Supplemental Table 1. Stakeholder Group

Name	*Role/ Perspsective Affiliation
William Abraham, MD, FACP, FACC, FAHA, FESC	*Principal Investigator, MIRACLE, MIRACLE ICD2 Studies Director, Division of Cardiovascular Medicine Professor of Internal Medicine, Physiology and Cell Biology at The Ohio State University Columbus, OH
Elise Berliner, PhD	*Federal/Non-government Funding Agency Director, Technology Assessment Program, Center for Outcomes and Evidence, AHRQ Rockville, MD
Michael Bristow, MD, PhD	*Principal Investigator, COMPANION Study Professor of Medicine and Cardiology, University of Colorado Denver, CO
Mark Carlson, MD	*Industry/Device Companies Vice President, Global Clinical Affairs, St. Jude Medical (Abbott Laboratories) Los Angeles, CA
John Cleland, MD, PhD, FRCP, FACC	*Principal Investigator, CARE-HF Study Professor of Clinical Cardiology, Imperial College of London London, United Kingdom
Anne Curtis, MD	*Principal Investigator, BLOCK-HF Study Chair, Department of Medicine, University at Buffalo, SUNY Buffalo, NY
David DeMets, PhD, FACMI	*Lead Statistician, COMPANION Study Professor of Statistics and Biostatistics, University of Wisconsin Madison, WI
Adam DeVore, MD, MHS	*Healthcare Provider Assistant Professor of Medicine in the Department of Medicine, Division of Cardiology, at Duke University School of Medicine Durham, NC
Gregg Fonarow, MD, FACC, FAHA	*Healthcare Provider Director, Ahmanson-UCLA Cardiomyopathy Center Co-Director, UCLA Preventative Cardiology Program Co-Chief, UCLA Division of Cardiology The Eliot Corday Chair in Cardiovascular Medicine and Science University of California, Los Angeles Los Angeles, CA
Michael Gold, MD, PhD, FHRS	*Principal Investigator, RESOLVE Study Director of the Division of Cardiology, Professor of Medicine, Medical University of South Carolina Charleston, SC

Name	*Role/ Perspsective Affiliation
Valentina Kutyifa, MD, MSc, PhD, FESC, FHRS, FACC	*Co-Representative for MADIT-CRT Study Research Associate Professor in Medicine/Cardiology, Heart Research Follow-Up Program, University of Rochester Medical Center Rochester, NY
Cecilia Linde, MD, PhD	*Principal Investigator, REVERSE Study Adjunct Professor, Department of Medicine, Karolinska Institutet, Stockholm, Sweden
Fred Masoudi, MD, MSPH, FACC, FACP, FAHA	*NCDR-ICD Registry representative Professor of Medicine in Cardiology at University of Colorado Denver, CO
Dan Matlock, MD, MPH	*Geriatric Care Perspective Associate Professor of Medicine – Geriatrics, University of Colorado Aurora, CO
David McManus, MD, ScM, FACC, FAHA, FHRS	*NCDR-ICD Registry representative Associate Professor, Depts of Medicine and Quantitative Health Sciences, UMass Medical School Director, Atrial Fibrillation Program, UMass Medical School Amherst, MA
Arthur Moss, MD	*Principal Investigator, MADIT-CRT Study Professor of Medicine, University of Rochester Rochester, NY
Pamela Peterson, MD, MSPH	*NCDR-ICD Registry representative Associate Professor of Medicine-Cardiology, University of Colorado Denver, CO
Andrea Russo, MD, FHRS	*Professional Society, Heart Rhythm Society Director of Electrophysiology and Arrhythmia Services at Cooper University Hospital, Director of the CCEP Fellowship program and Professor of Medicine at Cooper Medical School of Rowan University Glassboro, NJ
Samir Saba, MD, FACC, FHRS	*Healthcare Provider Chief, Cardiac Electrophysiology; Director, Cardiac Electrophysiology Laboratory; Associate Professor of Medicine in Division of Cardiology; University of Pittsburgh Pittsburgh, PA
Dan Schaber, PharmD	*Industry/Device Company Vice President, Heart Failure Clinical Research (Medtronic) Minneapolis, MN
Ken Stein, MD, FACC	*Industry/Device Company Senior Vice President and Chief Medical Officer for Rhythm Management and Global Health Policy (Boston Scientific) Boston, MA

Name	*Role/ Perspsective Affiliation
Anthony Tang, MD	*Principal Investigator, RAFT Study Chair, Cardiovascular Population Health, Western University
Paul Varosy, MD, FACC, FAHA, FHRS	*Member of the 2012 ACC/AHA Guideline, Healthcare Provider Associate Professor, Medicine-Cardiology, University of Colorado Associate Program Director, Clinical Cardiac Electrophysiology Fellowship Training Program, University of Colorado Denver, CO
George Wells, MSc, PhD	*Principal Investigator, RAFT study Professor of the School of Epidemiology, Public Health and Preventive Medicine at the University of Ottawa Professor in the Department of Medicine, Senior Scientist at the Ottawa Health Research Institute Director, Cardiovascular Research Methods Centre at the University of Ottawa Heart Institute Ottawa, Canada
Clyde Yancy, MD, MSc	*Professional Society, American College of Cardiology Chief of Cardiology at Northwestern University, Feinberg School of Medicine Associate Director of the Bluhm Cardiovascular Institute at Northwestern Memorial Hospital Chicago, IL
James Young, MD, FACC, FACP, FAHA, FESC	*Principal Investigator, MIRACLE ICD1 Study Professor of Medicine and Executive Dean, Cleveland Clinic Cleveland, Ohio

Supplemental Table 2. Expanded (Unranked) List of CRT Evidence Gaps

Evidence Gaps		Evidence Gap Identified By:
Specific populations or subgroups of interest		
1.	What is the comparative safety and effectiveness of CRT (vs. no CRT) among patients ≥75 years old? ≥80 years old?	Research group
2.	What is the association between heart failure duration and history of heart failure hospitalizations prior to implantation of CRT (vs. no CRT) with outcomes?	Stakeholders
3.	Do CRT outcomes differ based on patient race and ethnicity?	Stakeholders
4.	What is the relationship between gender, QRS morphology and duration, and outcomes for patients with either CRT-D or ICD?	Stakeholders
5.	What is the effectiveness of CRT among patients with paroxysmal, persistent, and permanent AF?	Research group
6.	What is the association between comorbid diseases (e.g., chronic kidney disease, chronic lung disease, atrial fibrillation, diabetes mellitus, arterial and pulmonary hypertension, right ventricular dysfunction, and patients on dialysis) as well as the burden of comorbidities and the effectiveness of CRT-P and CRT-D?	Research group/ Stakeholders
7.	What is the relationship between chronic lung disease, receipt of CRT vs. no CRT, and outcomes, particularly symptom burden and quality of life?	Research group
8.	Does CRT benefit (compared to no CRT) vary based on QRS duration (<150ms vs ≥ 150ms)?	Research group
9.	Do the location and extent of left ventricular dyssynchrony predict outcomes among CRT patients?	Stakeholders
10.	What is the relationship between height, weight, BMI, diabetes, and outcomes of CRT-D vs. ICD (i.e. does the obesity paradox apply to CRT patients and does diabetes modify this relationship)?	Research group
11.	What is the comparative safety and effectiveness of CRT compared with no CRT among patients with a LBBB and EF >35%?	Research group
12.	Is CRT more effective than an ICD at halting progressive remodeling in the subset of HF patients who do not demonstrate classic echocardiographic response (defined as 15% improvement in LV end systolic volume)?	Research group
13.	What is the comparative safety and effectiveness of CRT-D versus CRT-P overall and among subgroups defined by cardiomyopathy etiology and QRS morphology?	Research group
14.	In looking at the control arms of the available CRT trials, which patients are at the highest risk of heart failure or death?	Stakeholders
15.	In looking at the control arms of the available CRT, what are the predictors of worsening LVEF?	Stakeholders
Comparative safety and effectiveness of available interventions/comparators		
16.	What is the association between AV node ablation (vs. no AV node ablation) and CRT effectiveness among patients with AF and history of AF with rapid ventricular response?	Research group/ Stakeholders
17.	What is the minimum percentage of biventricular pacing required for CRT-D to be superior to ICD?	Research group
18.	What is the optimal percentage of biventricular pacing required to optimize outcomes among CRT recipients?	Research group

Evidence Gaps		Evidence Gap Identified By:
19.	What is the association of PVC burden prior and post CRT-D implantation on outcomes? Any data on associations of PVC ablation and outcomes?	Stakeholders
20.	Is the PR interval associated with the effectiveness of CRT (vs. no CRT)?	Research group
21.	Is AV delay programming and/or CRT optimization associated with any observed relationship between PR interval and outcomes among CRT patients?	Research group
22.	Is upgrade from a dual chamber pacemaker or defibrillator to a CRT device (vs. no upgrade) associated with HF free survival among patients with a high burden of RV pacing?	Research group
23.	Is there an association between time since MI/revascularization and CRT outcomes?	Stakeholders
24.	What is the EF threshold at which CRT is superior to dual chamber pacing in high grade or complete AV block?	Research group
25.	Does RV lead location predict outcomes among CRT patients?	Stakeholders
26.	Does CRT (compared to ICD) improve survival in very advanced HF as demonstrated by NYHA class and/or LV size/function?	Research group
27.	Is LV end systolic volume superior to EF at predicting whether CRT is superior to dual chamber pacing in high grade or complete AV block?	Research group
28.	What is the role of endocardial CRT especially in “non-responders” and with the advent of novel oral anticoagulants (NOACs)?	Stakeholders
Association of treatment with specific outcomes of interest		
29.	What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with improvement in quality of life and functional status in patients with CRT?	Research group
30.	What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with a short term and durable improvement in LVEF and other echocardiographic parameters in patients with CRT?	Research group
31.	What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with reductions in heart failure (HF) hospitalizations in patients with CRT?	Research group
32.	What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with improvement in overall survival in patients with CRT?	Research group
33.	What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with reduction in the risk of sudden cardiac death in patients with CRT?	Research group
34.	What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with reduction of cost in patients with CRT?	Stakeholders
35.	What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters	Research group

Evidence Gaps		Evidence Gap Identified By:
	associated with reduction in atrial and ventricular arrhythmias in patients with CRT?	
36.	What are the rates and predictors of appropriate and inappropriate ICD therapy events (shocks and/or ATP) among patients with CRT-D vs. ICD only?	Stakeholders
37.	What are the echocardiographic predictors of early death (within 30 days) after CRT implantation (i.e. are there echocardiographic predictors of CRT futility)?	Research group
38.	What is the distribution of modes of death in responders vs. non-responders to CRT?	Stakeholders
Optimal timing or setting for treatment		
39.	Do outcomes and complications vary based on timing relative to prior heart failure hospital admission?	Stakeholders
40.	Are the CRT outcomes observed in the community predicted by the available clinical trial evidence?	Research group

Abbreviations: AF=atrial fibrillation; AV=atrioventricular; CRT=cardiac resynchronization therapy; ECG=electrocardiogram; EF=ejection fraction; HF=heart failure; ICD=implantable cardiac device; LBBB=left bundle branch block; LVEF=left ventricular ejection fraction; NYHA=New York Heart Association; PVC=premature ventricular contraction; RCT=randomized controlled trial; RV=right ventricular

Supplemental Table 3: Search Strategy

Search date: November 9, 2018

Database: PubMed

Set	Terms
#1 CRT terms	"Cardiac Resynchronization Therapy"[Mesh] OR "Cardiac Resynchronization Therapy Devices"[Mesh] OR “Cardiac resynchronization therapy”[tiab] OR “Cardiac resynchronisation therapy”[tiab] OR “atrio biventricular pacing”[tiab] OR “atrio-biventricular pacing”[tiab] OR “biventricular pacing”[tiab] OR “biventricular pacemaker*”[tiab]
#2 Study design	(randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR randomised[tiab] OR randomization[tiab] OR randomisation[tiab] OR placebo[tiab] OR randomly[tiab] OR trial[tiab] OR Clinical trial[pt] OR “clinical trial”[tiab] OR “clinical trials”[tiab] OR "intervention study"[tiab] OR "intervention studies"[tiab] OR "prospective"[tiab] OR prospectively[tiab] OR "comparative study"[pt] OR "comparative study"[tiab]) NOT (Editorial[ptyp] OR Letter[pt] OR Case Reports[pt] OR Comment[pt]) NOT (animals[mh] NOT humans[mh])
#3	#1 AND #2
#4	#3, limit since October 2008 and English only

Database: Embase

Set	Terms
#1 CRT terms	'cardiac resynchronization therapy'/exp OR 'cardiac resynchronization therapy device'/exp OR ‘Cardiac resynchronization therapy’:ab,ti OR ‘Cardiac resynchronisation therapy’:ab,ti OR ‘atrio biventricular pacing’:ab,ti OR ‘atrio-biventricular pacing’:ab,ti OR ‘biventricular pacing’:ab,ti OR ‘biventricular pacemaker’:ab,ti

#2 Study design	'clinical trial'/exp OR 'clinical study'/exp OR 'controlled study'/exp OR randomized:ab,ti OR randomised:ab,ti OR randomization:ab,ti OR randomisation:ab,ti OR placebo:ab,ti OR 'clinical trial':ab,ti OR 'clinical trials':ab,ti OR 'clinical study':ab,ti OR 'clinical studies':ab,ti OR 'prospective':ab,ti OR 'comparative study'/exp OR 'comparative study':ab,ti OR 'comparative studies':ab,ti NOT ('case report'/exp OR 'case study'/exp OR 'editorial'/exp OR 'letter'/exp OR 'note'/exp OR 'conference abstract'/exp)
#3	#1 AND #2
#4	#3 AND [embase]/lim NOT [medline]/lim AND [humans]/lim AND [english]/lim AND [2008-2018]/py

Supplemental Table 4. Ranking of Evidence Gaps by Critical Importance

Question	NOT REALLY THAT IMPORTANT					IMPORTANT BUT NOT CRITICAL					CRITICAL IMPORTANCE				
	1	**2**	**3**	**1-3 N**	**1-3 %**	**4**	**5**	**6**	**4-6 N**	**4-6 %**	**7**	**8**	**9**	**7-9 N**	**7-9 %**
5. What is the effectiveness of CRT among patients with paroxysmal. persistent, and permanent AF?	0	0	0	0	0,00%	0	4	1	5	23,81%	4	8	4	16	76,19%
6. What is the association between comorbid diseases (e.g., chronic kidney disease, chronic lung disease, atrial fibrillation, diabetes mellitus, arterial and pulmonary hypertension, right ventricular dysfunction, and patients on dialysis) as well as the burden of comorbidities and the effectiveness of CRT-P and CRT-D?	0	0	0	0	0,00%	1	2	3	6	28,57%	8	6	1	15	71,43%
18. What is the optimal percentage of biventricular pacing required to optimize outcomes among CRT recipients?	0	0	0	0	0,00%	1	4	1	6	28,57%	6	9	0	15	71,43%

Question	NOT REALLY THAT IMPORTANT					IMPORTANT BUT NOT CRITICAL					CRITICAL IMPORTANCE				
	1	**2**	**3**	**1-3 N**	**1-3 %**	**4**	**5**	**6**	**4-6 N**	**4-6 %**	**7**	**8**	**9**	**7-9 N**	**7-9 %**
17. What is the minimum percentage of biventricular pacing required for CRT-D to be superior to ICD?	1	0	0	1	4,76%	1	4	0	5	23,81%	6	9	0	15	71,43%
4. What is the relationship between gender, QRS morphology and duration, and outcomes for patients with either CRT-D or ICD?	0	0	0	0	0,00%	2	4	1	7	33,33%	7	5	2	14	66,67%
24. What is the EF threshold at which CRT is superior to dual chamber pacing in high grade or complete AV block?	0	0	1	1	4,76%	2	2	2	6	28,57%	6	6	2	14	66,67%
16. What is the association between AV node ablation (vs. no AV node ablation) and CRT effectiveness among patients with AF and history of AF with rapid ventricular response?	0	0	0	0	0,00%	1	5	3	9	42,86%	5	6	1	12	57,14%
26. Does CRT (compared to ICD) improve survival in very advanced HF as	0	0	0	0	0,00%	1	3	5	9	42,86%	7	4	1	12	57,14%

Question	NOT REALLY THAT IMPORTANT					IMPORTANT BUT NOT CRITICAL					CRITICAL IMPORTANCE				
	1	**2**	**3**	**1-3 N**	**1-3 %**	**4**	**5**	**6**	**4-6 N**	**4-6 %**	**7**	**8**	**9**	**7-9 N**	**7-9 %**
demonstrated by NYHA class and/or LV size/function?															
40. Are the CRT outcomes observed in the community predicted by the available clinical trial evidence?	0	1	0	1	4,76%	1	4	3	8	38,10%	10	2	0	12	57,14%
32. What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with improvement in overall survival in patients with CRT?	0	0	0	0	0,00%	2	3	5	10	47,62%	7	3	1	11	52,38%
22. Is upgrade from a dual chamber pacemaker or defibrillator to a CRT device (vs. no upgrade) associated with HF free survival among patients with a high burden of RV pacing?	0	0	1	1	4,76%	1	6	2	9	42,86%	3	6	2	11	52,38%

Question	NOT REALLY THAT IMPORTANT					IMPORTANT BUT NOT CRITICAL					CRITICAL IMPORTANCE				
	1	**2**	**3**	**1-3 N**	**1-3 %**	**4**	**5**	**6**	**4-6 N**	**4-6 %**	**7**	**8**	**9**	**7-9 N**	**7-9 %**
11. What is the comparative safety and effectiveness of CRT compared with no CRT among patients with a LBBB and EF >35%?	0	0	2	2	9,52%	1	4	3	8	38,10%	4	3	4	11	52,38%
19. What is the association of PVC burden prior and post CRT-D implantation on outcomes? Any data on associations of PVC ablation and outcomes?	0	0	2	2	9,52%	2	1	5	8	38,10%	7	4	0	11	52,38%
8. Does CRT benefit (compared to no CRT) vary based on QRS duration (<150ms vs ≥ 150ms)?	0	0	0	0	0,00%	5	2	4	11	52,38%	4	3	3	10	47,62%
13. What is the comparative safety and effectiveness of CRT-D versus CRT-P overall and among subgroups defined by cardiomyopathy etiology and QRS morphology?	0	0	0	0	0,00%	2	4	5	11	52,38%	4	3	3	10	47,62%

Question	NOT REALLY THAT IMPORTANT					IMPORTANT BUT NOT CRITICAL					CRITICAL IMPORTANCE				
	1	**2**	**3**	**1-3 N**	**1-3 %**	**4**	**5**	**6**	**4-6 N**	**4-6 %**	**7**	**8**	**9**	**7-9 N**	**7-9 %**
1. What is the comparative safety and effectiveness of CRT (vs. no CRT) among patients ≥75 years old? ≥80 years old?	0	0	1	1	4,76%	4	4	3	11	52,38%	6	2	1	9	42,86%
29. What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with improvement in quality of life and functional status in patients with CRT?	0	0	3	3	14,29%	0	5	4	9	42,86%	5	3	1	9	42,86%
20. Is the PR interval associated with the effectiveness of CRT (vs. no CRT)?	0	0	5	5	23,81%	5	1	1	7	33,33%	5	2	2	9	42,86%
31. What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with reductions in heart failure (HF) hospitalizations in patients with CRT?	0	0	0	0	0,00%	3	3	7	13	61,90%	6	2	0	8	38,10%

Question	NOT REALLY THAT IMPORTANT					IMPORTANT BUT NOT CRITICAL					CRITICAL IMPORTANCE				
	1	**2**	**3**	**1-3 N**	**1-3 %**	**4**	**5**	**6**	**4-6 N**	**4-6 %**	**7**	**8**	**9**	**7-9 N**	**7-9 %**
33. What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with reduction in the risk of sudden cardiac death in patients with CRT?	0	0	0	0	0,00%	4	3	6	13	61,90%	6	2	0	8	38,10%
9. Do the location and extent of left ventricular dyssynchrony predict outcomes among CRT patients?	0	0	2	2	9,52%	6	2	3	11	52,38%	4	3	1	8	38,10%
21. Is AV delay programming and/or CRT optimization associated with any observed relationship between PR interval and outcomes among CRT patients?	0	0	2	2	9,52%	3	5	3	11	52,38%	3	4	1	8	38,10%
35. What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with reduction in atrial and ventricular arrhythmias in patients with CRT?	0	1	2	3	14,29%	3	4	3	10	47,62%	6	2	0	8	38,10%

Question	NOT REALLY THAT IMPORTANT					IMPORTANT BUT NOT CRITICAL					CRITICAL IMPORTANCE				
	1	**2**	**3**	**1-3 N**	**1-3 %**	**4**	**5**	**6**	**4-6 N**	**4-6 %**	**7**	**8**	**9**	**7-9 N**	**7-9 %**
36. What are the rates and predictors of appropriate and inappropriate ICD therapy events (shocks and/or ATP) among patients with CRT-D vs. ICD only?	0	0	0	0	0,00%	2	4	8	14	66,67%	5	1	1	7	33,33%
37. What are the echocardiographic predictors of early death (within 30 days) after CRT implantation (i.e. are there echocardiographic predictors of CRT futility)?	0	0	0	0	0,00%	4	7	3	14	66,67%	7	0	0	7	33,33%
30. What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with a short term and durable improvement in LVEF and other echocardiographic parameters in patients with CRT?	1	0	0	1	4,76%	5	4	4	13	61,90%	5	2	0	7	33,33%

Question	NOT REALLY THAT IMPORTANT					IMPORTANT BUT NOT CRITICAL					CRITICAL IMPORTANCE				
	1	**2**	**3**	**1-3 N**	**1-3 %**	**4**	**5**	**6**	**4-6 N**	**4-6 %**	**7**	**8**	**9**	**7-9 N**	**7-9 %**
10. What is the relationship between height, weight, BMI, diabetes, and outcomes of CRT-D vs. ICD (i.e. does the obesity paradox apply to CRT patients and does diabetes modify this relationship)?	0	0	2	2	9,52%	3	4	5	12	57,14%	2	5	0	7	33,33%
34. What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with reduction of cost in patients with CRT?	0	1	2	3	14,29%	3	4	4	11	52,38%	4	3	0	7	33,33%
2. What is the association between heart failure duration and history of heart failure hospitalizations prior to implantation of CRT (vs. no CRT) with outcomes?	0	2	3	5	23,81%	1	5	3	9	42,86%	5	2	0	7	33,33%
12. Is CRT more effective than an ICD at halting progressive remodeling in the subset of HF patients who do not demonstrate	2	2	1	5	23,81%	2	5	2	9	42,86%	3	4	0	7	33,33%

Question	NOT REALLY THAT IMPORTANT					IMPORTANT BUT NOT CRITICAL					CRITICAL IMPORTANCE				
	1	**2**	**3**	**1-3 N**	**1-3 %**	**4**	**5**	**6**	**4-6 N**	**4-6 %**	**7**	**8**	**9**	**7-9 N**	**7-9 %**
classic echocardiographic response (defined as 15% improvement in LV end systolic volume)?															
25. Does RV lead location predict outcomes among CRT patients?	0	0	1	1	4,76%	3	5	6	14	66,67%	3	2	1	6	28,57%
28. What is the role of endocardial CRT especially in “non-responders” and with the advent of novel oral anticoagulants (NOACs)?	0	2	0	2	9,52%	4	2	7	13	61,90%	4	2	0	6	28,57%
3. Do CRT outcomes differ based on patient race and ethnicity?	0	0	3	3	14,29%	2	6	4	12	57,14%	6	0	0	6	28,57%
7. What is the relationship between chronic lung disease, receipt of CRT vs. no CRT, and outcomes, particularly symptom burden and quality of life?	0	0	0	0	0,00%	1	8	7	16	76,19%	3	2	0	5	23,81%

Question	NOT REALLY THAT IMPORTANT					IMPORTANT BUT NOT CRITICAL					CRITICAL IMPORTANCE				
	1	**2**	**3**	**1-3 N**	**1-3 %**	**4**	**5**	**6**	**4-6 N**	**4-6 %**	**7**	**8**	**9**	**7-9 N**	**7-9 %**
14. In looking at the control arms of the available CRT trials, which patients are at the highest risk of heart failure or death?	0	0	2	2	9,52%	2	6	6	14	66,67%	3	2	0	5	23,81%
15. In looking at the control arms of the available CRT, what are the predictors of worsening LVEF?	0	1	1	2	9,52%	3	9	2	14	66,67%	3	2	0	5	23,81%
23. Is there an association between time since MI/revascularization and CRT outcomes?	0	0	3	3	14,29%	4	7	2	13	61,90%	3	1	1	5	23,81%
38. What is the distribution of modes of death in responders vs. non-responders to CRT?	0	1	2	3	14,29%	3	3	7	13	61,90%	2	2	1	5	23,81%
39. Do outcomes and complications vary based on timing relative to prior heart failure hospital admission?	0	2	1	3	14,29%	3	6	5	14	66,67%	3	1	0	4	19,05%
27. Is LV end systolic volume superior to EF at predicting whether CRT is superior to dual	0	2	2	4	19,05%	4	1	8	13	61,90%	3	1	0	4	19,05%

Question	NOT REALLY THAT IMPORTANT					IMPORTANT BUT NOT CRITICAL					CRITICAL IMPORTANCE				
	1	2	3	1-3 N	1-3 %	4	5	6	4-6 N	4-6 %	7	8	9	7-9 N	7-9 %
chamber pacing in high grade or complete AV block?															

Abbreviations: AF=atrial fibrillation; AV=atrioventricular; CRT=cardiac resynchronization therapy; ECG=electrocardiogram; EF=ejection fraction; HF=heart failure; ICD=implantable cardiac device; LBBB=left bundle branch block; LVEF=left ventricular ejection fraction; NYHA=New York Heart Association; PVC=premature ventricular contraction; RCT=randomized controlled trial; RV=right ventricular

Supplemental Table 5. Ranking of Research Priorities by Stakeholder Group. Listed in the ranked order by the complete stakeholder group

Question	Score (Healthcare Providers) N = 13	Score (Researchers/ Investigators). N = 17	Score (Product Makers) N= 2	Score (Pts/Public) N = 3	Score (All) N = 26
6. What is the association between comorbid diseases (e.g., chronic kidney disease, chronic lung disease, atrial fibrillation, diabetes mellitus, arterial and pulmonary hypertension, right ventricular dysfunction, and patients on dialysis) as well as the burden of comorbidities and the effectiveness of CRT-P and CRT-D?	13	13	2	4	19
5. What is the effectiveness of CRT among patients with paroxysmal, persistent, and permanent AF?	11	10	2	1	18
24. What is the EF threshold at which CRT is superior to dual chamber pacing in high grade or complete AV block?	11	13	3	1	17
4. What is the relationship between gender, QRS morphology and duration, and outcomes for patients with either CRT-D or ICD?	11	13	1	1	17

Question	Score (Healthcare Providers) N = 13	Score (Researchers/ Investigators). N = 17	Score (Product Makers) N= 2	Score (Pts/Public) N = 3	Score (All) N = 26
11. What is the comparative safety and effectiveness of CRT compared with no CRT among patients with a LBBB and EF >35%?	14	9	0	2	16
16. What is the association between AV node ablation (vs. no AV node ablation) and CRT effectiveness among patients with AF and history of AF with rapid ventricular response?	9	10	5	2	15
1. What is the comparative safety and effectiveness of CRT (vs. no CRT) among patients ≥75 years old? ≥80 years old?	13	10	0	1	14
32. What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with improvement in overall survival in patients with CRT?	4	11	0	3	13
17. What is the minimum percentage of biventricular pacing required for CRT-D to be superior to ICD?	9	11	0	1	13

Question	Score (Healthcare Providers) N = 13	Score (Researchers/ Investigators). N = 17	Score (Product Makers) N= 2	Score (Pts/Public) N = 3	Score (All) N = 26
22. Is upgrade from a dual chamber pacemaker or defibrillator to a CRT device (vs. no upgrade) associated with HF free survival among patients with a high burden of RV pacing?	6	11	3	1	12
8. Does CRT benefit (compared to no CRT) vary based on QRS duration (<150ms vs ≥ 150ms)?	3	10	3	1	11
26. Does CRT (compared to ICD) improve survival in very advanced HF as demonstrated by NYHA class and/or LV size/function?	9	8	0	1	11
13. What is the comparative safety and effectiveness of CRT-D versus CRT-P overall and among subgroups defined by cardiomyopathy etiology and QRS morphology?	7	6	2	3	10
29. What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with improvement in quality of life and functional status in patients with CRT?	4	8	0	3	10

Question	Score (Healthcare Providers) N = 13	Score (Researchers/ Investigators). N = 17	Score (Product Makers) N= 2	Score (Pts/Public) N = 3	Score (All) N = 26
18. What is the optimal percentage of biventricular pacing required to optimize outcomes among CRT recipients?	6	9	0	1	10
19. What is the association of PVC burden prior and post CRT-D implantation on outcomes? Any data on associations of PVC ablation and outcomes?	3	6	0	3	8
3. Do CRT outcomes differ based on patient race and ethnicity?	5	6	1	0	7
20. Is the PR interval associated with the effectiveness of CRT (vs. no CRT)?	4	6	0	0	7
31. What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with reductions in heart failure (HF) hospitalizations in patients with CRT?	3	6	0	0	7
28. What is the role of endocardial CRT especially in “non-responders” and with the advent of novel oral anticoagulants (NOACs)?	2	6	0	1	6

Question	Score (Healthcare Providers) N = 13	Score (Researchers/ Investigators). N = 17	Score (Product Makers) N= 2	Score (Pts/Public) N = 3	Score (All) N = 26
37. What are the echocardiographic predictors of early death (within 30 days) after CRT implantation (i.e. are there echocardiographic predictors of CRT futility)?	1	5	0	4	5
39. Do outcomes and complications vary based on timing relative to prior heart failure hospital admission?	1	4	1	3	5
34. What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with reduction of cost in patients with CRT?	1	5	0	2	5
33. What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with reduction in the risk of sudden cardiac death in patients with CRT?	2	3	0	2	5
40. Are the CRT outcomes observed in the community predicted by the available clinical trial evidence?	3	4	0	1	5

Question	Score (Healthcare Providers) N = 13	Score (Researchers/ Investigators). N = 17	Score (Product Makers) N= 2	Score (Pts/Public) N = 3	Score (All) N = 26
14. In looking at the control arms of the available CRT trials, which patients are at the highest risk of heart failure or death?	5	4	3	0	5
25. Does RV lead location predict outcomes among CRT patients?	5	5	0	0	5
21. Is AV delay programming and/or CRT optimization associated with any observed relationship between PR interval and outcomes among CRT patients?	4	3	0	0	5
15. In looking at the control arms of the available CRT, what are the predictors of worsening LVEF?	4	3	2	0	4
9. Do the location and extent of left ventricular dyssynchrony predict outcomes among CRT patients?	3	3	2	0	4
12. Is CRT more effective than an ICD at halting progressive remodeling in the subset of HF patients who do not demonstrate classic echocardiographic response (defined as 15% improvement in LV end systolic volume)?	2	4	0	0	4

Question	Score (Healthcare Providers) N = 13	Score (Researchers/ Investigators). N = 17	Score (Product Makers) N= 2	Score (Pts/Public) N = 3	Score (All) N = 26
2. What is the association between heart failure duration and history of heart failure hospitalizations prior to implantation of CRT (vs. no CRT) with outcomes?	4	3	0	0	4
10. What is the relationship between height, weight, BMI, diabetes, and outcomes of CRT-D vs. ICD (i.e. does the obesity paradox apply to CRT patients and does diabetes modify this relationship)?	3	2	0	0	4
23. Is there an association between time since MI/revascularization and CRT outcomes?	2	3	0	1	3
27. Is LV end systolic volume superior to EF at predicting whether CRT is superior to dual chamber pacing in high grade or complete AV block?	3	2	0	0	3
30. What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with a short term and durable	2	2	0	0	3

Question	Score (Healthcare Providers) N = 13	Score (Researchers/ Investigators). N = 17	Score (Product Makers) N= 2	Score (Pts/Public) N = 3	Score (All) N = 26
improvement in LVEF and other echocardiographic parameters in patients with CRT?					
7. What is the relationship between chronic lung disease, receipt of CRT vs. no CRT, and outcomes, particularly symptom burden and quality of life?	3	1	0	0	3
36. What are the rates and predictors of appropriate and inappropriate ICD therapy events (shocks and/or ATP) among patients with CRT-D vs. ICD only?	0	1	0	1	1
38. What is the distribution of modes of death in responders vs. non-responders to CRT?	0	1	0	1	1
35. What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with reduction in atrial and ventricular arrhythmias in patients with CRT?	0	0	0	0	0

Supplemental Table 6. Search Results from Horizon Scan of Published Literature and Clinicaltrials.gov for the 18 Top-Tier Evidence Gaps

Subtable 1. Published and ongoing studies potentially relevant to Evidence Gap 1 *[What is the comparative safety and effectiveness of CRT (vs. no CRT) among patients ≥75 years old? ≥80 years old?]*

Author, Year [NCT]	Title	N	Objective
RCTs			
Thomas, 2016 (1)	Cardiac Resynchronization in Different Age Groups: A MADIT-CRT Long-Term Follow-Up Substudy	1,281	To assess the association of age on heart failure and death as a post hoc analysis of the MADIT-CRT follow-up study.
Prospective Observational			
Adelstein, 2016 (2)	Clinical outcomes in cardiac resynchronization therapy-defibrillator recipients 80 years of age and older	258	To compare clinical outcomes in CRT-defibrillator (CRT-D) recipients >/=80 and <80 years old.
Antonio, 2010 (3)	Cardiac resynchronization therapy is effective even in elderly patients with comorbidities	87	To compare the effects of cardiac resynchronization therapy (CRT) in elderly patients (> or =65 years) with younger patients and to assess the impact of comorbidities in CRT remodeling response.
Brambatti, 2013 (4)	Cardiac resynchronization therapy improves ejection fraction and cardiac remodelling regardless of patients' age	65	To define CRT-related benefits in terms of left ventricular ejection fraction (LVEF) improvement in two subgroups of patients (<75 and >/=75 years old) and test possible differences between these two groups.
de la Cruz, 2015 (5)	Comparison of pharmacological treatment alone versus treatment combined with cardiac resynchronization therapy in patients over 75 years	607	To review the role of cardiac resynchronization therapy (CRT) in patients aged >/=75 years.
Doring, 2018 (6)	Cardiac resynchronization therapy in the ageing population - With or without an implantable defibrillator?	775	To evaluate the impact of an additional ICD on survival in elderly CRT recipients.
Foley, 2008 (7)	Long-term effects of cardiac resynchronization therapy in octogenarians: a comparative study with a younger population	330	To review the effectiveness of CRT in octogenarians compared to younger patients.

Author, Year [NCT]	Title	N	Objective
Fumagalli, 2011 (8)	Comparison of the usefulness of cardiac resynchronization therapy in three age-groups (<65, 65-74 and >/=75 Years) (from the InSync/InSync ICD Italian Registry)	1,787	To evaluate the existence of age-related differences in clinical effectiveness and outcomes of cardiac resynchronization therapy (CRT), alone or in combination with an implantable cardioverter-defibrillator (CRT-D), in a large, real-world registry.
Guha, 2014 (9)	The impact of age on clinical outcomes following cardiac resynchronisation therapy	177	To evaluate the impact of age on clinical outcomes following CRT.
Hoke, 2014 (10)	Left ventricular reverse remodeling, device-related adverse events, and long-term outcome after cardiac resynchronization therapy in the elderly	798	To evaluate the effect of CRT, device-related adverse events, and long-term outcome after CRT among elderly patients.
Kobe, 2017 (11)	Complications and 1-year benefit of cardiac resynchronization therapy in patients over 75 years of age - Insights from the German Device Registry	1,199	To examine the conflicting evidence on cardiac resynchronization therapy (CRT) in older patients which has major practical relevance as heart failure prevalence increases with age.
Kron, 2009 (12)	Benefit of cardiac resynchronization in elderly patients: results from the Multicenter InSync Randomized Clinical Evaluation (MIRACLE) and Multicenter InSync ICD Randomized Clinical Evaluation (MIRACLE-ICD) trials	839	To examine the little data available for which specifically address the effects of CRT in the elderly (>65).
Laish-Farkash, 2017 (13)	Morbidity and mortality with cardiac resynchronization therapy with pacing vs. with defibrillation in octogenarian patients in a real-world setting	246	To test if among octogenarians eligible for cardiac resynchronization therapy, CRT-P confers similar morbidity and mortality benefits as CRT-D.
Olechowski, 2015 (14)	Is cardiac resynchronisation therapy feasible, safe and beneficial in the very elderly?	439	To evaluate whether cardiac resynchronisation therapy (CRT) implantation was feasible and safe in octogenarians and the association with symptoms.
Penn, 2011 (15)	Improved outcome with preventive cardiac resynchronization therapy in the elderly: a MADIT-CRT substudy	1,820	To investigate the limited data that exist on the effectiveness of cardiac resynchronization therapy with defibrillator (CRT-D) in patients with mild HF symptoms in an elderly population.

Author, Year [NCT]	Title	N	Objective
Sardu, 2014 (16)	Impact of diabetes mellitus on the clinical response to cardiac resynchronization therapy in elderly people	72	To investigate the functional role of T2DM on the effectiveness of CRT at advanced age.
Suleiman, 2014 (17)	Clinical characteristics and outcomes of elderly patients treated with an implantable cardioverter-defibrillator or cardiac resynchronization therapy in a real-world setting: data from the Israeli ICD Registry	2,807	To provide real-world data regarding outcomes associated with device-based therapy in a large cohort of elderly patients enrolled in the Israeli ICD Registry.
Verbrugge, 2013 (18)	Response to cardiac resynchronization therapy in elderly patients (>/=70 years) and octogenarians	220	To investigate whether these benefits can be extrapolated to older patients, typically not included in randomized clinical trials.
Completed Studies (ClinicalTrials.gov)			
NCT00387803	Safety and Effectiveness of Cardiac Resynchronization Therapy With Defibrillation	581	Completed. The purpose of this study was to determine if cardiac resynchronization therapy when combined with defibrillation is safe and effective in the treatment of symptomatic heart failure. Patients enrolled received a device with cardiac resynchronization therapy (CRT) and defibrillation. Patients were randomized to CRT on or off for up to six months and evaluated for mortality, hospitalization, and functional outcomes including exercise capacity, quality of life, symptomatic status, and echocardiographic analysis.

Author, Year [NCT]	Title	N	Objective
NCT00271154	REsynchronization reVErses Remodeling in Systolic Left vEntricular Dysfunction (REVERSE)	684	Completed. Heart failure is a progressive disease that decreases the pumping action of the heart. This may cause a backup of fluid in the heart and may result in heart beat changes. When there are changes in the heart beat sometimes an implantable heart device is used to control the rate and rhythm of the heart beat. The purpose of the REVERSE clinical trial is to determine whether pacing in both the left and right ventricles using Cardiac Resynchronization Therapy (CRT) can help slow the progression of heart failure in people who have mild or previous symptoms and poor heart pumping function. This kind of therapy has previously been shown to reduce symptoms and improve exercise capacity in people with more advanced forms of heart failure.
NCT01294449	Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy Post Approval Registry	394	Completed. MADIT-CRT PAR is an FDA mandated follow-up registry for patients that participated in the MADIT-CRT IDE study examining long-term mortality. The registry is designed to determine the long-term mortality benefit as a result of Cardiac Resynchronization Therapy with Defibrillation (CRT-D) vs. Implantable Cardioverter Defibrillator (ICD) therapy in the MADIT-CRT study patient population. The registry will collect data on patients that previously participated at MADIT-CRT sites within the US through five years of participation from their original enrollment in the MADIT-CRT IDE study (MADIT-CRT IDE: NCT00180271).

Author, Year [NCT]	Title	N	Objective
NCT00251251	Resynchronization/Defibrillation for Ambulatory Heart Failure Trial	1,798	Completed. Congestive heart failure (CHF) is a common health problem that leads to frequent hospitalizations and an increased death rate. In spite of advances in drug therapy, it remains a significant public health problem. Recently, a new therapy has been developed for advanced heart failure patients with a ventricular conduction abnormality. This new therapy, called cardiac resynchronization (CRT), is a device which stimulates the atrium, the right ventricle, and the left ventricle providing synchronization of the contraction of the heart chambers. It is the addition of this therapy to an implantable cardioverter defibrillator (ICD) that will be evaluated in this study. This study will compare whether the implantation of this new therapy device, in combination with an implantable cardioverter defibrillator, will reduce total mortality and hospitalizations for CHF.
NCT00180258	Comparison of Medical Therapy, Pacing and Defibrillation in Heart Failure	2,200	Completed. The purpose of this study is to determine whether combined mortality and hospitalization in heart failure patients receiving optimal pharmacologic therapy can be reduced by combining optimal pharmacologic therapy and 1) biventricular pacing therapy alone or 2) biventricular pacing with defibrillation. Evaluation of new therapies for the treatment of heart failure should address mortality, morbidity, hospitalization, and cardiac symptoms and function when compared to standard pharmacologic therapy. The COMPANION trial is designed to address all of these objectives.

Author, Year [NCT]	Title	N	Objective
NCT01434615	Medtronic South Asian Systolic Heart Failure Registry	502	Completed. The purpose of this study is to (a) characterize the current management of patients with systolic heart failure (HF) in South Asia following an educational intervention of current guidelines and delivery of disease management tools and (b) to characterize the effect of current therapy on clinical outcomes in patients managed by tertiary care centers across South Asia. Current therapy includes characterization of the post market performance of any market released Medtronic cardiac resynchronization therapy (CRT) or cardiac resynchronization therapy plus implantable cardiac defibrillator (CRT-D) system for cardiac resynchronization therapy (CRT).
NCT00170300	Care-HF CArdiac Resynchronization in Heart Failure	813	Completed. The CARE-HF trial evaluates the effects of Cardiac Resynchronization (CR) therapy on the mortality and morbidity of patients with heart failure due to left ventricular systolic dysfunction already receiving diuretics and optimal medical therapy.
NCT00132977	RethinQ Study - Evaluating Pacing in Heart Failure Patients	250	Completed. The investigational portion of this trial involves the implantation of a market-approved CRT implantable cardioverter defibrillator (CRT-D) system in patients who do not meet the current criteria for a CRT implant. In order to receive a CRT-D implant today, patients must have heart failure symptoms, have a weakened heart muscle, and have uncoordinated pumping of the heart. To demonstrate this uncoordinated pumping of the heart, a test (electrocardiogram [ECG]) is done. It is believed that by using a different test (echocardiogram) to measure whether this uncoordinated pumping is present, more patients will be identified that will benefit from CRT-D therapy. This study will look at whether patients identified by using this echocardiogram test show a benefit from having this CRT-D therapy.
Ongoing Studies (ClinicalTrials.gov)			

Author, Year [NCT]	Title	N	Objective
NCT03031847	Cardiac Resynchronization in the Elderly	50	Recruiting. This pilot will enroll 50 HF patients (age ≥ 75 years) undergoing CRT device implantation at the hospitals of the University of Pittsburgh Medical Center, Duke University, Ohio State University, and the VA Pittsburgh Healthcare System. Patients will be randomized to CRT-P versus CRT-D and followed until study end. Rates of patient screening, enrollment, randomization, and retention as well as cost of care will be examined. The results of this pilot study will inform the design of a large pivotal non-inferiority trial and will be necessary for its success. Patients who refuse participation in the randomized pilot trial will be asked to enroll in a prospective observational cohort. Characteristics of patients who choose CRT-P vs. CRT-D will be compared and patients' level of satisfaction with their device decision will be measured.

Subtable 2. Published and ongoing studies potentially relevant to Evidence Gap 4 *[What is the relationship between gender, QRS morphology and duration, and outcomes for patients with either CRT-D or ICD?]*

Author, Year [NCT]	Title	N	Objective
RCTs			
Arshad, 2011 (19)	Cardiac resynchronization therapy is more effective in women than in men: the MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy) trial	1,820	To investigate the factors related to sex-specific outcomes for death and heart failure events in the MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy) trial.
Goldenberg, 2014 (20)	Survival with cardiac-resynchronization therapy in mild heart failure	1,691	To evaluate the effect of CRT-D on long-term survival in the MADIT-CRT population.
Jamerson, 2014 (21)	Early procedure-related adverse events by gender in MADIT-CRT	1,790	To investigate the type and frequency of procedure-related adverse events among those enrolled in MADIT-CRT and identified clinical predictors for gender-specific events.
Tang, 2010 (22)	Cardiac-resynchronization therapy for mild-to-moderate heart failure	1,798	To evaluate whether adding CRT to an ICD and optimal medical therapy might reduce mortality and morbidity among such patients.

Author, Year [NCT]	Title	N	Objective
Zareba, 2011 (23)	Effectiveness of Cardiac Resynchronization Therapy by QRS Morphology in the Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy (MADIT-CRT)	1,817	To determine whether QRS morphology identifies patients who benefit from cardiac resynchronization therapy with a defibrillator (CRT-D) and whether it influences the risk of primary and secondary end points in patients.
Prospective Observational			
Ahsan, 2013 (24)	An 8-year single-centre experience of cardiac resynchronisation therapy: procedural success, early and late complications, and left ventricular lead performance	402	To determine procedural success and early and late complications in CRT patients.
Amit, 2014 (25)	Sex differences in implantable cardioverter-defibrillator implantation indications and outcomes: lessons from the Nationwide Israeli-ICD Registry	3,544	To evaluate the indications for ICD implantation as well as outcomes in implanted women vs. men.
Biton, 2015 (26)	Long-term outcome with cardiac resynchronization therapy in mild heart failure patients with left bundle branch block from US and Europe MADIT-CRT	1,263	To compare the baseline clinical characteristics and clinical and echocardiographic long-term clinical response to CRT-D between MADIT-CRT patients with LBBB who were enrolled in USA (n = 871) and European centers (n = 392).
Biton, 2015 (27)	Sex Differences in Long-Term Outcomes With Cardiac Resynchronization Therapy in Mild Heart Failure Patients With Left Bundle Branch Block	1,281	To evaluate long-term clinical outcome of heart failure (HF) or death, death, and HF alone by sex and QRS duration (dichotomized at 150 ms) in left bundle-branch block patients with CRT with defibrillator backup (CRT-D) versus implantable cardioverter-defibrillator (ICD) only.
Cheng, 2012 (28)	Potential mechanisms underlying the effect of gender on response to cardiac resynchronization therapy: insights from the SMART-AV multicenter trial	846	To describe the effects of gender on response to CRT and to explore potential mechanisms behind these differences.
Gillis, 2014 (29)	Impact of cardiac resynchronization therapy on hospitalizations in the Resynchronization-Defibrillation for Ambulatory Heart Failure trial	682	To report the impact of cardiac resynchronization therapy (CRT) on hospitalizations in patients randomized to implantable cardioverter-defibrillator (ICD) or ICD-CRT in the Resynchronization-Defibrillation for Ambulatory Heart Failure Trial (RAFT).

Author, Year [NCT]	Title	N	Objective
Leyva, 2011 (30)	Female gender is associated with a better outcome after cardiac resynchronization therapy	550	To determine whether female gender influences long-term clinical outcome, symptomatic response as well as echocardiographic response after CRT.
Mooyaart, 2011 (31)	Comparison of long-term survival of men versus women with heart failure treated with cardiac resynchronization therapy	578	To elucidate the gender-related differences in long-term survival after CRT.
Providencia, 2016 (32)	Primary Prevention Implantable Cardioverter Defibrillator (ICD) Therapy in Women-Data From a Multicenter French Registry	5,539	To examine the sex differences in subjects' characteristics and outcomes using a large multicenter cohort of consecutive patients referred for ICD implantation for primary prevention (2002-2012), in ischemic and nonischemic cardiomyopathy.
Schuchert, 2013 (33)	Gender-related safety and efficacy of cardiac resynchronization therapy	393	To determine whether gender has an effect on the outcome of heart failure patients undergoing cardiac resynchronisation therapy.
Sciarra, 2018 (34)	Patients with left bundle branch block and left axis deviation show a specific left ventricular asynchrony pattern: Implications for left ventricular lead placement during CRT implantation	30	To assess if LBBB and LAD patients show a specific pattern of mechanical asynchrony.
Serdoz, 2011 (35)	Predictors for restoration of normal left ventricular function in response to cardiac resynchronization therapy measured at time of implantation	75	To find prognostic factors of full clinical and echocardiographic responses (i.e., >/=50% left ventricular ejection fraction [LVEF] and New York Heart Association class I) after 1 year of CRT.
Stabile, 2009 (36)	Long-term outcomes of CRT-PM versus CRT-D recipients	233	To compare the rates of all-cause mortality in recipients of cardiac resynchronization therapy devices with (CRT-PM) versus with defibrillator (CRT-D).
Tompkins, 2017 (37)	Sex Differences in Inappropriate ICD Device Therapies: MADIT-II and MADIT-CRT	610	To compare the frequency of inappropriate therapies (IT) between men and women enrolled in MADIT II and MADIT-CRT.
Van Bommel 2009 (38)	Characteristics of heart failure patients associated with good and poor response to cardiac resynchronization therapy: a PROSPECT (Predictors of Response to CRT) sub-analysis	286	To investigate the relationship between baseline characteristics and measures of response to CRT.

Author, Year [NCT]	Title	N	Objective
Varma, 2017 (39)	Sex-Specific Response to Cardiac Resynchronization Therapy: Effect of Left Ventricular Size and QRS Duration in Left Bundle Branch Block	130	To assess the impact of body and heart size on sex-specific cardiac resynchronization therapy (CRT) response rate, according to QRS duration (QRSd) as a continuum
Wilcox, 2014 (40)	Clinical effectiveness of cardiac resynchronization and implantable cardioverter-defibrillator therapy in men and women with heart failure: findings from IMPROVE HF	8,936	To determine the clinical effectiveness of CRT and ICD therapy as a function of sex in outpatients with heart failure and reduced ejection fraction
Xu, 2012 (41)	Cardiac resynchronization therapy: do women benefit more than men?	728	To investigate women are underrepresented in cardiac resynchronization therapy (CRT) trials. Whether there is a gender difference in the benefit derived from CRT has not been well studied.
Completed Studies (ClinicalTrials.gov)			
NCT00180271	MADIT-CRT: Multicenter Automatic Defibrillator Implantation With Cardiac Resynchronization Therapy	1,820	Completed. The MADIT-CRT trial is designed to determine if combined implantable cardiac defibrillator (ICD)-cardiac resynchronization therapy (CRT-D) will reduce the risk of mortality and heart failure (HF) events by approximately 25%, in subjects who are in New York Heart Association (NYHA) functional Class II with non-ischemic or ischemic cardiomyopathy and subjects who are in NYHA functional Class I with ischemic cardiomyopathy, left ventricular dysfunction (ejection fraction [EF] < or = 0.30), and prolonged intraventricular conduction (QRS duration > or = 130 ms).

Author, Year [NCT]	Title	N	Objective
NCT00271154	REsynchronization reVErses Remodeling in Systolic Left vEntricular Dysfunction (REVERSE)	684	Completed. Heart failure is a progressive disease that decreases the pumping action of the heart. This may cause a backup of fluid in the heart and may result in heart beat changes. When there are changes in the heart beat sometimes an implantable heart device is used to control the rate and rhythm of the heart beat. The purpose of the REVERSE clinical trial is to determine whether pacing in both the left and right ventricles using Cardiac Resynchronization Therapy (CRT) can help slow the progression of heart failure in people who have mild or previous symptoms and poor heart pumping function. This kind of therapy has previously been shown to reduce symptoms and improve exercise capacity in people with more advanced forms of heart failure.
NCT01294449	Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy Post Approval Registry	394	Completed. MADIT-CRT PAR is an FDA mandated follow-up registry for patients that participated in the MADIT-CRT IDE study examining long-term mortality. The registry is designed to determine the long-term mortality benefit as a result of Cardiac Resynchronization Therapy with Defibrillation (CRT-D) vs. Implantable Cardioverter Defibrillator (ICD) therapy in the MADIT-CRT study patient population. The registry will collect data on patients that previously participated at MADIT-CRT sites within the US through five years of participation from their original enrollment in the MADIT-CRT IDE study (MADIT-CRT IDE: NCT00180271).

Author, Year [NCT]	Title	N	Objective
NCT00251251	Resynchronization/Defibrillation for Ambulatory Heart Failure Trial	1,798	Completed. Congestive heart failure (CHF) is a common health problem that leads to frequent hospitalizations and an increased death rate. In spite of advances in drug therapy, it remains a significant public health problem. Recently, a new therapy has been developed for advanced heart failure patients with a ventricular conduction abnormality. This new therapy, called cardiac resynchronization (CRT), is a device which stimulates the atrium, the right ventricle, and the left ventricle providing synchronization of the contraction of the heart chambers. It is the addition of this therapy to an implantable cardioverter defibrillator (ICD) that will be evaluated in this study. This study will compare whether the implantation of this new therapy device, in combination with an implantable cardioverter defibrillator, will reduce total mortality and hospitalizations for CHF.
NCT00180258	Comparison of Medical Therapy, Pacing and Defibrillation in Heart Failure	2,200	Completed. The purpose of this study is to determine whether combined mortality and hospitalization in heart failure patients receiving optimal pharmacologic therapy can be reduced by combining optimal pharmacologic therapy and 1) biventricular pacing therapy alone or 2) biventricular pacing with defibrillation. Evaluation of new therapies for the treatment of heart failure should address mortality, morbidity, hospitalization, and cardiac symptoms and function when compared to standard pharmacologic therapy. The COMPANION trial is designed to address all of these objectives.

Author, Year [NCT]	Title	N	Objective
NCT01434615	Medtronic South Asian Systolic Heart Failure Registry	502	Completed. The purpose of this study is to (a) characterize the current management of patients with systolic heart failure (HF) in South Asia following an educational intervention of current guidelines and delivery of disease management tools and (b) to characterize the effect of current therapy on clinical outcomes in patients managed by tertiary care centers across South Asia. Current therapy includes characterization of the post market performance of any market released Medtronic cardiac resynchronization therapy (CRT) or cardiac resynchronization therapy plus implantable cardiac defibrillator (CRT-D) system for cardiac resynchronization therapy (CRT).
Ongoing Studies (ClinicalTrials.gov)			

Author, Year [NCT]	Title	N	Objective
NCT02493907	Corrected Left Ventricular Electrical Delay Predicting Response to Cardiac Resynchronization Therapy	60	Recruiting. Cardiac resynchronization therapy (CRT) is a well-established treatment for patients with severe systolic heart failure (HF) and ventricular desynchronization. Despite the consistently observed structural and functional improvements as well as reductions in HF events and mortality in large multicenter randomized trials, 30% patients remain classified as nonresponders. Present evidences showed that QRS duration was the most effective parameter to predict responsivity of CRT in patients with severe HF. But some studies showed that QRS duration could be influenced by obesity and gender. Accordingly, the simple QRS interval width of body surface electrocardiograph should not be the most satisfactory parameter for screening patients suitable for CRT. Recent study showed that left ventricular electrical delay, as measured by the time from the onset of QRS to the LV electrogram peak (QLV), predicted CRT response. At long QLV intervals, atrioventricular optimization (AVO) can increase the likelihood of structural response to CRT. However, it is unclear whether it is suitable for Chinese patients. The investigators would like to validate this relation in a Chinese population and explore if a corrected QLV might do better to predict the responsivity of CRT.
NCT02344420	Clinical Investigation on Differences in the Magnitude of CRT Response in WOmen Versus MEN	494	Recruiting. BIOWOMEN is a study designed to compare the Cardiac Resynchronization Therapy (CRT) response rate in a Heart Failure (HF) population with an equal distribution of men and women. Different clinical variables will be collected (QRSd, Left Bundle Brunch Block (LBBB), HF etiology…) and compared in order to demonstrate that women may respond even better than men.

Subtable 3. Published and ongoing studies potentially relevant to Evidence Gap 5 *[What is the effectiveness of CRT among patients with paroxysmal, persistent, and permanent AF?]*

Author, Year [NCT]	Title	N	Objective
RCTs			
Brignole, 2011 (42)	Cardiac resynchronization therapy in patients undergoing atrioventricular junction ablation for permanent atrial fibrillation: a randomized trial	186	To examine whether CRT was superior to conventional right ventricular (RV) pacing in reducing heart failure (HF) events.
Brignole, 2018 (43)	A randomized controlled trial of atrioventricular junction ablation and cardiac resynchronization therapy in patients with permanent atrial fibrillation and narrow QRS	102	To test our hypothesis that atrioventricular (AV) junction ablation in conjunction biventricular pacing [cardiac resynchronization (CRT)] pacing is superior to pharmacological rate-control therapy in reducing heart failure (HF) and hospitalization in patients with permanent atrial fibrillation (AF) and narrow QRS.
Healey, 2012 (44)	Cardiac resynchronization therapy in patients with permanent atrial fibrillation: results from the Resynchronization for Ambulatory Heart Failure Trial (RAFT)	229	To determine if cardiac resynchronization (CRT) prolongs survival in patients with systolic heart failure and QRS prolongation and atrial fibrillation
Plummer, 2018 (45)	A novel algorithm increases the delivery of effective cardiac resynchronization therapy during atrial fibrillation: The CRTee randomized crossover trial	71	To determine whether eCRTAF increases the amount of effective CRT delivered during AF compared to a currently available rate regularization algorithm.
Prospective Observational			
Abreu, 2017 (46)	Does permanent atrial fibrillation modify response to cardiac resynchronization therapy in heart failure patients?	101	To compare CRT response in patients in AF and in sinus rhythm (SR).
Aktas, 2009 (47)	Effect of biventricular pacing during a ventricular sensed event	32	To examine the effect of biventricular pacing during a ventricular sensed event.
Brignole, 2012 (48)	Predictors of clinical efficacy of 'Ablate and Pace' therapy in patients with permanent atrial fibrillation	171	To evaluate the 2-year clinical improvement after 'Ablate and Pace' therapy and to identify the variables able to influence the efficacy of this therapy in patients with permanent atrial fibrillation (AF).

Author, Year [NCT]	Title	N	Objective
Dong, 2010 (49)	Atrioventricular nodal ablation predicts survival benefit in patients with atrial fibrillation receiving cardiac resynchronization therapy	154	To assess the impact of AVN ablation on clinical and survival outcomes in a large atrial fibrillation and heart failure population that met the current indication for CRT and to determine whether AVN ablation is an independent predictor of survival in CRT recipients
Himmel, 2012 (50)	A strategy to achieve CRT response in permanent atrial fibrillation without obligatory atrioventricular node ablation	230	To evaluate the benefit of CRT in permanent AF with and without AVN ablation.
Kalscheur, 2017 (51)	Outcomes of cardiac resynchronization therapy in patients with intermittent atrial fibrillation or atrial flutter in the COMPANION trial	1,180	To describe CRT outcomes in patients with IAF/AFL and advanced HF.
Marques, 2016 (52)	Triple-site pacing for cardiac resynchronization in permanent atrial fibrillation - Acute phase results from a prospective observational study	40	To examine the effects of triple-site (Tri-V) vs. biventricular (Bi-V) pacing on hemodynamics and QRS duration in patients with permanent afib.
Nakajima, 2018 (53)	Development of Heart Failure From Transient Atrial Fibrillation Attacks in Responders to Cardiac Resynchronization Therapy	22	To investigate transient atrial fibrillation (AF) attacks themselves and the efficacy of cardiac resynchronization therapy (CRT) in patients with intermittent AF.
Tolosana, 2012 (54)	Cardiac resynchronization therapy in patients with permanent atrial fibrillation. Is it mandatory to ablate the atrioventricular junction to obtain a good response?	202	To compare the CRT response of patients in sinus rhythm (SR) vs. AF.
Uğurlu, 2018 (55)	Subclinical atrial fibrillation frequency and associated parameters in patients with cardiac resynchronization therapy	194	To examine subclinical atrial fibrillation frequency and associated parameters in patients with CRT.
Wilton, 2011 (56)	Association of rate-controlled persistent atrial fibrillation with clinical outcome and ventricular remodelling in recipients of cardiac resynchronization therapy	93	To examine whether patients with persistent atrial fibrillation (AF) obtain the same degree of benefit with cardiac resynchronization therapy (CRT) as those in sinus rhythm remains unclear.
Wo, 2011 (57)	Cardiac resynchronization therapy in patients with and without atrial fibrillation	56	To review the benefits of CRT in patients with atrial fibrillation (AF)
Completed Studies (ClinicalTrials.gov)			

Author, Year [NCT]	Title	N	Objective
NCT00111527	APAF: Assessment of Cardiac Resynchronization Therapy in Patients With Permanent Atrial Fibrillation	458	Completed. A suboptimal level of resynchronization (cardiac resynchronization therapy [CRT]) achieved in many patients with actual standards and techniques based on tissue-Doppler echocardiography could be more effective to obtain better CRT results. Eligible patients who successfully received atrioventricular (AV) junction ablation and biventricular (BiV) pacing are randomised to a comparison between a strategy of right ventricular (RV) apical pacing with delayed CRT based on clinical indications with a strategy of early optimal CRT based on an echocardiographic stratification.
NCT00268294	Restoring Sinus Rhythm With Cardiac Resynchronization in Patients With Atrial Fibrillation (ReSync AF)	20	Completed. The purpose of this study is to characterize the impact of cardiac resynchronization therapy versus cardiac resynchronization therapy with atrial therapies on the incidence, duration and termination of atrial tachyarrhythmias.
NCT00251251	Resynchronization/Defibrillation for Ambulatory Heart Failure Trial	1,798	Completed. Congestive heart failure (CHF) is a common health problem that leads to frequent hospitalizations and an increased death rate. In spite of advances in drug therapy, it remains a significant public health problem. Recently, a new therapy has been developed for advanced heart failure patients with a ventricular conduction abnormality. This new therapy, called cardiac resynchronization (CRT), is a device which stimulates the atrium, the right ventricle, and the left ventricle providing synchronization of the contraction of the heart chambers. It is the addition of this therapy to an implantable cardioverter defibrillator (ICD) that will be evaluated in this study. This study will compare whether the implantation of this new therapy device, in combination with an implantable cardioverter defibrillator, will reduce total mortality and hospitalizations for CHF.
Ongoing Studies (ClinicalTrials.gov)			

Author, Year [NCT]	Title	N	Objective
NCT01994252	Resynchronization/Defibrillation for Ambulatory Heart Failure Trial in Patients With Permanent Atrial Fibrillation	200	Recruiting. In these HF patients who are in AF all of the time, who would otherwise be a suitable candidate for an implantable defibrillator to prevent sudden cardiac death, we would like to determine whether adding pacing of both ventricles will reduce heart size (left ventricular end systolic volume index LVESVi) as measured by ultrasound, which can improve its function and help the heart pump more efficiently. Other studies have shown that adding pacing to both ventricles is of benefit in HF patients with mild to moderate symptoms and have a regular heart rhythm. The Investigators now want to explore if this therapy will benefit those patients with a permanent irregular heart rhythm (AF).

Subtable 4. Published and ongoing studies potentially relevant to Evidence Gap 6 *[What is the association between comorbid diseases (e.g., chronic kidney disease, chronic lung disease, atrial fibrillation, diabetes mellitus, arterial and pulmonary hypertension, right ventricular dysfunction, and patients on dialysis) as well as the burden of comorbidities and the effectiveness of CRT-P and CRT-D?]*

Author, Year [NCT]	Title	N	Objective
RCTs			
Daimee, 2015 (58)	Long-Term Outcomes With Cardiac Resynchronization Therapy in Patients With Mild Heart Failure With Moderate Renal Dysfunction	1,820	To determine the impact of renal function on long-term outcomes with cardiac resynchronization therapy with defibrillator among patients with mild heart failure (HF).
Szepietowska, 2015 (59)	Effect of Cardiac Resynchronization Therapy in Patients With Insulin-Treated Diabetes Mellitus	1,278	To analyze the risk for death, HF alone, combined end point HF/death, and ventricular tachycardia/ventricular fibrillation (VT/VF) in patients with mild HF without DM and in those with DM, further stratified by the presence of insulin treatment.
Tang, 2010 (22)	Cardiac-resynchronization therapy for mild-to-moderate heart failure	1,798	To evaluate whether adding CRT to an ICD and optimal medical therapy might reduce mortality and morbidity among such patients.
Prospective Observational			

Author, Year [NCT]	Title	N	Objective
Bai, 2008 (60)	Mortality of heart failure patients after cardiac resynchronization therapy: identification of predictors	542	To compare (CRT-D vs CRT-P) in a large CHF population and seeks to identify predictors of death in patients with different comorbidities.
Bogdan, 2015 (61)	Clinical Outcomes in Patients with Severe Renal Dysfunction Including Dialysis Following Defibrillator Implantation	2,289	To evaluate outcomes associated with the severity of renal dysfunction with or without dialysis
Boriani, 2009 (62)	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	1,480	To analyse the effectiveness of cardiac resynchronization therapy (CRT) in patients with valvular heart disease (a subset not specifically investigated in randomized controlled trials) in comparison with ischaemic heart disease or dilated cardiomyopathy patients.
Campbell, 2013 (63)	Right ventricular function, pulmonary pressure estimation, and clinical outcomes in cardiac resynchronization therapy	1,820	To determine whether therapy with CRT is influenced by or affects RV function and to define the relationship between RV function and outcomes
Damy, 2013 (64)	Interplay between right ventricular function and cardiac resynchronization therapy: an analysis of the CARE-HF trial (Cardiac Resynchronization-Heart Failure)	813	To investigate the impact of cardiac resynchronization therapy (CRT) on right ventricular (RV) function and the influence of RV dysfunction on the echocardiographic and clinical response to CRT among patients enrolled in the CARE-HF (Cardiac Resynchronization-Heart Failure) trial.
D'Andrea, 2009 (65)	Right ventricular myocardial function in patients with either idiopathic or ischemic dilated cardiomyopathy without clinical sign of right heart failure: effects of cardiac resynchronization therapy	110	To detect RV myocardial function in DCM using two-dimensional (2D) strain echocardiography and to assess the effects of cardiac resynchronization therapy (CRT) on RV myocardial strain during a 6-month follow-up.
Dominguez-Rodriguez, 2015 (66)	The impact of frailty in older patients with non-ischaemic cardiomyopathy after implantation of cardiac resynchronization therapy defibrillator	102	To look at frailty status impact that is unknown in patients with non-ischaemic cardiomyopathy after cardiac resynchronization therapy.

Author, Year [NCT]	Title	N	Objective
Friedman, 2015 (67)	Comparative Effectiveness of CRT-D Versus Defibrillator Alone in HF Patients With Moderate-to-Severe Chronic Kidney Disease	10,946	To assess the real-world comparative effectiveness of CRT with defibrillator (CRT-D) versus implantable cardioverter-defibrillator (ICD) alone in CRT-eligible patients with moderate-to-severe CKD.
George, 2012 (68)	Effectiveness of cardiac resynchronization therapy in diabetic patients with ischemic and nonischemic cardiomyopathy	552	To identify differences in response to cardiac resynchronization therapy with a defibrillator (CRT-D) among DM patients with ischemic or nonischemic cardiomyopathy.
Goldenberg, 2010 (69)	Relation between renal function and response to cardiac resynchronization therapy in Multicenter Automatic Defibrillator Implantation Trial--Cardiac Resynchronization Therapy (MADIT-CRT)	1,803	To test our hypothesis that assessment of markers of prerenal failure may help identify mildly symptomatic HF patients with diminished effective circulating blood volume who will benefit from CRT.
Herscovici, 2013 (70)	Risk factors and outcomes associated with the development of myocardial ischemic events in patients who receive cardiac resynchronization therapy	1,045	To evaluate risk factors for the development of ischemic events (IEs) among patients with ischemic cardiomyopathy (IC) who receive cardiac resynchronization therapy with a defibrillator (CRT-D) and their effect on the efficacy of the device.
Himmel, 2012 (50)	A strategy to achieve CRT response in permanent atrial fibrillation without obligatory atrioventricular node ablation	230	The aim of this study was to evaluate the benefit of CRT in permanent AF with and without AVN ablation.
Hoke, 2014 (10)	Left ventricular reverse remodeling, device-related adverse events, and long-term outcome after cardiac resynchronization therapy in the elderly	798	To evaluate the effect of CRT, device-related adverse events, and long-term outcome after CRT among elderly patients.
Hosoda, 2012 (71)	Impact of renal insufficiency on long-term clinical outcome in patients with heart failure treated by cardiac resynchronization therapy	67	To investigate the uncertainty in long-term clinical outcome of cardiac resynchronization therapy (CRT) in Japanese HF patients with renal insufficiency.

Author, Year [NCT]	Title	N	Objective
Kowalczyk, 2014 (72)	Contrast-induced acute kidney injury in patients undergoing cardiac resynchronization therapy-incidence and prognostic importance. Sub-analysis of data from randomized TRUST CRT trial	100	To assess the incidence, natural course and prognostic importance of this syndrome in CRT recipients.
Kubala, 2017 (73)	Utility of Frailty Assessment for Elderly Patients Undergoing Cardiac Resynchronization Therapy	151	To evaluate the impact of frailty in the elderly on response to cardiac resynchronization therapy (CRT).
Kutyifa, 2018 (74)	Comparison of Long-Term Survival Benefits With Cardiac Resynchronization Therapy in Patients With Mild Heart Failure With Versus Without Diabetes Mellitus (from the Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy [MADIT-CRT])	1,368	To investigate whether HF remission in DM patients with CRT-D translates into reduced mortality.
Mangiavacchi, 2008 (75)	Insulin-treated type 2 diabetes is associated with a decreased survival in heart failure patients after cardiac resynchronization therapy	447	To investigate the effect of diabetes and insulin treatment on outcome after CRT.
Martin, 2011 (76)	Cardiac resynchronization therapy reduces the risk of cardiac events in patients with diabetes enrolled in the multicenter automatic defibrillator implantation trial with cardiac resynchronization therapy (MADIT-CRT)	1,817	To investigate the limited data on whether the presence of diabetes mellitus (DM) influences the benefit of cardiac resynchronization with defibrillator therapy (CRT-D) in heart failure (HF) patients.
Mathew, 2012 (77)	Chronic kidney disease and cardiac remodelling in patients with mild heart failure: results from the REsynchronization reVErses Remodeling in Systolic Left vEntricular Dysfunction (REVERSE) study	610	To evaluate the effect of CKD on left ventricular (LV) remodelling among patients with mild heart failure.

Author, Year [NCT]	Title	N	Objective
Nakajima, 2018 (53)	Development of Heart Failure From Transient Atrial Fibrillation Attacks in Responders to Cardiac Resynchronization Therapy	22	To investigate transient atrial fibrillation (AF) attacks themselves and the efficacy of cardiac resynchronization therapy (CRT) in patients with intermittent AF.
Santangelo, 2011 (78)	Functional and clinical implications of cardiac resynchronization therapy on outcomes of diabetic patients with heart failure	68	To compare functional and structural changes of the left ventricle and long-term clinical outcomes in diabetic and nondiabetic patients with heart failure undergoing cardiac resynchronization therapy (CRT).
Sardu, 2014 (16)	Impact of diabetes mellitus on the clinical response to cardiac resynchronization therapy in elderly people	72	To investigate the functional role of T2DM on the effectiveness of CRT at advanced age.
Schaer, 2013 (79)	Changes in renal function over time in patients with cardiac resynchronisation therapy	284	To describe changes in glomerular filtration rate (GFR) from baseline compared with 1 and 2 years after CRT implantation.
Scuteri, 2009 (80)	Relevance of echocardiographic evaluation of right ventricular function in patients undergoing cardiac resynchronization therapy	44	To determine whether RV function might influence response to cardiac resynchronization therapy (CRT).
Singal, 2015 (81)	Renal Response in Patients with Chronic Kidney Disease Predicts Outcome Following Cardiac Resynchronization Therapy	260	To examine renal improvement after cardiac resynchronization therapy (CRT) and its potential impact on clinical outcomes, especially in patients with severe CKD.
Sredniawa, 2009 (82)	Sleep apnoea as a predictor of mid- and long-term outcome in patients undergoing cardiac resynchronization therapy	71	To assess the impact of baseline apnoea-hypopnoea index (AHI) on mid-term outcome and its change after 6 months of cardiac resynchronization therapy (CRT) on remote outcome.
Stabile, 2009 (36)	Long-term outcomes of CRT-PM versus CRT-D recipients	233	To compare the rates of all-cause mortality in recipients of cardiac resynchronization therapy devices with (CRT-PM) versus with defibrillator (CRT-D).
Szepietowska, 2016 (83)	Metabolic syndrome is associated with different clinical outcome after cardiac resynchronization therapy in patients with ischemic and non-ischemic cardiomyopathy	1,262	To evaluate the associations between obesity and metabolic features and the clinical outcome after cardiac resynchronization with defibrillator therapy (CRT-D), compared to an implantable cardioverter defibrillator (ICD).

Author, Year [NCT]	Title	N	Objective
Van Bommel 2011 (84)	Impaired renal function is associated with echocardiographic nonresponse and poor prognosis after cardiac resynchronization therapy	490	To investigate the effect of renal function on left ventricular (LV) reverse remodeling and long-term outcome after cardiac resynchronization therapy (CRT), and to explore the relation between LV reverse remodeling and changes in renal function at 6-month follow-up.
van Everdingen 2017 (85)	Echocardiographic Prediction of Cardiac Resynchronization Therapy Response Requires Analysis of Both Mechanical Dyssynchrony and Right Ventricular Function: A Combined Analysis of Patient Data and Computer Simulations	122	To investigate how RV dysfunction influences the association between mechanical dyssynchrony and left ventricular (LV) volumetric remodeling following CRT.
Verbrugge, 2013 (18)	Response to cardiac resynchronization therapy in elderly patients (>/=70 years) and octogenarians	220	To investigate whether these benefits can be extrapolated to older patients, typically not included in randomized clinical trials.
Completed Studies (ClinicalTrials.gov)			
NCT03077139	Cardiac Resynchronization Therapy in Pulmonary Hypertension	6	Completed. This study is being conducted to determine whether patients with advanced pulmonary hypertension when treated with cardiac resynchronization therapy improve hemodynamically and/or receive clinical benefit. This study aims to determine whether stimulating earlier activation of the failing right ventricle in pulmonary hypertension reduces the effects of interventricular dependence in human subjects, thereby improving overall cardiac function and symptoms in patients with pulmonary hypertension and right ventricle failure with NYHA Class 3-4 symptoms.

Author, Year [NCT]	Title	N	Objective
NCT03282136	Incretin and CRTd.	500	Completed. Incretin therapy is a treatment for type 2 diabetes (T2DM) affected by heart failure (HF). In this study the investigators will recruit T2DM patients affected by HF with depressed ejection fraction and treated by Cardiac resynchronization therapy (CRT). These patients will randomly be treated by incretin v/s conventional hypoglicemic drugs. In this patients investigators will report at follow up CRT-d responders rate, mortality, and hospital admission for HF worsening. Incretin may reduce hospital admissions for HF in T2DM v/s conventional hypoglicemic drugs.
NCT00208806	Resynchronization Therapy in Young Patients With and Without CHD	50	Completed. The hearts of children grow fast. It is important to be able to know if the pacemaker or problems from dilated cardiomyopathy are causing any changes in the heart that might cause problems. We expect to be able to use information we learn from this study to improve how we use pacemakers in the future to avoid problems that can happen over time.
NCT02164721	Multicenter Automatic Defibrillator Implantation Trial - Chemotherapy-Induced Cardiomyopathy	30	Active, not recruiting. The purpose of this trial or study is to determine if cardiac resynchronization therapy (CRT) can be a benefit to people who have impaired heart function due to past treatment with chemotherapy and/or chest radiation. The investigators are looking to enroll approximately 30 eligible subjects with heart failure in this trial. All patients enrolled and registered in the study will be implanted with a cardiac resynchronization therapy device that includes an implantable cardiac defibrillator (CRT-D). Clinical histories, physical exams, and external device testing will be collected both at the time of enrollment in the trial and during follow-up study visits. Following implantation of the CRT-D, patients will be contacted by phone at 3 months and will have a scheduled clinic visit follow-up at 6 months.

Author, Year [NCT]	Title	N	Objective
NCT00251251	Resynchronization/Defibrillation for Ambulatory Heart Failure Trial	1,798	Completed. Congestive heart failure (CHF) is a common health problem that leads to frequent hospitalizations and an increased death rate. In spite of advances in drug therapy, it remains a significant public health problem. Recently, a new therapy has been developed for advanced heart failure patients with a ventricular conduction abnormality. This new therapy, called cardiac resynchronization (CRT), is a device which stimulates the atrium, the right ventricle, and the left ventricle providing synchronization of the contraction of the heart chambers. It is the addition of this therapy to an implantable cardioverter defibrillator (ICD) that will be evaluated in this study. This study will compare whether the implantation of this new therapy device, in combination with an implantable cardioverter defibrillator, will reduce total mortality and hospitalizations for CHF.
NCT00180258	Comparison of Medical Therapy, Pacing and Defibrillation in Heart Failure	2,200	Completed. The purpose of this study is to determine whether combined mortality and hospitalization in heart failure patients receiving optimal pharmacologic therapy can be reduced by combining optimal pharmacologic therapy and 1) biventricular pacing therapy alone or 2) biventricular pacing with defibrillation. Evaluation of new therapies for the treatment of heart failure should address mortality, morbidity, hospitalization, and cardiac symptoms and function when compared to standard pharmacologic therapy. The COMPANION trial is designed to address all of these objectives.

Author, Year [NCT]	Title	N	Objective
NCT01434615	Medtronic South Asian Systolic Heart Failure Registry	502	Completed. The purpose of this study is to (a) characterize the current management of patients with systolic heart failure (HF) in South Asia following an educational intervention of current guidelines and delivery of disease management tools and (b) to characterize the effect of current therapy on clinical outcomes in patients managed by tertiary care centers across South Asia. Current therapy includes characterization of the post market performance of any market released Medtronic cardiac resynchronization therapy (CRT) or cardiac resynchronization therapy plus implantable cardiac defibrillator (CRT-D) system for cardiac resynchronization therapy (CRT).
NCT00170300	Care-HF CArdiac Resynchronization in Heart Failure	813	Completed. The CARE-HF trial evaluates the effects of Cardiac Resynchronization (CR) therapy on the mortality and morbidity of patients with heart failure due to left ventricular systolic dysfunction already receiving diuretics and optimal medical therapy.
NCT03095196	Multipolar CRT-d and Diabetes	190	Completed. One hundred and ninety five T2DM patients will receive a CRT-d treatment. Randomly the study population will receive a CRT-d via multipolar left ventricle (LV) lead pacing (n 99 as Multipolar group), v/s a CRT-d via bipolar LV pacing (n 96, as Bipolar group). These patients will be followed by clinical, and instrumental assessment, and telemetric device control at follow up. Study design will be to evaluate, in failing heart T2DM patients, cardiac deaths, all cause deaths, arrhythmic events, CRT-d responders rate, hospitalizations for HF worsening, phrenic nerve stimulation (PNS), and LV catheter dislodgment events (and re-intervention for LV catheter re-positioning), comparing multipolar CRT-d v/s bipolar CRT-d group of patients at follow up.

Author, Year [NCT]	Title	N	Objective
NCT00846001	Resynchronization Surgery Combined Unified Efficacy	178	Completed. The purpose of the study is to compare survivability and efficacy of the patients with severe ischemic heart failure after coronary artery bypass grafting alone and coronary artery bypass grafting with single-step implantation of CRT system (CABG alone vs CABG + CRT)
NCT00180271	MADIT-CRT: Multicenter Automatic Defibrillator Implantation With Cardiac Resynchronization Therapy	1,820	Completed. The MADIT-CRT trial is designed to determine if combined implantable cardiac defibrillator (ICD)-cardiac resynchronization therapy (CRT-D) will reduce the risk of mortality and heart failure (HF) events by approximately 25%, in subjects who are in New York Heart Association (NYHA) functional Class II with non-ischemic or ischemic cardiomyopathy and subjects who are in NYHA functional Class I with ischemic cardiomyopathy, left ventricular dysfunction (ejection fraction [EF] < or = 0.30), and prolonged intraventricular conduction (QRS duration > or = 130 ms).
Ongoing Studies (ClinicalTrials.gov)			
NCT01970423	Sleep Apnea and CRT Upgrading	80	Recruiting. Cardiac resynchronization therapy may reduce central sleep apnea, but there is no prospective randomized study so far demonstrating such an effect in patients with conventional pacemaker undergoing upgrading to CRT because of heart failure.
NCT03494933	Re-evaluation of Optimal Re-synchronisation Therapy in Patients With Chronic Heart Failure	2,030	Recruiting. The objective of the study is to demonstrate that in patients with chronic heart failure who receive optimal medical treatment for this condition and have indication for Cardiac Resynchronisation Therapy, the implantation of a pacemaker (index group) is not inferior to defibrillator (control group) with respect to all-cause mortality.

Subtable 5. Published and ongoing studies potentially relevant to Evidence Gap 8 *[Does CRT benefit (compared to no CRT) vary based on QRS duration (<150ms vs ≥ 150ms)?]*

Author, Year [NCT]	Title	N	Objective
RCTs			
Tang, 2010 (22)	Cardiac-resynchronization therapy for mild-to-moderate heart failure	1798	To evaluate whether adding CRT to an ICD and optimal medical therapy might reduce mortality and morbidity among such patients.
Prospective Observational			
Birnie, 2013 (86)	Impact of QRS morphology and duration on outcomes after cardiac resynchronization therapy: Results from the Resynchronization-Defibrillation for Ambulatory Heart Failure Trial (RAFT)	1,483	To review the impact of QRS morphology and duration on the effectiveness of cardiac resynchronization therapy (CRT) which has been usually assessed separately. The interaction between these 2 simple ECG parameters and their effect on CRT has not been systematically assessed in a large-scale clinical trial.
Biton, 2015 (27)	Sex Differences in Long-Term Outcomes With Cardiac Resynchronization Therapy in Mild Heart Failure Patients With Left Bundle Branch Block	1,281	To evaluate long-term clinical outcome of heart failure (HF) or death, death, and HF alone by sex and QRS duration (dichotomized at 150 ms) in left bundle-branch block patients with CRT with defibrillator backup (CRT-D) versus implantable cardioverter-defibrillator (ICD) only.
Biton, 2018 (87)	Baseline adverse electrical remodeling and the risk for ventricular arrhythmia in Cardiac Resynchronization Therapy Recipients (MADIT CRT)	961	To examine baseline adverse electrical remodeling and the risk for ventricular arrhythmia in CRT Recipients.
Gasparini, 2014 (88)	Absolute survival after cardiac resynchronization therapy according to baseline QRS duration: a multinational 10-year experience: data from the Multicenter International CRT Study	3,319	To determine whether baseline QRS duration relates to the absolute survival after CRT.
Gervais, 2009 (89)	Surface electrocardiogram to predict outcome in candidates for cardiac resynchronization therapy: a sub-analysis of the CARE-HF trial	803 (409 with MT and CRT)	To examine whether baseline and follow-up electrocardiographic characteristics might predict long-term outcome

Author, Year [NCT]	Title	N	Objective
Gold, 2012 (90)	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	610	To assess the impact of baseline QRS duration and morphology and the change in QRS duration with pacing on CRT outcomes in mild heart failure
Goldenberg, 2011 (91)	Predictors of response to cardiac resynchronization therapy in the Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT)	1,761	To examine the combined assessment of factors that are associated with favorable reverse remodeling after cardiac resynchronization-defibrillator therapy (CRT-D) which can be used to predict clinical response to the device.
Gorcsan, 2010 (92)	Relationship of echocardiographic dyssynchrony to long-term survival after cardiac resynchronization therapy	229	To test the hypothesis that baseline dyssynchrony is associated with long-term survival after CRT.
Hudak, 2017 (93)	The effectiveness of CRT on improvement of survival of heart failure patients in real life clinical settings	680	To compare the survival of patients with HF and wide QRS after cardiac resynchronization therapy (CRT) with survival of HF patients with narrow QRS and to assess factors predictive of non-response to CRT.
Moss, 2009 (94)	Cardiac-resynchronization therapy for the prevention of heart-failure events	1,820	To determine whether cardiac-resynchronization therapy (CRT) with biventricular pacing would reduce the risk of death or heart-failure events in patients with mild cardiac symptoms, a reduced ejection fraction, and a wide QRS complex
Rickard, 2011 (95)	Predictors of response to cardiac resynchronization therapy in patients with a non-left bundle branch block morphology	850	To investigate Predictors of response to cardiac resynchronization therapy in patients with a non-left bundle branch block morphology
Risum, 2014 (96)	Assessment of mechanical dyssynchrony in cardiac resynchronization therapy	67	To investigate if echocardiographic methods for evaluation of mechanical dyssynchrony, reflecting this fundamental pathophysiologic change, could predict response to CRT.
Saba, 2014 (97)	Influence of QRS duration on outcome of death or appropriate defibrillator therapy by strategy of left ventricular lead placement in cardiac resynchronization therapy recipients	183	To examine whether a strategy of EG LV lead placement equally improves outcome in CRT recipients with wide (>/=150 ms) versus intermediate (120-149 ms) QRS duration.
Completed Studies (ClinicalTrials.gov)			

Author, Year [NCT]	Title	N	Objective
NCT00846001	Resynchronization Surgery Combined Unified Efficacy	178	Completed. The purpose of the study is to compare survivability and efficacy of the patients with severe ischemic heart failure after coronary artery bypass grafting alone and coronary artery bypass grafting with single-step implantation of CRT system (CABG alone vs CABG + CRT)
NCT00132977	RethinQ Study - Evaluating Pacing in Heart Failure Patients	250	Completed. The investigational portion of this trial involves the implantation of a market-approved CRT implantable cardioverter defibrillator (CRT-D) system in patients who do not meet the current criteria for a CRT implant. In order to receive a CRT-D implant today, patients must have heart failure symptoms, have a weakened heart muscle, and have uncoordinated pumping of the heart. To demonstrate this uncoordinated pumping of the heart, a test (electrocardiogram [ECG]) is done. It is believed that by using a different test (echocardiogram) to measure whether this uncoordinated pumping is present, more patients will be identified that will benefit from CRT-D therapy. This study will look at whether patients identified by using this echocardiogram test show a benefit from having this CRT-D therapy.
NCT01577446	Narrow QRS Ischemic Patients Treated With Cardiac Resynchronization Therapy (NARROW CRT)	120	Completed. Current recommendations require a QRS duration of ≥120ms as a condition for prescribing cardiac resynchronization therapy (CRT). This study was designed to test the hypothesis that patients with heart failure of ischemic origin, current indications for defibrillator implantation and QRS <120ms may benefit from CRT in the presence of marked mechanical dyssynchrony.

Author, Year [NCT]	Title	N	Objective
NCT00387803	Safety and Effectiveness of Cardiac Resynchronization Therapy With Defibrillation	581	Completed. The purpose of this study was to determine if cardiac resynchronization therapy when combined with defibrillation is safe and effective in the treatment of symptomatic heart failure. Patients enrolled received a device with cardiac resynchronization therapy (CRT) and defibrillation. Patients were randomized to CRT on or off for up to six months and evaluated for mortality, hospitalization, and functional outcomes including exercise capacity, quality of life, symptomatic status, and echocardiographic analysis.
NCT00251251	Resynchronization/Defibrillation for Ambulatory Heart Failure Trial	1798	Completed. Congestive heart failure (CHF) is a common health problem that leads to frequent hospitalizations and an increased death rate. In spite of advances in drug therapy, it remains a significant public health problem. Recently, a new therapy has been developed for advanced heart failure patients with a ventricular conduction abnormality. This new therapy, called cardiac resynchronization (CRT), is a device which stimulates the atrium, the right ventricle, and the left ventricle providing synchronization of the contraction of the heart chambers. It is the addition of this therapy to an implantable cardioverter defibrillator (ICD) that will be evaluated in this study. This study will compare whether the implantation of this new therapy device, in combination with an implantable cardioverter defibrillator, will reduce total mortality and hospitalizations for CHF.

Author, Year [NCT]	Title	N	Objective
NCT00180258	Comparison of Medical Therapy, Pacing and Defibrillation in Heart Failure	2200	Completed. The purpose of this study is to determine whether combined mortality and hospitalization in heart failure patients receiving optimal pharmacologic therapy can be reduced by combining optimal pharmacologic therapy and 1) biventricular pacing therapy alone or 2) biventricular pacing with defibrillation. Evaluation of new therapies for the treatment of heart failure should address mortality, morbidity, hospitalization, and cardiac symptoms and function when compared to standard pharmacologic therapy. The COMPANION trial is designed to address all of these objectives.
NCT01434615	Medtronic South Asian Systolic Heart Failure Registry	502	Completed. The purpose of this study is to (a) characterize the current management of patients with systolic heart failure (HF) in South Asia following an educational intervention of current guidelines and delivery of disease management tools and (b) to characterize the effect of current therapy on clinical outcomes in patients managed by tertiary care centers across South Asia. Current therapy includes characterization of the post market performance of any market released Medtronic cardiac resynchronization therapy (CRT) or cardiac resynchronization therapy plus implantable cardiac defibrillator (CRT-D) system for cardiac resynchronization therapy (CRT).
NCT00170300	Care-HF CArdiac Resynchronization in Heart Failure	813	Completed. The CARE-HF trial evaluates the effects of Cardiac Resynchronization (CR) therapy on the mortality and morbidity of patients with heart failure due to left ventricular systolic dysfunction already receiving diuretics and optimal medical therapy.

Author, Year [NCT]	Title	N	Objective
NCT00821938	Cardiac Resynchronization Therapy (CRT)-Narrow-dp/Dt-Study	30	Completed. Goal is to examine the efficy of Cardiac Resynchronization Therapy in heart failure patients with narrow QRS complex and optimized medical treatment but echocardiographic desynchronization detection as well as the positve increase of the intraoperative pressureincreasespeed in reverse remodelling and a secondary improvement of functional parameters

Subtable 6. Published and ongoing studies potentially relevant to Evidence Gap 11 *[What is the comparative safety and effectiveness of CRT compared with no CRT among patients with a LBBB and EF >35%?]*

Author, Year [NCT]	Title	N	Objective
Prospective Observational			
Biton, 2015 (27)	Sex Differences in Long-Term Outcomes With Cardiac Resynchronization Therapy in Mild Heart Failure Patients With Left Bundle Branch Block	1,281	To evaluate long-term clinical outcome of heart failure (HF) or death, death, and HF alone by sex and QRS duration (dichotomized at 150 ms) in left bundle-branch block patients with CRT with defibrillator backup (CRT-D) versus implantable cardioverter-defibrillator (ICD) only.
Daubert, 2009 (99)	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	262	To determine the long-term effects of cardiac resynchronization therapy (CRT) in the European cohort of patients enrolled in the REVERSE (Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction) trial.
Foley, 2009 (100)	Cardiac resynchronization therapy in patients with mildly impaired left ventricular function	157	To determine the unknown effects of cardiac resynchronization therapy (CRT) in patients with a left ventricular ejection fraction (LVEF) >35%. Because of its technical limitations, echocardiography (Echo) may underestimate LVEF, compared with cardiovascular magnetic resonance (CMR).

Author, Year [NCT]	Title	N	Objective
Kutyifa, 2013 (101)	The influence of left ventricular ejection fraction on the effectiveness of cardiac resynchronization therapy: MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy)	1,809	To evaluate the relationship between left ventricular (LV) ejection fraction and clinical outcome to cardiac resynchronization therapy (CRT) in mild heart failure patients enrolled in MADIT-CRT
Linde, 2013 (102)	Impact of ejection fraction on the clinical response to cardiac resynchronization therapy in mild heart failure	177	To evaluate outcomes in patients with EF >35% who receive CRT
Schuchert, 2014 (103)	Relationship between pre-implant ejection fraction and outcome after cardiac resynchronization therapy in symptomatic patients	366	To assess the relationship between pre-implant LVEF and outcome of patients with advanced heart failure who received cardiac resynchronization therapy (CRT).
Completed Studies (ClinicalTrials.gov)			
NCT00271154	REsynchronization reVErses Remodeling in Systolic Left vEntricular Dysfunction (REVERSE)	684	Completed. Heart failure is a progressive disease that decreases the pumping action of the heart. This may cause a backup of fluid in the heart and may result in heart beat changes. When there are changes in the heart beat sometimes an implantable heart device is used to control the rate and rhythm of the heart beat. The purpose of the REVERSE clinical trial is to determine whether pacing in both the left and right ventricles using Cardiac Resynchronization Therapy (CRT) can help slow the progression of heart failure in people who have mild or previous symptoms and poor heart pumping function. This kind of therapy has previously been shown to reduce symptoms and improve exercise capacity in people with more advanced forms of heart failure.
Ongoing Studies (ClinicalTrials.gov)			

Author, Year [NCT]	Title	N	Objective
NCT03338374	Cardiac Resynchronisation Therapy Versus Rate-responsive Pacing in Heart Failure With Preserved Ejection Fraction	10	Recruiting. The investigators plan to assess the feasibility of using a prospective cohort study to assess the incremental benefit of CRT over and above RRP in patients with HFpEF. 10 patients with HFpEF and insufficient heart rate will be recruited and will undergo exercise testing, heart scanning and symptom questionnaires. A biventricular pacemaker will be implanted and programmed to RRP for 12 weeks before repeating the tests. After this, the investigators will non-invasively programme the pacemaker to CRT for 12 weeks and repeat the functional tests. If incremental benefit is shown with CRT the echocardiograms will be analysed in detail to determine the mechanism of change.
NCT03420833	Metabolic Mapping and Cardiac Resynchronization	100	Recruiting. The purpose of this study is to gather information on the safety and effectiveness of cardiac resynchronization therapy (CRT) in patients who have mild heart failure (HF) and left bundle branch block (LBBB).

Subtable 7. Published and ongoing studies potentially relevant to Evidence Gap 13 *[What is the comparative safety and effectiveness of CRT-D versus CRT-P overall and among subgroups defined by cardiomyopathy etiology and QRS morphology?]*

Author, Year [NCT]	Title	N	Objective
RCTs			
Barsheshet, 2011 (104)	Response to preventive cardiac resynchronization therapy in patients with ischaemic and nonischaemic cardiomyopathy in MADIT-CRT	1,820	To evaluate the outcome of patients enrolled in MADIT-CRT by ischaemic and non-ischaemic aetiology of cardiomyopathy (ICM and non-ICM, respectively).
Linde, 2010 (105)	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	600	To determine the effects of cardiac resynchronization therapy (CRT) with respect to heart failure etiology among patients in the REVERSE (REsynchronization reVErses Remodeling in Systolic Left vEntricular Dysfunction) study.
Prospective Observational			

Author, Year [NCT]	Title	N	Objective
Ahsan, 2013 (24)	An 8-year single-centre experience of cardiac resynchronisation therapy: procedural success, early and late complications, and left ventricular lead performance	402	To determine procedural success and early and late complications in CRT patients.
Barra, 2018 (106)	Device complications with addition of defibrillation to cardiac resynchronisation therapy for primary prevention	3,008	To determine whether adding defibrillator to CRT in the primary prevention setting impacts risk of other acute and late device-related complications.
Boriani, 2009 (62)	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	1,480	To analyse the effectiveness of cardiac resynchronization therapy (CRT) in patients with valvular heart disease (a subset not specifically investigated in randomized controlled trials) in comparison with ischaemic heart disease or dilated cardiomyopathy patients.
Daubert, 2009 (99)	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	262	To determine the long-term effects of cardiac resynchronization therapy (CRT) in the European cohort of patients enrolled in the REVERSE (Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction) trial.
Di Biase 2008 (107)	The magnitude of reverse remodelling irrespective of aetiology predicts outcome of heart failure patients treated with cardiac resynchronization therapy	398	To assess the relationship between cardiac resynchronization therapy (CRT)-induced reverse remodelling and mortality during a long-term follow-up in a prospective observational study.
Doring, 2018 (6)	Cardiac resynchronization therapy in the ageing population - With or without an implantable defibrillator?	775	To evaluate the impact of an additional ICD on survival in elderly CRT recipients.
Drozd, 2017 (108)	Cardiac resynchronization therapy outcomes in patients with chronic heart failure: cardiac resynchronization therapy with pacemaker versus cardiac resynchronization therapy with defibrillator	795	To investigate the long-term prognosis of patients who received CRT-P or CRT-D.

Author, Year [NCT]	Title	N	Objective
George, 2012 (68)	Effectiveness of cardiac resynchronization therapy in diabetic patients with ischemic and nonischemic cardiomyopathy	552	To identify differences in response to cardiac resynchronization therapy with a defibrillator (CRT-D) among DM patients with ischemic or nonischemic cardiomyopathy.
Gold, 2013 (109)	Implantable defibrillators improve survival in patients with mildly symptomatic heart failure receiving cardiac resynchronization therapy: analysis of the long-term follow-up of remodeling in systolic left ventricular dysfunction (REVERSE)	419	To examine the little available data comparing mortality between 2 device types, CRT-pacemakers as well as those devices with defibrillator backup (CRT-D).
Laish-Farkash, 2017 (13)	Morbidity and mortality with cardiac resynchronization therapy with pacing vs. with defibrillation in octogenarian patients in a real-world setting	246	To test if among octogenarians eligible for cardiac resynchronization therapy, CRT-P confers similar morbidity and mortality benefits as CRT-D.
Marijon, 2015{Marijon, 2015 #548}	Causes-of-death analysis of patients with cardiac resynchronization therapy: an analysis of the CeRtiTuDe cohort study	1,705	To examine the cause-of-death analysis among CRT-P, compared with CRT-D
McLeod, 2011 (110)	Differential outcome of cardiac resynchronization therapy in ischemic cardiomyopathy and idiopathic dilated cardiomyopathy	503	To evaluate whether heart failure etiology (ischemic cardiomyopathy [ICM] vs nonischemic dilated cardiomyopathy [DCM]) was associated with CRT outcome and implantable cardioverter-defibrillator (ICD) shocks.
Morani, 2013 (111)	Cardiac resynchronization therapy-defibrillator improves long-term survival compared with cardiac resynchronization therapy-pacemaker in patients with a class IA indication for cardiac resynchronization therapy: data from the Contak Italian Registry	620	To compare the long-term prognosis of patients who received CRT-D or CRT-P according to class IA recommendations of the European Society of Cardiology (ESC) and who were enrolled in a multicentre prospective registry.
Mukherjee, 2016 (112)	Quantitative assessment of cardiac mechanical dyssynchrony and prediction of response to cardiac resynchronization therapy in patients with non-ischaemic dilated cardiomyopathy using equilibrium radionuclide angiography	32	To evaluate equilibrium radionuclide angiography (ERNA) in prediction of response to cardiac resynchronization therapy (CRT) in non-ischaemic dilated cardiomyopathy (DCM) patients.

Author, Year [NCT]	Title	N	Objective
Stabile, 2009 (36)	Long-term outcomes of CRT-PM versus CRT-D recipients	233	To compare the rates of all-cause mortality in recipients of cardiac resynchronization therapy devices with (CRT-PM) versus with defibrillator (CRT-D).
Szepietowska, 2016 (83)	Metabolic syndrome is associated with different clinical outcome after cardiac resynchronization therapy in patients with ischemic and non-ischemic cardiomyopathy	1,262	To evaluate the associations between obesity and metabolic features and the clinical outcome after cardiac resynchronization with defibrillator therapy (CRT-D), compared to an implantable cardioverter defibrillator (ICD).
Verbrugge, 2013 (113)	Cardiac resynchronization therapy with or without defibrillator: experience from a high-volume Belgian implantation centre	221	To describe the experience of a high-volume Belgian implantation centre with CRT with/without defibrillator (CRT-D/P)
Wang, 2018 (114)	Cardiac resynchronization therapy pacemakers versus defibrillators in older non-ischemic cardiomyopathy patients	135	To investigate the survival of recipients of CRT pacemakers (CRT-P) versus CRT ICDs (CRT-D) in a cohort of older (>/=75 years) NICM patients at our institution.
Wikstrom, 2009 (115)	The effects of aetiology on outcome in patients treated with cardiac resynchronization therapy in the CARE-HF trial	813	To investigate the relatively unknown effect of the underlying cause of cardiac dysfunction on the response to cardiac resynchronization therapy (CRT).
Zhang, 2009 (116)	Difference in long-term clinical outcome after cardiac resynchronisation therapy between ischaemic and non-ischaemic aetiologies of heart failure	119	To examine the impact of heart failure (HF) aetiology on long-term outcome after cardiac resynchronisation therapy (CRT).
Completed Studies (ClinicalTrials.gov)			
NCT00846001	Resynchronization Surgery Combined Unified Efficacy	178	Completed. The purpose of the study is to compare survivability and efficacy of the patients with severe ischemic heart failure after coronary artery bypass grafting alone and coronary artery bypass grafting with single-step implantation of CRT system (CABG alone vs CABG + CRT)

Author, Year [NCT]	Title	N	Objective
NCT00251251	Resynchronization/Defibrillation for Ambulatory Heart Failure Trial	1798	Completed. Congestive heart failure (CHF) is a common health problem that leads to frequent hospitalizations and an increased death rate. In spite of advances in drug therapy, it remains a significant public health problem. Recently, a new therapy has been developed for advanced heart failure patients with a ventricular conduction abnormality. This new therapy, called cardiac resynchronization (CRT), is a device which stimulates the atrium, the right ventricle, and the left ventricle providing synchronization of the contraction of the heart chambers. It is the addition of this therapy to an implantable cardioverter defibrillator (ICD) that will be evaluated in this study. This study will compare whether the implantation of this new therapy device, in combination with an implantable cardioverter defibrillator, will reduce total mortality and hospitalizations for CHF.
NCT00180258	Comparison of Medical Therapy, Pacing and Defibrillation in Heart Failure	2200	Completed. The purpose of this study is to determine whether combined mortality and hospitalization in heart failure patients receiving optimal pharmacologic therapy can be reduced by combining optimal pharmacologic therapy and 1) biventricular pacing therapy alone or 2) biventricular pacing with defibrillation. Evaluation of new therapies for the treatment of heart failure should address mortality, morbidity, hospitalization, and cardiac symptoms and function when compared to standard pharmacologic therapy. The COMPANION trial is designed to address all of these objectives.

Subtable 8. Published and ongoing studies potentially relevant to Evidence Gap 16 *[What is the association between AV node ablation (vs. no AV node ablation) and CRT effectiveness among patients with AF and history of AF with rapid ventricular response?]*

Author, Year [NCT]	Title	N	Objective
RCTs			

Author, Year [NCT]	Title	N	Objective
Brignole, 2011 (42)	Cardiac resynchronization therapy in patients undergoing atrioventricular junction ablation for permanent atrial fibrillation: a randomized trial	186	To examine whether CRT was superior to conventional right ventricular (RV) pacing in reducing heart failure (HF) events.
Brignole, 2018 (43)	A randomized controlled trial of atrioventricular junction ablation and cardiac resynchronization therapy in patients with permanent atrial fibrillation and narrow QRS	102	To test if atrioventricular (AV) junction ablation in conjunction biventricular pacing [cardiac resynchronization (CRT)] pacing is superior to pharmacological rate-control therapy in reducing heart failure (HF) and hospitalization in patients with permanent atrial fibrillation (AF) and narrow QRS.
Orlov, 2010 (117)	Biventricular pacing improves cardiac function and prevents further left atrial remodeling in patients with symptomatic atrial fibrillation after atrioventricular node ablation	108	To demonstrate superiority of BiV pacing in patients with AF after AV node ablation, to evaluate its effects on cardiac structure and function, and to investigate additional benefits of Closed Loop Stimulation
Prospective Observational			
Abreu, 2017 (46)	Does permanent atrial fibrillation modify response to cardiac resynchronization therapy in heart failure patients?	101	To compare CRT response in patients in AF and in sinus rhythm (SR).
Brignole, 2008 (118)	Usefulness of echo-guided cardiac resynchronization pacing in patients undergoing "ablate and pace" therapy for permanent atrial fibrillation and effects of heart rate regularization and left ventricular resynchronization	50	To test if optimized CRP guided by tissue Doppler echocardiography would exert an additive beneficial hemodynamic effect to that of rate regularization achieved through atrioventricular junction ablation.
Brignole, 2012 (48)	Predictors of clinical efficacy of 'Ablate and Pace' therapy in patients with permanent atrial fibrillation	171	To evaluate the 2-year clinical improvement after 'Ablate and Pace' therapy and to identify the variables able to influence the efficacy of this therapy in patients with permanent atrial fibrillation (AF).
Dong, 2010 (49)	Atrioventricular nodal ablation predicts survival benefit in patients with atrial fibrillation receiving cardiac resynchronization therapy	154	To assess the impact of AVN ablation on clinical and survival outcomes in a large atrial fibrillation and heart failure population that met the current indication for CRT and to determine whether AVN ablation is an independent predictor of survival in CRT recipients

Author, Year [NCT]	Title	N	Objective
Garcia, 2016 (119)	Mortality After Atrioventricular Nodal Radiofrequency Catheter Ablation With Permanent Ventricular Pacing in Atrial Fibrillation: Outcomes From a Controlled Nonrandomized Study	9,122	To examine the uncertain long-term outcomes after AVNA, especially in light of irreversible pacemaker dependence.
Kia, 2016 (120)	Left and right approach atrioventricular junctional ablation in patients with permanent Atrial fibrillation	109	To compare the outcome of 2 AVNA approaches in AF.
Palmisano, 2017 (121)	Effect of fixed-rate vs. rate-RESPONSIve pacing on exercise capacity in patients with permanent, refractory atrial fibrillation and left ventricular dysfunction treated with atrioventricular junction aBLation and bivEntricular pacing (RESPONSIBLE): a prospective, multicentre, randomized, single-blind study	60	To examine the outcomes in permanent AF patients with uncontrolled rate who had undergone AVJ ablation and biventricular pacing.
Tolosana, 2012 (54)	Cardiac resynchronization therapy in patients with permanent atrial fibrillation. Is it mandatory to ablate the atrioventricular junction to obtain a good response?	202	To compare the CRT response of patients in sinus rhythm (SR) vs. AF.
Completed Studies (ClinicalTrials.gov)			
NCT01181414	Spanish Atrial Fibrillation And Resynchronization Study	60	Completed. The aim of the present study is to compare the response to cardiac resynchronization therapy (CRT) in patients with chronic advanced heart failure and permanent atrial fibrillation (AF) depending on atrio ventricular junction (AVJ) is ablated or not.

Author, Year [NCT]	Title	N	Objective
NCT00251251	Resynchronization/Defibrillation for Ambulatory Heart Failure Trial	1798	Completed. Congestive heart failure (CHF) is a common health problem that leads to frequent hospitalizations and an increased death rate. In spite of advances in drug therapy, it remains a significant public health problem. Recently, a new therapy has been developed for advanced heart failure patients with a ventricular conduction abnormality. This new therapy, called cardiac resynchronization (CRT), is a device which stimulates the atrium, the right ventricle, and the left ventricle providing synchronization of the contraction of the heart chambers. It is the addition of this therapy to an implantable cardioverter defibrillator (ICD) that will be evaluated in this study. This study will compare whether the implantation of this new therapy device, in combination with an implantable cardioverter defibrillator, will reduce total mortality and hospitalizations for CHF.
NCT00111527	APAF: Assessment of Cardiac Resynchronization Therapy in Patients With Permanent Atrial Fibrillation	458	Completed. A suboptimal level of resynchronization (cardiac resynchronization therapy [CRT]) achieved in many patients with actual standards and techniques based on tissue-Doppler echocardiography could be more effective to obtain better CRT results. Eligible patients who successfully received atrioventricular (AV) junction ablation and biventricular (BiV) pacing are randomised to a comparison between a strategy of right ventricular (RV) apical pacing with delayed CRT based on clinical indications with a strategy of early optimal CRT based on an echocardiographic stratification.
Ongoing Studies (ClinicalTrials.gov)			

Author, Year [NCT]	Title	N	Objective
NCT01522898	Cardiac Resynchronisation Therapy and AV Nodal Ablation Trial in Atrial Fibrillation Patients (CAAN-AF)	590	Recruiting. In the current study, we aim to test the hypothesis that ablating the AV node, which controls electrical conduction from the heart's atria (top chamber) to its ventricles (lower chambers), will improve survival and heart failure symptoms in CRT patients with co-existent AF. The results are important, because they will provide a way of passing on the benefits of CRT, such as improved survival, less heart failure symptoms, and better quality of life, to heart failure patients who also suffer from AF.
NCT02137187	Atrioventricular Junction Ablation and Biventricular Pacing for Atrial Fibrillation and Heart Failure	1,830	Recruiting. There is evidence of superiority of AV junction ablation strategy over pharmacological therapy only for symptoms of atrial fibrillation, but not for heart failure, hospitalization, morbidity and mortality. Hypothesis of trial is that AV junction ablation is superior to pharmacological therapy as regard hospitalization and mortality

Subtable 9. Published and ongoing studies potentially relevant to Evidence Gap 17 *[What is the minimum percentage of biventricular pacing required for CRT-D to be superior to ICD?]*

Author, Year [NCT]	Title	N	Objective
RCTs			
Atwater, 2017 (122)	The electromechanical substrate for response to cardiac resynchronization therapy in patients with right bundle branch block	9	To compare the frequency of dyssynchrony on baseline echocardiogram in patients with RBBB
Ruwald, 2014 (123)	Association between frequency of atrial and ventricular ectopic beats and biventricular pacing percentage and outcomes in patients with cardiac resynchronization therapy	801	To determine if increased ectopic beats reduce the chance of high biventricular pacing percentage and are associated with subsequent adverse outcomes.
Prospective Observational			

Author, Year [NCT]	Title	N	Objective
Ruwald, 2015 (124)	The association between biventricular pacing and cardiac resynchronization therapy-defibrillator efficacy when compared with implantable cardioverter defibrillator on outcomes and reverse remodelling	1,219	To determine the threshold of BIV pacing percentage needed for CRT-D to be superior to ICD
Completed Studies (ClinicalTrials.gov)			
NCT00180271	MADIT-CRT: Multicenter Automatic Defibrillator Implantation With Cardiac Resynchronization Therapy	1820	Completed. The MADIT-CRT trial is designed to determine if combined implantable cardiac defibrillator (ICD)-cardiac resynchronization therapy (CRT-D) will reduce the risk of mortality and heart failure (HF) events by approximately 25%, in subjects who are in New York Heart Association (NYHA) functional Class II with non-ischemic or ischemic cardiomyopathy and subjects who are in NYHA functional Class I with ischemic cardiomyopathy, left ventricular dysfunction (ejection fraction [EF] < or = 0.30), and prolonged intraventricular conduction (QRS duration > or = 130 ms).
NCT00251251	Resynchronization/Defibrillation for Ambulatory Heart Failure Trial	1798	Completed. Congestive heart failure (CHF) is a common health problem that leads to frequent hospitalizations and an increased death rate. In spite of advances in drug therapy, it remains a significant public health problem. Recently, a new therapy has been developed for advanced heart failure patients with a ventricular conduction abnormality. This new therapy, called cardiac resynchronization (CRT), is a device which stimulates the atrium, the right ventricle, and the left ventricle providing synchronization of the contraction of the heart chambers. It is the addition of this therapy to an implantable cardioverter defibrillator (ICD) that will be evaluated in this study. This study will compare whether the implantation of this new therapy device, in combination with an implantable cardioverter defibrillator, will reduce total mortality and hospitalizations for CHF.

Author, Year [NCT]	Title	N	Objective
NCT00271154	REsynchronization reVErses Remodeling in Systolic Left vEntricular Dysfunction (REVERSE)	684	Completed. Heart failure is a progressive disease that decreases the pumping action of the heart. This may cause a backup of fluid in the heart and may result in heart beat changes. When there are changes in the heart beat sometimes an implantable heart device is used to control the rate and rhythm of the heart beat. The purpose of the REVERSE clinical trial is to determine whether pacing in both the left and right ventricles using Cardiac Resynchronization Therapy (CRT) can help slow the progression of heart failure in people who have mild or previous symptoms and poor heart pumping function. This kind of therapy has previously been shown to reduce symptoms and improve exercise capacity in people with more advanced forms of heart failure.

Subtable 10. Published and ongoing studies potentially relevant to Evidence Gap 18 *[What is the optimal percentage of biventricular pacing required to optimize outcomes among CRT recipients?]*

Author, Year [NCT]	Title	N	Objective
RCTs			
Liang, 2018 (125)	Cessation of pacing in super-responders of cardiac resynchronization therapy: A randomized controlled trial	21	To examine the consequence of cessation of biventricular pacing in super-responders of cardiac resynchronization therapy (CRT)
Ruwald, 2014 (123)	Association between frequency of atrial and ventricular ectopic beats and biventricular pacing percentage and outcomes in patients with cardiac resynchronization therapy	801	To determine if increased ectopic beats reduce the chance of high biventricular pacing percentage and are associated with subsequent adverse outcomes.
Prospective Observational			
Ghotbi, 2015 (126)	Optimal Cardiac Resynchronization Therapy Pacing Rate in Non-Ischemic Heart Failure Patients: A Randomized Crossover Pilot Trial	12	To investigate the impact of changing basal pacing frequencies on autonomic nerve function, cardiopulmonary exercise capacity and self-perceived quality of life (QoL).

Author, Year [NCT]	Title	N	Objective
Mazurek, 2016 (127)	Do we need to monitor the percentage of biventricular pacing day by day?	304	To assess the value of daily remote monitoring in identifying prognostically critical burden of low CRT%.
Varma, 2017 (128)	Influence of automatic frequent pace-timing adjustments on effective left ventricular pacing during cardiac resynchronization therapy	60	To compare the morphological consistency of ventricular depolarizations and percentage effective LV pacing in CRT patients randomized to aCRT vs. echo-optimization.
Xu, 2013 (129)	Predictive factors and clinical effect of optimized cardiac resynchronization therapy	65	To assess the effectiveness of cardiac resynchronization therapy (CRT) by intracardiac delay optimization using echocardiography
Completed Studies (ClinicalTrials.gov)			
NCT00746356	Safety and Efficacy of Automatic Testing Feature in New ICDs and CRT-Ds	128	Completed. This study is a prospective, non-randomized, multi-center clinical trial that will assess the safety and effectiveness of investigational models of the Promote™ RF CRT-D and Current™ RF ICD devices. These new ICD and CRT-D devices have new features that allow the device to periodically check how much energy is needed to pace a patient's heart and to automatically adjust the amount of energy used to pace the heart.
NCT00251251	Resynchronization/Defibrillation for Ambulatory Heart Failure Trial	1,798	Completed. Congestive heart failure (CHF) is a common health problem that leads to frequent hospitalizations and an increased death rate. In spite of advances in drug therapy, it remains a significant public health problem. Recently, a new therapy has been developed for advanced heart failure patients with a ventricular conduction abnormality. This new therapy, called cardiac resynchronization (CRT), is a device which stimulates the atrium, the right ventricle, and the left ventricle providing synchronization of the contraction of the heart chambers. It is the addition of this therapy to an implantable cardioverter defibrillator (ICD) that will be evaluated in this study. This study will compare whether the implantation of this new therapy device, in combination with an implantable cardioverter defibrillator, will reduce total mortality and hospitalizations for CHF.

Author, Year [NCT]	Title	N	Objective
NCT00846001	Resynchronization Surgery Combined Unified Efficacy	178	Completed. The purpose of the study is to compare survivability and efficacy of the patients with severe ischemic heart failure after coronary artery bypass grafting alone and coronary artery bypass grafting with single-step implantation of CRT system (CABG alone vs CABG + CRT)

Subtable 11. Published and ongoing studies potentially relevant to Evidence Gap 19 *[What is the association of PVC burden prior and post CRT-D implantation on outcomes? Any data on associations of PVC ablation and outcomes?]*

Author, Year [NCT]	Title	N	Objective
RCTs			
Aktas, 2016 (130)	The Burden and Morphology of Premature Ventricular Contractions and their Impact on Clinical Outcomes in Patients Receiving Biventricular Pacing in the Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy (MADIT-CRT)	146	To investigate the premature ventricular contractions (PVCs) frequently occur in patients with left ventricular dysfunction. However, there are limited data regarding the burden and morphologic characteristics of PVCs in patients receiving cardiac resynchronization therapy.
Mittal, 2014 (131)	The impact of nonsustained ventricular tachycardia on reverse remodeling, heart failure, and treated ventricular tachyarrhythmias in MADIT-CRT	1,000	To determine whether the presence of nonsustained ventricular tachycardia (NSVT) was predictive of clinical events in MADIT-CRT (multicenter automatic defibrillator implantation trial-cardiac resynchronization therapy) patients treated with CRT-defibrillator.
Prospective Observational			
Ruwald, 2018 (132)	Postimplantation ventricular ectopic burden and clinical outcomes in cardiac resynchronization therapy-defibrillator patients: a MADIT-CRT substudy	698	To describe the association between post-CRT implantation ectopic burden and subsequent risk of clinical outcomes.
Completed Studies (ClinicalTrials.gov)			

Author, Year [NCT]	Title	N	Objective
NCT00251251	Resynchronization/Defibrillation for Ambulatory Heart Failure Trial	1,798	Completed. Congestive heart failure (CHF) is a common health problem that leads to frequent hospitalizations and an increased death rate. In spite of advances in drug therapy, it remains a significant public health problem. Recently, a new therapy has been developed for advanced heart failure patients with a ventricular conduction abnormality. This new therapy, called cardiac resynchronization (CRT), is a device which stimulates the atrium, the right ventricle, and the left ventricle providing synchronization of the contraction of the heart chambers. It is the addition of this therapy to an implantable cardioverter defibrillator (ICD) that will be evaluated in this study. This study will compare whether the implantation of this new therapy device, in combination with an implantable cardioverter defibrillator, will reduce total mortality and hospitalizations for CHF.

Subtable 12. Published and ongoing studies potentially relevant to Evidence Gap 20 *[Is the PR interval associated with the effectiveness of CRT (vs. no CRT)?]*

Author, Year [NCT]	Title	N	Objective
RCTs			
Sonne, 2014 (98)	Three-dimensional echocardiographic optimization improves outcome in cardiac resynchronization therapy compared to ECG optimization: a randomized comparison	77	To examine a novel combination of Doppler echocardiography (DE) and three-dimensional echocardiography (3DE) for individualized AV- and VV-interval optimization compared to conventional electrocardiogram (ECG) optimization.
Prospective Observational			
Januszkiewicz, 2015 (133)	Prognostic implication of baseline PR interval in cardiac resynchronization therapy recipients	283	To compare clinical outcomes and response to CRT in patients with normal (<200 ms) vs prolonged (>/=200 ms) baseline PR interval.

Author, Year [NCT]	Title	N	Objective
Kutyifa, 2014 (134)	PR interval identifies clinical response in patients with non-left bundle branch block: a Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy substudy	537	To examine if baseline PR interval modulates clinical response to CRT-D therapy in patients with non-LBBB.
Kyriacou, 2018 (135)	Distinct impacts of heart rate and right atrial-pacing on left atrial mechanical activation and optimal AV delay in CRT	20	To investigate the impact of heart rate and right atrial-pacing on left atrial mechanical activation and optimal AV delay in CRT.
Lee, 2014 (136)	Effects of atrioventricular conduction delay on the outcome of cardiac resynchronization therapy	403	To examine first-degree atrioventricular (AV) block in relation to the outcome of cardiac resynchronization therapy (CRT).
Senfield, 2017 (137)	The Impact of the PR Interval in Patients Receiving Cardiac Resynchronization Therapy: Results From the REVERSE Study	582	To evaluate the impact of baseline PR interval on cardiac resynchronization therapy (CRT) outcomes
Sohaib, 2015 (138)	Atrioventricular Optimized Direct His Bundle Pacing Improves Acute Hemodynamic Function in Patients With Heart Failure and PR Interval Prolongation Without Left Bundle Branch Block	16	To investigate whether heart failure patients with narrow QRS duration (or right bundle branch block) but with long PR interval gain acute hemodynamic benefit from atrioventricular (AV) optimization.
Stockburger, 2016 (139)	Sustained clinical benefit of cardiac resynchronization therapy in non-LBBB patients with prolonged PR-interval: MADIT-CRT long-term follow-up	534	To study the long-term outcome of non-LBBB patients by baseline PR-interval with CRT-D versus ICD-only.
Completed Studies (ClinicalTrials.gov)			
NCT00387803	Safety and Effectiveness of Cardiac Resynchronization Therapy With Defibrillation	581	Completed. The purpose of this study was to determine if cardiac resynchronization therapy when combined with defibrillation is safe and effective in the treatment of symptomatic heart failure. Patients enrolled received a device with cardiac resynchronization therapy (CRT) and defibrillation. Patients were randomized to CRT on or off for up to six months and evaluated for mortality, hospitalization, and functional outcomes including exercise capacity, quality of life, symptomatic status, and echocardiographic analysis.

Author, Year [NCT]	Title	N	Objective
NCT00251251	Resynchronization/Defibrillation for Ambulatory Heart Failure Trial	1,798	Completed. Congestive heart failure (CHF) is a common health problem that leads to frequent hospitalizations and an increased death rate. In spite of advances in drug therapy, it remains a significant public health problem. Recently, a new therapy has been developed for advanced heart failure patients with a ventricular conduction abnormality. This new therapy, called cardiac resynchronization (CRT), is a device which stimulates the atrium, the right ventricle, and the left ventricle providing synchronization of the contraction of the heart chambers. It is the addition of this therapy to an implantable cardioverter defibrillator (ICD) that will be evaluated in this study. This study will compare whether the implantation of this new therapy device, in combination with an implantable cardioverter defibrillator, will reduce total mortality and hospitalizations for CHF.
NCT00170300	Care-HF CArdiac Resynchronization in Heart Failure	813	Completed. The CARE-HF trial evaluates the effects of Cardiac Resynchronization (CR) therapy on the mortality and morbidity of patients with heart failure due to left ventricular systolic dysfunction already receiving diuretics and optimal medical therapy.
NCT00846001	Resynchronization Surgery Combined Unified Efficacy	178	Completed. The purpose of the study is to compare survivability and efficacy of the patients with severe ischemic heart failure after coronary artery bypass grafting alone and coronary artery bypass grafting with single-step implantation of CRT system (CABG alone vs CABG + CRT)

Author, Year [NCT]	Title	N	Objective
NCT00132977	RethinQ Study - Evaluating Pacing in Heart Failure Patients	250	Completed. The investigational portion of this trial involves the implantation of a market-approved CRT implantable cardioverter defibrillator (CRT-D) system in patients who do not meet the current criteria for a CRT implant. In order to receive a CRT-D implant today, patients must have heart failure symptoms, have a weakened heart muscle, and have uncoordinated pumping of the heart. To demonstrate this uncoordinated pumping of the heart, a test (electrocardiogram [ECG]) is done. It is believed that by using a different test (echocardiogram) to measure whether this uncoordinated pumping is present, more patients will be identified that will benefit from CRT-D therapy. This study will look at whether patients identified by using this echocardiogram test show a benefit from having this CRT-D therapy.

Subtable 13. Published and ongoing studies potentially relevant to Evidence Gap 22 *[Is upgrade from a dual chamber pacemaker or defibrillator to a CRT device (vs. no upgrade) associated with HF free survival among patients with a high burden of RV pacing?]*

Author, Year [NCT]	Title	N	Objective
RCTs			
Bank, 2010 (140)	Intramural dyssynchrony and response to cardiac resynchronization therapy in patients with and without previous right ventricular pacing	80	To assess whether HF patients paced from the right ventricle (RVp) adversely remodel and respond to cardiac resynchronization therapy (CRT) in a similar way to HF patients without right ventricular pacing(nRVp).
Kanzaki, 2015 (141)	Comparison of the acute effects of right ventricular apical pacing and biventricular pacing in patients with heart failure	37	To investigate the effects of BiV pacing in heart failure patients under RV apical pacing.
Stockburger, 2011 (142)	Preventing ventricular dysfunction in pacemaker patients without advanced heart failure: results from a multicentre international randomized trial (PREVENT-HF)	108	To explore differences in left ventricular (LV) remodelling during RV apical vs. biventricular (BIV) pacing in patients with AV block.

Author, Year [NCT]	Title	N	Objective
Taborsky, 2013 (143)	TUGENDHAT: a pilot randomized study on effects of biventricular pacing in patients with bradycardia pacing indication and normal systolic function on heart failure, atrial fibrillation and quality of life (results of 12 month follow-up)	127	To investigate whether cardiac resynchronization therapy (CRT) using biventricular (BiV) pacing can prevent the development of left ventricular (LV) dysfunction, LV remodelling, worsening of the clinical status and quality of life in chronically RV paced patients with normal LV ejection fraction
Prospective Observational			
Chang, 2014 (144)	Remote past left ventricular function before chronic right ventricular pacing predicts responses to cardiac resynchronization therapy upgrade	25	To examine factors that could predict response to cardiac resynchronization therapy (CRT) upgrade in patients who developed heart failure (HF) after long-term right ventricular (RV) pacing.
Delnoy, 2009 (145)	Long-term clinical response of cardiac resynchronization after chronic right ventricular pacing	284	To evaluate the clinical and echocardiographic response to cardiac resynchronization therapy after years of chronic RV pacing.
Gierula, 2013 (146)	Cardiac resynchronization therapy in pacemaker-dependent patients with left ventricular dysfunction	50	To determine if cardiac resynchronization therapy (CRT) at the time of pulse generator replacement (PGR) is of benefit in patients with unavoidable RV pacing and LVSD.
Lipar, 2016 (147)	Short-term outcome of cardiac resynchronization therapy - a comparison between newly implanted and chronically right ventricle-paced patients	165	To evaluate the benefit of CRT in patients with chronic RV pacing in comparison to previously non-paced heart failure patients.
Paparella, 2010 (148)	Long-term effects of upgrading to biventricular pacing: differences with cardiac resynchronization therapy as primary indication	42	To assess the clinical and hemodynamic impact of upgrading to biventricular pacing in patients with severe HF and permanent RVAP in comparison with patients who had CRT implantation as initial therapy
Rickard, 2013 (149)	QRS narrowing is associated with reverse remodeling in patients with chronic right ventricular pacing upgraded to cardiac resynchronization therapy	112	To identify baseline characteristics associated with response in patients upgraded to CRT from chronic RVP.
Sideris, 2014 (150)	Upgrading pacemaker to cardiac resynchronization therapy: an option for patients with chronic right ventricular pacing and heart failure	37	To assess the benefit from upgrading to CRT in chronically RV-paced patients with a low left ventricular ejection fraction (LVEF<35%).

Author, Year [NCT]	Title	N	Objective
van Geldorp 2010 (151)	Beneficial effects of biventricular pacing in chronically right ventricular paced patients with mild cardiomyopathy	36	To investigate whether cardiac resynchronization therapy (CRT) by means of biventricular (BiV) pacing can improve left ventricular (LV) function, remodelling and clinical status in chronically right ventricular (RV) paced patients with mild cardiomyopathy.
Vatankulu, 2009 (152)	Effect of long-term resynchronization therapy on left ventricular remodeling in pacemaker patients upgraded to biventricular devices	26	To assess the effects of long-term ventricular resynchronization therapy on echocardiographic parameters of left ventricular (LV) remodeling in patients with moderate to severe heart failure who were upgraded from single- to biventricular pacing.
Completed Studies (ClinicalTrials.gov)			
NCT01466621	Response to Cardiac Resynchronization Therapy of Previously Right Ventricular Paced Heart Failure Patients	743	Completed. The present proposal is designed to investigate the response to CRT in patients who were previously paced from the right ventricle (RV). The negative physiologic and structural changes associated with chronic RV pacing are well documented, but patient response following upgrade to CRT after chronic RV pacing has not been well characterized in a large cohort.
NCT01652248	Pacemaker Upgrade to Cardiac Resynchronisation Therapy in Patients With Left Ventricular Dysfunction Dependant Upon Right Ventricular Pacing	50	Completed. Patients with pacemakers often have undiagnosed heart muscle weakness. When a pacemaker battery has run down, it is easily replaced by a short procedure. In those with heart muscle weakness, who use their pacemaker most of the time (rather than acting just as a back-up) the investigators want to find out if adding a further lead to their pacemaker system improves their heart's function, kidney function and exercise capacity.
NCT01609738	Left Ventricular Septum Pacing in Patients by Transvenous Approach Through the Inter-ventricular Septum	12	Completed. The purpose of this study is to translate the findings from preclinical studies to the clinical situation by investigating the feasibility, long-term lead stability and safety of LV septum pacing by transvenous approach through the inter-ventricular septum in patients.

Author, Year [NCT]	Title	N	Objective
NCT00267098	Biventricular Versus Right Ventricular Pacing in Heart Failure Patients With Atrioventricular Block (BLOCK HF)	918	Completed. Heart failure is a progressive disease that decreases the pumping action of the heart. This may cause a backup of fluid in the heart and may result in heart beat changes. When there are changes in the heartbeat, sometimes a pacemaker is used to control the rate and rhythm of the heartbeat. In this trial, the researchers will test if pacing both the left and right lower half of the heart (ventricles) will: • decrease the number of hospital and clinic visits due to heart failure symptoms • extend life • delay heart failure symptoms as compared to those who are paced in only one ventricle (the right ventricle)
NCT00875732	Choosing the Right Pacing Mode in Heart Failure - The CHOICE Trial	22	Completed. The aim of the study is to see if biventricular pacemakers offer any advantage over conventional pacemakers in patients with heart failure who require pacemakers. The endpoints will be the 6 minute walking distance along with markers of cardiovascular function. The investigators' hypothesis is that biventricular pacing is preferable to conventional pacing in these heart failure patients.

Subtable 14. Published and ongoing studies potentially relevant to Evidence Gap 24 *[What is the EF threshold at which CRT is superior to dual chamber pacing in high grade or complete AV block?]*

Author, Year [NCT]	Title	N	Objective
RCTs			
Albertsen, 2011 (153)	Adverse effect of right ventricular pacing prevented by biventricular pacing during long-term follow-up: a randomized comparison	50	To investigate whether biventricular (BIV) pacing preserves left ventricular ejection fraction (LVEF) and reduces LV dyssynchrony when compared with standard dual-chamber right ventricular (RV) pacing in consecutive patients with high-grade atrioventricular block during 3 years of pacing.

Author, Year [NCT]	Title	N	Objective
Curtis, 2013 (154)	Biventricular pacing for atrioventricular block and systolic dysfunction	691	To evaluate whether biventricular pacing might reduce mortality, morbidity, and adverse left ventricular remodeling in such patients.
Taborsky, 2013 (143)	TUGENDHAT: a pilot randomized study on effects of biventricular pacing in patients with bradycardia pacing indication and normal systolic function on heart failure, atrial fibrillation and quality of life (results of 12 month follow-up)	127	To investigate whether cardiac resynchronization therapy (CRT) using biventricular (BiV) pacing can prevent the development of left ventricular (LV) dysfunction, LV remodelling, worsening of the clinical status and quality of life in chronically RV paced patients with normal LV ejection fraction
Prospective Observational			
Curtis, 2016 (155)	Improvement in Clinical Outcomes With Biventricular Versus Right Ventricular Pacing: The BLOCK HF Study	691	To examine clinical outcomes, including clinical composite score, quality of life (QOL), and change in New York Heart Association (NYHA) functional classification in patients with AV block and CRT vs RV pacing
Martinelli 2010 (156)	Conventional versus biventricular pacing in heart failure and bradyarrhythmia: the COMBAT study	60	To compare BiVP versus RVP in patients with symptomatic heart failure (HF) and atrioventricular (AV) block.
Vatankulu, 2009 (152)	Effect of long-term resynchronization therapy on left ventricular remodeling in pacemaker patients upgraded to biventricular devices	26	To assess the effects of long-term ventricular resynchronization therapy on echocardiographic parameters of left ventricular (LV) remodeling in patients with moderate to severe heart failure who were upgraded from single- to biventricular pacing.
Completed Studies (ClinicalTrials.gov)			
NCT00267098	Biventricular Versus Right Ventricular Pacing in Heart Failure Patients With Atrioventricular Block (BLOCK HF)	918	Completed. Heart failure is a progressive disease that decreases the pumping action of the heart. This may cause a backup of fluid in the heart and may result in heart beat changes. When there are changes in the heartbeat, sometimes a pacemaker is used to control the rate and rhythm of the heartbeat. In this trial, the researchers will test if pacing both the left and right lower half of the heart (ventricles) will: • decrease the number of hospital and clinic visits due to heart failure symptoms • extend life delay heart failure symptoms as compared to those who are paced in only one ventricle (the right ventricle)

Author, Year [NCT]	Title	N	Objective
NCT00875732	Choosing the Right Pacing Mode in Heart Failure - The CHOICE Trial	22	Completed. The aim of the study is to see if biventricular pacemakers offer any advantage over conventional pacemakers in patients with heart failure who require pacemakers. The endpoints will be the 6 minute walking distance along with markers of cardiovascular function. The investigators' hypothesis is that biventricular pacing is preferable to conventional pacing in these heart failure patients.

Subtable 15. Published and ongoing studies potentially relevant to Evidence Gap 26 *[Does CRT (compared to ICD) improve survival in very advanced HF as demonstrated by NYHA class and/or LV size/function?]*

Author, Year [NCT]	Title	N	Objective
RCTs			
Cruz, 2017 (157)	Relationship of left ventricular global longitudinal strain with cardiac autonomic denervation as assessed by (123)I-mIBG scintigraphy in patients with heart failure with reduced ejection fraction submitted to cardiac resynchronization therapy : Assessment of cardiac autonomic denervation by GLS in patients with heart failure with reduced ejection fraction submitted to CRT	81	To examine the relationship between myocardial contractility assessed by global longitudinal strain (GLS) and AD assessed by (123)I-mIBG scintigraphy in advanced HF.
Gorcsan, 2016 (158)	Association of persistent or worsened echocardiographic dyssynchrony with unfavourable clinical outcomes in heart failure patients with narrow QRS width: a subgroup analysis of the EchoCRT trial	614	To test if persistent or worsening dyssynchrony is associated with unfavourable clinical outcomes
Prospective Observational			
Anand, 2009 (159)	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	1,520	To examine the risk of hospitalizations in CRT patients with advance HF patients.
Bank, 2012 (160)	Comparison of cardiac resynchronization therapy outcomes in patients with New York Heart Association functional class I/II versus III/IV heart failure	667	To examine the cardiac resynchronization therapy (CRT) benefits in New York Heart Association (NYHA) functional class I/II heart failure (HF) patients, but also investigate if similar outcomes in the real-world are unknown.
Bhattacharya, 2010 (161)	Role of cardiac resynchronization in end-stage heart failure patients requiring inotrope therapy	759	To evaluate echocardiographic parameters after 6 months of cardiac resynchronization therapy (CRT) as well as long-term outcome in patients with the left ventricular (LV) lead positioned at the site of latest activation (concordant LV lead position) as compared with that seen in patients with a discordant LV lead position.

Author, Year [NCT]	Title	N	Objective
Castel, 2010 (162)	Survival in New York Heart Association class IV heart failure patients treated with cardiac resynchronization therapy compared with patients on optimal pharmacological treatment	40	To evaluate the effect of CRT on urgent transplant-free survival in NYHA class IV patients treated with CRT, compared with medication-only treatment.
Gopinathannair, 2018 (163)	Cardiac resynchronization therapy and clinical outcomes in continuous flow left ventricular assist device recipients	488	To assess the impact of CRT on clinical outcomes in CF-LVAD patients.
Gorcsan, 2010 (92)	Relationship of echocardiographic dyssynchrony to long-term survival after cardiac resynchronization therapy	229	To test the hypothesis that baseline dyssynchrony is associated with long-term survival after CRT.
Haghjoo, 2009 (164)	Effect of right ventricular lead location on response to cardiac resynchronization therapy in patients with end-stage heart failure	73	To investigate whether optimizing the site for placement of the RV lead could further improve the long-term response to CRT in patients with advanced heart failure.
Haugaa, 2014 (165)	Mechanical dyssynchrony after cardiac resynchronization therapy for severely symptomatic heart failure is associated with risk for ventricular arrhythmias	266	To test the hypothesis that mechanical dyssynchrony after CRT-D is a risk factor for ventricular arrhythmias.
Lepillier, 2009 (166)	Relationship between New York Heart Association class change and ventricular tachyarrhythmia occurrence in patients treated with cardiac resynchronization plus defibrillator	332	To examine the added benefit of an implantable cardioverter defibrillator (ICD) in HF patients with CRT.
Richardson, 2018 (167)	Prospective Randomized Evaluation of Implantable Cardioverter-Defibrillator Programming in Patients With a Left Ventricular Assist Device	83	To determine if an ultra-conservative ICD programming strategy in patients with LVAD affects ICD shocks.
Rickard, 2015 (168)	Comparative Efficacy of Cardiac Resynchronization Therapy in Africans Americans Compared With European Americans	662	To compare reverse ventricular remodeling and long-term outcomes in AAs versus European Americans (EAs) with advanced heart failure who underwent CRT.
Schuchert, 2013 (169)	One-year outcome after CRT implantation in NYHA class IV in comparison to NYHA class III patients	405	To compare the outcome of heart failure patients in New York Heart Association (NYHA) class IV to that of NYHA class III patients 1 year after implantation of a CRT device.
Suleiman, 2015 (170)	Outcome of Patients with Advanced Heart Failure Who Receive Device-Based Therapy for Primary Prevention of Sudden Cardiac Death: Insights from the Israeli ICD Registry	913	To examine the effect of HF functional class on the outcome of patients who receive device therapy in a real-world setting.

Author, Year [NCT]	Title	N	Objective
Tayal, 2017 (171)	Interaction of Left Ventricular Remodeling and Regional Dyssynchrony on Long-Term Prognosis after Cardiac Resynchronization Therapy	260	To examine the impact of LV dilatation on the association of measures of dyssynchrony with long-term prognosis and resynchronization potential after cardiac resynchronization therapy (CRT) remains unclear.
Van Bommel 2010 (172)	Effect of cardiac resynchronization therapy in patients with New York Heart Association functional class IV heart failure	61	To evaluate the effects of CRT in patients with NYHA functional class IV heart failure.
Versteeg, 2011 (173)	Effect of cardiac resynchronization therapy-defibrillator implantation on health status in patients with mild versus moderate symptoms of heart failure	169	To examine the influence of baseline NYHA functional class on health status changes in the first 12 months after implantation of a CRT with defibrillator (CRT-D).
Completed Studies (ClinicalTrials.gov)			
NCT01294449	Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy Post Approval Registry	394	Completed. MADIT-CRT PAR is an FDA mandated follow-up registry for patients that participated in the MADIT-CRT IDE study examining long-term mortality. The registry is designed to determine the long-term mortality benefit as a result of Cardiac Resynchronization Therapy with Defibrillation (CRT-D) vs. Implantable Cardioverter Defibrillator (ICD) therapy in the MADIT-CRT study patient population. The registry will collect data on patients that previously participated at MADIT-CRT sites within the US through five years of participation from their original enrollment in the MADIT-CRT IDE study (MADIT-CRT IDE: NCT00180271).

Author, Year [NCT]	Title	N	Objective
NCT00251251	Resynchronization/Defibrillation for Ambulatory Heart Failure Trial	1,798	Completed. Congestive heart failure (CHF) is a common health problem that leads to frequent hospitalizations and an increased death rate. In spite of advances in drug therapy, it remains a significant public health problem. Recently, a new therapy has been developed for advanced heart failure patients with a ventricular conduction abnormality. This new therapy, called cardiac resynchronization (CRT), is a device which stimulates the atrium, the right ventricle, and the left ventricle providing synchronization of the contraction of the heart chambers. It is the addition of this therapy to an implantable cardioverter defibrillator (ICD) that will be evaluated in this study. This study will compare whether the implantation of this new therapy device, in combination with an implantable cardioverter defibrillator, will reduce total mortality and hospitalizations for CHF.

Author, Year [NCT]	Title	N	Objective
NCT00180258	Comparison of Medical Therapy, Pacing and Defibrillation in Heart Failure	2,200	Completed. The purpose of this study is to determine whether combined mortality and hospitalization in heart failure patients receiving optimal pharmacologic therapy can be reduced by combining optimal pharmacologic therapy and 1) biventricular pacing therapy alone or 2) biventricular pacing with defibrillation. Evaluation of new therapies for the treatment of heart failure should address mortality, morbidity, hospitalization, and cardiac symptoms and function when compared to standard pharmacologic therapy. The COMPANION trial is designed to address all of these objectives.
NCT00180271	MADIT-CRT: Multicenter Automatic Defibrillator Implantation With Cardiac Resynchronization Therapy	1,820	Completed. The MADIT-CRT trial is designed to determine if combined implantable cardiac defibrillator (ICD)-cardiac resynchronization therapy (CRT-D) will reduce the risk of mortality and heart failure (HF) events by approximately 25%, in subjects who are in New York Heart Association (NYHA) functional Class II with non-ischemic or ischemic cardiomyopathy and subjects who are in NYHA functional Class I with ischemic cardiomyopathy, left ventricular dysfunction (ejection fraction [EF] < or = 0.30), and prolonged intraventricular conduction (QRS duration > or = 130 ms).

Subtable 16. Published and ongoing studies potentially relevant to Evidence Gap 29 *[What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with improvement in quality of life and functional status in patients with CRT?]*

Author, Year [NCT]	Title	N	Objective
RCTs			
Cruz, 2017 (157)	Relationship of left ventricular global longitudinal strain with cardiac autonomic denervation as assessed by (123)I-mIBG scintigraphy in patients with heart failure with reduced ejection fraction submitted to cardiac resynchronization therapy : Assessment of cardiac autonomic denervation by GLS in patients with heart failure with reduced ejection fraction submitted to CRT	81	To examine the relationship between myocardial contractility assessed by global longitudinal strain (GLS) and AD assessed by (123)I-mIBG scintigraphy in advanced HF.
Gold, 2018 (174)	The rationale and design of the SMART CRT trial	726	To assess the efficacy of an atrioventricular optimization algorithm to improve reverse remodeling among patients undergoing cardiac resynchronization therapy (CRT) in the presence of interventricular electrical delay.
Gu, 2017 (175)	Repetitive optimizing left ventricular pacing configurations with quadripolar leads improves response to cardiac resynchronization therapy: A single-center randomized clinical trial	52	To investigate if repetitive optimizing left ventricular pacing configurations (LVPCs) with quadripolar leads (QUAD) can improve response to cardiac resynchronization therapy
Knappe, 2011 (176)	Dyssynchrony, contractile function, and response to cardiac resynchronization therapy	1,077	To test if a combined assessment of left ventricular (LV) dyssynchrony and contractile function by strain-based imaging would identify patients who would most benefit from CRT.
Kockova, 2018 (177)	Cardiac resynchronization therapy guided by cardiac magnetic resonance imaging: A prospective, single-centre randomized study (CMR-CRT)	99	To investigate the impact of cardiac magnetic resonance (CMR)-guided left ventricular (LV) lead placement on clinical outcomes and LV reverse remodelling in CRT recipients.
Liang, 2018 (125)	Cessation of pacing in super-responders of cardiac resynchronization therapy: A randomized controlled trial	21	To examine the consequence of cessation of biventricular pacing in super-responders of cardiac resynchronization therapy (CRT)

Author, Year [NCT]	Title	N	Objective
Miranda, 2012 (178)	Maximal electric separation-guided placement of right ventricular lead improves responders in cardiac resynchronization defibrillator therapy	60	To test if placement of the RV lead guided by maximal electric separation (MES) would improve response to cardiac resynchronization therapy compared with standard apical placement.
Mittal, 2014 (131)	The impact of nonsustained ventricular tachycardia on reverse remodeling, heart failure, and treated ventricular tachyarrhythmias in MADIT-CRT	1,000	To determine whether the presence of nonsustained ventricular tachycardia (NSVT) was predictive of clinical events in MADIT-CRT (multicenter automatic defibrillator implantation trial-cardiac resynchronization therapy) patients treated with CRT-defibrillator.
Pouleur, 2011 (179)	Relationship between improvement in left ventricular dyssynchrony and contractile function and clinical outcome with cardiac resynchronization therapy: the MADIT-CRT trial	761	To assess long-term effects of cardiac resynchronization therapy (CRT) on left ventricular (LV) dyssynchrony and contractile function, by two-dimensional speckle-tracking echocardiography, compared with implantable cardioverter defibrillator (ICD) only in MADIT-CRT
Yan, 2018 (180)	Evaluation of the therapeutic effects of QuickOpt optimization in Chinese patients with chronic heart failure treated by cardiac resynchronization	392	To compare the long-term therapeutic effects and clinical improvements in Chinese chronic heart failure patients optimized by QuickOpt or echocardiography with atrioventricular (AV) and interventricular (VV) delay optimizations after cardiac resynchronization therapy (CRT) with pacing (CRT-P) or with pacing and defibrillator (CRT-D) therapy.
Yang, 2018 (181)	Outcomes of cardiac resynchronization therapy using left ventricular quadripolar leads	516	To determine the clinical outcomes of CRT using quadripolar leads.

Author, Year [NCT]	Title	N	Objective
Zareba, 2011 (23)	Effectiveness of Cardiac Resynchronization Therapy by QRS Morphology in the Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy (MADIT-CRT)	1,817	To determine whether QRS morphology identifies patients who benefit from cardiac resynchronization therapy with a defibrillator (CRT-D) and whether it influences the risk of primary and secondary end points in patients enrolled in the Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy (MADIT-CRT) trial.
Prospective Observational			
Bertini, 2013 (182)	Impact of clinical and echocardiographic response to cardiac resynchronization therapy on long-term survival	679	To establish which definition of response to CRT, clinical or echocardiographic, best predicts long-term prognosis
Biffi, 2018 (183)	Benefits of left ventricular endocardial pacing comparing failed implants and prior non-responders to conventional cardiac resynchronization therapy: A subanalysis from the ALSYNC study	118	To report how left ventricular endocardial pacing (LVEP) may offer enhanced possibility to deliver CRT in patients with a failed attempt at implantation and to improve clinical status of CRT non-responders.
Conraads, 2014 (184)	Physical activity measured with implanted devices predicts patient outcome in chronic heart failure	836	To examine the lesser known prognostic value in patients with chronic heart failure.
Coverstone, 2015 (185)	The postimplantation electrocardiogram predicts clinical response to cardiac resynchronization therapy	213	To investigate whether the presence or absence of RV1SI predicts heart failure outcomes within 1 year of CRT implant.
Curtis, 2016 (155)	Improvement in Clinical Outcomes With Biventricular Versus Right Ventricular Pacing: The BLOCK HF Study	691	To examine clinical outcomes, including clinical composite score, quality of life (QOL), and change in New York Heart Association (NYHA) functional classification in patients with AV block and CRT vs RV pacing
Delgado, 2011 (186)	Relative merits of left ventricular dyssynchrony, left ventricular lead position, and myocardial scar to predict long-term survival of ischemic heart failure patients undergoing cardiac resynchronization therapy	397	To evaluate the relative merits of left ventricular (LV) dyssynchrony, LV lead position, and myocardial scar to predict long-term outcome after cardiac resynchronization therapy.
Dong, 2013 (187)	Left ventricular 12 segmental strain imaging predicts response to cardiac resynchronization therapy	45	To identify echocardiographic parameters that would predict the response to CRT.

Author, Year [NCT]	Title	N	Objective
Forleo, 2012 (188)	Clinical and procedural outcome of patients implanted with a quadripolar left ventricular lead: early results of a prospective multicenter study	154	To evaluate the long-term procedural and clinical outcomes of CRT patients implanted with a quadripolar LV lead.
Gendre, 2017 (189)	Research of predictive factors for cardiac resynchronization therapy: a prospective study comparing data from phase-analysis of gated myocardial perfusion single-photon computed tomography and echocardiography : Trying to anticipate response to CRT	42	To evaluate gated myocardial perfusion single-photon emission computed tomography (GMPS) phase parameters as compared to echocardiography in the assessment of predictors for response to CRT before and after CRT activation.
Gold, 2011 (190)	The relationship between ventricular electrical delay and left ventricular remodelling with cardiac resynchronization therapy	426	To evaluate the relationship between left ventricular (LV) electrical delay, as measured by the QLV interval, and outcomes in a prospectively designed substudy of the SMART-AV Trial.
Gold, 2012 (90)	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	610	To assess the impact of baseline QRS duration and morphology and the change in QRS duration with pacing on CRT outcomes in mild heart failure
Gold, 2016 (191)	Interventricular Electrical Delay Is Predictive of Response to Cardiac Resynchronization Therapy	419	To test if interventricular electrical delay is associated with improved CRT outcomes.
Gold, 2017 (192)	The role of interventricular conduction delay to predict clinical response with cardiac resynchronization therapy	1,342	To assess the association between interventricular electrical delay and HF clinical outcomes.
Hansen, 2017 (193)	Left atrial size and function as assessed by computed tomography in cardiac resynchronization therapy: Association to echocardiographic and clinical outcome	138	To evaluate whether baseline left atrial (LA) volume and function were associated with clinical or echocardiographic response to cardiac resynchronization therapy
Hsing, 2011 (194)	Paced left ventricular QRS width and ECG parameters predict outcomes after cardiac resynchronization therapy: PROSPECT-ECG substudy	426	To analyze the ECGs collected before, during, and after CRT implantation in the PROSPECT Trial.
Iwano, 2013 (195)	Strain rate dispersion index can predict changes in left ventricular volume and adverse cardiac events following cardiac resynchronization therapy	40	To examine whether the SRDI can predict the chronic response. Additionally, if SRDI needs to be simplified for use in clinical practice.

Author, Year [NCT]	Title	N	Objective
Kalscheur, 2018 (196)	Machine Learning Algorithm Predicts Cardiac Resynchronization Therapy Outcomes: Lessons From the COMPANION Trial	595	To use a machine learning algorithm to develop a model to predict outcomes after CRT.
Kjaergaard, 2011 (197)	Tricuspid annular plane systolic excursion and response to cardiac resynchronization therapy: results from the REVERSE trial	420	To evaluate tricuspid annular plane systolic excursion (TAPSE) as a predictor of left ventricular (LV) reverse remodeling and clinical benefit of cardiac synchronization therapy (CRT) and to evaluate the effect of CRT on TAPSE in patients with mildly symptomatic systolic heart failure as a substudy of the REVERSE trial.
Kutyifa, 2013 (101)	The influence of left ventricular ejection fraction on the effectiveness of cardiac resynchronization therapy: MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy)	1809	To evaluate the relationship between left ventricular (LV) ejection fraction and clinical outcome to cardiac resynchronization therapy (CRT) in mild heart failure patients enrolled in MADIT-CRT
Lenarczyk, 2015 (198)	Quality of life in cardiac resynchronization recipients: association with response and impact on outcome	77	To assess the correspondence between response to CRT and improvements in QoL and to verify if a change in QoL after pacing influences outcome in CRT patients.
Linde, 2013 (102)	Impact of ejection fraction on the clinical response to cardiac resynchronization therapy in mild heart failure	177	To evaluate outcomes in patients with EF >35% who receive CRT
Linde, 2017 (199)	Predictors of short-term clinical response to cardiac resynchronization therapy	1591	To examine the uncertainty about which patient characteristics predict short-term clinical response.
Mascioli, 2012 (200)	Electrocardiographic criteria of true left bundle branch block: a simple sign to predict a better clinical and instrumental response to CRT	111	To verify if newly proposed criteria for true LBBB identify patients with a better clinical and instrumental response to CRT.

Author, Year [NCT]	Title	N	Objective
Menet, 2016 (201)	Prognostic value of left ventricular reverse remodeling and performance improvement after cardiac resynchronization therapy: A prospective study	170	To evaluate the respective value of left ventricular (LV) reverse remodeling (changes in LV end-systolic volume relative to baseline (DeltaLVESV)) or LV performance improvement (DeltaLV ejection fraction (DeltaLVEF) or DeltaGlobal longitudinal strain (GLS)) to predict long-term outcome in a prospective cohort of consecutive patients receiving routine cardiac resynchronization therapy (CRT).
Momomura, 2012 (202)	Clinical efficacy of cardiac resynchronization therapy with an implantable defibrillator in a Japanese population: results of the MIRACLE-ICD outcome measured in Japanese indication (MOMIJI) study	80	To compare the efficacy of CRT-D therapy in an all-Japanese population with the study conducted in the US.
Murin, 2015 (203)	Global myocardial contractile reserve assessed by high-dose dobutamine stress echocardiography predicts response to the cardiac resynchronization therapy	52	To test that myocardial contractile reserve assessed by high-dose dobutamine stress echocardiography (DSE) which could predict response to CRT.
Nagy, 2015 (204)	Role of Right Ventricular Global Longitudinal Strain in Predicting Early and Long-Term Mortality in Cardiac Resynchronization Therapy Patients	93	To investigate if RV dysfunction would predict outcome in CRT.
Nagy, 2018 (205)	Quality of life measured with EuroQol-five dimensions questionnaire predicts long-term mortality, response, and reverse remodelling in cardiac resynchronization therapy patients	130	To examine the predictive role of baseline QoL and QoL change at 6 months after CRT with EQ-5D on 5-year mortality and response.
Orlov, 2008 (206)	Baseline myocardial perfusion predicts response to cardiac resynchronization therapy: a prospective observational study	19	To determine whether preimplant myocardial perfusion imaging (MPI) predicts outcome with biventricular pacing (BiVP).
Park, 2013 (207)	Echocardiographic predictors of reverse remodeling after cardiac resynchronization therapy and subsequent events	334	To determine whether combining parameters would be more robust and sought to develop a multiparametric echocardiographic score for predicting CRT response.

Author, Year [NCT]	Title	N	Objective
Petrovic, 2012 (208)	Prediction of a good response to cardiac resynchronization therapy in patients with severe dilated cardyomyopathy: could conventional echocardiography be the answer after all?	70	To assess the performance of echocardiographic parameters to predict response to cardiac resynchronization therapy (CRT).
Petryka, 2012 (209)	Magnetic resonance imaging assessment of intraventricular dyssynchrony and delayed enhancement as predictors of response to cardiac resynchronization therapy in patients with heart failure of ischaemic and non-ischaemic etiologies	52	To assess the value of dyssynchrony and myocardial viability assessment by cardiac magnetic resonance (CMR) in prediction of response to cardiac resynchronization therapy (CRT) in patients with heart failure (HF) of both ischaemic and non-ischaemic etiologies.
Poposka, 2018 (210)	Electrocardiographic Parameters as Predictors of Response to Cardiac Resynchronization Therapy	102	To determine Electrocardiographic Parameters as Predictors of Response to Cardiac Resynchronization Therapy
Rocchi, 2009 (211)	Exercise stress echocardiography is superior to rest echocardiography in predicting left ventricular reverse remodelling and functional improvement after cardiac resynchronization therapy	64	To evaluate whether exercise dyssynchrony could select responders to CRT.
Sebag, 2012 (212)	Reverse electrical remodeling by cardiac resynchronization therapy: prevalence and clinical impact	85	To determine (1) if chronic CRT induces a relevant shortening of the intrinsic QRS (iQRS), (2) whether changes in the native conduction system correlate with clinical or echocardiographic response to CRT, and (3) to identify predictors of iQRS width shortening.
Separham, 2017 (213)	Vitamin D deficiency and functional response to CRT in heart failure patients	50	To examine the role of vitamin D in the response of HF patients to cardiac resynchronization therapy (CRT).
Serdoz, 2011 (35)	Predictors for restoration of normal left ventricular function in response to cardiac resynchronization therapy measured at time of implantation	75	To find prognostic factors of full clinical and echocardiographic responses (i.e., >/=50% left ventricular ejection fraction [LVEF] and New York Heart Association class I) after 1 year of CRT.
Shanmugam, 2013 (214)	Effect of atrioventricular optimization on circulating N-terminal pro brain natriuretic peptide following cardiac resynchronization therapy	72	To examine the effect of AV delay optimization on the prognostic biomarker NT-proBNP following CRT.

Author, Year [NCT]	Title	N	Objective
Şipal, 2018 (215)	Surface electrogram-guided left ventricular lead placement improves response to cardiac resynchronization therapy	80	To investigate the echocardiographic and clinical benefits of LV lead implantation guided by an intraoperative 12-lead surface electrocardiogram (ECG) in patients with multiple target veins
Sohal, 2013 (216)	Noninvasive assessment of LV contraction patterns using CMR to identify responders to CRT	52	To determine if a corresponding pattern of contraction could be identified using cardiac magnetic resonance (CMR) cine imaging and whether this predicted response to cardiac resynchronization therapy (CRT).
Sullivan, 2013 (217)	Do baseline diastolic echocardiographic parameters predict outcome after resynchronization therapy? Results from the PROSPECT trial	426	To test if diastolic echocardiographic parameters were associated with clinical and structural outcomes in CRT patients.
Thebault, 2012 (218)	Sites of left and right ventricular lead implantation and response to cardiac resynchronization therapy observations from the REVERSE trial	346	To ascertain the effects of the left (LV) and right (RV) ventricular lead tip position in response to cardiac resynchronization therapy (CRT).
Thomas, 2010 (219)	Heart rate deceleration after exercise predicts patients most likely to respond to cardiac resynchronisation therapy	37	To examine the relationship between heart rate recovery following exercise and subsequent response to cardiac resynchronisation therapy (CRT).
Truong, 2018 (220)	Utility of dual-source computed tomography in cardiac resynchronization therapy-DIRECT study	54	To determine whether dual-source CT predicts clinical CRT outcomes and reduces intraprocedural time.
Van Bommel 2009 (38)	Characteristics of heart failure patients associated with good and poor response to cardiac resynchronization therapy: a PROSPECT (Predictors of Response to CRT) sub-analysis	286	To investigate the relationship between baseline characteristics and measures of response to CRT.
Van't Sant 2015 (221)	Measurements of electrical and mechanical dyssynchrony are both essential to improve prediction of CRT response	227	To assess the incremental value of mechanical dyssynchrony besides electrical dyssynchrony for predicting CRT response.
Vegh, 2014 (222)	Device-measured physical activity versus six-minute walk test as a predictor of reverse remodeling and outcome after cardiac resynchronization therapy for heart failure	164	To investigate the prognostic value of device-measured physical activity data compared with a six-minute walk test (6MWT) in predicting clinical response to cardiac resynchronization therapy (CRT).

Author, Year [NCT]	Title	N	Objective
Verbrugge, 2013 (223)	Time from emerging heart failure symptoms to cardiac resynchronisation therapy: impact on clinical response	172	To investigate whether time from onset of heart failure signs and/or symptoms (ie, progression to stage C/D heart failure) until implantation affects reverse remodelling and clinical outcome after cardiac resynchronisation therapy (CRT).
Versteeg, 2016 (224)	Patient-reported health status prior to cardiac resynchronisation therapy identifies patients at risk for poor survival and prolonged hospital stays	139	To examine the independent value of pre-implantation patient reported health status in predicting four-year survival and cardiac-related hospitalization of CRT patients.
Vondrak, 2017 (225)	Cardiac resynchronisation therapy optimisation of interventricular delay by the systolic dyssynchrony index: A comparative, randomised, 12-month follow-up study	63	To compare the effect of interventricular (VV) delay optimisation in CRT recipients on the basis of systolic dyssynchrony index (SDI) derived from the three-dimensional echocardiography (3DE) versus QRS width assessment on left ventricle volume reduction at the 12-month follow-up.
Werys, 2016 (226)	Cine dyscontractility index: A novel marker of mechanical dyssynchrony that predicts response to cardiac resynchronization therapy	52	To investigate whether magnetic resonance imaging (MRI) cine-derived dyssynchrony indices provide additional information compared to conventional tagged MRI (tMRI) acquisitions in heart failure patients undergoing cardiac resynchronization therapy (CRT).
Wiliński, 2011 (227)	Baseline tissue Doppler imaging-derived echocardiographic parameters and left ventricle reverse remodelling following cardiac resynchronization therapy introduction	60	To assess the relation of baseline mechanical dyssynchrony with the left ventricular end-systolic volume (LVESV) decrease following cardiac resynchronization (CRT) therapy introduction.
Xu, 2013 (129)	Predictive factors and clinical effect of optimized cardiac resynchronization therapy	65	To assess the effectiveness of cardiac resynchronization therapy (CRT) by intracardiac delay optimization using echocardiography

Author, Year [NCT]	Title	N	Objective
Ypenburg, 2008 (228)	Optimal left ventricular lead position predicts reverse remodeling and survival after cardiac resynchronization therapy	243	To evaluate echocardiographic parameters after 6 months of cardiac resynchronization therapy (CRT) as well as long-term outcome in patients with the left ventricular (LV) lead positioned at the site of latest activation (concordant LV lead position) as compared with that seen in patients with a discordant LV lead position.
Zajac, 2018 (229)	Mechanical dyssynchrony alters left ventricular flow energetics in failing hearts with LBBB: a 4D flow CMR pilot study	22	To investigate the impact of mechanical dyssynchrony on diastolic function by comparing 4D flow in myopathic LVs with and without LBBB.
Ongoing Studies (ClinicalTrials.gov)			
NCT02258061	Optimal Cardiac Resynchronization Therapy Pacing Rate	15	Completed. The optimal pacing rate during cardiac resynchronization therapy (CRT) is not known. Investigators investigate the impact of changing basal pacing frequencies on autonomic nerve function, cardiopulmonary exercise capacity and self-perceived quality of life (QoL).
NCT01573091	Cardiac Resynchronization Therapy Modular Registry	500	Completed. The purpose of the study is to collect some parameters (clinical, electrical, radiographic, echocardiographic and ECG) able to predict response to cardiac resynchronization therapy.

Author, Year [NCT]	Title	N	Objective
NCT01100918	Utility of Tissue Doppler Echocardiography for Selecting Patients for Cardiac Resynchronisation Therapy	80	Completed. Currently the main selection tool for Cardiac Resynchronisation Therapy (CRT) is the QRS duration on the surface echocardiography (ECG) which has been shown to be a poor predictor of response. We sought to evaluate the use of tissue Doppler (TDI) assessment of dyssynchrony in prediction of response to CRT. The hypothesis is that the presence of mechanical dyssynchrony (measured using TDI echocardiography) successfully identifies heart failure patients who will respond to CRT. Conversely, the absence of mechanical dyssynchrony is associated with a low/no response to CRT. This is a three arm study. Group 1 comprises patients with dyssynchrony on TDI who are implanted with a biventricular ICD whereas Group 2 patients comprise patients who have no dyssynchrony. Group 2 patients are randomised 1:1 to either receive a biventricular ICD (2a) or an ICD (2b). All patients undergo a NYHA class assessment, a cardiopulmonary exercise test, and an echocardiogram at baseline and at 6 months follow up. Baseline and 6 months findings will be compared in all three groups.

Author, Year [NCT]	Title	N	Objective
NCT02080000	R-wave Optimisation in Cardiac Resynchronisation Therapy Study	6	Completed. The aim of this study is to investigate whether the use of a simple feature on the 12 lead electrocardiogram (ECG) to optimise pacemaker device programming can have clinically relevant benefit to patient management. More specifically it is to investigate whether using the R-wave in V1 of the surface ECG to guide the timings between left (LV) and right ventricular (RV) pacing improves response to Cardiac Resynchronisation Therapy.
NCT00489177	Optimal Programming to Improve Mechanical Indices, Symptoms and Exercise in Cardiac Resynchronization Therapy.	461	Completed. This international study is assessing if repeat adjustment of the timing between the three leads in a cardiac resynchronization therapy (CRT) defibrillator will increase the likelihood of benefit (symptoms and heart function) compared to usual device programming. The hypothesis is that QuickOpt facilitated serial optimization of sensed atrioventricular (sAV), paced atrioventricular (pAV), and inter-ventricular (VV) timing in the initial 9 months following successful CRT will increase the rate of clinical response and structural remodeling at 12 months compared to usual care.
NCT00158015	Prospective Minnesota Study of ECHO Tissue Doppler Imaging in Cardiac Resynchronization Therapy	70	Completed. The purpose of this study is to assess whether tissue doppler imaging is useful in predicting which patients will respond most to Cardiac Resynchronization therapy (a type of pacemaker)
NCT00748735	Left Ventricular Lead Position in Cardiac Resynchronization Therapy	55	Completed. Left ventricular (LV) lead position has crucial impact on cardiac resynchronization therapy (CRT) success. This study will compare fluoroscopy and myocardial deformation imaging for optimal definition of LV lead position.

Author, Year [NCT]	Title	N	Objective
NCT00359372	Predicting Response to Cardiac Resynchronization Therapy in Heart Failure	180	Completed. This study will explore which characteristics of patients with heart failure will likely predict improvement after cardiac resynchronization (CRT), implantation of a pacemaker to improve heart function. In spite of major medical advances, about 30% to 40% of patients with heart failure do not respond to CRT, and the reasons are not well understood. This study will involve magnetic resonance imaging (MRI), electrocardiogram (ECG), and echocardiography techniques to let researchers examine what may influence response to CRT.
NCT00677014	Comparison of AV Optimization Methods Used in Cardiac Resynchronization Therapy (CRT)	1,060	Completed. The primary objective of SMART-AV is to assess the effect of SmartDelay for determining optimal AV delay timing during CRT compared to both a fixed AV delay and echocardiography-determined optimal AV timing chronically over a 6-month period.
NCT00488410	SYNCHRO. Evaluation of the Forecasts Parameters of Real Time-three-dimensional Doppler Echocardiography in Selecting Patients With Chronic Heart Failure for Cardiac Resynchronisation Therapy	NA	Completed. Patients showing a normal value of SDI (< or + 8%) will randomly be assigned to CRT in "ON" or "OFF"mode at one month after implantation. In any case of emergency, an automated rescue mode is included in the device for the patients in "OFF" mode.
NCT00146848	PEGASUS CRT Study: Atrial Support Study in Cardiac Resynchronization Therapy	1,742	Completed. This study will look at different pacing modes (how a device is programmed to pace one's heart), and how these modes may assist in one's daily activities and how one is feeling.

Author, Year [NCT]	Title	N	Objective
NCT00941850	A Study of Triple-site Ventricular Pacing in Patients Who Have Not Responded to Conventional Dual Ventricular Site Cardiac Resynchronization Therapy	20	Completed. Patients are randomised to receive ongoing optimised device and medical therapy or triple ventricular site resynchronisation. The hypothesis states that patients receiving triple-site resynchronization will exhibit a better response.
NCT00187200	Response of Cardiac Resynchronization Therapy Optimization With Ventricle to Ventricle Timing in Heart Failure Patients	816	Completed. The purpose of the study is to evaluate the benefit of interventricular (V-V) delay optimization in reducing the non-responder rate in patients with cardiac resynchronization defibrillator (CRT-D) devices. The primary endpoint of this study is CRT responder rate.
NCT00253357	PROSPECT: Predictors of Response to Cardiac Re-Synchronization Therapy	450	Completed. The purpose of this study is to determine if using medical tests, Echocardiogram, can help in predicting which patients will improve. The types of patients needed for this study are those who have been diagnosed with moderate or severe heart failure.
NCT00737490	Does Echocardiographically Guided Ventriculo-Ventricular Optimization Yield a Sustained Improvement in Echocardiographic Parameters in Cardiac Resynchronization Therapy Patients? (DEVISE CRT)	40	Completed. The purpose of this study is to determine whether using an echocardiogram (a painless test where ultrasound is used to see your heart) while using mild electrical stimulation from your own CRT-D device to stimulate the ventricles (the lower chambers of the heart) to squeeze one slightly earlier than the other will show a sustained increase your heart's productivity (Cardiac Output (CO)), following implantation of a Cardiac Resynchronization Device (CRT-D). We believe that squeezing some parts of the heart earlier than others may make the heart a stronger pump.

Author, Year [NCT]	Title	N	Objective
NCT00271232	InSync III Marquis Model 7279 Cardioverter Defibrillator Cardiac Resynchronization System	238	Completed. People who have a dangerously fast hear beat, or whose heart is at risk of stopping beating, may be in need of an electronic device called an implantable cardioverter defibrillator (ICD). An ICD is implanted surgically just under the skin in the upper chest area and it sends a strong electrical impulse, or shock, to the heart to return it to a normal rhythm. If the heart is beating too slowly or at an abnormal rhythm, an ICD can also pace the heart to return the heart to its normal rhythm. The InSync III Marquis device can change the timing of when the left and right ventricles of the heart are paced to beat. This is called "V to V timing". V to V timing may further improve the pumping function of the heart. The purpose of this study is to determine whether or not this V to V timing feature of the InSync III Marquis system is safe and effective.
NCT01060449	Stimulus Intensity in Left Ventricular Leads	60	Completed. Cardiac resynchronization therapy (CRT) is a device implanted to improve the function of some people's hearts. CRT involves the placement of 3 wires in the heart through a vein near the front of your left or right shoulder into three pumping chambers of the heart, the most important being the left lower chamber, left ventricle (LV). The purpose of this study is to determine if pacing the wires in the left ventricular chamber of the heart using higher stimulus intensity improves the strength of the heart's contraction.

Author, Year [NCT]	Title	N	Objective
NCT00887237	Triple Site Ventricular Stimulation for Cardiac Resynchronization Therapy (CRT) Candidates	76	Completed. The present pilot trial was designed to examine the 6-month safety of biventricular stimulation with 2 right ventricular (RV) and 1 left ventricular (LV) leads - main objective- and to assess its clinical benefit.
NCT01831518	Predicting Response to CRT Using Body Surface ECG Mapping	20	Completed. Body surface ECG mapping is a new technique that assesses the electrical activation of the heart in more detail than the standard ECG. This study aims to determine whether this new technology may aid current selection criteria in predicting response to CRT.
NCT01258829	British Randomised Controlled Trial of Atrioventricular (AV) and Interventricular (VV) Optimisation (BRAVO)	403	Completed. Many patients who have cardiac resynchronisation therapy (a type of pacemaker) implanted for heart failure do not have the settings of their device optimised. The most widely available method for optimisation uses flow measured using cardiac ultrasound (echocardiography) to determine the optimal settings. However, this is not frequently performed because it is time consuming and requires two skilled operators. In this study the investigators will test a new non-invasive method for optimisation, which utilises pressure measurements (non-invasive blood pressure measured from the finger). Is optimising AV and VV delay using non-invasive haemodynamics at least equivalent, in terms of exercise capacity, to conventional echo optimisation.

Author, Year [NCT]	Title	N	Objective
NCT01270646	Impact of Intraventricular Electrical Activation in Resynchronization Therapy	18	Completed. Impact of intraventricular electrical activation in resynchronization therapy. We seek to evaluate the impact of Cardiac Resynchronization Therapy (CRT) on electrical activation of the Left Ventricle (LV). The first goal of the study is to evaluate if CRT is able to decrease the heterogeneity of LV activation in heart failure patients. A second goal is to evaluate the electrical determinant of clinical response to CRT using invasive and non-invasive mapping technology.
NCT02126241	Non-Invasive Cardiac Output Measurement for CRT Optimization	42	Completed. This proposal aims to evaluate the added clinical and echocardiographic benefit of using the non-invasive impedance-based cardiac output measurement system (NICaS) for optimizing atrio-ventricular and inter-ventricular delays in chronic (more than 6 months) CRT recipients.
NCT01172067	QuickOpt Chronic Study	400	Completed. The purpose of this study is to demonstrate that QuickOpt optimization can be as an alternative method for CRTP/D patients' optimization in clinical practice through the comparison of the improvement differences between the CRTP/D patients with different optimization at 12 months after implantation.The hypothesis is that the Heart Remolding parameter (LVESV) improvement of patients using QuickOpt parameters at 12 months after implant is not inferior (10%) to the patients by Echo optimization。

Author, Year [NCT]	Title	N	Objective
NCT01484613	Selected Site Pacing to Avoid Phrenic Nerve Stimulation in Cardiac Resynchronization Patients With Quadripolar Left Ventricular Leads	337	Completed. Cardiac resynchronization (CRT) therapy is well established for treatment of patients with severe heartfailure, reduced left ventricular (LV) function and ventricular dyssynchrony. Roughly 1/3 of CRT patients do not improve after CRT implant. One possible reason is interruption of biventricular pacing. This might be caused by several conditions, including elevated left ventricular (LV) pacing thresholds or presence of phrenic nerve stimulation (PNS). CRT devices with quadripolar LV leads offer 10 LV pacing vectors to choose from. It's the aim of this prospective observational study to investigate efficacy and reliability of cardiac resynchronization therapy (CRT) with quadripolar left ventricular leads. Hypothesis: In more than 90% of patients, who received a CRT system with quadripolar LV lead, at least one acceptable LV lead vector is available.
NCT02139891	Effects of Multipoint Pacing CRT-D on Neurohormonal Activation.	30	Completed. This study will examine the additional clinical benefit conferred by multipoint pacing (MPP) compared to standard CRT over a period of 3 months. Patients will be randomized to MPP ON vs. OFF and followed for a total of 6 months. This includes two crossover periods for each pacing modality (MPP on vs. off).

Author, Year [NCT]	Title	N	Objective
NCT00158951	Device Evaluation of Contak Renewal 2and Easytrak 2 - DECREASE-HF	360	Completed. The purpose of this clinical investigation is to demonstrate the safety and effectiveness of the CONTAK® RENEWAL™ 2/4/4HE cardiac resynchronization therapy defibrillator (CRT-D) family and EASYTRAK® 2 lead in delivering LV-CRT or BiV-CRT with an LV Offset for patients with heart failure and an indication for an ICD.
NCT00901212	Evaluation of Resynchronization Therapy for Heart Failure (EARTH)	120	Completed. Heart failure is a major health problem in Canada. Recent advances in medical and device therapy have helped to reduce the morbidity and mortality of patients with this problem. Among these treatments, cardiac resynchronization therapy (CRT) has very recently been shown to be effective to improve functional class, quality of life and exercise tolerance of the patients with the most severe symptoms of heart failure and a prolonged duration of the QRS on the 12-lead Electrocardiography (ECG).

Author, Year [NCT]	Title	N	Objective
NCT01439529	ECG Optimization of CRT: Evaluation of Mid-term Response	180	Completed. New simpler methods to optimize cardiac resynchronization therapy (CRT) are being evaluated, such as the use of the electrocardiogram. In this prospective, double-blind, study, the investigators will evaluate: Primary endpoint: To compare the clinical response to CRT in patients with the programming optimized by QRS versus the nominal suggested by the device. Secondary endpoints: To compare cardiac remodeling in patients with the programming optimized by QRS versus the nominal suggested by the device. To evaluate the degree of asynchrony in both groups (nominal versus optimization by QRS) with respect to the intrinsic rhythm. To evaluate the echocardiographic improvement in left ventricular (LV) filling in both groups. To evaluate the differences in the optimal atrioventricular (AV) delay with atrial sensing or atrial pacing. For that, 180 patients with an indication for CRT will be randomized to nominal programming of the device or optimization by the electrocardiogram for a narrower QRS. A clinical and echocardiographic evaluation will be done at baseline, 6 and 12 months.

Author, Year [NCT]	Title	N	Objective
NCT00251251	Resynchronization/Defibrillation for Ambulatory Heart Failure Trial	1798	Completed. Congestive heart failure (CHF) is a common health problem that leads to frequent hospitalizations and an increased death rate. In spite of advances in drug therapy, it remains a significant public health problem. Recently, a new therapy has been developed for advanced heart failure patients with a ventricular conduction abnormality. This new therapy, called cardiac resynchronization (CRT), is a device which stimulates the atrium, the right ventricle, and the left ventricle providing synchronization of the contraction of the heart chambers. It is the addition of this therapy to an implantable cardioverter defibrillator (ICD) that will be evaluated in this study. This study will compare whether the implantation of this new therapy device, in combination with an implantable cardioverter defibrillator, will reduce total mortality and hospitalizations for CHF.

Author, Year [NCT]	Title	N	Objective
NCT01434615	Medtronic South Asian Systolic Heart Failure Registry	502	Completed. The purpose of this study is to (a) characterize the current management of patients with systolic heart failure (HF) in South Asia following an educational intervention of current guidelines and delivery of disease management tools and (b) to characterize the effect of current therapy on clinical outcomes in patients managed by tertiary care centers across South Asia. Current therapy includes characterization of the post market performance of any market released Medtronic cardiac resynchronization therapy (CRT) or cardiac resynchronization therapy plus implantable cardiac defibrillator (CRT-D) system for cardiac resynchronization therapy (CRT).
NCT00821938	Cardiac Resynchronization Therapy (CRT)-Narrow-dp/Dt-Study	30	Completed. Goal is to examine the efficy of Cardiac Resynchronization Therapy in heart failure patients with narrow QRS complex and optimized medical treatment but echocardiographic desynchronization detection as well as the positve increase of the intraoperative pressureincreasespeed in reverse remodelling and a secondary improvement of functional parameters
NCT01179997	Tissue Doppler Imaging (TDI) Versus Electrocardiography (ECG) Interventricular Pacing Delay Optimization in Cardiac Resynchronization Therapy (CRT)	156	Completed. The aim of this study was to compare the response to cardiac resynchronization therapy when the interventricular pacing interval was optimized by Tissue Doppler Imaging (TDI) to response when it was optimized following QRS width criteria.

Author, Year [NCT]	Title	N	Objective
NCT01294527	Wireless Stimulation Endocardially for Cardiac Resynchronization Therapy	17	Completed. The WiCS-LV system is an alternative means to providing left ventricular stimulation for Cardiac Resynchronization Therapy (CRT). The purpose of this study is to evaluate the safety and performance of the WiCS-LV System in patients with indications for CRT.
NCT01603706	Radial Strain ECHO-Guided Implantation of Cardiac Resynchronization Therapy	172	Completed. The purpose of this study is to evaluate the use of radial strain imaging using speckle tracking analysis to predict the response to CRT in patients with ischemic cardiomyopathy (ICMP) with NYHA functional class 2-4 heart failure and a standard guideline-based CRT indication. Thus assessing the value of lead localization determined by radial strain imaging in a prospective, randomized manner.
NCT00996086	Risk Stratification and Benefits With Cardiac Resynchronization Therapy (CRT)	154	Completed. The purpose of the study is two-fold. First, to determine if an algorithm can be developed based on pre-implant clinical variables to predict response to CRT-D therapy. Second, the study aims to determine in patients implanted with CRT-D if the combined use of cTnT and BNP can further predict and risk-stratify HF improvement and all-cause mortality. Additionally, novel biochemical markers defining cardiac mortality in high risk patients detected by plasma proteomic analysis in the CRT-D patients will be evaluated.

Author, Year [NCT]	Title	N	Objective
NCT02525185	Contractile Reserve in Dyssynchrony: A Novel Principle to Identify Candidates for Cardiac Resynchronization Therapy	210	Active, not recruiting. Cardiac resynchronisation therapy (CRT) has been documented to be a powerful treatment in patients with severe congestive heart failure. However, 30-40% of patients receiving a CRT are non-responders. In this study the investigators will use a previously validated method to estimate myocardial segment work non-invasively by speckle-tracking echocardiography and blood pressure. Since segments which shorten in systole perform positive work, whereas segments which lengthen do negative work, the investigators will calculate wasted work as negative work in percentage of positive work. The main purpose of the study is to determine if wasted work can predict response to CRT.
NCT01323686	Empiric Versus Imaging Guided Left Ventricular Lead Placement in Cardiac Resynchronization Therapy	182	Completed. The aim of this study is to investigate if imaging guided optimal left ventricular (LV) lead placement improves the response rate to cardiac resynchronization therapy (CRT). Consecutive patients meeting the standard criteria for CRT are included in a prospective, double-blinded, randomized trial to LV lead positioning either 1) guided by cardiac imaging using echocardiography, single-photon emission computed tomography, and visualization of cardiac venous anatomy (cardiac computed tomography (CT), venography) to target an epicardial vein at the site of latest mechanical activation without scar tissue or 2) using standard LV lead placement.

Author, Year [NCT]	Title	N	Objective
NCT00399594	Effect of Targeting Left Ventricular Lead Position on the Rate of Response to Cardiac Resynchronization Therapy.	96	Completed. Identifying & optimizing strategies to reduce the burden of heart failure is vital. Despite advances in pharmacotherapy, patients with heart failure are at high risk for death & hospitalization. Cardiac resynchronization therapy (CRT) synchronizes ventricular mechanical activity, improves cardiac output & reduces HF symptoms. However, ~50% of patients do not clearly respond to CRT. Sub-optimal placement of the LV pacing lead appears to be an important reason for non-response. This study will assess whether targeted LV lead placement will result in an increased probability of CRT response at 52 weeks vs. usual (lateral wall) lead placement.
NCT00814840	Efficiency Study of Triple-Site Cardiac Resynchronization in Patients With Heart Failure	100	Completed. The purpose of this study is to assess the efficiency of permanent biventricular pacing using three ventricular leads in terms of reduction in adverse cardiac events rates, improvement in cardiac capacity and patients' functional status in subjects with congestive heart failure and a physiologic (sinus) rhythm.

Author, Year [NCT]	Title	N	Objective
NCT01426321	Combining Myocardial Strain and Cardiac CT to Optimize Left Ventricular Lead Placement in CRT Treatment	100	Active, not recruiting. For patients with advanced heart failure, Cardiac Resynchronization Therapy (CRT) has been a major improvement. The treatment improves symptoms and prolongs life in selected patients with heart failure. However, with the current selection criteria and methods for implanting the pacemaker, only 60-70% of the patients derive significant benefit from the treatment. New imaging techniques, including advanced ultrasound and computed tomography, in combination with new versatile multi-pole electrodes, have made an individually tailored therapy possible. Using these techniques in combination, the study will investigate the effect of individually based "optimal" placement of the pacemaker electrodes vs. standard care. The optimal LV electrode position is defined as pacing a viable segment with the latest mechanical delay, targeting a specific segment of the coronary sinus as visualised on cardiac CT. The hypothesis is that this will increase the number of positive responders from 65% to 85%.
NCT02350842	Triple-site Biventricular Stimulation in the Optimization of CRT	30	Active, not recruiting. The primary objective of this study is to demonstrate that individually optimized, triple-site biventricular pacing is superior to standard biventricular pacing in reverse ventricular modeling as demonstrated by Echo Left Ventricle End-Systolic Volume (LVESV) at 1 year in patients with non-LBBB morphology without increasing the risk of serious procedure and/or device related adverse events at 30 days.

Author, Year [NCT]	Title	N	Objective
NCT01805154	Advance Cardiac Resynchronization Therapy (CRT) Registry	1,500	Completed. The intent of this registry is to understand comprehensive clinical care strategies for Cardiac Resynchronization Therapy (CRT) patients especially non-responders in real-world clinical practice.
NCT01905670	Safety and Performance of Electrodes Implanted in the Left Ventricle	39	Active, not recruiting. The study is intended to demonstrate the safe implant of small receiver-electrodes into the endocardial surface of the left ventricle and to demonstrate its utility in providing cardiac resynchronization therapy in heart failure patients.
NCT02346097	Electrophysiological Optimization of Left Ventricular Lead Placement in CRT	122	Completed. The purpose of this study is to investigate if "optimal electrical resynchronization" achieved by targeting left ventricular lead placement to the myocardial region with the latest electrical activation combined with post-implant pacemakersettings for narrowing the paced QRS width causes an excess improvement in the pumping function of the heart (the left ventricular ejection fraction) in Cardiac Resynchronization Therapy (CRT)
NCT02832622	MultiPoint Pacing™ Post Market Study (MPP-PMS)	2,000	Active, not recruiting. This is a prospective, multicenter, non-randomized registry/observational study. The study will enroll up to 2,000 patients with successful St. Jude Medical (SJM) Cardiac Resynchronization Therapy (CRT) MP device implant from up to 140 centers undergoing CRT implantation.

Author, Year [NCT]	Title	N	Objective
NCT01059175	Dual-Site LV Pacing in CRT Non Responders: Multicenter Randomized Trial	84	Completed. Cardiac resynchronization therapy (CRT) is an effective treatment of heart failure (HF) refractory to optimal medical management, in presence of a depressed left ventricular (LV) ejection fraction and a wide QRS complex. It is mainly limited by a high proportion of non-responders. Attempts have been made, in small studies, to increase the number of stimulation sites in order to optimize the resynchronization therapy. V3 is a planned multicenter, randomized trial whose objective is to evaluate the clinical benefit conferred by the addition of a second endocardial or epicardial LV lead in non-responders after at least 6 months of standard biventricular stimulation. The V3 trial will examine the clinical benefit conferred by the addition of a second LV lead in non-responders compared to standard CRT.
NCT00111527	APAF: Assessment of Cardiac Resynchronization Therapy in Patients With Permanent Atrial Fibrillation	458	Completed. A suboptimal level of resynchronization (cardiac resynchronization therapy [CRT]) achieved in many patients with actual standards and techniques based on tissue-Doppler echocardiography could be more effective to obtain better CRT results. Eligible patients who successfully received atrioventricular (AV) junction ablation and biventricular (BiV) pacing are randomised to a comparison between a strategy of right ventricular (RV) apical pacing with delayed CRT based on clinical indications with a strategy of early optimal CRT based on an echocardiographic stratification.
Ongoing Studies (ClinicalTrials.gov)			

Author, Year [NCT]	Title	N	Objective
NCT02728336	MRI Assessment of Patient Suitability for Cardiac Resynchronization Therapy (CRT)	110	Recruiting. The goals of this project are to: 1) explore the potential use of magnetic resonance imaging (MRI) data for improved prediction of response to cardiac resynchronization (CRT), and 2) use the MRI-derived data together with a computer model of the cardiovascular system to study the relative roles of different factors in the mechanical effects of dyssynchrony in failure, and in the response (or lack thereof) to CRT.
NCT03183011	Cardiac Magnetic Resonance Imaging After Cardiac Resynchronization Therapy	40	Recruiting. This study is evaluating how MRI after CRT can provide key insights regarding LV function, structure, and mechanics resulting from CRT in patients with or without LV scar and inform optimal pacing strategies. The expected accurate and reproducible response assessment with cardiac MRI has important implications for evaluating CRT outcomes in clinical trials, and the insights from the post-CRT MRI promise to improve implementation of CRT.
NCT03366545	Observation of Clinical Routine Care for Heart Failure Patients Implanted With BIOTRONIK CRT Devices	3,000	Recruiting. The registry is primarily designed to assess outcome, efficacy and residual safety aspects of CRT based on long-term data from an unselected, real-life clinical set-up. Moreover, the observation of the patient status should help to find possible predictors for HF events and to identify areas of improvement for CRT and for CRT device settings.

Subtable 17. Published and ongoing studies potentially relevant to Evidence Gap 32 *[What is the predictive accuracy of a model that includes available clinical, ECG, echocardiography, and device parameters associated with improvement in overall survival in patients with CRT?]*

Author, Year [NCT]	Title	N	Objective
RCTs			
Bossard, 2014 (230)	Outcome of patients with cardiac resynchronisation defibrillator therapy and a follow-up of at least five years after implant	49	To evaluate the long-term outcome (>5 years) of patients with the main focus on device-associated events.
Brenyo, 2014 (231)	Predictors of spontaneous reverse remodeling in mild heart failure patients with left ventricular dysfunction	714	To examine the factors associated with spontaneous left ventricular reverse remodeling (S-LVRR) among mildly symptomatic heart failure (HF) patients and its prognostic implications on clinical outcomes.
Gold, 2015 (232)	The effect of reverse remodeling on long-term survival in mildly symptomatic patients with heart failure receiving cardiac resynchronization therapy: results of the REVERSE study	353	To assess the effect of CRT-induced reverse remodeling on long-term survival in patients with mildly symptomatic heart failure.
Gold, 2018 (174)	The rationale and design of the SMART CRT trial	726	To assess the efficacy of an atrioventricular optimization algorithm to improve reverse remodeling among patients undergoing cardiac resynchronization therapy (CRT) in the presence of interventricular electrical delay.
Knappe, 2011 (176)	Dyssynchrony, contractile function, and response to cardiac resynchronization therapy	1,077	To test if a combined assessment of left ventricular (LV) dyssynchrony and contractile function by strain-based imaging would identify patients who would most benefit from CRT.
Kockova, 2018 (177)	Cardiac resynchronization therapy guided by cardiac magnetic resonance imaging: A prospective, single-centre randomized study (CMR-CRT)	99	To investigate the impact of cardiac magnetic resonance (CMR)-guided left ventricular (LV) lead placement on clinical outcomes and LV reverse remodelling in CRT recipients.

Author, Year [NCT]	Title	N	Objective
Kuperstein, 2014 (233)	Left atrial volume and the benefit of cardiac resynchronization therapy in the MADIT-CRT trial	1,785	To test if LAV independently correlates with clinical outcomes in patients who receive cardiac resynchronization therapy with a defibrillator (CRT-D) and can be used for improved risk assessment in this population
Mittal, 2014 (131)	The impact of nonsustained ventricular tachycardia on reverse remodeling, heart failure, and treated ventricular tachyarrhythmias in MADIT-CRT	1,000	To determine whether the presence of nonsustained ventricular tachycardia (NSVT) was predictive of clinical events in MADIT-CRT (multicenter automatic defibrillator implantation trial-cardiac resynchronization therapy) patients treated with CRT-defibrillator.
Pouleur, 2011 (179)	Relationship between improvement in left ventricular dyssynchrony and contractile function and clinical outcome with cardiac resynchronization therapy: the MADIT-CRT trial	761	To assess long-term effects of cardiac resynchronization therapy (CRT) on left ventricular (LV) dyssynchrony and contractile function, by two-dimensional speckle-tracking echocardiography, compared with implantable cardioverter defibrillator (ICD) only in MADIT-CRT
Rickard, 2011 (234)	The impact of left ventricular size on response to cardiac resynchronization therapy	668	To examine changes in left ventricular ejection fraction (LVEF) and survival in patients with NDCM or SDCM compared with those with traditionally studied moderately dilated cardiomyopathy.
Sherazi, 2014 (235)	Comparison of low versus high (>40 mm Hg) pulse pressure to predict the benefit of cardiac resynchronization therapy for heart failure (from the Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy Trial)	754	To evaluate the relation between preimplantation PP and echocardiographic response to CRT-D and subsequent clinical outcome after 1 year.
Wilton, 2014 (236)	Left ventricular lead position and outcomes in the Resynchronization-Defibrillation for Ambulatory Heart Failure Trial (RAFT)	894	To evaluate the relationships between LV lead positions and the risk of death or hospitalization for heart failure (HF) in the cardiac resynchronization therapy arm of the Resynchronization-Defibrillation for Ambulatory Heart Failure Trial (RAFT).

Author, Year [NCT]	Title	N	Objective
Zareba, 2011 (23)	Effectiveness of Cardiac Resynchronization Therapy by QRS Morphology in the Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy (MADIT-CRT)	1,817	To determine whether QRS morphology identifies patients who benefit from cardiac resynchronization therapy with a defibrillator (CRT-D) and whether it influences the risk of primary and secondary end points in patients enrolled in the Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy (MADIT-CRT) trial.
Prospective Observational			
Aktas, 2014 (237)	The effect of weight loss on clinical outcomes in patients implanted with a cardiac resynchronization therapy device-A MADIT-CRT substudy	994	To evaluate the effect of weight loss on clinical outcomes in patients implanted with a cardiac resynchronization therapy with defibrillator (CRT-D).
Bai, 2008 (60)	Mortality of heart failure patients after cardiac resynchronization therapy: identification of predictors	542	To make a comparison (CRT-D vs CRT-P) in a large CHF population and seeks to identify predictors of death in patients with different comorbidities.
Baturova, 2018 (238)	Usefulness of Electrocardiographic Left Atrial Abnormality to Predict Response to Cardiac Resynchronization Therapy in Patients With Mild Heart Failure and Left Bundle Branch Block (a Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy Substudy)	941	To assess the impact of electrocardiographic LA abnormality for prognosis in patients with HF treated with CRT.
Berger, 2009 (239)	Relationships between cardiac resynchronization therapy and N-terminal pro-brain natriuretic peptide in patients with heart failure and markers of cardiac dyssynchrony: an analysis from the Cardiac Resynchronization in Heart Failure (CARE-HF) study	813	To evaluate whether the prognostic value of NT-proBNP was influenced by CRT and the effects of CRT stratified according to NT-proBNP.
Bertini, 2013 (182)	Impact of clinical and echocardiographic response to cardiac resynchronization therapy on long-term survival	679	To establish which definition of response to CRT, clinical or echocardiographic, best predicts long-term prognosis
Binda, 2018 (240)	Time course of secondary mitral regurgitation in patients with heart failure receiving cardiac resynchronization therapy: Impact on long-term outcome beyond left ventricular reverse remodelling	198	To evaluate the clinical significance of secondary MR

Author, Year [NCT]	Title	N	Objective
Biton, 2018 (87)	Baseline adverse electrical remodeling and the risk for ventricular arrhythmia in Cardiac Resynchronization Therapy Recipients (MADIT CRT)	961	To examine baseline adverse electrical remodeling and the risk for ventricular arrhythmia in CRT Recipients.
Biton, 2018 (241)	Predictors of long-term mortality with cardiac resynchronization therapy in mild heart failure patients with left bundle branch block	756	To test if clinical and echocardiographic variables can be used to develop a simple mortality risk stratification score in CRT.
Boriani, 2012 (242)	Impact of mitral regurgitation on the outcome of patients treated with CRT-D: data from the InSync ICD Italian Registry	659	To assess the influence of clinically significant mitral regurgitation (MR) on clinical-echocardiographic response and outcome in heart failure (HF) patients treated with a biventricular defibrillator (cardiac resynchronization therapy defibrillator [CRT-D]).
Botto, 2013 (243)	Clinical characteristics, mortality, cardiac hospitalization, and ventricular arrhythmias in patients undergoing CRT-D implantation: results of the ACTION-HF study	406	To assess 2-year outcomes in a population implanted with a CRT plus defibrillator device in accordance with the standard of care and to evaluate any independent association between clinical variables and outcome.
Brenyo, 2012 (244)	Baseline functional capacity and the benefit of cardiac resynchronization therapy in patients with mildly symptomatic heart failure enrolled in MADIT-CRT	1,765	To evaluate the association between FC and response to CRT-D in Multicenter Automatic Defibrillator Implantation Trial in Cardiac Resynchronization Therapy.
Brenyo, 2013 (245)	QRS axis and the benefit of cardiac resynchronization therapy in patients with mildly symptomatic heart failure enrolled in MADIT-CRT	1,820	To determine whether QRS axis deviation will be associated with differential benefit from CRT-D.
Cipriani, 2016 (246)	Prognostic implications of mitral regurgitation in patients after cardiac resynchronization therapy	1,122	To investigate the prognostic impact of baseline MR and MR persistence after CRT on outcomes of treated patients.
Cleland, 2012 (247)	Long-term mortality with cardiac resynchronization therapy in the Cardiac Resynchronization-Heart Failure (CARE-HF) trial	813	To report the long-term outcome during and subsequent to the randomized trial.
Clemens, 2012 (248)	The Seattle Heart Failure Model predicts survival in patients with cardiac resynchronization therapy: a validation study	427	To examine the Seattle Heart Failure Model (SHFM) which predicts mortality in patients with heart failure, but also investigate model performance in subjects with cardiac resynchronization therapy.

Author, Year [NCT]	Title	N	Objective
Conraads, 2014 (184)	Physical activity measured with implanted devices predicts patient outcome in chronic heart failure	836	To examine the lesser known prognostic value in patients with chronic heart failure.
Dauphin, 2011 (249)	Quantification of ventricular resynchronization reserve by radionuclide phase analysis in heart failure patients: a prospective long-term study	74	To quantify the cardiac resynchronization reserve, that is, the extent of response to cardiac resynchronization therapy (CRT), by radionuclide imaging could potentially identify patients who are best suited for CRT.
Delgado, 2011 (186)	Relative merits of left ventricular dyssynchrony, left ventricular lead position, and myocardial scar to predict long-term survival of ischemic heart failure patients undergoing cardiac resynchronization therapy	397	To evaluate the relative merits of left ventricular (LV) dyssynchrony, LV lead position, and myocardial scar to predict long-term outcome after cardiac resynchronization therapy.
Delgado-Montero, 2016 (250)	Additive Prognostic Value of Echocardiographic Global Longitudinal and Global Circumferential Strain to Electrocardiographic Criteria in Patients With Heart Failure Undergoing Cardiac Resynchronization Therapy	205	To examine that response to cardiac resynchronization therapy is most favorable in patients with heart failure with QRS duration >/=150 ms and left bundle branch block and less predictable in those with QRS width 120 to 149 ms or non-left bundle branch block.
Di Biase 2008 (107)	The magnitude of reverse remodelling irrespective of aetiology predicts outcome of heart failure patients treated with cardiac resynchronization therapy	398	To assess the relationship between cardiac resynchronization therapy (CRT)-induced reverse remodelling and mortality during a long-term follow-up in a prospective observational study.
Ellims, 2013 (251)	Utility of cardiac magnetic resonance imaging, echocardiography and electrocardiography for the prediction of clinical response and long-term survival following cardiac resynchronisation therapy	46	To compare electrocardiography (ECG), echocardiography, and cardiac magnetic resonance (CMR) imaging for the prediction of response to CRT.
Gasparini, 2012 (252)	Low-dose dobutamine test associated with interventricular dyssynchrony: a useful tool to identify cardiac resynchronization therapy responders: data from the LOw dose DObutamine stress-echo test in Cardiac Resynchronization Therapy (LODO-CRT) phase 2 study	221	To investigate the association between left ventricular contractile reserve (LVCR) and clinical and echocardiographic long-term CRT response.

Author, Year [NCT]	Title	N	Objective
Gasparini, 2014 (88)	Absolute survival after cardiac resynchronization therapy according to baseline QRS duration: a multinational 10-year experience: data from the Multicenter International CRT Study	3,319	To determine whether baseline QRS duration relates to the absolute survival after CRT.
Gasparini, 2015 (253)	Validation of a simple risk stratification tool for patients implanted with Cardiac Resynchronization Therapy: the VALID-CRT risk score	5,153	To design and validate a simple prognostic score for patients implanted with CRT, based on readily available clinical variables
Gervais, 2009 (89)	Surface electrocardiogram to predict outcome in candidates for cardiac resynchronization therapy: a sub-analysis of the CARE-HF trial	803	To examine whether baseline and follow-up electrocardiographic characteristics might predict long-term outcome
Ghani, 2015 (254)	Response to cardiac resynchronization therapy as assessed by time-based speckle tracking imaging	138	To assess the predictive value of longitudinal strain (LS) and radial strain (RS) speckle tracking measurements on echocardiographic and clinical response to CRT.
Ghani, 2016 (255)	Association of apical rocking with long-term major adverse cardiac events in patients undergoing cardiac resynchronization therapy	295	To assess the predictive value of left ventricular (LV) apical rocking on a long-term clinical outcome in patients treated with CRT.
Gold, 2012 (90)	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	610	To assess the impact of baseline QRS duration and morphology and the change in QRS duration with pacing on CRT outcomes in mild heart failure
Gold, 2017 (192)	The role of interventricular conduction delay to predict clinical response with cardiac resynchronization therapy	1,342	To assess the association between interventricular electrical delay and HF clinical outcomes.
Goldenberg, 2011 (91)	Predictors of response to cardiac resynchronization therapy in the Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT)	1,761	To examine the combined assessment of factors that are associated with favorable reverse remodeling after cardiac resynchronization-defibrillator therapy (CRT-D) which can be used to predict clinical response to the device.

Author, Year [NCT]	Title	N	Objective
Goldstein, 2013 (256)	Differing effects of cardiac resynchronization therapy on long-term mortality in patient subgroups of MADIT-CRT defined by baseline conduction and 1-year post-treatment left ventricular remodeling	1,196	To clarify influences on long-term mortality after CRT-D, we assessed MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy) patient outcomes by baseline conduction abnormality and 1-year posttreatment remodeling.
Guha, 2013 (257)	A reduction in total isovolumic time with cardiac resynchronisation therapy is a predictor of clinical outcomes	73	To examine how CRT shortens t-IVT, but the long-term clinical benefit of such reduction after CRT has not been studied in this patient group.
Hasselberg, 2016 (258)	Left ventricular markers of mortality and ventricular arrhythmias in heart failure patients with cardiac resynchronization therapy	170	To investigate for echocardiographic predictors of ventricular arrhythmias and fatal outcome and to explore how myocardial function is changed by biventricular pacing in heart failure.
Hsing, 2011 (194)	Paced left ventricular QRS width and ECG parameters predict outcomes after cardiac resynchronization therapy: PROSPECT-ECG substudy	426	To analyze the ECGs collected before, during, and after CRT implantation in the PROSPECT Trial.
Hsu, 2012 (259)	Predictors of super-response to cardiac resynchronization therapy and associated improvement in clinical outcome: the MADIT-CRT (multicenter automatic defibrillator implantation trial with cardiac resynchronization therapy) study	191	To investigate predictors of left ventricular ejection fraction (LVEF) super-response to cardiac resynchronization therapy with defibrillator (CRT-D) and whether super-response translated into improved event-free survival in patients with mildly symptomatic heart failure (HF).
Hudak, 2017 (93)	The effectiveness of CRT on improvement of survival of heart failure patients in real life clinical settings	680	To compare the survival of patients with HF and wide QRS after cardiac resynchronization therapy (CRT) with survival of HF patients with narrow QRS and to assess factors predictive of non-response to CRT.
Iwano, 2013 (195)	Strain rate dispersion index can predict changes in left ventricular volume and adverse cardiac events following cardiac resynchronization therapy	40	To examine whether the SRDI can predict the chronic response. Additionally, if SRDI needs to be simplified for use in clinical practice.
Jacobsson, 2016 (260)	Usefulness of the Sum Absolute QRST Integral to Predict Outcomes in Patients Receiving Cardiac Resynchronization Therapy	496	To examine if it is unknown whether SAI QRST is associated with all-cause mortality and HF hospitalizations in patients undergoing CRT.

Author, Year [NCT]	Title	N	Objective
Jin, 2018 (261)	Significant mitral regurgitation as a predictor of long-term prognosis in patients receiving cardiac resynchronisation therapy	296	To examine the association of baseline significant MR with long-term outcomes in patients undergoing CRT.
Kalscheur, 2018 (196)	Machine Learning Algorithm Predicts Cardiac Resynchronization Therapy Outcomes: Lessons From the COMPANION Trial	595	To use a machine learning algorithm to develop a model to predict outcomes after CRT.
Khatib, 2014 (262)	EAARN score, a predictive score for mortality in patients receiving cardiac resynchronization therapy based on pre-implantation risk factors	608	To identify the predictors of mortality in patients treated with CRT and to design a risk score for mortality.
Kiani, 2013 (263)	Relationship of electro-mechanical remodeling to survival rates after cardiac resynchronization therapy	40	To examine whether reverse remodeling predicts increased survival rates in non-trial settings.
Kjaergaard, 2011 (197)	Tricuspid annular plane systolic excursion and response to cardiac resynchronization therapy: results from the REVERSE trial	420	To evaluate tricuspid annular plane systolic excursion (TAPSE) as a predictor of left ventricular (LV) reverse remodeling and clinical benefit of cardiac synchronization therapy (CRT) and to evaluate the effect of CRT on TAPSE in patients with mildly symptomatic systolic heart failure as a substudy of the REVERSE trial.
Kobe, 2012 (264)	Prospective evaluation of electrocardiographic parameters in cardiac resynchronization therapy: detecting nonresponders by left ventricular pacing	102	To identify predictive parameters for cardiac resynchronization therapy (CRT) response.
Kubala, 2017 (73)	Utility of Frailty Assessment for Elderly Patients Undergoing Cardiac Resynchronization Therapy	151	To evaluate the impact of frailty in the elderly on response to cardiac resynchronization therapy (CRT)
Kutyifa, 2013 (101)	The influence of left ventricular ejection fraction on the effectiveness of cardiac resynchronization therapy: MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy)	1,809	To evaluate the relationship between left ventricular (LV) ejection fraction and clinical outcome to cardiac resynchronization therapy (CRT) in mild heart failure patients enrolled in MADIT-CRT
Lenarczyk, 2015 (198)	Quality of life in cardiac resynchronization recipients: association with response and impact on outcome	77	To assess the correspondence between response to CRT and improvements in QoL and to verify if a change in QoL after pacing influences outcome in CRT patients.

Author, Year [NCT]	Title	N	Objective
Leong, 2012 (265)	Predictors of long-term benefit of cardiac resynchronization therapy in patients with right bundle branch block	561	To characterize consecutive cardiac resynchronization therapy (CRT) recipients with right bundle branch block (RBBB) in comparison with left bundle branch block (LBBB) and (ii) to identify independent predictors of long-term outcome among CRT recipients with RBBB. The presence of RBBB has been associated with poorer prognosis after CRT compared with LBBB; however, little is known about the differences in cardiac mechanics between RBBB and LBBB patients. Furthermore, predictors of favourable outcome after CRT in patients with RBBB have not been identified.
Leshem, 2018 (266)	Impact of quadripolar LV leads on heart failure hospitalization rates among patients implanted with CRT-D: data from the Israeli ICD Registry	2,913	To review the clinical outcomes associated with quadripolar LV leads.
Leyva, 2009 (267)	Development and validation of a clinical index to predict survival after cardiac resynchronisation therapy	148	To develop and validate a prognostic risk index of cardiovascular mortality after cardiac resynchronisation therapy (CRT).
Leyva, 2011 (30)	Female gender is associated with a better outcome after cardiac resynchronization therapy	550	To determine whether female gender influences long-term clinical outcome, symptomatic response as well as echocardiographic response after CRT.
Linde, 2013 (268)	Long-term impact of cardiac resynchronization therapy in mild heart failure: 5-year results from the REsynchronization reVErses Remodeling in Systolic left vEntricular dysfunction (REVERSE) study	419	To examine the long-term stability of CRT.
Linde, 2013 (102)	Impact of ejection fraction on the clinical response to cardiac resynchronization therapy in mild heart failure	177	To evaluate outcomes in patients with EF >35% who receive CRT
Linde, 2017 (199)	Predictors of short-term clinical response to cardiac resynchronization therapy	1,591	To examine the uncertainty about which patient characteristics predict short-term clinical response.
Liu, 2017 (269)	The assessment of the long-term effects of elective CRT-D of coronary heart disease after PCI	124	To examine long-term effects of elective cardiac resynchronization therapy devices (CRT-D) of coronary heart disease after percutaneous coronary intervention

Author, Year [NCT]	Title	N	Objective
Mascioli, 2012 (200)	Electrocardiographic criteria of true left bundle branch block: a simple sign to predict a better clinical and instrumental response to CRT	111	To verify if newly proposed criteria for true LBBB identify patients with a better clinical and instrumental response to CRT.
Mathias, 2016 (270)	Clinical Implications of Complete Left-Sided Reverse Remodeling With Cardiac Resynchronization Therapy: A MADIT-CRT Substudy	533	To evaluate the rate and predictive value of complete left-sided reverse remodeling on heart failure (HF) and death events in CRT-D patients with left bundle branch block (LBBB) enrolled in MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy).
Menet, 2016 (271)	Prognostic importance of postoperative QRS widening in patients with heart failure receiving cardiac resynchronization therapy	237	To investigate the relationship between postoperative QRS widening relative to baseline and mortality in a prospective cohort of heart failure patients receiving CRT.
Menet, 2016 (201)	Prognostic value of left ventricular reverse remodeling and performance improvement after cardiac resynchronization therapy: A prospective study	170	To evaluate the respective value of left ventricular (LV) reverse remodeling (changes in LV end-systolic volume relative to baseline (DeltaLVESV)) or LV performance improvement (DeltaLV ejection fraction (DeltaLVEF) or DeltaGlobal longitudinal strain (GLS)) to predict long-term outcome in a prospective cohort of consecutive patients receiving routine cardiac resynchronization therapy (CRT).
Mooyaart, 2011 (31)	Comparison of long-term survival of men versus women with heart failure treated with cardiac resynchronization therapy	578	To elucidate the gender-related differences in long-term survival after CRT.
Nagy, 2015 (204)	Role of Right Ventricular Global Longitudinal Strain in Predicting Early and Long-Term Mortality in Cardiac Resynchronization Therapy Patients	93	To investigate if RV dysfunction would predict outcome in CRT.
Nagy, 2018 (205)	Quality of life measured with EuroQol-five dimensions questionnaire predicts long-term mortality, response, and reverse remodelling in cardiac resynchronization therapy patients	130	To examine the predictive role of baseline QoL and QoL change at 6 months after CRT with EQ-5D on 5-year mortality and response.

Author, Year [NCT]	Title	N	Objective
Nauffal, 2015 (272)	Predictors of mortality, LVAD implant, or heart transplant in primary prevention cardiac resynchronization therapy recipients: The HF-CRT score	305	To develop a risk prediction score incorporating variables associated with mortality, left ventricular assist device (LVAD) implant, or heart transplant in recipients of a primary prevention cardiac resynchronization therapy-defibrillator (CRT-D).
Park, 2013 (207)	Echocardiographic predictors of reverse remodeling after cardiac resynchronization therapy and subsequent events	334	To determine whether combining parameters would be more robust and sought to develop a multiparametric echocardiographic score for predicting CRT response.
Penn, 2011 (15)	Improved outcome with preventive cardiac resynchronization therapy in the elderly: a MADIT-CRT substudy	1,820	To examine elderly patients comprise a large portion of patients with heart failure (HF). Limited data exist on the effectiveness of cardiac resynchronization therapy with defibrillator (CRT-D) in patients with mild HF symptoms in this population.
Plesinger, 2018 (273)	Ventricular Electrical Delay Measured From Body Surface ECGs Is Associated With Cardiac Resynchronization Therapy Response in Left Bundle Branch Block Patients From the MADIT-CRT Trial (Multicenter Automatic Defibrillator Implantation-Cardiac Resynchronization Therapy)	676	To verify the diagnostic contribution and an optimized computerized approach to measuring ventricular electrical activation delay (VED) from body surface 12-lead ECGs.
Plonska-Gosciniak, 2016 (274)	Role of lowdose dobutamine echocardiography in predicting response to biventricular pacing. Results from the multicenter Viability in Cardiac Resynchronisation Therapy (ViaCRT) study	127	To identify mechanical dyssynchrony indices with combination of myocardial viability characteristics for predicting long-term response to CRT.
Qin, 2015 (275)	Can the Prognosis of Cardiac Resynchronization Therapy Be Predicted by Gated SPECT?	63	To evaluate the role of gated myocardial perfusion SPECT (GMPS) phase parameters (phase SD and histogram bandwidth) in predicting the short-term response to cardiac resynchronization therapy (CRT) as left ventricle (LV) remodeling and the long-term effect as all-cause mortality or cardiac transplantation and hospitalization for heart failure.

Author, Year [NCT]	Title	N	Objective
Reinsch, 2010 (276)	Iterative cardiac output measurement for optimizing cardiac resynchronization therapy: a randomized, blinded, crossover study	24	To evaluate whether an optimization of CRT can be obtained by noninvasive CO measurements and to evaluate whether acute hemodynamic improvements obtained by this approach relate into increase in cardiac exercise capacity
Rickard, 2011 (95)	Predictors of response to cardiac resynchronization therapy in patients with a non-left bundle branch block morphology	850	To investigate Predictors of response to cardiac resynchronization therapy in patients with a non-left bundle branch block morphology
Risum, 2013 (277)	Mechanical dyssynchrony evaluated by tissue Doppler cross-correlation analysis is associated with long-term survival in patients after cardiac resynchronization therapy	131	To test for association with long-term survival compared with other tissue Doppler imaging (TDI)-derived indices.
Risum, 2015 (278)	Identification of Typical Left Bundle Branch Block Contraction by Strain Echocardiography Is Additive to Electrocardiography in Prediction of Long-Term Outcome After Cardiac Resynchronization Therapy	208	To investigate whether the absence of a typical LBBB mechanical activation pattern by 2DSE was associated with unfavorable long-term outcome and if this is additive to electrocardiographic (ECG) morphology and duration.
Rocha, 2015 (279)	Development and Validation of Predictive Models of Cardiac Mortality and Transplantation in Resynchronization Therapy	116	to develop predictive models for the combined endpoint of cardiac death and transplantation (Tx) at different stages of cardiac resynchronization therapy (CRT).
Rocha, 2015 (280)	Echocardiographic Predictors of Worse Outcome After Cardiac Resynchronization Therapy	116	To develop an echocardiographic model to predict cardiac death or transplantation (Tx) 1 year after CRT.
Ruwald, 2014 (281)	The effect of intermittent atrial tachyarrhythmia on heart failure or death in cardiac resynchronization therapy with defibrillator versus implantable cardioverter-defibrillator patients: a MADIT-CRT substudy (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy)	1,264	To investigate the effect of both history of intermittent atrial tachyarrhythmias (IAT) and in-trial IAT on the risk of heart failure (HF) or death comparing cardiac resynchronization therapy with defibrillator (CRT-D) to implantable cardioverter-defibrillator (ICD) treatment in mildly symptomatic HF patients with left bundle branch block (LBBB).
Sade, 2014 (282)	The association of left ventricular lead position related to regional scar by speckle-tracking echocardiography with clinical outcomes in patients receiving cardiac resynchronization therapy	149	To test the hypothesis that left ventricular (LV) lead position in proximity to myocardial scar is associated with less favorable outcomes.

Author, Year [NCT]	Title	N	Objective
Schuchert, 2014 (103)	Relationship between pre-implant ejection fraction and outcome after cardiac resynchronization therapy in symptomatic patients	366	To assess the relationship between pre-implant LVEF and outcome of patients with advanced heart failure who received cardiac resynchronization therapy (CRT).
Seo, 2011 (283)	The role of echocardiography in predicting responders to cardiac resynchronization therapy	217	To identify both ability of echocardiographic parameters to detect cardiac resynchronization therapy (CRT) volume responders and relation of these parameters with clinical outcomes.
Smith, 2012 (284)	Performance of the Seattle Heart Failure Model in implantable defibrillator patients treated with cardiac resynchronization therapy	413	To assess the performance of the SHFM when applied to patients with heart failure who received cardiac resynchronization therapy devices with defibrillation.
Sood, 2014 (285)	Association between myocardial substrate, implantable cardioverter defibrillator shocks and mortality in MADIT-CRT	1,790	To assess a possible association between myocardial substrate, implantable cardioverter defibrillator (ICD) shocks, and subsequent mortality.
Sredniawa, 2009 (82)	Sleep apnoea as a predictor of mid- and long-term outcome in patients undergoing cardiac resynchronization therapy	71	To assess the impact of baseline apnoea-hypopnoea index (AHI) on mid-term outcome and its change after 6 months of cardiac resynchronization therapy (CRT) on remote outcome.
Stankovic, 2014 (286)	Dynamic relationship of left-ventricular dyssynchrony and contractile reserve in patients undergoing cardiac resynchronization therapy	58	To investigate, using apical rocking (ApRock) as surrogate dyssynchrony parameter, the dobutamine stress echocardiography (DSE)-induced changes in left-ventricular (LV) dyssynchrony and LVEF and their potential pathophysiological interdependence
Stankovic, 2017 (287)	The association of volumetric response and long-term survival after cardiac resynchronization therapy	356	To investigate the association of the extent of LV remodelling, mechanical dyssynchrony, and survival in patients undergoing CRT.
Sullivan, 2013 (217)	Do baseline diastolic echocardiographic parameters predict outcome after resynchronization therapy? Results from the PROSPECT trial	426	To test if diastolic echocardiographic parameters were associated with clinical and structural outcomes in CRT patients.
Takaya, 2014 (288)	Electrocardiographic predictors of response to cardiac resynchronization therapy in patients with intraventricular conduction delay	152	To investigate the benefits of CRT and significant variables on surface electrocardiogram (ECG) to predict response to CRT in those patients.

Author, Year [NCT]	Title	N	Objective
Tatsumi, 2014 (289)	Combined baseline strain dyssynchrony index and its acute reduction predicts mid-term left ventricular reverse remodeling and long-term outcome after cardiac resynchronization therapy	75	To test the hypothesis that combining assessment of baseline radial strain dyssynchrony index (SDI), that expressed both left ventricular (LV) dyssynchrony and residual myocardial contractility, and of acute changes in this index can yield more accurate prediction of mid-term responders and long-term outcome after cardiac resynchronization therapy (CRT).
Tayal, 2017 (171)	Interaction of Left Ventricular Remodeling and Regional Dyssynchrony on Long-Term Prognosis after Cardiac Resynchronization Therapy	260	To examine the impact of LV dilatation on the association of measures of dyssynchrony with long-term prognosis and resynchronization potential after cardiac resynchronization therapy (CRT) remains unclear.
Tepper, 2009 (290)	Optimal left ventricular lead position predicts reverse remodeling and survival after cardiac resynchronization therapy	244	To evaluate echocardiographic parameters after 6 months of cardiac resynchronization therapy (CRT) as well as long-term outcome in patients with the left ventricular (LV) lead positioned at the site of latest activation (concordant LV lead position) as compared with that seen in patients with a discordant LV lead position.
Tompkins, 2013 (291)	Effect on cardiac function of cardiac resynchronization therapy in patients with right bundle branch block (from the Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy [MADIT-CRT] trial)	219	To determine whether patients with specific RBBB conduction patterns responded to CRT in the Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT) trial.
Truong, 2018 (220)	Utility of dual-source computed tomography in cardiac resynchronization therapy-DIRECT study	54	To determine whether dual-source CT predicts clinical CRT outcomes and reduces intraprocedural time.
Uretsky, 2008 (292)	Predictors of mortality from pump failure and sudden cardiac death in patients with systolic heart failure and left ventricular dyssynchrony: results of the CARE-HF trial	428	To determine a specific death cause may facilitate individualized therapy in patients with heart failure (HF).

Author, Year [NCT]	Title	N	Objective
Van Bommel 2009 (38)	Characteristics of heart failure patients associated with good and poor response to cardiac resynchronization therapy: a PROSPECT (Predictors of Response to CRT) sub-analysis	286	To investigate the relationship between baseline characteristics and measures of response to CRT.
van der Bijl 2018 (293)	Reduced left ventricular mechanical dispersion at 6 months follow-up after cardiac resynchronization therapy is associated with superior long-term outcome	1.185	To relate LVMD to long-term prognosis in a large cohort of HF patients after 6 months of cardiac resynchronization therapy (CRT).
van der Bijl 2018 (294)	Effect of Functional Mitral Regurgitation on Outcome in Patients Receiving Cardiac Resynchronization Therapy for Heart Failure	1,313	To investigate the prevalence, evolution and impact on mortality of functional MR before and after CRT
Vegh, 2014 (222)	Device-measured physical activity versus six-minute walk test as a predictor of reverse remodeling and outcome after cardiac resynchronization therapy for heart failure	164	To investigate the prognostic value of device-measured physical activity data compared with a six-minute walk test (6MWT) in predicting clinical response to cardiac resynchronization therapy (CRT).
Végh, 2018 (295)	A new simplified electrocardiographic score predicts clinical outcome in patients treated with CRT	431	To examine the ability of a simple standard electrocardiogram (ECG)-based scoring system to predict clinical outcome.
Verbrugge, 2013 (223)	Time from emerging heart failure symptoms to cardiac resynchronisation therapy: impact on clinical response	172	To investigate whether time from onset of heart failure signs and/or symptoms (ie, progression to stage C/D heart failure) until implantation affects reverse remodelling and clinical outcome after cardiac resynchronisation therapy (CRT).
Verbrugge, 2014 (296)	Asymptomatic episodes of device-registered atrial tachyarrhythmia are not associated with worse cardiac resynchronization therapy response	112	To assess the influence of device-registered episodes of atrial tachyarrhythmia (AT) on the response to cardiac resynchronization therapy
Verna, 2012 (297)	Evaluation of baseline contractile reserve vs dyssynchrony as a predictor of functional improvement and long term outcome after resynchronization pacing therapy: a radionuclide stress study	57	To assess the predictive value of baseline ventricular dyssynchrony and myocardial contractile reserve (mCR) in identifying responders to cardiac resynchronization therapy (CRT).

Author, Year [NCT]	Title	N	Objective
Wang, 2012 (298)	Left ventricular discoordination index measured by speckle tracking strain rate imaging predicts reverse remodelling and survival after cardiac resynchronization therapy	97	To evaluate the predictive value of a baseline speckle tracking strain rate imaging-derived discoordination index for response to cardiac resynchronization therapy (CRT).
Werys, 2016 (226)	Cine dyscontractility index: A novel marker of mechanical dyssynchrony that predicts response to cardiac resynchronization therapy	52	To investigate whether magnetic resonance imaging (MRI) cine-derived dyssynchrony indices provide additional information compared to conventional tagged MRI (tMRI) acquisitions in heart failure patients undergoing cardiac resynchronization therapy (CRT).
Xu, 2012 (41)	Cardiac resynchronization therapy: do women benefit more than men?	728	To examine the gender differences in the benefits derived from CRT as women are underrepresented in cardiac resynchronization therapy (CRT) trials.
Zecchin, 2014 (299)	Long-term outcome of 'super-responder' patients to cardiac resynchronization therapy	62	To evaluate the long-term changes of clinical and echocardiographic parameters, the incidence of cardiac events and parameters associated with late cardiac events in 'super-responders' to cardiac resynchronization therapy (CRT) with [CRT defibrillator (CRT-D)] or without defibrillator back-up
Completed Studies (ClinicalTrials.gov)			

Author, Year [NCT]	Title	N	Objective
NCT03095196	Multipolar CRT-d and Diabetes	190	Completed. One hundred and ninety five T2DM patients will receive a CRT-d treatment. Randomly the study population will receive a CRT-d via multipolar left ventricle (LV) lead pacing (n 99 as Multipolar group), v/s a CRT-d via bipolar LV pacing (n 96, as Bipolar group). These patients will be followed by clinical, and instrumental assessment, and telemetric device control at follow up. Study design will be to evaluate, in failing heart T2DM patients, cardiac deaths, all cause deaths, arrhythmic events, CRT-d responders rate, hospitalizations for HF worsening, phrenic nerve stimulation (PNS), and LV catheter dislodgment events (and re-intervention for LV catheter re-positioning), comparing multipolar CRT-d v/s bipolar CRT-d group of patients at follow up.
NCT01179997	Tissue Doppler Imaging (TDI) Versus Electrocardiography (ECG) Interventricular Pacing Delay Optimization in Cardiac Resynchronization Therapy (CRT)	156	Completed. The aim of this study was to compare the response to cardiac resynchronization therapy when the interventricular pacing interval was optimized by Tissue Doppler Imaging (TDI) to response when it was optimized following QRS width criteria.
NCT01294527	Wireless Stimulation Endocardially for Cardiac Resynchronization Therapy	17	Completed. The WiCS-LV system is an alternative means to providing left ventricular stimulation for Cardiac Resynchronization Therapy (CRT). The purpose of this study is to evaluate the safety and performance of the WiCS-LV System in patients with indications for CRT.

Author, Year [NCT]	Title	N	Objective
NCT01603706	Radial Strain ECHO-Guided Implantation of Cardiac Resynchronization Therapy	172	Completed. The purpose of this study is to evaluate the use of radial strain imaging using speckle tracking analysis to predict the response to CRT in patients with ischemic cardiomyopathy (ICMP) with NYHA functional class 2-4 heart failure and a standard guideline-based CRT indication. Thus assessing the value of lead localization determined by radial strain imaging in a prospective, randomized manner.
NCT00996086	Risk Stratification and Benefits With Cardiac Resynchronization Therapy (CRT)	154	Completed. The purpose of the study is two-fold. First, to determine if an algorithm can be developed based on pre-implant clinical variables to predict response to CRT-D therapy. Second, the study aims to determine in patients implanted with CRT-D if the combined use of cTnT and BNP can further predict and risk-stratify HF improvement and all-cause mortality. Additionally, novel biochemical markers defining cardiac mortality in high risk patients detected by plasma proteomic analysis in the CRT-D patients will be evaluated.

Author, Year [NCT]	Title	N	Objective
NCT02525185	Contractile Reserve in Dyssynchrony: A Novel Principle to Identify Candidates for Cardiac Resynchronization Therapy	210	Active, not recruiting. Cardiac resynchronisation therapy (CRT) has been documented to be a powerful treatment in patients with severe congestive heart failure. However, 30-40% of patients receiving a CRT are non-responders. In this study the investigators will use a previously validated method to estimate myocardial segment work non-invasively by speckle-tracking echocardiography and blood pressure. Since segments which shorten in systole perform positive work, whereas segments which lengthen do negative work, the investigators will calculate wasted work as negative work in percentage of positive work. The main purpose of the study is to determine if wasted work can predict response to CRT.
NCT01323686	Empiric Versus Imaging Guided Left Ventricular Lead Placement in Cardiac Resynchronization Therapy	182	Completed. The aim of this study is to investigate if imaging guided optimal left ventricular (LV) lead placement improves the response rate to cardiac resynchronization therapy (CRT). Consecutive patients meeting the standard criteria for CRT are included in a prospective, double-blinded, randomized trial to LV lead positioning either 1) guided by cardiac imaging using echocardiography, single-photon emission computed tomography, and visualization of cardiac venous anatomy (cardiac computed tomography (CT), venography) to target an epicardial vein at the site of latest mechanical activation without scar tissue or 2) using standard LV lead placement.

Author, Year [NCT]	Title	N	Objective
NCT00399594	Effect of Targeting Left Ventricular Lead Position on the Rate of Response to Cardiac Resynchronization Therapy.	96	Completed. Identifying & optimizing strategies to reduce the burden of heart failure is vital. Despite advances in pharmacotherapy, patients with heart failure are at high risk for death & hospitalization. Cardiac resynchronization therapy (CRT) synchronizes ventricular mechanical activity, improves cardiac output & reduces HF symptoms. However, ~50% of patients do not clearly respond to CRT. Sub-optimal placement of the LV pacing lead appears to be an important reason for non-response. This study will assess whether targeted LV lead placement will result in an increased probability of CRT response at 52 weeks vs. usual (lateral wall) lead placement.
NCT00814840	Efficiency Study of Triple-Site Cardiac Resynchronization in Patients With Heart Failure	100	Completed. The purpose of this study is to assess the efficiency of permanent biventricular pacing using three ventricular leads in terms of reduction in adverse cardiac events rates, improvement in cardiac capacity and patients' functional status in subjects with congestive heart failure and a physiologic (sinus) rhythm.

Author, Year [NCT]	Title	N	Objective
NCT01426321	Combining Myocardial Strain and Cardiac CT to Optimize Left Ventricular Lead Placement in CRT Treatment	100	Active, not recruiting. For patients with advanced heart failure, Cardiac Resynchronization Therapy (CRT) has been a major improvement. The treatment improves symptoms and prolongs life in selected patients with heart failure. However, with the current selection criteria and methods for implanting the pacemaker, only 60-70% of the patients derive significant benefit from the treatment. New imaging techniques, including advanced ultrasound and computed tomography, in combination with new versatile multi-pole electrodes, have made an individually tailored therapy possible. Using these techniques in combination, the study will investigate the effect of individually based "optimal" placement of the pacemaker electrodes vs. standard care. The optimal LV electrode position is defined as pacing a viable segment with the latest mechanical delay, targeting a specific segment of the coronary sinus as visualised on cardiac CT. The hypothesis is that this will increase the number of positive responders from 65% to 85%.
NCT02350842	Triple-site Biventricular Stimulation in the Optimization of CRT	30	Active, not recruiting. The primary objective of this study is to demonstrate that individually optimized, triple-site biventricular pacing is superior to standard biventricular pacing in reverse ventricular modeling as demonstrated by Echo Left Ventricle End-Systolic Volume (LVESV) at 1 year in patients with non-LBBB morphology without increasing the risk of serious procedure and/or device related adverse events at 30 days.

Author, Year [NCT]	Title	N	Objective
NCT01805154	Advance Cardiac Resynchronization Therapy (CRT) Registry	1,500	Completed. The intent of this registry is to understand comprehensive clinical care strategies for Cardiac Resynchronization Therapy (CRT) patients especially non-responders in real-world clinical practice.
NCT01905670	Safety and Performance of Electrodes Implanted in the Left Ventricle	39	Active, not recruiting. The study is intended to demonstrate the safe implant of small receiver-electrodes into the endocardial surface of the left ventricle and to demonstrate its utility in providing cardiac resynchronization therapy in heart failure patients.
NCT02346097	Electrophysiological Optimization of Left Ventricular Lead Placement in CRT	122	Completed. The purpose of this study is to investigate if "optimal electrical resynchronization" achieved by targeting left ventricular lead placement to the myocardial region with the latest electrical activation combined with post-implant pacemakersettings for narrowing the paced QRS width causes an excess improvement in the pumping function of the heart (the left ventricular ejection fraction) in Cardiac Resynchronization Therapy (CRT)
NCT02832622	MultiPoint Pacing™ Post Market Study (MPP-PMS)	2,000	Active, not recruiting. This is a prospective, multicenter, non-randomized registry/observational study. The study will enroll up to 2,000 patients with successful St. Jude Medical (SJM) Cardiac Resynchronization Therapy (CRT) MP device implant from up to 140 centers undergoing CRT implantation.

Author, Year [NCT]	Title	N	Objective
NCT01059175	Dual-Site LV Pacing in CRT Non Responders: Multicenter Randomized Trial	84	Completed. Cardiac resynchronization therapy (CRT) is an effective treatment of heart failure (HF) refractory to optimal medical management, in presence of a depressed left ventricular (LV) ejection fraction and a wide QRS complex. It is mainly limited by a high proportion of non-responders. Attempts have been made, in small studies, to increase the number of stimulation sites in order to optimize the resynchronization therapy. V3 is a planned multicenter, randomized trial whose objective is to evaluate the clinical benefit conferred by the addition of a second endocardial or epicardial LV lead in non-responders after at least 6 months of standard biventricular stimulation. The V3 trial will examine the clinical benefit conferred by the addition of a second LV lead in non-responders compared to standard CRT.

Author, Year [NCT]	Title	N	Objective
NCT00251251	Resynchronization/Defibrillation for Ambulatory Heart Failure Trial	1,798	Completed. Congestive heart failure (CHF) is a common health problem that leads to frequent hospitalizations and an increased death rate. In spite of advances in drug therapy, it remains a significant public health problem. Recently, a new therapy has been developed for advanced heart failure patients with a ventricular conduction abnormality. This new therapy, called cardiac resynchronization (CRT), is a device which stimulates the atrium, the right ventricle, and the left ventricle providing synchronization of the contraction of the heart chambers. It is the addition of this therapy to an implantable cardioverter defibrillator (ICD) that will be evaluated in this study. This study will compare whether the implantation of this new therapy device, in combination with an implantable cardioverter defibrillator, will reduce total mortality and hospitalizations for CHF.
NCT00180258	Comparison of Medical Therapy, Pacing and Defibrillation in Heart Failure	2,200	Completed. The purpose of this study is to determine whether combined mortality and hospitalization in heart failure patients receiving optimal pharmacologic therapy can be reduced by combining optimal pharmacologic therapy and 1) biventricular pacing therapy alone or 2) biventricular pacing with defibrillation. Evaluation of new therapies for the treatment of heart failure should address mortality, morbidity, hospitalization, and cardiac symptoms and function when compared to standard pharmacologic therapy. The COMPANION trial is designed to address all of these objectives.

Author, Year [NCT]	Title	N	Objective
NCT01434615	Medtronic South Asian Systolic Heart Failure Registry	502	Completed. The purpose of this study is to (a) characterize the current management of patients with systolic heart failure (HF) in South Asia following an educational intervention of current guidelines and delivery of disease management tools and (b) to characterize the effect of current therapy on clinical outcomes in patients managed by tertiary care centers across South Asia. Current therapy includes characterization of the post market performance of any market released Medtronic cardiac resynchronization therapy (CRT) or cardiac resynchronization therapy plus implantable cardiac defibrillator (CRT-D) system for cardiac resynchronization therapy (CRT).

Author, Year [NCT]	Title	N	Objective
NCT01439529	ECG Optimization of CRT: Evaluation of Mid-term Response	180	Completed. New simpler methods to optimize cardiac resynchronization therapy (CRT) are being evaluated, such as the use of the electrocardiogram. In this prospective, double-blind, study, the investigators will evaluate: Primary endpoint: To compare the clinical response to CRT in patients with the programming optimized by QRS versus the nominal suggested by the device. Secondary endpoints: To compare cardiac remodeling in patients with the programming optimized by QRS versus the nominal suggested by the device. To evaluate the degree of asynchrony in both groups (nominal versus optimization by QRS) with respect to the intrinsic rhythm. To evaluate the echocardiographic improvement in left ventricular (LV) filling in both groups. To evaluate the differences in the optimal atrioventricular (AV) delay with atrial sensing or atrial pacing. For that, 180 patients with an indication for CRT will be randomized to nominal programming of the device or optimization by the electrocardiogram for a narrower QRS. A clinical and echocardiographic evaluation will be done at baseline, 6 and 12 months.

Author, Year [NCT]	Title	N	Objective
NCT01302470	Comparison of Epicardial Versus Conventional Lead Placement in Cardiac Resynchronization Therapy	30	Completed. The primary goal of this study is to evaluate the use of robotically - assisted device leads as a primary strategy for heart resynchronization.This trials aims to compare transvenous lead placement with robotic lead placement for cardiac resynchronization therapy.
NCT02369419	Frailty Score Assessment for Elderly Patients Undergoing Cardiac Resynchronization Therapy	150	Completed. Background: The cardiac resynchronization therapy (CRT) has been shown to improve symptoms and outcome of patients with congestive heart failure (HF), and depressed left ventricular ejection fraction (LVEF < 35 %). The rate of non-responders to CRT is estimated at 30 %. Yet, the impact of frailty on the response to CRT has not been studied, until now. Purpose : To assess the impact of frailty in the elderly, on the response to CRT.
NCT00273182	InSync Model 8040 (InSync) and InSync III Model 8042 (InSync III) Registry	1,999	Completed. The purpose of this study is to monitor the long-term performance of the InSync Model 8040 (InSync) and InSync III Model 8042 (InSync III) systems for cardiac resynchronization therapy (CRT).
NCT00453622	RISK Stratification Using a Combination of Cardiac Troponin T and Brain Natriuretic Peptide in Patients Receiving CRT-D	222	Completed. The purpose of the study is to identify if the combined use of cardiac troponin enzyme (cTnT) and brain natriuretic peptide (BNP) can predict Heart Failure (HF)improvement and all-cause mortality in patients implanted with cardiac pacemaker-defibrillation devices (CRT-D). Novel biochemical markers identifying patients with high risk cardiac mortality detected by plasma protein analysis will also be evaluated.
Ongoing Studies (ClinicalTrials.gov)			

Author, Year [NCT]	Title	N	Objective
NCT03183011	Cardiac Magnetic Resonance Imaging After Cardiac Resynchronization Therapy	40	Recruiting. This study is evaluating how MRI after CRT can provide key insights regarding LV function, structure, and mechanics resulting from CRT in patients with or without LV scar and inform optimal pacing strategies. The expected accurate and reproducible response assessment with cardiac MRI has important implications for evaluating CRT outcomes in clinical trials, and the insights from the post-CRT MRI promise to improve implementation of CRT.
NCT03366545	Observation of Clinical Routine Care for Heart Failure Patients Implanted With BIOTRONIK CRT Devices	3,000	Recruiting. The registry is primarily designed to assess outcome, efficacy and residual safety aspects of CRT based on long-term data from an unselected, real-life clinical set-up. Moreover, the observation of the patient status should help to find possible predictors for HF events and to identify areas of improvement for CRT and for CRT device settings.

Subtable 18. Published and ongoing studies potentially relevant to Evidence Gap 40 *[Are the CRT outcomes observed in the community predicted by the available clinical trial evidence?]*

Author, Year [NCT]	Title	N	Objective
RCTs			
Bossard, 2014 (230)	Outcome of patients with cardiac resynchronisation defibrillator therapy and a follow-up of at least five years after implant	49	To evaluate the long-term outcome (>5 years) of patients with the main focus on device-associated events.
Rickard, 2011 (234)	The impact of left ventricular size on response to cardiac resynchronization therapy	668	To examine changes in left ventricular ejection fraction (LVEF) and survival in patients with NDCM or SDCM compared with those with traditionally studied moderately dilated cardiomyopathy.
Prospective Observational			

Author, Year [NCT]	Title	N	Objective
Bank, 2012 (160)	Comparison of cardiac resynchronization therapy outcomes in patients with New York Heart Association functional class I/II versus III/IV heart failure	667	To examine the cardiac resynchronization therapy (CRT) benefits in New York Heart Association (NYHA) functional class I/II heart failure (HF) patients, but also investigate if similar outcomes in the real-world are unknown.
Bogale, 2012 (300)	The European CRT Survey: 1 year (9-15 months) follow-up results	2,438	To evaluate the contemporary implantation practice of cardiac resynchronization therapy (CRT) in Europe.
Boriani, 2009 (62)	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	1,480	To analyse the effectiveness of cardiac resynchronization therapy (CRT) in patients with valvular heart disease (a subset not specifically investigated in randomized controlled trials) in comparison with ischaemic heart disease or dilated cardiomyopathy patients.
Botto, 2013 (243)	Clinical characteristics, mortality, cardiac hospitalization, and ventricular arrhythmias in patients undergoing CRT-D implantation: results of the ACTION-HF study	406	To assess 2-year outcomes in a population implanted with a CRT plus defibrillator device in accordance with the standard of care and to evaluate any independent association between clinical variables and outcome.
Dichtl, 2013 (301)	Clinical outcome after 1 year of cardiac resynchronisation therapy: national results from the European CRT survey	150	To investigate the Clinical outcome after 1 year of cardiac resynchronisation therapy: national results from the European CRT survey.
Drozd, 2017 (108)	Cardiac resynchronization therapy outcomes in patients with chronic heart failure: cardiac resynchronization therapy with pacemaker versus cardiac resynchronization therapy with defibrillator	795	To investigate the long-term prognosis of patients who received CRT-P or CRT-D.
Khazanie, 2014 (302)	Clinical effectiveness of cardiac resynchronization therapy versus medical therapy alone among patients with heart failure: analysis of the ICD Registry and ADHERE	9,359	To examine the effectiveness of this therapy in clinical practice
Kiani, 2013 (263)	Relationship of electro-mechanical remodeling to survival rates after cardiac resynchronization therapy	40	To examine whether reverse remodeling predicts increased survival rates in non-trial settings.

Author, Year [NCT]	Title	N	Objective
Laish-Farkash, 2017 (13)	Morbidity and mortality with cardiac resynchronization therapy with pacing vs. with defibrillation in octogenarian patients in a real-world setting	246	To test if among octogenarians eligible for cardiac resynchronization therapy, CRT-P confers similar morbidity and mortality benefits as CRT-D.
Marijon, 2015{Marijon, 2015 #548}	Causes-of-death analysis of patients with cardiac resynchronization therapy: an analysis of the CeRtiTuDe cohort study	1,705	To examine the cause-of-death analysis among CRT-P, compared with CRT-D
Migowski, 2015 (303)	Seven years of use of implantable cardioverter-defibrillator therapies: a nationwide population-based assessment of their effectiveness in real clinical settings	3,295	To assess the effectiveness of ICD and CRT-D therapies within the Brazilian National Health System (SUS).
Suleiman, 2014 (17)	Clinical characteristics and outcomes of elderly patients treated with an implantable cardioverter-defibrillator or cardiac resynchronization therapy in a real-world setting: data from the Israeli ICD Registry	2,807	To provide real-world data regarding outcomes associated with device-based therapy in a large cohort of elderly patients enrolled in the Israeli ICD Registry.
van der Heijden 2015 (304)	The clinical course of patients with implantable cardioverter-defibrillators: Extended experience on clinical outcome, device replacements, and device-related complications	842	To evaluate the long-term outcome of ICD and CRT-D recipients.
Verbrugge, 2013 (18)	Response to cardiac resynchronization therapy in elderly patients (>/=70 years) and octogenarians	220	To investigate whether these benefits can be extrapolated to older patients, typically not included in randomized clinical trials.
Completed Studies (ClinicalTrials.gov)			
NCT01185392	European Cardiac Resynchronisation Therapy Survey	2,438	Completed. The primary objective of this Survey is to describe current European practice based on a broad sampling in 13 countries. The information collected will enable practice between centres and countries to be compared and permit benchmarking with national and international practice. The survey provides valuable quality assurance assessment for individual centres, permits limited economic analyses and broadly evaluates adherence to guideline recommendations.

Author, Year [NCT]	Title	N	Objective
NCT01173783	Deutsches Device Qualitative register	4,008	Completed. It is the aim of this register to document the development of therapies by implantation of Cardioverter/Defibrillators (ICDs) and/or Cardiac Resynchronization therapy (CRT)-Systems.
NCT00382525	PANORAMA Observational Study	8,586	Completed. To construct a computerized database of national profiles and epidemiological data on patients wearing Medtronic implantable pacemakers and cardioverter defibrillators (both with or without cardiac resynchronization therapy), implantable loop recorders and leads used within their intended use. Clinical variables will be analyzed in relation to device-based data and diagnostics.

REFERENCES TO SUPPLEMENTAL TABLE 4

1. Thomas S, Moss AJ, Zareba W et al. Cardiac Resynchronization in Different Age Groups: A MADIT-CRT Long-Term Follow-Up Substudy. J Card Fail. 2016;22:143-9.
2. Adelstein EC, Liu J, Jain S et al. Clinical outcomes in cardiac resynchronization therapy-defibrillator recipients 80 years of age and older. Europace. 2016;18:420-7.
3. Antonio N, Lourenco C, Teixeira R et al. Cardiac resynchronization therapy is effective even in elderly patients with comorbidities. J Interv Card Electrophysiol. 2010;27:61-8.
4. Brambatti M, Guerra F, Matassini MV et al. Cardiac resynchronization therapy improves ejection fraction and cardiac remodelling regardless of patients' age. Europace. 2013;15:704-10.
5. de la Cruz E, Cortes M, Farre J et al. Comparison of pharmacological treatment alone versus treatment combined with cardiac resynchronization therapy in patients over 75 years. J Interv Card Electrophysiol. 2015;43:13-20.
6. Doring M, Ebert M, Dagres N et al. Cardiac resynchronization therapy in the ageing population - With or without an implantable defibrillator? Int J Cardiol. 2018;263:48-53.
7. Foley PW, Chalil S, Khadjooi K, Smith RE, Frenneaux MP, Leyva F. Long-term effects of cardiac resynchronization therapy in octogenarians: a comparative study with a younger population. Europace. 2008;10:1302-7.

8. Fumagalli S, Valsecchi S, Boriani G et al. Comparison of the usefulness of cardiac resynchronization therapy in three age-groups (<65, 65-74 and >/=75 Years) (from the InSync/InSync ICD Italian Registry). Am J Cardiol. 2011;107:1510-6.
9. Guha K, Konstantinou D, Mantziari L et al. The impact of age on clinical outcomes following cardiac resynchronisation therapy. J Interv Card Electrophysiol. 2014;39:95-102.
10. Hoke U, Putter H, Van Der Velde ET et al. Left ventricular reverse remodeling, device-related adverse events, and long-term outcome after cardiac resynchronization therapy in the elderly. Circ Cardiovasc Qual Outcomes. 2014;7:437-44.
11. Kobe J, Andresen D, Maier S et al. Complications and 1-year benefit of cardiac resynchronization therapy in patients over 75 years of age - Insights from the German Device Registry. Int J Cardiol. 2017;228:784-789.
12. Kron J, Aranda JM, Jr., Miles WM et al. Benefit of cardiac resynchronization in elderly patients: results from the Multicenter InSync Randomized Clinical Evaluation (MIRACLE) and Multicenter InSync ICD Randomized Clinical Evaluation (MIRACLE-ICD) trials. J Interv Card Electrophysiol. 2009;25:91-6.
13. Laish-Farkash A, Bruoha S, Katz A et al. Morbidity and mortality with cardiac resynchronization therapy with pacing vs. with defibrillation in octogenarian patients in a real-world setting. Europace. 2017;19:1357-1363.
14. Olechowski B, Sands R, Zachariah D et al. Is cardiac resynchronisation therapy feasible, safe and beneficial in the very elderly? Journal of Geriatric Cardiology. 2015;12:497-501.
15. Penn J, Goldenberg I, Moss AJ et al. Improved outcome with preventive cardiac resynchronization therapy in the elderly: a MADIT-CRT substudy. J Cardiovasc Electrophysiol. 2011;22:892-7.
16. Sardu C, Marfella R, Santulli G. Impact of diabetes mellitus on the clinical response to cardiac resynchronization therapy in elderly people. J Cardiovasc Transl Res. 2014;7:362-8.
17. Suleiman M, Goldenberg I, Haim M et al. Clinical characteristics and outcomes of elderly patients treated with an implantable cardioverter-defibrillator or cardiac resynchronization therapy in a real-world setting: data from the Israeli ICD Registry. Heart Rhythm. 2014;11:435-41.
18. Verbrugge FH, Dupont M, De Vusser P et al. Response to cardiac resynchronization therapy in elderly patients (>/=70 years) and octogenarians. Eur J Heart Fail. 2013;15:203-10.
19. Arshad A, Moss AJ, Foster E et al. Cardiac resynchronization therapy is more effective in women than in men: the MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy) trial. J Am Coll Cardiol. 2011;57:813-20.
20. Goldenberg I, Kutyifa V, Klein HU et al. Survival with cardiac-resynchronization therapy in mild heart failure. N Engl J Med. 2014;370:1694-701.
21. Jamerson D, McNitt S, Polonsky S, Zareba W, Moss A, Tompkins C. Early procedure-related adverse events by gender in MADIT-CRT. J Cardiovasc Electrophysiol. 2014;25:985-989.
22. Tang AS, Wells GA, Talajic M et al. Cardiac-resynchronization therapy for mild-to-moderate heart failure. N Engl J Med. 2010;363:2385-95.

23. Zareba W, Klein H, Cygankiewicz I et al. Effectiveness of Cardiac Resynchronization Therapy by QRS Morphology in the Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy (MADIT-CRT). Circulation. 2011;123:1061-72.
24. Ahsan SY, Saberwal B, Lambiase PD et al. An 8-year single-centre experience of cardiac resynchronisation therapy: procedural success, early and late complications, and left ventricular lead performance. Europace. 2013;15:711-7.
25. Amit G, Suleiman M, Konstantino Y et al. Sex differences in implantable cardioverter-defibrillator implantation indications and outcomes: lessons from the Nationwide Israeli-ICD Registry. Europace. 2014;16:1175-80.
26. Biton Y, Kutyifa V, Zareba W et al. Long-term outcome with cardiac resynchronization therapy in mild heart failure patients with left bundle branch block from US and Europe MADIT-CRT. Heart Fail Rev. 2015;20:535-43.
27. Biton Y, Zareba W, Goldenberg I et al. Sex Differences in Long-Term Outcomes With Cardiac Resynchronization Therapy in Mild Heart Failure Patients With Left Bundle Branch Block. J Am Heart Assoc. 2015;4.
28. Cheng A, Gold MR, Waggoner AD et al. Potential mechanisms underlying the effect of gender on response to cardiac resynchronization therapy: insights from the SMART-AV multicenter trial. Heart Rhythm. 2012;9:736-41.
29. Gillis AM, Kerr CR, Philippon F et al. Impact of cardiac resynchronization therapy on hospitalizations in the Resynchronization-Defibrillation for Ambulatory Heart Failure trial. Circulation. 2014;129:2021-30.
30. Leyva F, Foley PW, Chalil S, Irwin N, Smith RE. Female gender is associated with a better outcome after cardiac resynchronization therapy. Pacing Clin Electrophysiol. 2011;34:82-8.
31. Mooyaart EA, Marsan NA, van Bommel RJ et al. Comparison of long-term survival of men versus women with heart failure treated with cardiac resynchronization therapy. Am J Cardiol. 2011;108:63-8.
32. Providencia R, Marijon E, Lambiase PD et al. Primary Prevention Implantable Cardioverter Defibrillator (ICD) Therapy in Women-Data From a Multicenter French Registry. J Am Heart Assoc. 2016;5.
33. Schuchert A, Muto C, Maounis T et al. Gender-related safety and efficacy of cardiac resynchronization therapy. Clin Cardiol. 2013;36:683-90.
34. Sciarra L, Golia P, Palamà Z et al. Patients with left bundle branch block and left axis deviation show a specific left ventricular asynchrony pattern: Implications for left ventricular lead placement during CRT implantation. Journal of Electrocardiology. 2018;51:175-181.
35. Serdoz LV, Daleffe E, Merlo M et al. Predictors for restoration of normal left ventricular function in response to cardiac resynchronization therapy measured at time of implantation. Am J Cardiol. 2011;108:75-80.
36. Stabile G, Solimene F, Bertaglia E et al. Long-term outcomes of CRT-PM versus CRT-D recipients. Pacing Clin Electrophysiol. 2009;32 Suppl 1:S141-5.
37. Tompkins CM, McNitt S, Polonsky B et al. Sex Differences in Inappropriate ICD Device Therapies: MADIT-II and MADIT-CRT. J Cardiovasc Electrophysiol. 2017;28:94-102.

38. van Bommel RJ, Bax JJ, Abraham WT et al. Characteristics of heart failure patients associated with good and poor response to cardiac resynchronization therapy: a PROSPECT (Predictors of Response to CRT) sub-analysis. Eur Heart J. 2009;30:2470-7.
39. Varma N, Lappe J, He J, Niebauer M, Manne M, Tchou P. Sex-Specific Response to Cardiac Resynchronization Therapy: Effect of Left Ventricular Size and QRS Duration in Left Bundle Branch Block. JACC: Clinical Electrophysiology. 2017;3:844-853.
40. Wilcox JE, Fonarow GC, Zhang Y et al. Clinical effectiveness of cardiac resynchronization and implantable cardioverter-defibrillator therapy in men and women with heart failure: findings from IMPROVE HF. Circ Heart Fail. 2014;7:146-53.
41. Xu YZ, Friedman PA, Webster T et al. Cardiac resynchronization therapy: do women benefit more than men? J Cardiovasc Electrophysiol. 2012;23:172-8.
42. 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.
43. Brignole M, Pokushalov E, Pentimalli F et al. A randomized controlled trial of atrioventricular junction ablation and cardiac resynchronization therapy in patients with permanent atrial fibrillation and narrow QRS. Eur Heart J. 2018.
44. Healey JS, Hohnloser SH, Exner DV et al. Cardiac resynchronization therapy in patients with permanent atrial fibrillation: results from the Resynchronization for Ambulatory Heart Failure Trial (RAFT). Circ Heart Fail. 2012;5:566-70.
45. Plummer CJ, Frank CM, Bari Z et al. A novel algorithm increases the delivery of effective cardiac resynchronization therapy during atrial fibrillation: The CRTee randomized crossover trial. Heart Rhythm. 2018;15:369-375.
46. Abreu A, Oliveira M, Silva Cunha P et al. Does permanent atrial fibrillation modify response to cardiac resynchronization therapy in heart failure patients? Rev Port Cardiol. 2017;36:687-694.
47. Aktas MK, Jeevanantham V, Sherazi S et al. Effect of biventricular pacing during a ventricular sensed event. Am J Cardiol. 2009;103:1741-5.
48. Brignole M, Botto GL, Mont L et al. Predictors of clinical efficacy of 'Ablate and Pace' therapy in patients with permanent atrial fibrillation. Heart. 2012;98:297-302.
49. Dong K, Shen WK, Powell BD et al. Atrioventricular nodal ablation predicts survival benefit in patients with atrial fibrillation receiving cardiac resynchronization therapy. Heart Rhythm. 2010;7:1240-5.
50. Himmel F, Reppel M, Mortensen K, Schunkert H, Bode F. A strategy to achieve CRT response in permanent atrial fibrillation without obligatory atrioventricular node ablation. Pacing Clin Electrophysiol. 2012;35:943-7.
51. Kalscheur MM, Saxon LA, Lee BK et al. Outcomes of cardiac resynchronization therapy in patients with intermittent atrial fibrillation or atrial flutter in the COMPANION trial. Heart Rhythm. 2017;14:858-865.
52. Marques P, Nobre Menezes M, Lima da Silva G et al. Triple-site pacing for cardiac resynchronization in permanent atrial fibrillation - Acute phase results from a prospective observational study. Rev Port Cardiol. 2016;35:331-8.
53. Nakajima I, Noda T, Kanzaski H et al. Development of Heart Failure From Transient Atrial Fibrillation Attacks in Responders to Cardiac Resynchronization Therapy. JACC: Clinical Electrophysiology. 2018;4:1227-1234.

54. Tolosana JM, Arnau AM, Madrid AH et al. Cardiac resynchronization therapy in patients with permanent atrial fibrillation. Is it mandatory to ablate the atrioventricular junction to obtain a good response? Eur J Heart Fail. 2012;14:635-41.
55. Uğurlu M, Kaypakli O, Şahin DY, Içen YK, Kurt İ H, Koç M. Subclinical atrial fibrillation frequency and associated parameters in patients with cardiac resynchronization therapy. Journal of Interventional Cardiac Electrophysiology. 2018;52:217-223.
56. Wilton SB, Kavanagh KM, Aggarwal SG et al. Association of rate-controlled persistent atrial fibrillation with clinical outcome and ventricular remodelling in recipients of cardiac resynchronization therapy. Can J Cardiol. 2011;27:787-93.
57. Wo HT, Chang PC, Chen TH, Wang CC. Cardiac resynchronization therapy in patients with and without atrial fibrillation. Acta Cardiologica Sinica. 2011;27:46-51.
58. Daimee UA, Moss AJ, Biton Y et al. Long-Term Outcomes With Cardiac Resynchronization Therapy in Patients With Mild Heart Failure With Moderate Renal Dysfunction. Circ Heart Fail. 2015;8:725-32.
59. Szepietowska B, Kutyifa V, Ruwald MH et al. Effect of Cardiac Resynchronization Therapy in Patients With Insulin-Treated Diabetes Mellitus. Am J Cardiol. 2015;116:393-9.
60. Bai R, Di Biase L, Elayi C et al. Mortality of heart failure patients after cardiac resynchronization therapy: identification of predictors. J Cardiovasc Electrophysiol. 2008;19:1259-65.
61. Bogdan S, Nof E, Eisen A et al. Clinical Outcomes in Patients with Severe Renal Dysfunction Including Dialysis Following Defibrillator Implantation. Am J Nephrol. 2015;42:295-304.
62. Boriani G, Gasparini M, Landolina M et al. 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;30:2275-83.
63. Campbell P, Takeuchi M, Bourgoun M et al. Right ventricular function, pulmonary pressure estimation, and clinical outcomes in cardiac resynchronization therapy. Circ Heart Fail. 2013;6:435-42.
64. Damy T, Ghio S, Rigby AS et al. Interplay between right ventricular function and cardiac resynchronization therapy: an analysis of the CARE-HF trial (Cardiac Resynchronization-Heart Failure). J Am Coll Cardiol. 2013;61:2153-60.
65. D'Andrea A, Salerno G, Scarafile R et al. Right ventricular myocardial function in patients with either idiopathic or ischemic dilated cardiomyopathy without clinical sign of right heart failure: effects of cardiac resynchronization therapy. Pacing Clin Electrophysiol. 2009;32:1017-29.
66. Dominguez-Rodriguez A, Abreu-Gonzalez P, Jimenez-Sosa A et al. The impact of frailty in older patients with non-ischaemic cardiomyopathy after implantation of cardiac resynchronization therapy defibrillator. Europace. 2015;17:598-602.
67. Friedman DJ, Singh JP, Curtis JP et al. Comparative Effectiveness of CRT-D Versus Defibrillator Alone in HF Patients With Moderate-to-Severe Chronic Kidney Disease. J Am Coll Cardiol. 2015;66:2618-2629.
68. George J, Barsheshet A, Moss AJ et al. Effectiveness of cardiac resynchronization therapy in diabetic patients with ischemic and nonischemic cardiomyopathy. Ann Noninvasive Electrocardiol. 2012;17:14-21.

69. Goldenberg I, Moss AJ, McNitt S et al. Relation between renal function and response to cardiac resynchronization therapy in Multicenter Automatic Defibrillator Implantation Trial--Cardiac Resynchronization Therapy (MADIT-CRT). Heart Rhythm. 2010;7:1777-82.
70. Herscovici R, Moss AJ, Kutyifa V et al. Risk factors and outcomes associated with the development of myocardial ischemic events in patients who receive cardiac resynchronization therapy. Am J Cardiol. 2013;112:1896-900.
71. Hosoda J, Ishikawa T, Matsushita K et al. Impact of renal insufficiency on long-term clinical outcome in patients with heart failure treated by cardiac resynchronization therapy. J Cardiol. 2012;60:301-5.
72. Kowalczyk J, Lenarczyk R, Kowalski O et al. Contrast-induced acute kidney injury in patients undergoing cardiac resynchronization therapy-incidence and prognostic importance. Sub-analysis of data from randomized TRUST CRT trial. J Interv Card Electrophysiol. 2014;40:1-8.
73. Kubala M, Guédon-Moreau L, Anselme F et al. Utility of Frailty Assessment for Elderly Patients Undergoing Cardiac Resynchronization Therapy. JACC: Clinical Electrophysiology. 2017;3:1523-1533.
74. Kutyifa V, Naqvi SY, Brown M et al. Comparison of Long-Term Survival Benefits With Cardiac Resynchronization Therapy in Patients With Mild Heart Failure With Versus Without Diabetes Mellitus (from the Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy [MADIT-CRT]). Am J Cardiol. 2018;121:1567-1574.
75. Mangiavacchi M, Gasparini M, Genovese S et al. Insulin-treated type 2 diabetes is associated with a decreased survival in heart failure patients after cardiac resynchronization therapy. Pacing Clin Electrophysiol. 2008;31:1425-32.
76. Martin DT, McNitt S, Nesto RW, Rutter MK, Moss AJ. Cardiac resynchronization therapy reduces the risk of cardiac events in patients with diabetes enrolled in the multicenter automatic defibrillator implantation trial with cardiac resynchronization therapy (MADIT-CRT). Circ Heart Fail. 2011;4:332-8.
77. Mathew J, Katz R, St John Sutton M et al. Chronic kidney disease and cardiac remodelling in patients with mild heart failure: results from the REsynchronization reVErses Remodeling in Systolic Left vEntricular Dysfunction (REVERSE) study. Eur J Heart Fail. 2012;14:1420-8.
78. Santangelo G, Dugo D, Mule M et al. Functional and clinical implications of cardiac resynchronization therapy on outcomes of diabetic patients with heart failure. J Cardiovasc Med (Hagerstown). 2011;12:396-400.
79. Schaer BA, Hitz L, Sticherling C et al. Changes in renal function over time in patients with cardiac resynchronisation therapy. Swiss Med Wkly. 2013;143:w13863.
80. Scuteri L, Rordorf R, Marsan NA et al. Relevance of echocardiographic evaluation of right ventricular function in patients undergoing cardiac resynchronization therapy. Pacing Clin Electrophysiol. 2009;32:1040-9.
81. Singal G, Upadhyay GA, Borgquist R et al. Renal Response in Patients with Chronic Kidney Disease Predicts Outcome Following Cardiac Resynchronization Therapy. Pacing Clin Electrophysiol. 2015;38:1192-200.
82. Sredniawa B, Lenarczyk R, Kowalski O et al. Sleep apnoea as a predictor of mid- and long-term outcome in patients undergoing cardiac resynchronization therapy. Europace. 2009;11:106-14.

83. Szepietowska B, McNitt S, Polonsky B et al. Metabolic syndrome is associated with different clinical outcome after cardiac resynchronization therapy in patients with ischemic and non-ischemic cardiomyopathy. Cardiol J. 2016;23:344-51.
84. Van Bommel RJ, Mollema SA, Borleffs CJ et al. Impaired renal function is associated with echocardiographic nonresponse and poor prognosis after cardiac resynchronization therapy. J Am Coll Cardiol. 2011;57:549-55.
85. van Everdingen WM, Walmsley J, Cramer MJ et al. Echocardiographic Prediction of Cardiac Resynchronization Therapy Response Requires Analysis of Both Mechanical Dyssynchrony and Right Ventricular Function: A Combined Analysis of Patient Data and Computer Simulations. J Am Soc Echocardiogr. 2017;30:1012-1020.e2.
86. Birnie DH, Ha A, Higginson L et al. Impact of QRS morphology and duration on outcomes after cardiac resynchronization therapy: Results from the Resynchronization-Defibrillation for Ambulatory Heart Failure Trial (RAFT). Circ Heart Fail. 2013;6:1190-8.
87. Biton Y, Ng CY, Xia X et al. Baseline adverse electrical remodeling and the risk for ventricular arrhythmia in Cardiac Resynchronization Therapy Recipients (MADIT CRT). Journal of Cardiovascular Electrophysiology. 2018;29:1017-1023.
88. Gasparini M, Leclercq C, Yu CM et al. Absolute survival after cardiac resynchronization therapy according to baseline QRS duration: a multinational 10-year experience: data from the Multicenter International CRT Study. Am Heart J. 2014;167:203-209.e1.
89. Gervais R, Leclercq C, Shankar A et al. Surface electrocardiogram to predict outcome in candidates for cardiac resynchronization therapy: a sub-analysis of the CARE-HF trial. Eur J Heart Fail. 2009;11:699-705.
90. Gold MR, Thebault C, Linde C 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;126:822-9.
91. Goldenberg I, Moss AJ, Hall WJ et al. Predictors of response to cardiac resynchronization therapy in the Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT). Circulation. 2011;124:1527-36.
92. Gorcsan J, 3rd, Oyenuga O, Habib PJ et al. Relationship of echocardiographic dyssynchrony to long-term survival after cardiac resynchronization therapy. Circulation. 2010;122:1910-8.
93. Hudak M, Kerekanic M, Misikova S, Komanova E, Boho A, Stancak B. The effectiveness of CRT on improvement of survival of heart failure patients in real life clinical settings. Acta Cardiologica. 2017;72:180-187.
94. 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.
95. 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.
96. Risum N. Assessment of mechanical dyssynchrony in cardiac resynchronization therapy. Dan Med J. 2014;61:B4981.

97. Saba S, Marek J, Alam MB et al. Influence of QRS duration on outcome of death or appropriate defibrillator therapy by strategy of left ventricular lead placement in cardiac resynchronization therapy recipients. J Interv Card Electrophysiol. 2014;41:211-5.
98. Sonne C, Bott-Flugel L, Hauck S et al. Three-dimensional echocardiographic optimization improves outcome in cardiac resynchronization therapy compared to ECG optimization: a randomized comparison. Pacing Clin Electrophysiol. 2014;37:312-20.
99. 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.
100. Foley PW, Stegemann B, Smith RE, Sanderson JE, Leyva F. Cardiac resynchronization therapy in patients with mildly impaired left ventricular function. Pacing Clin Electrophysiol. 2009;32 Suppl 1:S186-9.
101. Kutyifa V, Kloppe A, Zareba W et al. The influence of left ventricular ejection fraction on the effectiveness of cardiac resynchronization therapy: MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy). J Am Coll Cardiol. 2013;61:936-44.
102. Linde C, Daubert C, Abraham WT et al. Impact of ejection fraction on the clinical response to cardiac resynchronization therapy in mild heart failure. Circ Heart Fail. 2013;6:1180-9.
103. Schuchert A, Muto C, Maounis T, Ella RO, Polauck A, Padeletti L. Relationship between pre-implant ejection fraction and outcome after cardiac resynchronization therapy in symptomatic patients. Acta Cardiol. 2014;69:424-32.
104. Barsheshet A, Goldenberg I, Moss AJ et al. Response to preventive cardiac resynchronization therapy in patients with ischaemic and nonischaemic cardiomyopathy in MADIT-CRT. Eur Heart J. 2011;32:1622-30.
105. Linde C, Abraham WT, Gold MR, Daubert C. 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;56:1826-31.
106. Barra S, Providência R, Boveda S et al. Device complications with addition of defibrillation to cardiac resynchronisation therapy for primary prevention. Heart. 2018.
107. Di Biase L, Auricchio A, Sorgente A et al. The magnitude of reverse remodelling irrespective of aetiology predicts outcome of heart failure patients treated with cardiac resynchronization therapy. Eur Heart J. 2008;29:2497-505.
108. Drozd M, Gierula J, Lowry JE et al. Cardiac resynchronization therapy outcomes in patients with chronic heart failure: cardiac resynchronization therapy with pacemaker versus cardiac resynchronization therapy with defibrillator. J Cardiovasc Med (Hagerstown). 2017;18:962-967.
109. Gold MR, Daubert JC, Abraham WT et al. Implantable defibrillators improve survival in patients with mildly symptomatic heart failure receiving cardiac resynchronization therapy: analysis of the long-term follow-up of remodeling in systolic left ventricular dysfunction (REVERSE). Circ Arrhythm Electrophysiol. 2013;6:1163-8.

110. McLeod CJ, Shen WK, Rea RF et al. Differential outcome of cardiac resynchronization therapy in ischemic cardiomyopathy and idiopathic dilated cardiomyopathy. Heart Rhythm. 2011;8:377-82.
111. Morani G, Gasparini M, Zanon F et al. Cardiac resynchronization therapy-defibrillator improves long-term survival compared with cardiac resynchronization therapy-pacemaker in patients with a class IA indication for cardiac resynchronization therapy: data from the Contak Italian Registry. Europace. 2013;15:1273-9.
112. Mukherjee A, Patel CD, Naik N, Sharma G, Roy A. Quantitative assessment of cardiac mechanical dyssynchrony and prediction of response to cardiac resynchronization therapy in patients with non-ischaemic dilated cardiomyopathy using equilibrium radionuclide angiography. Europace. 2016;18:851-7.
113. Verbrugge FH, De Vusser P, Rivero-Ayerza M et al. Cardiac resynchronization therapy with or without defibrillator: experience from a high-volume Belgian implantation centre. Acta Cardiol. 2013;68:37-45.
114. Wang Y, Sharbaugh MS, Althouse AD, Mulukutla S, Saba S. Cardiac resynchronization therapy pacemakers versus defibrillators in older non-ischemic cardiomyopathy patients. Indian Pacing Electrophysiol J. 2018.
115. Wikstrom G, Blomstrom-Lundqvist C, Andren B et al. The effects of aetiology on outcome in patients treated with cardiac resynchronization therapy in the CARE-HF trial. Eur Heart J. 2009;30:782-8.
116. Zhang Q, Fung JW, Chan JY et al. Difference in long-term clinical outcome after cardiac resynchronisation therapy between ischaemic and non-ischaemic aetiologies of heart failure. Heart. 2009;95:113-8.
117. Orlov MV, Gardin JM, Slawsky M et al. Biventricular pacing improves cardiac function and prevents further left atrial remodeling in patients with symptomatic atrial fibrillation after atrioventricular node ablation. Am Heart J. 2010;159:264-70.
118. Brignole M, Menozzi C, Botto GL et al. Usefulness of echo-guided cardiac resynchronization pacing in patients undergoing "ablate and pace" therapy for permanent atrial fibrillation and effects of heart rate regularization and left ventricular resynchronization. Am J Cardiol. 2008;102:854-60.
119. Garcia B, Clementy N, Benhenda N et al. Mortality After Atrioventricular Nodal Radiofrequency Catheter Ablation With Permanent Ventricular Pacing in Atrial Fibrillation: Outcomes From a Controlled Nonrandomized Study. Circ Arrhythm Electrophysiol. 2016;9.
120. Kia M, Tabatabaei SA, Bagherzadeh AA, Nikdoust F. Left and right approach atrioventricular junctional ablation in patients with permanent Atrial fibrillation. Iranian Heart Journal. 2016;17:12-17.
121. Palmisano P, Aspromonte V, Ammendola E et al. Effect of fixed-rate vs. rate-RESPONSIve pacing on exercise capacity in patients with permanent, refractory atrial fibrillation and left ventricular dysfunction treated with atrioventricular junction aBLation and bivEntricular pacing (RESPONSIBLE): a prospective, multicentre, randomized, single-blind study. Europace. 2017;19:414-420.
122. Atwater BD, Wagner GS, Kisslo J, Risum N. The electromechanical substrate for response to cardiac resynchronization therapy in patients with right bundle branch block. Pacing Clin Electrophysiol. 2017;40:1358-1367.

123. Ruwald MH, Mittal S, Ruwald AC et al. Association between frequency of atrial and ventricular ectopic beats and biventricular pacing percentage and outcomes in patients with cardiac resynchronization therapy. J Am Coll Cardiol. 2014;64:971-81.
124. Ruwald AC, Kutyifa V, Ruwald MH et al. The association between biventricular pacing and cardiac resynchronization therapy-defibrillator efficacy when compared with implantable cardioverter defibrillator on outcomes and reverse remodelling. Eur Heart J. 2015;36:440-8.
125. Liang Y, Wang Q, Zhang M et al. Cessation of pacing in super-responders of cardiac resynchronization therapy: A randomized controlled trial. J Cardiovasc Electrophysiol. 2018.
126. Ghotbi AA, Sander M, Kober L et al. Optimal Cardiac Resynchronization Therapy Pacing Rate in Non-Ischemic Heart Failure Patients: A Randomized Crossover Pilot Trial. PLoS One. 2015;10:e0138124.
127. Mazurek M, Jedrzejczyk-Patej E, Lenarczyk R et al. Do we need to monitor the percentage of biventricular pacing day by day? Int J Cardiol. 2016;221:81-9.
128. Varma N, Stadler RW, Ghosh S, Kloppe A. Influence of automatic frequent pace-timing adjustments on effective left ventricular pacing during cardiac resynchronization therapy. Europace. 2017;19:831-837.
129. Xu GJ, Gan TY, Tang BP et al. Predictive factors and clinical effect of optimized cardiac resynchronization therapy. Exp Ther Med. 2013;5:355-361.
130. Aktas MK, Mittal S, Kutyifa V et al. The Burden and Morphology of Premature Ventricular Contractions and their Impact on Clinical Outcomes in Patients Receiving Biventricular Pacing in the Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy (MADIT-CRT). Ann Noninvasive Electrocardiol. 2016;21:41-8.
131. Mittal S, Aktas MK, Moss AJ et al. The impact of nonsustained ventricular tachycardia on reverse remodeling, heart failure, and treated ventricular tachyarrhythmias in MADIT-CRT. J Cardiovasc Electrophysiol. 2014;25:1082-7.
132. Ruwald AC, Aktas MK, Ruwald MH et al. Postimplantation ventricular ectopic burden and clinical outcomes in cardiac resynchronization therapy-defibrillator patients: a MADIT-CRT substudy. Annals of Noninvasive Electrocardiology. 2018;23.
133. Januszkiewicz L, Vegh E, Borgquist R et al. Prognostic implication of baseline PR interval in cardiac resynchronization therapy recipients. Heart Rhythm. 2015;12:2256-62.
134. Kutyifa V, Stockburger M, Daubert JP et al. PR interval identifies clinical response in patients with non-left bundle branch block: a Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy substudy. Circ Arrhythm Electrophysiol. 2014;7:645-51.
135. Kyriacou A, Rajkumar CA, Pabari PA et al. Distinct impacts of heart rate and right atrial-pacing on left atrial mechanical activation and optimal AV delay in CRT. PACE - Pacing and Clinical Electrophysiology. 2018;41:959-966.
136. Lee YH, Wu JH, Asirvatham SJ et al. Effects of atrioventricular conduction delay on the outcome of cardiac resynchronization therapy. J Electrocardiol. 2014;47:930-5.

137. Senfield J, Daubert C, Abraham WT et al. The Impact of the PR Interval in Patients Receiving Cardiac Resynchronization Therapy: Results From the REVERSE Study. JACC Clin Electrophysiol. 2017;3:818-826.
138. Sohaib SMA, Wright I, Lim E et al. Atrioventricular Optimized Direct His Bundle Pacing Improves Acute Hemodynamic Function in Patients With Heart Failure and PR Interval Prolongation Without Left Bundle Branch Block. JACC Clin Electrophysiol. 2015;1:582-591.
139. Stockburger M, Moss AJ, Klein HU 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;105:944-952.
140. Bank AJ, Kaufman CL, Burns KV et al. Intramural dyssynchrony and response to cardiac resynchronization therapy in patients with and without previous right ventricular pacing. Eur J Heart Fail. 2010;12:1317-24.
141. Kanzaki H, Satomi K, Noda T et al. Comparison of the acute effects of right ventricular apical pacing and biventricular pacing in patients with heart failure. Intern Med. 2015;54:1329-35.
142. Stockburger M, Gomez-Doblas JJ, Lamas G et al. Preventing ventricular dysfunction in pacemaker patients without advanced heart failure: results from a multicentre international randomized trial (PREVENT-HF). Eur J Heart Fail. 2011;13:633-41.
143. Taborsky M, Rihova D, Mraz T et al. TUGENDHAT: a pilot randomized study on effects of biventricular pacing in patients with bradycardia pacing indication and normal systolic function on heart failure, atrial fibrillation and quality of life (results of 12 month follow-up). Bratisl Lek Listy. 2013;114:323-9.
144. Chang PC, Wo HT, Chen TH, Wu D, Lin FC, Wang CC. Remote past left ventricular function before chronic right ventricular pacing predicts responses to cardiac resynchronization therapy upgrade. Pacing Clin Electrophysiol. 2014;37:454-63.
145. Delnoy PP, Ottervanger JP, Luttikhuis HO et al. Long-term clinical response of cardiac resynchronization after chronic right ventricular pacing. Am J Cardiol. 2009;104:116-21.
146. Gierula J, Cubbon RM, Jamil HA et al. Cardiac resynchronization therapy in pacemaker-dependent patients with left ventricular dysfunction. Europace. 2013;15:1609-14.
147. Lipar L, Srivathsan K, Scott LR. Short-term outcome of cardiac resynchronization therapy - a comparison between newly implanted and chronically right ventricle-paced patients. Int J Cardiol. 2016;219:195-9.
148. Paparella G, Sciarra L, Capulzini L et al. Long-term effects of upgrading to biventricular pacing: differences with cardiac resynchronization therapy as primary indication. Pacing Clin Electrophysiol. 2010;33:841-9.
149. Rickard J, Cheng A, Spragg D et al. QRS narrowing is associated with reverse remodeling in patients with chronic right ventricular pacing upgraded to cardiac resynchronization therapy. Heart Rhythm. 2013;10:55-60.
150. Sideris S, Poulidakis E, Aggeli C et al. Upgrading pacemaker to cardiac resynchronization therapy: an option for patients with chronic right ventricular pacing and heart failure. Hellenic J Cardiol. 2014;55:17-23.
151. van Geldorp IE, Vernooy K, Delhaas T et al. Beneficial effects of biventricular pacing in chronically right ventricular paced patients with mild cardiomyopathy. Europace. 2010;12:223-9.

152. 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.
153. Albertsen AE, Mortensen PT, Jensen HK, Poulsen SH, Egeblad H, Nielsen JC. Adverse effect of right ventricular pacing prevented by biventricular pacing during long-term follow-up: a randomized comparison. Eur J Echocardiogr. 2011;12:767-72.
154. Curtis AB, Worley SJ, Adamson PB et al. Biventricular pacing for atrioventricular block and systolic dysfunction. N Engl J Med. 2013;368:1585-93.
155. Curtis AB, Worley SJ, Chung ES, Li P, Christman SA, St John Sutton M. Improvement in Clinical Outcomes With Biventricular Versus Right Ventricular Pacing: The BLOCK HF Study. J Am Coll Cardiol. 2016;67:2148-2157.
156. Martinelli Filho M, de Siqueira SF, Costa R et al. Conventional versus biventricular pacing in heart failure and bradyarrhythmia: the COMBAT study. J Card Fail. 2010;16:293-300.
157. Cruz MC, Abreu A, Portugal G et al. Relationship of left ventricular global longitudinal strain with cardiac autonomic denervation as assessed by (123)I-mIBG scintigraphy in patients with heart failure with reduced ejection fraction submitted to cardiac resynchronization therapy : Assessment of cardiac autonomic denervation by GLS in patients with heart failure with reduced ejection fraction submitted to CRT. J Nucl Cardiol. 2017.
158. Gorcsan J, 3rd, Sogaard P, Bax JJ et al. Association of persistent or worsened echocardiographic dyssynchrony with unfavourable clinical outcomes in heart failure patients with narrow QRS width: a subgroup analysis of the EchoCRT trial. Eur Heart J. 2016;37:49-59.
159. Anand IS, Carson P, Galle E 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;119:969-77.
160. Bank AJ, Rischall A, Gage RM, Burns KV, Kubo SH. Comparison of cardiac resynchronization therapy outcomes in patients with New York Heart Association functional class I/II versus III/IV heart failure. J Card Fail. 2012;18:373-8.
161. Bhattacharya S, Abebe K, Simon M, Saba S, Adelstein E. Role of cardiac resynchronization in end-stage heart failure patients requiring inotrope therapy. J Card Fail. 2010;16:931-7.
162. Castel MA, Magnani S, Mont L et al. Survival in New York Heart Association class IV heart failure patients treated with cardiac resynchronization therapy compared with patients on optimal pharmacological treatment. Europace. 2010;12:1136-40.
163. Gopinathannair R, Roukoz H, Bhan A et al. Cardiac resynchronization therapy and clinical outcomes in continuous flow left ventricular assist device recipients. Journal of the American Heart Association. 2018;7.
164. Haghjoo M, Bonakdar HR, Jorat MV et al. Effect of right ventricular lead location on response to cardiac resynchronization therapy in patients with end-stage heart failure. Europace. 2009;11:356-63.
165. Haugaa KH, Marek JJ, Ahmed M et al. Mechanical dyssynchrony after cardiac resynchronization therapy for severely symptomatic heart failure is associated with risk for ventricular arrhythmias. J Am Soc Echocardiogr. 2014;27:872-9.

166. Lepillier A, Piot O, Gerritse B et al. Relationship between New York Heart Association class change and ventricular tachyarrhythmia occurrence in patients treated with cardiac resynchronization plus defibrillator. Europace. 2009;11:80-5.
167. Richardson TD, Hale L, Arteaga C et al. Prospective Randomized Evaluation of Implantable Cardioverter-Defibrillator Programming in Patients With a Left Ventricular Assist Device. J Am Heart Assoc. 2018;7.
168. Rickard J, Baranowski B, Cheng A et al. Comparative Efficacy of Cardiac Resynchronization Therapy in Africans Americans Compared With European Americans. Am J Cardiol. 2015;116:1101-5.
169. Schuchert A, Muto C, Maounis T et al. One-year outcome after CRT implantation in NYHA class IV in comparison to NYHA class III patients. Clin Res Cardiol. 2013;102:505-11.
170. Suleiman M, Goldenberg I, Samniah N et al. Outcome of Patients with Advanced Heart Failure Who Receive Device-Based Therapy for Primary Prevention of Sudden Cardiac Death: Insights from the Israeli ICD Registry. Pacing Clin Electrophysiol. 2015;38:738-45.
171. Tayal B, Sogaard P, Delgado-Montero A et al. Interaction of Left Ventricular Remodeling and Regional Dyssynchrony on Long-Term Prognosis after Cardiac Resynchronization Therapy. J Am Soc Echocardiogr. 2017;30:244-250.
172. van Bommel RJ, van Rijnsoever E, Borleffs CJ et al. Effect of cardiac resynchronization therapy in patients with New York Heart Association functional class IV heart failure. Am J Cardiol. 2010;106:1146-51.
173. Versteeg H, van den Broek KC, Theuns DA 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;108:1155-9.
174. Gold MR, Auricchio A, Leclercq C et al. The rationale and design of the SMART CRT trial. Pacing Clin Electrophysiol. 2018;41:1212-1216.
175. Gu M, Jin H, Hua W et al. Repetitive optimizing left ventricular pacing configurations with quadripolar leads improves response to cardiac resynchronization therapy: A single-center randomized clinical trial. Medicine (Baltimore). 2017;96:e8066.
176. Knappe D, Pouleur AC, Shah AM et al. Dyssynchrony, contractile function, and response to cardiac resynchronization therapy. Circ Heart Fail. 2011;4:433-40.
177. Kockova R, Sedlacek K, Wichterle D et al. Cardiac resynchronization therapy guided by cardiac magnetic resonance imaging: A prospective, single-centre randomized study (CMR-CRT). Int J Cardiol. 2018;270:325-330.
178. Miranda RI, Nault M, Johri A et al. Maximal electric separation-guided placement of right ventricular lead improves responders in cardiac resynchronization defibrillator therapy. Circ Arrhythm Electrophysiol. 2012;5:927-32.
179. Pouleur AC, Knappe D, Shah AM et al. 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;32:1720-9.
180. Yan J, Zhang S, Huang D et al. Evaluation of the therapeutic effects of QuickOpt optimization in Chinese patients with chronic heart failure treated by cardiac resynchronization. Sci Rep. 2018;8:4259.
181. Yang M, Li X, Liang J et al. Outcomes of cardiac resynchronization therapy using left ventricular quadripolar leads. Pacing Clin Electrophysiol. 2018.

182. Bertini M, Hoke U, van Bommel RJ et al. Impact of clinical and echocardiographic response to cardiac resynchronization therapy on long-term survival. Eur Heart J Cardiovasc Imaging. 2013;14:774-81.
183. Biffi M, Defaye P, Jais P et al. Benefits of left ventricular endocardial pacing comparing failed implants and prior non-responders to conventional cardiac resynchronization therapy: A subanalysis from the ALSYNC study. Int J Cardiol. 2018;259:88-93.
184. Conraads VM, Spruit MA, Braunschweig F et al. Physical activity measured with implanted devices predicts patient outcome in chronic heart failure. Circ Heart Fail. 2014;7:279-87.
185. Coverstone E, Sheehy J, Kleiger RE, Smith TW. The postimplantation electrocardiogram predicts clinical response to cardiac resynchronization therapy. Pacing Clin Electrophysiol. 2015;38:572-80.
186. Delgado V, van Bommel RJ, Bertini M et al. Relative merits of left ventricular dyssynchrony, left ventricular lead position, and myocardial scar to predict long-term survival of ischemic heart failure patients undergoing cardiac resynchronization therapy. Circulation. 2011;123:70-8.
187. Dong YX, Oh JK, Yang YZ, Cha YM. Left ventricular 12 segmental strain imaging predicts response to cardiac resynchronization therapy. Chin Med J (Engl). 2013;126:2620-4.
188. Forleo GB, Mantica M, Di Biase L et al. Clinical and procedural outcome of patients implanted with a quadripolar left ventricular lead: early results of a prospective multicenter study. Heart Rhythm. 2012;9:1822-8.
189. Gendre R, Lairez O, Mondoly P et al. Research of predictive factors for cardiac resynchronization therapy: a prospective study comparing data from phase-analysis of gated myocardial perfusion single-photon computed tomography and echocardiography : Trying to anticipate response to CRT. Ann Nucl Med. 2017;31:218-226.
190. Gold MR, Birgersdotter-Green U, Singh JP et al. The relationship between ventricular electrical delay and left ventricular remodelling with cardiac resynchronization therapy. Eur Heart J. 2011;32:2516-24.
191. Gold MR, Singh JP, Ellenbogen KA et al. Interventricular Electrical Delay Is Predictive of Response to Cardiac Resynchronization Therapy. JACC Clin Electrophysiol. 2016;2:438-447.
192. Gold MR, Yu Y, Wold N, Day JD. The role of interventricular conduction delay to predict clinical response with cardiac resynchronization therapy. Heart Rhythm. 2017;14:1748-1755.
193. Hansen PB, Sommer A, Norgaard BL, Kronborg MB, Nielsen JC. Left atrial size and function as assessed by computed tomography in cardiac resynchronization therapy: Association to echocardiographic and clinical outcome. Int J Cardiovasc Imaging. 2017;33:917-925.
194. Hsing JM, Selzman KA, Leclercq C et al. Paced left ventricular QRS width and ECG parameters predict outcomes after cardiac resynchronization therapy: PROSPECT-ECG substudy. Circ Arrhythm Electrophysiol. 2011;4:851-7.
195. Iwano H, Yamada S, Watanabe M et al. Strain rate dispersion index can predict changes in left ventricular volume and adverse cardiac events following cardiac resynchronization therapy. Circ J. 2013;77:2757-65.

196. Kalscheur MM, Kipp RT, Tattersall MC et al. Machine Learning Algorithm Predicts Cardiac Resynchronization Therapy Outcomes: Lessons From the COMPANION Trial. Circ Arrhythm Electrophysiol. 2018;11:e005499.
197. Kjaergaard J, Ghio S, St John Sutton M, Hassager C. Tricuspid annular plane systolic excursion and response to cardiac resynchronization therapy: results from the REVERSE trial. J Card Fail. 2011;17:100-7.
198. Lenarczyk R, Jedrzejczyk-Patej E, Mazurek M et al. Quality of life in cardiac resynchronization recipients: association with response and impact on outcome. Pacing Clin Electrophysiol. 2015;38:8-17.
199. Linde C, Abraham WT, Gold MR et al. Predictors of short-term clinical response to cardiac resynchronization therapy. Eur J Heart Fail. 2017;19:1056-1063.
200. Mascioli G, Padeletti L, Sassone B et al. Electrocardiographic criteria of true left bundle branch block: a simple sign to predict a better clinical and instrumental response to CRT. Pacing Clin Electrophysiol. 2012;35:927-34.
201. Menet A, Guyomar Y, Ennezat PV et al. Prognostic value of left ventricular reverse remodeling and performance improvement after cardiac resynchronization therapy: A prospective study. Int J Cardiol. 2016;204:6-11.
202. Momomura S, Tsutsui H, Sugawara Y et al. Clinical efficacy of cardiac resynchronization therapy with an implantable defibrillator in a Japanese population: results of the MIRACLE-ICD outcome measured in Japanese indication (MOMIJI) study. Circ J. 2012;76:1911-9.
203. Murin P, Mitro P, Valocik G, Spurny P. Global myocardial contractile reserve assessed by high-dose dobutamine stress echocardiography predicts response to the cardiac resynchronization therapy. Echocardiography. 2015;32:490-5.
204. Nagy VK, Szeplaki G, Apor A et al. Role of Right Ventricular Global Longitudinal Strain in Predicting Early and Long-Term Mortality in Cardiac Resynchronization Therapy Patients. PLoS One. 2015;10:e0143907.
205. Nagy KV, Szeplaki G, Perge P et al. Quality of life measured with EuroQol-five dimensions questionnaire predicts long-term mortality, response, and reverse remodelling in cardiac resynchronization therapy patients. Europace. 2018;20:1506-1512.
206. Orlov MV, Maysky M, Akrivakis ST et al. Baseline myocardial perfusion predicts response to cardiac resynchronization therapy: a prospective observational study. J Interv Card Electrophysiol. 2008;23:127-33.
207. Park JH, Negishi K, Grimm RA et al. Echocardiographic predictors of reverse remodeling after cardiac resynchronization therapy and subsequent events. Circ Cardiovasc Imaging. 2013;6:864-72.
208. Petrovic M, Petrovic MT, Milasinovic G et al. Prediction of a good response to cardiac resynchronization therapy in patients with severe dilated cardyomyopathy: could conventional echocardiography be the answer after all? Echocardiography. 2012;29:267-75.
209. Petryka J, Misko J, Przybylski A et al. Magnetic resonance imaging assessment of intraventricular dyssynchrony and delayed enhancement as predictors of response to cardiac resynchronization therapy in patients with heart failure of ischaemic and non-ischaemic etiologies. Eur J Radiol. 2012;81:2639-47.
210. Poposka L, Boskov V, Risteski D et al. Electrocardiographic Parameters as Predictors of Response to Cardiac Resynchronization Therapy. Open Access Maced J Med Sci. 2018;6:297-302.

211. Rocchi G, Bertini M, Biffi M et al. Exercise stress echocardiography is superior to rest echocardiography in predicting left ventricular reverse remodelling and functional improvement after cardiac resynchronization therapy. Eur Heart J. 2009;30:89-97.
212. Sebag FA, Martins RP, Defaye P et al. Reverse electrical remodeling by cardiac resynchronization therapy: prevalence and clinical impact. J Cardiovasc Electrophysiol. 2012;23:1219-27.
213. Separham A, Pourafkari L, Kazemi B et al. Vitamin D deficiency and functional response to CRT in heart failure patients. Herz. 2017.
214. Shanmugam N, Campos AG, Prada-Delgado O et al. Effect of atrioventricular optimization on circulating N-terminal pro brain natriuretic peptide following cardiac resynchronization therapy. Eur J Heart Fail. 2013;15:534-42.
215. Şipal A, Bozyel S, Aktaş M et al. Surface electrogram-guided left ventricular lead placement improves response to cardiac resynchronization therapy. Anatolian Journal of Cardiology. 2018;19:184-191.
216. Sohal M, Shetty A, Duckett S et al. Noninvasive assessment of LV contraction patterns using CMR to identify responders to CRT. JACC Cardiovasc Imaging. 2013;6:864-73.
217. Sullivan RM, Murillo J, Gerritse B et al. Do baseline diastolic echocardiographic parameters predict outcome after resynchronization therapy? Results from the PROSPECT trial. Pacing Clin Electrophysiol. 2013;36:214-20.
218. Thebault C, Donal E, Meunier C et al. Sites of left and right ventricular lead implantation and response to cardiac resynchronization therapy observations from the REVERSE trial. Eur Heart J. 2012;33:2662-71.
219. Thomas DE, Exton SA, Yousef ZR. Heart rate deceleration after exercise predicts patients most likely to respond to cardiac resynchronisation therapy. Heart. 2010;96:1385-9.
220. Truong QA, Szymonifka J, Picard MH et al. Utility of dual-source computed tomography in cardiac resynchronization therapy-DIRECT study. Heart Rhythm. 2018;15:1206-1213.
221. Van't Sant J, Ter Horst IA, Wijers SC et al. Measurements of electrical and mechanical dyssynchrony are both essential to improve prediction of CRT response. J Electrocardiol. 2015;48:601-8.
222. Vegh EM, Kandala J, Orencole M et al. Device-measured physical activity versus six-minute walk test as a predictor of reverse remodeling and outcome after cardiac resynchronization therapy for heart failure. Am J Cardiol. 2014;113:1523-8.
223. Verbrugge FH, Dupont M, Vercammen J et al. Time from emerging heart failure symptoms to cardiac resynchronisation therapy: impact on clinical response. Heart. 2013;99:314-9.
224. Versteeg H, Denollet J, Meine M, Pedersen SS. Patient-reported health status prior to cardiac resynchronisation therapy identifies patients at risk for poor survival and prolonged hospital stays. Netherlands Heart Journal. 2016;24:18-24.
225. Vondrak J, Marek D, Vecera J, Benesova K, Matejka J. Cardiac resynchronisation therapy optimisation of interventricular delay by the systolic dyssynchrony index: A comparative, randomised, 12-month follow-up study. Hellenic J Cardiol. 2017.
226. Werys K, Petryka-Mazurkiewicz J, Blaszczyk L et al. Cine dyscontractility index: A novel marker of mechanical dyssynchrony that predicts response to cardiac resynchronization therapy. J Magn Reson Imaging. 2016;44:1483-1492.

227. Wiliński J, Czarnecka D, Wojciechowska W et al. Baseline tissue Doppler imaging-derived echocardiographic parameters and left ventricle reverse remodelling following cardiac resynchronization therapy introduction. Archives of Medical Science. 2011;7:813-822.
228. Ypenburg C, van Bommel RJ, Delgado V et al. Optimal left ventricular lead position predicts reverse remodeling and survival after cardiac resynchronization therapy. J Am Coll Cardiol. 2008;52:1402-9.
229. Zajac J, Eriksson J, Alehagen U, Ebbers T, Bolger AF, Carlhall CJ. Mechanical dyssynchrony alters left ventricular flow energetics in failing hearts with LBBB: a 4D flow CMR pilot study. Int J Cardiovasc Imaging. 2018;34:587-596.
230. Bossard M, Sticherling C, Kuhne M, Frey S, Osswald S, Schaer B. Outcome of patients with cardiac resynchronisation defibrillator therapy and a follow-up of at least five years after implant. Swiss Med Wkly. 2014;144:w13938.
231. Brenyo A, Barsheshet A, Kutyifa V et al. Predictors of spontaneous reverse remodeling in mild heart failure patients with left ventricular dysfunction. Circ Heart Fail. 2014;7:565-72.
232. Gold MR, Daubert C, Abraham WT et al. The effect of reverse remodeling on long-term survival in mildly symptomatic patients with heart failure receiving cardiac resynchronization therapy: results of the REVERSE study. Heart Rhythm. 2015;12:524-530.
233. Kuperstein R, Goldenberg I, Moss AJ et al. Left atrial volume and the benefit of cardiac resynchronization therapy in the MADIT-CRT trial. Circ Heart Fail. 2014;7:154-60.
234. Rickard J, Brennan DM, Martin DO et al. The impact of left ventricular size on response to cardiac resynchronization therapy. Am Heart J. 2011;162:646-53.
235. Sherazi S, Goldenberg I, Moss AJ et al. Comparison of low versus high (>40 mm Hg) pulse pressure to predict the benefit of cardiac resynchronization therapy for heart failure (from the Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy Trial). Am J Cardiol. 2014;114:1053-8.
236. Wilton SB, Exner DV, Healey JS et al. Left ventricular lead position and outcomes in the Resynchronization-Defibrillation for Ambulatory Heart Failure Trial (RAFT). Can J Cardiol. 2014;30:413-9.
237. Aktas MK, Zareba W, Huang DT et al. The effect of weight loss on clinical outcomes in patients implanted with a cardiac resynchronization therapy device-A MADIT-CRT substudy. J Card Fail. 2014;20:183-9.
238. Baturova MA, Kutyifa V, McNitt S et al. Usefulness of Electrocardiographic Left Atrial Abnormality to Predict Response to Cardiac Resynchronization Therapy in Patients With Mild Heart Failure and Left Bundle Branch Block (a Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy Substudy). Am J Cardiol. 2018;122:268-274.
239. Berger R, Shankar A, Fruhwald F et al. Relationships between cardiac resynchronization therapy and N-terminal pro-brain natriuretic peptide in patients with heart failure and markers of cardiac dyssynchrony: an analysis from the Cardiac Resynchronization in Heart Failure (CARE-HF) study. Eur Heart J. 2009;30:2109-16.

240. Binda C, Menet A, Appert L et al. Time course of secondary mitral regurgitation in patients with heart failure receiving cardiac resynchronization therapy: Impact on long-term outcome beyond left ventricular reverse remodelling. Arch Cardiovasc Dis. 2018;111:320-331.
241. Biton Y, Costa J, Zareba W et al. Predictors of long-term mortality with cardiac resynchronization therapy in mild heart failure patients with left bundle branch block. Clin Cardiol. 2018;41:1358-1366.
242. Boriani G, Gasparini M, Landolina M et al. Impact of mitral regurgitation on the outcome of patients treated with CRT-D: data from the InSync ICD Italian Registry. Pacing Clin Electrophysiol. 2012;35:146-54.
243. Botto GL, Dicandia CD, Mantica M et al. Clinical characteristics, mortality, cardiac hospitalization, and ventricular arrhythmias in patients undergoing CRT-D implantation: results of the ACTION-HF study. J Cardiovasc Electrophysiol. 2013;24:173-81.
244. Brenyo A, Goldenberg I, Moss AJ et al. Baseline functional capacity and the benefit of cardiac resynchronization therapy in patients with mildly symptomatic heart failure enrolled in MADIT-CRT. Heart Rhythm. 2012;9:1454-9.
245. Brenyo A, Rao M, Barsheshet A et al. QRS axis and the benefit of cardiac resynchronization therapy in patients with mildly symptomatic heart failure enrolled in MADIT-CRT. J Cardiovasc Electrophysiol. 2013;24:442-8.
246. Cipriani M, Lunati M, Landolina M et al. Prognostic implications of mitral regurgitation in patients after cardiac resynchronization therapy. Eur J Heart Fail. 2016;18:1060-8.
247. Cleland JG, Freemantle N, Erdmann E et al. Long-term mortality with cardiac resynchronization therapy in the Cardiac Resynchronization-Heart Failure (CARE-HF) trial. Eur J Heart Fail. 2012;14:628-34.
248. Clemens M, Szegedi Z, Kardos L et al. The Seattle Heart Failure Model predicts survival in patients with cardiac resynchronization therapy: a validation study. J Card Fail. 2012;18:682-7.
249. Dauphin R, Nonin E, Bontemps L et al. Quantification of ventricular resynchronization reserve by radionuclide phase analysis in heart failure patients: a prospective long-term study. Circ Cardiovasc Imaging. 2011;4:114-21.
250. Delgado-Montero A, Tayal B, Goda A et al. Additive Prognostic Value of Echocardiographic Global Longitudinal and Global Circumferential Strain to Electrocardiographic Criteria in Patients With Heart Failure Undergoing Cardiac Resynchronization Therapy. Circ Cardiovasc Imaging. 2016;9.
251. Ellims AH, Pfluger H, Elsik M, Butler MJ, Hare JL, Taylor AJ. Utility of cardiac magnetic resonance imaging, echocardiography and electrocardiography for the prediction of clinical response and long-term survival following cardiac resynchronisation therapy. Int J Cardiovasc Imaging. 2013;29:1303-11.
252. Gasparini M, Muto C, Iacopino S et al. Low-dose dobutamine test associated with interventricular dyssynchrony: a useful tool to identify cardiac resynchronization therapy responders: data from the LOw dose DObutamine stress-echo test in Cardiac Resynchronization Therapy (LODO-CRT) phase 2 study. Am Heart J. 2012;163:422-9.
253. Gasparini M, Klersy C, Leclercq C et al. Validation of a simple risk stratification tool for patients implanted with Cardiac Resynchronization Therapy: the VALID-CRT risk score. Eur J Heart Fail. 2015;17:717-24.

254. Ghani A, Delnoy PP, Adiyaman A et al. Response to cardiac resynchronization therapy as assessed by time-based speckle tracking imaging. Pacing Clin Electrophysiol. 2015;38:455-64.
255. Ghani A, Delnoy PP, Ottervanger JP et al. Association of apical rocking with long-term major adverse cardiac events in patients undergoing cardiac resynchronization therapy. Eur Heart J Cardiovasc Imaging. 2016;17:146-53.
256. Goldstein RE, Haigney MC, Krone RJ, McNitt S, Zareba W, Moss AJ. Differing effects of cardiac resynchronization therapy on long-term mortality in patient subgroups of MADIT-CRT defined by baseline conduction and 1-year post-treatment left ventricular remodeling. Heart Rhythm. 2013;10:366-73.
257. Guha K, Mantziari L, Sharma R, McDonagh TA, Gibson D, Duncan AM. A reduction in total isovolumic time with cardiac resynchronisation therapy is a predictor of clinical outcomes. Int J Cardiol. 2013;168:382-7.
258. Hasselberg NE, Haugaa KH, Bernard A et al. Left ventricular markers of mortality and ventricular arrhythmias in heart failure patients with cardiac resynchronization therapy. Eur Heart J Cardiovasc Imaging. 2016;17:343-50.
259. Hsu JC, Solomon SD, Bourgoun M et al. Predictors of super-response to cardiac resynchronization therapy and associated improvement in clinical outcome: the MADIT-CRT (multicenter automatic defibrillator implantation trial with cardiac resynchronization therapy) study. J Am Coll Cardiol. 2012;59:2366-73.
260. Jacobsson J, Borgquist R, Reitan C et al. Usefulness of the Sum Absolute QRST Integral to Predict Outcomes in Patients Receiving Cardiac Resynchronization Therapy. Am J Cardiol. 2016;118:389-95.
261. Jin H, Yang S, Hua W et al. Significant mitral regurgitation as a predictor of long-term prognosis in patients receiving cardiac resynchronisation therapy. Kardiologia Polska. 2018;76:987-992.
262. Khatib M, Tolosana JM, Trucco E et al. EAARN score, a predictive score for mortality in patients receiving cardiac resynchronization therapy based on pre-implantation risk factors. Eur J Heart Fail. 2014;16:802-9.
263. Kiani J, Agarwal SK, Kamireddy S, Adelstein E, Saba S. Relationship of electro-mechanical remodeling to survival rates after cardiac resynchronization therapy. Tex Heart Inst J. 2013;40:268-73.
264. Kobe J, Dechering DG, Rath B et al. Prospective evaluation of electrocardiographic parameters in cardiac resynchronization therapy: detecting nonresponders by left ventricular pacing. Heart Rhythm. 2012;9:499-504.
265. Leong DP, Hoke U, Delgado V et al. Predictors of long-term benefit of cardiac resynchronization therapy in patients with right bundle branch block. Eur Heart J. 2012;33:1934-41.
266. Leshem E, Suleiman M, Laish-Farkash A et al. Impact of quadripolar LV leads on heart failure hospitalization rates among patients implanted with CRT-D: data from the Israeli ICD Registry. J Interv Card Electrophysiol. 2018;51:5-12.
267. Leyva F, Foley PW, Stegemann B et al. Development and validation of a clinical index to predict survival after cardiac resynchronisation therapy. Heart. 2009;95:1619-25.
268. Linde C, Gold MR, Abraham WT et al. Long-term impact of cardiac resynchronization therapy in mild heart failure: 5-year results from the REsynchronization reVErses Remodeling in Systolic left vEntricular dysfunction (REVERSE) study. Eur Heart J. 2013;34:2592-9.

269. Liu K, Hua BT, Guo T, Pu LJ. The assessment of the long-term effects of elective CRT-D of coronary heart disease after PCI. Eur Rev Med Pharmacol Sci. 2017;21:1313-1317.
270. Mathias A, Moss AJ, McNitt S et al. Clinical Implications of Complete Left-Sided Reverse Remodeling With Cardiac Resynchronization Therapy: A MADIT-CRT Substudy. J Am Coll Cardiol. 2016;68:1268-76.
271. Menet A, Bardet-Bouchery H, Guyomar Y et al. Prognostic importance of postoperative QRS widening in patients with heart failure receiving cardiac resynchronization therapy. Heart Rhythm. 2016;13:1636-43.
272. Nauffal V, Tanawuttiwat T, Zhang Y et al. Predictors of mortality, LVAD implant, or heart transplant in primary prevention cardiac resynchronization therapy recipients: The HF-CRT score. Heart Rhythm. 2015;12:2387-94.
273. Plesinger F, Jurak P, Halamek J et al. Ventricular Electrical Delay Measured From Body Surface ECGs Is Associated With Cardiac Resynchronization Therapy Response in Left Bundle Branch Block Patients From the MADIT-CRT Trial (Multicenter Automatic Defibrillator Implantation-Cardiac Resynchronization Therapy). Circ Arrhythm Electrophysiol. 2018;11:e005719.
274. Plonska-Gosciniak E, Kasprzak JD, Kukulski T et al. Role of lowdose dobutamine echocardiography in predicting response to biventricular pacing. Results from the multicenter Viability in Cardiac Resynchronisation Therapy (ViaCRT) study. Pol Arch Med Wewn. 2016;126:989-994.
275. Qin S, Shi H, Su Y, Chen S, Pan W, Ge J. Can the Prognosis of Cardiac Resynchronization Therapy Be Predicted by Gated SPECT? Clin Nucl Med. 2015;40:786-92.
276. Reinsch N, Konorza T, Woydowski D et al. Iterative cardiac output measurement for optimizing cardiac resynchronization therapy: a randomized, blinded, crossover study. Pacing Clin Electrophysiol. 2010;33:1188-94.
277. Risum N, Williams ES, Khouri MG et al. Mechanical dyssynchrony evaluated by tissue Doppler cross-correlation analysis is associated with long-term survival in patients after cardiac resynchronization therapy. Eur Heart J. 2013;34:48-56.
278. Risum N, Tayal B, Hansen TF et al. Identification of Typical Left Bundle Branch Block Contraction by Strain Echocardiography Is Additive to Electrocardiography in Prediction of Long-Term Outcome After Cardiac Resynchronization Therapy. J Am Coll Cardiol. 2015;66:631-41.
279. Rocha EA, Pereira FT, Abreu JS et al. Development and Validation of Predictive Models of Cardiac Mortality and Transplantation in Resynchronization Therapy. Arq Bras Cardiol. 2015;105:399-409.
280. Rocha EA, Pereira FT, Abreu JS et al. Echocardiographic Predictors of Worse Outcome After Cardiac Resynchronization Therapy. Arq Bras Cardiol. 2015;105:552-9.
281. Ruwald AC, Pietrasik G, Goldenberg I et al. The effect of intermittent atrial tachyarrhythmia on heart failure or death in cardiac resynchronization therapy with defibrillator versus implantable cardioverter-defibrillator patients: a MADIT-CRT substudy (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy). J Am Coll Cardiol. 2014;63:1190-1197.

282. Sade LE, Saba S, Marek JJ et al. The association of left ventricular lead position related to regional scar by speckle-tracking echocardiography with clinical outcomes in patients receiving cardiac resynchronization therapy. J Am Soc Echocardiogr. 2014;27:648-56.
283. Seo Y, Ito H, Nakatani S et al. The role of echocardiography in predicting responders to cardiac resynchronization therapy. Circ J. 2011;75:1156-63.
284. Smith T, Levy WC, Schaer BA et al. Performance of the Seattle Heart Failure Model in implantable defibrillator patients treated with cardiac resynchronization therapy. Am J Cardiol. 2012;110:398-402.
285. Sood N, Ruwald AC, Solomon S et al. Association between myocardial substrate, implantable cardioverter defibrillator shocks and mortality in MADIT-CRT. Eur Heart J. 2014;35:106-15.
286. Stankovic I, Aarones M, Smith HJ et al. Dynamic relationship of left-ventricular dyssynchrony and contractile reserve in patients undergoing cardiac resynchronization therapy. Eur Heart J. 2014;35:48-55.
287. Stankovic I, Belmans A, Prinz C et al. The association of volumetric response and long-term survival after cardiac resynchronization therapy. Eur Heart J Cardiovasc Imaging. 2017;18:1109-1117.
288. Takaya Y, Noda T, Nakajima I et al. Electrocardiographic predictors of response to cardiac resynchronization therapy in patients with intraventricular conduction delay. Circ J. 2014;78:71-7.
289. Tatsumi K, Tanaka H, Matsumoto K et al. Combined baseline strain dyssynchrony index and its acute reduction predicts mid-term left ventricular reverse remodeling and long-term outcome after cardiac resynchronization therapy. Echocardiography. 2014;31:464-73.
290. Tepper D, Harris S, Ip R. Optimal left ventricular lead position predicts reverse remodeling and survival after cardiac resynchronization therapy. Congestive Heart Failure. 2009;15:99.
291. Tompkins C, Kutyifa V, McNitt S et al. Effect on cardiac function of cardiac resynchronization therapy in patients with right bundle branch block (from the Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy [MADIT-CRT] trial). Am J Cardiol. 2013;112:525-9.
292. Uretsky BF, Thygesen K, Daubert JC et al. Predictors of mortality from pump failure and sudden cardiac death in patients with systolic heart failure and left ventricular dyssynchrony: results of the CARE-HF trial. J Card Fail. 2008;14:670-5.
293. van der Bijl P, Khidir MJH, Leung M et al. Reduced left ventricular mechanical dispersion at 6 months follow-up after cardiac resynchronization therapy is associated with superior long-term outcome. Heart Rhythm. 2018;15:1683-1689.
294. van der Bijl P, Khidir M, Ajmone Marsan N et al. Effect of Functional Mitral Regurgitation on Outcome in Patients Receiving Cardiac Resynchronization Therapy for Heart Failure. American Journal of Cardiology. 2018.
295. Végh EM, Kandala J, Januszkiewicz L et al. A new simplified electrocardiographic score predicts clinical outcome in patients treated with CRT. Europace. 2018;20:492-500.
296. Verbrugge FH, Nijst P, Van Herendael H et al. Asymptomatic episodes of device-registered atrial tachyarrhythmia are not associated with worse cardiac resynchronization therapy response. Europace. 2014;16:1197-204.

297. Verna E, Ghiringhelli S, Scotti S, Caravati F. Evaluation of baseline contractile reserve vs dyssynchrony as a predictor of functional improvement and long term outcome after resynchronization pacing therapy: a radionuclide stress study. J Nucl Cardiol. 2012;19:53-62.
298. Wang CL, Powell BD, Redfield MM et al. Left ventricular discoordination index measured by speckle tracking strain rate imaging predicts reverse remodelling and survival after cardiac resynchronization therapy. Eur J Heart Fail. 2012;14:517-25.
299. Zecchin M, Proclemer A, Magnani S et al. Long-term outcome of 'super-responder' patients to cardiac resynchronization therapy. Europace. 2014;16:363-71.
300. Bogale N, Priori S, Cleland JG et al. The European CRT Survey: 1 year (9-15 months) follow-up results. Eur J Heart Fail. 2012;14:61-73.
301. Dichtl W, Strohmer B, Fruhwald F. Clinical outcome after 1 year of cardiac resynchronisation therapy: national results from the European CRT survey. Wien Klin Wochenschr. 2013;125:750-4.
302. Khazanie P, Hammill BG, Qualls LG et al. Clinical effectiveness of cardiac resynchronization therapy versus medical therapy alone among patients with heart failure: analysis of the ICD Registry and ADHERE. Circ Heart Fail. 2014;7:926-34.
303. Migowski A, Ribeiro AL, Carvalho MS et al. Seven years of use of implantable cardioverter-defibrillator therapies: a nationwide population-based assessment of their effectiveness in real clinical settings. BMC Cardiovasc Disord. 2015;15:22.
304. van der Heijden AC, Borleffs CJ, Buiten MS et al. The clinical course of patients with implantable cardioverter-defibrillators: Extended experience on clinical outcome, device replacements, and device-related complications. Heart Rhythm. 2015;12:1169-76.