Implantable cardioverter defibrillator for primary prevention of sudden cardiac death ?

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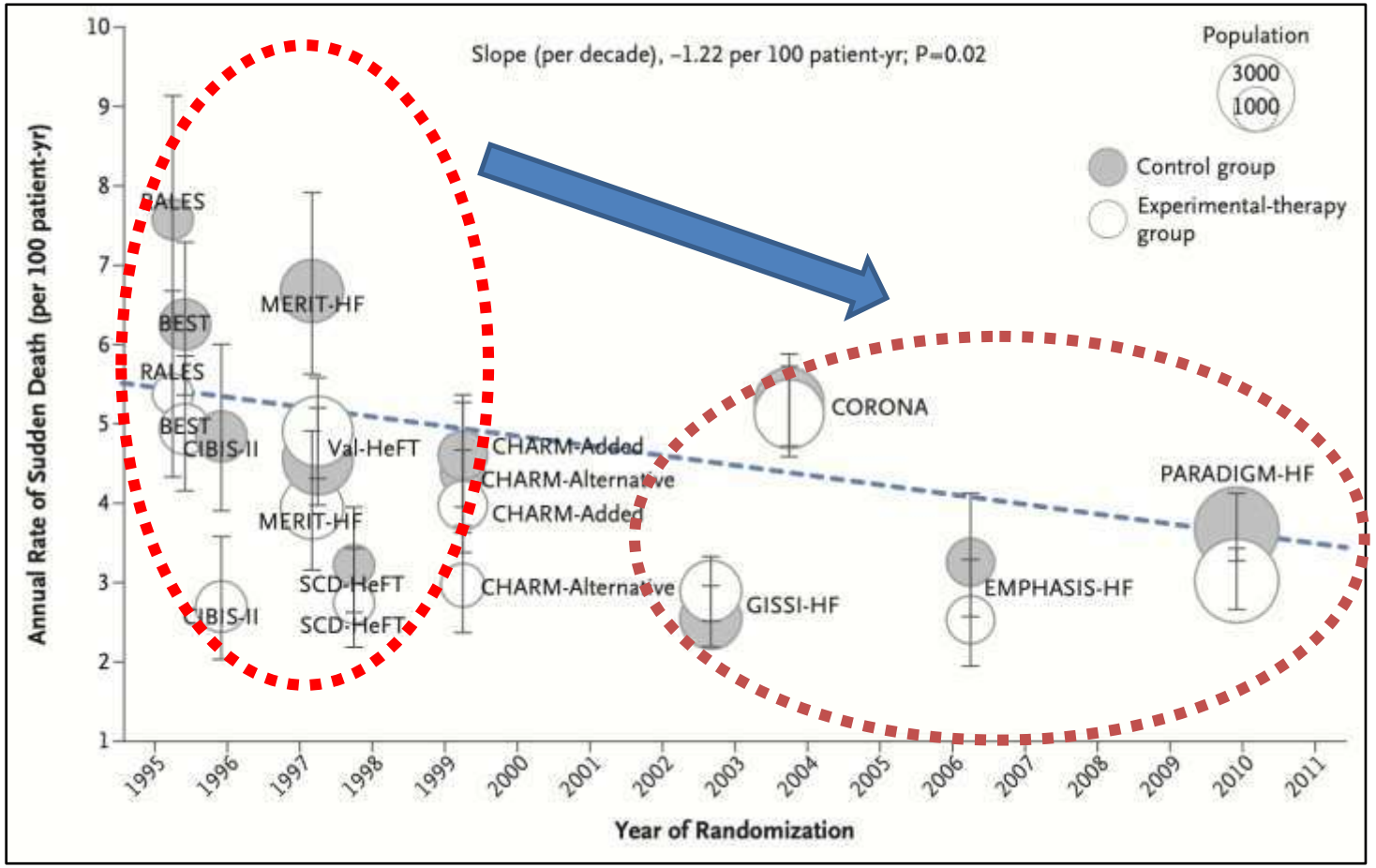
Declaration of interests of C Linde

- Nothing to declare

The current view

- ICD reduces mortality in HF patients
- Current ICD guidelines are based on studies earlier than 2005
- DANISH study raised questions on usefulness of ICDs in DCM
- Many ICD patients never get a shock
- *The benefits of ICD have been questioned*

Declining Risk of Sudden Death in HFrEF



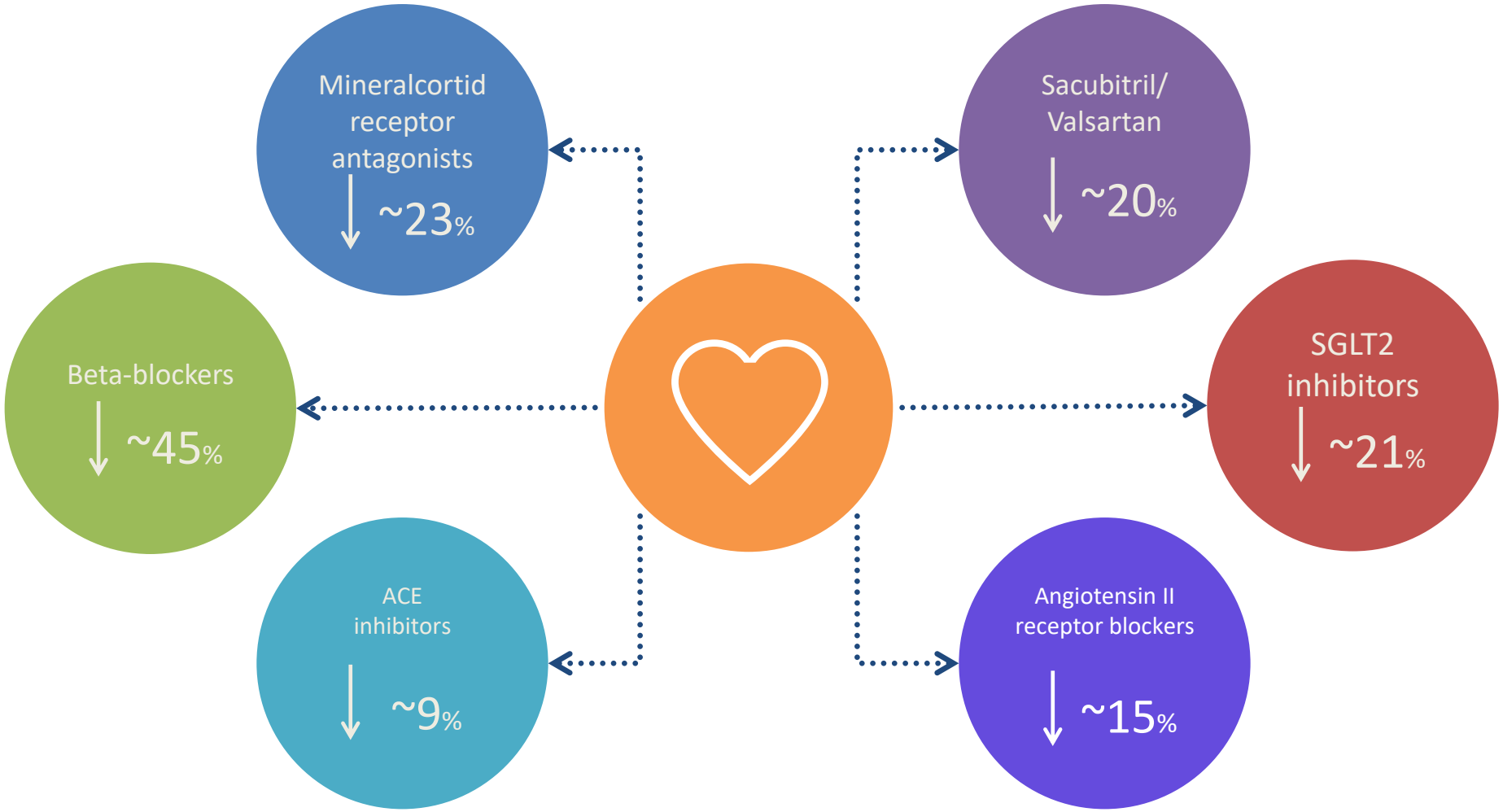
- RCTs in the late 90's reported annual rate of SCD of **6%**,
- More recent studies reported rates of **3%**
- **SCD rates have declined by 44% over the past 20 years**

Shen L et al. N Engl J Med. 2017 Jul 6;377(1):41-51.

Misperception 1

There is no clear benefit for ICDs in patients who are on guidelines indicated heart failure medical therapy

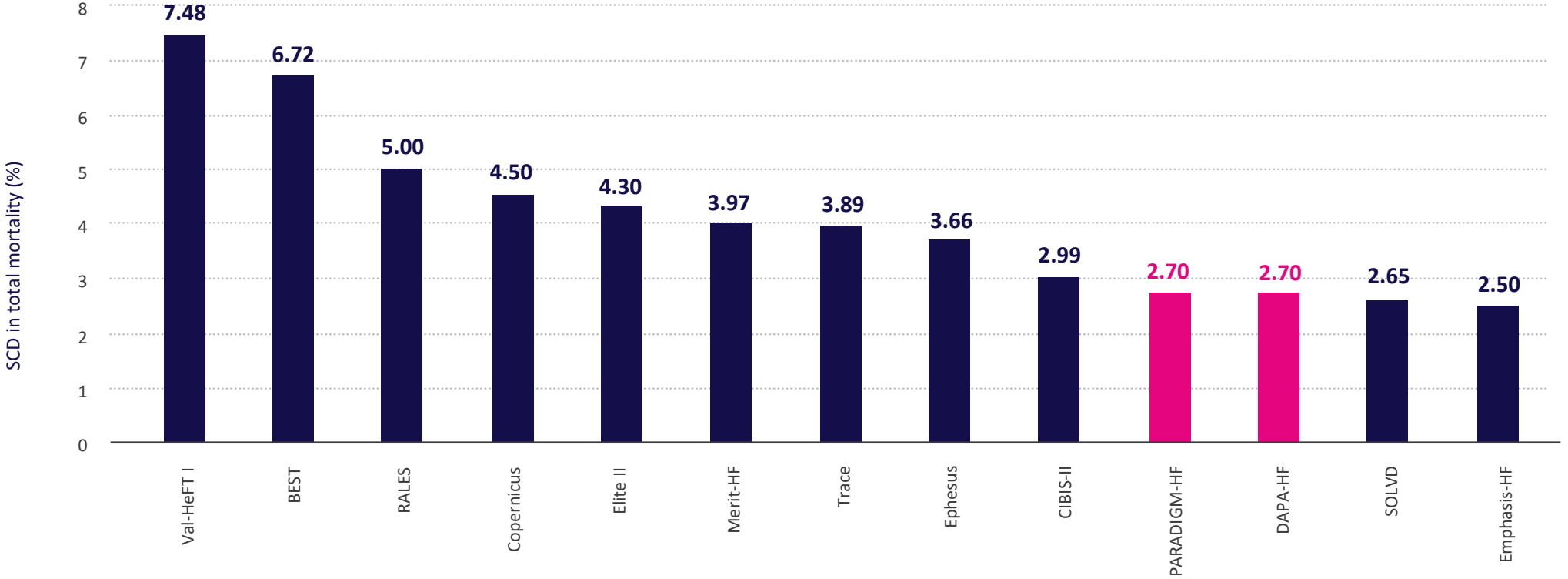
Estimated SCD risk reduction of HF medications for HFrEF in randomised trials



- Polovina M et al. *Eur J Heart Fail.* 2023; Oct 31

Residual risk of SCD remains high

rate of SCD (%) per 100 patient years in HF trials – incidence



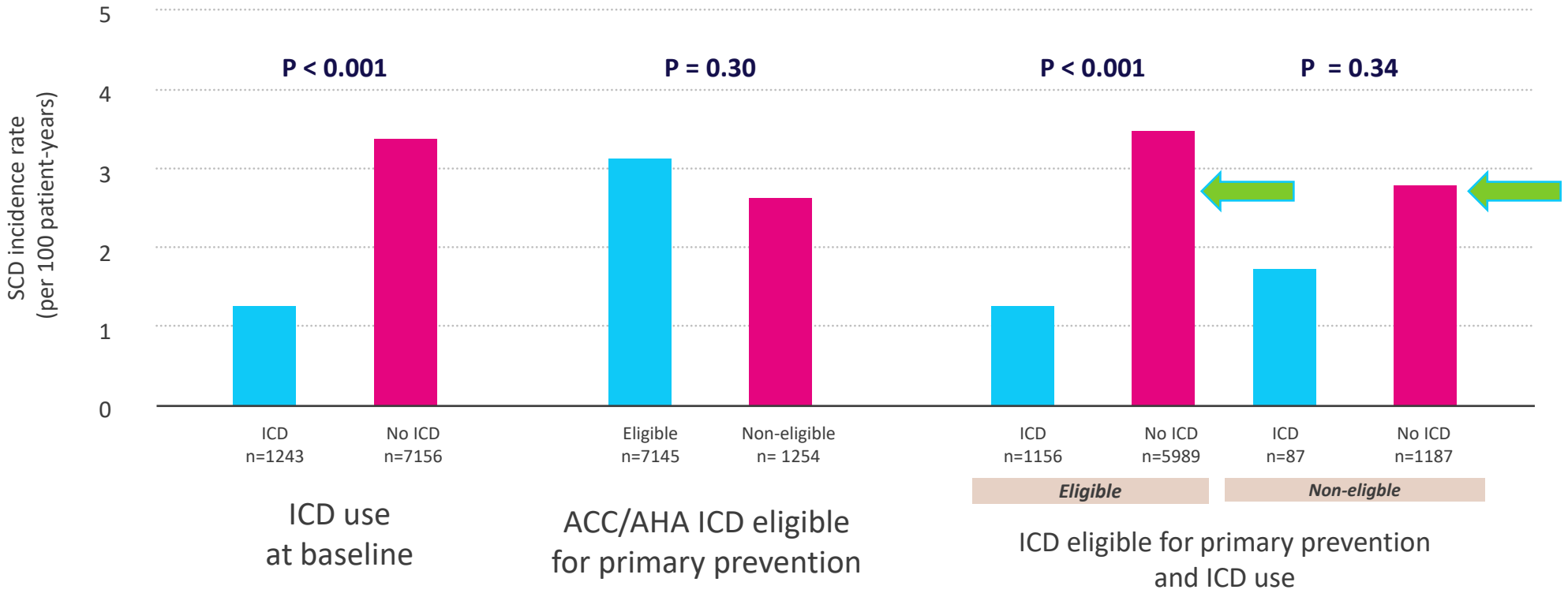
Residual risk of SCD in HF trials

The graph shows the rate of SCD (%) per 100 patient years in the intervention arm in HF trials.

Leyva F et al. Circulation. 2023;147:759-67

Sacubitril/Valsartan and sudden cardiac death according to ICD use

A PARADIGM-HF propensity score-adjusted analysis (n = 8,399)



Among patients who were potentially ICD-eligible or noneligible,

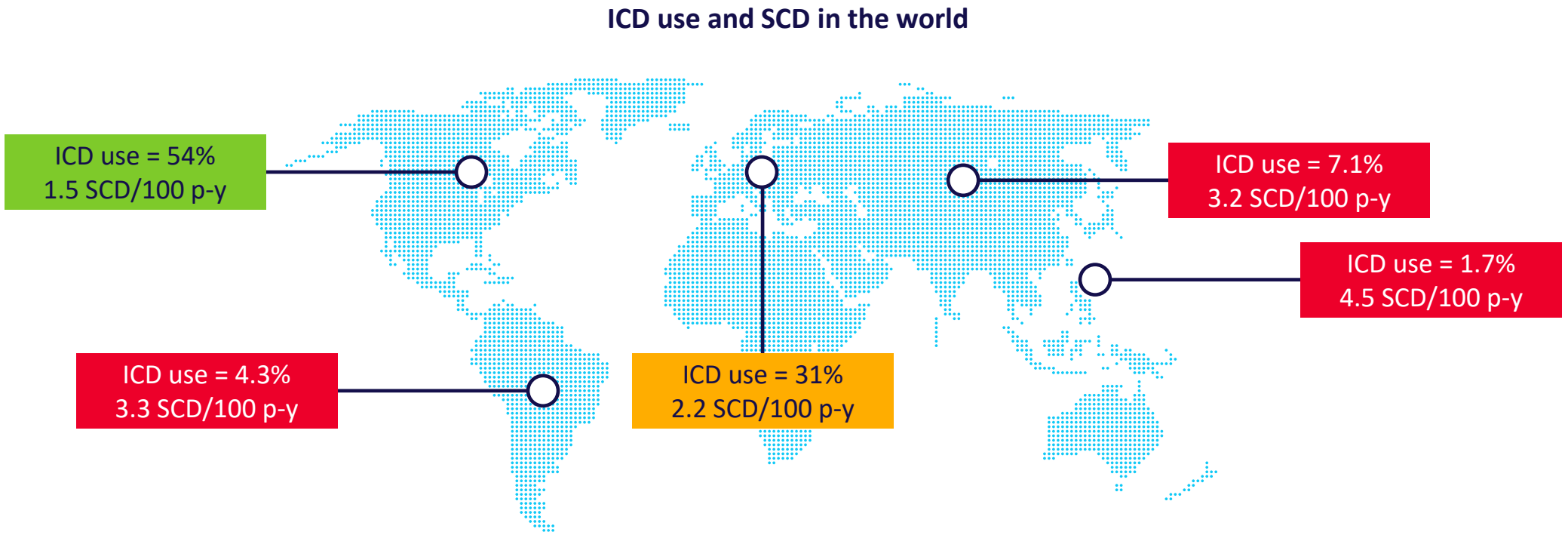
SCD incidence rates were 3.11% and 2.66% per 100 patient-years, respectively

Rohde LE et al. *JACC Heart Fail.* 2020;8:844-55

Geographical variation of ICD use taking the PARADIGM study as example

Rates of ICD implantation among eligible patients were low and inversed related to SCD risk

A PARADIGM-HF propensity score-adjusted analysis (n = 8,399)



Marked geographic variation in the prevalence of ICD implantation and SCD with inverse relationship was observed between the rate of ICD implantation and rates of SCD

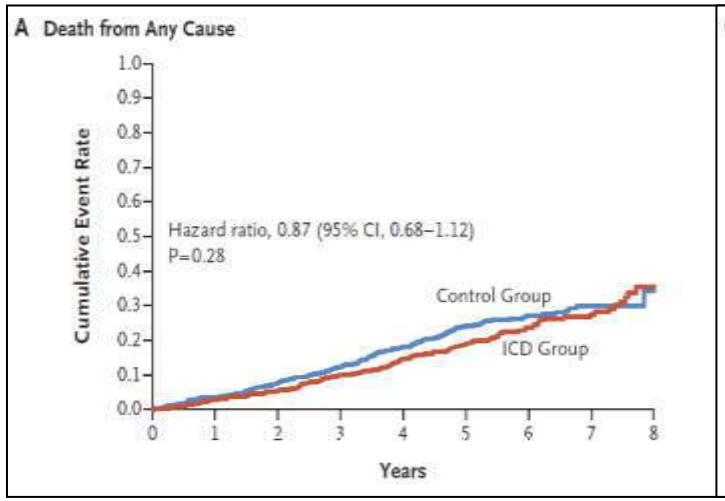
Rohde LE et al. *JACC Heart Fail.* 2020;8:844-55

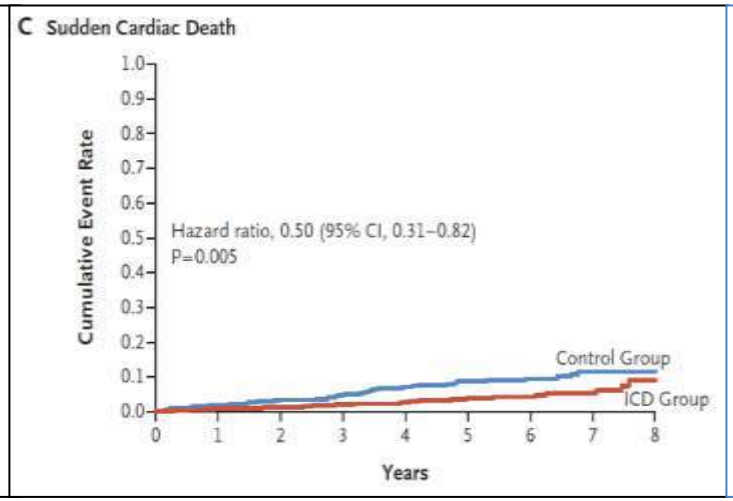
Misperception 2

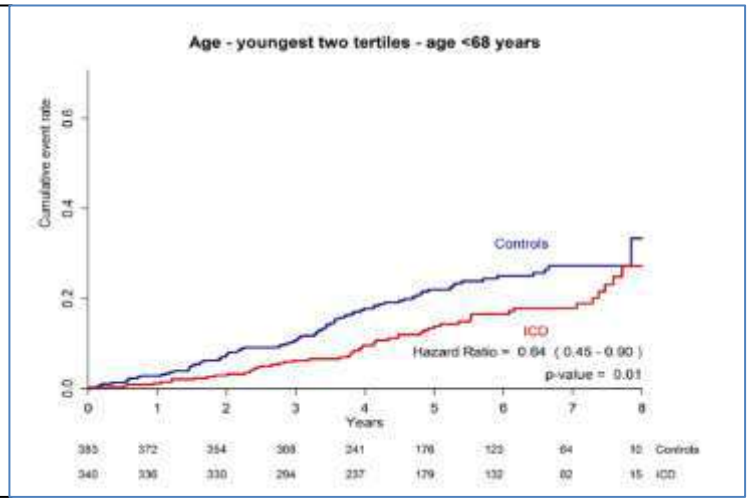
There is no benefit of primary preventive ICD in patients with non-ischemic heart disease

DANISH an RCT of ICD vs control in non-ischemic HF primary endpoint total mortality

- No mortality benefit of ICD therapy on top of OMT (CRT in 58%)
- but with a 50% reduction in SCD
- 36% mortality benefit of ICD in pts. <68 years



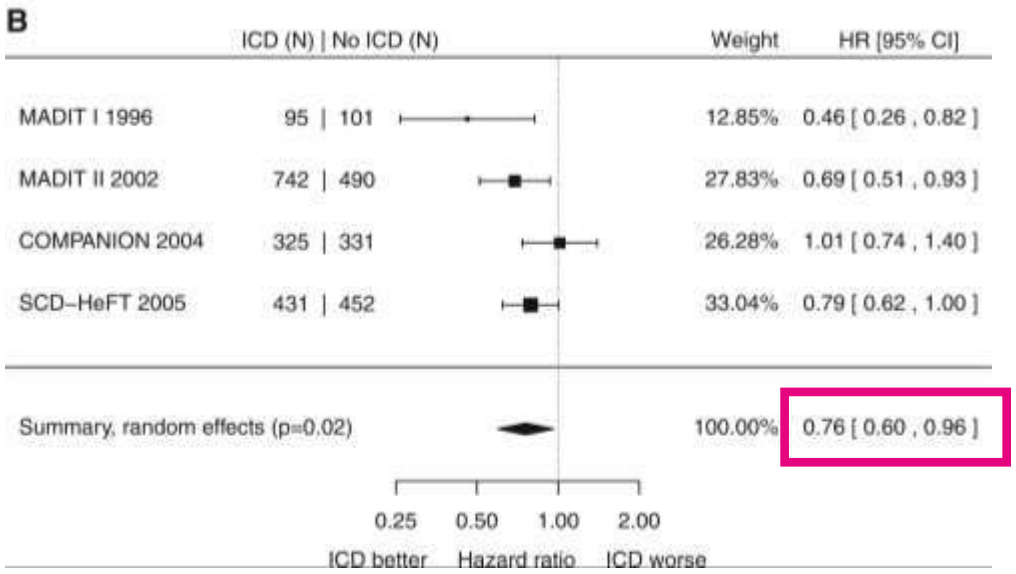




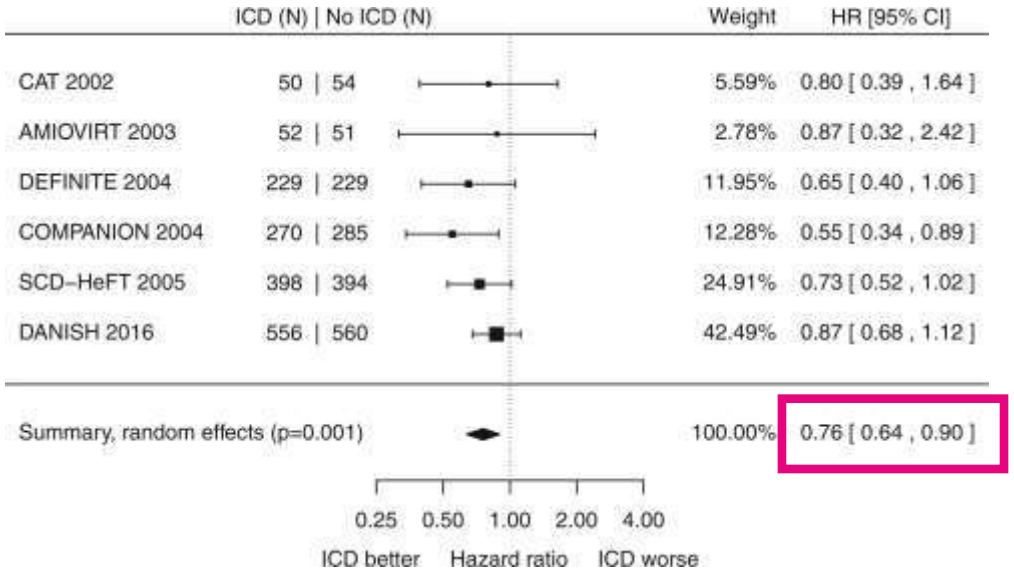
Köber L et al New Engl J Med 2016

ICDs for primary prevention in left ventricular dysfunction with and without ischemic heart disease: a meta-analysis of 8567 in 11 trials

Left ventricular dysfunction with ischemic heart disease:
impact of primary prevention ICD on all-cause mortality



Left ventricular dysfunction without ischemic heart disease:
impact of primary prevention ICD on all-cause mortality



Based on high-quality data from RCTs, primary prevention ICDs reduce all-cause mortality in patients both with and without ischemic heart disease.

2022 ESC Guidelines for VA and SCD

ESC European Society of Cardiology

European Heart Journal (2022) **00**, 1–130
https://doi.org/10.1093/eurheartj/ehac262

ESC GUIDELINES

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)

Authors/Task Force Members: Katja Zeppenfeld[*†] (Chairperson) (Netherlands), Jacob Tfelt-Hansen[*†] (Chairperson) (Denmark), Marta de Riva[**] (Task Force Coordinator) (Netherlands), Bo Gregers Winkel[**] (Task Force Coordinator) (Denmark), Elijah R. Behr (United Kingdom), Nico A. Blom[1] (Netherlands), Philippe Charron (France), Domenico Corrado (Italy), Nikolaos Dagres (Germany), Christian de Chillou (France), Lars Eckardt (Germany), Tim Friede (Germany), Kristina H. Haugaa (Norway), Mélèze Hocini (France), Pier D. Lambiase (United Kingdom), Eloi Marijon (France), Jose L. Merino (Spain), Petr Peichl (Czech Republic), Silvia G. Priori (Italy), Tobias Reichlin (Switzerland), Jeanette Schulz-Menger (Germany), Christian Sticherling (Switzerland), Stylianos Tzeis (Greece), Axel Verstrael (Belgium), Maurizio Volterrani (Italy), and ESC Scientific Document Group

Primary prevention ICD in current HF guidelines

Recommendations for ICD in patients with HFrEF – patients in sinus rhythm (1/2)			
AHA/ACC/HFSA 2022	**ESC 2022**	**JCS/JHFS 2017**	**CCS 2017**
In patients with **non-ischemic DCM** or **ischemic heart disease at least 40 days post-MI** with **LVEF ≤35%** and **NYHA class II or III** symptoms on **chronic GDMT**, who have **reasonable expectation of meaningful survival for >1 year**, ICD therapy is recommended for primary prevention of SCD to reduce total mortality (**1 A**).	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 **ischemic etiology** (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**).	Use of ICDs in patients who meet all the following criteria: (1) Have **coronary artery disease** (at least 40 days post myocardial infarction) or **non-ischemic dilated cardiomyopathy**; (2) Receiving **optimal medical therapy**; (3) Have **NYHA Class II or greater** symptoms; (4) **LVEF ≤35%**; (5) Have **non-sustained ventricular tachycardia** (**I A**).	We recommend consideration of primary ICD therapy in patients with: i. **Ischemic cardiomyopathy**, **NYHA class II-III**, **EF ≤35%**, measured at least 1 month post MI, and at least 3 months post coronary revascularization procedure (Strong Recommendation; High-Quality Evidence)
In patients **at least 40 days post-MI** with **LVEF ≤30%** and **NYHA class I** symptoms while **receiving GDMT**, who have **reasonable expectation of meaningful survival for >1 year**, ICD therapy is recommended for primary prevention of SCD to reduce total mortality (**1 B-R**).	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-ischemic etiology**, 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**).	Use of ICDs in patients who meet all the following criteria: (1) Have **coronary artery disease** (at least 40 days post myocardial infarction) or **non-ischemic dilated cardiomyopathy**; (2) Receiving **optimal medical therapy**; (3) Have **NYHA Class II or greater** symptoms; (4) **LVEF ≤35%** (**IIa B**).	ii. **Ischemic cardiomyopathy**, **NYHA class I** , and an **EF ≤30%** at least 1 month post MI, and at least 3 months post coronary revascularization procedure (Strong Recommendation; High-Quality Evidence)
In patients with **genetic arrhythmogenic cardiomyopathy with high-risk features of sudden death**, with **EF ≤45%,** implantation of ICD is reasonable to decrease sudden death (**2a B-NR**).			iii. **Nonischemic cardiomyopathy**, **NYHA class II-III**, **EF ≤35%,** measured at least 3 months after titration and optimization of GDMT (Strong Recommendation; High-Quality Evidence)

- Heidenreich PA et al. J Am Coll Cardiol. 2022;79:e263-e421; McDonagh TA et al. Eur Heart J. 2021;42:3599-726; Tsutsui H et al. Circ J. 2019;83:2084-184; Ezekowitz JA et al. Can J Cardiol. 2017;33:1342-433

Timing

When do you decide on implantation of a primary preventive ICD?

In non - HF

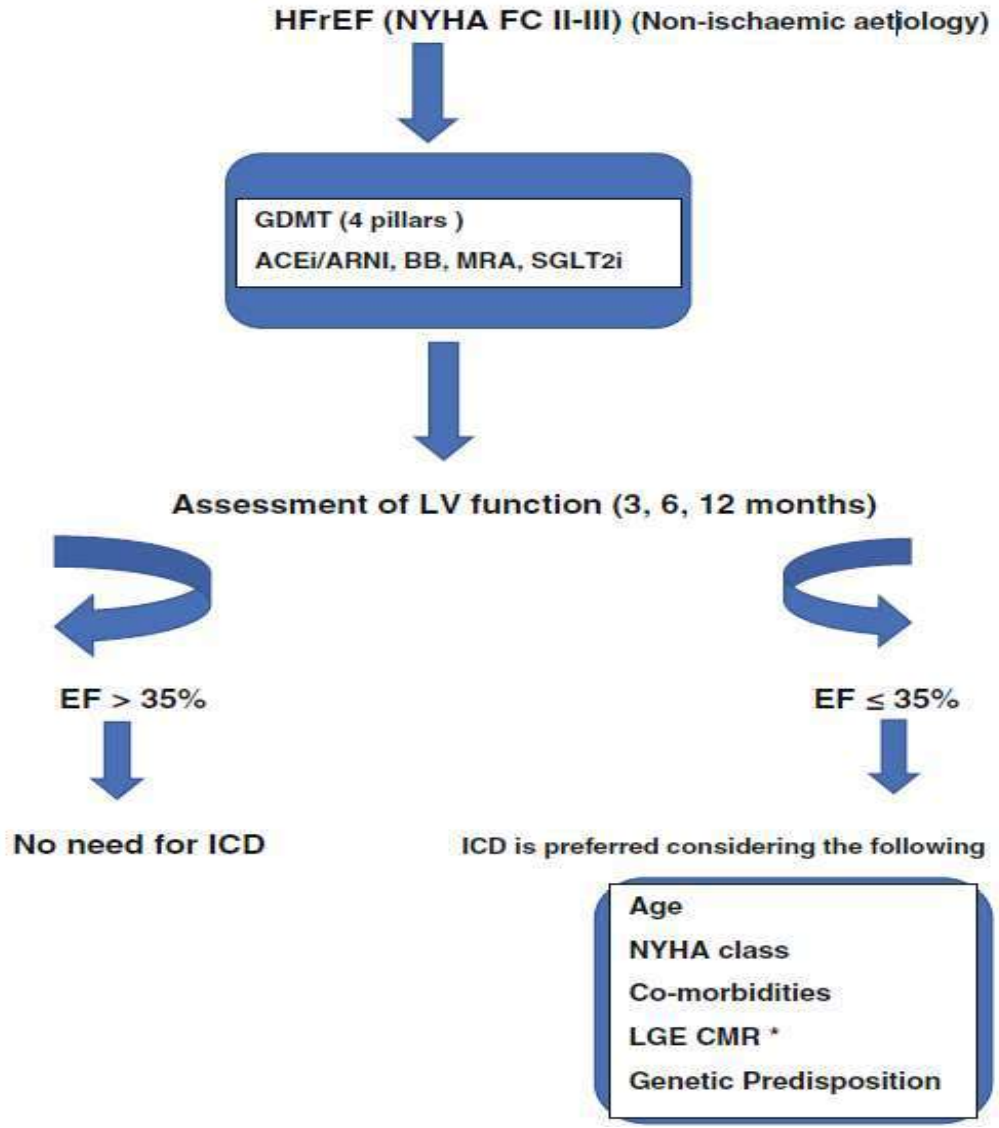
ESC European Society of Cardiology

European Journal of Heart Failure (2022) 24, 1460–1466
doi:10.1002/ejhf.2594

REVIEW ARTICLE

Prevention of sudden death in heart failure with reduced ejection fraction: do we still need an implantable cardioverter-defibrillator for primary prevention?

Magdy Abdelhamid[1]*, Giuseppe Rosano[2], Marco Metra[3], Stamatis Adamopoulos[4], Michael Böhm[5], Ovidiu Chioncel[6], Gerasimos Filippatos[7], Ewa A. Jankowska[8], Yury Lopatin[9], Lars Lund[10], Davor Milicic[11], Brenda Moura[12], Tuvia Ben Gal[13], Arsen Ristic[14], Amina Rakisheva[15], Gianluigi Savarese[10], Wilfried Mullens[16], Massimo Piepoli[17], Antoni Bayes-Genis[18], Thomas Thum[19], Stefan D. Anker[20], Petar Seferovic[21], and Andrew J.S. Coats[22]



After myocardial infarction

As a general rule, no value of ICD < 40 days of MI based on IRIS and DYNAMIT trials

Recommendation Table 23 — Recommendations for risk stratification and treatment of ventricular arrhythmias early after myocardial infarction

Recommendations	Class[a]	Level[b]
Risk stratification		
Early (before discharge) assessment of LVEF is recommended in all patients with acute MI[567,568]	I	B
In patients with pre-discharge LVEF ≤40%, re-evaluation of LVEF 6–12 weeks after MI is recommended to assess the potential need for primary prevention ICD implantation.[568,573,574]	I	C

Recommendation Table 15 — Recommendations for wearable cardioverter defibrillator

Recommendations	Class[a]	Level[b]
The WCD should be considered for adult patients with a secondary prevention ICD indication, who are temporarily not candidates for ICD implantation	IIa	C
The WCD may be considered in the early phase after MI in selected patients.[371,372]	IIb	B

Deciding on primary preventive ICDs

General ICD recommendations

Recommendation Table 11 — Recommendations for implantable cardioverter defibrillator implantation (general aspects)

Recommendations	Class[a]	Level[b]
Implantation of a cardioverter defibrillator is only recommended in patients who have an expectation of good quality survival >1 year	I	C
It is not recommended to implant an ICD in patients with incessant VAs until the VA is controlled.	III	C

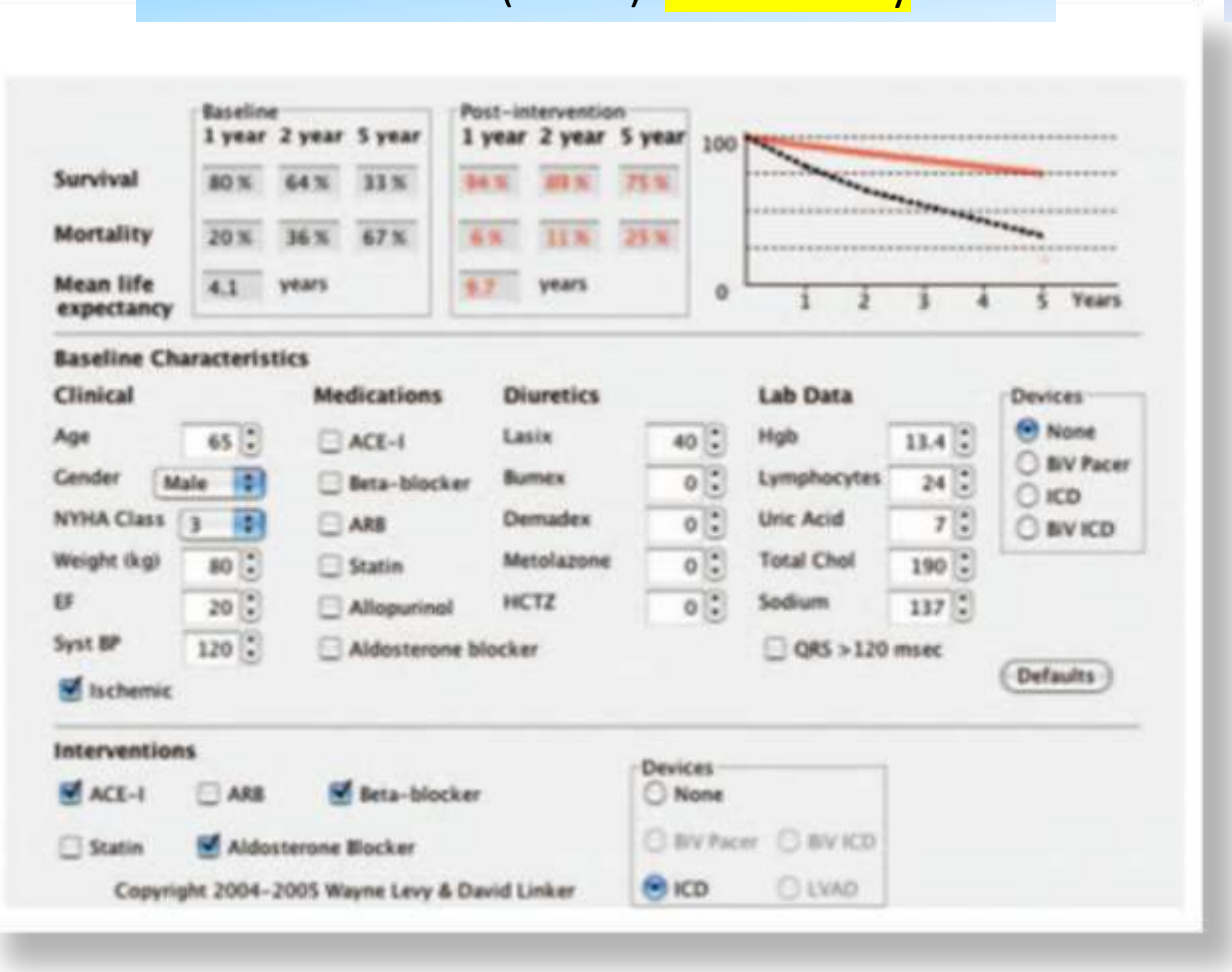
Recommendation Table 18 — Recommendations for psychosocial management after implantable cardioverter defibrillator implantation

Recommendations	Class[a]	Level[b]
Assessment of psychological status and treatment of distress is recommended in ICD patients.[421–423]	I	C
Communication between patient and physician/healthcare professional is recommended to address ICD-related concerns and to discuss quality-of-life issues before ICD implantation and during disease progression.[412,424]	I	C

Recommendation Table 14 — Recommendations for adding cardiac resynchronization therapy to implantable cardioverter defibrillator

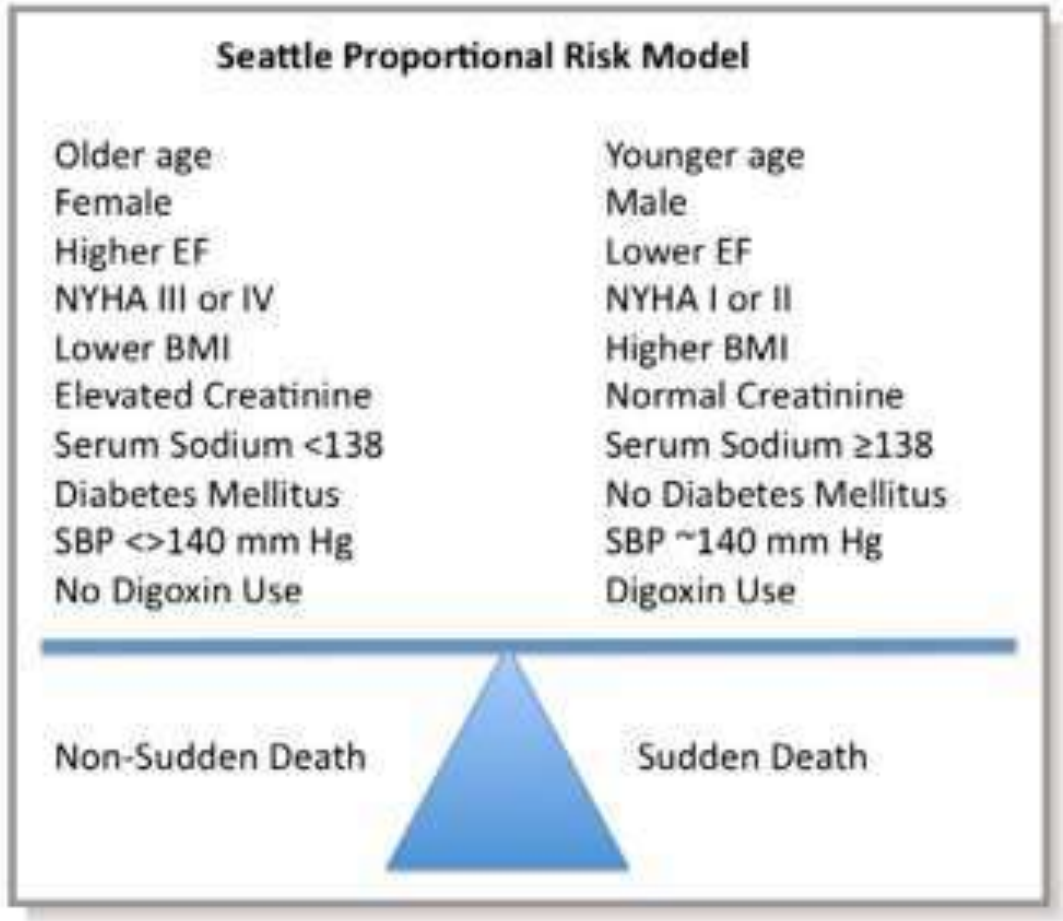
Recommendations	Class[a]	Level[b]
When an ICD is indicated, it is recommended to evaluate whether the patient could benefit from CRT-defibrillator.[367]	I	C

Seattle HF model (SHFM) for mortality



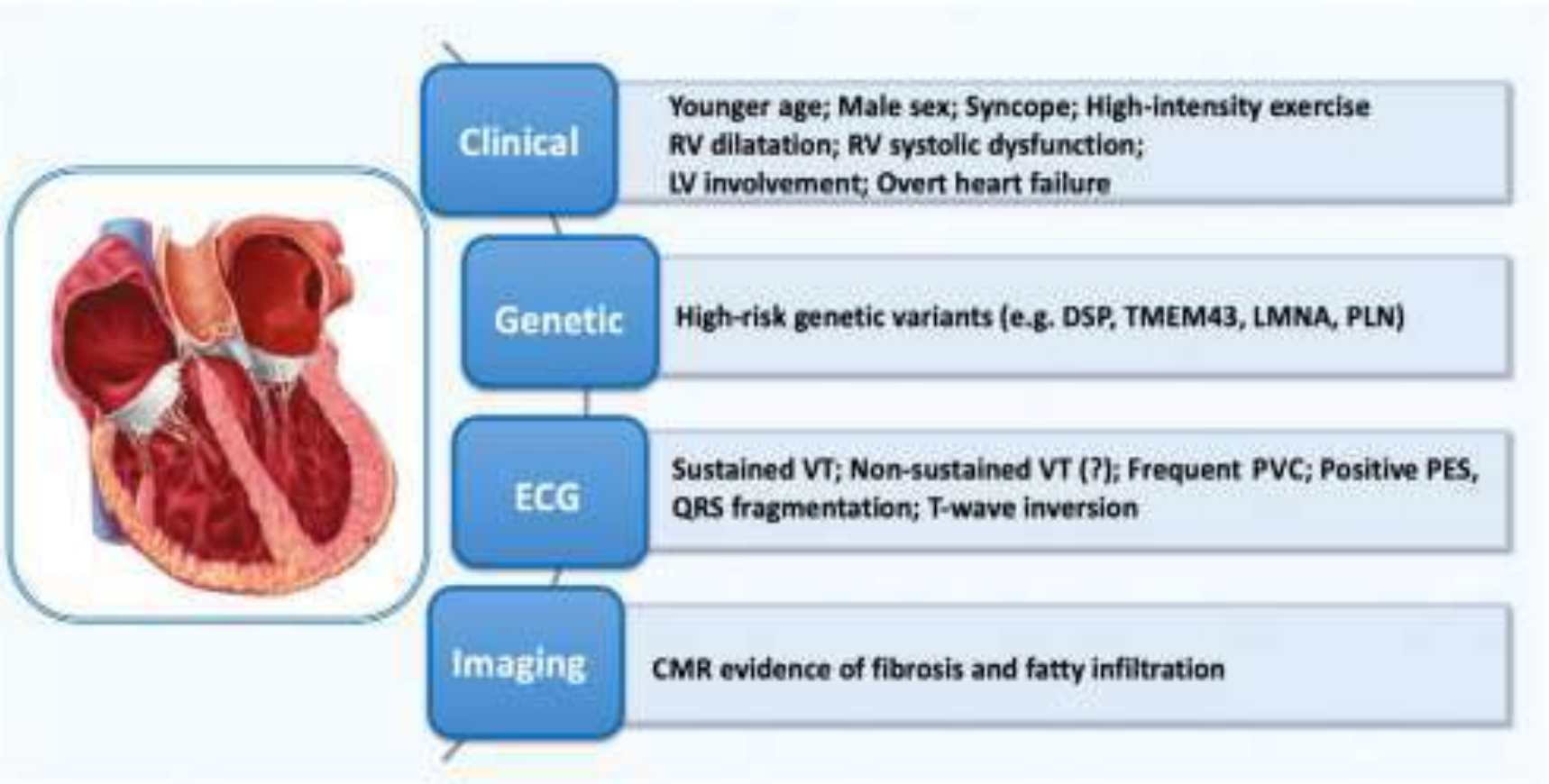
Levy WC et al Circulation 2006;113;1424

Seattle proportional Risk Model (SPRM) for SCD vs non–SCD



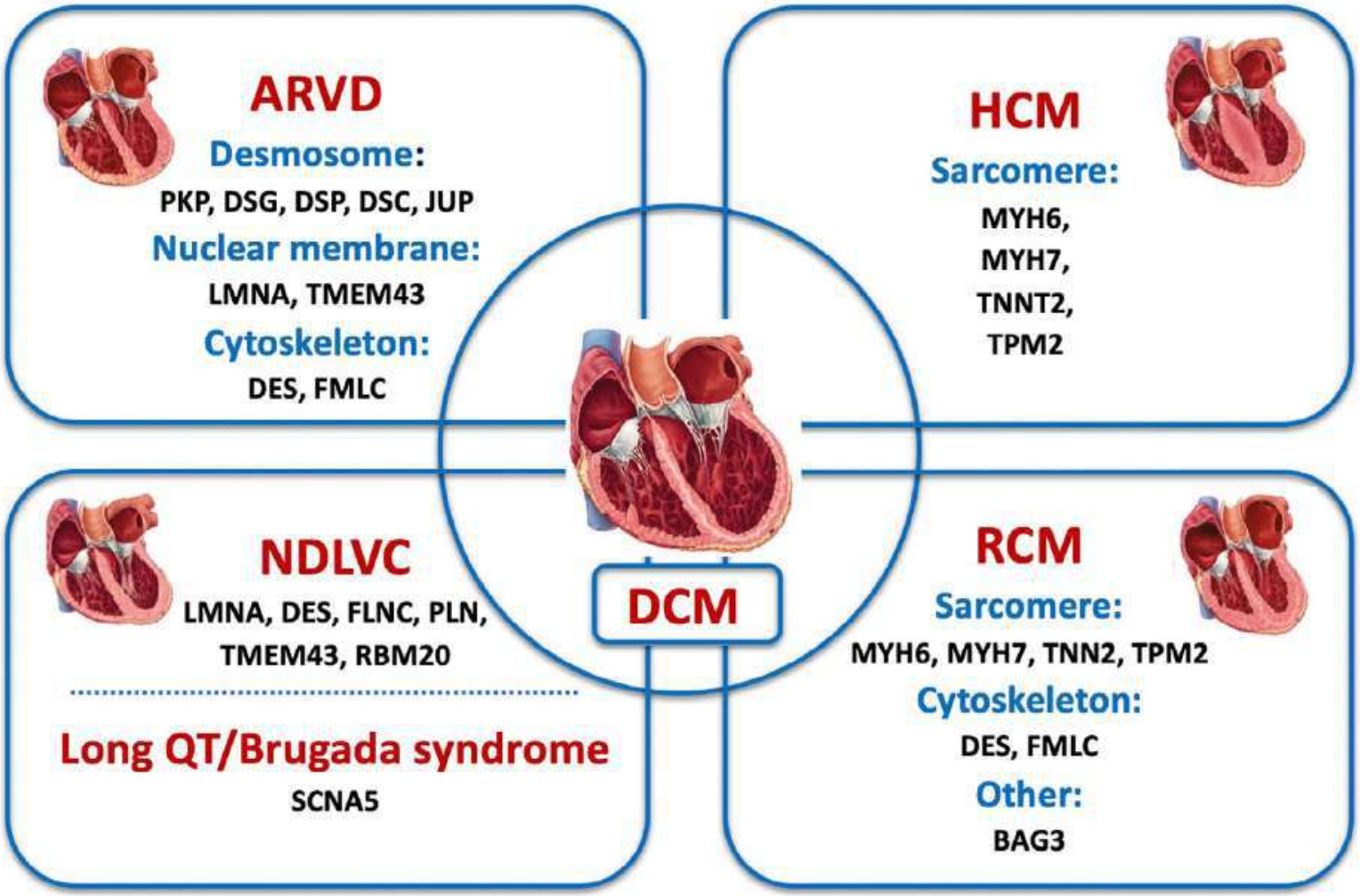
Levy WC et al JACC Clin electrophysiol 2017;3:291

Phenotype, genotype ECG and imaging



- Polovina M et al. *Eur J Heart Fail.* 2023; Oct 31

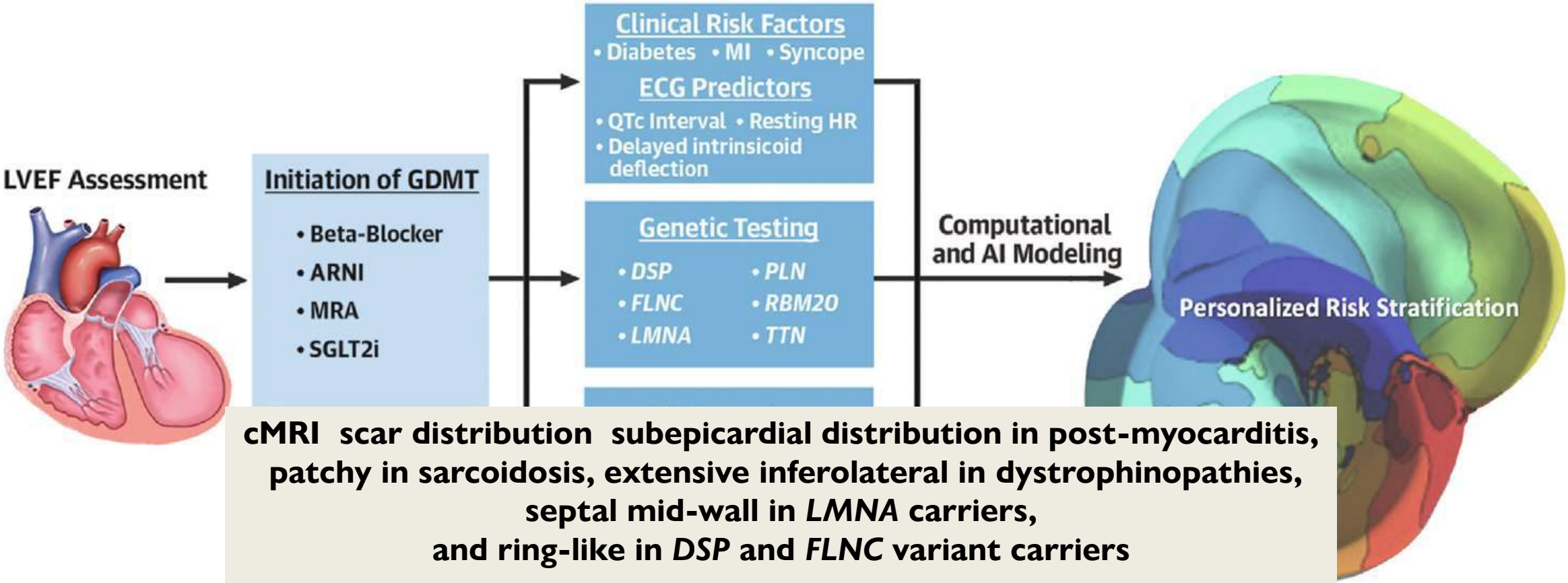
Overlapping genetic background in cardiomyopathies



Polovina M et al. *Eur J Heart Fail.* 2023; Oct 31 [Online ahead of print]

NDLVC = non dilated LV cardiomyopathy

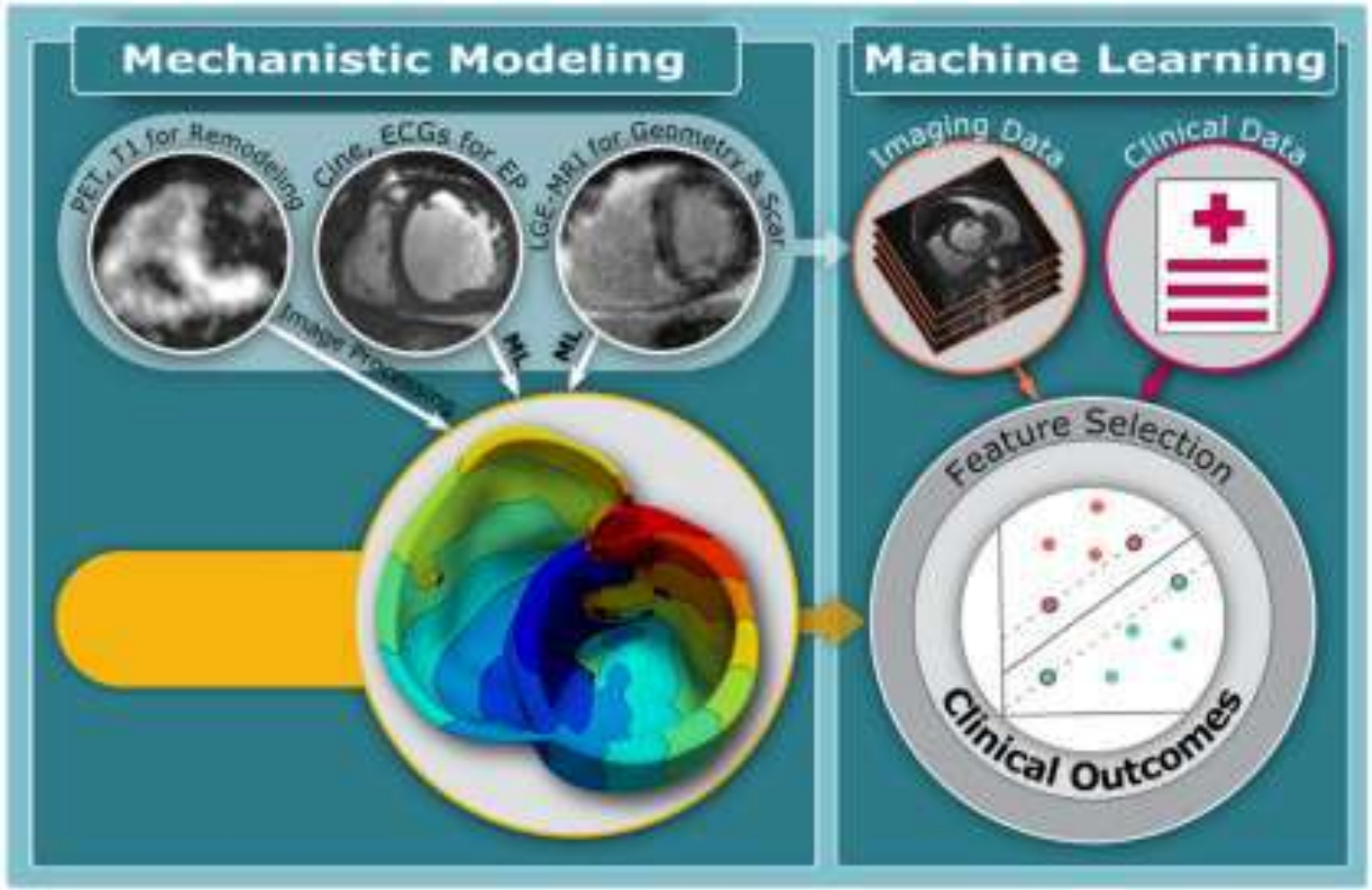
Future SCD risk stratification must synthesize clinical risk factors with genetic and morphofunctional data to develop personalized risk assessment



cMRI scar distribution subepicardial distribution in post-myocarditis, patchy in sarcoidosis, extensive inferolateral in dystrophinopathies, septal mid-wall in *LMNA* carriers, and ring-like in *DSP* and *FLNC* variant carriers

- Chrispin J et al. *J Am Coll Cardiol.* 2023;82:735-747

FIGURE 6 Personalized Heart Model for Sudden Cardiac Death Risk Stratification



Using mechanistic modeling with machine learning (ML), patient-specific sudden cardiac death risk stratification can be performed. ECG = electrocardiogram; EP = electrophysiology; PET = positron emission tomography; other abbreviations as in Figures 4 and 5.

- Christpin

Conclusions

- HF medication reduces SCD and total mortality in HFrEF
- ICDs (and over time CRT) reduce SCD
- HF medication and ICDs work synergistically
- Benefits of ICD may be smaller in patients with non -ischemic cardiomyopathy and in older patients with co-morbidities
- A personalized approach using machine learning is anticipated