Automatic Implantable Cardioverter Defibrillator (AICD)

Policy # 00008
Original Effective Date: 05/12/2003
Current Effective Date: 12/20/2017

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: "Biventricular Pacemakers for the Treatment of Congestive Heart Failure." is addressed in medical policy 00009.

ADULTS

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider the use of an automatic implantable cardioverter defibrillator (AICD) in adults to be **eligible for coverage**.

Primary Prevention

Patient Selection Criteria

Coverage eligibility the use of an automatic implantable cardioverter defibrillator (AICD) in adults will be considered when the following criteria are met:

- Ischemic cardiomyopathy with New York Heart Association functional Class II or Class III symptoms, a history of myocardial infarction at least 40 days before automatic implantable cardioverter defibrillator (AICD) treatment, and left ventricular ejection fraction (LVEF) of 35% or less; or
- Ischemic cardiomyopathy with New York Heart Association functional Class I symptoms, a history of myocardial infarction at least 40 days before automatic implantable cardioverter defibrillator (AICD) treatment, and left ventricular ejection fraction (LVEF) of 30% or less; or
- Nonischemic dilated cardiomyopathy and left ventricular ejection fraction (LVEF) of 35% or less, after reversible causes have been excluded, and the response to optimal medical therapy has been adequately determined; or
- Hypertrophic cardiomyopathy with 1 or more major risk factors for sudden cardiac death (history of premature hypertrophic cardiomyopathy-related sudden death in 1 or more first-degree relatives younger than 50 years; left ventricular hypertrophy greater than 30 mm; 1 or more runs of nonsustained ventricular tachycardia at heart rates of 120 beats per minute or greater on 24-hour Holter monitoring; prior unexplained syncope inconsistent with neurocardiogenic origin) and judged to be at high risk for sudden cardiac death by a physician experienced in the care of patients with hypertrophic cardiomyopathy.
- 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; OR
- Brugada syndrome; OR
- Short QT syndrome; OR
- Catecholaminergic polymorphic ventricular tachycardia.

Note: Symptomatic heart failure is defined as the presence of dyspnea on exertion, angina, palpitations or fatigue.

Secondary Prevention
Patient Selection Criteria
Coverage eligibility for the use of an automatic implantable cardioverter defibrillator (AICD) in adults will be considered when the following criteria are met:

- As a secondary prevention for patients 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.

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company may consider the use of an automatic implantable cardioverter defibrillator (AICD) in adults for primary prevention patients in the following situations to be **investigational*:**

- Have had an acute myocardial infarction (i.e., less than 40 days before automatic implantable cardioverter defibrillator (AICD) treatment);
- Have New York Heart Association Class IV congestive heart failure (unless patient is eligible to receive a combination cardiac resynchronization therapy automatic implantable cardioverter defibrillator device [AICD]);
- Have had cardiac revascularization procedure in past three months (coronary artery bypass graft [CABG] or percutaneous transluminal coronary angioplasty) or are candidates for a cardiac revascularization procedure; or
- Have noncardiac disease that would be associated with life expectancy less than one year.

Based on review of available data, the Company considers the use of an automatic implantable cardioverter defibrillator (AICD) when patient selection criteria are not met to be **investigational.***

Based on review of available data, the Company considers use of the automatic implantable cardioverter defibrillator (AICD) for secondary prevention in patients who do not meet the criteria for secondary prevention to be **investigational.***

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PEDIATRICS

When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider use of an automatic implantable cardioverter defibrillator (AICD) in children who meet any of the following criteria to be **eligible for coverage**:

- Survivors of cardiac arrest, after reversible causes have been excluded;
- Symptomatic, sustained ventricular tachycardia in association with congenital heart disease in patients who have undergone hemodynamic and electrophysiologic evaluation; or
- Congenital heart disease with recurrent syncope of undetermined origin in the presence of either ventricular dysfunction or inducible ventricular arrhythmias.
- Hypertrophic cardiomyopathy (HCM) with 1 or more major risk factors for sudden cardiac death (history of premature HCM-related sudden death in 1 or more first-degree relatives younger than 50 years; massive left ventricular hypertrophy based on age-specific norms; prior unexplained syncope inconsistent with neurocardiogenic origin) and judged to be at high risk for sudden cardiac death by a physician experienced in the care of patients with HCM.
- Diagnosis of any one of the following cardiac ion channelopathies and considered to be at high risk for sudden cardiac death:
    - Congenital long QT syndrome (LQTS); OR
    - Brugada syndrome (BrS); OR
    - Short QT syndrome (SQTS); OR
    - Catecholaminergic polymorphic ventricular tachycardia (CPVT).

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of the automatic implantable cardioverter defibrillator (AICD) for all other indications in pediatric patients to be **investigational.***

SUBCUTANEOUS ICD
When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider the use of a subcutaneous implantable cardioverter defibrillator (ICD) to be **eligible for coverage** in adults or children who have an indication for ICD implantation for primary or secondary prevention for any of the above reasons and meet all of the following criteria:

- Have a contraindication to a transvenous ICD due to one 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 patient with anticipated long-term need for ICD therapy); or (3) history of need for explantation of a transvenous ICD due to a complication, with ongoing need for ICD therapy.
- Have no indication for antibradycardia pacing; AND
- Do not have ventricular arrhythmias that are known or anticipated to respond to antitachycardia pacing.

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of a subcutaneous implantable cardioverter defibrillator (ICD) for individuals who do not meet the criteria outlined above to be **investigational.***

Policy Guidelines

This evidence review addresses the use of 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 are referring 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 patients 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 PATIENTS 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 patients with cardiac ion channelopathies derive from results of clinical input, a 2013 consensus statement from the HRS, European Heart Rhythm Association (EHRA), and the Asia-

Pacific Heart Rhythm Society on the diagnosis and management of patients with inherited primary arrhythmia syndromes (Priori et al, 2013), 2012 guidelines from ACC, AHA, and HRS on device-based therapy of cardiac rhythm abnormalities (Epstein et al, 2013), and a report from the HRS and EHRA's Second Consensus Conference on Brugada syndrome (Antzelevitch et al, 2005).

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

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

NOTE: For congenital LQTS, patients may have 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 patients with a family history of sudden cardiac death due to LQTS, infants with a diagnosis of LQTS with functional 2:1 atrioventricular block, patients with a diagnosis of LQTS in conjunction with a diagnosis of Jervell and Lange-Nielsen syndrome or Timothy syndrome, and patients with a diagnosis of LQTS with profound QT prolongation (>550 ms). These factors should be evaluated on an individualized basis by a clinician with expertise in LQTS when considering the need for ICD placement.

Background/Overview

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

ICDs monitor a patient's heart rate, recognize ventricular fibrillation (VF) or ventricular tachycardia (VT), and deliver an electric shock to terminate these arrhythmias to reduce the risk of SCD. Indications for ICD placement can be broadly subdivided into (1) secondary prevention, 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 VF.

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 shock when a malignant arrhythmia is recognized.

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

Several automatic ICDs have been approved by the U.S. Food and Drug Administration (FDA) through the premarket approval process. 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. In addition, devices typically have approval in the secondary prevention setting for patients with a previous myocardial infarction and reduced injection fraction.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration

Transvenous Implantable Cardioverter Defibrillators

A large number of ICDs have been approved by the U.S. FDA through the premarket approval (PMA) process (FDA product code: LWS). A 2014 review of FDA approvals of cardiac implantable devices reported that, between 1979 and 2012, 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.

Subcutaneous ICDs
In September 2012, the Subcutaneous Implantable Defibrillator (S-ICD™)‡ System was approved by FDA through the PMA process for the treatment of life-threatening ventricular tachyarrhythmias in patients who do not have symptomatic bradycardia, incessant ventricular tachycardia, or spontaneous, frequently recurring ventricular tachycardia that is reliably terminated with antitachycardia pacing (see Table 1).

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

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 (St. Paul, MN)	Jul 1993
Current® Plus ICD (originally: Cadence Tiered Therapy Defibrillation System)	St. Jude Medical (St. Paul, MN)	Jul 1993
Dynagen™, Inogen™, Origen™, and Teligen® Family (originally: Ventak, Vitality, Cofient family)	Boston Scientific (Marlborough, MA)	Jan 1998
Evera™ Family (originally: Virtuosos/Entrust/Maximo/ Intrisic/Marquis family)	Medtronic (Minneapolis, MN)	Dec 1998
Subcutaneous		
Subcutaneous Implantable Defibrillator System (S-ICD)	Cameron Health (San Clemente, CA); 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.

Centers for Medicare and Medicaid Services (CMS)
In January 2005, Medicare issued the following revised national coverage guideline for the use of ICDs.
The CMS determined that the evidence is adequate to conclude that an ICD is reasonable and necessary for the following:

- Patients with ischemic dilated cardiomyopathy (IDCM), documented prior MI, NYHA Class II and III heart failure, and measured LVEF of 35% or less;
- Patients with nonischemic dilated cardiomyopathy (NIDCM) >9 months, NYHA Class II and III heart failure, and measured LVEF of 35% or less;
- Patients who meet all current CMS coverage requirements for a cardiac resynchronization therapy (CRT) device and have NYHA Class IV heart failure;

For each of these groups, patients must not have:

- Cardiogenic shock or symptomatic hypotension while in a stable baseline rhythm;
- Had CABG or percutaneous transluminal coronary angioplasty (PTCA) within the past 3 months;
- Had an acute MI within the past 40 days;
- Clinical symptoms or findings that would make them a candidate for coronary revascularization;
- Irreversible brain damage from pre-existing cerebral disease;
- Any disease, other than cardiac disease (e.g., cancer, uremia, liver failure), associated with a likelihood of survival less than 1 year;

In addition, CMS specifies that the beneficiary receiving the ICD implantation for primary prevention must be enrolled in either a U.S. FDA-approved category B Investigational Device Exemption clinical trial (42 CFR §405.201), a trial under the CMS Clinical Trial Policy (NCD Manual §310.1), or a qualifying data collection system including approved clinical trials and registries.
The Medicare policy for ischemic and nonischemic dilated cardiomyopathy is consistent with this policy.

Rationale/Source

TRANSVENOUS IMPLANTABLE CARDIOVERTER DEFIBRILLATORS

Primary Prevention in Adults

Transvenous implantable cardioverter defibrillators (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 Nonischemic Dilated Cardiomyopathy

Randomized Controlled Trials

At least 13 RCTs of ICDs for primary prevention have been conducted. Five were in populations with ischemic cardiomyopathy with prior myocardial infarction (MI; usually ≥3 weeks post-MI):

- Multicenter Automatic Defibrillator Implantation Trial (MADIT);
- MADIT II;
- CABG Patch trial;
- Multicenter Unsustained Tachycardia Trial (MUSTT); and
- Sudden Cardiac Death in Heart Failure (SCD HeFT) trial.

Three trials were conducted in patients implanted with ICD in the first few weeks following MI (recent MI):

- Defibrillator in Acute Myocardial Infarction Trial (DINAMIT);
- Immediate Risk Stratification Improves Survival (IRIS) trial; and
- BEta-blocker STrategy plus ICD (BEST-ICD) trial.

Six trials were conducted in populations with NIDCM:

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

The characteristics and mortality results for these 3 groups of trails are shown in Table 2.

Most of the trials for both ischemic and nonischemic cardiomyopathy 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 statistical significant. However, the DINAMIT, IRIS, and BEST-ICD trials did not support a mortality benefit for ICD in the early weeks following MI and CABG-Patch showed no benefit in patients having recently undergone coronary revascularization. Another notable exception is the 2016 DANISH trial, which enrolled primarily outpatients with nonischemic cardiomyopathy (NICM) in stable condition who were almost all receiving β-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 2. RCTs of Implantable Cardiac Defibrillators 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% • Asymptomatic non-SVT • MI ≥3 wk prior • Inducible VT • NYHA class I-III	• ICD • Standard therapy	95 101	27 mo (trial stopped early by DSMB)	0.46	0.26 to 0.82
MADIT II (2002)	• LVEF ≤30% • No history of VT • MI ≥1 mo prior • NYHA class I-III	• ICD • Standard therapy	742 490	20 mo (trial stopped early by DSMB)	0.69	0.51 to 0.93
CABG Patch (1997)	• Scheduled for CABG • LVEF ≤35% • No sustained VT or VF • Age >80 y • Signal-averaged ECG abnormalities • 82% had prior MI, time since MI not reported	• ICD during CABG • No ICD	446 454	32 mo	1.07	0.81 to 1.42
MUSTT (1999)	• LVEF ≤40% • Asymptomatic non-SVT • Inducible VT • MI ≥4 d prior (median, ≈3 y prior) • No sustained VT or VF	• EPS-guided therapy (AAD with or without ICD) (202 got ICD) • Standard therapy	351 353	39 mo	**5-y outcomes[b]:** EPS-guided vs standard therapy • 0.80 ICD vs AAD alone • 0.42	 0.64 to 1.01 0.29 to 0.61
SCD HeFT (2005)	• LVEF ≤35% • NYHA class II-III • No asymptomatic SVT • 52% received ICM • Treated with ACE inhibitors and β-blockers	Ischemic patients: • ICD • Amiodarone • Placebo	 431 426 453	45 mo	**ICD vs placebo** Ischemic • 0.79[a] Overall • 0.77[a]	 0.60 to 1.04 0.62 to 0.96
ICM with recent MI						
DINAMIT (2004)	• LVEF ≤35% • NYHA class I-III • No asymptomatic SVT • MI in preceding 6-40 d (mean, 18 d) • Reduced HR variability or elevated resting HR	• ICD • Standard therapy	332 342	30 mo	1.08	0.76 to 1.55
IRIS (2009)	• MI in preceding 5-31 d • At least 1 of the following: ○ LVEF ≤40% and resting HR ≥90 or non-SVT	• ICD • Standard therapy	445 453	37 mo	1.04	0.81 to 1.35
BEST-ICD (2005)	• LVEF ≤35% • NYHA class I-III • No asymptomatic SVT	• EPS-guided therapy (24 got ICD) • Standard therapy	79 59	540 d	**1-year mortality[d]** • EPS-guided therapy: 14% • Conventional therapy: 18%	

Systematic Reviews

Woods et al (2015) published an individual patient data network meta-analysis of primary prevention RCTs of 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 12,638 patients overall. Patients included in the ICD arms had a mean age of 63.5, mean QRS interval of 140.5 ms, and mean ejection fraction of 23%. Twenty-one percent of patients were women. The overall estimated effect of ICD on mortality compared to medical therapy was 0.71 (95% CI, 0.63 to 0.80).

Four systematic reviews and meta-analyses of ICD trials in NICM were published in 2017 and incorporated the 2016 DANISH trial results and updating a previous meta-analysis. Two of the 2017 reviews included the CAT, AMIOVIRT, DEFINITE, SCD-HeFT, COMPANION, and DANISH trials; the other 2 reviews included all but the COMPANION trial. All 4 reviews concluded that there was a statistically significant overall reduction

in mortality for ICD versus medical therapy, ranging from 20% to 23%, even with the inclusion of the null DANISH results.

Risk for death varies by age, sex, and clinical characteristics such as LVEF and time since revascularization and comorbid conditions such as diabetes and kidney disease. Meta-analyses have examined whether there is a beneficial effect on mortality of ICD in these subgroups. The Agency for Healthcare Research and Quality sponsored a review of evidence for ICD across important clinical subgroups published in 2014. 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) and were combined to calculate a relative odds ratio (ROR) using random-effects meta-analyses. There was no statistically significant difference in the mortality benefit by sex (ROR=0.95; 95% CI, 0.75 to 1.27), age (ROR=0.93; 95% CI, 0.73 to 1.20), or QRS interval (ROR=1.13; 95% CI, 0.82 to 1.54). 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 2015 IPD 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, age less than 60 and 60 and older, and for men.[15] However, the effect on mortality in women was not statistically significant (HR=0.93; 95% CI, 0.73 to 1.18).

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

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

In 2015, Magnusson et al reported 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 VT or VF occurred in 77 (24%) patients, corresponding to an annual rate of appropriate discharges of 5.3%. At least 1 inappropriate shock occurred in 46 (14.3%) patients, corresponding to an annualized event rate of 3.0%. Ninety-two (28.7%) patients required at least 1 surgical intervention for an ICD-related complication, with a total of 150 ICD-related reinterventions. Most reinterventions (n=105 [70%]) were related to lead dysfunction.

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, SQTS, and 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

In 2010, Horner et al 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. Of patients treated with ICDs, 43 (84%) received the device as primary prevention. Twelve (24%) patients received appropriate VF or torsades de pointes–terminated ICD shocks. Factors associated with appropriate shocks included secondary prevention indications (p=0.008), QT corrected (QTc) 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

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 or antitachycardia pacing in 28 (15.9%) patients and 2 (1.1%) patients, respectively. However, 33 (18.7%) patients experienced inappropriate shocks. Eight (4.5%) patients died during follow-up, 3 of cardiac causes.
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 nonsustained VT during follow-up (HR=6.73; 95% CI, 1.27 to 35.7; p=0.025).

In data from a U.S. cohort of 33 BrS patients treated with ICDs, Steven et al (2011) reported that two-thirds of patients with a prior history of aborted SCD received appropriate shocks over a mean follow-up of 7.9 years -up, while none of the 30 patients without a history of aborted SCD had an arrhythmia detected. In a smaller registry (2012) that included 25 BrS patients treated with ICDs, over an average follow-up of 41.2 months, appropriate shocks were delivered in 3 patients, all of whom had prior cardiac arrest.

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.

Section Summary: Primary Prevention in Adults (Ischemic Cardiomyopathy, NICM, HCM, and Cardiac Ion Channelopathy)
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 a LVEF of 35% or less. The notable exceptions are that data from several RCTs, including the BEST-ICD, DINAMIT and IRIS trials and subanalyses 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. Less evidence is available for use of ICDs for primary prevention in patients with HCM. In a meta-analysis of cohort studies, the annual rates of appropriate ICD discharge was 3.3% and the mortality rate was 1%. Given the long-term high risk of SCD in patients with HCM, with the assumption that appropriate shocks are life-saving, these rates are considered adequate evidence for the use of SCDs in patients with HCM. 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 reported high rates of appropriate shocks. For BrS, more data are available and have suggested that rates appropriate shocks are similarly high. Studies comparing outcomes between patients treated and untreated with ICDs are not available. However, given the relatively small patient populations and the high risk of cardiac arrhythmias, clinical trials are unlikely. Given the long-term high risk of SCD in patients with inherited cardiac ion channelopathy, with the assumption that appropriate shocks are life-saving, these rates are considered adequate evidence for the use of SCDs in patients with inherited cardiac ion channelopathy.

Secondary Prevention in Adults
At least 5 trials comparing ICD plus medical therapy to 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) (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) (N=60). The trials are shown in Table 3. Mean length of follow-up varied from 18 to 57 months across trials. Lee et al (2003) combined the AVID, CASH, CIDS, and Wever 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 to the group receiving medical therapy alone. To support NICE guidance on use of ICDs, a meta-analysis of 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). Two other meta-analyses that included AVID, CIDS, and CASH reached similar conclusions.

Table 3. RCTs of ICDs for Secondary Prevention

Trials	Participants	Treatment Groups		Mortality Results	
		Group	N	RR	95% CI
AVID (1997)	Patients resuscitated from near-fatal VT/VF, SVT with syncope, or SVT with LVEF ≤40% and symptoms	• ICD • AAD	507 509	0.66	0.51 to 0.85
CASH (2000)	Patients resuscitated from cardiac arrest due to sustained ventricular arrhythmia	• ICD • Amiodarone • Metoprolol	99 92 97	0.82	0.60 to 1.11
CIDS (2000)	Patients with VF, out-of-hospital cardiac arrest requiring defibrillation, VT with syncope, VT with rate ≥150/min causing presyncope or angina in patient with LVEF ≤35% or syncope with inducible VT inducible	• ICD • Amiodarone	328 331	0.85	0.67 to 1.10
Wever et al (1995)	Patients with previous MI and resuscitated cardiac arrest due to VT or VF and inducible VT	• ICD • AAD	29 31	0.39	0.14 to 1.08
DEBUT (2003)	Patients were either SUDS survivors or probable SUDS with ECG abnormalities showing a RBBB-like pattern with ST elevation in the right precordial leads and inducible VT/VF	**Pilot** • ICD • β-blockade therapy **Main trial** • ICD • β-blockade therapy	 10 10 37 29	• RR not calculable (DSMB stopped trial early due to efficacy of ICD) • 7 deaths in β-blockade 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; RR: relative risk; SUDS: sudden unexplained death syndrome; SVT: sustained ventricular tachycardia; VF: ventricular fibrillation; VT: ventricular tachycardia.

An analysis by Chan and Hayward (2005) using the National Veterans Administration database previously confirmed that this mortality benefit is generalizable to the clinical setting. A cohort of 6996 patients in the National Veterans Administration database from Austin, Texas, 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 to no ICD was a relative risk of 0.72 (95% CI, 0.69 to 0.79) for all-cause mortality and a relative risk 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 to medical therapy. Analysis of data from a large administrative database confirms that this mortality benefit is generalizable to the clinical setting.

TV-ICDS 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. A review of some representative series is provided next.

The largest published series (2008) combined pediatric patients and patients with congenital heart disease from 4 clinical centers. Median age was 16 years, although some adults included were as old as 54 years. A total of 443 patients were included. The most common diagnoses were tetralogy of Fallot and HCM. ICD placement was performed for primary prevention in 52% of patients and for 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 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 1 inappropriate shock. Actuarial 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 with a mean age of 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. Fourteen (22%) patients experienced at least 1 appropriate shock and 17 (27%) had at least 1 inappropriate shock. Serious psychological sequelae developed in 27 (43%) patients.

Section Summary: 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 also be eligible ICD placement if they have inherited cardiac ion channelopathy (see ICDs in Patients With inherited cardiac ion channelopathy section).

ADVERSE EVENTS ASSOCIATED WITH TV-ICDS

Systematic Reviews: Mixed Adverse Events

Perrson et al (2014) conducted a systematic review of adverse events following ICD placement. They included data from 35 cohort studies, reported in 53 articles. 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%). Posthospitalization complication rates varied: device-related complications occurred in 0.1% to 6.4%; lead-related complications in 0.1% to 3.9% of patients; infection in 0.2% to 3.7%; thrombosis in 0.2% to 2.9%; and inappropriate shock in 3% to 21%.

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. Reviewers included 18 RCTs (total N=6796 patients). In pooled analysis, the overall AE rate was 9.1% (95% CI, 6.4% to 12.6%). Rates of access-related complications, lead-related complications, generator-related complications, and infection were 2.1% (91% CI, 1.3% to 3.3%), 5.8% (95% CI, 3.3% to 9.8%), 2.7% (95% CI, 1.3% to 5.7%), and 1.5% (95% CI, 0.8% to 2.6%), respectively. 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%] 5918 patients with at least 1 complication).

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

In 2016, Olde Nordkamp et al 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 SQTS). Overall, inappropriate shocks occurred in 20% of patients over a mean follow-up of 51 months, corresponding to an annual inappropriate shock rate of 4.7% (95% CI, 4.2% to 5.3%). Over a mean follow-up of 55 months, ICD-related complications occurred in 22%, most commonly lead malfunction (10.3% of patients). The pooled rate of ICD-related complications was 4.4% per year (95% CI, 3.6% to 5.2%).

Systematic Review: Specific Complications

Lead Failure

The failure of leads in specific ICD devices led the U.S. FDA to require St. Jude Medical to conduct 3-year postmarket surveillance studies to address concerns related to premature insulation failure and important questions related to follow-up of affected patients. A 2010 evaluation 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 (MAUDE) database.

In 2015, Providencia et al reported on a meta-analysis of 17 observational studies evaluating performance of 49,871 leads (5538 Durata, 10,605 Endotak Reliance, 16119 Sprint Quattro, 11,709 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 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 clinical predictors of failure for 3169 Sprint Fidelis leads implanted from 2003 to 2007 at 11 centers participating in the Canadian Heart Rhythm Society Device Committee 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 2011 study from 3 centers reporting on predictors of Fidelis lead failures, compared with Quattro lead failures, Hauser et al 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 an earlier study from 12 Canadian centers, Gould et al (2008) reported on outcomes from ICD replacements due to ICD advisories from 2004 to 2005, which included 451 replacements (of 2635 advisory ICD devices). Over 355 days of follow-up, 41 (9.1%) complications occurred, including 27 (5.9%) requiring surgical reintervention and 2 deaths.

In a large prospective multicenter study, Poole et al (2010) reported on complications rates associated with generator replacements and/or upgrade procedures of pacemaker or ICD devices, which included 1031 patients without a planned transvenous lead replacement (cohort 1) and 713 with a planned transvenous lead replacement (cohort 2). 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 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. 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 226,764 patients treated with an ICD between April 2006 and September 2008, lead dislodgement occurred in 2628 (1.2%). Factors associated with lead dislodgement were New York Heart Association class IV heart failure, AF or atrial flutter, a combined ICD and CRT device, and having the procedure performed by a nonelectrophysiologist. Lead dislodgement was associated with an increased risk for other cardiac adverse events and death.

In another single-center study, Faulknier et al (2010) reported on the time-dependent hazard of failure of Sprint Fidelis leads. 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 the rate of ICD-associated infections among consecutive patients treated with an ICD at a tertiary referral center. Twenty-four of 2417 patients had infections, for a rate of 1.0%. Twenty-two (91.7%) of the 24 patients with infections required device replacement. Factors associated with infection were device replacement (vs de novo implantation) and use of a complex device (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 vs 1 day) and chronic obstructive pulmonary disease (OR=9.8, p=0.02) were significant risk factors.

Chua et al (2000) described the diagnosis and management of infections in a retrospective case series that included 123 patients, 36 of whom were treated for ICD infections. Most (n=117 [95%]) patients required removal of the device and all lead material. Of those who had all hardware removed, 1 patient experienced a relapse, while 3 of the 6 patients who did not undergo hardware removal experienced a relapse.

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

Inappropriate Shocks

Inappropriate shocks may occur with ICDs due to faulty sensing or sensing of atrial arrhythmias with rapid ventricular conduction; these shocks may lead to reduced QOL and risk of ventricular arrhythmias. In the MADIT II trail (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 AEs associated with ICDs with built-in therapy-reduction programming. Six randomized trials and 2 nonrandomized cohort studies (total N=7687 patients) were included (3598 with conventional ICDs, 4089 therapy-reduction programming). A total of 267 (4.9%) patients received inappropriate ICD shocks, 99 (3.4%) in the therapy reduction group and 168 (6.9%) in the conventional programming group (RR=50%; 95% CI, 37% to 61%; p<0.001). Therapy-reduction programming was associated with a significantly lower risk of death than conventional programming (RR=30%; 95% CI, 16% to 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 study reported on a prespecified subgroup analysis of the PainFree SST trial, which compared standard and prolonged detection in patients receiving an ICD for secondary prevention. Patients treated for secondary prevention indications were randomized to a prolonged VF detection period ("Number of Intervals to Detect" VF 30/40; n=352) or a standard detection period ("Number of Intervals to Detect" VF 18/24; n=353). At 1 year, arrhythmic syncope-free rates were 96.9% in the 30/40 (intervention) group and 97.7% in the 18/24 (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 who 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 February 2007 through May 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 (hs-TnT) 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 hs-TnT 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 hs-TnT levels.

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

S-ICD Efficacy
Several observational studies have compared S-ICD to TV-ICD.

Observational Studies
The observational studies are briefly described in Table 4. All studies were performed in the United States and/or Europe.

Noncomparative Studies
The EFFORTLESS S-ICD Registry is a multicenter European registry reporting outcomes for patients treated with S-ICD. Several publications from EFFORTLESS, the pivotal trial submitted to FDA for the investigational device exemption, and other noncomparative studies are described in Table 5.

Table 4. Summary of Observational Studies of S-ICD to TV-ICD

Author	Study Type	N	Follow-Up	Results			
				Outcomes	TV-ICD	S-ICD	DC TV-ICD
Honarbakhsh (2017)	Propensity matched case-control	138 (69 matched pairs)	32 mo[a]	• Total device-related complications • Infections • Inappropriate shocks • Failure to cardiovert VA	29% 5.8% 8.7% 1.4%	9% 1.4% 4.3% 1.4%	
Kobe (2017)	Sex- and age-matched case-control	120 (60 pairs); 84 pairs analyzed	942 d vs 622 d	• Posttraumatic stress disorder • Major depression • SF-12 Physical well-being score • SF-12 Mental well-being score	14.3% 9.5% 40 52	14.3% 4.8% 47 52	
Pedersen (2016)	Retrospective analysis of propensity-matched cohort	334 (167 matched pairs)	6 mo	• SF-12 Physical well-being score • SF-12 Mental well-being score	43 45	44 45	
Brouwer (2016)	Retrospective analysis of propensity-matched cohort	280 (140 matched pairs)	5 y	• Overall complications • Lead complications • Non-lead complications • Infections • Appropriate ICD intervention (HR=2.4; 95% CI, NR; p=0.01) • Inappropriate ICD intervention (HR=1.3; 95% CI, NR; p=0.42) • Survival	18% 11.5% 2.2% 3.6% 31% 30% 95%	14% 0.8% 9.9% 4.1% 17% 21% 96%	
Friedman (2016)	Retrospective analysis of propensity-matched cohort from NCDR for ICD	5760 (1920 matched, groups)	NR	• Any in-hospital complication • Deaths • Infections • Lead dislodgements • Pneumothorax	0.6% 0.1% 0% 0.2% 0.2%	0.9% 0.2% 0.05% 0.1% 0%	1.5% 0.05% 0.1% 0.6% 0.3%
Kobe (2013)	Sex- and age-matched case-control	138 (69 matched pairs)	217 d[a]	• Pericardial effusion • Successful termination of induced VF • Appropriate shocks • Inappropriate shocks	1 91% 9 3	0 90% 3 5	
Pettitt (2013)	Case series	15 (6 TV-ICD, 9 S-ICD)	36 mo TV-ICD vs 20 mo S-ICD[b]	• Survival • Survival free of inappropriate therapy • Extractions	100% 25% 3	100% 89% 0	
Gold (2012); START study	Prospective cohort	64 (patients got TV-ICD and S-ICD)	NR	• Sensitivity for detecting induced VA • Specificity for detecting induced VA	99% 77%	100% 98%	

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.
[b] Median.

Inappropriate Shocks

Although Kobe et al reported no differences between inappropriate shock rates in patients treated TV-ICD or S-ICD, noncomparative studies have reported relatively high rates of inappropriate shocks with S-ICD. Inappropriate shocks from S-ICDs often result from T-wave oversensing. Because the sensing algorithm and the discrimination algorithm for arrhythmia detection are fixed in the S-ICD, management to reduce inappropriate shocks for an S-ICD differs from that for a TV-ICD. Kooiman et al (2014) reported inappropriate shock rates among 69 patients treated at a single center with an S-ICD between February 2009 and July 2012 who were not enrolled in 1 of 2 other concurrent trials. Over a total follow-up of 1316 months (median per patient, 21 months), the annual incidence of inappropriate shocks was 10.8%. In 8 patients, inappropriate shocks were related to T-wave oversensing. After patients underwent adjustment of the sensing vector, no further inappropriate shocks occurred in 87.5% of patients with T-wave oversensing.

Section Summary: Subcutaneous Implantable Cardioverter Defibrillators

Nonrandomized studies have suggested that S-ICDs are as effective as TV-ICDs at terminating laboratory-induced ventricular arrhythmias. Data from 2 large patient registries have suggested that S-ICDs are effective at terminating ventricular arrhythmias when they occur. Given the need for cardioverter

defibrillation for SCD risk in this population, with the assumption that appropriate shocks are life-saving, these rates suggest S-ICDs, in patients with contraindication to TV-ICD, are likely an improvement over medical management alone. However, no RCTs directly comparing TV-ICDs with S-ICDs were identified and therefore evidence is not sufficient to show that outcomes for S-ICDs are noninferior to those for TV-ICD for patients who could otherwise receive TV-ICD.

SUMMARY OF EVIDENCE

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

For individuals who have a high risk of SCD due to HCM in adulthood who receive TV-ICD placement for primary prevention, the evidence includes several large registry studies. Relevant outcomes are overall survival, morbid events, quality of life, and treatment-related mortality and morbidity. In these studies, the annual rate of appropriate ICD discharge ranged from 3.6% to 5.3%. Given the long-term high risk of SCD in patients with HCM, with the assumption that appropriate shocks are life-saving, these rates are considered adequate evidence to support use of ICDs in patients with HCM. The evidence is sufficient to determine that the technology results in a meaningful 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. Relevant outcomes are overall survival, morbid events, quality of life, and treatment-related mortality and morbidity. The limited evidence for patients with LQTS, CPVT, and BrS has reported high rates of appropriate shocks. No studies were identified on the use of ICDs for patients with SQTS. Studies comparing outcomes between patients treated and untreated with ICDs are not available. However, given the relatively small patient populations and the high risk of cardiac arrhythmias, clinical trials are unlikely. Given the long-term high risk of SCD in patients with inherited cardiac ion channelopathy, with the assumption that appropriate shocks are life-saving, these rates are considered adequate evidence to support use of TV-ICDs in patients with inherited cardiac ion channelopathy. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have who have had symptomatic life-threatening sustained VT or 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. Relevant outcomes are overall survival, morbid events, quality of life, and treatment-related mortality and morbidity. Systematic reviews of RCTs have demonstrated a 25% reduction in mortality for ICD compared to 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 a meaningful improvement in the net health outcome.

For individuals who need an ICD and have a contraindication to a TV-ICD but no indications for antibradycardia pacing and no antitachycardia pacing–responsive arrhythmias who receive S-ICD placement, the evidence includes nonrandomized studies and case series. Relevant outcomes are overall survival, morbid events, quality of life, and treatment-related mortality and morbidity. Nonrandomized controlled studies have reported success rates in terminating laboratory-induced VF that are similar to 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 rates are considered adequate evidence to support use of S-ICDs in patients with contraindication to TV-ICD. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have need for an ICD without contraindication to TV-ICD but no indications for antibradycardia pacing and no antitachycardia pacing–responsive arrhythmias who receive S-ICD placement, the evidence includes nonrandomized studies and case series. Relevant outcomes are overall survival, morbid events, quality of life, and treatment-related mortality and morbidity. Nonrandomized controlled studies have reported success rates in terminating laboratory-induced VF that are similar to TV-ICD. However, there is scant evidence on comparative clinical outcomes of both types of ICD over longer periods. Case series have reported high rates of detection and successful conversion of VT, and inappropriate shock rates in the range reported for TV-ICD. This evidence does not support conclusions on whether there are small differences in efficacy between the 2 types of devices, which may be clinically important due to the nature to the disorder being treated. Also, adverse event rate is uncertain, with variable rates reported. At least 1 RCT is currently underway comparing S-ICD with TV-ICD. The evidence is insufficient to determine the effects of the technology on health outcomes.

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Policy History

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04/25/2003	Medical Policy Committee review
05/12/2003	Managed Care Advisory Council approval
06/01/2004	Medical Director review
06/15/2004	Medical Policy Committee review Format revision. No substance change to policy.

06/28/2004	Managed Care Advisory Council approval
04/05/2005	Medical Director review
04/18/2005	Medical Director review
04/22/2005	Medical Director review
04/27/2005	Medical Policy Committee approval. Investigational designation for specific clinical scenarios added. Clinical criteria revision.
05/23/2005	Managed Care Advisory Council approval
05/03/2006	Medical Director review Format Revisions. Government regulations, literature updated; no change in policy statement.
05/17/2006	Medical Policy Committee review
08/15/2007	Medical Policy Committee review. Policy statement not medically necessary when patient selection criteria not met changed to investigational. Removed not medically necessary policy statement for selected conditions.
12/12/2007	Medical Director review
12/19/2007	Medical Policy Committee approval. No change to coverage eligibility. CMS added. FDA updated.
12/03/2008	Medical Director review
12/17/2008	Medical Policy Committee approval. Changed format and coverage by adopting BCBSA's.
12/04/2009	Medical Policy Committee approval
12/16/2009	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/01/2010	Medical Policy Committee approval
12/15/2010	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/08/2011	Medical Policy Committee review
12/21/2011	Medical Policy Implementation Committee approval. Policy statements specific to AICD indications in pediatric patients added to coverage section and Rationale. Policy statement revised to clarify the indications in ischemic cardiomyopathy with separate indications for class II/III and class I patients. Policy statement with waiting time in nonischemic cardiomyopathy was revised.
12/06/2012	Medical Policy Committee review
12/19/2012	Medical Policy Implementation Committee approval. Added new investigational statement "Based on review of available data, the Company considers the use of a subcutaneous ICD investigational for all indications in adult and pediatric patients."
02/04/2013	Coding revised
12/12/2013	Medical Policy Committee review
12/18/2013	Medical Policy Implementation Committee approval. No change to coverage.
12/04/2014	Medical Policy Committee review
12/17/2014	Medical Policy Implementation Committee approval. A clause "…after reversible causes (e.g., acute ischemia) have been excluded" added to current statement on secondary prevention in adults.
02/17/2015	Coding update.
08/03/2015	Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
12/03/2015	Medical Policy Committee review
12/16/2015	Medical Policy Implementation Committee approval. New S-ICD section added to policy statements and added new bullet points to both Pediatric and Adult coverage statements. Statement added for Adults that ICD for secondary prevention in pts who do not meet criteria is considered INV.
12/01/2016	Medical Policy Committee review
12/21/2016	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Automatic Implantable Cardioverter Defibrillator (AICD)

Policy # 00008
Original Effective Date: 05/12/2003
Current Effective Date: 12/20/2017

01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes
12/07/2017 Medical Policy Committee review
12/20/2017 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/17/2018 Coding update
Next Scheduled Review Date: 12/2018

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2016 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. *Applicable FARS/DFARS apply.*

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	33215, 33216, 33217, 33218, 33220, 33223, 33224, 33225, 33226, 33230, 33231, 33240, 33241, 33249, 33262, 33263, 33264, 33270, 33271, 33272, 33273, 93260, 93283, 93284, 93640, 93641
HCPCS	C1721, C1722, C1777, C1882, C1895, C1896, C1899
ICD-10 Diagnosis	I42.0-I42.9, I46.2-I46.9, I47.0-I47.2, I49.01, I49.9, Q20.0-Q24.9

*****Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association TEC or other nonaffiliated technology evaluation center(s);

2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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