Heart Failure and Sudden Cardiac Death

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What is sudden cardiac death?

Sudden Cardiac Death

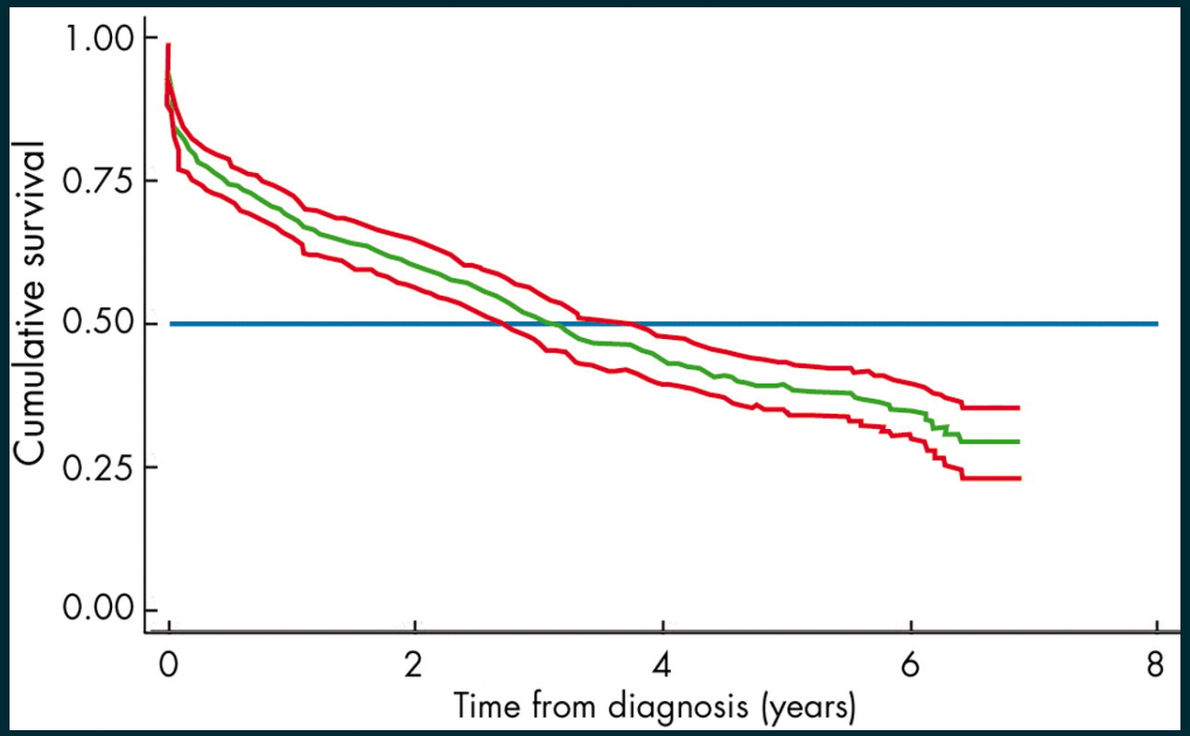
- Unexpected deaths from cardiovascular causes
- Preceded by a witnessed collapse
- Occur within 1 hour of an acute change in clinical condition
- Or < 24 hours after the person was known to be in usual state of health

SCD - Cause

- ICM
  - Ventricular fibrillation
  - Asystole / PEA (usually late after VF)
  - Recurrent MI (40 to 50%, early post MI)
  - Mechanical causes (very early post MI)
- NICM
  - Severe bradycardia / Asystole
  - Ventricular arrhythmias

Why is it a problem in patients with heart failure?

Survival in patients with heart failure

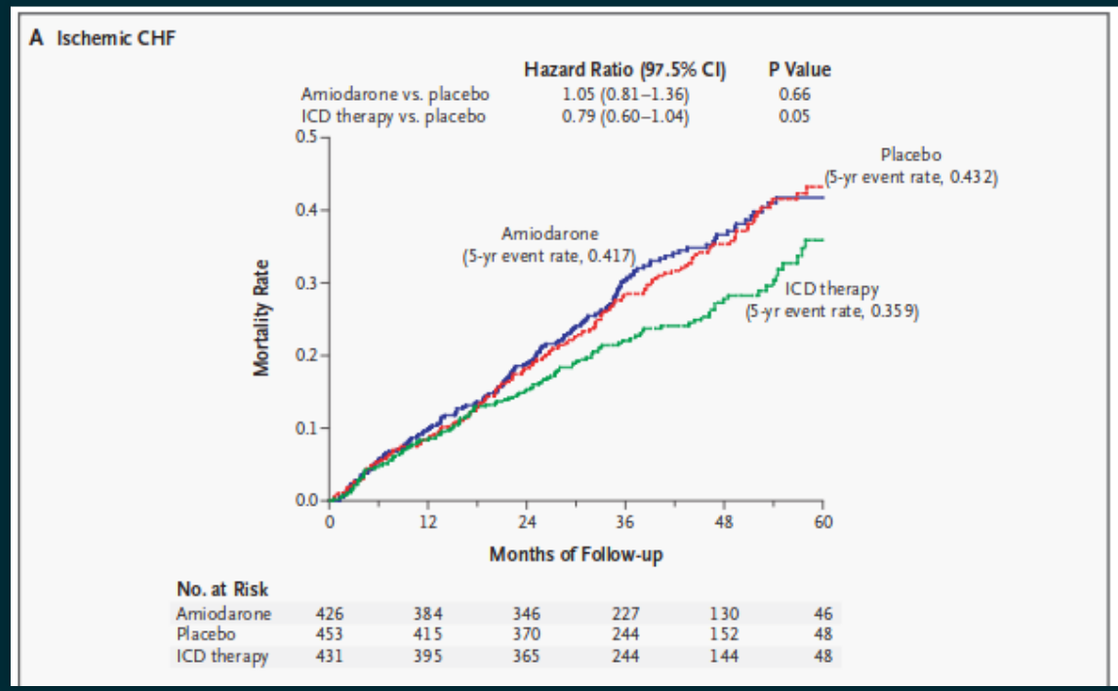


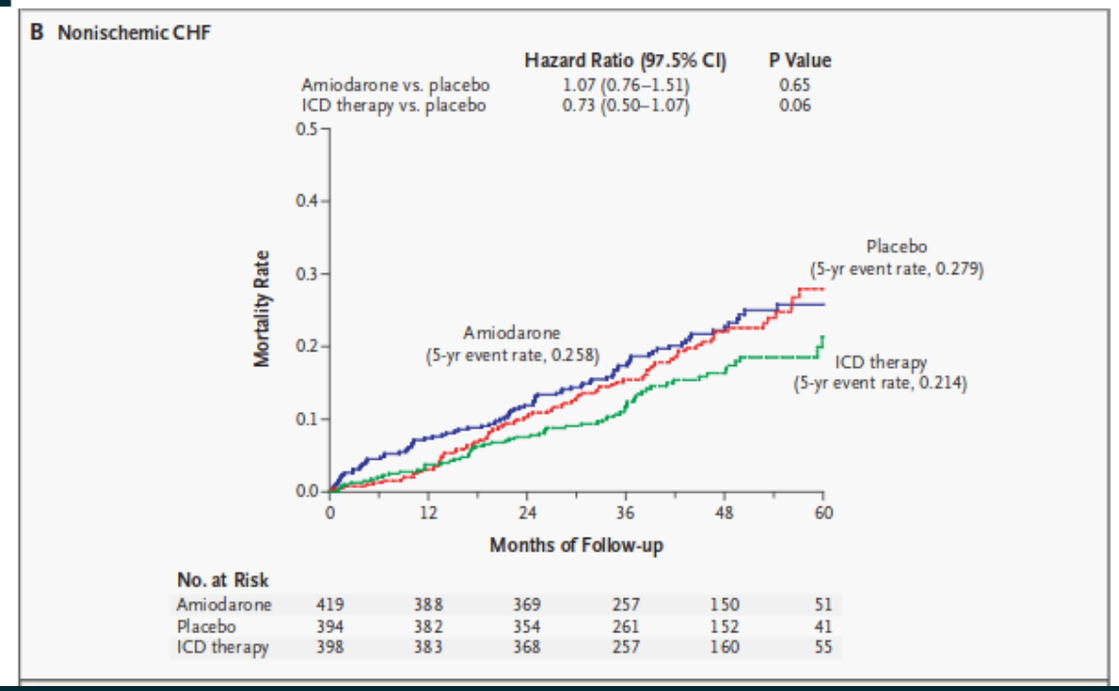
Lane RE, Cowie MR, Chow AWC. Prediction and prevention of sudden cardiac death in heart failure. Heart 2005;91:674-680.

SCD in heart failure

- CHF increases risk of SCD by 6-9 times
- Primarly in HFrEF
- About 3% per year now (20% per year previously)

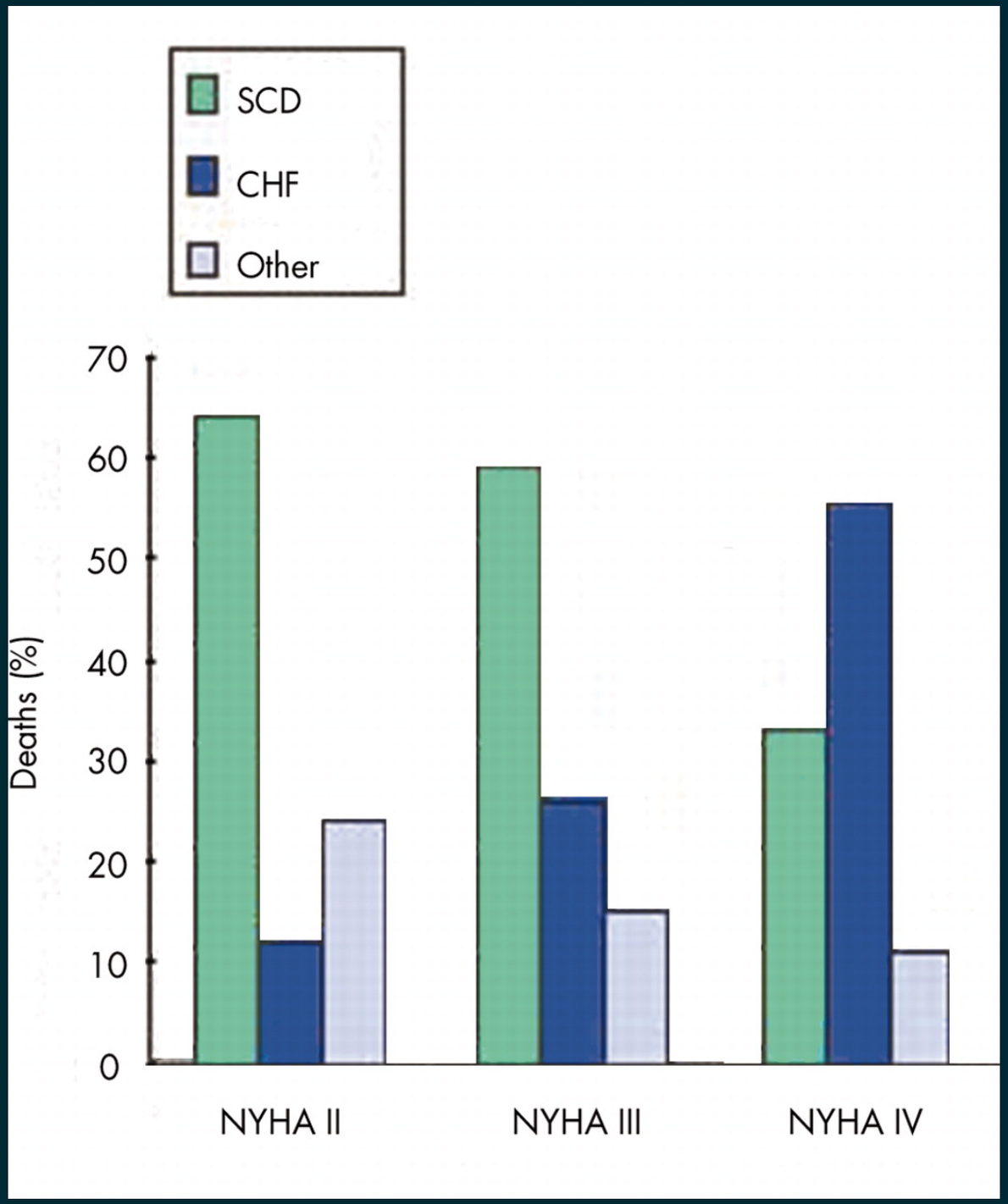
SCD HeFT





Bardy et a. Amiodarone or an Implantable Cardioverter–Defibrillator for Congestive Heart Failure. N Engl J Med 2005;352:225-37.

Mode of death and severity of symptoms



What can be done to identify and reduce risk

Identification of high risk patients

- LVEF is the one consistent marker
- Others - varying results across studies
  - NSVT
  - TWA
  - HRV
  - HRT
  - EP study
  - MRI

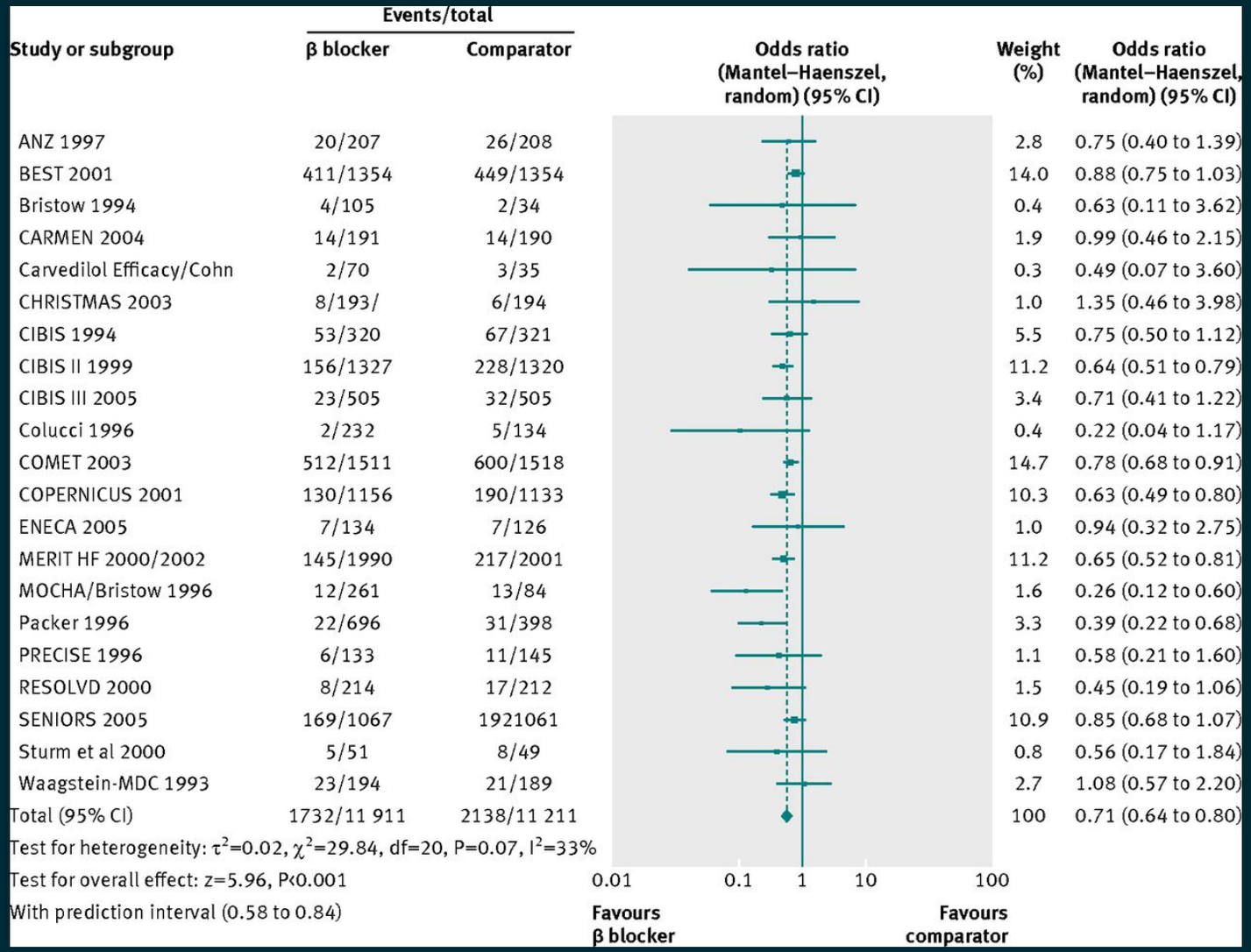
Non-pharmacologic

- Exercise
- Revascularization

Drugs

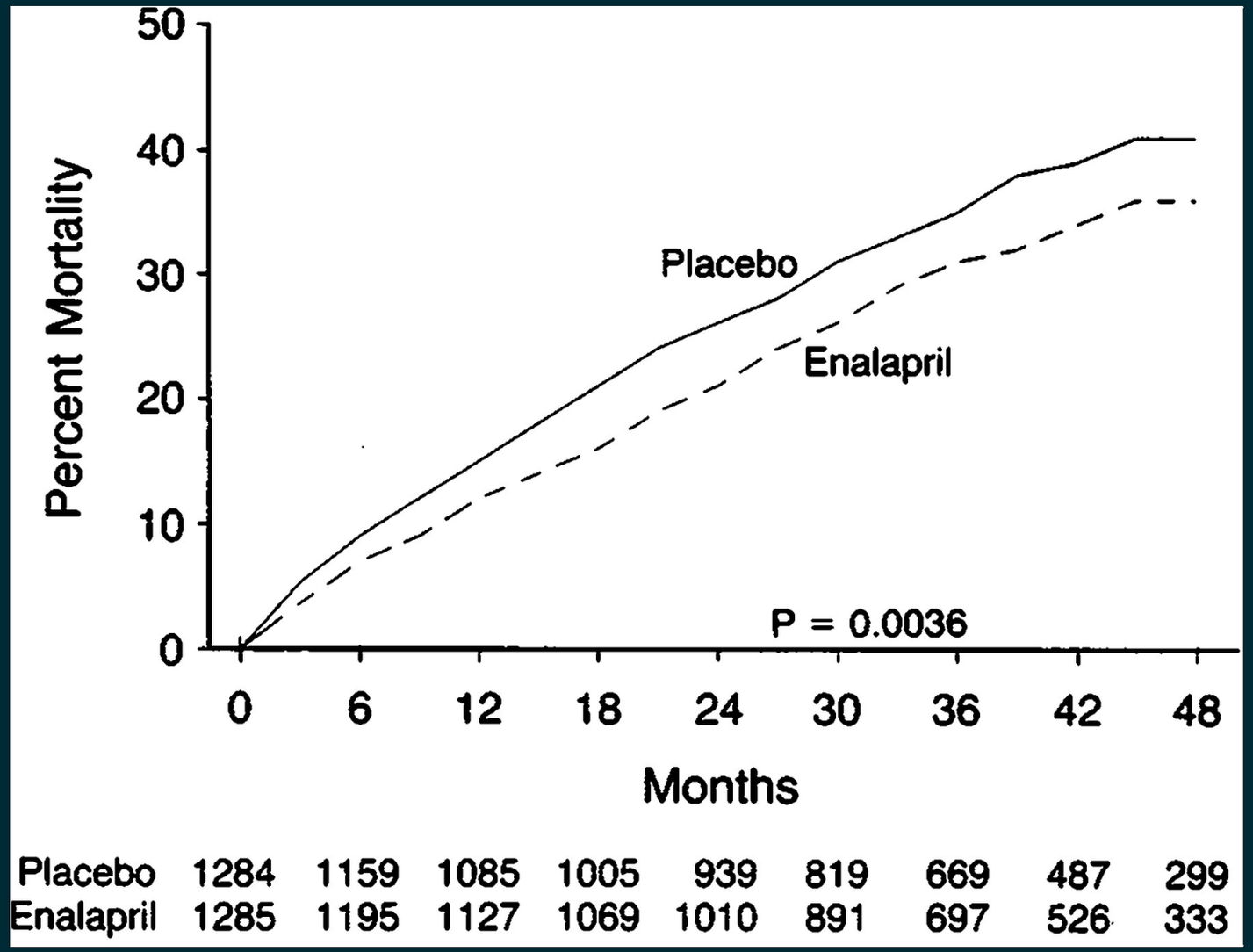
Beta blockers

- Consistently improves survival in patients with heart failure
- Around 50% reduction in SCD
- Best studied - Carvedilol, Bisoprolol and Metoprolol



Chatterjee Saurav et al. Benefits of β blockers in patients with heart failure and reduced ejection fraction: network meta-analysis BMJ 2013; 346 :f55

ACEI - SOLVD trial



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

SOLVD investigators. Effect of Enalapril on Survival in Patients with Reduced Left Ventricular Ejection Fractions and Congestive Heart Failure. N Engl J Med 1991; 325:293-302

ACEI

- Reduce total mortality
- Reduce arrhythmic mortality ?

Naccarella F et al. Do ACE inhibitors or angiotensin II antagonists reduce total mortality and arrhythmic mortality? A critical review of controlled clinical trials. Curr Opin Cardiol. 2002 Jan;17(1):6-18

ARB as compared to ACEI

- No difference in mortality with ARB as compared to ACEI (1)

Pitt et al. Effect of losartan compared with captopril on mortality in patients with symptomatic heart failure: randomised trial–the Losartan Heart Failure Survival Study ELITE II. Lancet. 2000 May 6;355(9215):1582-7.

Aldosterone antagonist

- Spironolactone - 30% reduction in mortality (1)
- Eplerenone - 15% reduction in overall mortality and 21% reduction in SCD (2)
- Especially important in early mortality reduction after MI when ICD has no benefit

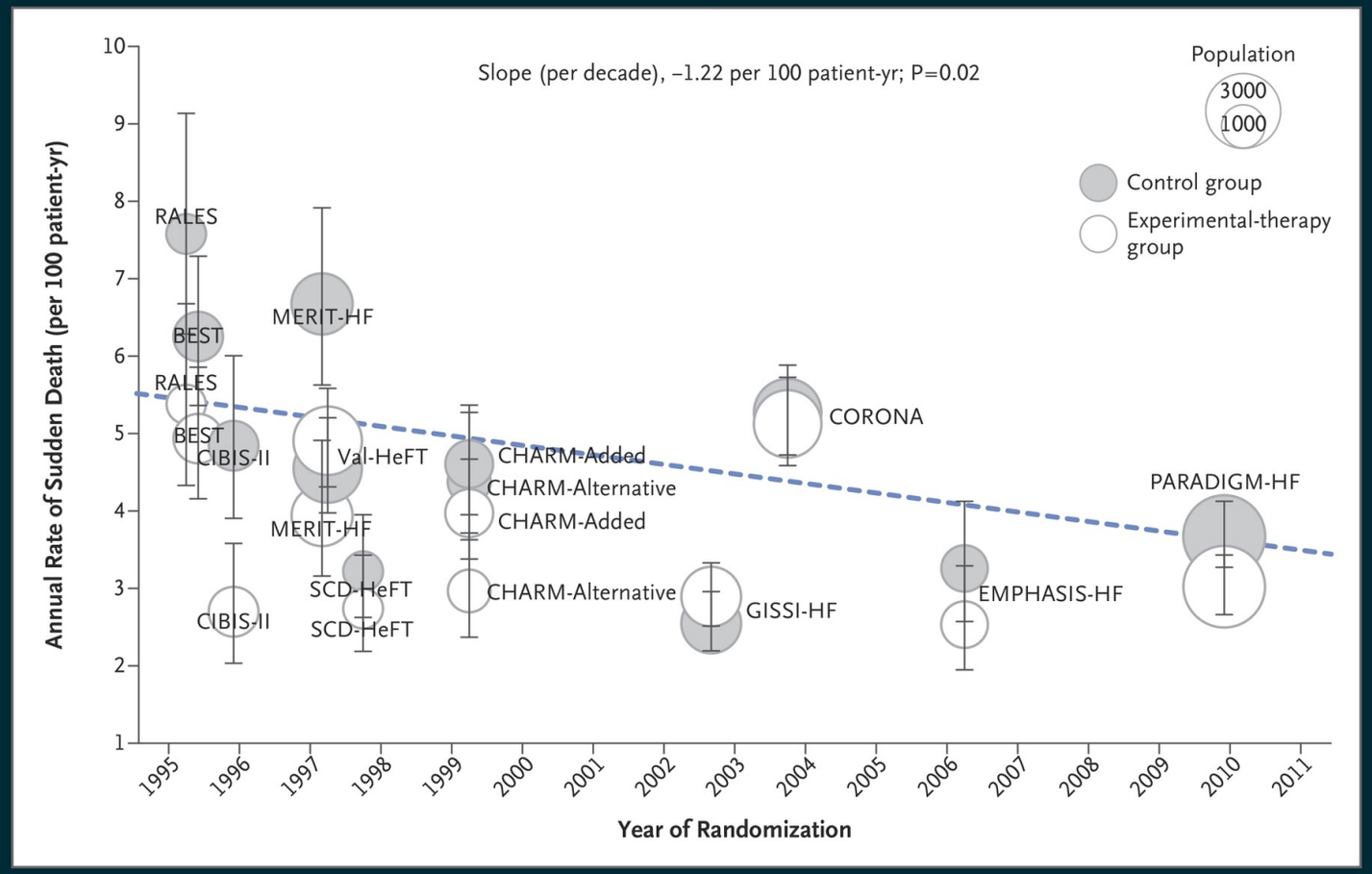
1. Pitt B, Zannad F, Remme WJ, et al. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomized aldactone evaluation study investigators. N Engl J Med1999;341:709–17
2. Pitt B, Remme W, Zannad F, et al. Eplerenone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction. N Engl J Med2003;348:1309–21.

Statins

- Lower rate of arrhythmias - MADIT II post hoc analysis (1)
- No SCD reduction in prospective trials (2,3)

1. Vyas AK et al. MADIT-II Research Group. Reduction in ventricular tachyarrhythmias with statins in the multicenter automatic defibrillator implantation trial (MADIT)-II. J Am Coll Cardiol 2006;47:769–73
2. Kjekshus et al, CORONA Group. Rosuvastatin in older patients with systolic heart failure. N Engl J Med 2007;357:2248–61
3. GISSI-HF Investigators. Effect of rosuvastatin in patients with chronic heart failure (the GISSI-HF trial): a randomised, double-blind, placebo-controlled trial. Lancet 2008;372:1231–9

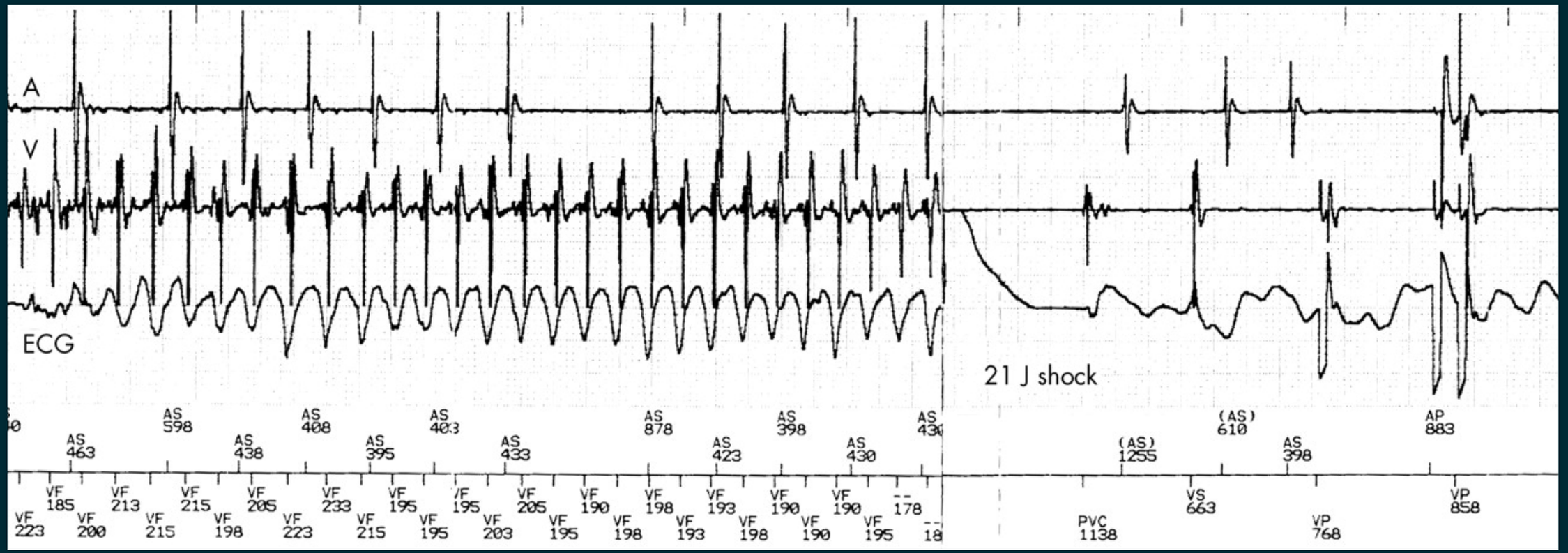
Optimal medical management - Huge impact



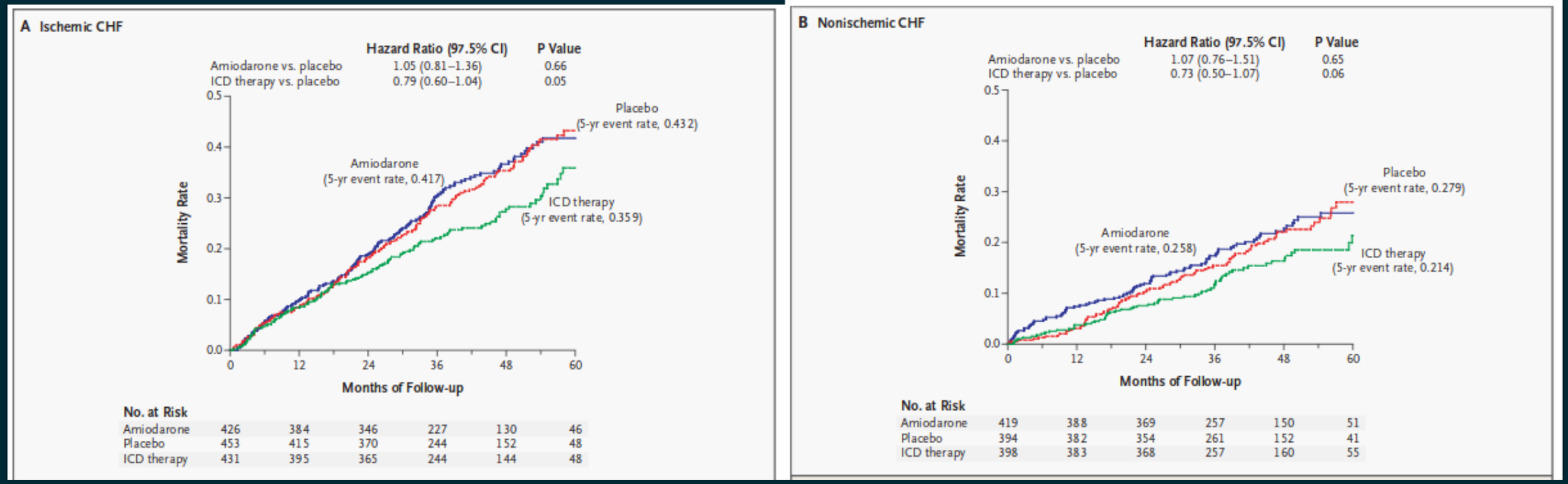
Li Shen et al. Declining Risk of Sudden Death in Heart Failure. N Engl J Med 2017; 377:41-51

Implantable devices

Implantable Cardioverter Defibrillator (ICD)



ICD - 20 to 30% reduction in deaths



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CRT

- Reduction of all cause mortality compared to optimal medical treatment (24%)

(COMPANION) - Bristow MR, Saxon LA, Boehmer J, et al. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med2004;350:2140–50

Role of Sacubitril-Valsartan

PARADIGM-HF

- Neprlisyn inhibitor with ARB
- About 4200 patients in each group
- 27 months follow up
- Significant reduction in composite endpoint (death + hospitalization for heart failure
- NNT 32 to prevent one cardiovascular death

McMurray et al. Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure. N Engl J Med 2014; 371:993-1004

Mode of death in PARADIGM-HF

- Cardiovascular deaths
  - Sudden - 44.8%
  - Heart failure related - 26.5%
- Less cardiovascular deaths with ARNI
- Benefit seen in both sudden and heart failure deaths
- Reduction in sudden death even in patients with ICD

Desai et al. Effect of the angiotensin-receptor-neprilysin inhibitor LCZ696 compared with enalapril on mode of death in heart failure patients. European Heart Journal, Volume 36, Issue 30, 7 August 2015, Pages 1990–1997

ARNI and survival in CHF patients

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	LCZ696 (N=4187)	Enalapril (N=4212)
Treatments at randomization — no. (%)		
Diuretic	3363 (80.3)	3375 (80.1)
Digitalis	1223 (29.2)	1316 (31.2)
Beta-blocker	3899 (93.1)	3912 (92.9)
Mineralocorticoid antagonist	2271 (54.2)	2400 (57.0)
Implantable cardioverter–defibrillator	623 (14.9)	620 (14.7)
Cardiac resynchronization therapy	292 (7.0)	282 (6.7)

Summary

- All patients with heart failure should receive
  - Beta blockers
  - ACEI
  - Aldosterone antagonists
- Patients at high risk of SCD should receive
  - ICD
- Patients with wide QRS may require
  - CRT

Should ARNI replace ACEI

- Existing evidence is compelling
- Guidelines suggests replacing ACEI (US) or using when patients still symptomatic (EUR)
- Single trial, no long term follow up
- When changing
  - High dose ACEI tolerated?
  - 36 hour washout
  - Cost benefit ratio