Table 1: Summary of trials analysing the impact of QRS duration in patients with DCM with different EF; as well as the role of CRT in these cohorts (Abbreviations: **ACM:** All-Cause Mortality; **AS**: Aortic Stenosis; **CAD:** Coronary Artery Disease; **CI:** Confidence Interval; **CRT:** Cardiac Resynchronization Therapy; **CRTD:** Cardiac Resynchronization Therapy – Defibrillator; **CRTP:** Cardiac Resynchronization Therapy – Pacemaker; **DCM:** Dilated Cardiomyopathy; **EF:** Ejection Fraction; **FU:** Follow-Up; **HF:** Heart Failure; **HR:** Hazard Ratio; **ICD:** Implantable Cardioverter-Defibrillator; **ICM:** Ischaemic Cardiomyopathy; **IVCD:** Intraventricular conduction delay; **LBBB:** Left Bundle Branch Block; **LVEDV:** Left ventricular end-diastolic volume; **LVEDVi:** Indexed LV End-Diastolic Volume; **LVEF:** Left Ventricular Ejection Fraction; **LVESVi:** Indexed LV End-Systolic Volume; **LVSD:** LV Systolic Dysfunction; **MI:** Myocardial Infarction; **MR:** Mitral Regurgitation; **NYHA:** New York Heart Association; **OMT:** Optimal Medical Therapy; **QoL:** Quality of Life; **RBBB:** Right Bundle Branch Block; **VT:** Ventricular Tachycardia; **VF:** Ventricular Fibrillation; **6MWT:** Six-Minute Walk Test.

Trial	Inclusion Criteria	Patient Numbers	Outcome
Impact of LBBB in Patients with Intermediate LVSD			
Outcomes with LBBB and mildly to moderately reduced LV function [8]	Patients with LBBB and **LVEF 36-50%.** Exclusion: EF ≤35; or > 50%; RBBB, IVCD	1436 patients. Mean LVEF 44 +/- 4%. Control group matched for age, sex and baseline EF but without IVCD. 35% of patients with LBBB had CAD; 7% previous MI and 5.4% had moderate+ AS	LBBB is associated with increased mortality - HR 1.17 (1-1.36 CI); p=0.04 LBBB associated with a higher incidence of LVEF reduction to ≤35% - HR 1.34 (1.09-1.63 CI) LBBB patients had similar rates of HF admission (11% vs 13% control; p-0.35) and similar incidence of VT/VF (15% vs 12% control; p=0.1) compared to non-LBBB controls.
CRT in Patients with Intermediate LVSD			
The Influence of LVEF on the effectiveness of CRT therapy: MADIT-CRT [e[13], e[17]]	MADIT criteria with EF<30%, Studied a subpopulation who had an **EF>30%** adjudicated by core lab compared to initially thought EF <30% by participating centre	1809 patients with CRT (696 patients with EF>30% by corelab – 450 of these with LBBB) Response to CRT was an improvement in LVEDV Primary endpoint was Heart failure or death. Secondary endpoint was ACM.	Patients with EF>30% had a 22.3% mean reduction in LVEDV with CRTD at 1 year. Reduced risk of HF hospitalization / death in EF>30% with CRT - HR 0.56 (CI .39-0.82; p=0.003).
CRT in patients with mildly impaired LV function [e[18]]	NYHA 3-4; QRS ≥120ms; TTE LVEF ≤35% on pre-implant TTE.	157 Patients with CRT Group A (n=130): CMR initial LVEF ≤35% vs Group B	CRT resulted in an Improvement in NYHA class; QoL scores; 6MWT distance in both groups.

	Sub-study with EF reclassification based on CMRI into those with **EF >35%.**	(n=27): CMR initial LVEF reclassified to >35%	Group A had a higher risk of ACM, hospitalization or major cardiovascular events.
CRT may benefit patients with LVEF>35%: a PROSPECT trial substudy. [e[12]]	The Prospect trial was a prospective, multicentred study recruiting patients with LVEF ≤35%; QRS ≥130ms; NYHA 3-4 on OMT This substudy assessed patients in whom corelab re-classified the initial **EF to >35%** versus EF <35% with CRT implantation.	361 Patients in the substudy – 86 (24%) had LVEF reclassified to >35% by corelab.	In patients with LVEF>35%, 63% improved in clinical composite score and 51% improved in LVESV. In patients with EF >35% and NYHA 3-4, QRS >130ms – CRT appears to provide clinical and structural benefits.
Long-term impact of CRT in mild heart failure: 5-year results from the REsynchronization reVErses Remodeling in Systolic left vEntricular dysfunction (REVERSE) study. [e[15], e[19], e[20]]	Randomized, double-blind study on CRT in NYHA 1-2; QRS ≥120ms and **LVEF≤40%**.	419 CRT Patients (256 patients with LBBB) Randomized CRT to switch on or off - after randomized phase, all patients had CRT switched on.	6min walk distance increased; mean LVESVi and LVEDVi decreased. Increase in mean LVEF with CRT-ON. Low rates of hospitalisation and mortality with CRT. Effects persist over 5 years.
Effect of CRT in patients with moderate LVSD and wide QRS complex: a prospective study [e[14]]	15 patients NYHA 3; **LVEF 36-44%** and QRS >120ms on OMT compared to 30 age, sex, NYHA class and HF-aetiology matched patients with conventional CRT indications.	15 case patients (EF 36-44%) compared to 30 control patients (EF≤ 35%).	Significant LV reverse remodelling by CRT in those with a wide QRS complex and moderate LVSD – significant reduction in LVEDV and LVESV and improvements in NYHA class and LVEF.
CRT in chronic heart failure with moderately reduced LVEF: Lessons from the Multicenter InSync Randomized Clinical Evaluation MIRACLE EF study. [e[21]]	Randomized, controlled, double-blind study with CRTP in NYHA 2-3, LBBB and **LVEF 36-50%.** Exclusion: Prior pacing or ICD.	44 patients (26 randomized). Patients Randomized 2:1 to CRTP-ON or CRTP-OFF. Minimum FU 24 months	Study prematurely stopped due to poor patient recruitment.
Biventricular pacing for atrioventricular block and systolic dysfunction – BLOCK HF [e[22]]	Patients with pacing Indications (AV block), NYHA 1-3; **LVEF ≤50%.** Primary outcome was time to ACM, urgent HF visit for intravenous diuretics or ≥15% increase in LVESVi	691 Patients (225 with LBBB) Randomized to CRT(P/D) vs RV pacing Mean FU 37 months	CRT resulted in significantly lower incidence of the primary outcome
CRT in Patients with Severe LVSD			
		813 Patients	

The effect of Cardiac Resynchronization on Morbidity and Mortality in Heart Failure – CARE-HF [9]	Age ≥18, NYHA 3-4, on OMT, **LVEF ≤35%**; indexed LVEDD ≥30mm, QRS ≥120ms	38% DCM Randomized to OMT vs CRT + OMT	CRT reduces the composite of ACM or hospitalization vs OMT (39% vs 55%). CRT reduces mortality (20% vs 30%). CRT improves EF, NYHA class and QoL. CRT reduces LVESVi and area of MR jet.
CRT with or without an ICD in advanced chronic heart failure - COMPANION [e[23]]	NYHA 3-4, on OMT, QRS ≥120ms; **LVEF ≤35%**, Sinus rhythm, Prior HF hospitalization in preceding 12 months Primary composite endpoint was time to all-cause mortality or hospitalization.	1520 patients Randomized 1:2:2 to OMT : CRTP : CRTD 70% in OMT group had LBBB (71% overall) 45% DCM	CRTP/D reduced rate of primary endpoint. CRTP/D both reduce risk of ACM compared to OMT. CRT has benefits in both DCM and ICM subgroups with respect to ACM / hospitalization.
CRT for mild-moderate heart failure (RAFT trial) [e[24]]	NYHA 2-3, **LVEF ≤30%**; QRS ≥120ms or paced QRS >200ms;	1798 patients Randomized ICD vs CRTD. Mean FU 40 months.	CRTD compared to ICD alone reduced rates of composite of death or HF hospitalization.