

Défibrillateur Automatique Implantable et Dysfonction Ventriculaire Gauche Chronique

Doit-on implanter un DAI à tous les patients avec FEVG $\leq 35\%$?

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Disclosure:

Speaker, Consultant, Research grants

*Novartis
ST Jude Medical
LivaNova Group*



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Before **DANISH**, everything looked clear!

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

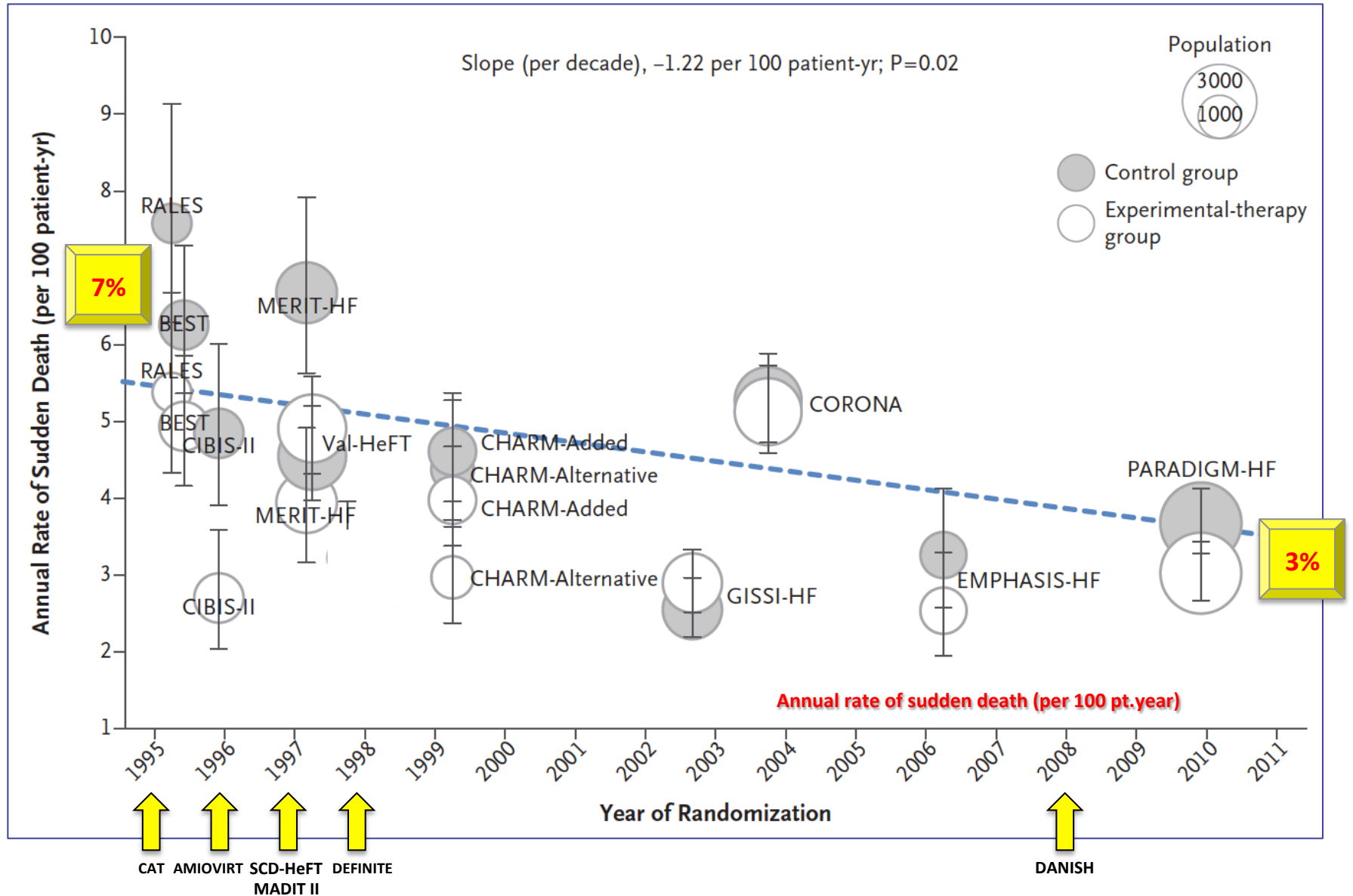
Primary prevention	Class ^a	Level ^b
<p>An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA Class II–III), and an LVEF ≤35% despite ≥3 months of OMT, provided they are expected to survive substantially longer than one year with good functional status, and they have:</p>		
<ul style="list-style-type: none"> • IHD (unless they have had an MI in the prior 40 days – see below). 	I	A
<ul style="list-style-type: none"> • DCM. 	I	B

P Ponikowski et al. European Heart Journal (2016) 37, 2129–2200

9 trials	Post-MI (ICM?)	NICM
≥15 years	MADIT I (1996) MUST (1999) MADIT II (2002)	CAT (2002) AMIOVIRT (2003)
≥10 years	DINAMIT (2004) SCD-HeFT (2005)*	DEFINITE (2004) SCD-HeFT (2005)*
<10 years	IRIS (2009)	

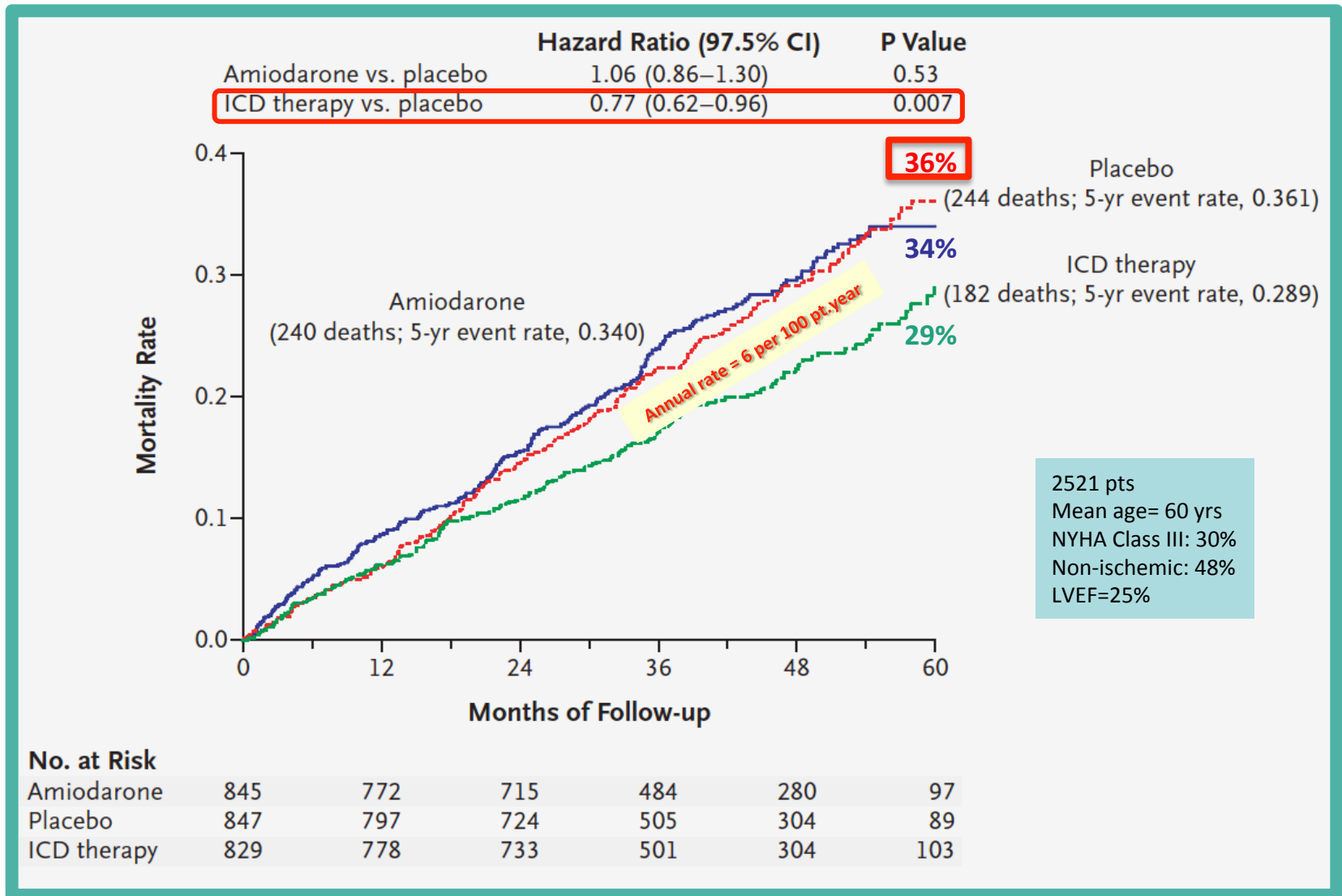
***SCD-HeFT**: no stratification by etiology at inclusion. Ischemic CHF was defined as left ventricular systolic dysfunction associated with >75% stenosis of at least one of the three major coronary arteries or a documented history of a myocardial infarction

Declining Risk of Sudden Death in Heart Failure



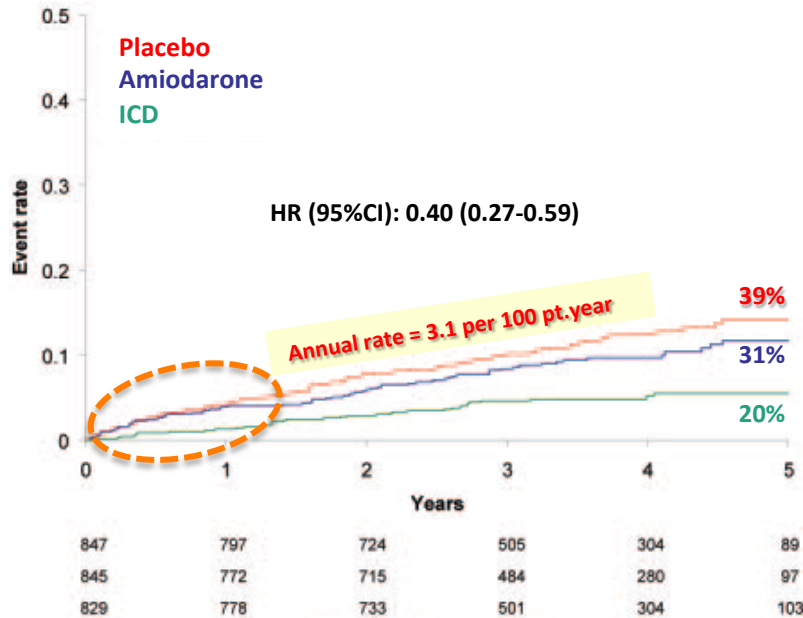
SCD-HeFT: All-cause mortality

HF patients who remained symptomatic in NYHA functional class II-III after drug treatment optimization with LVEF<35%

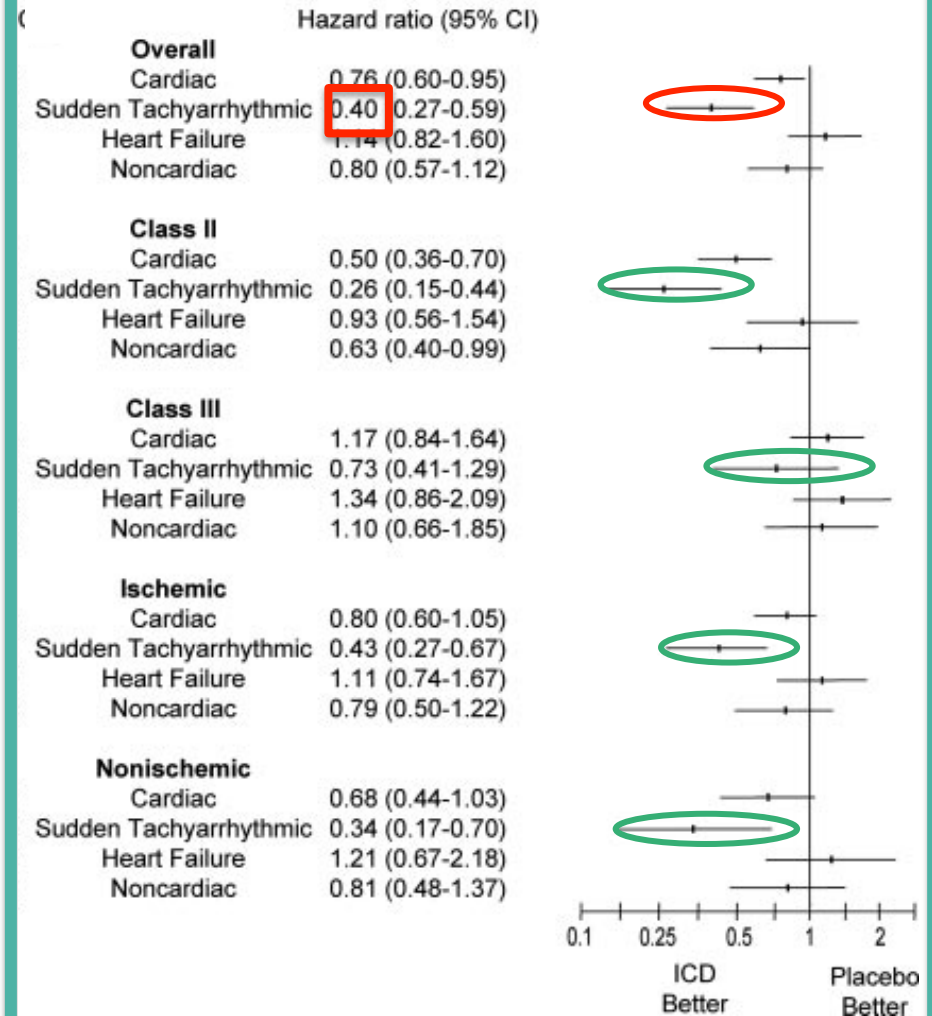


SCD-HeFT: Subgroup Analysis by Cause of Death

Sudden presumed arrhythmic death



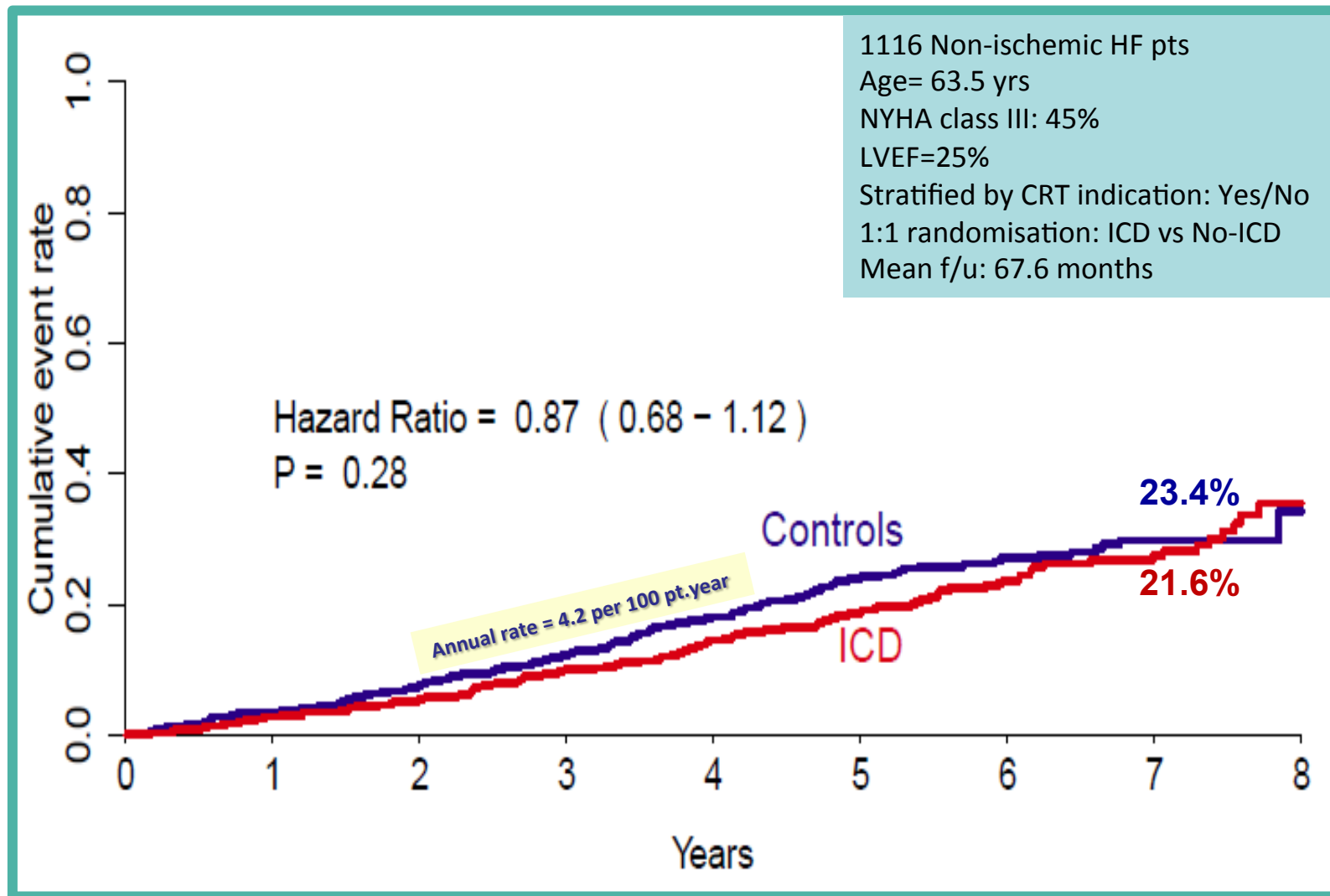
« This mode-of-death analysis of SCD-HeFT demonstrates that the reduction in all-cause mortality associated with ICD therapy was due exclusively to a reduction in cardiac mortality from sudden death presumed to be ventricular tachyarrhythmic »





DANISH: ICD in Non-ischemic Cardiomyopathy

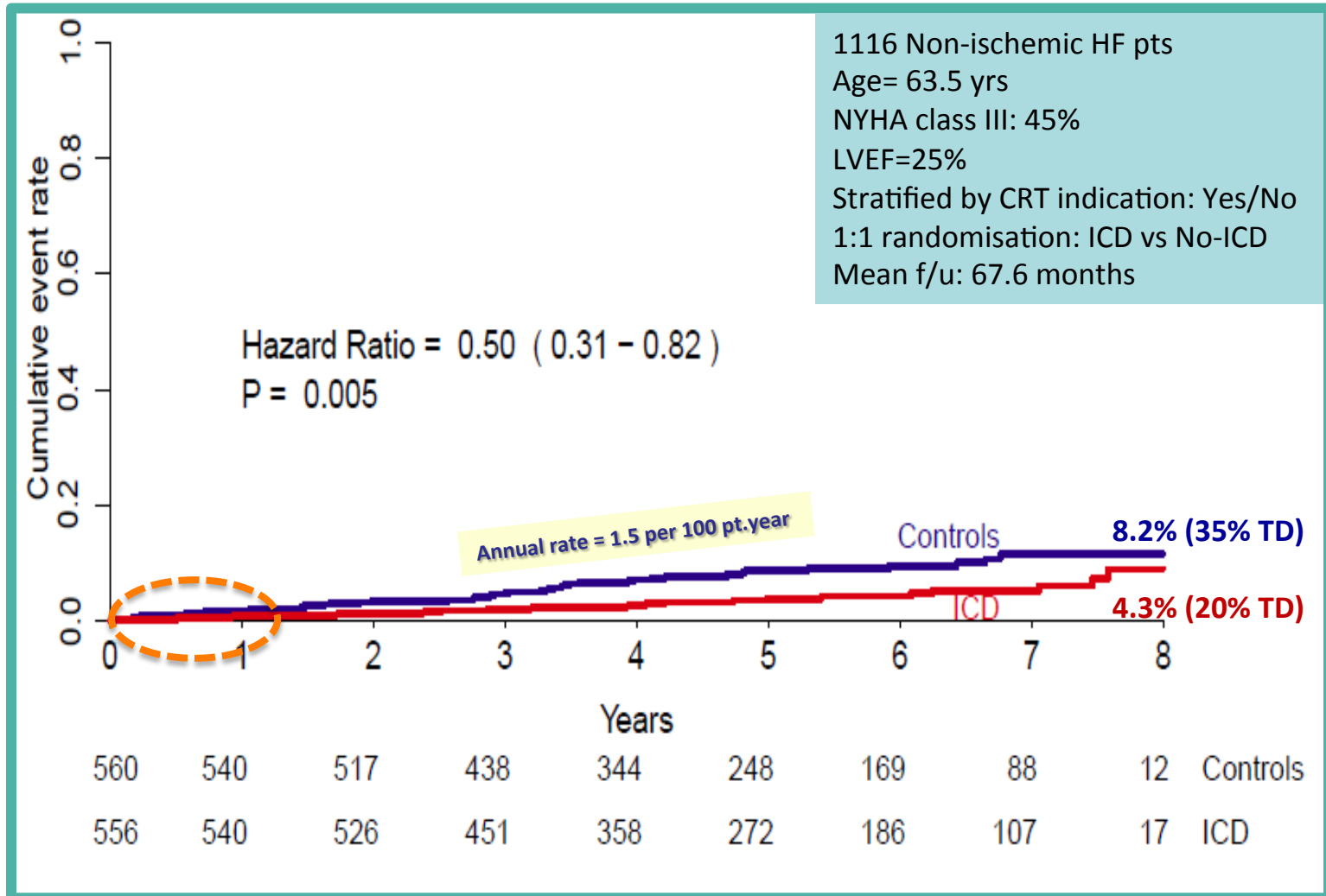
Primary outcome – all-cause mortality





DANISH: ICD in Non-ischemic Cardiomyopathy

Secondary outcome – Sudden death



How to Explain the *DANISH* results?

Wide heterogeneity in baseline characteristics between trials, in particular pharmacological treatment

	DEFINITE	SCD-HeFT <u>NICD</u>	DANISH
Enrollment	1998-2002	1997-2001	2008-2014
Year publication	2004	2005	2016
F/u (years)	2.4	3.8	5.6
N pts	458	794	1112
Age	58	60	63.5
% NYHA class III	21%	30%	45%
LVEF %	21	24.5	25
B-blockers %	85%	69%	92%
ACEI-ARB %	96%	85%	96.5%
MR Antagonists %	NR	20%	58%
Control group: annualized mortality rate	6.3%	6%	4.2%
Control group: annualized rate of SCD	3.2%	3.1%	1.5%

Before DANISH:

inclusion of younger, mildly symptomatic, suboptimally treated but at high-risk patients

Meta-analyses/Systematic literature reviews after **DANISH**

- H Golwala et al. Implantable cardioverter-defibrillator for non-ischemic cardiomyopathy: an updated meta-analysis. Circulation 2016; CIRCULATIONAHA.116.026056
- AM Barakat et al. Primary prevention implantable cardioverter defibrillator in patients with non-ischaemic cardiomyopathy: a meta-analysis of randomised controlled trials. BMJ Open 2017;7:e016352. doi:10.1136/bmjopen-2017-016352
- S Stavrakis et al. Implantable cardioverter defibrillators for primary prevention of mortality in patients with nonischemic cardiomyopathy. J Cardiovasc Electrophysiol 2017; 28: 659-665
- T Akel et al. Implantable cardioverter defibrillators for primary prevention in patients with nonischemic cardiomyopathy: a systematic review and meta-analysis. Cardiovasc Ther 2017; 35:
- FK Luni et al. Mortality effect of ICD in primary prevention of nonischemic cardiomyopathy: A meta-analysis of randomized controlled trials. J Cardiovasc Electrophysiol 2017; 28: 538-543
- MA Narayanab et al. Efficacy of Implantable Cardioverter-Defibrillator Therapy in Patients With Nonischemic Cardiomyopathy: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. J Am Coll Cardiol EP 2017; 3: 962-970
- M Kolodziejczak et al. Implantable cardioverter-defibrillators for primary prevention in patients with Ischemic or nonischemic cardiomyopathy: A systematic review and meta-analysis. Ann Int Med 2017; 167: 103-111
- S Al Khatib et al. Primary prevention implantable cardioverter defibrillators in patients with nonischemic cardiomyopathy: A meta-analysis. JAMA Cardiol 2017; 2: 685-688
- SA Beggs et al. Non-ischaemic cardiomyopathy, sudden death and implantable defibrillators: a review and meta-analysis. Heart Jan 2018
- AC Alba et al. Implantable cardiac defibrillator and mortality in nonischaemic cardiomyopathy: an updated meta-analysis. Heart Feb 2018
- ...

Summary: In NICM patients, ICD use remains associated with a significant reduction in

- **All-cause mortality: RRR= 16-25% (ULCI: 0.89-0.93)**
- **Sudden cardiac death: RRR= 53-59% (ULCI: 0.68-0.73)**

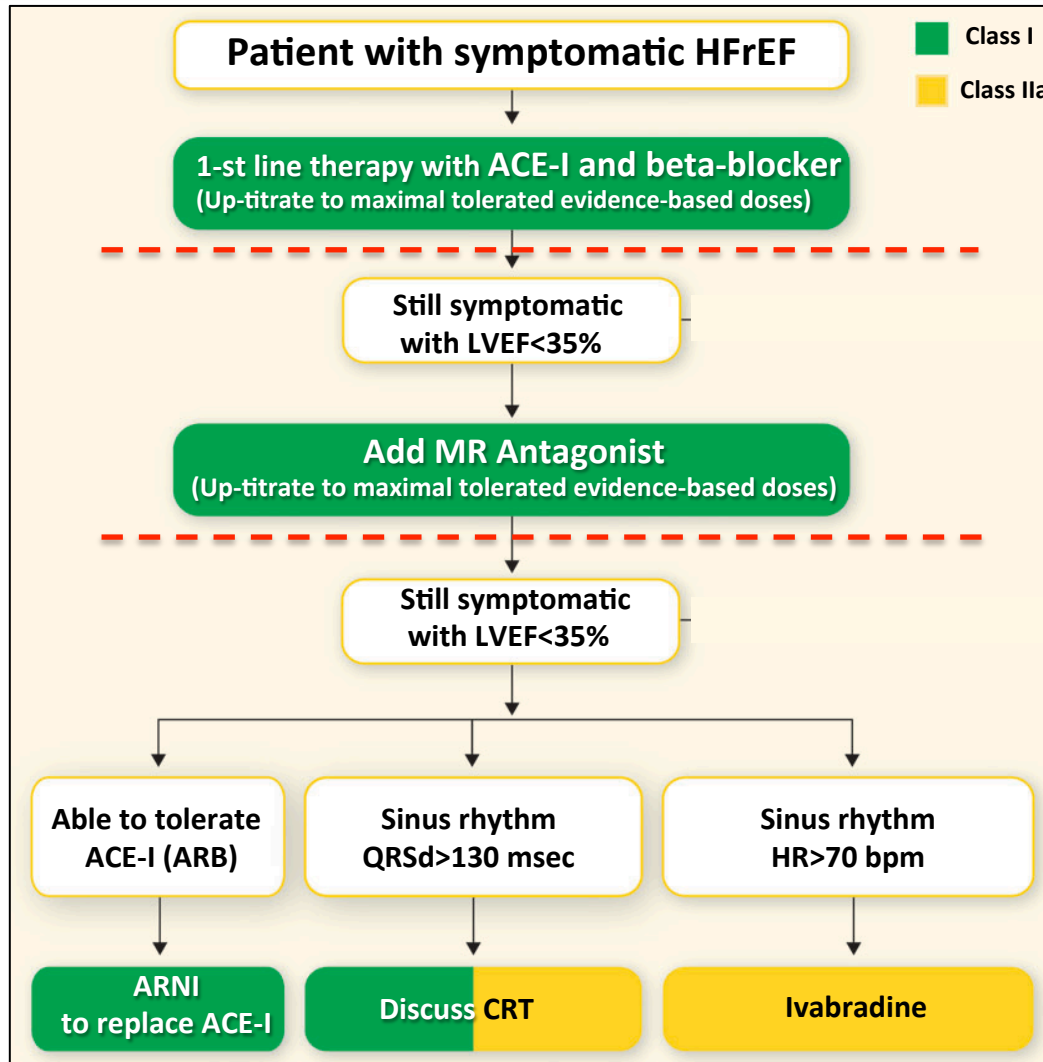
But, sensitivity analyses suggest that the mortality benefit is confined to patients who did not receive optimal medical treatment (B-blocker, ACE/ARB, MRA)

Determinants of ICD Efficacy in Primary Prevention in HFrEF

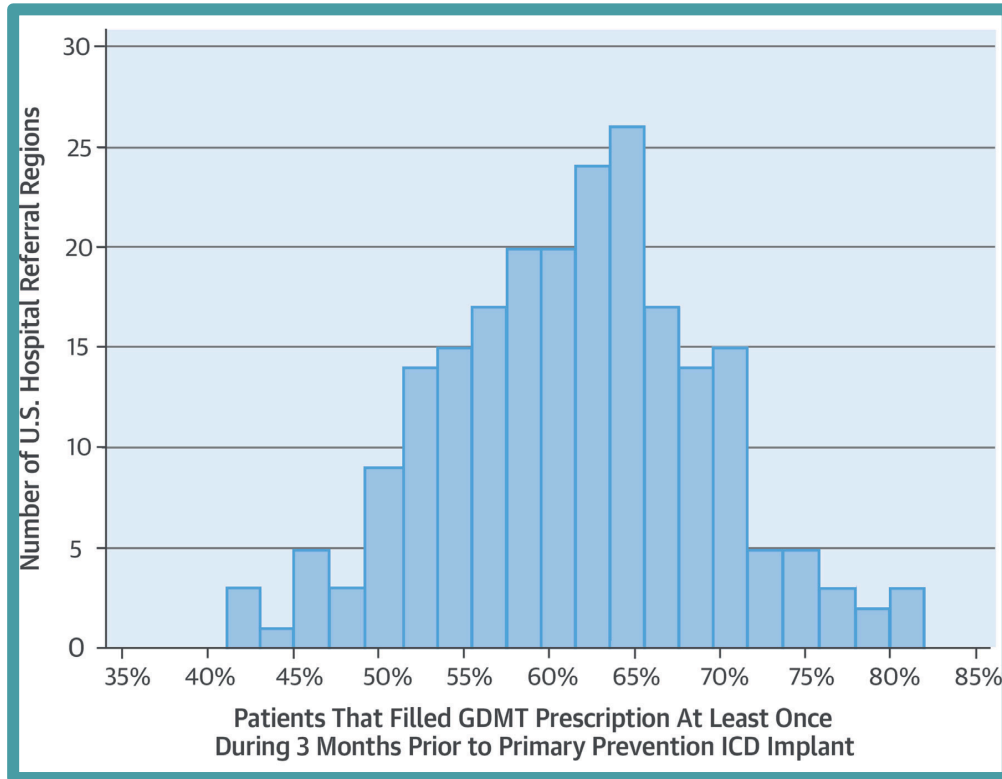
- **Optimal HF pharmacological treatment and Duration**
- **Age (*and co-morbidities*)**
- **Etiology: ischemic vs non-ischemic**

Primary prevention ICD:

An ICD is recommended in patients with symptomatic HF (NYHA Class II-III) and an LVEF $\leq 35\%$ despite ≥ 3 months of optimal medical treatment



Use of Guidelines-directed Medications Prior ICD Implantation: Current Practices



19773 pts (Medicare coverage)

222 US hospitals

Implantation period: 2007-2011

Mean age 74.9±6.2 yrs

35.4% females

	At any time	>80% time
ACE or ARB	74.3%	46.3%
HF Beta-blocker	80.7%	52.8%
ACE/ARB + HF BB	61.1%	28.3%
No GDMT	38.9%	71.7%

Total mortality at 1-year post-implant

GDMT patients: 11.1%

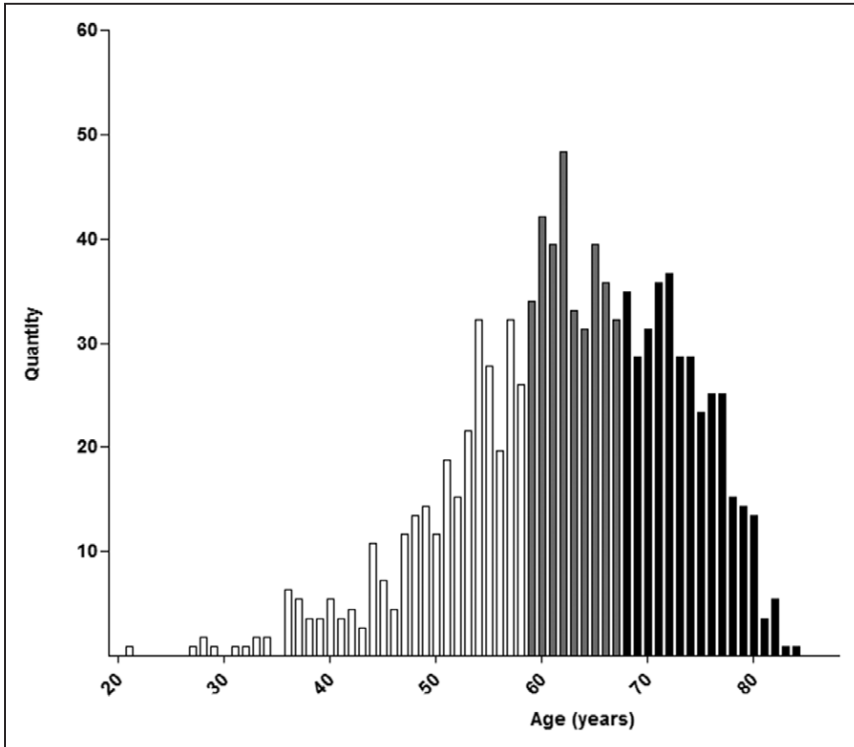
No-GDMT patients: 16.2%

Multivariate analysis: GDMT independent predictor of lower mortality ARR 0.80 (95%CI 0.73-0.87)

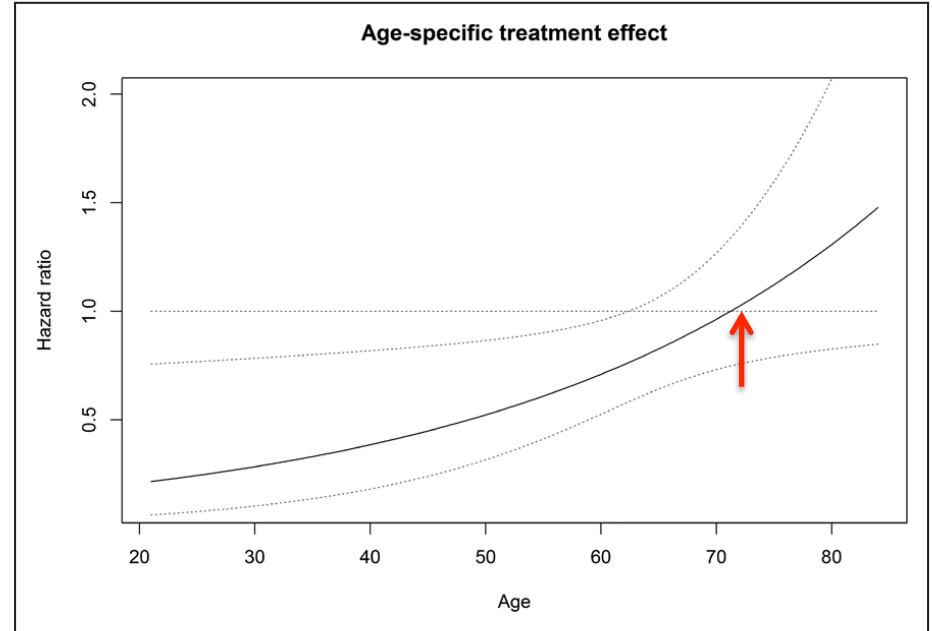
DANISH: Influence of Age

Age and Outcomes of Primary Prevention Implantable Cardioverter-Debrillators in Patients With Nonischemic Systolic Heart Failure

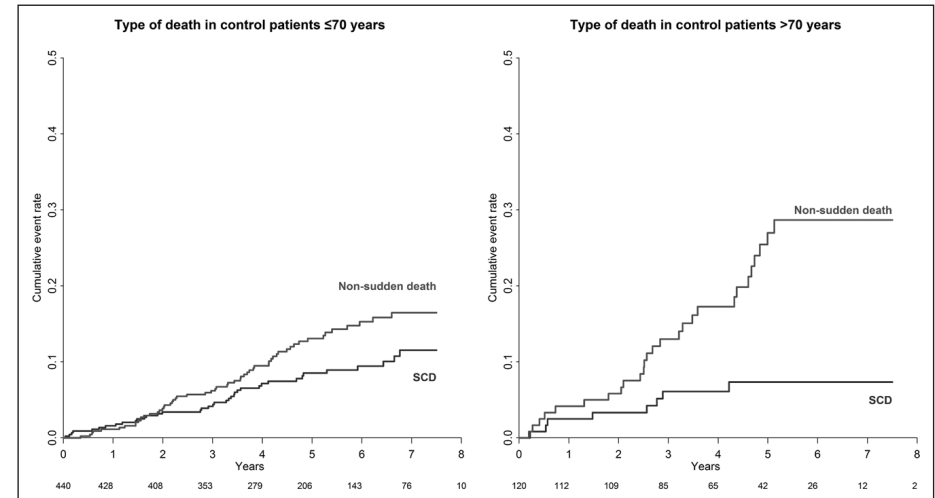
MB Elming et al. Circulation. 2017;136:1772–1780



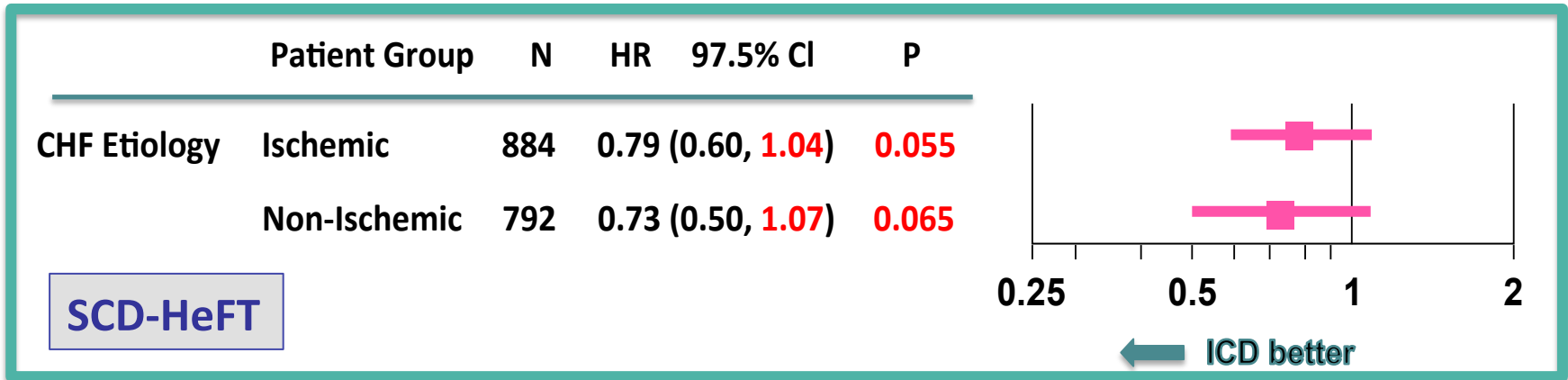
1116 Non-ischemic HF pts
Age= 63.5 yrs (21-84)
Age >70 yrs: 30%



Cumulated event rates of causes of death in the control group for patients ≤70 years and patients >70 years



HF Etiology: ICM vs NICM



GH Bardy et al N Engl J Med 2005;352:225-237

Implantable cardioverter-defibrillators for primary prevention in patients with Ischemic or nonischemic cardiomyopathy: A systematic review and meta-analysis.

All-cause mortality	HR 95% CI
Ischemic	0.82 (0.63-1.06)
Non-ischemic	0.81 (0.72-0.91)

Should we have to change the recommendations?

Recommendations for implantable cardioverter-defibrillator in patients with heart failure

<p>Secondary prevention An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients who have recovered from a ventricular arrhythmia causing haemodynamic instability, and who are expected to survive for >1 year with good functional status.</p>	I	A
<p>Primary prevention An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA Class II–III), and an LVEF ≤35% despite ≥3 months of OMT, provided they are expected to survive substantially longer than one year with good functional status</p> <ul style="list-style-type: none"> • IHD (unless they have had an MI in the prior 40 days – see below). • DCM. 	I	A
<p>ICD implantation is not recommended within 40 days of an MI as implantation at this time does not improve prognosis.</p>	III	A
<p>ICD therapy is not recommended in patients in NYHA Class IV with severe symptoms refractory to pharmacological therapy unless they are candidates for CRT, a ventricular assist device, or cardiac transplantation.</p>	III	C

P Ponikowski et al Eur Heart J 2016; 37: 2129-2200

Not Yet

Read the guidelines carefully and follow the recommendations

Personal Remarks

- Don't rush! Leave time in time (≥ 3 months)
- Take time to optimize medical (pharmacological and non-pharmacological) treatment
- Carefully weigh the pros and cons, especially in patients > 70 yrs and in patients with a clinical indication for CRT
- Main teaching of *DANISH*:
Yesterday's truth is not the truth of today.
The truth of today will probably not be tomorrow's
- Need to periodically reevaluate clinical evidence and adapt the clinical practices

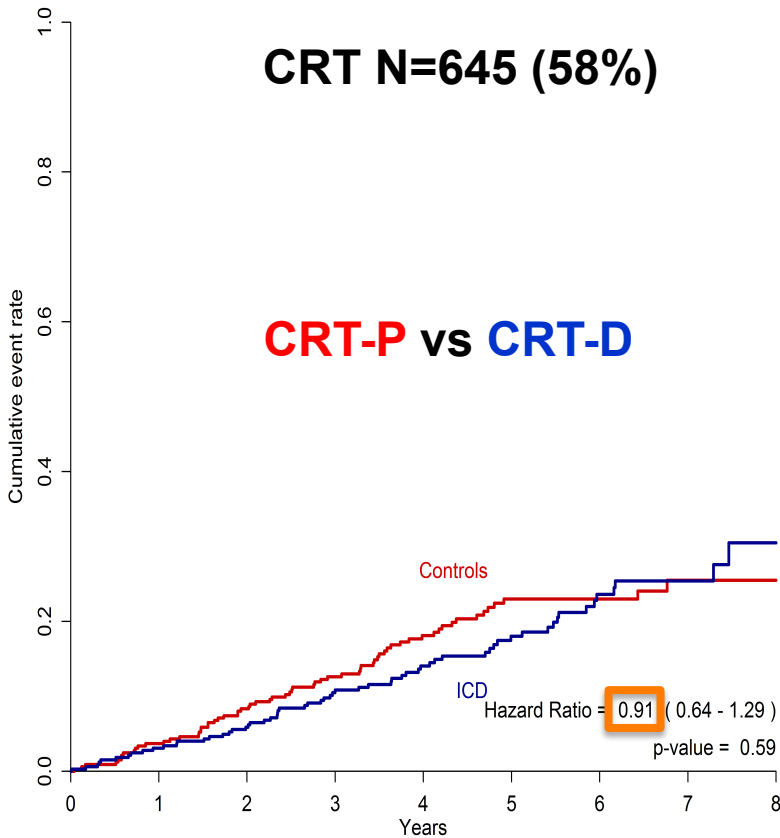
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Recommendations	Class ^a	Level ^b
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ICD therapy is not recommended in patients in NYHA Class IV with severe symptoms refractory to pharmacological therapy unless they are candidates for CRT, a ventricular assist device, or cardiac transplantation.	III	C
Patients should be carefully evaluated by an experienced cardiologist before generator replacement, because management goals and the patient's needs and clinical status may have changed.	IIa	B
A wearable ICD may be considered for patients with HF who are at risk of sudden cardiac death for a limited period or as a bridge to an implanted device.	IIb	C

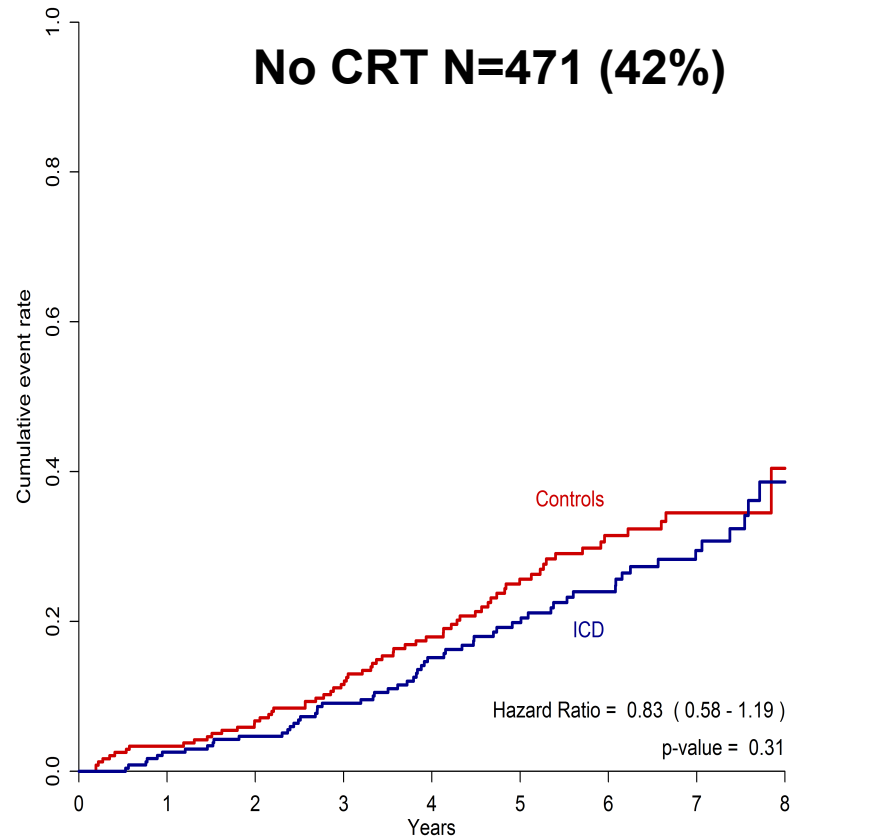


DANISH: Mortality in CRT vs No-CRT

Patients stratified at inclusion by clinical indication to CRT: Yes/No



323	311	296	246	192	132	89	42	5
322	312	303	255	202	147	91	48	6



237	229	221	192	152	116	80	46	7
234	228	223	196	156	125	95	59	11