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

Manufacturer's response to specification for further work following the appraisal committee meeting on 23rd April 2013

Executive Summary

Background

This document describes further analyses of a cost-effectiveness model developed by the ABHI group to meet a request made by NICE in their correspondence of 19th June 2013.

The original ABHI analysis included individual patient data from over 12,000 patients, representing 95% of the relevant randomised controlled trial evidence for the devices under evaluation. Analyses of this data set for the all-cause mortality endpoint demonstrated strong and statistically significant impacts of each device on all-cause mortality.

These results do not imply that every heart failure patient should receive an implantable device. The heart failure population that would be eligible for a device, be that CRT-P, CRT-D or ICD, and that is therefore considered in this appraisal, is a highly selected sub-population of heart failure patients. For all devices the potential patient population includes only those on optimal medical therapy, whom have undergone an echocardiography examination and been found to have ejection fraction (EF) < 35%. Furthermore, to be eligible for CRT patients must have wide QRS (>120 ms); and additionally the NYHA classification system would be applied to exclude NYHA IV patients from ICD devices.

New analyses

The analyses requested were:

- Aggregate ischaemic and non-ischaemic sub-groups and present summary tables at £30,000, £25,000 and £20,000 per QALY thresholds.
- Explore different durations of mortality treatment effect.
- Implement a treatment effect of 0.696 for CRT-D on hospitalisation.
- Include counselling costs.
- Conduct sensitivity analyses on cost parameters.
- Comment on device crossover/upgrade

Clinical experts confirmed that device crossover/upgrade was rare and its inclusion in the model would not be reflective of routine UK practice. Inclusion of counselling costs did not change the base case conclusions at any of the three thresholds considered. Further inspection of the model showed that a treatment effect of 0.696 for CRT-D on hospitalisation had in fact been used in the original base case submission. Cost parameter sensitivity analysis had minimal effect on the ICERs.

Combining ischaemic and non-ischaemic groups yields conclusions regarding the most cost-effective technologies that are consistent with summary tables presented at the first Committee meeting. Combining these groups has also increased the precision around the results, as each subgroup is now made up of a larger number of patients. Cost-effective interventions at the three requested thresholds are summarised in Table 1-3.

Table 1: Cost-effective interventions (threshold value = £30,000 per QALY gained)

NYHA	QRS <120ms	QRS ≥120-<150ms	QRS ≥150ms
I/II	ICD	ICD (no LBBB)	CRT-D (both LBBB groups)
		CRT-D (with LBBB)	
III	ICD	CRT-D (both LBBB groups)	CRT-D (both LBBB groups)
IV	OPT	CRT-P (both LBBB groups)	CRT-P (both LBBB groups)

Table 2: Cost-effective interventions (threshold value = £25,000 per QALY gained)

NYHA	QRS <120ms	QRS ≥120-<150ms	QRS ≥150ms
I/II	ICD	ICD (no LBBB)	CRT-D (both LBBB groups)
		CRT-D (with LBBB)	
III	OPT	CRT-D (both LBBB groups)	CRT-P (both LBBB groups)
IV	OPT	CRT-P (both LBBB groups)	CRT-P (both LBBB groups)

Table 31: Cost-effective interventions (threshold value = £20,000 per QALY gained)

NYHA	QRS <120ms	QRS ≥120-<150ms	QRS ≥150ms
I/II	OPT	ICD (no LBBB)	OPT (no LBBB)
		OPT (with LBBB)	CRT-D (with LBBB)
III/IV	OPT	OPT (no LBBB)	CRT-P (both LBBB groups)
		CRT-P (with LBBB)	

We would ask the Committee to note that in some cases, the ICERs are very close to threshold values, with the potential impact that very small differences in ICERs could change threshold-based decisions. The ICERs for all technologies will not be static and would be expected to decrease over time. As presented in ABHI original submission, real term prices (adjusted to 2011 equivalents) have fallen by 17% for CRT-P, 10.4% for CRT-D and 8% for ICD between 2006 and 2011. There is no Pharmaceutical Price Regulation Scheme (PPRS) for medical devices and historically market forces have driven acquisition costs down over time. Over the lifetime of this appraisal – all things being equal - the ICERs would therefore be expected to reduce.

Reducing the constant mortality benefit to 5 years (from the base case 7.5 years), followed by linear tapering to 20 years resulted in treatment choices as per the base case using the £30,000/QALY threshold with the exception of only one of the 24 subgroups:

- NYHA III patients with QRS ≥150ms and LBBB, the cost-effective option switches from CRT-D to CRT-P when the treatment effect duration is reduced to 5 years (ICER for CRT-D vs. CRT-P = £30,548/QALY)

Reducing the constant mortality benefit to 5 years (from the base case 7.5 years), followed by linear tapering to 20 years resulted in treatment choices as per the base case using the mid-point threshold value of £25,000/QALY. Exceptions occurred in only four of the 24 sub-groups:

- NYHA I/II patients with QRS duration<120ms, ICD becomes cost-ineffective if the treatment effect duration is reduced to 5 years (ICER for ICD vs. OPT = £25,714/QALY and £26,181/QALY in NYHA I and II respectively)
- NYHA II patients with QRS≥150ms and without LBBB, CRT-D becomes cost-ineffective if the treatment duration is reduced to 5 years, and ICD becomes the optimal treatment (ICER for CRT-D vs. ICD = £25,267/QALY)
- NYHA III patients with QRS ≥120ms and <150ms and LBBB, the cost-effective option switches from CRT-D to CRT-P when the treatment effect duration is reduced to 5 years (ICER for CRT-D vs. CRT-P = £26,192/QALY)

In each case, although the optimal decision at a threshold of £25,000/QALY changed, the ICERs for the base case preferred treatment option remained under £26,200/QALY.

The base case analysis assumes that the mortality benefit is constant for 7.5 years followed by a linear tapering until year 20. The duration of effect is based on the longest available follow-up from the individual patient data analysis. Longer term analyses of the post-protocol period have been presented 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.

End of Executive Summary

Base case results combining ischemic and non-ischemic patient groups

As per the specification document, we have generated results for 24 rather than 48 subgroups using the same format as in the original submission. The results for patients without Left Bundle Branch Block (LBBB) are presented in Table 2 and for patients with LBBB in Table 3. These tables are to be interpreted in the same way to the results tables in the original submission: the "CE sequence" section ranks the treatments in terms of incremental benefit and the "ICERs" section reports the fully incremental cost-effectiveness ratios compared to the next most effective intervention on the frontier (dominance/ extended dominance also reported).

Table 2: Original cost-effectiveness results (pooled ischemic and non-ischemic) for patients without LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	below £20k/QALY
I	<120ms	OPT	ICD	N/A	N/A	Referent	£24,074	N/A	N/A	ICD	ICD	OPT
I	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£16,253	N/A	ICD	ICD	ICD
I	>150ms	OPT	ICD	CRTD	N/A	Referent	£21,102	£21,759	N/A	CRTD	CRTD	OPT
II	<120ms	OPT	ICD	N/A	N/A	Referent	£24,465	N/A	N/A	ICD	ICD	OPT
II	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£16,813	N/A	ICD	ICD	ICD
II	>150ms	OPT	ICD	CRTD	N/A	Referent	£20,602	£23,738	N/A	CRTD	CRTD	OPT
III	<120ms	OPT	ICD	N/A	N/A	Referent	£27,826	N/A	N/A	ICD	OPT	OPT
III	>=120, <150 ms	OPT	CRTP	ICD	CRTD	Referent	£20,178	Ext Dominated	£23,349	CRTD	CRTD	OPT
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£13,930	£25,200	CRTD	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£22,578	£40,052	N/A	CRTP	CRTP	OPT
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£17,175	£35,811	N/A	CRTP	CRTP	CRTP

Table 3: Original cost-effectiveness results (pooled ischemic and non-ischemic) for patients with LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	below £20k/QALY
I	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
I	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	£20,677	£21,672	N/A	CRTD	CRTD	OPT
I	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£17,470	N/A	CRTD	CRTD	CRTD
II	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
II	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£20,704	N/A	CRTD	CRTD	OPT
II	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£17,664	N/A	CRTD	CRTD	CRTD
III	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
III	>=120, <150 ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£14,215	£24,875	CRTD	CRTD	CRTP
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£10,496	£28,646	CRTD	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£18,664	£37,104	N/A	CRTP	CRTP	CRTP
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£14,500	£40,449	N/A	CRTP	CRTP	CRTP

N/A values indicate where a device is not evaluated in a specific population. The rationale for these exclusions is detailed in the original submission.

The specification document also requested summaries of optimal strategies at cost-effectiveness threshold values of £20,000, £25,000 and £30,000 per QALY gained. These are reported in Table 4, Table 5 and Table 6.

Table 4: Cost-effective interventions (original analysis, threshold value = £30,000 per QALY gained)

NYHA	QRS <120ms	QRS ≥120-<150ms	QRS ≥150ms
I/II	ICD	ICD (no LBBB)	CRT-D (both LBBB groups)
		CRT-D (with LBBB)	
III	ICD	CRT-D (both LBBB groups)	CRT-D (both LBBB groups)
IV	OPT	CRT-P (both LBBB groups)	CRT-P (both LBBB groups)

Table 5: Cost-effective interventions (original analysis, threshold value = £25,000 per QALY gained)

NYHA	QRS <120ms	QRS ≥120-<150ms	QRS ≥150ms
I/II	ICD	ICD (no LBBB)	CRT-D (both LBBB groups)
		CRT-D (with LBBB)	
III	OPT	CRT-D (both LBBB groups)	CRT-P (both LBBB groups)
IV	OPT	CRT-P (both LBBB groups)	CRT-P (both LBBB groups)

Table 6: Cost-effective interventions (original analysis, threshold value = £20,000 per QALY gained)

NYHA	QRS <120ms	QRS ≥120-<150ms	QRS ≥150ms
I/II	OPT	ICD (no LBBB)	OPT (no LBBB)
		OPT (with LBBB)	CRT-D (with LBBB)
III/IV	OPT	OPT (no LBBB)	CRT-P (both LBBB groups)
		CRT-P (with LBBB)	

We request that the committee review specific ICERs as well as the summary tables, as in a number of cases the ICERs are very close to the threshold values used (see, for example, CRT-P vs. OPT in non-LBBB, NYHA III, QRS ≥120 and <150ms: £20,178/QALY and CRT-D vs. OPT in LBBB, NYHA II, QRS between 120 and 150ms: £20,704). In order to facilitate this we have provided Figure 1 and Figure 2 which show the cost-effective treatment option according to a continuous display of the threshold.

Figure 1: Graphic display of cost-effective option across cost-effectiveness threshold values for patients without LBBB

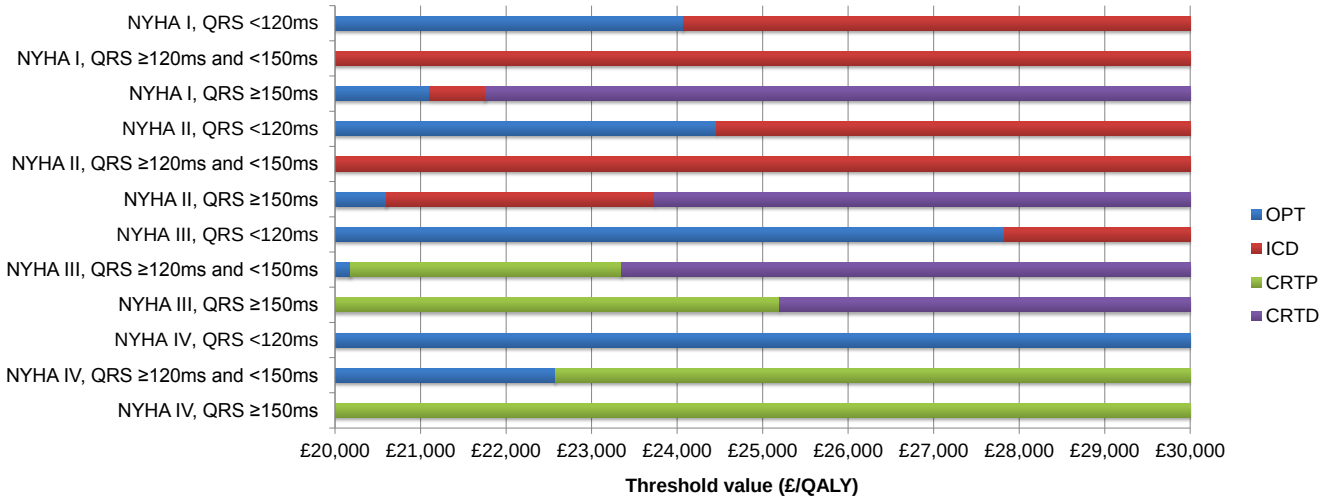
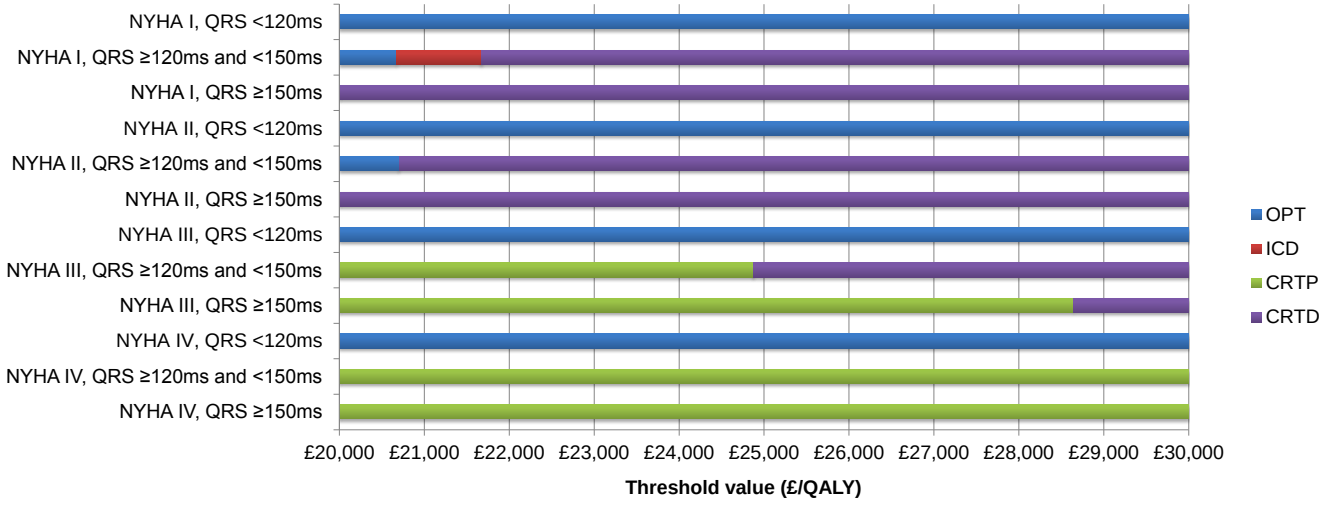


Figure 2: Graphic display of cost-effective option across cost-effectiveness threshold values for patients with LBBB



Requested scenario analyses

1) Duration of mortality treatment effects

The base case analysis assumes a constant duration of effect of 7.5 years for all-cause mortality followed by linear tapering up to year 20. In addition, sensitivity analyses using a life-long constant treatment effect and a five year treatment effect followed by linear tapering to year 20 were provided in the original ABHI submission. As requested, these sensitivity analyses are presented below using the revised presentation with 24 subgroups.

An additional analysis assuming that the duration of treatment effect is as per the average duration of follow-up in the trial database has also been run. As requested this scenario retains the tapering effects used in the base case (tapering until year 20). Mean follow-up was calculated using all patients included in the network meta-analysis. The analysis

comprised of using a Kaplan Meier analysis and calculating the restricted mean survival time[1]. The survival analysis was run with all loss to follow-up occurrences considered as events and all deaths considered as occurrences of censoring.

The results for each scenario are presented below, followed by a narrative and tabular summary.

a) Life-long constant mortality treatment effect

The results using the life-long constant treatment effects are presented as Table 7 and Table 8.

Table 7: Sensitivity analyses - constant life-long mortality treatment effect for patients without LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER below
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	£20k/QALY
I	<120ms	OPT	ICD	N/A	N/A	Referent	£18,321	N/A	N/A	ICD	ICD	ICD
I	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£13,153	N/A	ICD	ICD	ICD
I	>150ms	OPT	ICD	CRTD	N/A	Referent	£17,588	£18,558	N/A	CRTD	CRTD	CRTD
II	<120ms	OPT	ICD	N/A	N/A	Referent	£17,807	N/A	N/A	ICD	ICD	ICD
II	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£13,374	N/A	ICD	ICD	ICD
II	>150ms	OPT	ICD	CRTD	N/A	Referent	£16,782	£19,748	N/A	CRTD	CRTD	CRTD
III	<120ms	OPT	ICD	N/A	N/A	Referent	£24,153	N/A	N/A	ICD	ICD	OPT
III	>=120, <150 ms	OPT	CRTP	ICD	CRTD	Referent	£19,807	Ext Dominated	£21,438	CRTD	CRTD	CRTP
III	>150ms	OPT	CRTP	ICD	CRTD	Referent	£13,453	Ext Dominated	£22,217	CRTD	CRTD	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£22,500	£39,290	N/A	CRTP	CRTP	OPT
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£17,047	£34,627	N/A	CRTP	CRTP	CRTP

Table 8: Sensitivity analyses - constant life-long mortality treatment effect for patients with LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER below
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	£20k/QALY
I	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
I	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	£16,692	£17,267	N/A	CRTD	CRTD	CRTD
I	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£14,044	N/A	CRTD	CRTD	CRTD
II	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
II	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£16,302	N/A	CRTD	CRTD	CRTD
II	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£13,497	N/A	CRTD	CRTD	CRTD
III	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
III	>=120, <150 ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£13,664	£21,786	CRTD	CRTD	CRTP
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£9,928	£23,891	CRTD	CRTD	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£18,472	£35,479	N/A	CRTP	CRTP	CRTP
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£14,334	£38,283	N/A	CRTP	CRTP	CRTP

b) Constant mortality treatment effect for five years

The results using a five-year constant treatment effect followed by tapering until year 20 are presented as Table 9 and Table 10.

[1] This analysis is equivalent to calculating the area under the Kaplan Meier curve. In this case the Kaplan Meier curve is complete by definition; as all non-dead patients must be lost to follow-up/subject to administrative censoring.

Table 9: Sensitivity analyses - constant mortality treatment effect for five years for patients without LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER below
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	£20k/QALY
I	<120ms	OPT	ICD	N/A	N/A	Referent	£25,714	N/A	N/A	ICD	OPT	OPT
I	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£17,295	N/A	ICD	ICD	ICD
I	>150ms	OPT	ICD	CRTD	N/A	Referent	£22,366	£23,168	N/A	CRTD	CRTD	OPT
II	<120ms	OPT	ICD	N/A	N/A	Referent	£26,181	N/A	N/A	ICD	OPT	OPT
II	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£17,909	N/A	ICD	ICD	ICD
II	>150ms	OPT	ICD	CRTD	N/A	Referent	£21,888	£25,267	N/A	CRTD	ICD	OPT
III	<120ms	OPT	ICD	N/A	N/A	Referent	£29,309	N/A	N/A	ICD	OPT	OPT
III	>=120, <150 ms	OPT	CRTP	ICD	CRTD	Referent	£20,421	Ext Dominated	£24,311	CRTD	CRTD	OPT
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£14,203	£26,586	CRTD	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£22,702	£40,899	N/A	CRTP	CRTP	OPT
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£17,330	£36,934	N/A	CRTP	CRTP	CRTP

Table 10: Sensitivity analyses - constant mortality treatment effect for five years for patients with LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER below
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	£20k/QALY
I	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
I	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	£21,985	£23,080	N/A	CRTD	CRTD	OPT
I	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£18,615	N/A	CRTD	CRTD	CRTD
II	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
II	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£22,049	N/A	CRTD	CRTD	OPT
II	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£18,879	N/A	CRTD	CRTD	CRTD
III	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
III	>=120, <150 ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£14,489	£26,192	CRTD	CRTP	CRTP
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£10,769	£30,548	CRTP	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£18,817	£38,202	N/A	CRTP	CRTP	CRTP
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£14,666	£42,039	N/A	CRTP	CRTP	CRTP

c) Constant mortality treatment effect for average duration of follow up in trial database

The average (mean) follow up in the trial database was 2.54 years. The impact on cost-effectiveness of using this value for the fixed treatment effect period and tapering the treatment effect until year 20 is presented in Table 11 and Table 12.

Table 11: Sensitivity analyses - constant mortality treatment effect for mean trial follow up in patients without LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	below £20k/QALY
I	<120ms	OPT	ICD	N/A	N/A	Referent	£27,936	N/A	N/A	ICD	OPT	OPT
I	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£18,768	N/A	ICD	ICD	ICD
I	>150ms	OPT	ICD	CRTD	N/A	Referent	£24,196	£25,155	N/A	CRTD	ICD	OPT
II	<120ms	OPT	ICD	N/A	N/A	Referent	£28,463	N/A	N/A	ICD	OPT	OPT
II	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£19,442	N/A	ICD	ICD	ICD
II	>150ms	OPT	ICD	CRTD	N/A	Referent	£23,714	£27,389	N/A	CRTD	ICD	OPT
III	<120ms	OPT	ICD	N/A	N/A	Referent	£31,573	N/A	N/A	OPT	OPT	OPT
III	>=120, <150 ms	OPT	CRTP	ICD	CRTD	Referent	£20,864	Ext Dominated	£25,873	CRTD	CRTP	OPT
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£14,657	£28,735	CRTD	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£23,041	£42,813	N/A	CRTP	CRTP	OPT
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£17,683	£39,155	N/A	CRTP	CRTP	CRTP

Table 12: Sensitivity analyses - constant mortality treatment effect for mean trial follow up in patients with LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	below £20k/QALY
I	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
I	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	£23,830	£24,982	N/A	CRTD	CRTD	OPT
I	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£20,218	N/A	CRTD	CRTD	OPT
II	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
II	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£23,897	N/A	CRTD	CRTD	OPT
II	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£20,534	N/A	CRTD	CRTD	OPT
III	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
III	>=120, <150 ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£14,937	£28,244	CRTD	CRTP	CRTP
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£11,207	£33,410	CRTP	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£19,164	£40,371	N/A	CRTP	CRTP	CRTP
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£15,035	£45,049	N/A	CRTP	CRTP	CRTP

The impact of different treatment effect durations on treatment choice at the £30,000, £25,000 and £20,000 per QALY thresholds is shown in Table 13, Table 14 and Table 15.

At the £30,000 per QALY threshold the model is insensitive to the treatment effect duration. The duration of treatment effect alters the preferred treatment choice in only two subgroups. In patients with NYHA III, QRS<120ms and no LBBB use of the most conservative treatment effect duration switches the preferred treatment option from ICD to OPT. In patients with NYHA III, QRS≥150ms and LBBB use of a five-year treatment effect duration switches the preferred treatment option from CRT-D to CRT-P.

Table 13: Impact of duration of treatment effect on treatment choice using £30,000 per QALY threshold

	Duration of mortality treatment effect			
Subgroup	**Lifetime**	**7.5 years (base case)**	**5 years**	**Mean f/up**
	Individuals without LBBB			
NYHA I, QRS <120ms	ICD	ICD	ICD	ICD
NYHA I, QRS ≥120ms and <150ms	ICD	ICD	ICD	ICD
NYHA I, QRS ≥150ms	CRTD	CRTD	CRTD	CRTD
NYHA II, QRS <120ms	ICD	ICD	ICD	ICD
NYHA II, QRS ≥120ms and <150ms	ICD	ICD	ICD	ICD
NYHA II, QRS ≥150ms	CRTD	CRTD	CRTD	CRTD
NYHA III, QRS <120ms	ICD	ICD	ICD	OPT
NYHA III, QRS ≥120ms and <150ms	CRTD	CRTD	CRTD	CRTD
NYHA III, QRS ≥150ms	CRTD	CRTD	CRTD	CRTD
NYHA IV, QRS <120ms	OPT	OPT	OPT	OPT
NYHA IV, QRS ≥120ms and <150ms	CRTP	CRTP	CRTP	CRTP
NYHA IV, QRS ≥150ms	CRTP	CRTP	CRTP	CRTP
	Individuals with LBBB			
NYHA I, QRS <120ms	OPT	OPT	OPT	OPT
NYHA I, QRS ≥120ms and <150ms	CRTD	CRTD	CRTD	CRTD
NYHA I, QRS ≥150ms	CRTD	CRTD	CRTD	CRTD
NYHA II, QRS <120ms	OPT	OPT	OPT	OPT
NYHA II, QRS ≥120ms and <150ms	CRTD	CRTD	CRTD	CRTD
NYHA II, QRS ≥150ms	CRTD	CRTD	CRTD	CRTD
NYHA III, QRS <120ms	OPT	OPT	OPT	OPT
NYHA III, QRS ≥120ms and <150ms	CRTD	CRTD	CRTD	CRTD
NYHA III, QRS ≥150ms	CRTD	CRTD	CRTP	CRTP
NYHA IV, QRS <120ms	OPT	OPT	OPT	OPT
NYHA IV, QRS ≥120ms and <150ms	CRTP	CRTP	CRTP	CRTP
NYHA IV, QRS ≥150ms	CRTP	CRTP	CRTP	CRTP

At the £25,000 per QALY threshold the model is sensitive to the treatment effect duration being increased in three subgroups, and is sensitive to it being decreased in six subgroups. Use of a lifetime treatment effect switches the treatment choice from OPT to ICD in patients with NYHA III, QRS<120ms; switches the treatment choice from CRT-P to CRT-D in patients with NYHA III, QRS≥150ms for both the no LBBB and LBBB subgroups.

Use of a 5-year time horizon switches the treatment choice from ICD to OPT in patients with NYHA I and II with QRS<120ms; switches the treatment choice from CRT-D to ICD in patients with NYHA II and QRS≥150ms and no LBBB and switches the treatment choice from CRT-D to CRT-P in patients with NYHA III and QRS≥120ms and <150ms with LBBB.

Use of the most conservative assumption switches the treatment choice from CRT-D to ICD in patients with NYHA I, QRS≥150ms and without LBBB and from CRT-D to CRT-P in patients with NYHA III, QRS≥120ms and <150ms and no LBBB.

Table 14: Impact of duration of treatment effect on treatment choice using £25,000 per QALY threshold

	Duration of mortality treatment effect			
Subgroup	**Lifetime**	**7.5 years (base case)**	**5 years**	**Mean f/up**
	Individuals without LBBB			
NYHA I, QRS <120ms	ICD	ICD	OPT	OPT
NYHA I, QRS ≥120ms and <150ms	ICD	ICD	ICD	ICD
NYHA I, QRS ≥150ms	CRTD	CRTD	CRTD	ICD
NYHA II, QRS <120ms	ICD	ICD	OPT	OPT
NYHA II, QRS ≥120ms and <150ms	ICD	ICD	ICD	ICD
NYHA II, QRS ≥150ms	CRTD	CRTD	ICD	ICD
NYHA III, QRS <120ms	ICD	OPT	OPT	OPT
NYHA III, QRS ≥120ms and <150ms	CRTD	CRTD	CRTD	CRTP
NYHA III, QRS ≥150ms	CRTD	CRTP	CRTP	CRTP
NYHA IV, QRS <120ms	OPT	OPT	OPT	OPT
NYHA IV, QRS ≥120ms and <150ms	CRTP	CRTP	CRTP	CRTP
NYHA IV, QRS ≥150ms	CRTP	CRTP	CRTP	CRTP
	Individuals with LBBB			
NYHA I, QRS <120ms	OPT	OPT	OPT	OPT
NYHA I, QRS ≥120ms and <150ms	CRTD	CRTD	CRTD	CRTD
NYHA I, QRS ≥150ms	CRTD	CRTD	CRTD	CRTD
NYHA II, QRS <120ms	OPT	OPT	OPT	OPT
NYHA II, QRS ≥120ms and <150ms	CRTD	CRTD	CRTD	CRTD
NYHA II, QRS ≥150ms	CRTD	CRTD	CRTD	CRTD
NYHA III, QRS <120ms	OPT	OPT	OPT	OPT
NYHA III, QRS ≥120ms and <150ms	CRTD	CRTD	CRTP	CRTP
NYHA III, QRS ≥150ms	CRTD	CRTP	CRTP	CRTP
NYHA IV, QRS <120ms	OPT	OPT	OPT	OPT
NYHA IV, QRS ≥120ms and <150ms	CRTP	CRTP	CRTP	CRTP
NYHA IV, QRS ≥150ms	CRTP	CRTP	CRTP	CRTP

At the £20,000 per QALY threshold the model is sensitive to the treatment effect duration increasing in seven subgroups. This is because many of the ICERs lie just above £20,000 per QALY in the base case. Using of more conservative treatment effect durations alters the treatment choice in only two subgroups; patients with NYHA I or II with QRS≥150ms and LBBB switch from CRT-D to OPT only when the most conservative treatment effect duration is used.

Table 15: Impact of duration of treatment effect on treatment choice using £20,000 per QALY threshold

	Duration of mortality treatment effect			
Subgroup	Lifetime	7.5 years (base case)	5 years	Mean f/up
	Individuals without LBBB			
NYHA I, QRS <120ms	ICD	OPT	OPT	OPT
NYHA I, QRS ≥120ms and <150ms	ICD	ICD	ICD	ICD
NYHA I, QRS ≥150ms	CRTD	OPT	OPT	OPT
NYHA II, QRS <120ms	ICD	OPT	OPT	OPT
NYHA II, QRS ≥120ms and <150ms	ICD	ICD	ICD	ICD
NYHA II, QRS ≥150ms	CRTD	OPT	OPT	OPT
NYHA III, QRS <120ms	OPT	OPT	OPT	OPT
NYHA III, QRS ≥120ms and <150ms	CRTP	OPT	OPT	OPT
NYHA III, QRS ≥150ms	CRTP	CRTP	CRTP	CRTP
NYHA IV, QRS <120ms	OPT	OPT	OPT	OPT
NYHA IV, QRS ≥120ms and <150ms	OPT	OPT	OPT	OPT
NYHA IV, QRS ≥150ms	CRTP	CRTP	CRTP	CRTP
	Individuals with LBBB			
NYHA I, QRS <120ms	OPT	OPT	OPT	OPT
NYHA I, QRS ≥120ms and <150ms	CRTD	OPT	OPT	OPT
NYHA I, QRS ≥150ms	CRTD	CRTD	CRTD	OPT
NYHA II, QRS <120ms	OPT	OPT	OPT	OPT
NYHA II, QRS ≥120ms and <150ms	CRTD	OPT	OPT	OPT
NYHA II, QRS ≥150ms	CRTD	CRTD	CRTD	OPT
NYHA III, QRS <120ms	OPT	OPT	OPT	OPT
NYHA III, QRS ≥120ms and <150ms	CRTP	CRTP	CRTP	CRTP
NYHA III, QRS ≥150ms	CRTP	CRTP	CRTP	CRTP
NYHA IV, QRS <120ms	OPT	OPT	OPT	OPT
NYHA IV, QRS ≥120ms and <150ms	CRTP	CRTP	CRTP	CRTP
NYHA IV, QRS ≥150ms	CRTP	CRTP	CRTP	CRTP

The following evidence supports the assumption that treatment effects are maintained over the long term, and that the use of a 7.5 year constant treatment effect may be reasonable:

- The original data lock for the CARE-HF study found that at a mean follow-up of 29.4 months the hazard ratio for all cause-mortality was 0.64 [95% CI 0.48, 0.85] for CRT-P vs. OPT[2]. Long-term follow up recently published for CARE-HF[3] found that at a

[2] Cleland JG, Daubert JC, Erdmann E, Freemantle N, Gras D, Kappenberger L et al. The effect of cardiac resynchronization on morbidity and mortality in heart failure. New England Journal of Medicine 2005; 352(15):1539-1549.

mean follow-up of 56 (50) months in the CRT-P (OPT) arms the hazard ratio for all cause-mortality was 0.77 [0.63, 0.93], this is despite the fact that 156/404 (39%) of control patients crossed-over to a CRT device during follow-up.

- The original data lock for MADIT-II study found that at an average follow-up of 20 months, the hazard ratio for all cause-mortality was 0.69 [0.51, 0.93][4]. Long-term follow-up found that at a median follow-up of 7.6 years the hazard ratio for all cause-mortality was 0.77 [0.65, 0.91], this is despite the fact that 167/490 (34%) of control patients crossed-over to a device during follow-up[5]. Attempts to adjust for cross-over by censoring patients at the time of cross-over and including treatment as a time-dependent covariable provided treatment effect estimates of 0.67 [0.56, 0.80] and 0.66 [0.56, 0.78] respectively.
- As reported in the original submission (Section 4.5.3), there is no evidence from the overall IPD analysis that hazard ratios describing the device treatment effects on all-cause mortality vary over time. A test of the validity of the proportional hazards assumption which looks for any correlation between the scaled Schoenfeld residuals and survival time produced a global p-value for device terms of [redacted] (a p-value of less than 0.05 is considered to indicate violation of the proportionality assumption). The p-values for individual treatment coefficients were CRT-P: [redacted]; CRT-D: [redacted] and ICD: [redacted]; again suggesting no evidence of time-dependence in the treatment effects.

2) Effect of CRT-D on hospitalisation in NYHA III/IV patients

On review of the model inputs, the estimated [redacted] treatment effect for CRT-D in patients with NYHA III/IV was implemented in the base case and the reporting of this was inaccurate. A comparison of reported and used treatment effects are presented in Table 16. Small differences occurred for two of the CRT-D treatment effects.

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[3] Cleland JGF, Freemantle N, Erdmann E, Gras D, Kappenberger L, Tavazzi L et al. Long-term mortality with cardiac resynchronization therapy in the Cardiac Resynchronization-Heart Failure (CARE-HF) trial. Eur J Heart Fail. 14[6], 628-634. 2012.

[4] Moss AJ, Zareba W, Hall WJ, Klein H, Wilber DJ, Cannom DS et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. New England Journal of Medicine. 2002; 346(12):877-883.

[5] Goldenberg I, Gillespie J, Moss A, Hall J, Klein H, McNitt S, Brown M et al. Long-Term Benefit of Primary Prevention With an Implantable Cardioverter-Defibrillator: An Extended 8-Year Follow-Up Study of the Multicenter Automatic Defibrillator Implantation Trial II. Circulation. 2010;122:1265-1271.

Table 16: Comparison between reported and actual all-cause hospitalisation treatment effects in the ABHI model

	Reported as used in ABHI model			Actually used in ABHI model		
	NYHA I/II	NYHA III	NYHA IV	NYHA I/II	NYHA III	NYHA IV
ICD	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
CRT-P	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
CRT-D	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

We have therefore run a scenario using the approach reported in the submission i.e. using the values for CRT-P in NYHA III and IV patients to model the treatment effects for CRT-D in these groups. The impact of this scenario is presented in Table 17 and Table 18. This has a marginal impact on the ICERs and none of the treatment options at £20,000, £25,000 or £30,000 per QALY change from the base case.

Table 17: Sensitivity analyses – all-cause hospitalisation treatment effect for CRT-D set equal to CRT-P for patients without LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	below £20k/QALY
I	<120ms	OPT	ICD	N/A	N/A	Referent	£24,074	N/A	N/A	ICD	ICD	OPT
I	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£16,253	N/A	ICD	ICD	ICD
I	>150ms	OPT	ICD	CRTD	N/A	Referent	£21,102	£21,759	N/A	CRTD	CRTD	OPT
II	<120ms	OPT	ICD	N/A	N/A	Referent	£24,465	N/A	N/A	ICD	ICD	OPT
II	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£16,813	N/A	ICD	ICD	ICD
II	>150ms	OPT	ICD	CRTD	N/A	Referent	£20,602	£23,738	N/A	CRTD	CRTD	OPT
III	<120ms	OPT	ICD	N/A	N/A	Referent	£27,826	N/A	N/A	ICD	OPT	OPT
III	>=120, <150 ms	OPT	CRTP	ICD	CRTD	Referent	£20,178	Ext Dominated	£23,207	CRTD	CRTD	OPT
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£13,930	£25,050	CRTD	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£22,578	£38,459	N/A	CRTP	CRTP	OPT
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£17,175	£34,245	N/A	CRTP	CRTP	CRTP

Table 18: Sensitivity analyses - all-cause hospitalisation treatment effect for CRT-D set equal to CRT-P for patients with LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	below £20k/QALY
I	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
I	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	£20,677	£21,672	N/A	CRTD	CRTD	OPT
I	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£17,470	N/A	CRTD	CRTD	CRTD
II	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
II	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£20,704	N/A	CRTD	CRTD	OPT
II	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£17,664	N/A	CRTD	CRTD	CRTD
III	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
III	>=120, <150 ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£14,215	£24,707	CRTD	CRTD	CRTP
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£10,496	£28,467	CRTD	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£18,664	£35,384	N/A	CRTP	CRTP	CRTP
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£14,500	£38,722	N/A	CRTP	CRTP	CRTP

3) Inclusion of counselling costs

Heart Rhythm UK note in their statement on "Standards for the implantation and follow up of cardiac rhythm management devices in adults" that psychological support and counselling

service for ICD and CRT-D patients is a necessary part of device follow up[6]. They then go on to say that "*counselling prior to implant is essential and further counselling as and when required should be made available if a patient is having problems*".

Input from our clinical advisors indicated that the initial counselling session would be delivered by a member of the support team, typically an arrhythmia nurse and that long term a small proportion of patients would require psychiatric support (cognitive behavioural therapy, CBT). The following typical lifetime counselling protocol was provided by our clinical advisors:

1 x arrhythmic nurse consultation (incurred by 100% of patients)

1 x full psychiatry visit (incurred by 0.5% of patients)

4 x CBT sessions (incurred by 0.5% of patients)

All input data used in the model were taken from the latest version of the PSSRU[7]. Based on the unit cost of a specialist nurse consultation (£22, Table 10.7), a counselling consultation (£59, Table 2.7) and the per-person-per-session cost of CBT (£15, Table 2.6) the overall expected per-patient cost of counselling used in the model is £27.95. For simplicity, this value is applied in the first model cycle. Based on feedback from the committee, the Heart Rhythm UK statement and feedback from the clinical advisors this is applied to those receiving defibrillator therapy (CRT-D or ICD) and not to patients who receive CRT-P.

The results from this sensitivity analysis are presented in Table 19 and

Table 20. The overall impact on the ICERs in all subgroups was negligible with no changes to optional treatment choice at £20,000, £25,000 or £30,000 per QALY gained.

Table 19: sensitivity analysis – inclusion of counselling costs for patients without LBBB

[6] http://heartrhythmuk.org.uk/files/file/Docs/Position%20Statements/121214-1-Heart%20Rhythm%20UK%20standards%20for%20CRM%20devices%20in%20adults%202013.pdf
[7] http://www.pssru.ac.uk/project-pages/unit-costs/2012/

NYHA Class	QRS Duration	C-E Sequence 1st	2nd	3rd	4th	ICERs 1st	2nd	3rd	4th	Highest ICER below £30k/QALY	Highest ICER below £25k/QALY	Highest ICER below £20k/QALY
I	<120ms	OPT	ICD	N/A	N/A	Referent	£24,105	N/A	N/A	ICD	ICD	OPT
I	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£16,275	N/A	ICD	ICD	ICD
I	>150ms	OPT	ICD	CRTD	N/A	Referent	£21,131	£21,759	N/A	CRTD	CRTD	OPT
II	<120ms	OPT	ICD	N/A	N/A	Referent	£24,497	N/A	N/A	ICD	ICD	OPT
II	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£16,835	N/A	ICD	ICD	ICD
II	>150ms	OPT	ICD	CRTD	N/A	Referent	£20,630	£23,738	N/A	CRTD	CRTD	OPT
III	<120ms	OPT	ICD	N/A	N/A	Referent	£27,865	N/A	N/A	ICD	OPT	OPT
III	>=120, <150 ms	OPT	CRTP	ICD	CRTD	Referent	£20,178	Ext Dominated	£23,394	CRTD	CRTD	OPT
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£13,930	£25,248	CRTD	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£22,578	£40,138	N/A	CRTP	CRTP	OPT
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£17,175	£35,883	N/A	CRTP	CRTP	CRTP

Table 20: sensitivity analysis – inclusion of counselling costs for patients with LBBB

NYHA Class	QRS Duration	C-E Sequence 1st	2nd	3rd	4th	ICERs 1st	2nd	3rd	4th	Highest ICER below £30k/QALY	Highest ICER below £25k/QALY	Highest ICER below £20k/QALY
I	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
I	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	£20,705	£21,672	N/A	CRTD	CRTD	OPT
I	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£17,488	N/A	CRTD	CRTD	CRTD
II	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
II	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£20,724	N/A	CRTD	CRTD	OPT
II	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£17,681	N/A	CRTD	CRTD	CRTD
III	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
III	>=120, <150 ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£14,215	£24,922	CRTD	CRTD	CRTP
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£10,496	£28,701	CRTD	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£18,664	£37,179	N/A	CRTP	CRTP	CRTP
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£14,500	£40,532	N/A	CRTP	CRTP	CRTP

4) Device crossover or upgrade in clinical practice

(a) Likelihood

Information on crossover or upgrade rates in routine clinical practice is sparse. The latest UK devices survey[8] did not collect this information and recorded "upgrades" as new implants. Information is available from the Swedish annual ICD and pacemaker register prepared annually by the Karolinska Hospital department of cardiology[9]. In this document, the annual rate of upgrade to CRT (type unspecified) in ICD explant patients was 0.5%. Information on the rate of upgrades from CRT-P to CRT-D was not reported in this document.

A recent retrospective observational study from the UK[10] concluded that 3.8% of patients upgraded from ICD to CRT-D during a mean follow up period of 48 months. Data were again not reported for the proportion of CRT-P patients who upgrade to CRT-D.

The clinical experts consulted for this appraisal also confirmed that cross-overs or device upgrades are rare in UK clinical practice. They explained that upgrade procedures are complex and associated with increased lead and infective complications; and that they are also considered to be a waste of resources.

(b) Upgrade from CRT-P to CRT-D

We discussed the possibility of using CRT-D in patients currently indicated for a CRT-P on the basis that they may require defibrillation in the future with the clinical experts consulted for this appraisal. They both viewed that it was implausible that a patient with a CRT-P indication would be implanted with a CRT-D on the basis that they may develop a life-threatening arrhythmia at some point in the future but that defibrillation would not be switched on initially.

5) Deterministic sensitivity analyses for resource use and cost parameters

In response to the committee request for further deterministic sensitivity analyses for resource use and cost parameters we have run the following additional analyses:

- +/-25% change to HRG EA12Z (related to ICD/CRT-D based therapy) - used to model non-purchase costs in patients who get an ICD or CRT-D device.

[8]https://nicor5.nicor.org.uk/CRM/device.nsf/65153b7e3756850e80256aff003a2c78/$FILE/CRM%20National%20Annual%20Report%202011%20final%20release%20revised.pdf
[9]https://www.pacemakerregistret.se/icdpmr/start.do
[10]Scott et al. Pacing Clin Electrophysiol. 2012 Jan;35(1):73-80

- +/-25% change to HRG EA07Z (CRT-P based therapy) – unlike for CRT-D and ICD, a relevant tariff existed for CRT-P and this was used to cover all up front implant costs.
- +/-25% change to HRG EA39Z - this tariff value was applied to battery replacements for ICD and CRT-D therapy.
- Upper/lower quartile HF and non-HF Hospitalisation costs
- +/-25% change to cost of an outpatient visit

The raw cost-effectiveness results for all analyses are presented as Appendix 1 with a summary of where the preferred treatment option changes from those in the base case presented below. Where the results differ from the base case, three pieces of information are provided: the subgroup where the change occurs, the nature of the change ('from option X to option Y') and the respective absolute ICER that has driven the change in the optimal treatment choice at a given threshold.

In terms of absolute changes to all ICERs, the model was robust to all alterations, with none of the analyses having a dramatic impact. However, the analyses do highlight the fact that small changes to cost parameters can impact on the choice of treatment in a subset of the 24 patient groups. These groups are primarily those with NYHA I to III HF and very wide QRS duration (≥150ms) or NYHA III and wide QRS duration (≥120ms and <150ms). The results arise due to the base case ICERs being very close to the threshold values, and in particular the £25,000/QALY threshold in some subgroups. As such, the results in these tables should be read in conjunction with the relevant model outputs presented in Appendix 1.

Table 21: summary of additional deterministic sensitivity analyses for patients without LBBB

	Cost-effectiveness threshold (per QALY gained)		
Analysis	£30,000	£25,000	£20,000
		Alteration to HRG EA12Z (ICD / CRT-D non-purchase, £5,556)	
Increased by 25%	None	NYHA I, QRS <120ms,ICD → OPT, £24,074 → £25,645 NYHA II, QRS <120ms, ICD → OPT, ICD: £24,465 → £26,027 NYHA III, QRS ≥120ms and <150ms,CRT-D →CRT-P, CRT-D: £23,349 → £25,611	None
Decreased by 25%	None	NYHA III, QRS ≥150ms, CRT-P →CRT-D, CRT-D: £25,200 → £22,806	NYHA I, QRS ≥150ms, OPT→ ICD, ICD: £21,102 → £19,668 NYHA II, QRS ≥150ms, OPT→ ICD, ICD: £20,602 → £19,231
		Alteration to HRG EA07Z (total CRT-P implant cost, £8,281)	
Increased by 25%	NYHA IV, QRS ≥150ms, CRT-P → CRT-D, CRT-D: £35,811 → £29,881	NYHA III, QRS ≥150ms, CRT-P →CRT-D, CRT-D: £25,200 → £20,927 NYHA IV, QRS ≥120ms and <150ms CRT-P → OPT, CRT-P: £22,578 → £28,516	NYHA IV, QRS ≥150ms CRT-P → OPT, CRT-P: £17,175 → £21,618
Decreased by 25%	None	NYHA III, QRS ≥120ms and <150ms, CRT-D → CRT-P, CRT-D: £23,349 → £27,276	NYHA III, QRS ≥120ms and <150ms, OPT → CRT-P, CRT-P: £20,178 → £15,182
		Alteration to HRG EA39Z (ICD/CRT-D battery replacement cost, £2,748)	
Increased by 25%	None	None	None
Decreased by 25%	None	NYHA III, QRS ≥150ms, CRT-P→ CRT-D, CRT-D: £25,200 → £24,747	None
		HF and non-HF Hospitalisation costs (£2,295 and £2,448 respectively)	
Use of upper quartile data	None	None	NYHA III, QRS ≥120ms and <150ms,OPT → CRT-P, CRT-P: £20,178 → £19,724
Use of lower quartile data	None	NYHA III, QRS ≥150ms, CRT-P →CRT-D, CRT-D: £25,200 → £24,990	None
		Cost of an outpatient visit (£110)	
Increased by 25%	None	NYHA II, QRS ≥150ms,CRT-D → ICD, CRT-D: £23,768 → £25,403	None
Decreased by 25%	None	None	NYHA III, QRS ≥120ms and <150ms, OPT → CRT-P, CRT-P: £20,178 → £19,635

Table 22: summary of additional deterministic sensitivity analyses for patients with LBBB

	Cost-effectiveness threshold (per QALY gained)		
Analysis	£30,000	£25,000	£20,000
	Alteration to HRG EA12Z (ICD / CRT-D non-purchase,£5,556)		
Increased by 25%	NYHA III, QRS ≥150ms, CRT-D →CRT-P, CRT-D: £28,646 → £31,356	NYHA III, QRS ≥120ms and <150ms, CRT-D →CRT-P, CRT-D: £24,875→£27,232	None
Decreased by 25%	None	None	NYHA I, QRS ≥120ms and <150ms OPT →ICD, ICD: £20,677 → £19,303 NYHA II, QRS ≥120ms and <150ms, OPT →CRT-D, CRT-D: £20,704 → £19,683
	Alteration to HRG EA07Z (total CRT-P implant cost, £8,281)		
Increased by 25%	None	NYHA III, QRS ≥150ms, CRT-P → CRT-D, CRT-D: £28,646 → £23,709	NYHA IV, QRS≥120 and <150ms CRT-P → OPT, CRT-P: £18,664 → £23,546
Decreased by 25%	NYHA III, QRS ≥150ms, CRT-D →CRT-P, CRT-D: £28,646 → £33,583	NYHA III, QRS ≥120ms and <150ms, CRT-D → CRT-P, CRT-D: £24,875 → £29,070	None
	Alteration to HRG EA39Z (ICD/CRT-D battery replacement cost, £2,748)		
Increased by 25%	None	NYHA III, QRS ≥120ms and <150ms, CRT-D → CRT-P, CRT-D: £24,875 → £25,313	None
Decreased by 25%	None	None	None
	HF and non-HF Hospitalisation costs (£2,295 and £2,448 respectively		
Use of upper quartile data	None	NYHA III, QRS ≥120ms and <150ms, CRT-D →CRT-P, CRT-D: £24,875 → £25,100	None
Use of lower quartile data	None	None	None
	Cost of an outpatient visit (£110)		
Increased by 25%	None	NYHA III, QRS ≥120ms and <150ms,CRT-D → CRT-P, CRT-D: £24,875 → £25,037	None
Decreased by 25%	None	None	None

Appendix 1

HRG tariff EA12Z (ICD/CRT non-purchase costs tariff)

Lower value for HRG tariff

Table 23: Sensitivity analyses –a reduction in tariff EA12Z for patients without LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	below £20k/QALY
I	<120ms	OPT	ICD	N/A	N/A	Referent	£22,502	N/A	N/A	ICD	ICD	OPT
I	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£15,189	N/A	ICD	ICD	ICD
I	>150ms	OPT	ICD	CRTD	N/A	Referent	£19,668	£21,756	N/A	CRTD	CRTD	ICD
II	<120ms	OPT	ICD	N/A	N/A	Referent	£22,904	N/A	N/A	ICD	ICD	OPT
II	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£15,728	N/A	ICD	ICD	ICD
II	>150ms	OPT	ICD	CRTD	N/A	Referent	£19,231	£23,735	N/A	CRTD	CRTD	ICD
III	<120ms	OPT	ICD	N/A	N/A	Referent	£25,864	N/A	N/A	ICD	OPT	OPT
III	>=120, <150 ms	OPT	CRTP	ICD	CRTD	Referent	£20,178	Ext Dominated	£21,087	CRTD	CRTD	OPT
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£13,930	£22,806	CRTD	CRTD	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£22,578	£35,752	N/A	CRTP	CRTP	OPT
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£17,175	£32,215	N/A	CRTP	CRTP	CRTP

Table 24: Sensitivity analyses –a reduction in tariff EA12Z for patients with LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	below £20k/QALY
I	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
I	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	£19,303	£21,669	N/A	CRTD	CRTD	ICD
I	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£16,603	N/A	CRTD	CRTD	CRTD
II	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
II	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£19,683	N/A	CRTD	CRTD	CRTD
II	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£16,817	N/A	CRTD	CRTD	CRTD
III	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
III	>=120, <150 ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£14,215	£22,517	CRTD	CRTD	CRTP
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£10,496	£25,937	CRTD	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£18,664	£33,311	N/A	CRTP	CRTP	CRTP
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£14,500	£36,291	N/A	CRTP	CRTP	CRTP

Upper value for HRG tariff

Table 25: Sensitivity analyses –an increase in tariff EA12Z for patients without LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	below £20k/QALY
I	<120ms	OPT	ICD	N/A	N/A	Referent	£25,645	N/A	N/A	ICD	OPT	OPT
I	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£17,318	N/A	ICD	ICD	ICD
I	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£22,354	N/A	CRTD	CRTD	OPT
II	<120ms	OPT	ICD	N/A	N/A	Referent	£26,027	N/A	N/A	ICD	OPT	OPT
II	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£17,898	N/A	ICD	ICD	ICD
II	>150ms	OPT	ICD	CRTD	N/A	Referent	£21,973	£23,741	N/A	CRTD	CRTD	OPT
III	<120ms	OPT	ICD	N/A	N/A	Referent	£29,787	N/A	N/A	ICD	OPT	OPT
III	>=120, <150 ms	OPT	CRTP	ICD	CRTD	Referent	£20,178	Ext Dominated	£25,611	CRTD	CRTP	OPT
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£13,930	£27,594	CRTD	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£22,578	£44,353	N/A	CRTP	CRTP	OPT
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£17,175	£39,407	N/A	CRTP	CRTP	CRTP

Table 26: Sensitivity analyses –an increase in tariff EA12Z for patients with LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	below £20k/QALY
I	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
I	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£21,964	N/A	CRTD	CRTD	OPT
I	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£18,337	N/A	CRTD	CRTD	CRTD
II	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
II	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£21,725	N/A	CRTD	CRTD	OPT
II	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£18,511	N/A	CRTD	CRTD	CRTD
III	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
III	>=120, <150 ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£14,215	£27,232	CRTD	CRTP	CRTP
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£10,496	£31,356	CRTP	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£18,664	£40,896	N/A	CRTP	CRTP	CRTP
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£14,500	£44,608	N/A	CRTP	CRTP	CRTP

HRG tariff EA07Z (CRT-P tariff)

Lower value for HRG tariff

Table 27: Sensitivity analyses –a reduction in tariff EA07Z for patients without LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER below
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	£20k/QALY
I	<120ms	OPT	ICD	N/A	N/A	Referent	£24,074	N/A	N/A	ICD	ICD	OPT
I	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£16,253	N/A	ICD	ICD	ICD
I	>150ms	OPT	ICD	CRTD	N/A	Referent	£21,102	£21,759	N/A	CRTD	CRTD	OPT
II	<120ms	OPT	ICD	N/A	N/A	Referent	£24,465	N/A	N/A	ICD	ICD	OPT
II	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£16,813	N/A	ICD	ICD	ICD
II	>150ms	OPT	ICD	CRTD	N/A	Referent	£20,602	£23,738	N/A	CRTD	CRTD	OPT
III	<120ms	OPT	ICD	N/A	N/A	Referent	£27,826	N/A	N/A	ICD	OPT	OPT
III	>=120, <150 ms	OPT	CRTP	ICD	CRTD	Referent	£15,182	Ext Dominated	£27,276	CRTD	CRTP	CRTP
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£10,667	£29,473	CRTD	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£16,640	£46,934	N/A	CRTP	CRTP	CRTP
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£12,732	£41,740	N/A	CRTP	CRTP	CRTP

Table 28: Sensitivity analyses –a reduction in tariff EA07Z for patients with LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER below
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	£20k/QALY
I	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
I	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	£20,677	£21,672	N/A	CRTD	CRTD	OPT
I	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£17,470	N/A	CRTD	CRTD	CRTD
II	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
II	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£20,704	N/A	CRTD	CRTD	OPT
II	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£17,664	N/A	CRTD	CRTD	CRTD
III	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
III	>=120, <150 ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£10,848	£29,070	CRTD	CRTP	CRTP
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£8,177	£33,583	CRTP	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£13,783	£43,283	N/A	CRTP	CRTP	CRTP
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£11,028	£47,296	N/A	CRTP	CRTP	CRTP

Upper value for HRG tariff

Table 29: Sensitivity analyses –an increase in tariff EA07Z for patients without LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER below
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	£20k/QALY
I	<120ms	OPT	ICD	N/A	N/A	Referent	£24,074	N/A	N/A	ICD	ICD	OPT
I	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£16,253	N/A	ICD	ICD	ICD
I	>150ms	OPT	ICD	CRTD	N/A	Referent	£21,102	£21,759	N/A	CRTD	CRTD	OPT
II	<120ms	OPT	ICD	N/A	N/A	Referent	£24,465	N/A	N/A	ICD	ICD	OPT
II	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£16,813	N/A	ICD	ICD	ICD
II	>150ms	OPT	ICD	CRTD	N/A	Referent	£20,602	£23,738	N/A	CRTD	CRTD	OPT
III	<120ms	OPT	ICD	N/A	N/A	Referent	£27,826	N/A	N/A	ICD	OPT	OPT
III	>=120, <150 ms	OPT	CRTP	ICD	CRTD	Referent	Ext Dominated	Ext Dominated	£21,954	CRTD	CRTD	OPT
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£17,193	£20,927	CRTD	CRTD	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£28,516	£33,170	N/A	CRTP	OPT	OPT
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£21,618	£29,881	N/A	CRTD	CRTP	OPT

Table 30: Sensitivity analyses –an increase in tariff EA07Z for patients with LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER below
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	£20k/QALY
I	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
I	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	£20,677	£21,672	N/A	CRTD	CRTD	OPT
I	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£17,470	N/A	CRTD	CRTD	CRTD
II	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
II	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£20,704	N/A	CRTD	CRTD	OPT
II	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£17,664	N/A	CRTD	CRTD	CRTD
III	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
III	>=120, <150 ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£17,582	£20,679	CRTD	CRTD	CRTP
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£12,816	£23,709	CRTD	CRTD	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£23,546	£30,924	N/A	CRTP	CRTP	OPT
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£17,973	£33,602	N/A	CRTP	CRTP	CRTP

HRG tariff EA39Z (battery replacement for ICD/CRT-D)

Lower value for HRG tariff

Table 31: Sensitivity analyses –a reduction in tariff EA39Z for patients without LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	below £20k/QALY
I	<120ms	OPT	ICD	N/A	N/A	Referent	£23,690	N/A	N/A	ICD	ICD	OPT
I	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£16,020	N/A	ICD	ICD	ICD
I	>150ms	OPT	ICD	CRTD	N/A	Referent	£20,817	£21,572	N/A	CRTD	CRTD	OPT
II	<120ms	OPT	ICD	N/A	N/A	Referent	£24,056	N/A	N/A	ICD	ICD	OPT
II	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£16,566	N/A	ICD	ICD	ICD
II	>150ms	OPT	ICD	CRTD	N/A	Referent	£20,312	£23,544	N/A	CRTD	CRTD	OPT
III	<120ms	OPT	ICD	N/A	N/A	Referent	£27,493	N/A	N/A	ICD	OPT	OPT
III	>=120, <150 ms	OPT	CRTP	ICD	CRTD	Referent	£20,178	Ext Dominated	£22,971	CRTD	CRTD	OPT
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£13,930	£24,747	CRTD	CRTD	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£22,578	£39,687	N/A	CRTP	CRTP	OPT
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£17,175	£35,389	N/A	CRTP	CRTP	CRTP

Table 32: Sensitivity analyses –a reduction in tariff EA39Z for patients with LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	below £20k/QALY
I	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
I	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	£20,375	£21,495	N/A	CRTD	CRTD	OPT
I	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£17,244	N/A	CRTD	CRTD	CRTD
II	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
II	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£20,428	N/A	CRTD	CRTD	OPT
II	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£17,424	N/A	CRTD	CRTD	CRTD
III	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
III	>=120, <150 ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£14,215	£24,437	CRTD	CRTD	CRTP
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£10,496	£28,098	CRTD	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£18,664	£36,713	N/A	CRTP	CRTP	CRTP
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£14,500	£39,986	N/A	CRTP	CRTP	CRTP

Upper value for HRG tariff

Table 33: Sensitivity analyses –an increase in tariff EA39Z for patients without LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER below
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	£20k/QALY
I	<120ms	OPT	ICD	N/A	N/A	Referent	£24,457	N/A	N/A	ICD	ICD	OPT
I	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£16,487	N/A	ICD	ICD	ICD
I	>150ms	OPT	ICD	CRTD	N/A	Referent	£21,388	£21,947	N/A	CRTD	CRTD	OPT
II	<120ms	OPT	ICD	N/A	N/A	Referent	£24,874	N/A	N/A	ICD	ICD	OPT
II	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£17,061	N/A	ICD	ICD	ICD
II	>150ms	OPT	ICD	CRTD	N/A	Referent	£20,893	£23,932	N/A	CRTD	CRTD	OPT
III	<120ms	OPT	ICD	N/A	N/A	Referent	£28,158	N/A	N/A	ICD	OPT	OPT
III	>=120, <150 ms	OPT	CRTP	ICD	CRTD	Referent	£20,178	Ext Dominated	£23,727	CRTD	CRTD	OPT
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£13,930	£25,654	CRTD	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£22,578	£40,418	N/A	CRTP	CRTP	OPT
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£17,175	£36,233	N/A	CRTP	CRTP	CRTP

Table 34: Sensitivity analyses –an increase in tariff EA39Z for patients with LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER below
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	£20k/QALY
I	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
I	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	£20,979	£21,850	N/A	CRTD	CRTD	OPT
I	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£17,697	N/A	CRTD	CRTD	CRTD
II	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
II	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£20,980	N/A	CRTD	CRTD	OPT
II	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£17,904	N/A	CRTD	CRTD	CRTD
III	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
III	>=120, <150 ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£14,215	£25,313	CRTD	CRTP	CRTP
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£10,496	£29,194	CRTD	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£18,664	£37,494	N/A	CRTP	CRTP	CRTP
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£14,500	£40,913	N/A	CRTP	CRTP	CRTP

Hospitalisation costs (HF related and non-HF related)

For the purpose of this sensitivity analyses, the derived lower estimates for HF related and non-HF related hospitalisations are £1,804 and £1,859 respectively with the corresponding upper values being £2,804 and £2,941. These were derived by taking a weighted average of the lower and upper quartiles, weighting by activity.

Lower value for all NHS tariffs

Table 35: Sensitivity analyses –a reduction in all hospitalisation costs for patients without LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER below
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	£20k/QALY
I	<120ms	OPT	ICD	N/A	N/A	Referent	£24,147	N/A	N/A	ICD	ICD	OPT
I	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£16,250	N/A	ICD	ICD	ICD
I	>150ms	OPT	ICD	CRTD	N/A	Referent	£21,126	£21,898	N/A	CRTD	CRTD	OPT
II	<120ms	OPT	ICD	N/A	N/A	Referent	£24,552	N/A	N/A	ICD	ICD	OPT
II	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£16,819	N/A	ICD	ICD	ICD
II	>150ms	OPT	ICD	CRTD	N/A	Referent	£20,628	£23,907	N/A	CRTD	CRTD	OPT
III	<120ms	OPT	ICD	N/A	N/A	Referent	£27,875	N/A	N/A	ICD	OPT	OPT
III	>=120, <150 ms	OPT	CRTP	ICD	CRTD	Referent	£20,669	Ext Dominated	£23,123	CRTD	CRTD	OPT
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£14,168	£24,990	CRTD	CRTD	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£23,298	£39,283	N/A	CRTP	CRTP	OPT
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£17,745	£35,081	N/A	CRTP	CRTP	CRTP

Table 36: Sensitivity analyses –a reduction in all hospitalisation costs for patients with LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER below
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	£20k/QALY
I	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
I	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	£20,714	£21,853	N/A	CRTD	CRTD	OPT
I	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£17,498	N/A	CRTD	CRTD	CRTD
II	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
II	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£20,777	N/A	CRTD	CRTD	OPT
II	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£17,704	N/A	CRTD	CRTD	CRTD
III	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
III	>=120, <150 ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£14,492	£24,632	CRTD	CRTD	CRTP
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£10,600	£28,429	CRTD	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£19,303	£36,281	N/A	CRTP	CRTP	CRTP
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£14,750	£39,679	N/A	CRTP	CRTP	CRTP

Upper value for all NHS tariffs

Table 37: Sensitivity analyses –an increase in all hospitalisation costs for patients without LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	below £20k/QALY
I	<120ms	OPT	ICD	N/A	N/A	Referent	£24,007	N/A	N/A	ICD	ICD	OPT
I	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£16,257	N/A	ICD	ICD	ICD
I	>150ms	OPT	ICD	CRTD	N/A	Referent	£21,081	£21,630	N/A	CRTD	CRTD	OPT
II	<120ms	OPT	ICD	N/A	N/A	Referent	£24,386	N/A	N/A	ICD	ICD	OPT
II	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£16,809	N/A	ICD	ICD	ICD
II	>150ms	OPT	ICD	CRTD	N/A	Referent	£20,579	£23,581	N/A	CRTD	CRTD	OPT
III	<120ms	OPT	ICD	N/A	N/A	Referent	£27,781	N/A	N/A	ICD	OPT	OPT
III	>=120, <150 ms	OPT	CRTP	ICD	CRTD	Referent	£19,724	Ext Dominated	£23,559	CRTD	CRTD	CRTP
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£13,710	£25,396	CRTD	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£21,912	£40,767	N/A	CRTP	CRTP	OPT
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£16,647	£36,489	N/A	CRTP	CRTP	CRTP

Table 38: Sensitivity analyses –an increase in all hospitalisation costs for patients with LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	below £20k/QALY
I	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
I	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	£20,644	£21,505	N/A	CRTD	CRTD	OPT
I	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£17,444	N/A	CRTD	CRTD	CRTD
II	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
II	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£20,636	N/A	CRTD	CRTD	OPT
II	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£17,627	N/A	CRTD	CRTD	CRTD
III	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
III	>=120, <150 ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£13,958	£25,100	CRTD	CRTP	CRTP
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£10,400	£28,849	CRTD	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£18,073	£37,868	N/A	CRTP	CRTP	CRTP
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£14,270	£41,165	N/A	CRTP	CRTP	CRTP

Outpatient costs

Lower value

Table 39: Sensitivity analyses –a reduction in outpatient costs for patients without LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER below
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	£20k/QALY
I	<120ms	OPT	ICD	N/A	N/A	Referent	£24,005	N/A	N/A	ICD	ICD	OPT
I	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£16,182	N/A	ICD	ICD	ICD
I	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£20,855	N/A	CRTD	CRTD	OPT
II	<120ms	OPT	ICD	N/A	N/A	Referent	£24,397	N/A	N/A	ICD	ICD	OPT
II	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£16,742	N/A	ICD	ICD	ICD
II	>150ms	OPT	ICD	CRTD	N/A	Referent	£20,532	£22,074	N/A	CRTD	CRTD	OPT
III	<120ms	OPT	ICD	N/A	N/A	Referent	£27,742	N/A	N/A	ICD	OPT	OPT
III	>=120, <150 ms	OPT	CRTP	ICD	CRTD	Referent	£19,635	Ext Dominated	£23,190	CRTD	CRTD	CRTP
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£13,510	£25,040	CRTD	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£22,148	£39,864	N/A	CRTP	CRTP	OPT
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£16,769	£35,625	N/A	CRTP	CRTP	CRTP

Table 40: Sensitivity analyses –a reduction in outpatient costs for patients with LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER below
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	£20k/QALY
I	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
I	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£20,487	N/A	CRTD	CRTD	OPT
I	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£17,110	N/A	CRTD	CRTD	CRTD
II	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
II	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£20,273	N/A	CRTD	CRTD	OPT
II	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£17,279	N/A	CRTD	CRTD	CRTD
III	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
III	>=120, <150 ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£13,786	£24,713	CRTD	CRTD	CRTP
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£10,153	£28,483	CRTD	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£18,253	£36,915	N/A	CRTP	CRTP	CRTP
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£14,161	£40,260	N/A	CRTP	CRTP	CRTP

Upper value

Table 41: Sensitivity analyses –an increase in outpatient costs for patients without LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	below £20k/QALY
I	<120ms	OPT	ICD	N/A	N/A	Referent	£24,142	N/A	N/A	ICD	ICD	OPT
I	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£16,324	N/A	ICD	ICD	ICD
I	>150ms	OPT	ICD	CRTD	N/A	Referent	£21,173	£23,236	N/A	CRTD	CRTD	OPT
II	<120ms	OPT	ICD	N/A	N/A	Referent	£24,534	N/A	N/A	ICD	ICD	OPT
II	>=120, <150 ms	OPT	CRTD	ICD	N/A	Referent	Dominated	£16,884	N/A	ICD	ICD	ICD
II	>150ms	OPT	ICD	CRTD	N/A	Referent	£20,673	£25,403	N/A	CRTD	ICD	OPT
III	<120ms	OPT	ICD	N/A	N/A	Referent	£27,909	N/A	N/A	ICD	OPT	OPT
III	>=120, <150 ms	OPT	CRTP	ICD	CRTD	Referent	£20,722	Ext Dominated	£23,508	CRTD	CRTD	OPT
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£14,349	£25,360	CRTD	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£23,007	£40,240	N/A	CRTP	CRTP	OPT
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£17,580	£35,997	N/A	CRTP	CRTP	CRTP

Table 42: Sensitivity analyses –an increase in outpatient costs for patients with LBBB

		C-E Sequence				ICERs				Highest ICER below	Highest ICER	Highest ICER
NYHA Class	QRS Duration	1st	2nd	3rd	4th	1st	2nd	3rd	4th	£30k/QALY	below £25k/QALY	below £20k/QALY
I	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
I	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	£20,748	£23,247	N/A	CRTD	CRTD	OPT
I	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£17,830	N/A	CRTD	CRTD	CRTD
II	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
II	>=120, <150 ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£21,135	N/A	CRTD	CRTD	OPT
II	>150ms	OPT	ICD	CRTD	N/A	Referent	Ext Dominated	£18,049	N/A	CRTD	CRTD	CRTD
III	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
III	>=120, <150 ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£14,644	£25,037	CRTD	CRTP	CRTP
III	>150ms	OPT	ICD	CRTP	CRTD	Referent	Dominated	£10,840	£28,809	CRTD	CRTP	CRTP
IV	<120ms	OPT	N/A	N/A	N/A	Referent	N/A	N/A	N/A	OPT	OPT	OPT
IV	>=120, <150 ms	OPT	CRTP	CRTD	N/A	Referent	£19,076	£37,292	N/A	CRTP	CRTP	CRTP
IV	>150ms	OPT	CRTP	CRTD	N/A	Referent	£14,840	£40,639	N/A	CRTP	CRTP	CRTP