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# Implantable Cardioverter Defibrillators

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## Disclaimer

**Carefully check state regulations and/or the member contract.**
Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

## Coverage

**NOTE 1: This policy does not address implantable cardioverter defibrillators (ICD) combined with other pacing devices such as pacemakers for atrial fibrillation or biventricular pacemakers designed to treat heart failure. This policy addresses ICDs alone when used solely to treat individuals at risk for ventricular arrhythmias.**

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

Primary Prevention
1. Ischemic cardiomyopathy with New York Heart Association (NYHA) functional class II or III symptoms, a history of myocardial infarction (MI) at least 40 days before ICD treatment, and left ventricular ejection fraction (LVEF) of 35% or less; **OR**
2. Ischemic cardiomyopathy with NYHA functional class I symptoms, a history of MI at least 40 days before ICD treatment, and LVEF of 30% or less; **OR**

3. Nonischemic dilated cardiomyopathy and LVEF of 35% or less, after reversible causes have been excluded, and the response to optimal medical therapy has been adequately determined; **OR**
4. Hypertrophic cardiomyopathy (HCM) with 1 or more major risk factors for sudden cardiac death (history of premature HCM-related sudden death in ≥1 first-degree relatives younger than 50 years; left ventricular hypertrophy >30 mm; ≥1 runs of nonsustained ventricular tachycardia (VT) at heart rates of ≥120 beats per minute 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 individuals with HCM; **OR**
5. Diagnosis of cardiac sarcoid and considered to be at high risk for sudden cardiac death (see **NOTE 2**):
6. Diagnosis of any one of the following cardiac ion channelopathies and considered to be at high risk for sudden cardiac death (see **NOTE 3**):
   a. Congenital long QT syndrome (see **NOTE 4**);
   b. Brugada syndrome;
   c. Short QT syndrome; or
   d. Catecholaminergic polymorphic VT.

The use of the ICD **is considered experimental, investigational and/or unproven** in primary prevention individuals who:
1. Have had an acute MI (i.e., <40 days before ICD treatment); **OR**
2. Have NYHA class IV congestive heart failure (unless the individual 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 or percutaneous transluminal coronary angioplasty) or are candidates for a cardiac revascularization procedure; **OR**
4. Have noncardiac disease that would be associated with life expectancy less than 1 year.

<u>Secondary Prevention</u>
Individuals 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.

The use of the ICD for secondary prevention **is considered experimental, investigational and/or unproven** for individuals who do not meet the criteria for secondary prevention.

**Pediatrics**
The use of the ICD **may be considered medically necessary** in pediatric individuals who meet **any** of the following criteria:
1. Survivors of cardiac arrest due to VT or ventricular fibrillation (VF), after reversible causes have been excluded; **OR**
2. Long QT syndrome in individuals who are survivors of sudden cardiac arrest (in combination with beta-blockers); **OR**

3. Long QT syndrome in individuals who cannot take beta-blockers and for whom cardiac sympathetic denervation or other medications are not considered appropriate; **OR**
4. Catecholaminergic polymorphic VT in individuals who experience cardiac arrest despite maximally tolerated beta-blockers, flecainide, or cardiac sympathetic denervation; **OR**
5. Brugada syndrome in individuals who are survivors of sudden cardiac arrest or have documented spontaneous sustained VT; **OR**
6. Hypertrophic cardiomyopathy in individuals who are survivors of sudden cardiac arrest or have documented spontaneous sustained VT; **OR**
7. Arrhythmogenic cardiomyopathy in individuals who are survivors of sudden cardiac arrest or sustained VT that is not hemodynamically tolerated; **OR**
8. Nonischemic dilated cardiomyopathy in individuals who are survivors of sudden cardiac arrest or have documented spontaneous sustained VT that is not due to completely reversible causes; **OR**
9. Congenital heart disease in individuals who are survivors of sudden cardiac arrest, after reversible causes have been excluded; **OR**
10. Symptomatic, sustained VT in association with congenital heart disease in individuals who have undergone hemodynamic and electrophysiologic evaluation.

The use of the ICD **is considered experimental, investigational and/or unproven** for all other indications in pediatric individuals.

**Subcutaneous ICD**

The use of a subcutaneous ICD **may be considered medically necessary** for adult or pediatric individuals 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 no indication for antibradycardia pacing; **AND**
2. Do not have ventricular arrhythmias known or anticipated to respond to antitachycardia pacing; **AND**
3. Have a contraindication to a transvenous ICD due to 1 or more of the following:
   a. Lack of adequate vascular access;
   b. Compelling reason to preserve existing vascular access (i.e., need for chronic dialysis; younger individual 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.

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

**Extravascular Implantable Cardioverter Defibrillator**

The use of an extravascular ICD (also known as a substernal ICD) **is considered experimental, investigational and/or unproven**.

**NOTE 2: Criteria for ICD Implantation in Individuals with Cardiac Sarcoid**

Criteria for ICD placement in individuals with cardiac sarcoid derive from a 2014 consensus statement from the Heart Rhythm Society (HRS) and 2017 joint guidelines from the American Heart Association (AHA), American College of Cardiology (ACC), and HRS.

Indications for consideration of ICD placement in individuals 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; **OR**
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; **OR**
3. LVEF greater than 35%, if meaningful survival of greater than 1 year is expected; <u>and</u>
    a. Syncope or near-syncope, felt to be arrhythmic in etiology;
    b. Evidence of myocardial scar by cardiac MRI or positron emission tomographic (PET) scan; or
    c. Inducible sustained ventricular arrhythmias (>30 seconds of monomorphic VT or polymorphic VT) or clinically relevant VF; **OR**
4. An indication for permanent pacemaker implantation.

**NOTE 3: Criteria for ICD Implantation in Individuals with Cardiac Ion Channelopathies**
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.

Criteria for ICD placement in individuals 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 individuals with inherited primary arrhythmia syndromes, and a report from the HRS and EHRA's Second Consensus Conference on Brugada syndrome.

Indications for consideration for ICD placement for each cardiac ion channelopathy are as follows:

- Long QT syndrome (LQTS):
    a. Individuals with a diagnosis of LQTS who are survivors of cardiac arrest;
    b. Individuals with a diagnosis of LQTS who experience recurrent syncopal events while on beta-blocker therapy.
- Brugada syndrome (BrS):
    a. Individuals with a diagnosis of BrS who are survivors of cardiac arrest;
    b. Individuals with a diagnosis of BrS who have documented spontaneous sustained VT with or without syncope;
    c. Individuals with a spontaneous diagnostic type 1 electrocardiogram (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);

d. Individuals with a diagnosis of BrS who develop VF during programmed electrical stimulation.

- Catecholaminergic polymorphic ventricular tachycardia (CPVT):
  a. Individuals with a diagnosis of CPVT who are survivors of cardiac arrest;
  b. Individuals with a diagnosis of CPVT who experience recurrent syncope or polymorphic/bidirectional VT despite optimal medical management, and/or left cardiac sympathetic denervation.
- Short QT syndrome (SQTS):
  a. Individuals with a diagnosis of SQTS who are survivors of cardiac arrest;
  b. Individuals with a diagnosis of SQTS who are symptomatic and have documented spontaneous VT with or without syncope;
  c. Individuals with a diagnosis of SQTS who are asymptomatic or symptomatic and have a family history of sudden cardiac death.

**NOTE 4:** For congenital LQTS, individuals may have 1 or more clinical or historical findings other than those outlined above that could, alone or in combination, put them at higher risk for sudden cardiac death. They can include:
1. Individuals with a family history of sudden cardiac death due to LQTS; **OR**
2. Infants with a diagnosis of LQTS with functional 2:1 atrioventricular block; **OR**
3. Individuals with a diagnosis of LQTS in conjunction with a diagnosis of Jervell and Lange-Nielsen syndrome or Timothy syndrome; **OR**
4. Individuals 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 when considering the need for ICD placement.

## Policy Guidelines

None.

## Description

### 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 (LVEF) and prior myocardial infarction (MI); nonischemic dilated cardiomyopathy with reduced LVEF; hypertrophic cardiomyopathy and additional risk factors; congenital heart disease, particularly with recurrent syncope; and cardiac ion channelopathies.

<u>Treatment</u>
Implantable cardioverter defibrillators (ICDs) monitor a patient's heart rate, recognize ventricular fibrillation (VF) 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 (PMA). 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 MI and reduced ejection fraction.

**Regulatory Status**

Transvenous Implantable Cardioverter Defibrillators

A large number of ICDs have been approved by the FDA through the 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. (2) Many originally approved ICDs have received multiple supplemental applications. A selective summary of some currently available ICDs is provided in Table 1.

In April 2021, Medtronic issued a recall of the Evera, Viva, Brava, Claria, Amplia, Compia, and Visia ICDs and cardiac resynchronization therapy defibrillators (CRT-Ds) due to an unexpected and rapid decrease in battery life. (3) The decrease in battery life is caused by a short circuit and will cause some devices to produce a "Recommended Replacement Time" warning earlier than expected. Some devices may progress from this warning to full battery depletion within as little as 1 day. The device may stop functioning if the user does not respond to the first warning. In August 2022, Medtronic issued a recall of the Cobalt XT, Cobalt, and Crome ICDs and CRT-Ds because of risk that the devices may issue a short circuit alert and deliver a reduced energy electric shock instead of delivering a second phase of high voltage therapy. (4) The reduced energy electrical shock may fail to correct an arrhythmia or may cause an irregular heartbeat. In

July 2023, Medtronic issued a recall of the Cobalt XT, Cobalt, Crome, Visia AF, Visia AF MRI, Evera, Evera MRI, Prio, MRI, and Mirro MRI devices (along with some CRT-D devices) due to the potential for a reduced energy shock due to inappropriate activation of the short circuit protection feature. (5) The FDA identified all 3 of these events as Class I recalls, the most serious type of recall, indicating a situation in which use of these devices may cause serious injuries or death.

Subcutaneous ICDs

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. The 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. (6)

Extravascular Implantable Cardioverter Defibrillators

In 2023, the Aurora EV-ICD™ MRI SureScan device was approved by the FDA for patients who are at risk of life-threatening ventricular arrhythmias and have not had a prior sternotomy and do not need pacing. This was the first extravascular ICD to be approved in the United States. Extravascular ICD leads are placed in the anterior mediastinum rather than inside the heart or veins.

**Table 1. ICDs with FDA Approval**

| Device | Manufacturer | Original PMA Approval Date |
|---|---|---|
| **Transvenous** | | |
| Ellipse™/Fortify Assura™ Family (originally: Cadence Tiered Therapy Defibrillation System) | St. Jude Medical | July 1993 |
| Current® Plus ICD (originally: Cadence Tiered Therapy Defibrillation System) | St. Jude Medical | July 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 | Sept. 2012 |
| **Extravascular** | | |
| Aurora EV-ICD | Medtronic | Oct 2023 |

FDA: Food and Drug Administration; ICDs: implantable cardioverter defibrillators; PMA: premarket application.

**NOTE 5:** ICDs may be combined with other pacing devices, such as pacemakers for atrial fibrillation, or biventricular pacemakers designed to treat heart failure. This medical policy document addresses ICDs alone when used solely to treat individuals at risk for ventricular arrhythmias.

## Rationale

This medical policy was created in 1990 and has been updated regularly with searches of the PubMed database. The most recent literature update was performed through April 1, 2024.

Medical policies 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 (QOL), 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 transvenous implantable cardioverter defibrillators (T-ICD) placement is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with a high-risk of sudden cardiac death (SCD) due to ischemic or non-ischemic cardiomyopathy (NICM), inherited cardiac ion channelopathy, or cardiac sarcoid.

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

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

*Interventions*
The therapy being considered is T-ICD placement. An implantable cardioverter defibrillator (ICD) is a device designed to monitor a patient's heart rate, recognize ventricular fibrillation (VF) or ventricular tachycardia (VT), and deliver an electric shock to terminate these arrhythmias to reduce the risk of sudden death.

*Comparators*
Comparators of interest include medical management without ICD placement. Guideline-based medical management for ischemic cardiovascular disease including antihypertensive therapy and antiarrhythmic medications. Medical management for cardiac sarcoid includes steroid therapy.

*Outcomes*
The general outcomes of interest are overall survival (OS), morbid events, QOL, treatment-related mortality, and treatment-related morbidity. Table 2 describes outcomes of interest related to quality of life and treatment-related morbidity for individuals at high risk of SCD due to ischemic or non-ischemic cardiomyopathy.

**Table 2. Outcomes of Interest for Individuals at High Risk of Sudden Cardiac Death Due to Ischemic or Non-ischemic Cardiomyopathy in Adulthood**

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

<u>Study Selection Criteria</u>
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.

**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.

<u>Ischemic Cardiomyopathy and NIDCM</u>

*Randomized Controlled Trials*

At least 14 RCTs of ICDs for primary prevention have been conducted. Six 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);
- Sudden Cardiac Death in Heart Failure (SCD HeFT) trial; and
- Defibrillator After Primary Angioplasty (DAPA) 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 lCDs in Patients with Non-Ischemic Systolic Heart Failure on Mortality (DANISH).

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

Most trials for both ischemic cardiomyopathy and NICM 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 NICM in stable condition who were almost all receiving beta-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) (7) | • LVEF ≤35%<br>• Asymptomatic unsustained VT<br>• MI ≥3 wk prior<br>• Inducible VT<br>• NYHA class I-III | • ICD<br>• Standard therapy | • 95<br>• 101 | 27 mo (trial stopped early by DSMB) | 0.46 | 0.26 to 0.82 |
| MADIT II (2002) (8) | • LVEF ≤30%<br>• No history of VT<br>• MI ≥1 mo prior<br>• NYHA class I-III | • ICD<br>• Standard therapy | • 742<br>• 490 | 20 mo Trial (stopped early by DSMB) | 0.69 | 0.51 to 0.93 |
| CABG Patch (1997) (9) | • Scheduled for CABG<br>• LVEF ≤35%<br>• No sustained VT or VF<br>• Signal-averaged ECG abnormalities<br>• 82% had prior MI, time since MI not reported | • ICD during CABG<br>• No ICD | • 446<br>• 454 | 32 mo | 1.07 | 0.81 to 1.42 |
| MUSTT (1999) (10) | • LVEF ≤40%<br>• Asymptomatic unsustained VT<br>• Inducible VT<br>• MI ≥4 d prior (median, »3 y prior)<br>• No sustained VT or VF | • EPS-guided therapy (AAD with or without ICD (202 got ICD)<br>• Standard therapy | • 351<br>• 353 | 39 mo | 5-y outcomes[b]:<br>• EPS-guided vs standard therapy: 0.80<br>• ICD vs AAD alone: 0.42 | 0.64 to 1.01<br><br>0.29 to 0.61 |
| SCD HeFT (2005) (11) | • LVEF ≤35%<br>• NYHA class II-III | Ischemic patients: | • 431<br>• 426 | 45 mo | ICD vs. placebo | 0.60 to 1.04 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | • 52% received ICM<br>• Treated with ACE inhibitors and beta-blockers | • ICD<br>• Amiodarone<br>• Placebo | • 453 | | • Ischemic: 0.79[a]<br>• Overall: 0.77[a] | 0.62 to 0.96 |
| DAPA (2020) (12) | • LVEF <30% within 4 days post-STEMI<br>• Primary VF<br>• Killip class ≥2<br>• TIMI flow <3 after PCI | • ICD<br>• Standard therapy | • 131<br>• 135 | 3 years in 89% of patients | • 3-y outcomes:<br>• ICD vs standard therapy: 0.37<br>• 9-y outcomes:<br>• ICD vs standard therapy: 0.58 | 0.15 to 0.95<br><br>0.37 to 0.91 |
| **ICM with Recent MI** | | | | | | |
| DINAMIT (2004) (13) | • LVEF ≤35%<br>• NYHA class I-III<br>• MI in preceding 6-40 d (mean, 18 d)<br>• No sustained VT or VF for >48 h after index MI<br>• Reduced HR variability or elevated resting HR | • ICD<br>• Standard therapy | • 332<br>• 342 | 30 mo | 1.08 | 0.76 to 1.55 |
| IRIS (2009) (14) | • MI in preceding 5 to 31 d<br>• At least 1 of the following:<br>a. LVEF ≤40% and resting HR ≥90 bpm or unsustained VT | • ICD<br>• Standard therapy | • 445<br>• 453 | 37 mo | 1.04 | 0.81 to 1.35 |
| BEST-ICD (2005) (15) | • LVEF ≤35%<br>• NYHA class I-III<br>• No unsustained VT or sustained ventricular arrhythmias (except primary VF)<br>• MI in preceding 5 to 30 d<br>• At least 1 other risk factor | • EPS-guided therapy (24 got ICD)<br>• Standard therapy | • 79<br>• 59 | 540 d | 1-year mortality[d]<br>• EPS-guided therapy: 14%<br>• Conven-tional therapy: 18%<br>2-y mortality[d]<br>• EPS-guided | |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | therapy: 20%<br>• Conventional therapy: 29.5% | |
| **Nonischemic cardiomyopathy** | | | | | | |
| DEFINITE (2004) (16) | • LVEF ≤35%<br>• NYHA class II-IV | • ICD and medical therapy<br>• Medical therapy alone | • 229<br>• 229 | 29 mo | 0.65 (0.40 to 1.06) | |
| SCD HeFT (2005) (11) | • LVEF ≤35%<br>• NYHA class II-III<br>• 48% with non-ICM<br>• Treated with ACE inhibitor and beta-blocker | Nonischemic patients:<br>• ICD<br>• Amiodarone<br>• Placebo | • 398<br>• 419<br>• 394 | 45 mo | • ICD vs. placebo<br>• Non-ischemic: 0.73[a]<br>• Overall: 0.77[a] | • 0.50 to 1.07<br>• 0.62 to 0.96 |
| COMPANION (2004) (17) | • LVEF ≤35%<br>• NYHA class III-IV<br>• DCM | Nonischemic patients:<br>• CRT-D<br>• Medical therapy<br>• CRT | • 270<br>• 127<br>• 285 | 16 mo | • CRT-D vs medical therapy<br>• Non-ischemic: 0.50<br>• Overall: 0.64 | • 0.29 to 0.88<br>• 0.48 to 0.86 |
| AMIOVIRT (2003) (18) | • LVEF ≤35%<br>• NYHA class I-III<br>• DCM<br>• Asymptomatic unsustained VT | • ICD<br>• Amiodarone | • 51<br>• 52 | 2 years | 1-year survival[d]<br>• ICD: 96%<br>• Amio-darone: 90%<br>2-year survival[d]<br>• ICD: 88%<br>• Amio-darone: 87% | |
| CAT (2002) (19) | • LVEF ≤30%<br>• NYHA class II-III<br>• No symptomatic VT, VF, or bradycardia<br>• Recent-onset DCM | • ICD<br>• Control | • 50<br>• 54 | 23 mo (trial stopped early due to low event rates) | • ICD: 4 deaths (8%)[d]<br>• Control: 2 deaths (3.7%) | |
| DANISH (2016) (20) | • LVEF ≤35%<br>• NYHA class II-IV<br>• 58% received CRT | • ICD and medical therapy | • 556<br>• 560 | 5.6 years | 0.87 | 0.68 to 1.12 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | • Almost all patients on ACE inhibitors or beta-blockers;<br>o 60% treated with mineralo-corticoid-receptor antagonist | • Medical therapy | | | | |

AAD: antiarrhythmic drugs ; ACE: angiotensin-converting enzyme; CABG: coronary artery bypass grafting; Cl: confidence interval; CRT: cardiac resynchronization therapy; CRT-D: cardiac resynchronization therapy implantable cardioverter defibrillator; d: day; DCM: dilated cardiomyopathy; DSMB: Data Safety Monitoring Board; ECG: electrocardiogram; EPS: electrophysiologic study; HR: heart rate; ICD: implantable cardioverter defibrillator; ICM: ischemic cardiomyopathy; mo: month; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NYHA: New York Heart Association; PCI: percutaneous coronary intervention; RCT: randomized controlled trial; STEMI: ST-elevation myocardial infarction; TIMI Thrombolysis in Myocardial Infarction; VF: ventricular fibrillation; VT: ventricular tachycardia; wk: week; yr: year.

[a] 97.5% CI.

[b] Relative risk.

[c] Median.

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

*Systematic Reviews*

Characteristics and results of systematic reviews of primary prevention ICD trials are described in Tables 4 and 5. 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. (21) The COMPANION, DEFINITE, MADIT, MADIT II, SCD HeFT, AMIOVIRT, and CAT trials were included, representing 6,134 patients for the direct ICD comparisons and 12,638 patients overall. Jaiswal et al. (2024) conducted a meta-analysis of 13 RCTs in patients with both ICM and NICM (including all RCTs listed in Table 3 except BEST-ICD), which found that all-cause mortality and SCD were significantly lower with ICD therapy compared to standard therapy. (22) These outcomes were significant when patients with ICM and NICM were analyzed separately, as well as together.

Subsequent systematic reviews and meta-analyses of ICD trials in NICM incorporated the 2016 DANISH trial results. (23-27) Two reviews published in 2017 included the CAT, AMIOVIRT, DEFINITE, SCD HeFT, COMPANION, and DANISH trials; one review published in 2021 included the CAT, AMIOVIRT, DEFINITE, and DANISH trials; other reviews included all but the COMPANION trial. The majority of the reviews concluded that there was a statistically significant overall reduction in mortality for ICD vs 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. (28) 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 (OR) 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 years and older, and for men. (21) 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 |
|---|---|---|---|---|---|---|
| Jaiswal et al. (2020) (22) | 1996-2020 | 13 | Patients with ICM or NICM who received ICD | 7857 | RCT | Mean 3.1 years |
| Woods et al. (2015) (21) | 1990-2010 | 13 | Patients with heart failure who received ICD | 12,638 (17 to 2,521) | RCT | NR |
| Earley et al. (2014) (28) | 1996-2010 | 14 | Adults eligible to receive an ICD for primary prevention of SCD | NR | RCT, Nonrandomized comparative studies | NR |

ICD: implantable cardioverter defibrillator; ICM: ischemic cardiomyopathy; NICM: non-ischemic cardiomyopathy; 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 |
|---|---|
| **Jaiswal et al. (2020) (22)** | **Estimated Effect of ICD on All-Cause Mortality Compared with MT** |

| | |
|---|---|
| Overall population | 0.69 (95% CI, 0.55 to 0.87) |
| ICM | 0.66 (95% CI, 0.45 to 0.96) |
| NICM | 0.75 (95% CI, 0.62 to 0.89) |
| **Woods et al. (2015) (21)** | **Estimated Effect of ICD on Mortality Compared with MT** |
| | 0.71 (95% CI, 0.63 to 0.80) |
| **Earley et al. (2014) (28)** | **Mortality Benefit of Variables (ROR)** |
| Sex | 0.95 (95% CI, 0.75 to 1.27) |
| Age | 0.93 (95% CI, 0.73 to 1.20) |
| QRS Interval | 1.13 (95% CI, 0.82 to 1.54) |

CI: confidence interval; ICD: implantable cardioverter defibrillator; ICM: ischemic cardiomyopathy; NICM: non-ischemic cardiomyopathy; 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 1,514 patients implanted with Medtronic ICDs equipped with remote monitoring who were enrolled between 2012 and 2013. (29) The mean age of enrollees 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.

<u>High-Risk HCM</u>

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. (30) 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. (31) Over a mean follow-up of 5.4 years, appropriate ICD discharges in response to VT or 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.

<u>Inherited Cardiac Ion Channelopathy</u>

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.

Medeiros et al. (2023) conducted a systematic review of 36 studies in 2,750 patients with inherited arrhythmia syndromes (LQTS, short QT syndrome, BrS, CPVT, and early repolarization syndrome) who received ICD therapy. (32) Mean follow-up in the included studies was 69 months. Appropriate and inappropriate therapy occurred in 21% and 20% of patients overall, respectively. Appropriate therapy was more common than inappropriate therapy in the setting of CPVT, early repolarization, and LQTS. Inappropriate therapy was more common than appropriate therapy in patients with BrS and short QT syndrome. Inappropriate therapy consisted of SVT in 44% of cases, oversensing or device malfunction in 35% of cases, and other mechanisms in 21% of cases. Complications of ICD therapy were prevalent (22%), most commonly lead malfunction (46% overall) and infection (13% overall). This analysis is limited by inclusion of observational studies and incomplete information about the type of ICD device used.

*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. (33) 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=0.008), QT corrected duration greater than 500 ms (p<0.001), non-*LQT3* genotype (p=0.02), documented syncope (p=0.05), documented torsades de pointes (p=0.003), and a negative sudden family death history (p<0.001). 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. (34) 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 (ECG) 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 ECG findings who received an ICD at a single institution and were followed for at least 6 months. (35) 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. (36) 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=0.027) and nonsustained VT during follow-up (HR=6.73; 95% CI, 1.27 to 35.7; p=0.025).

*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. (37) The indication for ICD therapy was syncope despite maximal beta-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

Sarcoidosis is a systemic granulomatous disease of unknown etiology, with a worldwide prevalence of about 4.7 to 64 in 100,000. (38) The annual incidence of sarcoidosis in the United States has been estimated at 10.9 per 100,000 in White individuals and 35.5 per 100,000 in Black individuals. Cardiac involvement occurs in about 5% of systemic sarcoidosis 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. (39)

Mantini et al. (2012) published a review on the diagnosis and management of cardiac sarcoid, including a treatment algorithm. (40) 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 patients with cardiac sarcoid with electrical instability and help to determine who should get ICD.

Subsection Summary: T-ICD for Primary Prevention in Adults

*Ischemic Cardiomyopathy and NIDCM*

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.

*HCM*

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 T-ICDs 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 studies are considered adequate evidence for the use of T-ICDs 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 sarcoidosis), 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. (41) The 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. Defibrillator 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. (42) 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 to 30 years). (43) 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 of 6 and 21 years, who were treated with an ICD device. (44) 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.

Subsection 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 individuals 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 policy.

*Populations*
The relevant population of interest is individuals with life-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 VF or VT, and deliver an electric shock to terminate these arrhythmias to reduce the risk of sudden death.

*Comparators*
Comparators of interest include medical management without ICD placement.

*Outcomes*
The general outcomes of interest are OS, morbid events, QOL, 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.

**Secondary Prevention in Adults**
At least five 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 (45) (n=1016); Cardiac Arrest Survival in Hamburg (CASH) trial (46) (n=288); Canadian Implantable Defibrillator Study (CIDS) (47) (n=659); Defibrillator Versus Beta-Blockers for Unexplained Death in Thailand (DEBUT) trial (48) (n=66; pilot, n=20; main study, n=46); and Wever et al. (1995) (49) (n=60). The trials are shown in Table 6. The 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. (50) The mortality analysis included 2,023 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. (51) 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. (52, 53)

**Table 6. RCTs of ICDs for Secondary Prevention**

| Trials | Participants | Treatment Groups | | Mortality Results | |
|---|---|---|---|---|---|
| | | **Group** | **N** | **RR** | **95% CI** |
| AVID (1997) (45) | Patients resuscitated from near-fatal VT/VF, SVT with syncope, or SVT with LVEF ≤ 40% and symptoms | • ICD<br>• AAD | • 507<br>• 509 | 0.66 | 0.51 to 0.85 |
| CASH (2000) (46) | Patients resuscitated from cardiac arrest due to sustained ventricular arrhythmia | • ICD<br>• Amiodarone<br>• Metoprolol | • 99<br>• 92<br>• 97 | 0.82 | 0.60 to 1.11 |
| CIDS (2000) (47) | Patients with VF, out-of-hospital cardiac arrest requiring defibrillation, VT with syncope, VT with rate ≥ 150/min causing presyncope or angina in patients with LVEF ≤ 35% or syncope with inducible VT | • ICD<br>• Amiodarone | • 328<br>• 331 | 0.85 | 0.67 to 1.10 |
| Wever et al. (1995) (49) | Patients with previous MI and resuscitated cardiac arrest due to VT or VF and inducible VT | • ICD<br>• AAD | • 29<br>• 31 | 0.39 | 0.14 to 1.08 |
| DEBUT (2003) (48) | Patients with 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:<br>• ICD<br>• Beta-blocker therapy<br><br>Main trial:<br>• ICD<br>• beta-blocker therapy | <br>• 10<br>• 10<br><br>• 37<br>• 29 | • RR not calculable (DSMB stopped trial early due to efficacy of ICD)<br>• 7 deaths in beta-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. (54) A cohort of 6,996 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, 1,442 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.

Subsection 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).

Subsection 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 T-ICDs**

Systematic Reviews: Mixed Adverse Events

Characteristics and results of systematic reviews of adverse events associated with T-ICDs are described in Tables 7 and 8. Persson et al. (2014) conducted a systematic review of adverse events following ICD placement. (55) In-hospital serious adverse event rates ranged from 1.2% to 1.4%, most frequently pneumothorax (0.4% to 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. (56) 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<0.01). The overall complication rate was similar to that reported by Kirkfeldt 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%] of 5918 patients with at least 1 complication). (57)

Van Rees et al. (2011) reported on results of a systematic review of RCTs assessing implant-related complications of ICDs and cardiac resynchronization therapy (CRT) devices. (58) 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. (59) Reviewers included 63 cohort studies with a total of 4,916 patients (710 [10%] with arrhythmogenic right VT; 1,037 [21%] with BrS; 28 [0.6%] with CPVT; 2,466 [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 et al. (2014) (55) | 2005-2012 | • 53 trials;<br>• 35 cohorts | Patients receiving ICD placement | NR | Cohort studies | NR |
| Ezzat et al. (2015) (56) | 2001-2011 | 18 | Patients receiving ICD placement | 6,796 (16 to 1,530) | RCTs | NR |
| Olde Nordkamp et al. (2016) (59) | 1997-2014 | 63 | Patients with inherited arrhythmia syndromes receiving ICD placement | 4,916 (NR) | Cohort studies | 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 et al. (2014) (55)** | | |
| Range | 1.2% to 1.4%[1] | • Device-related: <0.1% to 6.4%<br>• Lead-related: <0.1% to 3.9%<br>• Infection: 0.2% to 3.7%<br>• Inappropriate shock: 3% to 21% |
| **Ezzat et al. (2015) (56)** | 9.1 (95% CI, 6.4% to 12.6%) | • Access-related: 2.1% (95% CI, 1.3% to 3.3%)<br>• Lead-related: 5.8% (95% CI, 3.3% to 9.8%)<br>• Generator-related: 2.7% (95% CI, 1.3% to 5.7%)<br>• Infection: 1.5% (95% CI, 0.8% to 2.6%) |
| **Olde Nordkamp et al. (2016) (59)** | 22% (4.4% per year; 95% CI, 3.6% to 5.2%; p<0.001) | • Lead malfunction: 10.3%<br>• Infection: 3.0% (0.53% per year)<br>• Inappropriate shock: 20% (4.7% per year; 95% CI, 4.2% to 5.3%; p<0.001) |

CI: confidence interval; T-ICD: transvenous implantable cardioverter defibrillator.
[1]Only 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.

<u>Systematic Review: Specific Complications</u>

*Lead Failure*

The failure of leads in specific ICD devices led the U.S. Food and Drug Administration (FDA) to require St. Jude Medical to conduct three-year post-market surveillance studies to address concerns related to premature insulation failure and important questions related to follow-up of affected patients. (60) 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 FDA's Manufacturers and User Defined Experience database. (61)

Providencia et al. (2015) reported on a meta-analysis of 17 observational studies evaluating the performance of 49,871 leads (5,538 Durata, 10,605 Endotak Reliance, 16,119 Sprint Quattro, 11,709 Sprint Fidelis, 5,900 Riata). (62) 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 non-recalled leads (Endotak Reliance, Durata, Sprint Quattro).

Birnie et al. (2012) reported on clinical predictors of failure for 3,169 Sprint Fidelis leads implanted from 2003 to 2007 at 11 centers participating in the Canadian Heart Rhythm Society study. (63) 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=0.005), 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<0.001). (64)

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 1,031 patients without a planned transvenous lead replacement (cohort 1) and 713 with a planned transvenous lead replacement (cohort 2). (65) 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. (66) 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. (67) Of 226,764 patients treated with an ICD between 2006 and 2008, lead dislodgement occurred in 2,628 (1.2%). Factors associated with lead dislodgement were New York Heart Association (NYHA) class IV heart failure, AF or atrial flutter, a combined ICD and CRT device, and having the procedure performed by a non-electrophysiologist. 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. (68) 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<0.001).

*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. (69) 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. (70) Twenty-four of 2,417 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. (71) On multivariate analysis, the presence of epicardial leads (odds ratio [OR]=9.7; p=0.03) and postoperative complications at the insertion site (OR=27.2, p<0.001) were significant risk factors for early infection. For late-onset infections, hospitalization for more than 3 days (OR=33.1, p<0.001 for 2 days vs. 1 day) and chronic obstructive pulmonary disease (OR=9.8, p=0.02) were significant risk factors.

Borleffs et al. (2010) also reported on complications after ICD replacement for pocket-related complications, including infection or hematoma in a single-center study. (72) Of 3,161 ICDs included, 145 surgical re-interventions were required for 122 ICDs in 114 patients. Ninety-five (66%) re-interventions were due to infection, and the remaining 50 (34%) were due to other causes. Compared with first-implanted ICDs, the occurrence of surgical re-intervention 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 QOL 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=0.02). (73)

Tan et al. (2014) conducted a systematic review to identify outcomes and adverse events associated with ICDs with built-in therapy-reduction programming. (74) Six randomized trials and 2 nonrandomized cohort studies (total N=7,687 patients) were included (3,598 with conventional ICDs, 4,089 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<0.001). 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<0.001).

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. (75) 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=0.003 for noninferiority).

Auricchio et al. (2015) assessed data from the PainFree SST trial, specifically newer ICD programming strategies for reducing inappropriate shocks. (76) A total of 2,790 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. (77) Of 3,340 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<0.01).

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. (78) The 13 subjects undergoing ICD placement alone had a median increase in high-sensitivity troponin T level of 95% (p=0.005), while the 13 undergoing implantation and testing had a median increase of 161% (p=0.005). Those undergoing testing alone demonstrated no significant change in high-sensitivity troponin T levels.

**SUBCUTANEOUS IMPLANTABLE CARDIOVERTER DEFIBRILLATORS IN INDIVIDUALS WITH A CONTRAINDICATION TO A TRANSVENOUS IMPLANTABLE CARDIOVERTER DEFIBRILLATOR**

Clinical Context and Therapy Purpose

The purpose of subcutaneous implantable cardioverter defibrillator (S-ICD) placement in individuals 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 following PICO was used to select literature to inform this policy.

*Populations*

The relevant population of interest is individuals 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:

- Individuals at high risk of infection, inadequate venous access, and any individual without a pacing indication.
- Younger individuals due to the expected longevity of the implanted leads and a desire to avoid chronic transvenous leads (e.g., individuals with HCM, congenital cardiomyopathies, or inherited channelopathies).
- Individuals at high risk for bacteremia, such as individuals on hemodialysis or with chronic indwelling endovascular catheters.
- Individuals with challenging vascular access or prior complications with T-ICDs.

*Interventions*

The therapy being considered is S-ICD. An ICD is a device designed to monitor an individual's heart rate, recognize VF or VT, and deliver an electric shock to terminate these arrhythmias to reduce the risk of sudden death. A S-ICD, which lacks transvenous leads, is intended to reduce lead-related complications. The S-ICD is intended for individuals 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 individuals with limited vascular access (including individuals 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.

*Comparators*

The comparator of interest is medical management without ICD placement.

*Outcomes*

The general outcomes of interest are OS, morbid events, QOL, treatment-related mortality, and treatment-related morbidity. Table 9 describes outcomes of interest related to quality of life and treatment-related morbidity for individuals who need an ICD and have a contraindication to a T-ICD.

**Table 9. Outcomes of Interest for Individuals Who Need an Implantable Cardioverter Defibrillator (ICD) and Have a Contraindication to a Transvenous ICD**

| Outcomes | Details | Timing |
|---|---|---|
| Quality of life | Can be assessed by patient reported data such as surveys and questionnaires | 1 week to 5 years |
| Treatment-related mortality | Can be assessed by 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.

Randomized Trials

Healey et al. (2022) published 2.5 year interim results of the randomized, multicenter Avoid Transvenous Leads in Appropriate Subjects (ATLAS S-ICD) trial. (79) This trial included 544 individuals (141 female) with a primary or secondary prevention indication for an ICD who were younger than 60 years, had a cardiogenetic phenotype, or had prespecified risk factors for lead complications. Of those, 503 were randomized to S-ICD (n=251) or T-ICD (n=252). The mean age of the included patients was 49 years. The primary outcome focused on perioperative complications that were lead-related. Within 6 months of implantation, perioperative, lead-related complications occurred in 1 patient (0.4%) with an S-ICD and in 12 patients (4.8%) with T-ICD (risk difference, -4.4%; 95% CI, -6.9 to -1.9; p=.001). Overall, complications between groups were similar at 6 months, including device-related infection requiring surgery (S-ICD, 11 patients vs. T-ICD, 14 patients; risk difference, -1.2; 95% CI, -2.4 to 0.1). More patients in the S-ICD group experienced ICD site pain on the day of implant (p<.001) and 1 month later (p=.035) compared to T-ICD patients. There were no differences in pain scores at 6 months. After a follow-up of 2.5 years, there was a trend for more inappropriate shocks with S-ICD (S-ICD, 16 patients vs. T-ICD, 7 patients; HR, 2.37; 95% CI, 0.98 to 5.77), but no increase in failed appropriate ICD shocks (HR, 0.61; 95% CI, 0.15 to 2.57); however, this trial was not powered to detect differences in clinical shock outcomes. Although the ATLAS trial found a decreased risk of lead-related perioperative complications, it was underpowered to detect differences in clinical shock outcomes; extended follow-up is ongoing.

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, the pivotal trial submitted to the FDA for the investigational device exemption, and other noncomparative 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 NYHA II/III heart failure or coronary artery disease. (80) 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 (PAS) and 18-month data from the UNTOUCHED study have been published; these studies are ongoing. The S-ICD System PAS is a nonrandomized, standard-of-care registry in the United States that has prospectively enrolled and followed S-ICD recipients. (81) 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. Gold et al. (2022) reported on the 3-year post implantation follow-up data of the S-ICD PAS. (82) Within 3 years, infection was observed in 55 patients (3.3%) with 69% of infections occurring within 90 days of implantation and the majority (92.7%) within 1 year of implantation. No patient included in the registry had more than 1 infection and no infections occurred after 2 years in the cohort. The annual post-infection mortality rate was 0.6%. Based on their findings, the authors developed a risk score for likelihood of developing an infection, with diabetes, age ≥55 years, previous ICD implant, or LVEF ≤30% all identified as contributing risk to S-ICD-related infection. This risk score has not been externally validated. The S-ICD PAS study has been completed (NCT01736618) but 5-year results have yet to be published. 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) (81)<br>S-ICD PAS<br>NCT01736618 | U.S. | 1637 | 1y | • Complication-free rate at 1 y<br>• Appropriate shock rate at 1 y<br>• Inappropriate shocks at 1 y<br>• Death at 1 y | • 92.5%<br>• 5.3%<br>• 6.5%<br>• 5.4% |
| Gold et al. (2021) (80)<br>UNTOUCHED | U.S., Canada, Europe | 1111 | 18 months | • Inappropriate shock-free rate at 18 months<br>• Appropriate shock-free rate at 18 months<br>• Complication-free rate at 18 months<br>• Overall survival rate at 18 months | • 94.8%<br>• 94.3%<br>• 92.7%<br>• 94.9% |
| Lambiase et al. (2014) (83); Olde Nordkamp et al. (2015) (84); Boersma et al. | 10 European countries | • 985<br>• 928<br>• 697<br>• 498<br>• 300<br>• 82 | • 3.1 y<br>• 1 y<br>• 2 y<br>• 3 y<br>• 4 y<br>• 5 y | • Complication rates by 360 d<br>• Inappropriate shocks by 360 d<br>• Complication rates through follow-up | • 8.4%<br>• 8.1%<br>• 11.7%<br>• 11.7%<br>• 13.5% |

| | | | | | |
|---|---|---|---|---|---|
| (2017) (85): EFFORTLESS S-ICD Registry | | | | • Inappropriate shocks through follow-up<br>• Appropriate shocks through follow-up | |
| Weiss et al. (2013) (86) IDE study | U.S., U.K., New Zealand, Netherlands | 330 | 11 mo | • Implanted successfully<br>• Complication-free at 180 d<br>• Inappropriate shocks<br>• Episodes of discrete spontaneous VT or VF, all successfully converted | • 95%<br>• 99%<br>• 13%<br>• 38 |
| Burke et al. (2015) (81); Boersma et al. (2016) (87); Lambiase et al. (2016) (88) EFFORTLESS and IDE studies | Multiple European countries, U.S., New Zealand | 882 | 651 d | • Complications within 3 y<br>• Infections requiring device removal or revision<br>• Annual mortality rate<br>• 2-y cumulative mortality<br>• Incidence of therapy for VT or VF:<br>  ○ 1 year<br>  ○ 2 years<br>  ○ 3 years<br>• Incidence of inappropriate shock at 3 y | • 11%<br>• 1.7%<br>• 1.6%<br>• 3.2%<br>• 5.3%<br>• 7.9%<br>• 10.5%<br>• 13.1% |
| Bardy et al. (2010) (89); Theuns et al. (2015) (90) | Europe, New Zealand | 55 | 5.8 y | • Devices replaced<br>• Devices explanted<br>• Replaced with T-ICD<br>• Shocks recorded in 16 (29%) patients | • 26 (47%)<br>• 5 (9%)<br>• 4 (7%)<br>• 119 |
| Olde Nordkamp et al. (2012) (91) | Netherlands | 118 | 18 mo | • All device-related complications<br>• Infections<br>• Dislodgements of device/leads<br>• Skin erosion<br>• Battery failure<br>• Replaced with T-ICD<br>• Appropriate shocks experienced in 8 patients | • 14%<br>• 5.9%<br>• 3.3%<br>• 1.7%<br>• 1.7%<br>• 1 (0.8%)<br>• 45<br>• 33<br>• 2 |

| | | | | | |
|---|---|---|---|---|---|
| | | | | • Total inappropriate shocks delivered to 15 (13%) patients<br>• Deaths (cancer, progressive heart failure) | |

d: day(s); FU: follow-up; mo: month(s); S-ICD: subcutaneous implantable cardioverter defibrillator; T-ICD: transvenous implantable cardioverter defibrillator; U.S.: United States; VF: ventricular fibrillation; VT: ventricular tachycardia; y: year(s).

Section Summary: Subcutaneous-Implantable Cardioverter Defibrillators in Individuals with a Contraindication to a Transvenous Implantable Cardioverter Defibrillator
An RCT found that S-ICD significantly decreased the risk of lead-related perioperative complications compared to T-ICD. However, this study was not powered to detect differences in the rates of failed shocks or inappropriate shocks and an extension study is ongoing. 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 studies suggest S-ICDs in patients with contraindication to T-ICD are likely improvements over medical management alone.

**SUBCUTANEOUS IMPLANTABLE CARDIOVERTER DEFIBRILLATORS IN INDIVIDUALS WITH NO CONTRAINDICATION TO A TRANSVENOUS IMPLANTABLE CARDIOVERTER DEFIBRILLATOR**
Clinical Context and Therapy Purpose
The purpose of S-ICD placement in individuals 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 following PICO was used to select literature to inform this policy.

*Populations*
The population of interest is individuals 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:
- Individuals at high risk of infection, inadequate venous access, and any individual without a pacing indication.
- Younger individuals due to the expected longevity of the implanted leads and a desire to avoid chronic transvenous leads (e.g., individuals with HCM, congenital cardiomyopathies, or inherited channelopathies).
- Individuals at high risk for bacteremia, such as individuals on hemodialysis or with chronic indwelling endovascular catheters.
- Individuals with challenging vascular access or prior complications with T-ICDs.

*Interventions*
The therapy being considered is S-ICD. An ICD is a device designed to monitor an individual's heart rate, recognize VF or VT, and deliver an electric shock to terminate these arrhythmias to reduce the risk of sudden death. An 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, QOL, 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

<u>Study Selection Criteria</u>
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.

<u>Randomized Controlled Trials</u>
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). (92) 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 LVEF was 30%.

The primary endpoint 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 endpoint event. The primary analysis was the modified intention-to-treat (ITT) 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% CI for the HR was set at 1.45.

The trial's main results are summarized in Tables 12 to 14. The S-ICD was noninferior to the T-ICD on the composite endpoint of device-related complications and inappropriate shocks. The HR for the primary endpoint 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%; HR, 1.23; 95% CI, 0.89 to 1.70), but the number of SCDs did not differ between groups (18 in each group). There were more appropriate shocks in the S-ICD group (19.2% vs. 11.5%; HR, 1.52; 95% CI, 1.08 to 2.12). Other secondary endpoints did not differ between the groups.

While the rate of SCD 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 HR 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 endpoint 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 HR (and 95% CI) for the primary endpoint.

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

**Table 11a. PRAETORIAN Trial Characteristics**

| Study | Countries | Sites | Dates | Participants |
|---|---|---|---|---|
| **PRAETORIAN** | | | | |

| Knops et al. (2020) (92) | | | | |
|---|---|---|---|---|
| | Europe (92.4%) and U.S. | 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. |

ICD: implantable cardioverter defibrillator; PRAETORIAN: Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter Defibrillator Therapy; S-ICD: subcutaneous implantable cardioverter defibrillator; U.S.: United States.

**Table 11b. PRAETORIAN Trial Characteristics**

| Study | Interventions | | Primary Endpoint Definitions |
|---|---|---|---|
| **PRAETORIAN<br>Knops et al. (2020) (92)** | | | |
| | **Active** | **Comparator** | |
| | S-ICD (N = 426) | T-ICD (N = 423) | Composite of device-related complications and inappropriate shocks. Inappropriate shocks were defined as shock therapy for anything else but VF or VT. 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:<br>• device infection that led to the extraction of the lead or generator;<br>• pocket hematoma that led to drainage, blood transfusion, or prolongation of hospitalization; |

| | | | |
|---|---|---|---|
| | | | • device-related thrombotic events;<br>• pneumothorax or hemothorax that led to intervention or prolongation of hospitalization;<br>• cardiac perforation or tamponade;<br>• lead repositioning or replacement;<br>• 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; S-ICD: subcutaneous implantable cardioverter defibrillator; T-ICD: transvenous implantable cardioverter defibrillator; VF: ventricular fibrillation; VT: ventricular tachycardia.

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

| Study | Endpoint (4-year cumulative incidence) | S-ICD (n = 426) | T-ICD (n = 423) | Hazard Ratio (95% CI) |
|---|---|---|---|---|
| **PRAETORIAN**<br><br>**Knops et al. (2020) (92)** | Primary composite endpoint (modified ITT analysis) | 68 (15.1%) | 68 (15.7%) | 0.99 (0.71 to 1.39); p=.01 for noninferiority; p=.95 for superiority |
| | Device-related complication | 31 (5.9%) | 44 (9.8%) | 0.69 (0.44 to 1.09) |
| | Inappropriate shock | 41 (9.7%) | 29 (7.3%) | 1.43 (0.89 to 2.30) |
| | Primary composite endpoint (as-treated analysis) | 68/428 (15.9%) | 68/421 (16.2%) | 0.98 (0.70 to 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; S-ICD: subcutaneous implantable cardioverter defibrillator; T-ICD: transvenous implantable cardioverter defibrillator.

**Table 13. PRAETORIAN Trial Results - Secondary Endpoints**

| Study | End Point | S-ICD (N=426) | T-ICD (N=423) | Hazard Ratio (95% CI) |
|---|---|---|---|---|
| **PRAETORIAN**<br><br>**Knops et al. (2020) (92)** | Death from any cause | 83 (16.4%) | 68 (13.1%) | 1.23 (0.89 to 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 to 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 to 1.11) |
| | Hospitalization for heart failure | 79 (17.4%) | 74 (16.1%) | 1.08 (0.79 to 1.49) |
| | Crossover to other study device | 18 (4.3%) | 11 (2.7%) | 1.64 (0.77 to 3.47) |

CI: confidence interval; ICD: implantable cardioverter defibrillator; PRAETORIAN: Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter Defibrillator Therapy; S-ICD: subcutaneous implantable cardioverter defibrillator; T-ICD: transvenous implantable cardioverter defibrillator.

**Table 14. PRAETORIAN Trial Results - Specific Complications**

| Study | Endpoint | S-ICD (N=426) | T-ICD (N=423) |
|---|---|---|---|
| **PRAETORIAN**<br><br>**Knops et al. (2020) (92)** | 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%) |
| | 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 S-ICD: subcutaneous implantable cardioverter defibrillator; T-ICD: transvenous implantable cardioverter defibrillator.

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 2 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 were collected but have not yet been published. These data could shed light on the relative importance to patients of adverse events such as inappropriate shocks and device replacement, especially if QOL 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] | Compartor[c] | Outcomes[d] | Duration of Follow-up[e] |
|---|---|---|---|---|---|
| **PRAETORIAN**<br><br>**Knops et al. (2020) (92)** | 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. Study population is unclear; 3. Study population not representative of intended use; 4, Enrolled populations do not reflect relevant diversity; 5. Other.

[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5: Other.

[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.

[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically

significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

**Table 16. Study Design and Conduct Limitations**

| Study | Allocation[a] | Blinding[b] | Selective Reporting[c] | Data Completeness[d] | Power[e] | Statistical[f] |
|---|---|---|---|---|---|---|
| **PRAETORIAN**<br><br>**Knops et al. (2020) (92)** | | 2. Clinical-events committee was not blinded to treatment assignment | 2. Quality of life data collected but not yet published | | | 5. Rationale for choice of noninferiority margin unclear |

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; 5. Other.
[b] Blinding key: 1. Participants or study staff not blinded; 2. Outcome assessors not blinded; 3. Outcome assessed by treating physician; 4. Other.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4. Other.
[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); 7. Other.
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference; 4. Other.
[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; 5. Other.

## 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) (93) | Matching based on dialysis | 182 (91 matched pairs) | 180 days | • Inappropriate shocks | 2.2%<br><br>1.1% | 1.1%<br><br>3.3% | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | status, sex, age | | | • Infection requiring explant<br>• Death from all causes<br>• Total with adverse event or death | 2.2%<br>7.7% | 2.2%<br>5.5% | |
| Honarbakhsh et al. (2017) (94) | Propensity matched case-control | 138 (69 matched pairs) | 32 months[a] | • Total device-related complication<br>• Infections<br>• Inappropriate shocks<br>• Failure to cardiovert VA | 29%<br>5.8%<br>8.7%<br>1.4% | 9%<br>1.4%<br>4.3%<br>1.4% | |
| Kobe et al. (2017) (95) | Sex- and age-matched case control | 120 (60 pairs); 84 pairs analyzed | 942 days vs 622 days | • Post-traumatic stress disorder<br>• Major depression<br>• SF-12 physical well-being score<br>• SF-12 mental well-being score | 14.3%<br>9.5%<br>40<br>52 | 14.3%<br>4.8%<br>47<br>52 | |
| Pedersen et al. (2016) (96) | Retrospective analysis of propensity-matched cohort | 334 (167 matched pairs) | 6 months | • SF-12 physical well-being score<br>• SF-12 mental well-being score | 43<br>45 | 44<br>45 | |
| Brouwer et al. (2016) (97) | Retrospective analysis of propensity-matched cohort | 280 (140 matched pairs) | 5 years | • Overall complications<br>• Lead complications<br>• Non-lead complications<br>• Infections<br>• Appropriate ICD intervention (HR=2.4; 95% CI, NR; p=0.01)<br>• Inappropriate ICD | 18%<br>11.5%<br>2.2%<br>3.6%<br>31%<br>30% | 14%<br>0.8%<br>9.9%<br>4.1%<br>17%<br>21% | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | intervention (HR=1.3; 95% CI, NR; p=0.42)<br>• Survival | <br><br><br>95% | <br><br><br>96% | |
| Friedman et al. (2016) (98) | Retrospective analysis of propensity-matched cohort from NCDR for ICD | 5,760 (1,920 matched groups) | NR | • Any in-hospital complications<br>• Deaths<br>• Infections<br>• Lead dislodgements<br>• Pneumothorax | 0.6%<br><br>0.1%<br>0%<br>0.2%<br><br>0.2% | 0.9%<br><br>0.2%<br>0.05%<br>0.1%<br><br>0% | 1.5%<br><br>0.05%<br>0.1%<br>0.6%<br><br>0.3% |
| Kobe et al. (2013) (99) | Sex- and age-matched case-control | 138 (69 matched pairs) | 217 days[a] | • Pericardial effusion<br>• Successful termination of induced VF<br>• Appropriate shocks<br>• Inappropriate shocks | 1<br><br>91%<br><br><br>9<br><br>3 | 0<br><br>90%<br><br><br>3<br><br>5 | |

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

Section Summary: Subcutaneous Implantable Cardioverter Defibrillators In Individuals 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 2 types of devices, and reported variable adverse event rates. Ongoing studies could provide additional evidence on complications and device safety over the longer term.

**Extravascular Implantable Cardioverter Defibrillators**

Clinical Context and Therapy Purpose

The purpose of extravascular ICD (E-ICD) placement in individuals 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 following PICO was used to select literature to inform this policy.

*Populations*
The population of interest is individuals who need an ICD.

There are no defined guidelines for the selection of E-ICD versus T-ICD.

*Interventions*
The therapy being considered is E-ICD. An ICD is a device designed to monitor an individual's heart rate, recognize VF or VT, and deliver an electric shock to terminate these arrhythmias to reduce the risk of sudden death. An E-ICD is intended as an alternative to T-ICD to reduce lead-related complications, and as an alternative to S-ICD since S-ICD are less effective at stopping ventricular arrhythmias. The E-ICD lead is placed substernally at the anterior mediastinum, and the pulse generator is placed at the left midaxillary region. The pulse generator size and energy capacity are similar to T-ICD devices, which overcomes some of the limitations of S-ICD devices. However, E-ICD still have a risk of cardiac injury or perforation.

*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.

<u>Study Selection Criteria</u>
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.

Nonrandomized Study

Following several smaller preliminary studies with E-ICD, Friedman et al. (2022) published a prospective, nonrandomized, global clinical study in patients who received an E-ICD. (100) All patients had a class I or IIa indication for ICD placement (81.6% for primary prevention, 18.0% for secondary prevention). At baseline, 83.9% had cardiomyopathy, 42.7% had ventricular arrhythmias, and 13.9% had atrial fibrillation. The primary efficacy endpoint was successful defibrillation at implantation, and safety was assessed for 6 months. Of the entire study population (N=356), 302 patients were successfully defibrillated after ventricular arrhythmia was induced; 98.7% of these patients had successful defibrillation. At 6 months, 92.6% of patients had not experienced a major complication. Major complications occurred in 23 patients, none of which had further sequelae. Inappropriate shocks (n=118) occurred in 29 patients during follow-up (median number of shocks per patient, 2). The most common reasons for inappropriate shocks were P-wave oversensing (34 episodes) and lead noise (19 episodes). Tables 18 and 19 summarize the characteristics and results, respectively.

**Table 18. Summary of Key Nonrandomized Trial Characteristics**

| Study | Study Type | Country | Dates | Participants | Treatment | Follow-Up |
|---|---|---|---|---|---|---|
| Friedman et al. (2022) (100) | Prospective | US, Europe, Asia, Oceania | 2019-2021 | Patients with a class I or IIa indication for ICD for primary or secondary prevention | E-ICD | Mean, 10.6 months |

E-ICD: extravascular implantable cardioverter defibrillator; ICD: implantable cardioverter defibrillator; US: United States.

**Table 19. Summary of Key Nonrandomized Trial Results**

| Study | Successful Defibrillation after Implantation | Freedom from Major System- or Procedure-Related Complications for 6 Months | Inappropriate Shocks |
|---|---|---|---|
| Friedman et al. (2022) (100) | N=302 | N=299 | N=299 |
| E-ICD | 98.7% | 92.6% | 9.7% |

E-ICD: extravascular implantable cardioverter defibrillator.

Section Summary: Extravascular Implantable Cardioverter Defibrillators
The largest available study with an E-ICD reported high rates of defibrillation after implantation and a low rate of major complications, with a numerically similar rate of inappropriate shocks compared to studies with T-ICD and S-ICD. The major limitation of the study is the lack of an active control group.

**Summary of Evidence**
Transvenous Implantable Cardioverter Defibrillators
For individuals who have a high-risk of sudden cardiac death (SCD) due to ischemic or nonischemic cardiomyopathy in adulthood who receive transvenous implantable cardioverter defibrillators (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 (QOL), 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 implantable cardioverter defibrillators (ICD) use following recent myocardial infarction (MI) did not support a benefit for immediate vs delayed implantation for at least 40 days. For nonischemic cardiomyopathy (NICM), there is less clinical trial data, but pooled estimates of available evidence from RCTs enrolling patients with NICM 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, QOL, 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 studies are considered adequate evidence to support the use of T-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, QOL, and treatment-related mortality and morbidity. The limited evidence for patients with long QT syndrome (LQTS), catecholaminergic polymorphic ventricular tachycardia (CPVT), and Brugada syndrome (BrS) 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 studies 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 sarcoidosis), 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 (VT) 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, QOL, 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 subcutaneous ICD (S-ICD) placement, the evidence includes an RCT, nonrandomized studies, and case series. Relevant outcomes are OS, morbid events, QOL, and treatment-related mortality and morbidity. An RCT found that S-ICD significantly decreases the risk of lead-related perioperative complications compared to T-ICD. However, this study was not powered to detect differences in the rates of failed shocks or inappropriate shocks and an extension study is ongoing. 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 studies 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 with no contraindication to a T-ICD, who receive

S-ICD placement, the evidence includes one RCT, nonrandomized studies, and case series. Relevant outcomes are OS, morbid events, QOL, and treatment-related mortality and morbidity. The Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter Defibrillator Therapy (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 (hazard ration [HR], 0.99; 95% confidence interval [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 2 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.

Extravascular Implantable Cardioverter Defibrillators
For individuals who need an ICD who receive an extravascular ICD (E-ICD), the evidence includes nonrandomized studies. Relevant outcomes are OS, morbid events, quality of life, and treatment-related mortality and morbidity. The largest available study with an E-ICD reported high rates of defibrillation after implantation and a low rate of major complications, with a numerically similar rate of inappropriate shocks compared to studies with T-ICD and S-ICD. The major limitation of the study is the lack of an active control group. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

**Practice Guidelines and Position Statements**
American Heart Association/American College of Cardiology et al. – Heart Failure (2022)
In 2022, the American Heart Association (AHA), American College of Cardiology (ACC), and the Heart Failure Society of America released a guideline for the management of heart failure. (101) This guideline includes ICD recommendations which are summarized in Table 20.

**Table 20. Guideline for the Management of Heart Failure - Recommendations for ICDs**

| Recommendation | COR | LOE |
|---|---|---|
| "In patients with nonischemic DCM or ischemic heart disease at least 40 days post-MI with LVEF ≤35% and NYHA class I or II symptoms on chronic GDMT, who have reasonable expectation of meaningful survival for >1 year, ICD therapy is recommended for primary prevention of SCD to reduce total mortality." | 1 | A |
| "A transvenous ICD provides high economic value in the primary prevention of SCD particularly when the patient's risk of death caused by ventricular arrhythmia is deemed high and the risk of nonarrhythmic | | A |

| | | |
|---|---|---|
| death (either cardiac or noncardiac) is deemed low based on the patient's burden of comorbidities and functional status." | | |
| "In patients at least 40 days post-MI with LVEF ≤30% and NYHA class I symptoms while receiving GDMT who have reasonable expectation of meaningful survival for >1 year, ICD therapy is recommended for primary prevention of SCD to reduce total mortality." | 1 | B-R |
| "In patients with genetic arrhythmogenic cardiomyopathy with high-risk features of sudden death with EF ≤45%, implantation of ICD is reasonable to decrease sudden death." | 2a | B-NR |
| "For patients whose comorbidities or frailty limit survival with good functional capacity to <1 year, ICD and CRT-D are not indicated." | No benefit | C-LD |

A: high; B-NR: moderate, non-randomized; B-R: moderate, randomized; C-LD: limited data; COR: class of recommendation; CRT-D: cardiac resynchronization therapy with defibrillation; DCM: dilated cardiomyopathy; EF: ejection fraction; GDMT: guideline-directed management and therapy; ICD: implantable cardioverter defibrillator: LOE: level of evidence; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NYHA: New York Heart Association; SCD: sudden cardiac death.

American Heart Association/American College of Cardiology et al. - Hypertrophic Cardiomyopathy (2020)

In 2020, the AHA and ACC published a joint guideline for the Diagnosis and Treatment of Patients with Hypertrophic Cardiomyopathy. (102) Recommendations relevant to this policy are summarized in Table 21.

**Table 21. Patient 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 HCM 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 | I | B-NR |

| | | |
|---|---|---|
| consideration patient preferences, lifestyle, and expected potential need for pacing for bradycardia or ventricular tachycardia termination. | | |

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

American Heart Association/American College of Cardiology et al. – Ventricular Arrhythmias and Prevention of Sudden Cardiac Death (2017)

The AHA, ACC, and Heart Rhythm Society (2017) published joint guidelines on the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. (103) This guideline supersedes the 2008 guideline for device-based therapy of cardiac rhythm abnormalities (104) and the subsequent 2012 focused update. (105) The most up-to-date recommendations on the use of T-ICD devices from the 2017 guidelines are presented in Tables 22 to 26. Table 27 summarizes the most up-to-date recommendations regarding S-ICDs.

**Table 22. Recommendations on Use of Implantable Cardioverter Defibrillators as Secondary Prevention of Sudden Cardiac Death of Ischemic Heart Disease or Nonischemic Cardiomyopathy**

| Recommendations | 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, an ICD is recommended if meaningful survival of greater than 1 year is expected." | I | B-R<br>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, an ICD is recommended if meaningful survival of greater than 1 year is expected." | I | B-NR |
| "In patients resuscitated from SCA due to coronary artery spasm in whom medical therapy is ineffective or not tolerated, an ICD is reasonable if meaningful survival of greater than 1 year is expected." | IIa | B-NR |
| "In patients resuscitated from SCA due to coronary artery spasm, an ICD in addition to medical therapy may be reasonable if meaningful survival of greater than 1 year is expected." | IIb | B-NR |
| "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, an ICD is recommended if meaningful survival of greater than 1 year is expected." | I | B-R<br>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 if meaningful survival of greater than 1 year is expected." | IIa | B-NR |
| "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%), and ICD is recommended if meaningful survival of greater than 1 year is expected." | I | B-NR |
| "In patients with arrhythmogenic right ventricular cardiomyopathy and syncope presumed due to VA, an ICD can be useful if meaningful survival of greater than 1 year is expected." | 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; NICM: nonischemic cardiomyopathy; RVEF: right ventricular ejection fraction; SCA: sudden cardiac arrest; SCD: sudden cardiac death; VA: ventricular arrhythmia; VF: ventricular fibrillation; VT: ventricular tachycardia

**Table 23. Recommendations on Use of ICDs as a Primary Prevention of Ischemic Heart Disease or Nonischemic Cardiomyopathy**

| Recommendations | 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 postrevascularization, and with NYHA class II or III HF despite GDMT, an ICD is recommended if meaningful survival of greater than 1 year is expected." | 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 postrevascularization, and with NYHA class I HF despite GDMT, an ICD is recommended if meaningful survival of greater than 1 year is expected." | 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, an ICD is recommended if meaningful survival of greater than 1 year is expected." | I | B-R |
| "In nonhospitalized patients with NYHA class IV symptoms who are candidates for cardiac transplantation or an LVAD, an ICD is reasonable if meaningful survival of greater than 1 year is expected." | 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 |
| "In patients with NICM, HF with NYHA class II-III symptoms and an LVEF of 35% or less, despite GDMT, an ICD is recommended if meaningful survival of greater than 1 year is expected." | I | A |
| "In patients with NICM due to a *Lamic A/C* mutation who have 2 or more risk factors (NSVT, LVEF <45%, nonmissense mutation, and male sex), an ICD can be beneficial if meaningful survival of greater than 1 year is expected." | IIa | B-NR |
| "In patients with NICM, HF with NYHA class I symptoms and an LVEF of 35% or less, despite GDMT, an ICD may be considered if meaningful survival of greater than 1 year is expected." | 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; CRT: cardiac resynchronization therapy; COR: class of recommendation; ICD: implantable cardioverter defibrillator; 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; MI: myocardial infarction; NICM: nonischemic cardiomyopathy; 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 24. Recommendations 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, an ICD is recommended if meaningful survival of greater than 1 year is expected." | I | B-NR |
| "In patients with HCM and 1 or more of the following risk factors, an ICD is reasonable if meaningful survival of greater than 1 year is expected:<br>• Maximum LV wall thickness ≥30 mm (LOE: B-NR).<br>• SCD in 1 or more first-degree relatives presumably caused by HCM (LOE: C-LD).<br>• 1 or more episodes of unexplained syncope within the preceding 6 months (LOE: C-LD)." | IIa | B-NR<br>C-LD<br>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 | IIa | B-NR<br>C-LD |

| | | |
|---|---|---|
| features an ICD is reasonable if meaningful survival of greater than 1 year is expected." | | |
| "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<br>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 25. Recommendations on Use of ICDs for Cardiac Sarcoidosis**

| **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 |
| "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 26. Recommendations 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, an ICD may be reasonable if meaningful survival of greater than 1 year is expected." | IIb | B-NR |
| "In patients with neuromuscular disorders, primary and secondary prevention ICDs are recommended for the same indications as for patients with NICM if meaningful survival of greater than 1 year is expected." | I | B-NR |
| "In patients with Emery-Dreifuss and limb-girdle type IB muscular dystrophies with progressive cardiac involvement, an ICD is reasonable if meaningful survival of greater than 1 year is expected." | IIa | B-NR |
| "In patients with myotonic dystrophy type 1 with an indication for a permanent pacemaker, an ICD may be considered to minimize the risk of SCA from VT if meaningful survival of greater than 1 year is expected." | IIb | B-NR |
| “In patients with a cardiac channelopathy and SCA, an ICD is recommended if meaningful survival of greater than 1 year is expected." | I | B-NR |
| "In high-risk patients with symptomatic long QT syndrome in whom a beta blocker is ineffective or not tolerated, intensification of therapy with additional medications (guided by consideration of the particular long QT syndrome type), left cardiac sympathetic denervation, and/or an ICD is recommended." | I | B-NR |
| “In patients with catecholaminergic polymorphic VT and recurrent sustained VT or syncope, while receiving adequate or maximally tolerated beta blocker, treatment intensification with either combination medication therapy, left cardiac sympathetic denervation, and/or an ICD is recommended." | 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, an ICD is recommended if meaningful survival of greater than 1 year is expected." | I | B-NR |
| "In patients with early repolarization pattern on ECG and cardiac arrest or sustained VA, an ICD is recommended if meaningful survival of greater than 1 year is expected." | I | B-NR |
| "In patients with short QT syndrome who have a cardiac arrest or sustained VA, an ICD is recommended if meaningful survival greater than 1 year is expected." | I | B-NR |
| “In patients resuscitated from SCA due to idiopathic polymorphic VT or VF, an ICD is recommended if meaningful survival of greater than 1 year is expected." | I | B-NR |

| | | |
|---|---|---|
| “For older patients and those with significant comorbidities, who meet indications for a primary prevention ICD, an ICD is reasonable if meaningful survival of greater than 1 year is expected." | IIa | B-NR |
| "In patients with adult congenital heart disease with SCA due to VT or VF in the absence of reversible causes, an ICD is recommended if meaningful survival of greater than 1 year is expected." | 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 if meaningful survival of greater than 1 year is expected." | 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 27. Recommendations 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; COR: class of recommendation; CRT: cardiac resynchronization therapy; ICD: implantable cardioverter defibrillator; LOE: level of evidence; VT: ventricular tachycardia.
[a] Harm.

<u>American Heart Association - Cardiomyopathy in Children (2023)</u>

In 2023, the AHA published a scientific statement on cardiomyopathy in children. (106) The statement recommends a discussion of benefit and risk, including the potential for sudden death and ICD discharges. The criteria for ICD implementation in children are the same as in adults after pediatric-specific risks are taken into account.

Heart Rhythm Society et al. - Position Paper (2022)

The Heart Rhythm Society, in conjunction with the European Heart Rhythm Association and the Asia Pacific Heart Rhythm Society published a position paper on several cardiac devices, including S-ICDs. (107) The authors reviewed the available literature and provided practical considerations for appropriate use. There was strong consensus that T-ICDs should be considered in all patients with an indication for preventing sudden cardiac death, and that non-T-ICDs can be considered in patients who do not require active pacing or who require a non-transvenous approach. There was general agreement that a T-ICD or leadless pacemaker could be added to a non-T-ICD if the patient develops a need for cardiac pacing. The position paper mentioned extravascular ICDs but did not provide any formal recommendations regarding their use due to a lack of available data.

Heart Rhythm Society – Arrhythmogenic Cardiomyopathy (2019)

In 2019, the Heart Rhythm Society published a consensus statement on evaluation, risk stratification, and management of arrhythmogenic cardiomyopathy. (108) Recommendations related to ICD risk stratification and placement decisions are shown in Table 28.

**Table 28. Recommendations 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 (2013)

The Heart Rhythm Society, 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). (109)

**Table 29. Recommendations on ICDs in 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:<br>• Are survivors of a cardiac arrest; and/or<br>• 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 stand-alone 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: | I |

| | |
|---|---|
| • Are survivors of cardiac arrest; and/or<br>• Have documented spontaneous VT with or without syncope. | |
| 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; HRS: Heart Rhythm Society; 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.

Heart Rhythm Society – Cardiac Sarcoidosis (2014)

In 2014, the Heart Rhythm Society published a consensus statement on the diagnosis and management of arrhythmias associated with cardiac sarcoidosis, including recommendations for ICD implantation in patients with cardiac sarcoidosis (Table 30). (38) The writing group concluded that although there are few data specific to ICD use in patients with cardiac sarcoidosis, 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 Sarcoidosis**

| Recommendation | COR[1] |
|---|---|
| ICD implantation **is recommended** in patients with cardiac sarcoidosis and one or more of the following:<br>• Spontaneous sustained ventricular arrhythmias, including prior cardiac arrest;<br>• 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 sarcoidosis, independent of ventricular function, and one or more of the following:<br>• An indication for permanent pacemaker implantation;<br>• Unexplained syncope or near-syncope, felt to be arrhythmic in etiology;<br>• 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:<br>• Incessant ventricular arrhythmias;<br>• Severe New York Heart Association class IV heart failure. | III |

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

Pediatric and Congenital Electrophysiology Society et al.

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. (110) The statement made the following recommendations on the use of ICD therapy in adults with congenital heart disease (see Table 31).

**Table 31. Recommendations on ICDs in 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, nonsustained ventricular tachycardia, QRS duration >180 ms, extensive right ventricular scarring, or inducible sustained ventricular tachycardia at electrophysiologic study. | IIa | B |
| 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 | Ib | C |

| | | |
|---|---|---|
| arrhythmia and in whom thorough invasive and noninvasive investigations have failed to define a cause. | | |
| 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.

In 2021, the Pediatric and Congenital Electrophysiology Society and Heart Rhythm Society also issued an expert consensus statement on the indications and management of cardiovascular implantable electronic devices in pediatric patients. (1) Table 32 summarizes recommendations for ICD therapy from this statement.

**Table 32. Recommendations for ICD Therapy in Pediatric Patients**

| Recommendation | COR | LOE |
|---|---|---|
| ICD implantation is indicated for survivors of SCA due to VT/VF if completely reversible causes have been excluded and an ICD is considered to be more beneficial than alternative treatments that may significantly reduce the risk of SCA. | I | B-NR |
| ICD implantation may be considered for patients with sustained VT that cannot be adequately controlled with medication and/or catheter ablation. | 2b | C-EO |
| ICD therapy may be considered for primary prevention of SCD in patients with genetic cardiovascular diseases and risk factors for SCA or pathogenic mutations and family history of recurrent SCA. | 2b | C-EO |
| ICD therapy is not indicated for patients with incessant ventricular tachyarrhythmias due to risk of ICD storm. | 3: Harm | C-EO |
| ICD therapy is not indicated for patients with ventricular arrhythmias that are adequately treated with medication and/or catheter ablation. | 3: Harm | C-LD |
| ICD therapy is not indicated for patients who have an expected survival <1 year, even if they meet ICD implantation criteria specified in the above recommendations. | 3: Harm | C-EO |
| ICD implantation along with the use of beta-blockade is indicated for patients with a diagnosis of LQTS who are survivors of SCA. | I | B-NR |
| ICD implantation is indicated in LQTS patients with symptoms in whom beta-blockade is either ineffective or not tolerated and cardiac sympathetic denervation or other medications are not considered effective alternatives. | I | B-NR |

| | | |
|---|---|---|
| ICD therapy may be considered for primary prevention in LQTS patients with established clinical risk factors and/or pathogenic mutations. | 2b | C-LD |
| ICD implantation is not indicated in asymptomatic LQTS patients who are deemed to be at low risk of SCA and have not been tried on beta-blocker therapy. | 3: Harm | C-LD |
| ICD implantation is indicated in patients with a diagnosis of CPVT who experience cardiac arrest of arrhythmic syncope despite maximally tolerated beta-blocker plus flecainide and/or cardiac sympathetic denervation. | I | C-LD |
| ICD implantation is reasonable in combination with pharmacologic therapy with or without cardiac sympathetic denervation when aborted SCA is the initial presentation of CPVT. Pharmacologic therapy and/or cardiac sympathetic denervation without ICD may be considered as an alternative. | 2a | C-LD |
| ICD therapy may be considered in CPVT patients with polymorphic/bidirectional VT despite optimal pharmacologic therapy with or without cardiac sympathetic denervation. | 2b | C-LD |
| ICD implantation is not indicated in asymptomatic patients with a diagnosis of CPVT. | 3: Harm | C-EO |
| ICD implantation is indicated in patients with a diagnosis of BrS who are survivors of SCA or have documented spontaneous sustained VT. | I | B-NR |
| ICD implantation is reasonable for patients with BrS with a spontaneous type I Brugada ECG pattern and recent syncope presumed due to ventricular arrhythmias. | 2a | B-NR |
| ICD implantation may be considered in patients with syncope presumed due to ventricular arrhythmias with a type I Brugada ECG pattern only with provocative medications. | 2b | C-EO |
| ICD implantation is not indicated in asymptomatic BrS patients in the absence of risk factors. | 3: No benefit | C-EO |
| ICD implantation is indicated in patients with HCM who are survivors of SCA or have spontaneous sustained VT. | I | B-NR |
| For children with HCM who have ≥1 primary risk factors, including unexplained syncope, massive left ventricular hypertrophy, nonsustained VT, or family history of early HCM-related SCD, ICD placement is reasonable after considering the potential complications of long-term ICD placement. | 2a | B-NR |
| ICD implantation may be considered in patients with HCM without the above risk factors but with secondary risk factors for SCA such as extensive LGE cardiac MRI or systolic dysfunction. | 2b | B-NR |
| ICD implantation is not indicated in patients with an identified HCM genotype in the absence of known pediatric SCA risk factors. | 3: Harm | C-LD |

| | | |
|---|---|---|
| ICD implantation is indicated in patients with ACM who have been resuscitated from SCA or sustained VT that is not hemodynamically tolerated. | I | B-NR |
| ICD implantation is reasonable in patients with ACM with hemodynamically tolerated sustained VT, syncope presumed due to ventricular arrhythmia, or an LVEF ≤35%. | 2a | B-NR |
| ICD implantation may be considered in patients with inherited ACM associated with increased risk of SCD based on an assessment of additional risk factors. | 2b | C-LD |
| ICD implantation is indicated in patients with NIDCM who either survive SCA or experience sustained VT not due to completely reversible causes. | I | B-NR |
| ICD implantation may be considered in patients with NIDCM and syncope or an LVEF ≤35%, despite optimal medical therapy. | 2b | C-LD |
| ICD implantation is not recommended in patients with medication-refractory advanced heart failure who are not cardiac transplantation or left ventricular assist device candidates. | 3: Harm | C-EO |
| ICD therapy is not indicated for patients with advanced heart failure who are urgently listed for cardiac transplantation and will remain in the hospital until transplantation, even if they meet ICD implantation criteria specified in the above recommendations. | 3: No benefit | C-EO |
| ICD implantation is indicated for CHD patients who are survivors of SCA after evaluation to define the cause of the event and exclude any completely reversible causes. | I | B-NR |
| ICD implantation is indicated for CHD patients with hemodynamically unstable sustained VT who have undergone hemodynamics and EP evaluation. | I | C-LD |
| ICD implantation is reasonable for CHD patients with systemic LVEF <35% and sustained VT or presumed arrhythmogenic syncope. | 2a | C-LD |
| ICD implantation may be considered for CHD patients with spontaneous hemodynamically stable sustained VT who have undergone hemodynamic and EP evaluation. | 2b | C-EO |
| ICD implantation may be considered for CHD patients with unexplained syncope in the presence of ventricular dysfunction, nonsustained VT, or inducible ventricular arrhythmias at EP study. | 2b | C-LD |
| ICD implantation may be considered for CHD patients with a single or systemic right ventricular ejection fraction ≤35%, particularly in the presence of additional risk factors such as VT, arrhythmic syncope, or severe systemic AV valve insufficiency. | 2b | C-EO |

ACM: arrhythmogenic cardiomyopathy; AV: atrioventricular; B-NR: moderate, non-randomized; BrS: Brugada syndrome; C-EO: consensus of expert opinion; CHD: coronary heart disease; C-LD: limited data; COR: class of recommendation; CPVT: catecholaminergic polymorphic ventricular tachycardia; ECG: electrocardiogram; EP: electrophysiology; HCM: hypertrophic cardiomyopathy; ICD: implantable cardioverter defibrillator; LGE: late gadolinium-enhanced; LOE: level of evidence; LQTS: long QT syndrome; LVEF: left ventricular ejection fraction; MRI: magnetic resonance imaging; NIDCM: nonischemic dilated cardiomyopathy; SCA: sudden cardiac arrest; SCD: sudden cardiac death; VF: ventricular fibrillation; VT: ventricular tachycardia.

**Medicare National Coverage**

There is a National Coverage Determination for ICDs. (111) According to the most recent publication (effective February 15, 2018), Centers for Medicare and Medicaid Services (CMS) will cover ICDs for the following patient indications:

1. Patients with a personal history of sustained VT or cardiac arrest due to Ventricular Fibrillation (VF).
2. Patients with a prior myocardial infarction (MI) and a measured Left Ventricular Ejection Fraction (LVEF) ≤ 0.30.
3. Patients who have severe ischemic dilated cardiomyopathy but no personal history of sustained VT or cardiac arrest due to VF, and have New York Heart Association (NYHA) Class II or III heart failure, LVEF≤ 35%.
4. Patients who have severe non-ischemic dilated cardiomyopathy but no personal history of cardiac arrest or sustained VT, NYHA Class II or III heart failure, LVEF ≤ 35%, and been on optimal medical therapy for at least three (3) months.
5. Patients with documented familial, or genetic disorders with a high risk of life-threatening tachyarrhythmias (sustained VT or VF), to include, but not limited to, long QT syndrome or hypertrophic cardiomyopathy.
6. Patients with an existing ICD may receive an ICD replacement if it is required due to the end of battery life, Elective Replacement Indicator (ERI), or device/lead malfunction.

For each group:

1. Patients must be clinically stable (e.g., not in shock from any etiology);
2. LVEF must be measured by echocardiography, radionuclide (nuclear medicine) imaging, cardiac Magnetic Resonance Imaging (MRI), or catheter angiography;
3. Patients must not have:
    - Significant, irreversible brain damage; or,
    - Any disease, other than cardiac disease (e.g., cancer, renal failure, liver failure) associated with a likelihood of survival less than one (1) year; or,
    - Supraventricular tachycardia such as atrial fibrillation with a poorly controlled ventricular rate.

**Ongoing and Unpublished Clinical Trials**

Some ongoing and unpublished trials that may influence this policy are listed in Table 33.

**Table 33. Summary of Key Trials**

| NCT Number | Trial Name | Planned Enrollment | Completion Date |
|---|---|---|---|
| ***Ongoing*** | | | |
| NCT02845531 | Implantable Cardioverter Defibrillator Versus Optimal Medical Therapy In Patients With Variant Angina | 140 | Jun 2030 |

| | | | |
|---|---|---|---|
| | Manifesting as Aborted Sudden Cardiac Death (VARIANT ICD) | | |
| NCT00673842[a] | Risk Estimation Following Infarction Noninvasive Evaluation - ICD Efficacy | 700 | Dec 2024 |
| 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 Ila Indication for ICD Without an Indication for Pacing | 850 | Dec 2023 (extended follow-up) |
| ***Unpublished*** | | | |
| NCT01085435[a] | Evaluation oF Factors Impacting Clinical Outcome and Cost Effectiveness of the S-ICD (The EFFORTLESS S-ICD Registry) | 994 | Jan 2024 |
| NCT02787785[a] | Multicenter Automatic Defibrillator Implantation Trial With Subcutaneous Implantable Cardioverter Defibrillator (MADIT S-ICD) | 40 | Oct 2023 |
| NCT01736618[a] | Subcutaneous Implantable Cardioverter Defibrillator System Post Approval Study (UNTOUCHED) | 1766 | Oct 2021 |

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

## Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

| | |
|---|---|
| **CPT Codes** | 0571T, 0572T, 0573T, 0574T, 0575T, 0576T, 0577T, 0578T, 0579T, 0580T, 0614T, 33216, 33217, 33218, 33220, 33223, 33230, 33231, 33240, 33241, 33243, 33244, 33249, 33262, 33263, 33264, 33270, 33271, 33272, 33273, 93260, 93261, 93282, 93283, 93284, 93285, 93287, 93289, 93295, 93296, 93297, 93298, 93640, 93641, 93642, 93644 |
| **HCPCS Codes** | C1721, C1722, C1882, C1895, C1896, C1899, G0448, [Deleted 1/1/2024: G2066] |

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## Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been changed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

## Policy History/Revision

| Date | Description of Change |
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| 02/15/2025 | Document updated with literature review. The following changes were made to Coverage: 1) Updated Coverage statements specific to pediatric indications for implantable cardioverter defibrillators; and 2) Added |

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| | experimental, investigational and/or unproven statement for extravascular implantable cardioverter defibrillators. Added references 1, 3-5, 12, 22, 27, 32, 79, 82, 100, 104, 106 and 107; others removed. |
| 01/01/2024 | Reviewed. No changes. |
| 10/01/2022 | Document updated with literature review. Coverage unchanged. Added/updated the following references: 2, 21, 74, 85, 93, 96, and 102. |
| 08/01/2021 | Reviewed. No changes. |
| 11/15/2020 | Document updated with literature review. The following changes were made to Coverage: 1) Added conditional coverage of an automatic implantable cardioverter defibrillator (ICD) in adults for primary prevention for diagnosis of cardiac sarcoid; and 2) Added a NOTE 2 specific to criteria for ICD implantation in patients with cardiac sarcoid. Added references: 29-31 and 94. |
| 11/01/2019 | Document updated with literature review. Coverage revised to include specific criteria for ICD implantation in patients with cardiac ion channelopathies as well as clinical or historical findings for patients with congenital long QT syndrome. References revised; some references removed; added references 25, 48, 69, 78, 93. Title changed from Automatic Implantable Cardioverter Defibrillator (AICD) and Subcutaneous Implantable Cardioverter Defibrillator (S-ICD). |
| 08/15/2017 | Reviewed. No changes. |
| 09/01/2016 | Document partially updated. 1) Coverage language for subcutaneous ICD (S-ICD®) modified to remove the wording "for patients <45 years of age who meet the criteria for an AICD listed" and replaced with the wording "who have an indication for ICD implantation for primary or secondary prevention". 2) Added the following to the bulleted criteria regarding pacing: no indication for biventricular pacing/resynchronization therapy; and no ventricular arrhythmias that are known or anticipated to respond to antitachycardia pacing; 3) changed to describe the previously described conditions for "increased procedural risk" conditions for transvenous ICD's to "contraindicated" for clarification. |
| 08/15/2016 | Document updated with literature review. The following conditions were added to the coverage statement for: "Patient's with familial or inherited conditions with a high risk of life-threatening VT's" such as: Brugada syndrome, short QT syndrome, or catecholaminergic polymorphic ventricular tachycardia. In addition, the following coverage criteria was modified or added regarding the medically necessary statement for subcutaneous ICD (S-ICD®): "for patients <45 years of age who meet the criteria for an AICD listed above AND both of the following: 1) There is no indication for antibradycardia pacing; and 2) When placement of the transvenous AICD is associated with increased procedural risk as evidenced by the patient having one of the following documented indications: Complex congenital heart disease or challenging vascular access, high risk for systemic infection, |

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| | Multiple prior transvenous endocardial leads, Compelling reason to preserve existing vascular access (i.e., need for chronic dialysis; younger patient with anticipated long-term need for ICD therapy), or History of need for explantation of a transvenous ICD due to a complication, with ongoing need for ICD therapy. |
| 05/01/2015 | Reviewed. No changes. |
| 12/01/2014 | CPT/HCPCS code(s) updated |
| 09/01/2014 | Document updated with literature review. The use of an FDA approved subcutaneous implantable cardioverter-defibrillator (S-ICD) is considered medically necessary when meeting criteria for an AICD listed above AND when placement of the transvenous AICD is associated with increased procedural risk as evidenced by the patient having one of the following documented indications: 1) Congenital heart disease that limits intracavitary lead placements, 2) Obstructed venous access, 3) Chronic indwelling catheters, or 4) Immunocompromised. CPT/HCPCS code(s) updated. |
| 01/01/2013 | Policy updated with literature review. The following was added: The use of a subcutaneous implantable defibrillator system (S-ICD) is considered experimental, investigational and unproven. Title changed from "Automatic Implantable Cardioverter Defibrillator (AICD)". CPT/HCPCS code(s) updated. |
| 06/01/2012 | Document updated with literature review. The following was added: 1) "New York Heart Association (NYHA) functional Class II or Class III symptoms" was added to the criteria for Primary Prevention for ischemic cardiomyopathy with a history of myocardial infarction at least 40 days before ICD treatment, and left ventricular ejection fraction of 35% or less, 2) "ischemic cardiomyopathy with NYHA functional Class I symptoms, was added to the criteria for Primary Prevention with a history of myocardial infarction at least 40 days before ICD treatment, and left ventricular ejection fraction of 30% or less" 3) "The use of the AICD may be considered medically necessary in children who meet any of the noted criteria in the coverage section. 4) "The use of the ICD is considered experimental, investigational and unproven for all other indications in pediatric patients". CPT/HCPCS code(s) updated. |
| 03/15/2010 | Intermediate partial policy update. Positive coverage criteria change for secondary prevention. Added the following additional indication for coverage: Patients with familial or inherited conditions with a high risk of life-threatening VT's such as long QT syndrome or hypertrophic cardiomyopathy. |
| 06/15/2009 | Coverage and rationale section revised. Removed requirement of more than nine months duration of symptomatic nonischemic dilated cardiomyopathy. Rationale modified. |
| 05/01/2009 | CPT/HCPCS code(s) updated |
| 01/15/2009 | Revised/updated entire document |
| 11/15/2006 | Revised/updated entire document |
| 10/24/2003 | Revised/updated entire document |

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| 03/01/2000 | CPT/HCPCS code(s) updated |
| 02/01/1998 | Revised/updated entire document |
| 11/01/1999 | CPT/HCPCS code(s) updated |
| 05/01/1995 | Revised/updated entire document |
| 10/01/1994 | Revised/updated entire document |
| 04/01/1992 | Revised/updated entire document |
| 05/01/1990 | New medical document |