Management of Heart Failure: State of the Art Update 2018

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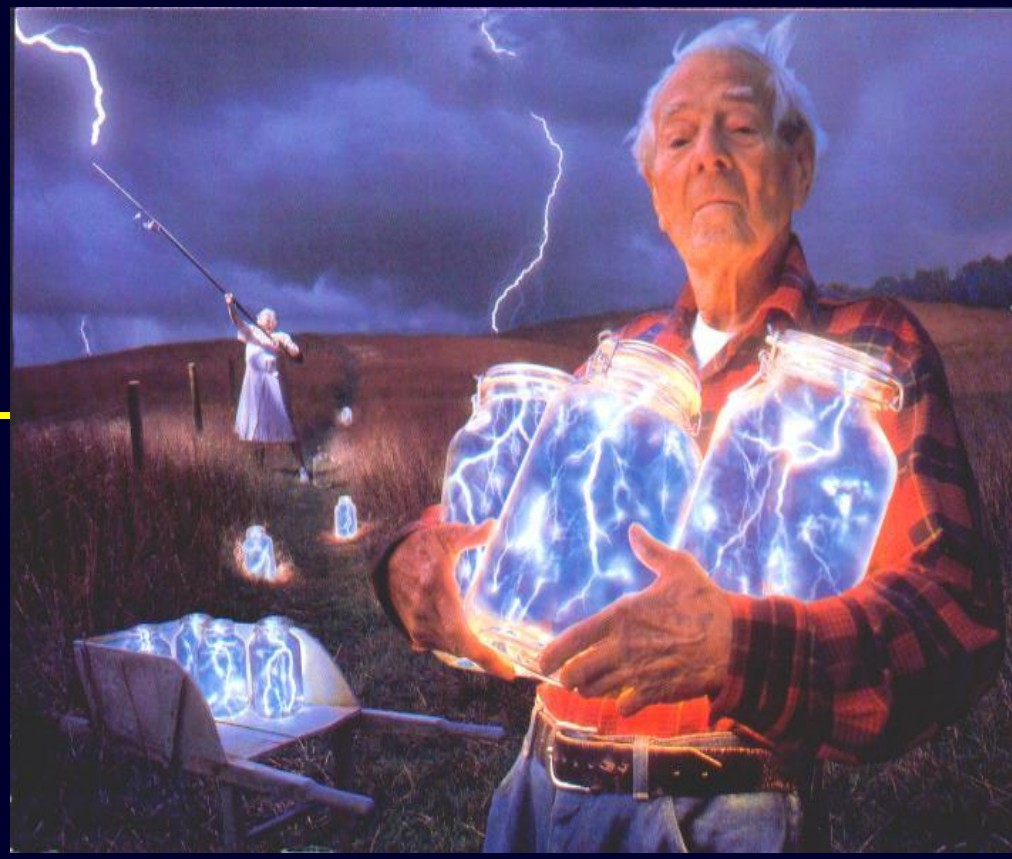


Disclosures

- Consulting – Abbott, Critical Diagnostics
- Speaking – Critical Diagnostics

Epidemiology and Pathophysiology of HF

Scope of heart failure

Population Group	Prevalence	Incidence	Mortality	Hospital Discharges	Cost[1]
Total Population	5,700,000	870,000	50% at 5 years	1,023,000	$30.7 billion

- Heart failure (HF) is a major public health problem resulting in substantial morbidity and mortality
- 23 million people with HF worldwide
- 6–12 million office visits
- Despite available effective treatments, a large number of eligible patients are not receiving optimal care

Mozaffarian D, et al. *Circulation*. 2015;131:e29-e322.
Jessup M. *Circulation*. 2014;129:2717-2722.

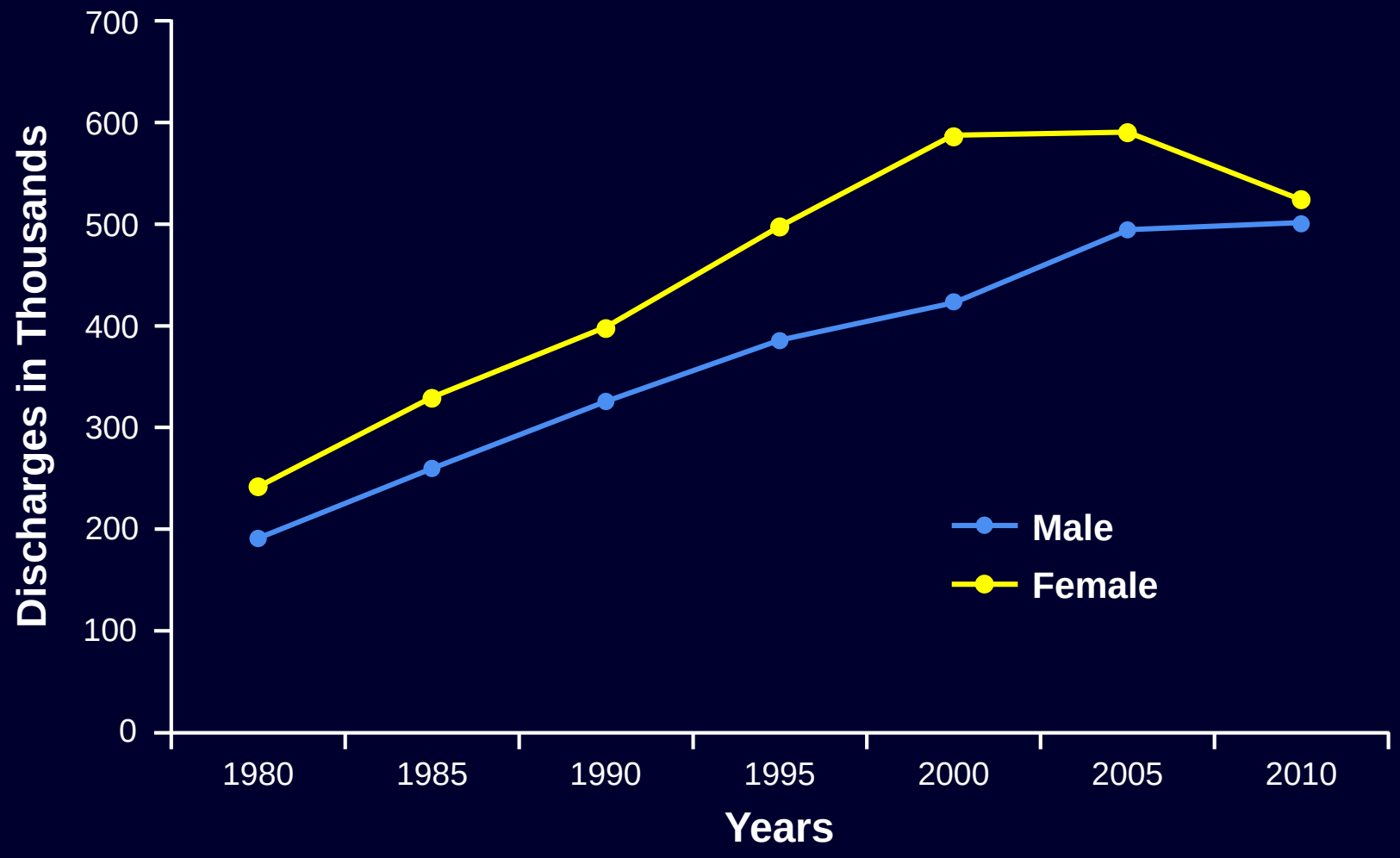
Risk factors for heart failure

- CAD
- Hypertension (LVH)
- Valvular heart disease
- Alcoholism
- Infection (viral)
- Diabetes
- Congenital heart defects
- Other:
  - Obesity
  - Age
  - Smoking
  - High or low hematocrit level
  - Obstructive sleep apnea

CAD = coronary artery disease; LVH = left ventricular hypertrophy.

Yancy CW, et al. *J Am Coll Cardiol*. 2013;62(16):e147-239.

Hospital discharges for HF



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

The short of breath pie

Musculoskeletal Pain

Pneumomediastinum

Mediastinitis

IVDA Pulm Infarction

Anxiety

Pulmonary Embolus

Panic Attack

Cyanide poisoning

Pneumothorax

Empyema

Pneumonia

MetHgb

Tietze's disease

Mondor's Syndrome

DKA

Metabolic acidosis

Asthma

COPD exacerbation

FB Aspiration

Breast Cancer

Chemical Exposure

Subdiaphrag Abcess

Anemia

Lung Cancer

Amniotic Fluid Embolus

Heart Failure

Anaphylaxis

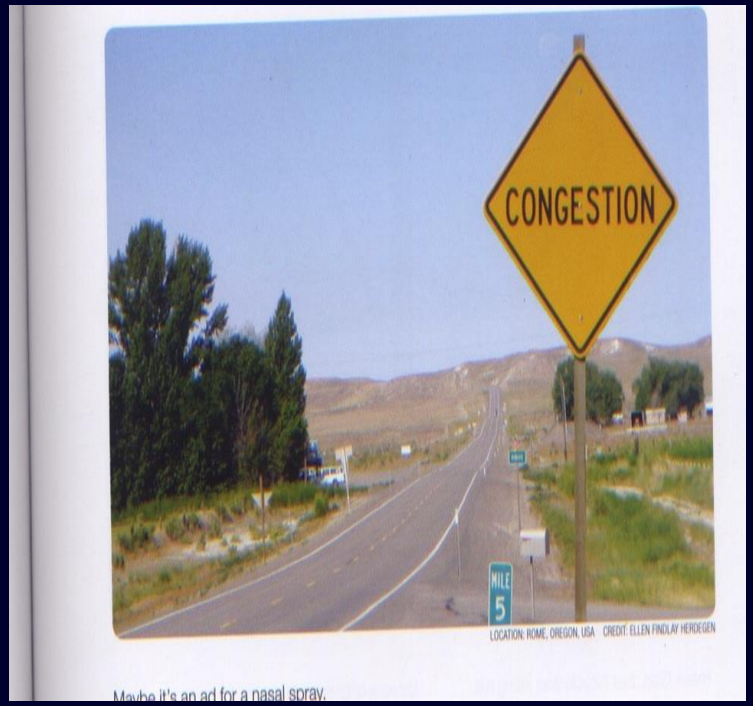
Diagnosis of HF

Differential Diagnosis

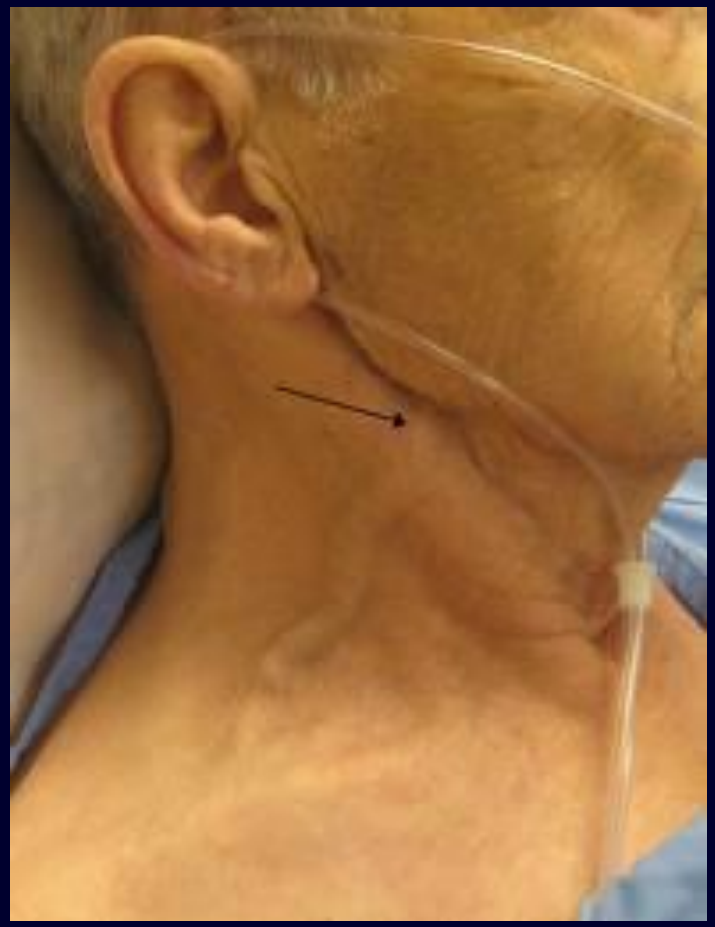
- Pulmonary infection
- Acute COPD / asthma exacerbation
- Acute coronary syndrome
- Pulmonary emboli
- Pneumothorax, pleural effusions
- Aortic dissection
- Renal failure

Congestion often does not translate in signs/symptoms

- Among pts. with severe heart failure [1] and PCWP 33 mmHg, CI 1.8 , LVEF 0.18 CXR: 27%
  - No congestion on x-ray: 41%
  - No rales: 84%,
  - No edema: 80%
  - No JVP: 50%

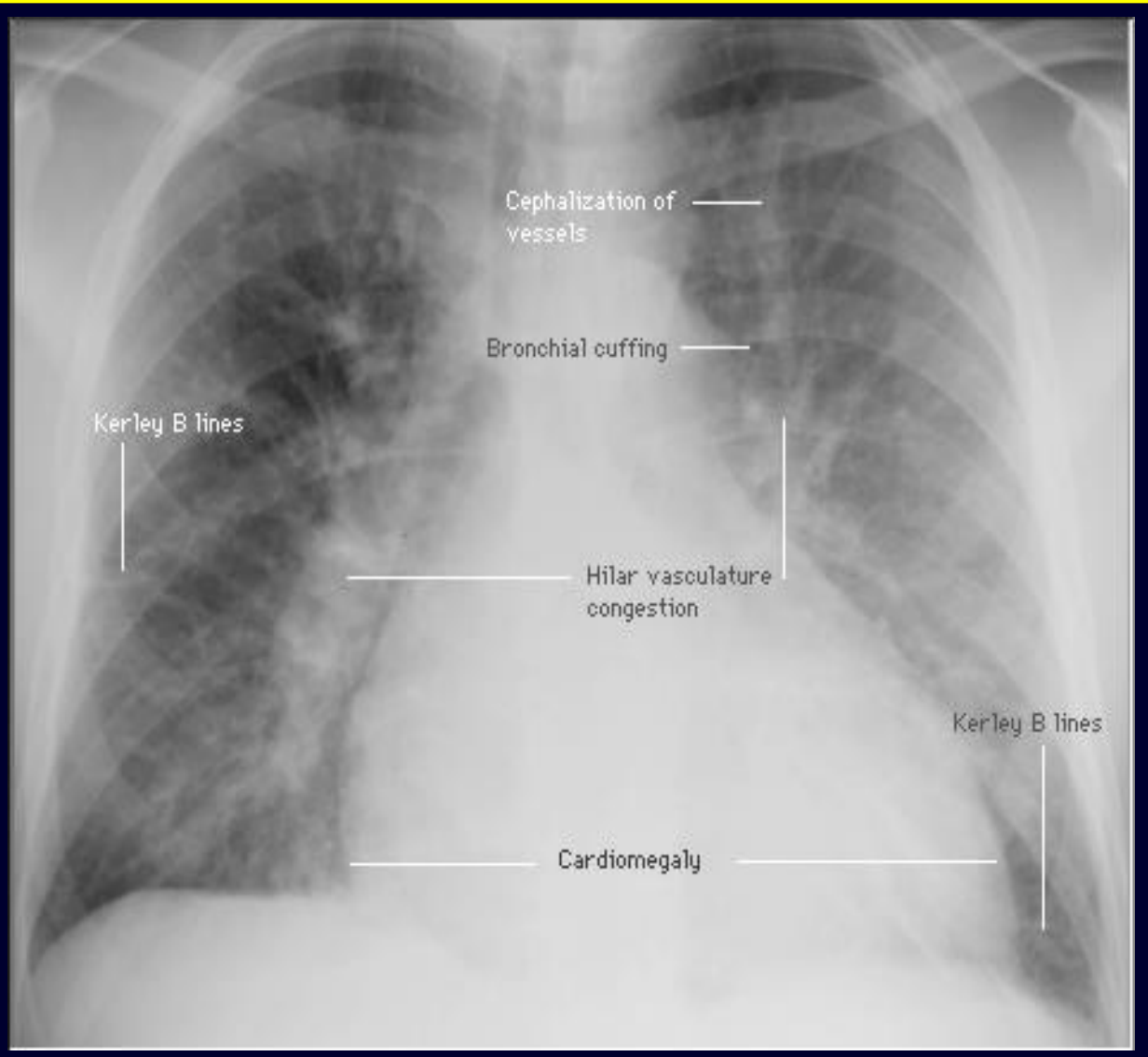


JVP- misconceptions

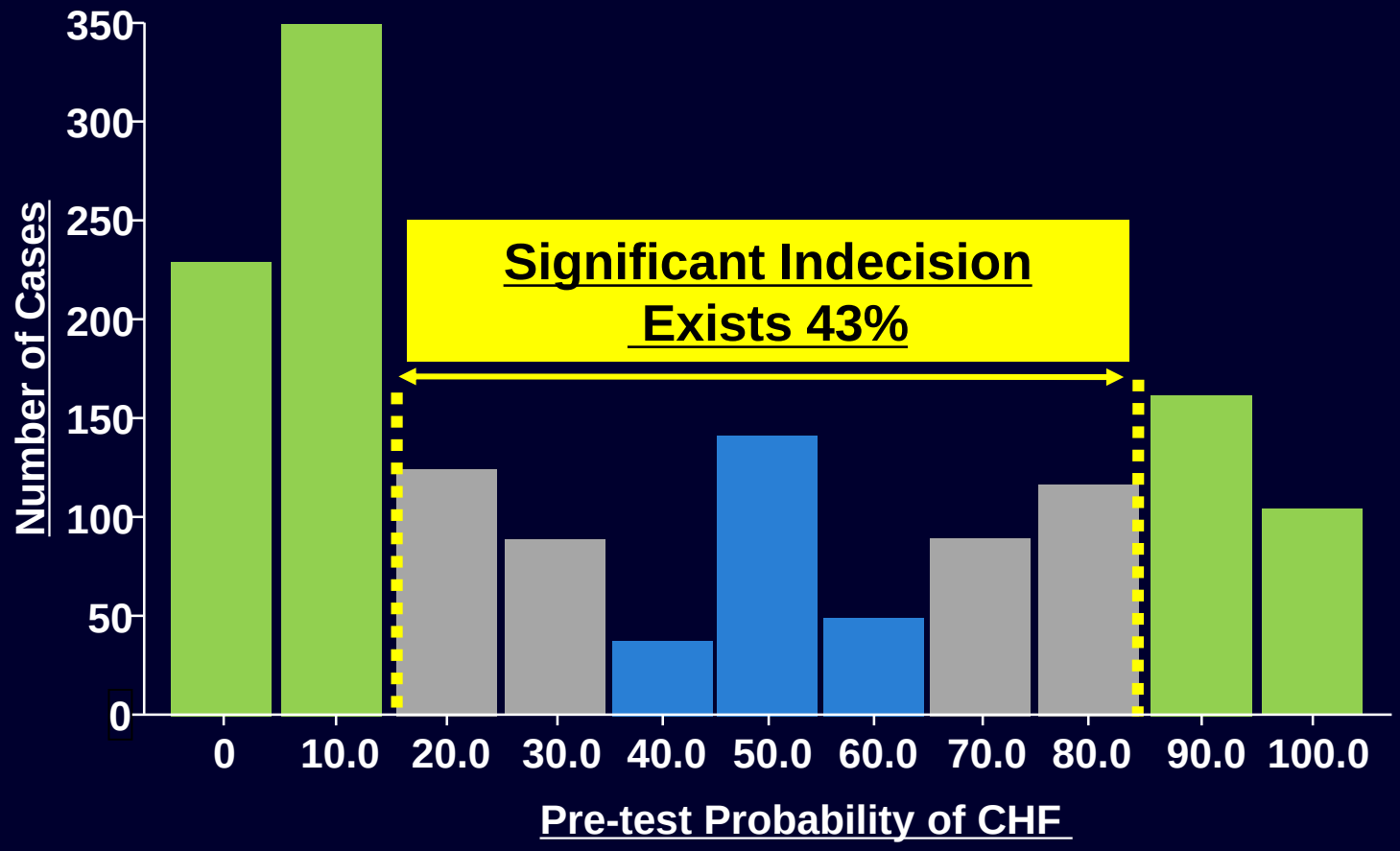


- When its very high it is often mistaken for carotid
- Docs tend to think if jvp is not elevated, it cant be heart failure
- Elevations only mean right sided- and might not explain sob

Chest X-Ray in HF



How sure are physicians in the ED about the diagnosis of HF?



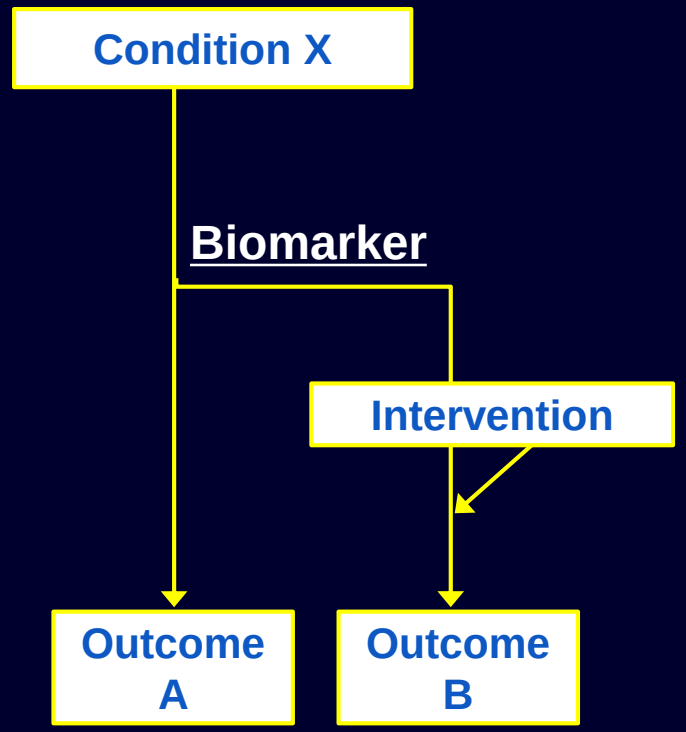
Adapted with permission from McCullough PA et al. *Circulation.* 2002;106:416−422.

Objectives of biomarker testing in HF

Diagnosis[1]
- To establish or refute a diagnosis
- To understand the underlying pathophysiologic processes

Risk Stratification/Screening[1]
- To determine the presence or severity of disease
- To detect adverse consequences

Monitoring/Therapeutic Guidance[1]
- To facilitate selection of an appropriate therapeutic intervention
- To guide or monitor responses to treatment



Many biomarkers may be risk factors themselves; therefore, may be potential targets of therapy[2]

HF, heart failure.

1. Morrow DA, et al. *Circulation.* 2007;115:949-952.
2. Kalogeropoulos AP, et al. *Prog Cardiovasc Dis.* 2012;55(1):3-13.

Breathing Not Properly STUDY

The New England
Journal of Medicine

VOLUME 347 JULY 18, 2002 NUMBER 3

RAPID MEASUREMENT OF B-TYPE NATRIURETIC PEPTIDE IN THE EMERGENCY DIAGNOSIS OF HEART FAILURE

ALAN S. MAISEL, M.D., PADMA KRISHNASWAMY, M.D., RICHARD M. NOWAK, M.D., M.B.A., JAMES MCCORD, M.D
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WILLIAM T. ABRAHAM, M.D., ALAN H.B. WU, PH.D., PAUL CLOPTON, M.S., PHILIPPE G. STEG, M.D.,
ARNE WESTHEIM, M.D., PH.D., M.P.H., CATHERINE WOLD KNUDSEN, M.D., ALBERTO PEREZ, M.D.,
RADMILA KAZANEGRA, M.D., HOWARD C. HERRMANN, M.D., AND PETER A. MCCULLOUGH, M.D., M.P.H.,
FOR THE BREATHING NOT PROPERLY MULTINATIONAL STUDY INVESTIGATORS*

Clinical Investigation and Reports

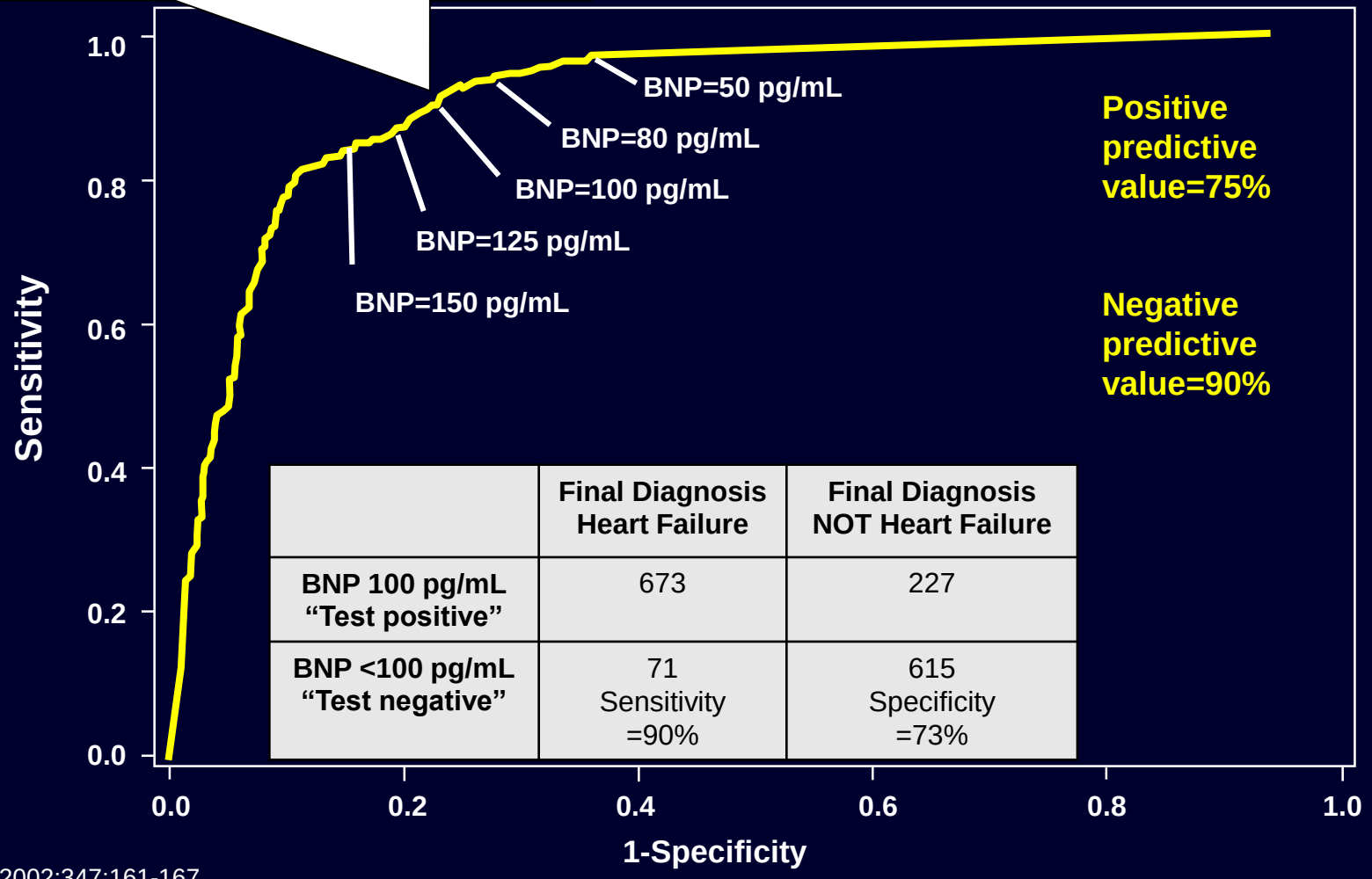
B-Type Natriuretic Peptide and Clinical Judgment in Emergency Diagnosis of Heart Failure

Analysis From Breathing Not Properly (BNP) Multinational Study

Peter A. McCullough, MD, MPH; Richard M. Nowak, MD, MBA; James McCord, MD;
Judd E. Hollander, MD; Howard C. Herrmann, MD; Philippe G. Steg, MD; Philippe Duc, MD;
Arne Westheim, MD, PhD; Torbjørn Omland, MD, PhD, MPH; Cathrine Wold Knudsen, MD;
Alan B. Storrow, MD; William T. Abraham, MD; Sumant Lamba, MD; Alan H.B. Wu, PhD;
Alberto Perez, MD; Paul Clopton, MS; Padma Krishnaswamy, MD; Radmila Kazanegra, MD;
Alan S. Maisel, MD; for the BNP Multinational Study Investigators

Accuracy is 90%

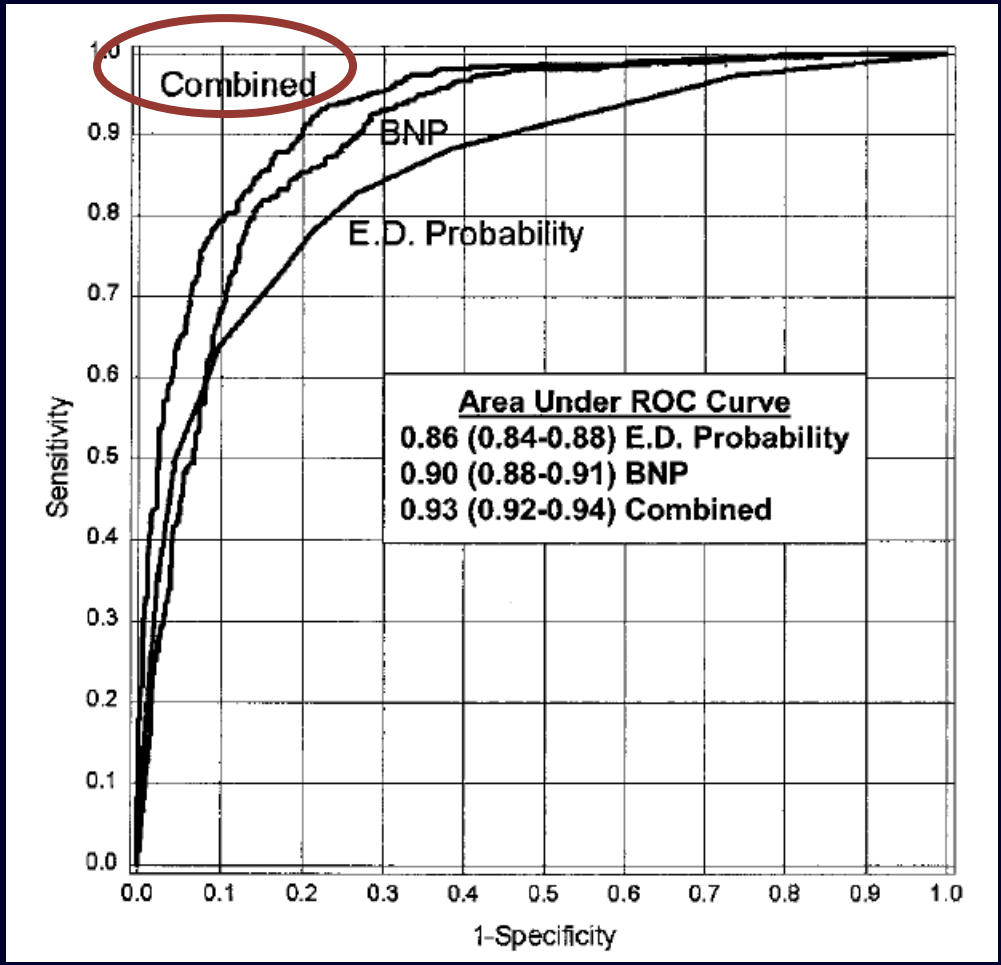
Optimal cut-off point determined @ 100 pg/mL



	Final Diagnosis Heart Failure	Final Diagnosis NOT Heart Failure
BNP 100 pg/mL "Test positive"	673	227
BNP <100 pg/mL "Test negative"	71 Sensitivity =90%	615 Specificity =73%

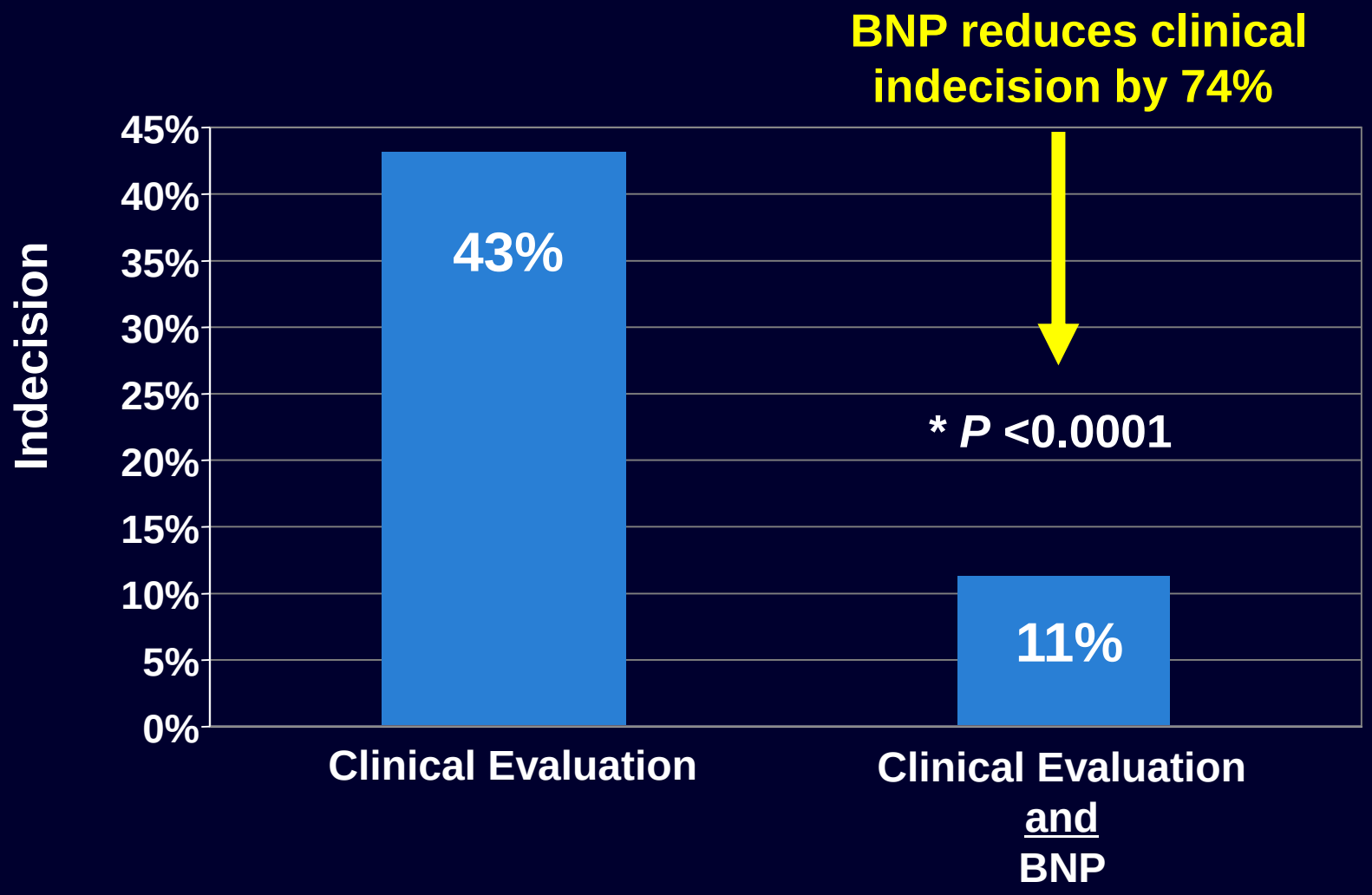
Maisel AS et al. *N Engl J Med.* 2002;347:161-167

BNP levels adds to the physician's ability



McCulough, M et al. *Circulation*. 2002;346:416-422.

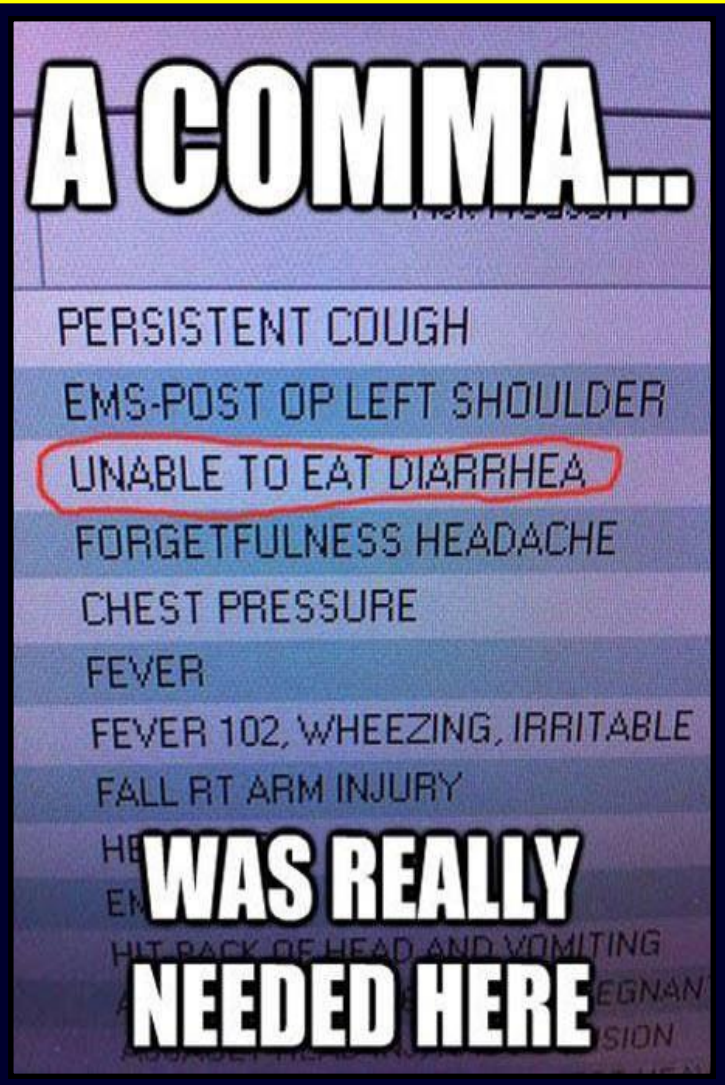
Clarification of diagnosis & BNP



NtproBNP cut-offs

1. 125 < 75 y.o. and 450 > 75 y.o.
2. 450, 900, 1800 based on age
3. 300 to rule out

Caveats to NP testing



- Dry versus wet BNP
- Gray Zone
- Renal dysfunction
- Obesity
- Heart Failure with normal levels

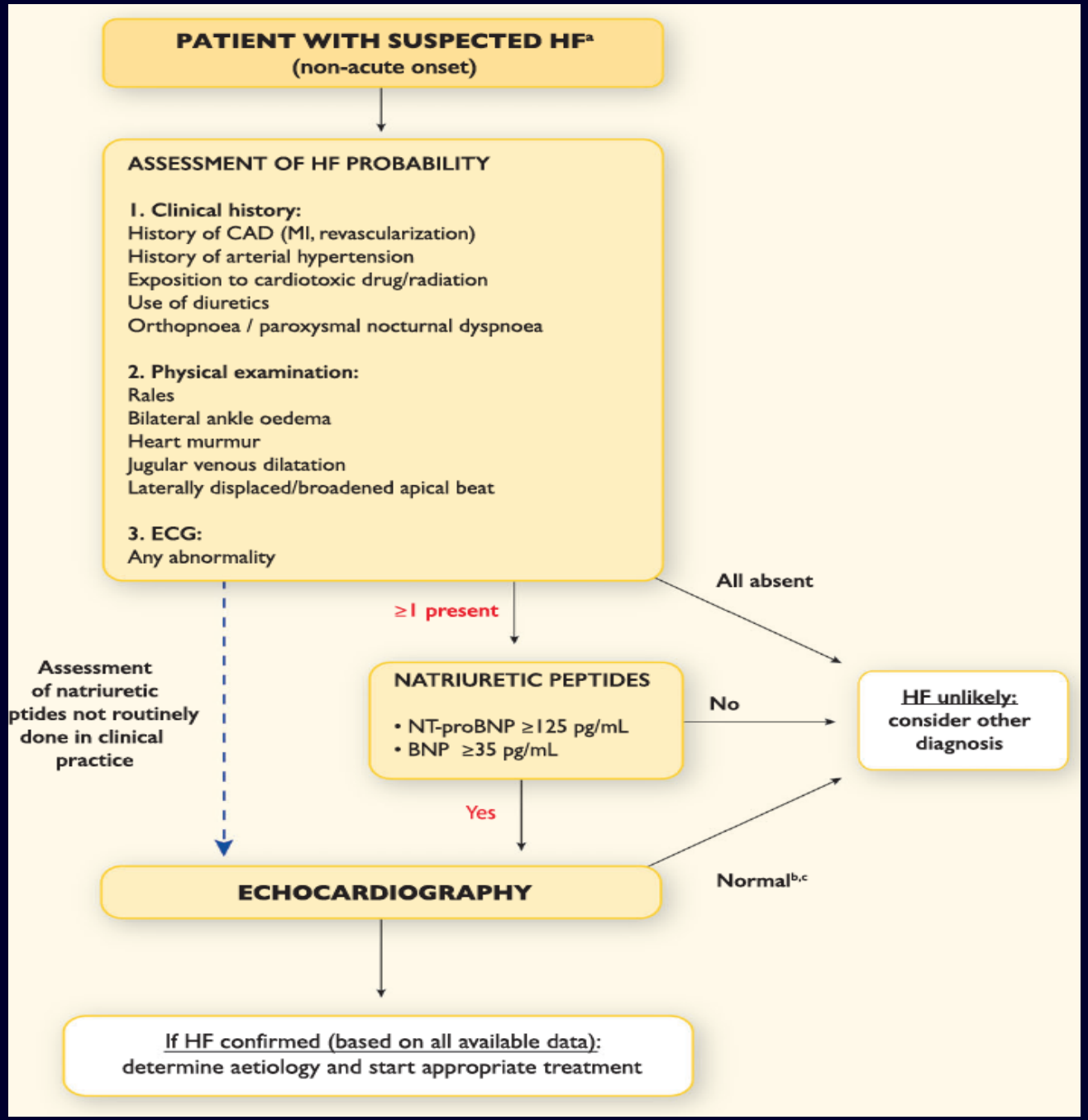
Obesity

- There appears to be a linear inverse relationship between BMI and NP levels
- Patients who are obese (BMI >35kg/m^2) should have their NP doubled to use the standard cut-points.

Maisel, Valle, Aspromente et al EJHF 2009

The use of NPs for rule-out heart failure in symptomatic patients in primary care

Identifying the right patients for echocardiography


PATIENT WITH SUSPECTED HF[a]
(non-acute onset)
ASSESSMENT OF HF PROBABILITY
1. Clinical history:
History of CAD (MI, revascularization)
History of arterial hypertension
Exposition to cardiotoxic drug/radiation
Use of diuretics
Orthopnoea / paroxysmal nocturnal dyspnoea
2. Physical examination:
Rales
Bilateral ankle oedema
Heart murmur
Jugular venous dilatation
Laterally displaced/broadened apical beat
3. ECG:
Any abnormality
All absent
≥1 present
Assessment of natriuretic ptides not routinely done in clinical practice
NATRIURETIC PEPTIDES
• NT-proBNP ≥125 pg/mL
• BNP ≥35 pg/mL
No
HF unlikely: consider other diagnosis
Yes
Normal[b,c]
ECHOCARDIOGRAPHY
If HF confirmed (based on all available data):
determine aetiology and start appropriate treatment

NATRIURETIC PEPTIDES

- NT-proBNP ≥125 pg/mL
- BNP ≥35 pg/mL

Non-HF causes of high NP's:

- Advanced age
- Renal dysfunction
- Acute coronary syndromes
- Pulmonary disease
  - E.g. ARDS, lung disease with right heart failure
- Pulmonary embolism
- High output states
  - E.g. sepsis, cirrhosis, hyperthyroidism
- Atrial fibrillation
- LV dysfunction

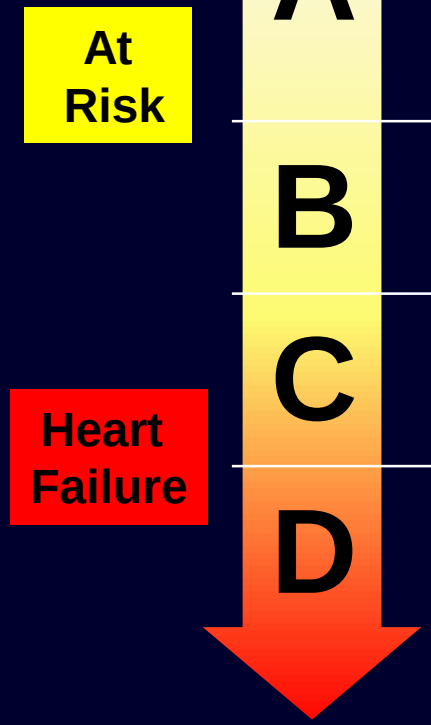
Guideline Recommended Medical Therapy for HF

Types of Heart Failure

Classification	Ejection Fraction	Description
I. Heart Failure with Reduced Ejection Fraction (HFrEF)	≤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)	≥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 patients 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.

Yancy CW, et al. *J Am Coll Cardiol*. 2013;62:1495-1539.

Approach to the Classification of Heart Failure



Stage	Patient Description
High risk for developing heart failure (HF)	▯ Hypertension ▯ CAD ▯ Diabetes mellitus ▯ Family history of cardiomyopathy
Asymptomatic HF	▯ Previous MI ▯ LV systolic dysfunction ▯ Asymptomatic valvular disease
Symptomatic HF	▯ Known structural heart disease ▯ Shortness of breath and fatigue ▯ Reduced exercise tolerance
Refractory end-stage HF	▯ Marked symptoms at rest despite maximal medical therapy (eg, those who are recurrently hospitalized or cannot be safely discharged from the hospital without specialized interventions)

Yancy CW et al. *J Am Coll Cardiol.* 2013;62:1495-1539.

Classification of Heart Failure

ACCF/AHA Stages of HF		NYHA Functional Classification	
A	At high risk for HF but without structural heart disease or symptoms of HF.	None	
B	Structural heart disease but without signs or symptoms of HF.	I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.
C	Structural heart disease with prior or current symptoms of HF.	I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.
		II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF.
		III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of HF.
		IV	Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest.
D	Refractory HF requiring specialized interventions.		

Yancy CW et al. *J Am Coll Cardiol.* 2013;62:1495-1539.

ACC/AHA HF Guidelines:
Management of HFrEF (Stage C)

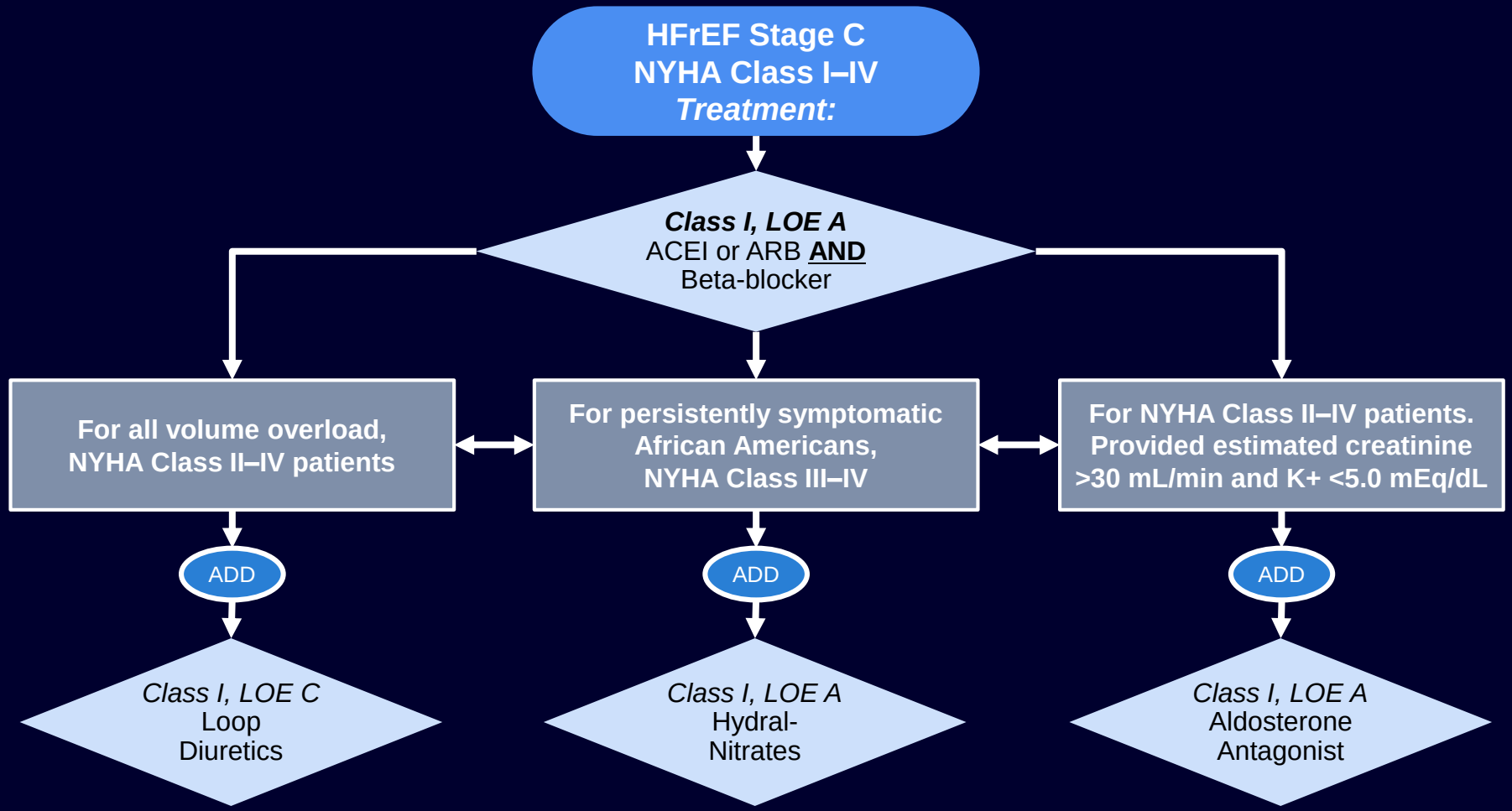
Life-Prolonging Medical Therapy

- ACE inhibitors or ARB (Class I, evidence A) in all patients without contraindications or intolerance.
- Evidence-based beta-blockers (Class I, evidence A) in all patients without contraindications or intolerance. This would include carvedilol (immediate or extended release), metoprolol succinate, or bisoprolol.
- Aldosterone antagonists (Class I, evidence A) in all patients with Class II–IV HF without contraindications or intolerance when close monitoring can be ensured.

ACE = angiotensin converting enzyme; ARB = angiotensin receptor blocker.

Yancy CW, et al. *J Am Coll Cardiol*. 2013;62:1495-1539.

Pharmacologic Treatment for Stage C HFrEF

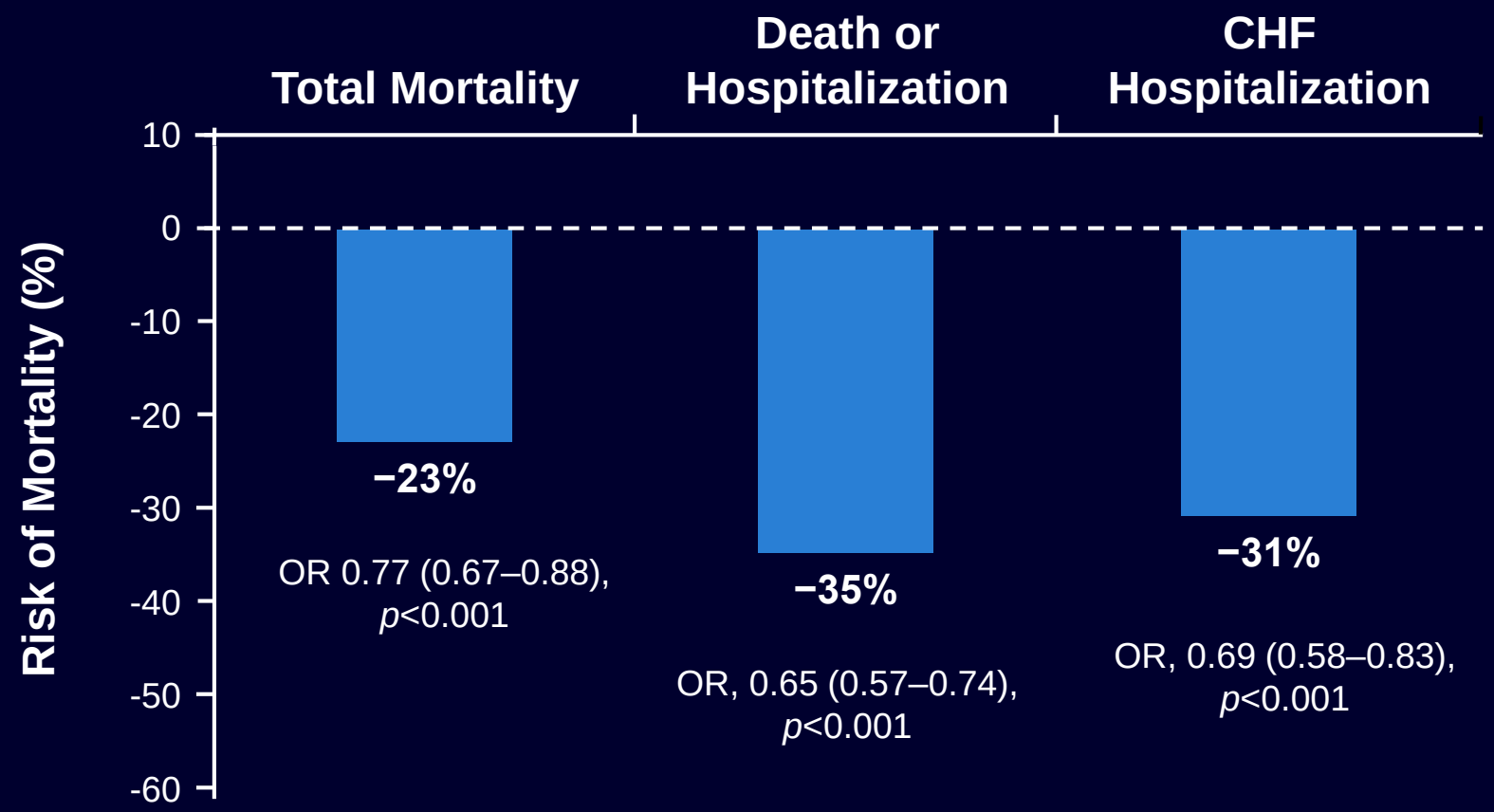


LOE = level of evidence.

Yancy CW, et al. *J Am Coll Cardiol*. 2013;62:1495-1539.

Effect of ACE inhibitors on mortality and hospitalizations in patients with HF

32 Trials of ACEI in Heart Failure: ACEI (n=3870) **vs. Placebo** (n=3235)



OR = odds ratio.

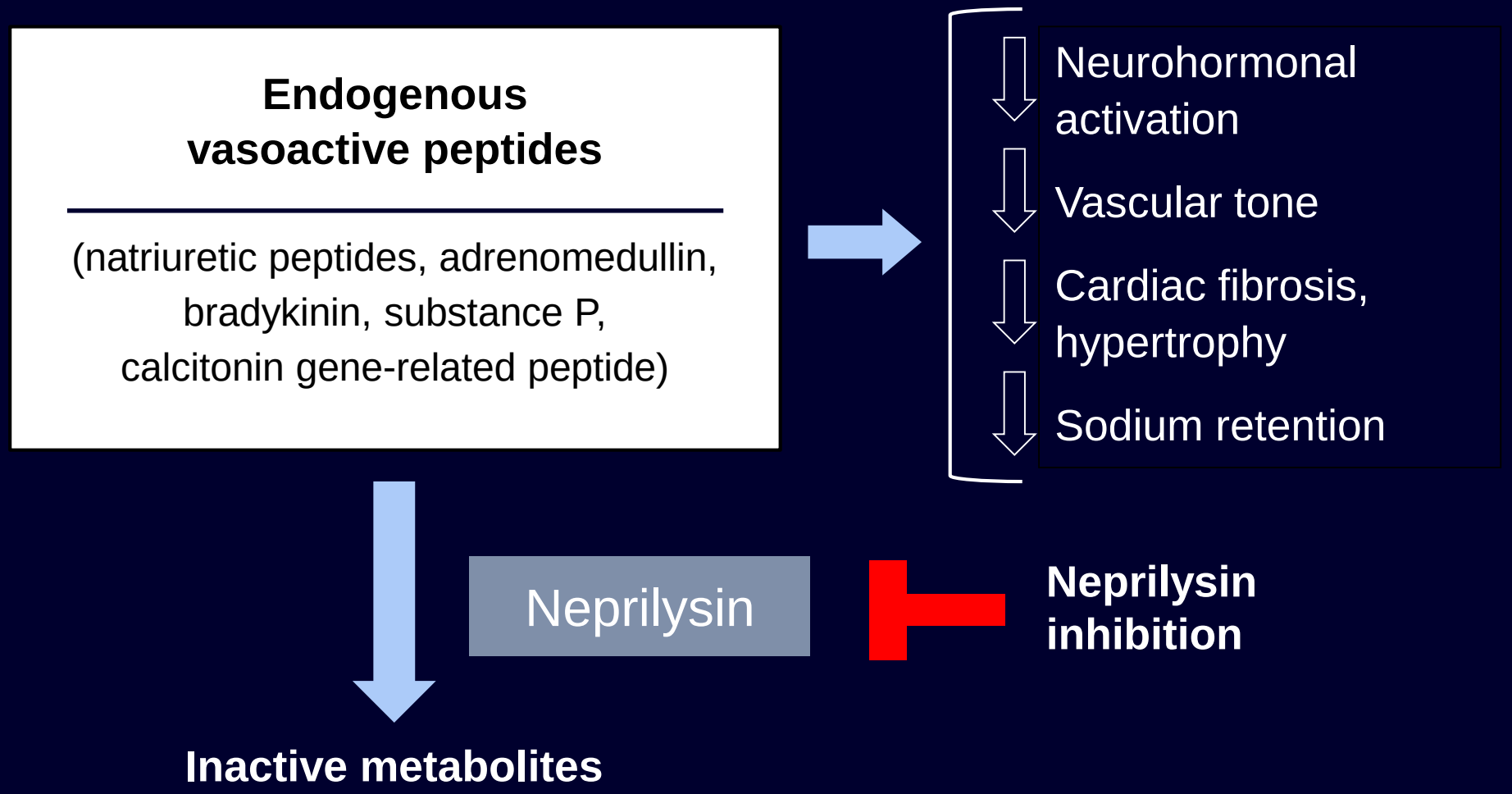
Collaborative Group on ACE Inhibitor Trials. *JAMA*. 1995;273:1450-1456.

ACEI/ARB in heart failure

- Indicated for all patients with asymptomatic LV dysfunction and for Class I to IV heart failure (contraindications: hyperkalemia, angioedema, pregnancy)
- Titrate to target doses (example enalapril 10 mg bid, lisinopril 20 qd, ramipril 10 mg qd, benazepril 40 qd, valsartan 160 mg bid, candesartan 32 mg qd)
- Monitor serum potassium and renal function. Advise checking chemistry panel 1–2 weeks after first dose
- Use of ACE inhibitor together with ARB reserved as a consideration only in patients not candidates for aldosterone antagonist

Yancy CW, et al. *J Am Coll Cardiol*. 2013;62:1495-1539.

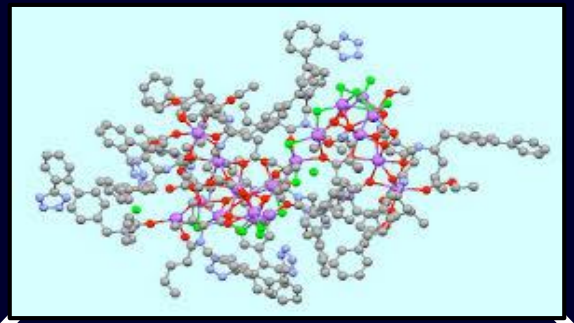
Effects of neprilysin inhibition in heart failure



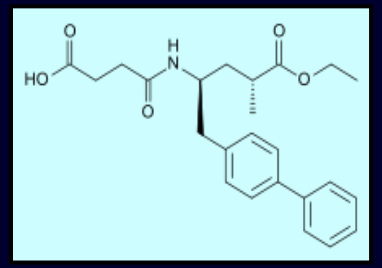
McMurray JJV, et al. *N Engl J Med*. 2014;371:993-1004.

Sacubitril/Valsartan: neprilysin angiotensin receptor inhibitor

Sacubitril/Valsartan



Inhibition of neprilysin



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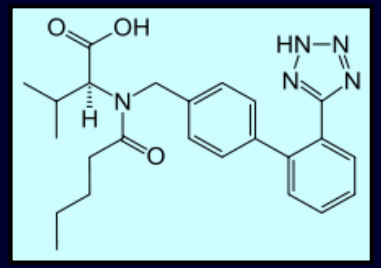
Angiotensin receptor blocker



Sacubitril/Valsartan = LCZ696.

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

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)

Sacubitril/Valsartan
97/103 mg twice daily

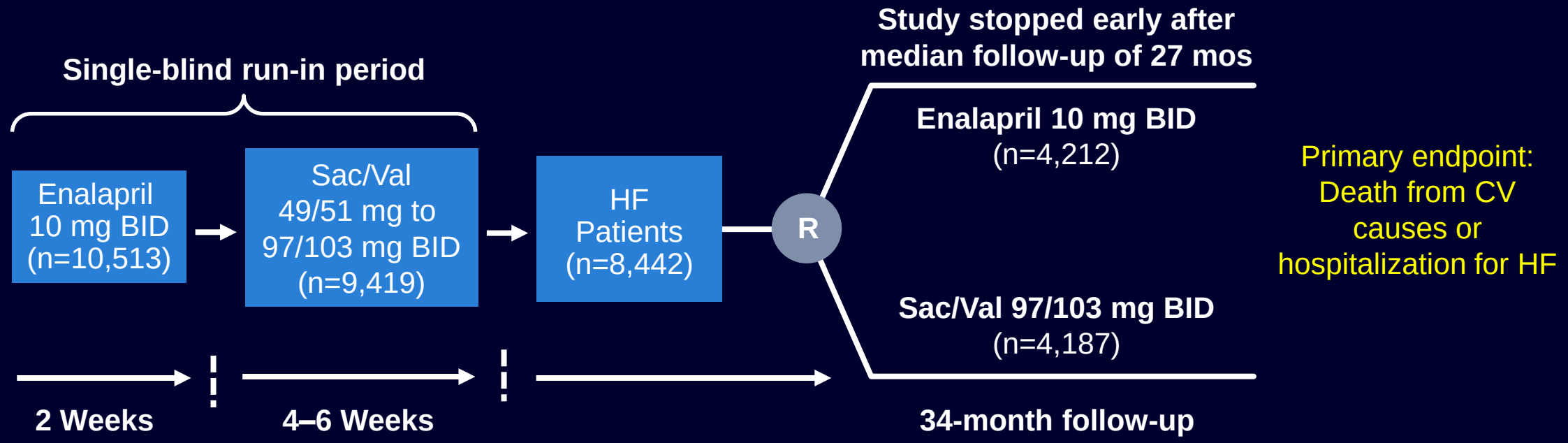
Enalapril
10 mg twice daily

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

PARADIGM-HF trial: design

Entry Criteria:

- NYHA Class II-IV HF, LVEF ≤40% → amended to ≤35%
- BNP ≥150 pg/mL (or NT-proBNP ≥ 600 pg/mL) or 1/3 lower if hospitalized for HF within 12 mos
- On a stable dose of ACEI or ARB equivalent to ≥10 mg of enalapril daily for ≥4 weeks
- Unless contraindicated, on stable dose of beta-blocker for ≥4 weeks
- SBP ≥95 mm Hg, eGFR ≥30 mL/min/1.73 m2 and serum K ≤5.4 mmol/L at randomization



Primary endpoint: Death from CV causes or hospitalization for HF

Sac/Val = Sacubitril/Valsartan.

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

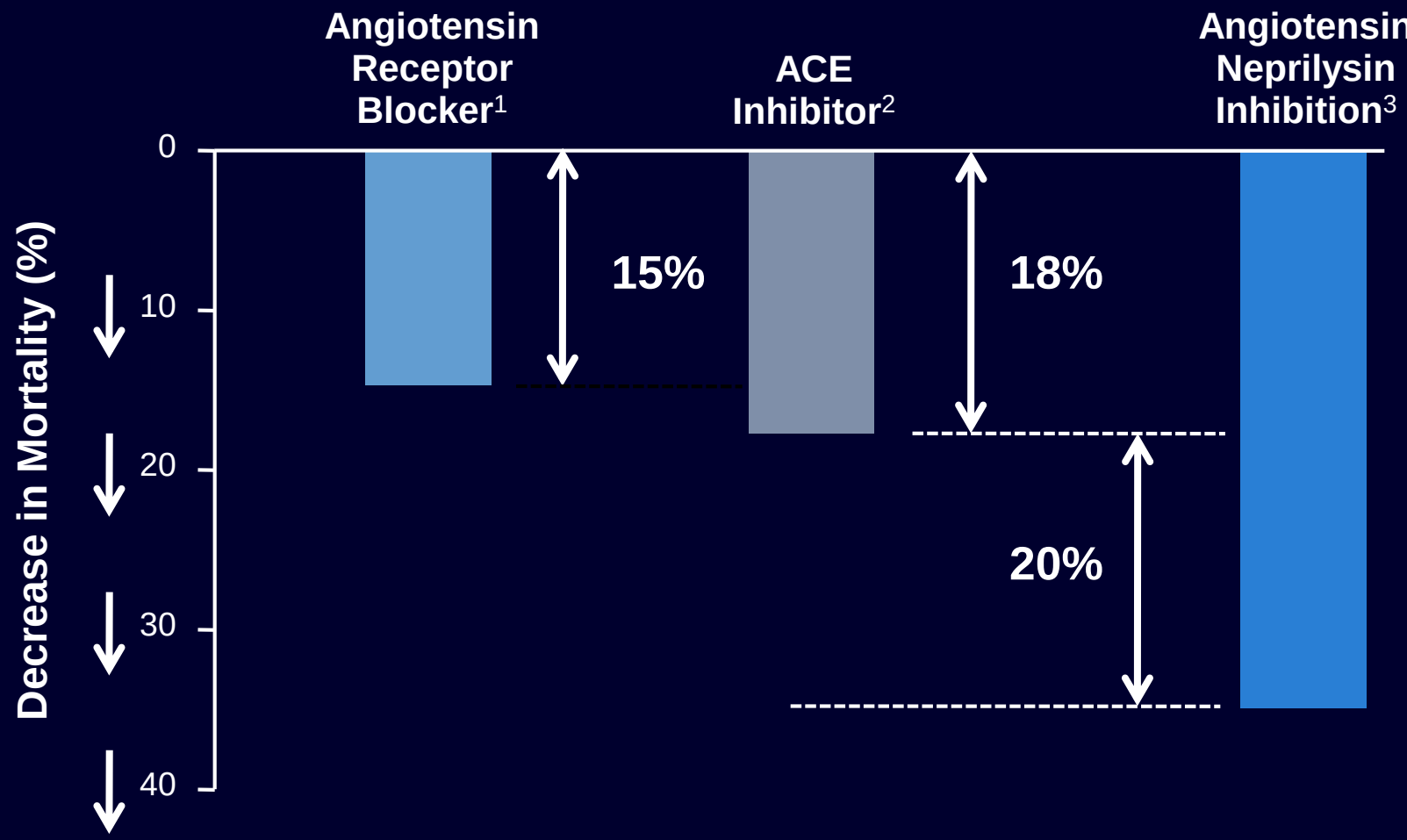
PARADIGM-HF: effect of Sac/Val vs. Enalapril on the primary endpoint and its components

	Sac/Val (n=4187)	Enalapril (n=4212)	Hazard Ratio (95% CI)	*p*-Value
Primary endpoint	914 (21.8%)	1117 (26.5%)	0.80 (0.73–0.87)	<0.001
Cardiovascular death	558 (13.3%)	693 (16.5%)	0.80 (0.71–0.89)	<0.001
Hospitalization for heart failure	537 (12.8%)	658 (15.6%)	0.79 (0.71–0.89)	<0.001

Sac/Val = Sacubitril/Valsartan.

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

Angiotensin neprilysin inhibition with Sac/Val doubles effect on CV death of current inhibitors of the RAS



1. Granger CB, et al. *Lancet*. 2003;362:772-776.
2. The SOLVD Investigators. *N Engl J Med*. 1991;325:293-302.
3. McMurray JJV, et al. *N Engl J Med*. 2014;371:993-1004.

Pharmacological treatment for stage C HF with reduced EF

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

COR	LOE	Recommendations	Comment/ Rationale
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.	NEW: New clinical trial data necessitated this recommendation.

Pharmacological treatment for stage C HF with reduced EF

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

COR	LOE	Recommendations	Comment/ Rationale
III: Harm	**B-R**	ARNI should not be administered concomitantly with ACE inhibitors or within 36 hours of the last dose of an ACE inhibitor.	NEW: Available evidence demonstrates a potential signal of harm for a concomitant use of ACE inhibitors and ARNI.
III: Harm	**C-EO**	ARNI should not be administered to patients with a history of angioedema.	NEW: New clinical trial data.

Beta-Blockers differ in their long-term effects on mortality in HF

Beta-Blocker	Long-Term Effect
Bisoprolol[1]	Beneficial
Bucindolol[2]	No effect
Carvedilol[3–5]	Beneficial
Metoprolol tartrate[6]	Not well studied
Metoprolol succinate[7]	Beneficial
Nebivolol[8]	No effect
Xamoterol[9]	Harmful

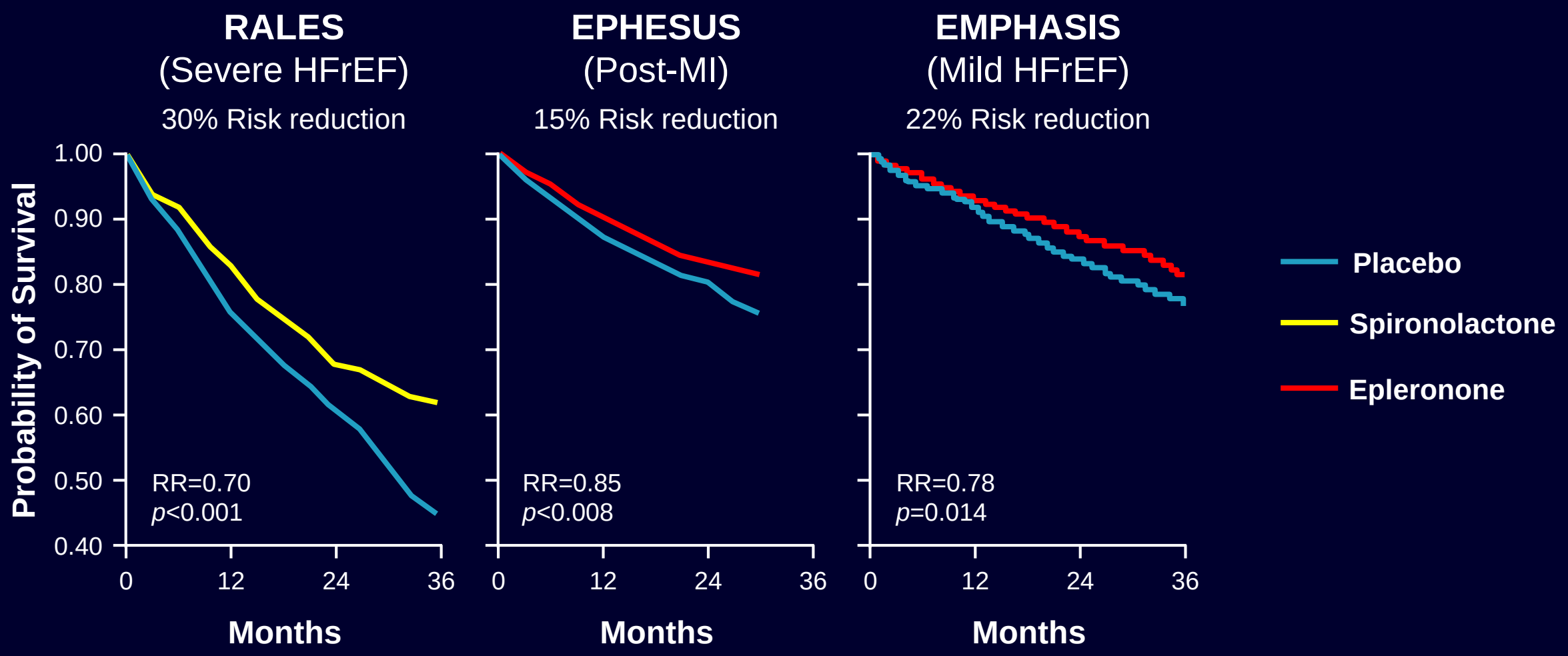
1. CIBIS II Investigators and Committees. *Lancet*. 1999;353:9-13. 2. The BEST Investigators. *N Engl J Med*. 2001; 344:1659-1667. 3. Colucci WS, et al. *Circulation*. 1996;94:2800-2806. 4. Packer M, et al. *N Engl J Med*. 2001;344:1651-1658. 5. The CAPRICORN Investigators. *Lancet*. 2001;357:1385-1390. 6. Waagstein F, et al. *Lancet*. 1993;342:1441-1446. 7. MERIT-HF Study Group. *Lancet*. 1999;353:2001-2007. 8. SENIORS Study Group. *Eur Heart J*. 2005; 26:215-225. 9. The Xamoterol in Severe Heart Failure Study Group. *Lancet*. 1990;336:1-6.

Beta-Blocker therapy in heart failure

- Indicated for all patients with asymptomatic LVD dysfunction and for Class I to IV Heart Failure with LVEF ≤0.40.
- Contraindications: cardiogenic shock, severe reactive airway disease, 2/3rd-degree HB.
- Use of one the 3 evidence-based beta-blockers in HF: e.g., carvedilol, metroprolol succinate, bisoprolol.
- Start at very low HF doses and up-titrate to target doses at two-week intervals or highest dose short of target dose that is well tolerated.
- Monitor HR and BP.

Yancy CW, et al. *J Am Coll Cardiol*. 2013;62:1495-1539.

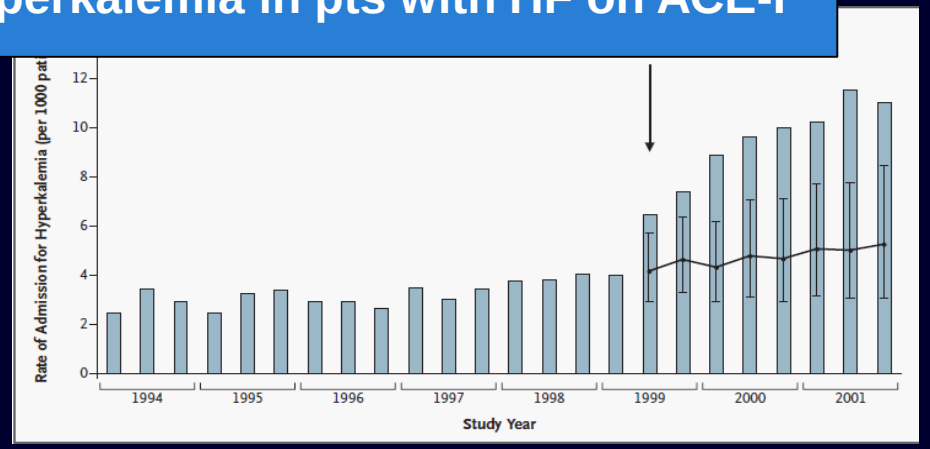
Aldosterone antagonists in HF



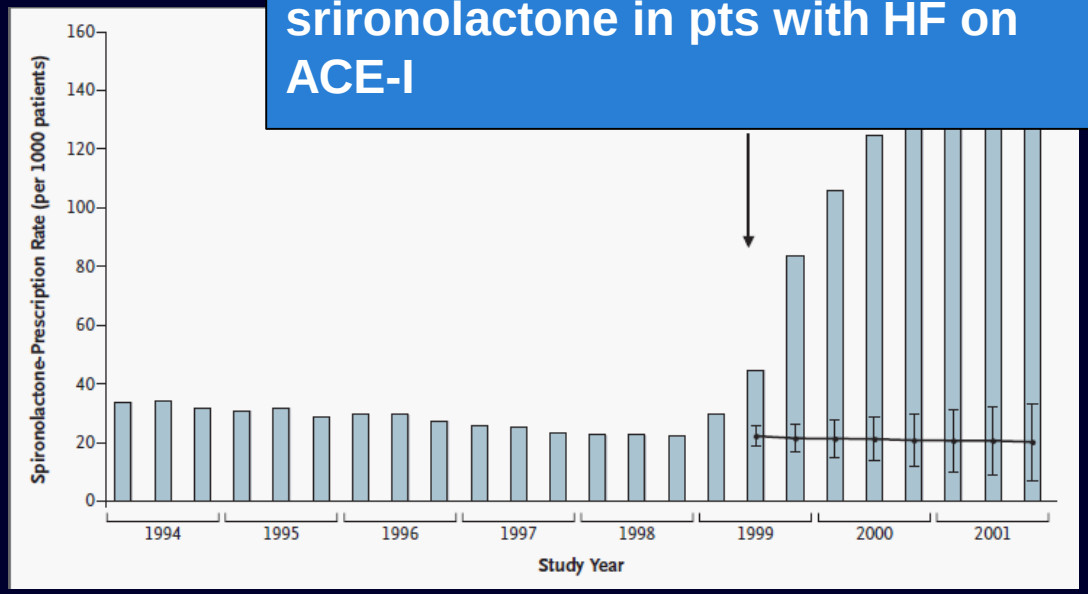
Pitt B, et al. *N Engl J Med*. 1999:341:709-717. Pitt B, et al. *N Engl J Med*. 2003;348:1309-1321.
Zannad F, et al. *N Engl J Med*. 2011;364:11-21.

Rate of Hyperkalemia after publication of RALES

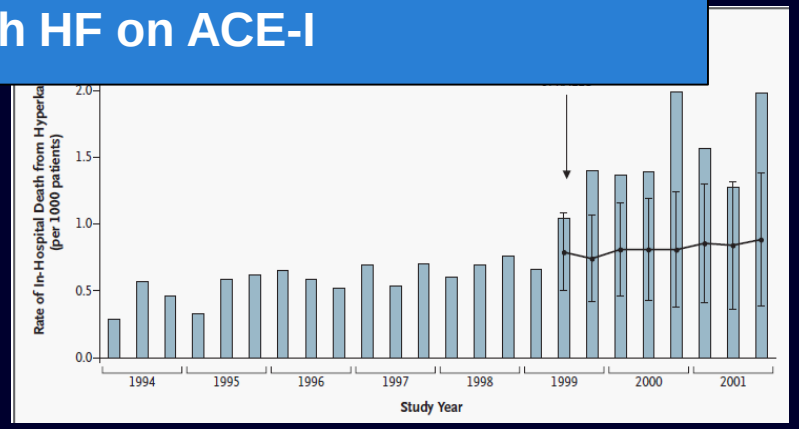
Number of admissions for hyperkalemia in pts with HF on ACE-I



Number of prescriptions of srironolactone in pts with HF on ACE-I



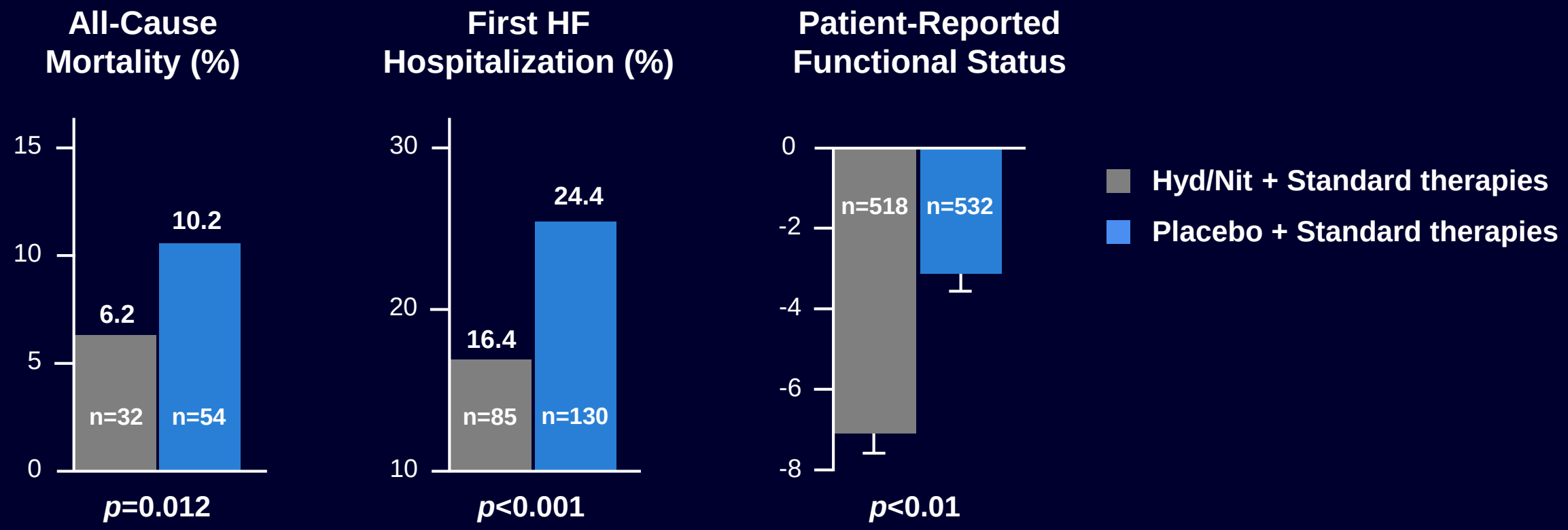
Death due to hyperkalemia in pts with HF on ACE-I



Jurleenk DN et al NEJM. 2004;351:543

AHeFT: Trial Summary

1050 African Americans with Class III to IV HF, LVEF 24%, on ACEI, BB, AA



AHeFT = African-American Heart Failure Trial; BB = beta-blocker; AA = aldosterone antagonist.

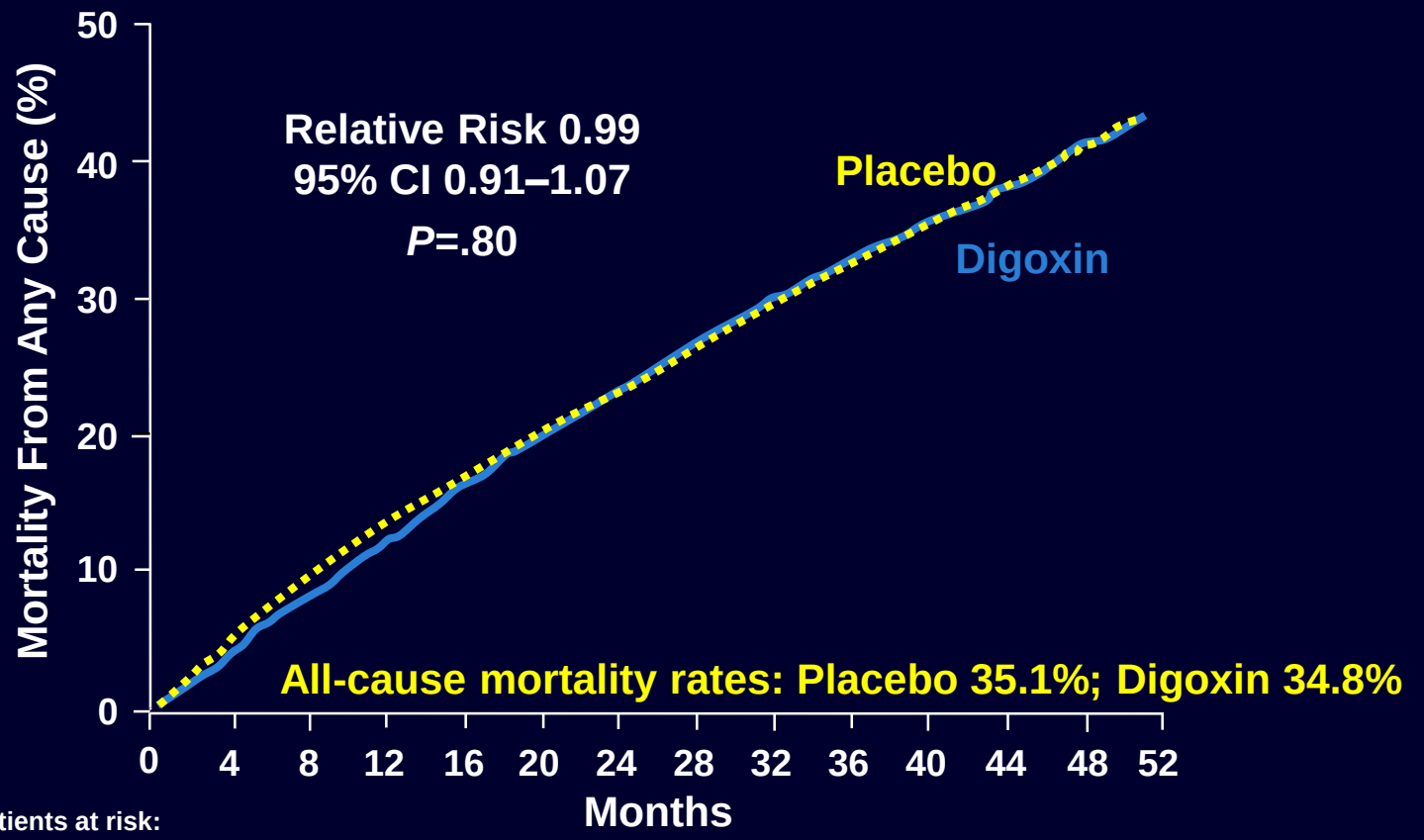
Adapted from Taylor AL et al. *N Engl J Med*. 2004;351:2052.

Effect of Digoxin on mortality in heart failure: The Digitalis Investigation Group

CV Mortality
↓ 0%

HF Hospitalizations
↓ 28%

Total Hospitalizations
↓ 6%



Number of patients at risk:

Placebo	3,403	3,239	3,105	2,976	2,868	2,758	2,652	2,551	2,205	1,881	1,506	1,168
	734	339										
Digoxin	3,397	3,269	3,144	3,019	2,882	2,759	2,644	2,531	2,184	1,840	1,475	1,156
	737	335										

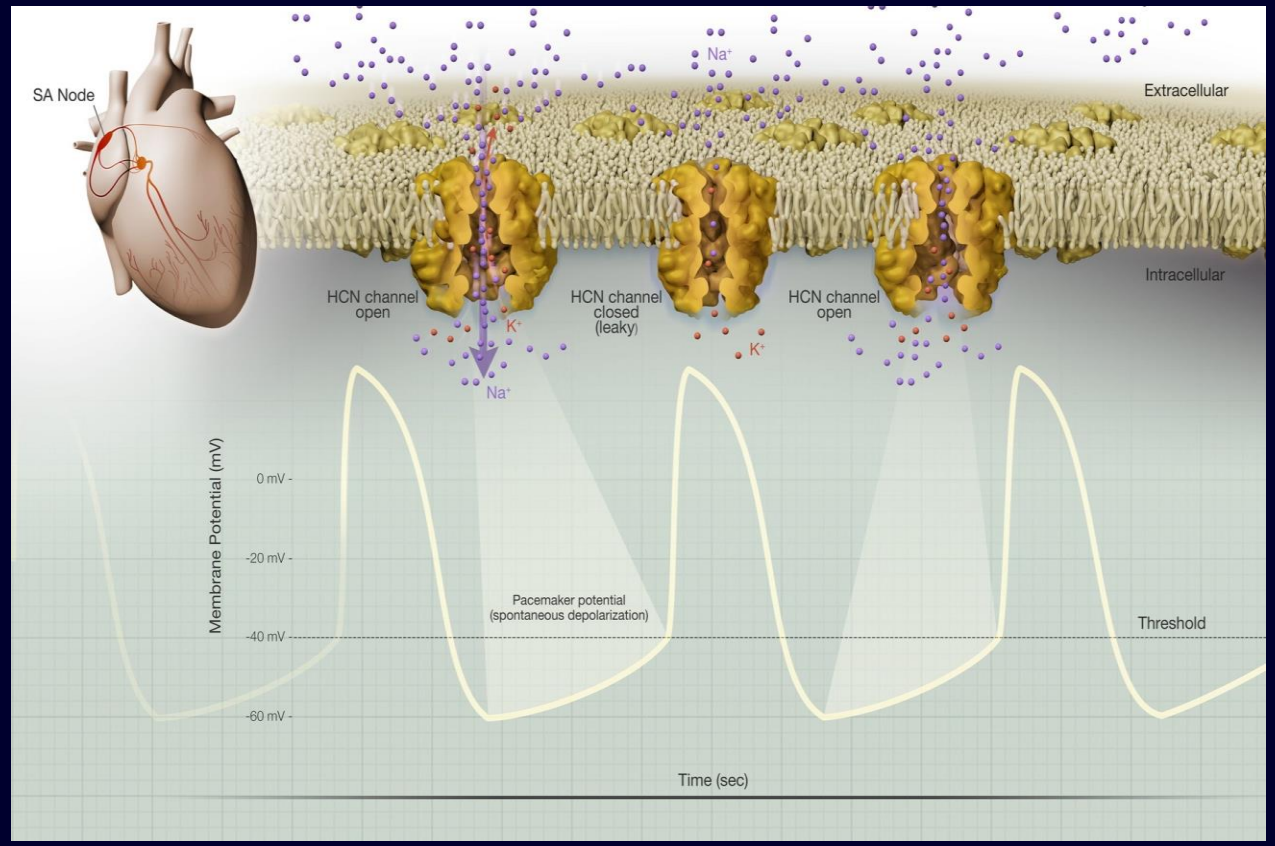
DIG (Digitalis Investigation Group): 6,800 patients with LVEF <45% randomized to digoxin (n=3,403) or placebo (n=3,397) in addition to therapy with diuretics and ACEI followed for 37 months.

The DIGITALIS Investigation Group. *N Engl J Med*. 1997;336:525–532.

Ivabradine Mechanism of Action

Funny current? (1970)

The *hyperpolarization-activated cyclic nucleotide-gated* (HCN) channel responsible for the cardiac pacemaker I_f current regulates heart rate

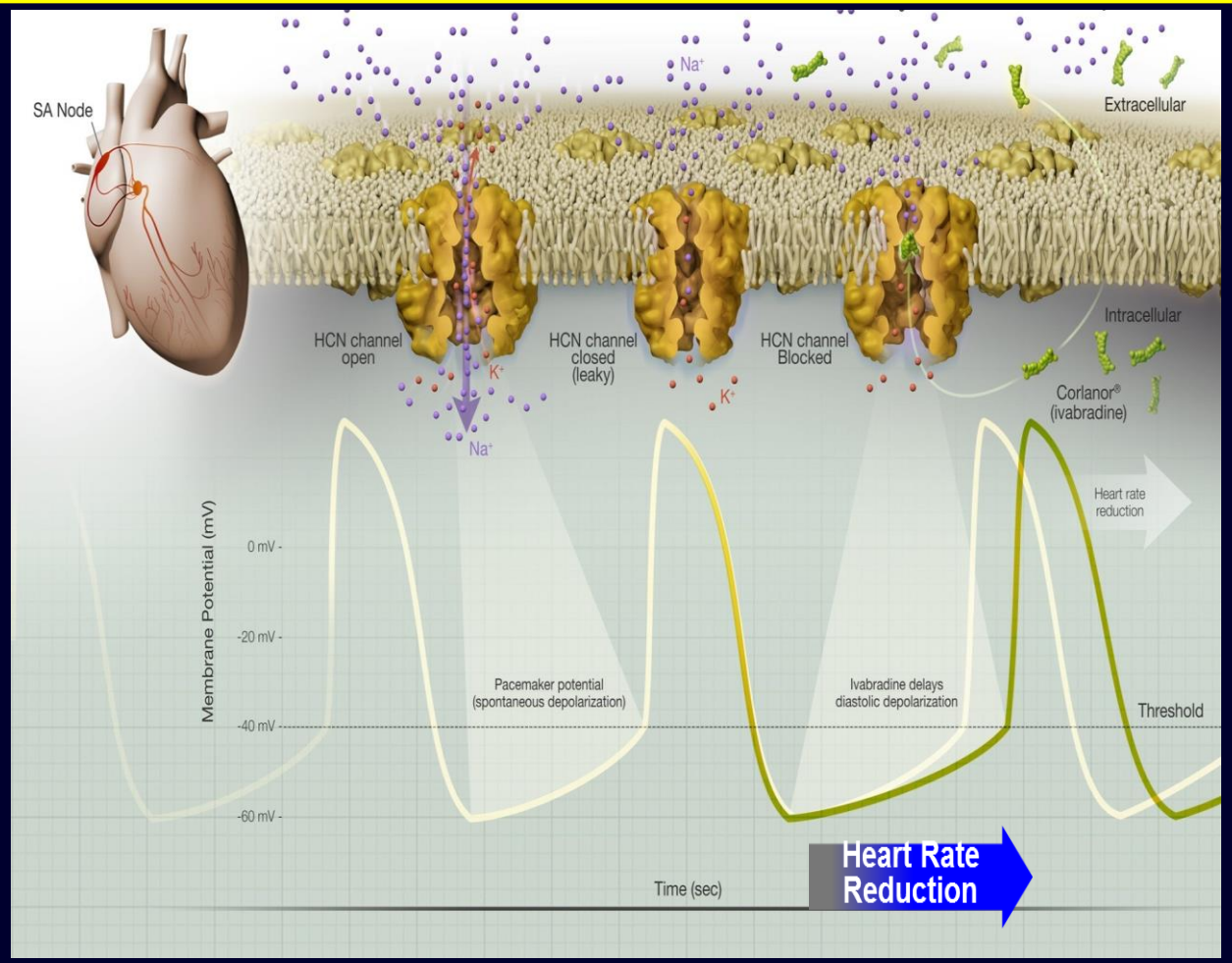


HCN, hyperpolarization-activated cyclic nucleotide-gated; K^+, potassium; N^+, sodium; SA, sinoatrial.

Adapted from: Postea O, et al. *Nature Reviews*. 2011;10:903-914.

Adapted from: DiFrancesco D, et al. *Drugs*. 2004;64:1757-1765.

Ivabradine blocks the HCN channel in the sinus node which reduces heart rate



Adapted from: Postea O, et al. *Nature Reviews*. 2011;10:903-914.
Adapted from: DiFrancesco D, et al. *Drugs*. 2004;64:1757-1765.
Corlanor® (ivabradine) Prescribing Information, Amgen.

SHIFT Study Design

- Subjects ≥ 18 years
- In sinus rhythm and had a resting HR ≥ 70 bpm
- NYHA Class II, III, or IV and in stable condition for ≥ 4 weeks
- LVEF ≤ 35%
- Optimal stable Standard of Care (SOC) therapy, including maximally tolerated doses of beta-blockers
- Hospitalization for worsening HF within ≤ 12 months

14-day run-in

Randomized, double-blind, parallel-group study to assess the effect of ivabradine in addition to guidelines-based treatment in 6,558 patients with HF, conducted from October 2006 through March 2010.

Randomization

Ivabradine 5 mg twice daily for 2 weeks (n = 3,268)

Ivabradine 7.5/5.0/2.5 mg twice daily according to HR and tolerability*

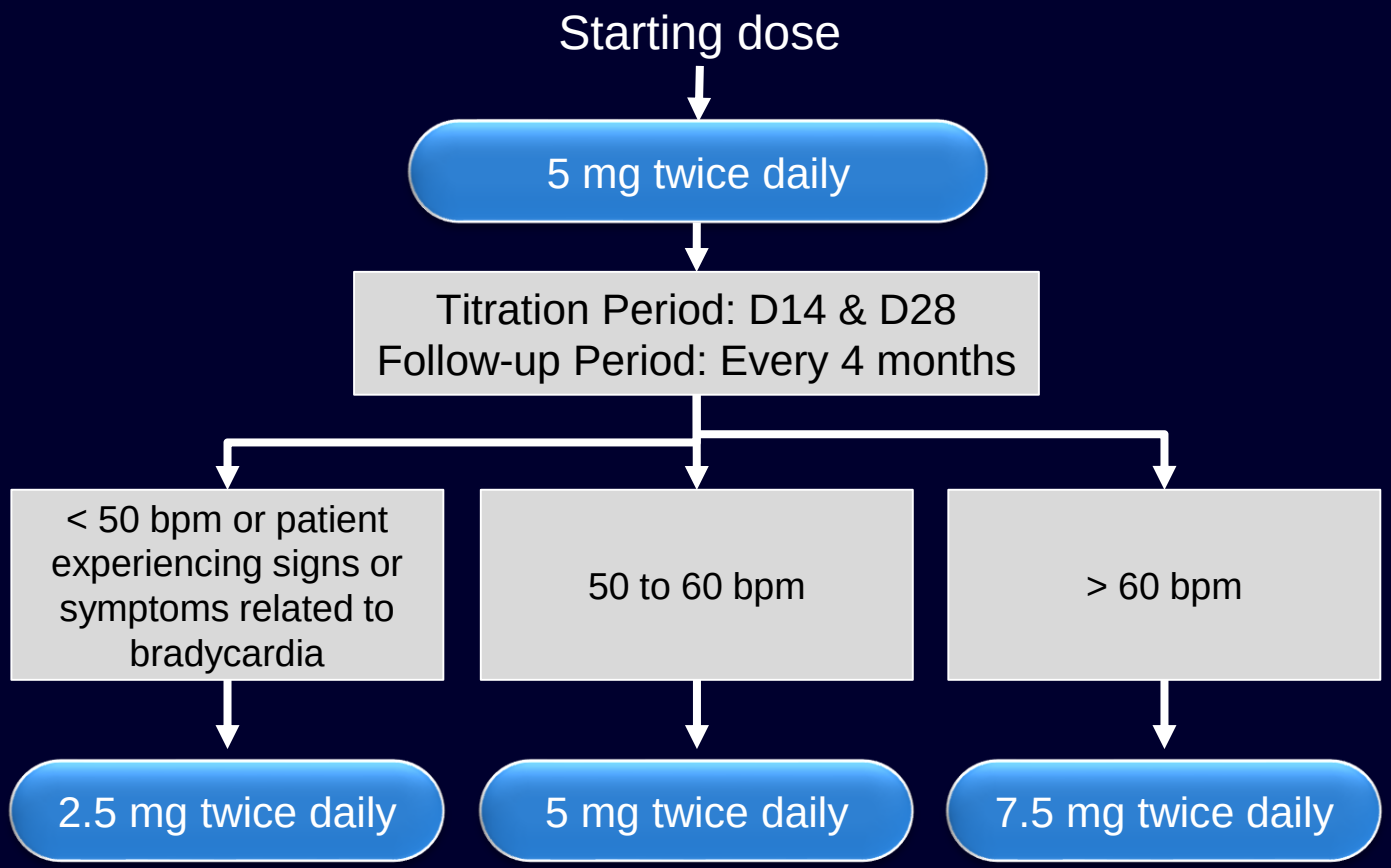
Placebo twice daily (n = 3,290)

Median follow-up duration: 22.9 months (interquartile range = 18 to 28 months)

HF, heart failure; HR, heart rate; LVEF, left ventricular ejection fraction.

Swedberg K, et al. *Lancet*. 2010;376:875-885.

Ivabradine Titration

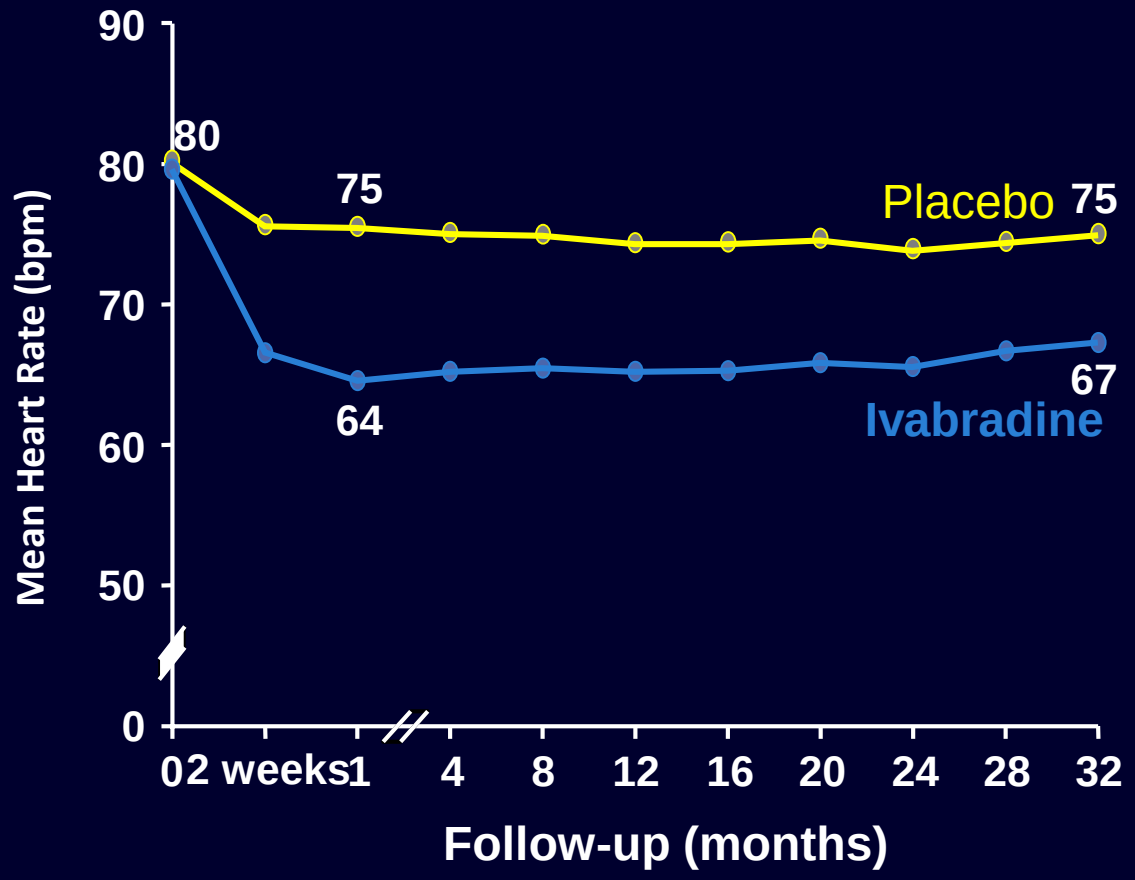


Treatment was discontinued if heart rate remained below 50 bpm or symptoms of bradycardia persisted after dose reduction.

D, day.

Swedberg K, et al. *Lancet*. 2010;376:875-885.
Corlanor® (ivabradine) Prescribing Information, Amgen.

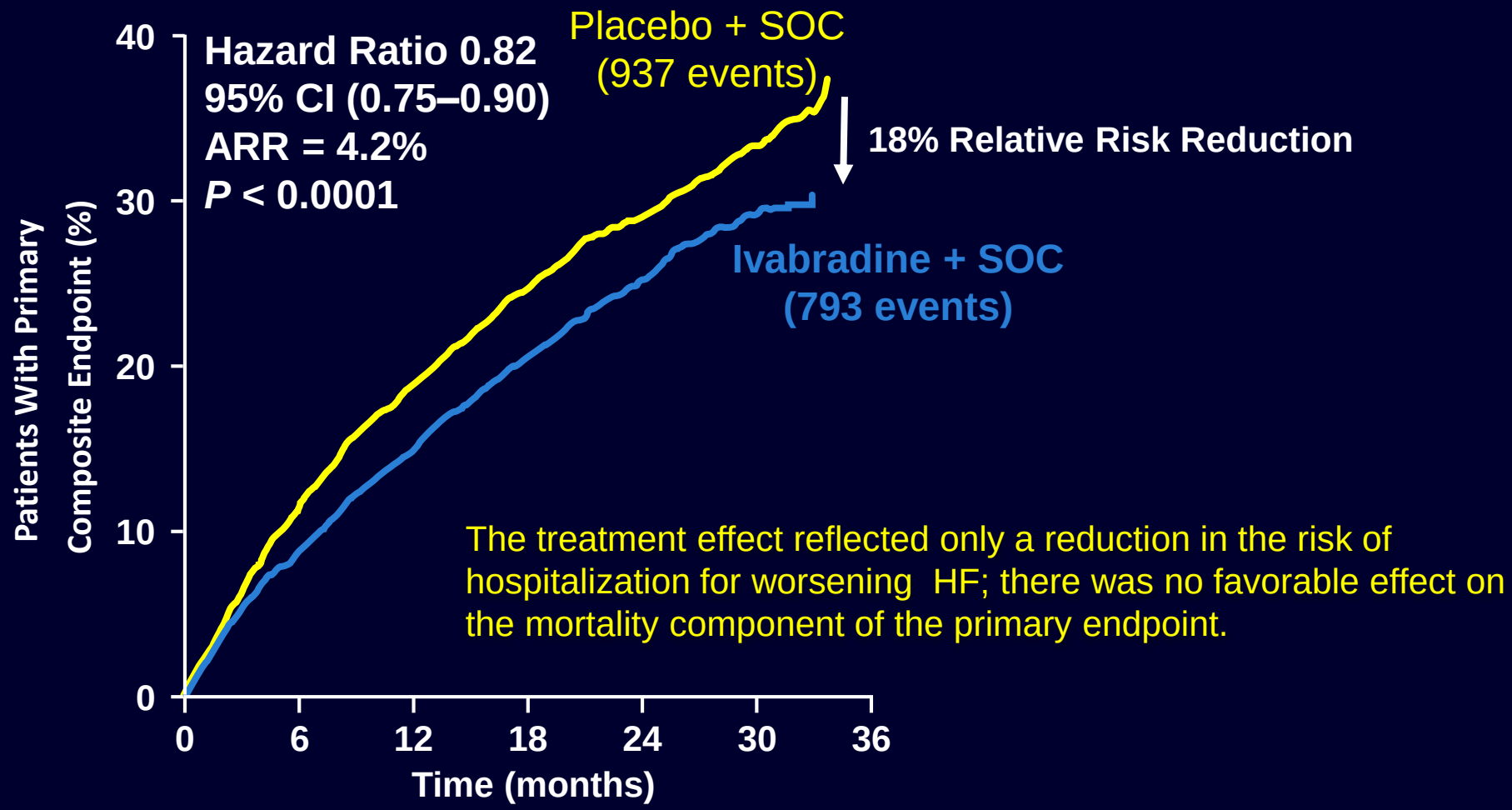
Difference in heart rate reduction between groups was early and sustained throughout study



Beta-blocker dose remained stable in 86% of the ivabradine group and 82% of the placebo group throughout the study

Swedberg K, et al. *Lancet*. 2010;376:875-885.
Data on file, Amgen.

Time to first event of hospitalization for worsening HF or CV death

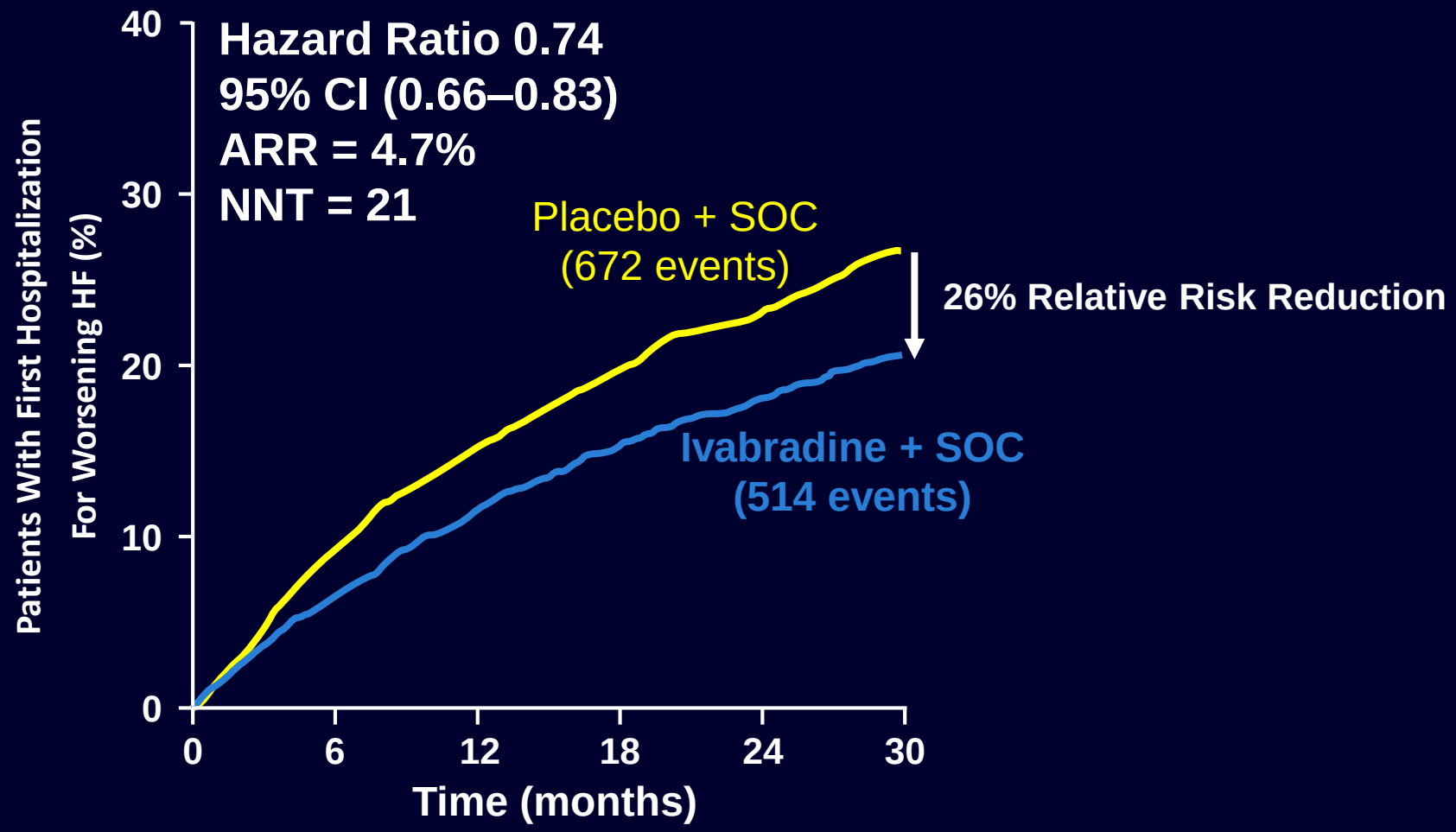


The treatment effect reflected only a reduction in the risk of hospitalization for worsening HF; there was no favorable effect on the mortality component of the primary endpoint.

Primary Composite Endpoint: Time to CV Death or First Hospitalization for Worsening HF.
ARR, absolute risk reduction; CI, confidence interval; SOC, standard of care.

Corlanor® (ivabradine) Prescribing Information, Amgen.
Swedberg K, et al. *Lancet*. 2010;376:875-885

Hospitalization for worsening HF at any time



Swedberg K, et al. *Lancet*. 2010;376:875-885.

Pharmacological Treatment for Stage C HF with Reduced EF

Ivabradine

COR	LOE	Recommendations	Comment/ Rationale
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.	NEW New clinical trial data.

Therapies approved for HF treatment over the past 4 decades

HFrEF

- ACEIs and ARBs
- Aldo receptor antagonists
- Beta blockers
- Hyd/ISDN
- Ivabradine
- ICDs
- BiVs
- LVADs

HFpEF

- None

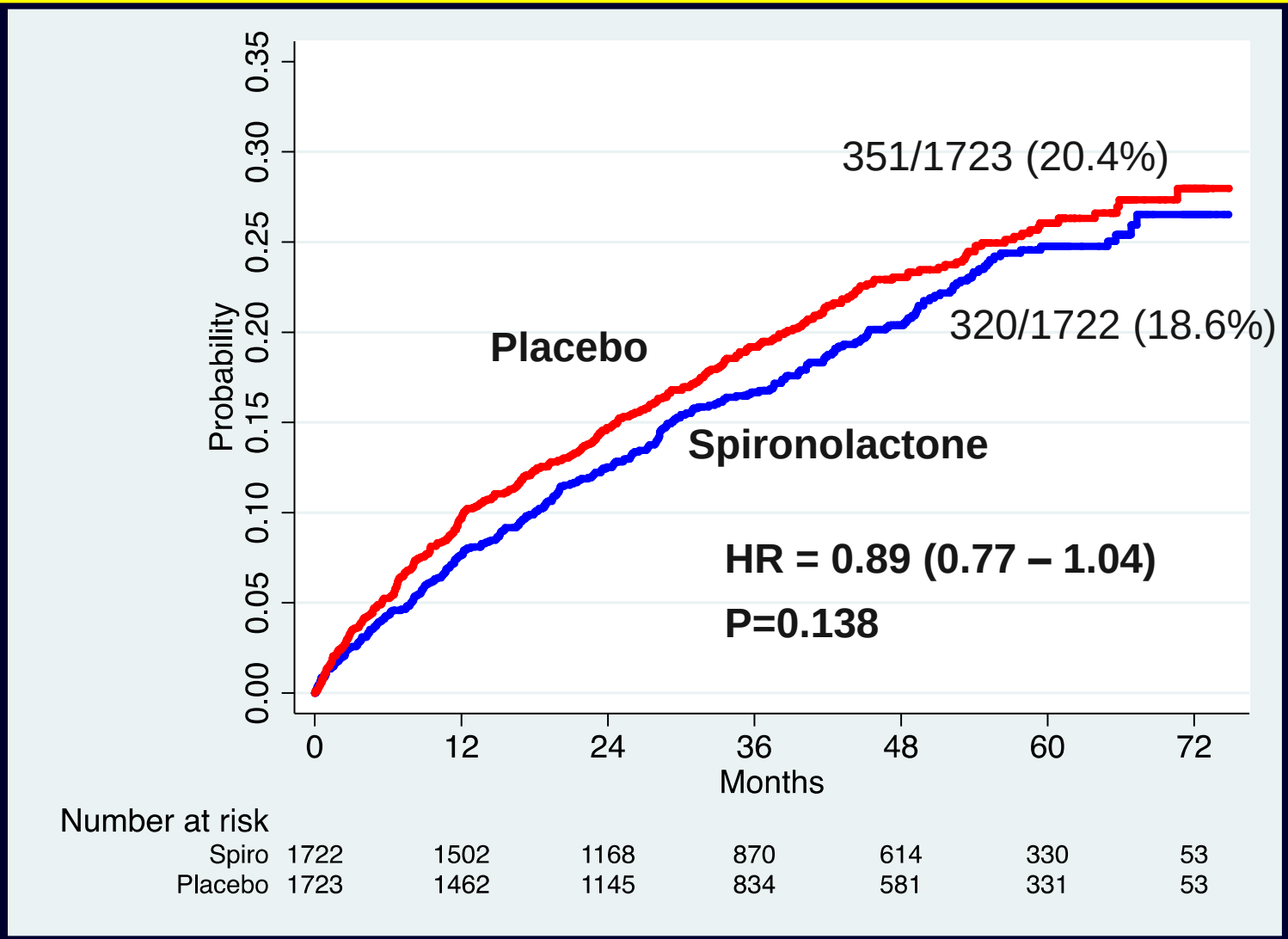
Pharmacological Treatment for Stage C HF With Preserved EF

COR	LOE	Recommendations	Comment/ Rationale
I	B	Systolic and diastolic blood pressure should be controlled in patients with HF*p*EF in accordance with published clinical practice guidelines to prevent morbidity	2013 recommendation remains current.
I	C	Diuretics should be used for relief of symptoms due to volume overload in patients with HF*p*EF.	2013 recommendation remains current.

Pharmacological Treatment for Stage C HF With Preserved EF

COR	LOE	Recommendations	Comment/ Rationale
IIa	C	Coronary revascularization is reasonable in patients with CAD in whom symptoms (angina) or demonstrable myocardial ischemia is judged to be having an adverse effect on symptomatic HF*p*EF despite GDMT.	2013 recommendation remains current.
IIa	C	Management of AF according to published clinical practice guidelines in patients with HF*p*EF is reasonable to improve symptomatic HF.	2013 recommendation remains current.
IIa	C	The use of beta-blocking agents, ACE inhibitors, and ARBs in patients with hypertension is reasonable to control blood pressure in patients with HF*p*EF.	2013 recommendation remains current.

Spironolactone in HFpEF: TOPCAT
1° Outcome: CV Death, HF Hosp, or Resuscitated Cardiac Arrest



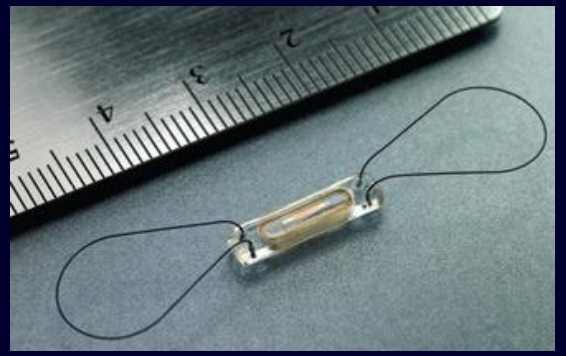
N Engl J Med. 2014 Apr 10;370(15):1383-92

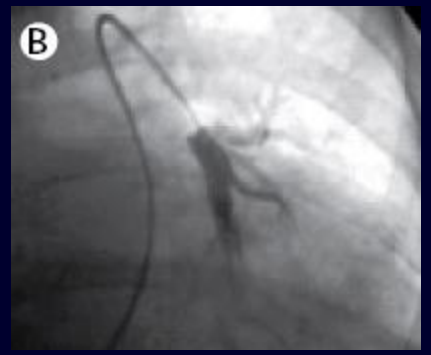
Class I recommendations for devices in patients with LV systolic dysfunction

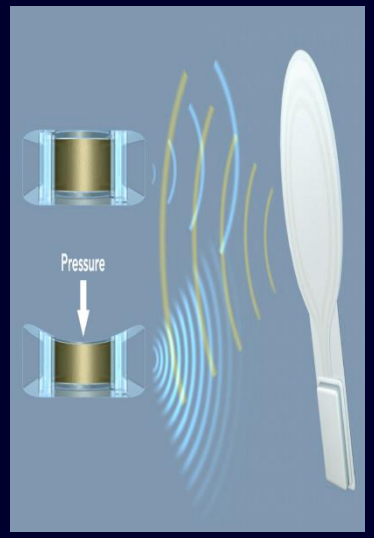
ICD	
Prior resuscitated cardiac arrest	Class I Level A
Ischaemic aetiology and >40 days of MI	Class I Level A
Non-ischaemic aetiology	Class I Level B
CRT	
NYHA Class III/IV and QRS >120 ms	Class I Level A
To improve symptoms/reduce hospitalization	Class I Level A
To reduce mortality	Class I Level A

Implantable Wireless Heart Sensor

No batteries or internal power source, sensor is powered by RF-energy provided by an external electronics module.

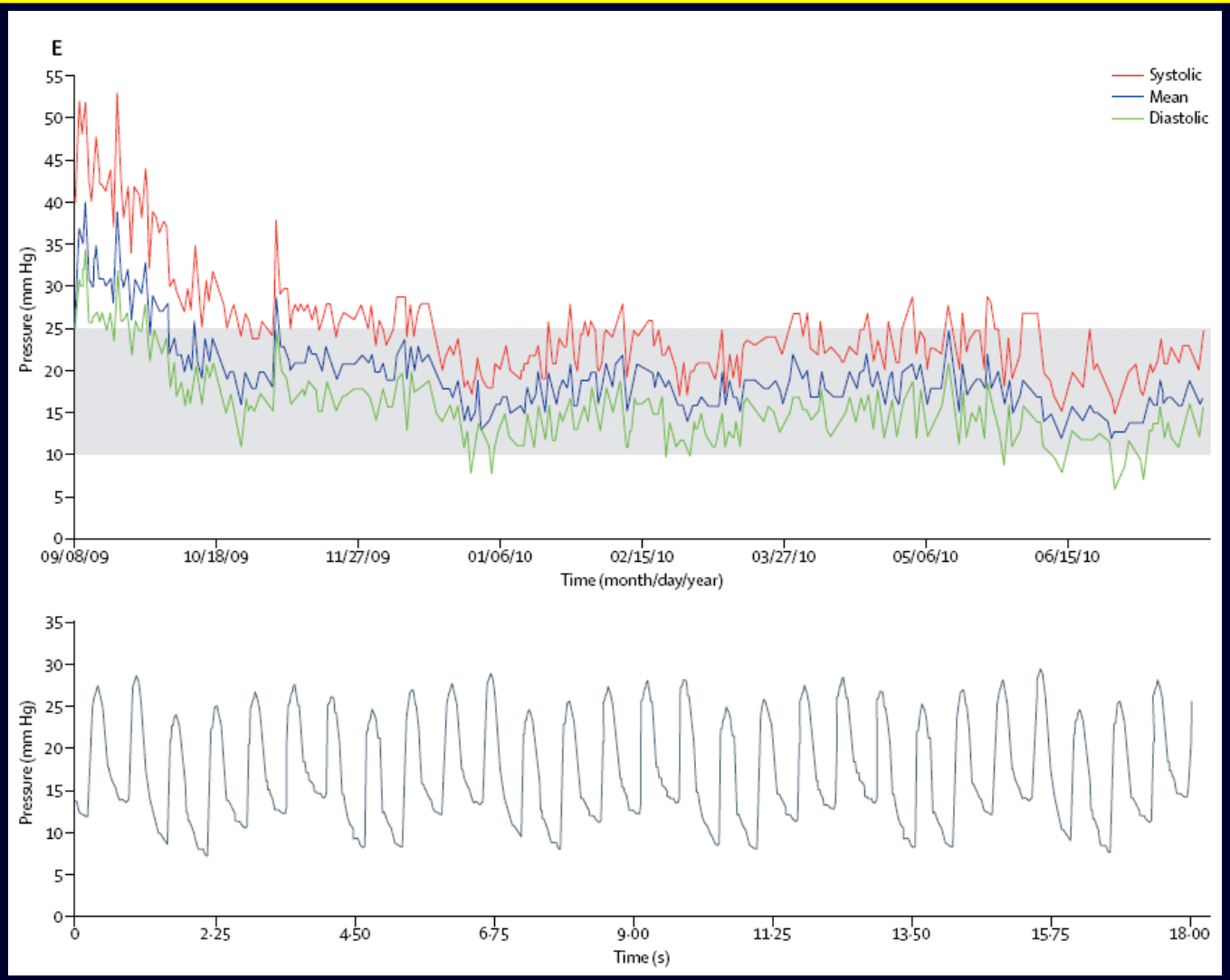






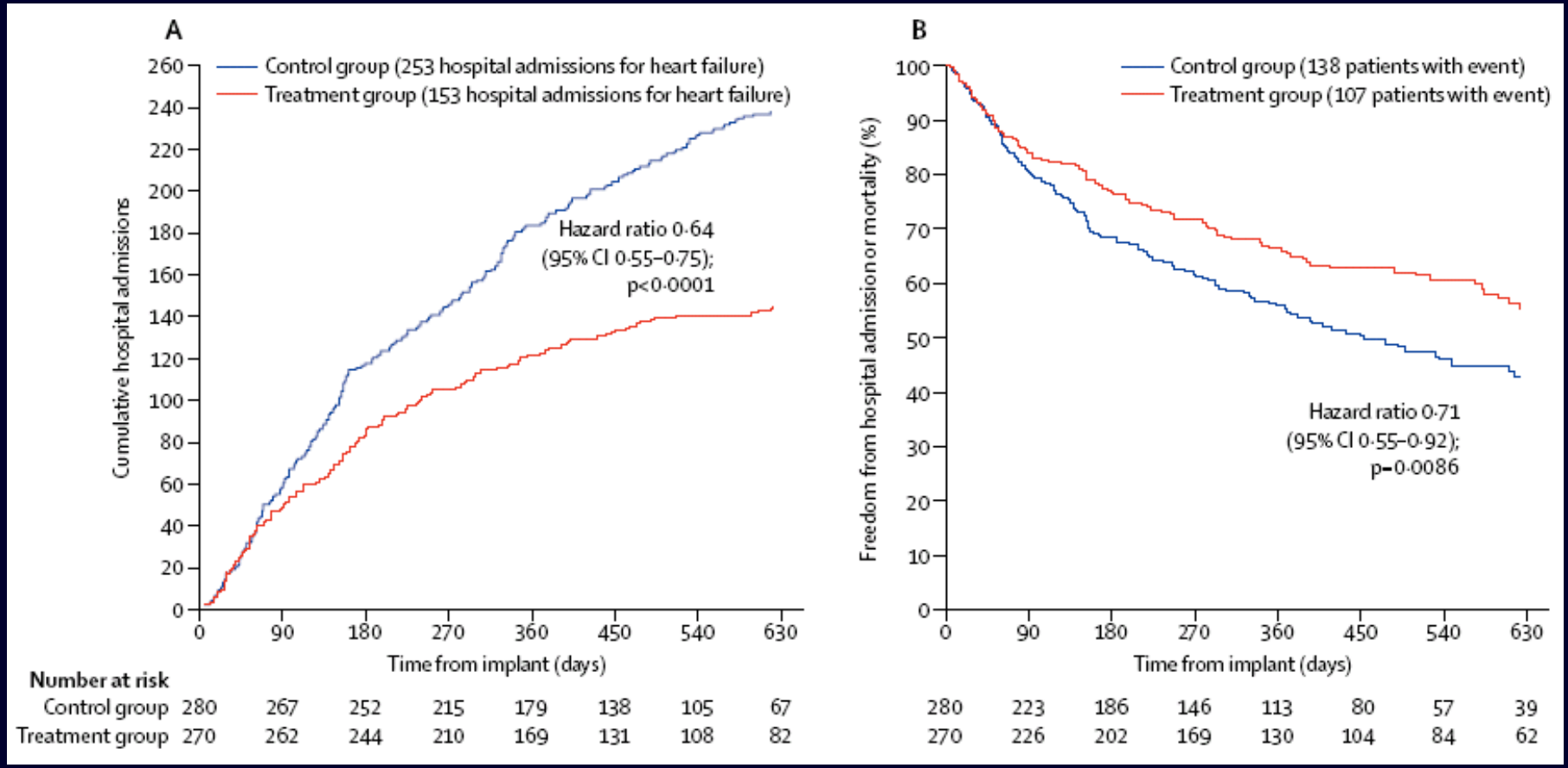
Coil and a pressure sensitive capacitor encased in a hermetically sealed silica capsule covered by silicone. The device has no leads or batteries. Two nitinol loops at the ends of the capsule serve as anchors in the pulmonary artery. The coil and capacitor form an electrical circuit that resonates at a specific frequency, and pressure applied to the sensor causes deflections of the pressure-sensitive surface. An external antenna provides power to the device, continuously measuring its resonant frequency, which is then converted to a pressure waveform. The interrogating device has an atmospheric barometer which automatically subtracts the ambient pressure from that measured from the implanted sensor.

Wireless pulmonary artery hemodynamic monitoring in chronic heart failure: CHAMPION



Abraham WT, et al Lancet. 2011 Feb 19;377(9766):658-66.

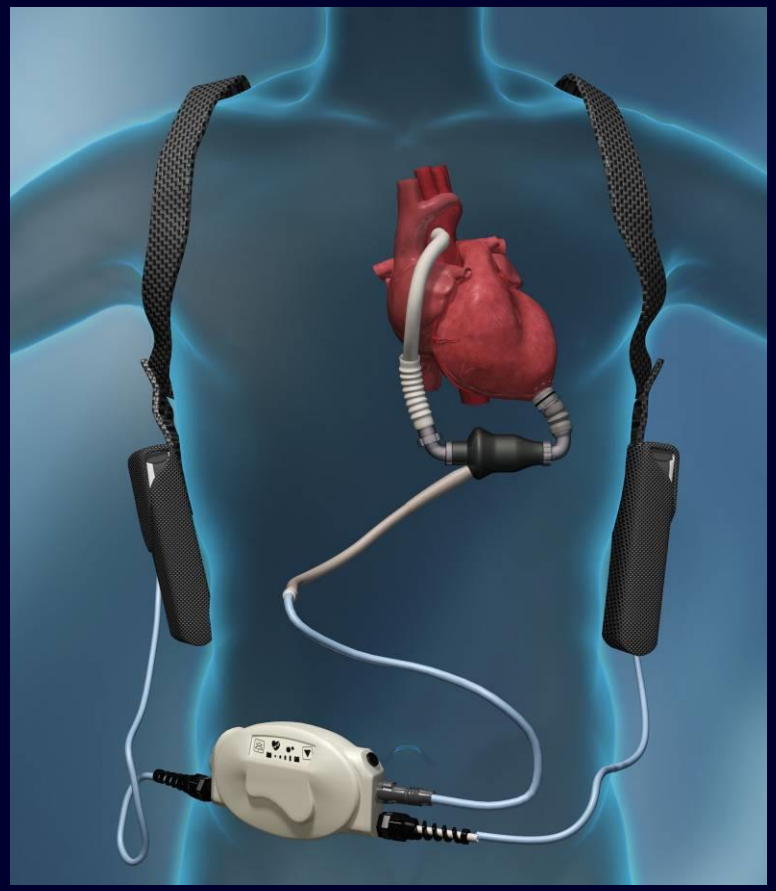
Wireless pulmonary artery hemodynamic monitoring in chronic heart failure: CHAMPION



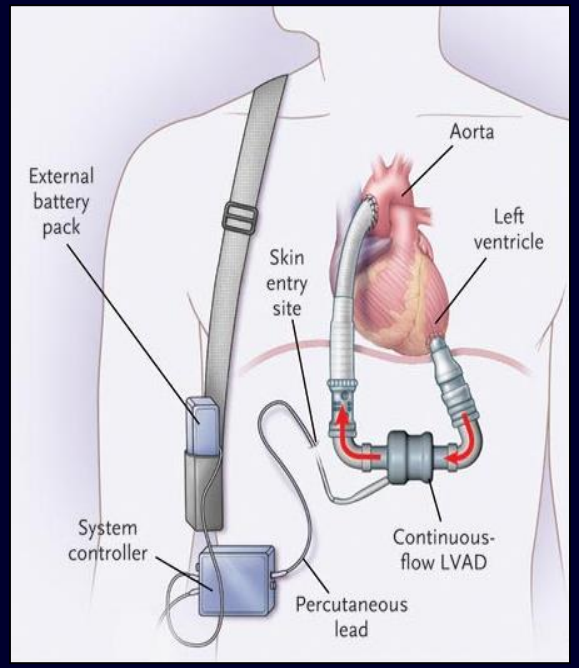
Abraham WT, et al Lancet. 2011 Feb 19;377(9766):658-66.

HeartMate II LVAS

- A surgically implanted, rotary continuous-flow device in parallel with the native left ventricle
  - Left ventricle to ascending aorta
- Percutaneous driveline
- Electrically powered
  - Batteries & line power
- Fixed speed operating mode
- Home discharge



Destination VAD therapy trials



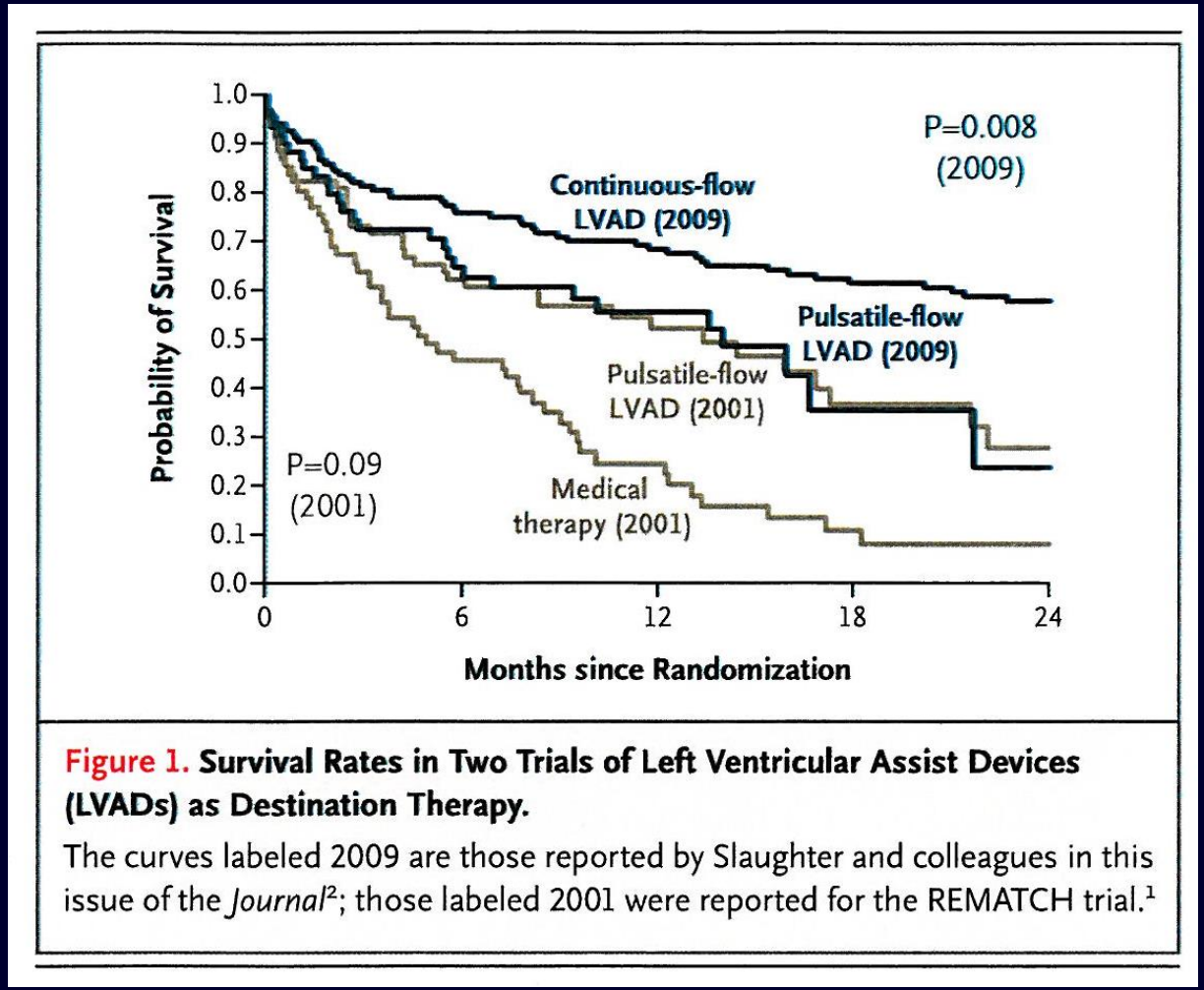


Figure 1. Survival Rates in Two Trials of Left Ventricular Assist Devices (LVADs) as Destination Therapy.

The curves labeled 2009 are those reported by Slaughter and colleagues in this issue of the *Journal*[2]; those labeled 2001 were reported for the REMATCH trial.[1]

NEJM 2009;361(23):2241-51.

Mechanical Circulatory Support (MCS)

Indications

- Failure to wean off CPB (post-cardiotomy syndrome)
- ESHD pt with inadequate organ perfusion despite optimal medical management (BT Tx)
- Acute myocarditis/post-partum CMY (BT Recovery)
- Acute, massive MI with shock
- Destination therapy (DT) for non-transplant candidates with end stage HD
- Incessant VT/cardiac arrest

CPB, cardiopulmonary bypass; ESHD, end-stage heart disease; BTT, bridge to transplant; CMY, cardiomyopathy; BTR, bridge to recovery; VT, ventricular tachycardia.

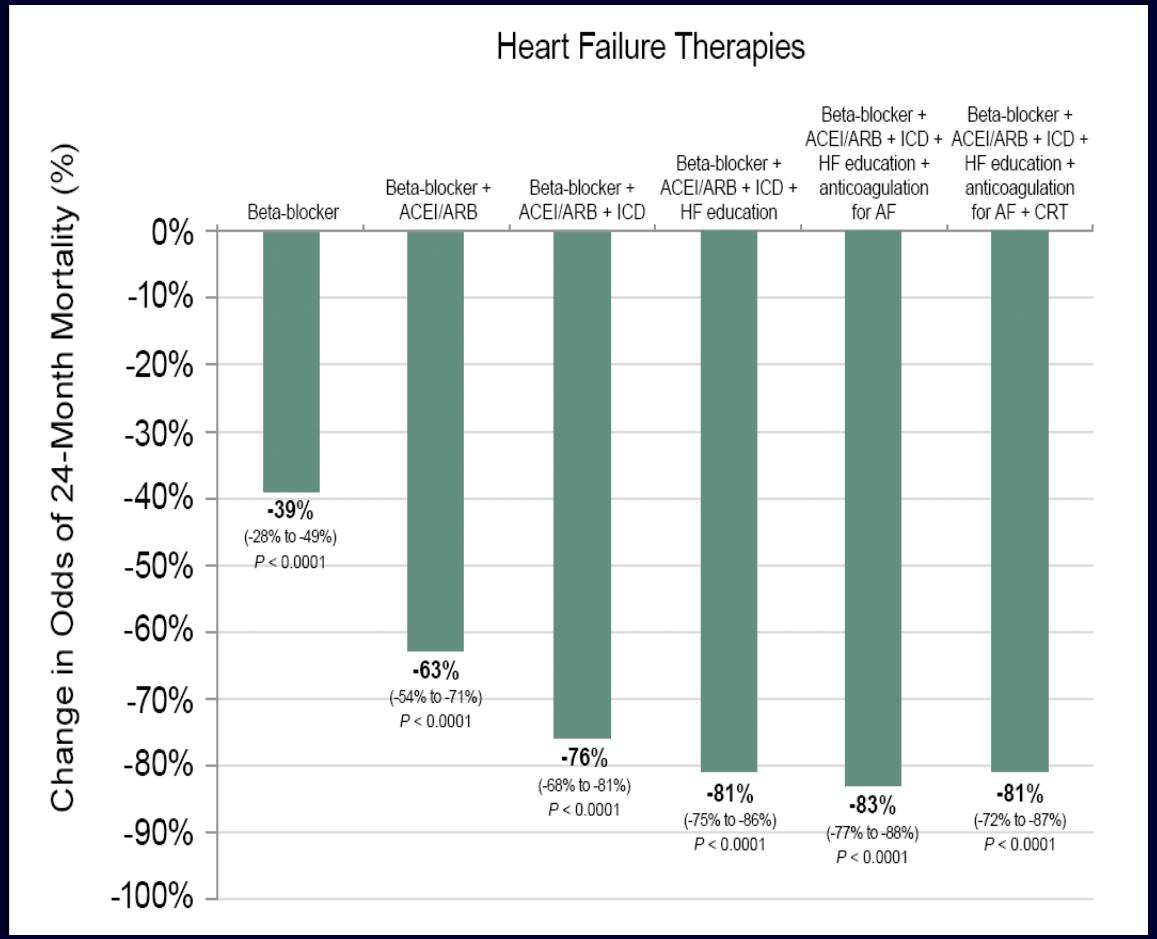
Final Takeaways

- The treatment of HF continues to evolve with new therapies and emerging new devices
- New treatment algorithms address the increasing complexity of HF therapy
- Application of GDMT for HFrEF markedly improves outcomes in clinical practice
- A specific intervention is now indicated for HFpEF, but mortality reducing therapies urgently needed
- Co-Morbidities matter; overzealous treatment may lead to harm
- PREVENTION of HF is essential

Improved Adherence to HF Guidelines Translates to Improved Clinical Outcomes in Real World Patients

- Each 10% improvement in guideline recommended composite care was associated with a 13% lower odds of 24-month mortality (adjusted OR 0.87; 95% CI, 0.84 to 0.90; *P<0.0001)*

ACC/AHA/HFSA Guideline Directed Therapy for Heart Failure Improves Outcomes



Fonarow GC, et al. *Circulation*. 2011;123:1601-1610.
Fonarow GC et al J Am Heart Assoc 2012;1:16-26

Advances in the Treatment of HF

- Increased attention to prevention
- ACEI / β-blocker / aldosterone antagonist combination established as the "cornerstone" of therapy
- ARNI further reduce morbidity and mortality
- Evidence that β-blockers' effects are not homogeneous
- Downgrade in recommendation for use of digoxin
- Integration of CRT and ICD device therapy into the standard therapeutic regimen
- Recognition that "special populations" of HF patients may benefit from or require different approaches
- New strategies to improve utilization of evidence based therapies

Revised from Yancy CW et al. *J Am Coll Cardiol.* 2013;62:1495-1539.