

APPENDIX 1: Literature Search Strategy for Clinical Effectiveness Studies

Guide to Search Syntax (DIALOG®)

- ! Explode the search term. Retrieve the search concept plus all narrower terms.
- ? Truncation symbol, single character. Retrieve plural and variant ending of search terms.
- " " Search phrases.
- () Proximity operator. Words must be adjacent.
- (l) Proximity operator. Links descriptors and subheadings.
- (n) Proximity operator. Words must be near each other in any order.
- (w) Proximity operator. Words must be adjacent.
- ab Search in article abstract.
- de Descriptor i.e., subject heading (a controlled, thesaurus term).
- dt Document type.
- id Identifier (includes CAS Registry Number and natural language indexing terms).
- rn CAS Registry Number.
- ti Search in titles.
- tn Brand name.
- tw Text word.

DATABASES	DATES / LIMITS	SUBJECT HEADINGS/KEYWORDS
DIALOG OneSearch® MEDLINE® BIOSIS Previews® EMBASE® PASCAL	Human 1980 -	<p>1. Defibrillators, Implantable/de [MeSH heading for MEDLINE®]</p> <p>OR</p> <p>(Automatic Cardioversion OR Cardioversion OR Defibrillator)/de [EMTREE terms for EMBASE®]</p> <p>OR</p> <p>(Implantable Defibrillator OR Implantable Cardioverter-Defibrillator OR Cardioversion)/de [BIOSIS Previews® thesaurus terms]</p> <p>OR</p> <p>(implant?(3n)defib? OR ((icd OR icds) NOT "icd()10") OR aicd OR implant?(2n)cardioversion OR implant?(2n)cardioverter? OR internal(2n)cardioversion OR internal(2n)cardioverter OR internal(2n)defib OR internal(2n)defibrillator? OR internal(2n)defibrillation)/ti,ab [Textwords searched in title, abstract]</p> <p>2. (Preventive Medicine OR Primary Prevention OR "prevention and control")/de [MeSH heading for MEDLINE®]</p> <p>OR</p> <p>(Heart Infarction Prevention OR Primary Prevention OR Preventive Health Service OR Preventive Medicine OR Prevention OR "prevention and control" OR Prophylaxis)/de</p>

		<p><i>[EMTREE terms for EMBASE®]</i></p> <p>OR</p> <p>(Prevention OR Preventive Medicine OR Primary Health Care OR Prophylaxis)/de <i>[BIOSIS Previews® thesaurus terms]</i></p> <p>OR</p> <p>(Primary Prevention OR Preventive Medicine OR Preventive Maintenance)/de <i>[Pascal vocabulary terms]</i></p> <p>OR</p> <p>(asymptomatic OR high()risk OR increase?()risk OR primary OR primar?(2n)prevent? OR prevent? OR prophyla?)/ti,ab <i>[Textwords searched in title, abstract]</i></p> <p>3. (Death, Sudden, Cardiac OR Death, Sudden)/de <i>[MeSH heading for MEDLINE®]</i></p> <p>OR</p> <p>Sudden Death/de <i>[EMTREE terms for EMBASE®]</i></p> <p>OR</p> <p>(Sudden Cardiac Death OR Sudden Death)/de <i>[BIOSIS Previews® thesaurus terms]</i></p> <p>OR</p> <p>(cardiac())sudden()death? OR sudden()cardiac()death? OR sudden()heart()death? OR sudden(2w)death? OR SCD OR SHD)/ti,ab <i>[Textwords searched in title, abstract]</i></p> <p>4. Cardiovascular Diseases!/de OR (Arrhythmia! AND Heart Ventricles)/de <i>[MeSH heading for MEDLINE®]</i></p> <p>OR</p> <p>Cardiovascular Disease!/de <i>[EMTREE terms for EMBASE®]</i></p> <p>OR</p> <p>(Cardiovascular Death OR Cardiovascular Disease OR Cardiovascular Events OR Cardiovascular Function OR Cardiovascular Morbidity OR Cardiovascular Mortality OR Coronary Disease OR Coronary Artery Disease OR Coronary Heart Disease OR Cerebrovascular Disease OR Cerebrovascular Disorders OR Heart Disease)/de <i>[BIOSIS Previews® thesaurus terms]</i></p>
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		<p><i>OR</i></p> <p>(Cardiovascular Disease OR Cardiovascular Diseases OR Coronary Artery Disease OR Coronary Heart Disease OR Cerebrovascular Disease OR Heart Disease)/de <i>[Pascal vocabulary terms]</i></p> <p><i>OR</i></p> <p>(arrhythmia? OR arrythmia? OR cardio(2n)disease? OR cardiovascular()disease? OR cardio()vascular()disease? OR cardiovascular()dysfunction? OR cardiovascular()event? OR coronary()artery()disease? OR coronary(2n)disease? OR CVD OR heart()attack? OR heart()disease? OR heart()failure OR myocardial()infarct? OR systolic()dysfunction? OR ventric?()dysfunction? OR ventric?()rhythm OR ventric?()fibrillation OR ventric?()tachycardia OR coronary(3n)(event? OR disease? OR bypass? OR thrombol? OR thrombos? OR angioplast?) OR cerebrovascular(5n)(disease? OR disorder?) OR vascular(3n)(disease? OR disorder?) OR myocard?(5n)(isch?emi? OR infarct?) OR heart(3n)(diseas? OR isch?emi? OR infarct?) OR angina)/ti,ab <i>[Textwords searched in title, abstract]</i></p> <p>5. (Controlled Clinical Trials! OR Epidemiologic Research Design!)/de <i>[MeSH headings for MEDLINE®]</i></p> <p><i>OR</i></p> <p>dt=(Multicenter Study OR Randomized Controlled Trial OR Controlled Clinical Trial) <i>[Document type in MEDLINE®]</i></p> <p><i>OR</i></p> <p>(Major Clinical Study OR Multicenter Study OR Controlled Study! OR Randomized Controlled Trial OR Evidence Based Medicine!)/de <i>[EMTREE terms for EMBASE®]</i></p> <p><i>OR</i></p> <p>(Multicenter Study OR Randomized Controlled Trial OR Randomized Clinical Trial OR Randomized Trial OR Evidence-Based Medicine)/de <i>[BIOSIS Previews® thesaurus terms]</i></p> <p><i>OR</i></p> <p>(random? OR sham? OR placebo? OR singl?()(blind? OR dumm? OR mask?) OR doubl?()(blind? OR dumm? OR mask?) OR tripl?()(blind? OR dumm? OR mask?) OR trebl?()(blind? OR dumm? OR mask?) OR control?()(study OR studies OR trial?) OR RCT? ? OR (multicent? OR multi()cent?)(study OR studies OR trial?))/ti,ab</p> <p><i>OR</i></p>
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		<p>(Meta-Analysis OR Technology Assessment, Biomedical!)/de [MeSH headings for MEDLINE®]</p> <p>OR</p> <p>dt=Meta-Analysis [Document type in MEDLINE®]</p> <p>OR</p> <p>Meta-Analysis/de [BIOSIS Previews® thesaurus term]</p> <p>OR</p> <p>Meta Analysis/de [EMTREE terms for EMBASE®]</p> <p>OR</p> <p>(meta()analy? OR metaanaly? OR met()analy? OR metanaly? OR health()technology()assessment? OR meta()regression? OR metaregression? OR mega()regression? OR systematic?()(literature()review? OR review? OR overview?) OR methodologic?()(literature()review? OR review? OR overview?) OR quantitative()(review? OR overview? OR syntheses?) OR research()(integration? OR overview?) OR integrative(2w)(review? OR overview?) OR collaborative()(review? OR overview?)/ti,ab</p> <p>6. ((1 AND 2 AND 4) OR (1 AND 3)) AND 5</p> <p><i>Search performed on 26 September 2005; monthly alerts set up on MEDLINE®, EMBASE® and BIOSIS Previews® and were ongoing until 01/25/2006.</i></p> <p><i>Total Hits = 2062 Records (2050 'clinical' results + 12 sys. review /meta-analysis results)</i></p>
Cochrane Library Issue 3 2005	1980 -	<p>Same MeSH and keywords as per MEDLINE® search, excluding study design filter. Appropriate syntax used.</p> <p><i>Initial search performed on 3 October 2005 and updated with subsequent database updates. Last update performed on 02/06/2006.</i></p> <p><u>Total Hits =</u> <i>Cochrane Database of Systematic Reviews = 1 Records, 1 Unique</i> <i>DARE = 7 Records, 4 Unique</i> <i>CENTRAL = 151 Records, 2 Unique</i> <i>Abstracts by INAHTA and other HTAs = 4 Records, 2 Unique</i></p>
Web sites of health technology assessment (HTA) and related agencies; trial registries; other databases		<p>AHRQ; National Research Register; University of York NHS Centre for Reviews and Dissemination – CRD databases; LILACS etc.</p>

APPENDIX 2: Literature Search Strategy for Cost-effectiveness Studies

DATABASES	DATES / LIMITS	SUBJECT HEADINGS/KEYWORDS
DIALOG OneSearch [®] MEDLINE [®] BIOSIS Previews [®] EMBASE [®] PASCAL	1980 -	<p>1. Defibrillators, Implantable/de <i>[MeSH heading for MEDLINE[®]]</i></p> <p>OR</p> <p>(Automatic Cardioversion OR Cardioversion OR Defibrillator)/de <i>[EMTREE terms for EMBASE[®]]</i></p> <p>OR</p> <p>(Implantable Defibrillator OR Implantable Cardioverter-Defibrillator OR Cardioversion)/de <i>[BIOSIS Previews[®] thesaurus terms]</i></p> <p>OR</p> <p>(implant?(3n)defib? OR ((icd OR icds) NOT "icd()10") OR aicd OR implant?(2n)cardioversion OR implant?(2n)cardioverter? OR internal(2n)cardioversion OR internal(2n)cardioverter OR internal(2n)defib OR internal(2n)defibrillator? OR internal(2n)defibrillation)/ti,ab <i>[Textwords searched in title, abstract]</i></p> <p>2. (Preventive Medicine OR Primary Prevention OR "prevention and control")/de <i>[MeSH heading for MEDLINE[®]]</i></p> <p>OR</p> <p>(Heart Infarction Prevention OR Primary Prevention OR Preventive Health Service OR Preventive Medicine OR Prevention OR "prevention and control" OR Prophylaxis)/de <i>[EMTREE terms for EMBASE[®]]</i></p> <p>OR</p> <p>(Prevention OR Preventive Medicine OR Primary Health Care OR Prophylaxis)/de <i>[BIOSIS Previews[®] thesaurus terms]</i></p> <p>OR</p> <p>(Primary Prevention OR Preventive Medicine OR Preventive Maintenance)/de <i>[Pascal vocabulary terms]</i></p> <p>OR</p>

		<p>(asymptomatic OR high()risk OR increase?()risk OR primary OR primar?(2n)prevent? OR prevent? OR prophyla?)/ti,ab <i>[Textwords searched in title, abstract]</i></p> <p>3. (Death, Sudden, Cardiac OR Death, Sudden)/de <i>[MeSH heading for MEDLINE®]</i></p> <p>OR</p> <p>Sudden Death/de <i>[EMTREE terms for EMBASE®]</i></p> <p>OR</p> <p>(Sudden Cardiac Death OR Sudden Death)/de <i>[BIOSIS Previews® thesaurus terms]</i></p> <p>OR</p> <p>(cardiac()sudden()death? OR sudden()cardiac()death? OR sudden()heart()death? OR sudden(2w)death? OR SCD OR SHD)/ti,ab <i>[Textwords searched in title, abstract]</i></p> <p>4. Cardiovascular Diseases!/de OR (Arrhythmia! AND Heart Ventricles)/de <i>[MeSH heading for MEDLINE®]</i></p> <p>OR</p> <p>Cardiovascular Disease!/de <i>[EMTREE terms for EMBASE®]</i></p> <p>OR</p> <p>(Cardiovascular Death OR Cardiovascular Disease OR Cardiovascular Events OR Cardiovascular Function OR Cardiovascular Morbidity OR Cardiovascular Mortality OR Coronary Disease OR Coronary Artery Disease OR Coronary Heart Disease OR Cerebrovascular Disease OR Cerebrovascular Disorders OR Heart Disease)/de <i>[BIOSIS Previews® thesaurus terms]</i></p> <p>OR</p> <p>(Cardiovascular Disease OR Cardiovascular Diseases OR Coronary Artery Disease OR Coronary Heart Disease OR Cerebrovascular Disease OR Heart Disease)/de <i>[Pascal vocabulary terms]</i></p> <p>OR</p> <p>(arrhythmia? OR arrythmia? OR cardio(2n)disease? OR cardiovascular()disease? OR cardio()vascular()disease? OR cardiovascular()dysfunction? OR cardiovascular()event? OR coronary()artery()disease? OR coronary(2n)disease? OR CVD OR</p>
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		<p>heart()attack? OR heart()disease? OR heart()failure OR myocardial()infarct? OR systolic()dysfunction? OR ventric?()dysfunction? OR ventric?()rhythm OR ventric?()fibrillation OR ventric?()tachycardia OR coronary(3n)(event? OR disease? OR bypass? OR thrombol? OR thrombos? OR angioplast?) OR cerebrovascular(5n)(disease? OR disorder?) OR vascular(3n)(disease? OR disorder?) OR myocard?(5n)(isch?emi? OR infarct?) OR heart(3n)(diseas? OR isch?emi? OR infarct?) OR angina)/ti,ab <i>[Textwords searched in title, abstract]</i></p> <p>5. (Economics OR ‘Costs and Cost Analysis’! OR Health Care Costs! OR Economic Value of Life OR Economics, Medical OR Economics, Pharmaceutical OR Models, Economic! OR Markov Chains OR Monte Carlo Method OR Decision Support Techniques! OR Uncertainty OR Quality of Life OR Quality-Adjusted Life Years OR Economics, Nursing OR Economics, Hospital)/de <i>[MeSH headings for MEDLINE®]</i></p> <p>OR</p> <p>(Health Economics! OR Economic Evaluation! OR Pharmacoeconomics! OR Economic Aspect! OR Quality Adjusted Life Year OR Quality of Life!)/de <i>[EMTREE terms for EMBASE®]</i></p> <p>OR</p> <p>(Economics OR Economic Model OR Pharmacoeconomics OR Cost Benefit Analysis OR Cost Efficiency Analysis OR Cost Utility Analysis OR Health Care Economics OR Medical Cost OR Expenditure OR Budget OR Budgeting OR Budget Control OR Budgetary Control OR Cost Estimation OR Cost Evaluation OR Cost Lowering OR Cost Minimization OR Cost Savings OR Cost Utility Analysis OR Cost Price OR Quality Adjusted Life Year OR Quality of Life)/de <i>[Pascal vocabulary terms]</i></p> <p>OR</p> <p>(Economic Impact OR Economic Value OR Pharmacoeconomics OR Health Care Cost OR Economic Factors OR Economics OR Cost Analysis OR Economic Analysis OR Cost OR Cost-Effectiveness OR Cost Effectiveness OR Costs OR Quality Of Life OR Health Care Cost OR Cost Savings OR Cost-Benefit Analysis OR Hospital Costs OR Medical Costs OR Quality-of-Life)/de <i>[BIOSIS Previews® thesaurus terms]</i></p> <p>OR</p> <p>(econom? OR cost OR costly OR costing OR costed OR price OR prices OR pricing OR priced OR discount OR discounts OR discounted OR discounting OR expenditure OR expenditures OR budget? OR afford? OR pharmacoeconomic? OR pharmaco(1n)economic? OR cost?(1n)(util? OR effective? OR efficac? OR benefit? OR consequence? OR analy? OR minimi? OR</p>
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		<p>saving? OR breakdown OR lowering OR estimate? OR variable? OR allocation))/ti,ab <i>[Textwords searched in title, abstract]</i></p> <p>OR</p> <p>(cost?(1n)(control OR illness OR sharing OR life OR lives OR affordabl? OR instrument? OR technolog? OR day? OR fee OR fees OR charge OR charges) OR unit(1n)cost OR unit?(1n)costs OR drug()cost OR drug()costs OR hospital()costs OR health(1n)care()costs OR medical(1n)cost OR medical(1n)costs OR markov OR markow OR monte()carlo OR decision(1n)(tree? OR analy? OR model?) OR (value OR values OR valuation)(2n)(money OR monetary OR life OR lives OR cost) OR QOL OR QOLY OR QOLYs OR HRQOL OR QALY OR QALYs OR quality(1n)life OR willingness(1n)pay OR quality(1n)adjusted()life)year? OR sensitivity()analys?s)/ti,ab <i>[Textwords searched in title, abstract]</i></p> <p>6. ((1 AND 2 AND 4) OR (1 AND 3)) AND 5</p> <p><i>Search performed on 26 September 2005; monthly alerts set up on MEDLINE[®], EMBASE[®] and BIOSIS Previews[®] and were ongoing until 01/25/2006.</i></p> <p><i>Total Hits = 584 Unique Records (i.e. records remaining after 'clinical' records from 1-A search NOT'd out)</i></p>
Cochrane Library Issue 3 2005	1980 -	<p>Same MeSH and keywords as per MEDLINE[®] search, excluding study design filter. Appropriate syntax used.</p> <p><i>Initial search performed on 3 October 2005 and updated with subsequent database updates. Last update performed on 02/06/2006.</i></p> <p><u>Total Hits =</u> <i>NHS EED = 20 Records, 3 Unique</i></p>
OHE-IFPMA Database Ltd. HEED: Health Economic Evaluations Database September 2005		<p>implantable defibrillator OR cardioverter OR cardioversion OR ICD OR sudden death OR (defibrillator* AND primary) [all fields], <i>0 Unique Relevant Results</i></p>
Websites of health economics research groups		<p>Health Economics Research Group (HERG); Health Economics Research Unit (HERU); etc.</p>

APPENDIX 3: Clinical Trial Data Extraction Form

Reviewer		
Study title		
Author		
ID number	Year	
Methods		
Study design	RCT	
Study duration		
Population <ul style="list-style-type: none"> • number of patients randomized • number of patients completing study 		
Diagnosis		
Eligibility criteria		
Jadad score <ul style="list-style-type: none"> • randomized? • randomization appropriately described? • blinded? • blinding appropriately described? • withdrawals described? 		
Country of origin		
Industry sponsorship	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown	
Baseline Characteristics of Study Participants		
<ul style="list-style-type: none"> • age • New York Heart Association class • ejection fraction • ischemic • diabetic • others 		
Outcomes	With ICD	Without ICD
Efficacy: number of patients with all-cause death or sudden cardiac death Safety <ul style="list-style-type: none"> • adverse events (AEs) • number of patients withdrawn because of AEs Psychosocial Ethical Comments		

APPENDIX 4: Economic Study Data Extraction Form

Reference ID, Author, Title, Journal	
Reviewer	
Date	
Study Characteristics	
1. Question and objective	
2. Population selection criteria	
3. Population characteristics	
4. Indication	
5. Intervention	
6. Comparator	
7. Type of economic analytic techniques	
8. Analysis type	
9. Currency and year	
10. Care setting or geographic location	
11. Perspective and justification if possible	
12. Discounting rate and justification	
13. Analysis time horizon	
Source of Data	
14. Effectiveness data	
15. Cost data	
Method for Estimation of Benefits and Costs	
16. Valuation for clinical outcomes or benefits	
17. Health outcomes	
18. Instruments to value health states	
19. Approach for health state assessment	
20. Estimated cost scope	
21. Cost components and justification	
22. Cost estimation approach	
23. Modelling (if model used)	
24. Sensitivity analysis type	
25. Key parameters on which sensitivity analysis was done	
26. Statistical analysis	
Subgroup analysis (if applicable)	
Results and Analysis	
27. Clinical outcomes and benefits	
28. Costs	
29. Synthesis of costs and benefits	
30. Statistical analysis	
31. Sensitivity analysis	
32. Subgroup analysis	

Conclusion	
33. Conclusion	
34. Limitation	
35. Other relevant publication	
36. Future study suggestion	
37. Funding source (if applicable)	
Reviewers' Comments	

APPENDIX 5: Clinical Trial Quality Assessment Form

Reference	Reviewer	Score
Study design		
1. large RCT (>50 in each arm): 5 points 2. small RCT: 3 points 3. prospective: 2 points 4. retrospective: 1 point If RCT* <ul style="list-style-type: none"> • randomization appropriately described? • blinded? • blinding appropriately described? • withdrawals described? 		
Study performance		
1. patient selection 2. description or specification of intervention 3. specification and analysis of study 4. patient disposal 5. outcomes reported <ul style="list-style-type: none"> • information missing=0 point, information limited=1 point, information satisfactory=2 points 		
Overall Score		
Category A (overall score 11.5 to 15.0): high quality (high degree of confidence in study findings) B (overall score 9.5 to 11.0): good quality (some uncertainty regarding study findings) C (overall score 7.5 to 9.0): fair to good quality (some limitations that should be considered in implementation of study findings) D (overall score 5.5 to 7.0): poor to fair quality (substantial limitations in study; findings should be used cautiously) E (overall score 1 to 5.0): poor quality (unacceptable uncertainty of study findings)		

*RCT gets full points if it addressed all four characteristics. Half a point deducted if one characteristic not addressed.

APPENDIX 6: List of Excluded Clinical Studies

Quantity of research available

Original electronic search: 2,273 citations

Citations excluded: 2,149

124 potentially relevant articles retrieved for full-text review

Number of reports excluded: 113

Reports included in review: Bänsch,¹⁸ Bardy,¹⁹ Bigger,²⁰ Buxton,²¹ Greenberg,²² Hohnloser,²³ Kadish,²⁴ Moss,²⁵ Moss,²⁶ Raviele,²⁷ Strickberger,²⁸

Reasons for exclusion

Study design inappropriate for review (63)

The Coronary Artery Bypass Graft (CABG) Patch Trial. The CABG Patch Trial Investigators and Coordinators. *Prog Cardiovasc Dis* 1993;36(2):97-114.

Summaries for patients. What are the clinical and economic implications of following MADIT-II criteria for surgically implanting automatic cardiac defibrillators? *Ann Intern Med* 2005;142(8):139.

Use of implantable cardioverter-defibrillators for prevention of sudden death in patients at high risk for ventricular arrhythmia. *Technol Eval Cent Asses Program Exec Summ* 2005;19(19):1-6. Available: http://www.bcbs.com/tec/Vol19/19_19.pdf (accessed 2005 Oct 31).

National Institute for Clinical Excellence. *Guidance on the use of implantable cardioverter defibrillators for arrhythmias* [Technology assessment report no 11]. London: The Institute; 2000. Available: <http://www.nice.org.uk/pdf/Nice+DEFIBRILATOR++guidance.pdf> (accessed 2005 Oct 31).

Almquist AK, Montgomery JV, Haas TS, Maron BJ. Cardioverter-defibrillator implantation in high-risk patients with hypertrophic cardiomyopathy. *Heart Rhythm* 2005;2(8):814-9.

Anderson JL, Hallstrom AP, Epstein AE, Pinski SL, Rosenberg Y, Nora MO, et al. Design and results of the antiarrhythmics vs implantable defibrillators (AVID) registry. *Circulation* 1999;99(13):1692-9. Available: <http://circ.ahajournals.org/cgi/reprint/99/13/1692> (accessed 2005 Oct 21).

Ashwath ML, Sogade FO. Ejection fraction and QRS width as predictors of event rates in patients with implantable cardioverter defibrillators. *South Med J* 2005;98(5):513-7.

Babuty D, Fauchier L, Charniot JC, Grimbert M, Tena-Carbi D, Poret P, et al. Complications à moyen terme du défibrillateur cardiaque automatique implantable. *Arch Mal Coeur Vaiss* 2000;93(11):1269-75.

Begley DA, Mohiddin SA, Tripodi D, Winkler JB, Fananapazir L. Efficacy of implantable cardioverter defibrillator therapy for primary and secondary prevention of sudden cardiac death in hypertrophic cardiomyopathy. *Pacing Clin Electrophysiol* 2003;26(9):1887-96.

Bhatia A, Cooley R, Berger M, Blanck Z, Dhala A, Sra J, et al. The implantable cardioverter defibrillator: technology, indications, and impact on cardiovascular survival. *Curr Probl Cardiol* 2004;29(6):303-56.

Bocker D, Haverkamp W, Block M, Borggrefe M, Hammel D, Breithardt G. Comparison of *d,l*-sotalol and implantable defibrillators for treatment of sustained ventricular tachycardia or fibrillation in patients with coronary artery disease. *Circulation* 1996;94(2):151-7. Available: <http://circ.ahajournals.org/cgi/content/full/94/2/151> (accessed 2005 Oct 21).

Botto GL, Proclemer A, Luzi M, Ruffa F, Gorgoglione MG, Ferrari G. Primary prevention of sudden cardiac death: indications for cardioverter-defibrillator implantation. *Ital Heart J* 2005;6(3):210-5.

Brunckhorst C, Binggeli C, Hellermann JP, Scharf C, Holzmeister J, Duru F. ICD-Therapie bei Patienten mit koronarer Herzkrankheit - Inzidenz adäquater Interventionen [ICD therapy in patients with coronary artery disease: incidence of adequate interventions]. *Ther Umsch* 2004;61(4):271-8.

Buxton AE. Risk stratification for sudden death: do we need anything more than ejection fraction? *Card Electrophysiol Rev* 2003;7(4):434-7.

Cannom DS. Matching cardiac rhythm management technology to patient needs: pacing/ablation/implantable cardioverter defibrillators. *Am J Cardiol* 2000;86(Suppl 9A):58-70K.

Cawley PJ, Al Khatib SM. Amiodarone versus implantable cardioverter defibrillator for asymptomatic nonsustained ventricular tachycardia in nonischemic dilated cardiomyopathy. *Am Heart J* 2004;147(5):790-1.

Chan PS, Hayward RA. Mortality reduction by implantable cardioverter-defibrillators in high-risk patients with heart failure, ischemic heart disease, and new-onset ventricular arrhythmia: an effectiveness study. *J Am Coll Cardiol* 2005;45(9):1474-81.

Crespo EM, Kim J, Selzman KA. The use of implantable cardioverter defibrillators for the prevention of sudden cardiac death: a review of the evidence and implications. *Am J Med Sci* 2005;329(5):238-46.

Desai AS, Fang JC, Maisel WH, Baughman KL. Implantable defibrillators for the prevention of mortality in patients with nonischemic cardiomyopathy: a meta-analysis of randomized controlled trials. *JAMA* 2004;292(23):2874-9.

Epstein AE. An update on implantable cardioverter-defibrillator guidelines. *Curr Opin Cardiol* 2004;19(1):23-5.

Evonich RF, Maheshwari A, Gardiner JC, Khasnis A, Kantipudi S, Ip JH, et al. Implantable cardioverter defibrillator therapy in patients with ischemic or non-ischemic cardiomyopathy and nonsustained ventricular tachycardia. *J Interv Card Electrophysiol* 2004;11(1):59-65.

Gasparini M, Lunati M, Bocchiardo M, Mantica M, Gronda E, Frigerio M, et al. Cardiac resynchronization and implantable cardioverter defibrillator therapy: preliminary results from the InSync Implantable Cardioverter Defibrillator Italian Registry. *Pacing Clin Electrophysiol* 2003;26(1 Pt 2):148-51.

Gillis AM. Rhythm control in atrial fibrillation: endpoints for device-based trials. *Heart Rhythm* 2004;1(2 Suppl):B52-7.

Greene HL. The implantable cardioverter-defibrillator. *Clin Cardiol* 2000;23(5):315-26.

Grimm W, Hoffmann J, Müller HH, Maisch B. Implantable defibrillator event rates in patients with idiopathic dilated cardiomyopathy, nonsustained ventricular tachycardia on holter and a left ventricular ejection fraction below 30%. *J Am Coll Cardiol* 2002;39(5):780-7.

Grimm W, Alter P, Maisch B. Arrhythmia risk stratification with regard to prophylactic implantable defibrillator therapy in patients with dilated cardiomyopathy. Results of MACAS, DEFINITE, and SCD-HeFT. *Herz* 2004;29(3):348-52.

Hauser RG, Kallinen L. Deaths associated with implantable cardioverter defibrillator failure and deactivation reported in the United States Food and Drug Administration Manufacturer and User Facility Device Experience Database. *Heart Rhythm* 2004;1(4):399-405.

Henry VR, Smart S, Akram S, McGrath K, Wright I, Blackman S, et al. Living with an ICD: the price of saving a life. *Br J Cardiol* 2004;11(4):261-2.

Hlatky MA, Sanders GD, Owens DK. Evidence-based medicine and policy: the case of the implantable cardioverter defibrillator. *Health Aff (Millwood)* 2005;24(1):42-51.

- Jayatileke I, Doolan A, Ingles J, McGuire M, Booth V, Richmond DR, et al. Long-term follow-up of implantable cardioverter defibrillator therapy for hypertrophic cardiomyopathy. *Am J Cardiol* 2004;93(9):1192-4.
- Kang S, Cannom DS. Current role of device therapy to reduce sudden cardiac death in heart failure. *Curr Heart Fail Rep* 2004;1(3):104-10.
- Korte T, Jung W, Ostermann G, Wolpert C, Spehl S, Esmailzadeh B, et al. Hospital readmission after transvenous cardioverter/defibrillator implantation. A single centre study. *Eur Heart J* 2000;21(14):1186-91.
- Kron J. Clinical significance of device-related complications in clinical trials and implications for future trials: insights from the Antiarrhythmics Versus Implantable Defibrillators (AVID) trial. *Card Electrophysiol Rev* 2003;7(4):473-8.
- Lee DS, Green LD, Liu PP, Dorian P, Newman DM, Grant FC, et al. Effectiveness of implantable defibrillators for preventing arrhythmic events and death: a meta-analysis. *J Am Coll Cardiol* 2003;41(9):1573-82.
- Levine JH, Waller T, Hoch D, Greenberg S, Goldberger J, Kadish A. Implantable cardioverter defibrillator: use in patients with no symptoms and at high risk. *Am Heart J* 1996;131(1):59-65.
- Maron BJ, Shen WK, Link MS, Epstein AE, Almquist AK, Daubert JP, et al. Efficacy of implantable cardioverter-defibrillators for the prevention of sudden death in patients with hypertrophic cardiomyopathy. *N Engl J Med* 2000;342(6):365-73.
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APPENDIX 7: Inclusion and Exclusion Criteria for RCTs Included in this Review

Study	Inclusion Criteria	Exclusion Criteria
Bänsch ¹⁹	18 to 70 years old, with symptomatic dilated cardiomyopathy for ≤ 9 months, impaired left ventricular function (LVEF $\leq 30\%$ obtained during left ventricular angiography), NYHA class II or III	coronary artery disease (coronary stenosis $>70\%$) excluded by angiography; history of MI, myocarditis, excessive alcohol consumption, symptomatic bradycardia, ventricular tachycardia, ventricular fibrillation; listing for heart transplantation at time of presentation; significant valvular disease and hypertrophic or restricted cardiomyopathy; NYHA class I or IV; mental inability to understand protocol
Bardy ²⁰	≥ 18 years of age, NYHA class II or III chronic stable CHF due to ischemic or non-ischemic causes, LVEF $\leq 35\%$	NR
Bigger ²¹	scheduled for coronary bypass surgery, <80 years old, LVEF <0.36 , abnormalities on signal averaged ECG	history of sustained ventricular tachycardia or fibrillation, diabetes mellitus with poor blood glucose control or recurrent infections, previous or concomitant aortic- or mitral-valve surgery, concomitant cerebrovascular surgery, serum creatinine >3 mg/dL (265 $\mu\text{mol/L}$), emergency coronary bypass surgery, non-cardiovascular condition with expected survival <2 years, inability to attend follow-up visits
Buxton ²²	coronary artery disease, LVEF $\leq 40\%$, asymptomatic unsustained ventricular tachycardia (lasting ≤ 3 beats) that occurred ≤ 6 months before enrolment, ≤ 4 days after most recent MI or revascularization procedure	history of syncope or sustained ventricular tachycardia or fibrillation >48 hours after onset of MI, unsustained ventricular tachycardia occurred only in setting of acute ischemia, metabolic disorders, drug toxicity
Greenberg ²³	post-infarction, EF $\leq 30\%$	NR
Hohnloser ²⁴	8 to 80 years old, MI 6 to 40 days previously, LVEF ≤ 0.35 and standard deviation of RR intervals ≤ 70 msec or mean RR interval ≤ 750 msec (heart rate ≥ 80 beats per minute) over 24-hour period, as assessed by 24-hour Holter monitoring performed >3 days after infarction	CHF or NYHA class IV at time of randomization, non-cardiac disease that limited life expectancy, CABG performed since qualifying infarction or planned to be performed <4 weeks after randomization, 3-vessel percutaneous coronary intervention performed since qualifying infarction, on waiting list for heart transplant, ongoing ICD therapy, prior implantation of permanent pacemaker, sustained ventricular tachycardia or fibrillation >48 hours after qualifying infarction, low probability that study ICD could be implanted <7 days after randomization, expected poor compliance with protocol
Kadish ²⁵	LVEF $<36\%$, presence of ambient arrhythmias, history of symptomatic heart failure, presence of non-ischemic dilated cardiomyopathy	NYHA class IV CHF, not candidate for implantation of cardioverter-defibrillator, electrophysiologic testing within 3 months before start of trial, permanent pacemaker; cardiac transplantation imminent, familial cardiomyopathy associated with sudden death, acute myocarditis or congenital heart disease

Moss ²⁷	25 to 80 years old, Q-wave or enzyme-positive MI ≥ 3 weeks before entry; episode of asymptomatic, unsustained ventricular tachycardia unrelated to acute MI, EF ≤ 0.35 ; NYHA class I, II, or III; no indications for CABG or coronary angioplasty on basis of cardiac evaluation within past 3 months	previous cardiac arrest or ventricular tachycardia causing syncope unassociated with acute MI, symptomatic hypotension while in stable rhythm, MI within past 3 weeks, CABG within past 2 months, coronary angioplasty within past 3 months, women of childbearing age not using medically prescribed contraceptives, advanced cerebrovascular disease, any condition other than cardiac disease associated with reduced likelihood of survival for duration of trial, participation in other clinical trials
Moss ²⁶	>21 years old; MI ≥ 1 month before entry; EF < 0.30 ; NYHA class I, II, III at time of enrolment	indication approved by FDA for implantable defibrillator, NYHA class IV at enrolment, coronary revascularization within preceding 3 months, MI within past month, advanced cerebrovascular disease, women of childbearing age not using medically prescribed contraceptives, any condition other than cardiac disease associated with high likelihood of death during trial, unwilling to sign consent form for participation
Raviele ²⁸	acute MI 5 to 30 days before enrolment; LVEF $\leq 35\%$; one or more of following risk factors: premature ventricular contractions (≥ 10 per hour), reduced heart rate variability with standard deviation of normal QRS complex intervals, positive signal averaged ECG; on and able to tolerate therapy with metoprolol at dosage of at least 25 mg/day	contraindications or intolerance to metoprolol, history of sustained ventricular arrhythmias associated or unassociated with acute MI (except primary ventricular fibrillation), non-sustained ventricular tachycardia during 24-hour Holter monitoring, residual myocardial ischemia for which early myocardial revascularization needed, cardiogenic shock, severe hypotension, NYHA class IV, life expectancy < 1 year, irreversible brain damage, refusal or inability to participate in study, participation in other trials, long distance from patient's residence to referring centre, other factors that made follow-up impossible
Strickberger ²⁹	non-ischemic dilated cardiomyopathy, EF ≤ 0.35 , asymptomatic non-sustained ventricular tachycardia, NYHA class I to III, ≥ 18 years old	syncope, pregnancy, contraindication to amiodarone or defibrillator therapy, concomitant therapy with class I antiarrhythmic drug

LVEF=left ventricular ejection fraction; NYHA=New York Heart Association; CHF=congestive heart failure; MI=myocardial infarction; NR=not reported; ECG=electrocardiogram; RR=relative risk.

APPENDIX 8: Characteristics of Patients Participating in RCTs Included in this Review

Study	Study Name	Inclusion Criteria	Treatment Arm	Age (years)	Male/Female (%)	Ischemic	Ejection Fraction (%)	NYHA Class (%)
Bänsch ¹⁹	CAT	age 18 to 70 years; symptomatic dilated cardiomyopathy ≤ 9 months; LVEF $\leq 30\%$; NYHA class II or III; no prior MI	with ICD	52 \pm 12*	86/14	no	24 \pm 6*	II 66.7 III 33.3
			without ICD	52 \pm 10*	74/26	no	25 \pm 8*	II 64.1 III 35.8
Bardy ²⁰	SCD-HeFT	age ≥ 18 years; NYHA class II or III chronic, stable CHF due to ischemic or non-ischemic causes; LVEF $\leq 35\%$	with ICD	60.1 (51.9 to 69.2) [†]	77/23	both	24 (19 to 30) [†]	II 68 III 32
			without ICD, with amiodarone	60.4 (51.7 to 68.3) [†]	76/24	both	25 (20 to 30) [†]	II 71 III 29
			without ICD, with placebo	59.7 (51.2 to 67.8) [†]	77/23	both	25 (20 to 30) [†]	II 70 III 30
Bigger ²¹	CABG Patch	age < 80 years; scheduled for coronary bypass surgery; LVEF < 0.36 ; abnormalities on signal averaged ECG	with ICD	64 \pm 9*	87/13	yes	27 \pm 6*	II or III 71
			without ICD	63 \pm 9*	82/18	yes	27 \pm 6*	II or III 74
Buxton ²²	MUSST	coronary artery disease; LVEF $\leq 40\%$; asymptomatic unsustained ventricular tachycardia (lasting ≤ 3 beats) occurred ≤ 6 months before enrolment; ≤ 4 days after most recent MI or revascularization procedure	with ICD	67 (60 to 72) [†]	90/10	yes	30 (20 to 35) [†]	I 37 II 39 III 24
			without ICD	66 (58 to 72) [†]	90/10	yes	29 (22 to 35) [†]	I 36 II 38 III 25
Hohnloser ²⁴	DINAMIT	age 18 to 80 years; MI 6 to 40 days previously; LVEF ≤ 0.35 ; standard deviation of RR intervals ≤ 70 msec or mean RR interval ≤ 750 msec (heart	with ICD	61.5 \pm 10.9*	75.9/24.1	yes	28 \pm 5*	I 13.5 II 60.9 III 25.6
			without ICD	62.1 \pm 10.6*	76.6/23.4	yes	28 \pm 5*	I 12.0 II 58.7 III 29.3

Study	Study Name	Inclusion Criteria	Treatment Arm	Age (years)	Male/Female (%)	Ischemic	Ejection Fraction (%)	NYHA Class (%)
		rate, ≥ 80 beats/minute) over 24-hour period, as assessed by 24-hour Holter monitoring performed at least 3 days after infarction						
Kadish ²⁵	DEFINITE	LVEF $< 36\%$; presence of ambient arrhythmias; history of symptomatic heart failure; presence of non-ischemic dilated cardiomyopathy	with ICD	58.4 (20.3 to 83.9) [‡]	72.5/27.5	no	20.9 (7 to 35) [‡]	I 25.3 II 54.2 III 20.5
			without ICD	58.1 (21.8 to 78.7) [‡]	69.9/30.1	no	21.8 (10 to 35) [‡]	I 17.9 II 60.7 III 21.4
Moss ²⁷	MADIT-I	age 25 to 80 years; Q-wave or enzyme-positive MI ≥ 3 weeks before entry; episode of asymptomatic, unsustained ventricular tachycardia unrelated to acute MI; LVEF ≤ 0.35 ; NYHA class I, II, or III; no indications for CABG or coronary angioplasty on basis of cardiac evaluation within past 3 months	with ICD	62 \pm 9 [*]	92/8	yes	27 \pm 7 [*]	II or III 63
			without ICD	64 \pm 9 [*]	92/8	yes	25 \pm 7 [*]	II or III 67
Moss ²⁶ and Greenberg ²³	MADIT-II	age > 21 years; MI ≥ 1 month before entry; LVEF < 0.30 ; NYHA class I, II, III at time of enrolment	with ICD	64 \pm 10 [*]	84/16	yes	23 \pm 5 [*]	I 35 II 35 III 25 IV 5
			without ICD	65 \pm 10 [*]	85/15	yes	23 \pm 6 [*]	I 39 II 34 III 23 IV 4
Raviele ²⁸	ICD	acute MI 5 to 30 days before enrolment; LVEF $\leq 35\%$; ≥ 1 of following	with EPS-ICD	66.5 \pm 9.0 [*]	69.6/30.4	yes	30.8 \pm 4.0 [*]	NR
			without ICD	66.3 \pm 10.5 [*]	72.9/27.1	yes	31.4 \pm 4.2 [*]	NR

Study	Study Name	Inclusion Criteria	Treatment Arm	Age (years)	Male/Female (%)	Ischemic	Ejection Fraction (%)	NYHA Class (%)
		risk factors: PVCs ≥ 10 per hour, reduced heart rate variability with standard deviation of normal QRS complex intervals, positive signal averaged ECG						
Strickberger ²⁹	AMIOVIRT	age ≥ 18 years; non-ischemic dilated cardiomyopathy; LVEF ≤ 0.35 ; asymptomatic non-sustained ventricular tachycardia; NYHA class I to III	with ICD	58 \pm 11*	67/33	no	23 \pm 8*	I 18 II 64 III 16
			without ICD, with amiodarone	60 \pm 12*	74/26	no	22 \pm 10*	I 13 II 63 III 24

*mean \pm SD; †median (interquartile range); ‡mean (range); ECG=electrocardiogram; MI=myocardial infarction; LVEF=left ventricular ejection fraction; NYHA=New York Heart Association; NR=not reported.

APPENDIX 9: Adverse Events (AEs)

Study	Number of Patients	AEs in Patients with ICD	AEs in Patients Without ICD
Bänsch <i>et al.</i> ¹⁹	ICD 50, without ICD 54	10 AEs in 7 patients (14%): electrode dislocation and sensing-isolation defects (7), infection with total device replacement (2), perforation (1)	NR
Bardy <i>et al.</i> ²⁰	ICD 829, without ICD 847	5% of patients at time of implantation experienced clinical events requiring surgical correction, hospitalization, or new drug therapy; 9% later during trial; inappropriate shocks averaged 2.4% per year over 5 years	with amiodarone: increased tremor and increased hypothyroidism; with placebo: NR
Bigger <i>et al.</i> ²¹	ICD 446, without ICD 454	postoperative complications (% of patients): atrial fibrillation (22.9); new or more severe heart failure (15.7); conduction defect (14.1); infection at wound or catheter site (12.3); MI (4.0); sustained ventricular tachycardia (5.8); ventricular fibrillation (3.4); bradycardia (2.9); shock (9.2); residual central nervous system deficit (3.6); bleeding treated with surgery (4.9); post pericardiotomy syndrome (0.9); deep sternal-wound infection (2.7); pneumonia (8.5); other infection (6.3); renal failure (6.7); long-term follow-up: hospitalization (61.4); new or worsening heart failure (42.5); angina pectoris (27.0); ventricular arrhythmias (19.4); atrial fibrillation (14.7); MI (0.5); percutaneous transluminal coronary angioplasty or atherectomy (2.9); permanent cardiac pacemaker (2.9)	postoperative complications (% of patients): atrial fibrillation (20.7); conduction defect (14.5); new or more severe heart failure (12.6); MI (3.5); sustained ventricular tachycardia (6.8); ventricular fibrillation (5.3); bradycardia (4.4); shock (7.5); residual central nervous system deficit (2.0); bleeding treated with surgery (3.1); post pericardiotomy syndrome (0.7); deep sternal-wound infection (0.4); infection at wound or catheter site (5.9); pneumonia (4.0); other infection (3.3); renal failure (4.8); long-term follow-up: hospitalization (55.2); new or worsening heart failure (42.5); angina pectoris (27.5); ventricular arrhythmias (14.3); atrial fibrillation (10.1); MI (4.2); repeat CABG surgery (0.7); percutaneous transluminal coronary angioplasty or atherectomy (2.1); permanent cardiac pacemaker (4.9)
Buxton <i>et al.</i> ²²	ICD 161, without ICD 158	1 death from infection during revision of lead system, 18 months after initial implantation	NR
Hohnloser <i>et al.</i> ²⁴	ICD 332, without ICD 342	in-hospital device-related complications occurred in 25 patients (7.5%); most common were lead dislodgment, pneumothorax, and inappropriate shocks	NR
Kadish <i>et al.</i> ²⁵	ICD 229, without ICD 229	during implantation (1.3%): hemothorax (1), pneumothorax (1), cardiac tamponade (1); during follow-up: lead dislodgment or lead fracture (6); venous thrombosis (3); infection (1); 49	during follow-up: syncope or heart failure with prolonged QRS interval resulted in 23 patients (10%) receiving ICDs

		patients received inappropriate ICD shocks (primarily for atrial fibrillation or sinus tachycardia)	
Moss <i>et al.</i> ²⁷	ICD 95, without ICD 101	patients with AEs=19 (20%); syncope (1); sinus bradycardia (3); pulmonary embolism (1); atrial fibrillation (4); pneumothorax (2); bleeding (1); venous thrombosis (1); surgical infection (2); problem with defibrillator lead (7); malfunction of defibrillator generator (3)	patients with AEs=12 (12%); hypotension (1); syncope (5); hypothyroidism (1); sinus bradycardia (3); pulmonary fibrosis (3); pulmonary embolism (1); malfunction of defibrillator generator (2) (patients crossed over from control arm)
Moss <i>et al.</i> ²⁶	ICD 742, without ICD 490	13 lead problems requiring surgical intervention (1.8%); 5 non-fatal infections requiring surgical intervention (0.7%); 148 patients (19.9%) hospitalized with heart failure, representing 11.3 patients per 1,000 months follow-up	73 patients (14.9%) hospitalized with heart failure, representing 9.4 patients per 1,000 months follow-up
Raviele <i>et al.</i> ²⁸	ICD 79, without ICD 59	4 inappropriate shocks (16%): for atrial fibrillation (3), for paroxysmal atrial tachycardia (1); no implantation-related complications	NR
Strickberger <i>et al.</i> ²⁹	ICD 51, without ICD 52	3.9% of patients experienced syncope due to ventricular tachycardia or ventricular fibrillation; 8 patients received amiodarone in follow-up for treatment of atrial fibrillation	5.8% of patients experienced syncope; 8 patients crossed over to ICD due to near-syncope with ventricular tachycardia (2); cardiac arrest (2); amiodarone intolerance (4)

ICD= implantable cardiac device; AEs=adverse events; NR=not reported.

APPENDIX 10: Economic Results

Author	Currency Year	Baseline Results	Sensitivity Analysis Results	Conclusion
Al-Khatib <i>et al.</i> ³³	2002 US\$	ICER per life year saved \$50,500; ICER per QALY gained \$57,300	in 1-way sensitivity analysis, ICER ranged from \$42,200 to \$123,400 per life year gained; in threshold analysis of \$50,000 per life year gained, hazard ratios should be <0.69, or ICD replacement cost down to \$10,000, and hazard ratio <0.72; for \$100,000 per life year gained threshold, hazard ratio <0.84, or ICD placement cost down to \$10,000, and hazard ratio <0.86	in range of survival benefit observed in MADIT-II, ICD therapy in these patients economically attractive; this therapy would be more attractive if cost reduced and longevity extended
Anderson <i>et al.</i> ³⁶	1991 UK£	cost efficacy of ICD, £42,500 per life year for patients with non-sustained ventricular tachycardia, £36,500 for patients at high risk after MI, £44,000 for patients with low EF and positive signal average ECG (with CABG Patch data), £16,000 for patients awaiting cardiac transplantation		present and possible future application of ICD seems expensive when compared with accepted treatments
Chen <i>et al.</i> ³⁰	2002 US\$	ICER per QALY gained \$97,863	in 1-way sensitivity analysis, no ICER under any plausible scenario was <\$50,000 per QALY gained; in threshold analysis of \$50,000 per QALY, utility at 2 nd year after ICD implantation needed to be as high as 1.0, or ICD implantation costs ≤\$9,600, or sudden death proportion of CHF fatalities >60%	unlikely that ICD would be cost-effective in preventing sudden death in CHF patients, when using conventional cost-effective thresholds
Mushlin <i>et al.</i> ³⁴	1995 US\$	ICER \$27,000 per life year saved	ICER ranged from \$3,300 to \$39,600 per life year	ICD cost-effective when used for prevention of sudden death in selected high risk patients; limited to clinical circumstance and patient characteristics included in trial from which data derived
Sanders <i>et al.</i> ³¹	1999 US\$	\$ per life year gained \$63,300 for EF ≤0.3 group; \$173,400 for EF 0.31 to 0.4 group;	in 1-way sensitivity analysis, ICER ranged from \$29,200 to \$557,900 per QALY depending on patient's EF and varying	in patients with past MI and severely depressed left ventricular function, use of ICD or amiodarone

		\$501,500 for EF >0.4 group (with ICD versus amiodarone and their efficacy moderate)	parameters; in probabilistic sensitivity analysis, ICD more effective but costs more than amiodarone among 97.4% of simulations, with median ICER of \$83,200 per QALY	may provide substantial clinical benefit at acceptable cost
Sanders <i>et al.</i> ³²	2003 US\$	ICER \$36,700 per life year saved; \$50,900 per QALY gained	in 1-way sensitivity analysis, ICER ranged from \$32,300 to \$372,500 per QALY gained; in threshold analysis, efficacy of ICD prevents 68.5% of SCD to reach ICER of \$50,000 per QALY, 31.2% to reach ICER of \$100,000/QALY; utility of patient with ICD >0.78 to reach ICER of \$100,000 per QALY; in worst case scenario, ICER was \$311,700 per QALY; in best case scenario, \$16,900 per QALY	based on 67% reduction in SCD observed in trial, ICER costs approximately \$51,000 per QALY gained; most important determinants include ICD efficacy in preventing SCD, effect of ICD on quality of life, cost of ICD, patients' age, frequency of generator replacement
Sanders <i>et al.</i> ³⁵	2005 US\$	ICER per life year saved, \$24,500 to \$50,700 depending on trials discussed; ICER per QALY gained, \$34,000 to \$70,200	in 1-way sensitivity analysis, ICD becomes more favourable as following values increase: ICD efficacy, QoL with ICD, duration of ICD, time horizon; less favourable as following values increase: ICD cost, frequency of ICD generator replacement, monthly inpatient costs; in threshold analysis of \$100,000 per QALY, utility associated with ICD had to be >0.84 (0.95 for \$50,000 per QALY gained threshold)	prophylactic implantation of ICD has ICER <\$100,000 per QALY gained in populations in which significant device-associated reduction in mortality has been demonstrated

ICER=incremental cost-effectiveness ratio; ICD=implantable cardiac device; MI=myocardial infarction; EF=ejection fraction; ECG=electrocardiogram; CABG=coronary artery bypass graft; QALY=quality-adjusted life year; SCD=sudden cardiac death.

APPENDIX 11: Estimated Target Population for Budget Impact Analysis

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Reference
Input Data								
mortality rate*								
without ICD	0.12	0.13	0.15	0.16	0.18	0.20	0.22	56
with ICD	0.09	0.10	0.11	0.12	0.14	0.09	0.1	
new ICD implant	3,500	4,500	5,500	6,500	6,500	6,500	6,500	12
Estimated Results								
alive population†								
without ICD	3,290	7,306	11,970	17,220	22,042	26,428	30,377	estimated
with ICD	3,343	7,473	12,336	17,876	23,070	27,988	32,639	estimated
death								
without ICD	210	484	836	1,250	1,678	2,114	2,551	estimated
with ICD	158	370	637	960	1,306	1,582	1,849	estimated
death in control therapy scenario that would have been prevented by ICD treatment	53	114	199	291	372	532	702	estimated

*Mortality rate obtained from Maurice *et al.* study.⁵⁶ We used their estimated results from constant mortality ratio model; †number of alive patients in mid year: for year 1= $[3,500+3,500 \times (1-\text{mortality rate})/2]$, for years 2 to 7= \sum alive patients of each year's cohort in mid year; over 7 years, 7 cohorts, which were 1st year cohort of 3,500 and 2nd to 7th year cohorts (all originally 3,700). Alive patients of each cohort in mid year= $1/2$ (patients of cohort at end of previous year+patients of cohort at end of this year). Patients of 1 cohort at end of 1 year=patients of cohort at end of previous year \times (1-mortality rate at year).

APPENDIX 12: Per-patient Cost Estimation Results

Scenario with ICD implantation	Estimated cost	Reference
Per patient with ICD		
Implant procedure		
ICD device	C\$19,500.00	Appendix 12
electrode (assumed 1:1 ratio, chance to use single chamber electrode versus chance to use double chamber electrode)	C\$2,250.00	Appendix 12
implant consumables	C\$175.00	Appendix 12
arterial line by anesthesiology	C\$31.00	Appendix 12
electrophysiology doctor consultation	C\$127.50	Appendix 12
nurse (2 hours/nurse × 2 nurses × C\$36/nurse/hour)	C\$144.00	Appendix 12
surgeon's work (assuming 1:1 ratio for single chamber electrode: double)=50% × (cost of surgeon's work for single chamber electrode ICD implantation+cost of surgeon's work for double chamber electrodes ICD implantation)	C\$1,008.50	Appendix 12
anesthetist's work (consulting cost+cost for 2-hour anesthesiology time=C\$103+C\$144)	C\$247.00	Appendix 12
Total	C\$23,483.00	estimated
Post implant		
chest x-ray test cost	C\$32.00	Appendix 12
electrocardiogram test cost	C\$15.00	Appendix 12
hospital ward stay (1.5 days × C\$649/day)	C\$973.50	estimated
Total	C\$1,020.50	estimated
Clinic follow-up		
1 st year (3 × C\$106.65/clinic visit, Appendix 12)	C\$319.95	estimated
2 nd year (discounted) (adjusted by considering inflation factor 2 × C\$106.65/clinic visit, this applied to subsequent year after first year of ICD implantation)	C\$207.09	estimated
3 rd year (discounted)	C\$201.06	estimated
4 th year (discounted)	C\$195.20	estimated
5 th year (discounted)	C\$189.51	estimated
6 th year (discounted)	C\$275.17	estimated
7 th year (discounted)	C\$178.64	estimated
Total cost attributable to clinic follow-up	C\$1,566.62	estimated
ICD-related complication treatment (∑ quantities of health care resources in Appendix 11 × corresponding unit cost in Appendix 12)		
lead displacement (assumed 7% chance)	C\$1,617.00	estimated
infection requiring explant (assumed 1.0% chance)	C\$34,733.50	estimated
pneumothorax (drain) (assumed 0.1% chance)	C\$2,755.00	estimated
pneumothorax (no drain) (assumed 1.0% chance)	C\$1,362.00	estimated
perforation (assumed 0.3% chance)	C\$3,850.00	estimated
Total cost of treating ICD-related complications (∑ unit cost of complications × chance)	C\$488.47	estimated

Scenario with ICD implantation	Estimated cost	Reference
Per patient with ICD	(discounted, rounded)	
1 st year (total cost for implant procedure+total cost for health care post-implant+clinic follow-up cost for 1 st year+total cost for ICD complication treatment)	C\$25,312	estimated
2 nd year (times of clinical follow up each year in Appendix 11 × corresponding unit cost in Appendix 12)	C\$207	estimated
3 rd year (times of clinical follow up each year in Appendix 11 × corresponding unit cost in Appendix 12)	C\$201	estimated
4 th year (times of clinical follow up each year in Appendix 11 × corresponding unit cost in Appendix 12)	C\$195	estimated
5 th year (times of clinical follow up each year in Appendix 11 × corresponding unit cost in Appendix 12)	C\$190	estimated
6 th year (total cost for 1 st year post-ICD implantation discounted)	C\$21,834	estimated
7 th year (times of clinical follow up each year in Appendix 11 × corresponding unit cost in Appendix 12)	C\$179	estimated
total (over 7 years)	C\$48,119	estimated
For entire study population		
1 st year (3,500 new ICD implants) (per-case cost in 1 st year due to ICD implant C\$25,312 × 3,500 ICD implants in year, as in Appendix 14)	C\$88.59 million	estimated
2 nd year (3,290 follow-up+4,500 new ICD implants) cost attributable for clinical follow-up of patients with ICD+cost of new ICD implantation)	C\$111.24 million	estimated
3 rd year (7,306 follow-up+5,500 new ICD implants) (cost attributable for clinical follow-up of patients with ICD+cost of new ICD implantation)	C\$132.65 million	estimated
4 th year (11,970 follow-up+6,500 new ICD implants) (cost attributable for clinical follow-up of patients with ICD+cost of new ICD implantation)	C\$152.84 million	estimated
5 th year (17,220 follow-up+6,500 new ICD implants) (cost attributable for clinical follow-up of patients with ICD+cost of new ICD implantation)	C\$149.38 million	estimated
6 th year (22,042 follow-up+6,500 new ICD implants) (cost attributable for clinical follow-up of patients with ICD+cost of new ICD implantation in year+cost due to ICD replacement)	C\$200.17 million	estimated
7 th year (26,428 follow-up+6,500 new ICD implants) (cost attributable for clinical follow-up of patients with ICD+cost of new ICD implantation)	C\$210.22 million	estimated
total budget (first 3 years) $\sum_{n=1}^3$ cost for year n	C\$332.48 million	estimated
total budget (first 5 years) $\sum_{n=1}^5$ cost for year n	C\$634.70 million	estimated
total budget (first 6 years) $\sum_{n=1}^6$ cost for year n	C\$834.87 million	estimated
total budget (7 years) $\sum_{n=1}^7$ cost for year n	C\$1.05 billion	estimated
Scenario with usual medical therapy		
if per-person cost associated with cardiac event as high as \$300 (\$6,500) (Appendix 12 shows total cost of 1 SCD)		
1 st year (number of deaths that would have been prevented by ICD treatment as in Appendix 14 × assumed cost of death)	C\$15.75 thousand (341.25 thousand)	estimated
2 nd year	C\$34.27 thousand (742.46 thousand)	estimated
3 rd year	C\$59.59 thousand (1.29 million)	estimated

Scenario with ICD implantation	Estimated cost	Reference
4 th year	C\$87.18 thousand (1.89 million)	estimated
5 th year	C\$111.52 thousand (2.42 million)	estimated
6 th year	C\$159.72 thousand (3.46 million)	estimated
7 th year	C\$210.55 thousand (4.56 million)	estimated
total budget (first 3 years)	C\$109.61 thousand (2.37 million)	estimated
total budget (first 5 years)	C\$308.31 thousand (6.68 million)	estimated
total budget (first 6 years)	C\$468.03 thousand (10.14 million)	estimated
total budget (7 years)	C\$678.58 thousand (14.70 million)	estimated

APPENDIX 13: Quantities of Health Care Resources*

Procedure	Initial Implant (unit)	Lead Dislodgment	Infection Requiring Removal	Pneumothorax (no drain)	Pneumothorax (drain)	Perforation
Implant procedure						
ICD device	1		1 unit			
electrode	1		1 unit			
EP doctor (process)	1					
number of nurses	2	1 unit	4 units			
nursing time	2 hours	1 unit	4 units			
anesthesiology time	2 hours	1 unit	2 units			
surgeon (process)	1		1 unit			
Post implant						
chest x-ray test	1	1 unit	2 units	2 units	3 units	1 unit
ECG test	1	1 unit	2 units			
days of hospital ward stay	1.5 days	1 day	14 days	2 days	4 days	5 days
Clinic follow-up						
times per year in 1 st year	3					
times per year in subsequent years	2					
additional health care resources		for lead repositioning	for explants including extraction and pulse generator change		for chest tube insertion	for pericardiocentesis and 3 times of echocardiography

*Ottawa Heart Institute; EP=electrophysiology; ECG=electrocardiogram.

APPENDIX 14: Cost Data

Variables	Value	Reference
Implant procedure		
assumed average unit cost of ICD device	C\$19,500.00	Ottawa Heart Institute ^a
average unit cost of electrodes (single chamber)	C\$2,000.00	Ottawa Heart Institute
average unit cost of electrodes (dual chamber)	C\$2,500.00	Ottawa Heart Institute
implant consumables (total)	C\$175.00	Ottawa Heart Institute
arterial line by anesthesiology (total)	C\$31.00	Ottawa Heart Institute
electrophysiology doctor consultation	C\$127.50	Ottawa Heart Institute
cost for nurse per hour	C\$36.00	Ottawa Heart Institute
cost for surgeon's work (single chamber)	C\$970.00	Ottawa Heart Institute
cost for surgeon's work (dual chamber)	C\$1,047.00	Ottawa Heart Institute
cost for anesthesiology consulting and 2 hours of time	C\$247.00	
cost for anesthesiology consultation	C\$103.00	Ottawa Heart Institute
cost for 2 hours of anesthesiology time	C\$144.00	Ottawa Heart Institute
Post implant		
chest x-ray test cost (chest x-ray post implant)	C\$32.00	Ottawa Heart Institute
electrocardiogram test cost	C\$15.00	Ottawa Heart Institute
cost per hospital ward stay	C\$649.00	Ottawa Heart Institute
Clinic follow-up		
technical cost per clinic visit	C\$47.65	Ottawa Heart Institute
professional cost per clinic visit	C\$29.00	Ottawa Heart Institute
other cost per clinic visit	C\$30.00	Ottawa Heart Institute
<i>Total</i>	C\$106.65	estimated
Complication-specific cost per time		
lead repositioning	C\$324.00	Ottawa Heart Institute
explant including extraction	C\$598.00	Ottawa Heart Institute
pulse generator change	C\$715.00	Ottawa Heart Institute
Pericardiocentesis	C\$131.00	Ottawa Heart Institute
chest tube insertion	C\$63.00	Ottawa Heart Institute
Echocardiography	C\$150.00	Ottawa Heart Institute
Potential savings to be offset against cost of ICDs*		
ambulance cost of attending cardiac arrest	C\$442.03	NICE ^b (converted to 2005C\$)
A&E, other high-cost investigation (died or admitted)	C\$348.71	NICE (converted to 2005C\$)
A&E, dead on arrival	C\$58.94	NICE (converted to 2005C\$)
A&E, observation unit episode	C\$719.52	NICE (converted to 2005C\$)
emergency admission for arrhythmia	C\$2,413.96	NICE (converted to 2005C\$)
cardiac intensive care	C\$2,517.10	NICE (converted to 2005C\$)
coronary care unit	C\$1,122.26	NICE (converted to 2005C\$)
total cost of 1 SCD	C\$300 [†] to 6,500 [‡]	assumed
Implant procedure		
assumed average unit cost of ICD device	C\$19,500.00	Ottawa Heart Institute
average unit cost of electrodes (single chamber)	C\$2000.00	Ottawa Heart Institute
average unit cost of electrodes (dual chamber)	C\$2500.00	Ottawa Heart Institute

implant consumables (total)	C\$175.00	Ottawa Heart Institute
arterial line by anesthesiology (total)	C\$31.00	Ottawa Heart Institute
electrophysiology doctor consult	C\$127.50	Ottawa Heart Institute
cost for nurse per hour	C\$36.00	Ottawa Heart Institute
cost for surgeon's work (single chamber)	C\$970.00	Ottawa Heart Institute
cost for surgeon's work (dual chamber)	C\$1047.00	Ottawa Heart Institute
cost for anesthesiology consulting and 2 hours of time	C\$247.00	
cost for anesthesiology consultation	C\$103.00	Ottawa Heart Institute
cost for 2 hours of anesthesiology time	C\$144.00	Ottawa Heart Institute
Post implant		
chest x-ray test cost (chest x-ray post implant)	C\$32.00	Ottawa Heart Institute
electrocardiogram test cost	C\$15.00	Ottawa Heart Institute
cost per hospital ward stay	C\$649.00	Ottawa Heart Institute
Clinic follow-up		
technical cost per clinic visit	C\$47.65	Ottawa Heart Institute
professional cost per clinic visit	C\$29.00	Ottawa Heart Institute
other cost per clinic visit	C\$30.00	Ottawa Heart Institute
<i>Total</i>	C\$106.65	estimated
Complication-specific cost per time		
lead repositioning	C\$324.00	Ottawa Heart Institute
explant including extraction	C\$598.00	Ottawa Heart Institute
pulse generator change	C\$715.00	Ottawa Heart Institute
Pericardiocentesis	C\$131.00	Ottawa Heart Institute
chest tube insertion	C\$63.00	Ottawa Heart Institute
Echocardiography	C\$150.00	Ottawa Heart Institute
Potential savings to be offset against cost of ICDs*		
ambulance cost of attending cardiac arrest	C\$442.03	NICE (converted to 2005C\$)
A&E, other high-cost investigation (died or admitted)	C\$348.71	NICE (converted to 2005C\$)
A&E, dead on arrival	C\$58.94	NICE (converted to 2005C\$)
A&E, observation unit episode	C\$719.52	NICE (converted to 2005C\$)
emergency admission for arrhythmia	C\$2,413.96	NICE (converted to 2005C\$)
cardiac intensive care	C\$2,517.10	NICE (converted to 2005C\$)
coronary care unit	C\$1,122.26	NICE (converted to 2005C\$)
total cost of 1 SCD	C\$300 [†] to 6,500 [‡]	assumed

*Adjusted to Canadian 2005 dollar (3% inflation rate; source for exchange rate: <http://www.bankofcanada.ca/pdf/nraa05.pdf>).

[†]Assumption of C\$300 based on cost for A&E investigation of death on arrival.

[‡]Assumption of C\$6,500 based on sum of costs for ambulance after cardiac arrest, emergency admission for arrhythmia, cardiac intensive care, and coronary care unit.

Source^a: DB, unpublished observations, 2006.

Source^b: *Costing template and costing report. Arrhythmia - implantable cardioverter defibrillators (ICDs)* [Technology appraisal no 95]. London: National Institute for Health and Clinical Excellence; 2006. Available: <http://www.nice.org.uk/pdf/TA095costing.xls> (accessed 2007 Feb 19).

APPENDIX 15: Budget Impact* Estimation for Canada (in 2005 Canadian dollars)

Time Post-implant	Budget if ICD Used [†]	Budget if No ICD Used [†]	Budget Impact [‡]
1 st year	C\$88.59 million	C\$15.75 (341.25) thousand**	C\$88.58 (88.25) million
2 nd year	C\$111.24 million	C\$34.27 (742.46) thousand	C\$111.21 (110.50) million
3 rd year	C\$132.65 million	C\$59.59 thousand (1.29 million)	C\$132.59 (131.36) million
4 th year	C\$152.84 million	C\$87.18 thousand (1.89 million)	C\$152.76 (150.95) million
5 th year	C\$149.38 million	C\$111.52 thousand (2.42 million)	C\$149.26 (146.96) million
6 th year	C\$200.17 million	C\$159.72 thousand (3.46 million)	C\$200.00 (196.71) million
7 th year	C\$210.22 million	C\$210.55 thousand (4.56 million)	C\$200.00 (205.65) million
total budget (first 3 years)	C\$332.48 million	C\$109.61 thousand (2.37 million)	C\$332.37 (330.11) million
total budget (first 5 years)	C\$634.70 million	C\$308.31 thousand (6.68 million)	C\$634.39 (628.02) million
total budget (first 6 years)	C\$834.87 million	C\$468.03 thousand (10.14 million)	C\$834.40 (824.73) million
total budget (7 years)	C\$1.05 billion	C\$678.58 thousand (14.70 million)	C\$1.04 (1.03) billion

* All budget estimates converted into 2005 value by considering annual inflation rate of 3%; [†]Appendix 13; [‡]budget if ICD implant–budget if no ICD use; ** budget estimation when per-patient cost due to cardiac event was \$300 (number in parentheses when cardiac event cost was \$6,500).