

World Congress of Cardiology 2006

2-6 September, Barcelona - Spain

www.worldcardio2006.org



Sudden cardiac death in heart failure

Implantable cardioverter-defibrillator

indications: the arrhythmia

specialist's point of view.

**Ignacio Fernández
Lozano**



World Congress of Cardiology 2006
2-6 September, Barcelona - Spain



**Joint meeting of
the European Society of Cardiology
& World Heart Federation**

DISCLOSURES

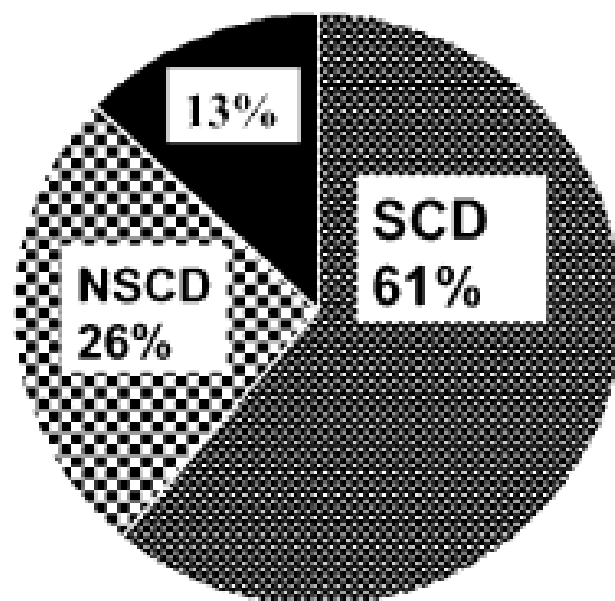
Multicenter Trials	Medtronic, SJM Guidant
Stock ownership	None
Consulting	SJM Sorin group
Speakers Bureau	None

All cause mortality and SCD in Heart Failure

- Despite improvements in medical therapy, symptomatic HF still confers a 20-25% risk of premature death in the first 2.5 yrs after diagnosis.
- 35-50% of these premature deaths are SCD
- SCD occurs at 6-9 times the rate of the general population.

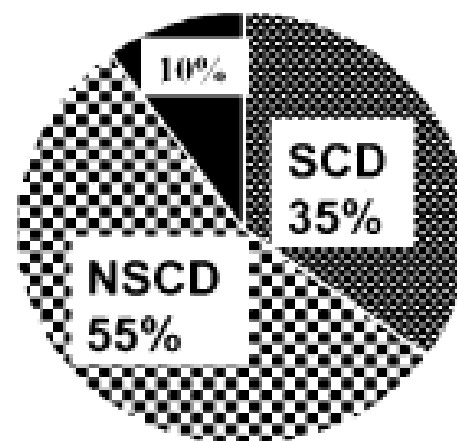
Analysis of Mortality Events in the Multicenter Automatic Defibrillator Implantation Trial (MADIT-II)

CONVENTIONAL GROUP



Cardiac Death: $80/490=16.3\%$

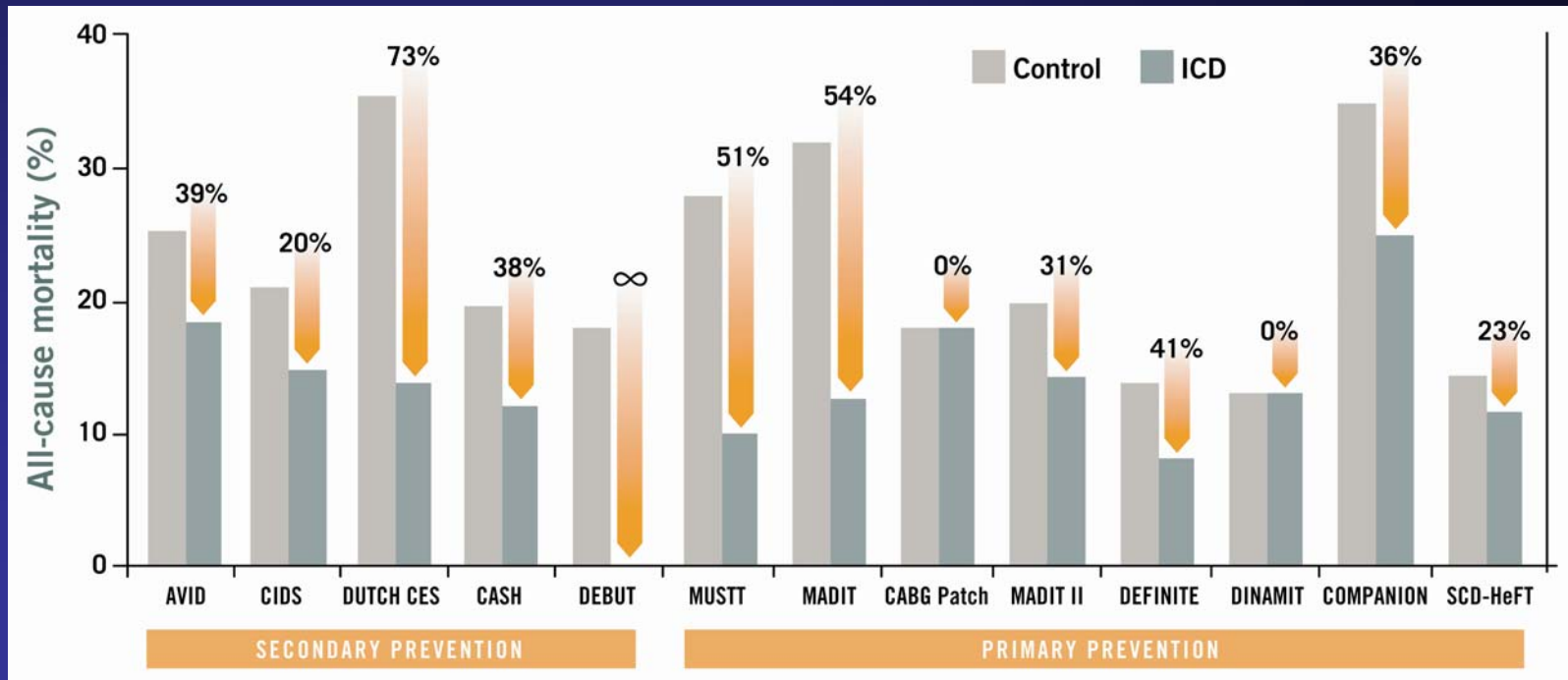
DEFIBRILLATOR GROUP



Cardiac Death: $79/742=10.6\%$

AICD

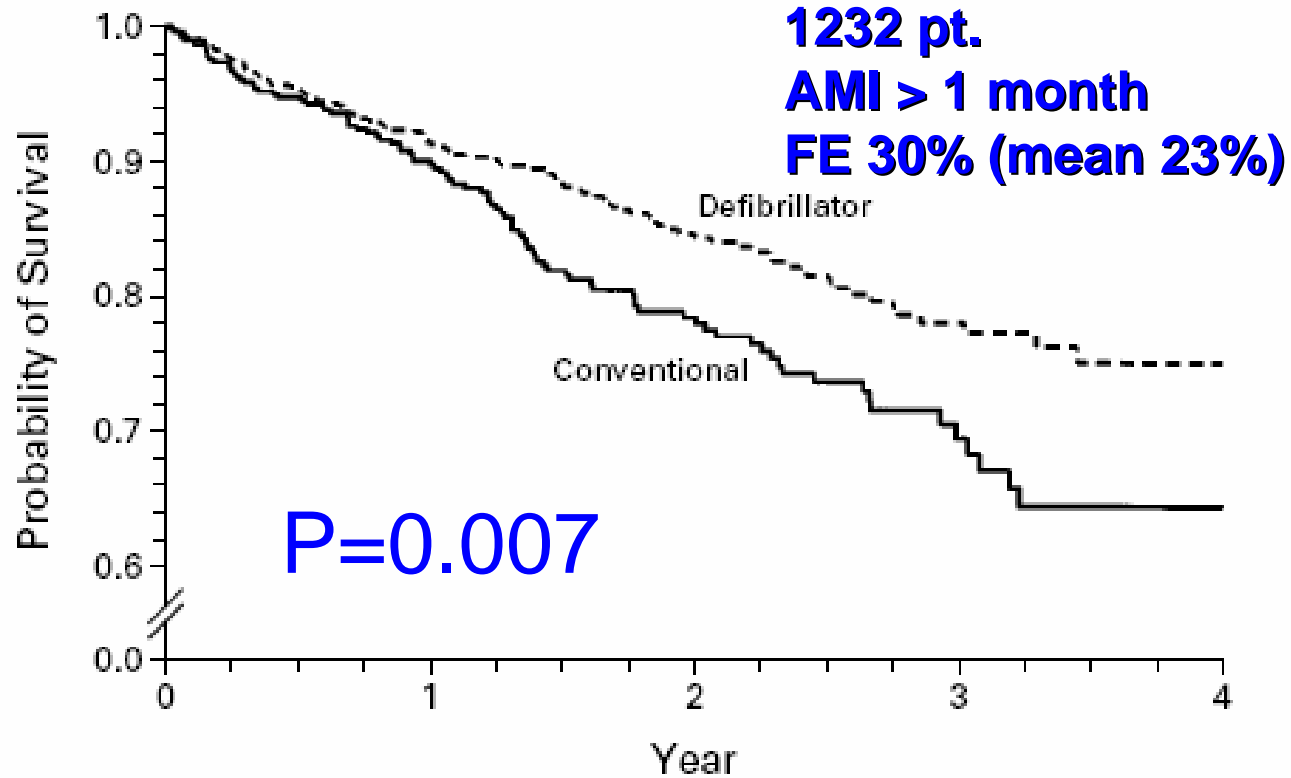
- AICD reduces total mortality ~30-50%.
- AICD reduces SD 65%.



MADIT II

PROPHYLACTIC IMPLANTATION OF A DEFIBRILLATOR IN PATIENTS WITH MYOCARDIAL INFARCTION AND REDUCED EJECTION FRACTION

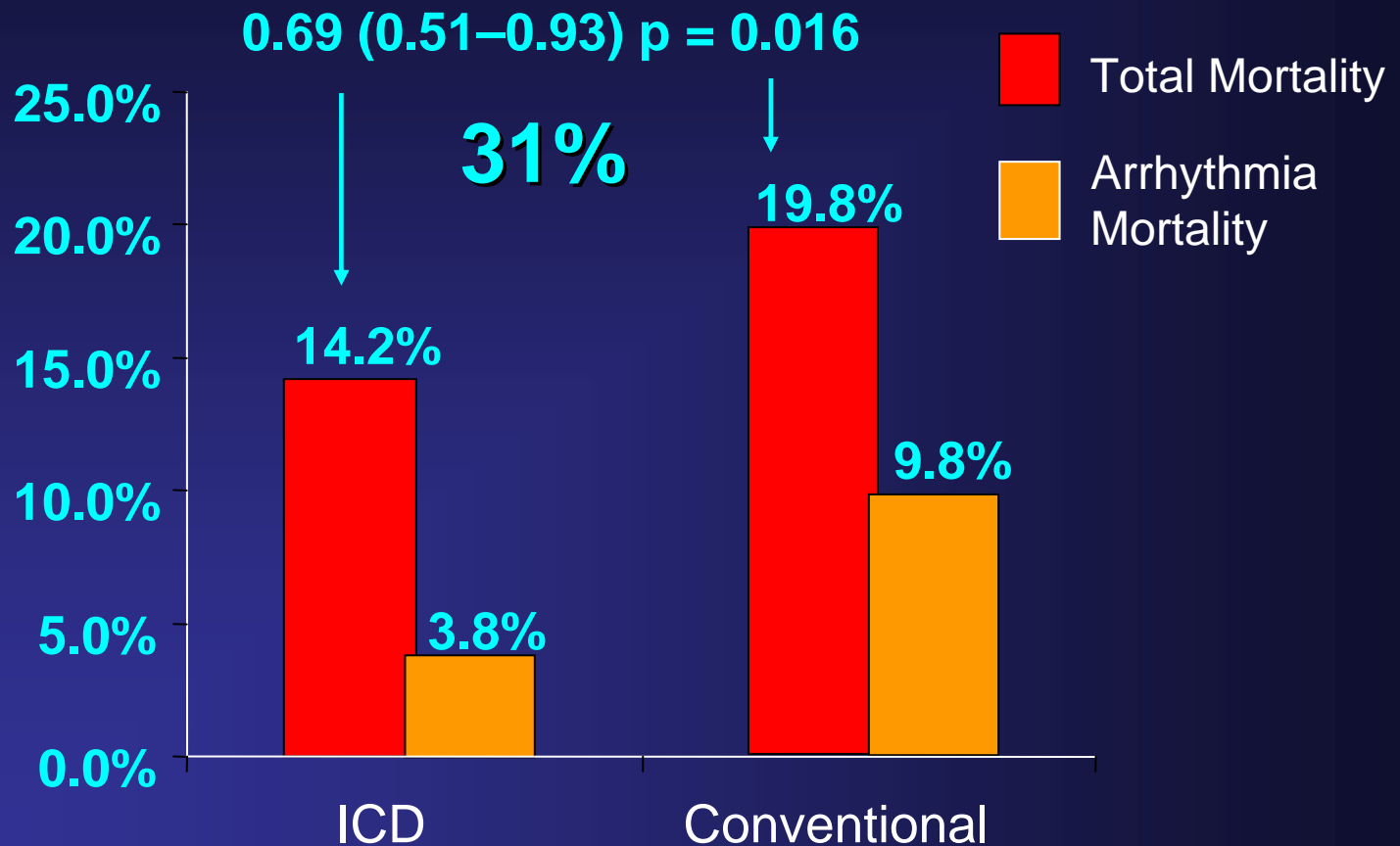
ARTHUR J. MOSS, M.D., WOJCIECH ZAREBA, M.D., PH.D., W. JACKSON HALL, PH.D., HELMUT KLEIN, M.D.,
DAVID J. WILBER, M.D., DAVID S. CANNOM, M.D., JAMES P. DAUBERT, M.D., STEVEN L. HIGGINS, M.D.,
MARY W. BROWN, M.S., AND MARK L. ANDREWS, B.B.S.,
FOR THE MULTICENTER AUTOMATIC DEFIBRILLATOR IMPLANTATION TRIAL II INVESTIGATORS*



No. AT Risk

Defibrillator	742	503 (0.91)	274 (0.84)	110 (0.78)	9
Conventional	490	329 (0.90)	170 (0.78)	65 (0.69)	3

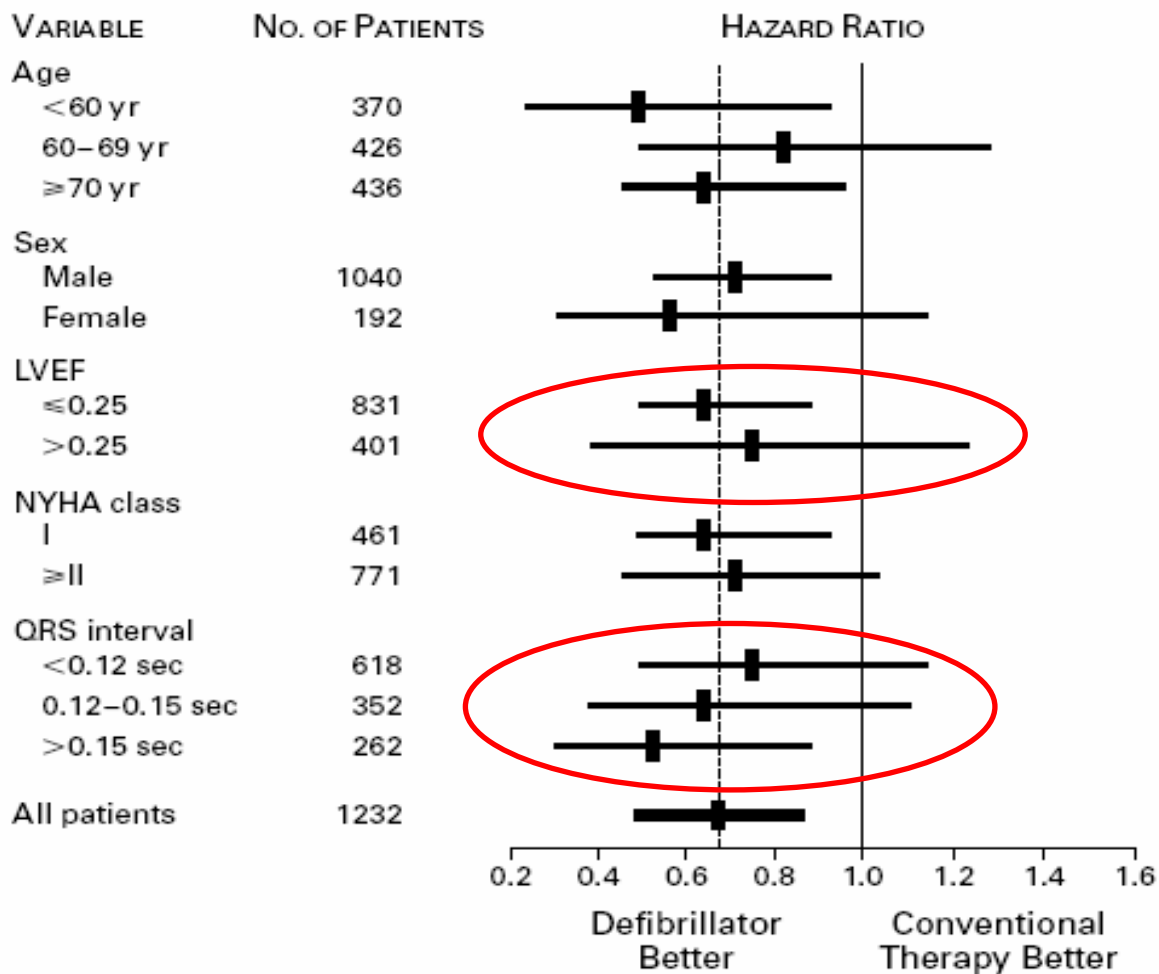
MADIT II: Impact of ICD therapy on total and arrhythmia mortality



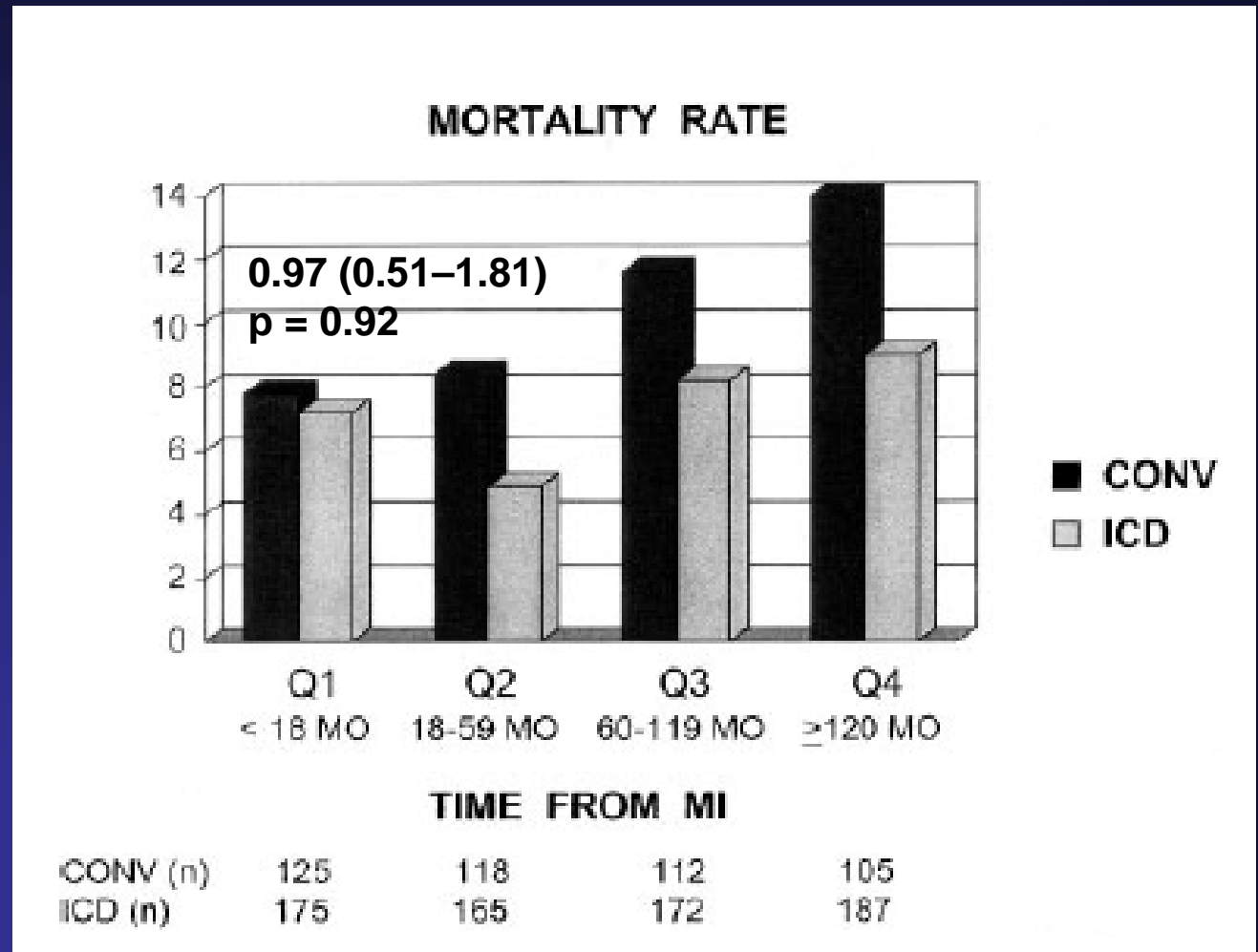
MADIT II

PROPHYLACTIC IMPLANTATION OF A DEFIBRILLATOR IN PATIENTS WITH MYOCARDIAL INFARCTION AND REDUCED EJECTION FRACTION

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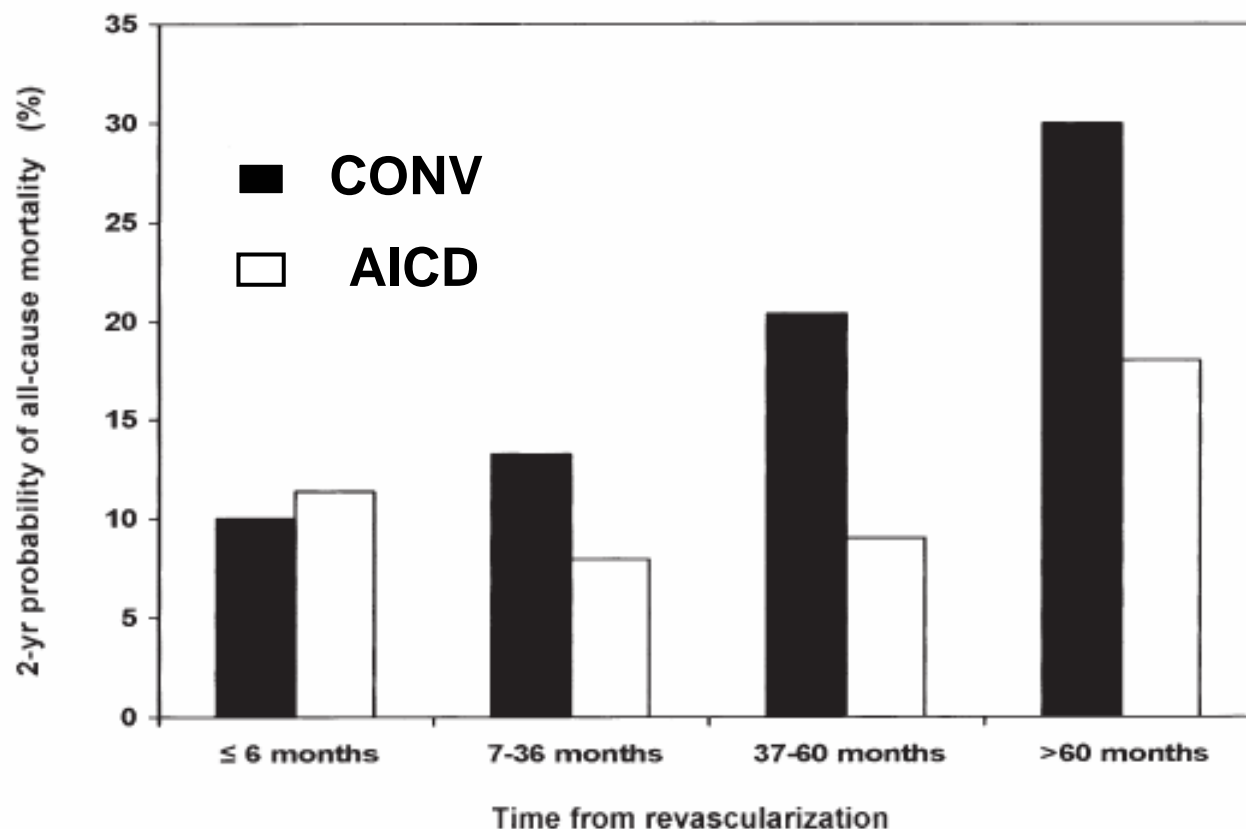
Time Dependence of Mortality Risk and Defibrillator Benefit After Myocardial Infarction



Time Dependence of Defibrillator Benefit After Coronary Revascularization in the Multicenter Automatic Defibrillator Implantation Trial (MADIT)-II

JACC Vol. 47, No. 9, 2006

May 2, 2006:1811-7



Conv: No. of deaths	6	15	11	43
No. of patients	60	113	54	144
ICD: No. of deaths	8	10	8	47
No. of patients	70	124	89	263

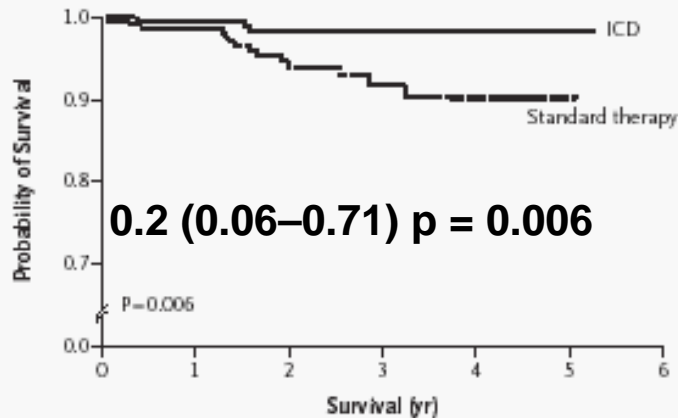
MADIT II

Prophylactic Defibrillator Implantation in Patients with Nonischemic Dilated Cardiomyopathy (DEFINITE)

DEFINITE

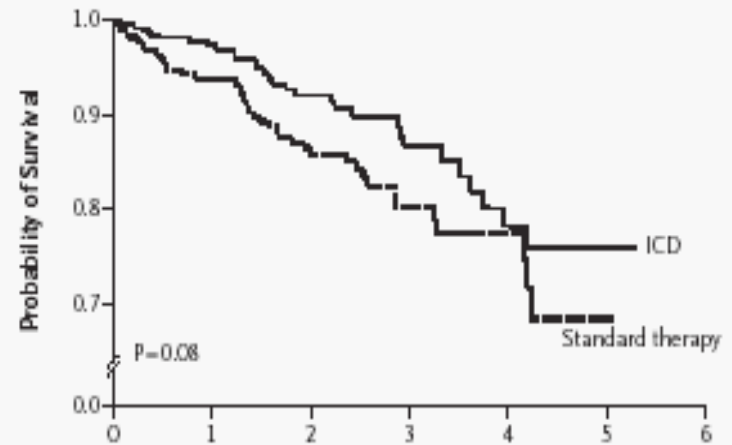
456 pt. NIDCM
FE <36% (mean 21%)
PVC or NSVT

B Sudden Death from Arrhythmia



No. at Risk	0	1	2	3	4	5	6
Standard-therapy group	229	210	131	67	32		
ICD group	229	218	140	77	41		

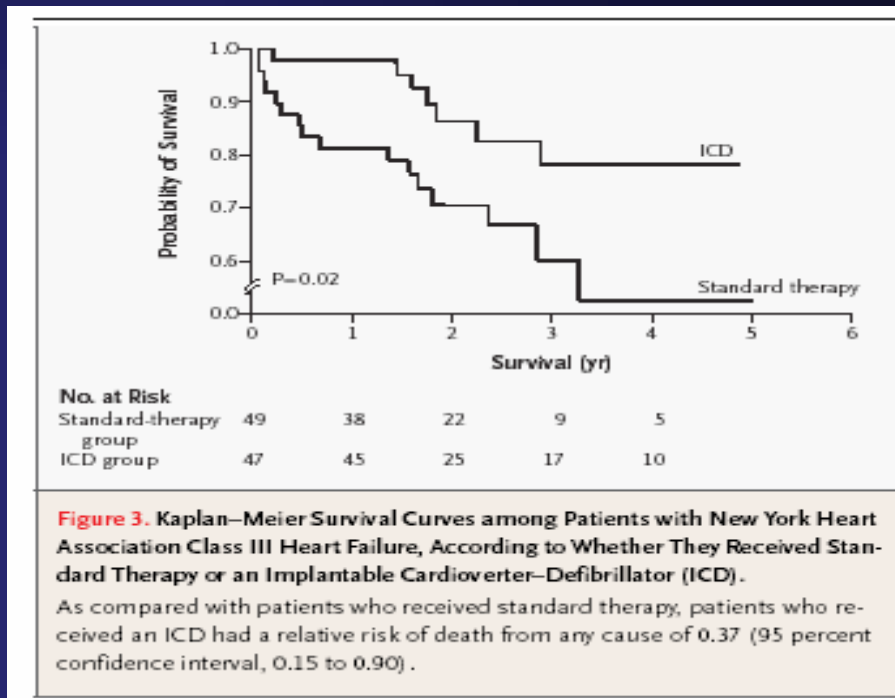
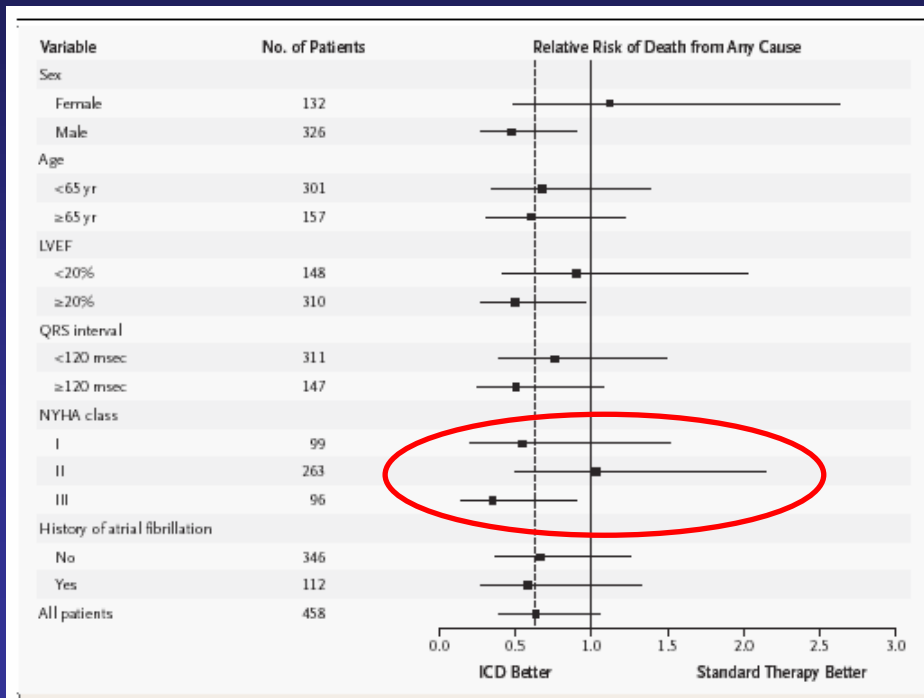
A Death from Any Cause



0.65 (0.4–1.06) p = 0.08

Prophylactic Defibrillator Implantation in Patients with Nonischemic Dilated Cardiomyopathy (DEFINITE)

DEFINITE



SCD-HeFT

2,521 patients with moderately symptomatic CHF (NYHA Class II or III) and LVEF \leq 35%

Mean EF 25%, 70% FC II – 30% FC III, 52% IC – 48% NIC

Conventional CHF Treatment + Amiodarone

Antiarrhythmic agent

- 800 mg Week 1, 400 mg Week 2-4

Chronic therapy:

- 200 mg/day if <150 lbs
- 300 mg/day if 150-200 lbs
- 400 mg/day if >200 lbs

Conventional CHF Treatment + ICD

Single lead implantable cardioverter defibrillator programmed for ventricular fibrillation (VF) treatment only

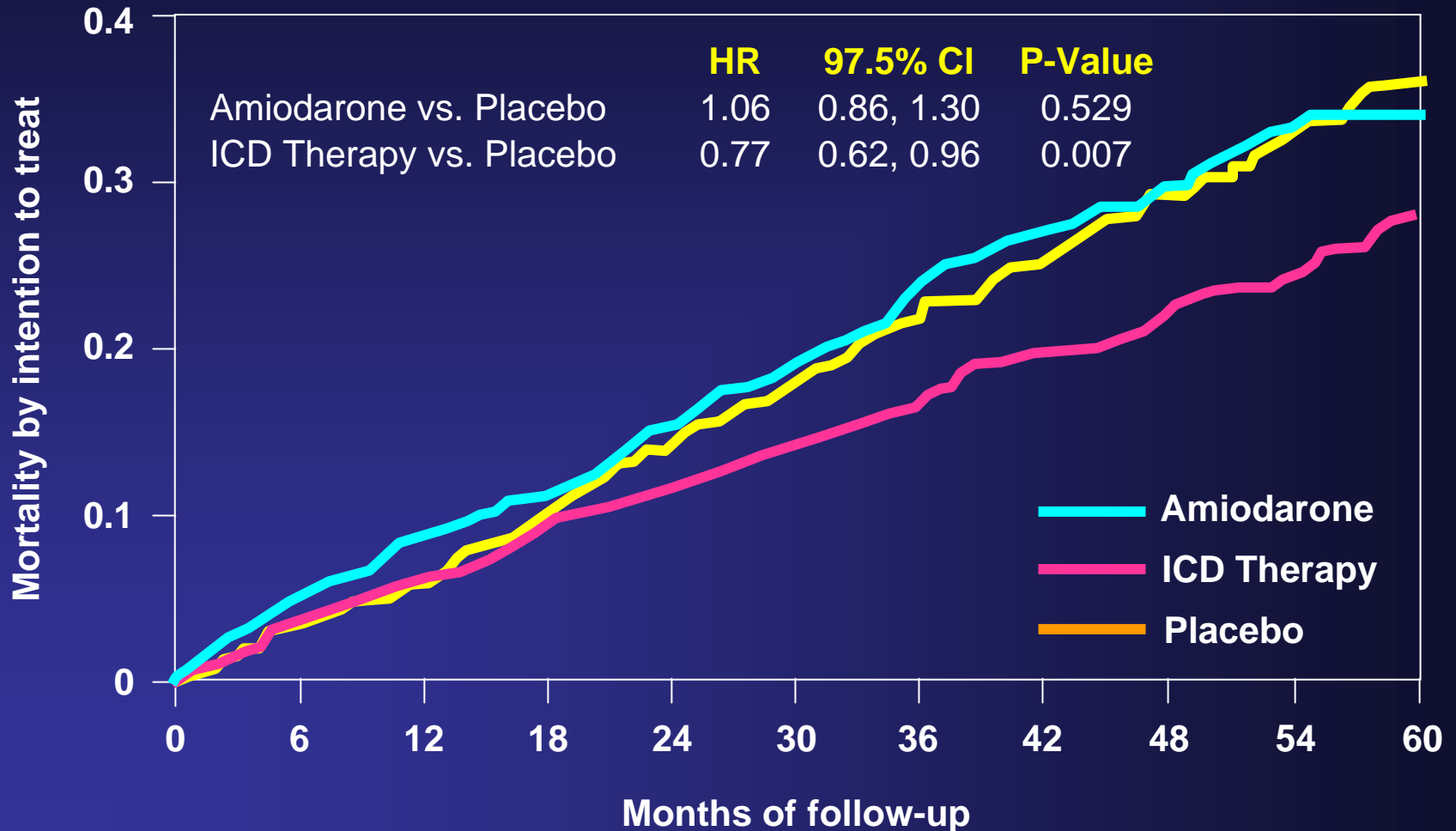
Conventional CHF Treatment + Placebo

Treatment

Endpoints (median 45.5 months):

All-cause mortality

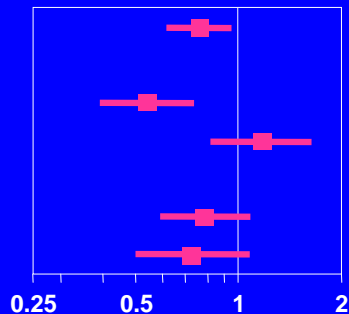
SCD-HeFT. Total mortality



- Median follow-up: 45.5 mo (34.8, 55.2)
- Vital status known on 100% of 2,521 patients

ICD vs. Placebo Hazard Ratios

Patient Group	N	HR	97.5% CI
All Patients	1676	0.77	0.62, 0.96
NYHA Class			
Class II	1160	0.54	0.40, 0.74
Class III	516	1.16	0.84, 1.61
CHF Etiology			
Ischemic	884	0.79	0.60, 1.04
Non-Ischemic	792	0.73	0.50, 1.04

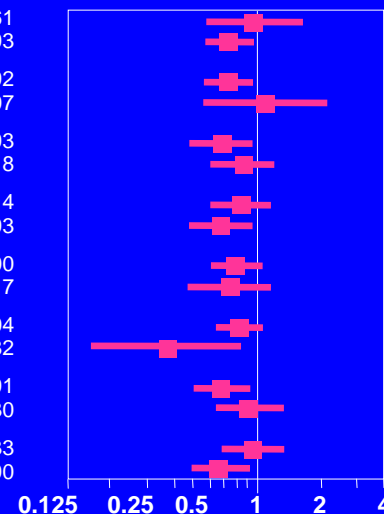


In the intention to treat analysis, ICD therapy significantly reduced all-cause mortality by clinically relevant 23% as compared to Placebo over the observation period of 5 years.



Additional Subgroups: ICD vs. Placebo

Patient Group	N	HR	97.5% CI
Gender			
Female	382	0.96	0.58, 1.61
Male	1294	0.73	0.57, 0.93
LVEF			
≤30%	1390	0.73	0.57, 0.92
> 30%	285	1.08	0.57, 2.07
Age			
< 65	1098	0.68	0.50, 0.93
≥ 65	578	0.86	0.62, 1.18
QRS Duration			
< 120 ms	977	0.84	0.62, 1.14
≥ 120 ms	699	0.67	0.49, 0.93
Race			
White	1283	0.78	0.61, 1.00
Non-White	393	0.75	0.48, 1.17
Enrolling Country			
U.S.	1512	0.82	0.65, 1.04
Non-U.S.	164	0.37	1.17, 0.82
Beta Blocker			
Yes	1157	0.68	0.51, 0.91
No	519	0.92	0.65, 1.30
Diabetes			
Yes	524	0.95	0.68, 1.33
No	1152	0.67	0.50, 0.90

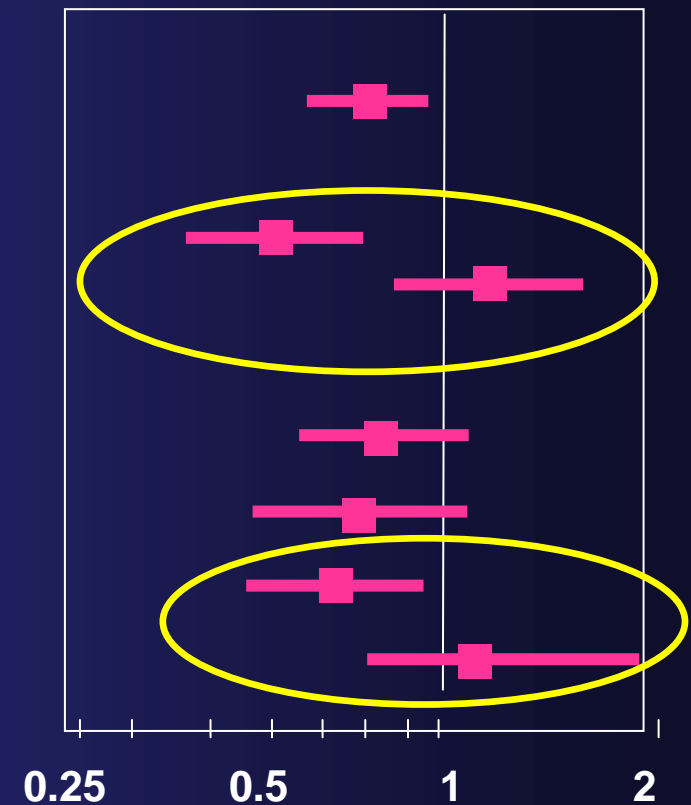


Subgroups in SCD-HeFT are too small and not powered to provide statistically significant results.

DAI vs. Placebo Hazard Ratios

SCD-HeFT

Patient Group		N	HR	97.5% CI
All Patients		1676	0.77	0.62, 0.96
NYHA Class	Class II	1160	0.54	0.40, 0.74
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CHF Etiology	Ischemic	884	0.79	0.60, 1.04
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LVEF	< 30%	1390	0.73	0.57, 0.92
	> 30%	285	1.08	0.57, 2.07



Cardiac-Resynchronization Therapy with or without an Implantable Defibrillator in Advanced Chronic Heart Failure

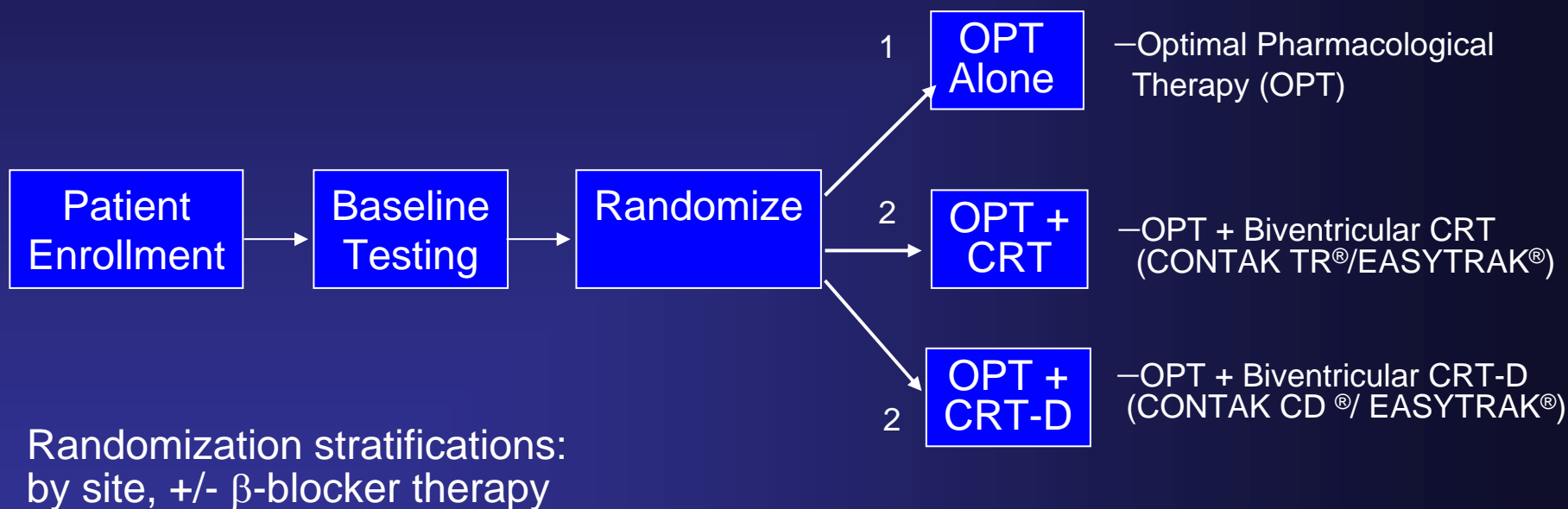
N Engl J Med 2004;350:2140-50.

- Normal Sinus Rhythm
- NYHA Class III (85%) or IV . ICM 56%
- QRS \geq 120 msec, PR interval $>$ 150msec
- LVEF \leq 35%, LVEDD \geq 60 mm
- Optimal pharmacological therapy
 - Beta blocker (for at least 3 months)
 - Diuretic, ACEI/ARB, spironolactone (1 month); +/- digoxin
- Hx of HF hospitalization (or RX equivalent) $<$ 12 months, $>$ 1 month prior to enrollment
- No bradycardia or tachyarrhythmia device indication at the time of enrollment

COMPANION

Cardiac-Resynchronization Therapy with or without an Implantable Defibrillator in Advanced Chronic Heart Failure

Patients randomized 1:2:2: to the following arms:



Target time to Implant ≤ 2 days from randomization

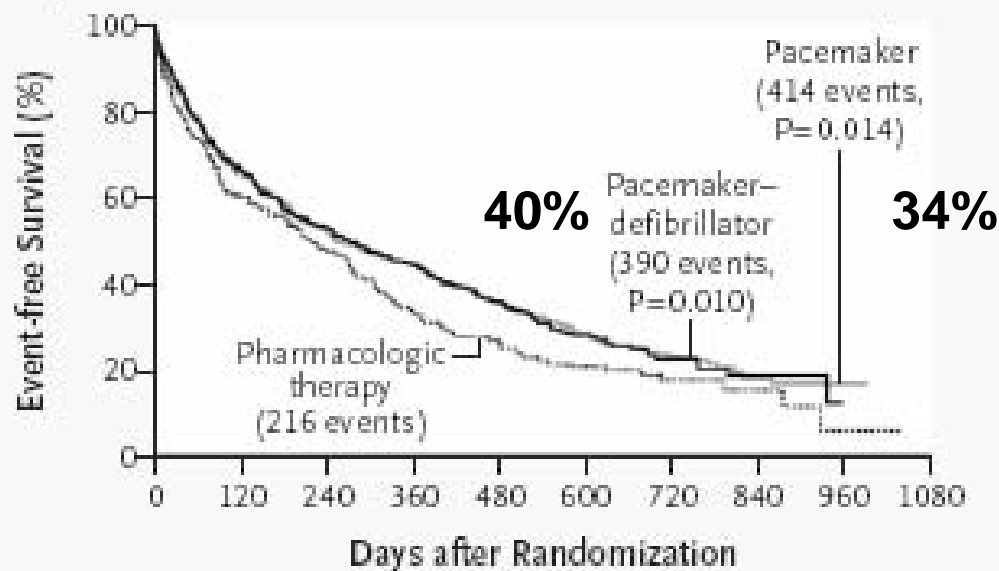
COMPANION

N Engl J Med 2004;350:2140-50.

Cardiac-Resynchronization Therapy with or without an Implantable Defibrillator in Advanced Chronic Heart Failure

N Engl J Med 2004;350:2140-50.

A Primary End Point



No. at Risk

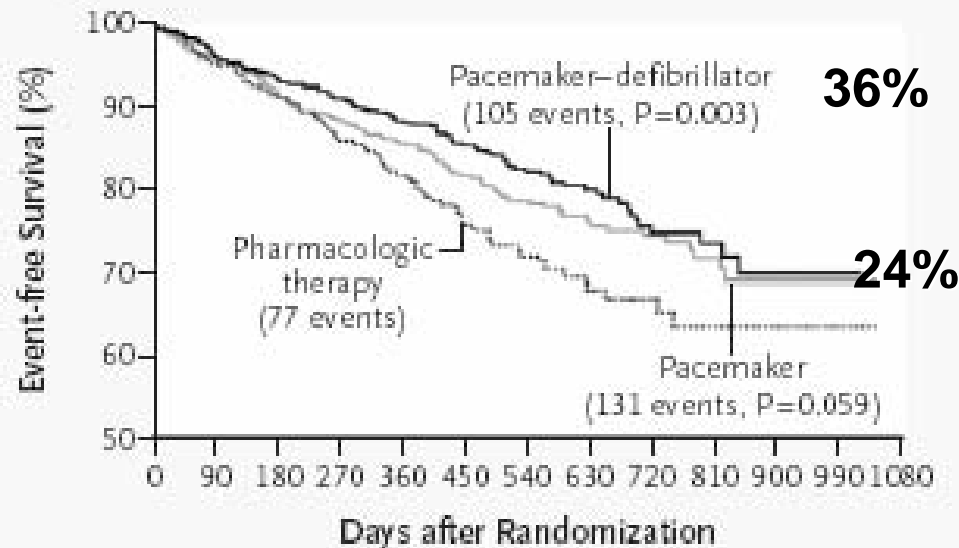
Pharmacologic therapy	308	176	115	72	46	24	16	6	1
Pacemaker	617	384	294	228	146	73	36	14	3
Pacemaker-defibrillator	595	385	283	217	128	61	25	8	0

COMPANION

Cardiac-Resynchronization Therapy with or without an Implantable Defibrillator in Advanced Chronic Heart Failure

N Engl J Med 2004;350:2140-50.

B Secondary End Point



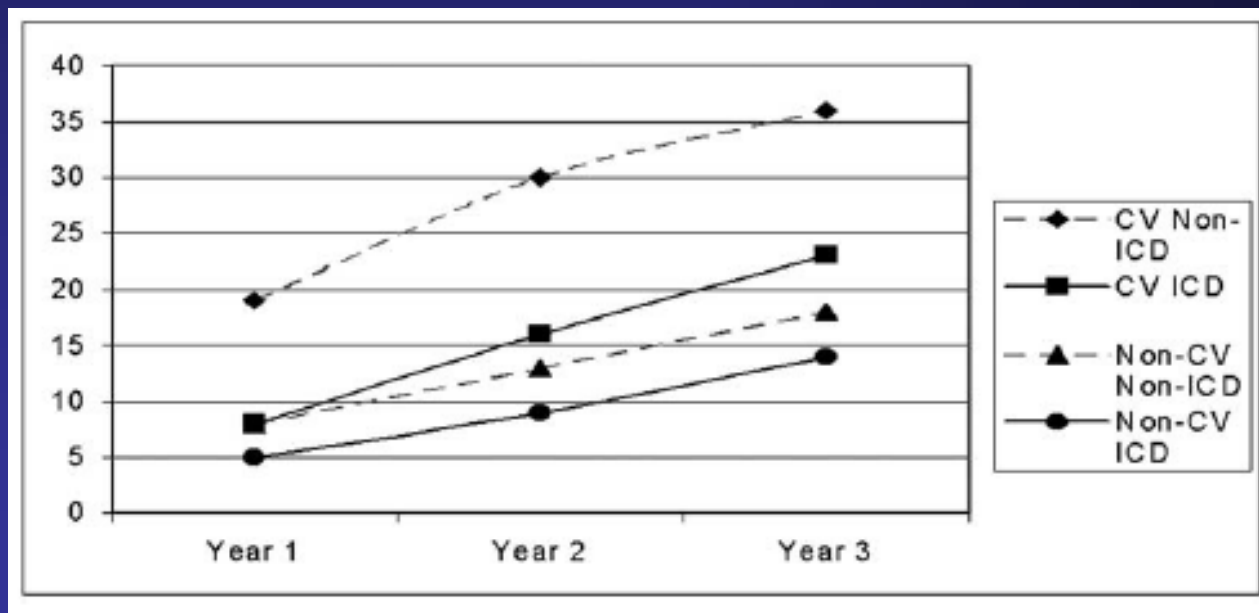
No. at Risk

Pharmacologic therapy	308	284	255	217	186	141	94	57	45	25	4	2
Pacemaker	617	579	520	488	439	355	251	164	104	60	25	5
Pacemaker-defibrillator	595	555	517	470	420	331	219	148	95	47	21	1

COMPANION

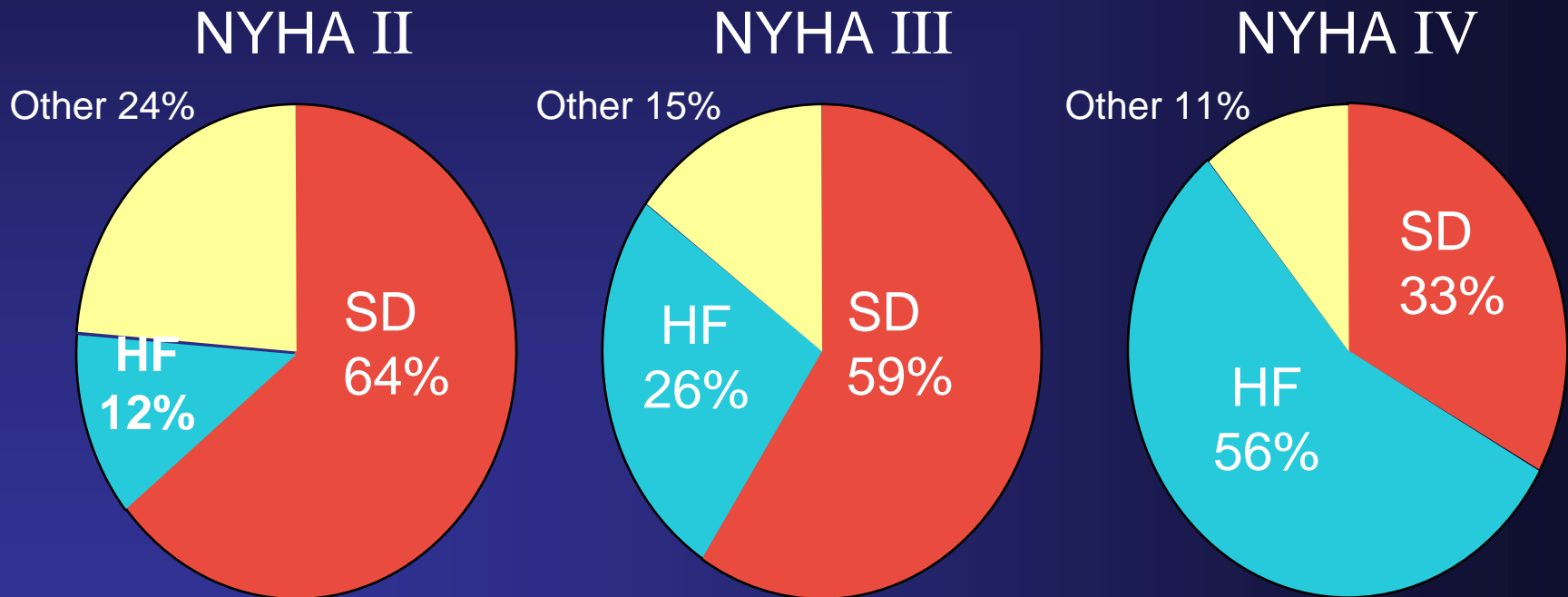
Mortality Reduction by Implantable Cardioverter-Defibrillators in High-Risk Patients With Heart Failure, Ischemic Heart Disease, and New-Onset Ventricular Arrhythmia

6.996 patients. IHD, CHF, VA
1.442 AICD
3 years follow up



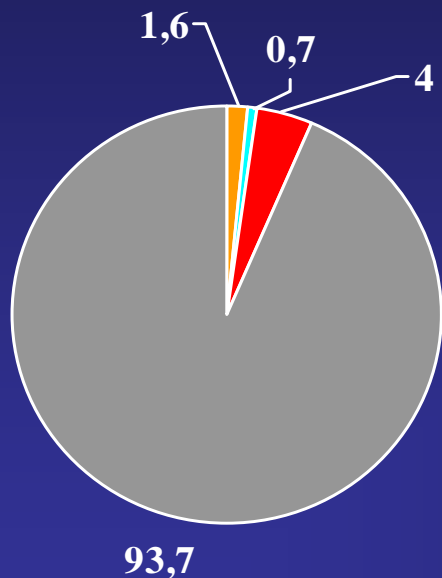
NYHA IV?

Mode of Death by NYHA Class

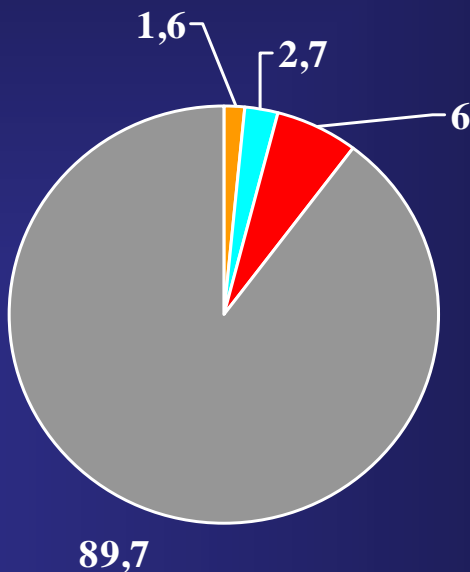


Mode of Death by NYHA Class

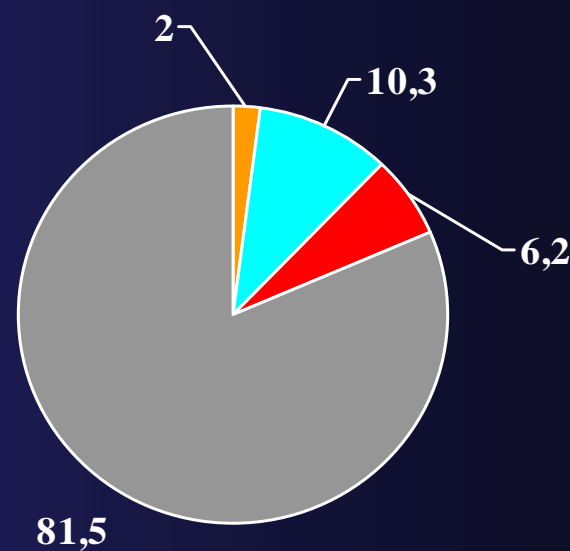
NYHA II

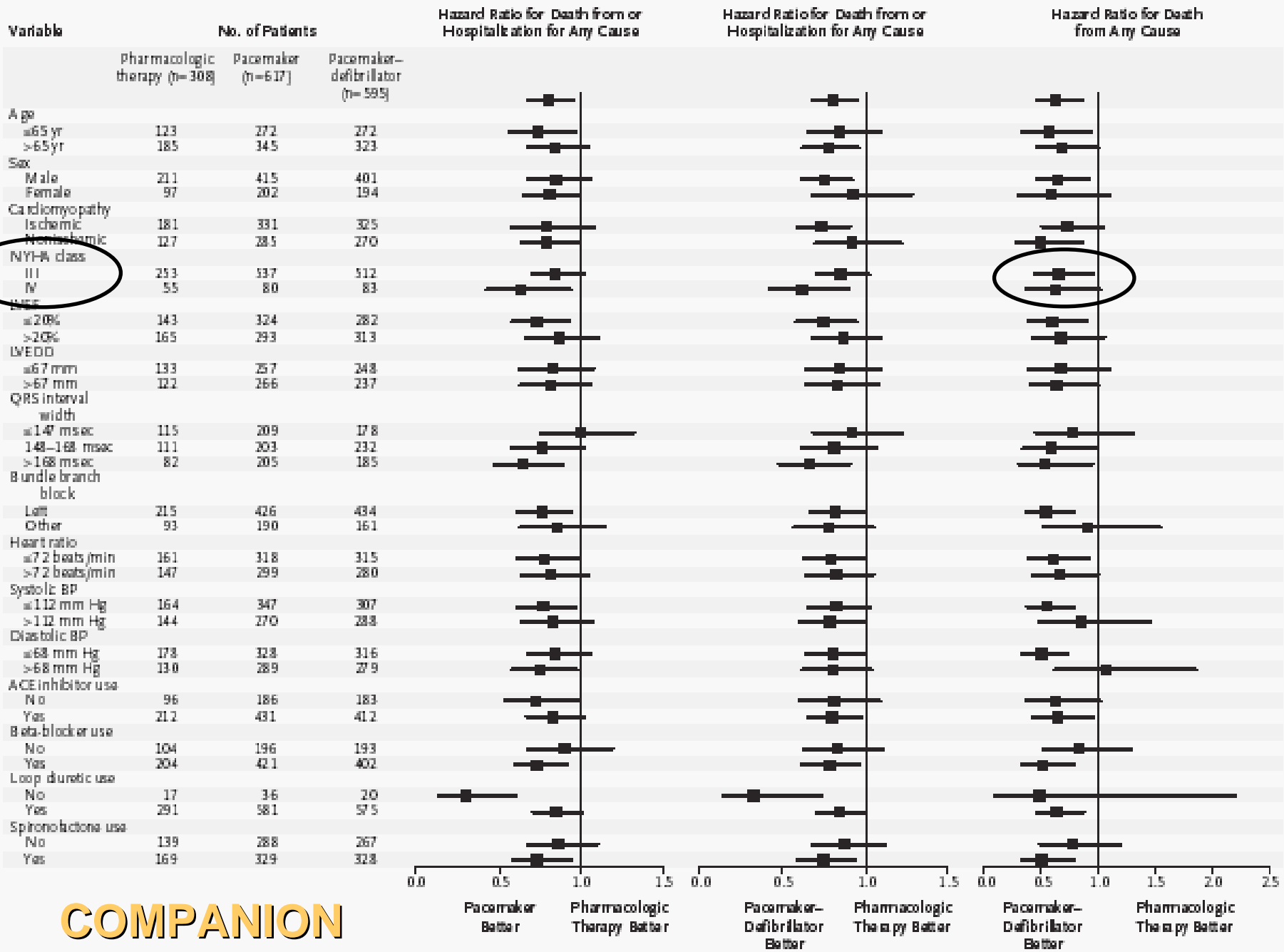


NYHA III



NYHA IV





COMPANION

Guidelines for the diagnosis and treatment of chronic heart failure: executive summary (update 2005)

- **“LVEF \leq 30-35%, not within 40 days of MI...”**
(Class 1 recommendation, level of evidence A)
- **CRT-D “in patients who remain symptomatic with HF NYHA Class III-IV, LVEF \leq 35%, and QRS \geq 120 ms**
(Class IIa recommendation, level of evidence B)

ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death—executive summary

1. Left ventricular dysfunction due to prior MI.

“Patients at least 40 d post-MI, EF \leq 30 to 40%, NYHA II or III ...”

(Class 1 recommendation, level of evidence A)

“Patients at least 40 d post-MI, EF \leq 30 to 35%, NYHA I...”

(Class IIa recommendation, level of evidence A)

2. Dilated cardiomyopathy

“Patients with NICM, EF \leq 30 to 35%, NYHA II or III...”

(Class I recommendation, level of evidence B)

“Patients with NICM, EF \leq 30 to 35%, NYHA I...”

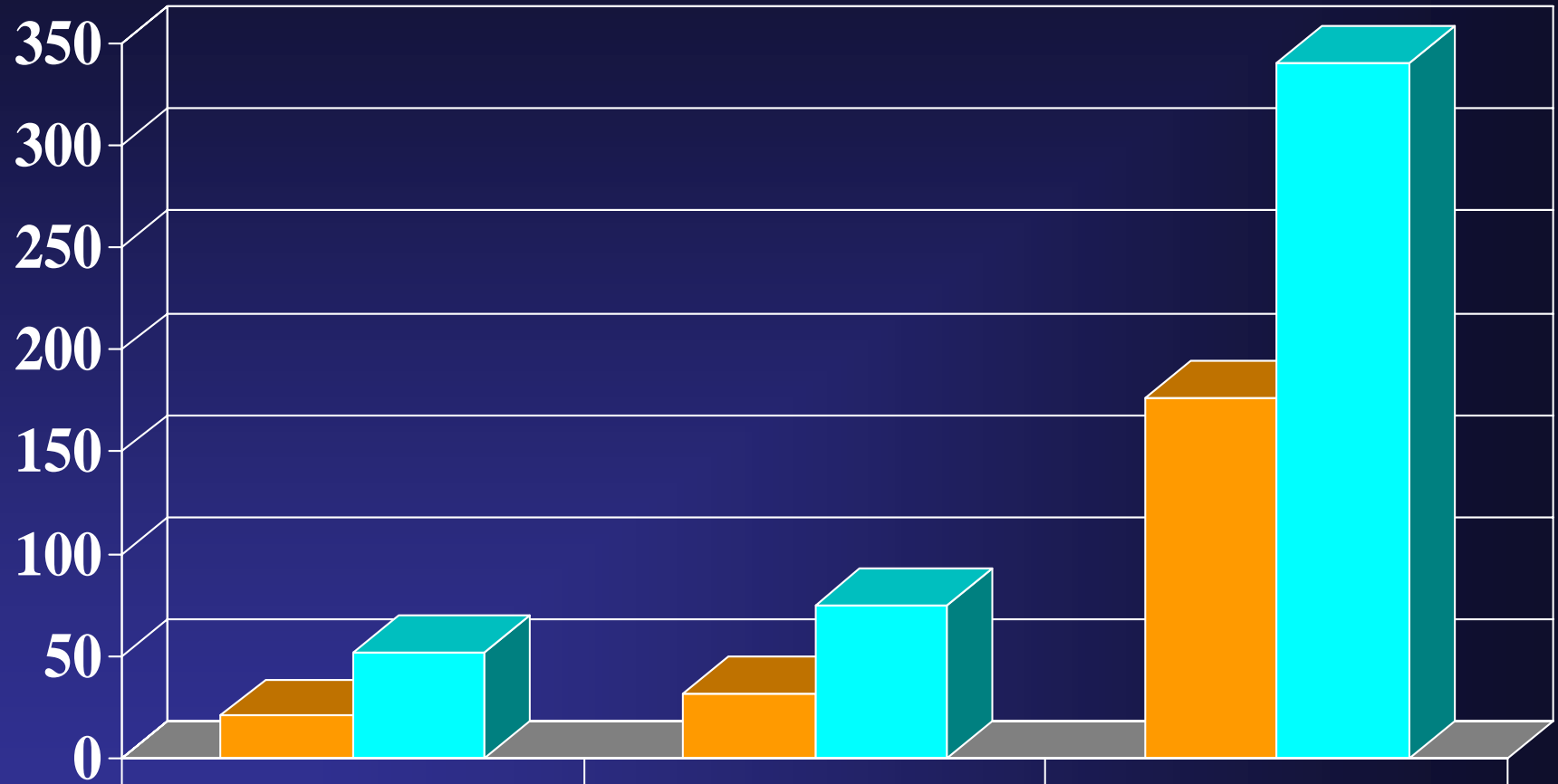
(Class IIb recommendation, level of evidence C)

3. Heart Failure.

CRT-D “in HF patients NYHA Class III-IV, SR, and QRS \geq 120 ms

(Class IIa recommendation, level of evidence B)

DAIs / 1999-2004



SPAIN

EUROPE

EEUU

1999

20,8

32,1

176,2

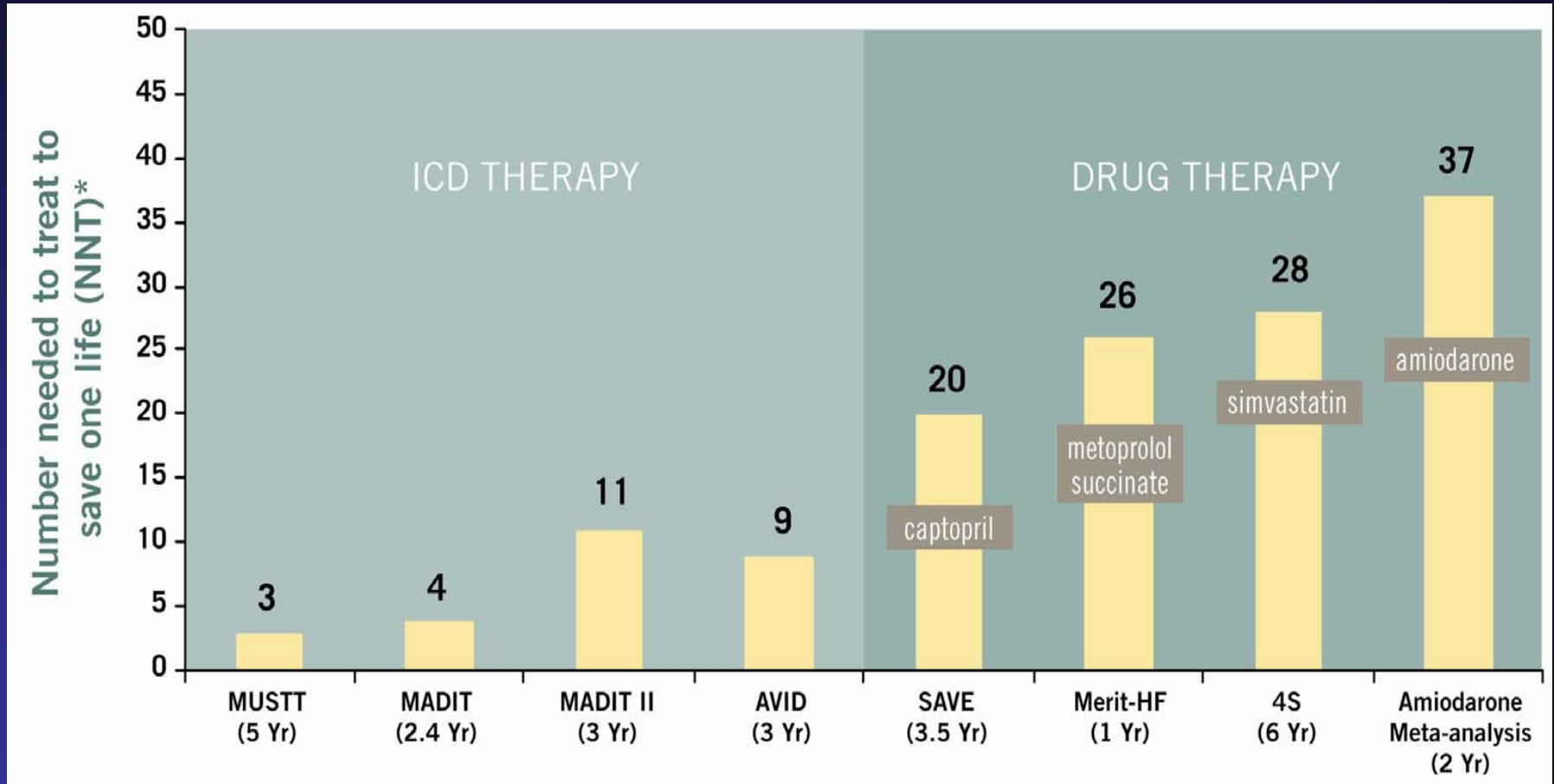
2004

52

75

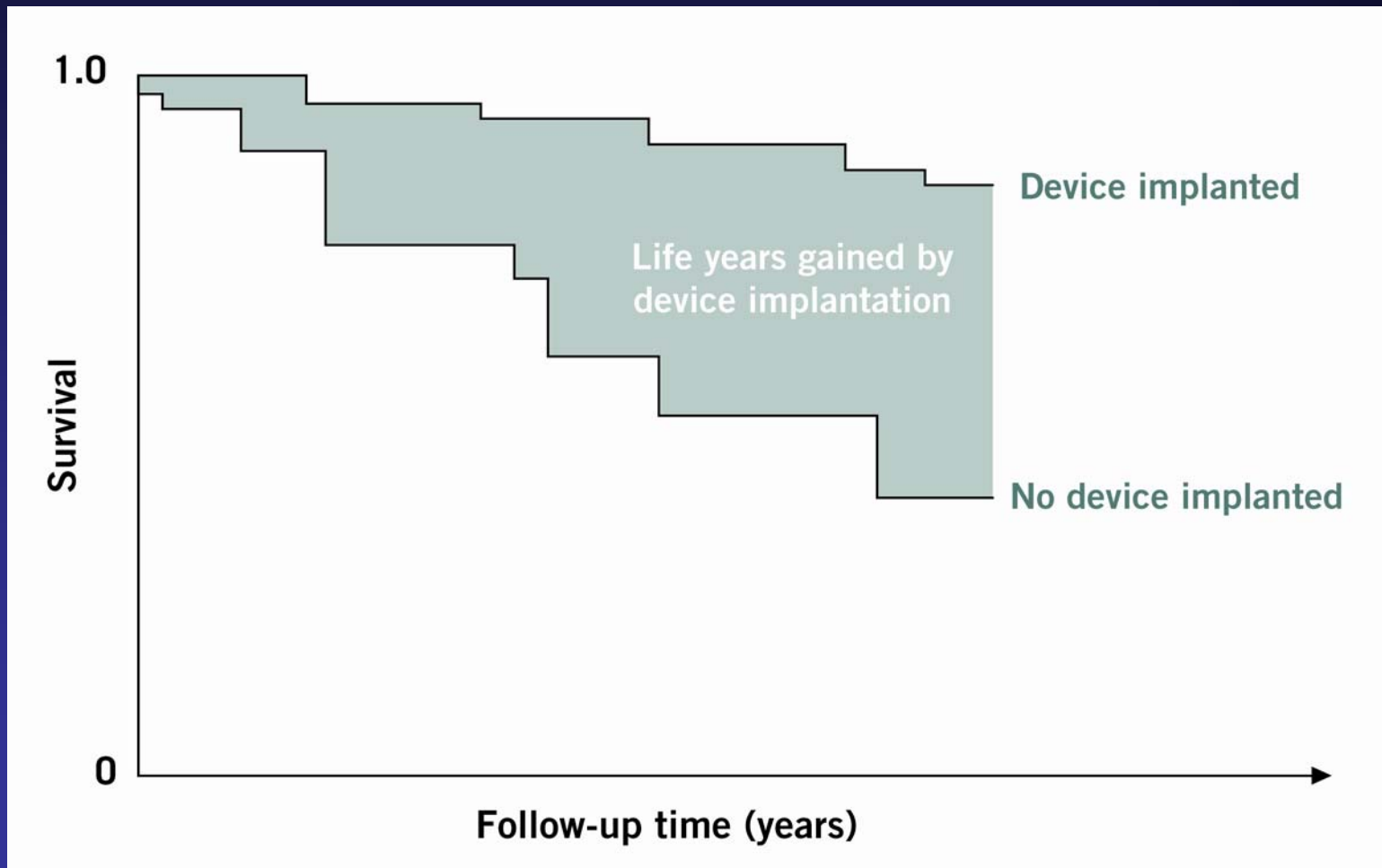
340

ICD Cost-effectiveness



Source: ¹ Guidant estimates ² EURO-MED-STAT 2004,
³ Ministry of Health-Italy, ⁴ Prescription Pricing Authority-NHS UK, ⁵
OECD Health Working Paper 2003

Benefits of AICD improves with time.




Conclusions

- The inclusion criteria have been too simple.
- We still need more data.
- MADIT II.
 - AMI > 18 months.
 - Broad QRS complex.
- Heart Failure.
 - FE < 30%.
 - CRT candidates.



Gr
a

CHAMPIONS



Gracias por su
atención ...