

Is an ICD Necessary in all HF Patients Receiving CRT?

David S. Cannom, M.D.

March 9, 2008

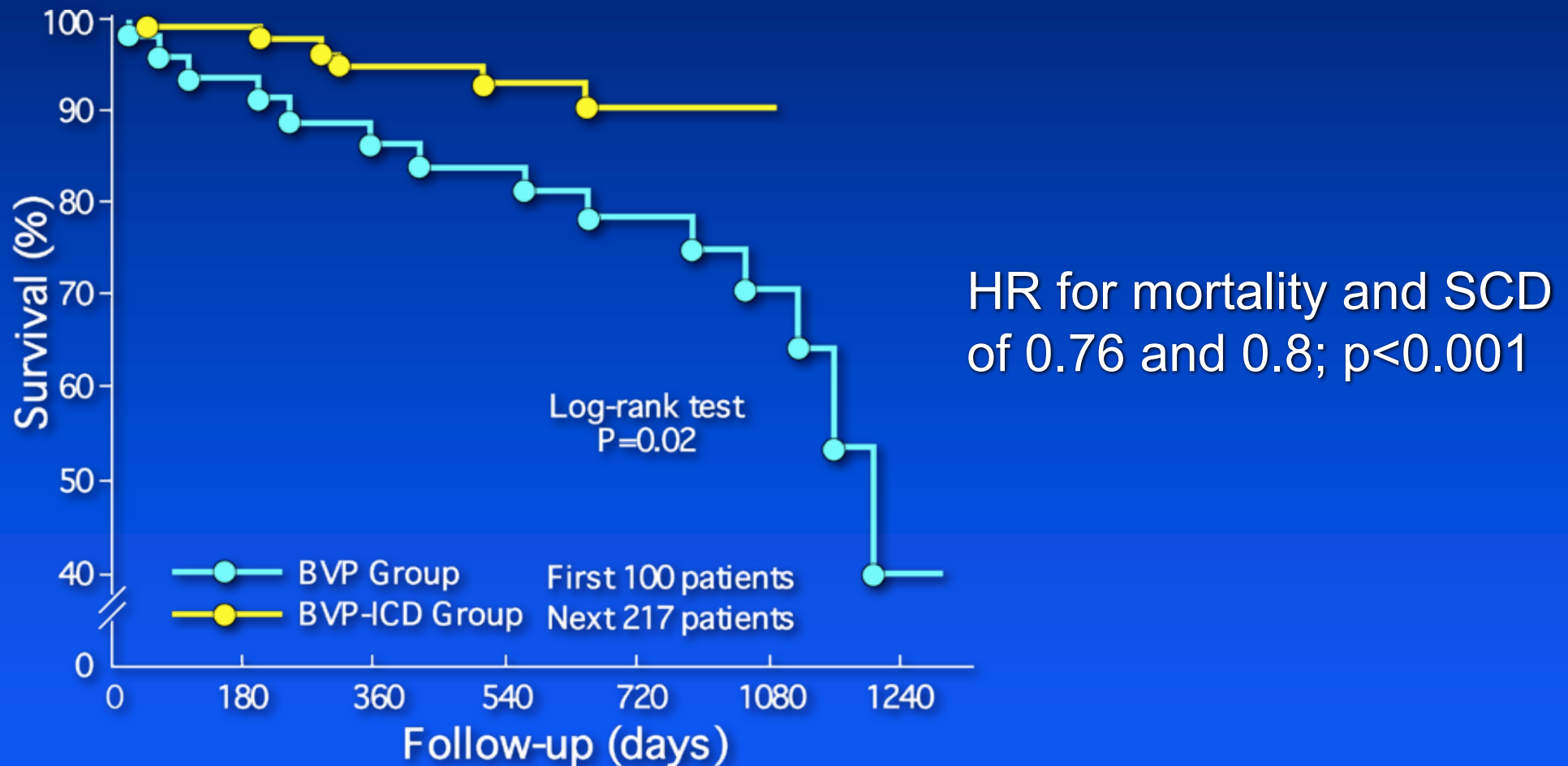
MIROWSKI / MOWER LEGACY of PIVOTAL THERAPIES

	ICD	CRT
Concept	1970	Mid 1970s
Patent	1971	1990
1 st Implant	1981	1991
FDA/CMS Approval	1984	2004
Pivotal Trials	MADIT I & II SCD-HEFT AVID CIDS	COMPANION CARE-HF

Concerns with Adding ICD to CRT

- It won't work to prevent sudden deaths in a heart failure population where the etiology of sudden death is diverse and not all tachyarrhythmic
- The risk of inappropriate shocks is high
- The cost is excessive for the number of lives saved
- If it works it will allow me to decide by my own standards, on an individual basis who gets to die 'mercifully' and who gets to die of pump death

Backup Defibrillation Prolongs Survival in Patients with Indications for CRT by Reducing Sudden Cardiac Death



Conclusions: the patients with CRT-D had far lower overall mortality and sudden deaths

ORIGINAL ARTICLE

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

Michael R. Bristow, M.D., Leslie A. Saxon, M.D., John Boehmer, M.D.,
Steven Krueger, M.D., David A. Kass, M.D., Teresa De Marco, M.D.,
Peter Carson, M.D., Lorenzo DiCarlo, M.D., David DeMets, Ph.D.,
Bill G. White, Ph.D., Dale W. DeVries, B.A., and Arthur M. Feldman, M.D., Ph.D.,
for the Comparison of Medical Therapy, Pacing, and Defibrillation
in Heart Failure (COMPANION) Investigators*

COMPANION: *Endpoints*

- Primary

- Time to death or hospitalization (both all-cause)
 - Definition of hospitalization: all-cause except elective admit for CRT or CRT-D; also includes treatment of decompensated HF with vasoactive drugs for a period of >4 hours, in an urgent care setting

- Secondary

- All-cause mortality, cardiac morbidity, maximal exercise other

- Tertiary

- Submaximal exercise, QoL, other

COMPANION

CARE HF

Inclusion

CL III - IV CHF

EF $\leq$ 35% (mean 21%)

QRS $\geq$ 120 msec
NSR

Ischemic (56%) &
nonischemic (44%)

No. Pts. = 1520

Inclusion

CL III - IV CHF

EF $\leq$ 35% (mean 25%)

QRS $\geq$ 120 msec
NSR

Ischemic (38%) &
nonischemic (62%)

No. Pts. = 813

Randomization

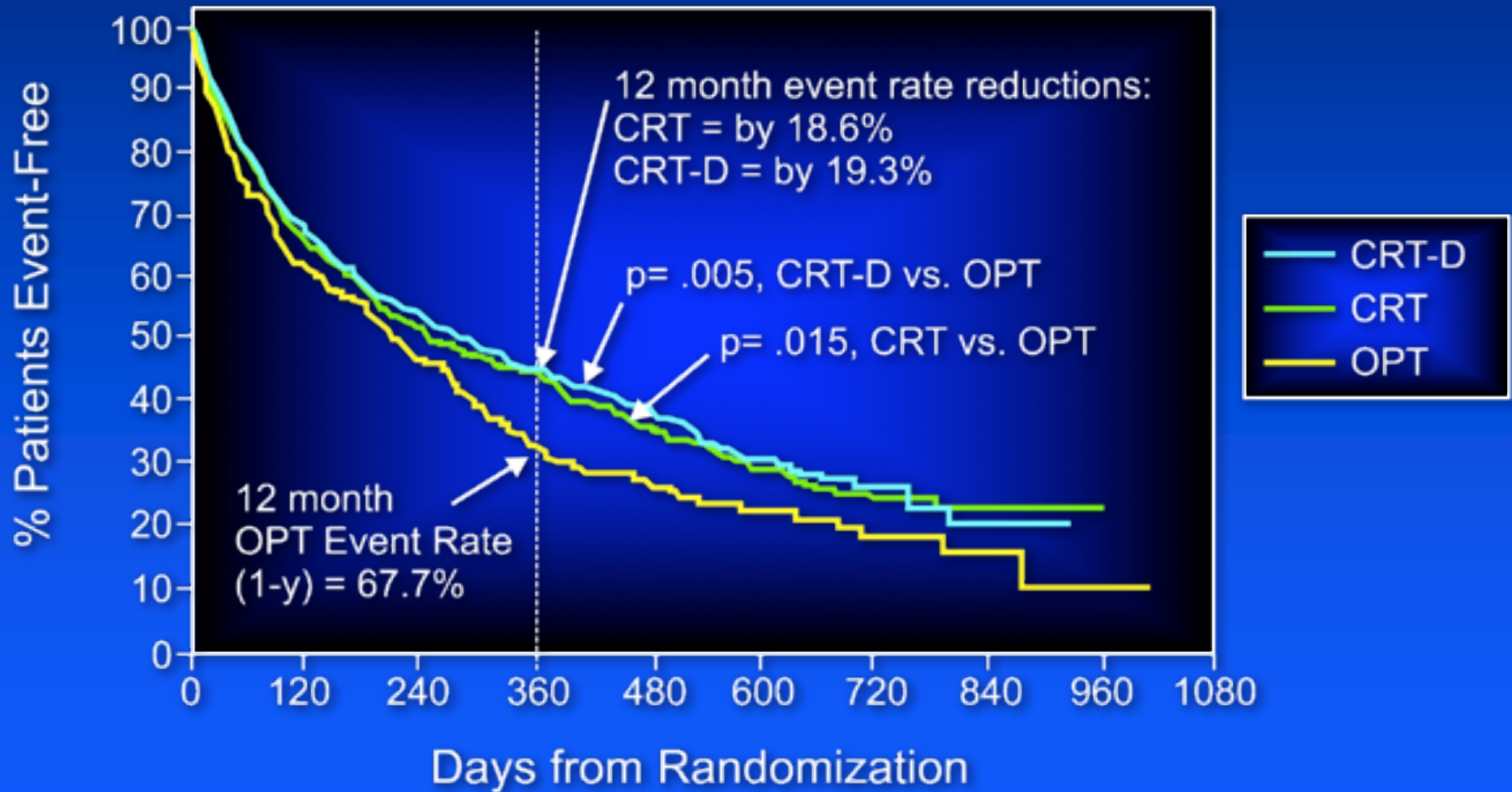
OPT vs CRT vs CRT D

Randomization

OPT vs CRT

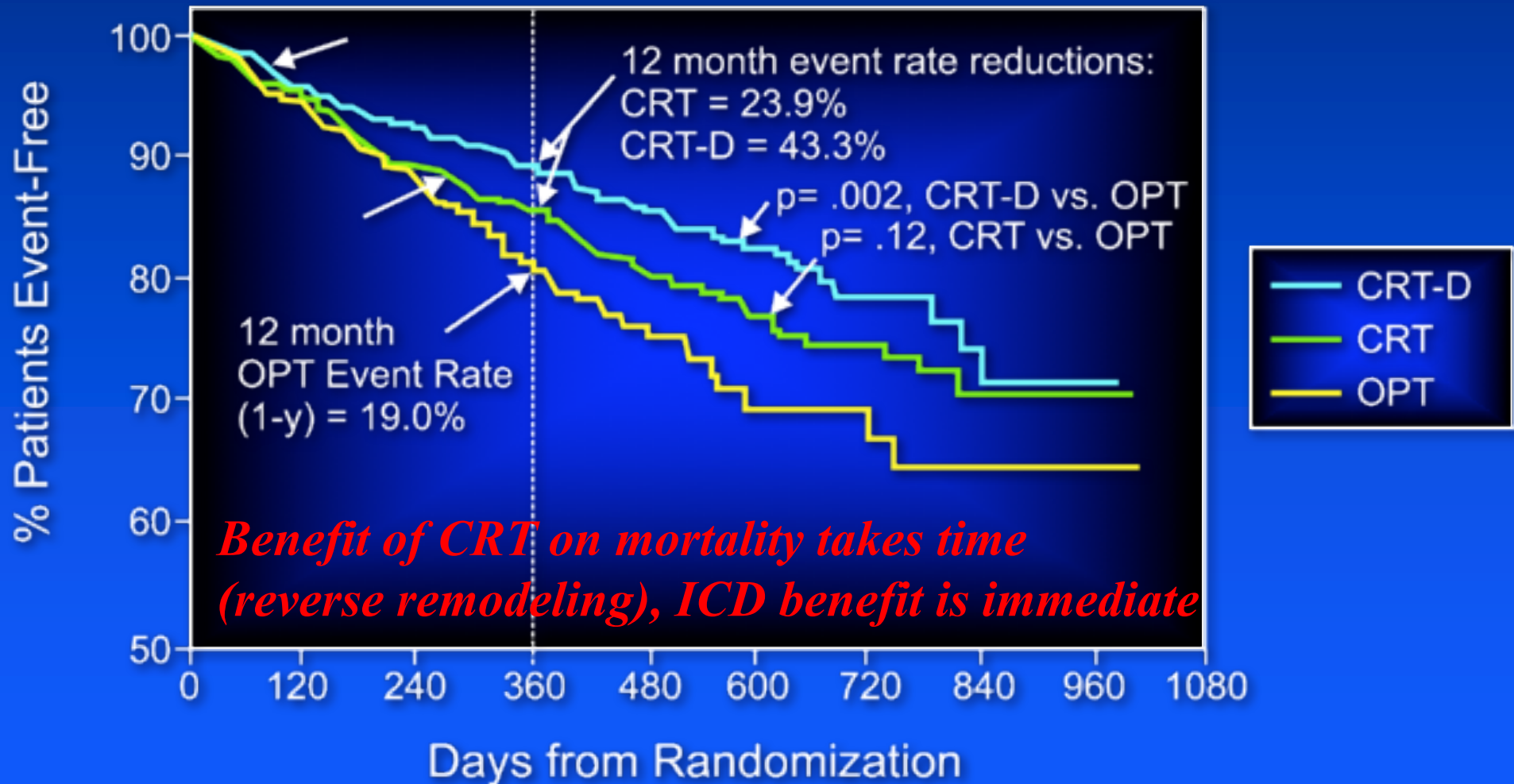
COMPANION: *Primary Endpoint*

Death or Any Hospitalization, IV Rx >4 hrs



COMPANION: Secondary Endpoint of All-Cause Mortality

Any Death



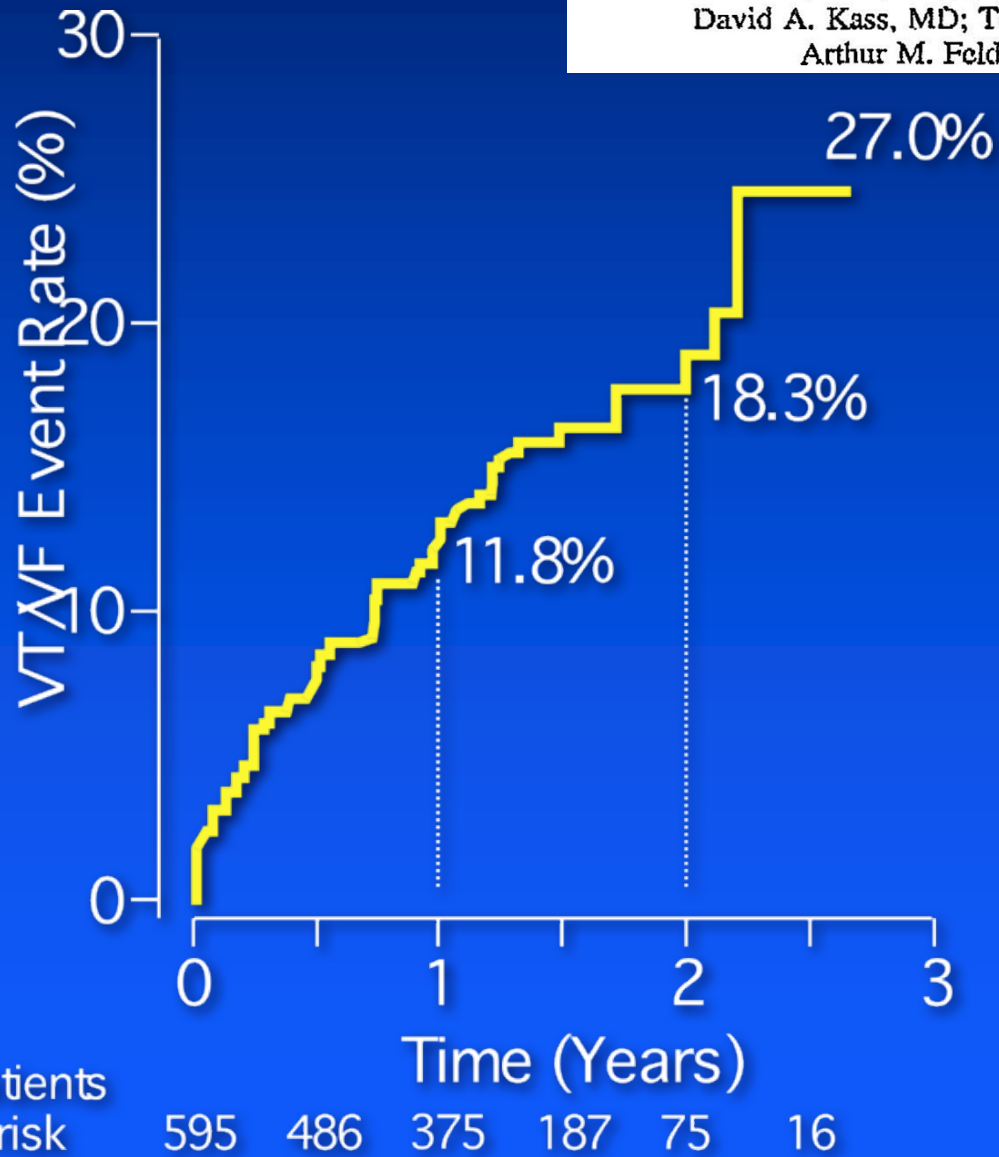
COMPANION Patient with ICD: True Shock



J.W.

Predictors of Sudden Cardiac Death and Appropriate Shock in the Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) Trial

Leslie A. Saxon, MD; Michael R. Bristow, MD; John Boehmer, MD; Steven Krueger, MD; David A. Kass, MD; Teresa De Marco, MD; Peter Carson, MD; Lorenzo DiCarlo, MD; Arthur M. Feldman, MD, PhD; Elizabeth Galle, MS; Fred Ecklund, MS



Risk of appropriate shock in CRT-D recipients.

COMPANION:

Summary of Major Outcomes

- Reduction in the combined endpoints of death + all-cause, CV or HF hospitalizations was due to CRT
- CRT was associated with a trend for reduction in mortality (24% reduction in the 12 month rate, HR 0.76)
- Therapy with an ICD in addition to CRT substantially increased the mortality reduction, attributable to reduction in SCD (HR 0.64)
- Followup only 12 months

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Sudden Death Risk

“The present study demonstrates that cardiac resynchronization therapy combined with an ICD favorably impacts sudden death risk.... the findings of the present study demonstrate a positive therapeutic association with CRT-D but not CRT therapy with regard to sudden death risk reduction.”



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

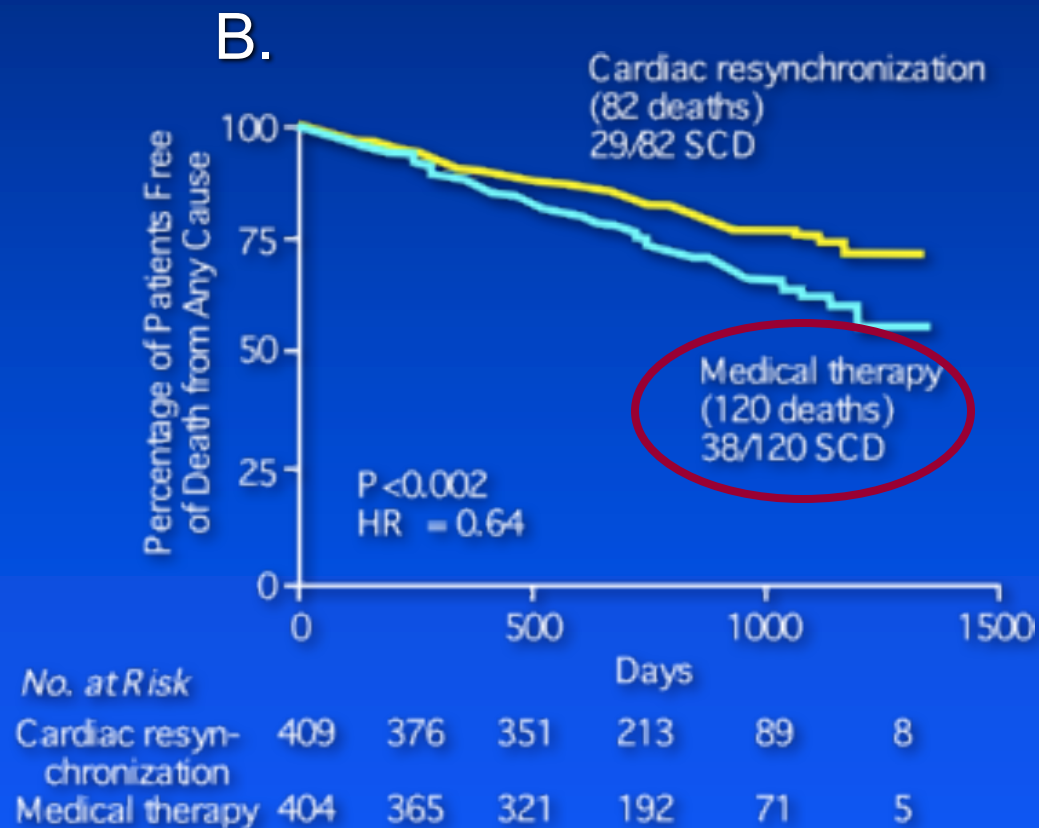
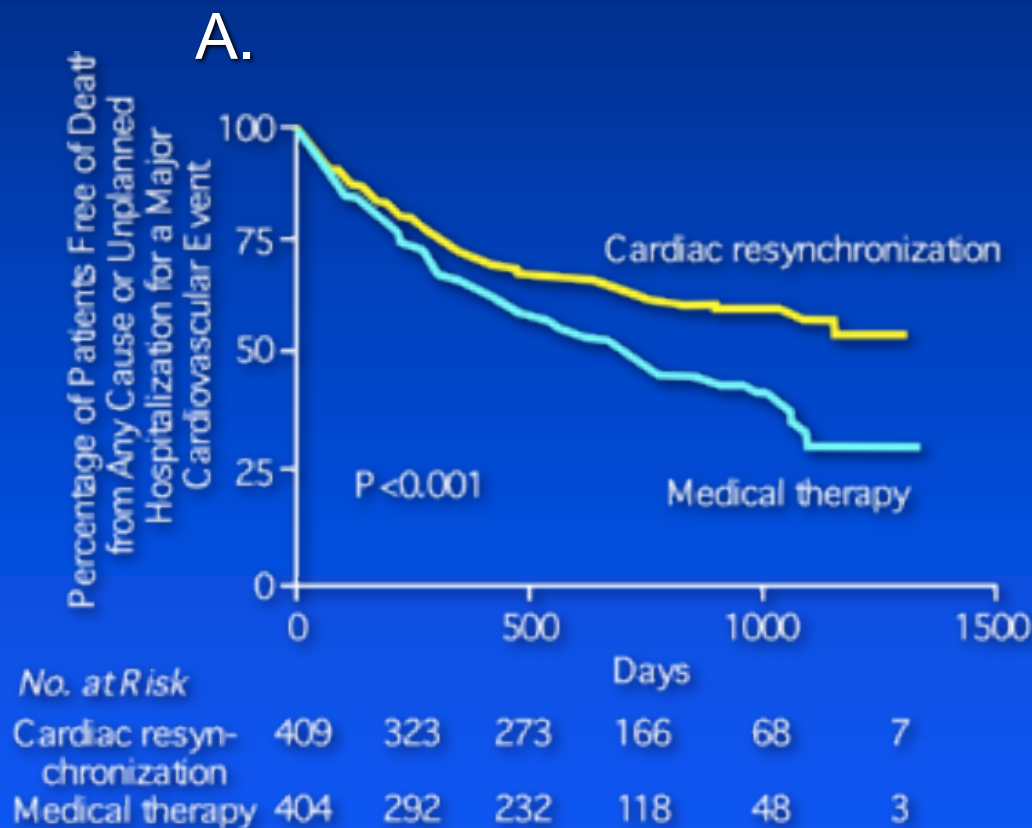
The Effect of Cardiac Resynchronization on Morbidity and Mortality in Heart Failure

John G.F. Cleland, M.D., Jean-Claude Daubert, M.D.,
Erland Erdmann, M.D., Nick Freemantle, Ph.D., Daniel Gras, M.D.,
Lukas Kappenberger, M.D., and Luigi Tavazzi, M.D.,
for the Cardiac Resynchronization — Heart Failure (CARE-HF) Study Investigators*

CARE HF

Primary endpoint was a composite of death from any cause or an unplanned hospitalization for a major cardiovascular event. Secondary endpoint was death from any cause classified according to endpoint.

Kaplan-Meier Estimates of the Time to the Primary End Point and the Principal Secondary Outcome



While only 7% of patients in the CRT arm died suddenly, sudden death accounted for 35% of all deaths in CARE-HF, 29 people died suddenly in the CRT group

COMPANION Patient with CRT only



J.G.

Conclusions of CARE-HF

- CRT vs OMT alone reduces total mortality by 30% vs 20% (HR 0.64)
- Effect continued over 18 months
- BNP level decreased by 1,100 pg/ml at 3 mos
- However a significant number of SCDs occurred in the CRT arm some of which can be prevented

Issues arising from CARE-HF publication

“Retarding the progression of cardiac dysfunction to prevent malignant arrhythmias may be a better strategy than treating malignant arrhythmias once they occur, because defibrillation is stressful to the patient and associated with an adverse prognosis owing either to the cause of the arrhythmia or to the effects of the shock.”

- In randomized ICD studies, patients' Quality of Life is better in the ICD arm than in the control arm!
- In COMPANION, Q-o-L same for CRT and CRT-D
- If patients had an “adverse prognosis with ICDs”, then the ICD studies would have turned out negative!

The box that's bad is not the ICD



Death, the ultimate in adverse prognosis-
In a box forever



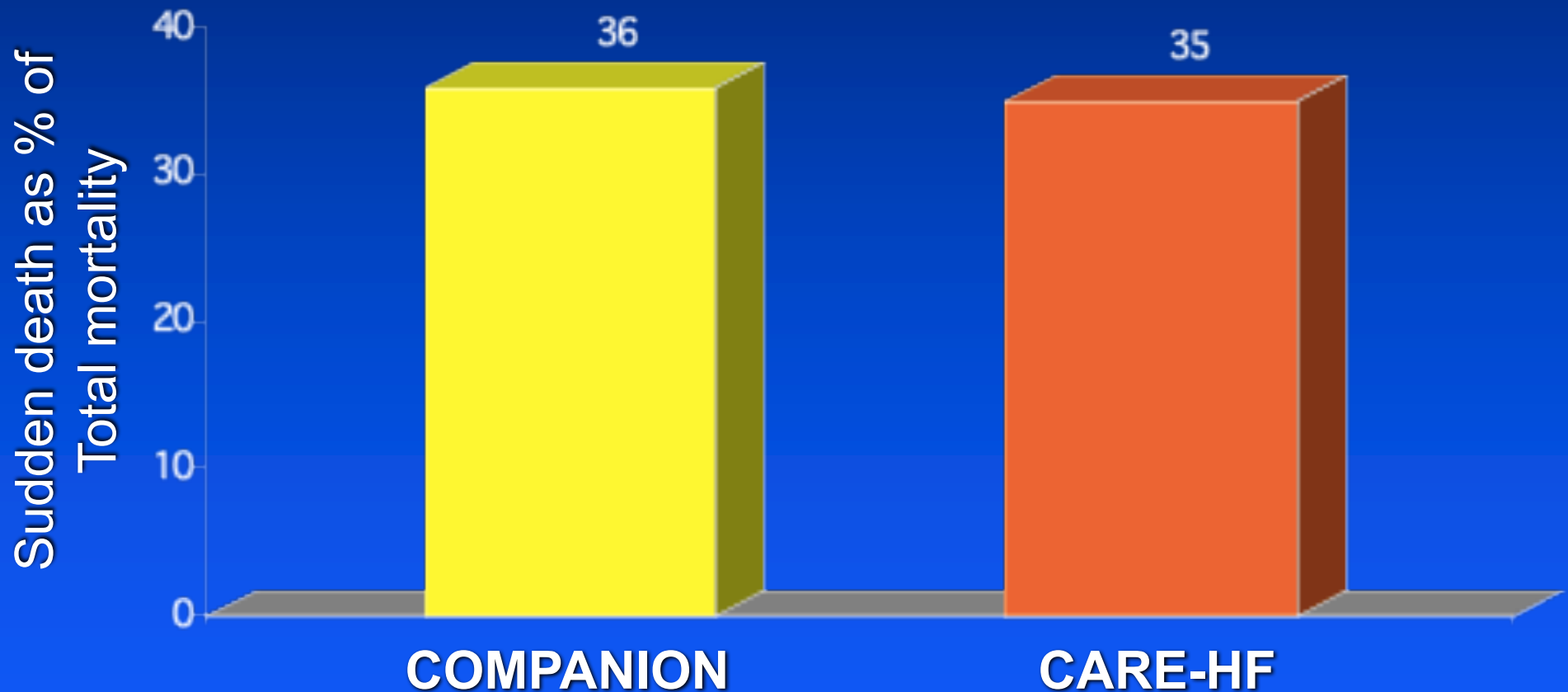
Stress-Something you can cope with
and still be alive

COMPANION somewhat higher risk population than CARE-HF

	CARE-HF (n=813)	COMPANION (n=1520)
Age	66.5	67.5
Male (%)	73.5	68
NYHA IV (%)	6.5	15.5
CAD (%)	38	56.5
LVEF (%)	25	21
QRS (msec)	160	159

One-year control group mortality:
COMPANION 19%, CARE-HG 12.6%

Sudden Cardiac Death Despite CRT



Sudden deaths account for ~35% of mortality in CRT-P

HF Predicts ICD Discharge and ICD Discharge Predicts HF Worsening

HR for shock HF Class III- 2.4

HR Death 3.4 with ICD Shock
Risk of HF Hosp 1 year 31%

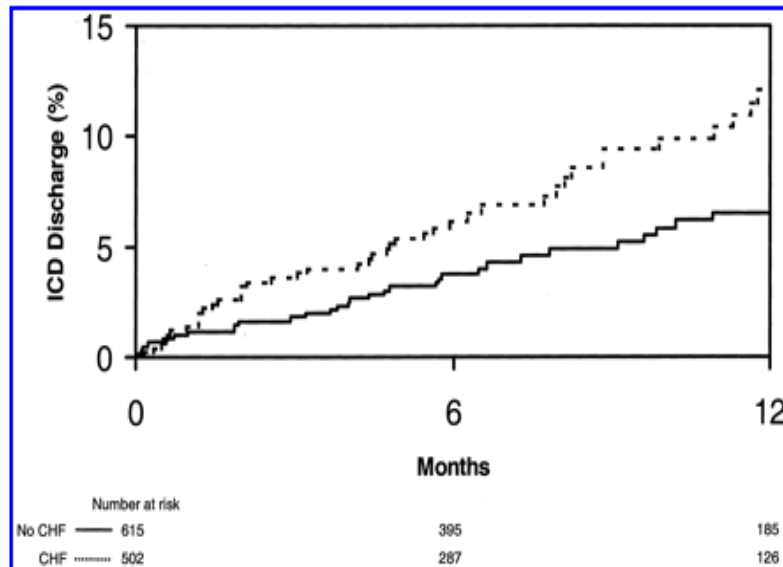


Figure 1. Time to ICD discharge by presence of CHF (P=0.01, log-rank test).

Wang W et al. Circulation. 2004 Mar 23;109(11):1386-91. Epub 2004 Mar 1.

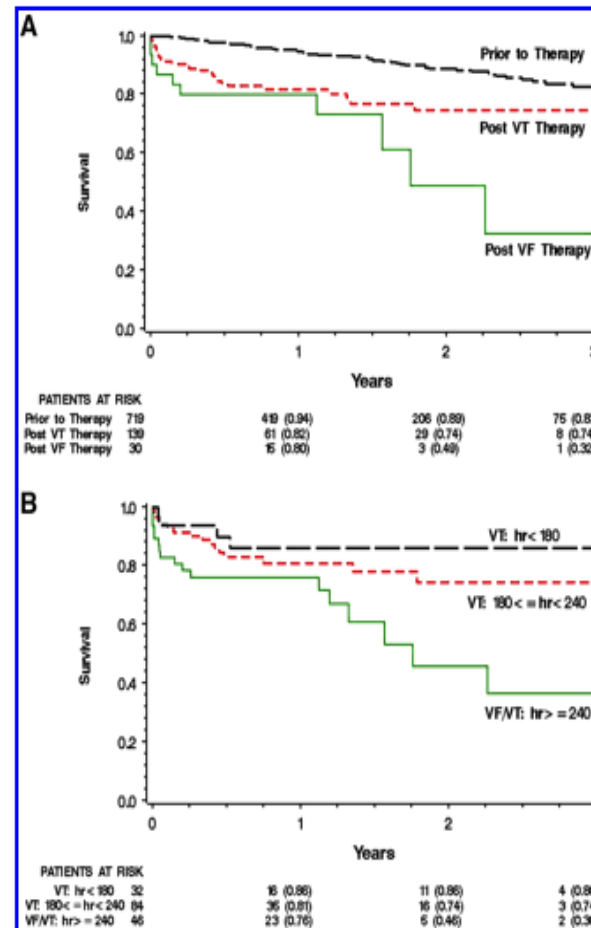


Figure 4. A, Kaplan-Meier estimates of probability of survival before and after first appropriate ICD therapy for VT or VF. When patients developed their first device therapy for VT or VF, they were censored from before-therapy group and moved to their respective posttherapy group. In before-therapy group, 1 patient had no interrogation follow-up. Difference in survival among 3 groups was significant (P<0.001), with difference in survival between post-VT and post-VF not significant (P=0.08). B, Kaplan-Meier estimates of probability of survival by rate of VT or VF terminated by first appropriate ICD therapy. Difference in survival among 3 heart rate (hr) groups in beats per minute was significant (P=0.01).

Moss AJ et al. Circulation. 2004 Dec 21;110(25):3760-5.

5.8% OPT
7.8% CRT
2.9% CRT-D

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Sudden Cardiac Death (n=83/1519)

Variable	Hazard Ratio	P Value	95% CI
CRT-D	0.47	0.02	0.24 to 0.91
CRT	1.21	0.48	0.71 to 2.09
LVEF>20%	0.55	0.01	0.35 to 0.87
QRS>160 ms	0.63	0.05	0.40 to 0.997
Female gender	0.47	<0.01	0.27 to 0.82
NYHA class IV	2.62	<0.01	1.61 to 4.20
Renal dysfunction	1.69	0.03	1.06 to 2.69

A futuristic perspective on clinical studies of cardiac resynchronization therapy for heart failure patients

Anthony S.L. Tang^a and Kenneth A. Ellenbogen^b

“COMPANION and CARE-HF provided good information that CRT-ICD and CRT pacing are superior to optimal medical therapy. By 2005, however, the standard-of-care in heart failure patients with LV dysfunction dictates that most of these patients are eligible for ICD.”

Changes in CRT-D and CRT-P use (data from GDT)

EUROPE

U.S.

CRT-D

CRT-P

CRT-D

CRT-P

2003

45%

55%

2004

55%

45%

2005

62%

38%

90%

10%

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"Your insurance only covers the basic model. You'll have to pay extra if you want a pacemaker with a built-in MP3 player and radar detector."

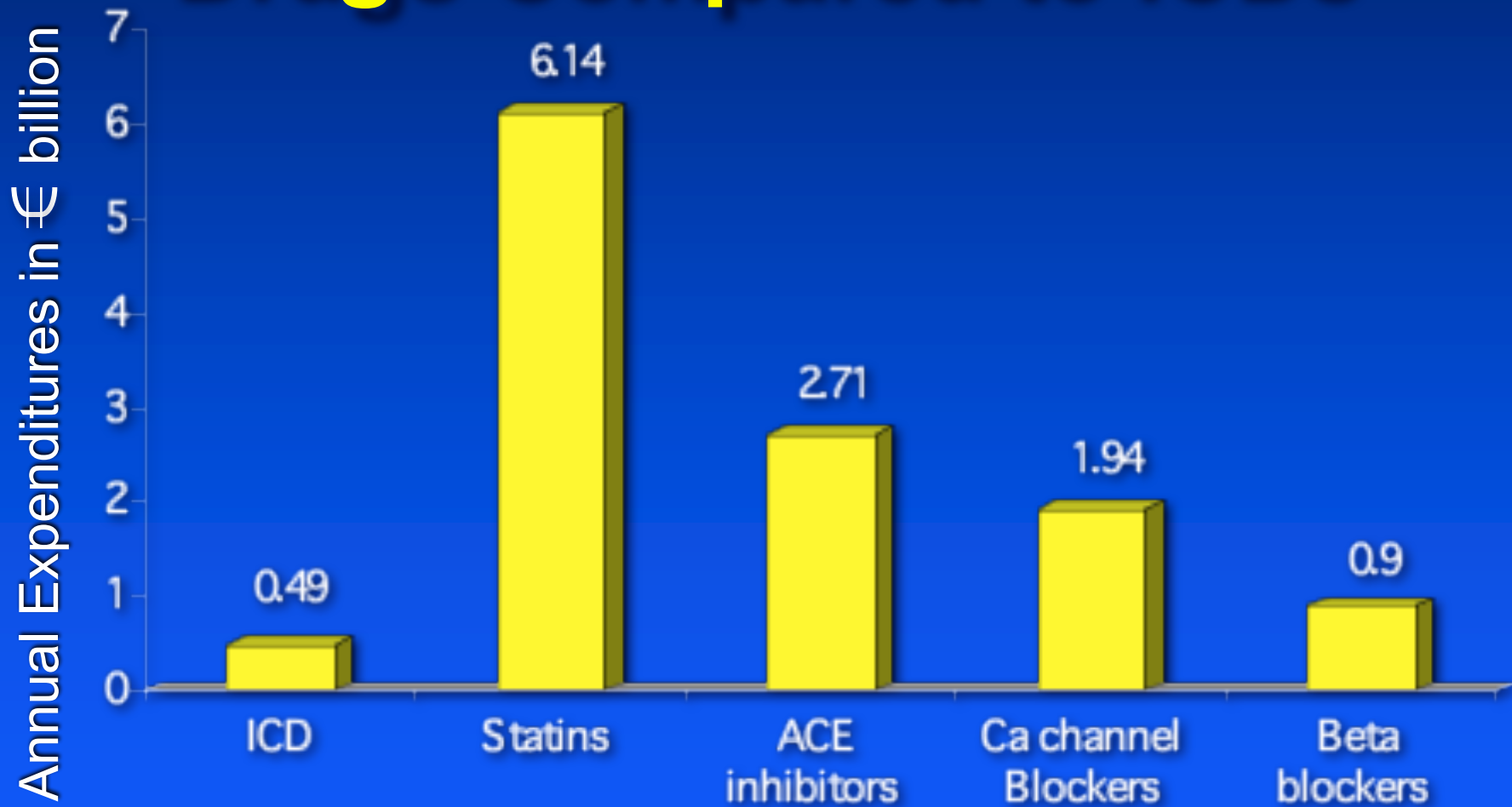
Who might receive a CRT only device?

- Pt with CI III/IV HF but significant comorbidity
- Pt understands the SCD risk
- Occasional unforgiving reimbursement environment (see LA County)

COMPANION & CARE-HF are concordant

- CRT reduces mortality and morbidity
- CRT (alone) reduces mortality
- Significant (35%) sudden death mortality remains despite CRT (and *at-risk* patients are not identifiable), so back-up defibrillation is usually needed

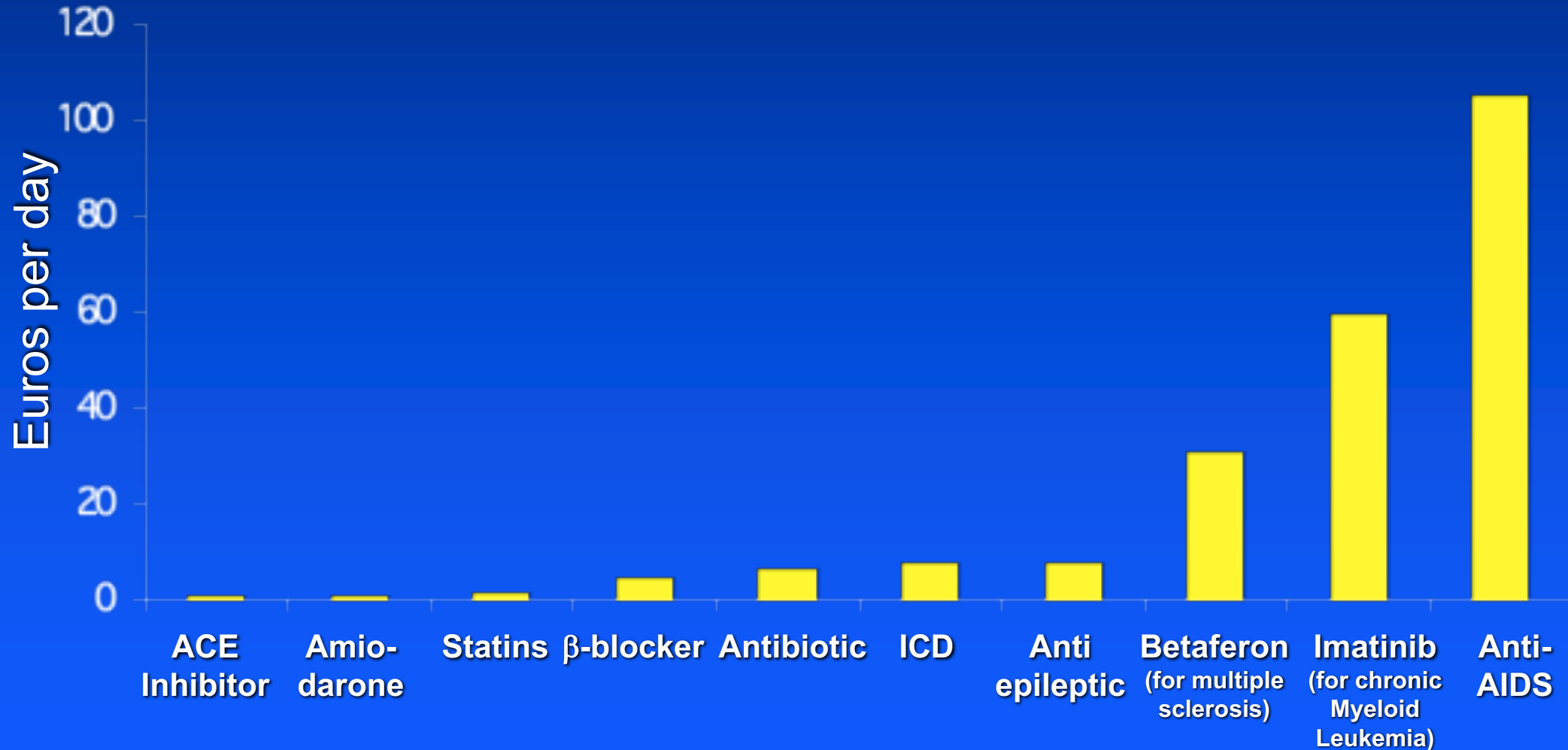
Costs* (annual) of Drugs Compared to ICDs



*France, Germany, Italy, UK

In press, A.J. Camm and S. Nisam, European Heart Journal

Cost/per/day of Drugs Compared to ICDs



In press, A.J. Camm and S. Nisam, European Heart Journal

Costs of ICDs Compared to Other Healthcare Costs* in W. Europe



In press, A.J. Camm and S. Nisam, European Heart Journal

Cost of ICDs Compared to Overall Healthcare Costs in W. Europe

2004 (est.) Europe
in-patient Expenditure

€ 286.7 bn



ICD expenditure =
0.2% of in-patient
expenditure

Current level of
ICD implants

€ 287.6 bn



ICD expenditure =
0.5% of in-patient
expenditure

3 x Current level
of ICD implants



Should we afford implantable cardioverter defibrillator therapy?

A. John Camm

“Many considerations could make it easy to restrict the use of ICDs. It is not the role of the medical profession, however, to collude with attempts to impede the proper use of life-saving therapy. That everything must be done to preserve life is a code to which physicians have adhered for centuries and must not now relinquish.”