New Approaches to Treat and Prevent Heart Failure

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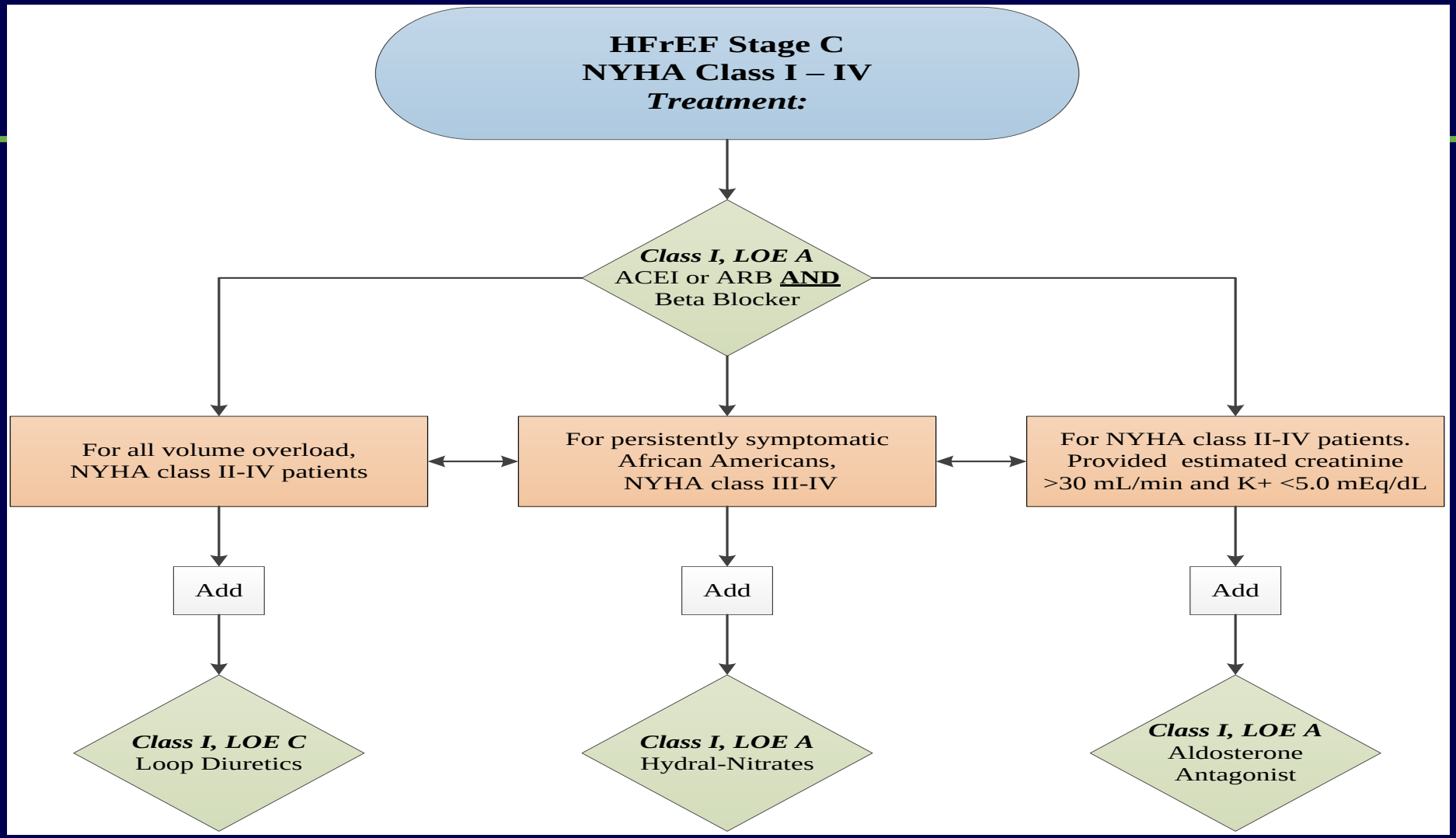
Heart Failure Background

Population Group	Prevalence	Incidence	Mortality	Hospital Discharges	Cost
Total population	5,700,000	915,000	300,122 (50% at 5 years)	1,023,000	$30.7 billion

- Heart failure (HF) is a major public health problem resulting in substantial morbidity, mortality, and healthcare expenditures
- Major cost driver of HF is high incidence of hospitalizations
- Despite treatment advances large number of eligible patients are not receiving one or more evidence-based HF therapies

American Heart Association. *2016 Heart and Stroke Statistical Update.* Dallas, Tex: American Heart Association; 2016.

Pharmacologic Treatment for Stage C HFrEF



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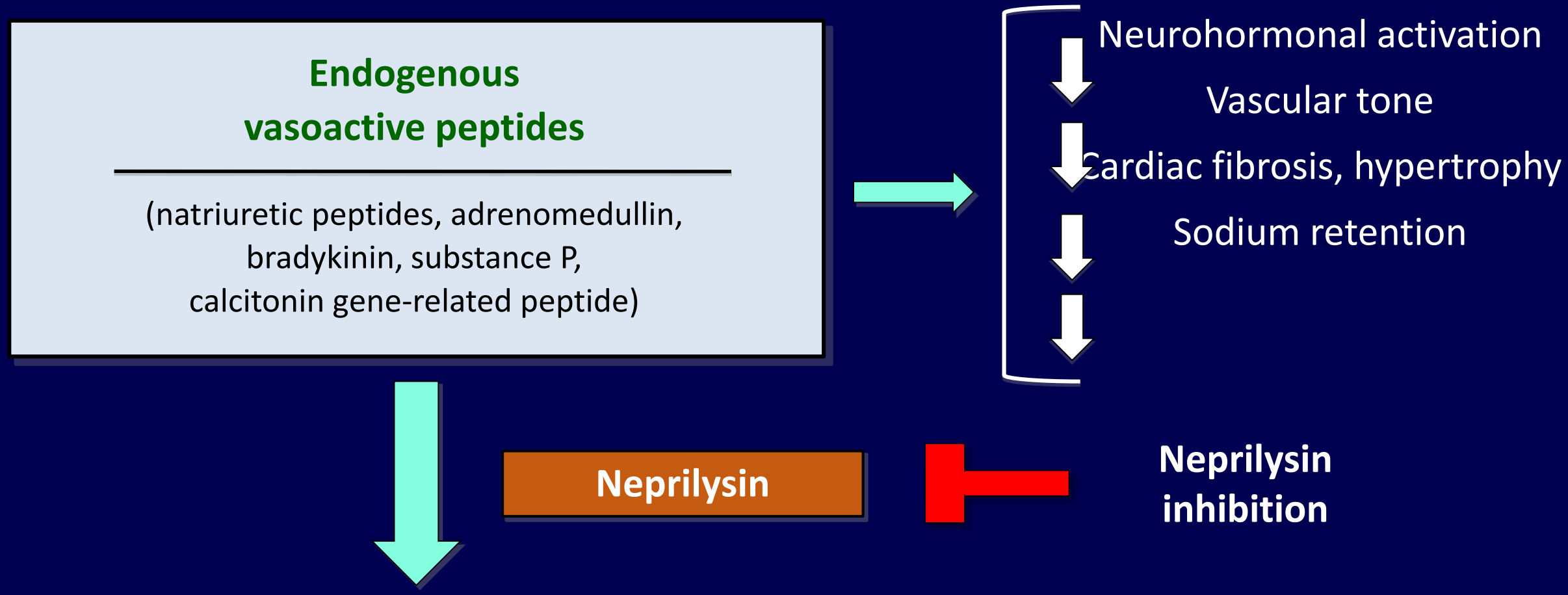
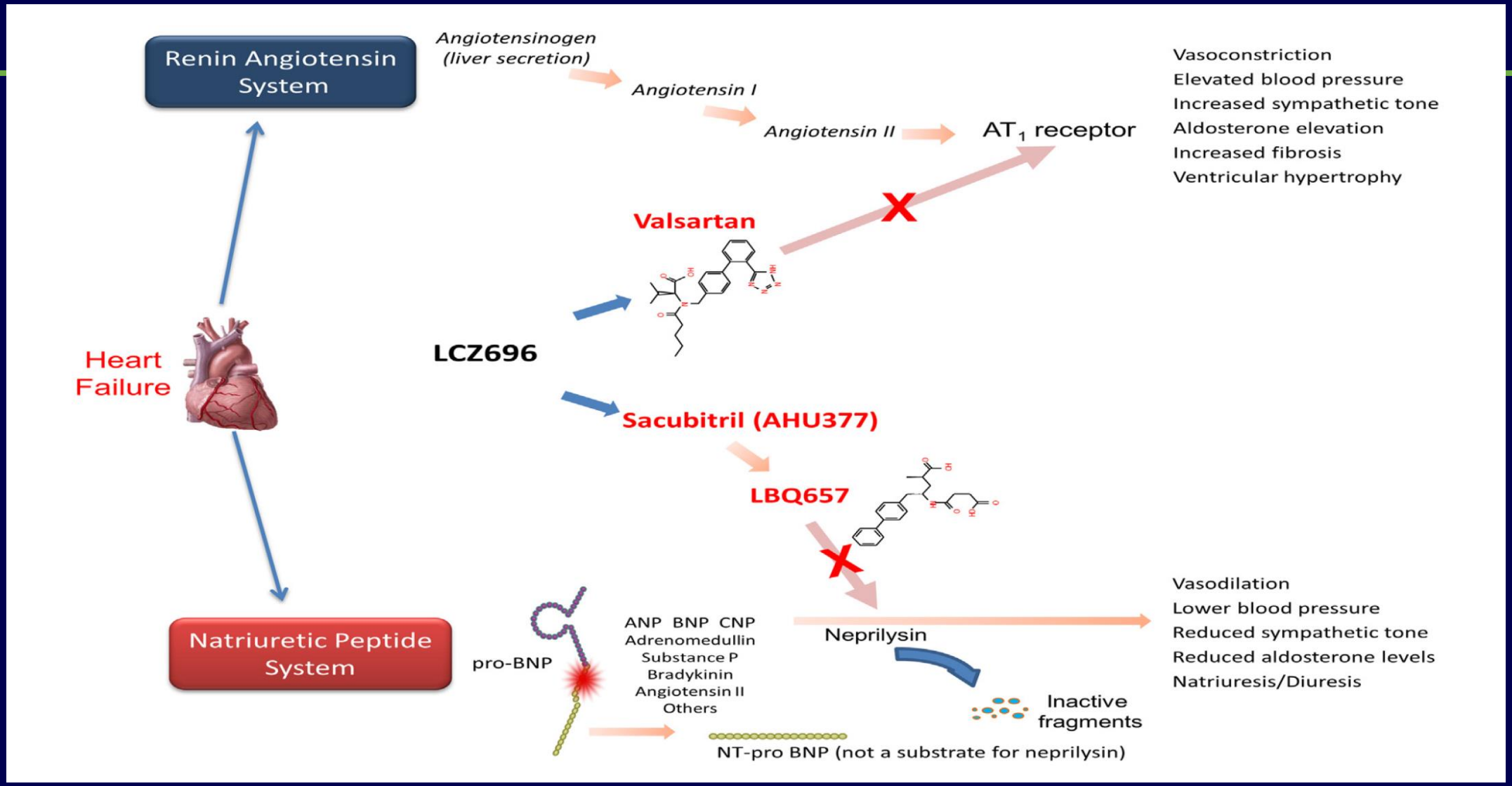
American Heart Association.

Neprilysin Inhibition Potentiates Actions of Endogenous Vasoactive Peptides That Counter Maladaptive Mechanisms in Heart Failure



McMurray JJ et al. N Engl J Med. 2014 Sep 11;371(11):993-1004.

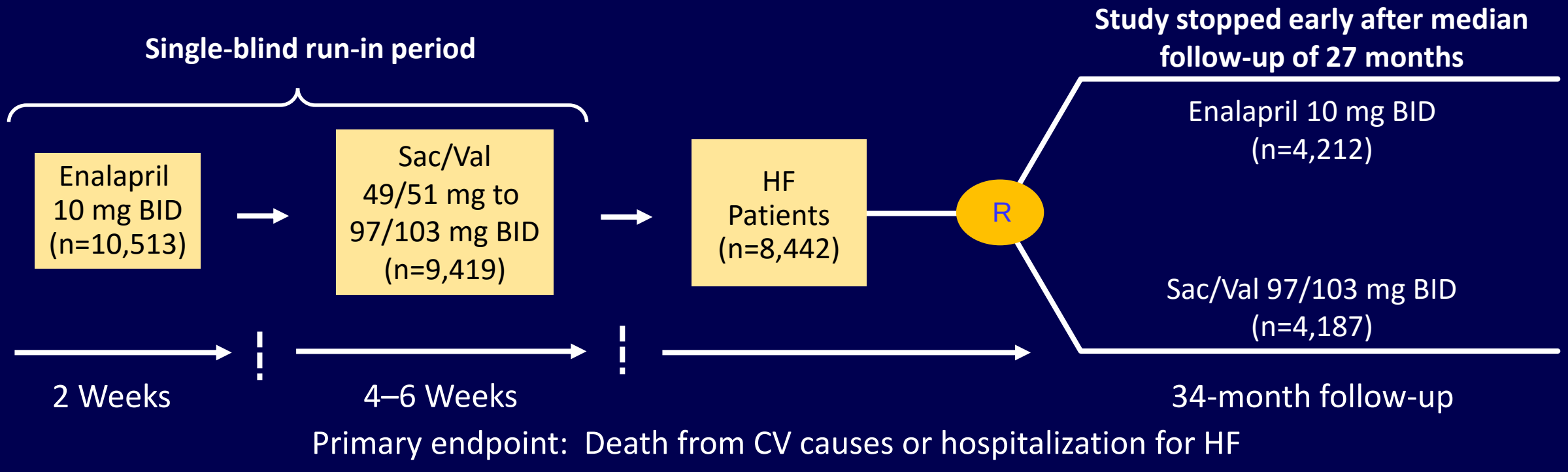
Sacubitril-Valsartan (LCZ696)
Mechanism of Action



PARADIGM-HF Trial: Design

Entry Criteria:

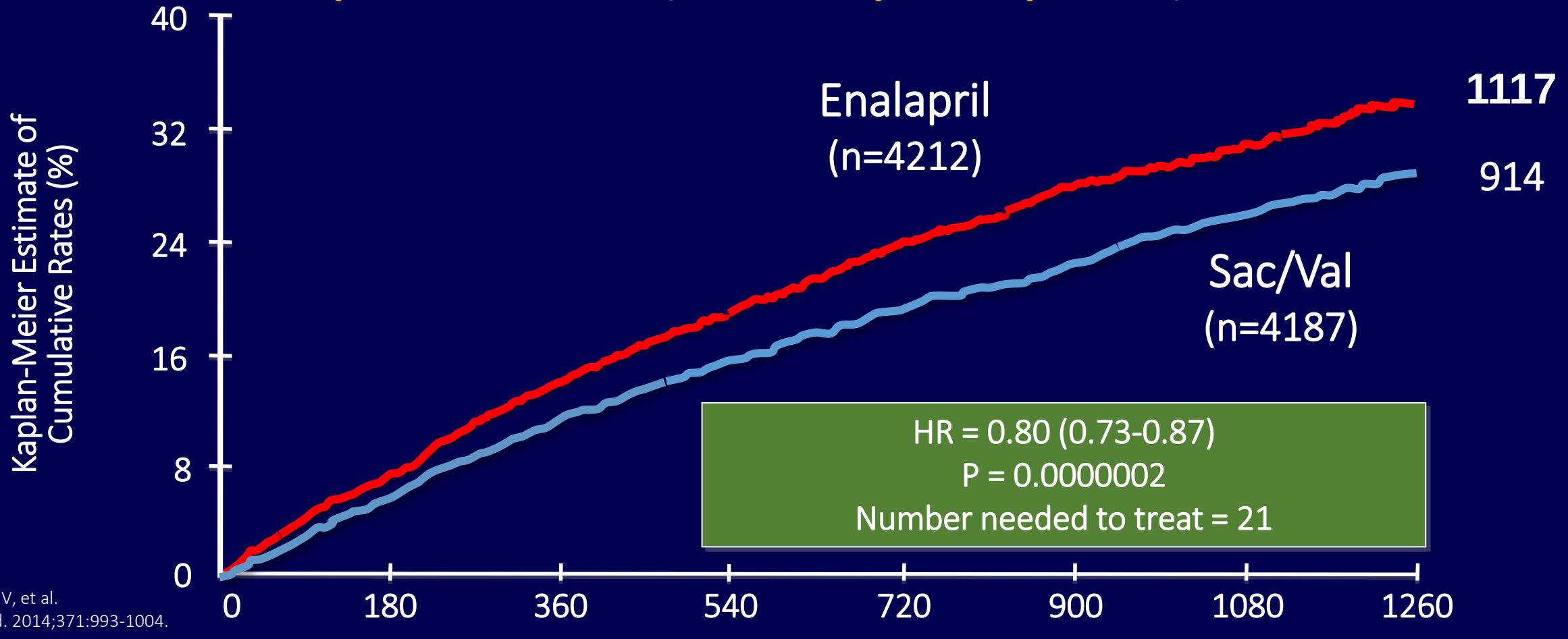
- NYHA Class II-IV HF, LVEF ≤40% → amended to ≤35%
- BNP ≥150 pg/mL (or NT-proBNP ≥ 600 pg/mL) or 1/3 lower if hospitalized for HF within 12 mos
- On a stable dose of ACEI or ARB equivalent to ≥10 mg of enalapril daily for ≥4 weeks
- Unless contraindicated, on stable dose of beta-blocker for ≥4 weeks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



Specifically designed to test replacing current use of ACEI and ARB as the cornerstone of the treatment of HF

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

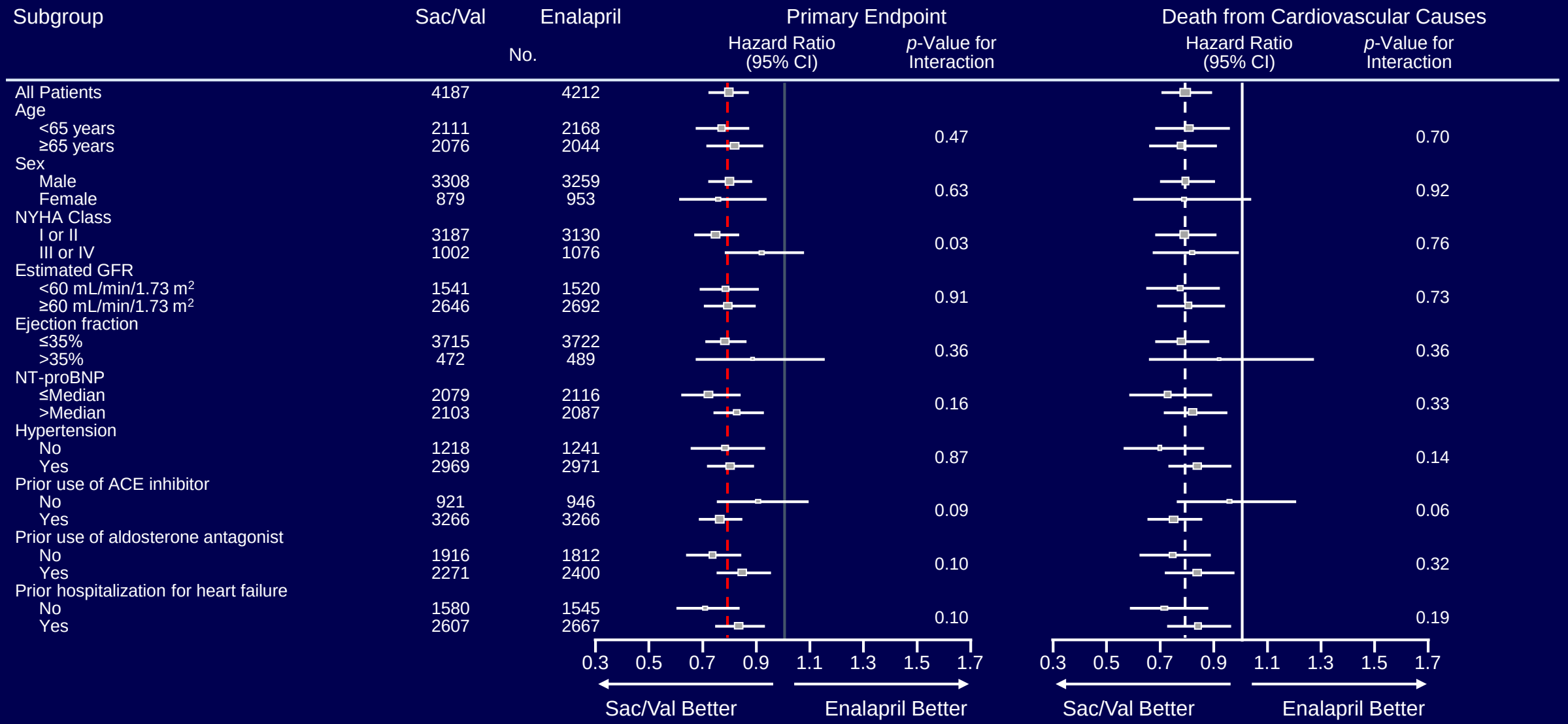
PARADIGM-HF: Cardiovascular Death or Heart Failure Hospitalization (Primary Endpoint)



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

Patients at Risk								
Sac/Val	4187	3922	3663	3018	2257	1544	896	249
Enalapril	4212	3883	3579	2922	2123	1488	853	236

Sac/Val vs. Enalapril on Primary Endpoint and on CV Death by Subgroups



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

PARADIGM-HF: Summary of Findings

In heart failure with reduced ejection fraction, when compared with recommended doses of enalapril:

Sac/Val was *more effective* than enalapril in . . .

- Reducing the risk of CV death and HF hospitalization
- Reducing the risk of CV death by *incremental* 20%
- Reducing the risk of HF hospitalization by *incremental* 21%
- Reducing all-cause mortality by *incremental* 16%
- *Incrementally* improving symptoms and physical limitations

Sac/Val was *better tolerated* than enalapril . . .

- Less likely to cause cough, hyperkalemia or renal impairment
- Less likely to be discontinued due to an adverse event
- More hypotension, but no increase in discontinuations
- Not more likely to cause serious angioedema

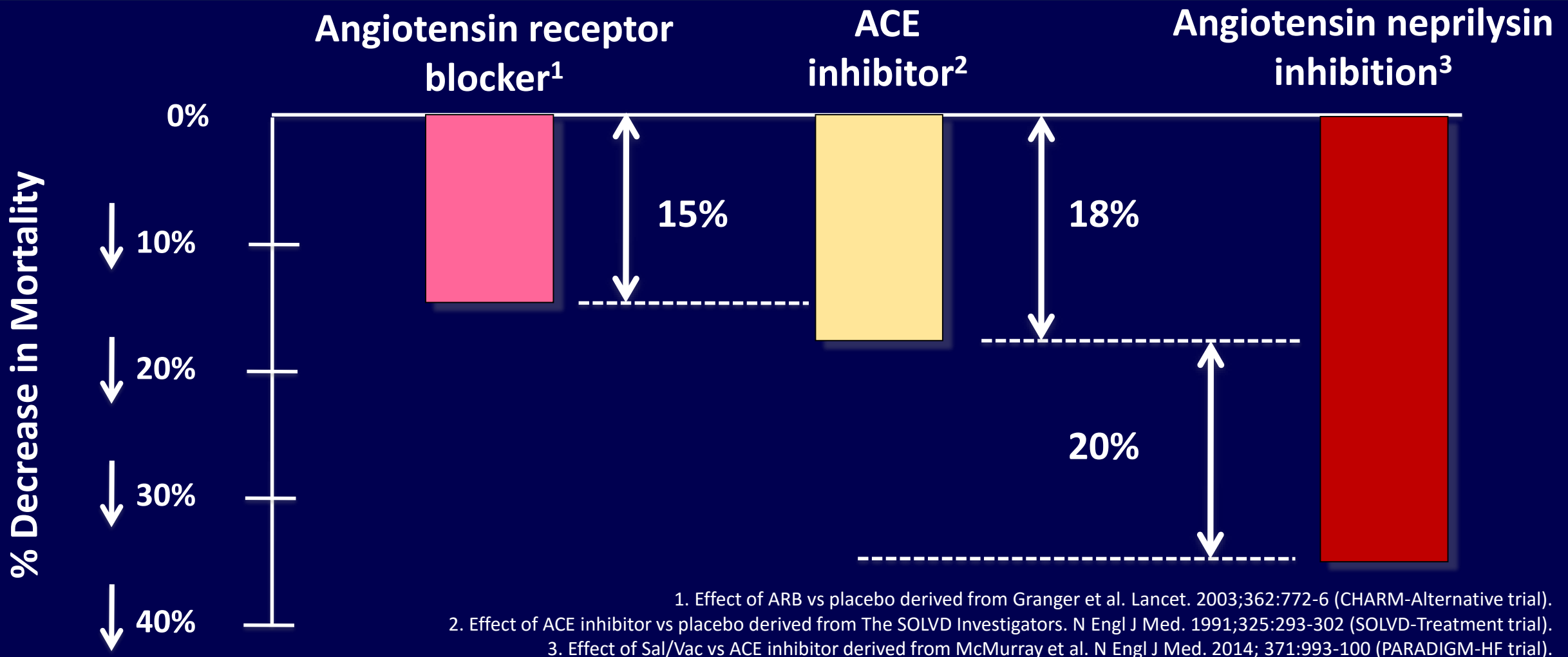
McMurray JJ et al. N Engl J Med. 2014 Sep 11;371(11):993-1004.

FDA-Approved Sacubitril-Valsartan

	Sacubitril/Valsartan
Brand name	Entresto
Indication	The fixed-dose combination of the neprilysin inhibitor sacubitril and the ARB valsartan is indicated to reduce the risk of CV death and HF hospitalization in patients with HF with reduced ejection fraction.
Dosage	Start with 49/51 mg twice daily. Double the dose after 2–4 weeks as tolerated to maintenance dose of 97/103 mg twice daily.
Renal/hepatic impairment	For patients not currently taking an ACEI or ARB, or for those with severe renal impairment (eGFR <30 mL/min/1.73 m^2) or moderate hepatic impairment, start with 24/26 mg twice daily.
Switching from an ACE inhibitor	Stop ACE inhibitor for 36 hours before starting treatment.
Contraindications	History of angioedema related to previous ACE inhibitor or ARB, concomitant use of ACE inhibitors, concomitant use of aliskiren in patients with diabetes. WARNING – pregnancy, hyperkalemia.
Side effects	Hypotension, hyperkalemia, cough, dizziness, renal failure, and angioedema (0.5% Sac/Val vs. 0.2% Enalapril).

http://www.pdr.net/full-prescribing-information/entresto?druglabelid=3756. Accessed October 20, 2015.

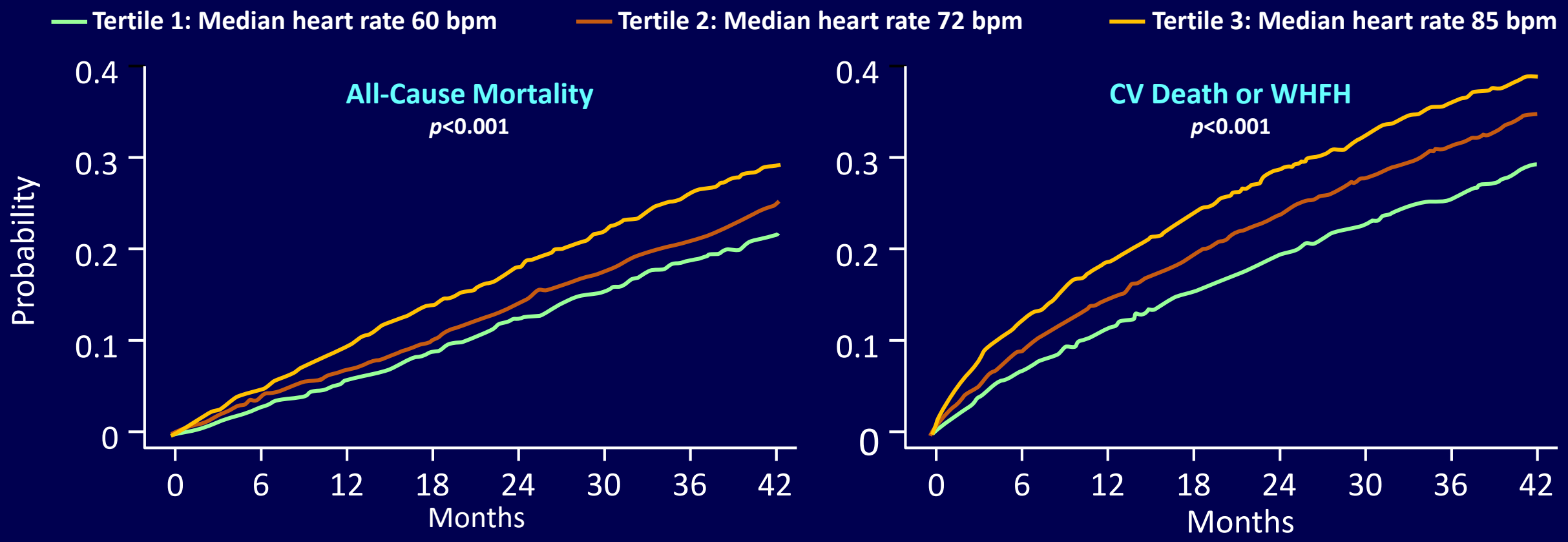
Angiotensin Neprilysin Inhibition With Sac/Val Doubles Effect on CV Death of Current RASI



1. Effect of ARB vs placebo derived from Granger et al. Lancet. 2003;362:772-6 (CHARM-Alternative trial).
2. Effect of ACE inhibitor vs placebo derived from The SOLVD Investigators. N Engl J Med. 1991;325:293-302 (SOLVD-Treatment trial).
3. Effect of Sal/Vac vs ACE inhibitor derived from McMurray et al. N Engl J Med. 2014; 371:993-100 (PARADIGM-HF trial).

Resting Heart Rate and CV Outcomes in Patients with HF

Retrospective analysis of 7,599 symptomatic HF* patients from the CHARM studies, who were followed for a median of 38 months to determine the relationship between resting heart rate at baseline and all-cause mortality, and fatal and nonfatal CV outcomes.



Resting heart rate is an important predictor of mortality and CV outcomes in patients with HF

WHFH = worsening heart failure hospitalization; *symptomatic HF defined as NYHA functional Class II to IV.

Adapted from: Castagno D, et al. J Am Coll Cardiol. 2012;59:1785-1795.

β-Blocker Dose and Heart Rate Reduction in Patients with Chronic Heart Failure

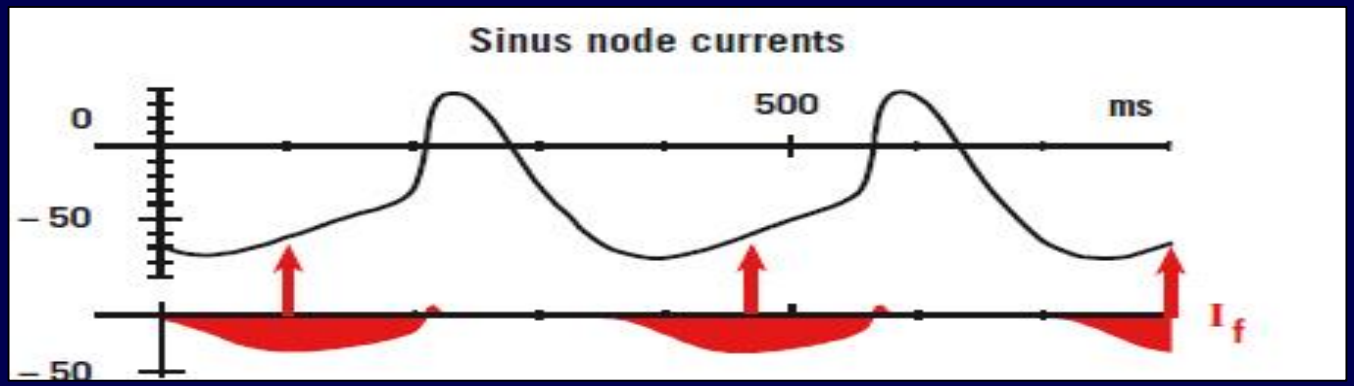
Results of univariable meta-regressions evaluating the effect of individual covariates on the potential mortality benefits of β-blockers in heart failure

Potential Modifier	# Trials	# Subjects	Ratio of Relative Risks (95% CI)	*P* Value
Heart rate reduction	17	17,831	0.82 (0.71-0.94) per 5 bpm	0.006
β-blocker dose	17	17,660	1.02 (0.93-1.10) per increment	0.69
Baseline heart rate	19	17,981	1.07 (0.88-1.32) per 5 bpm	0.47

Meta-analysis of 17 randomized trials in subjects with heart failure to examine whether the β-blocker dose or the magnitude of heart rate reduction could account for differences in treatment effects among heart failure β-blocker trials, 1966-2008.

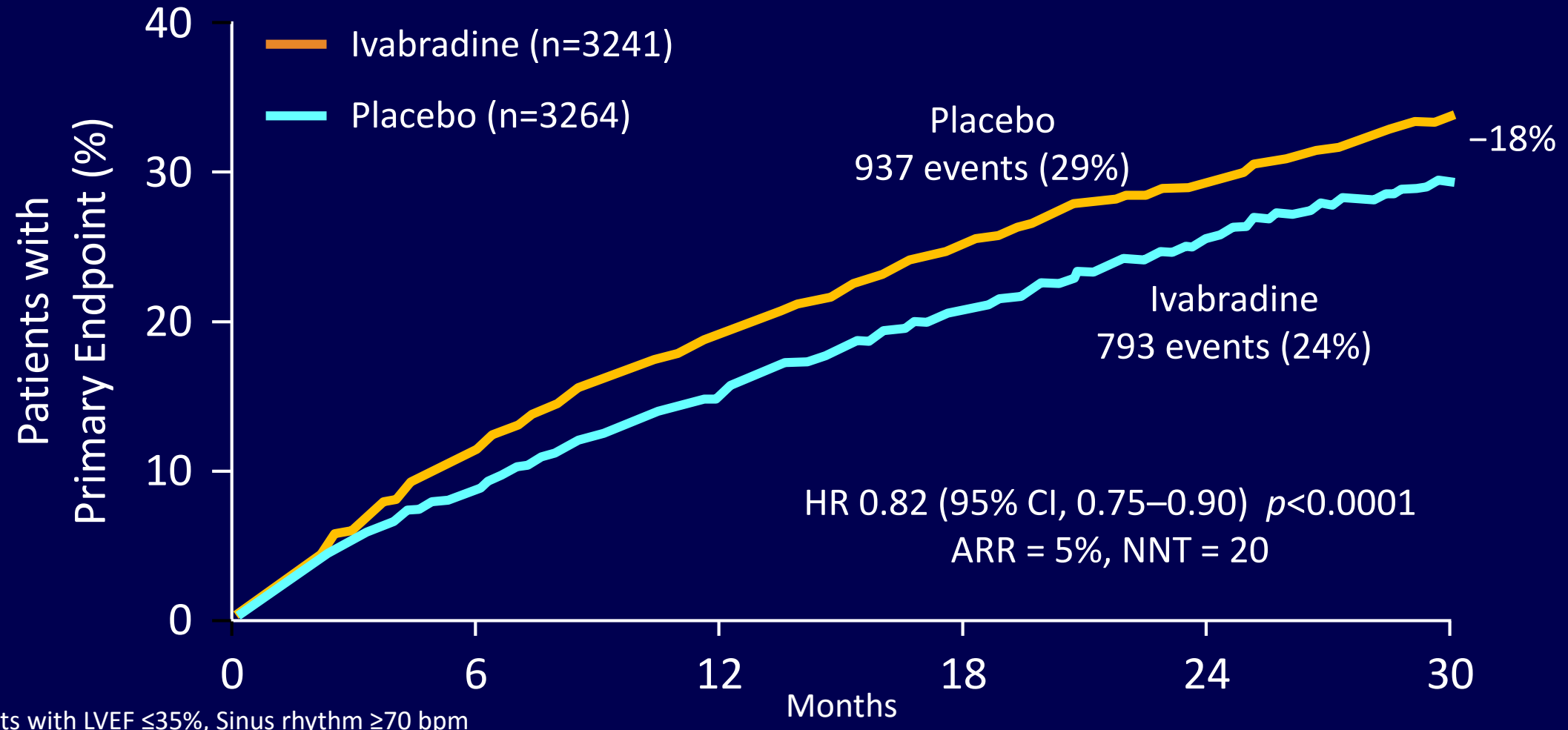
Ivabradine

- Specific inhibitor of the I_f current in SA node
- This so-called "funny" current controls the rate of spontaneous activity of SA node myocytes
- Reduces the slope for diastolic depolarization
  - Prolongs Diastolic Duration → Slows Heart Rate
- No action on other cardiac channels
- Does not modify contractility



DiFrancesco D. Pharmacol Res 2006;53:399-406; Savelieva I. Drug Saf 2008;31:95-107.

SHIFT Study: Primary Endpoint of CV Death or Hospitalization for Worsening HF



6558 patients with LVEF ≤35%, Sinus rhythm ≥70 bpm

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

Ivabradine and Outcomes in Chronic Heart Failure (SHIFT)

SHIFT: Hazard ratios for primary and individual outcomes, ivabradine vs placebo groups

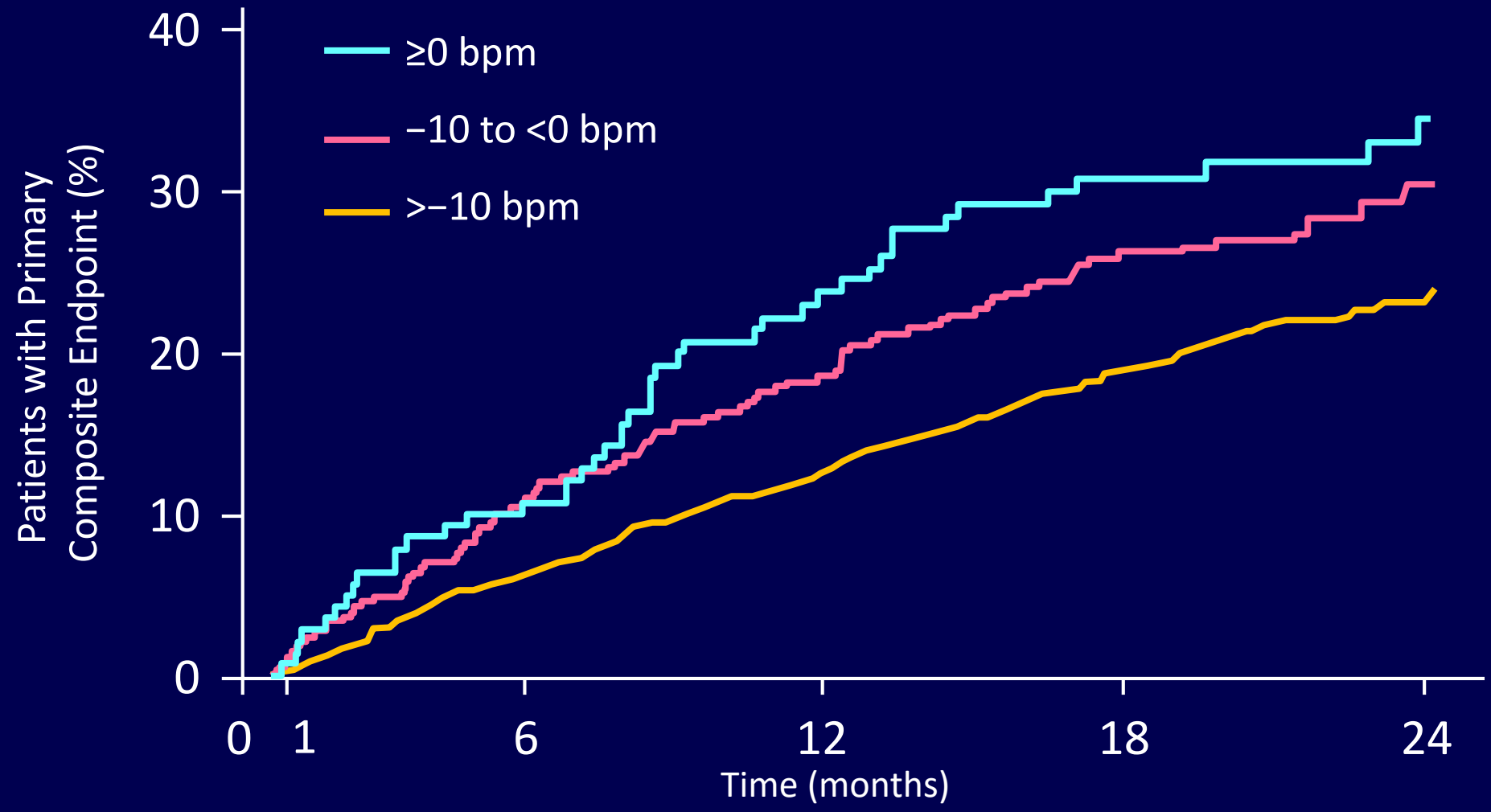
Outcomes in SHIFT	Ivabradine, n=3241 (%)	Placebo, n=3264 (%)	HR (95% CI)	p
CV death or HF hospitalization	24	29	0.82 (0.75-0.90)	<0.0001
Death from heart failure	3	5	0.74 (0.58-0.94)	0.014
HF hospitalization	16	21	0.74 (0.66-0.83)	<0.0001
CV death, HF hospitalization, or admission for nonfatal MI	25	30	0.82 (0.74-0.89)	<0.0001

The benefit of ivabradine appeared to go up with increasing heart rate (HR<77 HR 0.93; HR≥77 HR 0.75)

6558 patients with LVEF ≤35%, Sinus rhythm ≥70 bpm

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

Effect of Ivabradine on Outcomes According to Magnitude of HR Reduction



Böhm et al. Clin Res Cardiol. 2013;102(1):11-22.

FDA-Approved Ivabradine

	Ivabradine
Brand name	Corlanor
Indication	To reduce the risk of hospitalization for worsening HF in patients with stable, symptomatic chronic HF with LVEF ≤ 35% who are in sinus rhythm with resting HR ≥70 bpm and either are on maximally tolerated doses of beta-blockers or have a contraindication to beta-blocker use.
Dosage	Start with 5 mg twice daily. After 2 weeks of treatment, adjust dose based on HR. Max is 7.5 mg twice daily. In patients with conduction defects or in whom bradycardia could lead to hemodynamic compromise, start with 2.5 mg twice daily.
Contraindications	Acute decompensated HF; BP <90/50 mmHg; sick sinus syndrome or third-degree AV block, unless a functioning demand pacemaker is present; resting HR < 60 bpm prior to treatment; severe hepatic impairment; pacemaker dependence. WARNING – fetal toxicity.
Side effects	Occurring in ≥1% of patients are bradycardia, hypertension, atrial fibrillation, and luminous phenomena (phosphenes).

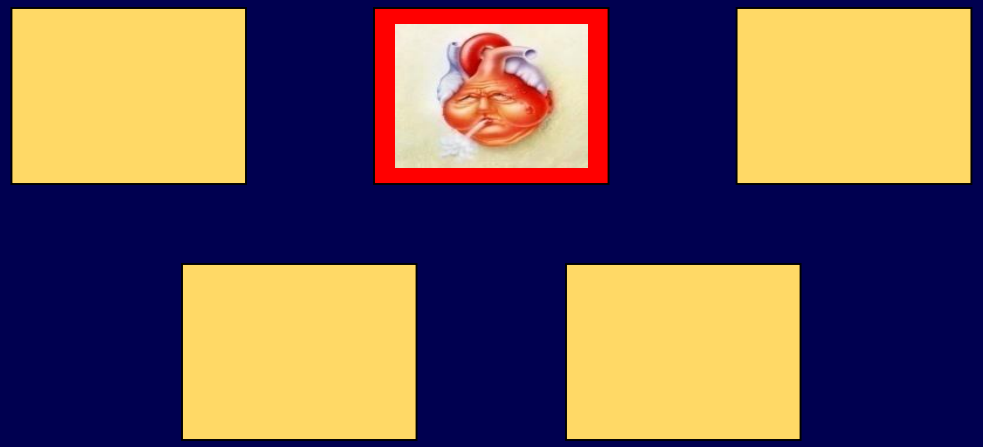
http://www.pdr.net/full-prescribing-information/corlanor?druglabelid=3713. Accessed October 20, 2015.

Heart Failure is Preventable

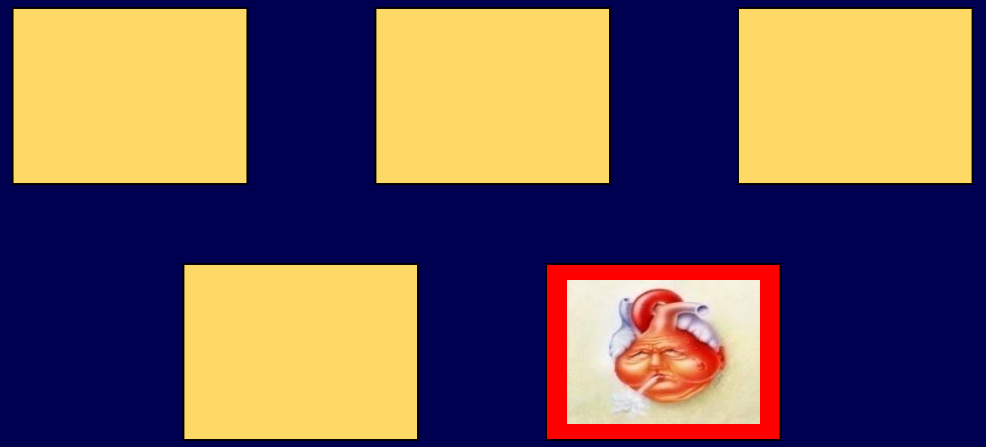
- There are large numbers of patients without any evidence of structural heart disease or symptoms who are at high risk for developing heart failure
- There will be 915,000 new cases of heart failure this year
- Better identification of patients at risk and the mechanisms by which risk factors result in heart failure may lead to better heart failure prevention strategies
- Modification of risk factors and medical therapies have been demonstrated to significantly reduce the risk of developing heart failure in these patients

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

Lifetime Risk for Developing Heart Failure



Men



Women

At age 40 years, the lifetime risk for CHF was 21.0% (95% CI 18.7% to 23.2%) for men and 20.3% (95% CI 18.2% to 22.5%) for women

Lloyd-Jones et al. Circulation 2002;106:3068-72.

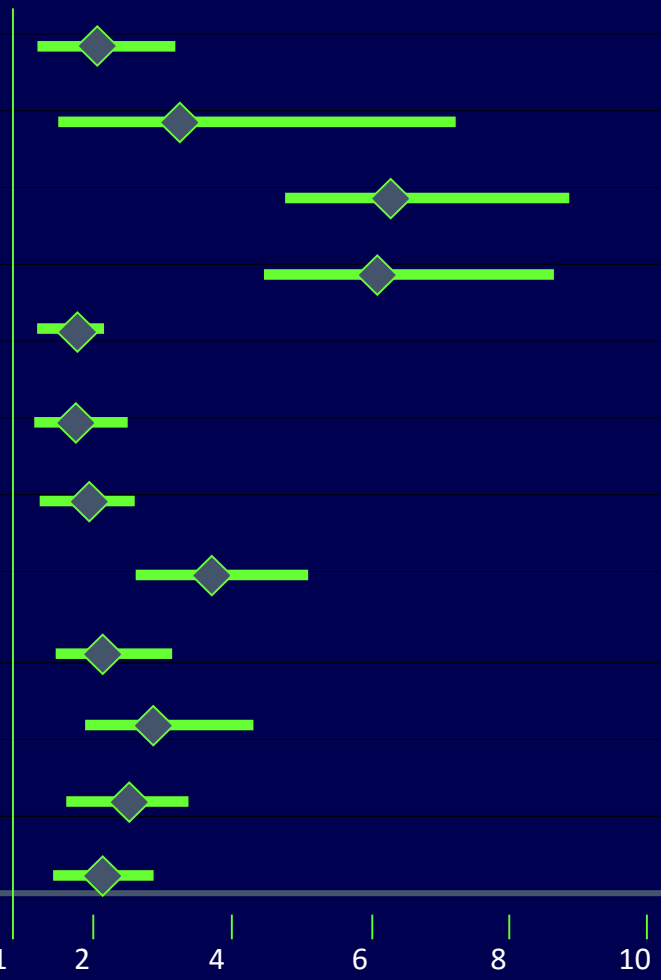
Established and Hypothesized Risk Factors For Developing HF

- Major Clinical RFs
  - Age, male sex
  - Hypertension, LVH
  - Myocardial infarction
  - Diabetes mellitus
  - Valvular heart disease
  - Obesity
- Minor Clinical RFs
  - Smoking
  - Dyslipidemia
  - Sleep-disordered breathing
  - Chronic kidney disease
  - Albuminuria
  - Homocysteine
  - Immune activation, IGF1, TNF, IL-6, CRP
  - Natriuretic peptides
  - Anemia
  - Dietary risk factors
- Minor Clinical RFs, con't
  - Increased HR
  - Sedentary lifestyle
  - Low socioeconomic status
- Toxic Risk Precipitants
  - Chemotherapy (anthracyclines, cyclophosphamide, 5-FU, trastuzumab)
  - Cocaine, NSAIDs
  - Thiazolidinediones
  - Doxazosin
  - Alcohol
- Genetic Risk Predictors
  - SNP (eg, 2CDel322-325, β1Arg389)
- Morphological Risk Predictors
  - Increased LVID, mass
  - Asymptomatic LV dysfunction
  - LV diastolic dysfunction

From Schocken et al. Circulation 2008;117:2544-2565.

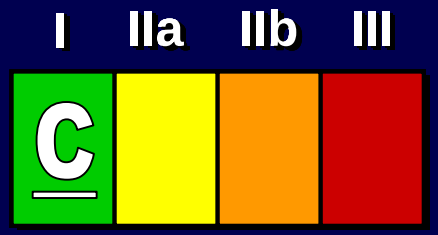
Risk Factors for the Development of HF

Risk Factor	Sex	Age- and Risk Factor–Adjusted Hazard Ratio† (95% CI)	Prevalence, %‡	Population-attributable Risk, %§
Hypertension	**M**		**60**	**39**
	F		**62**	**59**
Myocardial infarction	**M**		**10**	**34**
	F		**3**	**13**
Angina pectoris	**M**		**11**	**5**
	F		**9**	**5**
Diabetes	**M**		**8**	**6**
	F		**5**	**12**
Left ventricular hypertrophy	**M**		**4**	**4**
	F		**3**	**5**
Valvular heart disease	**M**		**5**	**7**
	F		**8**	**8**

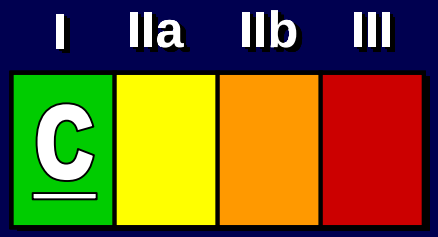


Levy D et al. JAMA. 1996;275:1557–1562

Patients at High Risk for Developing Heart Failure (Stage A): Identification

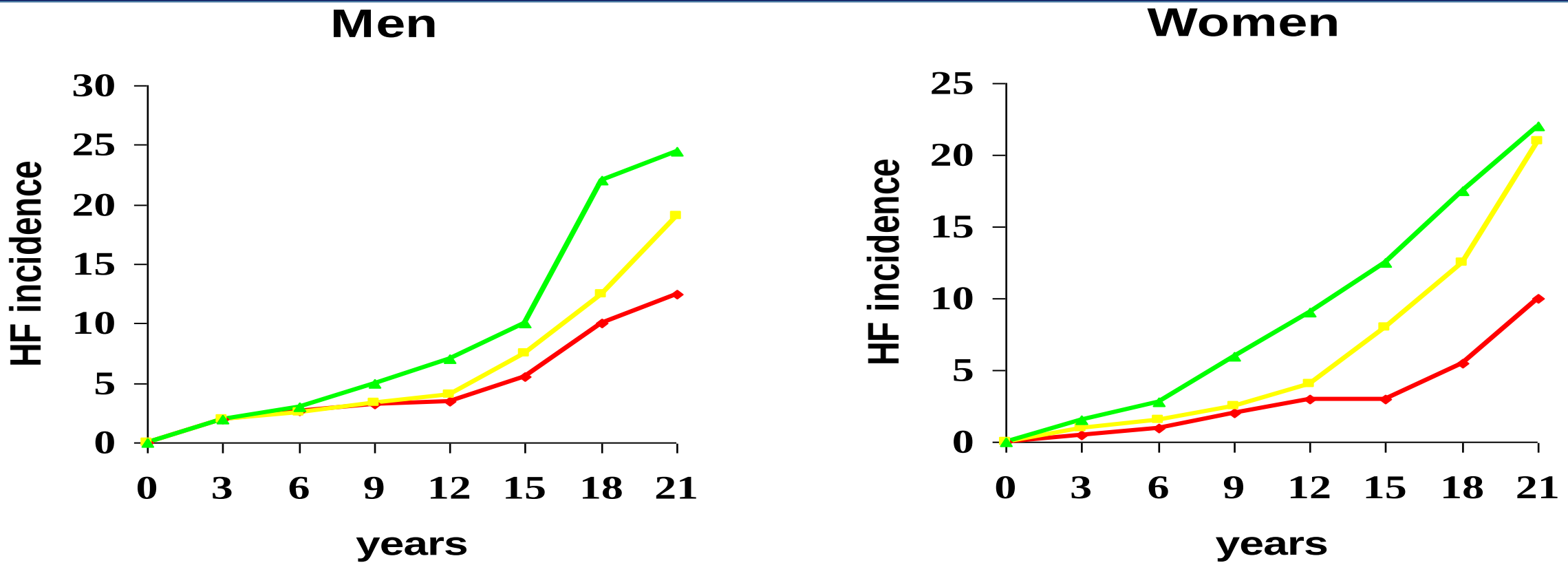


Healthcare providers should perform periodic evaluation for signs and symptoms of HF in patients at high risk for developing HF



Healthcare providers should perform a noninvasive evaluation of LV function (i.e., LVEF) in patients with a strong family history of cardiomyopathy or in those receiving cardiotoxic interventions

Obesity and the Risk of New Onset Heart Failure

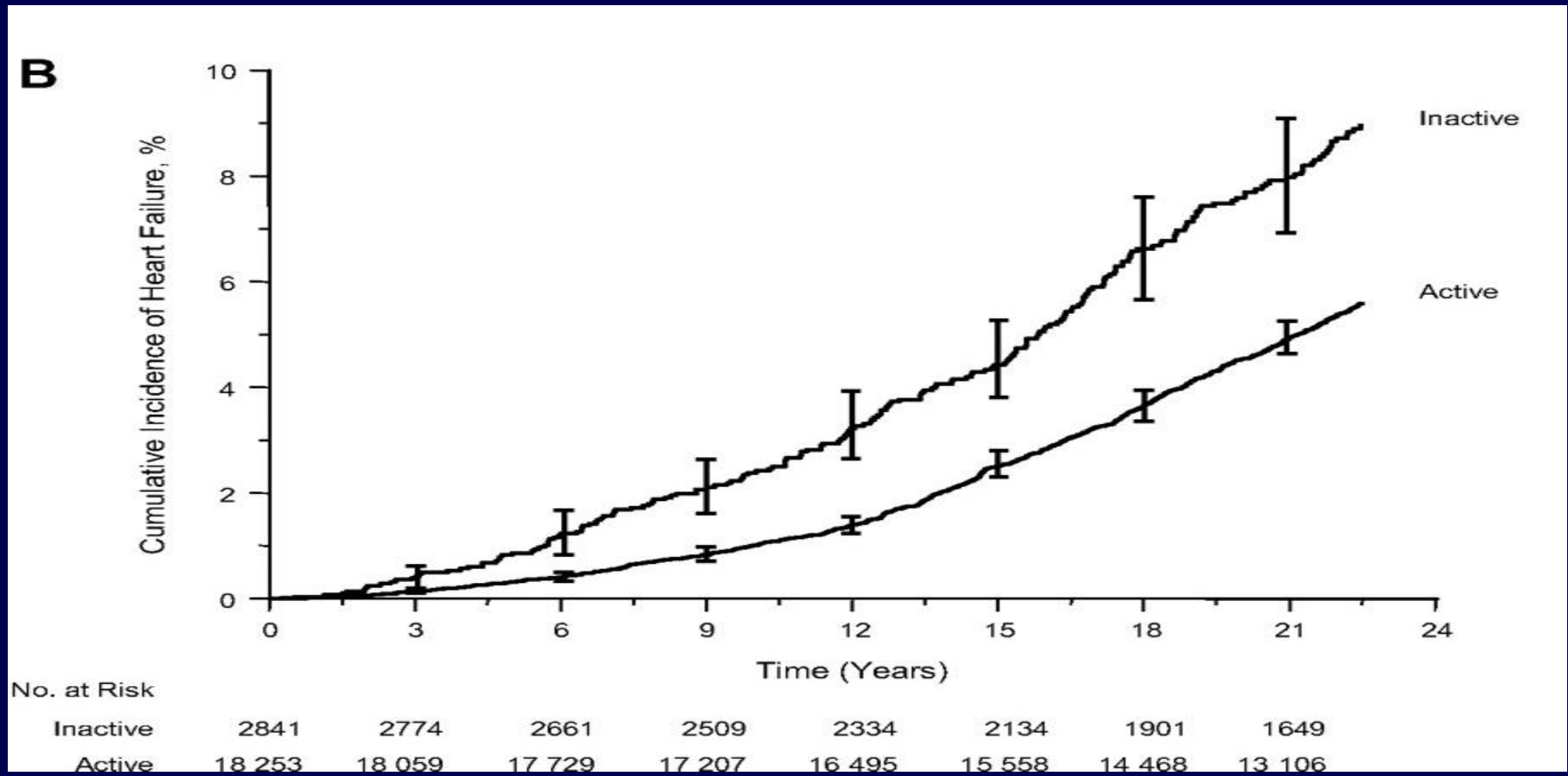


Framingham Cohort, n = 5881

Normal = BMI 18.5 – 24.9 kg/m^2; Overweight = 25 – 29.9 kg/m^2; Obese = BMI > 30 kg/m^2

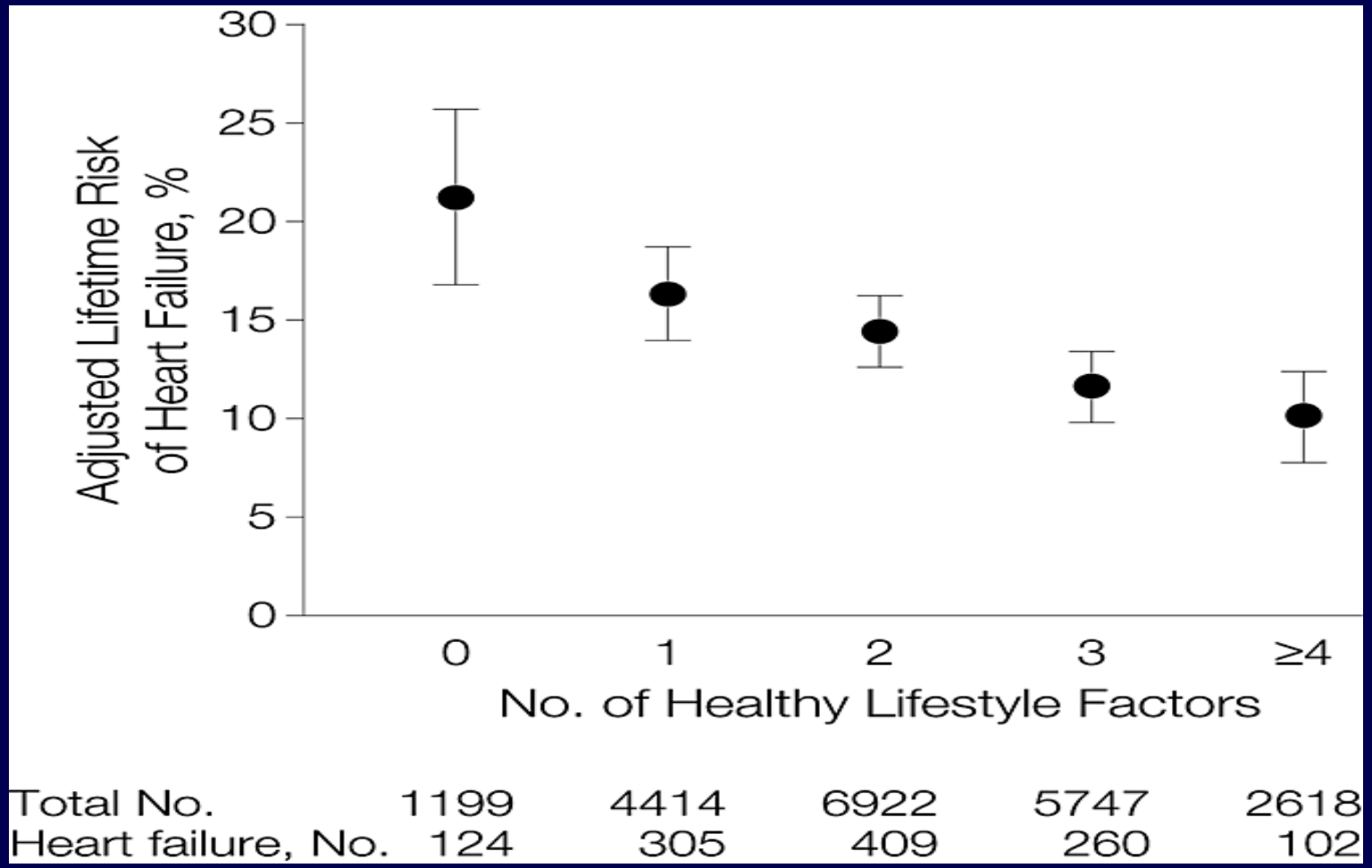
Kenchaiah. et al. NEJM 2002;347:305-313.

Cumulative Incidence of HF According to Categories of Physical Activity



Analysis of Physicians Health Study, Kenchaiah, et al. Circulation 2009;119:44-52

Lifetime Risk for Heart Failure According to Number of Healthy Lifestyle Factors



Djousse et al. JAMA. 2009;302(4):394-400.

Hypertension and Prevention of Heart Failure

- 60-80% of patients presenting with heart failure have a history of hypertension.
- Treatment of hypertension, especially systolic hypertension, significantly lowers the risk of developing heart failure
- Key target is SBP <140 mm Hg, DBP <90 mm Hg
- Despite identical blood pressure reduction, different antihypertensives may have different degrees of risk reduction for heart failure

American Heart Association. 2002 Heart and Stroke Statistical Update. Dallas, Tex: American Heart Association; 2001.
Hunt SA et al. J Am Coll Cardiol. 2001;38:2101–2113.

Impact of Blood Pressure Control on Heart Failure in Hypertension Trials

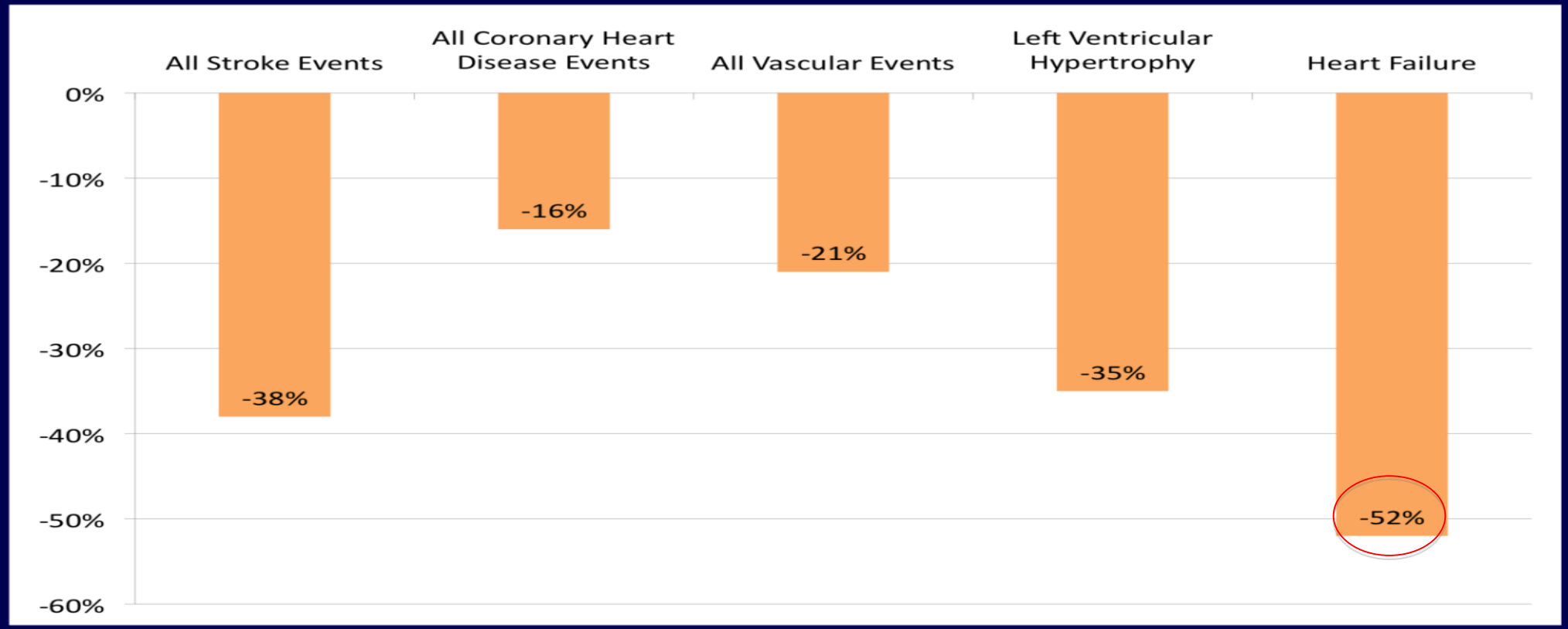
Trial	Treatment	% ↓ HF events (fatal & nonfatal)
SHEP[1] (n=4736) ≥60 years, ≥160/90 mm Hg	Diuretic, ß-blockers (n=2365) vs placebo (n=2371)	49% (102 placebo vs 48 active)
Syst-Eur[2]* (n=4695) ≥60 years, ≥160/<95 mm Hg	DHP-CCB, ACEI, diuretic (n=2398) vs placebo (n=2297)	29% (49 placebo vs 37 active)

*Terminated early

[1]SHEP Cooperative Research Group. JAMA 1991;265:3255

[2]Staessen JA et al. Lancet 1997;350:757

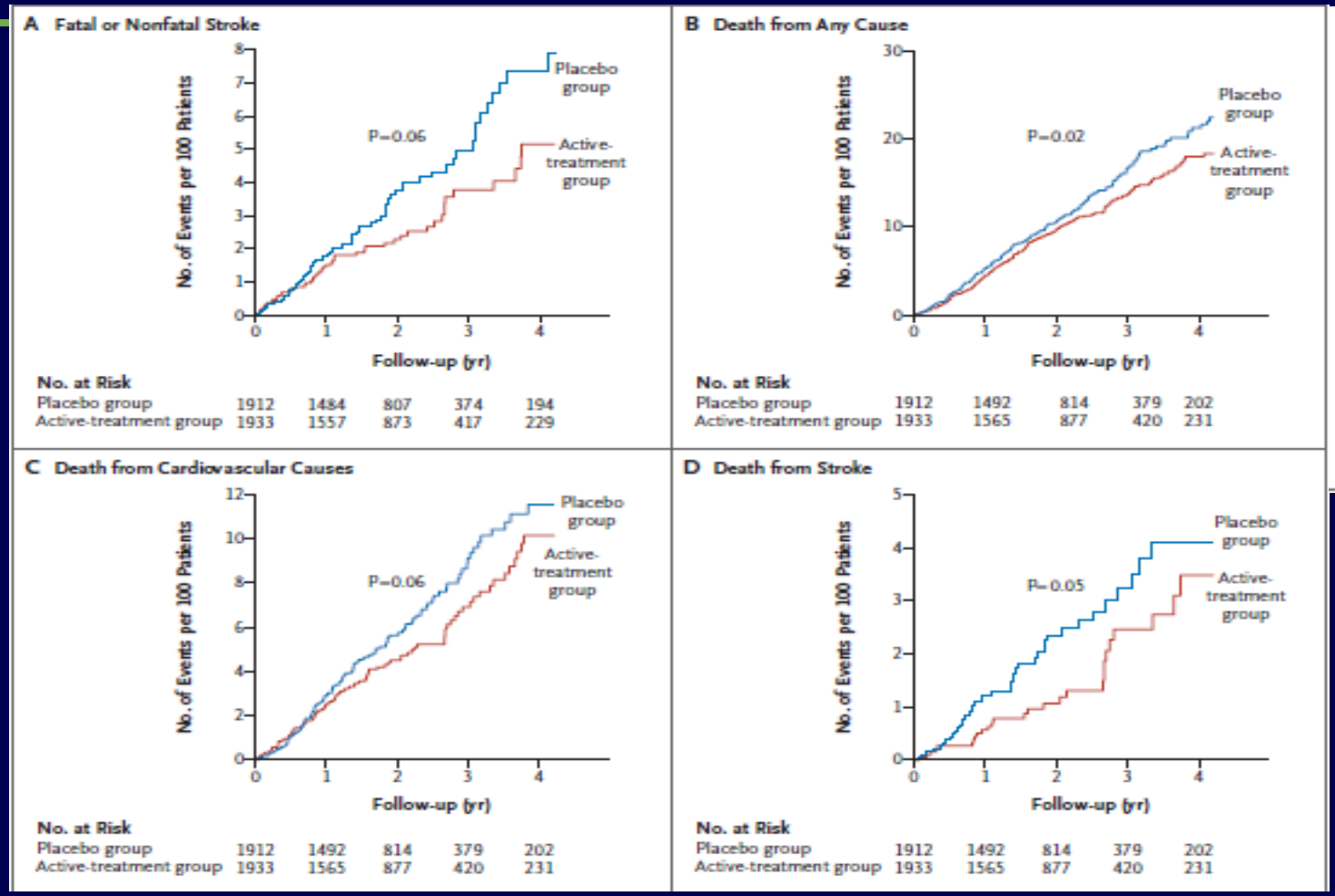
Beneficial Effect of HTN Treatment

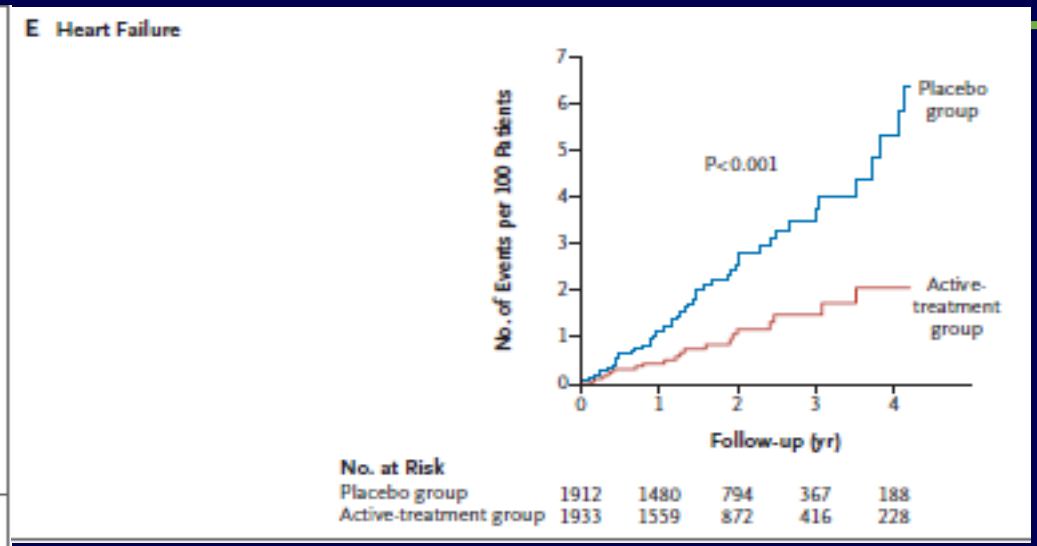


Meta-analyses of 12 randomized trials of antihypertensive medication therapy on the impact of BP reduction

Hebert et al. Arch Intern Med, 1993;153:849-858; Moser et al. J Am Coll Cardiol, 1996;27:1214-1218.

Treatment of Hypertension in Patients 80 Years or Older





64% reduction
in the rate of HF
95% CI, 42 to 78, P<0.001

HYVET . NEJM 2008;358:1887-98.

Diuretics ±ACE inhibitors

Systolic Blood Pressure Intervention Trial (SPRINT)

SPRINT enrolled 9361 participants, age 50 years or older with SBP 130 mm Hg or higher.

Participants must have a history of CVD or be at high risk for heart disease by having at least one additional risk factor, such as smoking or high blood cholesterol levels; or have chronic kidney disease.

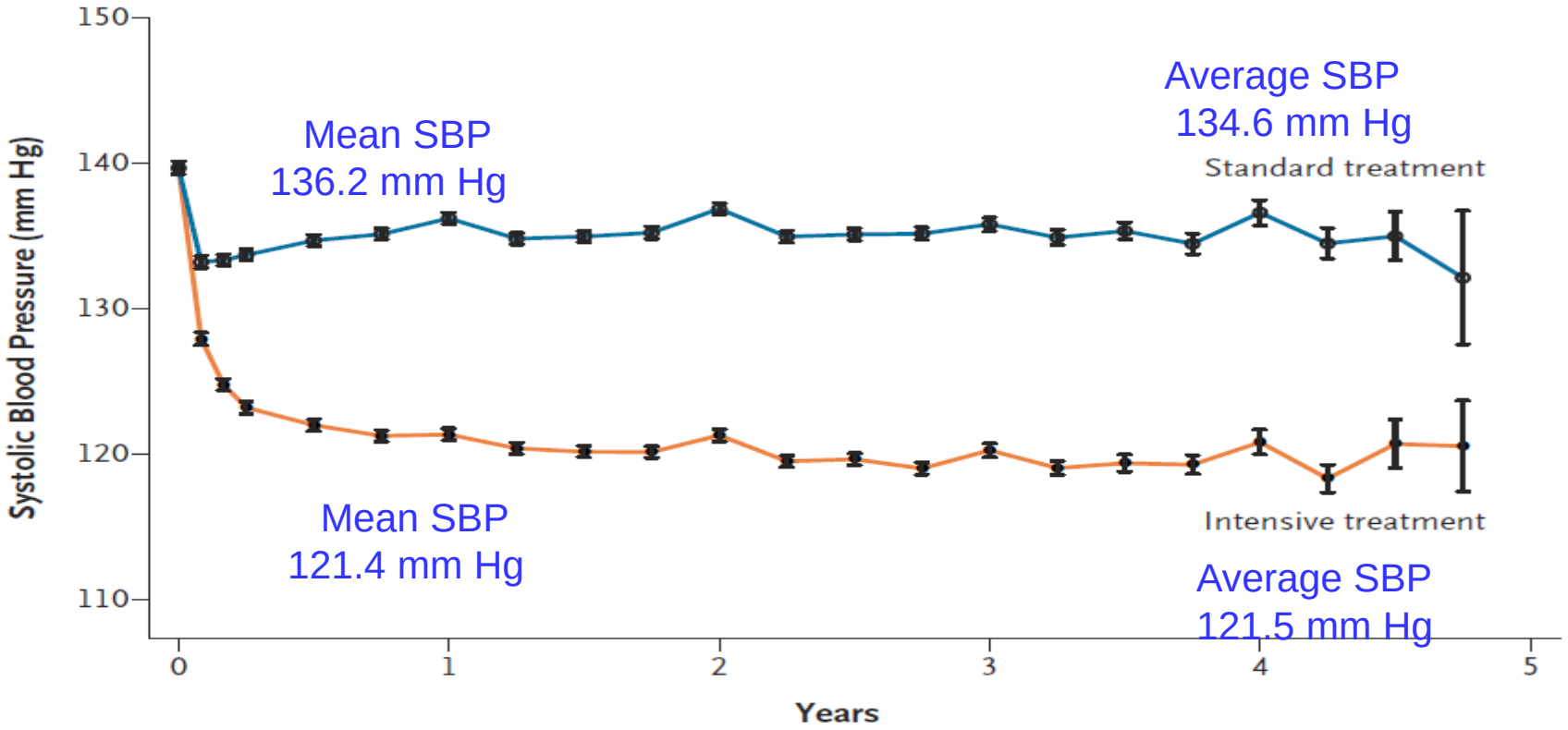
No history of diabetes or stroke

Participants randomly assigned to one of two groups: to treat SBP to the lower goal of less than 120 mm Hg or to treat to the standard goal of less than 140 mm Hg.

Primary Endpoint: First occurrence of a myocardial infarction (MI), acute coronary syndrome (ACS), stroke, heart failure (HF), or CVD death

ClinicalTrials.gov Identifier: NCT01206062

Systolic Blood Pressure Intervention Trial (SPRINT)



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

SPRINT Systolic Blood Pressure Intervention Trial

SPRINT Research Group. NEJM 2015 DOI: 10.1056/NEJMoa1511939

SPRINT Primary Outcome, Its Components, and Mortality

	Intensive (n=4678)		Standard (n=4683)			
	No. of Events	Rate, %/year	No. of Events	Rate, %/year	HR (95% CI)	P value
Primary Outcome	243	1.65	319	2.19	0.75 (0.64-0.89)	<0.001
All MI	97	0.65	116	0.78	0.83 (0.64-1.09)	0.19
Non-MI ACS	40	0.27	40	0.27	1.00 (0.64-1.55)	0.99
All Stroke	62	0.41	70	0.47	0.89 (0.63-1.25)	0.50
All HF	62	0.41	100	0.67	0.62 (0.45-0.84)	0.002
CVD Death	37	0.25	65	0.43	0.57 (0.38-0.85)	0.005
All-Cause Death	155	1.03	210	1.40	0.73 (0.60-0.90)	0.003

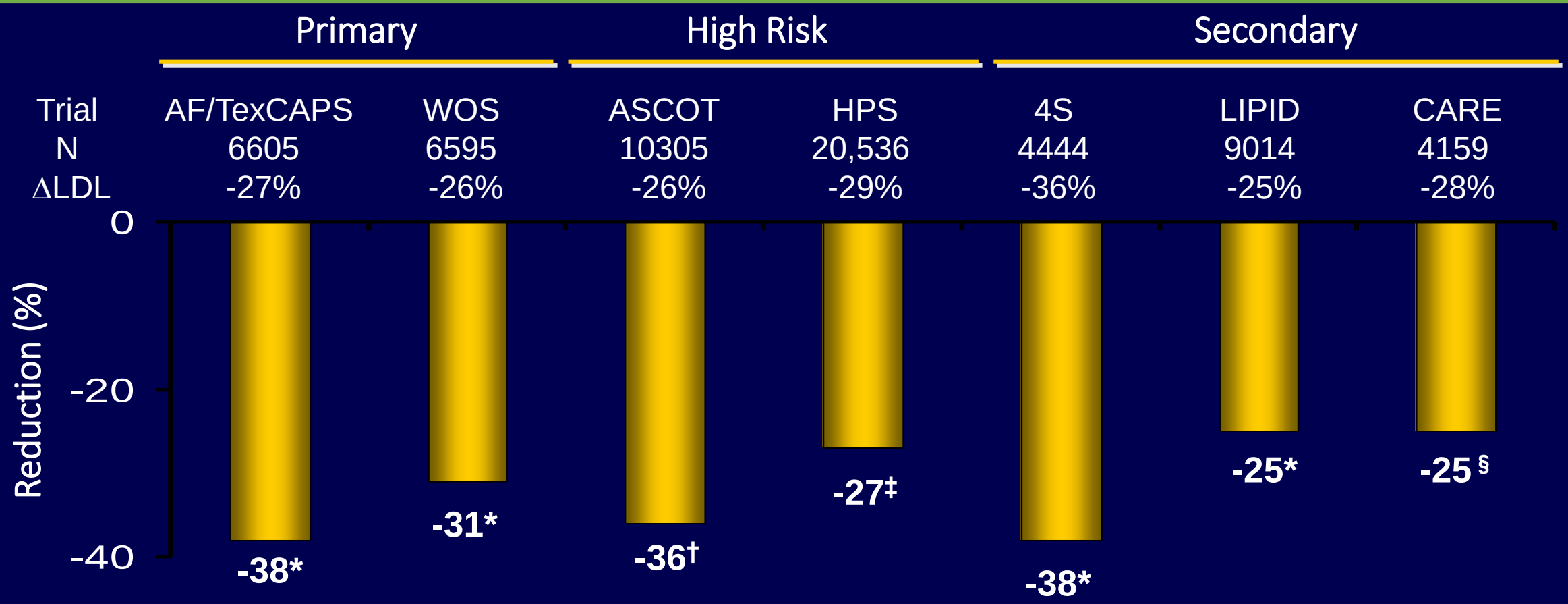
SPRINT Research Group. NEJM 2015 DOI: 10.1056/NEJMoa1511939

Hyperlipidemia, Coronary Artery Disease, and Prevention of HF

- 50-80% of patients presenting with heart failure have a history of coronary artery disease.
- Within 6 years of a recognized myocardial infarction, 22% of men and 46% of women will develop symptomatic heart failure.
- The use of effective treatments for coronary artery disease substantially reduces the risk of heart failure.

American Heart Association. 2002 Heart and Stroke Statistical Update. Dallas, Tex: American Heart Association; 2001.
Hunt SA et al. J Am Coll Cardiol. 2001;38:2101–2113.

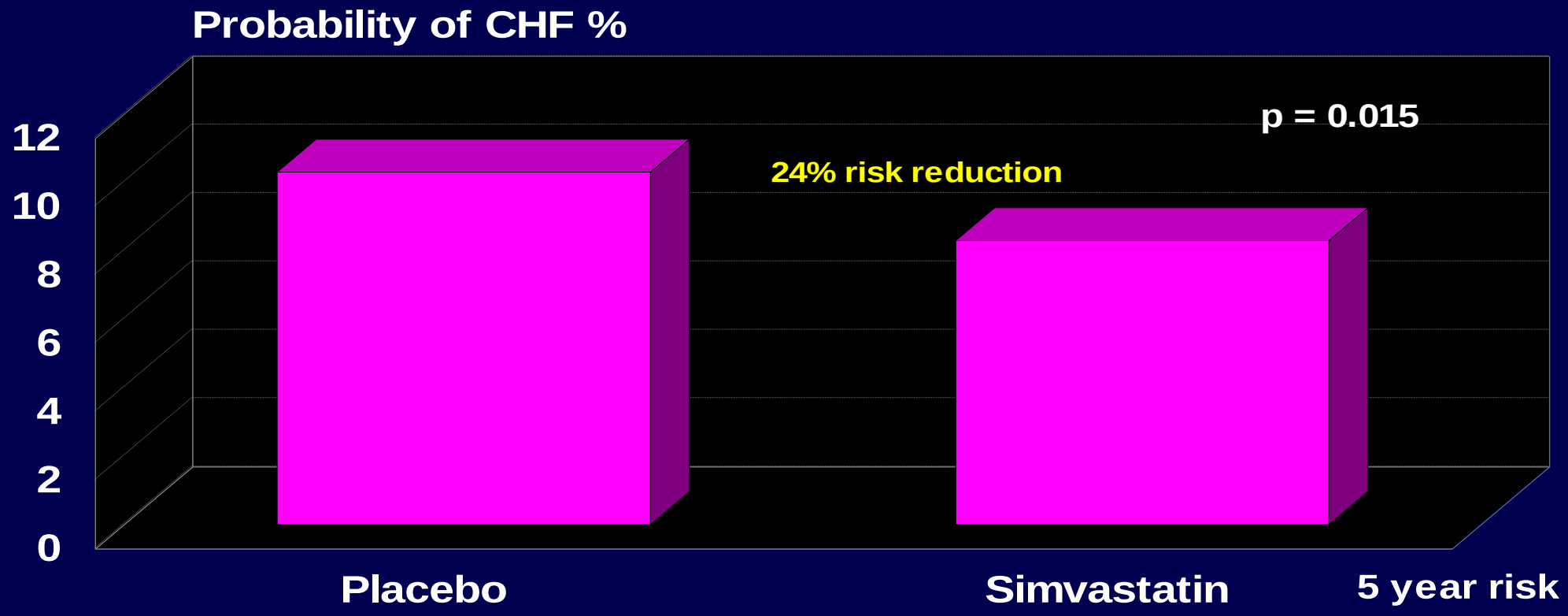
Statin Endpoint Clinical Trials: Reduction in Major Coronary Events



*P<0.001; †P=0.0005; ‡P<0.0001; § P=0.002.

HPS Collaborative Group. Lancet. 2002;360:7-22; LaRosa et al. JAMA. 1999;282:2340-2346; Sever et al. Lancet. 2003;361:1149-1158.

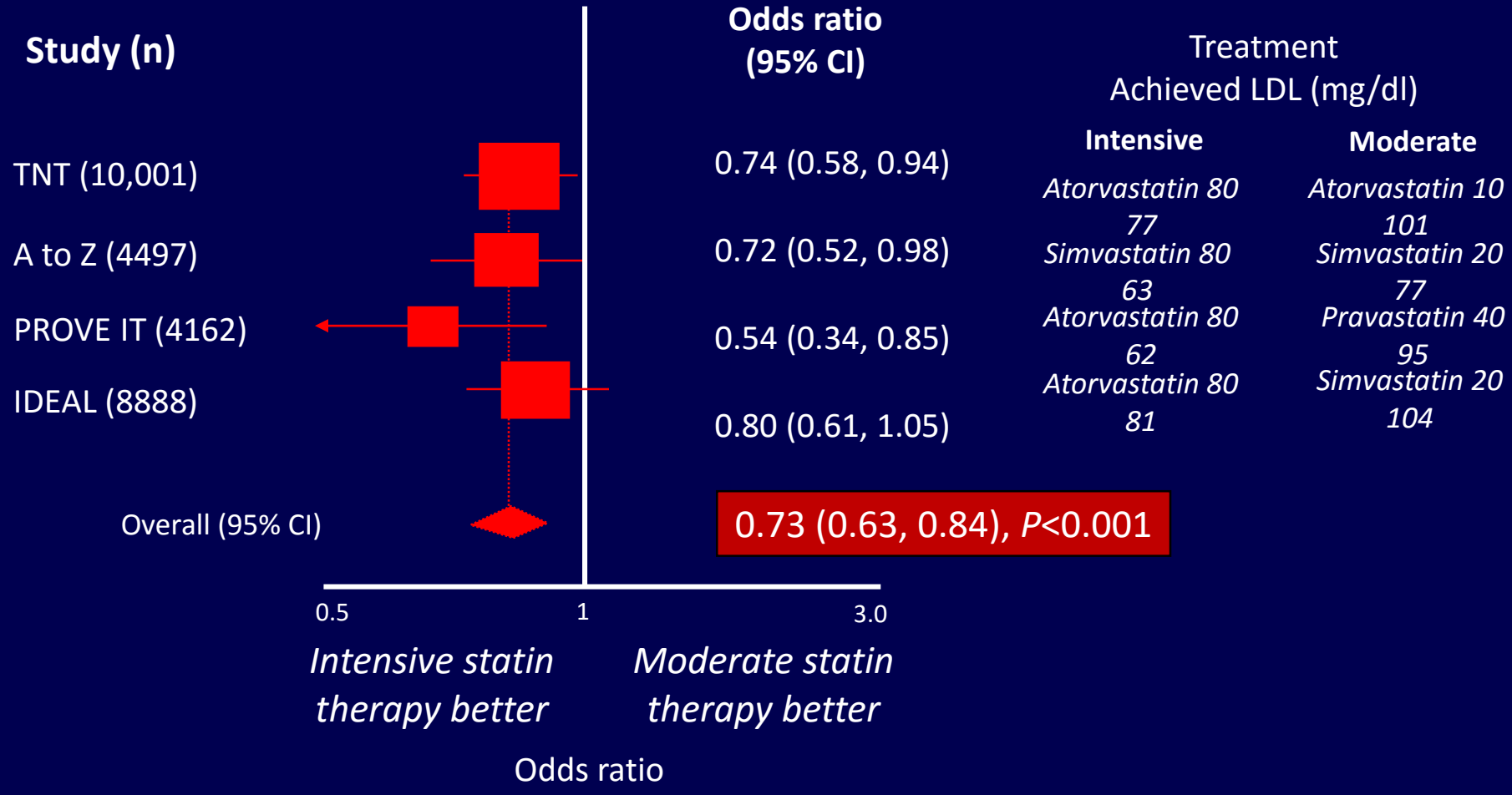
Impact of HMG CoA Reductase Inhibitor Therapy on Risk of Developing Heart Failure



Patients with coronary artery disease and cholesterol > 212 mg/dl

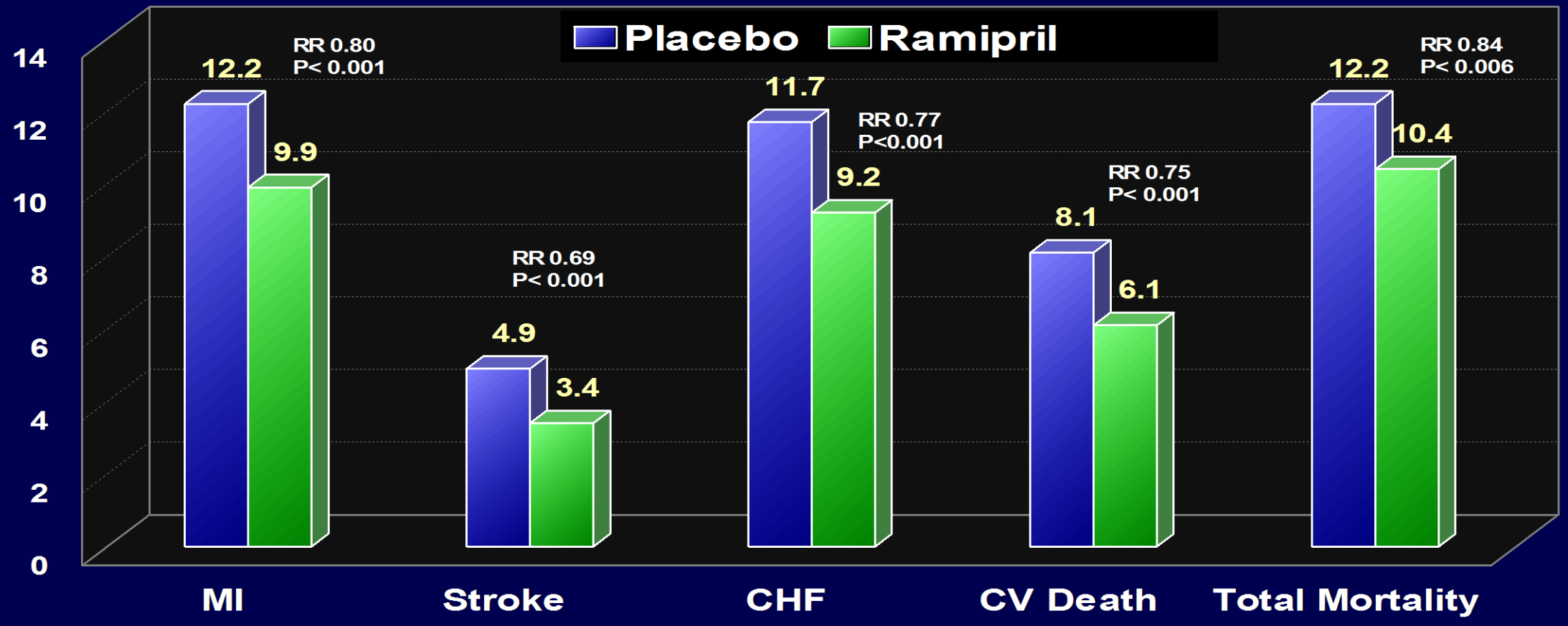
Kjekshus J Cardiac Failure. 1997;4:249-54

Intensive Statin Therapy and HF Risk in Stable CAD or ACS



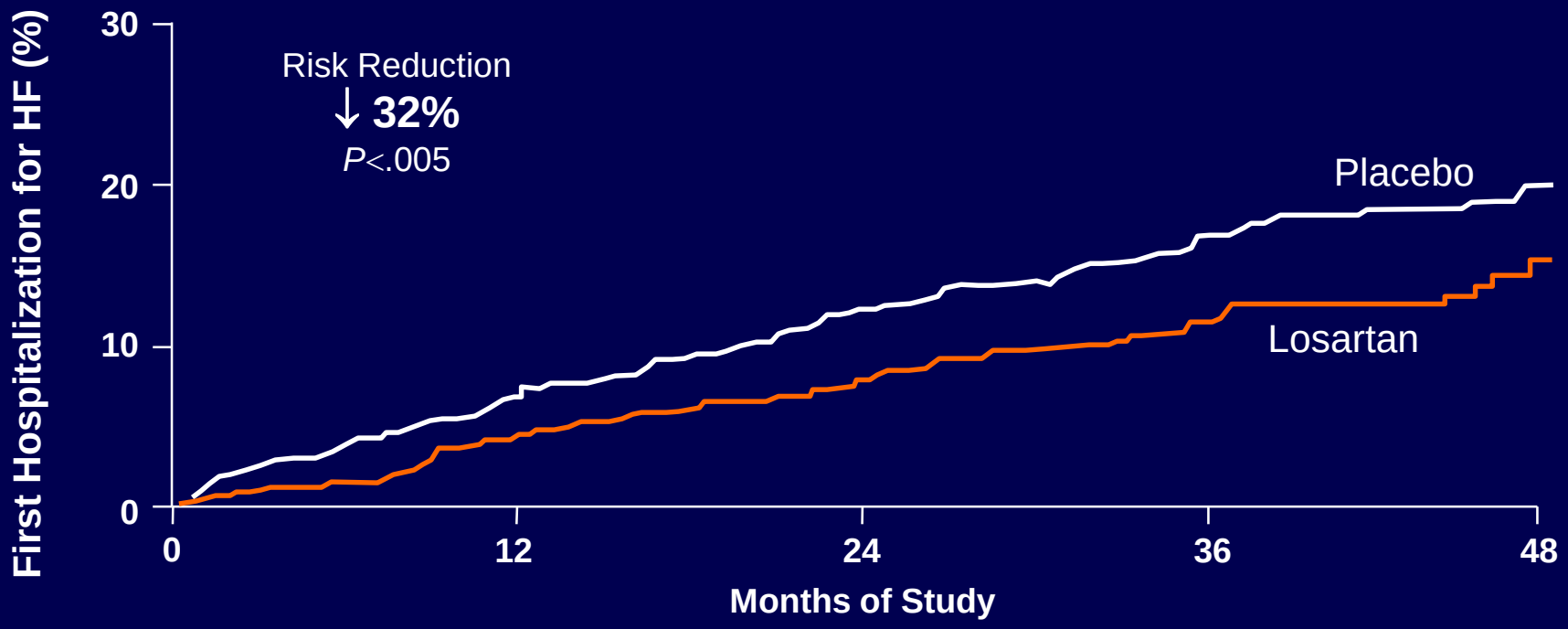
Scirica B et al. J Am Coll Cardiol. 2006;47:2326–2331.

Impact of ACE Inhibitor Therapy on Mortality in Patients With or at Risk for Cardiovascular Disease



HOPE Trial Ramipril 10 mg qd vs Placebo
9297 pts with vascular disease or diabetes plus one other cardiovascular risk factor
Yusuf. NEJM 2000;342:145.

RENAAL: Effect of Losartan on New-Onset Heart Failure in Diabetes



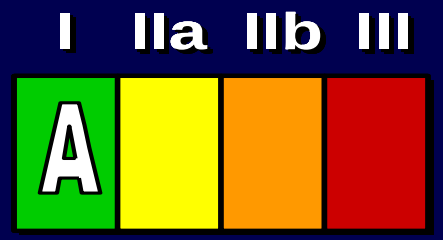
Number at risk:

Placebo	762	685	616	375	53
Losartan	751	701	637	388	74

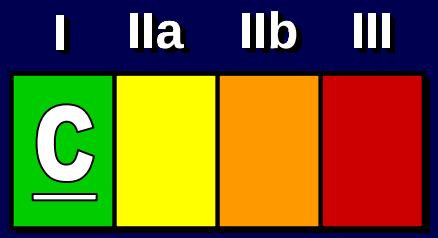
RENAAL (Reduction of Endpoints in Non–Insulin-Dependant Diabetes Mellitus With the Angiotensin II Antagonist Losartan): 1,513 patients with DM and nephropathy enrolled in a randomized, double-blind study comparing losartan (50–100 mg QD) to placebo, both on top of standard HTN therapy including CCBs (calcium channel blockers) diuretics, β-blockers, α-blockers, and centrally acting agents for 3.4 years.

Brenner B. N Engl J Med. 2001;345:861–869.

Patients at High Risk for Developing Heart Failure (Stage A): Treatment



ACE inhibitors can be useful to prevent HF in patients at high risk for developing HF who have a history of atherosclerotic vascular disease, diabetes mellitus, or hypertension with associated cardiovascular risk factors.



Angiotensin receptor blockers can be useful to prevent HF in patients at high risk for developing HF who have a history of atherosclerotic vascular disease, diabetes mellitus, or hypertension with associated cardiovascular risk factors.

Epidemiology of Diabetes and Incident Heart Failure

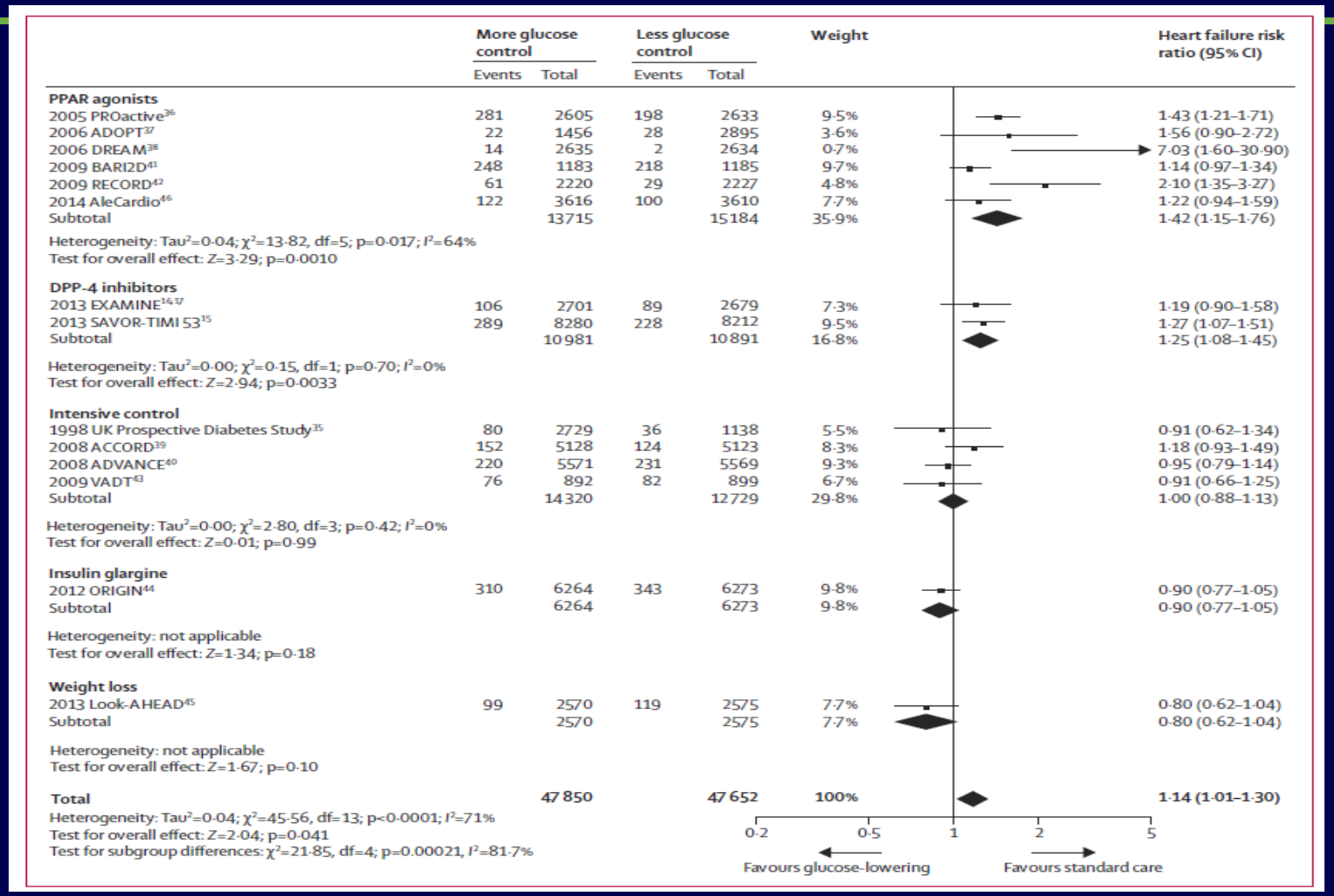
- Framingham study (risk of HF in diabetics)
  - 2x diabetic males
  - 5x diabetic females
  - 4x young diabetic males
  - 8x young diabetic females
- US HMO prevalence study

  With diabetes, incident HF developed at a rate of 3.3% per year
- Each 1% elevation in HbA_{1c} leads to a 15% increase in frequency of HF

Kannel WB et al. JAMA. 1979;241:2035–2038. Nichols GA. Diabetologia. 2000;43(suppl A2):7. Chue CL et al. Circulation. 1998;98(suppl 1):721.

Heart Failure Rates in Diabetes Glucose Control Trials

Risk of HF events with glucose-lowering drugs or strategies versus standard care



PPAR Agonists

DPP-4 Inhibitors

Intensive Control

Insulin

Weight loss

Udell et al. Lancet Diabetes Endocrinol 2015.http://dx.doi.org/10.1016/S2213-8587(15)00044-3

Effects of Intensive Glucose Lowering in Type 2 Diabetes: ACCORD

Table 4. Primary and Secondary Outcomes.*

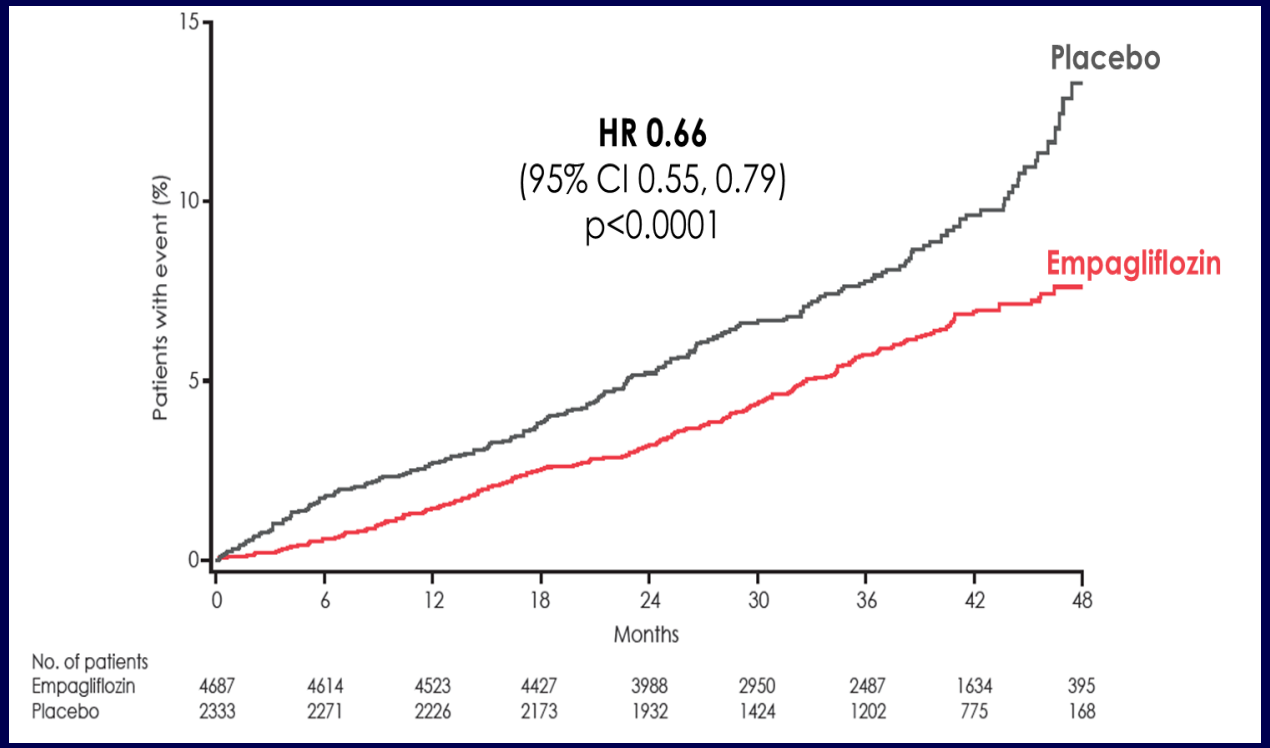
Outcome	Intensive Therapy (N = 5128)		Standard Therapy (N = 5123)		Hazard Ratio (95% CI)	P Value
	no. of patients (%)	*% per yr*	*no. of patients (%)*	*% per yr*		
Primary outcome	352 (6.9)	2.11	371 (7.2)	2.29	0.90 (0.78–1.04)	0.16
Secondary outcome						
Death						
Any cause	257 (5.0)	1.41	203 (4.0)	1.14	1.22 (1.01–1.46)	0.04
Cardiovascular causes	135 (2.6)	0.79	94 (1.8)	0.56	1.35 (1.04–1.76)	0.02
Nonfatal myocardial infarction	186 (3.6)	1.11	235 (4.6)	1.45	0.76 (0.62–0.92)	0.004
Nonfatal stroke	67 (1.3)	0.39	61 (1.2)	0.37	1.06 (0.75–1.50)	0.74
Fatal or nonfatal congestive heart failure	152 (3.0)	0.90	124 (2.4)	0.75	1.18 (0.93–1.49)	0.17

At 1 year, stable median glycated hemoglobin levels of 6.4% and 7.5% were achieved in the intensive-therapy group and the standard-therapy group, respectively

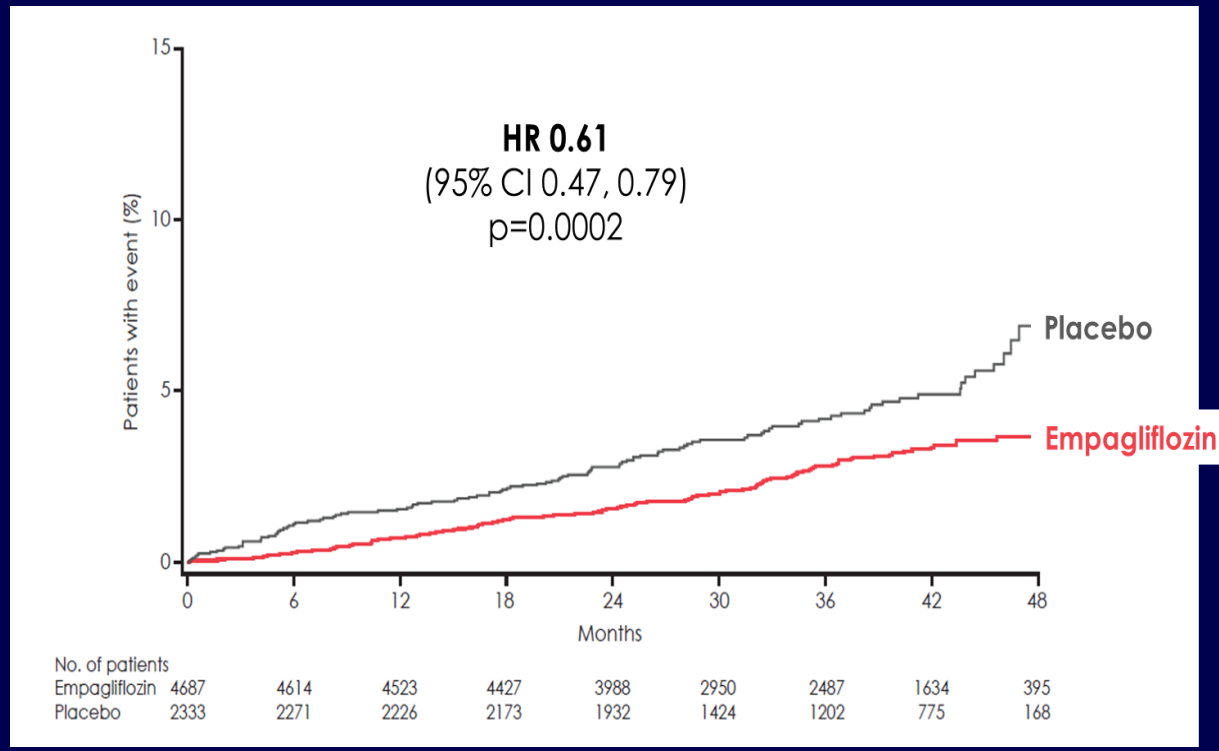
ACCORD Study Group N Engl J Med 2008;358:2545-59.

EMPA-REG OUTCOME Study

HF Hospitalization or CV Death



HF Hospitalization or HF Death



Empagliflozin is a highly selective inhibitor of SGLT2

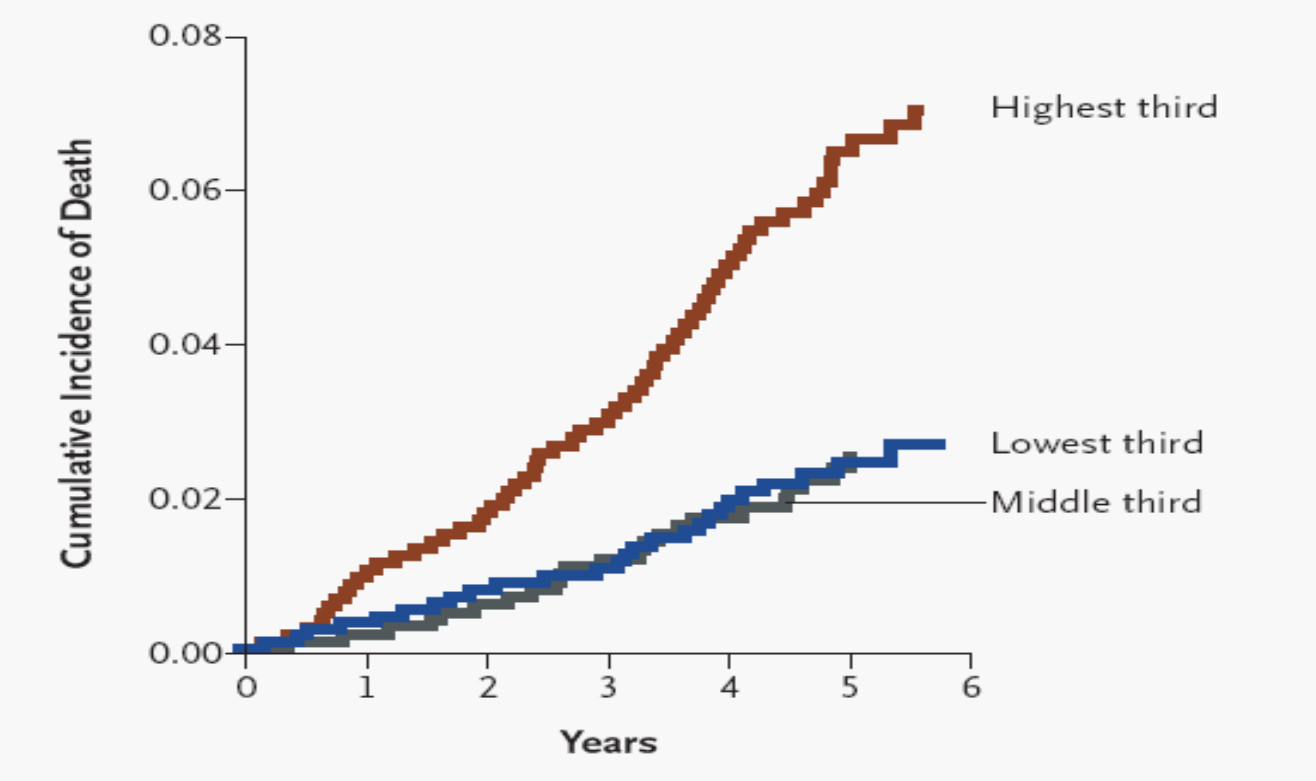
7020 adults with type 2 diabetes and established CVD

BMI ≤45 kg/m^2; HbA1c 7–10%; eGFR ≥30 mL/min/1.73m^2 (MDRD)

Zinman B et al. N Engl J Med 2015;373:2117-2128.

Precision Guided Prevention of Heart Failure

BNP as a Predictor of Risk in Asymptomatic Adults: The Framingham Heart Study



End point	Hazard ratio for 1 SD increment in log BNP value	p
Death	1.27	0.009
First major CV event	1.28	0.03
HF	1.77	<0.001
Atrial fibrillation	1.66	<0.001
Stroke or TIA	1.53	0.002
CHD event	1.1	0.37

Wang TJ et al. N Engl J Med 2004; 350:655-63.

The Saint Vincents Screening To Prevent Heart Failure (STOP-HF) Study

1374 Asymptomatic Adults >40 years of age

Routine PCP care

- Annual BNP not available to clinicians
- At least annual review by PCP
- Cardiology review only if requested by PCP

BNP-directed care

In addition to routine PCP care

- Annual BNP in all

If BNP >50 pg/ml at any time

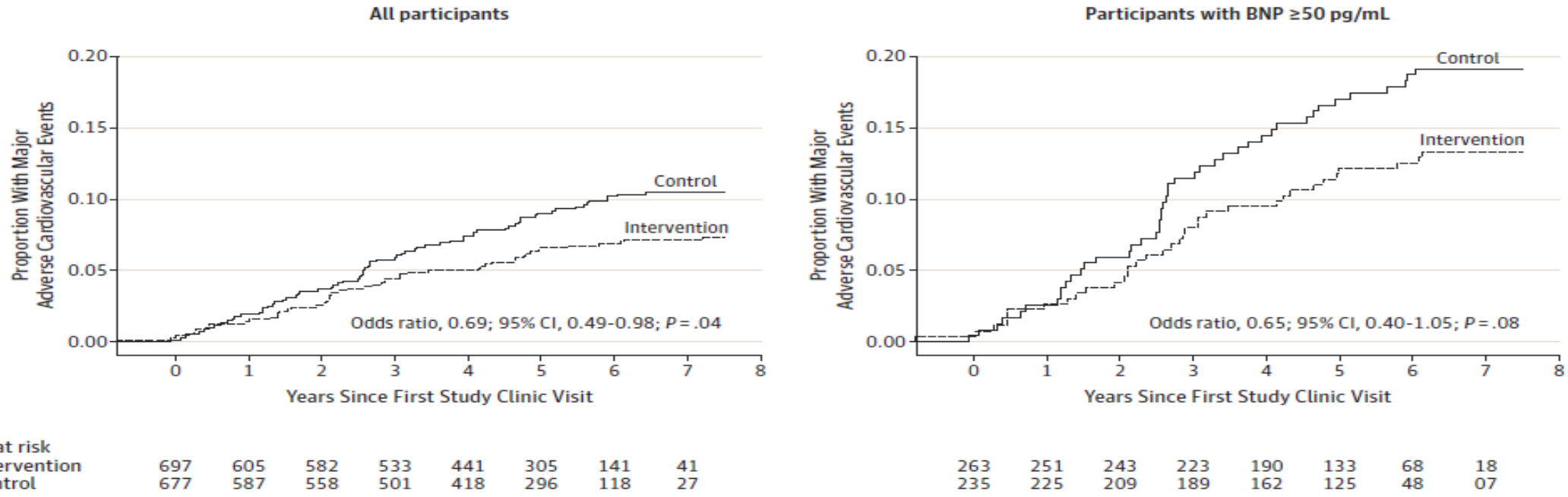
- Shared-care
  - Cardiology review
  - Echo-Doppler
  - Other CV investigations
  - CV nurse coaching
  - Preventative therapies
  - Regular Cardiology follow-up

Ledwidge. JAMA. 2013;310(1):66-74.

Natriuretic Peptide–Based Screening and Collaborative Care for Heart Failure

The STOP-HF Randomized Trial

Figure 2. Kaplan-Meier Analysis of Major Adverse Cardiovascular Events in the Full Study Sample and in Participants With BNP ≥50 pg/mL



Patients were randomly assigned to receive usual primary care (control condition; n=677) or screening with BNP testing (n=697). Intervention-group participants with BNP levels of 50 pg/mL or higher underwent echocardiography and collaborative care between their PCP and specialist cardiovascular service.

Ledwidge. JAMA. 2013;310(1):66-74.

Prevention of Heart Failure

Patients at risk for heart failure:

- Treat hypertension with substantial additional benefits with SBP treatment target of <120 mm Hg
- Treat diabetes according to guidelines, use SGLT-2 inhibitors
- Treat atherosclerosis according to guidelines
- Treat lipid disorders with statins according to guidelines
- Encourage smoking cessation
- Encourage exercise
- Discourage heavy alcohol intake, illicit drug use
- Consider ACEI or ARB and beta blocker use in those at risk for HF

Revised from Yancy CW et al. J Am Coll Cardiol. 2013;62:e147-1539.

Conclusions

- The economic burden of HF continues to grow and HF is one of the single most common, deadly, and expensive healthcare problems
- New treatments can further improve outcomes in HFrEF
- There will be over 915,000 new cases of HF this year, yet the majority of HF is preventable
- Because early modification of HF risk factors can reduce the risk of HF, the recommendation of appropriate medical interventions to patients with these risk factors provides the earliest opportunity to reduce the impact of HF on public and individual health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