Prevention of RV Pacing, Why & How

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I am a consultant for and receive honoraria from Medtronic, Boston Scientific, St. Jude Medical, Biotronik, Sorin, Inner Pulse, Spectranetics, Cook Vascular and Stereotaxis.

Pacing the Right Ventricle

RV stimulation is **BAD**

A. ICD Trials
B. Pacing Trials
C. Alternative RV sites
D. BiV Stimulation

Dual Chamber & VVI Implantable Defibrillator Trial

DAVID

October 2000 and September 2002 at 37 US Centers

Hypothesis

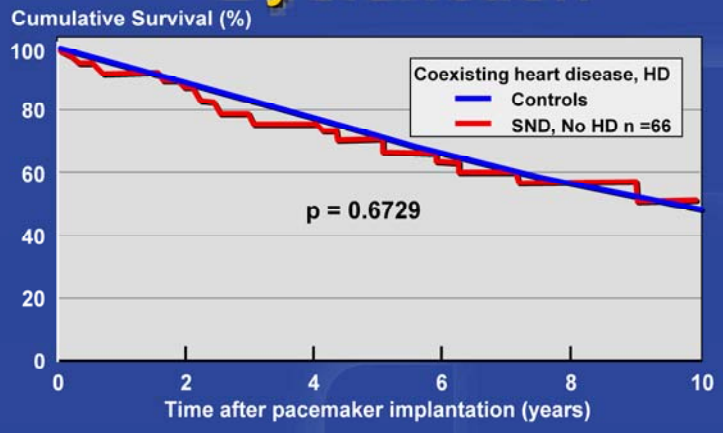
DDDR pacing …..

1). . . improves prognosis of patients treated with ICDs.

2) . . . Improves the Quality of life of patients treated with ICDs.

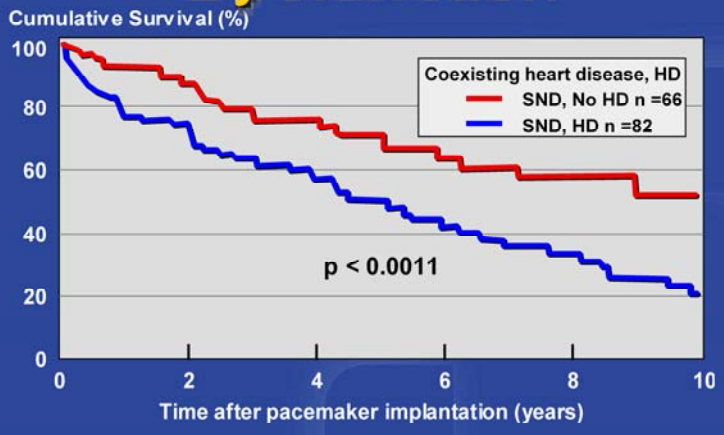
3) . . . Reduces the cost of treating patients with ICDs.

Sinus Node Dysfunction



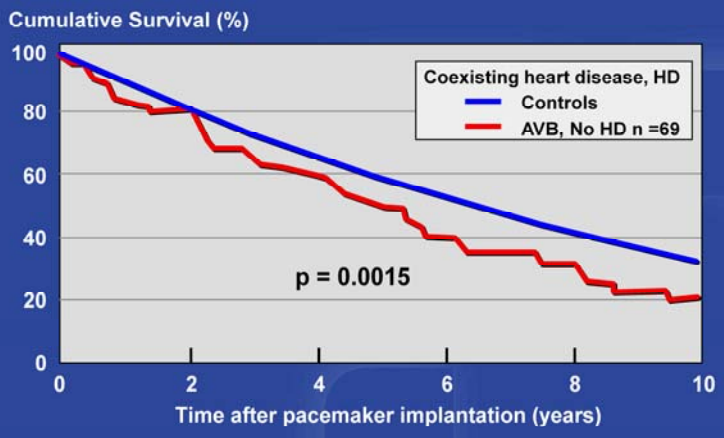
Am J Cardiol 74:1016. 1994

Sinus Node Dysfunction



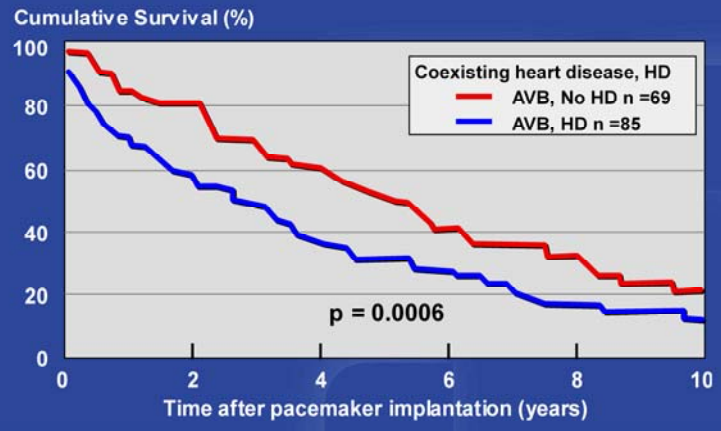
Am J Cardiol 74:1016. 1994

AV Block



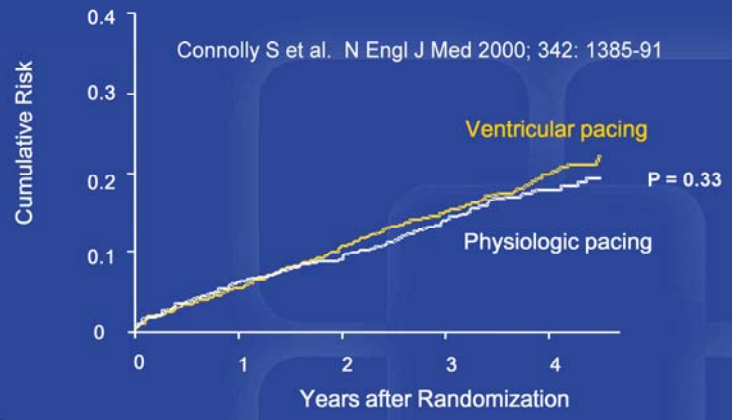
Am J Cardiol 74:1016. 1994

AV Block



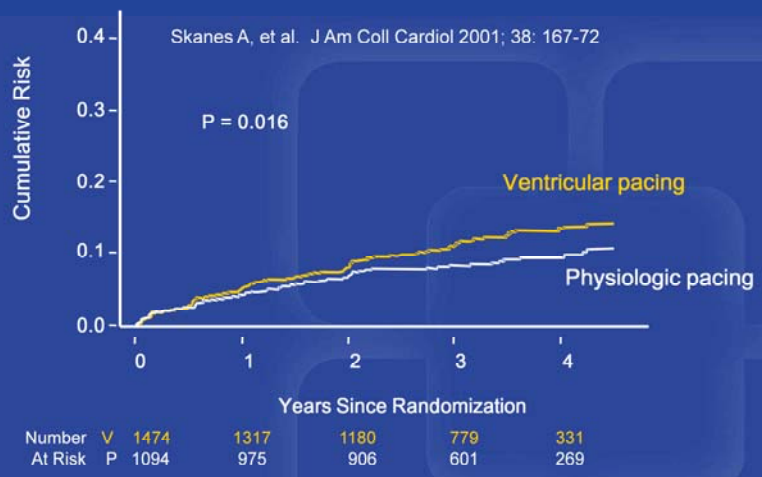
Am J Cardiol 74:1016. 1994

CTOPP
Cumulative Risk of Stroke or CV Death



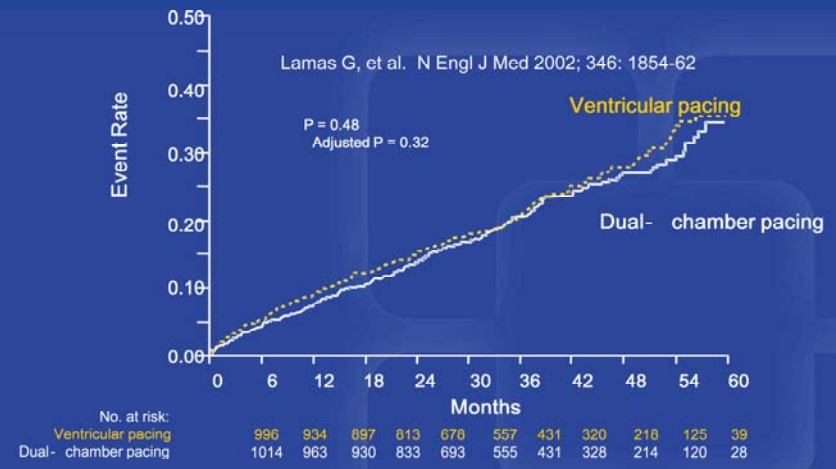
No. at risk:					
Ventricular pacing	1474	1369	1259	847	366
Physiologic pacing	1094	1005	954	637	287

CTOPP
Cumulative Risk of Chronic AF



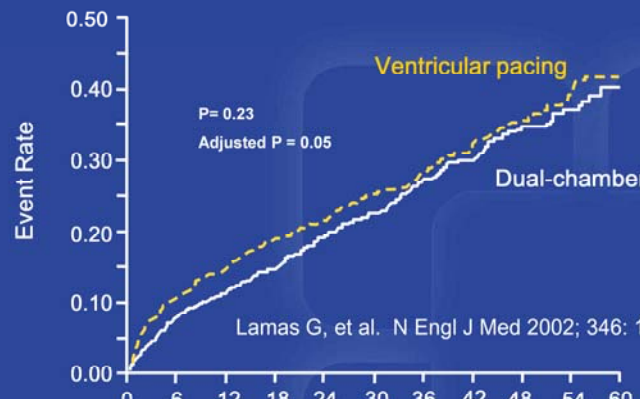
Number At Risk	V	1474	1317	1180	779	331
	P	1094	975	906	601	269

MOST
Total Mortality or Stroke



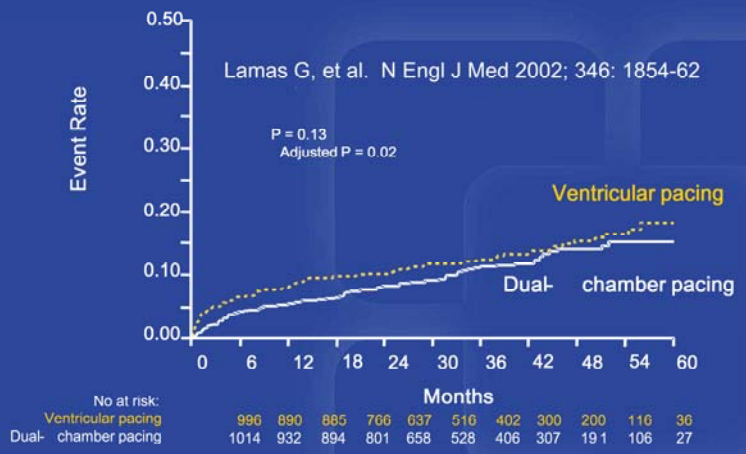
No. at risk:											
Ventricular pacing	996	934	897	813	676	557	431	320	218	125	39
Dual- chamber pacing	1014	963	930	833	693	555	431	328	214	120	28

MOST
Heart Failure, Stroke, or Death



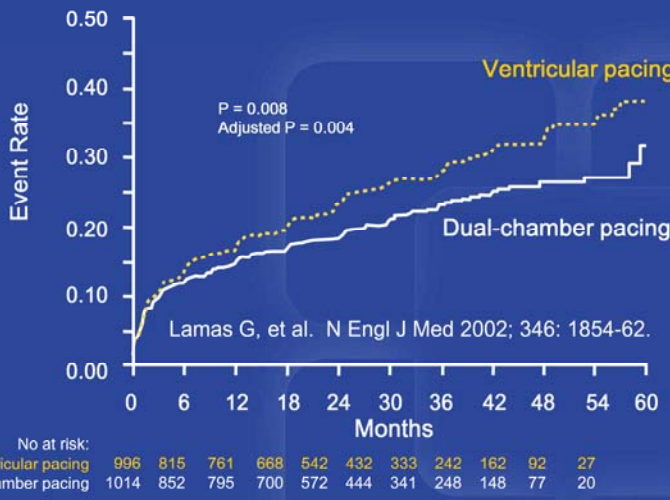
No at risk:										
Ventricular pacing	996	880	839	752	624	504	388	287	193	110	35
Dual-chamber pacing	1014	926	889	793	649	518	394	297	188	105	26

MOST
CHF Hospitalization



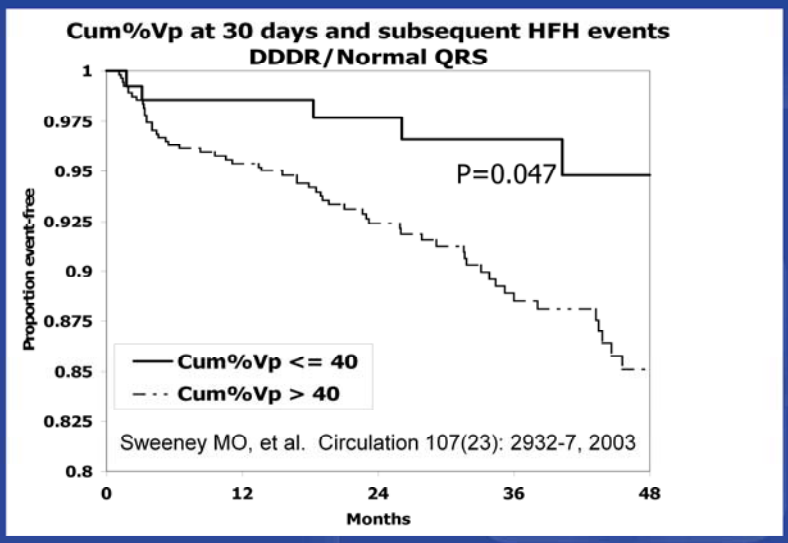
No at risk:											
Ventricular pacing	996	890	885	766	637	516	402	300	200	116	36
Dual- chamber pacing	1014	932	894	801	658	528	406	307	191	106	27

MOST
Atrial Fibrillation

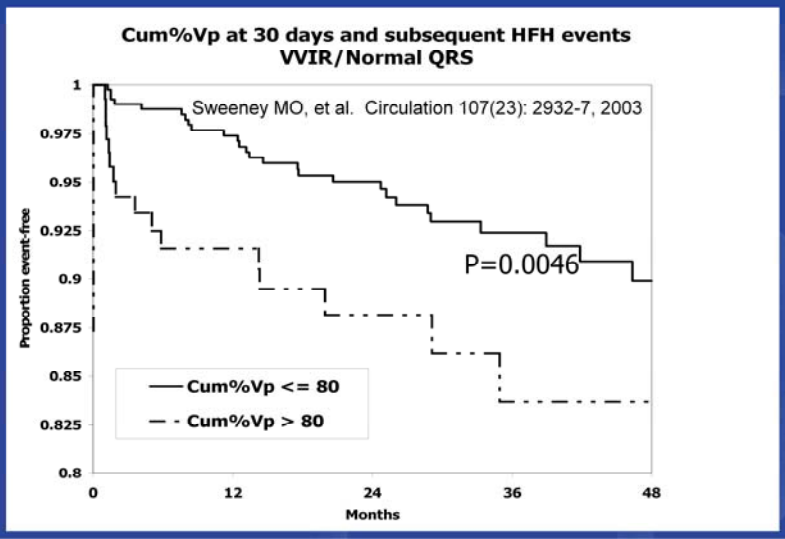


No at risk:											
Ventricular pacing	996	815	761	668	542	432	333	242	162	92	27
Dual-chamber pacing	1014	852	795	700	572	444	341	248	148	77	20

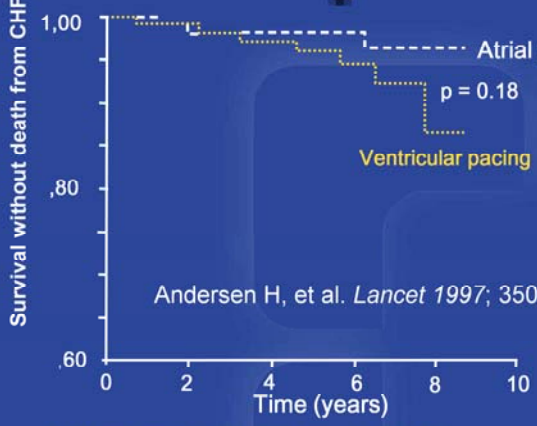
MOST Sub-Study



MOST Sub-Study



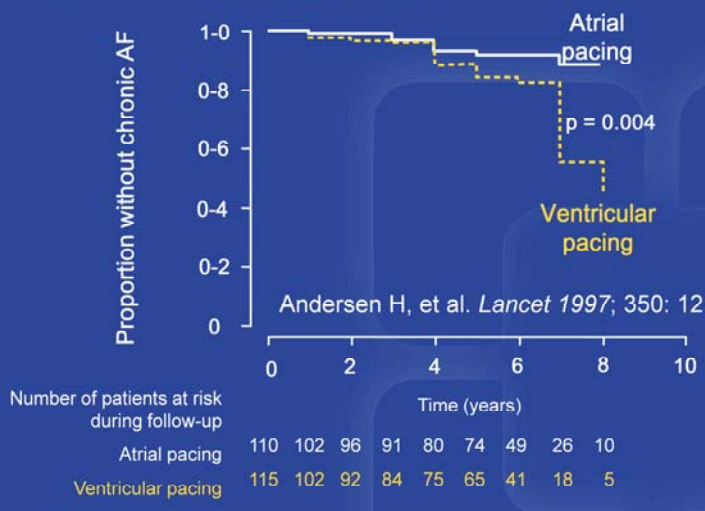
Danish Study Mortality-CHF



Andersen H, et al. *Lancet 1997*; 350: 1210-16.

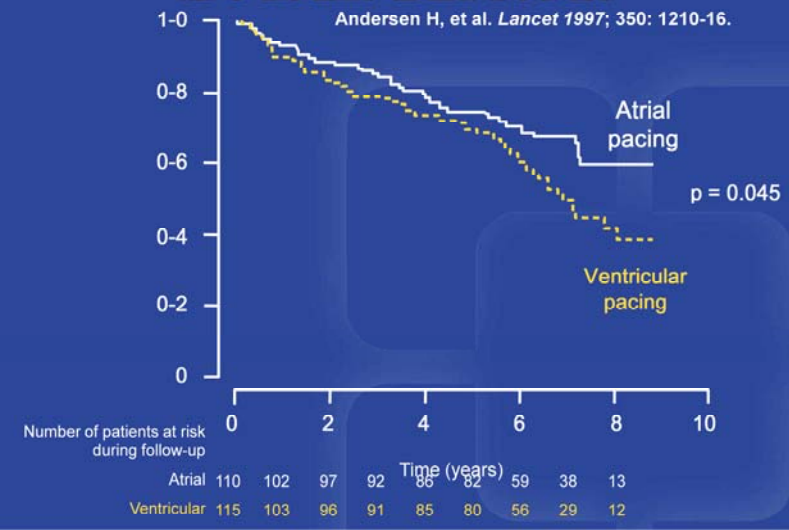
AAI:	110	102	97	92	86	82	59	38	13
VVI:	115	103	96	91	85	80	56	29	12

Danish Study
Cumulative risk of chronic AF

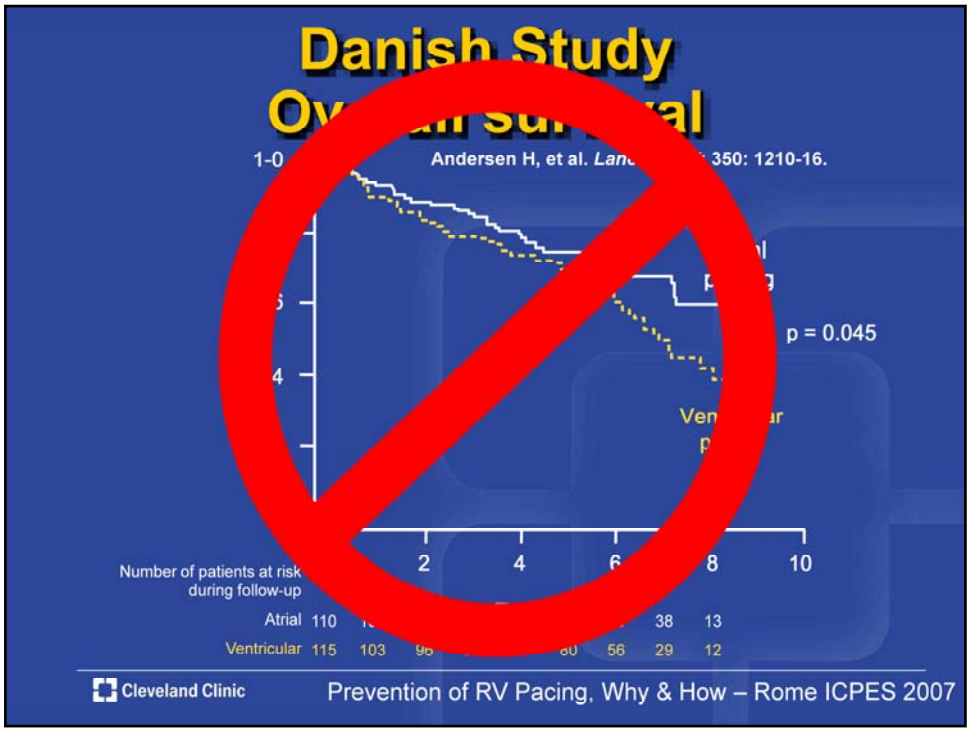


Number of patients at risk during follow-up									
Atrial pacing	110	102	96	91	80	74	49	26	10
Ventricular pacing	115	102	92	84	75	65	41	18	5

Danish Study
Overall survival

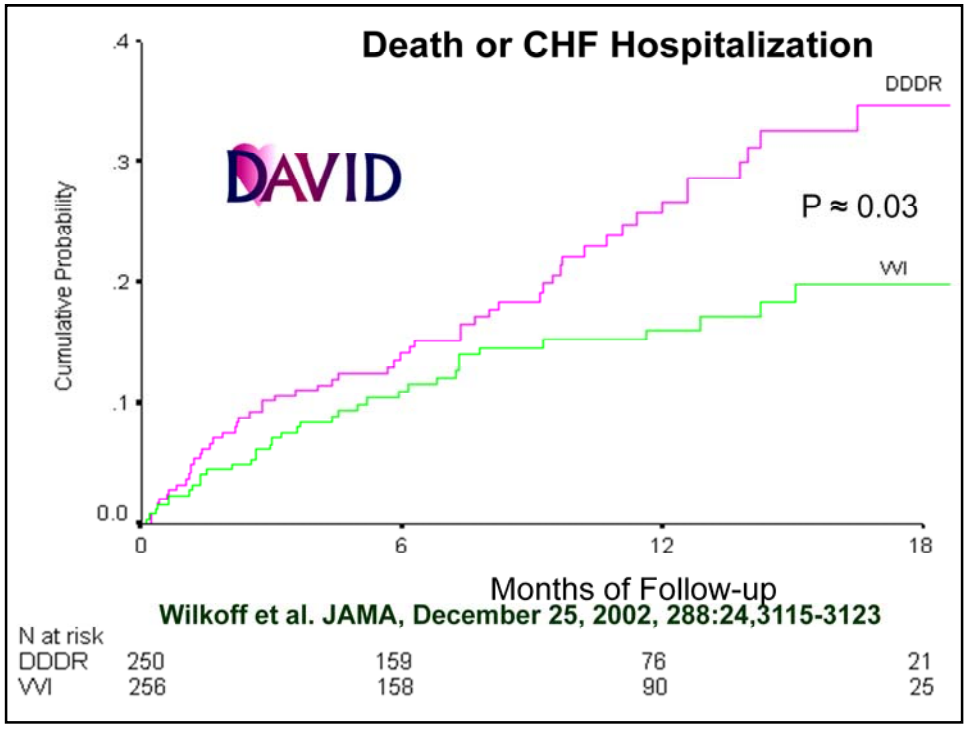


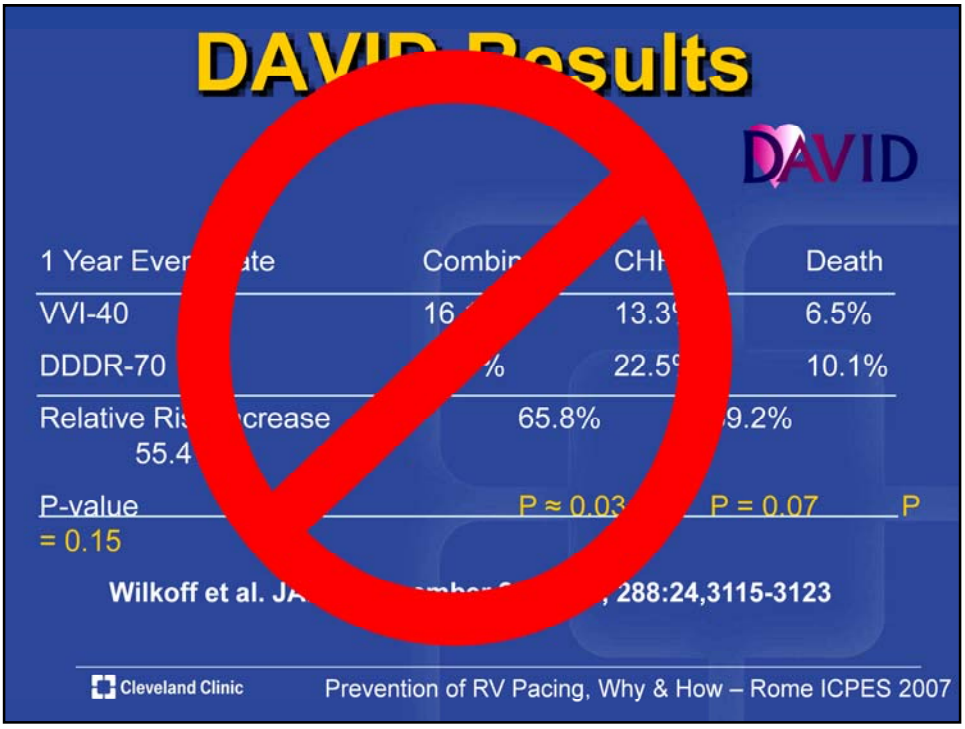
Danish Study



Implantation & Randomization

- Dual Chamber ICD (DDDR capable) Implantation
- Group 1
  - Optimal Pharmacologic Rx
  - DDDR Mode
  - Lower rate = 70 bpm
- Group 2
  - Optimal Pharmacologic Rx
  - VVI Mode
  - Lower rate = 40 bpm


Death or CHF Hospitalization
DDDR
VVI
P ≈ 0.03
Cumulative Probability
.4
.3
.2
.1
0.0
0
6
12
18
Months of Follow-up
Wilkoff et al. JAMA, December 25, 2002, 288:24,3115-3123
N at risk
DDDR 250 159 76 21
VVI 256 158 90 25


DAVID Results
DAVID
1 Year Ever ate
Combin
CH
Death
VVI-40
16
13.3
6.5%
DDDR-70
%
22.5
10.1%
Relative Ris crease
65.8%
9.2%
55.4
P-value
P ≈ 0.03
P = 0.07
P
= 0.15
Wilkoff et al. JA
, 288:24,3115-3123
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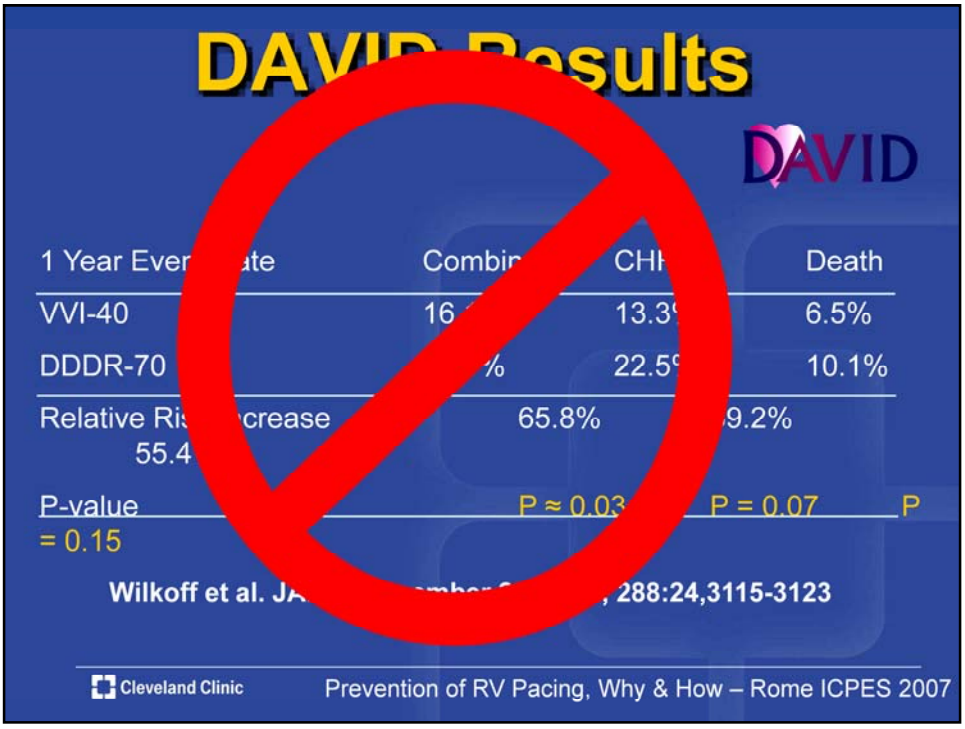
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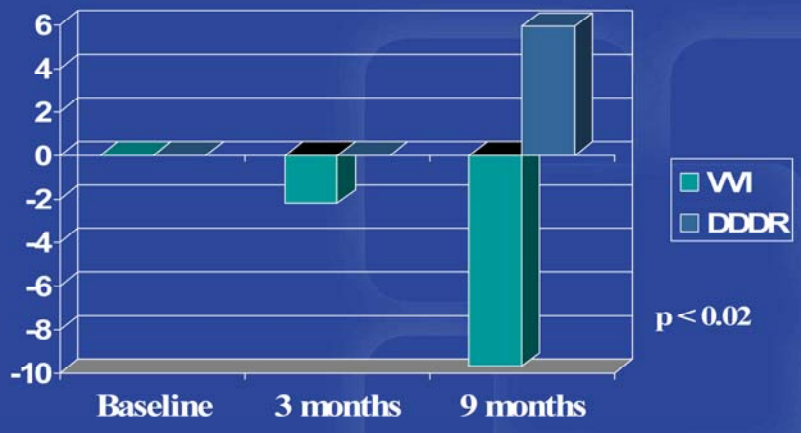
MLHF SCORE

(Lower is Better)



$p < 0.02$

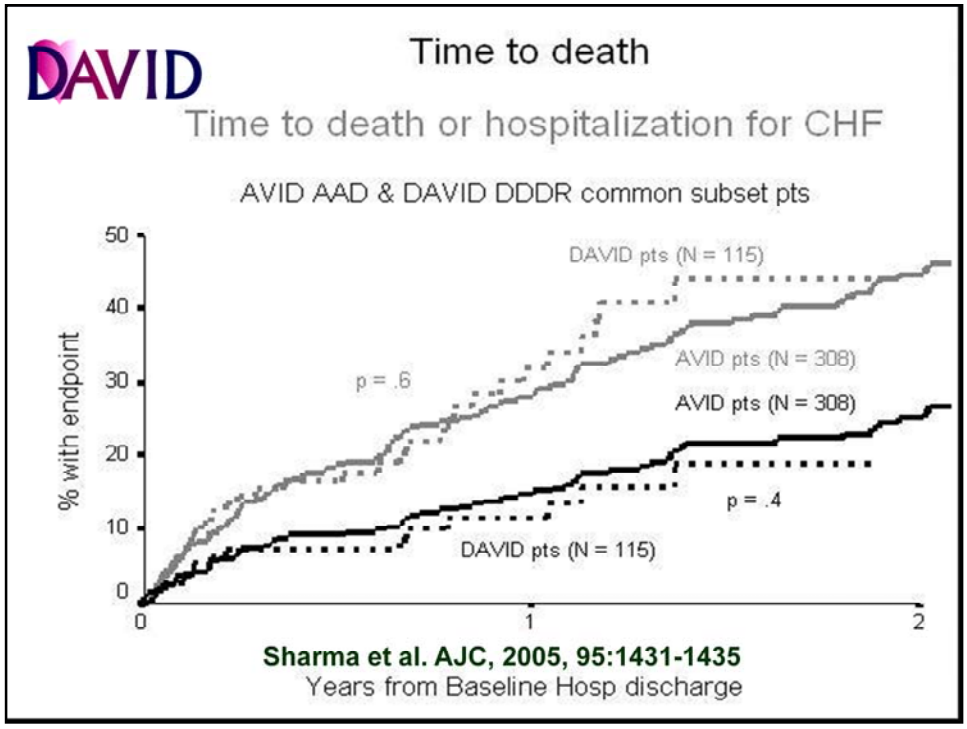
Conclusions

- DDDR pacing increases the combined endpoint of Heart Failure Hospitalization and death in comparison to ventricular backup pacing.
- No benefit and significant detriment is associated with DDDR pacing in ICD therapy indicated patient.

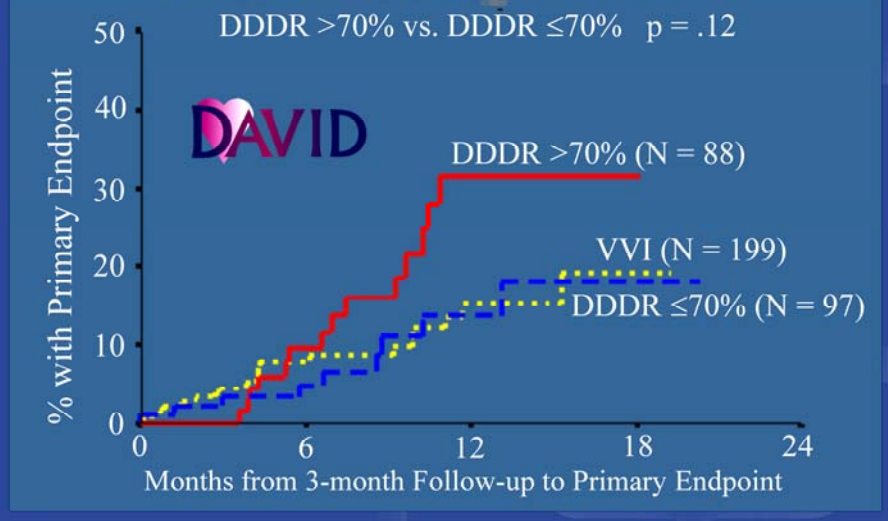
Implications

- Since DDDR pacing
  - Increases heart rate
  - Alters AV interval
  - Alters ventricular activation

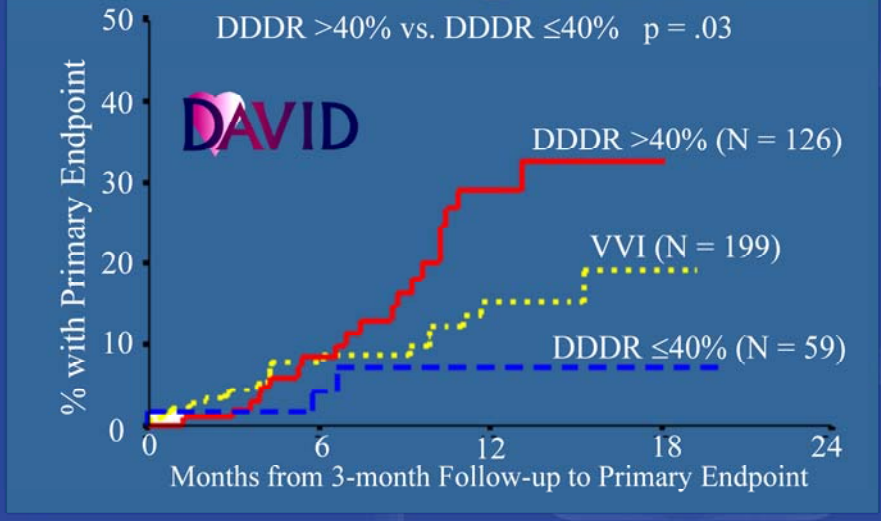
    AND
- Percent RV pacing correlates with poor outcomes
- The implication is that ventricular dyssynchrony caused by RV pacing produces this adverse outcome and should be avoided in ICD indicated patients without indications for antibradycardia pacemaker support.


DAVID
Time to death
Time to death or hospitalization for CHF
AVID AAD & DAVID DDDR common subset pts
% with endpoint
50
40
30
20
10
0
0
1
2
DAVID pts (N = 115)
AVID pts (N = 308)
p = .6
AVID pts (N = 308)
p = .4
DAVID pts (N = 115)
Sharma et al. AJC, 2005, 95:1431-1435
Years from Baseline Hosp discharge

Outcomes Analysis: 70% V-Pacing in DDDR

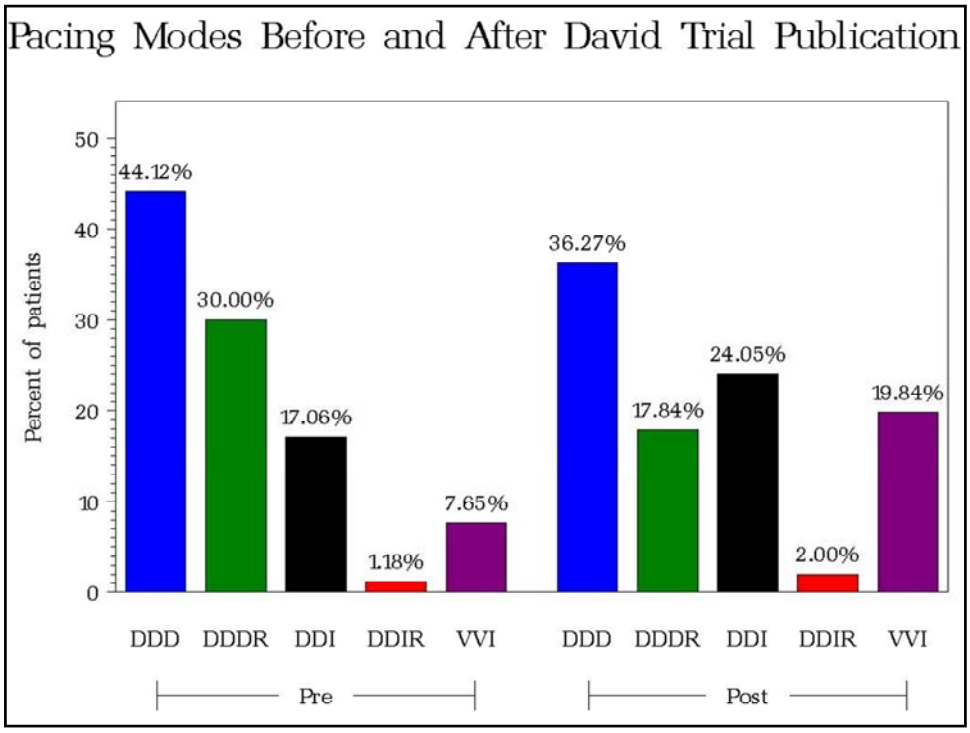


Outcomes Analysis: 40% V-Pacing in DDDR

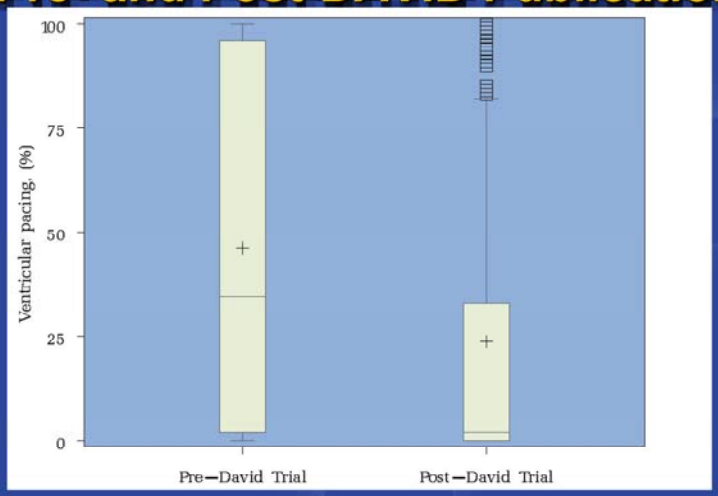


EMPIRIC Methodology

- Patients divided into 2 groups
  - Before DAVID Trial Publication
  - After DAVID trial Results – 12/25/02
- Pacing Mode:
  - Implant programming until first follow-up
- Percentage Ventricular Pacing
  - 3 month interrogation


Pacing Modes Before and After David Trial Publication
Percent of patients
50
40
30
20
10
0
44.12%
30.00%
17.06%
1.18%
7.65%
36.27%
17.84%
24.05%
2.00%
19.84%
DDD
DDDR
DDI
DDIR
VVI
DDD
DDDR
DDI
DDIR
VVI
Pre
Post

Percent Ventricular Pacing Pre- and Post-DAVID Publication



Before: 47% of patients paced over 40% of time
After: 23% of patients paced over 40% of time

Right Ventricular Outflow Versus Apical Pacing in Pacemaker Patients with Congestive Heart Failure and Atrial Fibrillation

Right Ventricular Pacing Site in Heart Failure. *Introduction:* Prior studies suggest that right ventricular apical (RVA) pacing has deleterious effects. Whether the right ventricular outflow tract (RVOT) is a more optimal site for permanent pacing in patients with congestive heart failure (CHF) has not been established.

Methods and Results: We conducted a randomized, cross-over trial to determine whether quality of life (QOL) is better after 3 months of RVOT than RVA pacing in 103 pacemaker recipients with CHF, left ventricular (LV) systolic dysfunction (LV ejection fraction $\leq 40\%$), and chronic atrial fibrillation (AF). An additional aim was to compare dual-site (RVOT + RVA, 31-ms delay) with single-site RVA and RVOT pacing. QRS duration was shorter during RVOT (167 ± 45 ms) and dual-site (149 ± 19 ms) than RVA pacing (180 ± 58 ms, $P < 0.0001$). At 6 months, the RVOT group had higher ($P = 0.01$) role-emotional QOL subscale scores than the RVA group. At 9 months, there were no significant differences in QOL scores between RVOT and RVA groups. Comparing RVOT to RVA pacing within the same patient, mental health subscale scores were better ($P = 0.03$) during RVOT pacing. After 9 months of follow-up, LVEF was higher ($P = 0.04$) in those assigned to RVA rather than RVOT pacing between months 6 and 9. After 3 months of dual-site RV pacing, physical functioning was worse ($P = 0.04$) than during RVA pacing, mental health was worse ($P = 0.02$) than during RVOT pacing, and New York Heart Association (NYHA) functional class was slightly better ($P = 0.03$) than during RVOT pacing. There were no other significant differences between RVA, RVOT and dual-site RV pacing in QOL scores, NYHA class, distance walked in 6 minutes, LV ejection fraction, or mitral regurgitation.

Conclusion: In patients with CHF, LV dysfunction, and chronic AF, RVOT and dual-site RV pacing shorten QRS duration but after 3 months do not consistently improve QOL or other clinical outcomes compared with RVA pacing. *(J Cardiovasc Electrophysiol, Vol. 14, pp. 1180-1186, November 2003)*

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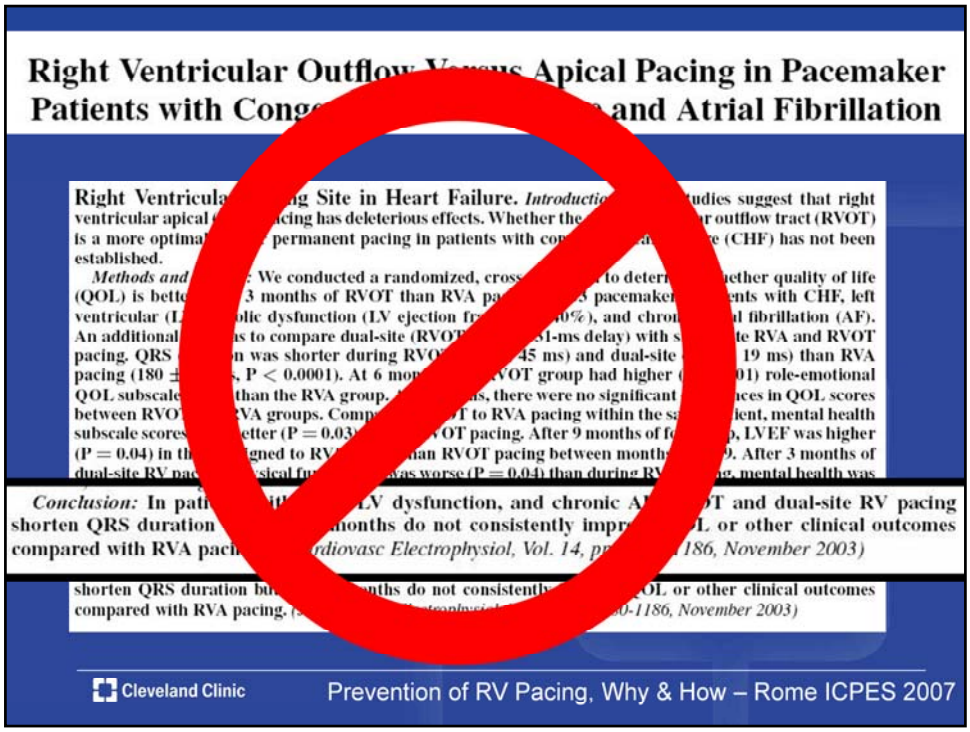
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Conclusion: In pati LV dysfunction, and chronic A T and dual-site RV pacing shorten QRS duration months do not consistently impr L or other clinical outcomes compared with RVA paci rdiovasc Electrophysiol, Vol. 14, pr 186, November 2003)
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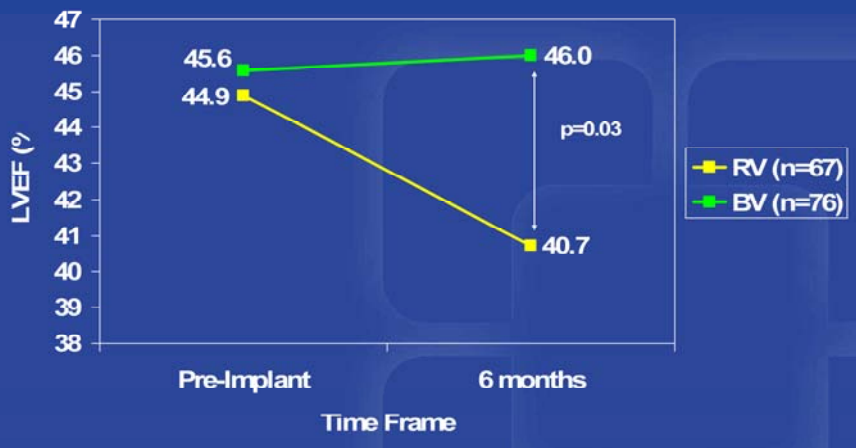
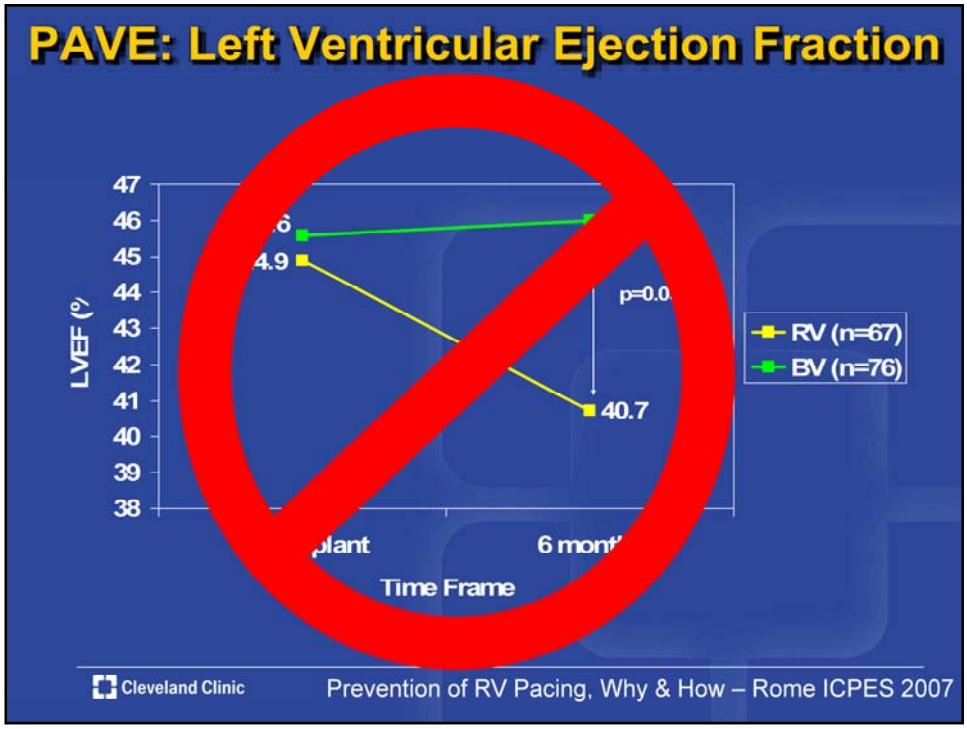
PAVE: Left Ventricular Ejection Fraction




PAVE: Left Ventricular Ejection Fraction
47
46
45
44
43
42
41
40
39
38
LVEF (%)
4.9
p=0.0
40.7
RV (n=67)
BV (n=76)
Time Frame
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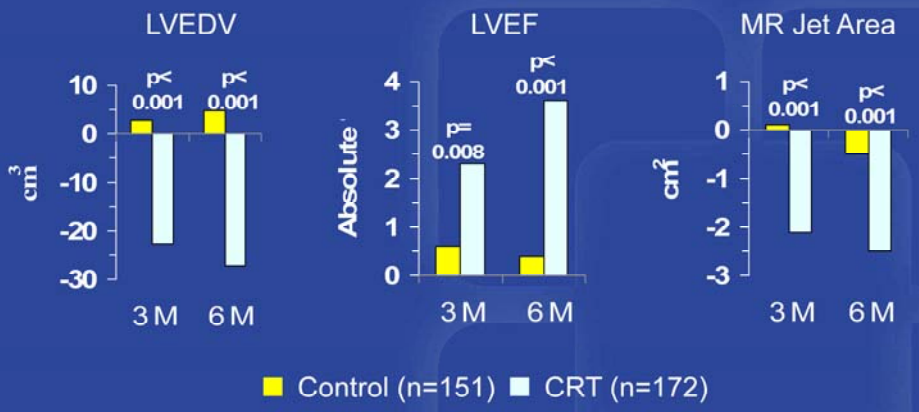
MIRACLE
Effect on LV Size and Function

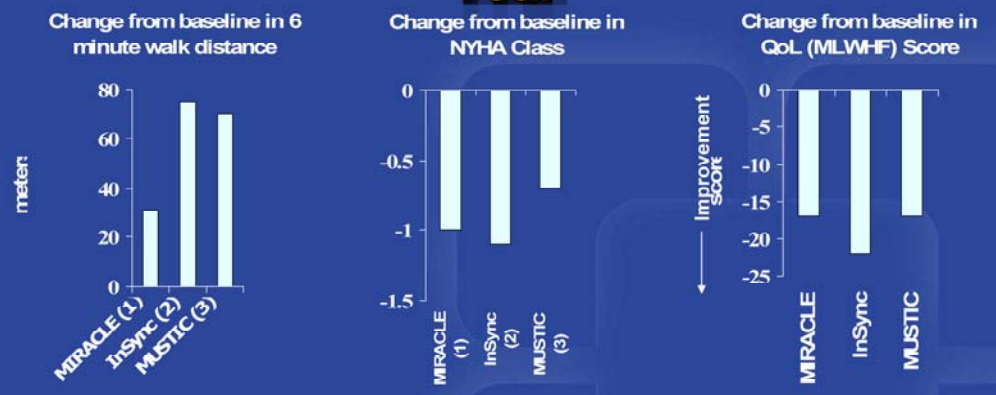
Paired, Median Changes from Baseline



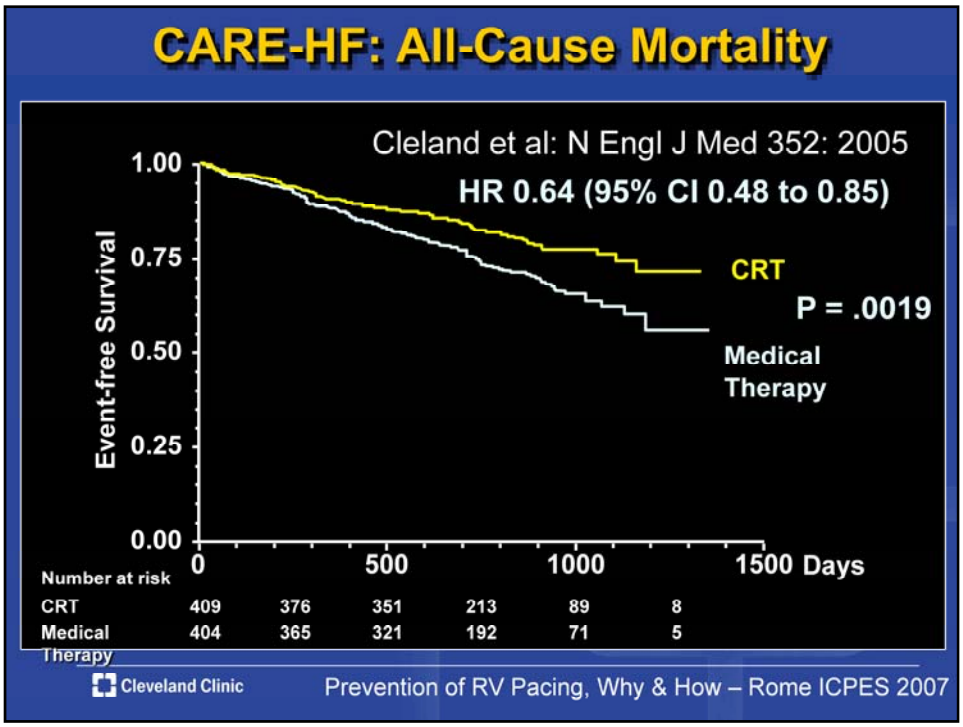
Control (n=151) CRT (n=172)

St. John Sutton M, et al. Circulation 2003;107:1985-1990

Therapy Benefits Sustained Through 1 Year



1. *World Congress of Cardiology 2002* (MIRACLE)
2. *Eur J Heart Fail* 2002;4:311-20 (InSync Europe & Canada)
3. *JACC* 2002;4:111-8 (MUSTIC)



There was a striking reduction in mortality in the CRT group. The absolute difference between control and CRT was 10%. Again, there was no early hazard and the curves begin to separate within the first 6 months of randomisation. A reduction in both sudden deaths and deaths due to worsening heart failure was observed. There were only 29 sudden deaths out of 82 in the CRT group.

The benefits of CRT are in addition to those of the above pharmacological therapy. The absolute difference in mortality at 2 years was 7.1%. This compares to 5.2% with enalapril in the SOLVD-treatment study and is similar to the estimated two-year mortality difference between placebo and bisoprolol in the CIBIS-II study or the 8.8% difference between placebo and carvedilol in COPERNICUS (which using the method of trial duration used in our study had a duration of about 15 months).

The hazard ratio of the effect of CRT in CARE-HF (0.64; 95% confidence interval 0.48 to 0.85; p=0.0019) was similar to that of CRT-D compared to control in the COMPANION trial (0.64, 95% confidence interval, 0.48 to 0.86; P=0.003) . The absolute estimated difference at 2 years in the COMPANION study between CRT-D and control was about 8% with CRT and CRT-D having similar effects in that study.

AAI ICD - Theoretical Advantages

- VT/VF therapy equivalent to VVI-ICD
- Electrophysiologic effects
  - Chronotropic benefit
  - Fewer shocks
  - Less atrial fibrillation
    - Fewer symptoms
    - Less CVA
- Hemodynamic benefits - Improved cardiac output
  - Better tolerance of CHF medications
  - Fewer CHF symptoms
  - Less CHF death
  - More energy
  - Improved quality of life

DAVID II

ICD Indication

Optimal CHF therapy

Endpoint: Death or CHF Hospitalization

Intention to Treat Analysis

DAVID I - V Pacing

Percent beats ventricular paced

	VVI	DDDR	p-value
3 months	1.5%	57.6%	0.001
6 months	0.7%	60.7%	0.001
12 months	2.9%	61.0%	0.001

DAVID II - Pacing at Follow-up

Ventricular pacing

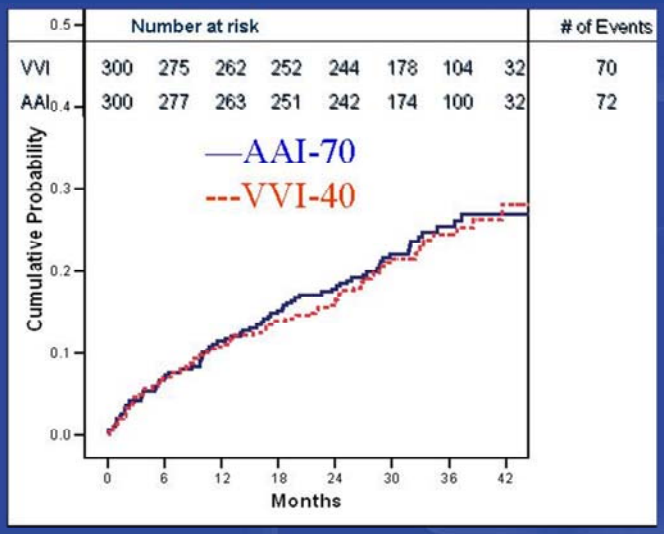
Follow-up	Beats paced (%)*	Range*
3-month	1.2	1 – 14
24-month	1.0	1 – 5

Atrial pacing

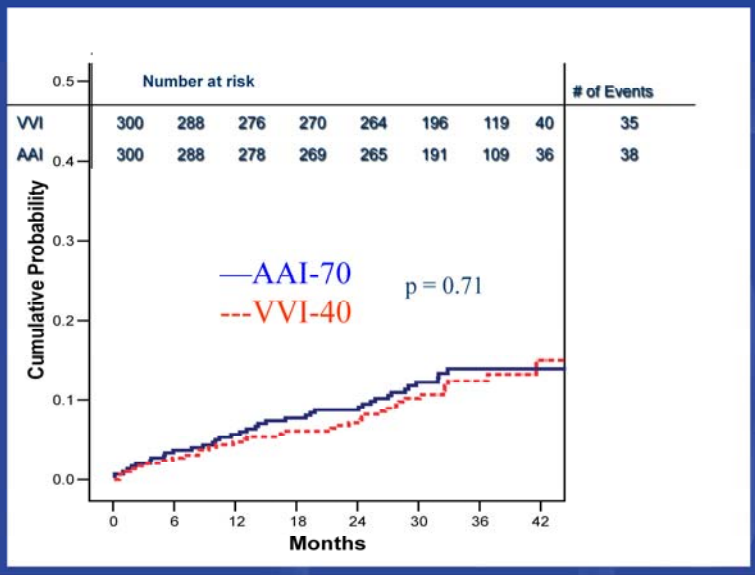
Follow-up	Beats paced (%)*	Range*
3-month	47	1 - 99
24-month	51	1 - 99

*among the ~90% of patients in both treatment arms who received pacing

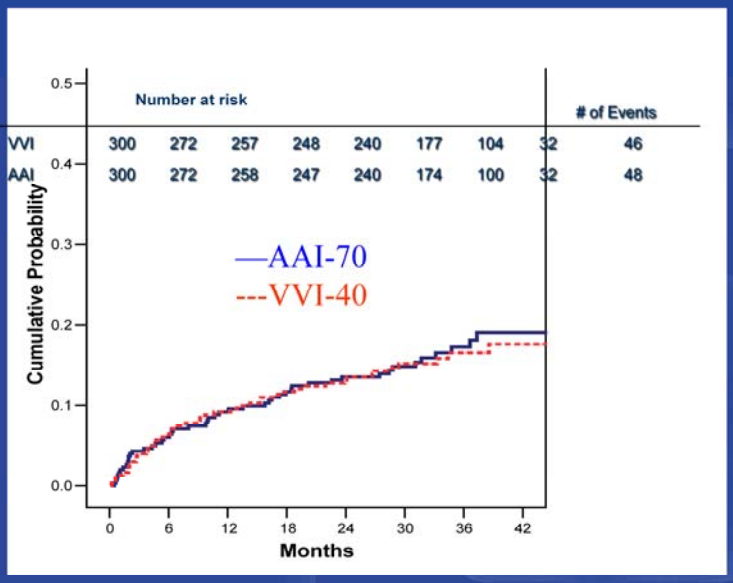
Primary Outcome
Death or Re-hospitalization for New/Worsened CHF

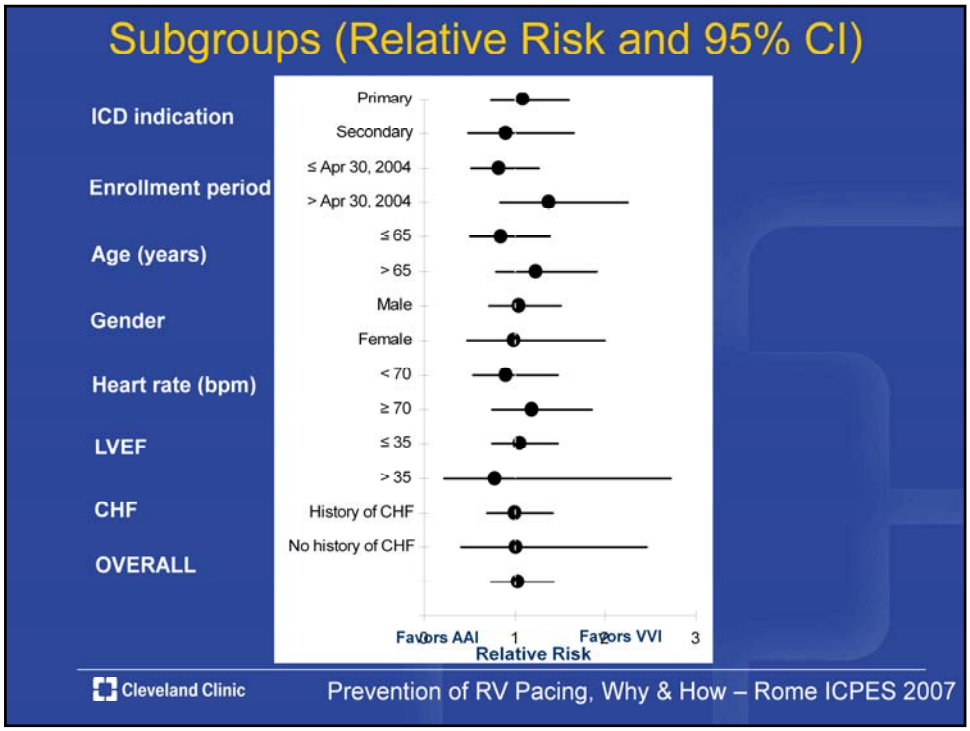


Death


Number at risk
# of Events
VVI 300 288 276 270 264 196 119 40 35
AAI 300 288 278 269 265 191 109 36 38
Cumulative Probability
0.5
0.4
0.3
0.2
0.1
0.0
—AAI-70
---VVI-40
p = 0.71
0 6 12 18 24 30 36 42
Months

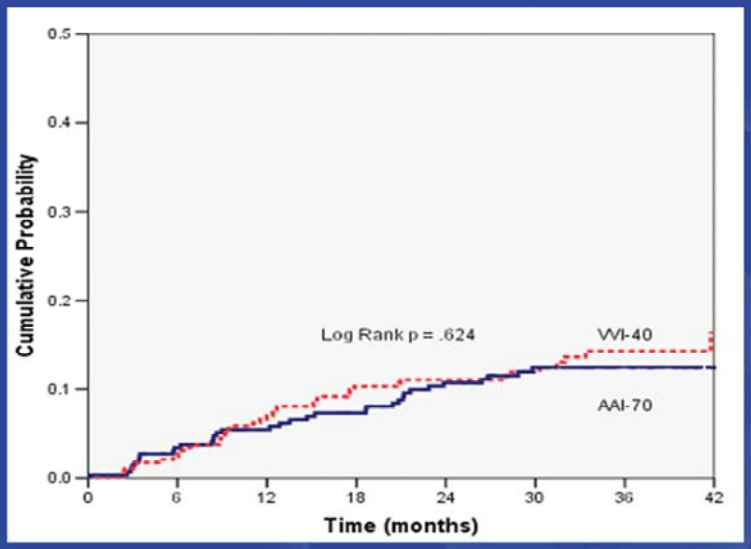
Re-hospitalization for New or Worsened CHF



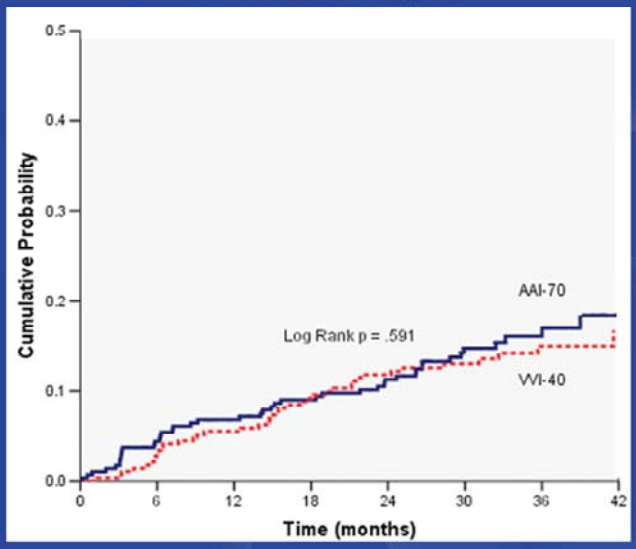


No subgroup results differed from the overall result.

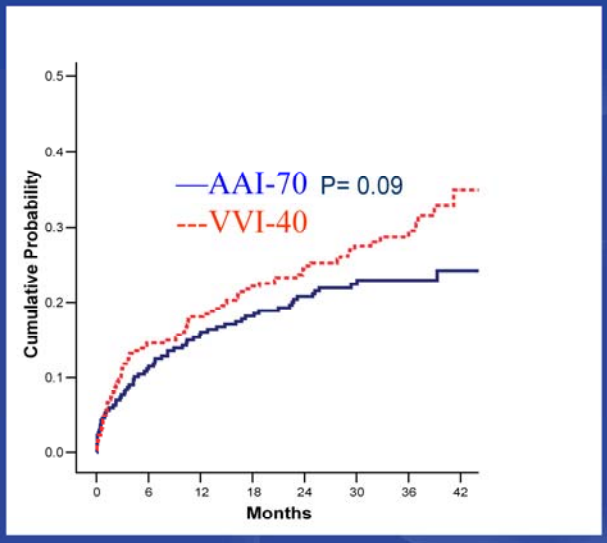
Atrial Fibrillation

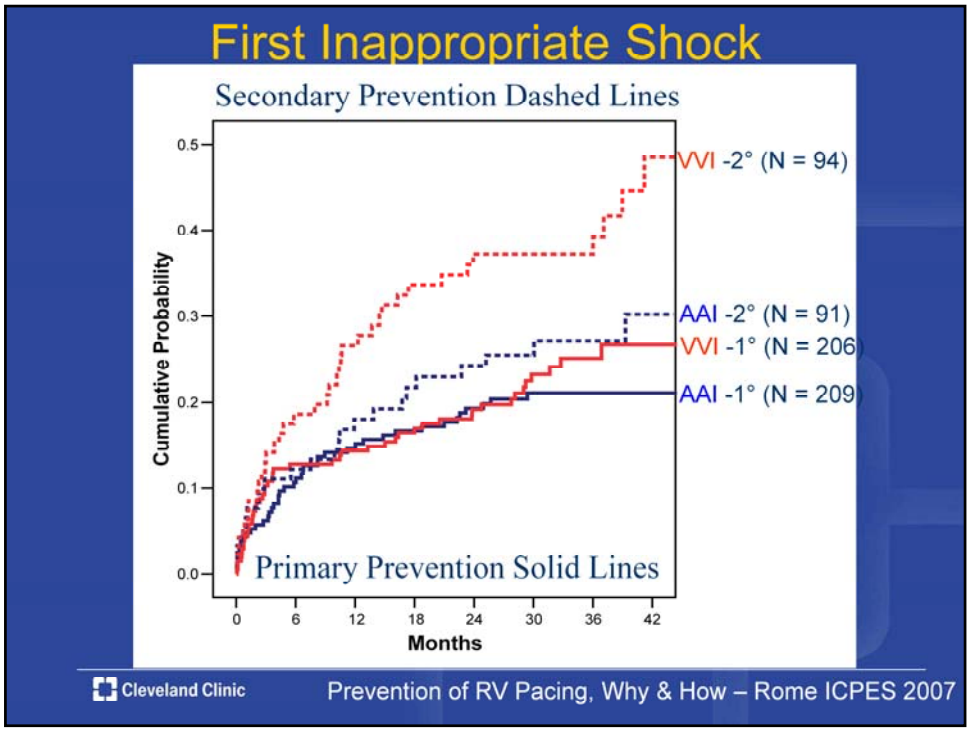


First Syncope

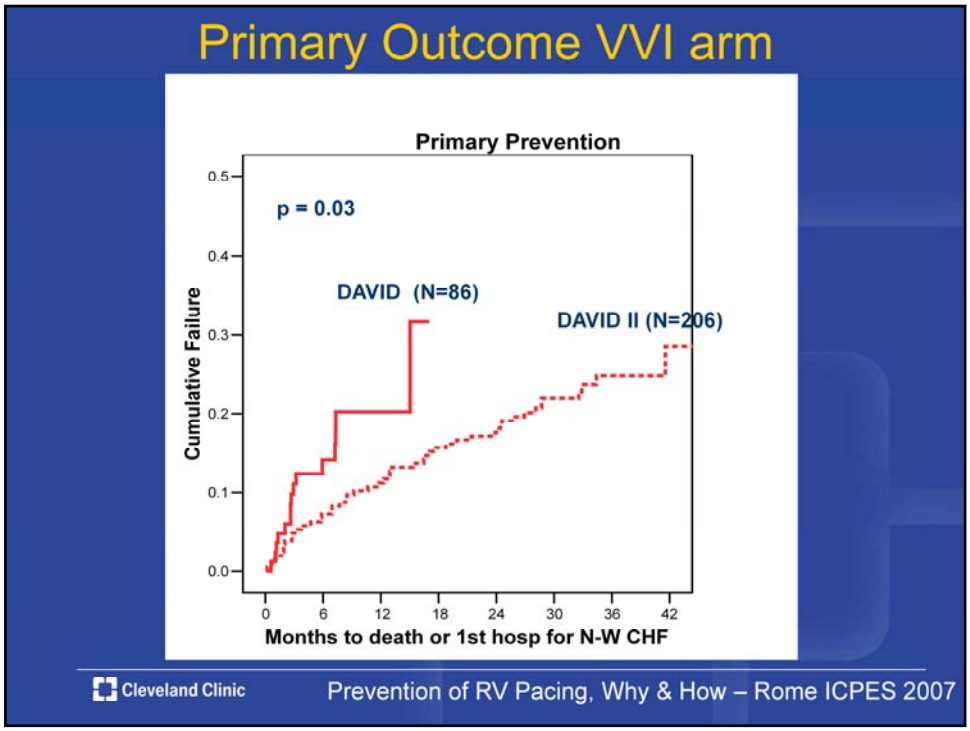


First Inappropriate Shock



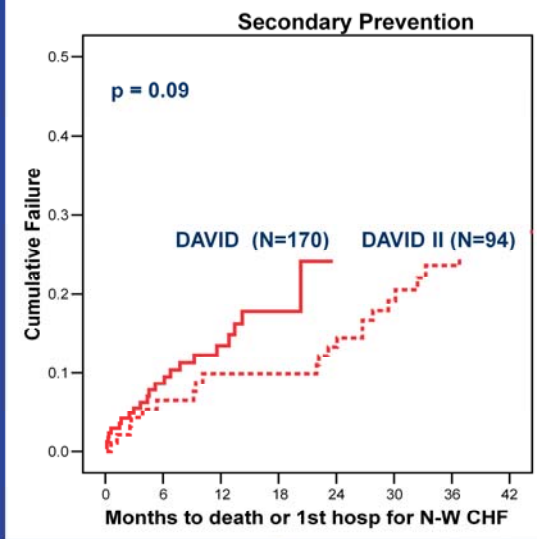


It is of interest that the benefit of AAI in reducing inappropriate shocks appears to be restricted to secondary prevention patients.



The primary outcome in DAVID II was below predicted based on DAVID, but in the end the same cumulative failure was obtained; that is, there is as much information in DAVID II as in DAVID.

Primary Outcome VVI arm



Summary

- No statistically significant differences in outcome between AAI-70 and VVI-40 treated patients
  - Mortality or CHF hospitalization
  - New onset AF
  - Syncope
  - Quality of life
- No differential benefit related to pacing mode among patient subgroups
- No significant impact of pacing mode on heart failure medication use in follow-up

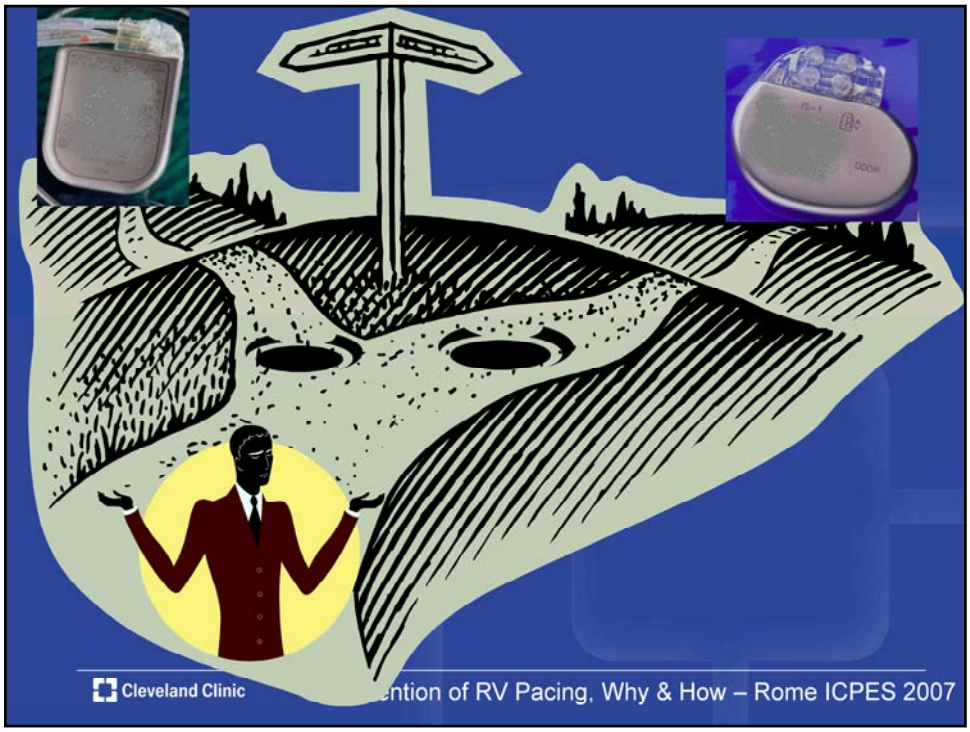
Conclusions

In patients with LV dysfunction who need an ICD but have no indications for pacing . . .

- The effect of atrial-based pacing (AAI-70) on event-free survival and quality of life is not substantially worse than, and is likely equivalent to ventricular back-up pacing (VVI-40)
- Atrial (AAI-70) pacing may be considered a "safe alternative," but affords no clear advantage nor disadvantage over ventricular back-up (VVI-40) pacing

Implications

- LV dysfunction + QRS duration are powerful predictors of Mortality
- Implantable devices have the potential to influence both LV function and QRS duration
- Ventricular stimulation, most common during dual chamber pacing, has the potential to adversely effect survival.
- AAI ICDs, VVI ICDs or BiV ICDs might be the only acceptable techniques for ICD therapy.


Cleveland Clinic
ention of RV Pacing, Why & How – Rome ICPES 2007