Arrhythmic risk and role of ICD in Dilated cardiomyopathy

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Tradition of Excellence

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Arrhythmic risk in dilated cardiomyopathy

- Recent trials on DCM patients with systolic HF and OMT report 5 year mortality 21-28%.

- SCD occur in up to 12 % – 25-35% of all deaths

Køber L, et al. . N Engl J Med 2016;375:1221 -1230
Weintraub RG, et al. Lancet 2017; 390:400–414.
Beggs SAS, el al. Heart 2018;104:144–150

ESC European Society of Cardiology
European Heart Journal (2022) 43, 3997–4126
https://doi.org/10.1093/eurheartj/ehac262

2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

Developed by the task force for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death of the European Society of Cardiology (ESC)

Endorsed by the Association for European Paediatric and Congenital Cardiology (AEPC)

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Primary prevention ICD trials in dilated cardiomyopathy

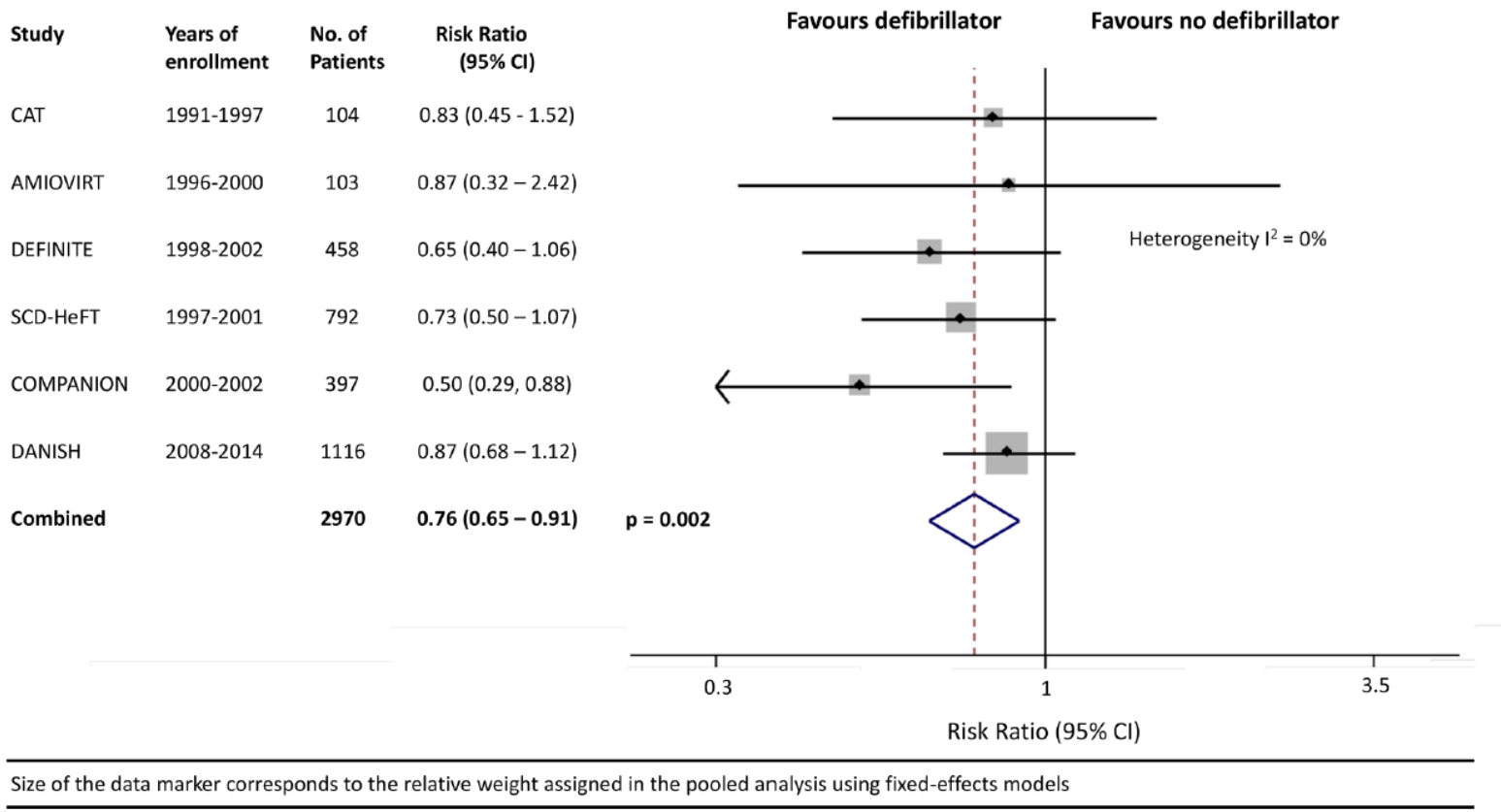
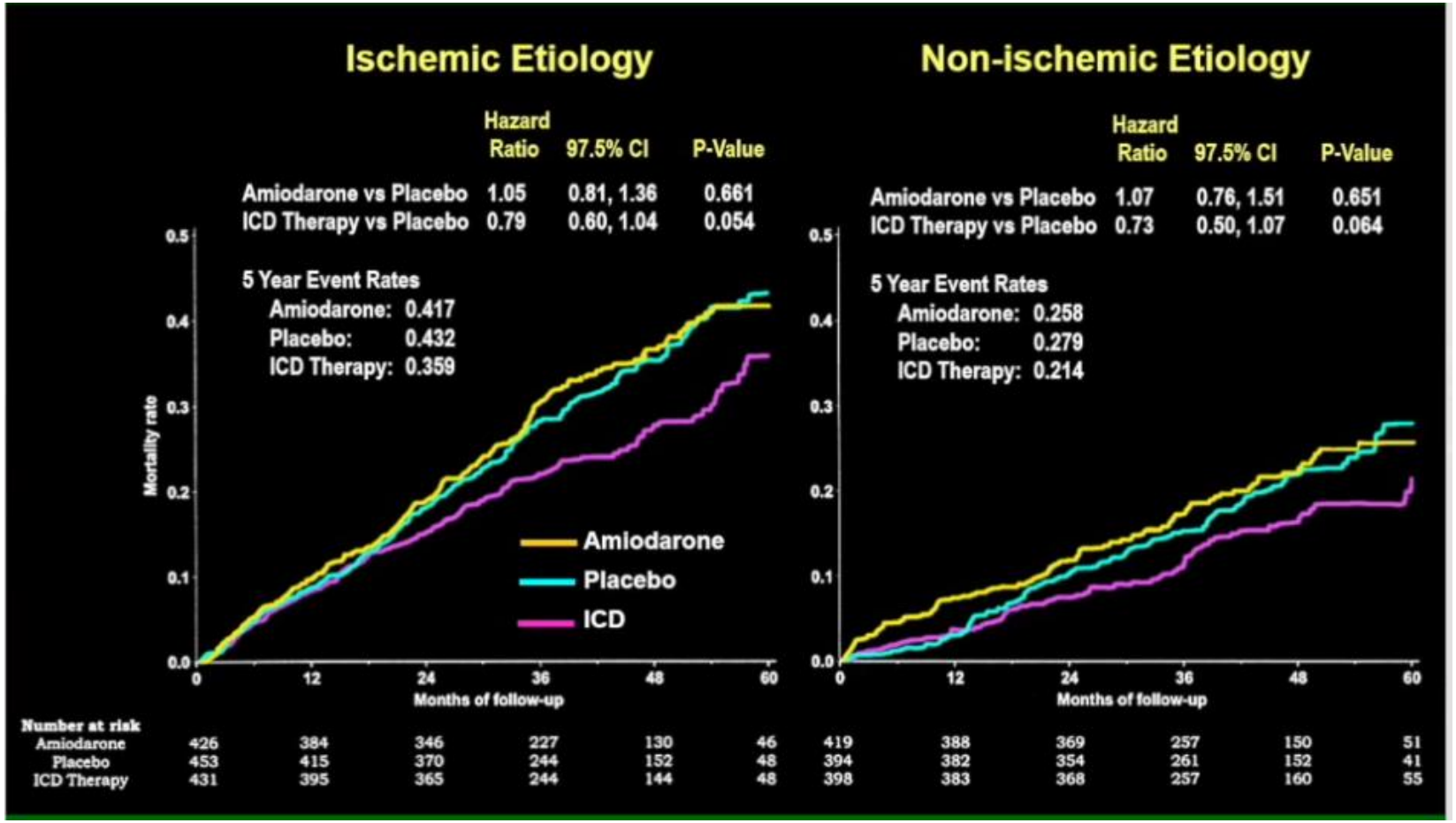


Figure 2 All cause mortality among patients with non-ischaemic cardiomyopathy randomised to implantable cardioverter defibrillator (ICD) or cardiac resynchronisation therapy defibrillator (CRT-D) versus medical therapy or medical therapy plus cardiac resynchronisation pacemaker (CRT-P) in primary prevention trials.

Beggs SAS, et al. Heart 2018;104:144–150

SCD-HeFT Trial

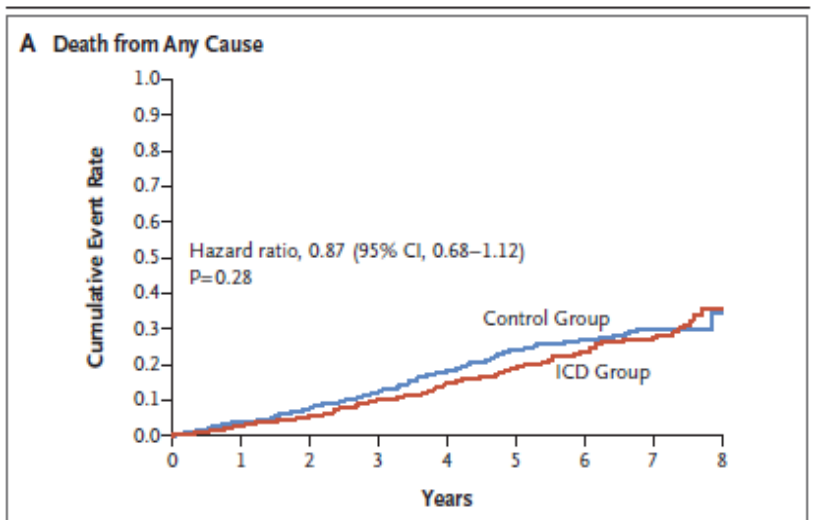
Mortality rate in subgroup of patients with ischemic and non ischemic Cardiomyopathy

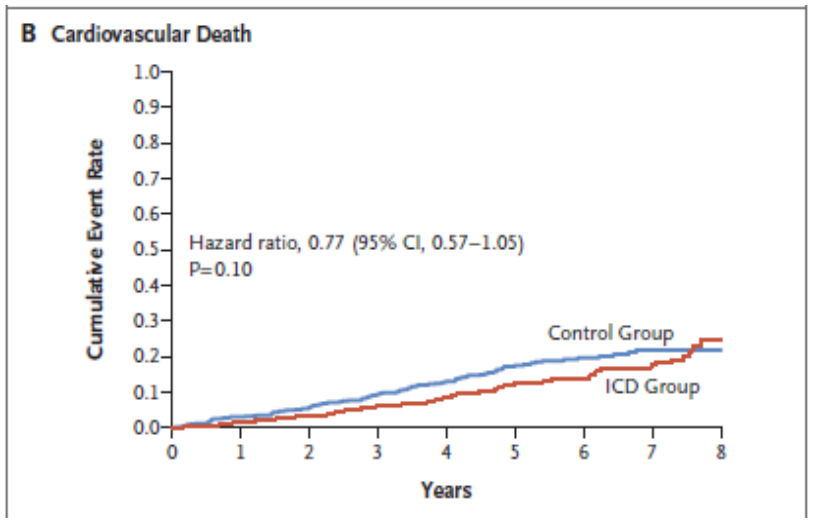


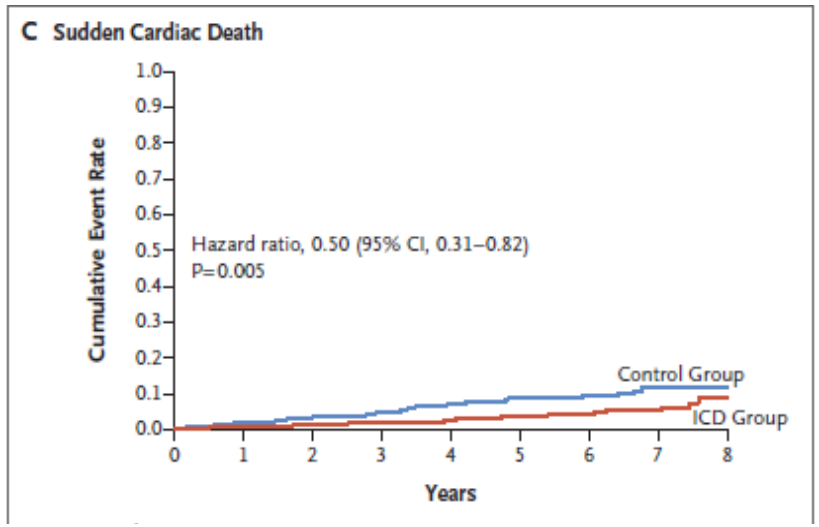
N Engl J Med 2005;352:225-37.

Defibrillator Implantation in Patients with Nonischemic Systolic Heart Failure

Lars Køber, M.D., D.M.Sc., Jens J. Thune, M.D., Ph.D., Jens C. Nielsen, M.D., D.M.Sc., Jens Haarbo, M.D., D.M.Sc., Lars Videbæk, M.D., Ph.D., Eva Korup, M.D., Ph.D., Gunnar Jensen, M.D., Ph.D., Per Hildebrandt, M.D., D.M.Sc., Flemming H. Steffensen, M.D., Niels E. Bruun, M.D., D.M.Sc., Hans Eiskjær, M.D., D.M.Sc., Axel Brandes, M.D., Anna M. Thøgersen, M.D., Ph.D., Finn Gustafsson, M.D., D.M.Sc., Kenneth Egstrup, M.D., D.M.Sc., Regitze Videbæk, M.D., Christian Hassager, M.D., D.M.Sc., Jesper H. Svendsen, M.D., D.M.Sc., Dan E. Høfsten, M.D., Ph.D., Christian Torp-Pedersen, M.D., D.M.Sc., and Steen Pehrson, M.D., D.M.Sc., for the DANISH Investigators*



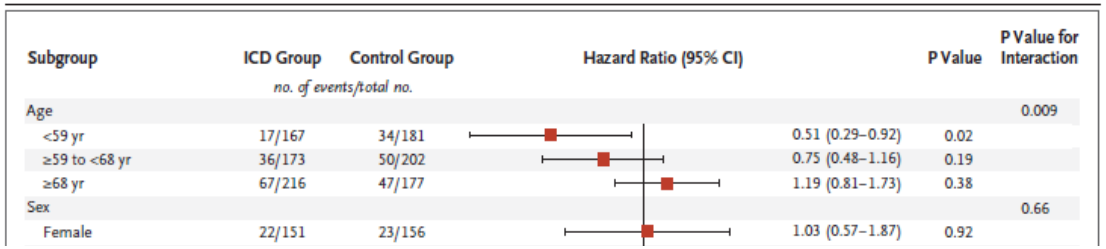




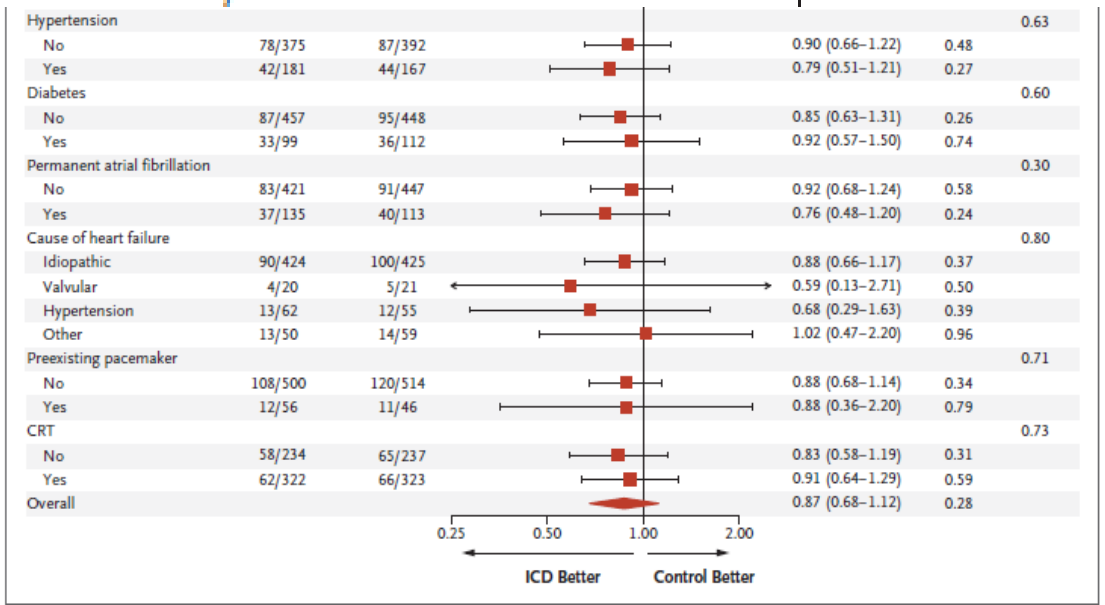
Randomized, controlled trial, 556 patients , Systolic HF, LVEF< 35%, non ischemic
ICD, Vs “usual clinical care” (control group).
58% of the patients received CRT.
Primary outcome of death from any cause.

N Engl J Med 2016;375:1221-30

Rate of death from any cause(primary outcome) in prespecified subgroups

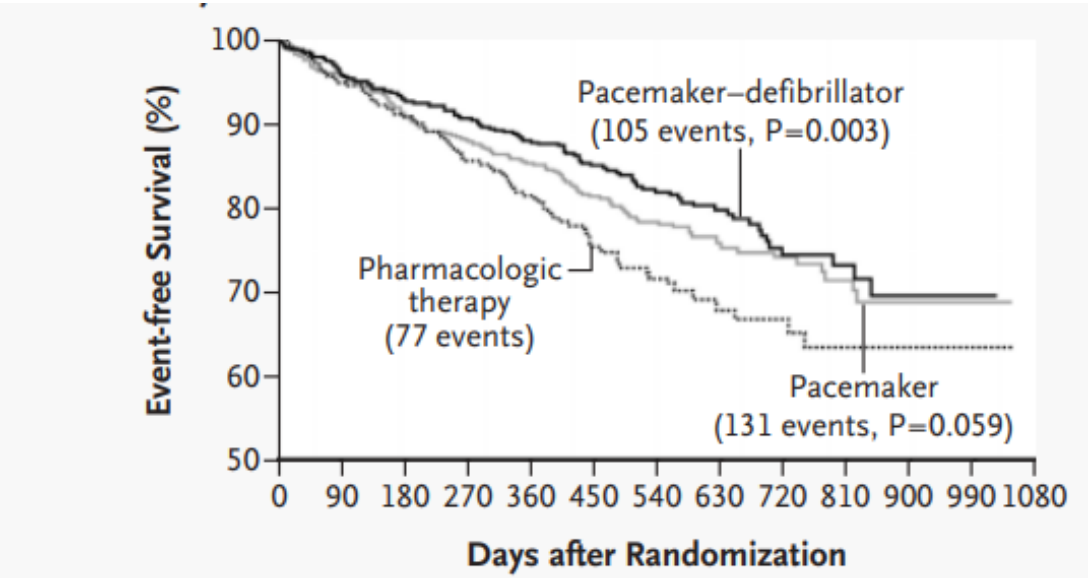


Subgroup	ICD Group	Control Group	Hazard Ratio (95% CI)	P Value	P Value for Interaction
	no. of events/total no.				
Age					0.009
<59 yr	17/167	34/181	0.51 (0.29–0.92)	0.02	
≥59 to <68 yr	36/173	50/202	0.75 (0.48–1.16)	0.19	
≥68 yr	67/216	47/177	1.19 (0.81–1.73)	0.38	
Sex					0.66
Female	22/151	23/156	1.03 (0.57–1.87)	0.92	



Subgroup	ICD Group	Control Group	Hazard Ratio (95% CI)	P Value	P Value for Interaction
	no. of events/total no.				
Hypertension					0.63
No	78/375	87/392	0.90 (0.66–1.22)	0.48	
Yes	42/181	44/167	0.79 (0.51–1.21)	0.27	
Diabetes					0.60
No	87/457	95/448	0.85 (0.63–1.31)	0.26	
Yes	33/99	36/112	0.92 (0.57–1.50)	0.74	
Permanent atrial fibrillation					0.30
No	83/421	91/447	0.92 (0.68–1.24)	0.58	
Yes	37/135	40/113	0.76 (0.48–1.20)	0.24	
Cause of heart failure					0.80
Idiopathic	90/424	100/425	0.88 (0.66–1.17)	0.37	
Valvular	4/20	5/21	0.59 (0.13–2.71)	0.50	
Hypertension	13/62	12/55	0.68 (0.29–1.63)	0.39	
Other	13/50	14/59	1.02 (0.47–2.20)	0.96	
Preexisting pacemaker					0.71
No	108/500	120/514	0.88 (0.68–1.14)	0.34	
Yes	12/56	11/46	0.88 (0.36–2.20)	0.79	
CRT					0.73
No	58/234	65/237	0.83 (0.58–1.19)	0.31	
Yes	62/322	66/323	0.91 (0.64–1.29)	0.59	
Overall			0.87 (0.68–1.12)	0.28	

COMPANION trial

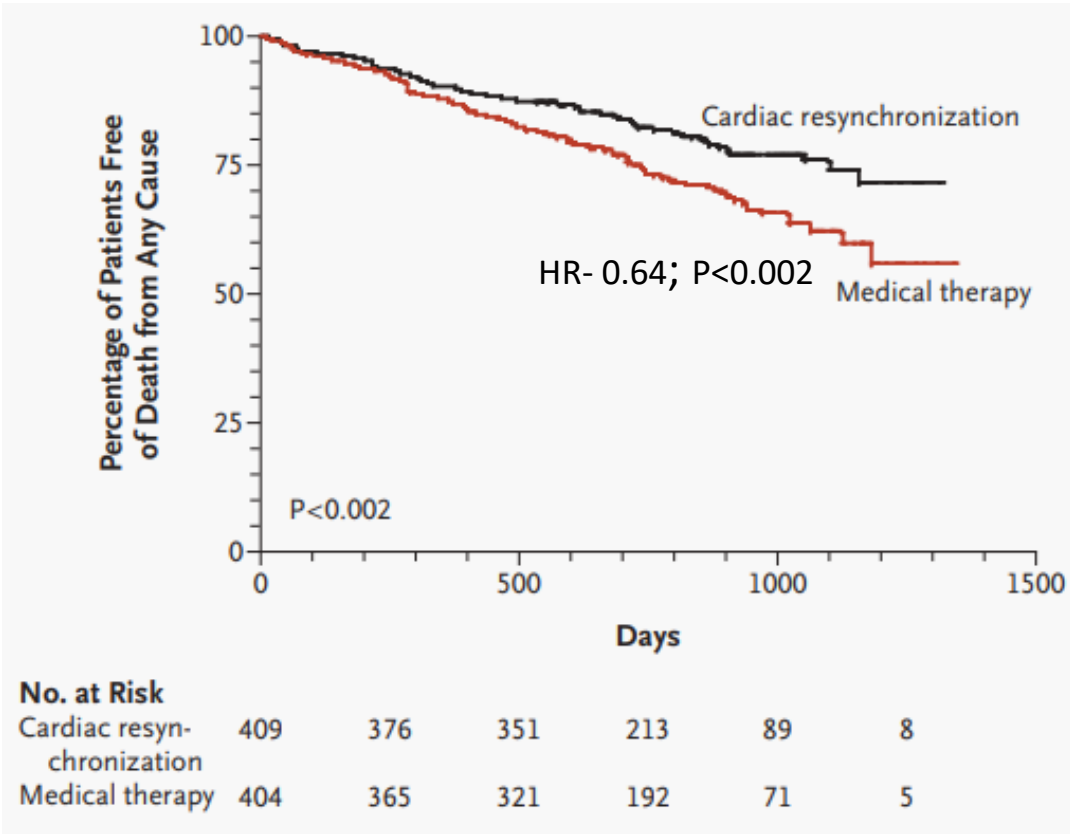


No. at Risk

Pharmacologic therapy	308	284	255	217	186	141	94	57	45	25	4	2
Pacemaker	617	579	520	488	439	355	251	164	104	60	25	5
Pacemaker–defibrillator	595	555	517	470	420	331	219	148	95	47	21	1

N Engl J Med. 2004;350:2140–2150

CARE HF trial



No. at Risk

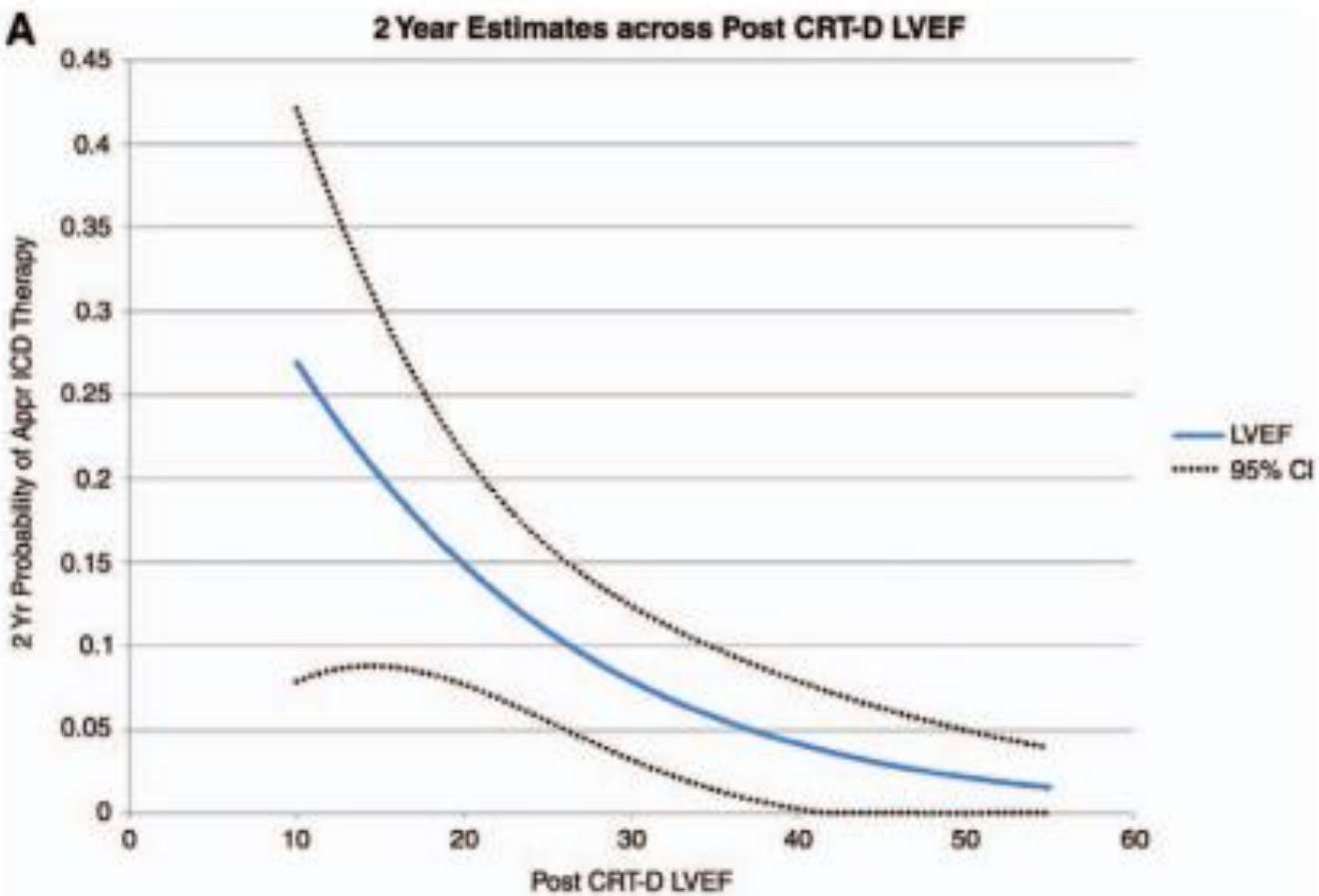
Cardiac resynchronization	409	376	351	213	89	8
Medical therapy	404	365	321	192	71	5

N Engl J Med 2005;352:1539-49.

Association Between Left Ventricular Ejection Fraction Post-Cardiac Resynchronization Treatment and Subsequent Implantable Cardioverter Defibrillator Therapy for Sustained Ventricular Tachyarrhythmias

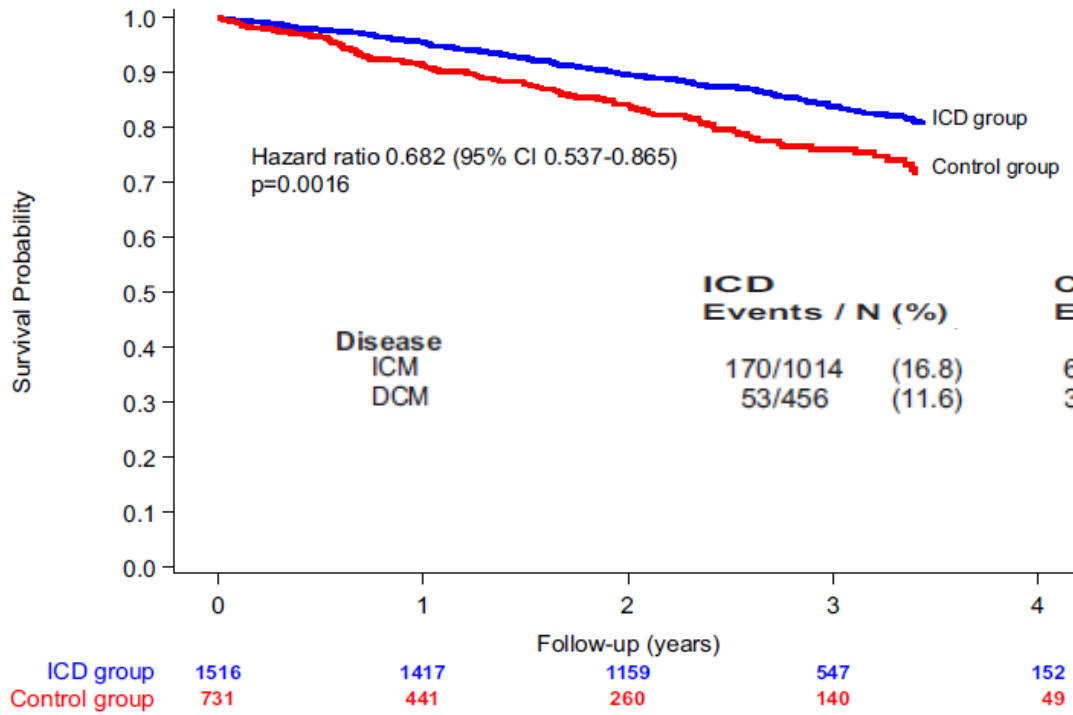
Joseph A. Manfredi, MD; Sana M. Al-Khatib, MD, MHS; Linda K. Shaw, MS; Laine Thomas, PhD; Richard I. Fogel, MD; Benzy Padanilam, MD; David Rardon, MD; Rosh Vatthyam, MD; Lee W. Gemma, MD; Keith Golden, MD; Eric N. Prystowsky, MD

Circ Arrhythm Electrophysiol. 2013;6:257-264.



ESC European Society of Cardiology
European Heart Journal (2020) **41**, 3437–3447
doi:10.1093/eurheartj/ehaa226

Clinical effectiveness of primary prevention implantable cardioverter-defibrillators: results of the EU-CERT-ICD controlled multicentre cohort study



Disease	ICD Events / N (%)		Control Events / N (%)		Hazard ratio (95% CI)
ICM	170/1014	(16.8)	66/387	(17.1)	0.786 (0.582, 1.061)
DCM	53/456	(11.6)	37/297	(12.5)	0.588 (0.380, 0.910)

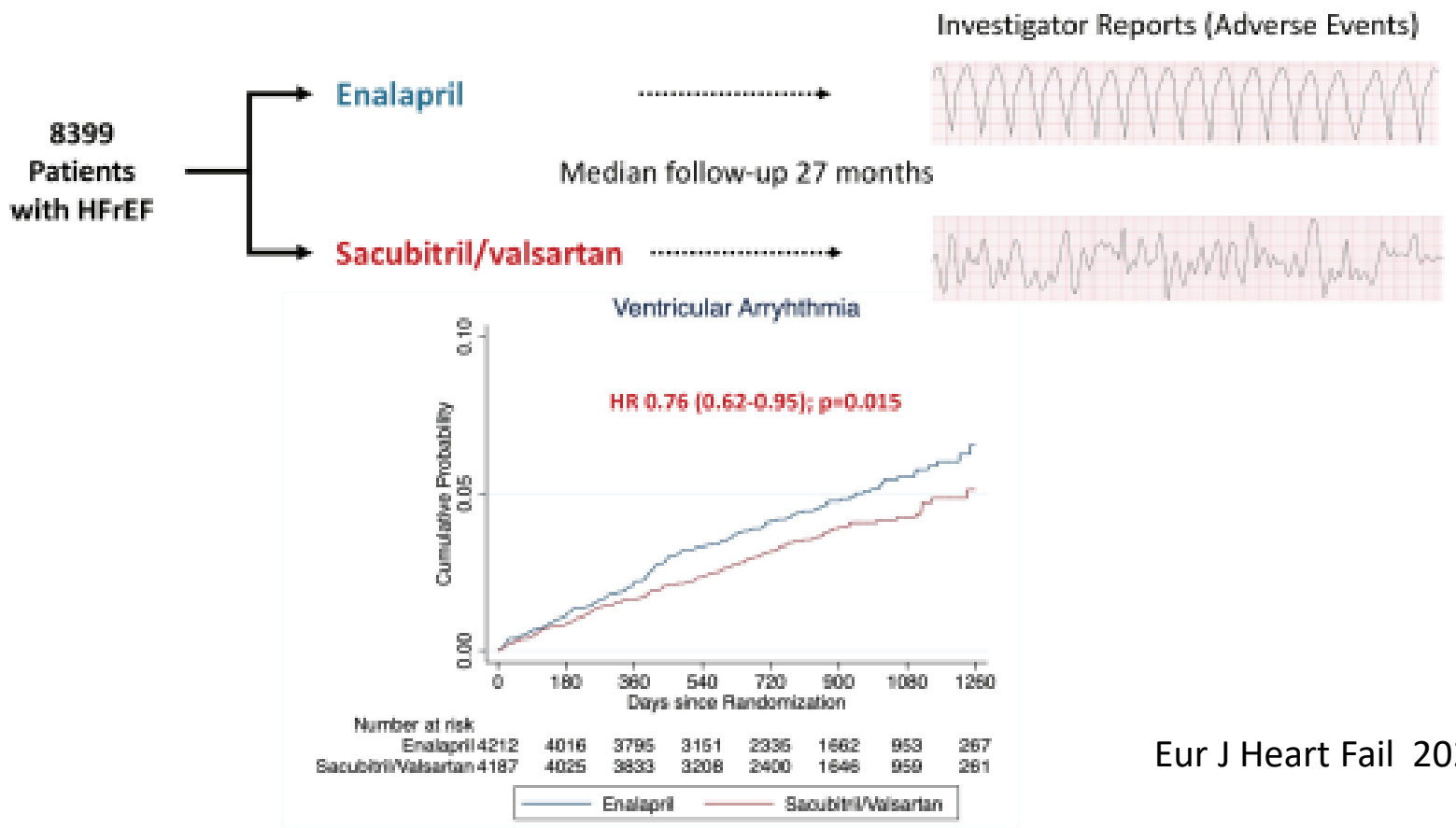
Take home figure Unadjusted all-cause mortality of the ICD group (blue line) and the control group (red line). There is an unadjusted 32% difference in survival between the ICD group and the control group. CI, confidence interval.

2022 ESC Guidelines

	2015	2022
Recommendations	**Class**	**Class**
DCM/HNDCM		
ICD implantation should be considered in patients with DCM/HNDCM, symptomatic heart failure (NYHA class II–III), and LVEF ≤ 35% after ≥ 3 months of OMT.	**I**	**IIa**

Effect of sacubitril/valsartan on investigator-reported ventricular arrhythmias in PARADIGM-HF

James P. Curtain[1], Alice M. Jackson[1], Li Shen[1,2], Pardeep S. Jhund[1], Kieran F. Docherty[1], Mark C. Petrie[1], Davide Castagno[3], Akshay S. Desai[4], Luis E. Rohde[4,5], Martin P. Lefkowitz[6], Jean-Lucien Rouleau[7], Michael R. Zile[8], Scott D. Solomon[4], Karl Swedberg[9], Milton Packer[10], and John J.V. McMurray[1]*

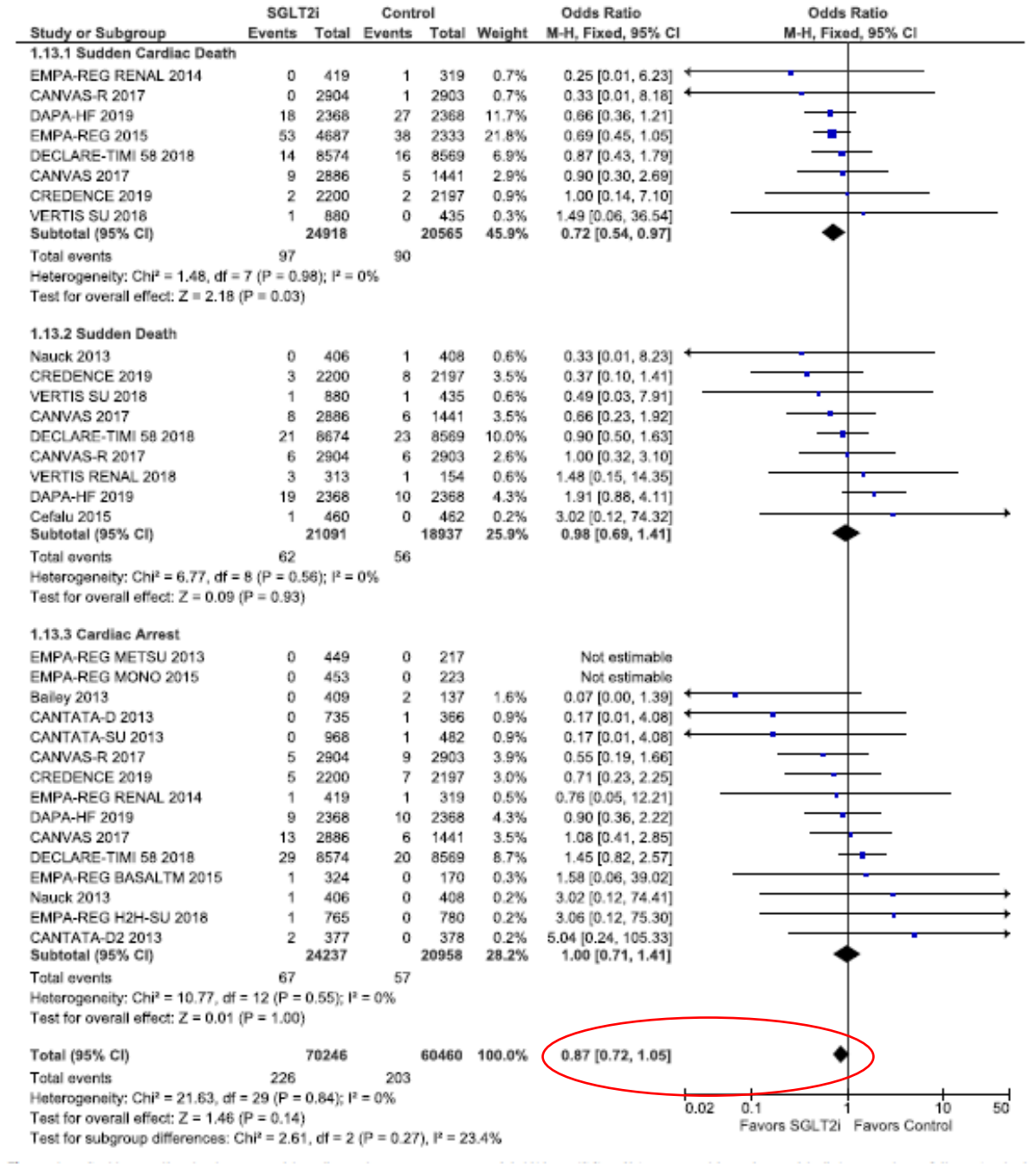


Eur J Heart Fail 2022 Mar;24(3):551-561

Association of SGLT2 inhibitors with arrhythmias and sudden cardiac death in patients with type 2 diabetes or heart failure: A meta-analysis of 34 randomized controlled trials

Gilson C. Fernandes, MD,* Amanda Fernandes, MD,† Rhanderson Cardoso, MD,‡ Jorge Penalver, MD,* Leonardo Knijnik, MD,† Raul D. Mitrani, MD, FHRS,* Robert J. Myerburg, MD,* Jeffrey J. Goldberger, MD, MBA, FHRS*

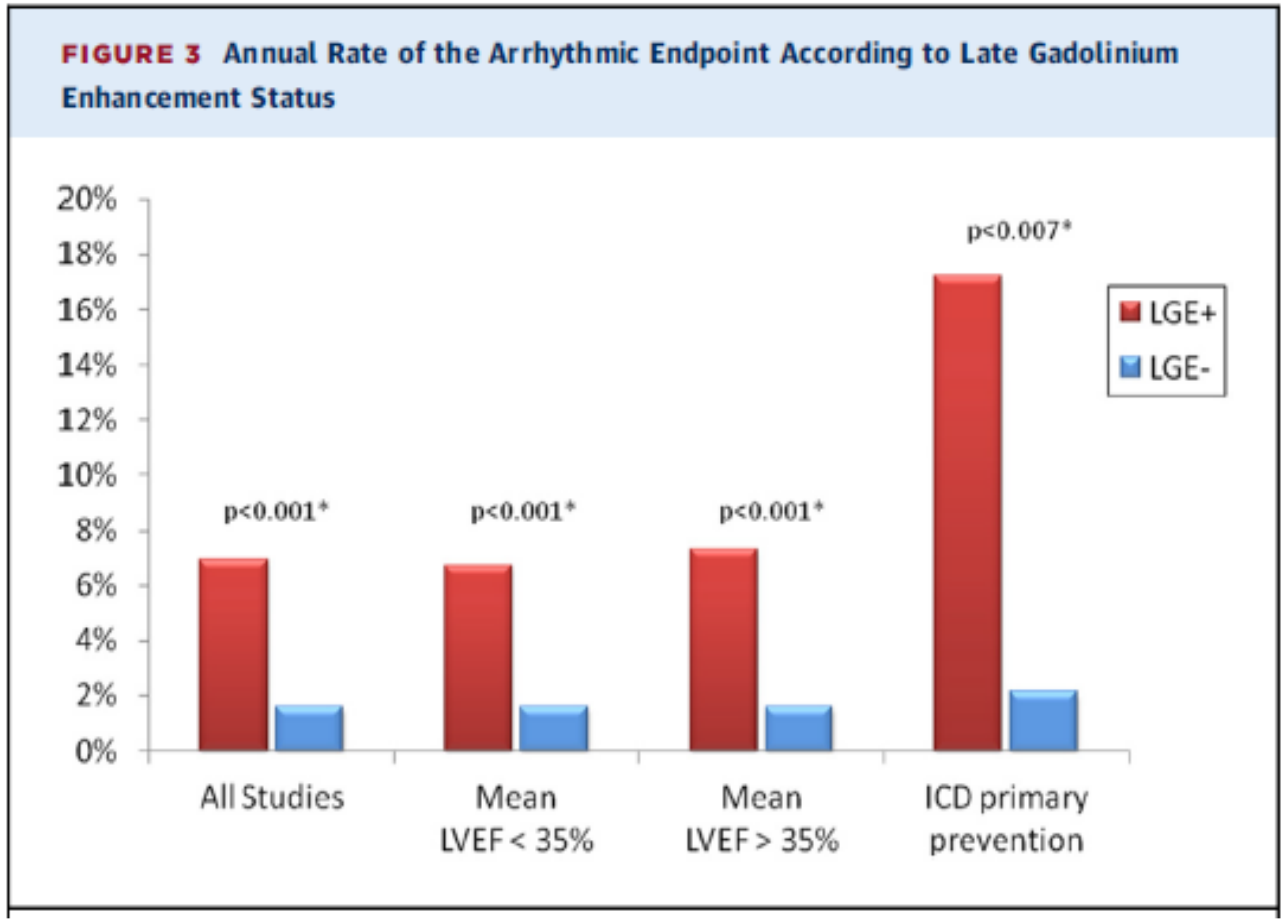
Heart Rhythm 2021;18:1098–1105



Late Gadolinium Enhancement and the Risk for Ventricular Arrhythmias of Sudden Death in Dilated Cardiomyopathy

Meta-Analysis

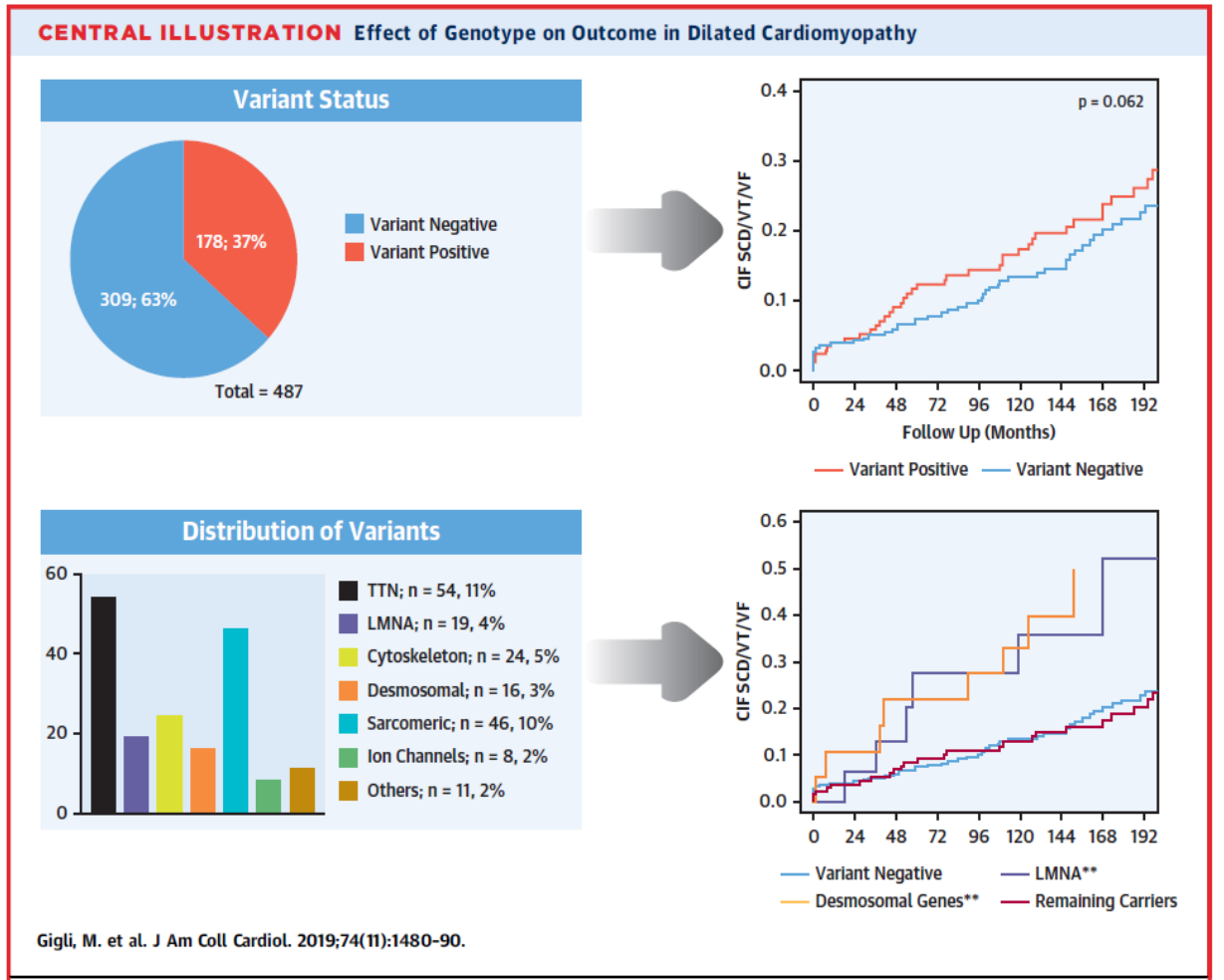
- 2,948 patients enrolled in 29 studies
- LGE was present inconsiderable proportion of patients with DCM (44%)
- LGE is a robust predictor of VA or SCD across a wide spectrum of patients with DCM (OR 7.8 in primary prevention)



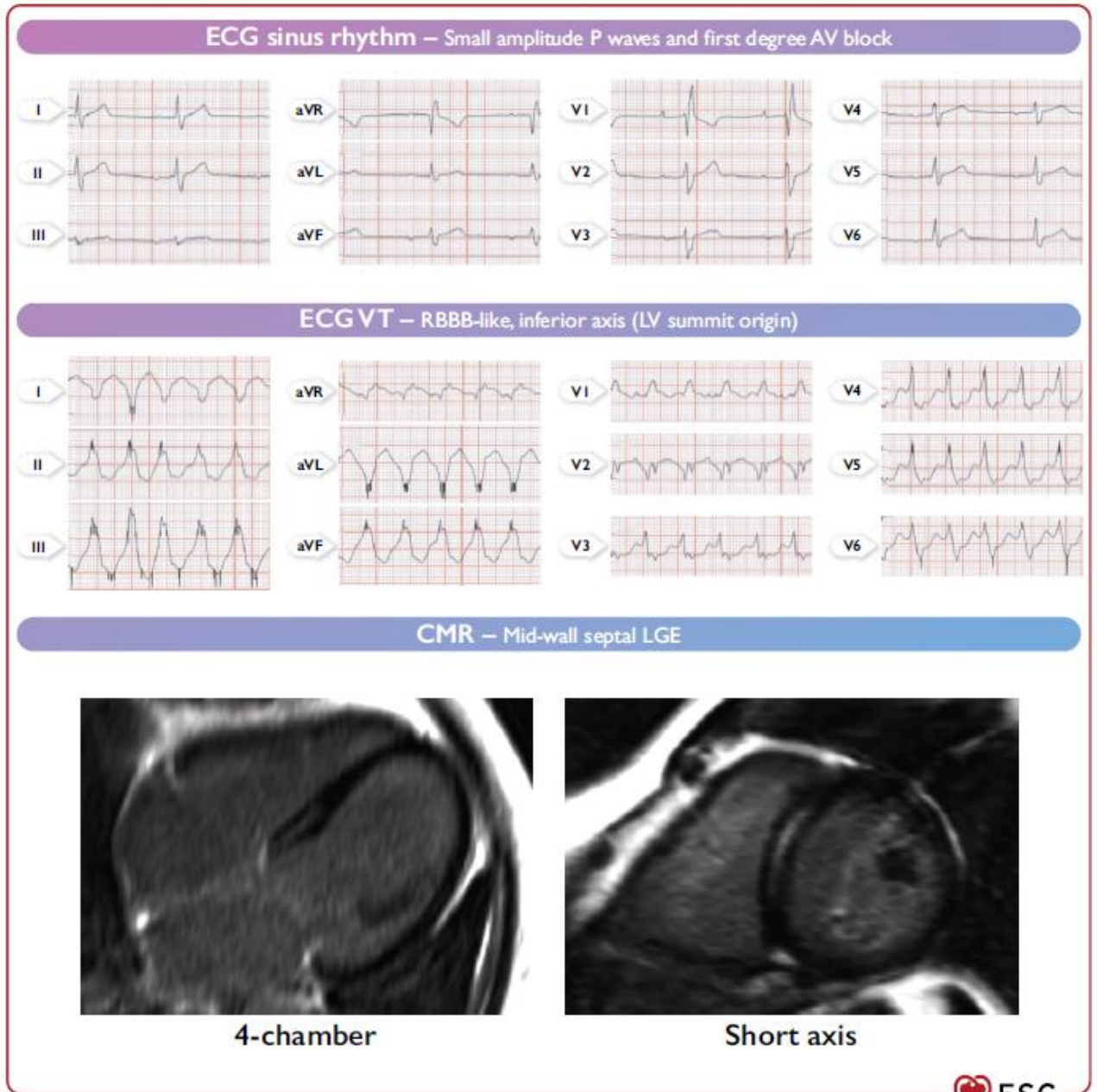
Am Coll Cardiol HF 2017;5:28–38

Genetic Risk of Arrhythmic Phenotypes in Patients With Dilated Cardiomyopathy

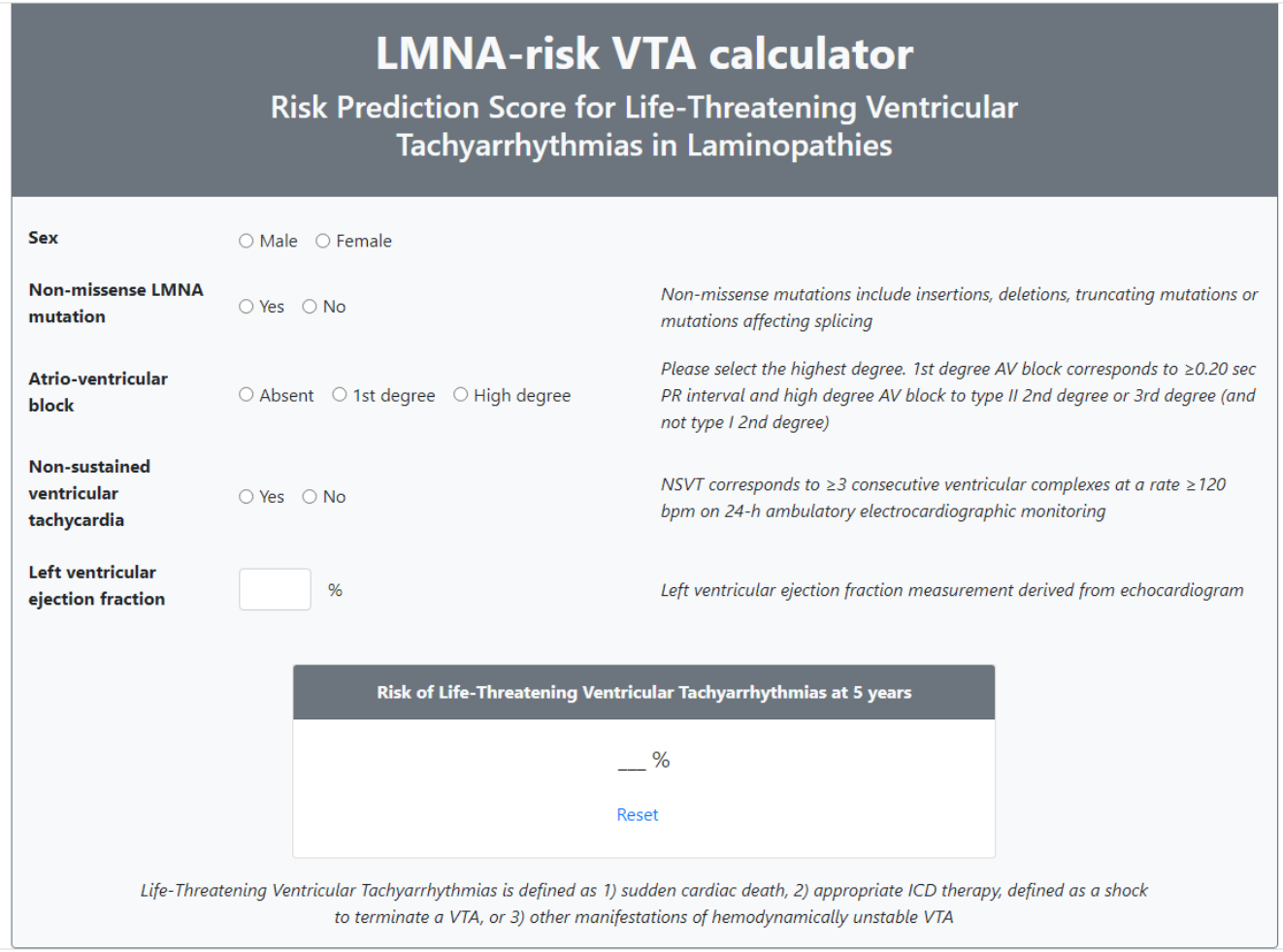
- More than 50 genes are currently considered to be disease-related, in 20% to 50% of all DCM cases.
- Carriers of desmosomal and LMNA variants experienced the highest rate of VA/SCD, in dependent of the LVEF



Typical features of dilated cardioyopathy with lamin A/C gene mutation



- In patients with a 5-year estimated risk ≥10% and a manifest cardiac phenotype (NSVT, LVEF < 50%, or AV conduction delay), a primary prevention ICD implantation should be considered



LMNA-risk VTA calculator

Risk Prediction Score for Life-Threatening Ventricular Tachyarrhythmias in Laminopathies

Sex	○ Male ○ Female	
Non-missense LMNA mutation	○ Yes ○ No	*Non-missense mutations include insertions, deletions, truncating mutations or mutations affecting splicing*
Atrio-ventricular block	○ Absent ○ 1st degree ○ High degree	*Please select the highest degree. 1st degree AV block corresponds to ≥0.20 sec PR interval and high degree AV block to type II 2nd degree or 3rd degree (and not type I 2nd degree)*
Non-sustained ventricular tachycardia	○ Yes ○ No	*NSVT corresponds to ≥3 consecutive ventricular complexes at a rate ≥120 bpm on 24-h ambulatory electrocardiographic monitoring*
Left ventricular ejection fraction	[ ] %	*Left ventricular ejection fraction measurement derived from echocardiogram*

Risk of Life-Threatening Ventricular Tachyarrhythmias at 5 years

___ %

Reset

Life-Threatening Ventricular Tachyarrhythmias is defined as 1) sudden cardiac death, 2) appropriate ICD therapy, defined as a shock to terminate a VTA, or 3) other manifestations of hemodynamically unstable VTA

https://lmna-riskvta.fr/

Prognostic value of programmed ventricular stimulation for sudden death in selected high risk patients with structural heart disease and preserved systolic function

Konstantinos A. Gatzoulis [a,*,1], Dimitris Tsiachris [a,1], Petros Arsenos [a,1], Stefanos Archontakis [a,1], Polychronis Dilaveris [a,1], Apostolis Vouliotis [a,1], Skevos Sideris [b,1], Ioannis Skiadas [b,1], Ioannis Kallikazaros [b,1], Christodoulos Stefanadis [a,1]

[a] *First Cardiology Division, University of Athens Medical School, Hippokration Hospital, Athens, Greece*
[b] *State Department of Cardiology, Hippokration Hospital, Athens, Greece*

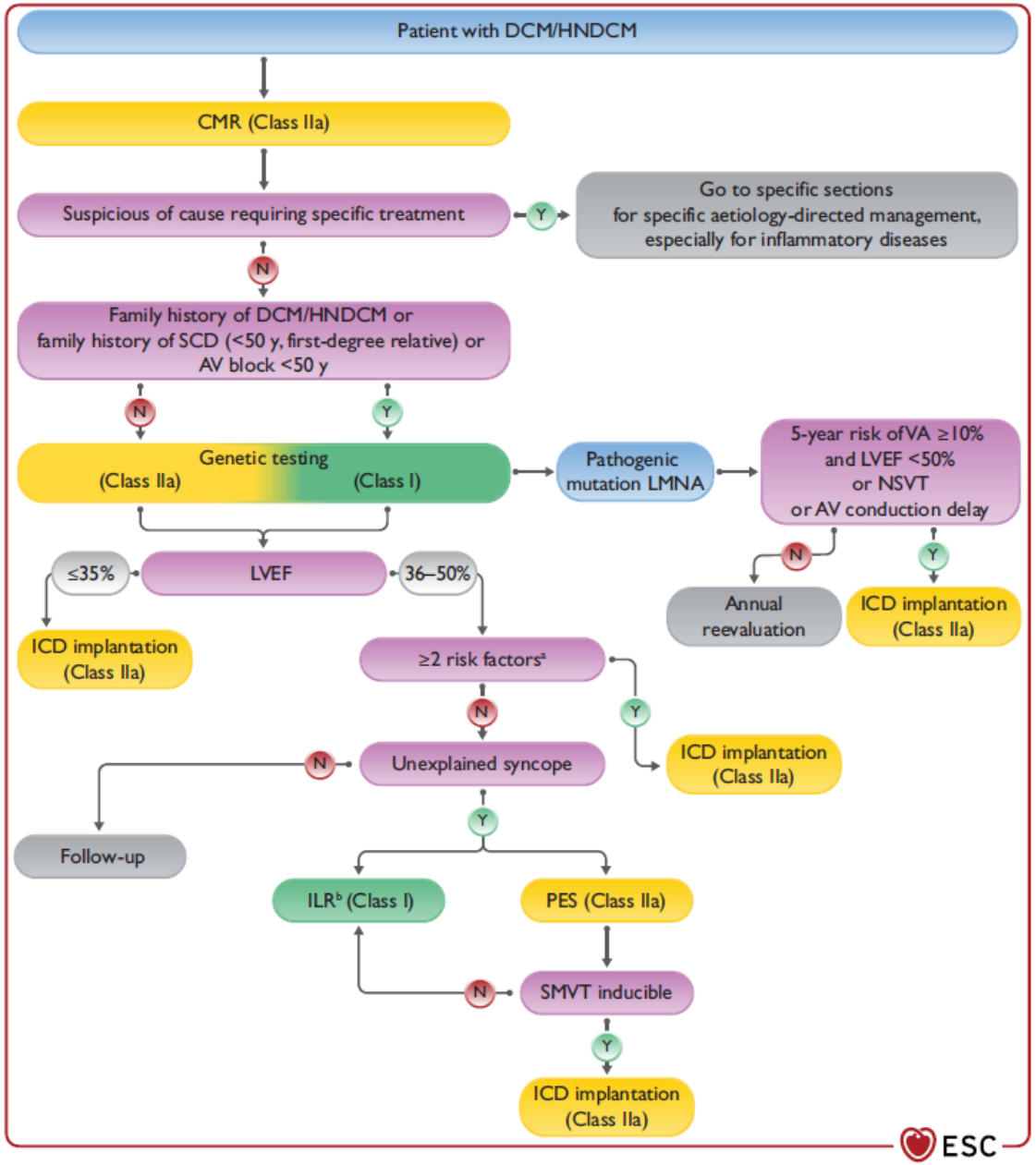
- Dilated cardiomyopathy (DCM) patients with LVEF ≥40%
- Assessed the prognostic role of programmed ventricular stimulation (PVS) in 42 DCM patients
- Mean follow-up period was 52.3 months.
- None of the non-inducible patients at baseline (29 patients) experienced SCD or cardiac death

Inter J Card 176 (2014) 1449–1451

Diagnostic evaluation and general recommendations		
Genetic testing (including at least *LMNA*, *PLN*, *RBM20*, and *FLNC* genes) is recommended in patients with DCM/HNDCM and AV conduction delay at <50 years, or who have a family history of DCM/HNDCM or SCD in a first-degree relative (at age <50 years).[641–645]	I	B
CMR with LGE should be considered in DCM/HNDCM patients for assessing the aetiology and the risk of VA/SCD.[129,651,667]	IIa	B
Genetic testing (including at least *LMNA*, *PLN*, *RBM20*, and *FLNC* genes) should be considered for risk stratification in patients with apparently sporadic DCM/HNDCM, who present at young age, or with signs suspicious for an inherited aetiology.[641–645]	IIa	C
Participation in high-intensity exercise including competitive sports is not recommended for individuals with DCM/HNDCM and a *LMNA* mutation.[655]	III	C

Risk stratification and primary prevention of SCD		
ICD implantation should be considered in patients with DCM/HNDCM, symptomatic heart failure (NYHA class II–III), and LVEF ≤35% after ≥3 months of OMT.[357,359,635,650]	IIa	A
ICD implantation should be considered in DCM/HNDCM patients with a pathogenic mutation in *LMNA* gene, if the estimated 5-year risk of life-threatening VA is ≥10%[c] *and* in the presence of NSVT or LVEF < 50% or AV conduction delay.[80,652,653]	IIa	B
ICD implantation should be considered in DCM/HNDCM patients with a LVEF <50% and ≥2 risk factors (syncope, LGE on CMR, inducible SMVT at PES, pathogenic mutations in *LMNA*,[d] *PLN*, *FLNC*, and *RBM20* genes).	IIa	C
In DCM/HNDM patients, electrophysiological evaluation should be considered when syncope remains unexplained after non-invasive evaluation.[661,668]	IIa	C

Algorithm for risk stratification and primary prevention of sudden cardiac death in patients with DCM/HNDCM



Risk factor:
-Unexplained syncope
-Pathogenic variants in PLN, FLNC, or RBM20
-LGE on CMR
-Inducible SMVT at PES.

Secondary prevention of sudden cardiac death and management of ventricular arrhythmias in DCM

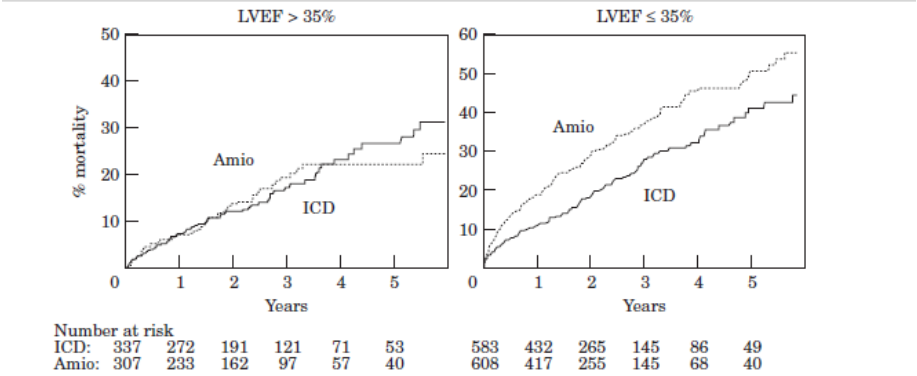


Figure 2 Cumulative risk of death for patients with left ventricular ejection fraction (LVEF) >35% and ≤35%.

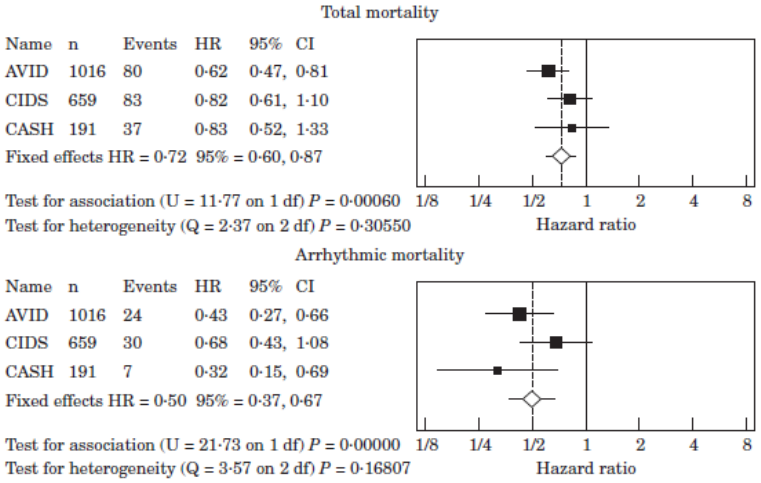
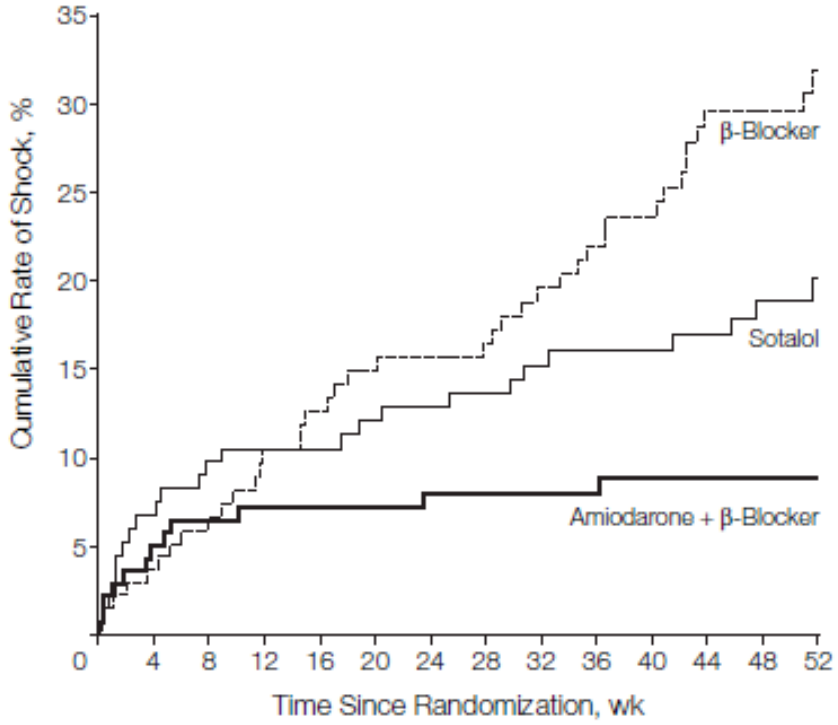


Figure 3 Results of the fixed effects meta-analysis (see text for explanation).

- 1963 patients, of whom only 292 (14.8%) had non-ischemic etiologies
- 28% reduction in the relative risk of death with the ICD that is due almost entirely to a 50% reduction in arrhythmic death

Eur Heart J 2000; 21, 2071–2078

- In the OPTIC trial, 412 patients with ICD implantation within 21 days of VT/VF were randomized to ***amiodarone plus beta-blockers***, ***sotalol*** alone,or ***beta-blocker*** alone



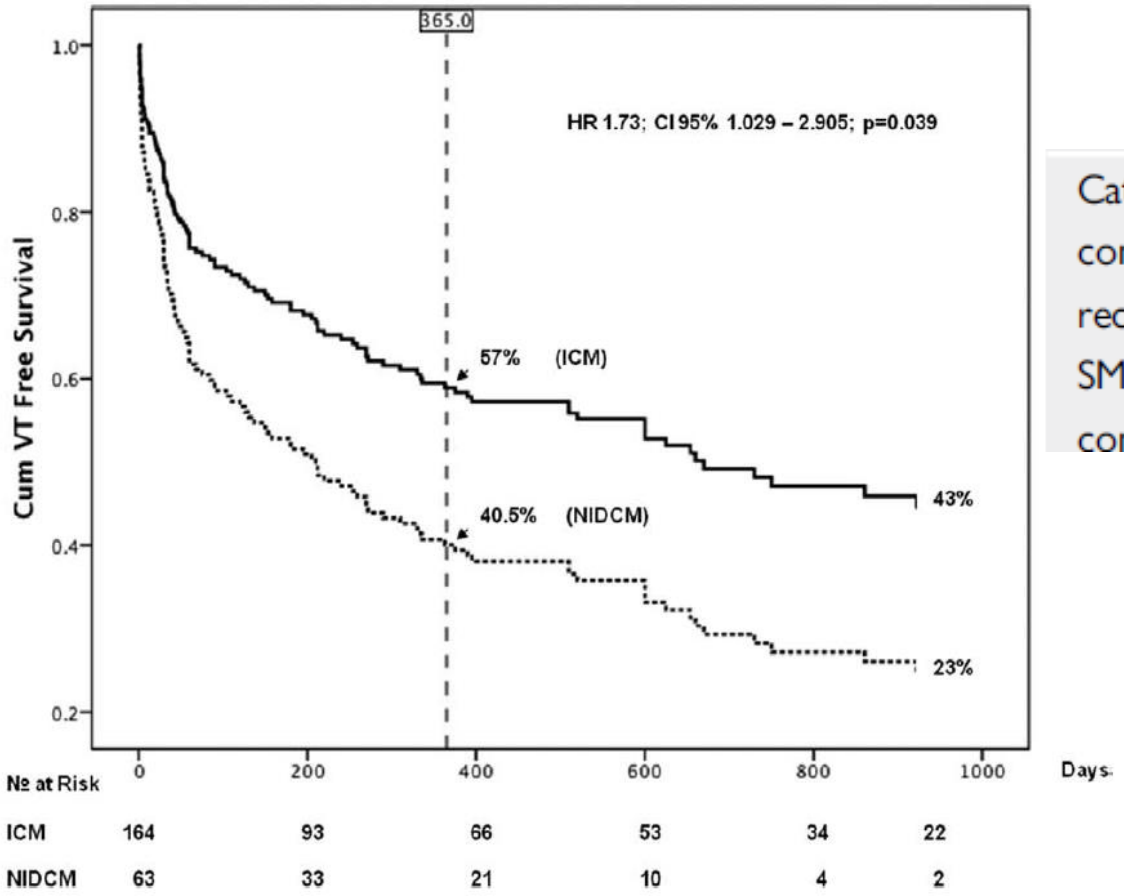
No. at Risk					
β-Blocker	138	119	109	91	42
Sotalol	134	118	108	94	35
Amiodarone + β-Blocker	140	124	115	106	56

- ICD shock rates after one year were 10.3%, 24.3%, and 38.5%, respectively

Outcomes in Catheter Ablation of Ventricular Tachycardia in Dilated Nonischemic Cardiomyopathy Compared With Ischemic Cardiomyopathy

Results From the Prospective Heart Centre of Leipzig VT (HELP-VT) Study

Borislav Dinov, MD; Lukas Fiedler, MD; Robert Schönbauer, MD; Andreas Bollmann, MD, PhD; Sascha Rolf, MD; Christopher Piorkowski, MD; Gerhard Hindricks, MD; Arash Arya, MD



Catheter ablation in specialized centres should be considered in patients with DCM/HNDCM and recurrent, symptomatic SMVT or ICD shocks for SMVT, in whom AADs are ineffective, contraindicated, or not tolerated.[481,497,664,669]	IIa	C

Circulation. 2014;129:728-736

SCD risk in DCM – future aspect

- LGE could be a powerful tool to improve risk stratification for SCD in patients with DCM

- Future studies need to confirm whether patients with LGE could benefit from primary prevention ICDs irrespective of their left ventricular ejection fractions, while patients without LGE might not need preventive ICDs despite having severe left ventricular dysfunction.

- In the era of improved medical therapy we should redefine the patients most likely will benefit from ICD therapy