Appendix A. Search Strategy

Databases:

1) **Ovid MEDLINE ®** 1948 to December Week 1 2012
2) **Ovid MEDLINE ® In-Process & Other Non-Indexed Citations** November 30, 2012
3) **EBM Reviews-Cochrane Central Register of Controlled Trials** 4th Quarter 2012

Search Terms:

#	Searches	Brief description of terms	Number of abstracts
1	defibrillators, implantable.sh.	Terms related to device of interest	9,770
2	(defibrillators and implantable).af.		10,520
3	implantable defibrillators.af.		656
4	(implantable and cardioverter and defibrillator).af.		5,507
5	implantable cardioverter defibrillator.af.		4,645
6	cardioverter defibrillators, implantable.af.		1
7	(death, sudden, cardiac and cardiac pacing, artificial).af.	Terms related to outcome of interest	310
8	or/1-7		**11,828**
9	randomized controlled trial.pt.	RCT module	623,823
10	controlled clinical trial.pt		164,766
11	randomized controlled trials/		83,169
12	Random Allocation/		93,931
13	Double-blind Method/		208,115
14	Single-Blind Method/		25,802
15	clinical trial.pt.		745,680
16	Clinical Trials.mp. or exp Clinical Trials/		304,982
17	(clinic$ adj25 trial$).tw.		270,192
18	((singl$ or doubl$ or trebl$ or tripl$) adj (mask$ or blind$)).tw.		238,018
19	Placebos/		50,936
20	placebo$.tw.		253,666
21	random$.tw.		877,789
22	trial$.tw.		687,536
23	(randomized control trial or clinical control trial).sd.		232,482
24	(latin adj square).tw.		3,834
25	Comparative Study.tw. or Comparative Study.pt.		1,718,659
26	exp Evaluation studies/		160,402
27	Follow-Up Studies/		472,156
28	Prospective Studies/		367,536
29	(control$ or prospectiv$ or volunteer$).tw.		2,861,505
30	Cross-Over Studies/		51,220
31	or/9-30		5,503,700
32	8 and 31	Comparative ICD studies	*5,457*
33	exp cohort studies/ or exp prospective studies/ or exp retrospective studies/ or exp epidemiologic studies/ or exp case-control studies/	Cohort module	1,471,173

34	(cohort or retrospective or prospective or longitudinal or observational or follow-up or followup or registry).af.		1,819,849
35	case-control.af. or (case adj10 control).tw.		175,858
36	ep.fs. *(epidemiology/floating subhead)*		1,046,431
37	or/33-36		2,709,357
38	8 not 31		6,437
39	37 and 38	Cohort ICD studies	*1,309*
40	**32 or 39**	**All ICD studies**	**6,766**

NOTE: The above search strategy was successfully tested against the major RCTs identified in the review by Passman R, Kadish A. Sudden death prevention with implantable devices. *Circulation* 2007:116:561-71; PMID: 17664385.

Appendix B. Excluded Studies

The 223 studies excluded after full-text review are listed in alphabetical order by first author under each main reason for exclusion (bold headings): adverse event paper published before 2002 (n=10), <500 adverse events (n=8), mixed primary and secondary prevention and no adverse effect (n=33), no outcomes of interest (n=28), and not comparison of interest (n=6), not intervention of interest (n=3), outcome numerator or denominator unclear (n=8), protocol (not full article) (n=5), review/editorial (n=4), secondary prevention (n=31), not study design of interest (n=59), wrong population (n=24), and other (n=4). PMIDs are given at the end of each reference, when available.

Adverse Event Paper Published Before 2002 (n=10)

1. Pacifico A, Johnson JW, Stanton MS, et al. Comparison of results in two implantable defibrillators. Jewel 7219D Investigators. Am J Cardiol 1998 Oct 1;82(7):875-80. PMID: 9781970.

2. Hoffmann E, Steinbeck G. Experience with pectoral versus abdominal implantation of a small defibrillator. A multicenter comparison in 778 patients. European Jewel Investigators. Eur Heart J 1998 Jul;19(7):1085-98. PMID: 9717045.

3. Rosenqvist M, Beyer T, Block M, et al. Adverse events with transvenous implantable cardioverter-defibrillators: a prospective multicenter study. European 7219 Jewel ICD investigators. Circulation 1998 Aug 18;98(7):663-70. PMID: 9715859.

4. Smith PN, Vidaillet HJ, Hayes JJ, et al. Infections with nonthoracotomy implantable cardioverter defibrillators: can these be prevented? Endotak Lead Clinical Investigators. Pacing Clin Electrophysiol 1998 Jan;21(1 Pt 1):42-55. PMID: 9474647.

5. Narasimhan C, Dhala A, Axtell K, et al. Comparison of outcome of implantable cardioverter defibrillator implantation in patients with severe versus moderately severe left ventricular dysfunction secondary to atherosclerotic coronary artery disease. Am J Cardiol 1997 Nov 15;80(10):1305-08. PMID: 9388103.

6. Panotopoulos PT, Axtell K, Anderson AJ, et al. Efficacy of the implantable cardioverter-defibrillator in the elderly. J Am Coll Cardiol 1997 Mar 1;29(3):556-60. PMID: 9060893.

7. Gold MR, Peters RW, Johnson JW, et al. Complications associated with pectoral implantation of cardioverter defibrillators. World-Wide Jewel Investigators. Pacing Clin Electrophysiol 1997 Jan;20(1 Pt 2):208-11. PMID: 9121991.

8. Gallik DM, Ben-Zur UM, Gross JN, et al. Lead fracture in cephalic versus subclavian approach with transvenous implantable cardioverter defibrillator systems. Pacing Clin Electrophysiol 1996 Jul;19(7):1089-94. PMID: 8823837.

9. Zipes DP, Roberts D. Results of the international study of the implantable pacemaker cardioverter-defibrillator. A comparison of epicardial and endocardial lead systems. The Pacemaker-Cardioverter-Defibrillator Investigators. Circulation 1995 Jul 1;92(1):59-65. PMID: 7788918.

10. Mosteller RD, Lehmann MH, Thomas AC, et al. Operative mortality with implantation of the automatic cardioverter-defibrillator. Am J Cardiol 1991 Nov 15;68(13):1340-45. PMID: 1951123.

Adverse Events N<500 (n=13)

1. Holst AG, Jensen HK, Eschen O, et al. Low disease prevalence and inappropriate implantable cardioverter defibrillator shock rate in Brugada syndrome: a nationwide study. Europace 2012 Jul;14(7):1025-29. PMID: 22286273.

2. Yu JB, Yang B, Xu DJ, et al. [Impact of metoprolol use in the treatment of patients with electrical-storm after cardioverter defibrillators implantation]. Zhonghua Xin Xue Guan Bing Za Zhi 2011 Aug;39(8):717-20. PMID: 22169417.

3. Forleo GB, Tesauro M, Panattoni G, et al. Impact of continuous intracardiac ST-segment monitoring on mid-term outcomes of ICD-implanted patients with coronary artery disease. Early results of a prospective comparison with conventional ICD outcomes. Heart 2012 Mar;98(5):402-07. PMID: 22115985.

4. Gojkovic O, Aliot EM, Capucci A, et al. Celivarone in patients with an implantable cardioverter-defibrillator: adjunctive therapy for the reduction of ventricular arrhythmia-triggered implantable cardioverter-defibrillator interventions. Heart Rhythm 2012 Feb;9(2):217-24. PMID: 21978965.

5. McLeod CJ, Shen WK, Rea RF, et al. Differential outcome of cardiac resynchronization therapy in ischemic cardiomyopathy and idiopathic dilated cardiomyopathy. Heart Rhythm 2011 Mar;8(3):377-82. PMID: 21070886.

6. Kettering K, Mewis C, Dornberger V, et al. Long-term experience with subcutaneous ICD leads: a comparison among three different types of subcutaneous leads. Pacing Clin Electrophysiol 2004 Oct;27(10):1355-61. PMID: 15511244.

7. Sandstedt B, Kennergren C, Schaumann A, et al. Short- and long-term performance of a tripolar down-sized single lead for implantable cardioverter defibrillator treatment: a randomized prospective European multicenter study. European Endotak DSP Investigator Group. Pacing Clin Electrophysiol 1998 Nov;21(11 Pt 1):2087-94. PMID: 9826861.

8. Mehta D, Nayak HM, Singson M, et al. Late complications in patients with pectoral defibrillator implants with transvenous defibrillator lead systems: high incidence of insulation breakdown. Pacing Clin Electrophysiol 1998 Oct;21(10):1893-900. PMID: 9793085.

9. Lelakowski J, Piekarz J, Rydlewska A, et al. Determinants of patient survival rate after implantation of a cardioverter-defibrillator without resynchronisation capability. Kardiol Pol 2012;70(11):1099-110. PMID: 23180517.

10. Codner P, Nevzorov R, Kusniec J, et al. Implantable cardioverter defibrillator with and without defibrillation threshold testing. Isr Med Assoc J 2012 Jun;14(6):343-46. PMID: 22891393.

11. Aschenbrenner T, Brockmeier J, Bramlage P, et al. Improved survival of patients with coronary artery disease and low ejection fraction with ICD implantation versus conventional therapy in a real world survey. BMC Res Notes 2012;5:382. PMID: 22840219.

12. Lovelock JD, Patel A, Mengistu A, et al. Generator exchange is associated with an increased rate of Sprint Fidelis lead failure. Heart Rhythm 2012 Oct;9(10):1615-18. PMID: 22683747.

13. Clementy N, Pierre B, Lallemand B, et al. Long-term follow-up on high-rate cut-off programming for implantable cardioverter defibrillators in primary prevention patients with left ventricular systolic dysfunction. Europace 2012 Jul;14(7):968-74. PMID: 22389416.

Mixed Primary and Secondary Prevention, No Adverse Effect (n=33)

1. Pedersen SS, Tekle FB, Hoogwegt MT, et al. Shock and patient preimplantation type D personality are associated with poor health status in patients with implantable cardioverter-defibrillator. Circ Cardiovasc Qual Outcomes 2012 May;5(3):373-80. PMID: 22570357.

2. Cho EY, von KR, Marten-Mittag B, et al. Determinants and trajectory of phobic anxiety in patients living with an implantable cardioverter defibrillator. Heart 2012 May;98(10):806-12. PMID: 22543838.

3. Berg SK, Higgins M, Reilly CM, et al. Sleep quality and sleepiness in persons with implantable cardioverter defibrillators: outcome from a clinical randomized longitudinal trial. Pacing Clin Electrophysiol 2012 Apr;35(4):431-43. PMID: 22303998.

4. Shalaby A, Brumberg G, El-Saed A, et al. Mood disorders and outcome in patients receiving cardiac resynchronization therapy. Pacing Clin Electrophysiol 2012 Mar;35(3):294-301. PMID: 22229659.

5. Flemme I, Johansson I, Stromberg A. Living with life-saving technology - coping strategies in implantable cardioverter defibrillators recipients. J Clin Nurs 2012 Feb;21(3-4):311-21. PMID: 21951323.

6. Habibovic M, van den Broek KC, Alings M, et al. Posttraumatic stress 18 months following cardioverter defibrillator implantation: shocks, anxiety, and personality. Health Psychol 2012 Mar;31(2):186-93. PMID: 21806300.

7. Pedersen SS, Hoogwegt MT, Jordaens L, et al. Relation of symptomatic heart failure and psychological status to persistent depression in patients with implantable cardioverter-defibrillator. Am J Cardiol 2011 Jul 1;108(1):69-74. PMID: 21529736.

8. Tzeis S, Kolb C, Baumert J, et al. Effect of depression on mortality in implantable cardioverter defibrillator recipients--findings from the prospective LICAD study. Pacing Clin Electrophysiol 2011 Aug;34(8):991-97. PMID: 21438895.

9. Chair SY, Lee CK, Choi KC, et al. Quality of life outcomes in chinese patients with implantable cardioverter defibrillators. Pacing Clin Electrophysiol 2011 Jul;34(7):858-67. PMID: 21410723.

10. Heatherly SJ, Simmons T, Fitzgerald DM, et al. Psychological effects of implantable cardioverter-defibrillator leads under advisory. Pacing Clin Electrophysiol 2011 Jun;34(6):694-99. PMID: 21410721.

11. von KR, Baumert J, Kolb C, et al. Chronic posttraumatic stress and its predictors in patients living with an implantable cardioverter defibrillator. J Affect Disord 2011 Jun;131(1-3):344-52. PMID: 21195483.

12. Marcus GM, Chan DW, Redberg RF. Recollection of pain due to inappropriate versus appropriate implantable cardioverter-defibrillator shocks. Pacing Clin Electrophysiol 2011 Mar;34(3):348-53. PMID: 21077915.

13. Suzuki T, Shiga T, Kuwahara K, et al. Prevalence and persistence of depression in patients with implantable cardioverter defibrillator: a 2-year longitudinal study. Pacing Clin Electrophysiol 2010 Dec;33(12):1455-61. PMID: 20946285.

14. Keren A, Sears SF, Nery P, et al. Psychological adjustment in ICD patients living with advisory fidelis leads.

J Cardiovasc Electrophysiol 2011 Jan;22(1):57-63. PMID: 20731739.

15. Pedersen SS, van den Broek KC, Erdman RA, et al. Pre-implantation implantable cardioverter defibrillator concerns and Type D personality increase the risk of mortality in patients with an implantable cardioverter defibrillator. Europace 2010 Oct;12(10):1446-52. PMID: 20719779.

16. Dickerson SS, Kennedy M, Wu YW, et al. Factors related to quality-of-life pattern changes in recipients of implantable defibrillators. Heart Lung 2010 Nov;39(6):466-76. PMID: 20561848.

17. Pedersen SS, Theuns DA, Jordaens L, et al. Course of anxiety and device-related concerns in implantable cardioverter defibrillator patients the first year post implantation. Europace 2010 Aug;12(8):1119-26. PMID: 20507853.

18. Kapa S, Rotondi-Trevisan D, Mariano Z, et al. Psychopathology in patients with ICDs over time: results of a prospective study. Pacing Clin Electrophysiol 2010 Feb;33(2):198-208. PMID: 19930108.

19. Pedersen SS, den Broek KC, Theuns DA, et al. Risk of chronic anxiety in implantable defibrillator patients: a multi-center study. Int J Cardiol 2011 Mar 17;147(3):420-23. PMID: 19896732.

20. Kim J, Pressler SJ, Welch JL, et al. Validity and reliability of the chronic heart failure questionnaire mastery subscale in patients with defibrillators. West J Nurs Res 2009 Dec;31(8):1057-75. PMID: 19783791.

21. Pinter A, Mangat I, Korley V, et al. Assessment of resynchronization therapy on functional status and quality of life in patients requiring an implantable defibrillator. Pacing Clin Electrophysiol 2009 Dec;32(12):1509-19. PMID: 19765233.

22. Fisher JD, Koulogiannis KP, Lewallen L, et al. The psychological impact of implantable cardioverter-defibrillator recalls and the durable positive effects of counseling. Pacing Clin Electrophysiol 2009 Aug;32(8):1012-16. PMID: 19659621.

23. van den Broek KC, Nyklicek I, Van d, V, et al. Risk of ventricular arrhythmia after implantable defibrillator treatment in anxious type D patients. J Am Coll Cardiol 2009 Aug 4;54(6):531-37. PMID: 19643315.

24. Pandya K, Patel MB, Natla J, et al. Predictors of hemodynamic compromise with propofol during defibrillator implantation: a single center experience. J Interv Card Electrophysiol 2009 Aug;25(2):145-51. PMID: 19263205.

25. Bilge AK, Ozben B, Demircan S, et al. Depression and anxiety status of patients with implantable cardioverter defibrillator and precipitating factors. Pacing Clin Electrophysiol 2006 Jun;29(6):619-26. PMID: 16784428.

26. Wathen MS, DeGroot PJ, Sweeney MO, et al. Prospective randomized multicenter trial of empirical antitachycardia pacing versus shocks for spontaneous rapid ventricular tachycardia in patients with implantable cardioverter-defibrillators: Pacing Fast Ventricular Tachycardia Reduces Shock Therapies (PainFREE Rx II) trial results. Circulation 2004 Oct 26;110(17):2591-96. PMID: 15492306.

27. Pedersen SS, van Domburg RT, Theuns DA, et al. Type D personality is associated with increased anxiety and depressive symptoms in patients with an implantable cardioverter defibrillator and their partners. Psychosom Med 2004 Sep;66(5):714-19. PMID: 15385696.

28. Shukla HH, Flaker GC, Jayam V, et al. High defibrillation thresholds in transvenous biphasic implantable defibrillators: clinical predictors and prognostic implications. Pacing Clin Electrophysiol 2003 Jan;26(1 Pt 1):44-48. PMID: 12685138.

29. Godemann F, Ahrens B, Behrens S, et al. Classic conditioning and dysfunctional cognitions in patients with panic disorder and agoraphobia treated with an implantable cardioverter/defibrillator. Psychosom Med 2001 Mar;63(2):231-38. PMID: 11292270.

30. Duru F, Buchi S, Klaghofer R, et al. How different from pacemaker patients are recipients of implantable cardioverter-defibrillators with respect to psychosocial adaptation, affective disorders, and quality of life? Heart 2001 Apr;85(4):375-79. PMID: 11250956.

31. Herbst JH, Goodman M, Feldstein S, et al. Health-related quality-of-life assessment of patients with life-threatening ventricular arrhythmias. Pacing Clin Electrophysiol 1999 Jun;22(6 Pt 1):915-26. PMID: 10392390.

32. Pacifico A, Hohnloser SH, Williams JH, et al. Prevention of implantable-defibrillator shocks by treatment with sotalol. d,l-Sotalol Implantable Cardioverter-Defibrillator Study Group. N Engl J Med 1999 Jun 17;340(24):1855-62. PMID: 10369848.

33. Dunbar SB, Jenkins LS, Hawthorne M, et al. Mood disturbance in patients with recurrent ventricular dysrhythmia before insertion of implantable cardioverter defibrillator. Heart Lung 1996 Jul;25(4):253-61. PMID: 8836741.

No Outcomes of Interest (n=43)

1. Barsheshet A, Moss AJ, Huang DT, et al. Applicability of a risk score for prediction of the long-term (8-year) benefit of the implantable cardioverter-defibrillator. J Am Coll Cardiol 2012 Jun 5;59(23):2075-79. PMID: 22651863.

2. 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 Jan;17(1):14-21. PMID: 22276624.

3. Versteeg H, Starrenburg A, Denollet J, et al. Monitoring device acceptance in implantable cardioverter defibrillator patients using the Florida Patient Acceptance Survey. Pacing Clin Electrophysiol 2012 Mar;35(3):283-93. PMID: 22229519.

4. Zecchin M, Merlo M, Pivetta A, et al. How can optimization of medical treatment avoid unnecessary implantable cardioverter-defibrillator implantations in patients with idiopathic dilated cardiomyopathy presenting with "SCD-HeFT criteria?". Am J Cardiol 2012 Mar 1;109(5):729-35. PMID: 22176998.

5. Sullivan RM, Russo AM, Berg KC, et al. Arrhythmia rate distribution and tachyarrhythmia therapy in an ICD population: results from the INTRINSIC RV trial. Heart Rhythm 2012 Mar;9(3):351-58. PMID: 22016074.

6. Hoogwegt MT, Kupper N, Theuns DA, et al. Beta-blocker therapy is not associated with symptoms of depression and anxiety in patients receiving an implantable cardioverter-defibrillator. Europace 2012 Jan;14(1):74-80. PMID: 21920910.

7. Sohail MR, Henrikson CA, Braid-Forbes MJ, et al. Mortality and cost associated with cardiovascular implantable electronic device infections. Arch Intern Med 2011 Nov 14;171(20):1821-28. PMID: 21911623.

8. 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 Oct 4;124(14):1527-36. PMID: 21900084.

9. Buber J, Klein H, Moss AJ, et al. Clinical course and outcome of patients enrolled in US and non-US centres in MADIT-CRT. Eur Heart J 2011 Nov;32(21):2697-704. PMID: 21642283.

10. Barsheshet A, Goldenberg I, Moss AJ, et al. Effect of elapsed time from coronary revascularization to implantation of a cardioverter defibrillator on long-term survival in the MADIT-II trial. J Cardiovasc Electrophysiol 2011 Nov;22(11):1237-42. PMID: 21615813.

11. 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 Jul;32(14):1720-29. PMID: 21609974.

12. Knappe D, Pouleur AC, Shah AM, et al. Dyssynchrony, contractile function, and response to cardiac resynchronization therapy. Circ Heart Fail 2011 Jul;4(4):433-40. PMID: 21602574.

13. Perrotta L, Pieragnoli P, Ricciardi G, et al. Multicenter experience with implantable defibrillators subject to recall. Pacing Clin Electrophysiol 2011 Aug;34(8):998-1002. PMID: 21438897.

14. Rordorf R, Canevese F, Vicentini A, et al. Delayed ICD lead cardiac perforation: comparison of small versus standard-diameter leads implanted in a single center. Pacing Clin Electrophysiol 2011 Apr;34(4):475-83. PMID: 21208240.

15. Linde C, Mealing S, Hawkins N, et al. Cost-effectiveness of cardiac resynchronization therapy in patients with asymptomatic to mild heart failure: insights from the European cohort of the REVERSE (Resynchronization Reverses remodeling in Systolic Left Ventricular Dysfunction). Eur Heart J 2011 Jul;32(13):1631-39. PMID: 21112898.

16. 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 Jul;32(13):1622-30. PMID: 21075774.

17. Barsheshet A, Moss AJ, Eldar M, et al. Time-dependent benefit of preventive cardiac resynchronization therapy after myocardial infarction. Eur Heart J 2011 Jul;32(13):1614-21. PMID: 21075773.

18. Sauer WH, Lowery CM, Bargas RL, et al. Utility of postoperative testing of implantable cardioverter-defibrillators. Pacing Clin Electrophysiol 2011 Feb;34(2):186-92. PMID: 21039640.

19. 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 Dec;7(12):1777-82. PMID: 20833266.

20. Mohamad T, Jacob S, Kommuri NV, et al. Low referral pattern for implantable defibrillator therapy in a tertiary hospital: referral physician survey and Monte Carlo simulation. Am J Ther 2011 Sep;18(5):350-54. PMID: 20335787.

21. Sumner AD, Boehmer JP, Saxon LA, et al. Statin use is associated with improved survival in patients with advanced heart failure receiving resynchronization therapy. Congest Heart Fail 2009 Jul;15(4):159-64. PMID: 19627288.

22. Saxon LA, Olshansky B, Volosin K, et al. Influence of left ventricular lead location on outcomes in the COMPANION study. J Cardiovasc Electrophysiol 2009 Jul;20(7):764-68. PMID: 19298563.

23. Belardinelli R, Capestro F, Misiani A, et al. Moderate exercise training improves functional capacity, quality of life, and endothelium-dependent vasodilation in chronic heart failure patients with implantable cardioverter defibrillators and cardiac resynchronization therapy. Eur J Cardiovasc Prev Rehabil 2006 Oct;13(5):818-25. PMID: 17001224.

24. Steinbeck G, Andresen D, Senges J, et al. Immediate Risk-Stratification Improves Survival (IRIS): study protocol. Europace 2004 Sep;6(5):392-99. PMID: 15294263.

25. Lampert R, Joska T, Burg MM, et al. Emotional and physical precipitants of ventricular arrhythmia. Circulation 2002 Oct 1;106(14):1800-05. PMID: 12356633.

26. Schulte B, Sperzel J, Carlsson J, et al. Dual-coil vs single-coil active pectoral implantable defibrillator lead systems: defibrillation energy requirements and probability of defibrillation success at multiples of the defibrillation energy requirements. Europace 2001 Jul;3(3):177-80. PMID: 11467457.

27. Whang W, Bigger JT, Jr. Diabetes and outcomes of coronary artery bypass graft surgery in patients with severe left ventricular dysfunction: results from The CABG Patch Trial database. The CABG Patch Trial Investigators and Coordinators. J Am Coll Cardiol 2000 Oct;36(4):1166-72. PMID: 11028466.

28. Bigger JT, Jr., Whang W, Rottman JN, et al. Mechanisms of death in the CABG Patch trial: a randomized trial of implantable cardiac defibrillator prophylaxis in patients at high risk of death after coronary artery bypass graft surgery. Circulation 1999 Mar 23;99(11):1416-21. PMID: 10086963.

29. Masoudi FA, Go AS, Magid DJ, et al. Longitudinal study of implantable cardioverter-defibrillators: methods and clinical characteristics of patients receiving implantable cardioverter-defibrillators for primary prevention in contemporary practice. Circ Cardiovasc Qual Outcomes 2012 Nov;5(6):e78-e85. PMID: 23170006.

30. Veazie PJ, Noyes K, Li Q, et al. Cardiac resynchronization and quality of life in patients with minimally symptomatic heart failure. J Am Coll Cardiol 2012 Nov 6;60(19):1940-44. PMID: 23062542.

31. Bilchick KC, Stukenborg GJ, Kamath S, et al. Prediction of mortality in clinical practice for medicare patients undergoing defibrillator implantation for primary prevention of sudden cardiac death. J Am Coll Cardiol 2012 Oct 23;60(17):1647-55. PMID: 23021331.

32. Flo GL, Glenny RW, Kudenchuk PJ, et al. Development and safety of an exercise testing protocol for patients with an implanted cardioverter defibrillator for primary or secondary indication. Cardiopulm Phys Ther J 2012 Sep;23(3):16-22. PMID: 22993498.

33. 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 Jun 19;59(25):2366-73. PMID: 22698490.

34. Barsheshet A, Moss AJ, Huang DT, et al. Applicability of a risk score for prediction of the long-term (8-year) benefit of the implantable cardioverter-defibrillator. J Am Coll Cardiol 2012 Jun 5;59(23):2075-79. PMID: 22651863.

35. Leenhardt A, Defaye P, Mouton E, et al. First inappropriate implantable cardioverter defibrillator therapy is often due to inaccurate device programming: analysis of the French OPERA registry. Europace 2012 Oct;14(10):1465-74. PMID: 22547767.

36. Martins RP, Blangy H, Muresan L, et al. Safety and efficacy of programming a

high number of antitachycardia pacing attempts for fast ventricular tachycardia: a prospective study. Europace 2012 Oct;14(10):1457-64. PMID: 22547765.

37. 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 Sep;9(9):1454-59. PMID: 22521920.

38. Ji SY, Gundewar S, Palma EC. Subclavian venoplasty may reduce implant times and implant failures in the era of increasing device upgrades. Pacing Clin Electrophysiol 2012 Apr;35(4):444-48. PMID: 22229641.

39. Sullivan RM, Russo AM, Berg KC, et al. Arrhythmia rate distribution and tachyarrhythmia therapy in an ICD population: results from the INTRINSIC RV trial. Heart Rhythm 2012 Mar;9(3):351-58. PMID: 22016074.

40. Kramer DB, Friedman PA, Kallinen LM, et al. Development and validation of a risk score to predict early mortality in recipients of implantable cardioverter-defibrillators. Heart Rhythm 2012 Jan;9(1):42-46. PMID: 21893137.

41. Fischer A, Ousdigian KT, Johnson JW, et al. The impact of atrial fibrillation with rapid ventricular rates and device programming on shocks in 106,513 ICD and CRT-D patients. Heart Rhythm 2012 Jan;9(1):24-31. PMID: 21835150.

42. Atary JZ, Borleffs CJ, van der Bom JG, et al. Right ventricular stimulation threshold at ICD implant predicts device therapy in primary prevention patients with ischaemic heart disease. Europace 2010 Nov;12(11):1581-88. PMID: 20639206.

43. Borleffs CJ, van Rees JB, van Welsenes GH, et al. Prognostic importance of atrial fibrillation in implantable cardioverter-defibrillator patients. J Am Coll Cardiol 2010 Mar 2;55(9):879-85. PMID: 20185038.

Not Comparison of Interest (n=6)

1. Gilliam FR, Hayes DL, Boehmer JP, et al. Real world evaluation of dual-zone ICD and CRT-D programming compared to single-zone programming: the ALTITUDE REDUCES study. J Cardiovasc Electrophysiol 2011 Sep;22(9):1023-29. PMID: 21627705.
Comparison: programming

2. Hauser RG, Maisel WH, Friedman PA, et al. Longevity of Sprint Fidelis implantable cardioverter-defibrillator leads and risk factors for failure: implications for patient management. Circulation 2011 Feb 1;123(4):358-63. PMID: 21242478.
Comparison: lead 1 vs. lead 2

3. Russo AM, Hafley GE, Lee KL, et al. Racial differences in outcome in the Multicenter UnSustained Tachycardia Trial (MUSTT): a comparison of whites versus blacks. Circulation 2003 Jul 8;108(1):67-72. PMID: 12821551.
Outcome not based on ICD vs. no ICD

4. Wilkoff BL, Cook JR, Epstein AE, et al. Dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator: the Dual Chamber and VVI Implantable Defibrillator (DAVID) Trial. JAMA 2002 Dec 25;288(24):3115-23. PMID: 12495391.
Comparison: programming

5. Kohn CS, Petrucci RJ, Baessler C, et al. The effect of psychological intervention on patients' long-term adjustment to the ICD: a prospective study. Pacing Clin Electrophysiol 2000 Apr;23(4 Pt 1):450-56. PMID: 10793433.
Comparison: Psych. therapy vs. control

6. Giorgberidze I, Saksena S, Krol RB, et al. Risk stratification and clinical outcome of minimally symptomatic and

asymptomatic patients with nonsustained ventricular tachycardia and coronary disease: a prospective single-center study. Am J Cardiol 1997 Sep 11;80(5B):3F-9F. PMID: 9291444.
Comparison: ICD or drug 1 vs. drug 2

Not Intervention of Interest (n=3)

1. Rodriguez Y, Garisto JD, Carrillo RG. Laser lead extraction in the octogenarian patient. Circ Arrhythm Electrophysiol 2011 Oct;4(5):719-23. PMID: 22007037.
Lead extraction

2. Mela T, McGovern BA, Garan H, et al. Long-term infection rates associated with the pectoral versus abdominal approach to cardioverter- defibrillator implants. Am J Cardiol 2001 Oct 1;88(7):750-53. PMID: 11589841.
Abdominal implants

3. Buxton AE, Lee KL, Fisher JD, et al. A randomized study of the prevention of sudden death in patients with coronary artery disease. Multicenter Unsustained Tachycardia Trial Investigators. N Engl J Med 1999 Dec 16;341(25):1882-90. PMID: 10601507.
Not an ICD trial

Outcome Numerator or Denominator Unclear (n=8)

1. Duggirala HJ, Herz ND, Canos DA, et al. Disproportionality analysis for signal detection of implantable cardioverter-defibrillator-related adverse events in the Food and Drug Administration Medical Device Reporting System. Pharmacoepidemiol Drug Saf 2012 Jan;21(1):87-93. PMID: 22095760.

2. Smith T, van Dessel PF, Theuns DA, et al. Health care utilisation after defibrillator implantation for primary prevention according to the guidelines in 2 Dutch academic medical centres. Neth Heart J 2011 Oct;19(10):405-11. PMID: 21773744.

3. Rodriguez Y, Baltodano P, Tower A, et al. Management of symptomatic inadvertently placed endocardial leads in the left ventricle. Pacing Clin Electrophysiol 2011 Oct;34(10):1192-200. PMID: 21671951.

4. van G, I, Phan HM, Wilkoff BL, et al. Prognostic significance of atrial arrhythmias in a primary prevention ICD population. Pacing Clin Electrophysiol 2011 Sep;34(9):1070-79. PMID: 21605131.

5. Smit J, Korup E, Schonheyder HC. Infections associated with permanent pacemakers and implanted cardioverter-defibrillator devices. A 10-year regional study in Denmark. Scand J Infect Dis 2010 Sep;42(9):658-64. PMID: 20465488.

6. Santini M, Lunati M, Defaye P, et al. Prospective multicenter randomized trial of fast ventricular tachycardia termination by prolonged versus conventional anti-tachyarrhythmia burst pacing in implantable cardioverter-defibrillator patients-Atp DeliVery for pAiNless ICD thErapy (ADVANCE-D) Trial results. J Interv Card Electrophysiol 2010 Mar;27(2):127-35. PMID: 20087760.

7. Wilkoff BL, Williamson BD, Stern RS, et al. Strategic programming of detection and therapy parameters in implantable cardioverter-defibrillators reduces shocks in primary prevention patients: results from the PREPARE (Primary Prevention Parameters Evaluation) study. J Am Coll Cardiol 2008 Aug 12;52(7):541-50. PMID: 18687248.

8. Wilkoff BL, Ousdigian KT, Sterns LD, et al. A comparison of empiric to physician-

tailored programming of implantable cardioverter-defibrillators: results from the prospective randomized multicenter EMPIRIC trial. J Am Coll Cardiol 2006 Jul 18;48(2):330-39. PMID: 16843184.

Protocol (n=6)

1. Pedersen SS, Lambiase P, Boersma LV, et al. Evaluation oF FactORs ImpacTing CLinical Outcome and Cost EffectiveneSS of the S-ICD: design and rationale of the EFFORTLESS S-ICD Registry. Pacing Clin Electrophysiol 2012 May;35(5):574-79. PMID: 22360677.

2. Pedersen SS, Spek V, Theuns DA, et al. Rationale and design of WEBCARE: a randomized, controlled, web-based behavioral intervention trial in cardioverter-defibrillator patients to reduce anxiety and device concerns and enhance quality of life. Trials 2009;10:120. PMID: 20030843.

3. Moss AJ, Brown MW, Cannom DS, et al. Multicenter automatic defibrillator implantation trial-cardiac resynchronization therapy (MADIT-CRT): design and clinical protocol. Ann Noninvasive Electrocardiol 2005 Oct;10(4 Suppl):34-43. PMID: 16274414.

4. Moss AJ et al. Multicenter automatic defibrillator implantation trial II (MADIT II): design and clinical protocol. Ann Noninvasive Electrocardiol. 2012

5. Kadish A, Quigg R, Schaechter A, et al. Defibrillators in nonischemic cardiomyopathy treatment evaluation. Pacing Clin Electrophysiol 2000 Mar;23(3):338-43. PMID: 10750134.

6. Schuger C, Daubert JP, Brown MW, et al. Multicenter automatic defibrillator implantation trial: reduce inappropriate therapy (MADIT-RIT): background, rationale, and clinical protocol. Ann Noninvasive Electrocardiol 2012 Jul;17(3):176-85. PMID: 22816536

Review/Editorial (n=4)

1. Atwater BD, Daubert JP. Implantable cardioverter defibrillators: risks accompany the life-saving benefits. Heart 2012 May;98(10):764-72. PMID: 22422588.

2. Gasparini M, Nisam S. Implantable cardioverter defibrillator harm? Europace 2012 Aug;14(8):1087-93. PMID: 22389417.

3. Kelly D, Mariathas M, Gough R, et al. Is a new high-voltage lead necessary? 6.6-French ICD lead failure: a UK tertiary center experience. Pacing Clin Electrophysiol 2012 Jan;35(1):1-2. PMID: 22077138.

4. Salukhe TV, Francis DP, Sutton R. Comparison of medical therapy, pacing and defibrillation in heart failure (COMPANION) trial terminated early; combined biventricular pacemaker-defibrillators reduce all-cause mortality and hospitalization. Int J Cardiol 2003 Feb;87(2-3):119-20. PMID: 12559527.

Secondary Prevention (n=31)

1. Ye S, Grunnert M, Thune JJ, et al. Circumstances and outcomes of sudden unexpected death in patients with high-risk myocardial infarction: implications

for prevention. Circulation 2011 Jun 14;123(23):2674-80. PMID: 21606398.

2. Redhead AP, Turkington D, Rao S, et al. Psychopathology in postinfarction patients implanted with cardioverter-defibrillators for secondary prevention. A cross-sectional, case-controlled study. J Psychosom Res 2010 Dec;69(6):555-63. PMID: 21109043.

3. Hallas CN, Burke JL, White DG, et al. A prospective 1-year study of changes in neuropsychological functioning after implantable cardioverter-defibrillator surgery. Circ Arrhythm Electrophysiol 2010 Apr;3(2):170-77. PMID: 20197542.

4. MacFadden DR, Tu JV, Chong A, et al. Evaluating sex differences in population-based utilization of implantable cardioverter-defibrillators: role of cardiac conditions and noncardiac comorbidities. Heart Rhythm 2009 Sep;6(9):1289-96. PMID: 19695966.

5. Bagherzadeh A, Emkanjoo Z, Haghjoo M, et al. Complications and mortality of single versus dual chamber implantable cardioverter defibrillators. Indian Pacing Electrophysiol J 2006;6(2):75-83. PMID: 16943899.

6. Kron J. Clinical significance of device-related complications in clinical trials and implications for future trials: insights from the Antiarrhytmics Versus Implantable Defibrillators (AVID) trial. Card Electrophysiol Rev 2003 Dec;7(4):473-78. PMID: 15071278.

7. Kamphuis HC, de L, Jr., Derksen R, et al. Implantable cardioverter defibrillator recipients: quality of life in recipients with and without ICD shock delivery: a prospective study. Europace 2003 Oct;5(4):381-89. PMID: 14753636.

8. Young JB, Abraham WT, Smith AL, et al. Combined cardiac resynchronization and implantable cardioversion defibrillation in advanced chronic heart failure: the MIRACLE ICD Trial. JAMA 2003 May 28;289(20):2685-94. PMID: 12771115.

9. Fries R, Konig J, Schafers HJ, et al. Triggering effect of physical and mental stress on spontaneous ventricular tachyarrhythmias in patients with implantable cardioverter-defibrillators. Clin Cardiol 2002 Oct;25(10):474-78. PMID: 12375806.

10. Hsu J, Uratsu C, Truman A, et al. Life after a ventricular arrhythmia. Am Heart J 2002 Sep;144(3):404-12. PMID: 12228776.

11. Takahashi T, Bhandari AK, Watanuki M, et al. High incidence of device-related and lead-related complications in the dual-chamber implantable cardioverter defibrillator compared with the single-chamber version. Circ J 2002 Aug;66(8):746-50. PMID: 12197599.

12. Pires LA, Sethuraman B, Guduguntla VD, et al. Outcome of women versus men with ventricular tachyarrhythmias treated with the implantable cardioverter defibrillator. J Cardiovasc Electrophysiol 2002 Jun;13(6):563-68. PMID: 12108497.

13. Cook JR, Rizo-Patron C, Curtis AB, et al. Effect of surgical revascularization in patients with coronary artery disease and ventricular tachycardia or fibrillation in the Antiarrhythmics Versus Implantable Defibrillators (AVID) Registry. Am Heart J 2002 May;143(5):821-26. PMID: 12040343.

14. Della BP. [Canadian Implantable Defibrillator Study (CIDS): a randomized trial of the implantable cardioverter defibrillator against amiodarone]. Ital Heart J Suppl 2000 Aug;1(8):1070-71. PMID: 10993020.

15. Connolly SJ, Gent M, Roberts RS, et al. Canadian implantable defibrillator study (CIDS) : a randomized trial of the implantable cardioverter defibrillator against amiodarone. Circulation 2000 Mar 21;101(11):1297-302. PMID: 10725290.

16. Dunbar SB, Kimble LP, Jenkins LS, et al. Association of mood disturbance and

arrhythmia events in patients after cardioverter defibrillator implantation. Depress Anxiety 1999;9(4):163-68. PMID: 10431681.

17. Trappe HJ, Achtelik M, Pfitzner P, et al. Single-chamber versus dual-chamber implantable cardioverter defibrillators: indications and clinical results. Am J Cardiol 1999 Mar 11;83(5B):8D-16D. PMID: 10089834.

18. Heller SS, Ormont MA, Lidagoster L, et al. Psychosocial outcome after ICD implantation: a current perspective. Pacing Clin Electrophysiol 1998 Jun;21(6):1207-15. PMID: 9633062.

19. Bourke JP, Turkington D, Thomas G, et al. Florid psychopathology in patients receiving shocks from implanted cardioverter-defibrillators. Heart 1997 Dec;78(6):581-83. PMID: 9470875.

20. Schuster PM, Phillips S, Dillon DL, et al. The psychosocial and physiological experiences of patients with an implantable cardioverter defibrillator. Rehabil Nurs 1998 Jan;23(1):30-37. PMID: 9460456.

21. Domanski MJ, Saksena S, Wyse G, et al. Clinical and socioeconomic profile of patients with malignant ventricular arrhythmias in 1993 to 1995. AVID investigators. Antiarrhythmics Versus Implantable Defibrillator. Am J Cardiol 1997 Aug 1;80(3):299-301. PMID: 9264422.

22. Hegel MT, Griegel LE, Black C, et al. Anxiety and depression in patients receiving implanted cardioverter-defibrillators: a longitudinal investigation. Int J Psychiatry Med 1997;27(1):57-69. PMID: 9565714.

23. Haffajee C, Martin D, Bhandari A, et al. A multicenter, randomized trial comparing an active can implantable defibrillator with a passive can system. Jewel Active Can Investigators. Pacing Clin Electrophysiol 1997 Jan;20(1 Pt 2):215-19. PMID: 9121993.

24. Ector H, Jordaens L, Vanhaecke J. Survival analysis and clinical medicine. An observational comparison of the implantable cardioverter defibrillator, amiodarone treatment, and heart transplantation. Eur Heart J 1996 Sep;17(9):1444-47. PMID: 8880032.

25. Fleurant E, Lacroix D, Klug D, et al. [Automatic implantable defibrillator and antiarrhythmic surgery in ischemic cardiopathies. Apropos of 53 cases]. Arch Mal Coeur Vaiss 1995 Nov;88(11):1627-34. PMID: 8745998.

26. Arteaga WJ, Windle JR. The quality of life of patients with life-threatening arrhythmias. Arch Intern Med 1995 Oct 23;155(19):2086-91. PMID: 7575068.

27. Clinical outcome of patients with malignant ventricular tachyarrhythmias and a multiprogrammable implantable cardioverter-defibrillator implanted with or without thoracotomy: an international multicenter study. PCD Investigator Group. J Am Coll Cardiol 1994 Jun;23(7):1521-30. PMID: 8195508.

28. Trappe HJ, Klein H, Wenzlaff P, et al. Role of interventional therapy in patients with coronary heart disease and life-threatening ventricular tachyarrhythmias. Eur Heart J 1993 Sep;14 Suppl E:120-27. PMID: 8223748.

29. Gross JN, Sackstein RD, Song SL, et al. The antitachycardia pacing ICD: impact on patient selection and outcome. Pacing Clin Electrophysiol 1993 Jan;16(1 Pt 2):165-69. PMID: 7681565.

30. Pinski SL, Mick MJ, Arnold AZ, et al. Retrospective analysis of patients undergoing one- or two-stage strategies for myocardial revascularization and implantable cardioverter defibrillator implantation. Pacing Clin Electrophysiol 1991 Jul;14(7):1138-47. PMID: 1715551.

31. Thomas AC, Moser SA, Smutka ML, et al. Implantable defibrillation: eight years clinical experience. Pacing Clin Electrophysiol 1988 Nov;11(11 Pt 2):2053-58. PMID: 2463587.

Not Study Design of Interest (n=66)

1. Hickman RL, Jr., Pinto MD, Lee E, et al. Exploratory and confirmatory factor analysis of the decision regret scale in recipients of internal cardioverter defibrillators. J Nurs Meas 2012;20(1):21-34. PMID: 22679707. *Reason for Exclusion: cross-sectional*

2. van Rees JB, Borleffs CJ, van Welsenes GH, et al. Clinical prediction model for death prior to appropriate therapy in primary prevention implantable cardioverter defibrillator patients with ischaemic heart disease: the FADES risk score. Heart 2012 Jun;98(11):872-77. PMID: 22581736. *Reason for Exclusion: Cohort study, no adverse events or N<500*

3. Carroll SL, Markle-Reid M, Ciliska D, et al. Age and mental health predict early device-specific quality of life in patients receiving prophylactic implantable defibrillators. Can J Cardiol 2012 Jul;28(4):502-07. PMID: 22425267. *Reason for Exclusion: Cohort study, no adverse events or N<500*

4. Bruggenjurgen B, Israel CW, Klesius AA, et al. Health services research in heart failure patients treated with a remote monitoring device in Germany-a retrospective database analysis in evaluating resource use. J Med Econ 2012;15(4):737-45. PMID: 22409232. *Reason for Exclusion: Cohort study, no adverse events or N<500*

5. Ziegler PD, Koehler JL, Verma A. Continuous versus intermittent monitoring of ventricular rate in patients with permanent atrial fibrillation. Pacing Clin Electrophysiol 2012 May;35(5):598-604. PMID: 22394432. *Reason for Exclusion: Cohort study, no adverse events or N<500*

6. James CA, Tichnell C, Murray B, et al. General and disease-specific psychosocial adjustment in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy with implantable cardioverter defibrillators: a large cohort study. Circ Cardiovasc Genet 2012 Feb 1;5(1):18-24. PMID: 22238189. *Reason for Exclusion: Cohort study, no adverse events or N<500*

7. Epstein AJ, Polsky D, Yang F, et al. Geographic variation in implantable cardioverter-defibrillator use and heart failure survival. Med Care 2012 Jan;50(1):10-17. PMID: 22167063. *Reason for Exclusion: Cohort study, no adverse events or N<500*

8. Scott PA, Whittaker A, Zeb M, et al. Rates of upgrade of ICD recipients to CRT in clinical practice and the potential impact of the more liberal use of CRT at initial implant. Pacing Clin Electrophysiol 2012 Jan;35(1):73-80. PMID: 22054072. *Reason for Exclusion: Cohort study, no adverse events or N<500*

9. Cesarino CB, Beccaria LM, Aroni MM, et al. Quality of life of patients with implantable cardioverser-defibrillator: the usage of SF-36 questionnaire. Rev Bras Cir Cardiovasc 2011 Apr;26(2):238-43. PMID: 21894414. *Reason for Exclusion: Cohort study, no adverse events or N<500*

10. Kramer DB, Friedman PA, Kallinen LM, et al. Development and validation of a risk score to predict early mortality in recipients of implantable cardioverter-defibrillators. Heart Rhythm 2012 Jan;9(1):42-46. PMID: 21893137. *Reason for Exclusion: Cohort study, no adverse events or N<500*

11. Sack S, Wende CM, Nagele H, et al. Potential value of automated daily screening of cardiac resynchronization therapy defibrillator diagnostics for prediction of major cardiovascular events: results from Home-CARE (Home Monitoring in Cardiac Resynchronization Therapy) study. Eur J Heart Fail 2011 Sep;13(9):1019-27. PMID: 21852311. *Reason for Exclusion: Cohort study, no adverse events or N<500*

12. Fischer A, Ousdigian KT, Johnson JW, et al. The impact of atrial fibrillation with rapid ventricular rates and device programming on shocks in 106,513 ICD and CRT-D patients. Heart Rhythm 2012 Jan;9(1):24-31. PMID: 21835150. *Reason for Exclusion: Cohort study, no adverse events or N<500*

13. Lazarus A, Biondi N, Thebaut JF, et al. Implantable cardioverter-defibrillators in France: practices and regional variability. Europace 2011 Nov;13(11):1568-73. PMID: 21784742. *Reason for Exclusion: cross-sectional*

14. Tavenaux M, Ginzburg DM, Boukacem A, et al. [Changes in depression, anxiety, and vital exhaustion in patients after ICD implantation. Comparison of clinical subgroups]. Herzschrittmacherther Elektrophysiol 2011 Sep;22(3):174-79. PMID: 21773789. *Reason for Exclusion: Cohort study, no adverse events or N<500*

15. Pedersen SS, Versteeg H, Nielsen JC, et al. Patient-reported outcomes in Danish implantable cardioverter defibrillator patients with a Sprint Fidelis lead advisory notification. Europace 2011 Sep;13(9):1292-98. PMID: 21616945. *Reason for Exclusion: cross-sectional*

16. Flemme I, Hallberg U, Johansson I, et al. Uncertainty is a major concern for patients with implantable cardioverter defibrillators. Heart Lung 2011 Sep;40(5):420-28. PMID: 21459446. *Reason for Exclusion: Cohort study, no adverse events or N<500*

17. Probst V, Plassard-Kerdoncuf D, Mansourati J, et al. The psychological impact of implantable cardioverter defibrillator implantation on Brugada syndrome patients. Europace 2011 Jul;13(7):1034-39. PMID: 21427091. *Reason for Exclusion: Cohort study, no adverse events or N<500*

18. Mellert F, Schneider C, Esmailzadeh B, et al. Implantation of left ventricular epicardial leads in cardiosurgical patients with impaired cardiac function--a worthwhile procedure in concomitant surgical interventions? Thorac Cardiovasc Surg 2012 Feb;60(1):64-69. PMID: 21425053. *Reason for Exclusion: Cohort study, no adverse events or N<500*

19. Alla VM, Anand K, Hundal M, et al. Impact of moderate to severe renal impairment on mortality and appropriate shocks in patients with implantable cardioverter defibrillators. Cardiol Res Pract 2010;2010:150285. PMID: 21197424. *Reason for Exclusion: Cohort study, no adverse events or N<500*

20. Cross NJ, McCrae CS, Smith KM, et al. Comparison of actigraphic and subjective measures of sleep in implantable cardioverter defibrillator and coronary artery disease patients. Clin Cardiol 2010 Dec;33(12):753-59. PMID: 21184559. *Reason for Exclusion: Cohort study, no adverse events or N<500*

21. Arnous S, Murphy NF, Pyne-Daly P, et al. Clinical and psychological impact of prophylactic implantable cardioverter-defibrillators in a community heart failure population. Ir J Med Sci 2011 Jun;180(2):369-74. PMID: 21153928. *Reason for Exclusion: Cohort study, no adverse events or N<500*

22. Leistner DM, Schmitt J, Palm S, et al. Intracoronary administration of bone marrow-derived mononuclear cells and arrhythmic events in patients with chronic heart failure. Eur Heart J 2011 Feb;32(4):485-91. PMID: 21138937. *Reason for Exclusion: Cohort study, no adverse events or N<500*

23. Bilchick KC, Kamath S, DiMarco JP, et al. Bundle-branch block morphology and other predictors of outcome after cardiac resynchronization therapy in Medicare patients. Circulation 2010 Nov 16;122(20):2022-30. PMID: 21041691. *Reason for Exclusion: Cohort study, no adverse events or N<500*

24. Hager CS, Jain S, Blackwell J, et al. Effect of renal function on survival after implantable cardioverter defibrillator placement. Am J Cardiol 2010 Nov 1;106(9):1297-300. PMID: 21029827. *Reason for Exclusion: Cohort study, no adverse events or N<500*

25. Versteeg H, Baumert J, Kolb C, et al. Somatosensory amplification mediates sex differences in psychological distress among cardioverter-defibrillator patients. Health Psychol 2010 Sep;29(5):477-83. PMID: 20836602. *Reason for Exclusion: cross-sectional*

26. Chen TB, Cheng KA, Gao P, et al. Primary prevention of sudden cardiac death by implantable cardioverter-defibrillator therapy in Chinese patients with heart failure: a single-center experience. Chin Med J (Engl) 2010 Apr 5;123(7):848-51. PMID: 20497676. *Reason for Exclusion: Cohort study, no adverse events or N<500*

27. Marijon E, Trinquart L, Otmani A, et al. Predictors for short-term progressive heart failure death in New York Heart Association II patients implanted with a cardioverter defibrillator--the EVADEF study. Am Heart J 2010 Apr;159(4):659-64. PMID: 20362726. *Reason for Exclusion: Cohort study, no adverse events or N<500*

28. Salukhe TV, Briceno NI, Ferenczi EA, et al. Is there benefit in implanting defibrillators in patients with severe heart failure? Heart 2010 Apr;96(8):599-603. PMID: 20357388. *Reason for Exclusion: Cohort study, no adverse events or N<500*

29. Desai H, Aronow WS, Ahn C, et al. Incidence of appropriate cardioverter-defibrillator shocks and mortality in patients with heart failure treated with combined cardiac resynchronization plus implantable cardioverter-defibrillator therapy versus implantable cardioverter-defibrillator therapy. J Cardiovasc Pharmacol Ther 2010 Mar;15(1):37-40. PMID: 19966176. *Reason for Exclusion: Cohort study, no adverse events or N<500*

30. Borleffs CJ, van Welsenes GH, van Bommel RJ, et al. Mortality risk score in primary prevention implantable cardioverter defibrillator recipients with non-ischaemic or ischaemic heart disease. Eur Heart J 2010 Mar;31(6):712-18. PMID: 19933693. *Reason for Exclusion: Cohort study, no adverse events or N<500*

31. Kim JS, Pressler SJ, Welch JL, et al. Physical function of patients with implantable cardioverter-defibrillators. J Cardiovasc Nurs 2009 Sep;24(5):398-409. PMID: 19707100. *Reason for Exclusion: Cohort study, no adverse events or N<500*

32. Otmani A, Trinquart L, Marijon E, et al. Rates and predictors of appropriate implantable cardioverter-defibrillator therapy delivery: results from the EVADEF cohort study. Am Heart J 2009 Aug;158(2):230-37. PMID: 19619699. *Reason for Exclusion: Cohort study, no adverse events or N<500*

33. Srivatsa UN, Hoppe BL, Narayan S, et al. Ventricular arrhythmia discriminator programming and the impact on the incidence of inappropriate therapy in patients with implantable cardiac defibrillators. Indian Pacing Electrophysiol J 2007;7(2):77-84. PMID:

17538699. *Reason for Exclusion: Cohort study, no adverse events or N<500*

34. Baumert J, Schmitt C, Ladwig KH. Psychophysiologic and affective parameters associated with pain intensity of cardiac cardioverter defibrillator shock discharges. Psychosom Med 2006 Jul;68(4):591-97. PMID: 16868269. *Reason for Exclusion: cross-sectional*

35. Klein T, Schonecke O, Wollny H, et al. [Clinical significance of stress reactivity for frequency of electric shock discharges in patients with implanted cardioverter-defibrillators]. Dtsch Med Wochenschr 2004 Oct 22;129(43):2291-94. PMID: 15483767. *Reason for Exclusion: Cohort study, no adverse events or N<500*

36. Godemann F, Butter C, Lampe F, et al. Panic disorders and agoraphobia: side effects of treatment with an implantable cardioverter/defibrillator. Clin Cardiol 2004 Jun;27(6):321-26. PMID: 15237689. *Reason for Exclusion: Cohort study, no adverse events or N<500*

37. Ricci R, Quesada A, Pignalberi C, et al. Dual defibrillator improves quality of life and decreases hospitalizations in patients with drug refractory atrial fibrillation. J Interv Card Electrophysiol 2004 Feb;10(1):85-92. PMID: 14739755. *Reason for Exclusion: Cohort study, no adverse events or N<500*

38. Hamilton GA, Carroll DL. The effects of age on quality of life in implantable cardioverter defibrillator recipients. J Clin Nurs 2004 Feb;13(2):194-200. PMID: 14723671. *Reason for Exclusion: Cohort study, no adverse events or N<500*

39. Carroll DL, Hamilton GA, Kenney BJ. Changes in health status, psychological distress, and quality of life in implantable cardioverter defibrillator recipients between 6 months and 1 year after implantation. Eur J Cardiovasc Nurs 2002 Oct;1(3):213-19. PMID: 14622676. *Reason for Exclusion: Cohort study, no adverse events or N<500*

40. Bolse K, Flemme I, Ivarsson A, et al. Life situation related to the ICD implantation; self-reported uncertainty and satisfaction in Swedish and US samples. Eur J Cardiovasc Nurs 2002 Dec;1(4):243-51. PMID: 14622654. *Reason for Exclusion: Cohort study, no adverse events or N<500*

41. Pelletier D, Gallagher R, Mitten-Lewis S, et al. Australian implantable cardiac defibrillator recipients: quality-of-life issues. Int J Nurs Pract 2002 Apr;8(2):68-74. PMID: 11993579. *Reason for Exclusion: Cohort study, no adverse events or N<500*

42. Flemme I, Bolse K, Ivarsson A, et al. Life situation of patients with an implantable cardioverter defibrillator: a descriptive longitudinal study. J Clin Nurs 2001 Jul;10(4):563-72. PMID: 11822504. *Reason for Exclusion: Cohort study, no adverse events or N<500*

43. Wathen MS, Sweeney MO, DeGroot PJ, et al. Shock reduction using antitachycardia pacing for spontaneous rapid ventricular tachycardia in patients with coronary artery disease. Circulation 2001 Aug 14;104(7):796-801. PMID: 11502705. *Reason for Exclusion: Cohort study, no adverse events or N<500*

44. Ahmad M, Bloomstein L, Roelke M, et al. Patients' attitudes toward implanted defibrillator shocks. Pacing Clin Electrophysiol 2000 Jun;23(6):934-38. PMID: 10879375. *Reason for Exclusion: Cohort study, no adverse events or N<500*

45. Pelletier D, Mitten-Lewis S, Gallagher RD, et al. Implantable defibrillator recipients' responses to device implantation and design. Biomed Instrum Technol 1999 May;33(3):224-29. PMID: 10360211. *Reason for*

Exclusion: Cohort study, no adverse events or N<500

46. Pauli P, Wiedemann G, Dengler W, et al. Anxiety in patients with an automatic implantable cardioverter defibrillator: what differentiates them from panic patients? Psychosom Med 1999 Jan;61(1):69-76. PMID: 10024069. *Reason for Exclusion: Cohort study, no adverse events or N<500*

47. Grubman EM, Pavri BB, Shipman T, et al. Cardiac death and stored electrograms in patients with third-generation implantable cardioverter-defibrillators. J Am Coll Cardiol 1998 Oct;32(4):1056-62. PMID: 9768732. *Reason for Exclusion: Cohort study, no adverse events or N<500*

48. Crow SJ, Collins J, Justic M, et al. Psychopathology following cardioverter defibrillator implantation. Psychosomatics 1998 Jul;39(4):305-10. PMID: 9691699. *Reason for Exclusion: Cohort study, no adverse events or N<500*

49. Craney JM, Mandle CL, Munro BH, et al. Implantable cardioverter defibrillators: physical and psychosocial outcomes. Am J Crit Care 1997 Nov;6(6):445-51. PMID: 9354222. *Reason for Exclusion: Cohort study, no adverse events or N<500*

50. Jessurun ER, Hutten BA, van Hemel NM, et al. [Good experiences with an implantable automatic defibrillator with transvenous electrodes for patients with life-threatening arrhythmias]. Ned Tijdschr Geneeskd 1997 Jul 26;141(30):1475-80. PMID: 9542881. *Reason for Exclusion: Cohort study, no adverse events or N<500*

51. Herrmann C, von zur MF, Schaumann A, et al. Standardized assessment of psychological well-being and quality-of-life in patients with implanted defibrillators. Pacing Clin Electrophysiol 1997 Jan;20(1 Pt 1):95-103. PMID: 9121977. *Reason for Exclusion: Cohort study, no adverse events or N<500*

52. Li H, Axtell K, Biehl M, et al. Sudden death in patients with implantable cardioverter-defibrillators. Am Heart J 1996 Nov;132(5):986-88. PMID: 8892772. *Reason for Exclusion: Cohort study, no adverse events or N<500*

53. Jung W, Luderitz B. Quality of life and driving in recipients of the implantable cardioverter-defibrillator. Am J Cardiol 1996 Sep 12;78(5A):51-56. PMID: 8820836. *Reason for Exclusion: Cohort study, no adverse events or N<500*

54. Daoud EG, Strickberger SA, Man KC, et al. Comparison of early and late complications in patients undergoing coronary artery bypass graft surgery with and without concomitant placement of an implantable cardioverter defibrillator. Am Heart J 1995 Oct;130(4):780-85. PMID: 7572586. *Reason for Exclusion: Cohort study, no adverse events or N<500*

55. Vitale MB, Funk M. Quality of life in younger persons with an implantable cardioverter defibrillator. Dimens Crit Care Nurs 1995 Mar;14(2):100-11. PMID: 7889798. *Reason for Exclusion: Cohort study, no adverse events or N<500*

56. Bainger EM, Fernsler JI. Perceived quality of life before and after implantation of an internal cardioverter defibrillator. Am J Crit Care 1995 Jan;4(1):36-43. PMID: 7894553. *Reason for Exclusion: Cohort study, no adverse events or N<500*

57. Luderitz B, Jung W, Deister A, et al. [The quality of life after the implantation of a cardioverter/defibrillator in malignant arrhythmias]. Dtsch Med Wochenschr 1993 Mar 5;118(9):285-89. PMID: 8444109. *Reason for Exclusion: Cohort study, no adverse events or N<500*

58. Nisam S, Mower MM, Thomas A, et al. Patient survival comparison in three generations of automatic implantable cardioverter defibrillators: review of 12 years, 25,000 patients. Pacing Clin

Electrophysiol 1993 Jan;16(1 Pt 2):174-78. PMID: 7681567. *Reason for Exclusion: Cohort study, no adverse events or N<500*

59. Pycha C, Calabrese JR, Gulledge AD, et al. Patient and spouse acceptance and adaptation to implantable cardioverter defibrillators. Cleve Clin J Med 1990 Jul;57(5):441-44. PMID: 2372924. *Reason for Exclusion: Cohort study, no adverse events or N<500*

60. Boriani G, Botto G, Lunati M, et al. Influence of time between last myocardial infarction and prophylactic implantable defibrillator implant on device detections and therapies. "Routine Practice" data from the SEARCH MI registry. BMC Cardiovasc Disord 2012;12:72. PMID: 22966862. *Reason for Exclusion: Cohort study, no adverse events or N<500*

61. Kreuz J, Horlbeck F, Schrickel J, et al. Kidney dysfunction and deterioration of ejection fraction pose independent risk factors for mortality in implantable cardioverter-defibrillator recipients for primary prevention. Clin Cardiol 2012 Sep;35(9):575-79. PMID: 22707222. *Reason for Exclusion: Cohort study, no adverse events or N<500*

62. Parkash R, Sapp JL, Basta M, et al. Use of primary prevention implantable cardioverter-defibrillators in a population-based cohort is associated with a significant survival benefit. Circ Arrhythm Electrophysiol 2012 Aug 1;5(4):706-13. PMID: 22685111. *Reason for Exclusion: historic (not concurrent) control group*

63. van Rees JB, Borleffs CJ, van Welsenes GH, et al. Clinical prediction model for death prior to appropriate therapy in primary prevention implantable cardioverter defibrillator patients with ischaemic heart disease: the FADES risk score. Heart 2012 Jun;98(11):872-77. PMID: 22581736. *Reason for Exclusion: Cohort study, no adverse events or N<500*

64. Thijssen J, van Rees JB, Venlet J, et al. The mode of death in implantable cardioverter-defibrillator and cardiac resynchronization therapy with defibrillator patients: results from routine clinical practice. Heart Rhythm 2012 Oct;9(10):1605-12. PMID: 22522066. *Reason for Exclusion: Cohort study, no adverse events or N<500*

65. Carroll SL, Markle-Reid M, Ciliska D, et al. Age and mental health predict early device-specific quality of life in patients receiving prophylactic implantable defibrillators. Can J Cardiol 2012 Jul;28(4):502-07. PMID: 22425267. *Reason for Exclusion: Cohort study, no adverse events or N<500*

66. Biasucci LM, Bellocci F, Landolina M, et al. Risk stratification of ischaemic patients with implantable cardioverter defibrillators by C-reactive protein and a multi-markers strategy: results of the CAMI-GUIDE study. Eur Heart J 2012 Jun;33(11):1344-50. PMID: 22285581. *Reason for Exclusion: Cohort study, no adverse events or N<500*

Wrong Population (n=37)

1. Viola GM, Awan LL, Ostrosky-Zeichner L, et al. Infections of cardiac implantable electronic devices: a retrospective multicenter observational study. Medicine (Baltimore) 2012 May;91(3):123-30. PMID: 22543626.

2. Athan E, Chu VH, Tattevin P, et al. Clinical characteristics and outcome of infective endocarditis involving implantable cardiac devices. JAMA 2012 Apr 25;307(16):1727-35. PMID: 22535857.

3. Deharo JC, Quatre A, Mancini J, et al. Long-term outcomes following infection of cardiac implantable electronic devices: a prospective matched cohort study. Heart 2012 May;98(9):724-31. PMID: 22523057.

4. Powell BD, Asirvatham SJ, Perschbacher DL, et al. Noise, artifact, and oversensing related inappropriate ICD shock evaluation: ALTITUDE noise study. Pacing Clin Electrophysiol 2012 Jul;35(7):863-69. PMID: 22519674.

5. Viganego F, O'Donoghue S, Eldadah Z, et al. Effect of early diagnosis and treatment with percutaneous lead extraction on survival in patients with cardiac device infections. Am J Cardiol 2012 May 15;109(10):1466-71. PMID: 22356796.

6. Greenspon AJ, Prutkin JM, Sohail MR, et al. Timing of the most recent device procedure influences the clinical outcome of lead-associated endocarditis results of the MEDIC (Multicenter Electrophysiologic Device Infection Cohort). J Am Coll Cardiol 2012 Feb 14;59(7):681-87. PMID: 22322085.

7. Jacob S, Panaich SS, Zalawadiya SK, et al. Phantom shocks unmasked: clinical data and proposed mechanism of memory reactivation of past traumatic shocks in patients with implantable cardioverter defibrillators. J Interv Card Electrophysiol 2012 Aug;34(2):205-13. PMID: 22183617.

8. 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 Jan;14(1):61-73. PMID: 22179034.

9. Bogale N, Witte K, Priori S, et al. The European Cardiac Resynchronization Therapy Survey: comparison of outcomes between de novo cardiac resynchronization therapy implantations and upgrades. Eur J Heart Fail 2011 Sep;13(9):974-83. PMID: 21771823.

10. Le KY, Sohail MR, Friedman PA, et al. Impact of timing of device removal on mortality in patients with cardiovascular implantable electronic device infections. Heart Rhythm 2011 Nov;8(11):1678-85. PMID: 21699855.

11. Tompkins C, McLean R, Cheng A, et al. End-stage renal disease predicts complications in pacemaker and ICD implants. J Cardiovasc Electrophysiol 2011 Oct;22(10):1099-104. PMID: 21489029.

12. Powell BD, Cha YM, Asirvatham SJ, et al. Implantable cardioverter defibrillator electrogram adjudication for device registries: methodology and observations from ALTITUDE. Pacing Clin Electrophysiol 2011 Aug;34(8):1003-12. PMID: 21453341.

13. Sohail MR, Hussain S, Le KY, et al. Risk factors associated with early- versus late-onset implantable cardioverter-defibrillator infections. J Interv Card Electrophysiol 2011 Aug;31(2):171-83. PMID: 21365264.

14. Krahn AD, Lee DS, Birnie D, et al. Predictors of short-term complications after implantable cardioverter-defibrillator replacement: results from the Ontario ICD Database. Circ Arrhythm Electrophysiol 2011 Apr;4(2):136-42. PMID: 21325209.

15. Cengiz M, Okutucu S, Ascioglu S, et al. Permanent pacemaker and implantable cardioverter defibrillator infections: seven years of diagnostic and therapeutic experience of a single center. Clin Cardiol 2010 Jul;33(7):406-11. PMID: 20641117.

16. Tompkins C, Cheng A, Dalal D, et al. Dual antiplatelet therapy and heparin "bridging" significantly increase the risk of bleeding complications after pacemaker or implantable cardioverter-defibrillator device implantation. J Am Coll Cardiol 2010 May 25;55(21):2376-82. PMID: 20488310.

17. Nery PB, Fernandes R, Nair GM, et al. Device-related infection among patients with pacemakers and implantable defibrillators: incidence, risk factors, and consequences. J Cardiovasc Electrophysiol 2010 Jul;21(7):786-90. PMID: 20102431.

18. de Oliveira JC, Martinelli M, Nishioka SA, et al. Efficacy of antibiotic prophylaxis before the implantation of pacemakers and cardioverter-defibrillators: results of a large, prospective, randomized, double-blinded, placebo-controlled trial. Circ Arrhythm Electrophysiol 2009 Feb;2(1):29-34. PMID: 19808441.

19. Curtis LH, Al-Khatib SM, Shea AM, et al. Sex differences in the use of implantable cardioverter-defibrillators for primary and secondary prevention of sudden cardiac death. JAMA 2007 Oct 3;298(13):1517-24. PMID: 17911496.

20. Gunderson BD, Patel AS, Bounds CA, et al. An algorithm to predict implantable cardioverter-defibrillator lead failure. J Am Coll Cardiol 2004 Nov 2;44(9):1898-902. PMID: 15519026.

21. Cabell CH, Heidenreich PA, Chu VH, et al. Increasing rates of cardiac device infections among Medicare beneficiaries: 1990-1999. Am Heart J 2004 Apr;147(4):582-86. PMID: 15077071.

22. Giudici MC, Paul DL, Bontu P, et al. Pacemaker and implantable cardioverter defibrillator implantation without reversal of warfarin therapy. Pacing Clin Electrophysiol 2004 Mar;27(3):358-60. PMID: 15009863.

23. Newman DM, Dorian P, Paquette M, et al. Effect of an implantable cardioverter defibrillator with atrial detection and shock therapies on patient-perceived, health-related quality of life. Am Heart J 2003 May;145(5):841-46. PMID: 12766741.

24. Gronefeld GC, Mauss O, Li YG, et al. Association between atrial fibrillation and appropriate implantable cardioverter defibrillator therapy: results from a prospective study. J Cardiovasc Electrophysiol 2000 Nov;11(11):1208-14. PMID: 11083241.

25. Hua W, Niu H, Fan X, et al. Preventive effectiveness of implantable cardioverter defibrillator in reducing sudden cardiac death in the Chinese population: a multicenter trial of ICD therapy versus non-ICD therapy. J Cardiovasc Electrophysiol 2012 Nov;23 Suppl 1:S5-S9. PMID: 23140347.

26. Dougherty CM, Thompson EA, Kudenchuk PJ. Development and testing of an intervention to improve outcomes for partners following receipt of an implantable cardioverter defibrillator in the patient. ANS Adv Nurs Sci 2012 Oct;35(4):359-77. PMID: 23107992.

27. Chen S, Yin Y, Krucoff MW. Effect of cardiac resynchronization therapy and implantable cardioverter defibrillator on quality of life in patients with heart failure: a meta-analysis. Europace 2012 Nov;14(11):1602-07. PMID: 23104857.

28. Rho RW, Patton KK, Poole JE, et al. Important differences in mode of death between men and women with heart failure who would qualify for a primary prevention implantable cardioverter-defibrillator. Circulation 2012 Nov 13;126(20):2402-07. PMID: 23072904.

29. 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 Sep 1;5(5):566-70. PMID: 22896584.

30. Ipek EG, Guray U, Demirkan B, et al. Infections of implantable cardiac rhythm devices: predisposing factors and outcome. Acta Cardiol 2012 Jun;67(3):303-10. PMID: 22870738.

31. Brignole M, Occhetta E, Bongiorni MG, et al. Clinical evaluation of defibrillation testing in an unselected population of 2,120 consecutive patients undergoing first implantable cardioverter-defibrillator implant. J Am Coll Cardiol 2012 Sep 11;60(11):981-87. PMID: 22858384.

32. Roig IL, Darouiche RO, Musher DM, et al. Device-related infective endocarditis,

with special consideration of implanted intravascular and cardiac devices in a predominantly male population. Scand J Infect Dis 2012 Oct;44(10):753-60. PMID: 22681242.

33. Hoogwegt MT, Kupper N, Theuns DA, et al. Undertreatment of anxiety and depression in patients with an implantable cardioverter-defibrillator: impact on health status. Health Psychol 2012 Nov;31(6):745-53. PMID: 22545981.

34. Powell BD, Asirvatham SJ, Perschbacher DL, et al. Noise, artifact, and oversensing related inappropriate ICD shock evaluation: ALTITUDE noise study. Pacing Clin Electrophysiol 2012 Jul;35(7):863-69. PMID: 22519674.

35. Boriani G, Santini M, Lunati M, et al. Improving thromboprophylaxis using atrial fibrillation diagnostic capabilities in implantable cardioverter-defibrillators: the multicentre Italian ANGELS of AF Project. Circ Cardiovasc Qual Outcomes 2012 Mar 1;5(2):182-88. PMID: 22373906.

36. Koopman HM, Vrijmoet-Wiersma CM, Langius JN, et al. Psychological functioning and disease-related quality of life in pediatric patients with an implantable cardioverter defibrillator. Pediatr Cardiol 2012 Apr;33(4):569-75. PMID: 22314365.

37. Marshall P, Ketchell A, Maclean J. Comparison of male and female psychological outcomes related to implantable cardioverter defibrillators (COMFORTID). Eur J Cardiovasc Nurs 2012 Sep;11(3):313-21. PMID: 21802370.

Other (n=4)

1. Sayfo S, Vakil KP, Alqaqa'a A, et al. A retrospective analysis of proceduralist-directed, nurse-administered propofol sedation for implantable cardioverter-defibrillator procedures. Heart Rhythm 2012 Mar;9(3):342-46. PMID: 22001710. *Reason for Exclusion: inpatient adverse effect, not NCDR ICD database*

2. Swindle JP, Rich MW, McCann P, et al. Implantable cardiac device procedures in older patients: use and in-hospital outcomes. Arch Intern Med 2010 Apr 12;170(7):631-37. PMID: 20386008. *Reason for Exclusion: Inpatient adverse effect, not NCDR ICD database*

3. Bhavnani SP, Kluger J, Coleman CI, et al. The prognostic impact of shocks for clinical and induced arrhythmias on morbidity and mortality among patients with implantable cardioverter-defibrillators. Heart Rhythm 2010 Jun;7(6):755-60. PMID: 20211275. *Reason for Exclusion: No data about population*

4. Zaman S, Sivagangabalan G, Narayan A, et al. Outcomes of early risk stratification and targeted implantable cardioverter-defibrillator implantation after ST-elevation myocardial infarction treated with primary percutaneous coronary intervention. Circulation 2009 Jul 21;120(3):194-200. PMID: 19581496. *Reason for Exclusion: intervention arms not comparable*

Appendix C. Supplemental Tables

Appendix Table 1. Baseline data

Study Author, Year PMID	Intervention (Control)	Baseline characteristics Intervention (Control)					
		Age, y (mean or median)	%Male	%LVEF	%NYHA class	%DM	QRS interval
ICD vs. no ICD							
AMIOVIRT Strickberger, 2003 12767651	ICD (Amiodarone)	58 (60)	67 (74)	22 (23)	Class I: 18 (13); Class II:64 (63); Class III: 16 (24)	31 (36)	nd
CABG-Patch Bigger, 1997 9371853	ICD (No ICD)	64 (63)	87 (82)	27 (27)	Class II or III: 71 (74)	36 (40)	QRS complex >100 msec: 71 (74)
CAT Bansch, 2002 11914254	ICD (Control)	52 (52)	86 (74)	24 (25)	Class II: 67 (64); Class III: 33 (36)	NR	"Abnormal": 27 (45)
Chan, 2009 20031808	ICD (No ICD)	66 (66)	80 (75)	26 (28)	nd	35 (37)	%QRS interval >120 msec: 32 (21)
COMPANION Bristow, 2004 15152059	ICD + CRT (No ICD)	66 (68)	67 (69)	22 (22)	Class III: 86 (82)	41 (45)	160 (158)
DEFINITE Kadish, 2004 15152060	ICD (No ICD)	58 (58)	73 (70)	21 (22)	Class I: 25 (18); Class II: 54 (61); Class III: 21 (21)	23 (23)	115 (116)
Hohnloser, 2004 15590950 DINAMIT	ICD (No ICD)	62 (62)	76 (77)	28 (28)	Class I: 14 (12); Class II:31 (59); Class III: 26 (29)	31 (29)	107 (105)
Fonarow, 2000 10760339	ICD (Control)	49 (48)	68 (58)	21 (21)	Class III: 48 (49); Class IV: 52 (51)	NR	nd
IRIS Steinbeck, 2009 19812399	ICD (No ICD)	63 (62)	78 (76)	NR	At hospital discharge post-MI, the NYHA Class could be assessed in 885 of the surviving patients and was judged to be Class I in 247 patients (28%), Class II in 531 (60%), and Class III in 106 (12%); the Class changed to IV in 1 patient (0.1%).	37 (30)	nd
MADIT Moss, 1996 8960472	ICD (No ICD)	62 (64)	97 (91)	27 (25)	Class II or III: 63 (67)	7 (5)	nd
MADIT II Moss, 2002 11907286	ICD (No ICD)	64 (65)	84 (85)	23 (23)	Class I: 35 (39); Class II:35 (34); Class III: 25 (23); Class IV: 5 (4)	33 (38)	%QRS interval ≥120 msec: 50 (51)

Study Author, Year PMID	Intervention (Control)	Baseline characteristics Intervention (Control)					
		Age, y (mean or median)	%Male	%LVEF	%NYHA class	%DM	QRS interval
Mezu, 2011 21640321	ICD (No ICD)	82 (86)	77 (67)	24 (27)	Class III or IV: 44 (72)	34 (63)	nd
OPTIMIZE-HF and GWTG-H Hernandez, 2010 20009044	ICD (No ICD)	74 (75)	74 (58)	23 (25)	nd	37 (44)	nd
SCD-HeFT Bardy, 2005 15659722	ICD (No ICD/placebo)	60 (60)	77 (76)	Median: 24 (25)	nd	31 (29)	nd
ICD vs. CRT-D							
Diab, 2011 21700757	ICD (CRT-D)	65 (67)	90 (88)	27 (25)	Class III: 89 (88) Mean: 3.2 (3.1)	NR	142 (134)
MADIT-CRT Moss, 2009 19723701	ICD (CRT-D)	64 (65)	76 (75)	24 (24)	Class I (all ischemic): 16 (14); Class II (ischemic): 39 (41); Class II (nonischemic): 45 (45)	31 (30)	%QRS duration ≥150 msec: 65 (64)
MENDMI Chung, 2010 20852059	ICD (CRT-D)	55 (58)	68 (81)	29 (28)	Class I: 16 (17); Class II: 34 (29); Class III: 34 (38); Unknown: 16 (17)	11 (5)	91 (86)
RAFT Tang, 2010 21073365	ICD (CRT-D)	66 (66)	81 (85)	23 (23)	Class II: 81 (79); Class III: 19(21)	35 (33)	Intrinsic: 158 (157); Paced: 210 (207)

AMIOVERT=Amiodarone versus Implantable Cardioverter-Defibrillator Randomized Trial, CABG-Patch=Coronary Artery Bypass Graft Patch, CAT=Cardiomyopathy Trial, COMPANION=Comparison of Medical Therapy, Pacing and Defibrillation in Heart Failure, CRT-D=cardiac resynchronization therapy defibrillator, DEFINITE=Defibrillators in Nonischemic Cardiomyopathy Treatment Evaluation, DINAMIT=Defibrillator in Acute Myocardial Infarction Trial, DM=diabetes, GWTG-HF= Get With the Guidelines-Heart Failure, ICD=implantable cardiac defibrillator, IRIS=Immediate Risk Stratification Improves Survival, LVEF=left ventricular ejection fraction, MADIT=Multicenter Automatic Defibrillator Implantation Trial, MADIT-CRT=Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy, MENDMI=Prevention of Myocardial Enlargement and Dilation Post Myocardial Infarction Study, MI= myocardial infarction, msec, millisecond, nd=not documented, NYHA=New York Heart Association, OPTIMIZE-HF=Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure, SCD-HeFT= Sudden Cardiac Death in Heart Failure Trial, VT=ventricular tachycardia

Appendix Table 2. Concomitant medications

Study Author, Year PMID	Intervention (Control)	Medications Intervention (Control)				
		%Antiarrhythmic drug Class I	%Antiarrhythmic drug Class III	%Beta blocker	%ACEi or ARB	Control (Verbatim)
ICD vs. no ICD						
AMIOVIRT Strickberger, 2003 12767651	ICD (Amiodarone)	nd	Amiodarone: 0 (100)	Last follow-up: 53 (50)	Last follow-up: 90 (81)	Subjects were randomly assigned to receive either amiodarone or an ICD.
CABG-Patch Bigger, 1997 9371853	ICD (No ICD)	17 (12)	Amiodarone: 4 (3); Sotalol: 1 (0.2)	18 (24)	ACEi: 55 (54)	Patients were randomly assigned to the defibrillator or control group within randomly permuted blocks. The trial protocol prohibited the use of antiarrhythmic drugs for asymptomatic ventricular arrhythmia and specified that patients without contraindications should be treated with aspirin.
CAT Bansch, 2002 11914254	ICD (Control)	nd	nd	4 (4)	ACEi: 94 (98)	Patients with recent onset of DCM (9 months) and an ejection fraction 30% were randomly assigned to the implantation of an ICD or control.
Chan, 2009 20031808	ICD (No ICD)	1 (0.4)	Class III: 8 (8)	86 (83)	86 (86)	The study cohort comprised 965 patients (751 [77.8%] ischemic; 214 [22.2%] nonischemic), of whom 494 (51.2%) received ICDs.
COMPANION Bristow, 2004 15152059	ICD + CRT (No ICD)	nd	nd	68 (66)	90 (89)	Eligible patients who provided written informed consent were randomly assigned in a 1:2:2 ratio to treatment with protocol-mandated optimal pharmacologic therapy alone, optimal pharmacologic therapy plus cardiac-resynchronization therapy with a pacemaker, or optimal pharmacologic therapy plus cardiac-resynchronization therapy with a pacemaker–defibrillator. The pharmacologic therapy used in all groups consisted of diuretics (unless they were not needed), ACEi (unless they were not tolerated, where-upon ARBs could be substituted), beta-blockers (unless they were not tolerated or were contraindicated), and spironolactone (unless it was not tolerated). Digoxin and other medications used to treat heart failure could be given at the investigator's discretion.

Study Author, Year PMID	Intervention (Control)	Medications Intervention (Control)				
		%Antiarrhythmic drug Class I	%Antiarrhythmic drug Class III	%Beta blocker	%ACEi or ARB	Control (Verbatim)
DEFINITE Kadish, 2004 15152060	ICD (No ICD)	nd	Amiodarone: 4 (7)	86 (84)	ACEi: 84 (87); ARB: 14 (9)	Patients were randomly assigned to receive either standard oral medical therapy for heart failure or standard oral medical therapy plus an ICD. All patients received ACEi unless they were contraindicated. Patients who were unable to tolerate ACE inhibitors received hydralazine or nitrates or ARBs. In addition, beta-blocker therapy was required unless patients were unable to tolerate it. Carvedilol was the beta-blocker of choice on the basis of data available when the study was designed. The doses of ACEi and beta-blockers were adjusted to the levels recommended for patients with heart failure or to the highest tolerated doses. Digoxin and diuretics were used when necessary to manage clinical symptoms. The use of antiarrhythmic drugs such as amiodarone was discouraged. However, it was recognized that some patients had symptomatic atrial fibrillation or supraventricular arrhythmias requiring treatment with amiodarone, and these conditions did not constitute exclusion criteria. No other antiarrhythmic drugs were used.
DINAMIT Hohnloser, 2004 15590950	ICD (No ICD)	nd	nd	87 (87)	95 (94)	Patients were randomly assigned in a 1:1 ratio either to receive an ICD (the ICD group) or not to receive an ICD (the control group). The study protocol mandated that patients receive the best conventional medical therapy. Investigators were encouraged to treat all study patients with ACEi, beta-blockers, aspirin, and lipid-lowering drugs, as appropriate.
Fonarow, 2000 10760339	ICD (Control)	4 (12)	Amiodarone: 40 (36)	0 (5)	ACEi: 83 (74)	Of the 147 patients, 122 were treated with conventional medical therapy. Patients with atrial fibrillation or frequent nonsustained VT received low-dose amiodarone (200 mg/day) after varied loading protocols. Type I antiarrhythmic agents for nonsustained VT or atrial fibrillation were generally discontinued.

Study Author, Year PMID	Intervention (Control)	Medications Intervention (Control)				
		%Antiarrhythmic drug Class I	%Antiarrhythmic drug Class III	%Beta blocker	%ACEi or ARB	Control (Verbatim)
IRIS Steinbeck, 2009 19812399	ICD (No ICD)	"Anti-arrhythmic drugs (mainly amiodarone): 13 (17)	"Anti-arrhythmic drugs (mainly amiodarone): 13 (17)	89 (86)	82 (82)	The remaining 898 patients (86% of whom were still in the hospital) were randomly assigned to a study treatment — 445 to receive an ICD and 453 to receive medical therapy alone — at a mean (±SD) of 13±7 days after infarction.
MADIT Moss, 1996 8960472	ICD (No ICD)	At 1 mo: 12 (10)	At 1 mo: Amiodarone: 2 (74); Sotalol: 1 (7); Sotatol and beta-blockers: 27 (15)	At 1 mo: 26 (8)	At 1 mo: ACEi: 60 (55)	The choice of conventional medical therapy, including the decision whether to use antiarrhythmic medications, was left to the patient's attending physician. Antiarrhythmic drugs approved and released by the FDA could be administered to patients in either group.
MADIT II Moss, 2002 11907286	ICD (No ICD)	3 (2)	Amiodarone: 13 (10)	70 (70)	ACEi: 68 (72)	The patients were randomly assigned in a 3:2 ratio to receive either an implantable defibrillator or conventional medical therapy. The appropriate use of beta-blockers, ACEi, and lipid-lowering drugs was strongly encouraged in both study groups.
Mezu, 2011 21640321	ICD (No ICD)	I and III: 9 (22)	I and III: 9 (22)	70 (61)	ACEi: 77 (65)	We identified all patients who received an ICD at our institution from January 2000 through December 2008 and were 80 years of age at the time of their ICD implantation.
OPTIMIZE-HF and GWTG-HF Hernandez, 2010 20009044	ICD (No ICD)	nd	nd	84 (78)	78 (72)	We identified patients with heart failure who were aged 65 years or older and were eligible for an ICD, had left ventricular ejection fraction of 35% or less, and were discharged alive from hospitals participating in the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure and the Get With the Guidelines–Heart Failure quality-improvement programs during the period January 1, 2003, through December 31, 2006. We matched the patients to Medicare claims to examine long-term outcomes.
SCD-HeFT Bardy, 2005 15659722	ICD (No ICD/placebo)	nd	nd	At enrollment: 69 (69)	At enrollment: 94 (97)	From September 16, 1997, to July 18, 2001, we randomly assigned 2521 patients in equal proportions to receive placebo, amiodarone, or a single-chamber ICD programmed to shock-only mode.
ICD vs. CRT-D						
Diab, 2011 21700757	ICD (CRT-D)	nd	nd	73 (71)	100 (98)	All patients underwent a device implantation procedure but were blinded to whether they received a CRT-D or an ICD device.

Study Author, Year PMID	Intervention (Control)	Medications Intervention (Control)				
		%Antiarrhythmic drug Class I	%Antiarrhythmic drug Class III	%Beta blocker	%ACEi or ARB	Control (Verbatim)
MADIT-CRT Moss, 2009 19723701	ICD (CRT-D)	0.4 (1)	Amiodarone: 7 (7)	93 (93)	ACEi: 77 (77); ARB: 20 (21)	The patients were randomly assigned in a 3:2 ratio to receive either CRT with an ICD (CRT–ICD group) or only an ICD (ICD-only group) and were stratified according to clinical center and ischemic status with the use of an algorithm that ensured near balance in each stratum.
MENDMI Chung, 2010 20852059	ICD (CRT-D)	nd	nd	94 (94)	94 (88)	Eligible patients were randomized 1:1 in blocks of 4 stratified per center to therapy CRT-D or control (ICD) between 3 and 14 days of their presenting MI.
RAFT Tang, 2010 21073365	ICD (CRT-D)	nd	nd	89 (90)	97 (96)	Eligible patients were randomly assigned in a 1:1 ratio to receive an ICD or an ICD with CRT and were stratified according to clinical center, atrial rhythm (atrial fibrillation or flutter or sinus–atrial pacing), and a planned implantation of a single- or dual-chamber ICD.

ACEi=angiotensin-converting-enzyme inhibitor, ARB=angiotensin receptor blockers, CRT-D=cardiac resynchronization therapy defibrillator, ICD=implantable cardiac defibrillator, nd=not documented, VT=ventricular tachycardia

For study names, see Appendix Table 1.

Appendix Table 3. ICD vs. No ICD: Results for all-cause mortality at longest follow-up

Study Author, Year PMID	Outcome name	Timepoint	Outcome description	Intervention (Control)	Events Intervention (Control)	N analyzed Intervention (Control)	Metric	Results (95% CI)	p-value between arms
≥4 year									
MADIT II Barsheshet, 2011 210448997	Death, all-cause longest follow-up	8 y	nd	ICD (No ICD)	~44%[1] (~55%)	567 (490)	Adjusted HR	0.55 (0.46-0.67)	<0.001
CAT Bansch, 2002 11914254	Death, all-cause longest follow-up	5 y	nd	ICD (No ICD)	13 (17)	50 (54)	nd	nd	nd
DEFINITE Kadish, 2004 15152060	Death, all-cause longest follow-up	5 y	nd	ICD (No ICD)	28 (40)	229 (229)	Unadjusted HR[2]	0.65 (0.40-1.06)	0.08
MADIT Moss, 1996 8960472	Death, all-cause longest follow-up	5 y	nd	ICD (No ICD)	15 (39)	95 (101)	HR	0.46 (0.26-0.82)	0.009
SCD-HeFT Bardy, 2005 15659722	Death, all-cause longest follow-up	5 y	nd	ICD (No ICD/placebo)	182 (240)	829 (845)	nd	nd	nd
MADIT II Moss, 2002 11907286	Death, all-cause longest follow-up	4 y	nd	ICD (No ICD)	105 (97)	742 (490)	HR	0.69 (0.51-0.93)	0.016
2-3 y									
Chan, 2009 20031808	Death, all-cause longest follow-up	3 y	Death at 34 ± 16 mo in ICD arm; Death at 33 ± 16 mo in No ICD arm	ICD (No ICD)	102 (115)	494 (471)	Adjusted HR	0.69 (0.50-0.96)	0.03
OPTIMIZE-HF and GWTG-HF Hernandez, 2010 20009044	Death, all-cause longest follow-up	3 y	Death at 3 y	ICD (No ICD)	101 (1771)	376 (4,309)	Inverse-weighted HR (control for meds)	0.71 (0.56-0.91)[3]	<0.001

1 Estimated from figure
2 Adjusted model "unchanged" at 0.65 but CI not reported
3 Unadjusted HR 0.67 (0.52-0.87)

Study Author, Year PMID	Outcome name	Timepoint	Outcome description	Intervention (Control)	Events Intervention (Control)	N analyzed Intervention (Control)	Metric	Results (95% CI)	p-value between arms
AMIOVIRT Strickberger, 2003 12767651	Death, all-cause longest follow-up	2 y	Duration of follow-up 2.2 y ion ICD arm and 1.8 y in Amiodarone arm	ICD (Amiodarone)	6 (7)	51 (52)	nd	nd	0.8
DEFINITE Kadish, 2004 15152060	Death, all-cause longest follow-up	2 y	nd	ICD (No ICD)	7.9% (14.1%)	229 (229)	nd	nd	nd
Fonarow, 2000 10760339	Death, all-cause longest follow-up	2 y	nd	ICD (No ICD)	2 (31)	25 (122)	nd	nd	nd
MADIT II Moss, 2002 11907286	Death, all-cause longest follow-up	2 y	nd	ICD (No ICD)	~15%[4] (~31%)	742 (490)	% difference	-28% (-46%, 4%)	NS
Mezu, 2011 21640321	Death, all-cause longest follow-up	2 y	Death during study	ICD (No ICD)	58 (35)	99 (53)	nd	nd	nd
OPTIMIZE-HF and GWTG-HF Hernandez, 2010 20009044	Death, all-cause longest follow-up	2 y	Death at 2 y	ICD (No ICD)	90 (1550)	376 (4,309)	nd	nd	<0.001
CABG-Patch Bigger, 1997 9371853	Death, all-cause longest follow-up	3 y	Death at 32 ± 16 mo	ICD (No ICD)	101 (95)	446 (454)	HR, Cox adjusted for 10 prespecified covariates	1.03 (0.75-1.41)	NS
DINAMIT Hohnloser, 2004 15590950	Death, all-cause longest follow-up	3 y	All cause mortality at 30 ± 13 mo	ICD (No ICD)	62 (58)	332 (342)	HR	1.08 (0.76-1.55)	0.66
IRIS Steinbeck, 2009 19812399	Death, all-cause longest follow-up	3 y	nd	ICD (No ICD)	116 (117)	445 (453)	HR	1.04 (0.81-1.35)	0.15
		2 y			15.4% (18.2%)	445 (453)	nd	nd	nd

4 Estimated from figure

Study Author, Year PMID	Outcome name	Timepoint	Outcome description	Intervention (Control)	Events Intervention (Control)	N analyzed Intervention (Control)	Metric	Results (95% CI)	p-value between arms
1 y									
AMIOVIRT Strickberger, 2003 12767651	Death, all-cause longest follow-up	1 y	nd	ICD (Amiodarone)	96% (90%)	51 (52)	nd	nd	nd
CAT Bansch, 2002 11914254	Death, all-cause longest follow-up	1 y	nd	ICD (No ICD)	4 (2)	50 (54)	nd	nd	nd
COMPANION Bristow, 2004 15152059	Death, all-cause longest follow-up	1 y	Death from any cause	ICD + CRT (No ICD)	105 (77)	595 (308)	HR	0.76 (0.58-1.01)	0.059 (Adjusted 0.06)
DEFINITE Kadish, 2004 15152060	Death, all-cause longest follow-up	1 y	nd	ICD (No ICD)	2.6% (6.2%)	229 (229)	nd	nd	nd
Fonarow, 2000 10760339	Death, all-cause longest follow-up	1 y	nd	ICD (Control)	6.7% (24.5%)	25 (122)	nd	nd	nd
MADIT II Moss, 2002 11907286	Death, all-cause longest follow-up	1 y	nd	ICD (No ICD)	~8%[5] (~10%)	742 (490)	% difference	-12% (-40%, 27%)	NS
Mezu, 2011 21640321	Death, all-cause longest follow-up	1 y	Death at 1 y	ICD (No ICD)	72% (52%)	99 (53)	Adjusted HR[6]	0.78 (0.44-1.30)	0.312
OPTIMIZE-HF and GWTG-HF Hernandez, 2010 20009044	Death, all-cause longest follow-up	1 y	Death at 1 y	ICD (No ICD)	65 (1102)	376 (4,309)	nd	nd	<0.001
IRIS Steinbeck, 2009 19812399	Death, all-cause longest follow-up	1 y	nd	ICD (No ICD)	10.6% (12.5%)	445 (453)	nd	nd	nd

CI=confidence interval, HR=hazards ratio, ICD=implantable cardiac defibrillator, mo=month, nd=not documented, NS=not significant, y=year
For study names, see Appendix Table 1.

[5] Estimated from figure
[6] Adjusted for age, Charlson comorbidity index, LVEF, GFR

Appendix Table 4. ICD plus CRT versus ICD alone: Results for all-cause mortality at longest followup

Study Author, Year PMID	Outcome name	Timepoint	Outcome description	Intervention (Control)	Events Intervention (Control)	N analyzed Intervention (Control)	Metric	Results (95% CI)	p-value between arms
≥4 year									
MADIT-CRT Moss, 2009 19723701	Death, all-cause longest followup	5 y	nd	CRT-D (ICD)	74 (53)	nd	HR	1.00 (0.69-1.44)	0.99
3 years									
RAFT Tang, 2010 21073365	Death, all-cause longest followup	3 y	Death from any cause	CRT-D (ICD)	186 (236)	894 (904)	HR	0.75 (0.62-0.91)	0.003
1 y									
Diab, 2011 21700757	Death, all-cause longest followup	1 y	Mortality	CRT-D (ICD)	0 (2)	nd	nd	nd	nd
MENDMI Chung 2010 20852059	Death, all-cause longest followup	1 y	All–cause mortality	CRT-D (ICD)	1 (1)	42 (38)	nd	nd	1.00

CI=confidence interval, CRT-D=cardiac resynchronization therapy defibrillator, HR=hazards ratio, nd=not documented, y=year

For study names, see Appendix Table 1.

Appendix Table 5. Subgroup analyses of ICD vs. no ICD for all-cause death

Study, Author, Year, PMID	Subgroups HR/RR (95% CI)		P Interaction
Age			
MADIT, Moss, 1996, 8960472	Continuous: nd		P>0.2
CABG-Patch, Bigger, 1997, 9371853	Continuous: nd		NS
MADIT II, Moss, 2002, 11907286	<60 y: 0.5 (0.2, 0.9) ≥70 y: 0.6 (0.45, 0.95)	60-69 y: 0.8 (0.5, 1.3)	NS
DINAMIT, Hohnloser, 2004, 15590950	<60 y: 0.9 (0.4, 1.9)	≥60 y: 1.2 (0.8, 1.9)	P=0.46
Chan, 2009, 20031808*	<65 y: 0.74 (0.43,1.28) ≥75 y: 0.59 (0.39, 0.90)	65-74 y: 0.76 (0.45, 1.29)	P=0.43
COMPANION, Bristow, 2004, 15152059	≤65 y: 0.6 (0.3, 0.95)	>65 y: 0.7 (0.5, 1.0)	nd
SCD-HeFT, Bardy 2005 15659722	<65 y: 0.68 (0.50, 0.93)†	≥65 y: 0.86 (0.62, 1.18)†	nd
DEFINITE, Kadish, 2004, 15152060	<65y; 0.7 (0.3, 1.4)	≥65 y: 0.6 (0.3, 1.2)	NS
IRIS, Steinbeck, 2009, 19812399	<65 y: 0.95 (0.6, 1.5)	≥65 y: 1.05 (0.8, 1.5)	P=0.73
OPTIMIZE-HF and GWTG-H, Hernandez, 2010, 20009044*	65-74 y: 0.65 (0.47, 0.89)	75-84 y: 0.80 (0.62, 1.03)	P=0.31
Sex			
CABG-Patch, Bigger, 1997, 9371853	Female: nd	Male: nd	NS
COMPANION, Bristow, 2004, 15152059	0.6 (0.3, 1.1)	0.65 (0.4, 0.9)	nd
DEFINITE, Kadish, 2004, 15152060	1.1 (0.5-2.6)	0.49 (0.27, 0.90)	NS
DINAMIT, Hohnloser, 2004, 15590950	1.0 (0.5-2.1)	1.1 (0.7-1.7)	P=0.82
IRIS, Steinbeck, 2009, 19812399	1.0 (0.6-1.7)	1.1 (0.8-1.5)	P=0.85
MADIT II Moss, 2002, 11907286	0.6 (0.3-1.1)	0.7 (0.5-0.9)	NS
MADIT, Moss, 1996, 8960472	nd	nd	P>0.2
OPTIMIZE-HF and GWTG-H, Hernandez, 2010, 20009044*	0.58 (0.41,0.83)	0.80 (0.63,1.01)	P=0.15
SCD-HeFT, Russo 2008 18373605	0.90 (0.56, 1.43)†	0.71 (0.57, 0.88)†	P=0.54‡
Race/Ethnicity			
SCD-HeFT, Mitchell, 2008, 18294487	AA: 0.65 (0.43, 0.99)†	White: 0.73 (0.58, 0.90)†	P=0.53
Bardy 2005 15659722	Non-white: 0.75 (0.48, 1.17)†	White: 0.78 (0.61, 1.00)†	nd
NYHA Class			
CABG-Patch, Bigger, 1997, 9371853	nd		NS
COMPANION, Bristow, 2004, 15152059	III: 0.6 (0.4, 0.97)	IV: 0.6 (0.4, 1.0)	nd
DEFINITE, Kadish, 2004, 15152060	I: 0.5 (0.2, 1.5) III: 0.37 (0.15, 0.90)	II: 1.0 (0.5, 2.2)	NS
DINAMIT, Hohnloser, 2004, 15590950	0-II: 1.1 (0.7, 1.7)	III: 1.0 (0.5, 2.3)	P=0.87
MADIT, Moss, 1996, 8960472	nd		P>0.2
MADIT II Moss, 2002, 11907286	I 0.6 (0.5, 0.9)	II-IV: 0.7 (0.45, 1.0)	NS
SCD-HeFT, Bardy 2005 15659722	II: 0.54 (0.40, 0.74)†	III: 1.16 (0.84, 1.61)†	**P<0.001**

Study, Author, Year, PMID	Subgroups HR/RR (95% CI)				P Interaction
Heart Failure					
CABG-Patch, Bigger, 1997, 9371853	Yes:	nd	No:	nd	NS
Chan, 2009, 20031808*		0.69 (0.50, 0.93)		0.70 (0.35, 1.41)	P=0.59
MADIT, Moss, 1996, 8960472		nd		nd	P>0.2
IRIS, Steinbeck, 2009, 19812399		1.0 (0.7, 1.4)		1.2 (0.8, 1.8)	P=0.56
Time Since Heart Failure Diagnosis					
DEFINITE, Kadish, 2006, 16781376	≤3 mo:	0.38 (0.14, 1.000)	>3 mo:	0.80 (0.46,1.41)	P=0.19
	≤9 mo:	0.46 (0.216, 0.986)	>9 mo:	0.86 (0.46,1.61)	P=0.22
LVEF					
CABG-Patch, Bigger, 1997, 9371853		nd			NS
Chan, 2009, 20031808*	≤25%:	0.73 (0.51, 1.04)	26-35%:	0.59 (0.37, 0.93)	P=0.61
COMPANION, Bristow, 2004, 15152059	≤20:	0.6 (0.4, 0.9)	20-35%:	0.7 (0.4, 1.1)	nd
DEFINITE, Kadish, 2004, 15152060	<20%:	0.9 (0.4, 2.0)	20-36%:	0.5 (0.3,0.95)	NS
DINAMIT, Hohnloser, 2004, 15590950	<26%:	1.5 (0.8, 2.7)	26-35%:	0.85 (0.5, 1.5)	P=0.16
OPTIMIZE-HF and GWTG-H, Hernandez, 2010, 20009044*	≤30%:	0.76 (0.59, 0.98)§	All patients:	0.71 (0.56, 0.91)§	NA
MADIT, Moss, 1996, 8960472	Continuous:	nd			P>0.2
MADIT II, Moss, 2002, 11907286	≤25%:	0.6 (0.5, 0.9)	25-30%	0.7 (0.4, 1.2)	NS
SCD-HeFT, Bardy 2005 15659722	≤30%:	0.73 (0.57, 0.92)†	30-35%:	1.08 (0.57, 2.07)†	nd
LBBB					
COMPANION, Bristow, 2004, 15152059	LBBB:	0.5 (0.4, 0.8)	Other:	0.9 (0.5, 1.6)	nd
MADIT, Moss, 1996, 8960472	LBBB:	nd	No LBBB:	nd	P>0.2
MADIT II, Moss, 2002, 11907286	LBBB:	nd	No LBBB:	nd	NS
QRS Duration					
CABG-Patch, Bigger, 1997, 9371853	≤100 msec:	nd	>100 msec:	nd	NS
COMPANION, Bristow, 2004, 15152059	≤147 msec: >168 msec:	0.8 (0.4, 1.3) 0.5 (0.3, 0.97)	148-168 msec:	0.6 (0.3, 1.0)	nd
DEFINITE, Kadish, 2004, 15152060	<120 msec:	0.75 (0.4, 1.5)	≥120 msec:	0.5 (0.2, 1.1)	NS
DINAMIT, Hohnloser, 2004, 15590950	<120 msec:	0.85 (0.5, 1.4)	≥120 msec:	1.5 (0.8, 2.9)	P=0.13
MADIT II, Moss, 2002, 11907286	<120 msec: ≥150 msec:	0.7 (0.5, 1.2) 0.5 (0.3, 0.9)	120-150 msec:	0.6 (0.4, 1.1)	NS
SCD-HeFT, Bardy 2005 15659722	<120 msec:	0.84 (0.62, 1.14)†	≥120 msec:	0.67 (0.49, 0.93)†	nd
Heart Disease					
COMPANION, Bristow, 2004, 15152059	Ischemic:	0.73 (0.52, 1.04)	Non-ischemic:	0.5 (0.29, 0.88)	NS
Time Since Myocardial Infarction					
SCD-HeFT, Piccini, 2011, 21109025	<18 mo: 52-111 mo:	0.7 (0.37, 1.31)† 1.47 (0.75, 2.87)†	18-51 mo: >111 mo:	0.54 (0.3, 0.98)† 0.75 (0.44, 1.29)†	P=0.33
MADIT, Moss, 1996, 8960472	<6 mo:	nd	≥6 mo:	nd	P>0.2
MADIT II, Moss, 2002, 11907286	<6 mo:	nd	≥6 mo:	nd	NS

Study, Author, Year, PMID	Subgroups HR/RR (95% CI)				P Interaction
MADIT II, Wilber, 2004, 14993128	<18 mo:	0.97 (0.51, 1.81)	≥18 mo:	0.55 (0.39, 0.78)	P=0.27
	18-59 mo	0.52 (0.26, 1.05)	60-119 mo	0.50 (0.26, 0.91)	nd
	≥120 mo:	0.62 (0.36, 1.08)			
Prior Coronary Revasc					
MADIT, Moss, 1996, 8960472	CR:	nd	No CR:	nd	P>0.2
SCD-HeFT, Al-Khatib 2008 18479330	CABG:	0.87 (0.62, 1.22)	No CABG:	0.66 (0.47, 0.94)	P=0.39
	PCI:	0.66 (0.36, 1.22)	No PCI:	0.82 (0.53, 1.29)	P=0.93
Time Since Coronary Revasc					
MADIT II, Goldenberg, 2006, 16682305	≤6 mo:	1.19 (0.40, 3.54)	>6 mo:	0.64 (0.45, 0.90)	P=0.29
	7-60 mo:	0.55 (0.31, 0.97)	>60 mo	0.67 (0.43, 1.03)	nd
SCD-HeFT, Al-Khatib 2008 18479330	CABG ≤2 y:	1.40 (0.61, 3.24)	CABG >2 y:	0.71 (0.49, 1.04)	P=0.09
	Time since PCI:	nd			P=0.51
Diabetes Mellitus					
CABG-Patch, Bigger, 1997, 9371853	Yes:	nd	No:	nd	NS
Chan, 2009, 20031808*		0.68 (0.45, 1.03)		0.69 (0.48, 1.01)	P=0.95
DINAMIT, Hohnloser, 2004, 15590950		0.9 (0.5, 1.5)		1.2 (0.8, 2.0)	P=0.38
IRIS, Steinbeck, 2009, 19812399		nd		nd	NS
MADIT II, Moss, 2002, 11907286		nd		nd	NS
SCD-HeFT, Bardy 2005 15659722		0.95 (0.68, 1.33)†		0.67 (0.50, 0.90)†	nd
Blood Urea Nitrogen					
MADIT, Moss, 1996, 8960472	≤25 mg/dL:	nd	>25 mg/dL:	nd	P>0.2
MADIT II Moss, 2002, 11907286	≤25 mg/dL:	nd	>25 mg/dL:	nd	NS
Kidney Disease					
Chan, 2009, 20031808*	Kidney failure:	0.52 (0.11, 2.48)	No kidney failure:	0.70 (0.53, 0.94)	P=0.21
MADIT II, Goldenberg, 2006, 16893702	eGFR ≥35:	1.09 (0.49, 2.43)	eGFR <35:	0.68 (0.50, 0.93)	P=0.29
	eGFR 35-59:	0.74 (0.48, 1.15)	eGFR ≥60:	0.66 (0.43, 1.02)	nd

AA = African American, CABG = coronary artery bypass graft, CI =confidence interval, CR = coronary revascularization, eGFR = estimated glomerular filtration rate (in mL/min/m^2), HR = hazard ratio, ICD = implantable cardiac defibrillator, LBBB = left bundle branch block, LVEF = left ventricular ejection fraction, mo = month, NA = not applicable, nd =no data, NS = Not statistically significant (no P-value documented), PCI = percutaneous coronary revascularization, PMID = PubMed ID, Revasc = revascularization, RR = risk ratio, y = years. See page 16 for study acronyms

* Nonrandomized comparative study
† 97.5% confidence interval
‡ P value refers to comparison of subgroups across all three study arms. (ICD, amiodarone, and placebo).
§ Only the LVEF <30% subgroup analysis was reported. The alternative group given here is from the total analysis, regardless of LVEF.

Appendix Table 6. ICD vs. No ICD: Results for 30 d mortality

Study Author, Year PMID	Outcome name	Timepoint	Outcome description	Intervention (Control)	Events Intervention (Control)	N analyzed Intervention (Control)	Metric	Results (95% CI)	p-value between arms
CABG-Patch Bigger, 1997 9371853	Death, all-cause at 30 d	30 d	Death in the first 30 days	ICD (No ICD)	24 (20)	446 (454)	nd	nd	0.60
MADIT Moss, 1996 8960472	Death, all-cause at 30 d	30 d	NR	ICD (No ICD)	0 (0)	95 (101)	nd	nd	nd

CI=confidence interval, d= day, ICD=implantable cardiac defibrillator, nd=not documented

Appendix Table 7. ICD vs. No ICD: Results for sudden cardiac (arrhythmic) death

Study Author, Year PMID	Outcome name	Timepoint	Outcome description	Intervention (Control)	Events Intervention (Control)	N analyzed Intervention (Control)	Metric	Results (95% CI)	p-value between arms
5 y									
MADIT Moss, 1996 8960472	Death, cardiac arrhythmia	5 y	Classification of Hinkle and Thaler 13 was used to evaluate the suspected mechanism of death from cardiac causes (arrhythmic or nonarrhythmic). "Abrupt loss of consciousness and disappearance of pulse without prior collapse of the circulation" (w/ or w/o CHF; witnessed or not)	ICD (No ICD)	3 (13)	95 (101)	nd	nd	nd
3 y									
Chan, 2009 20031808	Death, cardiac arrhythmia	3 y	Death arrhythmic, Modified Hinkle and Thaler: unwitnessed deaths (if stable when last observed within 24 hours before death), witnessed instantaneous deaths, and sequelae of cardiac arrest.	ICD (No ICD)	46 (105)	494 (471)	Adjusted HR	0.65 (0.40-1.03)	0.07
DINAMIT Hohnloser, 2004 15590950	Death, cardiac arrhythmia	3 y	Death due to cardiac arrhythmia from witnesses, family, death certificate, hospital records, autopsy. Not ICD telemetry	ICD (No ICD)	12 (29)	332 (342)	HR	0.42 (0.22-0.83)	0.009
IRIS Steinbeck, 2009 19812399	Death, cardiac arrhythmia	3 y	A death, either in the hospital or out of the hospital, was assumed to be a sudden cardiac death if a cardiac death occurred within minutes after the onset of acute symptoms, resulted from a documented cardiac arrhythmia, or was not witnessed and occurred unexpectedly and without recognizable causes (e.g., during sleep). Furthermore, a death was classified as a sudden cardiac death regardless of the underlying condition.	ICD (No ICD)	27 (60)	445 (453)	HR	0.55 (0.31-1.00)	0.049
2 y									
AMIOVIRT Strickberger, 2003 12767651	Death, cardiac arrhythmia	2 y	Sudden cardiac death (actual death); Cardiac death, SCD, duration of follow up 2.2 y	ICD (Amiodarone)	1 (2)	51 (52)	nd	nd	0.7
DEFINITE Kadish, 2004 15152060	Death, cardiac arrhythmia	2 y	Sudden death from arrhythmia	ICD (No ICD)	3 (14)	229 (229)	HR	0.20 (0. 60-0.71)	0.001

Study Author, Year PMID	Outcome name	Timepoint	Outcome description	Intervention (Control)	Events Intervention (Control)	N analyzed Intervention (Control)	Metric	Results (95% CI)	p-value between arms
Fonarow, 2000 10760339	Death, cardiac arrhythmia	2 y	Witnessed cardiac arrest or death within at least 1 hour after onset of acute symptoms or unexpected, unwitnessed death in a patient known to have been well within the previous 24 hours	ICD (Control)	0 (18)	25 (122)	nd	nd	0.05
			Actuarial survival	ICD (Control)	100% (78.3%)	25 (122)	nd	nd	0.05
1 y									
CAT Bansch, 2002 11914254	Death, all-cause longest follow-up	1 y	Sudden cardiac death	ICD (No ICD)	0 (0)	50 (54)	nd	nd	nd

CHF=chronic heart failure, CI=confidence interval, CRT-D=cardiac resynchronization therapy defibrillator, HR=hazards ratio, ICD=implantable cardiac defibrillator, mo=month, nd=not documented, y=year

For study names, see Appendix Table 1.

Appendix Table 8. Risk of bias

Study Author, Year PMID	Overall	Random'n	Alloc Conc	Blinding	Attr'n	ITT	Base Similar	Coint'n	Other Factors	Crossover to ICD	Crossover to no ICD
ICD vs. no ICD											
AMIOVIRT Strickberger, 2003 12767651	Good	Low	Unclear	Low	Low	Low	Low	Low	Yes, highly underpowered	8/52 (15%)	3/51 (6%) heart transplants; 11/51 (22%) also started amiodarone
CABG-Patch Bigger, 1997 9371853	Fair[7]	Low	Low	High	Low	Low	Low	Low	Yes, differential crossover	18/454 (4%)	52/446 (12%)
CAT Bansch, 2002 11914254	Good	Low	Low	Unclear	Low	Low	Low	Low	Yes, highly underpowered	nd	nd
Chan, 2009 20031808	--	--	--	--	--	--	--	--	Yes, observational study	77/456 (17%)	nd
COMPANION Bristow, 2004 15152059	Fair	Low (implied)	Unclear	High	High	Low	Low	Low	Yes, differential attrition and crossover (patients censored when crossed over)	26%	6.5%
DEFINITE Kadish, 2004 15152060	Fair	Low	Unclear	Low	Low	Low	Low	Low	Yes, differential crossover	23/229 (10%)	4/229 (2%)
DINAMIT Hohnloser, 2004 15590950	Good	Low	Low	Low	Low	Low	Low	Low	No	nd	22/332 (7%)
Fonarow, 2000 10760339	--	--	--	--	--	--	--	--	Yes, observational study	0/122 (0%)	1/25 (4%)
IRIS Steinbeck, 2009 19812399	Good	Low (implied)	Unclear	Low	Low	Low	Low	Low	No	39/463 (8%)	45/445 (10%)
MADIT Moss, 1996 8960472	Good	Low	Unclear	Unclear	Low (14%)	Low	Low	Low	No	11/101 (11%)	7/95 (7%)
MADIT II Moss, 2002 11907286	Good[8]	Low (implied)	Unclear	High	Low	Low	Low	Low	No	22/490 (4%)	44/742 (6%)

[7] Poor outcome other than all-cause mortality

Study Author, Year PMID	Overall	Random'n	Alloc Conc	Blinding	Attr'n	ITT	Base Similar	Coint'n	Other Factors	Crossover to ICD	Crossover to no ICD
Mezu, 2011 21640321	--	--	--	--	--	--	--	--	Yes, observational study	nd	nd
OPTIMIZE-HF and GWTG-HF Hernandez, 2010 20009044	--	--	--	--	--	--	--	--	Yes, observational study	nd	nd
SCD-HeFT Bardy, 2005 15659722	Fair	Low (implied)	Unclear	Unclear	Low	Low	Low	High	Yes, differential crossover; differential use of beta blockers[9]	118/1676 (11%)	50/829 (6%)
ICD vs. CRT-D											
Diab, 2011 21700757	Good	Low	Low	Low	Low	Low	Low	Low	Yes, powered for echo outcomes	nd	nd
MADIT-CRT Moss, 2009 19723701	Good	Low (implied)	Unclear	Low	Low	Low	Low	Low	No	ICD->CRT 91/731 (12%); CRT->ICD 82/1089 (8%)	30/1820 (2%)
MENDMI Chung, 2010 20852059	Fair	Low (implied)	Unclear	Unclear	High	Low	Low	Low	Yes, powered for LVEDV	nd	nd
RAFT Tang, 2010 21073365	Good	Low	Unclear	Low	Low	Low	Low	Low	Yes, powered for the primary outcome, a composite of death or hospitalization for heart failure	nd	nd

Random'n: Randomization—What is the risk of selection bias (biased allocation to interventions) due to inadequate generation of a randomized sequence?

Alloc Conc: Allocation Concealment—What is the risk of selection bias (biased allocation to interventions) due to inadequate concealment of allocations before assignment?

Blinding: Outcome Assessor Blinding—For each main outcome or class of outcomes, what was the risk of detection bias due to knowledge of the allocated interventions by outcome assessment (lack of outcome assessor blinding)?

Attr'n: Attrition—For each main outcome or class of outcomes, what is the risk of attrition bias due to amount, nature, or handling of incomplete outcome data?

ITT: Intention-to-Treat—Were all randomized participants analyzed in the group to which they were allocated?

Base Similar: Groups Similarity—Were the groups similar at baseline regarding the most important prognostic indicators?

Coint'n: Cointerventions—Were co-interventions avoided or similar?

Other Factors: Are there other risks of bias? If yes, describe them in Notes?

Crossovers: Numbers of crossovers from one intervention to the other.

---

[8] Fair outcomes other than all-cause mortality

[9] Except in the use of beta-blockers at the time of the last follow-up visit (P<0.001). Amiodarone 72%; Placebo 79%; ICD 82%

nd=not documented
For study names, see Appendix Table 1.

Appendix Table 9. Quality of life in comparative studies of ICDs for primary prevention of SCD

Study Author, Year PMID	N	Study Duration	Intervention	QoL Instrument	Favors*	Net Difference†	95% CI†	Test Range "Worst"	Test Range "Best"	P Value
MADIT II Noyes, 2007 17446823	1,232	3 y	ICD vs. conventional treatment	Health Utility Index 3	0	-0.068	-	-0.371	1.0	NS
AMIOVIRT Strickberger, 2003 12767651	103	1 y	ICD vs. Amiodarone	Quality of Well-being Schedule	0	+7	-0.1, +14	0	110	NS
				State Trait Anxiety Inventory	0	-2	-10, +6	40	160	NS
CABG Patch Namerow, 1999 10527011	490	6 mo	ICD vs. control	SF-36: Physical Limitations	0	-7.5	-	0	100	NS
				Role - Physical	0	-3.5	-	0	100	NS
				Bodily Pain	0	-1.4	-	0	100	NS
				General Health	0	-3.5	-	0	100	NS
				Social Limitations	0	-0.3	-	0	100	NS
				Role - Emotional	No ICD	-11.9	-	0	100	0.003
				Mental Health	No ICD	-4.7	-	0	100	0.004
				Perception of Health Transition	No ICD	+0.3	-	5	1	0.030

CABG Patch= Coronary Artery Bypass Graft Patch; CI=confidence interval; HRQOL=health-related quality of life; ICD=implantable cardioverter–defibrillator; MADIT II=Multicenter Automatic Defibrillator Implantation Trial II; mo=month; NS=not statistically significant; PMID=PubMed ID; QOL=quality of life; y=year

* Notes arm with statistically significantly better change in QOL
† (ΔQOL ICD arm – ΔQOL Treatment arm), data calculated

Health Utility Index (HUI3) "is a questionnaire that assesses HRQOL across 8 attributes: vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain and discomfort and can take values between -0.371 and 1, with -0.371 being the worst possible health state, 0 being death, and 1 being the best possible health state." PMID 17446823

Perception of Health Transition Patients assess their current health status relative to 1 year before. Higher scores represent the perception that health status has gotten worse. PMID 10527011

Quality of Well-being Schedule "A higher level of general well-being is associated with a greater value." The score range is 0 to 110. PMID 12767651

SF-36 "The Medical Outcomes Study 36-Item Short-Form health survey is a widely used health status questionnaire comprised of 36 items… The SF-36 health survey taps 8 health concepts: physical functioning, role limitations due to physical problems, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems, mental health, health transition (perceived change in health)." PMID 10747763

State Trait Anxiety Inventory (STAI) "The score range is 40 to 160. A greater value is associated with a lower level of anxiety." [PMID 12767651] The scale and direction of this scale is different from other reports using STAI.

Appendix Table 10. Relationship between shocks and quality of life in patients with ICDs for primary prevention of SCD

Study Author, Year PMID	N	Study Duration	Comparison	% With Any Shock	QoL Instrument	Favors*	Net Difference†	Test "Worst"	Range "Best"	P Value
MADIT-II Noyes, 2009 19929037	983	3 y	Shock (with ICD) vs. no shock (with or without ICD)	nd	Health Utility Index 3	No shocks	-0.044 adjusted ‡	-0.371	1.0	0.037
CABG Patch Namerow, 1999 10527011	262	6 mo	Shock vs. no shock (all with ICD)	38.5%	SF-36: Physical Limitations	0	-8.0	0	100	NS
					Physical Functioning	0	-8.3	0	100	NS
					Bodily Pain	0	-1.0	0	100	NS
					General Health	0	-4.5	0	100	NS
					Social Functioning	0	-2.8	0	100	NS
					Role Emotional	0	-10.4	0	100	NS
					Mental Health	0	-3.0	0	100	NS
					Perception of Health Transition	0	+0.2	5	1	NS

CABG Patch= Coronary Artery Bypass Graft Patch; ICD=implantable cardioverter–defibrillator; MADIT II=Multicenter Automatic Defibrillator Implantation Trial II; mo=month; NS=not statistically significant; PMID=PubMed ID; QOL: quality of life; y: year.

* Notes whether shocks or no shocks have a statistically significant association with better QOL.

†(ΔQOL ICD arm – ΔQOL Treatment arm)

‡ Effect size of ICD shock since last HRQOL assessment (at 3, 12, 24 and 36 mo after randomization) adjusted for clinical events and randomization to ICD vs. no ICD arm. On Health Utility Index 3 scale, 1 represents perfect health, 0 represents death, and negative values implies HRQOL worse than death.

Appendix Table 11. Quality of reporting for adverse events

Study, Author, Year, PubMed ID	Q1	Q1a	Q2	Q3	Q4	Q5	Q6*	Q7†	Q8
Comparative studies									
ADRIA, Sticherling, 2011, 21156772	Yes	Yes	Yes	Yes	nd	Yes	Yes	Yes	Yes‡
ALTITUDE, Saxon, 2010, 21098452	Yes	Yes	Yes	Yes	nd	Yes	Yes	Yes	No
MADIT-CRT Moss, 2009, 19723701 Moss, 2005, 16274414 (protocol)	No	--	--	Yes	nd	Yes	Yes	Yes	No
MADIT-RIT Moss, 2012 , 23131066	Yes	Yes	Yes	Yes	nd	Yes	Yes	Yes	Yes
MENDMI, Chung, 2010, 20852059	Yes	No	Yes	Yes	nd	Yes	Yes	Yes	Yes‡
Morrison, 2011, 21737019	Yes	Yes	Yes	Yes	nd	Yes	Yes	Yes	Yes
RAFT, Tang, 2010, 21073395 Parkash, 2012, 23159551 Tang, 2009, 19102034 (protocol)	No	--	--	Yes	nd	Yes	Yes	Yes	Yes‡
RIGHT, Gold, 2012, 21978966	Yes	Yes	Yes	Yes	nd	Yes	Yes	Yes	Yes
ICD arms from RCTs									
MADIT II, Moss, 2002, 11907286 §	No	--	--	nd	nd	No	Yes	Yes	--
SCD-HeFT, Bardy, 2005, 15659722 Freudenberger, 2007, 17485579	No	--	--	Yes	nd	Yes	Yes	Yes	--
Cohort studies									
NCDR ICD Database, 11 papers ||	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	--
EPD-Vision 2009-2012, 5 papers ¶	Yes	Yes	Yes	Yes	nd	Yes	Yes	Yes	--
Birnie, 2012, 22311781	Yes	Yes	Yes	nd	nd	No	Yes	Yes	--
Bode, 2012, 22753865	Yes	Yes	Yes	nd	nd	Yes	Yes	Yes	--
Brullmann 2012, 22154315	No	--	--	Yes**	nd	Yes	Yes	Yes	--
Brumberg, 2012, 22519559	Yes	Yes	Yes	nd	nd	No	Yes	Yes	--
Charytan, 2011, 21664735	Yes	Yes	Yes	nd	nd	No	Yes	Yes	--
Cheung, 2012, 22923271	Yes	Yes	Yes	Yes	nd	Yes	Yes	Yes	--
Desai, 2010, 20403488	Yes	Yes	Yes	Yes	nd	Yes	Yes	Yes	--
Ditchl, 2011, 21678454	Yes	Yes	Yes	Yes	nd	Yes	Yes	Yes	--
Gradeus, 2003, 12914630	Yes	No	Yes	Yes	nd	Yes	Yes	Yes	--
Hauser, 2012, 22396584	Yes	Yes	Yes	Yes	nd	Yes	Yes	Yes	--
Landolina, 2011, 21576653	Yes	Yes	Yes	Yes	nd	Yes	Yes	Yes	--

Study, Author, Year, PubMed ID	Q1	Q1a	Q2	Q3	Q4	Q5	Q6*	Q7†	Q8
Larsen, 2010, 20186244	Yes	Yes	Yes	nd	nd	No	Yes	Yes	--
Lee, 2010 20170816; McFadden 2012, 22312139	Yes	Yes	Yes	Yes	nd	Yes	Yes	Yes	--
Lyman, 2011, 21795298	Yes	Yes	Yes	nd	nd	No	Yes	Yes	--
Kleeman, 2012, 22313314	Yes	Yes	Yes	Yes	nd	Yes	Yes	Yes	--
Porterfield, 2010, 19925609	Yes	Yes	Yes	nd	nd	Yes	Yes	Yes	--
Remmelts, 2009, 19325900	Yes	Yes	Yes	nd	nd	No	Yes	Yes	--
Sandesara, 2011, 21086086	Yes	Yes	Yes	Yes	nd	Yes	Yes	Yes	--
Schaer, 2011, 21712284	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	--
Sengupta, 2012, 22314669	No	--	--	nd	nd	No	Yes	Yes	--
Sweeney, 2012, 22387371	Yes	Yes	Yes	Yes	nd	Yes	No††	Yes	--
Sweeney, 2010, 21085109	Yes	No	Yes	Yes	nd	No	Yes	Yes	--
Sweeney, 2005, 15927965	Yes	Yes	Yes	Yes	nd	Yes	Yes	Yes	--
Tsai, 2010, 19262366	No	--	--	nd	nd	No	Yes	Yes	--
Tzogias, 2012, 22314669	Yes	Yes	Yes	nd	nd	No	Yes	Yes	--
Varma, 2010, 20716717	Yes	Yes	Yes	Yes	nd	Yes	Yes	Yes	--
Total Yes/Total	**31/38**	**27/31**	**27/27**	**26/38**	**2/38**	**27/38**	**37/38**	**38/38**	**6/8**

Modified McHarms

Q1. Were any harms prespecified (*a priori)* in Methods section?
Q1a. If yes, were any of them prespecified with *a priori* standardized or precise definitions?
Q2. Were all prespecified harms reported?
Q3. Was the mode of harms collection ACTIVE (sought to collect information on AEs)?
Q4. Was the mode of harms collection PASSIVE? (Participants are not specifically asked about or tested for the occurrence of adverse events. Rather, adverse events are identified based on patient reports made on their own initiative.)
Q5. Did the study specify the TIMING and/or FREQUENCY of collection of harms?
Q6. Is the number of participants who experience harms provided for each arm?
Q7. Is the number at risk for harms (denominator) provided for each arm?
Q8. For studies comparing adverse events across two or more arms: Is there a STATISTICAL analysis of relative harms between groups?

EPD-Vision=Cardiology Information System, Leiden University Medical Center; ICD=implantable cardioverter-defibrillator; NCDR: National Cardiovascular Data Registry; nd=not documented; RCT=randomized, controlled trial. For study name abbreviations, see Appendix Tables 1 and 16.

* Studies had to report number of patients affected.
† Studies had to report number of patients at risk.
‡ Not all outcomes
§ Additional information from protocol paper: Moss et al. *Annals of Noninvasive Electrocardiology* 1999. 4 (1): 83-91.

|| PMIDs: 22095828, 21878667, 21537001, 19383957, 21050975, 21867834, 20863954, 21487093, 19879533, 21883101 and 19221223
¶ PMIDs: 21208947, 19808497, 22056722, 22094073 and 21272746
** Active collection for inappropriate shocks. No data for other outcomes.
†† Number of patients affected not documented. Study used for subgroup table only.

Appendix Table 12. Early (in-hospital) adverse events from the NCDR ICD database - Study characteristics

Author, Year PMID	N	Primary Prevention	Dates	# Sites*	Exclusion Criteria (Prior ICD excluded, unless noted)
Freeman, 2012 22095828	356,515	82%	04/06-03/10	1473	Epicardial lead placement Missing physician data
Haines, 2011 21537001	268,701	78%	01/06-06/08	1300	Pts requiring thoracotomy Includes patients with prior ICD
Cheng, 2010 21050975	226,764	nd	04/06-09/08	nd	
Freeman, 2010 20863954	224,233	81%	01/06-12/08	1356	Epicardial lead placement Hospitals not reporting all implants per quarter of data
Aggarwal, 2009 19879533	164,069	68%†	01/06-12/07	1241	Missing ESRD status data
Peterson, 2009 19221223	161,470	72%	01/06-12/07	1224	
Tsai, 2011 21878667	150,264	100%	01/06-12/08	nd	Secondary prevention Hospitals only submitting data on Medicare patients
Curtis, 2009 19383957	111,293	83%	01/06-06/07	1062	Age <18 Epicardial lead placement Physician <10 procedures during study
Dewland, 2011 21867834	104,049	82%	01/06-12/07	nd	Biventricular ICD
Wei, 2011 21487093	53,198	77%†	01/06-12/08	1300	No data for serum BNP May include prior ICD as this is not stated as exclusion
Tsai, 2011 21883101 Subgroup only	44,805	100%	01/06-12/08	nd	Do not meet MADIT II criteria, which are MI >40 days, LVEF ≤ 30%, NYHA I, II or III

ESRD=end stage renal disease; ICD=implantable cardioverter–defibrillator; LVEF=left ventricular ejection fraction; MADIT II=Multicenter Automatic Defibrillator Implantation Trial II; MI=myocardial infarction; NCDR=National Cardiovascular Data Registry; nd=not documented; NYHA=New York Heart Association; PMID=PubMed ID

* Number of sites is limited to sites achieving NCDR Data Reporting Quality thresholds. It is unclear if and why this would be different in studies with same time period.

† Calculated

Appendix Table 13. Percentage of patients with early (in-hospital) adverse events in NCDR ICD database

	Author	Freeman	Haines	Cheng	Freeman	Aggarwal	Peterson	Tsai	Curtis	Dewland	Wei
	Year	2012	2011	2010	2010	2009	2009	2011	2009	2011	2011 *
	PMID	22095828	21537001	21050975	20863954	19879533	19221223	21878667	19383957	21867834	21487093
	N	356,515	268,701	226,764	224,233	164,069	161,470	150,264	111,293	104,049	53,198
Outcomes	**Range***										
Any adverse event	2.77–3.55	3.08	3.05	--	3.19	3.6†	3.55	3.26	3.7	2.77†	4.59†
Any serious adverse event	1.17–1.35	1.17	--	--	1.20	1.3†	1.35	1.2†‡	--	--	--
Any adverse event or death	1.5–3.37	--	3.2	--	--	--	--	3.37	1.5	--	1.97†
Arteriovenous fistula	<0.1	--	<0.01	--	--	0.01†	0.01	0	<0.1	<0.01†	0.01†
Cardiac arrest	0.26–0.34	0.29	0.30	0.32†	0.3	0.3†	0.34	0.26	0.3	0.28†	0.69†
Cardiac perforation	0.06–0.1	--	0.07	0.08†	--	0.08†	0.08	0.07	0.1	0.06†	0.07†
Cardiac valve injury	<0.1	--	<0.01	--	--	§	0	--	<0.1	<0.01†	--
Conduction block	0.03–0.1	--	0.03	--	--	0.04†	0.04	0.04	0.1	0.03†	0.04†
Coronary venous dissection	0.08–0.15	0.12	0.12	--	--	0.15†	0.15	--	0.1	0.08†	0.19†
Drug reaction	0.09–0.11	--	0.09	0.09†	--	0.1†	0.11	--	0.1	0.10†	0.15†
Hematoma	0.84–1.1	0.86	0.93	1.01†	--	1.0†	1.06	0.94	1.1	0.84†	1.39†
Hemothorax	0.07–0.1	--	0.08	0.09†	0.9	0.1†	0.10	0.09	0.1	0.07†	0.12†
Infection related to device	<0.1	--	0.03	0.02†	--	0.03†	0.03	--	<0.1	0.03*	0.06*
Lead dislodgement	0.73–1.2	1.02	0.93	1.2	1.0	1.1†	1.09	--	1.0	0.73†	1.24†
Myocardial infarction	<0.1	--	0.02	--	--	0.03†	0.03	0.03	<0.1	0.03†	0.05†
Pericardial tamponade	0.07–0.1	--	0.07	--	--	0.1†	0.09	0.10	0.1	0.07†	0.08†
Peripheral embolism	<0.1	--	0.03	0.03†	--	0.03†	0.03	--	0	0.03†	0.06†
Peripheral nerve injury	<0.1	--	<0.01	--	--	§	0	--	<0.1	<0.01†	0.01†
Phlebitis, deep	<0.1	--	0.02	--	--	0.03†	0.03	--	<0.1	0.02†	0.06†
Phlebitis, superficial	0.04–0.1	--	0.04	0.04†	--	0.1†	0.05	--	0.1	0.05†	0.07†
Pneumothorax	0.42–0.51	0.44	0.42	0.48†	0.5	0.5†	0.51	0.45	0.5	0.46†	0.58†
Stroke/CVA	0.05–0.1	--	0.06	--	--	0.1†	0.07	0.05	0.1	0.06†	0.12†
Transient ischemic attack	<0.1	--	0.02	--	--	0.02†	0.02	0.03	<0.1	0.02†	0.04†

CVA=cerebrovascular accident; ICD=implantable cardioverter–defibrillator; NCDR=National Cardiovascular Data Registry; PMID=PubMed ID

* Data from Wei, 2011 PMID 21487093 are outliers and are not included. All patients in this study had B-type natriuretic peptide (BNP) measurement which may represent patients with heart failure. Also the study did not explicitly exclude patients with prior ICD.
† Calculated.
‡ From figure.
§ Likely error in original paper: rate for cardiac valve injury (3%) and peripheral nerve injury (8%) are inconsistent with other studies from NCDR ICD database.

Appendix Table 14: P values for comparisons of early (in-hospital) adverse events by patient subgroup in the NCDR ICD database

	Primary vs. Secondary Prevention	Dual- vs. Single-chamber ICD*	CRT-D vs. Single-chamber ICD*	Older age†	Female‡	Race / Ethnicity	DM	ESRD§	Lower physician implant volume||	Lower hospital implant volume¶
Any adverse event	--	**P<0.001** (I) **P<0.05**** (B) nd (A,D,H)	**P<0.05**** (B) nd (A,D,H)	**P<0.001** (K) **P<0.05****(B)†† nd (G)	**P<0.001** (F) **P<0.05**** (B)	--	--	**P<0.0001** (E)	**P<0.0001** (A)	**P<0.0001** (D) nd (A)
Any serious adverse event	--	nd (A,D)	nd (A,D)	nd (G)	**P<0.001** (F)	--	--	**P<0.0001** (E)	**P<0.0001** (A)	**P<0.0001** (D)
Any adverse event or death	NS (B)	**P<0.001** (G) nd (H)	**P<0.001** (G) nd (H)	**P<0.0001** (B) **P<0.05** (G)‡‡	**P<0.0001** (B) **P<0.001**(G)	**P<0.01** (G)§§ Higher for Black	NS (B)	**P<0.0001** (B) **P<0.001** (G)	--	--
Arteriovenous fistula	--	NS (I) ¶¶	--	nd (G) ¶¶	NS (F) ¶¶	--	--	NS (E)	--	--
Cardiac arrest	--	**P=0.01** (I) nd (A)	nd (A)	nd (G)	NS (F)	--	--	**P<0.0001** (E)	--	--
Cardiac perforation	--	NS (I)	--	nd (G) ¶¶	**P<0.001** (F)	--	--	NS (E)	--	--
Cardiac valve injury	--	NS (I) ¶¶	--	--	NS (F) ¶¶	--	--	***	--	--
Conduction block	--	NS (I) ¶¶	--	nd (G) ¶¶	**P<0.001** (F)	--	--	NS (E)	--	--
Coronary venous dissection	--	**P<0.001** (I) ¶¶ nd (A)	nd (A)	--	**P<0.001** (F)	--	--	**P=0.05** (E) § Lower in ESRD	--	--
Drug reaction	--	NS (I)	--	--	**P=0.015** (F)	--	--	**P<0.0001** (E)	--	--
Hemothorax	--	NS (I)	--	nd (G)	**P<0.001** (F)	--	--	**P=0.01** (E)	--	--
Hematoma	--	**P<0.001** (I) nd (A)	nd (A)	nd (G)	NS (F)	--	--	**P<0.0001** (E)	--	--
Infection related to device	--	NS (I)	--	--	NS (F)	--	--	NS (E)	--	--
Lead dislodgement	--	**P<0.001** (I) **P<0.05**** (C) nd (A)	**P<0.05**(C) ¶¶ nd (A)	NS (C)	**P=0.002** (F) **P<0.001** (C)	**P=0.005** (C) Higher for White†††	NS (C)	NS (E)	--	--
Myocardial infarction	--	**P=0.05** (I) ¶¶	--	nd (G) ¶¶	NS (F)	--	--	NS (E)	--	--
Pericardial tamponade	--	**P=0.01** (I)	--	nd (G)	**P<0.001** (F)	--	--	NS (E)	--	--
Peripheral nerve injury	--	NS (I) ¶¶	--	--	NS (F) ¶¶	--	--	***	--	--

	Primary vs. Secondary Prevention	Dual- vs. Single-chamber ICD*	CRT-D vs. Single-chamber ICD*	Older age†	Female‡	Race / Ethnicity	DM	ESRD§	Lower physician implant volume||	Lower hospital implant volume¶
Peripheral embolism	--	NS (I) ¶¶	--	--	**P=0.014** (F)	--	--	NS (E)	--	--
Phlebitis - deep	--	NS (I) ¶¶	--	--	**P=0.008** (F)	--	--	NS (E)	--	--
Phlebitis - superficial	--	**P=0.009**(I)	--	--	NS (F)	--	--	NS (E)	--	--
Pneumothorax	--	**P<0.001** (I) nd (A)	nd (A)	nd (G)	**P<0.001** (F)	--	--	NS (E)	--	--
Stroke/CVA	--	NS (I)	--	nd (G) ¶¶	NS (F)	--	--	NS (E)	--	--
Transient ischemic attack	--	NS (I) ¶¶	--	nd (G) ¶¶	NS (F) ¶¶	--	--	NS (E)	--	--
Number of papers (reporting statistics)	1 (1)	7 (4)	5 (2)	4 (3)	4 (4)	2 (2)	2 (2)	4 (4)	1 (1)	2 (1)

A-J in parentheses indicate the specific studies. See Study Key, below.
P values <0.05 indicate statistically higher rates of AE in subgroup in column header, unless otherwise noted. NS indicates no statistical difference in AE between subgroups. "nd" indicates paper reported rates of AE by subgroup but did not report statistical comparison between groups.

AE=adverse event; CRT-D=cardiac resynchronization therapy-defibrillator; CVA=cerebrovascular accident; DM=diabetes mellitus; ESRD=end-stage renal disease; ICD=implantable cardioverter–defibrillator; NCDR=National Cardiovascular Data Registry;

* More leads resulted in higher rates of adverse events unless difference between groups NS.
† Adverse events were higher in older patients unless difference between groups NS. Age cutoffs varied between papers.
‡ Female sex resulted in higher rates of adverse events, unless difference between groups NS.
§ Rate of adverse events are higher in patients with ESRD unless difference between groups NS, with the following exception: rates of coronary venous dissection are 0.06% and 0.15%, for ESRD and non-ESRD groups, respectively (E).
|| Rates of adverse events decrease with higher physician implant volume, p=p trend.
¶ Rates of adverse events decrease with higher hospital implant volume, p=p trend.
** Paper reports odds or hazards ratio with confidence interval that does not cross 1.0. No p-value reported.
†† Rates of any adverse event increased statistically across the age groups ≤65, 65-75 and ≥75 (K) and with age >70 (B).
‡‡ Rates of any adverse event or death were statistically for age ≥75 (G) and with age >70 (B).
§§ Rates of any adverse event or death are higher in black subgroup, reference group not documented (G).
¶¶ Less than 10 events in at least one subgroup.
*** Paper reports NS between groups. However rate data is inconsistent in order of magnitude within paper and with other papers.
††† Rates of lead dislodgement differed across White, Black, Hispanic and Other subgroups with Whites having more events (C).

Study Key (author, year, PubMed ID)

A	Freeman, 2012	22095828	E	Aggarwal, 2009	19879533	I	Dewland, 2011	21867834
B	Haines, 2011	21537001	F	Peterson, 2009	19221223	J	Wei, 2011	21487093
C	Cheng, 2010	21050975	G	Tsai, 2011	21878667	K	Tsai, 2011	21883101
D	Freeman, 2010	20863954	H	Curtis, 2009	19383957			

Appendix Table 15. Study characteristics of comparative studies of ICDs with adverse event data

Study Author, Year PMID	Country	N	Primary Prevention	Study Duration	No. Sites	Study Design	Inclusion/Exclusion Criteria	Age (Mean)	Male (%)
ICD vs. CRT-D									
ALTITUDE Saxon, 2010 21098452	US	185,778	nd	2006-05/09*	2096	Prospective cohort	Inclusion: All patients receiving ICD or CRT-D with Boston Scientific remote monitoring device	67	74%
MADIT-CRT Moss , 2009, 19723701	US	1,820	100%	12/04-04/08	110	RCT	Inclusion: Age ≥21, ischemic cardiomyopathy (NYHA class I or II) or nonischemic cardiomyopathy (NYHA class II only), sinus rhythm, ejection fraction ≤30% and prolonged intraventricular conduction with a QRS duration ≥130 msec Exclusion: An existing indication for CRT, implanted pacemaker, ICD or CRT, NYHA class III or IV sympotoms, previous CABG, percutaneous coronary intervention, or MI within 3 mo; atrial fibrillation within 1 mo	65	75%
RAFT Tang, 2010 21073365 Parkash, 2012 23159551	Canada, Europe, Turkey, Australia	1798	86%	01/03-08/10	34	RCT	Inclusion: Primary or secondary prevention, NHYA class II or III symptoms of heart failure despite receiving optimal medical therapy, LVEF ≤30% , ischemic or nonischemic causes, an intrinsic QRS duration ≥120 msec or paced QRS duration ≥200 msec, sinus rhythm or permanent atrial fibrillation or flutter with a controlled ventricular rate or planned atrioventricular-junction ablation after device implantation. Exclusion: Major coexisting illness or a recent cardiovascular event.	66	83%
MENDMI Chung, 2010 20852059	US	80	100%	04/05-03/08	nd	RCT	Inclusion: Recent MI, QRS duration <120 msec, LVEF ≤35%, abnormal wall motion in at least 5 of 16 possible segments measured 2 to 14 days after presentation Exclusion: Permanent or persistent atrial tachyarrhythmia, cardiogenic shock, 2° or 3° heart block, marked renal dysfunction, CABG within 30 days, NYHA class IV, previous ICD or pacemaker or CRT device.	57	75%

Study Author, Year PMID	Country	N	Primary Prevention	Study Duration	No. Sites	Study Design	Inclusion/Exclusion Criteria	Age (Mean)	Male (%)
Single- vs. Dual-	**Chamber**								
ADRIA Sticherling, 2011 21156772	Germany & Switzerland	249	nd	nd	10	RCT	Inclusion: age≥18, indication for ICD; Exclusion: Antibradycardia pacing, permanent atrial fibrillation	63	87%

ADRIA= A+ versus DR Clinical Investigation of Arrhythmia Discrimination; ALTITUDE= the acronym is undefined CABG=Coronary Artery Bypass Graft; CRT-D=cardiac resynchronization therapy-defibrillator; ICD=implantable cardioverter–defibrillator; LVEF=left ventricular ejection fraction; MADIT-CRT=Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy; MENDMI=Prevention of Myocardial Enlargement and Dilation Post Myocardial Infarction Study; MI=myocardial infarction; nd=not documented; No=number; NYHA=New York Heart Association; PMID=PubMed ID; RAFT= Resynchronization–Defibrillation for Ambulatory Heart Failure Trial; RCT=randomized, controlled trial; US=United States

*Month in 2006 in which data collection began was not documented.

Appendix Table 16. Adverse events from comparative studies of ICDs

Study Author, Year PMID	N	Primary Prevention	Intervention	Early Adverse Events			Late Adverse Events & Inappropriate shock		
				Followup	Outcome	% (P value*)	Followup	Outcome	% (P value*)
ICD vs. CRT-D									
ALTITUDE Saxon, 2010 21098452	185,778	nd	ICD vs. CRT-D	--			5 y	Inappropriate shocks	16% vs. 17%
MADIT-CRT Moss, 2009 19723701	1,820	100%	ICD vs. CRT-D	In-hospital	Coronary venous dissection with pericardial effusion	0% vs. 0.5%	2.4 y	Total device-related AE	5.2 vs. 4.5 †
				30 days	Pneumothorax	0.8% vs. 1.7%			
					Infection	0.70% vs. 1.10%			
					Pocket hematoma req. evacuation	2.5% vs. 3.3%			
RAFT Tang, 2010 21073365	1798	86%	ICD vs. CRT-D	30 days	Hemothorax or pneumothorax	0.9% vs. 1.2%	--		
					Hematoma req. intervention	1.2% vs.1.6%			
					Pocket infection req. intervention	1.8% vs. 2.4%			
					Lead dislodgement req. intervention	2.2% vs. 6.9%			
					Pocket problems req. revision	0.1% vs. 0.5%			
					Coronary sinus dissection	0% vs. 1.2%			
MENDMI Chung, 2010 20852059	80	100%	ICD vs. CRT-D	--			1 y	Total AE	42% vs. 52% (NS) ‡
Single- vs. Dual-Chamber									
ADRIA Sticherling, 2011 21156772	249	nd	Single-chamber vs. dual-chamber ICD §	In-hospital	Pneumothorax	0.8% vs. 0.8% (NS)||	1 y	Inappropriate shocks	5.6% vs. 5.6%¶
					Ventricular perforation	0% vs. 0.8% (NS)||		Ventricular lead-related AE	5.6% vs. 4.0% (NS)**

ADRIA= A+ versus DR Clinical Investigation of Arrhythmia Discrimination; AE=adverse events; ALTITUDE= the acronym is undefined; CRT-D=cardiac resynchronization therapy-defibrillator; ICD=implantable cardioverter–defibrillator; MADIT-CRT=Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy; MENDMI=Prevention of Myocardial Enlargement and Dilation Post Myocardial Infarction Study; nd=not documented; PMID=PubMed ID; req=requiring; y=year

* P-value provided only if documented.

† Total device-related AE per 100 device-months

‡ Data calculated. Prespecified composite AE: Left ventricular lead dislodgement, postimplantation left ventricular lead repositioning, permanent failure to deliver biventricular pacing, ventricular tachyarrythmia, hospitalization due to cardiac causes and all-cause mortality.

§ ICD with a single-lead with an integrated atrial sensing rings mounted 15 to 18 cm from the tip of the ICD lead versus a dual lead (dual chamber) ICD

|| Data calculated

¶ Data calculated. 34 episodes in 7 patients vs. 12 episodes in 7 patients.
** Data calculated. Ventricular lead dislocation or high threshold. Follow-up time unclear (in-hospital or 12 months)

Appendix Table 17. Characteristics of studies of late adverse events and inappropriate shock

Author, Year PMID, Country	N	Primary Prevention	Study Duration	# Sites	Study Design	Inclusion/Exclusion Criteria	Age (mean)	Male (%)
ICD arms from RCTs*								
SCD-HeFT Bardy, 2005 15659722, US	829	100%	09/97-10/03	multiple	RCT	Inclusion: Age≥18, NYHA II–III, CHF due to ischemic or nonischemic causes, LVEF ≤35%	60 median	77†
MADIT II Moss, 2002 11907286 US & Europe	742	100%	07/97-11/01	76	RCT	Inclusion: Age ≥21, >1 mo since MI and LVEF≤30 within 3 mo before entry, primary prevention Exclusion: Coronary revascularization within 3 mo, MI within 1 mo, NYHA class IV, advanced cerebrovascular disease	64	84
Other Studies								
Birnie, 2012 22311781, Canada	3,169	67%	12/03-11/07	11	Retrospective cohort	Inclusion: All pts receiving ICDs with Sprint Fidelis leads	63	82†
Bode, 2012 22753865, Germany	903	nd	01/93-12/09 (implant date)	1	Retrospective cohort	Inclusion: All pts receiving first transvenous ICD	64	81
Borleffs, 2009 19808497, NL	2,068‡	55%	1992-02/08	1	Prospective cohort	Inclusion: All pts receiving ICDs Exclusion: Receiving abdominal system or leads with coaxial construction or polyurethane coating	61	80
Brumberg, 2012 22519559, US	621	nd	05/04-12/07 (implant date)	1	Retrospective cohort	Inclusion: All pts receiving initial ICD, revision or upgrade with Fidelis lead	66	75
Brullman, 2012 22154315 Austria, Switzerland	936§	42%†	1987-2009 (implant dates)	2	Prospective cohort	Inclusion: Age ≥18 receiving first ICD for primary or secondary prevention or syncope [2]	63 median	85
Charytan, 2011 21664735, US	9,528	<50%	1994-2006	nd	Registry	Inclusion: Age ≥21, all dialysis pts in USRDS implanted with ICD or CRT	65	70
Cheung, 2012 22923271, US	732	91%	09/04-10/07 (implant date)	1	Retrospective cohort	Inclusion: All pts receiving Sprint Fidelis leads Exclusion: <90 days followup	67	76†
De Bie, 2012 22056722, NL	2,476 ‡	66%	01/00-09/09 (implant date)	1	Prospective cohort	Inclusion: All pts receiving first ICD or CRT-D	62	79
Desai, 2010 20403488, US	549	nd	nd	1	Retrospective cohort	Inclusion: Pts with heart failure receiving ICDs	74	79†
Dichtl, 2011 21678454 Austria, Switzerland	1,117§	40%	nd	2	Prospective cohort	nd	nd ‖	81
RIGHT, Gold, 2012 21978966 US, Canada, Europe	1962	85%†	nd	130	RCT	Inclusion: Pts scheduled to receive ICD	64	79†

Author, Year PMID, Country	N	Primary Prevention	Study Duration	# Sites	Study Design	Inclusion/Exclusion Criteria	Age (mean)	Male (%)
Gradaus, 2003 12914630 Germany	3,344	7.1%	01/98-10/00 (implant date)	62	Retrospective cohort	Inclusion: All pts receiving ICDs	61	80
Hauser, 2002 22396584, US	2,710	75%†	11/01-11/09	3	Retrospective cohort	Inclusion: All pts receiving Sprint Fidelis or Quattro Secure leads	64†	77†
Kleeman, 2012 22313314, Germany	1,411	32%†	1992-05/08 (implant date)	1	Prospective cohort	Inclusion: pts receiving ICDs for primary or secondary prevention	66	79†
Landolina, 2011 21576653 Italy	3,253	87%	2004-2009 (implant date)	117	Prospective cohort	Inclusion: Consecutive pts receiving first single- or dual-chamber ICD or CRT-D systems including pts with preexisting pacemakers.	67	80
Larsen, 2010 20186244 New Zealand	702	27%†	01/00-12/07 (implant date)	2	Retrospective cohort	Inclusion: All pts receiving first ICD	53	77
Lee, 2010 20170816 Canada	3,340¶	70%†	02/07-05/09	nd	Registry	Inclusion: De novo single- or dual-chamber ICD or CRT-D. Exclusion: <45 day followup	64	79
Lyman, 2011 21795298, US	38,992	100	1997-2006	nd	Retrospective cohort	Inclusion: All primary ICD implantation admissions	66	77
MacFadden, 2012 22312139, Canada	5,213¶	72%†	02/07-07/10	nd	Registry	Inclusion: De novo single- or dual-chamber ICD or CRT-D for primary or secondary prevention	65	79
Morrison, 2011 21737019, US	2,671	75%	11/01-12/08 (implant date)	3	Prospective cohort	Inclusion: All pts receiving ICDs with Sprint Fidelis or Quattro Secure leads	65†	77†
MADIT-RIT Moss, 2012 23131066 US & other**	1,500	100%	09/09-07/12	98	RCT	Inclusion: ≥21 yrs, ischemic or nonishchemic heart disease, sinus rhythm, standard indication for ICD or CRT-D for primary prevention Exclusion: Prior ICD, Pacemaker or CRT; Atrial fibrillation; CABG, PCI or MI within 3 mo	63†	71†
RAFT Parkash, 2012 23159551	1787	86%	01/03-08/10	34	RCT	Inclusion: Primary or secondary prevention, NHYA class II or III, LVEF ≤30% , ischemic or nonischemic causes, an intrinsic QRS duration ≥120 msec or paced QRS duration ≥200 msec. (See Appendix Table 14) Exclusion: Major coexisting illness or a recent cardiovascular event.	66	83
Porterfield, 2010 19925609 US, Germany	15,387	nd	06/01-11/07	28	Retrospective cohort	Inclusion: Pts implanted with Riata lead model numbers from 1500 and 7000 series	66	76
Remmelts, 2009 19325900, NL	667	nd	01/96-10/06 (implant date)	1	Retrospective cohort	Inclusion: All pts receiving first ICD Exclusion: Pulse generator inserted in abdominal	58	77

Author, Year PMID, Country	N	Primary Prevention	Study Duration	# Sites	Study Design	Inclusion/Exclusion Criteria	Age (mean)	Male (%)
						pocket or epicardial lead system		
INTRINSIC RV Sandesara, 2011 21086086, US	1,528	nd	nd	108	Post-hoc analysis of RCT	Inclusion: Indication for ICD and VITALITY AVT ICD implanted	65	81†
ALTITUDE Saxon, 2010 21098452, US	185,778	nd	2006-05/09	2096	Prospective cohort	Inclusion: All pts receiving ICD or CRT-D with Boston Scientific remote monitoring device	68†	75†
Schaer, 2011 21712284, NL	536	100%	1998-2008	2	Retrospective cohort	Inclusion: All pts with CAD receiving ICD or CRT-D for primary prevention	63	88
Sengupta, 2012 22314669 US	1644	55%	08/94-05/04 (implant date)	1	Retrospective cohort	Inclusion: All pts receiving first ICD Exclusion: Pts receiving investigational ICDs or ICDs with unclear advisory/non-advisory status	63	78
Sweeney,2012 22387371, US Subgroups only	1,464	100%	08/05-04/11	134	Prospective cohort	Inclusion:All pts receiving Medtronic ICD or CRT-D for primary prevention and LVEF ≤35%	67	72
Sweeney, 2010 20185109, US	2,135	67%	nd	nd	Post-hoc analysis of 4 Trials††	Inclusion:All pts had Medtronic ICDs implanted less than 4 wks before enrollment	66	80
PainFree RX II Sweeney, 2005 15927965, US Subgroups only	582‡‡	43%†	nd	nd	RCT	Inclusion: Pts receiving ICDs Exclusion: Pts unlikely to have substrate for stable monomorphic VT susceptible to pace termination	68	79
Thijssen,2012 22094073, NL	3,194‡	62%	1996-04/11	1	Prospective cohort	Inclusion: All pts receiving ICDs	62	78
Tsai, 2010 19262366, US	1,060	nd	nd	1	Retrospective cohort	Inclusion: All pts receiving ICDs	70	80
Tzogias, 2012 22314669, US	971	85%	09/04-07/07 (implant date)	1	Retrospective cohort	Inclusion: Al pts receiving Sprint Fidelis 6949 lead	68	73
Van Rees, 2012 22352338, NL	1,602‡	58%	1996-02/11	1	Prospective cohort	Inclusion: All pts receiving ICDs with transvenous leads Exclusion: Pts with Sprint Fidelis or Riata leads	61	80
Van Rees, 2011 21272746, NL Subgroups only	1,544‡	56%	1996-2006	1	Prospective cohort	Inclusion: All pts receiving ICDs	61	79
Van Rees, 2012 21920909, NL Subgroups only	1,395‡	100%	01/96-01/09	1	Prospective cohort	Inclusion: All pts receiving ICDs for primary prevention Exclusion: Congenital structural or monogenetic heart disease	63	79
Van Welsenes 2011 21208947, NL	2,134‡	61%	1996-01/08	1	Prospective cohort	Inclusion: All pts receiving ICD Exclusion: Congenital monogenetic cardiac	63	81†

Author, Year PMID, Country	N	Primary Prevention	Study Duration	# Sites	Study Design	Inclusion/Exclusion Criteria	Age (mean)	Male (%)
						disease, hypertrophic obstructive cardiomyopathy, long-QT syndrome, Brugada syndrome, and idiopathic VF, related to an increased risk of cardiac arrhythmia		
TRUST Varma, 2010 20716717, US	1,339	73%†	08/05-05/09	102	RCT (remote monitoring vs. conventional)	Inclusion: Recipients of single- or dual-chamber ICDs for class I/II indications Exclusion: Pacemaker dependent	64†	72†

ALTITUDE=acronym is undefined; CABG=coronary artery bypass grafting; CAD=coronary artery disease; CHF=congestive heart failure; CRT-D=cardiac resynchronization therapy-defibrillator; ICD=implantable cardioverter–defibrillator; INTRINSIC RV= Inhibition of Unnecessary RV Pacing with AV Search Hysteresis in ICDs; LVEF=left ventricular ejection fraction; MADIT II= Multicenter Automatic Defibrillator Implantation Trial II; MADIT-RIT= Multicenter automatic defibrillator implantation trial: reduce inappropriate therapy; MI=myocardial infarction; mo=month; nd=not documented; NL: Netherlands; NYHA=New York Heart Association; PCI=percutaneous coronary intervention; PMID:=PubMed ID; pts=patients; RCT=randomized, controlled trial; RIGHT=Rhythm ID Goes Head to Head Trial; RV=right ventricular; SCD-HeFT= Sudden Cardiac Death in Heart Failure Trial; TRUST= Lumos-T Safely Reduces Routine Office Device Follow Up; US=United States; USRDS=United States Renal Data System; VF=ventricular fibrillation; VT=ventricular tachycardia

* Includes ICD arm of trials from Key Question 1 with ≥500 patients with ICDs and non-ICD control groups.
† calculated
‡ Likely patient overlap between Van Welsenes [21208947], Borleffs [19808497], de Bie [22056722], Thijssen [22094073], Van Rees [21920909], [22352338] and [21272746]. All data from Leiden University Medical Center Cardiology Information System (EPD-Vision).
§ Likely patient overlap between Brullman [22154315] and Ditchl [21678454].
|| 19.3% of patients age >70yr
¶ Patients in Lee [20170816] included in MacFadden [22312139].
** US, Canada, Israel, Japan and Europe
†† Four trials incorporating ATP to reduce shocks (PainFREE Rx, PainFREE Rx II, EMPIRIC, and PREPARE)
‡‡ All patients included in Sweeney, 2010, PMID 20185109

Appendix Table 18. Inappropriate shock (among studies with N ≥500)

Study Author, Year PMID	N	Mean followup	Device Type	Model	Patients with Inappropriate Shock (%)	Between Arm Comparison
Comparative studies						
Morrison, 2011	1,030	34 mo	ICD or CRT-D	Medtronic Sprint Fidelis 6931, 6948, 6949	20%	P<0.001
21737019	1,641	40 mo		Medtronic Quattro Secure 6947	14%	
RIGHT	985	18 mo	Single- or dual-chamber ICD	Guidant Vitality 2 with Rhythm ID	18%*	P<0.001†
Gold, 2012	977			Medtronic Maximo Marquis, Intrinsic, Virtuoso, or Entrust with Wavelet or Enhanced PR logic	12%*	
21978966						
MADIT-RIT	514	17 mo*	Dual-chamber ICD or CRT-D	Conventional programming‡	6%	--
Moss, 2012	500			High-rate therapy‡	3%	P=0.01 vs. conventional
23131066	486			Delayed therapy‡	3%	P=0.03 vs. conventional
ICD arms from RCTs[§]						
SCD-HeFT Bardy, 2005 15659722	829	46 mo median	Single-chamber ICD	Medtronic 7223	2.4% per year	--
Other Studies						
ALTITUDE[‖] Saxon, 2010 21098452	185,778	60 mo	Single- or dual-chamber ICD or CRT-D	Boston Scientific remote-monitoring capable device	16%*[‖]	--
Brullman, 2012 22154315	936[¶]	43 mo	Single- or dual-chamber ICD or CRT-D	nd	21%	--
Van Welsenes, 2011 21208947	2,134	41 mo*	Single- or dual-chamber ICD or CRT-D	Biotronik, Medtronic, Boston Scientific/ Guidant, St. Jude Medical/Ventritex	14%**	--
Desai, 2010 20403488	549	41 mo††	ICD	nd	13%‡‡	--
Larsen, 2010 20186244	702	40 mo median	Single- or dual-chamber ICD or CRT-D	nd	16%	--
Kleemann, 2012 22313314	1,411	36 mo*	Single- or dual-chamber ICD or CRT-D	Biotronik, Medtronic, ELA Medical, Guidant, St. Jude Medical	21%[§§]	--
Dichtl, 2011 21678454	1,117[¶]	35 mo*	Single- or dual-chamber ICD or CRT-D	nd	21%	--
Schaer, 2011 21712284	536	30 mo	Single- or dual-chamber ICD or CRT-D	nd	8.0%	--
MacFadden, 2012, 22312139	5,213	12 mo	Single- or dual-chamber ICD or CRT-D	nd	3.0%	--
INTRINSIC RV Sandesara,2011 21086086	1,528	12 mo	Dual-chamber ICD	Guidant Vitality AVT	6.3%*	

Study Author, Year PMID	N	Mean followup	Device Type	Model	Patients with Inappropriate Shock (%)	Between Arm Comparison
Sweeney, 2010 20185109	2,135	12 mo*	ICD	Medtronic	8.6%*‖‖‖‖	

ATP=antitachycardia pacing; bpm=beats per minute; CRT-D=cardiac resynchronization therapy-defibrillator; ICD=implantable cardioverter–defibrillator; mo=month; nd=not documented; PMID=PubMed ID; VF=ventricular fibrillation; VT=ventricular tachycardia. For study name acronyms see Appendix Table 16.

* calculated

† Single chamber ICDs Guidant vs. Medtronic p=0.003; dual chamber ICDs Guidant vs. Medtronic p=0.006

‡ Boston Scientific ICDs. Conventional programming: For 170 bpm (VT), 2.5 second delay, atrial discriminators on, ATP+shock. For 200 bpm (VF) 1.0 second delay, ATP+shock. High rate therapy: For 170 bpm (VT), monitor only. For 200 bpm (VF) 2.5 second delay, ATP+shock Delayed therapy For 170 bpm (VT-1), rhythm detection on, 60 second delay, ATP+shock For 200 bpm (VT) rhythm detection on, 12 second delay ATP+shock. For 250 bpm (VF) 2.5 second delay ATP+shock. In all devices, ATP was followed by shock therapy only if pacing did not terminate the tachycardia.

§ Includes ICD arm of trials from Key Question 1 with ≥500 patients with ICDs and non-ICD control groups.

‖ ALTITUDE study is also included in Appendix Table 15

¶ Likely patient overlap between Brullman [22154315] and Ditchl [21678454].

** Patients receiving inappropriate shocks experienced 2.9 +/- 4.5 shocks (mean.) Additional papers published from EPD-Vision Database with smaller numbers of patients and similar or shorter follow-up periods report rates of inappropriate shocks ranging from 10%-15% [PMID 21272746, 20185038, 20639206].

†† Unclear if follow-up begins at implantation.

‡‡ 187 inappropriate shocks in 71 patients

§§ 297 patients received 948 inappropriate shocks

‖‖‖‖ Four trials incorporating ATP to reduce shocks (PainFREE Rx, PainFREE Rx II, EMPIRIC, and PREPARE). Pain FREE RX II trial alone reports 9.1% of patients experiencing inappropriate shocks (PMID 15927965) with a followup of 11 months.

Appendix Table 19. Late adverse events: Device- and lead-related adverse events

Study Author, Year PMID	N	Mean Followup	Device Type [Model]*	Device-Related Adverse Events	%	/100 Pt-Y	Lead-Related Adverse Events	%	/100 Pt-Y
ICD arms from RCTs†									
MADIT II Moss, 2002 11907286	742	20 mo	ICD [Guidant]	--			Lead problems requiring surgical intervention	1.8%	--
Other Studies									
Hauser, 2002 22396584	1,675	86 mo maximum	ICD [Quattro Secure 6947]	--			Lead failure	1.4%	--
Sengupta, 2012 22314669	940	70 mo	Single- or dual-chamber ICD or CRT-D	Device malfunction (P<0.001 vs. advisory)	1.6%	--			
Thijssen,2012 22094073	3,194‡	49 mo	Single- or dual-chamber ICD or CRT-D [Multiple] §	System malfunction requiring replacement	2.6%	--	--		
Bode, 2012 22753865	903	49 mo	ICD [High voltage RV lead]	--			High voltage lead defect	7.0%	--
Brullman, 2012 22154315	936||	43 mo	Single- or dual-chamber ICD or CRT-D	--			Lead revision	19%	--
van Rees, 2012 22352338	1,602‡	41 mo	ICD¶	--			Lead failure	3.9%	1.14
							Cumulative lead failure at 8 yr	11.5%	--
Morrison, 2011 21737019	1,641	40 mo	ICD or CRT-D [Quattro Secure 6947]	--			Lead survival: 98.7%	--	--
RAFT Parkash, 2012 23159551	969	39 mo median	ICD or CRT-D	--			Lead failure	0.2%	--
Tsai, 2010 19262366	1,060	38 mo	ICD	ICD malfunction requiring replacement	0.5%	--	Lead repositioning required	0.3%	--
							Lead fracture requiring revision	3.4%	--
Borleffs, 2009 19808497	2,068‡	36 mo	Single- or dual-chamber ICD or CRT-D [Multiple] §	--			Lead failure	3.8%	1.4**
							Lead dislodgement within 6 mo	0.6%††	--
Dichtl, 2011 21678454	1,117||	35 mo††	Single- or dual-chamber ICD or CRT-D	--			Lead dysfunction (undefined)	16.5%	--
Porterfield, 2010 19925609	15,387	18.0 mo	ICD or CRT-D [St. Jude Riata leads 1500 or 7000 series]	--			Total lead-related AE‡‡	3.6%§§	--
							Lead dislodgement	0.9%	--
							Lead malfunction, electrical ||||	0.5%	
							Lead malfunction, other¶¶	1.9%	--

Study Author, Year PMID	N	Mean Followup	Device Type [Model]*	Device-Related Adverse Events	%	/100 Pt-Y	Lead-Related Adverse Events	%	/100 Pt-Y
Landolina, 2011 21576653	3,253	18 mo median	Single- or dual-chamber ICD or CRT-D [Medtronic]	ICD surgical revision	6.4%††	5.2***	Lead malfunction	--	1.2†††
							Lead dislodgement	--	2.8†††
Charytan, 2011 21664735	9,528 ESRD	16.8 mo††	ICD or CRT-D	Generator replacement	--	3.9	Lead removal / change	--	3.4
TRUST Varma, 2010 20716717	1,339	13.4 mo††	Single- or dual-chamber ICD [Biotronik] ‡‡‡	ICD replacement	<0.1%††	0.1	Lead revision	0.9%††	0.8
							Lead replacement	0.4%††	0.34
							ICD explanted due to lead fracture	<0.1%	0.07
Lyman, 2011 21795298	38,992	3 mo	ICD	ICD mechanical complications	4.2%	--	--		
		12 mo		ICD revision procedure	2.2%	--			
Gradaus, 2003 12914630	2,554	2.6 mo	Single- or dual-chamber ICD	ICD dislocation	1.9%	--	Lead dislocation	1.4%	--
MacFadden, 2012 22312139	4,830	1.5 mo††	Single- or dual-chamber ICD or CRT-D	--			Lead replacement	1.0%††	--
							Lead repositioning, any	1.2%††	--
							Lead dislodgement, repositioned	0.6%††	--
							Lead dislodgement, not repositioned	2.5%††	--

AE=adverse event; CRT-D=cardiac resynchronization therapy-defibrillator; ESRD=end stage renal disease; ICD=implantable cardioverter–defibrillator; mo=month; PMID=PubMed ID; Pt-y=Patient-year; RV=right ventricular; y=year. For study name acronyms see Appendix Table 16.

* Generator and/or lead models noted if documented.
† Includes ICD arm of trials from Key Question 1 with ≥500 patients with ICDs.
‡ Likely patient overlap between Thijssen,2012 [22094073], Borleffs [19808497] and Van Rees [22352338]. All data from Leiden University Medical Center Cardiology Information System (EPD-Vision).
§ Implanted systems were manufactured by Biotronik, Medtronic, Boston Scientific/Guidant, and St. Jude Medical/Ventritex
|| Likely patient overlap between Brullman [22154315] and Ditchl [21678454].
¶ These analyses exclude patients receiving Sprint Fidelis or Riata leads.
** per 100 lead-years.
†† calculated
‡‡ Includes perforations (0.38%), dislodgements, electrical malfunctions and other lead-related AEs.
§§573 events in 561 patients
|||| Insulation damage, conductor fracture, impedance issues
¶¶ Sensing issues, elevated threshold, loss of capture, diaphragmatic simulation, High DFT, unclassified
*** 220 events in 210 patients. From figure.
††† Includes 44 lead failures among 1985 patients with Sprint Fidelis (1.5 per 100 pt-yrs.)
‡‡‡ Biotronik generators capable of automatic remote home monitoring (Lumax 300 DR-T (1.3%), Lumax 300 VR-T (1.1%), Lumax 340 DR-T (22.2%), Lumax 340 VR-T (11.9%), Lumos DR-T (33.9%), Lumos

Appendix Table 20. Late adverse events: Device- and lead-related adverse events in patients with advisory leads or devices

Study Author, Year PMID	N	Mean Followup	Device Type [Model]*	Device- or Lead-Related Adverse Events	%
Advisory Devices					
Sengupta, 2012 22314669	704	70 mo	Single- or dual-chamber ICD or CRT-D [Advisory]	Device malfunction	6.1% †
Advisory Leads					
Hauser, 2002 22396584	1,035	86 mo maximum	ICD [Fidelis leads 6931, 6948, 6949]	Lead failure	8.1%
Tzogias, 2012 22314669, US	971	46 mo	Single- or dual-chamber ICD or CRT-D [Fidelis 6949 leads]	Lead failure	7.1%
				Lead fracture leading to failure	6.8% ‡
Cheung, 2012 22923271	602	42 mo median	ICD [Fidelis leads models 6949, 6931, 6948]	Lead failure	8.4%
Birnie, 2012 22311781	3,169	41 mo median	ICD [Fidelis leads]	Lead failure	7.9%
RAFT Parkash, 2012 23159551	818	39 mo median	ICD or CRT-D [Fidelis leads]	Lead failure	5.5%§
				Lead fracture	1.65% per year
Morrison, 2011 21737019	1,030	34 mo	ICD or CRT-D [Fidelis leads 6931, 6948, 6949]	Lead survival: 87.0%‖	--
Brumberg, 2012 22519559	621	32 mo	Single- or dual-chamber ICD or CRT-D [Fidelis leads]	Lead malfunction	8.4% ‡

CRT-D=cardiac resynchronization therapy-defibrillator; ICD=implantable cardioverter–defibrillator; mo=month; PMID=PubMed ID.

* Generator and/or lead models noted if documented.

† 4.0% advisory-related malfunctions. Device malfunction is patients with non-advisory devices: 1.6% (see Appendix Table 18). P<0.001 advisory versus non-advisory devices.

‡ Calculated

§ Lead failure in patients with non-Fidelis leads: 0.2%. (see Appendix Table 18A). P<0.0001 Fidelis vs. non-Fidelis leads.

‖ Lead survival in patients with non-advisory leads: 98.7% (see Appendix Table 18A). P<0.001 advisory versus non-advisory leads.

Appendix Table 21. Late adverse events: Infection and deep vein thrombosis

Study Author, Year PMID	N	Mean Followup	Device Type [Model]*	Infection	%	/100 Pt-Y	Thrombosis	%
ICD arms from RCTs†								
SCD-HeFT Freudenberger, 2007 17485579	681‡	45.5 mo Median	Single-chamber ICD [Medtronic 7223]	--			Any thrombo-embolic event	2.9%
MADIT II Moss, 2002, 1190728(	742	20 mo	ICD [Guidant]	Non-fatal infection requiring surgical intervention	0.7%	--	--	
Other Studies								
Thijssen,2012 22094073	3,194§	49 mo	Single- or dual-chamber ICD or CRT-D [Multiple‖]	Infection requiring ICD replacement	3.7%	--	--	
Bode, 2012 22753865	903	49 mo	ICD	--			Symptomatic subclavian venous thrombosis	0.9%
van Rees, 2012 22352338	1,602§	41 mo	ICD ¶	Infection (undefined)	2.7%		--	
Tsai, 2010 19262366	1,060	38 mo	ICD	Lead infection requiring antibiotics	0.5%	--	--	
Borleffs, 2009 19808497	2,068§	36 mo	Single- or dual-chamber ICD or CRT-D [Multiple‖]	Pocket infection requiring lead removal	1.7%**	--	--	
De Bie, 2012 22056722	2,476§	30 mo median	ICD or CRT-D [Multiple‖]	Infection requiring device and lead removal	2.6%	--	--	
Landolina, 2011 21576653	3,253	18 mo median	Single- or dual-chamber ICD or CRT-D [Medtronic]	Incisional infection treated conservatively	--	0.3**	--	
				Infection requiring system removal	--	0.7††		
Charytan, 2011 21664735	9,528 ESRD	16.8 mo**	ICD or CRT-D	Severe infection during 1st year ‡‡	--	98.8	--	
				Subsequent years (N=4,552)	--	63.9		
				Device infection	--	4.2		
Gradaus, 2003 12914630	1,033	12 mo	Single- or dual-chamber ICD	Infection of ICD device	0.9%**	--	--	
Remmelts, 2009 19325900	667	10 mo**	Single- or dual-chamber ICD or CRT-D	Pocket infection with or without bacteremia or ICD-related endocarditis	1.0%§§	1.2	--	
Lyman, 2011 21795298	38,992	3 mo	ICD	Infection	1.2%	--	Deep venous thrombosis	1.0%
Lee, 2010 20170816	3,340	1.5 mo	Single- or dual-chamber ICD or CRT-D	Pocket infection requiring debridement	1.0%	--	Subclavian venous thrombosis	0.2%
				Sepsis	0.2%	--		

CRT-D=cardiac resynchronization therapy-defibrillator; ESRD=end stage renal disease; ICD=implantable cardioverter–defibrillator; MADIT II=Multicenter Automatic Defibrillator Implantation Trial II; mo=month; PMID=PubMed ID; Pt-Y=patient-year; SCD-HeFT= Sudden Cardiac Death in Heart Failure Trial.

* Generator and/or lead models noted if documented.
† Includes ICD arm of trials from key question 1 with ≥500 patients with ICDs.
‡ Excludes patients with atrial fibrillation or flutter at baseline.
§ Likely patient overlap between Borleffs [19808497], de Bie [22056722], Thijssen [22094073] and Van Rees [22352338]. All data from Leiden University Medical Center Cardiology Information System (EPD-Vision).
|| Implanted systems were manufactured by Biotronik, Medtronic, Boston Scientific/Guidant, and St. Jude Medical/Ventritex
¶ Excludes patients receiving Sprint Fidelis or Riata leads
** Calculated
†† From figure
‡‡ Severe infection defined as any of the following: episodes coded as device infections, postoperative infections, bacteremia, septicemia, and all episodes in which patients received intravenous vancomycin.
§§ Data calculated. Includes N=2 (0.3%) post-operative infections.

Appendix Table 22. P values for comparisons of late adverse events and inappropriate shock by patient subgroup

Adverse Event	Primary vs. Secondary Prevention	LVEF	NYHA Class IV vs. III	Dual- vs. Single-chamber ICD	Single-chamber ICD vs. CRT-D	Age	Female*	DM	Lower Physician Volume	Lower Hospital Volume	OR vs. CCL
Inappropriate shocks	NS (A, E, F,U) **P<0.001** (M) worse for secondary	NS (P)†	NS (P)	**P=0.02** (C) worse for single-chamber NS (A, I)	NS (A)	**P<0.01** (A), **P<0.04** (K) **P<0.05** (Q,M‡) nd (D) worse for younger	NS (A, M, O)	**P=0.0076** (D) NS (J,M)	--	--	--
Surgical intervention / revision	NS (G§)‖	--	--	**P=0.004** (H) worse for dual-chamber	**P<0.001** (H) worse for CRT-D	--	--	--	NS (N)	**P<0.01** (N)¶	--
Lead dislodgement, requiring intervention or undefined	NS (H**)	--	--	--	--	NS (H**,Q)	NS (H**, O§)	NS (J)	--	--	--
Lead dislodgement, no intervention	--	--	--	--	--	--	**P=0.003** (O)	--	--	--	--
Lead malfunction / replacement / failure	--	--	--	--	--	NS (Q)	**P<0.001** (O)	--	--	--	--
Recalled lead malfunction / failure	NS (R, S, T)	**P=0.026** (R) worse for higher; NS (S, T, V) ††	NS (V)	NS (L) NS (T) ‡‡	**P=0.0021** worse for CRT (V§§); NS (L, T‡‡)	**P=0.016** worse for older (R); NS (L, T, V)	**P=0.028** (L) **P=0.005** (R) **P=0.02** (S), NS (T, V)	NS (T)	--	--	--
Infection	NS (H)	--	--	nd (B§)	--	NS (H,Q)	NS (H,O§)	NS (H, J)	NS (N)	NS (N)	nd (B§)
Deep vein thrombosis	--	--	--	--	--	--	**P=0.004** (O§)	--	**P<0.01** (N)¶	NS (N)	--
Number of papers (reporting statistics)	10 (10)	5 (5)	2 (2)	7 (6)	5 (5)	10 (9)	9 (9)	5 (5)	1 (1)	1 (1)	1 (0)

A-R in parentheses indicate specific studies. (See Study Key, below)
P values <0.05 indicate statistically higher rates of AE in subgroup, unless otherwise noted. NS indicates no statistical difference in AE between subgroups. nd indicates paper reported rates of AE by subgroup but did not report statistical comparison between groups.

CCL=cardiac catheterization lab; CRT-D=cardiac resynchronization therapy-defibrillator; DM=diabetes mellitus; ICD=implantable cardioverter–defibrillator; LVEF=left ventricular ejection fraction; MADIT II=Multicenter Automatic Defibrillator Implantation Trial II; MADIT-CRT=Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy; NYHA=New York Heart Association; OR=operating room; PMID=PubMed ID

* Adverse events are higher or NS different in females compared with males.
† LVEF 31-35% vs. ≤30%
‡ Paper reports hazard ratio with confidence interval that does not cross 1.0.
§ Less than 10 events in at least one subgroup.

|| Patients receiving ICDs for primary prevention compared with "other indications".
¶ Higher rates of AEs with lower ICD implantation volume.
** Left ventricular lead dislodgement in CRT-D patients
†† Worse for each 10% absolute increase in LVEF (R); not statistically significantly different for continuous LVEF (S, T) or LVEF >23% vs. ≤23% (V).
‡‡ No statistically significant difference across three subgroups: single-chamber ICD, dual-chamber ICD and CRT-D.
§§ Single- or dual-chamber ICD vs. CRT-D

Study Key (Author, Year, PMID)

A	Van Rees, 2011, 21272746	H	Landolina, 2011, 21576653	O	McFadden, 2012, 22312139
B	Remmelts, 2009, 19325900	I	MADIT II, Berenbom, 2005, 16255753	P	Sweeney, 2012, 22387371
C	Larsen, 2010, 20186244	J	MADIT-CRT, Martin, 2011, 21350054	Q	van Rees, 2012, 21920909
D	Sandesara, 2011, 21086086	K	Brullman, 2012, 22154315	R	Birnie, 2012, 22311781
E	Van Welsenes, 2011, 21208947	L	Brumberg, 2012, 22519559	S	Cheung, 2012, 22923271
F	Ditchl, 2011, 21678454	M	Kleemann, 2012, 2232331	T	Tzogias, 2012, 22314669
G	Varma, 2010, 20716717	N	Lyman, 2011, 21795298	U	Sweeney, 2005, 15927965
				V	RAFT, Parkash, 2012, 23159551

Appendix Table 23. Eligibility criteria

Study Author, Year PMID Country	Study type (# of centers)	Total N (Study duration)	Inclusion						Specification regarding:		
			Age, y	Etiology	1° prevention	LVEF	NYHA	QRS interval	MI	Revascularization excluding CABG	CABG
Studies of patients with ischemic cardiomyopathy and remote MI (>30 or 40 days)											
ICD vs. no ICD											
MADIT Moss, 1996 8960472 US and EU	RCT (32)	196 (5 y, mean 27 mo)	25-80	Ischemic	Yes	≤35	I, II, III	nd	Inc: Q-wave or enzyme-positive MI ≥3 wk	Exc: Coronary angioplasty within the past 3 mo	Exc: CABG within the past 2 mo
MADIT II Moss, 2002 11907286 US and EU	RCT (76)	1232 (mean 20 mo; range 6 d-53 mo)	>21	Ischemic	Yes	≤30	I, II, III	nd	Inc: MI ≥1 mo Exc: MI within the past mo	Exc: Coronary revascularization within prior 3 mo	nd
Studies of patients with nonischemic cardiomyopathy											
ICD vs. no ICD											
AMIOVIRT Strickberger, 2003 12767651 US	RCT (10)	103 (5 y)	≥18	Nonischemic	Yes	≤35	I, II, III	nd	nd	nd	nd
CAT Bansch, 2002 11914254 Germany	RCT (15)	104 (6 y)	18-70	Nonischemic	Yes	≤30	II, III	nd	Exc: History of prior MI	nd	nd
DEFINITE Kadish, 2004 15152060 US	RCT (25)	458 (5 y; mean 2.4 y)	nd	Nonischemic	Yes	<36	I, II, III	nd	nd	nd	nd

Study Author, Year PMID Country	Study type (# of centers)	Total N (Study duration)	Inclusion						Specification regarding:		
			Age, y	Etiology	1° prevention	LVEF	NYHA	QRS interval	MI	Revascularization excluding CABG	CABG
Fonarow, 2000 10760339 US	Retrospective cohort (1)	147 (mean 22 mo)	nd	Nonischemic	Yes	<35	III, IV	nd	nd	nd	nd
Studies of patients with mixed ischemic and nonischemic cardiomyopathy											
ICD vs. no ICD											
Chan, 2009 20031808 US	Prospective cohort (7)	965 (5 y)	≥18	Ischemic, nonischemic	Yes	≤35	nd	>120 ms	Inc: MI of ≥30 d	nd	nd
COMPANION Bristow, 2004 15152059 US	RCT (128)	1520 (3.0 y; median 14 mo)	nd	Ischemic, nonischemic	Yes	≤35	III, IV	≥120 ms	nd	nd	nd
Mezu, 2011 21640321 US	Retrospective cohort (1)	152 (4 y; mean 2.3 y)	≥80	Ischemic, nonischemic	Yes	≤35	I, II, III (class I only if prior MI)	nd	nd	nd	nd
OPTIMIZE-HF and GWTG-HF Hernandez, 2010 20009044 US	Retrospective cohort, registry (nd)	4685 (3 y)	65-84	Ischemic, nonischemic	Yes	≤35	nd	nd	nd	nd	nd
SCD-HeFT Bardy, 2005 15659722 US	RCT (nd)	2521 (6 y; median 46 mo)	>18	Ischemic, nonischemic	Yes	≤35	II, III	nd	nd	nd	nd
ICD vs. CRT-D											
Diab, 2011 21700757 UK	RCT (1)	73 (6 mo)	nd	Ischemic, nonischemic	nd	≤35	III, IV	≥120 ms	nd	nd	nd

Study Author, Year PMID Country	Study type (# of centers)	Total N (Study duration)	Inclusion						Specification regarding:		
			Age, y	Etiology	1° prevention	LVEF	NYHA	QRS interval	MI	Revascularization excluding CABG	CABG
MADIT-CRT Moss, 2009 19723701 US, Canada, EU	RCT (110)	1820 (4 y; mean 2.4 y)	≥21	Ischemic, nonischemic	nd	≤30	I, II	≥130 ms	Exc: MI within 3 mo	Exc: PCI within 3 mo	Exc: Previous CABG within 3 mo
RAFT Tang 2010 21073365 Multi	RCT	1798 (mean 40 mo)	nd	Ischemic, nonischemic	nd (86% were primary prevention)	≤30	II, III	Intrinsic: ≥120 ms; Paced: ≥200ms	nd	nd	nd
Studies of patients with ischemic cardiomyopathy and recent MI (<30 days) or revascularization											
ICD vs. no ICD											
CABG-Patch Bigger, 1997 9371853 US and Germany	RCT (37)	900 (4 y; mean 2.7 y)	<80	Ischemic	Yes	<36	nd	≥114 ms	nd	nd	Inc: Scheduled for CABG Exc: Emergency CABG
DINAMIT Hohnloser, 2004 15590950 Multi	RCT (73)	674 (4 y; mean 2.5 y)	18-80	Ischemic	Yes	≤35	I, II, III	nd	Inc: MI (6-40 d prior)	Exc: 2-vessel PCI since the qualifying MI	Exc: CABG since the qualifying MI or planned within 4 wk
IRIS Steinbeck, 2009 19812399 Germany	RCT (nd)	898 (6 y; mean 37 mo)	18-80	Ischemic	Yes	≤40	I, II, III	nd	Inc: MI (5-31 d prior)	nd	Exc: An indication for CABG
ICD vs. CRT-D											

Study Author, Year PMID Country	Study type (# of centers)	Total N (Study duration)	Inclusion						Specification regarding:		
			Age, y	Etiology	1° prevention	LVEF	NYHA	QRS interval	MI	Revascularization excluding CABG	CABG
MENDMI Chung, 2010 20852059 US	RCT (29)	80 (12 mo)	nd	Ischemic	nd	≤35	I, II, III	<120 ms	Inc: Anterior MI 3-14 d	nd	Exc: CABG 30 d before or after enrollment

1°=primary, CABG=coronary artery bypass graft, EU=Europe, ICD=implantable cardiac defibrillator, LVEF=left ventricular ejection fraction, MI=myocardial infarction, mo=month, ms=millisecond, nd=not documented, NYHA=New York Heart Association, RCT=randomized controlled trial, UK, United Kingdom, US=United States, wk=week, y=year
For study names, see Appendix Table 1.