

Non-Pharmacologic Treatment in Heart Failure

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Device-based treatment of heart failure

Function of device

Examples

Monitor heart failure condition

Implantable hemodynamic monitors, home scales, home monitoring systems

Prevent or treat rhythm disturbances

Pacemakers for bradycardia, ICD, LifeWest Wearable AED (LIFECOR, Inc, PA)

Improve mechanical efficiency of the heart

Left ventricular or multisite pacing, Biventricular pacing, CorCap (Accorn, MN) Myosplint (Myocor, MN)

Cardiac replacement therapy

LVAD, BiVAD, TAH

Adapted from Boehmer, Am J Cardiol, 2003

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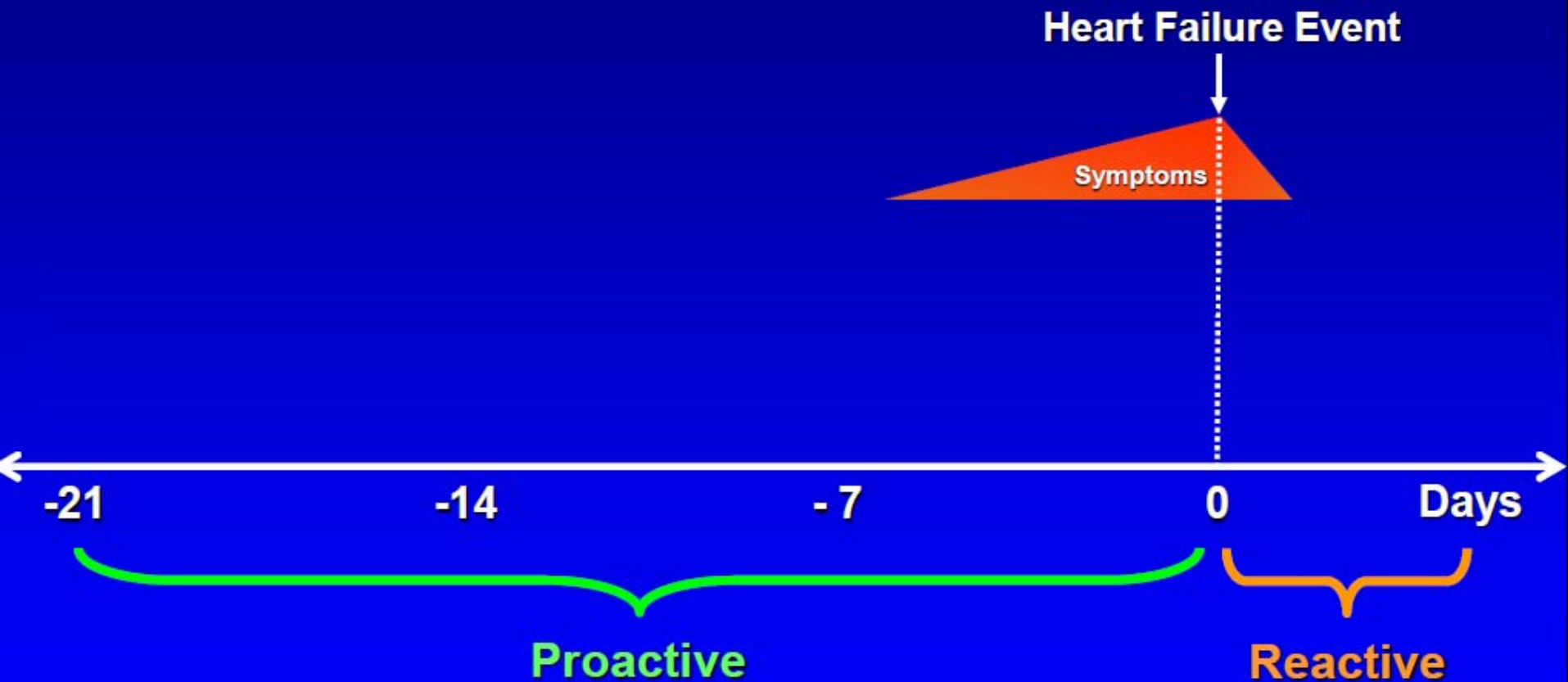
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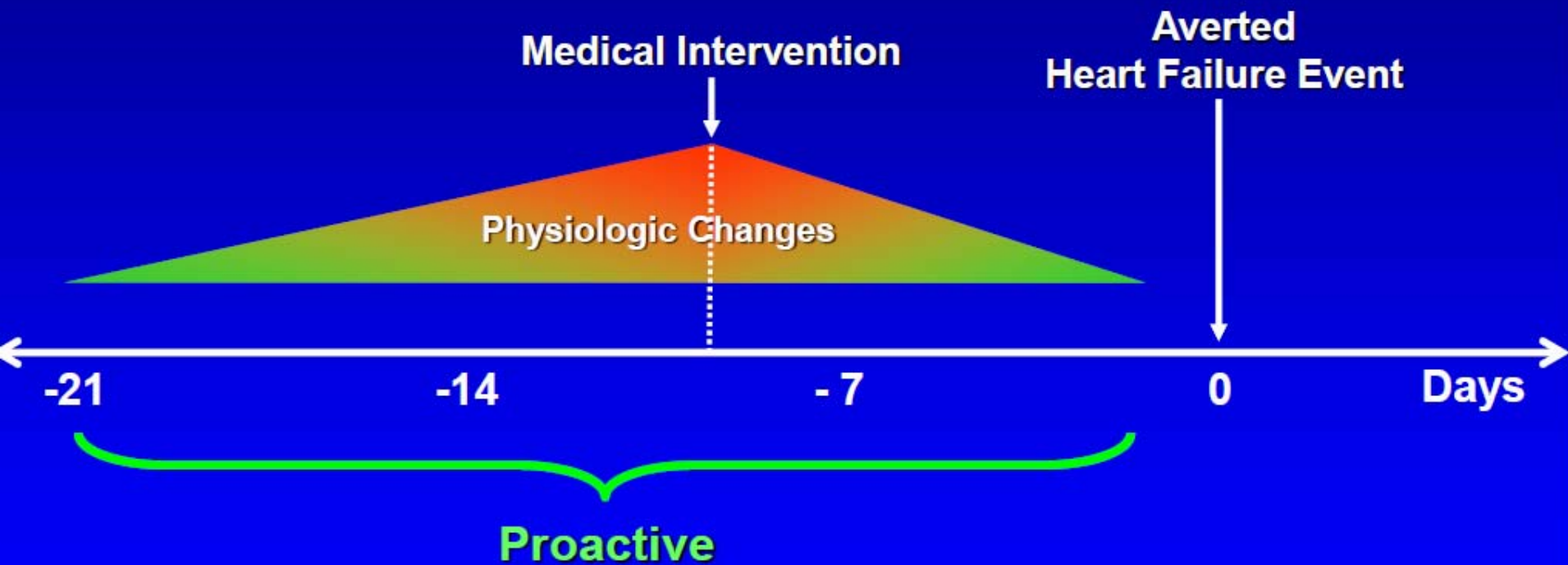
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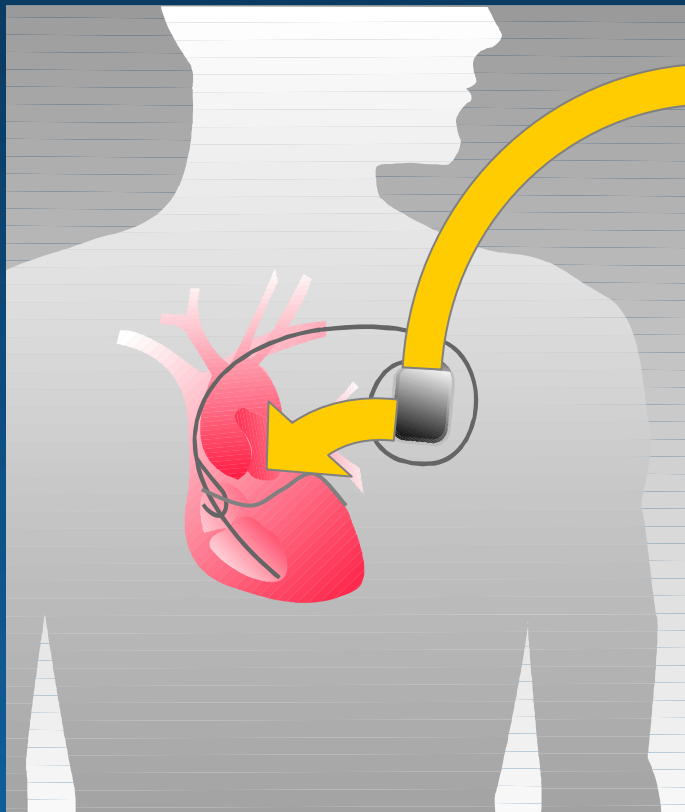
Physiological Premise of Implantable HF Device Diagnostics (1)



Physiological Premise of Implantable HF Device Diagnostics (2)



Devices in heart failure



Diagnostic capabilities

- Arrhythmia monitoring
- Heart rate
- Percent pacing
- Physical activity
- Heart rate variability
- Intrathoracic impedance
- RV pressures

Implantable Hemodynamic Monitors



PA Pressure Sensors



RV Pressure Sensors



LV Pressure Sensor



LA Pressure Sensor

The Chronicle[®]

Implantable continuous hemodynamic monitor (ICHM)



External
Pressure
Reference



- Heart rate
- Syst RV pressure
- Diast RV pressure
- RV pulse pressure
- ePAD
- pos dP/dt_{max}
- neg dP/dt_{max}
- PEI
- STI
- Activity

Randomized Controlled Trial of an Implantable Continuous Hemodynamic Monitor in Patients With Advanced Heart Failure

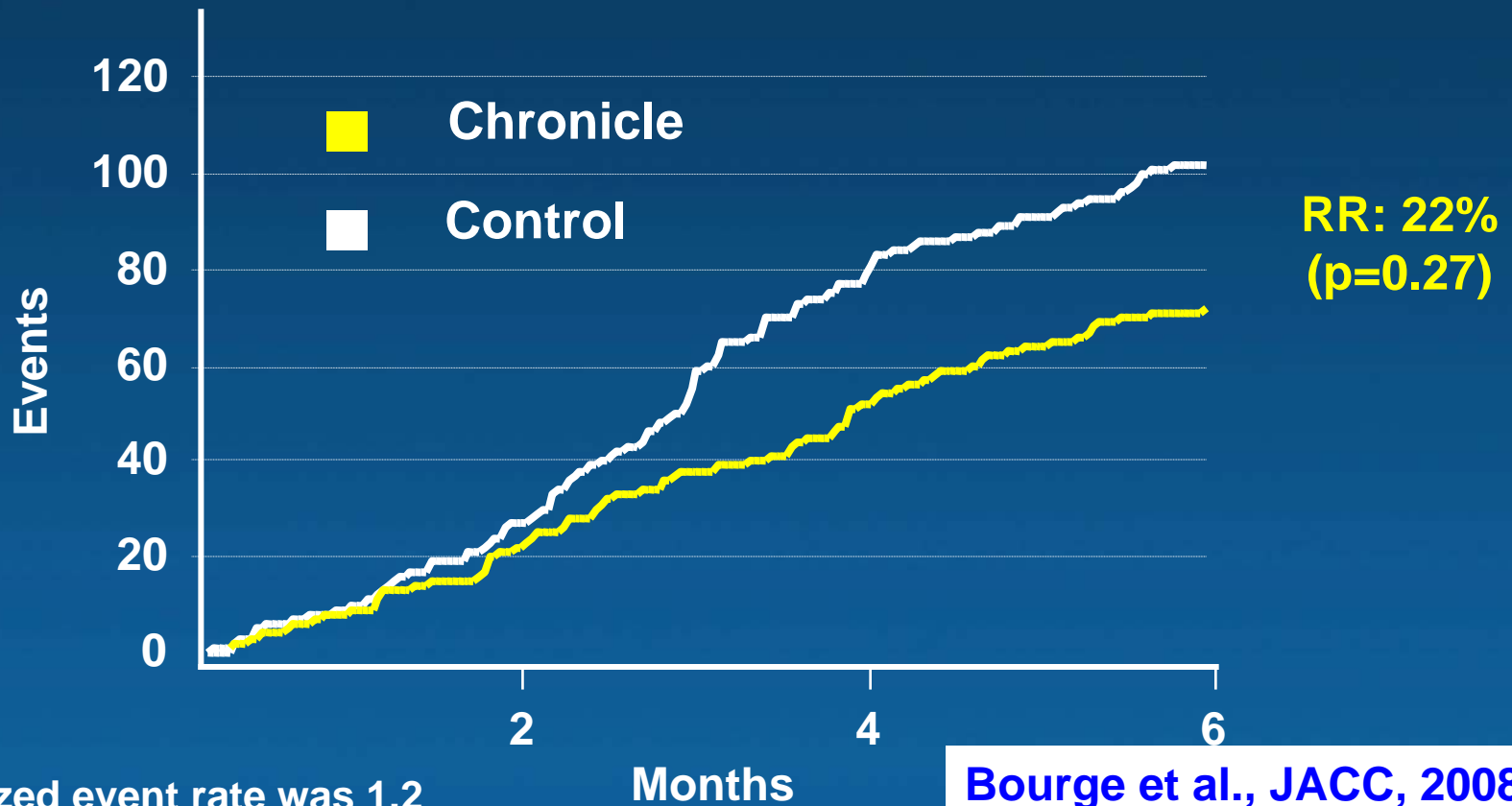
The COMPASS-HF Study

- 1 Primary Effectiveness end-point - the Chronicle group would have a 30% lower rate of combined HF-related events (hospitalizations, emergency department and urgent clinic visits requiring intravenous therapy) compared with the control group.

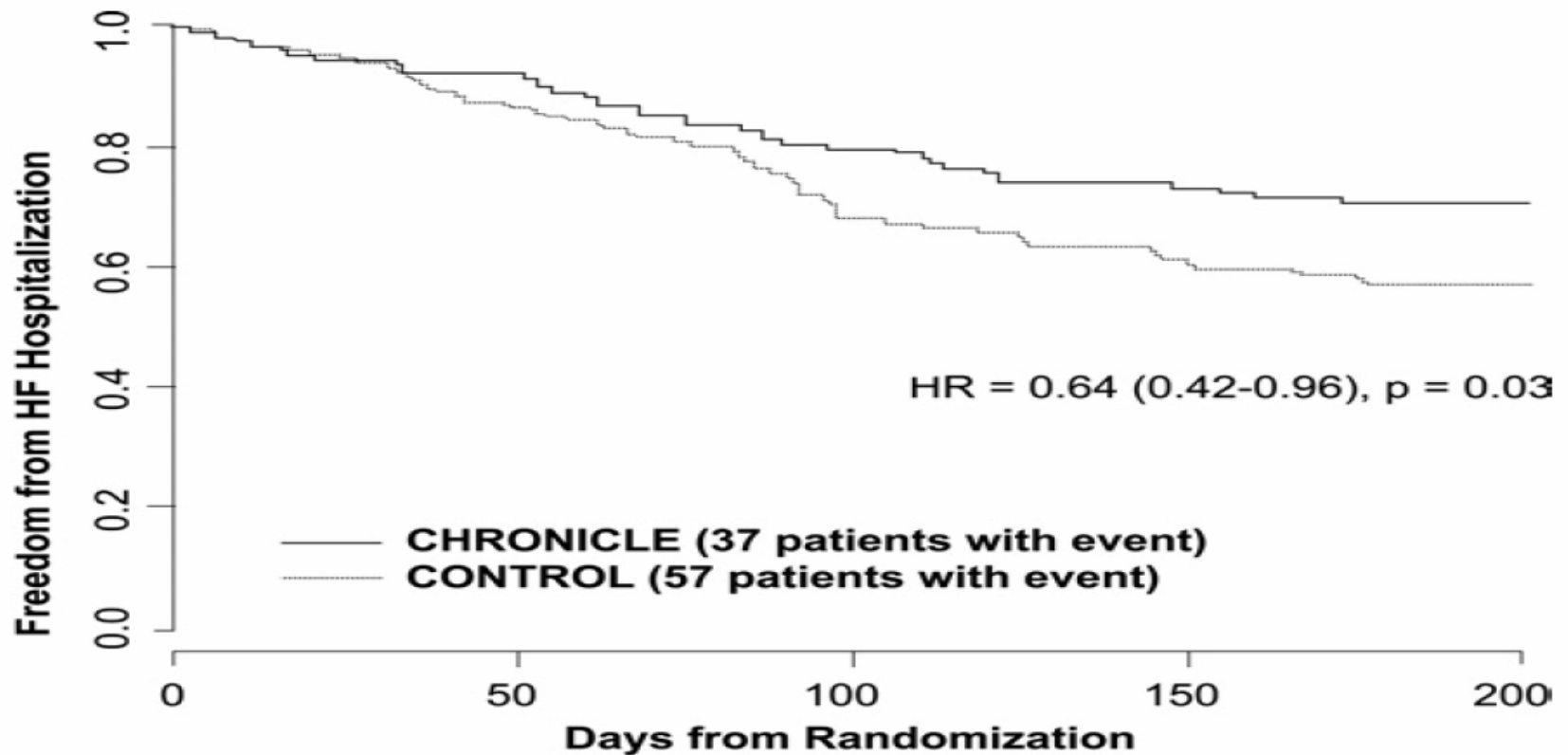
Bourge et al., JACC, 2008

COMPASS-HF

HF-related Hospitalization Cumulative Events



Reduction in relative risk of a first heart failure related hospitalization



Number at Risk

CHRONICLE	124	120	108	101	93	89	84	4
CONTROL	132	119	110	91	87	80	77	3

Conclusions

- 1 In patients with moderate to severe HF, the addition of an ICHM to optimal medical management did not significantly reduce the rate of all HF-related events.
- 1 Additional trials will be necessary to establish clinical benefit of ICHM-guided care in this patient population.

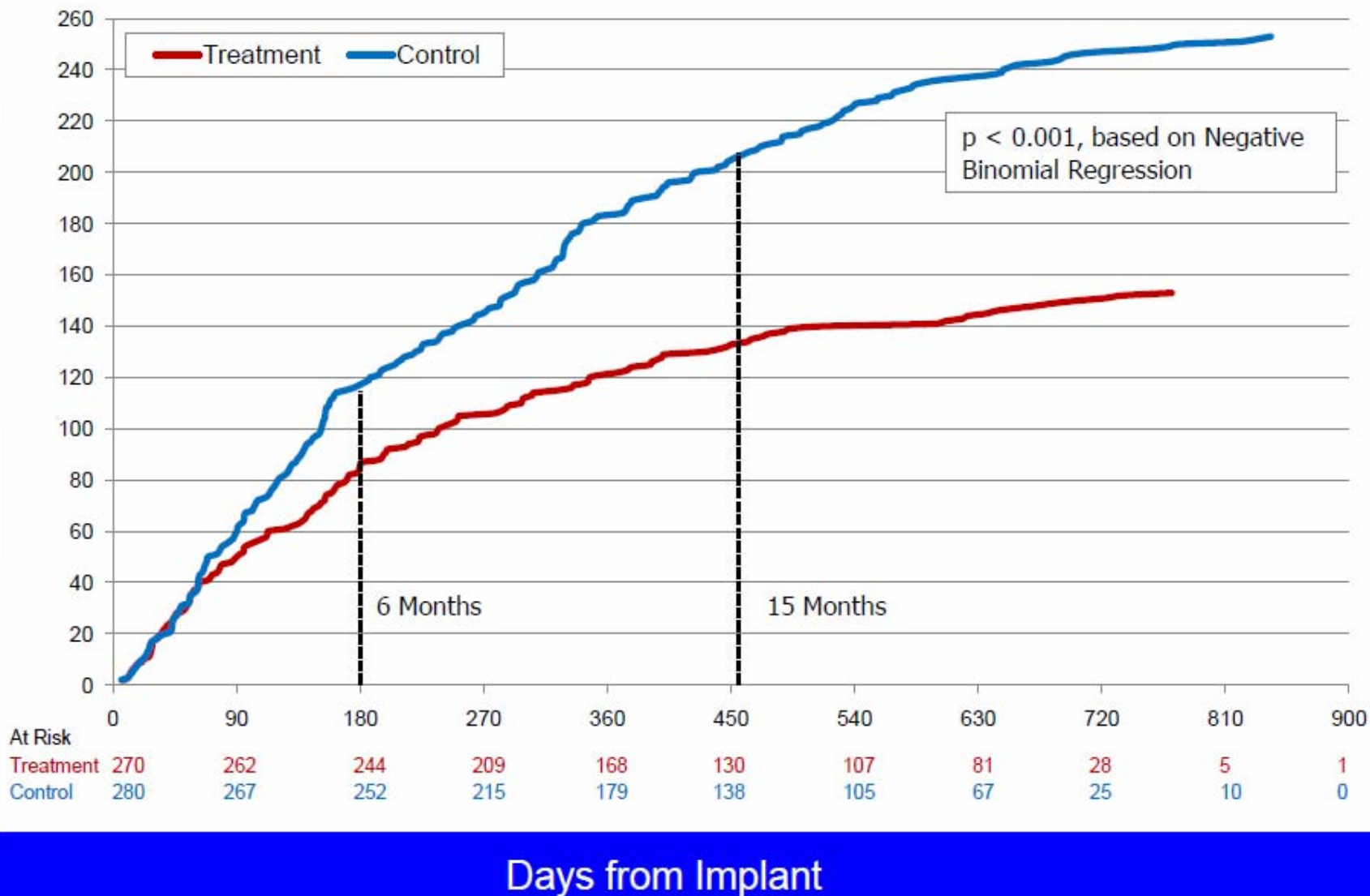
**Primary Results of the CardioMEMS
Heart Sensor Allows Monitoring of
Pressure to Improve Outcomes in NYHA
Class III Heart Failure Patients
(CHAMPION) Trial**

William T. Abraham, MD and Philip B. Adamson, MD
On behalf of the CHAMPION Trial Committees
and Study Group

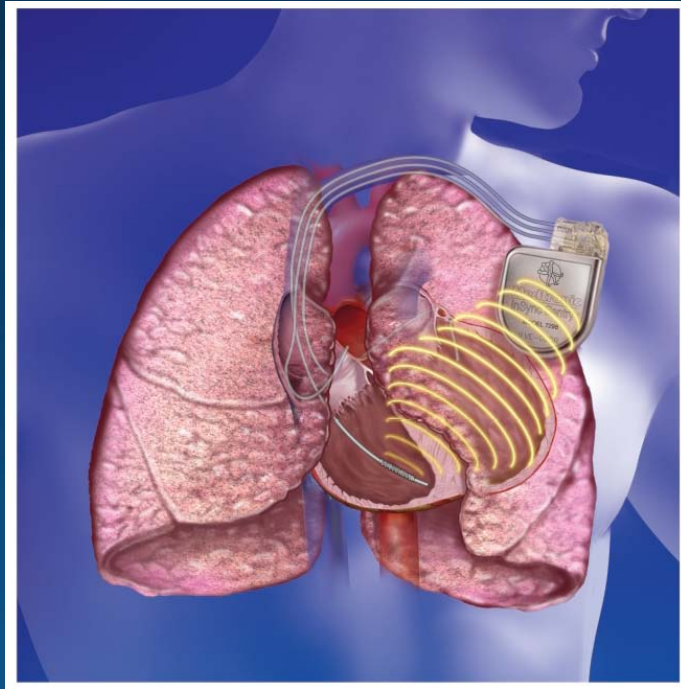
Presented at ESC-HF 2010

Cumulative HF Hospitalizations Over Entire Randomized Follow-Up Period

Cumulative Number of HF Hospitalizations



Intrathoracic impedance



Dryer lungs

Impedance



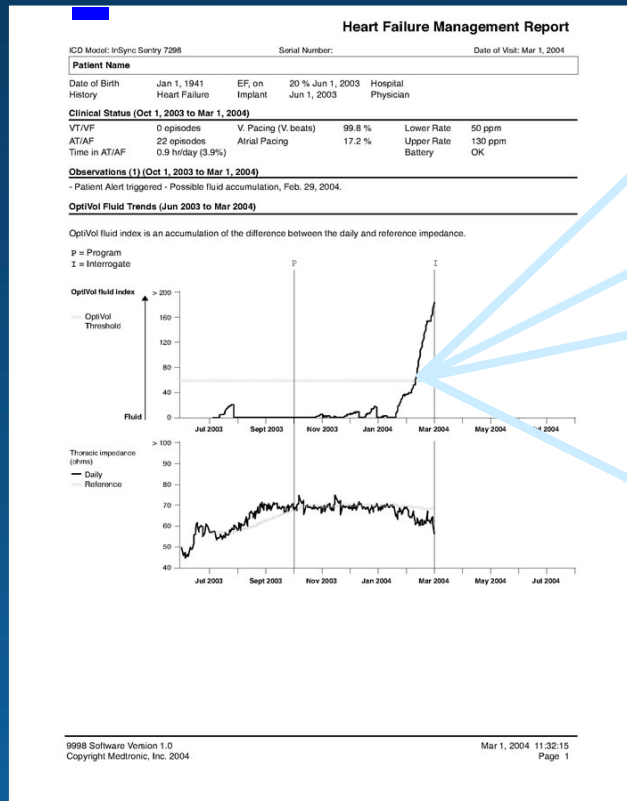
Wetter lungs

Impedance



Intrathoracic impedance

Fluid Accumulation Notification Options



- Observations with Trends
- Device audible alert
- SentryCheck™
- Patient look indicator





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SOCIETY OF
CARDIOLOGY®

European Heart Journal (2007) 28, 1835–1840
doi:10.1093/eurheartj/ehl506

European
Heart Journal

Clinical research
Heart failure/cardiomyopathy

Clinical utility of intrathoracic impedance monitoring to alert patients with an implanted device of deteriorating chronic heart failure

- 1 640 pts with heart failure eligible for CRT-D (InSync Sentry®, Medtronic Inc, USA) implantation were enrolled in 42 countries.**
- 1 Lack of FU reports in 267 pts.**
- 1 Finally 373 pt files were analyzed.**

Vollmann et al., 2008

Main Findings

- 1 The device alert detected HF deterioration with an adjusted sensitivity and an adjusted PPV of 60% each.
- 1 Failure of the alert algorithm to detect clinical HF deterioration was in 55% of the cases associated with an increase of the fluid index that was yet below the programmable alert threshold.
- 1 Half of the false-positive alerts were related to other clinical findings or therapeutic interventions.

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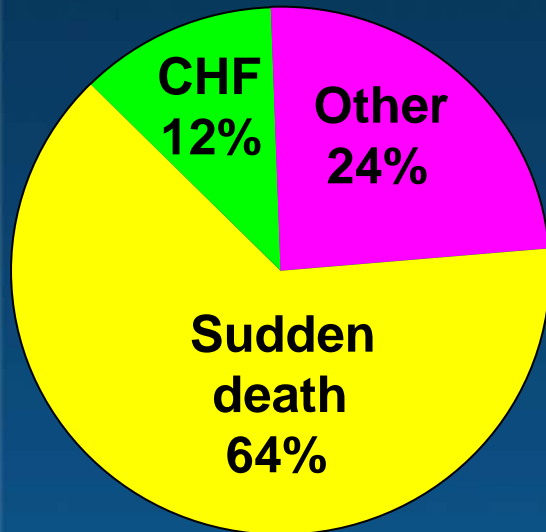
Cardiac replacement therapy

LVAD, BiVAD, TAH

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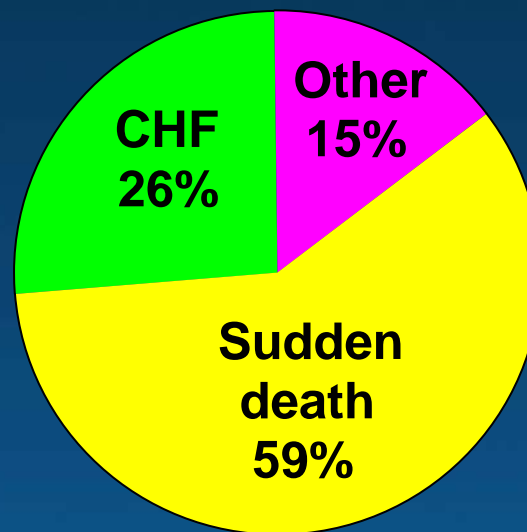
Severity of Heart Failure and Mode of Death

NYHA II



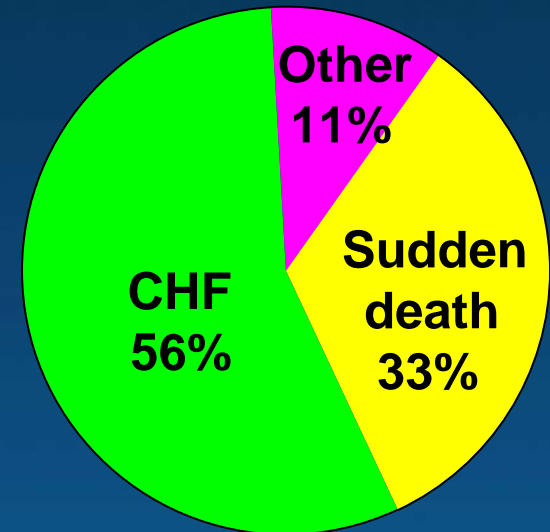
N=103

NYHA III



N=232

NYHA IV

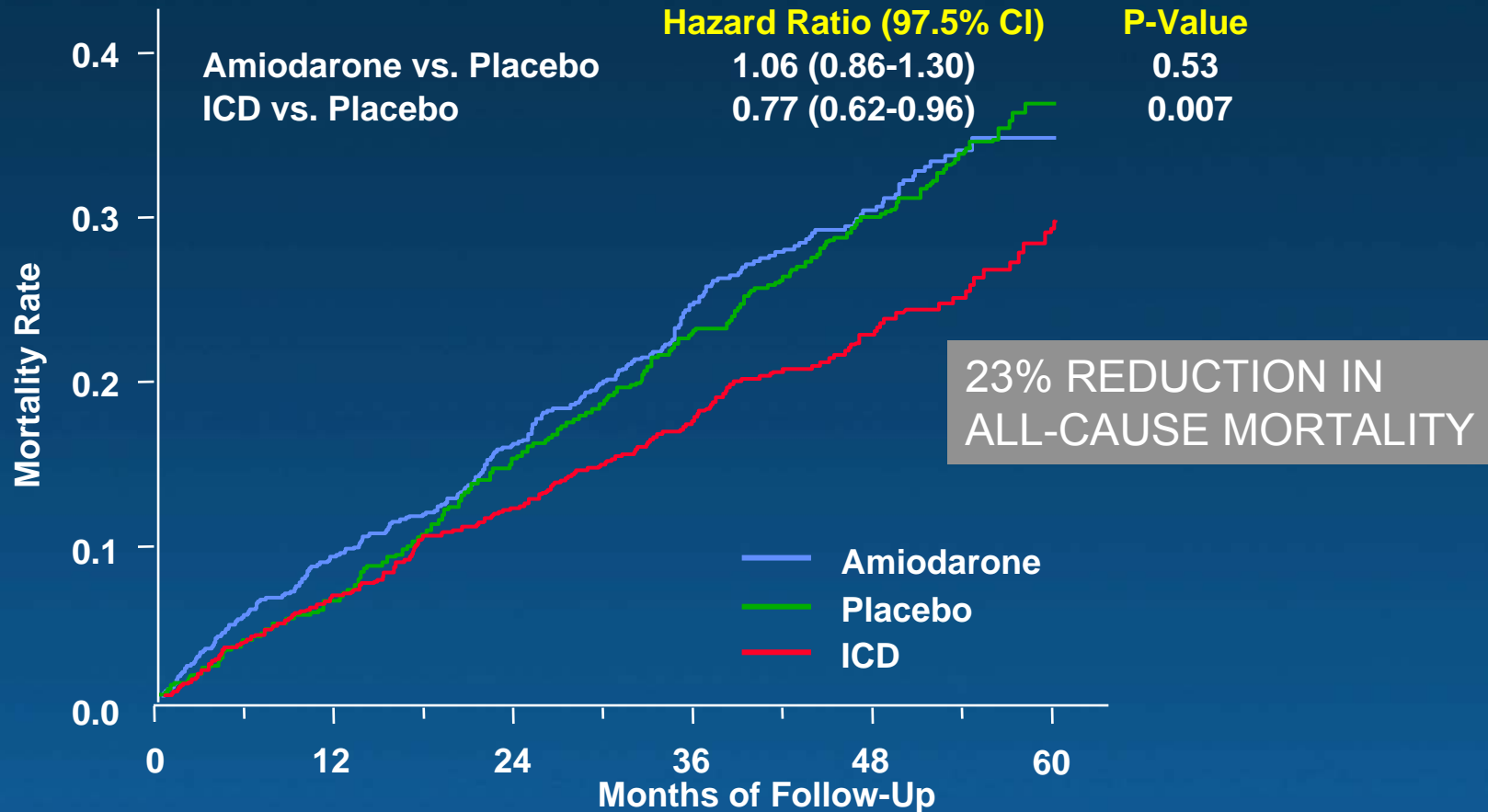


N=27

N = number of deaths

SCD-HeFT

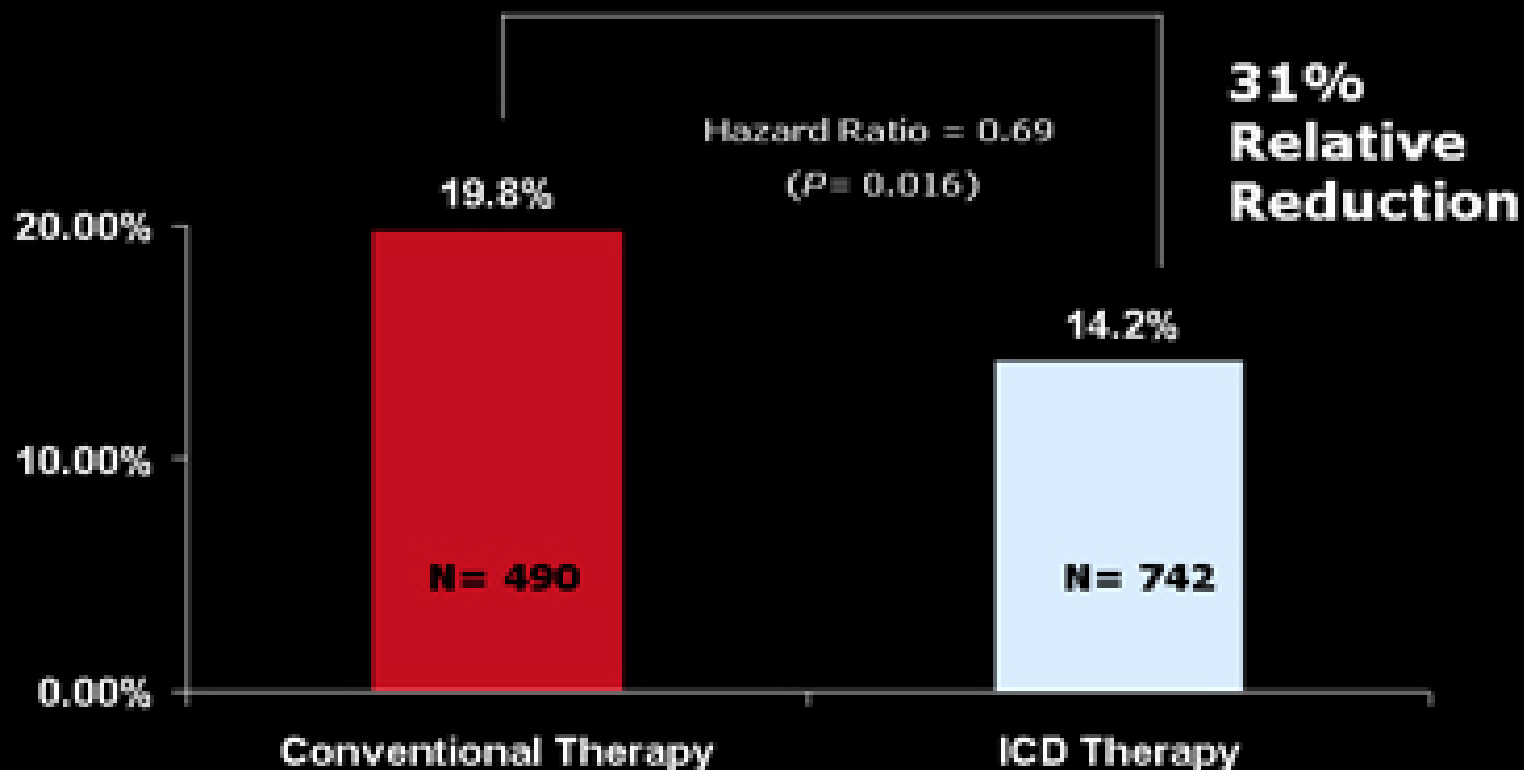
Mortality Rate Overall Results



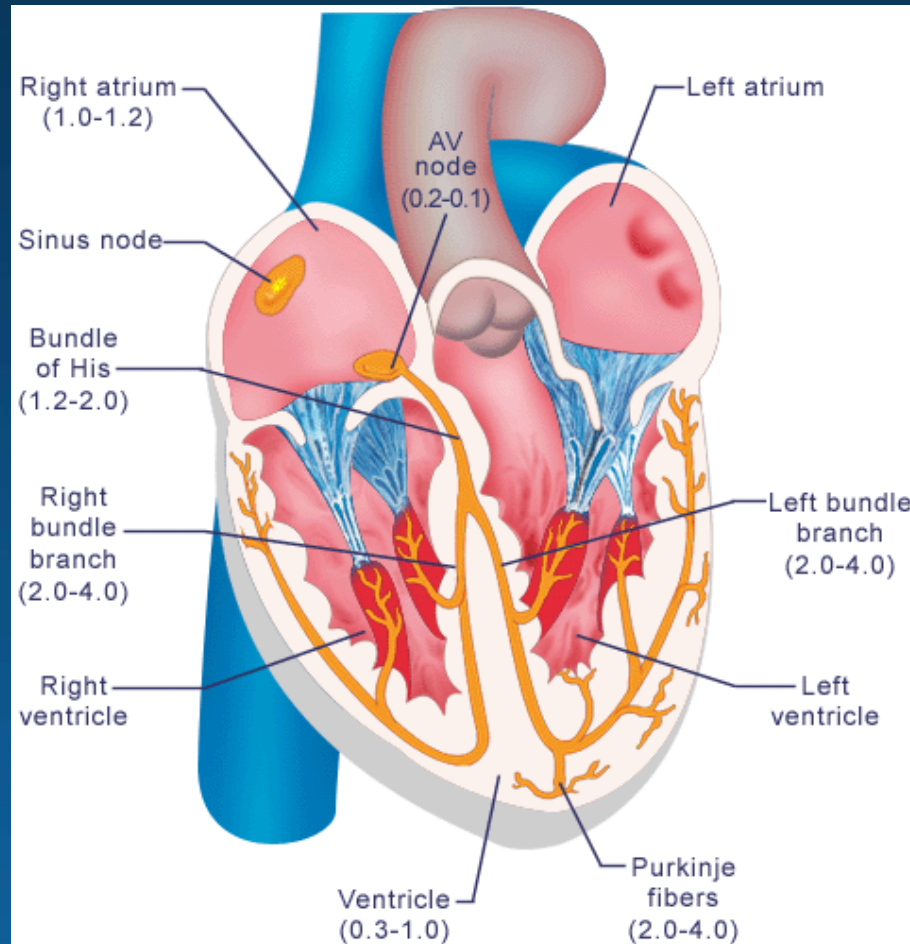
No. at Risk

	0	12	24	36	48	60
Amiodarone	845	772	715	484	280	97
Placebo	847	797	724	505	304	89
ICD	829	778	733	501	304	103

MADIT II: Multicenter Automatic Defibrillator Implantation Trial II



Contraction Depends on Activation



HF1 ASW

Healthy heart



Heart failure heart

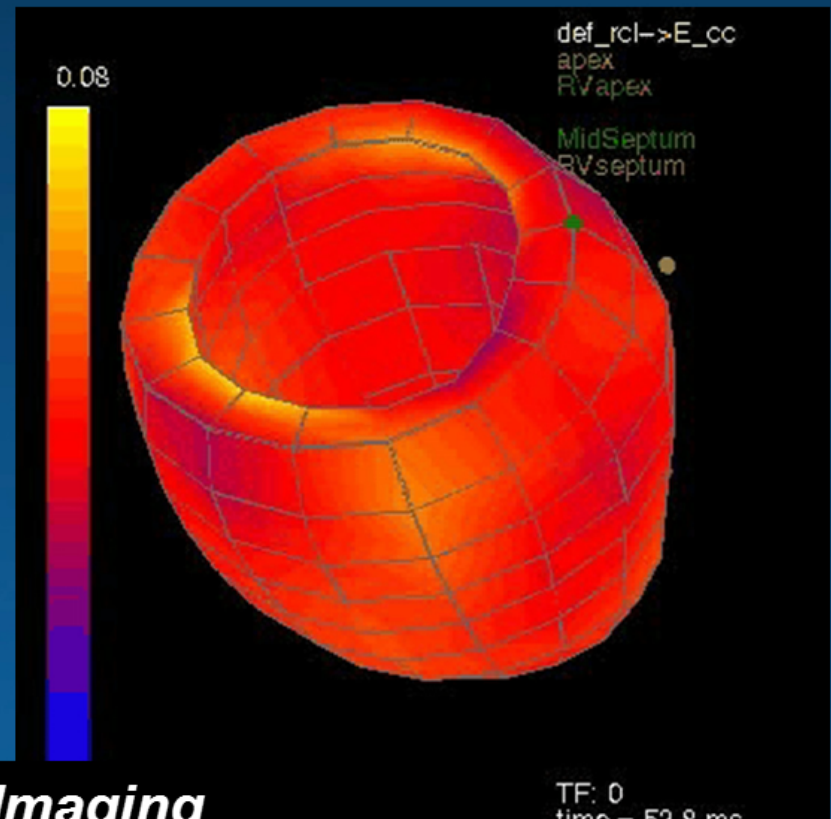
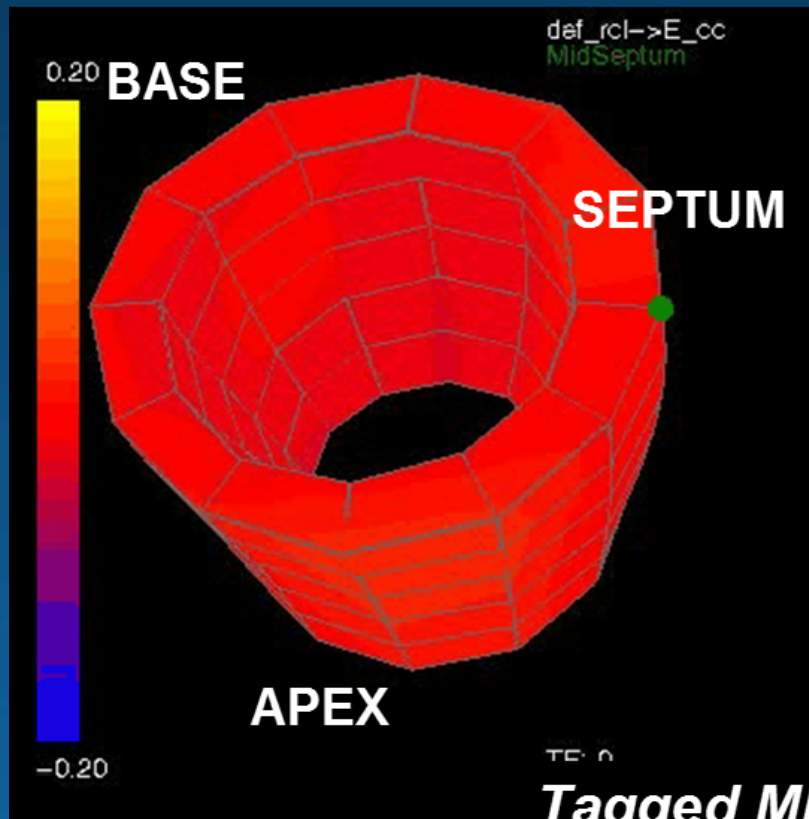


Normal vs Abnormal Contraction

Mechanical Dyssynchrony with IVCD

Normal

Dilated Cardiomyopathy



Tagged MRI Imaging

Dysynchrony - Consequences

- Abnormal septal motion¹
- Reduced dP/dt^{3,4}
- Reduced pulse pressure⁴
- Lower ejection fraction⁴
- Reduced diastolic filling^{1,2,4}
- Mitral regurgitation^{1,2,4}

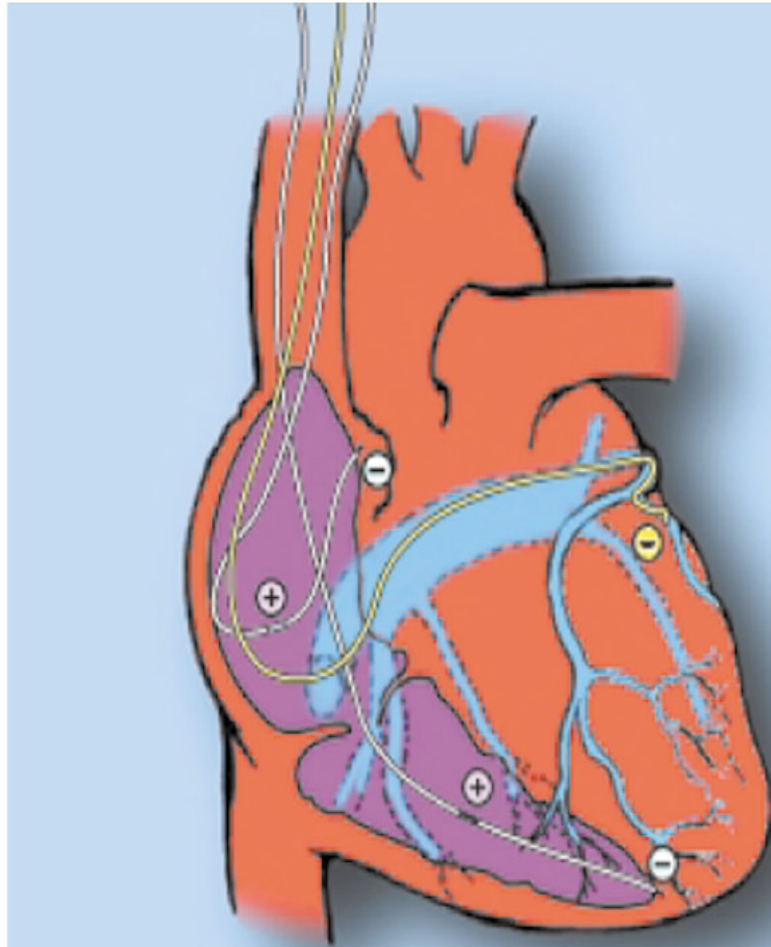
1 Grines CL, Bashore TM, Boudoulas H, et al. *Circulation* 1989;79:845-853.

2 Xiao, HB, Lee CH, Gibson DG. *Br Heart J* 1991;66:443-447.

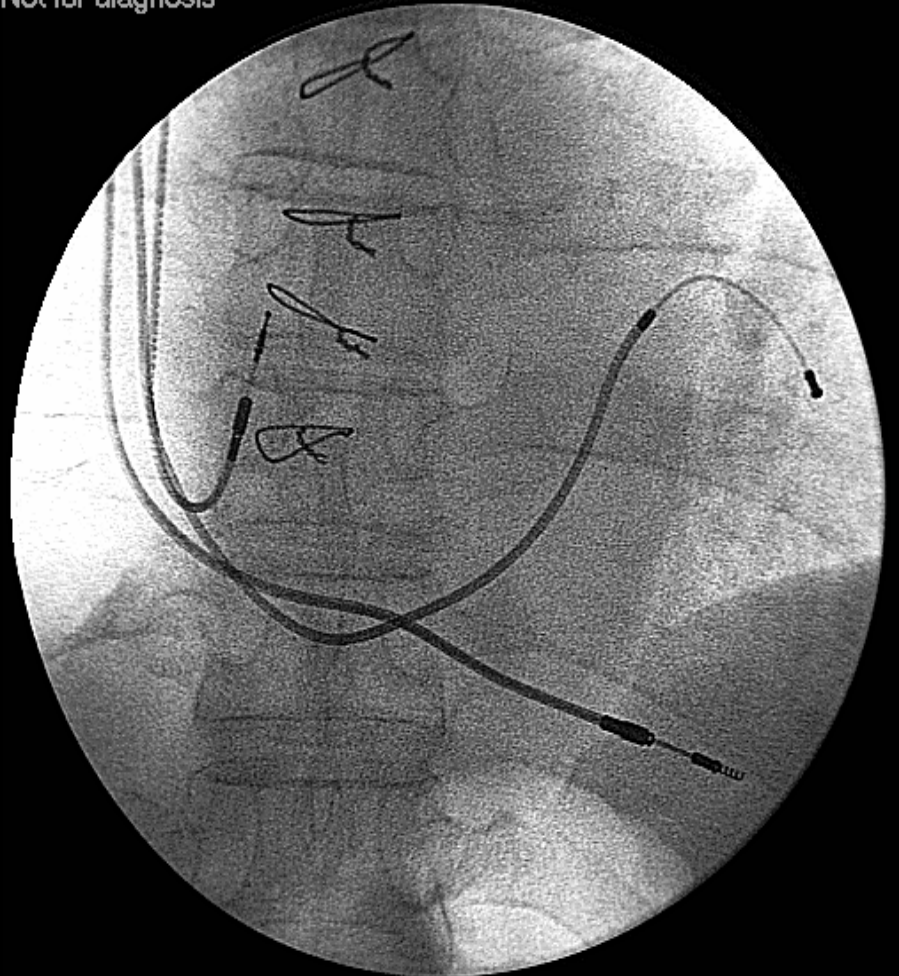
3 Xiao HB, Brecker SJD, Gibson DG. *Br Heart J* 1992;68:403-407.

4 Yu C-M, Chau E, Sanderson JE, et al. *Circulation*. 2002;105:438-445.

Biventricular pacemaker leads



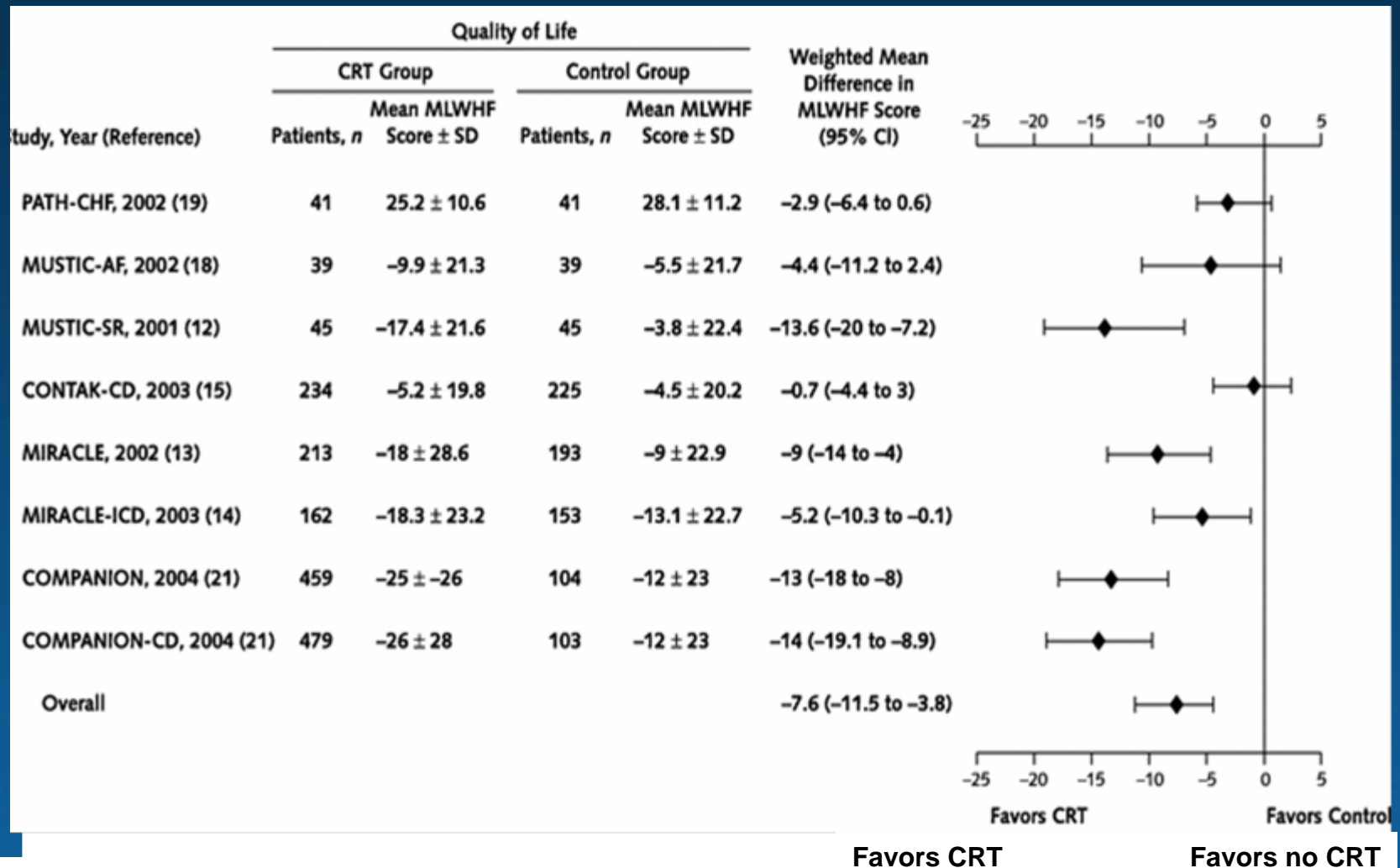
Not for diagnosis



CRT Background

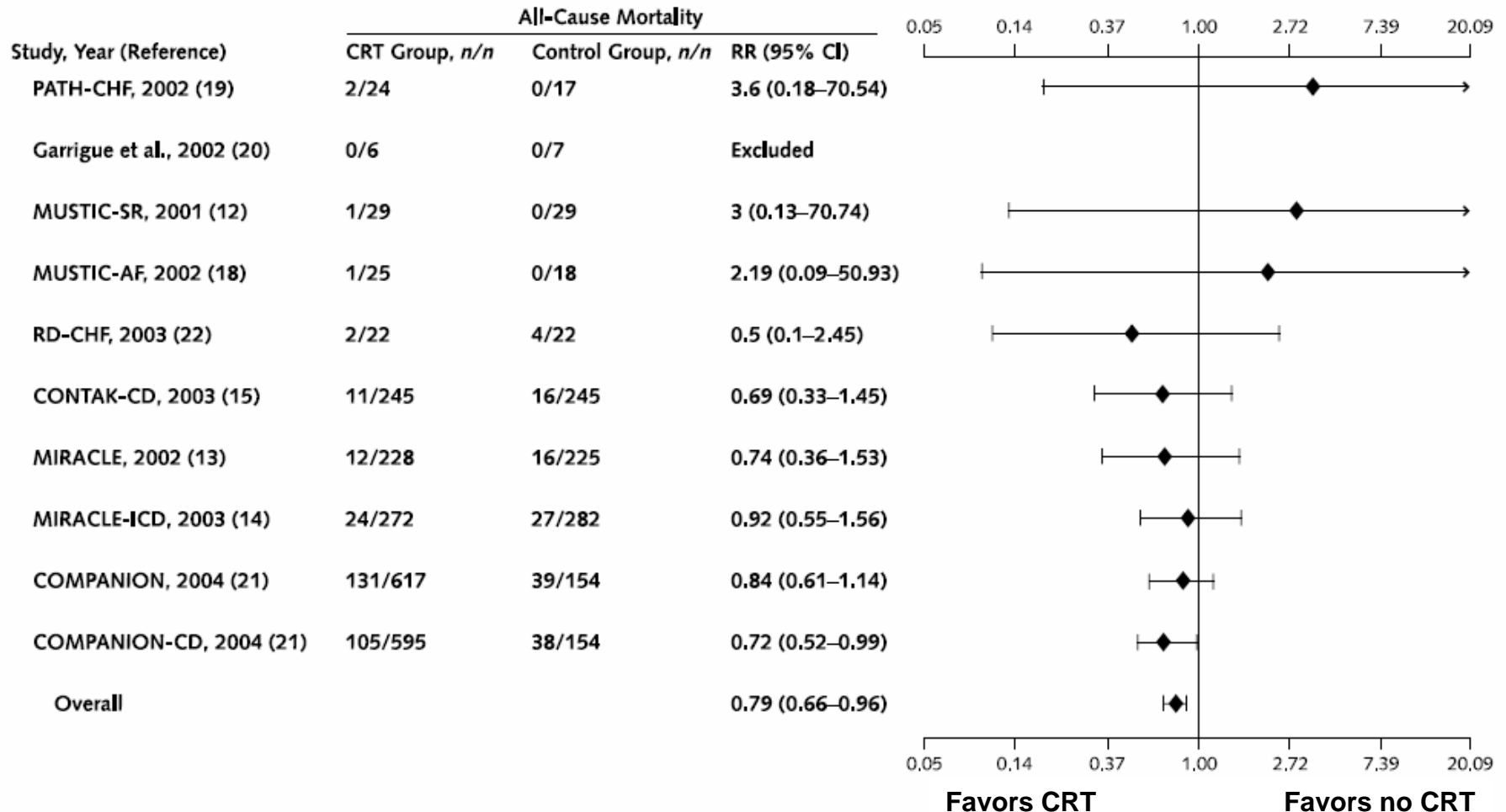
- CRT has been shown to be consistently associated with:
 - Reductions in LV size and volume
 - Increased Stroke Volume
 - Increased Ejection Fraction
 - Reduced Mitral Regurgitation
 - Improved exercise capacity
 - Improved QOL and functional capacity

Quality of Life and CRT



Does CRT Prevent Death?

All Cause Mortality and CRT



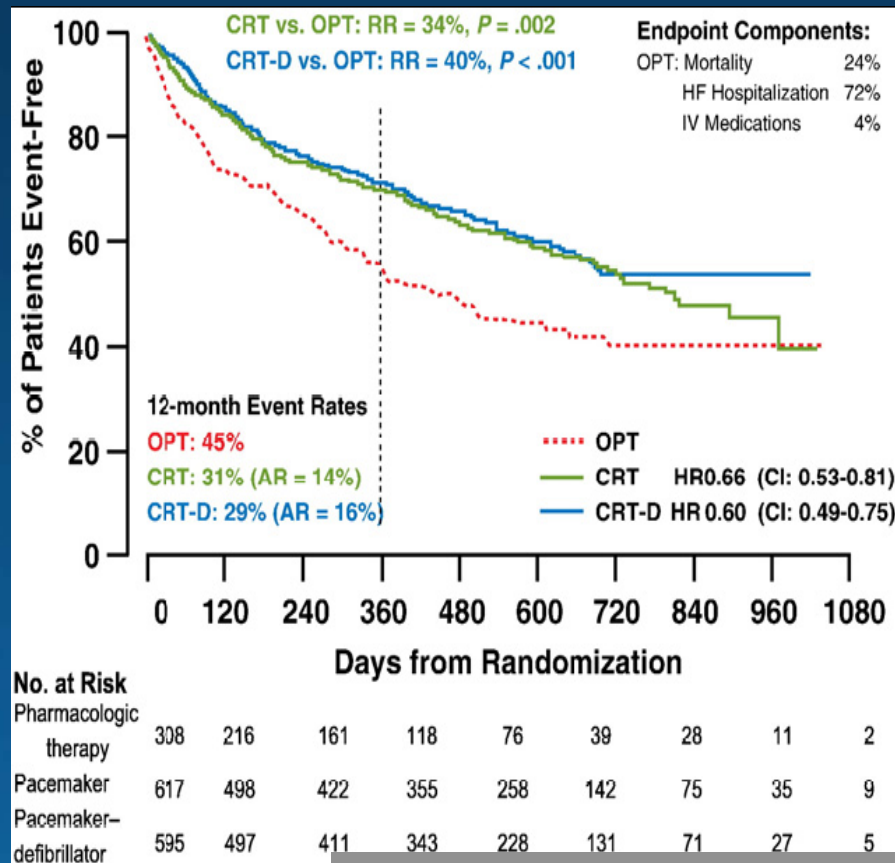
The COMPANION Trial

- 1520 patients* enrolled at 30 centers
- NYHA FC III/IV, LVEF ≤ 0.35 , QRS ≥ 120 ms
- Optimal medical therapy vs. CRTp vs. CRTd with optimal medical therapy

**stopped early by DSMB; 2200 planned*

COMPANION: 1^o Endpoint

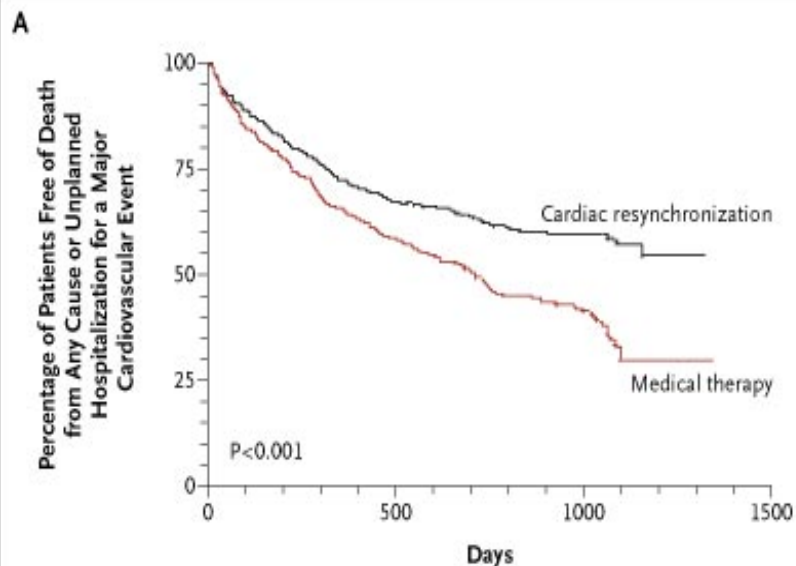
Death, Hospitalization or Outpatient Medication



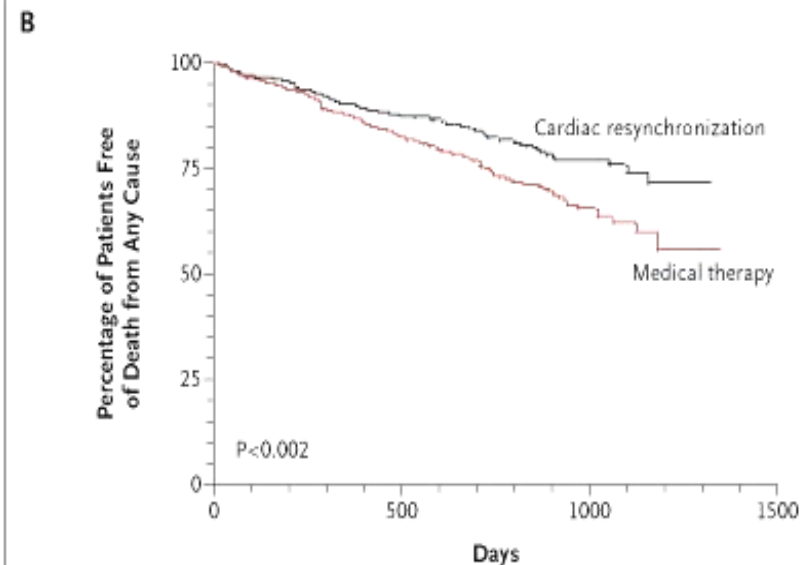
CARE – HF Study

Maybe CRTp is all that is needed

36% reduction in all-cause mortality,
10% absolute risk reduction



No. at Risk	0	500	1000	1500
Cardiac resynchronization	409	323	273	166
Medical therapy	404	292	232	118



No. at Risk	0	500	1000	1500
Cardiac resynchronization	409	376	351	213
Medical therapy	404	365	321	192

PROSPECT - Predictors of Response to CRT

(*Circulation*. 2008;117:2608-2616)

- 53 European, American and Hong Kong centers
- 498 pts with standard CRT indications
- Twelve echo parameters of dyssynchrony were evaluated.
- Outcomes - improved clinical composite score and $\geq 15\%$ reduction in LVESV at 6 months
- $AUC < 0.62$

PROSPECT - Predictors of Response to CRT

(*Circulation*. 2008;117:2608-2616)

- *Conclusion*

- Given the modest sensitivity and specificity in this multicenter setting despite training and central analysis, no single echocardiographic measure of dyssynchrony may be recommended to improve patient selection for CRT beyond current guidelines.

Recommendation in patients with heart failure in NYHA function class III/IV

Recommendation	Patient Population	Class	LoE
CRT-P/CRT-D* is recommended to reduce morbidity and mortality	NYHA function class III/IV LVEF \leq 35%, QRS \geq 120 ms, SR Optimal medical therapy Class IV patients should be ambulatory**	I	A

* Reasonable expectation of survival with good functional status for >1 year for CRT-D.
Patients with a secondary prevention indication for an ICD should receive a CRT-D.

** No admissions for HF during the last month and a reasonable expectation of survival >6 months.

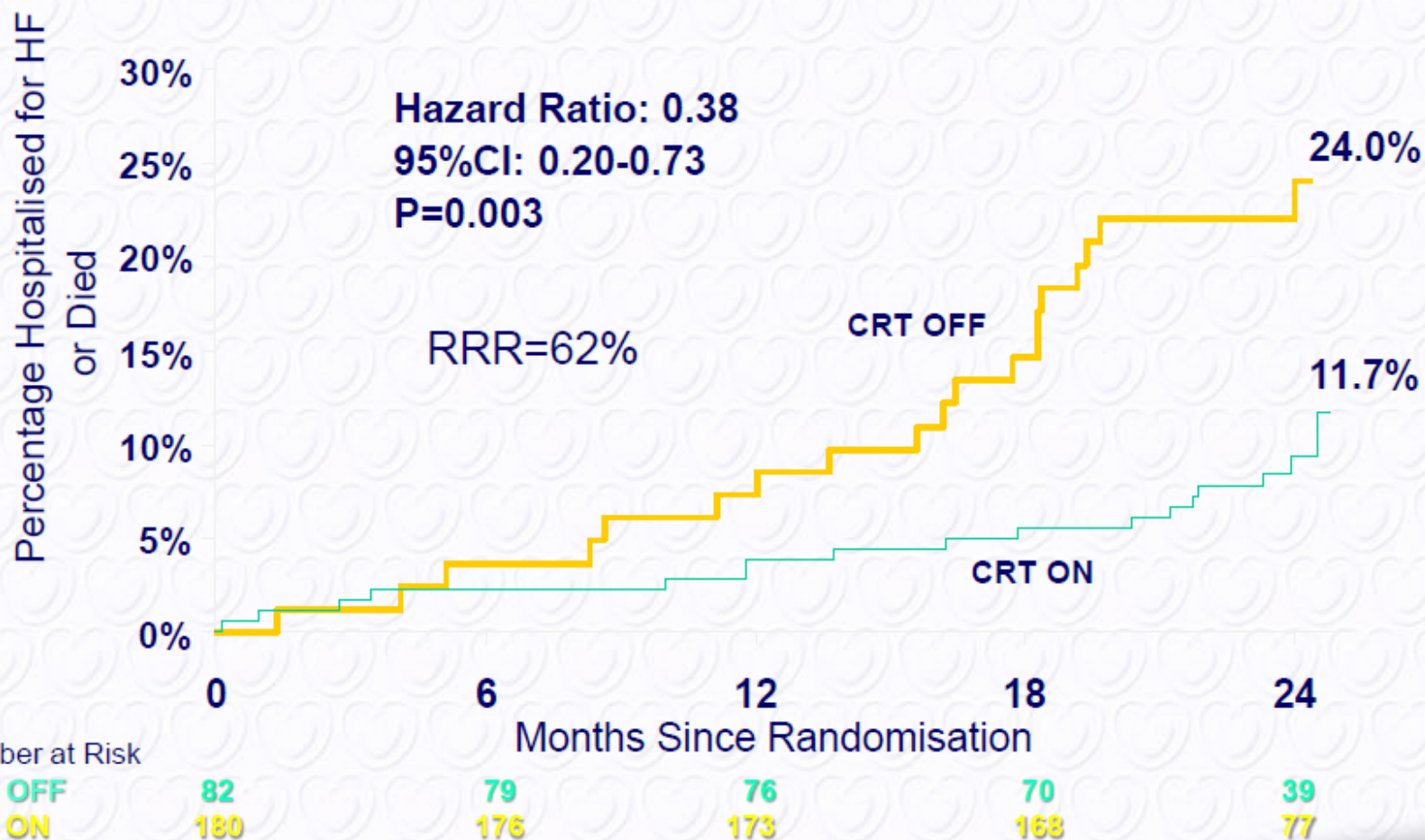
CRT-P/CRT-D in patients with heart failure in NYHA function class III/IV

Key points:

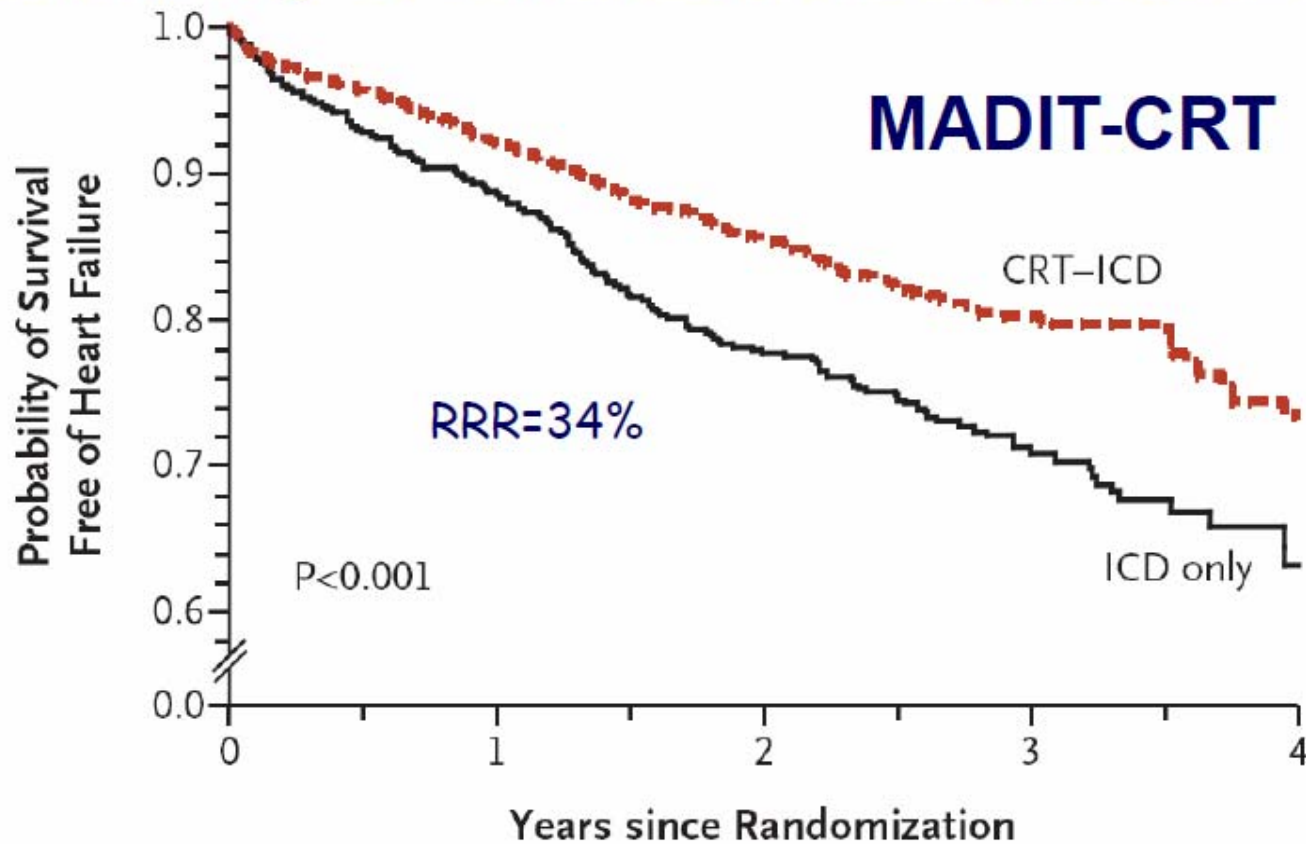
- **New: LV dilatation no longer required**
- **New: Class IV patients should be ambulatory**
- **New: Reasonable expectation of survival with good functional status for >1 year for CRT-D**
- **Evidence is strongest for patients with typical LBBB**
- **Similar level of evidence for CRT-P and CRT-D**

REVERSE 24-months analysis:

Reductions in risk of first HF hospitalisation or death



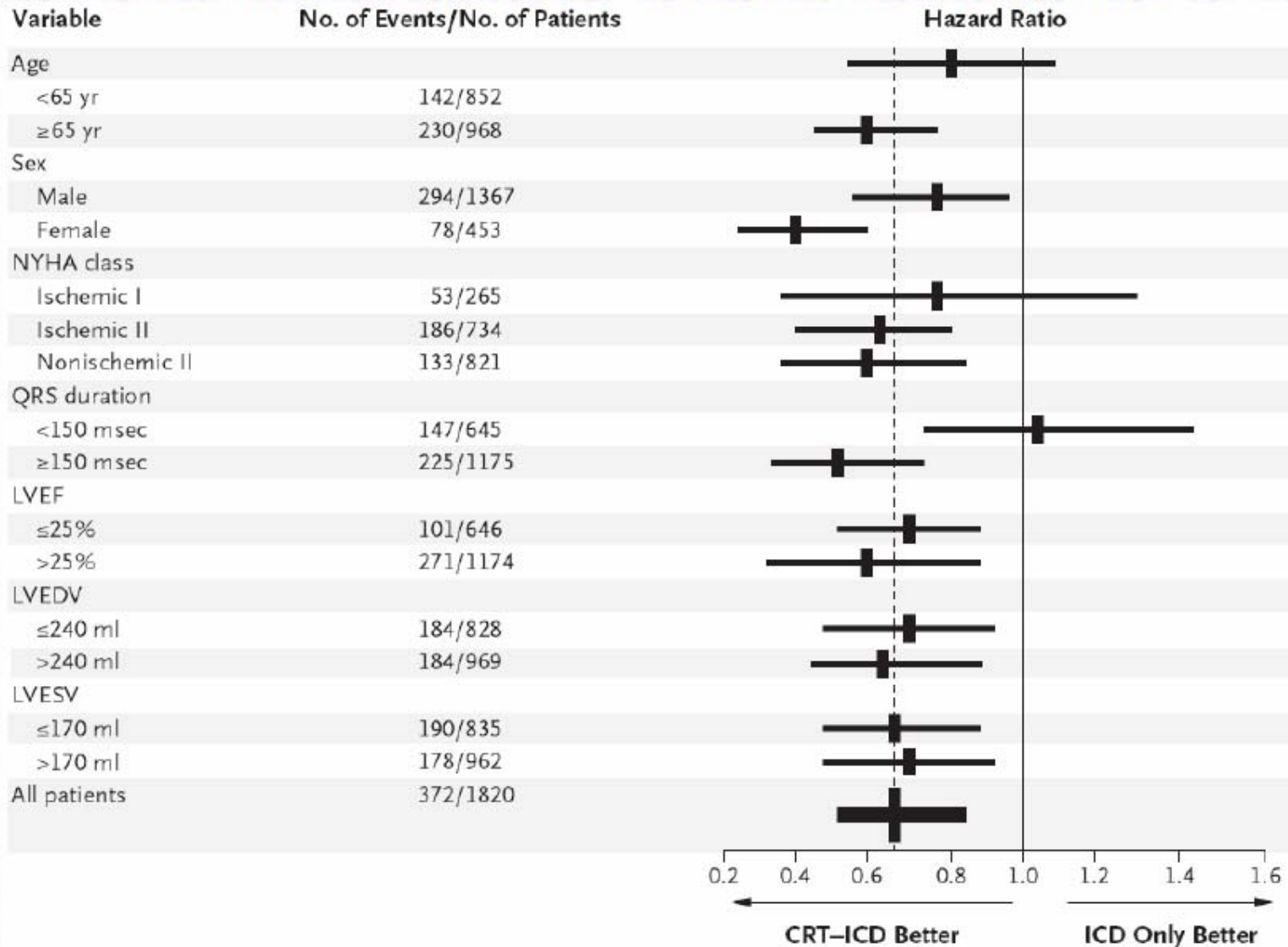
Probability of Survival Free of Heart Failure



No. at Risk (Probability of Survival)

ICD only	731	621 (0.89)	379 (0.78)	173 (0.71)	43 (0.63)
CRT-ICD	1089	985 (0.92)	651 (0.86)	279 (0.80)	58 (0.73)

MADIT-CRT: Risk of death or heart failure



Recommendation in patients with heart failure in NYHA function class II

Recommendation	Patient Population	Class	Level
CRT preferentially by CRT-D is recommended to reduce morbidity or to prevent disease progression*	NYHA function class II LVEF \leq 35%, QRS \geq 150 ms, SR Optimal medical therapy	I	A

* The guideline indication has been restricted to patients with HF in NYHA function class II with a QRS width \geq 150 ms, a population with a high likelihood of a favourable response.

CRT-D in patients with heart failure in NYHA function class I/II

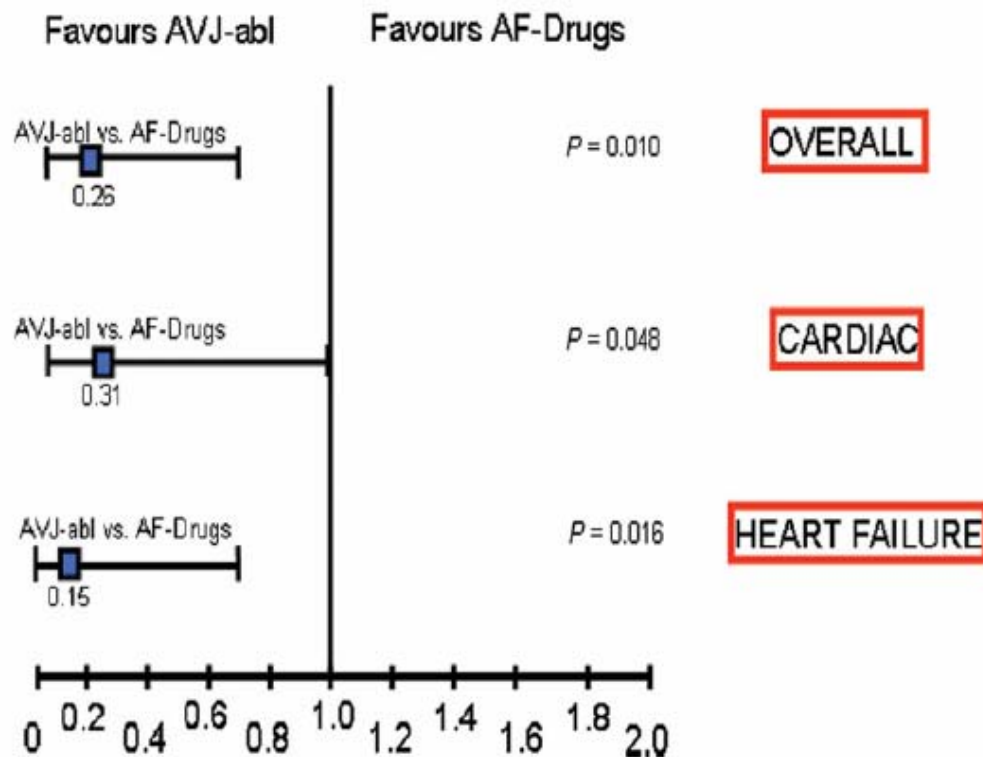
Key points:

- 2 recent, randomised, prospective, multicentre trials in mild HF (MADIT-CRT and REVERSE) demonstrate reduced morbidity
- 18% of patients in REVERSE and 15% of patients in MADIT-CRT were in NYHA I class at baseline
- Improvement primarily seen in patients with $QRS \geq 150$ ms and/or typical LBBB
- Women with LBBB showed a particularly favourable response
- Survival advantage not established
- In MADIT-CRT the extent of reverse remodelling was concordant with and predictive of improvement in clinical outcomes

Adjusted hazard ratios for death AV ablation vs. AF drug therapy

Atrial Fibrillation

Hazard ratio estimates on the mode of death were adjusted for centre, age, gender, aetiology, NYHA class, QRS width, left ventricular ejection fraction, and device type.



Recommendations in patients with heart failure and permanent atrial fibrillation

Recommendations	Patient Population	Class	Level
CRT-P/CRT-D* should be considered to reduce morbidity	NYHA function class III/IV LVEF \leq 35%, QRS \geq 130 ms Pacemaker dependency induced by AV nodal ablation	Ila	B
CRT-P/CRT-D* should be considered to reduce morbidity	NYHA function class III/IV LVEF \leq 35%, QRS \geq 130 ms Slow ventricular rate and frequent pacing**	Ila	C

* Reasonable expectation of survival with good functional status for >1 year for CRT-D. Patients with a secondary prevention indication for an ICD should receive a CRT-D.

** Frequent pacing is defined as \geq 95% pacemaker dependency

CRT-P/CRT-D in patients with heart failure and permanent atrial fibrillation

Key points:

- **Approximately 1/5 of CRT implantations in Europe are in patients with permanent AF**
- **NYHA class III/IV symptoms and an LVEF $\leq 35\%$ are well-established indications for ICD**
- **Frequent pacing is defined as $\geq 95\%$ pacemaker dependency**
- **AV nodal ablation may be required to assure adequate pacing**
- **Evidence strongest for patients with an LBBB pattern**
- **Insufficient evidence for mortality recommendation**

Recommendations in patients with heart failure and a concomitant class I pacemaker indication

Recommendations	Patient Population	Class	Level
CRT-P/CRT-D* is recommended to reduce morbidity	NYHA function class III/IV LVEF \leq 35%, QRS \geq 120 ms	I	B
CRT-P/CRT-D* should be considered to reduce morbidity	NYHA function class III/IV LVEF \leq 35%, QRS $<$ 120 ms	IIa	C
CRT-P/CRT-D* may be considered to reduce morbidity	NYHA function class II LVEF \leq 35%, QRS $<$ 120 ms	IIb	C

* Reasonable expectation of survival with good functional status for >1 year for CRT-D. Patients with a secondary prevention indication for an ICD should receive a CRT-D.

CRT-P/CRT-D in patients with heart failure and a conventional pacemaker indication

Key points:

- **In patients with a conventional indication for pacing, NYHA III/IV symptoms, LVEF $\leq 35\%$, QRS width ≥ 120 ms, a CRT-P/CRT-D is indicated**
- **RV pacing will induce dyssynchrony**
- **Chronic RV pacing in patients with LV dysfunction should be avoided**
- **CRT may permit adequate uptitration of beta-blocker treatment**

Evidence table 1: Inclusion criteria in RCTs evaluating CRT in heart failure

Trial	Patients	NYHA class	LVEF(%)	LVEDD (mm)	SR/AF	QRS (ms)	ICD
MUSTIC-SR (16)	58	III	≤35%	≥60	SR	≥150	No
MIRACLE (5)	453	III,IV	≤35%	≥55	SR	≥130	No
MUSTIC AF (35)	43	III	≤35%	≥60	AF	≥200	No
PATH CHF (6)	41	III,IV	≤35%	NA	SR	≥120	No
MIRACLE ICD (8)	369	III,IV	≤35%	≥55	SR	≥130	Yes
CONTAK CD (55)	227	II,IV	≤35%	NA	SR	≥120	Yes
MIRACLE ICD II (9)	186	II	≤35%	≥55	SR	≥130	Yes
PATH CHF II (56)	89	III,IV	≤35%	NA	SR	≥120	Yes/No
COMPANION (10)	1520	III,IV	≤35%	NA	SR	≥120	Yes/No
CARE HF (11)	814	III,IV	≤35%	≥30	SR	≥120	No
CARE HF (17)	813	III,IV	≤35%	≥30	SR	≥120	No
REVERSE (21, 22)	610	I,II	≤40%	≥55	SR	≥120	Yes/No
MADIT CRT (20)	1800	I,II	≤30%	NA	SR	≥130 ms	Yes
RAFT (57)	1800 Canada	II,III	≤30%	>60	SR/AF	≥130 ≥200 *	Yes

Evidence table 2: Endpoints, design and main findings of the RCTs evaluating CRT in heart failure

Trial	Endpoints	Design	Main findings
MUSTIC-SR (16)	6MWT, QoL, pVO ₂ , Hosp	Single-blinded, controlled, crossover, 6 months	CRT-P improved: 6MWT, QOL, pVO ₂ ; reduced Hosp
MIRACLE (8)	NYHA class, QoL, pVO ₂	Double-blinded, controlled, 6 months	CRT-P improved: NYHA, pVO ₂ , 6MWT
MUSTIC AF (35)	6MWT, QoL, pVO ₂ , Hosp	Single-blinded, controlled, crossover, 6 months	CRT-P improved all; reduction of Hosp
PATH CHF (6)	6MWT, pVO ₂	Single-blinded, controlled, crossover, 12 months	CRT-P improved: 6MWT; pVO ₂
MIRACLE ICD (8)	6MWT, QoL, Hosp	Double-blinded, ICD vs. CRT-D 6 months	CRT-D improved all from baseline (not ICD)
CONTAK CD (54)	All-cause death + HF Hosp, pVO ₂ , 6MWT, NYHA class, QoL, LVEDD, LVEF	Double-blinded, ICD vs. CRT-D 6 months	CRT-D improved: pVO ₂ , 6MWT; reduced LVEDD and increased LVEF
MIRACLE ICD II (9)	VE/CO ₂ , pVO ₂ , NYHA, QoL, 6MWT, LV volumes, LVEF	Double-blinded, ICD vs. CRT-D 6 months	CRT-D improved: NYHA, VE/CO ₂ ; volumes, LVEF
COMPANION (10)	(1) All-cause death or Hosp	Double-blinded, controlled, OPT, CRT-D, CRT-P, about 15 months	CRT-P/CRT-D: reduced (1)
CARE-HF (11)	(1) All-cause death or CV event (2) All-cause death	Double-blinded, controlled, OPT, CRT-P, 29 months	CRT-P reduced (1) and (2)
REVERSE (21)	(1) % worsened by clinical composite endpoint, (2) LVESVi, (3) HF hosp, (4) all-cause death	Double-blinded, controlled, OPT, CRT-P ±ICD, 12months	Primary endpoint NS CRT-P/CRT-D reduced (2) and (3) hosp but not (4)
MADIT-CRT (20)	(1) HFevent or death (2) All-cause death (3) LVESV	Controlled, CRTP, CRT-D, 2.4 years	CRT-D reduced (1) and (3c) but not (2)

Summary of indications for CRT in patients with heart failure

Recommendations	Patient population	CoR	LoE
CRT-P/CRT-D* is recommended to reduce morbidity and mortality	NYHA class III/IV symptoms LVEF≤35%, QRS≥120 ms, SR Optimal medical therapy Class IV patients should be ambulatory**	I	A
CRT preferentially by CRT-D* is recommended to reduce morbidity or to prevent disease progression	NYHA class II symptoms LVEF≤35%, QRS≥150 ms, SR	I	A
CRT-P/CRT-D* should be considered to reduce morbidity	Permanent Atrial Fibrillation NYHA class III/IV LVEF≤35%, QRS≥130 ms Pacemaker dependency induced by AV nodal ablation	IIa	B
CRT-P/CRT-D* should be considered to reduce morbidity	Permanent Atrial Fibrillation NYHA class III/IV LVEF≤35%, QRS≥130 ms Slow ventricular rate and frequent pacing***	IIa	C
CRT-P/CRT-D* is recommended to reduce morbidity	Class I indication for pacemaker NYHA class III/IV LVEF≤35%, QRS ≥120 ms	I	B
CRT-P/CRT-D* should be considered to reduce morbidity	Class I indication for pacemaker NYHA class III/IV LVEF≤35%, QRS<120 ms	IIa	C
CRT-P/CRT-D* may be considered to reduce morbidity	Class I indication for pacemaker NYHA class II LVEF≤35%, QRS<120 ms	IIb	C
LVAD may be considered as destination treatment to reduce mortality	NYHA IIIB/IV symptoms Ineligible for cardiac transplantation LVEF≤25%	IIb	B

Possible Risks for Implantable Devices

- Vascular complications
- Long-term risk of infections
- Leads may break/fracture
- Recalls

BUT:

Significant benefits –evaluate patients carefully

Devices are very reliable and improving constantly

The Importance of Patient Selection

- Maintain relationship with EP/patient and family
- Need to understand:
 - Why treatment is indicated
 - What are the downsides
 - Will continue with medical therapy
 - Possibility of inappropriate shocks

IMPROVE HF: Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting

- 167 outpatient cardiology practices surveyed in the USA
- 15 381 pts with HF, previous MI/LV Dx
- Results for utilization of device therapy in eligible patients:
 - ICD/CRT-D 51%
 - CRT – 39%
- Median 27% of pts received all HF therapies for which they were potentially eligible on the basis of chart documentation.
- Use of guideline-recommended therapies by practices varied widely
- Need to translate outcomes of RCTs, guidelines into clinical practice

Stages of Therapy

