Implantable cardioverter defibrillators for the treatment of arrhythmias and cardiac resynchronisation therapy for the treatment of heart failure (review of TA95 and TA120) [ID481]

Manufacturers' Comments on Appraisal Consultation Document (ACD)

The ABHI would like to thank NICE for the opportunity to comment on the ACD. We are grateful for the collaborative engagement with device manufacturers and other stakeholders that has been undertaken in arriving at the provisional recommendations.

Executive Summary

While the recommendations contained within the ACD would improve patient access in certain patient groups to ICD and CRT devices, we are concerned that in some instances the recommendations do not represent a sound basis for guidance to the NHS.

1. QRS < 120ms, NYHA I-III, LVEF < 35%

To exclude the option of ICD therapy in patients with QRS <120ms would place NICE guidance at odds with European and North American guidance. Patients within this group are at high risk of sudden cardiac death and thus gain a mortality benefit from an ICD. To exclude these patients would be counter to the aims of NHS Outcomes Framework Domain 1 'preventing people from dying prematurely'.

The Committee did not recommend within this group on the basis of cost-effectiveness. However, the ICERs presented in this group of patients are similar to those in other groups that have received a recommendation for device therapy. The ICERs reduced significantly when the model is re-run using recently collated 2013-14 prices/tariffs (see below).

2. QRS 120-149, LBBB, NHYA II, LVEF < 35%

ICD has been recommended in this group despite being extendedly dominated by CRT-D with an ICER of £22,049.

Three individual studies have been cited as the reason for this recommendation. It seems contrary to the principles of evidence evaluation in a Technology Appraisal to select out individual studies that have already been taken into account in the ABHI review of the relevant available data that informs device treatment in this group of patients.

Each of the individual studies referred to in the ACD have significant limitations that apparently were not considered. For instance, the Echo-CRT study only is informative about the lack of value of echocardiography in selecting patients with QRS <130ms for CRT. It does not indicate a lack of benefit of CRT in QRS 120-149ms, NYHA II, LVEF <35% patients.

3. QRS >150, LBBB, NYHA III, LVEF < 35%

It is clinically counter-intuitive not to recommend CRT-D as an option for these patients when patients without LBBB can be offered CRT-D. Sudden Cardiac Death (SCD) is the most common cause of death in these patients and to exclude patients from the protection offered by CRT-D would be counter to the aims of NHS Outcomes Framework Domain 1 'preventing people from dying prematurely'.

The ICER is marginally above £30,000 per QALY when a 5-year constant mortality effect is assumed, however, it is below £30,000 when the 7.5 year constant mortality effect is considered. This effect duration is more conservative than that deemed acceptable in the previous appraisal.

Concluding remarks

The ABHI and clinical representation have articulated already, and would like to emphasize, that the indications proposed herein for ICD and CRT devices do not imply there is a device for every heart failure patient. The heart failure population eligible for any of the devices in this appraisal is a highly selected sub population.

The uncertainty that the Committee noted to be present in some of the clinical and economic evidence in this appraisal is remarkably decreased compared to the previous appraisals in TA 095 & 120. The ABHI believes that given the evidence presented for this appraisal, the level of uncertainty is generally at acceptable levels.

Provisional Guidance

The recommendations for ICD are unchanged in secondary prevention and familial conditions and patients who have undergone surgical repair of congenital heart disease. These indications were not re-evaluated in the current review. The recommendations in this review are:

Table 1. ACD recommendations (with ABHI highlights for discussion)

	With LBBB	NYHA I	NYHA II	NYHA III	NYHA IV
< 120 ms	No	OMT	OMT	OMT	OMT
120-149 ms	No	ICD	ICD	ICD	CRT-P
	Yes	ICD	ICD	CRT-P or CRT-D	CRT-P
>150ms	No	CRT-D	CRT-D	CRT-P or CRT-D	CRT-P
	Yes	CRT-D	CRT-D	CRT-P	CRT-P

All patients must have LVEF ≤ 35%

General comments on Provisional Guidance

The Provisional Guidance includes positive developments on TA095 and TA120:

- Selected non-ischaemic cardiomyopathy patients are added to the recommended indications for an ICD;
- Patients with QRS > 150 ms in NYHA class I-II with LVEF ≤ 35% are added to the recommended indications for a CRT-D; and
- Non-sustained VT, positive VT stimulation study and dys-synchrony proven by echocardiography have been removed as selection criteria.

However, the Provisional Guidance has excluded patient groups or device choices, despite the clinical and cost-effectiveness evidence provided by the ABHI that supports the interventions as an efficient use of NHS resources:

1. ICD excluded for patients with QRS < 120ms, NYHA I-III, LVEF ≤ 35%
2. CRT-D excluded for patients with QRS 120-149ms, LBBB, NHYA II, LVEF ≤ 35%
3. CRT-D excluded for patients with QRS ≥150ms, LBBB, NYHA III, LVEF ≤ 35%

The ABHI requests the Committee to consider comments which concern four topics:

- Duration of constant mortality benefit included in cost effectiveness model
- The consideration of evidence for the use of interventions in three subgroups:
  - ICD for patients with QRS < 120ms, NYHA I-III, LVEF ≤ 35%;
  - CRT-D for patients with QRS 120-149ms, LBBB, NHYA II, LVEF < 35%
  - CRT-D for patients with QRS ≥150ms, LBBB, NYHA III, LVEF < 35%

Estimated duration of constant mortality benefit

The base case analysis submitted by the ABHI assumes that the mortality benefit is constant for 7.5 years followed by a linear tapering until year 20. However, the ACD communicates that the Committee concluded in favour of a constant mortality benefit for 5 years followed by tapering up to 20 years as the most reasonable assumption.

The ABHI provided the following evidence in support of a 7.5 year constant mortality benefit:

- Longer term analyses of the post-protocol period for two large trials, CARE-HF and MADIT-II. These analyses support that strong treatment effects for devices are maintained at 4.2-7.6 years average follow-up despite high degrees of cross-over from the control to the active trial arms.
- Analyses testing the validity of the proportional hazards assumption within the individual patient database found no evidence to suggest that treatment effects waned over time, supporting the use of a 7.5-year mortality benefit.

The ABHI is concerned that the Committee has taken an overly conservative assumption about the duration of a constant mortality benefit. The assumption taken in the ABHI submission already was more conservative than any previous analysis by NICE for ICD and CRT, which have assumed that the benefit of treatment is constant over time. Thus the Committee actually has taken a conservative assumption by the ABHI and made it even more conservative. Unlike medicines, patient non-compliance with a dosing regimen is not a concern, there is no evidence waning of the performance of ICD and CRT devices themselves. We request that the Committee reconsider this decision.

Using the model as originally submitted, the Committee's decision to reduce the duration of the constant mortality effect in the cost effectiveness model is important because it increases the cost effectiveness ratios for several patient groups, as follows, to levels that the Committee considered to be not cost effective:

- ICER for CRT-D vs. CRT-P became £30,548/QALY in NYHA III patients with QRS ≥150ms, LBBB;
- ICERs for ICD vs. OPT became £25,714/QALY, £26,181/QALY and £29,309/QALY in NYHA I, II and III respectively with QRS duration < 120ms,

On the other hand, if a constant mortality effect was assumed as in previous evaluations, the results could be acceptable for these two patient groups:

- ICERs for ICD vs. OPT become £18,321/QALY, £17,807/QALY and £24,153/QALY in NYHA I, II and III respectively in patients with QRS duration <120ms,
- ICER for CRT-D vs. CRT-P becomes £23,891/QALY in NYHA III patients with QRS ≥150ms, LBBB;

For patients QRS 120-149, LBBB, NHYA II, LVEF < 35%, ICD has been recommended in the ACD despite being extendedly dominated by CRT-D with an ICER of £22,049. With a constant mortality effect, ICD still is extendedly dominated by CRT-D and the ICER for CRT-D becomes £16,302.

ICD for patients with QRS < 120ms, NYHA I-III, LVEF < 35%

ICD is not recommended in the ACD for patients with QRS < 120ms, NYHA I-III, LVEF < 35%. The ABHI is concerned about three aspects of this:

1. ABHI analyses indicated cost effectiveness of ICD therapy is in an acceptable range irrespective of QRS duration (within NYHA I-III, LVEF < 35%); and
2. a decision to restrict ICD therapy to patients with QRS >=120ms is based on insufficient clinical evidence of an increased treatment effect of ICD in QRS >=120ms compared to QRS < 120ms
3. a NICE recommendation against ICD use in patients with QRS < 120 ms would be mis-aligned with European and USA clinical practice guidelines, which threatens to undermine this NICE Guideline in clinical practice because it cannot be soundly explained, for the reasons given above.

We are concerned about the basis for excluding this group on cost effectiveness grounds. In ICD patients with QRS < 120ms with NYHA I-III and LVEF < 35%, the ICERS in the original model are £25,714/QALY, £26,181/QALY and £29,309/QALY in NYHA I, II and III respectively in the base-case scenario preferred by NICE. The ACD communicates that the Committee decided ICD is not cost-effective in this group taking into consideration the uncertainties of evidence synthesis and the lack of a full exploration of parameter uncertainty in the model.

As presented in ABHI original submission, real term prices (adjusted to 2011 equivalents) had fallen by 17% for CRT-P, 10.4% for CRT-D and 8% for ICD between 2006 and 2011 (see Appendix 1). The cost effectiveness ratios presented in the ABHI submission used device and procedure costs from 2011. The ABHI recently was able to obtain cost information for 2013, which show an 11% decrease since 2011 in the total implant costs (device cost and implant procedure cost) for ICD (see Appendix 1). Using 2013 costs, recalculated ICERs are shown in the Table 2.

Table 2: Incremental cost-effectiveness ratios (£/QALY gained) with 2013 ICD costs

Mortality treatment effect duration	**NYHA Class**	**QRS Duration**	**ICER (ICD vs. OPT)**
5 years	I	<120ms	£23,509
5 years	II	<120ms	£23,976
5 years	III	<120ms	£26,648
7.5 years	I	<120ms	£21,394
7.5 years	II	<120ms	£21,747
7.5 years	III	<120ms	£24,770

It appears the Committee accepted ICERs of £26,192 and £26,586 for other patient groups in this appraisal. The ACD communicates that although the Committee was conscious of the uncertainties surrounding the ICERs in the patient groups with these ICERs, it considered those ICERs acceptable given the severity of the symptoms and the clinical plausibility of benefit. However, the ICERs for ICD in patients with QRS < 120ms, LVEF < 35% in NYHA class I - III are lower or at least on a par with the above ICERs which were accepted. Given the function of an ICD device is to prevent SCD, and it has a cost effectiveness ratio in NYHA class I-II that is apparently at an acceptable level for other patient groups in this appraisal, we request NICE to reconsider this recommendation.

The level of uncertainty about the ICER for ICD in this patient group is not more uncertain than other groups. As shown in Table 3 (below), the network meta-analysis included sizeable patient numbers in each of the ICD patient groups with QRS < 120 ms.

Table 3: Size of network meta-analysis database in each of the 20 decision categories

	LBBB	NYHA I	NYHA II	NYHA III	NYHA IV
< 120 ms	No	3.0%	13.3%	6.2%	0.4%
120-149 ms	No	2.0%	8.8%	5.1%	0.6%
	Yes	0.9%	7.7%	4.8%	0.5%
>150ms	No	1.0%	5.4%	2.7%	0.2%
	Yes	1.8%	20.4%	13.8%	1.6%

It is clearly of interest to identify ways to improve the patient risk stratification for ICD devices. As documented in the ACD, QRS duration is understood to impact upon the efficacy of CRT, however, the importance of QRS duration is less well understood as a predictor of ICD efficacy.

The relationship between prolonged QRS duration and SCD in patients with heart failure became a controversial issue in 2004 when the US Centers for Medicare and Medicaid (CMS) decided to limit reimbursement coverage of ICDs to patients who meet specific QRS width criteria (> 120 ms) on the basis of a subgroup analysis of the MADIT II trial. The same sub-group analysis led to the previous NICE Guidance for ICDs (TA95) to restrict ICD therapy to those with QRS duration >120ms and LVEF≤30% in the post-MI population. However, this QRS restriction was removed by CMS when data became available from the SCD-HeFT trial. QRS duration was retained in the final IPD NMA model due to the importance of this variable in predicting CRT efficacy (Table 38, manufacturer submission). The estimated variation in ICD efficacy across QRS duration bands may not represent a sound basis for making different recommendations for ICD use according to QRS duration.

Neither of the principal European nor USA clinical practice guidelines advocate that ICD therapy be restricted according to QRS duration, based on the clinical evidence. The European Society of Cardiology (ESC) recommend ICD regardless of QRS duration in NYHA II-III patients with EF≤35%. Clinical guidance from the US recommends ICD in the same group as well as in NYHA I patients with LV dysfunction due to prior MI who are at least 40 days post-MI, and have LVEF less than 30% (see Appendix 2 for full details).

In alignment with the international clinical practice guidelines, a recent meta-analysis (Katritsis et al, 2013) of primary prevention randomized controlled trials comparing ICD and standard medical therapy concluded that QRS duration does not appear to confer any additional value for selection of ICD therapy.[1]

CRT in patients with QRS 120-149ms, LBBB, NYHA II, LVEF < 35%

The ACD communicates that the NICE Committee was concerned that in terms of CRT benefit, the subgroups with a QRS duration between 120 -149 ms were heterogeneous, containing some patients in whom CRT may be inappropriate. Thus, ICD has been

[1] Katritsis et al. Effect of left ventricular ejection fraction and QRS duration on the survival benefit of implantable cardioverter-defibrillators: Meta-analysis of primary prevention trials. 2013:Heart Rhythm 2013;10:200–206.

recommended in this group despite being extendedly dominated by CRT-D with an ICER of £22,049.

The cost effectiveness ratios presented in the ABHI submission used device and procedure costs from 2011, so the ABHI obtained updated cost information for 2013 (see Appendix 1). The updated ICER indicates that ICD is no longer extendedly dominated, and has an ICER of £20,590. CRT-D now has an ICER versus ICD of £25,233.

Two studies and an individual patient meta-analysis are mentioned – the EchoCRT trial, the RethinQ trial, and the Cleland 2013 meta-analysis. From EchoCRT, it is mentioned that that in patients with QRS durations of less than 130 ms, the prognosis could be adversely affected with CRT-D. From RethinQ, it was noted that in this small trial in people with narrow or slightly prolonged QRS durations of less than 130 ms, it was inconclusive overall on mortality, with wide confidence intervals, but the point estimate of effect favoured ICDs. From the analysis by Cleland et al, 2013, it was reported that the clinical benefit of CRT in patients with QRS durations between 120-140 ms was uncertain.

ABHI is concerned about the informal way in which these three studies appear to have influenced the Committee's recommendation regarding CRT in patients with intermediate QRS durations (120-149 ms). We wish to draw the attention of the Committee to additional information which must be considered about these studies prior to letting them perhaps unduly influence a decision:

- The Echocardiography Guided Cardiac Resynchronization Therapy (EchoCRT) study included patients with NYHA III or IV heart failure, a LVEF < 35%, QRS < 130 ms. In addition, patients were required to have echocardiographic evidence of mechanical dyssynchrony (differences in the timing of contraction of different myocardial segments). Mean baseline QRS in this study was 105 ms, which is far below the minimum QRS of 120 ms conventionally accepted in CRT trials. CRT use in patients with QRS duration of less than 120 ms is unwarranted and should not be considered. The novel result of this study simply is to negate the use of echocardiographic measures of mechanical dyssynchrony in patients with a QRS < 130 ms as a means of identifying those who are most likely to have a good response to CRT.
- The RethinQ trial was a small study (172 patients) with a short duration of follow-up (6 months) in patients who had an indication for an ICD and QRS < 130ms. The primary end-point was the proportion of patients with an increase in peak oxygen consumption of at least 1.0 ml per kilogram of body weight per minute during cardiopulmonary exercise testing at 6 months. Thus we consider the study does not provide substantive evidence regarding the benefit of CRT in this evaluation. Conversely, if the Committee believes the study has some relevance, it is noted that the sub-group of patients with QRS > 120 ms experienced a significant improvement in the primary end-point of peak oxygen consumption (P = 0.02).
- The Cleland et al, 2013, individual patient data level meta-analysis has an important limitation compared to the ABHI analysis submitted to NICE: the lack of access to individual patient data from two large CRT trials. The COMPANION trial (1520 patients) and the MADIT-CRT trial (1820 patients). This analysis found that the "estimated HR crossed 1.0 at 126 ms for all-cause mortality" and the "95% confidence bounds excluded 1.0 beginning at ~140 ms". This analysis excluded 18% of the patients randomised to the CRT trials considered in the ABHI analysis. It is not therefore credible to base decisions on these point estimate or statistical significance results. Unlike the findings of the manufacturer network meta-analysis, Cleland et al, 2013 found that after adjusting for QRS duration, LBBB morphology was not a significant predictor of the benefits of CRT. However, their dataset was considerably smaller than the dataset presented to NICE, and furthermore the trials they included

were overwhelmingly made up of patients with LBBB (73-87%), thus their analysis may have lacked power to estimate the effects of CRT in patients with or without LBBB.

CRT-D in patients with QRS >150, LBBB, NYHA III, LVEF < 35%

In NYHA III patients with QRS ≥150ms with LBB B, ICERs for CRT-D vs. CRT-P were estimated at £30,548, £28,646 or £23,891 per QALY gained depending on whether a 5 year, 7.5 year or life-long constant treatment effect is assumed. The Committee preferred a 5 year constant treatment effect (discussed above) and it appears that the Committee decided not to recommend CRT-D in this patient group based on the ICER being marginally above £30,000/QALY in that scenario.

SCD is the most common cause of death for HF patients in NYHA class III, accounting for 59% of deaths observed in the ABHI network meta-analysis. We are concerned that the Provisional Guidance would exclude defibrillator use in this population. Secondly, it will be illogical and difficult to justify to either a clinician or a patient that someone with QRS >150, NYHA III with LVEF < 35% who does *not* have LBBB may receive a CRT-D device; whereas a similar patient who has LBBB will not be given the option of a CRT-D device, despite having the same risk of SCD.

The ACD view that CRT-D is not cost effective seems to be based largely on the ICER being £30,548/QALY, i.e. marginally above a £30,000 threshold. The ICERs for all devices in this appraisal are not static and are expected to decrease over time: as presented in ABHI original submission, real term prices (adjusted to 2011 equivalents) fell by 17% for CRT-P, 10.4% for CRT-D and 8% for ICD between 2006 and 2011.

The cost effectiveness ratios presented in the ABHI submission used device and procedure costs from 2011, so the ABHI obtained updated cost information for 2013. Total implant costs (device cost and implant procedure cost) for CRT-P and CRT-D have fallen by a further 3% and 1% in the meantime, with the effect that the ICER for CRT-D is practically unchanged. The cost effectiveness results are presented in Tables 3 and 4.

We request the Committee to recommend CRT-D in patients with QRS >150, LBBB, NYHA III, LVEF < 35% given the ICER between £30,548, £28,646 or £23,891 per QALY gained depending on whether a 5 year, 7.5 year or life-long constant treatment effect (as per original submission).

Table 3: Cost-effectiveness for patients with NYHA III (treatment effect duration = 5 years)

QRS duration	CE sequence				ICER			
	1st	2nd	3rd	4th	1st	2nd	3rd	4th
Patients without LBBB								
<120ms	OPT	ICD	N/A	N/A	Referent	£26,648	N/A	N/A
≥120ms, <150ms	OPT	CRT-P	ICD	CRT-D	Referent	£19,788	Ext Dom	£24,488
≥150ms	OPT	ICD	CRT-P	CRT-D	Referent	Dominated	£13,785	£26,799
Patients with LBBB								
≥120ms, <150ms	OPT	ICD	CRT-P	CRT-D	Referent	Dominated	£14,058	£26,399
≥150ms	OPT	ICD	CRT-P	CRT-D	Referent	Dominated	£10,469	£30,810

Table 4: Cost-effectiveness for patients with NYHA III (treatment effect duration = 7.5 years)

QRS duration	CE sequence				ICER			
	1st	2nd	3rd	4th	1st	2nd	3rd	4th
Patients without LBBB								
<120ms	OPT	ICD	N/A	N/A	Referent	£24,770	N/A	N/A
≥120ms, <150ms	OPT	CRT-P	ICD	CRT-D	Referent	£19,553	£22,662	£24,667
≥150ms	OPT	ICD	CRT-P	CRT-D	Referent	Dominated	£13,522	£25,402
Patients with LBBB								
≥120ms, <150ms	OPT	ICD	CRT-P	CRT-D	Referent	Dominated	£13,793	£25,071
≥150ms	OPT	ICD	CRT-P	CRT-D	Referent	Dominated	£10,206	£28,892

Internationally, CRT-D is widely used in this patient group. Details of the international clinical practice guidelines are included in Appendix 2.

Additional comments

- A minority of heart failure patients receiving an ICD might need frequent ventricular pacing, which means right ventricular (RV) pacing in the case of an ICD. It's been shown that RV pacing is deleterious because it can worsen heart failure and increase the risk of atrial fibrillation. In the ACD, NYHA I-III patients with QRS 120-149 for the most part are eligible for an ICD only. In patients where a high percentage of ventricular pacing is to be expected, we request the Committee to consider if CRT could be made an available choice.

- It was remarked in the ACD that in general, patients in the trials were about 10 years younger than the average age of people with heart failure in the UK. However, the UK devices registry data indicate that the average age of patients who receive a device in the UK is similar patients in the trials.

ABHI

10th February 2014

(On behalf of the manufacturers: Biotronik, Boston Scientific, Medtronic, Sorin and St Jude Medical)

Appendix 1

2013 device costs

As noted in the original submission, the acquisition cost of ICD and CRT therapy are falling in real terms over time.

The following plots show changes in absolute device costs over time. These data were supplied by ABHI and they are average selling prices by device type across all manufacturers, thus these prices represent the actual costs paid in the UK NHS. All of the devices have had a reduction in absolute costs over time (the reduction in real terms costs will be even more pronounced). Device tariffs also have reduced over time (information not shown).

Figure 1: UK ICD average selling price (all manufacturers)

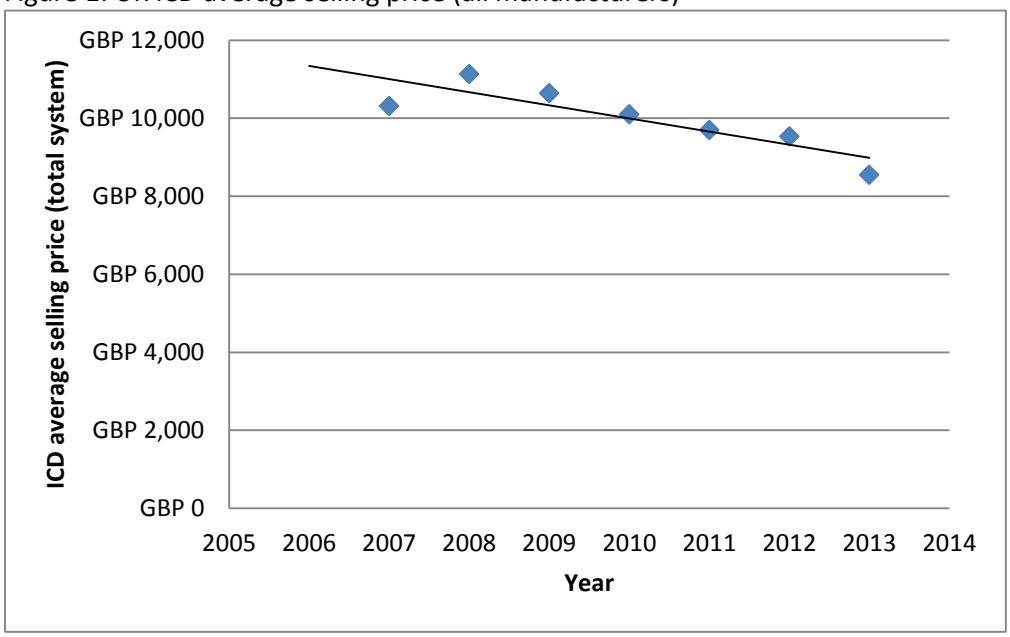


Figure 2: UK CRT-P average selling price (all manufacturers)

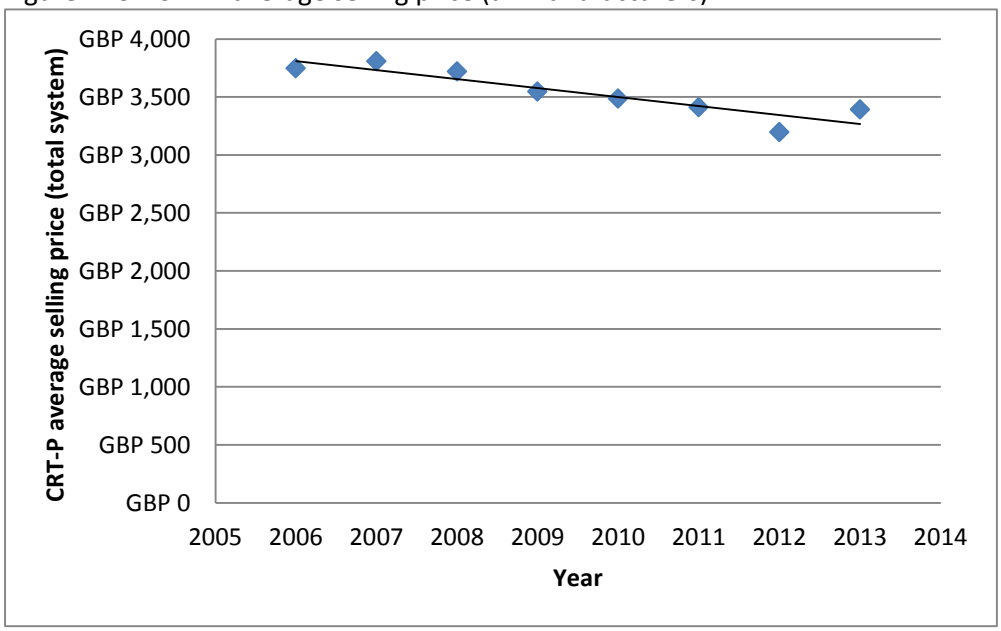
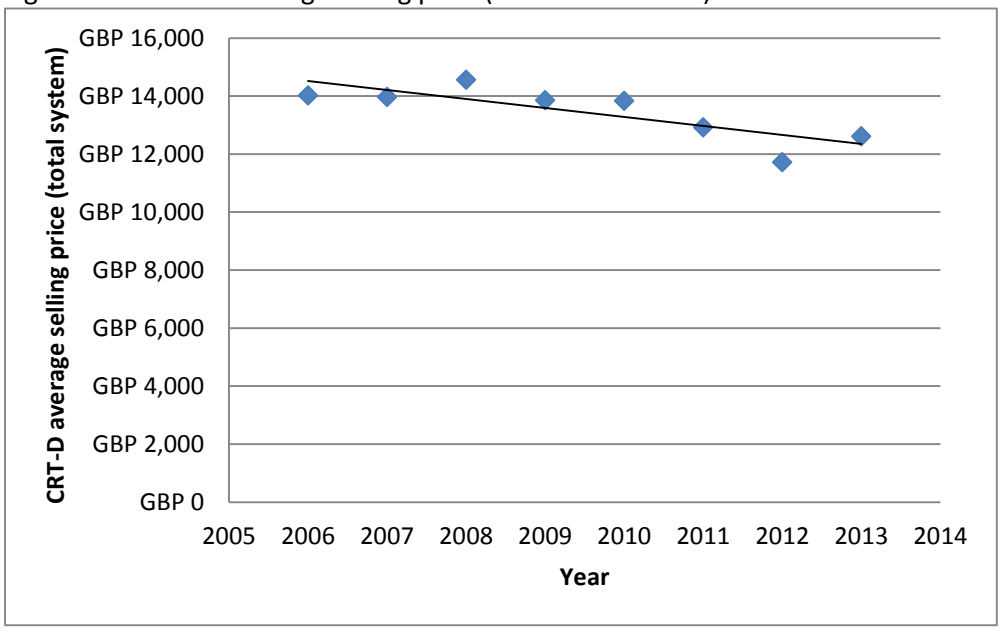


Figure 3: UK CRT-D average selling price (all manufacturers)



ABHI sourced revised average selling prices from Eucomed since the values used in the model were from a cost-year of 2011. We have also taken the opportunity to include the most recent HRG tariff values into the model since the originals were out of date. The values used in the model are reported in Table 5.

Table 5: revised cost estimates used in the ABHI analysis

Parameter	Original value	New value	Source for new value
HRG code E07Z	£8,821	£8,022	NHS 2014-15 Tariffs*
HRG code EA12Z	£5,556	£4,975	NHS 2014-15 Tariffs*
HRG EA39Z	£2,748	£2,494	NHS 2014-15 Tariffs*
CRT-P whole system costs	£3,411	£3,392	Eucomed (cost year = 2013)
CRT-D whole system costs	£12,293	£12,615	Eucomed (cost year = 2013)
ICD whole system costs	£9,692	£8,549	Eucomed (cost year = 2013)

* Value used will be in effect by the time NICE guidance is issued

Appendix 2

International Clinical Practice Guidelines

ICD
In the European Society of Cardiology (ESC) clinical practice guidelines (20122), ICD is recommended in a patient with symptomatic HF (NYHA class II–III) and an EF ≤35% despite ≥3 months of treatment with optimal pharmacological therapy, who is expected to survive for >1 year with good functional status, to reduce the risk of sudden death, in (i) Ischaemic aetiology and >40 days after acute myocardial infarction; and (ii) Non-ischaemic aetiology.

Similar to European ESC Guideline, in USA ICD therapy is indicated in patients with LVEF less than 35% in NYHA functional Class II or III. Additionally, for patients in NYHA class I, ICD therapy is indicated in patients with LV dysfunction due to prior MI who are at least 40 days post-MI, and have LVEF less than 30% (20083).

CRT
In the European Society of Cardiology (ESC) clinical practice guidelines (20124), CRT is recommended in chronic HF patients and LVEF≤35% who remain in NYHA II, III and ambulatory IV despite adequate medical treatment. The ESC recommendations favour CRT particularly in patients with LBBB, either with QRS >120ms or with QRS > 150ms thresholds. In patients without LBBB, the ESC Guidelines state that CRT *should be considered* if QRS duration >150 ms, whereas it *may be considered* if QRS is 120-49 ms.

When CRT is recommended, there is a choice between CRT-P and CRT-D. The ESC Guidelines Taskforce decided not to be prescriptive. They said the "Task Force is of the opinion that no strict recommendations can be made, and prefers to merely offer guidance regarding the selection of patients for CRT-D or CRT-P, based on overall clinical condition, device-related complications and cost". Specifically the Taskforce identified the following factors in favour of using CRT-D (Life expectancy >1 year, stable heart failure NYHA II, ischaemic heart disease, lack of comorbidities), versus some factors in favour of using CRT-P (advanced heart failure, severe renal insufficiency or dialysis, other major co-morbidities, frailty and cachexia).

Identical to European ESC Guideline, in the USA Guidelines (2012[5]) CRT is recommended in chronic HF patients and LVEF≤35% who remain in NYHA functional class II, III and ambulatory IV despite adequate medical treatment. The recommendation is again more favourable for CRT in patients with LBBB, either with QRS >120ms or with QRS > 150ms thresholds. In patients without LBBB, the recommendation is that CRT *should be* considered if QRS duration >150 ms, whereas it *may be* considered if QRS is 120-49 ms.

In patients in NYHA class III and ambulatory class IV, CRT-D may be chosen so long as the addition of an ICD is expected to produce a meaningful survival benefit.

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[2] The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC
[3] ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines
[4] 2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy
[5] 2012 ACCF/AHA/HRS Focused Update of the 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities