



*National Institute for
Health and Clinical Excellence*

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Cardiac resynchronisation therapy for the treatment of heart failure

NICE technology appraisal guidance 120

Cardiac resynchronisation therapy for the treatment of heart failure

Ordering information

You can download the following documents from www.nice.org.uk/TA120

- The full guidance (this document).
- A quick reference guide for healthcare professionals.
- Information for people with heart failure and their carers ('Understanding NICE guidance').
- Details of all the evidence that was looked at and other background information.

For printed copies of the quick reference guide or 'Understanding NICE guidance', phone the NHS Response Line on 0870 1555 455 and quote:

- N1265 (quick reference guide)
- N1266 ('Understanding NICE guidance').

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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1 Guidance

This guidance should be read in conjunction with 'Implantable cardioverter defibrillators for arrhythmias' (NICE technology appraisal guidance 95 – see appendix C). This guidance on cardiac resynchronisation therapy provides additional treatment options for some of the groups of people covered in the guidance on implantable cardioverter defibrillators (ICDs).

1.1 Cardiac resynchronisation therapy with a pacing device (CRT-P) is recommended as a treatment option for people with heart failure who fulfil all the following criteria.

- They are currently experiencing or have recently experienced New York Heart Association (NYHA) class III–IV symptoms.
- They are in sinus rhythm:
 - **either** with a QRS duration of 150 ms or longer estimated by standard electrocardiogram (ECG)
 - **or** with a QRS duration of 120–149 ms estimated by ECG **and** mechanical dyssynchrony that is confirmed by echocardiography.
- They have a left ventricular ejection fraction of 35% or less.
- They are receiving optimal pharmacological therapy.

1.2 Cardiac resynchronisation therapy with a defibrillator device (CRT-D) may be considered for people who fulfil the criteria for implantation of a CRT-P device in section 1.1 and who also separately fulfil the criteria for the use of an ICD device as recommended in NICE technology appraisal guidance 95.

2 Clinical need and practice

2.1 Heart failure is a complex syndrome that can result from any structural or functional cardiac disorder that impairs the heart's ability to function efficiently as a pump to support physiological circulation. In a healthy heart, the lower chambers (ventricles) pump at the same time and in

synchrony with the upper chambers (atria). This appraisal considered the treatment of people with heart failure caused by left ventricular systolic dysfunction, in which the left ventricle fails to pump in synchrony with some or all of the other chambers of the heart. If the contractions lack synchrony (because of either poor atrioventricular synchrony or lack of synchrony between the two ventricles), the heart becomes less efficient as a pump.

- 2.2 The incidence and prevalence of heart failure increase steeply with age, and the average age at first diagnosis is 76 years. The incidence of heart failure in the UK is 140 per 100,000 men and 120 per 100,000 women. Although the incidence is higher in men, evidence suggests higher mortality in women with the condition. Around 3% of people aged 65–74 years have heart failure; this increases to about 7% of those aged 75–84 years, and to just over 14% in those aged 85 years and older. The prevalence of heart failure in the UK is 40 per 1000 in men and 30 per 1000 in women.
- 2.3 Heart failure has a poor prognosis, with about 40% of patients dying within 1 year of diagnosis. More severely ill patients are more likely to die because of pump failure (congestive heart failure), while those with less severe heart failure are more likely to experience sudden cardiac death.
- 2.4 Heart failure is characterised by symptoms such as breathlessness, reduced exercise tolerance, fatigue and fluid retention, together with signs of reduced cardiac output. The extent to which the symptoms of heart failure affect quality of life can be measured using the New York Heart Association (NYHA) classification: from class I (no limitations) to class IV (inability to carry out any physical activity without discomfort). Among people with heart failure due to left ventricular systolic dysfunction, 27% are in NYHA class I, 50% in class II, 11% in class III and 12% in class IV.
- 2.5 The diagnosis of heart failure is based on a combination of patient history, physical examination and appropriate investigations to assess cardiac

function (chest X-ray, electrocardiography or tests for elevated plasma concentrations of brain natriuretic peptide). People with heart failure who can be considered for cardiac resynchronisation therapy (CRT) have a reduced left ventricular ejection fraction (the fraction of blood pumped out of the left ventricle with each heart beat expressed as a percentage of the total volume), and characteristic changes on an ECG (which measures electrical dyssynchrony) due to abnormal electrical conductivity.

Echocardiographic assessment, which measures aspects of mechanical dyssynchrony, can also be used to identify patients whose condition is likely to respond to CRT.

- 2.6 Treatment for heart failure aims to improve life expectancy and quality of life. Heart failure should initially be managed pharmacologically in accordance with the NICE clinical guideline 'Chronic heart failure: management of chronic heart failure in adults in primary and secondary care' (NICE clinical guideline 5). However, as the condition becomes more severe, symptoms may no longer be controlled by pharmacological treatment.

3 The technology

- 3.1 The aim of CRT (also known as biventricular pacing) is to improve the heart's pumping efficiency by resynchronising the pumping action of the chambers. CRT involves implantation in the upper chest of a pulse generator from which three leads descend via veins into the heart. Leads are placed in the right atrium and the right ventricle, and a third lead (the left ventricular lead) is usually placed via the coronary sinus. CRT pacing (CRT-P) devices allow both regulation of atrioventricular delay and restoration of synchronous contraction by pacing the right atrium and both ventricles. A cardioverter defibrillator function can be included with the pulse generator to defibrillate the heart internally should an acute arrhythmic event occur, and in this case the device is known as a CRT-D device.

- 3.2 The costs of CRT devices based on NHS Purchasing and Supply Agency estimates are £3809 for a CRT-P device and £16,001 for a CRT-D device (both including leads, and excluding VAT). Costs may vary in different settings because of negotiated procurement discounts.
- 3.3 In 2004, 1224 CRT devices were implanted (504 CRT-P and 720 CRT-D devices) across 154 centres in England and Wales. The rate of increase of implantation for both devices is about 50% per annum.

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 Literature searches identified a total of 10 studies of CRT compared with optimal pharmacological therapy: five systematic reviews and five randomised controlled trials (RCTs). In the RCTs, a total of 3434 patients were randomised to receive either CRT in addition to optimal pharmacological therapy, or optimal pharmacological therapy alone. Of the five RCTs, four compared CRT-P with optimal pharmacological therapy (CARE-HF, COMPANION, MIRACLE and MUSTIC-SR), two compared CRT-D with optimal pharmacological therapy (COMPANION and CONTAK-CD), and one compared CRT-P, CRT-D and optimal pharmacological therapy (COMPANION). Three of the studies (CONTAK-CD, MIRACLE and MUSTIC-SR) randomised people to different pacing modes (CRT-P or CRT-D switched on compared with switched off) and two studies (CARE-HF and COMPANION) randomised people to receive either a device or optimal pharmacological therapy alone.
- 4.1.2 Outcomes for which the relative effectiveness of CRT-P and/or CRT-D devices compared with optimal pharmacological therapy alone was measured included mortality (all-cause mortality, heart failure deaths, cardiac death and sudden cardiac death), morbidity (hospitalisation and

symptoms of worsening heart failure), NYHA class, exercise capacity, adverse events and health-related quality of life.

- 4.1.3 The estimate of perioperative death associated with CRT (CRT-P and CRT-D pooled) in the RCTs was 0.8% (95% confidence interval [CI] 0.5% to 1.2 %). CRT devices were implanted successfully on average in 90.8% of patients (95% CI 89.6% to 92.0%). The most common causes of implant failure were related to the placement of the left ventricle (LV) lead, and the most common postoperative event was lead dislodgement. The COMPANION trial reported no significant difference in the rate of device- and surgery-related adverse events between CRT-P (10% compared with optimal pharmacological therapy) and CRT-D (8% compared with optimal pharmacological therapy).
- 4.1.4 Estimates of the proportion of patients who have a CRT device implanted successfully without an improvement in their condition range from 11% to 46% (patients' condition is assessed by clinical [NYHA class] and echocardiographic parameters). Clinical specialists did not consider there to be a difference between CRT-D and CRT-P devices in the number of patients whose condition did not improve.

CRT-P versus optimal pharmacological therapy alone

- 4.1.5 Four RCTs (CARE-HF, COMPANION, MIRACLE and MUSTIC-SR) evaluated the effectiveness of CRT-P compared with optimal pharmacological therapy alone. The smallest RCT (MUSTIC-SR) randomised 67 patients to CRT-P or optimal pharmacological therapy alone and did not show any statistically significant difference between the treatment arms for any of the outcomes measured except exercise capacity and health-related quality of life.
- 4.1.6 All four RCTs reported on the incidence of all-cause mortality. The three large RCTs (CARE-HF, COMPANION and MIRACLE) demonstrated a statistically significant reduction in all-cause mortality for CRT-P compared with optimal pharmacological therapy alone. The MUSTIC-SR trial

reported no significant difference. A meta-analysis of all four trials demonstrated a statistically significant reduction in all-cause mortality for CRT-P compared with optimal pharmacological therapy alone (pooled hazard ratio [HR] 0.71, 95% CI 0.58 to 0.87).

- 4.1.7 CARE-HF and COMPANION reported on the rate of death from heart failure and showed conflicting results: CARE-HF (n = 813) reported a statistically significant reduction in the incidence of death from heart failure for CRT-P compared with optimal pharmacological therapy alone, whereas COMPANION (n = 1520) reported no difference in treatment effect. Pooled analysis demonstrated a statistically significant reduction in death from heart failure for CRT-P compared with optimal pharmacological therapy alone (HR 0.62, 95% CI 0.46 to 0.83).
- 4.1.8 All four RCTs reported the incidence of sudden cardiac death. Only CARE-HF, the RCT with the longest follow-up, found a statistically significant difference between CRT-P and optimal pharmacological therapy alone. Meta-analysis of all four RCTs demonstrated no significant difference in the rate of sudden cardiac death for CRT-P compared with optimal pharmacological therapy alone (HR 0.75, 95% CI 0.45 to 1.18).
- 4.1.9 CARE-HF, MUSTIC-SR and MIRACLE reported on the rate of hospitalisation for heart failure, and the meta-analysis of these RCTs showed a statistically significant reduction in the rate of hospitalisation for CRT-P compared with optimal pharmacological therapy alone (pooled HR 0.48, 95% CI 0.37 to 0.61).
- 4.1.10 MIRACLE and CARE-HF found a statistically significant reduction in the risk of worsening heart failure for CRT-P compared with optimal pharmacological therapy (pooled HR 0.67, 95% CI 0.46 to 0.84). The MUSTIC-SR trial reported no significant difference in the risk of worsening heart failure for CRT-P compared with optimal pharmacological therapy.

- 4.1.11 Three RCTs (CARE-HF, COMPANION and MIRACLE) reported statistically significant improvements in NYHA class with CRT-P compared with optimal pharmacological therapy. All four RCTs showed consistent improvements in exercise capacity and health-related quality of life for CRT-P compared with optimal pharmacological therapy alone. There was no difference in the rate of atrial arrhythmias. Subgroup analysis showed no difference in the effectiveness of CRT-P between patients with ischaemic and non-ischaemic heart failure.

CRT-D versus optimal pharmacological therapy alone

- 4.1.12 Two RCTs (COMPANION and CONTAK-CD) evaluated the effectiveness of CRT-D compared with optimal pharmacological therapy alone.
- 4.1.13 COMPANION and CONTAK-CD reported on the effect of CRT-D on all-cause mortality, which was statistically significant in one of the trials. Meta-analysis demonstrated a statistically significant reduction in all-cause mortality for CRT-D compared with optimal pharmacological therapy alone (HR 0.65, 95% CI 0.49 to 0.85).
- 4.1.14 COMPANION also reported improvements in the effectiveness of CRT-D compared with optimal pharmacological therapy alone for rate of death from heart failure (HR 0.73, 95% CI 0.47 to 1.11, $p = 0.143$), rate of sudden cardiac death (HR 0.44, 95% CI 0.23 to 0.86, $p = 0.02$) and NYHA class (pooled RR 1.40, 95% CI 1.13 to 1.75, $p < 0.0001$). COMPANION reported a significant improvement in the number of patients hospitalised due to heart failure with CRT-D (rate ratio 0.59, 95% CI 0.49 to 0.70, $p < 0.0001$). CONTAK-CD reported no significant difference in the number of hospitalisations due to heart failure with CRT-D compared with optimal pharmacological therapy alone (risk ratio 0.82, 95% CI 0.52 to 1.26, $p = 0.326$)

CRT-D versus CRT-P

- 4.1.15 COMPANION was the only RCT that provided a direct comparison between the effectiveness of CRT-P and CRT-D. However, this RCT was

designed to test the effectiveness of CRT-D compared with optimal pharmacological therapy alone, and was not powered to detect differences in the effectiveness of CRT-D compared with CRT-P. This study did not demonstrate any differences in the effectiveness of CRT-D and CRT-P for any of the outcomes except the incidence of cardiac death and sudden cardiac death. CRT-D was associated with a statistically significant reduction in the incidence of both cardiac death (12.8% for CRT-D compared with 17.1% for CRT-P) and sudden cardiac death (2.9% for CRT-D compared with 7.8% for CRT-P, $p = 0.0001$) compared with CRT-P.

4.2 Cost effectiveness

- 4.2.1 Literature searches identified six relevant studies that evaluated the cost effectiveness of CRT in the treatment of heart failure: three modelling studies, two based on the COMPANION trial and one based on the CARE-HF trial. However, these studies were of limited relevance because none were conducted from a UK perspective.
- 4.2.2 Two models were submitted by consultees: a joint submission on behalf of Biotronik UK, Guidant, Medtronic, Sorin Biomedical CRM UK and St Jude Medical UK, and a separate submission by Guidant. All models calculated the incremental cost-effectiveness ratios (ICERs) of CRT compared with optimal pharmacological therapy alone for a 5-year time horizon. Neither of the manufacturers' analyses directly analysed the cost effectiveness of CRT-D compared with CRT-P. The results from the manufacturers' models gave ICERs of £2800 for CRT-P and £22,400 for CRT-D (each compared with optimal pharmacological therapy alone) based on effectiveness data from the COMPANION RCT, and an ICER of £15,600 for CRT-P compared with optimal pharmacological therapy based on effectiveness data from the CARE-HF RCT.
- 4.2.3 The Assessment Group developed separate models that compared the costs and outcomes of CRT-P versus optimal pharmacological therapy,

CRT-D versus optimal pharmacological therapy and CRT-D versus CRT-P. The Assessment Group constructed a lifetime model, which was populated by a mixed-age cohort of patients with clinical characteristics that are representative of the general population of people with heart failure. The model included device-related adverse events (device replacement, perioperative complications, infection, device upgrade, lead dislodgement), hospitalisation due to heart failure or arrhythmia, heart transplant, surgical failure, death and failure to respond. These events could be experienced in each arm of the model (CRT-P, CRT-D and optimal pharmacological therapy).

- 4.2.4 Estimates of clinical effectiveness of CRT devices and transition probabilities for moving between health states were based on pooled HRs from the systematic review and meta-analysis, where appropriate. This required extrapolation from the 36-month trial data for the remainder of the lifetime model. Effectiveness data and transition probabilities for ICDs were based on values in the literature.
- 4.2.5 The Assessment Group's model used hardware costs based on NHS Purchasing and Supply Agency estimates of the purchase price of CRT-P devices (mean cost of £3809 including leads) and CRT-D devices (mean cost of £16,001 including leads) (excluding VAT). These costs represent the average purchase costs of devices, which are likely to represent a large discount on the list (published) prices. Costs for optimal pharmacological therapy were provided by clinicians, and drug costs were taken from the 'British national formulary', edition 51 (March 2006).
- 4.2.6 In the base-case analysis, CRT-P was associated with an incremental cost of £11,630 and a quality-adjusted life year (QALY) gain of 0.70 (equivalent to 256 days of full health) compared with optimal pharmacological therapy, to give an ICER of £16,735 per QALY when a lifetime time horizon was considered. One-way sensitivity analysis demonstrated that the model was not sensitive to changes in most of the

model parameters (such as age of population, device costs and utilities). The model was sensitive to changes in the time horizon of the model, HR for the risk of death, worsening heart failure and sudden cardiac death. Probabilistic sensitivity analysis demonstrated that CRT-P is approximately 95% likely to be cost effective at a willingness to pay of £30,000 per QALY and 72% likely to be cost effective at a willingness to pay of £20,000 per QALY compared with optimal pharmacological therapy alone.

4.2.7 In the base-case analysis, CRT-D was associated with an incremental cost of £23,320 and a QALY gain of 0.99 (equivalent to 361 days of full health) compared with optimal pharmacological therapy, to give an ICER of £23,650 per QALY when a lifetime time horizon was considered. One-way sensitivity analysis demonstrated that the model was not sensitive to changes in most of the model parameters (such as age of population, device costs and utilities). The model was sensitive to changes in the time horizon of the model, HR for the risk of death, worsening heart failure and sudden cardiac death. Probabilistic sensitivity analysis demonstrated that CRT-P is approximately 80% likely to be cost effective at a willingness to pay of £30,000 per QALY and 30% likely to be cost effective at a willingness to pay of £20,000 per QALY compared with optimal pharmacological therapy alone.

4.2.8 The Assessment Group assessed the cost effectiveness of CRT-D compared with CRT-P. In the base-case analysis, CRT-D was associated with an incremental cost of £11,689 and a QALY gain of 0.29 (equivalent to 106 days of full health), to give an ICER of £40,160 per QALY when a lifetime time horizon was considered. One-way sensitivity analysis showed that the ICER was sensitive to the relative risk of sudden cardiac death with CRT-D compared with CRT-P devices.

4.3 Consideration of the evidence

- 4.3.1 The Appraisal Committee reviewed the data available on the clinical and cost effectiveness of CRT, having considered evidence on the nature of the condition and the value placed on the benefits of CRT by people with heart failure, those who represent them and clinical specialists. The Committee also considered the evidence on the clinical and cost effectiveness of CRT in light of current NICE guidance on the use of ICDs for the treatment of arrhythmias (NICE technology appraisal 95 – see appendix C). It was also mindful of the need to take account of the effective use of NHS resources.
- 4.3.2 The Committee understood that the benefits of implantation of a CRT device are related to improvements in the symptoms of heart failure, the extension of life of those with heart failure and a reduction in the incidence of sudden cardiac death. The risk of sudden cardiac death is related to the presence of both heart failure associated with ventricular dyssynchrony and other underlying cardiac conditions that could add to the risk of sudden cardiac death. The Committee heard from clinical specialists that in patients with a diagnosis of heart failure associated with left ventricular systolic dysfunction, the use of CRT is based primarily on a diagnosis of electrical dyssynchrony as indicated by a widened QRS complex of more than 150 ms on a standard ECG. The Committee also understood from the clinical specialists that confirmation of the presence of mechanical dyssynchrony by echocardiography was considered appropriate in patients with electrical dyssynchrony as indicated by a QRS duration of between 120 ms and 149 ms. The Committee noted that this approach was the same as the inclusion criteria for the CARE-HF trial.
- 4.3.3 The Committee considered the inclusion criteria for patients entered into the RCTs identified, which included symptomatic heart failure at NYHA class II–IV, a QRS duration greater than 120 ms or 150 ms, and a left ventricular ejection fraction of less than 35%. All of these RCTs excluded

patients with atrial fibrillation. Clinical specialists advised that most patients included in the RCTs had a QRS duration greater than 150 ms, and that patients who have a greater degree of electrical dyssynchrony (QRS duration greater than 150 ms) may derive more benefit from CRT. The Committee was aware that there is uncertainty as to the exact mechanism of this benefit and of the direct relationship between the degree of dyssynchrony and the degree of benefit derived from CRT-P. The Committee also heard from the clinical specialists that echocardiography alone is not a good predictor of response to CRT, and agreed that QRS duration should be the primary criterion by which patient eligibility for CRT is determined. The Committee noted that in one of the large studies (CARE-HF) additional evidence of mechanical dyssynchrony from echocardiography was required in patients with a QRS duration of between 120 ms and 150 ms, and was therefore persuaded that such a requirement would be appropriate to use in clinical practice.

- 4.3.4 The Committee was aware that the severity of the symptoms of heart failure, as indicated by the NYHA class, may vary from day to day. However, it accepted that on average the NYHA class is relatively stable over the medium term and will tend to worsen over the long term. The Committee was persuaded that patients with current or recent NYHA class III and IV symptoms (similar to the patients enrolled in the principal clinical trials) would derive most benefit from CRT.
- 4.3.5 The Committee considered there to be insufficient evidence on the effectiveness of CRT in patients with heart failure associated with atrial fibrillation for it to make recommendations for this group, and emphasised the need for further research on the effectiveness of CRT in these patients.
- 4.3.6 The Committee considered the evidence from RCTs, clinical specialists and patient experts on the benefits and risks of CRT compared with optimal pharmacological therapy alone. The Committee concluded that

the implantation of a CRT-P or CRT-D device led to significant improvements in all-cause mortality, hospitalisation for heart failure and health-related quality of life compared with optimal pharmacological therapy alone. The Committee heard from the clinical specialists that some patients with heart failure who initially have a CRT-P device inserted may require an upgrade to a defibrillator (CRT-D) device because of the progression of underlying disease and the emergence of additional risk of sudden cardiac death.

- 4.3.7 The Committee noted that the only evidence on the effectiveness of CRT-D compared with CRT-P was based on the results of the COMPANION trial, which was not powered to detect a difference between the two device types. However, the Committee agreed that there is sufficient evidence from this trial to suggest that the incidence of sudden cardiac death is lower after CRT-D device implantation than after CRT-P device implantation. The Committee heard from the clinical specialists that implantation of a CRT-P device is more technically challenging than for standard pacemaker devices, and that implantation of a CRT-D device is even more so. In addition, the success of implantation increases with operator experience.
- 4.3.8 The Committee additionally heard from the clinical specialists that CRT-D devices may deliver inappropriate defibrillating shocks, which may be distressing for patients and impair their quality of life, especially for patients who are at low risk of sudden cardiac death. The Committee understood that the risks and benefits of the use of a defibrillator device would need to be evaluated on a case-by-case basis.
- 4.3.9 The Committee heard from the clinical specialists that the decision whether to implant a CRT-D or a CRT-P device usually depends on whether the patient has additional risk factors for sudden cardiac death, over and above those associated with cardiac dyssynchrony, which might have led them to consider the use of an ICD. The Committee was also

mindful that people who have a CRT-P device implanted may go on to develop additional risk factors for sudden cardiac death and thus might require an upgrade to a CRT-D device.

- 4.3.10 The Committee noted that a proportion of patients (11–46%) who have a CRT device implanted successfully do not respond to treatment. The clinical specialists advised that this occurs either because the leads, in particular the left ventricular lead, are not at the optimal site for ventricular stimulation, or because the condition of some patients fails to respond to CRT. The Committee understood that there was no definitive evidence relating to clinical factors that would allow patients whose condition might not respond to be identified before the device is implanted.
- 4.3.11 The Committee reviewed all data on the cost effectiveness of CRT in the manufacturers' and Assessment Group's models. The Committee considered a 5-year time horizon to be inappropriate because many patients (depending on the severity of underlying disease) are alive 5 years after the implant, and therefore a 5-year time horizon would not incorporate all of the costs of CRT, in particular the cost of device replacement. The Committee considered the ICERs generated by the Assessment Group's model that used a lifetime time horizon would be more appropriate, because this model incorporated all costs and benefits of CRT compared with optimal pharmacological therapy alone, and also included the probability of not responding to therapy. The Committee noted the higher average age of patients in the Assessment Group's model (74 years) compared with that in the RCTs (65 years in CARE-HF and 67 years in COMPANION). It considered the age range used in the Assessment Group's model to be appropriate because it reflects the average age of patients in England and Wales with heart failure.
- 4.3.12 The Committee considered the evidence on the cost effectiveness of CRT-P versus optimal pharmacological therapy alone and the associated ICER of £17,000 per QALY obtained using the Assessment Group's

model. The Committee concluded that CRT-P is cost effective for the treatment of heart failure caused by left ventricular systolic dysfunction in people who: have NYHA class III–IV symptoms; are in sinus rhythm either with a QRS duration of 150 ms or longer estimated by standard ECG or a QRS duration of 120–149 ms and mechanical dyssynchrony that is confirmed by echocardiography; have a left ventricular ejection fraction of 35% or less; and are receiving optimal pharmacological therapy.

- 4.3.13 The Committee considered the evidence on the cost effectiveness of CRT-D. It noted that the device costs for CRT-D are higher than those for CRT-P, and agreed that CRT-D should be compared with the next most effective treatment, which is CRT-P. The Committee therefore considered an incremental analysis of CRT-D compared with CRT-P to be the most relevant analysis. The Committee noted that implantation of a CRT-D device instead of a CRT-P device in the total population included in the RCTs would be associated with an ICER of £40,000 per QALY, and considered that this would not represent an efficient use of NHS resources.
- 4.3.14 The Committee considered a subgroup of people with heart failure who have additional risk factors for sudden cardiac death, and concluded that these patients would require both resynchronisation and defibrillation. The Committee heard from the Assessment Group that the cost effectiveness of CRT-D would be considerably improved in people with additional risk factors for sudden cardiac death. Thus the Committee concluded that for people who present with heart failure due to left ventricular systolic dysfunction fulfilling the criteria in section 1.1 (also listed in section 4.3.12) for the implantation of a CRT-P device and who also have additional risk factors for sudden cardiac death that separately fulfil the criteria for the use of an ICD device (as in NICE technology appraisal guidance 95 – see appendix C), the addition of the defibrillator function in the form of a CRT-D device could be considered. The Committee advised that consideration should be given to an early review of the guidance on ICDs, in particular

focusing on the patient group who could be considered for either an ICD or a CRT-D device.

5 Implementation

- 5.1 The Healthcare Commission assesses the performance of NHS organisations in meeting core and developmental standards set by the Department of Health in 'Standards for better health' issued in July 2004. The Secretary of State has directed that the NHS provides funding and resources for medicines and treatments that have been recommended by NICE technology appraisals normally within 3 months from the date that NICE publishes the guidance. Core standard C5 states that healthcare organisations should ensure they conform to NICE technology appraisals.
- 5.2 'Healthcare Standards for Wales' was issued by the Welsh Assembly Government in May 2005 and provides a framework both for self-assessment by healthcare organisations and for external review and investigation by Healthcare Inspectorate Wales. Standard 12a requires healthcare organisations to ensure that patients and service users are provided with effective treatment and care that conforms to NICE technology appraisal guidance. The Assembly Minister for Health and Social Services issued a Direction in October 2003 which requires Local Health Boards and NHS Trusts to make funding available to enable the implementation of NICE technology appraisal guidance, normally within 3 months.
- 5.3 NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (www.nice.org.uk/TA120).
- Local costing template incorporating a costing report to estimate the savings and costs associated with implementation.
 - Audit criteria to monitor local practice.

6 Recommendations for further research

- 6.1 The Appraisal Committee recommends further research to evaluate the clinical and cost effectiveness of CRT in people with heart failure associated with left ventricular systolic dysfunction and concomitant atrial fibrillation.

7 Related NICE guidance

- MI: secondary prevention in primary and secondary care for patients following a myocardial infarction. NICE clinical guideline 48 (2007). Available from: www.nice.org.uk/CG048
- Implantable cardioverter defibrillators for arrhythmias (review of technology appraisal guidance 11). NICE technology appraisal guidance 95 (2006). Available from: www.nice.org.uk/TA095
- Atrial fibrillation: the management of atrial fibrillation. NICE clinical guideline 36 (2006). Available from: www.nice.org.uk/CG036
- Chronic heart failure: management of chronic heart failure in adults in primary and secondary care. NICE clinical guideline 5 (2003). Available from: www.nice.org.uk/CG005

8 Review of guidance

- 8.1 The review date for a technology appraisal refers to the month and year in which the Guidance Executive will consider whether the technology should be reviewed. This decision will be taken in the light of information gathered by the Institute, and in consultation with consultees and commentators.
- 8.2 Guidance on the use of a defibrillator device (CRT-D or ICD) for the subpopulation of people with heart failure and additional risk factors for sudden cardiac death will be considered for review in 2008.

- 8.3 The guidance on this technology for people who do not have additional risk factors for sudden cardiac death will be considered for review in July 2010.

Andrew Dillon
Chief Executive
May 2007

Appendix A. Appraisal Committee members and NICE project team

A *Appraisal Committee members*

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 three times a month except in December, when there are no meetings. The Committee membership is split into three branches, each with a chair and vice-chair. 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 declarations of interests, are posted on the NICE website.

Dr Jeff Aronson

Reader in Clinical Pharmacology, Radcliffe Infirmary

Dr Darren Ashcroft

Senior Clinical Lecturer, School of Pharmacy and Pharmaceutical Sciences,
University of Manchester

Professor David Barnett (Chair)

Professor of Clinical Pharmacology, University of Leicester

Dr Peter Barry

Consultant in Paediatric Intensive Care, Leicester Royal Infirmary

Professor Stirling Bryan

Director of the Health Economics Facility, University of Birmingham

Professor John Cairns

Public Health and Policy, London School of Hygiene and Tropical Medicine

Dr Mark Chakravarty

Head of Government Affairs and NHS Policy, Procter and Gamble Pharmaceuticals (UK) Ltd

Professor Christopher Fowler

Professor of Surgical Education, University of London

Dr Fergus Gleeson

Consultant Radiologist, Churchill Hospital

Mrs Barbara Greggains

Company Director, Greggains Management Limited

Lynn Field

Nurse Director, Pan Birmingham Cancer Network

Mr Terence Lewis

Mental Health Consultant, National Institute for Mental Health in England

Professor Gary McVeigh

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Dr Neil Milner

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Dr Rubin Minhas

General Practitioner, CHD Clinical Lead, Medway PCT

Dr John Pounsford

Consultant Physician, North Bristol NHS Trust

Dr Rosalind Ramsay

Consultant Psychiatrist, Adult Mental Health Services, Maudsley Hospital

Dr Stephen Saltissi

Consultant Cardiologist, Royal Liverpool University Hospital

Mr Roderick Smith

Corporate lead, finance, West Sussex PCT

Dr Ken Stein

Senior Lecturer in Public Health, Peninsula Medical School, University of Exeter

Mr Cliff Snelling

Lay member

Professor Andrew Stevens

Professor of Public Health, University of Birmingham

B NICE project team

Each technology appraisal is assigned to a team consisting of one or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

Eleanor Donegan

Technical Lead

Elisabeth George

Technical Adviser

Chris Feinmann

Project Manager

Appendix B. Sources of evidence considered by the Committee

- A. The assessment report for this appraisal was prepared by Peninsula Technology Assessment Group, Universities of Exeter and Plymouth.
- Fox M, Mealing S, Anderson R et al. The effectiveness and cost effectiveness of cardiac resynchronisation (biventricular pacing) for heart failure: a systematic review and economic model, September 2006.
- B. The following organisations accepted the invitation to participate in this appraisal. They were invited to comment on the draft scope, assessment report and appraisal consultation document (ACD). Organisations listed in I and II were also invited to make written submissions and have the opportunity to appeal against the final appraisal determination.
- I. Manufacturers/sponsors:
- Biotronik UK Ltd
 - Guidant Ltd
 - Medtronic Ltd
 - Sorin Biomedica CRM UK Ltd
 - St Jude Medical UK Ltd
- II. Professional/specialist and patient/carer groups:
- British Cardiac Society
 - British Society for Heart Failure
 - Primary Care Cardiovascular Society
 - Royal College of General Practitioners
 - Royal College of Nursing
 - Royal College of Physicians of Edinburgh
 - Royal College of Physicians' Cardiology Committee
 - Action Heart

- Arrhythmia Alliance
- British Heart Foundation
- Cardiac Risk in the Young

III. Commentator organisations (without the right of appeal):

- Association of British Healthcare Industries (ABHI)
- EUCOMED
- Medicines and Healthcare products Regulatory Agency (MHRA)
- NHS Quality Improvement Scotland
- British Society for Cardiovascular Research
- Cardiac and Cardiology Research Department – Barts and The London, Queen Mary's School of Medicine and Dentistry

C. The following individuals were selected from clinical specialist and patient advocate nominations from the non-manufacturer/sponsor consultees and commentators. They participated in the Appraisal Committee discussions and provided evidence to inform the Appraisal Committee's deliberations. They gave their expert personal view on CRT for the treatment of heart failure by attending the initial Committee discussion and/or providing written evidence to the Committee. They were also invited to comment on the ACD.

- Professor John Cleland, Professor of Cardiology, Castle Hill Hospital, nominated by the Cochrane Heart Group – clinical specialist
- Dr Peter J Cowburn, Consultant Cardiologist, Southampton General Hospital, nominated by the British Society for Heart Failure – clinical specialist
- Robert Hall, Chief Executive, Cardiomyopathy Association, nominated by the Cardiomyopathy Association – patient expert
- Mr Terence Mounce, nominated by the Cochrane Heart Group – patient expert

Appendix C. Guidance on the use of Implantable cardioverter defibrillators for arrhythmias (NICE technology appraisal guidance 95)

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.