2007년 순환기관련학회 춘계통합학술대회

Device Therapies in Arrhythmias

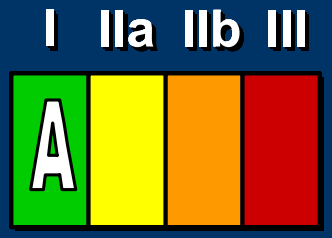
CRT-D vs CRT-P

# CRT-P is good enough

BEXCO, BUSAN

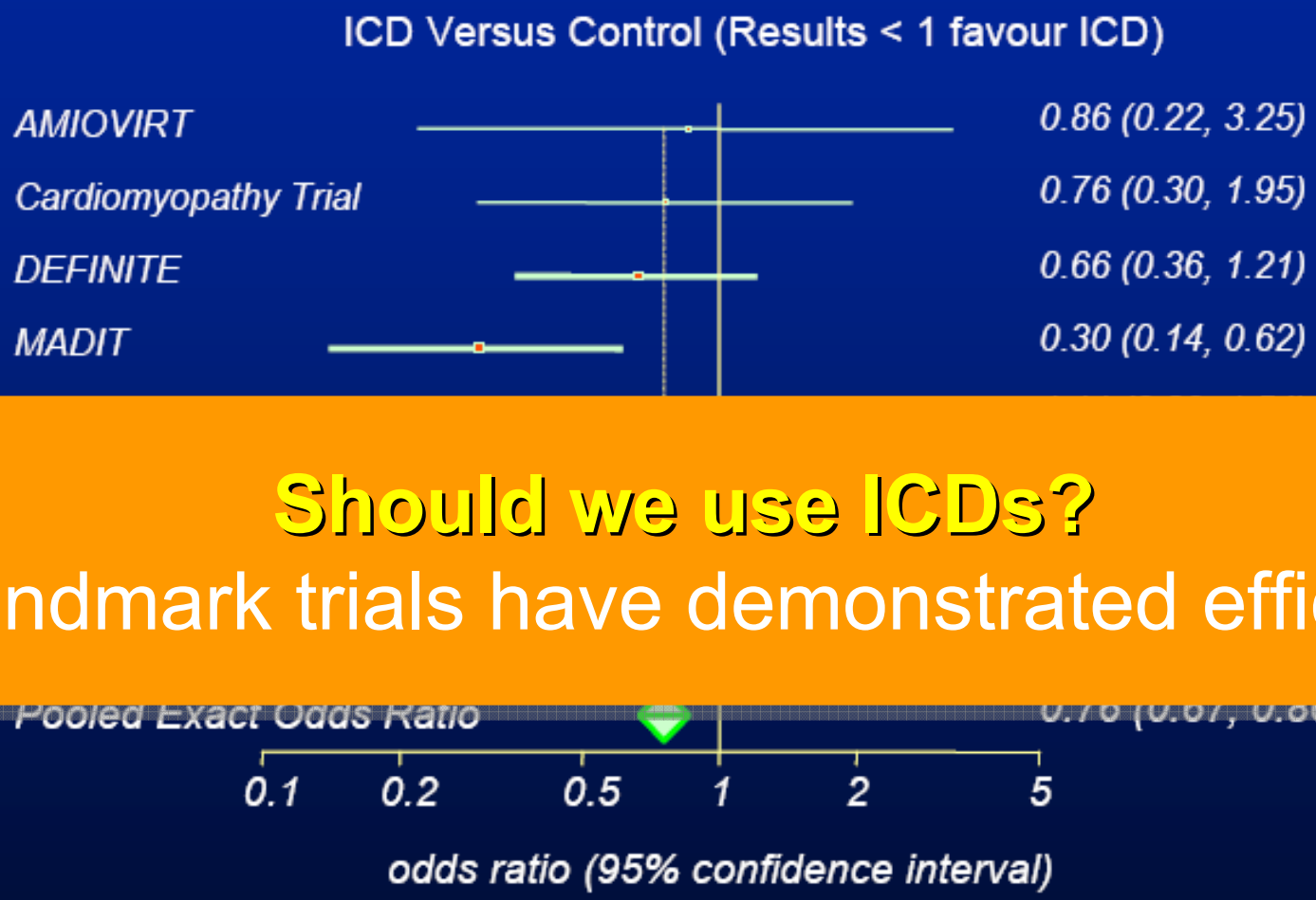
# Stage C Therapy (Reduced LVEF with Symptoms)

## Cardiac Resynchronization




Patients with LVEF less than or equal to 35%, sinus rhythm, and NYHA functional class III or ambulatory class IV symptoms despite recommended, optimal medical therapy and who have cardiac dyssynchrony, which is currently defined as a QRS duration greater than 120 ms, should receive cardiac resynchronization therapy unless contraindicated.

# Primary Prevention Studies with ICDs



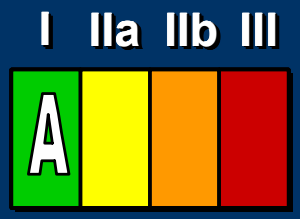

**Should we use ICDs?**

Landmark trials have demonstrated efficacy

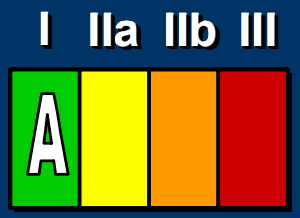
*Cleland et al Eur J Heart Fail 2004*

# Stage C Therapy (Reduced LVEF with Symptoms)

## Implantable Cardioverter-Defibrillators (ICDs)



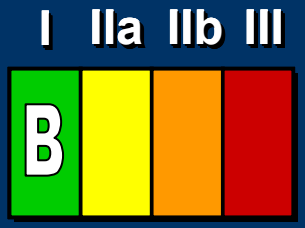

An ICD is recommended as **secondary prevention** to prolong survival in patients with current or prior symptoms of HF and reduced LVEF who have a history of cardiac arrest, ventricular fibrillation, or hemodynamically destabilizing ventricular tachycardia.



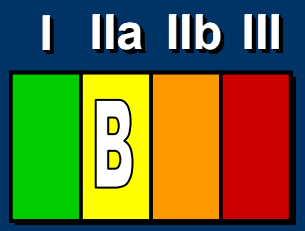

ICD therapy is recommended for **primary prevention** to reduce total mortality by a reduction in sudden cardiac death in patients with **ischemic heart disease** who are at least 40 days post-MI, have an LVEF less than or equal to 30%, with NYHA functional class II or III symptoms while undergoing chronic optimal medical therapy, and have reasonable expectation of survival with a good functional status for more than 1 year.

# Stage C Therapy (Reduced LVEF with Symptoms)

## Implantable Cardioverter-Defibrillators (ICDs)




ICD therapy is recommended for primary prevention to reduce total mortality by a reduction in sudden cardiac death in patients with nonischemic cardiomyopathy who have an LVEF less than or equal to 30%, with NYHA functional class II or III symptoms while undergoing chronic optimal medical therapy, and who have reasonable expectation of survival with a good functional status for more than 1 year.

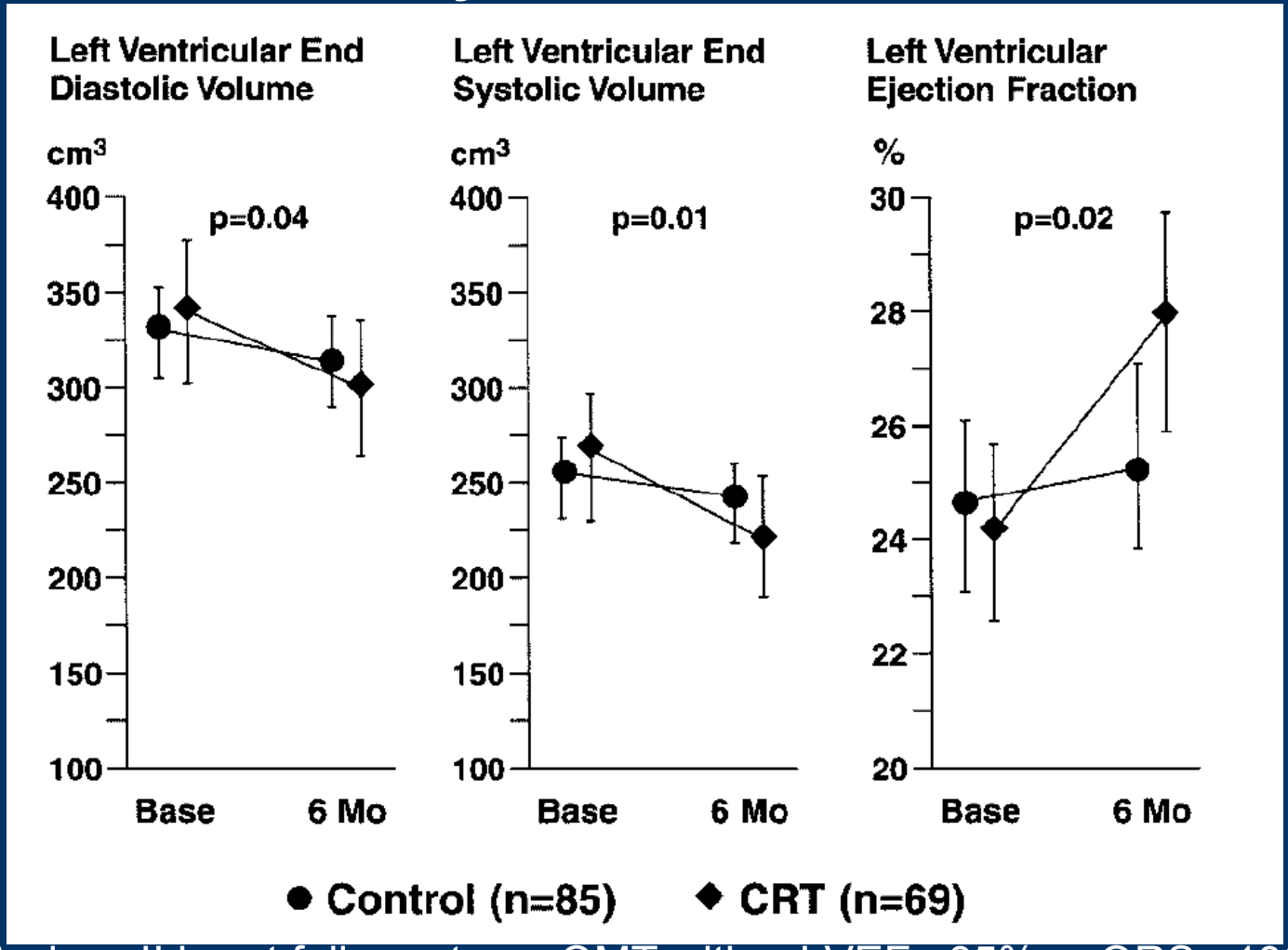



Placement of an ICD is reasonable in patients with LVEF of 30% to 35% of any origin with NYHA functional class II or III symptoms who are taking chronic optimal medical therapy and who have reasonable expectation of survival with good functional status of more than 1 year.

# Should Every Resynchronization Candidate Receive a Defibrillator?

# Effects of CRT on Disease Progression in LVSD Patients

**MIRACLE ICD II study. *Circulation*. 2004;110:2864-2868**




NYHA class II heart failure pts on OMT with a LVEF≤ 35%, a QRS ≥130 ms, and a class I indication for an ICD

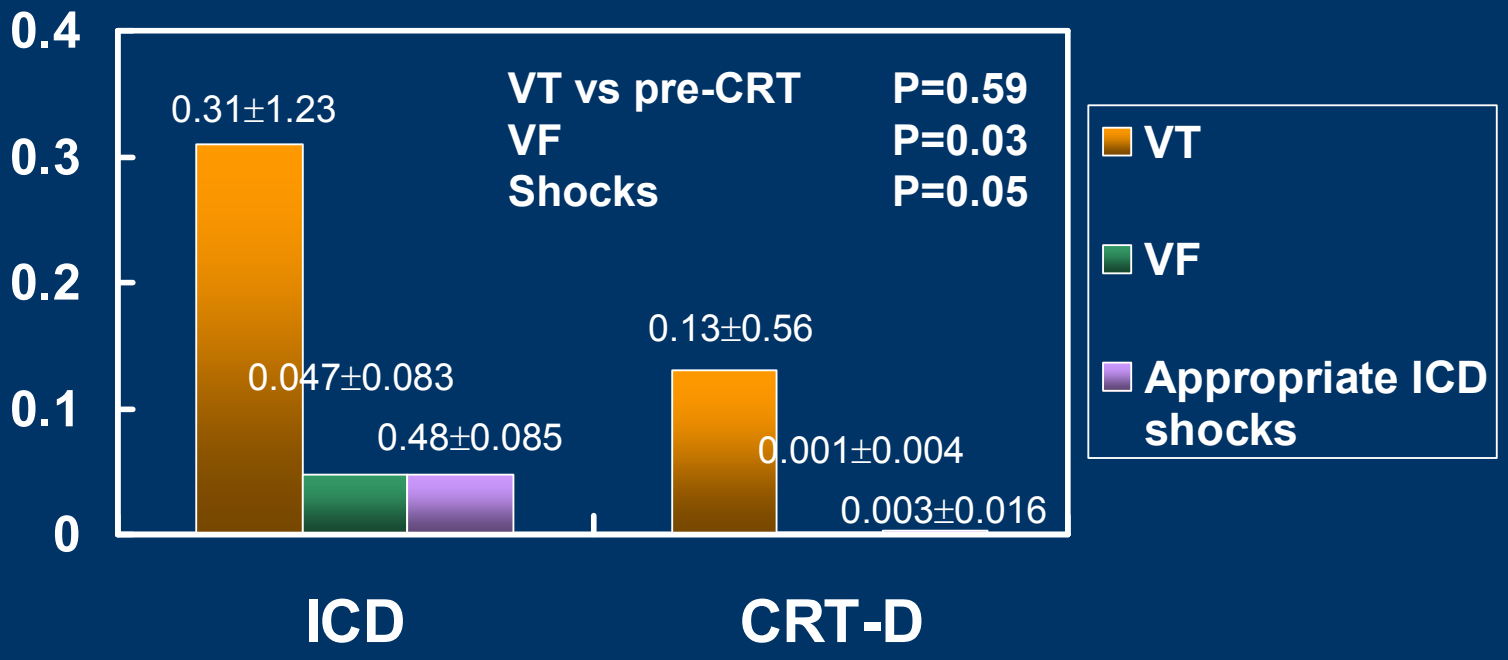
# Consistent Evidence of Reverse Remodelling by CRT in NYHA III-IV

- *PATH-CHF I : C Stellbrink, JACC 2001*
- MUSTIC : *C Linde, JACC 2002 (1-year FU)*
  *A Duncan, Eur Heart J 2003*
- *VIGOR-CHF : L Saxon, Circulation 2002*
- MIRACLE : *W Abraham, N Engl J Med 2002*
  *M St John Sutton, Circulation 2003*
- *CONTAK-CD : S Higgins, JACC (2004)*

**Reduces LVESD/V 8-15%**
**Increases LVEF 4-6%**

# Impact of Upgrade to CRT on VA frequency in patients with ICD

**CRT ameliorate ventricular tachyarrhythmia susceptibility in HF patients.**




J Am Coll Cardiol. 2005 Dec 20;46(12):2258-63

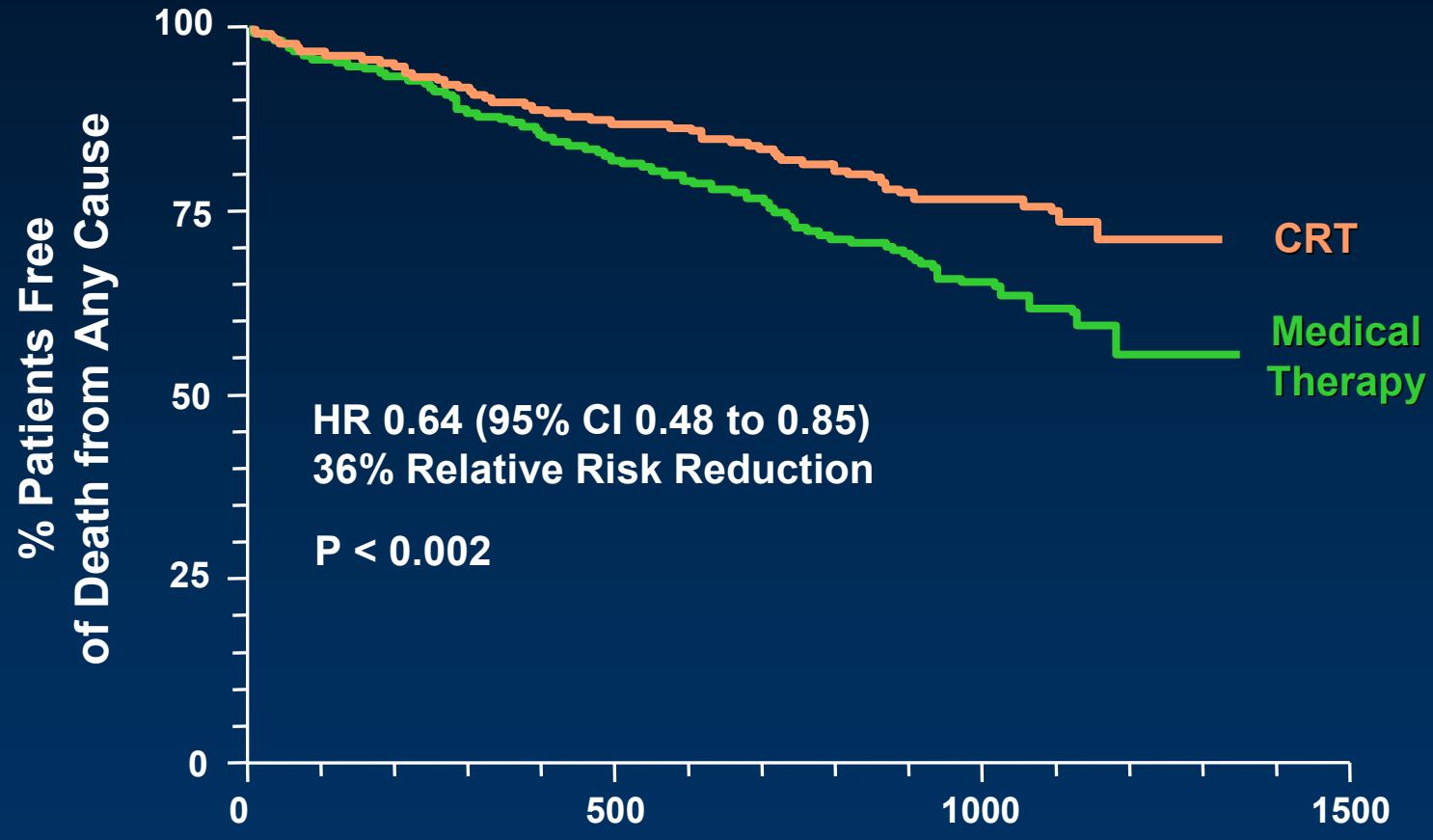
# Effect of CRT on the incidence of VA in patients with an ICD

- Sixty-five patients(58 $\pm$ 13 years) with an ICD
- 31 Biventricular and 34 dual-chamber ICDs
- 36 ischemic and 29 dilated cardiomyopathy
- Thirty-two (49%) patients received $\geq$ 1 appropriate ICD therapy during follow-up of 11 $\pm$ 8 months.
- Thirty-five percent and 62% of patients with biventricular (n = 11) and dual-chamber ICDs (n = 21), respectively, received appropriate ICD therapy during the follow-up period (odds ratio = 0.340, P = .048).
- Biventricular pacing was associated with a decreased incidence of sustained ventricular arrhythmias requiring ICD therapy

Heart Rhythm. 2005 Oct;2(10):1094-8

# CARE-HF

## *Death from Any Cause Results*

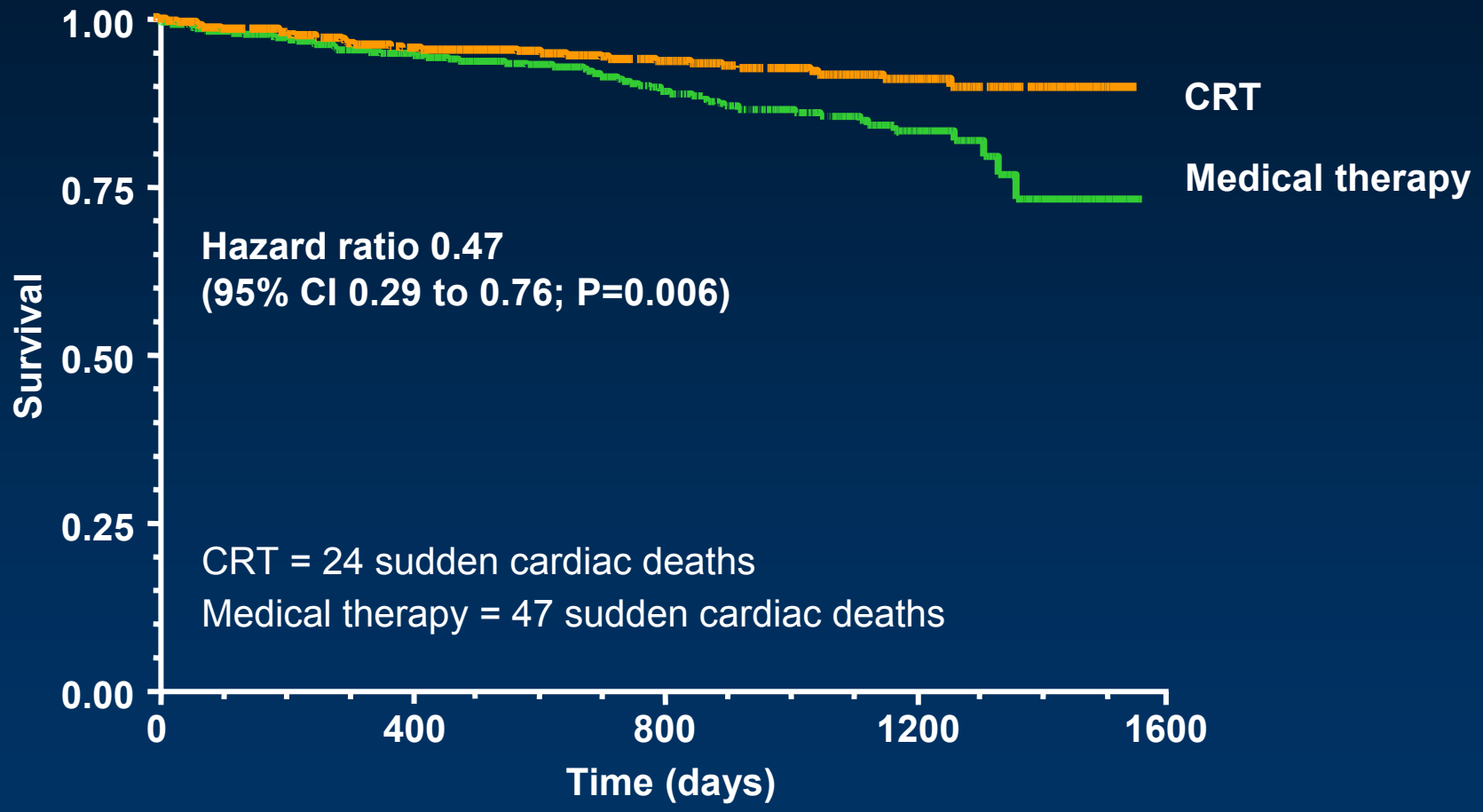



| No. at Risk | | | | | | |
|---|---|---|---|---|---|---|
| CRT | 409 | 376 | 351 | 213 | 89 | 8 |
| Medical Therapy | 404 | 365 | 321 | 192 | 71 | 5 |

Cleland JGF. *N Engl J Med.* 2005;352:1539-1549.

# CARE-HF Causes of Death Sub-Study

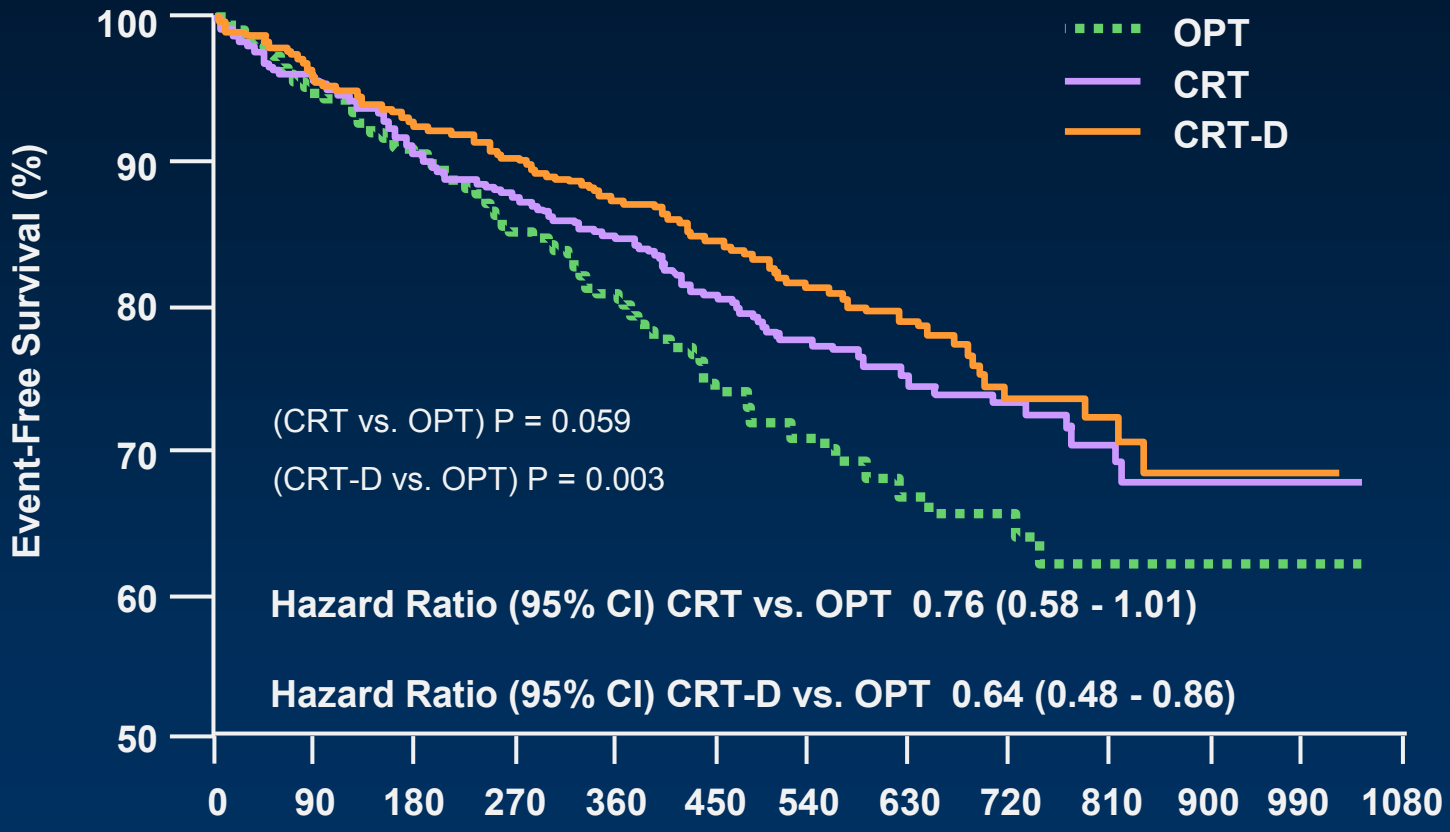
## *Time to sudden cardiac death*




Uretsky BF. Causes of Death in the CARE-HF Trial. Presented at Heart Rhythm Society 2006; May 19, 2006;
Boston, MA, USA

# COMPANION

## *All-Cause Death Results*




| No. at Risk | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| OPT | 308 | 284 | 255 | 217 | 186 | 141 | 94 | 57 | 45 | 25 | 4 | 2 |
| CRT | 617 | 579 | 520 | 488 | 439 | 355 | 251 | 164 | 104 | 60 | 25 | 5 |
| CRT-D | 595 | 555 | 517 | 470 | 420 | 331 | 219 | 148 | 95 | 47 | 21 | 1 |

Bristow M. *N Engl J Med*. 2004;350:2140-2150.

# COMPANION: Conclusion

When added to optimal pharmacological therapy in patients with moderate-severe LV dysfunction, NYHA Class III or IV symptoms and QRS lengthening:

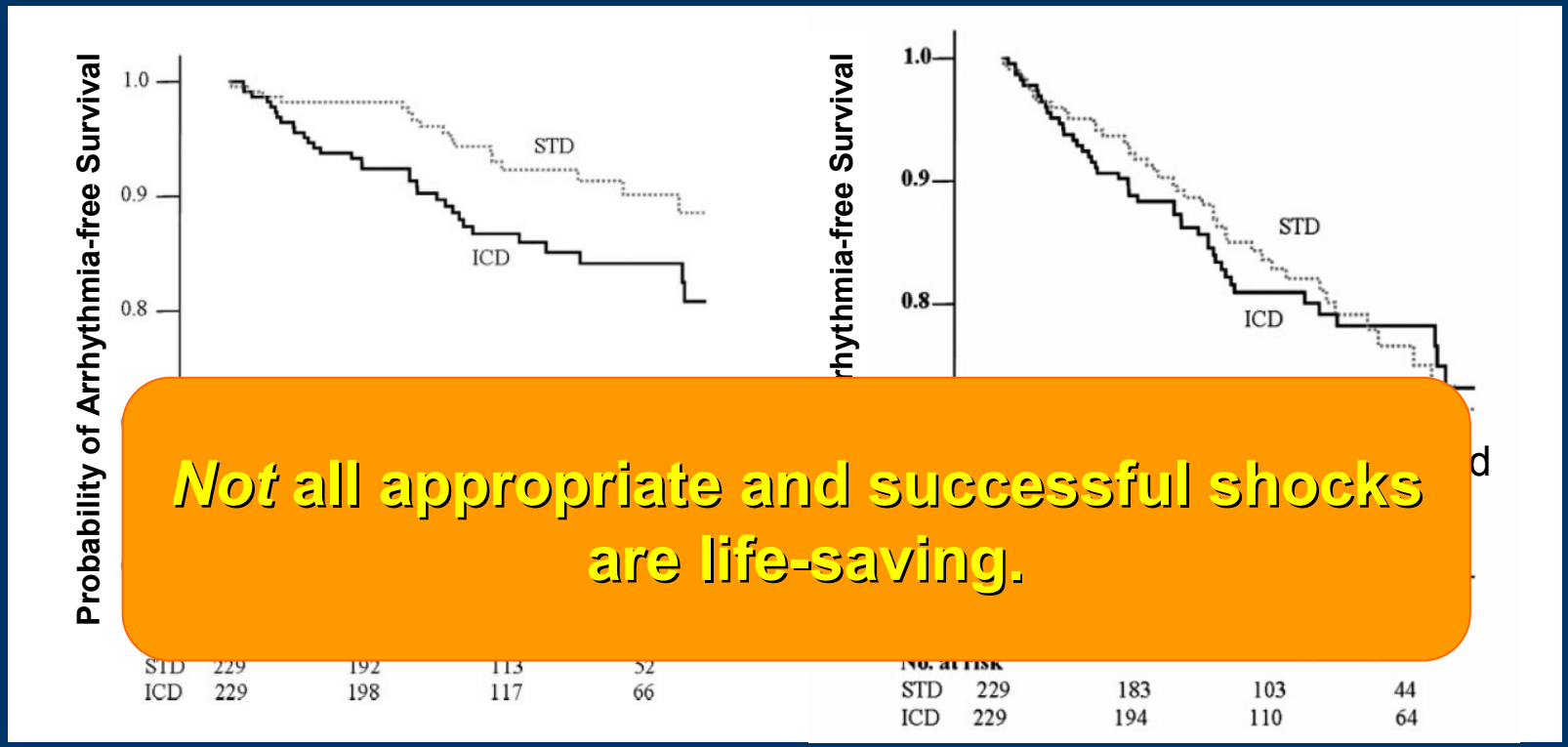
- CRT or CRT-D reduces Mortality+Hospitalization
- CRT-D reduces Mortality

  -2/3 of the effect size can be attributed to CRT

Bristow MR. N Eng J Med 2004;350:2140-50

# ICD shocks are not a surrogate marker for SCD in patients with NICM

- the number of appropriate ICD shocks will not equal the mortality benefit incurred by ICD implantation
- ICD shocks overestimate the true efficacy of ICD therapy, because many episodes of tachycardia terminate spontaneously

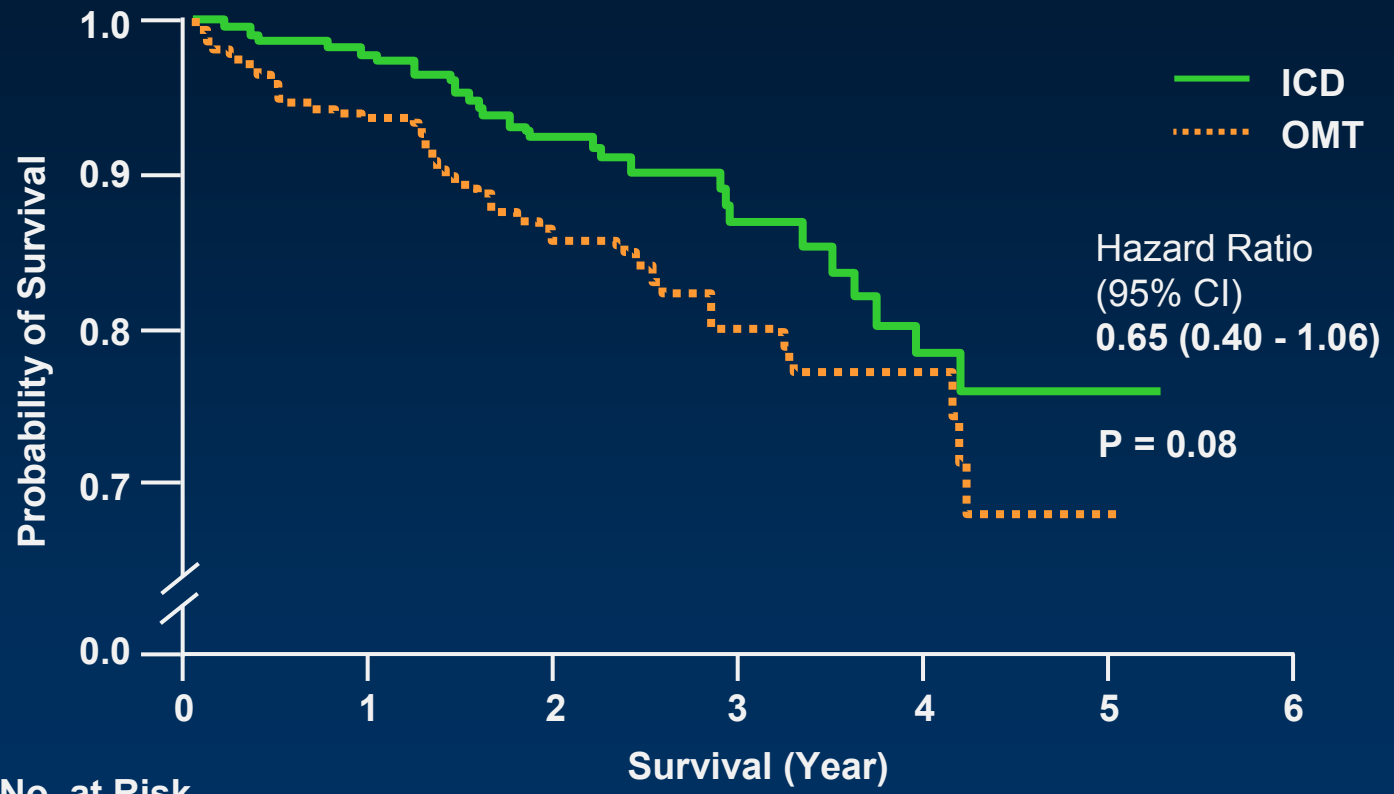



***Not* all appropriate and successful shocks are life-saving.**

DEFINITE substudy Circulation. 2006 Feb 14;113(6):776-82.

# DEFINITE

## *Death from Any Cause Results*




| No. at Risk | | | | | |
|---|---|---|---|---|---|
| OMT | 229 | 210 | 131 | 67 | 32 |
| ICD | 229 | 218 | 140 | 77 | 41 |

Kadish A. *N Engl J Med*. 2004;350:2151-2158.

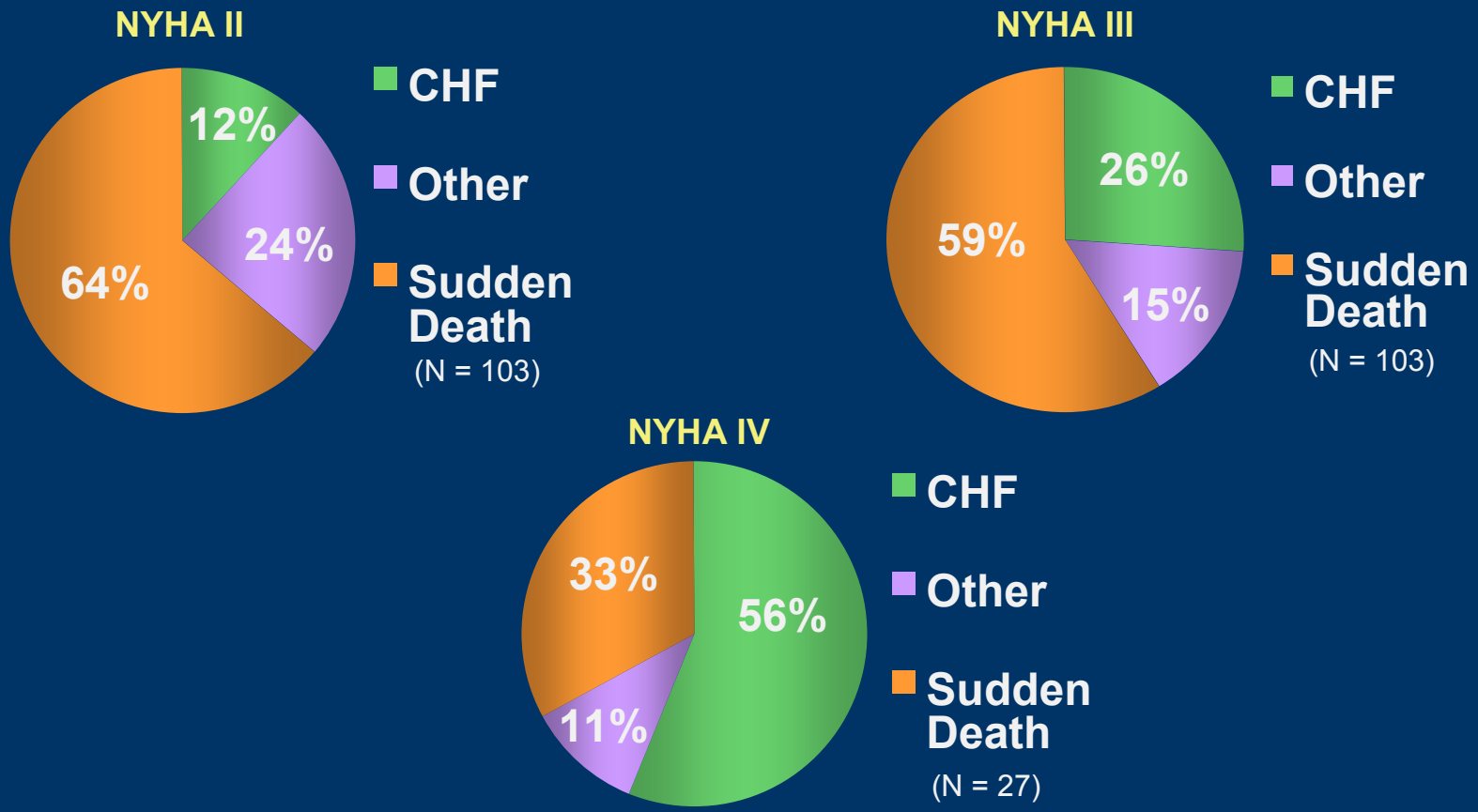
# DEFINITE

On the basis of our results, the routine Implantation of a cardioverter–defibrillator cannot be recommended for all patients with nonischemic cardiomyopathy and severe left ventricular dysfunction.
However, findings of a reduction in sudden death from arrhythmia and an apparent benefit of ICDs in subgroup analyses suggest that the use of these devices should be considered on a case-by-case basis.

N Engl J Med 2004;350:2151-8.

# Severity of Heart Failure

## Modes of Death*

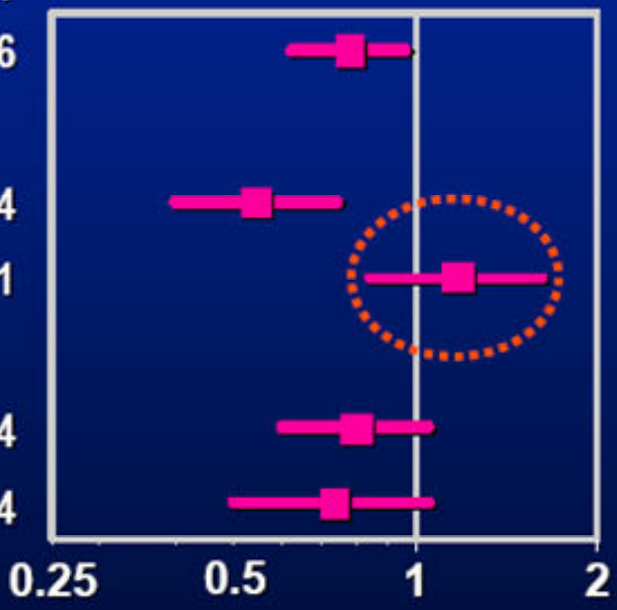



- Most patients who suffer from sudden death (60%) are the patients who are minimally symptomatic with Class II and III heart failure
- The sickest, most symptomatic patients (Class IV) experience heart failure deaths (56%) from pump failure rather than sudden death (33%)

* MERIT-HF Study Group. Lancet. 1999;353:2001-2007.

# ICD vs. Control
## Hazard Ratios

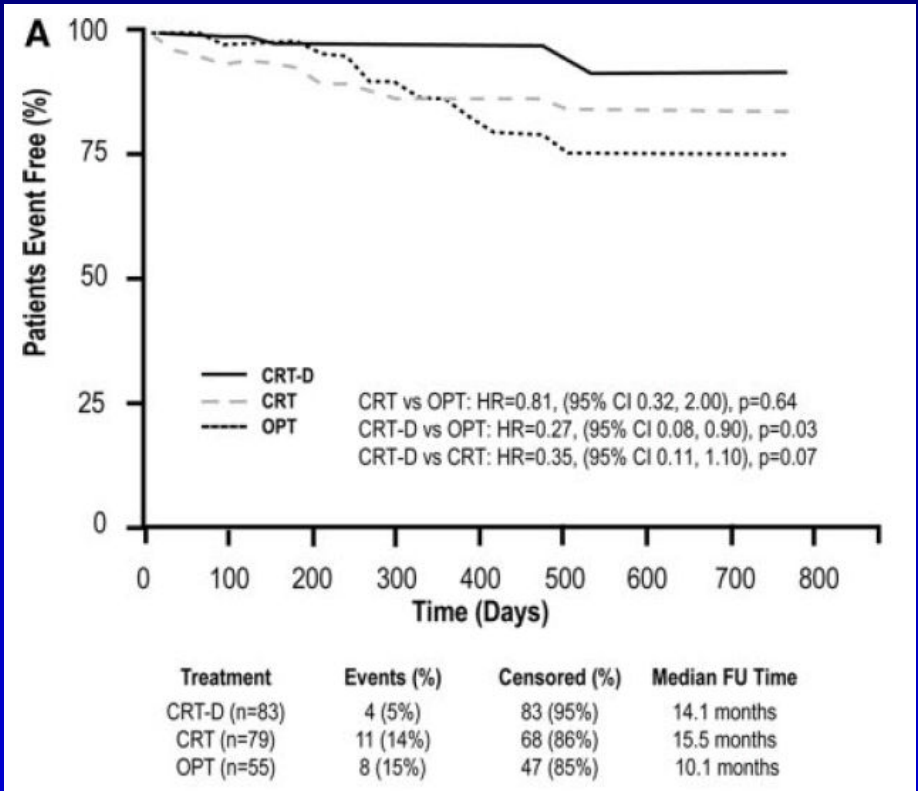
| Patient Group | | N | HR | 97.5% CI |
|---|---|---|---|---|
| All Patients | | 1676 | 0.77 | 0.62, 0.96 |
| NYHA Class | Class II | 1160 | 0.54 | 0.40, 0.74 |
| | Class III | 516 | 1.16 | 0.84, 1.61 |
| CHF Etiology | Ischemic | 884 | 0.79 | 0.60, 1.04 |
| | Non-Ischemic | 792 | 0.73 | 0.50, 1.04 |




SCD HeFT study. Bardy GH. *N Engl J Med.* 2005;352:225-237.

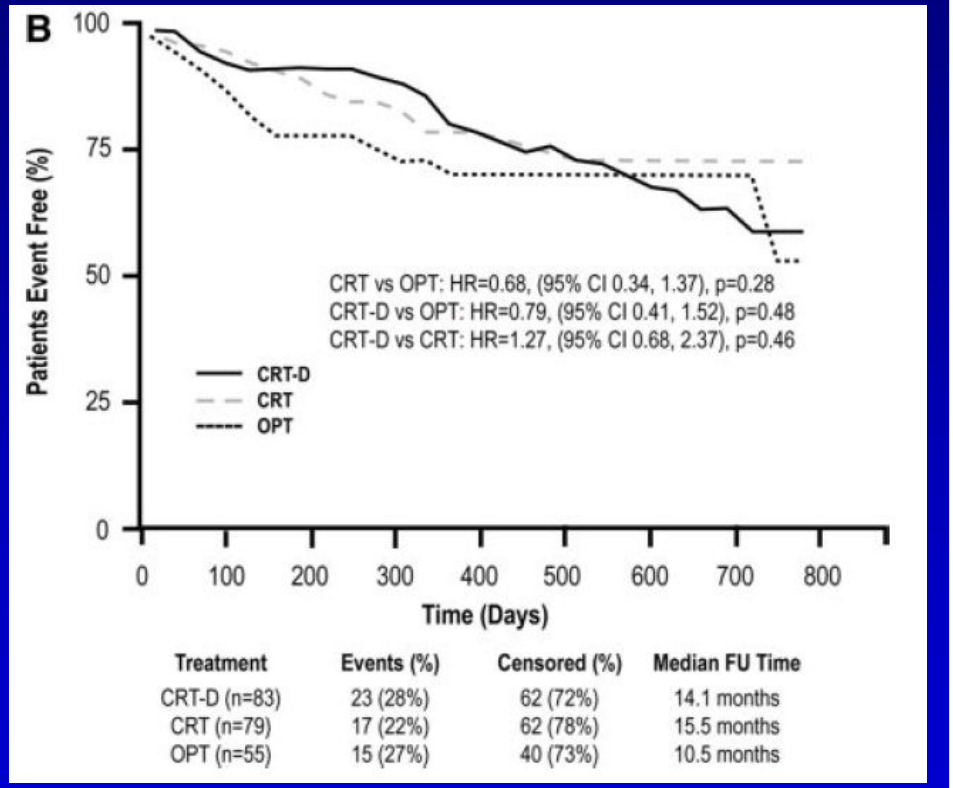
# Effects of CRT With or Without a Defibrillator on Survival and Hospitalizations in NYHA Class IV Heart Failure

## COMPANION -Subanalysis




| Treatment | Events (%) | Censored (%) | Median FU Time |
|---|---|---|---|
| CRT-D (n=83) | 4 (5%) | 83 (95%) | 14.1 months |
| CRT (n=79) | 11 (14%) | 68 (86%) | 15.5 months |
| OPT (n=55) | 8 (15%) | 47 (85%) | 10.1 months |

**Time to Sudden death**



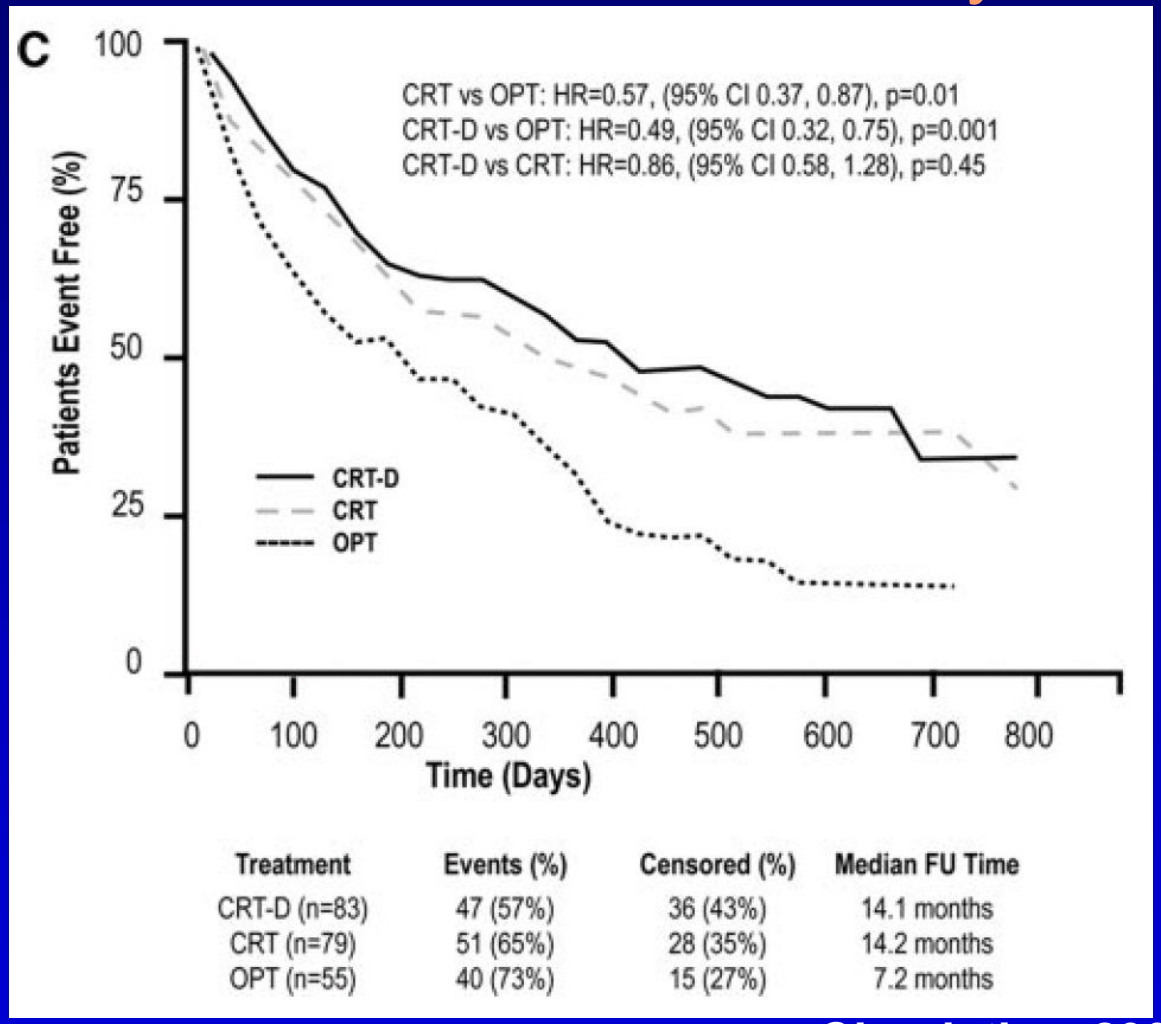

| Treatment | Events (%) | Censored (%) | Median FU Time |
|---|---|---|---|
| CRT-D (n=83) | 23 (28%) | 62 (72%) | 14.1 months |
| CRT (n=79) | 17 (22%) | 62 (78%) | 15.5 months |
| OPT (n=55) | 15 (27%) | 40 (73%) | 10.5 months |

**Time to HF death**

***Circulation*. 2007;115:204-212**

# Effects of CRT With or Without a Defibrillator on Survival and Hospitalizations in NYHA Class IV Heart Failure

## COMPANION -Subanalysis



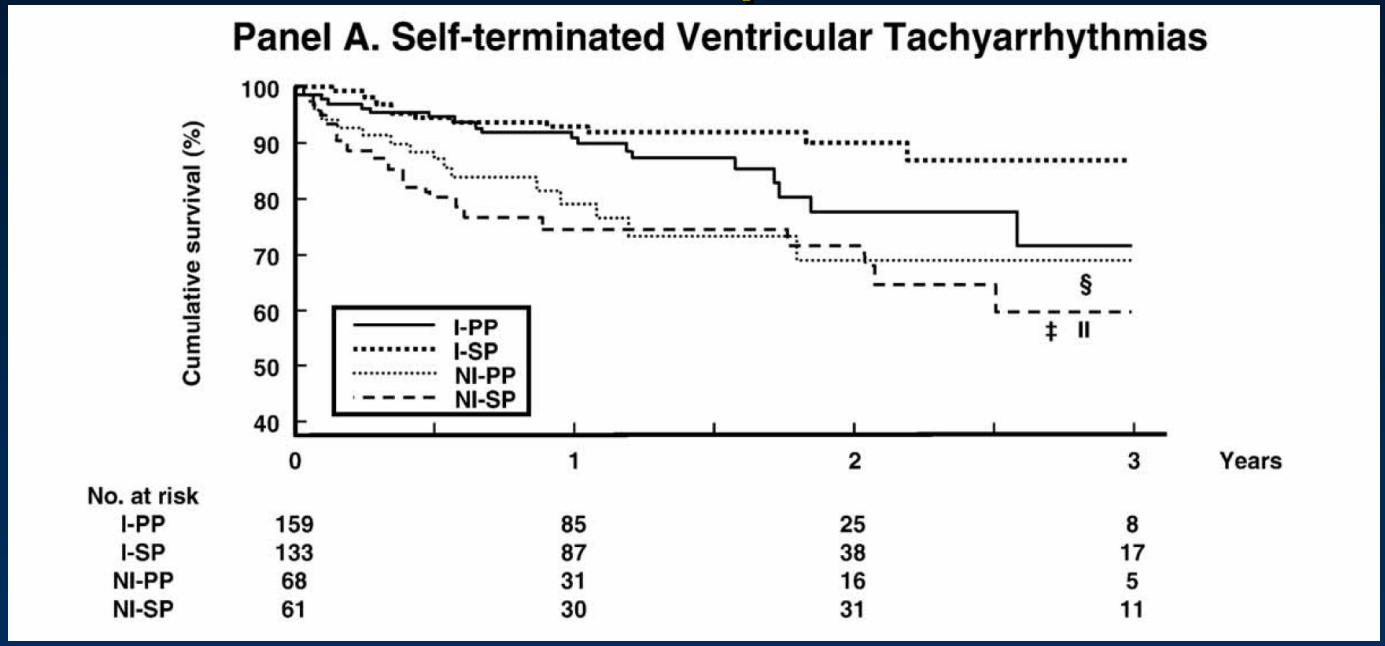

| Treatment | Events (%) | Censored (%) | Median FU Time |
|---|---|---|---|
| CRT-D (n=83) | 47 (57%) | 36 (43%) | 14.1 months |
| CRT (n=79) | 51 (65%) | 28 (35%) | 14.2 months |
| OPT (n=55) | 40 (73%) | 15 (27%) | 7.2 months |

***Circulation*. 2007;115:204-212**

# ICD and Advanced CHF

- No ancillary benefit from ICD in very symptomatic patients treated with CRT
- Limitations in the evidence for ICD use in CHF

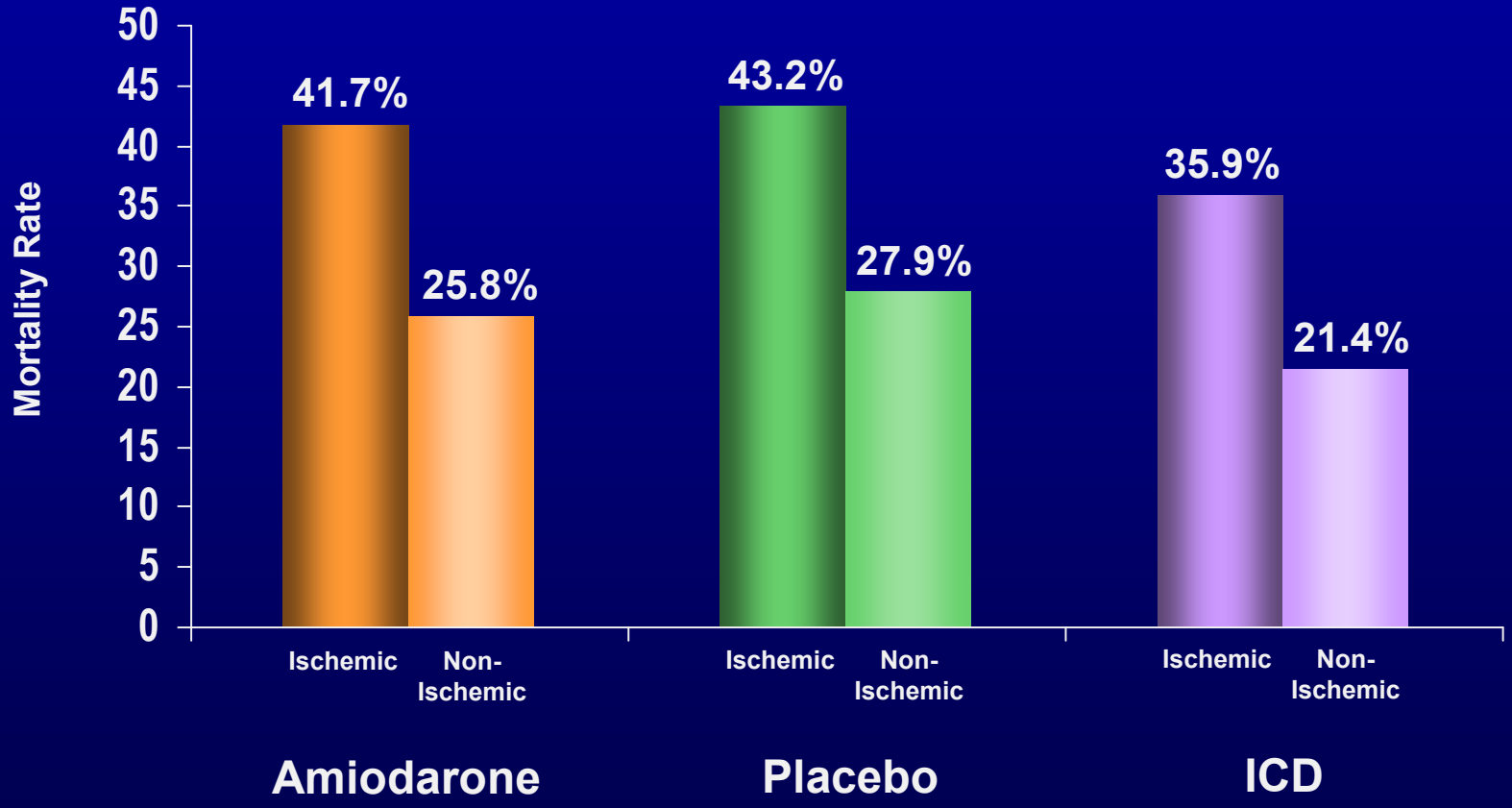
# Characteristics of VA occurring in ischemic vs nonischemic patients implanted with a CRT-D for 1° or 2° prevention of SD




- The incidence of overall ventricular tachyarrhythmias in nonischemic patients in secondary prevention (35.7% at 1 year) was higher than in ischemic patients implanted for either indication (16.5% and 22.9% at 1 year, respectively).
- The incidence of self-terminating ventricular tachyarrhythmias was greater in patients with nonischemic heart disease, regardless of indication. Patients with ischemic heart disease in primary prevention had a lower occurrence of VTs, whereas nonischemic patients in primary prevention had faster VTs.

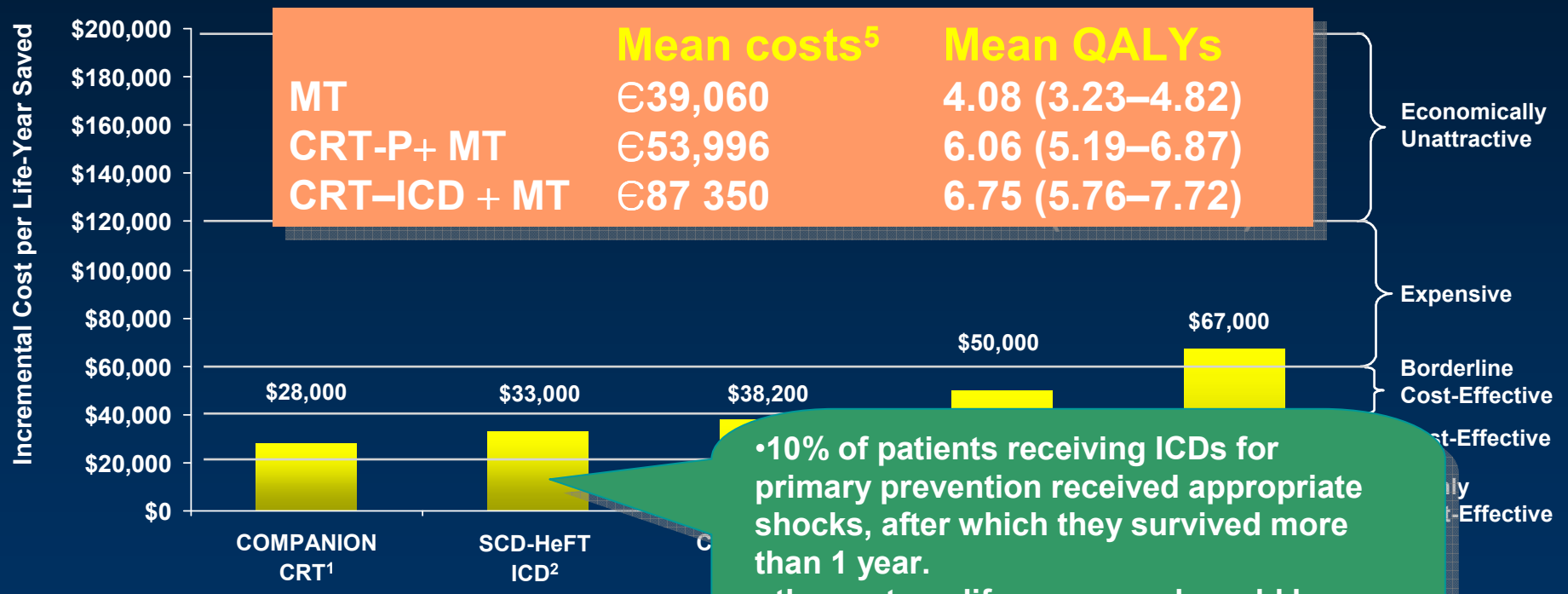
Am Heart J. 2006 Sep;152(3):527.e1-11

# SCD-HeFT 5-Year Mortality Rate Ischemic vs. Non-Ischemic




Bardy GH. *N Engl J Med.* 2005;352:225-237.

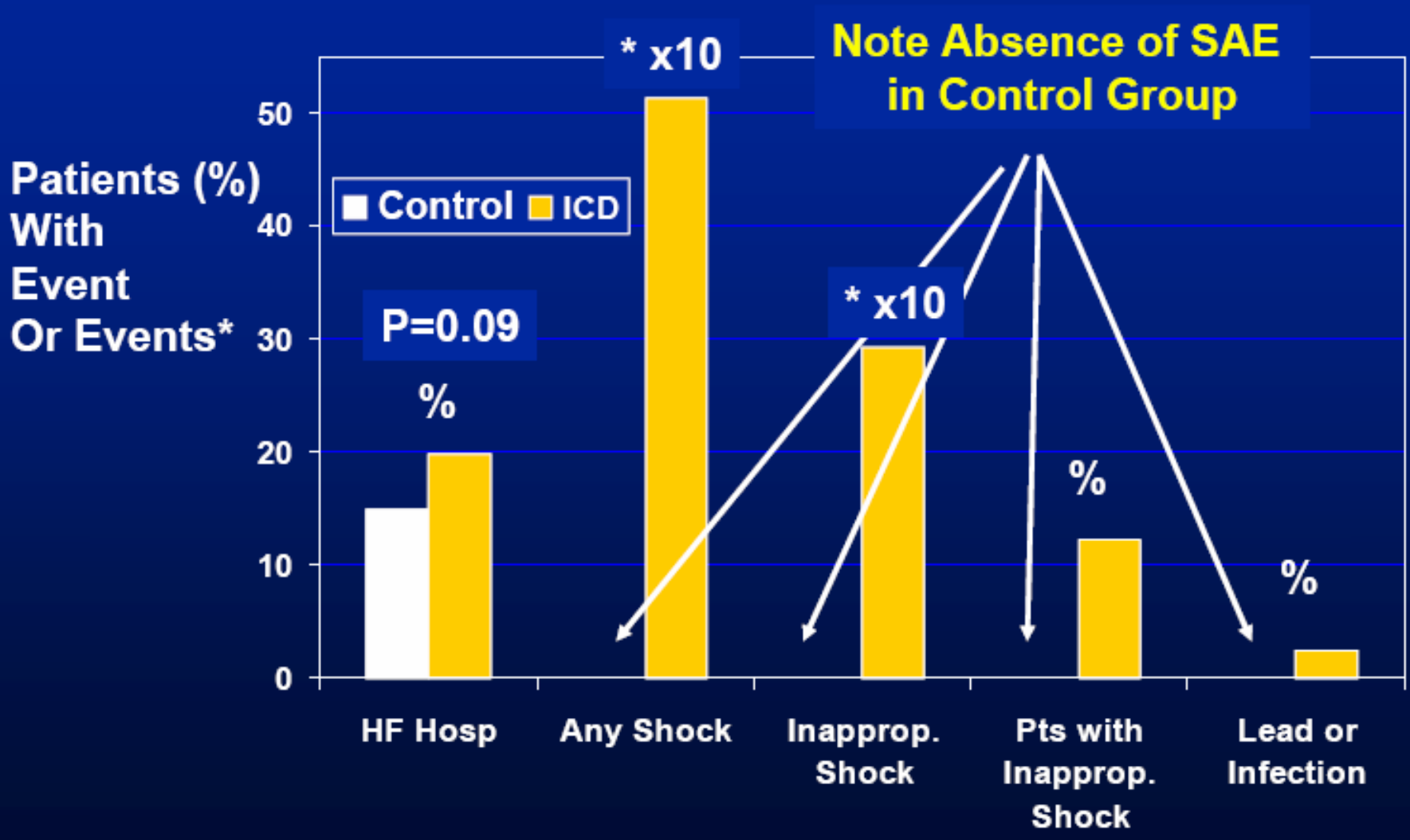
# Cost-Effectiveness ICD, CRT, and CRT-D Therapies





1 Feldman AM. www.theheart.org. ACC News.
2 Mark DB. www.theheart.org. AHA News. Novem
3 Ak-Khatib S. *Ann Intern Med.* 2005;142:593-600.
4 Larsen G. *Circulation.* 2002;105:2049-2057.
5. Based on CARE-HF and COMPANION study. Yao G et al European Heart Journal (2007) 28, 42–51
6. Stevenson LW. Circulation. 2006 Jul 11;114(2):101-3.

# Adverse Events in MADIT II



# ICDs and Morbidity

Substantial morbidity with ICDs

# Conclusions

- ICDs are proven to prolong life in patients with CHF and LV systolic dysfunction, but still limited in evidence
- Fairly small survival benefit
- Important morbidity
- Cost-effective?
- ICDs should be considered on a case-by-case basis in CRT patients.

감사합니다.

# Cost-Effectiveness of Defibrillator Therapy or Amiodarone in Chronic Stable Heart Failure

## Results From the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT)

Daniel B. Mark, MD, MPH; Charlotte L. Nelson, MS; Kevin J. Anstrom, PhD; Sana M. Al-Khatib, MD; Anastasios A. Tsiatis, PhD; Patricia A. Cowper, PhD; Nancy E. Clapp-Channing, RN, MPH; Linda Davidson-Ray, MA; Jeanne E. Poole, MD; George Johnson, BSEE; Jill Anderson, RN; Kerry L. Lee, PhD; Gust H. Bardy, MD; for the SCD-HeFT Investigators

**”Prophylactic use of single-lead, shock-only ICD therapy is economically attractive in patients with stable, moderately symptomatic heart failure with an ejection fraction <35%, particularly those in NYHA class II, as long as the benefits of ICD therapy observed in the SCD-HeFT persist for at least 8 years.”**

# ICD versus CRT

- No clear additional benefit of ICD in symptomatic patients treated with CRT

# CRT combined with ICD(CRT-D) Provides Incremental Survival Benefits

- While CRT alone reduces mortality, CRT-D provides incremental survival benefits, attributed to the reduction in sudden cardiac death