

PRECISION MEDICINE IN CARDIOLOGY

TOWARDS A STRATEGY FOR THE PREVENTION
OF SUDDEN CARDIAC DEATH
IN THE YOUNG

INHERITED NET GR

By Aris Anastasakis MD PhD

GSRT
GENERAL SECRETARIAT FOR
RESEARCH AND TECHNOLOGY

**Unit of Inherited and Rare Cardiovascular Diseases
Onassis Cardiac Surgery Centre**



Ωνάσειο
Καρδιοχειρουργικό
Κέντρο

ΜΟΝΑΔΑ

K.κα.πα

Sudden death in YOUNG



ΕΛΛΗΝΙΚΗ ΔΗΜΟΚΡΑΤΙΑ
Υπουργείο Υγείας



ΕΚΑΕ - ΟΑΚΑ

**PREPARTICIPATION
SCREENING
ATHLETES CARD**

**HIGH RISK
GROUP**

GSRT
GENERAL SECRETARIAT FOR
RESEARCH AND TECHNOLOGY

**FIRST AID IN
THE
COMMUNITY-
BLS**



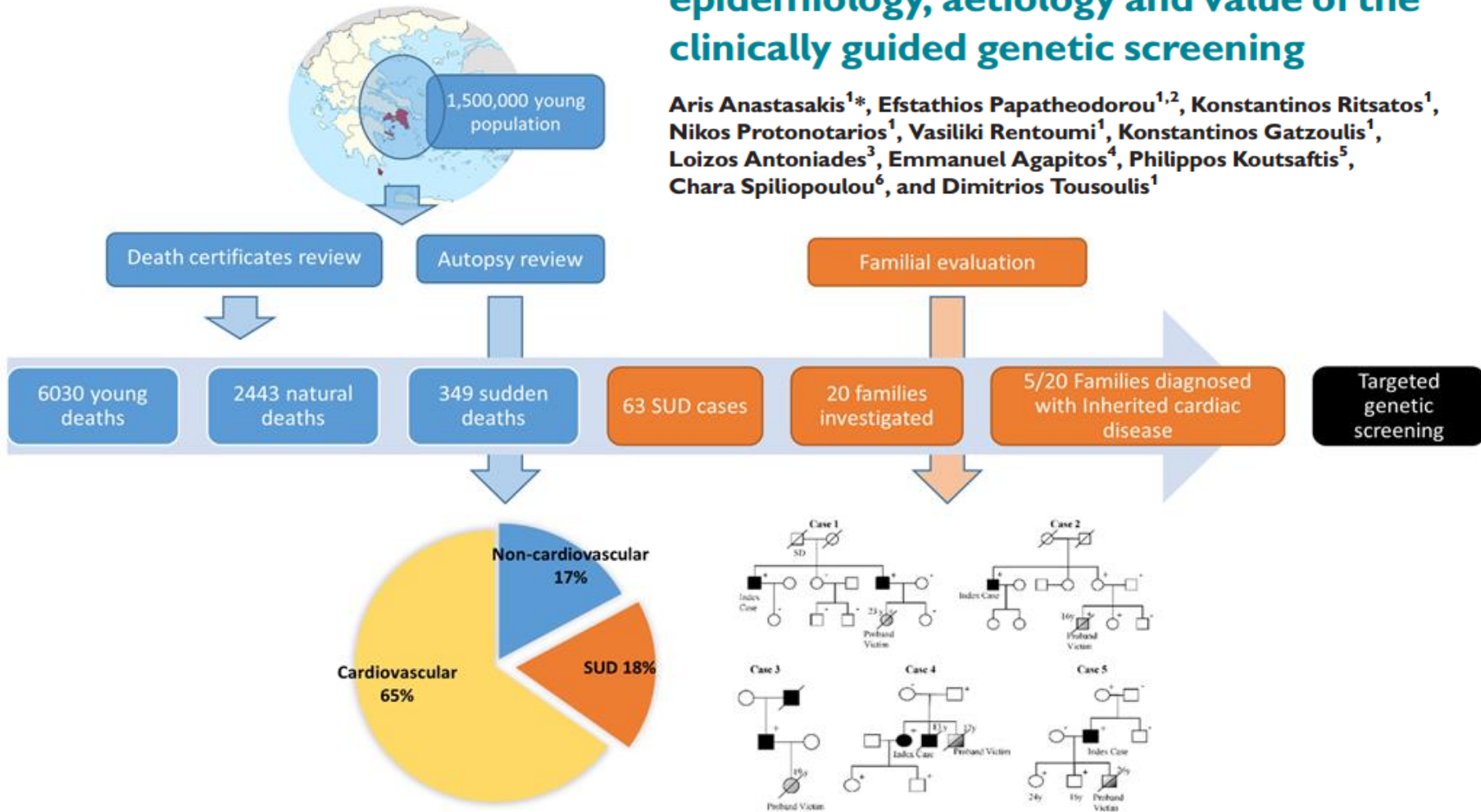
ΕΛΛΗΝΙΚΗ ΚΑΡΔΙΟΛΟΓΙΚΗ ΕΤΑΙΡΕΙΑ
-1948-



Ωνάσειο
Καρδιοχειρουργικό
Κέντρο

Sudden unexplained death in the young: epidemiology, aetiology and value of the clinically guided genetic screening

Aris Anastasakis^{1*}, Efstathios Papatheodorou^{1,2}, Konstantinos Ritsatos¹, Nikos Protonotarios¹, Vasiliki Rentoumi¹, Konstantinos Gatzoulis¹, Loizos Antoniadis³, Emmanuel Agapitos⁴, Philippos Koutsaftis⁵, Chara Spiliopoulou⁶, and Dimitrios Tousoulis¹

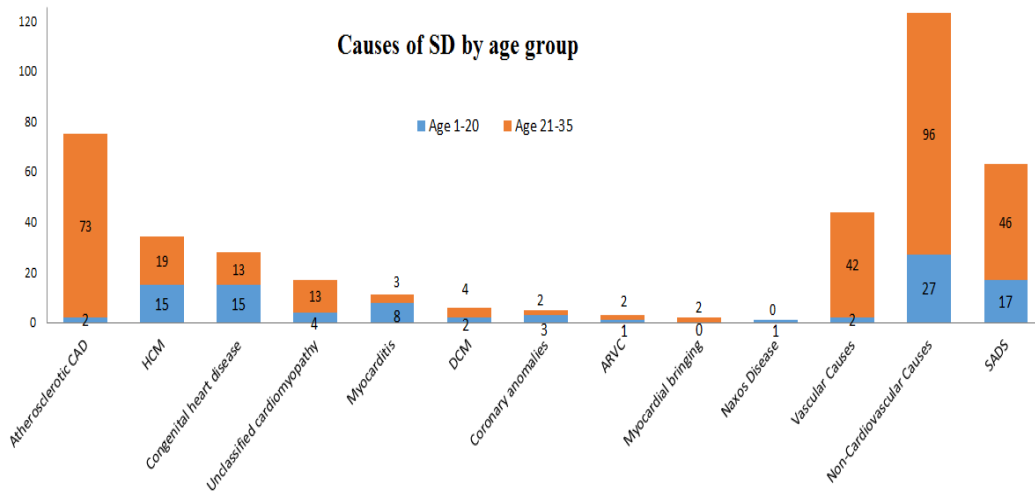


INHERITED CARDIAC DISEASES 1ST CAUSE OF SCD IN AGE < 20 Y OLD

Sudden unexplained death in the young: epidemiology, aetiology and value of the clinically guided genetic screening

Aris Anastasakis^{1*}, Efstathios Papatheodorou^{1,2}, Konstantinos Ritsatos¹, Nikos Protonotarios¹, Vasiliki Rentoumi¹, Konstantinos Gatzoulis¹, Loizos Antoniades³, Emmanuel Agapitos⁴, Philippos Koutsaftis⁵, Chara Siliopoulou⁶, and Dimitrios Tousoulis¹

- 2002-2010 Attica region
- 1.500.000 young population
- 349 young Sudden Deaths
- 4 young deaths / month in Attica
- **10-15 young deaths /month Greece**



**150 -200
SD/year
GREECE**

EUROPACE 2018

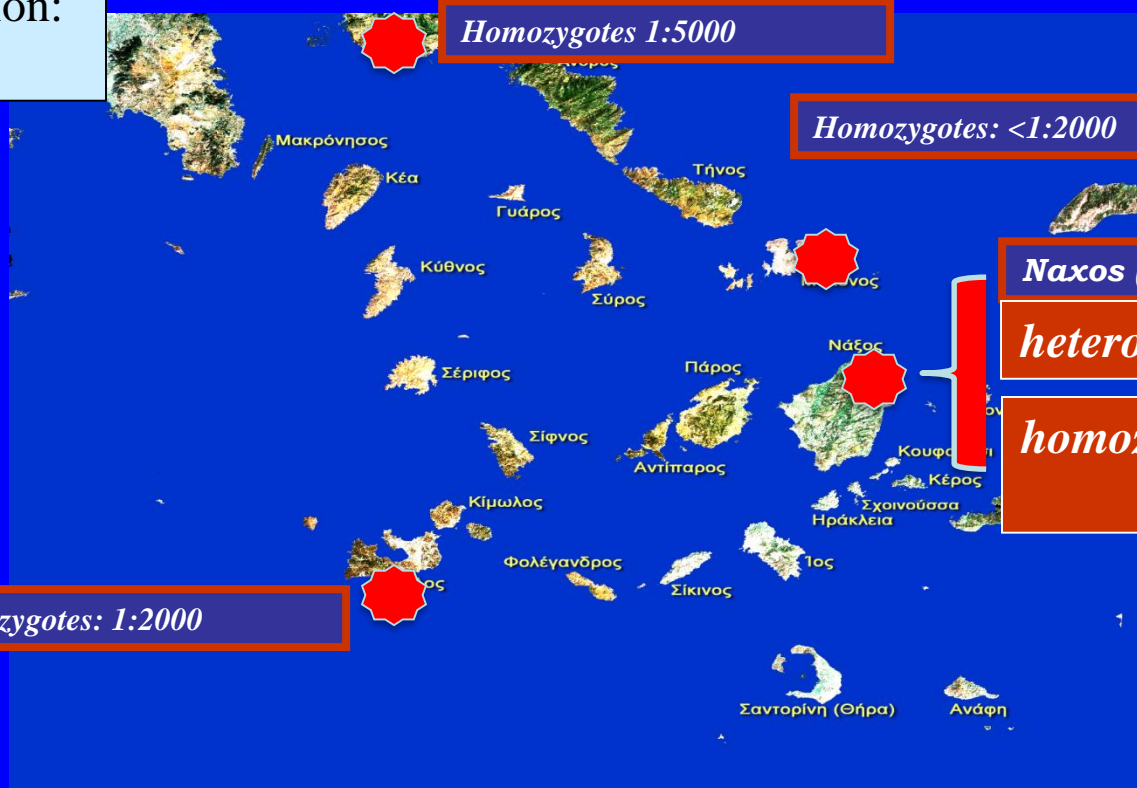
Causes of sudden cardiac death in the young

- **Hypertrophic cardiomyopathy**
 - **Arrhythmogenic cardiomyopathy**
 - **LQTS , BRUGADA , CPVT, SQTS**
-
- **Premature coronary artery disease**
 - **Myocarditis**
 - **Marfan syndrome**
-
- **Coronary artery anomalies**

Naxos disease

NIKOS PROTONOTARIOS PROJECT

Total Population:
265.153



The locality of
rare Inherited
CV diseases

McKoy G, Protonotarios N, Crosby A, Tsatsopoulou A,
Anastasakis A, Coonar A, Norman M, Baboonian C,
Jeffery S, McKenna WJ. *Lancet* 2000;355:2119-2124

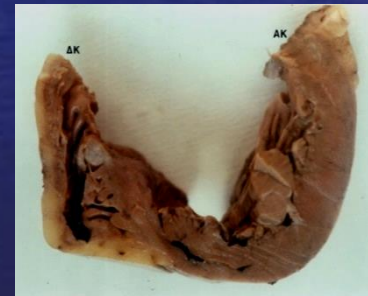
Lancet 2000



NAXOS DISEASE GENE

2000

Plakoglobin mutation JUP 2157del2



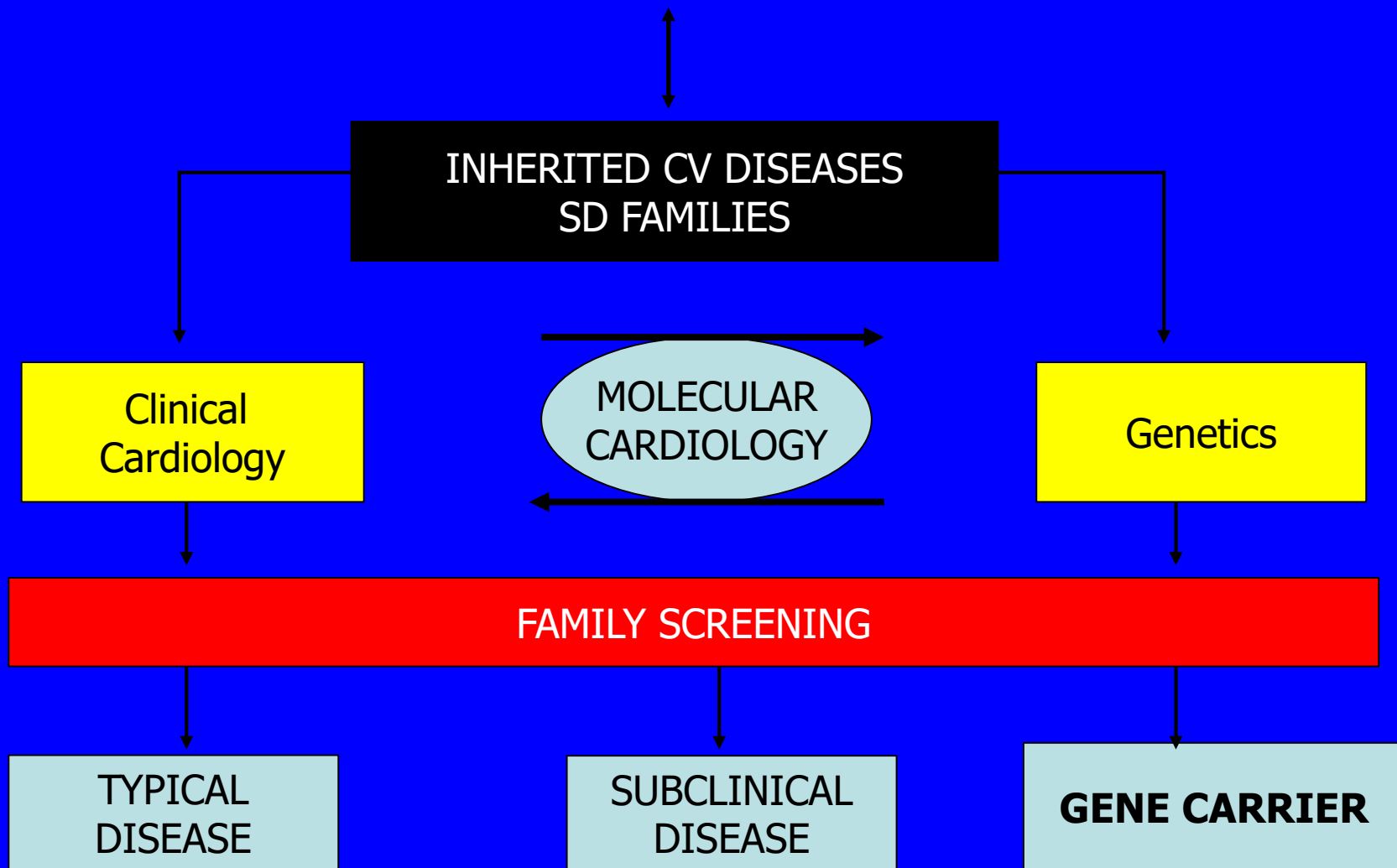
McKoy G, Protonotarios N, Crosby A, Tsatsopoulou A, Anastasakis A, Coonar A, Norman M, Baboonian C, Jeffery S, McKenna WJ. Lancet 2000;355:2119-2124

SPECIAL CHARACTERISTICS

- SUBSTRATE and TRIGGERING FACTOR
Sports Corrado et al JACC 2003
- **ASYMPTOMATIC** C Glinge J Cardiovasc Electrophysiology 2015
- **SUBCLINICAL FORMS** Mckenna Heart 1997

**SCD CAN BE THE FIRST CLINICAL
EXPRESSION OF THE DISEASE**

National Network for the management of inherited CV diseases and SCD prevention in the Young



NATIONAL NET WORK FOR THE PREVENTION OF SD IN THE YOUNG



Ωνάσειο
Καρδιοχειρουργικό
Κέντρο

SUDDEN DEATH IN THE YOUNG



GENERAL SECRETARIAT FOR
RESEARCH AND TECHNOLOGY

STUDENT HEALTH
CARD

PREPARTICIPATION
SCREENING

ATHLETES CARD

HIGH RISK
GROUP

SD DEATH

INHERITED
CV DISEASES

FAMILY SCREENING

FIRST AID IN
THE
COMMUNITY-
BLS

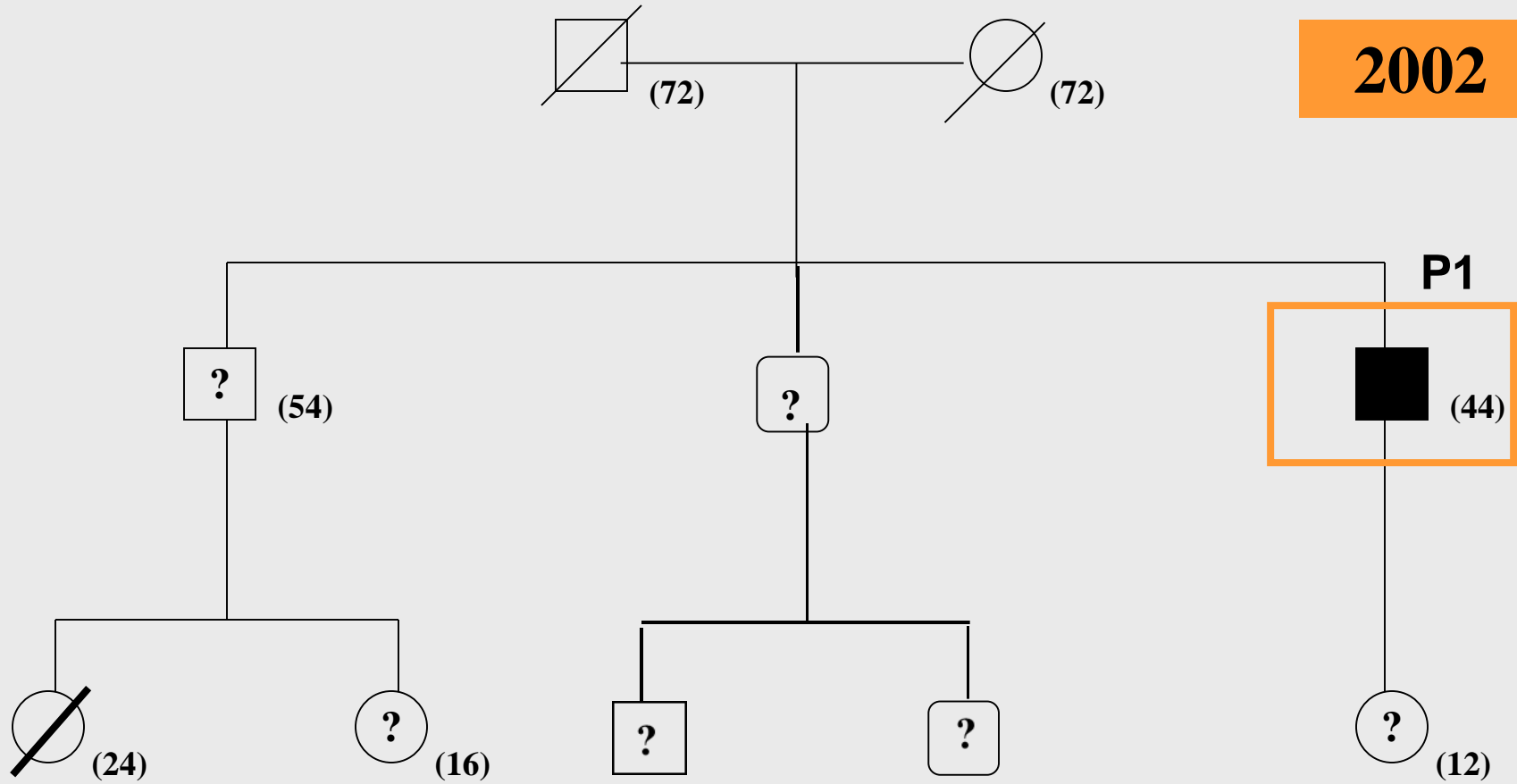
HCS/EKE

NSI/EKAE
HCS/EKE



RESEARCH
& INNOVATION

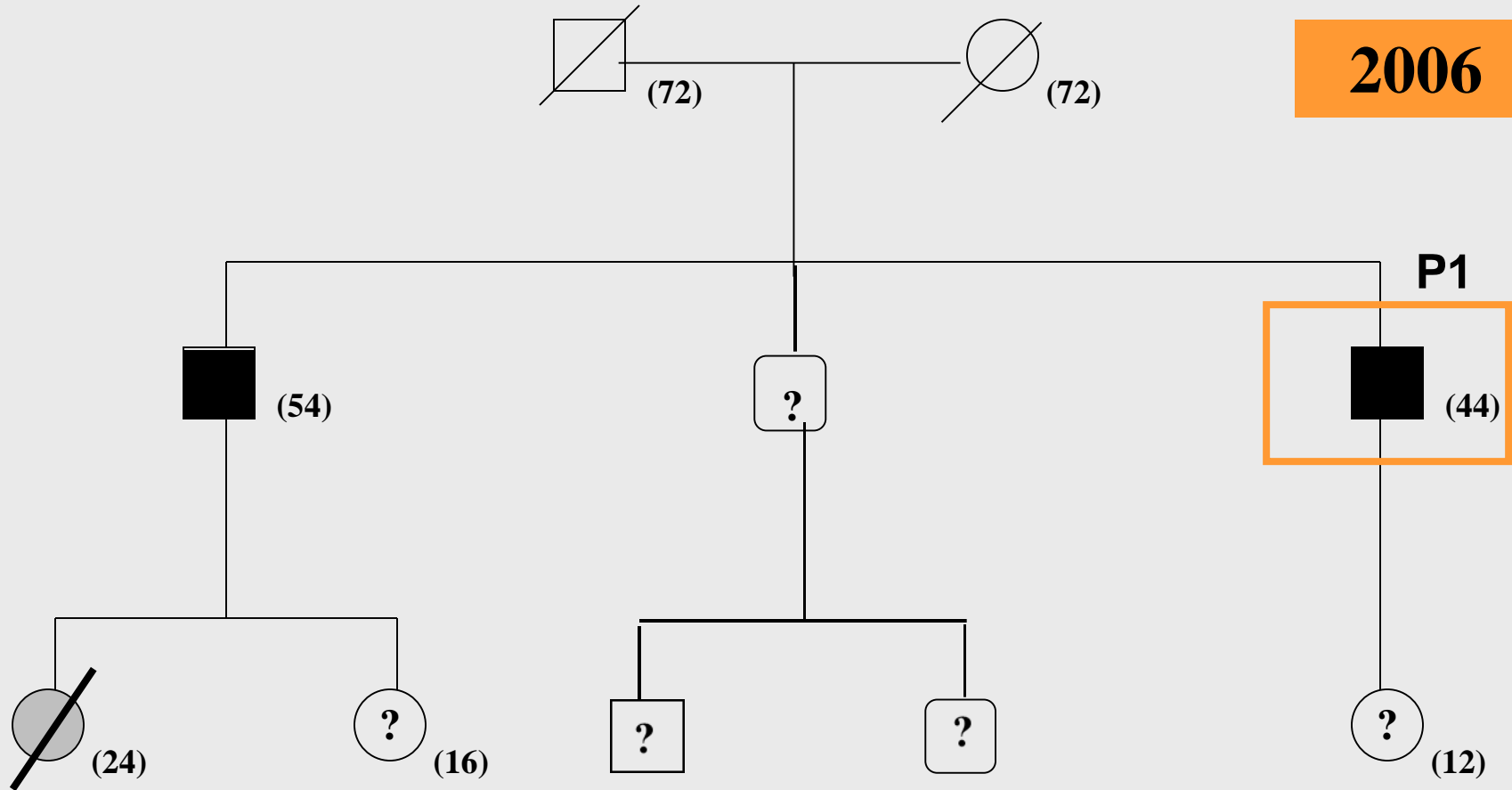
Case A



POST MORTEM

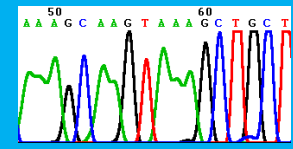
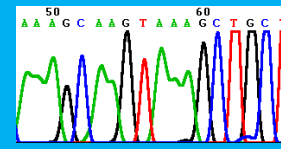
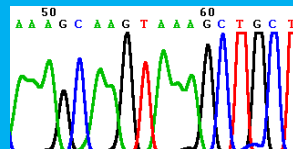
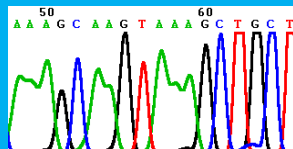
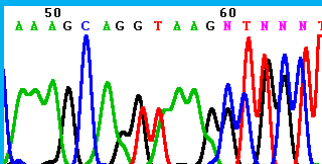
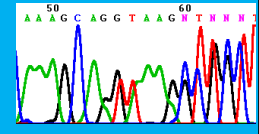
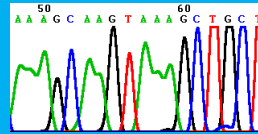
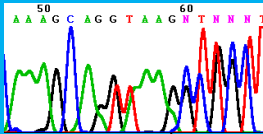
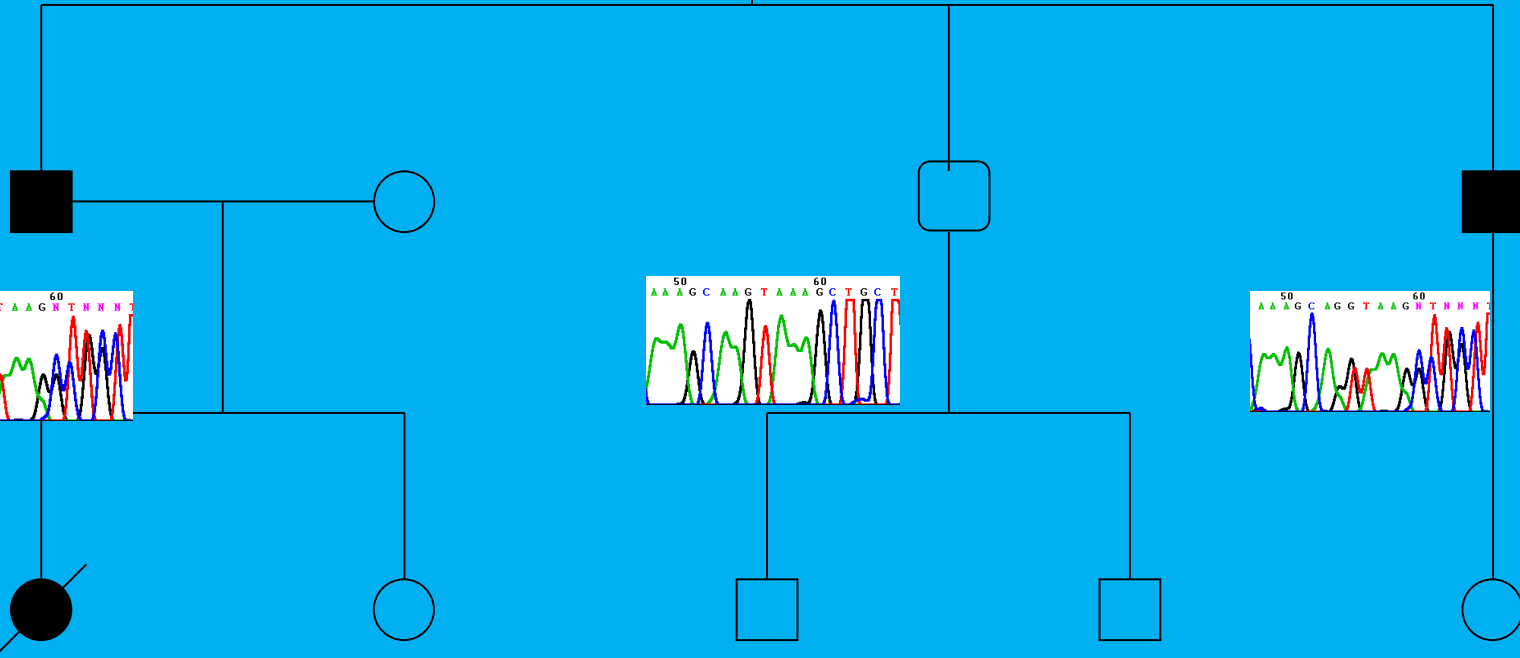
- UNKNOWN CAUSE SD

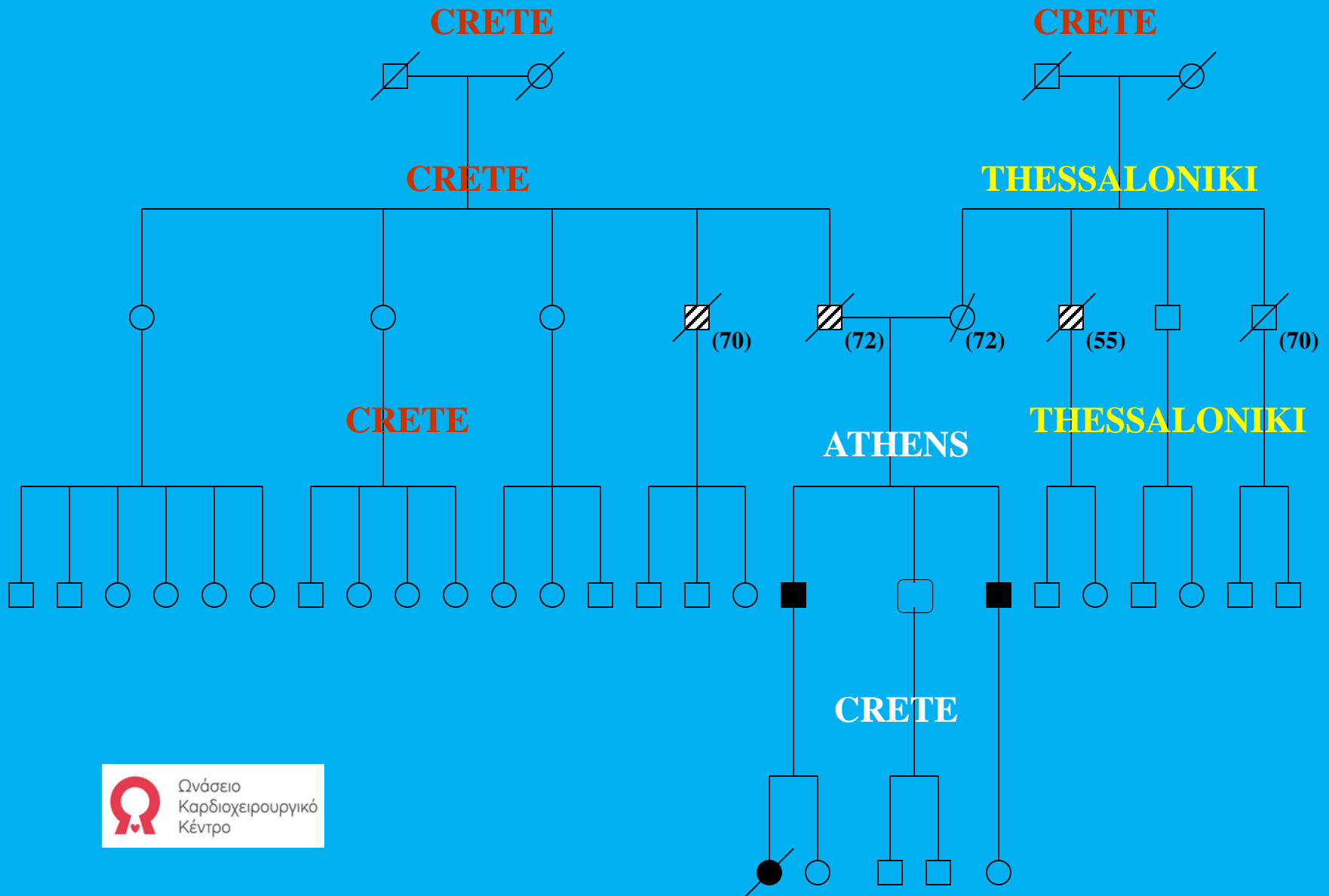
Case A



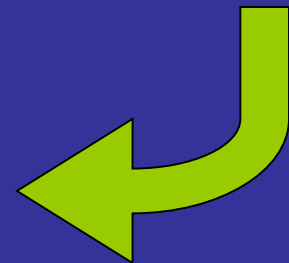
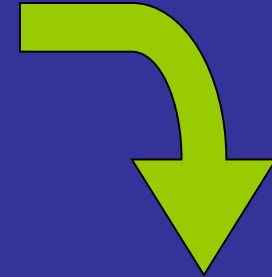
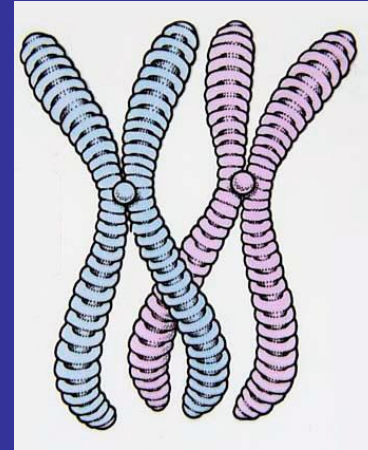
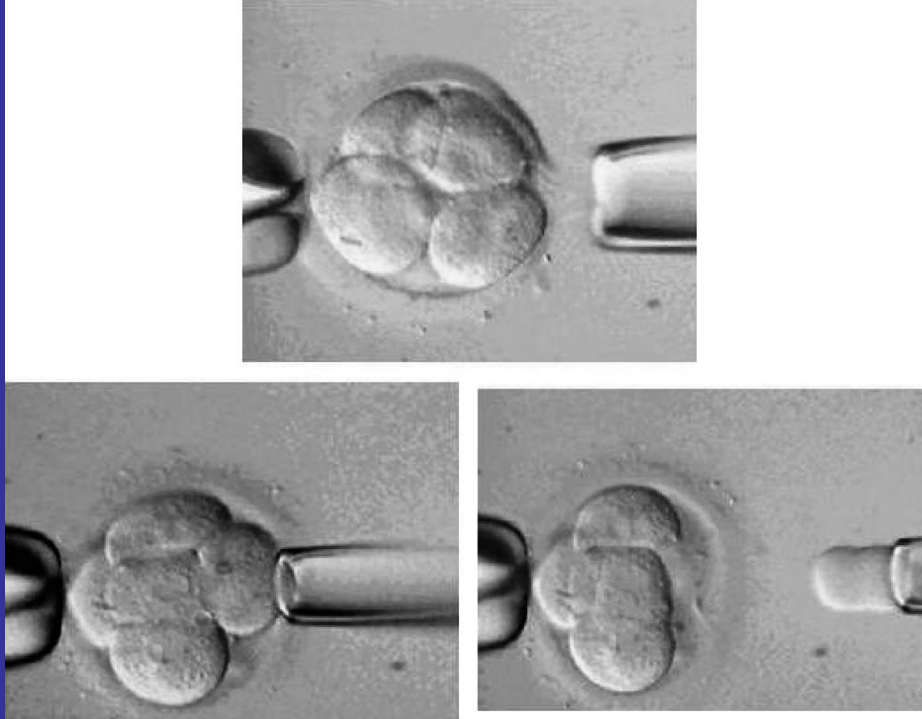
CASE A

SD (72)   (72)





Preimplantation diagnosis



**HARPER et al
UCLH 2012**

NATIONAL NET WORK FOR THE PREVENTION OF SD IN THE YOUNG



Ωνάσειο
Καρδιοχειρουργικό
Κέντρο

SUDDEN DEATH IN THE YOUNG

STUDENT HEALTH
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HIGH RISK GROUP

GERT
GENERAL SECRETARIAT FOR
RESEARCH AND TECHNOLOGY



SD DEATH
INHERITED CV
DISEASES

FAMILY SCREENING

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RESEARCH
& INNOVATION

GSRT

GENERAL SECRETARIAT FOR
RESEARCH AND TECHNOLOGY

FORENSIC
MEDICINE DPT
UNIVERSITY
OF ATHENS

ONASSIS
UNIT OF
INHERITED
DISEASES

**NATIONAL CLINICAL AND GENETIC DATA
NATIONAL MAP OF INHERITED CV DIASESES**

NSI

**NATIONAL
OBSERVATORY OF
SD**

SD IN
THE
YOUNG

**NATIONAL
DATABANK OF
INHERITED CV
DISEASES**

LARISSA

ALEXANDRUPOLI

IIOANNIA

**MINISTRY OF
RESEARCH**

**MINISTRY
OF
RESEARCH**

HIPPOKRAT
EION
HOSP

EVAGELI
SMOS
HOSP

DPT
CARDIOLOGY
UNIV. CRETE

ITE

PATRAS

ΑΧΕΠΑ
THESSALO
NIKI

EKETA

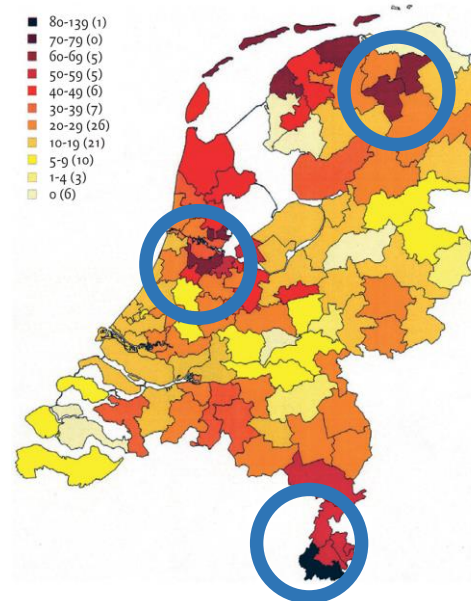
HIPPOKRAT
EION
THESS

RESEARCH
& INNOVATION

LQTS index per 10⁶ inhabitants



- ♥ Large differences between regions
 - ♥ Min. 3 per 10⁶ persons
 - ♥ Max. 110 per 10⁶ persons




State of the art of Rare Cardiovascular Disease activities in the Netherlands

Hofman, et al. NTvG. 2007.

Ice berg phenomenon

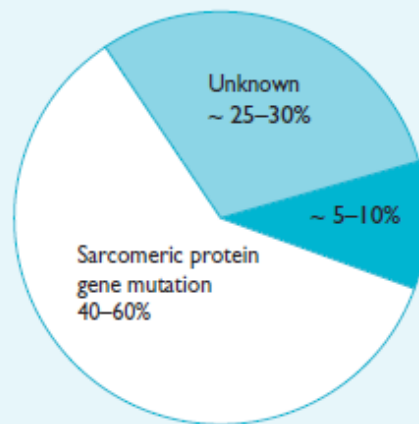
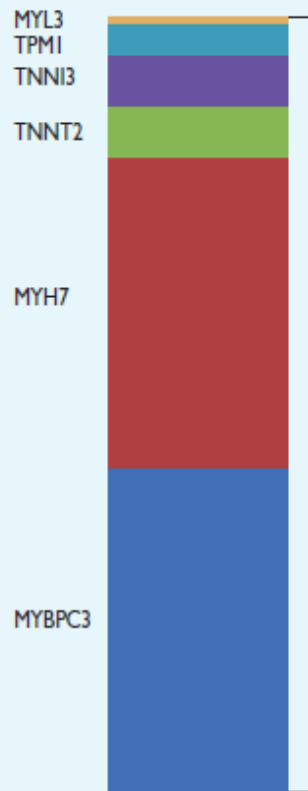
NATIONAL CLINICAL AND GENETIC DATABANK

A photograph of an iceberg floating in the ocean. The tip of the iceberg is visible above the water surface, while the much larger, submerged part is visible below. The water is a deep blue, and the sky is light blue with some clouds.

**Sudden death
In the young**

30 MILLION PEOPLE IN EU

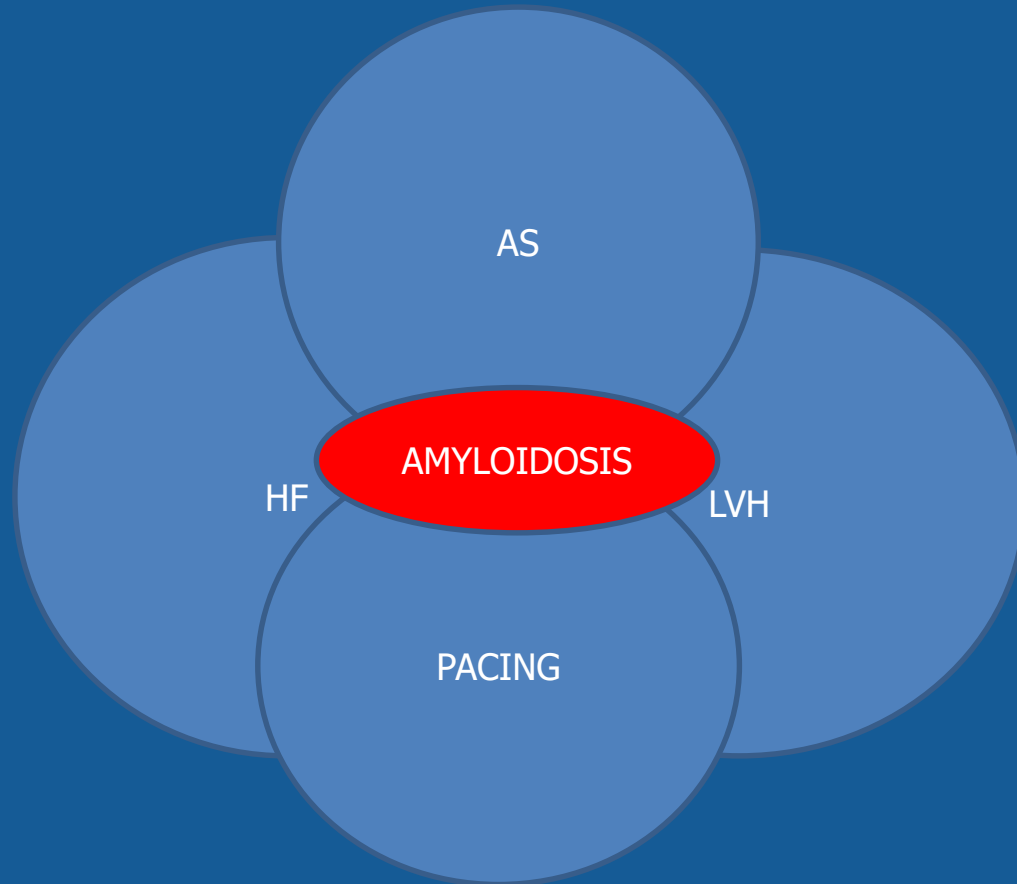
Inherited cv and rare diseases



Other genetic and non-genetic causes

- **Inborn errors of metabolism**
 - Glycogen storage diseases:
 - Pompe
 - Danon
 - AMP-Kinase (PRKAG2)
 - Carnitine disorders
 - Lysosomal storage diseases
 - Anderson-Fabry
- **Neuromuscular diseases**
 - Friedreich's ataxia
 - FHLI
- **Mitochondrial diseases**
 - MELAS
 - MERFF
- **Malformation Syndromes**
 - Noonan
 - LEOPARD
 - Costello
 - CFC
- **Amyloidosis**
 - Familial ATTR
 - Wild type TTR (senile)
 - AL amyloidosis
- **Newborn of diabetic mother**
- **Drug-induced**
 - Tacrolimus
 - Hydroxychloroquine
 - Steroids

Hidden amyloidosis





European Reference Network

for rare or low prevalence complex diseases

 **Network**
Heart Diseases
(ERN GUARD-HEART)

Gateway to Uncommon And Rare Diseases of the Heart

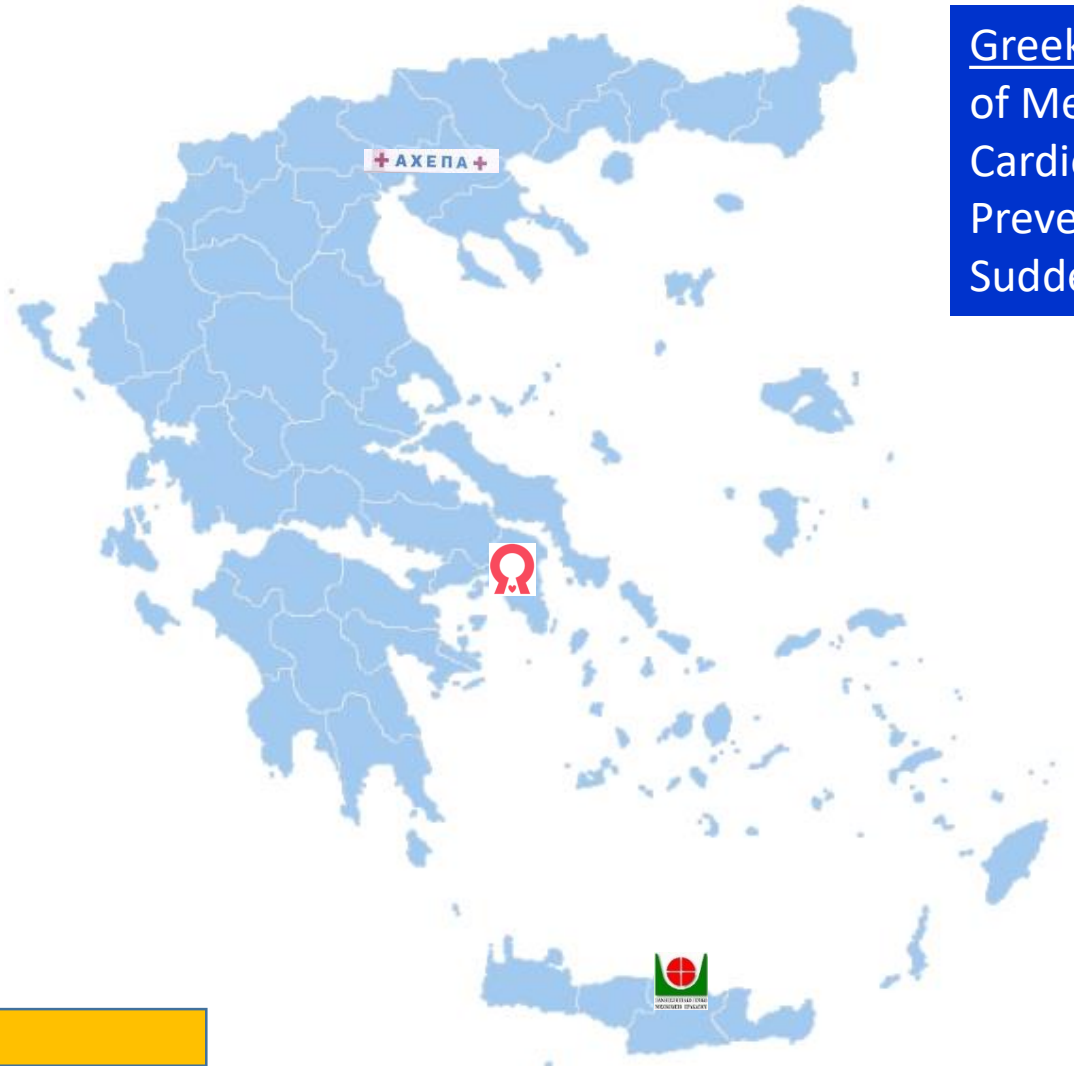
EUROPEAN REFERENCE NETWORKS
FOR RARE, LOW-PREVALENCE AND COMPLEX DISEASES

Share. Care. Cure.



**Network
Evolution**

Greek National Network
of Medical Precision in
Cardiology and
Prevention of Juvenile
Sudden Death

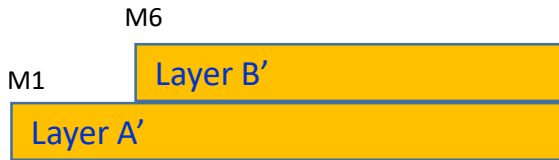


M1

Layer A'

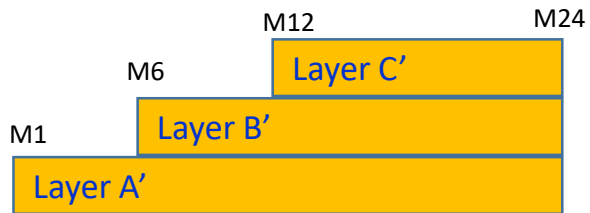
**Network
Evolution**

Greek National Network
of Medical Precision in
Cardiology and
Prevention of Juvenile
Sudden Death



Network Evolution

Greek National Network of Medical Precision in Cardiology and Prevention of Juvenile Sudden Death



**National
Coverage**

**Greek National Network
of Medical Precision in
Cardiology and
Prevention of Juvenile
Sudden Death**





Network Vision

- National Coverage
- Southeastern Europe Range
- Reference Network in European and International Level

GUARD- HEART 2017-2018



ERN GUARD-HEART Centres

Member State	City	Centre
Belgium	Brussels	University Hospital Brussels
Belgium	Leuven	University Hospitals Leuven
Czech Republic	Prague	University Hospital Motol
Denmark	Copenhagen	Copenhagen University Hospital Rigshospitalet
Finland	Helsinki	Helsinki University Hospital
France	Lyon	Louis Pradel Cardiovascular Hospital
France	Nantes	Nantes University Hospital
France	Paris	AP-HP Pitié Salpêtrière Hospital
Germany	Münster	University Hospital Münster
Italy	Milan	Istituto Auxologico Italiano IRCCS
Italy	Napels	AORN dei Colli/Monaldi Hospital
Italy	Padua	Padua University Hospital
Italy	Pavia	Clinical Scientific Institutes Maugeri IRCCS
Italy	Pavia	Foundation Policlinico San Matteo IRCCS
Italy	Rome	Bambino Gesù Children's Hospital
Netherlands	Amsterdam	Academic Medical Center
Romania	Bucharest	Emergency Institute for Cardiovascular Diseases
Spain	Barcelona	Sant Joan de Déu – Barcelona Children's Hospital
Spain	Madrid	University Hospital Puerta de Hierro Majadahonda
Spain	Murcia	University Hospital Virgen Arrixaca
Sweden	Umeå	Umeå University Hospital
United Kingdom	London	Barts Health NHS Trust
United Kingdom	London	Great Ormond Street Hospital NHS Trust

ERN GUARD-HEART Centres

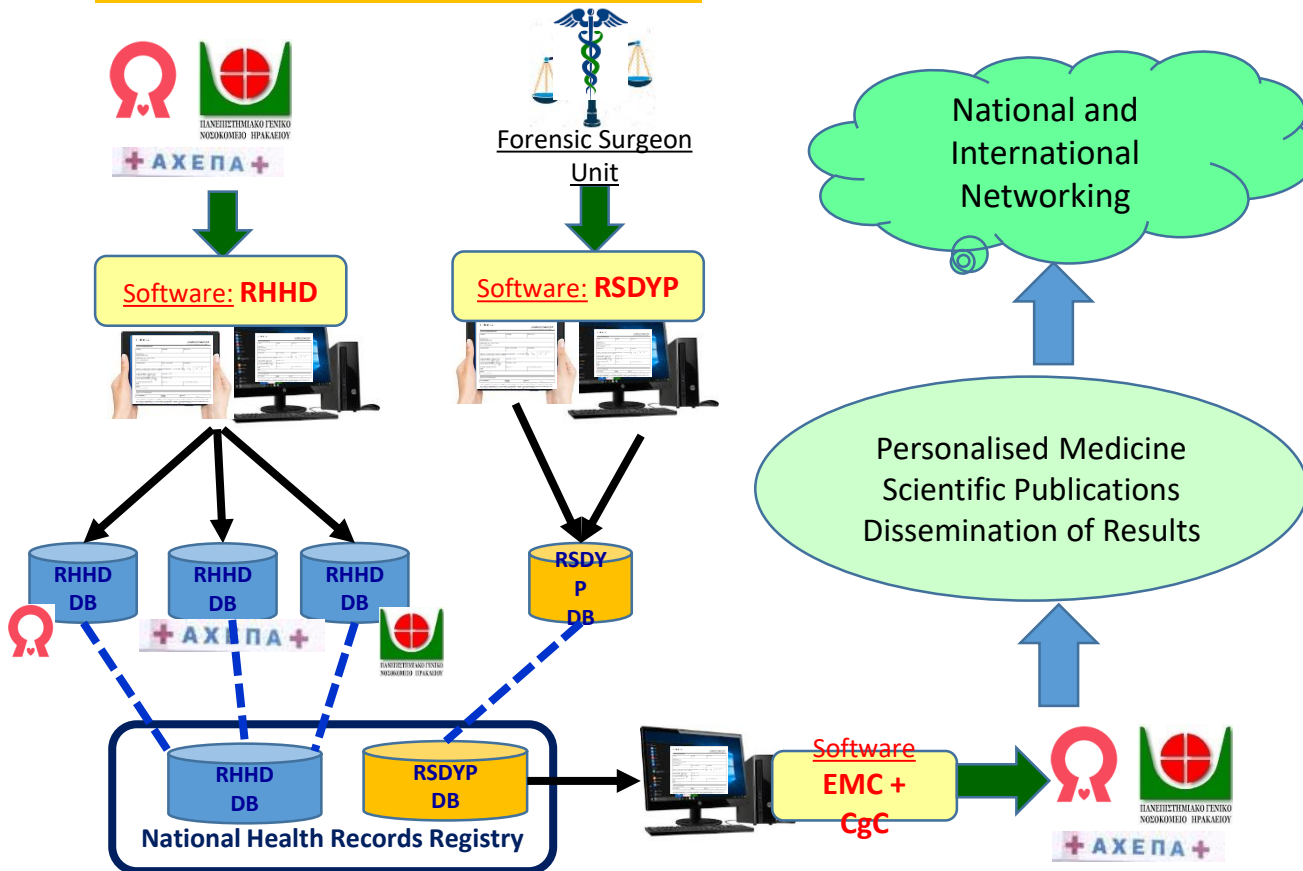


Member State	City	Centre
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Italy	Padua	Padua University Hospital
Italy	Pavia	Clinical Scientific Institutes Maugeri IRCCS
Italy	Pavia	Foundation Policlinico San Matteo IRCCS
Italy	Rome	Bambino Gesù Children’s Hospital
Netherlands	Amsterdam	Academic Medical Center
Romania	Bucharest	Emergency Institute for Cardiovascular Diseases
Spain	Barcelona	Sant Juan de Déu – Barcelona Children’s Hospital
Spain	Madrid	University Hospital Puerta de Hierro Majadahonda
Spain	Murcia	University Hospital Virgen Arrixaca
Sweden	Umeå	Umeå University Hospital
United Kingdom	London	Barts Health NHS Trust
United Kingdom	London	Great Ormond Street Hospital NHS Trust

GREECE 2019 ?

Greek National Network of Medical Precision in Cardiology and Prevention of Juvenile Sudden Death

LAYER A'



SOFTWARE APPLICATIONS/MODULES

RHHD: Software Application for the Registry of Hereditary Heart Diseases

RSDYP: Software Application for the Registry of the Sudden Death of Young People

RSDYP: Software Application for the Epidemiological Map of the Country

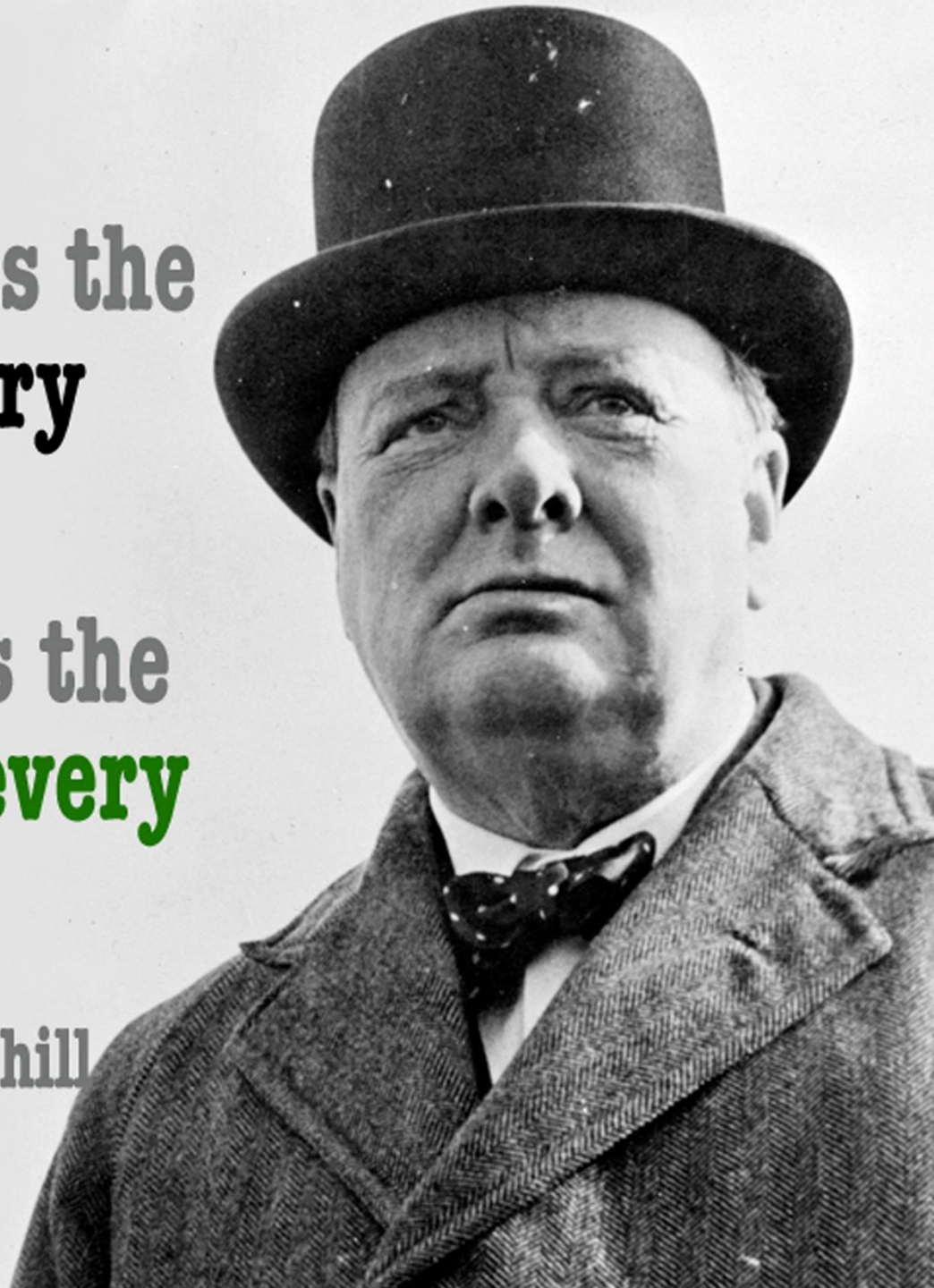
CgC: Software Module for Clinic-genital Correlations



**“A pessimist sees the
difficulty in every
opportunity;**

**an optimist sees the
opportunity in every
difficulty.”**

~ Winston Churchill





GR INHERITED NETWORK IN CARDIOLOGY
NETWORK OF SUDDEN DEATH PREVENTION IN THE
YOUNG AND PRECISION MEDICINE IN CARDIOLOGY

GSRT
GENERAL SECRETARIAT FOR
RESEARCH AND TECHNOLOGY

HEART IS AN ORGAN OF FIRE