ELECTRA

5-6 DÉCEMBRE 2024

HOTEL VILLA MASSALIA,
MARSEILLE I FRANCE

18èmes journées françaises
pratiques de rythmologie
& de stimulation cardiaque

2004 - 2024
20 ans
ELECTRA

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Session : Génétique et rythmologie

Du phénotype au génotype : quand et comment envoyer au généticien ?

Fabrice Extramiana

AP-HP. Nord Université Paris Cité
Hôpital Bichat Claude-Bernard AP-HP

Université Paris Cité

Centre de Référence des Maladies Cardiaques Héréditaires ou Rares

cardiogen
filière nationale de santé maladies cardiaques héréditaires

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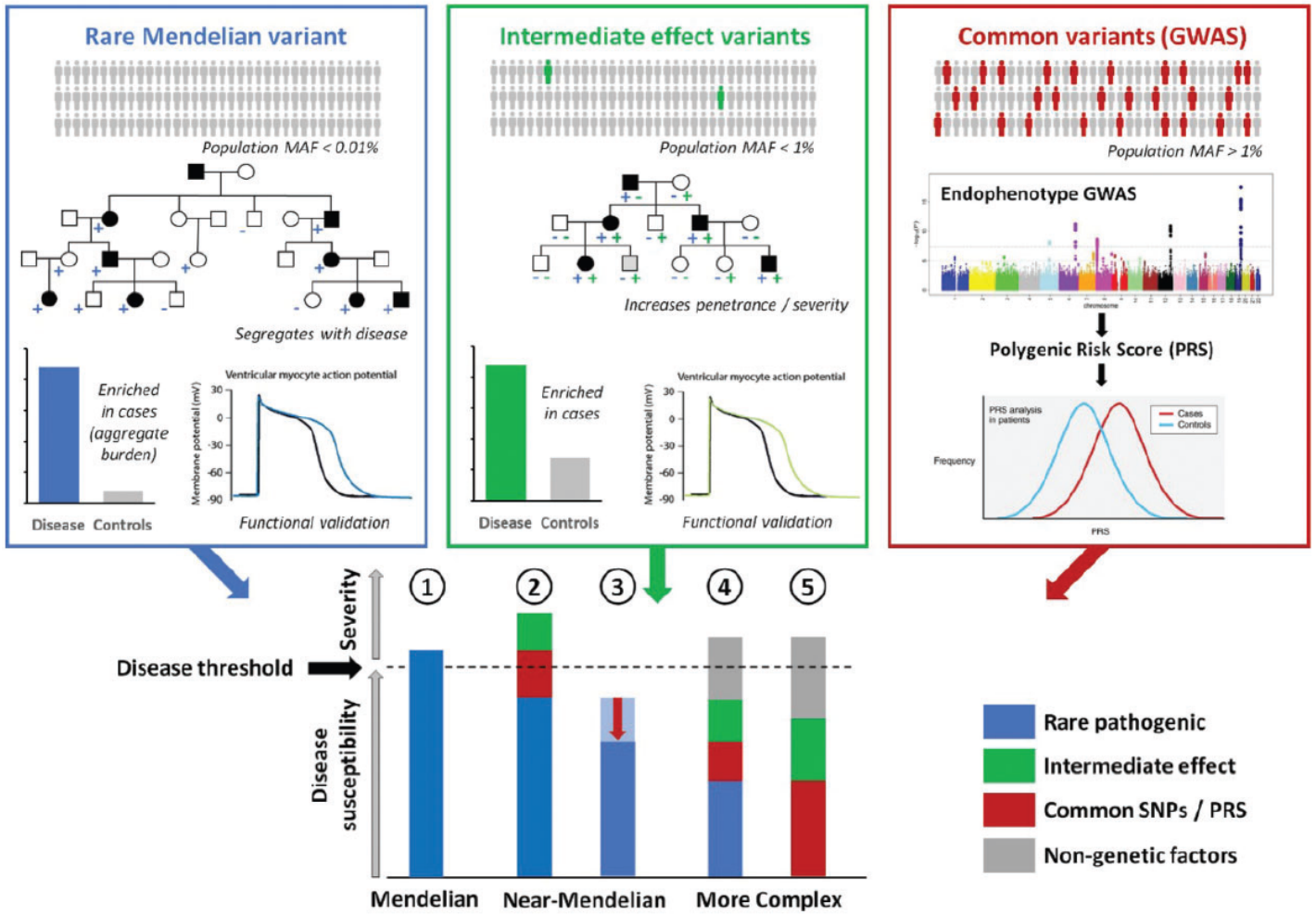
Conflits d'intérêts

- Biosense-Webster : Lecture fees

European Heart Rhythm Association (EHRA)/ Heart Rhythm Society (HRS)/Asia Pacific Heart Rhythm Society (APHRS)/Latin American Heart Rhythm Society (LAHRS) Expert Consensus Statement on the state of genetic testing for cardiac diseases

Europace 2022; 24:1307–1367



- Forme d'emblée familiale : origine génétique certaine ou très probable
- Forme apparemment sporadique, origine génétique mendélienne variable selon les pathologies
  - -certaine ou très probable (CMH, CVDA/DVDA),
  - -importante (QT long)
  - -plus modeste (CMD) ou
  - -mal connue (Brugada, PVM, ….)

European Heart Rhythm Association (EHRA)/ Heart Rhythm Society (HRS)/Asia Pacific Heart Rhythm Society (APHRS)/Latin American Heart Rhythm Society (LAHRS) Expert Consensus Statement on the state of genetic testing for cardiac diseases

Europace 2022; 24:1307–1367

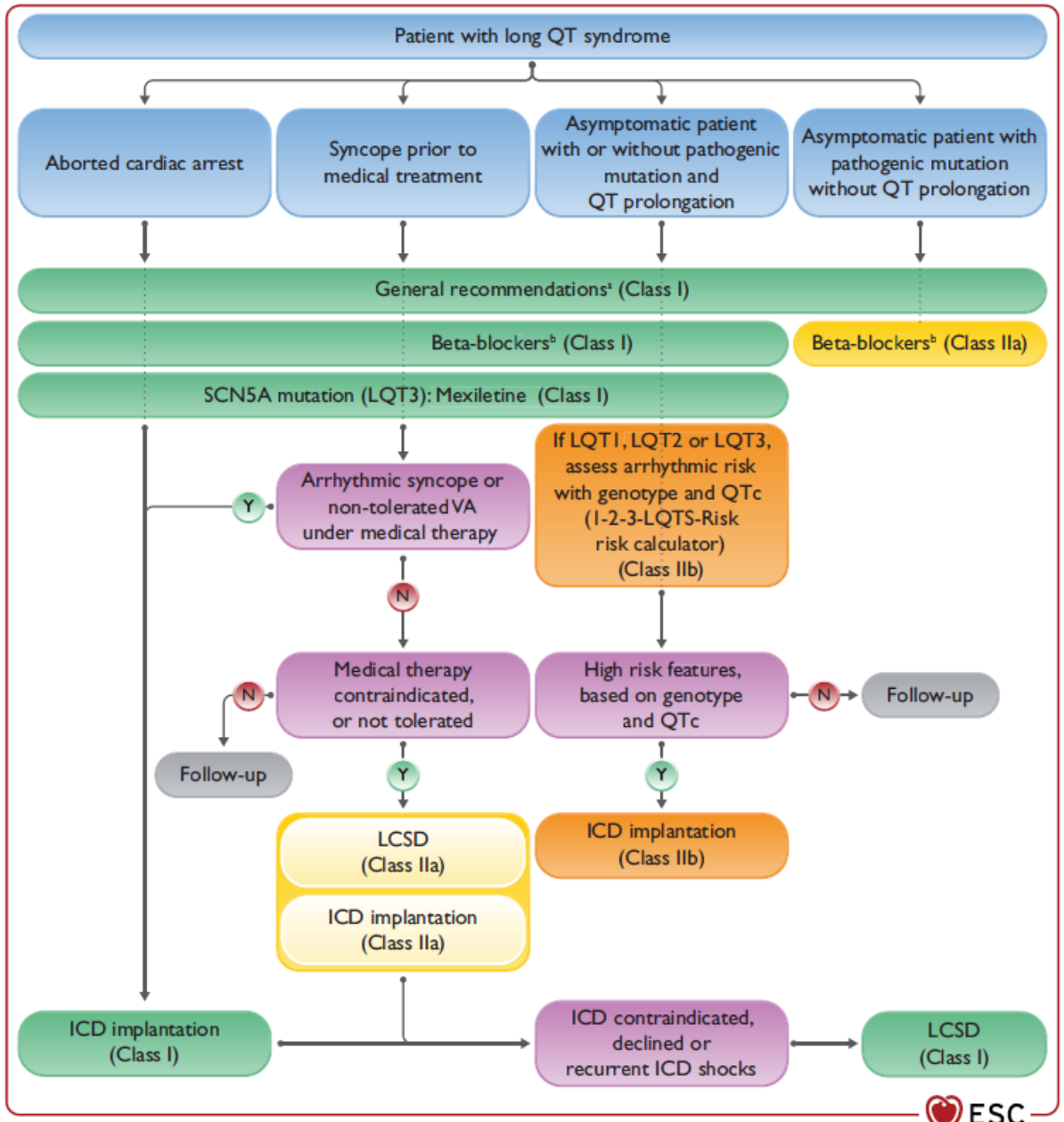
Table 5 Impact of genetic testing for the proband

Disease	Diagnostic	Prognostic	Therapeutic
Arrhythmia syndromes			
Long QT syndrome	+++	+++	+++
CPVT	+++	+	+
Brugada syndrome	+	+	+
Progressive cardiac conduction disease	+	+	+
Short QT syndrome	+	+	+
Sinus node disease	–	+	–
Atrial fibrillation	–	+	–
Early repolarization syndrome	–	–	–
Cardiomyopathies			
Hypertrophic cardiomyopathy	+++	++	++
Dilated cardiomyopathy	++	+++	++
Arrhythmogenic cardiomyopathy	+++	++	++
Left ventricular non-compaction	+	+	–
Restrictive cardiomyopathy	+	+	+
Congenital heart disease			
Syndromic CHD	+++	+	–
Non-syndromic CHD	+	–	–
Familial CHD	++	–	–

2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

Recommendation Table 41 — Recommendations for the management of patients with long QT syndrome

Recommendations	Class[a]	Level[b]
Diagnosis		
It is recommended that LQTS is diagnosed with either QTc ≥480 ms in repeated 12-lead ECGs with or without symptoms or LQTS diagnostic score >3.	I	C
In patients with clinically diagnosed LQTS, genetic testing and genetic counselling are recommended.	I	C
It is recommended that LQTS is diagnosed in the presence of a pathogenic mutation, irrespective of the QT duration.	I	C
The LQTS diagnosis should be considered in the presence of a QTc ≥460 ms and <480 ms in repeated 12-lead ECGs in patients with an arrhythmic syncope in the absence of secondary causes for QT prolongation.[952,962,963]	IIa	C



2023 ESC Guidelines for the management of cardiomyopathies

Developed by the task force on the management of cardiomyopathies of the European Society of Cardiology (ESC)

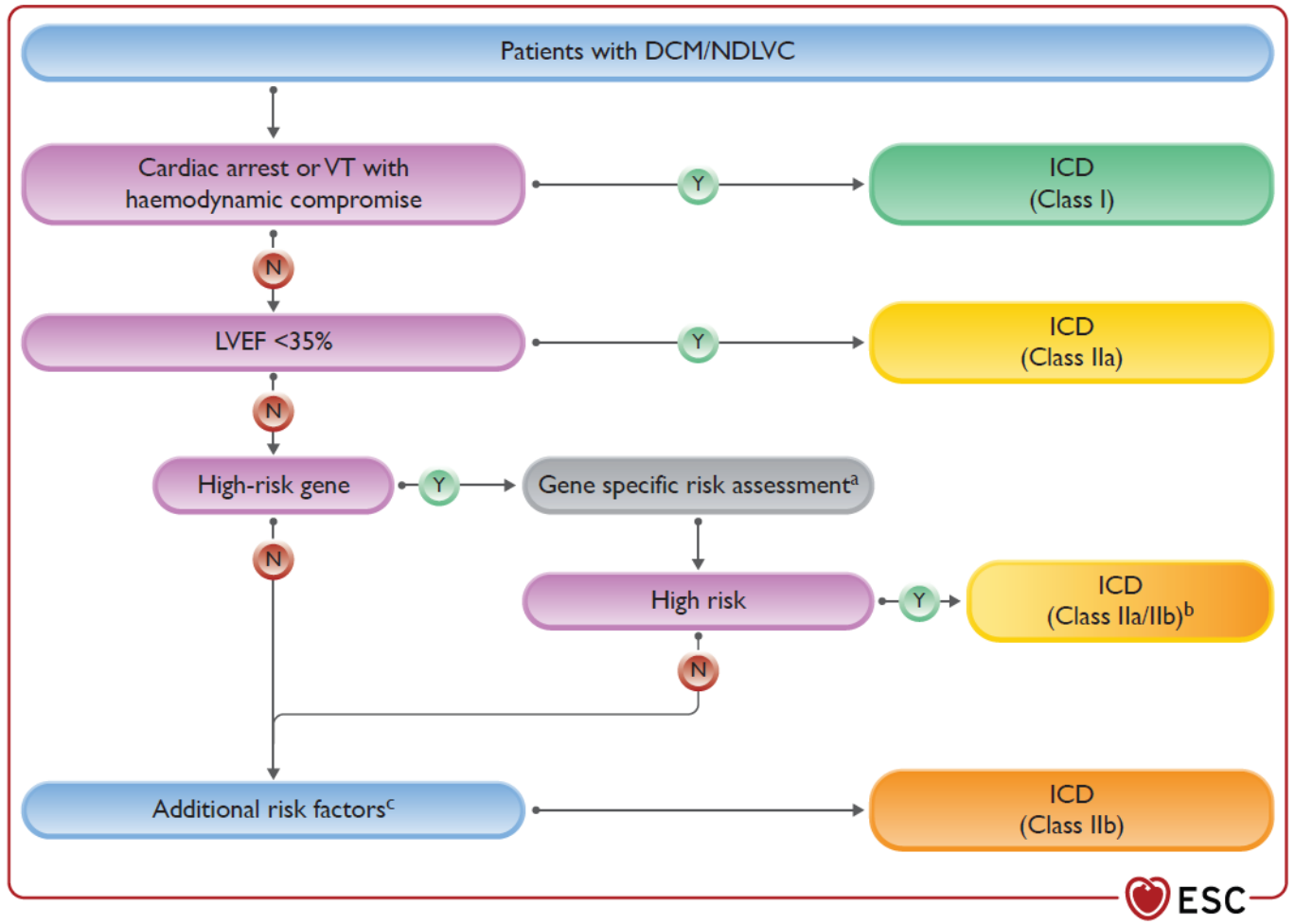


Table 21 High-risk genotypes and associated predictors of sudden cardiac death

Gene	Annual SCD rate	Predictors of SCD
LMNA[185,186,438,541,865,878,879]	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[868,881]	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%

2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

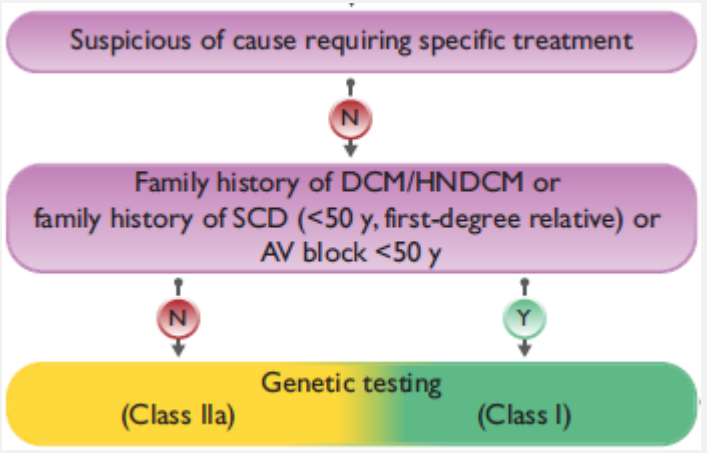
HOTEL VILLA MASSALIA

Recommendation Table 2 — Recommendations for genetic testing

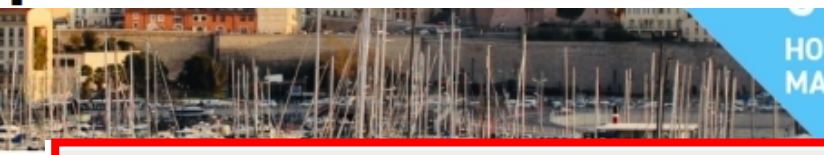
Recommendations	Class[a]	Level[b]
Genetic testing is recommended when a condition is diagnosed in a living or deceased individual with a likely genetic basis and a risk of VA and SCD.[56,183]	I	B
It is not recommended to undertake genetic testing in index patients with insufficient evidence of a genetic disease.	III	C

LQTS – Class I
BrS – Class I
CPVT – Class I
SQTS – Class I
IVF – Class IIb
ERS – Class IIb

ARVC – Class I
HCM – Class I
DCM



2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death



SCD

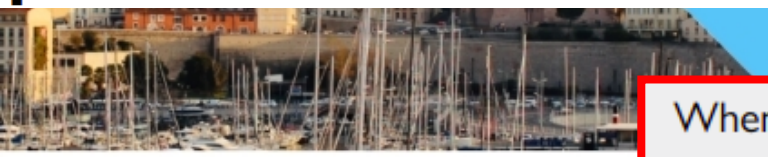
In SCA survivors, collection of blood samples at presentation is recommended for potential toxicology and genetic testing.[56,214]	I	B

ACA

Retrieval of recordings from CIEDs and wearable monitors is recommended for all SCA survivors.[217,218]	I	B
In SCA survivors, repeated 12-lead ECGs during stable rhythm (including high precordial lead ECG), as well as continuous cardiac monitoring, are recommended.[220,222]	I	B
Echocardiography is recommended for evaluation of cardiac structure and function in all SCA survivors.	I	C
Coronary imaging and CMR with LGE are recommended for evaluation of cardiac structure and function in all SCA survivors without a clear underlying cause.[62,222,223,226]	I	B
Sodium channel blocker test and exercise testing is recommended in SCA survivors without a clear underlying cause.[117,222,258–260]	I	B
In SCA survivors, ergonovine, acetylcholine, or hyperventilation testing may be considered for the diagnosis of coronary vasospasm.[240,261]	IIb	B

In cases of SCD, it is recommended to retain samples suitable for DNA extraction and consult a cardiac pathologist when an inherited cause is suspected or the cause of death unexplained.[264,265]	I	B
For SCD where the cause is known or suspected to be heritable, genetic testing targeted to the cause is recommended.[56,266,269]	I	B
Following SADS, post-mortem genetic testing targeted to primary electrical disease is recommended when the decedent is young (<50) and/or the circumstances and/or family history support a primary electrical disease.[56,183,223]	I	B
In non-autopsied cases of SD where inherited cardiac disease is suspected, it is recommended to refer first-degree relatives for cardiac assessment in a specialized clinic.[223,253,273]	I	B
Following SADS, post-mortem genetic testing in the decedent for additional genes may be considered.	IIb	C
Following SADS, hypothesis-free post-mortem genetic testing using exome or genome sequencing is not recommended.[274,275]	III	B

2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death



When a putative causative variant is first identified, evaluation for pathogenicity is recommended using an internationally accepted framework.[176]	I	C
When a Class IV or Class V variant has been identified in a living or deceased individual with a condition that carries a risk of VA and SCD, genetic testing of first-degree and symptomatic relatives and obligate carriers is recommended.	I	C
It is recommended that genetic testing and counselling on its potential consequences should be undertaken by an expert multidisciplinary team.[179]	I	C
It is recommended that Class III (variants of uncertain significance) and Class IV variants should be evaluated for segregation in families where possible, and the variant re-evaluated periodically.	I	C

A global reference for human genetic variation

The 1000 Genomes Project Consortium*

Nature 2015;256

The 1000 Genomes Project set out to provide a comprehensive description of common human genetic variation by applying whole-genome sequencing to a diverse set of individuals from multiple populations. Here we report completion of the project, having reconstructed the genomes of 2,504 individuals from 26 populations using a combination of low-coverage whole-genome sequencing, deep exome sequencing, and dense microarray genotyping. We characterized a broad spectrum of genetic variation, in total over 88 million variants (84.7 million single nucleotide polymorphisms (SNPs), 3.6 million short insertions/deletions (indels), and 60,000 structural variants), all phased onto high-quality haplotypes. This resource includes >99% of SNP variants with a frequency of >1% for a variety of ancestries. We describe the distribution of genetic variation across the global sample, and discuss the implications for common disease studies.

Genome Aggregation Database (gnomAD)

bioinformatics | genetic | genomic | life sciences | population | population genetics | short read sequencing | whole genome sequencing

Description

The Genome Aggregation Database (gnomAD) is a resource developed by an international coalition of investigators that aggregates and harmonizes both exome and genome data from a wide range of large-scale human sequencing projects. The summary data provided here are released for the benefit of the wider scientific community without restriction on use. The v4.1 data set (GRCh38) spans 730,947 exome sequences and 76,215 whole-genome sequences from unrelated individuals, of diverse ancestries, sequenced sequenced as part of various disease-specific and population genetic studies. The gnomAD Principal Investigators and team can be found here, and the groups that have contributed data to the current release are listed here. Sign up for the gnomAD mailing list here.

Update Frequency

Data from new releases are made public as soon as they are available. New releases, including both minor and major versions, have historically been issued on the order of once per year.

Resources on AWS

Description
gnomAD summary data aggregated from large-scale human genome and exome sequencing projects.

Resource type
S3 Bucket

Amazon Resource Name (ARN)
`arn:aws:s3:::gnomad-public-us-east-1`

AWS Region
`us-east-1`

AWS CLI Access (No AWS account required)
`aws s3 ls --no-sign-request s3://gnomad-public-us-east-1/`

Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology

Genet Med. 2015; 17:405-424

	Benign		Pathogenic			
	Strong	Supporting	Supporting	Moderate	Strong	Very Strong
Population data	MAF > 5% in public exome databases (BA1) MAF is too high for disorder (BS1)			Absent in public exome databases (PM2)	Prevalence in affecteds statistically increased over controls w/ OR ≥ 5 (PS4)	
Computational and predictive data		Multiple lines of computational evidence suggest no impact on gene/gene product (BP4) Missense gene where only truncating cause disease (BP1) Silent variant with no predicted splice impact (BP7) In-frame indels in repeat w/out known function (BP3)	Multiple lines of computational evidence support a deleterious effect on the gene /gene product (PP3)	Novel missense change at an amino acid residue where a different pathogenic missense change has been seen before (PM5) Protein length changing variant (PM4)	Same amino acid change as an established pathogenic variant (PS1)	Predicted null variant in a gene where LOF is a known mechanism of disease (PVS1)
Functional data	Well-established functional studies show no deleterious effect (BS3)		Missense in gene with low rate of benign missense variants and path. missense common (PP2)		Well-established functional studies show a deleterious effect (PS3)	
Family data	Non-segregation with disease (BS4)		Co-segregation with disease in multiple affected family members (PP1)	Increased segregation data →		
De novo data				*De novo* (without paternity & maternity confirmed) (PM4)	*De novo* (paternity & maternity confirmed) (PS2)	
Allelic data		Observed in *trans* with a dominant variant (BP2) Observed in *cis* with a pathogenic variant (BP2)		For recessive disorders, detected in trans with a pathogenic variant (PM3)		
Other data-base		Reputable source w/out shared data = benign (BP6)	Reputable database = pathogenic (PP5)			
Other data		Found in case with an alternate cause (BP5)	Patient's phenotype or FH highly specific for gene (PP4)			

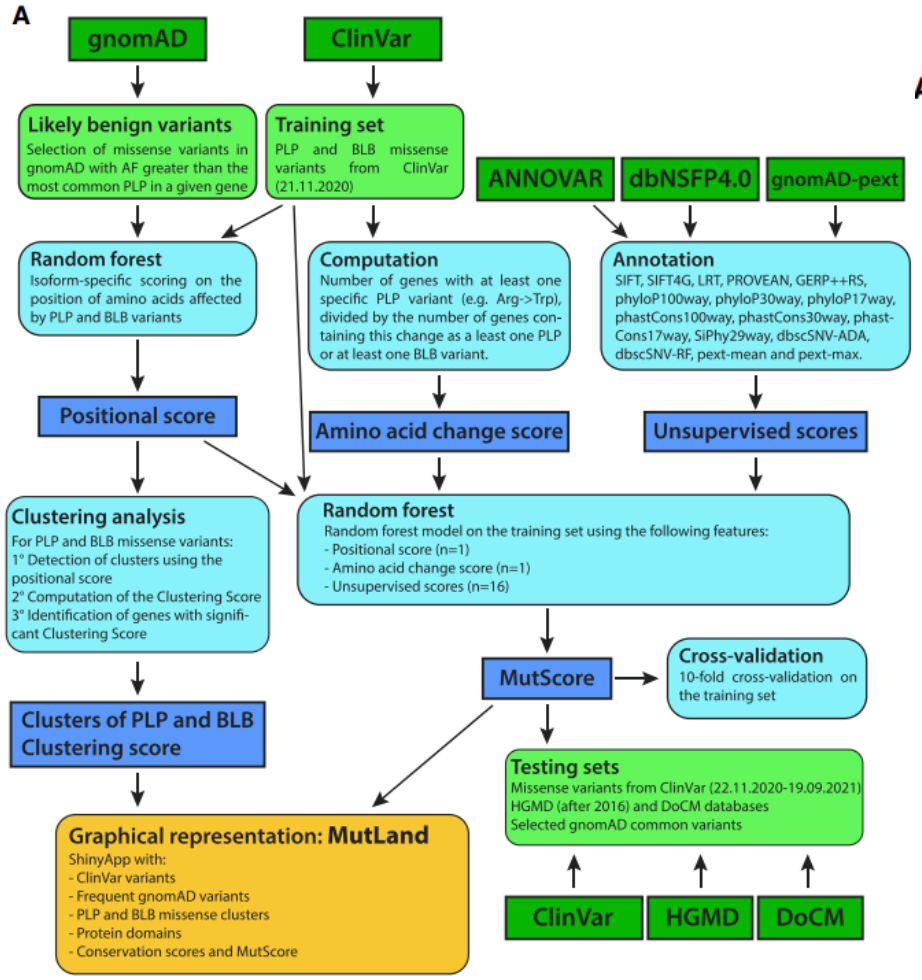
Table 2 In silico predictive algorithms

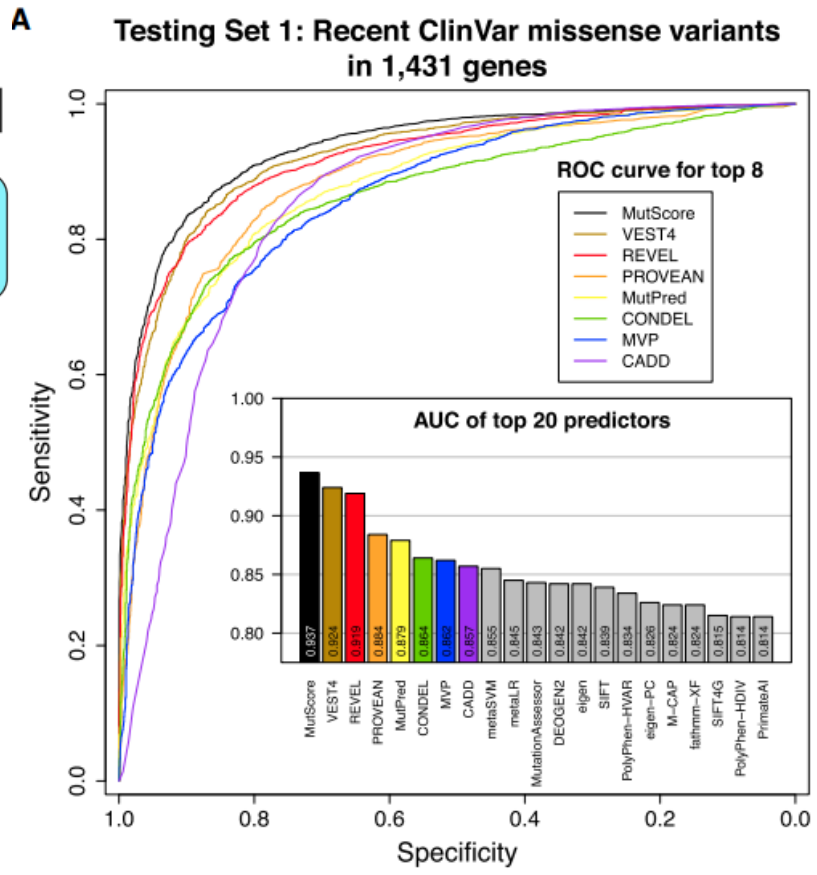
Category	Name
Missense prediction	ConSurf FATHMM MutationAssessor PANTHER PhD-SNP SIFT SNPs&GO Align GVGD MAPP MutationTaster MutPred PolyPhen-2 PROVEAN nsSNPAnalyzer Condel CADD
Splice site prediction	GeneSplicer Human Splicing Finder MaxEntScan NetGene2 NNSplice FSPLICE
Nucleotide conservation prediction	GERP PhastCons PhyloP

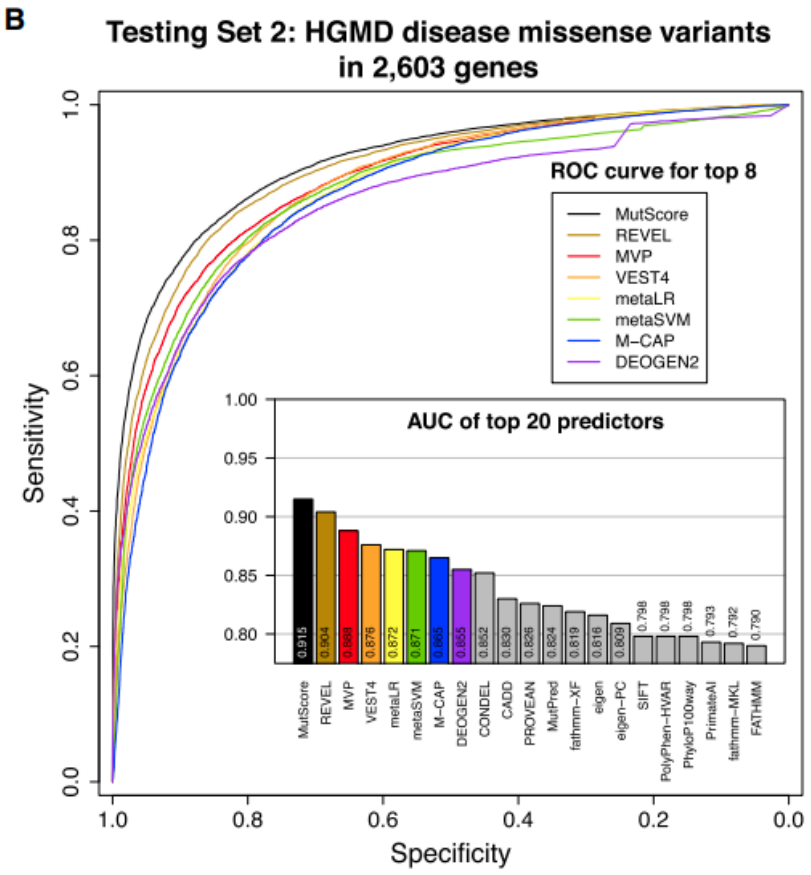
Analysis of missense variants in the human genome reveals widespread gene-specific clustering and improves prediction of pathogenicity

Mathieu Quinodoz,[1,2,3] Virginie G. Peter,[1,2,3,4] Katarina Cisarova,[5] Beryl Royer-Bertrand,[5] Peter D. Stenson,[6] David N. Cooper,[6] Sheila Unger,[5] Andrea Superti-Furga,[5] and Carlo Rivolta[1,2,3,*]

Am J Hum Genet. 2022;109:457-470







2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

When a putative causative variant is first identified, evaluation for pathogenicity is recommended using an internationally accepted framework.[176]	I	C
When a Class IV or Class V variant has been identified in a living or deceased individual with a condition that carries a risk of VA and SCD, genetic testing of first-degree and symptomatic relatives and obligate carriers is recommended.	I	C
It is recommended that genetic testing and counselling on its potential consequences should be undertaken by an expert multidisciplinary team.[179]	I	C
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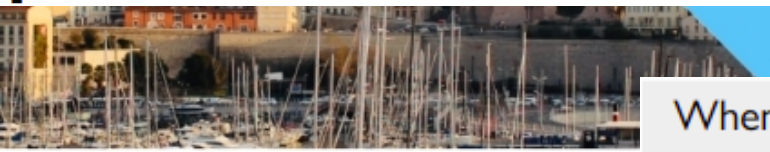

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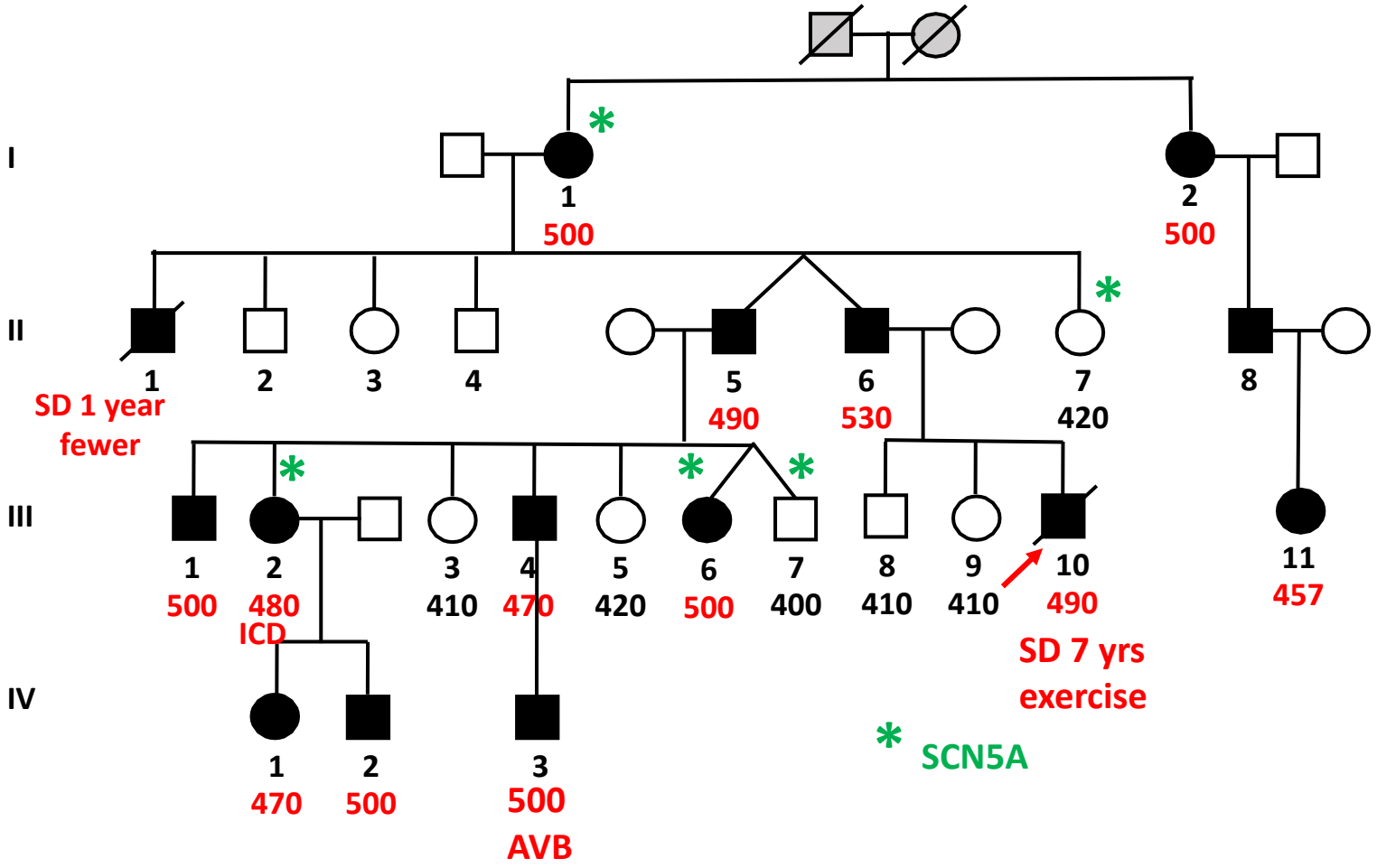
Cas index: garçon de 7 ans - MS inaugurale FV à l'effort - QTc 490 ms

Oncle : MS à 14 mois pendant épisode fébrile;

Apparentés asymptomatiques QTc ↗

Génétique : Variant familial SCN5A – classé IV



Absence de ségrégation variant / phénoype

Variant déclassé III (VSI)

2ème panel (à l'époque)

Variant Calmoduline

Classe IV

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Pre-symptomatic diagnosis +++

Pre-birth diagnosis

Pre-implantation diagnosis

Diagnostic PréNatal (DPN)
Dépistage prénatal non invasif (DPNI)
Diagnostic PréImplantatoire (DPI)

Même cadre législatif « affection d'une particulière **gravité** réputée comme **incurable** au moment du diagnostic »

- –Pas de liste de maladies
- –Pas de limite de terme
- –Variation génétique classe 4 & 5

Lois de bioéthique depuis 1994

Révisions successives en 2004 puis 2011 puis 2013 puis 2021

Centres Pluridisciplinaires de Diagnostic PréNatal (CPDPN)

Cardiogénétique: peu de cas

-Marfan et certains Sd apparentés

-Laminopathies, CMH sévères

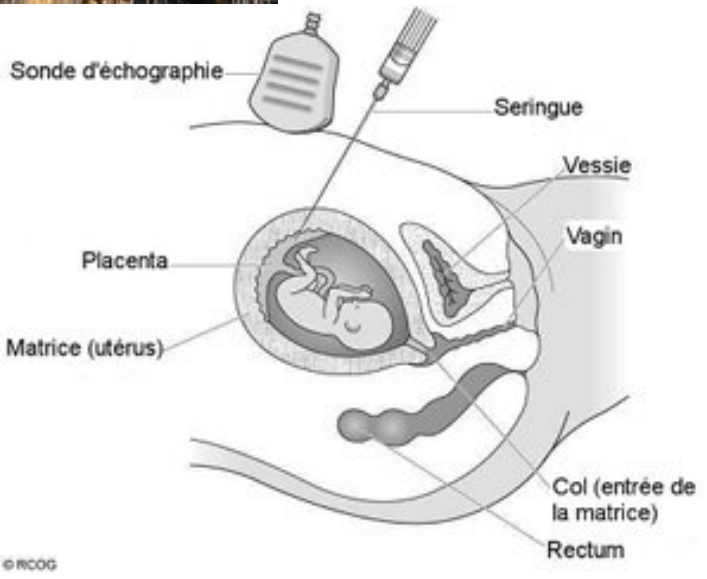
-Syndrome de Jervell

-TDR sévère (MS familiales)

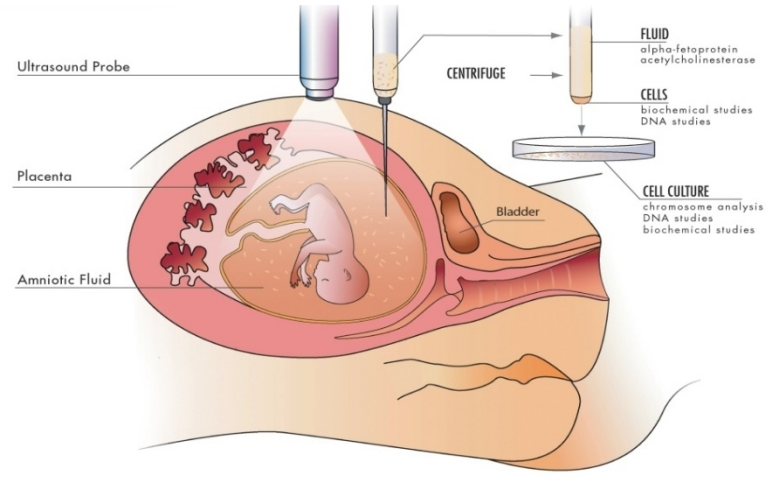
Discussion au cas par cas

Chaque famille est unique

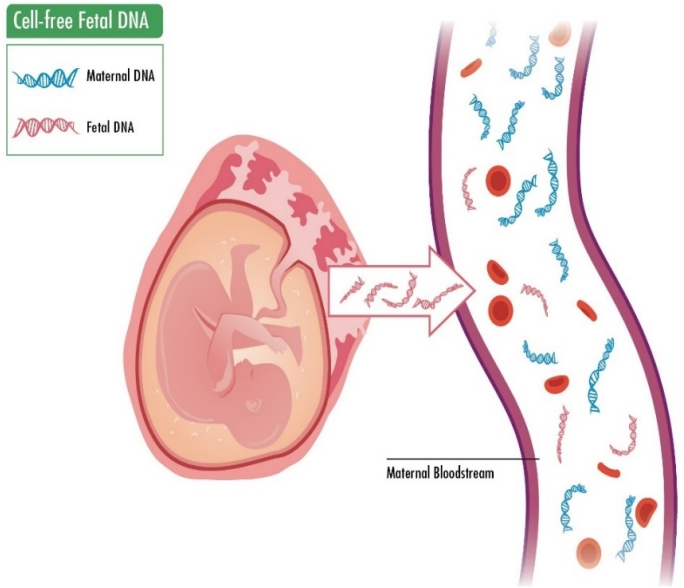
Diagnostic PréNatal (DPN)
Dépistage prénatal non invasif (DPNI)



LA CHORIOCENTESE :
Entre 11 et 14 SA
Prélèvement de villosités choriales
Risque de fausse couche :
Env 0,5%



L'AMNIOCENTESE
A partir de 15 SA
Prélèvement de liquide amniotique
Risque de fausse couche :
Env 1%



ADN libre fœtal circulant dans le plasma maternelle (prise de sang maternelle)

Possible dès 10 SA

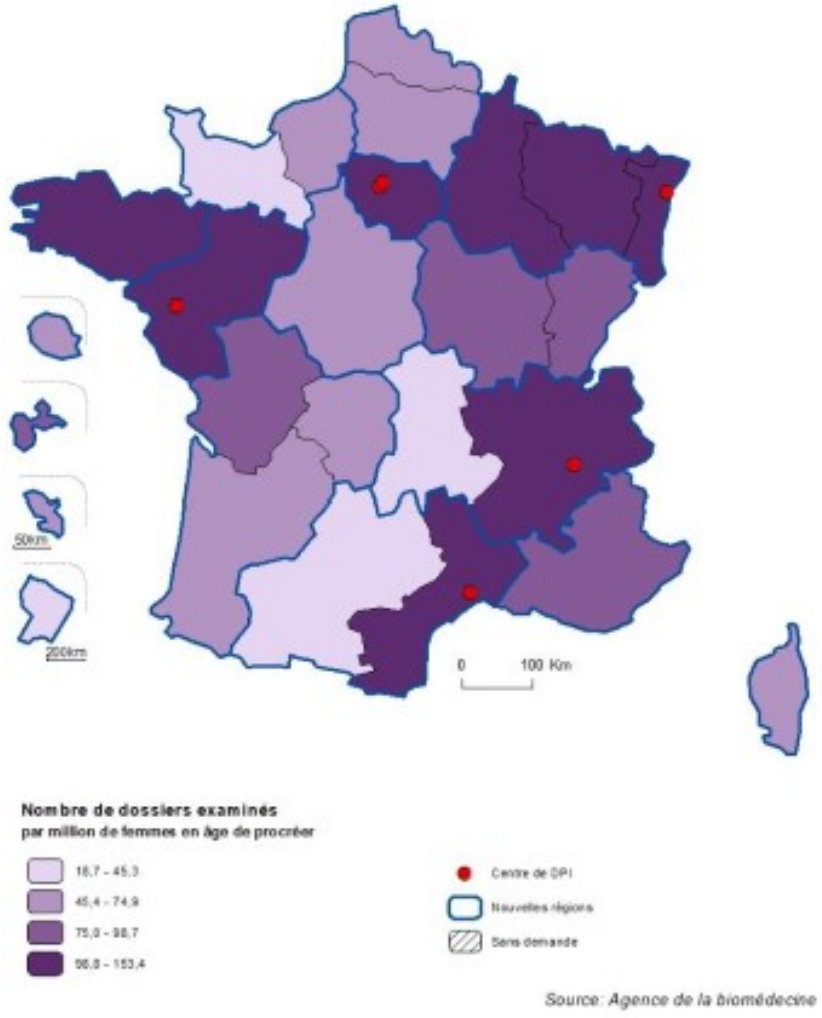
Analyse par PCR digitale

Mise au point technique

(prélèvement sanguin des 2 parents)

DPI = Diagnostic Pré-Implantatoire

= Diagnostic à partir d'une ou deux cellules d'embryons conçus *in vitro*, en vue d'un transfert *in utero* d'embryon(s) non atteint(s) de la maladie génétique recherchée



Rencontre du couple avec l'équipe pluridisciplinaire
généticien, gynécologue, biologiste, anesthésiste, psychologue, sage-femme…
Evaluation du dossier par le CPDPN (médical, éthique)
Evaluation de la faisabilité de la FIV
spermogramme, bilan ovarien…
Evaluation de la faisabilité génétique (mises au point techniques)
Demande de prise en charge DPI

Stimulation ovarienne
Ponction d'ovocytes / Prélèvement de sperme
Fécondation in vitro
Biopsie embryonnaire (à J3 ou J5, prélèvement d'1 à 2 cellules)
Transfert embryonnaire (1 à 2 embryons) d'un embryon sains +/- congélation des embryons surnuméraire

Grossesse

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HOPITAUX UNIVERSITAIRES LA PITIE-SALPETRIERE- CHARLES-FOIX
Unité Fonctionnelle de Cardiogénétique et Myogénétique
Centre de Génétique et Cytogénétique
http://www.cgmc-psl.fr ou http:/psl-cfx-manuelprelevement.fr

Bâtiment de Pharmacie, rue de l'infirmerie générale
47/83, boulevard de l'Hôpital
75651 PARIS cedex 13

Chef de Service : Pr. Dominique ROUSSELOT
Biologiste en charge du secteur Rythmologie : Dr. Véronique Fressart email : vero.fressart@aphp.fr
Biologiste Assistant spécialiste : Dr Adrien Bloch email : adrien.bloch@aphp.fr
Ingénieur Hospitalier : Mme Emile Blin email : emilie.blin@aphp.fr
Fax 01 42 17 76 18

Réception des échantillons: du lundi au jeudi, de 9h à 17h ; le vendredi, de 9h à 12h

DEMANDE DE DIAGNOSTIC MOLECULAIRE DE PATHOLOGIE RYTHMOLOGIQUE

Syndrome de QTL, Jerwell, QT court, Syndrome de Brugada, Trouble de conduction, Dysplasie arythmogène du ventricule droit (CMA), TVC, FVI, Trouble du rythme supraventriculaire.

PRESCRIPTEUR (SENIOR) ou Etquette
N° ADELI ou RPPS : .....
Nom et prénom : .....
Service : .....
Institution :.....
Adresse :

Téléphone :
Fax :
courriel :

PRELEVEUR
Nom et prénom :.....
Service :.....

Date :
Heure (facultatif) :

A COMPLETER ou Etiquette
IDENTITE PATIENT
Nom : .....
Prénom : .....
Sexe : ❑M ❑F
Nom de jeune fille :
Date de naissance : .....
Lieu et pays de naissance :
Statut du patient
❑ **Proband**
❑ **Apparenté**

A COMPLETER
Echantillon
❑ **1er prélèvement**
❑ **2ème prélèvement (dit de contrôle)**

Nature de l'échantillon
❑ **SANG (Tube EDTA)**
❑ **ADN**
❑ **Autre (préciser)**

Orientation diagnostique Proband ou Apparenté

❑ Syndrome du QT long congénital (105)
❑ Syndrome de Jerwell (106)
❑ Syndrome de QT court (108)
❑ Syndrome de Brugada (107)
❑ Troubles de conduction cardiaque (109)
❑ Tachycardie Ventriculaire Catécholaminergique TVC (111)
❑ Fibrillation Ventriculaire Idiopathique FVI (110)
Orage rythmique
❑ Mort Subite (114)

❑ Arythmie ventriculaire droite DVDA/CMA (102)

❑ Trouble du rythme supra ventriculaire (à préciser) (112)

Diagnostic moléculaire chez les apparentés
Recherche Directe chez un apparenté de Mutation connue ou confirmation (deuxième détermination)
(Cotation : N353 ; BHN720)

❑ **Diagnostic pré symptomatique**

❑ Phénotype Indemne

❑ Phénotype Douteux

❑ Phénotype Atteint

A COMPLETER
N° de Famille : .....
Gène : .....

Mutation : .....

(Ou photocopie du résultat précédent)

DEMANDE DE DIAGNOSTIC MOLECULAIRE DE PATHOLOGIE RYTHMOLOGIQUE

Syndrome de QTL, QT court, Syndrome de Brugada, Dysplasie arythmogène du ventricule droit, trouble de conduction, Trouble du rythme auriculaire

Renseignements cliniques ; A remplir obligatoirement ou associer un compte rendu d'hospitalisation ou de consultation
sauf pour les diagnostics présymptomatiques

Syndrome du QTL /Jerwell ou QT court **Valeur du QTc** :
❑ Asymptomatique ❑ Symptomatique :
Syncopes ❑OUI ❑NON Circonstances de la syncope :
Mort Subite ❑OUI ❑NON

Syndrome de Brugada / trouble de Conduction
❑ Asymptomatique ❑ Symptomatique
Syncopes ❑OUI ❑NON Circonstances de la syncope :
Mort Subite ❑OUI ❑NON

ECG au repos : Sus décalage du segment ST>2 mm ❑OUI ❑NON
Valeur de l'espace PR Présence de BAV ❑OUI ❑NON Type

Test à l'Ajmaline ❑ Positif (sus décalage sup à 2mm) ❑Négatif

Dysplasie Arythmogène du VDt ❑ Asymptomatique ❑ Symptomatique :
Nombre de critères mineurs :
Nombre de critères majeurs :
Anomalie du VDt à l'Echographie cardiaque, à l'angiographie, à l'IRM ❑OUI ❑NON
Présence d'anomalie à l'ECG ; ondes T négatives en V,2,3 ❑OUI ❑NON
Présence d'une onde epsilon ❑OUI ❑NON

Autres pathologies rythmiques :

ANALYSE MOLECULAIRE CHEZ LE PROBAND

Gènes majeurs par séquençage à haut débit (Cotation : N351)

Syndrome du QT long congénital /Jerwell: ***KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CALM1,2,3.***
Syndrome de QT court : ***CACNA1C, KCNQ1, KCNH2, KCNJ2, CACNB2***
Syndrome de Brugada : ***SCN5A***
Troubles de conduction : ***SCN5A, LMNA, NKX2.5, TRPM4***
Tachycardie Ventriculaire Cathécholaminergique (TVC) : ***RYR2, CASQ2, KCNJ2, CALM1,2,3, TRDN***
Arythmie ventriculaire droite (DVDA) : **PKP2, DSG2, DSC2, DSP, LMNA,TMEM43, CDH2, FLNC, DES, PLN, RYR2, HCN4, TNNT2, RBM20**
Trouble du rythme Supra Ventriculaire : ***KCNQ1; SCN5A; LMNA; NKX2-5; HCN4 ; GJA1 ; GJA5 ; CASQ2; RYR2 KCNJ5; CACNA2D1***
Mort subite et FVI : panel 71 gènes impliqués dans les troubles du rythme cardiaque

DOCUMENTS A JOINDRE IMPERATIVEMENT AVEC LA DEMANDE
* Un compte rendu d'hospitalisation ou de consultation
* **Un bon de commande (pour les patients hors APHP)**
* Un arbre généalogique
***Une photocopie du consentement écrit et signé du patient et du prescripteur**

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* Un compte rendu d'hospitalisation ou de consultation
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ELECTRA
5-6 DÉCEMBRE 2024
HOTEL VILLA MASSALIA,
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18èmes journées françaises
pratiques de rythmologie
& de stimulation cardiaque

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Mort subite et FVI : panel 71 gènes impliqués dans les troubles du rythme cardiaque

Mises à jour CARDIOGEN régulières

Strategies for molecular Diagnosis (National network CARDIOGEN)

- **Hypertrophic Cardiomyopathy**

Panel CMH (16 genes) — N351 → 30-50 % positive → NEGATIVE → least 2 affected

ACTC1, ACTN2, FHL1, FLNC, GLA, LAMP2, MYBPC3, MYH7, MYL2, MYL3, PRKAG2, TNNC1, TNNI3, TNNT2, TPM1, TTR

Mt-TL1 if MELAS suspected

- **Dilated Cardiomyopathy**
- **Restrictive Cardiomyopathy**
- **Left Ventricle Non Compaction**
- **Arrythmogenic Right ventricle CM**
- **Fetal, neonatal and pediatric CM**

Panel CM (80 gènes) — N352 → 30-50 % positive → NEGATIVE → At least 2 affected

ABCC9, ACAD9, ACTC1, ACTN2, ALPK3, ANKRD1, BAG3, CALR3, CAV3, CRYAB, CSRP3, CTNNA3, DES, DSC2, DSG2, DSP, DTNA, EMD, EYA4, FBN1, FHL1, FLNC, GAA, GATA4, GLA, HCN4, HEY2, JPH2, KRAS, LAMA4, LAMP2, LDB3, LMNA, MYBPC3, MYH6, MYH7, MYL2, MYL3, MYLK2, MYOM1, MYOZ2, MYPN, NEBL, NEXN, NKX2-5, PDLIM3, PKP2, PLN, PRDM16, PRKAG2, PTPN11, RAF1, RBM20, RYR2, SCN5A, SDHA, SGCD, SLC25A4, SOS1, SYNPO2, TAZ, TCAP, TMEM43, TMPO, TNNC1, TNNI3, TNNT2, TPM1, TTN, TTR, VCL

- **Cardiac Sudden Death**

Targeted panel CM + Arrythmias (115 genes)

SEQOIA Médecine génomique

AURA GEN

FRANCE MÉDECINE GÉNOMIQUE 2025

aviesan

Plan France Médecine génomique 2025

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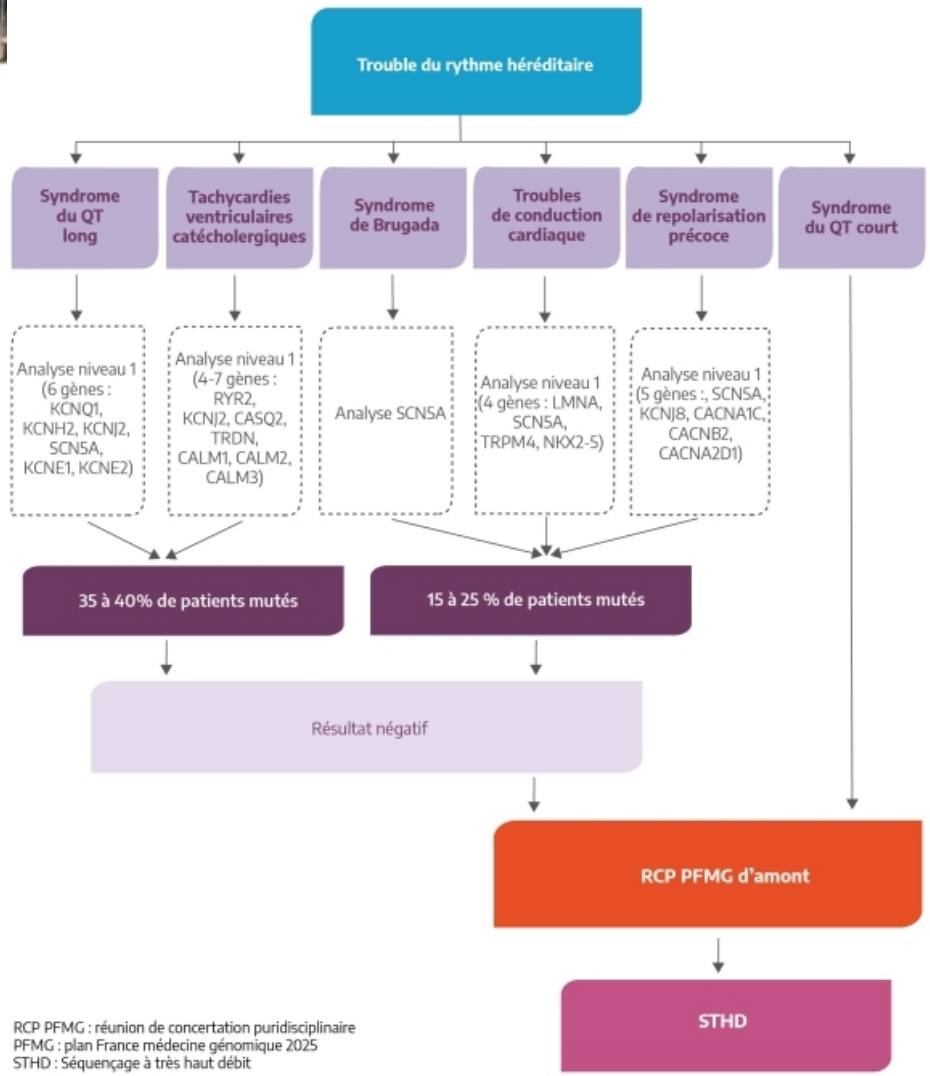
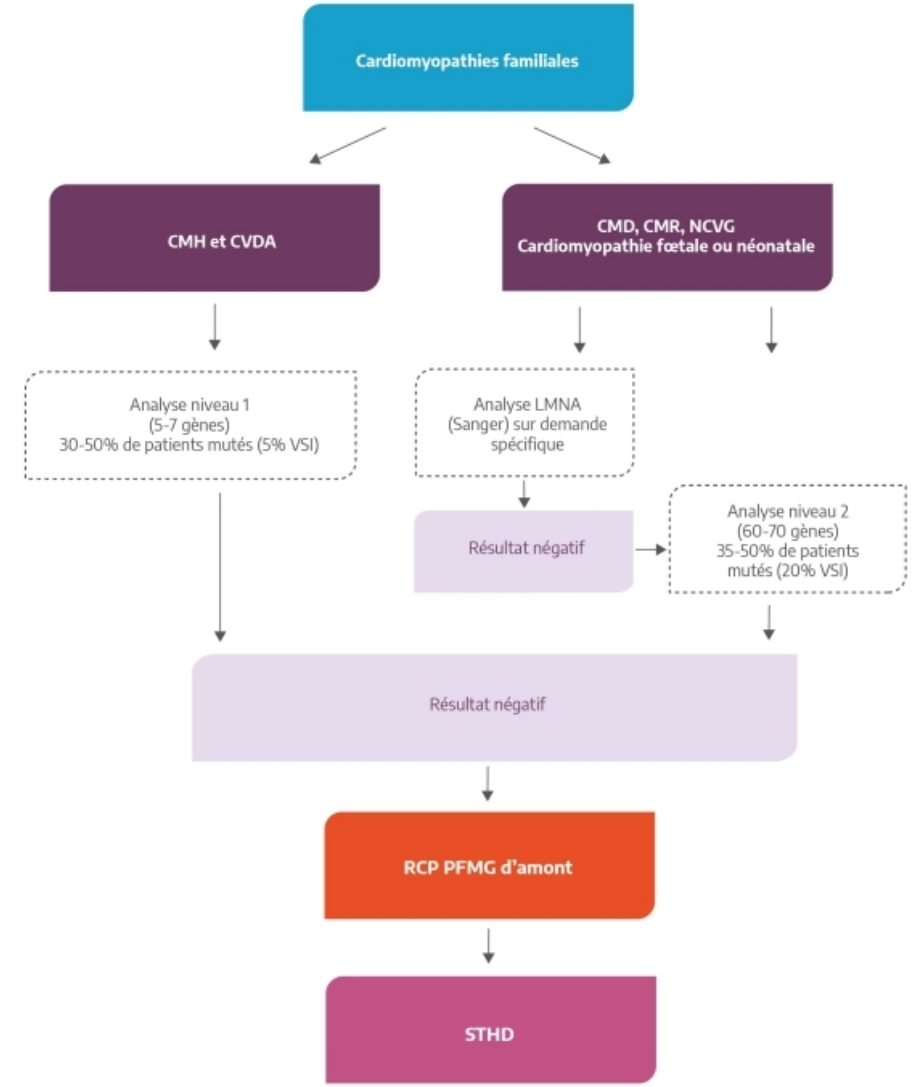


RCP PFMG : réunion de concertation puridisciplinaire
PFMG : plan France médecine génomique 2025
STHD : Séquençage à très haut débit



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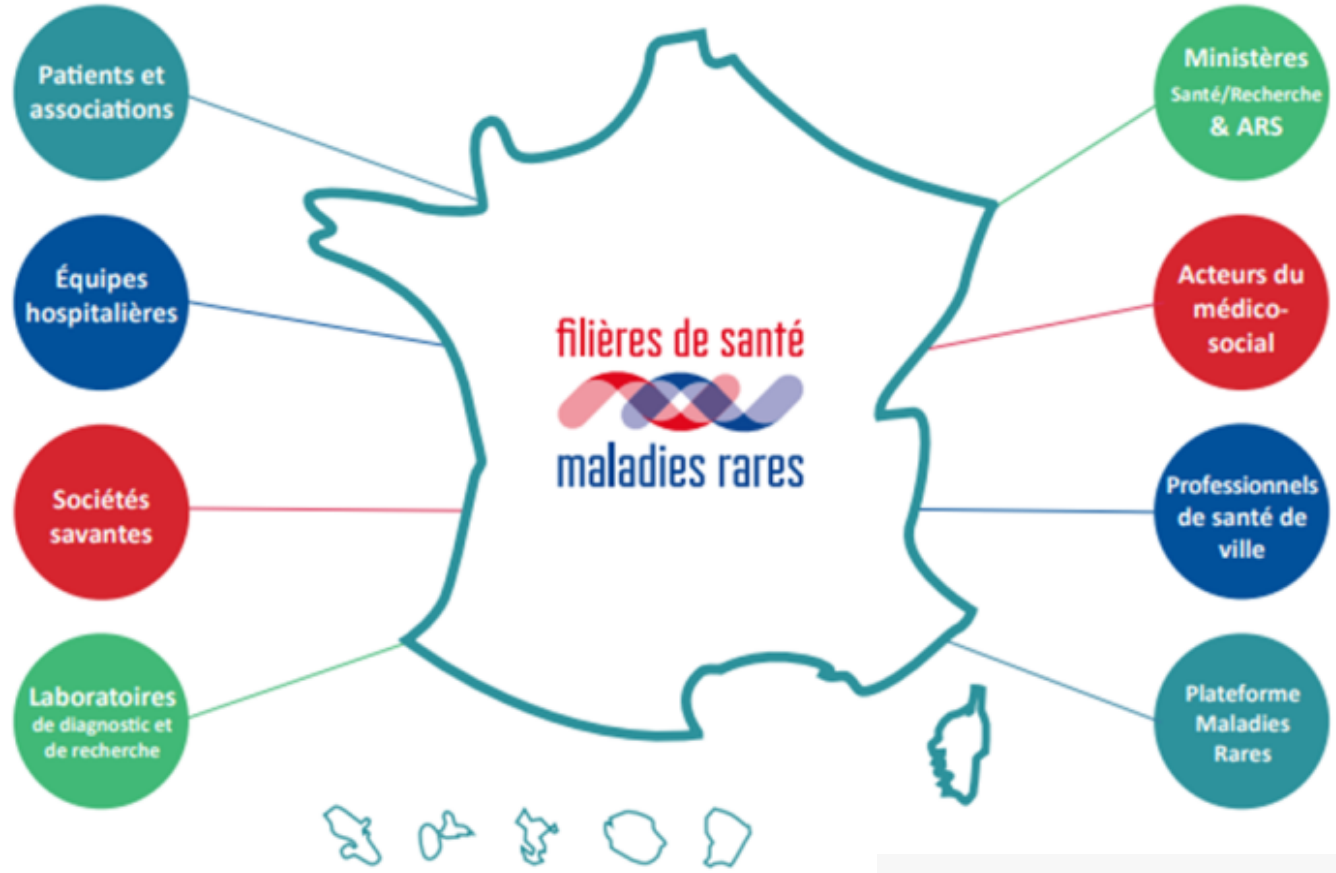

cardiogen

filière nationale de santé maladies cardiaques héréditaires

Du phénotype au génotype : quand et comment envoyer au généticien ?

2004 - 2024

2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

Quand ?

Recommendations	Class[a]
Genetic testing is recommended when a condition is diagnosed in a living or deceased individual with a likely genetic basis and a risk of VA and SCD.[56,183]	I
It is not recommended to undertake genetic testing in index patients with insufficient evidence of a genetic disease.	III
When a putative causative variant is first identified, evaluation for pathogenicity is recommended using an internationally accepted framework.[176]	I
It is recommended that genetic testing and counselling on its potential consequences should be undertaken by an expert multidisciplinary team.[179]	I

Où ?

cardiogen
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maladies cardiaques héréditaires

Conséquences ?

When a Class IV or Class V variant has been identified in a living or deceased individual with a condition that carries a risk of VA and SCD, genetic testing of first-degree and symptomatic relatives and obligate carriers is recommended.	I
It is recommended that Class III (variants of uncertain significance) and Class IV variants should be evaluated for segregation in families where possible, and the variant re-evaluated periodically.	I

Risque
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Centre de référence des maladies cardiaques héréditaires ou rares

Service de cardiologie

Centre de Référence des Maladies Cardiaques Héréditaires ou Rares

Petit aperçu de notre grande équipe

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Cardiologue Rythmologue et Coordonnateur du centre
Dr Isabelle DENJOY,
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Genetic testing for inherited arrhythmia syndromes and cardiomyopathies: results of the European Heart Rhythm Association survey

Ivan Zeljkovic [1], Anaïs Gauthey [2], Martin Manninger [3], Katarzyna Malaczynska-Rajpold [4], Jacob Tfelt-Hansen [5,6†‡], Lia Crotti [7,8†‡], Elijah R. Behr [9†‡], Federico Migliore [10], Arthur Wilde [11†‡], Julian Chun [12], and Giulio Conte [13,14*‡]

Europace. 2024; 26:euae216

Graphical Abstract

Genetic testing for inherited arrhythmia syndromes and cardiomyopathies: a physician-based EHRA survey

Methods/participants

- 28 question online
- EHRA platform & social media
- 57% 40–59 years, 34%
- 357 respondents/69 countries
  - 48/57 ESC countries + 21 rest of the
- 62% cardiac electrophysiologists
- 63% affiliated to university hospitals

Results

- 40% dedicated clinic & 27% genetic lab
- 78% face limitations in genetic testing
  - 35% no units/lab
  - 25% reimbursement issues
- 55% use genetic testing for diagnostics
- 92% offer testing w prior genetic counselling

Significant variability in genetic testing access and provision, mainly due to:

1. Dedicated units/genetic lab availability
2. Reimbursement issues

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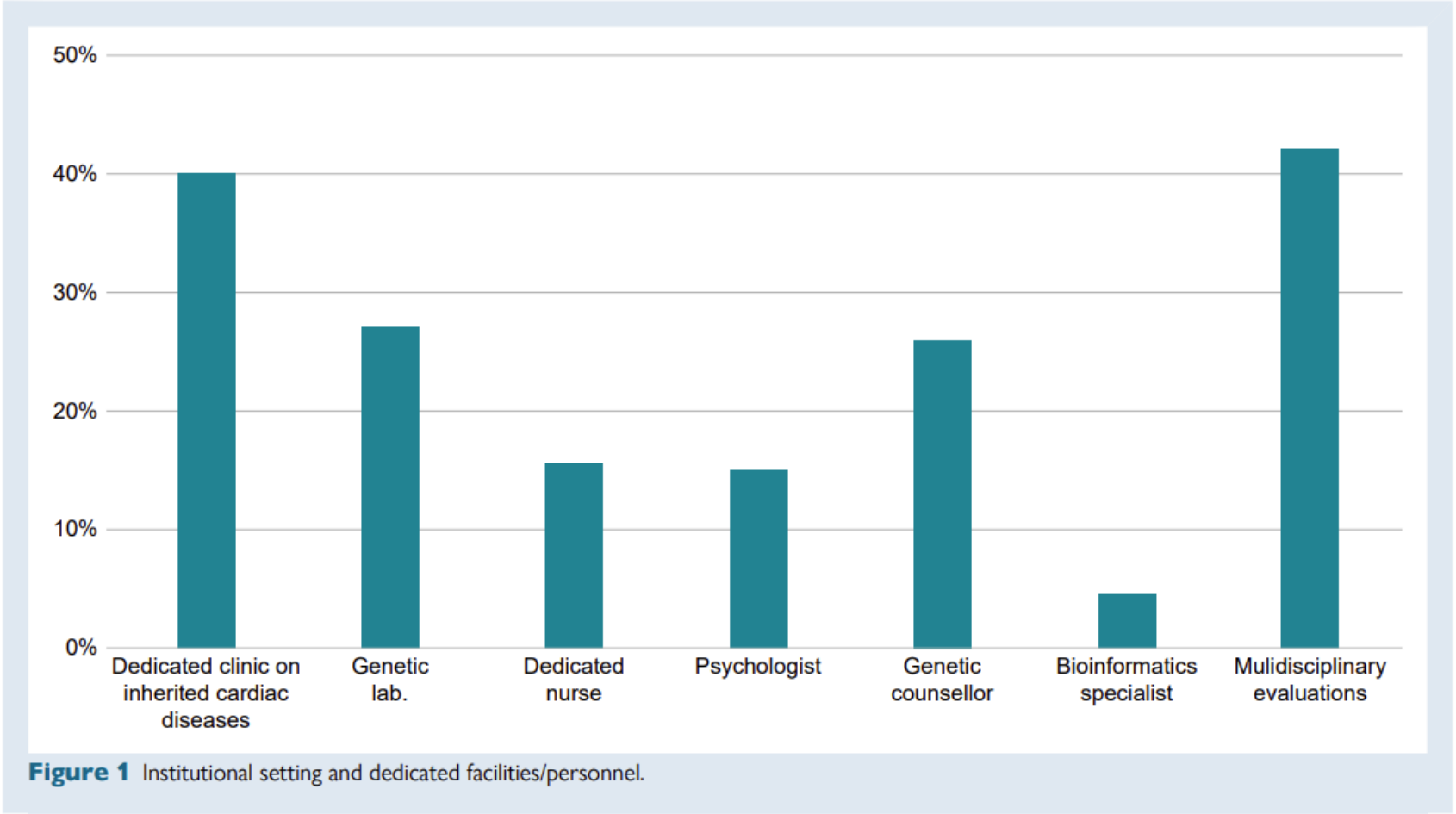

Figure 1 Institutional setting and dedicated facilities/personnel.

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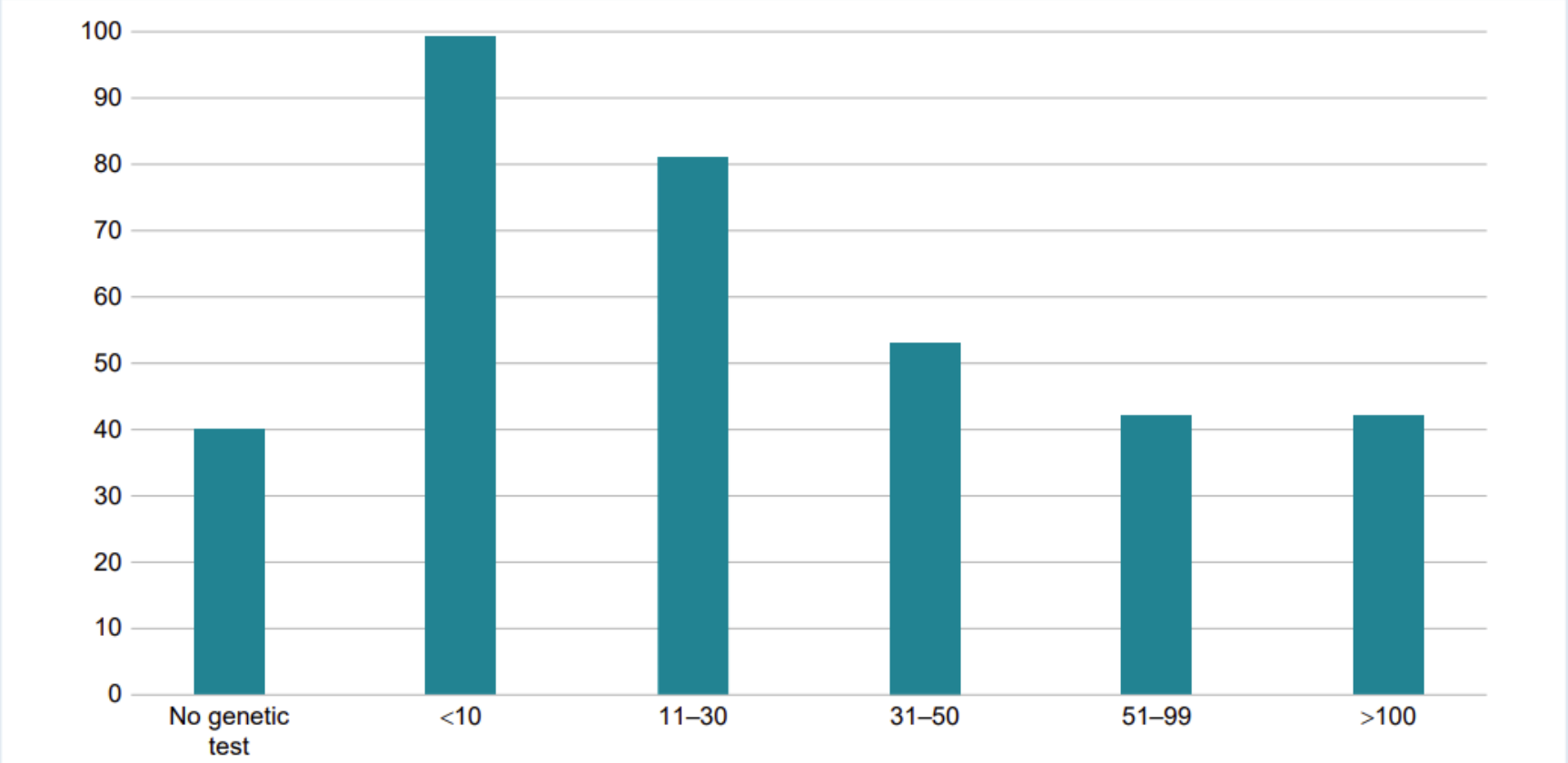

Figure 2 Number of genetic tests in the last 12 months.

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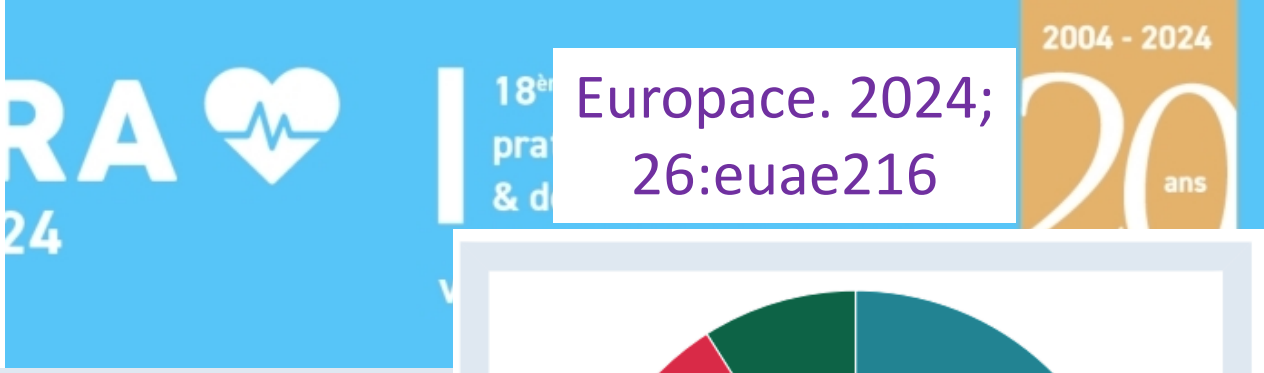

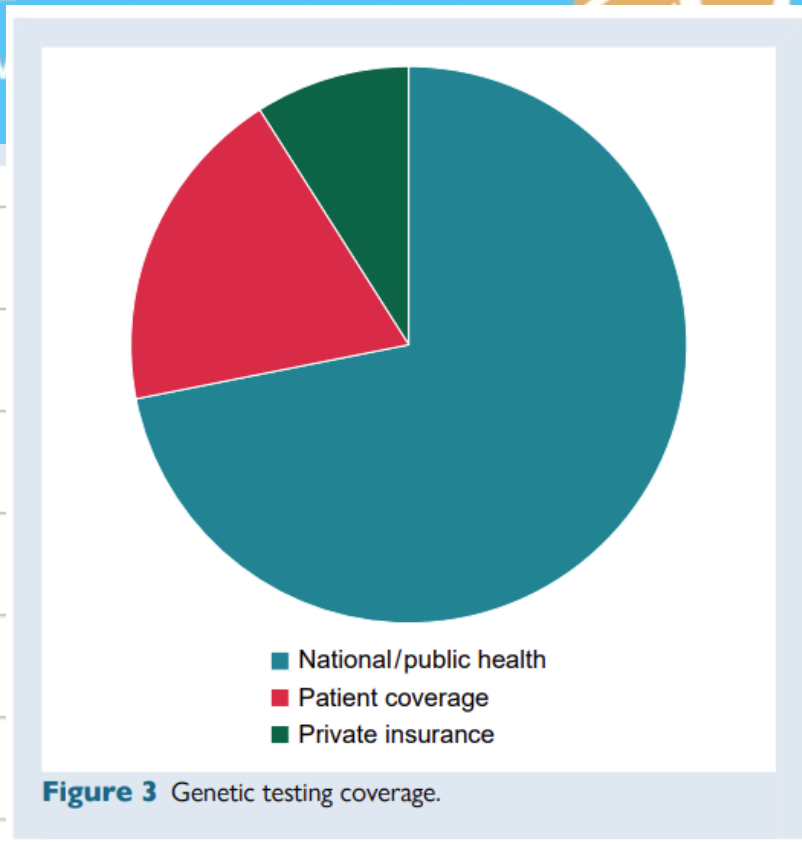

Figure 3 Genetic testing coverage.

Figure 6 Reasons for not providing genetic testing or for limited access (<10/year).

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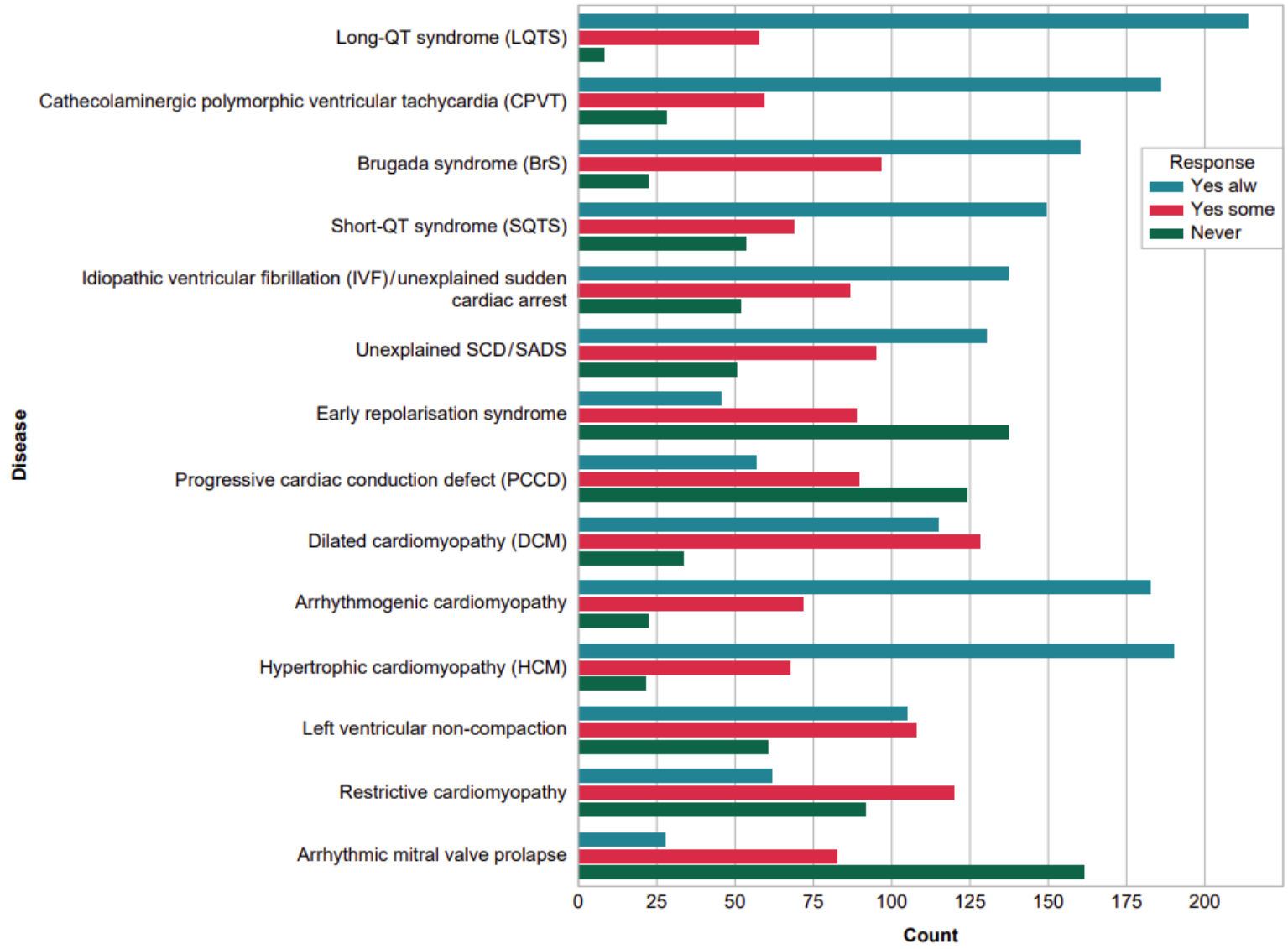

Figure 4 Diagnostic assessment by genetic testing of specific cardiac genetic diseases.