Benefits of CRT-D in CHF

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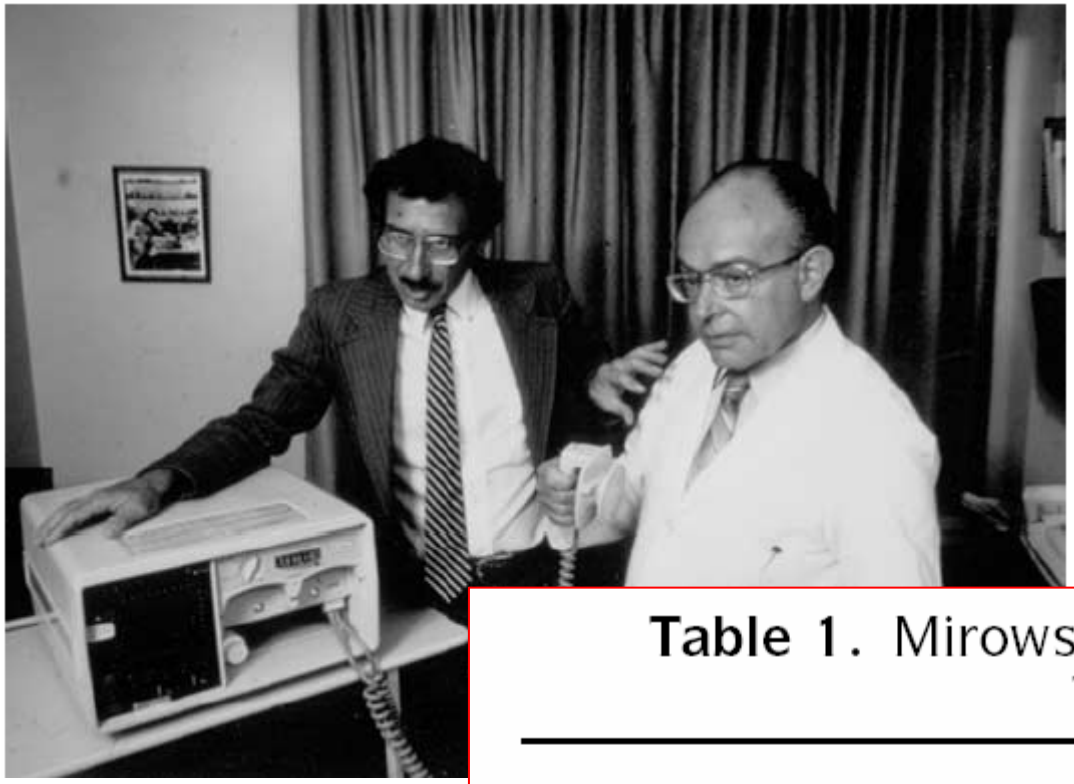
최 기 준



ICD and CRT : The Perfect Marriage?

Michel Mirowski a
: Two Baltimore ca

Table 1. Mirowski/Mower Legacy of Pivotal Therapies

	ICD	CRT
Concept	1970	Mid 1970s
Patent	1971	1990
First implant	1981	1991
FDA/CMS approval	1984	2004
Pivotal trials	MADIT I & II	COMPANION
	SCD-HeFT	CARE-HF
	AVID	
	CIDS	

If CRT-P alone provide predictable SCD prevention (or anti-arrhythmic benefit), Physician's decision making would be simple.

If CRT-D has same cost with CRT-P and/or government (medical insurance) covers all CRT-D cases, Physician's decision making would be simple.

In Real World --

	Price (Device)	Price (Device + leads)	환자부담 (10%) *
CRT-P	1010만원	1300만원	130만원
CRT-D	2150만원	2500만원	250만원
ICD (dual chamber)	2030만원	2300만원	230만원

* 6개월간 보험적용 입원비 중 최대 300만원만 본인 부담

Practice : CRT-D vs. CRT-P

	CRT-D (%)
USA	73% of all CRT in 2005 91% of all CRT in 2006 (expected)
Europe	50-60% of all CRT in 2005
Korea	25% (25/102) *(54% (7/13) in AMC)*

Saxon LA et al. European HJ 2006;27:1891

- Decision Summary (2005)
  - CMS determined ICD is reasonable and necessary for the followings :

1. Patients with **ischemic CMP**, prior MI, NYHA class II-III heart failure and measured LVEF ≤30%
2. Patients with **non-ischemic dilated CMP**

   > 9 months, NYHA class II-III heart failure and measured LVEF ≤30%

www.cms.hhs.gov/mcd

한국에서의 ICD 보험 인정기준

1. 일시적이거나 가역적인 원인이 없는 심실세동이나 심실빈맥에 의한 심정지
2. 기질적 심질환이 있는 자발적 지속성 심실빈맥 환자
3. 기질적 심질환이 없는 자발적 지속성 심실빈맥 환자에서 다른 치료 방법으로 조절되지 않는 경우
4. 원인을 알 수 없는 실신

   + 전기생리학 검사에서 혈역동학적으로 의미있는 심실빈맥의 유발

   + 약물치료는 효과가 없거나 복용을 못하는 경우

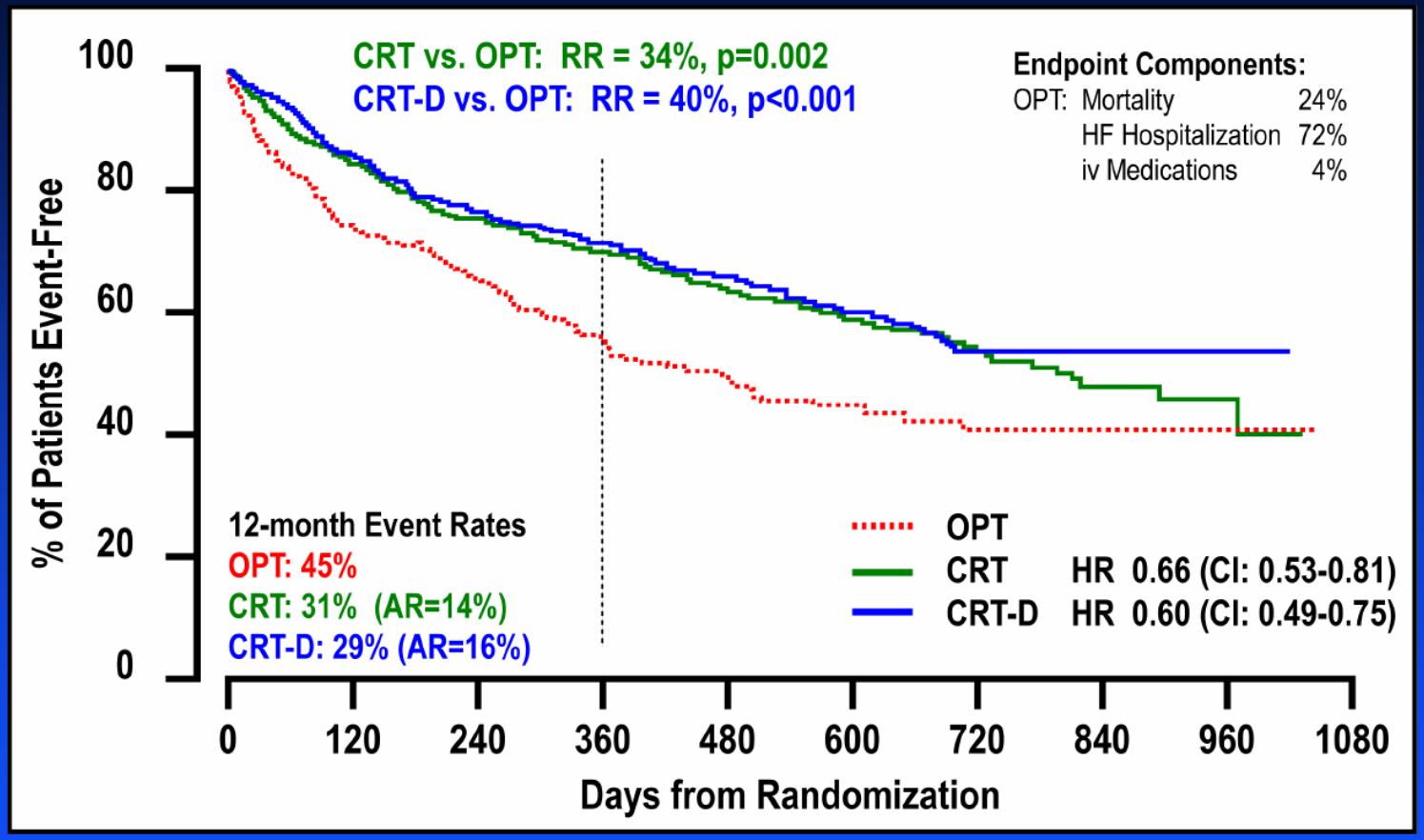
5. 이전의 심근경색 환자, 관상동맥질환 환자, 좌심실기능 부전 환자에서 다음 세가지 조건에 해당
   - 30% 이하의 low EF
   - 비지속성 심실빈맥
   - 전기생리학 검사에서 심실세동이나 지속성 심실빈맥의 유발
6. Brugada 증후군 환자에서 ---
7. 비후성 심근증 환자로 ---
8. Long QT 증후군 환자에서 ---

COMPANION study

- N=1520
- Advanced heart failure(NYHA class III or IV)
- Ischemic or non-ischemic
- QRS interval ≥ 120msec

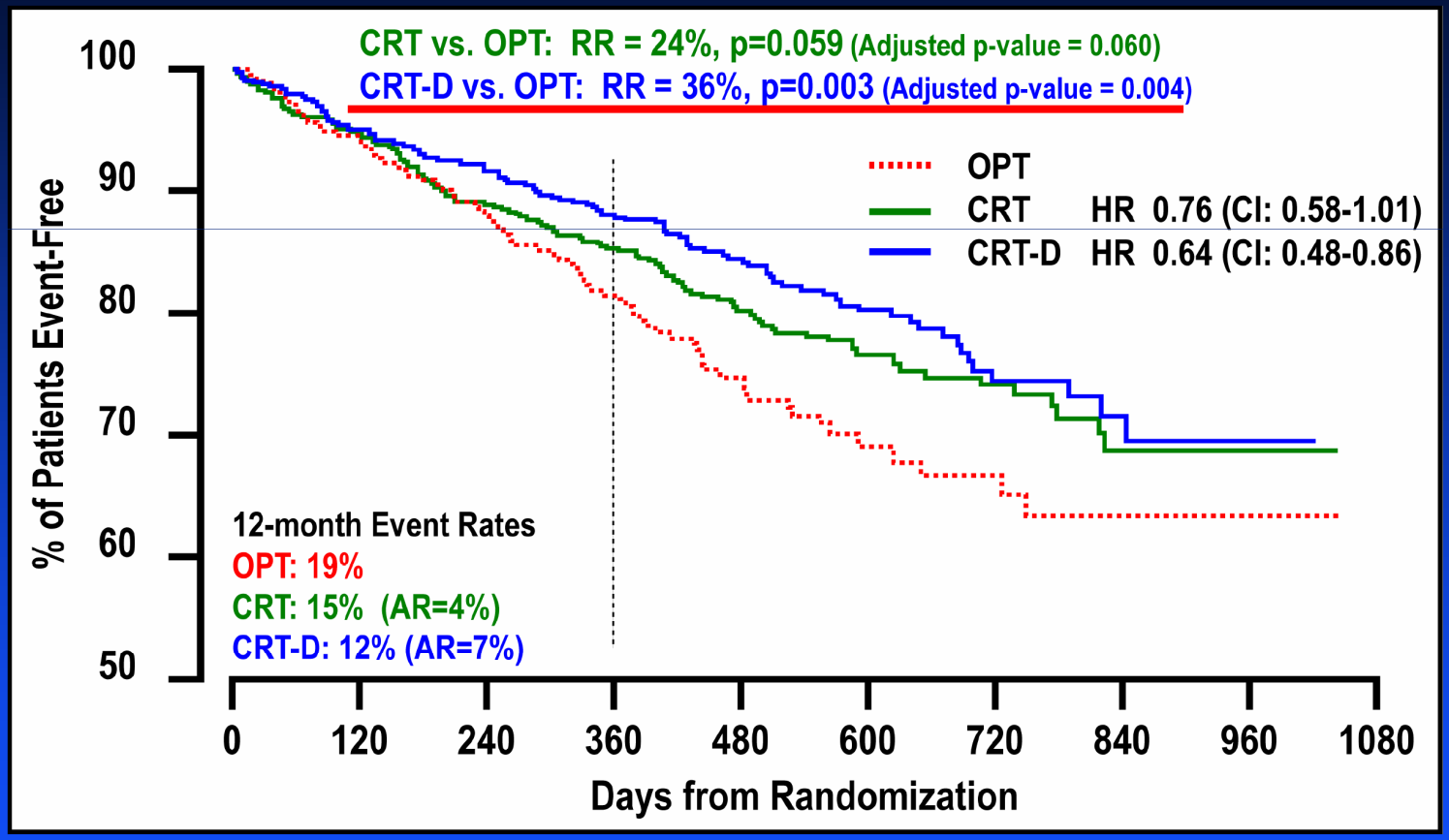
➢ 1) OPT (Optimal pharmacologic therapy)
2) CRT-P (CRT-Pacemaker)
3) CRT-D (CRT-Defibrillator)

COMPANION: *Death or HF Hospitalization*



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

COMPANION: *Secondary Endpoint of All-Cause Mortality*



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

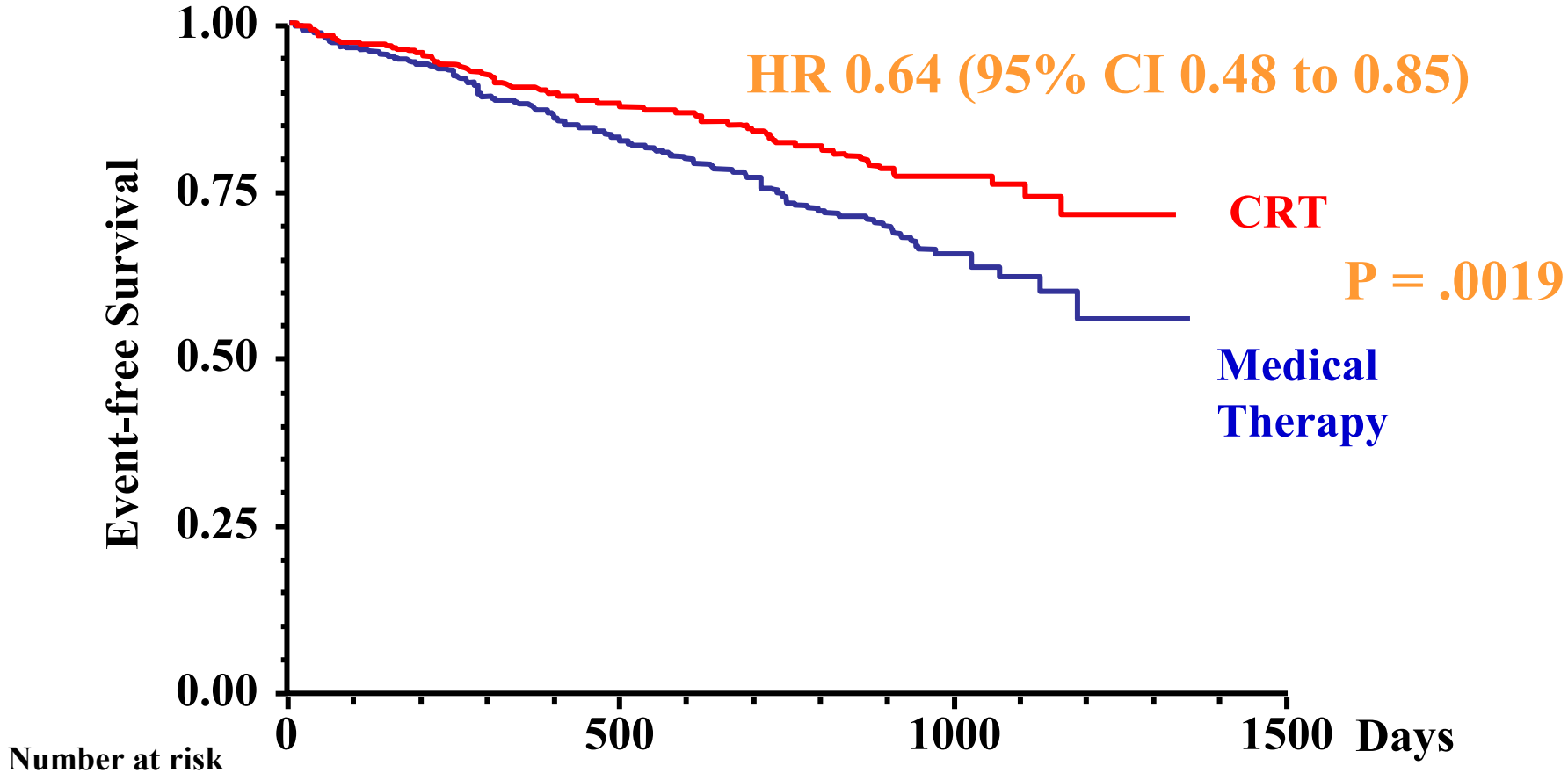
The CARE-HF Study

CArdiac REsynchronisation in Heart Failure

: Inclusion Criteria *- NEJM 352(15), 1539-49, 2005 -*

- **Currently in NYHA class III/IV**
- **LV systolic dysfunction and dilation**
  - **EF ≤35%; EDD ≥30mm/height in metres**
- **QRS ≥120 ms**
  - **Dyssynchrony confirmed by echo if QRS 120-149ms**
    - Aortic pre-ejection delay >140 ms
    - Interventricular mechanical delay >40 ms
    - Delayed activation of postero-lateral LV wall
- ***Patients with AF or requiring pacing or ICD excluded***

CARE-HF : All-Cause Mortality



Number at risk						
CRT	409	376	351	213	89	8
Medical Therapy	404	365	321	192	71	5

Issues--

- SCD prevention by CRT?

  Is it enough?

- Risk predictors of sudden death in CRT patients?

  – NYHA Functional class III or IV?

SCD prevention by CRT-P?

- CARE-HF(2005) : mortality benefit (+), SCD (-)
- CARE-HF extended phase (European Heart J 2006; 27:1928) : SCD prevention (+)
- Mechanism
  - Reduced ventricular volume
  - Improved cardiac output
  - Reduced wall stretch
  - Diminished catecholamine

→ reduced tachyarrhythmia risk

Mortality and mode of death

	Mean follow-up (months)	Total mortality (%)/pump death (%)[a]/sudden death (%)[a]		
		OPT	CRT	CRT-D
COMPANION	16	25/44/23	21/40/37	17/50/16
CARE-HF	29	30/47/32	20/40/35	—
CARE-HF extension	37	38/42/36	25/38/32	—

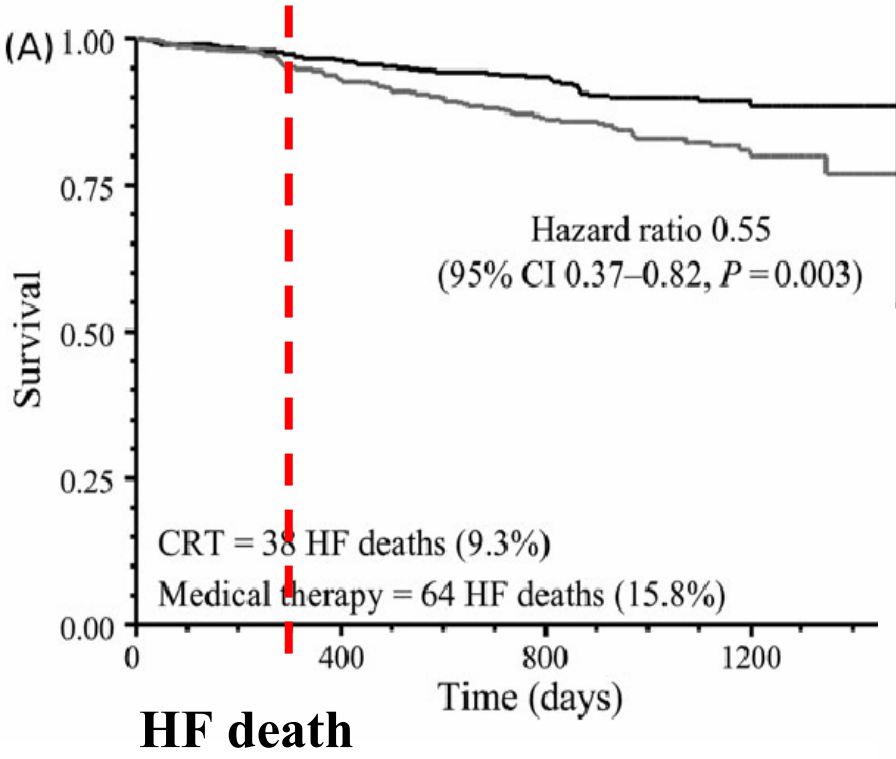
[a]Per cent of deaths within each treatment group.

Europace 2006;8:499

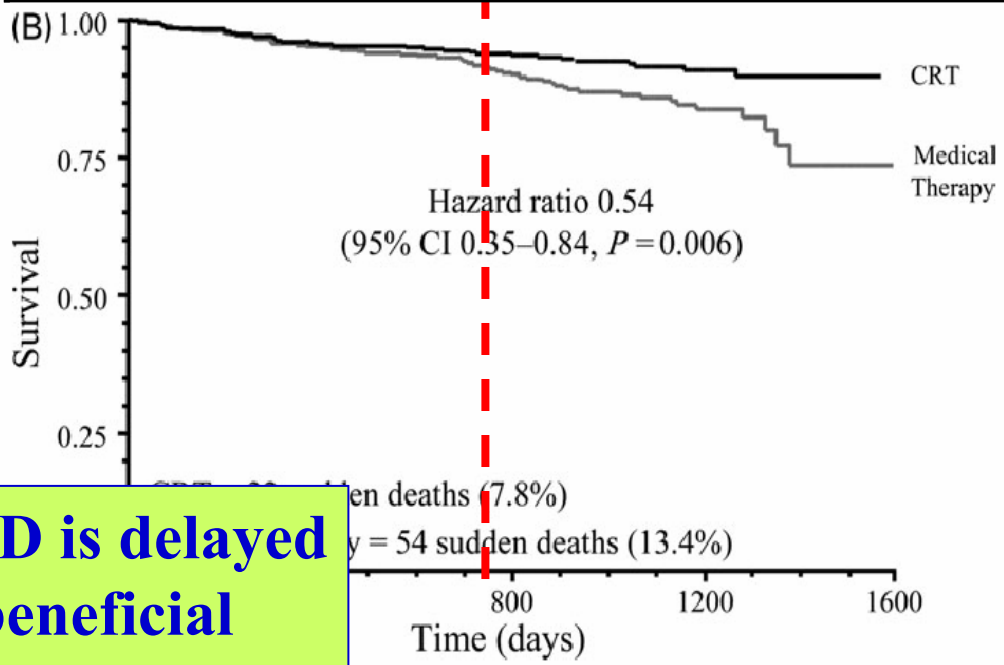
50% reduction of SD risk by CRT-D compared to CRT-P in these study
→ ***Strongly suggest added value of ICD for CRT recipients.***

CARE-HF trial extension phase

	F/U	SCD in med. Tx	SCD in CRT
CARE-HF	29m	**38**/404 vs.	**29**/409
CARE-HF exten.	37m	**54**/404 vs.	**32**/409



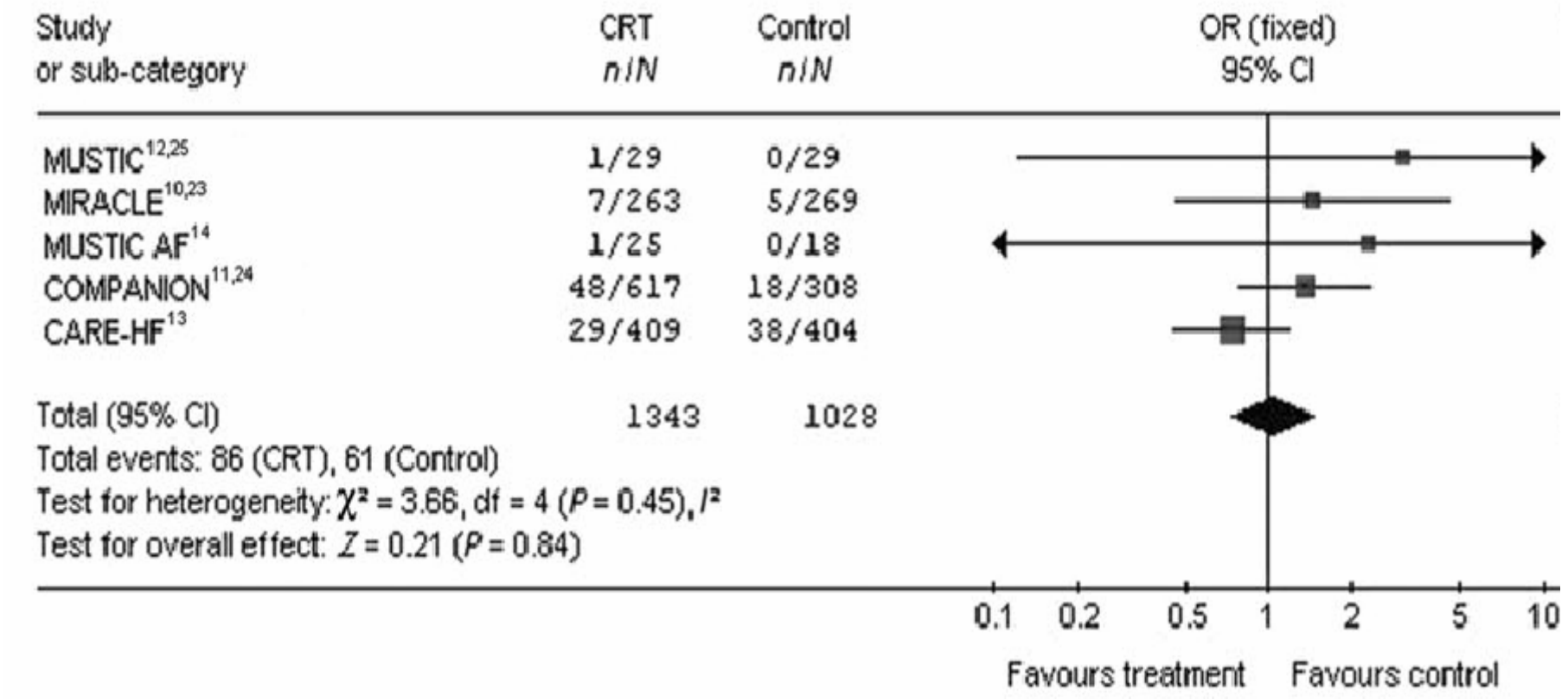
HF death



Sudden death

Ability of CRT-P to reduce SCD is delayed and potentially dependent on beneficial ventricular remodeling

Effects of cardiac resynchronization therapy on overall mortality and mode of death: a meta-analysis of randomized controlled trials



Effect of CRT alone vs. control on SCD

European HJ 2006;27:2682

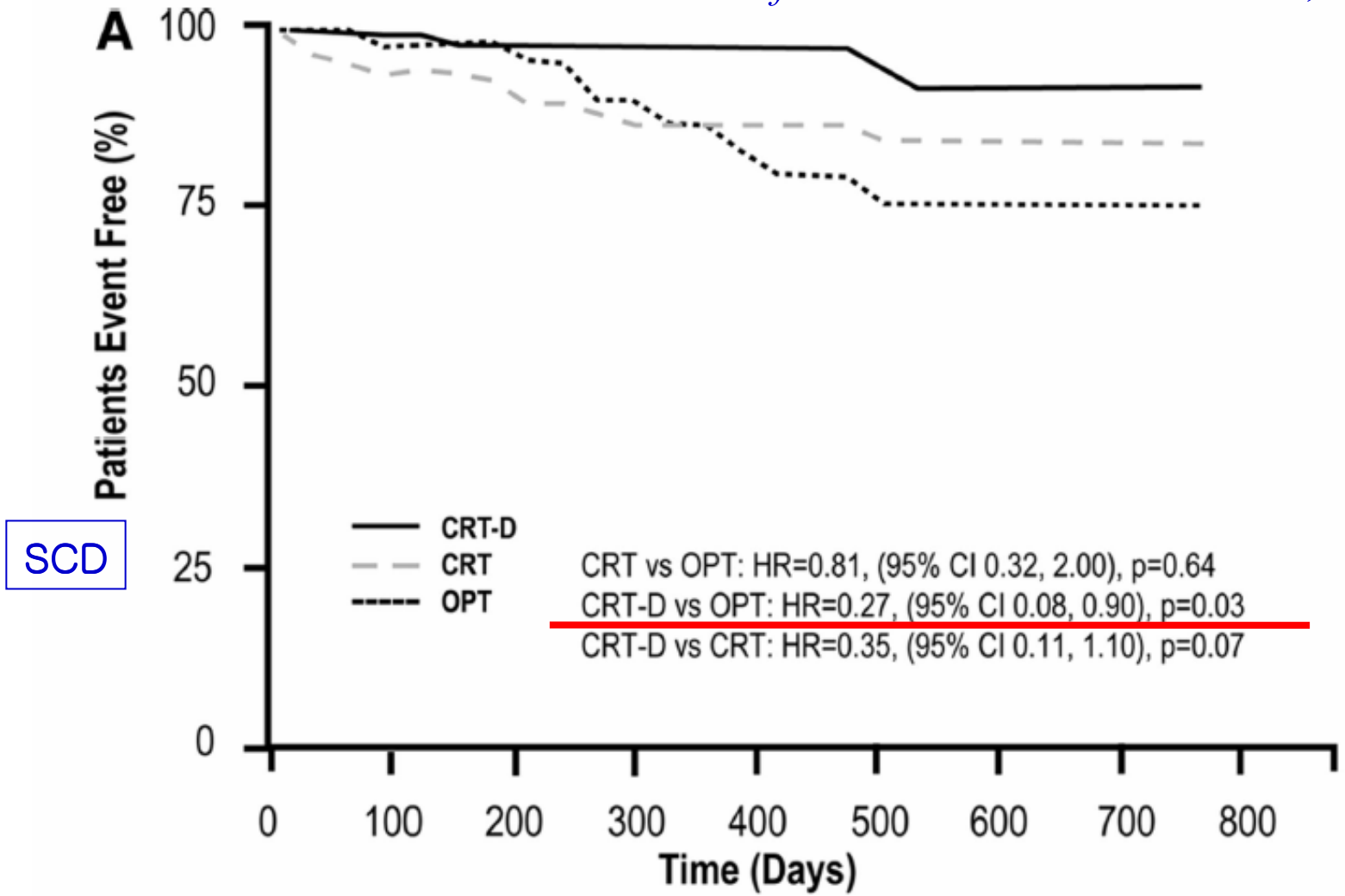
Risk stratification of SCD in CRT patients

- Predictors of ICD therapy in CRT-D patients
  - Ventak CHF / Contak CD study, n=501
  - Retrospective analysis during 6 months post-implant.
  - 14% (73/501) – appropriate ICD therapy
  - Two independent predictors
  - ➢ Hx of spontaneous, sustained ventricular arrhythmia
  - ➢ NYHA class IV CHF

Desai AD et al. J Cardiovasc Electrophysiol 2006;17:486

COMPANION subgroup : Class IV

- Lindenfeld J et al. Circulation 2007;115:204 -



SCD

NYHA class III vs. IV?

- Much greater mortality from SCD in NYHA class III vs. class IV HF : ~60% vs. ~20-33%

  (Lehmann MH et al. J Cardiovasc Electrophysiol 2006;17:491)

- Individuals with severe LV dysfunction and worsening HF may be more prone to die from disease complication other than ventricular tachyarrhythmias, not reversed by defibrillators

  (Ermis C et al. Europace 2006;8:499)

- *Still no reasonable risk predictor for CRT-D*

Benefit of CRT-D in HF with and without ventricular arrhythmias

- N=191

  : advanced HF, EF<35% and QRSd>120 msec

  – 71 with Hx of VA (secondary prevention)

  – 120 without VA (primary prevention)

- During 18±4 months F/U, ICD therapy in

  – 21% of primary prevention patients

  – 35% of secondary prevention patients ($p<0.05$)

- No predictors of ICD therapy in primary prevention patients

Ypenburg C et al. JACC 2006;48:464

No direct comparison study?
: CRT-P vs CRT-D

- Study require 1300 patients per group and follow-up period equivalent to CARE-HF (mean F/U 29m)
- Who will undertake such a study?

Conclusions

- Currently, there is no strong scientific evidence indicating that CRT-D must be offered to all CRT candidates **(at least, CRT-D for secondary prevention or younger patients without major comorbidities)**
- Because CRT improves functional class, it is likely that the relative risk for sudden death remains high and provide **a rationale for ICD as an excellent complement to CRT therapy.**