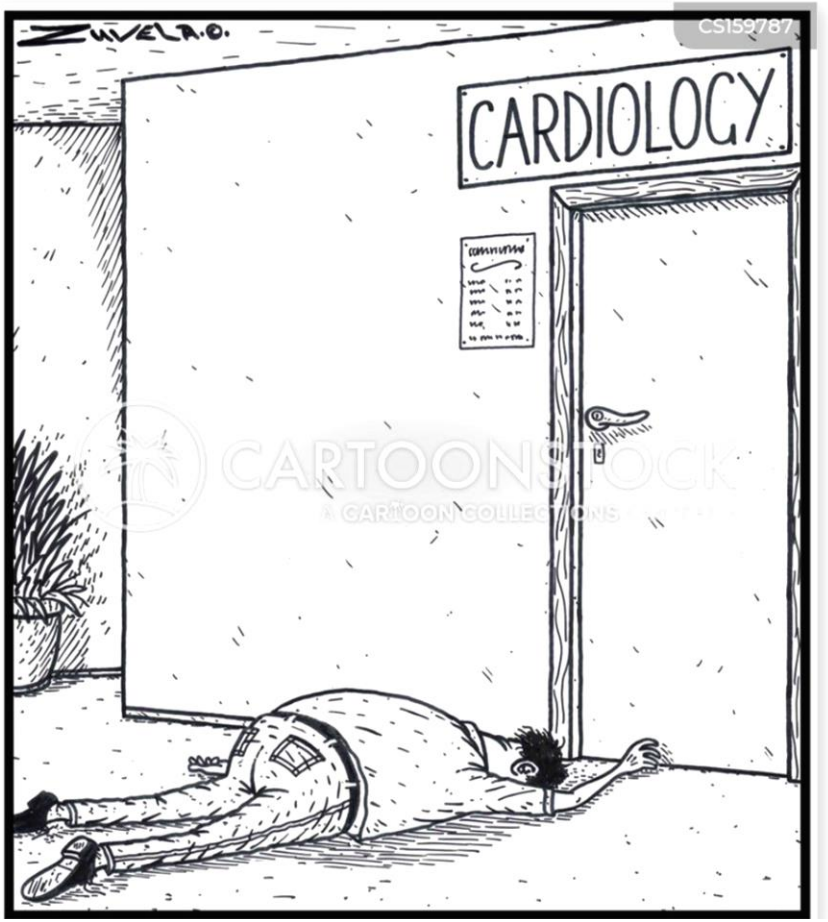
Sudden Cardiac Death in Heart Failure Risk Assessment and Prevention

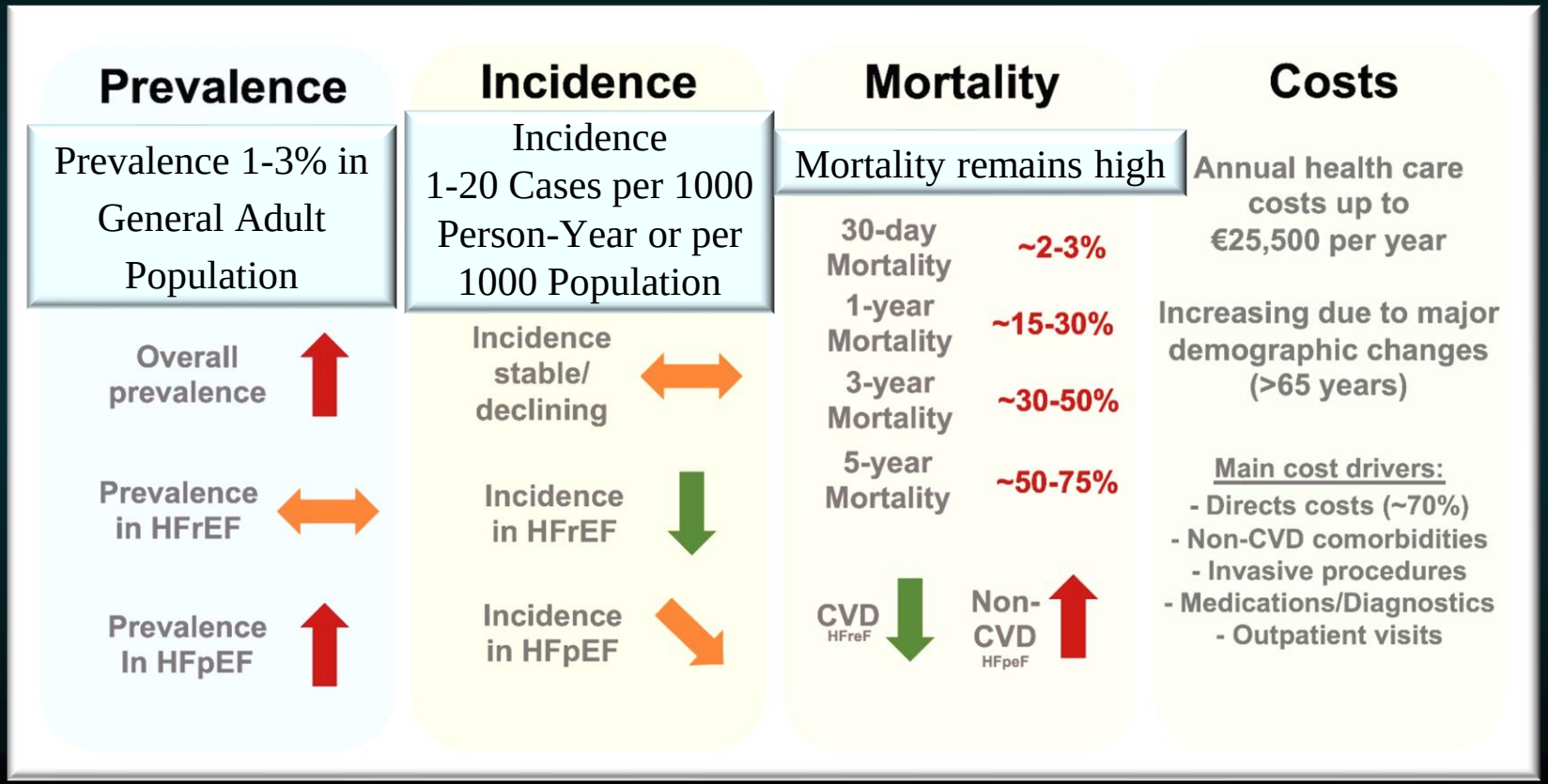
Ng Wai Kiat
Pantai Hospital, Kuala Lumpur

I Have Nothing to Disclose Related to Current Presentation Apart from My Love to Durian and Chocolate

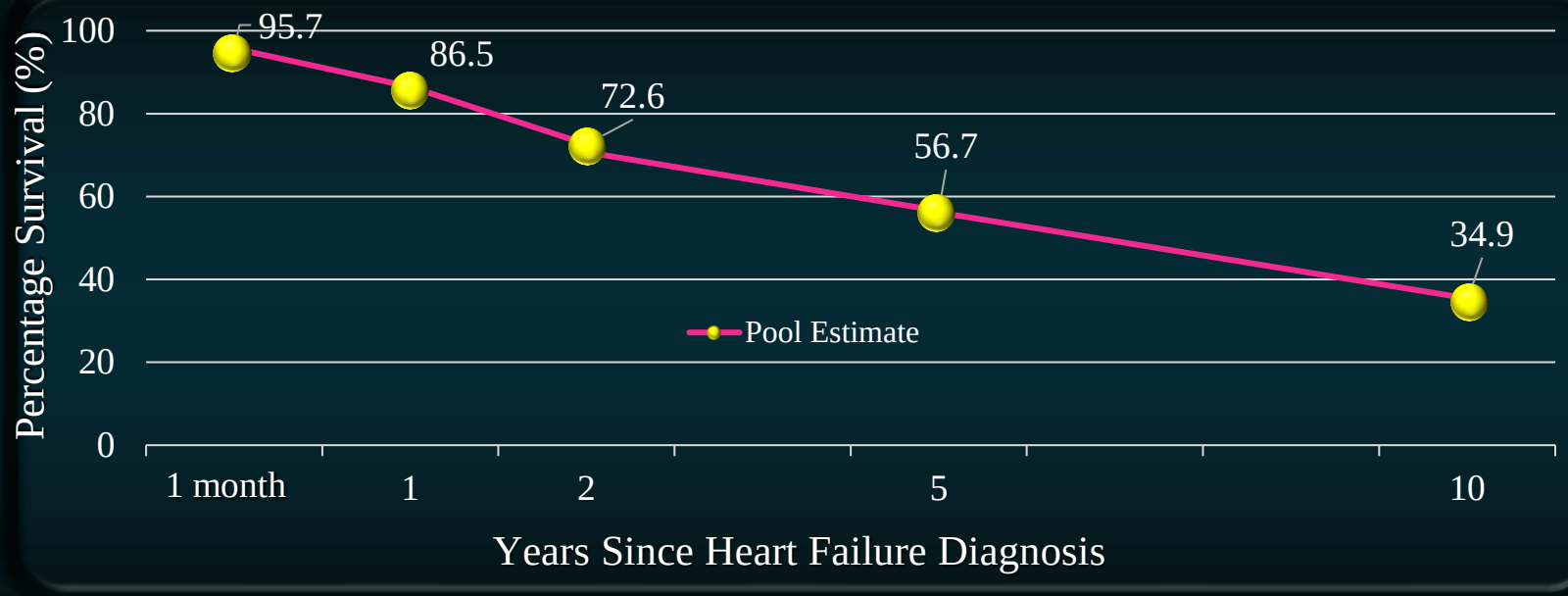


A man just died suddenly about to enter a cardiology centre

Global Burden of Heart Failure



Meta-Analysis: Patients with Heart Failure Survival Rates



Eur J Heart Fail. 2019 Nov; 21(11): 1306–1325

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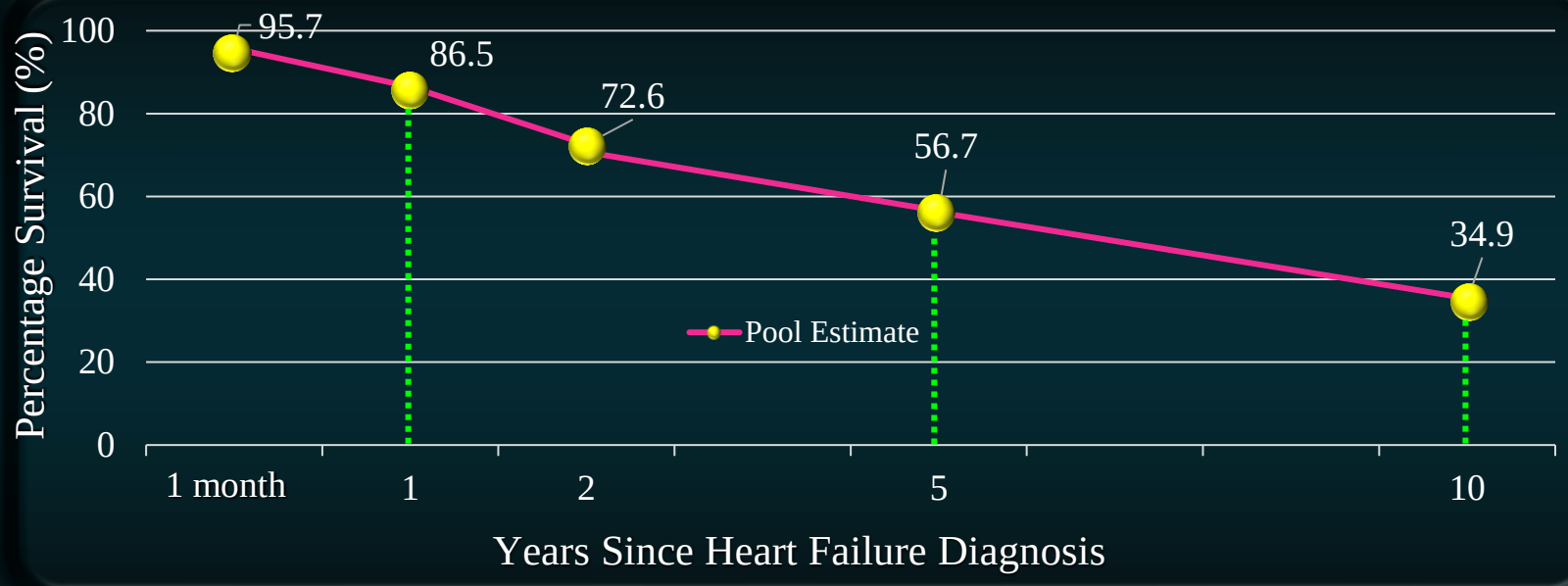
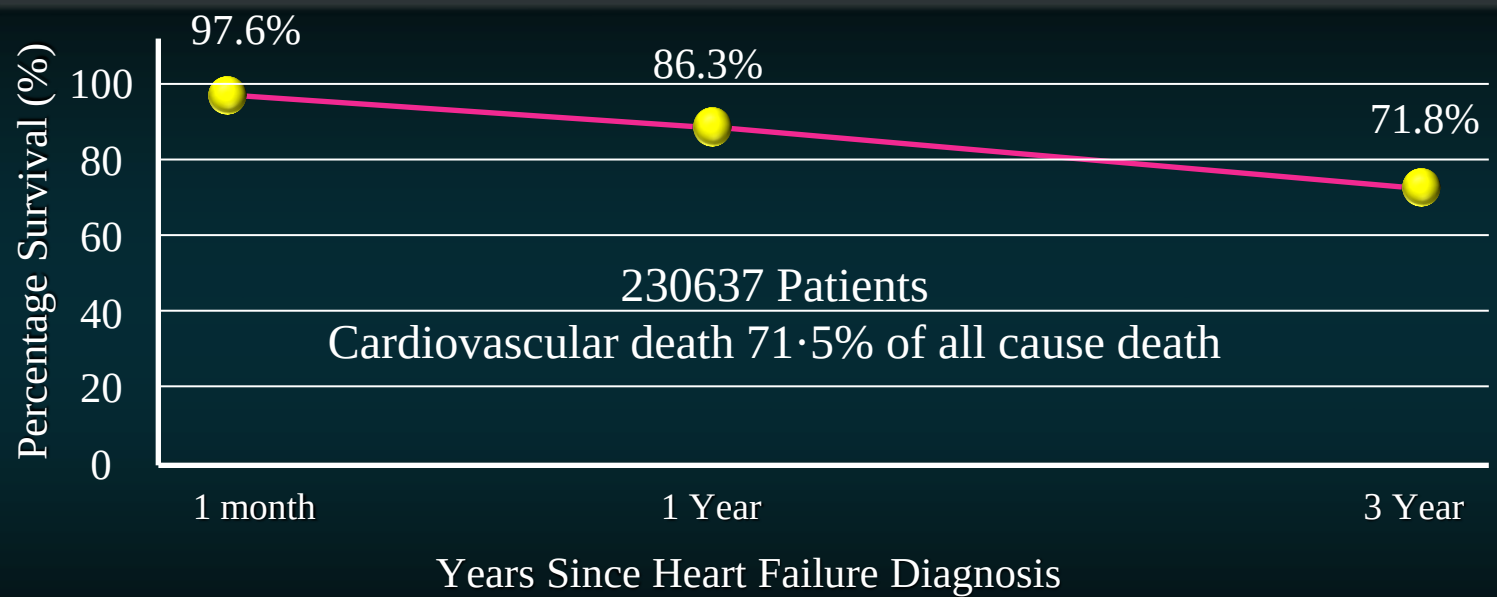


Eur J Heart Fail. 2019 Nov; 21(11): 1306–1325

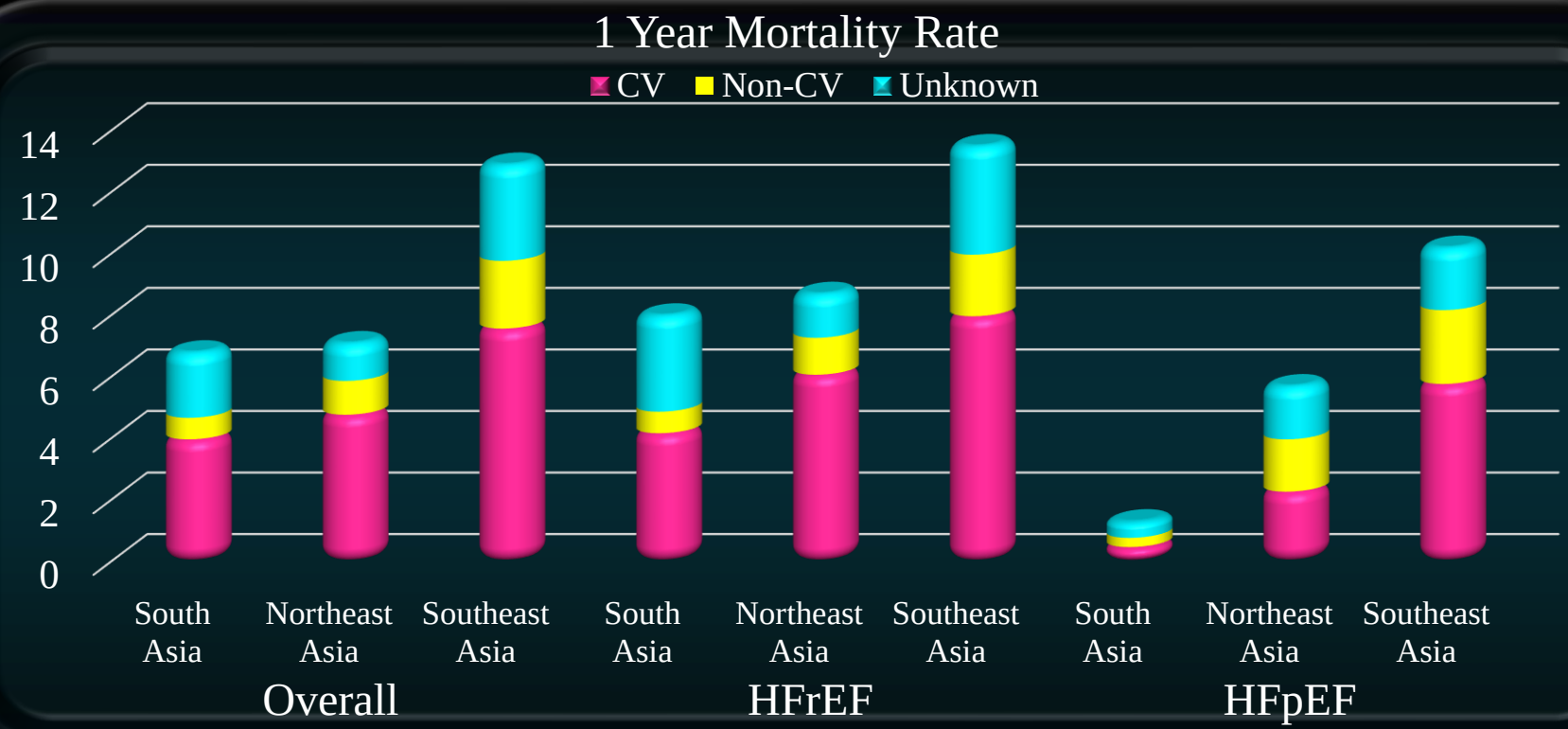
China Cardiovascular Association Database-Heart Failure Centre Registry 2017-2021



Lancet 2024 12;4:E611-E622

ASIAN HF Registry

(J Am Heart Assoc. 2020;9: e012199)



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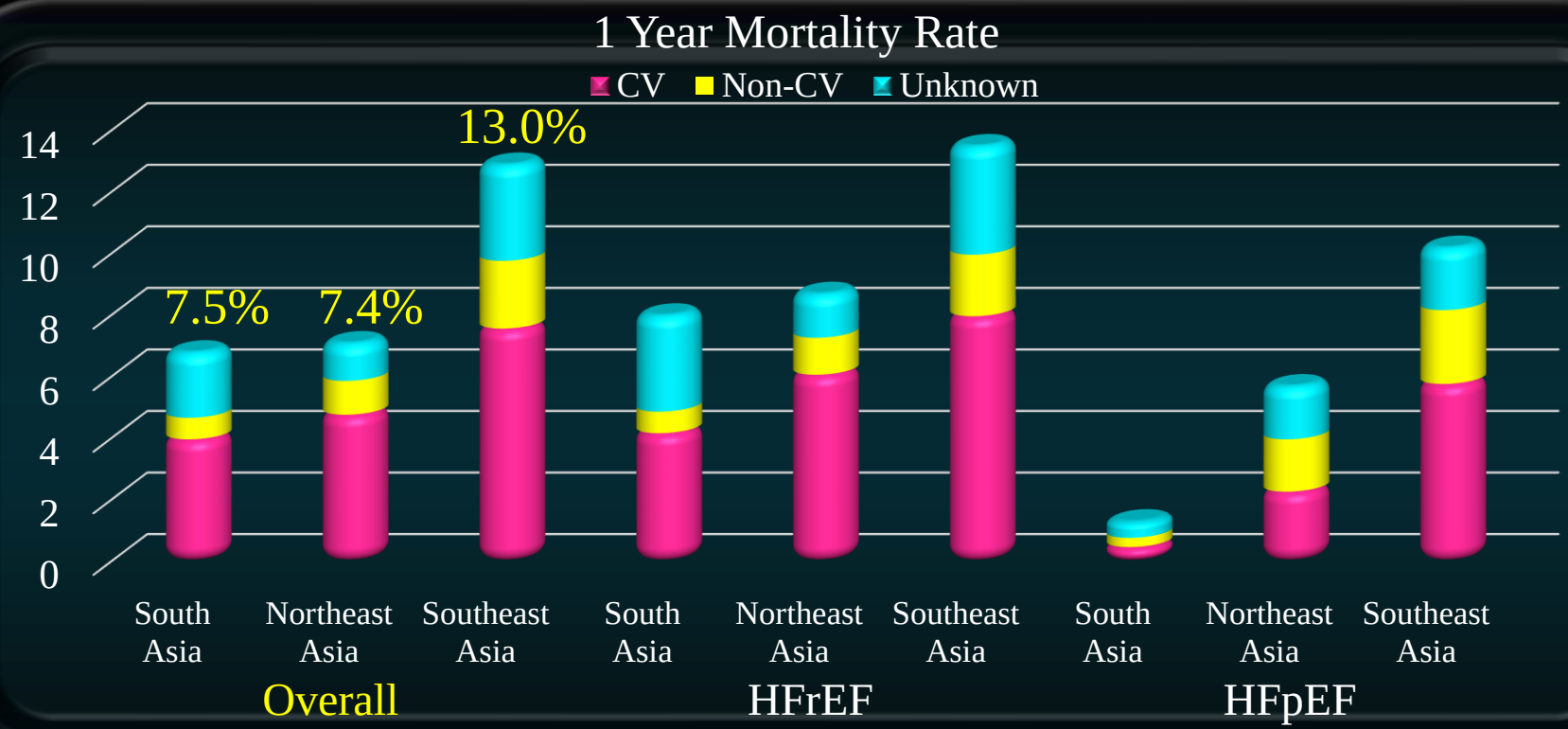

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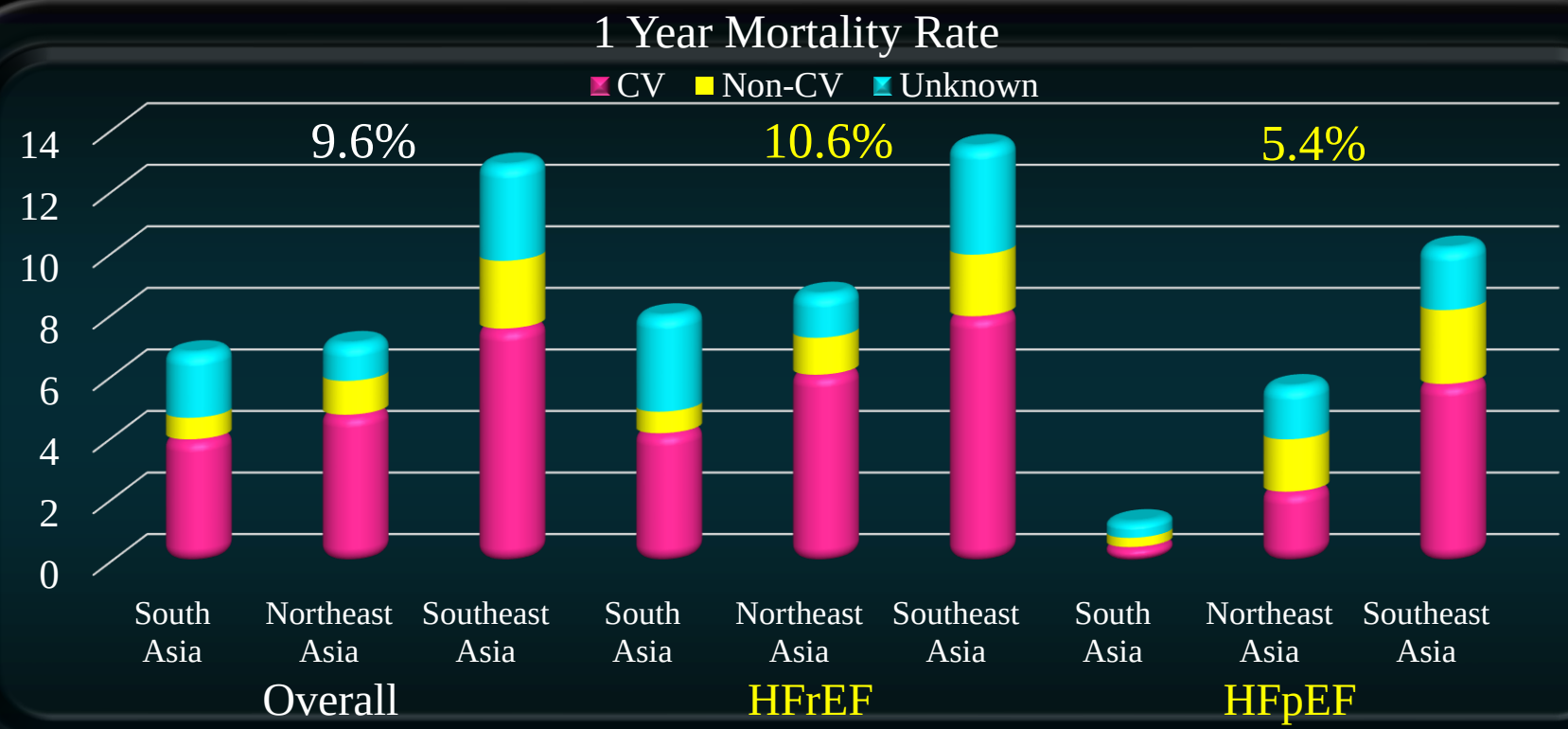

Asian HF Registry
One-Year Cause-Specific Mortality Rates

	Overall			HFrEF			HFpEF		
	South Asia	Northeast Asia	Southeast Asia	South Asia	Northeast Asia	Southeast Asia	South Asia	Northeast Asia	Southeast Asia
No. of cardiovascular deaths	64	104	173	61	97	151	3	7	22
Specific cause of cardiovascular death									
Sudden death	41 (64.0)	43 (41.3)	49 (28.3)	41 (67.2)	41 (42.3)	47 (31.1)	0 (0.0)	2 (28.6)	2 (9.1)
HF death	18 (28.1)	52 (50.0)	41 (23.7)	17 (27.9)	47 (48.4)	39 (25.8)	1 (33.3)	5 (71.4)	2 (9.1)
AMI death	4 (6.3)	5 (4.8)	14 (8.1)	3 (4.9)	5 (5.2)	11 (7.3)	1 (33.3)	0 (0.0)	3 (13.6)
Stroke death	1 (1.6)	2 (1.9)	7 (4.0)	0 (0.0)	2 (2.21)	6 (4.0)	1 (33.3)	0 (0.0)	1 (4.6)
Cardiovascular haemorrhage death	0 (0.0)	1 (1.0)	4 (2.3)	0 (0.0)	1 (1.0)	2 (1.3)	0 (0.0)	0 (0.0)	2 (9.1)
Procedure death	0 (0.0)	1 (1.0)	2 (1.2)	0 (0.0)	1 (1.0)	2 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)
Other cardiovascular death	0 (0)	0 (0)	56 (32.4)	0 (0.0)	0 (0.0)	44 (29.1)	0 (0.0)	0 (0.0)	12 (55.5)

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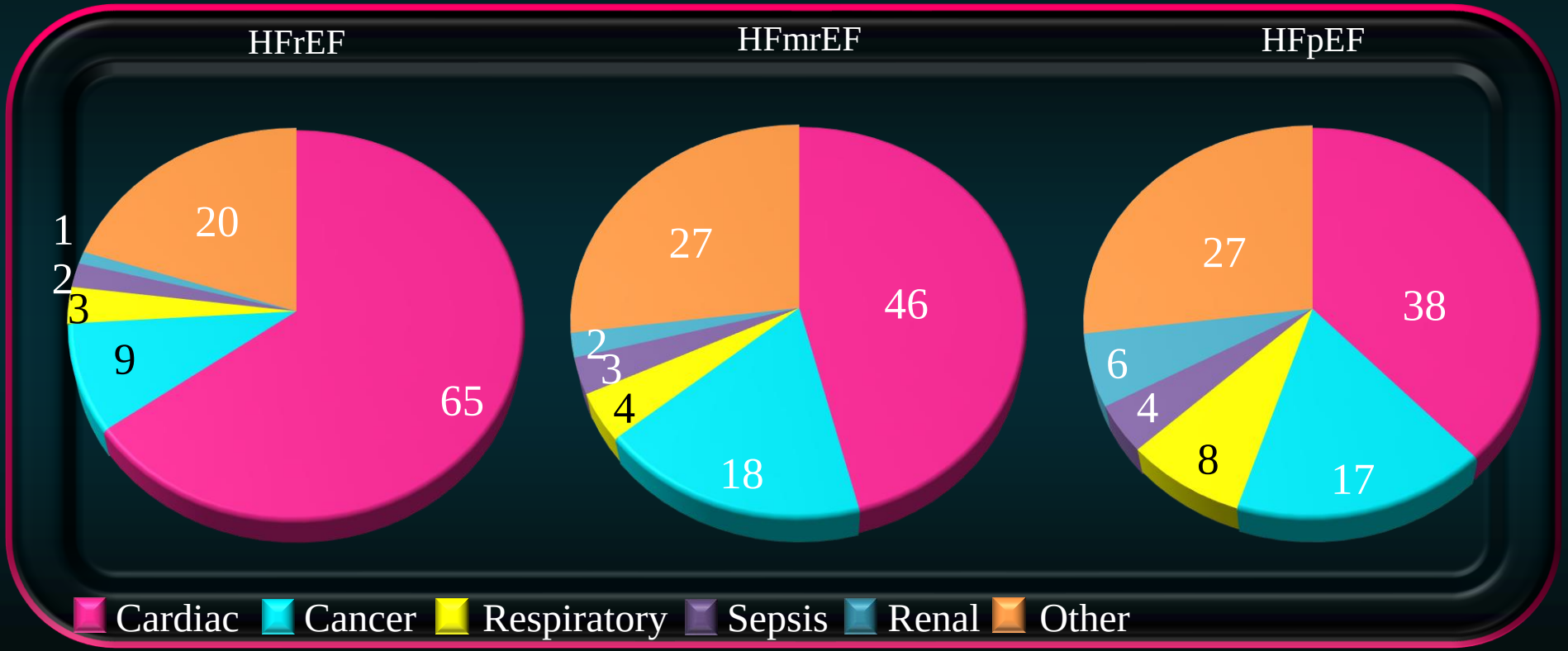
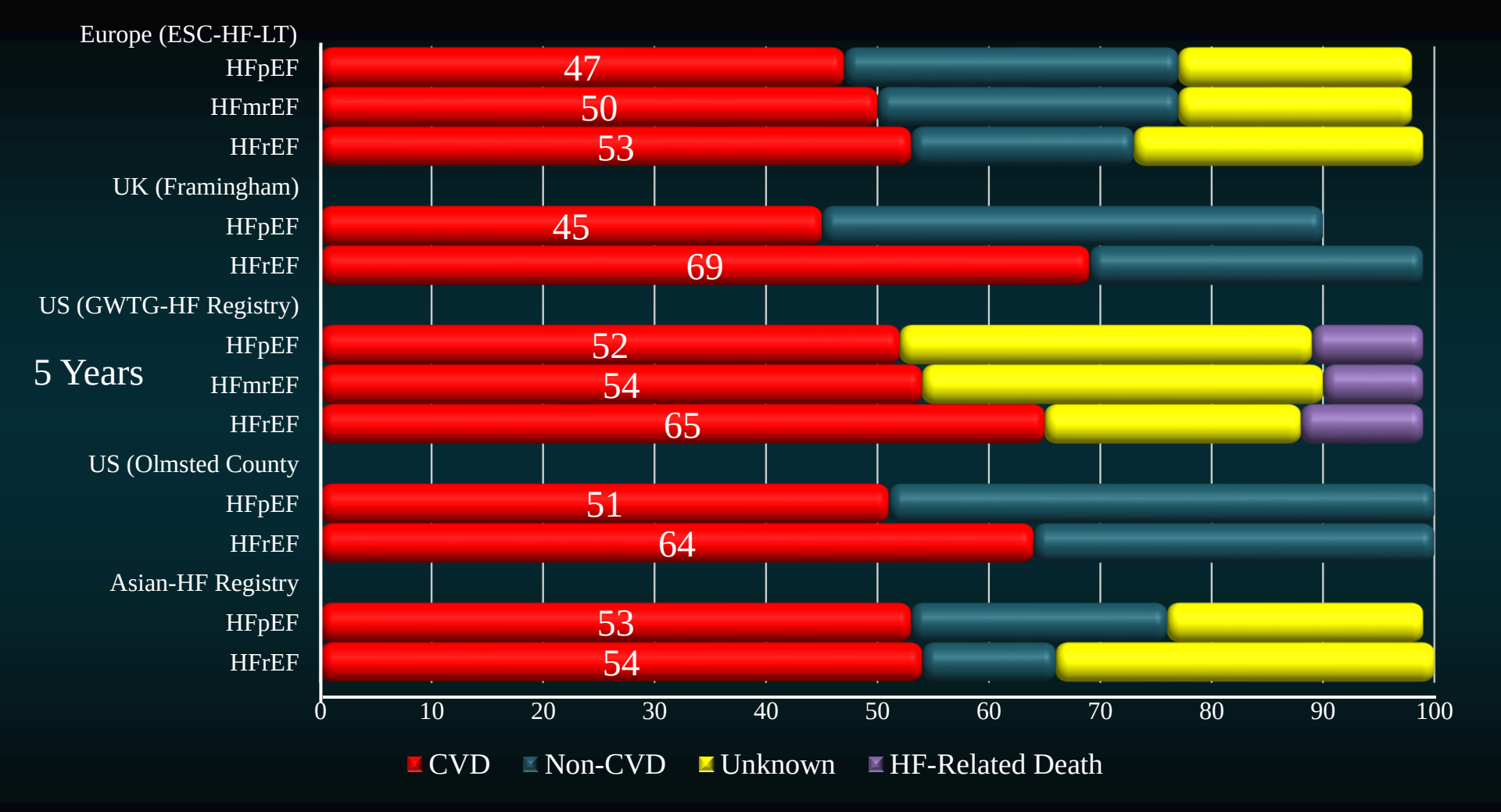
Causes of Death in Patients with HFrEF, HFmrEF, and HFpEF

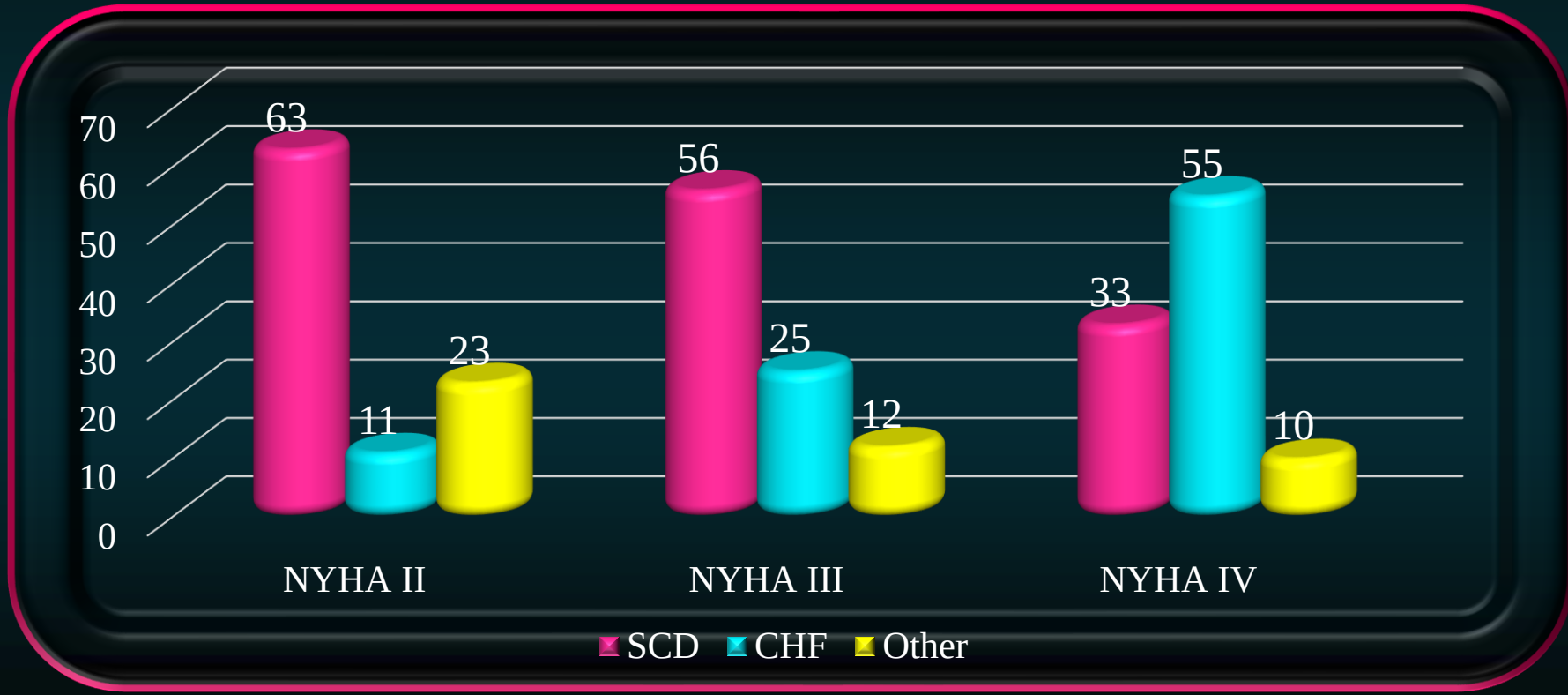


J Am Heart Assoc. 2019;8:e013441



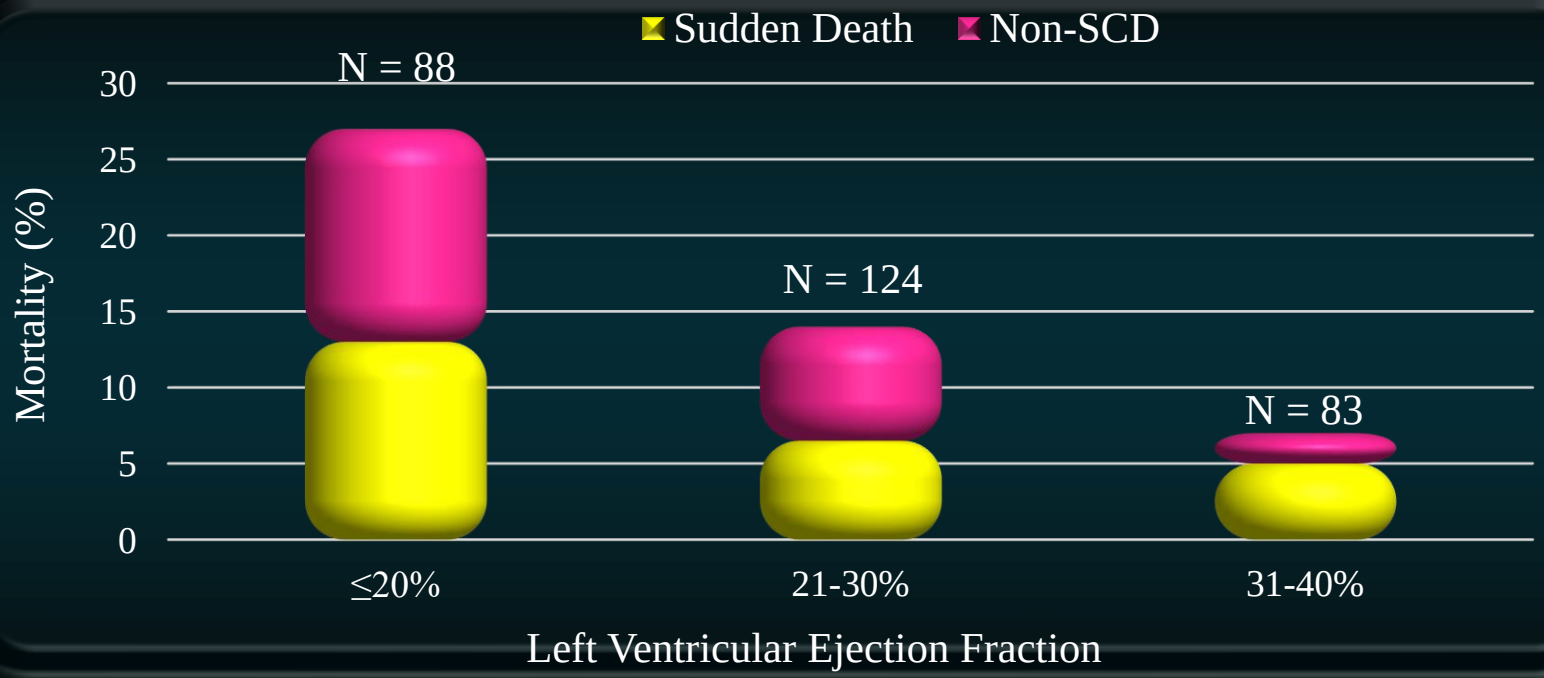
Cardiovascular Research, 2022 118;17: 3272–3287

MERIT-HF: Mode of Death by NYHA Class



Lancet 1999;353:9169, 2001 - 2007

Relation Between Baseline LVEF and Mortality Rate



JACC 1989;14.564-70)

Mortality: HFrEF Versus HFpEF

- HFrEF patients
  - SCD account for ~45% of cardiovascular deaths
  - Worsening heart failure ~25%
  - Cardiac dysrhythmias are responsible for majority of SCD in patients with HFrEF

- HFpEF patients
  - SCD accounted for ~40% of cardiovascular mortality
  - Worsening heart failure accounted for 20–30% of cardiovascular deaths
  - Burden of lethal and non-lethal arrhythmias in HFpEF is unknown

JACC 2017; 69: 556–569

Arrhythmia in HFmrEF and HFpEF: VIP-HF Study

- 113 patients consisting of combined HFmrEF and HFpEF patients implanted with implantable loop recorders to capture incident tachyarrhythmias and bradyarrhythmias
  - 0.6, 11.5, and 3.2 per 100 person-years incidence of sustained VT, non-sustained VT, and bradyarrhythmia, respectively, during a median follow-up of 1.8 years

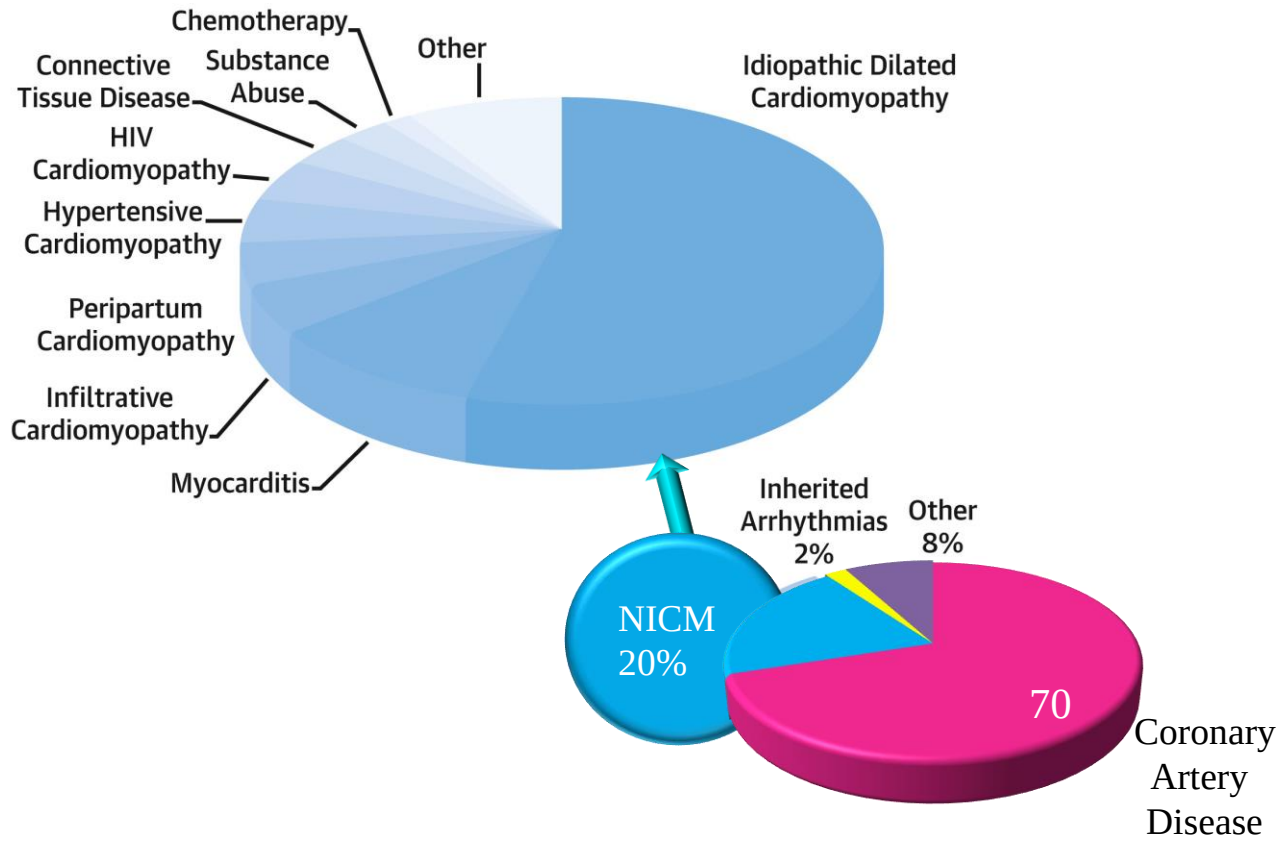
Eur J Heart Fail. 2020; 22: 1923–1929

Aetiology for Sudden Cardiac Death

Risk Factors
Age
Male
Diabetes
Chronic Kidney Disease
Genetics

Myocardial Substrate
Replacement Fibrosis
Interstitial Fibrosis
Hypertrophy
Abnormal Ca^{+} Handling
Dispersion of Repolarization
Impaired Myocardial Cell Coupling

Triggers
Ischemia
Heart Failure
Metabolic Disturbances
Electrolyte Abnormalities
Autonomic Dysfunction
Inflammation



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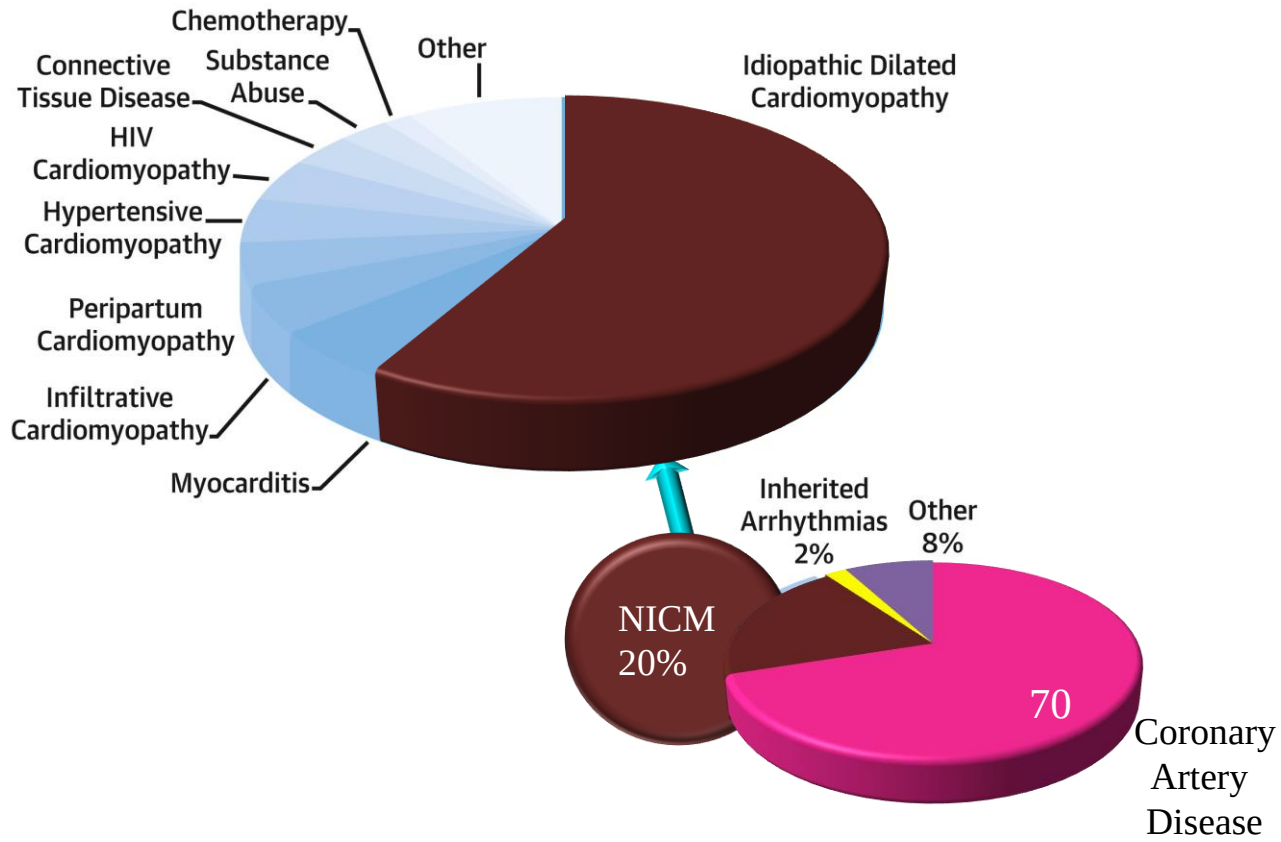
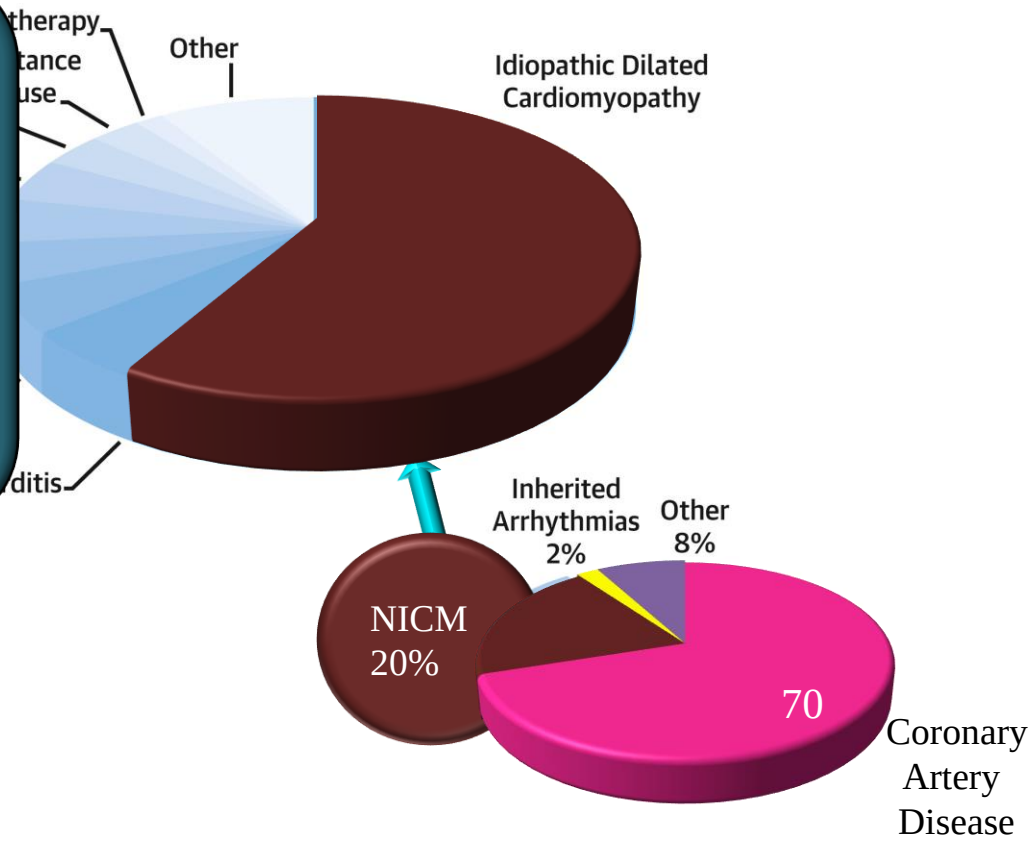


What Causes Sudden Cardiac Death in Heart Failure?

Myocardial Substrate
Replacement Fibrosis
Interstitial Fibrosis
Hypertrophy
Abnormal Ca+ Handling
Dispersion of Repolarisation
Impaired Myocardial Cell Coupling



Triggers
Ischemia
Heart Failure
Metabolic Disturbances
Electrolyte Abnormalities
Autonomic Dysfunction
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What Causes Sudden Cardiac Death in Heart Failure?

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Myocardial Substrate
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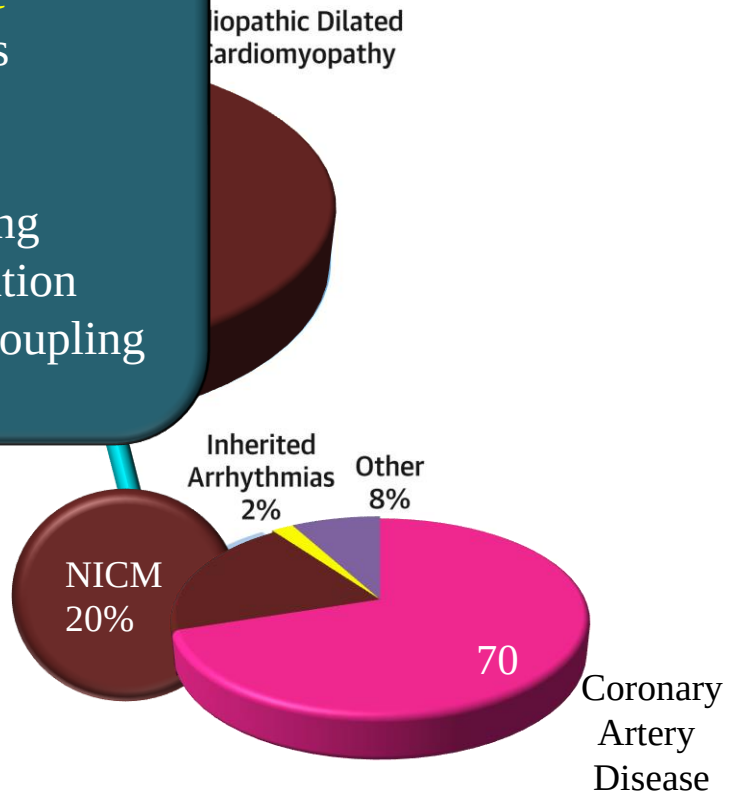
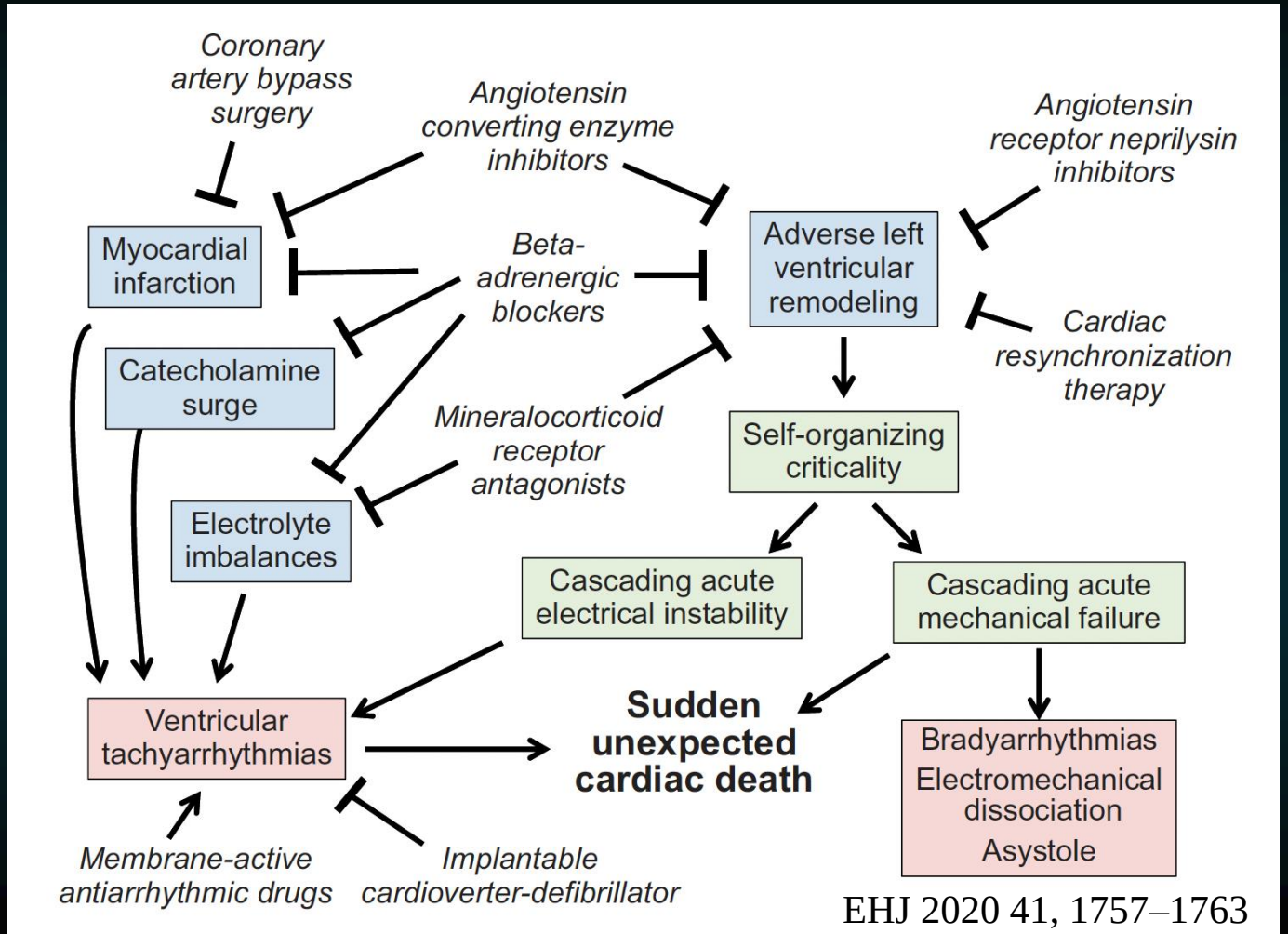
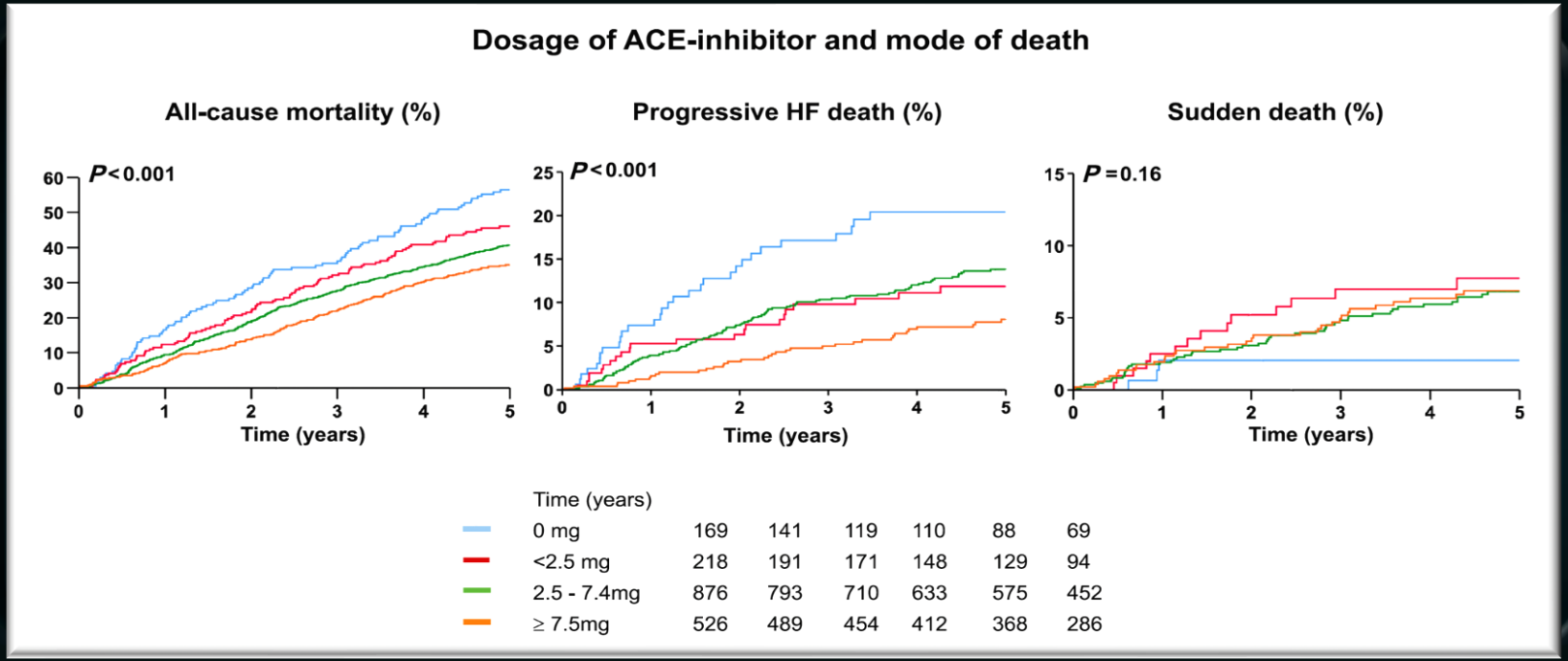


Interventions to Reduce the Risk of SCD in Chronic Heart Failure

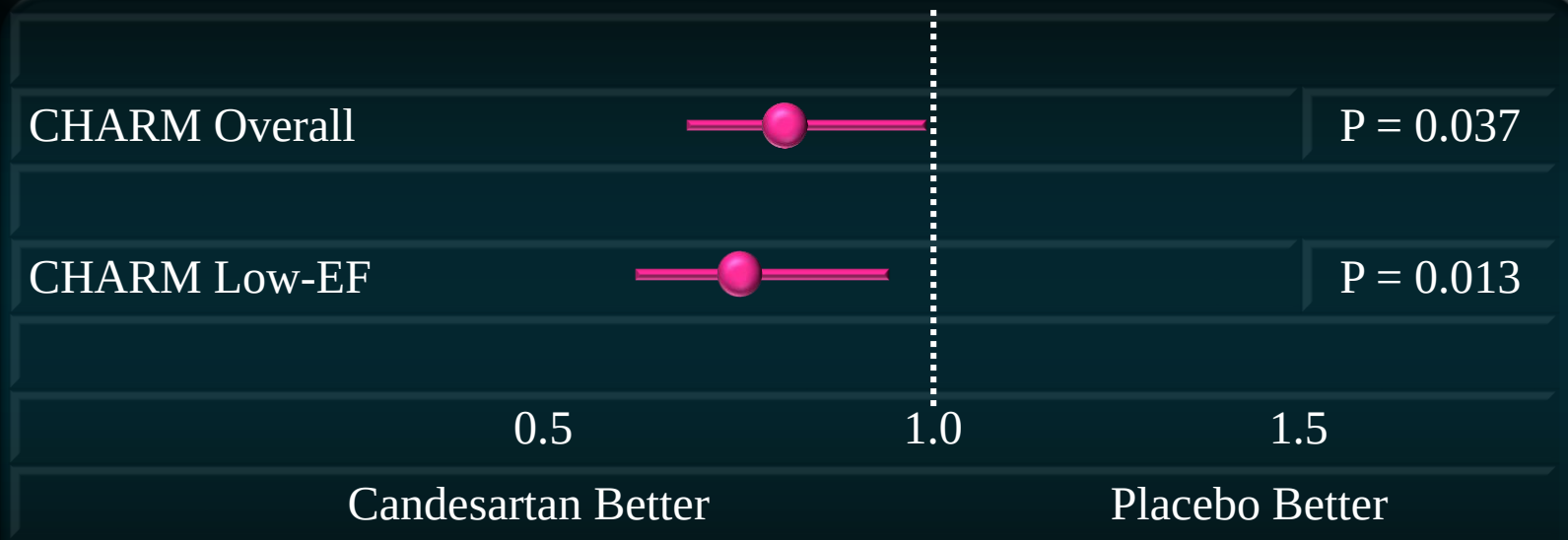


EHJ 2020 41, 1757–1763

Dosage of ACE-Inhibitor and Mode of Death



ARB and Sudden Death in Heart Failure

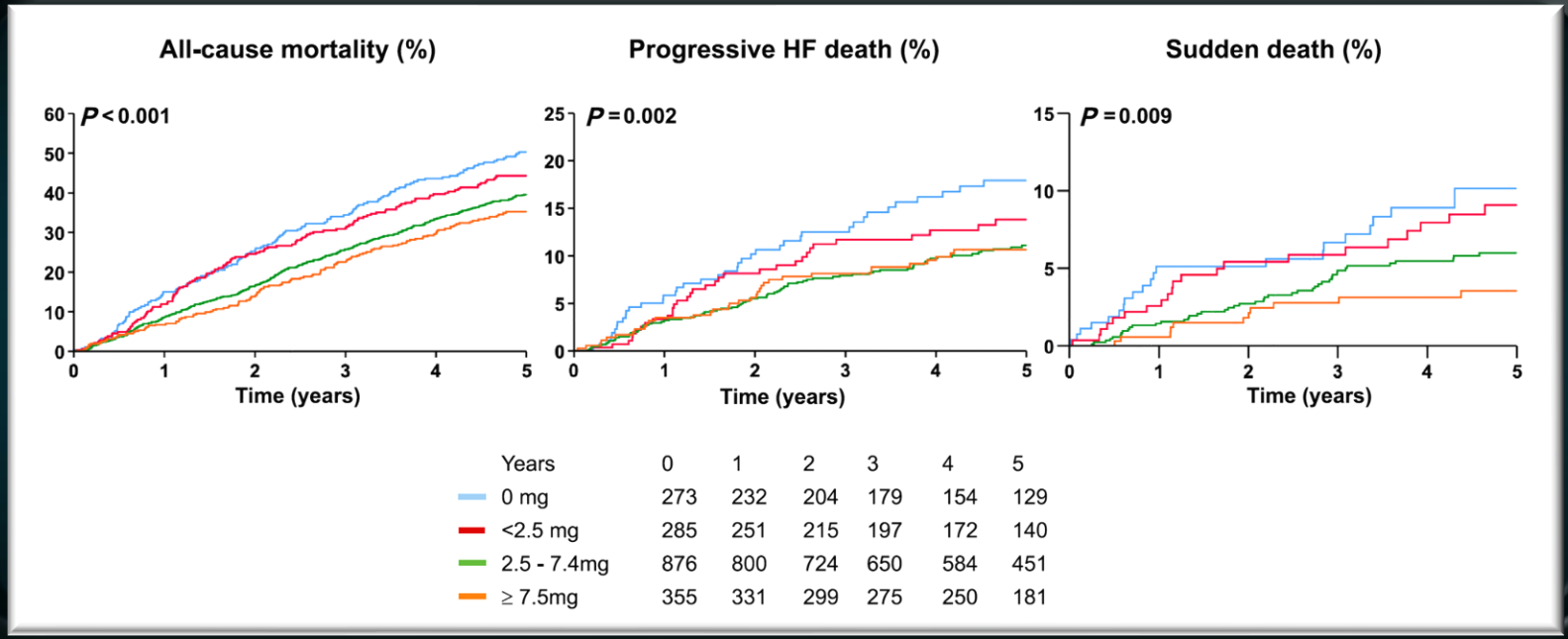


Circulation 2004;110:2180-3

Beta-Blockers, Heart Failure and SCD

- Beta-blockers decrease the risk of SCD and all-cause mortality in patients with HFrEF
  - 31% reduction in SCD (95% CI 0.62–0.77)
  - 33% reduction in all-cause mortality (95% CI 0.59–0.76)

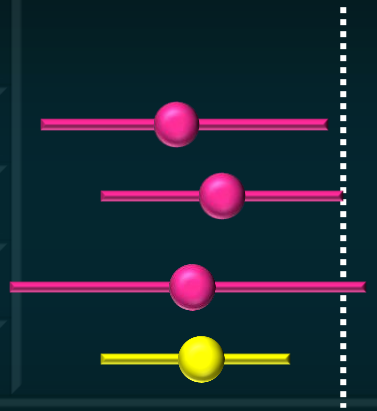
Dosage of Beta-Blocker and Mode of Death



ESC Heart Failure 2020; 7: 3859–3870

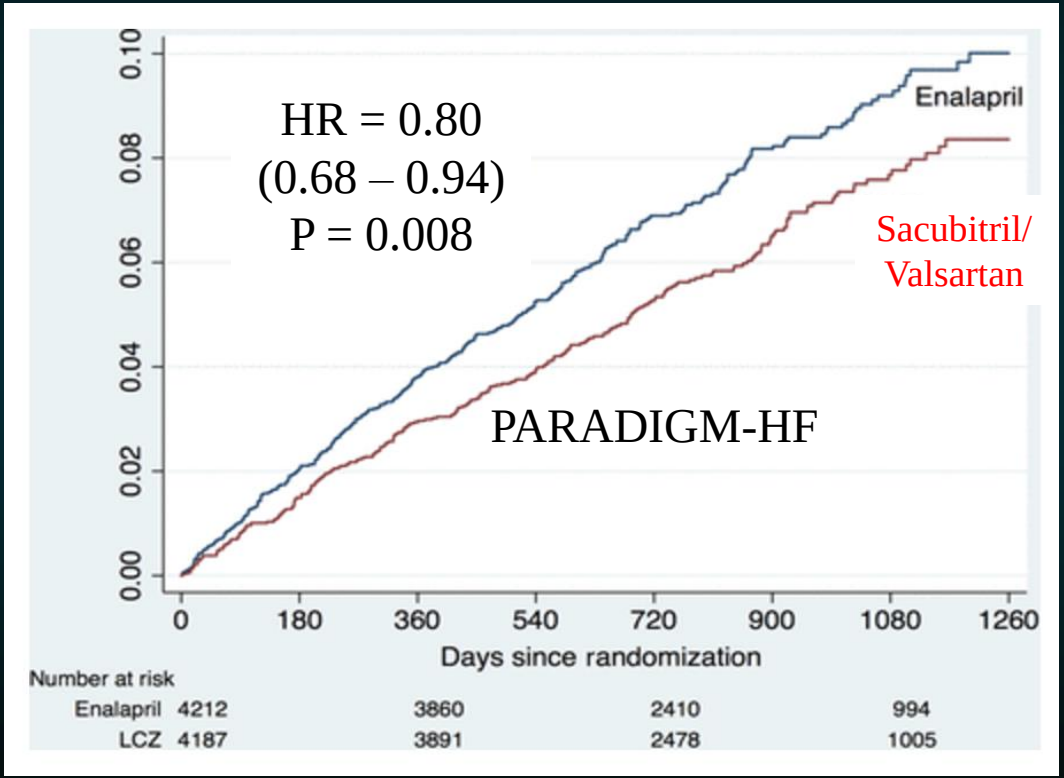
MRA, Sudden Cardiac Death and Heart Failure

Study	Patients Number	SCD MRA Number	SCD Placebo Number	Adjusted HR (95% CI	P Value
Rales	1652	110	82	0.70 (0.53-0.94)	0.017
EPHESUS	6229	201	162	0.80 (0.64-1.00)	0.053
EMPHASIS-HF	2562	76	61	0.74 (0.52-1.05)	0.091
Overall	10443	387	305	0.76 (0.65-0.89)	0.001



Clin Res Cardiol 2019 May;108(5):477-486

ARNI, Sudden Cardiac Death and Heart Failure



Eur Heart J, 2015;36:30 1990–1997

PARADIGM: Ventricular Arrhythmia Outcome

Outcome	Sacubitril/Valsartan		Enalapril		Hazard Ratio (95% CI)
	n/N (%)	Event Rate per 100 patient years (95% CI)	n/N (%)	Event Rate per 100 patient years (95% CI)	Analysis
Ventricular Arrhythmia	145/4187 (3.5%)	1.6 (1.4 – 1.9)	188/4212 (4.5)	2.1 (1.8 – 2.4)	0.76 (0.62-0.95) P = 0.015
Ventricular Arrhythmia/ICD	165/4187 (3.9)	1.8 (1.6 – 2.1)	207/4212 (4.9)	2.3 (2.0 – 2.6)	0.79 (0.65 – 0.97) P = 0.0025
VT/VF/Ventricular flutter/Torsades de pointes	133/4175 (3.2)	1.5 (1.2 – 1.7)	171/4195 (4.1)	1.9 (1.6 – 2.2)	0.77 (0.62 - 0.97) P = 0.027

DISCOVER-ARNI and ICD

351 Patients with HFrEF
Referred for treatment with Sacubitril/Valsartan
65±10 years Mean LVEF 29±6%

225 (64%)
ICD Carriers
64±11 Years
Mean LVEF 28±6%

126 (36%) Patients Without ICD

13 (10%) Patients
Without ICD Indication
at Baseline
Mean LVEF 35-40%

113 Patients
65±11 Years
Mean LVEF 30±5%

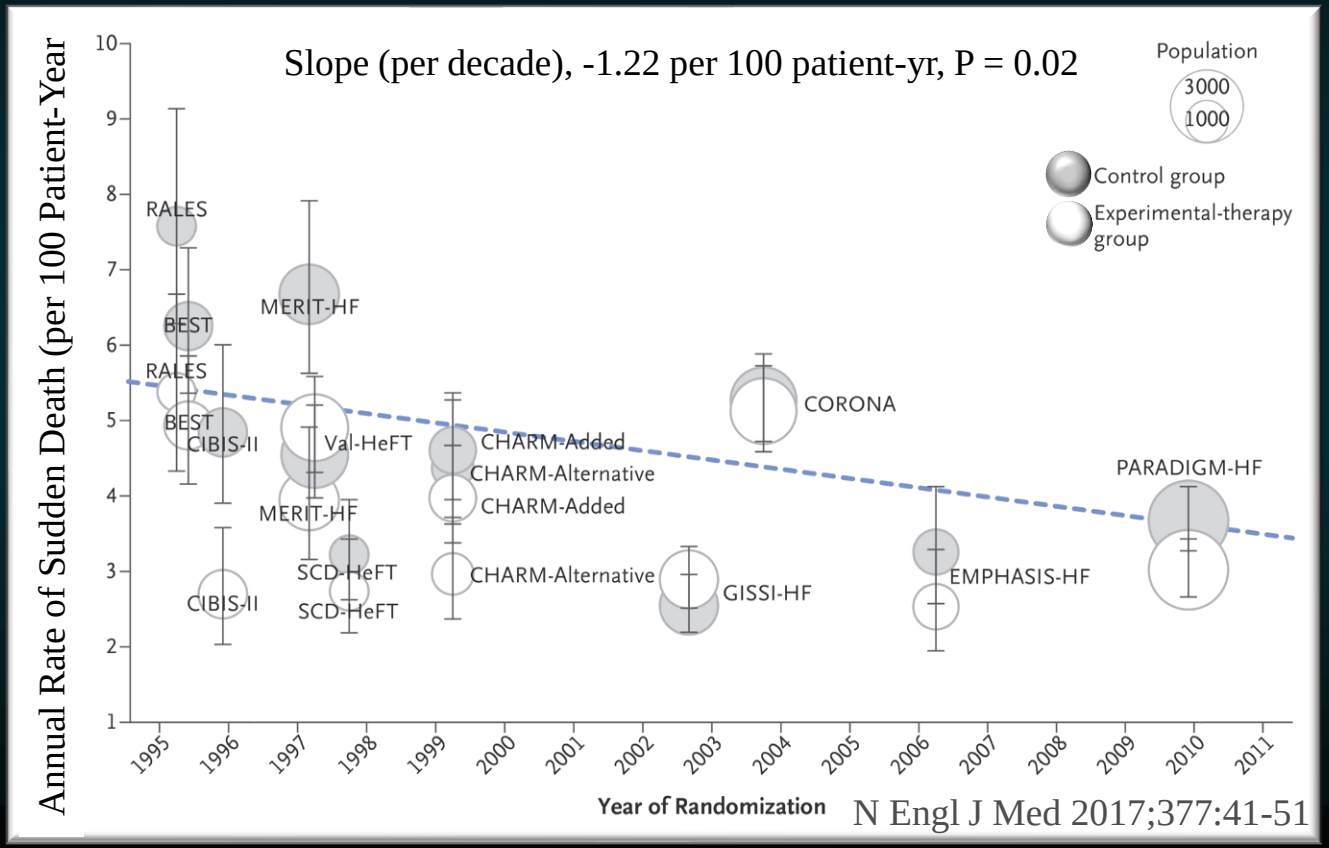
6 Months Treatment with Sacubitril/Valsartan

44 Patients (40%)
Still ICD Indication
LVEF ≤35% or NYHA = II-III

69 Patients (60%)
No ICD Indication
LVEF ≥35% or NYHA = I

Eur Heart J Open 2021 Dec 21;2(1):oeab046. doi

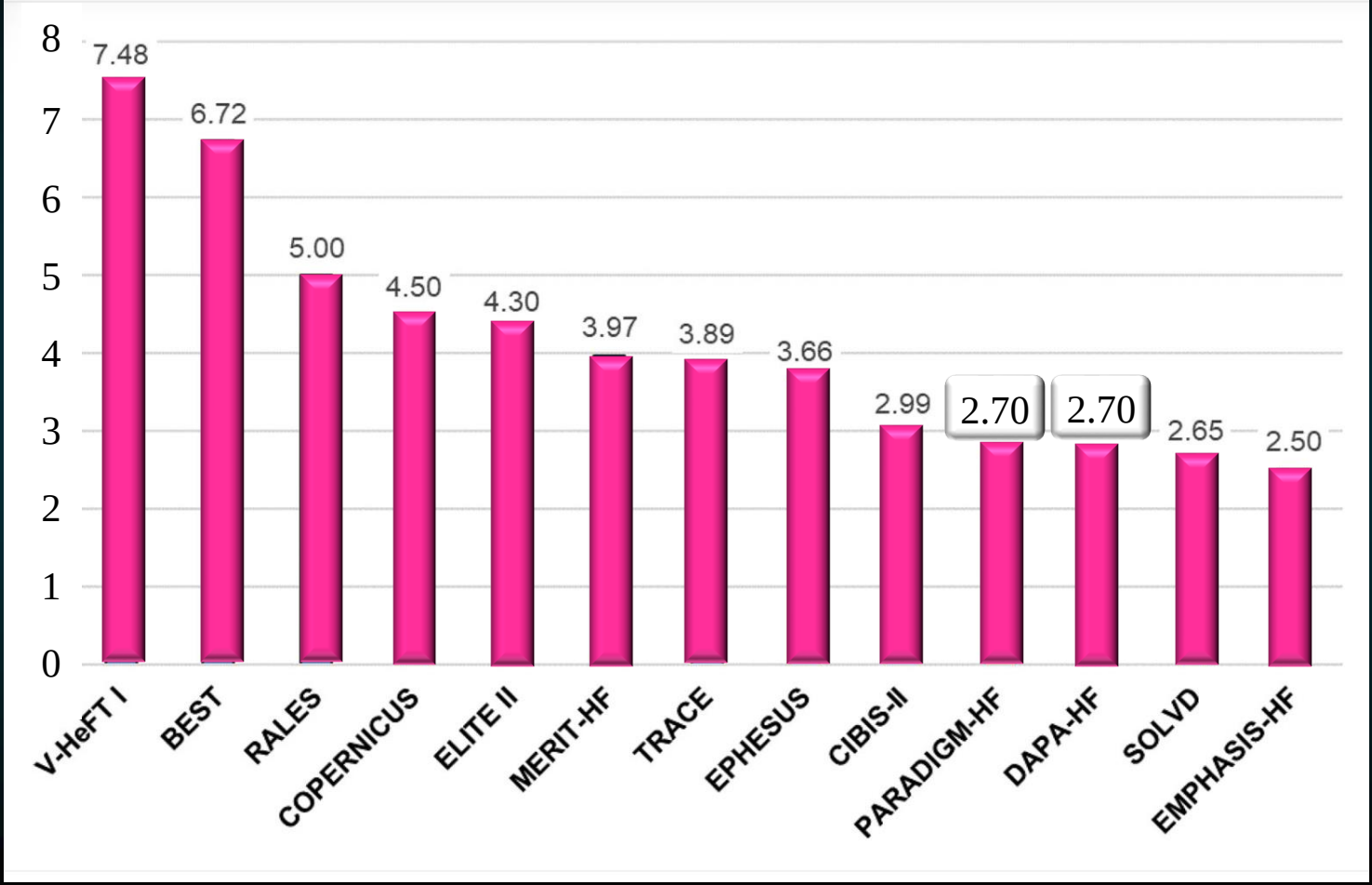
Trends in the Rate of Sudden Death across Trial Groups over Time



N Engl J Med 2017;377:41-51

Do We Still Need ICD for Primary Prevention of Sudden Death in HFrEF?

Residual Risk of SCD in HF trials



Results in Primary Prevention of Sudden Death With Implantation of an Implantable Cardioverter Defibrillator

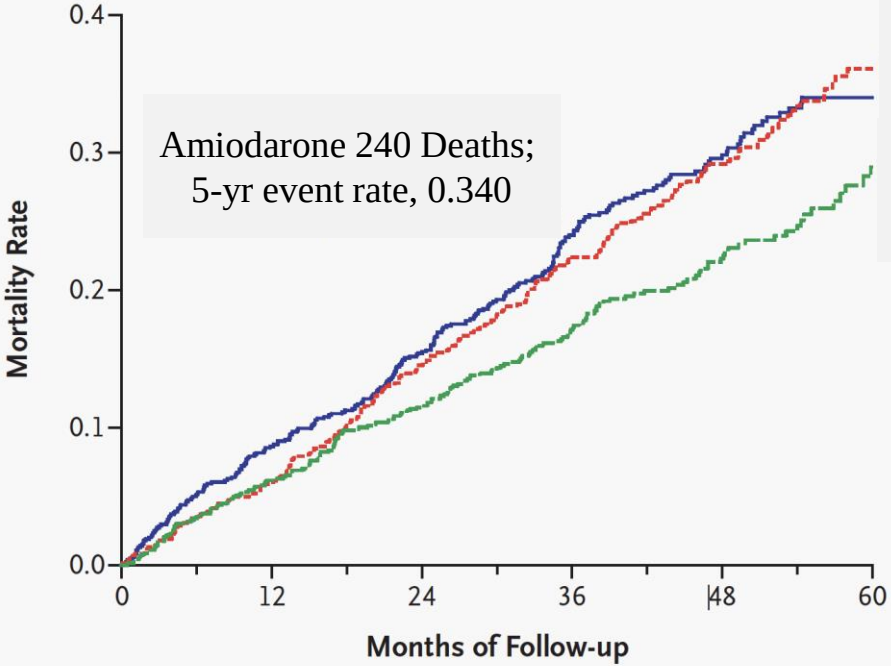
Study	N	Patient	Inclusion Criteria	Treatment Group	Sudden Death
MADIT	196	ICM	LVEF<35%, previous AMI, NSVT, SMVT in EPS, NYHA I-III	ICD vs AAD	Reduction
CABG PATCH	900	ICM	LVEF<36%, surgical revascularization, positive SAE, NYHA I-IV	ICD vs Control	Reduction
MUSTT	704	ICM	LVEF 40%, previous AMI, NSVT, SMVT in EPS, NYHA I-III	ICD vs AAD vs Control	Reduction
MADIT II	1232	ICM	LVEF 30%, previous AMI, NYHA I-III	ICD vs Control	Reduction

Results in Primary Prevention of Sudden Death With Implantation of an Implantable Cardioverter Defibrillator

Study	N	Patient	Inclusion Criteria	Treatment Group	Sudden Death
CAT	104	NICM	LVEF ≤30%, recent onset of NICM (9 months), NYHA II-III	ICD vs Control	Same
AMIOVIRT	103	NICM	LVEF ≤35%, NSVT, NYHA I-III	ICD vs Amiodarone	Same
DANISH	1116	NICM	LVEF ≤35%	ICD vs Control	Same
DEFINITE-ICD	458	NICM	LVEF ≤35%, NSVT or VE, NYHA I-III	ICD vs Control	HR 0.20; 0.06 to 0.71 P=0.006
SCD-HeFT	2500	NICM +ICM	LVEF ≤35%, NYHA II-III	ICD vs Amiodarone vs Control	HR 0.30; 0.62 to 0.96; P=0.007

SCD-HeFT Trial

	Hazard Ratio (97.5% CI)	P Value
Amiodarone vs Placebo	1.06 (0.86-1.30)	0.53
ICD therapy vs Placebo	0.77 (0.62-0.96)	0.007



Amiodarone 240 Deaths;
5-yr event rate, 0.340

Placebo 244 Deaths;
5-yr event rate, 0.361

ICD Therapy182 Deaths;
5-yr event rate, 0.289

ESC Recommendations for an Implantable Cardioverter-Defibrillator in Patients with Heart Failure

Recommendations	Class	Level
An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA class II–III) of an ischaemic aetiology (unless they have had a MI in the prior 40 days), and an LVEF ≤35% despite ≥3 months of OMT, provided they are expected to survive substantially longer than 1 year with good functional status	I	A

ESC Recommendations for an Implantable Cardioverter-Defibrillator in Patients with Heart Failure

Recommendations	Class	Level
An ICD should be considered to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA class II–III) of a non-ischaemic aetiology, and an LVEF ≤35% despite ≥3 months of OMT, provided they are expected to survive substantially longer than 1 year with good functional status	IIa	A

Risk Stratification for Sudden Death in Dilated Cardiomyopathy

- LVEF has been used as a key criterion for selecting patients with DCM for an ICD for primary prevention purposes
  - Registry data suggest that many patients with DCM and an out-of-hospital cardiac arrest do not have a markedly reduced left ventricular ejection fraction
  - Many patients with reduced LVEF die of non-sudden causes of death

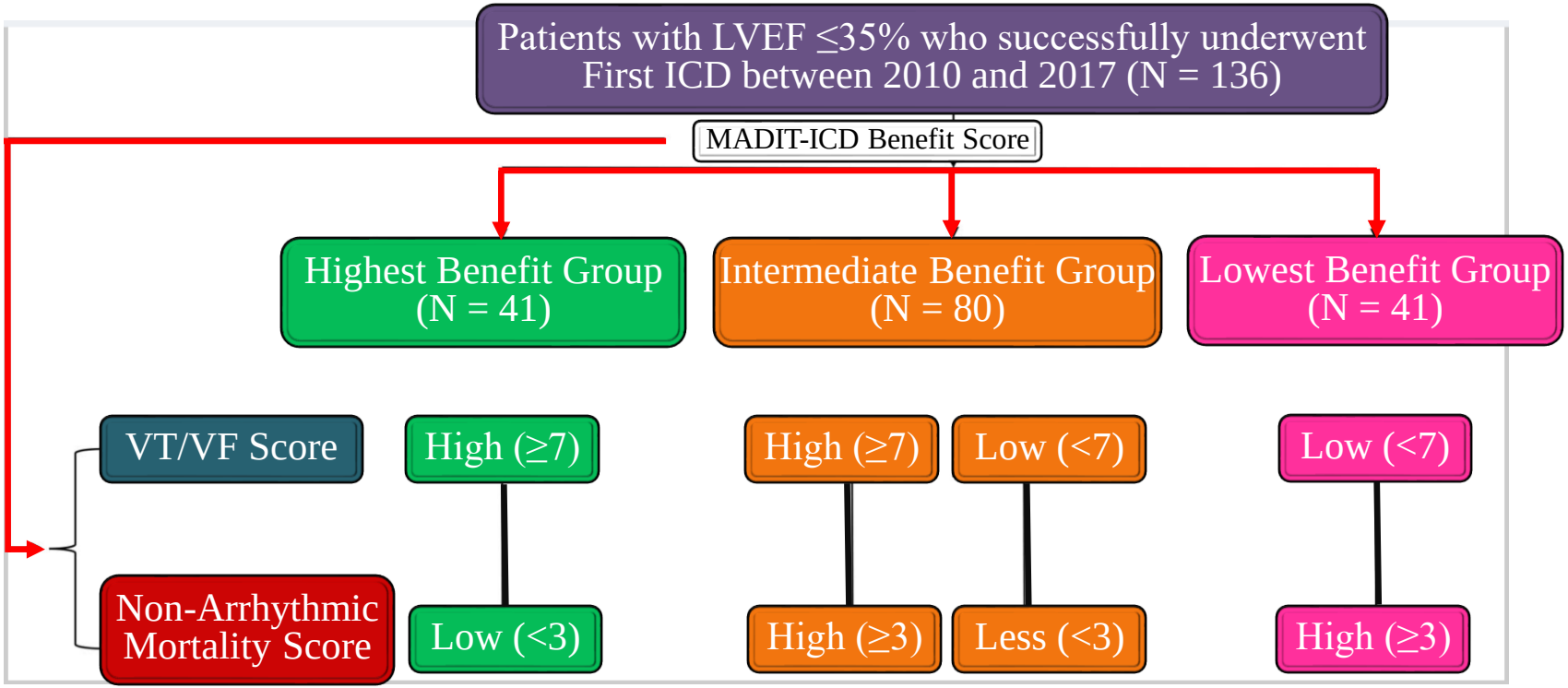
MADIT-ICD benefit group	Lowest	Intermediate		Highest
VT/VF score	Low (<7)	Low (<7)	High (≧7)	High (≧7)
Non-arrhythmic mortality score	High (≧3)	Low (<3)	High (≧3)	Low (<3)

VT/VF score	
Variable	Points
LVEF≦25%	+1
Atrial arrhythmia	
Heart Rate>75bpm	
SBP<140mmHg	+2
Myocardial Infarction	
Age<75yrs	
Male	
Prior NSVT	

Non-arrhythmic mortality score	
Variable	Points
CRT	-1
NYHA class≧II	+1
Diabetes	
BMI<23kg/m^2	+2
Atrial arrhythmia	
LVEF≦25%	
Age≧75yrs	

Eur Heart J. 2021;42:1676-1684.

MADIT-ICD: ICD or Not ICD



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ORIGINAL RESEARCH

Prediction Efficiency of MADIT-ICD Benefit Score for Outcome in Asian Patients with Implantable Cardioverter-Defibrillator

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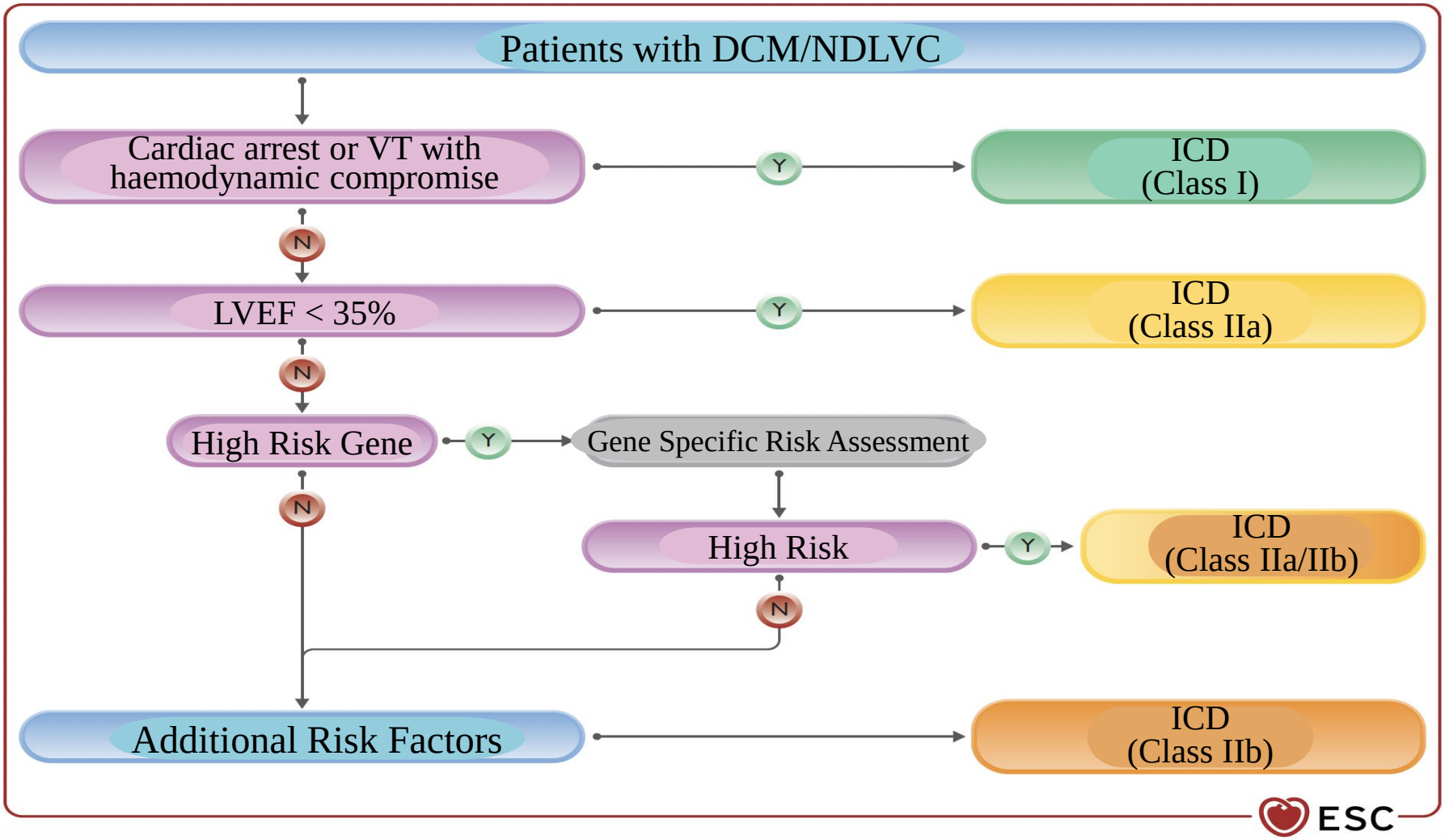
Background: Not all patients with heart failure derive consistent benefit from prophylactic implantable cardioverter-defibrillator (ICD). We aimed to evaluate the role of MADIT-ICD benefit score in risk-stratifying in Asian patients with left ventricular ejection fraction (LVEF) ≤35%.

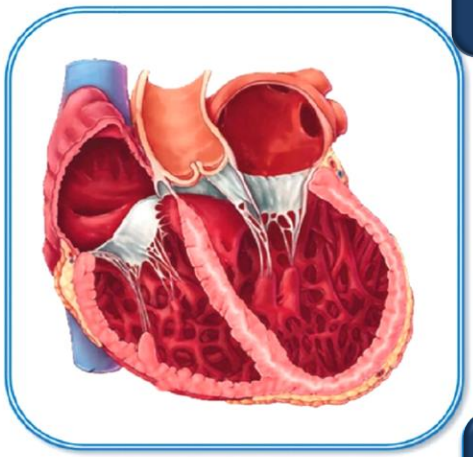
Methods: In this two-center, retrospective study, a total of 136 patients with LVEF ≤35% who received an ICD for primary prevention were enrolled. The endpoints were defined as the ventricular tachycardia ≥200bpm (VT) or ventricular fibrillation (VF) and non-arrhythmic death. Based on the MADIT-ICD benefit score system, all patients were categorized into three groups: highest benefit group (n = 41), intermediate benefit group (n = 80), and lowest benefit group (n = 15).

Results: Forty patients experienced VT/VF and seven died of non-arrhythmic causes during a median follow-up of 44.8 ± 28.9 months. Kaplan–Meier curves showed that patients in highest benefit group had a worse VT/VF occurrence compared to those in other groups. In the highest benefit group, the predicted risk of VT/VF was 17-fold higher than the risk of non-arrhythmic mortality (41.5% vs 2.4%, P < 0.001). In the intermediate benefit group, the predicted risk of VT/VF was 4.2-fold higher than the risk of non-arrhythmic mortality (26.3% vs 6.3%, P = 0.001). In the lowest benefit group, however, the difference in the corresponding predicted risks was

Conclusion: We demonstrate that MADIT-ICD benefit score can be used for the assessment of ICD primary prevention benefits in Asian patients with LVEF ≤35%

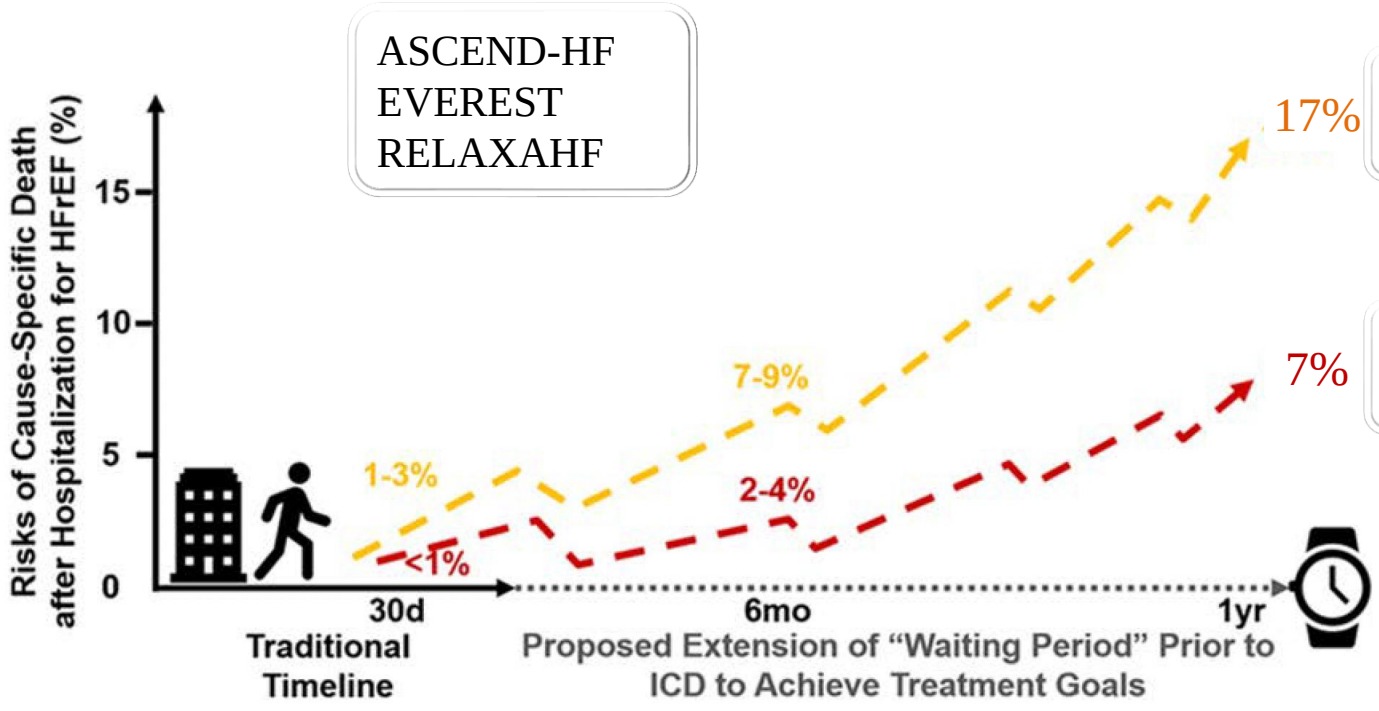

Patients with DCM/NDLVC
Cardiac arrest or VT with haemodynamic compromise
Y
ICD (Class I)
N
LVEF < 35%
Y
ICD (Class IIa)
N
High Risk Gene
Y
Gene Specific Risk Assessment
N
High Risk
Y
ICD (Class IIa/IIb)
N
Additional Risk Factors
ICD (Class IIb)
ESC

Establish and Emerging Risk Factors for SCD in DCM

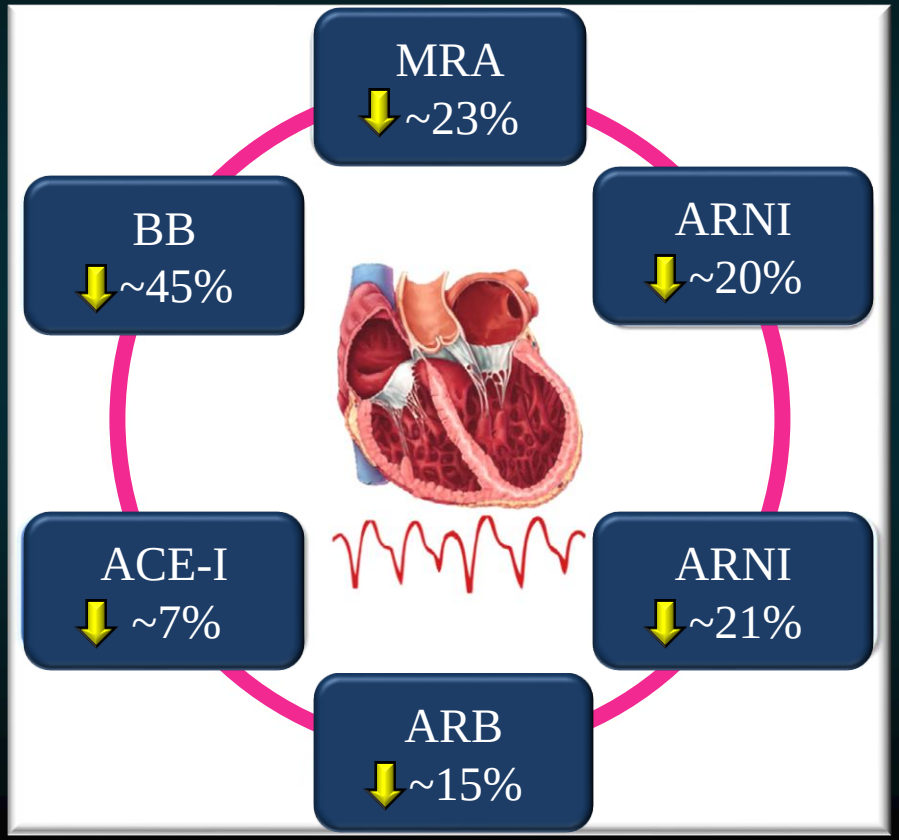


Clinical	Younger age; ↓LVEF; NYHA Class I-II; Syncope; SCD modifiers; comorbidities
Genetic	High risk genetic variants (eg LMNA, DSP, FLMC, RBM20)
ECG	QRS fragmentation; T wave alternans; Conduction abnormalities; Positive PES
Imaging	LGE on CMR; T1 mapping values

Effect of the Waiting Period on SCD and Non-SCD Risk Before ICD Implantation



Summary



Conclusion

- Sudden death is responsible for most deaths in patients with HF
- OMT should be the key first step in SCD risk reduction
- Identification and prevention of SCD in HF is of critical importance in patients with HFrEF
- Goal is to identify patients that is most likely to benefit from ICD therapy

Thank you for your attention