

Issue date: January 2006

Review date: July 2007

Implantable cardioverter defibrillators for arrhythmias

Review of Technology Appraisal 11

Technology Appraisal 95

Ordering information

You can download the following documents from www.nice.org.uk/TA095

- The full guidance for this technology appraisal (this document).
- A quick reference guide, which has been distributed to healthcare professionals working in the NHS in England.
- Information for people with arrhythmias, their families and carers, and the public.
- The assessment report – details of all the studies that were looked at.

For printed copies of the quick reference guide or information for the public, phone the NHS Response Line on 0870 1555 455 and quote:

- N0973 (quick reference guide)
- N0974 (information for the public).

This guidance is written in the following context

This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

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Contents

1	Guidance	4
2	Clinical need and practice	5
3	The technology	7
4	Evidence and interpretation	8
5	Recommendations for further research	19
6	Implications for the NHS	19
7	Implementation and audit	20
8	Related guidance	21
9	Review of guidance	21
	Appendix A. Appraisal Committee members and NICE project team.	23
	Appendix B. Sources of evidence considered by the Committee	26
	Appendix C. Detail on criteria for audit of the use of ICDs for arrhythmias	29

NOTE: This guidance replaces Technology Appraisal Guidance no. 11 issued in September 2000.

The Institute reviews each piece of guidance it issues.

The review and re-appraisal of the use of implantable cardioverter defibrillators (ICDs) for arrhythmias has resulted in a change in the guidance. The recommendation on the use of ICDs for the primary prevention of sudden cardiac death (SCD) has been expanded to include patients with a left ventricular ejection fraction (LVEF) of less than 30% (no worse than class III of the New York Heart Association functional classification of heart failure) and a QRS duration of equal to or more than 120 milliseconds, without the need for electrophysiological testing. It also includes patients who have undergone surgical repair for congenital heart conditions.

1 Guidance

This appraisal does not cover the use of implantable defibrillators for non-ischaemic dilated cardiomyopathy.

1.1 ICDs are recommended for patients in the following categories.

1.1.1 'Secondary prevention', that is, for patients who present, in the absence of a treatable cause, with one of the following:

- having survived a cardiac arrest due to either ventricular tachycardia (VT) or ventricular fibrillation (VF)
- spontaneous sustained VT causing syncope or significant haemodynamic compromise
- sustained VT without syncope or cardiac arrest, and who have an associated reduction in ejection fraction (LVEF of less than 35%) (no worse than class III of the New York Heart Association functional classification of heart failure).

1.1.2 'Primary prevention', that is, for patients who have:

- a history of previous (more than 4 weeks) myocardial infarction (MI) and:
 - either**
 - left ventricular dysfunction with an LVEF of less than 35% (no worse than class III of the New York Heart Association functional classification of heart failure), **and**
 - non-sustained VT on Holter (24-hour electrocardiogram [ECG]) monitoring, **and**
 - inducible VT on electrophysiological (EP) testing
 - or**
 - left ventricular dysfunction with an LVEF of less than 30% (no worse than class III of the New York Heart Association functional classification of heart failure) **and**
 - QRS duration of equal to or more than 120 milliseconds
- a familial cardiac condition with a high risk of sudden death, including long QT syndrome, hypertrophic cardiomyopathy, Brugada syndrome or arrhythmogenic right ventricular dysplasia (ARVD), or have undergone surgical repair of congenital heart disease.

2 Clinical need and practice

2.1 Sudden cardiac death (SCD) is defined as death from cardiac causes occurring unexpectedly within 1 hour of onset of symptoms. About 80% of SCDs are due to ventricular tachyarrhythmia (abnormal heart rate in the ventricles) – that is, VT and VF. The remaining 20% consists of a number of conditions, including cardiomyopathies (10–15%), other structural heart defects (less than 5%) and bradycardia (slow heartbeats).

- 2.2 SCD occurs in approximately 50,000–70,000 people annually in the UK and represents the largest proportion of the deaths attributable to coronary heart disease. Approximately 85–90% of SCD is due to the first recognised arrhythmic event; the remaining 10–15% is due to recurrent events.
- 2.3 The survival rates for out-of-hospital sudden cardiac episodes are less than 5% in most industrialised countries, including the UK. People who survive a first episode of a life-threatening ventricular arrhythmia are at high risk of further episodes. Half will be rehospitalised within 1 year, and approximately 40% will die within 2 years. However, some survivors live for many years without treatment, and the average length of survival for those discharged from hospital is of the order of 5–7 years.
- 2.4 Prevention of SCD is either primary, defined as prevention of a first life-threatening arrhythmic event, or secondary, which refers to the prevention of an additional life-threatening event in survivors of sudden cardiac events or patients with recurrent unstable rhythms.
- 2.5 Apart from a previous sudden cardiac event, risk factors for SCD include previous VT, a prior MI, coronary artery disease, heart failure, left ventricular ejection fraction (LVEF) of less than 35%, prolonged QRS duration, and genetic factors such as a family history of SCD and familial cardiac conditions (for example, long QT syndrome). The incidence of SCD increases with age.
- 2.6 Survivors of cardiac arrest, and those with low LVEF, who have a high relative risk for SCD, are a small proportion of the total population burden of SCD.
- 2.7 Identifying individuals at the highest risk of SCD is difficult. Risk stratification may involve the use of EP studies, signal-averaged ECGs and heart-rate variability, although the evidence base for these is often not strong. In addition, increased risk of SCD may also be conferred by the presence of ventricular asynchrony as evidenced by prolonged QRS duration on the ECG.

- 2.8 Many patients presenting with tachyarrhythmias with or without symptoms are treated with anti-arrhythmic drug therapy and other drug treatments specific to the underlying cardiac pathology. Currently, only a minority of patients is implanted with an ICD.
- 2.9 Anti-arrhythmic drugs are separated into classes I to IV. Class III drugs, which include amiodarone, are the most commonly used for long-term management of ventricular arrhythmias. Chronic prophylactic anti-arrhythmic drug therapy aims to suppress the development of arrhythmias, but does not terminate an arrhythmia once it is initiated.
- 2.10 Amiodarone is the most common anti-arrhythmic drug used as an alternative to ICD implantation for the treatment of ventricular tachyarrhythmias, although its overall long-term mortality benefit is open to question. Empiric anti-arrhythmic drug therapy or EP-guided anti-arrhythmic drug therapy is not effective in improving mortality for high-risk patients.

3 The technology

- 3.1 An ICD is a device implanted into the upper chest below the left shoulder, with leads into the heart to pace, sense and defibrillate. An ICD senses continuously until an arrhythmia is recognised, at which time a shock is delivered to the heart.
- 3.2 Implantation of current devices requires only local anaesthesia and a length of stay in hospital of 2–4 days. ICDs are battery operated with a battery life of up to 7 years, depending on the number of therapeutic shocks delivered. They may be programmed to optimise the detection of abnormalities in heartbeat and provide diagnostics and specific treatment for a patient.
- 3.3 Dual-function ICDs are available that combine pacemaker and conventional ICD capabilities in one device. Hence the device may also act as a pacemaker in some circumstances. The technology recognises and discriminates between a number of arrhythmias, which may enable it to

provide more appropriate therapy, in particular lessening the incidence of inappropriate shocks.

- 3.4 UK implantation rates are currently of the order of 50 per million per year.
- 3.5 ICD costs have fallen considerably since 2000; including leads and accessories, they range from slightly below £10,000 to about £15,000. With the cost of overheads and implantation (but not EP testing) added, the average cost appears to be about £16,000 per unit. Costs may vary in different settings because of negotiated procurement discounts.

4 Evidence and interpretation

The Appraisal Committee (Appendix A) considered evidence from a number of sources (see Appendix B).

4.1 Clinical effectiveness

- 4.1.1 For secondary prevention, no new trials have been completed since the original appraisal in 2000. Three trials involving a total of 1850 survivors of cardiac arrest (AVID, 1997; CASH, 2000; and CIDS, 1993 and 2000) have since been the subject of three different meta-analyses. These meta-analyses reported that, compared with amiodarone or another anti-arrhythmic drug, treatment with ICDs resulted in a 50% reduction in the risk of cardiac death (95% confidence interval [CI] average, 35% to 65%, with small differences between meta-analyses) and a 25–28% risk reduction in all-cause mortality (95% CI average, 10% to 40%, with small differences between meta-analyses).
- 4.1.2 For primary prevention, the three trials reported for the 2000 appraisal (MADIT I, 1996; CABG-Patch, 1997; and MUSTT, 1999) were supplemented by two further trials (MADIT II, 2002 and CAT, 2002) in the Assessment Report. A further six randomised controlled trials (RCTs) were also available to the Committee, including two trials that examined

the use of cardiac resynchronisation therapy (COMPANION and CARE-HF).

4.1.3 The trials reviewed in the Assessment Report had normal medical management as the comparator. That is, for most trials, patients in the ICD arm and the control arm had similar medication, with the addition of an ICD in the treatment arm. In the large MADIT II trial, for example, only about 10% (in both arms) were treated with amiodarone, whereas between 50% and 80% were treated with one or more of angiotensin-converting enzyme inhibitors, beta-blockers, digitalis, diuretics and statins. The population for the CABG-Patch trial consisted of people who had just undergone a coronary artery bypass graft operation and was therefore a rather different population group from those of the other trials. The CAT study, where patients had dilated cardiomyopathy and an LVEF of less than or equal to 30%, was stopped early, as deaths were too infrequent to allow statistical significance to be reached. The populations involved in the main primary prevention trials differed substantially from one trial to another. For example, the MUSTT trial compared EP-guided therapy (either ICDs or anti-arrhythmic drugs, non-randomised) in one arm with no anti-arrhythmic therapy in the other arm. The MADIT I trial comprised patients who had had a previous MI, had an LVEF of less than 35% and who were positive on EP testing. The MADIT II trial comprised patients who had a previous MI and an LVEF of less than 30%, but did not require EP testing. This represents a considerable widening of eligibility for an ICD compared with the MADIT I trial.

4.1.4 The Assessment Group reported heterogeneity between studies for primary prevention and thought that a meta-analysis would not be appropriate. Nevertheless, the Assessment Report notes two meta-analyses from previous systematic reviews in which the relative risk of death from cardiac causes was estimated to be 0.37 (95% CI, 0.27 to 0.50) in one study and 0.34 (95% CI, 0.23 to 0.50) in the other. For

all-cause mortality, the corresponding relative risks were 0.72 (95% CI, 0.63 to 0.84) and 0.66 (95% CI, 0.46 to 0.96), respectively, for fixed-effects estimates, and 0.69 (95% CI, 0.46 to 1.03) for the random-effects estimate for the first of the two reviews.

- 4.1.5 One of the most probable reasons for the heterogeneity is that the MADIT I and MUSTT trials in post-MI patients required patients to undergo EP testing, and only those who had sustained VT on testing were eligible for the trial. In the MADIT I trial the control group's annual mortality was 20% and the relative risk for those given an ICD was 0.46; for MUSTT, the baseline risk of mortality was 13% and the relative risk for ICD patients compared with those in the EP arm of the trial was 0.42. By contrast, in MADIT II, the baseline risk was 12% per year and the relative risk was 0.69.
- 4.1.6 A similar analysis in the manufacturers' submission demonstrates Kaplan-Meier estimates of the probability of survival in the ICD and conventional therapy groups for the MADIT II trial. The survival curves represent a reduction in death rates in the ICD group of 12% at 1 year, 28% at 2 years and 29% at 3 years.
- 4.1.7 Of the six trials published since the Assessment Report, CAT, AMIOVERT and DEFINITE have recruited exclusively non-ischaemic cardiomyopathy patients, so are outside the scope of this appraisal. SCD-HeFT, which included some patients with ischaemic heart failure, had a population exhibiting a lower baseline risk (7.2% per year) and a relative risk of 0.77 compared with conventional therapy and 0.73 compared with amiodarone.
- 4.1.8 Serious adverse events due to ICDs were reported infrequently. However, recorded complications included infection, haematomas and bleeding, lead dislodgement and migration, cardiac perforation, pleural effusion and pneumothorax, and device dysfunction/malfunction of the generator. Additionally, some people for whom defibrillation is initiated

while they remain conscious report that they become fearful of the severe jolt to the thorax occasioned by device activation.

4.2 Cost effectiveness

4.2.1 Several economic evaluations relating to primary and secondary use of ICDs were available to the Committee. The Assessment Group reviewed 11 published economic evaluations and one unpublished analysis (the Buxton and Sharples model), and performed their own evaluation. The ICD manufacturers also jointly submitted an evaluation of primary and secondary SCD prevention.

Secondary prevention

4.2.2 One published evaluation, performed from a UK perspective, indicated an incremental cost-effectiveness ratio (ICER) of approximately £15,000 per life year gained. The manufacturers' evaluation suggested that the ICER per quality-adjusted life year (QALY) gained was between £26,000 and £47,000, depending on the time horizon of the analysis.

4.2.3 The Buxton and Sharples model estimated that the mean ICER for the base case for a 20-year model for secondary prevention was £76,000 per QALY against amiodarone as a comparator.

4.2.4 Following discussion in the Appraisal Committee meeting, the Decision Support Unit (DSU) was asked to prepare ICER estimates based on the Buxton and Sharples model for a new base case for secondary prevention to include only patients with an LVEF of less than 35%. It was also asked to explore the effects of reducing the implantation and device cost of ICDs in line with more recent data, changing relative risks of SCD in different subgroups, changing assumptions about reliability of ICDs to reflect recent usage, and assuming different patient utility and a reduced need for hospital admissions for people implanted with ICDs.

4.2.5 The base-case ICER reported by the DSU decreased only marginally from the previous estimate, from £76,000 to £72,000. However, also reducing the total cost of the device and implantation to £16,250 (down from £23,800), and reducing the relative risk/hazard ratio of SCD to 0.66, the estimated ICER was £28,000 per QALY gained when a lifetime horizon was assumed.

Primary prevention

4.2.6 None of the published economic evaluations related to a UK setting. The joint manufacturers' submission for primary prevention yielded an estimated mean ICER of between £39,000 and £83,000 per QALY gained, based on information derived from MADIT II.

4.2.7 To fully explore the cost effectiveness of ICDs, the Committee requested that the Buxton and Sharples model be extended to include primary prevention of SCD. In one scenario, the relative risk was set at 0.43 to reflect the MADIT I/MUSTT populations, and the following assumptions were made: EP testing at a cost of approximately £3000 per test and an average patient utility of 0.75 for both treatment and control (amiodarone). The estimated mean ICERs were £32,000 (assuming a baseline risk of 20%) and £35,000 (assuming a baseline risk of 13%). When the cost of the device and implantation was reduced from £23,800 to £16,250, the estimated mean ICERs were reduced to between £27,000 and £28,500 per QALY gained, with regard to baseline risk, respectively.

4.2.8 In another scenario, the assumptions made were a relative risk of 0.73, to reflect the population of MADIT II and, in line with that trial, that no EP testing was required. For a 12% baseline risk, and the base case using the same additional assumptions as described in 4.2.7, the estimated mean ICER was £69,000, falling to £55,000 when the initial cost fell to £16,250. For a 7% baseline risk (SCD-HeFT), the corresponding figures were £86,000 and £68,000, respectively. Using a lifetime horizon

reduced the ICER to between £33,000 and £46,000 per QALY gained, depending on the assumed baseline risk of death.

4.2.9 The Committee requested further analysis of the clinical risk factors among patients that might predict whether an ICD would, on average, be cost effective for primary prevention of SCD in addition to or instead of the use of EP testing. The capacity of a number of factors to identify patients at high risk of SCD were considered in this analysis, including age, degree of clinical heart failure according to NYHA classification, presence of atrial fibrillation, different degrees of impairment of LVEF, QRS duration and renal function. The principal analysis considered individuals having similar inclusion criteria to the MADIT II population (LVEF of less than 30%, NYHA groups I, II or III and previous MI). The subgroup of this population was analysed using the pooled relative risk reduction of death from the MADIT II, DEFINITE and SCD-HeFT trials. In this analysis, in individuals with a QRS duration of greater than or equal to 120 milliseconds, implantation of an ICD was associated with a 38% reduction in mortality (relative risk, 0.62). The estimated ICER for this scenario based on a lifetime horizon was £30,300 per QALY gained. For the subgroup with a QRS duration of greater than or equal to 120 milliseconds within the MADIT II population alone, the relative risk reduction was 43%, so the cost per QALY gained would therefore be somewhat lower than £30,000. None of the other factors examined had an appreciable differential effect on risk reduction or, therefore, on the ICER.

4.3 Consideration of the evidence

4.3.1 The Committee reviewed the data available on the clinical and cost effectiveness of ICDs, having considered evidence on the nature of the condition and the value placed on the benefits of ICDs by people with arrhythmias, those who represent them, and clinical experts. It was also

mindful of the need to take account of the effective use of NHS resources.

- 4.3.2 The Committee heard that the total cost of purchasing and implanting ICDs ranged from £10,000 to £25,000. The Committee discussed this issue with the clinical experts, who agreed that £16,250 was an appropriate estimate of the current average cost to be used in the cost-effectiveness calculations. (This figure was the mid-point of a range of costs supplied in the joint manufacturers' submission.)
- 4.3.3 The Committee considered a lifetime horizon to be the appropriate horizon for the economic modelling. This was because it allowed any differential in mortality between the different treatment options to be fully quantified for the different treatment populations that might be considered for the insertion of an ICD.
- 4.3.4 The Committee recognised the need to consider both the absolute level of utility for people at risk of SCD and whether different utilities should be ascribed to patients receiving an ICD or medical management alone. The Committee reasoned that the average utility for someone implanted with an ICD should not be higher than that for a matched person of the same age from the general population. It heard that the average utility of the age-matched UK population is estimated to be about 0.78, and concluded that a utility of 0.75 for people implanted with an ICD was consistent with this. The Committee considered the effects on the quality of life of people on long-term amiodarone or following insertion of an ICD. Taking all factors into account, and in discussion with the clinical experts, the Committee concluded that there is currently insufficient evidence to support the notion that the utility ascribed to patients with an ICD differs from that of those on long-term amiodarone therapy.
- 4.3.5 A number of consultees questioned whether amiodarone therapy is the relevant comparator for ICD treatment. The Committee was persuaded that current evidence indicates that although amiodarone therapy may

provide some symptomatic relief by reducing the number of tachyarrhythmias, it has little or no effect on mortality. It also understood that removing this arm from the Buxton and Sharples model (and effectively assuming that the control arm was equivalent to a placebo) would do little to alter the cost-effectiveness estimate of either primary or secondary prevention because the cost of amiodarone treatment is relatively low.

- 4.3.6 The Committee heard that the rate at which ICDs are replaced is dependent on a number of factors including the number of shocks administered. Evidence collected by Buxton and Sharples suggested that the rate of hospitalisation for all reasons, including device maintenance and replacement, was 6% per annum. However, more recent evidence from Heart Rhythm UK suggested that this rate was nearer 3% for the first 3 years, although it rose steeply in year 4 to 15%. The Committee recognised that the Buxton and Sharples data related to a period during which there were rapid advances in device technology; however, it noted that a replacement rate of 3% per annum implied an average device life expectancy of approximately 30 years, compared with 15 years if a rate of 6% was assumed. On the basis of this evidence, the Committee concluded that a replacement rate of 6% was a more realistic figure.

Secondary prevention

- 4.3.7 The Committee noted that there had been no new RCTs but that several new economic evaluations had been carried out since publication of the 2000 guidance. However, the estimates generated by these evaluations differed considerably. The re-worked assessment in the Buxton and Sharples model produced a base-case analysis of approximately £72,000 per QALY gained (for patients with an LVEF of less than 35%), although the joint manufacturers' analysis suggested that this figure was much lower.

4.3.8 The Committee also agreed that the subgroup-specific relative risk of death (for patients with an LVEF of less than 35%) of 0.66 (derived in a meta-analysis) was appropriate for the analysis. Combining the Committee's preferred assumptions regarding utilities, costs and time horizon produced an ICER of approximately £28,000 per additional QALY. The Committee concluded that this estimate was within acceptable limits of cost effectiveness. It therefore agreed that there was no reason to change the original guidance regarding secondary prevention.

Primary prevention

4.3.9 The Committee understood that the evidence base for primary prevention had extended since the 2000 guidance, with the publication of the MADIT II, DEFINITE and SCD-HeFT trials. The important difference between the newer trials and the MADIT I/MUSTT trials is the lack of a requirement for patients to undergo EP testing to assess inducibility of their arrhythmia on enrolment, which was a requirement in MADIT I/MUSTT. This was also a requirement of the 2000 guidance for the use of ICDs in primary prevention.

4.3.10 The Committee discussed the need for EP testing. It carefully considered the new clinical evidence from MADIT II, DEFINITE and SCD-HeFT. It was persuaded that patients in whom EP testing had shown inducibility of their arrhythmia were at higher baseline risk of subsequent SCD and had more to gain from implantation of an ICD. Conversely, patients in the trials in whom inducibility of the arrhythmia had not been tested were at lower risk of subsequent SCD. Consequently, the Committee was also persuaded that the relative risk of death for patients who had shown inducibility of their arrhythmia was greater than for patients who had not been tested.

4.3.11 The Committee considered that the trials in which inducibility of the arrhythmia was not an entry requirement included heterogeneous

populations of patients, both those who would and would not have shown inducibility on an EP test. The Committee therefore concluded that, in the newer trials, the average relative risk of SCD for the non-EP tested group might have been substantially lower if those who would have been positive on testing had been stratified separately.

4.3.12 The Committee additionally considered that the cost of EP testing to determine the need for an ICD would be a little over £3000 per device implanted. The Committee concluded that this additional cost would not influence the resulting ICERs significantly.

4.3.13 The Committee discussed with the clinical experts their concerns about the use of EP testing. In particular, it is uncomfortable for patients with a small but significant risk of death; the necessary human and technical resources for undertaking this testing are not widespread currently in the NHS; and the population of patients who are not inducible by EP testing might still be at significantly high risk of SCD. The experts also stated that instead of using EP testing, the risk of SCD in this patient population could be assessed by alternative clinical methods such as the presence of very low LVEF (for example, less than 20%), prolonged QRS duration or clinical evidence of heart failure.

4.3.14 The Committee noted that the economic evaluation jointly submitted by the manufacturers (which was based on MADIT II criteria; that is, not including the need for EP testing) suggested that the cost effectiveness of primary prevention compared with medical management alone was approximately £39,000 per additional QALY. The Buxton and Sharples economic evaluation for this group (assuming a life-time horizon, LVEF of less than 35%, a replacement rate of 6%, and an ICD acquisition and implantation cost of £16,250) suggested that the incremental cost per QALY was between £33,000 and £46,000, depending on whether the baseline risk of death was 7% or 12%. However, the Committee noted that the ICER associated with MADIT II criteria would be higher than

these figures suggest if it was incrementally compared with a strategy of EP testing (MADIT I criteria).

- 4.3.15 Results from the final Buxton and Sharples model for the EP testing strategy to identify a high-risk population (assuming three EP tests to identify one person at high risk of SCD) were in the range of £21,000 to £23,000 per additional QALY for people with an LVEF of less than or equal to 35% when a lifetime horizon was assumed. Given its considerations in sections 4.3.2 to 4.3.6, the Committee concluded that the use of EP testing would identify a group of individuals at high risk of SCD in whom the use of ICDs for primary prevention is cost effective.
- 4.3.16 The Committee considered the use of alternative clinical risk factors that could identify those at high risk of SCD other than the use of EP testing. They requested the further subgroup and modelling evidence that is reported in 4.2.9. From this evidence, the Committee concluded that in patients who have suffered an MI and who have an LVEF of less than 30%, the finding of a QRS duration of greater than or equal to 120 milliseconds conferred an additional relative risk of SCD that indicated a cost-effective use of ICD implantation.
- 4.3.17 The Committee, however, was not persuaded by the current evidence before it and the analyses undertaken that EP testing should be excluded as a cost-effective means of identifying high-risk individuals and determining whether an ICD should be implanted. It therefore agreed that the guidance from the original appraisal regarding primary prevention using EP testing should be maintained. The Committee was also not persuaded that extending the use of ICDs for primary prevention to the totality of MADIT II-type populations (that is, those in whom EP testing for arrhythmia inducibility had not been carried out) was a cost-effective use of NHS resources. It considered that neither the baseline risks (7–12%) of patients in this category nor specifically the patients' capacity to benefit as indicated by the relative risk reduction of SCD

(approximately 25–30%) were sufficient to allow this extension of ICD implantation to all patients within this group. However, within the population of patients included in the MADIT II trial, the Committee recognised that a group existed (LVEF of less than 30% and a QRS duration greater than or equal to 120 milliseconds) for whom implantation of an ICD was clinically and cost effective.

4.3.18 The Committee understood that the clinical evidence base relating to familial cardiac conditions with a high risk of sudden cardiac death, including long QT syndrome, hypertrophic cardiomyopathy, Brugada syndrome, arrhythmogenic right ventricular dysplasia, and following surgical repair of Tetralogy of Fallot has not changed since the publication of the previous NICE guidance. On this basis, the Committee concluded that this part of the guidance should not change, other than to take account of a comment from public consultation that the repair of other congenital conditions should be included along with the repair of Tetralogy of Fallot.

5 Recommendations for further research

5.1 Further analysis is required to better establish risk factors other than EP testing that can inform future economic evaluations.

6 Implications for the NHS

6.1 Since the final appraisal determination was issued, NICE has carried out more detailed costing analysis to support implementation of the guidance. The following costing tools are available from the NICE website (www.nice.org.uk/TA095).

- A national costing report, which estimates the overall resource impact associated with implementation.
- A local costing template: a simple spreadsheet that can be used to estimate the local cost of implementation.

7 Implementation and audit

7.1 Clinicians caring for people who are at risk of SCD should review their current practice and policies to take account of the guidance set out in Section 1.

7.2 Local guidelines, protocols or care pathways that refer to the care of people who have experienced VT, VF, MI, left ventricular dysfunction, long QRS duration, a familial cardiac condition with a high risk of sudden death or surgical repair for congenital heart disease should incorporate the guidance.

7.3 To measure compliance locally with the guidance, the following criteria could be used. Further details on suggestions for audit are presented in Appendix C.

7.3.1 An ICD is provided for a person who is in one of the following categories.

7.3.1.1 A person presents, in the absence of a treatable cause, with one of the following:

- having survived a cardiac arrest due to either VT or VF, **or**
- spontaneous sustained VT causing syncope or significant haemodynamic compromise, **or**
- sustained VT without syncope or cardiac arrest, and who has an associated reduction in EF and is no worse than class III of the New York Heart Association functional classification of heart failure.

7.3.1.2 A person has a history of an MI more than 4 weeks previously and **either:**

- **all of the following:**
 - left ventricular dysfunction with an LVEF of less than 35%**and**

- no worse than class III NYHA functional classification of heart failure **and**
- non-sustained VT on Holter monitoring **and**
- inducible VT on EP testing
- **or all of the following:**
 - left ventricular dysfunction with an LVEF of less than 30% **and**
 - no worse than class III NYHA functional classification of heart failure **and**
 - QRS duration of equal to or more than 120 milliseconds.

7.3.1.3 A person has a familial cardiac condition with a high risk of sudden death.

7.3.1.4 A person has undergone surgical repair of congenital heart disease.

8 Related guidance

- Dual-chamber pacemakers for the treatment of symptomatic bradycardia. *NICE Technology Appraisal Guidance* No. 88 (2005). Available from: www.nice.org.uk/TA088
- Chronic heart failure. *NICE Clinical Guideline* No. 5 (2003). Available from: www.nice.org.uk/CG005
- Heart failure – biventricular pacing (cardiac resynchronisation). *NICE Technology Appraisal* (expected date of publication March 2007)

9 Review of guidance

9.1 The Institute will consider the need to review this guidance following completion of the appraisal for biventricular pacing (cardiac resynchronisation) for the treatment of heart failure, which is due to be published in July 2007.

Andrew Dillon
Chief Executive
January 2006

Appendix A. Appraisal Committee members and NICE project team.

A. Appraisal Committee members

NOTE The Appraisal Committee is a standing advisory committee of the Institute. Its members are appointed for a 3-year term. A list of the Committee members who took part in the discussions for this appraisal appears below. The Appraisal Committee meets twice a month other than in December, when there are no meetings. The Committee membership is split into two branches, with the chair, vice chair and a number of other members attending meetings of both branches. Each branch considers its own list of technologies and ongoing topics are not moved between the branches.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each Appraisal Committee meeting, which include the names of the members who attended and their declaration of interests, are posted on the NICE website.

Professor A E Ades

MRC Senior Scientist, MRC Health Services Research Collaboration, Department of Social Medicine, University of Bristol

Dr Tom Aslan

General Practitioner, Stockwell, London

Professor David Barnett (Chair)

Professor of Clinical Pharmacology, University of Leicester

Professor Sheila Bird

MRC Biostatistics Unit, Cambridge

Mrs Elizabeth Brain

Lay Representative, Registered General Nurse

Dr Karl Claxton

Health Economist, University of York

Dr Richard Cookson

Senior Lecturer, Health Economics, Centre for Health Economics, University of York

Professor Christopher Eccleston

Director, Pain Management Unit, University of Bath

Professor Terry Feest

Professor of Clinical Nephrology, Southmead Hospital

Ms Alison Forbes

Lay Representative, Health Consultant Associate, Eden Insight

Mr John Goulston

Director of Finance, Barts and the London NHS Trust

Dr Rowan Hillson

Consultant Physician, Diabeticare, The Hillingdon Hospital

Dr Catherine Jackson

Clinical Lecturer in Primary Care Medicine, Alyth Health Centre, Angus, Scotland

Ms Judith Paget

Chief Executive, Caerphilly Local Health Board, Wales

Dr Ann Richardson

Lay Representative, Independent Research Consultant

Professor Philip Routledge

Professor of Clinical Pharmacology, College of Medicine, University of Wales, Cardiff

Dr Debbie Stephenson

Head of HTA Strategy, Eli Lilly and Company

Professor Andrew Stevens (Vice Chair)

Professor of Public Health, University of Birmingham

Dr Cathryn Thomas

General Practitioner, and Senior Lecturer, Department of Primary Care & General Practice, University of Birmingham

Dr Norman Vetter

Reader, Department of Epidemiology, Statistics and Public Health, College of Medicine, University of Wales, Cardiff

Dr Paul Watson

Medical Director, Essex Strategic Health Authority

Dr David Winfield

Consultant Haematologist, Royal Hallamshire Hospital

B. NICE Project Team

Each appraisal of a technology is assigned to a Health Technology Analyst and a Technology Appraisal Project Manager within the Institute.

Alastair Fischer

Technical Lead, NICE project team

Alec Miners

Technical Advisor, NICE project team

Alana Miller

Project Manager, NICE project team

Appendix B. Sources of evidence considered by the Committee

A The assessment reports for this appraisal were prepared by Southampton Health Technology Assessment Centre:

Jackie Bryant, Hakan Brodin, Emma Loveman, Elizabeth Payne and Andrew Clegg, *The clinical effectiveness and cost effectiveness of implantable cardioverter defibrillator: arrhythmias*, January 2004

Steve Palmer (University of York), Martin Buxton (Brunel University), Linda Sharples (MRC Biostatistics Unit), Chris Jackson (MRC Biostatistics Unit), Alec Miners (NICE) and Alastair Fischer (NICE), *Implantable cardioverter defibrillators for arrhythmias*, June 2004

Martin Buxton (Brunel University), Linda Sharples (MRC Biostatistics Unit), Chris Jackson (MRC Biostatistics Unit), *A model of cost effectiveness and cost–utility of Implantable Cardioverter Defibrillators used for primary prevention in a UK context*, March 2005

B The following organisations accepted the invitation to participate in this appraisal. They were invited to make submissions and comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD). Consultee organisations are provided with the opportunity to appeal against the Final Appraisal Determination.

I Manufacturer/sponsors:

- Biotronik UK Ltd
- ELA Medical UK
- Guidant
- Medtronic UK Ltd
- St Jude Medical UK Ltd

II Professional/specialist and patient/carer group:

- ABHI
- Action Heart
- Billericay, Brentwood and Wickford Primary Care Trust
- British Association for Nursing in Cardiac Care
- British Cardiac Patients Association
- British Cardiac Society
- British Cardiovascular Interventional Society
- British Heart Foundation
- British Society for Heart Failure
- Cardiomyopathy Association
- Department of Health
- Heart Rhythm UK (formerly known as British Pacing and Electrophysiology Group)
- Long Term Medical Conditions Alliance
- Royal College of Physicians
- Royal College of Physicians Cardiology Committee
- Society for Cardiological Science and Technology
- Society of Cardiothoracic Surgeons of Great Britain and Ireland
- Sudden Adult Death Trust
- Welsh Assembly Government

III Commentator organisations (without the right of appeal):

- Cochrane Heart Group
- National Coordinating Centre for Chronic Conditions
- NCCHTA

- NHS Confederation
- NHS Purchasing and Supplies Agency
- NHS Quality Improvement Scotland
- Southampton Health Technology Assessment Centre
- Wellcome Trust Cardiovascular Research Initiative

C The following individuals were selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups. They participated in the Appraisal Committee discussions and provided evidence to inform the Appraisal Committee's deliberations. They gave their expert personal view on implantable cardioverter defibrillators for arrhythmias by attending the initial Committee discussion and/or providing written evidence to the Committee. They were also invited to comment on the ACD.

- Dr Campbell Cowan, Cardiologist, Leeds General Infirmary, Clinical Expert nominated by the British Cardiac Society
- Ms Anne Jolly, Patient Expert nominated by SADS UK
- Dr Janet McComb, President, Heart Rhythm UK (formerly British Pacing and Electrophysiology Group), Clinical Expert
- Dr John Morgan, Consultant Cardiologist and Electrophysiologist, Southampton General Hospital, Clinical Expert nominated by the British Cardiac Society
- Ms Louise Powers, Patient Expert nominated by SADS UK

Appendix C. Detail on criteria for audit of the use of implantable cardioverter defibrillators for arrhythmias

Possible objectives for an audit

An audit could be carried out on the appropriateness of use of ICDs.

Possible patients to be included in the audit

In order to determine if clinicians are providing ICDs for all eligible patients, the audit could include all of the following patients:

- those who present, without a treatable cause, having survived a cardiac arrest due to either ventricular tachycardia (VT) or ventricular fibrillation (VF); or with spontaneous sustained VT causing syncope or significant haemodynamic compromise; or with sustained VT without syncope or cardiac arrest and an associated reduction in ejection fraction (EF) (LVEF of less than 35%) and are no worse than class III of the New York Heart Association (NYHA) functional classification of heart failure
- those with a history of previous MI (more than 4 weeks) and either all of: (a) left ventricular dysfunction with an LVEF of less than 35% and (b) no worse than class III NYHA and (c) non-sustained VT on Holter monitoring and (d) inducible VT on EP testing, or all of: (a) left ventricular dysfunction with an LVEF of less than 30% and (b) no worse than class III NYHA and (c) QRS duration greater than or equal to 120 milliseconds
- those with a familial cardiac condition with a high risk of sudden death
- those having undergone surgical repair of congenital heart disease.

To find these patients on a retrospective basis, the records of patients who have survived a cardiac arrest may have to be hand sorted to find patients whose arrest was due to VT or VF and who would therefore be eligible for an ICD as secondary prevention. The records of patients who have experienced VT may have to be hand sorted to find those who would be eligible for an ICD as secondary prevention.

To determine those who would be eligible for an ICD as primary prevention, the records of patients who have experienced an MI may have to be hand sorted to find those who have left ventricular dysfunction with an LVEF of less than 35%, no worse than class III NYHA and non-sustained VT on Holter monitoring and inducible VT on EP testing, or those who have left ventricular dysfunction with an LVEF of less than 30%, no worse than class III NYHA and a QRS duration of greater than or equal to 120 milliseconds.

In addition, to determine those who would be eligible for an ICD as primary prevention because of a familial cardiac condition or because of having undergone surgical repair of congenital heart disease, clinicians may need to decide on a reliable method for identifying these patients, particularly those with long QT syndrome.

The measures below do not apply to the use of implantable defibrillators for non-ischaemic dilated cardiomyopathy and these patients may be excluded from the audit.

An alternative is to establish a prospective data collection system that will capture whether or not eligible patients are being considered for an ICD, and if they are not, the reasons.

Measures that could be used as a basis for an audit

The measures that could be used in an audit of the use of ICDs are as follows.

Criterion	Standard	Exception	Definition of terms
<p>1. A person who presents, in the absence of a treatable cause, with one of the following is provided with an ICD as secondary prevention:</p> <p>a. having survived a cardiac arrest due to either VT or VF, or</p> <p>b. spontaneous sustained VT causing syncope or significant haemodynamic compromise, or</p> <p>c. sustained VT without syncope or cardiac arrest and an associated reduction in EF and is no worse than class III of the NYHA functional classification of heart failure</p>	<p>100% of patients presenting with the conditions listed in a–c</p>	<p>A. The person declines the ICD following a complete explanation by the person's clinician of the device and the reason for its use</p>	<p>'Secondary prevention' refers to the prevention of an additional life-threatening event in a survivor of a sudden cardiac event or a patient with recurrent unstable rhythms.</p> <p>'Associated reduction in EF' means LVEF < 35%.</p> <p>Clinicians will need to agree locally on how eligible cases can be identified, for audit purposes.</p>
<p>2. A patient with a history of previous myocardial infarction is provided with an ICD as primary prevention if the patient has all of the following:</p> <p>a. left ventricular dysfunction with an LVEF < 35%, and</p> <p>b. no worse than class III of the NYHA functional classification of heart failure and</p>	<p>100% of patients with a history of previous MI and all the conditions listed in a–d or all of the conditions in e–g</p>	<p>A. The person declines the ICD following a complete explanation by the person's clinician of the device and the reason for its use</p>	<p>'Primary prevention' refers to prevention of a first life-threatening arrhythmic event.</p> <p>'History of previous MI' means > 4 weeks.</p> <p>'Holter' refers to 24-hour ECG monitoring. EP testing refers to electrophysiological testing.</p>

<p>c. non-sustained VT on Holter monitoring and</p> <p>d. inducible VT on EP testing</p> <p>or has all of the following:</p> <p>e. left ventricular dysfunction with an LVEF < 30% and</p> <p>f. no worse than class III of the NYHA functional classification of heart failure and</p> <p>g. QRS duration of ≥ 120 milliseconds</p>			<p>Clinicians will need to agree locally on how eligible cases can be identified, for audit purposes.</p>
<p>3. A patient with either of the following is provided with an ICD as primary prevention:</p> <p>a. a familial cardiac condition with a high risk of sudden death or</p> <p>b. having undergone surgical repair of congenital heart disease</p>	<p>100% of patients with either a or b</p>	<p>A. The person declines the ICD following a complete explanation by the person's clinician of the device and the reason for its use</p>	<p>'Familial cardiac condition with a high risk of sudden death' includes the following: long QT syndrome, hypertrophic cardiomyopathy, Brugada syndrome or arrhythmogenic right ventricular dysplasia (ARVD). Clinicians will need to agree locally on how eligible cases can be identified, for audit purposes.</p>

Calculation of compliance

Compliance (%) with each measure described in the table above is calculated as follows.

$$\frac{\text{Number of patients whose care is consistent with the **critierion** **plus** number of patients who meet any **exception** listed}{\text{Number of patients to whom the **measure** applies}} \times 100$$

Clinicians should review the findings of measurement, identify whether practice can be improved, agree on a plan to achieve any desired improvement and repeat the measurement of actual practice to confirm that the desired improvement is being achieved.