Supporting Information

Supplementary material

This appendix was part of the submitted manuscript and has been peer reviewed.
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Appendix to: Gray MP, Fatkin D, Ingles J, et al. Genetic testing in cardiovascular disease. *Med J Aust* 2024; doi: 10.5694/mja2.52278.

Disease/Condition	ClinGen *(as of 29 March 2023)*		Sample Genetic Testing Recommendations	
	Clinical Significance	Main Genes	Index Patient	Family Members
LIPID METABOLISM				
Familial hypercholesterolaemia (FH)	Definitive	*APOB, LDLR, LDLRAP1, PCSK9*	"The diagnosis of FH should be made using both phenotypic criteria…and genetic testing, but when genetic testing is not available the diagnosis should be made phenotypically (1-A)"[1] "When possible, genetic testing should be used to confirm the diagnosis of FH, especially if cascade testing…is planned (1-A)"[1]	"Cascade testing…should be carried out using both a phenotypic and genotypic strategy, but if genetic testing is not available a phenotypic strategy should be used (1-A)"[1] "Variant specific genetic testing is more cost-effective than phenotypic testing and should be employed to screen family members after a pathogenic, or likely pathogenic, gene variant has been identified in the family (1-A)"[1] "Genetic cascade testing should initially be prioritised for first-degree relatives of a variant carrier and sequentially extended as additional carriers are identified… (1-A)"[1] "Genetic testing for FH should generally be offered to diagnose children after a pathogenic or likely pathogenic gene variant has been identified in a parent or first-degree relative (1-B)"[1]
THORACIC AORTIC DISEASE				
Heritable thoracic aortic disease (HTAD)	Definitive	*ACTA2, FBN1, MYH11, SMAD3, TGFBR2, TGFBR1, TGFBR2*	"In patients with aortic root/ascending aortic aneurysms or aortic dissection and risk factors for [heritable thoracic aortic disease], genetic testing to identify pathogenic/likely pathogenic variants…is recommended (1-B)"[2]	"In patients with an established pathogenic or likely pathogenic variant, genetic testing of at-risk biological relatives (i.e., cascade testing) is recommended (1-B)"[2] "In a family with aortic root/ascending aortic aneurysms or aortic dissection, if the disease-causing variant is not identified with genetic
	Strong	*LOX, MYLK, PRKG1*		

				testing, screening aortic imaging…of at-risk biological relatives (i.e., cascade testing) is recommended (1-B).”[2]
INHERITED CARDIOMYOPATHIES				
Hypertrophic cardiomyopathy (HCM)	Definitive	*ALPK3, PRKAG2, MYBPC3, MYL2, ACTC1, MYL3, MYH7, TNNT2, TNNI3, TPM1*	“In patients with HCM, genetic testing is beneficial to elucidate the genetic basis to facilitate the identification of family members at risk for developing HCM (cascade testing) (1-B)”[3] “In patients with an atypical clinical presentation of HCM or when another genetic condition is suspected to be the cause, a work-up including genetic testing for HCM and other genetic causes of unexplained cardiac hypertrophy…is recommended (1-B)”[3]	“…Cascade genetic testing (when a pathogenic/likely pathogenic variant has been identified in the proband) should be offered (1-B)”[3]
Dilated cardiomyopathy (DCM)	Definitive	*BAG3, DES, FLNC, LMNA, MYH7, RBM20, SCN5A, TNNC1, TNNT2, TTN*	Genetic testing indicated in “[all] patients with a diagnosis of DCM or [hypokinetic non-dilated cardiomyopathy]…in order to identify genetically affected individuals at a preclinical phase.”[4]	Genetic testing indicated in “all first-degree adult relatives of [DCM] patients and a definite disease-causing mutation, regardless of their phenotype….”[4]
Arrhythmogenic right ventricular cardiomyopathy (ARVC)	Definitive	*DSC2, DSG2, DSP, JUP, PKP2, TMEM43*	Genetic testing is recommended “in patients with a suspected or definite diagnosis of ARVC (I-B)”[5]	“Mutation-specific genetic testing is recommended for family members and appropriate relatives following the identification of the…ARVC-causative mutation in an index case.”[5]
INHERITED ARRHYTHMIC DISORDERS				
Long QT syndrome (LQTS)	Definitive	*CALM1, CALM2, CALM3, KCNH2, KCNQ1, SCN5A*	Genetic testing is recommended “in patients with clinically diagnosed LQTS (1-C)”[5] “Molecular genetic testing for definitive disease associated genes…should be offered to all index patients with ahigh	“Variant-specific genetic testing is recommended for family members and appropriate relatives following the identification of the disease-causing variant.”[6]
	Strong	*TRDN*		

			probability of LQTS, based on examination of the patient's clinical history, family history, and ECG characteristics obtained at baseline, during ECG Holter recording and exercise stress testing."[6]	
Catecholaminergic polymorphic ventricular tachycardia (CPVT)	Definitive	*CASQ2, RYR2, TECRL, TRDN*	"In any patient satisfying the diagnostic criteria for CPVT…, molecular genetic testing is recommended for the currently established definite/strong evidence CPVT-susceptibility genes."[6]	"Variant-specific testing is recommended for family members and appropriate relatives following the identification of the disease-causative variant."[6] "Predictive genetic testing in related children at risk of inheriting a [pathogenic or likely pathogenic] variant is recommended from birth onward (any age)."[6]
Brugada syndrome (BrS)	Definitive	*SCN5A*	"Genetic testing for *SCN5A* gene is recommended for probands with BrS (1-C)"[5]	"Variant-specific genetic testing is recommended for family members and appropriate relatives following the identification of the disease-causative variant."[6]
Short QT syndrome (SQTS)	Definitive	*KCNH2*	"Genetic testing is indicated in patients diagnosed with SQTS (1-C)"[5]	"Variant-specific genetic testing is recommended for family members and appropriate relatives following the identification of the disease-causative variant."[6]
	Strong	*KCNQ1*		

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