
IMPRO

Séminaire
Winter Arrhythmia
School
Annual Cardiac Arrhythmia Meeting
Division of Cardiology, University of Toronto

ICD
Non Ischemic Population
PRO

François Philippon, MD, FRCPC, FHRS, FCCS

14th Annual
Collingwood, Ontario,
February 10 -12, 2017

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Guidelines

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USA

Class I

5. ICD therapy is indicated in patients with non-ischemic DCM who have an LVEF less than or equal to 35% and who are in NYHA functional Class II or III. (*Level of Evidence: B*)[16,333,369,379]

Class IIb

1. ICD therapy may be considered in patients with nonischemic heart disease who have an LVEF of less than or equal to 35% and who are in NYHA functional Class I. (*Level of Evidence: C*)

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Circulation January 22, 2013

Europe

Implantable cardioverter defibrillator in patients with left ventricular dysfunction

Recommendations	Class[a]	Level[b]	Ref.[c]
ICD therapy is recommended to reduce SCD in patients with symptomatic HF (NYHA class II–III) and LVEF ≤35% after ≥3 months of optimal medical therapy who are expected to survive for at least 1 year with good functional status:			
– Ischaemic aetiology (at least 6 weeks after myocardial infarction).	I	A	63,64
– Non-ischaemic aetiology.	I	B	64,316, 317

European Heart Journal (2015) **36**, 2793–2867

Canadian

Canadian Journal of Cardiology 33 (2017) 174–188

Society Guidelines

Canadian Cardiovascular Society/Canadian Heart Rhythm Society 2016 Implantable Cardioverter-Defibrillator Guidelines

Primary Panel: Matthew Bennett, MD (Co-Chair),[a] Ratika Parkash, MD,[b] Pablo Nery, MD,[c] Mario Sénéchal, MD,[d] Blandine Mondesert, MD,[e] David Birnie, MD,[c] Laurence D. Sterns, MD,[f] Claus Rinne, MD,[g] Derek Exner, MD,[h] François Philippon, MD (Co-Chair),[d] **Secondary Panel:** Debra Campbell, RN,[i] Jafna Cox, MD,[b] Paul Dorian, MD,[j] Vidal Essebag, MD,[k] Andrew Krahn, MD,[a] Jaimie Manlucu, MD,[l] Franck Molin, MD,[d] Michael Slawnych, MD,[h] and Mario Talajic, MD[e]

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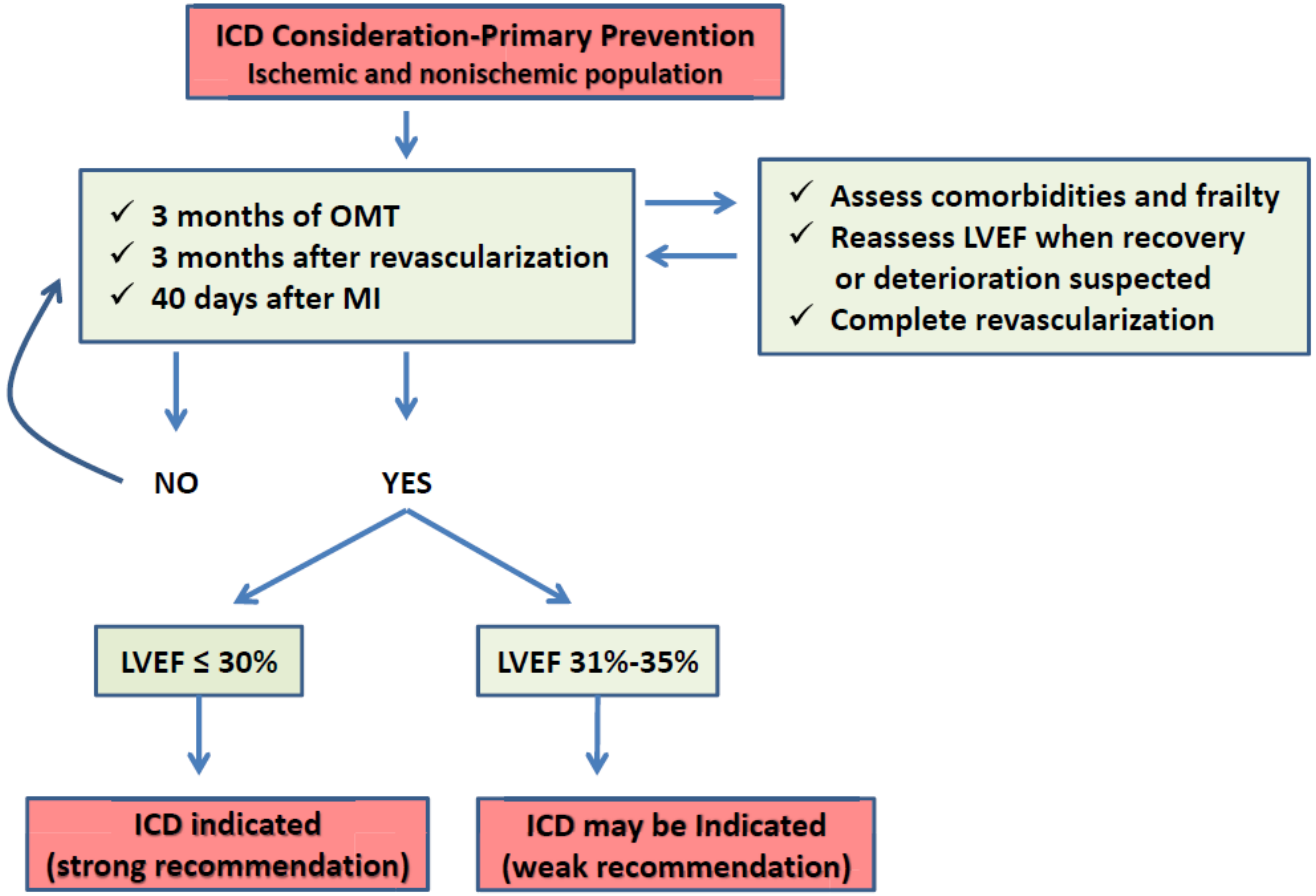

Figure 1. Aid in decision-making for primary prevention ICD. ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; MI, myocardial infarction; OMT, optimal medical therapy.

RECOMMENDATION

1. We recommend that patients with persistent left ventricular dysfunction due to either ischemic or NICM and ejection fraction $\leq$ 30% receive an ICD, when persistent refers to at least 3 months of OMT in all patients and, in patients with ischemic heart disease, at least 3 months after revascularization and at least 40 days after an MI (Strong Recommendation; High-Quality Evidence).
2. We suggest an ICD be considered for patients with persistent left ventricular dysfunction due to either ischemic or NICM and ejection fraction 31%-35% when persistent refers to at least 3 months of OMT in all patients and, in patients with ischemic heart disease, at least 3 months after revascularization and at least 40 days after an MI (Weak Recommendation; Moderate-Quality Evidence).
3. We recommend that patients likely to have left ventricular dysfunction 3 months after revascularization for MI or 40 days after MI without revascularization or 3 months following OMT in NICM undergo an assessment of ejection fraction at those time points (Strong Recommendation; Low-Quality Evidence).

Canadian Journal of Cardiology
Volume 33 2017

Controversial Issues

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EUROPEAN SOCIETY OF CARDIOLOGY®

Europace (2016) **18**, 413–419
doi:10.1093/europace/euv212

CLINICAL RESEARCH
Sudden death and ICDs

Adding the implantable cardioverter-defibrillator to cardiac resynchronization therapy is associated with improved long-term survival in ischaemic, but not in non-ischaemic cardiomyopathy

Christoffer Tobias Witt[1]*, Mads Brix Kronborg[1], Ellen Aagaard Nohr[2], Peter Thomas Mortensen[1], Christian Gerdes[1], Henrik Kjærulf Jensen[1], and Jens Cosedis Nielsen[1]

Methods and results

In this observational study, consecutive patients with an ejection fraction ≤35% and QRS width ≥120 ms receiving a CRT device at Aarhus University Hospital, Denmark from 2000 to 2010 were included. Baseline characteristics were retrieved from patient files and survival data were obtained from the Danish Civil Registration System. The primary outcome was all-cause mortality. The effect of ICD backup was estimated using Cox proportional hazards model, and the multivariate analyses were adjusted for a priori selected variables. We included 917 HF patients, 427 with NICM, and 490 with ICM. Median follow-up was 4.0 years. Adjusted hazard ratio (aHR) for all-cause mortality was 0.76 [95% confidence interval (95% CI), 0.60–0.97; $P = 0.03$] in all patients; 0.96 (95% CI, 0.60–1.51; $P = 0.85$) in patients with NICM, and 0.74 (95% CI, 0.56–0.97; $P = 0.03$) in patients with ICM. In patients with NICM, ICD backup seemed to be associated with improved survival among non-responders to CRT ($P = 0.08$), but not among responders ($P = 0.61$).

Conclusion

Adding an ICD backup is associated with better survival in CRT recipients. This effect was evident among patients with ICM, but not in patients with NICM.

Observational, retrospective study
All CRT patients
Who knows who will respond to CRT ?

Europace (2016) **18**, 413–419

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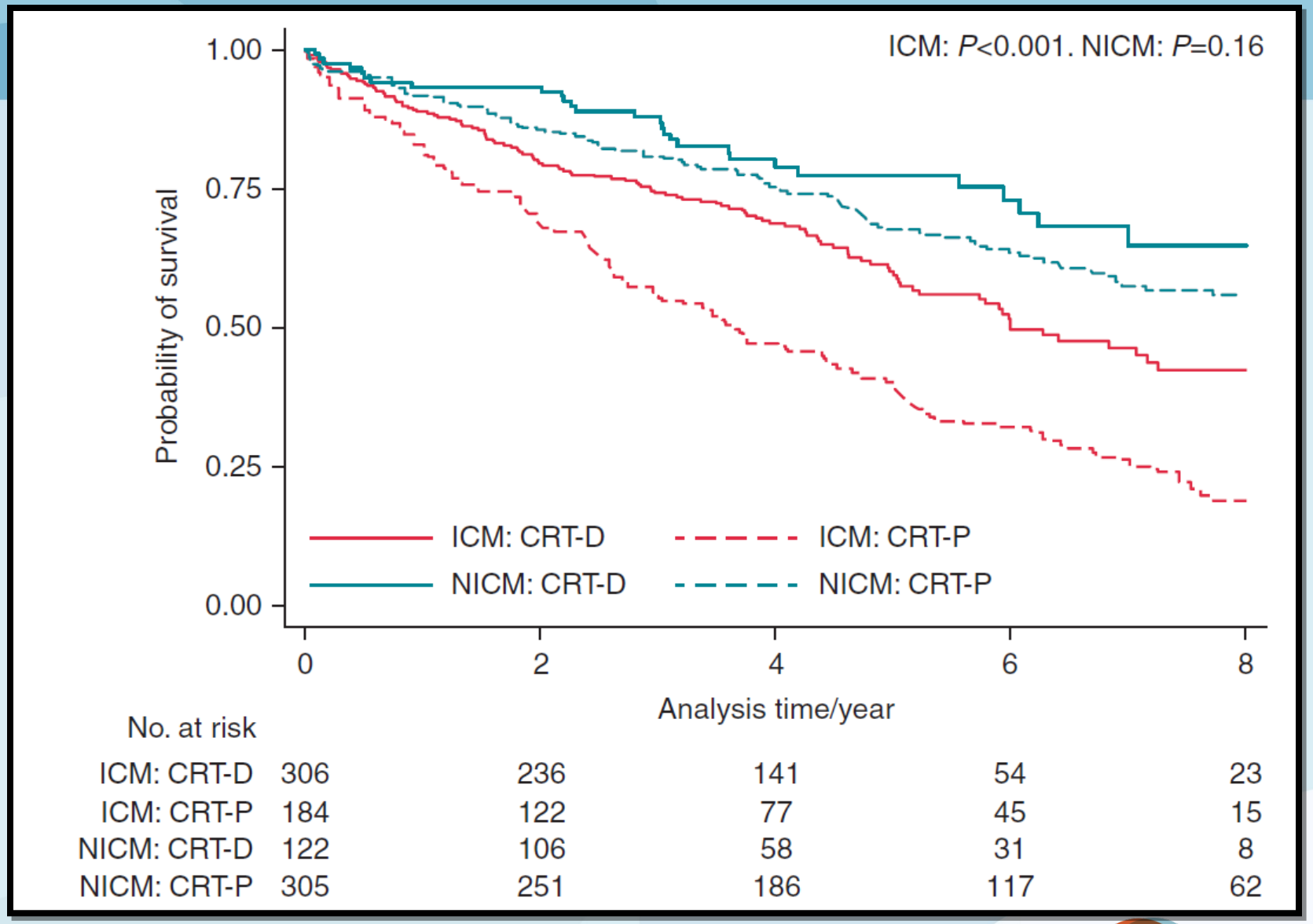

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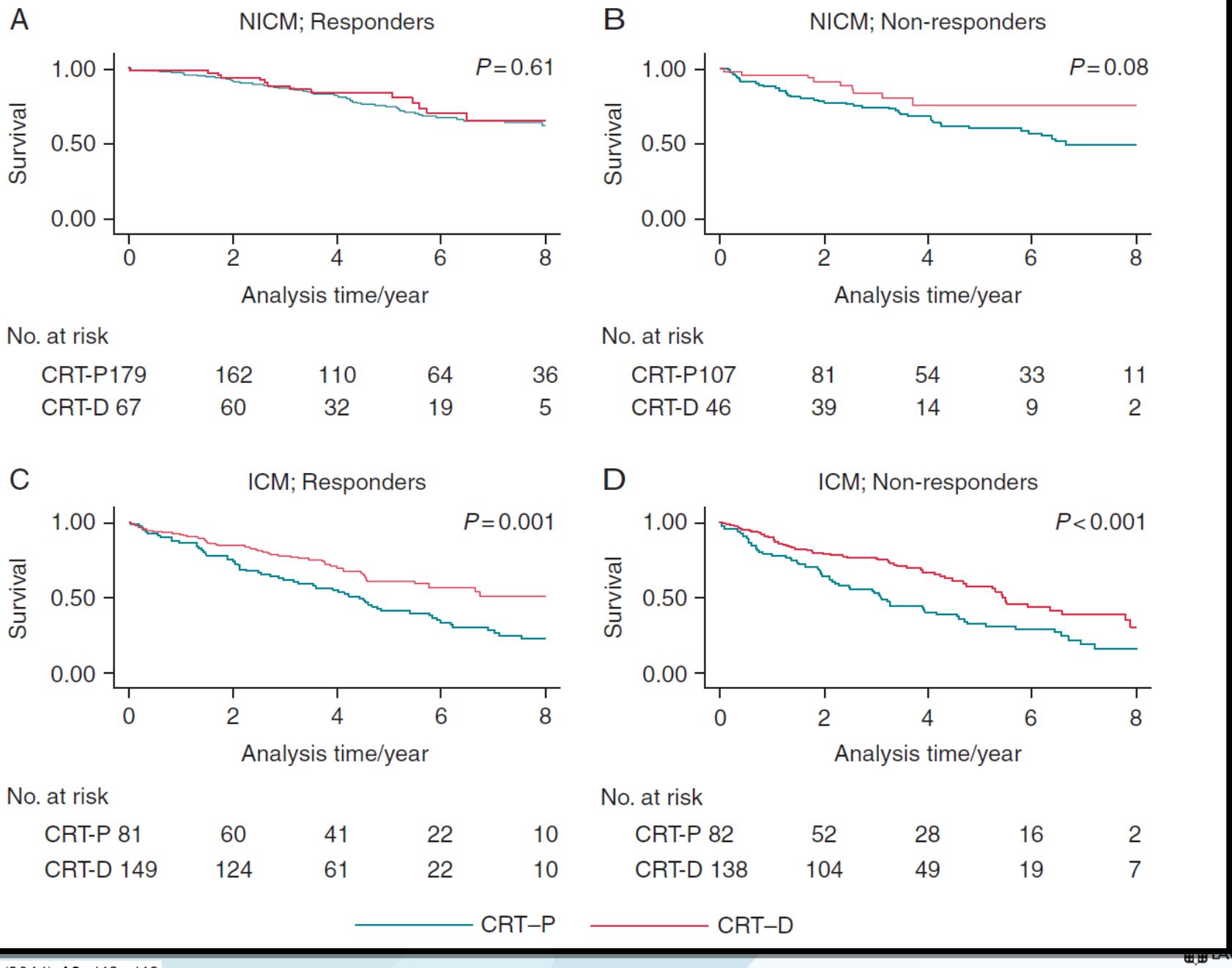
Europace (2016) **18**, 413–419



Europace (2016) **18**, 413–419

Implantable Defibrillators for the Prevention of Mortality in Patients With Nonischemic Cardiomyopathy

A Meta-analysis of Randomized Controlled Trials

Y 2004

JAMA, December 15, 2004—Vol 292, No. 23

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Study Selection Eligible studies were prospective randomized controlled trials of ICD or combined cardiac resynchronization therapy and defibrillator (CRT-D) vs medical therapy enrolling at least some individuals with NICM and reporting all-cause mortality as an outcome. Of 675 potentially relevant articles screened initially, 8 reports of randomized trials enrolling a total of 2146 patients with NICM were included.

Data Extraction Included studies were reviewed to determine the number of patients randomized, mean duration of follow-up, primary end point, mortality of ICD cohort, and mortality of control cohort.

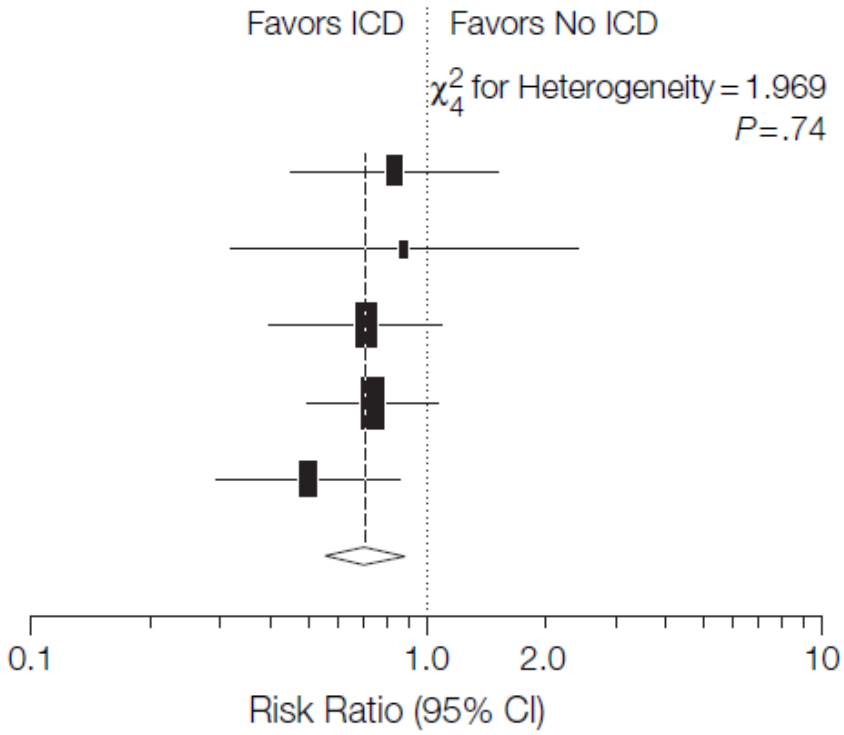
Data Synthesis Five primary prevention trials enrolling 1854 patients with NICM were identified; pooled analysis suggested a significant reduction in total mortality among patients randomized to ICD or CRT-D vs medical therapy (risk ratio [RR], 0.69; 95% confidence interval [CI], 0.55-0.87; *P*=.002). Mortality reduction remained significant even after elimination of CRT-D trials. Two of the 3 secondary prevention trials presented subgroup estimates for ICD efficacy in NICM. Pooled analysis of these secondary prevention trials (n=256 patients with NICM) indicated an equivalent but nonsignificant mortality reduction with ICD therapy (RR, 0.69; 95% CI, 0.39-1.24; *P*=.22). Analysis of all 7 trials combined demonstrated a statistically significant 31% overall reduction in mortality with ICD therapy (RR, 0.69; 95% CI, 0.56-0.86; *P*=.002).

Conclusion ICD therapy appears to significantly reduce mortality in selected patients with NICM.

JAMA. 2004;292:2874-2879 www.jama.com

Figure 3. All-Cause Mortality Among Patients With NICM Randomized to ICD or CRT-D vs Medical Therapy in Primary Prevention

Study	Years of Enrollment	No. of Patients	Risk Ratio (95% CI)
CAT[16]	1991-1997	104	0.83 (0.45-1.82)
AMIOVIRT[17]	1996-2000	103	0.87 (0.31-2.42)
DEFINITE[15]	1998-2002	458	0.65 (0.40-1.06)
SCD-HeFT[14]	1997-2001	792	0.73 (0.50-1.04)
COMPANION[21]	2000-2002	397	0.50 (0.29-0.88)
Combined		**1854**	**0.69 (0.55-0.87)**



Annual mortality 7%, absolute risk reduction 2%/yr, NNT = 25 in 2yrs (NNT in ischemic: 18 in ~20mos from MADIT II)

JAMA, December 15, 2004—Vol 292, No. 23

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 29, 2016 VOL. 375 NO. 13

Defibrillator Implantation in Patients with Nonischemic Systolic Heart Failure

CONCLUSIONS

In this trial, prophylactic ICD implantation in patients with symptomatic systolic heart failure not caused by coronary artery disease was not associated with a significantly lower long-term rate of death from any cause than was usual clinical care. (Funded by Medtronic and others; DANISH ClinicalTrials.gov number, NCT00542945.)

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N Engl J Med 2016;375:1221-30.

PATIENTS

Symptomatic patients (NYHA class II or III, or NYHA class IV if CRT was planned) with non-ischemic systolic heart failure (left ventricular ejection fraction ≤35%) and an increased level (>200 pg per milliliter) of N-terminal pro–brain natriuretic peptide (NT-proBNP) were eligible for enrollment.

In the current study, 31% of deaths were attributed to noncardiovascular causes.

N Engl J Med 2016;375:1221-30.

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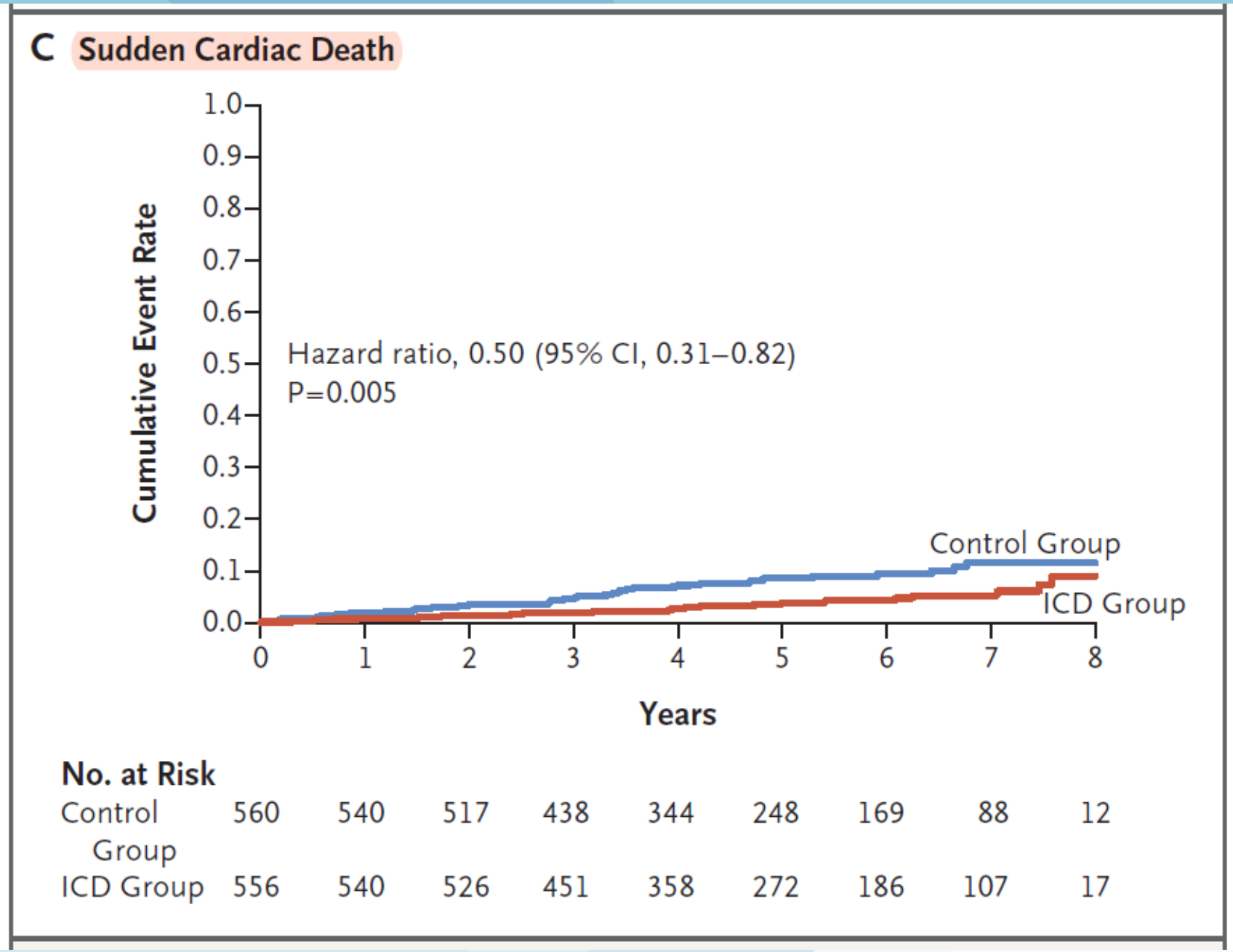
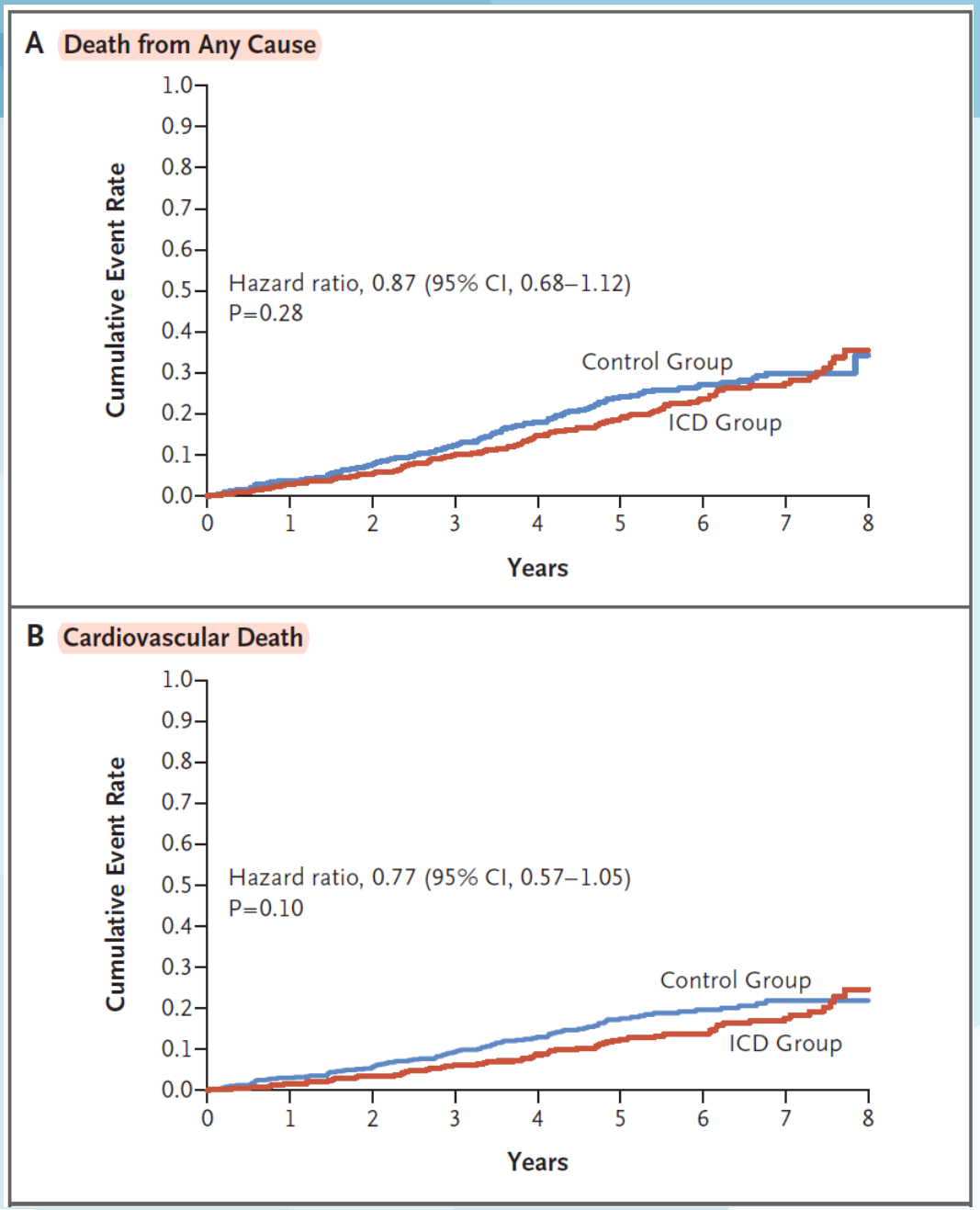


N Engl J Med 2016;375:1221-30.

NNT 25/ median 5.5yrs



N Engl J Med 2016;375:1221-30.

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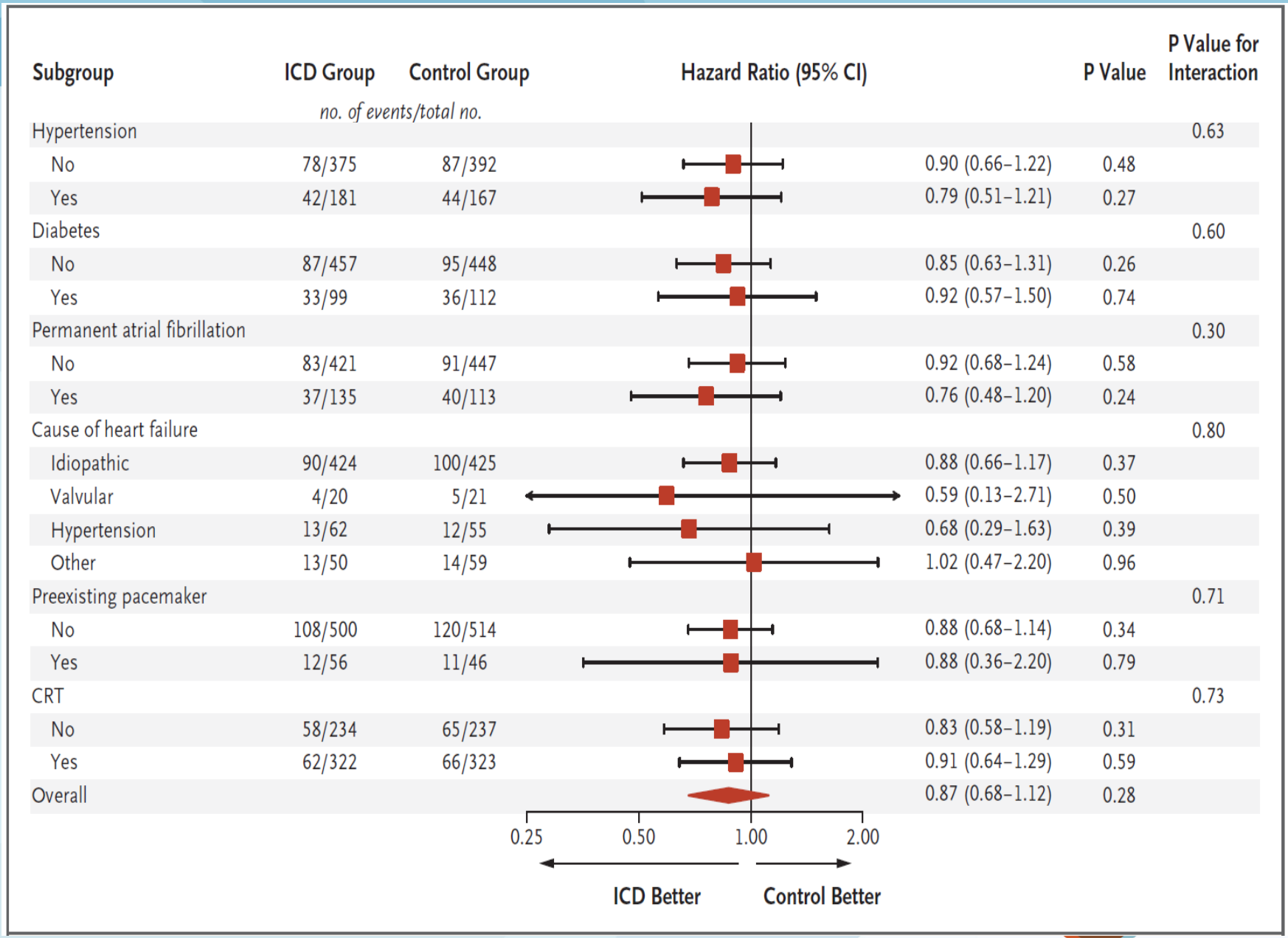
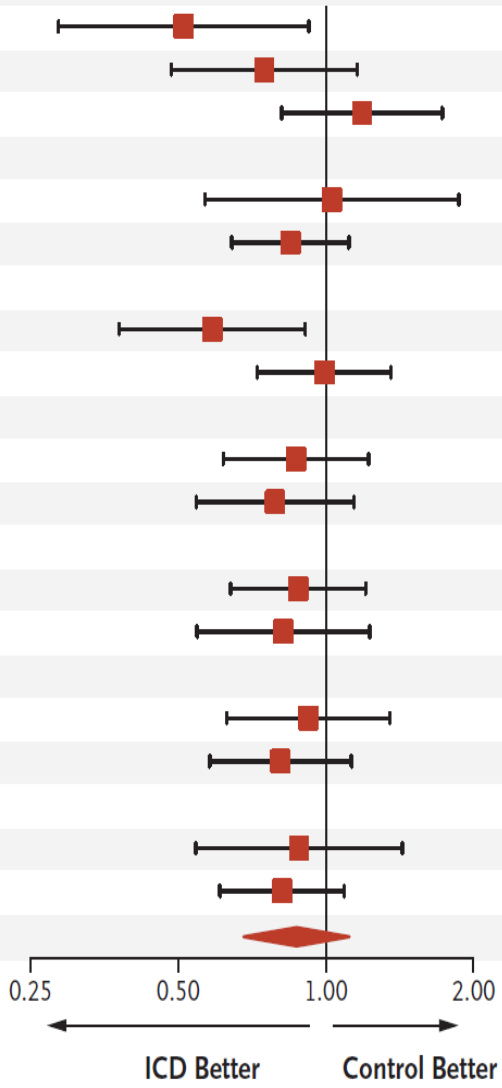


N Engl J Med 2016;375:1221-30.

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	
Male	98/405	108/404	0.85 (0.64–1.12)	0.24	
NT-proBNP					0.06
<1177 pg/ml	32/266	74/268	0.59 (0.38–0.91)	0.02	
≥1177 pg/ml	57/292	88/290	0.99 (0.73–1.36)	0.96	
LV ejection fraction					0.69
<25%	70/264	65/242	0.87 (0.62–1.22)	0.42	
≥25%	50/292	66/318	0.79 (0.54–1.14)	0.21	
Estimated GFR					0.86
<73 ml/min/1.73 m^2	75/272	80/278	0.88 (0.64–1.21)	0.42	
≥73 ml/min/1.73 m^2	45/283	50/280	0.82 (0.55–1.23)	0.33	
NYHA functional class					0.71
II	52/297	54/300	0.92 (0.63–1.35)	0.68	
III–IV	68/259	77/260	0.81 (0.58–1.13)	0.21	
Heart failure duration					0.73
<18 mo	31/254	36/277	0.88 (0.54–1.43)	0.61	
≥18 mo	89/301	95/283	0.81 (0.61–1.09)	0.17	
Overall			0.87 (0.68–1.12)	0.28	



N Engl J Med 2016;375:1221-30.

Implantable Cardioverter-Defibrillator for Nonischemic Cardiomyopathy

An Updated Meta-Analysis

Circulation. 2017;135:201–203. DOI: 10.1161/CIRCULATIONAHA.116.026056

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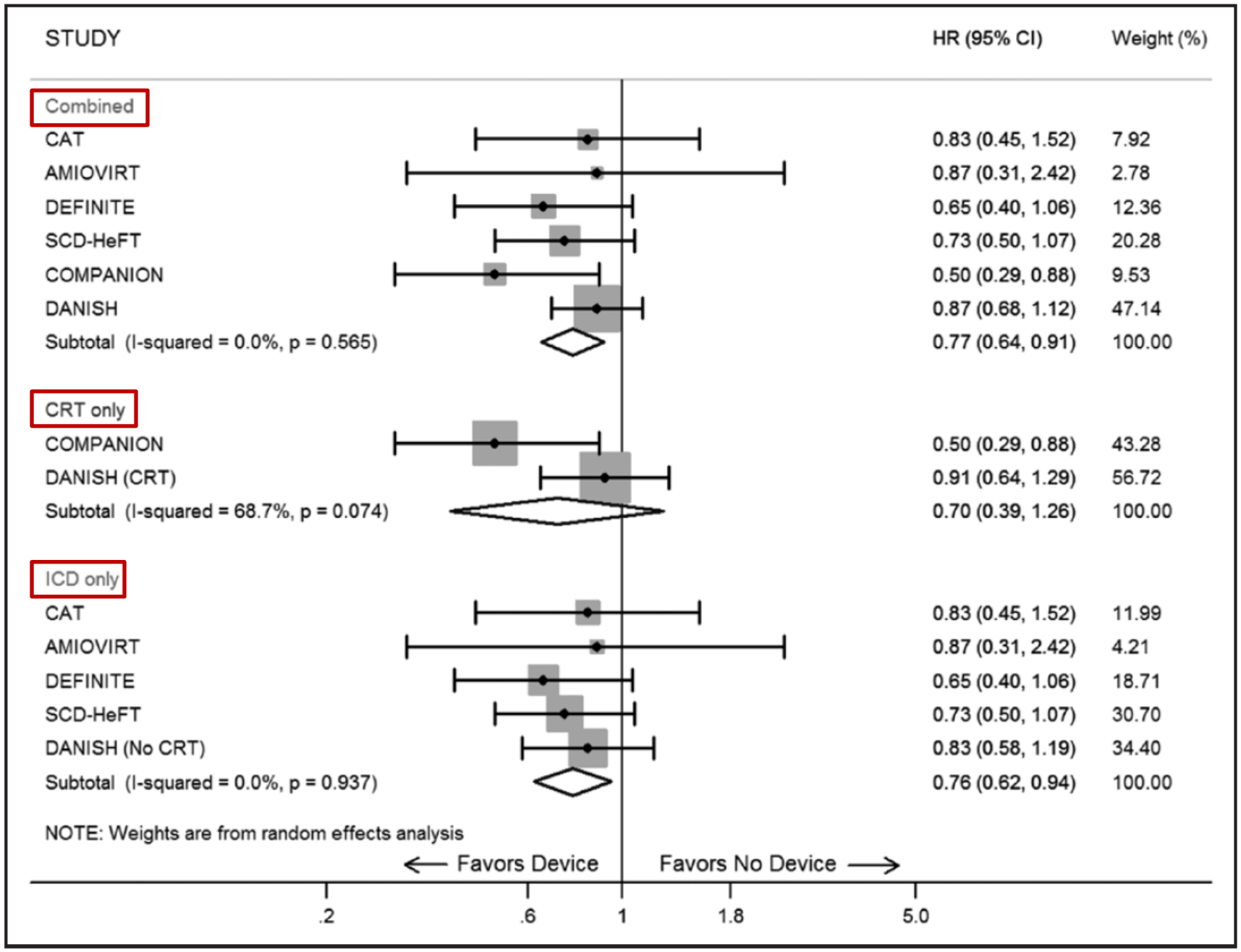

Circulation. 2017;135:201–203. DOI: 10.1161/CIRCULATIONAHA.116.026056

It may be plausible that, because of the high use of CRT in the DANISH trial (60% in each arm), ICD failed to demonstrate statistically significant effect on all-cause mortality in patients with NICM.

Taken collectively, despite the neutral results of the recently published DANISH trial, our meta-analysis of all the published RCTs to date demonstrates significant clinical benefit on all-cause mortality in favor of ICD use for primary prevention in patients with NICM. Improvement in risk prediction models can help overcome the traditional reliance on ejection fraction for risk stratification of sudden cardiac death in NICM patients. Furthermore, adequately powered randomized studies are needed before recommending any change in existing guidelines, and clinical judgment should prevail while assessing risk of sudden cardiac death in NICM patients with reduced ejection fraction.

Circulation. 2017;135:201–203. DOI: 10.1161/CIRCULATIONAHA.116.026056

Not Ready for a change in Guidelines…

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Mike’s editorial comments

- DANISH trial was important, but not the only body of evidence
- There is a clear benefit to an ICD in the nonischemic; the question is whom and when
- We knew from before that the benefit was LESS; DANISH highlights the importance of
  - optimal HF therapy including CRT
  - potential impact of age on ICD benefit

Mike’s editorial comments

- Is it better to give a CRT-P and wait for non-response before upgrading to a CRT-D?
- Risk stratification is the holy grail; does that include our expectation of ACHIEVING optimal medical therapy?
- Ischemic cardiomyopathy is one cardiomyopathy; nonischemic cardiomyopathy is EVERYTHING ELSE

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Patient Selection

- Optimal medical therapy in 2017 includes CRT in eligible patients
- We can't know in advance who will be a responder?
- Young patients, less comorbidities
- Not all NICM pts will have a CRT, then and ICD?
- What is the future role of sacubitril/valsartan ?
- Is there place for a RCT?

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