2017 AHA/ACC/HRS Systematic Review for the Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death Data Supplement

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Abbreviation List:

1° indicates primary; 2°, secondary; ACC, American College of Cardiology; AF, atrial fibrillation; AHA, American Heart Association; BMI, body mass index; BUN, blood urea nitrogen; CABG, coronary artery bypass graft surgery; CAD indicates coronary artery disease; CCI, charlson comorbidity index; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ECG, electrocardiogram; EP, electrophysiologic; ESRD, end stage renal disease; FDA, food and drug administration; HF, heart failure; HR, hazard ratio; HTN, hypertension; IHD, ischemic heart disease; ICD, implantable cardioverter defibrillator; LV, left ventricular; LVEF, ejection fraction; MI, myocardial infarction; N/A, not available; NYHA, New York Heart Association; NICM, nonischemic cardiomyopathy; PCI, primary coronary intervention; PES, programmed electrical stimulation; OR, odds ratio; RCT, randomized control trial; RR, relative risk; SBP, systolic blood pressure; SCD, sudden cardiac disease; TIA, transient ischemic attack; VA, ventricular arrhythmia; VF, ventricular fibrillation; and VT, ventricular tachycardia.

Part 1. For Asymptomatic Patients With Brugada Syndrome, What is the Association Between an Abnormal Programmed Ventricular Stimulation Study and Sudden Cardiac Death and Other Arrhythmia Endpoints?

Study Acronym; Author; Year Published	Aim of Study; Study Design; Study Size (N)	Patient Population	Study Intervention (# pts) / Study Comparator (# pts)	Endpoint Results (Absolute Event Rates, P values; OR or RR; & 95% CI)	Relevant 2° Endpoint (if any); Study Limitations; Adverse Events
● Sacher F 2006 (1) ● 17116772	**Aim:** The main objective of the present study was to assess both the clinical benefit and the complication rate at implantation and during follow-up in a group of Brugada syndrome pts implanted with an ICD for primary and secondary prevention of SCD **Study design:** **Size:** 220 Retrospective Observational	**Inclusion Criteria:** - Brugada syndrome - Implanted with an ICD - Type 1 ECG at baseline on at least one occasion or after provocation with a class I antiarrhythmic drug **Exclusion Criteria:** Not Reported	Resuscitated N=18 Syncope N=88 Asymptomatic N=114 Asymptomatic Inducible N=95 Asymtomatic Non-Inducible N=15	Resuscitated: ICD, Shocks, Appropriate – Median 25.5 mo - 4 (22%) - (N=18) ICD, Shocks, Inappropriate - Median 25.5 mo - 3 (17%) - (N=18) ICD, Complications – Median 25.5 mo - 5 (28%) - (N=18) Syncope: ICD, Shocks, Appropriate - Median 39.5 mo - 9 (10%) - (N=88) ICD, Shocks, Inappropriate – Median 39.5 mo - 19 (22%) - (N=88) ICD, Complications - Median 39.5 mo - 22 (25%) - (N=88) Asymptomatic: ICD, Shocks, Appropriate – Median 31 mo - 5 (4%) - (N=114) ICD, Shocks, Inappropriate – Median 31 mo - 23 (20%) - (N=114) ICD, Complications – Median 31 mo - 35 (31%) - (N=114) Asymptomatic Inducible: ICD, Shocks, Appropriate - NR - 5 (5.3%) - (N=95) Asymptomatic Non-Inducible:	

				ICD, Shocks, Appropriate - NR - 0 (0%) - (N=18)	

● Takagi M 2007 (2) ● 17900255	**Aim:** We compared the clinical and ECG characteristics of symptomatic and asymptomatic pts with Brugada syndrome to identify new markers for high-risk pts. **Study design:** Retrospective Observational **Size:** 188	**Inclusion Criteria** - Brugada Syndrome - J point amplitude >0.2mV - Either spontaneous or drug-induced coved-type ST segment elevation (>0.1 mV) in at least two of the three right precordial leads (V1 to V3) on resting 12-lead ECG - Normal findings on physical examination **Exclusion Criteria** - Abnormality in right ventricular morphology demonstrated by chest radiography - Abnormality in LV morphology demonstrated by chest radiography - Abnormality in right ventricular function demonstrated by echocardiography - Abnormality in LV function demonstrated by echocardiography	Asymptomatic N=98 Asymptomatic Inducible N=50 Asymptomatic Non-Inducible N=13 Syncope N=57 VF N=33	Asymptomatic: Cardiac Event - NR - 0 (0%) (N=82) SCD - Baseline - 3y - 0 (0%) - (N=82) Ventricular Fibrillation - Baseline – 3 y - 0 (0%) - (N=82) Asymptomatic Inducible: Cardiac Event - NR - 0 (0%) - (N=50) SCD - Baseline – 3 y - 0 (0%) - (N=50) VF - Baseline – 3 y - 0 (0%) - (N=50) Asymptomatic Non-Inducible: Cardiac Event - NR - 0 (0%) - (N=13) SCD - Baseline – 3 y - 0 (0%) - (N=13) VF - Baseline – 3 y - 0 (0%) - (N=13) Syncope: Cardiac Event - NR - 3 (6%) - (N=51) VF: Cardiac Event - NR - 10 (30%) - (N=33)	
● Brugada P 2003 (3) ● 12776858	**Aim:** We report here data on the prognostic value of PES in 443 pts with Brugada syndrome, which to the best of our knowledge is the largest population collected to date. **Study design:** Prospective Observational **Size:** 443	**Inclusion Criteria** - Brugada Syndrome - ECG showed a pattern resembling a right bundle branch block with ST segment elevation of at least 0.2 mV at the J wave - Slowly descending ST segment in continuation with a flat or negative T wave in the right precordial	Asymptomatic N=263 Asymptomatic Inducible N=91 Asymptomatic Non-Inducible N=172	Asymptomatic: Arrhythmic Event - Mean 31 mo - 13 (5%) - (N=263) Asymptomatic Inducible: Arrhythmic Event - Mean 31 mo - 11 (12.1%) - (N=91) Asymptomatic Non-Inducible: Arrhythmic Event - Mean 31 mo - 2 (1.2%) - (N=172)	

		leads V1 to V3 **Exclusion Criteria** Not Reported	Cardiac Arrest N=80 Cardiac Arrest Inducible N=65 Cardiac Arrest Non-Inducible N=15 Syncope N=100 Syncope Inducible N=61 Syncope Non-Inducible N=39 Symptomatic N=180	Cardiac Arrest: Arrhythmic Event - Mean 31 mo - 36 (45%) - (N=80) Cardiac Arrest Inducible: Arrhythmic Event - Mean 31 mo - 35 (53.8%) - (N=65) Cardiac Arrest Non-Inducible: Arrhythmic Event - Mean 31 mo - 1 (6.7%) - (N=15) Syncope: Arrhythmic Event - Mean 31 mo - 16 (16%) - (N=100) Syncope Inducible: Arrhythmic Event - Mean 31 mo - 14 (23%) N=61 Syncope Non-Inducible: Arrhythmic Event - Mean 31 mo - 2 (5.1%) - (N=39) Symptomatic: Arrhythmic Event - Mean 31 mo - 52 (28.9%) - (N=180)	
● Conte G 2015 (4) ● 25744005	**Aim:** To assess the clinical features and the long-term follow-up of pts with Brugada Syndrome who underwent ICD placement and the evolution of device-based management over the past 2 decades. **Study design:** Prospective Observational	**Inclusion Criteria** - Brugada Syndrome, Type I, Spontaneous, ECG Diagnosis or Brugada Syndrome, Type I, Drug-Induced, ECG Diagnosis - ICD implantation - Continuous follow-up at UZ Brussel-VUB	Aborted SCD N=25 Syncope N=105 Asymptomatic N=46	Aborted SCD: ICD, Shocks, Appropriate - Mean 83.8 mo - 11 (44%) - (N=25) ICD, Shocks, Inappropriate - Mean 83.8 mo - 8 (32%) - (N=25) Syncope: ICD, Shocks, Appropriate - Mean 83.8 mo - 11 (10.5%) - (N=105) ICD, Shocks, Inappropriate - Mean 83.8	

	Size: 176	**Exclusion Criteria** - Underlying structural cardiac abnormalities		mo - 18 (17.1%) - (N=105) Asymptomatic: ICD, Shocks, Appropriate - Mean 83.8 mo - 6 (13%) - (N=46) ICD, Shocks, Inappropriate - Mean 83.8 mo - 7 (15.2%) - (N=46)	
● Sacher F 2013 (5) ● 23995538	**Aim:** We report the outcome of pts with Brugada syndrome implanted with an ICD in a large multicenter registry. **Study design:** Retrospective Observational **Size:** 378	**Inclusion Criteria** - Brugada Syndrome - Implanted with an ICD - Type 1 Brugada pattern on ECG at baseline on at least 1 occasion or after provocation with a class I antiarrhythmic drug **Exclusion Criteria** - Acute ischemia - Metabolic disturbances - Electrolyte disturbances - Underlying structural heart disease	Asymptomatic N=166 Asymptomatic Inducible N=130 Asymptomatic Non-Inducible N=20 Aborted Sudden Cardiac Arrest N=31 Syncope N=181	Asymptomatic: ICD, Removal without Reimplantation - Mean 85 mo - 7 (4%) - (N=166) Lead Failure - Mean 85 mo - 28 (17%) - (N=166) ICD, Shocks, Appropriate - Mean 85 mo - 12 (7%) - (N=166) ICD, Shocks, Appropriate - Baseline–1 y - 2 (1%) - (N=166) ICD, Shocks, Appropriate - Baseline–2 y - 3 (2%) - (N=166) ICD, Shocks, Appropriate - Baseline–3 y - 7 (4%) - (N=166) ICD, Shocks, Appropriate - Baseline–4 y - 10 (6%) - (N=166) ICD, Shocks, Appropriate - Baseline–5 y - 10 (6%) - (N=166) ICD, Shocks, Appropriate - Baseline–10y - 20 (12%) - (N=166) ICD, Shocks, Inappropriate - Mean 85 mo - 47 (28%) - (N=166) Asymptomatic Inducible: ICD, Shocks, Appropriate - NR - 11 (8.5%) - (N=130) Asymptomatic Non-Inducible: ICD, Shocks, Appropriate - NR - 1 (5%) - (N=20) Aborted Sudden Cardiac Arrest:	

				ICD, Removal without Reimplantation - Mean 67 mo - 0 (0%) - (N=31) Lead Failure - Mean 85 mo - 3 (10%) - (N=31) ICD, Shocks, Appropriate - Mean 85 mo - 12 (39%) - (N=31) ICD, Shocks, Appropriate - Baseline-1 y - 8 (25%) - (N=31) ICD, Shocks, Appropriate - Baseline-2 y - 9 (30%) - (N=31) ICD, Shocks, Appropriate - Baseline-3 y - 11 (36%) - (N=31) ICD, Shocks, Appropriate - Baseline-4 y - 13 (41%) - (N=31) ICD, Shocks, Appropriate - Baseline-5 y - 15 (48%) - (N=31) ICD, Shocks, Appropriate - Baseline-10 y - 15 (48%) - (N=31) ICD, Shocks, Inappropriate - Mean 67 mo - 6 (19%) - (N=31) Syncope: ICD, Removal without Reimplantation - Mean 71 mo - 3 (1.7%) - (N=181) Lead Failure - Mean 85 mo - 29 (16%) - (N=181) ICD, Shocks, Appropriate - Mean 85 mo - 22 (12%) - (N=181) ICD, Shocks, Appropriate - Baseline-1 y - 5 (3%) - (N=181) ICD, Shocks, Appropriate - Baseline-2 y - 11 (6%) - (N=181) ICD, Shocks, Appropriate - Baseline-3 y - 13 (7%) - (N=181) ICD, Shocks, Appropriate - Baseline-4 y - 18 (10%) - (N=181) ICD, Shocks, Appropriate - Baseline-5 y - 20 (11%) - (N=181)	

				ICD, Shocks, Appropriate - Baseline-10 y - 34 (19%) - (N=181) ICD, Shocks, Inappropriate - Mean 71 mo - 38 (21%) - (N=181)	
● Sieira J 2015 (6) ● 26215662	**Aim:** To investigate the clinical characteristics, management, and long-term prognosis of asymptomatic Brugada syndrome pts. **Study design:** Prospective Observational **Size:** 363	**Inclusion Criteria** - Brugada Syndrome, Type I, Spontaneous, ECG Diagnosis or Brugada Syndrome, Type I, Drug-Induced, ECG Diagnosis **Exclusion Criteria** - Underlying structural cardiac abnormalities - Brugada Syndrome, Symptomatic - Syncope, History of - SCD, History of	Asymptomatic N=363 Asymptomatic Inducible N=32 Asymptomatic Non-Inducible N=289	Asymptomatic: Fracture of Ventricular Electrode - Mean 73.2 mo - 5 (8.2%) - (N=61) ICD, Complications - Mean 73.2 mo - 6 (9.8%) - (N=61) Infection, Any - Mean 73.2 mo - 1 (1.6%) - (N=61) Arrhythmic Event - Mean 73.2 mo - 9 (3%) - (N=303) ICD, Shocks, Appropriate - Mean 73.2 mo - 6 (2%) - (N=303) ICD, Shocks, Inappropriate - Mean 34.2 mo - 9 (14.8%) - (N=61) SCD - Mean 73.2 mo - 2 (0.7%) - (N=303) SCD, Aborted- Mean 73.2 mo - 1 (0.3%) - (N=303) Asymptomatic Inducible: Arrhythmic Event - Mean 73.2 mo - 5 (15.6%) - (N=32) ICD, Shocks, Appropriate - Mean 73.2 mo - 5 (15.6%) - (N=32) SCD - Mean 73.2 mo - 0 (0%) - (N=32) SCD, Aborted - Mean 73.2 mo - 0 (0%) - (N=32) Asymptomatic Non-Inducible: Arrhythmic Event - Mean 73.2 mo - 3 (1%) - (N=289) ICD, Shocks, Appropriate - Mean 73.2 mo - 1 (0.3%) - (N=289) SCD - Mean 73.2 mo - 1 (0.3%) - (N=289)	

				SCD, Aborted - Mean 73.2 mo - 1 (0.3%) - (N=289)	
● Sieira J 2015 (7) ● 25904495	**Aim:** The purpose of this study was to analyze our single-center experience of PES VA inducibility in pts with BS gathered in the last 20 y, since the first description of the syndrome. **Study design:** Retrospective Observational **Size:** 404	**Inclusion Criteria** - Brugada Syndrome - Brugada Syndrome, Type I, Drug-Induced, ECG Diagnosis or Brugada Syndrome, Type I, Spontaneous, ECG Diagnosis - Follow-up longer than 1 y achieved - PES VT induction protocol performed **Exclusion Criteria** - Underlying structural cardiac abnormalities, found by noninvasive methods, including echocardiogram - Underlying structural cardiac abnormalities, found by noninvasive methods, including stress tests - Underlying structural	Asymptomatic N=273 Asymptomatic Non-Inducible N=241 Asymptomatic Inducible N=32 Aborted Sudden Death N=17 Aborted Sudden Death Non-Inducible N=13 Syncope N=114	Asymptomatic: SCD, Aborted - Mean 74.3 mo - 1 (0.4%) - (N=273) Asymptomatic Non-Inducible: Arrhythmic Event - Mean 74.3 mo - 2 (0.8%) - (N=241) ICD, Shocks, Appropriate - Mean 74.3 mo - 1 (0.4%)- (N=241) SCD, Aborted - Mean 74.3 mo - 1 (0.4%)- (N=241) Asymptomatic Inducible: SCD, Aborted - Mean 74.3 mo - 0 (0%) - (N=32) Aborted Sudden Death: SCD, Aborted - Mean 74.3 mo - 0 (0%) - (N=17) Aborted Sudden Death Non-Inducible: Arrhythmic Event - Mean 74.3 mo - 3	

		cardiac abnormalities, found by noninvasive methods, including nuclear magnetic resonance - Underlying structural cardiac abnormalities, found by invasive methods, including coronary angiograph - Underlying structural cardiac abnormalities, found by invasive methods, including left ventriculography - Underlying structural cardiac abnormalities, found by invasive methods, including right ventriculography - Underlying structural cardiac abnormalities, found by invasive methods, including myocardial biopsies	Syncope Non-Inducible N=77 Aborted Sudden Death Inducible N=4 Syncope Inducible N=37	(23.1%) - (N=13) ICD, Shocks, Appropriate - Mean 74.3 mo - 3 (23.1%) - (N=13) SCD, Aborted - Mean 74.3 mo - 0 (0%) - (N=13) Syncope: SCD, Aborted - Mean 74.3 mo - 0 (0%) - (N=114) Syncope Non-Inducible: Arrhythmic Event - Mean 74.3 mo - 4 (5.2%) - (N=77) ICD, Shocks, Appropriate - Mean 74.3 mo - 4 (5.2%) - (N=77) SCD, Aborted - Mean 74.3 mo - 0 (0%) - (N=77) Aborted Sudden Death Inducible: SCD, Aborted - Mean 74.3 mo - 0 (0%) - (N=4) Syncope Inducible: SCD, Aborted - Mean 74.3 mo - 0 (0%) - (N=37)	

● **PRELUDE** ● Priori SG 2012 (8) ● 22192666	**Aim:** The PRELUDE prospective registry was designed to assess the predictive accuracy of sustained VT/VF inducibility and to identify additional predictors of arrhythmic events in Brugada syndrome pts without history of VT/VF **Study design:** Prospective Observational **Size:** 308	**Inclusion Criteria** - Brugada Syndrome - Age >18 y - Spontaneous or a pharmacologically induced type I ECG pattern - Coved ST-segment elevation >2mm in at least 2 right precordial leads **Exclusion Criteria** - Experienced cardiac arrest - Experienced sustained VT - Structural cardiac abnormalities verified by echocardiography - Structural cardiac abnormalities verified by exercise stress test - Previous MI, verified by echocardiography - Cardiomyopathies, verified by echocardiography - Angina, verified by echocardiography - LV hypertrophy, verified by echocardiography - Previous MI, verified by exercise stress test - Cardiomyopathies, verified by exercise stress test - Angina, verified by exercise stress test - LV hypertrophy, verified by exercise stress test - Cardiac diseases, verified by echocardiography	Asymptomatic N=244 Asymptomatic Non-Inducible N=NR Asymptomatic Inducible N=NR Syncope N=64 Syncope Inducible N=NR Syncope Non-Inducible N=NR	Asymptomatic: Arrhythmic Event - Mean 36 mo - 7 (2.9%) - (N=244) Cardiac Arrest, Resuscitated - Mean 36 mo - 1 (0.4%) - (N=244) ICD, Shocks, Appropriate - Mean 36 mo - 6 (2.5%) - (N=244) SCD - Mean 36 mo - 0 (0%) - (N=244) Asymptomatic Non-Inducible: Arrhythmic Event - Mean 36 mo - 4 (NR%) - (N=NR) Cardiac Arrest, Resuscitated - Mean 36 mo - 1 (NR%) - (N=NR) ICD, Shocks, Appropriate - Mean 36 mo - 3 (NR%) - (N=NR) SCD - Mean 36 mo - 0 (0%) - (N=NR) Asymptomatic Inducible: Arrhythmic Event - Mean 36 mo - 3 (NR%) - (N=NR) Cardiac Arrest, Resuscitated - Mean 36 mo - 0 (0%) - (N=NR) ICD, Shocks, Appropriate - Mean 36 mo - 3 (NR%) - (N=NR) SCD - Mean 36 mo - 0 (0%) - (N=NR) Syncope: Arrhythmic Event - Mean 36 mo - 7 (10.9%) - (N=64) Cardiac Arrest, Resuscitated - Mean 36 mo - 0 (0%) - (N=64) ICD, Shocks, Appropriate - Mean 36 mo - 7 (10.9%) - (N=64) SCD - Mean 36 mo - 0 (0%) - (N=64) Syncope Inducible: Arrhythmic Event - Mean 36 mo - 2	

		- Cardiac diseases, verified by exercise stress test		(NR%) - (N=NR) Cardiac Arrest, Resuscitated - Mean 36 mo - 0 (0%) - (N=NR) ICD, Shocks, Appropriate - Mean 36 mo - 2 (NR%) - (N=NR) SCD - Mean 36 mo - 0 (0%) - (N=NR) Syncope Non-Inducible: Arrhythmic Event - Mean 36 mo - 5 (NR%) - (N=NR) Cardiac Arrest, Resuscitated - Mean 36 mo - 0 (0%) - (N=NR) ICD, Shocks, Appropriate - Mean 36 mo - 5 (NR%) - (N=NR) SCD - Mean 36 mo - 0 (0%) - (N=NR)	

● Giustetto C 2009 (9) ● 19193676	**Aim:** The aim of this study was to prospectively evaluate the incidence of arrhythmic events and the prognostic role of clinical presentation, ECG, and of a standardized PES protocol in consecutive cases from a community-based population. **Study design:** Prospective Observational **Size:** 166	**Inclusion Criteria** - Brugada Syndrome - Brugada type 1 ECG spontaneously or after pharmacological testing with class 1 C drugs **Exclusion Criteria** Not Reported	Asymptomatic Inducible N=17 Asymptomatic Non-Inducible N=64 Asymptomatic N=103 Syncope Inducible N=26 Syncope Non-Inducible N=24 Aborted Sudden Death Inducible N=3 Aborted Sudden Death Non-Inducible N=1 Syncope N=58 Aborted Sudden Death N=5 Symptomatic N=63	Asymptomatic Inducible: Arrhythmic Event - Mean 30 mo - 0 (0%) - (N=17) SCD - Mean 30 mo - 0 (0%) - (N=17) Ventricular Arrhythmias, Sustained - Mean 30 mo - 0 (0%) - (N=17) Asymptomatic Non-Inducible: Arrhythmic Event - Mean 30 mo - 0 (0%) - (N=64) SCD - Mean 30 mo - 0 (0%) - (N=64) Ventricular Arrhythmias, Sustained - Mean 30 mo - 0 (0%) - (N=64) Asymptomatic: Arrhythmic Event - Mean 30 mo - 1 (1%) - (N=103) ICD, Shocks, Appropriate - Mean 30 mo - 1 (1%) - (N=103) SCD - Mean 30 mo - 1 (1%) - (N=103) Ventricular Arrhythmias, Sustained - Mean 30 mo - 0 (0%) - (N=103) Syncope Inducible: Arrhythmic Event - Mean 30 mo - 0 (0%) - (N=26) ICD, Shocks, Appropriate - Mean 30 mo - 5 (19.2%) - (N=26) SCD - Mean 30 mo - 0 (0%) - (N=26) Ventricular Arrhythmias, Sustained - Mean 30 mo - 5 (19.2%) - (N=26) Syncope Non-Inducible: Arrhythmic Event - Mean 30 mo - 0 (0%) - (N=24) SCD - Mean 30 mo - 0 (0%) - (N=24) Ventricular Arrhythmias, Sustained - Mean 30 mo - 0 (0%) - (N=24)	

				Aborted Sudden Death Inducible: Arrhythmic Event - Mean 30 mo - 0 (0%) - (N=3) ICD, Shocks, Appropriate - Mean 30 mo - 2 (66.7%) - (N=3) SCD - Mean 30 mo - 0 (0%) - (N=3) Ventricular Arrhythmias, Sustained - Mean 30 mo - 2 (66.7%) - (N=3) Aborted Sudden Death Non-Inducible: Arrhythmic Event - Mean 30 mo - 0 (0%) - (N=1) SCD - Mean 30 mo - 0 (0%) - (N=1) Ventricular Arrhythmias, Sustained - Mean 30 mo - 0 (0%) - (N=1) Syncope: Arrhythmic Event - Mean 30 mo - 5 (8.6%) - (N=58) ICD, Shocks, Appropriate - Mean 30 mo - 5 (8.6%) - (N=58) SCD - Mean 30 mo - 0 (0%) - (N=58) Ventricular Arrhythmias, Sustained - Mean 30 mo - 5 (8.6%) - (N=58) Aborted Sudden Death: Arrhythmic Event - Mean 30 mo - 3 (60%) - (N=5) ICD, Shocks, Appropriate - Mean 30 mo - 3 (60%) - (N=5) SCD - Mean 30 mo - 0 (0%) - (N=5) Ventricular Arrhythmias, Sustained - Mean 30 mo - 3 (60%) - (N=5)	

● Priori SG 2000 (10) ● 11076825	**Aim:** From a large cohort of Brugada syndrome pts, we present data at variance with the current view and propose that in analogy with the long-QT syndrome,7 the Brugada syndrome is characterized by incomplete penetrance and heterogeneous clinical phenotype (S.G.P., unpublished data, 1999). **Study design:** Prospective Observational **Size:** 60	**Inclusion Criteria** - Brugada Syndrome, Clinical Diagnosis - Brugada Syndrome, ECG Diagnosis **Exclusion Criteria** - Structural heart disease, defined by evaluation of blood enzymes - Structural heart disease, defined by evaluation of electrolytes - Structural heart disease, defined by Holter monitoring - Structural heart disease, defined by echocardiogram with careful evaluation of the right ventricle - Structural heart disease, defined by stress test - Structural heart disease, defined by nuclear MR	Asymptomatic N=30 Asymptomatic Inducible N=13 Asymptomatic Non-Inducible N=6 Cardiac Arrest N=17 Syncope N=13 Symptomatic N=30	Asymptomatic: Cardiac Arrest - Mean 33 mo - 0 (0%) - (N=30) VF - Mean 33 mo - 0 (0%) - (N=30) VT, Non-Sustained - Mean 33 mo - 2 (6.7%) - (N=30) VT, Sustained - Mean 33 mo - 0 (0%) - (N=30) Asymptomatic Inducible: Cardiac Arrest - Mean 33 mo - 0 (0%) - (N=13) VF - Mean 33 mo - 0 (0%) - (N=13) VT, Sustained - Mean 33 mo - 0 (0%) - (N=13) Asymptomatic Non-Inducible: Cardiac Arrest - Mean 33 mo - 0 (0%) - (N=6) VF - Mean 33 mo - 0 (0%) - (N=6) VT, Sustained - Mean 33 mo - 0 (0%) - (N=6) Cardiac Arrest: Cardiac Arrest - Mean 33 mo - 5 (29.4%) - (N=17) Syncope: Cardiac Arrest - Mean 33 mo - 0 (0%) - (N=13) Symptomatic: Cardiac Arrest - Mean 33 mo - 5 (16.7%) - (N=30) VF - Mean 33 mo - 5 (16.7%) - (N=30)	

● Kamakura S. 2009 (11) ● 19843917	**Aim:** To investigate the long-term prognosis of probands with noncoved type ST-elevation in leads V1–V3, prospectively, and compared it with that of probands with the type 1 ST-elevation. **Study design:** Prospective Observational **Size:** 330	**Inclusion Criteria** - Brugada Syndrome - Normal findings on physical examination - Proband - J-point (QRS-ST junction) amplitude of ≥0.1 mV (1 mm) with either coved or saddle back type ST-segment elevation in at least 2 of the 3 precordial leads (V1–V3) on resting standard 12-lead ECG **Exclusion Criteria** - Abnormality in right ventricular morphology demonstrated by chest radiography - Abnormality in LV morphology demonstrated by chest radiography - Abnormality in right ventricular function demonstrated by echocardiography - Abnormality in LV function demonstrated by echocardiography - Vasospastic angina - Vasovagal syncope - Abnormality in right ventricular function demonstrated by chest radiography - Abnormality in LV function demonstrated by chest radiography	Asymptomatic N=207 Asymptomatic Inducible N =61 Asymptomatic Non-Inducible N=62 Asymptomatic Type 1 Spontaneous N=108 Asymptomatic Type 1 Spontaneous Inducible N=32 Asymptomatic Type 1 Spontaneous Non-Inducible N=25 Asymptomatic Type 1 Drug-Induced N=46 Asymptomatic Type 1 Drug-Induced Inducible N=20 Asymptomatic Type 1 Drug-Induced Non-Inducible N=14	Asymptomatic Arrhythmic Event, Fatal - Mean 47.7 mo - 3 (1.4%) - (N=207) Asymptomatic Inducible: Arrhythmic Event, Fatal - Mean 47.7 mo - 1 (1.6%) - (N=61) Asymptomatic Non-Inducible: Arrhythmic Event, Fatal - Mean 47.7 mo - 2 (3.2%) - (N=62) Asymptomatic Type 1 Spontaneous: Arrhythmic Event, Fatal - Mean 47.7 mo - 3 (2.8%) - (N=108) Asymptomatic Type 1 Spontaneous Inducible: Arrhythmic Event, Fatal - Mean 47.7 mo - 1 (3.1%) - (N=32) Asymptomatic Type 1 Spontaneous Non-Inducible: Arrhythmic Event, Fatal - Mean 47.7 mo - 2 (8%) - (N=25) Asymptomatic Type 1 Drug-Induced: Arrhythmic Event, Fatal - Mean 47.7 mo - 0 (0%) - (N=46) Asymptomatic Type 1 Drug-Induced Inducible: Arrhythmic Event, Fatal - Mean 47.7 mo - 0 (0%) - (N=20) Asymptomatic Type 1 Drug-Induced Non-Inducible: Arrhythmic Event, Fatal - Mean 47.7 mo	

		- Abnormality in right ventricular morphology demonstrated by echocardiography - Abnormality in LV morphology demonstrated by echocardiography	Asymptomatic Non-Type 1 Inducible N=9 Asymptomatic Non-Type 1 Non-Inducible N=23 Asymptomatic Type 1 N=154 Asymptomatic Non-Type 1 N=53 VF N=56 Syncope N=67 Symptomatic N=123 VF Non-Inducible N=18 VF Inducible N=34 VF Type 1 Spontaneous N=35 VF Type 1	- 0 (0%) - (N=14) Asymptomatic Non-Type 1 Inducible: Arrhythmic Event, Fatal - Mean 47.7 mo- 0 (0%) - (N=9) Asymptomatic Non-Type 1 Non-Inducible: Arrhythmic Event, Fatal - Mean 47.7 mo - 0 (0%) - (N=23) Asymptomatic Type 1: Arrhythmic Event, Fatal - Mean 47.7 mo - 3 (2%) - (N=154) Asymptomatic Non-Type 1: Arrhythmic Event, Fatal - Mean 47.7 mo - 0 (0%) - (N=53) VF: Arrhythmic Event, Fatal - Mean 51.9 mo - 19 (33.9%) - (N=56) Syncope: Arrhythmic Event, Fatal - Mean 48.5 mo - 2 (3%) - (N=67) VF Non-Inducible: Arrhythmic Event, Fatal - Mean 51.9 mo - 4 (22.2%) - (N=18) VF Inducible: Arrhythmic Event, Fatal - Mean 51.9 mo - 13 (38.2%) - (N=34) VF Type 1 Spontaneous: Arrhythmic Event, Fatal - Mean 51.9 mo - 12 (34.3%) - (N=35)	

			Spontaneous Inducible N=22 VF Type 1 Spontaneous Non-Inducible N=10 VF Type 1 Drug-Induced N =10 VF Type 1 Drug-Induced Inducible N=5 VF Type 1 Drug-Induced Non-Inducible N=4 VF Non-Type 1 Inducible N=7 VF Non-Type 1 Non-Inducible N=4 Syncope Inducible N=43 Syncope Non-Inducible N=14 Syncope Type 1	VF Type 1 Spontaneous Inducible: Arrhythmic Event, Fatal - Mean 51.9 mo - 8 (36.4%) - (N=22) VF Type 1 Spontaneous Non-Inducible: Arrhythmic Event, Fatal - Mean 51.9 mo - 3 (30%) - (N=10) VF Type 1 Drug-Induced: Arrhythmic Event, Fatal - Mean 51.9 mo - 3 (30%) - (N=10) VF Type 1 Drug-Induced Inducible: Arrhythmic Event, Fatal - Mean 51.9 mo - 2 (40%) - (N=5) VF Type 1 Drug-Induced Non-Inducible: Arrhythmic Event, Fatal - Mean 51.9 mo - 0 (0%) - (N=4) VF Non-Type 1 Inducible: Arrhythmic Event, Fatal - Mean 51.9 mo - 3 (42.9%) - (N=7) VF Non-Type 1 Non-Inducible: Arrhythmic Event, Fatal - Mean 51.9 mo - 1 (25%) - (N=4) Syncope Inducible: Arrhythmic Event, Fatal - Mean 48.5 mo - 2 (4.7%) - (N=43) Syncope Non-Inducible: Arrhythmic Event, Fatal - Mean 48.5 mo - 0 (0%) - (N=14) Syncope Type 1 Spontaneous:	

			Spontaneous N=30 Syncope Type 1 Spontaneous Inducible N=19 Syncope Type 1 Spontaneous Non-Inducible N=7 Syncope Type 1 Drug-Induced N=16 Syncope Type 1 Drug-Induced Inducible N=12 Syncope Type 1 Drug-Induced Non-Inducible N=2 Syncope Non-Type 1 Inducible N=12 Syncope Non-Type 1 Non-Inducible N=5 VF Type 1 N=45	Arrhythmic Event, Fatal - Mean 48.5 mo - 1 (3.3%) - (N=30) Syncope Type 1 Spontaneous Inducible: Arrhythmic Event, Fatal - Mean 48.5 mo - 1 (5.3%) - (N=19) Syncope Type 1 Spontaneous Non-Inducible: Arrhythmic Event, Fatal - Mean 48.5 mo - 0 (0%) - (N=7) Syncope Type 1 Drug-Induced: Arrhythmic Event, Fatal - Mean 48.5 mo - 0 (0%) - (N=16) Syncope Type 1 Drug-Induced Inducible: Arrhythmic Event, Fatal - Mean 48.5 mo - 0 (0%) - (N=12) Syncope Type 1 Drug-Induced Non-Inducible: Arrhythmic Event, Fatal - Mean 48.5 mo - 0 (0%) - (N=2) Syncope Non-Type 1 Inducible: Arrhythmic Event, Fatal - Mean 48.5 mo - 1 (8.3%) - (N=12) Syncope Non-Type 1 Non-Inducible: Arrhythmic Event, Fatal - Mean 48.5 mo - 0 (0%) - (N=5) VF Type 1: Arrhythmic Event, Fatal - Mean 51.9 mo - 15 (33%) - (N=45) Syncope Type 1:	

			Syncope Type 1 N=46 VF Non-Type 1 N=11 Syncope Non-type 1 N=21	Arrhythmic Event, Fatal - Mean 48.5 mo - 1 (2%) - (N=46) VF Non-Type 1: Arrhythmic Event, Fatal - Mean 51.9 mo - 4 (36%) - (N=11) Syncope Non-type 1: Arrhythmic Event, Fatal - Mean 48.5 mo - 1 (5%) - (N=21)	

● Eckardt L. 2005 (12) ● 15642768	**Aim:** Brugada et al very recently reported on a large number of individuals with an ECG diagnostic of Brugada syndrome and no previous cardiac arrest. During a mean follow-up of 2 y, 8% of these pts suffered SCD or had documented VF. In contrast, Priori et al. demonstrated that asymptomatic individuals and in particular individuals with only transient ECG abnormalities are at low risk of SCD. Therefore, our goal was to verify these 2 opposite standpoints and to present long-term follow-up data on clinical and EP parameters in a large number of individuals with a so-called type 1 ECG compatible with Brugada syndrome. **Study design:** Prospective Observational **Size:** 212	**Inclusion Criteria** - Brugada Syndrome, ECG Diagnosis - Type 1 ECG at baseline or after provocation with a class I antiarrhythmic drug **Exclusion Criteria** - Underlying structural heart disease confirmed by echocardiography - Underlying structural heart disease confirmed by cardiac catheterization - Underlying structural heart disease confirmed by chest x-ray - Underlying structural heart disease confirmed by exercise testing - Acute ischemia confirmed by laboratory tests - Metabolic disturbances confirmed by laboratory tests - Electrolyte disturbances confirmed by laboratory tests - Only saddle-type ECG changes not changing to a type 1 pattern after drug testing with a class I agent	Asymptomatic N=123 Asymptomatic Inducible N=38 Asymptomatic Non-Inducible N=60 Aborted SCD N=24 Syncope N=65	Asymptomatic: Arrhythmic Event - Mean 33.7 mo - 1 (0.8%) - (N=123) SCD - Mean 33.7 mo - 0 (0%) - (N=123) VF - Mean 33.7 mo - 1 (0.8%) - (N=123) Asymptomatic Inducible: Arrhythmic Event - NR - 1 (2.6%) - (N=38) SCD - NR - 0 (0%) - (N=38) VF - NR - 1 (2.6%) - (N=38) Asymptomatic Non-Inducible: Arrhythmic Event - NR - 0 (0%) - (N=60) SCD - NR - 0 (0%) - (N=60) VF - NR - 0 (0%) - (N=60) Aborted SCD: Arrhythmic Event - Mean 83.2 mo - 4 (17%) - (N=24) Syncope: Arrhythmic Event - Mean 38.9 mo - 4 (6%) - (N=65)	

● **FINGER** ● Probst V. 2010 (13) ● 20100972	**Aim:** The aim of the present study was to evaluate the prognosis and risk factors of SCD in Brugada syndrome pts in the FINGER Brugada syndrome registry. **Study design:** Prospective Observational **Size:** 1029	**Inclusion Criteria** - Brugada Syndrome - Type 1 ECG **Exclusion Criteria** - Diseases that mimic Brugada Syndrome - Children <16y old	Asymptomatic N=654 Asymptomatic Inducible N=137 Asymptomatic Non-Inducible N=232 Cardiac Arrest N=62 Cardiac Arrest Inducible N=16 Cardiac Arrest Non-Inducible N=20 Symptomatic N=375 Symptomatic Inducible N=125 Symptomatic Non-Inducible N=144 Syncope N=313 Syncope Inducible N=109 Syncope Non-Inducible N=124	Asymptomatic: Arrhythmic Event - Median 31 mo - 10 (1.5%) - (N=654) Asymptomatic Inducible: Arrhythmic Event - NR - 4 (2.8%) - (N=137) Asymptomatic Non-Inducible: Arrhythmic Event - NR - 3 (1.3%) - (N=232) Cardiac Arrest: Arrhythmic Event - Median 44 mo - 22 (35%) - (N=62) Cardiac Arrest Inducible: Arrhythmic Event - NR - 0 (0%) - (N=16) Cardiac Arrest Non-Inducible: Arrhythmic Event - NR - 0 (0%) - (N=20) Symptomatic: Arrhythmic Event - NR - 41 (10.9%) - (N=375) Symptomatic Inducible: Arrhythmic Event - NR - 10 (8%) - (N=125) Symptomatic Non-Inducible: Arrhythmic Event - NR - 6 (4.2%) - (N=144) Syncope: Arrhythmic Event - Median 34 mo - 19 (6%) - (N=313) Syncope Inducible: Arrhythmic Event - NR - 10 (9.2%) - (N=109) Syncope Non-Inducible: Arrhythmic Event - NR - 6 (4.8%) - (N=124)	

Part 2. What is the Impact of ICD Implantation for Primary Prevention in Older Patients and Patients with Significant Comorbidities?

Study Acronym; Author; Year Published	Aim of Study; Study Design; Study Size (N)	Patient Population	Study InterventioN (# pts) / Study Comparator (# pts)	Endpoint Results (Absolute Event Rates, P values; OR or RR; & 95% CI)	Relevant 2° Endpoint (if any); Study Limitations; Adverse Events
● **MADIT II** ● Moss AJ 2002 (14) ● 11907286	**Aim:** To evaluate the effect of an ICD on survival in pts with reduced LV function after MI. **Study type:** RCT **Size:** 1,232	**Inclusion Criteria:** - Age ≥21 y - EF ≤0.30 within 3 mo before entry, as assessed by angiography, radionuclide scanning, or echocardiography - MI ≥1 mo before entry - Documented finding of an abnormal Q wave on electrocardiography, elevated cardiac-enzyme levels on laboratory testing during hospitalization for suspected MI, a fixed defect on thallium scanning, or localized akinesis on ventriculography with evidence of obstructive coronary disease on angiography **Exclusion Criteria:** - Indication approved by the FDA for an ICD. - NYHA functional class IV at enrollment - Undergone coronary revascularization within the preceding 3 mo - MI within the past mo, as evidenced by measurement of	ICD N=742 Conventional Therapy N=490	The 1° endpoint was death from any cause. Results adjusted for sequential monitoring ICD: Mortality, All-Cause - 20 mo - 105 (14.2%) - (N=742) Conventional Therapy: Mortality, All-Cause - 20 mo - 97 (19.8%) - (N=490)	● ICD: ICD, Complications, Lead Problems, Requiring Surgical Intervention - Mean 20 mo – 13 (1.8%) - (N=742) ● ICD, Complications, Infection, Nonfatal, Requiring Surgical Intervention - Mean 20 mo – 5 (0.7%) - (N=742)

		cardiac-enzyme levels - Advanced cerebrovascular disease - Childbearing age and not using medically prescribed contraceptive measures - Any condition other than cardiac disease that was associated with a high likelihood of death during the trial			
● **MADIT II** ● Huang DT 2007 (15) ● 17537209	**Aim:** To evaluate the mortality benefit from ICD therapy in eligible elderly pts. **Study type:** RCT **Size:** 1232	**Inclusion Criteria:** - Prior MI >1 mo before enrollment - LVEF ≤30 % **Exclusion Criteria:** - Advanced cerebrovascular disease - Undergone coronary revascularization within the preceding 3 mo from the time of enrollment - Preexisting indications for an ICD - NYHA functional class IV - Any other condition that was associated with a high likelihood of death during the trial	ICD; Age <75y N= 614 ICD; Age ≥75y N=128 Conventional Therapy; Age <75y N=414 Conventional Therapy; Age ≥75y N=76	Not Reported	● ICD; Age <75y: ● ICD, Complications, Difficult Lead Position - Mean 20.8 mo – 4 (0.7%) - (N=599) ● ICD, Complications, Elevated Defibrillation Threshold - Mean 20.8 mo – 1 (0.2%) - (N=599) ● ICD, Complications, Lead Dislodgement - Mean 20.8 mo – 9 (1.5%) - (N=599) ● ICD, Complications, Pericardial Effusion - Mean 20.8 mo – 1 (0.2%) - (N=599) ● ICD, Complications, Pneumothorax - Mean 20.8 mo –1 (0.2%) - (N=599) ● ICD, Complications, Pocket Erosion/Infection - Mean 20.8 mo – 3 (0.5%) - (N=599) ● ICD; Age ≥75 y: ● CD, Complications, Difficult Lead Position - Mean 17.2 mo – 0 (0%) - (N= 121) ● ICD, Complications, Elevated Defibrillation Threshold - Mean 17.2 mo – 1 (0.8%) - N=121)

					● ICD, Complications, Lead Dislodgement - Mean 17.2 mo – 3 (2.5%) - (N=121) ● ICD, Complications, Pericardial Effusion - Mean 17.2 mo – 0 (0%) - (N=121) ● ICD, Complications, Pneumothorax - Mean 17.2 mo – 0 (0%) - (N=121) ● ICD, Complications, Pocket Erosion/Infection - Mean 17.2 mo – 0 (0%) - (N=121)
● **MADIT II** ● Goldenberg I 2006 (16) ● 16893702	**Aim:** The present investigation was an analysis of the relation among the severity of renal dysfunction, risk of arrhythmic mortality, and ICD benefit in pts enrolled in the prospective MADIT-II **Study type:** RCT **Size:** 1232	**Inclusion Criteria:** - MI, History of - LVEF ≤30 % **Exclusion Criteria:** - HF, NYHA Class IV - Renal Failure - Coronary revascularization within the previous 3 mo - Elapsed interval from their most recent MI of <1 mo - Advanced medical co-morbidity	ICD N=738 Conventional Therapy N=485 ICD; eGFR <35 mL/ min/1.73 m^2 N=41 ICD; eGFR=35–59 mL/min/1.73 m^2 N=227 ICD; eGFR ≥60 mL/min/1.73 m^2 N=470 ICD; eGFR ≥35 mL/ min/1.73/ m^2 N=697 ICD; eGFR=35–49 mL/min/1.73 m^2 N=107	Not Reported	● ICD: ● SCD - Mean 20 mo - NR - (N=742) ● Conventional Therapy: ● SCD - Mean 20 mo - NR - (N=490) ● ICD; eGFR <35 ml per min per 1.73 m^2: ● SCD - Mean 20 mo - NR - (N=41) ● ICD; eGFR 35–59 mL/min/1.73 m^2 ● SCD - Mean 20 mo - NR - (N=227) ● ICD; eGFR ≥60 mL/min/1.73 m^2 ● SCD - Mean 20 mo - NR - (N=470) ● ICD; eGFR ≥35 mL/min/1.73 m^2 ● SCD - Mean 20 mo - NR - (N=697) ● ICD; eGFR 35–49 ml p mL/min/1.73 m^2: ● SCD - Mean 20 mo - NR - (N=107)

			ICD; eGFR=50–59 mL/min/1.73 m^2 N=120 ICD; eGFR=60–89 mL/ min/1.73 m^2 N=338 ICD; eGFR≥90 ml mL/min/1.73 m^2 N=132 Conventional Therapy; eGFR <35 mL/min/1.73 m^2 N=39 Conventional Therapy; eGFR=35–59 mL/min/1.73 m^2 N=160 Conventional Therapy; eGFR ≥60 mL/min/1.73 m^2 N=286 Conventional Therapy; eGFR ≥35 mL/min/1.73 m^2 N=446 Conventional Therapy; eGFR=35–49 mL/min/1.73 m^2 N=77 Conventional Therapy;		● ICD; eGFR 50–59 mL/min/1.73 m^2: ● SCD - Mean 20 mo - NR - (N=120) ● ICD; eGFR 60–89 mL/min/1.73 m^2: ● SCD - Mean 20 mo - NR - (N=338) ● ICD; eGFR ≥90 mL/min/1.73 m^2 ● SCD - Mean 20 mo - NR - (N=132) ● Conventional Therapy; eGFR <35 mL/min/1.73 m^2: ● SCD - Mean 20 mo - NR - (N=39) ● Conventional Therapy; eGFR 35–59 mL/min/1.73 m^2: ● SCD - Mean 20 mo - NR - (N=160) ● Conventional Therapy; eGFR ≥60 mL/min/1.73 m^2: ● SCD - Mean 20 mo - NR - (N=286) ● Conventional Therapy; eGFR ≥35 mL/min/1.73 m^2 ● SCD - Mean 20 mo - NR - (N=446) ● Conventional Therapy; eGFR 35–49 mL/min/1.73 m^2 ● SCD - Mean 20 mo - NR - (N=77) ● Conventional Therapy; eGFR 50–59 mL/min/1.73 m^2: ● SCD - Mean 20 mo - NR - (N=83) ● Conventional Therapy; eGFR 60–89 mL/min/1.73 m^2:

			eGFR=50–59 mL/min/1.73 m^2 N=83 Conventional Therapy; eGFR=60–89 mL/min/1.73 m^2 N=216 Conventional Therapy; eGFR≥90 mL/min/1.73 m^2 N=70		● SCD - Mean 20 mo - NR - (N=216) ● Conventional Therapy; eGFR ≥90 mL/min/1.73 m^2: ● SCD - Mean 20 mo - NR - (N=70)
● **MADIT II** ● Greenberg H 2004 (17) ● 15093884	**Aim:** To determine the efficacy of ICD therapy in preventing SCD in post-infarction pts with advanced LV dysfunction. **Study type:** RCT **Size:** 1232	**Inclusion Criteria:** - Previous MI - LVEF ≤30 % **Exclusion Criteria:** NA	ICD N=742 Conventional Therapy N=490	The 1° endpoint was total mortality. ICD: Mortality, All-Cause - NR - 105 (14.2%) - (N= 742) Conventional Therapy: Mortality, All-Cause - NR - 97 (19.8%) - (N =490)	● ICD: ● SCD, Clinical Classification Scheme - NR - 24 (3.2%) - (N=742) ● SCD, LV Dysfunction, Severe, modified Hinkle-Thaler Scheme - NR - 10 (1.3%) - (N=742) ● SCD, LV Dysfunction, Severe, modified Hinkle-Thaler Scheme, None - NR - 18 (2.4%) - (N=742) ● SCD, modified Hinkle-Thaler Scheme - NR - 28 (3.8%) - (N=742) ● SCD, Primary Arrhythmia, Clinical Classification Scheme - NR - 22 (3%) - (N=742) ● SCD, Secondary Arrhythmia, Clinical Classification Scheme - NR - 2 (0.3%) - (N=742) ● Conventional Therapy: ● SCD, Clinical Classification Scheme - NR - 48 (9.8%) - (N=490)

					● SCD, LV Dysfunction, Severe, modified Hinkle-Thaler Scheme - NR - 15 (3.1%) - (N=490) ● SCD, LV Dysfunction, Severe, modified Hinkle-Thaler Scheme, None - NR - 34 (6.9%) - (N=490) ● SCD, modified Hinkle-Thaler Scheme - NR - 49 (10%) - (N=490) ● SCD, Primary Arrhythmia, Clinical Classification Scheme - NR - 41 (8.4%) - (N=490) ● SCD, Secondary Arrhythmia, Clinical Classification Scheme - NR - 7 (1.4%) - (N=490)
● Razak E 2010 (18) ● 20487355	**Aim:** To examine the effect of the ICD on total mortality in pts with COPD and depressed LVEF who otherwise have an indication for ICD implantation for the primary prevention of SCD according to published guidelines. **Study type:** Retrospective Observational **Size:**100	**Inclusion Criteria:** - COPD - LVEF ≤ 35 % - Cardiomyopathy **Exclusion Criteria:** - Prior diagnosis of cardiac arrest - Lethal VA	ICD N=30 No ICD N=70	The 1° endpoint was all-cause mortality. Results adjusted for: 1. covariates incorporated into the multivariate model including pts' LVEF and the QRS interval on surface ECG as continuous variables and for race, the use of β-blockers and steroids as categorical variables. These covariates were examined for interactions and were found to be independent. 2. Presence of comorbidities using the CCI.	● Not Reported

				3. Predictors of ICD implantation using the propensity score method, as previously described. ICD: Mortality, All-Cause - Mean 3.1y - 11 (36.7%) - (N=30) Mortality, All-Cause - Mean 3.1y - NR - (N=30); Adjusted for QRS interval etc. Mortality, All-Cause - Mean 3.1y - NR - (N=30); Adjusted for Charlson Comorbidity Mortality, All-Cause - Mean 3.1y - NR - (N=30); Adjusted for Propensity Score Conventional Therapy: Mortality, All-Cause - Mean 3.1y - 35 (50%) - (N=70) Mortality, All-Cause - Mean 3.1y - NR - (N=70); Adjusted for QRS interval etc. Mortality, All-Cause - Mean 3.1y - NR - (N=70); Adjusted for Charlson Comorbidity Mortality, All-Cause - Mean 3.1y - NR - (N=70); Adjusted for Propensity Score	

● **MADIT II** ● Zareba W 2005 (19) ● 15950580	**Aim:** To determine the efficacy of ICD therapy in high-risk subgroups defined by NYHA functional class, EF, and BUN levels. **Study type:** RCT **Size:**1232	**Inclusion Criteria:** - HF - MI within 1 mo - LVEF≤ 30 % **Exclusion Criteria:** - Undergone recent revascularization procedures - NYHA class IV at enrollment - Major comorbidities	ICD N=742 Conventional Therapy N=490 ICD; BUN ≤25 mg/dl N=522 ICD; BUN >25 mg/dl N=213 Conventional Therapy; BUN ≤25 mg/dl N=328 Conventional Therapy; BUN >25 mg/dl N=155	Not Reported	● Not Reported
● **GWTG-HF & OPTIMIZE-HF** ● Hernandez AF 2010 (20) ● 20009044	**Aim:** We conducted a retrospective cohort study of the clinical effectiveness of ICD therapy in older pts with HF by using data from the OPTIMIZE-HF registry, the GWTG-HF registry, and long-term outcome data from Medicare claims files. **Study type:** Retrospective Observational **Size:**4685	**Inclusion Criteria:** - Age ≥65 y - Eligible for an ICD - LVEF ≤35 % - Discharged alive from hospitals participating in the OPTIMIZE-HF and GWTG-HF quality-improvement programs during the period January 1, 2003, through December 31, 2006 - Hospitalized with a diagnosis of HF **Exclusion Criteria**: - Discharged to a skilled nursing facility - Died before discharge - New-onset HF	ICD N=376 No ICD N=4309 ICD; Age 65–74 N=188 ICD; Age 75–84 N=188 No ICD; Age 65–74 N=1851 No ICD; Age 75–84 N=2458	The 1° endpoint was all-cause mortality within 3 y of the index hospitalization for HF. Results adjusted for the probability of treatment, other prognostic variables, and medical therapy at discharge. ICD: Mortality, All-Cause - Baseline – 3 y - 101 (26.9%) - (N=376) No ICD: Mortality, All-Cause - Baseline – 3 y - 1771	● Not Reported

		- LVEF > 35% - Transferred to another acute care hospital - Left hospital against medical advice - Discharged to hospice - Unknown discharge status - ICD at admission - Documented contraindication, defined as a specific contraindication or any reason documented by a physician for not using ICD therapy - Not receiving optimal medical therapy - Acute MI within 40 d - Life-threatening illness that would compromise 1 y survival with good functional status - Economic reasons for not using ICD therapy - Social reasons for not using ICD therapy - Religious reasons for not using ICD therapy - Compliance-related reasons for not using ICD therapy - Admitted to hospital that did not provide ICD therapy - Aged ≥85 y - Admitted electively for ICD therapy		(41.1%) - (N=4309) ICD; Age 65–74: Mortality, All-Cause - Baseline – 3 y - NR - (N=188) Mortality, All-Cause - Baseline – 3 y - NR - (N=188); Adjusted using Inverse Probability Weighted model ICD; Age 75–84: Mortality, All-Cause - Baseline – 3 y - NR - (N=188) Mortality, All-Cause - Baseline – 3 y - NR - (N=188); Adjusted using Inverse Probability Weighted model No ICD; Age 65–74: Mortality, All-Cause - Baseline - 3y - NR - (N=1851) Mortality, All-Cause - Baseline - 3y - NR - (N=1851); Adjusted using Inverse Probability Weighted model No ICD; Age 75–84: Mortality, All-Cause - Baseline - 3y - NR - (N=2458) Mortality, All-Cause - Baseline - 3y - NR -	

				(N=2458): Adjusted using Inverse Probability Weighted model.	
● **GWTG-HF & NCDR** ● Al-Khatib SM 2014 (21) ● 24893088	**Aim:** To characterize pts with LVEF between 30% and 35% and compare the survival of those with and without ICDs **Study type:** Retrospective Observational **Size:**816	**Inclusion Criteria:** - Age ≥ 65 y - Prophylactic ICD received between January 1, 2006 through December 31, 2007 in those pts from the NCDR - Hospitalized for HF from January 1, 2005, through December 31, 2009, in those pts from the GWTG-HF database - Primary insurance was Medicare - LVEF 30%–35 % **Exclusion Criteria**: - Recent MI - Potential contraindication to an ICD - Recent-onset of HF - CABG - New-onset HF, in those pts from the GWTG-HF database - Left hospital against medical advice, in those pts from the GWTG-HF database - Transferred to another acute care facility, in those pts from the GWTG-HF database - Discharged to hospice, in those pts from the GWTG-HF database - Discharged to skilled nursing facility, in those pts from the GWTG-HF database	ICD N=408 No ICD N=408	The 1° endpoint was all-cause mortality. Results adjusted using Cox models which include age, sex, race, LVEF, IHD, prior atrial arrhythmia, SBP, diabetes, hypertension, and baseline use of angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, calcium channel blocker, digoxin, diuretic, or statin ICD: Mortality, All-Cause - Median 4.4 y - 248 (60.8%) - (N=408) Mortality, All-Cause - Baseline – 1 y - 97 (23.8%) - (N=408) Mortality, All-Cause - Baseline – 3 y - 196 (48%) - (N=408) No ICD: Mortality, All-Cause - Median 2.9 y - 249 (61%) - (N=408) Mortality, All-Cause - Baseline – 1 y - 99 (24.3%) - (N=408) Mortality, All-Cause -	● Not Reported

		- Discharged to a rehabilitation center, in those pts from the GWTG-HF database - NYHA class IV HF symptoms (entered as a reason for not receiving an ICD), in those pts from the GWTG-HF database - No reasonable expectation of survival to at least 1 year, in those pts from the GWTG-HF database - Received an ICD, in those pts in the Get With the Guidelines-Heart Failure (GWTG-HF) database - Physician-documented reason for not receiving an ICD - NYHA class IV HF symptoms, in those pts from the National Cardiovascular Data Registry (NCDR) - Received a secondary prevention ICD, in those pts from the National Cardiovascular Data Registry (NCDR) - Received an ICD with cardiac resynchronization therapy, in those pts from the NCDR - Received ICD device replacements, in those pts from the NCDR		Baseline – 3 y - 204 (50%) - (N=408)	

● Mezu U 2011 (22) ● 21640321	**Aim:** To examine the effect of ICDs, age, and multiple co-morbidities on survival in elderly pts who otherwise meet implantation criteria for primary prevention of SCD **Study type:** Retrospective Observational **Size:**152	**Inclusion Criteria:** - LVEF ≤35% - Age ≥80y	ICD N=99 No ICD N=53	The 1° endpoint for the study was all-cause mortality. Results adjusted for the following confounding variables: (1) age only; (2) age and CCI; (3) age, CCI, and LVEF; (4) age, CCI, and GFR; and (5) age, CCI, LVEF, and GFR. ICD: Mortality, All-Cause - Mean 2.3y - 58 (59%) - (N=99) No ICD: Mortality, All-Cause - Mean 2.3y - 35 (66%) - (N=53)	● Not Reported

● **GWTG-HF & NCDR** ● Pokorney SD 2015 (23) ● 25504649	**Aim:** To investigate the association between primary prevention ICDs and mortality among Medicare, racial and ethnic minority pts in clinical practice. **Study type:** Retrospective Observational **Size:**2922	**Inclusion Criteria:** - Age ≥65 y - Fee-for-service Medicare beneficiaries - Hospitalized for a diagnosis of HF **Exclusion Criteria:** - Recent MI - LVEF >35% - No documented LVEF - Recent CABG - Class IV HF symptoms	ICD; Minority N=426 ICD; White, Non-Hispanics N=1035 No ICD; Minority N=426 No ICD; White, Non-Hispanics N=1035	The 1° endpoint for this analysis was all-cause mortality. Results adjusted for race (white versus other), age, past medical history (previous atrial arrhythmia, IHD, HTN, and diabetes mellitus), concomitant medications (beta blocker, calcium channel blocker angiotensin converting enzyme inhibitor, angiotensin receptor blocker, statin, digoxin, and diuretic), and clinical characteristics (SBP and LVEF). NYHA class and QRS duration were not available in the GWTG®-HF database. ICD; Minority: Mortality, All-Cause - Baseline - 5.9y - 234 (54.9%) - (N=426) Mortality, All-Cause - Baseline - 1y - 67 (22.4%) [Cl 95%: 21.9-22.9] - (N=297) Mortality, All-Cause - Baseline - 3y - 80 (44.9%) [Cl 95%: 44.2-45.7] - (N=179) ICD; White, Non-Hispanics:	● Not Reported

				Mortality, All-Cause - Baseline - 6y - 637 (61.5%) - (N=1035) Mortality, All-Cause - Baseline - 1y - 185 (24.2%) [Cl 95%: 23.9-24.5] - (N=766) Mortality, All-Cause - Baseline - 3y - 234 (47.8%) [Cl 95%: 47.3-48.3] - (N=490) No ICD; Minority: Mortality, All-Cause - Baseline - 6.7y - 239 (56.1%) - (N=426) Mortality, All-Cause - Baseline - 1y - 79 (28.4%) [Cl 95%: 27.9-29] - (N=279) Mortality, All-Cause - Baseline - 3y - 66 (54.3%) [Cl 95%: 53.4 - 55.1] - (N=121) No ICD; White, Non-Hispanics: Mortality, All-Cause - Baseline - 6.8y - 646 (62.4%) - (N =1035) Mortality, All-Cause - Baseline - 1y - 203 (30.6%) [Cl 95%: 30.2–31] - (N=663) Mortality, All-Cause - Baseline - 3y - 174 (57.3%) [Cl 95%: 56.8–57.9] - (N=303)	

● **GWTG-HF & NCDR** ● Khazanie P 2015 (24) ● 26251283	**Aim:** We analyzed 2 large national registries linked with Medicare claims to examine the characteristics and outcomes of HF pts aged >65 y in clinical practice who received an ICD for primary prevention compared with eligible pts who did not receive an ICD. We also examined the associations between mortality and comorbidities and between mortality and HF burden to better inform clinical decision making in this population. **Study type:** Retrospective Observational **Size:**2974	**Inclusion Criteria:** - HF - Age ≥ 65 y - Enrolled in fee-for-service Medicare for at least 12 mo before the index admission - Discharged alive - LVEF ≤ 35 % **Exclusion Criteria:** - Discharged to a skilled nursing facility - Discharged to a hospice - Left hospital against medical advice	ICD N=1487 No ICD N=1487 ICD; ≤ 3 Comorbidities N=1202 ICD; >3 Comorbidities N=283 No ICD; ≤3 Comorbidities N=978 No ICD; >3 Comorbidities N=278	The 1° endpoint was all-cause mortality. Results were adjusted for the following covariates: patient demographic characteristics (age, sex, race), medical history IHD, prior atrial arrhythmia, diabetes, HTN, chronic renal disease, chronic lung disease, cerebrovascular disease), laboratory tests and vital signs (LVEF, SBP), and discharge medications (angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, beta-blocker, diuretic, calcium channel blocker, digoxin, statin). NYHA class and QRS duration were not available in the GWTG-HF database. ICD: Mortality, All-Cause - Baseline - 6y - 876 (58.9%) - (N=1487) Mortality, All-Cause - Baseline - 1y - 348 (23.4%) [Cl 95%: 23.1–23.7] - (N=1487) Mortality, All-Cause -	● Not Reported

				Baseline - 3y - 694 (46.7%) [Cl 95%: 46.2–47.2] - (N=1487) Mortality, All-Cause - Baseline - 5y - NR - (N=1487) No ICD: Mortality, All-Cause - Baseline - 6.7y - 896 (60.3%) - (N=1487) Mortality, All-Cause - Baseline - 1y - 439 (29.5%) [Cl 95%: 29.2–29.9] - (N=1487) Mortality, All-Cause - Baseline - 3y - 830 (55.8%) [Cl 95%: 55.3–56.3] - (N=1487) Mortality, All-Cause - Baseline - 5y - NR - (N=1487) ICD; ≤3 Comorbidities: Mortality, All-Cause - Baseline - 6y - 677 (56.3%) - (N=1202) Mortality, All-Cause - Baseline - 1y - 261 (21.7%) [Cl 95%: 21.4–22.2] - (N=1202) Mortality, All-Cause - Baseline - 3y - 532 (44.3%) [Cl 95%: 43.7–44.8] - (N=1202) Mortality, All-Cause - Baseline - 5y - NR - (N=1202)	

				ICD; >3 Comorbidities: Mortality, All-Cause - Baseline - 5.9 y - 198 (70%) - (N=283) Mortality, All-Cause - Baseline - 1y - 84 (29.8%) [Cl 95%: 29.2–30.5] - (N=283) Mortality, All-Cause - Baseline - 3y - 162 (57.2%) [Cl 95%: 56.2–58.1] - (N=283) Mortality, All-Cause - Baseline - 5y - NR - (N=283) No ICD; ≤3 Comorbidities: Mortality, All-Cause - Baseline - 6.7y - 566 (57.9%) - (N=978) Mortality, All-Cause - Baseline - 1y - 266 (27.2%) [Cl 95%: 26.8–27.6] - (N=978) Mortality, All-Cause - Baseline - 3y - 516 (52.8%) [Cl 95%: 52.2–53.4] - (N=978) Mortality, All-Cause - Baseline - 5y - NR - (N=978) No ICD; >3 Comorbidities: Mortality, All-Cause - Baseline - 6y - 200 (71.9%) - (N =2 78) Mortality, All-Cause - Baseline - 1y - 102 (36.8%) [Cl 95%: 36–37.6] - (N=278)	

				Mortality, All-Cause - Baseline - 3y - 185 (66.4%) [Cl 95%: 65.5–67.4] - (N=278) Mortality, All-Cause - Baseline - 5y - NR - (N=278)	
● **GWTG** ● Zeitler EP 2016 (25) ● 26758365	**Aim:** To examine clinical practice data to compare survival rates among women with HF with or without a primary prevention ICD. **Study type:** Retrospective Observational **Size:**2578	**Inclusion Criteria:** - Primary insurance was Medicare - Linked to Centers for Medicare data - Linked to Centers for Medicaid Services data - LVEF ≤ 35% - At least 65y old - In the GWTG-HF registry - Discharged from the hospital to home - Reasonable expectation of survival to 1 year **Exclusion Criteria:** - Class IV HF symptoms - Received comfort care only - Missing medical history data - Contraindication to ICD	ICD; Women N=430 ICD; Men N=859 No ICD; Women N=430 No ICD; Men N=859	All-cause mortality was the 1° endpoint of this analysis. Results adjusted for Age, White race, LVEF, SBP, IHD, Prior atrial arrhythmia, Diabetes mellitus, HTN, Chronic renal insufficiency, Depression, COPD, Anemia, Previous cerebrovascular attack or transient ischemic attack, Angiotensin-converting enzyme-inhibitor or angiotensin receptor blocker, Beta-blocker, Calcium channel blocker, Digoxin, Diuretic, Statin, Sodium, Blood urea nitrogen, Creatinine, Hemoglobin	● Not Reported

		- MI within 40d - Coronary Revascularization - PCI within 90d - Coronary artery bypass grafting within 90d - Received cardiac resynchronization therapy - Records of subsequent hospitalizations - Missing LVEF data - Recent onset of HF (i.e., HF diagnosis not predating the index admission) - Died during hospital admission - Already had an ICD in place		ICD; Women: Mortality, All-Cause - Baseline - 1y - 79 (18.3%) [Cl 95%: 17.6–19] - (N=430) (Propensity-matched and propensity-adjusted analysis) Mortality, All-Cause - Baseline - 3y - 168 (39.1%) [Cl 95%: 38–40.3] - (N=430) (Propensity-matched and propensity-adjusted analysis) Mortality, All-Cause - Baseline - 1y - 73 (17.3%) [Cl 95%: 13.9–21.3] - (N=422) (Propensity-matched 30d landmark analysis) Mortality, All-Cause - Baseline - 3y - 169 (40.1%) [Cl 95%: 35.3–45.3] - (N=422) (Propensity-matched 30-d landmark analysis) ICD; Men: Mortality, All-Cause - Baseline - 1y - 183 (21.3%) [Cl 95%: 20.7–21.8] - (N=859) (Propensity-matched and propensity-adjusted analysis) Mortality, All-Cause - Baseline - 3y - 380 (44.2%) [Cl 95%: 43.3–45] - (N=859) (Propensity-matched and	

				propensity-adjusted analysis) Mortality, All-Cause - Baseline - 1y - 163 (19.4%) [Cl 95%: 16.8–22.3] - (N=839) (Propensity-matched 30-d landmark analysis) Mortality, All-Cause - Baseline - 3y - 363 (43.3%) [Cl 95%: 39.9–47] - (N=839) (Propensity-matched 30d landmark analysis) No ICD; Women: Mortality, All-Cause - Baseline - 1y - 99 (23.1%) [Cl 95%: 22.3–23.9] - (N=430) (Propensity-matched and propensity-adjusted analysis) Mortality, All-Cause - Baseline - 3y - 203 (47.1%) [Cl 95%: 45.9–48.3] - (N=430) (Propensity-matched and propensity-adjusted analysis) Mortality, All-Cause - Baseline - 1y - 100 (23.6%) [Cl 95%: 19.8–28.1] - (N=422) (Propensity-matched 30d landmark analysis) Mortality, All-Cause - Baseline - 3y - 205 (48.6%) [Cl 95%: 43.6–54] - (N=422) (Propensity-matched 30d landmark analysis)	

				No ICD; Men: Mortality, All-Cause - Baseline - 1 y - 229 (26.7%) [Cl 95%: 26–27.3] - (N=859) (Propensity-matched and propensity-adjusted analysis) Mortality, All-Cause - Baseline - 3y - 451 (52.5%) [Cl 95%: 51.6–53.4] - (N=859) (Propensity-matched and propensity-adjusted analysis) Mortality, All-Cause - Baseline - 1y - 210 (25%) [Cl 95%: 22.2–28.2] - (N=839) (Propensity-matched 30-d landmark analysis) Mortality, All-Cause - Baseline - 3y - 427 (50.9%) [Cl 95%: 47.3–54.7] - (N=839) (Propensity-matched 30d landmark analysis)	
● Nakhoul GN 2015 (26) ● 26111859	**Aim:** To examine the survival benefits of ICDs placed for primary prevention in those with CKD not on dialysis (estimated glomerular filtration rate <60 mL/min per 1.73 m^2). **Study type:** Retrospective Observational **Size:**1262	**Inclusion Criteria:** - CKD - Echocardiogram at the Cleveland Clinic (between 2001 and October 2011) - At least one face-to-face outpatient encounter with a Cleveland Clinic health care provider - Two estimated glomerular filtration rate (27) values <60mL/min/1.73m^2, calculated using the CKD Epidemiology	ICD N=631 No ICD N=631 ICD; eGFR, 45–59 mL/min/1.73m^2 N=303 ICD; eGFR, 30–44 mL/min/1.73m^2	The 1° endpoint of interest was all-cause mortality. Results adjusted for demographics, comorbid conditions, use of cardioprotective medications, eGFR, LVEF, and ventricular arrhythmia. ICD: Mortality, All-Cause -	● Not Reported

		Collaboration (CKD-EPI) equation >90d apart **<u>Exclusion Criteria:</u>** - Aged <18y - Diagnosed with ESRD needing dialysis before CKD diagnosis - Diagnosed with ESRD needing renal transplantation before CKD diagnosis	N=227 ICD; eGFR, <30 mL/min/1.73m^2 N=101 No ICD; eGFR, 45–59 mL/min/1.73m^2 N=305 No ICD; eGFR, 30–44 mL/min/1.73m^2 N=219 No ICD; eGFR, <30 mL/min/1.73m^2 N=107	Median 2.9y - NR - (N=631) Mortality, All-Cause - Median 2.9y - NR - (N=631); Adjusted No ICD: Mortality, All-Cause - Median 2.9y - NR - (N=631) Mortality, All-Cause - Median 2.9y - NR - (N=631); Adjusted ICD; eGFR, 45–59 mL/min/1.73m^2: Mortality, All-Cause - Median 2.9y - NR - (N=303) Mortality, All-Cause - Median 2.9y - NR - (N=303); Adjusted ICD; eGFR, 30–44 mL/min/1.73m^2 Mortality, All-Cause - Median 2.9y - NR - (N=227) Mortality, All-Cause - Median 2.9y - NR - (N=227); Adjusted ICD; eGFR, <30 mL/min/1.73m^2 Mortality, All-Cause - Median 2.9y - NR - (N=101) Mortality, All-Cause - Median 2.9y - NR - (N=101); Adjusted No ICD; eGFR, 45–59 mL/min/1.73m^2:	

				Mortality, All-Cause - Median 2.9y - NR - (N=305) Mortality, All-Cause - Median 2.9y - NR - (N=305); Adjusted No ICD; eGFR, 30–44 mL/min/1.73m^2: Mortality, All-Cause - Median 2.9y - NR - (N=219) Mortality, All-Cause - Median 2.9y - NR - (N=219); Adjusted No ICD; eGFR, <30 mL/min/1.73m^2: Mortality, All-Cause - Median 2.9y - NR - (N=107) Mortality, All-Cause - Median 2.9y - NR - (N=107); Adjusted	
● **GWTG-HF & NCDR** ● Zeitler EP 2015 (28) ● PMC4461749	**Aim:** To assess the benefit of primary prevention ICDs in women. **Study type:** Retrospective Observational **Size:** 2946	**Inclusion Criteria:** - Age ≥65 y - LVEF ≤35% **Exclusion Criteria:** - Recent MI - Class IV HF symptoms - Recent onset of HF - CABG - Contraindication to an ICD - No documented LVEF	ICD N=1473 No ICD N=1473 ICD; Female N=490 ICD; Male N=983 No ICD; Female N=490 No ICD; Male N=983	The 1° endpoint was all-cause mortality. Results adjusted for Age, White race, LVEF, SBP, IHD, Prior atrial arrhythmia, Diabetes mellitus, HTN, Chronic renal insufficiency, Depression, COPD, Anemia, Previous cerebrovascular attack or TIA, Angiotensin-converting enzyme-inhibitor or angiotensin receptor blocker, Beta-blocker, Calcium channel blocker, Digoxin, Diuretic,	● Not Reported

				Statin, Sodium, BUN, Creatinine, Hemoglobin ICD: Mortality, All-Cause - Median 4.6y - 868 (58.9%) - (N=1473) No ICD: Mortality, All-Cause - Median 3.2y - 874 (59.3%) - (N=1473) ICD; Female: Mortality, All-Cause - Baseline - 1y - 106 (21.7%) [Cl 95%: 21.2–22.2] - (N=490) Mortality, All-Cause - Baseline - 3y - 217 (44.3%) [Cl 95%: 43.5–45.1] - (N=490) Mortality, All-Cause - Median 4.6y - 286 (58.4%) - (N=490) ICD; Male: Mortality, All-Cause - Baseline - 1y - 231 (23.5%) [Cl 95%: 23.2–23.9] - (N=983) Mortality, All-Cause - Baseline - 3 - 465 (47.3%) [Cl 95%: 46.7–47.9] - (N=983) Mortality, All-Cause - Median 4.4y - 582 (59.2%) - (N=983)	

				No ICD; Female: Mortality, All-Cause - Baseline - 1y - 139 (28.3%) [Cl 95%: 27.7–28.8] - (N=490) Mortality, All-Cause - Baseline - 3y - 267 (54.5%) [Cl 95%: 53.7–55.3] - (N=490) Mortality, All-Cause - Median 3.1y - 273 (55.7%) - (N=490) No ICD; Male: Mortality, All-Cause - Baseline - 1y - 300 (30.5%) [Cl 95%: 30.1–31] - (N=983) Mortality, All-Cause - Baseline - 3y - 567 (57.7%) [Cl 95%: 57.1–58.3] - (N=983) Mortality, All-Cause - Median 3y - 601 (61.1%) - (N=983)	
● **GWTG-HF & NCDR** ● Pun PH 2015 (29) ● 25404241	**Aim:** To compare the mortality of dialysis pts receiving a primary prevention ICD with matched controls. **Study type:** Retrospective Observational **Size:**172	**Inclusion Criteria:** - Age ≥65y - Dialysis - LVEF ≤35% - Cardiomyopathy - Renal Failure **Exclusion Criteria:** - Class IV HF symptoms - MI within 40 d prior to implant - CABG surgery within 90 d prior to implant - New-onset HF (<3 mo)	ICD N=86 No ICD N=86	The 1° endpoint was all-cause mortality. Results adjusted for demographic characteristics, LVEF, comorbid conditions (history of IHD and arrhythmias), blood pressure readings, cardiovascular medication use and serum creatinine values.	● Not Reported

				ICD: Mortality, All-Cause - Baseline – 1 y - 37 (43.4%) - (N=86) Mortality, All-Cause - Baseline – 3 y - 64 (74%) - (N=86) No ICD: Mortality, All-Cause - Baseline – 1 y - 34 (39.7%) - (N=86) Mortality, All-Cause - Baseline – 3 y - 66 (76.6%) - (N=86)	

● **DINAMIT** ● Dorian P 2010 (30) ● 21135366	**Aim:** To investigate possible mechanisms underlying the lack of mortality benefit in the DINAMIT. **Study type:** RCT **Size:**653	**Inclusion Criteria:** - Age 18–80 y - MI 6–40 d before randomization - Evidence of impaired cardiac autonomic function - LVEF ≤35% - SD of N-N intervals ≤70 ms or average heart rate >80 bpm on a 24 h Holter monitor performed ≥3 d after the index MI **Exclusion Criteria:** - NYHA class IV HF symptoms at the time of randomization - CABG - 3-vessel PCI immediately after the acute MI - 3-vessel percutaneous coronary intervention planned at the time of randomization - Prior ICD therapy	ICD N=311 No ICD N=342	The 1° endpoint in DINAMIT was death resulting from any cause. The analysis adjusted for treatment effect by taking into account potentially differential effects of the risk factors for the different causes of death ICD: Mortality, All-Cause - Mean 30 mo - 54 (17.4%) - (N=311) Mortality, Cardiac, Non-Arrhythmic - Mean 30 mo - 30 (9.6%) - (N=311) Mortality, Non-Cardiac - Mean 30 mo - 14 (4.5%) - (N=311) No ICD: Mortality, All-Cause - Mean 28 mo - 54 (16%) - (N=342) Mortality, Cardiac, Non-Arrhythmic - Mean 28 mo - 17 (5%) - (N=342) Mortality, Non-Cardiac - Mean 30 mo - 8 (2.3%) - (N=342)	● ICD: ● SCD, Presumed Arrhythmic - Mean 30 mo - 10 (3.2%) - (N=311) ● No ICD: ● SCD, Presumed Arrhythmic - Mean 28 mo - 29 (8.5%) - (N=342)

● **MADIT II** ● Goldenberg I 2010 (31) ● 20837894	**Aim:** To evaluate the benefit of primary prevention with an ICD during an extended 8 y follow-up of the MADIT-II population **Study type:** RCT **Size:**1232	**Inclusion Criteria:** - Ischemic LV dysfunction - EF≤30% - MI ≥1 mo before entry	ICD N =630 No ICD N=390 ICD; Age <65 N=309 ICD; Age ≥65 N=321 ICD; Age <65 N=200 ICD; Age ≥65 N=190	The 1° endpoint of the present study was the occurrence of all-cause mortality during 8y after enrollment Results were adjusted for covariates in the multivariate models, including age (as a continuous variable), NYHA functional class II, QRS duration 120ms, EF 25%, gender, and blood urea nitrogen levels 25mg/dL. ICD: Mortality, All-Cause - Baseline - 8y - NR - (N=630); Adjusted Mortality, All-Cause - Baseline - 4y - NR - (N=630) Mortality, All-Cause - 5 y - 8y - NR - (N=630) Mortality, All-Cause - Baseline - 8y - NR - (N=630); ITT & Adjusted Mortality, All-Cause - Baseline - 8y - NR - (N=630); Adjusted moA & Follow-up time was censored No ICD: Mortality, All-Cause - Baseline - 8y - NR -	• Not Reported

				(N=390); Adjusted Mortality, All-Cause - Baseline - 4y - NR - (N=390) Mortality, All-Cause - 5 y - 8y - NR - (N=390) Mortality, All-Cause - Baseline - 8y - NR - (N=390); ITT & Adjusted Mortality, All-Cause - Baseline - 8y - NR - (N=390); Adjusted & Follow-up time was censored ICD; Age <65y Mortality, All-Cause - Baseline - 8y - NR - (N=309); Adjusted ICD; Age ≥65y: Mortality, All-Cause - Baseline - 8y - NR - (N=321); Adjusted No ICD; Age <65y: Mortality, All-Cause - Baseline - 8y - NR - (N=200); Adjusted No ICD; Age ≥65y: Mortality, All-Cause - Baseline - 8y - NR - (N=190); Adjusted	

● Hiremath S 2010 (32) ● 20714135	**Aim:** To evaluate the impact of an ICD on survival in ESRD pts. **Study type:** Retrospective Observational **Size:**100	**Inclusion Criteria:** - Renal Failure	ICD N=50 No ICD N=50	The 1° endpoint was all-cause mortality. The study included age, use of blockade and amiodarone, LVEF, and history of prior CAD as covariates in the multivariable analysis. ICD: Mortality, All-Cause - NR - 20 (40%) - (N=50) Mortality, All-Cause - NR - NR - (N=50); Adjusted Mortality, All-Cause - NR - NR - (N=50); Sensitivity Analysis No ICD: Mortality, All-Cause - NR - 29 (58%) - (N=50) Mortality, All-Cause - NR - NR - (N=50); Adjusted Mortality, All-Cause - NR - NR - (N=50); Sensitivity Analysis	● Not Reported

● **MADIT II** ● Wittenberg SM 2005 (33) ● 16054472	**Aim:** The present study used data from the second MADIT II to characterize the mortality experience of a contemporary diabetic cohort with a depressed LVEF after MI and to evaluate the relative benefit of ICD therapy in this group compared with nondiabetic pts enrolled in the trial. **Study type:** RCT **Size:**1231	**Inclusion Criteria**: - MI >1 mo before study entry - LVEF ≤0.30 documented within 3 mo before entry	ICD N=742 Conventional Therapy N=489 ICD; Diabetes N=249 ICD; No Diabetes N=493 Conventional Therapy; Diabetes N=184 Conventional Therapy; No Diabetes N=305	The 1° endpoint: was death from any cause. Results are adjusted for adjustment for renal insufficiency, NYHA class, and BMI. ICD; Diabetes: Mortality, All-Cause - Baseline - 2 y - NR - (N=249) ICD; No Diabetes: Mortality, All-Cause - Baseline - 2 y - NR - (N=493) Conventional Therapy; Diabetes: Mortality, All-Cause - Baseline - 2 y - 46 (25%) - (N=184) Conventional Therapy; No Diabetes: Mortality, All-Cause - Baseline - 2 y - 61 (20%) - (N=305)	● Not Reported

● **DEFINITE** ● Kadish A. 2004 (34) ● 15152060	**Aim:** To test the hypothesis that an ICD will reduce the risk of death in pts with nonischemic cardiomyopathy and moderate-to-severe LV dysfunction. **Study type:** RCT **Size:** 458	**Inclusion Criteria** - History of symptomatic HF - LVEF <36% - Ambient arrhythmias defined by an episode of NSVT on Holter or telemetric monitoring (3–15 beats at a rate of more than 120 beats per minute) or an average of at least 10 premature ventricular complexes per hour on 24h Holter monitoring - NICM **Exclusion Criteria** - NYHA class IV HF - CHD - Acute myocarditis - Clinically significant CAD as the cause of the cardiomyopathy - Not candidates for the ICD - Underwent EP testing within the prior 3 mo - Cardiac transplantation appeared to be imminent - Familial cardiomyopathy associated with sudden death - Permanent pacemakers	ICD N=229 Standard Therapy N=229 ICD (Age <65 y) N=NR ICD (Age ≥65y) N=NR Standard Therapy (Age <65 y) N=NR Standard Therapy (Age ≥65 y) N=NR	The 1° endpoint of the study was death from any cause. Results Adjusted for duration of HF ICD Mortality, All-Cause - Mean 29 mo - 28 (12.2%) - (N=229) Mortality, HF - Mean 29 mo - 9 (3.9%) - (N=229) Mortality, ICD, Procedure-Related - Implantation of ICD - 0 (0%) - (N=229) Mortality, Unknown Cause - Mean 29 mo - 2 (0.9%) - (N=229) Standard Therapy Mortality, All-Cause - Mean 29 mo - 40 (17.5%) - (N=229) Mortality, Cardiac, Suspected - Mean 29 mo - 1 (0.4%) - (N=229) Mortality, HF - Mean 29 mo - 11 (4.8%) - (N=229) Mortality, Unknown Cause - Mean 29 mo - 2 (0.9%) - (N=229) ICD (Age <65y) Mortality, All-Cause - Mean 29 mo - NR - (N=NR) ICD (Age ≥65y)	● ICD Cardiac Tamponade - Implantation of ICD - 1 (0.4%) - (N=229) ● Hemothorax - Implantation of ICD - 1 (0.4%) - (N=229) ● ICD, Complications - Mean 29 mo - 10 (4.4%) - (N=229) ● ICD, Complications - Implantation of ICD - 3 (1.3%) - (N=229) ● ICD, Complications, Lead Dislodgement or ICD, **Complications**, Lead Fractures - Mean 29 mo - 6 (2.6%) - (N=229) ● Infection, Any - Mean 29 mo - 1 (0.4%) - (N=229) ● Pneumothorax - Implantation of ICD - 1 (0.4%) - (N=229) ● Venous Thrombosis - Mean 29 mo - 3 (1.3%) - (N=229) ● SCD - Mean 29 mo - 3 (1.3%) - (N=229) ● Standard Therapy SCD - Mean 29 mo - 14 (6.1%) - (N=229)

				Mortality, All-Cause - Mean 29 mo - NR - (N=NR) Standard Therapy (Age <65 y) Mortality, All-Cause - Mean 29 mo - NR - (N=NR) Standard Therapy (Age ≥65 y) Mortality, All-Cause - Mean 29 mo - NR - (N=NR)	

● **SCD-HeFT** ● Bardy Gust H 2005 ● 15659722	**Aim:** To evaluate the hypothesis that amiodarone or a conservatively programmed shock-only, single-lead ICD would decrease the risk of death from any cause in a broad population of pts with mild to-moderate HF. **Study type:** RCT **Size:**2521	**Inclusion Criteria** - Age ≥18 y - NYHA class II or III chronic - Stable HF due to ischemic or nonischemic causes - LVEF ≤35 %	ICD N=829 Amiodarone N=845 Placebo N=847 ICD (Age <65 y) N=NR ICD (Age ≥65 y) N=NR Amiodarone (Age <65 y) N=NR Amiodarone (Age ≥65 y) N=NR Placebo (Age <65 y) N =NR Placebo (Age ≥65 y) N=NR ICD (Diabetes, Type Unknown) N=253 ICD (Diabetes, None) N=576	The primary end point was death from any cause. Results adjusted for the NYHA class and the cause of CHF. ICD Mortality, All-Cause - Median 45.5 mo - 182 (22%) - (N=829) Amiodarone Mortality, All-Cause - Median 45.5 mo - 237 (28%) - (N=845) Placebo Mortality, All-Cause - Median 45.5 mo - 246 (29%) - (N=847) ICD (Age <65 y) Mortality, All-Cause - Median 45.5 mo - NR - (N=NR) ICD (Age >=65 y) Mortality, All-Cause - Median 45.5 mo - NR - (N=NR) Amiodarone (Age <65 y) Mortality, All-Cause - Median 45.5 mo - NR - (N=NR) Amiodarone (Age ≥65 y)	● **i**CD, Complications - Median 45.5 mo - 75 (9%) - (N=829)

			Amiodarone (Diabetes, Type Unknown) N=243 Amiodarone (Diabetes, None) N=602 Placebo (Diabetes, Type Unknown) N=271 Placebo (Diabetes, None) N=576	Mortality, All-Cause - Median 45.5 mo - NR - (N=NR) Placebo (Age <65 y) Mortality, All-Cause - Median 45.5 mo - NR - (N=NR) Placebo (Age ≥65 y) Mortality, All-Cause - Median 45.5 mo - NR - (N=NR) ICD (Diabetes, Type Unknown) Mortality, All-Cause - Median 45.5 mo - NR - (N=253) ICD (Diabetes, None) Mortality, All-Cause - Median 45.5 mo - NR - (N=576) Amiodarone (Diabetes, Type Unknown) Mortality, All-Cause - Median 45.5 mo - NR - (N=243) Amiodarone (Diabetes, None) Mortality, All-Cause - Median 45.5 mo - NR - (N=602)	

				Placebo (Diabetes, Type Unknown) Mortality, All-Cause - Median 45.5 mo - NR - (N=271) Placebo (Diabetes, None) Mortality, All-Cause - Median 45.5 mo - NR - (N=576)	
● **MADIT I, MADIT II & SCD-HeFT** ● Pun PH 2014 (35) ● 24518128	**Aim:** To evaluate benefit of primary prevention ICD among pts with CKD **Study type:** Meta-analysis of RCT **Size:**2867	**Inclusion criteria:** - Symptomatic HF NYHA class <IV - LVEF ≤35% - Assignment to either an ICD or usual care. - Kidney function was determined by calculating estimated GFR (27) at study enrollment. CKD-EPI (CKD Epidemiology Collaboration) creatinine equation was used,	ICD N= 1533 Usual Care N=1334 ICD; eGFR< 60 N=541 Usual care; eGFR< 60 N=499	The 1° endpoint was mortality, re-hospitalizations, and effect modification by eGFR. Results adjusted for demographic characteristics, LVEF, comorbid conditions (history of IHD and arrhythmias), blood	

		which uses age, race, and sex in addition to serum creatinine concentration to determine eGFR. For consistency with prior literature and for simplicity, the cohort was dichotomized into 2 strata of eGFR: 1. eGFR < 60 (CKD stages 3–5) 2. eGFR ≥ 60 mL/min1.73m^2. They also examined outcomes by finer categories of eGFR (eGFR <45, 45–59, 60–89, and ≥ 90 mL/min1.73m^2). **Exclusion criteria**: -Patients without HF symptoms or with NYHA class IV symptoms - Patients with LVEF > 35% - Patient who were missing data on prior MI - Patients who had a MI in the 40 days preceding randomization - Patients whose time from randomization was unknown were excluded	ICD; eGFR ≥ 60 N=992 ICD; eGFR ≥ 60 N=835	pressure readings, cardiovascular medication use and serum creatinine values. Kaplan-Meier estimate of the probability of death during follow-up was: - 43.3% for 1,334 pts receiving usual care - 35.8% for 1,533 ICD recipients ICD and Sudden Death in CKD: GFR <45 HR (Adjusted) – 0.77; 95% CI= 0.36–1.32 GFR 45–60 HR (Adjusted) – 0.8; 95% CI= 0.38–1.48 GFR 60–90 HR (Adjusted) – 0.46; 95% CI = 0.22–0.83 GFR 90+ HR (Adjusted) – 0.45; 95% CI = 0.19–0.89	

● **MADIT I, MADIT II, DEFINITE, SCD-HeFT** ● Steinberg BA 2014 (36) ● 25306452	**Aim:** The aim of this study was to determine if the benefit of ICDs is modulated by medical comorbidity. **Study type:** Meta-analysis of RCT **Size:** 3,348	**Inclusion criteria:** - LVEF ≤35% - Either no prior MI or time from MI to randomization >40 d - Availability of data on important covariates. Seven comorbidities were selected for assessment: - Smoking - IHD - CKD - Diabetes - Pulmonary disease - AF - Peripheral vascular disease **Exclusion criteria:** - Patients with NYHA functional class IV HF were excluded.	ICD N=1771 Control N=1527 ICD, <2 Comorbidities N=442 Control, <2 Comorbidities N=388 ICD, ≥2 Comorbidities N=1329 ICD, ≥2 Comorbidities N=1189	The 1° endpoint was all-cause mortality at last follow-up. Adjusted (Mean) Survival Difference Between ICD and Control at 5y: 0 Comorbidity: 0.13; 95% CI = 0.06 – 0.19 1 Comorbidity: 0.13; 95% CI = 0.07 – 0.19 2 Comorbidities: 0.13; 95% CI = 0.08 – 0.18 3 Comorbidities: 0.11; 95% CI = 0.06 – 0.15 4 Comorbidities: 0.06; 95% CI = 0.0 – 0.14 5 Comorbidities: 0.00; 95% CI = -0.10 – 0.12 6 Comorbidities: -0.05; 95% CI = -0.18 – 0.09 - Use of an ICD resulted in significant improvement in survival in pts: - low comorbidity (unadjusted HR: 0.59; 95% CI: 0.40–0.87) - Patients with extensive comorbid illness (unadjusted HR: 0.71; 95% CI: 0.61–0.84)	● 2° endpoint included all-cause re-hospitalization and cause-specific mortality. ● The proportion of deaths due to arrhythmia were higher for pts in the control group (40% and 37% of deaths with <2 and ≥2 comorbidities, respectively) compared with pts in the ICD group (12% and 22% of deaths with <2 and ≥2 comorbidities, respectively). ● Hospitalization rates were lowest in pts with <2 comorbidities who did not receive an ICD (54%) and highest for pts with ≥2 comorbidities who received an ICD (74%). ● Adverse event rates were lowest in pts with low comorbidity not receiving an ICD (0%) and highest in pts with high comorbidity receiving an ICD (21%).

● **MADIT I, MADIT II, MUSTT, DEFINITE, SCD-HeFT** ● Hess PL 2015 ● 25669833	**Aim:** The aim was to assess the impact of patient age on the risks of death or re-hospitalization after 1° prevention ICD placement. **Study type:** Meta-analysis of RCT **Size:**3530	**Inclusion criteria:** - HF (NYHA I-III) - LVEF of ≤35% - Availability of important covariates. **Exclusion criteria:** - Patients without HF symptoms or with NYHA IV symptoms - LVEF of >35% - Time from MI to randomization <40 d - Those missing values for variables that define the inclusion criteria	ICD N=1837 Conventional Medical Therapy N=1693 ICD, age <55 y N=527 Conventional Medical Therapy, age <55 y N=483 ICD, age 55–64 y N=529 Conventional Medical Therapy, age 55–64 y N=526 ICD, age 65–74 y N=555 Conventional Medical Therapy, age 65–74 y N=520 ICD, age >75 y N=226 Conventional Medical Therapy, age >75 y N=164	The 1° endpoint: was all-cause mortality. No. of events (death) ICD, age <55 y N=43 Conventional Medical Therapy, age <55 y N=84 ICD, age 55–64 y N=97 Conventional Medical Therapy, age 55–64 y N=139 ICD, age 65–74 y N=127 Conventional Medical Therapy, age 65–74 y N=174 ICD, age >75 y N=56 Conventional Medical Therapy, age >75 y N=66 - ICD benefit in older pts: DEFINITE HR 0.48; 95% CI: 0.30–0.79 MADIT-I HR 0.37; 95% CI: 0.22–0.61	● The 2° endpoint was re-hospitalization for any reason.

				MADIT-II HR: 0.44; 95% CI: 0.31–0.59 MUSTT HR: 0.27; 95% CI: 0.14–0.49 SCD-HeFT HR: 0.58; 95% CI: 0.45–0.74 Overall HR: 0.41; 95% CI: 0.21–0.71	

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