Success for Failure:

Heart Failure Management in 2017

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No relevant disclosures

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Objectives

- Clinical presentation and diagnosis
- Evaluation and treatment strategies
- Chronic disease management and hospitalization prevention

Heart failure disease burden

- Lifetime risk of 20% in Americans ≥ 40 years old
- >650,000 new HF cases / yr
- Nearly 6 million HF patients in the US and 1 million hospitalizations with HF as primary diagnosis
- Nearly one in four patients hospitalized with HF is rehospitalized within 30 days of discharge
- 12-15 million outpatient visits a year
- Absolute mortality of 50% within 5 years
- Direct costs >$30 billion / yr

Yancy CW et al. *J Am Coll Cardiol*. 2013;62:e147-e239.

Clinical Diagnosis

MAJOR CRITERIA

- Orthopnea/paroxysmal nocturnal dyspnea
- Rales
- Cardiomegaly
- Acute pulmonary edema
- Jugular venous distention
- Hepatojugular reflux
- S3

MINOR CRITERIA

- Ankle edema
- Night cough
- Exertional dyspnea
- Hepatomegaly
- Pleural effusion
- Tachycardia (>120 bpm)
- Decreased vital capacity
- Weight loss with HF treatment

HF = 2 major or 1 major + 1 minor

McKee PA et al. *N Engl J Med*. 1971;285:1441-1446.

Definition of HF based on LVEF

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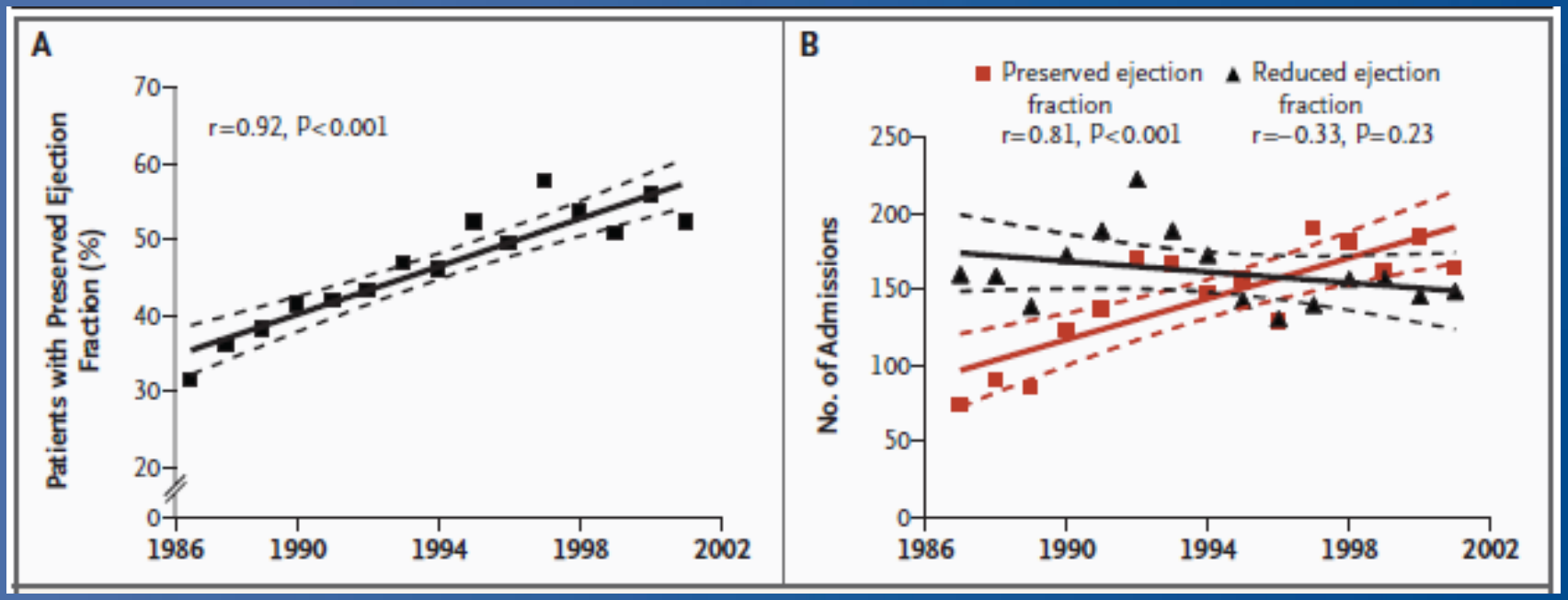
Classification	Ejection Fraction	Description
I. Heart Failure with Reduced Ejection Fraction (HF*r*EF)	≤40%	Also referred to as systolic HF. Randomized clinical trials have mainly enrolled patients with HF*r*EF and it is only in these patients that efficacious therapies have been demonstrated to date.
II. Heart Failure with Preserved Ejection Fraction (HF*p*EF)	≥50%	Also referred to as diastolic HF. Several different criteria have been used to further define HF*p*EF. The diagnosis of HF*p*EF 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. HF*p*EF, 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 HF*p*EF.
b. HF*p*EF, Improved	>40%	It has been recognized that a subset of patients with HF*p*EF previously had HF*r*EF. 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.

Epidemiology

Prevalence of HFpEF is estimated at 50% of all HF

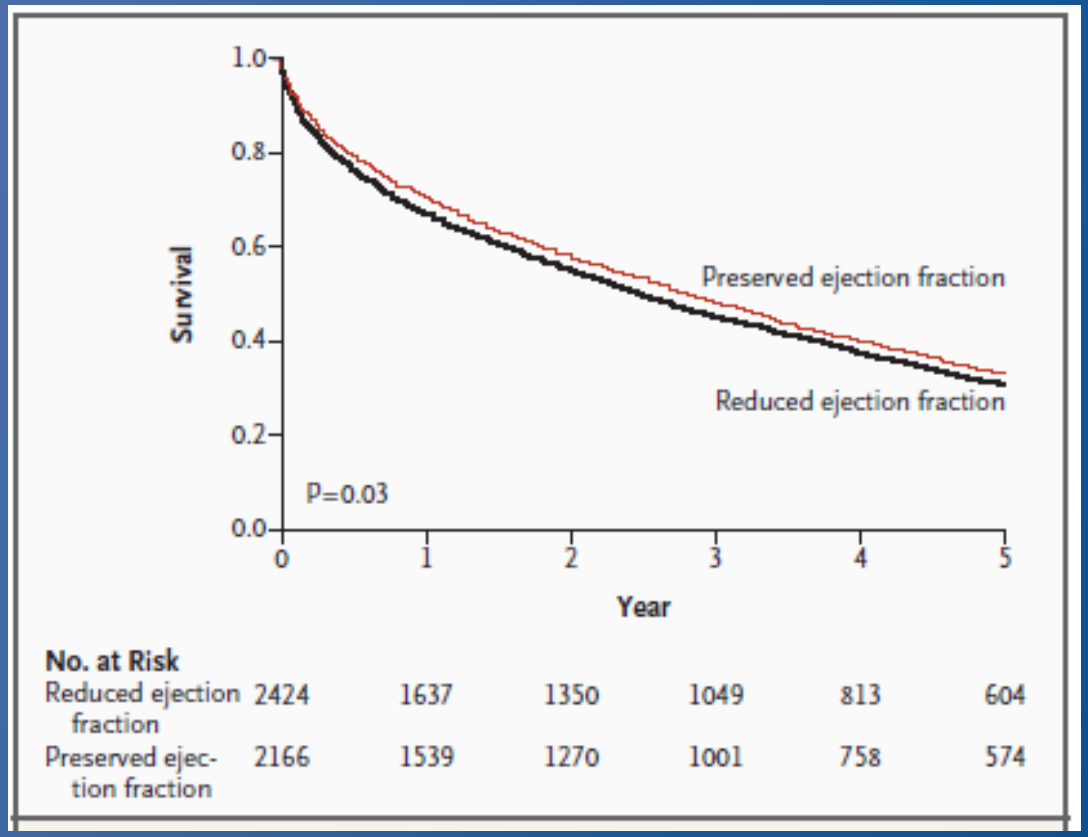


Prevalence of HFpEF

Number of admissions for HFpEF and HFrEF

Owan TE, et al. *NEJM* 2006;355:251-9.

Epidemiology



K-M survival curves for HFpEF v. HFrEF patients

Owan TE, et al. *NEJM* 2006;355:251-9.

Evaluation

HF Etiologies

- Ischemic
- Familial
- Metabolic
- Thyroid
- Toxic (etoh, cocaine, chemo)
- Nutritional
- Tachycardia-induced
- Myocarditis
- HIV
- Chagas
- Connective tissue disease
- Peripartum
- Iron overload
- Amyloidosis
- Sarcoidosis
- Stress
- Storage disease
- Hypertrophic
- ARVC
- HFpEF

Yancy CW et al. *J Am Coll Cardiol*. 2013;62:e147-e239.

Initial evaluation

In all cases:

- History, exam, ECG
- Echocardiogram
- Laboratory testing
- Assessment of functional capacity
- Assessment for CAD in patients at risk

In selected cases:

- Cardiac catheterization
- Cardiac MRI
- Endomyocardial biopsy
- Genetic testing

Yancy CW et al. *J Am Coll Cardiol*. 2013;62:e147-e239.

Initial evaluation

A **complete history and physical examination** should be obtained/performed in patients presenting with HF to identify cardiac and non-cardiac disorders or behaviors that might cause or accelerate the development or progression of HF.

In patients w idiopathic DCM, a **3-generational family history** should be obtained to aid in establishing the diagnosis of familial DCM.

Volume status and vital signs should be assessed at each patient encounter:

- Weight
- JVP
- Peripheral edema
- Orthopnea

Diagnosis

Initial labs in patients presenting with HF should include:

- CBC, BMP with BUN and Cr, Hepatic Panel
- UA, TSH, Lipid Profile

Serial monitoring, when indicated, should include serum electrolytes and renal function.

A 12-lead **ECG** should be performed initially on all patients presenting with HF.

Screening for hemochromatosis or HIV is reasonable in selected patients who present with HF.

Diagnostic tests for rheumatologic disease, amyloid, pheo are reasonable, when suspected.

Classification of HF

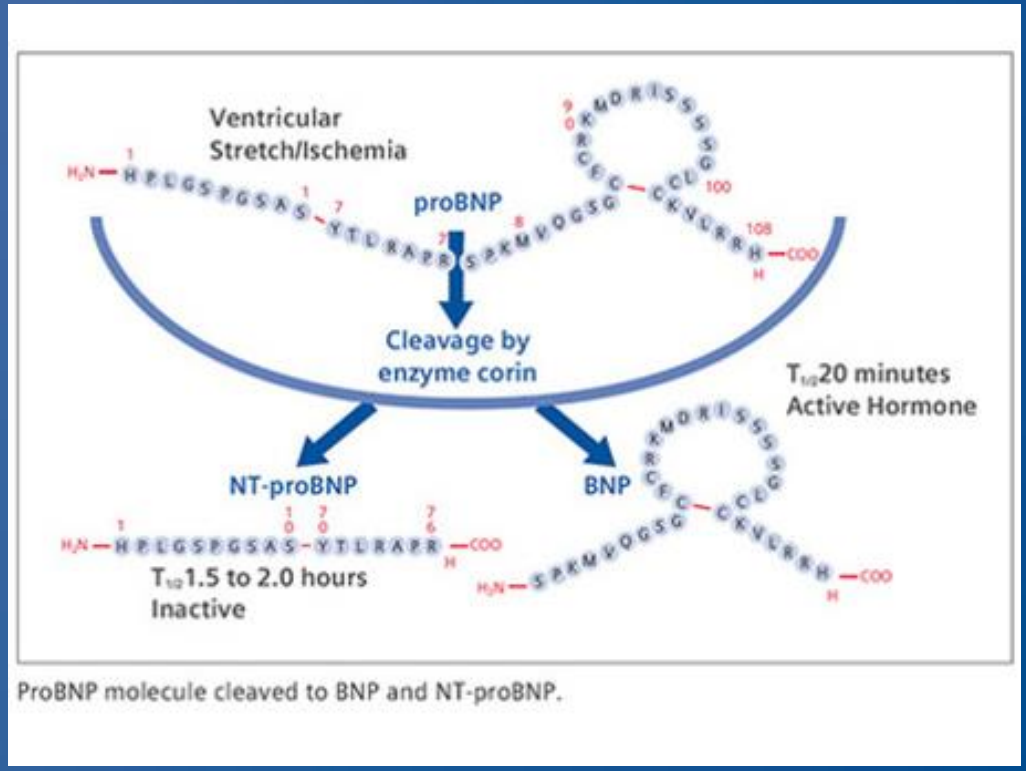
ACCF/AHA Stages of HF		NYHA Functional Classification	
A	At high risk for HF but without structural heart disease or symptoms of HF.	None	
B	Structural heart disease but without signs or symptoms of HF.	I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.
C	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:e147-e239.

Brain natriuretic peptide

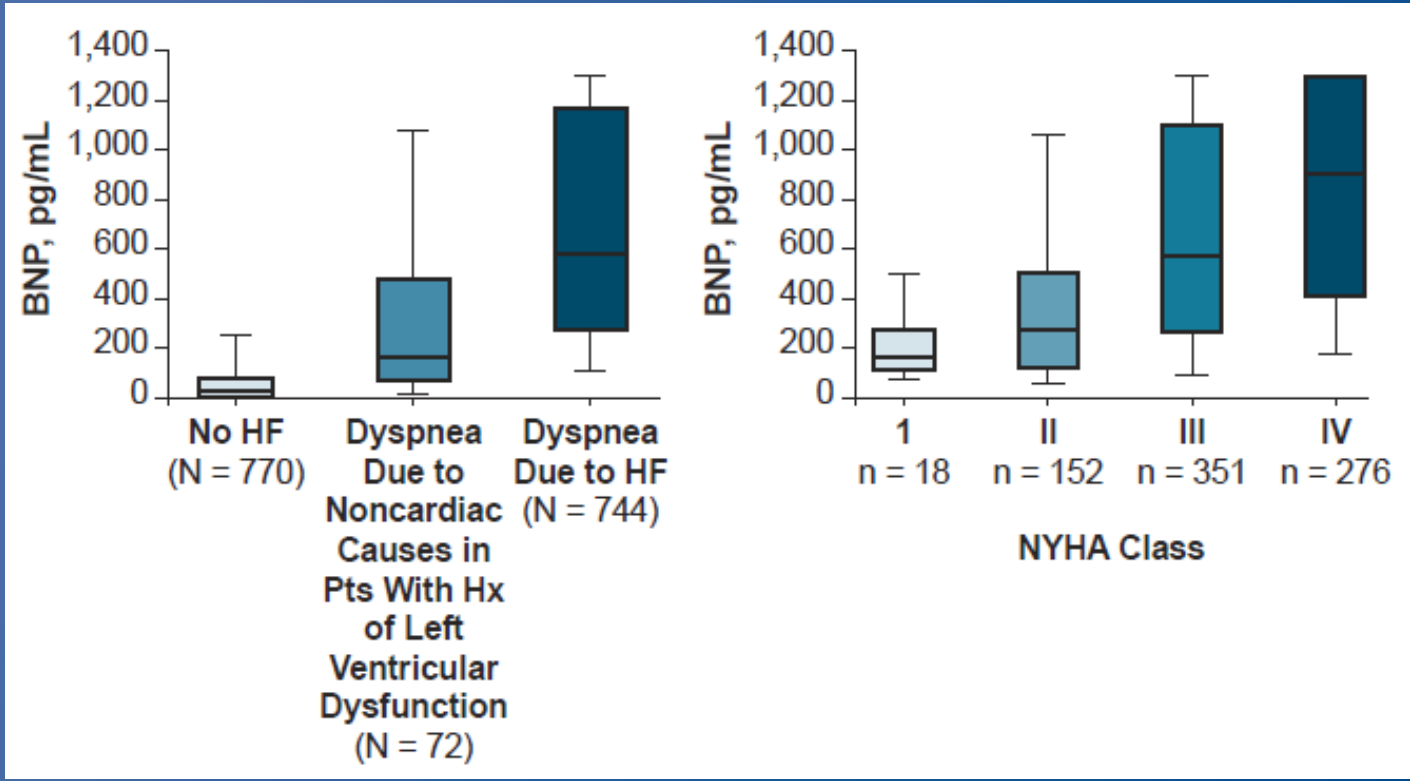
Pro-BNP = common 108-AA precursor

Cleaved into BNP and NT-pro BNP



ProBNP molecule cleaved to BNP and NT-proBNP.

BNP in ER patients with dyspnea



BNP ≥100 pg/mL:
Positive predictive value 79%
Negative predictive value 89%

NT-proBNP ≥900 pg/mL:
Positive predictive value 77%
Negative predictive value 92%

Maisel AS et al. *N Engl J Med*. 2002;347:161-167.
Krauser DG et al. *Am Heart J.* 2005;149:744-750.

BNP: Limitations

- Levels may increase with age, female gender, pressure overload, CKD
- Levels decrease with obesity, treatment (eg, carvedilol, spironolactone)
- Levels are lower in HF with preserved EF

- BNP-guided therapy trials: mixed results
  - Favorable metanalyses
  - Ongoing prospective trial

Cardiac Failure Review , 2015; 1 (2):96–101

Recommendations for BNP

In ambulatory patients with dyspnea, pro-BNP is useful to support the **diagnosis of HF**, especially when uncertain.

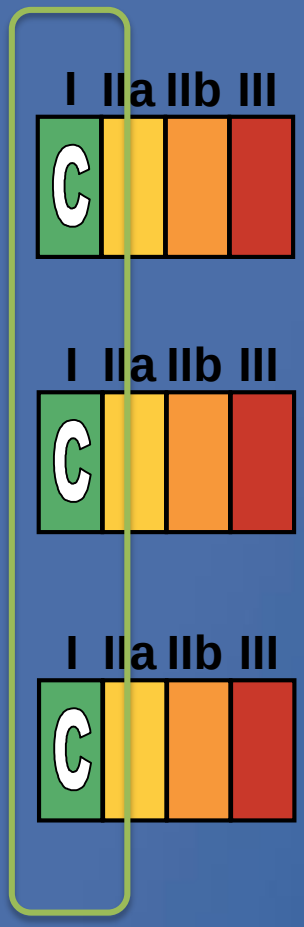
Measurement of BNP or NT-proBNP is useful for **establishing prognosis or disease severity** in chronic HF.

BNP- or NT-proBNP guided HF therapy can be useful to achieve optimal dosing of GDMT in select clinically euvolemic patients.

Using serial BNPs to reduce hospitalization

Using other biomarkers for additive stratification

Noninvasive Cardiac Imaging



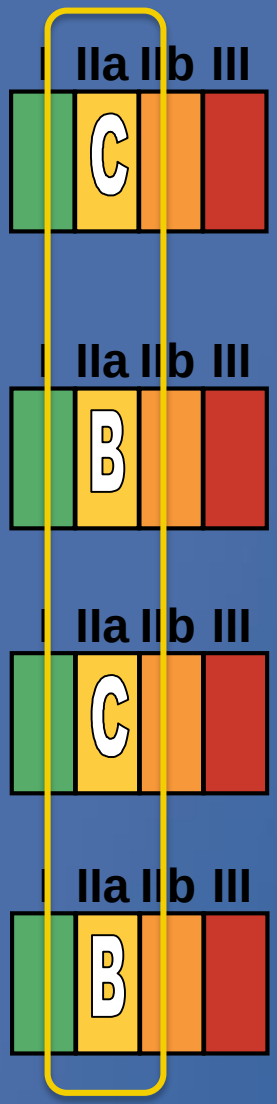
Patients with suspected or new-onset HF, or ADHF, should undergo a **chest x-ray** to assess heart size and pulmonary congestion, and detect items on differential diagnosis

A **2-dimensional echocardiogram with Doppler** should be performed during initial evaluation to assess ventricular function, size, wall thickness, wall motion, and valve function.

Repeat measurement of EF and measurement of the severity of structural remodeling are useful to provide information in patients with HF who:

1. Have had a significant change in clinical status
2. Have experienced or recovered from a clinical event
3. Have received treatment, including GDMT, that might have had a significant effect on cardiac function
4. May be candidates for device therapy.

Noninvasive Cardiac Imaging



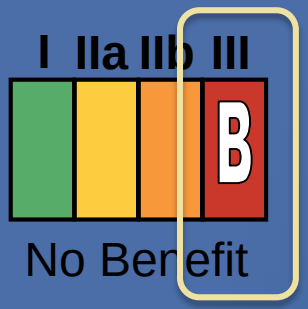
Noninvasive detection of myocardial ischemia and viability is reasonable in patients presenting with de novo HF who have known CAD and no angina, unless the patient is not eligible for revascularization of any kind.

Viability assessment is reasonable in select situations when planning revascularization in HF patients with CAD.

Ventriculogram or **magnetic resonance imaging** can be useful to assess LVEF and volume when echocardiography is inadequate.

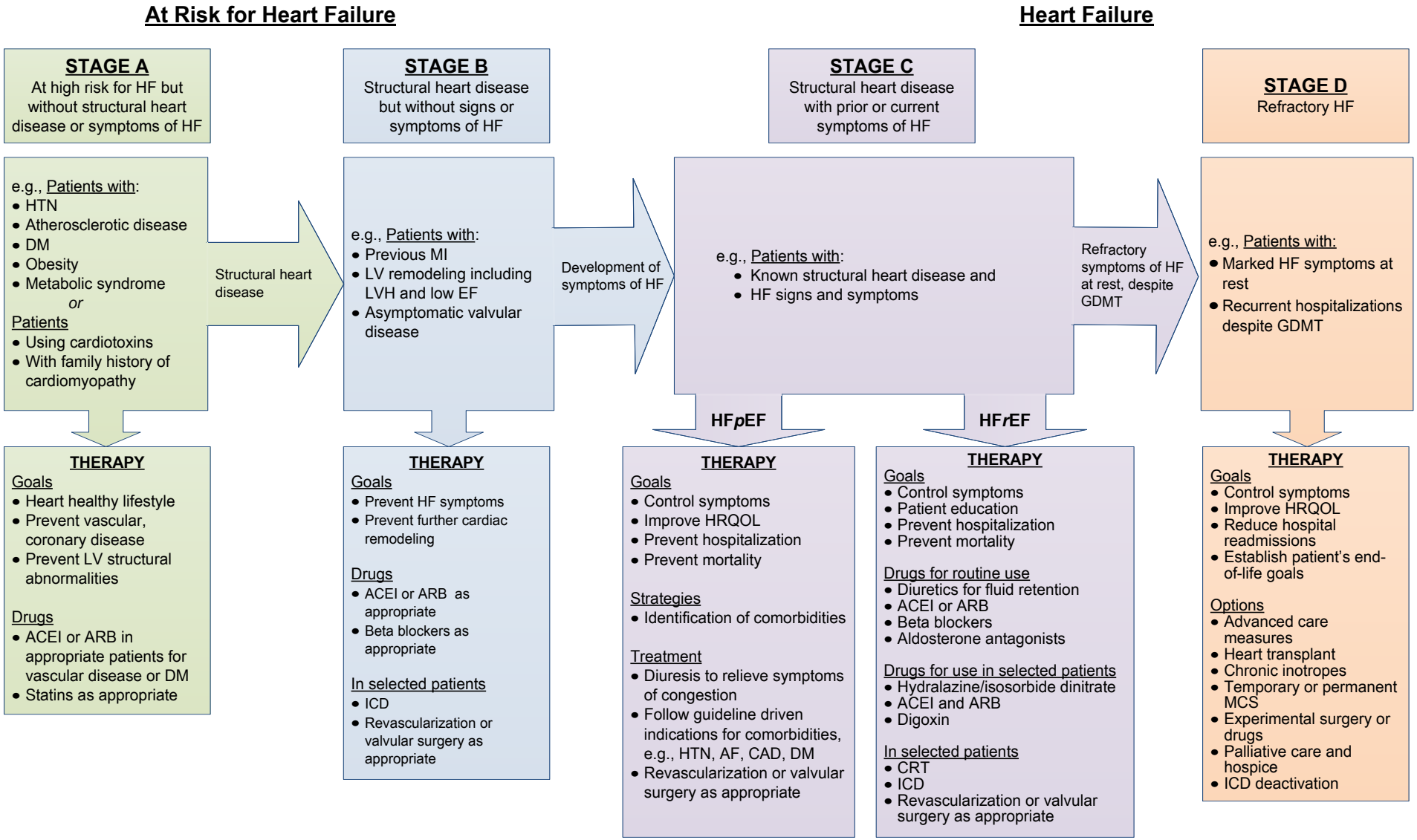
Magnetic resonance imaging is reasonable when assessing myocardial infiltrative processes or scar burden.

Noninvasive Cardiac Imaging



Routine repeat measurement of LV function assessment in the absence of clinical status change or treatment interventions should not be performed.

Treatment strategy



Yancy CW et al. *J Am Coll Cardiol*. 2013;62:e147-e239.

HFrEF Guideline-Directed Medical Treatment

ACE/ARB
- First line therapy
- NYHA Class I-IV

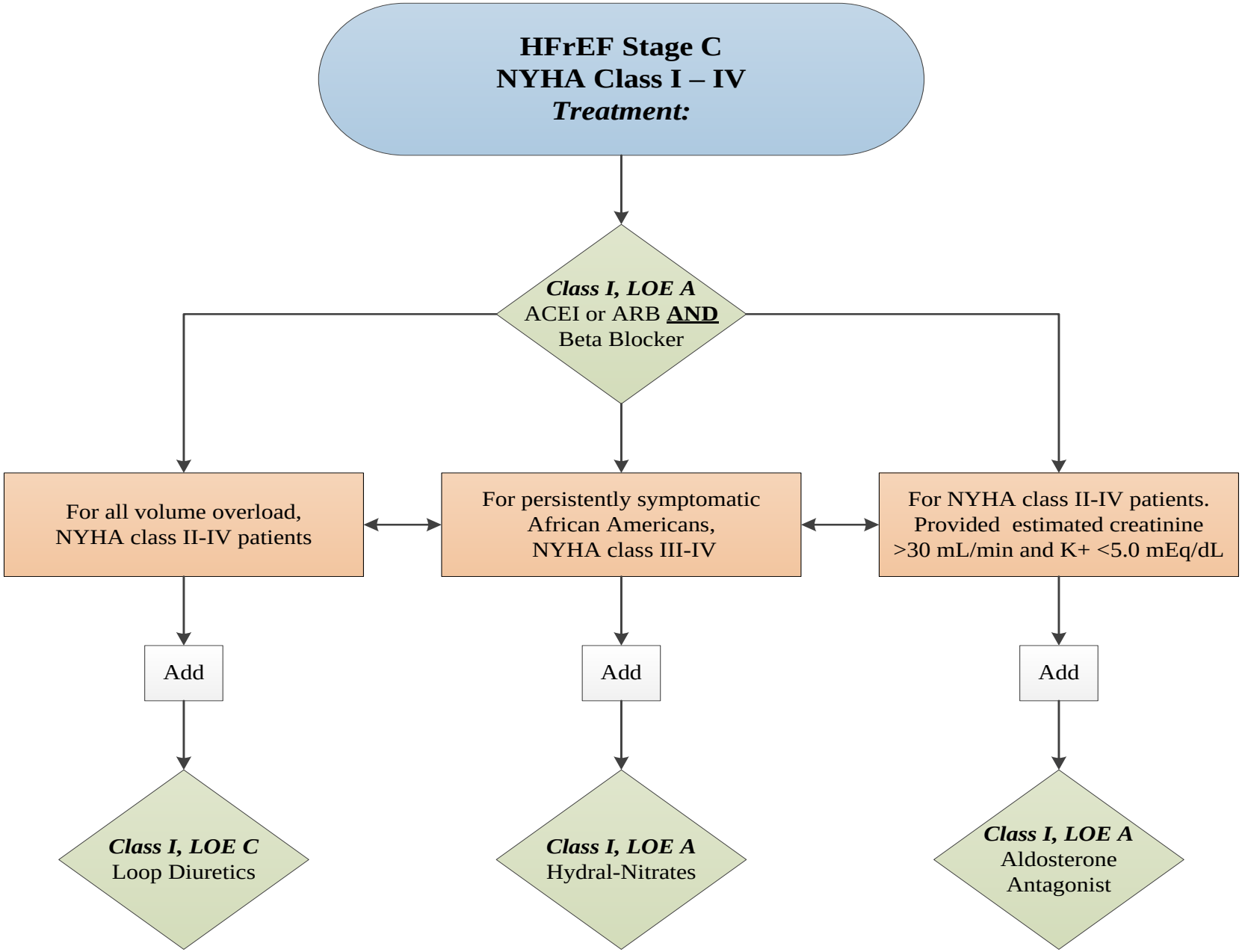
Beta-Blockers
- First line therapy
- NYHA Class I-IV
- Carvedilol, metoprolol succinate, bisoprolol

Aldosterone Antagonists
- Underutilized
- Indicated in almost all NYHA II-IV
- Lab cutoffs: K < 5.0, GFR > 30, SCr < 2.5 (Men) and 2.0 (Women)

Hydralazine-ISDN
- Consider in African-American with NYHA III-IV HFrEF
- Alternative to Ace/Arb

Strong evidence!

Study Name	LVEF	Rx	Year	Findings
VHeFT-I	< 45	Hyd-ISDN	1986	↓mortality @ 36 months; prazosin bad
VHeFT-II	< 45	Hyd-ISDN vs. Enalapril	1991	Enalapril > Hyd-ISDN (mortality)
A-HeFT	≤ 35	Hyd-ISDN in Af Am	2004	↓mort/hosp/better QOL in Af Am NYHA III-IV
CONSENSUS	CXR/IV	Enalapril vs. Placebo	1987	↓mortality (250 pts)
SOLVD	≤ 35	Enalapril vs. Placebo	1991/2	Improved survival and prevention of CHF
ELITE-2	≤ 40	Losartan vs. Captopril	2000	No change in mortality, SCD
Val-HeFT	<40	Valsartan BID vs. Placebo	2001	ARB > placebo; none if added to ACE/BB
CHARM	≤ 40	Cande + ACE (added) Cande vs. Placebo (altern)	2004	Candesartan ↓ CV death/HF independent of ACEI
US Carvedilol	≤ 35	Coreg vs. Placebo	1996	↓ mortality
MOCHA	≤ 35	Coreg 6.25 range to 25 BID	1996	Benefit at 6.25, but best at 25 BID
MERIT-HF	< 40	Metop Succ vs. Placebo	1999	↓ death, CV death, SCD, HF
COPERNICUS	< 25	Coreg in severe HF	2001	↓ mortality, even in sick patients
COMET	< 35	Coreg 25 vs Metop 50 BID	2003	Coreg > Metop tartrate
RALES	≤ 35/III-IV	Spiro vs. Placebo	1999	↓ mortality
EPHESUS	≤ 40 p MI + HF/DM	Eplerenone vs. Placebo	2003	↓ mortality/HF
EMPHASIS	≤ 30/II	Eplerenone vs. Placebo	2011	↓ mortality/HF
DIG	*≤ 45*	*Digoxin vs. Placebo*	*1997*	*no mortality change, ↓HF hosp*
PARADIGM	*< 40*	*Entresto vs. Enalapril*	*2014*	*↓ death/HF hosp*
SHIFT	*≤ 35*	*Ivabradine vs. Placebo*	*2010*	*↓ HF admission*



Yancy CW et al. *J Am Coll Cardiol*. 2013;62:e147-e239.

Medical Therapy for Stage C HF*r*EF: Magnitude of Benefit Demonstrated in RCTs

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Table. Demonstrated Benefits of Evidence-Based Therapies for Patients With Heart Failure and Reduced Ejection Fraction

Evidence-Based Therapy	Relative Risk Reduction in All-Cause Mortality in Pivotal Randomized Clinical Trial(s), %	NNT to Prevent All-Cause Mortality Over Time	NNT for All-Cause Mortality[a]
ACEI/ARB	17	22 over 42 mo	77
ARNI[b]	16	36 over 27 mo	80
β-Blocker	34	28 over 12 mo	28
Aldosterone antagonist	30	9 over 24 mo	18
Hydralazine/ nitrate	43	25 over 10 mo	21
CRT	36	12 over 24 mo	24
ICD	23	14 over 60 mo	70

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; CRT cardiac resynchronization therapy; ICD, implantable cardioverter defibrillator, NNT, number needed to treat.

[a] Standardized to 12 months.

[b] Benefit of ARNI therapy incremental to that achieved with ACEI therapy. For the other medications shown, the benefits are based on comparisons to placebo control.

Fonorow G. JAMA Cardiology; 2016

Heart Failure 2016 Guideline Update

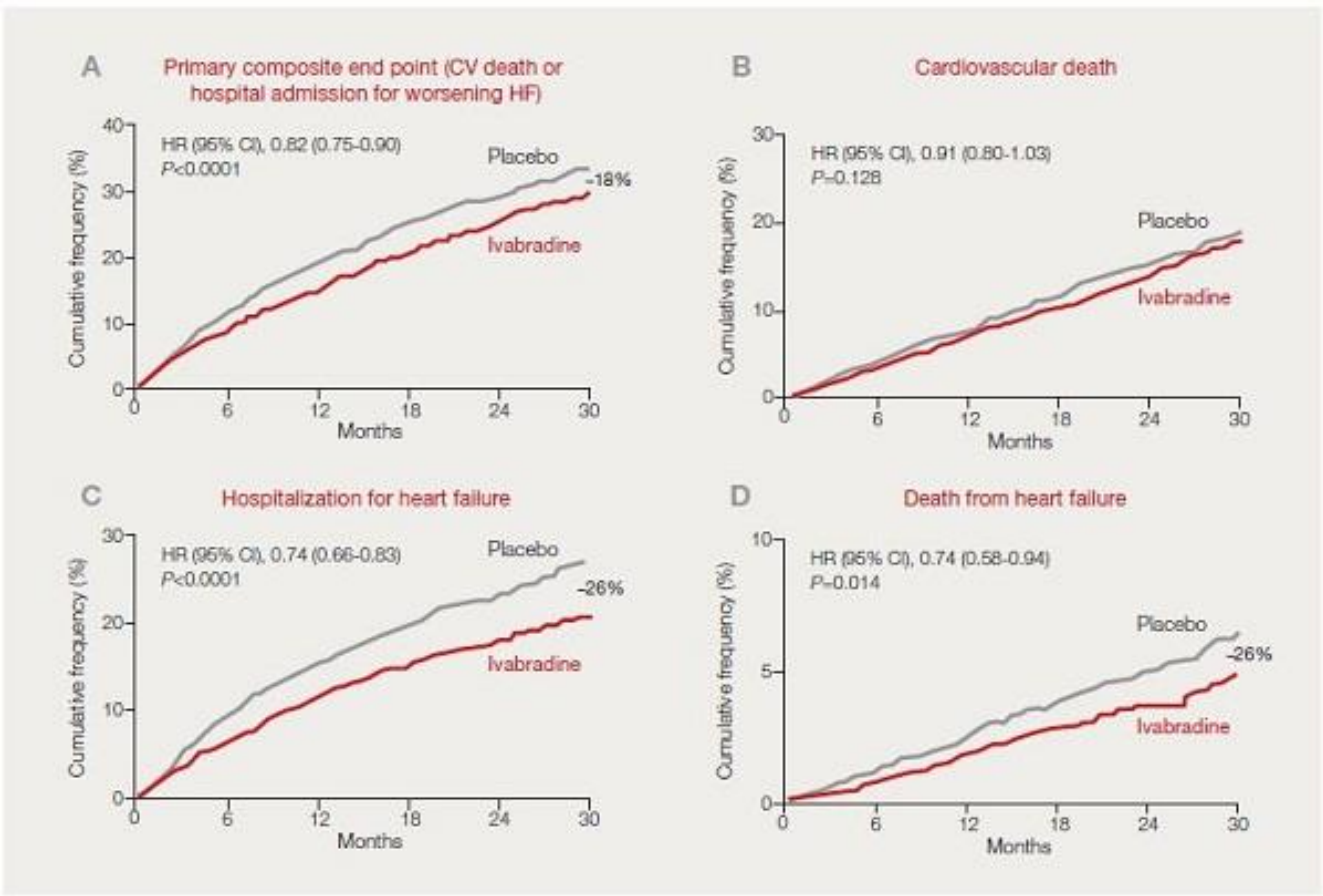
- Ivabradine
- Neprilysin inhibition

SHIFT Trial: Ivabradine

Inclusion Criteria
- NYHA II-IV
- Hospital in prior year
- LVEF < 35%
- NSR
- HR > 70 bpm

Primary endpoint
24 versus 29%
(CV Death/HF Hosp)

Does not reduce Death



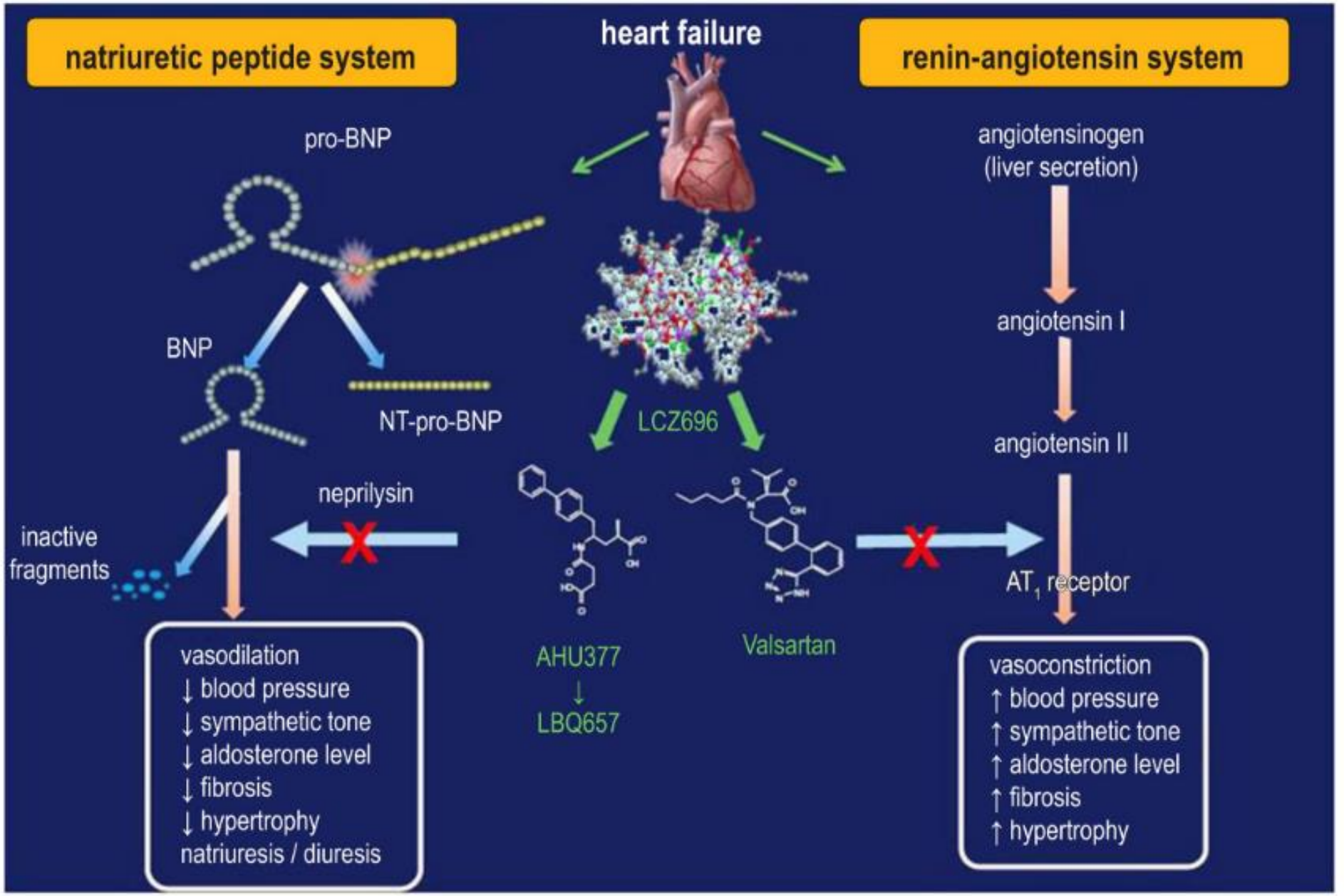
Swedberg K et al. *Lancet*. 2010;376:875-885.

Ivabradine—Guideline update

COR	LOE	Recommendations
IIa	B-R	Ivabradine can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA class II-III), stable, chronic HFrEF (LVEF ≤35%) who are receiving GDMT, including a β blocker at maximally tolerated dose, and who are in sinus rhythm with a heart rate ≥70 bpm at rest

- Incremental benefits of ivabradine are more pronounced in patients with higher resting heart rates
- Magnitude of heart rate reduction achieved with ivabradine + β blockade is the principal determinant of subsequent outcome

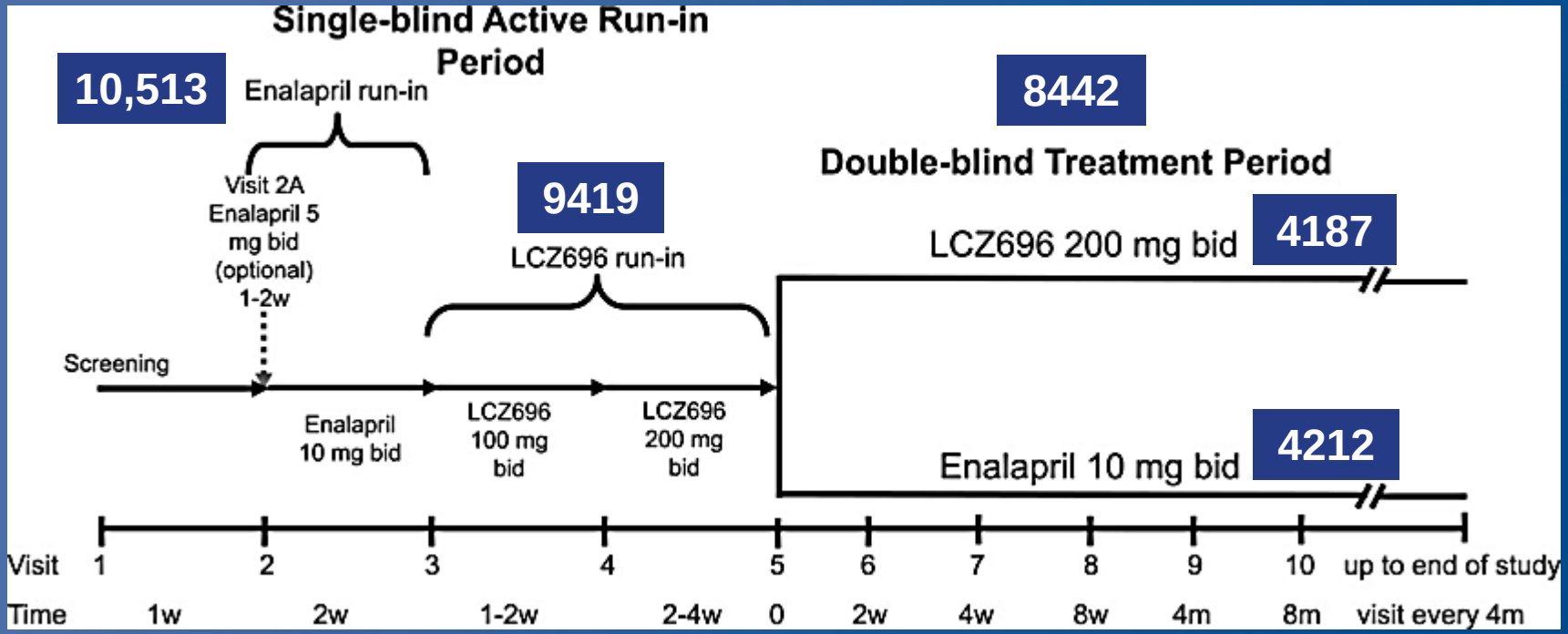
Yancy CW et al. *J Am Coll Cardiol*. 2016;68:1476-1488.



Solomon, S et al. Lancet. 2012

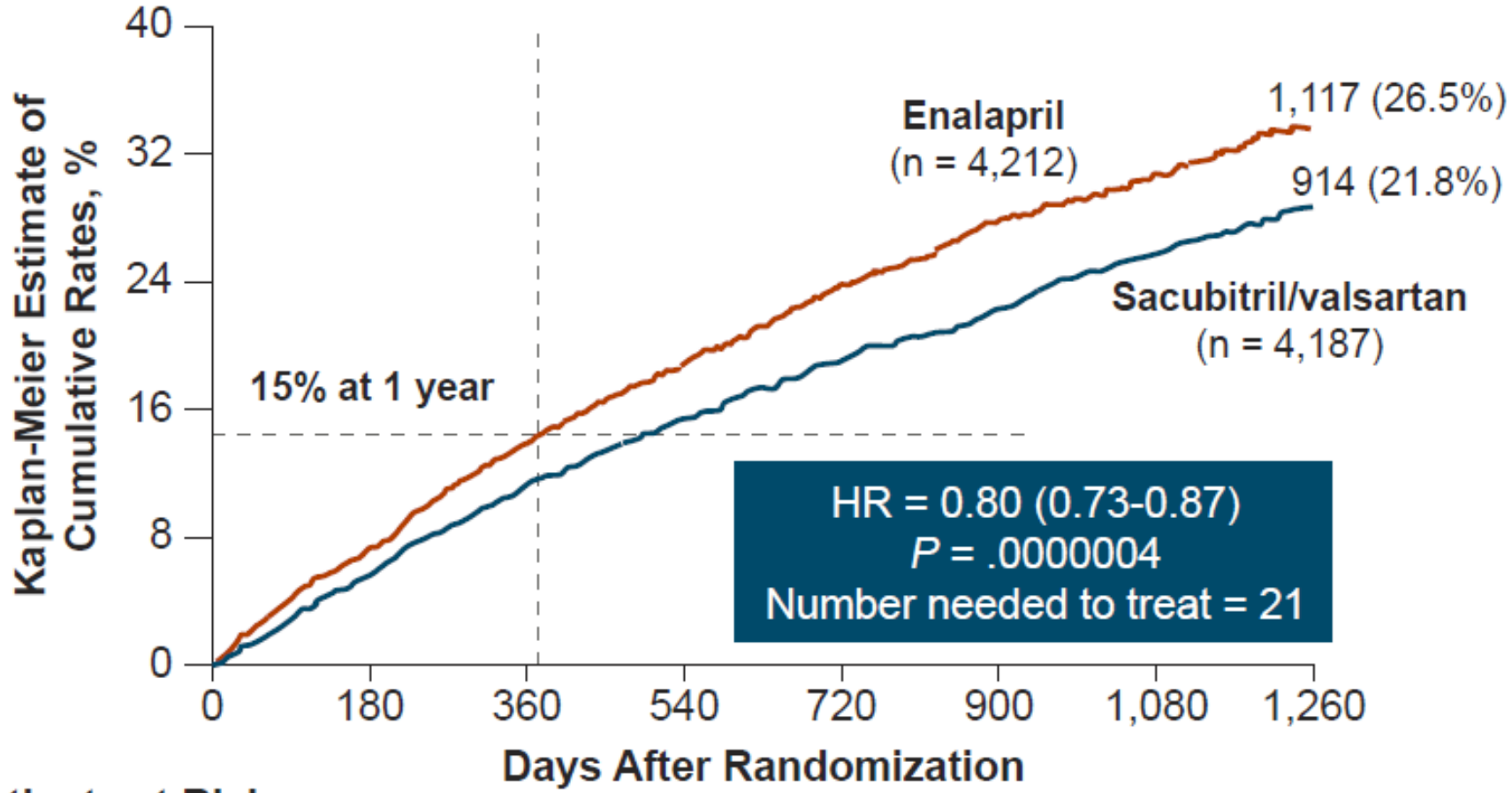
PARADIGM: Study design

Multicenter, international RCT



McMurray JJ, et. al. *Eur J Heart Fail.* 2013 Sep;15(9):1062-73

Primary endpoint: CV death/HF hospitalization

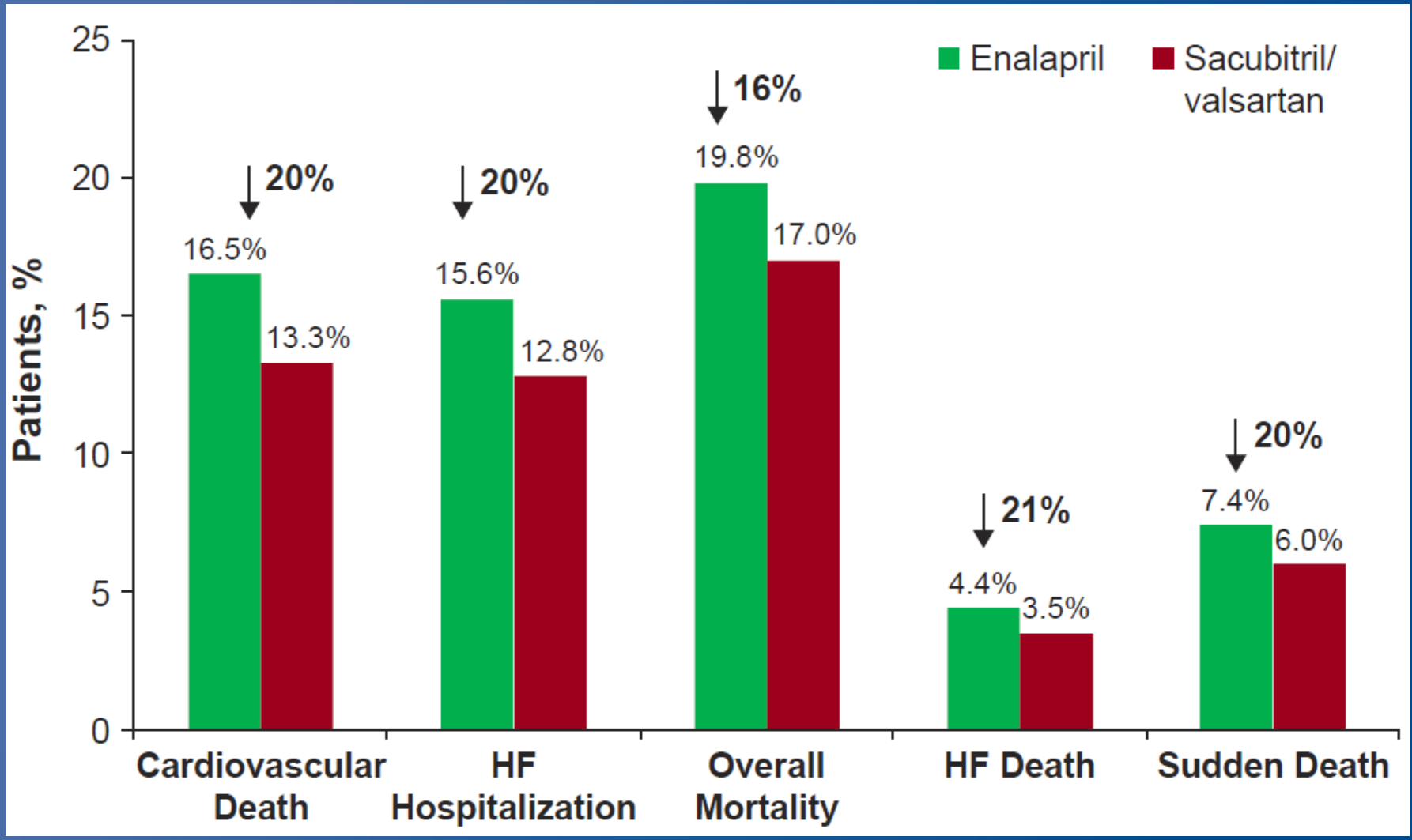


Patients at Risk

LCZ696	4,187	3,922	3,663	3,018	2,257	1,544	896	249
Enalapril	4,212	3,883	3,579	2,922	2,123	1,488	853	236

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

PARADIGM: endpoints



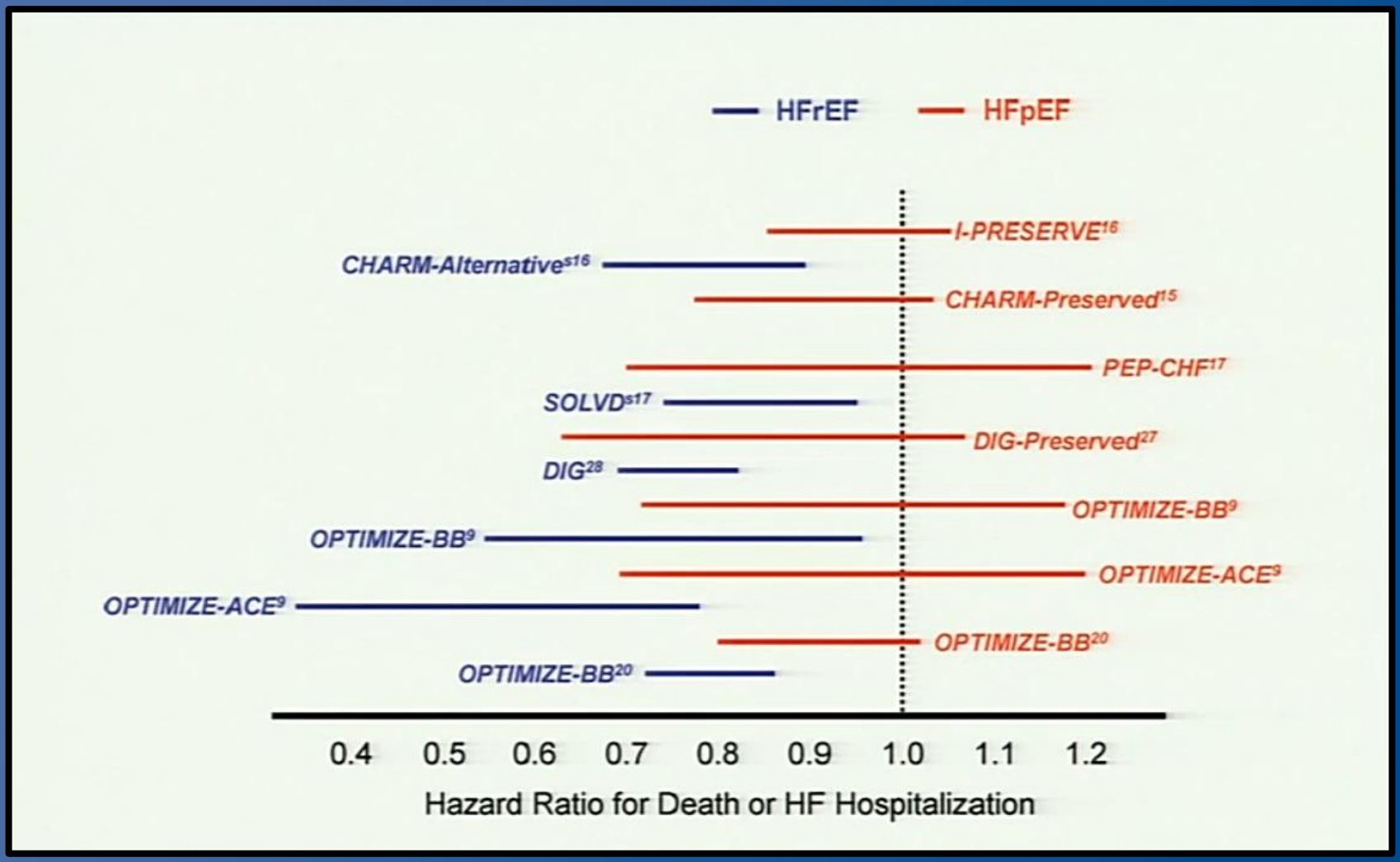
McMurray JJ et al. *N Engl J Med*. 2014;371:993-1004.
Desai AS et al. *Eur Heart J.* 2015;36:1990-1997.

ARNI—Guideline update

COR	LOE	Recommendation
I	B-R	ACEI **or** ARB **or** ARNI in conjunction with β blockers + MRA (where appropriate) is recommended for patients with chronic HFrEF to reduce morbidity and mortality
I	B-R	In patients with chronic, symptomatic HFrEF NYHA class II or III who tolerate and ACEI or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality
III	B-R	ARNI should NOT be administered concomitantly with ACEI or within 36 hours of last ACEI dose
III	C-EO	ARNI should NOT be administered to patients with a history of angioedema

Yancy CW et al. *J Am Coll Cardiol*. 2016;68:1476-1488.

What about HFpEF?



Borlaug BA, Redfied MM. Circ 2011;123:2006-2014

Guidelines for Treatment of HFpEF

- **Class I:**
  - Diuretics
  - HTN management
- **Class IIA:**
  - Management of AF
  - Coronary revascularization
  - Use beta blockers, ACE/ARB for HTN
- **Class IIB:**
  - ARBs to decrease hospitalization

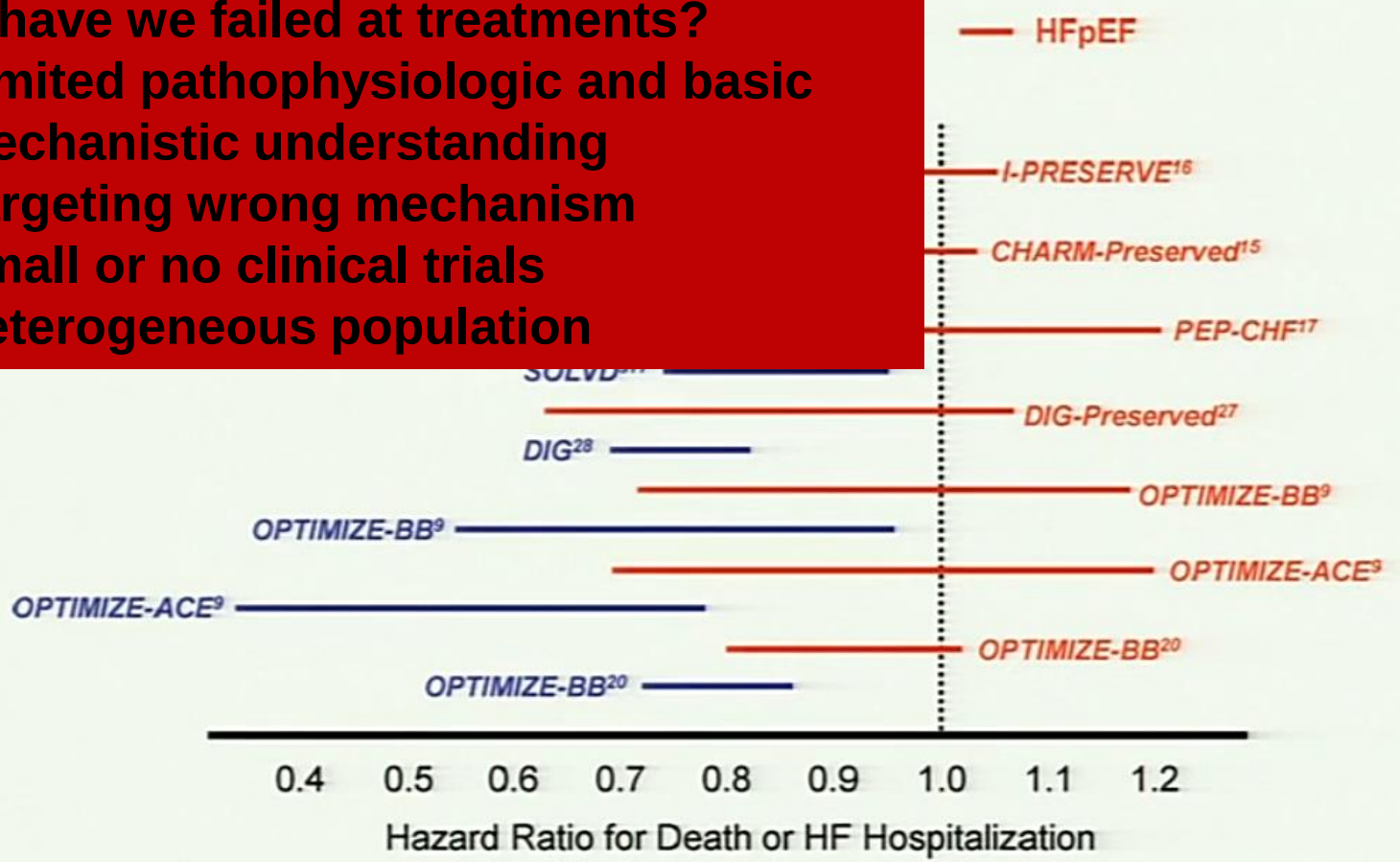
Yancy CW et al. *J Am Coll Cardiol*. 2013;62:e147-e239.

Signs/Symptom:	Pearls:
• Fluid overload, renovascular congestion	Diuretics; consider change to Torsemide, Bumetanide Ultrafiltration
• RV Dysfunction	Digoxin
• Acute HF	? Dopamine
• Hospitalization	ARB, Cardiomems, spironolactone

What about HFpEF?

Why have we failed at treatments?

- **Limited pathophysiologic and basic mechanistic understanding**
- **Targeting wrong mechanism**
- **Small or no clinical trials**
- **Heterogeneous population**



Borlaug BA, Redfied MM. Circ 2011;123:2006-2014

AHA Strategically Focused Research Network: *Go Red for Women*

Heart Failure with Preserved Ejection Fraction:

Female Sex Hormones and Cyclic GMP-PKG Modulation of Cardiac Disease and Metabolism

Center PI: Pamela Ouyang, MBBS
Clinical Site PI: Kavita Sharma, MD
Basic PI: David Kass, MD
Population PI: Wendy Post, MD MS

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HFpEF Future Directions

- Inorganic Nitrate Studies
  - Increased exercise capacity
  - Improved cardiac output reserve and ventricular reserve in setting of stress (exercise)
- Novel PDE targets
- LA mechanical unloading
  - Potential benefit seen in simulation model of low-flow, micropump-based LA decompression device

Disease Management and Hospitalization Prevention

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Hospitalization for Heart Failure

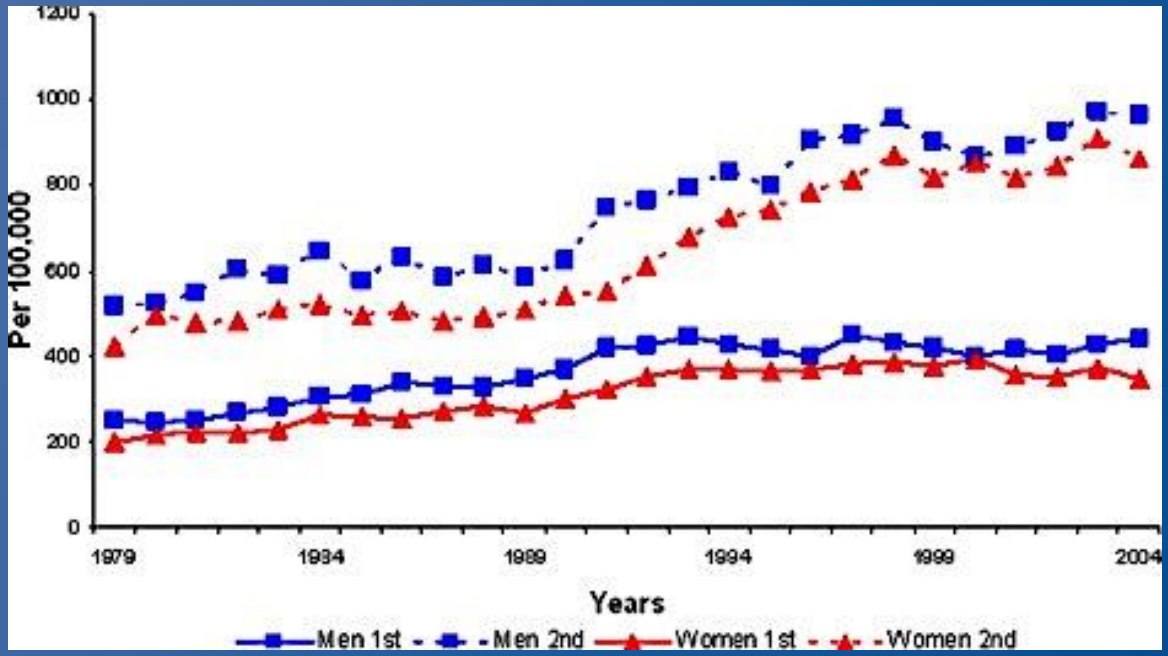
New-onset or worsening HF requiring urgent therapy and hospitalization

- 15% mortality and 30% readmission rate in the 3-6 months after discharge

- Comprised of:
  - Worsening chronic HF (80%)
  - New-onset HF (15%)
  - Advanced/end-stage HF (5%)

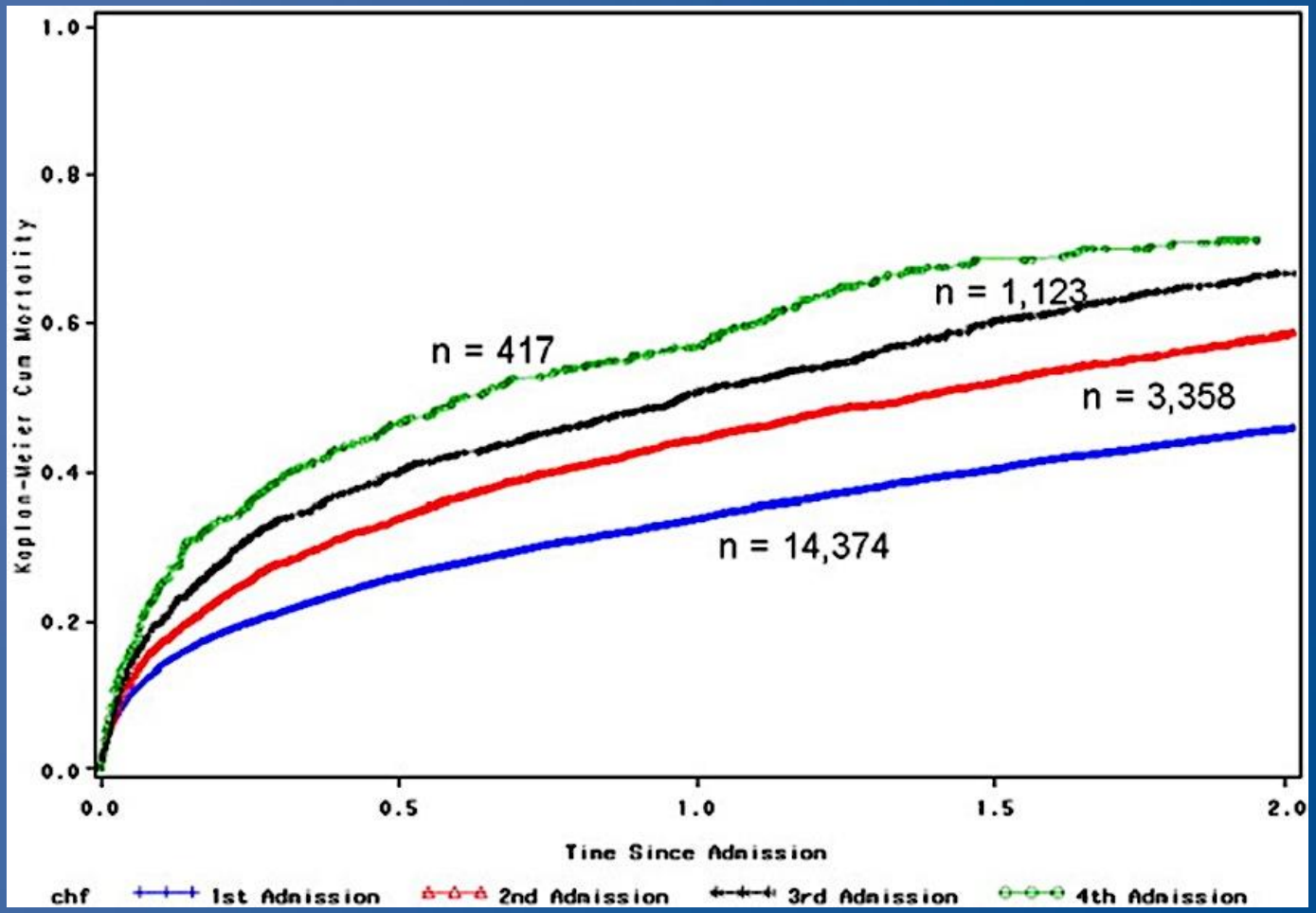
Gheorghiade M et al. JACC 2013;61:391-403

HF hospitalizations increasing



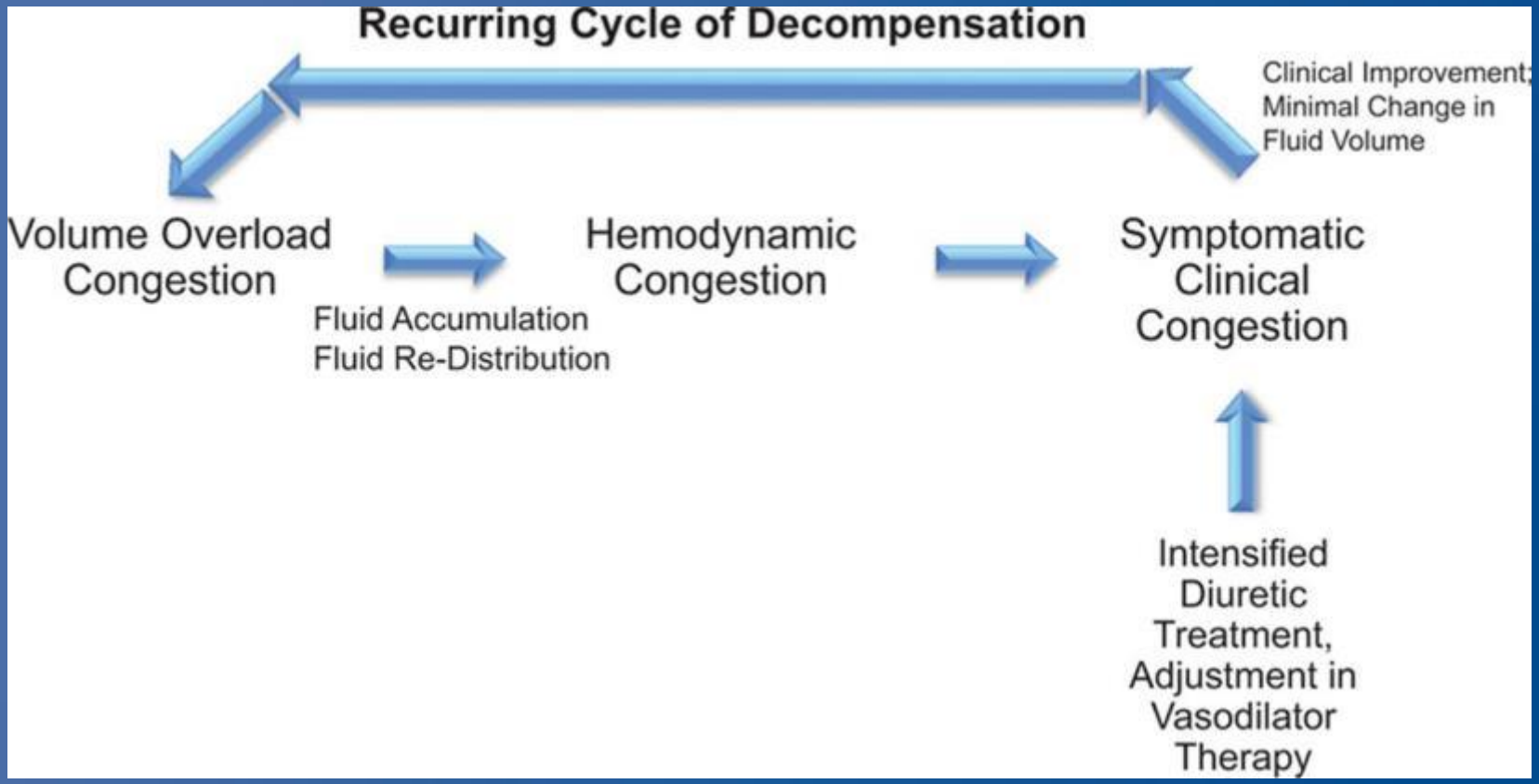
Fang J et al. JACC 2008;52:428-434

HF hospitalizations and mortality



Setoguchi S et al. Am Heart J 2007;154:26026

Concept of recurring symptomatic clinical volume overload and congestion in chronic heart failure.



Wayne L. Miller Circ Heart Fail. 2016;9:e002922

Recurrent congestion is common

- EVEREST trial: discharge composite congestion score

Table 4 Outcomes (*n*, %) by composite congestion score at discharge

	Discharge CCS				Overall[a]
	0	1	2	3–9	
Total (*n*)	890	505	247	297	2061
HHF	233, 26.2%	176, 34.9%	86, 34.8%	103, 34.7%	629, 30.5%
ACM	170, 19.1%	125, 24.8%	62, 25.1%	127, 42.8%	543, 26.4%
ACM + HHF	317, 35.6%	231, 45.7%	113, 45.8%	177, 60.0%	912, 44.3%

Ambrosy AP et al. European Heart Jour 2013;34:835-843

Decongestion and outcomes

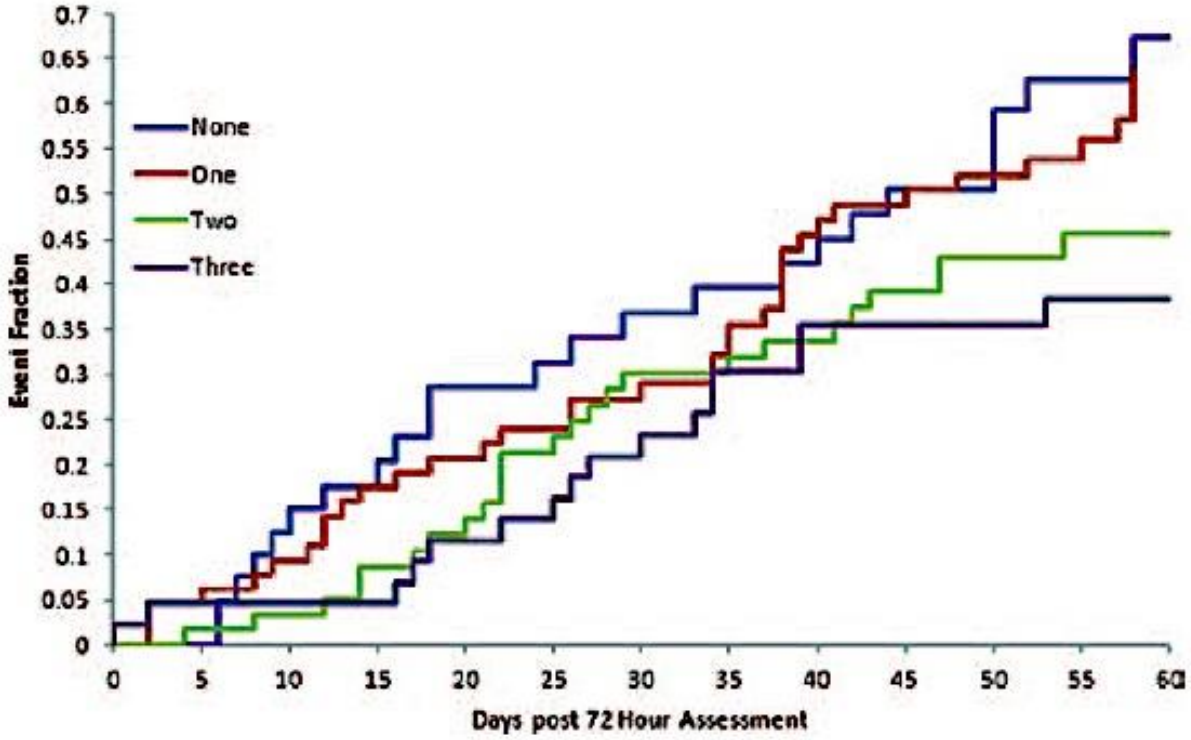
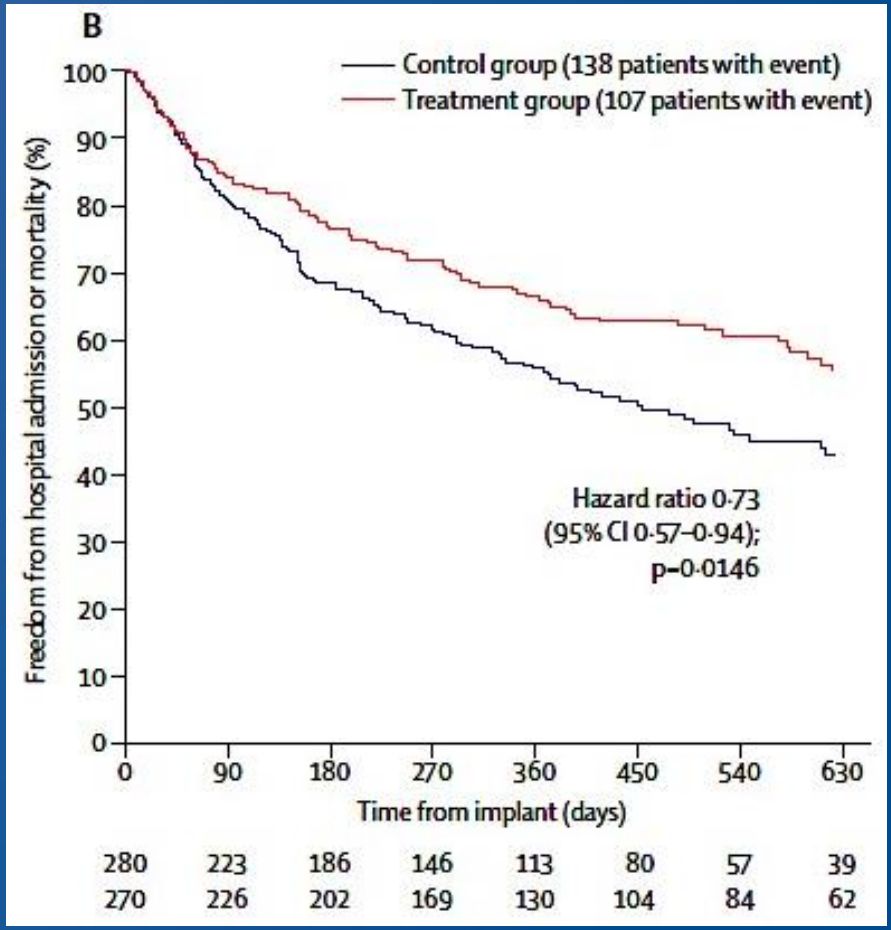


Figure. Relationship between number of markers of decongestion above median* and time to 60-day risk of emergency department (ED) visit, rehospitalization, or death. *Median net fluid loss, 3.8 L; median net weight loss, 6.5 lbs; median percent reduction in N terminal B-type natriuretic peptide 24.3%.

Kociol RD et al. Circ Heart Fail 2013

Implantable monitors

- CHAMPION:
  - CardioMEMS pulmonary artery sensor
  - 550 pts, NYHA III
  - 28% absolute reduction in HF hospitalizations at 6 mon
  - Had recommendations on how to guide therapy



Abraham W et. al. Lancet 2011;377:658-666

Transitioning from hospital to home

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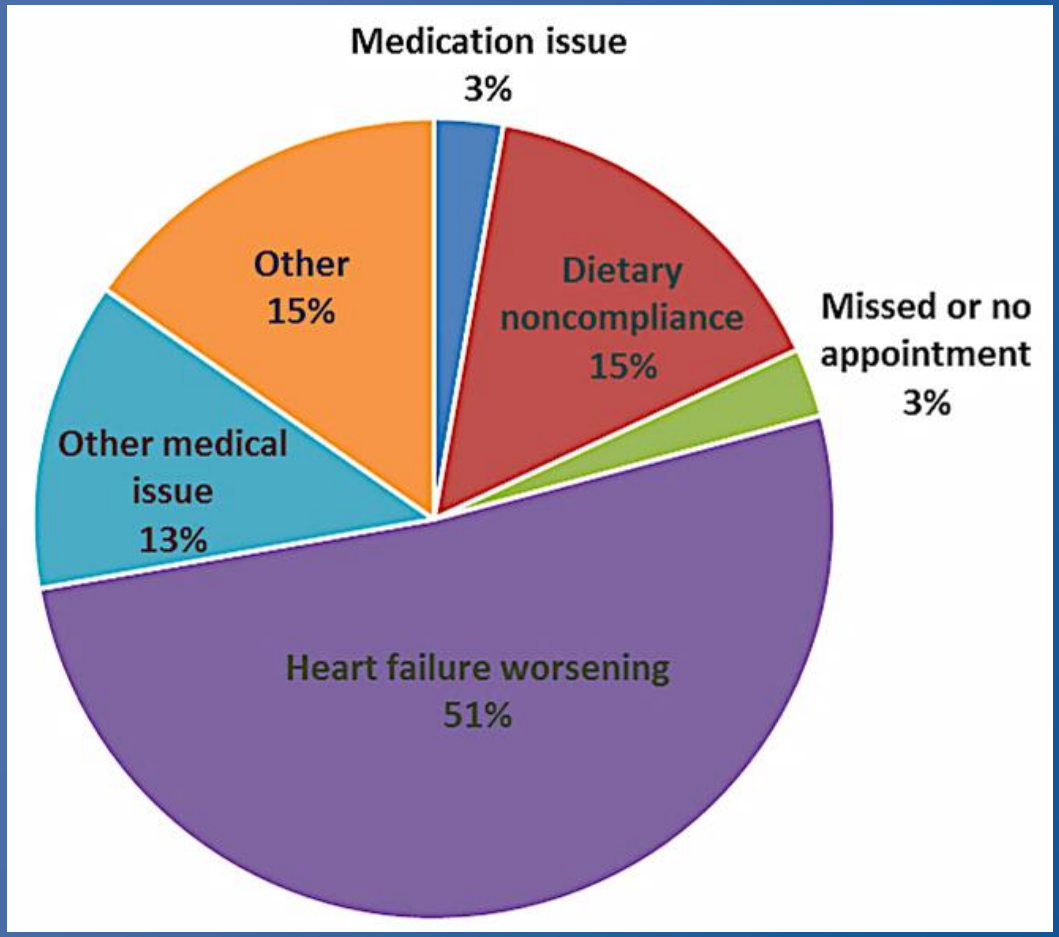
Predischarge	Bridging the Transition	Postdischarge
• Patient education • Discharge planning • Medica reconci • Appoint scheduled before discharge	• Transition coach • Provider continuity	• Timely follow-up • Timely PCP • Patient hotline • Home visit

Patient self-care and monitoring

Hansen L et al. *Ann Intern Med*. 2011;155:520-528.

What patients are saying…

What patients are saying…

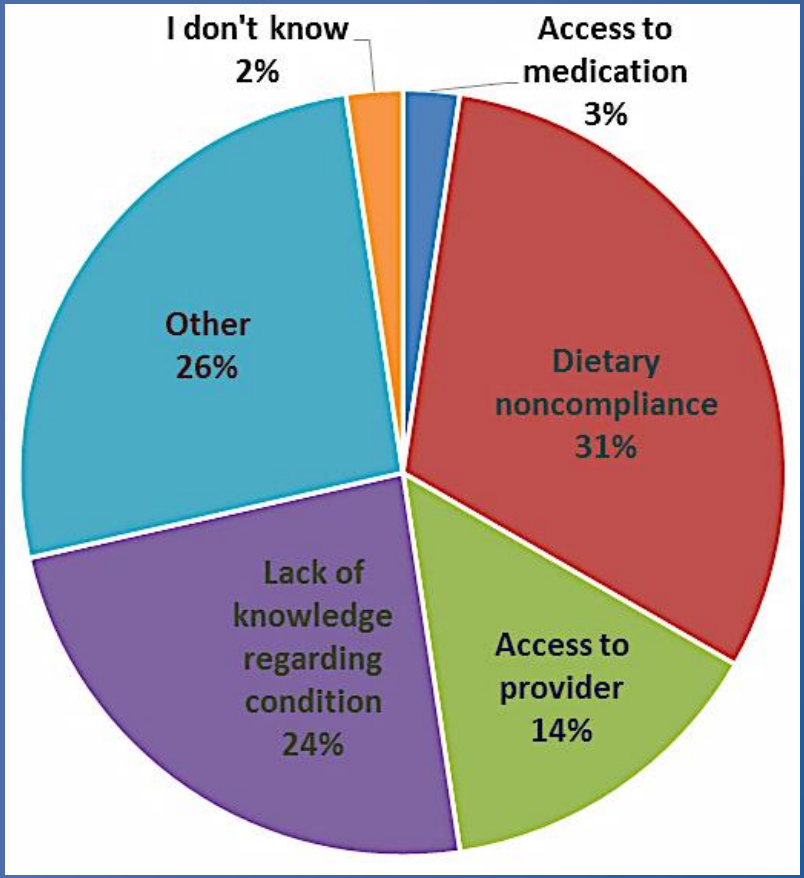


Patient-identified reason for HF hospitalization, n=72

Reason for admission did not correlate with readmission rate

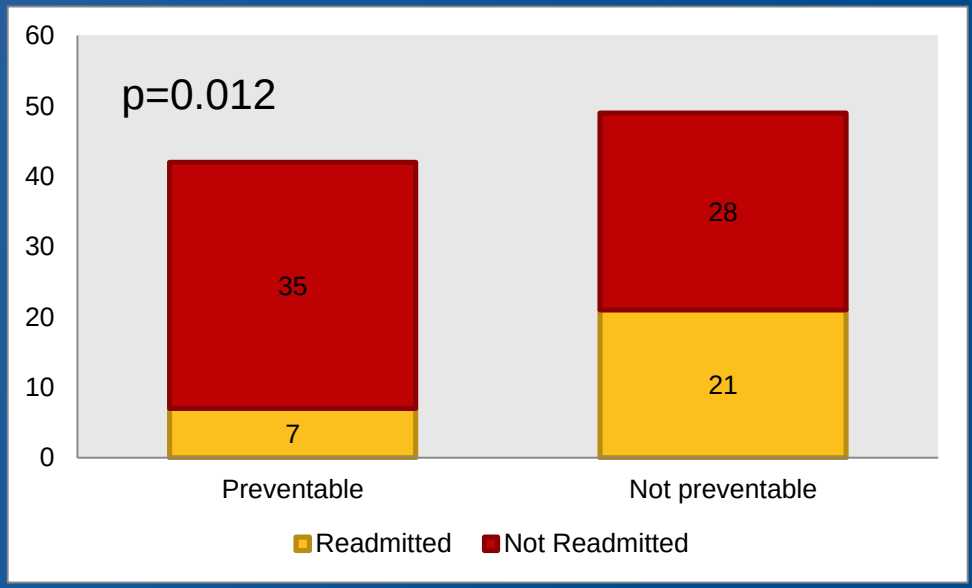
Gilotra, NA et al. *J Card Fail*. 2016

What patients are saying…

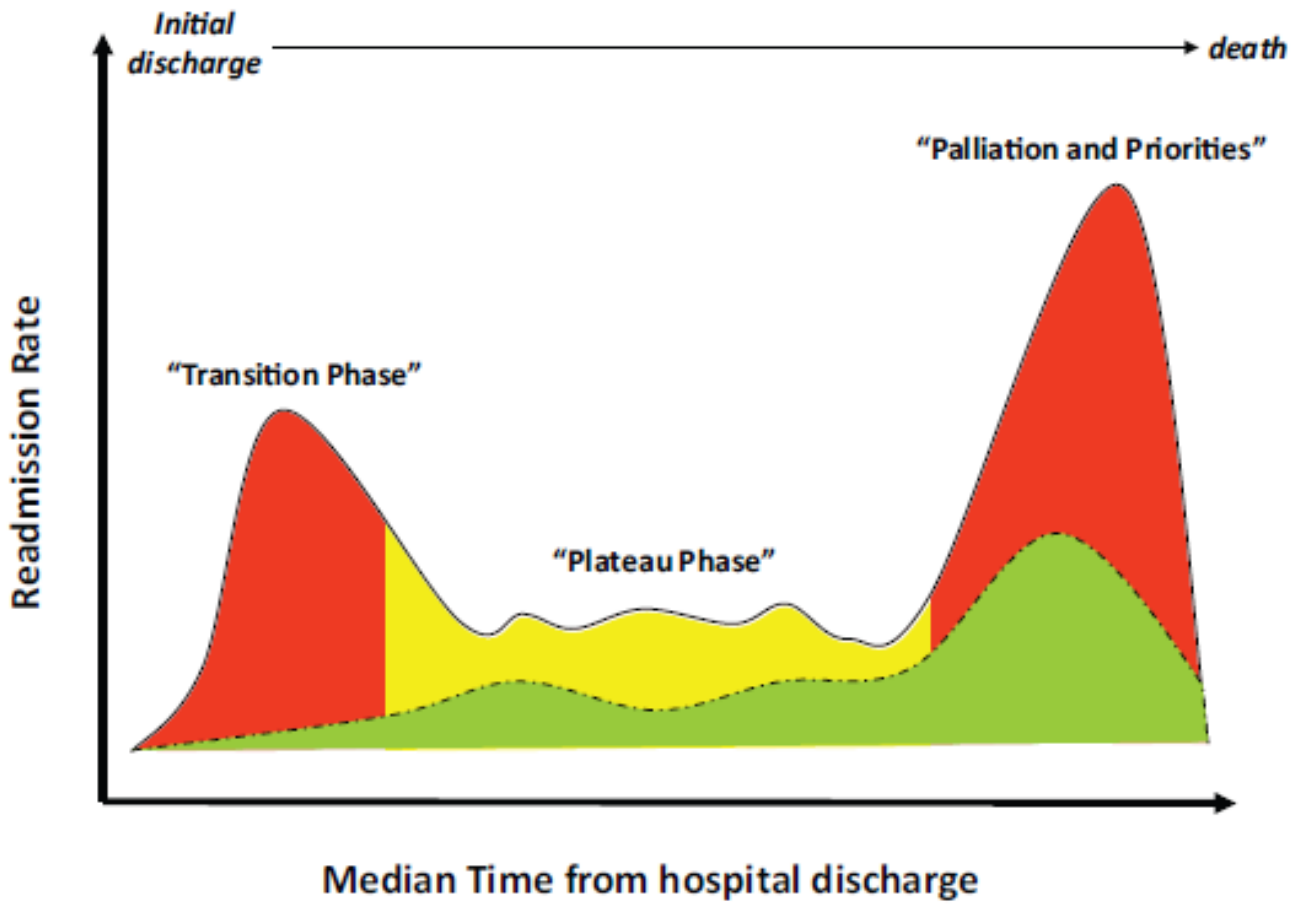


Patient-identified reason that admission was preventable, n=42

- 42/92 thought hospitalization was preventable
- Upon two physician review, 19 were felt to be preventable by both, 19 by one, and 54 by neither
  - Diet and meds



Gilotra, NA et al. *J Card Fail*. 2016



Desai A, Stevenson LW. Circ 2012;126:501-506

Follow-up

- 38% of HF patients are seen by a clinician within one week of discharge
- Higher early follow up = lower 30-d readmission risk
- Patients more likely to be seen if appointment made before discharge

Hernandez AF et al. JAMA 2010;5:1716-1722

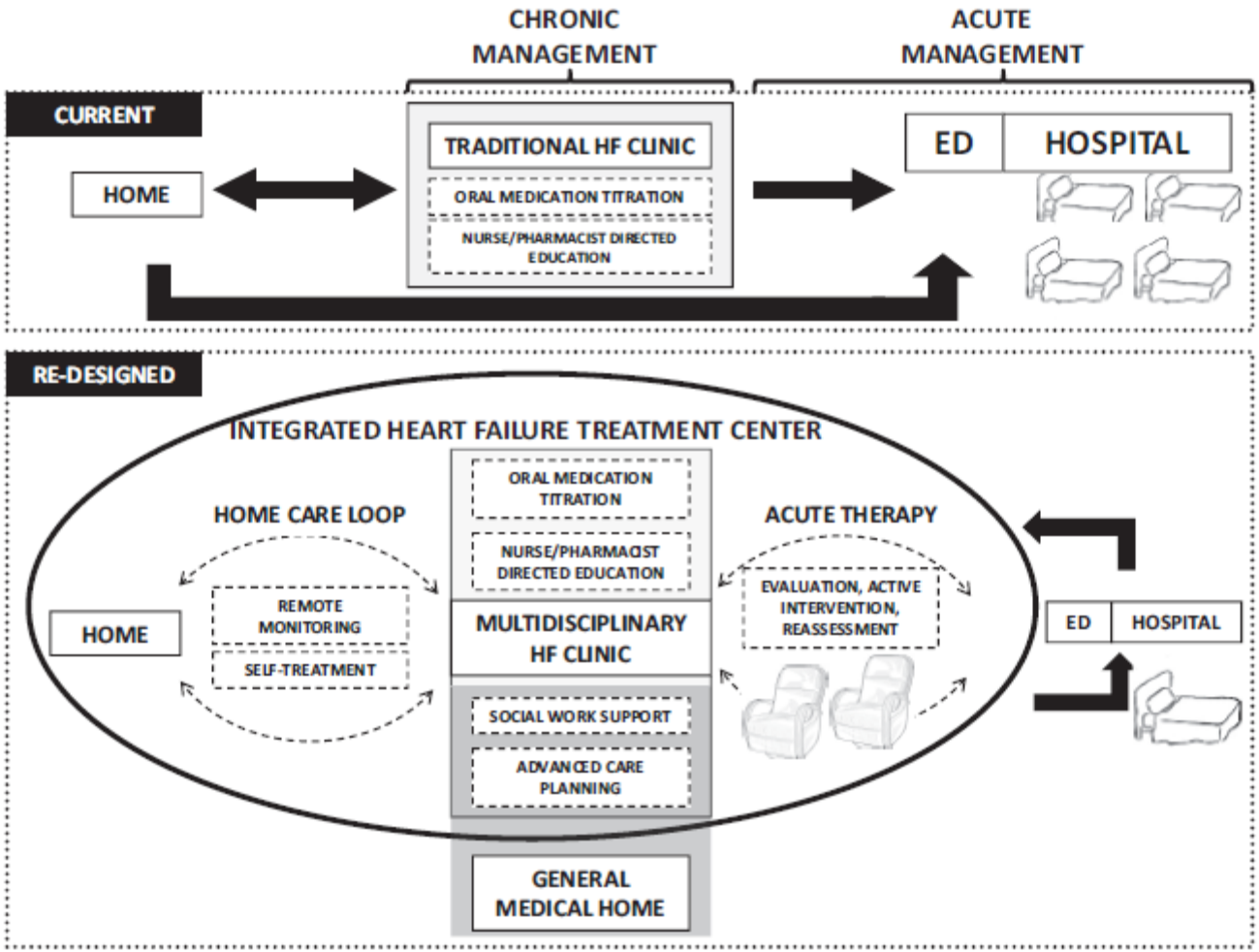


Figure 2. Models of HF care. The first panel reflects the traditional model of the ambulatory heart failure clinic as a focal point for intermittent assessment and chronic heart failure management. The second panel reflects a reengineered ambulatory heart failure treatment center with tighter linkage to home surveillance and options for active treatment as an alternative to hospitalization. HF indicates heart failure; ED, emergency department.

Desai A, Stevenson LW. Circ 2012;126:501-506

Heart failure disease management programs

- Improve medication dosing
- Decrease hospitalizations

- Outpatient IV diuresis clinics:
  - Less common
  - Literature describes referral of symptomatic patients only

Whellan DJ, Russell SD et al. Arch Intern Med 2001;161:2223-2228
Hebert K et al. Congest Heart Fail. 2011;17:309-313
Ryder M et al. Eur Jour Heart Fail. 2008;10:267-272

JHH Heart Failure Bridge Clinic

- Opened in 2012
- Early post-discharge follow-up
- Nurse practioner run
- Multidisciplinary approach: education, treatment, medication reconciliation
- Transition from hospitalization to home and establishment of outpatient specialty care
- Prevention of readmissions
- Referral to palliative care

JHH HFBC Experience

- May 2014 - July 2016
- 5070 clinic visits, 1336 unique patients seen an average of 3.8±4.3 times
- IV furosemide administered 728 times to 300 patients
- Mean IV furosemide dose was 129±43 mg
- The 30 day all-cause readmission rate for HFBC patients was 12.8% compared to 31.9% for those not seen in HFBC

Gilotra, NA et al. *ACC* Scientific Sessions March 2017.

Summary

- HF growing epidemic with rising hospitalizations and costs
- HF is a clinical diagnosis with broad etiologies
- HFrEF: goal is to get them on GDMT, referral for advanced therapies as needed
- HFpEF: treat comorbidities and volume overload, much to be learned about pathogenesis and treatment strategies
- Safe transitions, education and close follow up key in preventing hospitalizations

Thank you

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