

# SCD and inherited arrhythmia in Asian

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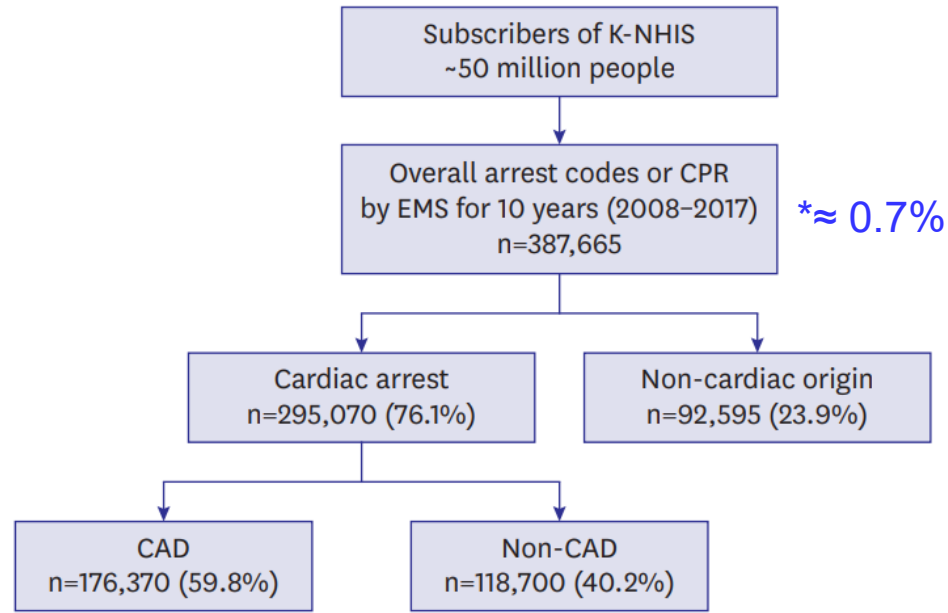
Korea University College of Medicine and Korea University Hospital



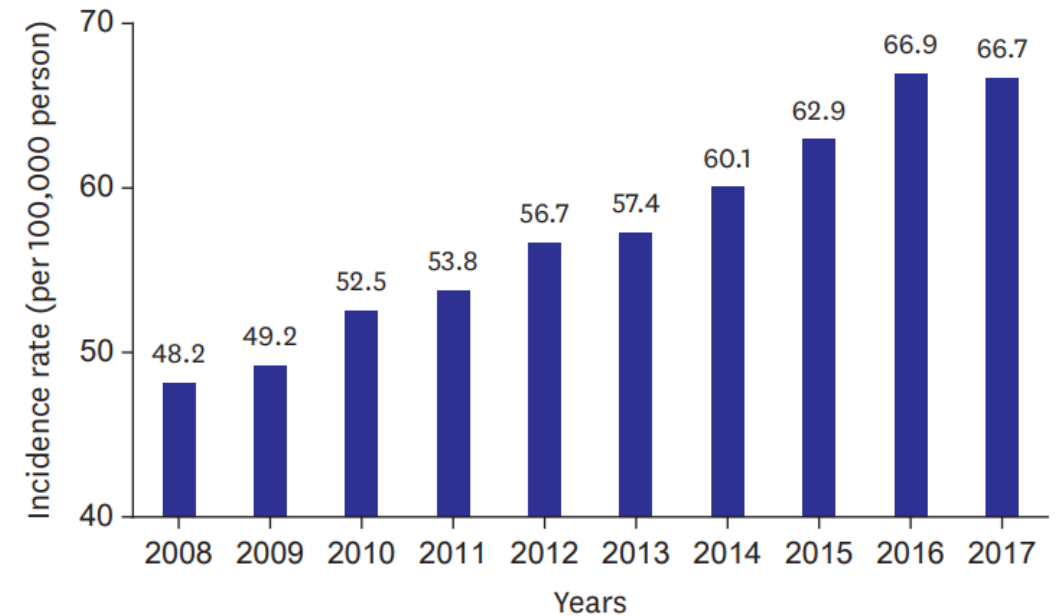
# **The spectrum of epidemiology underlying SCD**

# The 10-year trend of out-of-hospital cardiac arrests

## : a Korean nationwide population-based study



### Age- and sex-adjusted incidence of out-of-hospital cardiac arrest



### One-year mortality rate after out-of-hospital cardiac arrest

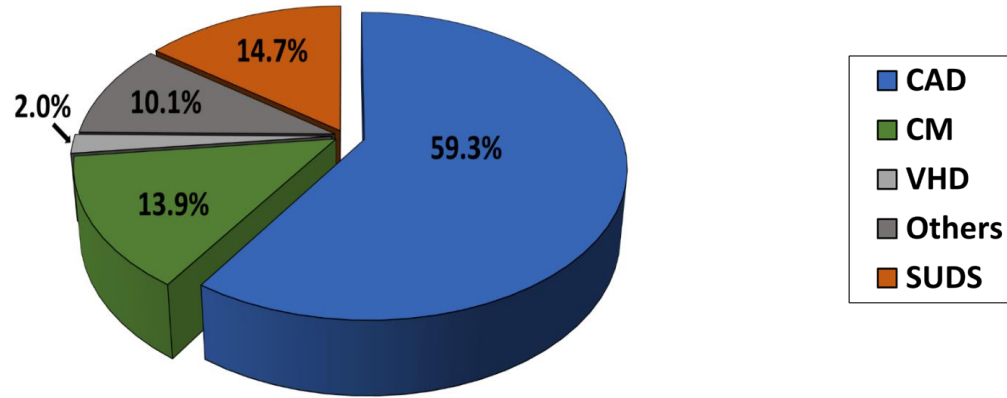
Year	Unadjusted rate (per 1,000)	Adjusted rate (per 1,000)	Age- and sex-adjusted HR (95% CI)	p value for trend
2008	913.9	869.0	1.00 (Reference)	
2009	916.5	870.3	1.00 (0.98-1.02)	
2010	914.5	866.4	1.00 (0.98-1.02)	
2011	914.6	864.6	1.00 (0.98-1.01)	
2012	908.6	857.3	0.99 (0.969-1.00)	<0.0001
2013	908.4	856.5	0.99 (0.97-1.00)	
2014	904.4	851.5	0.98 (0.96-1.00)	
2015	904.1	848.9	0.98 (0.96-0.99)	
2016	899.7	843.9	0.97 (0.95-0.99)	
2017	883.9	836.7	0.96 (0.95-0.98)	

CI = confidence interval; HR = hazard ratio.

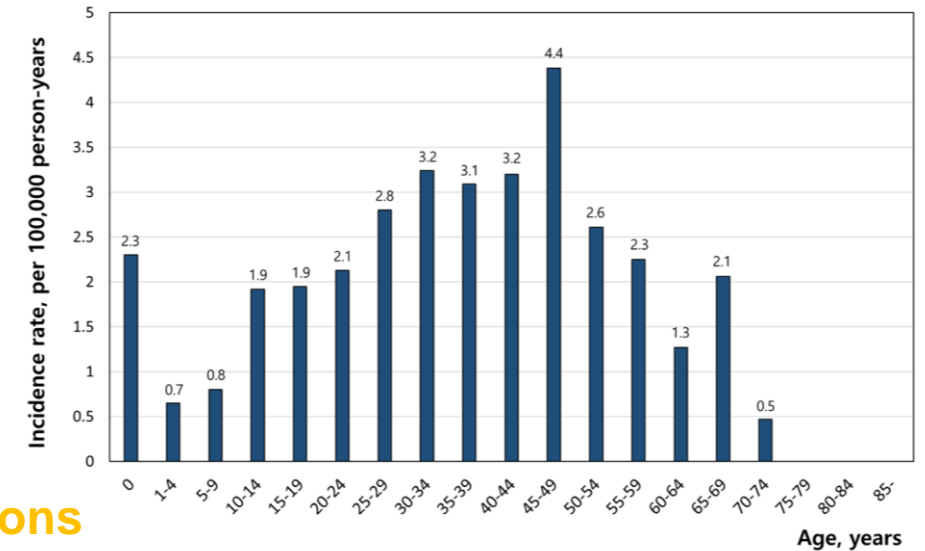
# Korean National Health Insurance Cohort dataset (1,125,691 individuals from 2007 to 2015)

## Incidence of SCA related to SUDS

2.36 per 100,000 person-years (95% CI 2.11-2.65)

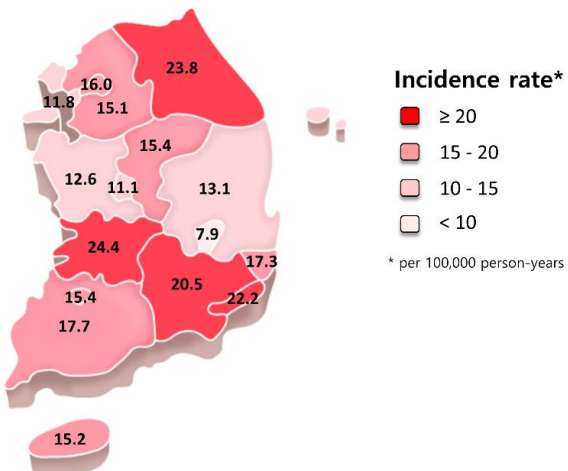


## Sudden unexplained death syndrome

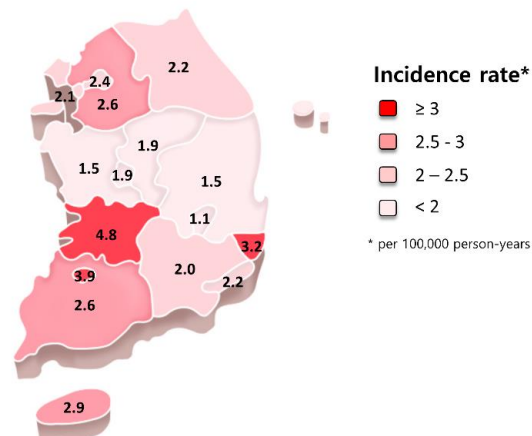


## Regional and Seasonal Variations

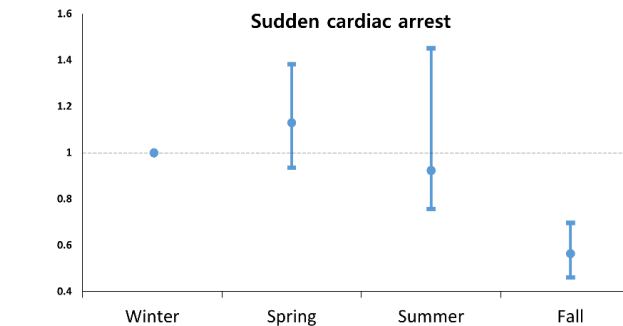
Sudden cardiac arrest



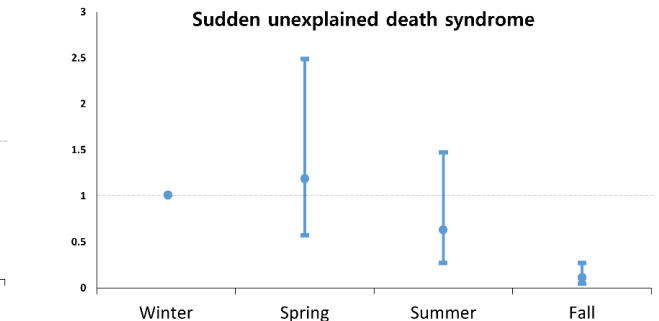
Sudden unexplained death syndrome



Hazard ratio (95% CI)

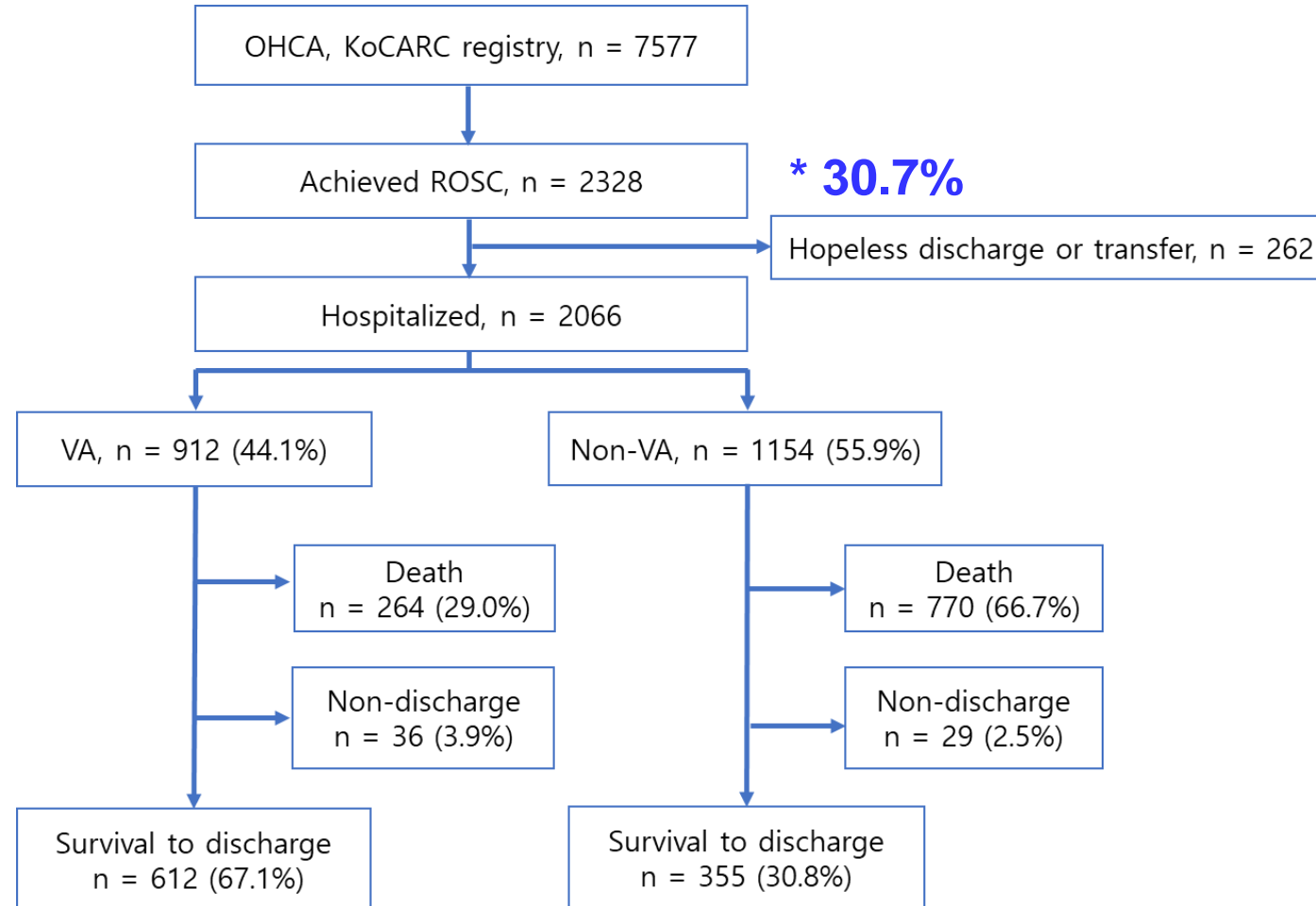


Hazard ratio (95% CI)

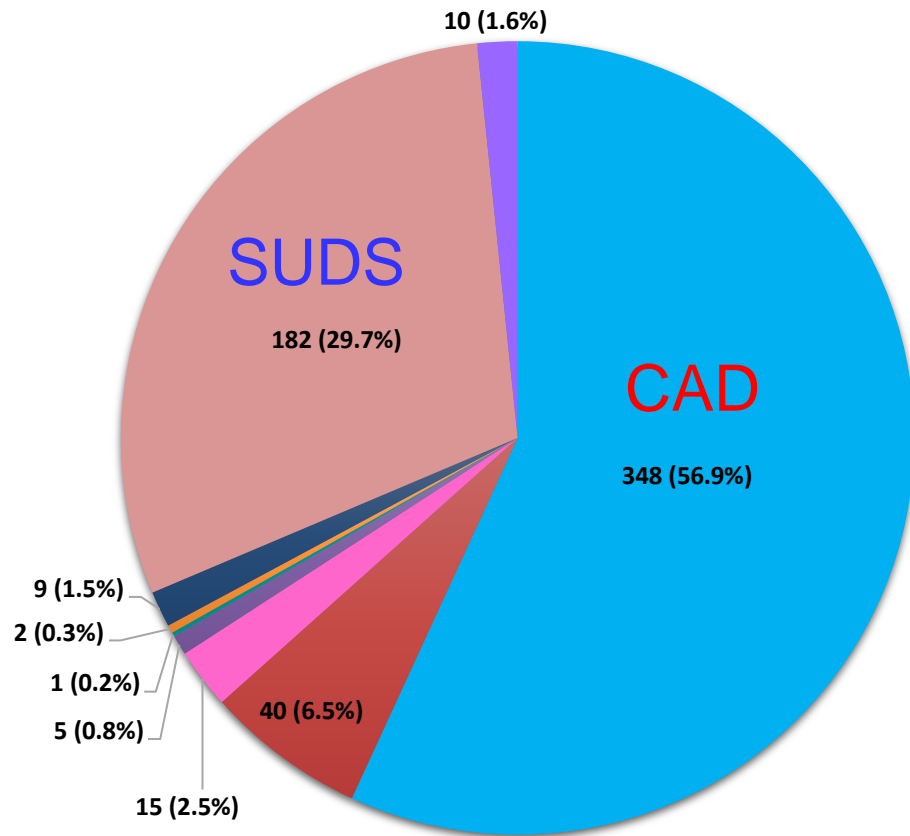


# Out-of-hospital cardiac arrest survivors and approach for secondary prevention in South Korea

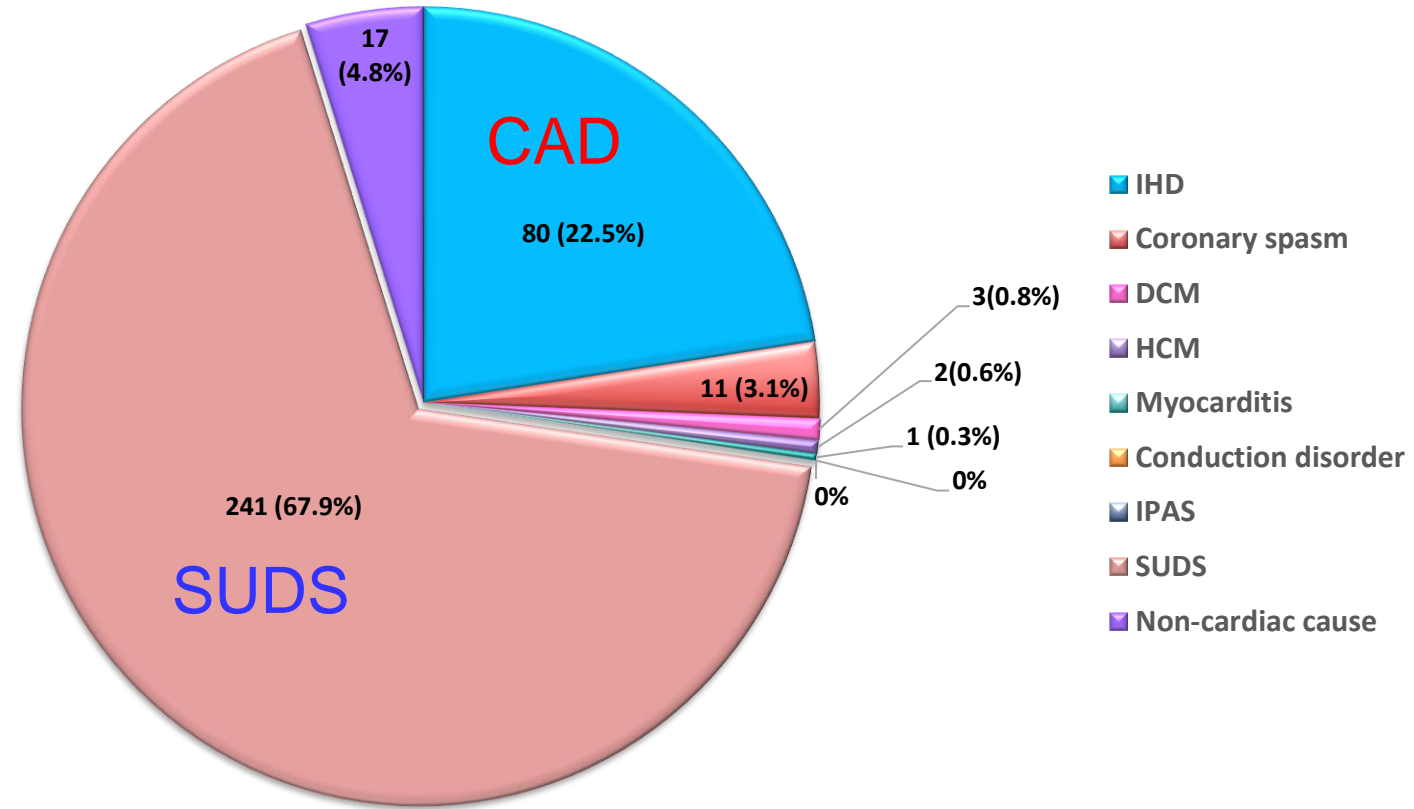
➤ Data from **Korean Cardiac Arrest Research Consortium (KoCARC)** registry



# Etiologies of aborted OHCA patients in VA and non-VA group



VA group, n = 612



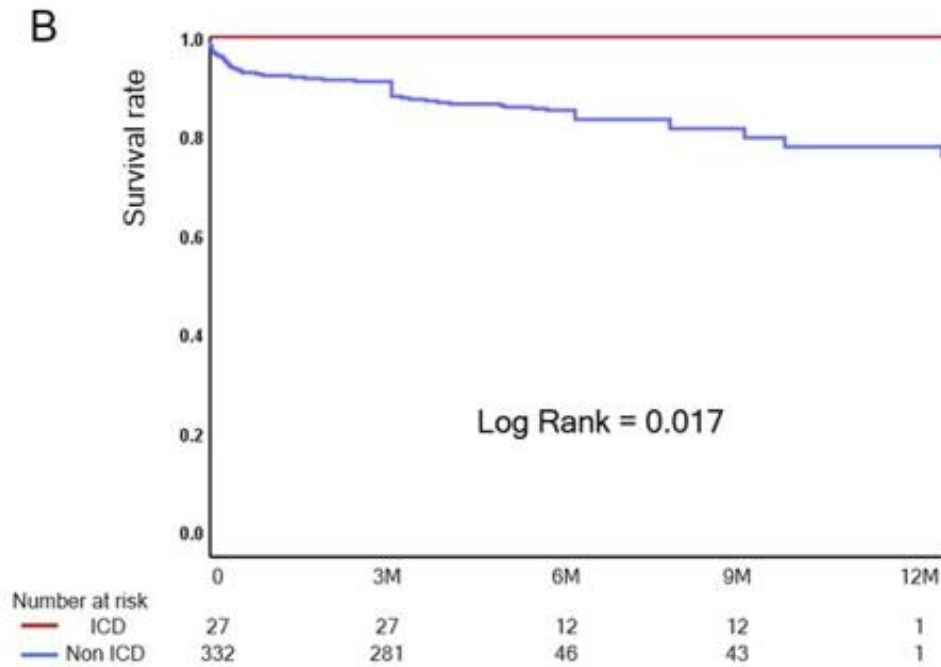
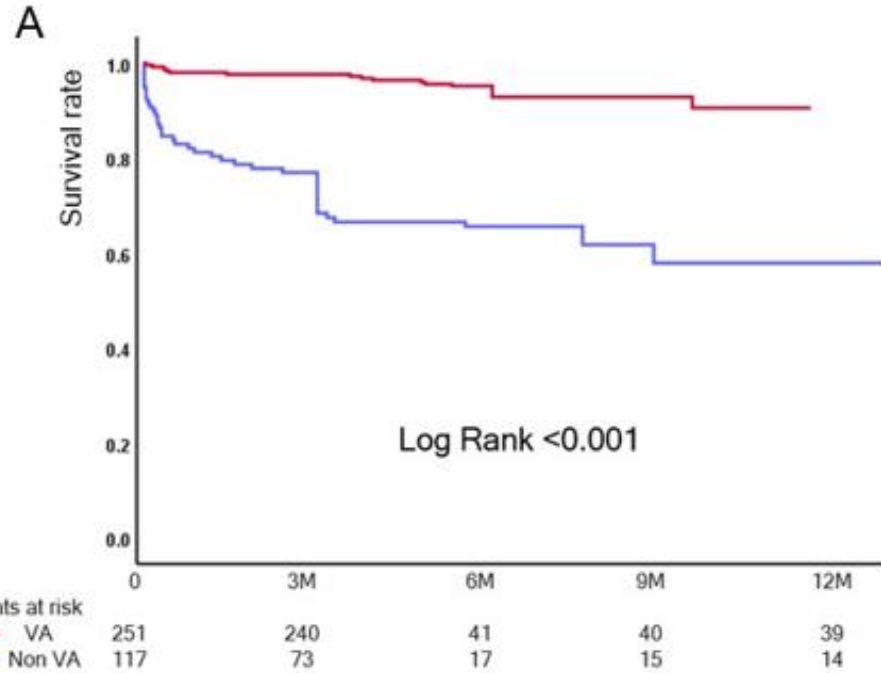
non-VA group, n = 355

- IHD
- Coronary spasm
- DCM
- HCM
- Myocarditis
- Conduction disorder
- IPAS
- SUDS
- Non-cardiac cause

OHCA : Out-of-hospital cardiac arrest ; VA : Ventricular arrhythmia ; IHD : Ischemic heart disease ; DCM : Dilated cardiomyopathy ; HCM : Hypertrophic cardiomyopathy ; IPAS : Inherited primary arrhythmia syndrome ; SUDS : sudden unexplained death syndrome.

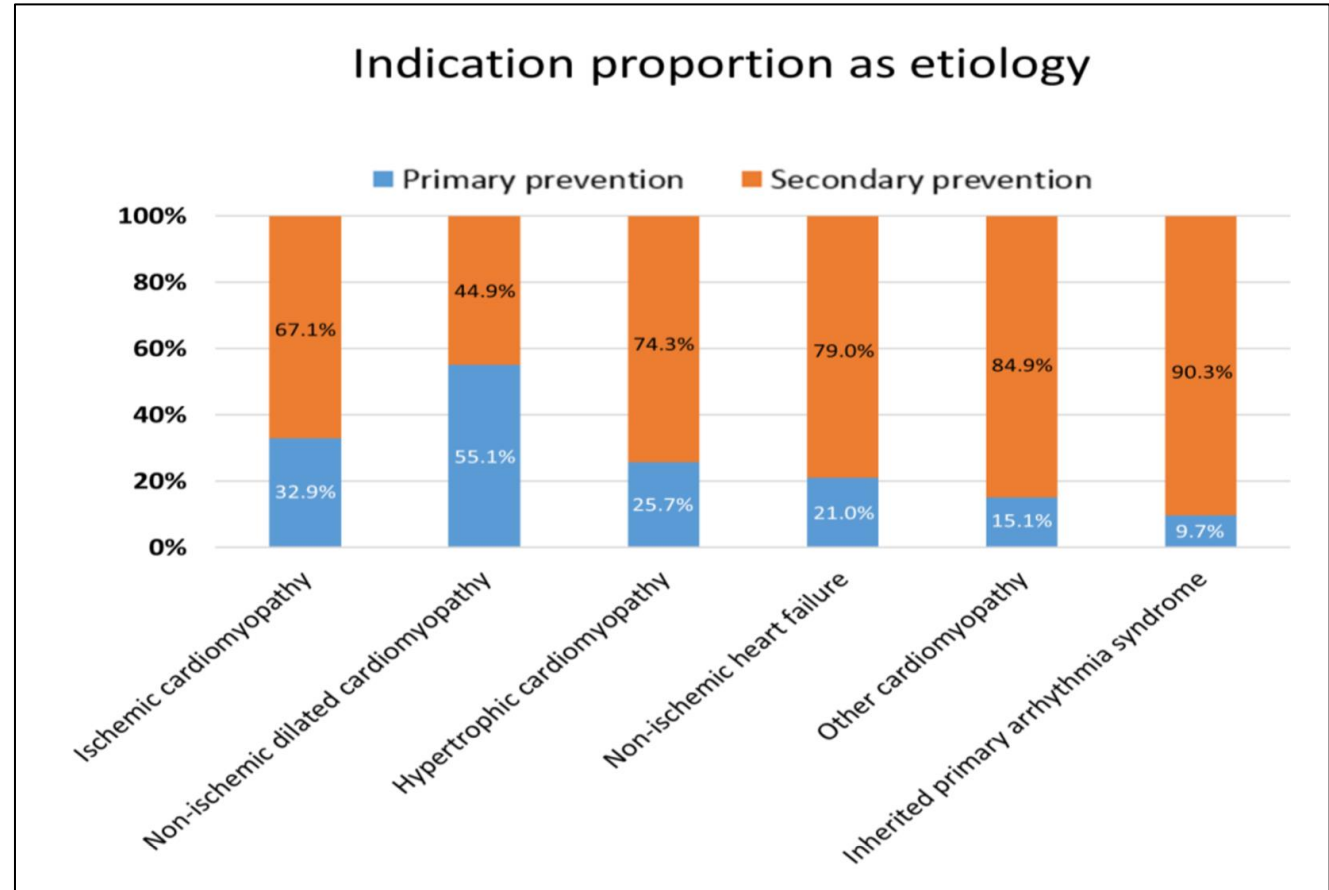
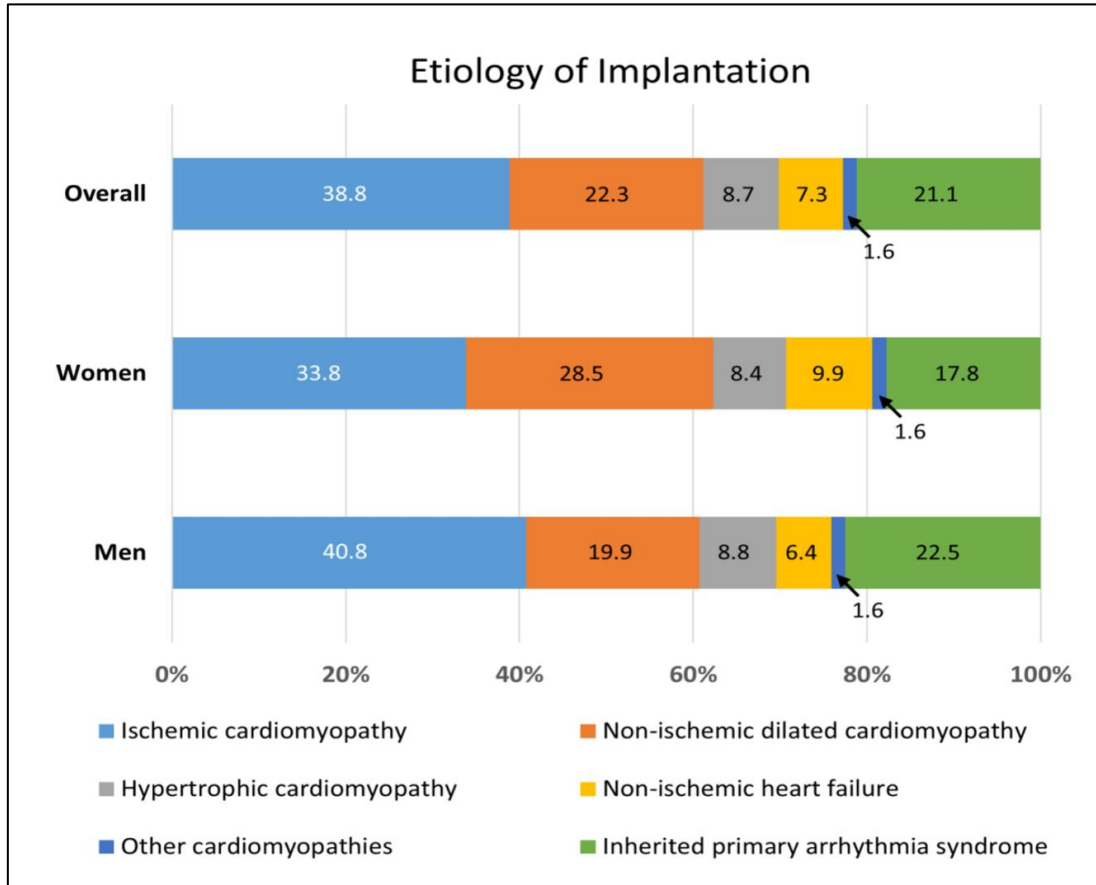


# Kaplan-Meier curves of survival after discharge



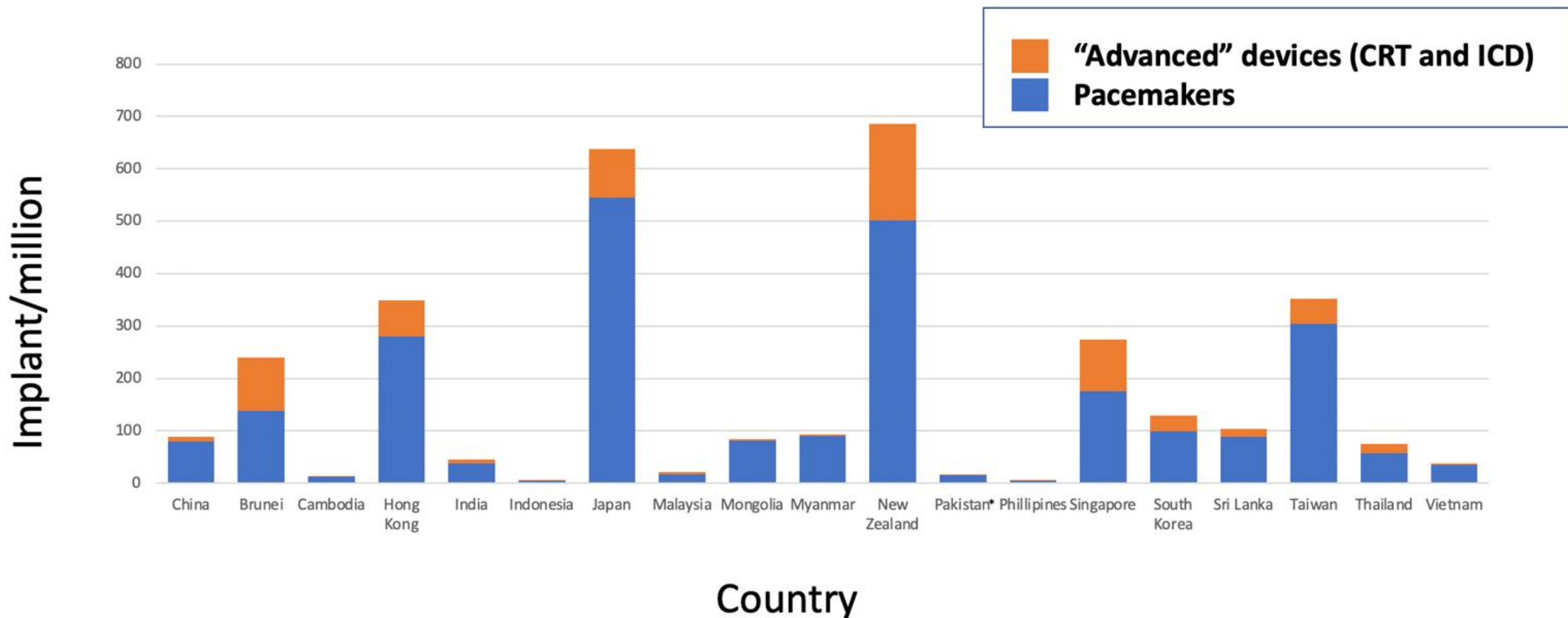
# Indication of ICD implantation in South Korea

(50 million people: Health Insurance Review and Assessment Service database)





# CIED implant rates (implants/million) for different countries in the Asia-Pacific region in 2020(\*Pakistan) and 2021



Sources: APHRS White Book 2021 and 2022; [WWW.Statista.com](http://WWW.Statista.com); [WWW.macrotrends.net](http://WWW.macrotrends.net); data. [Worldbank.org](http://Worldbank.org)

## Percentage of doctors in the general population & doctors who implant pacemakers

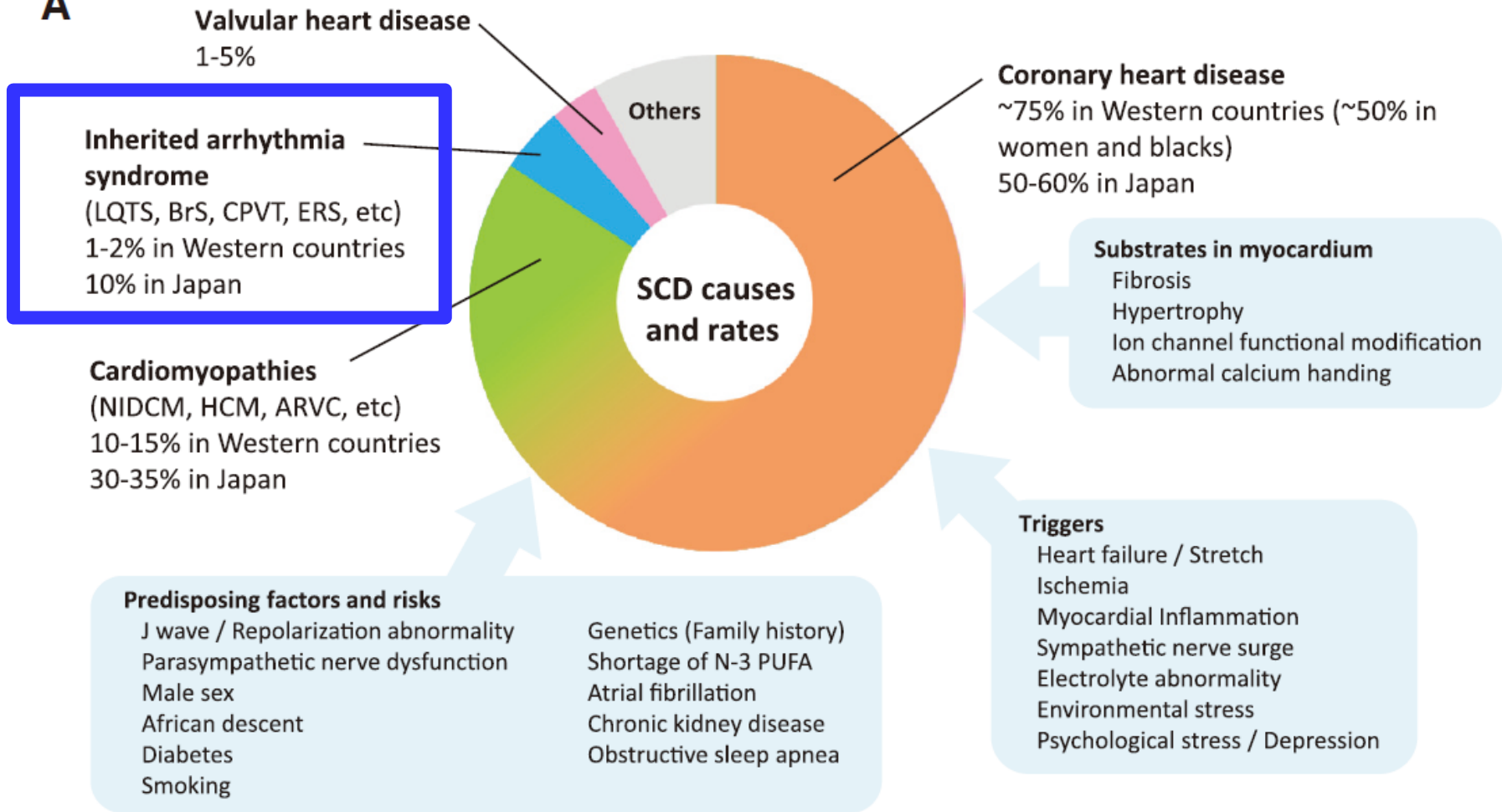
Country	Percentage of physicians in the general population	Percentage of physicians who implant pacemakers
China	0.29%	0.10%
Brunei	0.15%	0.75%
Cambodia	0.00%	20.45%
Hong Kong	<b>0.21%</b>	NA
India	0.10%	NA
Indonesia	0.08%	0.05%
Japan	0.13%	NA
Malaysia	0.00%	3.69%
Mongolia	0.38%	0.05%
Myanmar	0.01%	5.41%
New Zealand	0.32%	0.30%
Pakistan	0.04%	0.02%
Phillipines	0.12%	0.04%
Singapore	0.28%	0.16%
South Korea	<b>0.25%</b>	<b>0.09%</b>
Sri Lanka	0.09%	0.06%
Taiwan	0.22%	1.81%
Thailand	0.06%	NA
Vietnam	0.11%	0.12%

## Country specific barriers to providing best arrhythmia care

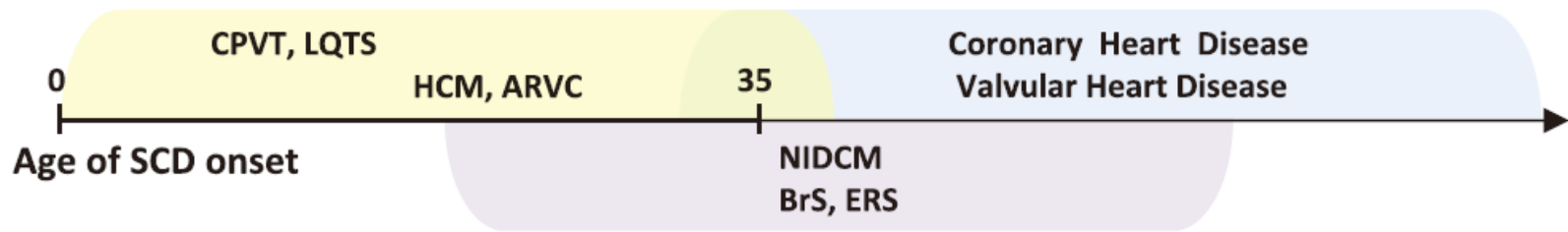
Country	Significant Obstacle
China	<ul style="list-style-type: none"> <li>Lack of reimbursement and financial resources</li> </ul>
Brunei	<ul style="list-style-type: none"> <li>None</li> </ul>
Cambodia	<ul style="list-style-type: none"> <li>Lack of centers</li> <li>Lack of reimbursement and financial resources</li> <li>Lack of trained personnel</li> <li>Lack of operators</li> </ul>
India	<ul style="list-style-type: none"> <li>Lack of reimbursement and financial resources</li> <li>Lack of trained personnel</li> <li>Lack of awareness of guidelines</li> </ul>
Indonesia	<ul style="list-style-type: none"> <li>Lack of reimbursement and financial resources</li> </ul>
Japan	<ul style="list-style-type: none"> <li>None</li> </ul>
Malaysia	<ul style="list-style-type: none"> <li>Lack of reimbursement and financial resources</li> <li>Lack of trained personnel</li> <li>Lack of referral</li> <li>Lack of awareness of guidelines</li> <li>Lack of operators</li> </ul>
Mongolia	<ul style="list-style-type: none"> <li>Lack of centers</li> <li>Lack of awareness of guidelines</li> <li>Lack of trained personnel</li> <li>Lack of operators</li> </ul>
Myanmar	<ul style="list-style-type: none"> <li>Lack of reimbursement and financial resources</li> </ul>
New Zealand	<ul style="list-style-type: none"> <li>None</li> </ul>
Pakistan (2021)	<ul style="list-style-type: none"> <li>Lack of centers</li> </ul>
Philippines	<ul style="list-style-type: none"> <li>Lack of reimbursement and financial resources</li> <li>Lack of awareness of guidelines</li> <li>Lack of trained personnel</li> <li>Lack of operators</li> </ul>
Singapore	<ul style="list-style-type: none"> <li>None</li> </ul>
Sri Lanka	<ul style="list-style-type: none"> <li>Lack of centers</li> <li>Lack of reimbursement and financial resources</li> </ul>
South Korea	<ul style="list-style-type: none"> <li>None</li> </ul>
Taiwan	<ul style="list-style-type: none"> <li>Lack of reimbursement and financial resources</li> </ul>
Thailand	<ul style="list-style-type: none"> <li>Lack of reimbursement and financial resources</li> <li>Lack of referral</li> <li>Lack of awareness of guidelines</li> </ul>
Vietnam	<ul style="list-style-type: none"> <li>Lack of reimbursement and final resources</li> <li>Lack of referral</li> <li>Lack of trained personnel</li> </ul>

# **Inherited arrhythmia predisposing to SCD**

**A**

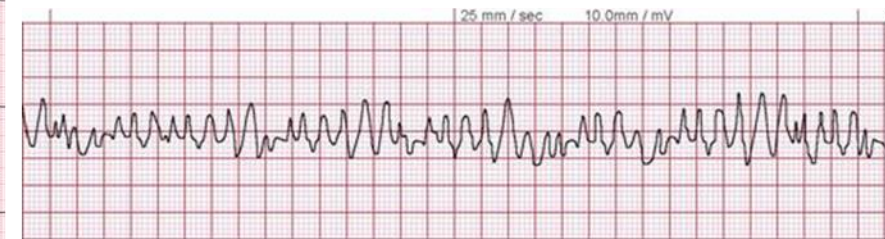
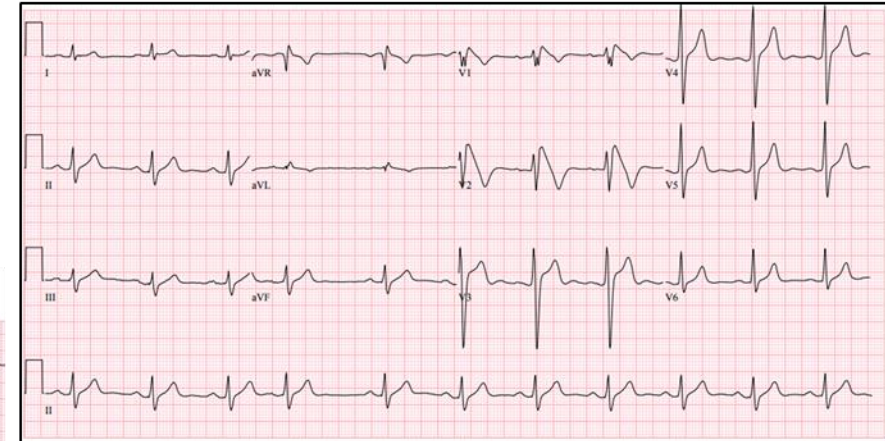
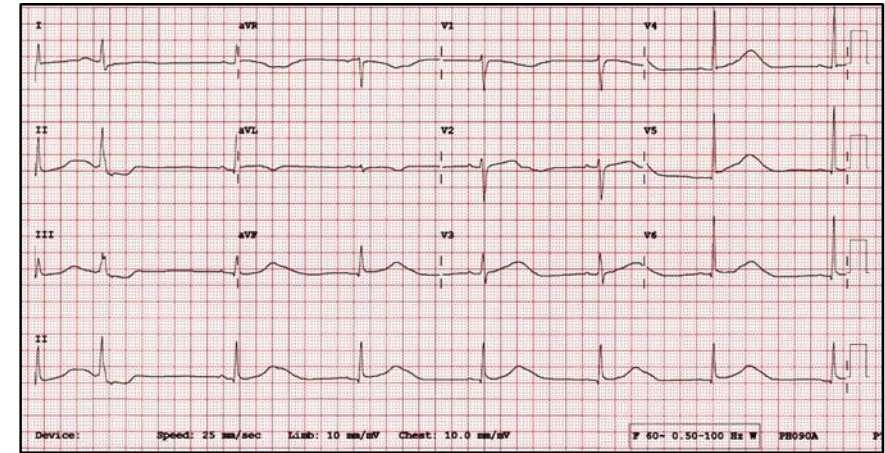


**B**



# Inherited arrhythmia syndrome or primary electrical disorder

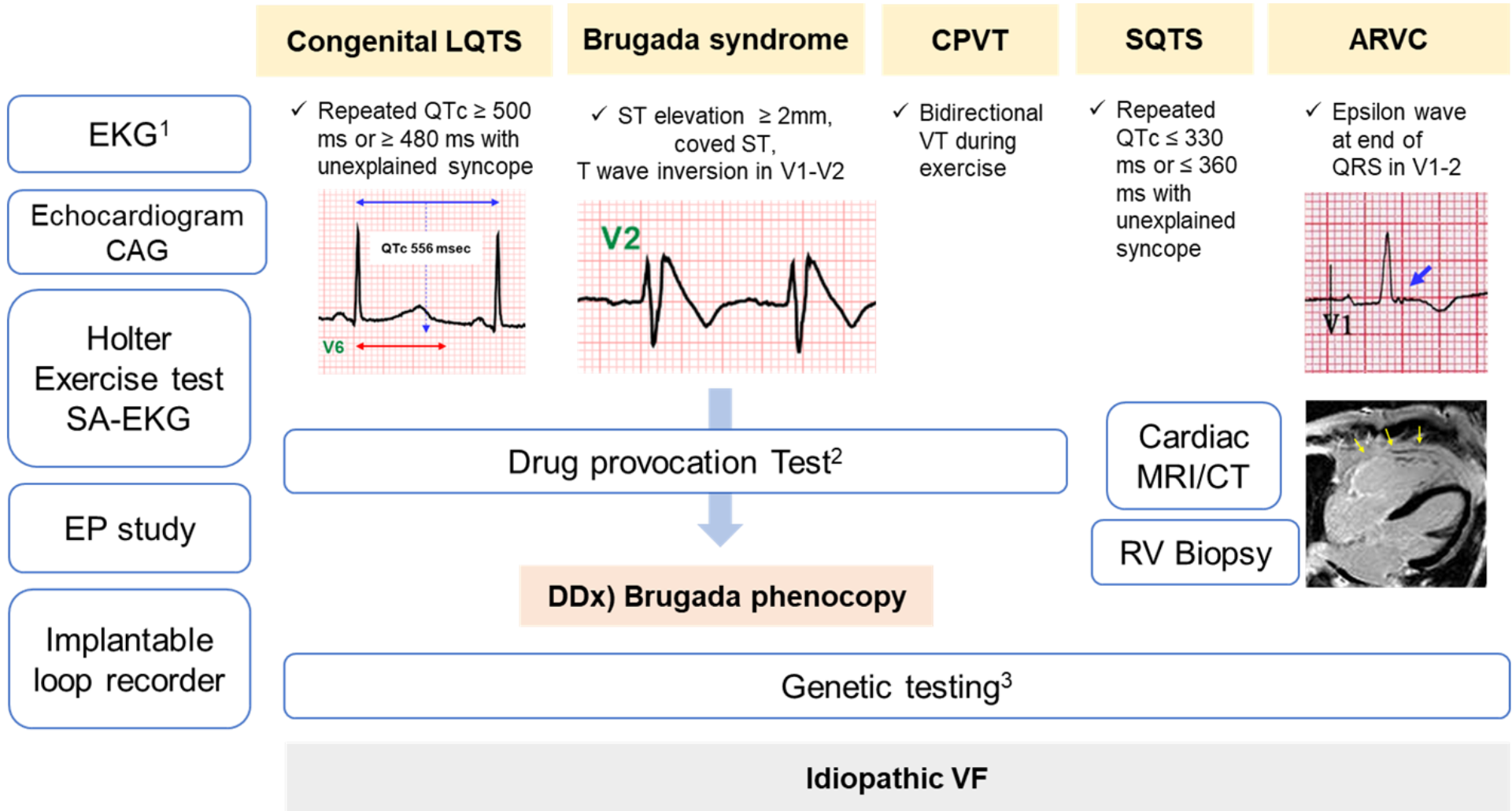
- Long QT syndrome
- Brugada syndrome
- Short QT syndrome
- Catecholaminergic polymorphic ventricular tachycardia
- Early repolarization (J wave) syndrome
- Idiopathic ventricular fibrillation
- Arrhythmogenic right ventricular cardiomyopathy



- 1<sup>st</sup> manifestation-SCA, syncope
- Early prediction
- Genetic/familial-not curable
- Mostly young-socioeconomic impact
- ICD

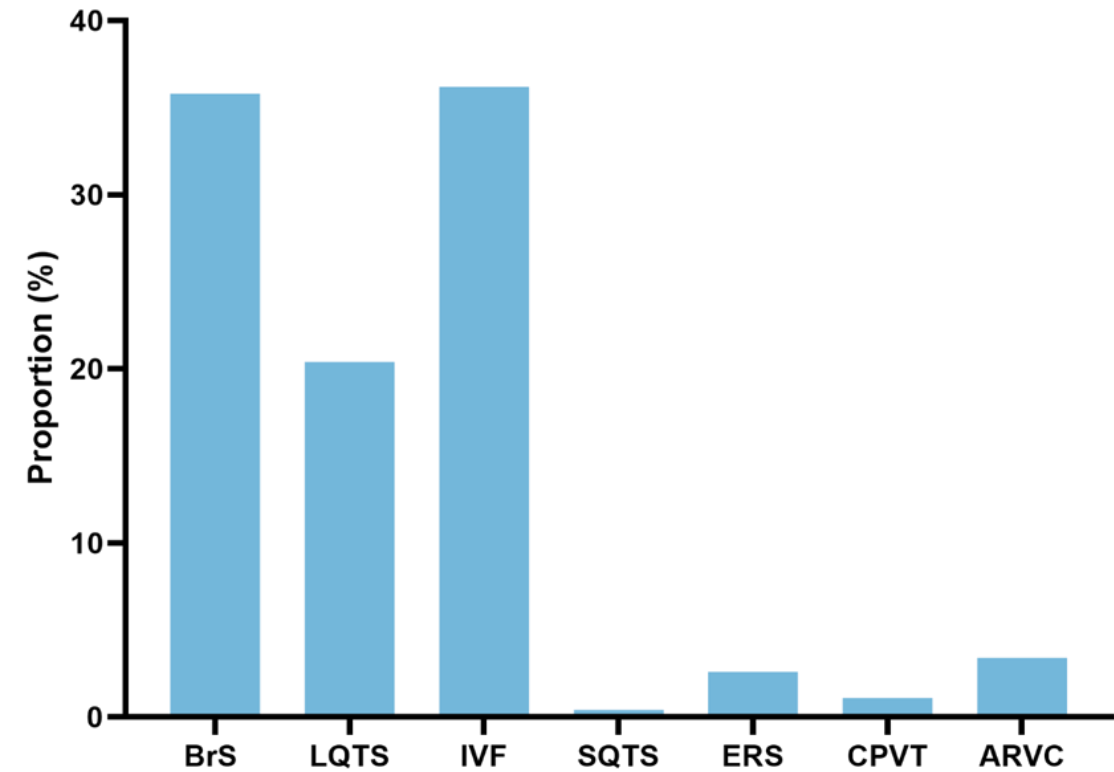
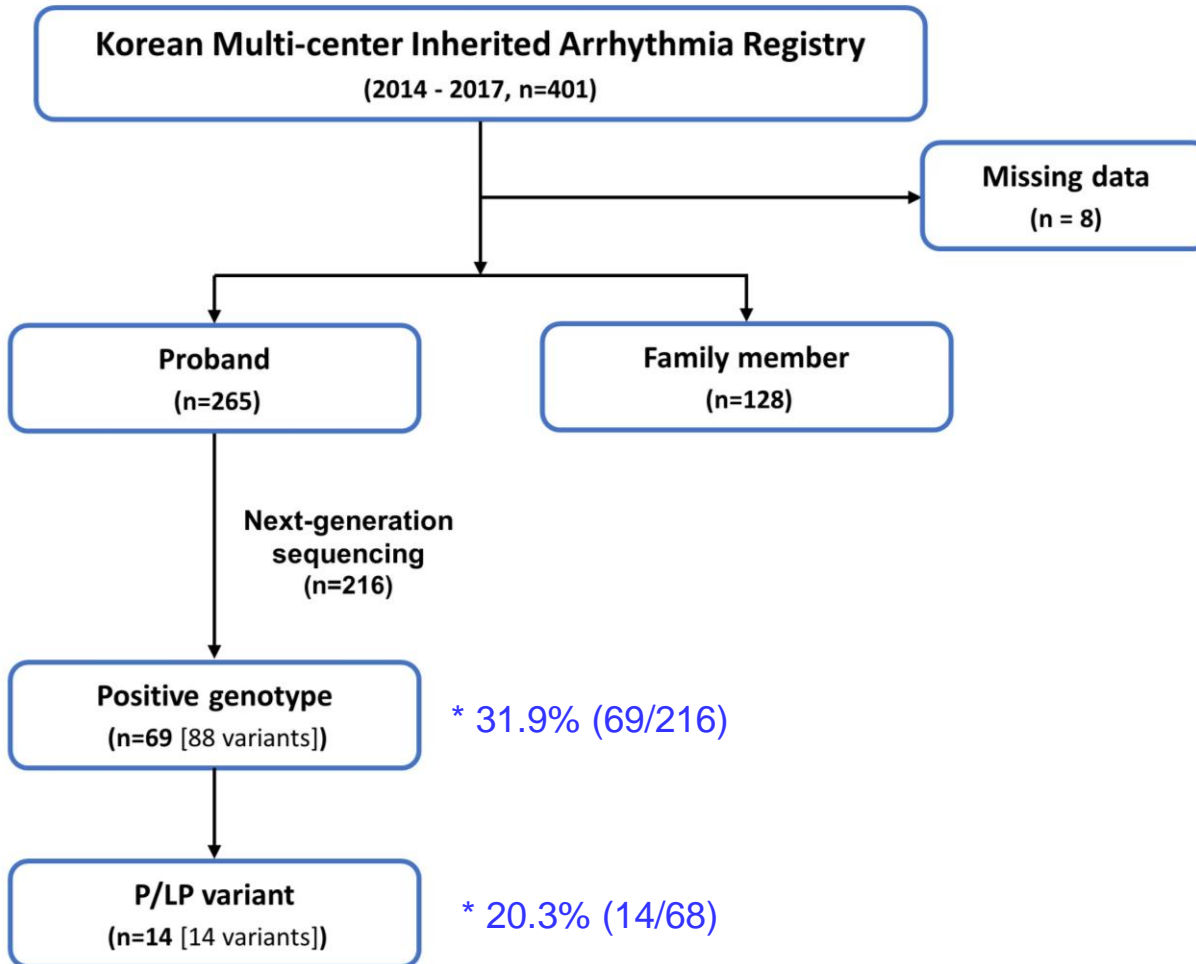


# A diagnostic algorithm in inherited arrhythmia syndrome



1. Bazett or Fridericia formula; standard & upper level (up to the 2<sup>nd</sup> or 3<sup>rd</sup> intercostal space)
2. Epinephrine for LQTS, CPVT; procainamide or flecainide for Brugada Syndrome
3. Next-generation sequencing panels for channelopathies and cardiomyopathies

# Clinical and genetic features of Korean inherited arrhythmia probands



# Clinical characteristics of patients with LQTS in the international registries

	Korean IA registry (n=54)	Korean single center <sup>1</sup> (n=62)	Burns et al. <sup>2</sup> (Australia) (n=78)	Earle et al. <sup>3</sup> (New Zealand) (n=309)	Goldenberg et al. <sup>4</sup> (7 Multi-national) (n=1861)	Sauer et al. <sup>5</sup> (International LQTS registry) (n=812)
Mean age (years)	38±17	15.8	40±18	30	NA	32
Female (n, %)	42 (78%)	34 (55%)	57 (73%)	184 (60%)	1075 (58%)	469 (58%)
History of syncope (n, %)	18 (33%)	26 (42%)	39 (50%)	72 (23%)	655 (35%)	NA
History of SCD (n, %)	27 (50%)	15 (24%)	25 (32%)	48 (16%)	191 (10%)	NA
Family history of SCD (n, %)	8 (15%)	NA	NA	40 (13%)	NA	NA
ICD implantation (n, %)	33 (61%)	6 (10%)	40 (51%)	NA	223 (12%)	9 (1%)
QTc interval (msec)	504	539	515	480	480	489
Beta-blocker (n, %)	41 (76%)	41 (66%)	66 (85%)	NA	930 (50%)	149 (18%)

1. J Korean Med Sci 2013; 28: 1454-1460

2. J Arrhythm. 2016;32:456-461

3. Earle Heart Rhythm 2013;10:233–238

4. Golden J Am Coll Cardiol. 2011;57:51–59

5. Sauer J Am Coll Cardiol 2007;49:329–37



# Clinical characteristics of patients with BrS in the international registries

	Korean IA registry (n=90)	Japanese multi-center registry <sup>1</sup> (n=415)	Sieira et al. <sup>2</sup> (Belgium) (n=404)	Delise et al. <sup>3</sup> (Italy) (n=320)	FINGER registry <sup>4</sup> (n=1029)	Eckardt et al. <sup>5</sup> (Europe) (n=212)	Brugada et al. <sup>6</sup> (Europe) (n=443)	Silvia et al. <sup>7</sup> (Italy) (n=200)	Brugada et al. <sup>8</sup> (n=334)
Mean age (years)	41±13	46±14	43±16	43	45	45±6	42±14	41±18	42±16
Male (n, %)	84 (93%)	403 (97%)	235 (58.2%)	258 (81%)	745 (72%)	152 (72%)	342 (77%)	152 (76%)	225 (67%)
History of syncope (n, %)	27 (30%)	99 (24%)	114 (28%)	105 (34%)	313 (30%)	65 (31%)	100 (23%)	34 (17%)	73 (22%)
History of SCD (n, %)	50 (56%)	88 (21%)	17 (4.2%)	NA	62 (6%)	24 (11%)	80 (18%)	22 (11%)	71 (21%)
FHx of SCD (n, %)	23 (26%)	64 (15%)	187 (47%)	94 (29%)	264 (26%)	60 (28%)	NA	26/130 (22%)	180 (54%)
ICD implantation (n, %)	70 (78%)	241 (58%)	168 (42%)	110 (34%)	433 (42%)	113 (53%)	NA	52 (26%)	129 (39%)
Type I ECG (n, %)	50/56 (89%)	299 (72%)	NA	174 (54%)	468 (45%)	125 (59%)	NA	90/176 (51%)	NA
SCN5A genotype (n, %)	NA	60 (14%)	53 (22%)	NA	185 (18%)	57/183 (31%)	NA	28/130 (22%)	NA

1 Circulation. 2017;135:2255–2270

2 Circ Arrhythm Electrophysiol. 2015;8:777–784.

3 Eur Heart J. 2011;32:169–176

4 Circulation. 2010;121:635–643

5 Circulation. 2005;111:257–263

6 J Cardiovasc Electrophysiol 2003;14:455–457

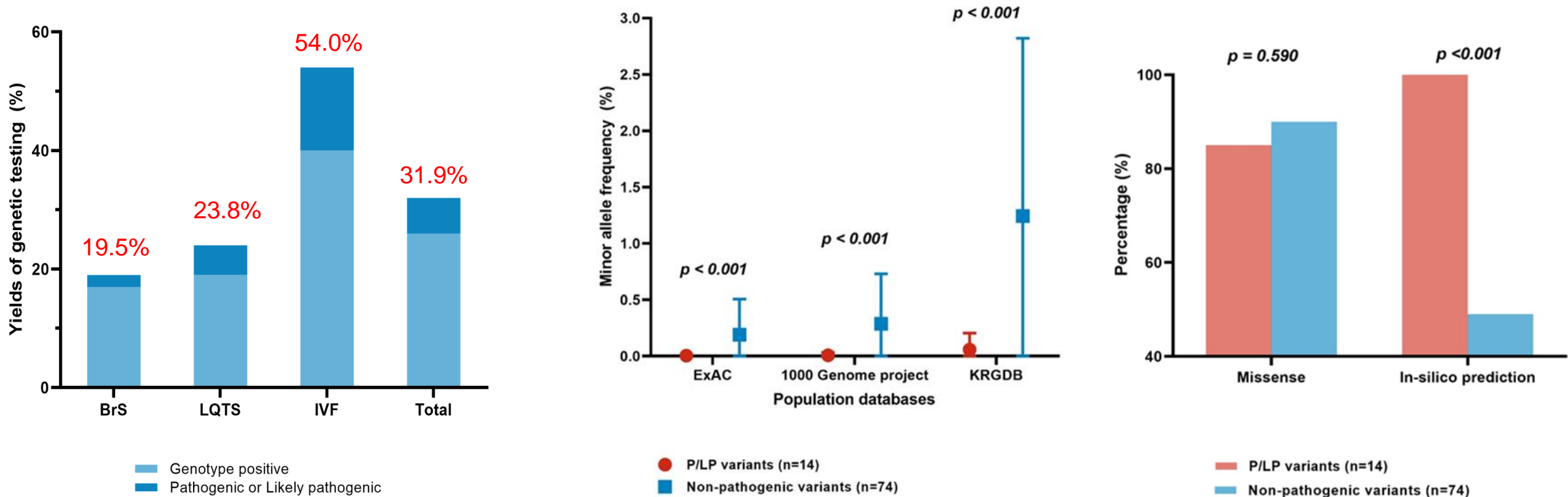
7 Circulation. 2002;105:1342–1347

8 Circulation. 2002;105:73–78

# **Genetic testing in patients with inherited arrhythmia**

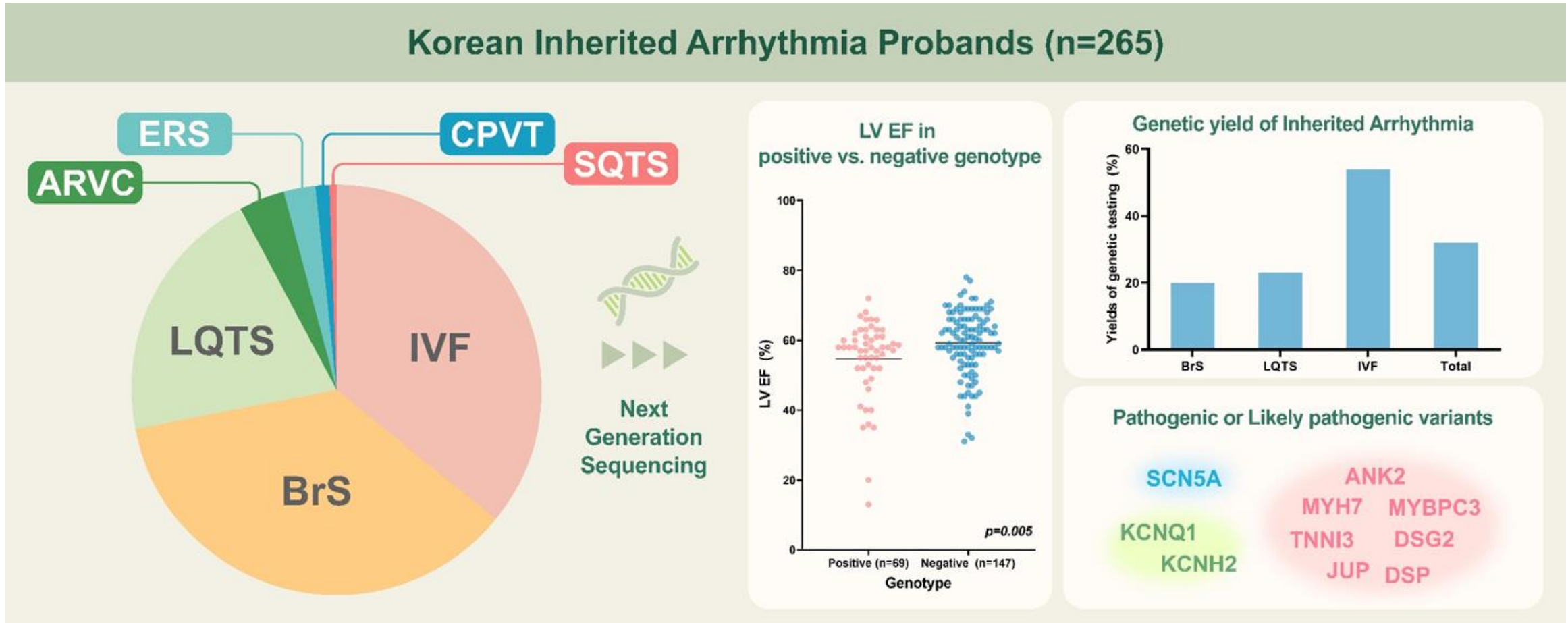
# Yield of genetic testing according to diagnosis

## From the Korea Inherited Arrhythmia Registry (2014~2017)



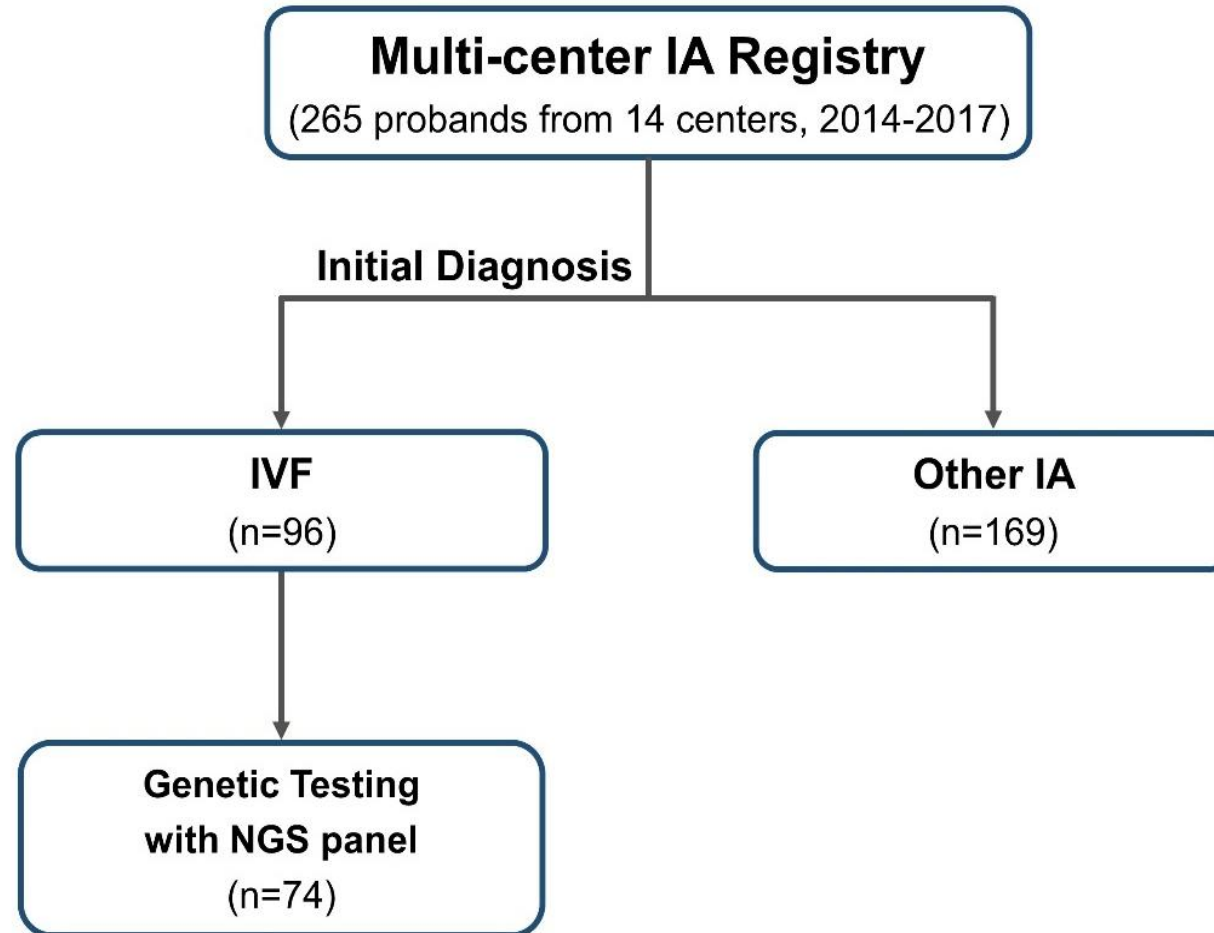
- The large-volume gene panel did not provide better yield for BrS and LQTS.
- Multiple genetic sequencing might enable the molecular diagnosis of concealed phenotypes in IVF, which might change management strategies in the future.

# Distribution and characteristics of Korean inherited arrhythmia probands

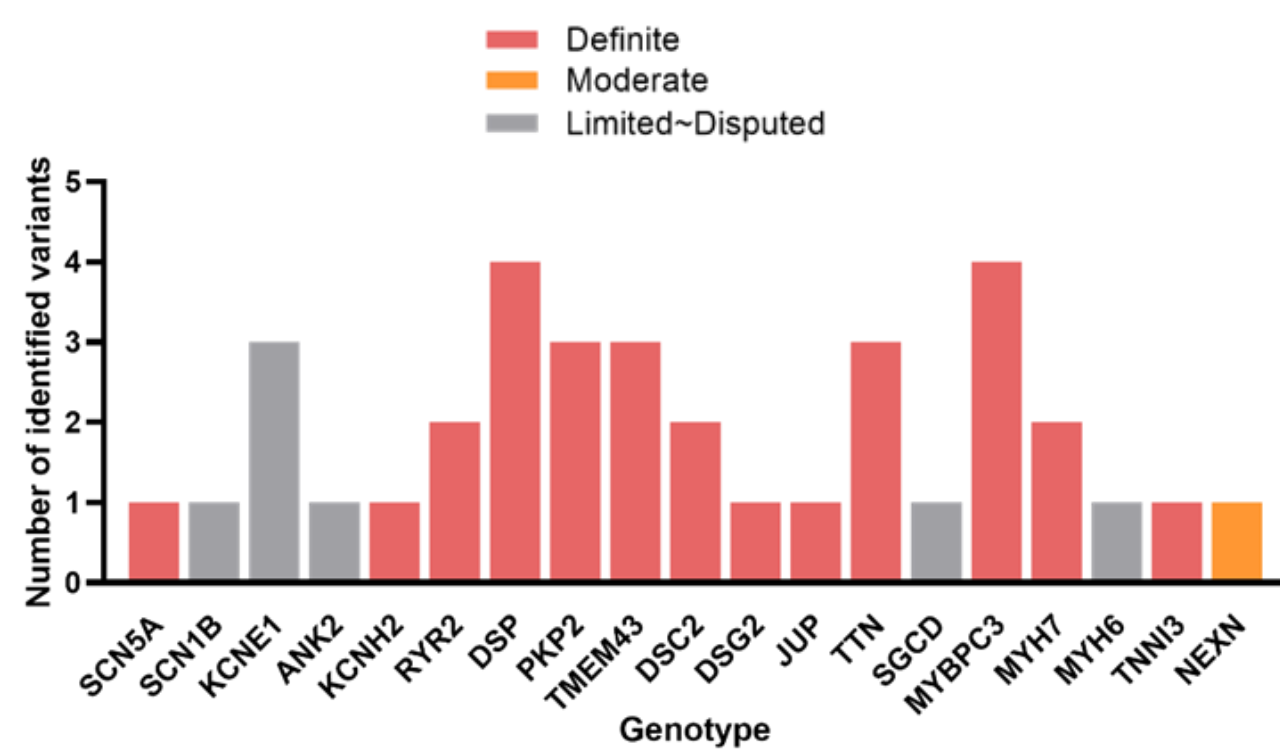


- In IVF probands, genetic screening for cardiovascular disease-associated genes may be promising to unveil hidden phenotype such as concealed cardiomyopathy.

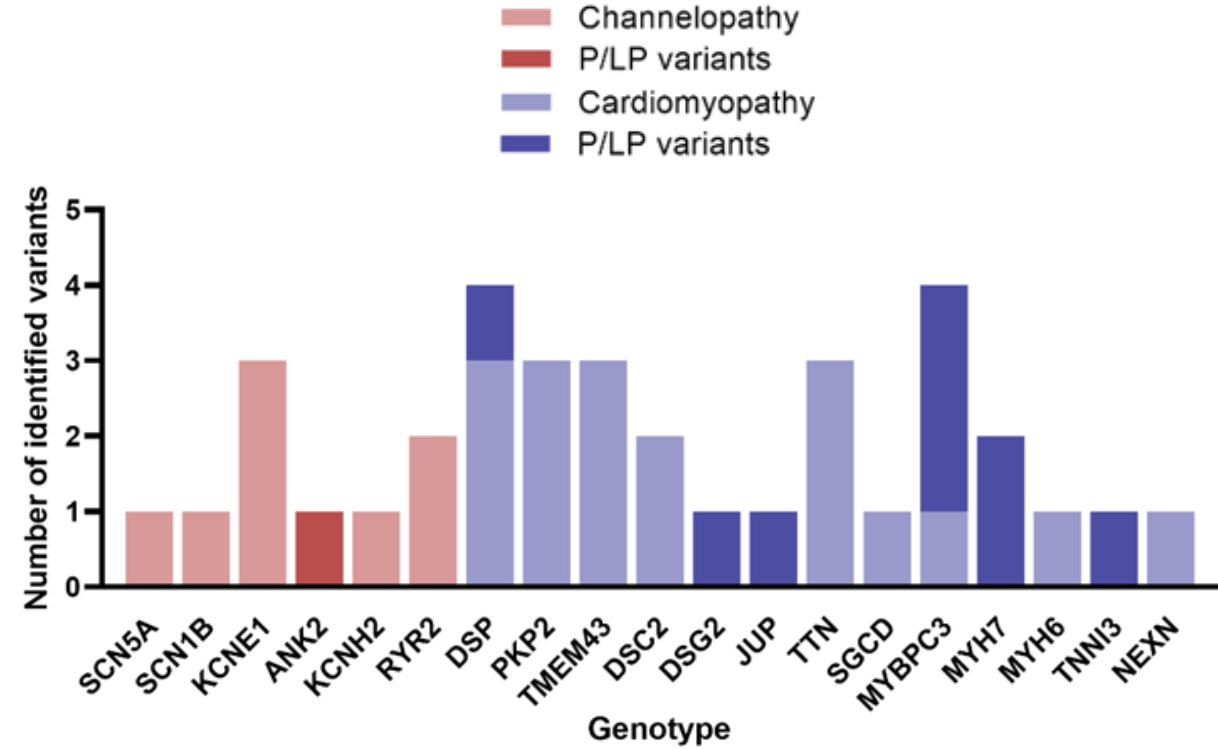
# NGS-based genetic testing in patients initially diagnosed *Idiopathic Ventricular Fibrillation*



# Results of NGS-based genetic testing in IVF probands

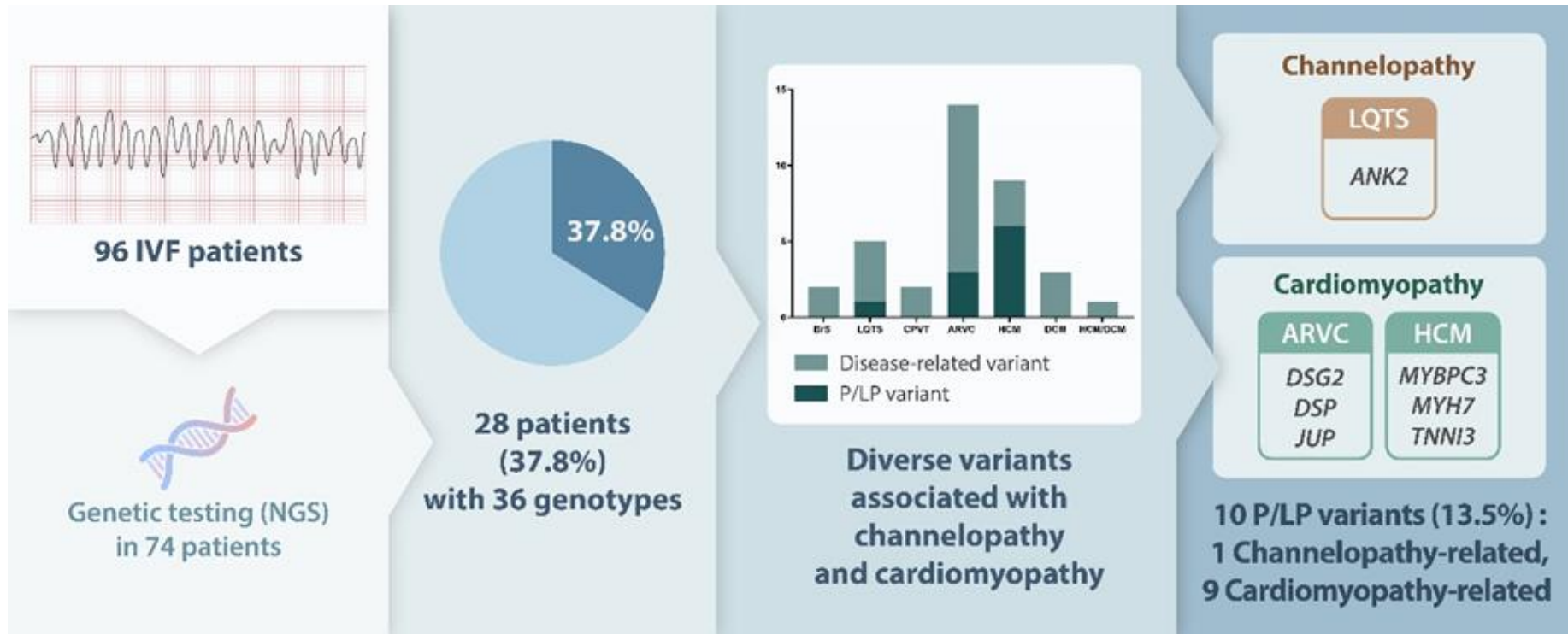


\*Level of evidence supported by gene/disease relationship curated by ClinGen



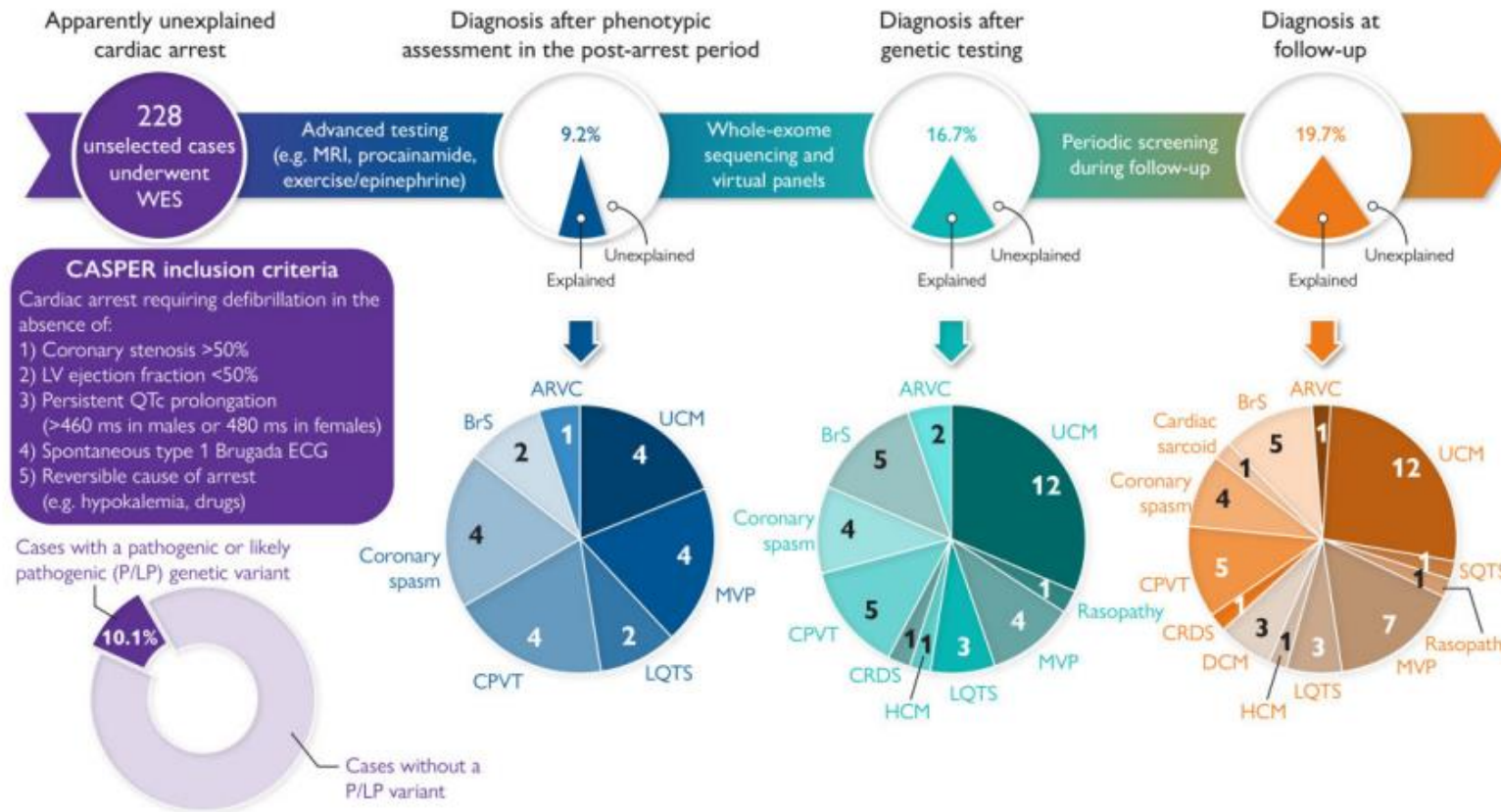
\*Identified variants were classified by channelopathy/cardiomyopathy and pathogenicity

# Concealed arrhythmia syndrome using NGS–based genetic testing in patients initially diagnosed idiopathic ventricular fibrillation



- NGS-based genetic testing could detect causal genetic variants up to **13.5% (LP/P)** in patients initially diagnosed with IVF, suggesting genetic testing with strong to definite evidence genes of cardiomyopathy may enable molecular diagnosis in patients with IVF.
- Patients with positive genotypes should be consistently monitored to unveil concealed underlying causes of their conditions.

# Genetic testing in unexplained cardiac arrest in Caucasian



- Genetic testing identifies a disease-causing variant in **10%** of apparent UCA survivors.
- The majority of disease-causing variants was located in **cardiomyopathy-associated genes**, highlighting the arrhythmogenic potential of such variants in the absence of an overt cardiomyopathy diagnosis.
- The present study supports the **use of genetic testing including assessment of arrhythmia and cardiomyopathy genes in survivors of UCA.**



# Summary

## Sudden cardiac death & inherited arrhythmia

- The incidence of OHCA in South Korea had been increased during the past decade. The post OHCA 1-year mortality rate showed a poor outcome, but improved gradually.
  - ICD implantation rate is still low in South Korea (esp, primary prevention in CAD & IA)
  - SUDS accounted for 14.7% of total SCAs: mostly inherited arrhythmias
  - NGS-based genetic testing in patients with IA has been widely used.
  - Disease-causing variants (mostly, cardiomyopathy) were often found in unexplained cardiac arrest or IVF.
- **Comprehensive evaluation** including **genetic testing** is mandatory in patients with IA.

***Thank you for your attention!***

***“Save one life, Save the entire world”***