

PRACTICE GUIDELINE

2012 ACCF/AHA/HRS Focused Update of the 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

Developed in Collaboration With the American Association for Thoracic Surgery, Heart Failure Society of America, and Society of Thoracic Surgeons

2012 WRITING GROUP MEMBERS*

Cynthia M. Tracy, MD, FACC, FAHA, Chair; Andrew E. Epstein, MD, FACC, FAHA, FHRM, Vice Chair*; Dawood Darbar, MD, FACC, FHRM[†]; John P. DiMarco, MD, PhD, FACC, FHRM[‡]; Sandra B. Dunbar, RN, DSN, FAAN, FAHA[†]; N.A. Mark Estes III, MD, FACC, FAHA, FHRM[§]; T. Bruce Ferguson, Jr, MD, FACC, FAHA^{||¶}; Stephen C. Hammill, MD, FACC, FHRM[‡]; Pamela E. Karasik, MD, FACC, FHRM[†]; Mark S. Link, MD, FACC, FHRM[†]; Joseph E. Marine, MD, FACC, FHRM[†]; Mark H. Schoenfeld, MD, FACC, FAHA, FHRM[†]; Amit J. Shanker, MD, FACC, FHRM[‡]; Michael J. Silka, MD, FACC[†]; Lynne Warner Stevenson, MD, FACC[#]; William G. Stevenson, MD, FACC, FAHA, FHRM^{***}; Paul D. Varosy, MD, FACC, FHRM[†]

2008 WRITING COMMITTEE MEMBERS

Andrew E. Epstein, MD, FACC, FAHA, FHRM, Chair; John P. DiMarco, MD, PhD, FACC, FHRM; Kenneth A. Ellenbogen, MD, FACC, FAHA, FHRM; N.A. Mark Estes III, MD, FACC, FAHA, FHRM; Roger A. Freedman, MD, FACC, FHRM; Leonard S. Gettes, MD, FACC, FAHA; A. Marc Gillinov, MD, FACC, FAHA; Gabriel Gregoratos, MD, FACC, FAHA; Stephen C. Hammill, MD, FACC, FHRM; David L. Hayes, MD, FACC, FAHA, FHRM; Mark A. Hlatky, MD, FACC, FAHA; L. Kristin Newby, MD, FACC, FAHA; Richard L. Page, MD, FACC, FAHA, FHRM; Mark H. Schoenfeld, MD, FACC, FAHA, FHRM; Michael J. Silka, MD, FACC; Lynne Warner Stevenson, MD, FACC; Michael O. Sweeney, MD, FACC

**Writing group members are required to recuse themselves from voting on sections to which their specific relationships with industry and other entities may apply; see [Appendix 1](#) for recusal information.*

[†]ACCF/AHA Representative.

[‡]Heart Rhythm Society Representative.

[§]ACCF/AHA Task Force on Performance Measures Liaison.

^{||}American Association for Thoracic Surgery Representative.

[¶]Society of Thoracic Surgeons Representative.

[#]Heart Failure Society of America Representative.

^{***}ACCF/AHA Task Force on Practice Guidelines Liaison.

ACCF/AHA TASK FORCE MEMBERS

Jeffrey L. Anderson, MD, FACC, FAHA, Chair; Alice K. Jacobs, MD, FACC, FAHA, Immediate Past Chair; Jonathan L. Halperin, MD, FACC, FAHA, Chair-Elect; Nancy M. Albert, PhD, CCNS, CCRN; Mark A. Creager, MD, FACC, FAHA; David DeMets, PhD; Steven M. Ettinger, MD, FACC; Robert A. Guyton, MD, FACC; Judith S. Hochman, MD, FACC, FAHA; Frederick G. Kushner, MD, FACC, FAHA; E. Magnus Ohman, MD, FACC; William Stevenson, MD, FACC, FAHA; Clyde W. Yancy, MD, FACC, FAHA

TABLE OF CONTENTS

Preamble	1738
1. Introduction.....	1740
1.1. Methodology and evidence review	1740
1.2. Organization of the writing group	1741
1.3. Document review and approval	1741
1.4. Scope of the focused update	1741
2. Indications for pacing.....	1742
2.4. Pacing for hemodynamic indications.....	1742
2.4.1. Cardiac resynchronization therapy.....	1742
2.8. Pacemaker follow-up.....	1746
2.8.3. Remote follow-up and monitoring.....	1746
References.....	1747
Appendix 1. Author Relationships With Industry and Other Entities (Relevant).....	1749
Appendix 2. Reviewer Relationships With Industry and Other Entities (Relevant).....	1751
Appendix 3. Indications for CRT Therapy—Algorithm.....	1753

Preamble

Keeping pace with the stream of new data and evolving evidence on which guideline recommendations are based is an ongoing challenge to timely development of clinical practice guidelines. In an effort to respond promptly to new evidence, the American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) Task Force on Practice Guidelines (Task Force) has created a “focused update” process to revise the existing guideline recommendations that are affected by evolving data or opinion. New evidence is reviewed in an ongoing fashion to more efficiently respond to important science and treatment trends that could have a major

KEYWORDS ACC Practice Guideline; arrhythmias; cardiac resynchronization therapy; focused update; heart failure; pacemaker (Heart Rhythm 2012;9: 1737–1753)

This document was approved by the American College of Cardiology Foundation Board of Trustees, the American Heart Association Science Advisory and Coordinating Committee, and the Heart Rhythm Society Board of Trustees in May 2012. The American College of Cardiology Foundation requests that this document be cited as follows: Tracy CM, Epstein AE, Darbar D, DiMarco JP, Dunbar SB, Estes NAM 3rd, Ferguson TB Jr, Hammill SC, Karasik PE, Link MS, Marine JE, Schoenfeld MH, Shanker AJ, Silka MJ, Stevenson LW, Stevenson WG, Varosy PD. 2012 ACCF/AHA/HRS focused update of the 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. *J Am Coll Cardiol* 2012;60:1297–1313. This article is copublished in *Circulation*, *Heart Rhythm*, and *Journal of Thoracic and Cardiovascular Surgery*. Copies: This document is available on the World Wide Web sites of the American College of Cardiology (www.cardiosource.org), the American Heart Association (my.americanheart.org), and the Heart Rhythm Society (www.hrsonline.org). For copies of this document, please contact Elsevier Inc. Reprint Department, fax (212) 633-3820, e-mail reprints@elsevier.com. Permissions: Multiple copies, modification, alteration, enhancement, and/or distribution of this document are not permitted without the express permission of the American College of Cardiology Foundation. Please contact Elsevier's permission department at healthpermissions@elsevier.com.

impact on patient outcomes and quality of care. Evidence is reviewed at least twice a year, and updates are initiated on an as-needed basis and completed as quickly as possible while maintaining the rigorous methodology that the ACCF and AHA have developed during their partnership of >20 years.

These focused updates are prompted following a thorough review of late-breaking clinical trials presented at national and international meetings, in addition to other new published data deemed to have an impact on patient care (Section 1.1, “Methodology and Evidence Review”). Through a broad-based vetting process, the studies included are identified as being important to the relevant patient population. The focused update is not intended to be based on a complete literature review from the date of the previous guideline publication but rather to include pivotal new evidence that may affect changes to current recommendations.

Specific criteria or considerations for inclusion of new data include the following:

- publication in a peer-reviewed journal;
- large, randomized, placebo-controlled trial(s);
- nonrandomized data deemed important on the basis of results affecting current safety and efficacy assumptions, including observational studies and meta-analyses;
- strength/weakness of research methodology and findings;
- likelihood of additional studies influencing current findings;
- impact on current and/or likelihood of need to develop new performance measure(s);
- request(s) and requirement(s) for review and update from the practice community, key stakeholders, and other sources free of industry relationships or other potential bias;
- number of previous trials showing consistent results; and
- need for consistency with a new guideline or guideline updates or revisions.

In analyzing the data and developing recommendations and supporting text, the writing group uses evidence-based methodologies developed by the Task Force (1). The Class of Recommendation (COR) is an estimate of the size of the treatment effect, with consideration given to risks versus benefits, as well as evidence and/or agreement that a given treatment or procedure is or is not useful/effective and in some situations may cause harm. The Level of Evidence (LOE) is an estimate of the certainty or precision of the treatment effect. The writing group reviews and ranks evidence supporting each recommendation, with the weight of evidence ranked as LOE A, B, or C, according to specific definitions that are included in Table 1. Studies are identified as observational, retrospective, prospective, or randomized, as appropriate. For certain conditions for which inadequate data are available, recommendations are based on expert consensus and clinical experience and are ranked as LOE C. When recommendations at LOE C are supported by historical clinical data, appropriate references (including clinical reviews) are cited if available. For issues for which sparse data are available, a survey of current practice among

Table 1 Applying Classification of Recommendations and Level of Evidence

A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Although randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

†For comparative effectiveness recommendations (Class I and IIa; Level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

the clinicians on the writing group is the basis for LOE C recommendations, and no references are cited. The schema for COR and LOE is summarized in [Table 1](#), which also provides suggested phrases for writing recommendations within each COR. A new addition to this methodology is separation of the Class III recommendations to delineate whether the recommendation is determined to be of “no benefit” or is associated with “harm” to the patient. In addition, in view of the increasing number of comparative effectiveness studies, comparator verbs and suggested phrases for writing recommendations for the comparative effectiveness of one treatment or strategy versus another have been added for COR I and IIa, LOE A or B only.

In view of the advances in medical therapy across the spectrum of cardiovascular diseases, the Task Force has designated the term *guideline-directed medical therapy (GDMT)* to represent optimal medical therapy as defined by ACCF/AHA guideline (primarily Class I)—recommended therapies. This new term, GDMT, will be used herein and throughout all future guidelines.

Because the ACCF/AHA practice guidelines address patient populations (and healthcare providers) residing in North America, drugs that are not currently available in North America are discussed in the text without a specific COR. For studies performed in large numbers of subjects outside North America, each writing group reviews the

potential impact of different practice patterns and patient populations on the treatment effect and relevance to the ACCF/AHA target population to determine whether the findings should inform a specific recommendation.

The ACCF/AHA practice guidelines are intended to assist healthcare providers in clinical decision making by describing a range of generally acceptable approaches to the diagnosis, management, and prevention of specific diseases or conditions. The guidelines attempt to define practices that meet the needs of most patients in most circumstances. The ultimate judgment about care of a particular patient must be made by the healthcare provider and patient in light of all the circumstances presented by that patient. As a result, situations may arise in which deviations from these guidelines may be appropriate. Clinical decision making should consider the quality and availability of expertise in the area where care is provided. When these guidelines are used as the basis for regulatory or payer decisions, the goal should be improvement in quality of care. The Task Force recognizes that situations arise in which additional data are needed to inform patient care more effectively; these areas will be identified within each respective guideline when appropriate.

Prescribed courses of treatment in accordance with these recommendations are effective only if they are followed. Because lack of patient understanding and adherence may adversely affect outcomes, physicians and other healthcare providers should make every effort to engage the patient's active participation in prescribed medical regimens and lifestyles. In addition, patients should be informed of the risks, benefits, and alternatives to a particular treatment and should be involved in shared decision making whenever feasible, particularly for COR IIa and IIb, for which the benefit-to-risk ratio may be lower.

The Task Force makes every effort to avoid actual, potential, or perceived conflicts of interest that may arise as a result of industry relationships or personal interests among the members of the writing group. All writing group members and peer reviewers of the guideline are required to disclose all current healthcare-related relationships, including those existing 12 months before initiation of the writing effort. In December 2009, the ACCF and AHA implemented a new policy for relationships with industry and other entities (RWI) that requires the writing group chair plus a minimum of 50% of the writing group to have no relevant RWI (Appendix 1 includes the ACCF/AHA definition of relevance). These statements are reviewed by the Task Force and all members during each conference call and/or meeting of the writing group and are updated as changes occur. All guideline recommendations require a confidential vote by the writing group and must be approved by a consensus of the voting members. Members are not permitted to draft or vote on any text or recommendations pertaining to their RWI. Members who recused themselves from voting are indicated in the list of writing group members, and specific section recusals are noted in Appendix 1.

Authors' and peer reviewers' RWI pertinent to this guideline are disclosed in Appendixes 1 and 2, respectively. Additionally, to ensure complete transparency, writing group members' comprehensive disclosure information—including RWI not pertinent to this document—is available as an online supplement. Comprehensive disclosure information for the Task Force is also available online at www.cardiosource.org/ACC/About-ACC/Leadership/Guidelines-and-Documents-Task-Forces.aspx. The work of the writing group is supported exclusively by the ACCF, AHA, and the Heart Rhythm Society (HRS) without commercial support. Writing group members volunteered their time for this activity.

In an effort to maintain relevance at the point of care for practicing physicians, the Task Force continues to oversee an ongoing process improvement initiative. As a result, in response to pilot projects, several changes to these guidelines will be apparent, including limited narrative text, a focus on summary and evidence tables (with references linked to abstracts in PubMed), and more liberal use of summary recommendation tables (with references that support LOE) to serve as a quick reference.

In April 2011, the Institute of Medicine released 2 reports: *Finding What Works in Health Care: Standards for Systematic Reviews* and *Clinical Practice Guidelines We Can Trust* (2,3). It is noteworthy that the ACCF/AHA practice guidelines were cited as being compliant with many of the standards that were proposed. A thorough review of these reports and our current methodology is under way, with further enhancements anticipated.

The recommendations in this focused update are considered current until they are superseded in another focused update or the full-text guideline is revised. Guidelines are official policy of both the ACCF and AHA.

Jeffrey L. Anderson, MD, FACC, FAHA
Chair, ACCF/AHA Task Force on Practice Guidelines

1. Introduction

1.1. Methodology and evidence review

Late-breaking clinical trials presented at the annual scientific meetings of the ACC, AHA, HRS, and European Society of Cardiology (2008 through 2010), as well as other selected data reported through January 2012, were reviewed by the guideline writing group along with the Task Force and other experts to identify trials and other key data that might affect guideline recommendations. On the basis of the criteria and considerations noted previously (Preamble), recently published trial data and other clinical information were considered important enough to prompt a focused update of the "ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities" (4).

To provide clinicians with a comprehensive set of data, the absolute risk difference and number needed to treat or harm, if they were published and their inclusion was deemed appropriate, are provided in the guideline, along with confidence intervals (CIs) and data related to the rel-

ative treatment effects, such as odds ratio, relative risk (RR), hazard ratio (HR), or incidence rate ratio.

Consult the full-text version of the “ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities” for policy on clinical areas not covered by the focused update (4). The individual recommendations in this focused update will be incorporated into future revisions or updates of the full-text guideline.

1.2. Organization of the writing group

For this focused update, selected members of the 2008 Device-Based Therapy (DBT) Writing Committee were invited to participate on the basis of areas of expertise, requirements for committee rotation, and the current RWI policy; those who agreed are referred to as the 2012 Focused Update Writing Group. The HRS was invited to be a partner on this focused update and has provided representation. The writing group also included representatives from the American Association for Thoracic Surgery, Heart Failure Society of America, and Society of Thoracic Surgeons.

1.3. Document review and approval

This document was reviewed by 2 official reviewers each nominated by the ACCF, AHA, and HRS, as well as 1 reviewer each from the American Association for Thoracic Surgery, Heart Failure Society of America, and Society of Thoracic Surgeons, and 21 individual content reviewers. All information on reviewers' RWI was collected and distributed to the writing group and is published in this document (Appendix 2).

This document was approved for publication by the governing bodies of the ACCF, AHA, and HRS and was endorsed by the American Association for Thoracic Surgery, Heart Failure Society of America, and Society of Thoracic Surgeons.

1.4. Scope of the focused update

Studies relevant to the management of patients treated with DBT for cardiac rhythm abnormalities were identified and reviewed as described previously in Section 1.1, “Methodology and Evidence Review.” On the basis of these data, the writing group determined that updates to the 2008 guideline were necessary for cardiac resynchronization therapy (CRT) and device follow-up.

Many clinical circumstances come into question in daily practice as to the appropriate use of implantable cardioverter-defibrillator (ICD)/CRT devices. Many of these clinical scenarios are both common and of great importance but have not or cannot be addressed by multicenter clinical trials, so many of these will be addressed in the “Appropriate Use Criteria (AUC) for Implantable Cardioverter-Defibrillators and Cardiac Resynchronization Therapy” document that is currently in development. Unlike comprehensive guidelines, AUC documents blend evidence-based information and clinical experience that can help guide allocation of healthcare resources, and they focus on the most common patient scenarios for which procedures may be considered. The AUC document

will help define when it is reasonable to perform a procedure and, importantly, when it is not reasonable. Some of the scenarios included in the AUC may be outside guideline indications. As such, AUC are complementary to guidelines and should be used in conjunction with them for determining patient care. Furthermore, the ACCF and AHA are currently undertaking a revision of the guidelines for management of heart failure (HF). The DBT and HF guideline writing committees have worked to maintain concordance on the recommendations with regard to indications for CRT.

The writing group also thoroughly reviewed the following sections from the 2008 DBT guideline (4) and determined that although some new information may be available, the recommendations remain current.

1. **Hypertrophic Cardiomyopathy**—The management of hypertrophic cardiomyopathy is addressed in the “2011 ACCF/AHA Guideline for the Diagnosis and Treatment of Hypertrophic Cardiomyopathy” (5). In that document, the indications for ICDs have been modified on the basis of reassessment of significance of risk factors. The present writing group did not analyze the source documents that led to these changes and refer the reader to the ACCF/AHA Guideline for full discussion of ICDs in hypertrophic cardiomyopathy.
2. **Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy**—The writing group reviewed all published evidence since the publication of the 2008 DBT guideline related to arrhythmogenic right ventricular dysplasia/cardiomyopathy and determined that no changes to the current recommendations for ICD indications were warranted.
3. **Genetic Arrhythmia Syndromes**—The writing group acknowledges that recent guidelines and data suggest that there may be a limited role for primary-prevention ICDs in individuals with a genetically confirmed diagnosis of long QT but without symptoms (6–8). Nevertheless, it is the consensus of this writing group that until more definitive trials or studies are completed, further refinement of criteria for ICD implantation in this patient group would not be appropriate. Therefore, the class of recommendations for ICD implantation in asymptomatic patients with a genetically confirmed mutation will remain unchanged.
4. **Congenital Heart Disease**—As with other forms of structural heart disease, there has been increased use of ICDs for primary prevention of sudden cardiac death in patients with congenital heart disease (4,9). Although randomized clinical trials have not been performed, multiple observational studies have consistently reported that systemic ventricular dysfunction in patients with congenital heart disease is the risk factor most predictive of subsequent sudden cardiac death or appropriate ICD rescue (10–12). These studies support consideration of an expanded role of ICDs in future revisions of the guideline, provided that consistent benefit with the use of ICDs in patients with congenital heart disease and advanced ventricular dysfunction is demonstrated. Never-

theless, the current recommendations are not changed at this time. There remain insufficient data to make specific recommendations about CRT in patients with congenital heart disease (13).

5. **Primary Electrical Disease**—The writing group reviewed all published evidence since the publication of the 2008 DBT guideline related to primary electrical disease and determined that no changes were warranted in the current recommendations for ICD indications with regard to idiopathic ventricular fibrillation, short-QT syndrome, Brugada syndrome, and catecholaminergic polymorphic ventricular tachycardia.
6. **Terminal Care**—Patients with cardiovascular implantable electronic devices (CIEDs) are living longer, with more surviving to develop comorbid conditions such as dementia or malignancy that may ultimately define their clinical course. This was recognized in the terminal care section of the 2008 DBT guideline. Recommendations on management of CIEDs in patients nearing end of life or requesting withdrawal of therapy were expanded upon in 2 subsequent HRS expert consensus statements in an effort to provide guidance to caregivers dealing with this increasingly prevalent and difficult issue (14,15).

2. Indications for Pacing

2.4. Pacing for Hemodynamic Indications

Although most commonly used to treat or prevent abnormal rhythms, pacing can alter the activation sequence in the paced chambers, influencing regional contractility and hemodynamics. These changes are frequently insignificant clinically but can be beneficial or harmful in some conditions. Pacing to decrease symptoms for patients with obstructive hypertrophic cardiomyopathy is discussed separately in the full-text guideline, Section 2.4.2, “Obstructive Hypertrophic Cardiomyopathy.”

2.4.1. Cardiac Resynchronization Therapy

(See Table 2 and the Online Data Supplement for additional data on the trials that comprise the basis for the recommendations in this focused update.)

The present document proposes several changes in recommendations for CRT, compared with the 2008 document. The most significant changes are 1) limitation of the Class I indication to patients with QRS duration ≥ 150 ms; 2) limitation of the Class I indication to patients with left bundle-branch block (LBBB) pattern; 3) expansion of Class I indication to New York Heart Association (NYHA) class II (and with LBBB with QRS duration ≥ 150 ms); and 4) the addition of a Class IIb recommendation for patients who have left ventricular ejection fraction (LVEF) $\leq 30\%$, ischemic etiology of HF, sinus rhythm, LBBB with a QRS duration ≥ 150 ms, and NYHA class I symptoms. These changes may have important implications for patient selection in clinical practice, and the justification for these changes is discussed in the following paragraphs.

Progression of left ventricular (LV) systolic dysfunction to clinical HF is frequently accompanied by impaired electromechanical coupling, which may further diminish effective ventricular contractility. The most common disruptions are prolonged atrioventricular conduction (first-degree atrioventricular block) and prolonged interventricular conduction, most commonly LBBB. Prolonged interventricular and intraventricular conduction causes regional mechanical delay within the left ventricle that can result in reduced ventricular systolic function, altered myocardial metabolism, functional mitral regurgitation, and adverse remodeling with ventricular dilatation (31). Prolongation of the QRS duration occurs in approximately one third of patients with advanced HF (32,33) and has been associated with ventricular electromechanical delay (“dyssynchrony”), as identified by multiple sophisticated echocardiographic indices. QRS duration and dyssynchrony both have been identified as predictors of worsening HF, sudden cardiac death, and total death (34).

Modification of ventricular electromechanical delay with multisite ventricular pacing (commonly called “biventricular pacing” or CRT) can improve ventricular systolic function, reduce metabolic costs, ameliorate functional mitral regurgitation, and, in some patients, induce favorable remodeling with reduction of cardiac chamber dimensions (35–37). Functional improvement has been demonstrated for exercise capacity, with peak oxygen consumption in the range of 1 to 2 mL/kg/min and a 50- to 70-meter increase in 6-minute walking distance, as well as a 10-point or greater reduction of HF symptoms on the 105-point Minnesota Living with Heart Failure scale (16,38,39).

Meta-analyses of initial clinical experiences and larger subsequent trials of CRT confirmed an approximately 30% decrease in hospitalizations and a mortality rate benefit of 24% to 36% (40). In the COMPANION (Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure) trial (NYHA class III/IV HF, QRS duration >120 ms, and LVEF $\leq 35\%$ on GDMT), GDMT was compared to CRT pacing therapy without backup defibrillation (CRT-Pacemaker) and to CRT therapy with defibrillation backup (CRT-D) (17). Both CRT-Pacemaker and CRT-D reduced the risk of the primary composite endpoint by approximately 20% as compared with GDMT alone. CRT-D reduced the mortality rate by 36% compared with medical therapy, but there was insufficient evidence to conclude that CRT-Pacemaker was inferior to CRT-D. The CARE-HF (Cardiac Resynchronization in Heart Failure) trial (18) limited subjects to a QRS duration >150 ms (89% of patients) or QRS duration 120 to 150 ms with echocardiographic evidence of dyssynchrony (11% of patients). It was the first study to show a significant (36%) reduction in death rate for resynchronization therapy unaccompanied by backup defibrillation compared with GDMT (18).

In the present document, we give a Class I recommendation for CRT in patients with QRS duration ≥ 150 ms.

Table 2 Recommendations for CRT in Patients With Systolic Heart Failure

2012 DBT Focused Update Recommendations	Comments
Class I	
1. CRT is indicated for patients who have LVEF less than or equal to 35%, sinus rhythm, LBBB with a QRS duration greater than or equal to 150 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT. (<i>Level of Evidence: A for NYHA class III/IV (16–19); Level of Evidence: B for NYHA class II (20,21)</i>)	Modified recommendation (specifying CRT in patients with LBBB of ≥ 150 ms; expanded to include those with NYHA class II symptoms).
Class IIa	
1. CRT can be useful for patients who have LVEF less than or equal to 35%, sinus rhythm, LBBB with a QRS duration 120 to 149 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT (16–18,20–22). (<i>Level of Evidence: B</i>)	New recommendation
2. CRT can be useful for patients who have LVEF less than or equal to 35%, sinus rhythm, a non-LBBB pattern with a QRS duration greater than or equal to 150 ms, and NYHA class III/ambulatory class IV symptoms on GDMT (16–18,21). (<i>Level of Evidence: A</i>)	New recommendation
3. CRT can be useful in patients with atrial fibrillation and LVEF less than or equal to 35% on GDMT if a) 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 (23–26,26a,48). (<i>Level of Evidence: B</i>)	Modified recommendation (wording changed to indicate benefit based on ejection fraction rather than NYHA class; level of evidence changed from C to B).
4. CRT can be useful for patients on GDMT who have LVEF less than or equal to 35% and are undergoing new or replacement device placement with anticipated requirement for significant ($>40\%$) ventricular pacing (25,27–29). (<i>Level of Evidence: C</i>)	Modified recommendation (wording changed to indicate benefit based on ejection fraction and need for pacing rather than NYHA class); class changed from IIb to IIa).
Class IIb	
1. CRT may be considered for patients who have LVEF less than or equal to 30%, ischemic etiology of heart failure, sinus rhythm, LBBB with a QRS duration of greater than or equal to 150 ms, and NYHA class I symptoms on GDMT (20,21). (<i>Level of Evidence: C</i>)	New recommendation
2. CRT may be considered for patients who have LVEF less than or equal to 35%, sinus rhythm, a non-LBBB pattern with QRS duration 120 to 149 ms, and NYHA class III/ambulatory class IV on GDMT (21,30). (<i>Level of Evidence: B</i>)	New recommendation
3. CRT may be considered for patients who have LVEF less than or equal to 35%, sinus rhythm, a non-LBBB pattern with a QRS duration greater than or equal to 150 ms, and NYHA class II symptoms on GDMT (20,21). (<i>Level of Evidence: B</i>)	New recommendation
Class III: No Benefit	
1. CRT is not recommended for patients with NYHA class I or II symptoms and non-LBBB pattern with QRS duration less than 150 ms (20,21,30). (<i>Level of Evidence: B</i>)	New recommendation
2. CRT is not indicated for patients whose comorbidities and/or frailty limit survival with good functional capacity to less than 1 year (19). (<i>Level of Evidence: C</i>)	Modified recommendation (wording changed to include cardiac as well as noncardiac comorbidities).

See Appendix 3, "Indications for CRT Therapy—Algorithm."

CRT indicates cardiac resynchronization therapy; DBT, device-based therapy; GDMT, guideline-directed medical therapy; LBBB, left bundle-branch block; LVEF, left ventricular ejection fraction; and NYHA, New York Heart Association.

The differential classification seen in this document related to QRS duration is based on the results of multiple analyses of CRT benefit. The prevalence of mechanical dyssynchrony has been documented in $>40\%$ of patients with dilated cardiomyopathy and QRS duration >120 ms, and is as high as 70% among patients with QRS duration >150 ms and intraventricular mechanical delay, as identified by several echocardiographic techniques (34,41). However, the aggregate clinical experience has consistently demonstrated that a significant clinical benefit from CRT is greatest among patients with QRS duration >150 ms (42,43). In a meta-analysis of 5 trials involving 6,501 patients, CRT significantly decreased the primary endpoint of death or hospitalization for HF in patients with QRS duration ≥ 150 ms (HR: 0.58; 95% CI: 0.50 to 0.68; $p < 0.00001$) but not in patients with QRS dura-

tion <150 ms (HR: 0.95; 95% CI: 0.83 to 1.10; $p = 0.51$) (42). In addition, subgroup analyses from several studies have suggested that a QRS duration <150 ms is a risk factor for failure to respond to CRT therapy (43,44). The observed differential benefit of CRT was seen across patients in NYHA classes I through IV. It has not been possible to reliably identify those with shorter QRS durations who may benefit. Patients with shorter QRS durations who otherwise qualify for CRT are afforded Class II recommendations in these guidelines.

An additional difference in the present document compared with the 2008 DBT guideline (4) is the limitation of the recommendation for Class I indication to patients with LBBB pattern as compared to those with non-LBBB. For patients with QRS duration ≥ 120 ms who do not have a complete LBBB (non-LBBB patterns), evidence for benefit

with CRT is less compelling than in the presence of LBBB (45–47). The impact of the specific QRS morphology on clinical event reduction with CRT was evaluated in a meta-analysis of 4 clinical trials including 5,356 patients (43). In those with LBBB, CRT significantly reduced composite adverse clinical events (RR: 0.64; 95% CI: 0.52 to 0.77; $p=0.00001$). No benefit was observed for patients with non-LBBB conduction abnormalities (RR: 0.97; 95% CI: 0.82 to 1.15; $p=0.75$). Specifically, there was no benefit in patients with right bundle-branch block (RR: 0.91; 95% CI: 0.69 to 1.20; $p=0.49$) or nonspecific intraventricular conduction delay (RR: 1.19; 95% CI: 0.87 to 1.63; $p=0.28$). Overall, the difference in effect of CRT between LBBB versus non-LBBB patients was highly statistically significant ($p=0.0001$) (43). Nevertheless, other studies have shown that CRT is more likely to be effective in patients with advanced HF and non-LBBB morphologies if they have a markedly prolonged QRS duration (21,30) (see RAFT [Resynchronization-Defibrillation for Ambulatory Heart Failure Trial] (21) discussion below). Furthermore, patients with QRS prolongation due to frequent right ventricular apical pacing may benefit from CRT when other criteria for CRT are met (23,25,48). No large trial has yet demonstrated clinical benefit among patients without QRS prolongation, even when they have been selected with echocardiographic measures of dyssynchrony (49).

The observed heterogeneity of response even among those who would appear to be excellent candidates for CRT also may result from factors such as suboptimal lead location and the location of conduction block from fibrosis in relation to the pacing site. Several recent studies have emphasized the importance of LV lead placement. For example, wider LV–right ventricular lead separation has been shown to provide better results (50). A subanalysis of MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy) (20) showed that an apical LV lead position, as compared with a basal or midventricular position, resulted in a significant increased risk for HF or death (51).

Clinical trials of resynchronization included mainly patients in sinus rhythm. However, prospective experience among patients with permanent atrial fibrillation and with decreased LV systolic function suggests that benefit may result from biventricular pacing when the QRS duration is >120 ms, although it may be most evident in patients in whom atrioventricular nodal ablation has been performed, such that right ventricular pacing is obligate (24,26,52). The benefit of CRT in patients with atrial fibrillation is more pronounced in those with depressed ejection fraction (25). Similarly, patients receiving prophylactic ICDs often evolve progressively to dominant ventricular pacing, which may reflect both intrinsic chronotropic incompetence and aggressive up-titration of beta-adrenergic–blocking agents.

When device implantation or reimplantation is being considered for patients who require ventricular pacing, it is prudent to recall the results of the DAVID (Dual Chamber and VVI Implantable Defibrillator) trial (53). In this trial,

dual-chamber rate-responsive pacing increased HF admissions and mortality rate as compared to sinus rhythm. A cutoff of approximately 40% right ventricular pacing was seen as deleterious (54). Similarly, in a substudy from MADIT-II (Multicenter Automatic Defibrillator Implantation Trial II), patients who were right ventricular paced $>50\%$ of the time had a higher rate of new or worsened HF than those right ventricular paced $\leq 50\%$ of the time (55).

The major experience with resynchronization derives from patients with NYHA class III symptoms of HF and LVEF $\leq 35\%$. Patients with NYHA class IV symptoms of HF have accounted for only 10% of all patients in clinical trials of resynchronization therapy. These patients were highly selected ambulatory outpatients who were taking oral medications and had no history of recent hospitalization (56). Although a benefit has occasionally been described in patients with more severe acute decompensation that required brief positive intravenous inotropic therapy to aid diuresis, CRT is not generally used as a “rescue therapy” for such patients. Patients with dependence on intravenous inotropic therapy, refractory fluid retention, or advanced chronic kidney disease represent the highest-risk population for complications of any procedure and for early death after hospital discharge, and they are also unlikely to receive a meaningful mortality risk benefit from concomitant defibrillator therapy (19,57).

Patients with NYHA class IV HF symptoms who derive functional benefit from resynchronization therapy may return to a better functional status, in which prevention of sudden death becomes a relevant goal. Even among the selected NYHA class IV patients identified within the COMPANION trial (17), there was no difference in 2-year survival rate between the CRT patients with and without backup defibrillation, although more of the deaths in the CRT-Pacemaker group were classified as sudden deaths (56).

Perhaps the most significant changes in the present document compared to the 2008 DBT Guideline (4) are the expansion of the Class I recommendation for CRT to include patients with LBBB, QRS duration ≥ 150 ms, and NYHA class II and the addition of a Class IIb recommendation for patients who have LVEF $\leq 30\%$, ischemic etiology of HF, sinus rhythm, LBBB with a QRS duration of ≥ 150 ms, and NYHA class I symptoms. These recommendations are based on 4 studies in which CRT was evaluated in patients with minimal or mild symptoms of HF in the setting of low LVEF. These include MADIT-CRT, RAFT, REVERSE (Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction), and MIRACLE ICD II (Multicenter InSync ICD Randomized Clinical Evaluation II), all of which are discussed in the following paragraphs (20–22,58).

MADIT-CRT (20) randomized patients with NYHA class I or II ischemic and NYHA class II nonischemic cardiomyopathy, LVEF $\leq 30\%$, and QRS duration ≥ 130 ms on GDMT to CRT-D or ICD alone. Of note, only 15% of the total cohort of patients were NYHA class I. The primary

endpoint, a composite of death or HF event, was reduced by 34% by CRT-D (HR: 0.66), with comparable benefit for both ischemic and nonischemic etiology of HF. HF events were reduced by 41%, without significant reduction in mortality rate. CRT-D therapy was demonstrated to be of more benefit in women than in men (HR: 0.37 and 0.76, respectively) and in patients with QRS duration ≥ 150 ms than in patients with QRS duration < 150 ms (HR: 0.48 and 1.06, respectively) (20). Patients with LBBB had a significant reduction in ventricular tachycardia, ventricular fibrillation, and death compared to non-LBBB patients, who derived no benefit (HR: 0.47 and 1.24, respectively) (10).

RAFT (21) reported the use of CRT-D in patients with NYHA class II or class III ischemic or nonischemic cardiomyopathy, LVEF $\leq 30\%$, and QRS duration ≥ 120 ms, as compared to those treated with an ICD alone. The primary outcome of death or hospitalization for HF occurred in 33% of patients receiving CRT-D and in 40% of patients receiving ICD only. RAFT not only showed a significant reduction in hospitalization for HF (HR: 0.68; 95% CI: 0.56 to 0.83; $p < 0.001$) but also was the first study to show a statistically significant reduction in death (HR: 0.75; 95% CI: 0.62 to 0.91; $p = 0.003$) in mildly symptomatic patients with NYHA class II symptoms. However, CRT-D was associated with a higher risk of adverse device- or implantation-related complications at 30 days after implantation ($p < 0.001$) compared with an ICD and no CRT. Patients with LBBB had a better outcome than did non-LBBB patients, but the statistical interaction between benefit and QRS morphology was weak in this trial ($p = 0.046$). CRT-D therapy was effective in patients with QRS duration ≥ 150 ms but of no benefit in patients with QRS duration < 150 ms (HR for QRS duration ≥ 150 ms: 0.59; 95% CI: 0.48 to 0.73; HR for QRS duration < 150 ms: 0.99; 95% CI: 0.77 to 1.27; $p = 0.002$ for interaction). Thus, both MADIT-CRT and RAFT showed benefit in NYHA class II patients treated with CRT-D and demonstrated that the benefit was primarily achieved in patients with QRS duration ≥ 150 ms and LBBB (20,21).

The REVERSE trial consisted of 610 patients. This study assessed CRT-D therapy in patients with NYHA class I or II HF symptoms on maximum medical therapy, LVEF $\leq 40\%$, and QRS duration ≥ 120 ms followed for 12 months and showed that 16% of patients receiving CRT and 21% without CRT worsened ($p = 0.10$). The time to first HF hospitalization was delayed in patients receiving CRT therapy (HR: 0.47). The primary echocardiographic endpoint of ventricular remodeling assessed by LV end-systolic volume index was significantly improved (reduction in end-systolic volume index) in patients treated with CRT therapy ($p < 0.0001$). REVERSE did not report a mortality rate benefit of CRT-D therapy (22). The lack of reported mortality rate benefit may be related to the higher ejection fraction enrollment criterion (LVEF $\leq 40\%$) and the relatively short-term follow-up (12 months) (22).

MIRACLE ICD II included patients with NYHA class II HF on GDMT with LVEF $\leq 35\%$ and QRS duration ≥ 130 ms who were undergoing implantation of an otherwise indicated ICD (58). In these patients, CRT did not alter exercise capacity but did result in significant improvement in cardiac structure and function and composite clinical response over 6 months.

Analysis of the multiple clinical trials of CRT is complicated because trials encompass a range of LVEFs in their entry criteria, as well as a range of measured outcomes. For mortality rate, the trials showing benefit in NYHA class III and IV patients typically included those with LVEF $\leq 35\%$ (22,58). For patients with NYHA class II, trials showing mortality rate benefit included those with LVEF $\leq 30\%$ (20,21). A mortality rate benefit with CRT has not been shown for patients who are NYHA class I (21). In terms of demonstrating improvement in cardiac function (e.g., significant reduction in LV size and improvement in ejection fraction), trials have included patients with LVEF $\leq 35\%$ who are NYHA class III and IV (58). Similarly, for patients with LVEF $\leq 40\%$, trials demonstrating improvement in function have included those who are NYHA class I and II (22). The congruence of results from the totality of CRT trials with regard to remodeling and HF events provides evidence supporting a common threshold of 35% for benefit from CRT in patients with NYHA class II through IV HF symptoms. Although there is evidence for benefit in both CRT-D and CRT-Pacemaker patients with NYHA class III and IV symptoms, for NYHA class I and II HF, all of the trials tested only CRT-D and not CRT-Pacemaker, and as such, recommendations for these classes of patients can be made only for CRT-D (20–22,58).

Taken together, the evidence from the randomized trials of CRT-D in patients with reduced LVEF and NYHA class I or II shows that CRT can provide functional improvement and decrease the risk of HF events and composite outcomes (20,22,58,59). Still, CRT-D also has been shown to decrease the mortality rate for patients with NYHA class II but not for those who have NYHA class I HF (20,21). As a result, the data support a Class I recommendation for CRT implantation in patients with LBBB and QRS duration ≥ 150 ms and NYHA class II. Because of the lack of mortality rate benefit and smaller sample size, we believe CRT may be considered for patients who have LVEF $< 30\%$, ischemic etiology of HF, sinus rhythm, LBBB with a QRS duration ≥ 150 ms, and NYHA class I symptoms on GDMT (*Class IIb; LOE: B*).

For all patients, optimal outcomes with CRT require effective placement of ventricular leads, ongoing HF management with neurohormonal antagonists and diuretic therapy, and in some cases, later optimization of device programming, especially atrioventricular (A-V) and interventricular (V-V) intervals (51,60).

Consistent with entry criteria for studies upon which these recommendations are based, CRT implantation should be performed only when the LVEF meets guideline criteria for patients with nonischemic cardiomyopathy who have received

>3 months of GDMT, or for patients with ischemic cardiomyopathy >40 days after myocardial infarction receiving GDMT when there was no intervening revascularization, or >3 months if revascularization was performed. It is assumed that the final decision to recommend CRT will be based on an assessment of LVEF made after any appropriate waiting period has concluded, during which GDMT has been applied. Finally, the pivotal trials demonstrating the efficacy of CRT took place in centers that provided expertise in device and HF therapy both at implantation and during long-term follow-up.

Two other organizational guidelines by the Heart Failure Society of America (61) and the European Society of Cardiology (62) have recently been published that address indications for CRT. For the patient categories in common between the Heart Failure Society of America document and the present focused update, there was a good deal of concordance. Although there are many areas of agreement, some differences exist between the present guideline and the European Society of Cardiology document. One difference is that in the present guideline, CRT is recommended in NYHA class I patients who have LVEF ≤30%, have ischemic heart disease, are in sinus rhythm, and have a LBBB with a QRS duration ≥150 ms (Class IIb; LOE: C) (20,21). There is no similar recommendation in the European Society of Cardiology document. The European Society of Cardiology recommendations include patients with QRS duration <120 ms. We have not recommended CRT for any functional class or ejection fraction with QRS durations <120 ms. We also have elected to consider the presence of LBBB versus non-LBBB in the class of recommendations, on the basis of perceived differential benefit by functional class, QRS morphology, and QRS duration.

2.8. Pacemaker Follow-Up

2.8.3. Remote Follow-Up and Monitoring

Since the publication of the 2008 DBT guideline, important changes have occurred related to follow-up and remote monitoring of CIEDs (4,15,63). CIEDs include pacemakers, ICDs, CRTs, implantable loop recorders, and implantable cardiovascular monitors. The current technology for follow-up, evidence supporting its use, and clinical practice of CIED monitoring have evolved. Routine in-person office follow-up supplemented by transtelephonic monitoring with limited remote follow-up for pacemakers was the standard approach before 2008 (4,15). Transtelephonic monitoring, with monitors that transmit the patient’s heart rhythm by converting electrocardiographic information to sound and transmitting it via telephone lines to a decoding machine that then converts the sound back into a rhythm strip, is now a dated technique (4,15,63) because it allows for limited monitoring of heart rate, rhythm, and battery status of only pacemakers (63).

Contemporary remote monitoring uses bidirectional telemetry with encoded and encrypted radiofrequency signals, allowing transmission and receipt of information from CIEDs (pacemakers, ICDs, CRTs, implantable loop recorders, and implantable hemodynamic monitors) (63). All major CIED manufacturers have developed proprietary sys-

tems to allow patients to have their devices interrogated remotely, and many use wireless cellular technology to extend the bidirectional telemetry links into the patient’s location (15,63). The information is analyzed, formatted, and transmitted to a central server, where it can be accessed by clinicians through the Internet. Information provided through remote follow-up includes virtually all of the stored information that would be obtained in an in-office visit, including battery voltage, charge time in ICDs, percent pacing, sensing thresholds, automatically measured pacing thresholds when available, pacing and shock impedance, and stored arrhythmia events with electrograms (15,63). CIEDs with wireless telemetry capability may be programmed at a face-to-face evaluation to subsequently send automatic alerts for a variety of issues that the clinician deems significant, such as abnormal battery voltage, abnormal lead parameters, or increased duration or frequency of arrhythmia episodes (15). Remote transmissions can be made at predetermined intervals or at unscheduled times for prespecified alerts related to device function or activated by the patient for clinical reasons (63). A detailed description of techniques, indications, personnel, and frequency has been published as a consensus document (15).

Several prospective randomized trials have been conducted evaluating the effect of remote monitoring on clinical outcomes (64–67) since the publication of the 2008 DBT Guideline (4). Collectively, these trials have demonstrated that remote monitoring is a safe alternative to office visits to evaluate CIEDs. Compared with in-person office visits to evaluate CIEDs, remote monitoring leads to early

Table 3 Minimum Frequency of CIED In-Person or Remote Monitoring*

Type and Frequency	Method
Pacemaker/ICD/CRT	
Within 72 h of CIED implantation	In person
2–12 wk postimplantation	In person
Every 3–12 mo for pacemaker/ CRT-Pacemaker	In person or remote
Every 3–6 mo for ICD/CRT-D	In person or remote
Annually until battery depletion	In person
Every 1–3 mo at signs of battery depletion	In person or remote
Implantable loop recorder	
Every 1–6 mo depending on patient symptoms and indication	In person or remote
Implantable hemodynamic monitor	
Every 1–6 mo depending on indication	In person or remote
More frequent assessment as clinically indicated	In person or remote

CIED indicates cardiovascular implantable electronic device; CRT, cardiac resynchronization therapy; CRT-D, cardiac resynchronization therapy defibrillator; CRT-Pacemaker, cardiac resynchronization therapy pacemaker; and ICD, implantable cardioverter-defibrillator.

Modified from Wilkoff et al (15).

*More frequent in-person or remote monitoring may be required for all the above devices as clinically indicated.

discovery of clinically actionable events, decreased time to clinical decision in response to these events, and fewer office visits (64–67). Long-term survival rates of patients monitored remotely with ICDs in a practice setting compare favorably with survival rates of patients in clinical trials (68).

Current suggestions for the minimum frequency of in-office and remote monitoring of patients with CIEDs are summarized in Table 3 (15). Issues such as lead malfunction, unreliable battery life indicators, and other device or lead recalls influence clinical decisions, which may change the appropriate minimum follow-up.

Presidents and Staff

American College of Cardiology Foundation

William A. Zoghbi, MD, FACC, President

Thomas E. Arend, Jr, Esq, CAE, Interim Chief Staff Officer

Charlene May, Senior Director, Science and Clinical Policy

American College of Cardiology Foundation/American Heart Association

Lisa Bradfield, CAE, Director, Science and Clinical Policy
Debjani Mukherjee, MPH, Associate Director, Evidence-Based Medicine

Ezaldeen Ramadhan III, Specialist, Science and Clinical Policy

American Heart Association

Gordon F. Tomaselli, MD, FAHA, President

Nancy Brown, Chief Executive Officer

Rose Marie Robertson, MD, FAHA, Chief Science Officer

Gayle R. Whitman, PhD, RN, FAHA, FAAN, Senior Vice President, Office of Science Operations

Judy L. Bezanson, DSN, RN, CNS-MS, FAHA, Science and Medicine Advisor, Office of Science Operations

Jody Hundley, Production Manager, Scientific Publications, Office of Science Operations

References

- ACCF/AHA Task Force on Practice Guidelines. Methodology Manual and Policies From the ACCF/AHA Task Force on Practice Guidelines. American College of Cardiology Foundation and American Heart Association, Inc. 2010. Available at: http://assets.cardiosource.com/Methodology_Manual_for_ACC_AHA_Writing_Committees.pdf and http://my.americanheart.org/ids/groups/ahamah-public/@wcm/@sop/documents/downloadable/ucm_319826.pdf. Accessed May 16, 2012.
- Committee on Standards for Systematic Reviews of Comparative Effectiveness Research, Institute of Medicine. Finding What Works in Health Care: Standards for Systematic Reviews. Washington, DC: The National Academies Press; 2011.
- Committee on Standards for Developing Trustworthy Clinical Practice Guidelines, Institute of Medicine. Clinical Practice Guidelines We Can Trust. Washington, DC: The National Academies Press; 2011.
- Epstein AE, DiMarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices). *J Am Coll Cardiol*. 2008;51:e1–62.
- Gersh BJ, Maron BJ, Bonow RO, et al. 2011 ACCF/AHA guideline for the diagnosis and treatment of hypertrophic cardiomyopathy: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2011;58:e212–60.
- Ackerman MJ, Priori SG, Willems S, et al. HRS/EHRA expert consensus statement on the state of genetic testing for the channelopathies and cardiomyopathies. *Heart Rhythm*. 2011;8:1308–39.
- Horner JM, Kinoshita M, Webster TL, et al. Implantable cardioverter defibrillator therapy for congenital long QT syndrome: a single-center experience. *Heart Rhythm*. 2010;7:1616–22.
- Schwartz PJ, Spazzolini C, Priori SG, et al. Who are the long-QT syndrome patients who receive an implantable cardioverter-defibrillator and what happens to them? Data from the European Long-QT Syndrome Implantable Cardioverter-Defibrillator (LQTS ICD) Registry. *Circulation*. 2010;122:1272–82.
- Berul CI, Van Hare GF, Kertesz NJ, et al. Results of a multicenter retrospective implantable cardioverter-defibrillator registry of pediatric and congenital heart disease patients. *J Am Coll Cardiol*. 2008;51:1685–91.
- Barsheshet A, Wang PJ, Moss AJ, et al. Reverse remodeling and the risk of ventricular tachyarrhythmias in the MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial—Cardiac Resynchronization Therapy). *J Am Coll Cardiol*. 2011;57:2416–23.
- Silka MJ, Bar-Cohen Y. Should patients with congenital heart disease and a systemic ventricular ejection fraction less than 30% undergo prophylactic implantation of an ICD? Patients with congenital heart disease and a systemic ventricular ejection fraction less than 30% should undergo prophylactic implantation of an implantable cardioverter defibrillator. *Circ Arrhythm Electrophysiol*. 2008;1:298–306.
- Khairy P, Harris L, Landzberg MJ, et al. Implantable cardioverter-defibrillators in tetralogy of Fallot. *Circulation*. 2008;117:363–70.
- van der Hulst AE, Delgado V, Blom NA, et al. Cardiac resynchronization therapy in paediatric and congenital heart disease patients. *Eur Heart J*. 2011;32:2236–46.
- Lampert R, Hayes DL, Annas GJ, et al. HRS expert consensus statement on the management of cardiovascular implantable electronic devices (CIEDs) in patients nearing end of life or requesting withdrawal of therapy. *Heart Rhythm*. 2010;7:1008–26.
- Wilkoff BL, Auricchio A, Brugada J, et al. HRS/EHRA expert consensus on the monitoring of cardiovascular implantable electronic devices (CIEDs): description of techniques, indications, personnel, frequency and ethical considerations. *Heart Rhythm*. 2008;5:907–25.
- Abraham WT, Fisher WG, Smith AL, et al. Cardiac resynchronization in chronic heart failure. *N Engl J Med*. 2002;346:1845–53.
- Bristow MR, Saxon LA, Boehmer J, et al. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. *N Engl J Med*. 2004;350:2140–50.
- Cleland JGF, Daubert J-C, Erdmann E, et al. The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med*. 2005;352:1539–49.
- Hunt SA, Abraham WT, Chin MH, et al. 2009 Focused update incorporated into the ACC/AHA 2005 guidelines for the diagnosis and management of heart failure in adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2009;119:e391–479.
- Moss AJ, Hall WJ, Cannom DS, et al. Cardiac-resynchronization therapy for the prevention of heart-failure events. *N Engl J Med*. 2009;361:1329–38.
- Tang ASL, Wells GA, Talajic M, et al. Cardiac-resynchronization therapy for mild-to-moderate heart failure. *N Engl J Med*. 2010;363:2385–95.
- Linde C, Abraham WT, Gold MR, et al. 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;52:1834–43.
- Brignole M, Gammage M, Puggioni E, et al. Comparative assessment of right, left, and biventricular pacing in patients with permanent atrial fibrillation. *Eur Heart J*. 2005;26:712–22.
- Brignole M, Botto G, Mont L, et al. Cardiac resynchronization therapy in patients undergoing atrioventricular junction ablation for permanent atrial fibrillation: a randomized trial. *Eur Heart J*. 2011;32:2420–9.
- Doshi RN, Daoud EG, Fellows C, et al. Left ventricular-based cardiac stimulation post AV nodal ablation evaluation (the PAVE study). *J Cardiovasc Electrophysiol*. 2005;16:1160–5.
- Gasparini M, Auricchio A, Regoli F, 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;48:734–43.
- Wilton SB, Leung AA, Ghali WA, et al. Outcomes of cardiac resynchronization therapy in patients with versus those without atrial fibrillation: a systematic review and meta-analysis. *Heart Rhythm*. 2011;8:1088–94.

27. Wilkoff BL, Cook JR, Epstein AE, et al. Dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator: the Dual Chamber and VVI Implantable Defibrillator (DAVID) Trial. *JAMA*. 2002;288:3115–23.
28. 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;22:905–11.
29. Vatankulu MA, Goktekin O, Kaya MG, et al. Effect of long-term resynchronization therapy on left ventricular remodeling in pacemaker patients upgraded to biventricular devices. *Am J Cardiol*. 2009;103:1280–4.
30. Rickard J, Bassiouny M, Cronin EM, 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.
31. Masci PG, Marinelli M, Piacenti M, et al. Myocardial structural, perfusion, and metabolic correlates of left bundle branch block mechanical derangement in patients with dilated cardiomyopathy: a tagged cardiac magnetic resonance and positron emission tomography study. *Circ Cardiovasc Imaging*. 2010;3:482–90.
32. Kashani A, Barold SS. Significance of QRS complex duration in patients with heart failure. *J Am Coll Cardiol*. 2005;46:2183–92.
33. Doval HC, Nul DR, Grancelli HO, et al. Randomised trial of low-dose amiodarone in severe congestive heart failure: Grupo de Estudio de la Sobrevida en la Insuficiencia Cardiaca en Argentina (GESICA). *Lancet*. 1994;344:493–8.
34. Bleeker GB, Schaliq MJ, Molhoek SG, et al. Relationship between QRS duration and left ventricular dyssynchrony in patients with end-stage heart failure. *J Cardiovasc Electrophysiol*. 2004;15:544–9.
35. Blanc JJ, Etienne Y, Gilard M, et al. Evaluation of different ventricular pacing sites in patients with severe heart failure: results of an acute hemodynamic study. *Circulation*. 1997;96:3273–7.
36. Prinzen FW, Vernooij K, De Boeck BWL, et al. Mechano-energetics of the asynchronous and resynchronized heart. *Heart Fail Rev*. 2011;16:215–24.
37. Ukkonen H, Sundell J, Knuuti J. Effects of CRT on myocardial innervation, perfusion and metabolism. *Europace*. 2008;10 Suppl 3:iii114–7.
38. Cazeau S, Leclercq C, Lavergne T, et al. Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay. *N Engl J Med*. 2001;344:873–80.
39. Stellbrink C, Breithardt OA, Franke A, et al. Impact of cardiac resynchronization therapy using hemodynamically optimized pacing on left ventricular remodeling in patients with congestive heart failure and ventricular conduction disturbances. *J Am Coll Cardiol*. 2001;38:1957–65.
40. Bradley DJ, Bradley EA, Baughman KL, et al. Cardiac resynchronization and death from progressive heart failure: a meta-analysis of randomized controlled trials. *JAMA*. 2003;289:730–40.
41. Haghjoo M, Bagherzadeh A, Fazelifar AF, et al. Prevalence of mechanical dyssynchrony in heart failure patients with different QRS durations. *Pacing Clin Electrophysiol*. 2007;30:616–22.
42. 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.
43. Sipahi I, Carrigan TP, Rowland DY, et al. Impact of QRS duration on clinical event reduction with cardiac resynchronization therapy: meta-analysis of randomized controlled trials. *Arch Intern Med*. 2011;171:1454–62.
44. Saxon LA, Ellenbogen KA. Resynchronization therapy for the treatment of heart failure. *Circulation*. 2003;108:1044–8.
45. Bilchick KC, Kamath S, DiMarco JP, Stukenborg GJ. Bundle-branch block morphology and other predictors of outcome after cardiac resynchronization therapy in Medicare patients. *Circulation*. 2010;122:2022–30.
46. Adelstein EC, Saba S. Usefulness of baseline electrocardiographic QRS complex pattern to predict response to cardiac resynchronization. *Am J Cardiol*. 2009;103:238–42.
47. Rickard J, Kumbhani DJ, Gorodeski EZ, et al. Cardiac resynchronization therapy in non-left bundle branch block morphologies. *Pacing Clin Electrophysiol*. 2010;33:590–5.
48. Upadhyay GA, Choudhry NK, Auricchio A, et al. Cardiac resynchronization in patients with atrial fibrillation: a meta-analysis of prospective cohort studies. *J Am Coll Cardiol*. 2008;52:1239–46.
49. Beshai JF, Grimm RA, Nagueh SF, et al. Cardiac-resynchronization therapy in heart failure with narrow QRS complexes. *N Engl J Med*. 2007;357:2461–71.
50. Ariga R, Tayebjee MH, Benfield A, et al. Greater three-dimensional ventricular lead tip separation is associated with improved outcome after cardiac resynchronization therapy. *Pacing Clin Electrophysiol*. 2010;33:1490–6.
51. Singh JP, Klein HU, Huang DT, et al. Left ventricular lead position and clinical outcome in the multicenter automatic defibrillator implantation trial-cardiac resynchronization therapy (MADIT-CRT) trial. *Circulation*. 2011;123:1159–66.
52. Linde C, Leclercq C, Rex S, et al. Long-term benefits of biventricular pacing in congestive heart failure: results from the Multisite Synchronization in cardiomyopathy (MUSTIC) study. *J Am Coll Cardiol*. 2002;40:111–8.
53. Sweeney MO, Prinzen FW. A new paradigm for physiologic ventricular pacing. *J Am Coll Cardiol*. 2006;47:282–8.
54. Sharma AD, Rizo-Patron C, Hallstrom AP, et al. Percent right ventricular pacing predicts outcomes in the DAVID trial. *Heart Rhythm*. 2005;2:830–4.
55. Steinberg JS, Fischer A, Wang P, et al. The clinical implications of cumulative right ventricular pacing in the Multicenter Automatic Defibrillator Trial II. *J Cardiovasc Electrophysiol*. 2005;16:359–65.
56. Lindenfeld J, Feldman AM, Saxon L, 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;115:204–12.
57. Amin MS, Fox AD, Kalahasty G, et al. Benefit of primary prevention implantable cardioverter-defibrillators in the setting of chronic kidney disease: a decision model analysis. *J Cardiovasc Electrophysiol*. 2008;19:1275–80.
58. Abraham WT, Young JB, León AR, et al. 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;110:2864–8.
59. Daubert C, Gold MR, Abraham WT, et al. Prevention of disease progression by cardiac resynchronization therapy in patients with asymptomatic or mildly symptomatic left ventricular dysfunction: insights from the European cohort of the REVERSE (Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction) trial. *J Am Coll Cardiol*. 2009;54:1837–46.
60. Singh JP, Gras D. Biventricular pacing: current trends and future strategies. *Eur Heart J*. 2012;33:305–13.
61. Stevenson WG, Hernandez AF, Carson PE, et al. Indications for cardiac resynchronization therapy: 2011 update from the Heart Failure Society of America Guideline Committee. *J Card Fail*. 2012;18:94–106.
62. Dickstein K, Vardas PE, Auricchio A, et al. 2010 Focused update of ESC guidelines on device therapy in heart failure: an update of the 2008 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure and the 2007 ESC guidelines for cardiac and resynchronization therapy. *Eur Heart J*. 2010;31:2677–87.
63. Dubner S, Auricchio A, Steinberg JS, et al. ISHNE/EHRA expert consensus on remote monitoring of cardiovascular implantable electronic devices (CIEDs). *Europace*. 2012;14:278–93.
64. Crossley GH, Chen J, Choucair W, et al. Clinical benefits of remote versus transtelephonic monitoring of implanted pacemakers. *J Am Coll Cardiol*. 2009;54:2012–9.
65. Crossley GH, Boyle A, Vitense H, et al. The CONNECT (Clinical Evaluation of Remote Notification to Reduce Time to Clinical Decision) trial: the value of wireless remote monitoring with automatic clinician alerts. *J Am Coll Cardiol*. 2011;57:1181–9.
66. Varma N, Epstein AE, Irimpen A, et al. Efficacy and safety of automatic remote monitoring for implantable cardioverter-defibrillator follow-up: the Lumos-T Safely Reduces Routine Office Device Follow-up (TRUST) trial. *Circulation*. 2010;122:325–32.
67. Mabo P, Victor F, Bazin P, et al. A randomized trial of long-term remote monitoring of pacemaker recipients (the COMPAS trial). *Eur Heart J*. 2012;33:1105–11.
68. Saxon LA, Hayes DL, Gilliam FR, et al. Long-term outcome after ICD and CRT implantation and influence of remote device follow-up: the ALTITUDE survival study. *Circulation*. 2010;122:2359–67.

Appendix 1 Author Relationships With Industry and Other Entities (Relevant)—2012 ACCF/AHA/HRS Focused Update of the 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities

Committee Member	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness	Voting Recusals by Section*
Cynthia M. Tracy, Chair	George Washington University Medical Center—Associate Director and Professor of Medicine	None	None	None	None	None	None	None
Andrew E. Epstein, Vice Chair	University of Pennsylvania—Professor of Medicine Philadelphia VA Medical Center—Chief, Cardiology Section	<ul style="list-style-type: none"> ● Boston Scientific (DSMB)† ● Medtronic‡ ● Medtronic/CryoCath (DSMB) ● St. Jude Medical (DSMB)† ● ZOLL—Advisory Board 	None	None	<ul style="list-style-type: none"> ● Biotronik ● Boston Scientific‡ ● Cameron Health† ● Medtronic‡ ● St. Jude Medical† 	<ul style="list-style-type: none"> ● Boston Scientific ● Medtronic ● St. Jude Medical 	None	2.4.1
Dawood Darbar	Vanderbilt University School of Medicine—C. Sydney Burwell Associate Professor Medicine Pharmacology Vanderbilt Arrhythmia Service—Director	None	None	None	None	None	None	None
John P. DiMarco	University of Virginia—Director, Clinical EP Laboratory	<ul style="list-style-type: none"> ● Medtronic ● St. Jude Medical 	None	None	● Boston Scientific	None	None	2.4.1
Sandra B. Dunbar	Emory University, Nell Hodgson Woodruff School of Nursing—Associate Dean for Academic Advancement, Charles Howard Candler Professor	None	None	None	None	None	None	None
N.A. Mark Estes III	Tufts University—Professor of Medicine	<ul style="list-style-type: none"> ● Boston Scientific‡ ● Boston Scientific, EP Fellowship Educational Symposium† ● Medtronic ● United Healthcare—Advisory Board 	None	None	● Boston Scientific—MADIT-RIT (Co-PI)	None	None	2.4.1
T. Bruce Ferguson, Jr	East Carolina University—Professor of Surgery and Physiology	None	None	None	None	None	None	2.4.1
Stephen C. Hammill	Mayo Clinic—Professor of Medicine	None	None	None	None	None	None	None
Pamela E. Karasik	Georgetown University Medical School—Associate Professor of Medicine VA Medical Center, Washington, DC—Acting Chief of Cardiology	None	None	None	None	None	None	None
Mark S. Link	Tufts Medical Center—Professor of Medicine	None	None	None	● Boston Scientific—MADIT-RIT (Co-PI)	None	None	2.4.1
Joseph E. Marine	Johns Hopkins University—Associate Professor of Medicine	None	None	None	None	None	None	None
Mark H. Schoenfeld	Yale University School of Medicine—Clinical Professor of Medicine	● United Healthcare—Advisory Board	None	None	None	None	None	2.4.1

Appendix 1 Continued

Committee Member	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness	Voting Recusals by Section*
Amit J. Shanker	Center for Advanced Arrhythmia Medicine—Director Columbia University College of Physicians and Surgeons—Assistant Professor of Medicine	None	None	None	None	None	None	None
Michael J. Silka	University of Southern California—Professor of Pediatrics Children's Hospital Los Angeles—Chief, Division of Cardiology	None	None	None	None	None	None	None
Lynne Warner Stevenson	Brigham & Women's Hospital—Director, Cardiomyopathy and Heart Failure	None	None	None	● Biosense Webster†‡	None	None	2.4.1
William G. Stevenson	Brigham & Women's Hospital—Director, Clinical Cardiac EP	None	None	None	● Biosense Webster†‡	None	None	2.4.1
Paul D. Varosy	VA Eastern Colorado Health Care System—Director of Cardiac EP University of Colorado Denver—Assistant Professor of Medicine	None	None	None	None	None	None	None

This table represents the relationships of committee members with industry and other entities that were determined to be relevant to this document. These relationships were reviewed and updated in conjunction with all meetings and/or conference calls of the writing group during the document development process. The table does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of $\geq 5\%$ of the voting stock or share of the business entity, or if the interest represents ownership of $\geq \$10,000$ of the fair market value of the business entity, or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted.

According to the ACCF/AHA, a person has a *relevant* relationship IF: (a) the *relationship or interest* relates to the same or similar subject matter, intellectual property or asset, topic, or issue addressed in the *document*; or (b) the *company/entity* (with whom the relationship exists) makes a drug, drug class, or device addressed in the *document* or makes a competing drug or device addressed in the *document*; or (c) the *person or a member of the person's household* has a reasonable potential for financial, professional, or other personal gain or loss as a result of the issues or content addressed in the *document*.

DSMB indicates Data Safety Monitoring Board; EP, electrophysiology; MADIT-RIT, Multicenter Automatic Defibrillator Implantation Trial—Reduce Inappropriate Therapy; PI, principal investigator; and VA, Veterans Affairs.

*Writing group members are required to recuse themselves from voting on sections to which their specific relationships with industry and other entities may apply. Section numbers pertain to those in the full-text guideline.

†Significant relationship.

‡No financial benefit.

Appendix 2 Reviewer Relationships With Industry and Other Entities (Relevant)—2012 ACCF/AHA/HRS Focused Update of the 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities

Peer Reviewer	Representation	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Sana Al-Khatib	Official Reviewer—AHA	Duke Clinical Research Institute and Duke University Medical Center	None	● Medtronic	None	None	None	None
Hugh Calkins	Official Reviewer—HRS	Johns Hopkins Hospital	● Biosense Webster ● Boston Scientific ● Medtronic*	None	None	● Boston Scientific* ● Medtronic* ● St. Jude Medical*	None	None
James R. Edgerton	Official Reviewer—STS	The Heart Hospital Baylor Plano	None	None	None	None	None	None
Michael M. Givertz	Official Reviewer—HFSA	Brigham and Women's Hospital	None	None	None	None	None	None
Jonathan L. Halperin	Official Reviewer—ACCF/ AHA Task Force on Practice Guidelines	Mount Sinai Medical Center	● Biotronik*	None	None	None	None	None
Bradley P. Knight	Official Reviewer—HRS	Northwestern Medical Center	● Boston Scientific ● Cameron Health†	● Biosense Webster ● Biotronik ● Boston Scientific ● Medtronic	None	● Cameron Health*	None	None
Thomas J. Lewandowski	Official Reviewer—ACCF Board of Governors	Appleton Cardiology Thedacare	None	None	None	None	None	None
Henry M. Spotnitz	Official Reviewer—AATS	Columbia University	None	None	● Strategic Pacing Systems†	None	None	None
C. Michael Valentine	Official Reviewer—ACCF Board of Trustees	The Cardiovascular Group	● Medtronic*	None	None	None	None	None
Paul J. Wang	Official Reviewer—AHA	Stanford University Medical Center	● Medtronic	None	None	● Medtronic*	None	None
John F. Beshai	Content Reviewer—ACCF EP Committee	University of Chicago Medical Center	None	None	None	None	● Medtronic* ● St. Jude Medical*	None
George H. Crossley	Content Reviewer	St. Thomas Heart	● Boston Scientific ● Medtronic	● Boston Scientific ● Medtronic	None	None	● Boston Scientific ● Medtronic*	None
Jennifer E. Cummings	Content Reviewer—ACCF EP Committee	University of Toledo	None	● Boston Scientific ● Medtronic ● St. Jude	None	None	None	None
Kenneth A. Ellenbogen	Content Reviewer	Virginia Commonwealth University Medical Center	● Cameron Health ● Boston Scientific ● Medtronic	● Biotronik ● Boston Scientific ● Medtronic ● St. Jude Medical	None	None	● Biosense Webster* ● Boston Scientific* ● Medtronic* ● St. Jude Medical*	None
Roger A. Freedman	Content Reviewer	University of Utah Health Sciences Center	● Boston Scientific ● Sorin ● Spectranetics ● St. Jude Medical	None	None	● Medtronic* ● St. Jude Medical*	None	● Defendant, 2011, pacemaker battery depletion
Gabriel Gregoratos	Content Reviewer	University of California—San Francisco	None	None	None	None	None	None
David L. Hayes	Content Reviewer	Mayo Clinic	● Biotronik ● Boston Scientific ● Medtronic* ● Sorin ● St. Jude Medical	None	None	None	None	None

Appendix 2 Continued

Peer Reviewer	Representation	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Mark A. Hlatky	Content Reviewer	Stanford University School of Medicine	None	None	None	None	None	None
Sandeep K. Jain	Content Reviewer	University of Pittsburgh Physicians, UPMC Heart and Vascular Institute	None	None	None	● Medtronic*	None	None
Samuel O. Jones	Content Reviewer	San Antonio Military Medical Center	None	None	None	None	● Medtronic† ● St. Jude Medical†	None
Kousik Krishnan	Content Reviewer	Rush University Medical Center	● Boston Scientific ● St. Jude Medical	None	None	None	● Biotronik* ● Boston Scientific—MADIT-RIT* ● Medtronic*	None
Michael Mansour	Content Reviewer	Cardiovascular Physicians	None	None	None	None	None	None
Steven M. Markowitz	Content Reviewer—ACCF EP Committee	New York Hospital	● Biotronik ● Boston Scientific ● Medtronic ● St. Jude Medical	None	None	None	● Biosense Webster* ● Boston Scientific* ● Medtronic* ● St. Jude Medical*	None
Marco A. Mercader	Content Reviewer	George Washington University	None	None	None	None	None	None
Simone Musco	Content Reviewer	Saint Patrick Hospital	● Boston Scientific	None	None	None	None	None
L. Kristin Newby	Content Reviewer	Duke University Medical Center	None	None	None	None	None	None
Brian Olshansky	Content Reviewer—ACCF EP Committee	University of Iowa Hospitals	● Boston Scientific ● Guidant ● Medtronic	None	None	None	None	None
Richard L. Page	Content Reviewer	University of Wisconsin Hospital and Clinics	None	None	None	None	None	None
Allen J. Solomon	Content Reviewer	Medical Faculty Associates	None	None	None	None	None	None
John S. Strobel	Content Reviewer	Internal Medicine Associates	None	None	None	● Medtronic*	None	None
Stephen L. Winters	Content Reviewer	Morristown Medical Center	● Biosense Webster	None	None	None	● Boston Scientific ● Medtronic ● St. Jude Medical	● Defendant, 2011, complication of ICD placement

This table represents the relationships of reviewers with industry and other entities that were disclosed at the time of peer review and determined to be relevant. It does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of $\geq 5\%$ of the voting stock or share of the business entity, or if the interest represents ownership of $\geq \$10,000$ of the fair market value of the business entity, or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. A relationship is considered to be modest if it is less than significant under the preceding definition. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted. Names are listed in alphabetical order within each category of review.

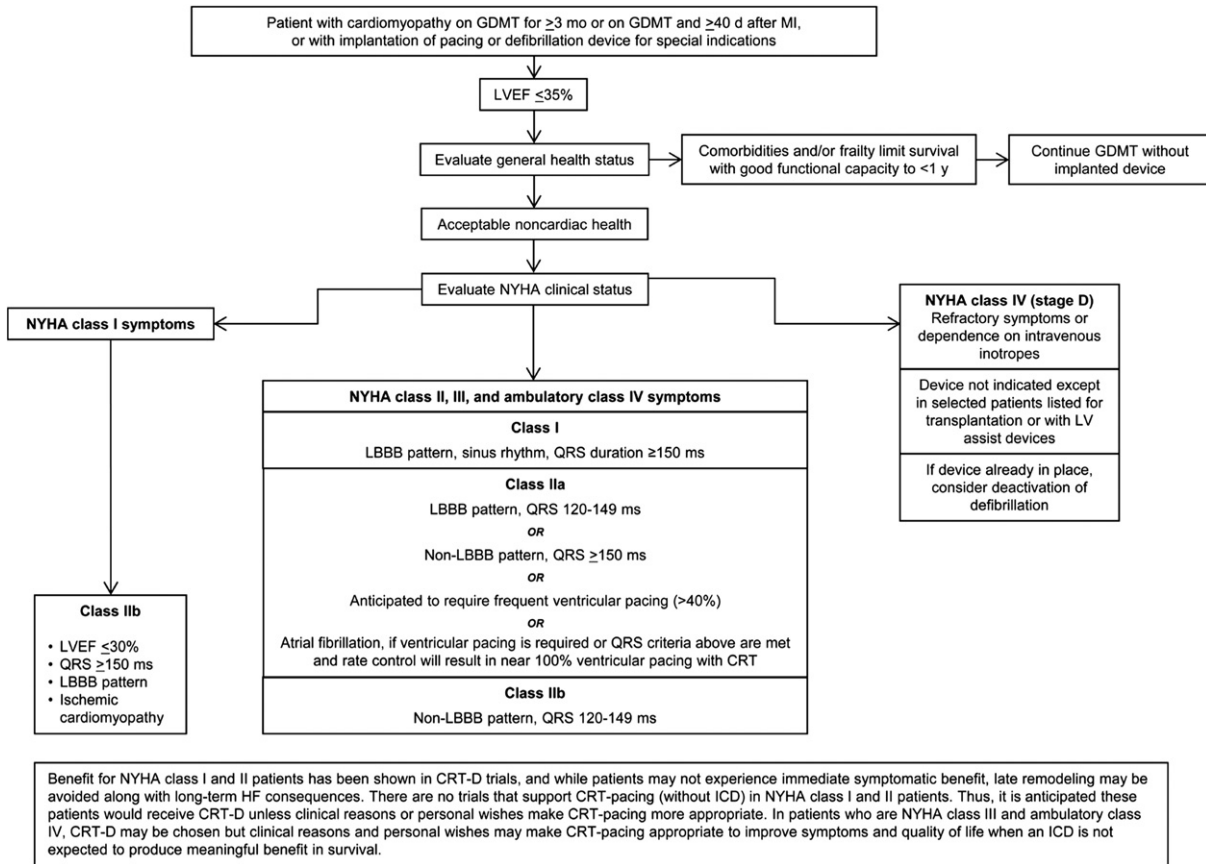
According to the ACCF/AHA, a person has a *relevant* relationship IF: (a) the *relationship or interest* relates to the same or similar subject matter, intellectual property or asset, topic, or issue addressed in the *document*; or (b) the *company/entity* (with whom the relationship exists) makes a drug, drug class, or device addressed in the *document* or makes a competing drug or device addressed in the *document*; or (c) the *person or a member of the person's household* has a reasonable potential for financial, professional, or other personal gain or loss as a result of the issues or content addressed in the *document*.

AATS indicates American Association for Thoracic Surgery; ACCF, American College of Cardiology Foundation; AHA, American Heart Association; EP, Electrophysiology; HFSA, Heart Failure Society of America; HRS, Heart Rhythm Society; ICD, implantable cardioverter-defibrillator; MADIT-RIT, Multicenter Automatic Defibrillator Implantation Trial—Reduce Inappropriate Therapy; and STS, Society of Thoracic Surgeons.

*Significant relationship.

†No financial benefit.

Appendix 3 Indications for CRT Therapy—Algorithm



CRT indicates cardiac resynchronization therapy; CRT-D, cardiac resynchronization therapy defibrillator; GDMT, guideline-directed medical therapy; ICD, implantable cardioverter-defibrillator; LV, left ventricular; LVEF, left ventricular ejection fraction; LBBB, left bundle-branch block; MI, myocardial infarction; and NYHA, New York Heart Association.