Medical Policy

BlueCross BlueShield Kansas
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Title: Implantable Cardioverter Defibrillators

Related Policy: Wearable Cardioverter Defibrillators

Professional
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Current Effective Date: August 2, 2021

Populations	Interventions	Comparators	Outcomes
Individuals: • With a high risk of sudden cardiac death due to ischemic cardiomyopathy in adulthood	Interventions of interest are: • Transvenous implantable cardioverter defibrillator placement	Comparators of interest are: • Medical management without implantable cardioverter defibrillator placement	Relevant outcomes include: • Overall survival • Morbid events • Quality of life • Treatment-related mortality • Treatment-related morbidity
Individuals: • With a high risk of sudden cardiac death due to nonischemic cardiomyopathy in adulthood	Interventions of interest are: • Transvenous implantable cardioverter defibrillator placement	Comparators of interest are: • Medical management without implantable cardioverter defibrillator placement	Relevant outcomes include: • Overall survival • Morbid events • Quality of life • Treatment-related mortality • Treatment-related morbidity

Populations	Interventions	Comparators	Outcomes
Individuals: • With a high risk of sudden cardiac death due to hypertrophic cardiomyopathy in adulthood	Interventions of interest are: • Transvenous implantable cardioverter defibrillator placement	Comparators of interest are: • Medical management without implantable cardioverter defibrillator placement	Relevant outcomes include: • Overall survival • Morbid events • Quality of life • Treatment-related mortality • Treatment-related morbidity
Individuals: • With a high risk of sudden cardiac death due to an inherited cardiac ion channelopathy	Interventions of interest are: • Transvenous implantable cardioverter defibrillator placement	Comparators of interest are: • Medical management without implantable cardioverter defibrillator placement	Relevant outcomes include: • Overall survival • Morbid events • Quality of life • Treatment-related mortality • Treatment-related morbidity
Individuals: • With life-threatening ventricular tachyarrhythmia or fibrillation or who have been resuscitated from sudden cardiac arrest	Interventions of interest are: • Transvenous implantable cardioverter defibrillator placement	Comparators of interest are: • Medical management without implantable cardioverter defibrillator placement	Relevant outcomes include: • Overall survival • Morbid events • Quality of life • Treatment-related mortality • Treatment-related morbidity
Individuals: • Who need an implantable cardioverter defibrillator and have a contraindication to transvenous ICD	Interventions of interest are: • Subcutaneous implantable cardioverter defibrillator placement	Comparators of interest are: • Medical management without implantable cardioverter defibrillator placement	Relevant outcomes include: • Overall survival • Morbid events • Quality of life • Treatment-related mortality • Treatment-related morbidity
Individuals: • Who need an implantable cardioverter defibrillator and have no contraindication to transvenous ICD	Interventions of interest are: • Subcutaneous implantable cardioverter defibrillator placement	Comparators of interest are: • Transvenous implantable cardioverter defibrillator placement	Relevant outcomes include: • Overall survival • Morbid events • Quality of life • Treatment-related mortality • Treatment-related morbidity
Individuals: • With a high risk of sudden cardiac death due to cardiac sarcoid	Interventions of interest are: • Transvenous implantable cardioverter defibrillator placemen	Comparators of interest are: • Medical management without implantable cardioverter defibrillator placement	Relevant outcomes include: • Overall survival • Morbid events • Quality of life • Treatment-related mortality • Treatment-related morbidity

DESCRIPTION

An implantable cardioverter defibrillator (ICD) is a device designed to monitor a patient's heart rate, recognize ventricular fibrillation or ventricular tachycardia, and deliver an electric shock to terminate these arrhythmias to reduce the risk of sudden death. A subcutaneous ICD (S-ICD), which lacks transvenous leads, is intended to reduce lead-related complications.

OBJECTIVE

The objective of this evidence review is to determine whether implantable cardioverter defibrillators improve the net health outcome for individuals with high-risk of cardiac death.

BACKGROUND

Ventricular Arrhythmia and Sudden Cardiac Death

The risk of ventricular arrhythmia and sudden cardiac death (SCD) may be significantly increased in various cardiac conditions such as ischemic cardiomyopathy, particularly when associated with reduced left ventricular ejection fraction and prior myocardial infarction; nonischemic dilated cardiomyopathy with reduced left ventricular ejection fraction; hypertrophic cardiomyopathy and additional risk factors; congenital heart disease, particularly with recurrent syncope; and cardiac ion channelopathies.

Treatment

Implantable cardioverter defibrillators (ICDs) monitor a patient's heart rate, recognize ventricular fibrillation or ventricular tachycardia (VT), and deliver an electric shock to terminate these arrhythmias to reduce the risk of SCD. Indications for ICD placement can be broadly subdivided into (1) secondary prevention, i.e., use in patients who have experienced a potentially life-threatening episode of VT (near SCD); and (2) primary prevention, i.e., use in patients who are considered at high risk for SCD but who have not yet experienced life-threatening VT or ventricular fibrillation.

The standard ICD placement surgery involves placement of a generator in the subcutaneous tissue of the chest wall. Transvenous leads are attached to the generator and threaded intravenously into the endocardium. The leads sense and transmit information on cardiac rhythm to the generator, which analyzes the rhythm information and produces an electrical ventricular fibrillation shock when a malignant arrhythmia is recognized.

A subcutaneous ICD (S-ICD) has been developed. It does not use transvenous leads and thus avoids the need for venous access and complications associated with the insertion of venous leads. Rather, the S-ICD uses a subcutaneous electrode implanted adjacent to the left sternum. The electrodes sense the cardiac rhythm and deliver countershocks through the subcutaneous tissue of the chest wall.

Several automatic ICDs have been approved by the U.S. Food and Drug Administration (FDA) through the premarket approval process. The FDA labeled indications generally include patients who have experienced life-threatening VT associated with cardiac arrest or VT associated with hemodynamic compromise and resistance to pharmacologic treatment. Also, devices typically have approval in the secondary prevention setting for patients with previous myocardial infarction and reduced e ejection fraction.

REGULATORY STATUS

Transvenous Implantable Cardioverter Defibrillators

A large number of ICDs have been approved by the FDA through the premarket approval (PMA) process (FDA product code: LWS). A 2014 review of the FDA approvals of cardiac implantable devices reported that, between 1979 and 2012, the FDA approved 19 ICDs (7 pulse generators, 3 leads, 9 combined systems) through new PMA applications.[1,] Many originally approved ICDs have received multiple supplemental applications. A selective summary of some currently available ICDs is provided in Table 1.

Subcutaneous Implantable Cardioverter Defibrillators

In 2012, the Subcutaneous Implantable Defibrillator (S-ICD™) System was approved by the FDA through the PMA process for the treatment of life-threatening ventricular tachyarrhythmias in

patients who do not have symptomatic bradycardia, incessant VT, or spontaneous, frequently recurring VT that is reliably terminated with antitachycardia pacing (see Table 1).

In 2015, the Emblem™ S-ICD (Boston Scientific), which is smaller and longer-lasting than the original S-ICD, was approved by the FDA through the PMA supplement process.

In February 2021, Boston Scientific issued a recall of the Emblem S-ICD because of increased risk of device fractures. FDA designated the recall a Class I event, the most serious type of recall, indicating a situation in which there is a reasonable probability that the use of the device may cause serious injuries or death.[2,]

Table 1. Implantable Cardioverter Defibrillators with FDA Approval

Device	Manufacturer	Original PMA Approval Date
Transvenous		
Ellipse™/Fortify Assura™ Family (originally: Cadence Tiered Therapy Defibrillation System)	St. Jude Medical	Jul 1993
Current® Plus ICD (originally: Cadence Tiered Therapy Defibrillation System)	St. Jude Medical	Jul 1993
Dynagen™, Inogen™, Origen™, and Teligen® Family (originally: Ventak, Vitality, Cofient family)	Boston Scientific	Jan 1998
Evera™ Family (originally: Virtuosos/Entrust/Maximo/ Intrisic/Marquis family)	Medtronic	Dec 1998
Subcutaneous		
Subcutaneous Implantable Defibrillator System (S-ICD)	Cameron Health; acquired by Boston Scientific	Sep 2012

FDA: Food and Drug Administration; PMA: premarket application.
NOTE: ICDs may be combined with other pacing devices, such as pacemakers for atrial fibrillation, or biventricular pacemakers designed to treat heart failure. This evidence review addresses ICDs alone when used solely to treat patients at risk for ventricular arrhythmias.

POLICY

I. Adults

A. The use of the automatic implantable cardioverter defibrillator (ICD) may be considered **medically necessary** in adults who meet the following criteria:

1. Primary Prevention
   a) Ischemic cardiomyopathy with New York Heart Association (NYHA) functional class II or class III symptoms, a history of myocardial infarction at least 40 days before ICD treatment, and left ventricular ejection fraction of 35% or less; or
   b) Ischemic cardiomyopathy with NYHA functional class I symptoms, a history of myocardial infarction at least 40 days before ICD treatment, and left ventricular ejection fraction of 30% or less; or
   c) Nonischemic dilated cardiomyopathy and left ventricular ejection fraction of 35% or less, after reversible causes have been excluded, and the response to optimal medical therapy has been adequately determined; or
   d) Hypertrophic cardiomyopathy (HCM) or arrhythmogenic right ventricular cardiomyopathy with 1 or more major risk factors for sudden cardiac death (history of premature HCM-related sudden death in 1 or more first-degree relatives younger than 50 years; left ventricular hypertrophy greater than 30 mm; 1 or more runs of nonsustained ventricular tachycardia at heart rates of 120 beats per minute or greater on 24-hour Holter monitoring; prior unexplained syncope inconsistent with neurocardiogenic origin) and judged to be at high risk for sudden cardiac death by a physician experienced in the care of patients with cardiomyopathy.
   e) Diagnosis of any one of the following cardiac ion channelopathies and considered to be at high risk for sudden cardiac death (see Policy Guidelines):
      i. Congenital long QT syndrome; **OR**
      ii. Catecholaminergic polymorphic ventricular tachycardia; **OR**
      iii. Brugada syndrome; **OR**
      iv. Short QT syndrome.

2. Secondary Prevention
   a) Patients with a history of a life-threatening clinical event associated with ventricular arrhythmic events such as sustained ventricular tachyarrhythmia, after reversible causes (e.g., acute ischemia) have been excluded.

B. The use of the ICD is considered **experimental / investigational** in primary prevention patients who:

1. Have had an acute myocardial infarction (i.e., less than 40 days before ICD treatment); **OR**

2. Have New York Heart Association (NYHA) Class IV congestive heart failure (unless patient is eligible to receive a combination cardiac resynchronization therapy ICD device); **OR**

3. Have had a cardiac revascularization procedure in the past 3 months (coronary artery bypass graft [CABG] or percutaneous transluminal coronary angioplasty [PTCA]) or are candidates for a cardiac revascularization procedure; **OR**

4. Have noncardiac disease that would be associated with life expectancy less than 1 year

C. The use of the ICD for secondary prevention is considered **experimental / investigational** for patients who do not meet the criteria for secondary prevention.

II. Pediatrics

A. The use of the ICD may be considered **medically necessary** in children who meet any of the following criteria:

1. Survivors of cardiac arrest, after reversible causes have been excluded; **OR**

2. Symptomatic, sustained ventricular tachycardia in association with congenital heart disease in patients who have undergone hemodynamic and electrophysiologic evaluation; **OR**

3. Congenital heart disease with recurrent syncope of undetermined origin in the presence of either ventricular dysfunction or inducible ventricular arrhythmias; **OR**

4. Hypertrophic cardiomyopathy (HCM) or arrhythmogenic right ventricular cardiomyopathy with 1 or more major risk factors for sudden cardiac death (history of premature HCM-related sudden death in 1 or more first-degree relatives younger than 50 years; massive left ventricular hypertrophy based on age-specific norms; prior unexplained syncope inconsistent with neurocardiogenic origin) and judged to be at high risk for sudden cardiac death by a physician experienced in the care of patients with cardiomyopathy; **OR**

5. Diagnosis of any one of the following cardiac ion channelopathies and considered to be at high risk for sudden cardiac death (see Policy Guidelines):
   a) Congenital long QT syndrome; **or**
   b) Brugada syndrome; **or**
   c) Short QT syndrome; **or**
   d) Catecholaminergic polymorphic ventricular tachycardia.

B. The use of the ICD is considered **experimental / investigational** for all other indications in pediatric patients.

III. Subcutaneous ICDs

A. The use of a subcutaneous ICD may be considered **medically necessary** for adults or children who have an indication for ICD implantation for primary or secondary prevention for any of the above reasons and meet all of the following criteria:

1. Have a contraindication to a transvenous ICD due to 1 or more of the following:
   a) lack of adequate vascular access; **or**
   b) compelling reason to preserve existing vascular access (i.e., need for chronic dialysis; younger patient with anticipated long-term need for ICD therapy); **or**
   c) history of need for explantation of a transvenous ICD due to a complication, with ongoing need for ICD therapy.

2. Have no indication for antibradycardia pacing; **AND**

3. Do not have ventricular arrhythmias that are known or anticipated to respond to antitachycardia pacing.

B. The use of a subcutaneous ICD is considered **experimental / investigational** for individuals who do not meet the criteria outlined above.

Policy Guidelines

1. This policy addresses the use of implantable cardioverter defibrillator (ICD) devices as stand-alone interventions, not as combination devices to treat heart failure (i.e., cardiac resynchronization devices) or in combination with pacemakers. Unless specified, the policy statements and rationale are referring to transvenous ICDs.
2. Indications for pediatric ICD use are based on American College of Cardiology / American Heart Association/Heart Rhythm Society (ACC/AHA/HRS) guidelines published in 2008 (updated in 2012), which acknowledged the lack of primary research in this field on pediatric patients (see Rationale section). These are derived from nonrandomized studies, extrapolation from adult clinical trials, and expert consensus.
3. Criteria for ICD Implantation in Patients with Cardiac Ion Channelopathies
   a. Individuals with cardiac ion channelopathies may have a history of a life-threatening clinical event associated with ventricular arrhythmic events such as sustained ventricular tachyarrhythmia, after reversible causes, in which case they should be considered for ICD implantation for secondary prevention, even if they do not meet criteria for primary prevention.
   b. Criteria for ICD placement in patients with cardiac ion channelopathies derive from results of clinical input, a 2013 consensus statement from the HRS, European Heart Rhythm Association (EHRA), and the Asia-Pacific Heart Rhythm Society on the diagnosis and management of patients with inherited primary arrhythmia syndromes (Priori et al [2013]), 2017 guidelines from ACC, AHA, and HRS on the management of heart failure (Al-Khatib et al [2017]), and a report from the HRS and EHRA's Second Consensus Conference on Brugada syndrome.
   c. Indications for consideration for ICD implantation for each cardiac ion channelopathy are as follows:
      1) Long QT syndrome (LQTS):
         i. Patients with a diagnosis of LQTS who are survivors of cardiac arrest.
         ii. Patients with a diagnosis of LQTS who experience recurrent syncopal events while on beta-blocker therapy.
      2) Brugada syndrome (BrS):
         i. Patients with a diagnosis of BrS who are survivors of cardiac arrest.
         ii. Patients with a diagnosis of BrS who have documented spontaneous sustained ventricular tachycardia (VT) with or without syncope.
         iii. Patients with a spontaneous diagnostic type 1 ECG who have a history of syncope, seizure, or nocturnal agonal respiration judged to be likely caused by ventricular arrhythmias (after noncardiac causes have been ruled out).
         iv. Patients with a diagnosis of BrS who develop ventricular fibrillation (VF) during programmed electrical stimulation.
      3) Catecholaminergic polymorphic ventricular tachycardia (CPVT):
         i. Patients with a diagnosis of CPVT who are survivors of cardiac arrest.
         ii. Patients with a diagnosis of CPVT who experience recurrent syncope or polymorphic/bidirectional ventricular tachycardia (VT) despite optimal medical management, and/or left cardiac sympathetic denervation.
      4) Short QT syndrome (SQTS):
         i. Patients with a diagnosis of SQTS who are survivors of cardiac arrest.

ii. Patients with a diagnosis of SQTS who are symptomatic and have documented spontaneous VT with or without syncope.
iii. Patients with a diagnosis of SQTS or are asymptomatic or symptomatic and have a family history of sudden cardiac death.

NOTE: For congenital LQTS, patients may have one or more clinical or historical findings other than those outlined above that may, alone or in combination, put them at higher risk for sudden cardiac death. These may include patients with a family history of sudden cardiac death due to LQTS, infants with a diagnosis of LQTS with functional 2:1 atrioventricular block, patients with a diagnosis of LQTS in conjunction with a diagnosis of Jervell and Lange-Nielsen syndrome or Timothy syndrome, and patients with a diagnosis of LQTS with profound QT prolongation (>550 ms). These factors should be evaluated on an individualized basis by a clinician with expertise in LQTS in considering the need for an ICD implantation.

4. Criteria for ICD Implantation in Patients with Cardiac Sarcoid
   a. Criteria for ICD placement in patients with cardiac sarcoid derive from a 2014 consensus statement from the Heart Rhythm Society (HRS) and 2017 joint guidelines from the American Heart Association, American College of Cardiology, and HRS.
   b. Indications for consideration of ICD placement in patients diagnosed with cardiac sarcoid are as follows:
      1) Spontaneous sustained ventricular arrhythmias, including prior cardiac arrest, if meaningful survival of greater than 1 year is expected;
      2) LVEF 35% or less, despite optimal medical therapy and a period of immunosuppression (if there is active inflammation), if meaningful survival of greater than 1 year is expected;
      3) LVEF greater than 35%, if meaningful survival of greater than 1 year is expected; AND
         i. syncope or near-syncope, felt to be arrhythmic in etiology OR
         ii. evidence of myocardial scar by cardiac MRI or positron emission tomographic (PET) scan OR
         iii. Inducible sustained ventricular arrhythmias (>30 seconds of monomorphic VT or polymorphic VT) or clinically relevant VF
      4) An indication for permanent pacemaker implantation.

RATIONALE

This evidence review has been updated with searches of the PubMed database. The most recent literature update was performed through April 8, 2021.

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life, and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, two domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For

some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

TRANSVENOUS IMPLANTABLE CARDIOVERTER DEFIBRILLATORS FOR PRIMARY PREVENTION

Clinical Context and Therapy Purpose

The purpose of T-ICD placement is to provide a treatment option that is an alternative to or an improvement on existing therapies in patients with a high risk of sudden cardiac death (SCD) due to ischemic or non-ischemic cardiomyopathy, inherited cardiac ion channelopathy, or cardiac sarcoid.

The question addressed in this evidence review is: Do ICDs improve the net health outcome in individuals with ischemic cardiomyopathy in adulthood who are at high risk of cardiac death?

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with a high risk of SCD due to ischemic or non-ischemic cardiomyopathy, inherited cardiac ion channelopathy, or cardiac sarcoid.

Interventions

The therapy being considered is T-ICD placement. An ICD is a device designed to monitor a patient's heart rate, recognize ventricular fibrillation or ventricular tachycardia, and deliver an electric shock to terminate these arrhythmias to reduce the risk of sudden death. Patients with a high risk of SCD due to ischemic cardiomyopathy in adulthood are actively managed by cardiologists, cardiovascular surgeons, neurologists, and primary care providers.

Comparators

Comparators of interest include medical management without ICD placement. Guideline based medical management for ischemic cardiovascular disease includes antihypertensive therapy and antiarrhythmic medications. Medical management for cardiac sarcoid includes steroid therapy. These patients are managed by cardiologists and primary care providers in an outpatient clinical setting.

Outcomes

The general outcomes of interest are overall survival (OS), morbid events, quality of life, treatment-related mortality, and treatment-related morbidity.

Table 2. Outcomes of Interest for Individuals at high risk of sudden cardiac death due to ischemic cardiomyopathy in adulthood

Outcomes	Details	Timing
Quality of life	Can be assessed patient reported data such as surveys and questionnaires	1 week to 5 years

Outcomes	Details	Timing
Treatment-related morbidity	Can be assessed rates of adverse events, including inappropriate shock, lead failure, infection, and other complications	1 week to 5 years

Study Selection Criteria
Methodologically credible studies were selected using the following principles:
- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE
Primary Prevention in Adults
T-ICDs have been evaluated for primary prevention in a number of populations considered at high risk of SCD, including those with ischemic cardiomyopathy, nonischemic dilated cardiomyopathy (NIDCM), and hypertrophic cardiomyopathy (HCM). There is a large body of evidence, including a number of RCTs and systematic reviews of these trials, addressing the role of ICDs for primary prevention and identifying specific populations who may benefit.

ISCHEMIC CARDIOMYOPATHY AND NONISCHEMIC DILATED CARDIOMYOPATHY
Randomized Controlled Trials
At least 13 RCTs of ICDs for primary prevention have been conducted. Five were in populations with ischemic cardiomyopathy with prior myocardial infarction (MI; usually ≥3 weeks post-MI):
- Multicenter Automatic Defibrillator Implantation Trial (MADIT);
- MADIT II;
- Coronary Artery Bypass Graft (CABG) Patch trial;
- Multicenter Unsustained Tachycardia Trial (MUSTT); and
- Sudden Cardiac Death in Heart Failure (SCD HeFT) trial.

Three trials were conducted in patients implanted with ICD in the first few weeks following MI (recent MI):
- Defibrillator in Acute Myocardial Infarction Trial (DINAMIT);
- Immediate Risk Stratification Improves Survival (IRIS) trial; and
- BEta-blocker STrategy plus ICD (BEST-ICD) trial.

Six trials were conducted in populations with NIDCM:
- Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial;
- Amiodarone Versus Implantable Cardioverter-Defibrillator (AMIOVIRT) trial;
- Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) trial;
- SCD HeFT trial;
- Cardiomyopathy Trial (CAT); and
- Danish Study to Assess the Efficacy of ICDs in Patients with Non-Ischemic Systolic Heart Failure on Mortality (DANISH).

The characteristics and mortality results for these 3 groups of trials are shown in Table 3.

Most trials for both ischemic and nonischemic cardiomyopathy have reported results consistent with a mortality benefit for ICD in patients with left ventricular systolic dysfunction or with heart failure and reduced ejection fraction, although not all trials were powered for the mortality outcome and some findings were not statistically significant. However, the DINAMIT, IRIS, and BEST-ICD trials did not support a mortality benefit for ICD in the early weeks following MI, and CABG Patch showed no benefit in patients having recently undergone coronary revascularization. Another notable exception is the 2016 DANISH trial, which enrolled primarily outpatients with nonischemic cardiomyopathy (NICM) in stable condition who were almost all receiving b-blocker or angiotensin-converting enzyme inhibitors, with the majority also receiving mineralocorticoid-receptor antagonists. While overall mortality did not differ significantly between the ICD and medical therapy groups in DANISH, SCD was significantly reduced in the ICD group (4% vs 8%; hazard ratio [HR], 0.50; 95% confidence interval [CI], 0.31 to 0.82).

Table 3. Characteristics and Results of RCTs of ICDs for Primary Prevention

Trial	**Participants**	**Treatment Groups**		**Mean Follow-Up**	**Mortality Results**	
		Group	*n*		*Hazard Ratio*	*95% CI*
ICM with prior MI						
MADIT (1996)[3,]	• LVEF ≤35% • Asymptomatic non-SVT • MI ≥3 wk prior • Inducible VT • NYHA class I-III	• ICD • Standard therapy	• 95 • 101	27 mo (trial stopped early by DSMB)	0.46	0.26 to 0.82
MADIT II (2002)[4,]	• LVEF ≤30% • No history of VT • MI ≥1 mo prior • NYHA class I-III	• ICD • Standard therapy	• 742 • 490	20 mo (trial stopped early by DSMB)	0.69	0.51 to 0.93
CABG Patch (1997)[5,]	• Scheduled for CABG • LVEF ≤35% • No sustained VT or VF • Signal-averaged ECG abnormalities • 82% had prior MI, time since MI not reported	• ICD during CABG • No ICD	• 446 • 454	32 mo	1.07	0.81 to 1.42
MUSTT (1999)[6,]	• LVEF ≤40% • Asymptomatic non-SVT • Inducible VT • MI ≥4 d prior (median, »3 y prior) • No sustained VT or VF	• EPS-guided therapy (AAD with or without ICD) (202 got ICD) • Standard therapy	• 351 • 353	39 mo	• 5-y outcomes[b]: • EPS-guided vs standard therapy: 0.80	• 0.64 to 1.01 • 0.29 to 0.61

Trial	Participants	Treatment Groups		Mean Follow-Up	Mortality Results	
					• ICD vs AAD alone: 0.42	
SCD HeFT (2005)[7,]	• LVEF ≤35% • NYHA class II-III • No asymptomatic SVT • 52% received ICM • Treated with ACE inhibitors and β-blockers	Ischemic patients: • ICD • Amiodarone • Placebo	• 431 • 426 • 453	45 mo	• ICD vs placebo • Ischemic: 0.79[a] • Overall: 0.77[a]	• 0.60 to 1.04 • 0.62 to 0.96
ICM with recent MI						
DINAMIT (2004)[8,]	• LVEF ≤35% • NYHA class I-III • No asymptomatic SVT • MI in preceding 6-40 d (mean, 18 d) • Reduced HR variability or elevated resting HR	• ICD • Standard therapy	• 332 • 342	30 mo	1.08	0.76 to 1.55
IRIS (2009)[9,]	• MI in preceding 5-31 d • At least 1 of the following: ○ LVEF ≤40% and resting HR ≥90 or non-SVT	• ICD • Standard therapy	• 445 • 453	37 mo	1.04	0.81 to 1.35
BEST-ICD (2005)[10,]	• LVEF ≤35% • NYHA class I-III • No asymptomatic SVT • MI in preceding 5-30 d • At least 1 other risk factor	• EPS-guided therapy (24 got ICD) • Standard therapy	• 79 • 59	540 d	1-year mortality[d] • EPS-guided therapy: 14% • Conventional therapy: 18% 2-y mortality[d] • EPS-guided therapy: 20% • Conventional therapy: 29.5%	
Nonischemic cardiomyopathy						
DEFINITE (2004)[11,]	• LVEF ≤35% • NYHA class II-IV	• ICD and medical therapy • Medical therapy alone	• 229 • 229	29 mo	• 0.65 (0.40 to 1.06)	

Trial	Participants	Treatment Groups		Mean Follow-Up	Mortality Results	
SCD HeFT (2005)[7,]	• LVEF ≤35% • NYHA class II-III • No asymptomatic SVT • 48% with non-ICM • Treated with ACE inhibitor and β-blocker	Nonischemic patients: • ICD • Amiodarone • Placebo	• 398 • 419 • 394	45 mo	• ICD vs placebo • Nonischemic: 0.73[a] • Overall: 0.77[a]	• 0.50 to 1.07 • 0.62 to 0.96
COMPANION (2004)[12,]	• LVEF ≤35% • NYHA class III-IV • DCM	Nonischemic patients: • CRT-D • Medical therapy • CRT	• 270 • 127 • 285	16 mo	• CRT-D vs medical therapy Nonischemic: 0.50 • Overall: 0.64	• 0.29 to 0.88 • 0.48 to 0.86
AMIOVIRT (2003)[13,]	• LVEF ≤35% • NYHA class I-III • DCM • Asymptomatic non-SVT	• ICD • Amiodarone	• 51 • 52	2 y	1-y survival[d] • ICD: 96% • Amiodarone: 90% 2-y survival[d] • ICD: 88% • Amiodarone: 87%	
CAT (2002)[14,]	• LVEF ≤30% • NYHA class II-III • No symptomatic VT, VF, or bradycardia • Recent-onset DCM	• ICD • Control	• 50 • 54	23 mo (trials stopped early due to low event rates)	• ICD: 4 deaths (8%)[d] • Control: 2 deaths (3.7%)	
DANISH (2016)[15,]	• LVEF ≤35% • NYHA class II-IV • 58% received CRT • Almost all patients on ACE inhibitors or β-blockers; ○ 60% treated with mineralocorticoid-receptor antagonist	• ICD and medical therapy • Medical therapy	• 556 • 560	5.6 y	0.87	0.68 to 1.12

AAD: antiarrhythmic drugs; ACE: angiotensin-converting enzyme; CABG: coronary artery bypass grafting; CI: confidence interval; CRT: cardiac resynchronization therapy; CRT-D: cardiac resynchronization therapy implantable cardioverter defibrillator; DCM: dilated cardiomyopathy; DSMB: Data Safety Monitoring Board; ECG: electrocardiogram; EPS: electrophysiologic study; HR: heart rate; ICD: implantable cardioverter defibrillator; ICM: ischemic cardiomyopathy; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NYHA: New York Heart Association; RCT: randomized controlled trial; SVT: sustained ventricular tachycardia; VF: ventricular fibrillation; VT: ventricular tachycardia.

[a] 97.5% CI.

[b] Relative risk.

[c] Median.

[d] Hazard ratio not given, no significant differences.

Systematic Reviews

Woods et al (2015) published an individual patient data network meta-analysis of primary prevention RCTs evaluating implantable cardiac devices, including studies of patients with heart failure and reduced ejection fraction and excluding studies of patients with recent MI or coronary revascularization.[16,] The COMPANION, DEFINITE, MADIT, MADIT II, SCD HeFT, AMIOVIRT, and CAT trials were included, representing 6134 patients for the direct ICD comparisons and 12638 patients overall.

Subsequent systematic reviews and meta-analyses of ICD trials in NICM incorporated the 2016 DANISH trial results.[17,18,19,20,] Two reviews published in 2017 included the CAT, AMIOVIRT, DEFINITE, SCD HeFT, COMPANION, and DANISH trials; other reviews included all but the COMPANION trial. All reviews have concluded that there was a statistically significant overall reduction in mortality for ICD versus medical therapy, ranging from 20% to 23%, even with the inclusion of the null DANISH results.

The risk for death varies by age, sex, and clinical characteristics such as LVEF and time since revascularization and comorbid conditions (e.g., diabetes, kidney disease). Meta-analyses have examined whether there is a beneficial effect on mortality of ICD in these subgroups. Earley et al (2014) conducted a review of evidence for the Agency for Healthcare Research and Quality on use of ICD across important clinical subgroups.[21,] Reviewers included 10 studies that provided subgroup analyses. Subgroup data were available from at least 4 studies for sex, age (<65 years vs ≥65 years), and QRS interval (<120 ms vs ≥120 ms); they were combined to calculate a relative odds ratio using random-effects meta-analyses. Other comparisons of subgroups were not meta-analyzed because too few studies compared them; however, no consistent differences between subgroups were found across studies for diabetes. The Woods et al (2015) individual patient data network meta-analysis (described previously) also examined ICD and medical therapy in various subgroups, and similarly concluded that ICD reduced mortality in patients with heart failure and reduced ejection for QRS interval less than 120 ms, 120 to 149 ms, and 150 ms or higher, ages less than 60 and 60 and older, and for men.[16,] However, the effect on mortality in women was not statistically significant (HR=0.93; 95% CI, 0.73 to 1.18).

Table 4. Characteristics of Systematic Reviews & Meta-Analysis of ICDs for Primary Prevention

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Woods (2015)[16,]	1990-2010	13	Patients with heart failure who received ICD	12,638 (17–2,521)	RCT	NR
Earley (2014)[21,]	1996-2010	14	Adults eligible to receive an ICD for primary prevention of SCD	NR	RCT, Nonrandomized comparative studies	NR

ICD: implantable cardioverter defibrillator; NR: not reported; RCT: randomized controlled trial; SCD: sudden cardiac death.

Table 5. Results of Systematic Reviews & Meta-Analysis of ICDs for Primary Prevention

Study	Mortality
Woods (2015)[16,]	**Estimated Effect of ICD on Mortality Compared with MT**
	0.71 (CI 0.63–0.80)
Earley (2014)[21,]	**Mortality Benefit of Variables (ROR)**
Sex	0.95 (CI 0.75–1.27)
Age	0.93 (CI 0.73–1.20)
QRS interval	1.13 (CI 0.82–1.54)

CI: 95% confidence interval;ICD: implantable cardioverter defibrillator; MT: medical therapy; ROR: relative odds ratio.

Registry Studies

Fontenla et al (2016) reported on results from the Spanish UMBRELLA Registry, a multicenter, observational, prospective nationwide registry of 1514 patients implanted with Medtronic ICDs equipped with remote monitoring (NTC01561144) who were enrolled between 2012 and 2013.[22,] Mean age was 64 years; 82% of the patients were men; and 65% received an ICD for primary prevention. Fifty-one percent of the patients had ischemic heart disease, 30% had NICM, 7% had HCM, 3% had Brugada syndrome (BrS), and 1.4% had long QT syndrome (LQTS). Mean follow-up was 26 months. The cumulative incidence of sustained ventricular arrhythmias was 15% (95% CI, 13% to 16%) at 1 year, 23% (95% CI, 21% to 25%) at 2 years, and 31% (95% CI, 28% to 34%) at 3 years. Thirteen percent of the episodes of sustained ventricular arrhythmias self-terminated and did not require shocks. One hundred seventy-five (12%) patients had 482 appropriate shocks, and 76 (5%) patients had 190 inappropriate shocks.

High-Risk Hypertrophic Cardiomyopathy

Schinkel et al (2012) conducted a systematic review and meta-analysis of 27 observational studies (16 cohorts, 2190 patients) reporting outcomes after ICD therapy for HCM.[23,] Most patients (83%) received an ICD for primary prevention of SCD. Mean age was 42, 38% of patients were women, and patients had a mean of 1.8 risk factors for SCD. With a mean follow-up of 3.7 years, 14% of patients had an appropriate ICD intervention with an annualized rate of 3.3%. Twenty percent of patients had an inappropriate ICD intervention, for an annualized rate of 4.8%. The annualized cardiac mortality rate was 0.6%, the noncardiac mortality rate was 0.4%, and heart transplantation rate was 0.5%.

Magnusson et al (2015) reported on outcomes for 321 patients with HCM treated with an ICD and enrolled in a Swedish registry.[24,] Over a mean follow-up of 5.4 years, appropriate ICD discharges in response to ventricular tachycardia (VT) or ventricular fibrillation (VF) occurred in 77 (24%) patients, corresponding to an annual rate of appropriate discharges of 5.3%. At least 1 inappropriate shock occurred in 46 (14.3%) patients, corresponding to an annualized event rate of 3.0%. Ninety-two (28.7%) patients required at least 1 surgical intervention for an ICD-related complication, with a total of 150 ICD-related reinterventions. Most reinterventions (n=105 [70%]) were related to lead dysfunction.

Inherited Cardiac Ion Channelopathy
ICDs have been used for primary and secondary prevention in patients with a number of hereditary disorders (also called cardiac ion channelopathies) that predispose to ventricular arrhythmias and SCD, including LQTS, BrS, short QT syndrome, and catecholaminergic polymorphic ventricular tachycardia (CPVT). Some of these conditions are extremely rare. Use of ICDs has been described in small cohorts of patients with LQTS, BrS, and CPVT.

Long QT Syndrome
Horner et al (2010) reported on outcomes for 51 patients with genetically confirmed LQTS treated with an ICD from 2000 to 2010 who were included in a single-center retrospective analysis of 459 patients with genetically confirmed LQTS.[25,] Of patients treated with ICDs, 43 (84%) received the device as primary prevention. Twelve (24%) patients received appropriate VF or torsades de pointes-terminated ICD shocks. Factors associated with appropriate shocks included secondary prevention indications (p=.008), QT corrected duration greater than 500 ms (p<0.001), non-*LQT3* genotype (p=.02), documented syncope (p=.05), documented torsades de pointes (p=.003), and a negative sudden family death history (p<.001). Inappropriate shocks were delivered in 15 (29%) patients. Patients with the *LQT3* genotype only received inappropriate shocks.

Brugada Syndrome
Hernandez-Ojeda et al (2017) reported on results from a single-center registry of 104 patients with BrS who were treated with ICDs.[26,] Ten (9.6%) patients received an ICD for secondary prevention and in 94 (90.4%) patients received an ICD for primary prevention. During an average 9.3-year follow-up, 21 (20.2%) patients received a total of 81 appropriate shocks. In multivariate analysis, type 1 electrocardiogram with syncope and secondary prevention indication were significant predictors of appropriate therapy. Nine (8.7%) patients received 37 inappropriate shocks. Twenty-one (20.2%) patients had other ICD-related complications.

Conte et al (2015) described outcomes for a cohort of 176 patients with spontaneous or drug-induced Brugada type 1 electrocardiographic (ECG) findings who received an ICD at a single institution and were followed for at least 6 months.[27,] Before ICD implantation, 14.2% of subjects had a history of aborted SCD due to sustained spontaneous ventricular arrhythmias, 59.7% had at least 1 episode of syncope, and 25.1% were asymptomatic. Over a mean follow-up of 83.8 months, 30 (17%) patients had spontaneous sustained ventricular arrhythmias detected. Sustained ventricular arrhythmias were terminated by ICD shocks in 28 (15.9%) patients and antitachycardia pacing in 2 (1.1%) patients. However, 33 (18.7%) patients experienced inappropriate shocks.

Dores et al (2015) reported on results of a Portuguese registry that included 55 patients with BrS, 36 of whom were treated with ICDs for primary or secondary prevention.[28,] Before ICD placement, 52.8% of subjects were asymptomatic, 30.6% had a history of syncope with suspected arrhythmic cause, and 16.7% had a history of aborted SCD. Over a mean follow-up of 74 months, 7 patients experienced appropriate shocks, corresponding to an incidence rate of 19.4% and an annual event rate of 2.8%. In multivariable analysis, predictors of appropriate shocks were a history of aborted SCD (HR=7.87; 95% CI, 1.27 to 49.6; p=.027) and nonsustained VT during follow-up (HR=6.73; 95% CI, 1.27 to 35.7; p=.025).

Catecholaminergic Polymorphic Ventricular Tachycardia

Roses-Noguer et al (2014) reported on results of a small retrospective study of 13 patients with CPVT who received an ICD.[29,] The indication for ICD therapy was syncope despite maximal β-blocker therapy in 6 (46%) patients and aborted SCD in 7 (54%) patients. Over a median follow-up of 4.0 years, 10 (77%) patients received a median of 4 shocks. For 96 shocks, 87 ECGs were available for review; of those, 63 (72%) were appropriate and 24 (28%) inappropriate. Among appropriate shocks, 20 (32%) restored sinus rhythm.

Cardiac Sarcoid

Sarcoiditis is a systemic granulomatous disease of unknown etiology, with a worldwide prevalence of about 4.7–64 in 100,000.[30,] The annual incidence of sarcoidosis in the United States has been estimated at 10.9 per 100,000 in whites and 35.5 per 100,000 in blacks. Cardiac involvement occurs in about 5% of systemic sarcoiditis cases. Steroid therapy is recommended as first-line treatment based on small cohort studies showing benefit, although there is conflicting evidence about its efficacy on long-term disease outcomes[31,].

Mantini et al (2012) published a review on the diagnosis and management of cardiac sarcoid, including a treatment algorithm.[32,] Limited evidence from small cohort studies suggested that an ICD could prevent dangerous arrhythmias or SCD even in patients with a relatively preserved LVEF. Evidence from case series also suggested that programmed electrical stimulation could identify cardiac sarcoid patients with electrical instability and help to determine who should get ICD.

SECTION SUMMARY: TRANSVENOUS IMPLANTABLE CARDIOVERTER DEFIBRILLATOR FOR PRIMARY PREVENTION IN ADULTS

Ischemic Cardiomyopathy and Nonischemic Dilated Cardiomyopathy

A large body of RCTs has addressed the effectiveness of T-ICD implantation for primary prevention in patients at high risk of SCD due to ischemic cardiomyopathy and NICM. Evidence from several RCTs has demonstrated improvements in outcomes with ICD treatment for patients with symptomatic heart failure due to ischemic or NICM with an LVEF of 35% or less. The notable exceptions are that data from several RCTs, including the BEST-ICD, DINAMIT and IRIS trials and subgroup analyses from earlier RCTs, have shown that outcomes with ICD therapy do not appear to improve for patients treated with an ICD within 40 days of recent MI and the CABG Patch trial did not find a benefit for patients undergoing coronary revascularization.

Hypertrophic Cardiomyopathy

Less evidence is available for the use of ICDs for primary prevention in patients with HCM. In a meta-analysis of cohort studies, the annual rates of appropriate ICD discharge were 3.3%, and the mortality rate was 1%. Given the long-term high-risk of SCD in patients with HCM, with the assumption that appropriate shocks are life-saving, these rates are considered adequate evidence for the use of SCDs in patients with HCM.

Inherited Cardiac Ion Channelopathy

The evidence related to the use of ICDs in patients with inherited cardiac ion channelopathy includes primarily single-center cohort studies or registries of patients with LQTS, BrS, and CPVT that have reported on appropriate shock rates. Patient populations typically include a mix of those requiring ICD placement for primary or secondary prevention. The limited available data for ICDs for LQTS and CPVT have indicated high rates of appropriate shocks. For BrS, more data are available and have suggested that rates of appropriate shocks are similarly high. Studies

comparing outcomes between patients treated and untreated with ICDs are not available. However, given the relatively small patient populations and the high-risk of cardiac arrhythmias, clinical trials are unlikely. Given the long-term high-risk of SCD in patients with inherited cardiac ion channelopathy, with the assumption that appropriate shocks are life-saving, these rates are considered adequate evidence for the use of SCDs in patients with inherited cardiac ion channelopathy.

Cardiac Sarcoid

The evidence related to the use of ICDs in patients with cardiac sarcoid includes small cohort studies of patients with cardiac sarcoid treated with ICDs who received appropriate shocks. Studies comparing outcomes between patients treated and untreated with ICDs are not available. However, given the relatively small number of patients with cardiac sarcoid (5% of those with systemic sarcoiditis), clinical trials are unlikely. Given the long-term high-risk of SCD in patients with cardiac sarcoid, with the assumption that appropriate shocks are life-saving, these studies are considered adequate evidence to support the use of T-ICDs in patients with cardiac sarcoid who have not responded to optimal medical therapy.

Primary Prevention in Pediatric Populations

There is limited direct evidence on the efficacy of ICDs in the pediatric population. Most published studies have retrospectively analyzed small case series that included mixed populations with mixed indications for device placement. Some representative series are reviewed next.

The largest published series, by Berul et al (2008), combined pediatric patients and patients with congenital heart disease from 4 clinical centers.[33,] Median age was 16 years, although some adults included were as old as 54 years. A total of 443 patients were included. The most common diagnoses were tetralogy of Fallot and HCM. ICD placement was performed for primary prevention in 52% of patients and secondary prevention in 48%. Over a 2-year follow-up, appropriate shocks occurred in 26% of patients and inappropriate shocks occurred in 21%.

Silka et al (1993) compiled a database of 125 pediatric patients treated with an ICD through a query of the manufacturers of commercially available devices.[34,] Indications for ICD placement were survivors of cardiac arrest (95 [76%] patients), drug-refractory VT (13 [10%] patients), and syncope with heart disease and inducible VT (13 [10%] patients). During a mean follow-up of 31 months, 73 (59%) patients received at least 1 appropriate shock and 25 (20%) received at least 1 inappropriate shock. Actual rates of SCD-free survival were 97% at 1 year, 95% at 2 years, and 90% at 5 years.

Alexander et al (2004) reported on 90 ICD procedures in 76 young patients (mean age, 16 years; range, 1-30 years).[35,] Indications for placement were 27 (36%) patients with cardiac arrest or sustained VT, 40 (53%) with syncope, 17 (22%) with palpitations, 40 (53%) with spontaneous ventricular arrhythmias, and 36 (47%) with inducible VT. Numerous patients had more than one indication for ICD in this study. Over a median follow-up of 2 years, 28% of patients received an appropriate shock and 25% received an inappropriate shock. Lewandowski et al (2010) reported on long-term follow-up for 63 patients, between the ages 6 and 21 years, who were treated with an ICD device.[36,] At 10-year follow-up, 13 (21%) patients had surgical infections. Fourteen (22%) patients experienced at least 1 appropriate shock and 17 (27%) had at least 1 inappropriate shock. Serious psychological sequelae developed in 27 (43%) patients.

Section Summary: Primary Prevention in Pediatric Populations
The available evidence for the use of ICDs in pediatric patients is limited and consists primarily of small case series that include mixed populations with mixed indications for device placement. Overall, these studies have reported both relatively high rates of appropriate and inappropriate shocks. Pediatric patients may be eligible for ICD placement if they have inherited cardiac ion channelopathy (see Inherited Cardiac Ion Channelopathy section).

TRANSVENOUS IMPLANTABLE CARDIOVERTER DEFIBRILLATORS FOR SECONDARY PREVENTION

Clinical Context and Therapy Purpose

The purpose of T-ICD placement is to provide a treatment option that is an alternative to or an improvement on existing therapies in patients with life-threatening ventricular tachyarrhythmia or fibrillation or who have been resuscitated from sudden cardiac arrest.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals wife-threatening ventricular tachyarrhythmia or fibrillation or who have been resuscitated from sudden cardiac arrest.

Interventions

The therapy being considered is T-ICD placement. An ICD is a device designed to monitor a patient's heart rate, recognize ventricular fibrillation or ventricular tachycardia, and deliver an electric shock to terminate these arrhythmias to reduce the risk of sudden death. Patients with life-threatening ventricular tachyarrhythmia or fibrillation or who have been resuscitated from sudden cardiac arrest are actively managed by cardiologists, cardiovascular surgeons, neurologists, and primary care providers.

Comparators

Comparators of interest include medical management without ICD placement.

Outcomes

The general outcomes of interest are overall survival (OS), morbid events, quality of life, treatment-related mortality, and treatment-related morbidity.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Secondary Prevention in Adults

At least 5 trials comparing ICD plus medical therapy with medical therapy alone have been conducted in the secondary prevention setting: the Antiarrhythmics Versus Implantable

Defibrillators (AVID) trial[37,] (n=1016), Cardiac Arrest Survival in Hamburg (CASH) trial[38,] (n=288), Canadian Implantable Defibrillator Study (CIDS)[39,] (n=659), Defibrillator Versus beta-Blockers for Unexplained Death in Thailand (DEBUT)[40,] trial (n=66; pilot, n=20; main study, n=46), and Wever et al (1995)[41,] (N=60). The trials are shown in Table 6. Mean length of follow-up varied from 18 to 57 months across trials. Lee et al (2003) combined the AVID, CASH, CIDS, and Wever et al (1995) trials in a meta-analysis of secondary prevention trials.[42,] The mortality analysis included 2023 participants and 518 events. In combined estimates, the ICD group had a significant reduction in both mortality (HR=0.75; 95% CI, 0.64 to 0.87) and SCD (HR=0.50; 95% CI, 0.34 to 0.62) compared with the group receiving medical therapy alone. To support National Institute for Health and Care Excellence guidance on the use of ICDs, AVID, CASH, CIDS, and the pilot DEBUT participants were combined in a meta-analysis.[43,] The results were similar, indicating a reduction in mortality for ICDs compared with medical therapy alone (relative risk [RR], 0.75; 95% CI, 0.61 to 0.93). Two other meta-analyses that included AVID, CIDS, and CASH reached similar conclusions.[44,45,]

Table 6. RCTs of ICDs for Secondary Prevention

Trials	Participants	Treatment Groups		Mortality Results	
		Group	N	RR	95% CI
AVID (1997)[37,]	Patients resuscitated from near-fatal VT/VF, SVT with syncope, or SVT with LVEF ≤40% and symptoms	• ICD • AAD	• 507 • 509	0.66	0.51 to 0.85
CASH (2000)[38,]	Patients resuscitated from cardiac arrest due to sustained ventricular arrhythmia	• ICD • Amiodarone • Metoprolol	• 99 • 92 • 97	0.82	0.60 to 1.11
CIDS (2000)[39,]	Patients with VF, out-of-hospital cardiac arrest requiring defibrillation, VT with syncope, VT with rate ≥150/min causing presyncope or angina in patient with LVEF ≤35% or syncope with inducible VT inducible	• ICD • Amiodarone	• 328 • 331	0.85	0.67 to 1.10
Wever et al (1995)[41,]	Patients with previous MI and resuscitated cardiac arrest due to VT or VF and inducible VT	• ICD • AAD	• 29 • 31	0.39	0.14 to 1.08
DEBUT (2003)[40,]	Patients were either SUDS or probable SUDS survivors with ECG abnormalities showing a RBBB-like pattern with ST elevation in the right precordial leads and inducible VT/VF	Pilot • ICD • β-blocker therapy Main trial • ICD • β-blocker therapy	 • 10 • 10 • 37 • 29	• RR not calculable (DSMB stopped trial early due to efficacy of ICD)	

Trials	Participants	Treatment Groups		Mortality Results	
				• 7 deaths in β-blockers vs 0 in ICD	

AAD: antiarrhythmic drugs; CI: confidence interval; DSMB: data safety monitoring board; ECG: electrocardiogram; ICD: implantable cardioverter defibrillator; LVEF: left ventricular ejection fraction; MI: myocardial infarction; RBBB: right bundle-branch block; RCT: randomized controlled trial; RR: relative risk; SUDS: sudden unexplained death syndrome; SVT: sustained ventricular tachycardia; VF: ventricular fibrillation; VT: ventricular tachycardia.

An analysis by Chan and Hayward (2005) using the National Veterans Administration database previously confirmed that this mortality benefit is generalizable to the clinical setting.[46,] A cohort of 6996 patients in the National Veterans Administration database, from 1995 to 1999, who had new-onset ventricular arrhythmia and preexisting ischemic heart disease and congestive heart failure were included. Of those, 1442 patients had received an ICD. Mortality was determined through the National Death Index at three years from the hospital discharge date. The cohort was stratified by quintiles of a multivariable propensity score created using many demographic and clinical confounders. The propensity score-adjusted mortality reduction for ICD compared with no ICD was an RR of 0.72 (95% CI, 0.69 to 0.79) for all-cause mortality and an RR of 0.70 (95% CI, 0.63 to 0.78) for cardiovascular mortality.

Section Summary: Secondary Prevention in Adults
Systematic reviews of RCTs in patients who have experienced symptomatic life-threatening sustained VT or VF or have been successfully resuscitated from sudden cardiac arrest have shown a 25% reduction in mortality for ICD compared with medical therapy. Analysis of data from a large administrative database has confirmed that this mortality benefit is generalizable to the clinical setting.

Secondary Prevention in Pediatric Populations
There is limited direct evidence on the efficacy of ICDs in the pediatric population. Most published studies have retrospectively analyzed small case series that included mixed populations with mixed indications for device placement. Some representative series were reviewed above (see Primary Prevention in Pediatric Populations section).

Section Summary: Secondary Prevention in Pediatric Populations
The available evidence for the use of ICDs in pediatric patients is limited and consists primarily of small case series that include mixed populations with mixed indications for device placement. Overall, these studies have reported both relatively high rates of appropriate and inappropriate shocks. Pediatric patients may be eligible for ICD placement if they have inherited cardiac ion channelopathy (see Inherited Cardiac Ion Channelopathy section).

ADVERSE EVENTS ASSOCIATED WITH TRANSVENOUS-IMPLANTABLE CARDIOVERTER DEFIBRILLATORS

Systematic Reviews: Mixed Adverse Events

Persson et al (2014) conducted a systematic review of adverse events following ICD placement.[47,] In-hospital serious adverse event rates ranged from 1.2% to 1.4%, most frequently pneumothorax (0.4%-0.5%) and cardiac arrest (0.3%).

In another systematic review of adverse events following ICD placement, Ezzat et al (2015) compared event rates reported in clinical trials of ICDs with those reported in the U.S. National

Cardiovascular Data Registry.[48,] Complication rates in the RCTs were higher than those in the U.S. registry, which reports only in-hospital complications (9.1% in the RCTs vs 3.08% in the U.S. registry, p<.01). The overall complication rate was similar to that reported by Kirkfelt et al (2014), in a population-based cohort study including all Danish patients who underwent a cardiac implantable electronic device procedure from 2010 to 2011 (562 [9.5%] 5918 patients with at least 1 complication).[49,]

Van Rees et al (2011) reported on results of a systematic review of RCTs assessing implant-related complications of ICDs and CRT devices.[50,] Reviewers included 18 trials and 3 subgroup analyses. Twelve trials assessed ICDs, 4 of which used both thoracotomy and nonthoracotomy ICDs (n=951) and 8 of which used nonthoracotomy ICDs (n=3828). For nonthoracotomy ICD placement, the rates for in-hospital and 30-day mortality were 0.2% and 0.6%, respectively, and pneumothorax was reported in 0.9% of cases. For thoracotomy ICD placement, the average in-hospital mortality rate was 2.7%. For nonthoracotomy ICD placement, the overall lead dislodgement rate was 1.8%.

Olde Nordkamp et al (2016) reported on a systematic review and meta-analysis of studies reporting on ICD complications in individuals with inherited arrhythmia syndromes.[51,] Reviewers included 63 cohort studies with a total of 4916 patients (710 [10%] with arrhythmogenic right VT; 1037 [21%] with BrS; 28 [0.6%] with CPVT; 2466 [50%] with HCM; 162 [3.3%] with lamin *A/C* gene variants; 462 [9.4%] with LQTS; 51 [1.0%] with short QT syndrome).

Table 7. Systematic Reviews & Meta-Analysis Characteristics for Adverse Events Associated With T-ICDs

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Persson (2014)[47,]	2005-2012	• 53 trials; • 35 cohorts	Patients receiving ICD placement	NR	Cohort studies	NR
Ezzat (2015)[48,]	2001-2011	18	Patients receiving ICD placement	6796 (16–1530)	RCT	NR
Olde Nordkamp (2016)[51,]	1997-2014	63	Patients with inherited arrhythmia syndromes receiving ICD placement	4916 (NR)	Cohort	NR

ICD: implantable cardioverter defibrillator; NR: not reported; RCT: randomized controlled trials; T-ICD: transvenous implantable cardioverter defibrillator.

Table 8. Systematic Reviews & Meta-Analysis Results for Adverse Events Associated With T-ICDs

Study	Rate of Adverse Events	Rates of Specific Complications
Persson (2014)[47,]		
Range	1.2%–1.4%[1]	• Device-related: <0.1%–6.4% • Lead-related: <0.1%–3.9% • Infection: 0.2%– 3.7% • Inappropriate shock: 3%–21%

Study	Rate of Adverse Events	Rates of Specific Complications
Ezzat (2015)[48,]	9.1 (CI 6.4%–12.6%)	• Access-related: 2.1% (CI 1.3%–3.3%) • Lead-related: 5.8% (CI 3.3%–9.8%) • Generator-related: 2.7% (CI 1.3%–5.7%) • Infection: 1.5% (CI 0.8%–2.6%)
Olde Nordkamp (2016)[51,]	22% (4.4% per year; 3.6%–5.2%; p<.001)	• Lead malfunction: 10.3% • Infection: 3.0% (0.53% per year)Inappropriate shock: 20% (4.7% per year; CI 4.2%–5.3%; p<.001)

CI: 95% confidence interval; T-ICD: transvenous implantable cardioverter defibrillator.
1Only serious adverse events, which included cardiac arrest, cardiac perforation, cardiac valve injury, coronary venous dissection, hemothorax, pneumothorax, deep phlebitis, transient ischemic attack, stroke, myocardial infarction, pericardial tamponade, arteriovenous fistula, and, in one study, lead dislodgement.

SYSTEMATIC REVIEW: SPECIFIC COMPLICATIONS

Lead Failure

The failure of leads in specific ICD devices led the U.S. Food and Drug Administration to require St. Jude Medical to conduct three-year postmarket surveillance studies to address concerns related to premature insulation failure and important questions related to follow-up of affected patients.[52,] An evaluation by Hauser et al (2010) found that 57 deaths and 48 serious cardiovascular injuries associated with device-assisted ICD or pacemaker lead extraction were reported to the Food and Drug Administration's Manufacturers and User Defined Experience database.[53,]

Providencia et al (2015) reported on a meta-analysis of 17 observational studies evaluating the performance of 49871 leads (5538 Durata, 10605 Endotak Reliance, 16119 Sprint Quattro, 11709 Sprint Fidelis, 5900 Riata).[54,] Overall, the incidence of lead failure was 0.93 per 100 lead-years (95% CI, 0.88 to 0.98). In an analysis of studies restricted to head-to-head comparisons of leads, there were no significant differences in the lead failure rates among nonrecalled leads (Endotak Reliance, Durata, Sprint Quattro).

Birnie et al (2012) reported on clinical predictors of failure for 3169 Sprint Fidelis leads implanted from 2003 to 2007 at 11 centers participating in the Canadian Heart Rhythm Society study.[55,] A total of 251 lead failures occurred, corresponding to a 5-year lead failure rate of 16.8%. Factors associated with higher failure rates included female sex (HR=1.51; 95% CI, 1.14 to 2.04; p=.005), axillary vein access (HR=1.94; 95% CI, 1.23 to 3.04), and subclavian vein access (HR=1.63; 95% CI, 1.08 to 2.46). In a study from 3 centers reporting on predictors of Fidelis lead failures, compared with Quattro lead failures, Hauser et al (2011) reported a failure rate for the Fidelis lead of 2.81% per year (vs 0.42% per year for Quattro leads; p<.001).[56,]

In an earlier study from 12 Canadian centers, Gould et al (2008) reported on outcomes from ICD replacements due to ICD advisories from 2004 to 2005, which included 451 replacements (of 2635 advisory ICD devices).[57,] Over 355 days of follow-up, 41 (9.1%) complications occurred, including 27 (5.9%) requiring surgical reintervention and 2 deaths.

In a large prospective multicenter study, Poole et al (2010) reported on complications rates associated with generator replacements and/or upgrade procedures of pacemaker or ICD devices, which included 1031 patients without a planned transvenous lead replacement (cohort 1) and 713 with a planned transvenous lead replacement (cohort 2).[58,] A total of 9.8% and

21.9% of cohort 1 and 19.2% and 25.7% of cohort 2 had a single chamber ICD and a dual chamber ICD, respectively, at baseline. Overall periprocedural complication rates for those with a planned transvenous lead replacement were a cardiac perforation in 0.7%, pneumothorax or hemothorax in 0.8%, cardiac arrest in 0.3%, and, most commonly, need to reoperate because of lead dislodgement or malfunction in 7.9%. Although rates were not specifically reported for ICD replacements, complication rates were higher for ICDs and CRT devices than pacemakers.

Ricci et al (2012) evaluated the incidence of lead failure in a cohort of 414 patients given an ICD with Sprint Fidelis leads.[59,] Patients were followed for a median of 35 months. Lead failures occurred in 9.7% (40/414) of patients, for an annual rate of 3.2% per patient-year. Most lead failures (87.5%) were due to lead fracture. Median time until recognition of lead failure, or until an adverse event, was 2.2 days. A total of 22 (5.3%) patients received an inappropriate shock due to lead failure.

Cheng et al (2010) examined the rate of lead dislodgements in patients enrolled in a national cardiovascular registry.[60,] Of 226764 patients treated with an ICD between 2006 and 2008, lead dislodgement occurred in 2628 (1.2%). Factors associated with lead dislodgement were New York Heart Association class IV heart failure, AF or atrial flutter, a combined ICD and CRT device, and having the procedure performed by a nonelectrophysiologist. Lead dislodgement was associated with an increased risk for other cardiac adverse events and death.

In another single-center study, Faulknier et al (2010) reported on the time-dependent hazard of failure of Sprint Fidelis leads.[61,] Over an average follow-up of 2.3 years, 38 (8.9%) of 426 leads failed. There was a 3-year lead survival rate of 90.8% (95% CI, 87.4% to 94.3%), with a hazard of fracture increasing exponentially over time by a power of 2.13(95% CI, 1.98 to 2.27; p<.001).

Infection Rates

Several publications have reported on infection rates in patients receiving an ICD. Smit et al (2010) published a retrospective, descriptive analysis of the types and distribution of infections associated with ICDs over a 10-year period in Denmark.[62,] Of 91 total infections identified, 39 (42.8%) were localized pocket infections, 26 (28.6%) were endocarditis, 17 (18.7%) were ICD-associated bacteremic infections, and 9 (9.9%) were acute postsurgical infections. Nery et al (2010) reported on the rate of ICD-associated infections among consecutive patients treated with an ICD at a tertiary referral center.[63,] Twenty-four of 2417 patients had infections, for a rate of 1.0%. Twenty-two (91.7%) of the 24 patients with infections required device replacement. Factors associated with infection were device replacement (vs de novo implantation) and use of a complex device (e.g., combined ICD plus CRT or dual-/triple-chamber devices). Sohail et al (2011) performed a case-control study evaluating the risk factors for an ICD-related infection in 68 patients and 136 matched controls.[64,] On multivariate analysis, the presence of epicardial leads (odds ratio [OR], 9.7; p=.03) and postoperative complications at the insertion site (OR=27.2, p<.001) were significant risk factors for early infection. For late-onset infections, hospitalization for more than 3 days (OR=33.1, p<.001 for 2 days vs1 day) and chronic obstructive pulmonary disease (OR=9.8, p=.02) were significant risk factors.

Chua et al (2000) described the diagnosis and management of infections in a retrospective case series that included 123 patients, 36 of whom were treated for ICD infections.[65,] Most (n=117 [95%]) patients required removal of the device and all lead material. Of those who had all hardware removed, one patient experienced a relapse, while three of the six patients who did not undergo hardware removal experienced a relapse.

Borleffs et al (2010) also reported on complications after ICD replacement for pocket-related complications, including infection or hematoma, in a single-center study.[66,] Of 3161 ICDs included, 145 surgical reinterventions were required for 122 ICDs in 114 patients. Ninety-five (66%) reinterventions were due to infection, and the remaining 50 (34%) were due to other causes. Compared with first-implanted ICDs, the occurrence of surgical reintervention in replacements was 2.5 (95% CI, 1.6 to 3.7) times higher for infection and 1.7 (95% CI, 0.9 to 3.0) times higher for non-infection-related causes.

Inappropriate Shocks

Inappropriate shocks may occur with ICDs due to faulty sensing or sensing of atrial arrhythmias with rapid ventricular conduction; these shocks may lead to reduced quality of life and risk of ventricular arrhythmias. In the MADIT II trial (described above), 1 or more inappropriate shocks occurred in 11.5% of ICD subjects and were associated with a greater likelihood of mortality (HR=2.29; 95% CI, 1.11 to 4.71; p=.02).[67,]

Tan et al (2014) conducted a systematic review to identify outcomes and adverse events associated with ICDs with built-in therapy-reduction programming.[68,] Six randomized trials and 2 nonrandomized cohort studies (total n=7687 patients) were included (3598 with conventional ICDs, 4089 therapy-reduction programming). A total of 267 (4.9%) patients received inappropriate ICD shocks, 99 (3.4%) in the therapy-reduction group and 168 (6.9%) in the conventional programming group (RR=0.50; 95% CI, 0.37 to 0.61; p<.001). Therapy-reduction programming was associated with a significantly lower risk of death than conventional programming (RR=0.30; 95% CI, 0.16 to 0.41; p<.001.)

Sterns et al (2016) reported on results of an RCT comparing a strategy using a prolonged VF detection time to reduce inappropriate shocks with a standard strategy among secondary prevention patients.[69,] This trial reported on a prespecified subgroup analysis of the PainFree SST trial, which compared standard with prolonged detection in patients receiving an ICD for secondary prevention. Patients treated for secondary prevention indications were randomized to a prolonged VF detection period (n=352) or a standard detection period (n=353). At 1 year, arrhythmic syncope-free rates were 96.9% in the intervention group, and 97.7% in the control group (rate difference, -1.1%; 90% lower confidence limit, -3.5%; above the prespecified noninferiority margin of -5%; p=.003 for noninferiority).

Auricchio et al (2015) assessed data from the PainFree SST trial, specifically newer ICD programming strategies for reducing inappropriate shocks.[70,] A total of 2790 patients with an indication for ICD placement were given a device programmed with a SmartShock Technology designed to differentiate between ventricular arrhythmias and other rhythms. The inappropriate shock incidence for dual-/triple-chamber ICDs was 1.5% at 1 year (95% CI, 1.0% to 2.1%), 2.8% at 2 years (95% CI, 2.1% to 3.8%), and 3.9% at 3 years (95% CI, 2.8% to 5.4%).

Other Complications

Lee et al (2010) evaluated rates of early complications among patients enrolled in a prospective, multicenter population-based registry of all newly implanted ICDs in Ontario, from 2007 through 2009.[71,] Of 3340 patients receiving an ICD, major complications (lead dislodgement requiring intervention, myocardial perforation, tamponade, pneumothorax, infection, skin erosion, hematoma requiring intervention) within 45 days of implantation occurred in 4.1% of new implants. Major complications were more common in women, in patients who received a combined ICD-CRT device, and in patients with a left ventricular end-systolic size of larger than

45 mm. Direct implant-related complications were associated with a major increase in early death (HR=24.9; p<.01).

Furniss et al (2015) prospectively evaluated changes in high-sensitivity troponin T levels and ECG results that occur during ICD placement alone, ICD placement with testing, and ICD testing alone.[72,] The 13 subjects undergoing ICD placement alone had a median increase in high-sensitivity troponin T level of 95% (p=.005) while the 13 undergoing implantation and testing had a median increase of 161% (p=.005). Those undergoing testing alone demonstrated no significant change in high-sensitivity troponin T levels.

SUBCUTANEOUS IMPLANTABLE CARDIOVERTER DEFIBRILLATORS IN PATIENTS WITH A CONTRAINDICATION TO A TRANSVENOUS IMPLANTABLE CARDIOVERTER DEFIBRILLATOR

Clinical Context and Therapy Purpose

The purpose of S-ICD placement in patients with a contraindication to transvenous T-ICD is to provide a treatment option that is an alternative to or an improvement on existing therapies such as medical management without ICD placement.

The question addressed in this evidence review is: Do S-ICDs improve the net health outcome in individuals who have an indication for cardioversion and have a contraindication to T-ICD?

The following PICO was used to select literature to inform this review.

Populations

The population of interest is patients who need an ICD and have a contraindication to a T-ICD.

There are no defined guidelines for the selection of S-ICD versus T-ICD. Currently, S-ICDs are generally considered in the following situations:

- Patients at high risk of infection, inadequate venous access, and any patient without a pacing indication
- Younger patients due to the expected longevity of the implanted leads and a desire to avoid chronic transvenous leads (e.g., patients with hypertrophic cardiomyopathy, congenital cardiomyopathies, or inherited channelopathies)
- Patients at high risk for bacteremia, such as patients on hemodialysis or with chronic indwelling endovascular catheters.
- Patients with challenging vascular access or prior complications with T-ICDs
- Sudden cardiac death resulting from cardiac arrhythmia is a leading case of CV mortality (50% of CV deaths worldwide).

Interventions

The therapy being considered is S-ICD.

An ICD is a device designed to monitor a patient's heart rate, recognize ventricular fibrillation or ventricular tachycardia, and deliver an electric shock to terminate these arrhythmias to reduce the risk of sudden death. A subcutaneous ICD (S-ICD, which lacks transvenous leads, is intended to reduce lead-related complications. The S-ICD is intended for patients who have standard indications for an ICD, but who do not require pacing for bradycardia or antitachycardia overdrive pacing for VT. The S-ICD is proposed to benefit patients with limited vascular access (including

patients undergoing renal dialysis or children) or those who have had complications requiring T-ICDs explantation.

The S-ICD is comprised of a pulse generator and single shocking coil running along the left parasternal margin. These are both implanted subcutaneously without endovascular access. The electrode is designed to be implanted using anatomical landmarks only without the need for fluoroscopy or other medical imaging systems during the surgical implant procedure.

Patients who need an ICD and have a contraindication to T-ICD are actively managed by cardiologists, cardiovascular surgeons, neurologists, and primary care providers.

Comparators
The comparator of interest is medical management without ICD placement

Outcomes
The general outcomes of interest are OS, morbid events, quality of life, treatment-related mortality, and treatment-related morbidity.

Table 9. Outcomes of interest for individuals who need an implantable cardioverter defibrillator and have a contraindication to a transvenous ICD

Outcomes	Details	Timing
Quality of life	Can be assessed patient reported data such as surveys and questionnaires	1 week to 5 years
Treatment-related morbidity	Can be assessed rates of adverse events, including inappropriate shock, lead failure, infection, and other complications	1 week to 5 years

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

The S-ICD is intended for patients who have standard indications for an ICD, but who do not require pacing for bradycardia or antitachycardia overdrive pacing for VT. The S-ICD has been proposed to benefit patients with limited vascular access (including patients undergoing renal dialysis or children) or those who have had complications requiring T-ICDs explantation. No RCTs were identified comparing the performance of an S-ICD with that of T-ICDs. The first multicenter, randomized trial (PRAETORIAN; NCT01296022) to directly compare S-ICDs with T-ICDs is underway.

REVIEW OF EVIDENCE

Nonrandomized Trials

Several nonrandomized trials and registry studies have reported outcomes for patients receiving a S-ICD, with follow-up periods up to 5.8 years (Table 10). The Implant and Midterm Outcomes of the Subcutaneous Implantable Cardioverter-Defibrillator Registry (EFFORTLESS) is a multicenter European registry reporting outcomes for patients treated with S-ICD. Several publications from EFFORTLESS (Evaluation of Factors Impacting Clinical Outcome and Cost Effectiveness of the S-ICD), the pivotal trial submitted to the Food and Drug Administration for the investigational device exemption, and other studies are summarized in Table 10. In the EFFORTLESS registry, among 472 enrolled patients, the complication-free rate was 94% at 360 days and there was a 13.1% inappropriate shock rate at 3 years' follow-up. Gold et al (2021) reported 18-month data from the UNTOUCHED study, a multinational, prospective trial designed to assess the performance of the S-ICD in primary prevention patients with a low LVEF and New York Heart Association II/III heart failure or coronary artery disease.[73,]At 18 months, the complication-free rate was 92.7% and the inappropriate shock-free rate was 95.9%. One-year data from the S-ICD Post Approval Study and 18-month data from the UNTOUCHED study have been published; these studies are ongoing. The S-ICD System Post-Approval Study (PAS) is a nonrandomized, standard-of-care registry in the United States that has prospectively enrolled and followed S-ICD recipients.[74,] Over the first 1 year post implantation, complications were observed in 119 patients, with a complication-free rate at 1 year of 92.5%. The most common complication was device system infection in 44 of 1,637 patients. This 5-year study is expected to be completed in October 2021, with a total of 1766 participants. Five-year data from the PAS should provide more information on longer-term adverse events such as lead failure and need for device replacement.

Table 10. Summary of Nonrandomized Trials of Subcutaneous Implantable Cardioverter Defibrillators

Study; Trial	Countries	N	Mean FU	Results	
				Outcomes	Values
Burke et al (2020)[74,]S-ICD PASNCT01736618	US	1637	1 y	• Complication-free rate at 1 y • Appropriate shock rate at 1 y • Inappropriate shocks at 1 y • Death at 1 y	• 92.5% • 5.3% • 6.5% • 5.4%
Gold et al (2021)[73,] UNTOUCHED NCT02433379	US, Canada, Europe	1111	18 months	• Inappropriate shock-free rate at 18 months • Appropriate shock-free rate at 18 months • Complication-free rate at 18 months • Overall survival rate at 18 months	• 94.8% • 94.3% • 92.7% • 94.9%
Lambiase et al (2014)[75,]; Olde Nordkamp et al	10 European countries	• 985 • 928 • 697	• 3.1 y • 1 y • 2 y	• Complication-rates by 360 d	• 8.4% • 8.1% • 11.7%

Study; Trial	Countries	N	Mean FU	Results	
(2015)[76]; Boersma et al (2017)[77], EFFORTLESS S-ICD Registry		• 498 • 300 • 82	• 3 y • 4 y • 5 y	• Inappropriate shocks by 360 d • Complication rates through follow-up • Inappropriate shocks through follow-up • Appropriate shocks through follow-up	• 11.7% • 13.5%
Weiss et al (2013)[78], IDE study	U.S., U.K., New Zealand, Netherlands	330	11 mo	• Implanted successfully: • Complication-free at 180 d • Inappropriate shocks • Episodes of discrete spontaneous VT or VF, all successfully converted	• 95% • 99% • 13% • 38

Burke et al (2015)[74]; Boersma et al (2016)[79]; Lambiase et al (2016)[80], EFFORTLESS and IDE studies	Multiple European countries, U.S., New Zealand	882	651 d	• Complications within 3 y
				• Infections requiring device removal or revision
				• Annual mortality rate
				• 2-y cumulative mortality
				• Incidence of therapy for VT or VF:
				  ○ 1 year
				  ○ 2 years
				  ○ 3 years
				• Incidence of inappropriate shock at 3 y
					• 11%
					• 1.7%
					• 1.6%
					• 3.2%
					• 5.3%
					• 7.9%
					• 10.5%
					• 13.1%

Bardy et al (2010)[81]; Theuns et al (2015)[82],	Europe, New Zealand	55	5.8 y	• Devices replaced • Devices explanted • Replaced with T-ICD • Shocks recorded in 16 (29%) patients	• 26 (47%) • 5 (9%) • 4 (7%) • 119
Olde-Nordkamp et al (2012)[83],	Netherlands	118	18 mo	• All device-related complications • Infections • Dislodgements of device/leads • Skin erosion • Battery failure • Replaced with T-ICD	• 14% • 5.9% • 3.3% • 1.7% • 1.7% • 1 (0.8%) • 45 • 33 • 2

Study; Trial	Countries	N	Mean FU	Results	
				• Appropriate shocks experienced in 8 patients • Total inappropriate shocks delivered to 15 (13%) patients • Deaths (cancer, progressive heart failure)	

FU: follow-up; S-ICD: subcutaneous implantable cardioverter defibrillator; T-ICD: transvenous implantable cardioverter defibrillator; VF: ventricular fibrillation; VT: ventricular tachycardia.

Section Summary: Subcutaneous-Implantable Cardioverter Defibrillators in Patients with a Contraindication to a Transvenous Implantable Cardioverter Defibrillator
Nonrandomized studies have suggested that S-ICDs are as effective as T-ICDs at terminating laboratory-induced ventricular arrhythmias. Data from large patient registries have suggested that S-ICDs are effective at terminating ventricular arrhythmias when they occur. Given the need for cardioverter defibrillation for SCD risk in this population, with the assumption that appropriate shocks are life-saving, these rates suggest S-ICDs, in patients with contraindication to T-ICD, are likely improvements over medical management alone.

SUBCUTANEOUS IMPLANTABLE CARDIOVERTER DEFIBRILLATORS IN PATIENTS WITH NO CONTRAINDICATION TO A TRANSVENOUS IMPLANTABLE CARDIOVERTER DEFIBRILLATOR

Clinical Context and Therapy Purpose
The purpose of S-ICD placement in patients with no contraindication to a T-ICD is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Do S-ICDs improve the net health outcome in individuals who have an indication for cardioversion and no contraindication to a T-ICD?

The following PICO was used to select literature to inform this review.

Populations
The population of interest is patients who need an ICD and have no contraindication to a T-ICD.

There are no defined guidelines for the selection of S-ICD versus T-ICD. Currently, S-ICDs are generally considered in the following situations:

- Patients at high risk of infection, inadequate venous access, and any patient without a pacing indication
- Younger patients due to the expected longevity of the implanted leads and a desire to avoid chronic transvenous leads (e.g., patients with hypertrophic cardiomyopathy, congenital cardiomyopathies, or inherited channelopathies)
- Patients at high risk for bacteremia, such as patients on hemodialysis or with chronic indwelling endovascular catheters.
- Patients with challenging vascular access or prior complications with T-ICDs
- Sudden cardiac death resulting from cardiac arrhythmia is a leading case of CV mortality (50% of CV deaths worldwide).

Interventions
The therapy being considered is S-ICD.

An ICD is a device designed to monitor a patient's heart rate, recognize ventricular fibrillation or ventricular tachycardia, and deliver an electric shock to terminate these arrhythmias to reduce the risk of sudden death. A subcutaneous ICD (S-ICD, which lacks transvenous leads, is intended as an alternative to T-ICD to reduce lead-related complications. The S-ICD is comprised of a pulse generator and single shocking coil running along the left parasternal margin. These are both implanted subcutaneously without endovascular access. The electrode is designed to be implanted using anatomical landmarks only without the need for fluoroscopy or other medical imaging systems during the surgical implant procedure.

Comparators
The comparator of interest is T-ICD placement.

Outcomes
The general outcomes of interest are OS, morbid events, quality of life, treatment-related mortality, and treatment-related morbidity. Outcomes should be assessed from 1 week to 5 years or longer.

Specific outcomes include the following:
- Sudden cardiac death
- All-cause mortality
- Adverse events including nonlead-related complications (device infection, hematoma, pneumothorax, pericardial effusion), inappropriate shocks, device failure; and lead-related complications
- Cardiovascular mortality
- Health-related quality of life
- Hospital re-admission

Study Selection Criteria
Methodologically credible studies were selected using the following principles:
- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE
Randomized Controlled Trial
The Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter Defibrillator Therapy (PRAETORIAN) trial was a noninferiority RCT that compared S-ICD to T-ICD in 849 patients with an indication for ICD but no indication for pacing (Table 11).[84,] The trial is the only RCT on the effect of an S-ICD with health outcomes. Patients were eligible if they were 18 years and older with a class I or IIa indication for ICD therapy for primary or secondary prevention, according to professional society guidelines, and no indication for pacing. The median age of enrolled patients was 63 years (interquartile range, 55 to 70). Most

enrolled patients were diagnosed with ischemic and nonischemic cardiomyopathy and 19.7% were women. The median left ventricular ejection fraction was 30%.

The primary end point in PRAETORIAN was the composite of device-related complications and inappropriate shocks (see Table 11 for outcome definitions). The trial was designed to test the hypothesis of noninferiority of the S-ICD as compared with the T-ICD with respect to the time from device implantation to the first occurrence of a primary end point event. The primary analysis was the modified intention-to-treat cohort (i.e. patients were analyzed in accordance to the treatment group to which they were originally assigned, regardless of withdrawals, losses to follow-up or crossovers). Patients who did not receive a device and patients who proved ineligible for one of the treatments due to incomplete or inadequate screening were excluded from this analysis. In the as-treated cohort, patients were analyzed in the group of the specific ICD type which they received at initial implantation regardless of randomization result, withdrawals, losses to follow-up or crossovers. The noninferiority margin for the upper boundary of the 95% confidence interval for the hazard ratio was set at 1.45.

The trial's main results are summarized in Tables 12-14. The S-ICD was noninferior to the T-ICD on the composite endpoint of device-related complications and inappropriate shocks. The hazard ratio for the primary end point was 0.99 (95% CI, 0.71 to 1.39; noninferiority margin, 1.45; p =.01 for noninferiority; p =.95 for superiority). Results for the modified ITT analysis and as-treated analysis did not differ. There were more device related complications in the T-ICD group and more inappropriate shocks in the S-ICD group, but the trial was not powered for these endpoints. Secondary endpoints and mortality results are summarized in Table 13. There were more deaths from any cause in the S-ICD group than in the T-ICD group (16.4% vs 13.1%; hazard ratio 1.23; 95% CI, 0.89 to 1.70), but the number of sudden cardiac deaths did not differ between groups (18 in each group). There were more appropriate shocks in the S-ICD group (19.2% vs 11.5%; hazard ratio 1.52; 95% CI 1.08 to 2.12). Other secondary endpoints did not differ between the groups.

While the rate of sudden cardiac death in the PRAETORIAN trial was low (18 patients in each group), the number of overall deaths was 151, and actually occurred more frequently than the composite outcome (Table 13). The hazard ratio for all-cause mortality was 1.23 (95% CI, 0.89 to 1.70). The PRAETORIAN trial investigators conducted competing risks analyses to account for discontinuation of follow-up before the primary end point had occurred in (1) the modified ITT population with competing risk of death, and (2) the true ITT population with competing risk of death and discontinuation of follow-up. These analyses led to consistent estimates of the hazard ratio (and 95% confidence interval) for the primary end point.

Device and lead complications occurred more frequently in the T-ICD group (Table 14).

Table 11. PRAETORIAN Trial Characteristics

Study	Countries	Sites	Dates	Participants	Interventions		Primary Endpoint Definitions
PRAETORIAN Knops et al (2020)[84,]					Active	Comparator	

Study	Countries	Sites	Dates	Participants	Interventions		Primary Endpoint Definitions
	Europe (92.4%) and US	39	March 2011 through January 2017	Eligibility:18 years and older Class I or IIa indication for ICD therapy for primary or secondary prevention, according to professional society guidelines. Exclusions: Previous ICD implantation, unsuitability for S-ICD therapy according to QRS-T–wave sensing analysis, and indications for either bradycardia pacing or biventricular pacing.	Subcutaneous ICD (N = 426)	Transvenous ICD (N = 423)	Composite of device-related complications and inappropriate shocks Inappropriate shocks were defined as shock therapy for anything else but ventricular fibrillation or ventricular tachycardia, for example supraventricular tachycardia with fast ventricle response (including sinus tachycardia and atrial fibrillation), T-wave oversensing, detection of physiological- or other non-cardiac activity and lead- or device failure. Complications included: • device infection that led to the extraction of the lead or generator; • pocket hematoma that led to drainage, blood transfusion, or prolongation of hospitalization; • device-related thrombotic events;

Study	Countries	Sites	Dates	Participants	Interventions		Primary Endpoint Definitions
							• pneumothorax or hemothorax that led to intervention or prolongation of hospitalization; • cardiac perforation or tamponade; • lead repositioning or replacement; • other complications related to the lead or generator that led to medical or surgical intervention.

ICD: implantable cardioverter defibrillator; PRAETORIAN: Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter Defibrillator Therapy

Table 12. PRAETORIAN Trial Results- Primary Composite Endpoint and Components

Study	Endpoint **(4-year cumulative incidence)**	**Subcutaneous ICD (n = 426)**	**Transvenous ICD (n = 423)**	**Hazard Ratio (95% CI)**
PRAETORIAN Knops et al (2020)[84,]	Primary Composite Endpoint (modified ITT analysis)	68 (15.1%)	68 (15.7%)	0.99 (0.71–1.39) p =.01 for noninferiority; p =.95 for superiority
	Device-related complication	31 (5.9%)	44 (9.8%)	0.69 (0.44–1.09)
	Inappropriate shock	41 (9.7%)	29 (7.3%)	1.43 (0.89–2.30)
	Primary Composite Endpoint (as-treated analysis)	68/428 (15.9%)	68/421 (16.2%)	0.98 (0.70–1.37)

CI: confidence interval; ICD: implantable cardioverter defibrillator; ITT: intention-to-treat; PRAETORIAN: Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter Defibrillator Therapy

Table 13. PRAETORIAN Trial Results- Secondary Endpoints

Study	End Point	Subcutaneous ICD (N=426)	Transvenous ICD (N=423)	Hazard Ratio (95% CI)
PRAETORIAN Knops et al (2020)[84,]	Death from any cause	83 (16.4%)	68 (13.1%)	1.23 (0.89–1.70)
	Sudden cardiac death	18 (4.2%)	18 (4.3%)	
	Other cardiovascular death	34 (8.0%)	28 (6.6%)	
	Noncardiovascular death	31 (7.3%)	22 (5.2%)	
	Appropriate shock therapy	83 (19.2%)	57 (11.5%)	1.52 (1.08–2.12)
	Antitachycardia pacing (appropriate)	6 (0.6%)	54 (12.9%)	
	Antitachycardia pacing (inappropriate)	1 (0.3%)	30 (7.2%)	
	Major adverse cardiac event	64 (13.3%)	80 (16.4%)	0.80 (0.57–1.11)
	Hospitalization for heart failure	79 (17.4%)	74 (16.1%)	1.08 (0.79–1.49
	Crossover to other study device	18 (4.3%)	11 (2.7%)	1.64 (0.77–3.47)

CI: confidence interval; ICD: implantable cardioverter defibrillator; PRAETORIAN: Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter Defibrillator Therapy

Table 14. PRAETORIAN Trial Results- Specific Complications

Study	Endpoint	Subcutaneous ICD (N=426)	Transvenous ICD (N=423)
PRAETORIAN Knops et al (2020)[84,]	Complications within the first 30 days	3.8%	4.7%
	Lead-related complications	1.4%	6.6%
	Device-related complications	31 (5.9%)	44 (9.8%)

Study	Endpoint	Subcutaneous ICD (N=426)	Transvenous ICD (N=423)
	Infection	4 (1 lead-related)	8 (5 lead-related)
	Bleeding	8	2
	Thrombotic event	1	2
	Pneumothorax	0	4
	Lead perforation	0	4
	Tamponade	0	2
	Lead repositioning	2	7
	Other lead or device complication	19	20
	Lead replacement	3	9
	Device malfunction	4	6
	Sensing issues	4	0
	Pacing indication	5	1
	Implantation failure	0	3
	Defibrillation test failure	3	0
	Pain or discomfort	2	3

CI: confidence interval; ICD: implantable cardioverter defibrillator: Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter Defibrillator Therapy

Study relevance, design and conduct limitations of PRAETORIAN are summarized in Tables 15 and 16. The choice of a composite primary endpoint poses several challenges to interpreting the results of PRAETORIAN. In PRAETORAN, the components of the composite endpoint were discordant; device-related complications were expected to favor S-ICD and inappropriate shocks were expected to favor T-ICD. The timing of the components of the composite outcome assessment is important in interpreting the study results and explaining expected treatment results to patients. Early benefit could favor one treatment over another, and results could change with longer follow-up. This is an important point to consider when assessing complications such as lead failure, which continue to increase over the life of the device. Additionally, because the composite was not used in earlier trials of the active comparator, there is no historical data on which to derive the expected performance of the active control. The inappropriate shock rate was based on results from the MADIT-RT trial, which compared programmed high-rate or delayed T-ICD therapy, and the expected rate of complications was based on results from MADIT-RT and the SCD-HeFT trial, which compared amiodarone to T-ICD. To estimate the expected event rate in PRAETORIAN, the researchers combined these two endpoints to arrive at the expected 17.2% event rate for the composite primary outcome. The study authors do not cite any previous RCTs that used the composite endpoint of complications and inappropriate shocks. All-cause mortality was a primary endpoint in several previous RCTs of T-ICD. However, the PRAETORIAN trial protocol (2012) noted that all-cause mortality was not chosen as the primary endpoint because "mortality event rates in both groups are presumed to be low, leading to an extremely large trial size if this would serve as a primary endpoint." The protocol also states that safety and efficacy of the S-ICD have been demonstrated in earlier trials

and that the composite endpoint was "preferred above all-cause mortality, as practical, reasonably achievable, and pertinent to most cardiologists."

Another major limitation of PRAETORIAN was that the median 48-month follow-up was not long enough to determine complications over the life of the device. In fact, the PRAETORIAN study authors note in their discussion, "longer-term follow-up of this cohort will be important because the incidence of lead-related complications increases over time with the transvenous ICD and because battery longevity is a limiting factor for the subcutaneous ICD." Five-year data from the S-ICD PAS should provide more information on longer-term adverse events such as lead failure and need for device replacement.

Quality of life data from PRAETORIAN was collected but has not yet been published. This data could shed light on the relative importance to patients of adverse events such as inappropriate shocks and device replacement, especially if quality of life data were reported by subgroups of patients who experienced shocks. For example, these data might indicate that inappropriate shocks are so distressing to patients that they outweigh any potential benefits of S-ICDs.

Finally, the under enrollment of women in the trial (19.7%) potentially limits the applicability of its results, although a subgroup analysis by sex was consistent with the primary analysis on the composite endpoint (HR in women 0.65; 95% CI 0.28 to 1.47).

Table 15. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-up[e]
PRAETORIAN Knops et al (2020)[84,]	4. Women under enrolled (19.7%)			6. composite endpoint with discordant outcomes;	2. 4-year median follow-up not sufficient to assess complications over the life of the device

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 16. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
PRAETORIAN Knops et al (2020)[84,]		2. clinical-events committee was not blinded to	2. Quality of life data collected but not yet published.			Rationale for choice of noninferiority margin unclear

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
		treatment assignment				

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Comparative Observational Studies

Several observational studies have directly compared T-ICD to S-ICD. These studies are briefly described in Table 17. All studies were performed in the U.S. and/or Europe. Nonrandomized controlled studies have reported success rates in terminating laboratory-induced VF that are similar to T-ICD. However, there is scant evidence on comparative clinical outcomes of both types of ICD over longer periods. Adverse event rates are uncertain, with variable rates reported.

Table 17. Summary of Observational Comparative Studies of S-ICD and T-ICD

Study	Study Type	N	Follow-Up	Results			
				Outcomes	*T-ICD*	*S-ICD*	*DC T-ICD*
Mithani et al (2018)[85,]	Matching based on dialysis status, sex, age	182 (91 matched pairs)	180 d	• Inappropriate shocks • Infection requiring explant • Death from all causes • Total with adverse event or death	• 2.2% • 1.1% • 2.2% • 7.7%	• 1.1% • 3.3% • 2.2% • 5.5%	
Honarbakhsh et al (2017)[86,]	Propensity matched case-control	138 (69 matched pairs)	32 mo[a]	• Total device-related complications • Infections • Inappropriate shocks • Failure to cardiovert VA	• 29% • 5.8% • 8.7% • 1.4%	• 9% • 1.4% • 4.3% • 1.4%	

Study	Study Type	N	Follow-Up	Results			
Kobe et al (2017)[87,]	Sex- and age-matched case-control	120 (60 pairs); 84 pairs analyzed	942 d vs 622 d	• Posttraumatic stress disorder • Major depression • SF-12 physical well-being score • SF-12 mental well-being score	• 14.3% • 9.5% • 40 • 52	• 14.3% • 4.8% • 47 • 52	
Pedersen et al (2016)[88,]	Retrospective analysis of propensity-matched cohort	334 (167 matched pairs)	6 mo	• SF-12 physical well-being score • SF-12 mental well-being score	• 43 • 45	• 44 • 45	
Brouwer et al (2016)[89,]	Retrospective analysis of propensity-matched cohort	280 (140 matched pairs)	5 y	• Overall complications • Lead complications • Non-lead complications • Infections • Appropriate ICD intervention (HR=2.4; 95% CI, NR; p=.01) • Inappropriate ICD intervention (HR=1.3; 95% CI, NR; p=.42) • Survival	• 18% • 11.5% • 2.2% • 3.6% • 31% • 30% • 95%	• 14% • 0.8% • 9.9% • 4.1% • 17% • 21% • 96%	
Friedman et al (2016)[90,]	Retrospective analysis of propensity-matched cohort from NCDR for ICD	5760 (1920 matched, groups)	NR	• Any in-hospital complication • Deaths • Infections • Lead dislodgements • Pneumothorax	• 0.6% • 0.1% • 0% • 0.2% • 0.2%	• 0.9% • 0.2% • 0.05% • 0.1% • 0%	• 1.5% • 0.05% • 0.1% • 0.6% • 0.3%
Kobe et al (2013)[91,]	Sex- and age-matched case-control	138 (69 matched pairs)	217 d[a]	• Pericardial effusion	• 1 • 91% • 9 • 3	• 0 • 90% • 3 • 5	

Study	Study Type	N	Follow-Up	Results			
				• Successful termination of induced VF • Appropriate shocks • Inappropriate shocks			

CI: confidence interval; DC: dual chamber; HR: hazard ratio; ICD: implantable cardioverter defibrillator; NCDR: National Cardiovascular Data Registry; NR: not reported; SF-12: 12-Item Short-Form Health Survey; S-ICD: subcutaneous implantable cardioverter defibrillator; T-ICD: transvenous implantable cardioverter defibrillator; VA: ventricular arrhythmia; VF: ventricular fibrillation.
a Mean.
b Median.

Section Summary: Subcutaneous Implantable Cardioverter Defibrillators In Patients With No Contraindications to a Transvenous Implantable Cardioverter Defibrillator
The PRAETORIAN trial is the only RCT on the effect of an S-ICD with health outcomes. PRAETORIAN found that S-ICD was noninferior to T-ICD on a composite outcome of complications and inappropriate shock at 48 months (HR, 0.99; 95% CI, 0.71 to 1.39; noninferiority margin, 1.45; p =.01 for noninferiority; p =.95 for superiority). There were more device related complications in the T-ICD group and more inappropriate shocks in the S-ICD group, but the trial was not powered for these endpoints. There is uncertainty over the applicability and interpretation of PRAETORIAN based on the choice of a composite outcome with discordant results, unclear rationale for choice of the noninferiority margin, inadequate length of follow-up to determine rates of complications, and lack of reporting of quality of life data. Comparative observational studies are insufficient to draw conclusions on whether there are small differences in efficacy between the two types of devices, and reported variable adverse event rates. Ongoing studies could provide additional evidence on complications and device safety over the longer term.

SUMMARY OF EVIDENCE

Transvenous Implantable Cardioverter Defibrillators

For individuals who have a high risk of sudden cardiac death (SCD) due to ischemic or to nonischemic cardiomyopathy in adulthood who receive transvenous ICD (T-ICD) placement for primary prevention, the evidence includes multiple well-designed and well-conducted randomized controlled trials (RCTs) as well as systematic reviews of these trials. Relevant outcomes are overall survival (OS), morbid events, quality of life, and treatment-related mortality and morbidity. Multiple, well-done RCTs have shown a benefit in overall mortality for patients with ischemic cardiomyopathy and reduced ejection fraction. RCTs assessing early ICD use following recent myocardial infarction did not support a benefit for immediate versus delayed implantation for at least 40 days. For nonischemic cardiomyopathy, there is less clinical trial data, but pooled estimates of available evidence from RCTs enrolling patients with nonischemic cardiomyopathy and from subgroup analyses of RCTs with mixed populations have supported a survival benefit for this group. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have a high risk of SCD due to hypertrophic cardiomyopathy (HCM) in adulthood who receive T-ICD placement for primary prevention, the evidence includes several

large registry studies. Relevant outcomes are OS, morbid events, quality of life, and treatment-related mortality and morbidity. In these studies, the annual rate of appropriate ICD discharge ranged from 3.6% to 5.3%. Given the long-term high-risk of SCD in patients with HCM, with the assumption that appropriate shocks are life-saving, these rates are considered adequate evidence to support the use of ICDs in patients with HCM. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have a high risk of SCD due to an inherited cardiac ion channelopathy who receive T-ICD placement for primary prevention, the evidence includes small cohort studies of patients with these conditions treated with ICDs. Relevant outcomes are OS, morbid events, quality of life, and treatment-related mortality and morbidity. The limited evidence for patients with long QT syndrome, catecholaminergic polymorphic ventricular tachycardia, and Brugada syndrome has reported high rates of appropriate shocks. No studies were identified on the use of ICDs for patients with short QT syndrome. Studies comparing outcomes between patients treated and untreated with ICDs are not available. However, given the relatively small patient populations with these channelopathies and the high-risk of cardiac arrhythmias, clinical trials are unlikely. Given the long-term high-risk of SCD in patients with inherited cardiac ion channelopathy, with the assumption that appropriate shocks are life-saving, these rates are considered adequate evidence to support the use of T-ICDs in patients with inherited cardiac ion channelopathy. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have a high risk of SCD due to cardiac sarcoid who receive T-ICD placement for primary prevention, the evidence includes small cohort studies of patients with cardiac sarcoid treated with ICDs who received appropriate shocks. Studies comparing outcomes between patients treated and untreated with ICDs are not available. However, given the relatively small number of patients with cardiac sarcoid (5% of those with systemic sarcoiditis), clinical trials are unlikely. Given the long-term high-risk of SCD in patients with cardiac sarcoid, with the assumption that appropriate shocks are life-saving, these studies are considered adequate evidence to support the use of T-ICDs in patients with cardiac sarcoid who have not responded to optimal medical therapy. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have had symptomatic life-threatening sustained ventricular tachycardia or ventricular fibrillation (VF) or who have been resuscitated from sudden cardiac arrest (secondary prevention) who receive T-ICD placement, the evidence includes multiple well-designed and well-conducted RCTs as well as systematic reviews of these trials. Relevant outcomes are OS, morbid events, quality of life, and treatment-related mortality and morbidity. Systematic reviews of RCTs have demonstrated a 25% reduction in mortality for ICD compared with medical therapy. Analysis of data from a large administrative database has confirmed that this mortality benefit is generalizable to the clinical setting. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Subcutaneous Implantable Cardioverter Defibrillators

For individuals who need an ICD and have a contraindication to a T-ICD but no indications for antibradycardia pacing and no antitachycardia pacing-responsive arrhythmias who receive S-ICD placement, the evidence includes nonrandomized studies and case series. Relevant outcomes are OS, morbid events, quality of life, and treatment-related mortality and morbidity. Nonrandomized controlled studies have reported success rates in terminating laboratory-induced VF that are

similar to T-ICD. Case series have reported high rates of detection and successful conversion of VF, and inappropriate shock rates in the range reported for T-ICD. Given the need for ICD placement in this population at risk for SCD, with the assumption that appropriate shocks are life-saving, these rates are considered adequate evidence to support the use of S-ICDs in patients with contraindication to T-ICD. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who need an ICD and have no indications for antibradycardia pacing or antitachycardia pacing-responsive arrhythmias and have no contraindication to a T-ICD, who receive S-ICD placement, the evidence includes 1 RCT, nonrandomized studies and case series. Relevant outcomes are OS, morbid events, quality of life, and treatment-related mortality and morbidity. The PRAETORIAN (Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter Defibrillator Therapy) trial is the only RCT on the effect of an S-ICD with health outcomes. PRAETORIAN found that S-ICD was noninferior to T-ICD on a composite outcome of complications and inappropriate shock at 48 months (HR, 0.99; 95% CI, 0.71 to 1.39; noninferiority margin, 1.45; p =.01 for noninferiority; p =.95 for superiority). There were more device related complications in the T-ICD group and more inappropriate shocks in the S-ICD group, but the trial was not powered for these endpoints. There is uncertainty over the applicability and interpretation of PRAETORIAN based on the choice of a composite outcome with discordant results, unclear rationale for choice of the noninferiority margin, inadequate length of follow-up to determine rates of complications, and lack of reporting of quality of life data. Comparative observational studies are insufficient to draw conclusions on whether there are small differences in efficacy between the two types of devices, and reported variable adverse event rates. Ongoing studies could provide additional evidence on complications and device safety over the longer term. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

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.

2020 Medical Advisory Panel

In October 2020, the BCBSA Medical Advisory Panel (MAP) reviewed the evidence for individuals who need an ICD and have no contraindication to transvenous ICD placement and agreed that for this indication, the evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

2015 Input

In response to requests, input was received from 1 physician specialty society (4 responses) and 5 academic medical centers, for a total of 9 responses, while this policy was under review in 2015. Input focused on the use of implantable cardioverter defibrillators (ICDs) as primary prevention for cardiac ion channelopathies and use of the subcutaneous implantable cardioverter defibrillator. Reviewers generally indicated that an ICD should be considered medically necessary

for primary prevention of ventricular arrhythmias in adults and children with a diagnosis of long QT syndrome, Brugada syndrome, short QT syndrome, and catecholaminergic polymorphic ventricular tachycardia. Reviewers generally indicated that the subcutaneous implantable cardioverter defibrillator should be considered medically necessary particularly for patients with indications for an ICD but who have difficult vascular access or have had transvenous ICD lead explantation due to complications.

2011 Input

In response to requests, input was received from 6 academic medical centers while this policy was under review in 2011. For most policy indications, including pediatric, there was general agreement from those providing input. On the question of timing of ICD placement, input was mixed, with some commenting about the potential role of early implantation in select patients. Reviewers indicated that a waiting period of nine months for patients with nonischemic cardiomyopathy was not supported by the available evidence or consistent with the prevailing practice patterns in academic medical centers. Input emphasized the difficulty of prescribing strict timeframes given the uncertainty of establishing the onset of cardiomyopathy and the inability to risk-stratify patients based on time since onset of cardiomyopathy.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Heart Association, American College of Cardiology, and Heart Rhythm Society Guidelines on Heart Failure (2017)

The AHA, American College of Cardiology, and Heart Rhythm Society (HRS) (2017) published joint guidelines on the management of heart failure, which updated their 2012 guidelines.[92,93,] These guidelines made the following recommendations on the use of ICD devices (see Tables 18-25). The recommendations for the use of an ICD apply only if meaningful survival is expected to be greater than 1 year.

Table 18. Guidelines on Device-Based Therapy of Cardiac Rhythm Abnormalities

Recommendation	COR	LOE
"In patients with ischemic heart disease, who either survive SCA due to VT/VF or experience hemodynamically unstable VT (LOE: B-R) or stable VT (LOE: B-NR) not due to reversible causes..."	I	B-R B-NR
"A transvenous ICD provides intermediate value in the secondary prevention of SCD particularly when the patient's risk of death due to a VA is deemed high and the risk of nonarrhythmic death (either cardiac or noncardiac) is deemed low based on the patient's burden of comorbidities and functional status."		B-R
"In patients with ischemic heart disease and unexplained syncope who have inducible sustained monomorphic VT on electrophysiological study..."	I	B-NR
"In patients resuscitated from SCA due to coronary artery spasm in whom medical therapy is ineffective or not tolerated..."	IIa	B-NR
"In patients resuscitated from SCA due to coronary artery spasm, an ICD in addition to medical therapy may be reasonable..."	IIb	B-NR

Recommendation	COR	LOE
"In patients with arrhythmogenic right ventricular cardiomyopathy and an additional marker of increased risk of SCD (resuscitated SCA, sustained VT, significant ventricular dysfunction with RVEF or LVEF ≤35%)..."	I	B-NR
"In patients with arrhythmogenic right ventricular cardiomyopathy and syncope presumed due to VA..."	IIa	B-NR

B-NR: moderate, non-randomized; B-R: moderate, randomized; COR: class of recommendation; ICD: implantable cardioverter defibrillator; LOE: level of evidence; LVEF: left ventricular ejection fraction; RVEF: right ventricular ejection fraction; SCA: sudden cardiac arrest; SCD: sudden cardiac death; VA: ventricular arrhythmia; VF: ventricular fibrillation; VT: ventricular tachycardia.

Table 19. Guidelines on Use of ICDs as a Primary Prevention of Ischemic Heart Disease

Recommendation	COR	LOE
"In patients with LVEF of 35% or less that is due to ischemic heart disease who are at least 40 days' post-MI and at least 90 days post revascularization, and with NYHA class II or III HF despite GDMT..."	I	A
" In patients with LVEF of 30% or less that is due to ischemic heart disease who are at least 40 days' post-MI and at least 90 days post revascularization, and with NYHA class I HF despite GDMT..."	I	A
"A transvenous ICD provides high value in the primary prevention of SCD particularly when the patient's risk of death due to a VA is deemed high and the risk of nonarrhythmic death (either cardiac or noncardiac) is deemed low based on the patient's burden of comorbidities and functional status..."		B-R
"In patients with NSVT due to prior MI, LVEF of 40% or less and inducible sustained VT or VF at electrophysiological study..."	I	B-R
"In nonhospitalized patients with NYHA class IV symptoms who are candidates for cardiac transplantation or an LVAD..."	IIa	B-NR
"An ICD is not indicated for NYHA class IV patients with medication-refractory HF who are not also candidates for cardiac transplantation, an LVAD, or a CRT defibrillator that incorporates both pacing and defibrillation capabilities."	III[a]	C-EO

A: high; B-NR: moderate, non-randomized; B-R: moderate, randomized; C-EO: consensus of expert opinion; CRT: cardiac resynchronization therapy; COR: class of recommendation; ICD: implantable cardioverter defibrillator; GDMT: guideline-directed management and therapy; HF: heart failure; LOE: level of evidence; LVAD: left ventricular assist device; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NSVT: nonsustained ventricular tachycardia; NYHA: New York Heart Association; SCD: sudden cardiac death; VA: ventricular arrhythmia; VF: ventricular fibrillation; VT: ventricular tachycardia.
a No benefit.

Table 20. Guidelines on Use of ICDs for Nonischemic Cardiomyopathy

Recommendation	COR	LOE
"In patients with NICM who either survive SCA due to VT/VF or experience hemodynamically unstable VT (LOE: B-R) (1-4) or stable VT (LOE: B-NR) (5) not due to reversible causes..."	I	B-R B-NR
" In patients with NICM who experience syncope presumed to be due to VA and who do not meet indications for a primary prevention ICD, an ICD or an electrophysiological study for risk stratification for SCD can be beneficial..."	IIa	B-NR

Recommendation	COR	LOE
"In patients with NICM, HF with NYHA class II-III symptoms and an LVEF of 35% or less, despite GDMT..."	IIa	B-R
"In patients with NICM, HF with NYHA class I symptoms and an LVEF of 35% or less, despite GDMT..."	IIb	B-R
"In patients with medication-refractory NYHA class IV HF who are not also candidates for cardiac transplantation, an LVAD, or a CRT defibrillator that incorporates both pacing and defibrillation capabilities, an ICD should not be implanted."	III[a]	C-EO

A: high; B-NR: moderate, non-randomized; B-R: moderate, randomized; C-EO: consensus of expert opinion; COR: class of recommendation; CRT: cardiac resynchronization therapy; GDMT: guideline-directed management and therapy; HF: heart failure; ICD: implantable cardioverter defibrillator: LOE: level of evidence; LVAD: left ventricular assist device; LVEF: left ventricular ejection fraction; NICM: nonischemic cardiomyopathy; NYHA: New York Heart Association; SCA: sudden cardiac arrest; SCD: sudden cardiac death; VA: ventricular arrhythmia; VF: ventricular fibrillation; VT: ventricular tachycardia.
a No benefit.

Table 21. Guidelines on Use of ICDs for HCM

Recommendation	COR	LOE
"In patients with HCM who have survived an SCA due to VT or VF, or have spontaneous sustained VT causing syncope or hemodynamic compromise..."	I	B-NR
"In patients with HCM and 1 or more of the following risk factors... • Maximum LV wall thickness ≥30 mm (LOE: B-NR). • SCD in 1 or more first-degree relatives presumably caused by HCM (LOE: C-LD). • 1 or more episodes of unexplained syncope within the preceding 6 months (LOE: C-LD)"	IIa	 B-NR C-LD C-LD
"In patients with HCM who have spontaneous NSVT (LOE: C-LD) or an abnormal blood pressure response with exercise (LOE: B-NR), who also have additional SCD risk modifiers or high risk features..."	IIa	B-NR C-LD
"In patients with HCM who have NSVT (LOE: B-NR) or an abnormal blood pressure response with exercise (LOE: B-NR) but do not have any other SCD risk modifiers, an ICD may be considered, but its benefit is uncertain."	IIB	B-NR B-NR
"In patients with an identified HCM genotype in the absence of SCD risk factors, an ICD should not be implanted"	III[a]	B-NR

B-NR: moderate, non-randomized; C-LD: limited data; COR: class of recommendation; HCM: hypertrophic cardiomyopathy; ICD: implantable cardioverter defibrillator; LOE: level of evidence; LV: left ventricular; NSVT: nonsustained ventricular tachycardia; SCA: sudden cardiac arrest; SCD: sudden cardiac death; VF: ventricular fibrillation; VT: ventricular tachycardia.
a No benefit.

Table 22. Guidelines on Use of Subcutaneous ICDs for Cardiac Sarcoiditis

Recommendation	COR	LOE
"In patients with cardiac sarcoidosis who have sustained VT or are survivors of SCA or have an LVEF of 35% or less, an ICD is recommended, if meaningful survival of greater than 1 year is expected."	I	B-NR
"In patients with cardiac sarcoidosis and LVEF greater than 35% who have syncope and/or evidence of myocardial scar by cardiac MRI or positron emission tomographic (PET) scan, and/or have an indication for permanent pacing, implantation of an ICD is reasonable, provided that meaningful survival of greater than 1 year is expected."	IIa	B-NR

Recommendation	COR	LOE
"In patients with cardiac sarcoidosis and LVEF greater than 35%, it is reasonable to perform an electrophysiological study and to implant an ICD, if sustained VA is inducible, provided that meaningful survival of greater than 1 year is expected."	IIa	C-LD
"In patients with cardiac sarcoidosis who have an indication for permanent pacing, implantation of an ICD can be beneficial."	IIa	C-LD

B-NR: moderate, non-randomized; C-LD: limited data; COR: class of recommendation; ICD: implantable cardioverter defibrillator; LOE: level of evidence; LVEF: left ventricular ejection fraction; MRI: magnetic resonance imaging; SCA: sudden cardiac arrest; VA: ventricular arrhythmia; VT: ventricular tachycardia.

Table 23. Guidelines on Use of ICDs for Other Conditions

Recommendation	COR	LOE
"In patients with HFrEF who are awaiting heart transplant and who otherwise would not qualify for an ICD (e.g., NYHA class IV and/or use of inotropes) with a plan to discharge home, an ICD is reasonable"	IIa	B-NR
"In patients with an LVAD and sustained VA, an ICD can be beneficial."	IIa	C-LD
"In patients with a heart transplant and severe allograft vasculopathy with LV dysfunction..."	IIb	B-NR
"In patients with neuromuscular disorders, primary and secondary prevention ICDs are recommended for the same indications as for patients with NICM..."	I	B-NR
In patients with a cardiac channelopathy (see Guideline Tables 7.9 and 7.9.1)	I	B-NR
In patients with catecholaminergic polymorphic ventricular tachycardia and recurrent sustained VT or syncope (see Guideline Table 7.9.1.2)	I	B-NR
"In patients with Brugada syndrome with spontaneous type 1 Brugada electrocardiographic pattern and cardiac arrest, sustained VA or a recent history of syncope presumed due to VA..."	I	B-NR
"In patients with early repolarization pattern on ECG and cardiac arrest or sustained VA..."	I	B-NR
"In patients resuscitated from SCA due to idiopathic polymorphic VT or VF..."	I	B-NR
"For older patients and those with significant comorbidities, who meet indications for a primary prevention ICD, an ICD is reasonable."	IIa	B-NR
"In patients with adult congenital heart disease with SCA due to VT or VF in the absence of reversible causes..."	I	B-NR
"In patients with repaired moderate or severe complexity adult congenital heart disease with unexplained syncope and at least moderate ventricular dysfunction or marked hypertrophy, either ICD implantation or an electrophysiological study with ICD implantation for inducible sustained VA is reasonable..."	IIa	B-NR

B-NR: moderate, non-randomized; C-LD: limited data; COR: class of recommendation; ECG: electrocardiogram; HFrEF; heart failure with reduced ejection fraction; ICD: implantable cardioverter defibrillator; LOE: level of evidence; LV: left ventricle; LVAD: left ventricular assist device; NICM: nonischemic cardiomyopathy; NYHA: New York Heart Association; SCA: sudden cardiac arrest; VA: ventricular arrhythmia; VF: ventricular fibrillation; VT: ventricular tachycardia.

Table 24. Guidelines on Use of Subcutaneous ICDs

Recommendation	COR	LOE
"In patients who meet criteria for an ICD who have inadequate vascular access or are at high risk for infection, and in whom pacing for bradycardia or VT termination or as part of CRT is neither needed nor anticipated, a subcutaneous implantable cardioverter-defibrillator is recommended."	I	B-NR
"In patients who meet indication for an ICD, implantation of a subcutaneous implantable cardioverter-defibrillator is reasonable if pacing for bradycardia or VT termination or as part of CRT is neither needed nor anticipated."	IIa	B-NR
"In patients with an indication for bradycardia pacing or CRT, or for whom antitachycardia pacing for VT termination is required, a subcutaneous implantable cardioverter-defibrillator should not be implanted."	III[a]	B-NR

B-NR: moderate, non-randomized; CRT: cardiac resynchronization therapy; COR: class of recommendation; ICD: implantable cardioverter defibrillator; LOE: level of evidence; VT: ventricular tachycardia.
a Harm.

The 2013 update made the following recommendations on ICD therapy for children (see Table 25).[92,]

Table 25. Guidelines on ICD Therapy for Children

Recommendation	COR	LOE
ICD implantation is indicated in the survivor of cardiac arrest after evaluation to define the cause of the event and to exclude any reversible causes.	I	B
ICD implantation is indicated for patients with symptomatic sustained VT in association with congenital heart disease who have undergone hemodynamic and electrophysiological evaluation. Catheter ablation or surgical repair may offer possible alternatives in carefully selected patients.	I	C
ICD implantation is reasonable for patients with congenital heart disease with recurrent syncope of undetermined origin in the presence of either ventricular dysfunction or inducible ventricular arrhythmias at electrophysiological study.	IIa	B
ICD implantation may be considered for patients with recurrent syncope associated with complex congenital heart disease and advanced systemic ventricular dysfunction when thorough invasive and noninvasive investigations have failed to define a cause.	IIb	C
All class III recommendations found in Section 3, "Indications for Implantable Cardioverter-Defibrillator Therapy," apply to pediatric patients and patients with congenital heart disease, and ICD implantation is not indicated in these patient populations.	III[a]	C

COR: class of recommendation; ICD: implantable cardioverter defibrillator; LOE: level of evidence; VT: ventricular tachycardia.
a Not recommended.

American Heart Association/American College of Cardiology Guidelines on Hypertrophic Cardiomyopathy (2020)

In 2020, the American Heart Association and American College of Cardiology published a joint Guideline for the Diagnosis and Treatment of Patients with Hypertrophic Cardiomyopathy.[94,] Recommendations relevant to this review are summarized in Table 26.

Table 26. Patients Selection for ICD Placement in High-Risk Patients With Hypertrophic Cardiomyopathy

Recommendation	COR	LOE
For patients with HCM, and previous documented cardiac arrest or sustained ventricular tachycardia, ICD placement is recommended.	I	B-NR
For adult patients with HCM with 1 or more major risk factors for SCD, it is reasonable to offer an ICD	2a	B-NR
For children with HCM who have 1 or more conventional risk factors, ICD placement is reasonable after considering the relatively high complication rates of long-term ICD placement in younger patients	2a	B-NR
For patients 16 years and older with HCM and 1 or more major SCD risk factors, discussion of the estimated 5-year sudden death risk and mortality rates can be useful during the shared decision-making process for ICD placement	2a	B-NR
In patients with HCM without risk factors, ICD placement should not be performed	3: Harm	B-NR
In patients with HCM, ICD placement for the sole purpose of participation in competitive athletics should not be performed	3: Harm	B-NR
In patients with hypertrophic cardiomyopathy who are receiving an ICD, either a single chamber transvenous ICD or a subcutaneous ICD is recommended after a shared decision-making discussion that takes into consideration patient preferences, lifestyle, and expected potential need for pacing for bradycardia or ventricular tachycardia termination	I	B-NR

B-NR: moderate, non-randomized; COR: class of recommendation; HCM: hypertrophic cardiomyopathy; ICD: implantable cardioverter defibrillator; LOE: level of evidence; SCD: sudden cardiac death

ICD Therapy in Patients Not Well Represented in Clinical Trials

The HRS, the American College of Cardiology, and AHA (2014) published an expert consensus statement on the use of ICD therapy for patients not included or poorly represented in ICD clinical trials.[95,] The statement presented a number of consensus-based guidelines on the use of ICDs in select patient populations.

American Heart Association

AHA (2010) issued a scientific statement, endorsed by HRS, on cardiovascular implantable electronic device infections and their management.[96,] This statement made the following recommendations on the removal of device-related infections (see Table 27).

Table 27. Guidelines on the Management of CIED Infections

Recommendation	COR	LOE
Complete device and lead removal is recommended for all patients with definite CIED infection, as evidenced by valvular and/or lead endocarditis or sepsis.	I	A
Complete device and lead removal is recommended for all patients with CIED pocket infection as evidenced by abscess formation, device erosion, skin adherence, or chronic draining sinus without clinically evident involvement of the transvenous portion of the lead system.	I	B
Complete device and lead removal is recommended for all patients with valvular endocarditis without definite involvement of the lead(s) and/or device.	I	B

Recommendation	COR	LOE
Complete device and lead removal is recommended for patients with occult staphylococcal bacteremia.	I	B

CIED: cardiovascular implantable electronic device; COR: class of recommendation; LOE: level of evidence.

Heart Rhythm Society- Arrhythmogenic Cardiomyopathy

In 2019, the HRS published a consensus statement on evaluation, risk stratification, and management of arrhythmogenic cardiomyopathy.[97,] Recommendations related to ICD risk stratification and placement decisions are shown in Table 28.

Table 28. Guidelines on Risk Stratification and ICD Decisions

Recommendation	COR[1]	LOE[2]
In individuals with ARVC with hemodynamically tolerated sustained VT, an ICD is reasonable.	IIa	B-NR
ICD implantation is reasonable for individuals with ARVC and three major, two major and two minor, or one major and four minor risk factors for ventricular arrhythmia.	IIa	B-NR
ICD implantation may be reasonable for individuals with ARVC and two major, one major and two minor, or four minor risk factors for ventricular arrhythmia.	IIb	B-NR
In individuals with ACM with LVEF 35% or lower and NYHA class II-III symptoms and an expected meaningful survival of greater than 1 year, an ICD is recommended.	I	B-R
In individuals with ACM with LVEF 35% or lower and NYHA class I symptoms and an expected meaningful survival of greater than 1 year, an ICD is reasonable.	IIa	B-R
In individuals with ACM (other than ARVC) and hemodynamically tolerated VT, an ICD is recommended.	I	B-NR
In individuals with phospholamban cardiomyopathy and LVEF <45% or NSVT, an ICD is reasonable.	IIa	B-NR
In individuals with lamin A/C ACM and two or more of the following: LVEF <45%, NSVT, male sex, an ICD is reasonable.	IIa	B-NR
In individuals with FLNC ACM and an LVEF <45%, an ICD is reasonable.	IIa	C-LD
In individuals with lamin A/C ACM and an indication for pacing, an ICD with pacing capabilities is reasonable.	IIa	C-LD

ACM: arrhythmogenic cardiomyopathy;ARVC: arrhythmogenic right ventricular cardiomyopathy;COR: Class of Recommendation;FLNC: filamin-C; ICD: Implantable cardioverter defibrillator; LOE: Level of Evidence; LVEF: left ventricular ejection fraction; NSVT: nonsustained ventricular tachycardia; NYHA: New York Heart Association; VT: ventricular tachycardia.
[1] Class I: Strong; Class IIa: Moderate; Class IIb: Weak. [2] B-R: Randomized; B-NR: nonrandomized; C-LD: limited data

Heart Rhythm Society et al- Inherited Primary Arrhythmia Syndromes

The HRS, the European Heart Rhythm Association, and the Asia-Pacific Heart Rhythm Society (2013) issued a consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes, which included recommendations on ICD use in patients with long QT syndrome, Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia, and short QT syndrome (see Table 29).[98,]

Table 29. Guidelines on the Diagnosis and Management of Inherited Primary Arrhythmia Syndromes

Recommendation	COR
Long QT syndrome	
ICD implantation is recommended for patients with a diagnosis of LQTS who are survivors of a cardiac arrest	I
ICD implantation can be useful in patients with a diagnosis of LQTS who experience recurrent syncopal events while on beta-blocker therapy	IIa
Except under special circumstances, ICD implantation is not indicated in asymptomatic LQTS patients who have not been tried on beta-blocker therapy	III[a]
Brugada syndrome	
ICD implantation is recommended in patients with a diagnosis of BrS who: • Are survivors of a cardiac arrest and/or • Have documented spontaneous sustained VT with or without syncope.	I
ICD implantation can be useful in patients with a spontaneous diagnostic type I ECG who have a history of syncope judged to be likely caused by ventricular arrhythmias.	IIa
ICD implantation may be considered in patients with a diagnosis of BrS who develop VF during programmed electrical stimulation (inducible patients).	IIb
ICD implantation is not indicated in asymptomatic BrS patients with a drug-induced type I ECG and on the basis of a family history of SCD alone.	III[a]
Catecholaminergic polymorphic ventricular tachycardia	
ICD implantation is recommended for patients with a diagnosis of CPVT who experience cardiac arrest, recurrent syncope or polymorphic/bidirectional VT despite optimal medical management, and/or left cardiac sympathetic denervation.	I
ICD as a standalone therapy is not indicated in an asymptomatic patient with a diagnosis of CPVT	III[a]
Short QT syndrome	
ICD implantation is recommended in symptomatic patients with a diagnosis of SQTS who: Are survivors of cardiac arrest and/or Have documented spontaneous VT with or without syncope.	I
ICD implantation may be considered in asymptomatic patients with a diagnosis of SQTS and a family history of sudden cardiac death.	IIb

BrS: Brugada syndrome; COR: class of recommendation; CPVT: catecholaminergic polymorphic ventricular tachycardia; ECG: electrocardiogram; ICD: implantable cardioverter defibrillator; LQTS: long QT syndrome; SCD: sudden cardiac death; SQTS: short QT syndrome; VF: ventricular fibrillation; VT: ventricular tachycardia.
a Not recommended.

ICD implantation may be considered in patients with LVEF in the range of 36%–49% and/or RV ejection fraction <40%, despite optimal medical therapy and a period of immunosuppression (if indicated).

Heart Rhythm Society - Cardiac Sarcoid

In 2014, the HRS published a consensus statement on the diagnosis and management of arrhythmias associated with cardiac sarcoiditis, including recommendations for ICD implantation in patients with cardiac sarcoid (Table 30).[30,] The writing group concluded that although there are few data specific to ICD use in patients with cardiac sarcoid, data from the major primary and

secondary prevention ICD trials were relevant to this population and recommendations from the general device guideline documents apply to this population.

Table 30. Recommendations for ICD Implantation in Patients with Cardiac Sarcoid

Recommendation	COR[1]
ICD implantation **is recommended** in patients with cardiac sarcoid and one or more of the following: • Spontaneous sustained ventricular arrhythmias, including prior cardiac arrest • LVEF <35%, despite optimal medical therapy and a period of immunosuppression (if there is active inflammation).	I
ICD implantation **can be useful** in patients with cardiac sarcoid, independent of ventricular function, and one or more of the following: • An indication for permanent pacemaker implantation; • Unexplained syncope or near-syncope, felt to be arrhythmic in etiology; • Inducible sustained ventricular arrhythmias (>30 seconds of monomorphic VT or polymorphic VT) or clinically relevant VF.*	IIa
ICD implantation **may be considered** in patients with LVEF in the range of 36%–49% and/or an RV ejection fraction <40%, despite optimal medical therapy for heart failure and a period of immunosuppression (if there is active inflammation).	IIb
ICD implantation **is not recommended** in patients with no history of syncope, normal LVEF/RV ejection fraction, no LGE on CMR, a negative EP study, and no indication for permanent pacing. However, these patients should be closely followed for deterioration in ventricular function. ICD implantation **is not recommended** in patients with one or more of the following: • Incessant ventricular arrhythmias; • Severe New York Heart Association class IV heart failure.	III

COR: Class of Recommendation; ICD: Implantable cardioverter defibrillator; LGE-CMR: late gadolinium-enhanced cardiovascular magnetic resonance; LOE: Level of Evidence; LVEF: left ventricular ejection fraction; RV: right ventricular.
[1]Class I: Strong; Class IIa: Moderate; Class IIb: Weak.

Pediatric and Congenital Electrophysiology Society and Heart Rhythm Society

The Pediatric and Congenital Electrophysiology Society and HRS (2014) issued an expert consensus statement on the recognition and management of arrhythmias in adult congenital heart disease. The statement made the following recommendations on the use of ICD therapy in adults with congenital heart disease (see Table 31).[99,]

Table 31. Guidelines on the Management of CHD

Recommendation	COR	LOE
ICD therapy is indicated in adults with CHD who are survivors of cardiac arrest due to ventricular fibrillation or hemodynamically unstable ventricular tachycardia after evaluation to define the cause of the event and exclude any completely reversible etiology.	I	B
ICD therapy is indicated in adults with CHD and spontaneous sustained ventricular tachycardia who have undergone hemodynamic and electrophysiologic evaluation.	I	B
ICD therapy is indicated in adults with CHD and a systemic left ventricular ejection fraction <35%, biventricular physiology, and NYHA class II or III symptoms.	I	B
ICD therapy is reasonable in selected adults with tetralogy of Fallot and multiple risk factors for sudden cardiac death, such as left ventricular systolic or diastolic dysfunction,	IIa	B

Recommendation	COR	LOE
nonsustained ventricular tachycardia, QRS duration >180 ms, extensive right ventricular scarring, or inducible sustained ventricular tachycardia at electrophysiologic study.		
ICD therapy may be reasonable in adults with a single or systemic right ventricular ejection fraction <35%, particularly in the presence of additional risk factors such as complex ventricular arrhythmias, unexplained syncope, NYHA functional class II or III symptoms, QRS duration >140 ms, or severe systemic AV valve regurgitation.	IIb	C
ICD therapy may be considered in adults with CHD and a systemic ventricular ejection fraction <35% in the absence of overt symptoms (NYHA class I) or other known risk factors.	Ib	C
ICD therapy may be considered in adults with CHD and syncope of unknown origin with hemodynamically significant sustained ventricular tachycardia or fibrillation inducible at electrophysiologic study.	Ib	B
ICD therapy may be considered for nonhospitalized adults with CHD awaiting heart transplantation.	Ib	C
ICD therapy may be considered for adults with syncope and moderate or complex CHD in whom there is a high clinical suspicion of ventricular arrhythmia and in whom thorough invasive and noninvasive investigations have failed to define a cause.	Ib	C
Adults with CHD and advanced pulmonary vascular disease (Eisenmenger syndrome) are generally not considered candidates for ICD therapy.	III[a]	
Endocardial leads are generally avoided in adults with CHD and intracardiac shunts. Risk assessment regarding hemodynamic circumstances, concomitant anticoagulation, shunt closure prior to endocardial lead placement, or alternative approaches for lead access should be individualized.	III[a]	

AV: arteriovenous; CHD: coronary heart disease; COR: class of recommendation; ICD: implantable cardioverter defibrillator; LOE: level of evidence; NYHA: New York Heart Association.
[a] Not recommended.

U.S. Preventive Services Task Force Recommendations

Not applicable.

Ongoing and Unpublished Clinical Trials

Some unpublished trials that may influence this review are listed in Table 32.

Table 32. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT02121158	CSP #592 - Efficacy and Safety of ICD Implantation in the Elderly	100	Aug 2021
NCT00673842[a]	Risk Estimation Following Infarction Noninvasive Evaluation - ICD Efficacy	1000	Dec 2021
NCT02845531	Implantable Cardioverter Defibrillator Versus Optimal Medical Therapy In Patients With Variant Angina Manifesting as Aborted Sudden Cardiac Death (VARIANT ICD)	140	Jun 2023

NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT01296022[a]	Randomized Trial to Study the Efficacy and Adverse Effects of the Subcutaneous and Transvenous Implantable Cardioverter Defibrillator (ICD) in Patients With a Class I or IIa Indication for ICD Without an Indication for Pacing	850	Dec 2023 (extended follow-up)
NCT01736618[a]	Subcutaneous Implantable Cardioverter Defibrillator System Post Approval Study (UNTOUCHED)	1766	Oct 2021
NCT02881255	Avoid Transvenous Leads in Appropriate Subjects (Atlas)	500	Feb 2022
NCT01085435[a]	Evaluation of Factors Impacting Clinical Outcome and Cost Effectiveness of the S-ICD (The EFFORTLESS S-ICD Registry)	994	Dec 2023
NCT02787785[a]	Multicenter Automatic Defibrillator Implantation Trial With Subcutaneous Implantable Cardioverter Defibrillator (MADIT S-ICD)	40	Dec 2023

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

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

CPT/HCPCS

33216 Insertion of a single transvenous electrode, permanent pacemaker or implantable defibrillator
33217 Insertion of 2 transvenous electrodes, permanent pacemaker or implantable defibrillator
33218 Repair of single transvenous electrode, permanent pacemaker or implantable defibrillator
33220 Repair of 2 transvenous electrodes for permanent pacemaker or implantable defibrillator
33223 Relocation of skin pocket for implantable defibrillator
33230 Insertion of implantable defibrillator pulse generator only; with existing dual leads
33231 Insertion of implantable defibrillator pulse generator only; with existing multiple leads
33240 Insertion of implantable defibrillator pulse generator only; with existing single lead
33241 Removal of implantable defibrillator pulse generator only
33243 Removal of single or dual chamber implantable defibrillator electrode(s); by thoracotomy

33244 Removal of single or dual chamber implantable defibrillator electrode(s); by transvenous extraction
33249 Insertion or replacement of permanent implantable defibrillator system, with transvenous lead(s), single or dual chamber
33262 Removal of implantable defibrillator pulse generator with replacement of implantable defibrillator pulse generator; single lead system
33263 Removal of implantable defibrillator pulse generator with replacement of implantable defibrillator pulse generator; dual lead system
33264 Removal of implantable defibrillator pulse generator with replacement of implantable defibrillator pulse generator; multiple lead system
33270 Insertion or replacement of permanent subcutaneous implantable defibrillator system, with subcutaneous electrode, including defibrillation threshold evaluation, induction of arrhythmia, evaluation of sensing for arrhythmia termination, and programming or reprogramming of sensing or therapeutic parameters, when performed
33271 Insertion of subcutaneous implantable defibrillator electrode
33272 Removal of subcutaneous implantable defibrillator electrode
33273 Repositioning of previously implanted subcutaneous implantable defibrillator electrode
93260 Programming device evaluation (in person) with iterative adjustment of the implantable device to test the function of the device and select optimal permanent programmed values with analysis, review and report by a physician or other qualified health care professional; implantable subcutaneous lead defibrillator system
93261 Interrogation device evaluation (in person) with analysis, review and report by a physician or other qualified health care professional, includes connection, recording and disconnection per patient encounter; implantable subcutaneous lead defibrillator system
93282 Programming device evaluation (in person) with iterative adjustment of the implantable device to test the function of the device and select optimal permanent programmed values with analysis, review and report by a physician or other qualified health care professional; single lead transvenous implantable defibrillator system
93283 Programming device evaluation (in person) with iterative adjustment of the implantable device to test the function of the device and select optimal permanent programmed values with analysis, review and report by a physician or other qualified health care professional; dual lead transvenous implantable defibrillator system
93284 Programming device evaluation (in person) with iterative adjustment of the implantable device to test the function of the device and select optimal permanent programmed values with analysis, review and report by a physician or other qualified health care professional; multiple lead transvenous implantable defibrillator system
93287 Peri-procedural device evaluation (in person) and programming of device system parameters before or after a surgery, procedure, or test with analysis, review and report by a physician or other qualified health care professional; single, dual, or multiple lead implantable defibrillator system
93289 Interrogation device evaluation (in person) with analysis, review and report by a physician or other qualified health care professional, includes connection, recording and disconnection per patient encounter; single, dual, or multiple lead transvenous implantable defibrillator system, including analysis of heart rhythm derived data elements

93295	Interrogation device evaluation(s) (remote), up to 90 days; single, dual, or multiple lead implantable defibrillator system with interim analysis, review(s) and report(s) by a physician or other qualified health care professional
93296	Interrogation device evaluation(s) (remote), up to 90 days; single, dual, or multiple lead pacemaker system, leadless pacemaker system, or implantable defibrillator system, remote data acquisition(s), receipt of transmissions and technician review, technical support and distribution of results
93297	Interrogation device evaluation(s), (remote) up to 30 days; implantable cardiovascular physiologic monitor system, including analysis of 1 or more recorded physiologic cardiovascular data elements from all internal and external sensors, analysis, review(s) and report(s) by a physician or other qualified health care professional
93640	Electrophysiologic evaluation of single or dual chamber pacing cardioverter-defibrillator leads including defibrillation threshold evaluation (induction of arrhythmia, evaluation of sensing and pacing for arrhythmia termination) at time of initial implantation or replacement;
93641	Electrophysiologic evaluation of single or dual chamber pacing cardioverter-defibrillator leads including defibrillation threshold evaluation (induction of arrhythmia, evaluation of sensing and pacing for arrhythmia termination) at time of initial implantation or replacement; with testing of single or dual chamber pacing cardioverter-defibrillator pulse generator
93642	Electrophysiologic evaluation of single or dual chamber transvenous pacing cardioverter-defibrillator (includes defibrillation threshold evaluation, induction of arrhythmia, evaluation of sensing and pacing for arrhythmia termination, and programming or reprogramming of sensing or therapeutic parameters)
93644	Electrophysiologic evaluation of subcutaneous implantable defibrillator (includes defibrillation threshold evaluation, induction of arrhythmia, evaluation of sensing for arrhythmia termination, and programming or reprogramming of sensing or therapeutic parameters)
C1721	Cardioverter-defibrillator, dual chamber (implantable)
C1722	Cardioverter-defibrillator, single chamber (implantable)
C1824	Generator, cardiac contractility modulation (implantable)
C1882	Cardioverter-defibrillator, other than single or dual chamber (implantable)
C1895	Lead, cardioverter-defibrillator, endocardial dual coil (implantable)
C1896	Lead, cardioverter-defibrillator, other than endocardial single or dual coil (implantable)
C1899	Lead, pacemaker/cardioverter-defibrillator combination (implantable)

ICD-10 Diagnoses

I25.5	Ischemic Cardiomyopathy
I42.1	Obstructive hypertrophic cardiomyopathy
I42.2	Other hypertrophic cardiomyopathy
I42.8	Other cardiomyopathies
I45.81	Long QT syndrome
I45.89	Other specified conduction disorders
I46.2	Cardiac arrest due to underlying cardiac condition
I46.8	Cardiac arrest due to other underlying condition

I46.9	Cardiac arrest, cause unspecified
I47.2	Ventricular tachycardia
I49.01	Ventricular fibrillation
I49.9	Cardiac arrhythmia, unspecified
Q20.0	Common arterial trunk
Q20.1	Double outlet right ventricle
Q20.2	Double outlet left ventricle
Q20.3	Discordant ventriculoarterial connection
Q20.4	Double inlet ventricle
Q20.5	Discordant atrioventricular connection
Q20.6	Isomerism of atrial appendages
Q20.8	Other congenital malformations of cardiac chambers and connections
Q20.9	Congenital malformation of cardiac chambers and connections, unspecified
Q21.0	Ventricular septal defect
Q21.1	Atrial septal defect
Q21.2	Atrioventricular septal defect
Q21.3	Tetralogy of Fallot
Q21.4	Aortopulmonary septal defect
Q21.8	Other congenital malformations of cardiac septa
Q22.0	Pulmonary valve atresia
Q22.1	Congenital pulmonary valve stenosis
Q22.2	Congenital pulmonary valve insufficiency
Q22.3	Other congenital malformations of pulmonary valve
Q22.4	Congenital tricuspid stenosis
Q22.5	Ebstein's anomaly
Q22.6	Hypoplastic right heart syndrome
Q22.8	Other congenital malformations of tricuspid valve
Q23.0	Congenital stenosis of aortic valve
Q23.1	Congenital insufficiency of aortic valve
Q23.2	Congenital mitral stenosis
Q23.3	Congenital mitral insufficiency
Q23.4	Hypoplastic left heart syndrome
Q23.8	Other congenital malformations of aortic and mitral valves
Q24.0	Dextrocardia
Q24.1	Levocardia
Q24.2	Cor triatriatum
Q24.3	Pulmonary infundibular stenosis
Q24.4	Congenital subaortic stenosis
Q24.5	Malformation of coronary vessels
Q24.6	Congenital heart block
Q24.8	Other specified congenital malformations of heart
Q24.9	Congenital malformation of heart, unspecified

REVISIONS

04-22-2011	Description section updated
	In Policy section: ▪ Clarified wording for C. Automatic External Defibrillators for Home Use From: "The use of automatic external defibrillators by lay persons is considered experimental and investigational because they have not been proven to reduce mortality

	compared to implantable cardioverter defibrillators or cardiopulmonary resuscitation by first responders. The coverage of automatic external defibrillators used by lay persons is an exclusion of the member's contract." To: "The purchase or rental of an automated external defibrillator is an exclusion of the member's contract." ▪ There is no change in the policy intent.
	In Coding section: ▪ Removed CPT code: 33222
	Rationale section added
	References updated
02-01-2012	In Policy section: ▪ In A 7 removed the word "documented" to read, "Ischemic dilated cardiomyopathy (IDCM) with NYHA Class II or III heart failure, prior myocardial infarction (MI), at least 40 days post MI, and measured left ventricular ejection fraction (LVEF) less than or equal to 35%;" ▪ In B 1 added "b. ischemic dilated cardiomyopathy; or c. non-ischemic dilated cardiomyopathy with NYHA Class II or III heart failure and left ventricular ejection fraction (LVEF) less than or equal to 35%" ▪ In B 2 removed the following indications: "a. Patients with a history of an acute myocardial infarction (MI) within the last 40 days b. Patients with drug-refractory class IV congestive heart failure (CHF) who are not candidates for heart transplantation c. Patients with a history of psychiatric disorders that interfere with the necessary care and follow-up d. Patients in whom a reversible triggering factor for VT/VF can be definitely identified, such as ventricular tachyarrhythmias in evolving acute myocardial infarction or electrolyte abnormalities e. Patients with terminal illnesses"
	In Coding section: ▪ Revised CPT nomenclature (effective 01/01/12): 33218, 33220, 33224, 33225, 33226, 33240, 33241, 33249 ▪ Added CPT codes (effective 01/01/12): 33230, 33231, 33262, 33263, 33264 ▪ Added Diagnosis codes: 411.0, 412, 414.00-414.07, 425.11, 425.18, 426.82, 745.0-745.9, 746.0-746.9
04-08-2013	Updated Description section
	In Policy section: ▪ Updated Implantable Cardioverter-Defibrillators (ICD) policy wording to the current wording from: "A. Implantable Cardioverter-Defibrillators The use of an implantable cardioverter-defibrillator is considered medically necessary for the treatment of ventricular tachyarrhythmias and for the prevention of sudden cardiac death when one of the following indications is present: 1.History of cardiac arrest due to ventricular fibrillation (VF) or ventricular tachycardia (VT) and which is not due to reversible or transient causes; or 2. Spontaneous sustained VT, in patients with structural heart disease; or 3. Spontaneous sustained VT, in patients without structural heart disease, that is not amenable to other treatments; or 4. Syncope of undetermined origin with clinically relevant, hemodynamically significant, sustained VT or VF induced at electrophysiological study when drug therapy is ineffective, not tolerated, or not preferred; or 5. Familial or inherited conditions with a high risk for life-threatening ventricular tachyarrhythmias such as long QT syndrome or hypertrophic cardiomyopathy; or

	6. Previous myocardial infarction and coronary artery disease (CAD), at least 40 days post myocardial infarction and three months post coronary artery revascularization surgery with an ejection fraction equal to or less than 35% after maximal medical therapy; or 7. Ischemic dilated cardiomyopathy (IDCM) with NYHA Class II or III heart failure, prior myocardial infarction (MI), at least 40 days post MI, and measured left ventricular ejection fraction (LVEF) less than or equal to 35%; or 8. Non-ischemic dilated cardiomyopathy (NIDCM) of greater than 9 months duration along with, NYHA Class II or III heart failure, and measured LVEF less than or equal to 35%." ▪ Added indication for Subcutaneous ICD as experimental / investigational to read, "The use of a subcutaneous ICD is considered experimental / investigational for all indications in adult and pediatric patients." ▪ Updated Wearable Cardioverter-Defibrillators policy wording to the current wording from: "B. Wearable Cardioverter Defibrillators (WCD) 1. The wearable cardioverter defibrillator is considered medically necessary for patients at high-risk of sudden cardiac arrest, who meet the following criteria: a. Patients must meet the medical necessity criteria for an implantable cardioverter defibrillator (ICD); or b. ischemic dilated cardiomyopathy; or c. non-ischemic dilated cardiomyopathy with NYHA Class II or III heart failure and left ventricular ejection fraction (LVEF) less than or equal to 35% AND d. Patients must have ONE of the following documented medical contraindications to ICD implantation: 1) Patients awaiting a heart transplantation - on waiting list and meets medical necessity criteria for heart transplantation; or 2) Patients with a previously implanted ICD that requires explantation due to infection with waiting period before ICD reinsertion; or 3) Patients with an infectious process or other temporary condition that precludes initial implantation of an ICD. 2. The wearable cardioverter defibrillator is considered not medically necessary for all other indications."
	Updated Rationale section
	In Coding section: ▪ Added CPT codes: 0319T, 0320T, 0321T, 0322T, 0323T, 0324T, 0325T, 0326T, 0327T, 0328T (effective 01-01-2013) ▪ Removed CPT codes: 33202, 33203, 33226 as these codes were determined to be not applicable to this policy. ▪ Updated nomenclature for CPT codes: 33218, 93292, 93745
	Removed Revision details from the 08-3-2010 revision.
	Updated References
01-01-2014	In Coding section: ▪ Revised nomenclature for CPT code: 33223 (Eff 01-01-2014) ▪ Added ICD-10 codes.
01-01-2015	In Coding section: ▪ Added CPT Codes: 33270, 33271, 33272, 33273, 93260, 93261, 93644 (Effective January 1, 2015) ▪ Deleted CPT Codes: 0319T, 0320T, 0321T, 0322T, 0323T, 0324T, 0325T, 0326T, 0327T, 0328T (Effective January 1, 2015)
05-01-2016	Policy title revised from "Cardioverter-Defibrillators." Policy separated into "Implantable Cardioverter Defibrillators" and "Wearable Cardioverter Defibrillators."
	Updated Description section.
	In Policy section: ▪ In Item I, removed "Implantable Cardioverter-Defibrillators (ICD)" and added "Adults."

	▪ In Item I A, removed "one of" to read "The use of the automatic implantable cardioverter defibrillator (ICD) may be considered medically necessary in adults who meet the following criteria:" ▪ Added Item I A 1. Previous numbered items are now alpha. ▪ In Item I A 1 a, removed "no" and "for" and added "New York Heart Association (NYHA) functional class II or class III symptoms" and "a". ▪ Added Item I A 1 b. ▪ In Item I A 1 d, added "(history of premature HCM-related sudden death in 1 or more first degree relatives younger than 50 years; left ventricular hypertrophy greater than 30 mm; 1 or more runs of nonsustained ventricular tachycardia at heart rates of 120 beats per minute or greater on 24-hour Holter monitoring; prior unexplained syncope inconsistent with neurocardiogenic origin)" and "by a physician experienced in the care of patients with HCM." ▪ Added Item I A 1 e. ▪ Removed previous Item I A 4. ▪ Item I A 2 includes "after reversible causes (eg, acute ischemia) have been excluded. ▪ Added Item I C. ▪ Added Section II. ▪ In Section III, revised subcutaneous ICD from experimental / investigational to medically necessary with criteria. ▪ Removed information regarding Wearable Cardioverter-Defibrillators and Automatic External Defibrillators for Home Use. ▪ Added Policy Guidelines.
	Updated Rationale section.
	Updated References section.
11-09-2016	Updated Description section.
	In Policy section: ▪ In Item I A 1 d, added "or arrhythmogenic right ventricular cardiomyopathy" and "cardiomyopathy" and removed "HCM" to read, "Hypertrophic cardiomyopathy (HCM) with 1 or more major risk factors for sudden cardiac death (history of premature HCM-related sudden death in 1 or more first degree relatives younger than 50 years; left ventricular hypertrophy greater than 30 mm; 1 or more runs of nonsustained ventricular tachycardia at heart rates of 120 beats per minute or greater on 24-hour Holter monitoring; prior unexplained syncope inconsistent with neurocardiogenic origin) and judged to be at high risk for sudden cardiac death by a physician experienced in the care of patients with cardiomyopathy." ▪ In Item II A 4, added "or arrhythmogenic right ventricular cardiomyopathy" and "cardiomyopathy" and removed "HCM" to read, "Hypertrophic cardiomyopathy (HCM) with 1 or more major risk factors for sudden cardiac death (history of premature HCM-related sudden death in 1 or more first degree relatives younger than 50 years; left ventricular hypertrophy greater than 30 mm; 1 or more runs of nonsustained ventricular tachycardia at heart rates of 120 beats per minute or greater on 24-hour Holter monitoring; prior unexplained syncope inconsistent with neurocardiogenic origin) and judged to be at high risk for sudden cardiac death by a physician experienced in the care of patients with cardiomyopathy."
	Updated Rationale section.
	In Coding section: ▪ Corrected nomenclature to CPT code 33273. ▪ Removed CPT/HCPCS codes: 00534, 33224, 33225, 93287, 93295, 93296, C1777, C1895, C1896, C1899. ▪ Removed ICD-10 codes: I24.1, I25.10, I25.110, I25.111, I25.118, I25.2, I25.710, I25.711, I25.718, I25.720, I25.721, I25.728, I25.730, I25.731, I25.738, I25.750, I25.751, I25.758, I25.760, I25.761, I25.768, I25.791, I25.798, I25.810, I25.811, I25.812, I42.0, I42.5, I47.0, I49.02.

	▪ Added ICD-10 codes: I45.89, I46.2, I46.8, I46.9.
	Updated References section.
07-11-2017	Updated Description section.
	In Policy Section: ▪ In Item III A 1 b, added "younger patient with anticipated long-term need for ICD therapy" to read, "compelling reason to preserve existing vascular access (ie, need for chronic dialysis; younger patient with anticipated long-term need for ICD therapy);" ▪ In Policy Guidelines, updates made to items 2 and 3 b.
	Updated Rationale section.
	Updated References section.
07-18-2018	Updated Description section.
	Updated Rationale section.
	In Coding section: ▪ Added HCPCS codes: C1895, C1896, C1899. ▪ Removed ICD-9 codes.
	Updated References section.
07-03-2019	Updated Description section.
	Updated Rationale section.
	In Coding section: ▪ Added CPT codes: 93287, 93295, 93296, 93297.
	Updated References section.
05-14-2021	Updated Description section
	In Policy Section: 3b Removed 2012 guidelines from the ACC, AHA, and HRS on device-based therapy of cardiac rhythm abnormalities (Epstein et al, 2013), and a report from the HRS/EHRA's Second Consensus Conference on Brugada syndrome (Antzelevitch et al, 2005). Added 2017 guidelines from ACC, AHA, and HRS on the management of heart failure (Al-Khatib et al [2017]), and a report from the HRS and EHRA's Second Consensus Conference on Brugada syndrome.
	Updated Rationale section
	Updated References section
08-02-2021	Updated Description section.
	Updated Rationale section.
	In Coding section: ▪ Added code C1824 ▪ Added ICD 10 diagnosis code I25.5
	Updated References section.

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