UPDATES IN MANAGEMENT OF HF

Jennifer R Brown MD, MS
Heart Failure Specialist
Medstar Cardiology Associates

DC ACP Meeting
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Disclosures:

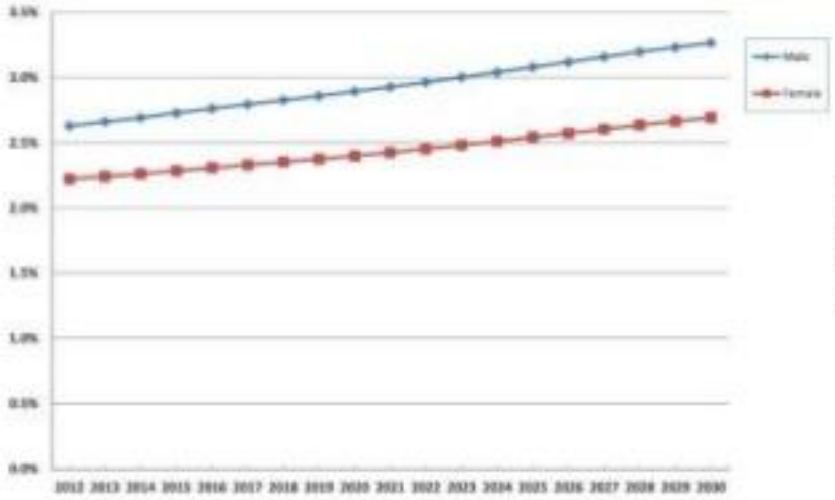
speaker bureau for novartis

speaker bureau for actelion

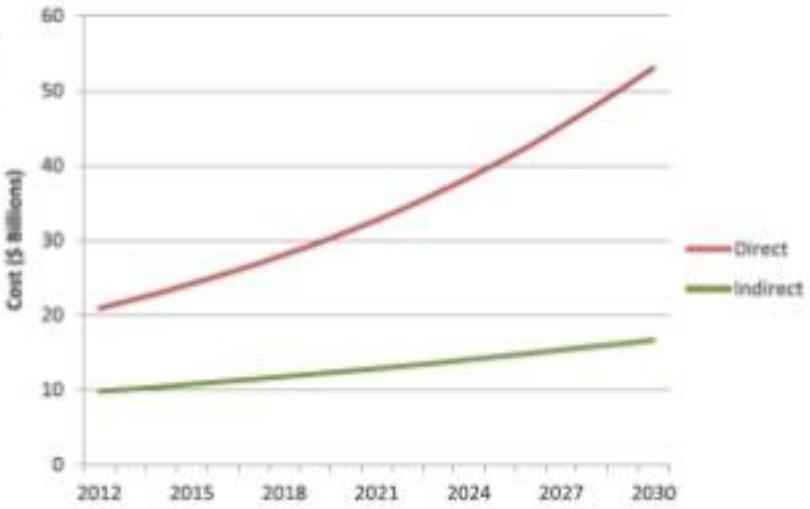
I will not discuss off-label use of any products

Forecasting the Impact of Heart Failure in the United States

Projected Prevalence



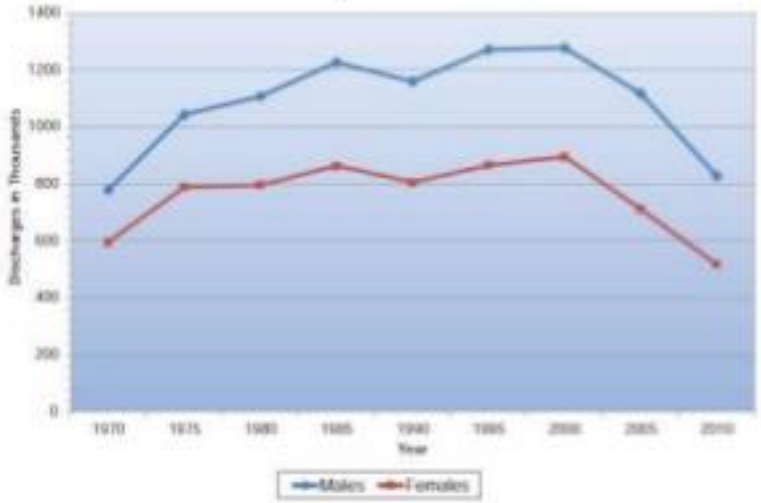
Projected Cost Increases



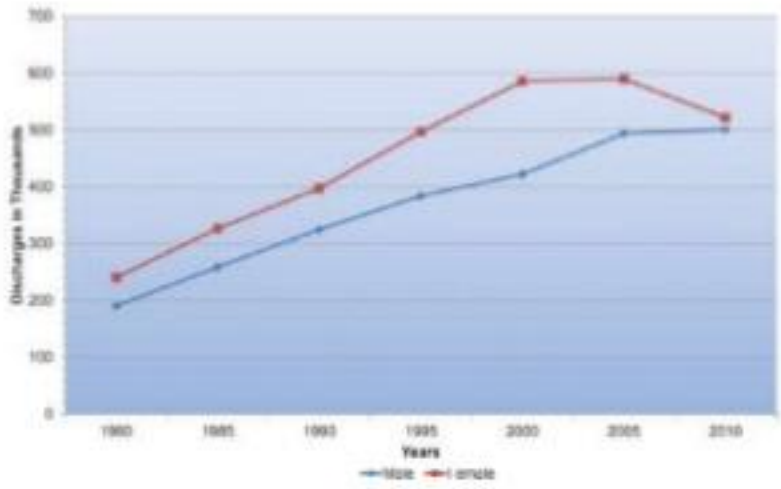
Heidenreich PA et al. Circ Heart Failure. 2013;6(3):606-19

Heart Failure Hospitalizations Remain Common

Coronary Heart Disease



Heart Failure



Mozaffarian D et al. Circulation. 2015;131:e29-e322.

Improvement in Heart Failure Assessment and Management is Needed

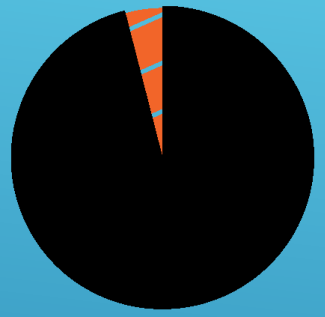
- Direct and indirect cost estimates for HF up to $56 billion USD annually
- Average HF Admission costs between $7,000 - $13,000 USD/admission
- Re-hospitalization rate: 50% within 6 months
- ACA has made HF readmission a major focus for improvement

Berkowitz et al Lippincotts Case Manag. 2005

Schlendorf et al Curr Treat Options in Cardiovasc Med 2011

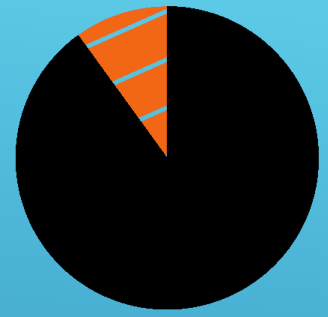
AHF MORTALITY RATES

~4%



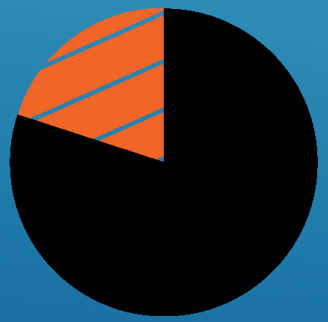
OF PATIENTS WITH AHF DIE DURING HOSPITALIZATION[10]*

10%



OF PATIENTS DIE WITHIN 30 DAYS FOLLOWING HOSPITALIZATION FOR AHF[9†]

>20%



OF PATIENTS DIE WITHIN 180 DAYS OF AN ACUTE HF EVENT[7‡]

~30%

OF PATIENTS DIE WITHIN 1 YEAR OF AN ACUTE HF EVENT[5§]

IN PATIENTS WITH HEART FAILURE

≥24%
DIE WITHIN 1 YEAR OF DIAGNOSIS[3]

~50%
DIE WITHIN 5 YEARS OF DIAGNOSIS[4]

Main challenges:
heart failure hospitalization

>1 million

Annual hospitalizations in both the United States and Europe[1]

1-4%

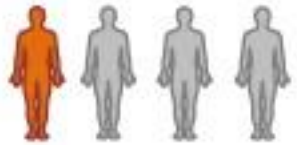
Heart failure hospitalizations as a percentage of total hospital admissions[2]

Up to 9/10 patients

Hospitalized due to worsening chronic heart failure as compared with de novo heart failure[3]

5-10 days

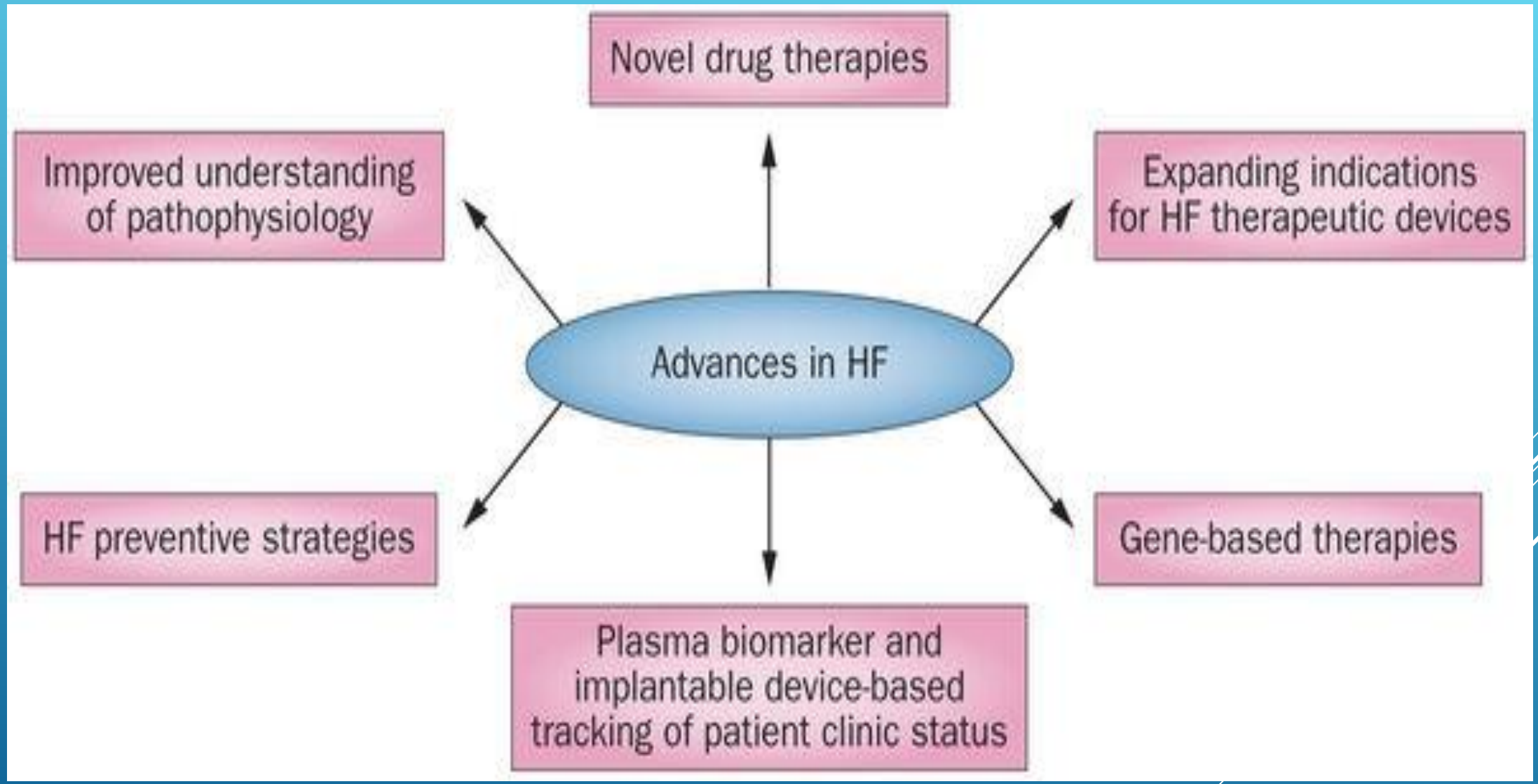
Average length of hospital stay[3]



Almost 1 out of 4 hospitalized patients (24%) are rehospitalized for heart failure within the **30-day post discharge period**[4]

Nearly 1 out of 2 patients (46%) are rehospitalized for heart failure within the **60-day post discharge period**[4]

1. Ambrosy PA et al. The Global Health and Economic Burden of Hospitalizations for Heart Failure. Lessons Learned From Hospitalized Heart Failure Registries. *J Am Coll Cardiol.* 2014;63:1123–1133. 2. Cowie MR et al. Improving care for patients with acute heart failure. 2014. Oxford PharmaGenesis. ISBN 978-1-903539-12-5. Available online at: http://www.oxfordhealthpolicyforum.org/reports/acute-heart-failure/improving-care-for-patients-with-acute-heart-failure . 3. Butler J, Braunwald E, Gheorghiade M. Recognizing worsening chronic heart failure as an entity and an end point in clinical trials. *JAMA.* 2014;312(8):789-90. 4. O'Connor CM et al. Causes of death and rehospitalization in patients hospitalized with worsening heart failure and reduced left ventricular ejection fraction: results from efficacy of vasopressin antagonism in heart failure outcome study with tolvaptan (EVEREST) program. *Am*


Novel drug therapies
Improved understanding of pathophysiology
Expanding indications for HF therapeutic devices
Advances in HF
HF preventive strategies
Gene-based therapies
Plasma biomarker and implantable device-based tracking of patient clinic status

AMERICAN COLLEGE of CARDIOLOGY

2017 ACC/AHA/HFSA

Focused Update Guideline for the Management of Heart Failure

Biomarkers:

For *prevention*:

The 2017 Focused Update gives a Class IIa recommendation (Level of Evidence: B-R) for utilizing natriuretic peptide biomarker-based screening for those at risk of developing HF, followed by team-based care including a cardiovascular specialist optimizing guideline-directed medical therapy (GDMT), to prevent the development of left ventricular dysfunction (systolic or diastolic) or new-onset HF.

For *diagnosis*:

The 2017 Focused Update gives a Class I recommendation (Level of Evidence: A) for measurement of natriuretic peptide biomarkers in patients presenting with dyspnea, to support a diagnosis or exclusion of HF.

For *prognosis or added risk stratification:*

The 2017 Focused Update gives a:

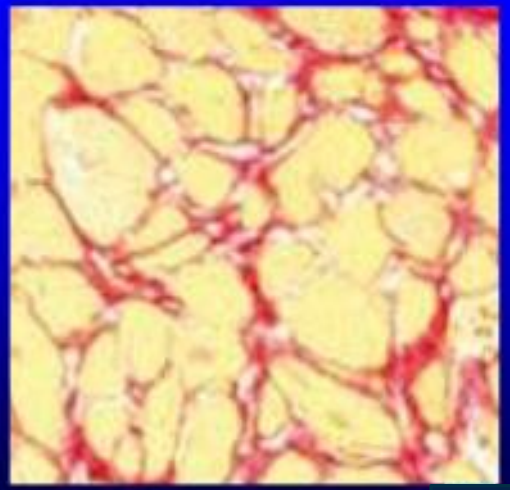
- Class I recommendation (Level of Evidence: A) for measurement of B-type natriuretic peptide (BNP) or N-terminal (NT)-proBNP for establishing prognosis or disease severity in chronic HF.
- Class I recommendation (Level of Evidence: A) for measurement of baseline natriuretic peptide biomarkers and/or cardiac troponin on admission to the hospital to establish a prognosis in acutely decompensated HF.
- Class IIa recommendation (Level of Evidence: B-NR) for measurement of a predischarge natriuretic peptide level during a HF hospitalization, to establish a post-discharge prognosis.
- Class IIa recommendation (Level of Evidence: B-NR) for measurement of other clinically available tests, such as biomarkers of myocardial injury or fibrosis, in patients with chronic HF for additive risk stratification.

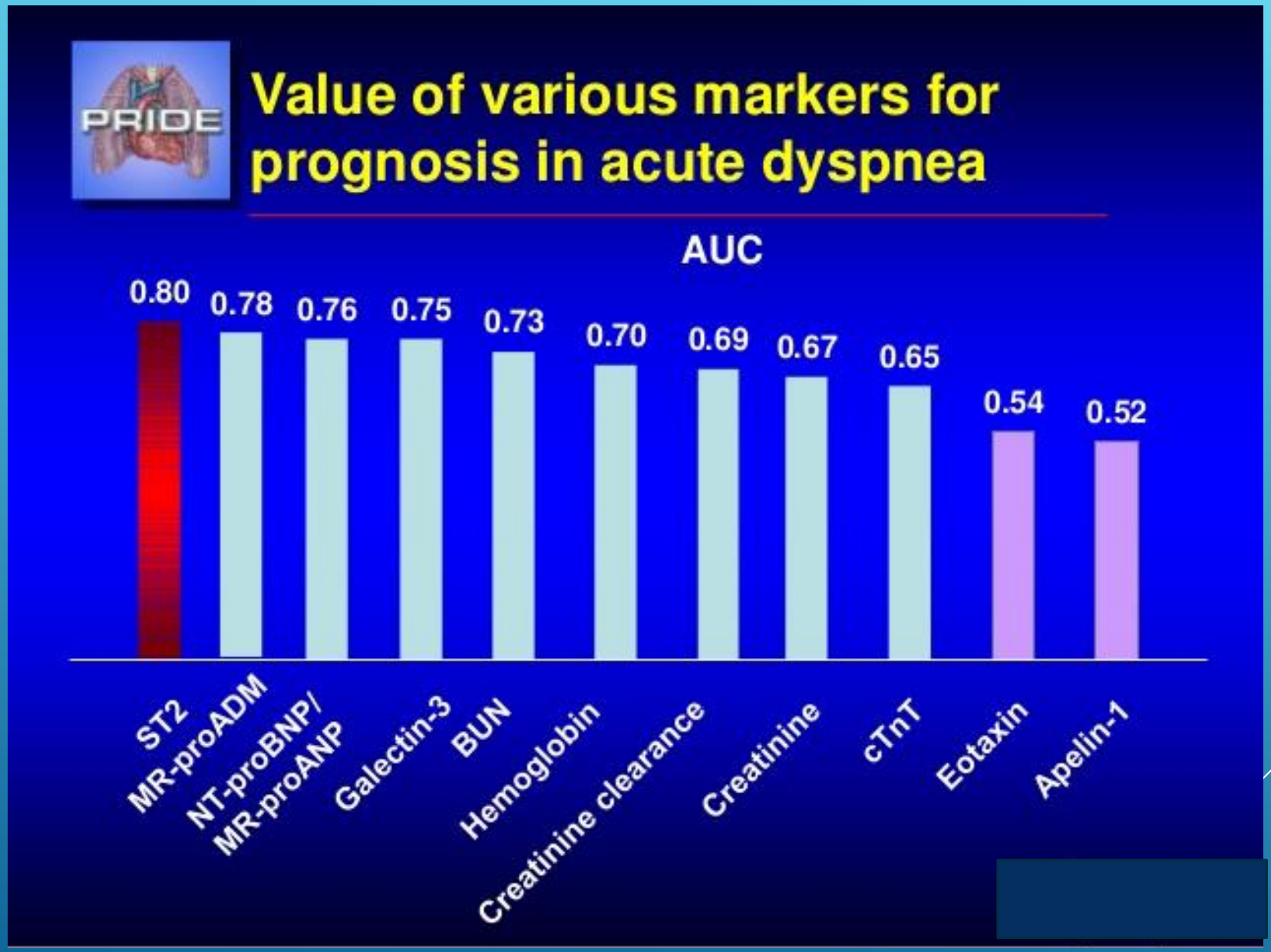
ST2 plays a role in reducing cardiomyocyte hypertrophy and fibrosis

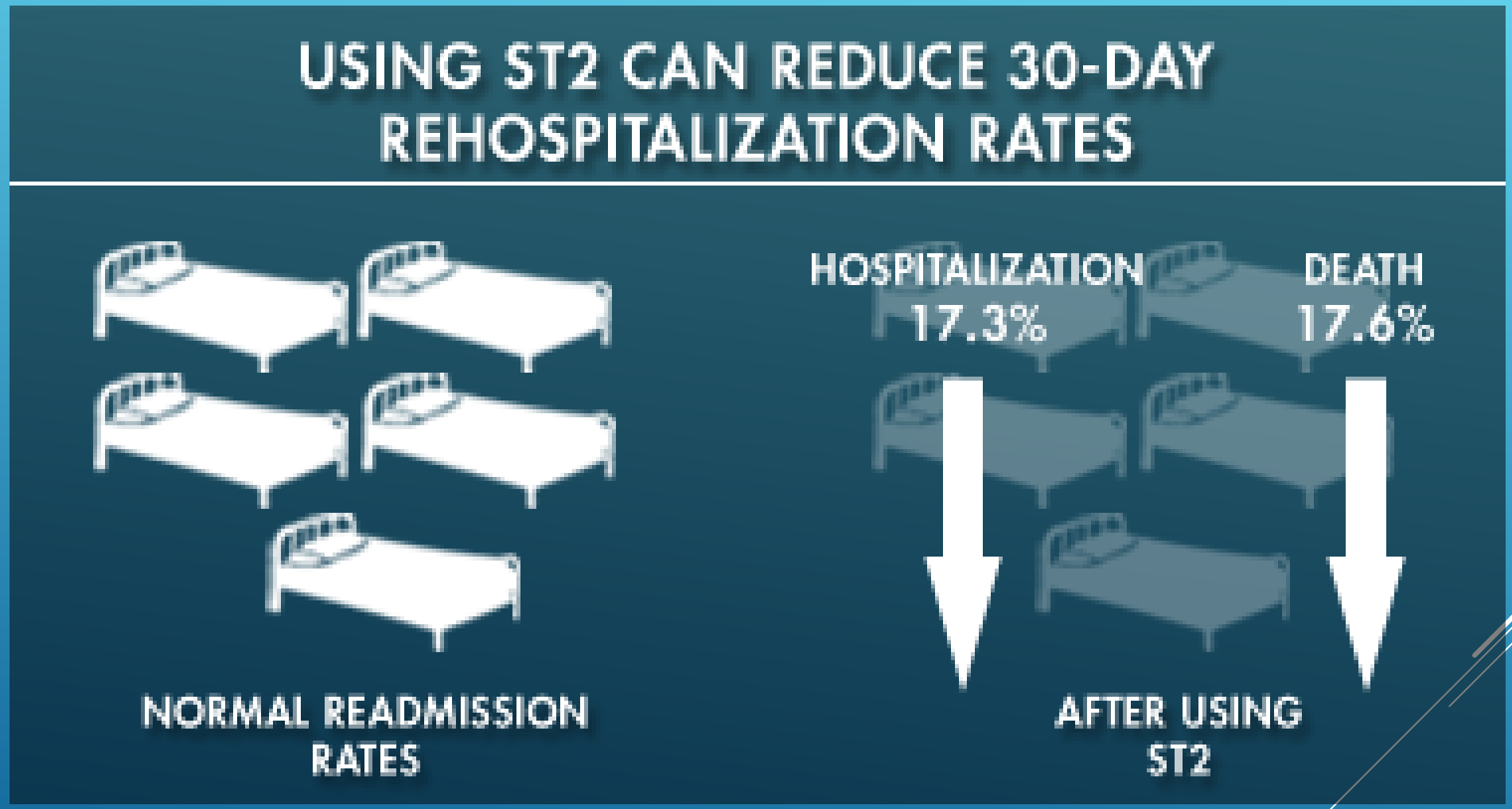
Abnormalities in ST2 experimentally result in severe cardiac remodeling and heart failure

Intact sST2

sST2 knock out




PRIDE
Value of various markers for prognosis in acute dyspnea
AUC
0.80
0.78
0.76
0.75
0.73
0.70
0.69
0.67
0.65
0.54
0.52
ST2
MR-proADM
NT-proBNP/ MR-proANP
Galectin-3
BUN
Hemoglobin
Creatinine clearance
Creatinine
cTnT
Eotaxin
Apelin-1


USING ST2 CAN REDUCE 30-DAY REHOSPITALIZATION RATES
NORMAL READMISSION RATES
HOSPITALIZATION 17.3%
DEATH 17.6%
AFTER USING ST2

st2 in the heart failure guidelines:

The role of st2 is as a useful additive biomarker to BNP and nt pro-bnp as detailed below:

Biomarker, Application	Setting	COR	LOE	References
Natriuretic peptides				
Diagnosis or exclusion of HF	Ambulatory, Acute	I	A	212, 217–223, 245–250
Prognosis of HF	Ambulatory, Acute	I	A	222, 224–229, 248, 251–258
Achieve GDMT	Ambulatory	IIa	B	230–237
Guidance for acutely decompensated HF therapy	Acute	IIb	C	259, 260
Biomarkers of myocardial injury				
Additive risk stratification	Acute, Ambulatory	I	A	238–241, 248, 253, 256–267
Biomarkers of myocardial fibrosis				
Additive risk stratification	Ambulatory	IIb	B	242–244
	Acute	IIb	A	248, 253, 256, 258–260, 262, 264–267

ST2

COR indicates Class of Recommendation; GDMT, guideline-directed medical therapy; HF, heart failure; and LOE, Level of Evidence.

Stage C HF With Preserved EF (HFpEF):

The 2017 Focused Update gives the following:

- Class IIa recommendation (Level of Evidence: B-R) for use of aldosterone antagonists in appropriately selected patients with HFpEF (with EF ≥45%, elevated BNP or HF admission within 1 year, estimated glomerular filtration rate >30 and creatinine <2.5 mg/dl, potassium <5.0 mEq /L), to decrease hospitalizations.
- Class III recommendation (Level of Evidence: B-R) for routine use of nitrates or phosphodiesterase-5 inhibitors to increase activity or quality of life (QoL) in patients with HFpEF, as there is no benefit.
- Class III recommendation (Level of Evidence: B-C) for routine use of nutritional supplements in patients with HFpEF, as there is no benefit.

Anemia:

The 2017 Focused Update gives a:

- Class IIb recommendation (Level of Evidence: B-R) for intravenous iron replacement in patients with New York Heart Association (NYHA) class II and III HF and iron deficiency (ferritin <100 ng/ml or 100-300 ng/ml if transferrin saturation <20%), to improve functional status and QoL.

- Class III recommendation (Level of Evidence: B-R) that erythropoietin stimulating agents should not be used in patients with HF and anemia to improve morbidity and mortality, as there is no benefit.

Hypertension:

The 2017 Focused Update gives a:

- Class I recommendation (Level of Evidence: B-R) for targeting an optimal blood pressure (BP) of <130/80 mm Hg in those with hypertension and at increased risk (stage A HF).
- Class I recommendation (Level of Evidence: C-EO) for titration of GDMT to attain systolic BP (SBP) <130 mm Hg in patients with HFrEF and hypertension.
- Class I recommendation (Level of Evidence: C-LD) for titration of GDMT to attain SBP <130 mm Hg in patients with HFpEF and persistent hypertension after management of volume overload.

Sleep-Disordered Breathing:

The 2017 Focused Update gives a:

- Class IIa recommendation (Level of Evidence: C-LD) for a formal sleep assessment in patients with NYHA class II–IV HF and suspicion of sleep-disordered breathing or excessive daytime sleepiness.
- Class IIb recommendation (Level of Evidence: B-R) for utilization of continuous positive airway pressure in patients with cardiovascular disease and obstructive sleep apnea, to improve sleep quality and daytime sleepiness.
- Class III recommendation: Harm (Level of Evidence: B-R) for use of adaptive servo-ventilation in patients with NYHA class II–IV HFrEF and central sleep apnea, as it causes harm.

Ivabradine and outcomes in chronic heart failure (SHIFT)

Background

Chronic heart failure is associated with high mortality and morbidity. Raised resting heart rate is a risk factor for adverse outcomes. We aimed to assess the effect of heart-rate reduction by the selective sinus-node inhibitor ivabradine on outcomes in heart failure.

Findings

6558 patients were randomly assigned to treatment groups (3268 ivabradine, 3290 placebo). 793 (24%) patients in the ivabradine group and 937 (29%) of those taking placebo had a primary endpoint event (HR 0·82, 95% CI 0·75–0·90, p<0·0001). The effects were driven mainly by hospital admissions for worsening heart failure (672 [21%] placebo *vs* 514 [16%] ivabradine; HR 0·74, 0·66–0·83; p<0·0001) and deaths due to heart failure (151 [5%] *vs* 113 [3%]; HR 0·74, 0·58–0·94, p=0·014).

The results support the importance of heart-rate reduction with ivabradine for improvement of clinical outcomes in heart failure and confirm the important role of heart rate in the pathophysiology of this disorder.

SHIFT (Systolic Heart Failure Treatment with the I_f Inhibitor Ivabradine Trial)

M Komajda (Groupe Hospitalier Pitié-Salpêtrière, Paris, France)
European Society of Cardiology 2010 Congress

- Background:

  Ivabradine is a selective inhibitor of a sodium-potassium channel highly expressed in the sinoatrial node, on which it has a mild dampening effect

- Population and treatment:

  >6500 patients with NYHA class 2–4 heart failure, an LVEF <35%, a resting heart rate >70 bpm, and HF hospitalization within the previous year

  Randomized to placebo or ivabradine at a starting dose of 5 mg twice daily, with adjustments to achieve a resting HR of 50 to 60 bpm; all patients were on standard HF medications according to guidelines

- Primary outcome:

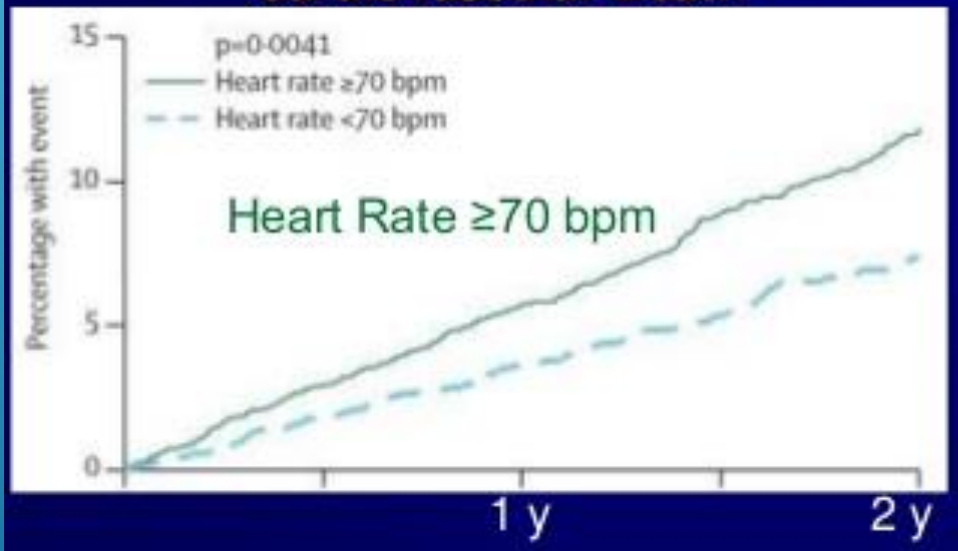
  Composite of CV death or HF hospitalization

HR=heart rate

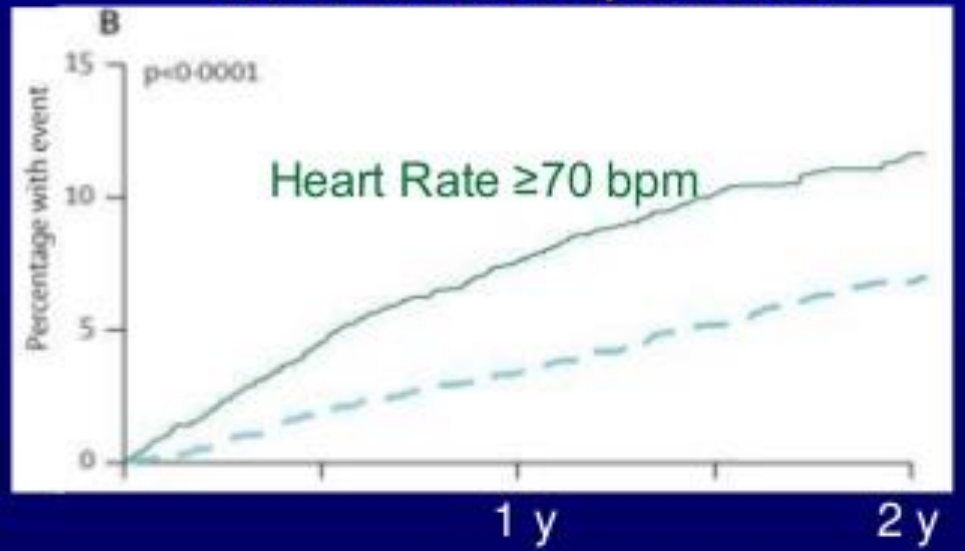
Heart Rate: A Prognostic Risk Factor in Heart Failure

Patients with CAD and EF < 40%

Cardiovascular Death

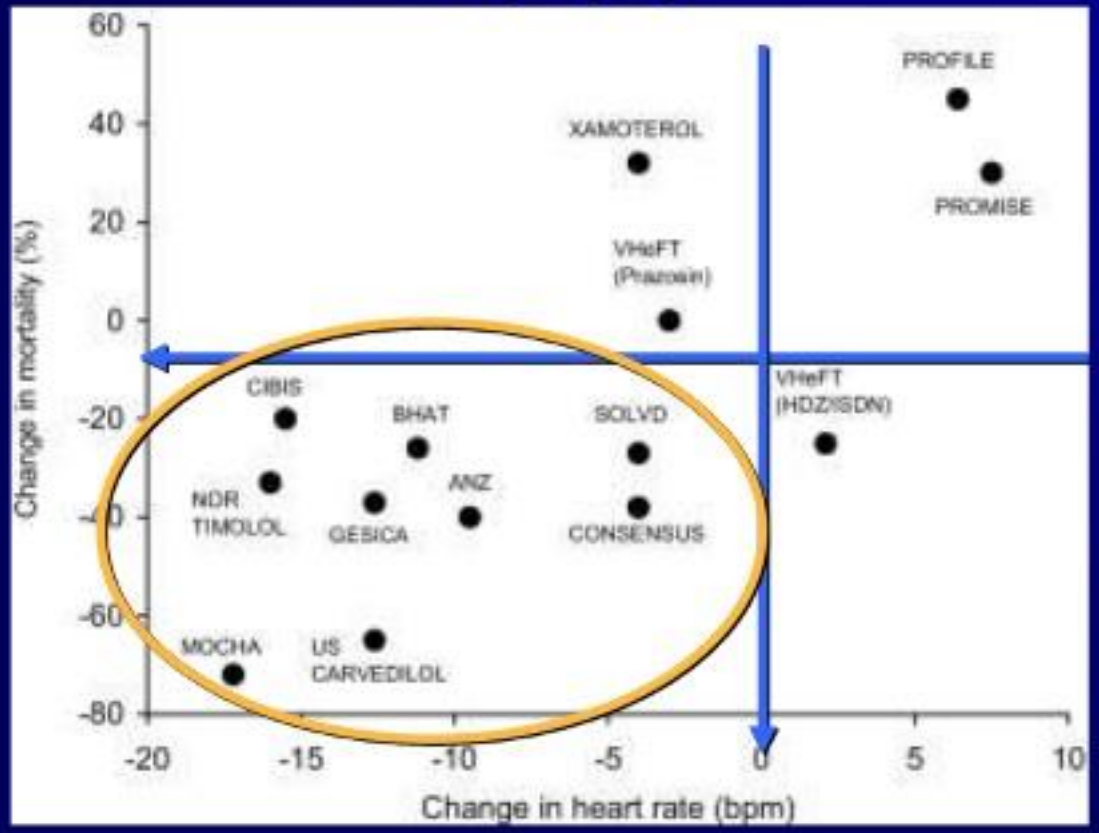


Heart Failure Hospitalization



Fox K, *et al*. Lancet 2008

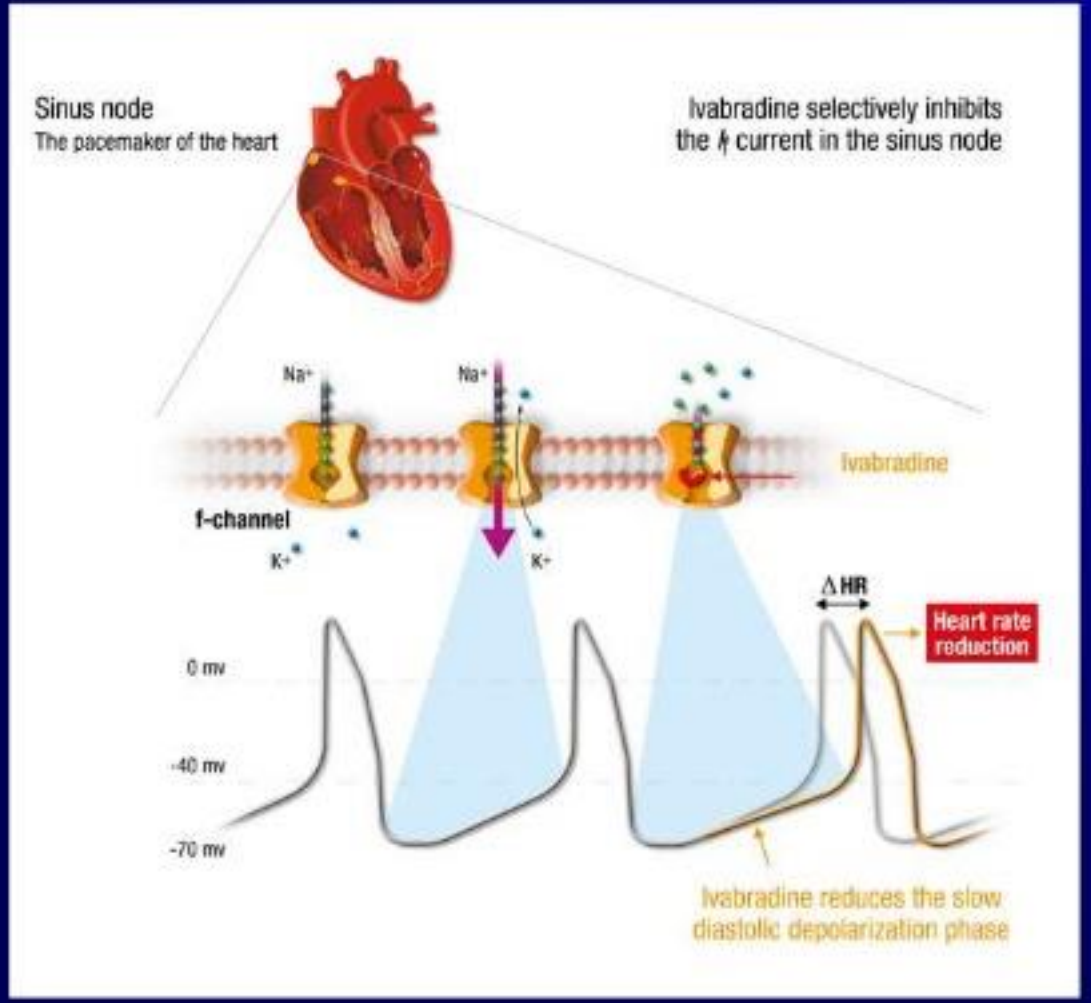
Heart Rate Reduction and Mortality in Heart Failure



- Major criticism of COMET (carvedilol vs metoprolol)

Kjekshus J. Eur Heart J 1999.

Ivabradine



Ivabradine selectively inhibits the "funny" current in the sinus node

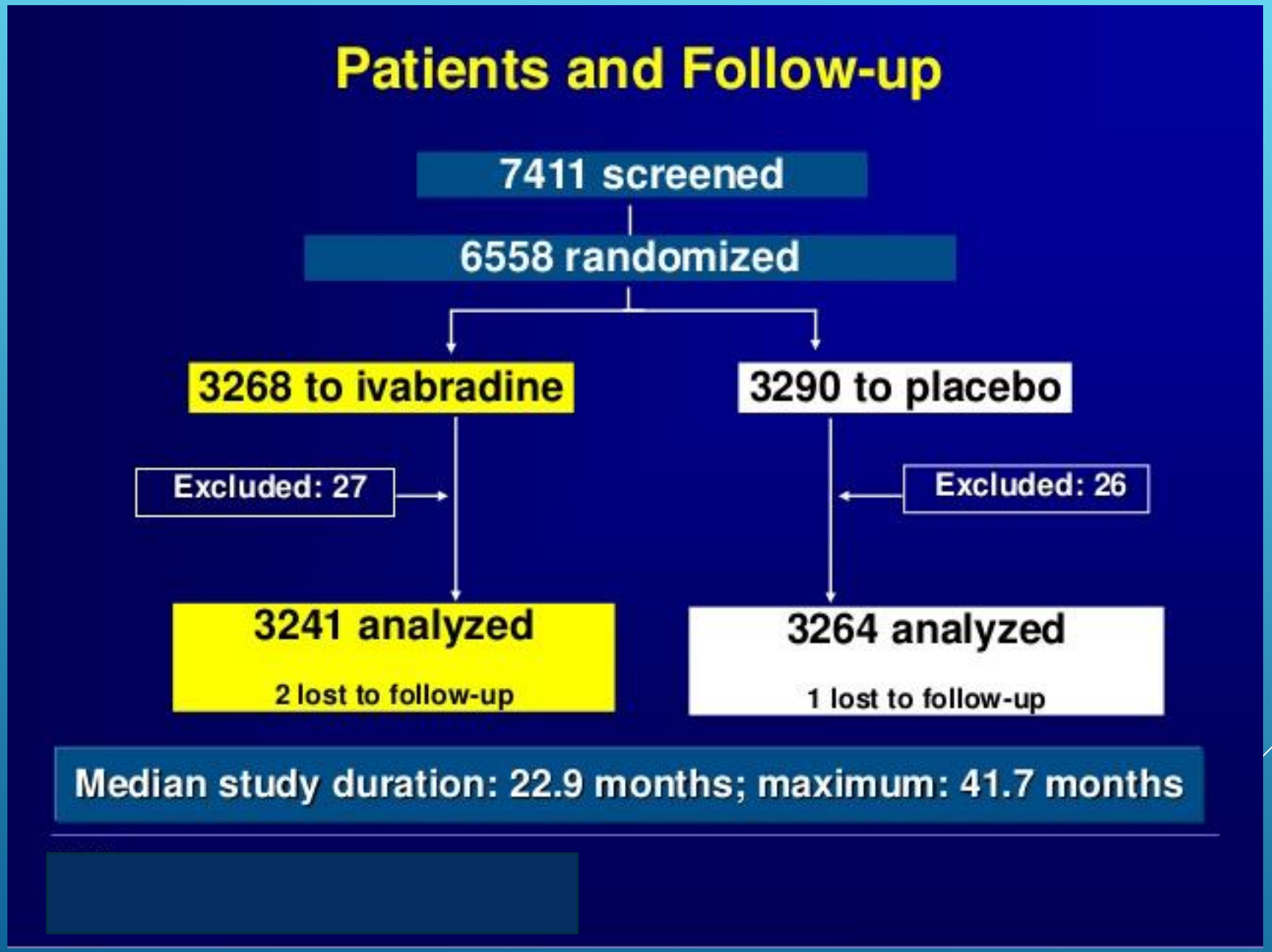
Slows HR independent of BB effect "less ngetive inotropy"

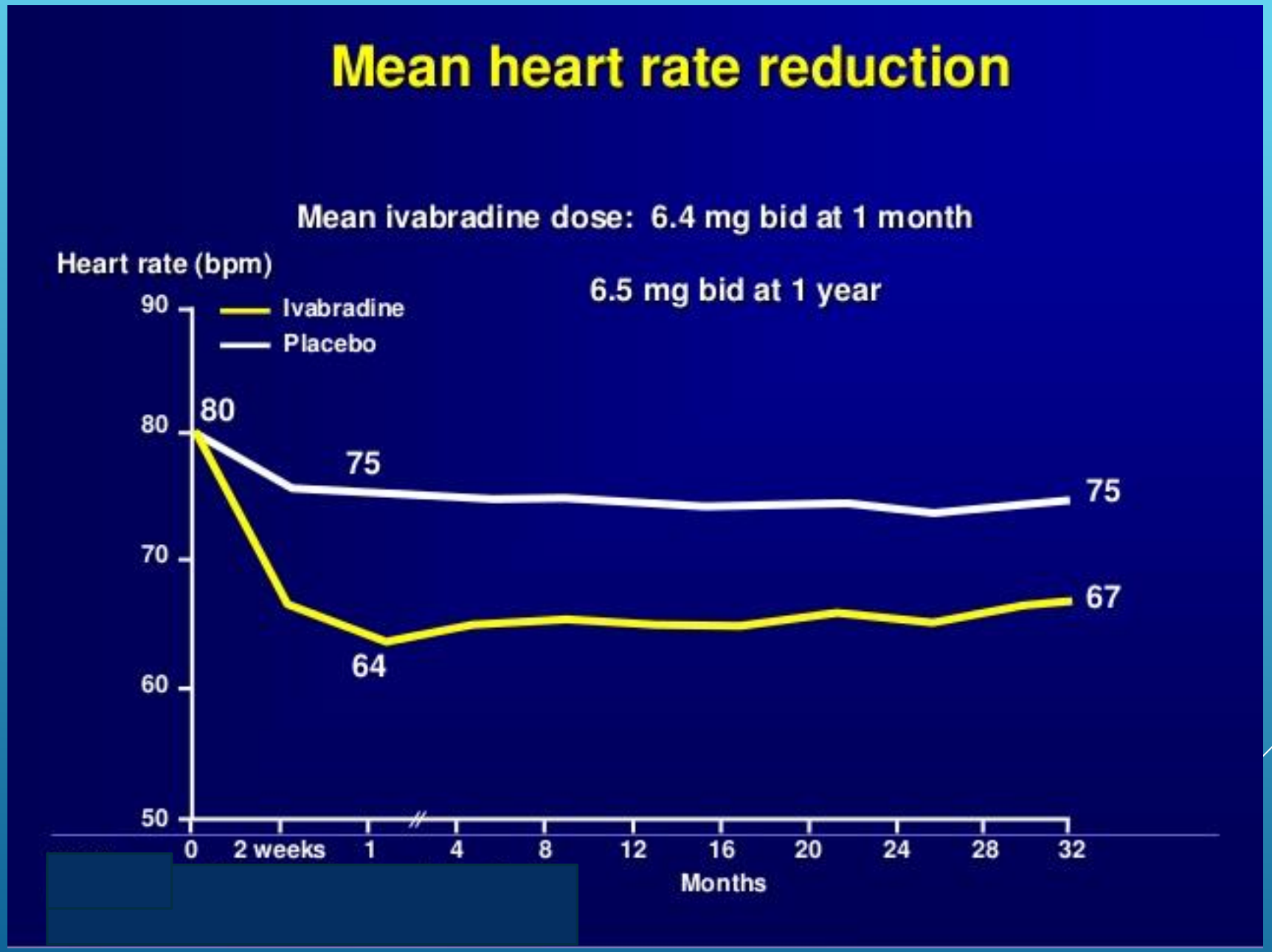
Implications for patients with impaired stroke volume

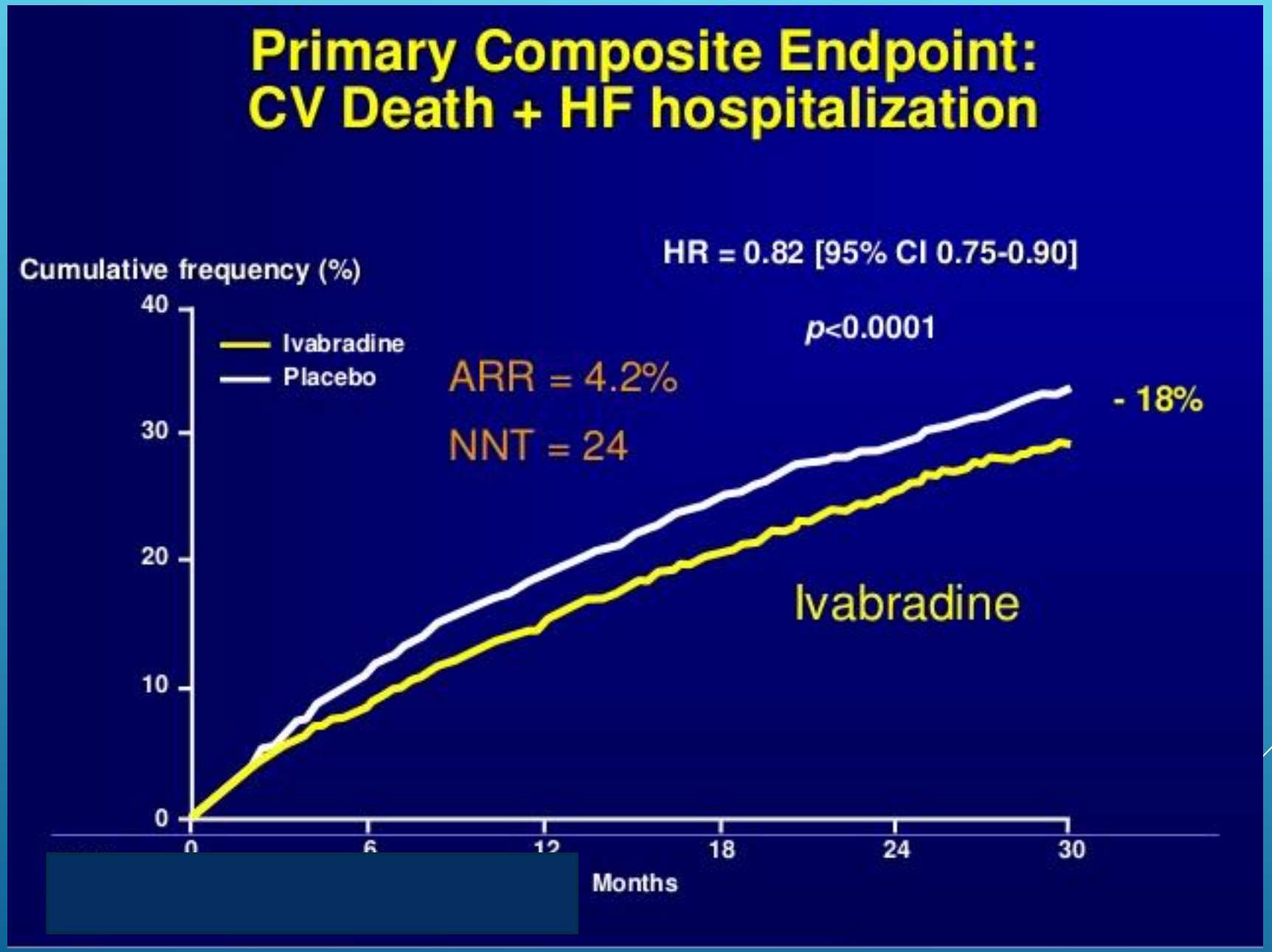
Systolic Heart failure treatment with the *If* inhibitor ivabradine Trial

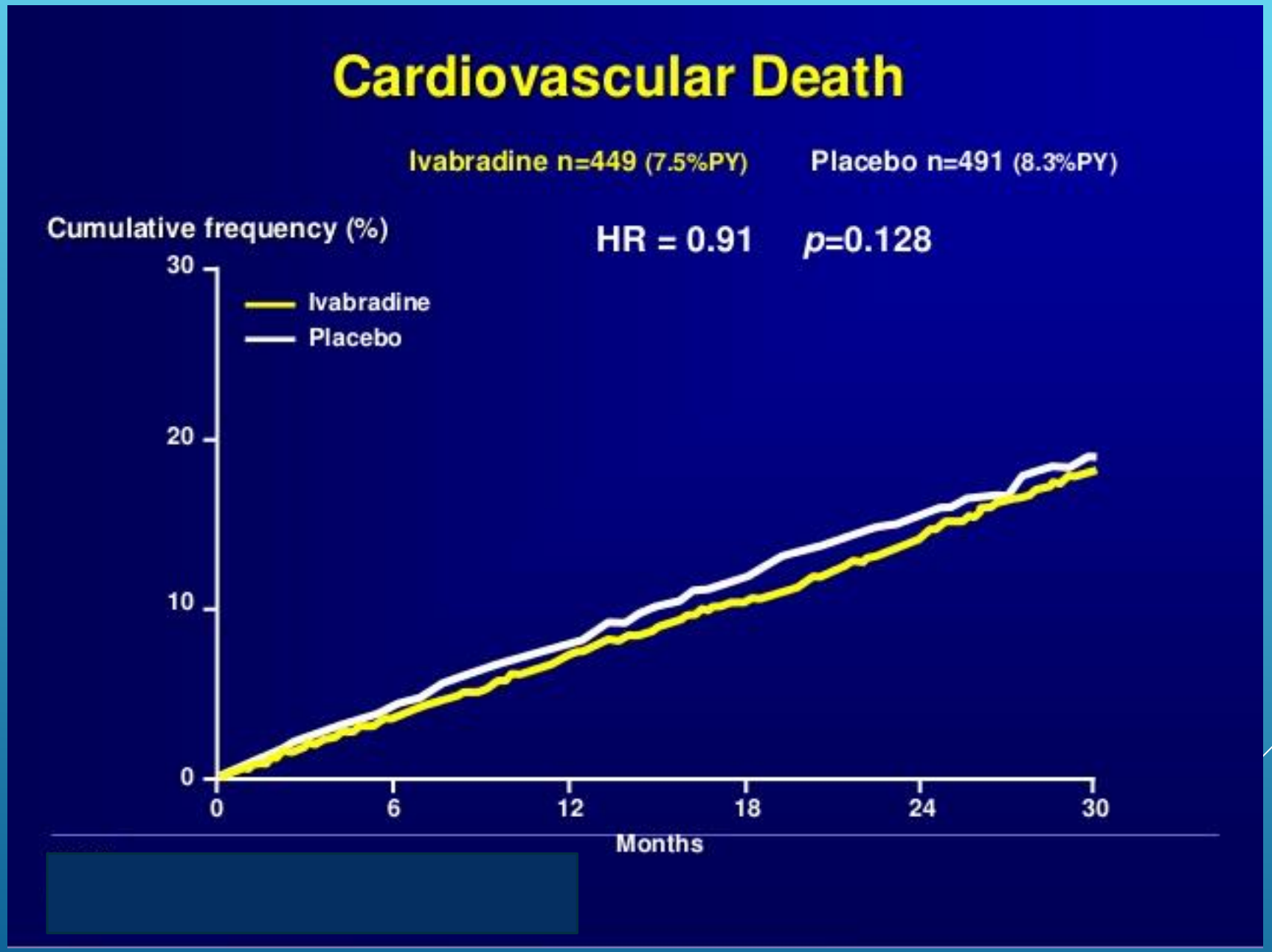
To evaluate whether the I_f inhibitor ivabradine improves cardiovascular outcomes in patients with

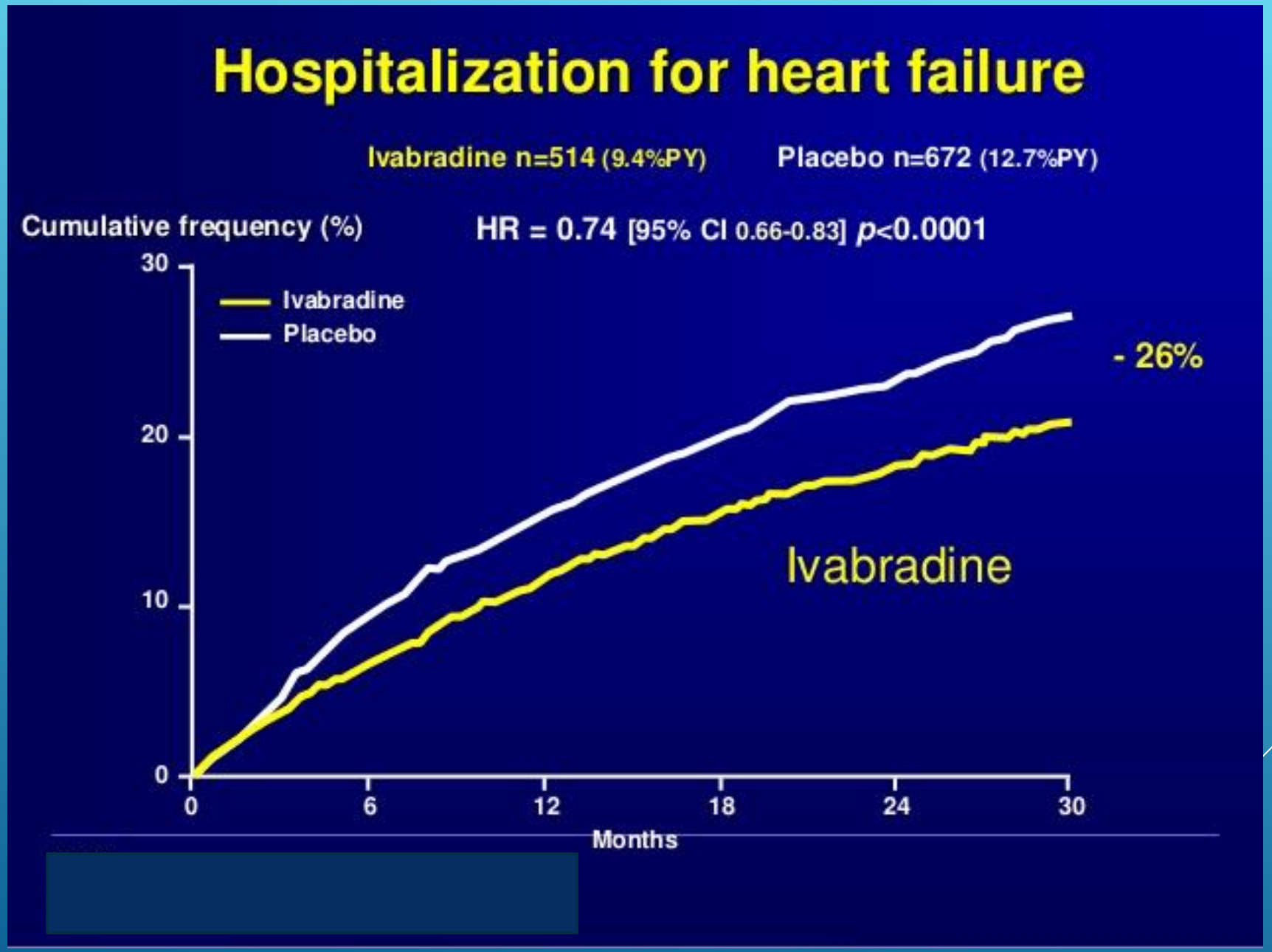
1. Moderate to severe chronic HF
2. Left ventricular EF ≤35%
3. Heart rate ≥70 bpm and
4. Recommended therapy


Patients and Follow-up
7411 screened
6558 randomized
3268 to ivabradine
3290 to placebo
Excluded: 27
Excluded: 26
3241 analyzed
2 lost to follow-up
3264 analyzed
1 lost to follow-up
Median study duration: 22.9 months; maximum: 41.7 months


Mean heart rate reduction
Mean ivabradine dose: 6.4 mg bid at 1 month
6.5 mg bid at 1 year
Heart rate (bpm)
Ivabradine
Placebo
90
80
70
60
50
80
75
64
75
67
0
2 weeks
1
4
8
12
16
20
24
28
32
Months


Primary Composite Endpoint:
CV Death + HF hospitalization
HR = 0.82 [95% CI 0.75-0.90]
p<0.0001
Cumulative frequency (%)
40
30
20
10
0
Ivabradine
Placebo
ARR = 4.2%
NNT = 24
- 18%
Ivabradine
0
6
12
18
24
30
Months


Cardiovascular Death
Ivabradine n=449 (7.5%PY)
Placebo n=491 (8.3%PY)
Cumulative frequency (%)
HR = 0.91
p=0.128
Ivabradine
Placebo
30
20
10
0
0
6
12
18
24
30
Months


Hospitalization for heart failure
Ivabradine n=514 (9.4%PY)
Placebo n=672 (12.7%PY)
Cumulative frequency (%)
HR = 0.74 [95% CI 0.66-0.83] p<0.0001
30
20
10
0
Ivabradine
Placebo
- 26%
Ivabradine
0
6
12
18
24
30
Months

SHIFT: Results

- Significant 18% reduction in HR for CV death or hospitalization for worsening HF with ivabradine vs control group—driven by significant 26% HR reductions for the individual secondary end points of death from HF and hospitalization for worsening HF

Primary and secondary end points[a]

Outcomes	Ivabradine (n=3241), %	Placebo (n=3264), %	HR (95% CI)	p
Primary end point	24	29	0.82 (0.75–0.90)	<0.001
Death from HF	3	5	0.74 (0.58–0.94)	0.014
HF hospitalization	16	21	0.74 (0.66–0.83)	<0.001
CV death, HF hospitalization, or admission for nonfatal MI	25	30	0.82 (0.74–0.89)	<0.001

a. Mean follow-up of 23 months
b. HR=hazard ratio

Ivabradine
Guideline Recommendations

2016 ACC/AHA/HFSA Heart Failure Update

Recommendation for Ivabradine		
COR	LOE	Recommendation
IIa	B-R	Ivabradine can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HF*r*EF (LVEF≤ 35%) who are receiving GDEM, including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 bpm or greater at rest (37-40).

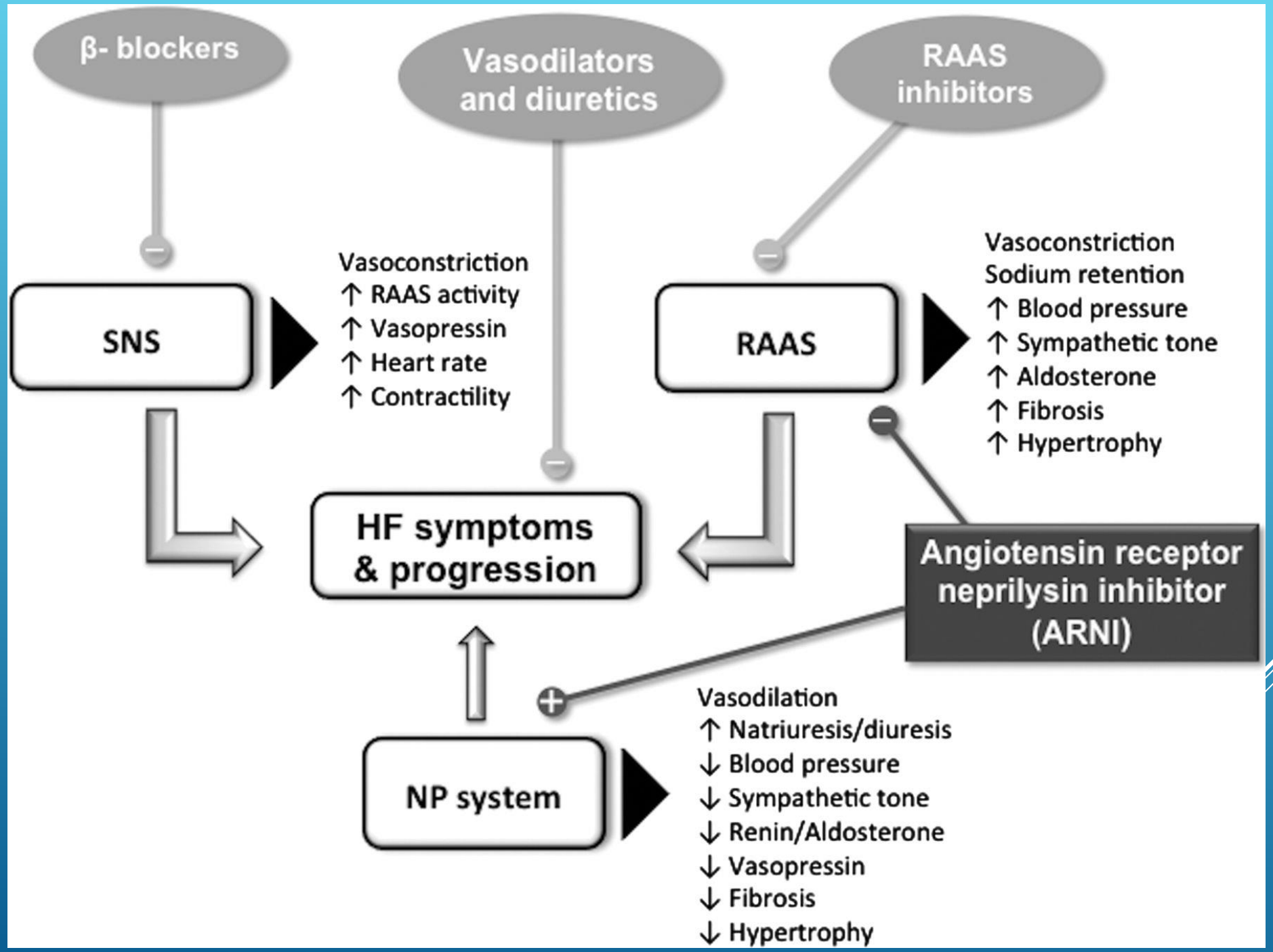
Yancy CW, et al. JACC 2016

2012 European HF Guidelines

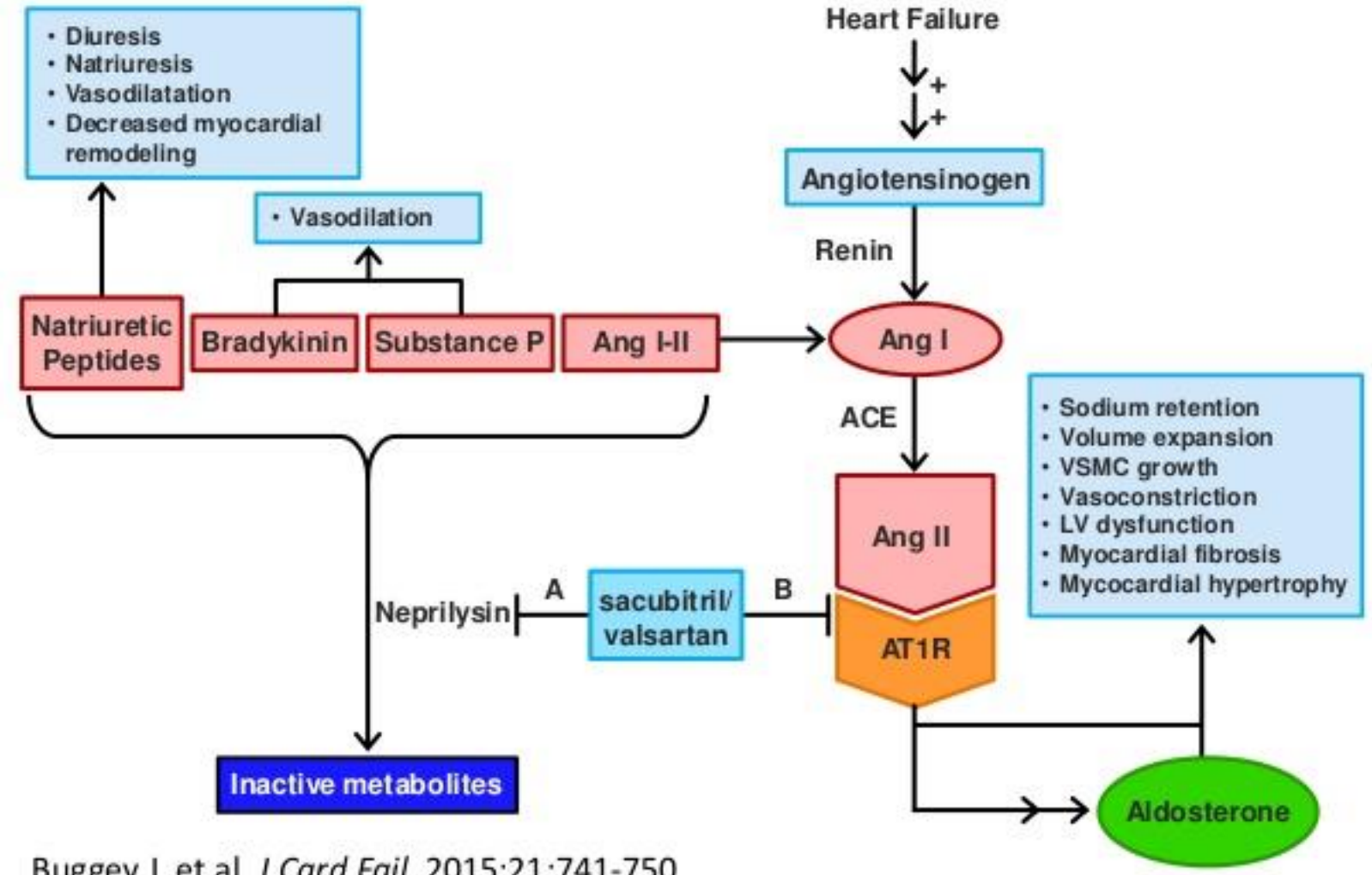
Should be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF ≤35%, a heart rate remaining ≥70 b.p.m., and persisting symptoms (NYHA class II–IV) despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE inhibitor (or ARB), and an MRA (or ARB).*	IIa	B
May be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF ≤35% and a heart rate ≥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).*	IIb	C

McMurray JJV, et al. EHJ 2012

LCZ-696


β- blockers
Vasodilators and diuretics
RAAS inhibitors
SNS
Vasoconstriction
↑ RAAS activity
↑ Vasopressin
↑ Heart rate
↑ Contractility
RAAS
Vasoconstriction
Sodium retention
↑ Blood pressure
↑ Sympathetic tone
↑ Aldosterone
↑ Fibrosis
↑ Hypertrophy
HF symptoms & progression
Angiotensin receptor neprilysin inhibitor (ARNI)
NP system
Vasodilation
↑ Natriuresis/diuresis
↓ Blood pressure
↓ Sympathetic tone
↓ Renin/Aldosterone
↓ Vasopressin
↓ Fibrosis
↓ Hypertrophy

Dual Effects of Sacubitril/Valsartan



Buggey J, et al. *J Card Fail.* 2015;21:741-750.

Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure: Paradigm Trial

BACKGROUND

We compared the angiotensin receptor–neprilysin inhibitor LCZ696 with enalapril in patients who had heart failure with a reduced ejection fraction. In previous studies, enalapril improved survival in such patients.

RESULTS

The trial was stopped early, after a median follow-up of 27 months, because of the benefit with LCZ696. The primary outcome occurred in 914 patients (21.8%) in the LCZ696 group and 1117 patients (26.5%) in the enalapril group (hazard ratio in the LCZ696 group, 0.80; 95% confidence interval [CI], 0.73 to 0.87; P<0.001). A total of 711 patients (17.0%) receiving LCZ696 and 835 patients (19.8%) receiving enalapril died. As compared with enalapril, LCZ696 also reduced the risk of hospitalization for heart failure by 21% (P<0.001) and decreased the symptoms and physical limitations of heart failure (P=0.001).

CONCLUSIONS

LCZ696 was superior to enalapril in reducing the risks of death and of hospitalization for heart failure.

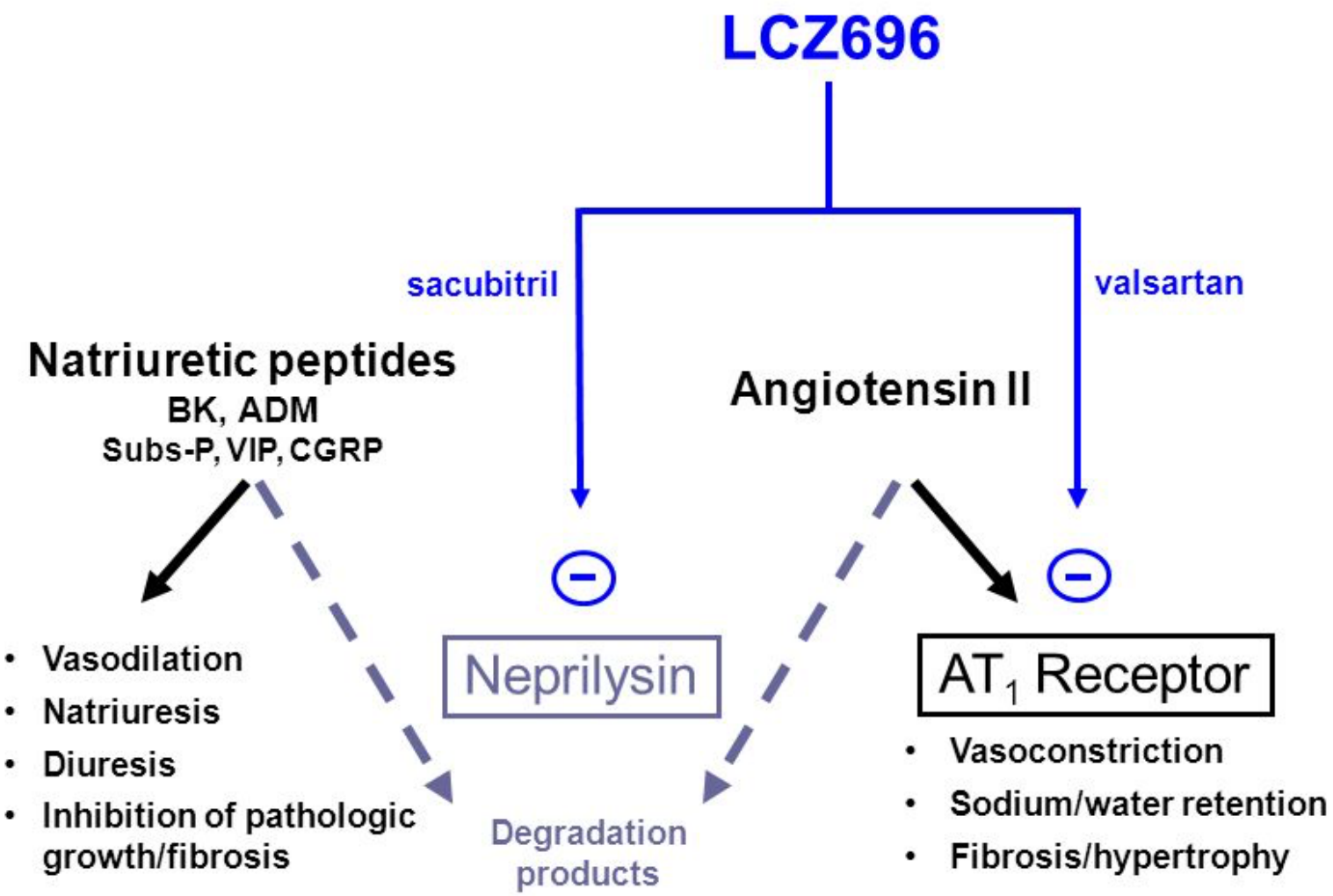
Aim of the PARADIGM-HF Trial

Prospective comparison of ARNI with ACEI to Determine Impact on Global Mortality and morbidity in Heart Failure trial (PARADIGM-HF)

LCZ696 400 mg daily ⟷ **Enalapril 20 mg daily**

SPECIFICALLY DESIGNED TO REPLACE CURRENT USE OF ACE INHIBITORS AND ANGIOTENSIN RECEPTOR BLOCKERS AS THE CORNERSTONE OF THE TREATMENT OF HEART FAILURE

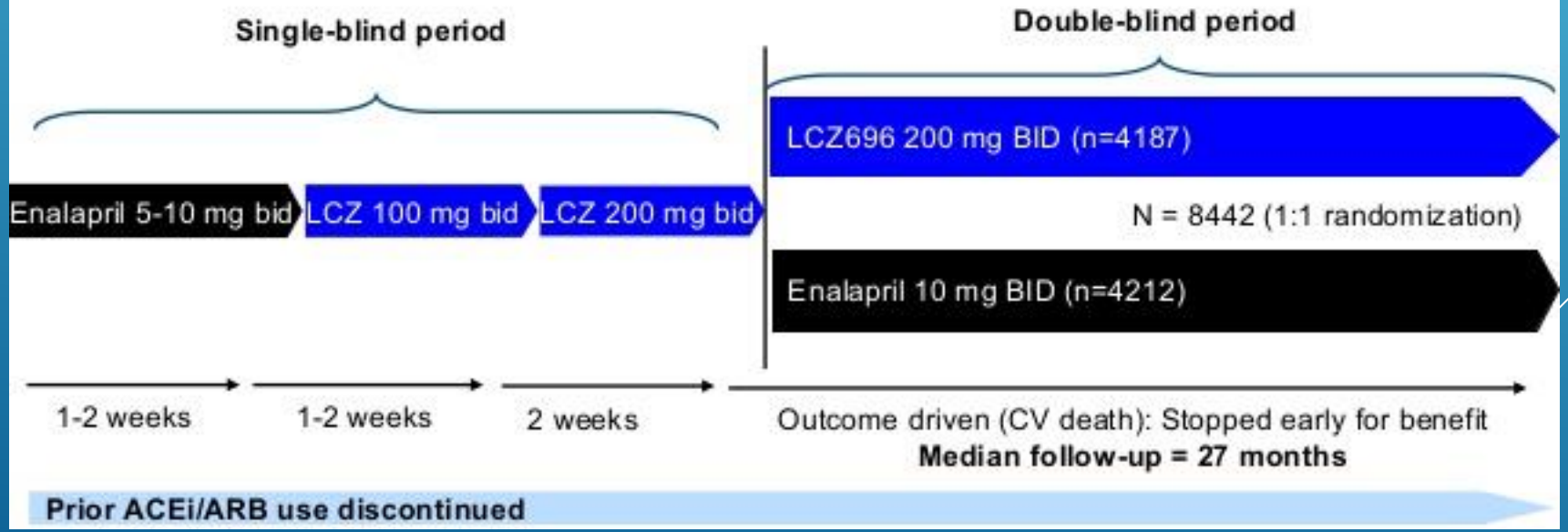
Angiotensin Receptor Neprilysin Inhibition (ARNI): LCZ696



PARADIGM-HF

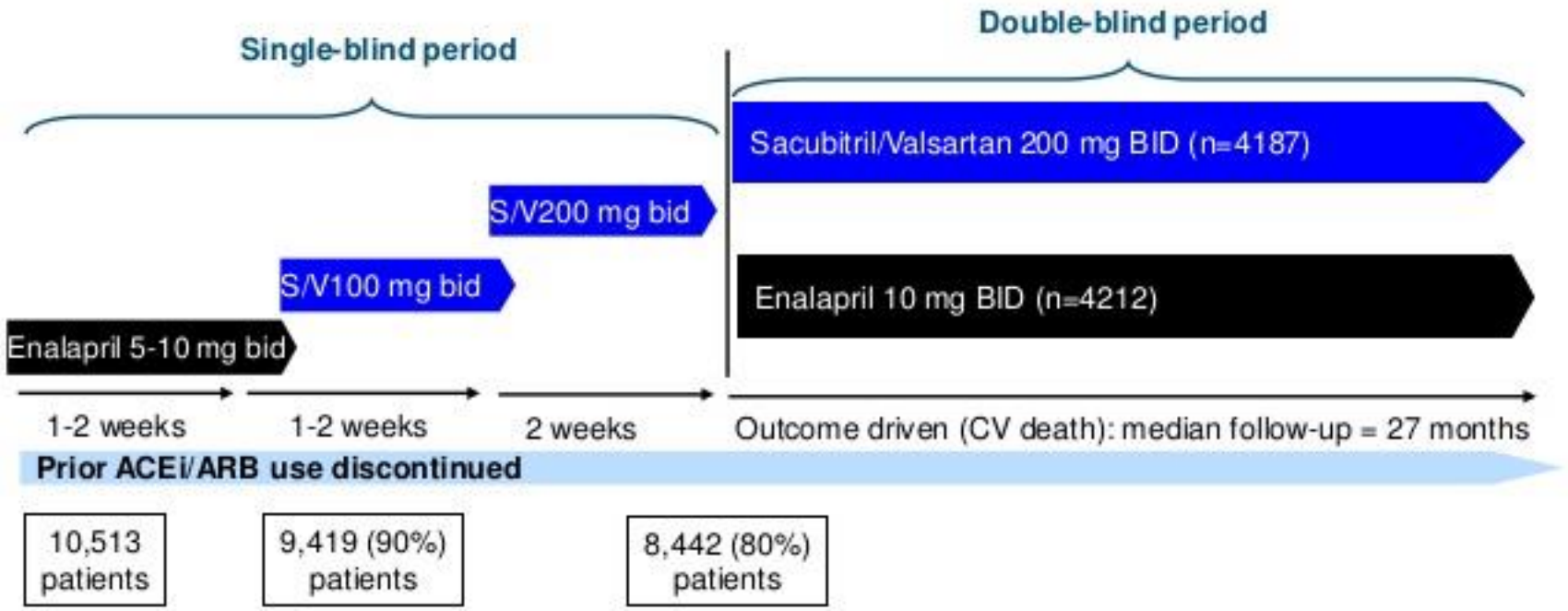
Prospective comparison of ARNI with ACEI to Determine Impact on Global Mortality and morbidity in Heart Failure trial

- Age ≥18 years. NYHA class II-IV. LVEF ≤0.40 (amended to ≤0.35).
- BNP ≥150 pg/ml (NTpro-BNP ≥600 pg/ml) or if HF hosp. within12 mo. BNP ≥100 pg/ml (NTpro-BNP ≥400 pg/ml)
- Background RAS blocker therapy equivalent to enalapril ≥10 mg/d
- Beta-blocker and MRA as recommended by guidelines
- SBP ≥100 mmHg run-in/ ≥95 mmHg at randomization
- eGFR ≥30 ml/min/1.73m^2 /no decrease >25% (amended to 35%)
- Potassium ≤5.2 mmol/l run-in/ ≤5.2 mmol/l at randomization



PARADIGM-HF

Prospective comparison of ARNI with ACEI to Determine Impact on Global Mortality and morbidity in Heart Failure trial



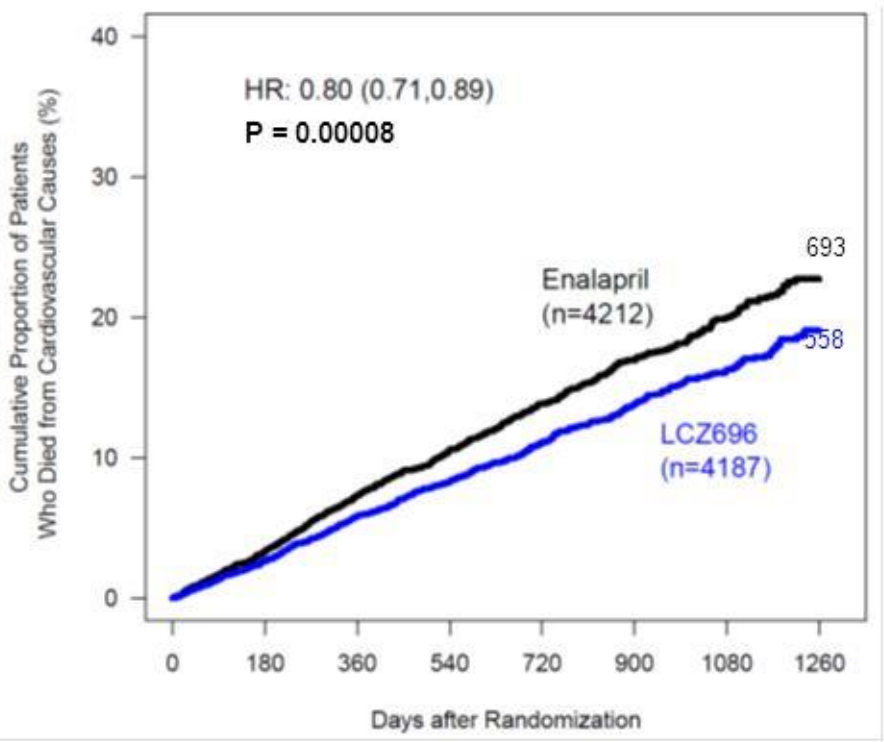
Age: 64 years. Female: 22%. Black: 5.1%.
NYHA class II 70% (class III 24%). Mean LVEF 29%.
NT pro BNP: 1613 pg/ml. eGFR 68 ml/min/1.73m^2. A-Fib 37%.
Diuretic use 80%, β-blocker 93%, MRA 56%. ICD15%. CRT 7%.

PARADIGM-HF

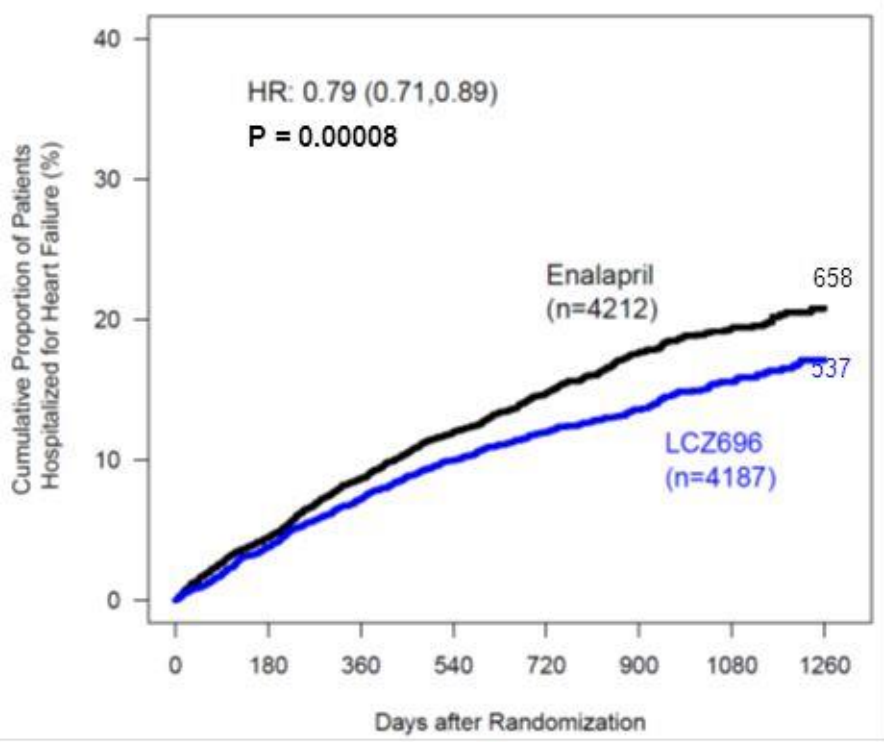
Prospective comparison of ARNI with ACEI to Determine Impact on Global Mortality and morbidity in Heart Failure trial

Primary composite outcome
HR: 0.80 (0.73, 0.87) p = 0.0000004

Death from CV causes
20% risk reduction



HF hospitalization
21% risk reduction

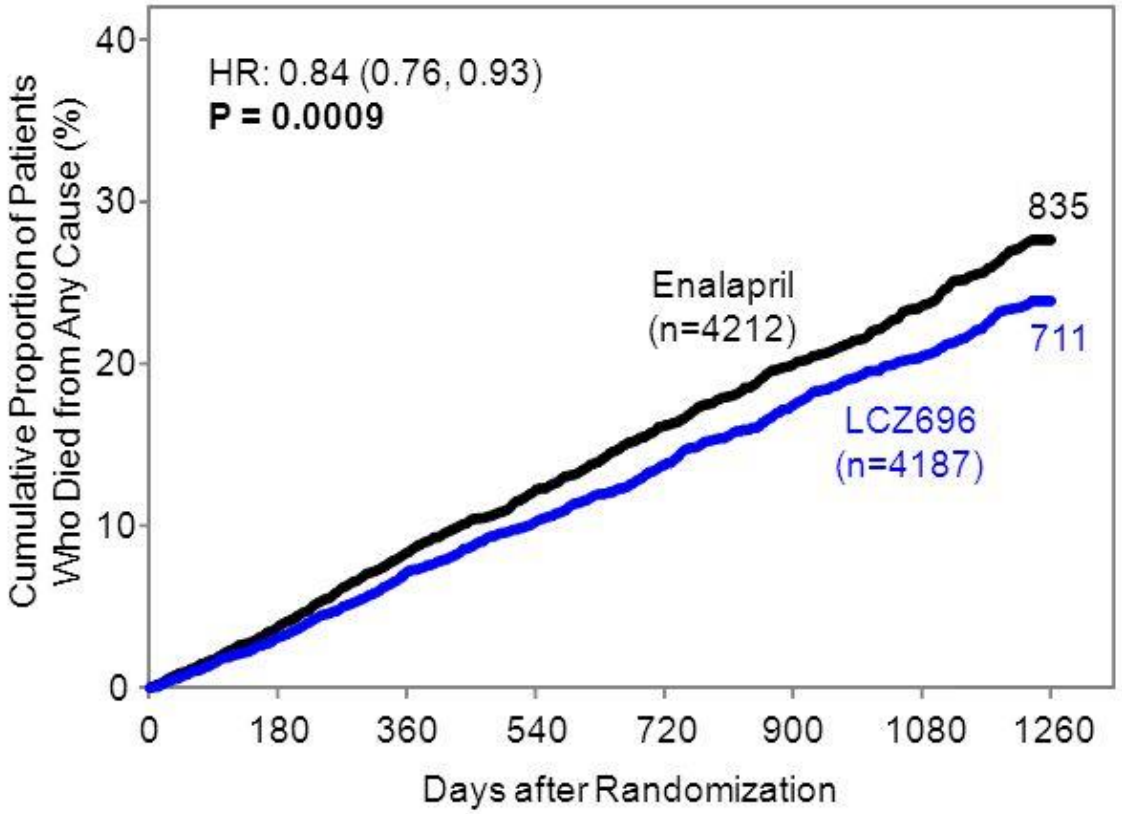


McMurray, Packer et al NEJM 2014

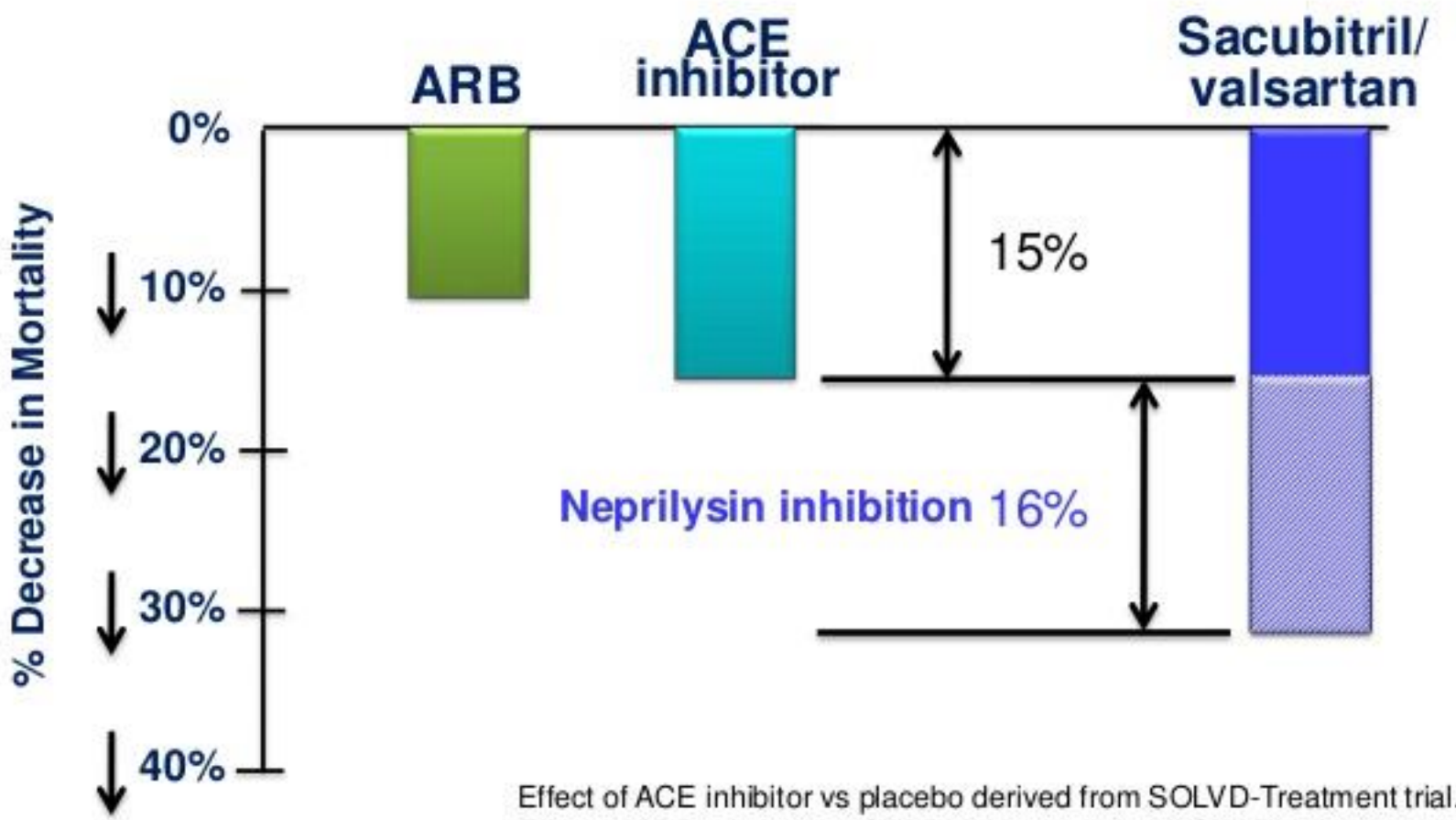
PARADIGM-HF

Prospective comparison of ARNI with ACEI to Determine Impact on Global Mortality and morbidity in Heart Failure trial

Death from any cause
16% risk reduction



Sacubitril/valsartan doubles the survival benefit of current renin-angiotensin inhibitors



Effect of ACE inhibitor vs placebo derived from SOLVD-Treatment trial.
Effect of ARB vs placebo CHARM-Alternative and CHARM-Added,
Effect of LCZ696 vs ACE inhibitor derived from PARADIGM-HF trial.

CV mortality: Baseline ICD use (*post hoc* analysis)

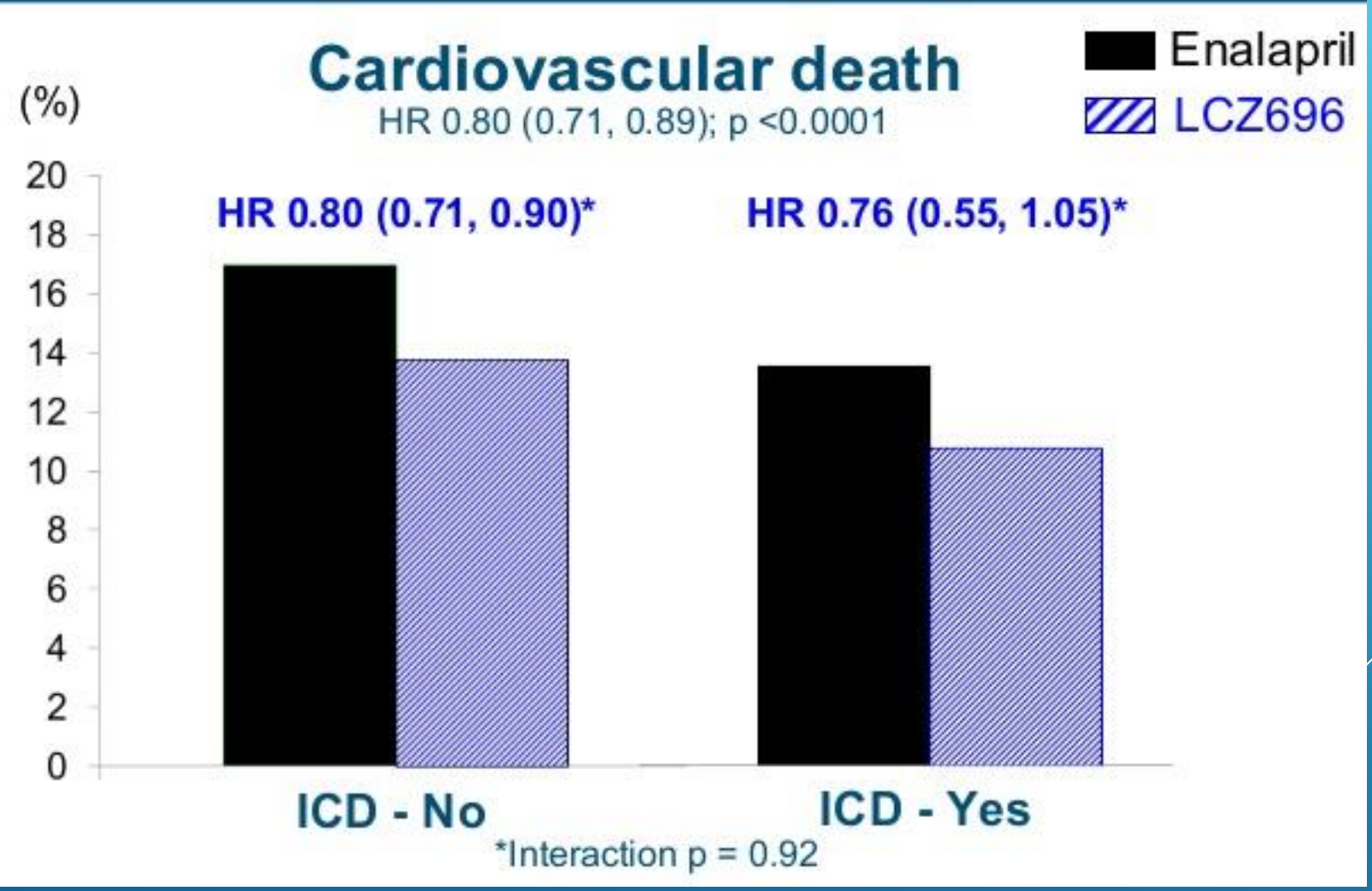


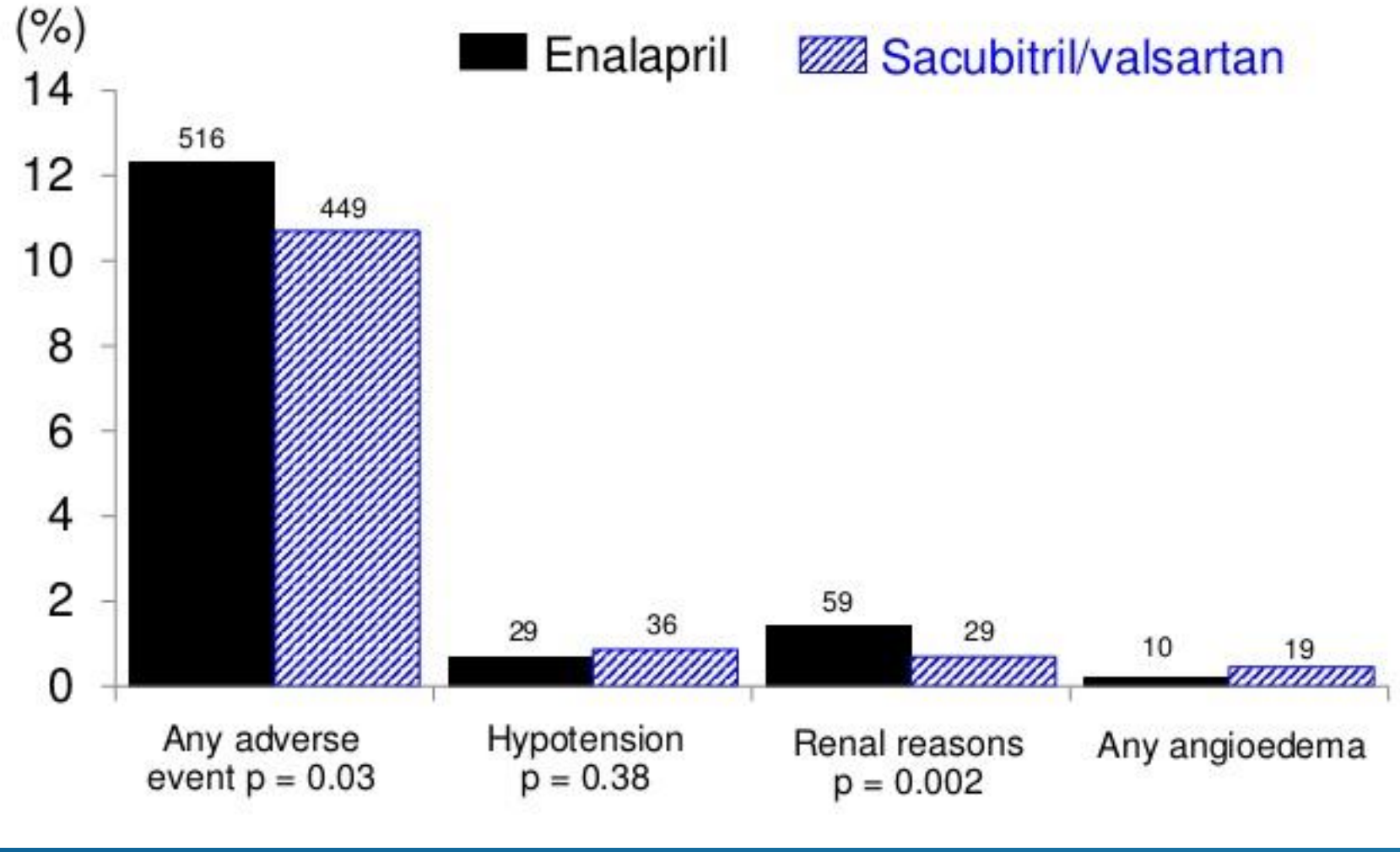
Table 3. Adverse Events during Randomized Treatment.*

Event	LCZ696 (N=4187)	Enalapril (N=4212)	P Value
	no. (%)		
Hypotension			
Symptomatic	588 (14.0)	388 (9.2)	<0.001
Symptomatic with systolic blood pressure <90 mm Hg	112 (2.7)	59 (1.4)	<0.001
Elevated serum creatinine			
≥2.5 mg/dl	139 (3.3)	188 (4.5)	0.007
≥3.0 mg/dl	63 (1.5)	83 (2.0)	0.10
Elevated serum potassium			
>5.5 mmol/liter	674 (16.1)	727 (17.3)	0.15
>6.0 mmol/liter	181 (4.3)	236 (5.6)	0.007
Cough	474 (11.3)	601 (14.3)	<0.001
Angioedema†			
No treatment or use of antihistamines only	10 (0.2)	5 (0.1)	0.19
Use of catecholamines or glucocorticoids without hospitalization	6 (0.1)	4 (0.1)	0.52
Hospitalization without airway compromise	3 (0.1)	1 (<0.1)	0.31
Airway compromise	0	0	—

* Shown are results of the analyses of prespecified safety events at any time after randomization. The numbers of patients who permanently discontinued a study drug were as follows: for hypotension, 36 (0.9%) in the LCZ696 group and 29 (0.7%) in the enalapril group (P=0.38); for renal impairment, 29 (0.7%) and 59 (1.4%), respectively (P=0.002); and for hyperkalemia, 11 (0.3%) and 15 (0.4%), respectively (P=0.56).

† Angioedema was adjudicated in a blinded fashion by an expert committee.

PARADIGM-HF: Adverse events leading to permanent study drug discontinuation



Recommendations for Renin-Angiotensin System Inhibition With ACE Inhibitor or ARB or ARNI		
COR	**LOE**	**Recommendations**
I	ACE: A	The clinical strategy of inhibition of the renin-angiotensin system with ACE inhibitors *(Level of Evidence: A)*, **OR** ARBs *(Level of Evidence: A)*, **OR** ARNI *(Level of Evidence: B-R)* in conjunction with evidence-based beta blockers, and aldosterone antagonists in selected patients, is recommended for patients with chronic HF*r*EF to reduce morbidity and mortality.
	ARB: A	
	ARNI: B-R	

Recommendations for Renin-Angiotensin System Inhibition With ACE Inhibitor or ARB or ARNI

COR	LOE	Recommendations
I	ARNI:B-R	In patients with chronic symptomatic HF*r*EF NYHA class II or III who tolerate an ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality.

Highlighting Key Recommendations

Recommendation	COR	LOE
The clinical strategy of inhibition of the renin-angiotensin system with ACE inhibitors or ARBs or ARNI, in conjunction with evidence-based β-blockers and aldosterone antagonists in selected patients, is recommended for patients with chronic HF*r*EF to reduce morbidity and mortality.	I	ACE: A; ARB: A; ARNI: B-R
The use of ACE inhibitors is beneficial for patients with prior or current symptoms of chronic HF*r*EF to reduce morbidity and mortality.	I	ACE: A
The use of ARBs to reduce morbidity and mortality is recommended in patients with prior or current symptoms of chronic HF*r*EF who are intolerant to ACE inhibitors because of cough or angioedema.	I	ARB: A
In patients with chronic symptomatic HF*r*EF NYHA class II or III who tolerate an ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality.	I	ARNI: B-R
ARNI should not be administered concomitantly with ACE inhibitors or within 36 hours of the last dose of an ACE inhibitor.	III: Harm	B-R
ARNI should not be administered to patients with a history of angioedema.	III: Harm	C-EO
Ivabradine can be beneficial to reduce heart failure hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HF*r*EF (LVEF ≤35%) who are receiving GDEM, including a β-blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 bpm or greater at rest.	IIa	B-R

Abbreviations: ARB, angiotensin receptor blockers; ARNI, angiotensin receptor-neprilysin inhibitor; COR, class of recommendation; GEDM, guideline-directed evaluation and management; HF*r*EF, heart failure with reduced ejection fraction; LOE, level of evidence; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

Source: Adapted from: Yancy C, et al. *Circulation*. 2016 May 20 [Epub ahead of print].

How do you switch from ace-I to arni?

- 36 hour wash out period

- if on equivalent of < 10 mg PO BID enalapril, start low dose ARNI (24/26 mg PO BID), then up-titrate every 2-4 weeks

- If on equivalet of > 10 mg PO BID enalapril, start mid dose arni (49/51 mg PO bid), then up-titrate every 2-4 weeks

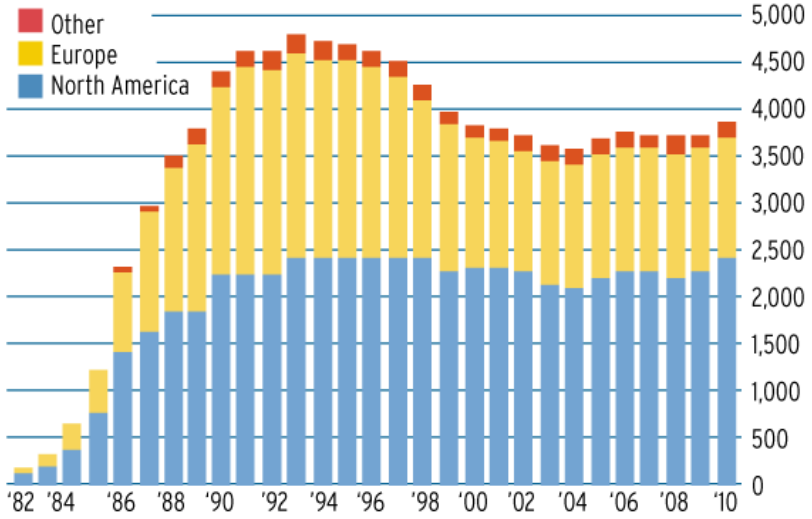
How do you switch from an aRB to arni?

- no wash out period

- if on equivalent of < 160 mg PO losartan, start low dose ARNI (24/26 mg PO BID), then up-titrate every 2-4 weeks

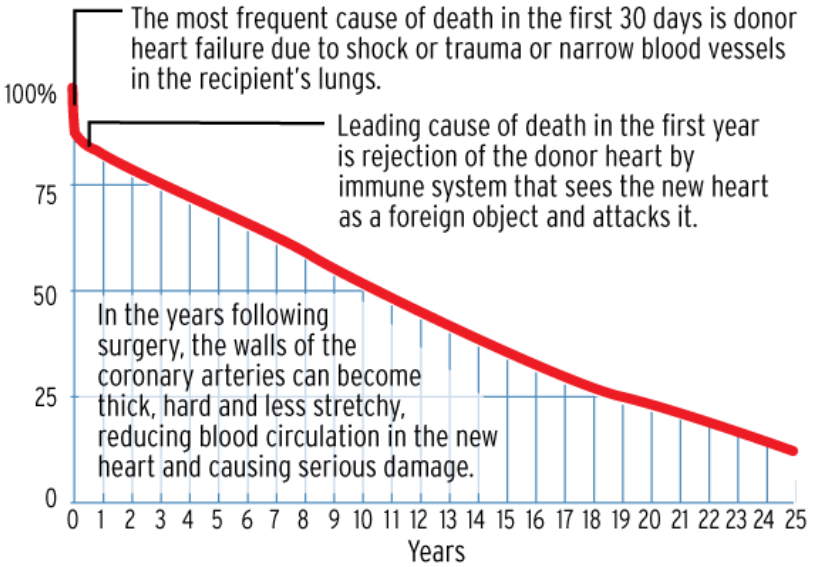
- If on equivalet of > 160 mg PO losartan, start mid dose arni (49/51 mg PO bid), then up-titrate every 2-4 weeks

Heart transplants worldwide



Note: Figures include only transplants reported to the ISHLT Transplant Registry

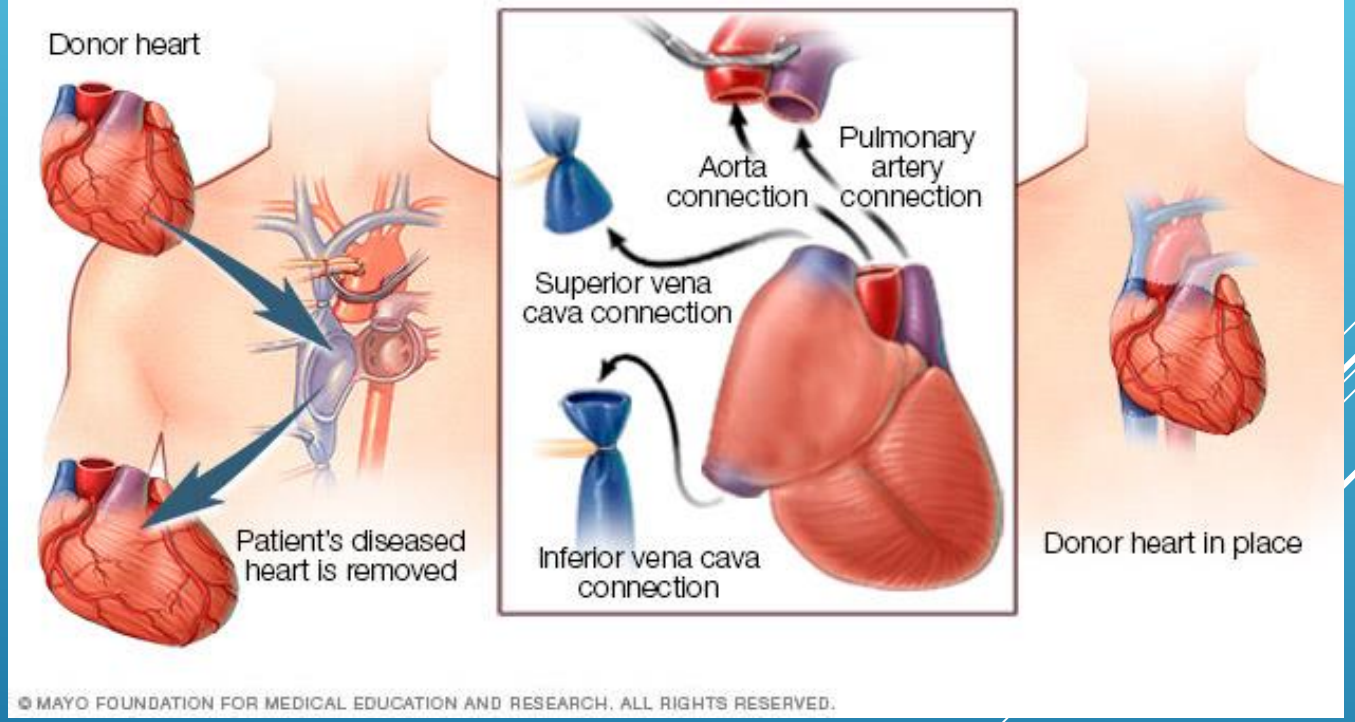
Years of survival after a heart transplant



Source: International Society for Heart & Lung Transplantation; National Heart Lung and Blood Institute

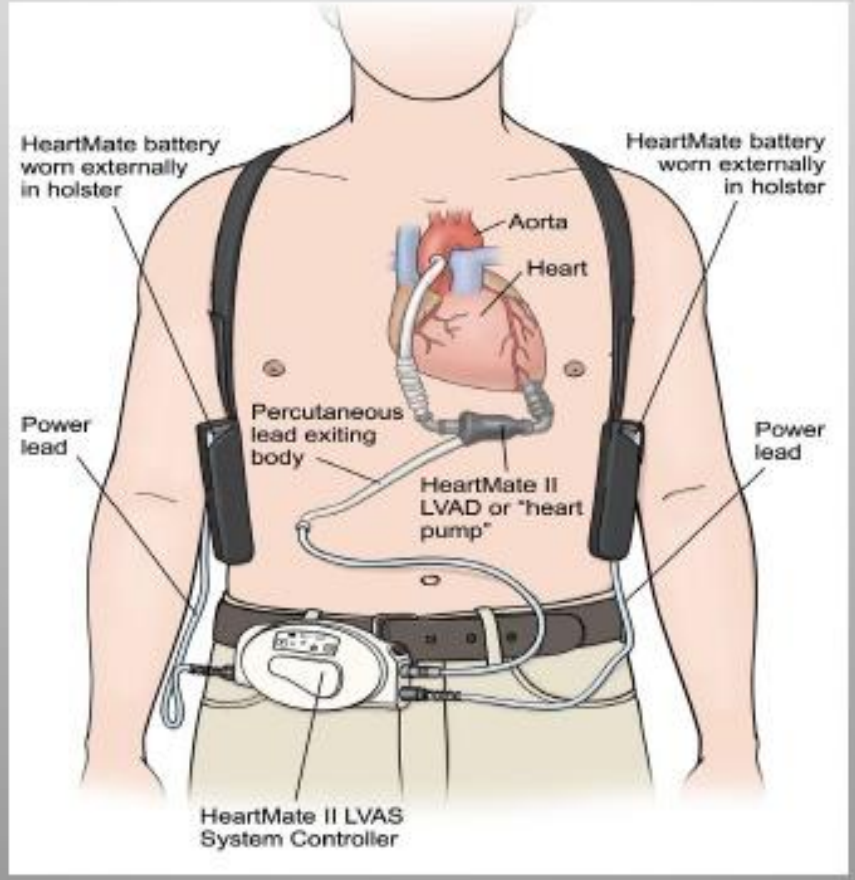
The Register

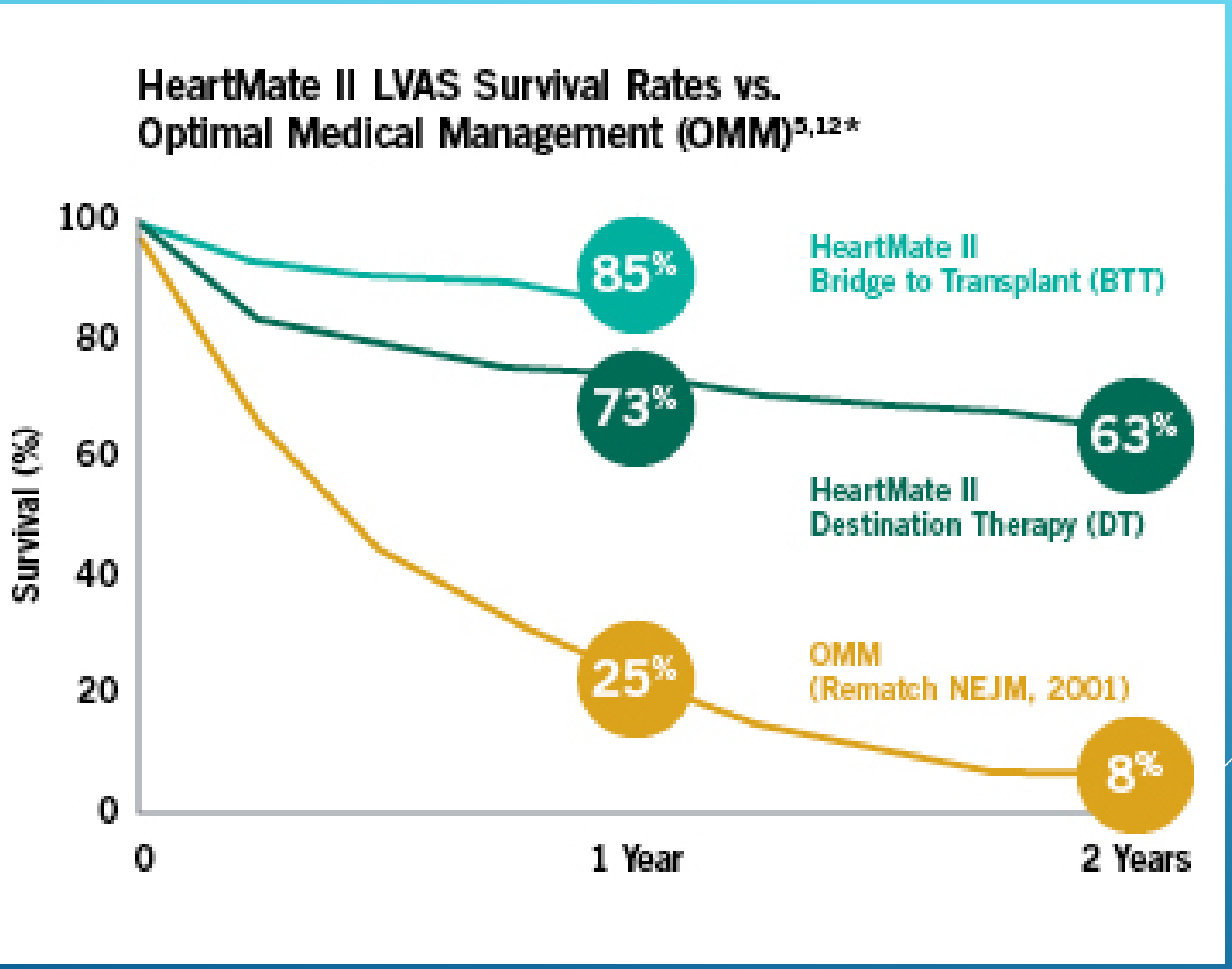
Heart transplant procedure



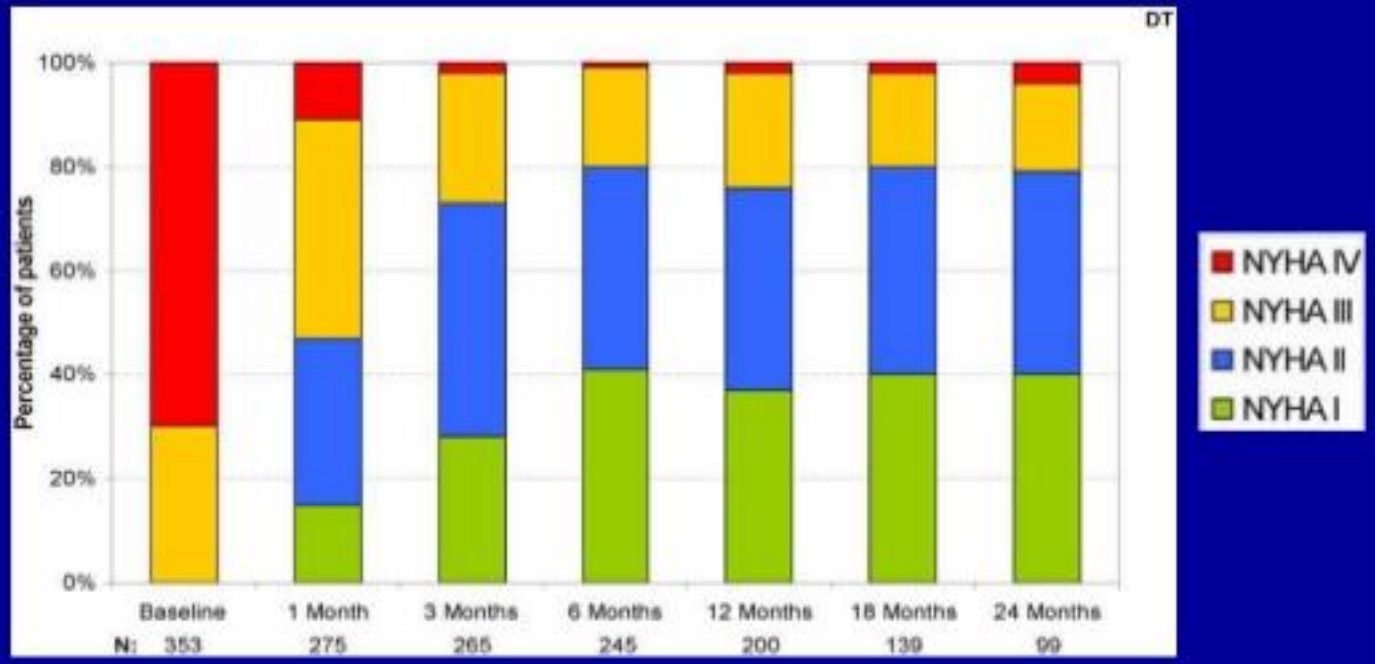
Heart Mate II

The VAD is a surgically implanted artificial heart pump used to treat patients with advanced congestive heart failure.




HeartMate II LVAS Survival Rates vs.
Optimal Medical Management (OMM)[5,12]*
Survival (%)
100
80
60
40
20
0
0
1 Year
2 Years
85%
73%
63%
25%
8%
HeartMate II
Bridge to Transplant (BTT)
HeartMate II
Destination Therapy (DT)
OMM
(Rematch NEJM, 2001)

Improvement in NYHA functional class Heartmate II DT LVAD trial



Joseph G. Rogers , Keith D. Aaronson , Andrew J. Boyle , Stuart D. Russell , Carmelo A. Milano , Francis D. Pagani...

Continuous Flow Left Ventricular Assist Device Improves Functional Capacity and Quality of Life of Advanced Heart Failure Patients

Journal of the American College of Cardiology Volume 55, Issue 17 2010 1826 - 1834

MOMENTUM 3

The MOMENTUM 3 U.S. IDE Clinical Trial is a prospective, multi-center, unblinded randomized study comparing the HeartMate 3 Left Ventricular Assist System (LVAS) to the HeartMate II LVAS in advanced stage heart failure patients.

Learn more

Expanding HF Choices & Decisions

1989

- Digoxin
- Diuretics
- Vasodilators

2017

- ACE inhibitors/ARBs
- Beta-blockers
- Aldosterone antagonists
- ARB/Neprilysin Inhibitor
- Hydralazine/Nitrates
- Ivabradine
- ICD and CRT
- Mechanical circulatory support
- CardioMEMS
- Disease management
- Palliative care

Applying Evidence to Health Care Delivery

It takes an average of 17 years for new knowledge generated by randomized controlled trails to be incorporated into practice, and even then application is highly uneven

Conclusions

- The prevalence of heart failure is increasing though HFpEF is becoming more common
- Exciting time to be caring for patients with HFrEF with multiple new therapeutic options
- New challenges to implementation of evidence-based chronic medical therapies