Wong et al (2014) assessed the yield of clinical history and cardiac and genetic evaluations in 112 pediatric relatives of 61 probands with SADS.[70] All subjects underwent initial cardiac investigations included a 12-lead ECG, transthoracic 2-dimensional echocardiogram, exercise ECG when possible, and 24-hour Holter monitoring, with additional investigations, including signal-averaged ECG, cardiac MRI, and ajmaline provocation tests as indicated. A probable diagnosis of an inherited cardiac condition was made in 18 (29.5%) of 61 families, most often (15/18 [83%]) after evaluation of an adult relative of the proband. BrS was the most common diagnosis, affecting 13 (72%) families, with LQTS in 3 (17%) families and CPVT in 2 (11%). The targeted genetic diagnosis was undertaken in 14 (78%) of 18 families with an inherited cardiac condition diagnosis. Two (20%) of 10 families with BrS were identified with an *SCN5A* variant. The testing yield was 50% for both LQTS (1 *KCNH2* variant detected) and CPVT (1 *RyR2* variant detected).

Bagnall et al (2016) reported on prospectively collected data for cases of SCD in children and young adults (up to age 35) in Australia and New Zealand from 2010 to 2012.[71] Of the 490 cases of SCD, 198 (40%) were unexplained after the autopsy. Of the unexplained deaths, 113 underwent genetic analysis of at least 59 cardiac arrhythmia and cardiomyopathy genes. Thirty-six pathogenic and probably pathogenic variants were found in 31 cases of unexplained SCD. Screening of families was performed in 91 of the 198 families in which an unexplained SCD occurred. A clinical diagnosis was established in 12 of the 91 families; inherited arrhythmogenic diseases were identified in 7 families.

Section Summary: Genetic Testing in Family Members of Probands Experiencing SCD

The evidence on the clinical validity of genetic testing for cardiac ion channelopathies in family members of probands with unexplained cardiac death or individuals with unexplained cardiac arrest consists of cohort studies that describe the genetic testing yield. In all studies identified, genetic testing was obtained only after a specific diagnosis was suspected based on other findings. In most studies, the yield was less than 50%.

There is potential for the utility of genetic testing of family members in the setting of a proband with SCD or unexplained cardiac arrest. However, identified studies related to testing yields in this setting used testing only after a specific channelopathy was suspected based on history or ancillary testing. Genetic testing can be part of a diagnostic strategy for patients with family members who experienced unexplained sudden cardiac arrest, but it should be preceded by thorough clinical evaluation.

Summary of Evidence

Long QT Syndrome

For individuals with suspected congenital LQTS who receive genetic testing for variants associated with congenital LQTS, the evidence includes observational studies reporting on the testing yield. Relevant outcomes are overall survival, test accuracy and validity, other test performance measures, changes in reproductive decision making, and morbid events. A genetic variant can be identified in approximately 72% to 80% of those with LQTS. Most are point mutations identified by gene sequencing analysis; however, a small number are deletions and duplications are best identified by chromosomal microarray analysis. The clinical validity of testing in LQTS is high, in the range of 70% to 80%. The clinical utility of genetic testing for LQTS is high when there is a moderate-to-high pretest probability and when the diagnosis cannot be made with certainty by other methods. There is a strong chain of evidence to suggest that testing for variants associated with LQTS in individuals who are suspected to have these disorders, but in whom the diagnosis cannot be made by other methods, leads to improved outcomes. A definitive diagnosis of LQTS leads to treatment with β-blockers in most cases, and sometimes to treatment with an implantable cardiac defibrillator (ICD). As a result, confirming the diagnosis is likely to lead to a health outcome benefit by reducing the risk for ventricular arrhythmias and sudden cardiac death. While there is evidence suggesting that different genotypes are associated with varying risk of sudden cardiac death, there is insufficient evidence on the effects of changes in clinical management based on different genotypes. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are asymptomatic with close relative(s) with a known LQTS variant who receive genetic testing for variants associated with congenital LQTS, the evidence includes observational studies reporting on changes in management. Relevant outcomes are overall survival, test accuracy and validity, other test performance measures, changes in reproductive decision making, and morbid events. The studies conducted cardiologic and genetic evaluations of surviving family members of probands and determined whether the family members had the genetic variant. For close relatives of patients with known LQTS variants who were found to have a pathologic variant, preventive treatment was initiated. The studies did not provide follow-up information on the family members with the variant who received preventive treatment. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Brugada Syndrome

For individuals with suspected BrS who receive genetic testing for variants associated with BrS, the evidence includes observational studies reporting on testing yields and a meta-analysis. Relevant outcomes are overall survival, test accuracy and validity, other test performance measures, changes in reproductive decision making, and morbid events. The clinical validity of testing for BrS is low: a genetic variant can only be identified in approximately 25% to 35% of BrS. BrS management changes, primarily use of ICDs, are directed by clinical symptoms. A meta-analysis reported that the presence of an *SCN5A* variant in patients with BrS was not predictive of the occurrence of a cardiac event, while a registry study published after the meta-analysis reported that the presence of the variant was related to a higher rate of cardiac events. There is limited evidence on changes in management based on genetic testing in a symptomatic proband without a definitive diagnosis. It is not clear that a genetic diagnosis in the absence of other clinical signs and symptoms leads to a change in management that improves outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who are asymptomatic with a close relative(s) with a known BrS variant who receive genetic testing for variants associated with congenital BrS, the evidence includes observational studies reporting on testing yields. Relevant outcomes are overall survival, test accuracy and validity, other test performance measures, changes in reproductive decision making, and morbid events. BrS management changes, primarily use of ICDs, are directed by clinical symptoms. There is limited evidence on the effect of changes in management based on genetic testing in an individual with family members who have a known variant. However, a negative test would allow family members to defer further testing. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Given the limited available evidence on genetic testing for BrS, clinical input was obtained. There was a consensus among the specialty societies and academic medical centers providing clinical input that genetic testing for BrS is medically necessary to establish a definitive diagnosis in patients with BrS symptoms and to evaluate family members of an individual with a known genetic variant of BrS. A review of guidelines from American and international cardiac specialty societies (American Heart Association, Heart Rhythm Society, European Heart Rhythm Association, Asia Pacific Heart Rhythm Society) was also conducted. The guidelines acknowledged that although the evidence is weak, genetic testing is recommended for both individuals with a suspected but not a definitive diagnosis of BrS and asymptomatic family members of individuals with known BrS variants.

Catecholaminergic Polymorphic Ventricular Tachycardia

For individuals with suspected CPVT who receive genetic testing for variants associated with congenital CPVT, the evidence includes observational studies reporting on testing yields. Relevant outcomes are overall survival, test accuracy and validity, other test performance measures, changes in reproductive decision making, and morbid events. A genetic variant can be identified in approximately 51% to 75% of CPVT patients. The clinical validity of testing in CPVT is moderate, in the range of 50% to 75%. The clinical utility of genetic testing for CPVT is high when there is a moderate-to-high pretest probability and when the diagnosis cannot be made with certainty by other methods. There is a strong chain of evidence to suggest that testing for variants associated with CPVT in individuals who are suspected to have these disorders, but in whom the diagnosis cannot be made by other methods, leads to improved outcomes. Confirming the diagnosis of CPVT is likely to lead to a health outcome benefit by initiating changes in management that reduce the risk of ventricular arrhythmias and sudden cardiac death. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are asymptomatic with a close relative(s) with a known CPVT variant who receive genetic testing for variants associated with congenital CPVT, the evidence includes observational studies reporting testing yields. Relevant outcomes are overall survival, test accuracy and validity, other test performance measures, changes in reproductive decision making, and morbid events. For close relatives of patients with known CPVT variants who are found to have a pathologic variant, preventive treatment can be initiated. Also, a negative test in the setting of a known familial variant should have a high negative predictive value. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Short QT Syndrome

For individuals with suspected SQTS who receive genetic testing for variants associated with SQTS, the evidence includes limited data on testing yields. Relevant outcomes are overall survival, test accuracy and validity, other test performance measures, changes in reproductive decision making, and morbid events. The clinical validity of testing for SQTS is low: a genetic variant can only be identified in approximately 15% to 20% of SQTS patients. SQTS management changes, primarily use of ICDs, are directed by clinical symptoms. There is limited evidence on changes in management based on genetic testing in a symptomatic proband without a definitive diagnosis. It is not clear that a genetic diagnosis in the absence of other clinical signs and symptoms leads to a change in management that improves outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who are asymptomatic with a close relative(s) with a known SQTS variant who receive genetic testing for variants associated with congenital SQTS, the evidence includes observational studies reporting on testing yields. Relevant outcomes are overall survival, test accuracy and validity, other test performance measures, changes in reproductive decision making, and morbid events. For patients with SQTS, management changes, primarily use of ICDs, are directed by clinical symptoms. There is limited evidence on changes in management based on genetic testing in an individual with family members who have a known variant. It is not clear that a genetic diagnosis in the absence of other clinical signs and symptoms leads to a change in management that improves outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

Given the limited available evidence on genetic testing for SQTS, clinical input was obtained. Among the specialty societies and academic medical centers providing input, there was no consensus on the use of genetic testing for variants associated with SQTS; however, there was consensus that genetic testing to predict future risk of disease in individuals with close relatives who have a known variant associated with SQTS is useful in management that may lead to improved outcomes. A review of guidelines was also conducted. The use of genetic testing for patients with suspected SQTS was not addressed in many guidelines; however, one did state that testing may be considered if a cardiologist has established a strong clinical index of suspicion. Additionally, the guidelines acknowledged that although the evidence is weak, genetic testing may be considered for asymptomatic family members of individuals with known SQTS variants.

For individuals who are asymptomatic with a close family member(s) who experienced sudden cardiac death specific diagnosis has been made who receive genetic testing for variants associated with cardiac ion channelopathies, the evidence includes cohort studies that describe the genetic testing yield. In all studies identified, genetic testing was obtained only after a specific diagnosis was suspected based on history or ancillary testing. The evidence is insufficient to determine the effects of the technology on health outcomes.

Supplemental Information

Clinical Input From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 3 specialty societies (4 reviewers) and 4 academic medical centers (9 reviewers) while this policy was under review in 2015. Input was limited to the use of genetic testing for Brugada syndrome (BrS) and short QT syndrome (SQTS). There was a consensus that genetic testing for BrS is medically necessary to establish the diagnosis of BrS in an individual with a suspected but not definitive diagnosis of BrS and to evaluate family members of an individual with a known pathogenic genetic variant for BrS. There was less consensus on whether genetic testing for variants associated with SQTS is medically necessary to establish the diagnosis of SQTS in an individual with a suspected but not definitive diagnosis of SQTS, but there was consensus that testing for SQTS to evaluate family members of an individual with a known pathogenic genetic variant for SQTS is medically necessary. However, reviewers acknowledged that the rarity of SQTS somewhat limited conclusions that could be made.

Practice Guidelines and Position Statements

American Heart Association, American College of Cardiology, and the Heart Rhythm Society

In 2017, the American Heart Association, American College of Cardiology, and the Heart Rhythm Society published guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death.[72] Table 7 summarizes the recommendations relating to cardiac ion channelopathies.

Table 7. Recommendations for Genetic Testing in Cardiac Channelopathies

Consensus Recommendation	COR	LOE
In first-degree relatives of patients who have a causative mutation for long QT syndrome, catecholaminergic polymorphic ventricular tachycardia, short QT syndrome, or Brugada	I (strong)	B-NR

Consensus Recommendation	COR	LOE
syndrome, genetic counseling and mutation-specific genetic testing are recommended.		
In patients with clinically diagnosed long QT syndrome, genetic counseling and genetic testing are recommended. Genetic testing offers diagnostic, prognostic, and therapeutic information.	I (strong)	B-NR
In patients with catecholaminergic polymorphic ventricular tachycardia and with clinical VT or exertional syncope, genetic counseling and genetic testing are reasonable. Genetic testing may confirm a diagnosis; however, therapy for these patients is not guided by genotype status.	IIa (moderate)	B-NR
In patients with suspected or established Brugada syndrome, genetic counseling and genetic testing may be useful to facilitate cascade screening of relatives, allowing for lifestyle modification and potential treatment.	IIb (weak)	C-EO
In patients with short QT syndrome, genetic testing may be considered to facilitate screening of first-degree relatives.	IIb (weak)	C-EO

B-NR: moderate level of evidence, nonrandomized studies; C-EO: consensus of expert opinion based on clinical experience; COR: class of recommendation; LOE: level of evidence; VT: ventricular tachycardia.

Heart Rhythm Society, European Heart Rhythm Association, et al

In 2013, the Heart Rhythm Society, the European Heart Rhythm Association, and the Asia Pacific Heart Rhythm Society issued an expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes.[73] The consensus statement refers to the 2011 guidelines on genetic testing for channelopathies and cardiomyopathies discussed next for the indications for genetic testing in patients affected by inherited arrhythmias and their family members and for diagnostic, prognostic, and therapeutic implications of the results of genetic testing. The 2013 consensus statement provided guidance for the evaluation of patients with idiopathic ventricular fibrillation, sudden unexplained death syndrome, and sudden unexplained death in infancy. Guidance on genetic testing for these patients was included (see Table 8). Idiopathic ventricular fibrillation is defined as a resuscitated cardiac arrest victim, preferably with documentation of ventricular fibrillation, in whom known cardiac, respiratory, metabolic, and toxicologic etiologies have been excluded through clinical evaluation.

The guidelines defined several terms related to specific types of sudden cardiac death, including sudden unexpl ained death syndrome, which refers to an unexplained sudden death in an individual older than 1 year of age, sudden arrhythmic death syndrome, which refers to a sudden unexplained death syndrome case with negative pathologic and toxicologic assessment, and sudden unexplained death in infancy, which refers to an unexplained sudden death in an individual younger than 1 year of age with negative pathologic and toxicologic assessment.

Table 8. Recommendations for Genetic Testing in IVF, SUDS, and SUDI

	Consensus Recommendation	Class
IVF	Genetic testing in IVF can be useful when there is suspicion of a specific	IIa

	Consensus Recommendation	Class
	genetic disease following clinical evaluation of the IVF patient and/or family members.	
	Genetic screening of a large panel of genes in IVF patients in whom there is no suspicion of an inherited arrhythmogenic disease after clinical evaluation should not be performed.	III
SUDS	Collection of blood and/or suitable tissue for molecular autopsy/postmortem genetic testing is recommended in all SUDS victims.	I
	Genetic screening of the first-degree relatives of a SUDS victim is recommended whenever a pathogenic mutation in a gene associated with increased risk of sudden death is identified by molecular autopsy in the SUDS victim.	I
SUDI	Collection of blood and/or suitable tissue for molecular autopsy is recommended in all SUDI victims.	I
	An arrhythmia syndrome-focused molecular autopsy/postmortem genetic testing can be useful for all SUDI victims.	IIa
	Genetic screening of the first-degree relatives of a SUDI victim is recommended whenever a pathogenic mutation in a gene associated with increased risk of sudden death is identified by molecular autopsy in the SUDI victim. Obligate mutations carriers should be prioritized.	I

IVF: idiopathic ventricular fibrillation; SUDI: sudden unexplained death in infancy; SUDS: sudden unexplained death syndrome.

In 2011, Heart Rhythm Society and European Heart Rhythm Association jointly published an expert consensus statement on genetic testing for channelopathies and cardiomyopathies.[19] This document made the following specific recommendations on testing for long QT syndrome (LQTS), Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia, and short QT syndrome (see Table 9).

Table 9. Cardiac Ion Channelopathy Testing Recommendations

	Consensus Recommendation	Class[a]	LOE[b]
LQTS	• Comprehensive or LQT1-3 (*KCNQ1*, *KCNH2*, *SCN5A*) targeted LQTS genetic testing is recommended for any patient in whom a cardiologist has established a strong clinical index of suspicion for LQTS based on examination of the patient's clinical history, family history, and expressed electrocardiographic (resting 12-lead ECGs and/or provocative stress testing with exercise or catecholamine infusion) phenotype. • Comprehensive or LQT1-3 (*KCNQ1*, *KCNH2*, *SCN5A*) targeted LQTS genetic testing is recommended for any asymptomatic patient with QT prolongation in the absence of other clinical conditions that might prolong the QT interval (such as electrolyte abnormalities, hypertrophy, bundle branch block, etc., ie, otherwise idiopathic) on serial 12-lead ECGs defined as QTc .480 ms (prepuberty) or .500 ms (adults). • Mutation-specific genetic testing is recommended for family members and other appropriate relatives subsequently following the identification of the LQTS-causative mutation in an index case.	I	C
	• Comprehensive or LQT1-3 (*KCNQ1*, *KCNH2*, *SCN5A*) targeted LQTS genetic testing may be considered for any asymptomatic patient with otherwise idiopathic QTc values .460 ms (prepuberty) or .480 ms (adults) on serial 12-lead ECGs.	IIb	C
BrS	• Mutation-specific genetic testing is recommended for family members and appropriate relatives following the identification of	I	C

	Consensus Recommendation	Class[a]	LOE[b]
	the BrS-causative mutation in an index case.		
	• Comprehensive or BrS1 (*SCN5A*) targeted BrS genetic testing can be useful for any patient in whom a cardiologist has established a clinical index of suspicion for BrS based on examination of the patient's clinical history, family history, and expressed electrocardiographic (resting 12-lead ECGs and/or provocative drug challenge testing) phenotype.	IIa	C
	• Genetic testing is not indicated in the setting of an isolated type 2 or type 3 Brugada ECG pattern.	III	C
CPVT	• Comprehensive or *CPVT1* and *CVPT2* (*RYR2*, *CASQ2*) targeted CPVT genetic testing is recommended for any patient in whom a cardiologist has established a clinical index of suspicion for CPVT based on examination of the patient's clinical history, family history, and expressed electrocardiographic phenotype during provocative stress testing with cycle, treadmill, or catecholamine infusion. Mutation-specific genetic testing is recommended for family members and appropriate relatives following the identification of the CPVT-causative mutation in an index case.	I	C
SQTS	• Mutation-specific genetic testing is recommended for family members and appropriate relatives following the identification of the SQTS-causative mutation in an index case.	I	C
	• Comprehensive or SQT1-3 (*KCNH2*, *KCNQ1*, *KCNJ2*) targeted SQTS genetic testing may be considered for any patient in whom a cardiologist has established a strong clinical index of suspicion for SQTS based on examination of the patient's clinical history, family history, and electrocardiographic phenotype.	IIb	C

BrS: Brugada syndrome; CPVT: catecholaminergic polymorphic ventricular tachycardia; ECG: electrocardiogram; LOE: level of evidence; LQTS: long QT syndrome; QTc: corrected QT; SQTS: short QT syndrome.
[a] Class I: "is recommended" when an index case has a sound clinical suspicion for the presence of a channelopathy with a high positive predictive value for the genetic test (>40%) with a signal-to-noise ratio of >10 and/or the test may provide diagnostic or prognostic information or may change therapeutic choices; Class IIa: "can be useful"; Class IIb: "may be considered"; Class III ("is not recommended"): The test fails to provide any additional benefit or could be harmful in the diagnostic process.
[b] Only consensus opinion of experts, case studies or standard of care.

American College of Cardiology et al

The American College of Cardiology, American Heart Association, and European Society of Cardiology issued joint guidelines in 2006 on the management of patients with ventricular arrhythmias and the prevention of sudden death.[74] These guidelines made a general statement that "In patients affected by LQTS, genetic analysis is useful for risk stratification and therapeutic decisions." These guidelines did not address the use of genetic testing for the diagnosis of LQTS.

The guidelines also stated that genetic testing for catecholaminergic polymorphic ventricular tachycardia, Brugada syndrome, or short QT syndrome might identify silent carriers for clinical monitoring but does not assist with risk stratification.

Canadian Cardiovascular Society and Canadian Heart Rhythm Society

The Canadian Cardiovascular Society and Canadian Heart Rhythm Society published a joint position paper in 2011.[22] Genetic testing was recommended for cardiac arrest survivors with LQTS for the purpose of familial screening, as well as those with syncope with corrected QT (QTc) prolongation, as well as asymptomatic patients with QTc prolongation with a high clinical suspicion of LQTS. For clinically suspect catecholaminergic polymorphic ventricular tachycardia, testing was recommended for familial screening. Genetic testing was also recommended for cardiac arrest survivors with a type I Brugada electrocardiogram pattern for familial screening, as well as in patients with syncope and type I Brugada electrocardiogram pattern or asymptomatic patients with type I Brugada electrocardiogram pattern and high clinical suspicion. No recommendations are given for short QT syndrome.

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 10.

Table 10. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01705925[a]	Multicenter Evaluation of Children and Young Adults With Genotype Positive Long QT Syndrome	500	Dec 2019
NCT02876380	Prospective Identification of Long QT Syndrome in Fetal Life	600	Dec 2020
NCT02425189	The Canadian National Long QT Syndrome Registry (LQTSREG)	600	Dec 2021
NCT02014961	Worm Study: Modifier Genes in Sudden Cardiac Death	223	Apr 2025

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

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Billing Coding/Physician Documentation Information

81280 Long QT syndrome gene analyses (eg, KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, and ANK2); full sequence analysis (Deleted code 1/1/2017)

81281 Long QT syndrome gene analyses (eg, KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, and ANK2); known familial sequence variant (Deleted code 1/1/2017)

81282 Long QT syndrome gene analyses (eg, KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, and ANK2); duplication/deletion variants (Deleted code 1/1/2017)

81403 Molecular pathology procedure, Level 4 (eg, analysis of single exon by DNA sequence analysis, analysis of >10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons)

81405 Molecular pathology procedure, Level 6 (eg, analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons, regionally targeted cytogenomic array analysis)

81406 Molecular pathology procedure, Level 7 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia)

81407 Molecular pathology procedure, Level 8 (eg, analysis of 26-50 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of >50 exons, sequence analysis of multiple genes on one platform)

81408 Molecular pathology procedure, Level 9 (eg, analysis of >50 exons in a single gene by DNA sequence analysis)

81413 Cardiac ion channelopathies (eg, Brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia); genomic sequence analysis panel, must include sequencing of at least 10 genes, including ANK2, CASQ2, CAV3, KCNE1,

	KCNE2, KCNH2, KCNJ2, KCNQ1, RYR2, and SCN5A (new code 1/1/2017)
81414	Cardiac ion channelopathies (eg, Brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia); duplication/deletion gene analysis panel, must include analysis of at least 2 genes, including KCNH2 and KCNQ1 (new code 1/1/2017)
S3861	Genetic testing, sodium channel, voltage-gated, type V, alpha subunit (SCN5A) and variants for suspected Brugada Syndrome

	ICD-10 Codes
I45.81	Long QT syndrome
Z13.6	Encounter for screening for cardiovascular disorders
Z13.79	Encounter for other screening for genetic and chromosomal anomalies

Effective in 2017, there are CPT genomic sequencing procedure codes for this testing:

81413: Cardiac ion channelopathies (eg, Brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia); genomic sequence analysis panel, must include sequencing of at least 10 genes, including *ANK2*, *CASQ2*, *CAV3*, *KCNE1*, *KCNE2*, *KCNH2*, *KCNJ2*, *KCNQ1*, *RYR2*, and *SCN5A*
81414: ; duplication/deletion gene analysis panel, must include analysis of at least 2 genes, including *KCNH2* and *KCNQ1*

Other analyses related to this testing are listed under the following CPT tier 2 molecular pathology codes:

Under code 81403:

KCNJ2 (potassium inwardly-rectifying channel, subfamily J, member 2) (eg, Andersen-Tawil syndrome), full gene sequence

Under code 81405:

CASQ2 (calsequestrin 2 [cardiac muscle]) (eg, catecholaminergic polymorphic ventricular tachycardia), full gene sequence

Under code 81406:

KCNH2 (potassium voltage-gated channel, subfamily H[ead-related], member 2) (eg, short QT syndrome, long QT syndrome), full gene sequence
KCNQ1 (potassium voltage-gated channel, KQT-like subfamily, member 1) (eg, short QT syndrome, long QT syndrome), full gene sequence

Under code 81407:

SCN5A (sodium channel, voltage-gated, type V, alpha subunit) (eg, familial dilated cardiomyopathy), full gene sequence

Under code 81408:

RYR2 (ryanodine receptor 2 [cardiac]) (eg, catecholaminergic polymorphic ventricular tachycardia, arrhythmogenic right ventricular dysplasia), full gene sequence or targeted sequence analysis of > 50 exons

There is a HCPCS S code for testing for suspected Brugada syndrome:

S3861: Genetic testing, sodium channel, voltage-gated, type V, alpha subunit (SCN5A) and variants for suspected Brugada syndrome.

Additional Policy Key Words

N/A

Policy Implementation/Update Information

6/1/07	New policy; considered investigational.
6/1/08	Policy statement revised to state some indications of genetic testing for long QT syndrome may be considered medically necessary.
6/1/09	No policy statement changes.
6/1/10	No policy statement changes.
6/1/11	No policy statement changes.
6/1/12	No policy statement changes.
6/1/13	No policy statement changes.
11/1/13	No policy statement changes.
11/1/14	Policy title changed to "Genetic Testing for Cardiac Ion Channelopathies". Medically necessary statement added for CPVT when criteria are met. Investigational statements added for Brugada syndrome and short QT syndrome. Added CPT codes.
11/1/15	Additional policy statement added that genetic testing for LQTS or CPVT is investigational for all other situations when criteria are not met.
11/1/16	Medically necessary statements added for diagnostic testing for Brugada syndrome and testing of an asymptomatic individual with a known familial mutation associated with Brugada syndrome or SQTS.
11/1/17	No policy statement changes.
11/1/18	No policy statement changes.

Appendix

Appendix Table 1. Categories of Genetic Testing Addressed in Policy No. 2.04.43

Category	Addressed
1. Testing of an affected individual's germline to benefit the individual	
1a. Diagnostic	X
1b. Prognostic	X
1c. Therapeutic	

2. Testing cancer cells from an affected individual to benefit the individual	
2a. Diagnostic	
2b. Prognostic	
2c. Therapeutic	
3. Testing an asymptomatic individual to determine future risk of disease	X
4. Testing of an affected individual's germline to benefit family members	
5. Reproductive testing	
5a. Carrier testing: preconception	
5b. Carrier testing: prenatal	
5c. In utero testing: aneuploidy	
5d. In utero testing: familial variants	
5e. In utero testing: other	
5f. Preimplantation testing with in vitro fertilization	