Primary Care Update
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New Approaches for Systolic Heart Failure

Thomas Cimato, MD, PhD, FACC, FAHA
Associate Professor
Division of Cardiovascular Medicine

UB|MD INTERNAL MEDICINE

University at Buffalo The State University of New York
Jacobs School of Medicine and Biomedical Sciences

Educational Goals:

- Review the definition, diagnostic criteria and medical therapy for congestive heart failure
- Understand why sacubatril-valsartan is superior to ACE inhibitor therapy in chronic systolic heart failure
- Understand the benefits and adverse reactions of sacubatril-valsartan therapy in patients with systolic heart failure

Question 1:

Sacubatril-valsartan is recommended in patients with NYHA Class II-III systolic congestive heart failure who can tolerate an ACE inhibitor or ARB with prior hospitalization in the past 12 months?

A. True

B. False

Question 2:

Therapy with sacubatril-valsartan reduces hospitalization for congestive heart failure?

A. True

B. False

Question 3:

Which of the following statements regarding use of sacubatril-valsartan treatment are true?

A. It can cause angioedema

B. It cannot be given with an ACEi or ARB

C. It cannot be used in patients with systolic blood pressure < 100 mm Hg

D. It cannot be used in patients with eGFR < 30

E. All of the above

Congestive Heart Failure- Definition

- A disorder of EITHER cardiac filling (diastole) or contraction (systole) resulting in symptoms of shortness of breath
- How do we know that the shortness of breath is due to heart failure and not another cause? What are the criteria for the diagnosis of heart failure?

Congestive Heart Failure-Definition

Table 1. Framingham Criteria for CHF

Major criteria
- Paroxysmal nocturnal dyspnea or orthopnea
- Neck-vein distention
- Rales
- Cardiomegaly
- Acute pulmonary edema
- S_3 gallop
- Increased venous pressure >16 cm of water
- Circulation time ≥25 s
- Hepatojugular reflux

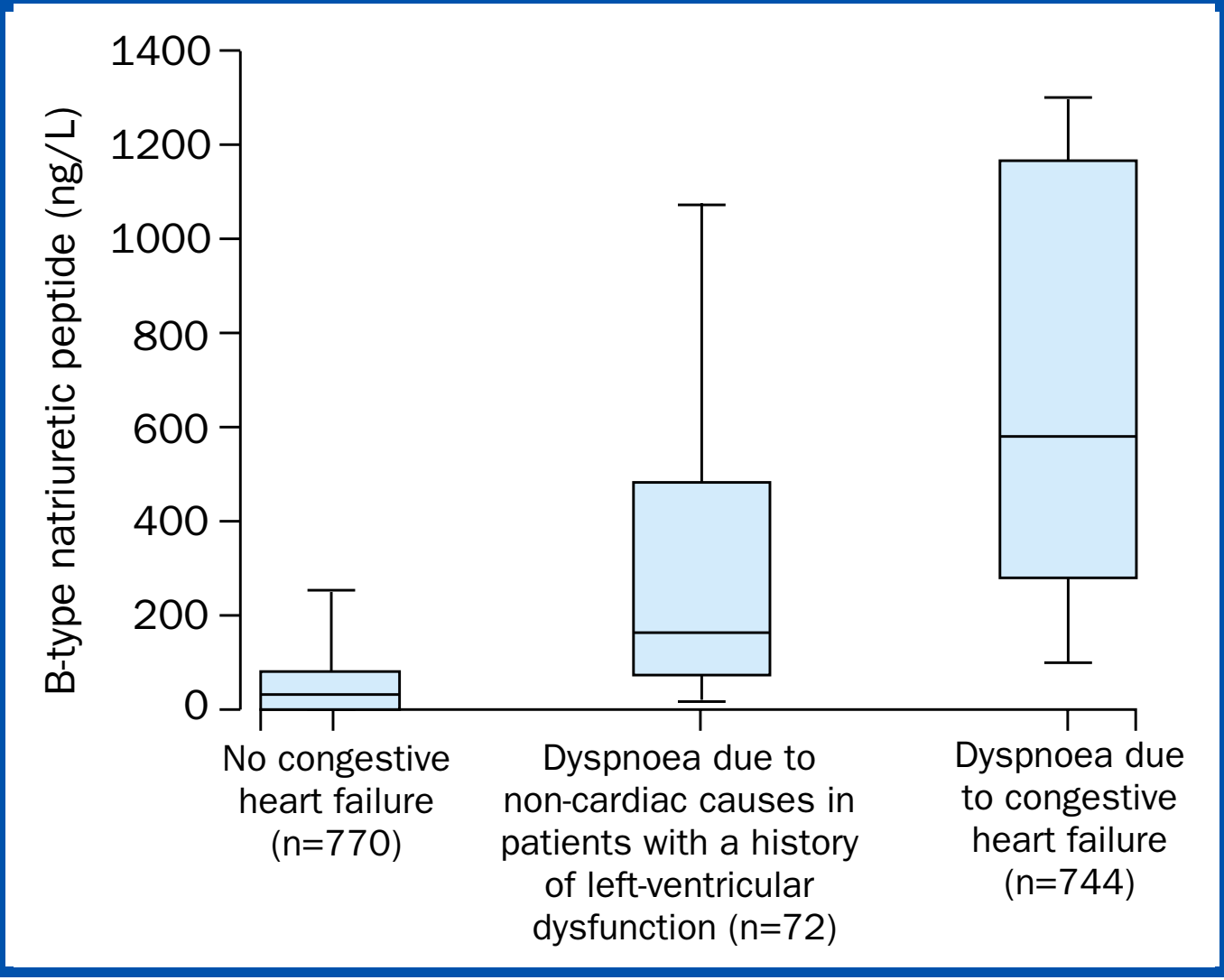
Minor criteria
- Ankle edema
- Night cough
- Dyspnea on exertion
- Hepatomegaly
- Pleural effusion
- Vital capacity ↓1/3 from maximum
- Tachycardia (range of ≥120/min)

Major or minor criteria
- Weight loss ≥4.5 kg in 5 days in response to treatment

For establishing a definite diagnosis of CHF, 2 major criteria or 1 major and 2 minor criteria must be present.

Yturralde and Gaasch (2005) Prog Cardiovasc Dis 47(5): 314-9

BNP Levels in Diagnosis of Heart Failure



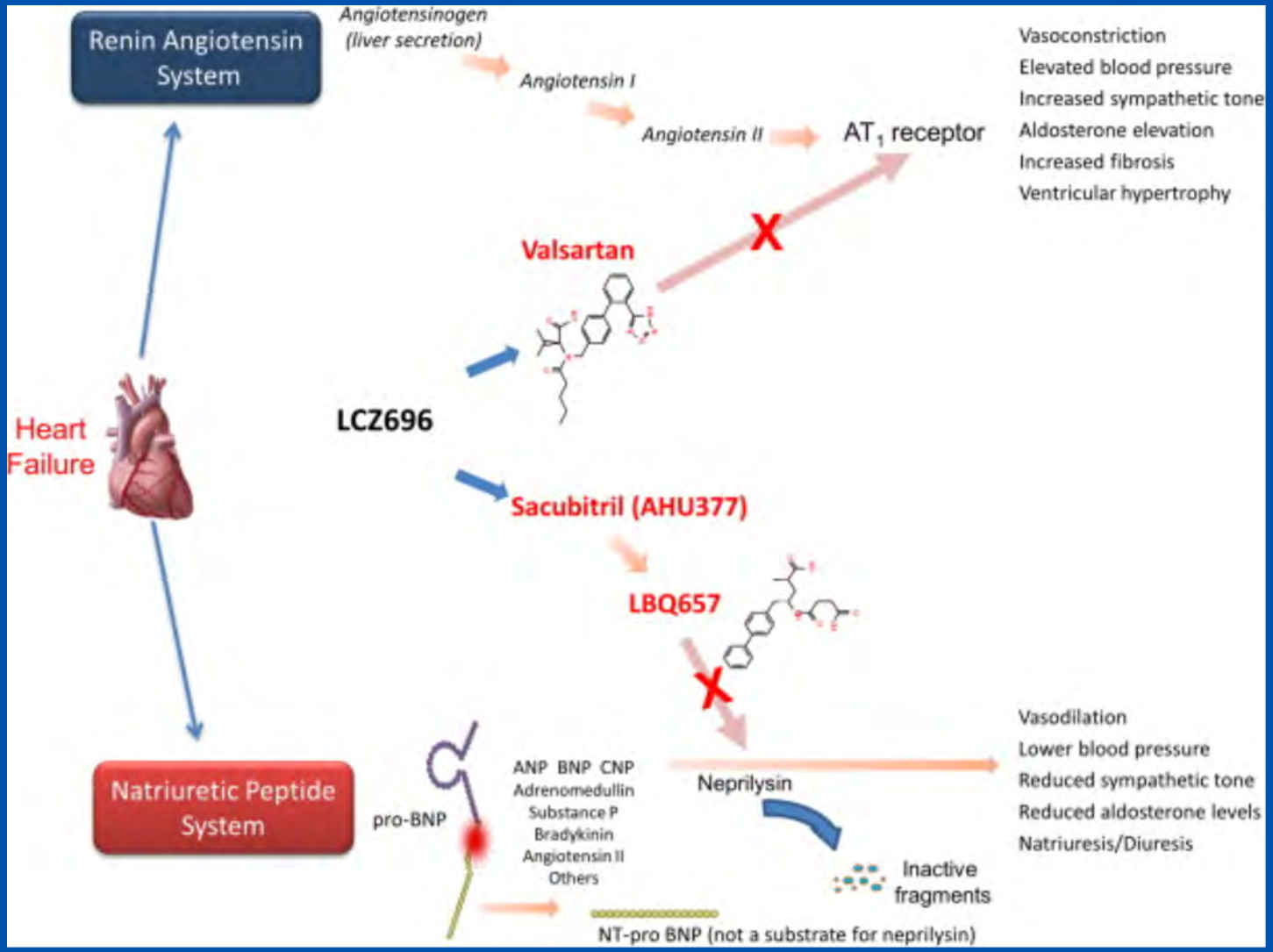
Guideline Directed Therapy for Congestive Heart Failure

Guideline-Directed Medical Therapy – "GDMT"

	Post-MI LV dysfunction	*Mild CHF*	*Moderate CHF*	*Severe CHF*
ACE inhibitor	AIRE/SAVE/TRACE (ramipril/captopril/ trandolapril)	SOLVD Treatment (enalapril)		CONSENSUS (enalapril)
Beta-blocker	CAPRICORN (carvedilol)	USCT / MERIT-HF / CIBIS II (carvedilol / metoprolol succinate/ bisoprolol)		COPERNICUS (carvedilol)
Aldo antagonist	EPHESUS (eplerenone)	EMPHASIS-HF (eplerenone)		RALES (spironolactone)
ARB	VALIANT (valsartan)	Val-HeFT / CHARM (valsartan / candesartan)		
Hydralazine -nitrates				A-HeFT (hydralazine-nitrates)
ICD/CRT	MADIT-II (ICD)	SCD-HeFT / CARE / MADIT-CRT / RAFT (ICD / CRT)		

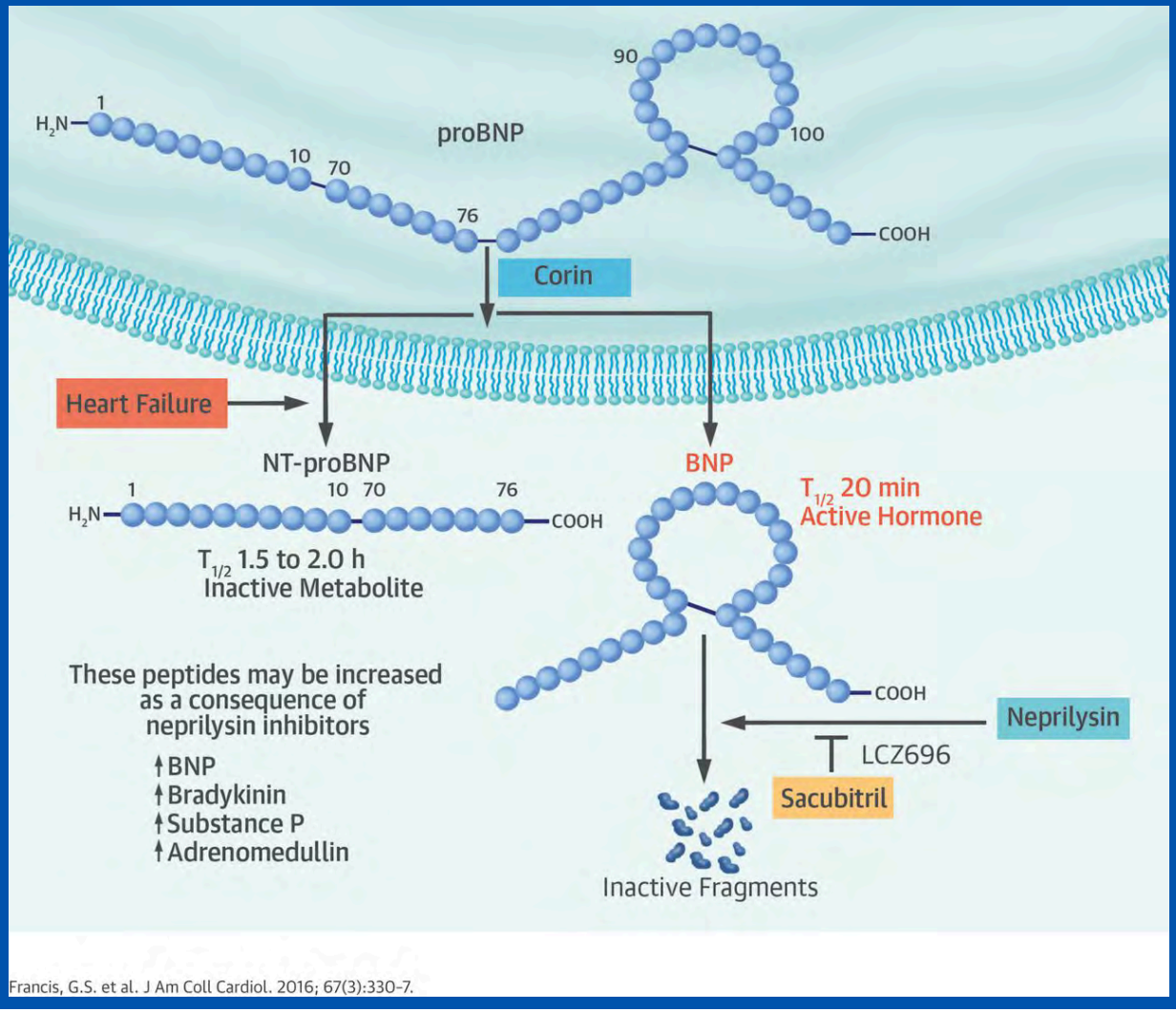
Adapted from Yancy et al, *Circulation* 2013

Combined Neprilysin and RAS Inhibition for Treatment of Heart Failure



JCHF. 2014;2(6):663-670. doi:10.1016/j.jchf.2014.09.001

Sacubatril-Valsartan Inhibits Degradation of BNP



Francis, G.S. et al. J Am Coll Cardiol. 2016; 67(3):330-7.

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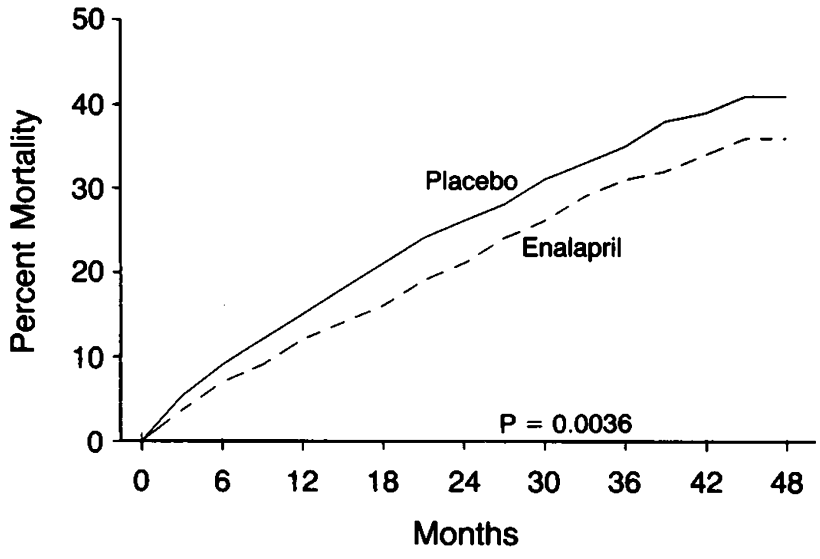
EFFECT OF ENALAPRIL ON SURVIVAL IN PATIENTS WITH REDUCED LEFT VENTRICULAR EJECTION FRACTIONS AND CONGESTIVE HEART FAILURE

THE SOLVD INVESTIGATORS*



Placebo	1284	1159	1085	1005	939	819	669	487	299
Enalapril	1285	1195	1127	1069	1010	891	697	526	333

Figure 1. Mortality Curves in the Placebo and Enalapril Groups.
The numbers of patients alive in each group at the end of each period are shown at the bottom of the figure. P = 0.0036 for the comparison between groups by the log-rank test.

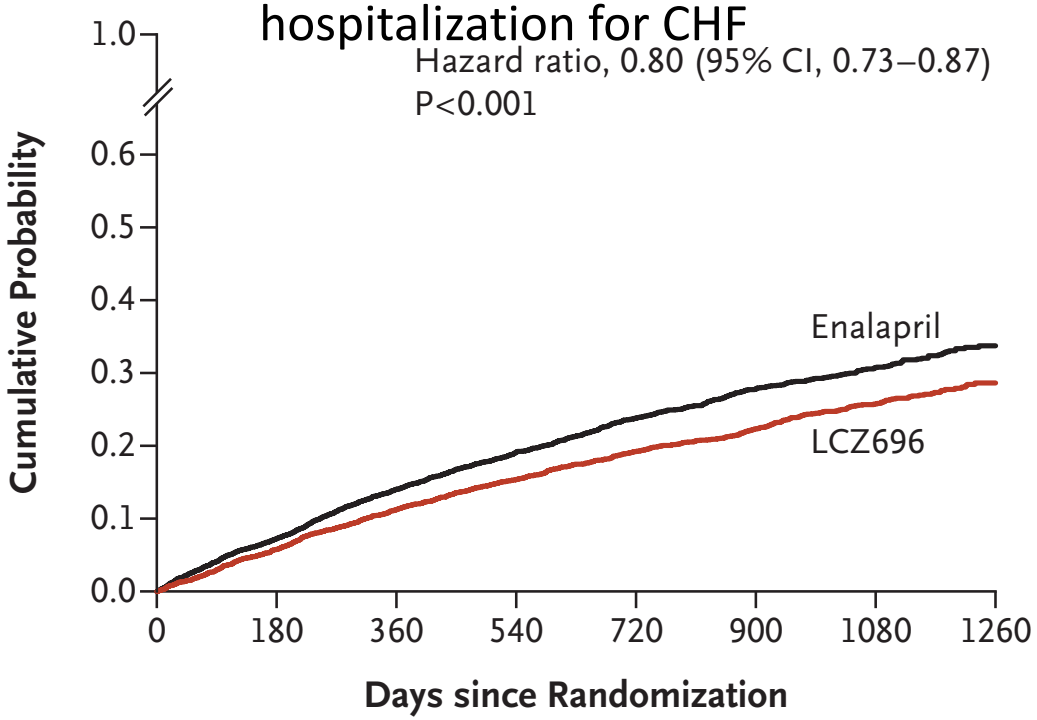
- SOLVD was the Only trial in HF To show a significant reduction in mortality With an ACE inhibitor

Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure

John J.V. McMurray, M.D., Milton Packer, M.D., Akshay S. Desai, M.D., M.P.H., Jianjian Gong, Ph.D., Martin P. Lefkowitz, M.D., Adel R. Rizkala, Pharm.D., Jean L. Rouleau, M.D., Victor C. Shi, M.D., Scott D. Solomon, M.D., Karl Swedberg, M.D., Ph.D., and Michael R. Zile, M.D., for the PARADIGM-HF Investigators and Committees*

A Primary End Point

Death CV causes or hospitalization for CHF



No. at Risk

LCZ696	4187	3922	3663	3018	2257	1544	896	249
Enalapril	4212	3883	3579	2922	2123	1488	853	236

Neprilysin Inhibition — A Novel Therapy for Heart Failure

Mariell Jessup, M.D.

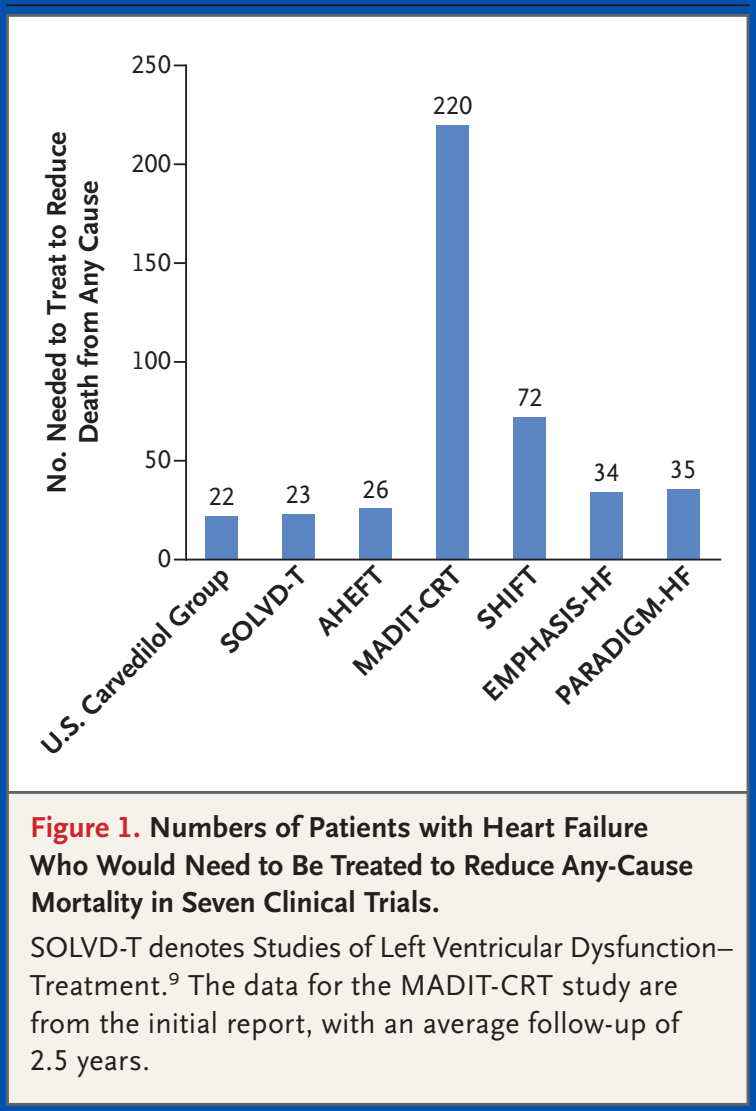
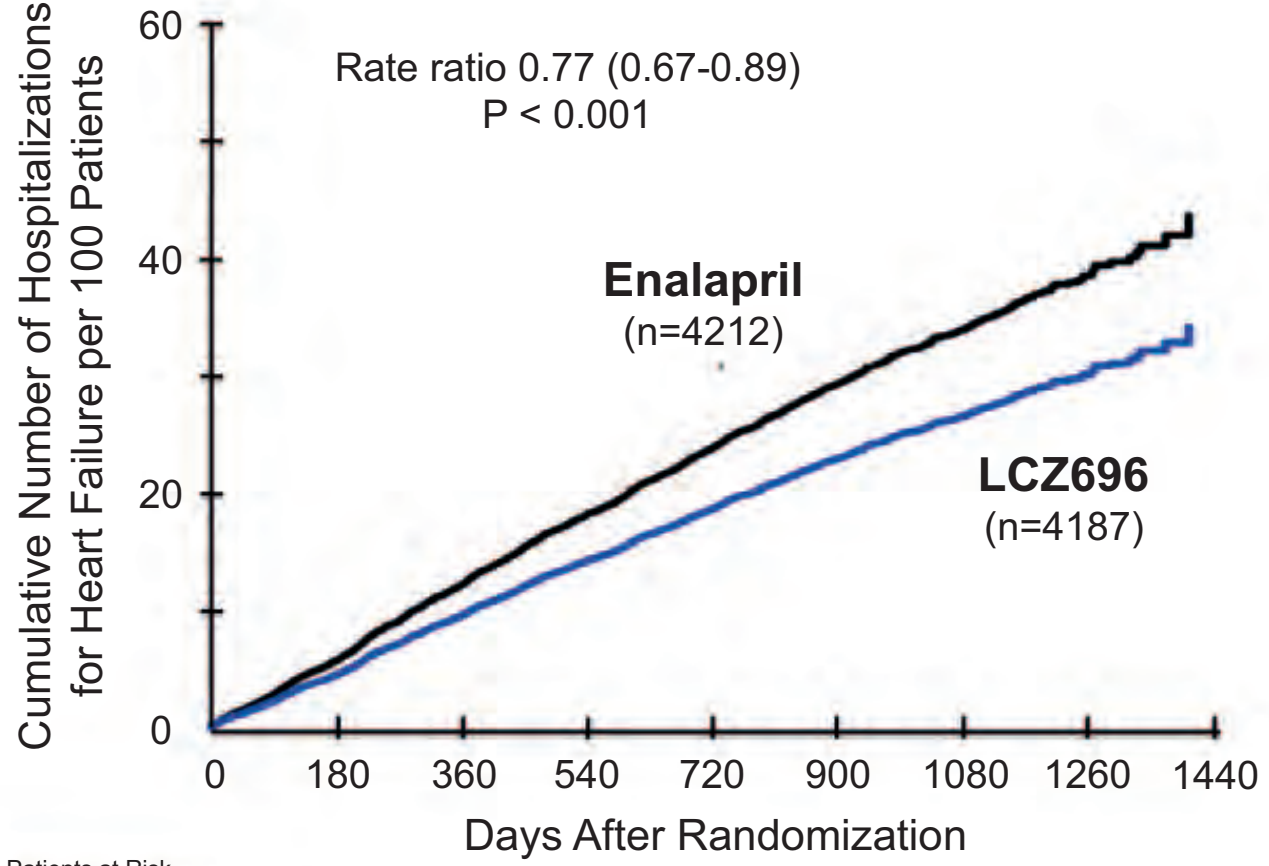


Figure 1. Numbers of Patients with Heart Failure Who Would Need to Be Treated to Reduce Any-Cause Mortality in Seven Clinical Trials.

SOLVD-T denotes Studies of Left Ventricular Dysfunction–Treatment.[9] The data for the MADIT-CRT study are from the initial report, with an average follow-up of 2.5 years.

Angiotensin Receptor Neprilysin Inhibition Compared With Enalapril on the Risk of Clinical Progression in Surviving Patients With Heart Failure

Cumulative Hospitalizations



Patients at Risk

LCZ696	4187	4054	3885	3276	2472	1710	1001	279	12
Enalapril	4212	4049	3857	3228	2408	1724	993	278	17

Circulation. 2015;131:54–61. DOI: 10.1161/CIRCULATIONAHA.114.013748

Who should be treated with sacubatril-valsartan?

- **ARNI therapy (valsartan/sacubitril) is recommended in patients with NYHA Class II or III systolic congestive heart failure who can tolerate an ACE inhibitor or ARB as disease modifying therapy with:**
- **Elevated brain derived natriuretic peptide > 150 pg/mL or NT-pro-BNP > 600 pg/mL**
- **Elevated brain derived natriuretic peptide > 100 pg/mL or NT-pro-BNP > 400 pg/mL WITH a prior hospitalization for congestive heart failure in the past 12 months**

Who should be treated with sacubatril-valsartan?

- ARNI should not be administered with ACE inhibitors or ARBs within 36 hours of the last dosage.
- Valsartan/sacubitril is not intended for subjects with low systolic blood pressure < 100 mm Hg, eGFR < 30 mL/min/1.73m^2, or potassium > 5.2 mmol/L.
- Hypotension and angioedema are potential effects of the drug.