European Reference Network
for rare or low prevalence complex diseases
Network Heart Diseases (ERN GUARD-HEART)

ASUGI
Azienda Sanitaria Universitaria Giuliano Isontina
REGIONE AUTONOMA FRIULI VENEZIA GIULIA

UNIVERSITÀ DEGLI STUDI DI TRIESTE

Sudden risk prevention in NICM: a multiparametric approach

Marco Merlo,

Centre for Diagnosis and Management of Cardiomyopathies.
Azieda Sanitaria Universitaria Giuliano Isontina (ASUGI)
and University of Trieste

European Reference Network
for rare or low prevalence complex diseases

Network Heart Diseases (ERN GUARD-HEART)

ASUGI Azienda Sanitaria Universitaria Giuliano Isontina

REGIONE AUTONOMA FRIULI VENEZIA GIULIA

UNIVERSITÀ DEGLI STUDI DI TRIESTE

DISCLOSURES

NONE RELATED TO THE PRESENT PRESENTATION

KARDIGAN; BAYER; PFIZER (consultancy)

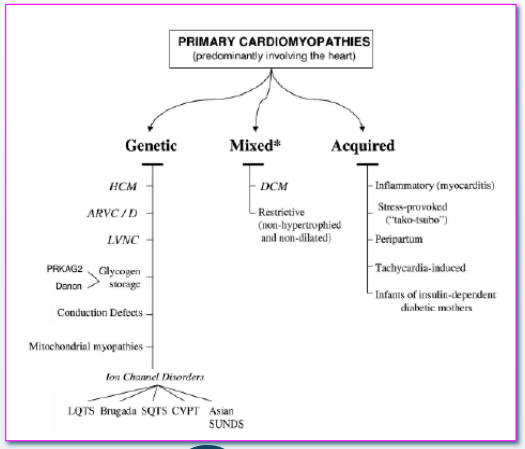
GENERAL (Support for attendance to International Meetings; Fees at meetings and Advisory Boards):

- **ALNYLAM**
- **BAYER**
- **PFIZER**
- **NOVONORDISK**
- **ASTRA ZENECA**

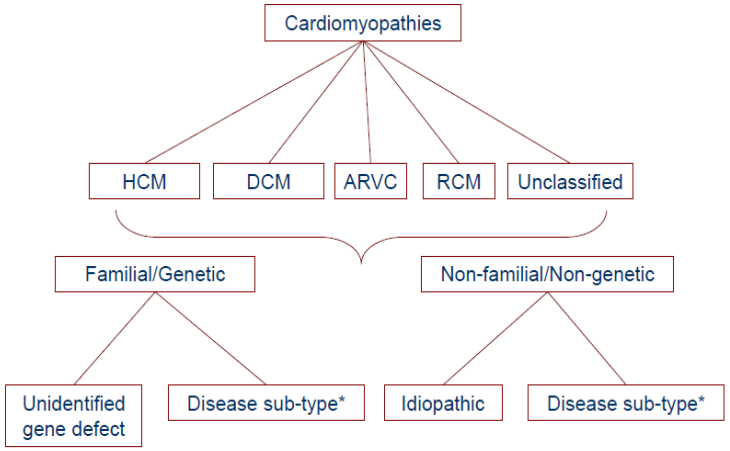
Once upon a time….a long journey

AHA Scientific Statement

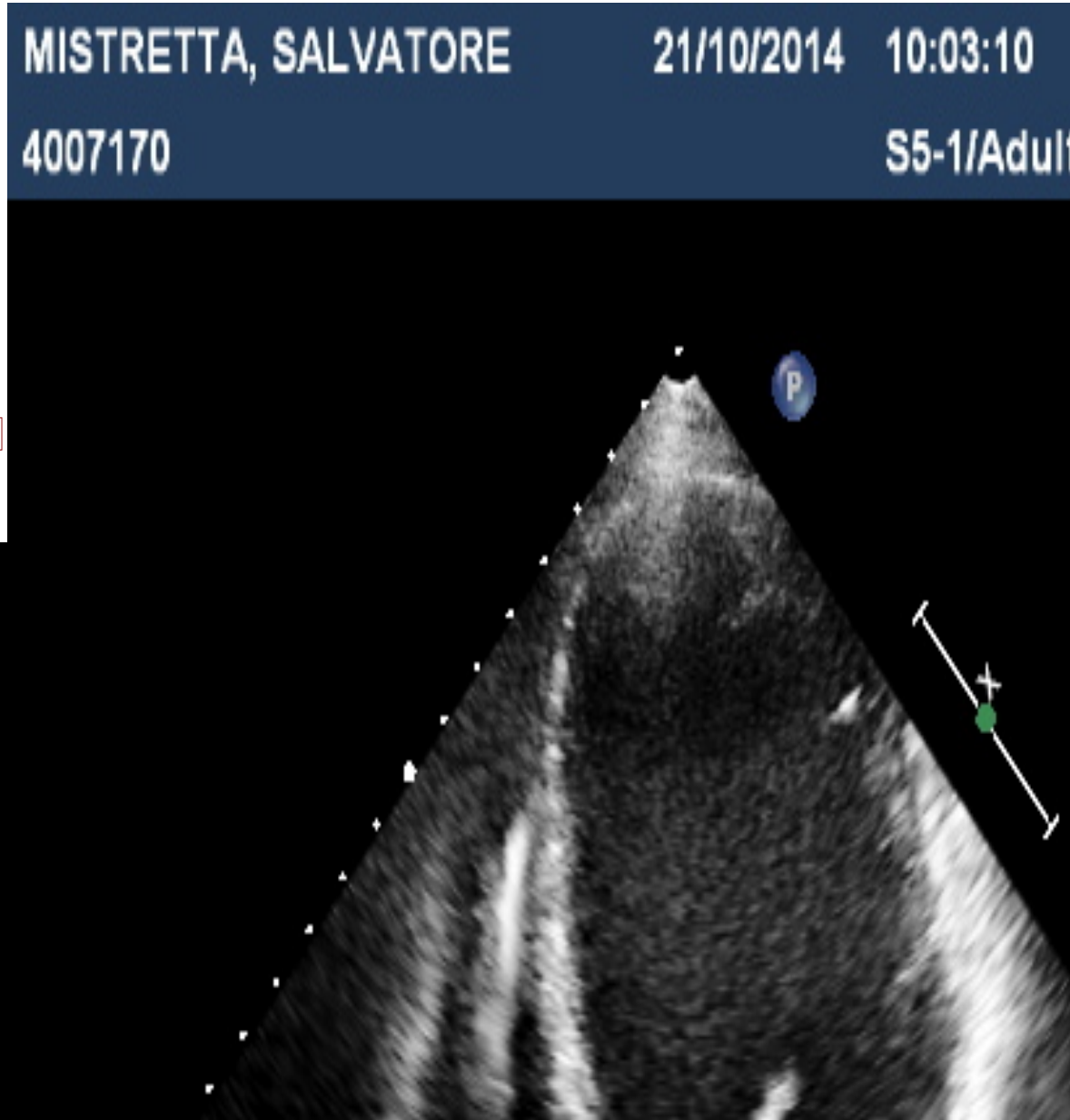
Contemporary Definitions and Classification of the Cardiomyopathies

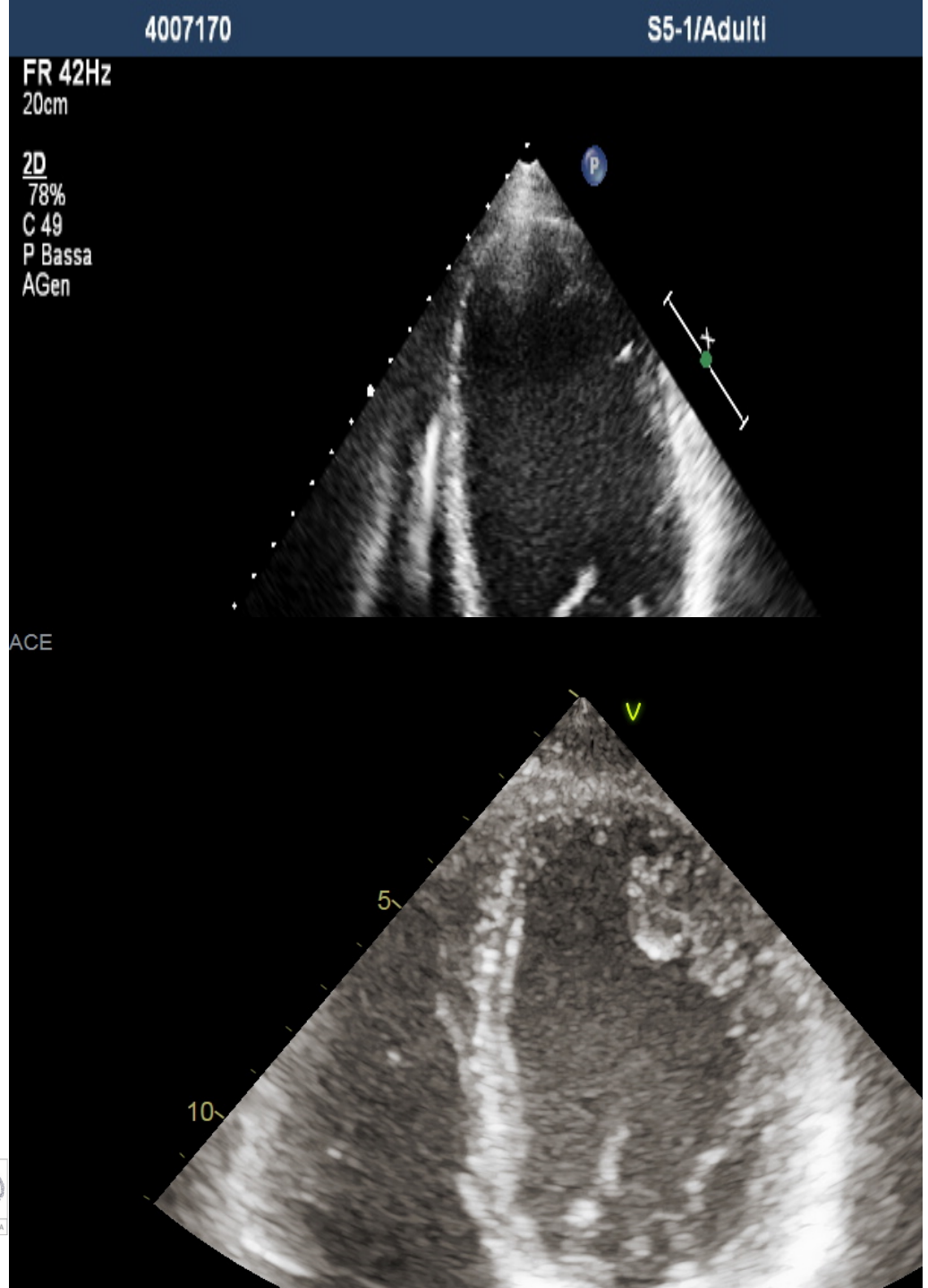


Maron BJ et al. Circulation 2006;113:1807-16



European WG on Myocardial and Pericardial Diseases (Elliott P et al. EHJ 2007)





Clinical scenario

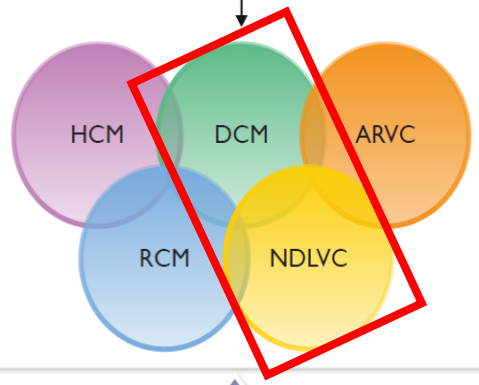
Symptoms	Incidental findings	Family screening
· Dyspnoea · Chest pain · Palpitation · Syncope/presyncope · Cardiac arrest	· Abnormal ECG · Murmur · Arrhythmia	· I[st] degree relative with CMP · Family history of sudden death

Morphological/functional characterization

Suspected cardiomyopathy

Ventricular morphology/function	Ventricular scar/fatty replacement
· Hypertrophy · Dilatation · Systolic/diastolic function	· Non-ischaemic ventricular scar on CMR/pathological examination · Other tissue characterization parameters on CMR

Phenotype



Additional traits

Arrhythmias/conduction disease
(atrial, ventricular, atrioventricular block)

Pedigree analysis | Genetic testing | Extracardiac involvement

Laboratory markers | Pathology

Phenotype-based integrated aetiological diagnosis

GENES RELATED TO CMPs

Gene Category	Gene	HCM	DCM / NDLVC	ARVC	AFD / hATTR
Sarcomeric	*MYH7*	●●●	●●●	○	—
	MYBPC3	●●●	○	○	—
	TNNT2	●●●	●●●	○	—
	TNNI3	●●●	●●	○	—
	TPM1	●●●	●●	—	—
	ACTC1	●●●	●●	—	—
	TNNC1	●●●	●●●	—	—
	MYL2 / MYL3	●●●	—	—	—
Desmosomal / Cytoskeletal	*DSP*	○	●●●	●●●	—
	PKP2	—	—	●●●	—
	DSG2 / DSC2	—	—	●●●	—
	JUP	—	—	●●●	—
	TTN (truncating)	○	●●●	○	—
	FLNC	●●● (missense)	●●● (truncating)	●●	—
	NEXN	○	●●	—	—
	DES	●●●	●●●	●●	
Ion Channel / Ca^{2+} Handling/ Splicing factors	*PLN*	●●●	●●●	●●	—
	RBM20	○	●●●	—	—
	SCN5A	—	●●●	○	—
	TMEM43	—	●●●	●●●	—
Nuclear Envelope	*LMNA*	○	●●●	○	—

Merlo M et al. Adapted and updated from ESC Guidelines on Cardiomyopathies. unpublished

Cardiac-MRI

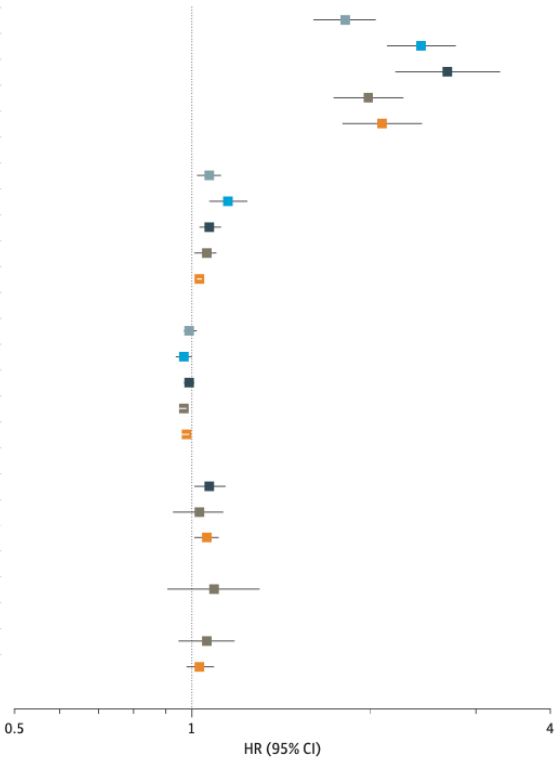
JAMA | Original Investigation

Risk Stratification in Nonischemic Dilated Cardiomyopathy Using CMR Imaging

A Systematic Review and Meta-Analysis

Figure 1. Cardiac Magnetic Resonance (CMR) Imaging Parameters and Clinical Outcomes

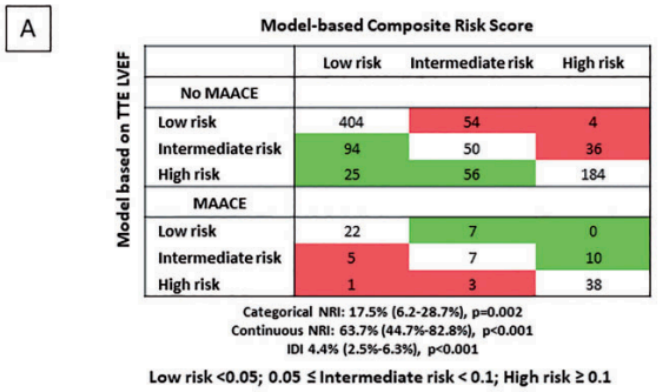
Parameter	Studies/ patients, No.	HR (95% CI)
Late gadolinium enhancement presence (yes/no)		
All-cause mortality	23/9738	1.81 (1.60-2.04)
Cardiovascular mortality	19/5228	2.43 (2.13-2.78)
Arrhythmia	40/13791	2.69 (2.20-3.30)
Heart failure	32/9464	1.98 (1.73-2.27)
MACE	54/12040	2.09 (1.79-2.44)
Late gadolinium enhancement extent (per 1%)		
All-cause mortality	4/1852	1.07 (1.02-1.12)
Cardiovascular mortality	3/1323	1.15 (1.07-1.24)
Arrhythmia	9/2086	1.07 (1.03-1.12)
Heart failure	6/1686	1.06 (1.01-1.10)
MACE	13/3004	1.03 (1.02-1.04)
Left ventricular ejection fraction (per 1%)		
All-cause mortality	5/3220	0.99 (0.97-1.02)
Cardiovascular mortality	7/3522	0.97 (0.94-1.00)
Arrhythmia	12/5055	0.99 (0.97-1.01)
Heart failure	10/4576	0.97 (0.95-0.98)
MACE	24/5446	0.98 (0.96-0.99)
T1 relaxation time (per 10 ms)		
Arrhythmia	5/1778	1.07 (1.01-1.14)
Heart failure	3/2198	1.03 (0.93-1.13)
MACE	3/962	1.06 (1.01-1.11)
Extracellular volume (per 1%)		
Heart failure	3/1372	1.09 (0.91-1.30)
Global longitudinal strain (per 1%)		
Heart failure	3/1001	1.06 (0.95-1.18)
MACE	7/1397	1.03 (0.94-1.14)



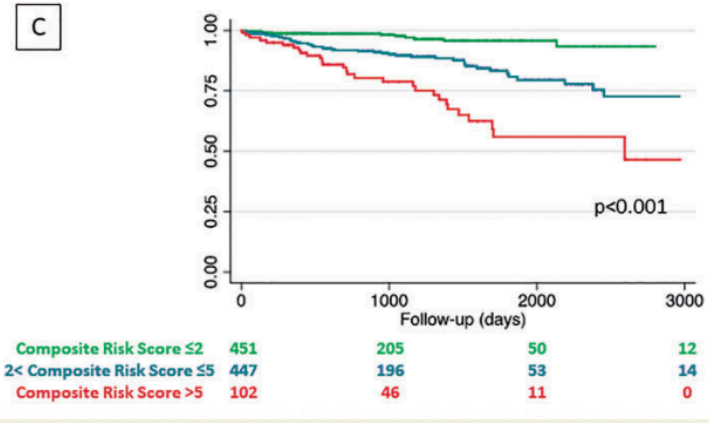
JAMA 2024;332;(18):1535-1550.

CarDiac magnEtic Resonance for prophylactic Implantable-cardioVerter defibrillAtor ThErapy in Non-Ischaemic dilated CardioMyopathy: an international Registry

Andrea Igoren Guaricci[1†], Pier Giorgio Masci[2†], Giuseppe Muscogiuri[3‡], Marco Guglielmo[3‡], Andrea Baggiano[3‡], Laura Fusini[3], Valentina Lorenzoni[4], Chiara Martini[5§], Daniele Andreini[3‡], Anna Giulia Pavon[6], Giovanni D. Aquaro[7], Andrea Barison[7], Giancarlo Todiere[7], Mark G. Rabbat[8], Emily Tat[8], Claudia Raineri[9], Adele Valentini[10], Akos Varga-Szemes[11], U. Joseph Schoepf[11], Carlo N. De Cecco[11,12], Jan Bogaert[13], Monica Dobrovie[13], Rolf Symons[13], Marta Focardi[14], Annalaura Gismondi[14], Jordi Lozano-Torres[15], Josè F. Rodriguez-Palomares[15,16], Chiara Lanzillo[17], Mauro Di Roma[17], Claudio Moro[18], Gabriella Di Giovine[19], Davide Margonato[19], Manuel De Lazzari[20], Martina Perazzolo Marra[20], Alberto Nese[21], Grazia Casavecchia[22], Matteo Gravina[23], Francesca Marzo[24], Samuela Carigi[24], Silvia Pica[25], Massimo Lombardi[25], Stefano Censi[26], Angelo Squeri[26], Alessandro Palumbo[5], Nicola Gaibazzi[27], Giovanni Camastra[28], Stefano Sbarbati[29], Patrizia Pedrotti[30], Ambra Masi[30], Nazario Carrabba[31], Silvia Pradella[32], Mauro Timpani[33], Gloria Cicala[5§], Cristina Presicci[5§], Sara Puglisi[5§], Nicola Sverzellati[5§], Vincenzo Ezio Santobuono[1], Mauro Pepi[3], Juerg Schwitter[6,34†], and Gianluca Pontone[3*,†,‡]



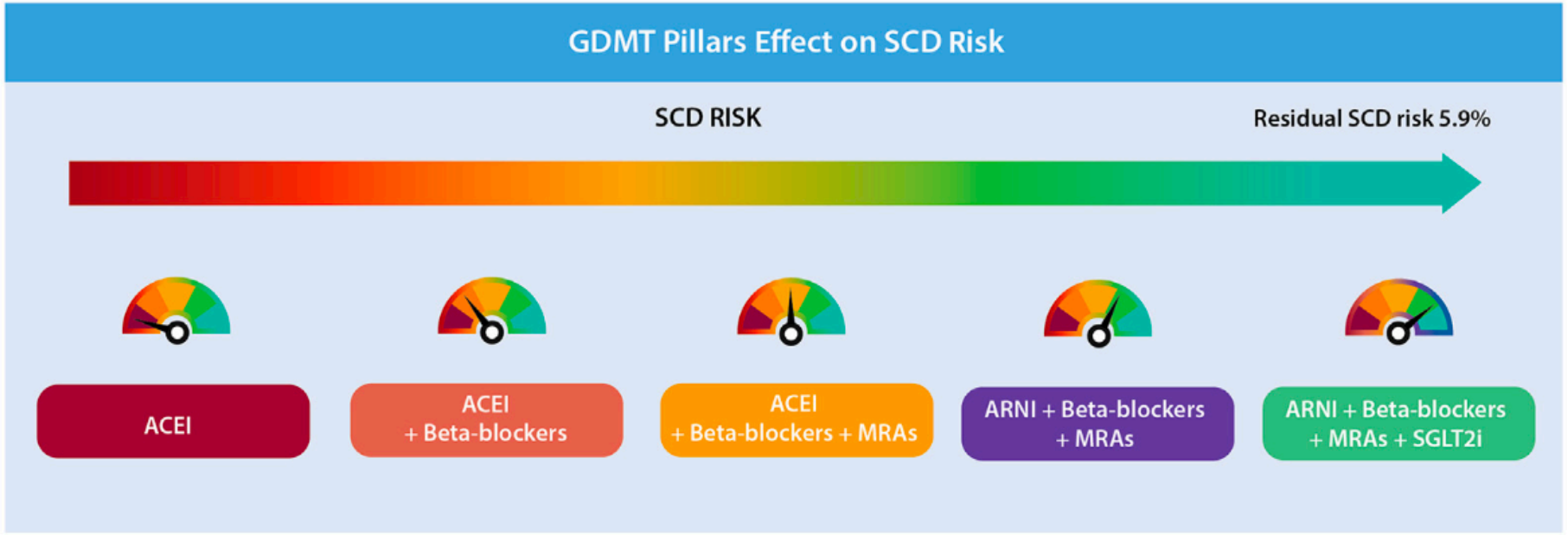
Major Adverse Arrhythmic Cardiac Events



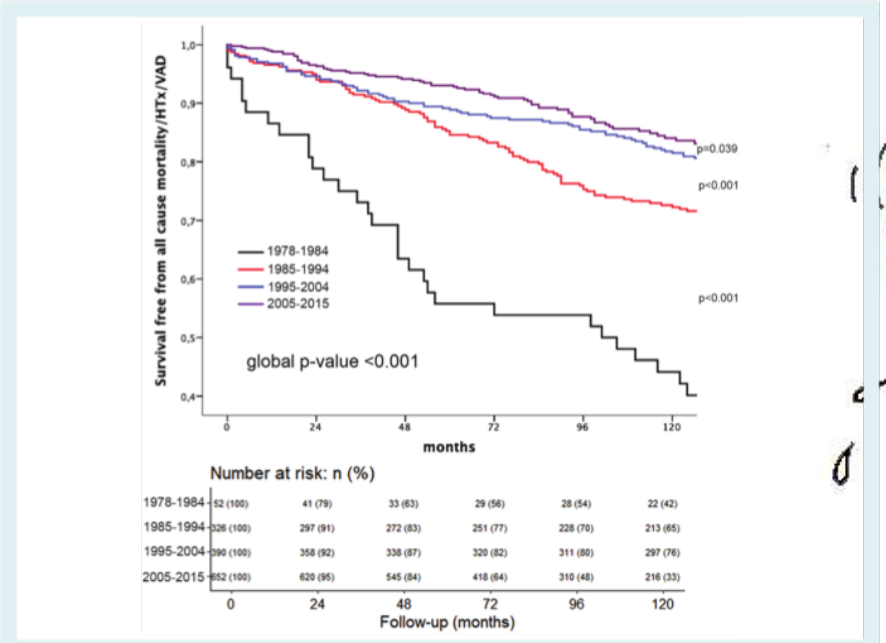
Strongest predictors:

- Male sex
- Higher LV end-diastolic volume index (LVEDVi)
- Presence of extensive midwall fibrosis (>3 segments on LGE)

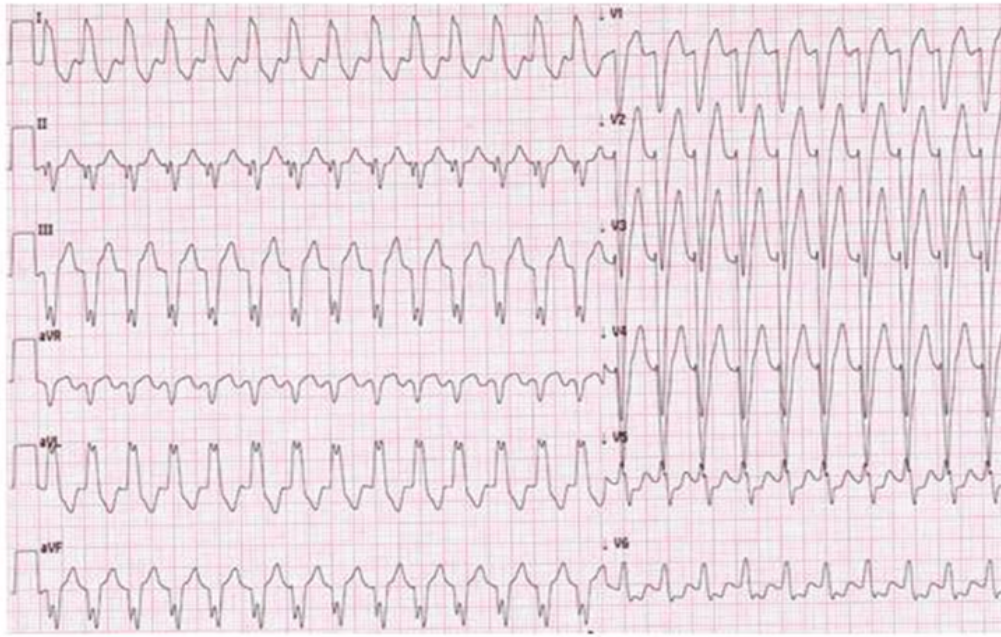
Europace (2021) **23**, 1072–1083
doi:10.1093/europace/euaa401



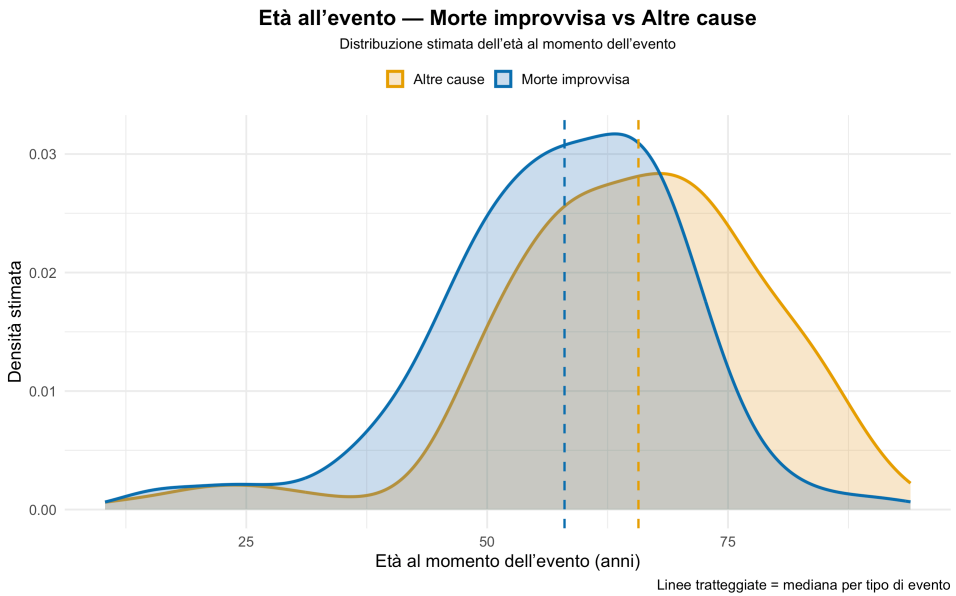
Yehya A, et al. JACC Heart Fail. 2025;13(1):1–13.



Merlo M, et al. EJHF 2020



Registro Cardiomiopatie Trieste
Aggiornamento 10-2025



Unpublished

ESC European Society of Cardiology
European Journal of Heart Failure (2020)
doi:10.1002/ejhf.1914
RESEARCH ARTICLE

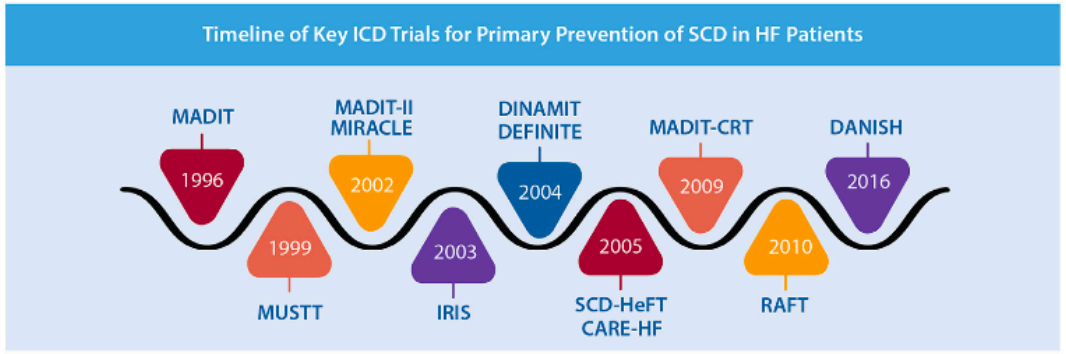
Contemporary survival trends and aetiological characterization in non-ischaemic dilated cardiomyopathy

Marco Merlo[1*†], Antonio Cannatà[1,2†], Carola Pio Loco[1], Davide Stolfo[1], Giulia Barbati[3], Jessica Artico[1], Piero Gentile[1], Valerio De Paris[1], Federica Ramani[1], Massimo Zecchin[1], Marta Gigli[1], Bruno Pinamonti[1], Renata Korcova[1], Andrea Di Lenarda[4], Mauro Giacca[2], Luisa Mestroni[5], Paolo G. Camici[6], and Gianfranco Sinagra[1]

[1]Cardiovascular Department, Centre for Diagnosis and Management of Cardiomyopathies, Azienda Sanitaria Universitaria Integrata di Trieste (ASUITS), University of Trieste, Trieste, Italy; [2]Department of Cardiovascular Sciences, Faculty of Life Sciences & Medicine, King's College London, London, UK; [3]Biostatistics Unit, University of Trieste, Trieste, Italy; [4]Cardiovascular Centre, Azienda Sanitaria Universitaria Integrata of Trieste (ASUITS), University of Trieste, Trieste, Italy; [5]Cardiovascular Institute and Adult Medical Genetics Program, University of Colorado Anschutz Medical Campus, Aurora, CO, USA; and [6]Vita Salute University and San Raffaele Hospital, Milan, Italy

NDLVC

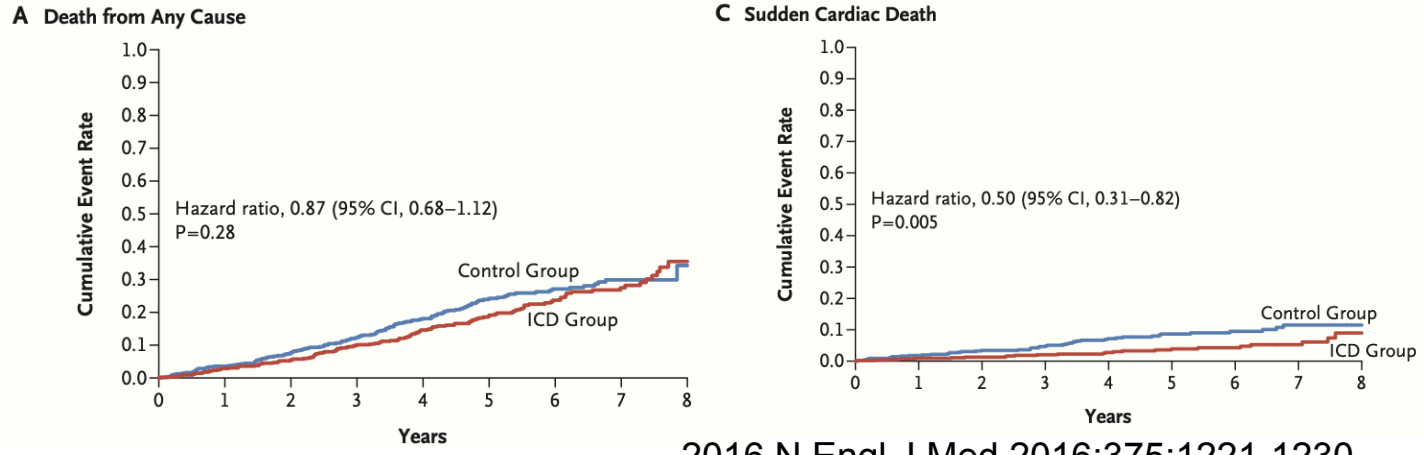
Sudden Cardiac Death Main Trials



Yehya A, et al. JACC Heart Fail. 2025;13(1):1–13.

DANISH-Trial (2016)

-Inclusion criteria: EF<35% non-ischemic.
-Follow up: 67 months.



2016 N Engl J Med 2016;375:1221-1230

DANISH-Trial-Age analysis (2017)

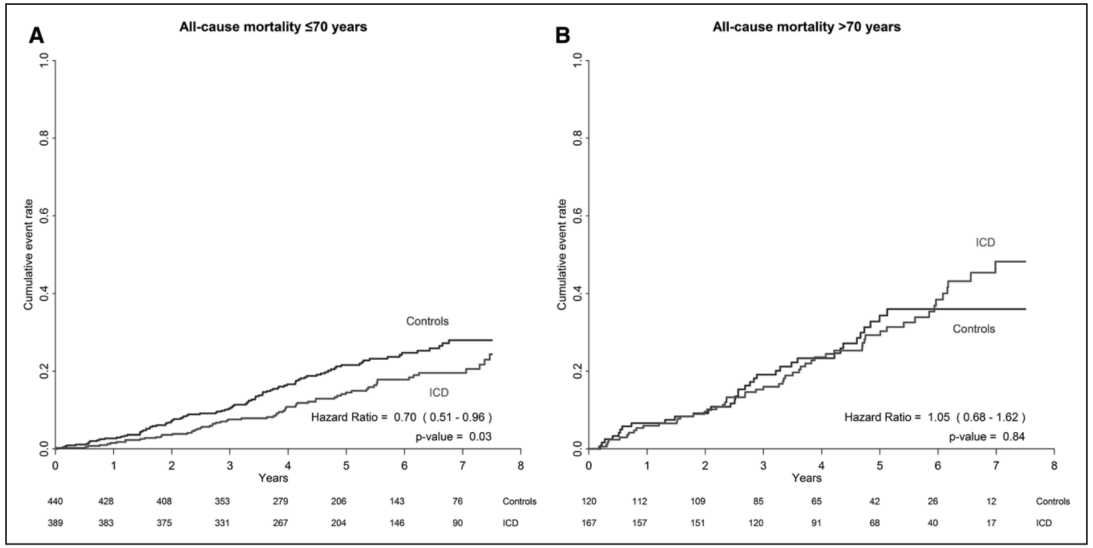
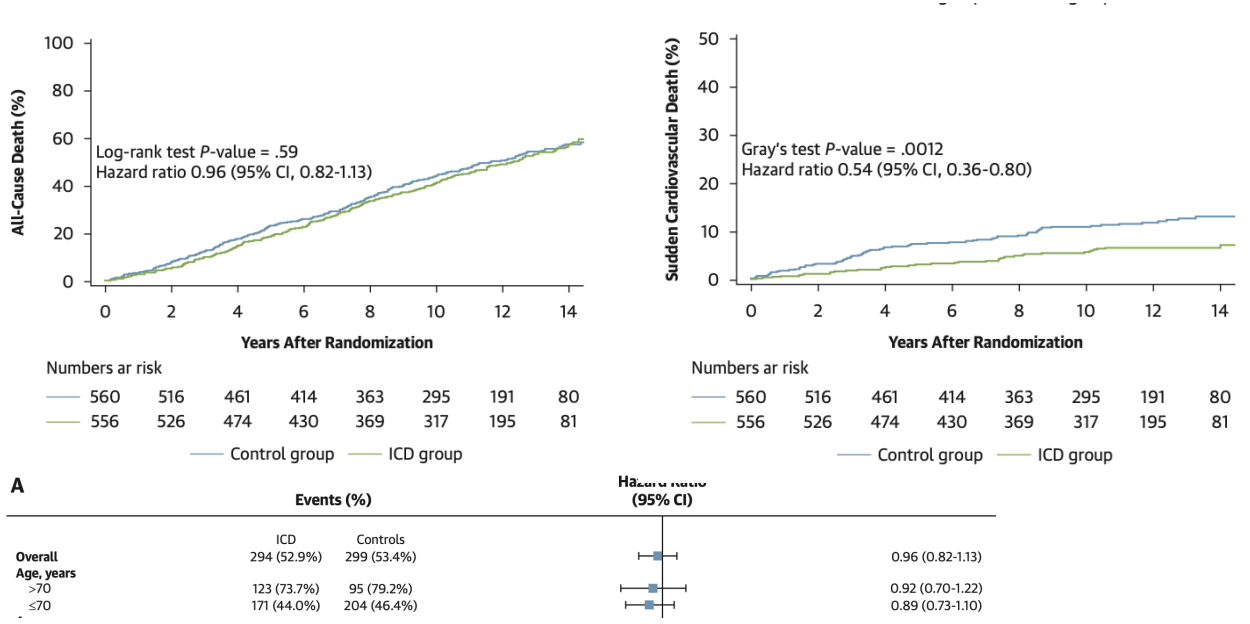


Figure 4. All-cause mortality for the entire population in (A) patients ≤70 years old and (B) patients >70 years old. Black lines represent patients in the control group; gray lines, patients randomized to implantable cardioverter-defibrillator (ICD) treatment.

Circulation. 2017;136:1772–1780.

Extended Follow-Up Analysis of DANISH (2025)



Extended Follow-Up Analysis of DANISH-JACC 2025 JACC; 2025

Why EF isn’t enough?

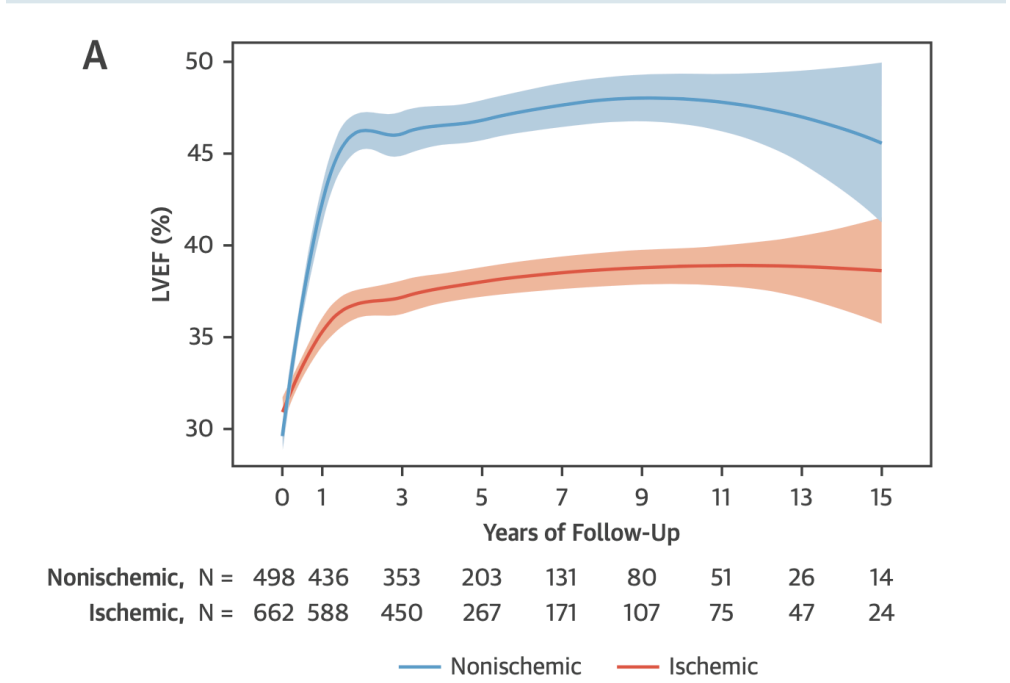
- **SINGLE.** Older age, frailty, CKD, diabetes, or recurrent HF hospitalization increase non-arrhythmic mortality — reducing the proportion of deaths that an ICD can prevent.
- **IMPRECISE:** arrhythmic risk depends on the **substrate**, not just pump function. Genetics, fibrosis on CMR drive arrhythmic vulnerability independently of EF.

ORIGINAL INVESTIGATIONS

Dynamic Trajectories of Left Ventricular Ejection Fraction in Heart Failure

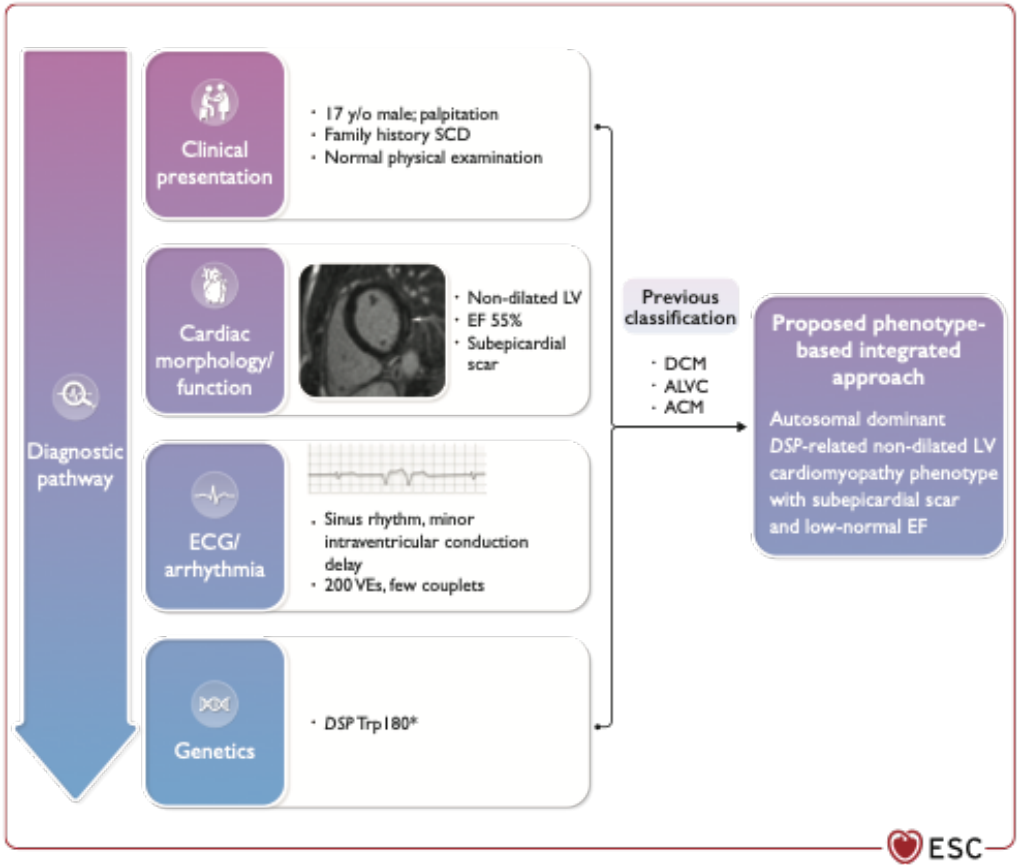
Josep Lupón, MD, PhD,[a,b,c,d] Giovana Gavidia-Bovadilla, MSc,[e,f] Elena Ferrer, MD,[b] Marta de Antonio, MD, PhD,[a,b] Alexandre Perera-Lluna, PhD,[f,g,h] Jorge López-Ayerbe, MD,[b] Mar Domingo, MD, PhD,[a] Julio Núñez, MD, PhD,[d,i,j] Elisabet Zamora, MD, PhD,[a,b,c,d] Pedro Moliner, MD,[a,b] Patricia Díaz-Ruata, MSc,[f,g] Javier Santesmases, MD,[a] Antoni Bayés-Genís, MD, PhD[a,b,c,d]

JACC vol 72, no 6, 2018:591-601



TIME DEPENDENT EVALUATION

CARDYOPATHY MINDSET



THE ERA OF THE SCORES!

Suspected cardiomyopathy

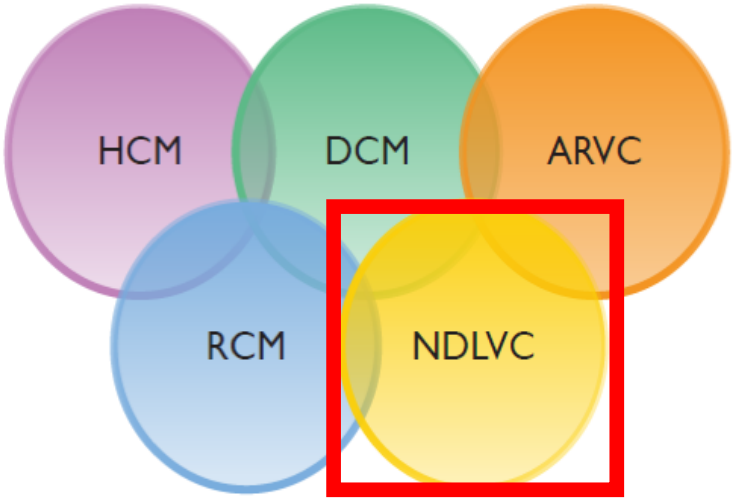
r morphology/function

ny

stolic function

Ventricular scar/fatty replacement

- Non-ischaemic ventricular scar on CMR/pathological examination
- Other tissue characterization parameters on CMR



Arrhythmias/conduction disease
(atrial, ventricular, atrioventricular block)

analysis

Genetic testing

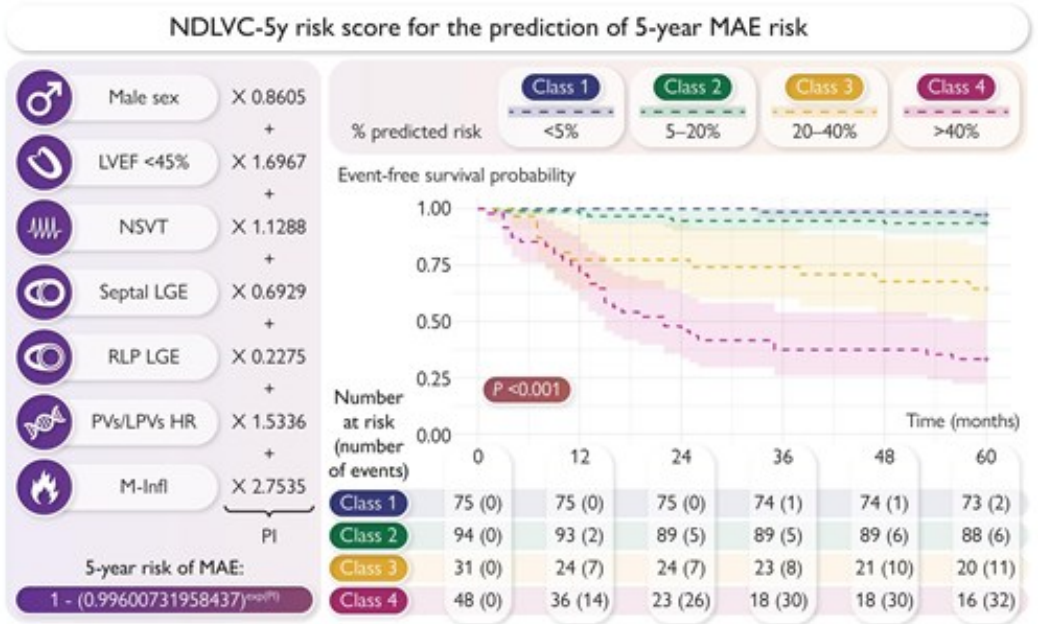
Extracardiac involvement

NDLVC

Key Question
What predicts the occurrence of the first major arrhythmic event (MAE) in non-dilated left ventricular cardiomyopathy (NDLVC)?

Key Finding
In NDLVC, male sex, non-sustained ventricular tachycardia, left ventricular ejection fraction <45%, septal and ring-like late gadolinium enhancement, high-risk genotypes, and myocardial inflammation predicted the first episode of MAE by 60 months. A new risk score (NDLVC-5y) was subsequently derived.

Take Home Message
A multi-parametric approach improves the arrhythmic risk stratification of NDLVC.



Peretto G, Merlo M et al. Eur Heart J 2025

DOI: 10.1093/eurheartj/ehaf477

European Reference Network for rare or low prevalence complex diseases
Network Heart Diseases (ERN GUARD-HEART)
ASUGI Azienda Sanitaria Universitaria Giuliano Isontina
REGIONE AUTONOMA FRIULI VENEZIA GIULIA
UNIVERSITÀ DEGLI STUDI DI TRIESTE

GENES IN RISK SCORES

5 y risk of major arrhythmic event according to genotype

NDLVC Score: 15,65%

Male sex: Yes

LVEF <45%: No

Nonsustained ventricular tachycardia: Yes

Septal LGE: No

Ring-like pattern LGE: Yes

Pathogenic/likely pathogenic variants in "high-risk" genes: Yes

Myocardial inflammation: No

LMNA score: 25%

Genetic Sex:

Female | Male

History of NSVT:

yes | No

Non-Missense Mutation:

yes | No

1st Degree AV Block:

yes | No

2nd or 3rd Degree AV Block:

yes | No

Left Ventricular Ejection Fraction:

48

DSP score: 10%

Genetic Sex:

Female | Male

History of NSVT:

yes | No

Left Ventricular Dysfunction (EF < 50%):

yes | No

Right Ventricular Dysfunction (Moderate to Severe):

yes | No

24 hour PVC Burden on Ambulatory Monitoring:

170

FLNC score: 39,2%

Age (years):

1 | 41 | 93

1 11 21 31 41 51 61 71 81 93

Sex:

Male

Non-sustained ventricular tachycardia (NSVT):

Yes

History of syncope:

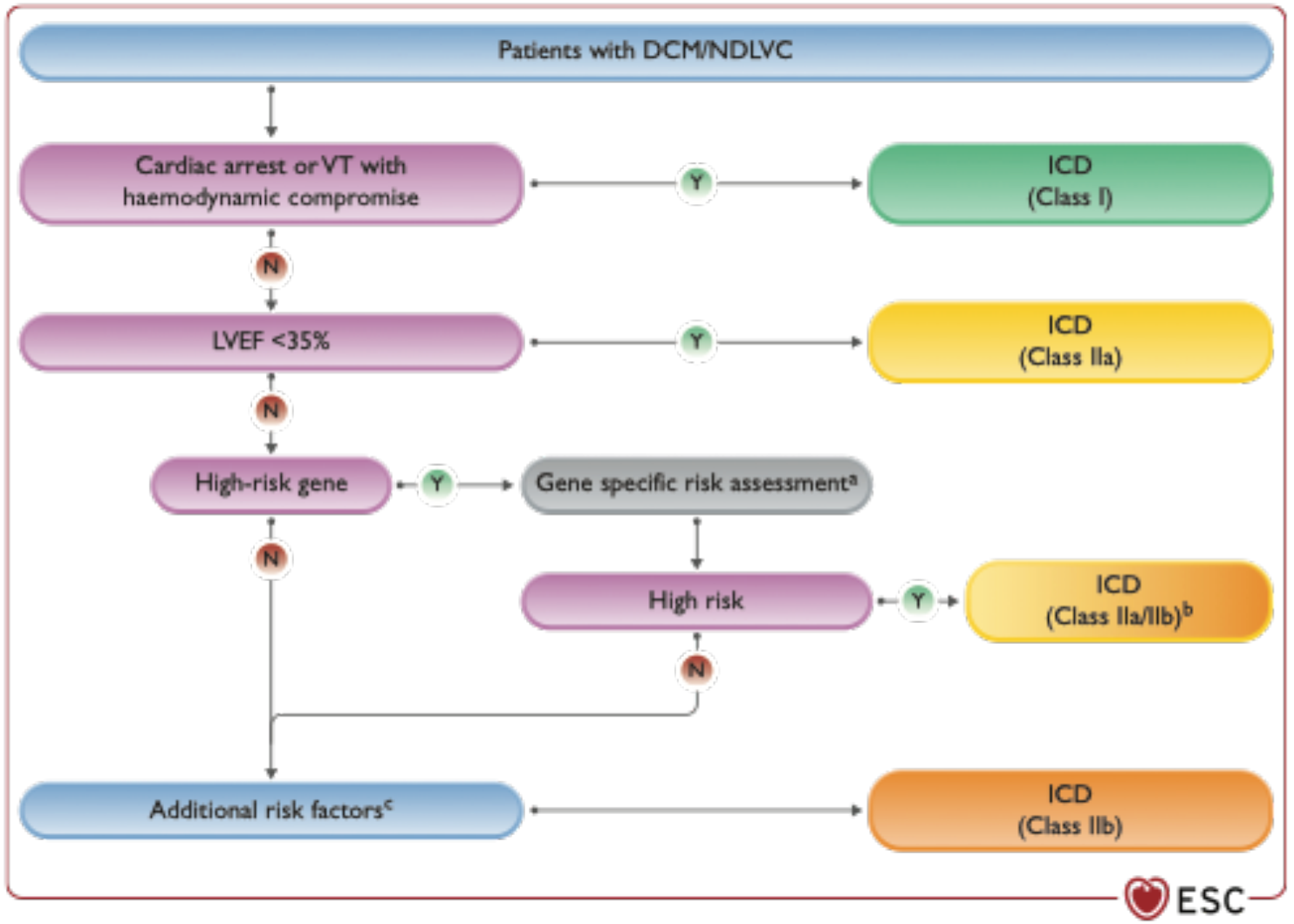
No

LVEF (%):

10 | 48 | 75

10 17 24 31 38 45 52 59 66 75

DCM/NDLVC: 2023 ESC guidelines



Gene	Annual SCD rate	Predictors of SCD
LMNA[185,186,430,541,865,878,879]	5–10%	Estimated 5-year risk of life-threatening arrhythmia using *LMNA* risk score (https://lmna-risk-vta.fr)
FLNC-truncating variants[866,867,880]	5–10%	LGE on CMR LVEF < 45%
TMEM43[860,881]	5–10%	Male Female and any of the following: LVEF <45%, NSVT, LGE on CMR, >200 VE on 24h Holter ECG
PLN[542,882,883]	3–5%	Estimated 5-year risk of life-threatening arrhythmia using *PLN* risk score (https://plnriskcalculator.shinyapps.io/final_shiny) LVEF < 45% LGE on CMR NSVT
DSP[185,186]	3–5%	LGE on CMR LVEF < 45%
RBM20[869]	3–5%	LGE on CMR LVEF < 45%

ESC 2023 cardiomyopathies guidelines

The role of genetics

nature reviews cardiology

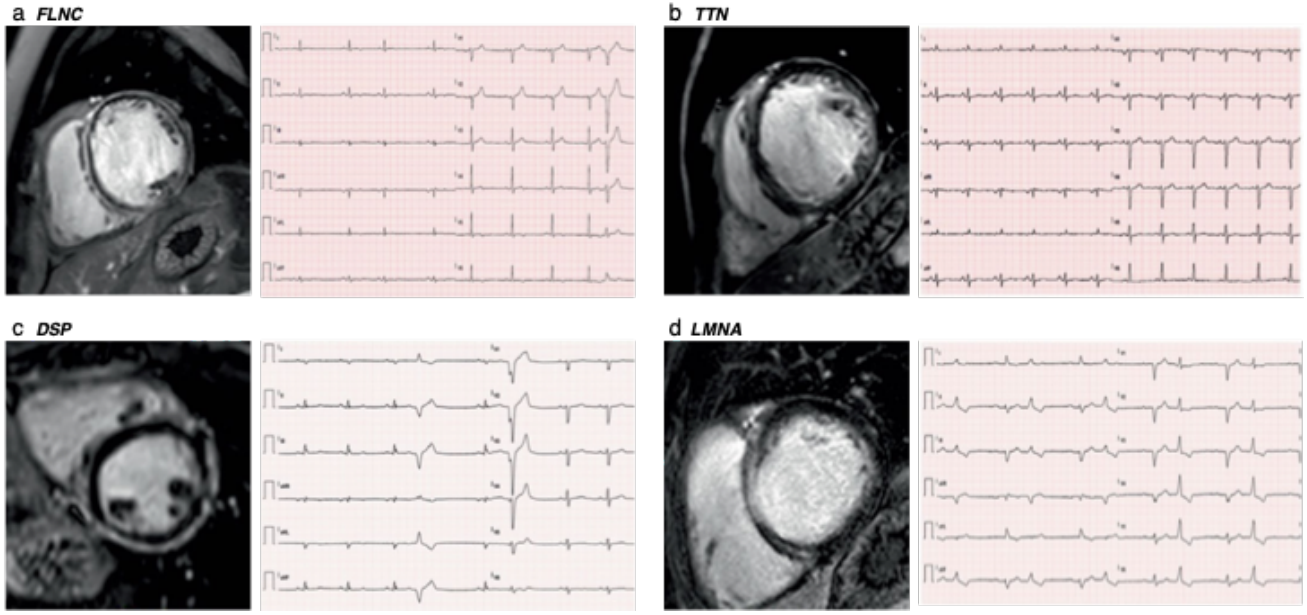
https://doi.org/10.1038/s41569-024-01074-2

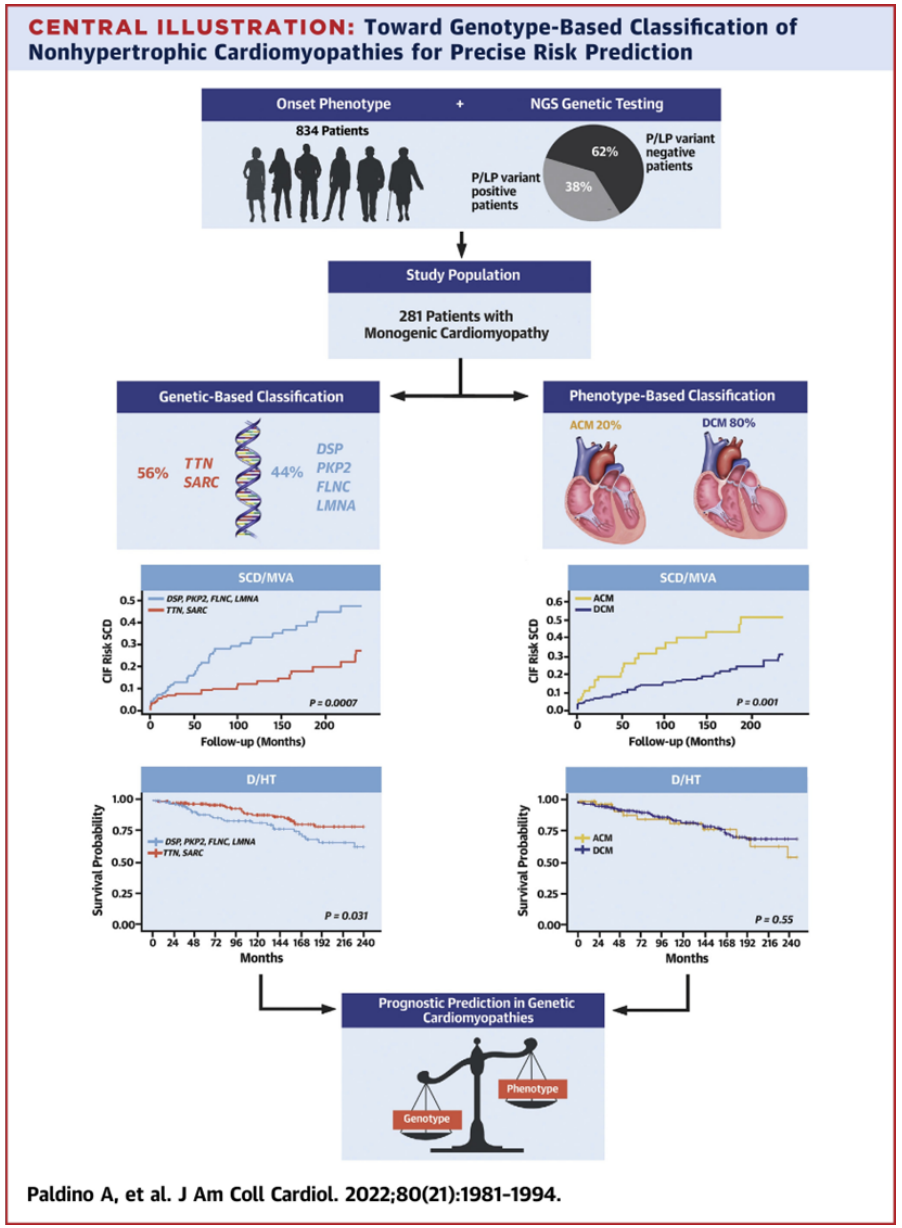
Review article

Check for updates

Pathophysiology of dilated cardiomyopathy: from mechanisms to precision medicine

Marta Gigli[1], Davide Stolfo[1,2], Marco Merlo[1], Gianfranco Sinagra[1], Matthew R. G. Taylor[3] & Luisa Mestroni[4]





Paldino A, et al. J Am Coll Cardiol. 2022;80(21):1981-1994.

GENES → DROWBACKS

INTERPRETABILITY → VUS!!

INTER-DISCIPLINARY TEAMS

ANXIETY AND PSYCHOLOGICAL ISSUES

RE-CLASSIFICATION

DROWBACKS – referral centers

GENERAL POPULATION
«genotype-first»

Titin-truncating variants affect heart function in disease cohorts and the general population

nature genetics

PLOS ONE

Prevalence of Titin Truncating Variants in General Population

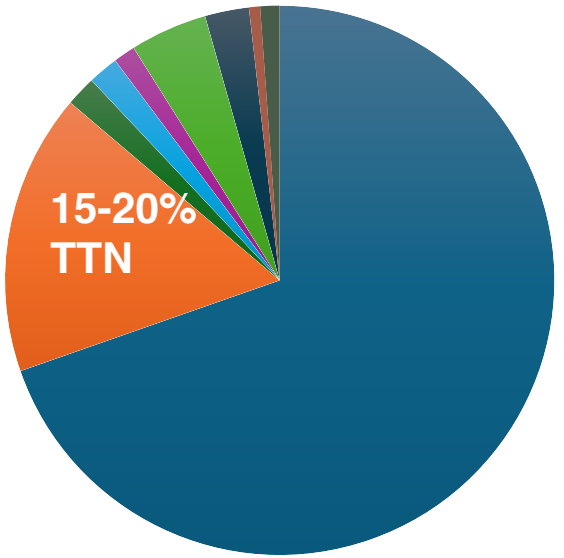
Oyediran Akinrinade[1], Juha W. Koskenvuo[2,3], Tero-Pekka Alastalo[1,2]*

Prevalence of DCM-associated TTNtv:

0.36% to 0.5%

≤37.5 million people may carry a DCM-associated TTNtv and potentially at an increased risk of developing heart failure and cardiac arrhythmia

REGISTRIES
«phenotype-first»



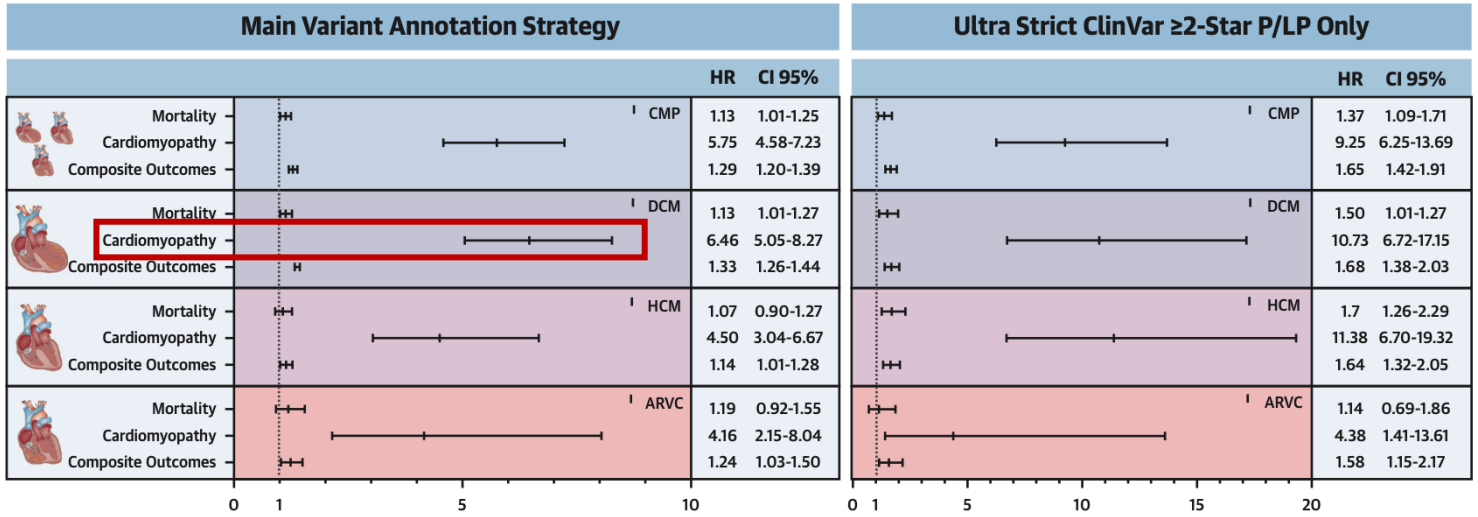
Schafer et al., *Nat Gen,* 2017
Akinrinade et al., *Plos One*, 2015

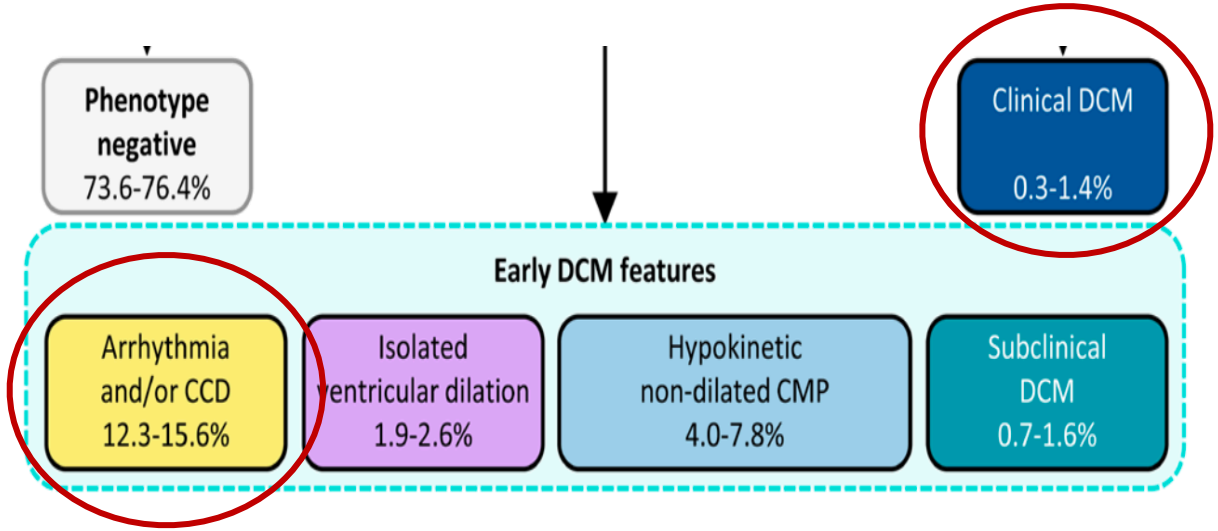
European Reference Network for rare or low prevalence complex diseases
Network Heart Diseases (ERN GUARD-HEART)
ASUGI Azienda Sanitaria Universitaria Giuliano Isontina
REGIONE AUTONOMA FRIULI VENEZIA GIULIA
UNIVERSITÀ DEGLI STUDI DI TRIESTE

DROWBACKS – referral centers

GENERAL POPULATION PENETRANCE **REGISTRIES**

Genetic background VARIABLE EXPRESSIVITY ***Overt phenotype***



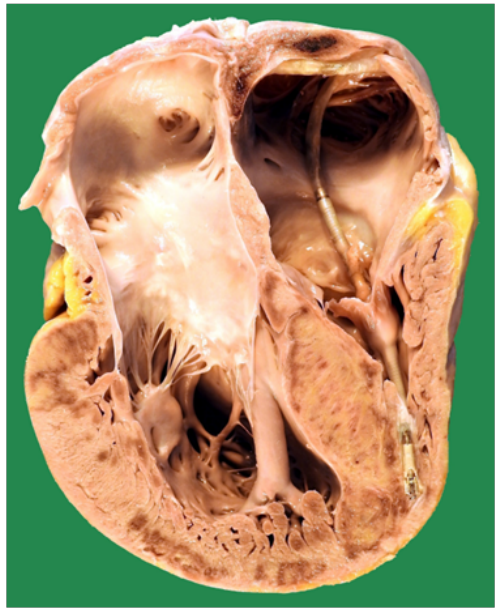


Asatryan et al, *JACC HF*, 2023
Shah et al., *Circulation,* 2022

European Reference Network for rare or low prevalence complex diseases
Network Heart Diseases (ERN GUARD-HEART)
ASUGI Azienda Sanitaria Universitaria Giuliano Isontina
REGIONE AUTONOMA FRIULI VENEZIA GIULIA
UNIVERSITÀ DEGLI STUDI DI TRIESTE

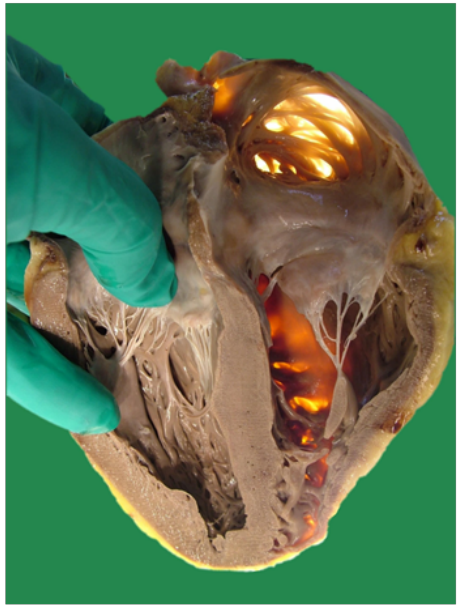
Diagnostic yield in the current era of whole genetic testing

HCM



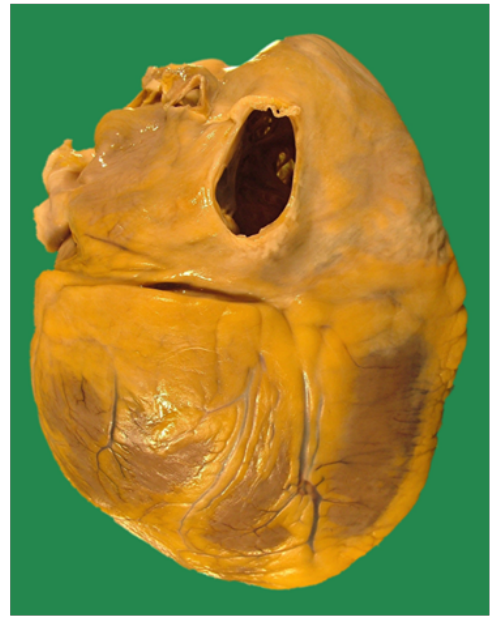
up to 50%

ARVC



60-70%

DCM



30-40%

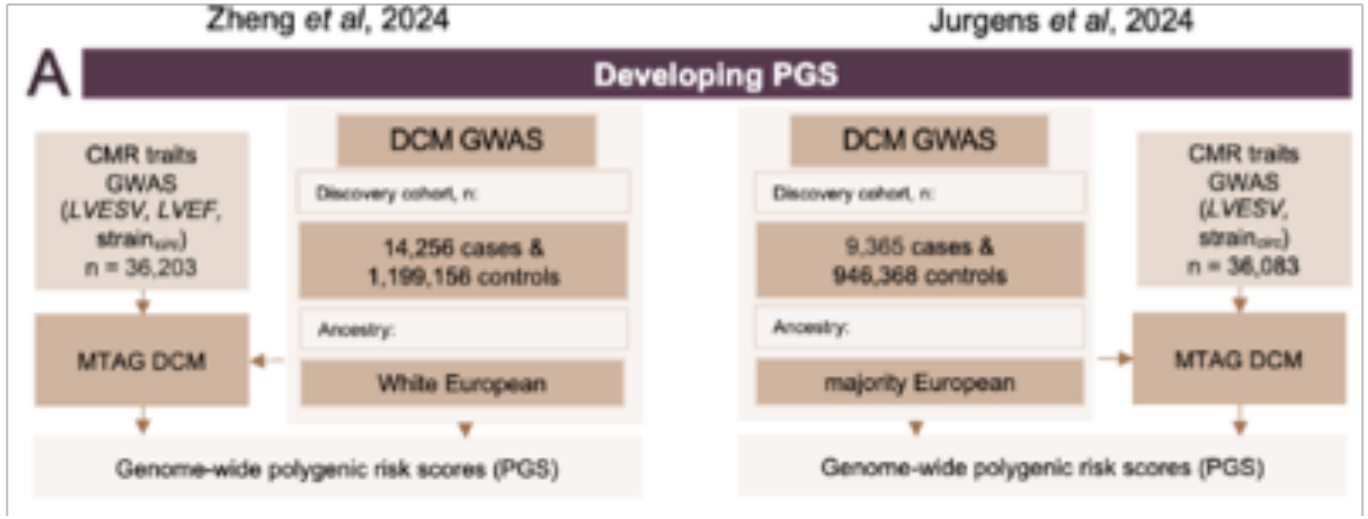
THE MAJORITY OF CARCIOMYOPATHY PTs IN CLINICAL PRACTICE ARE GENE ELUSIVE!!

European Reference Network for rare or low prevalence complex diseases
Network Heart Diseases (ERN GUARD-HEART)
ASUGI Azienda Sanitaria Universitaria Giuliano Isontina
REGIONE AUTONOMA FRIULI VENEZIA GIULIA
UNIVERSITÀ DEGLI STUDI DI TRIESTE

POLYGENIC RISK SCORES

Polygenic Risk Scores in Dilated Cardiomyopathy: Towards the Future

Daria R. Kramarenko[1,4] · Sean J. Jurgens[1,2,3] · Yigal M. Pinto[1,4,5] · Connie R. Bezzina[1,4] · Ahmad S. Amin[1,4,5]



Curr Cardiol Reports 2025

B

Testing PGS

PGS from MTAG (~700K SNPs)

DCM/NI-DCM risk (UKB)

Cohort	OR per SD	[95%CI]	AUC
UKB	1.76	[1.64-1.76]	0.71

Comparing risk of individuals from different centiles

	OR	[95%CI]
Top 1% vs middle 20%	3.83	[2.52-5.79]
Top 1% vs bottom 1%	7.04	[2.42-20.5]

Cumulative hazards for lifetime DCM diagnosis

	HR	[95%CI]
Top 1% vs bottom 20%	6.10	[3.90-9.40]

PGS in genotype positive cohort (UKB)

Cumulative hazards for lifetime DCM diagnosis

	HR	[95%CI]
Top 20% vs median 20%	2.30	[1.20-4.30]
Top 20% vs bottom 20%	4.40	[2.10-9.40]

Association with CMR traits (UKB)

Outcome	Per PGS SD	[95%CI]
LVEF, %	-0,66	[-0,73 to -0,59]
LVEDV, ml	2,12	[1,83 to 2,41]
LVESV, ml	1,89	[1,71 to 2,07]

PGS from MTAG (~1.1M SNPs)

DCM/NI-DCM risk

Cohort	OR per SD	[95%CI]	AUC
AoU	1.64	[1.54–1.75]	0.73
AUMC	1.93	[1.79-2.07]	0.73

Different ancestries (AoU)

Cohort	OR per SD	[95%CI]	AUC
European	1.73	[1.59–1.88]	0.75
African	1.61	[1.39–1.87]	0.67
Adm. American	1.34	[1.11–1.62]	0.74

Genetic sex (AUMC)

Cohort	OR per SD	[95%CI]	AUC
Females	2.00	[1.79–2.24]	0.73
Males	1.87	[1.70–2.06]	0.71

PGS in genotype positive vs negative cohort (AUMC)

	OR per SD	[95%CI]	AUC
Gen + vs controls	1.54	[1.33–1.79]	0.69
Gen - vs controls	2.05	[1.81–2.32]	0.73

PGS in gen + is significantly lower compared to gen - (p=0.0015)

Association with systolic HF (AoU)

Outcome	OR per SD	[95%CI]
Syst. HF (excl. DCM/HCM)	1.24	[1.20–1.28]

C

Comparison by Jurgens et al.

DCM/NIDCM risk

Cohort	OR per SD [95%CI]	AUC (univ) [95%CI]	R^2
AoU EUR	1.70 [1.45-1.99]	0.64 [0.62-0.67]	0.07
UKB EUR	1.83 [1.65-2.05]	0.66 [0.64-0.67]	0.08
AUMC EUR	1.87 [1.55-2.26]	0.66 [0.64-0.68]	0.1

DCM/NIDCM risk

Cohort	OR per SD [95%CI]	AUC (univ) [95%CI]	R^2
AoU EUR	1.73 [1.46-2.04]	0.66 [0.63-0.68]	0.08
UKB EUR	1.91 [1.69-2.15]	0.68 [0.66-0.69]	0.1
AUMC EUR	1.93 [1.58-2.35]	0.67 [0.65-0.69]	0.11

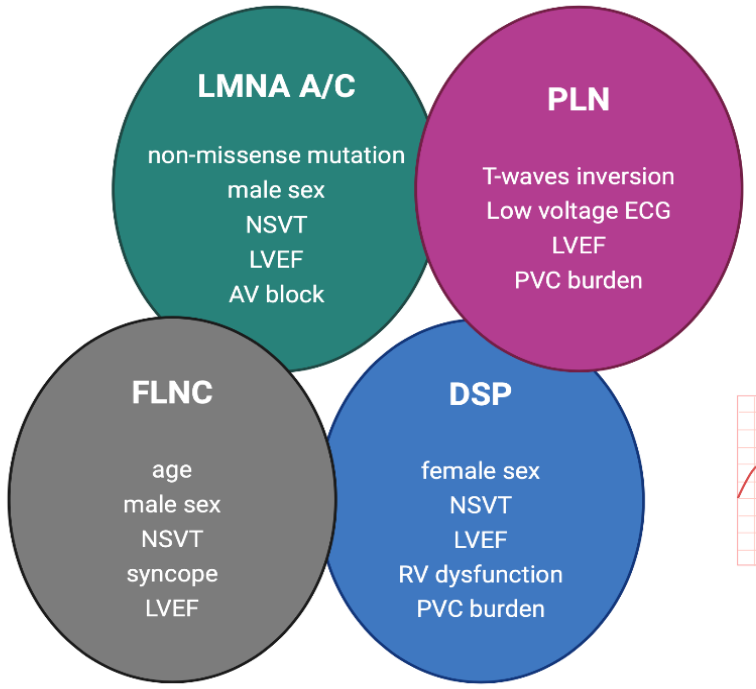
DCM/NDLVC: MULTIPARAMETRIC APPROACH deep phenotype the gene!

ESC European Society of Cardiology
European Journal of Heart Failure (2025)
doi:10.1002/ejhf.70042
RESEARCH ARTICLE

Future development of arrhythmogenic risk scores in patients with heart failure and inherited dilated cardiomyopathy. A scientific statement of the Heart Failure Association of the ESC

Marta Gigli[1†], Job A.J. Verdonschot[2,3†], Pablo Garcia-Pavia[4,5†], Davide Stolfo[1,6], Lorenzo Monserrat[7], Sanjay Prasad[8,9], Andrea Mazzanti[10,11], Folkert W Asselbergs[12,13,14†], Barbara Bauce[15†], Philippe Charron[16†], Dana Dawson[17], Brian P Halliday[8,9], Luisa Mestroni[18], Petar Seferovic[19,20,21], Upasana Tayal[8,9], Maria Teresa Tome Esteban[22], Peter Van Tintelen[23†], Stephane Heymans[3†], Antonis Pantazis[24], Marco Metra[25], and Gianfranco Sinagra[1*†]

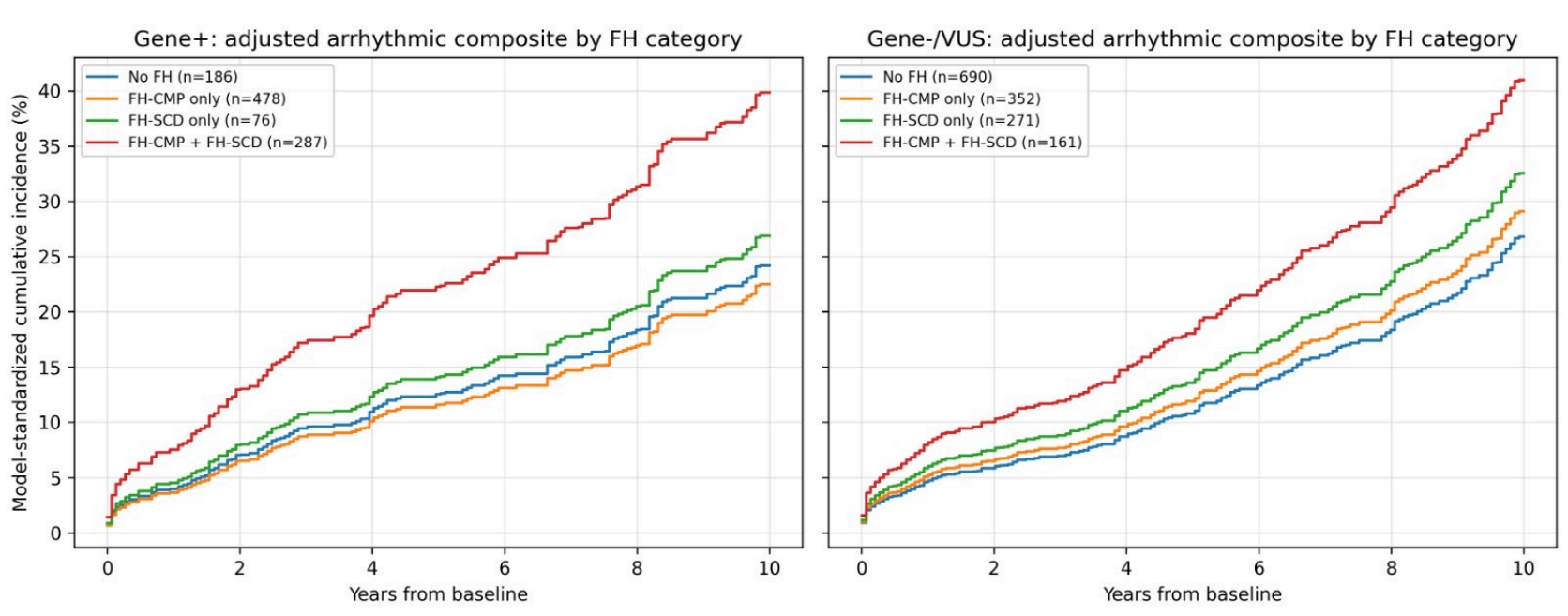
Gene-specific personalized risk estimation



European Reference Network for rare or low prevalence complex diseases
Network Heart Diseases (ERN GUARD-HEART)
ASUGI Azienda Sanitaria Universitaria Giuliano Isontina
REGIONE AUTONOMA FRIULI VENEZIA GIULIA
UNIVERSITÀ DEGLI STUDI DI TRIESTE

FIMILY HISTORY

SHARE REGISTRY – 2545 PATIENTS



Detailed categories

No FH

FH-CMP only

FH-SCD only

FH-CMP + FH-SCD

Highest risk:
combined FH-CMP + FH-SCD

This supports a graded familial burden: the highest risk appears when cardiomyopathy and sudden death coexist in the pedigree.

Unpublished

European Reference Network
for rare or low prevalence complex diseases
Network Heart Diseases (ERN GUARD-HEART)

ASUGI
Azienda Sanitaria Universitaria Giuliano Isontina

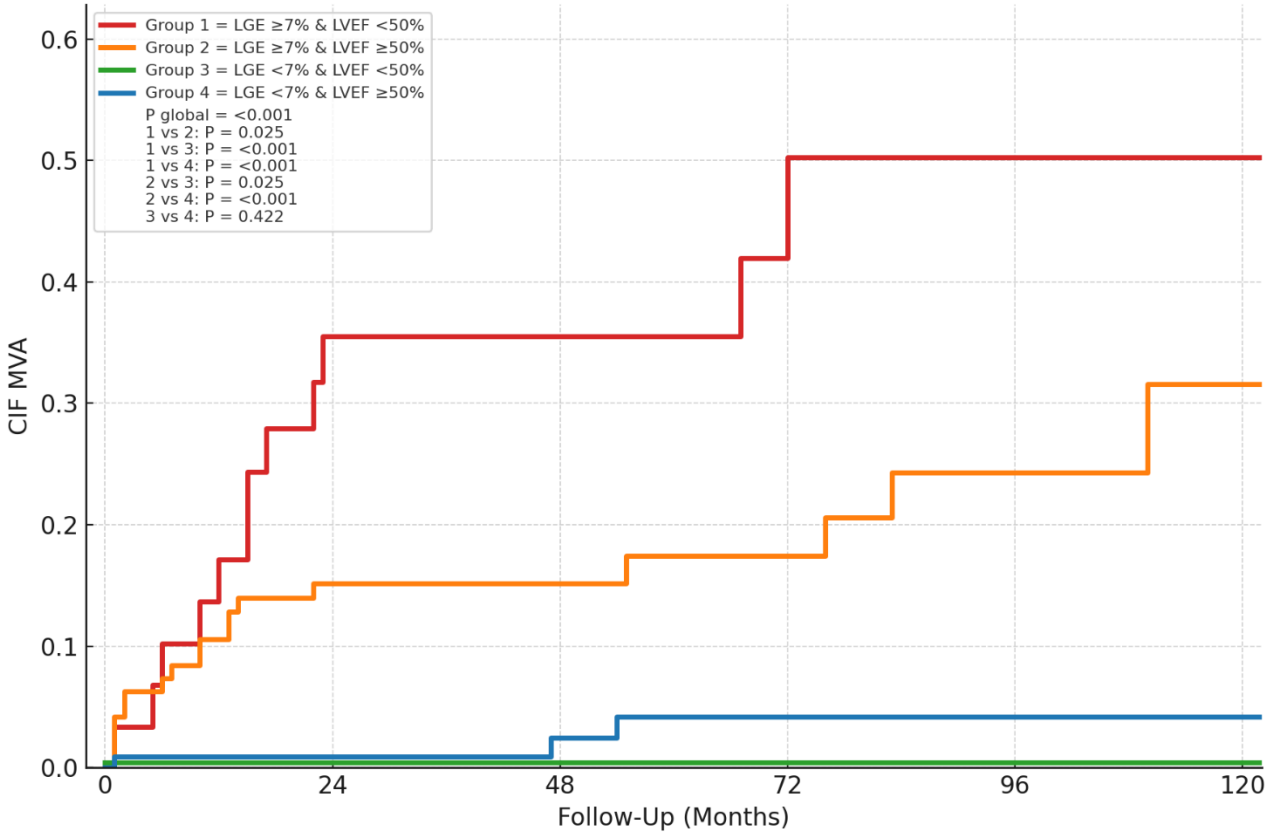
REGIONE AUTONOMA FRIULI VENEZIA GIULIA

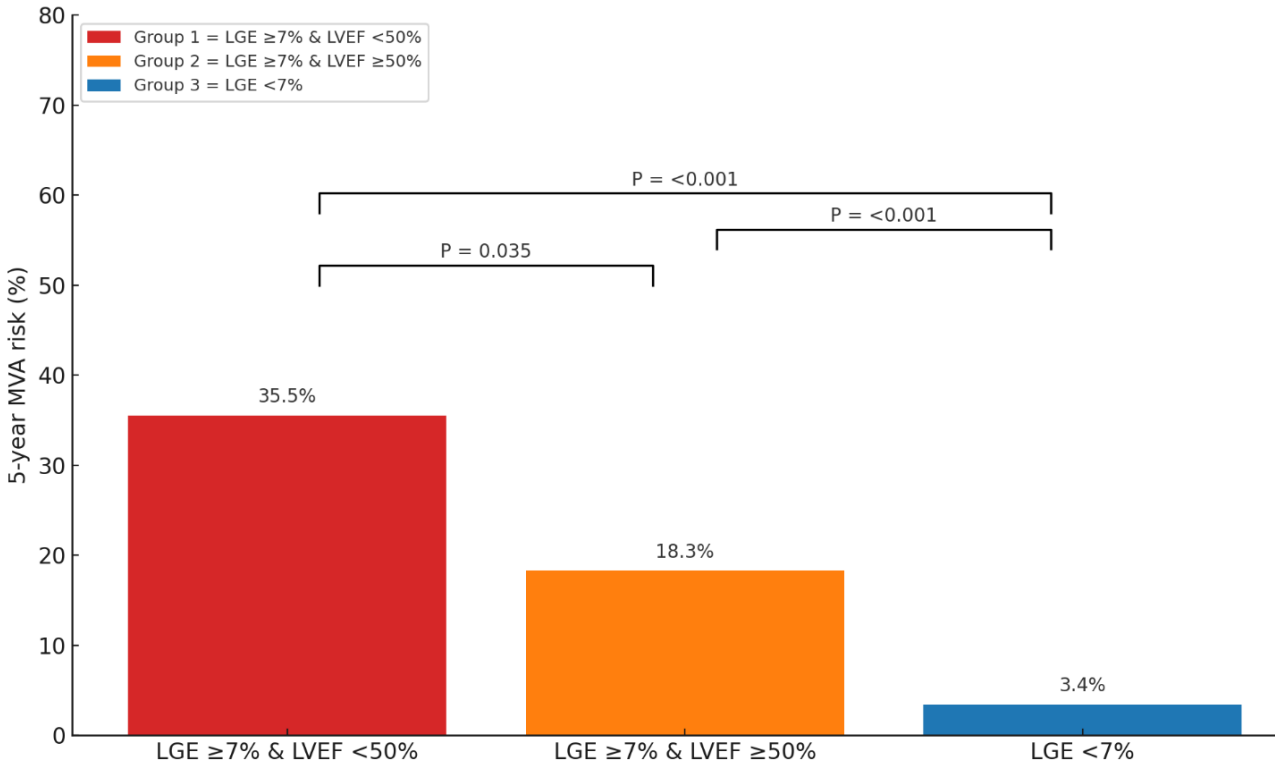
UNIVERSITÀ DEGLI STUDI DI TRIESTE

NDLVC

Radesich C, ….Merlo M, SUBMITTED

NDLVC





Burelli M, ….Merlo M, SUBMITTED

GENES IN NATURAL HISTORY: LVRR

Association between mutation status and left ventricular reverse remodelling in dilated cardiomyopathy

Matteo Dal Ferro,[1] Davide Stolfo,[1] Alessandro Altinier,[1]
Marta Gigli,[1] Martina Perrieri,[1] Federica Ramani,[1] Giulia Barbati,[1] Alberto Pivetta,[1]
Francesca Brun,[1] Lorenzo Monserrat,[2] Mauro Giacca,[3] Luisa Mestroni,[4] Marco Merlo,[1]
Gianfranco Sinagra[1]

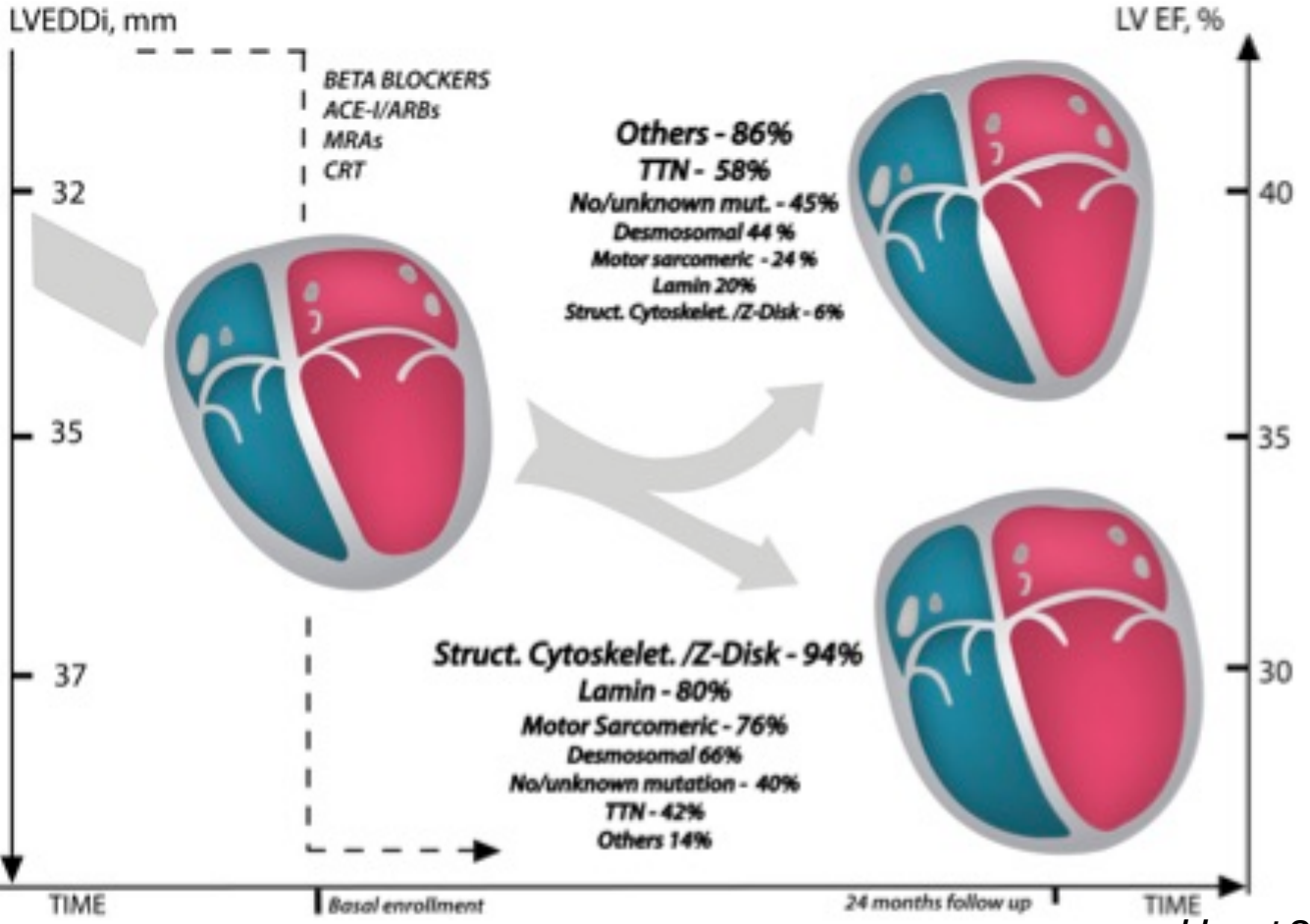


Table 5 Association between structural cytoskeleton Z-disk gene mutations and absence of left ventricular reverse remodelling at multivariable logistic regression analysis.

(5a) Only pathogenic and likely pathogenic variant carriers included

	OR	95% CI	p
Structural cytoskeleton Z-disk genes	0.065	0.008 to 0.535	0.011
LBBB	0.385	0.160 to 0.926	0.033
LVEF*	0.955	0.920 to 0.992	0.016
SBP*	1.017	0.994 to 1.039	0.145

(5b) Pathogenic, likely pathogenic and possibly pathogenic rare variants (PPrV) carriers included

	OR	95% CI	p
Structural cytoskeleton Z-disk genes	0.131	0.035 to 0.490	0.003
LBBB	0.365	0.150 to 0.886	0.026
LVEF*	0.995	0.920 to 0.992	0.016
SBP*	1.017	0.994 to 1.039	0.147

OR estimation is referred to every unit increase or decrease for continuous variables. Previously established clinical predictors of LVRR were entered into the multivariable model.[8]
LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; SBP, systolic blood pressure.

Heart 2017;**0**:1–7. doi:10.1136/

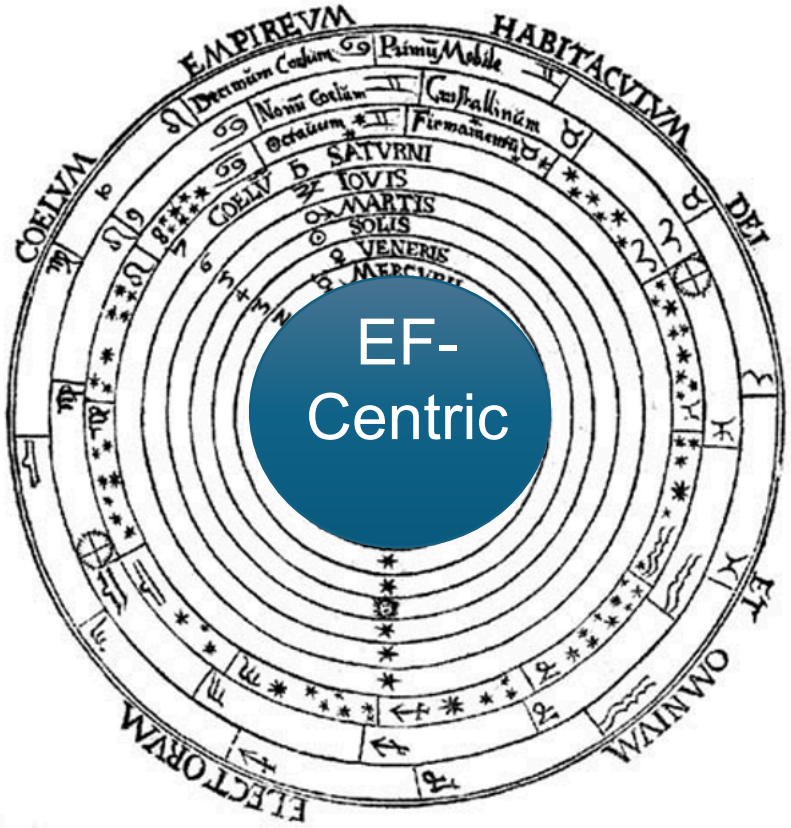
European Reference Network
for rare or low prevalence complex diseases
Network Heart Diseases (ERN GUARD-HEART)

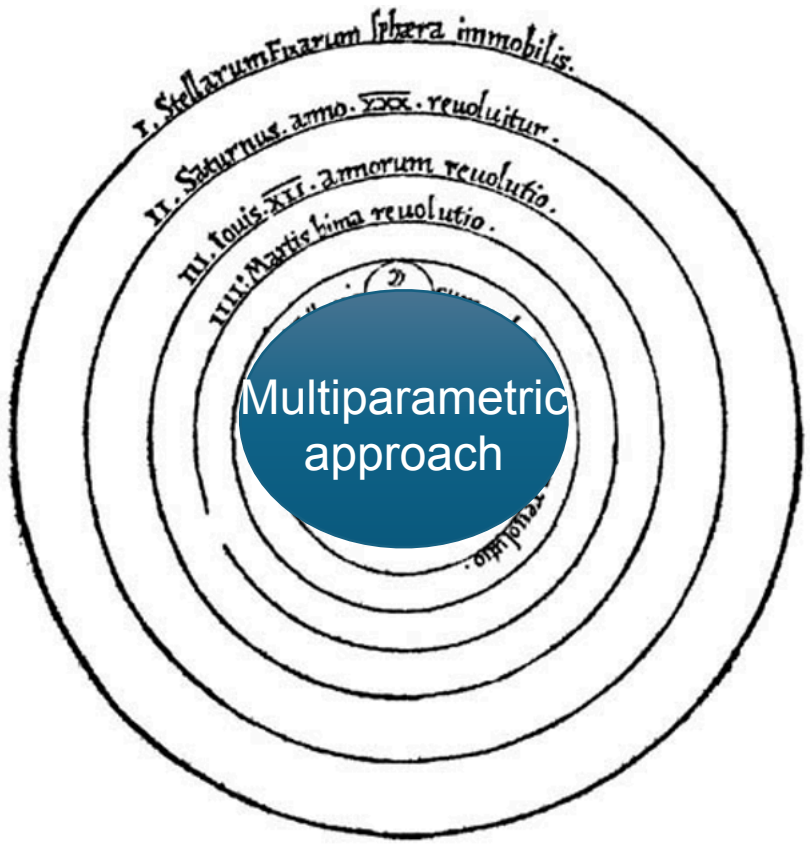
ASUGI
Azienda Sanitaria Universitaria Giuliano Isontina

REGIONE AUTONOMA FRIULI VENEZIA GIULIA

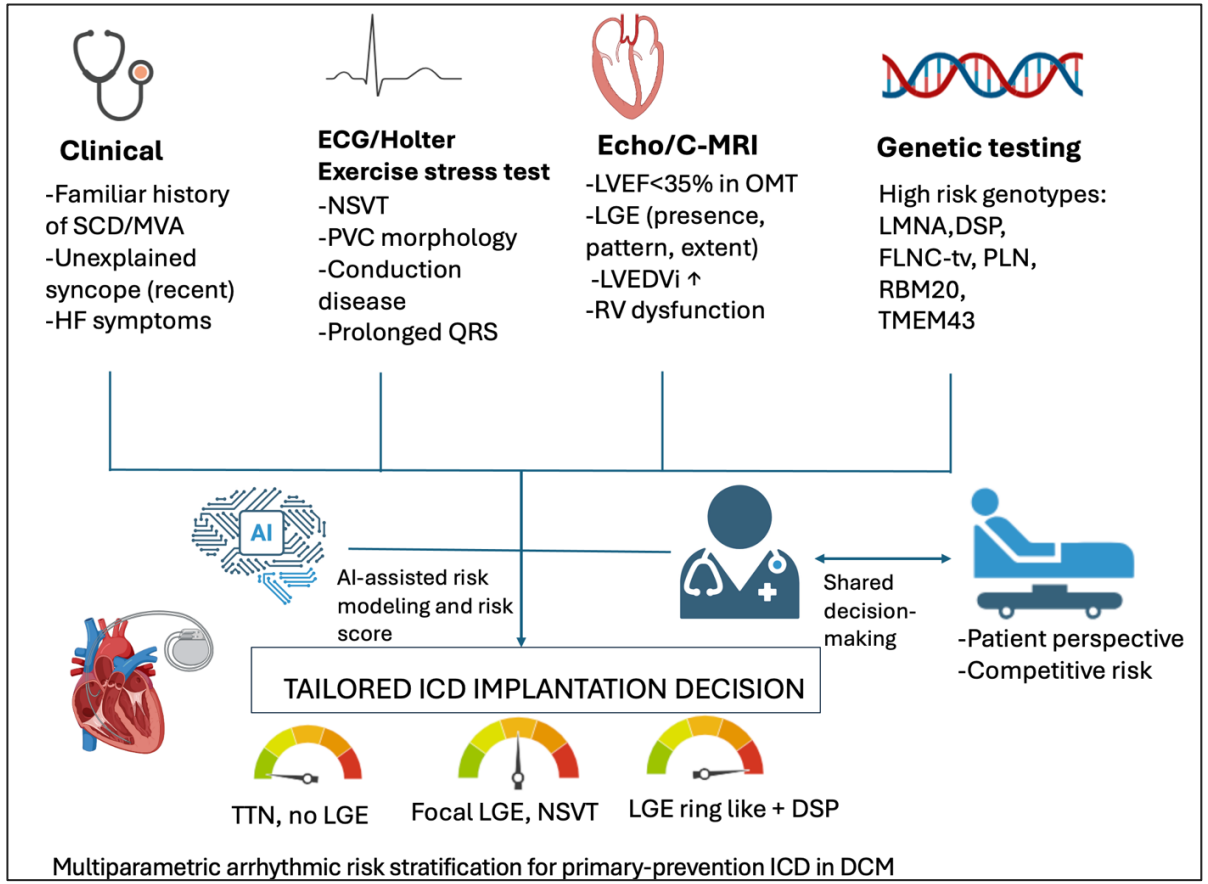
UNIVERSITÀ DEGLI STUDI DI TRIESTE

The Copernican revolution



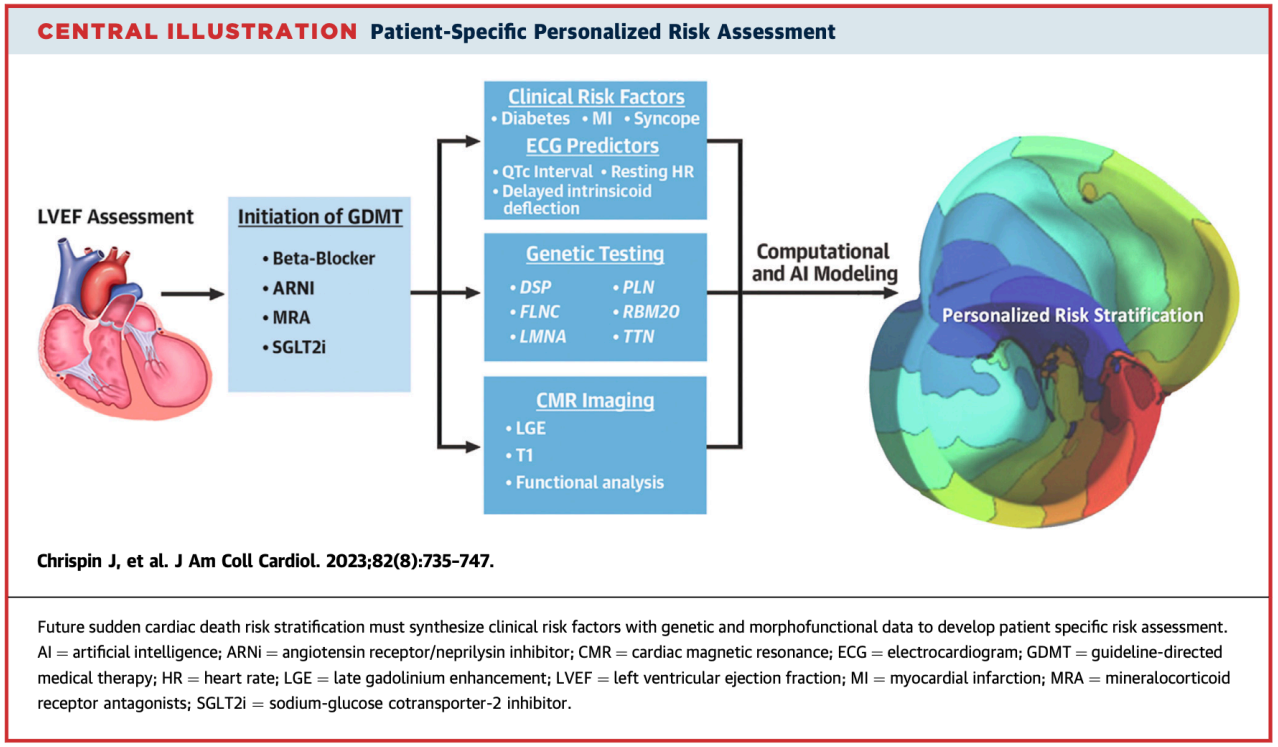


We need a multiparametric approach!



Multiparametric arrhythmic risk stratification for primary-prevention ICD in DCM

Garoia F. ..Merlo M., Sinagra G. et al, 2025 (Springer Book- Cardiomyopathies in Practice-From Deep Phenotyping to Precision Medicine-Submitted)



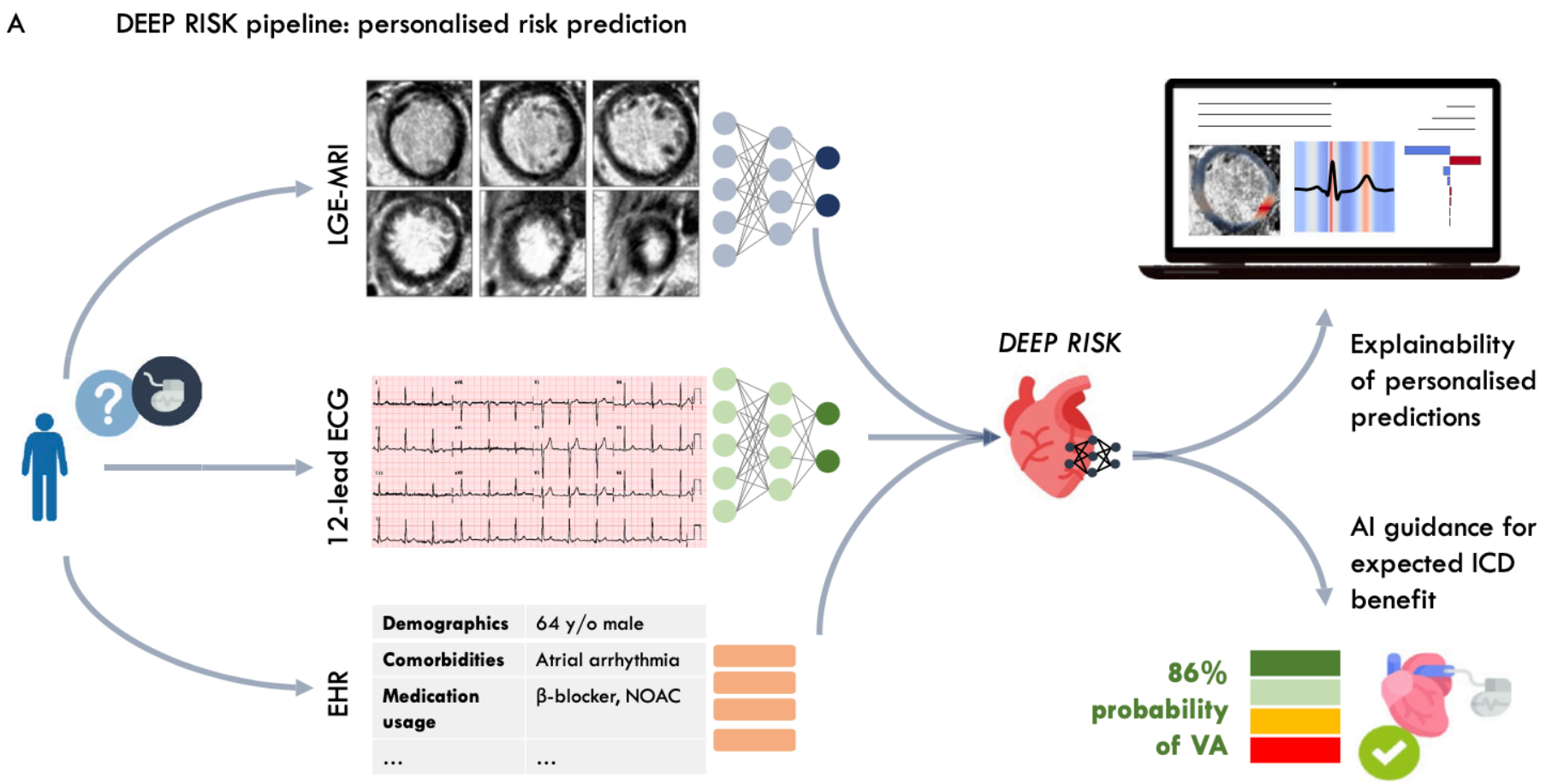
Future directions

scientific reports

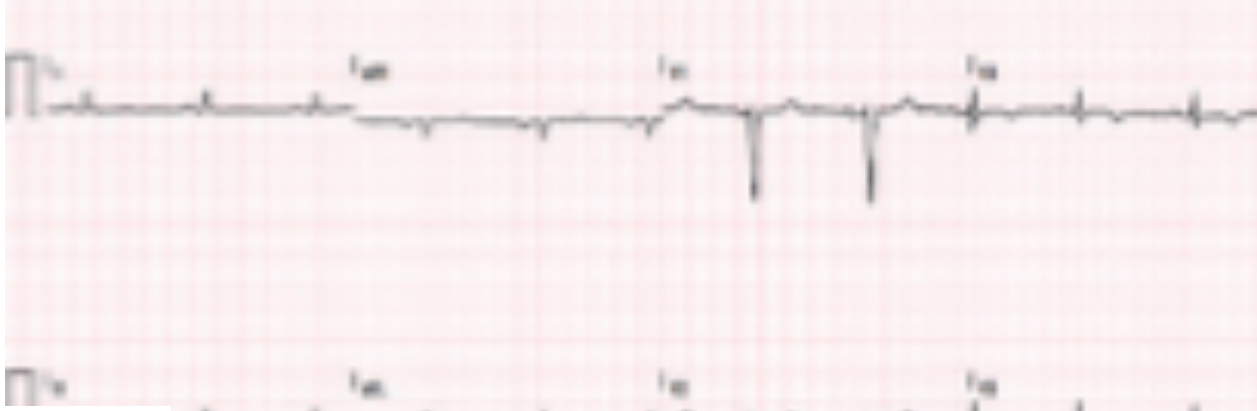
OPEN

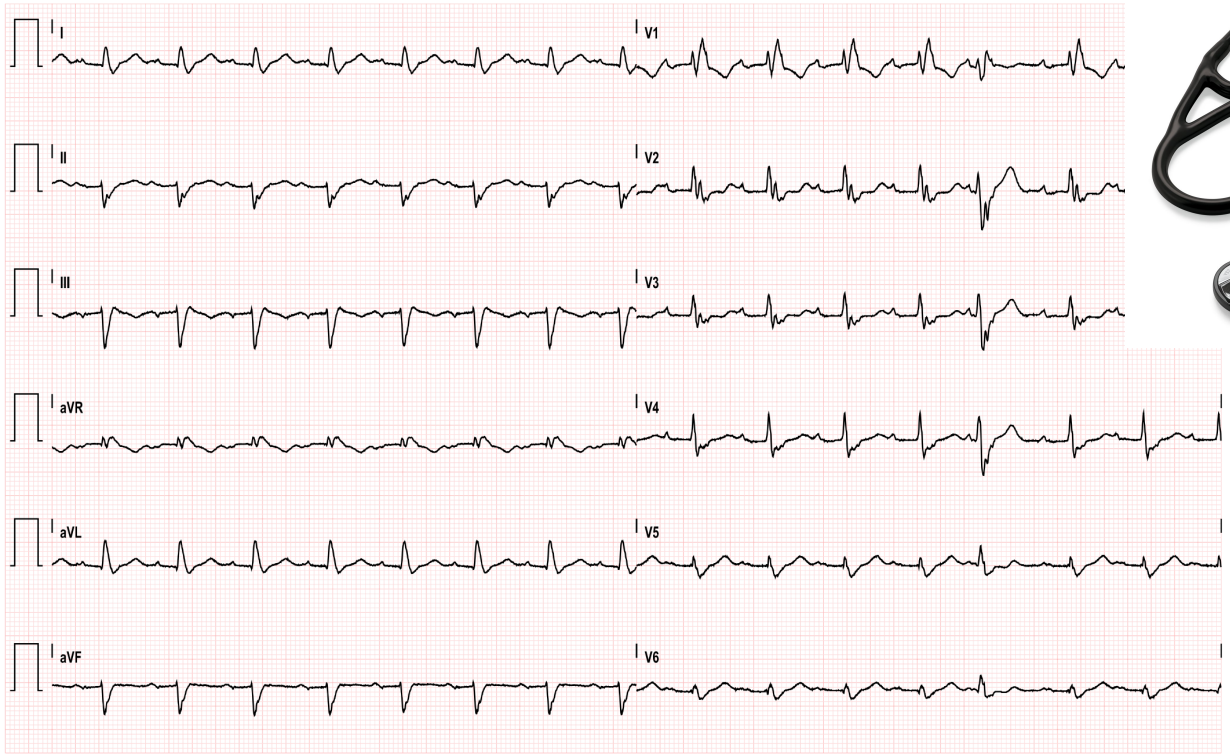
Multimodal explainable artificial intelligence identifies patients with non-ischaemic cardiomyopathy at risk of lethal ventricular arrhythmias

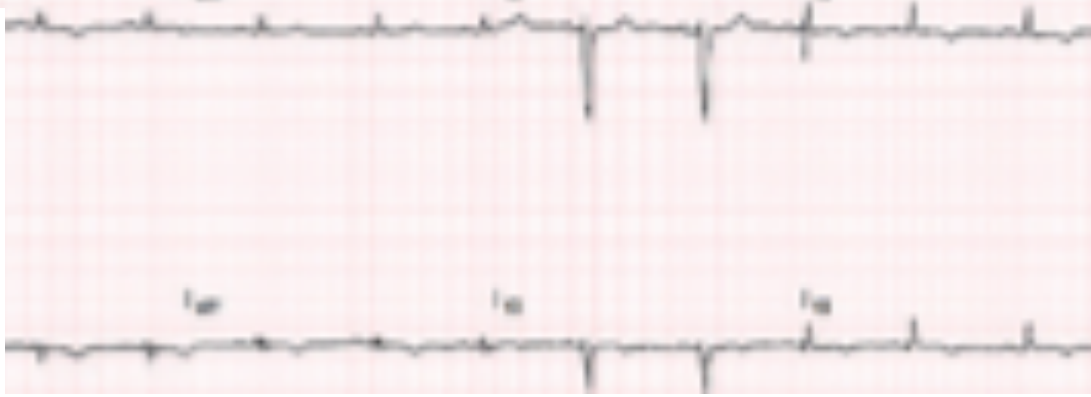
Maarten Z. H. Kolk[1,2], Samuel Ruipérez-Campillo[3,4], Cornelis P. Allaart[5], Arthur A. M. Wilde[1,2], Reinoud E. Knops[1,2], Sanjiv M. Narayan[3], Fleur V. Y. Tjong[1,2,3] & DEEP RISK investigators*



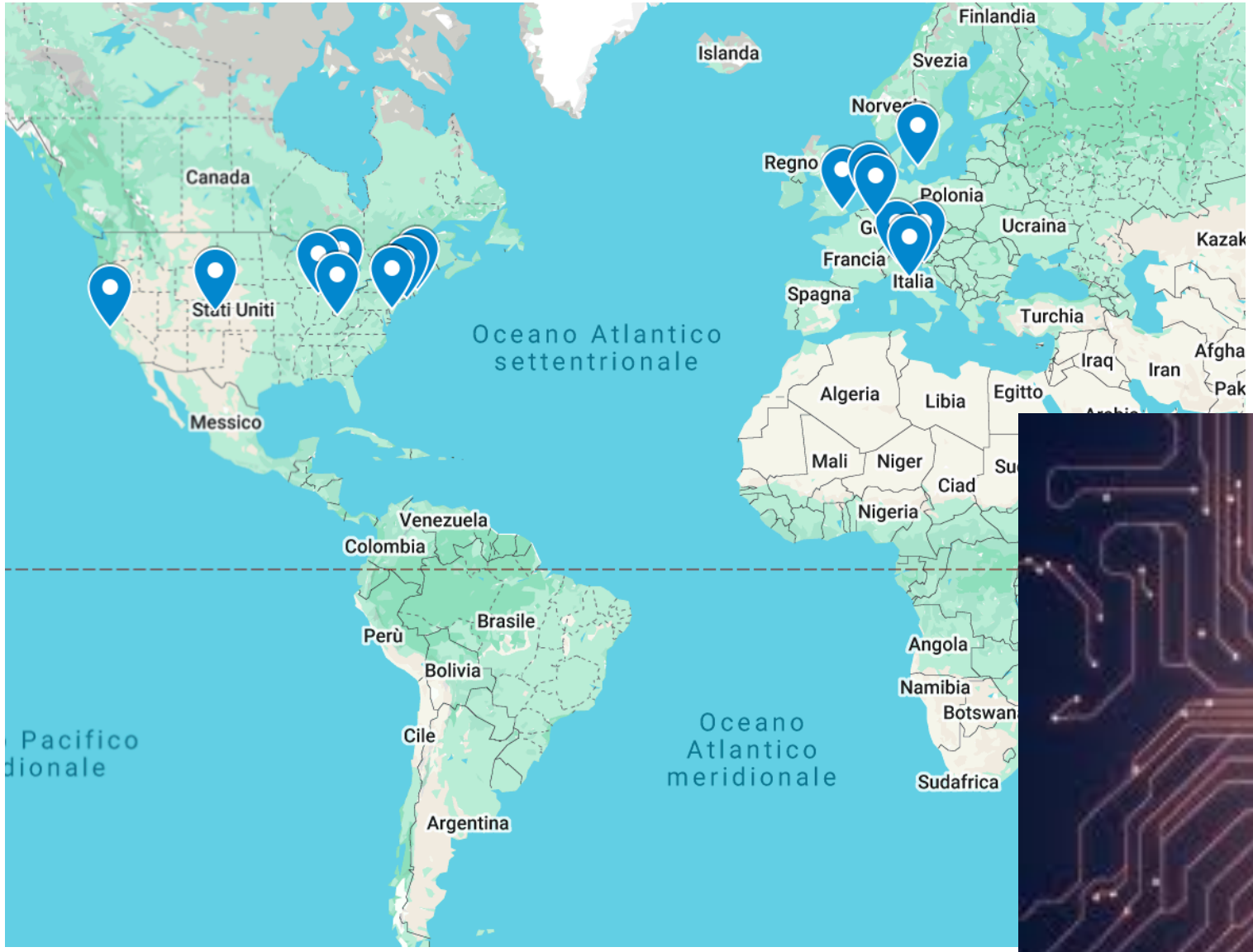
Nature, 2024. Kolk at







Share center



SHARE

ASUGI
Azienda Sanitaria Universitaria Giuliano Isontina
REGIONE AUTONOMA FRIULI VENEZIA GIULIA

European Reference Network
for rare or low prevalence complex diseases
Network Heart Diseases
(ERN GUARD-HEART)

UNIVERSITÀ DEGLI STUDI DI TRIESTE

GRAZIE