
Heart
Science
Amplified

Improving Guideline-Directed Heart Failure Care:

New Considerations in HF incl.- ACC/AHA/HFSA Heart Failure Guidelines

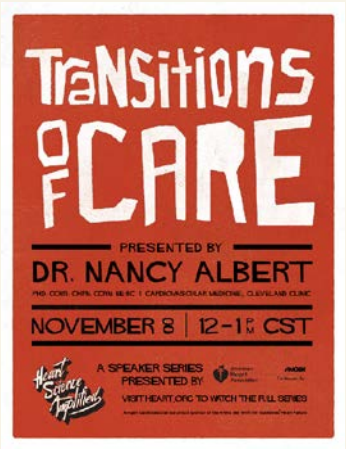
Tuesday October 18, 2016

1:00pm – 2:00pm Central

Presenter: Clyde W. Yancy, MD, MSc

Amgen Cardiovascular proudly sponsors Heart Science Amplified: An Online Speaker Series and Get With The Guidelines™-Heart Failure.

AMGEN Cardiovascular | American Heart Association



November 8, 12-1pm Central

Transitions of Care

Presented by Dr. Nancy Albert, PhD, CCNS, CHFN, CCRN, NE-BC

Register:

https://engage.vevent.com/rt/ahaevents~110816

November 13 - Scientific Sessions

HeartQuarters Live Webinar Series Wrap-up

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Professional.heart.org

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Get With The Guidelines Webinar: New Considerations in HF incl.- ACC/AHA/HFSA Heart Failure Guidelines

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No relevant disclosures

DISCLOSURES

- **Consultant/speaker/honoraria: none**

- **JAMA Cardiology*, Deputy Editor;* ; Journal of the American College of Cardiology- *senior associate editor (HF);* American Journal of Cardiology - *associate editor, supplements*; American Heart Journal, Circulation; Circulation-Heart Failure- *editorial boards***
- **Guideline writing committees: Chair, ACC/AHA, chronic HF; member, atrial fibrillation; hypertrophic cardiomyopathy; syncope guideline committees. Chair, Performance Measures, Sudden Cardiac Death**

- **Federal appointments: FDA: Immediate Past Chair, Cardiovascular Device Panel; ad hoc consultant; NIH – Scientific Management and Review Board; AHRQ- adhoc consultant; NHLBI- consultant; PCORI- former methodology committee member; IOM- writing group member**

- **Volunteer Appointments: American Heart Association- President, American Heart Association, 2009-2010; American College of Cardiology, Founder- CREDO**

Agenda

- New Epidemiology of Heart Failure
- New Prevention Strategies
- New Treatment Paradigms

From: **A Contemporary Appraisal of the Heart Failure Epidemic in Olmsted County, Minnesota, 2000 to 2010**

JAMA Intern Med. 2015;175(6):996-1004. doi:10.1001/jamainternmed.2015.0924

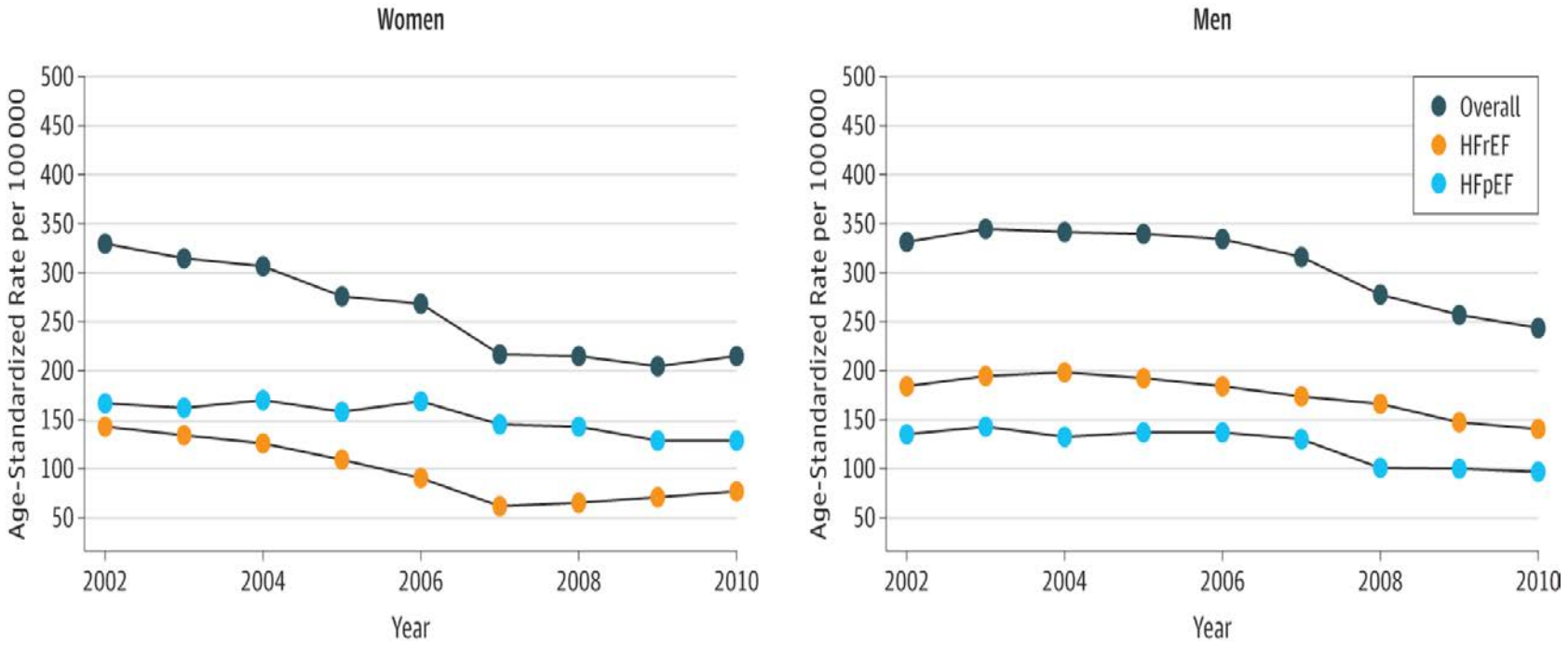


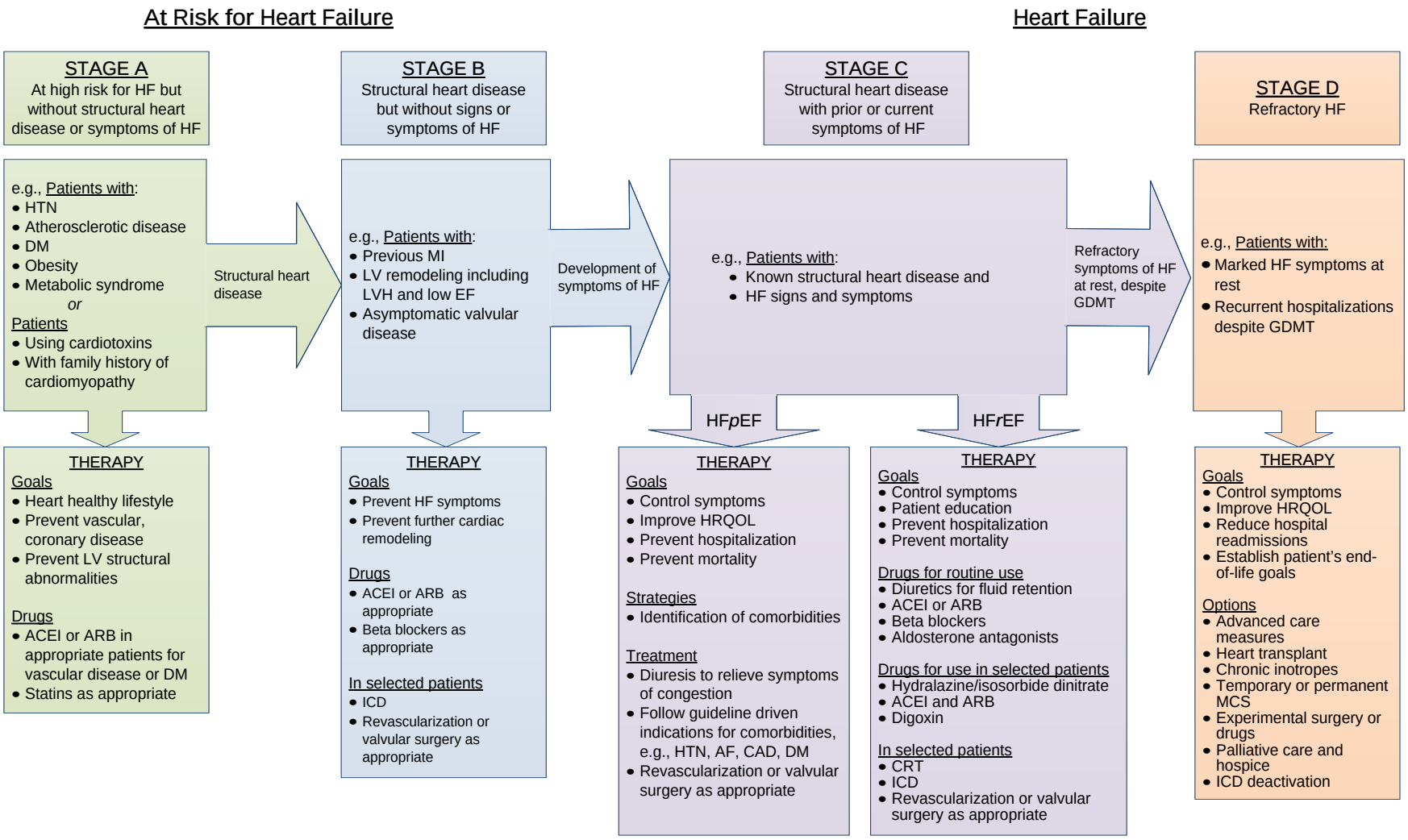
Figure Legend:

Temporal Trends in Heart Failure Incidence Rates Overall and by Reduced or Preserved Ejection Fraction Among Women and Men in Olmsted County, Minnesota, 2000 to 2010Yearly rates (smoothed using 3-year moving average) per 100 000 persons have been standardized by the direct method to the age distribution of the US population in 2010. HFpEF indicates heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction.

Agenda

- New Epidemiology of Heart Failure
- New Prevention Strategies
- New Treatment Paradigms

Stages, Phenotypes and Treatment of HF



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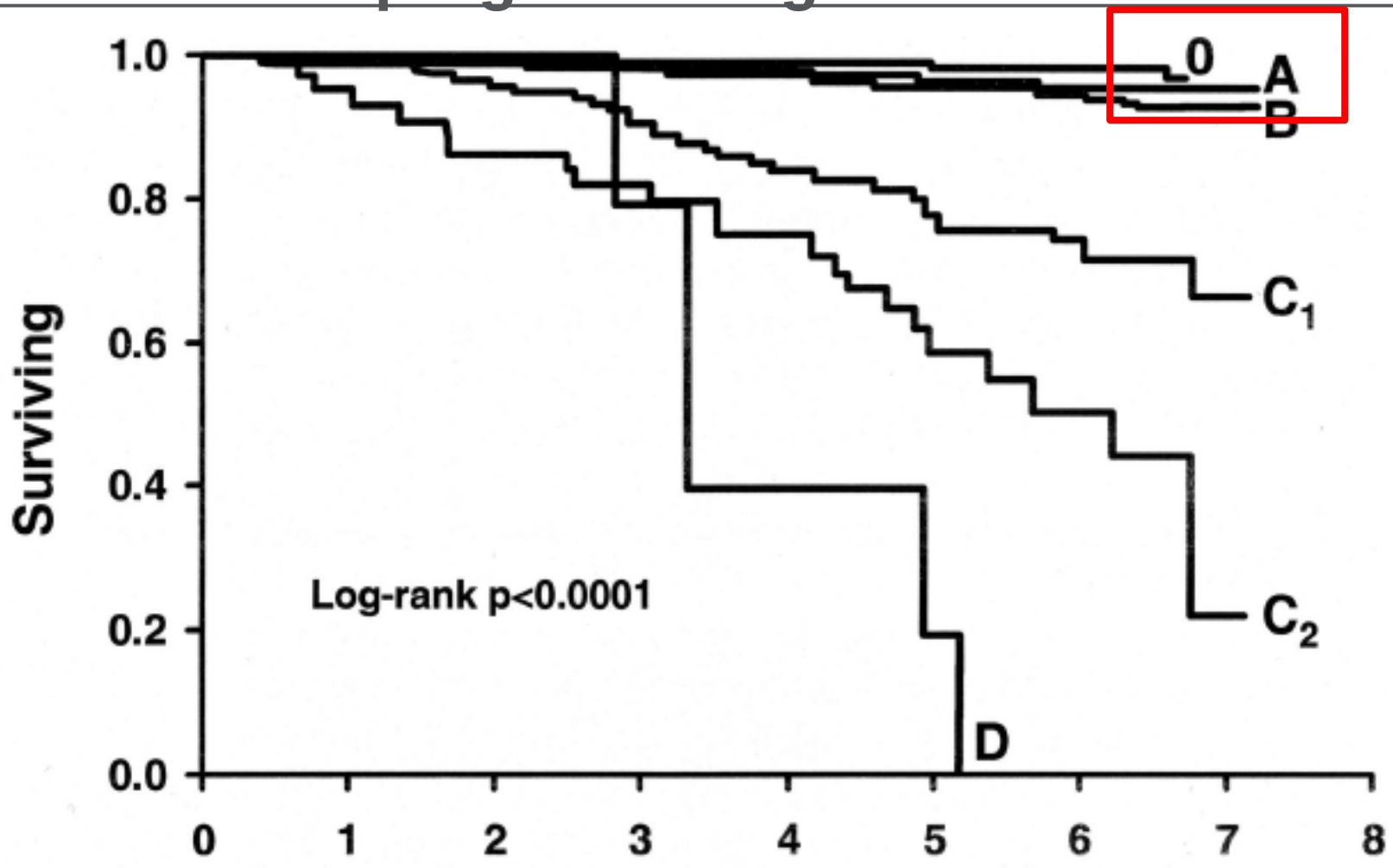
Prevalence and prognostic significance of HF Stages



Ammar et al. *Circulation* 2007; 115:1563

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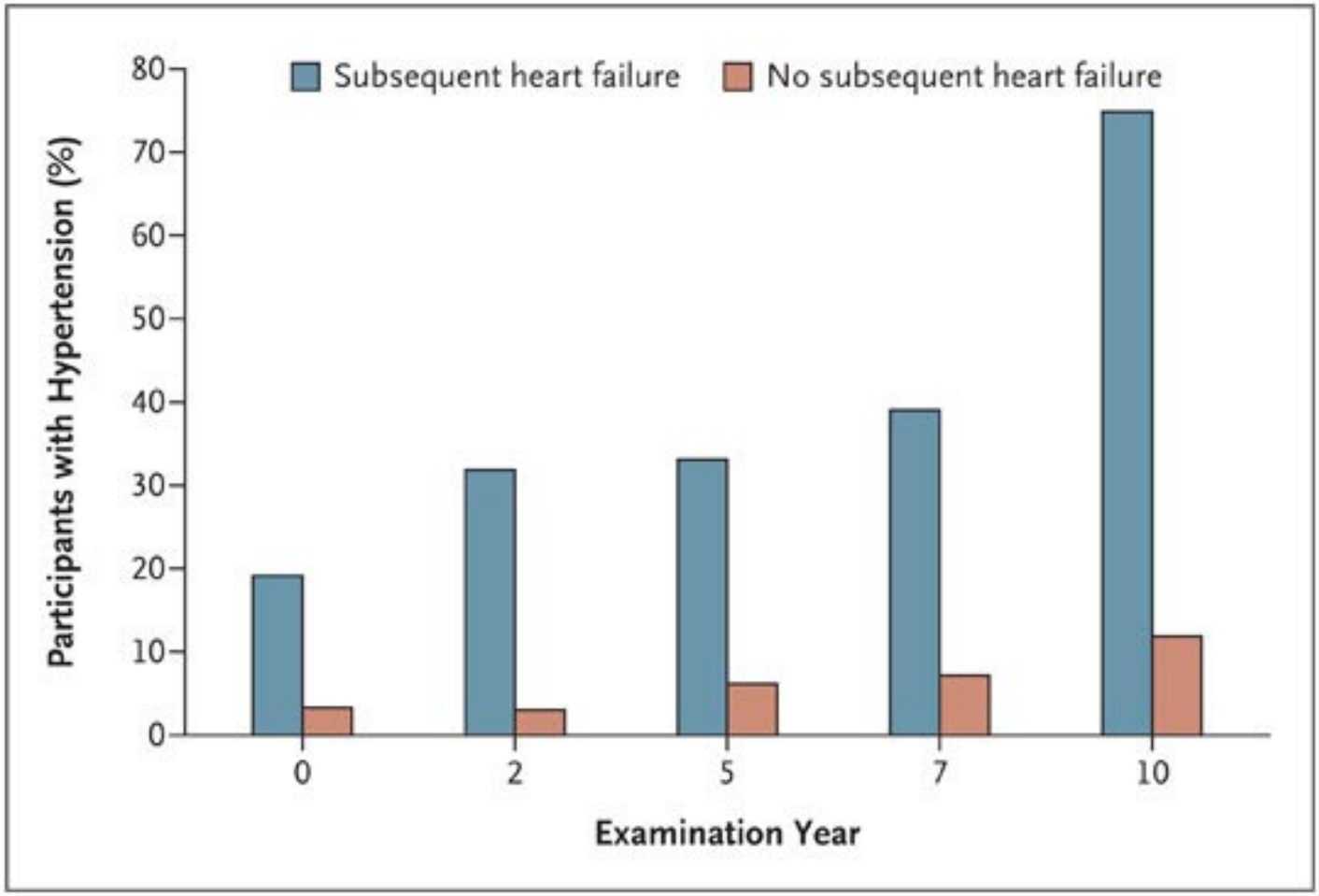
STAGE A HF:
Hypertension as a Risk Factor for HF in African Americans



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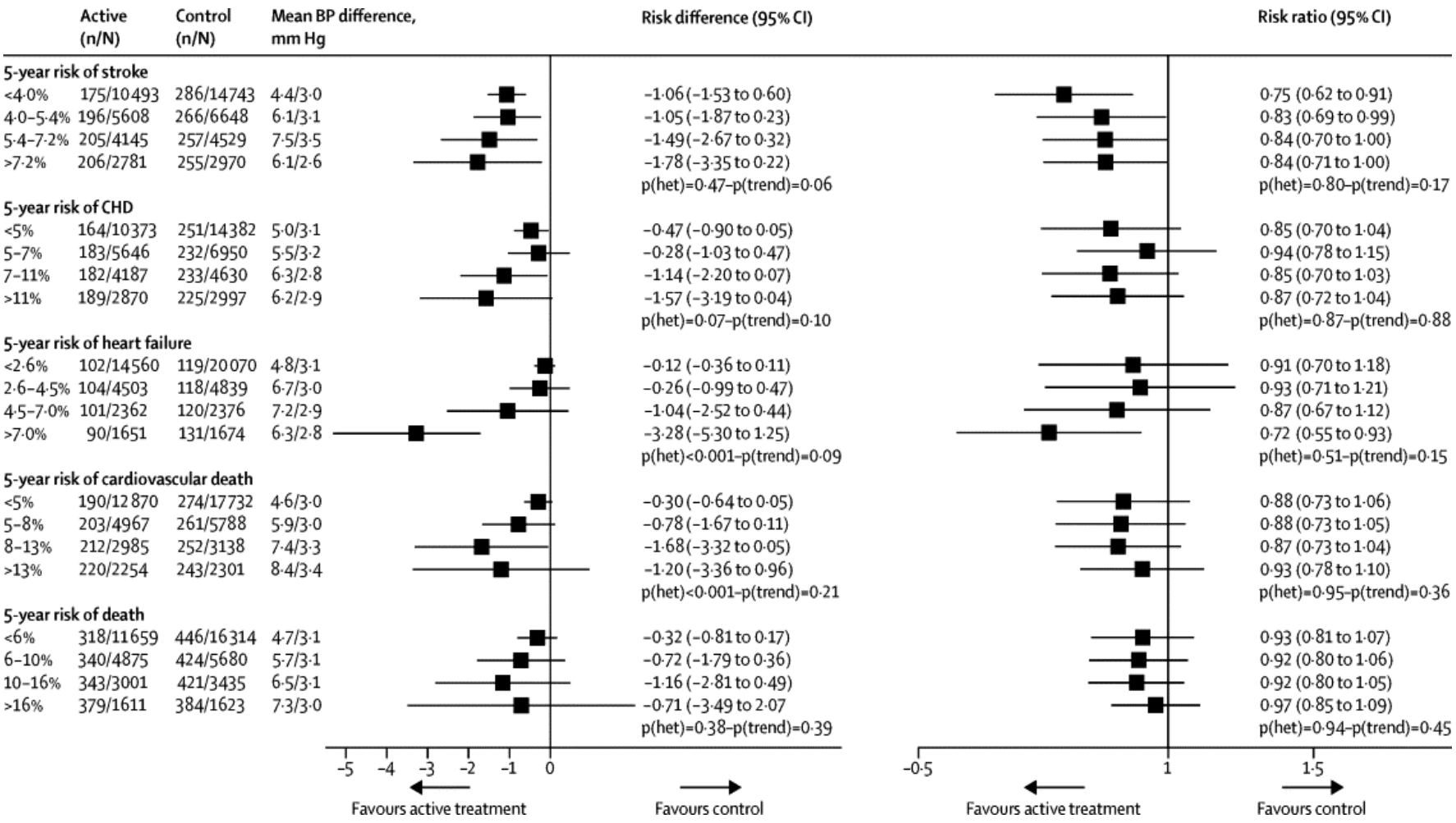
Bibbins-Domingo et al. N Engl J Med. 360(12):1179-1190

Blood Pressure Lowering Treatment Based on CV Risk: A Meta-analysis of Individual Patient Data



Lancet 2014; 384 (August 16 2014)

SPRINT Hypertension Trial

- Study Type: Interventional Study Design: Allocation: Randomized
  Endpoint Classification: Efficacy Study
  Intervention Model: Parallel Assignment
  Masking: Single Blind (Outcomes Assessor)
  Official Title: Systolic Blood Pressure Intervention Trial

  Primary Outcome Measures: First occurrence of a myocardial infarction (MI), acute coronary syndrome (ACS), stroke, heart failure (HF), or CVD death [Time Frame: 6 years] [Designated as safety issue: No]

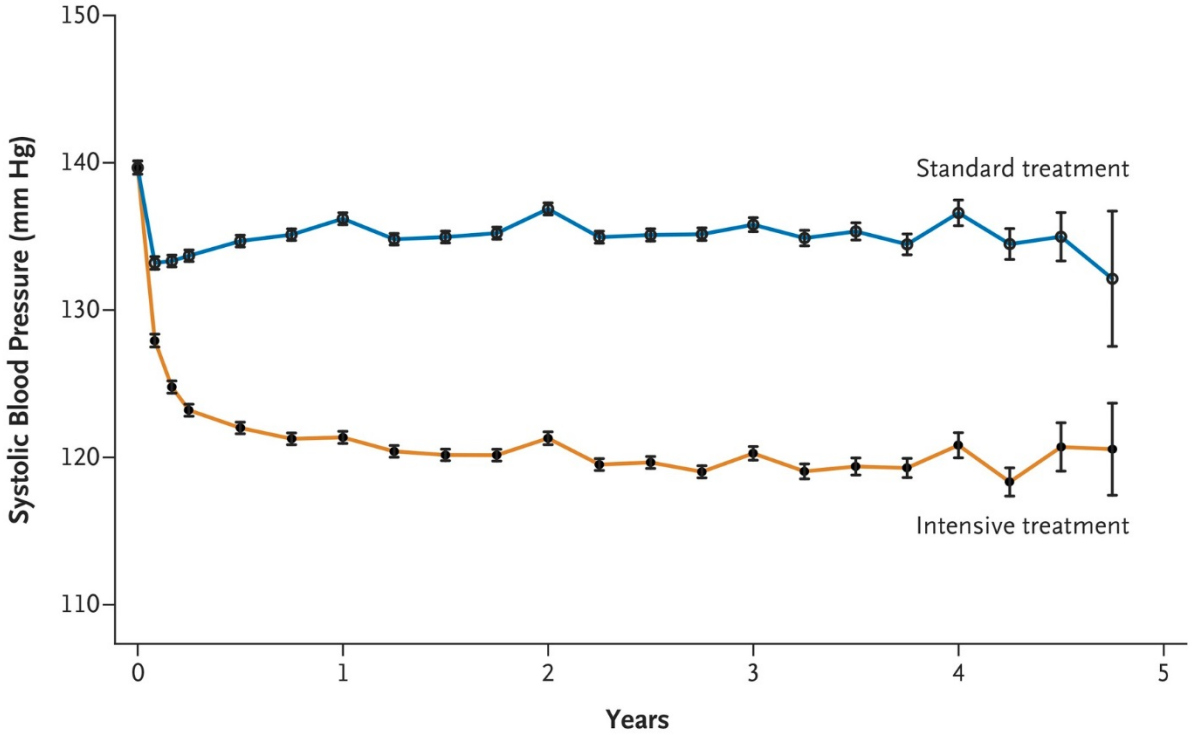
  Secondary Outcome Measures: All-cause mortality ; Development of end stage renal disease (ESRD), Dementia, Decline in cognitive function, Small vessel cerebral ischemic disease

- Estimated Enrollment: 9250 Study Start Date: October 2010 Estimated Study Completion Date: December 2018 Estimated Primary Completion Date: October 2018 (Final data collection date for primary outcome measure)

Increased CV risk as defined by SPRINT:

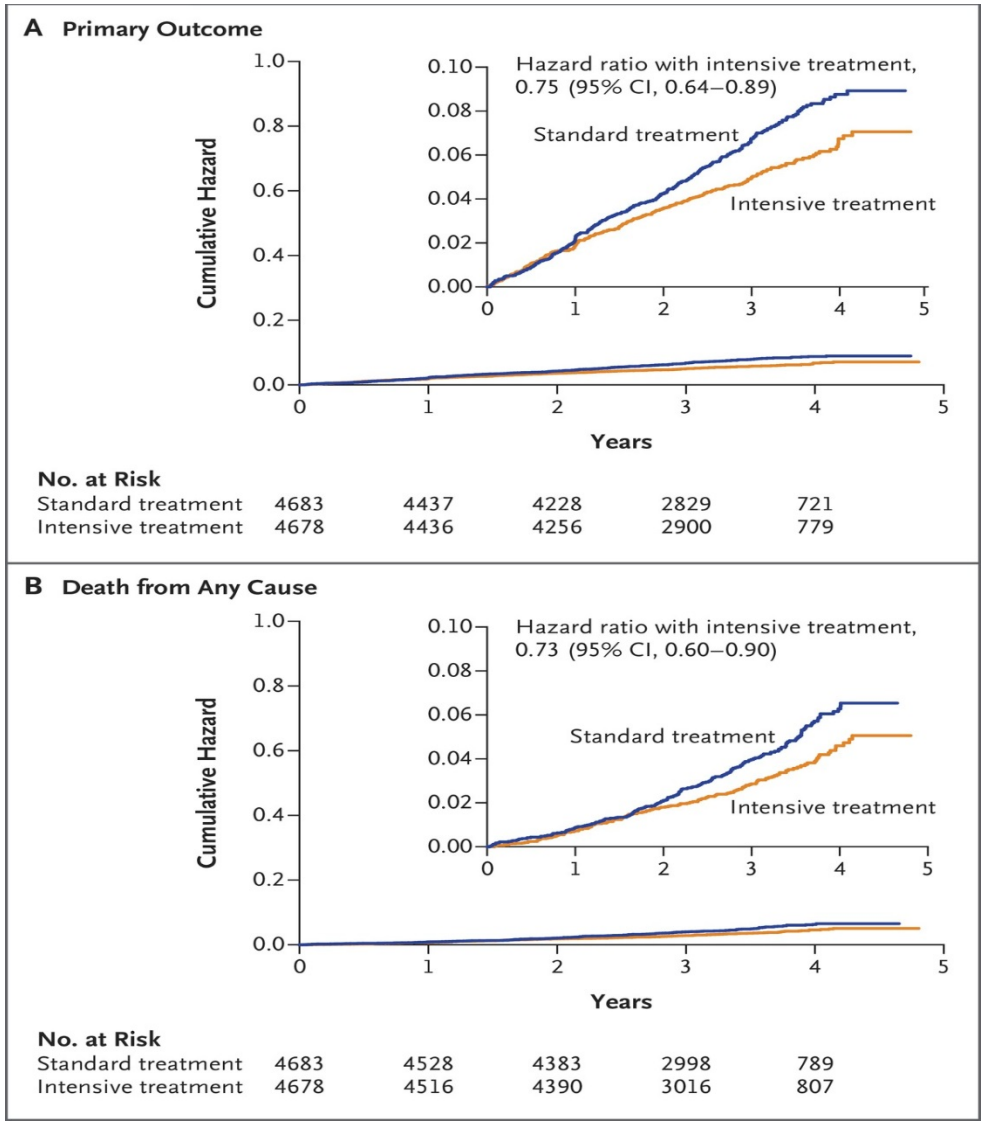
- clinical or subclinical cardiovascular disease other than stroke;
- chronic kidney disease, excluding polycystic kidney disease, with an estimated glomerular filtration rate (eGFR) of 20 to less than 60 ml per minute per 1.73 m^2 of body-surface area, calculated with the use of the four-variable Modification of Diet in Renal Disease equation;
- a 10-year risk of cardiovascular disease of 15% or greater on the basis of the Framingham risk score;
- or an age of 75 years or older

Systolic Blood Pressure in the Two Treatment Groups over the Course of the Trial.



No. with Data										
Standard treatment	4683	4345	4222	4092	3997	3904	3115	1974	1000	274
Intensive treatment	4678	4375	4231	4091	4029	3920	3204	2035	1048	286
Mean No. of Medications										
Standard treatment	1.9	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.9
Intensive treatment	2.3	2.7	2.8	2.8	2.8	2.8	2.8	2.8	2.8	3.0

Primary Outcome and Death from Any Cause.



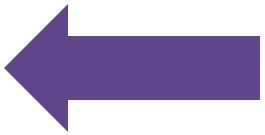
The SPRINT Research Group. N Engl J Med 2015;373:2103-2116

Primary and Secondary Outcomes and Renal Outcomes.

Table 2. Primary and Secondary Outcomes and Renal Outcomes.*

Outcome	Intensive Treatment		Standard Treatment		Hazard Ratio (95% CI)	P Value
	no. of patients (%)	*% per year*	*no. of patients (%)*	*% per year*		
All participants	**(N=4678)**		**(N=4683)**			
Primary outcome†	243 (5.2)	1.65	319 (6.8)	2.19	0.75 (0.64–0.89)	<0.001
Secondary outcomes						
Myocardial infarction	97 (2.1)	0.65	116 (2.5)	0.78	0.83 (0.64–1.09)	0.19
Acute coronary syndrome	40 (0.9)	0.27	40 (0.9)	0.27	1.00 (0.64–1.55)	0.99
Stroke	62 (1.3)	0.41	70 (1.5)	0.47	0.89 (0.63–1.25)	0.50
Heart failure	62 (1.3)	0.41	100 (2.1)	0.67	0.62 (0.45–0.84)	0.002
Death from cardiovascular causes	37 (0.8)	0.25	65 (1.4)	0.43	0.57 (0.38–0.85)	0.005
Death from any cause	155 (3.3)	1.03	210 (4.5)	1.40	0.73 (0.60–0.90)	0.003
Primary outcome or death	332 (7.1)	2.25	423 (9.0)	2.90	0.78 (0.67–0.90)	<0.001
Participants with CKD at baseline	**(N=1330)**		**(N=1316)**			
Composite renal outcome‡	14 (1.1)	0.33	15 (1.1)	0.36	0.89 (0.42–1.87)	0.76
≥50% reduction in estimated GFR§	10 (0.8)	0.23	11 (0.8)	0.26	0.87 (0.36–2.07)	0.75
Long-term dialysis	6 (0.5)	0.14	10 (0.8)	0.24	0.57 (0.19–1.54)	0.27
Kidney transplantation	0		0			
Incident albuminuria¶	49/526 (9.3)	3.02	59/500 (11.8)	3.90	0.72 (0.48–1.07)	0.11
Participants without CKD at baseline‖	**(N=3332)**		**(N=3345)**			
≥30% reduction in estimated GFR to <60 ml/min/1.73 m^2§	127 (3.8)	1.21	37 (1.1)	0.35	3.49 (2.44–5.10)	<0.001
Incident albuminuria¶	110/1769 (6.2)	2.00	135/1831 (7.4)	2.41	0.81 (0.63–1.04)	0.10

* CI denotes confidence interval, and CKD chronic kidney disease.
† The primary outcome was the first occurrence of myocardial infarction, acute coronary syndrome, stroke, heart failure, or death from cardiovascular causes.
‡ The composite renal outcome for participants with CKD at baseline was the first occurrence of a reduction in the estimated GFR of 50% or more, long-term dialysis, or kidney transplantation.
§ Reductions in the estimated GFR were confirmed by a second laboratory test at least 90 days later.
¶ Incident albuminuria was defined by a doubling of the ratio of urinary albumin (in milligrams) to creatinine (in grams) from less than 10 at baseline to greater than 10 during follow-up. The denominators for number of patients represent those without albuminuria at baseline.
‖ No long-term dialysis or kidney transplantation was reported among participants without CKD at baseline.



TheSPRINT Research Group. N Engl J Med 2015;373:2103-2116

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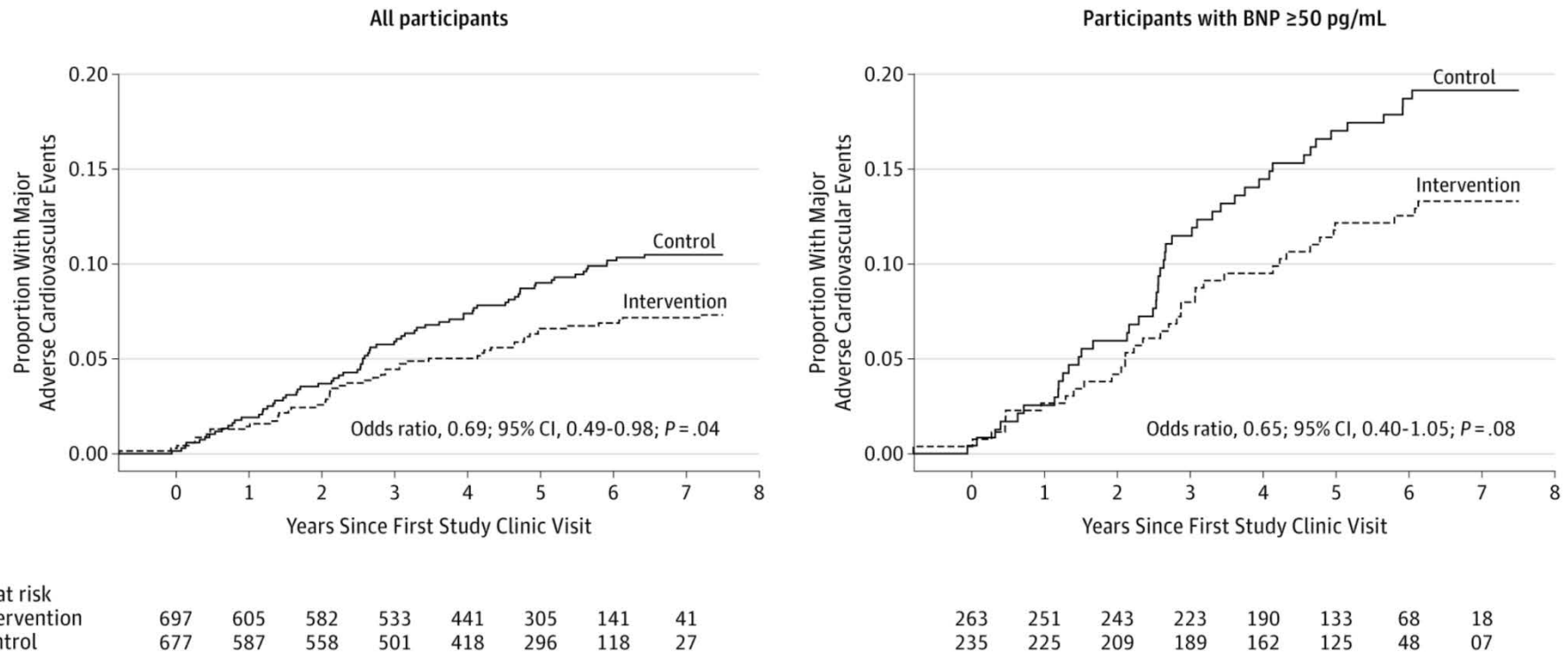
The NEW ENGLAND JOURNAL of MEDICINE

09/11/2015; Announcement of premature termination of SPRINT for benefit

- **"… treating high-risk hypertensive adults 50 years of age and older to a target of 120 mm Hg significantly reduced cardiovascular events by 30% and reduced all-cause mortality by nearly 25% when compared with patients treated to a target of 140 mm Hg…"**

From: **Natriuretic Peptide–Based Screening and Collaborative Care for Heart Failure: The STOP-HF Randomized Trial**

JAMA. 2013;310(1):66-74. doi:10.1001/jama.2013.7588



No. at risk								
Intervention	697	605	582	533	441	305	141	41
Control	677	587	558	501	418	296	118	27

263	251	243	223	190	133	68	18
235	225	209	189	162	125	48	07

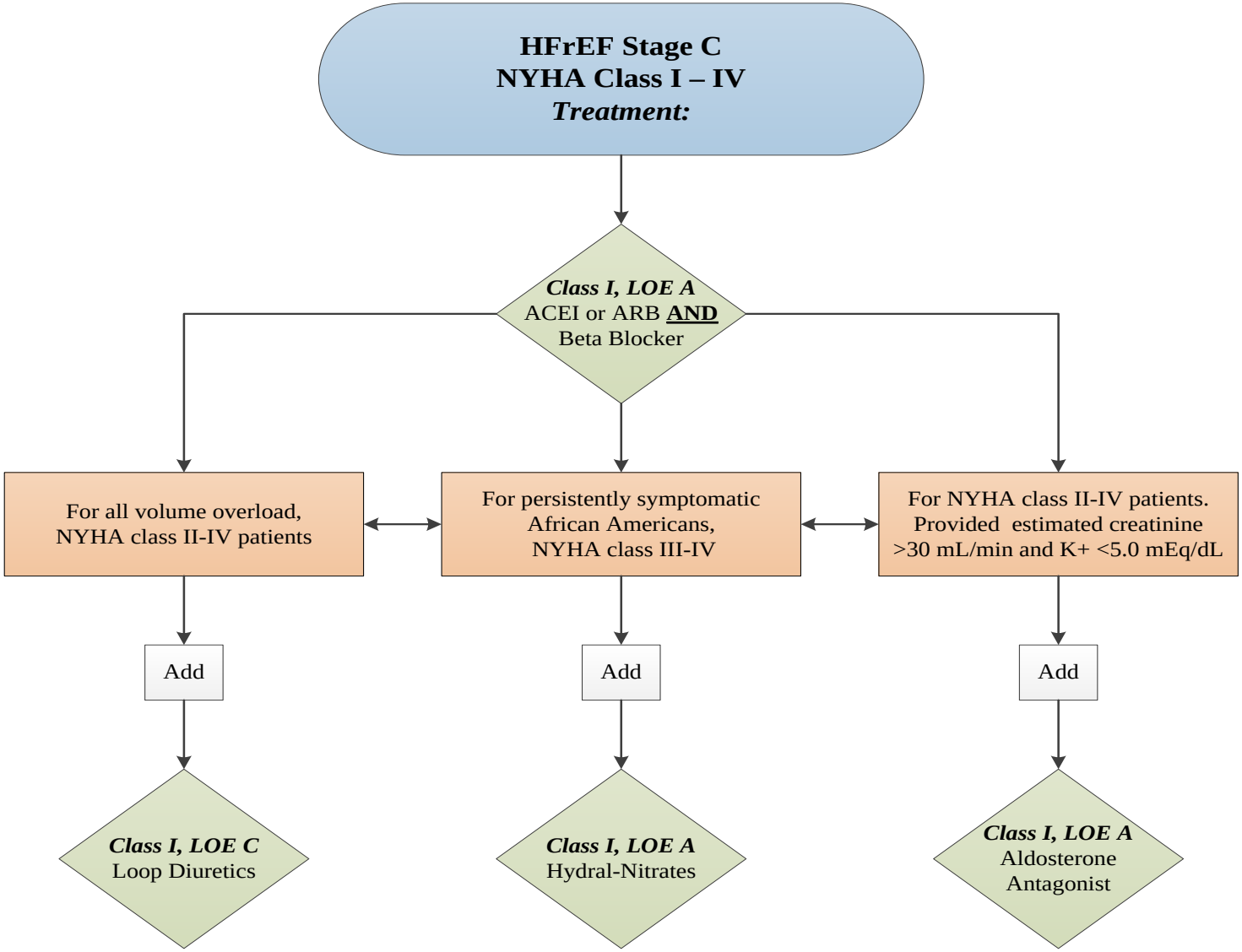
Figure Legend:

Kaplan-Meier Analysis of Major Adverse Cardiovascular Events in the Full Study Sample and in Participants With BNP ≥50 pg/mLBNP indicates brain-type natriuretic peptide. Major adverse cardiovascular events included arrhythmia, transient ischemic attack, stroke, myocardial infarction, peripheral or pulmonary thrombosis/embolus, or heart failure. In the full sample, 51 (7.3%) of 697 patients were admitted for major adverse cardiovascular events in the intervention group and 71 (10.5%) of 677 were admitted in the control group. In participants with BNP ≥50 pg/mL, 35 (13.3%) of 263 were admitted for major adverse cardiovascular events in the intervention group and 45 (19.1%) of 235 were admitted in the control group.

Agenda

- New Epidemiology of Heart Failure
- New Prevention Strategies
- New Treatment Paradigms

2013 ACCF/AHA Heart Failure Guidelines Pharmacologic Treatment for Stage C HFrEF



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Yancy C et al. Circulation, 2013

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

GDMT	RR Reduction in Mortality	NNT for Mortality Reduction (Standardized to 36 mo)	RR Reduction in HF Hospitalizations
ACE inhibitor or ARB	17%	26	31%
Beta blocker	34%	9	41%
Aldosterone antagonist	30%	6	35%
Hydralazine/nitrate	43%	7	33%

Fonarow, G, Yancy, C. American Heart Journal, 2012.

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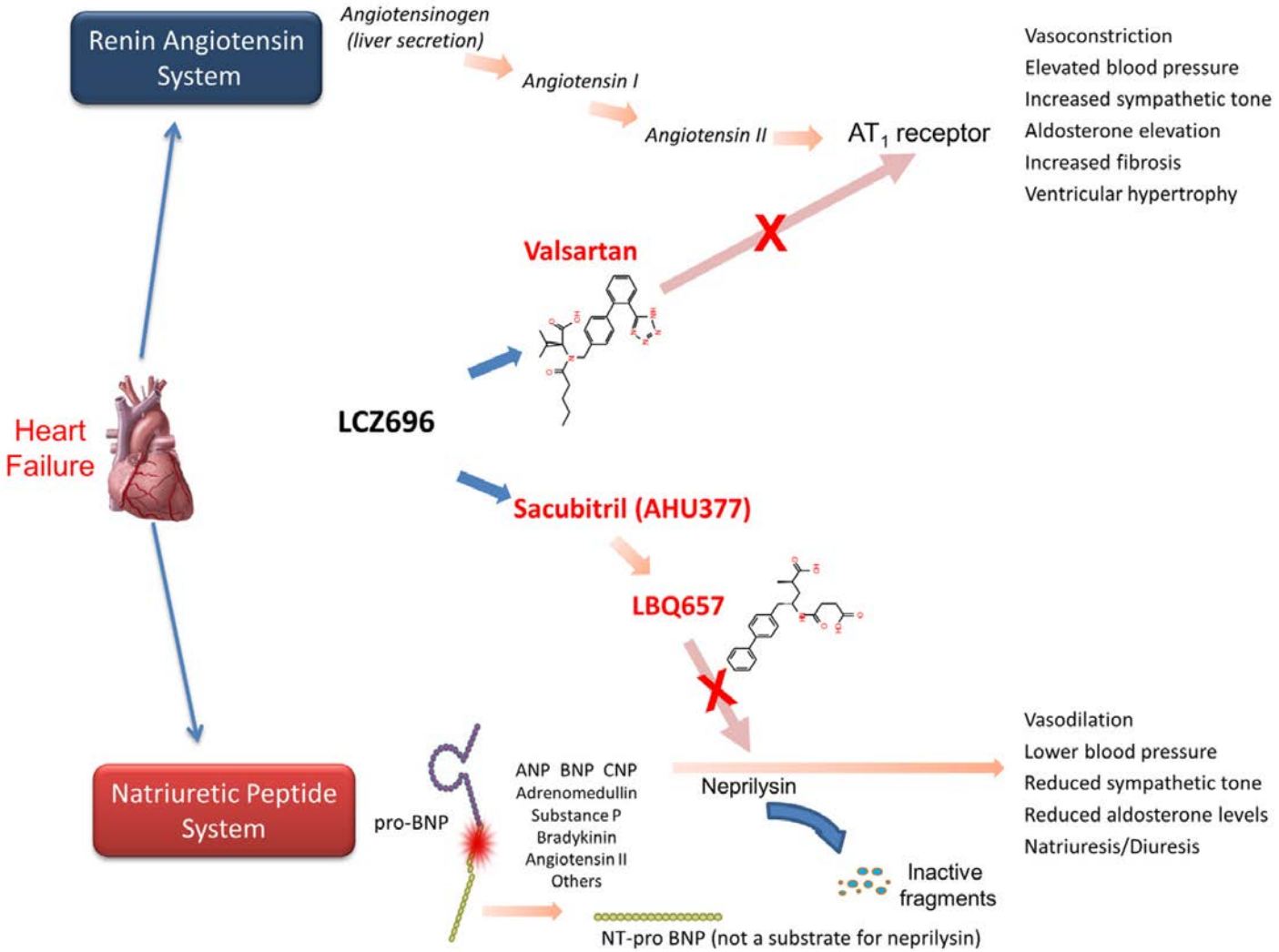
Mechanism of Action of LCZ696



Vardney O et al. JACC:Heart Failure. 2014;2:663-670.

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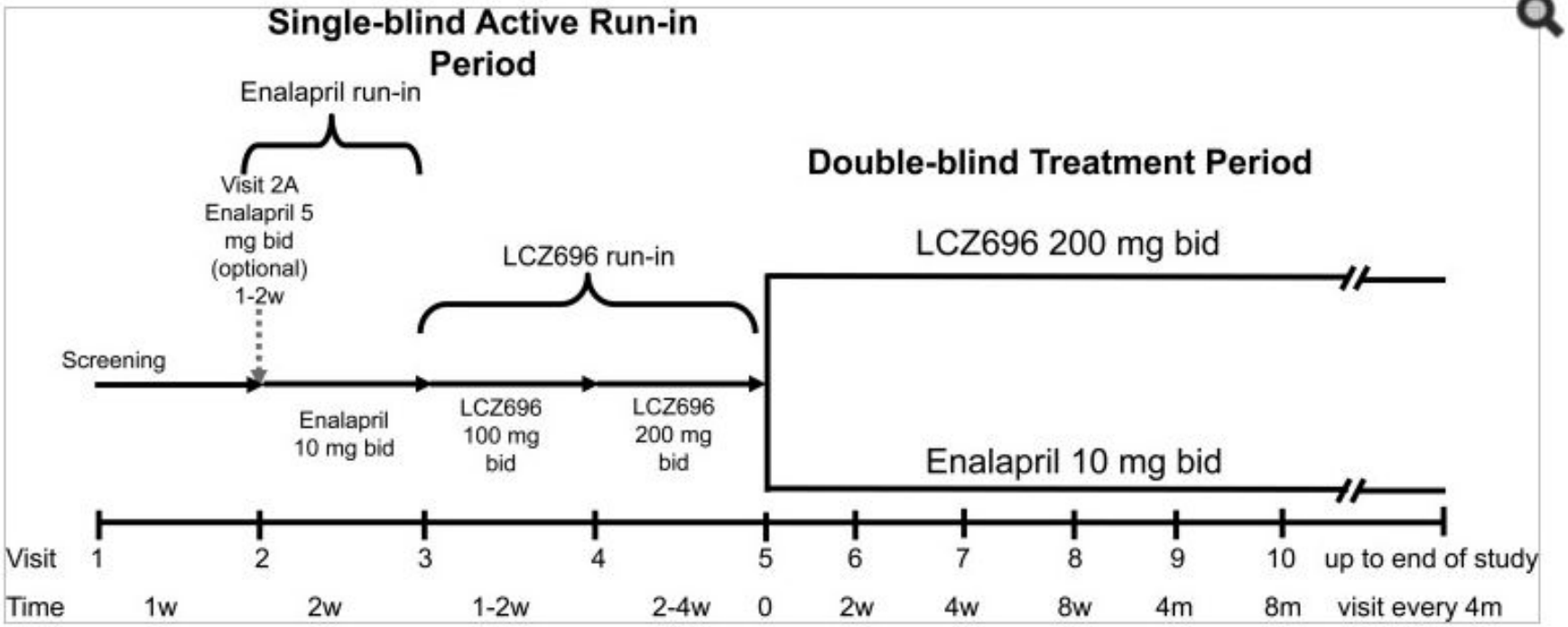
PARADIGM HF

Figure 1

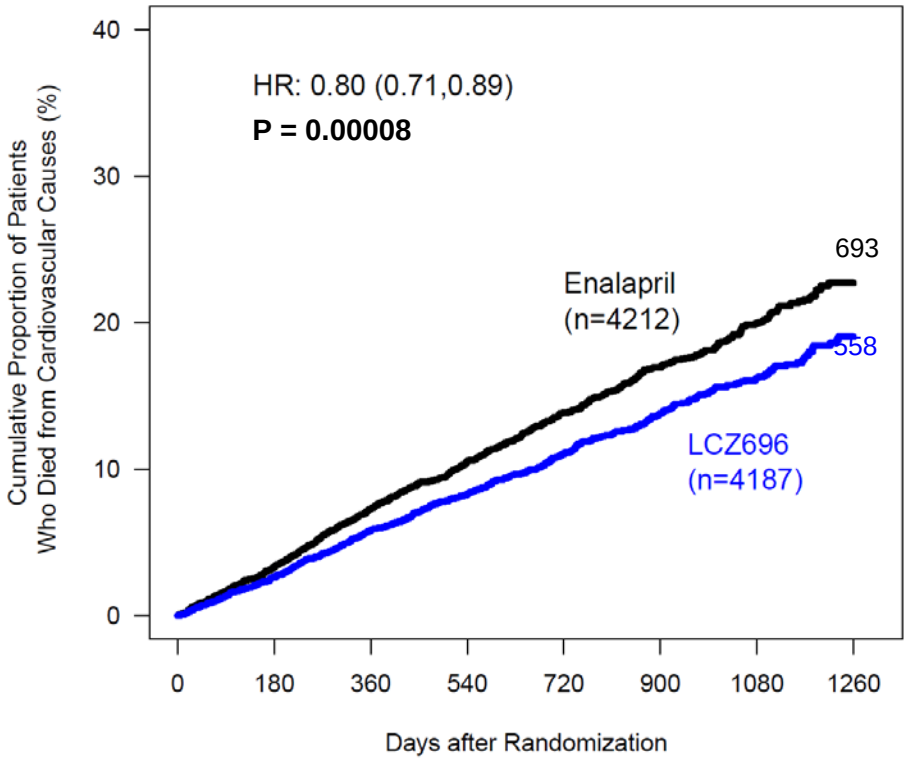


PARADIGM-HF study schema.

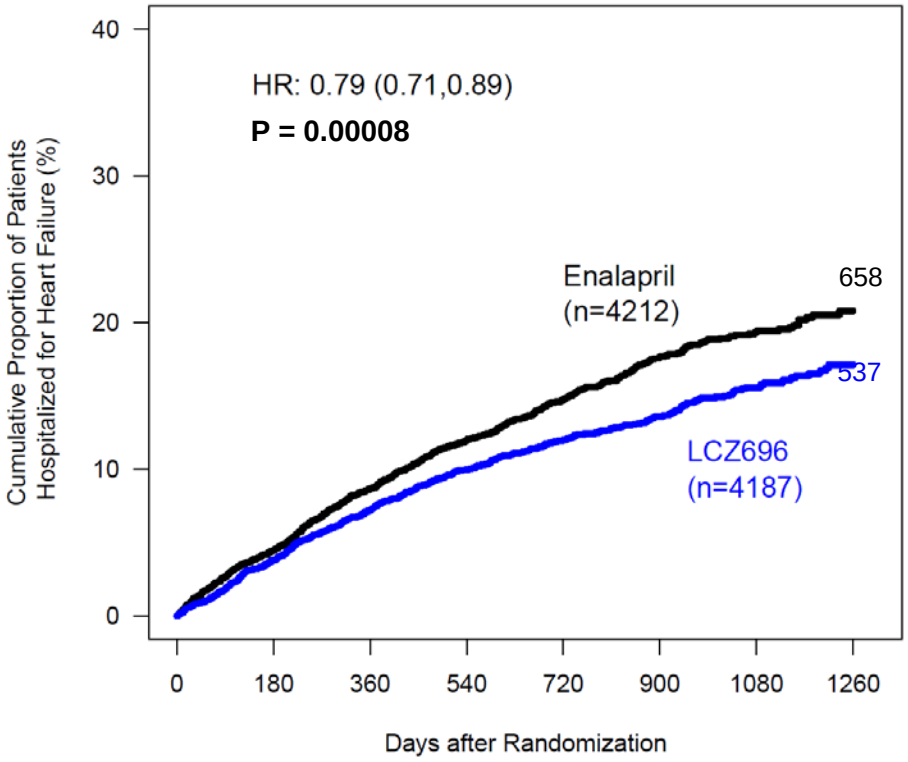
PARADIGM-HF
(Prospective Comparison of ARNI with ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure trial)

HR: 0.80 (0.73, 0.87) p = 0.0000004

Death from CV causes
20% risk reduction



HF hospitalization
21% risk reduction



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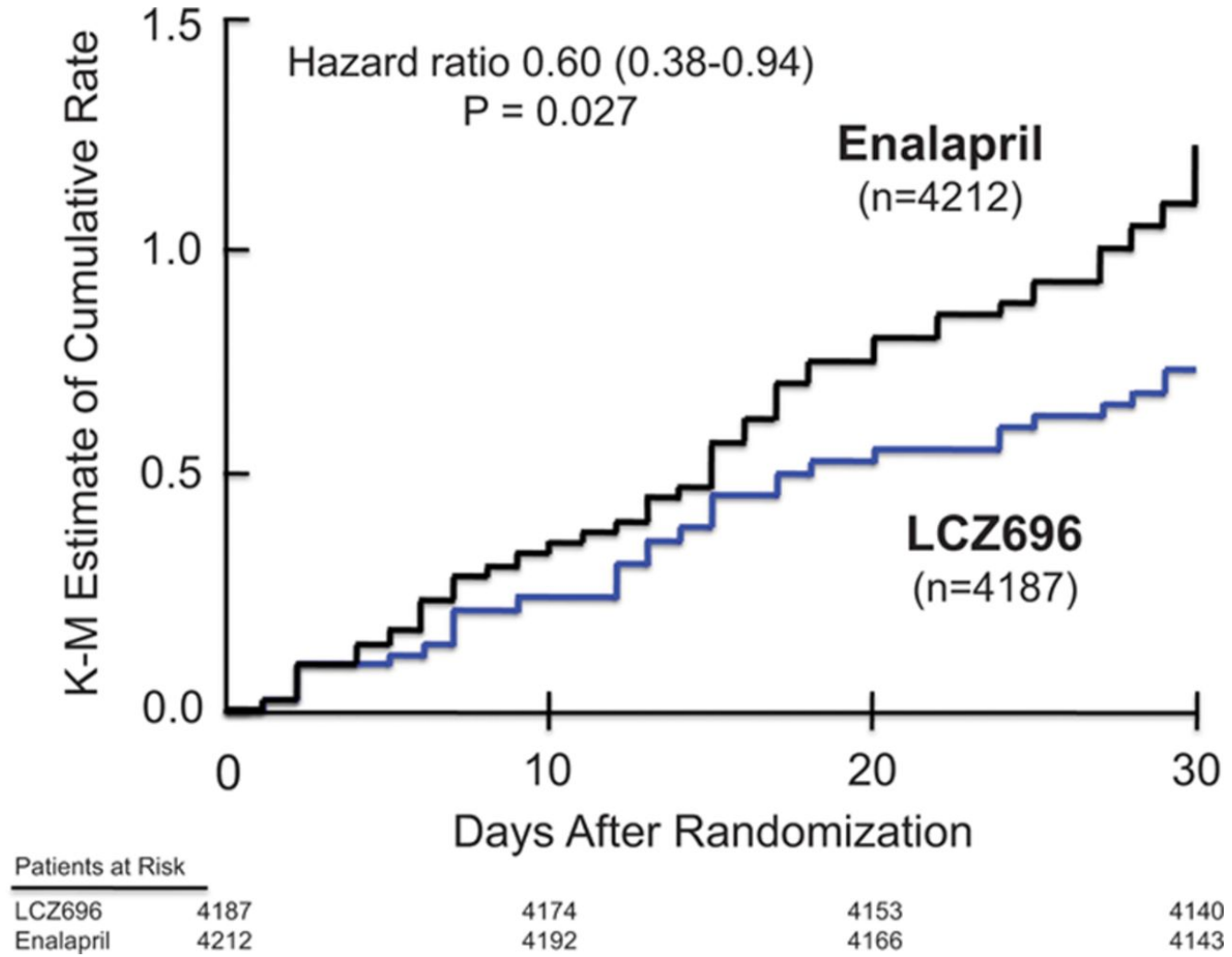
McMurray, Packer et al NEJM 2014

Kaplan–Meier Curve for the Time to First Hospitalization for Heart Failure During First 30 Days After Randomization, According to Study Group



Packer M et al. Circulation. 2015;131:54-61

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Pharmacologic Treatment for Stage C HFrEF- 2016

Strategies:

Disease Management

Genetic Counseling

Frailty Assessments

Palliative Care

Co-morbidities

Anemia

Sleep disordered breathing

Hypertension

Atrial Fibrillation

Devices

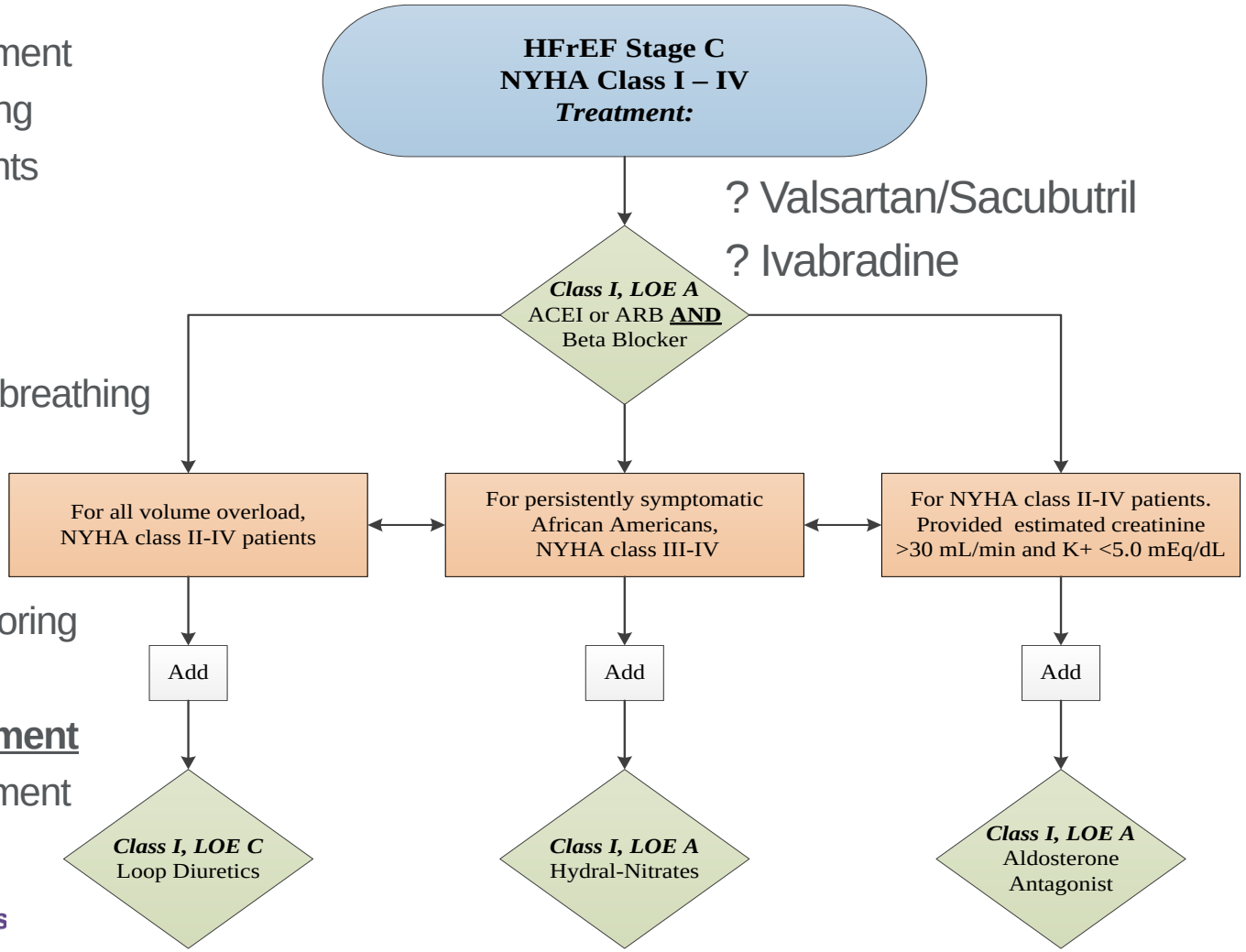
Remote PA monitoring

Wearable Vests

Quality Improvement

Process Improvement

Patient Education



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New Guidelines Have Emerged- 2016

Yancy, CW, et al.
Heart Failure Focused Update on Pharmacological Therapy

2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America

Developed in Collaboration With the International Society for Heart and Lung Transplantation

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COR/LOE 2016

Yancy, CW, et al.
Heart Failure Focused Update on Pharmacological Therapy

Table 1. Applying Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care* (Updated August 2015)

CLASS (STRENGTH) OF RECOMMENDATION

CLASS I (STRONG) — **Benefit >>> Risk**

Suggested phrases for writing recommendations:
- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

CLASS IIa (MODERATE) — **Benefit >> Risk**

Suggested phrases for writing recommendations:
- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

CLASS IIb (WEAK) — **Benefit ≥ Risk**

Suggested phrases for writing recommendations:
- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well established

CLASS III: No Benefit (MODERATE) — **Benefit = Risk**
(Generally, LOE A or B use only)

Suggested phrases for writing recommendations:
- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

CLASS III: Harm (STRONG) — **Risk > Benefit**

Suggested phrases for writing recommendations:
- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

LEVEL (QUALITY) OF EVIDENCE‡

LEVEL A
- High-quality evidence‡ from more than 1 RCT
- Meta-analyses of high-quality RCTs
- One or more RCTs corroborated by high-quality registry studies

LEVEL B-R (Randomized)
- Moderate-quality evidence‡ from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

LEVEL B-NR (Nonrandomized)
- Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

LEVEL C-LD (Limited Data)
- Randomized or nonrandomized observational or registry studies with limitations of design or execution
- Meta-analyses of such studies
- Physiological or mechanistic studies in human subjects

LEVEL C-EO (Expert Opinion)

Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

RAAS inhibition- 2016

7.3.2. Pharmacological Treatment for Stage C HF With Reduced Ejection Fraction: Recommendations

7.3.2.10. Renin-Angiotensin System Inhibition With Angiotensin-Converting Enzyme Inhibitor or Angiotensin Receptor Blocker or ARNI: Recommendations

See the *Online Data Supplement* (http://jaccjacc.acc.org/Clinical_Document/2016_Heart_Failure_Focused_Update_Data_Supplement_New_Therapy_Only_S5.pdf) for evidence supporting these recommendations.

Recommendations for Renin-Angiotensin System Inhibition With ACE Inhibitor or ARB or ARNI		
COR	LOE	Recommendations
I	ACE: A ARB: A ARNI: B-R	The clinical strategy of inhibition of the renin-angiotensin system with ACE inhibitors *(Level of Evidence: A)* (9-14), OR ARBs *(Level of Evidence: A)* (15-18), OR ARNI *(Level of Evidence: B-R)* (19) in conjunction with evidence-based beta blockers (20-22), and aldosterone antagonists in selected patients (23, 24), is recommended for patients with chronic HF*r*EF to reduce morbidity and mortality.

RAASi in Heart Failure and Post-MI LV Dysfunction

	Post-MI Low EF	Mild-Mod CHF Low EF	CHF Severe HF	CHF Preserved EF
ACEi[1]	AIRE SAVE	SOLVD	CONSENSUS	PEP-CHF (perindopril)
MRA	EPHESUS[1] (eplerenone)	EMPHASIS[1] (eplerenone)	RALES[1] (spironolactone)	TOPCAT[2] (spironolactone)
ARB[1]	OPTIMAAL VALIANT	ELITE-II HEALL VAL-HeFT CHARM		CHARM-Preserved I-PRESERVE
ARNI[3]		PARADIGM-HF (LCZ-696)		

RAASi=renin-angiotensin-aldosterone inhibitor; MI=myocardial infarction; EF: ejection fraction; CHF=chronic heart failure; ACEi=angiotensin-converting enzyme inhibitor; MRA=mineralocorticoid receptor antagonist; ARB=angiotensin II receptor blocker; ARNI=angiotensin receptor-neprilysin inhibitor.

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1. Mentz RJ, et al. *Int J Cardiol.* 2013:167:1677-1687.
2. Pitt B, et al. *N Engl J Med*. 2014;370(15):1383-1392.
3. McMurray JJV, et al. *N Engl J Med* 2014;371:993-1004.

ACE-I & ARB- 2016

I	ACE: A	**The use of ACE inhibitors is beneficial for patients with prior or current symptoms of chronic HF*r*EF to reduce morbidity and mortality (9-14, 25).**
See Online Data Supplement 18.		ACE inhibitors have been shown in large RCTs to reduce morbidity and mortality in patients with HF*r*EF with mild, moderate, or severe symptoms of HF, with or without coronary artery disease (9-14). Data suggest that there are no differences among available ACE inhibitors in their effects on symptoms or survival (25). ACE inhibitors should be started at low doses and titrated upward to doses shown to reduce the risk of cardiovascular events in clinical trials. ACE inhibitors can produce angioedema and should be given with caution to patients with low systemic blood pressures, renal insufficiency, or elevated serum potassium (>5.0 mEq/L). Angioedema occurs in <1% of patients who take an ACE inhibitor, but it occurs more frequently in blacks and women (26). Patients should not be given ACE inhibitors if they are pregnant or plan to become pregnant. ACE inhibitors also inhibit kininase and increase levels of bradykinin, which can induce cough in up to 20% of patients but also may contribute to beneficial vasodilation. If maximal doses are not tolerated, intermediate doses should be tried; abrupt withdrawal of ACE inhibition can lead to clinical deterioration and should be avoided. Although the use of an ARNI in lieu of an ACE inhibitor for HF*r*EF has been found to be superior, *for those patients for whom ARNI is not appropriate, continued use of an ACE inhibitor for all classes of HFrEF remains strongly advised.*
I	ARB: 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 (15-18, 27, 28).**

ARNI 2016

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 (19).**
See Online Data Supplements 1 and 18.		Benefits of ACE inhibitors with regard to decreasing HF progression, hospitalizations, and mortality rate have been shown consistently for patients across the clinical spectrum, from asymptomatic to severely symptomatic HF. Similar benefits have been shown for ARBs in populations with mild-to-moderate HF who are unable to tolerate ACE inhibitors. In patients with mild-to-moderate HF (characterized by either 1) mildly elevated natriuretic peptide levels, BNP [B-type natriuretic peptide] >150 pg/mL or NT-proBNP [N-terminal pro-B-type natriuretic peptide] ≥600 pg/mL; or 2) BNP ≥100 pg/mL or NT-proBNP ≥400 pg/mL with a prior hospitalization in the preceding 12 months) who were able to tolerate both a target dose of enalapril (10 mg twice daily) and then subsequently an ARNI (valsartan/sacubitril; 200 mg twice daily, with the ARB component equivalent to valsartan 160 mg), hospitalizations and mortality were significantly decreased with the valsartan/sacubitril compound compared with enalapril. The target dose of the ACE inhibitor was consistent with that known to improve outcomes in previous landmark clinical trials (10).

ARNI – (Harm) 2016

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 (31, 32).**
See Online Data Supplement 3.		Oral neprilysin inhibitors, used in combination with ACE inhibitors can lead to angioedema and concomitant use is contraindicated and should be avoided. A medication that represented both a neprilysin inhibitor and an ACE inhibitor,

Ivabradine 2016

7.3.2.11. Ivabradine: Recommendation

See the *Online Data Supplement*

(http://jacc.jacc.acc.org/Clinical_Document/2016_Heart_Failure_Focused_Update_Data_Supplement_New_Therapy_Only_S5.pdf) for evidence supporting this recommendation.

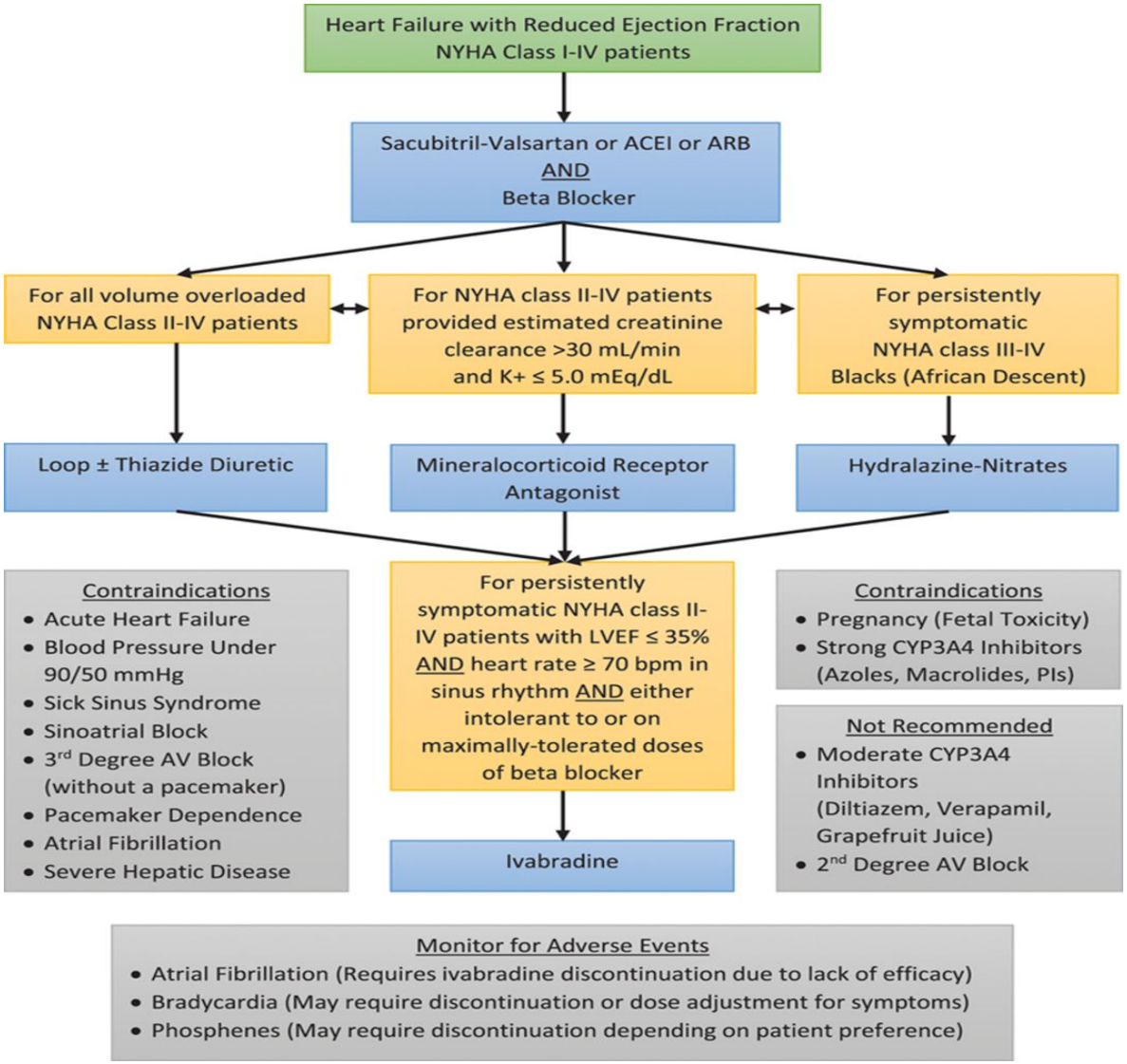
Recommendation for Ivabradine		
COR	**LOE**	**Recommendation**
IIa	**B-R**	**Ivabradine can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HF*r*EF (LVEF ≤35%) who are receiving GDEM, including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 bpm or greater at rest (37-40).**
See Online Data Supplement 4.		Ivabradine is a new therapeutic agent that selectively inhibits the I_f current in the sinoatrial node, providing heart rate reduction. One RCT demonstrated the efficacy of ivabradine in reducing the composite endpoint of cardiovascular death or HF hospitalization (38). The benefit of ivabradine was driven by a reduction in HF hospitalization. The study included patients with HF*r*EF (NYHA class II-IV, albeit with only a modest representation of NYHA class IV HF) and left ventricular ejection fraction (LVEF) ≤35%, in sinus rhythm with a resting heart rate of ≥70 beats per minute. Patients enrolled included a small number with paroxysmal atrial fibrillation (<40% of the time) but otherwise in

SUMMARY OF ACC/AHA/HFSA 2016 HF Guidelines; Focused Update

Table 1 | **Pharmacological treatment recommendations for patients with stage C HFrEF**[5,6]

Patient population	Treatment	Recommendation and LOE
2013 ACC/AHA guidelines		
For all patients with HFrEF with volume overload, NYHA class II–IV	• Loop diuretics • In addition to ACE inhibitor or ARB and β-blocker	Class I, LOE C
For persistently symptomatic African American patients, NYHA class III–IV, to reduce morbidity and mortality	• Hydral-nitrates • In addition to ACE inhibitor, or ARB and β-blocker	Class I, LOE A
For patients with NYHA class II–IV with eGFR >30 ml/min/1.73m^2 and K^+ <5.0 mEq/l, to reduce morbidity and mortality	• Mineralocorticoid-receptor antagonists • In addition to ACE inhibitor or ARB in conjunction with β-blocker	Class I, LOE A
2016 ACC/AHA/HFSA guideline update		
For patients with chronic HFrEF, to reduce morbidity and mortality	• ARNI in conjunction with β-blocker	Class I, LOE B-R
For patients with chronic symptomatic HFrEF, NYHA class II–III, who tolerate an ACE inhibitor or ARB	• ARNI to replace an ACE inhibitor or ARB	Class I, LOE B-R
For patients with stable chronic HFrEF (LVEF ≤35%), NYHA class II–III, who are in sinus rhythm with a heart rate ≥70 bpm at rest, to reduce heart failure hospitalization	• Ivabradine in addition to ACE inhibitor or ARB and β-blocker	Class IIa, LOE B-R

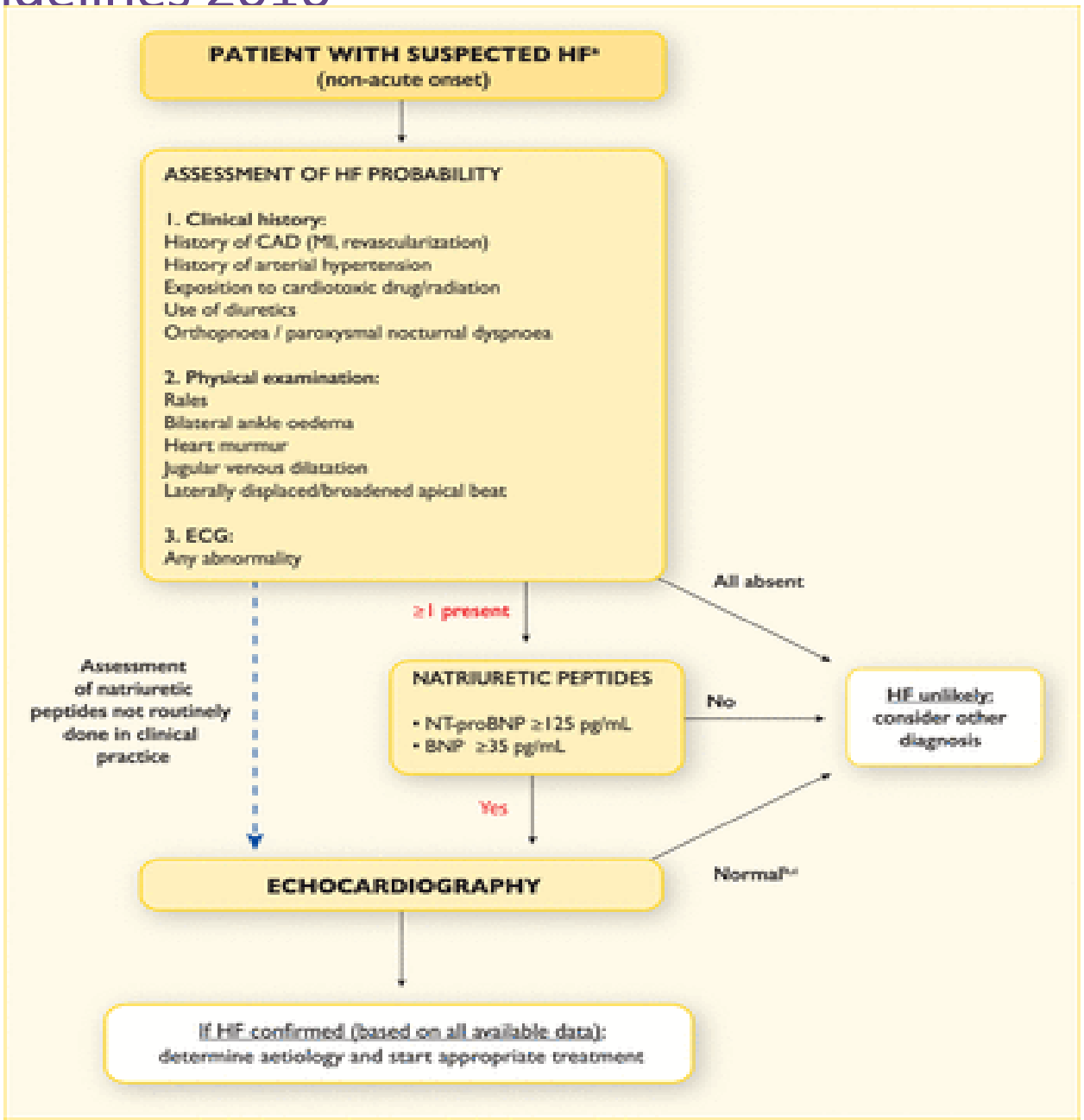
Evidence-based medical therapy.



Mitchell A. Psotka, and John R. Teerlink Circulation. 2016;133:2066-2075

American Heart Association. tern

ESC HF Guidelines 2016



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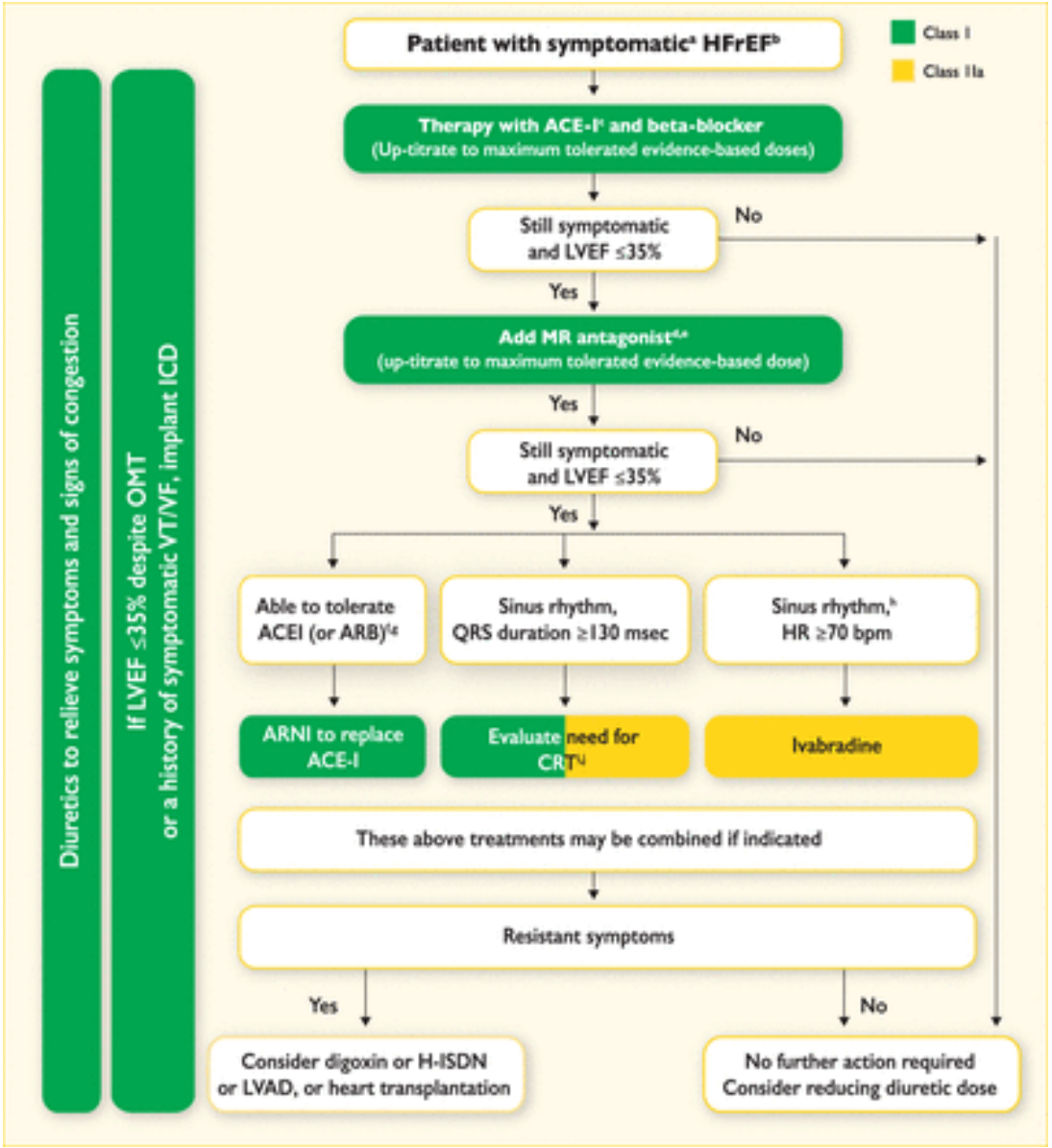
ESC HFrEF Treatment Algorithm



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A new classification?

ESC HF GUIDELINES 2016

Table 3.1

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

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

2013 ACCF/AHA Guideline for the Management of Heart Failure

Developed in Collaboration With the American Academy of Family Physicians, American College of Chest Physicians, Heart Rhythm Society, and International Society for Heart and Lung Transplantation

Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation

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Definition of Heart Failure

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.

From: **Characteristics and Outcomes of Adult Outpatients With Heart Failure and Improved or Recovered Ejection Fraction**

JAMA Cardiol. Published online July 06, 2016. doi:10.1001/jamacardio.2016.1325

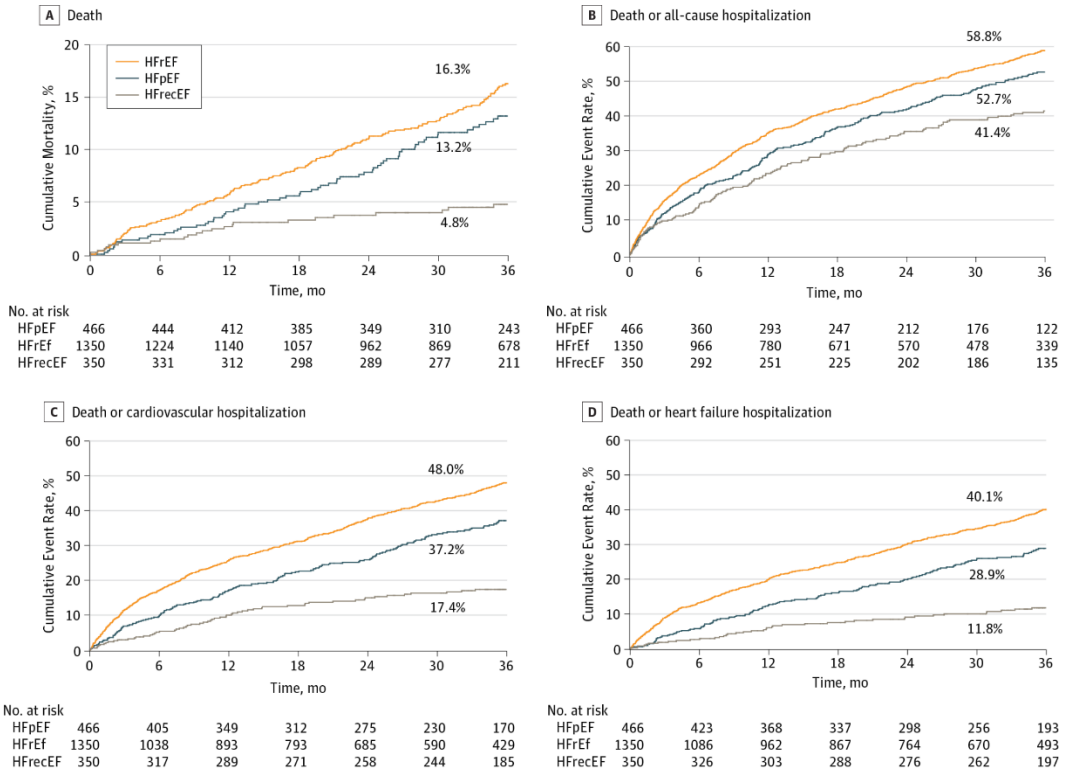

Figure Legend:

Kaplan-Meier Curves, Adjusted for Age and Sex, Across the 3 Heart Failure GroupsThe stratified log-rank χ^2_2 was 15.0 ($P < .001$) for difference in mortality between groups. HFpEF indicates heart failure with preserved ejection fraction; HFrecEF, heart failure with recovered ejection fraction; and HFrEF, heart failure with reduced ejection fraction.

Nature Reviews Cardiology, Vol. 13, October 2016

PERSPECTIVES

VIEWPOINT

2016 ESC and ACC/AHA/HFSA heart failure guideline update — what is new and why is it important?

Mariell Jessup, Thomas H. Marwick, Piotr Ponikowski, Adriaan A. Voors and Clyde W. Yancy

Abstract | Heart failure (HF) is a global epidemic affecting millions of individuals worldwide. Although important progress has been made in the management of HF, this condition remains a common cause of morbidity and death. Since the publication of the previous sets of guidelines for the management of HF, new

and today no one would dispute that, by applying evidence-based discoveries, HF has become a treatable disease.

The Task Force on the 2016 ESC HF guidelines[4], which we had the privilege to co-chair, decided to write a full document that, in its final form, is the result of extensive interactions between the Task Force, the review team, and the ESC Committee for Practice Guidelines. In parallel, on the other side of the Atlantic, a distinguished group of US colleagues has issued entirely independently the *2016 ACC/AHA/HFSA focused update on new pharmacological therapy for heart failure* document[5], summarizing an update on new pharmacotherapy for HF. We see these two documents as presenting similar

From: **Potential Mortality Reduction With Optimal Implementation of Angiotensin Receptor Neprilysin Inhibitor Therapy in Heart Failure**

JAMA Cardiol. Published online June 22, 2016. doi:10.1001/jamacardio.2016.1724

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.

Table Title:

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

THANK YOU

More Questions about Get With The Guidelines?

Visit heart.org/QualityHF to find your local Get With The Guidelines representative.

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