**NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE**

# Implantable cardioverter defibrillators for the treatment of arrhythmias and cardiac resynchronisation therapy for the treatment of heart failure (review of TA95 and TA120)

## Draft scope

## Appraisal objective[1]

To review and update as necessary guidance to the NHS in England and Wales on the clinical and cost effectiveness of implantable cardioverter defibrillators for the treatment of arrhythmias (January 2006[2] ) and cardiac resynchronisation therapy for the treatment of heart failure (May 2007[3])

## Background

### Arrhythmias

Abnormal heart rhythms are known as arrhythmias. Arrhythmias are caused by an abnormality in the electrical conduction system resulting in a reduction in cardiac efficiency. There are many different types of fast arrhythmias, some arise from above the ventricles and include supraventricular tachycardia, atrial fibrillation and atrial flutter and others arise from the ventricles and are called ventricle arrhythmias. There are two types of ventricular arrhythmias, ventricular tachycardia and ventricular fibrillation. Ventricular tachycardia is where the ventricles beat faster than normal (between 120 and 200 beats per minute) but the rate in the atria is normal. Ventricular fibrillation is where there is chaotic electrical activation of the ventricles resulting in no effective output from the heart. Arrhythmias arising in the ventricles can result in insufficient blood being pumped by the heart to sustain life. Ventricular arrhythmias can happen suddenly and unexpectedly, and sometimes can be fatal. Approximately 8 in every 10 sudden unexpected deaths from heart problems, known as sudden cardiac deaths (SCD), are caused by ventricular tachycardia or ventricular fibrillation.

Ventricular arrhythmias have many different causes but they most commonly happen in people with underlying heart disease. This includes people who are having or just had a heart attack; people with cardiomyopathy (a disease of the heart muscle), and people who have heart failure. Less commonly, ventricular arrhythmias can happen in people who do not have structural heart

[1] The original Department of Health and Welsh Assembly remits to the institute were to appraise the clinical and cost of : implantable cardioverter defibrillators in the treatment of arrhythmias and biventricular pacing (cardiac resynchronisation) to restore synchronous cardiac contraction in patients with advanced heart failure

[2] Implantable cardioverter defibrillators for arrhythmias (No 95, January 2006)

[3] Cardiac resynchronisation therapy for the treatment of heart failure (No. 120, May 2007)

disease, for example those people with long QT syndrome (a heart condition in which delayed repolarization of the heart following a heartbeat).

Treatment of ventricular arrhythmias consists of anti-arrhythmic drug therapy and other drug treatments specific to the underlying heart disease. Chronic prophylactic anti-arrhythmic drug therapy aims to suppress the development of arrhythmias, but does not terminate an arrhythmia once it is initiated. People with arrhythmias at risk of SCD may be given an implantable cardioverter defibrillator (ICD) device to detect and treat such arrhythmia. NICE technology appraisal guidance 95 recommends ICDs for both secondary prevention (that is, prevention of a further life-threatening event in survivors of a sudden cardiac episode or patients with recurrent unstable rhythms) and primary prevention (that is, prevention of a first-life threatening arrhythmic event).

**Heart failure**

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 in and in synchrony with the upper chambers (atria). 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. Some patients have heart failure as a result of left ventricular systolic dysfunction (LVSD) in which the left ventricle does not pump in synchrony with some or all of the other chambers of the heart. LVSD is associated with 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). Other people have heart failure with a preserved ejection fraction, which is usually associated with impaired left ventricular relaxation, rather than left ventricular contraction, and is characterised by a normal or preserved left ventricular ejection fraction. LVSD is the most common underlying cardiac abnormality in people with heart failure in the UK.

The incidence of heart failure in the UK is 140 per 100,000 men and 120 per 100,000 women. Approximately 900,000 people in England and Wales have heart failure, of which at least half have LVSD. Heart failure has a poor prognosis, with about 40% of patients dying within 1 year of diagnosis. The incidence and prevalence of heart failure increases with age and the average age at first diagnosis is 76 years.

Symptoms of heart failure include shortness of breath, swelling in the ankles or legs, weight gain, and fatigue. The New York Heart Association (NYHA) Functional Classification provides a way of classifying the severity of the symptoms of heart failure. It places the condition in one of four categories according to limitations in physical activity and symptoms related to shortness of breath and/ or angina pain (Class 1 [no limitations] to class IV [inability to carry out any physical activity without discomfort]).

Treatment of 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 108 'Chronic heart failure: management of chronic failure in adults in primary and secondary care' (NICE clinical guideline 108). However, as the condition becomes more severe, cardiac function and symptoms may no longer be controlled by pharmacological treatment and require invasive procedures. Cardiac function and heart failure symptoms may be improved by the implantation of a cardiac rhythm device which can sense and stimulate the atria, right and left ventricles independently. The devices are known as cardiac resynchronisation pacemaker (CRT-P) or cardiac resynchronisation defibrillator (CRT-D). The decision to implant CRT is also guided by left ventricular ejection fraction. NICE technology appraisal guidance120 recommends cardiac resynchronisation therapy with a pacing device (CRT-P) for people with heart failure who are currently experiencing or have recently experienced NYHA class III-IV symptoms; are in sinus rhythm, have a left ventricular ejection fraction of 35% or less and are receiving optimal pharmacological therapy. NICE technology appraisal guidance 120 also recommends cardiac resynchronisation therapy with a defibrillator device (CRT-D) for people who fulfil the criteria for implantation of a CRT-P device in section 1.1 in NICE technology appraisal guidance 120 and who also separately fulfil the criteria for the use of an ICD device as recommended in NICE technology appraisal guidance 95.

## The technologies

### Implantable cardioverter defibrillators

A transvenous ICD is a device implanted into the upper chest below the left shoulder, with leads into the heart to pace, sense and defibrillate.. Dual-function transvenous 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. A subcutaneous ICD (the S-ICD system) is implanted in the vicinity of the left fifth and sixth intercostal spaces, near the mid-axillary line, and has no leads either in or on the heart. All ICDs sense continuously until an arrhythmia is recognised at which time a shock is delivered to the heart. The technology recognises and differentiates between a number of arrhythmias, which may enable it to provide more appropriate therapy, in particular lessening the incidence of inappropriate shocks.

### Cardiac resynchronisation therapy

Traditional pacemakers use one or two leads to sense and pace the right atrium and right ventricle or both, thus keeping the right atrium and right ventricle working together (AV Synchrony). CRT uses a third lead to pace (CRT-P) the left ventricle via the coronary sinus. After the atria contract, both ventricles are paced to contract at the same time, causing the heart to contract in a more efficient manner, resulting in improved cardiac function.

A cardioverter defibrillator can be included with the pulse generator to defibrillate the heart internally should an acute arrhythmic event occur, and this the device is known as a CRT-D device.

There are 6 manufacturers of ICD and CRT devices that have gained a CE mark. These are Biotronik UK, Boston scientific, Cameron health, Medtronic, St Jude medical and Sorin Group

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| **Intervention(s)** | Implantable cardioverter defibrillators (ICDs) in addition to optimal pharmacological treatment | Cardiac resynchronisation therapy (CRT-P or CRT-D) in addition to optimal pharmacological treatment | Cardiac resynchronisation therapy with a defibrillator device (CRT-D) in addition to optimal pharmacological treatment |
| **Population(s)** | People at increased risk of sudden cardiac death as a result of ventricular arrhythmias despite optimal pharmacological treatment | People with heart failure as a result of left ventricular systolic dysfunction and cardiac dyssynchrony despite optimal pharmacological treatment | People with both conditions described to the left |
| **Comparators** | • standard care (optimal pharmacological treatment without ICD) | • CRT-P and CRT-D will be compared with each other<br>• standard care (optimal pharmacological treatment without CRT) | • ICD<br>• standard care (optimal pharmacological treatment without CRT-D) |
| **Outcomes** | • mortality<br>• adverse effects of treatment<br>• health related quality of life<br>• symptoms and complications related to tachyarrhythmias<br>• heart failure hospitalisations<br>• change in NYHA class<br>• change in left ventricular ejection fraction | | |

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| **Economic analysis** | The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.<br>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.<br>Costs will be considered from an NHS and Personal Social Services perspective. |
| **Other considerations** | Guidance will only be issued in accordance with the CE marking of the technologies |
| **Current NICE Guidance** | ***Technology Appraisal No 95 January 2006 Implantable cardioverter defibrillators for arrhythmias***.<br>This appraisal does not cover the use of implantable defibrillators for non-ischaemic dilated cardiomyopathy.<br>1.1 ICDs are recommended for patients in the following categories.<br>1.1.1 'Secondary prevention', that is, for patients who present, in the absence of a treatable cause, with one of the following:<br>• having survived a cardiac arrest due to either ventriculartachycardia (VT) or ventricular fibrillation (VF)<br>• spontaneous sustained VT causing syncope or significant haemodynamic compromise<br>• 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).<br>1.1.2 'Primary prevention', that is, for patients who have:<br>• a history of previous (more than 4 weeks) myocardial infarction (MI) and:<br>**either** |

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| | − 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<br>− non-sustained VT on Holter (24-hour electrocardiogram [ECG]) monitoring, and<br>− inducible VT on electrophysiological (EP) testing<br>**or**<br>− 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<br>− QRS duration of equal to or more than 120 milliseconds<br>• 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.<br><br>***Technology Appraisal No 120 May 2007 Cardiac resynchronisation therapy for the treatment of heart failure.***<br>This guidance should be read in conjunction with 'Implantable cardioverter defibrillators for arrhythmias' 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).<br>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.<br>• They are currently experiencing or have recently experienced New York Heart Association (NYHA) class III–IV symptoms.<br>• They are in sinus rhythm:<br>− **either** with a QRS duration of 150 ms or longer estimated by standard electrocardiogram |

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| | (ECG)<br>– **or** with a QRS duration of 120–149 ms estimated by ECG and mechanical dyssynchrony that is confirmed by echocardiography.<br>• They have a left ventricular ejection fraction of 35% or less.<br>• They are receiving optimal pharmacological therapy.<br>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. |
| **Related NICE Guidance** | Related Guidelines:<br>Clinical Guideline No 36 June 2006 Atrial Fibrillation<br>Clinical Guideline No 108 August 2010 Chronic Heart Failure<br>Related Quality standards<br>Ongoing Quality standard. Quality standard in preparation, 'Chronic Heart Failure' Earliest anticipated date of publication June 2011<br>Related NICE Pathways:<br>Chronic Heart Failure |

**Questions for consultation**

Have the three populations in this scope been defined correctly?

Have the most appropriate comparators for implantable cardioverter defibrillators and cardiac resynchronisation therapy been included in the scope? Please note that for the purpose of this appraisal a comparator is defined as current clinical practice in the NHS.

In particular:

- Should ICDs be included as a comparator to CRT-D given that the MIRACLE ICD trial (referenced in the ESC Guidelines 2010 on device therapy in heart failure) compared CRT-D with ICD in patients with heart failure in NYHA class III-IV and with a conventional indication for an ICD?

- Should standard care (optimal pharmacological treatment without CRT-D) be included as comparator to CRT-D?

Have the most appropriate outcomes for implantable cardioverter defibrillators and cardiac resynchronisation therapy been included in the scope? In particular should exercise capacity be included given that it was an outcome measure in Technology Appraisal no.120?

Please consider whether in the remit or the scope there are any issues relevant to equality. Please pay particular attention to whether changes need to be made to the remit or scope in order to promote equality, eliminate unlawful discrimination, or foster good relations between people who share a characteristic protected by the equalities legislation and those who do not share it, or if there is information that could be collected during the assessment process which would enable NICE to take account of equalities issues when developing guidance.

Do you consider the technologies to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a ‘step-change’ in the management of the condition)?

Do you consider that the use of these technologies can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits