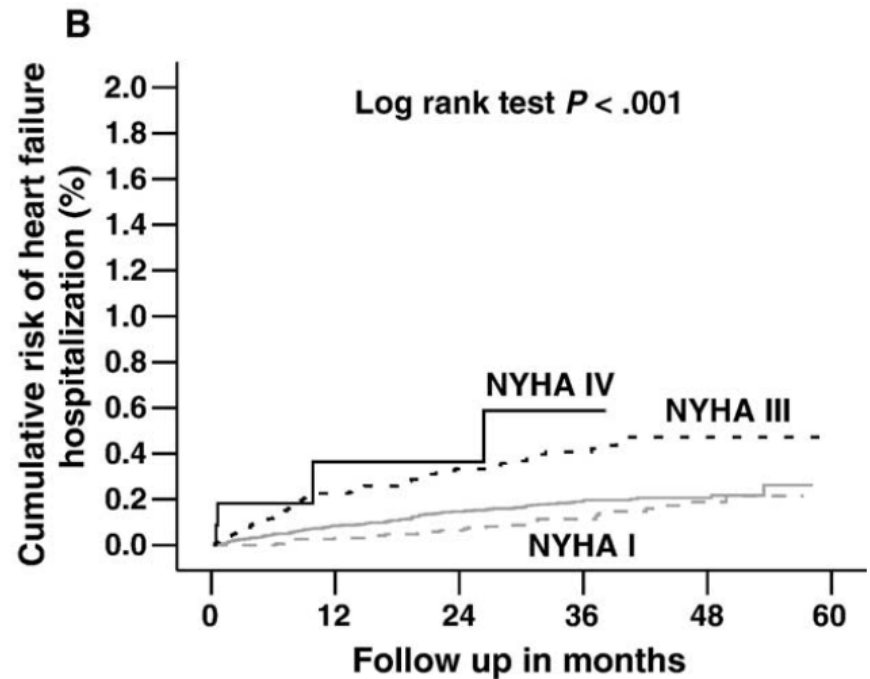
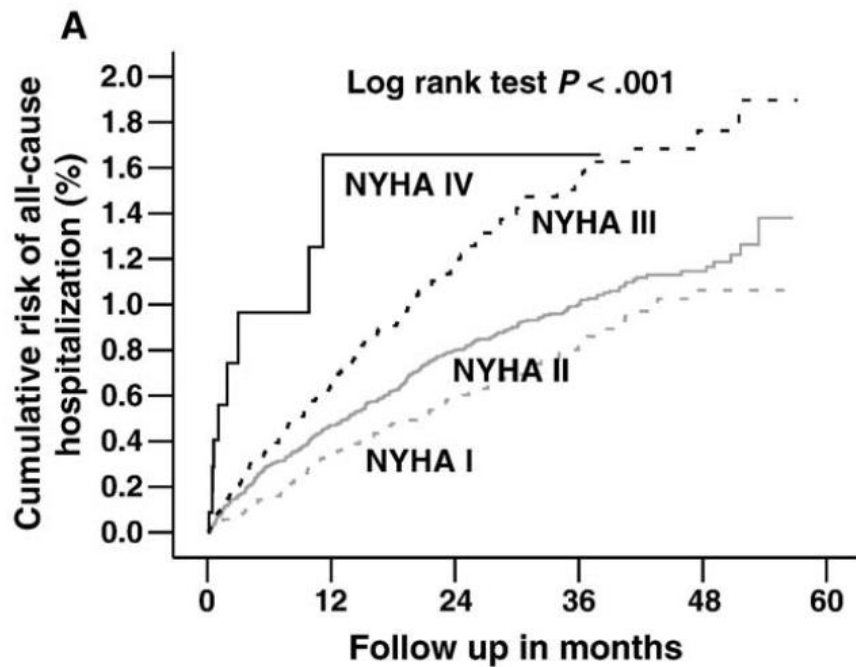
HF progressive clinical course



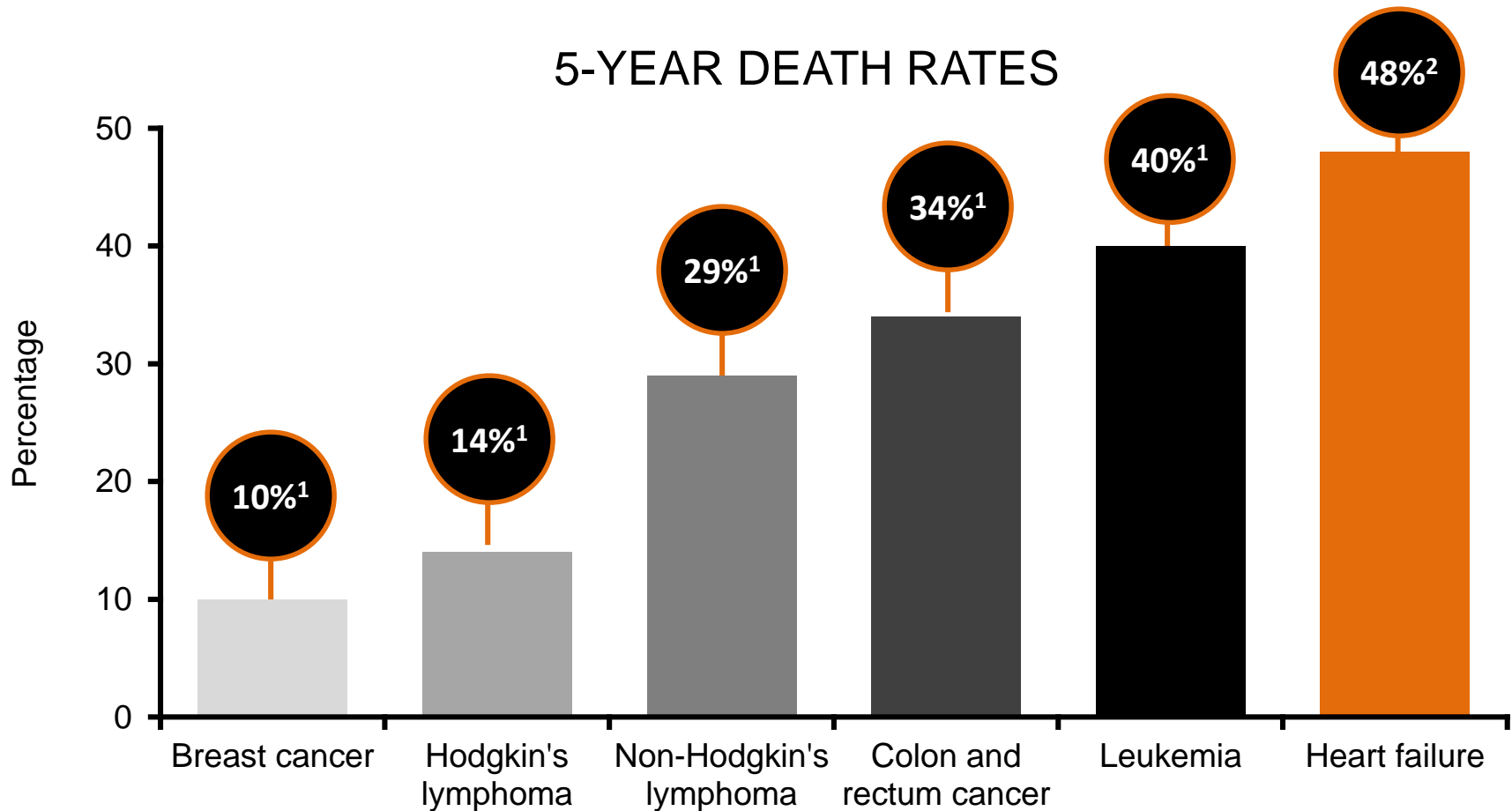
All cause mortality and HF mortality by NYHA functional class



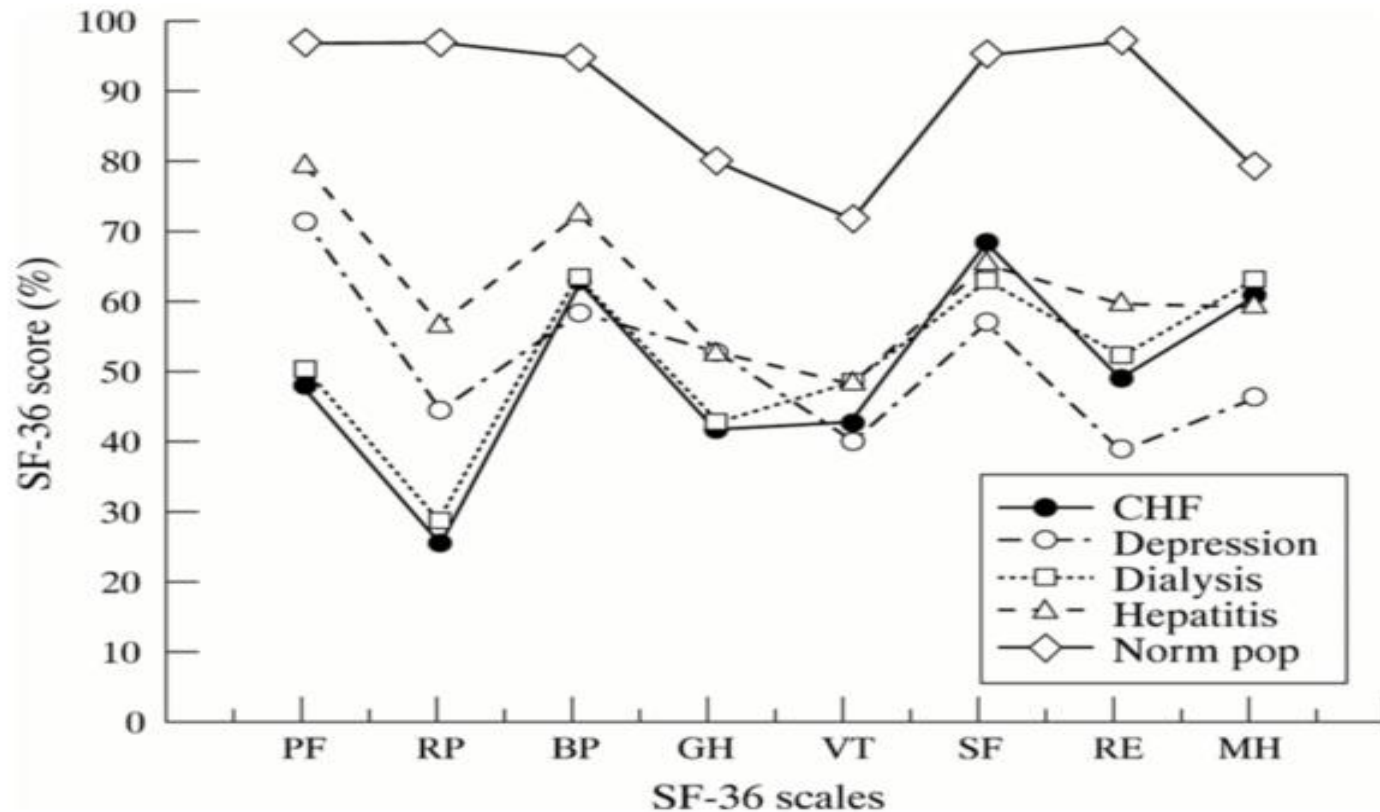
All cause hospitalization and hospitalization due to HF by NYHA functional class



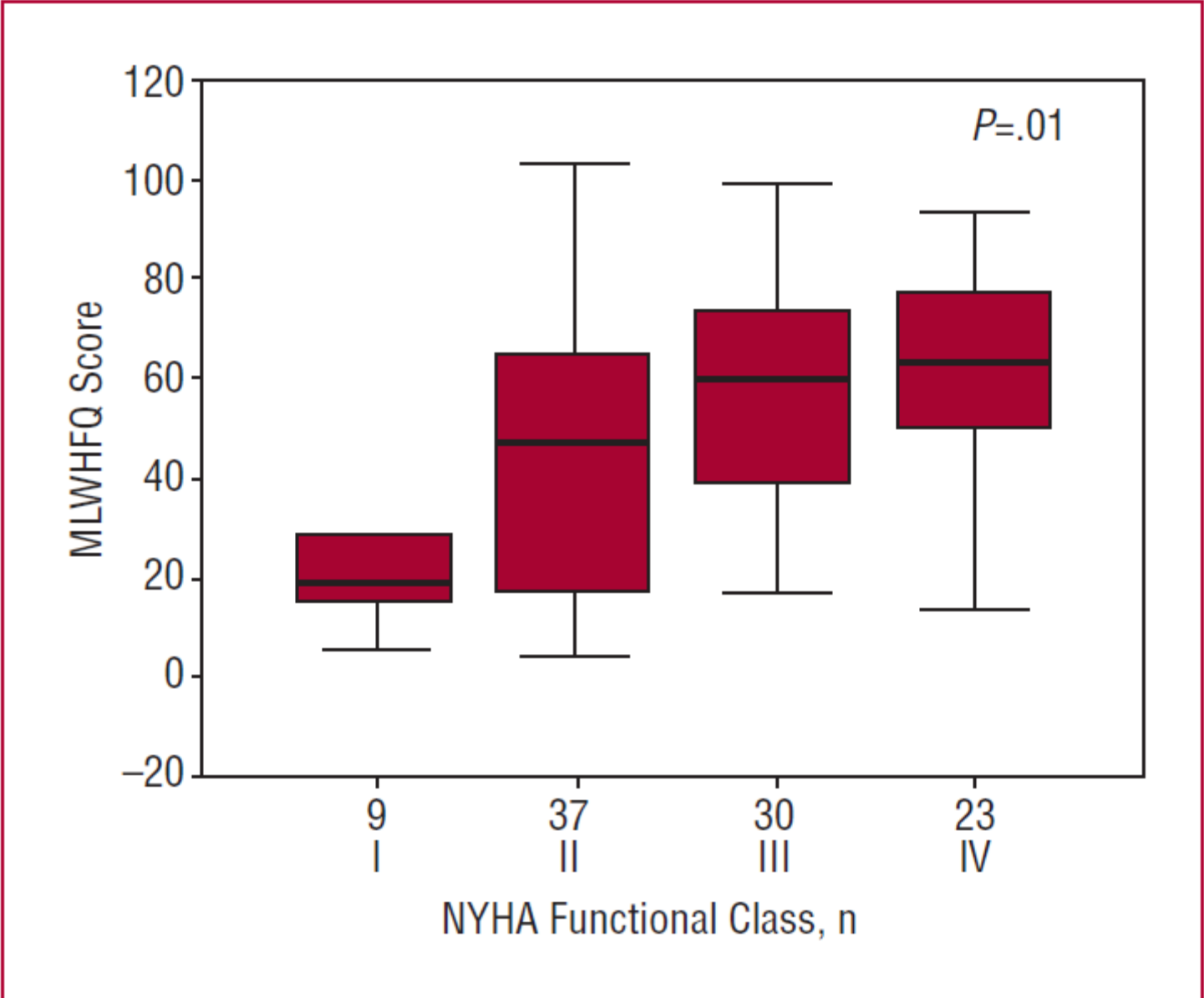
HFHF is deadlier than many cancers is deadlier than many cancers



Quality of life of patients with chronic HF is similar to other chronic diseases



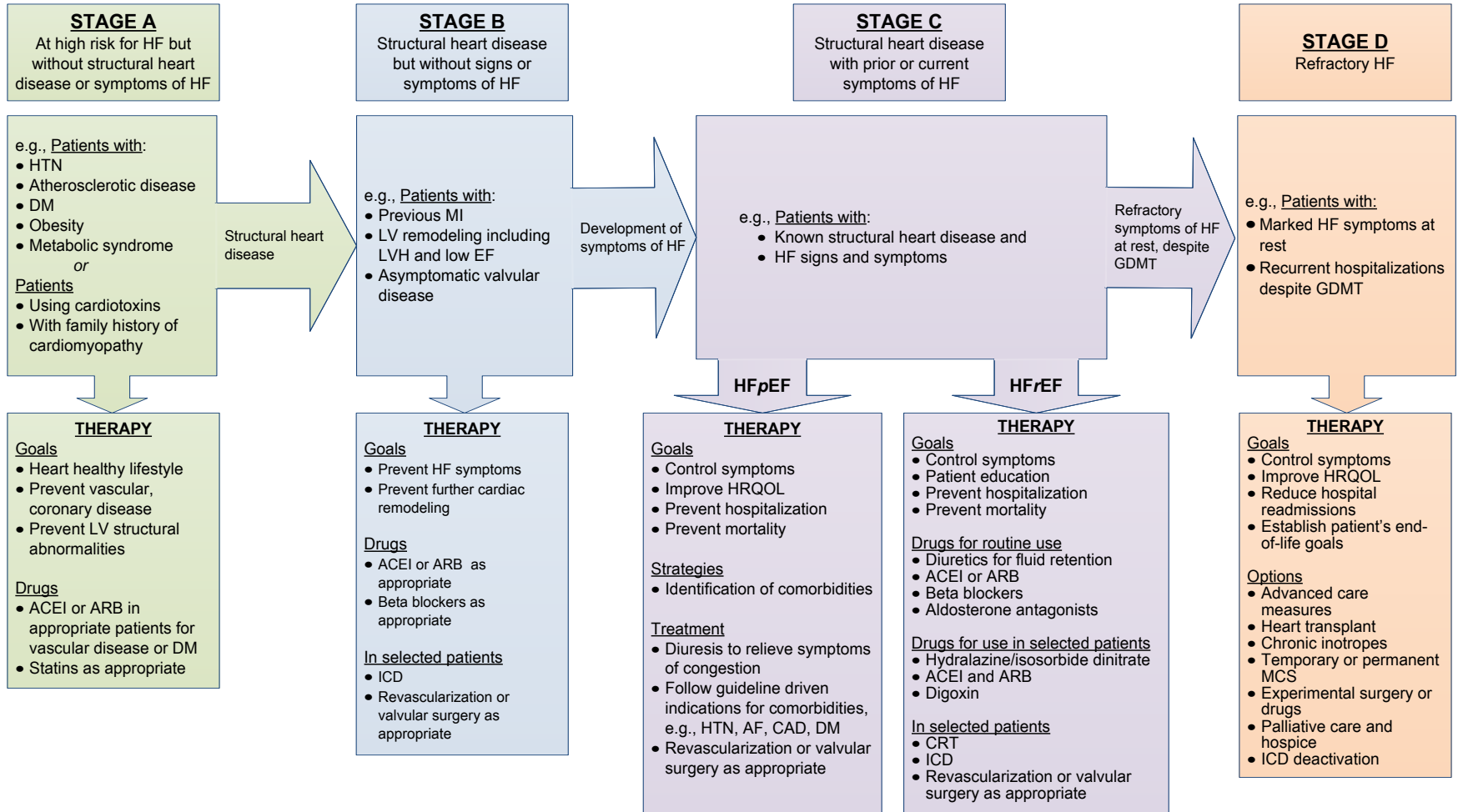
BP=bodily pain; CHF=chronic HF; GH=general health perceptions; MH=mental health; PF=physical functioning; RE=role limitations caused by emotional problems; RP=role limitations due to physical limitations; SF=social functioning; SF-36=short-form health survey; VT=vitality



Stages, Phenotypes and Treatment of HF

At Risk for Heart Failure

Heart Failure

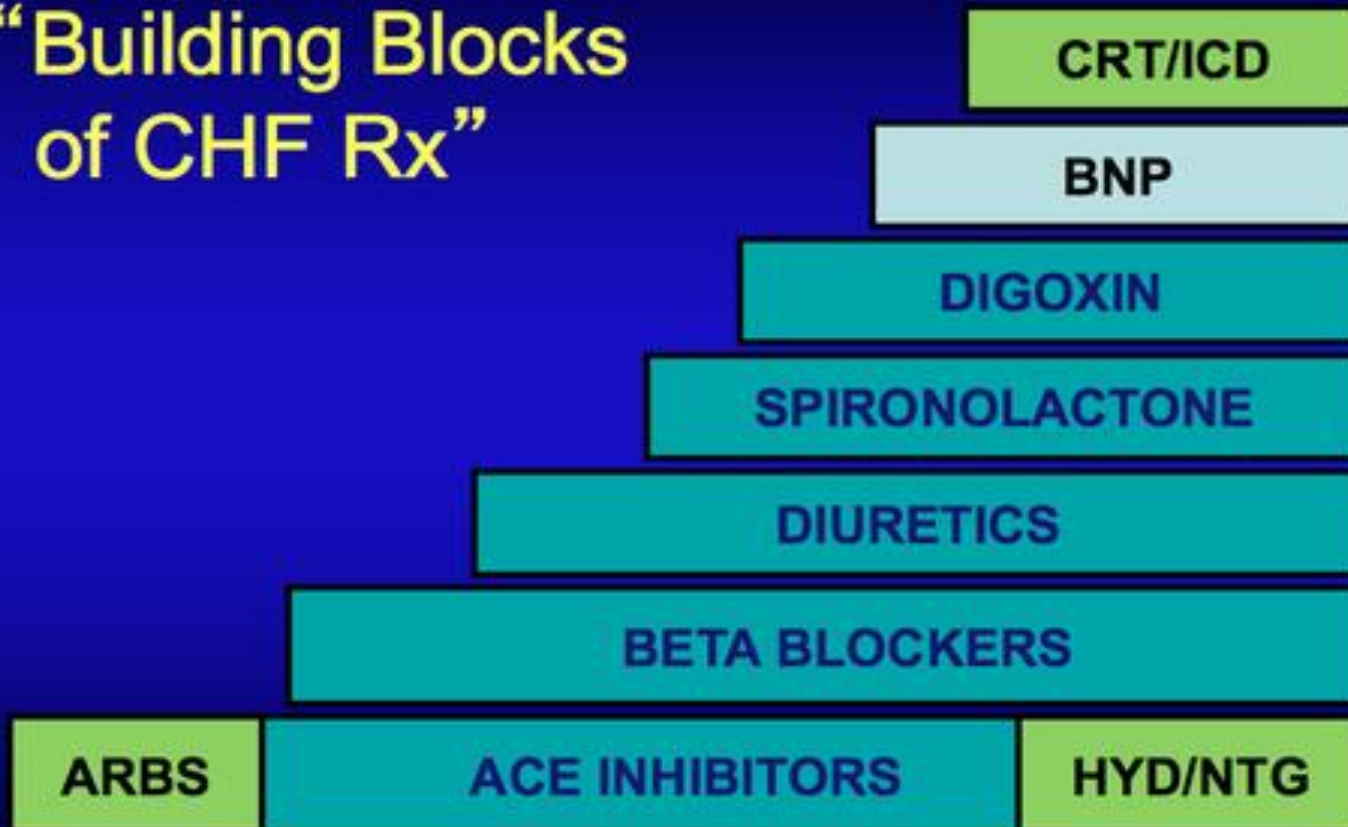


LV function in Heart Failure

Classification	Ejection Fraction	Description
I. Heart Failure with Reduced Ejection Fraction (HFrEF)	$\leq 40\%$	Also referred to as systolic HF. Randomized clinical trials have mainly enrolled patients with HFrEF and it is only in these patients that efficacious therapies have been demonstrated to date.
II. Heart Failure with Preserved Ejection Fraction (HFpEF)	$\geq 50\%$	Also referred to as diastolic HF. Several different criteria have been used to further define HFpEF. The diagnosis of HFpEF is challenging because it is largely one of excluding other potential noncardiac causes of symptoms suggestive of HF. To date, efficacious therapies have not been identified.
a. HFpEF, Borderline	41% to 49%	These patients fall into a borderline or intermediate group. Their characteristics, treatment patterns, and outcomes appear similar to those of patient with HFpEF.
b. HFpEF, Improved	$>40\%$	It has been recognized that a subset of patients with HFpEF previously had HFrEF. These patients with improvement or recovery in EF may be clinically distinct from those with persistently preserved or reduced EF. Further research is needed to better characterize these patients.

Medications

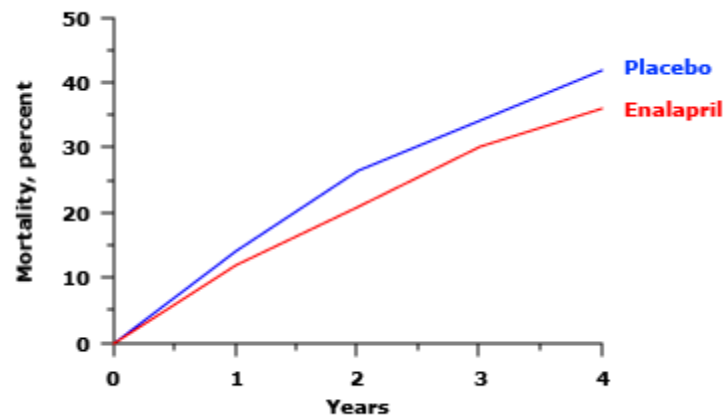
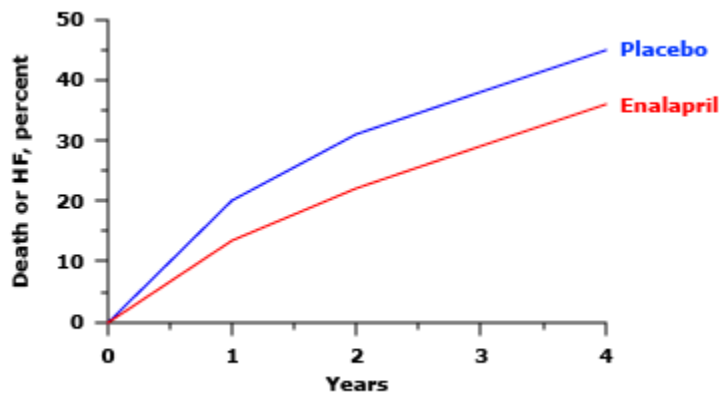
“Building Blocks
of CHF Rx”



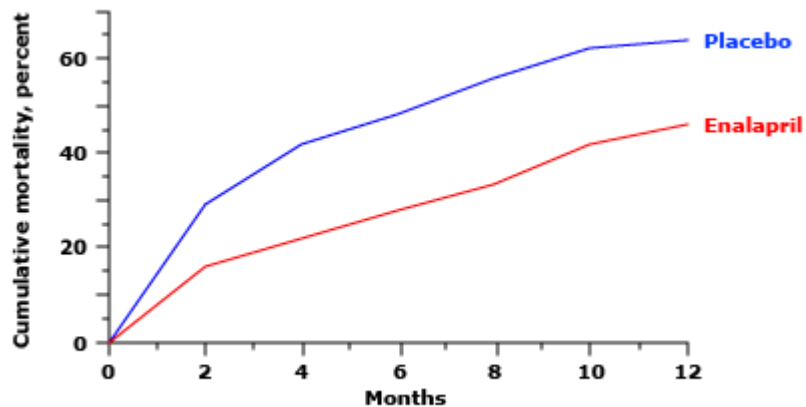
Angiotensin Converting Enzyme Inhibitors

asymptomatic LV dysfunction

in moderate HF



in advanced HF

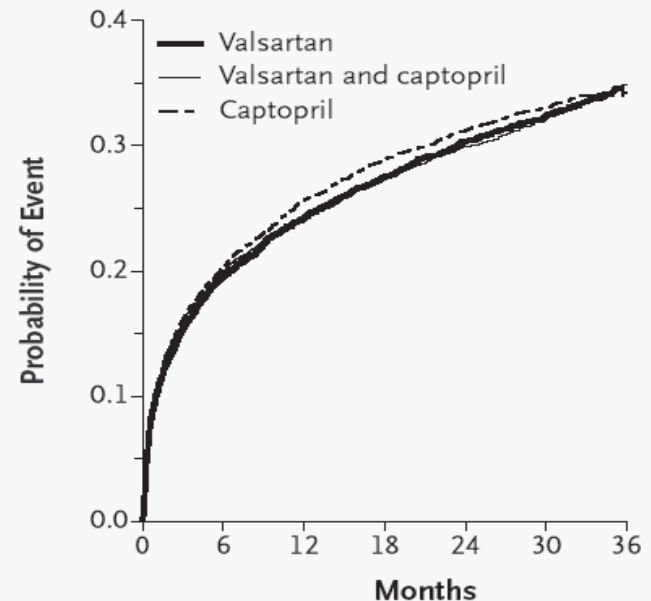


- ACE inhibitors are recommended for routine administration to symptomatic and asymptomatic patients with LVEF \leq 40%. (Strength of Evidence A)
- ACE inhibitors should be titrated to doses used in clinical trials, as tolerated

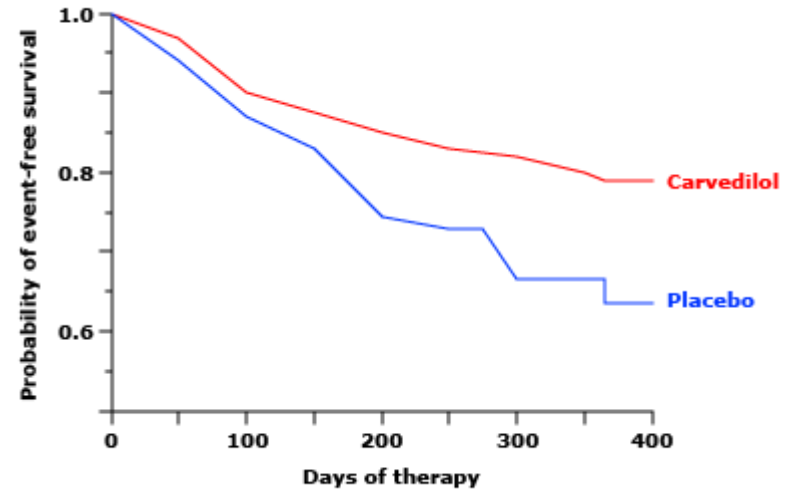
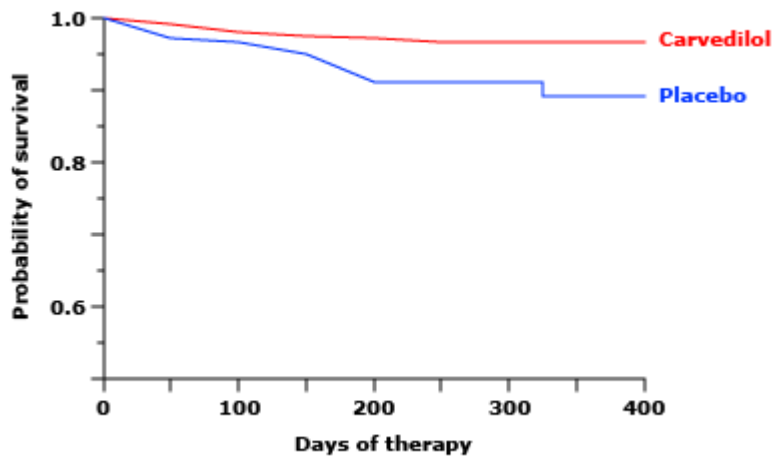
Angiotensin Receptor Blockers

- ACEI remain the first choice for inhibition of the renin-angiotensin system in chronic HF,
- ARBs can be considered a reasonable alternative

Combined Cardiovascular End Point

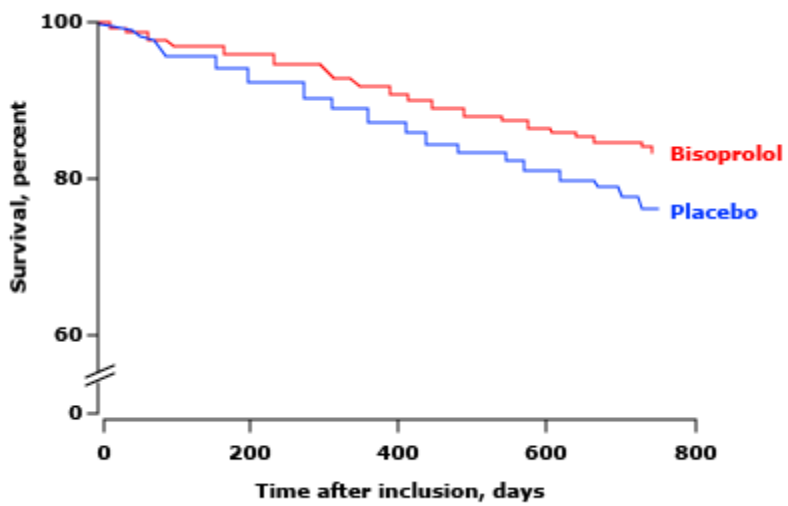
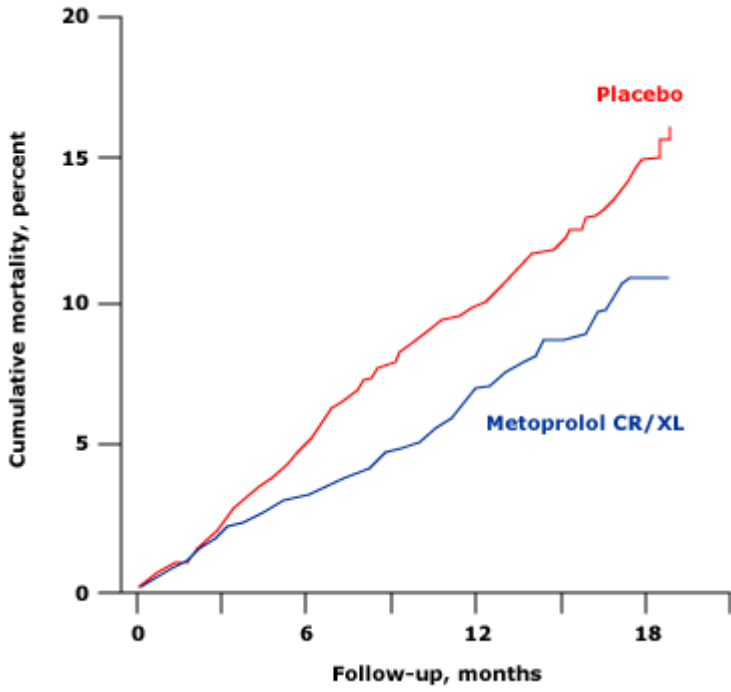


Beta Blockers



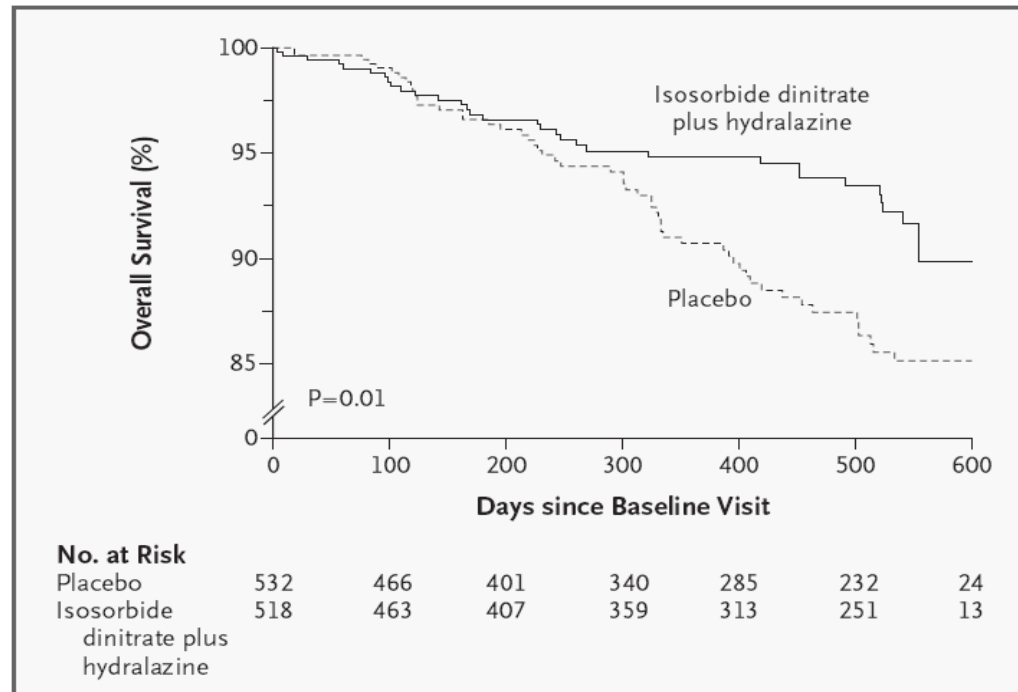
N Engl J Med 1996; 334:1349.

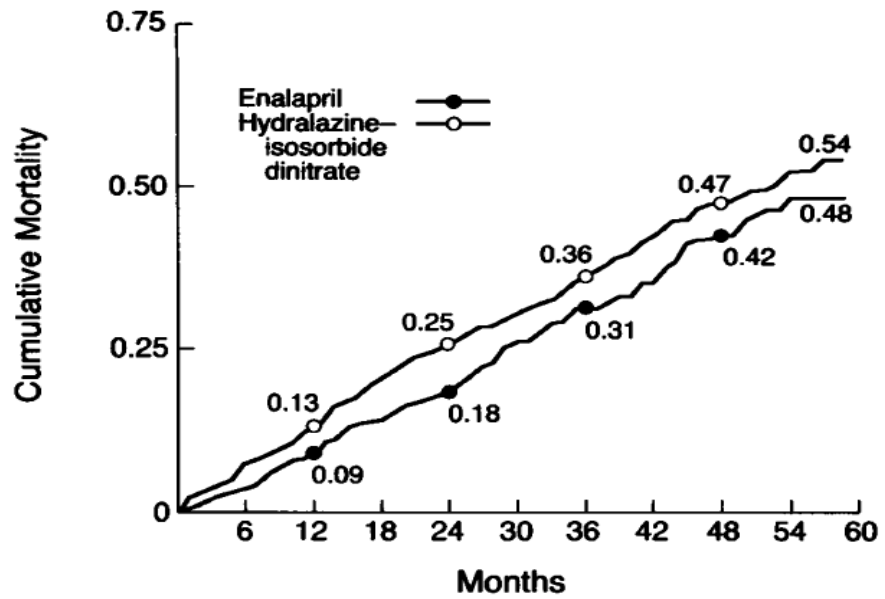
The MERIT-HF Study Group, Lancet 1999; 353:2001



CIBIS-II Investigators and Committees. Lancet 1999; 353:9

Hydralazine / Nitrates





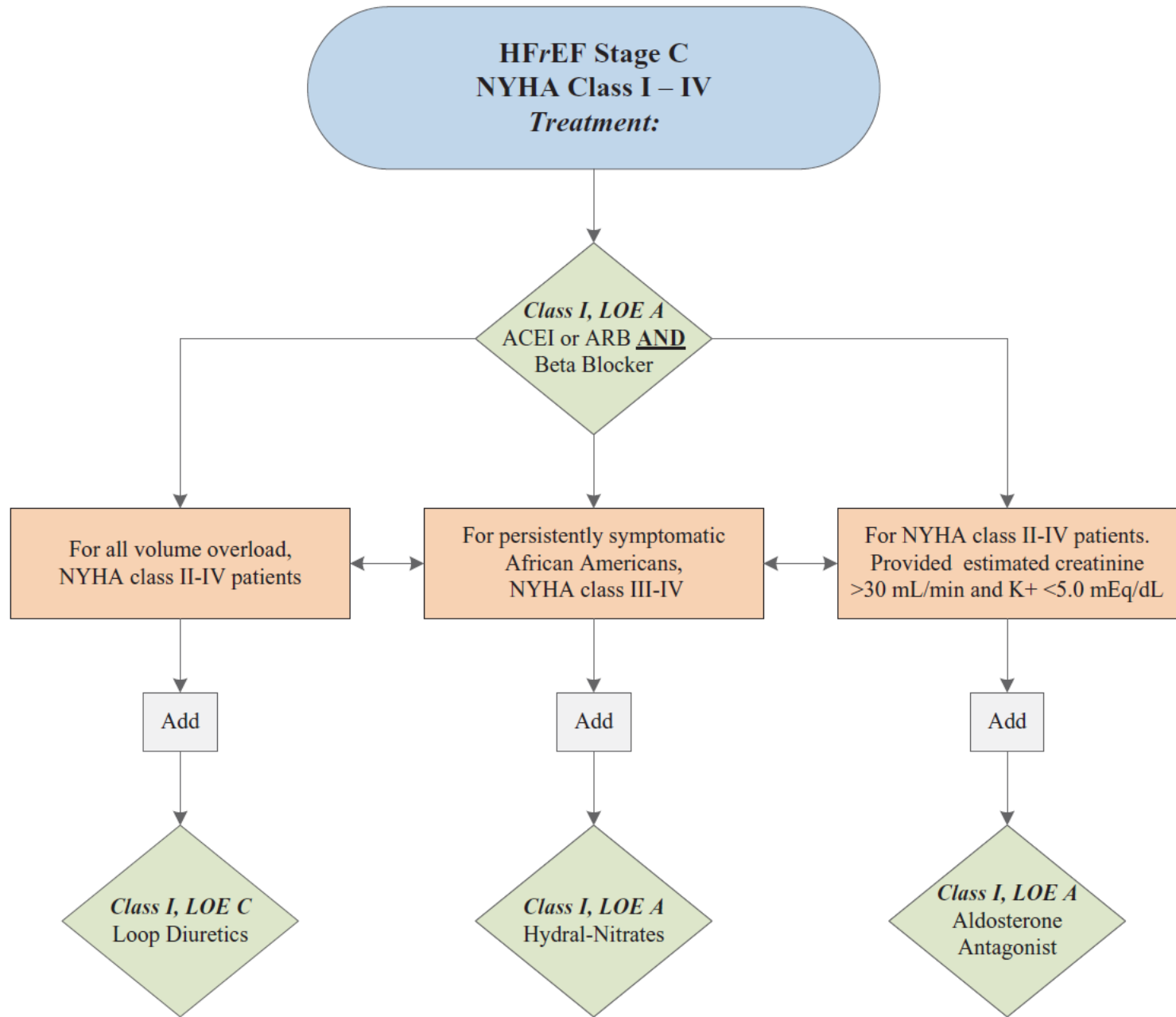
- Treatment with a combination of hydralazine plus nitrate in patients with HF and reduced LVEF who are unable to take ACE inhibitor or ARB
- Patients with persistent NYHA class III to IV HF and LVEF <40 percent despite optimal therapy the addition of the combination of hydralazine and an oral nitrate is recommended

MRA

- NYHA class II-IV
- Post MI, LVEF <40%
- HF symptoms or DM
- Spironolactone vs. Eplerenone

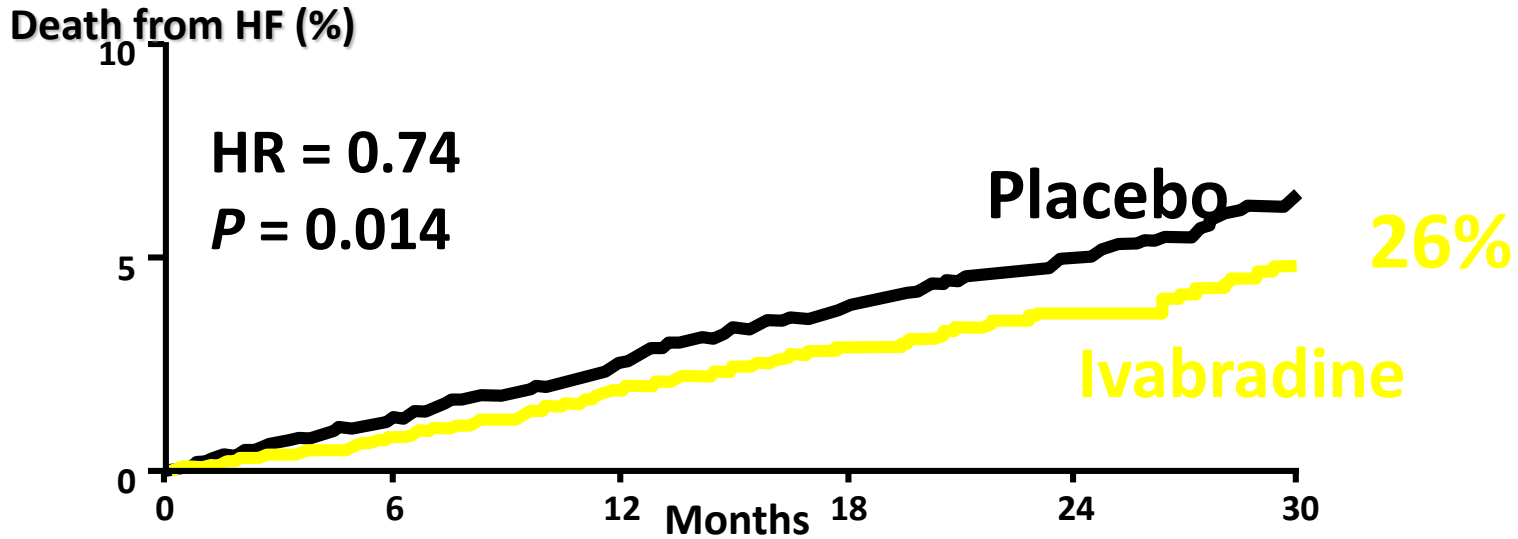
- Aldosterone receptor antagonists (or mineralocorticoid receptor antagonists) are recommended in patients with NYHA class II–IV HF and who have LVEF of 35% or less, to reduce morbidity and mortality.

- Aldosterone receptor antagonists are recommended to reduce morbidity and mortality following an acute MI in patients who have LVEF of 40% or less who develop symptoms of HF or who have a history of diabetes mellitus





Ivabradine reduced death from heart failure



Cause of heart failure

Non-Ischaemic (n=2087)

218 (21.3%)

296 (27.9%)

0.72 (0.60-0.85)

Ischaemic (n=4418)

575 (26.0%)

641 (29.1%)

0.87 (0.78-0.97)

p=0.059

0.5

1.0

1.5

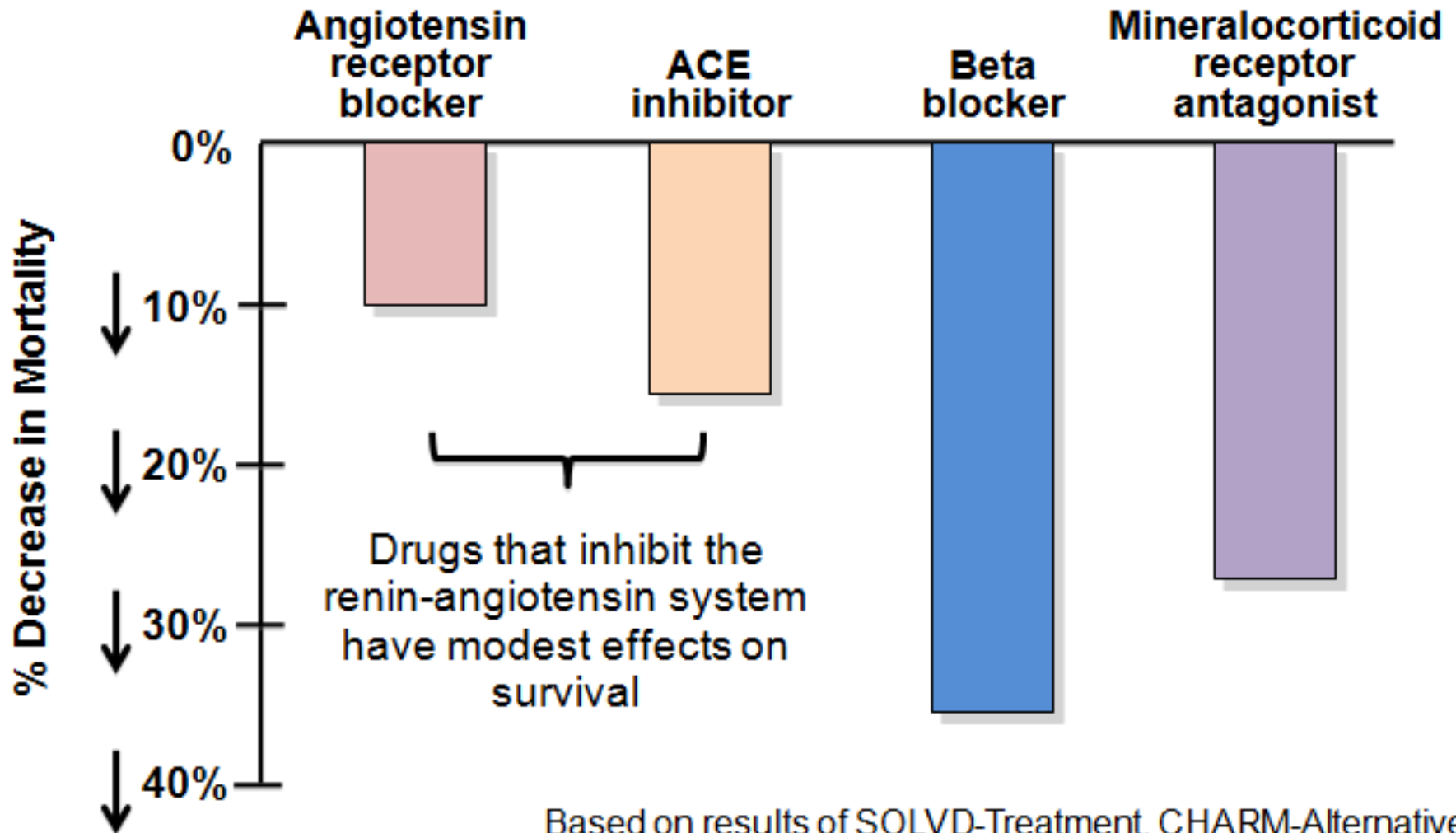
Favours ivabradine

Favours placebo

ESC Guidelines

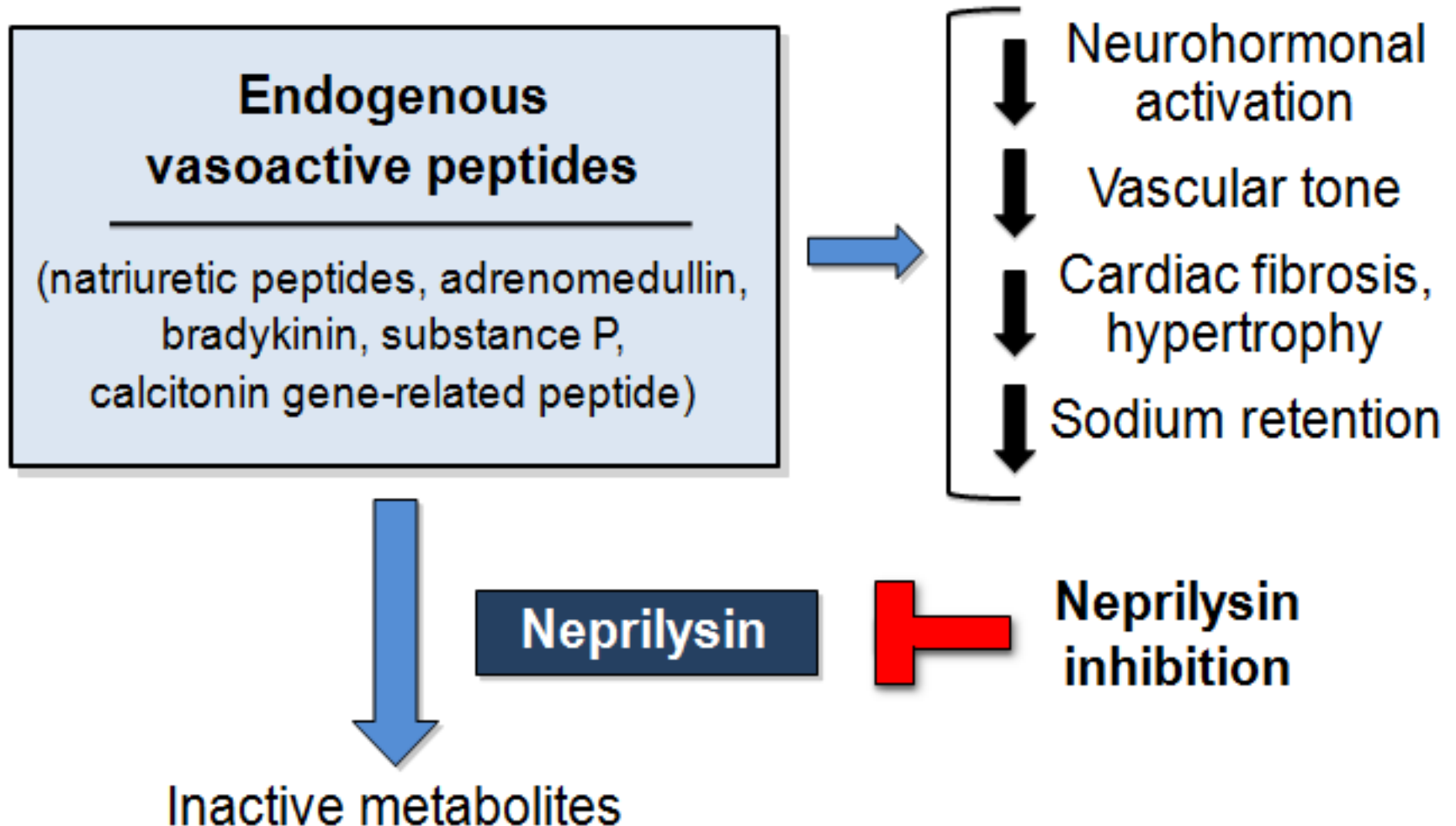
Ivabradine		
Should be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF \leq 35%, a heart rate remaining \geq 70 b.p.m., and persisting symptoms (NYHA class II–IV) despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE inhibitor (or ARB), and an MRA (or ARB). ^a	IIa	B
May be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF \leq 35% and a heart rate \geq 70 b.p.m. who are unable to tolerate a beta-blocker. Patients should also receive an ACE inhibitor (or ARB) and an MRA (or ARB). ^a	IIb	C
Digoxin		

Drugs That reduce Mortality in Heart Failure With Reduced EF

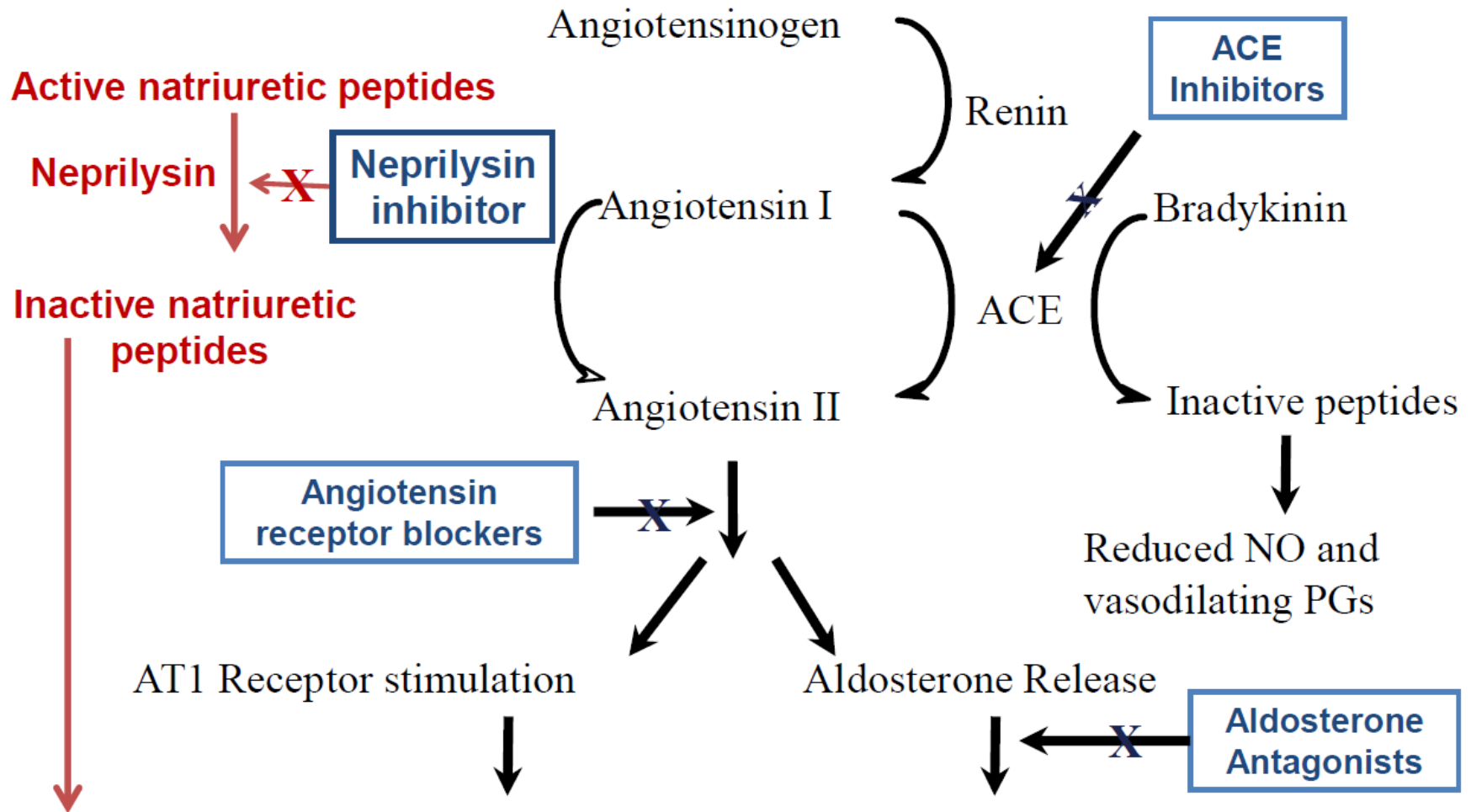


Based on results of SOLVD-Treatment, CHARM-Alternative, COPERNICUS, MERIT-HF, CIBIS II, RALES and EMPHASIS-HF

Neprilysin Inhibition Potentiate Actions of Vasoactive Peptides That counter Maladaptive Mechanisms in Heart Failure

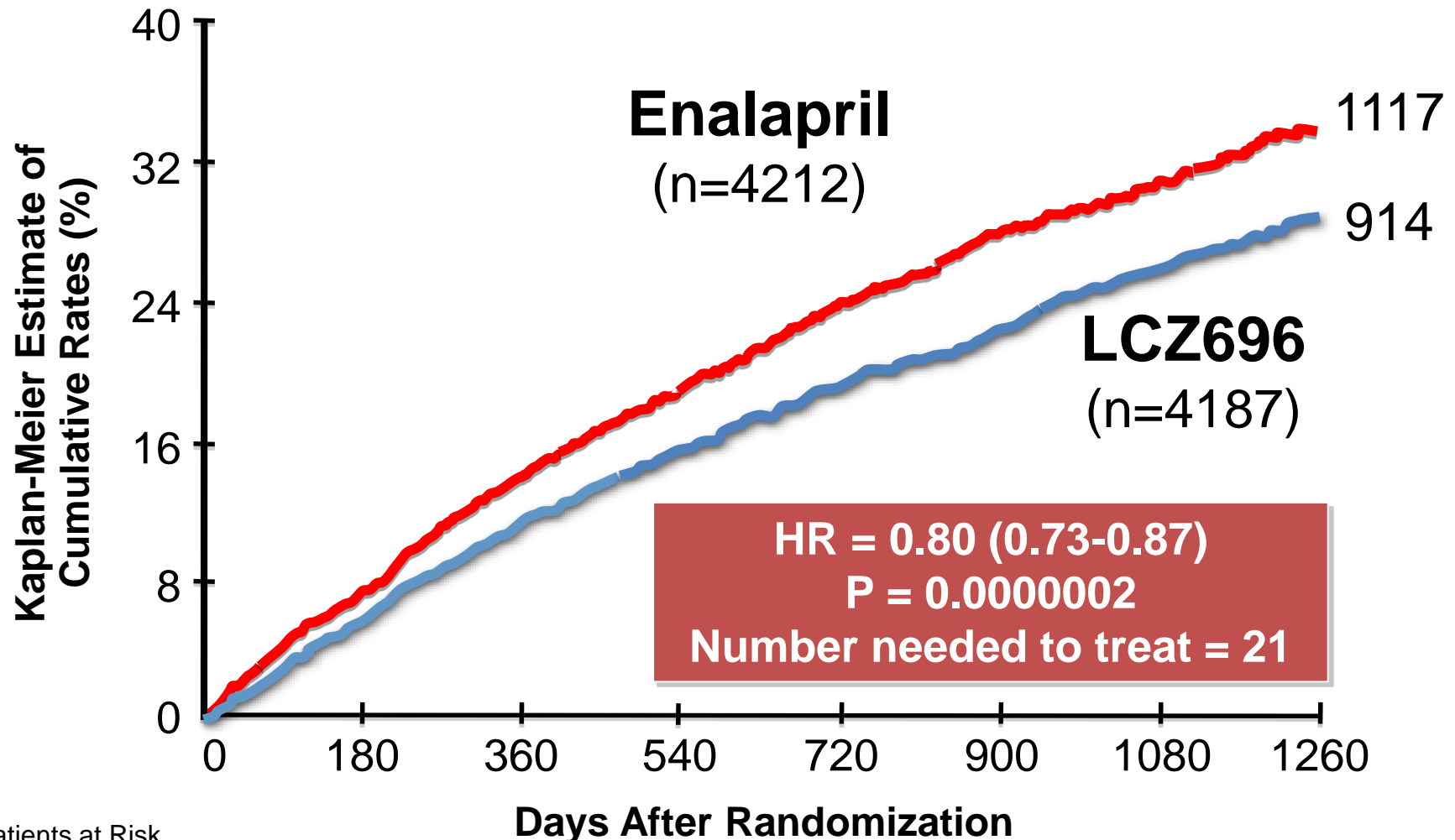


Neurohormonal blockade in HF – revisited



Vasoconstriction, Na retention, myocyte hypertrophy and apoptosis, endothelial dysfunction, sympathetic activation, free radical generation, etc

PARADIGM-HF: Cardiovascular Death or Heart Failure Hospitalization (Primary Endpoint)

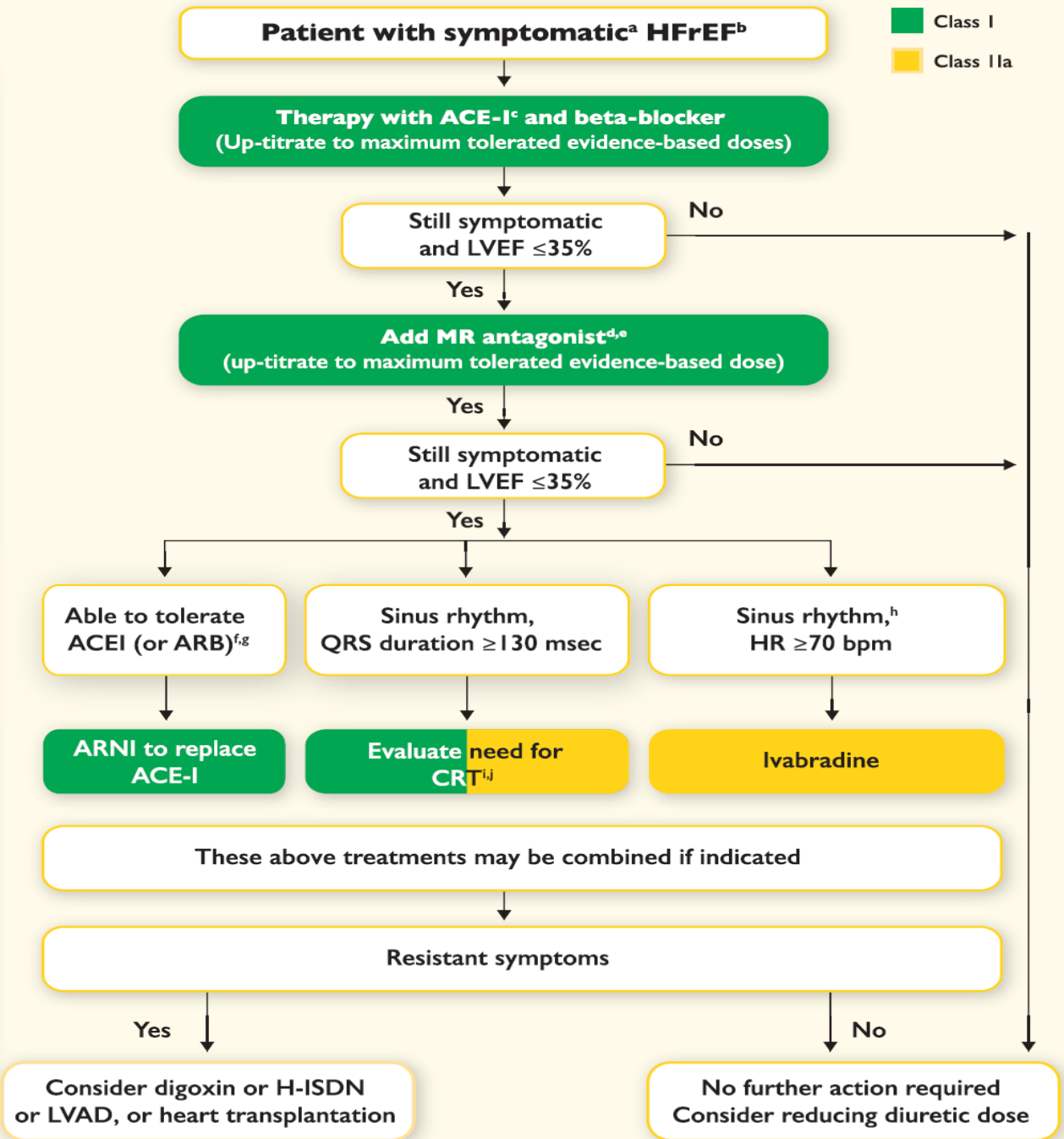


Patients at Risk

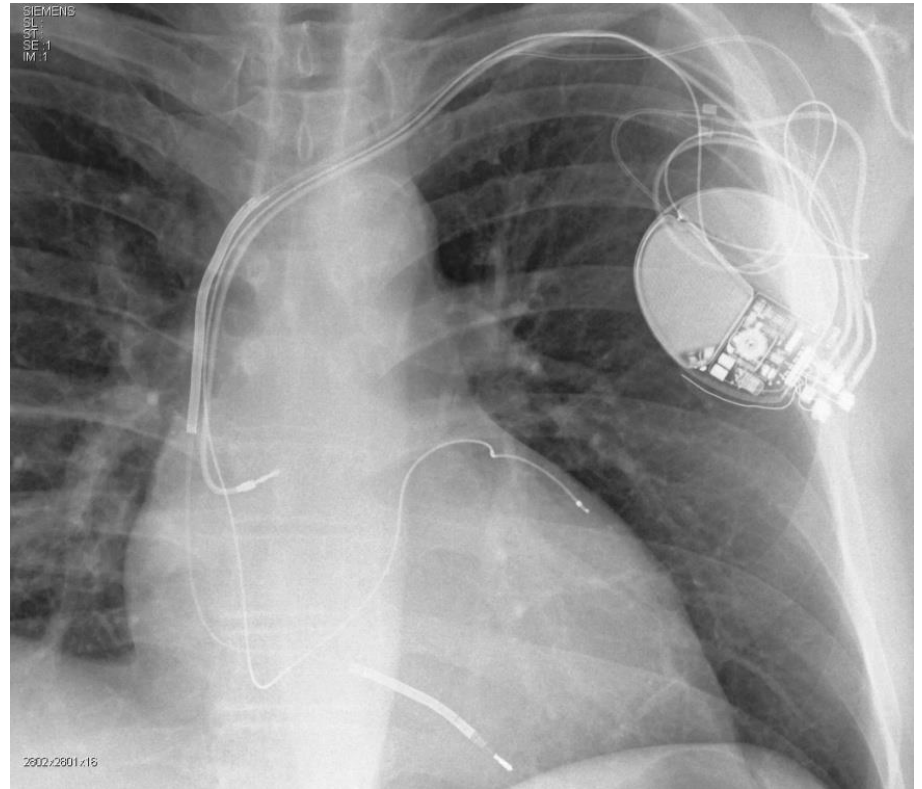
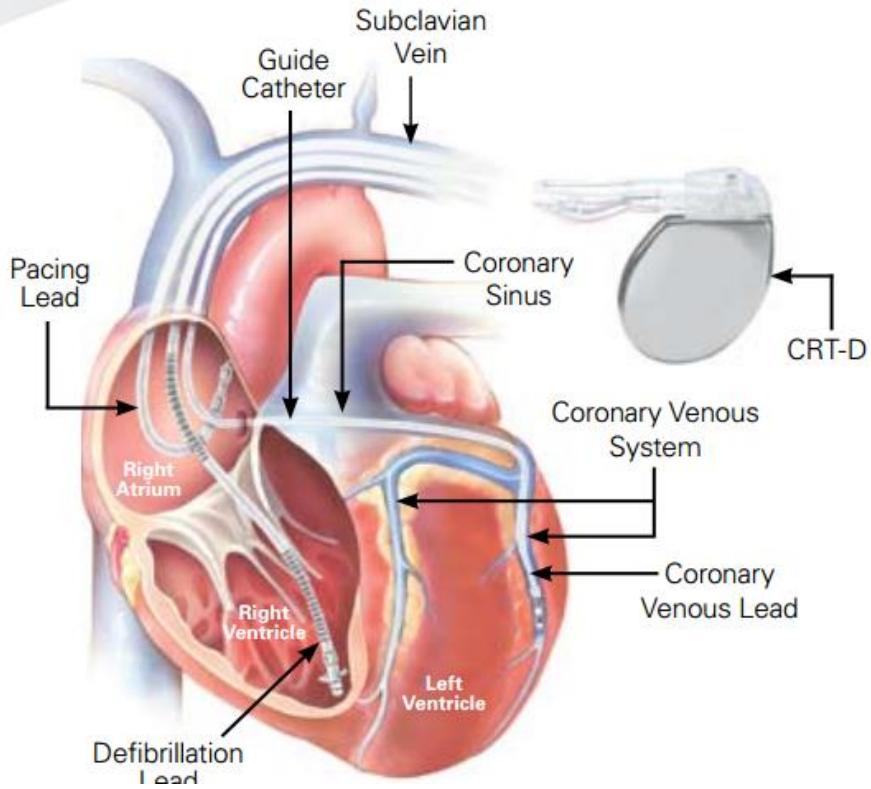
	0	180	360	540	720	900	1080	1260
LCZ696	4187	3922	3663	3018	2257	1544	896	249
Enalapril	4212	3883	3579	2922	2123	1488	853	236

Diuretics to relieve symptoms and signs of congestion

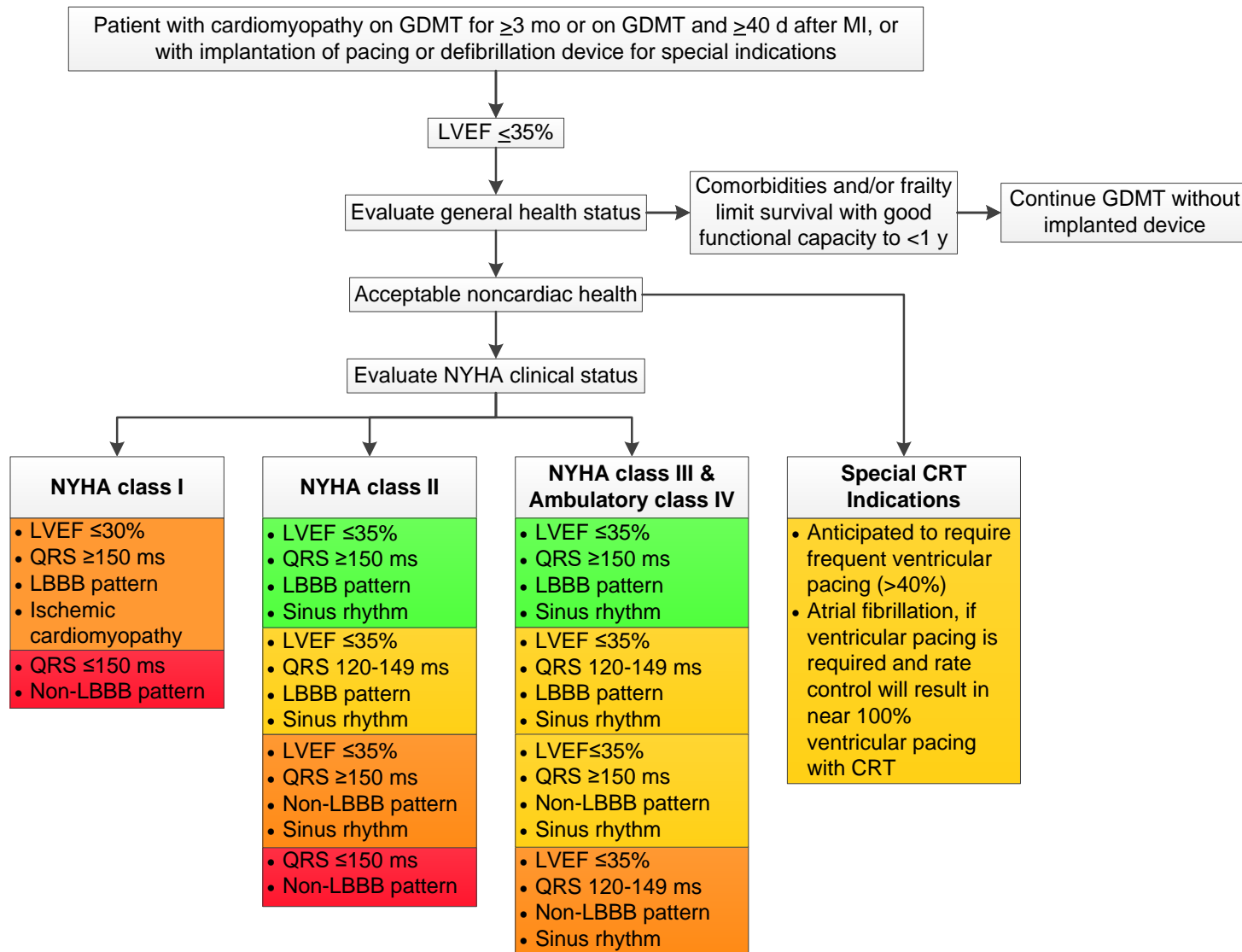
If LVEF $\leq 35\%$ despite OMT or a history of symptomatic VT/VF, implant ICD



Devices



Indications for CRT Therapy



Colors correspond to the class of recommendations in the ACCF/AHA Table 1.

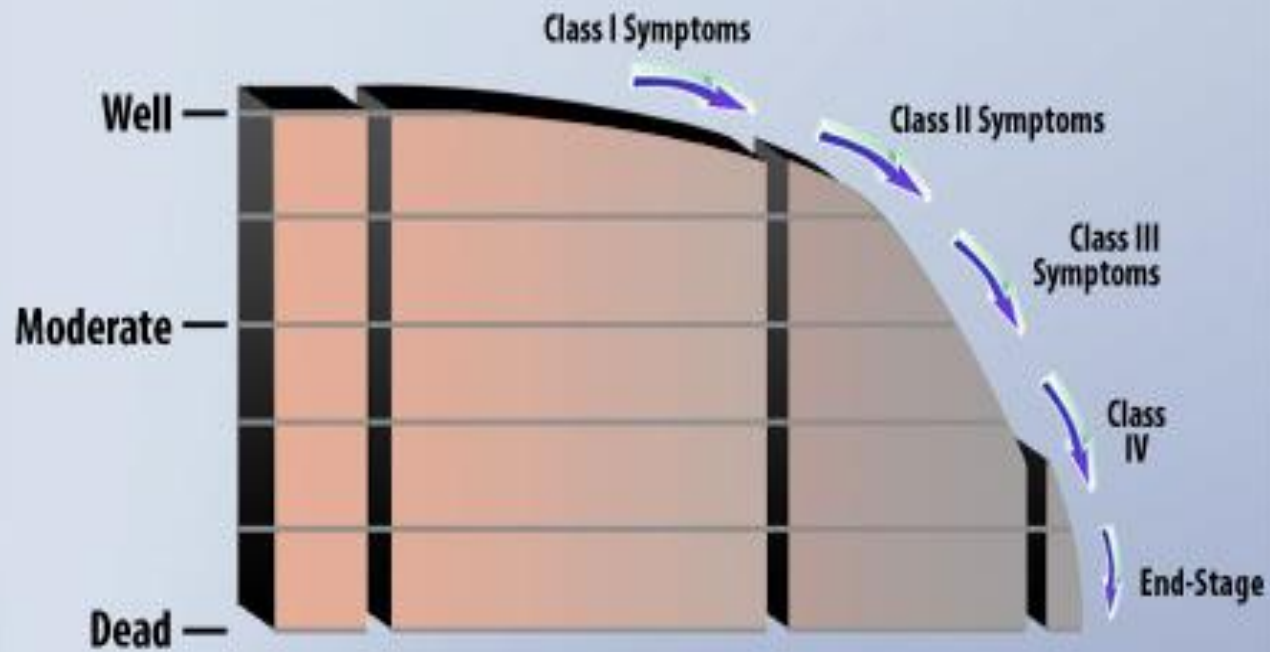
Benefit for NYHA class I and II patients has only been shown in CRT-D trials, and while patients may not experience immediate symptomatic benefit, late remodeling may be avoided along with long-term HF consequences. There are no trials that support CRT-pacing (without ICD) in NYHA class I and II patients. Thus, it is anticipated these patients would receive CRT-D unless clinical reasons or personal wishes make CRT-pacing more appropriate. In patients who are NYHA class III and ambulatory class IV, CRT-D may be chosen but clinical reasons and personal wishes may make CRT-pacing appropriate to improve symptoms and quality of life when an ICD is not expected to produce meaningful benefit in survival.



Advanced heart failure

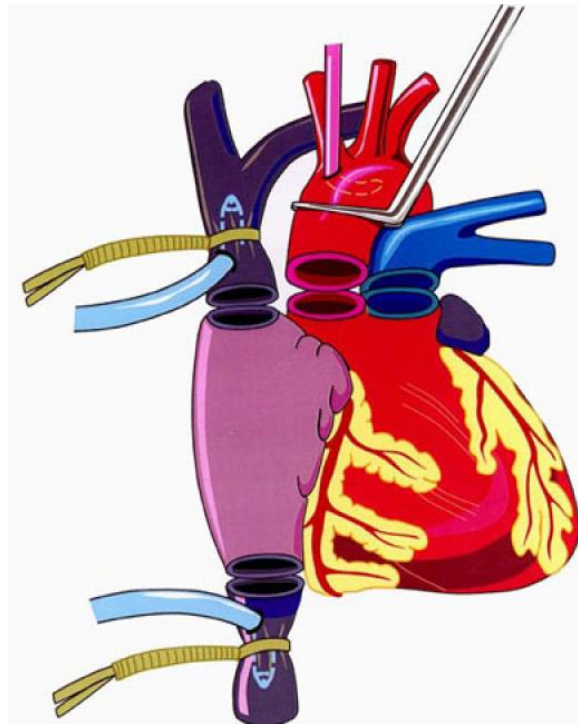
- *Defined* as persistent symptoms (NYHA class III–IV) that limit daily life despite routine therapy with agents of known benefit
- End-stage, refractory heart failure, probably accounts for 5% to 10% of the total population
- This group, consumes >60% of health-care expenditures for all patients with heart failure

New York Heart Association (NYHA) Classifications

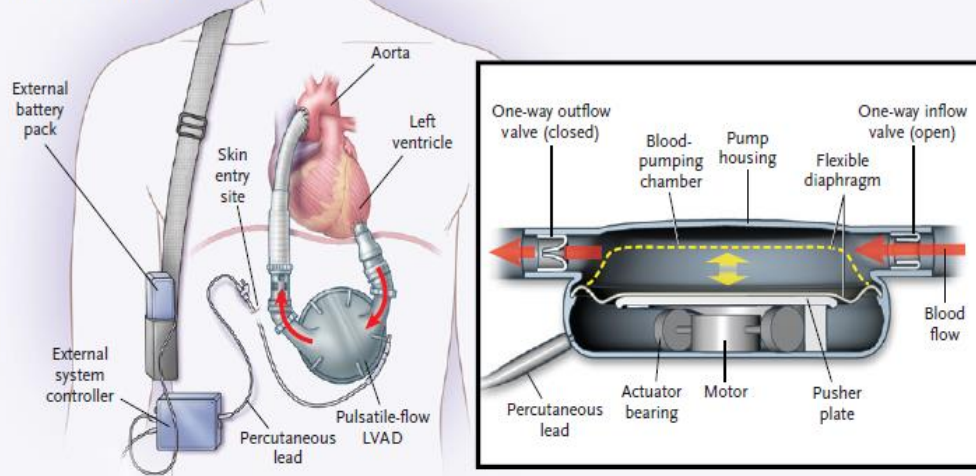


Heart Transplantation

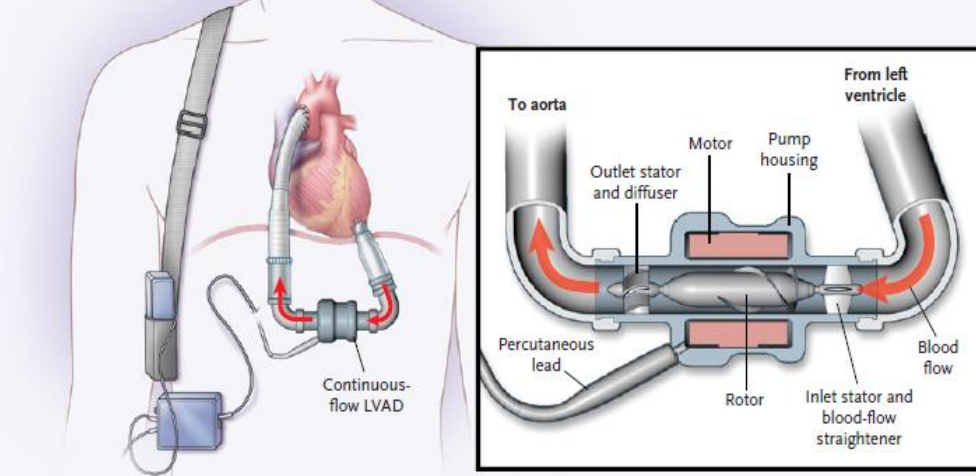
- Orthotopic cardiac transplantation remains the definitive therapy for terminal heart failure
- 5-year survival of 70%,
- 10-year survival of 60%,
- Markedly improved quality of life
- Donor organ availability has remained static even as the waiting list for heart transplant grows

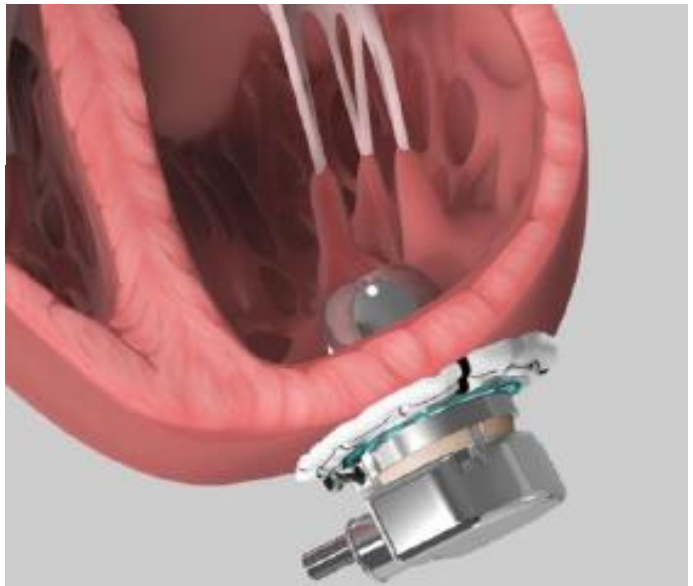


A Pulsatile-Flow LVAD

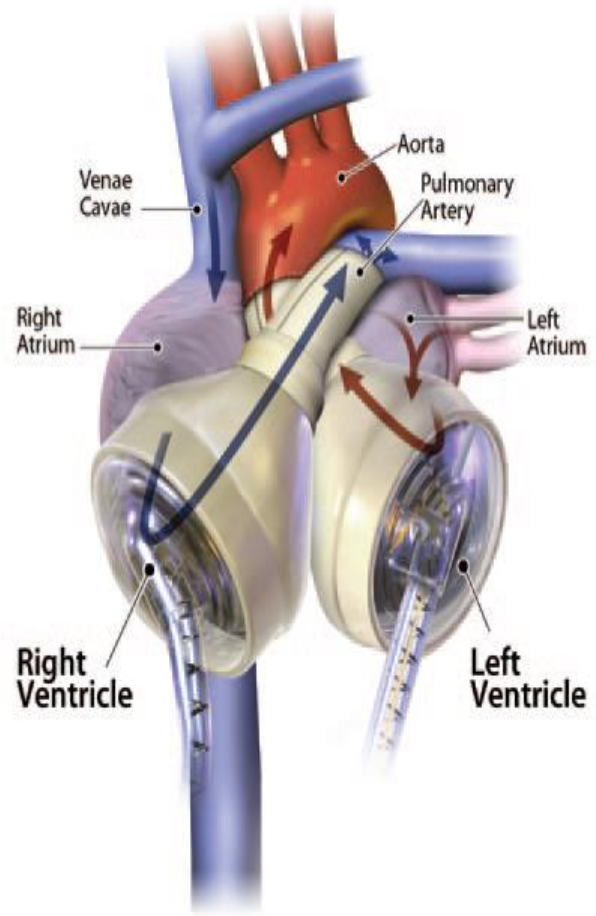
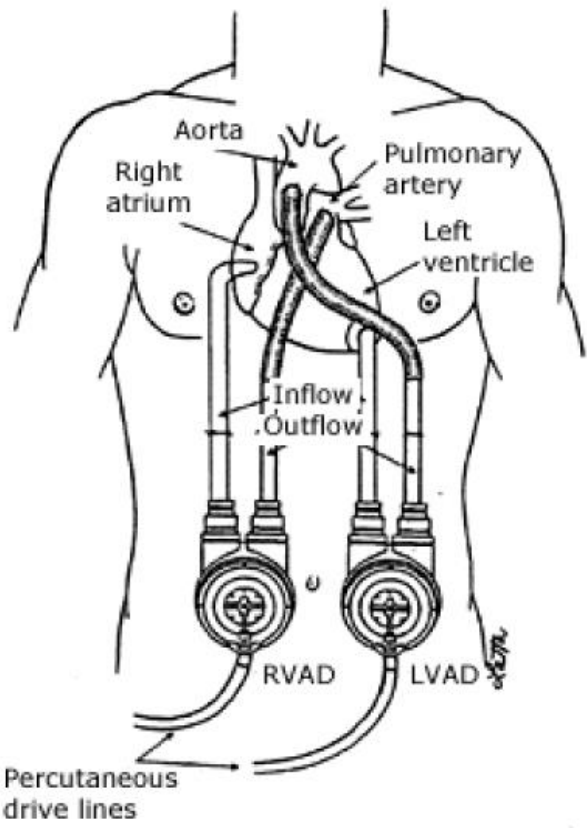


B Continuous-Flow LVAD





BiVAD





THANK YOU