Medical Coverage Policy

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Cardiac Resynchronization Therapy (CRT) and Advanced Cardiac Pacing Technologies

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Overview

This Coverage Policy addresses the use of a biventricular pacemaker (alone or combined with an implantable cardioverter defibrillator [ICD]) for cardiac resynchronization therapy (CRT), triple-site or triventricular pacing CRT, wireless pacing CRT, conduction system pacing, and leadless pacemakers.

Coverage Policy

The use of a biventricular pacemaker alone or in combination with an implantable cardioverter defibrillator (ICD)* for cardiac resynchronization therapy (CRT) is considered medically necessary for ANY of the following indications when the individual has been on an optimal pharmacologic regimen before consideration of implantation:

- **Ischemic cardiomyopathy, left ventricular ejection fraction (LVEF) ≤ 35%, no prior implant, sinus rhythm (SR) for ANY of the following:**
  - QRS 120-149 milliseconds (ms), left bundle branch block (LBBB), New York Heart Association (NYHA) Class I, II, III-IV
  - QRS ≥ 150 ms, LBBB, NYHA Class I, II, III-IV
  - QRS 120-149 ms, non-LBBB, NYHA Class III-IV
  - QRS ≥ 150 ms, non-LBBB, NYHA Class II, III-IV
- **Nonischemic cardiomyopathy, LVEF ≤ 30%, no prior implant, SR for ANY of the following:**
  - QRS 120-149 ms, LBBB, NYHA Class II,III-IV
  - QRS ≥ 150 ms, LBBB, NYHA Class I, II, III-IV
  - QRS 120-149 ms, non-LBBB, NYHA Class III-IV
  - QRS ≥ 150 ms, non-LBBB, NYHA Class I, II, III-IV
- **Nonischemic cardiomyopathy, LVEF 31-35%, no prior implant, SR for ANY of the following:**
  - QRS 120-149 ms, LBBB, NYHA Class I, II, III-IV
  - QRS ≥ 150 ms, LBBB, NYHA Class I, II, III-IV
  - QRS 120-149 ms, non-LBBB, NYHA Class III-IV
  - QRS ≥ 150 ms, non-LBBB, NYHA Class I, II, III-IV
- **LVEF > 35% of any etiology, ICD indicated, no prior implant, SR, QRS ≥ 150 ms, LBBB, NYHA Class III-IV**

- **LVEF ≤ 35% of any etiology, NYHA Class IV on intravenous inotropic support, no prior implant for EITHER of the following:**

  - QRS 120-149 ms, LBBB
  - QRS ≥ 150 ms, LBBB or non-LBBB

- **Pre-existing or anticipated right ventricular (RV) pacing with a clinical indication for ICD or pacemaker implantation, intrinsic narrow QRS for EITHER of the following:**

  - RV pacing anticipated ≤ 40%, LVEF ≤ 35%, NYHA Class III-IV
  - RV pacing anticipated > 40%, NYHA Class I, II, III-IV

- **Refractory NYHA Class III/IV heart failure < 3 months post revascularization and/or ≤ 40 days post-myocardial infarction (MI) and ALL of the following:**

  - LVEF ≤ 35%
  - QRS > 120 ms
  - LBBB or non-LBBB
  - no other indication for ventricular pacing

***Note: Please reference Cigna Medical Coverage policy "Implantable Cardioverter Defibrillator (ICD)" for conditions of coverage of an ICD device.**

Replacement of a biventricular pacemaker generator alone or in combination with an implantable cardioverter defibrillator and/or leads is considered medically necessary.

The use of a biventricular pacemaker alone or combined with an implantable cardioverter defibrillator for CRT for any other indication is considered not medically necessary.

Each of the following is considered experimental, investigational or unproven for any indication:

- triple-site or triventricular pacing CRT
- wireless pacing CRT
- conduction system pacing (i.e., His bundle pacing [HBP]; left bundle branch pacing [LBBP])
- leadless pacemaker

General Background

Heart Failure

Congestive heart failure (CHF), or heart failure (HF), is a serious medical condition in which the heart does not pump blood as efficiently as it should. Approximately one-third of people with heart failure will also develop an arrhythmia (irregular heartbeat) which can cause the contraction of the heart's two lower chambers (ventricles) to become uncoordinated (ventricular dyssynchrony). Dyssynchrony is evidenced by a wide QRS interval seen on electrocardiogram (ECG). Ventricular dyssynchrony can worsen the heart's ability to pump effectively and exacerbate heart failure symptoms. It is also associated with an increased risk of serious illness and death.

The most frequently used measure of heart function is the left ventricular ejection fraction (LVEF). Normal LVEF ranges from 50–75% at rest. Severe heart failure can reduce LVEF to < 35%. Treatment for heart failure includes medications, which may include a combination of diuretics, digoxin, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB), beta-blockers, and aldosterone antagonists. Some patients may remain symptomatic despite drug therapy. The definitive therapy for end-stage heart failure patients is heart transplantation.

The New York Heart Association (NYHA) classification of heart failure is a four-tier system that categorizes patients based on a subjective impression of the degree of functional compromise. The chart below defines the four NYHA functional classes. Advanced heart failure is categorized as NYHA Class III and Class IV (Colucci, 2022).

Class I	Patients with cardiac disease but without resulting limitation of physical activity; ordinary physical activity does not cause undue fatigue, palpitation, dyspnea or anginal pain; symptoms only occur on severe exertion
Class 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
Class III	Patients with cardiac disease resulting in marked limitation of physical activity; they are comfortable at rest; less than ordinary activity (e.g., mild exertion) causes fatigue, palpitation, dyspnea or anginal pain
Class IV	Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort; symptoms of cardiac insufficiency or anginal syndrome is present at rest; if any physical activity is undertaken, discomfort is increased

Cardiac Resynchronization Therapy (CRT)

Despite the combination of various therapies for heart failure, some patients remain symptomatic. Of the various non-drug approaches, biventricular pacing or cardiac resynchronization therapy (CRT) has gained interest since its introduction in the early 1990s. CRT is the term applied to reestablishing coordinated contraction between the left ventricular free wall and the ventricular septum in an attempt to improve left ventricular efficiency and, subsequently, to improve NYHA functional class. Generally, CRT has been used to describe biventricular pacing, but cardiac resynchronization can be achieved by left ventricular pacing only in some patients. Selected patients with mild to severe heart failure may benefit from CRT. Combined with stable optimal medical therapy, CRT may help the ventricles beat together and improve the heart's ability to supply blood and oxygen to the body.

An implantable biventricular pacemaker is an advanced version of a standard implantable pacemaker. The biventricular pacemaker is implanted in the muscle tissue of the chest, below the collarbone, or in the abdomen. Three leads or wires, (one atrial lead and two ventricular leads), are transvenously connected from the pacemaker to the heart. The pacing leads are typically placed in the right atrium, the right ventricle, and the coronary sinus, which results in stimulation of the left ventricle. In a small percentage of cases, it may not be possible to place the left ventricular lead transvenously. In such situations, some centers are opting for an epicardial approach if the transvenous approach is unsuccessful. The pacemaker sends out electrical impulses to the heart through the leads. Placement of a biventricular pacemaker can usually be accomplished in an outpatient setting under sedation or general anesthesia. A short inpatient stay may be required for epicardial left ventricular lead placement. Once the pacemaker is implanted, it is programmed so that both ventricles are stimulated to contract after atrial contraction, with the

goals of improving left ventricle (LV) function, reducing presystolic mitral regurgitation, and improving LV diastolic filling time.

The benefits of CRT need to be weighed against the risks of the procedure, along with the adverse effects of having a CRT device implanted long term. The reported risks of the procedure are uncommon but some events may be serious, such as pericardial effusion with tamponade or coronary dissection. Minor reported adverse events such as lead dislodgement are more common and may result in repeat procedures.

CRT plus Implantable Cardioverter Defibrillator (ICD) System (CRT-D)
Some individuals with heart failure are also at high risk for life-threatening heart rhythms, including ventricular tachycardia and ventricular fibrillation. Patients with heart failure who are at high risk for ventricular tachycardia and ventricular fibrillation may require a CRT system that includes implantable cardioverter defibrillator (ICD) therapy. The CRT plus ICD system (CRT-D) is designed to help the right and left ventricles beat at the same time in a normal sequence. Additionally, should an individual experience an episode of ventricular tachycardia or ventricular fibrillation, the CRT-D system will detect the life-threatening arrhythmia and automatically correct the heart's rhythm.

CRT-D may be considered for people who fulfill the criteria for implantation of a CRT-pacing (CRT-P) device and who also separately fulfill the criteria for the use of an ICD device. Clinical indications for ICD devices are discussed in further detail in Cigna Medical Coverage policy "Implantable Cardioverter Defibrillator (ICD)".

Device Replacement
When a biventricular pacemaker nears the end of its battery life, it is replaced; the expected lifespan of a biventricular pacemaker pulse generator varies among manufacturers. In addition, leads may become dislodged or fracture and require replacement.

U.S. Food and Drug Administration (FDA)
Multiple biventricular pacemakers have been approved by the U.S. Food and Drug Administration (FDA) through the Premarket Approval (PMA) process for biventricular pacing alone (CRT-P) or biventricular pacing and defibrillation (CRT-D). CRT-P and CRT-D devices are FDA Class III devices, with associated product codes NKE and NIK, respectively. Manufacturers of biventricular devices include Medtronic (Mounds View, MN), Guidant Corp. (St. Paul, MN), and ELA Medical, Inc. (Plymouth, MN).

The FDA device approval notifications and manufacturer labels include the following contraindications to CRT-P and CRT-D devices:

- Asynchronous pacing is contraindicated in the presence or likelihood of competitive paced and intrinsic rhythms.
- Unipolar pacing is contraindicated in individuals with an ICD because it may cause unwanted delivery or inhibition of defibrillator or ICD therapy.
- CRT-D devices are contraindicated for patients whose ventricular tachyarrhythmias may have transient or reversible causes and for patients with incessant ventricular tachycardia or ventricular fibrillation.
- CRT-D devices are contraindicated for dual chamber atrial pacing in patients with chronic refractory atrial tachyarrhythmias (FDA, 2014).

Literature Review
CRT in NYHA Class III and IV: Evidence in the published peer-reviewed literature, including randomized controlled trials, meta-analyses and systematic reviews, indicates that cardiac

resynchronization therapy is effective at improving quality of life, patient functional capacity and heart failure symptoms in a subgroup of patients with heart failure, with or without ICD indications, decreased cardiac function and ventricular dyssynchrony who are on optimal pharmacologic regimen before implantation. The following benchmark large-scale trials included primarily NYHA Class III and IV patients with a wide QRS complex: MUltisite STimulation In Cardiomyopathies (MUSTIC); Multicenter InSync Randomized Clinical Evaluation (MIRACLE); Multicenter InSync ICD Randomized Clinical Evaluation (MIRACLE ICD); Contak CD; Cardiac Resynchronization — Heart Failure (CARE-HF); and Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION). (Deng, et al., 2015; Cleland, et al., 2009; Upadhyay, et al., 2008; Auricchio, et al., 2007; McAlister, et al., 2007a; Lindenfeld, et al., 2007; Delnoy, et al., 2007; Sutton, et al., 2006; Gasparini, et al., 2006; Cleland, et al., 2005; Molhoek, et al., 2005; Doshi, et al., 2005; Molhoek, et al., 2004; Bristow, et al., 2004; Garrigue, et al., 2003; Higgins, et al., 2003; Abraham, et al., 2002; Leclercq, et al., 2002; Leon, et al., 2002).

CRT in NYHA Class I and II: The majority of newer research in CRT is to evaluate whether the benefits of CRT extend to patients with mild or less severe heart failure (NYHA Class I/II). While lower morbidity and reduction or alleviation of symptoms are the goals of CRT in advanced heart failure, preventing heart failure progression is the primary objective for CRT in NYHA Classes I and II. The role of CRT in patients with mild or less severe heart failure is less established. Four key randomized controlled trials have been published in the peer-reviewed literature: Resynchronization–Defibrillation for Ambulatory Heart Failure Trial (RAFT), Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction (REVERSE), Multicenter InSync ICD Randomized Clinical Evaluation II (MIRACLE ICD II) and Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT). These trials enrolled 4,414 patients which included patients with NYHA Class I or II heart failure, at least 25 patients per treatment group, and reported on at least one relevant health outcome with follow-up ranging from six months to 2.4 years (Tang, et al., 2010; Moss, et al., 2009; Linde, et al., 2008, Abraham, et al., 2004).

Evidence in the published peer-reviewed literature, including randomized controlled trials and a meta-analysis (Al-Majed, et al., 2011), indicates that there is a consistent benefit for CRT in reducing hospitalizations for a subgroup of patients with mild heart failure (NYHA Class I or II) and in improving echocardiographic parameters. Data indicates that biventricular resynchronization therapy may not demonstrate a benefit on quality of life, functional status, or progression to more advanced stages of heart failure. The evidence on mortality differs among the available studies. Of the two largest studies, MADIT-CRT and RAFT, one reported a mortality difference while the other did not. The RAFT trial had patients with more severe illness, a higher baseline death rate, and a longer follow-up period concluding that CRT is likely to improve mortality for patients with NYHA class II heart failure. A subanalysis of the RAFT study found that women in particular benefitted from CRT-D, and had a significantly reduced incidence of death and heart failure hospitalization as compared to men ($p<0.001$) (de Waard, et al., 2019). Robust evidence to support biventricular resynchronization therapy in patients with asymptomatic left ventricular dysfunction or NYHA Class I symptoms is inconclusive resulting in the inability to draw strong conclusions regarding the impact on health outcomes (Santangeli, et al., 2011; Al-Majed, et al., 2011; Adabag, et al., 2011; Zareba, et al., 2011; Versteeg, et al., 2011; Pouleur, et al., 2011; Solomon, et al., 2010; Tang, et al., 2010; Moss, et al., 2009; Linde, et al., 2008; Abraham, et al., 2004).

Patient Selection Criteria: Biventricular pacing is an established method of CRT, and is most effective for individuals experiencing heart failure with reduced ejection fraction (EF), left bundle branch block (LBBB), and a wide QRS. Pacing is also supported in individuals with a low EF receiving a new or replacement device and who require ≥ 40% ventricular pacing. However, approximately 30-50% of patients do not improve with biventricular pacing due to anatomical variances, a narrow QRS, non-LBBB presentation, or other factors (Sharma and Vijayaraman,

2021). Since some patients do not respond favorably after undergoing CRT, studies addressing optimal patient selection criteria for CRT are ongoing.

QRS Duration: Some patients with narrower QRS complexes have echocardiographic evidence of left ventricular mechanical dyssynchrony and may also benefit from CRT. Results of published trials are insufficient at this time to demonstrate that the use of CRT in heart failure patients with a narrow QRS complex (i.e., < 120 ms) benefits patient outcomes.

The Evaluation of Resynchronization Therapy for Heart Failure (LESSER-EARTH) trial was a randomized, double-blind, 12-center study that was designed to compare the effects of active and inactive cardiac resynchronization therapy in patients with severe left ventricular dysfunction and a QRS duration < 120 ms (Thibault, et al., 2013). The trial was interrupted prematurely by the Data Safety and Monitoring Board because of futility and safety concerns after 85 patients were randomized. The authors reported that in patients with a LVEF ≤ 35%, symptoms of heart failure, and a QRS duration < 120 ms, CRT did not improve clinical outcomes or left ventricular remodeling and was associated with potential harm (Thibault, et al., 2013).

Stavrakis et al. (2012) conducted a meta-analysis of randomized clinical trials to evaluate the impact of QRS duration on the efficacy of CRT. Only trials that reported subgroup data according to QRS duration were included. Five trials involving 6501 patients (4437 with QRS ≥ 150 ms and 2064 with QRS < 150 ms) were included. Three trials, enrolling patients with mild to moderate HF, compared CRT-implantable cardioverter defibrillator with CRT, whereas CRT versus medical therapy was compared in the other two trials, which included patients with advanced HF. In patients with intrinsic QRS duration ≥ 150 ms, pooled analysis of the five trials revealed a significant 42% reduction in the incidence of the of the primary endpoint of death or hospitalization for HF with the use of CRT compared to control (HR = 0.58, 95% CI: 0.50-0.68; p<0.00001), but not in patients with QRS < 150 ms (HR = 0.95, 95% CI: 0.83-1.10; p=0.51). These results were consistent across all degrees of HF severity. In patients with intrinsic QRS duration <150 ms, pooled analysis of the five trials showed no significant benefit from CRT (with or without ICD) compared to control (HR = 0.95, 95% CI: 0.83–1.10; p=0.51). The lack of benefit was consistent between the two subgroups based on the severity of heart failure.

Sipahi et al. (2011) conducted a meta-analysis of published randomized controlled trials that evaluated whether patients with modest prolongation of the QRS complex benefited from CRT. This study identified five trials enrolling a total of 5813 patients that reported on outcomes stratified by QRS duration. There was some variability in the definition of QRS categories, but the authors were able to categorize studies into those with moderately prolonged QRS, generally 120-149 ms, and severely prolonged QRS, generally ≥150 ms. For patients with a moderately prolonged QRS, there was no significant benefit for CRT in reducing composite outcomes of adverse cardiac events (Risk ratio [RR]: 0.95, 95% CI: 0.82 to 1.10, p=0.49). In contrast, for patients with a severely prolonged QRS, there was a 40% relative reduction in the composite outcomes (RR: 0.60, 95% CI: 0.53 to 0.67, p<0.001). Multiple limitations to these findings were reported including use of summary versus individual data in the meta-analysis; use of heterogeneous enrollment criteria by the five included trials with variable composite outcome measures; unknown morphology of the QRS complex in participants with a QRS duration less than 150 ms; and unknown percentages of study participants with RBBB (right bundle branch block). The authors reported that further analysis of individual subject-specific data from all relevant clinical trials can further refine the QRS cutoffs for different types of conduction abnormalities.

In a prospective randomized clinical trial, Beshai et al. (2007) enrolled 172 patients who had a standard indication for an ICD. Patients received a CRT-D device and were randomly assigned to the CRT group or to a control group (no CRT) for six months. The primary end point was the proportion of patients with an increase in peak oxygen consumption of at least 1.0 ml per

kilogram of body weight per minute during cardiopulmonary exercise testing at six months. At six months, the CRT group and the control group did not differ significantly in the proportion of patients with the primary end point (46% and 41%, respectively). In a pre-specified subgroup with a QRS interval of ≥ 120 ms, the peak oxygen consumption increased in the CRT group (p=0.02), but it was unchanged in a subgroup with a QRS interval of ≤ 120 ms (p=0.45). There were 24 heart failure events requiring intravenous therapy in 14 patients in the CRT group (16.1%) and 41 events in 19 patients in the control group (22.3%), but the difference was not significant. The authors reported that CRT did not improve peak oxygen consumption in patients with moderate-to-severe heart failure, providing evidence that patients with heart failure and narrow QRS intervals may not benefit from CRT.

In a prospective pilot study, Bleeker et al. (2006a) studied the effects of CRT in heart failure patients with narrow QRS complex (<120 ms) and evidence of LV dyssynchrony on tissue Doppler imaging (TDI). The study participants included a total of 33 consecutive patients with narrow QRS complex and 33 consecutive patients with wide QRS complex (control group). Patient inclusion criteria included: LV dyssynchrony ≥ 65 ms on TDI, NYHA functional Class III/IV heart failure, and LVEF ≤ 35%. Baseline characteristics, particularly LV dyssynchrony, were comparable between patients with narrow and wide QRS complex (p=NS). No significant relationship was observed between baseline QRS duration and LV dyssynchrony (p=NS). The improvement in clinical symptoms and LV reverse remodeling was comparable between patients with narrow and wide QRS complex (mean NYHA functional class reduction 0.9 versus 1.1; p=NS) and mean LV end-systolic volume reduction 39 versus 44 ml (p=NS). The authors reported that, "CRT appears to be beneficial in patients with narrow QRS complex and severe LV dyssynchrony on TDI, with similar improvement in symptoms and comparable LV reverse remodeling. These effects need confirmation in studies with larger populations." The authors noted that color-coded TDI measures the velocity of the myocardium, which may not always equal active myocardial contraction. Large, comparative studies are needed to define which technique is most accurate in the assessment of LV dyssynchrony.

QRS morphology: In a retrospective study, Dupont et al. (2012) evaluated the relative impact of QRS morphology and duration in echocardiographic responses to CRT and clinical outcomes. Baseline characteristics, clinical and echocardiographic response, and outcomes of all patients who received CRT at a single center were evaluated. Patients were stratified into four groups according to their baseline QRS morphology and QRS duration. A total of 496 patients were included in the study; 216 (43.5%) had LBBB and a QRS 150 ≥ ms, 85 (17.1%) had LBBB and QRS < 150 ms, 92 (18.5%) had non-LBBB and a QRS ≥150 ms, and 103 (20.8%) had non-LBBB and QRS <150 ms. Echocardiographic response (change in ejection fraction) was better in patients with LBBB and QRS ≥150 than in those with LBBB and QRS < 150 ms, non-LBBB and QRS ≥150, and non-LBBB and QRS >150 ms (p<0.0001). In a multivariate stepwise model with change in ejection fraction as the dependent variable, the presented classification was the most important independent variable (p=0.0003). Long-term survival was better in LBBB patients with QRS ≥ 150 (p=0.02), but this difference was not significant after adjustment for other baseline characteristics (p=0.15) suggesting that comorbid conditions may confound the treatment responses. The authors stated that "due to the lack of sufficiently powered trials in these subgroups, guideline committees have the difficult task of using this and similar studies to refine patient selection for CRT".

In a meta-analysis, Sipah et al. (2012) evaluated the effect of CRT on clinical events (including death and heart failure hospitalizations) with regards to bundle branch block morphologies. Four randomized controlled trials totaling 5356 patients met the inclusion criteria. The authors reported that in patients with a LBBB, CRT was very effective in reducing adverse events with a relative risk reduction of 36% (p=0.00001). However, no benefit was observed in patients with other types of conduction abnormalities and a QRS duration > 120 milliseconds.

Atrial Fibrillation: The use of CRT in atrial fibrillation (AF) is a growing area of study. Evidence in the published peer-reviewed literature is limited, but generally supportive, of CRT in individuals with AF with reduced ejection fraction on guideline-directed medical therapy, when criteria for CRT are otherwise met, and atrioventricular nodal ablation or pharmacological rate control will allow near 100% ventricular pacing with CRT (Heidenreich, et al., 2022; Steinberg, et al., 2022; Brignole, et al., 2021).

Other Cardiac Resynchronization and Pacing Technologies

To further evaluate potential solutions for CRT "nonresponders", studies have investigated alternative lead placement strategies, including triple-site (triventricular), conduction system, and wireless pacing.

Triple-site CRT (Triventricular Pacing)
Triple-site cardiac resynchronization or triventricular pacing involves the addition of another ventricular pacing lead. The typical triventricular configuration involves implanting the right ventricular and atrial leads as in conventional CRT, with the third ventricular lead joined in parallel with a Y-connector and connected to the left ventricular port of the CRT system. An alternate approach is using two RV leads and one LV lead.

Triventricular pacing has been proposed as an alternative approach to improve the response rate in CRT recipients. It has been suggested that failure of response to biventricular pacing is probably due to a combination of factors including placement of the pacing lead over a zone of slow conduction, the presence of scar within the left ventricle, variable electrical response of the diseased ventricle to pacing, or suboptimal positioning of the pacing leads with regard to the area of latest contraction (Rogers, et al., 2012).

Literature Review: Elliott et al. (2022) conducted a meta-analysis of six randomized controlled trials (RCTs; n=415 subjects) to evaluate the efficacy of multi-lead pacing compared to conventional biventricular CRT. Multi-lead pacing with two left ventricular (LV) leads and one right ventricular (RV) lead was utilized in four studies; one study used two RV leads and one LV lead; and one study used both configurations. Included were RCTs comparing standard biventricular CRT and multi-lead pacing CRT with follow up ≥ three months. Observational studies, nonrandomized studies, case reports, narrative reviews, and studies with only acute hemodynamic data were excluded. Outcome measures included echocardiographic outcomes; symptomatic outcomes using the six-minute walk test (6MWT), the Minnesota Living with Heart Failure Questionnaire (MLWHF) and New York Heart Association (NYHA) class; and mortality. Analysis demonstrated a statistically significant improvement in MLWHF score for multi-lead pacing versus conventional CRT ($p=0.05$), however the difference was not significant when only those patients receiving LV-only multi-lead pacing were included ($p=0.25$). There were no statistically significant differences between the groups in the remaining outcomes. The authors noted significant disadvantages to multi-lead pacing, including technical challenges, higher rates of battery depletion, and prolonged procedure times. Limitations of the meta-analysis included heterogeneity among the included studies in terms of inclusion criteria, study design, outcome reporting, and lead configuration. There was also a consistent underrepresentation of women across the included studies. The authors concluded the findings did not support the use of multi-lead pacing for CRT, although there may be a potential benefit to select patients (e.g., in atrial fibrillation or ischemic cardiomyopathy). Further RCTs to evaluate multi-lead pacing CRT in these subgroups are needed.

Gould et al. (2022) conducted the STRIVE HF (Standard care vs. TRIVEntricular pacing in Heart Failure; n=95) randomized controlled trial to evaluate whether triventricular (TriV) pacing was feasible and superior to standard BiV pacing in heart failure patients with left bundle branch block (LBBB) with a moderately prolonged QRS duration (120–150 ms). Subjects in the TriV group

underwent placement of two left ventricular (LV) leads and one right ventricular (RV) lead which were connected to a TriV device (Paradym TriV CRT-D) via an internal parallel Y-port. Subjects in the BiV group underwent placement of a quadripolar LV lead and CRT-defibrillator (CRT-D) device. The devices in both groups were programmed similarly. The study included patients with LBBB, QRS duration 120-150 ms, and age ≥ 18 years. Pregnant persons were excluded from the study. The primary outcome measure was the feasibility of TriV pacing. Other outcomes included reverse remodeling; N-terminal (NT)-pro hormone BNP (NTpro-BNP) value; six-minute walk test (6MWT); device shock therapy; quality of life scores; hospitalizations; adverse events; and mortality. Follow up occurred after six months. Successful device implantation occurred in 91.3% of subjects in the TriV group, and 95.9% of subjects in the BiV group. Pacing was maintained in 90% of the TriV subjects and 97.7% of the BiV subjects. Both groups showed a significant increase in left ventricular ejection fraction (LVEF) (TriV p=0.018, BiV p=0.007), and reduction in left ventricular end diastolic volume (p<0.001 each). Procedure time was significantly longer in the TriV group compared to the BiV group (192.6 ± 107.6 vs 133.9 ± 50.9 min, respectively; p<0.001). Mean LV pacing thresholds at implant were significantly higher in the TriV group versus the BiV group (1.3 ± 0.5 vs 1.0 ± 0.5 V, respectively; p=0.004). Battery longevity was significantly lower in the TriV group (5.5 ± 2.3 vs 8.6 ± 2.7 years, respectively; p<0.001). There were no significant between-group differences in the remaining outcomes. TriV pacing was deactivated in six patients after the study period due to threshold rises. There was one lead displacement reported in each group, and there was a limited coronary sinus dissection in the TriV group. Six deaths occurred during the study: two in the TriV group and four in the BiV group (one of which was thought to be procedure-related). The authors concluded that there was insufficient evidence to demonstrate that TriV pacing improved CRT response or provided any clinical benefit to patients with LBBB and intermediate QRS prolongation. Limitations of the study included short duration of follow up, unblinding of patients and investigators during follow up, lack of power calculation, and differences in leads used.

Zhang et al. (2017) conducted a meta-analysis of randomized controlled trials (RCTs) and comparative observational studies (n=251) comparing the benefits of triple-site ventricular (Tri-V pacing) versus Bi-V pacing on the left ventricular (LV) remodeling, quality of life, and exercise capacity in patients with heart failure (HF). The meta-analysis included one RCT, two randomized crossover studies, and two nonrandomized comparative studies. Two different pacing modalities were used. One type used one lead in the right ventricle and leads in two different tributaries in the left ventricle. The other used two leads in the right ventricle. Patients in the triple-site pacing group had greater improvement in LVEF (p<0.001) and NYHA classes (p=0.001) compared with the control group. There were no significant differences in left ventricular geometry, six-minute walk distance, or Minnesota Living With Heart Failure Questionnaire score between the two groups. The subgroup analyses showed there might be a greater improvement in LVEF in the Tri-V pacing group in patients with QRS duration ≥ 155 ms (p<0.001). The studies were limited by small sample size, short-term follow-up and lack of randomization. No study in this meta-analysis had power to assess the benefits of Tri-V pacing in terms of mortality, mobility, or other clinical outcomes.

There is a paucity of evidence in the peer-reviewed literature supporting the long-term safety and efficacy of triple-site resynchronization, compared to conventional biventricular pacing.

CRT with Wireless Left Ventricle Endocardial Pacing

The WiSE Cardiac Resynchronization Therapy System® (ebrSystems©, Sunnyvale, CA) is a wireless left ventricle (LV) pacing system that works with a conventional pacemaker and/or defibrillator for individuals in whom CRT is indicated. The WiSE CRT System is proposed to be used for patients who have failed conventional CRT or are not candidates for coronary sinus lead placement. The WiSE CRT system eliminates the need for a LV pacing wire in the coronary sinus. An ultrasonic transmitter attached to a battery unit and a tiny wireless receiver, measuring 10 x

2.6 millimeters (mm) acts as a pacing electrode. The transmitter is implanted in a left intercostal space, and the electrode is inserted into the LV via a retrograde aortic approach in a catheter-based procedure. After pacing-sensing mapping of the LV for site selection, the electrode is attached to the endocardial surface with a fixation barb. Sensing of RV pacing output from the conventional pacemaker device triggers ultrasonic energy transmission to the LV electrode from the transmitter, which stimulates synchronous contraction of the LV. The system allows the provider to customize electrode placement to the optimal location for pacing, which varies among patients; this differs significantly from conventional LV pacing leads, which are limited by coronary sinus anatomy.

U.S. Food and Drug Administration (FDA): The WiSE CRT System is approved by the FDA Investigational Device Exemption (IDE) approval process. On September 10, 2019, the manufacturer announced that the FDA had granted the WiSE CRT system breakthrough device designation status for the treatment of heart failure. A U.S. regulatory filing for the device has not yet been submitted. The U.S. pivotal Stimulation Of the Left Ventricle Endocardially (SOLVE) CRT study began in January 2018 and is ongoing.

Literature Review: There have been a limited number of studies published in the peer-reviewed literature addressing the use of this technology. The studies are primarily nonrandomized, have small patient populations, short term follow up, and lack a formal comparator group (Cang, et al., 2022; Wijesuriya, et al., 2022; Okabe, et al., 2021; Sidhu, et al., 2021; Sieniewicz, et al., 2020; Sidhu, et al., 2020; Singh, et al., 2019; Reddy, et al., 2017; Gamble, et al., 2018; Auricchio, et al., 2014). There is a lack of published randomized controlled trials evaluating CRT with wireless LV endocardial pacing. Clinical trials are ongoing.

Conduction System Pacing in Cardiac Resynchronization Therapy (CRT)
In conventional biventricular pacing, the pacing leads are placed in the right ventricle and in the coronary sinus (a large vein on the posterior surface of the heart) which then paces the left ventricle, causing the ventricles to beat synchronously. Conventional biventricular CRT is an established treatment for heart failure patients with low ejection fraction and ventricular dyssynchrony, and is effective in the majority of patients. However, around 30% of patients have a suboptimal response or do not respond to biventricular pacing CRT. This may be due to the patient's anatomy, atypical conduction disease, and/or coronary sinus lead dislodgement. Alternative strategies to achieve resynchronization have been studied, including conduction system pacing (CSP). Conduction system pacing is a technique of pacing that involves implanting permanent pacing leads at different sites along the cardiac conduction system, and includes His bundle pacing and left bundle branch pacing. These techniques are proposed to engage the intrinsic cardiac conduction system, with the intent to mimic the native ventricular activation sequence.

His Bundle Pacing (HBP): HBP was initially performed using standard pacing leads by reshaping the stylet or using a deflectable stylet to precisely position the lead at a site near the electrophysiology mapping catheter demonstrating the largest His deflection. This approach was technically challenging and time consuming. Case reports and review articles report that HBP may be an alternative approach in an attempt to achieve cardiac resynchronization in technically challenging cases where the standard endovascular approach via the coronary sinus is not possible. However HBP has been associated with atrial oversensing, higher capture thresholds, and increased risk for lead complications requiring revision (Lewis, et al., 2019; Vijayaraman, et al., 2019; Vijayaraman, 2018).

Left Bundle Branch Pacing (LBBP): Similar to His bundle pacing, LBBP (or left bundle branch area pacing [LBBAP]) is another conduction system pacing strategy being investigated as an alternative to conventional lead placement in CRT. LBBP is a more recent approach which involves

placing the pacing lead deep in the interventricular septum at the LBB region to capture the LV septum or proximal left conduction system. The premise is this placement will bypass the pathological or disease-vulnerable region in the conduction system such as the atrioventricular (AV) node or the His bundle, where AV block and bundle branch block likely occur (Chen, et al., 2019; Vijayaraman, et al., 2019). The limitations and complications of LBBP are reportedly similar to HBP; notably, cases of lead dislodgement and interventricular septal perforation have been reported in the literature.

U.S. Food and Drug Administration (FDA): In June 2018, the FDA granted Premarket Approval (PMA) to expand the indication for use of the Medtronic SelectSecure 3830 lead, to include pacing at the bundle of His.

In October 2022, the FDA approval for the SelectSecure 3830 lead was expanded to include pacing at the left bundle branch area as an alternative to right ventricular pacing.

Literature Review: There is a paucity of large randomized controlled clinical trials or comparative studies in the peer-reviewed literature assessing the impact of CRT with His bundle pacing or left bundle branch pacing on long-term health outcomes, compared to conventional biventricular pacing with traditional coronary sinus or epicardial LV leads. Evidence is primarily in the form of case studies, small case series, retrospective studies, and noncomparative observational feasibility studies, with limited follow up. Long-term efficacy and safety data are lacking (Wang, et al., 2022; Gui, et al., 2022; Tan, et al., 2021; Wu, et al., 2021; Vijayaraman, et al., 2021; Zweerink, et al., 2021; Huang, et al., 2020; Huang, et al., 2019; Boczar, et al., 2019, 2018; Vijayaraman, et al., 2019; Sharma, et al., 2018, 2017; Vijayaraman, 2018; Bhatt, et al., 2017; Huang, et al., 2017; Teng, et al., 2016; Lustgarten, et al., 2015).

Whinnett et al. (2023) conducted a randomized crossover trial to evaluate the effects of atrioventricular (AV) optimized His pacing CRT in select patients with heart failure. The study, conducted in the United Kingdom, included 167 participants (90% male; 82% White). The study inclusion criteria were symptomatic heart failure and left ventricular ejection fraction (LVEF) ≤ 40%; PR interval ≥ 200 milliseconds (ms), and either narrow QRS (≤ 140 ms) or right bundle branch block (RBBB, of any QRS duration). Excluded from the study were individuals with permanent or persistent atrial fibrillation; or paroxysmal AF with fewer than six months of maintained sinus rhythm. Participants were randomized to the "pacing" or "no pacing" groups. His bundle pacing was attempted in all patients, with either selective or non-selective capture accepted. When His bundle capture was not possible, an LV lead was placed. Patients also received an RA lead and a third lead which was either an RV defibrillator lead (where indicated) or an LV coronary sinus lead (used for backup pacing in the "no pacing" period, and/or as an alternative pacing lead if the His lead failed). After six months, subjects crossed over to the opposite treatment group. Twenty five (15%) participants were lost to follow up. The primary outcome measure was peak oxygen uptake on cardiopulmonary exercise testing. Other outcome measures included quality of life; LV dimensions; LVEF; plasma BNP; and incidence of ventricular arrhythmias. The authors found that His bundle pacing did not increase peak exercise oxygen consumption (+0.25 ml/kg/min, 95% confidence interval [CI] −0.23 to 0.73, p=0.3). The Minnesota Living with Heart Failure Questionnaire (MLHFQ) score improved significantly (−3.7, 95% CI −7.1 to −0.3, p=0.03) although the generic quality of life score (EQ-5D VAS) did not show a statistically significant improvement (+1.9, 95% CI −1.6 to 5.5, p=0.28). Left ventricular dimensions, LVEF, plasma BNP and incidence of ventricular arrhythmias did not change significantly with His bundle pacing. There were 19 heart failure admissions in each period/group (pacing and no pacing), and a total of 11 deaths were reported (six with pacing on and five with pacing off). The authors noted the study was not powered to detect a difference in these endpoints. Further limitations included the underrepresentation of non-male and non-White

participants; limited treatment time and follow up; and crossover design (i.e., lack of separate control group).

Wang et al. (2022) conducted a randomized controlled pilot trial (n=40) comparing the efficacy of left bundle branch pacing (LBBP)-CRT with biventricular pacing (BiVP)-CRT in patients with heart failure. Subjects were randomized 1:1 to either the LBBP group or the BiVP (control) group. During the LBBP procedure, a Select Secure pacing lead was placed on the right side of the interventricular septum into the LV septal subendocardium, until LBB capture was confirmed. Subjects in the BiVP group underwent standard biventricular CRT lead placement. The study inclusion criteria were age 18 to 80 years; sinus rhythm; nonischemic cardiomyopathy; complete LBBB; and New York Heart Association (NYHA) functional class II-IV. Excluded from the study were persons with ischemic cardiomyopathy; non-LBBB QRS; persistent atrial fibrillation; or who were pregnant. The mean age was 63.7 years, and 50% of subjects were female. The primary outcome measure was change in left ventricular ejection fraction (LVEF). Other endpoints included changes in echocardiographic measurements; N-terminal pro–B-type natriuretic peptide (NT-proBNP) value; NYHA functional class; 6-minute walk distance (6MWD); paced QRSd; and echocardiographic response to CRT. Follow ups were completed at three and six months. Four subjects in the BiVP group crossed over to the LBBP group, and two LBBP subjects crossed over to the BiVP group. The LBBP group had a significantly higher LVEF improvement at six months post-procedure, compared to the BiVP group (mean difference: 5.6%; 95% CI: 0.3-10.9; p=0.039). The remaining outcomes were comparable between the groups. One subject in the LBBP group had dislodgement of the coronary sinus LV lead two days post-procedure; one subject in the BiVP group experienced a pneumothorax. No revisions, hospitalizations, or deaths were reported. Limitations of the study included the small sample size; short duration of follow up; and relatively wide confidence intervals. The study was also limited to subjects with nonischemic cardiomyopathy and LBBB, which makes it difficult to generalize findings. The authors noted that the sample size was only designed to detect the difference in the change of LVEF, but not the other measures. Additional large randomized controlled trials with longer duration of follow up are needed to effectively compare left bundle branch pacing CRT with biventricular pacing CRT.

Chen et al. (2022) conducted a multicenter prospective nonrandomized observational study (n=100) to evaluate the feasibility and efficacy of CRT with left bundle branch pacing (LBBP-CRT) compared with optimized biventricular pacing with adaptive algorithm (BVP-aCRT) in patients with heart failure. Subjects were divided into each group per physician and patient choice. Left bundle branch pacing was performed on the LBBP-CRT group with pacing lead placement deep in the interventricular septum. The LBBP lead was programmed as pacing only or pacing prior to LV or RV lead if AV block occurred due to intraprocedural RBB injury. The LBBP lead was programmed back to pacing only once RBB injury resolved during follow up. In the BVP-aCRT group, pacing leads were placed in the RV apex and coronary sinus. Post-procedure, the devices in the BVP-aCRT group underwent adaptive optimization algorithm programming (aCRT; available on select devices). The study inclusion criteria were: symptomatic heart failure with NYHA class II-IV; LVEF ≤ 35%; sinus rhythm; QRS duration (QRSd) ≥ 150 ms; typical LBBB; age > 18 years; life expectancy > 1 year. Excluded from the study were persons with P-R interval > 200 ms, persistent atrial fibrillation, or intraventricular conduction defect. Outcome measures included implantation success rate; QRSd; pacing threshold; LVEF; echocardiographic measurements; NYHA class; and complications. Follow ups occurred at six and 12 months. The implant success rate for LBBP and BVP was 98.00% and 91.07%, respectively. Five subjects in the BVP-aCRT group crossed over to the LBBP-CRT group, and one subject in the LBBP-CRT group crossed over to the BVP-aCRT group. A significant reduction in QRSd was observed in both groups (p<0.001), with LBBP achieving the greatest reduced QRSd compared to BVP-aCRT (126.54 ± 11.67 ms vs 102.61 ± 9.66 ms, respectively; p<0.001). Pacing threshold at implantation was lower in the LBBP-CRT group than the BVP-aCRT group (0.92 ± 0.20 V/0.5ms vs 1.45 ± 0.39 V/0.5ms, respectively; p<0.001). The LBBP-CRT group had a significantly higher LVEF at six-month follow

up compared to the BVP-aCRT group (47.58 ± 12.02% vs 41.24 ± 10.56%, respectively; p=0.008). CRT with LBBP demonstrated a greater improvement in absolute LVEF at six and 12 months, compared to BVP-aCRT (18.52 ± 13.19% vs 12.89± 9.73%, respectively; p=0.020; and 20.90 ± 11.80% vs 15.20 ± 9.98%, respectively; p=0.015). There was no significant difference between the groups overall in response rate, however higher super-response rate (a > 20% improvement and a normalization of LVEF [> 50%]) was seen in the LBBP-CRT group as compared to the BVP-aCRT group at six months (53.06% vs 36.59%, respectively; p=0.016) and 12 months (61.22% v. 39.22%, respectively; p=0.028). Both groups demonstrated significant improvement in clinical heart function when evaluating the percentage of NYHA classification III–IV subjects, at follow up as compared to the subjects' baseline (all p<0.05); the percentage was significantly lower in the LBBP-CRT group compared to the BVP-aCRT group at 12 months (4.08% vs 19.61%, respectively; p=0.028). Both groups has a significant decrease in echocardiographic measurements (all p<0.05). Right bundle branch injury occurred during lead placement in 10 (20%) of LBBP-CRT subjects. Dislodgement of the LV lead occurred in one BVP-aCRT subject. Two subjects in the LBBP-CRT group and five subjects in BVP-aCRT group reported a heart failure hospitalization (no significant between-group difference). Author-noted limitations of the study included a relatively small cohort, non-randomized group allocation with risk of considerable selection bias, and overrepresentation of subjects with dilated cardiomyopathy, thus limiting the generalizability of results to persons with heart failure with atypical LBBB and other etiologies. Additionally, the comparator was BVP CRT utilizing an adaptive optimization algorithm, rather than conventional biventricular pacing, which may further limit the generalizability of the study results.

Vinther et al. (2021) conducted a pilot randomized controlled trial (n=50) to compare outcomes of CRT with His-bundle pacing (His-CRT) and with biventricular pacing (BiV-CRT) in symptomatic heart failure patients with left bundle branch block (LBBB). All subjects received a CRT-P or CRT-D device and were implanted with a standard RV-pacing lead or ICD lead and a standard atrial lead. For the His-CRT group, the third lead was implanted in the bundle of His and His capture was confirmed. For the BiV-CRT group, the third lead was implanted via the coronary sinus. Seven subjects crossed over from His-pacing to LV-pacing in the His-CRT group due to high capture thresholds or inability to capture. One subject crossed over from LV-pacing to His-pacing in the BiV-CRT group due to dissection in the coronary sinus ostium. The study inclusion criteria were: age ≥ 18 years; LVEF ≤ 35%; NYHA class II-IV; and LBBB by strict ECG/Strauss criteria. The exclusion criteria were: existing BiV pacing system; permanent atrial fibrillation; severe kidney disease; and acute myocardial infarct or coronary artery bypass graft within 3 months prior to study. Outcome measures included implant and capture success rate; procedure and radiation exposure; lead stability; complications; and improvements in QRS duration, LVEF and LV systolic volume, symptoms, NYHA class, walking distance, and N-terminal pro–B-type natriuretic peptide (NT-proBNP). Follow up was completed at six months post-procedure. Intention-to-treat implantation success rates were 72% for the His-CRT group and 96% for the BiV-CRT group. At six months, the His-CRT group maintained His bundle capture and LBBB correction. Procedure time was significantly longer for subjects in the His-CRT group versus the BiV-CRT group (137 ± 46 min vs. 102 ± 34 min; p<0.01). Lead thresholds were significantly higher in the His-CRT group compared with the BiV-CRT group at implantation (1.8 ± 1.4 V vs 1.2 ± 0.8 V; p<0.05) and at six month follow up (2.3 ± 1.4 V vs. 1.4 ± 0.5 V; p<0.01). From baseline to six months, both groups showed significant improvement in QRS duration, LVEF, LVESV, NT-proBNP, six-minute walk distance, and NYHA functional class (p<0.05), with no statistically significant between-group differences. One subject in the BiV-CRT group had dislodgement of the LV-lead and underwent replacement. One BiV-CRT subject had fever and positive blood cultures three weeks post-procedure and underwent device removal and reimplantation. The authors noted that this study was designed as a pilot study to provide estimates of crossover between groups and differences in various parameters to be used in future studies. A core laboratory for assessment of TTE parameters was not used. Further limitations of the study included the small sample size, short

duration of follow up, and overrepresentation of subjects with nonischemic cardiomyopathy, which may limit generalizability of findings.

Upadhyay et al. (2019a) published an on-treatment analysis of the His-SYNC pilot study randomized controlled trial (n=41), which aimed to assess the feasibility and efficacy of His bundle pacing cardiac resynchronization therapy (His-CRT) compared to biventricular pacing (BiV-CRT). Subjects had a diagnosis of heart failure, were 18 years or older, and met American College of Cardiology Foundation (ACCF)/American Heart Association (AHA)/Heart Rhythm Society (HRS) class I or II guideline indications for CRT. Excluded from the study were persons with an existing CRT device or who were pregnant. Most participants (n=35) had LBBB, and 33% had atrial fibrillation. His-CRT was performed utilizing the Medtronic SelectSecure Model 3830 lead. The BiV-CRT group underwent standard lead placements for CRT. Intraprocedural group crossover for patients randomized to His-CRT was required if the paced QRS width did not narrow by at least 20% or to a QRS width of ≤130 ms, or if placement of the HBP lead could not be performed with sufficient stability or pacing output. Similarly, crossover for patients randomized to the BiV-CRT group occurred when an LV lead could not be placed, or when diaphragmatic stimulation occurred due to phrenic nerve capture. Ultimately, crossover occurred in 48% of patients assigned to the His-CRT group, and 26% of patients in the BiV-CRT arm; a total of 16 subjects received His-CRT. The His-CRT group demonstrated a significant decrease in QRS duration ($p<0.001$) and significant increase in LVEF ($p<0.001$) at six months. Limitations of the study include the high rates of intraprocedural crossover, small study population, and short term follow up. Additional well-designed randomized controlled trials with large patient populations and long term follow-up are needed to support the clinical effectiveness of His bundle pacing CRT.

Qian et al. (2019) conducted a systematic review and meta-analysis to evaluate the efficacy of HBP in patients with heart failure and LV dyssynchrony. The successful rate of implantation, QRS duration, pacing threshold, LV function at baseline and follow-up, and mortality rates were extracted and summarized. Eleven studies including 494 patients were included in this analysis. The average age of the patients was 71.9 years and 63.2% of patients were male. Patients with ischemic etiology accounted for 32.8% of the population. Four studies reported 173 patients with atrial fibrillation (AF) and cardiomyopathy undergoing atrioventricular (AV) node ablation. The other seven studies focused on CRT candidates including de novo implantation, CRT nonresponders, patients with pacing-induced cardiomyopathy, and failed LV lead placement. The overall successful rate for implantation was 82.4%. The main indications for HBP were CRT candidates and cardiomyopathy with atrial fibrillation undergoing atrioventricular node ablation. Permanent HBP resulted in narrow QRS duration of 116.3 ± 13.9 ms after implantation. LV functions, including echocardiographic parameters and clinical outcomes, significantly improved at follow-up ($p<0.001$). However, there was a trend of increased capture and bundle branch block correction thresholds at follow-up compared to baseline ($p=0.01$ and 0.02, respectively). During a mean follow-up of 23.7 months, 5.9% of the patients experienced heart failure-related hospitalization and the mortality rate was 9.1%. The authors reported limitations of this meta-analysis include the limited sample size and most of the studies were cohort studies with inherent limitations that reduced the internal validity compared to randomized controlled trials. There was limited data on the effect size of HBP on outcomes as the studies included were observational and did not all have comparative arms. Next, some data, including pacing pulse width and follow-up time, were variable and inconsistent, which may influence the study uniformity. In addition, there was no uniformity in measuring QRS durations with selective and nonselective HBP. The authors concluded that although HBP has shown promising results in small and nonrandomized studies in several clinical situations, long-term safety and pacing threshold are needed.

Ali et al. (2018) concluded in a report on HBP that there was limited published data available for His pacing in any clinical setting. Although pacing thresholds for His pacing in bradycardia appear to be stable, there is limited long-term follow-up data available. When His pacing is used to deliver

ventricular resynchronization in patients with bundle branch block, the pacing thresholds can be relatively high, though comparable to left ventricular pacing thresholds. This has potential implications on battery longevity, though pacing is only required via a single lead (compared to biventricular pacing). Success rates for His lead implantation have been as low as 60% without dedicated tools and experience. Success rates have improved with the development of dedicated tools; however, the range of tools currently available are still limited, and these could be further improved. Adequately powered randomized control trials are required to investigate whether the theoretical advantages of physiological ventricular activation are achieved with His pacing and if the encouraging results in observational studies translate into clinical benefit (Ali, et al., 2018).

Ezzeddine et al. (2018) reported that certain problems unique to HBP are faced with conventional active fixation pacing leads, including a higher pacing threshold owing to the fibrous structure of the His bundle and due to current limitations in lead design and delivery. In addition, higher pacing thresholds can lead to increased battery drain and shorter battery longevity compared with traditional RV pacing. Other limitations of permanent HBP include inability to perform lead implantation in 10%-20% of patients, particularly in patients with dilated and remodeled atria or other structural heart disease, which makes mapping of the His bundle and delivery of the lead difficult. Ventricular undersensing, atrial oversensing on the ventricular channel, and atrial capture can also occur and need to be carefully avoided or excluded at the time of implantation. Long-term randomized safety and efficacy data are needed.

Permanent Leadless Pacemaker
Traditional cardiac pacemakers are implanted through a small incision and fitted into a pocket created under the skin of the upper chest near the collarbone with the pacemaker leads placed via transvenous access to the heart chambers and attached to the generator. The leads transmit information from the heart to the generator, and electrical impulses from the generator to heart muscle. Leadless pacemaker systems utilize a self-contained system which includes both the pulse generator and the electrode within a single unit that is placed into the right ventricle via a transvenous approach. Compared to traditional transvenous pacemakers, leadless pacemakers have been reported to have higher rates of pericardial effusion and/or perforation, cardiac tamponade, and death (Garg, et al., 2023; Mararenko, et al., 2023; Hauser, et al., 2021; Piccini, et al., 2021).

U.S. Food and Drug Administration (FDA): In April 2016, the FDA granted premarket approval (PMA) for the Micra™ Transcatheter Pacemaker System (TPS) (Medtronic, Mounds View, MN). This device is indicated for use in patients who have experienced one or more of the following conditions:

- symptomatic paroxysmal or permanent high-grade atrioventricular (AV) block in the presence of atrial fibrillation (AF)
- symptomatic paroxysmal or permanent high-grade AV block in the absence of AF, as an alternative to dual chamber pacing, when atrial lead placement is considered difficult, high risk, or not deemed necessary for effective therapy
- symptomatic bradycardia-tachycardia syndrome or sinus node dysfunction (sinus bradycardia or sinus pauses), as an alternative to atrial or dual chamber pacing, when atrial lead placement is considered difficult, high risk, or not deemed necessary for effective therapy

Rate-responsive pacing is indicated to provide increased heart rate appropriate to increasing levels of activity.

The Micra device is contraindicated for patients who have implanted devices that would interfere with the pacemaker, who are severely obese, or who have an intolerance to materials in the device or the blood thinner heparin. It is also contraindicated for patients with veins that are unable to accommodate the 7.8 millimeter introducer sheath or pacemaker implant.

On November 17, 2021, the FDA issued a letter to healthcare providers reaffirming the risk of major complications should cardiac perforation occur during leadless pacemaker implantation. Cardiac perforation is a rare complication of any pacemaker implantation, and the overall risk of perforation associated with leadless pacemaker implantation appears similar to the risk associated with traditional pacing implants. However, per the statement issued: "the Medtronic Micra leadless pacemaker premarket clinical studies suggested major complications related to cardiac perforation appeared to be more severe for patients who received a leadless pacing system compared to patients who received a transvenous pacemaker. The FDA continues to evaluate outcomes in patients who receive leadless pacing systems. Information from real-world use suggests that cardiac perforations associated with Micra leadless pacemakers are more likely to be associated with serious complications, such as cardiac tamponade or death, than with traditional pacemakers" (FDA, 2021).

The Nanostim™ leadless pacemaker (St. Jude Medical, now Abbott Medical, Sylmar, CA) was investigated as part of a Phase I clinical trial between 2013 and 2016; a total of 1,423 devices were implanted. The trial was halted in 2016 and the device recalled due to battery malfunction and difficulty with device retrieval. The Nanostim device was later modified and released under the name Aveir™ VR Leadless System (Abbott Medical, Sylmar, CA). The Aveir single chamber device received FDA premarket approval in March 2022. Per the approval, the Aveir device is indicated for patients with bradycardia and:

- normal sinus rhythm with only rare episodes of AV block or sinus arrest
- chronic atrial fibrillation
- severe physical disability
- Rate-Modulated Pacing is indicated for patients with chronotropic incompetence and for those who would benefit from increased stimulation rates concurrent with physical activity

A 10-year post-approval study is ongoing (FDA, 2022; Reddy, et al., 2022).

In June 2023, the Aveir™ DR dual chamber leadless pacemaker system (Abbott Medical, Sylmar, CA) received FDA premarket approval. Per the supplemental approval:
"The Aveir DR Leadless System is indicated for management of one or more of the following permanent conditions:

- Syncope
- Pre-syncope
- Fatigue
- Disorientation

Rate-Modulated Pacing is indicated for patients with chronotropic incompetence, and for those who would benefit from increased stimulation rates concurrent with physical activity.

Dual-Chamber Pacing is indicated for patients exhibiting:

- Sick sinus syndrome
- Chronic, symptomatic second- and third-degree AV block
- Recurrent Adams-Stokes syndrome
- Symptomatic bilateral bundle branch block when tachyarrhythmia and other causes have been ruled out

Atrial Pacing is indicated for patients with:

- Sinus node dysfunction and normal AV and intraventricular conduction systems

Ventricular Pacing is indicated for patients with:

- Significant bradycardia and normal sinus rhythm with only rare episodes of AV block or sinus arrest
- Chronic atrial fibrillation

- Severe physical disability”

Literature Review: In a prospective registry, El-Chami et al. (2018) compared the outcomes of the Micra transcatheter pacing system (TPS) to a historical transvenous pacing cohort implanted with dual-chamber pacemakers. The authors report updated performance of the Micra TPS from a worldwide post approval registry (PAR) and compare it with The Micra Investigational Device Exemption (IDE) study as well as a transvenous historical control. The safety objective of the analysis was system- or procedure-related major complications through 12 months postimplantation. A comparison of the major complication rate with that of the 726 patients from the IDE and with a reference data set of 2667 patients with transvenous pacemakers. The Micra device was successfully implanted in 1801 of 1817 patients (99.1%). The mean follow-up period was 6.8 months. Through 12 months, the major complication rate was 2.7%. The risk of major complications for Micra PAR patients was 63% lower than that for patients with transvenous pacemakers through 12 months postimplantation. The major complication rate trended lower in the PAR than in the IDE study, driven by the lower pericardial effusion rate in the PAR. There were three cases of infection associated with the procedure, but none required device removal and there were no battery or telemetry issues. Pacing thresholds were low and stable through 12 months postimplantation. A reported limitation of this study is lack of a randomized controlled study which would allow a direct comparison and would clearly define the benefits and drawbacks of leadless pacing compared to traditional transvenous pacemakers.

Roberts et al. (2017) reported acute performance of the Micra transcatheter pacemaker from a worldwide Post-Approval Registry, a prospective single-arm observational study designed to assess the safety and effectiveness of Micra in the post-approval setting. The safety end point was system or procedure-related major complications at 30 days post implant. Major complication rates were compared with that of the 726 patients from the investigational study (Reynolds, et al., 2016). Electrical performance was also characterized. The device was successfully implanted in 792 of 795 registry patients (99.6%) by 149 implanters at 96 centers in 20 countries. Through 30 days post implant, a total of 13 major complications occurred in 12 patients, for a major complication rate of 1.51% (95%). Major complications included cardiac effusion/perforation (1, 0.13%), device dislodgement (1, 0.13%), and sepsis (1, 0.13%). After adjusting for baseline differences, the rate of major complications in the registry trended lower than the investigational trial. Early pacing capture thresholds were low and stable. The data does not include all patients implanted with Micra TPS worldwide. This report is an interim analysis with limited follow-up, including patients who had not yet been followed for 30 days, and it reflects the geographies of enrolled patients who were primarily from Europe. However, enrollment of patients in the United States is continuing, and patients in the registry will be followed for a minimum of nine years. Few patients had follow-up electrical data available, and thus battery projections are preliminary and based on only 54 patients.

In a multicenter prospective international study, the Micra Transcatheter Pacing Study, Duray et al. (2017) reported on long-term safety of Micra at 12 months and electrical performance through 24 months. Enrolled patients met class I or II guideline recommendations for de novo ventricular pacing. The long-term safety objective was freedom from a system- or procedure-related major complication at 12 months. A predefined historical control group of 2667 patients with transvenous pacemakers was used to compare major complication rates. The long-term safety objective was achieved with a freedom from major complication rate of 96.0% at 12 months. The risk of major complications for patients with Micra (n=726) was 48% lower than that for patients with transvenous systems through 12 months postimplant. Across subgroups of age, sex, and comorbidities, Micra reduced the risk of major complications compared to transvenous systems. Electrical performance was excellent through 24 months, with a projected battery longevity of 12.1 years.

In a prospective observational study (n=30), Martinez-Sande et al. (2017) reported on the safety and efficacy of the Micra leadless pacemaker. Outcome measures were major complication (defined as death, serious deterioration of patient's condition, event resulting in vital risk requiring intervention, or hospitalization ≥48 hrs). Successful implantation was accomplished in all patients referred for leadless implantation. The mean age was 79.4 years; 20 (66.6%) were men and 28 had permanent atrial fibrillation (93.3%); one had atrial tachycardia and one had sinus rhythm. Concomitant atrioventricular node ablation was performed immediately after implantation in five patients (16.6%), and implantation was performed after transcatheter aortic valve implantation in two. With the exception of one moderate pericardial effusion without tamponade, there were no severe complications. The mean follow up was 5.3 months and four patients had more than one year of follow-up. Sensing and pacing parameters were stable both at implantation and during the short- to mid-term follow-up.

Reynolds et al. (2016) reported on interim analysis of an on-going prospective, nonrandomized, single-study-group, multisite, clinical study to evaluate the safety and efficacy of the Micra Transcatheter Pacemaker System (Medtronic). Transcatheter pacemaker was implanted in 725 patients with guideline-based indications for ventricular pacing, with 719 (99.2%) successfully implanted and followed for six months. The primary safety end point was freedom from system-related or procedure-related major complications. The primary efficacy end point was the percentage of patients with low and stable pacing capture thresholds at six months (≤2.0 V at a pulse width of 0.24 ms and an increase of ≤1.5 V from the time of implantation). The safety and efficacy end points were evaluated against performance goals (based on historical data) of 83% and 80%, respectively. A post hoc analysis was completed in which the rates of major complications was compared with a control cohort of 2667 patients with transvenous pacemakers from six previously published studies. The Kaplan–Meier estimate of the rate of the primary safety end point was 96.0% (95% confidence interval [CI], 93.9 to 97.3; p<0.001 for the comparison with the safety performance goal of 83%); there were 28 major complications in 25 of 725 patients, and no dislodgements. The rate of the primary efficacy for 297 patients end point was 98.3% (95% CI, 96.1 to 99.5; p<0.001 for the comparison with the efficacy performance goal of 80%) among 292 of 297 patients with paired 6-month data. Patients with transcatheter pacemakers had fewer major complications than did the control patients (hazard ratio, 0.49; 95% CI, 0.33 to 0.75; p=0.001). The study was limited by the lack of randomization, the comparator was historical data and this was an interim analysis of less than half the participants at six months.

Professional Societies/Organizations
American Heart Association (AHA)/American College of Cardiology (ACC)/Heart Failure Society of America (HFSA) Guideline for the Management of Heart Failure: The updated AHA/ACC/HFSA guidelines for the management of heart failure (HF) were published in 2022. To develop the guidelines, the committee used evidence-based methodologies to assign each recommendation a Class of Recommendation and a Level of Evidence:

Class (Strength) of Recommendation

- Class 1 (Strong)
  Benefit >>> Risk
  Intervention is recommended; is indicated/useful/effective/beneficial
- Class 2a (Moderate)
  Benefit >> Risk
  Intervention is reasonable; can be useful/effective/beneficial
- Class 2b (Weak)
  Benefit ≥ Risk
  Intervention may be reasonable; may be considered; its usefulness/ effectiveness is unknown/unclear/uncertain or not well-established

- Class 3: No Benefit (Moderate)
  Benefit = Risk
  Intervention is not recommended/indicated/useful/effective/beneficial; it should not be performed/ administered
- Class 3: Harm (Strong)
  Risk > Benefit
  Intervention is potentially harmful; causes harm; is associated with excess morbidity/mortality; should not be performed/administered

Level of Evidence (LOE)

- Level A
  High-quality evidence from more than one RCT
  Meta-analyses of high-quality RCTs
  One or more RCTs corroborated by high-quality registry studies
- Level B-R (Randomized)
  Moderate-quality evidence from one or more RCTs
  Meta-analyses of moderate-quality RCTs
- Level B-NR (Nonrandomized)
  Moderate-quality evidence from one or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
  Meta-analyses of such studies
- Level C-LD (Limited Data)
  Randomized or nonrandomized observational or registry studies with design or execution limitations
  Meta-analyses of such studies
  Physiological or mechanistic studies in human subjects
- Level C-EO (Expert Opinion)
  Consensus of expert opinion based on clinical experience

To reduce total mortality and hospitalizations, and improve symptoms and quality of life (QOL) in patients with heart failure with reduced ejection fraction (HFrEF), the committee made the following recommendations concerning cardiac resynchronization therapy (CRT) (Heidenreich, et al, 2022):

- Strong recommendation:
  - For individuals with left ventricular ejection fraction (LVEF) ≤ 35%, sinus rhythm, left bundle branch block (LBBB) with a QRS duration ≥ 150 ms, and New York Heart Association (NYHA) class II, III, or ambulatory IV symptoms on guideline-directed medical therapy (GDMT), CRT is indicated (Class of Recommendation: 1; Level of Evidence: B-R)

- Moderate recommendation:
  - For individuals with LVEF ≤ 35%, sinus rhythm, non-LBBB pattern with a QRS duration ≥ 150 ms, and NYHA class II, III, or ambulatory class IV symptoms on GDMT, CRT can be useful (Class of Recommendation: 2a; Level of Evidence: B-R)
  - For individuals with high-degree or complete heart block and LVEF of 36% to 50%, CRT is reasonable (Class of Recommendation: 2a; Level of Evidence: B-R)
  - For individuals with LVEF ≤ 35%, sinus rhythm, LBBB with a QRS duration of 120 to 149 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT, CRT can be useful (Class of Recommendation: 2a; Level of Evidence: B-NR)
  - For individuals with atrial fibrillation (AF) and LVEF ≤ 35% on GDMT, CRT can be useful if: a) the patient requires ventricular pacing or otherwise meets CRT criteria and b) atrioventricular nodal ablation or pharmacological rate control will allow near

100% ventricular pacing with CRT (Class of Recommendation: 2a; Level of Evidence: B-NR)
  - For individuals with LVEF ≤ 35% on GDMT and undergoing placement of a new or replacement device implantation with anticipated requirement for significant (> 40%) ventricular pacing, CRT can be useful (Class of Recommendation: 2a; Level of Evidence: B-NR)

- Weak recommendation:
  - For individuals with LVEF ≤ 35%, sinus rhythm, a non-LBBB pattern with QRS duration of 120 to 149 ms, and NYHA class III or ambulatory class IV on GDMT, CRT may be considered (Class of Recommendation: 2b; Level of Evidence: B-NR)
  - For individuals with LVEF ≤ 30%, ischemic cause of HF, sinus rhythm, LBBB with a QRS duration ≥ 150 ms, and NYHA class I symptoms on GDMT, CRT may be considered (Class of Recommendation: 2b; Level of Evidence: B-NR)

- Not recommended:
  - For individuals with QRS duration <120 ms, CRT is not recommended (Class of Recommendation: 3 – no benefit; Level of Evidence: B-R)
  - For individuals with NYHA class I or II symptoms and non-LBBB pattern with QRS duration < 150 ms, CRT is not recommended (Class of Recommendation: 3 – no benefit; Level of Evidence: B-NR)
  - For individuals whose comorbidities or frailty limit survival with good functional capacity to < 1 year, ICD and cardiac resynchronization therapy with defibrillation (CRT-D) are not indicated (Class of Recommendation: 3 – no benefit; Level of Evidence: C-LD)

Heart Rhythm Society (HRS)/Asia Pacific Heart Rhythm Society (APHRS)/Latin American Heart Rhythm Society (LAHRS): In 2023 these societies published a clinical practice guideline on cardiac physiologic pacing for the avoidance and mitigation of heart failure. The guideline defined cardiac physiologic pacing (CPP) as "as any form of cardiac pacing intended to restore or preserve synchrony of ventricular contraction", achieved via conduction system pacing (CSP; including His bundle pacing [HBP]and left bundle branch area pacing [LBBAP]), or CRT via biventricular (BiV) pacing using a coronary sinus branch or epicardial LV pacing lead. Scientific evidence was systematically reviewed and interpreted to develop several recommendations, which were then assigned a class of recommendation and a level of evidence using the ACC/AHA recommendation system described above. Among the highest-rated recommendations were the following:

Class of Recommendation: 1; Level of Evidence: A
- In patients with LVEF ≤ 35%, sinus rhythm, LBBB with QRS duration ≥150 ms, and NYHA class II–IV symptoms on guideline-directed medical therapy (GDMT), CRT with BiV pacing is indicated to improve symptoms and reduce morbidity and mortality.
- In patients with select characteristics (e.g., female) who have LVEF ≤ 35%, sinus rhythm, LBBB with QRS duration 120–149 ms, and NYHA class II–IV symptoms on GDMT, CRT with BiV pacing is recommended to reduce mortality and HF events and to improve LVEF.

Class of Recommendation: 1; Level of Evidence: B-R
- In patients undergoing CRT implant, a quadripolar LV lead is recommended to assist with lead stability, lower capture thresholds, avoid phrenic nerve pacing, and decrease need for lead repositioning.

Class of Recommendation: 2a; Level of Evidence: A

- In patients who have LVEF ≤35%, sinus rhythm, a non-LBBB pattern with QRS duration ≥150 ms, and NYHA class III or ambulatory class IV symptoms on GDMT, CRT with BiV pacing can be useful to improve functional class, cardiac structure, and LVEF.

Class of Recommendation: 2a; Level of Evidence: B-R

- In patients with LVEF ≤ 35%, sinus rhythm, LBBB with QRS duration 120–149 ms, and NYHA class II–IV symptoms on GDMT, CRT with BiV pacing is reasonable to reduce mortality and HF and to improve LVEF.
- In patients with an indication for permanent pacing with an LVEF 36%–50% who are anticipated to require substantial ventricular pacing, CPP is reasonable to reduce the risk of pacing-induced cardiomyopathy (Note: Level of Evidence B-R is for CRT, and B-NR for HBP, LBBAP).
- In patients with an indication for permanent pacing with LVEF >35% who are anticipated to require less than substantial ventricular pacing, it is reasonable to choose a traditional RV lead placement and minimize right ventricular pacing.
- In patients with atrial fibrillation undergoing atrioventricular junction ablation with LVEF ≤ 50%, CRT with BiV pacing is reasonable to improve heart failure hospitalization, reverse structural remodeling, and improve quality of life, exercise capacity, LVEF, and potentially mortality.

Regarding the evidence to support the use of biventricular pacing/CRT versus conduction system pacing (CSP), the authors noted "The strength of evidence for CRT in heart failure (HF) is substantially greater than what is available to support CSP. Multiple randomized controlled trials have shown a beneficial effect of CRT in reducing HF symptoms and hospitalization, improving left ventricular function, and increasing survival. The majority of data on CSP are observational, and long-term data on lead survival are lacking. Ongoing and planned studies are likely to provide future guidance on the use of CSP compared to CRT" (Chung, et al., 2023).

American Heart Association (AHA)/American College of Cardiology (ACC) Guideline for the Diagnosis and Treatment of Patients With Hypertrophic Cardiomyopathy: The 2020 AHA/ACC clinical practice guideline for the care of patients with hypertrophic cardiomyopathy (HCM) included the recommendation that cardiac resynchronization therapy (CRT) for symptom reduction is reasonable in selected adult patients with nonobstructive HCM receiving an ICD who have NYHA class II to ambulatory class IV HF, left bundle branch block (LBBB), and LV ejection fraction (LVEF) < 50% (Class of Recommendation: 2a; Level of Evidence: C-LD) (Ommen, et al., 2020).

American College of Cardiology (ACC)/American Heart Association (AHA)/Heart Rhythm Society (HRS) 2018 Guideline on the Evaluation and Management of Patients With Bradycardia and Cardiac Conduction Delay: The 2018 ACC/AHA/HRS document makes the following recommendations for permanent pacing techniques in persons with atrioventricular block:

- In patients with atrioventricular block who have an indication for permanent pacing with a LVEF between 36% and 50% and are expected to require ventricular pacing more than 40% of the time, it is reasonable to choose pacing methods that maintain physiologic ventricular activation (e.g., cardiac resynchronization therapy [CRT] or His bundle pacing) over right ventricular pacing (Class of Recommendation: 2a; Level of Evidence: B-R)
- In patients with atrioventricular block who have an indication for permanent pacing with a LVEF between 36% and 50% and are expected to require ventricular pacing less than 40% of the time, it is reasonable to choose right ventricular pacing over pacing methods that maintain physiologic ventricular activation (e.g., CRT or His bundle pacing) (Class of Recommendation: 2a; Level of Evidence: B-R)

- In patients with atrioventricular block at the level of the atrioventricular node who have an indication for permanent pacing, His bundle pacing may be considered to maintain physiologic ventricular activation (Class of Recommendation: 2b; Level of Evidence: B-R)

The guideline described His bundle pacing as a "promising pacing option". Supportive evidence consisted of small nonrandomized studies. The authors noted that "more studies are needed to better characterize His bundle pacing and compare it to RV and CRT pacing in atrioventricular block patients".

Regarding leadless pacemakers, the guideline further notes "pacing with entirely leadless devices is…an emerging area of interest, but the role of these new devices in real-world practice, and their potential interaction with other cardiac devices, is not yet clear" (Kusumoto, et al., 2019).

American College of Cardiology Foundation (ACCF)/Heart Rhythm Society (HRS)/American Heart Association (AHA)/American Society of Echocardiography (ASE)/Heart Failure Society of America (HFSA)/Society for Cardiovascular Angiography and Interventions (SCAI)/Society of Cardiovascular Computed Tomography (SCCT)/Society for Cardiovascular Magnetic Resonance (SCMR) 2013 Appropriate Use Criteria for Implantable Cardioverter-Defibrillators and Cardiac Resynchronization Therapy: The 2013 ACCF/HRS/AHA/ASE/HFSA/SCAI/SCCT/SCMR document addresses the appropriate use of implantable cardioverter-defibrillators (ICDs) and cardiac resynchronization therapy (CRT) for selected patient populations (Russo, et al., 2013). The authors state that the appropriate use criteria should be used in conjunction with the ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities and the 2012 focused update (Epstein, et al., 2013; Epstein, et al., 2008).

The indications for ICD and CRT were developed by a multidisciplinary writing team and scored by a separate independent technical panel. The final score reflects the median score of the 17 technical panel members and has been labeled according to the categories of Appropriate (median 7 to 9), May Be Appropriate (median 4 to 6), and Rarely Appropriate (median 1 to 3). The authors state that "The relationship of these criteria to existing guidelines was provided to the technical panel. In addition, extensive links to clinical trials and other literature regarding the role of ICD and CRT in each clinical scenario were provided to technical panel members. This document represents the current understanding of the clinical utility of ICD and CRT implantation in clinical practice as measured by physicians with a variety of backgrounds and areas of expertise. It is the goal that these criteria will help provide a guide to inform medical decisions and help clinicians and stakeholders understand areas of consensus as well as uncertainty, while identifying areas where there are gaps in knowledge that warrant additional investigation" (Russo, et al., 2013).

The authors also state that, "Atrial arrhythmias (including atrial fibrillation, atrial flutter, and atrial tachycardia) are not included in the indication tables. There are fewer data available for CRT in patients with persistent atrial arrhythmias, and the writing group elected to avoid additional scenarios for practical reasons, as the document already includes a large number of scenarios. However, it is assumed that the presence of intermittent or persistent atrial arrhythmias would not preclude CRT implantation, and the benefits of CRT would also apply to patients with persistent atrial arrhythmias, as long as CRT is maintained nearly 100% of the time" (Russo, et al., 2013).

Ambulatory class IV is defined as class IV heart failure with: 1) no active acute coronary syndrome; 2) no inotropes; and 3) on guideline-direct medical therapy (GDMT). A normal LVEF is defined as ≥ 50%. The authors stated that, "GDMT for heart failure in the setting of LV systolic dysfunction requires individualization but typically should include the combination of an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker and beta blocker therapy adjusted to target doses as tolerated, with diuretics adjusted if/as needed to control fluid

retention. In selected patients, the addition of aldosterone antagonists and hydralazine plus nitrate combinations should be considered. Patients who are going to receive substantial benefit from medical treatment alone usually show some clinical improvement during the first 3 to 6 months. Medical therapy is also assumed to include adequate rate control for tachyarrhythmias, including atrial fibrillation. Therefore, it is recommended that GDMT be provided for at least 3 months before planned reassessment of LV function to consider device implantation. If LV function improves to the point where primary prevention indications no longer apply, then device implantation is not indicated" (Russo, et al., 2013).

Recommendations are provided based on the following scoring method:

- **Median score 7-9:** Appropriate care: An appropriate option for management of patients in this population due to benefits generally outweighing risks; effective option for individual care plans, although not always necessary, depending on physician judgment and patient-specific preferences (i.e., procedure is generally acceptable and is generally reasonable for the indication).
- **Median score 4-6:** May be appropriate for care: At times an appropriate option for management of patients in this population due to variable evidence or agreement regarding the benefit/risk ratio, potential benefit based on practice experience in the absence of evidence, and/or variability in the population; effectiveness for individual care must be determined by a patient's physician in consultation with the patient based on additional clinical variables and judgment along with patient preferences (i.e., procedure may be acceptable and may be reasonable for the indication).
- **Median score 1-3:** Rarely appropriate care: Rarely an appropriate option for management of patients in this population due to the lack of a clear benefit/risk advantage; rarely an effective option for individual care plans; exceptions should have documentation of the clinical reasons for proceeding with this care option (i.e., procedure is not generally acceptable and is not generally reasonable for the indication).

Generally, criteria that have been deemed Appropriate or May Be Appropriate in these scenarios are supported by a critical mass of existing data, or were deemed by the technical panel to meet sufficient clinical judgment to be reasonable and appropriate.

Indications rated as Appropriate or May be Appropriate are detailed below; indications rated as Rarely Appropriate (median score 1-3) are outlined in the appropriate use criteria document described above.

The following indications were rated as Appropriate Care (median score 7-9):

Ischemic cardiomyopathy, left ventricular ejection fraction (LVEF) ≤ 30%, no prior implant, sinus rhythm (SR) for ANY of the following:

- QRS 120-149 milliseconds (ms), left bundle branch block (LBBB), New York Heart Association (NYHA) Class II (7), III-IV (8)
- QRS ≥ 150 ms, LBBB, NYHA Class I (7) II (8), III-IV (9)
- QRS ≥ 150 ms, non-LBBB, NYHA Class III-IV (7)

Ischemic cardiomyopathy, LVEF 31-35%, no prior implant, SR for ANY of the following:

- QRS 120-149 ms, LBBB, NYHA Class II (7), III-IV (8)
- QRS ≥ 150 ms, LBBB, NYHA Class II (8), III-IV (9)
- QRS ≥ 150 ms, non-LBBB, NYHA Class III-IV (7)

Nonischemic cardiomyopathy, LVEF ≤ 30%, no prior implant, SR for ANY of the following:

- QRS 120-149 ms, LBBB, NYHA Class II (7), III-IV (8)
- QRS ≥ 150 ms, LBBB, NYHA Class II (9), III-IV (9)
- QRS ≥ 150 ms, non-LBBB, NYHA Class III-IV (8)

Nonischemic cardiomyopathy, LVEF 31-35%, no prior implant, SR for ANY of the following:
- QRS 120-149 ms, LBBB, NYHA Class II (7), III-IV (8)
- QRS ≥ 150 ms, LBBB, NYHA Class II (8), III-IV (9)
- QRS ≥ 150 ms, non-LBBB, NYHA Class III-IV (7)

Pre-Existing or anticipated right ventricular (RV) pacing with a clinical indication for ICD or pacemaker implantation, intrinsic narrow QRS, LVEF ≤ 35% when RV pacing anticipated is > 40%, NYHA Class I-II (7), III-IV (8).

Refractory Class III/IV heart failure < 3 months post revascularization and/or ≤ 40 days post-myocardial infarction (MI), no other indication for ventricular pacing, LVEF ≤ 35% for ANY of the following:
- QRS 120-149 ms, LBBB (7)
- QRS ≥ 150 ms, LBBB (8)
- QRS ≥ 150 ms, non-LBBB (7)

The following indications were rated as May Be Appropriate for Care (median score 4-6):

Ischemic cardiomyopathy, LVEF ≤ 30%, no prior implant, SR for ANY of the following:
- QRS 120-149 ms, LBBB, NYHA Class I (5)
- QRS 120-149 ms, non-LBBB, NYHA Class III-amb. IV (6)
- QRS ≥ 150 ms, non-LBBB, NYHA Class I (4), II (6)

Ischemic cardiomyopathy, LVEF 31-35%, no prior implant, SR for ANY of the following:
- QRS 120-149 ms, LBBB, NYHA Class I (5)
- QRS ≥ 150 ms, LBBB, NYHA Class I (6)
- QRS 120-149 ms, non-LBBB, NYHA Class III-IV (6)
- QRS ≥ 150 ms, non-LBBB, NYHA Class I (4), Class II (6)

Nonischemic cardiomyopathy, LVEF ≤ 30%, no prior implant, SR for ANY of the following:
- QRS 120-149 ms, LBBB, NYHA Class I (4)
- QRS ≥ 150 ms, LBBB, NYHA Class I (6)
- QRS 120-149 ms, non-LBBB, NYHA Class III-IV (6)
- QRS ≥ 150 ms, non-LBBB, NYHA Class I (5), II (6)

Nonischemic cardiomyopathy, LVEF 31-35%, no prior implant, SR for ANY of the following:
- QRS 120-149 ms, LBBB, NYHA Class I (5)
- QRS ≥ 150 ms, LBBB, NYHA Class I (6)
- QRS 120-149 ms, non-LBBB, NYHA Class III-IV (6)
- QRS ≥ 150 ms, non-LBBB, NYHA Class I (5), II (6)

LVEF > 35% of any etiology (ICD Indicated), no prior implant, SR:
- QRS 120-149 ms, LBBB, NYHA Class III-IV (4)
- QRS ≥ 150 ms, LBBB, NYHA Class I-II (4), III-IV (5)
- QRS ≥ 150 ms, non-LBBB, NYHA Class III-IV (4)

LVEF ≤ 35% of any etiology (NYHA Class IV on Intravenous Inotropic Support), no prior implant:
- QRS 120-149 ms, LBBB (6) or non-LBBB (4)

- QRS ≥ 150 ms, LBBB (6) or non-LBBB (5)

Pre-Existing or anticipated RV pacing with a clinical indication for ICD or pacemaker implantation-intrinsic narrow QRS:

- LVEF ≤ 35%, RV pacing anticipated ≤ 40%, NYHA Class I-II (4), III-amb. IV (5)
- LVEF > 35%, RV pacing anticipated ≤ 40%, NHYA Class III-IV (4)
- LVEF > 35%, RV pacing anticipated > 40%, NHYA Class I-II (5), III-IV (6)

Refractory Class III/IV heart failure < 3 months post revascularization and/or ≤ 40 days post-MI, no other indication for ventricular pacing:

- LVEF ≤ 35%, QRS 120-149 ms, non-LBBB (5)
- LVEF 36-50%, QRS ≥ 150, LBBB (4)

American College of Cardiology Foundation (ACCF), American Heart Association (AHA) and Heart Rhythm Society (HRS) Guideline for Device-Based Therapy for Cardiac Rhythm Abnormalities: The 2012 ACCF/AHA/HRS focused update incorporated into the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities addresses recommendations for CRT (Epstein, et al., 2013). Guideline recommendations are classified as Class I, Class IIa, Class IIb, and Class III. The classification system is described as follows:

- Class I: Benefit >>> Risk; Procedure/Treatment should be performed/administered
- Class IIa: Benefit >> Risk; Additional studies with focused objectives needed. It is reasonable to perform procedure/administer treatment.
- Class IIb: Benefit ≥ Risk; Additional studies with broad objectives needed; additional registry data would be helpful. Procedure/treatment may be considered.
- Class III: No Benefit or Harm
  - Class of Recommendation (COR) III: No Benefit
    - Procedure/Test: not helpful
    - Treatment: no proven benefit
  - COR III: Harm
    - Procedure/Test: excess cost w/o benefit or harmful
    - Treatment: harmful to patients

The weight of evidence supporting each recommendation is classified as follows:

- Level A: Multiple populations evaluated. Data derived from multiple randomized clinical trials or meta-analyses.
- Level B: Limited populations evaluated. Data derived from a single randomized trial or nonrandomized studies.
- Level C: Very limited populations evaluated. Only consensus opinion of experts, case studies, or standard of care.

The updated guideline proposes several changes in recommendations for CRT, compared with the 2008 document. The most significant changes are limitation of the Class I indication to patients with QRS duration ≥150 ms; limitation of the Class I indication to patients with left bundle-branch block (LBBB) pattern; expansion of Class I indication to New York Heart Association (NYHA) class II (and with LBBB with QRS duration ≥150 ms); and the addition of a Class IIb recommendation for patients who have LVEF ≤30%, ischemic etiology of heart failure (HF), sinus rhythm, LBBB with a QRS duration ≥150 ms, and NYHA class I symptoms.

The following recommendations for CRT placement are included in the 2012 guideline:

Class I

- CRT is indicated for patients who have LVEF ≤ 35%, sinus rhythm, LBBB with a QRS duration ≥ 150 ms, and NYHA class II, III, or ambulatory IV symptoms on guideline directed medical therapy (GDMT) (Level of Evidence: A for NYHA class III/IV; Level of Evidence: B for NYHA class II).

Class IIa

- CRT can be useful for patients who have LVEF ≤ 35%, sinus rhythm, LBBB with a QRS duration 120 to 149 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT (Level of Evidence: B).
- CRT can be useful for patients who have LVEF ≤ 35%, sinus rhythm, a non-LBBB pattern with a QRS ≥ 150 ms, and NYHA class III/ambulatory class IV symptoms on GDMT (Level of Evidence: A).
- CRT can be useful in patients with atrial fibrillation and LVEF ≤ 35% on GDMT if the patient requires ventricular pacing or otherwise meets CRT criteria and b) AV nodal ablation or pharmacologic rate control will allow near 100% ventricular pacing with CRT (Level of Evidence: B).
- CRT can be useful for patients on GDMT who have LVEF ≤ 35% and are undergoing new or replacement device placement with anticipated requirement for significant (> 40%) ventricular pacing (Level of Evidence: C).

Class IIb

- CRT may be considered for patients who have LVEF ≤ 30%, ischemic etiology of heart failure, sinus rhythm, LBBB with a QRS duration of ≥150 ms, and NYHA class I symptoms on GDMT (Level of Evidence: C).
- CRT may be considered for patients who have LVEF ≤ 35%, sinus rhythm, a non-LBBB pattern with QRS duration 120 to 149 ms, and NYHA class III/ambulatory class IV on GDMT (Level of Evidence: B).
- CRT may be considered for patients who have LVEF ≤ 35%, sinus rhythm, a non-LBBB pattern with a QRS duration ≥ 150 ms, and NYHA class II symptoms on GDMT (Level of Evidence: B).

Class III: No Benefit

- CRT is not recommended for patients with NYHA class I or II symptoms and non-LBBB pattern with QRS duration less than 150 ms (Level of Evidence: B).
- CRT is not indicated for patients whose comorbidities and/or frailty limit survival with good functional capacity to less than 1 year (Level of Evidence: C).

European Society of Cardiology (ESC) Guidelines on Cardiac Pacing and Cardiac Resynchronization Therapy: The updated 2021 ESC guidelines on cardiac pacing and CRT include expanded recommendations for CRT, and new sections which include leadless pacing and alternative pacing strategies/sites (Glikson, et al., 2021). Guideline recommendations are classified as Class I, Class IIa, Class IIb, and Class III. The classification system is described as follows:

- Class I: Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.
- Class II: Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.
  - Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.
  - Class IIb: Usefulness/efficacy is less well established by evidence/opinion.
- Class III: Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.

The weight of evidence supporting each recommendation is classified as follows:

- Level of evidence A: Data derived from multiple randomized clinical trials or meta-analyses.
- Level of evidence B: Data derived from a single randomized clinical trial or large non-randomized clinical trials.
- Level of evidence C: Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

Recommendations for CRT in patients in sinus rhythm (SR):

- CRT is recommended for symptomatic patients with heart failure (HF) with LVEF ≤ 35%, QRS duration ≥ 150 ms, and left bundle branch block (LBBB) QRS morphology despite optimal medical treatment (OMT) in order to improve symptoms and reduce morbidity and mortality (Class I, Level A)
- CRT should be considered for symptomatic patients with HF with LVEF ≤ 35%, QRS duration 130 – 149 ms, and LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity and mortality (Class IIa, Level B)
- CRT should be considered for symptomatic patients with HF LVEF ≤ 35%, QRS duration ≥ 150 ms, and non-LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity (Class IIa, Level B)
- CRT may be considered for symptomatic patients with HF with LVEF ≤ 35%, QRS duration 130 – 149 ms, and non-LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity (Class IIb, Level B)
- CRT is not indicated in patients with HF and QRS duration <130 ms without an indication for RV pacing (Class III, Level A)

Recommendations for CRT in patients with persistent or permanent atrial fibrillation (AF):

- Patients with HF with permanent AF who are candidates for CRT:
  - CRT should be considered for patients with HF and LVEF ≤ 35% in NYHA class III or IV despite OMT if they are in AF and have intrinsic QRS ≥ 130 ms, provided a strategy to ensure biventricular capture is in place, in order to improve symptoms and reduce morbidity and mortality (Class IIa, Level C)
  - Atrioventricular junction (AVJ) ablation should be added in the case of incomplete biventricular pacing (<90 – 95%) due to conducted AF (Class IIa, Level B)
- Patients with symptomatic AF and an uncontrolled heart rate who are candidates for AVJ ablation (irrespective of QRS duration):
  - CRT is recommended in patients with HF with reduced ejection fraction (<40%) (Class I, Level B)
  - CRT rather than standard right ventricular (RV) pacing should be considered in patients with HF with mildly reduced ejection fraction (40 - 49%) (Class IIa, Level C)
  - RV pacing should be considered in patients with HF with preserved ejection fraction (≥ 50%) (Class IIa, Level B)
  - CRT may be considered in patients with HF with preserved ejection fraction (≥ 50%) (Class IIb, Level C)

Recommendation for upgrade from RV pacing to CRT:

- Patients who have received a conventional pacemaker or an ICD and who subsequently develop symptomatic HF with LVEF ≤ 35% despite OMT, and who have a significant proportion of RV pacing, should be considered for upgrade to CRT (Class IIa, Level B)

Recommendation for patients with HF and atrioventricular block (AVB):

- CRT rather than RV pacing is recommended for patients with HF with reduced ejection fraction (<40%) regardless of NYHA class who have an indication for ventricular pacing and high-degree AVB in order to reduce morbidity. This includes patients with AF (Class I, Level A)

The document also acknowledges the growing interest in His bundle pacing, left bundle branch area pacing, and leadless pacemakers, however the authors note that large RCTs and long-term follow up are still lacking (Glikson, et al., 2021).

National Institute for Health and Care Excellence (NICE): In 2021, NICE published procedural guidance for the use of permanent His-bundle pacemakers to treat heart failure. The recommendation asserted that permanent His-bundle pacemaker implantation should only be used in a research context, as safety and efficacy data was inadequate in quality and quantity. The guidance further noted that the procedure was technically challenging, and should only be done in specialty centers with experience in cardiac pacing (NICE, 2021).

An August 2018 NICE interventional procedures guidance on leadless cardiac pacemaker implantation for bradyarrhythmias states that "evidence on the safety of leadless cardiac pacemaker implantation for bradyarrhythmias shows that there are serious but well-recognized complications. The evidence on efficacy is inadequate in quantity and quality. Clinicians wishing to do leadless cardiac pacemaker implantation for bradyarrhythmias in people who cannot have conventional cardiac pacemaker implantation should ensure that patients and their carers understand the uncertainty about the procedure's safety and efficacy compared with conventional pacemaker implantation, and provide them with clear written information. Further research in people who could have conventional cardiac pacemaker implantation should report the patient selection criteria and compare leadless pacemakers with conventional pacemakers. Follow-up should be for at least 5 years and outcomes should include adverse events, symptom relief, quality of life and device durability in the long-term".

In 2014, NICE published guidance on the use of implantable cardioverter defibrillators and cardiac resynchronization therapy (CRT-P and CRT-D devices) for arrhythmias and heart failure. The authoring committee made the following recommendations for CRT treatment options in persons with heart failure who have left ventricular dysfunction, and an EF ≤ 35%:

- QRS < 120 milliseconds (ms): CRT not indicated
- QRS 120 – 149 ms
  - Without left bundle branch block (LBBB)
    - NYHA Class I – III: CRT not indicated
    - NYHA Class IV: CRT-P
  - With LBBB
    - NYHA Class I: CRT not indicated
    - NYHA Class II: CRT-D
    - NYHA Class III: CRT-P or CRT-D
    - NYHA Class IV: CRT-P
- QRS ≥ 150 ms
  - With or without LBBB
    - NYHA Class I and II: CRT-D
    - NYHA Class III: CRT-P or CRT-D
    - NYHA Class IV: CRT-P

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD	National	Leadless Pacemakers (20.8.4)	1/18/2017
LCD	Palmetto GBA	Cardiac Resynchronization Therapy (CRT) (L39080)	12/12/2021

Note: Please review the current Medicare Policy for the most up-to-date information.
(NCD = National Coverage Determination; LCD = Local Coverage Determination)

Coding Information

Notes:

1. This list of codes may not be all-inclusive since the American Medical Association (AMA) and Centers for Medicare & Medicaid Services (CMS) code updates may occur more frequently than policy updates.
2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when used to report the insertion or replacement of a biventricular pacemaker alone or when combined with an implantable cardioverter defibrillator (ICD) and/or leads:

CPT®* Codes	Description
33202	Insertion of epicardial electrode(s); open incision (eg, thoracotomy, median sternotomy, subxiphoid approach)
33203	Insertion of epicardial electrode(s); endoscopic approach (eg, thoracoscopy, pericardioscopy)
33208	Insertion of new or replacement of permanent pacemaker with transvenous electrode(s); atrial and ventricular
33211	Insertion or replacement of temporary transvenous dual chamber pacing electrodes (separate procedure)
33213	Insertion of pacemaker pulse generator only; with existing dual leads
33214	Upgrade of implanted pacemaker system, conversion of single chamber system to dual chamber system (includes removal of previously placed pulse generator, testing of existing lead, insertion of new lead, insertion of new pulse generator)
33217	Insertion of 2 transvenous electrodes, permanent pacemaker or implantable defibrillator
33221	Insertion of pacemaker pulse generator only; with existing multiple leads
33222	Relocation of skin pocket for pacemaker
33223	Relocation of skin pocket for implantable defibrillator
33224	Insertion of pacing electrode, cardiac venous system, for left ventricular pacing, with attachment to previously placed pacemaker or implantable defibrillator pulse generator (including revision of pocket, removal, insertion, and/or replacement of existing generator)
33225	Insertion of pacing electrode, cardiac venous system, for left ventricular pacing, at time of insertion of implantable defibrillator or pacemaker pulse generator (eg, for upgrade to dual chamber system) (List separately in addition to code for primary procedure)
33226	Repositioning of previously implanted cardiac venous system (left ventricular) electrode (including removal, insertion and/or replacement of existing generator)
33228	Removal of permanent pacemaker pulse generator with replacement of pacemaker pulse generator; dual lead system

CPT®* Codes	Description
33229	Removal of permanent pacemaker pulse generator with replacement of pacemaker pulse generator; multiple lead system
33249	Insertion or replacement of permanent implantable defibrillator system, with transvenous lead(s), single or dual chamber
33263	Removal of implantable defibrillator pulse generator with replacement of implantable defibrillator pulse generator; dual lead system
33264	Removal of implantable defibrillator pulse generator with replacement of implantable defibrillator pulse generator; multiple lead system

HCPCS Codes	Description
C1721	Cardioverter-defibrillator, dual chamber (implantable)
C1722	Cardioverter-defibrillator, single chamber (implantable)
C1777	Lead, cardioverter-defibrillator, endocardial single coil (implantable)
C1779	Lead, pacemaker, transvenous VDD single pass
C1785	Pacemaker, dual chamber, rate-responsive (implantable)
C1786	Pacemaker, single chamber, rate-responsive (implantable)
C1882	Cardioverter-defibrillator, other than single or dual chamber (implantable)
C1895	Lead, cardioverter-defibrillator, endocardial dual coil (implantable)
C1896	Lead, cardioverter-defibrillator, other than endocardial single or dual coil (implantable)
C1898	Lead, pacemaker, other than transvenous VDD single pass
C1899	Lead, pacemaker/cardioverter-defibrillator combination (implantable)
C1900	Lead, left ventricular coronary venous system
C2619	Pacemaker, dual chamber, non rate-responsive (implantable)
C2620	Pacemaker, single chamber, non rate-responsive (implantable)
C2621	Pacemaker, other than single or dual chamber (implantable)

Considered Experimental/Investigational/Unproven:

CPT®* Codes	Description
33274	Transcatheter insertion or replacement of permanent leadless pacemaker, right ventricular, including imaging guidance (eg, fluoroscopy, venous ultrasound, ventriculography, femoral venography) and device evaluation (eg, interrogation or programming), when performed
33275	Transcatheter removal of permanent leadless pacemaker, right ventricular, including imaging guidance (eg, fluoroscopy, venous ultrasound, ventriculography, femoral venography), when performed
33999†	Unlisted procedure, cardiac surgery
0515T	Insertion of wireless cardiac stimulator for left ventricular pacing, including device interrogation and programming, and imaging supervision and interpretation, when performed; complete system (includes electrode and generator [transmitter and battery])
0516T	Insertion of wireless cardiac stimulator for left ventricular pacing, including device interrogation and programming, and imaging supervision and interpretation, when performed; electrode only
0517T	Insertion of wireless cardiac stimulator for left ventricular pacing, including device interrogation and programming, and imaging supervision and

CPT®* Codes	Description
	interpretation, when performed; pulse generator component(s) (battery and/or transmitter) only
0518T	Removal of only pulse generator component(s) (battery and/or transmitter) of wireless cardiac stimulator for left ventricular pacing
0519T	Removal and replacement of wireless cardiac stimulator for left ventricular pacing; pulse generator component(s) (battery and/or transmitter)
0520T	Removal and replacement of wireless cardiac stimulator for left ventricular pacing; pulse generator component(s) (battery and/or transmitter), including placement of a new electrode
0521T	Interrogation device evaluation (in person) with analysis, review and report, includes connection, recording, and disconnection per patient encounter, wireless cardiac stimulator for left ventricular pacing
0522T	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, including review and report, wireless cardiac stimulator for left ventricular pacing
0795T	Transcatheter insertion of permanent dual-chamber leadless pacemaker, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography, right ventriculography, femoral venography) and device evaluation (eg, interrogation or programming), when performed; complete system (ie, right atrial and right ventricular pacemaker components)
0796T	Transcatheter insertion of permanent dual-chamber leadless pacemaker, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography, right ventriculography, femoral venography) and device evaluation (eg, interrogation or programming), when performed; right atrial pacemaker component (when an existing right ventricular single leadless pacemaker exists to create a dual-chamber leadless pacemaker system)
0797T	Transcatheter insertion of permanent dual-chamber leadless pacemaker, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography, right ventriculography, femoral venography) and device evaluation (eg, interrogation or programming), when performed; right ventricular pacemaker component (when part of a dual-chamber leadless pacemaker system)
0798T	Transcatheter removal of permanent dual-chamber leadless pacemaker, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography, right ventriculography, femoral venography), when performed; complete system (ie, right atrial and right ventricular pacemaker components)
0799T	Transcatheter removal of permanent dual-chamber leadless pacemaker, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography, right ventriculography, femoral venography), when performed; right atrial pacemaker component
0800T	Transcatheter removal of permanent dual-chamber leadless pacemaker, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography, right ventriculography, femoral venography), when performed; right ventricular pacemaker component (when part of a dual-chamber leadless pacemaker system)
0801T	Transcatheter removal and replacement of permanent dual-chamber leadless pacemaker, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography, right ventriculography, femoral venography) and device

CPT®* Codes	Description
	evaluation (eg, interrogation or programming), when performed; dual-chamber system (ie, right atrial and right ventricular pacemaker components)
0802T	Transcatheter removal and replacement of permanent dual-chamber leadless pacemaker, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography, right ventriculography, femoral venography) and device evaluation (eg, interrogation or programming), when performed; right atrial pacemaker component
0803T	Transcatheter removal and replacement of permanent dual-chamber leadless pacemaker, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography, right ventriculography, femoral venography) and device evaluation (eg, interrogation or programming), when performed; right ventricular pacemaker component (when part of a dual-chamber leadless pacemaker system
0804T	Programming device evaluation (in person) with iterative adjustment of implantable device to test the function of device and to select optimal permanent programmed values, with analysis, review, and report, by a physician or other qualified health care professional, leadless pacemaker system in dual cardiac chambers
0823T	Transcatheter insertion of permanent single-chamber leadless pacemaker, right atrial, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography and/or right ventriculography, femoral venography, cavography) and device evaluation (eg, interrogation or programming), when performed
0824T	Transcatheter removal of permanent single-chamber leadless pacemaker, right atrial, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography and/or right ventriculography, femoral venography, cavography), when performed
0825T	Transcatheter removal and replacement of permanent single-chamber leadless pacemaker, right atrial, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography and/or right ventriculography, femoral venography, cavography) and device evaluation (eg, interrogation or programming), when performed
0826T	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, leadless pacemaker system in single-cardiac chamber
0861T	Removal of pulse generator for wireless cardiac stimulator for left ventricular pacing; both components (battery and transmitter)
0862T	Relocation of pulse generator for wireless cardiac stimulator for left ventricular pacing, including device interrogation and programming; battery component only
0863T	Relocation of pulse generator for wireless cardiac stimulator for left ventricular pacing, including device interrogation and programming; transmitter component only

†Note: Considered Experimental/Investigational/Unproven when used to report conduction system pacing for any indication

References

1. Abbott Medical Cardiovascular. ©2023. Accessed Nov 27, 2023. Available at URL address: https://www.cardiovascular.abbott/us/en/hcp.html

2. Abraham WT, Fisher WG, Smith AL, Delurgio DB, Leon AR, Loh E, et al. MIRACLE Study Group. Multicenter InSync Randomized Clinical Evaluation. Cardiac resynchronization in chronic heart failure. N Engl J Med. 2002 Jun 13;346(24):1845-53.

3. Abraham WT, Young JB, León AR, Adler S, Bank AJ, Hall SA, et al; Multicenter InSync ICD II Study Group. Effects of cardiac resynchronization on disease progression in patients with left ventricular systolic dysfunction, an indication for an implantable cardioverter-defibrillator, and mildly symptomatic chronic heart failure. Circulation. 2004 Nov 2;110(18):2864-8.

4. Achilli A, Sassara M, Ficili S, Pontillo D, Achilli P, Alessi C, et al. Long-term effectiveness of cardiac resynchronization therapy in patients with refractory heart failure and "narrow" QRS. J Am Coll Cardiol. 2003 Dec 17;42(12):2117-24.

5. Adabag S, Roukoz H, Anand IS, Moss AJ. Cardiac resynchronization therapy in patients with minimal heart failure: a systematic review and meta-analysis. J Am Coll Cardiol. 2011 Aug 23;58(9):935-41.

6. Adelstein E, Saba S. Cardiac resynchronization therapy in heart failure: Indications and choice of system. Last updated Jun 14, 2023. In: UpToDate, Dardas TF (Ed). UpToDate, Waltham, MA. Accessed Dec 4, 2023.

7. Adelstein E, Schwartzman D, Gorcsan J 3rd, Saba S. Predicting hyperresponse among pacemaker-dependent nonischemic cardiomyopathy patients upgraded to cardiac resynchronization. J Cardiovasc Electrophysiol. 2011 Aug;22(8):905-11.

8. Al-Khatib SM, Stevenson WG, Ackerman MJ, Bryant WJ, Callans DJ, Curtis AB, et al. 2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Heart Rhythm. 2017 Oct 26.

9. Al-Majed NS, McAlister FA, Bakal JA, Ezekowitz JA. Meta-analysis: cardiac resynchronization therapy for patients with less symptomatic heart failure. Ann Intern Med. 2011 Mar 15;154(6):401-12.

10. Ali N, Keene D, Arnold A, Shun-Shin M, Whinnett ZI, Afzal Sohaib SM. His Bundle Pacing: A New Frontier in the Treatment of Heart Failure. Arrhythm Electrophysiol Rev. 2018 Jun;7(2):103-110.

11. Anand IS, Carson P, Galle E, Song R, Boehmer J, Ghali JK, et al. Cardiac resynchronization therapy reduces the risk of hospitalizations in patients with advanced heart failure: results from the Comparison of Medical Therapy, Pacing and Defibrillation in Heart Failure (COMPANION) trial. Circulation. 2009 Feb 24;119(7):969-77.

12. Anselme F, Bordachar P, Pasquié JL, Klug D, Leclercq C, Milhem A, et al. Safety, feasibility, and outcome results of cardiac resynchronization with triple-site ventricular stimulation compared to conventional cardiac resynchronization. Heart Rhythm. 2016 Jan;13(1):183-9.

13. Auricchio A, Metra M, Gasparini M, Lamp B, Klersy C, Curnis A, et al; Multicenter Longitudinal Observational Study (MILOS) Group. Long-term survival of patients with heart failure and ventricular conduction delay treated with cardiac resynchronization therapy. Am J Cardiol. 2007 Jan 15;99(2):232-8.

14. Auricchio A, Delnoy PP, Butter C, Brachmann J, Van Erven L, Spitzer S, et al; Collaborative Study Group. Feasibility, safety, and short-term outcome of leadless ultrasound-based endocardial left ventricular resynchronization in heart failure patients: results of the wireless stimulation endocardially for CRT (WiSE-CRT) study. Europace. 2014 May;16(5):681-8.

15. Arbelo E, Protonotarios A, Gimeno JR, Arbustini E, Barriales-Villa R, Basso C, Bezzina CR, Biagini E, Blom NA, de Boer RA, De Winter T, Elliott PM, Flather M, Garcia-Pavia P, Haugaa KH, Ingles J, Jurcut RO, Klaassen S, Limongelli G, Loeys B, Mogensen J, Olivotto I, Pantazis A, Sharma S, Van Tintelen JP, Ware JS, Kaski JP; ESC Scientific Document Group. 2023 ESC Guidelines for the management of cardiomyopathies. Eur Heart J. 2023 Oct 1;44(37):3503-3626.

16. Barsheshet A, Wang PJ, Moss AJ, Solomon SD, Al-Ahmad A, McNitt S, et al. Reverse remodeling and the risk of ventricular tachyarrhythmias in the MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy). J Am 34 Coll Cardiol. 2011;57:2416-23.

17. Bernard ML. Pacing Without Wires: Leadless Cardiac Pacing. Ochsner J. 2016 Fall;16(3):238-42.

18. Bertoldi EG, Polanczyk CA, Cunha V, Ziegelmann PK, Beck-da-Silva L, Rohde LE. Mortality reduction of cardiac resynchronization and implantable cardioverter-defibrillator therapy in heart failure: an updated meta-analysis. Does recent evidence change the standard of care? J Card Fail. 2011 Oct;17(10):860-6.

19. Beshai JF, Grimm RA, Nagueh SF, Baker JH 2nd, Beau SL, Greenberg SM, et al; RethinQ Study Investigators. Cardiac-resynchronization therapy in heart failure with narrow QRS complexes. N Engl J Med. 2007 Dec 13;357(24):2461-71.

20. Beurskens NEG, Breeman KTN, Dasselaar KJ, Meijer AC, Quast ABE, Tjong FVY, Knops RE. Leadless cardiac pacing systems: current status and future prospects. Expert Rev Med Devices. 2019 Nov;16(11):923-930.

21. Bhatt AG, Musat DL, Preminger MW, Sichrovsky T, Mittal S. Obstacles preventing biventricular pacing mitigated with lead extraction and His bundle pacing to achieve effective cardiac resynchronization. HeartRhythm Case Rep. 2017 Aug 31;3(11):531-535.

22. Bleeker GB, Schalij MJ, Holman ER, Steendijk P, van der Wall EE, Bax JJ. Cardiac resynchronization therapy in patients with systolic left ventricular dysfunction and symptoms of mild heart failure secondary to ischemic or nonischemic cardiomyopathy. Am J Cardiol. 2006a Jul 15;98(2):230-235.

23. Bleeker GB, Holman ER, Steendijk P, Boersma E, van der Wall EE, Schalij MJ, Bax JJ. Cardiac resynchronization therapy in patients with a narrow QRS complex. J Am Coll Cardiol. 2006b Dec 5;48(11):2243-50.

24. Boczar K, Sławuta A, Ząbek A, Dębski M, Vijayaraman P, Gajek J, Lelakowski J, Małecka B. Cardiac resynchronization therapy with His bundle pacing. Pacing Clin Electrophysiol. 2019 Mar;42(3):374-380.

25. Boczar K, Sławuta A, Ząbek A, Dębski M, Gajek J, Lelakowski J, Małecka B. Cardiac resynchronization therapy with His bundle pacing as a method of treatment of chronic heart failure in patients with permanent atrial fibrillation and left bundle branch block. J Electrocardiol. 2018 May - Jun;51(3):405-408.

26. Bordachar P, Gras D, Clementy N, Defaye P, Mondoly P, Boveda S, et al. Clinical impact of an additional left ventricular lead in cardiac resynchronization therapy nonresponders: The V(3) trial. Heart Rhythm. 2018 Jun;15(6):870-876.

27. Boriani G, Gasparini M, Landolina M, Lunati M, Biffi M, Santini M, et al; on behalf of the InSync/InSync ICD Italian Registry Investigators. Effectiveness of cardiac resynchronization therapy in heart failure patients with valvular heart disease: comparison with patients affected by ischaemic heart disease or dilated cardiomyopathy. The InSync/InSync ICD Italian Registry. Eur Heart J. 2009 Jun 10.

28. Boriani G, Muller CP, Seidl KH, Grove R, Vogt J, Danschel W, et al. Resynchronization for the Hemodynamic Treatment for Heart Failure Management II Investigators. Randomized comparison of simultaneous biventricular stimulation versus optimized interventricular delay in cardiac resynchronization therapy. The Resynchronization for the Hemodynamic Treatment for Heart Failure Management II implantable cardioverter defibrillator (RHYTHM II ICD) study. Am Heart J. 2006 May;151(5):1050-8.

29. Boston Scientific. ©2023. Accessed Dec 4, 2023. Available at URL address: https://www.bostonscientific.com/en-US/medical-specialties/heart-failure.html

30. Boveda S, Marijon E, Lenarczyk R, Iliodromitis KE, Marin F, Defaye P, et al. Factors influencing the use of leadless or transvenous pacemakers: Results of the European Heart Rhythm Association prospective survey. Europace. 2020;22(4):667-673.

31. Bradley DJ, Bradley EA, Baughman KL, Berger RD, Calkins H, Goodman SN, et al. Cardiac resynchronization and death from progressive heart failure: a meta-analysis of randomized controlled trials. JAMA. 2003 Feb 12;289(6):730-40.

32. Braunschweig F, Mortensen PT, Gras D, Reiser W, Lawo T, Mansour H, et al. InSync III Study Investigators. Monitoring of physical activity and heart rate variability in patients with chronic heart failure using cardiac resynchronization devices. Am J Cardiol. 2005 May 1;95(9):1104-7.

33. Brignole M, Botto G, Mont L, Iacopino S, De Marchi G, Oddone D, et al. Cardiac resynchronization therapy in patients undergoing atrioventricular junction ablation for permanent atrial fibrillation: a randomized trial. Eur Heart J. 2011 Oct;32(19):2420-9.

34. Brignole M, Pentimalli F, Palmisano P, Landolina M, Quartieri F, Occhetta E, Calò L, Mascia G, Mont L, Vernooy K, van Dijk V, Allaart C, Fauchier L, Gasparini M, Parati G, Soranna D, Rienstra M, Van Gelder IC; APAF-CRT Trial Investigators. AV junction ablation and cardiac

resynchronization for patients with permanent atrial fibrillation and narrow QRS: the APAF-CRT mortality trial. Eur Heart J. 2021 Dec 7;42(46):4731-4739. Erratum in: Eur Heart J. 2021 Oct 16; Erratum in: Eur Heart J. 2021 Dec 08.

35. Bristow MR, Feldman AM, Saxon LA. Heart failure using implantable devices for ventricular resynchronization: Comparison of Medical Therapy, Pacing, and Defibrillation in Chronic Heart Failure (COMPANION) trial. COMPANION Steering Committee and COMPANION Clinical Investigators. J Card Fail. 2000 Sep;6(3):276-85.

36. Bristow MR, Saxon LA, Boehmer J, Krueger S, Kass DA, DeMarco T, et al. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med. 2004 May 20;350(21):2140-50.

37. Cang J, Liu Y, Zhu D, Liu S, Shen J, Miao H, Zhou Q, Chen L. WiSE CRT Is Beneficial for Heart Failure Patients as a Rescue Therapy: Evidence From a Meta-Analysis. Front Cardiovasc Med. 2022 Mar 15;9:823797.

38. Cantillon DJ, Dukkipati SR, Ip JH, Exner DV, Niazi IK, Banker RS, et al. Comparative study of acute and mid-term complications with leadless and transvenous cardiac pacemakers. Heart Rhythm. 2018 Jul;15(7):1023-1030.

39. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determinations (LCDs) alphabetical index. Accessed Nov 29, 2023. Available at URL address: https://www.cms.gov/medicare-coverage-database/reports/local-coverage-final-lcds-alphabetical-report.aspx?lcdStatus=all

40. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determination (LCD) for Cardiac Resynchronization Therapy (CRT) (L39080). Accessed Nov 29, 2023. Available at URL address: https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=39080

41. Centers for Medicare and Medicaid Services (CMS). National Coverage Determinations (NCDs) alphabetical index. Accessed Nov 29, 2023. Available at URL address: https://www.cms.gov/medicare-coverage-database/reports/national-coverage-ncd-report.aspx?chapter=all&sortBy=title

42. Centers for Medicare and Medicaid Services (CMS). National Coverage Determination (NCD) for Leadless Pacemakers (20.8.4). Accessed Nov 29, 2023. Available at URL address: https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=370

43. Chen K, Li Y, Dai Y, Sun Q, Luo B, Li C, Zhang S. Comparison of electrocardiogram characteristics and pacing parameters between left bundle branch pacing and right ventricular pacing in patients receiving pacemaker therapy. Europace. 2019 Apr 1;21(4):673-680.

44. Chen X, Ye Y, Wang Z, Jin Q, Qiu Z, Wang J, Qin S, Bai J, Wang W, Liang Y, Chen H, Sheng X, Gao F, Zhao X, Fu G, Ellenbogen KA, Su Y, Ge J. Cardiac resynchronization therapy via left bundle branch pacing vs. optimized biventricular pacing with adaptive algorithm in heart failure with left bundle branch block: a prospective, multi-centre, observational study. Europace. 2022 May 3;24(5):807-816.

45. Chung MK, Patton KK, Lau CP, Dal Forno ARJ, Al-Khatib SM, Arora V, Birgersdotter-Green UM, Cha YM, Chung EH, Cronin EM, Curtis AB, Cygankiewicz I, Dandamudi G, Dubin AM,

Ensch DP, Glotzer TV, Gold MR, Goldberger ZD, Gopinathannair R, Gorodeski EZ, Gutierrez A, Guzman JC, Huang W, Imrey PB, Indik JH, Karim S, Karpawich PP, Khaykin Y, Kiehl EL, Kron J, Kutyifa V, Link MS, Marine JE, Mullens W, Park SJ, Parkash R, Patete MF, Pathak RK, Perona CA, Rickard J, Schoenfeld MH, Seow SC, Shen WK, Shoda M, Singh JP, Slotwiner DJ, Sridhar ARM, Srivatsa UN, Stecker EC, Tanawuttiwat T, Tang WHW, Tapias CA, Tracy CM, Upadhyay GA, Varma N, Vernooy K, Vijayaraman P, Worsnick SA, Zareba W, Zeitler EP. 2023 HRS/APHRS/LAHRS guideline on cardiac physiologic pacing for the avoidance and mitigation of heart failure. Heart Rhythm. 2023 Sep;20(9):e17-e91.

46. Cleland JG, Calvert MJ, Verboven Y, Freemantle N. Effects of cardiac resynchronization therapy on long-term quality of life: an analysis from the CArdiac Resynchronisation-Heart Failure (CARE-HF) study. Am Heart J. 2009 Mar;157(3):457-66.

47. Cleland JG, Daubert JC, Erdmann E, Freemantle N, Gras D, Kappenberger L, Tavazzi L; Cardiac Resynchronization-Heart Failure (CARE-HF) Study Investigators. The effect of cardiac resynchronization on morbidity and mortality in heart failure. N Engl J Med. 2005 Apr 14;352(15):1539-49.

48. Colucci WS. Predictors of survival in heart failure with reduced ejection fraction. Updated Nov 1, 2022. In: UpToDate, Dardas TF, Gottlieb SS, Jaffe AS, (Eds.) UpToDate, Waltham, MA. Accessed Dec 4, 2023.

49. Crossley GH, Piccini JP, Longacre C, Higuera L, Stromberg K, El-Chami MF. Leadless versus transvenous single-chamber ventricular pacemakers: 3 year follow-up of the Micra CED study. J Cardiovasc Electrophysiol. 2023 Apr;34(4):1015-1023.

50. Curtis AB, Tomaselli GF. Approach to the Patient with Cardiac Arrhythmias. In: Libby P, Bonow RO, Mann DL, Tomaselli GF, Bhatt DL, Solomon SD. Braunwald's Heart Disease: A Textbook of Cardiovascular Disease. 12th ed. Elsevier; 2022. 1145-1162.e7.

51. Darlington D, Brown P, Carvalho V, Bourne H, Mayer J, Jones N, Walker V, Siddiqui S, Patwala A, Kwok CS. Efficacy and safety of leadless pacemaker: A systematic review, pooled analysis and meta-analysis. Indian Pacing Electrophysiol J. 2022 Mar-Apr;22(2):77-86.

52. de Waard D, Manlucu J, Gillis AM, Sapp J, Bernick J, Doucette S, Tang A, Wells G, Parkash R. Cardiac Resynchronization in Women: A Substudy of the Resynchronization-Defibrillation for Ambulatory Heart Failure Trial. JACC Clin Electrophysiol. 2019 Sep;5(9):1036-1044

53. Delnoy PP, Ottervanger JP, Luttikhuis HO, Elvan A, Misier AR, Beukema WP, van Hemel NM. Comparison of usefulness of cardiac resynchronization therapy in patients with atrial fibrillation and heart failure versus patients with sinus rhythm and heart failure. Am J Cardiol. 2007 May 1;99(9):1252-7.

54. DeMarco T, Wolfel E, Feldman AM, Lowes B, Higginbotham MB, Ghali JK, et al. Impact of cardiac resynchronization therapy on exercise performance, functional capacity, and quality of life in systolic heart failure with QRS prolongation: COMPANION trial sub-study. J Card Fail. 2008 Feb;14(1):9-18.

55. Deng JL, Wu YX, Liu J. Efficacy of implantable cardioconverter defibrillator or cardiac resynchronization therapy compared with combined therapy in survival of patients with heart failure: a meta-analysis. Medicine (Baltimore). 2015 Feb;94(5):e418.

56. Diab IG, Hunter RJ, Kamdar R, Berriman T, Duncan E, Richmond L, et al. Does ventricular dyssynchrony on echocardiography predict response to cardiac resynchronisation therapy? A randomised controlled study. Heart. 2011 Sep;97(17):1410-6.

57. Doshi RN, Daoud EG, Fellows C, Turk K, Duran A, Hamdan MH, Pires LA; PAVE Study Group. Left ventricular-based cardiac stimulation post AV nodal ablation evaluation (the PAVE study). J Cardiovasc Electrophysiol. 2005 Nov;16(11):1160-5.

58. Dupont M, Rickard J, Baranowski B, Varma N, Dresing T, Gabi A, et al. Differential response to cardiac resynchronization therapy and clinical outcomes according to QRS morphology and QRS duration. J Am Coll Cardiol. 2012 Aug 14;60(7):592-8.

59. Duray GZ, Ritter P, El-Chami M, Narasimhan C, Omar R, Tolosana JM, et al; Micra Transcatheter Pacing Study Group. Long-term performance of a transcatheter pacing system: 12-Month results from the Micra Transcatheter Pacing Study. Heart Rhythm. 2017 May;14(5):702-709.

60. ebrSystems, Inc. WiSE CRT System®. ©2023. Accessed Dec 4, 2023. Available at URL address: https://ebrsystemsinc.com/

61. El-Chami MF, Al-Samadi F, Clementy N, Garweg C, Martinez-Sande JL, Piccini JP, et al. Updated performance of the Micra transcatheter pacemaker in the real-world setting: A comparison to the investigational study and a transvenous historical control. Heart Rhythm. 2018 Dec;15(12):1800-1807.

62. El-Chami MF, Bockstedt L, Longacre C, Higuera L, Stromberg K, Crossley G, Kowal RC, Piccini JP. Leadless vs. transvenous single-chamber ventricular pacing in the Micra CED study: 2-year follow-up. Eur Heart J. 2022 Mar 21;43(12):1207-1215.

63. El-Chami MF, Garweg C, Iacopino S, Al-Samadi F, Martinez-Sande JL, Tondo C, Johansen JB, Prat XV, Piccini JP, Cha YM, Grubman E, Bordachar P, Roberts PR, Soejima K, Stromberg K, Fagan DH, Clementy N. Leadless pacemaker implant, anticoagulation status, and outcomes: Results from the Micra Transcatheter Pacing System Post-Approval Registry. Heart Rhythm. 2022 Feb;19(2):228-234.

64. Elliott MK, Mehta V, Wijesuriya N, Sidhu BS, Gould J, Niederer S, Rinaldi CA. Multi-lead pacing for cardiac resynchronization therapy in heart failure: a meta-analysis of randomized controlled trials. Eur Heart J Open. 2022 Feb 26;2(2):oeac013.

65. Epstein AE, Dimarco JP, Ellenbogen KA, Estes NA 3rd, Freedman RA, Gettes LS, et al. American College of Cardiology; American Heart Association Task Force on Practice Guidelines; American Association for Thoracic Surgery; Society of Thoracic Surgeons. ACC/AHA/HRS 2008 Guidelines for device-based therapy of cardiac rhythm abnormalities. Heart Rhythm. 2008 Jun;5(6):e1-62.

66. Epstein AE, DiMarco JP, Ellenbogen KA, Estes NAM III, Freedman RA, Gettes LS, Gillinov AM, Gregoratos G, Hammill SC, Hayes DL, Hlatky MA, Newby LK, Page RL, Schoenfeld MH, Silka MJ, Stevenson LW, Sweeney MO 2012 ACCF/AHA/HRS focused update incorporated into the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2013;61:e6–75.

67. European Heart Rhythm Association (EHRA); European Society of Cardiology (ESC); Heart Rhythm Society; Heart Failure Society of America (HFSA); American Society of Echocardiography (ASE); American Heart Association (AHA); European Association of Echocardiography (EAE) of ESC; Heart Failure Association of ESC (HFA), Daubert JC, Saxon L, Adamson PB, Auricchio A, Berger RD, Beshai JF, et al. 2012 EHRA/HRS expert consensus statement on cardiac resynchronization therapy in heart failure: implant and follow-up recommendations and management. Europace. 2012 Sep;14(9):1236-86.

68. Ezzeddine FM, Dandamudi G. His Bundle Pacing: Is It Ready for Prime Time? Card Electrophysiol Clin. 2018 Mar;10(1):87-98.

69. Gamble JHP, Herring N, Ginks M, Rajappan K, Bashir Y, Betts TR. Endocardial left ventricular pacing for cardiac resynchronization: systematic review and meta-analysis. Europace. 2018 Jan 1;20(1):73-81.

70. Ganesan AN, Brooks AG, Roberts-Thomson KC, Lau DH, Kalman JM, Sanders P. Role of AV nodal ablation in cardiac resynchronization in patients with coexistent atrial fibrillation and heart failure a systematic review. J Am Coll Cardiol. 2012 Feb 21;59(8):719-26.

71. Garg J, Shah K, Bhardwaj R, Contractor T, Mandapati R, Turagam MK, Lakkireddy D. Adverse events associated with AveirTM VR leadless pacemaker: A Food and Drug Administration MAUDE database study. J Cardiovasc Electrophysiol. 2023 Jun;34(6):1469-1471.

72. Garrigue S, Bordachar P, Reuter S, Jais P, Haissaguerre M, Clementy J. Comparison of permanent left ventricular and biventricular pacing in patients with heart failure and chronic atrial fibrillation: a prospective hemodynamic study. Card Electrophysiol Rev. 2003 Dec;7(4):315-24.

73. Gasparini M, Auricchio A, Regoli F, Fantoni C, Kawabata M, Galimberti P, et al. Four-year efficacy of cardiac resynchronization therapy on exercise tolerance and disease progression: the importance of performing atrioventricular junction ablation in patients with atrial fibrillation. J Am Coll Cardiol. 2006 Aug 15;48(4):734-43.

74. Ghosh S, Silva JN, Canham RM, et al. Electrophysiologic substrate and intraventricular left ventricular dyssynchrony in nonischemic heart failure patients undergoing cardiac resynchronization therapy. Heart Rhythm. 2011;8(5):692-699.

75. Glikson M, Nielsen JC, Kronborg MB, Michowitz Y, Auricchio A, Barbash IM, Barrabés JA, Boriani G, Braunschweig F, Brignole M, Burri H, Coats AJS, Deharo JC, Delgado V, Diller GP, Israel CW, Keren A, Knops RE, Kotecha D, Leclercq C, Merkely B, Starck C, Thylén I, Tolosana JM; ESC Scientific Document Group; ESC National Cardiac Societies. 2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy. Eur Heart J. 2021 Sep 14;42(35):3427-3520.

76. Gold MR, Padhiar A, Mealing S, Sidhu MK, Tsintzos SI, Abraham WT. Long-Term Extrapolation of Clinical Benefits Among Patients With Mild Heart Failure Receiving Cardiac Resynchronization Therapy: Analysis of the 5-Year Follow-Up From the REVERSE Study. JACC Heart Fail. 2015 Sep;3(9):691-700.

77. Gold MR, Thébault C, Linde C, Abraham WT, Gerritse B, Ghio S, et al. Effect of QRS duration and morphology on cardiac resynchronization therapy outcomes in mild heart

failure: results from the Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction (REVERSE) study. Circulation. 2012 Aug 14;126(7):822-9.

78. Goldenberg I, Hall WJ, Beck CA, Moss AJ, Barsheshet A, McNitt S, et al. Reduction of the risk of recurring heart failure events with cardiac resynchronization therapy: MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy). J Am Coll Cardiol. 2011 Aug 9;58(7):729-37.

79. Goldenberg I, Moss AJ, Hall WJ, Foster E, Goldberger JJ, Santucci P, et al.; MADIT-CRT Executive Committee. Predictors of response to cardiac resynchronization therapy in the Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT). Circulation. 2011 Oct 4;124(14):1527-36.

80. Gould J, Claridge S, Jackson T, Sieniewicz BJ, Sidhu BS, Porter B, Elliott MK, Mehta V, Niederer S, Chadwick H, Kamdar R, Adhya S, Patel N, Hamid S, Rogers D, Nicolson W, Chan CF, Whinnett Z, Murgatroyd F, Lambiase PD, Rinaldi CA. Standard care vs. TRIVEntricular pacing in Heart Failure (STRIVE HF): a prospective multicentre randomized controlled trial of triventricular pacing vs. conventional biventricular pacing in patients with heart failure and intermediate QRS left bundle branch block. Europace. 2022 May 3;24(5):796-806.

81. Gui Y, Ye L, Wu L, Mai H, Yan Q, Wang L. Clinical Outcomes Associated With His-Purkinje System Pacing vs. Biventricular Pacing, in Cardiac Resynchronization Therapy: A Meta-Analysis. Front Cardiovasc Med. 2022 Feb 11;9:707148.

82. Hauser RG, Gornick CC, Abdelhadi RH, Tang CY, Casey SA, Sengupta JD. Major adverse clinical events associated with implantation of a leadless intracardiac pacemaker. Heart Rhythm. 2021 Jul;18(7):1132-1139.

83. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, Deswal A, Drazner MH, Dunlay SM, Evers LR, Fang JC, Fedson SE, Fonarow GC, Hayek SS, Hernandez AF, Khazanie P, Kittleson MM, Lee CS, Link MS, Milano CA, Nnacheta LC, Sandhu AT, Stevenson LW, Vardeny O, Vest AR, Yancy CW. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. 2022 May 3;79(17):e263-e421.

84. Heist EK. Cardiac resynchronization therapy in atrial fibrillation. Last updated Nov 9, 2022. In: UpToDate, Dardas TF (Ed), UpToDate, Waltham, MA. Accessed Dec 4, 2023.

85. Hernández-Madrid A, Paul T, Abrams D, Aziz PF, Blom NA, Chen J, Chessa M, Combes N, Dagres N, Diller G, Ernst S, Giamberti A, Hebe J, Janousek J, Kriebel T, Moltedo J, Moreno J, Peinado R, Pison L, Rosenthal E, Skinner JR, Zeppenfeld K; ESC Scientific Document Group. Arrhythmias in congenital heart disease: a position paper of the European Heart Rhythm Association (EHRA), Association for European Paediatric and Congenital Cardiology (AEPC), and the European Society of Cardiology (ESC) Working Group on Grown-up Congenital heart disease, endorsed by HRS, PACES, APHRS, and SOLAECE. Europace. 2018 Nov 1;20(11):1719-1753.

86. Higgins SL, Hummel JD, Niazi IK, Giudici MC, Worley SJ, Saxon LA, Boehmer JP, Higginbotham MB, De Marco T, Foster E, Yong PG. Cardiac resynchronization therapy for the treatment of heart failure in patients with intraventricular conduction delay and malignant ventricular tachyarrhythmias. J Am Coll Cardiol. 2003 Oct 15;42(8):1454-9.

87. Huang W, Su L, Wu S, Xu L, Xiao F, Zhou X, Ellenbogen KA. A Novel Pacing Strategy With Low and Stable Output: Pacing the Left Bundle Branch Immediately Beyond the Conduction Block. Can J Cardiol. 2017 Dec;33(12):1736.e1-1736.e3

88. Huang W, Su L, Wu S, et al. Long-term outcomes of His bundle pacing in patients with heart failure with left bundle branch block. Heart 2019;105:137-143.

89. Huang W, Wu S, Vijayaraman P, Su L, Chen X, Cai B, Zou J, Lan R, Fu G, Mao G, Ellenbogen KA, Whinnett ZI, Tung R. Cardiac Resynchronization Therapy in Patients With Nonischemic Cardiomyopathy Using Left Bundle Branch Pacing. JACC Clin Electrophysiol. 2020 Jul;6(7):849-858.

90. Khazanie P, Greiner MA, Al-Khatib SM, Piccini JP, Turakhia MP, Varosy PD, et al; National Cardiovascular Data Registry. Comparative Effectiveness of Cardiac Resynchronization Therapy Among Patients With Heart Failure and Atrial Fibrillation: Findings From the National Cardiovascular Data Registry's Implantable Cardioverter-Defibrillator Registry. Circ Heart Fail. 2016 Jun;9(6).

91. Knight BP. Cardiac resynchronization therapy and conduction system pacing in heart failure: System implantation and programming. In: UpToDate, Dardas TF (ed). Sep 26, 2023. UpToDate, Waltham, MA. Accessed Dec 4, 2023.

92. Knops RE, Reddy VY, Ip JE, Doshi R, Exner DV, Defaye P, Canby R, Bongiorni MG, Shoda M, Hindricks G, Neužil P, Rashtian M, Breeman KTN, Nevo JR, Ganz L, Hubbard C, Cantillon DJ; Aveir DR i2i Study Investigators. A Dual-Chamber Leadless Pacemaker. N Engl J Med. 2023 Jun 22;388(25):2360-2370.

93. Knops RE, Tjong FV, Neuzil P, Sperzel J, Miller MA, Petru J, et al. Chronic performance of a leadless cardiac pacemaker: 1-year follow-up of the LEADLESS trial. J Am Coll Cardiol. 2015 Apr 21;65(15):1497-504.

94. Kusumoto FM, Schoenfeld MH, Barrett C, Edgerton JR, Ellenbogen KA, Gold MR, Goldschlager NF, Hamilton RM, Joglar JA, Kim RJ, Lee R, Marine JE, McLeod CJ, Oken KR, Patton KK, Pellegrini CN, Selzman KA, Thompson A, Varosy PD. 2018 ACC/AHA/HRS Guideline on the Evaluation and Management of Patients With Bradycardia and Cardiac Conduction Delay: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. 2019 Aug 20;74(7):e51-e156.

95. Landolina M, Lunati M, Gasparini M, Santini M, Padeletti L, Achilli A, et al; InSync/InSync ICD Italian Registry Investigators. Comparison of the effects of cardiac resynchronization therapy in patients with class II versus class III and IV heart failure (from the InSync/InSync ICD Italian Registry). Am J Cardiol. 2007 Sep 15;100(6):1007-12.

96. Leclercq C, Burri H, Delnoy PP, Rinaldi CA, Sperzel J, Calò L, Concha JF, Fusco A, Al Samadi F, Lee K, Thibault B. Cardiac resynchronization therapy non-responder to responder conversion rate in the MORE-CRT MPP trial. Europace. 2023 Oct 5;25(10):euad294.

97. Leclercq C, Walker S, Linde C, Clementy J, Marshall AJ, Ritter P, et al. Comparative effects of permanent biventricular and right-univentricular pacing in heart failure patients with chronic atrial fibrillation. Eur Heart J. 2002 Nov;23(22):1780-7.

98. Lenarczyk R, Boveda S, Mansourati J, Russo V, Marijon E, Lane DA, et al. Peri-procedural management, implantation feasibility, and short-term outcomes in patients undergoing implantation of leadless pacemakers: European snapshot survey. Europace. 2020;22(5):833-838.

99. Lenarczyk R, Kowalski O, Sredniawa B, Pruszkowska-Skrzep P, Mazurek M, Jędrzejczyk-Pate J Cardiovasc Electrophysiol. 2012 Nov;23(11):1228-36 j E, Implantation feasibility, procedure-related adverse events and lead performance during 1-year follow-up in patients undergoing triple-site cardiac resynchronization therapy: a substudy of TRUST CRT randomized trial. J Cardiovasc Electrophysiol. 2012 Nov;23(11):1228-36.

100. Leon AR, Abraham WT, Curtis AB, Daubert JP, Fisher WG, Gurley J, et al. MIRACLE Study Program. Safety of transvenous cardiac resynchronization system implantation in patients with chronic heart failure: combined results of over 2,000 patients from a multicenter study program. J Am Coll Cardiol. 2005 Dec 20;46(12):2348-56.

101. Leon AR, Greenberg JM, Kanuru N, Baker CM, Mera FV, Smith AL, et al. Cardiac resynchronization in patients with congestive heart failure and chronic atrial fibrillation: effect of upgrading to biventricular pacing after chronic right ventricular pacing. J Am Coll Cardiol. 2002 Apr 17;39(8):1258-63.

102. Lewis AJM, Foley P, Whinnett Z, Keene D, Chandrasekaran B. His Bundle Pacing: A New Strategy for Physiological Ventricular Activation. J Am Heart Assoc. 2019 Mar 19;8(6):e010972. Erratum in: J Am Heart Assoc. 2019 Jun 4;8(11):e002310.

103. Linde C, Abraham WT, Gold MR, Daubert C; REVERSE Study Group. Cardiac resynchronization therapy in asymptomatic or mildly symptomatic heart failure patients in relation to etiology: results from the REVERSE (REsynchronization reVErses Remodeling in Systolic Left vEntricular Dysfunction) study. J Am Coll Cardiol. 2010 Nov 23;56(22):1826-31.

104. Linde C, Abraham WT, Gold MR, St John Sutton M, Ghio S, Daubert C; REVERSE (REsynchronization reVErses Remodeling in Systolic left vEntricular dysfunction) Study Group. Randomized trial of cardiac resynchronization in mildly symptomatic heart failure patients and in asymptomatic patients with left ventricular dysfunction and previous heart failure symptoms. J Am Coll Cardiol. 2008 Dec 2;52(23):1834-43.

105. Lindenfeld J, Feldman AM, Saxon L, Boehmer J, Carson P, Ghali JK, et al. Effects of cardiac resynchronization therapy with or without a defibrillator on survival and hospitalizations in patients with New York Heart Association class IV heart failure. Circulation. 2007 Jan 16;115(2):204-12.

106. Lindenfeld J, Zile MR. Devices for Monitoring and Managing Heart Failure. In: Libby P, Bonow RO, Mann DL, Tomaselli GF, Bhatt DL, Solomon SD. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. 12th ed. Philidelphia, PA: Elsevier Inc.; 2022. 1107-1118.

107. Lustgarten DL, Crespo EM, Arkhipova-Jenkins I, Lobel R, Winget J, Koehler J, et al. His-bundle pacing versus biventricular pacing in cardiac resynchronization therapy patients: A crossover design comparison. Heart Rhythm. 2015 Jul;12(7):1548-57.

108. Mararenko A, Udongwo N, Pannu V, Miller B, Alshami A, Ajam F, Odak M, Tavakolian K, Douedi S, Mushtaq A, Asif A, Sealove B, Almendral J, Zacks E, Heaton J. Intracardiac

leadless versus transvenous permanent pacemaker implantation: Impact on clinical outcomes and healthcare utilization. J Cardiol. 2023 Nov;82(5):378-387.

109. Marques P, Nobre Menezes M, Lima da Silva G, Guimarães T, Bernardes A, Cortez-Dias N, et al. Triple-site pacing for cardiac resynchronization in permanent atrial fibrillation: follow-up results from a prospective observational study. Europace. 2018 Jun 1;20(6):986-992.

110. Martínez-Sande JL, García-Seara J, Rodríguez-Mañero M, Fernández-López XA, González-Melchor L, et al. The Micra Leadless Transcatheter Pacemaker. Implantation and Mid-term Follow-up Results in a Single Center. Rev Esp Cardiol (Engl Ed). 2017 Apr;70(4):275-281.

111. Massacesi C, Ceriello L, Maturo F, Porreca A, Appignani M, Di Girolamo E. Cardiac resynchronization therapy with multipoint pacing via quadripolar lead versus traditional biventricular pacing: A systematic review and meta-analysis of clinical studies on hemodynamic, clinical, and prognostic parameters. Heart Rhythm O2. 2021 Dec 17;2(6Part B):682-690.

112. McAlister FA, Ezekowitz J, Hooton N, Vandermeer B, Spooner C, Dryden DM, et al. Cardiac resynchronization therapy for patients with left ventricular systolic dysfunction: a systematic review. JAMA. 2007a Jun 13;297(22):2502-14.

113. McAlister FA, Ezekowitz J, Dryden DM, Hooton N, Vandermeer B, Friesen C, et al. Cardiac Resynchronization Therapy and Implantable Cardiac Defibrillators in Left Ventricular Systolic Dysfunction. Evidence Report/Technology Assessment No. 152 (Prepared by the University of Alberta Evidence-based Practice Center under Contract No. 290-02-0023). AHRQ Publication No. 07-E009. Rockville, MD: Agency for Healthcare Research and Quality. Jun 2007b.

114. Medtronic. Cardiac Resynchronization Therapy (CRT) Systems. Last updated Jul 2022. Accessed Dec 4, 2023. Available at URL address: https://www.medtronic.com/us-en/healthcare-professionals/products/cardiac-rhythm/crt-systems.html

115. Molhoek SG, Bax JJ, Bleeker GB, Boersma E, van Erven L, Steendijk P, et al. Comparison of response to cardiac resynchronization therapy in patients with sinus rhythm versus chronic atrial fibrillation. Am J Cardiol. 2004 Dec 15;94(12):1506-9.

116. Molhoek SG, Bax JJ, Bleeker GB, Holman ER, van Erven L, Bootsma M, et al. Long-term follow-up of cardiac resynchronization therapy in patients with end-stage heart failure. J Cardiovasc Electrophysiol. 2005 Jul;16(7):701-7.

117. Morgan JM, Biffi M, Gellér L, Leclercq C, Ruffa F, Tung S, et al; ALSYNC Investigators. ALternate Site Cardiac ResYNChronization (ALSYNC): a prospective and multicentre study of left ventricular endocardial pacing for cardiac resynchronization therapy. Eur Heart J. 2016 Jul 14;37(27):2118-27.

118. Moss AJ, Hall WJ, Cannom DS, Klein H, Brown MW, Daubert JP, et al; MADIT-CRT Trial Investigators. Cardiac-resynchronization therapy for the prevention of heart-failure events. N Engl J Med. 2009 Oct 1;361(14):1329-38.

119. Mulia EPB, Amadis MR, Julario R, Dharmadjati BB. Left bundle branch pacing: An evolving site for physiological pacing. J Arrhythm. 2021 Sep 20;37(6):1578-1584.

120. National Institute for Health and Care Excellence (NICE). NICE interventional procedure guidance 626. Leadless cardiac pacemaker implantation for bradyarrhythmias. Aug 29, 2018. Accessed Dec 1, 2023. Available at URL address: https://www.nice.org.uk/guidance/ipg626

121. National Institute for Health and Care Excellence (NICE). NICE interventional procedure guidance 694. Permanent His-bundle pacemaker implantation for treating heart failure. May 5, 2021. Accessed Dec 1, 2023. Available at URL address: https://www.nice.org.uk/guidance/ipg694

122. National Institute for Health and Care Excellence (NICE). Technology appraisal guidance 314. Implantable cardioverter defibrillators and cardiac resynchronization therapy for arrhythmias and heart failure. Jun 25, 2014. Accessed Dec 1, 2023. Available at URL address: https://www.nice.org.uk/guidance/ta314

123. Neugebauer F, Noti F, van Gool S, Roten L, Baldinger SH, Seiler J, Madaffari A, Servatius H, Ryser A, Tanner H, Reichlin T, Haeberlin A. Leadless atrioventricular synchronous pacing in an outpatient setting: Early lessons learned on factors affecting atrioventricular synchrony. Heart Rhythm. 2022 May;19(5):748-756.

124. Ngo L, Nour D, Denman RA, Walters TE, Haqqani HM, Woodman RJ, Ranasinghe I. Safety and Efficacy of Leadless Pacemakers: A Systematic Review and Meta-Analysis. J Am Heart Assoc. 2021 Jul 6;10(13):e019212.

125. Normand C, Linde C, Singh J, Dickstein K. Indications for Cardiac Resynchronization Therapy: A Comparison of the Major International Guidelines. JACC Heart Fail. 2018 Apr;6(4):308-316.

126. Okabe T, Hummel JD, Bank AJ, Niazi IK, McGrew FA, Kindsvater S, Oza SR, Scherschel JA, Walsh MN, Singh JP. Leadless left ventricular stimulation with WiSE-CRT System - Initial experience and results from phase I of SOLVE-CRT Study (nonrandomized, roll-in phase). Heart Rhythm. 2021 Jul 23:S1547-5271(21)01808-7.

127. Ommen SR, Mital S, Burke MA, Day SM, Deswal A, Elliott P, Evanovich LL, Hung J, Joglar JA, Kantor P, Kimmelstiel C, Kittleson M, Link MS, Maron MS, Martinez MW, Miyake CY, Schaff HV, Semsarian C, Sorajja P. 2020 AHA/ACC Guideline for the Diagnosis and Treatment of Patients With Hypertrophic Cardiomyopathy: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2020 Dec 22;142(25):e558-e631.Erratum in: Circulation. 2020 Dec 22;142(25):e633.

128. Padeletti L, Musilli N, Porciani MC, Colella A, Di Biase L, Ricciardi G, et al. Atrial fibrillation and cardiac resynchronization therapy: the MASCOT study. Europace. 2004 Sep;5 Suppl 1:S49-54.

129. Padeletti L, Muto C, Maounis T, Schuchert A, Bongiorni MG, Frank R, et al; Management of Atrial fibrillation Suppression in AF-HF COmorbidity Therapy Study Group. Atrial fibrillation in recipients of cardiac resynchronization therapy device: 1-year results of the randomized MASCOT trial. Am Heart J. 2008 Sep;156(3):520-6.

130. Piccini JP, El-Chami M, Wherry K, Crossley GH, Kowal RC, Stromberg K, Longacre C, Hinnenthal J, Bockstedt L. Contemporaneous Comparison of Outcomes Among Patients

Implanted With a Leadless vs Transvenous Single-Chamber Ventricular Pacemaker. JAMA Cardiol. 2021 Oct 1;6(10):1187-1195. Erratum in: JAMA Cardiol. 2021 Sep 8.

131. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, et al.; Authors/Task Force Members; Document Reviewers. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail. 2016 Aug;18(8):891-975.

132. Pouleur AC, Knappe D, Shah AM, Uno H, Bourgoun M, Foster E, et al; MADIT-CRT Investigators. Relationship between improvement in left ventricular dyssynchrony and contractile function and clinical outcome with cardiac resynchronization therapy: the MADIT-CRT trial. Eur Heart J. 2011 Jul;32(14):1720-9.

133. Qian Z, Zou F, Wang Y, Qiu Y, Chen X, Jiang H, Hou X. Permanent His bundle pacing in heart failure patients: A systematic review and meta-analysis. Pacing Clin Electrophysiol. 2019 Feb;42(2):139-145.

134. Reddy VY, Exner DV, Doshi R, Tomassoni G, Bunch TJ, Estes NAM, Neužil P, Paulin FL, Garcia Guerrero JJ, Cantillon DJ; LEADLESS II Investigators. Primary Results on Safety and Efficacy From the LEADLESS II-Phase 2 Worldwide Clinical Trial. JACC Clin Electrophysiol. 2022 Jan;8(1):115-117.

135. Reddy VY, Knops RE, Sperzel J, Miller MA, Petru J, Simon J, et al. Permanent leadless cardiac pacing: results of the LEADLESS trial. Circulation. 2014 Apr 8;129(14):1466-71.

136. Reddy VY, Miller MA, Neuzil P, Søgaard P, Butter C, Seifert M, et al. Cardiac Resynchronization Therapy With Wireless Left Ventricular Endocardial Pacing: The SELECT-LV Study. J Am Coll Cardiol. 2017 May 2;69(17):2119-2129.

137. Reynolds D, Duray GZ, Omar R, Soejima K, Neuzil P, Zhang S, et al.; Micra Transcatheter Pacing Study Group. A Leadless Intracardiac Transcatheter Pacing System. N Engl J Med. 2016 Feb 11;374(6):533-41.

138. Rickard J, Bassiouny M, Cronin EM, Martin DO, Varma N, Niebauer MJ, et al. Predictors of response to cardiac resynchronization therapy in patients with a non-left bundle branch block morphology. Am J Cardiol. 2011;108:1576-80.

139. Rickard J, Jackson K, Biffi M, Vernooy K, Bank A, Cerkvenik J, Ghosh S, Gold MR. The ECG Belt for CRT response trial: Design and clinical protocol. Pacing Clin Electrophysiol. 2020 Oct;43(10):1063-1071.

140. Ritter P, Duray GZ, Steinwender C, Soejima K, Omar R, Mont L, et al.; Micra Transcatheter Pacing Study Group. Early performance of a miniaturized leadless cardiac pacemaker: the Micra Transcatheter Pacing Study. Eur Heart J. 2015 Oct 1;36(37):2510-9.

141. Roberts PR, Clementy N, Al Samadi F, Garweg C, Martinez-Sande JL, Iacopino S, et al. A leadless pacemaker in the real-world setting: The Micra Transcatheter Pacing System Post-Approval Registry. Heart Rhythm. 2017 Sep;14(9):1375-1379.

142. Rogers DP, Lambiase PD, Lowe MD, Chow AW. A randomized double-blind crossover trial of triventricular versus biventricular pacing in heart failure. Eur J Heart Fail. 2012 May;14(5):495-505.

143. Russo AM, Stainback RF, Bailey SR, Epstein AE, Heidenreich PA, Jessup M, et al. ACCF/HRS/AHA/ASE/HFSA/SCAI/SCCT/SCMR 2013 appropriate use criteria for implantable cardioverter-defibrillators and cardiac resynchronization therapy: a report of the American College of Cardiology Foundation appropriate use criteria task force, Heart Rhythm Society, American Heart Association, American Society of Echocardiography, Heart Failure Society of America, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance. J Am Coll Cardiol. 2013 Mar 26;61(12):1318-68.

144. Saba S, McLaughlin T, He M, Althouse A, Mulukutla S, Hernandez I. Cardiac resynchronization therapy using pacemakers vs defibrillators in patients with nonischemic cardiomyopathy: The United States experience from 2007 to 2014. Heart Rhythm. 2019 Jul;16(7):1065-1071.

145. Santangeli P, Di Biase L, Pelargonio G, Dello Russo A, Casella M, Bartoletti S, et al. Cardiac resynchronization therapy in patients with mild heart failure: a systematic review and meta-analysis. J Interv Card Electrophysiol. 2011;32:125-35.

146. Sharma PS, Naperkowski A, Bauch TD, Chan JYS, Arnold AD, Whinnett ZI, et al. Permanent His Bundle Pacing for Cardiac Resynchronization Therapy in Patients With Heart Failure and Right Bundle Branch Block. Circ Arrhythm Electrophysiol. 2018 Sep;11(9):e006613.

147. Sharma PS, Vijayaraman P. Conduction System Pacing for Cardiac Resynchronisation. Arrhythm Electrophysiol Rev. 2021;10(1):51-58.

148. Sharma PS, Vijayaraman P. His Bundle Pacing Or Biventricular Pacing For Cardiac Resynchronization Therapy In Heart Failure: Discovering New Methods For An Old Problem. J Atr Fibrillation. 2016 Dec 31;9(4):1501.

149. Sidhu BS, Porter B, Gould J, et al. Leadless left ventricular endocardial pacing in nonresponders to conventional cardiac resynchronization therapy [published online ahead of print, 2020 Apr 24]. Pacing Clin Electrophysiol. 2020;10.1111/pace.13926.

150. Sidhu BS, Sieniewicz B, Gould J, Elliott MK, Mehta VS, Betts TR, James S, Turley AJ, Butter C, Seifert M, Boersma LVA, Riahi S, Neuzil P, Biffi M, Diemberger I, Vergara P, Arnold M, Keane DT, Defaye P, Deharo JC, Chow A, Schilling R, Behar JM, Leclercq C, Auricchio A, Niederer SA, Rinaldi CA. Leadless left ventricular endocardial pacing for CRT upgrades in previously failed and high-risk patients in comparison with coronary sinus CRT upgrades. Europace. 2021 Oct 9;23(10):1577-1585.

151. Sieniewicz, Benjamin J et al. Real-world experience of leadless left ventricular endocardial cardiac resynchronization therapy: A multicenter international registry of the WiSE-CRT pacing system. Heart rhythm vol. 17,8 (2020): 1291-1297.

152. Singh JP, Abraham WT, Auricchio A, Delnoy PP, Gold M, Reddy VY, et al. Design and rationale for the Stimulation Of the Left Ventricular Endocardium for Cardiac Resynchronization Therapy in non-responders and previously untreatable patients (SOLVE-CRT) trial. Am Heart J. 2019 Apr 9;217:13-22.

153. Singh JP, Klein HU, Huang DT, Reek S, Kuniss M, Quesada A, et al. Left ventricular lead position and clinical outcome in the multicenter automatic defibrillator implantation trial-cardiac resynchronization therapy (MADIT-CRT) trial. Circulation. 2011 Mar 22;123(11):1159-66.

154. Sipahi I, Carrigan TP, Rowland DY, Stambler BS, Fang JC. Impact of QRS duration on clinical event reduction with cardiac resynchronization therapy: meta-analysis of randomized controlled trials. Arch Intern Med. 2011 Sep 12;171(16):1454-62.

155. Sipahi I, Chou JC, Hyden M, Rowland DY, Simon DI, Fang JC. Effect of QRS morphology on clinical event reduction with cardiac resynchronization therapy: meta-analysis of randomized controlled trials. Am Heart J. 2012 Feb;163(2):260-7.

156. Sohaib SM, Finegold JA, Nijjer SS, Hossain R, Linde C, Levy WC, et al. Opportunity to increase life span in narrow QRS cardiac resynchronization therapy recipients by deactivating ventricular pacing: evidence from randomized controlled trials. JACC Heart Fail. 2015 Apr;3(4):327-36.

157. Solomon SD, Foster E, Bourgoun M, Shah A, Viloria E, Brown MW, et al. MADIT-CRT Investigators. Effect of cardiac resynchronization therapy on reverse remodeling and relation to outcome: multicenter automatic defibrillator implantation trial: cardiac resynchronization therapy. Circulation. 2010 Sep 7;122(10):985-92.

158. Sperzel J, Burri H, Gras D, Tjong FV, Knops RE, Hindricks G, Steinwender C, Defaye P. State of the art of leadless pacing. Europace. 2015 Oct;17(10):1508-13.

159. St John Sutton M, Ghio S, Plappert T, Tavazzi L, Scelsi L, Daubert C, et al; REsynchronization reVErses Remodeling in Systolic left vEntricular dysfunction (REVERSE) Study Group. Cardiac resynchronization induces major structural and functional reverse remodeling in patients with New York Heart Association class I/II heart failure. Circulation. 2009 Nov 10;120(19):1858-65.

160. Stavrakis S, Lazzara R, Thadani U. The benefit of cardiac resynchronization therapy and QRS duration: a meta-analysis. J Cardiovasc Electrophysiol. 2012;23:163-8.

161. Steinberg JS, Gorcsan J, Mazur A, Jain SK, Rashtian M, Greer GS, Zarraga I, Vloka M, Cook MM, Salam T, Mountantonakis S, Beck H, Silver J, Aktas M, Henrikson C, Schaller RD, Epstein AE, McNitt S, Schleede S, Peterson D, Goldenberg I, Zareba W. Junctional AV ablation in patients with atrial fibrillation undergoing cardiac resynchronization therapy (JAVA-CRT): results of a multicenter randomized clinical trial pilot program. J Interv Card Electrophysiol. 2022 Aug;64(2):519-530.

162. Steinwender C, Khelae SK, Garweg C, Chan JYS, Ritter P, Johansen JB, et al. Atrioventricular synchronous pacing using a leadless ventricular pacemaker: results from the MARVEL 2 study. JACC Clin Electrophysiol. 2020;6(1):94-106.

163. Stevenson WG, Hernandez AF, Carson PE, Fang JC, Katz SD, Spertus JA, et al; Heart Failure Society of America Guideline Committee. Indications for cardiac resynchronization therapy: 2011 update from the Heart Failure Society of America Guideline Committee. J Card Fail. 2012 Feb;18(2):94-106.

164. Stockburger M, Moss AJ, Klein HU, Zareba W, Goldenberg I, Biton Y, et al. Sustained clinical benefit of cardiac resynchronization therapy in non-LBBB patients with prolonged PR-interval: MADIT-CRT long-term follow-up. Clin Res Cardiol. 2016 Nov;105(11):944-952.

165. Sutton MG, Plappert T, Hilpisch KE, Abraham WT, Hayes DL, Chinchoy E. Sustained reverse left ventricular structural remodeling with cardiac resynchronization at one year is a function of etiology: quantitative Doppler echocardiographic evidence from the Multicenter InSync Randomized Clinical Evaluation (MIRACLE). Circulation. 2006 Jan 17;113(2):266-72.

166. Tan JL, Lee JZ, Terrigno V, Saracco B, Saxena S, Krathen J, Hunter K, Cha YM, Russo AM. Outcomes of Left Bundle Branch Area Pacing for Cardiac Resynchronization Therapy: An Updated Systematic Review and Meta-analysis. CJC Open. 2021 Jun 16;3(10):1282-1293.

167. Tang AS, Wells GA, Talajic M, Arnold MO, Sheldon R, Connolly S, et al. Cardiac-resynchronization therapy for mild-to-moderate heart failure. N Engl J Med. 2010 Dec 16;363(25):2385-95.

168. Teng AE, Massoud L, Ajijola OA. Physiological mechanisms of QRS narrowing in bundle branch block patients undergoing permanent His bundle pacing. J Electrocardiol. 2016 Sep-Oct;49(5):644-8.

169. Thibault B, Harel F, Ducharme A, White M, Ellenbogen KA, Frasure-Smith N, et al.; LESSER-EARTH Investigators. Cardiac resynchronization therapy in patients with heart failure and a QRS complex <120 milliseconds: the Evaluation of Resynchronization Therapy for Heart Failure (LESSER-EARTH) trial. Circulation. 2013 Feb 26;127(8):873-81.

170. Upadhyay GA, Choudhry NK, Auricchio A, Ruskin J, Singh JP. Cardiac resynchronization in patients with atrial fibrillation: a meta-analysis of prospective cohort studies. J Am Coll Cardiol. 2008 Oct 7;52(15):1239-46.

171. Upadhyay GA, Tung R. His Bundle Pacing for Cardiac Resynchronization. Card Electrophysiol Clin. 2018 Sep;10(3):511-517.

172. Upadhyay GA, Vijayaraman P, Nayak HM, Verma N, Dandamudi G, Sharma PS, Saleem M, Mandrola J, Genovese D, Oren JW, Subzposh FA, Aziz Z, Beaser A, Shatz D, Besser S, Lang RM, Trohman RG, Knight BP, Tung R; His-SYNC Investigators. On-treatment comparison between corrective His bundle pacing and biventricular pacing for cardiac resynchronization: A secondary analysis of the His-SYNC Pilot Trial. Heart Rhythm. 2019a Dec;16(12):1797-1807.

173. Upadhyay GA, Vijayaraman P, Nayak HM, Verma N, Dandamudi G, Sharma PS, Saleem M, Mandrola J, Genovese D, Tung R; His-SYNC Investigators. His Corrective Pacing or Biventricular Pacing for Cardiac Resynchronization in Heart Failure. J Am Coll Cardiol. 2019b Jul 9;74(1):157-159.

174. U.S. Food Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). Premarket approval (PMA). Abbott Medical Aveir™ DR Leadless System. P150035/S003. Jun 29, 2023. Accessed Nov 27, 2023. Available at URL address: https://www.accessdata.fda.gov/cdrh_docs/pdf15/P150035S003A.pdf

175. U.S. Food Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). Premarket approval (PMA). Abbott Medical Aveir™ VR Leadless System. P150035. Mar 31,

2022. Accessed Dec 1, 2023. Available at URL address: https://www.accessdata.fda.gov/cdrh_docs/pdf15/P150035A.pdf

176. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). Premarket Approval (PMA) Database. InSync™ biventricular pacing system. P010015. Aug 28, 2001. Accessed Dec 1, 2023. Available at URL address: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=p010015

177. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). Premarket Approval (PMA) Database. St. Jude Medical® Epic™ and Atlas® + HF dual chamber implantable cardioverter defibrillator systems with cardiac resynchronization therapy. P030054. Jun 30, 2004. Accessed Dec 1, 2023. Available at URL address: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=p030054

178. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). Premarket Approval (PMA) Database. Anthem and Frontier II biventricular pacing systems. P030035. May 13, 2004. Accessed Dec 4, 2023. Available at URL address: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=p030035

179. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). Premarket Approval (PMA) Database. Guidant cardiac resynchronization therapy defibrillator system including the CONTAK CD pulse generator and the EASYTRAK left ventricular coronary venous lead. P010012. May 2, 2002. Accessed Dec 1, 2023. Available at URL address: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=p010012

180. U.S. Food Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). Premarket approval (PMA) Database. Medtronic Micra Transcatheter Pacemaker System. Apr 6, 2016. Accessed Dec 1, 2023. Available at URL address: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=p150033

181. U.S. Food Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). Premarket approval (PMA) Database. Medtronic Cardiac Rhythm Disease Management SelectSecure MRI SureScan Lead. P030036 Supplement S100. Jun 28, 2018. Accessed Dec 1, 2023. Available at URL address: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P030036S100

182. U.S. Food Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). Premarket approval (PMA) Database. Medtronic Cardiac Rhythm Disease Management SelectSecure MRI SureScan Lead. P030036 Supplement S139. Oct 3, 2022. Accessed Dec 4, 2023. Available at URL address: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P030036S139

183. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). Premarket Approval (PMA) Database. Ovatio CRT-D. P060027. May 15, 2008. Accessed Dec 4, 2023. Available at URL address: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=p060027

184. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). Premarket Approval (PMA) Database. Expanded indications for use of CRT-P devices. P010015/S205 and P010031/S381. Apr 10, 2014. Accessed Dec 4, 2023. Available at URL address: https://www.accessdata.fda.gov/cdrh_docs/pdf/P010015S205b.pdf

185. U.S. Food and Drug Administration (FDA). Medical Device Safety. Letters to Health Care Providers. Leadless Pacing Systems: Risk of Major Complications Related to Cardiac Perforation During Implantation - Letter to Health Care Providers. Nov 17, 2021. Accessed Dec 5, 2023. Available at URL address: https://www.fda.gov/medical-devices/letters-health-care-providers/leadless-pacing-systems-risk-major-complications-related-cardiac-perforation-during-implantation

186. U.S. Food Drug Administration (FDA). News Release. FDA approves first leadless pacemaker to treat heart rhythm disorders. Apr 6, 2016. Accessed Dec 5, 2023. Available at URL address: https://www.fda.gov/news-events/press-announcements/fda-approves-first-leadless-pacemaker-treat-heart-rhythm-disorders

187. U.S. National Library of Medicine. ClinicalTrials.gov. Accessed Nov 6, 2023. Available at URL address: https://clinicaltrials.gov

188. Vaidya VR, Dai M, Asirvatham SJ, Rea RF, Thome TM, Srivathsan K, et al. Real-world experience with leadless cardiac pacing. Pacing Clin Electrophysiol. 2019 Mar;42(3):366-373.

189. Valiton V, Graf D, Pruvot E, Carroz P, Fromer M, Bisch L, et al. Leadless pacing using the transcatheter pacing system (Micra TPS) in the real world: initial Swiss experience from the Romandie region. Europace. 2018 Sep 6.

190. van Bommel RJ, Marsan NA, Delgado V, Borleffs CJ, van Rijnsoever EP, et al. Cardiac resynchronization therapy as a therapeutic option in patients with moderate-severe functional mitral regurgitation and high operative risk. Circulation. 2011 Aug 23;124(8):912-9.

191. van der Zee S, Doshi SK. Expert Analysis. Permanent Leadless Cardiac Pacing. Mar 23, 2016. American College of Cardiology. Accessed Dec 5, 2023. Available at URL address: https://www.acc.org/latest-in-cardiology/articles/2016/03/23/08/09/permanent-leadless-cardiac-pacing

192. van Geldorp IE, Vernooy K, Delhaas T, Prins MH, Crijns HJ, Prinzen FW, Dijkman B. Beneficial effects of biventricular pacing in chronically right ventricular paced patients with mild cardiomyopathy. Europace. 2010 Feb;12(2):223-9.

193. Vatankulu MA, Goktekin O, Kaya MG, Ayhan S, Kucukdurmaz Z, Sutton R, Henein M. Effect of long-term resynchronization therapy on left ventricular remodeling in pacemaker patients upgraded to biventricular devices. Am J Cardiol. 2009 May 1;103(9):1280-4.

194. Versteeg H, van den Broek KC, Theuns DA, Mommersteeg PM, Alings M, van der Voort PH, et al. Effect of cardiac resynchronization therapy-defibrillator implantation on health status in patients with mild versus moderate symptoms of heart failure. Am J Cardiol. 2011 Oct 15;108(8):1155-9.

195. Vijayaraman P, Chung MK, Dandamudi G, Upadhyay GA, Krishnan K, Crossley G, et al; ACC's Electrophysiology Council. His Bundle Pacing. J Am Coll Cardiol. 2018 Aug 21;72(8):927-947.

196. Vijayaraman P, Ponnusamy S, Cano Ó, Sharma PS, Naperkowski A, Subsposh FA, Moskal P, Bednarek A, Dal Forno AR, Young W, Nanda S, Beer D, Herweg B, Jastrzebski M. Left Bundle Branch Area Pacing for Cardiac Resynchronization Therapy: Results From the

International LBBAP Collaborative Study Group. JACC Clin Electrophysiol. 2021 Feb;7(2):135-147.

197. Vijayaraman P, Subzposh FA, Naperkowski A, Panikkath R, John K, Mascarenhas V, Bauch TD, Huang W. Prospective evaluation of feasibility and electrophysiologic and echocardiographic characteristics of left bundle branch area pacing. Heart Rhythm. 2019 Dec;16(12):1774-1782.

198. Vinther M, Risum N, Svendsen JH, Møgelvang R, Philbert BT. A Randomized Trial of His Pacing Versus Biventricular Pacing in Symptomatic HF Patients With Left Bundle Branch Block (His-Alternative). JACC Clin Electrophysiol. 2021 Nov;7(11):1422-1432.

199. Wang Y, Zhu H, Hou X, Wang Z, Zou F, Qian Z, Wei Y, Wang X, Zhang L, Li X, Liu Z, Xue S, Qin C, Zeng J, Li H, Wu H, Ma H, Ellenbogen KA, Gold MR, Fan X, Zou J; LBBP-RESYNC Investigators. Randomized Trial of Left Bundle Branch vs Biventricular Pacing for Cardiac Resynchronization Therapy. J Am Coll Cardiol. 2022 Sep 27;80(13):1205-1216.

200. Wells G, Parkash R, Healey JS, Talajic M, Arnold JM, Sullivan S, et al. Cardiac resynchronization therapy: a meta-analysis of randomized controlled trials. CMAJ. 2011 Mar 8;183(4):421-9.

201. Whinnett ZI, Shun-Shin MJ, Tanner M, Foley P, Chandrasekaran B, Moore P, Adhya S, Qureshi N, Muthumala A, Lane R, Rinaldi A, Agarwal S, Leyva F, Behar J, Bassi S, Ng A, Scott P, Prasad R, Swinburn J, Tomson J, Sethi A, Shah J, Lim PB, Kyriacou A, Thomas D, Chuen J, Kamdar R, Kanagaratnam P, Mariveles M, Burden L, March K, Howard JP, Arnold A, Vijayaraman P, Stegemann B, Johnson N, Falaschetti E, Francis DP, Cleland JGF, Keene D. Effects of haemodynamically atrio-ventricular optimized His bundle pacing on heart failure symptoms and exercise capacity: the His Optimized Pacing Evaluated for Heart Failure (HOPE-HF) randomized, double-blind, cross-over trial. Eur J Heart Fail. 2023 Feb;25(2):274-283.

202. Wijesuriya N, Elliott MK, Mehta V, Sidhu BS, Behar JM, Niederer S, Rinaldi CA. Leadless left ventricular endocardial pacing for cardiac resynchronization therapy: A systematic review and meta-analysis. Heart Rhythm. 2022 Jul;19(7):1176-1183.

203. Wilkoff BL, Cook JR, Epstein AE, Greene HL, Hallstrom AP, Hsia H, et al; Dual Chamber and VVI Implantable Defibrillator Trial Investigators. Dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator: the Dual Chamber and VVI Implantable Defibrillator (DAVID) Trial. JAMA. 2002 Dec 25;288(24):3115-23.

204. Wilkoff BL, Filippatos G, Leclercq C, Gold MR, Hersi AS, Kusano K, Mullens W, Felker GM, Kantipudi C, El-Chami MF, Essebag V, Pierre B, Philippon F, Perez-Gil F, Chung ES, Sotomonte J, Tung S, Singh B, Bozorgnia B, Goel S, Ebert HH, Varma N, Quan KJ, Salerno F, Gerritse B, van Wel J, Schaber DE, Fagan DH, Birnie D; AdaptResponse investigators. Adaptive versus conventional cardiac resynchronisation therapy in patients with heart failure (AdaptResponse): a global, prospective, randomised controlled trial. Lancet. 2023 Sep 30;402(10408):1147-1157. Erratum in: Lancet. 2023 Sep 30;402(10408):1132.

205. Wilton SB, Leung AA, Ghali WA, Faris P, Exner DV. Outcomes of cardiac resynchronization therapy in patients with versus those without atrial fibrillation: a systematic review and meta-analysis. Heart Rhythm. 2011 Jul;8(7):1088-94.

206. Wu S, Su L, Vijayaraman P, Zheng R, Cai M, Xu L, Shi R, Huang Z, Whinnett ZI, Huang W. Left Bundle Branch Pacing for Cardiac Resynchronization Therapy: Nonrandomized On-Treatment Comparison With His Bundle Pacing and Biventricular Pacing. Can J Cardiol. 2021 Feb;37(2):319-328.

207. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Colvin MM, et al. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation. 2017 Apr 28.

208. Yancy CW, Jessup M, Bozkurt B, Masoudi FA, Butler J, McBride PE, et al.; ACCF/AHA Task Force Members. 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2013 Jun 5. pii: S0735-1097(13)02114-1.

209. Young JB, Abraham WT, Smith AL, Leon AR, Lieberman R, Wilkoff B, et al; Multicenter InSync ICD Randomized Clinical Evaluation (MIRACLE ICD) Trial Investigators. Combined cardiac resynchronization and implantable cardioversion defibrillation in advanced chronic heart failure: the MIRACLE ICD Trial. JAMA. 2003 May 28;289(20):2685-94.

210. Zanon F, Ellenbogen KA, Dandamudi G, Sharma PS, Huang W, Lustgarten DL, et al. Permanent His-bundle pacing: a systematic literature review and meta-analysis. Europace. 2018 Nov 1;20(11):1819-1826.

211. Zareba W, Klein H, Cygankiewicz I, Hall WJ, McNitt S, Brown M, et al; MADIT-CRT Investigators. Effectiveness of Cardiac Resynchronization Therapy by QRS Morphology in the Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy (MADIT-CRT). Circulation. 2011 Mar 15;123(10):1061-72.

212. Zhang B, Guo J, Zhang G. Comparison of triple-site ventricular pacing versus conventional cardiac resynchronization therapy in patients with systolic heart failure: A meta-analysis of randomized and observational studies. J Arrhythm. 2017 Dec 21;34(1):55-64.

213. Zweerink A, Zubarev S, Bakelants E, Potyagaylo D, Stettler C, Chmelevsky M, Lozeron ED, Hachulla AL, Vallée JP, Burri H. His-Optimized Cardiac Resynchronization Therapy With Ventricular Fusion Pacing for Electrical Resynchronization in Heart Failure. JACC Clin Electrophysiol. 2021 Jul;7(7):881-892.

Revision Details

Type of Revision	Summary of Changes	Date
Annual review	• Revised statement for biventricular pacemaker for all other indications. • Removed policy statement for body surface potential mapping.	1/15/2024