Cardio Risk

is a genomic tool at the service of precision medicine and genetic counseling

> ***As doctors we are used to seeing the most severe cases, but with genetics you are anticipating.***
>
> **Dr. Luis Izquierdo | Chief Medical Officer Veritas Genetics**

CardioRisk

Human and technological commitment for diagnosis and counseling.

What is CardioRisk?

It is a service for the diagnosis of hereditary cardiovascular disease that integrates:

- Veritas whole exome sequencing, with an optimized design to achieve a more homogeneous sequencing depth of the exome.
- The analysis, under the Double-check methodology, of 100 genes selected by an expert team in the classification of variants in the field of heart disease.[1,2]
- Pre-test and post-test counseling to the specialist provided by medical geneticists.
- The storage of sequencing data with a bioinformatic tool that allows subsequent access and re-analysis of the information, if necessary.

The ESC, AHA and CCS[3,4,5,6,7] recommend that patients with cardiomyopathy and channelopathy receive genetic counseling.

Scientific publications show that genetic studies in the field of familial heart disease are cost-effective.[8,9]

The test includes all the genes recommended by the American Heart Association (Scientific Statement 2020).[10]

Types of sample

The following sample types are accepted:

- Saliva in specific kit provided by Veritas
- Whole blood in EDTA
- DNA extracted according to Veritas specifications

Counseling to the specialist

Veritas provides a differential service by providing counseling to the specialist for the interpretation of the results of the patient, when needed.

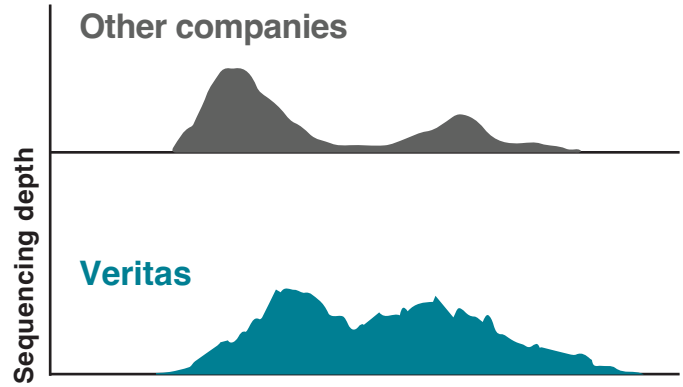
Additional services

Once CardioRisk test has been performed, the genetic analysis can be expanded to include:

- Other genes of interest based on the specialist criteria.
- Exome Diagnostic Service.
- Data reanalysis service for the patient to benefit from advances in scientific knowledge.[11]

Veritas whole exome technical information

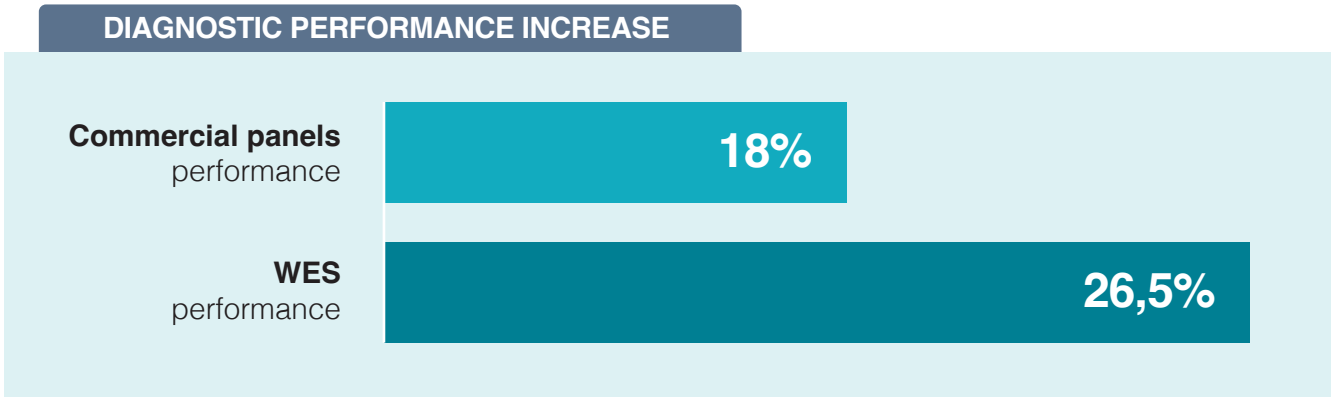
- Whole exome sequencing (WES) with 100x average coverage, sequencing more than 99% of the genes of interest at ≥20x.
- More than 19,000 genes covered.
- The classification of the variants is performed according to the American College of Medical Genetics and Genomics (ACMG) guidelines.
- Veritas has a team of expert curators who perform the interpretation of the variants based on the most up-to-date scientific knowledge, with a specialized software developed for a detailed variant classification.



Example of the different coverage of a specific region in the exome with Veritas WES versus other companies.

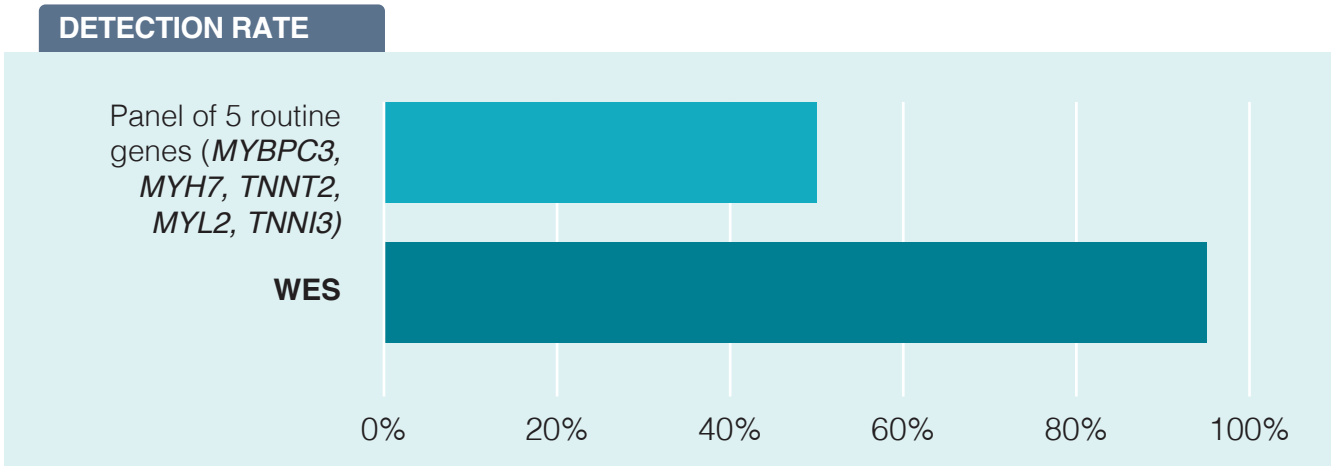
Whole exome sequencing (WES) is a suitable tool to address the genetic heterogeneity present in hereditary cardiovascular disease.

- Recent studies show a very significant improvement in diagnostic performance using exome sequencing compared to the use of panels.[12,13]
- A high number of cases present several mutations simultaneously.[13]
- The advantages of the exome are more prominent in those cases in which there is no high clinical suspicion as well as those in which the patient has recovered after an episode of sudden death.[12]



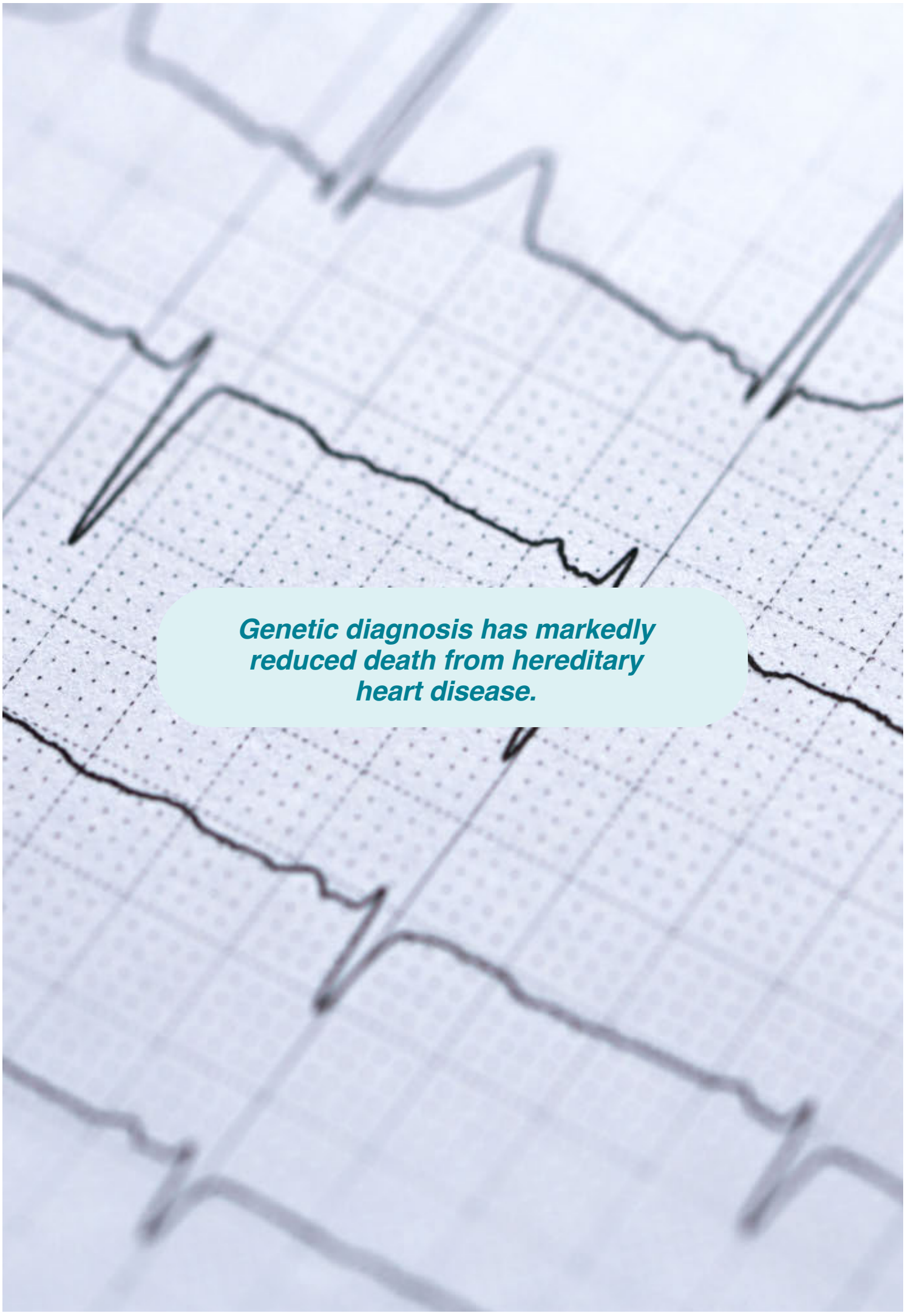
Circulation: Cardiovascular Genetics - AHA Journals

A study carried out by the Yale School of Medicine, on 200 cases of consecutive entry, in the framework of hereditary-based cardiovascular disease (CVD), a diagnostic increase from 18% to 26.5% was observed with the use of the exome p = 0.04 [12]



Archives of Cardiovascular Diseases Supplements

Multicenter study on 200 cases of hypertrophic cardiomyopathy. The diagnostic yield appreciated is 95% compared to the 50% obtained with a reduced panel of 5 genes [13] *(60% with the usual genes in routine practice in Spain)* [4,14]


Genetic diagnosis has markedly reduced death from hereditary heart disease.

LIST OF FAMILY HEART DISEASES AND ASSOCIATED GENES
(GROUPED BY CONDITION)

Primary cardiomyopathies	Hypertrophic cardiomyopathy	*ACTC1, ACTN2, COX15, CSRP3, FHL1, FLNC, FXN, JPH2, LAMP2, LDB3, MYBPC3, MYH7, MYL2, MYL3, NEXN, NF1, PLN, PRKAG2, SLC25A4, TCAP, TNNC1, TNNI3, TNNT2, TPM1, TTN, VCL*
	Dilated cardiomyopathy	*ABCC9, ACTC1, ACTN2, BAG3, CRYAB, CSRP3, DES, DSG2, FKTN (FCMD), LDB3, LMNA, MYBPC3, MYH7, NEXN, NF1, PLN, RBM20, SCN5A, TAZ, TCAP, TMEM43, TNNC1, TNNI3, TNNT2, TPM1, TTN, VCL*
	Left ventricular noncompaction	*ACTC1, CSRP3, LDB3, LMNA, MYBPC3, MYH7, SCN5A, TAZ, TNNT2, TPM1, TTN*
	Arrhythmogenic right ventricular cardiomyopathy	*DES, DSC2, DSG2, DSP, JUP, LMNA, PKP2, PLN, RYR2, TGFB3, TMEM43, TTN*
	Familial restrictive cardiomyopathy	*ACTC1, BAG3, DES, FLNC, MYH7, MYL2, MYL3, TNNI3, TNNT2, TPM1, TTN*
Metabolic cardiomyopathies	Fabry disease	*GLA*
	Pompe disease	*GAA*
	Danon disease	*LAMP2*
	Barth syndrome	*TAZ*
	Transthyretin-related familial amyloidotic cardiomyopathy	*TTR*
Channelopathies - Arrhythmias	Short QT syndrome	*KCNH2, KCNJ2, KCNQ1*
	Long QT & Romano-Ward syndrome	*CALM1, CALM2, CAV3, KCNE1, KCNE2, KCNH2, KCNQ1, SCN5A*
	Jervel and Lange-Nielsen syndrome	*KCNE1, KCNQ1*
	Brugada syndrome	*CACNA1C, SCN5A*
	Catecholaminergic polymorphic ventricular tachycardia	*CALM1, CALM3, CASQ2, RYR2, TRDN*
	KATP channelopathies	*ABCC9*
	Familial atrial fibrillation	*ABCC9, KCNE2, KCNH2, KCNJ2, KCNQ1, LMNA, PRKAG2, RYR2, SCN5A, TNNI3, TNNT2*
	Wolf-Parkinson-White	*PRKAG2*
	Familial progressive cardiac conduction defect	*SCN5A*
Syndromes with vascular involvement	Marfan syndrome	*FBN1*
	Loeys-Dietz syndrome	*SMAD3, TGFB2, TGFB3, TGFBR1, TGFBR2*
	Congenital contractural arachnodactyly (Beals syndrome)	*FBN2*
	Familial thoracic aortic aneurysm	*ACTA2, ELN, FBN1, FLNA, LOX, MYH11, MYLK, NOTCH1, PRKG1, SMAD3, SKI, SLC2A10, SMAD4, TGFBR1, TGFBR2*
	Ehlers-Danlos syndrome type IV (vascular type)	*COL3A1*
RASopathies	Noonan syndrome	*BRAF, KRAS, MAP2K1, NRAS, PTPN11, RAF1, RIT1, SOS1, SOS2*
	LEOPARD syndrome	*BRAF, MAP2K1, PTPN11, RAF1*
	Cardiofaciocutaneous syndrome	*BRAF, KRAS, MAP2K1, MAP2K2*
	Costello syndrome	*HRAS*
	Noonan-like syndrome with loose anagen hair (OMIM # 607721 # 617506)	*PPP1CB, SHOC2*
	Noonan-like syndrome with or without juvenile myelomonocytic leukemia	*CBL*
Other syndromes linked to heart disease	Friedreich ataxia with associated cardiomyopathy	*FXN*
	Andersen-Tawil syndrome	*KCNJ2*
	Cantu syndrome	*ABCC9*
	Fatal infantile cardioencephalomyopathy with COX deficiency	*COX15*
	Charcot-Marie-Tooth	*BAG3, LMNA*
	Cutis Laxa	*EFEMP2*
	Limb-Girdle muscular dystrophy	*CAV3, FKTN (FCMD), LMNA, TCAP, TTN*
	Distal muscular dystrophy	*MYH7*
	Emery-Dreifuss muscular dystrophy	*EMD, FHL1, LMNA, TMEM43*
	Fukuyama muscular dystrophy	*FKTN (FCMD)*
	Muscular dystrophy linked to LMNA	*LMNA*
	Leigh syndrome	*COX15*
	Early onset myopathy with lethal cardiomyopathy (OMIM # 611705)	*TTN*
	Neurofibromatosis	*NF1*
	Timothy syndrome	*CACNA1C*
	Walker-Walburg syndrome	*FKTN (FCMD)*
Other risk factors (Ischemic Heart Disease)	Familial hypercholesterolemia	*ABCG5, ABCG8, APOE, APOB, LDLR, LDLRAP1 (ARH), LIPA, PCSK9*

References

1. Ingles J, et al. Evaluating the clinical validity of hypertrophic cardiomyopathy genes. Circ Genom Precis Med. 2019;12:e002460. doi:10.1161/CIRCGEN.119.002460.
2. Walsh R, et al. Defining the genetic architecture of hypertrophic cardiomyopathy: re-evaluating the role of non-sarcomeric genes. Eur Heart J. 2017;38:3461–3468. doi:10.1093/eurheartj/ehw603.
3. Ackerman MJ, et al. HRS/EHRA expert consensus statement on the state of genetic testing for the channelopathies and cardiomyopathies: this document was developed as a partnership between the Heart Rhythm Society (HRS) and the European Heart Rhythm Association (EHRA). Europace 2011;13(8):1077-1109. doi:10.1093/europace/eur245.
4. Authors/Task Force members, et al. 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy: the Task Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC). Eur Heart J. 2014;35(39):2733-2779. doi:10.1093/eurheartj/ehu284.
5. Charron P, et al. Genetic counselling and testing in cardiomyopathies: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. Eur Heart J. 2010;31(22):2715-26. doi:10.1093/eurheartj/ehq271.
6. Gersh BJ, et al. 2011 ACCF/AHA guideline for the diagnosis and treatment of hypertrophic cardiomyopathy: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines developed in collaboration with the American Association for Thoracic Surgery, American Society of echocardiography, American Society of nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol. 2011;58(25):e212-e260. doi:10.1016/j.jacc.2011.06.011.
7. Gollob MH, et al. Recommendations for the use of genetic testing in the clinical evaluation of inherited cardiac arrhythmias associated with sudden cardiac death: Canadian Cardiovascular Society/Canadian Heart Rhythm Society joint position paper. Can J Cardiol. 2011;27(2):232-245. doi:10.1016/j.cjca.2010.12.078.
8. Ingles J, et al. A cost-effectiveness model of genetic testing for the evaluation of families with hypertrophic cardiomyopathy. Heart. 2012;98(8):625-630. doi:10.1136/heartjnl-2011-300368.
9. Perez MV, et al. Cost-effectiveness of genetic testing in family members of patients with long-QT syndrome. Circ Cardiovasc Qual Outcomes. 2011;4:76-84. doi:10.1161/CIRCOUTCOMES.110.957365.
10. Musunuru K, et al. Genetic testing for inherited cardiovascular diseases: a scientific statement from the American Heart Association. Circ Genom Precis Med. 2020;13:e000067. doi:10.1161/HCG.0000000000000067.
11. Baker SW, et al. Automated clinical exome reanalysis reveals novel diagnoses. J Mol Diagn. 2019 Jan;21(1):38-48. doi:10.1016/j.jmoldx.2018.07.008.
12. Seidelmann SB, et al. Application of whole exome sequencing in the clinical diagnosis and management of inherited cardiovascular diseases in adults. Circ Cardiovasc Genet. 2017;10(1):e001573. doi:10.1161/CIRCGENETICS.116.001573.
13. Nguyen K, et al. Genetic spectrum of hypertrophic cardiomyopathy revisited. Whole Exome Sequencing reveals extreme genetic heterogeneity, new gene mutations in a multicenter series of 200 patients. Archives of Cardiovascular Diseases Supplements. 2019;11(1):29. doi:10.1016/j.acvdsp.2018.10.059.
14. Binder J, et al. Echocardiography-guided genetic testing in hypertrophic cardiomyopathy: septal morphological features predict the presence of myofilament mutations. Mayo Clin Proc. 2006;81(4):459-467. doi:10.4065/81.4.459.

Bibliography

- Zook JM. et al. Extensive sequencing of seven human genomes to characterize benchmark reference materials. Sci Data 2016;3:160025 doi: 10.1038/sdata.2016.25. PMID: 27271295

- Mandelker D et al. Navigating highly homologous genes in a molecular diagnostic setting: a resource for clinical next-generation sequencing. Genet Med 2016;18:1282-1289. PMID: 27228465

- Landrum MJ et al. ClinVar: public archive of interpretations of clinically relevant variants. Nuc Acids Res 2016;44(1):D862–D868. doi: 10.1093/nar/gkv1222. PMID 26582918

- Richards S et al. 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. PMID 25741868

- Stenson PD et al. The Human Gene Mutation Database: towards a comprehensive repository of inherited mutation data for medical research, genetic diagnosis and next-generation sequencing studies. Hum Genet 2017;136:665-677. PMID: 28349240

About Veritas

Veritas Genetics, a *LetsGetChecked* company, is one of the world leaders in advanced genetic sequencing and clinical interpretation of the exome and whole genome, driving the transition to personalized and preventive medicine.

Using state-of-the-art technologies and the highest safety standards, Veritas Genetics helps individuals, healthcare professionals and institutions worldwide to understand and anticipate genetic risks, enabling more informed and proactive health decisions.

With a focus on innovation and accessibility, Veritas Genetics transforms the way we understand and care for health at every stage of life.

Veritas

a LetsGetChecked company

info@veritasint.com | veritasint.com

MB.MC_EN_V3.0
07/03/2025