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# Subcutaneous Implantable Cardioverter Defibrillator (ICD) System

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| **Lines of Business:** HMO; PPO; QUEST Integration | **Original Effective Date:** July 01, 2015 |
| **Place of Service:** Inpatient, Outpatient | **Precertification:** Not Required |

## I. Description

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

**Transvenous ICDs**

For individuals who have a high-risk of sudden cardiac death (SCD) due to ischemic or nonischemic cardiomyopathy in adulthood who receive transvenous ICD (TV-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. The 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 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 nonischemic cardiomyopathy and from subgroup analyses of RCTs with mixed populations have supported a survival benefit for this group. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have a high-risk of SCD due to hypertrophic cardiomyopathy (HCM) in adulthood who receive TV-ICD placement for primary prevention, the evidence includes several large registry studies. The 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 lifesaving, these rates are considered adequate evidence to support the use of ICDs in patients with HCM. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have a high-risk of SCD due to an inherited cardiac ion channelopathy who receive TV-ICD placement for primary prevention, the evidence includes small cohort studies of patients with these conditions treated with ICDs. The relevant outcomes are OS, morbid events, QOL, and treatment-related mortality and morbidity. The limited evidence for patients with long QT syndrome, catecholaminergic polymorphic ventricular tachycardia, and Brugada syndrome has

reported high rates of appropriate shocks. No studies were identified on the use of ICDs for patients with short QT syndrome. Studies comparing outcomes between patients treated and untreated with ICDs are not available. However, given the relatively small patient populations with these channelopathies and the high-risk of cardiac arrhythmias, clinical trials are unlikely. Given the long-term high-risk of SCD in patients with inherited cardiac ion channelopathy, with the assumption that appropriate shocks are life-saving, these studies are considered adequate evidence to support the use of TV-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 TV-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 lifesaving, these studies are considered adequate evidence to support the use of TV-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 TV-ICD placement, the evidence includes multiple well-designed and well-conducted RCTs as well as systematic reviews of these trials. The 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 ICDs**

For individuals who need an ICD and have a contraindication to a TV-ICD but no indications for anti-bradycardia pacing and no anti-tachycardia pacing-responsive arrhythmias who receive S-ICD placement, the evidence includes an RCT, nonrandomized studies and case series. The 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 TV-ICD. Case series have reported high rates of detection and successful conversion of VF, and inappropriate shock rates in the range reported for TV-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 TV-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 anti-bradycardia pacing or anti-tachycardia pacing-responsive arrhythmias with no contraindication to a T-ICD, who receive S-ICD placement, the evidence includes 1 RCT, nonrandomized studies and case series. Relevant outcomes are OS, morbid events, quality of life, and treatment-related mortality and morbidity. The PRAETORIAN (Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter Defibrillator Therapy) trial is the only RCT on the effect of an S-ICD with health outcomes. PRAETORIAN found that S-ICD was noninferior to T-ICD on a composite outcome of complications and inappropriate shock at 48 months (Hazard Ratio [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 the effects of the technology on health outcomes.

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

## II. Policy Criteria

The use of a subcutaneous ICD is covered (subject to Limitations and Administrative Guidelines) when **ALL** of the following criteria are met:

A. The patient has a contraindication to a transvenous ICD due to **1 OR MORE** of the following:
   1. Lack of adequate vascular access.
   2. Compelling reason to preserve existing vascular access (ie, need for chronic dialysis; younger individual with anticipated long-term need for ICD therapy).
   3. History of need for explantation of a transvenous ICD due to a complication, with ongoing need for ICD therapy.

B. The individual does not have an indication for anti-bradycardia pacing.

C. The individual does not have ventricular arrhythmias known or anticipated to respond to anti-tachycardia pacing.

D. The individual has **AT LEAST 1** of the following indications for an ICD:
   1. For primary prevention in an adult individual when **ONE** of the following criteria is met:
      a. Ischemic cardiomyopathy with New York Heart Association (NYHA) functional class II or III symptoms, a history of myocardial infarction at least 40 days before ICD treatment and left ventricular ejection fraction (LVEF) of 35% or less.
      b. Ischemic cardiomyopathy with NYHA functional class I symptoms, a history of myocardial infarction at least 40 days before ICD treatment and LVEF of 30% or less.
      c. 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.

d. 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 greater than 30 mm; ≥1 runs of non-sustained ventricular tachycardia 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.
e. Diagnosis of any **ONE** of the following cardiac ion channelopathies and considered to be at high risk for sudden cardiac death (see Policy Guidelines section):
   - congenital long QT syndrome
   - Brugada syndrome
   - short QT syndrome
   - catecholaminergic polymorphic ventricular tachycardia
f. Diagnosis of cardiac sarcoid and considered to be at high risk for sudden cardiac death (see Policy Guidelines section)

2. For secondary prevention in an adult individual with a history of a life-threatening clinical event associated with ventricular arrhythmic events such as sustained ventricular tachyarrhythmia, after reversible causes (eg, acute ischemia) have been excluded
3. For a pediatric individual when **ONE** of the following criteria is met:
   a. Survivor of cardiac arrest, after reversible causes have been excluded
   b. Symptomatic, sustained ventricular tachycardia in association with congenital heart disease in individuals who have undergone hemodynamic and electrophysiologic evaluation
   c. Congenital heart disease with recurrent syncope of undetermined origin in the presence of ventricular dysfunction or inducible ventricular arrhythmias
   d. HCM with 1 or more major risk factors for sudden cardiac death (history of premature HCM- related sudden death in ≥1 first-degree relatives <50 years; massive left ventricular hypertrophy based on age-specific norms; prior unexplained syncope inconsistent with neurocardiogenic origin) and judged to be at high risk for sudden cardiac death by a physician experienced in the care of individuals with HCM
   e. Diagnosis of **ANY ONE** of the following cardiac ion channelopathies and considered to be at high risk for sudden cardiac death (see Policy Guidelines):
      - congenital long QT syndrome
      - Brugada syndrome
      - short QT syndrome
      - catecholaminergic polymorphic ventricular tachycardia

## III. Policy Guidelines

This evidence review addresses the use of implantable cardioverter defibrillator (ICD) devices as stand-alone interventions, not as combination devices to treat heart failure (ie, cardiac resynchronization devices) or in combination with pacemakers. Unless specified, the policy statements and rationale refer to transvenous ICDs.

Indications for pediatric ICD use are based on American College of Cardiology (ACC), American Heart Association (AHA), and Heart Rhythm Society (HRS) guidelines published in 2008 (updated in 2012), which acknowledged the lack of primary research on pediatric individuals in this field (see Rationale section). These indications derive from nonrandomized studies, extrapolation from adult clinical trials, and expert consensus.

**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 patients 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):
  - Individuals with a diagnosis of LQTS who are survivors of cardiac arrest
  - Individuals with a diagnosis of LQTS who experience recurrent syncopal events while on β-blocker therapy
- Brugada syndrome (BrS):
  - Individuals with a diagnosis of BrS who are survivors of cardiac arrest
  - Individuals with a diagnosis of BrS who have documented spontaneous sustained ventricular tachycardia (VT) with or without syncope
  - 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)
  - Individuals with a diagnosis of BrS who develop ventricular fibrillation during programmed electrical stimulation.
- Catecholaminergic polymorphic ventricular tachycardia (CPVT):
  - Individuals with a diagnosis of CPVT who are survivors of cardiac arrest
  - 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):
  - Individuals with a diagnosis of SQTS who are survivors of cardiac arrest
  - Individuals with a diagnosis of SQTS who are symptomatic and have documented spontaneous VT with or without syncope
  - Individuals with a diagnosis of SQTS who are asymptomatic or symptomatic and have a family history of sudden cardiac death

NOTE: 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 individuals with a family history of sudden cardiac death due to LQTS, infants with a diagnosis of LQTS with functional 2:1 atrioventricular block, individuals with a diagnosis of LQTS in conjunction with a diagnosis of Jervell and Lange-Nielsen syndrome or Timothy syndrome, and 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.

**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, American College of Cardiology, and HRS.

Indications for consideration of ICD placement in individuals diagnosed with cardiac sarcoid are as follows:

- Spontaneous sustained ventricular arrhythmias, including prior cardiac arrest, if meaningful survival of greater than1 year is expected
- Left ventricular ejection fraction (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
- LVEF greater than 35%, if meaningful survival of greater than 1 year is expected; AND
  - syncope or near-syncope, felt to be arrhythmic in etiology OR
  - evidence of myocardial scar by cardiac magnetic resonance imaging (MRI) or positron emission tomographic (PET) scan OR
  - Inducible sustained ventricular arrhythmias (>30 seconds of monomorphic VT or polymorphic VT) or clinically relevant VF
- An indication for permanent pacemaker implantation

## IV. Limitations

A. The use of a subcutaneous ICD is not covered for individuals who do not meet the criteria outlined above (see II), as it is not known to be effective in improving health outcomes
B. The use of the ICD is not indicated for primary prevention for adult individuals in the following situations, as it is not known to be effective in improving health outcomes:
   1. Have had an acute MI (ie, <40 days before ICD treatment)
   2. Have NYHA class IV congestive heart failure (unless the individual is eligible to receive a combination cardiac resynchronization therapy ICD device)
   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
   4. Have noncardiac disease that would be associated with life expectancy less than 1 year
C. The use of the ICD for secondary prevention is not covered for adult individuals who do not meet the criteria for secondary prevention (see II.D.2), as it is not known to be effective in improving health outcomes
D. The use of the ICD is not covered for pediatric patients who do not meet the above criteria (see II.D.3.a-e), as it is not known to be effective in improving health outcomes.

## V. Administrative Guidelines

Precertification is not required. HMSA reserves the right to perform retrospective review using the above criteria to validate if services rendered met payment determination criteria.

Documentation supporting that the payment determination criteria were met should be maintained in the patient's medical record and must be made available to HMSA upon request. HMSA reserves the right to perform retrospective review using the above criteria to validate if services rendered met payment determination criteria.

| CPT Code | Description |
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|---|---|
| 33241 | Removal of implantable defibrillator pulse generator only |
| 33270 | Insertion or replacement of permanent subcutaneous implantable defibrillator system, with subcutaneous electrode, including defibrillation threshold evaluation, induction of arrhythmia, evaluation of sensing for arrhythmia termination, and programming or |
| 33271 | Insertion of subcutaneous implantable defibrillator electrode |
| 33272 | Removal of subcutaneous implantable defibrillator electrode |
| 33273 | Repositioning of previously implanted subcutaneous implantable defibrillator electrode |
| 93282-93284 | Programming device evaluation (in person) with iterative adjustment of the implantable device to test the function of the device and select optimal permanent programmed values with analysis, review and report by a physician or other qualified health care professional, codes specific to the type of device |
| 93260 | Programming device evaluation (in person) with iterative adjustment of the implantable device to test the function of the device and select optimal permanent programmed values with analysis, review and report by a physician or other qualified health care professional; implantable subcutaneous lead defibrillator system |
| 93261 | Interrogation device evaluation (in person) with analysis, review and report by a physician or other qualified health care professional, includes connection, recording and disconnection per patient encounter; implantable subcutaneous lead defibrillator system |
| 93289 | Interrogation device evaluation (in person) with analysis, review and report by a physician or other qualified health care professional, includes connection, recording and disconnection per patient encounter; codes specific to the type of device |
| 93640-93644 | Electrophysiologic evaluation; codes specific to the type of device |
| **HCPCS code** | |
| C1722 | Cardioverter-defibrillator, single chamber (implantable) |
| C1896 | Lead, cardioverter-defibrillator, other than endocardial single or dual coil (implantable) |

## VI. Scientific Background

### Ventricular Arrhythmia and Sudden Cardiac Death

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

### Treatment

ICDs monitor a patient's heart rate, recognize ventricular fibrillation or 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, ie, use in patients who have experienced a potentially life-threatening episode of VT (near SCD); and (2) primary prevention, ie, 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 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 s-iof 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 (PMA) process. The FDA-labeled indications generally include patients who have experienced life-threatening VT associated with cardiac arrest or VT associated with hemodynamic compromise and resistance to pharmacologic treatment. Also, devices typically have approval in the secondary prevention setting for patients with previous myocardial infarction and reduced injection 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. 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. 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. The reduced energy electrical shock may fail to correct an arrhythmia or may cause an irregular heartbeat. The FDA identified both 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 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 anti-tachycardia 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.

**Table 1. Implantable Cardioverter Defibrillators With FDA Approval**

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

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

## Rationale

This evidence review was created in March 1996 and has been updated regularly with a search of the PubMed database. The most recent literature update was performed through April 3, 2023.

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, 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, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 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 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

#### Clinical Context and Therapy Purpose

The purpose of transvenous implantable cardioverter defibrillator (T-ICD) placement is to provide a treatment option that is an alternative to or an improvement on existing therapies in patients with a high-risk of sudden cardiac death (SCD) due to ischemic cardiomyopathy in adulthood.

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

**Populations**
The relevant population of interest are individuals who are at high-risk SCD due to ischemic or non-ischemic cardiomyopathy, inherited cardiac ion channelopathy, or cardiac sarcoid.

**Interventions**
The therapy being considered is TV-ICD placement. An ICD is a device designed to monitor a patient's heart rate, recognize ventricular fibrillation or ventricular tachycardia, and deliver an electric shock to terminate these arrhythmias to reduce the risk of sudden death.

**Comparators**
Comparators of interest include medical management without ICD placement. Guideline based medical management for ischemic cardiovascular disease including antihypertensive therapy and antiarrhythmic medications.

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

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

| Outcomes | Details | Timing |
|---|---|---|
| Quality of life | Can be assessed 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 |

**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

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

**Ischemic Cardiomyopathy and NIDCM**

**Randomized Controlled Trials**

At least 13 RCTs of ICDs for primary prevention have been conducted. 5 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

3 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
- BEta-blocker STrategy plus ICD (BEST-ICD) trial

6 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)
- Danish Study to Assess the Efficacy of ICDs in Patients with Non-Ischemic Systolic Heart Failure on Mortality (DANISH)

The characteristics and mortality results for these 3 groups of trials are shown in Table 3.
Most trials for both ischemic and nonischemic cardiomyopathy have reported results consistent with a mortality benefit for ICD in patients with left ventricular systolic dysfunction or with heart failure and reduced ejection fraction, although not all trials were powered for the mortality outcome and some findings were not statistically significant. However, the DINAMIT, IRIS, and BEST-ICD trials did not support a mortality benefit for ICD in the early weeks following MI, and=-0

CABG Patch showed no benefit in patients having recently undergone coronary revascularization. Another notable exception is the 2016 DANISH trial, which enrolled primarily outpatients with nonischemic cardiomyopathy (NICM) in stable condition who were almost all receiving b-blocker or angiotensin-converting enzyme inhibitors, with the majority also receiving mineralocorticoid-receptor antagonists. While overall mortality did not differ significantly between the ICD and medical therapy groups in DANISH, SCD was significantly reduced in the ICD group (4% vs 8%; hazard ratio [HR], 0.50; 95% confidence interval [CI], 0.31 to 0.82).

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

| Trial | Participants | Treatment Groups | | Mean Follow-Up | Mortality Results | |
|---|---|---|---|---|---|---|
| | | Group | N | | Hazard Ratio | 95% CI |
| **ICM with prior MI** | | | | | | |
| MADIT (1996) | • LVEF ≤35%<br>• Asymptomatic unsustained VT | • ICD<br>• Standard therapy | 95<br>101 | 27 mo (trial stopped | 0.46 | 0.26 to 0.82 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | • MI ≥3 wk prior<br>• Inducible VT<br>• NYHA class I to III | | | early by DSMB) | | |
| MADIT II (2002) | • LVEF ≤30%<br>• No history of VT<br>• MI ≥1 mo prior<br>• NYHA class I to 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) | • 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) | • 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><br><br><br>353 | 39 mo | 5-y outcomes[b]:<br>EPS-guided vs standard therapy: 0.80<br><br>ICD vs AAD alone: 0.42 | <br>0.64 to 1.01<br><br>0.29 to 0.61 |
| SCD HeFT (2005) | • LVEF ≤35%<br>• NYHA class II to III<br>• 52% received ICM<br>• Treated with ACE inhibitors and b-blockers | Ischemic patients:<br>• ICD<br>• Amiodarone<br>• Placebo | <br>431<br>426<br>453 | 45 mo | • ICD vs placebo<br>• Ischemic: 0.79[a]<br>Overall: 0.77[a] | <br>0.60 to 1.04<br>0.62 to 0.96 |
| **ICM with recent MI** | | | | | | |
| DINAMIT (2004) | • LVEF ≤35%<br>• NYHA class I to 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) | • MI in preceding 5-31 d<br>• At least 1 of the following:<br>o LVEF ≤40% and resting HR ≥90 or unsustained VT | • ICD<br>• Standard therapy | 445<br>453 | 37 mo | 1.04 | 0.81 to 1.35 |
| BEST-ICD (2005) | • LVEF ≤35%<br>• NYHA class I to III<br>• No unsustained VT or sustained ventricular | • EPS-guided therapy (24 got ICD) | 79 | 540 d | 1-year mortality[d]<br>• EPS-guided therapy: 14% | |

| | | | | | | |
|---|---|---|---|---|---|---|
| | arrhythmias (except primary VF)<br>• MI in preceding 5-30 d<br>• At least 1 other risk factor | • Standard therapy | | | • Conventional therapy: 18%<br>2-y mortality[d]<br>• EPS-guided therapy: 20%<br>• Conventional therapy: 29.5% | |
| **Nonischemic cardiomyopathy** | | | | | | |
| DEFINITE (2004) | • LVEF ≤35%<br>• NYHA class II to IV | • ICD and medical therapy<br>• Medical therapy alone | 229<br>229 | 29 mo | 0.65 (0.40 to 1.06) | |
| SCD HeFT (2005) | • LVEF ≤35%<br>• NYHA class II to III<br>• 48% with non-ICM<br>• Treated with ACE inhibitor and b-blocker | Nonischemic patients:<br>• ICD<br>• Amiodarone<br>• Placebo | 398<br>419<br>394 | 45 mo | ICD vs placebo<br>Nonischemic: 0.73[a]<br>Overall: 0.77[a] | 0.50 to 1.07<br>0.62 to 0.96 |
| COMPANION (2004) | • LVEF ≤35%<br>• NYHA class III to 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>**Nonischemic: 0.50**<br>Overall: 0.64 | 0.29 to 0.88<br>0.48 to 0.86 |
| AMIOVIRT (2003) | • LVEF ≤35%<br>• NYHA class I to III<br>• DCM<br>• Asymptomatic unsustained VT | • ICD<br>• Amiodarone | 51<br>52 | 2 y | 1-y survival[d]<br>• ICD: 96%<br>• Amiodarone: 90%<br>2-y survival[d]<br>• ICD: 88%<br>• Amiodarone: 87% | |
| CAT (2002) | • LVEF ≤30%<br>• NYHA class II to III<br>• No symptomatic VT, VF, or bradycardia<br>• Recent-onset DCM | • ICD<br>• Control | 50<br>54 | 23 mo (trials stopped early due to low event rates) | ICD: 4 deaths (8%)[d]<br>Control: 2 deaths (3.7%) | |
| DANISH (2016) | • LVEF ≤35%<br>• NYHA class II to IV<br>• 58% received CRT<br>• Almost all patients on ACE inhibitors or b-blockers; »60% treated with | • ICD and medical therapy<br>• Medical therapy | 556<br>560 | 5.6 y[c] | 0.87 | 0.68 to 1.12 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | mineralocorticoid-receptor antagonist | | | | | |

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

[a] 97.5% CI

[b] Relative risk

[c] Median

[d] Hazard ratio not given, no significant differences

**Systematic Reviews**

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. The COMPANION, DEFINITE, MADIT, MADIT II, SCD HeFT, AMIOVIRT, and CAT trials were included, representing 6134 patients for the direct ICD comparisons and 12638 patients overall.

Subsequent systematic reviews and meta-analyses of ICD trials in NICM incorporated the 2016 DANISH trial results. 2 reviews published in 2017 included the CAT, AMIOVIRT, DEFINITE, SCD HeFT, COMPANION, and DANISH trials; 1 review published in 2021 included the CAT, AMIOVIRT, DEFINITE, and DANISH trials; other reviews included all but the COMPANION trial. All reviews have concluded that there was a statistically significant overall reduction in mortality for ICD 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 (eg, 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. Reviewers included 10 studies that provided subgroup analyses. Subgroup data were available from at least 4 studies for sex, age (<65 years vs ≥65 years), and QRS interval (<120 ms vs ≥120 ms); they were combined to calculate a relative odds ratio) using random-effects meta-analyses. Other comparisons of subgroups were not meta-analyzed because too few studies compared them; however, no consistent differences between subgroups were found across studies for diabetes. The Woods et al (2015) individual patient data network meta-analysis (described previously) also examined ICD and medical therapy in various subgroups, and similarly concluded that ICD reduced mortality in patients with heart failure and reduced ejection for QRS interval less than 120 ms, 120 to 149 ms, and 150 ms or higher, ages less than 60 and 60 and older, and for men. However, the effect on mortality in women was not statistically significant (HR=0.93; 95% CI, 0.73 to 1.18).

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

| Study | Dates | Trials | Participants | N (Range) | Design | Duration |
|---|---|---|---|---|---|---|

| | | | | | | |
|---|---|---|---|---|---|---|
| Woods (2015) | 1990-2010 | 13 | Patients with heart failure who received ICD | 12,638 (17–2,521) | RCT | NR |
| Earley (2014) | 1996-2010 | 14 | Adults eligible to receive an ICD for primary prevention of SCD | NR | RCT, Nonrandomized comparative studies | NR |

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

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

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

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

**Registry Studies**

Fontenla et al (2016) reported on results from the Spanish UMBRELLA Registry, a multicenter, observational, prospective nationwide registry of 1514 patients implanted with Medtronic ICDs equipped with remote monitoring who were enrolled between 2012 and 2013. The mean age of enrollees was 64 years; 82% of the patients were men; and 65% received an ICD for primary prevention. 51% 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. 13% of the episodes of sustained ventricular arrhythmias self-terminated and did not require shocks. 175 (12%) patients had 482 appropriate shocks, and 76 (5%) patients had 190 inappropriate shocks.

**High-Risk HCM**

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. Most patients (83%) received an ICD for primary prevention of SCD. The 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%. 20% 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. Over a mean follow-up of 5.4 years, appropriate ICD discharges in response to ventricular tachycardia (VT) or ventricular fibrillation (VF) occurred in 77 (24%) patients, corresponding to an annual rate of appropriate discharges of 5.3%. At least 1 inappropriate shock occurred in 46 (14.3%) patients, corresponding to an annualized event rate of 3.0%. 92 (28.7%) patients required at least 1 surgical intervention for an ICD-related complication, with a total of 150 ICD-related reinterventions. Most reinterventions (n=105 [70%]) were related to lead dysfunction.

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

**Long QT Syndrome**
Horner et al (2010) reported on outcomes for 51 patients with genetically confirmed LQTS treated with an ICD from 2000 to 2010 who were included in a single-center retrospective analysis of 459 patients with genetically confirmed LQTS.24, Of patients treated with ICDs (84%) received the device as primary prevention. 12 (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. 10 (9.6%) patients received an ICD for secondary prevention and 94 (90.4%) patients received an ICD for primary prevention. During an average 9.3-year follow-up, 21 (20.2%) patients received a total of 81 appropriate shocks. In multivariate analysis, type 1 electrocardiogram with syncope and secondary prevention indication were significant predictors of appropriate therapy. 9 (8.7%) patients received 37 inappropriate shocks. 21 (20.2%) patients had other ICD-related complications.

Conte et al (2015) described outcomes for a cohort of 176 patients with spontaneous or drug-induced Brugada type 1 electrocardiographic (ECG) findings who received an ICD at a single institution and were followed for at least 6 months. 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 anti-tachycardia 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. 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 non-sustained 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. The indication for ICD therapy was syncope despite maximal β-blocker

therapy in 6 (46%) patients and aborted SCD in 7 (54%) patients. Over a median follow-up of 4.0 years, 10 (77%) patients received a median of 4 shocks. For 96 shocks, 87 ECGs were available for review; of those, 63 (72%) were appropriate and 24 (28%) inappropriate. Among appropriate shocks, 20 (32%) restored sinus rhythm.

**Cardiac Sarcoid**

Sarcoidosis is a systemic granulomatous disease of unknown etiology, with a worldwide prevalence of about 4.7–64 in 100,000. 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

Mantini et al (2012) published a review on the diagnosis and management of cardiac sarcoid, including a treatment algorithm. 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.

**Section Summary: TV-ICD for Primary Prevention in Adults**

**Ischemic Cardiomyopathy and Nonischemic Dilated Cardiomyopathy**

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

**Hypertrophic Cardiomyopathy**

Less evidence is available for the use of ICDs for primary prevention in patients with HCM. In a meta-analysis of cohort studies, the annual rates of appropriate ICD discharge were 3.3%, and the mortality rate was 1%. Given the long-term high-risk of SCD in patients with HCM, with the assumption that appropriate shocks are life-saving, these rates are considered adequate evidence for the use of TV-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 TV-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 TV-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. The median age was 16 years, although some adults included were as old as 54 years. A total of443 patients were included. The most common diagnoses were tetralogy of Fallot and HCM. ICD placement was performed for primary prevention in 52% of patients and secondary prevention in 48%. Over a 2-year follow-up, appropriate shocks occurred in 26% of patients and inappropriate shocks occurred in 21%.

Silka et al (1993) compiled a database of 125 pediatric patients treated with an ICD through a query of the manufacturers of commercially available devices. 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 1inappropriate shock. Actutimes rates of SCD-free survival were 97% at 1 year, 95% at 2 years, and 90% at 5 years.

Alexander et al (2004) reported on 90 ICD procedures in 76 young patients (mean age, 16 years; range, 1-30 years). 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 1 indication for ICD in this study. Over a median follow-up of 2 years, 28% of patients received an appropriate shock and 25% received an inappropriate shock. Lewandowski et al (2010) reported on long-term follow-up for 63 patients, between the ages 6 and 21 years, who were treated with an ICD device. At 10-year follow-up, 13 (21%) patients had surgical infections. 14 (22%) patients experienced at least 1 appropriate shock and 17 (27%) had at least 1 inappropriate shock. Serious psychological sequelae developed in 27 (43%) patients.

**Section Summary: Primary Prevention in Pediatric Populations**
The available evidence for the use of ICDs in pediatric patients is limited and consists primarily of small case series that include mixed populations with mixed indications for device placement. Overall, these studies have reported both relatively high rates of appropriate and inappropriate

shocks. Pediatric patients may be eligible for ICD placement if they have inherited cardiac ion channelopathy (see Inherited Cardiac Ion Channelopathy section).

**Transvenous Implantable Cardioverter Defibrillators for Secondary Prevention**
**Clinical Context and Therapy Purpose**
The purpose of TV-ICD placement is to provide a treatment option that is an alternative to or an improvement on existing therapies in patients with life-threatening ventricular tachyarrhythmia or fibrillation or who have been resuscitated from sudden cardiac arrest.

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

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

**Interventions**
The therapy being considered is TV-ICD placement. An ICD is a device designed to monitor a patient's heart rate, recognize ventricular fibrillation or ventricular tachycardia, and deliver an electric shock to terminate these arrhythmias to reduce the risk of sudden death.

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

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

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

**Secondary Prevention in Adults**
At least 5 trials comparing ICD plus medical therapy with medical therapy alone have been conducted in the secondary prevention setting: the Antiarrhythmics Versus Implantable Defibrillators (AVID) trial (n=1016), Cardiac Arrest Survival in Hamburg (CASH) trial (n=288), Canadian Implantable Defibrillator Study (CIDS)31, (n=659), Defibrillator Versus beta-Blockers for Unexplained Death in Thailand (DEBUT) trial (n=66; pilot, n=20; main study, n=46), and Wever et al (1995)33, (n=60). The trials are shown in Table 6. Mean length of follow-up varied from 18 to 57 months across trials. Lee et al (2003) combined the AVID, CASH, CIDS, and Wever et al (1995) trials in a meta-analysis of secondary prevention trials. The mortality analysis included 2023 participants and 518 events. In combined estimates, the ICD group had a significant reduction in both mortality (HR=0.75; 95% CI, 0.64 to 0.87) and SCD (HR=0.50; 95% CI, 0.34 to 0.62) compared with the group

receiving medical therapy alone. To support National Institute for Health and Care Excellence guidance on the use of ICDs, AVID, CASH, CIDS, and the pilot DEBUT participants were combined in a meta-analysis. 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). 2 other meta-analyses that included AVID, CIDS, and CASH reached similar conclusions.

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

| Trials | Participants | Treament Groups | | Mortality Groups | |
|---|---|---|---|---|---|
| | | **Group** | **N** | **RR** | **95% CI** |
| AVID (1997) | Patients resuscitated from near-fatal VT/VF, sustained VT with syncope, or sustained VT with LVEF ≤40% and symptoms | • ICD<br>• AAD | 507<br>509 | 0.66 | 0.51 to 0.85 |
| CASH (2000) | 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) | Patients with VF, out-of-hospital cardiac arrest requiring defibrillation, VT with syncope, VT with rate ≥150/min causing presyncope or angina in patient with LVEF ≤35% or syncope with inducible VT | • ICD<br>• Amiodarone | 329<br>331 | 0.85 | 0.67 to 1.10 |
| Wever et al (1995) | 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) | 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>• β-blocker therapy<br><br>**Main trial**<br>• ICD<br>• β-blocker therapy | <br>10<br>10<br><br><br>3 7<br>29 | • RR not calculable (DSMB stopped trial early due to efficacy of ICD)<br>• 7 deaths in β-blockers vs 0 in ICD | |

AAD: antiarrhythmic drugs; CI: confidence interval; DSMB: data safety monitoring board; ECG: electrocardiogram; ICD: implantable cardioverter defibrillator; LVEF: left ventricular ejection fraction; MI: myocardial infarction; RBBB: right bundle-branch block; RCT: randomized controlled trial; RR: relative risk; SUDS: sudden unexplained death syndrome; 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. A cohort of 6996 patients in the National Veterans Administration database, from 1995 to 1999, who had new-onset ventricular arrhythmia and preexisting ischemic heart disease and congestive heart failure were included. Of those, 1442 patients had received an ICD. Mortality was determined through the National Death Index at 3 years from the hospital discharge date. The cohort was stratified by quintiles of a multivariable propensity score created using many demographic and clinical confounders. The propensity score-adjusted mortality reduction for ICD compared with no ICD was an RR of 0.72 (95% CI, 0.69 to 0.79) for all-cause mortality and an RR of 0.70 (95% CI, 0.63 to 0.78) for cardiovascular mortality.

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

**Section Summary: TV-ICDs 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 TV-ICDs**
**Systematic Reviews: Mixed Adverse Events**
Characteristics and results of systematic reviews of adverse events associated with transvenous ICDs are described in Tables 7and 8. Persson et al (2014) conducted a systematic review of adverse events following ICD placement. In-hospital serious adverse event rates ranged from 1.2% to 1.4%, most frequently pneumothorax (0.4%-0.5%) and cardiac arrest (0.3%).

In another systematic review of adverse events following ICD placement, Ezzat et al (2015) compared event rates reported in clinical trials of ICDs with those reported in the U.S. National Cardiovascular Data Registry. 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 Kirkfelt et al (2014), in a population-based cohort study including all Danish patients who underwent a cardiac implantable electronic device procedure from 2010 to 2011 (562 [9.5%] of 5918 patients with at least 1 complication).

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. Reviewers included 18 trials and 3 subgroup analyses. 12 trials assessed ICDs, 4 of which used both thoracotomy and non-thoracotomy ICDs (n=951) and 8 of which used non-thoracotomy ICDs (n=3828). For non-thoracotomy 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 non-thoracotomy 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. Reviewers included 63 cohort studies with a total of 4916 patients (710 [10%] with arrhythmogenic right VT; 1037 [21%] with BrS; 28 [0.6%] with CPVT; 2466 [50%] with HCM; 162 [3.3%] with lamin *A/C* gene variants; 462 [9.4%] with LQTS; 51 [1.0%] with short QT syndrome).

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

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

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

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

| Study | Rate of Adverse Events | Rates of Specific Complications |
|---|---|---|
| Persson (2014) | | |
| Range | 1.2%–1.4%[1] | Device-related: <0.1%–6.4%<br>Lead-related: <0.1%–3.9%<br>Infection: 0.2%– 3.7%<br>Inappropriate shock: 3%–21% |
| Ezzat (2015) | 9.1 (CI 6.4% to 12.6%) | Access-related: 2.1% (CI 1.3%–3.3%)<br>Lead-related: 5.8% (CI 3.3%–9.8%)<br>Generator-related: 2.7% (CI 1.3%–5.7%)<br>Infection: 1.5% (CI 0.8%–2.6%) |
| Olde Nordkamp (2016) | 22% (4.4% per year; 3.6%–5.2%; p<0.001) | Lead malfunction: 10.3%<br>Infection: 3.0% (0.53% per year) Inappropriate shock: 20% (4.7% per year; CI 4.2%–5.3%; p<0.001) |

CI: 95% confidence interval; TV-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

**Systematic Reviews: Specific Complications**

**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 3-year post-market surveillance studies to address concerns related to premature insulation failure and important questions related to follow-up of affected patients. 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.

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

Birnie et al (2012) reported on clinical predictors of failure for 3169 Sprint Fidelis leads implanted from 2003 to 2007 at 11 centers participating in the Canadian Heart Rhythm Society study. 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).

In a large prospective multicenter study, Poole et al (2010) reported on complications rates associated with generator replacements and/or upgrade procedures of pacemaker or ICD devices, which included 1031 patients without a planned transvenous lead replacement (cohort 1) and 713 with a planned transvenous lead replacement (cohort 2). 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. 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. The 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. Of 226764 patients treated with an ICD between 2006 and 2008, lead dislodgement occurred in 2628 (1.2%). Factors associated with lead dislodgement were New York Heart Association class IV heart failure, AF or atrial flutter, a combined ICD and CRT device, and having the procedure performed by a 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. 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. 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. 24 of 2417 patients had infections, for a rate of 1.0%. 22 (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 (eg, 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. 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 vs1 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. Of 3161 ICDs included, 145 surgical reinterventions were required for 122 ICDs in 114 patients. 95 (66%) reinterventions were due to infection, and the remaining 50 (34%) were due to other causes. Compared with first-implanted ICDs, the occurrence of surgical reintervention in replacements was 2.5 (95% CI, 1.6 to 3.7) times higher for infection and 1.7 (95% CI, 0.9 to 3.0) times higher for non-infection-related causes.

**Inappropriate Shocks**

Inappropriate shocks may occur with ICDs due to faulty sensing or sensing of atrial arrhythmias with rapid ventricular conduction; these shocks may lead to reduced 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).

Tan et al (2014) conducted a systematic review to identify outcomes and adverse events associated with ICDs with built-in therapy-reduction programming. 6 randomized trials and 2 nonrandomized cohort studies (total n=7687 patients) were included (3598 with conventional ICDs, 4089 therapy-reduction programming). A total of 267 (4.9%) patients received inappropriate ICD shocks, 99 (3.4%) in the therapy-reduction group and 168 (6.9%) in the conventional programming group (RR=0.50; 95% CI, 0.37 to 0.61; p<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. 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. A total of 2790 patients with an indication for ICD placement were given a device programmed with a SmartShock Technology designed to differentiate between ventricular arrhythmias and other rhythms. The inappropriate shock incidence for dual-/triple-chamber ICDs was 1.5% at 1 year (95% CI, 1.0% to 2.1%), 2.8% at 2 years (95% CI, 2.1% to 3.8%), and 3.9% at 3 years (95% CI, 2.8% to 5.4%).

**Other Complications**
Lee et al (2010) evaluated rates of early complications among patients enrolled in a prospective, multicenter population-based registry of all newly implanted ICDs in Ontario, from 2007 through 2009. Of 3340 patients receiving an ICD, major complications (lead dislodgement requiring intervention, myocardial perforation, tamponade, pneumothorax, infection, skin erosion, hematoma requiring intervention) within 45 days of implantation occurred in 4.1% of new implants. Major complications were more common in women, in patients who received a combined ICD-CRT device, and in patients with a left ventricular end-systolic size of larger than 45 mm. Direct implant-related complications were associated with a major increase in early death (HR=24.9; p<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. 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 defibrillators (S-ICD) placement 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 review.

**Populations**
The 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 patient 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., patients with hypertrophic cardiomyopathy, congenital cardiomyopathies, or inherited channelopathies)

Individuals at high risk for bacteremia, such as patients on hemodialysis or with chronic indwelling endovascular catheters.
Patients with challenging vascular access or prior complications with T-ICDs

**Interventions**
The therapy being considered is S-ICD. An ICD is a device designed to monitor an individual's heart rate, recognize ventricular fibrillation or ventricular tachycardia, and deliver an electric shock to terminate these arrhythmias to reduce the risk of sudden death. A subcutaneous ICD (S-ICD, which lacks transvenous leads, is intended to reduce lead-related complications. The S-ICD is intended for individuals who have standard indications for an ICD, but who do not require pacing for bradycardia or anti-tachycardia overdrive pacing for VT. The S-ICD is proposed to benefit

individuals with limited vascular access (including patients undergoing renal dialysis or children) or those who have had complications requiring T-ICDs explanation.

**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. 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 ICD and have a contraindication to a T-ICD**

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

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

**Review of Evidence**
**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. 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 cadiogenetic phenotype, or had prespecified risk factors for lead complications. Of those, 503 were randomized to S-ICD (n=251) or T-ICD (n=252). Mean age of included patients was 49 years. The primary outcome focused on perioperative complications that are 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 under-powered to detect differences in clinical shock outcomes, however, extended follow-up is ongoing.

**Non-randomized 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 outcome for patients treated with S-ICD. Several publications from EFFORTLESS (Evaluation of Factors Impacting Clinical Outcome and Cost Effectiveness of the S-ICD), the pivotal trial submitted to the Food and Drug Administration for the investigational device exemption, and other studies are summarized in Table 10. In the EFFORTLESS registry, among 472 enrolled patients, the complication-free rate was 94% at 360 days and there was a 13.1% inappropriate shock rate at 3 years' follow-up. Gold et al (2021) reported 18-month data from the UNTOUCHED study, a multinational, prospective trial designed to assess the performance of the S-ICD in primary prevention patients with a low LVEF and New York Heart Association II/III heart failure or coronary artery disease. At 18 months, the complication-free rate was 92.7% and the inappropriate shock-free rate was 95.9%. 1-year data from the S-ICD Post Approval Study and 18-month data from the UNTOUCHED study have been published; these studies are ongoing. The S-ICD System Post-Approval Study (PAS) is a nonrandomized, standard-of-care registry in the United States that has prospectively enrolled and followed S-ICD recipients. 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. 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. 5-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 S-ICD**

| Study; Trial | Countries | N | Mean FU | Results | |
|---|---|---|---|---|---|
| | | | | **Outcomes** | **Values** |
| Burke et al (2020) S-ICD PASNCT01736618 | US | 1637 | 1 y | • 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)<br><br>UNTOUCHED | US, Canada, Europe | 1111 | 18 months | • Inappropriate shock-free rate at 18 months<br>• Appropriate shock-free rate at 18 months<br>• Complication-free rae 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); Olde Nordkamp et al (2015); Boersma et al (2017) EFFORTLESS S-ICD Registry | 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<br>• Inappropriate shocks through follow-up<br>• Appropriate shocks through follow-up | 8.4%<br>8.1%<br>11.7%<br>11.7%<br>13.5% |
| Weiss et al (2013) 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); Boersma et al (2016); Lambiase et al (2016) 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>o 1 year<br>o 2 years<br>o 3 years<br>• Incidence of inappropriate shock at 3 y | 11%<br>1.7%<br><br>1.6%<br>3.2%<br><br><br>5.3%<br>7.9%<br>10.5%<br>13.1% |
| Bardy et al (2010); Theuns et al (2015) | Europe, New Zealand | 55 | 5.8 y | • Devices replaced<br>• Devices explanted<br>• Replaced with TV-ICD<br>• Shocks recorded in 16 (29%) patients | 26 (47%)<br>5 (9%)<br>4 (7%)<br>119 |

| | | | | | |
|---|---|---|---|---|---|
| Olde-Nordkamp et al (2012) | Netherlands | 118 | 18mo | • All device-related complications<br>• Infections<br>• Dislodgements of device/leads<br>• Skin erosion<br>• Battery failure<br>• Replaced with TV-ICD<br>• Appropriate shocks experienced in 8 patients<br>• Total inappropriate shocks delivered to 15 (13%) patients<br>• Deaths (cancer, progressive heart failure) | 14%<br>5.9%<br>3.3%<br>1.7%<br>1.7%<br>1 (0.8%)<br>45<br>33<br>2 |

FU: follow-up; S-ICD: subcutaneous implantable cardioverter defibrillator; TV-ICD: transvenous implantable cardioverter defibrillator; VF: ventricular fibrillation; VT: ventricular tachycardia
[a] Median

**Section Summary: Subcutaneous-Implantable Cardioverter Defibrillators in Individuals with a Contraindication to a Transvenous Implantable Cardioverter Defibrillator**
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 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 Patients 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 review.

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

**Comparators**
The comparator of interest is T-ICD placement.

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

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

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

**Review of Evidence**

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

age of enrolled patients was 63 years (interquartile range, 55 to 70). Most enrolled patients were diagnosed with ischemic and nonischemic cardiomyopathy and 19.7% were women. The median left ventricular ejection fraction was 30%.

The primary end point in PRAETORIAN was the composite of device-related complications and inappropriate shocks (see Table 11 for outcome definitions). The trial was designed to test the hypothesis of noninferiority of the S-ICD as compared with the T-ICD with respect to the time from device implantation to the first occurrence of a primary end point event. The primary analysis was the modified intention-to-treat cohort (i.e. patients were analyzed in accordance to the treatment group to which they were originally assigned, regardless of withdrawals, losses to follow-up or crossovers). Patients who did not receive a device and patients who proved ineligible for 1 of the treatments due to incomplete or inadequate screening were excluded from this analysis. In the as-treated cohort, patients were analyzed in the group of the specific ICD type which they received at initial implantation regardless of randomization result, withdrawals, losses to follow-up or crossovers. The noninferiority margin for the upper boundary of the 95% confidence interval for the hazard ratio was set at 1.45.

The trial's main results are summarized in Tables 12-14. The S-ICD was noninferior to the T-ICD on the composite endpoint of device-related complications and inappropriate shocks. The hazard ratio for the primary end point was 0.99 (95% confidence interval [CI], 0.71 to 1.39; noninferiority margin, 1.45; P =.01 for noninferiority; P =.95 for superiority). Results for the modified ITT analysis and as-treated analysis did not differ. There were more device related complications in the T-ICD group and more inappropriate shocks in the S-ICD group, but the trial was not powered for these endpoints. Secondary endpoints and mortality results are summarized in Table 13. There were more deaths from any cause in the S-ICD group than in the T-ICD group (16.4% vs 13.1%; hazard ratio 1.23; 95% CI, 0.89 to 1.70), but the number of 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%; hazard ratio 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 hazard ratio for all-cause mortality was 1.23 (95% CI, 0.89 to 1.70). The PRAETORIAN trial investigators conducted competing risks analyses to account for discontinuation of follow-up before the primary end point had occurred in (1) the modified ITT population with competing risk of death, and (2) the true ITT population with competing risk of death and discontinuation of follow-up. These analyses led to consistent estimates of the hazard ratio (and 95% confidence interval) for the primary end point.

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

**Table 11. PRAETORIAN Trial Characteristics**

| Study | Countries | Sites | Dates | Participants | Interventions | | Primary Endpoint Definitions |
|---|---|---|---|---|---|---|---|
| **PRAETORIAN**<br><br>**Knops et al (2020)** | | | | | **Active** | **Comparator** | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Europe (92.4%) and US | 39 | March 2011 through January 2017 | Eligibility:18 years and older Class I or IIa indication for ICD therapy for primary or secondary prevention, according to professional society guidelines. Exclusions: Previous ICD implantation, unsuitability for S-ICD therapy according to QRS-T–wave sensing analysis, and indications for either bradycardia pacing or biventricular pacing. | Subcutaneous ICD (N = 426) | Transvenous ICD (N = 423) | Composite of device-related complications and inappropriate shocks. Inappropriate shocks were defined as shock therapy for anything else but ventricular fibrillation or ventricular tachycardia, for example supraventricular tachycardia with fast ventricle response (including sinus tachycardia and atrial fibrillation), T-wave oversensing, detection of physiological- or other non-cardiac activity and lead- or device failure. Complications included:<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;<br>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; VF: ventricular fibrillation; VT: ventricular tachycardia

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

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

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

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

| Study | End Point | Subcutaneous IC (N=426) | Transvenous ICD (N=423) | Hazard Ratio (95% CI) |
|---|---|---|---|---|
| **PRAETORIAN**<br><br>**Knops et al (2020)** | Death from any cause | 83 (16.4%) | 68 (13.1%) | 1.23 (0.89–1.70) |
| | Sudden cardiac death | 18 (4.2%) | 18 (4.3%) | |
| | Other cardiovascular death | 34 (8.0%) | 28 (6.6%) | |
| | Non-cardiovascular death | 31 (7.3%) | 22 (5.2%) | |
| | Appropriate shock therapy | 83 (19.2%) | 57 (11.5%) | 1.52 (1.08–2.12) |
| | Anti-tachycardia pacing (appropriate) | 6 (0.6%) | 54 (12.9%) | |
| | Anti-tachycardia pacing (inappropriate) | 1 (0.3%) | 30 (7.2%) | |
| | Major adverse cardiac event | 64 (13.3%) | 80 (16.4%) | 0.80 (0.57–1.11) |
| | Hospitalization for heart failure | 79 (17.4%) | 74 (16.1%) | 1.08 (0.79–1.49 |

| | | | | |
|---|---|---|---|---|
| | Crossover to other study device | 18 (4.3%) | 11 (2.7%) | 1.64 (0.77–3.47) |

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

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

| Study | End Point | Subcutaneous IC (N=426) | Transvenous ICD (N=423) |
|---|---|---|---|
| **PRAETORIAN**<br><br>**Knops et al (2020)** | 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; ITT: intention-to-treat; PRAETORIAN: Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter Defibrillator Therapy

Study relevance, design and conduct limitations of PRAETORIAN are summarized in Tables 15 and 16. The choice of a composite primary endpoint poses several challenges to interpreting the results of PRAETORIAN. In PRAETORAN, the components of the composite endpoint were discordant; device-related complications were expected to favor S-ICD and inappropriate shocks were expected to favor T-ICD. The timing of the components of the composite outcome assessment is important in interpreting the study results and explaining expected treatment results to patients. Early benefit could favor 1 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." 5-year data from the S-ICD PAS should provide more information on longer-term adverse events such as lead failure and need for device replacement.

Quality of life data from PRAETORIAN was collected but has not yet been published. This data could shed light on the relative importance to patients of adverse events such as inappropriate shocks and device replacement, especially if quality of life data were reported by subgroups of patients who experienced shocks. For example, these data might indicate that inappropriate shocks are so distressing to patients that they outweigh any potential benefits of S-ICDs.
Finally, the under-enrollment of women in the trial (19.7%) potentially limits the applicability of its results, although a subgroup analysis by sex was consistent with the primary analysis on the composite endpoint (Hazard Ratio in women 0.65; 95% CI 0.28 to 1.47).

**Table 15. Study Relevance Limitations**

| Study | Population[a] | Intervention[a] | Comparator[c] | Outcomes[d] | Duration of Follow-Up[e] |
|---|---|---|---|---|---|
| PRAETORIAN<br><br>Knops et al (2020) | 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] | Date Completeness[d] | Power[e] | Statistical[f] |
|---|---|---|---|---|---|---|
| **PRAETORIAN**<br><br>**Knops et al (2020)** | | 2. clinical-events committee was not blinded to treatment assignment | 2. Quality of life data collected but not yet published. | | | 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.

### 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 Nonrandomized Trials of Subcutaneous Implantable Cardioverter Defibrillators**

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

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | • Failure to cardiovert VA | | | |
| Kobe et al (2017) | Sex- and age-matched case-control | 120 (60 pairs); 84 pairs analyzed | 942 d vs 622 d | • Posttraumatic 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) | Retrospective analysis of propensity-matched cohort | 334 (167 matched pairs) | 6 mo | • SF-12 physical well-being score<br>• SF-12 mental well-being score | 43<br>45 | 44<br>45 | |
| Brouwer et al (2016) | Retrospective analysis of propensity-matched cohort | 280 (140 matched pairs) | 5 y | • 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 intervention (HR=1.3; 95% CI, NR; p=0.42)<br>• Survival | 18%<br>11.5%<br>2.2%<br>3.6%<br>31%<br>30%<br>95% | 14%<br>0.8%<br>9.9%<br>4.1%<br>17%<br>21%<br>96% | |
| Friedman et al (2016) | Retrospective analysis of propensity-matched cohort from NCDR for ICD | 5760 (1920 matched, groups) | NR | • Any in-hospital complication<br>• Deaths<br>• Infections<br>• Lead dislodgements<br>• Pneumothorax | 0.6%<br>0.1%<br>0%<br>0.2%<br>0.2% | 0.9%<br>0.2%<br>0.05%<br>0.1%<br>0% | 1.5%<br>0.05%<br>0.1%<br>0.6%<br>0.3% |
| Kobe et al (2013) | Sex- and age-matched case-control | 138 (69 matched pairs) | 217 d[a] | • Pericardial effusion<br>• Successful termination of induced VF<br>• Appropriate shocks<br>• Inappropriate shocks | 1<br>91%<br>9<br>3 | 0<br>90%<br>3<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-Item Short-Form Health Survey; S-ICD: subcutaneous

implantable cardioverter defibrillator; TV-ICD: transvenous implantable cardioverter defibrillator; VA: ventricular arrhythmia; VF: ventricular fibrillation
[a] Mean

**Section Summary: Subcutaneous Implantable Cardioverter Defibrillators In Patients With No Contraindications to a Transvenous Implantable Cardioverter Defibrillator**

The PRAETORIAN trial is the only RCT on the effect of an S-ICD with health outcomes. PRAETORIAN found that S-ICD was noninferior to T-ICD on a composite outcome of complications and inappropriate shock at 48 months (Hazard Ratio 0.99; 95% confidence interval, 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.

## VII. Supplemental Information

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

**Clinical Input from Physician Specialty Societies and Academic Medical Centers**

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

**2020 Medical Advisory Panel**

In October 2020, the BCBSA Medical Advisory Panel (MAP) reviewed the evidence for individuals who need an ICD and have no contraindication to TV ICD placement and agreed that for this indication, the evidence is insufficient to determine the effects of the technology on health outcomes.

**2015 Input**

In response to requests, input was received from 1 physician specialty society (4 responses) and 5 academic medical centers, for a total of 9 responses, while this policy was under review in 2015. Input focused on use of ICDs as primary prevention for cardiac ion channelopathies and on use of the subcutaneous implantable cardioverter defibrillator (S-ICD). Reviewers generally indicated that an ICD should be considered medically necessary for primary prevention of ventricular arrhythmias in adults and children with a diagnosis of long QT syndrome, Brugada syndrome, short QT syndrome, and catecholaminergic polymorphic ventricular tachycardia. Reviewers generally indicated that the S-ICD should be considered medically necessary particularly for patients with indications for an ICD but who have difficult vascular access or have had transvenous ICD lead explantation due to complications.

**2011 Input**

In response to requests, input was received from 6 academic medical centers while this policy was under review in 2011. For most policy indications, including pediatric, there was general agreement from those providing input. On the question of timing of ICD placement, input was mixed, with some commenting about the potential role of early implantation in select patients. Reviewers indicated that a waiting period of 9 months for patients with nonischemic cardiomyopathy was not supported by the available evidence or consistent with the prevailing practice patterns in academic medical centers. Input emphasized the difficulty of prescribing strict timeframes given the uncertainty of establishing the onset of cardiomyopathy and the inability to risk-stratify patients based on time since onset of cardiomyopathy.

**Practice Guidelines and Position Statements**

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

**American Heart Association/ American College of Cardiology 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. This guideline includes ICD recommendations which are summarized in Table 18.

**Table 18. 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 non-arrhythmic death (either cardiac or noncardiac) is deemed low based on the patient's burden of comorbidities and functional status." | | A |
| "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. Recommendations relevant to this review are summarized in Table 19.

**Table 19. 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-yearsudden 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 consideration patient preferences, lifestyle, and expected potential need for pacing for bradycardia or ventricular tachycardia termination. | I | B-NR |

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

**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 (HRS) (2017) published joint guidelines on the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. This guideline supersedes the 2008 guideline for device-based therapy of cardiac rhythm abnormalities and the subsequent 2012 focused update. The most up-to-date recommendations on the use of transvenous ICD devices from the 2017 guidelines are presented in Tables 20 to 24. Table 25 summarizes the most up-to-date recommendations regarding S-ICDs.

**Table 20. Recommendations on Use of ICDs as Secondary Prevention of SCD of Ischemic Heart Disease or Nonischemic Cardiomyopathy**

| Recommendation | COR | LOE |
|---|---|---|
| "In patients with ischemic heart disease, who either survive SCA due to VT/VF or experience hemodynamically unstable VT (LOE: B-R) or stable sustained 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 |
| "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 non arrhythmic 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 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-R<br>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%), an ICD is recommended if meaningful survival of greater than 1 year is expected." | I | 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%), an 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 21. Recommendations on Use of ICDs as a Primary Prevention of Ischemic Heart Disease or Nonischemic Cardiomyopathy**

| Recommendation | COR | LOE |
|---|---|---|
| "In patients with LVEF of 35% or less that is due to ischemic heart disease who are at least 40 days' post-MI and at least 90 days post-revascularization, and with NYHA class II or III HF despite GDMT, 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 post-revascularization, 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 non-arrhythmic 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 non-hospitalized 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." | IIIa | 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%, non missense 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." | IIIa | C-EO |

A: high; B-NR: moderate, non-randomized; B-R: moderate, randomized; C-EO: consensus of expert opinion; CRT: cardiac resynchronization therapy; COR: class of recommendation; ICD: implantable cardioverter defibrillator; GDMT: guideline-directed management and therapy; HF: heart failure; LOE: level of evidence; LVAD: left ventricular assist device; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NICM: nonischemic cardiomyopathy; NSVT: non-sustained ventricular tachycardia; NYHA: New York Heart Association; SCD: sudden cardiac death; VA: ventricular arrhythmia; VF: ventricular fibrillation; VT: ventricular tachycardia

[a] No benefit

**Table 22. 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..." | I | B-NR |
| "In patients with HCM and 1 or more of the following risk factors...<br>a. Maximum LV wall thickness ≥30 mm (LOE: B-NR).<br>b. SCD in 1 or more first-degree relatives presumably caused by HCM (LOE: C-LD).<br>c. 1 or more episodes of unexplained syncope within the preceding 6 months (LOE: C-LD)" | IIa | <br>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 features..." | IIa | B-NR<br>C-LD |
| "In patients with HCM who have NSVT (LOE: B-NR) or an abnormal blood pressure response with exercise (LOE: B-NR) but do not have any other SCD risk modifiers, an ICD may be considered, but its benefit is uncertain." | IIB | B-NR<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 23. Recommendations on Use of Subcutaneous 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 1year 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; ICD: implantable cardioverter defibrillator; COR: class of recommendation; LOE: level of evidence; VT: ventricular tachycardia; SCA: sudden cardiac arrest; LVEF: left ventricular ejection fraction; MRI: magnetic resonance imaging; VA: ventricular arrhythmia

**Table 24. 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 25. 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; C-LD: limited data; CRT: cardiac resynchronization therapy; COR: class of recommendation; ICD: implantable cardioverter defibrillator; LOE: level of evidence; VT: ventricular tachycardia
[a] Harm

### Heart Rhythm Society- Arrhythmogenic Cardiomyopathy (2019)

In 2019, the HRS published a consensus statement on evaluation, risk stratification, and management of arrhythmogenic cardiomyopathy. Recommendations related to ICD risk stratification and placement decisions are shown in Table 26.

**Table 26. Recommendations on Risk Stratification and ICD Decisions**

| Recommendation | COR1 | LOE2 |
|---|---|---|
| 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, 2 major and 2 minor, or 1 major and 4 minor risk factors for ventricular arrhythmia. | IIa | B-NR |
| ICD implantation may be reasonable for individuals with ARVC and 2 major, 1 major and 2 minor, or 4 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 2 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 |

ICD: Implantable cardioverter defibrillator; ACM: arrhythmogenic cardiomyopathy; ARVC: arrhythmogenic right ventricular cardiomyopathy; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; NSVT: non-sustained ventricular tachycardia; VT: ventricular tachycardia; FLNC: filamin-C; HRS: Heart Rhythm Society; COR: Class of Recommendation; LOE: Level of Evidence1 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 HRS, the European Heart Rhythm Association, and the Asia-Pacific Heart Rhythm Society (2013) issued a consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes, which included recommendations on ICD use in patients with long QT syndrome, Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia, and short QT syndrome (see Table 27).

**Table 27. 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 standalone therapy is not indicated in an asymptomatic patient with a diagnosis of CPVT | III[a] |
| Short QT syndrome | |
| ICD implantation is recommended in symptomatic patients with a diagnosis of SQTS who:<br>• Are survivors of cardiac arrest and/or<br>• Have documented spontaneous VT with or without syncope. | I |
| ICD implantation may be considered in asymptomatic patients with a diagnosis of SQTS and a family history of sudden cardiac death. | IIb |

BrS: Brugada syndrome; COR: class of recommendation; CPVT: catecholaminergic polymorphic ventricular tachycardia; ECG: electrocardiogram; 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 Sarcoid (2014)**

In 2014, the HRS published a consensus statement on the diagnosis and management of arrhythmias associated with cardiac sarcoidosis, including recommendations for ICD implantation in patients with cardiac sarcoid (Table 28). The writing group concluded that although there are few data specific to ICD use in patients with cardiac sarcoid, data from the major primary and secondary prevention ICD trials were relevant to this population and recommendations from the general device guideline documents apply to this population.

**Table 28. Recommendations for ICD Implantation in Patients with Cardiac Sarcoid**

| Recommendation | COR 1 |
|---|---|
| ICD implantation is recommended in patients with cardiac sarcoidosis and 1 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 1 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 LGEon 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 1 or more of the following:<br>• Incessant ventricular arrhythmias;<br>• Severe New York Heart Association class IV heart failure. | III |

**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. The statement made the following recommendations on the use of ICD therapy in adults with congenital heart disease (see Table 29).

**Table 29. 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, non-sustained 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 non-hospitalized adults with CHD awaiting heart transplantation. | Ib | C |
| ICD therapy may be considered for adults with syncope and moderate or complex CHD in whom there is a high clinical suspicion of ventricular arrhythmia and in whom thorough invasive and noninvasive investigations have failed to define a cause. | Ib | C |
| Adults with CHD and advanced pulmonary vascular disease (Eisenmenger syndrome) are generally not considered candidates for ICD therapy. | III[a] | |
| Endocardial leads are generally avoided in adults with CHD and intracardiac shunts. Risk assessment regarding hemodynamic circumstances, concomitant anticoagulation, shunt closure prior to endocardial lead placement, or alternative approaches for lead access should be individualized. | III[a] | |

AV: arterioventricular; CHD: congenital 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. Table 30 summarizes recommendations for ICD therapy from this statement.

**Table 30. 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, non-sustained 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, non-sustained 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: congenital 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: non-ischemic dilated cardiomyopathy; SCA: sudden cardiac arrest; SCD: sudden cardiac death; VF: ventricular fibrillation; VT: ventricular tachycardia

**U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS**

Not applicable

**MEDICARE NATIONAL COVERAGE**

There is a National Coverage Determination for ICDs. 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 VF.
2. Patients with a prior MI and a measured 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 tachyarrhytmias (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
   - Any disease, other than cardiac disease (e.g., cancer, renal failure, liver failure) associated with a likelihood of survival less than 1 year
   - Supraventricular tachycardia such as atrial fibrillation with a poorly controlled ventricular rate

**Ongoing and Unpublished Clinical Trials**

Some currently unpublished trials that might influence this review are listed in Table 31.

**Table 31. Summary of Key Trials**

| NCT No. | Trial Name | Planned Enrollment | Completion Date |
|---|---|---|---|

| | | | |
|---|---|---|---|
| *Ongoing* | | | |
| NCT02845531 | Implantable Cardioverter Defibrillator Versus Optimal Medical Therapy In Patients With Variant Angina Manifesting as Aborted Sudden Cardiac Death (VARIANT ICD) | 140 | Jun 2023 |
| NCT01296022a | Randomized Trial to Study the Efficacy and Adverse Effects of the Subcutaneous and Transvenous Implantable Cardioverter Defibrillator (ICD) in Patients With a Class I or IIa Indication for ICD Without an Indication for Pacing | 850 | Dec 2023 (extended follow-up) |
| NCT01085435[a] | Evaluation oF Factors Impacting Clinical Outcome and Cost Effectiveness of the S-ICD (The EFFORTLESS S-ICD Registry) | 994 | Dec 2023 |
| NCT02787785[a] | Multicenter Automatic Defibrillator Implantation Trial With Subcutaneous Implantable Cardioverter Defibrillator (MADIT S-ICD) | 40 | Dec 2023 |
| *Unpublished* | | | |
| NCT01736618[a] | Subcutaneous Implantable Cardioverter Defibrillator System Post Approval Study (UNTOUCHED) | 1766 | Oct 2021 |
| NCT00673842a | Risk Estimation Following Infarction Noninvasive Evaluation - ICD Efficacy | 1000 | Dec 2021 |

NCT: national clinical trial

[a] Denotes industry-sponsored or cosponsored trial

## VIII. Important Reminder

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii's Patients' Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), and for QUEST members, under Hawaii Administrative Rules (HAR 1700.1-42), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA's determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

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## X. Appendix

**Table 1. New York Heart Association (NYHA) Functional Classification**

| Class | Patient Symptoms |
|---|---|
| I | Patients with cardiac disease but without resulting limitations of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain. |
| II | Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain. |
| III | Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary physical activity causes fatigue, palpitation, dyspnea, or anginal pain. |
| IV | Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency or of the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased. |

## XI. Policy History

| Action Date | Action |
|---|---|
| September 16, 2014 | Policy reviewed by Medical Director Stefanie Park, M.D. |
| February 17, 2015 | Policy approved by Medical Directors |
| February 27, 2015 | Policy approved by UMC |
| January 19, 2016 | Policy approved by Medical Directors |
| January 22, 2016 | Policy approved by UMC |
| February 17, 2017 | Policy reviewed by Medical Director Stefanie Park, M.D. |
| February 21, 2017 | Policy approved by Medical Directors |
| March 24, 2017 | Policy approved by UMC |
| August 02, 2018 | Policy reviewed by Medical Director Rupal Gohil, M.D. |
| August 07, 2018 | Policy approved by Medical Directors |
| August 29, 2018 | Policy approved by UMC |
| January 01, 2019 | 90 Day Notice |
| November 14, 2019 | Policy reviewed by Medical Director Rupal Gohil, M.D. |
| November 19, 2019 | Policy approved by Medical Directors |
| December 20, 2019 | Policy approved by UMC |
| November 24, 2020 | Policy reviewed by Medical Director Rupal Gohil, M.D. |
| December 1, 2020 | Policy approved by Medical Directors |
| December 18, 2020 | Policy approved by UMC |
| November 9, 2021 | Policy reviewed by Medical Director Rupal Gohil, M.D. |
| November 16, 2021 | Policy approved by Medical Directors |
| November 19, 2021 | Policy approved by UMC |
| June 28, 2022 | Policy reviewed by Medical Director Christopher Kwock, M.D. |
| July 5, 2022 | Policy approved by Medical Directors |

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| July 22, 2022 | Policy approved by UMC |
| May 15, 2023 | Policy reviewed by Medical Director Christopher Kwock, M.D. |
| June 6, 2023 | Policy approved by Medical Directors |
| June 23, 2023 | Policy approved by UMC |
| October 1, 2023 | Policy effective date following notification period |