Association between implantable cardioverter-defibrillator use for primary prevention and mortality: a prospective propensity-score matched study.

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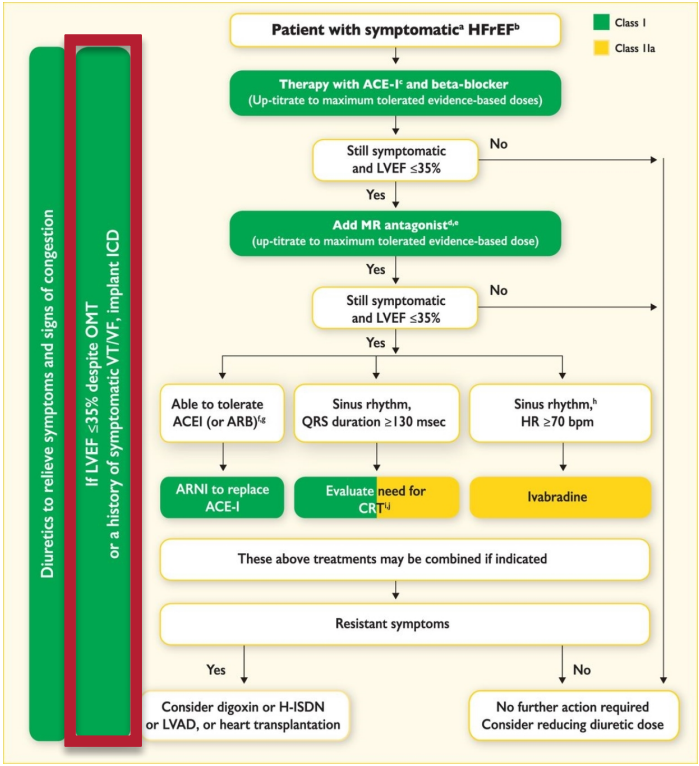
SwedeHF
Heart Failure Registry

ESC Congress Paris 2019
Together with World Congress of Cardiology

Conflict of interest

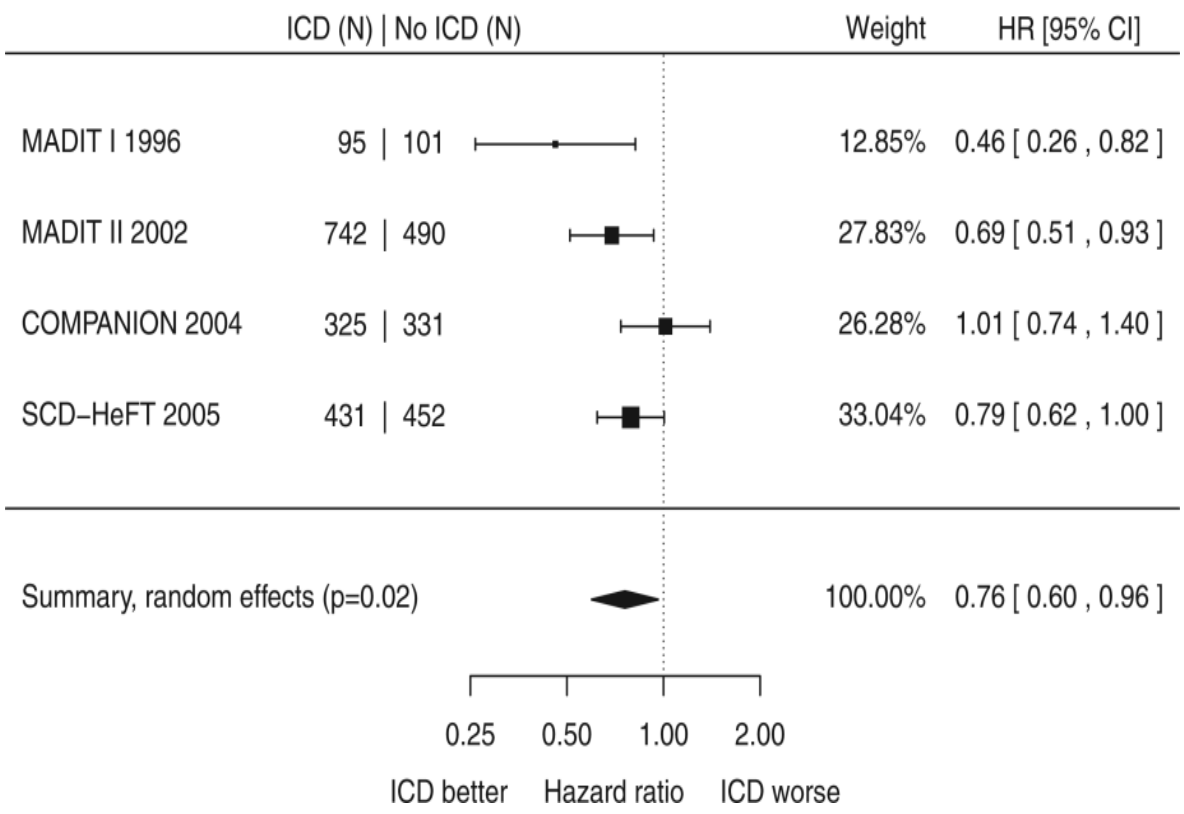
- I do not have a conflict of interest in regard to this study. Outside: Funding by the German Research Foundation and honoraria from AstraZeneca.
- This study received funding from Boston Scientific and the EU/EFPIA Innovative Medicines Initiative 2 Joint Undertaking BigData@Heart grant.

Guideline recommendation for primary prevention ICD in HFrEF



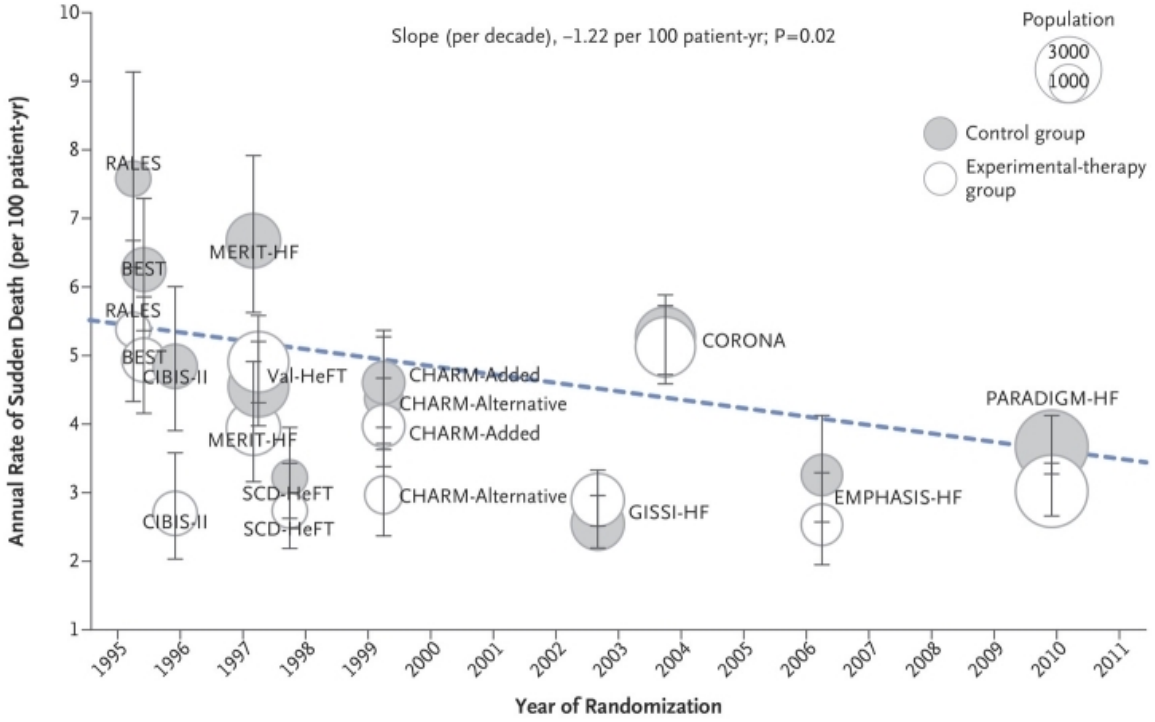
Ponikowski et al., ESC Heart Failure Guidelines 2016

Recommendation based on RCTs initiated ≥ 20 years ago



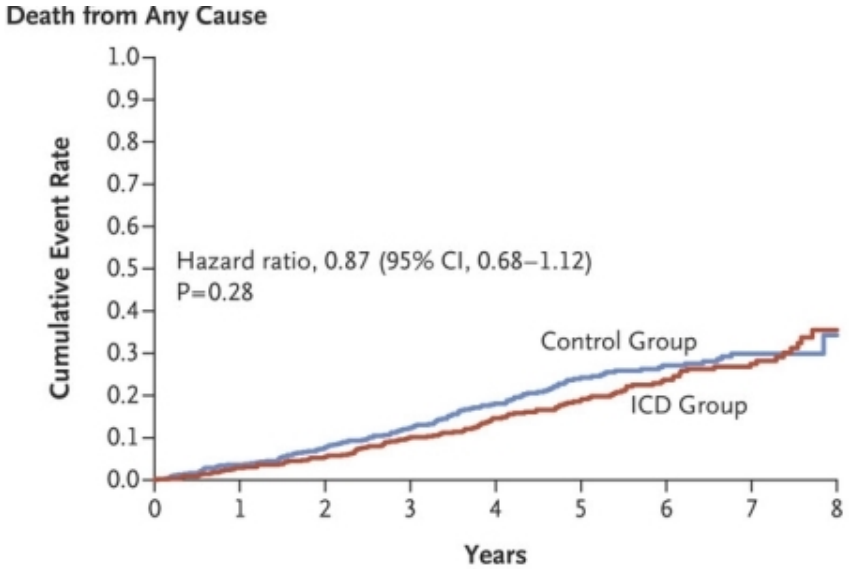
Shun-Shin et al., EHJ, 2017

Declining rate of SCD and improved HFrEF therapy



Shen et al., NEJM, 2017

DANISH questions ICD in non-ischaemic HFrEF and older patients



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	

Køber et al., NEJM, 2016

Aim

To evaluate the association between primary prevention ICD and all-cause mortality in a large, contemporary cohort of HFrEF patients with a focus on prespecified subgroups (e.g. ischaemic heart disease, age, time of enrolment and sex).

Study population

- Study based on the Swedish Heart Failure Registry:
  - Patients ≥18 years
  - Clinician judged heart failure
  - Enrolment between 2000 and 2016
  - Linkage to the National Patient Registry and Cause of Death Registry

SwedeHF Heart Failure Registry

- Inclusion criteria in accordance with ESC 2016 HF guidelines:
  - EF <40% (which is a categorized variable in SwedeHF, i.e. <30%, 30-39%, 40-49%, and ≥50%)
  - HF duration ≥3 months
  - NYHA class ≥II
  - No missing data on ICD use

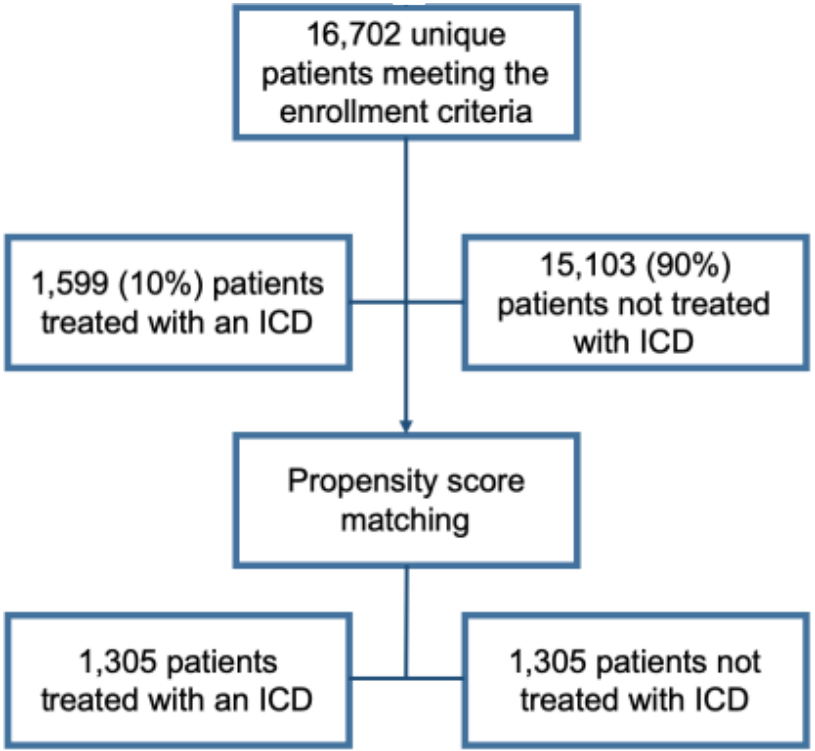
Ponikowski et al., ESC Heart Failure Guidelines 2016
Savarese et al., UJoMS, 2019

Statistical methods

- Chained equation multiple imputation to handle missing data.
- Calculation of propensity scores for ICD based on 31 clinically relevant variables.
- 1:1 propensity score matching (caliper 0.05) to compare ICD recipients vs. non-recipients.
- Primary outcome: One-year and five-year all-cause mortality.
- Secondary outcome: One-year and five year cardiovascular mortality.
- Negative control analysis: composite endpoint of non-cardiovascular hospitalisation.

SwedeHF Heart Failure Registry

Overall study cohort



- Mean age 73 (±11) years and 28% were female
- Ejection fraction <30% in 51%, NYHA class III in 48% of the cases
- High prevalence of comorbidities (atrial fibrillation 59%, ischaemic heart disease 65%)
- Patients with an ICD were younger, more likely male and more likely to receive optimal medical therapy.

Matched study cohort

	ICD patients (N=1,305)	Matched controls (N=1,305)	SD
Age (years)	68 (±11)	68 (±13)	1.0%
Female sex	228 (17.5%)	216 (16.6%)	2.4%
Ejection fraction <30%	842 (64.5%)	861 (66.0%)	3.1%
NYHA class III	653 (50.1%)	670 (51.4%)	2.7%
Ischaemic heart disease	997 (76.4%)	1,007 (77.2%)	1.8%
Atrial fibrillation	758 (58.1%)	770 (59.0%)	1.9%
Anaemia	420 (33.5%)	438 (34.4%)	1.8%
Diabetes mellitus	423 (32.4%)	426 (32.6%)	0.5%
Valvular heart disease	349 (26.7%)	345 (26.4%)	0.7%
CRT	449 (34.4%)	427 (32.7%)	3.6%
Beta-blocker	1,257 (96.6%)	1,254 (96.2%)	2.4%
RAS inhibitors	1,236 (99.8%)	1,209 (99.8%)	3.7%
MRA	703 (54.2%)	699 (53.7%)	1.5%

SD: absolute standard difference

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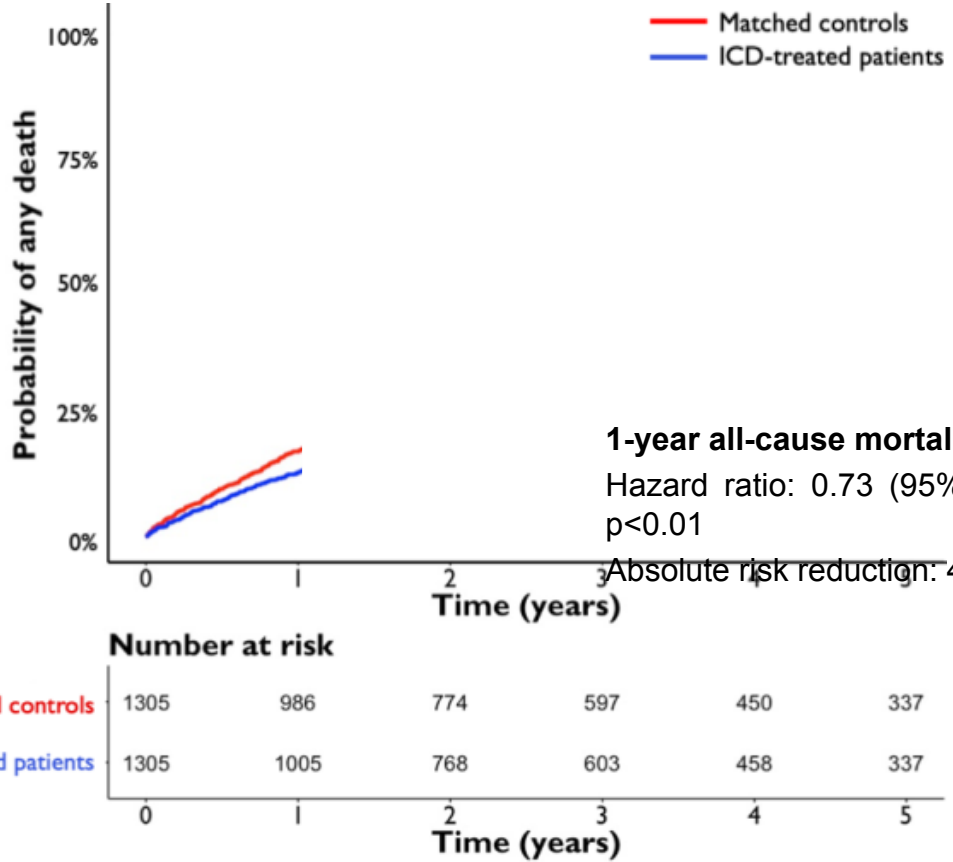
One-year all-cause mortality



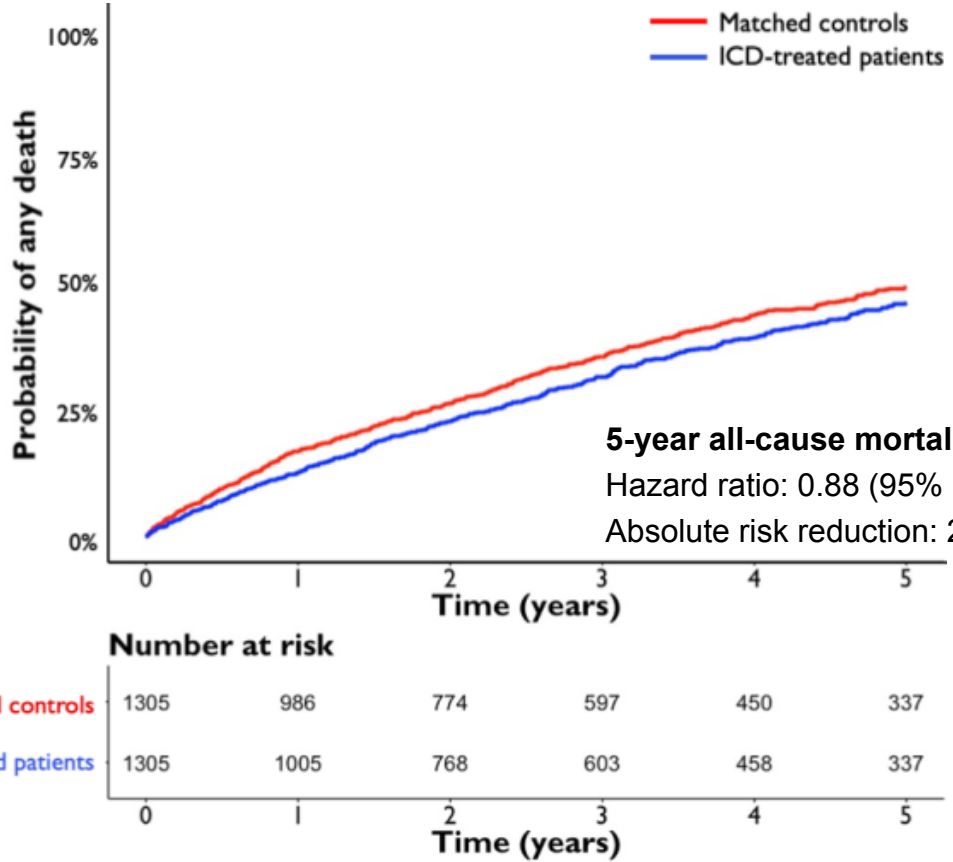
1-year all-cause mortality

Hazard ratio: 0.73 (95% CI 0.60 - 0.90), p<0.01

Absolute risk reduction: 4.2%

Median follow-up:
2.64 (IQR 0.99 – 5.00) years

Five-year all-cause mortality



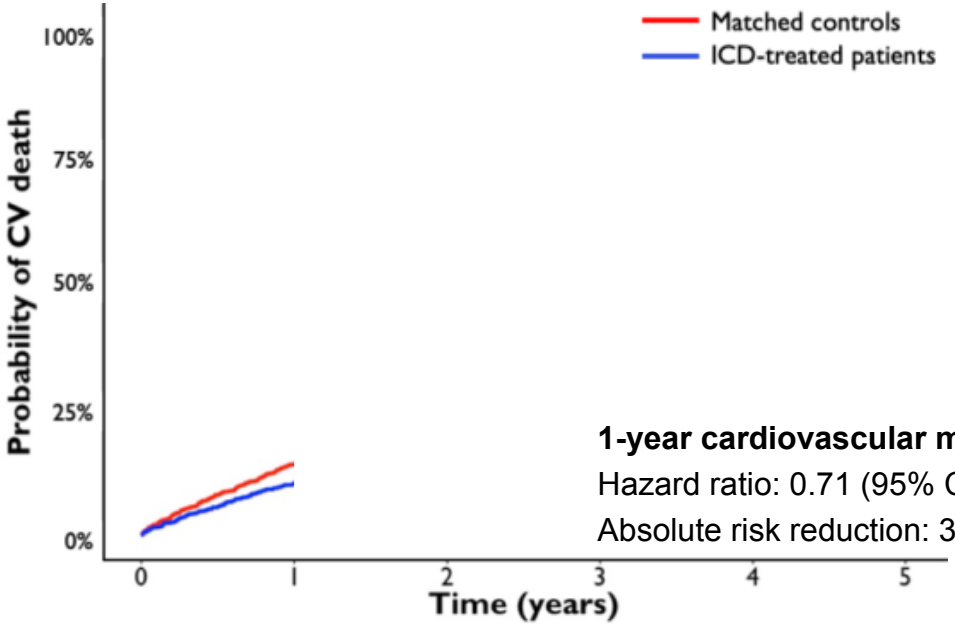
5-year all-cause mortality

Hazard ratio: 0.88 (95% CI 0.78 - 0.99), p=0.04

Absolute risk reduction: 2.1%

Median follow-up:
2.64 (IQR 0.99 – 5.00) years

One-year cardiovascular mortality



1-year cardiovascular mortality

Hazard ratio: 0.71 (95% CI 0.57 - 0.90), p<0.01

Absolute risk reduction: 3.8%

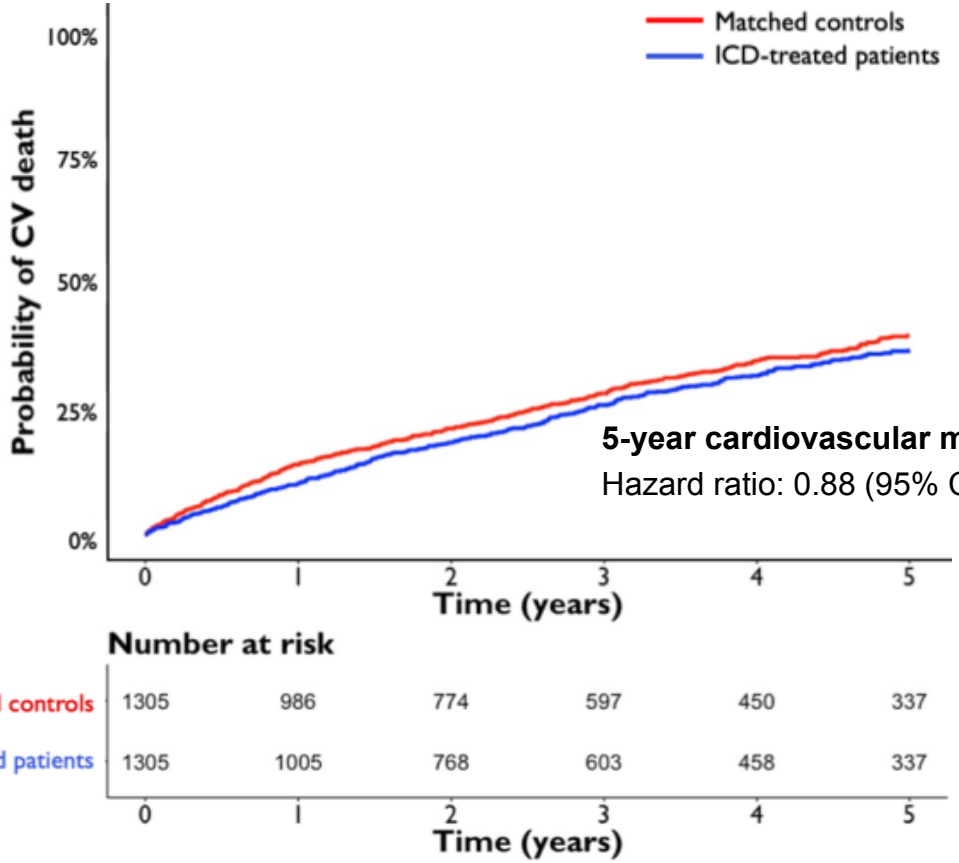
Number at risk

	0	1	2	3	4	5
Matched controls	1305	986	774	597	450	337
ICD-treated patients	1305	1005	768	603	458	337

Time (years)

Median follow-up:
2.64 (IQR 0.99 – 5.00) years

Five-year cardiovascular mortality



5-year cardiovascular mortality

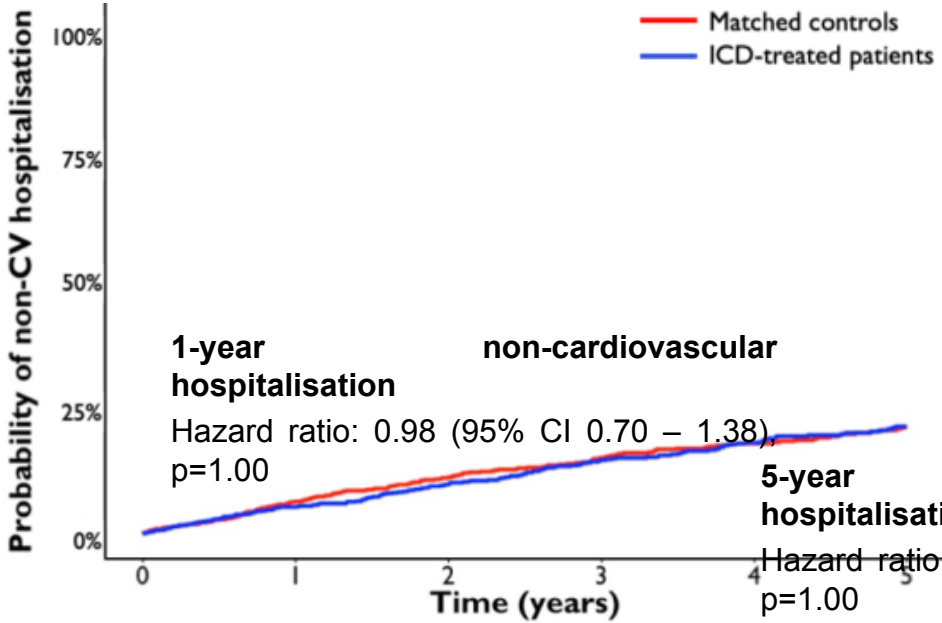
Hazard ratio: 0.88 (95% CI 0.77 - 1.02), p=0.10

Median follow-up:
2.64 (IQR 0.99 – 5.00) years

Negative control analysis

Non-cardiovascular hospitalisation:

Composite of hospitalisation for renal failure, dialysis, chronic lower respiratory disease, influenza and pneumonia, liver disease, rheumatoid arthritis.



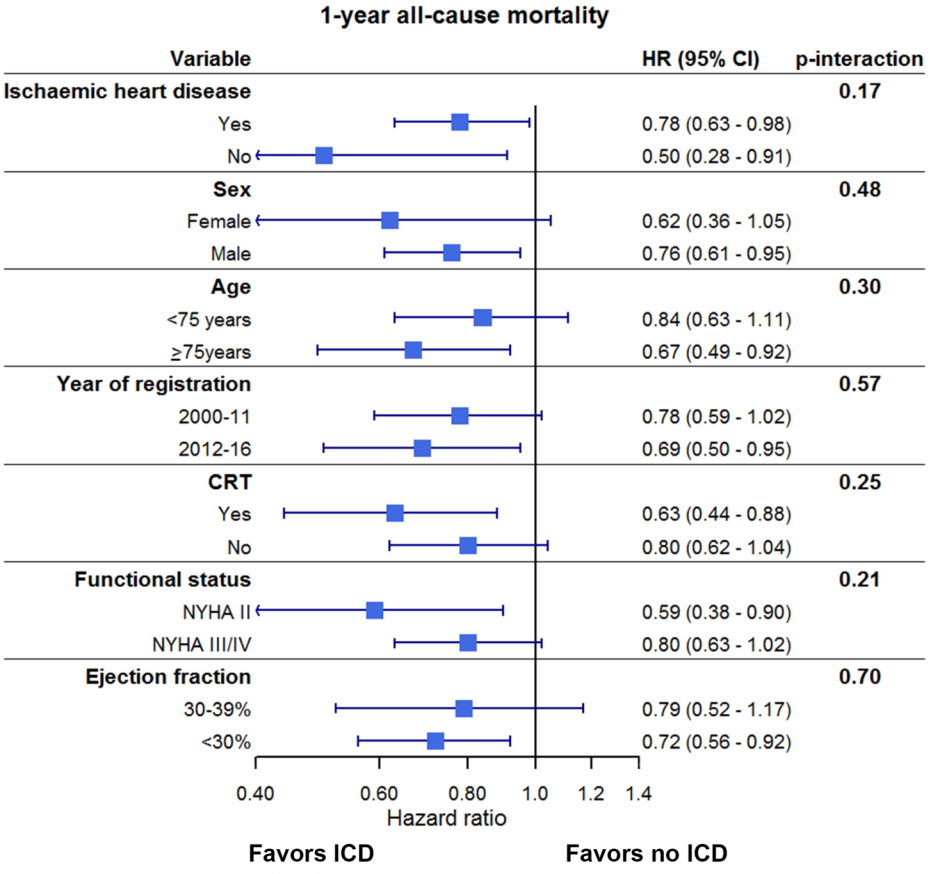
1-year non-cardiovascular hospitalisation

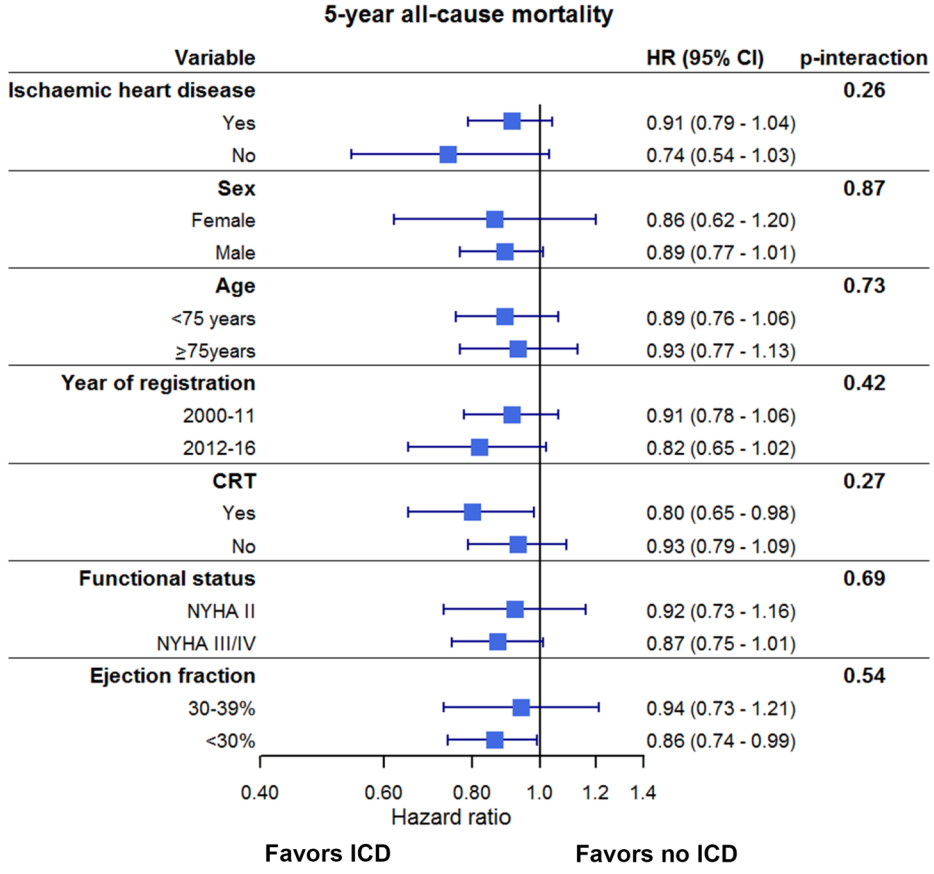
Hazard ratio: 0.98 (95% CI 0.70 – 1.38), p=1.00

5-year non-cardiovascular hospitalisation

Hazard ratio: 0.98 (95% CI 0.80 – 1.21), p=1.00

Sub-group analyses





Limitations

- Potential impact of residual and unmeasured confounders.
- ICD was considered at baseline – Potential cross-over.
- No outcome data on sudden cardiac death or data on antiarrhythmic drugs.
- Our data did not allow to capture whether some patients received ICD for secondary prevention of sudden cardiac death.
- Limited sample size of the matched cohort might have prevented to observe significant differences in the sub-group analysis.
- Observational study – Association between exposure and outcome; not causality.

Conclusion

In this large and contemporary HFrEF cohort:

- ICD was underused.
- Primary prevention ICD was associated with reduced short-term and long-term mortality, which was consistent in all the evaluated sub-groups.

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In this large and contemporary HFrEF cohort:

- ICD was underused.
- Primary prevention ICD was associated with reduced short-term and long-term mortality, which was consistent in all the evaluated sub-groups.

These findings support the current guideline recommendations for primary prevention ICD in HFrEF and call for better implementation of ICD in clinical practice.

Karolinska Institutet

Thank you very much for your attention!

Universitäres Herz- und Gefäßzentrum UKE Hamburg

Circulation

ORIGINAL RESEARCH ARTICLE

Association between use of primary prevention implantable cardioverter-defibrillators and mortality in patients with heart failure.

A prospective propensity-score matched analysis from the Swedish heart failure registry.

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