# CRT Survey II: An ESC Survey of Cardiac Resynchronization Therapy in 11088 patients – *Who is doing What to Whom and How*?

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The work was supported by the European Heart Rhythm Association; the Heart Failure Association; Biotronik; Boston Scientific; Medtronic; Sorin; St. Jude; Abbott; Bayer, Bristol-Myers Squibb and Servier.

Word count: 5569

**Abstract**

Background

Cardiac resynchronisation therapy (CRT) reduces morbidity and mortality in appropriately selected patients with heart failure and is strongly recommended for such patients by guidelines. An ESC CRT Survey conducted in 2008-09 showed considerable variation in guideline adherence and large individual, national and regional differences in patient selection, implantation practice and follow-up. Accordingly, two ESC associations, EHRA and the HFA designed a second prospective survey to describe contemporary clinical practice regarding CRT.

Methods and Results

A survey of the clinical practice of CRT-P and CRT-D implantation was conducted from October 2015 to December 2016 in 42 ESC member countries. Implanting centres provided information about their hospital and CRT service and were asked to complete a web-based case report form collecting information on patients' characteristics, investigations, implantation procedures and complications during the index hospitalisation.

The 11,088 patients enrolled represented 11% of the total number of expected implantations in participating countries during the survey period; 32% of patients were aged ≥75 years, 22% of procedures were upgrades from a permanent pacemaker or implantable cardiac defibrillator and 30% were CRT-P rather than CRT-D. Most patients (88%) had a QRS duration ≥130ms, 73% had LBBB and 26% were in atrial fibrillation at the time of implantation. Large geographical variations in clinical practice were observed.

Conclusion

CRT Survey II provides a valuable source of information on contemporary clinical practice with respect to CRT implantation in a large sample of ESC member states. The Survey permits assessment of guideline adherence and demonstrates variations in patient selection, management, implantation procedure and follow-up strategy.

## Introduction

Randomised controlled trials (RCTs) and meta-analyses have demonstrated that Cardiac Resynchronisation Therapy (CRT) reduces morbidity and mortality in appropriately selected patients with symptomatic heart failure (HF), reduced left ventricular ejection fraction (LVEF) and QRS prolongation on the electrocardiogram. [1-7] Accordingly, the benefits of CRT for such patients were accorded high levels of evidence and strong recommendations in European Society of Cardiology (ESC) and other international guidelines. [8-12]

The first ESC CRT Survey, performed in 2008-09 in 13 ESC countries, demonstrated that implanters often extrapolated the benefits of CRT to a broader population including patient groups that were not well represented in RCTs: such as patients aged >75 years or with a QRS duration <120 ms, atrial fibrillation (AF) or requiring an upgrade from an existing permanent pacemaker (PPM) or implantable cardiac defibrillator (ICD). The first CRT Survey also showed considerable regional and national differences in implantation practices. [13] Since this Survey was published, several important modifications of ESC Guideline recommendations concerning CRT indications have been made by both the Heart Failure Association (HFA) and European Heart Rhythm Association (EHRA).[8, 9, 12] Therefore, these two ESC Associations decided to collaborate and undertake a pan-European Survey designed to describe current clinical practice regarding implantation of CRT devices in a larger sample of patients and greater number of ESC member countries. CRT Survey II was not designed to compare results with the first Survey. There was limited overlap between the cohorts of the two Surveys and substantial differences in the data collected precluding valid comparison. Lessons learned from conducting the first

Survey were used to improve both the design and performance of CRT Survey II, which involved many more countries. CRT Survey II provides insights into contemporary clinical practice that is useful for patients, clinicians, administrators, the pharmaceutical and device industry as well as for parties who fund healthcare. Further analyses confined to the subset of countries participating in both surveys are planned.

## Methods

### Survey Infrastructure

The Survey was designed as a joint initiative between EHRA and the HFA. These two ESC Associations co-coordinated the Survey with sponsorship from all five companies that manufacture CRT devices as well as from several pharmaceutical and diagnostic companies (see acknowledgements). The design and rationale of CRT Survey II, along with the detailed contents of the electronic case report form (eCRF) have been published previously. [14]

A Scientific Committee (SC) was established, composed of equal number of members from each Association, together with non-voting representatives from each of the five CRT device companies. The SC regularly monitored the progress of the Survey and agreed on logistical adjustments during the period of data collection.

### Recruitment

The 47 ESC member states detailed in the 2014 EHRA White Book, which provided information on the number of sites implanting CRT and volume of activity in these

countries, were invited to participate.[15] Each participating ESC member country was represented by a National Coordinator (NC) who was nominated by the President of their National Cardiology Society. The NCs were responsible for obtaining national Institutional Review Board (IRB) approval if required, recruiting centres in their country and distributing information from the Scientific Committee (SC) to their implanters. Of the 47 invited ESC member countries 42 agreed to participate. The NCs were requested to contact CRT implanters in their countries and invite them to participate in the Survey. Sites were then asked to enter consecutive patients implanted with a CRT during the inclusion period. 288 individual centres participated in CRT Survey II.

Data collection, management and analyses

For the first ESC CRT Survey, the web-based eCRF used for data collection was developed by Institut für Herzinfarktforschung Ludwigshafen (IHF). [16] They also conducted data-management and statistical analyses. Therefore, the Associations decided that IHF should support similar functions for CRT Survey II. Together with the SC, the IHF revised the eCRF, developed the statistical analysis plan and was responsible for data-monitoring and verification. No imputation for missing data was done. All percentages are relative to the total number of patients with available information.

Each participating country had their data-points collected in the eCRF benchmarked against the total cohort. The day-to-day operational running of the Survey was conducted by Tessa Baak at Stavanger University Hospital, University of Bergen, Norway.

Survey population

Any patient in the 42 participating countries was eligible for inclusion if he/she was implanted with either a CRT with pacemaker function (CRT-P) or a CRT with an incorporated defibrillator (CRT-D). This included both successful and un-successful implantations as well as both de-novo CRT devices and upgrades from a PPM or ICD. Generator replacements or revisions of existing CRT devices were excluded as the Survey was designed to capture only new CRT implantations.

The One-time Site Questionnaire

Each implanting centre was requested to complete a one-time site questionnaire, which provided information on hospital type, size, population served, operator speciality, infrastructure, facilities and implantation routines for their CRT device programme. The data collected also provided useful information related to health-care resource utilisation. [14]

The electronic case report form (eCRF)

Implanting centres were asked to complete a web-based eCRF of consecutive patients scheduled to receive a CRT device. The eCRF collected information on patients' characteristics, investigations, indications for CRT, implant procedures and short-term outcomes including adverse events and complications during the index hospitalization [14]. Information on longer-term outcome was not collected. The eCRF was reviewed by ESC data-protection consultants to ensure patient anonymity. This, together with the fact that the Survey did not include follow-up data after discharge, obviated the necessity for formal IRB approval in most countries. Most centres were

simply required to notify their local or national ethical committee of their participation in the Survey.

Timelines

The first patient was included on October 1, 2015. The Survey was initially planned to run for 9 months. However, the SC decided to extend the enrolment by 6 months to December 31, 2016 in order to increase sample size and improve representativeness and therefore the ability to compare differences in practice amongst participating countries.

## Results

The CRT Survey II recruited 11,088 patients from 42 ESC countries. The number of patients included per country is shown in Table 1. Using data from the EHRA White Book 2015 on national implantation rates we estimated representativeness, [17] that is, the number of patients enrolled compared with expected total implants in that country. This metric was updated continuously and permitted us to estimate how representative of the predicted national implantation rates was the data collected in the Survey.

Overall, the Survey collected data on 11% of expected implantations during the enrolment period of the Survey. Of the 42 countries, 34 (81%) had >10% of the expected total number of implants for that country.

Table 2-6 report key findings from the total cohort and the number of patients contributing to each data-point.

Hospital demographics (Table 2)

University hospitals accounted for 59% of participating centres. The median (Interquartile range, IQR) number of CRT implants per hospital per year was 52 (30-96) and 76% of centres were participating in a national device registry. Device remote monitoring was employed by 59% of centres and 99% of centres had either partial or total reimbursement from public health providers.

Patient Characteristics (Table 3)

The median (IQR) age at implantation was 70 (62-76), 32% of patients were aged ≥75 years and 24% were women. Half of the patients had ischaemic heart disease, 41% had a prior history of AF of which 42% of these were permanent AF, 31% had diabetes mellitus and 47% had a HF hospitalization during the previous year.

Pre-implantation clinical evaluation (Table 4)

Most patients were in New York Heart Association (NYHA) functional class III or IV (60%) and the natriuretic peptide levels were generally substantially elevated. The ECG at the time of implantation showed AF in 26%, a QRS duration of <130ms in 13% and ≥150ms in 69% of patients and 73% had LBBB. On imaging, 28% of patients had an LVEF >35%, the median (IQR) LV end-diastolic diameter was 63 (58-69) mm and 34% had either moderate or severe mitral regurgitation. The clinical indication for CRT implantation was HF with a wide QRS in 60% of cases, HF or LV dysfunction and indication for an ICD in 48%. In 10% of patients the sole clinical indication for CRT was HF and a PPM indication with expected RV pacing dependence.

CRT Implantation procedure (Table 5)

Hospital admission was elective for 77% of implants, 77% of which were performed by electrophysiologists; 97% of procedures were successful, 70% of devices implanted were CRT-D and only 25% were referrals from other centres. The median duration of the procedure (IQR) was 90 (65-120) minutes. The RV lead was implanted first in 84% of cases and the LV lead was multipolar in 57%. The LV position was evaluated by biplane X-ray projection in 88% of patients. The left anterior oblique site was lateral in 84% and the right anterior oblique site was middle in 71%. The peri-procedural complication rate was 6%. The most common complications were coronary sinus dissection, bleeding and pneumothorax.

Post CRT Implantation data (Table 6).

The median (IQR) hospital stay was 3 (2-7) days. In 5% of patients an adverse event was reported and 0.4% died during the index hospitalization. Follow up was planned at the implanting centre in 86% of patients. AV programming was performed prior to discharge in 58% and VV programming in 56% of patients. Device-based software was used to optimize programming in 36%. Heart failure medications at discharge included loop diuretics (81%), β -blockers (89%), angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) (86%) and mineralocorticoid receptor antagonists (MRAs) (63%). Overall, 47% of patients were anticoagulated, mostly (70%) with warfarin; 10% of anticoagulated patients had no history of AF.

Benchmarking the top 10 recruiting countries (Figure 1; Panels A-G)

Data from the 10 countries that enrolled the most patients were compared. There were substantial differences amongst countries in the mean age of patients implanted (Panel A). The symptom severity varied substantially amongst countries (Panel B). The proportion of patients with AF was about 26% with a range of 16 to 29%. In all countries, most patients had LBBB but this ranged from as low as 61 to 82% (Panel C). The percentage of patients with a QRS duration <130 ms ranged from 7 to 19% but most patients had a QRS duration >150 ms (panel D). The percentage of patients upgraded from another device was between 21 to 39% (Panel E) and those receiving a CRT-P ranged from 2 to 37% (Panel F). The median duration of hospitalization varied markedly (Panel G), with a median of 3 days.

## Discussion

This second, larger survey of CRT implantations in ESC member countries provides a valuable source of clinical information describing 'who is doing what to whom and how', permits benchmarking across Europe and provides essential feedback on guideline adherence, which supports the development of future guidelines.

The '*Who*' are implanters, and as expected, primarily electrophysiologists, although a considerable number of implanters are not (23%). The '*What*' are primarily CRT-D devices (70%) but in many countries up to 40% of implants are CRT-P devices. The '*Whom*' (patients selected for CRT implantation) are predominantly men, <75 years, with an LVEF <35%, in sinus rhythm, with LBBB and a QRS duration ≥150ms. The '*How*' reveals that most implantations are elective with a low peri-procedural mortality

(<1%). Referrals from non-implanting centres accounted for only 25%, indicating that patients outside university or teaching hospital settings have limited access to CRT. The Swedish HF Registry, which included 12,807 patients, demonstrated that underutilization was associated with demographic, organizational and socio-economic characteristics as well as clinical information. For example, the likelihood of being considered for CRT was much higher if the patients were managed by cardiologists rather than other specialists or primary care physicians.[18]

An excellent overview of the diverse issues that serve to explain why only about one-third of CRT candidates are actually implanted with a device has recently been published. [19] CRT Survey II also confirms that clinicians continue to extrapolate data from RCTs to patients who are not well represented in the evidence base. Clinical practice may be guided by clinical trials but differences in practice exist because clinicians have accumulated experience and try to offer the best treatment to individual patients, many of whom do not fulfil the selection criteria for the RCTs. Many devices were implanted in patients, with AF or relatively narrow QRS complexes, or requiring a device upgrade. In these patient groups, guidelines either contra-indicate CRT or make only weak recommendations. Compared to patients enrolled in RCTs, patients in this Survey were generally older, had more comorbidities, were less likely to have ischaemic heart disease, had higher LVEF, narrower QRS complexes and more AF but a similar proportion were women. [20]

Compared to men, the low number of women receiving CRT is of concern. Women with HF with reduced ejection fraction (HFrEF) are more likely to have LBBB and may benefit from CRT at a shorter QRS duration than men. [21, 22] However, women with heart failure are older and less likely to have a reduced EF.[23] Accordingly, the low number of women receiving CRT may reflect the relatively lower number of women

aged <75 years with HFrEF rather than a lower proportion of such women who are eligible for CRT.

CRT implants were upgrades from a previous PPM or ICD device in 28% of procedures. The landmark trials of CRT, with the exception of RAFT, excluded patients with a prior device. In RAFT an upgrade from an ICD or PPM was not associated with benefit. [7] Accordingly, the 2012 HFA Guidelines do not provide guidance on upgrades. Although the ESC EHRA 2013 Guidelines provided a Class I recommendation level of evidence B for device upgrade for patients with persistent symptoms compatible with heart failure [9] the 2016 HFA Guidelines offered only a Class IIb recommendation. [8] Although a pacing generally prolongs QRS duration, its clinical significance with respect to CRT may differ. The importance of atrio-ventricular resynchronization may be as or more important than bi-ventricular resynchronization and the benefit of upgrading devices to CRT is not well established.

The rhythm at implantation was AF for 26% patients in this survey. The EHRA 2013 and HFA 2012 and 2016 guidelines provide either a IIa or IIb recommendation for patients with AF but emphasise the importance of pharmacological rate control or AV nodal ablation in order to adequate ensure bi-ventricular capture. [8, 9, 12] No substantial trial has compared CRT to a pharmacological control group for patients with AF. A subgroup of patients in the RAFT study had AF and did not appear to benefit, which was ascribed to inadequate ventricular capture. [7] Similarly, a recent report from COMPANION also suggested that patients with a prior history of AF did not benefit from CRT, although incident AF did not appear to reduce benefit in CARE-HF [4, 24]. At least two trials have compared CRT to RV pacing after AV node ablation. These suggest that CRT is superior. [25, 26] However, whether this reflects a benefit

from CRT or simply avoiding the harm of RV pacing is unclear. For this reason, some experts think that current guidelines provide an unduly strong recommendation for CRT in patients with AF.

This Survey shows that 8% of implants were in patients with a QRS <120 ms and that a further 5% had a QRS duration 120-129ms. The HFA 2012 Guidelines recommended CRT implantation only when QRS duration was >120 ms in the presence of more severe symptoms and LBBB, >130ms when symptoms were mild and LBBB was present or when QRS duration was >150ms in the absence of LBBB. [12] In May 2016 the most recent version of the HFA Guidelines, based on the results of ECHO-CRT and an individual-patient data (IPD) meta-analysis, suggested that CRT is contra- indicated when QRS duration is <130ms. [8, 27-29] This Survey ran from October 2015 to December 2016. Future analyses will determine whether practice evolved over the course of the survey. [9, 12] Of note, the median QRS duration was narrower (144 ms compared with 160 ms) for patients implanted only for the clinical indication 'PM indicated and expected RV pacing dependence' compared to the overall cohort. 10% of the Survey population were implanted with only this clinical indication and 22% of this group had a QRS duration <120 ms. However, most patients in this Survey had a QRS duration ≥150 ms. IPD meta-analyses of RCTs have convincingly shown that longer QRS durations predict greater long-term benefit from CRT. [28, 30]

Patients in this Survey were generally treated with loop diuretics (81%), ACE inhibitors / ARBs (86%), β-blockers (89%), and MRAs (63%) at discharge from hospital. Guidelines recommend implantation of CRT only after patients have been optimally medically managed. Although the proportion of patients in the Survey discharged on disease-modifying medications is less than ideal and less than

observed in some registries, it is still similar or greater than observed in most of the landmark clinical trials that proved the efficacy of CRT, many other registries or in clinical practice.[18, 31]

The process of developing evidence-based guidelines includes both adequate evaluation by randomised clinical trials as well as feedback from surveys and registries. Survey and registries demonstrate the degree to which guidelines are adopted in practice. Therefore, the extensive observational data that we have collected highlights both which guideline recommendation are or are not being adhered to as well as how physicians extrapolate existing data to clinical challenges they encounter in practice where evidence is lacking. These gaps in evidence are intentionally included in all ESC guidelines in order to identify potentially fruitful area for future research.

The one-time site questionnaire included information such as total number of beds per hospital, type of hospital, number of CRT devices implanted annually and the number and speciality of implanters, which provides valuable information related to health care resource demands and capacity. A dedicated health care resource utilization paper will be published.

The data selected for benchmarking is directly related to patient selection, clinical practice and health care resource utilization in the top 10 recruiting countries. Benchmarking of these countries in the Survey revealed remarkable similarities with regards to patient selection. However, there were also many highly significant differences between countries (Figure 1) especially the populations aged ≥ 75 years with QRS <130 ms, NYHA Class III or IV as well as choice of device (CRT-P vs CRT-D).

Particularly striking was the difference in index hospitalization duration between the top 10 countries. Hospitalization for implantation of a CRT can facilitate initiation and up-titration of optimal medical therapy, which can prolong hospital stay. Differences in the length of hospital stay depend both on the implanting centre and the collaboration with the outpatient HF services. Some of the observed differences in these countries' CRT implantation practice will be related to the country's economic strength, the proportion of their budget allocated to healthcare and the demographics of the population. The initial cost of CRT is substantial due to the device itself, the implantation procedure, hospitalisation and follow-up. However, the symptomatic improvement following CRT and the reduction in HF hospitalization makes it an effective use of resources. Countries with limited financial resources may select patients most likely to respond and also may prefer CRT-P to CRT-D due to the reduced cost. In Europe, physicians may be more willing to extrapolate beyond the existing evidence and guidelines for CRT because the risk of medical litigation is relatively low. Most procedures are funded partly or entirely by public funding and there is limited formal audit of adherence to guidelines.

## Limitations

The strength and ability of a survey to address questions are related to the strength of its methodology, its representativeness and size. Although the number of patients enrolled in this Survey was large, there were substantial differences amongst countries. Overall, we estimate that about 11% of patients implanted with CRT in participating countries were enrolled in the Survey. We cannot assess the degree of selection bias in the choice of enrolled patients. Sites may have been less likely to

report unsuccessful implants or cases with a poor outcome, accounting for low complication and mortality rates. The number of implanting sites ranged from 1 to 37. In countries with few participating centres, these centres' practice will have a great impact on the national results.

The eCRF was designed to be as user-friendly as possible in order to maximise the number of patients enrolled. Unavailable patient data could be omitted; the analyses were based on the available data, which explains the variation in the sample size for each data point. Furthermore, the interpretation of questions was up to the discretion of the investigator. Although there was no formal independent monitoring of the data collection, the IHF conducted 'front-end' data check and post database lock quality control analyses designed to prevent incorrect data being analysed. The most recent ESC HF Guidelines were released during the enrolment period of the Survey.[8] It requires time before new guidelines are adopted into evolving clinical practice. It is difficult to quantify the effect that this had on the selection and enrolment of patients subsequent to the release of the most recent ESC Guidelines.

## Conclusion

CRT Survey II provides a valuable source of information on contemporary clinical practice with respect to CRT implantation in a large sample of ESC member states. The Survey demonstrates important similarities as well as substantial differences in patient selection, implantation procedure and follow-up. The data collected are sufficient to permit meaningful benchmarking between the highest recruiting countries and for assessing guideline adherence and healthcare resource utilisation. This

should assist in educational initiatives and identifying appropriate directions for future research.

Acknowledgments

A special thanks to Tessa Baak, Operation for her dedication and excellent organisational skills. Thanks to our sponsors. The work was supported by the European Heart Rhythm Association; the Heart Failure Association; Biotronik; Boston Scientific; Medtronic; Sorin; St. Jude; Abbott; Bayer, Bristol-Myers Squibb and Servier. Thanks to the industry representatives Joel Courville, Thomas Herrmann, Dave Hollants, Marijke Laarakker , Art Pilmeyer, Nico Uwents and Alphons Vincent. Thanks to the National Coordinators and the implanters for providing us with such a wealth of data.

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## Legend Figure 1

Asterisks demonstrate the level of statistical significance of the bottom red category for each country as compared to the total cohort. One asterisk denotes a p-value of <0.01 and two asterisks a p-value <0.001.

Table 1 CRT Survey II Total Cohort

| Country | National coordinator | Patients entered |
|---|---|---|
| Algeria | Seddik Ait-Messaoudene | 66 |
| Armenia | Svetlana Grigoryan | 2 |
| Austria | Marianne Gwechenberger | 407 |
| Belgium | JB le Polain de Waroux | 262 |
| Bulgaria | Svetoslav Iovev | 264 |
| Croatia | Sandro Brusich | 115 |
| Czech Republic | Alan Bulava | 931 |
| Denmark | Helen Høgh Petersen | 254 |
| Egypt | Mostafa Nawar | 22 |
| Estonia | Jüri Voitk | 58 |
| Finland | Sami Pakarinen | 351 |
| France | Christophe Leclercq | 754 |
| Georgia | Giorgi Papiashvili | 24 |
| Germany | Carsten W. Israel | 675 |
| Greece | Antonis Sideris | 137 |
| Hungary | Gabor Duray | 467 |
| Iceland | Sigfús Gizurarson | 19 |
| Ireland | Ricky Sheahan | 85 |
| Israel | Michael Geist | 39 |
| Italy | Gianlucca Botto | 526 |
| Kazakhstan | Roin Rekvava | 34 |
| Latvia | Oskars Kalejs | 79 |
| Lebanon | Marwan M. Refaat | 30 |
| Lithuania | Germanas Marinskis | 173 |
| Luxembourg | Laurent Groben | 36 |
| Macedonia FYR | Nikola Gjorgov | 70 |
| Malta | Mark Sammut | 26 |
| Montenegro | Ljilja Music | 6 |
| Morocco | Salima Abdelali | 12 |
| Netherlands | Alexander Maass | 202 |
| Norway | Torkel Steen | 370 |
| Poland | Maciej Sterlinski | 1241 |
| Portugal | Francisco Morgado | 58 |
| Romania | Dan DOBREANU | 214 |
| Russian Federation | Amiran Revishvili | 71 |
| Slovakia | Peter Margitfalvi | 472 |
| Slovenia | Igor Zupan | 119 |
| Spain | Oscar Cano Pérez | 847 |
| Sweden | Elena Sciaraffia | 255 |
| Switzerland | Christian Sticherling | 320 |
| Turkey | Umutay Nedim Sarigül | 424 |
| United Kingdom | Chris Plummer | 571 |
| **Total** | | **11088** |

Table 2 Hospital Demographics

| **Hospital Demographics** | **n =288** |
|---|---|
| **Inhabitants of area** median (in 100.000) (IQR) | 5 (3-10) |
| **Total number of hospital beds** median (IQR) | 600 (357-964) |
| **Number of cardiology beds** median (IQR) | 57 (34-80) |
| **Type of hospital** | |
| University hospital | 59 % (162/274) |
| Teaching hospital (non-university) | 23 % (64/274) |
| Community hospital | 10 % (27/274) |
| Private hospital | 8 % (21/274) |
| **CRT implantations per year** median (IQR) | 52 (30-96) |
| **Pacemaker implantations per year** median (IQR) | 250 (175-400) |
| **ICD implantations per year** median (IQR) | 80 (40-132) |
| **Cardiac surgery on site** | 69 % (190/274) |
| **Angiography/PCI on site** | 96 % (262/273) |
| **Dedicated electrophysiological labs** median(IQR) | 1 (1-2) |
| **Number of CRT implanters** median (IQR) | |
| Electrophysiologists | 2 (1-4) |
| Interventional cardiologists | 0 (0-4) |
| Heart failure physicians | 0 (1-2) |
| **Follow-Up** | |
| Implanting centre | 93 % (254/272) |
| Heart failure clinic | 68 % (186/273) |
| Dedicated CRT clinic | 59 % (161/273) |
| Remote device monitoring service | 70 % (191/272) |

| | |
|---|---|
| **Centre uses device monitoring by telemetry** | 59 % (169/288) |
| **Dedicated lead extraction/management program** | 45 % (123/272) |
| **Participation in a national device registry** | 76 % (207/273) |
| **Use electronic medical health records** | 81 % (221/273) |
| **Source of reimbursement for CRT** | |
| Public health provider | 99 % (270/274) |
| Private insurance | 12 % (32/274) |
| Private payer | 7 % (20/274) |

IQR – interquartile range, CRT – Cardiac Resynchronization therapy, ICD- Implantable cardiac defibrillator, PCI –percutaneous coronary intervention. In parenthesis, we indicated the number of centres in each category compared to the total cohort for each data-point.

Table 3 Patient Demographics

| **Demographic** | **n=11088** |
|---|---|
| **Age** median (years) (IQR) | 70 (62-76) |
| **Age >=75** | 32 % (3536/11039) |
| **Female** | 24 % (2686/11052) |
| **Primary HF aetiology** | |
| Ischaemic | 45 % (4875/10953) |
| Non-ischaemic | 55 % (6078/10953) |
| **Past history and major comorbidity** | |
| Previous myocardial infarction | 36 % (3957/10926) |
| Prior revascularization (PCI/CABG) | 39 % (4245/10924) |
| Hypertension | 64 % (6962/10900) |
| Atrial fibrillation | 41 % (4459/10920) |
| Valvular heart disease | 27 % (2968/10920) |
| Obstructive lung disease | 12 % (1315/10922) |
| Diabetes | 31 % (3428/10921) |
| Anaemia | 15 % (1640/10916) |
| Chronic kidney disease (eGFR <60) | 31 % (3395/10907) |
| **Previous device (PPM or ICD)** | 22 %(2434/10992) |
| **HF hospitalization during past year** | 47 % (5078/10917) |
| **Currently enrolled in a clinical trial** | 8 % (918/11028) |

IQR – interquartile range, PCI –percutaneous coronary intervention, CABG- coronary artery bypass grafting, eGFR –estimated glomerular filtration rate, PPM –permanent pacemaker, ICD –implantable

cardiac defibrillator, HF- heart failure. In parenthesis, we indicated the number of patients in each category compared to the total cohort for each data-point.

Table 4 Pre-implant clinical evaluation

| **Pre-implant clinical evaluation** | **n=11088** |
|---|---|
| **NYHA class** | |
| I | 3 % (370/10848) |
| II | 38 % (4083/10848) |
| III | 55 % (5909/10848) |
| IV | 5 % (486/10848) |
| **BMI** median (kg/m²) (IQR) | 27 (25-31) |
| **Systolic blood pressure** median (mmHg) (IQR) | 122 (110-137) |
| **Diastolic blood pressure** median (mmHg) (IQR) | 72 (66-80) |
| **Laboratory measurement** median (most recent) (IQR) | |
| BNP (ng/L) | 422 (150-1115) |
| NT-proBNP (ng/) | 2400 (1049-5517) |
| Serum Creatinine (µmol/l) | 100 (83-129) |
| Haemoglobin (g/dl) | 13 (12-15) |
| **Pre-implant ECG** | |
| Heart rate median bpm (IQR) | 70 (60-80) |
| **Atrial rhythm** | |
| Sinus | 69 % (7496/10836) |
| Atrial fibrillation | 26 % (2778/10836) |
| Atrial paced | 3 % (303/10836) |
| Other | 2 % (259/10836) |
| **PR interval** median (IQR) (ms) | 180 (160-210) |
| **AV block II/III** | 19 % (2026/10700) |

| | |
|---|---|
| **Pacemaker dependant** | 14 % (1511/10752) |
| **Intrinsic QRS morphology** | |
| LBBB | 73 % (7861 /10800) |
| Non LBBB | 27 % (2939 /10800) |
| **Intrinsic QRS duration** | |
| Median (IQR) | 160 (140 -174) |
| < 120 ms | 8 % (711/9535) |
| 120 -129 ms | 5 % (505/9535) |
| 130 -149 ms | 19 % (1779/9535) |
| 150 -179 ms | 47 % (4486/9535) |
| >180 ms | 22 % (2054/9535) |
| **Clinical indication for CRT** | |
| HF with wide QRS | 60 % (6550/10923) |
| HF or LV dysfunction and indication for ICD | 48 % (5228/10923) |
| PM indication and expected RV pacing dependence | 23 % (2494/10923) |
| Evidence of mechanical dyssynchrony | 12 % (1260/10923) |
| Other | 5 % (487/10923) |
| **LVEF** | |
| Median (IQR) | 29 (23-34) |
| LVEF <25 | 28 % (2979/10805) |
| LVEF 25 -35% | 60 % (6426/10805) |
| LVEF >35 % | 13 % (1400/10805) |
| **LVEDD** median (IQR) (mm) | 63 (58-69) |
| **Mitral regurgitation** | |
| Mild | 46 % (4644/10000) |
| Moderate | 27 % (2646/10000) |

| | |
|---|---|
| Severe | 7 % (690/10000) |
| None | 20 % (2020/10000) |

NYHA – New Year Heart Association, BMI- body mass index, IQR- interquartile range, BNP –brain natriuretic peptide, NT pro-BNP- N-terminal pro BNP, bpm- beats per minute, LBBB –left bundle branch block, CRT – Cardiac Resynchronization Therapy, HF- heart failure, LV- left ventricle, ICD – implantable cardiac defibrillator , PM –pacemaker, RV- right ventricular, EF- ejection fraction. Note: total can = > 100% due to rounding off. In parenthesis, we indicated the number of patients in each category compared to the total cohort for each data-point.

Table 5, CRT Implantation Procedure

| **CRT Implantation Procedure** | **n= 11088** |
|---|---|
| **Elective admission** | 77 % (8422/10946) |
| **Referral from another centre** | 25 % (2770/10938) |
| **Admission to implantation time** median (IQR) (day) | 1 (1-4) |
| **Successful implantation** | 97 % (10798/11100) |
| **Non-successful implantation** | 3 % (302/11100) |
| **Number of attempts per patient** | |
| One attempt per patient | 99 % (10971/11088) |
| Two attempts per patient | 1 % (106/11088) |
| Three attempts per patient | <1% (11/11088) |
| **Type of device** | |
| CRT-P | 30 % (3256/10769) |
| CRT-D | 70 % (7513/10769) |
| **Operator** | |
| Electrophysiologist | 77 % (8302/10779) |
| HF physician | 5 % (541/10779) |
| Invasive cardiologist | 12 % (1330/10779) |
| Surgeon | 4 % (464/10779) |
| Other | 1 % (142/10779) |
| **Duration of procedure,** median (min) (IQR) | 90 (65-120) |
| **Fluoroscopy time,** median (min) (IQR) | 14 (8-22) |
| **Prophylactic antibiotics** | 99 % (10527/10672) |
| **Which lead was implanted first** | |

| | |
|---|---|
| RV | 84 % (8816/10555) |
| LV | 16 % (1733/10555) |
| **RV lead placement** | |
| Apex | 61 % (6280/10253) |
| Septum | 36 % (3733/10253) |
| RVOT | 2 % (240/10253) |
| **LV lead placement successful** | 99 % (10533/10594) |
| **LV lead type** | |
| Unipolar | 1 % (77/10601) |
| Bipolar | 42 % (4478/10601) |
| Multipolar | 57 % (6046/10601) |
| **Coronary venogram performed** | 92 % (9636/10529) |
| **Venogram performed with occlusion** | 47 % (4486/9522) |
| **Dilatation of coronary vein performed** | 2 % (251/10538) |
| **Phrenic nerve stimulation tested** | 90 % (9556/10568) |
| **LV lead position evaluation** | 97 % (9943/10302) |
| Biplane x-ray projection | 88 % (8771/9943) |
| Monoplane LAO | 11 % (1105/9943) |
| Monoplane RAO | 1 % (67/9943) |
| **LAO site** | |
| Lateral | 84 % (8665/10300) |
| Posterior | 12 % (1188/10300) |
| Anterior | 4 % (447/10300) |
| **RAO site** | |
| Middle | 71 % (7200/10119) |
| Basal | 15 % (1505/10119) |

| | |
|---|---|
| Apical | 14 % (1414/10119) |
| **LV position optimized** | 34 % (3484/10307) |
| **Peri-procedural complications** | 6 % (624/11088) |
| Death | 0.1 % (8/11088) |
| Bleeding | 1.0 % (108/11088) |
| Bleeding requiring intervention | 0.3 % (35/11088) |
| Pocket hematoma | 0.8 % (85/11088) |
| Pneumothorax | 1.0 % (112/11088) |
| Haemothorax | 0.1 % (9/11088) |
| Coronary sinus dissection | 1.9 % (214/11088) |
| Pericardial tamponade | 0.3%(28/11088) |
| Other | 1.6 % (172/11088) |

CRT – Cardiac Resynchronization Therapy, IQR – interquartile range, P-pacemaker, D-defibrillator, HF –heart failure, RV- right ventricle, LV – left ventricle, RVOT –right ventricular outflow tract, LAO – left anterior oblique, RAO –right anterior oblique. Note: total can = > 100% due to rounding off. In parenthesis, we indicated the number of patients in each category compared to the total cohort for each data-point.

Table 6 Post CRT Implantation

| **Post CRT Implantation** | **n=11088** |
|---|---|
| **Post-implant ECG** | |
| Paced QRS duration median (ms) (IQR) | 137 (120-151) |
| **Device programming** | |
| AV programming performed prior to discharge | 58 % (6132/10593) |
| VV programming performed prior to discharge | 56 % (5962/10577) |
| Device-based software optimization for AV or VV | 36 % (3821/10500) |
| **Discharge status** | |
| Alive | 99.6 % (10801/10845) |
| Dead | 0.1% (45/10845) |
| **Total length of hospital stay** median (days) (IQR) | 3 (2-7) |
| **Major adverse events after Implantation** | 5 % (528/11088) |
| Myocardial Infarction | 0.1 % (8/10816) |
| Stroke | 0.1 % (6/10816) |
| Infection | 0.6 % (60/10816) |
| Worsening heart failure | 0.7 % (78/10816) |
| Worsening renal function | 1.0% (104/10816) |
| Arrhythmias | 1.2 % (128/10816) |
| Other | 1.9 % (208/10816) |
| **Planned Follow-Up** | |
| Implanting centre | 86 % (9345/10818) |
| Other hospital | 8 % (873/10818) |
| Cardiologist in private practice | 5 % (569/10818) |

| | |
|---|---|
| Primary care physician | 1 % (92/10818) |
| CRT/ pacemaker clinic | 10 % (1124/10818) |
| Heart failure management clinic | 3 % (273/10818) |
| Other | 0 % (34/10818) |
| **Drug therapy at discharge** | |
| Loop diuretic | 81 % (8621/10635) |
| ACE inhibitor/ARB | 86 % (9163/10603) |
| MRA (aldosterone antagonist) | 63 % (6682/10573) |
| β-blocker | 89 % (9472/10648) |
| Ivabradine | 6 % (593/10543) |
| Digoxin | 10 % (1100/10544) |
| Calcium channel blocker | 9 % (946/10531) |
| Amiodarone | 17 % (1825/10547) |
| Other anti-arrhythmic agent | 2 % (181/10531) |
| **Oral anticoagulant** | 47 % (4928/10577) |
| Warfarin (Coumadin) | 33 % (3463/10577) |
| Dabigatran | 3 % (327/10577) |
| Rivaroxaban | 6 % (611/10577) |
| Apixaban | 5 % (509/10577) |
| Edoxaban | <1 % (18/10577) |
| **Anti-platelet agent** | 44 % (4846/11088) |
| Aspirin | 41 % (4357/10547) |
| Clopidogrel | 12 % (1304/10547) |
| Ticagrelor | 1 % (136/10547) |
| Prasugrel | <1 % (31/10547) |

ECG- electrocardiogram, IQR -interquartile range, AV –atrioventricular, VV-ventriculo-ventricular, CRT- Cardiac Resynchronization Therapy, ACE –angiotensin enzyme, ARB –angiotensin II receptor blocker, MRA- mineralocorticoid receptor antagonist. In parenthesis, we indicated the number of patients in each category compared to the total cohort for each data-point.

Figure 1, Panel A - Age of Patients Implanted with CRT by Countries

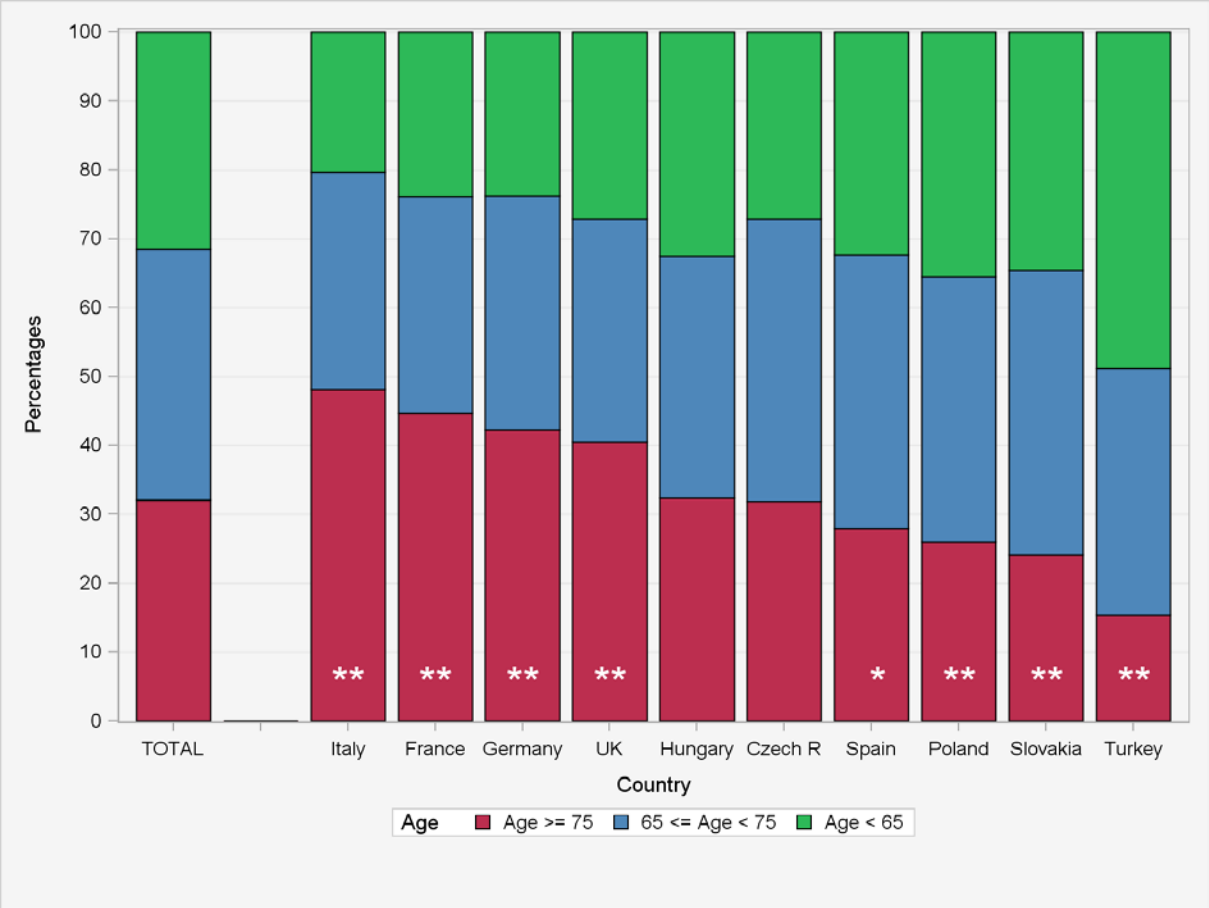


Figure 1, Panel B - NYHA Classification across Countries

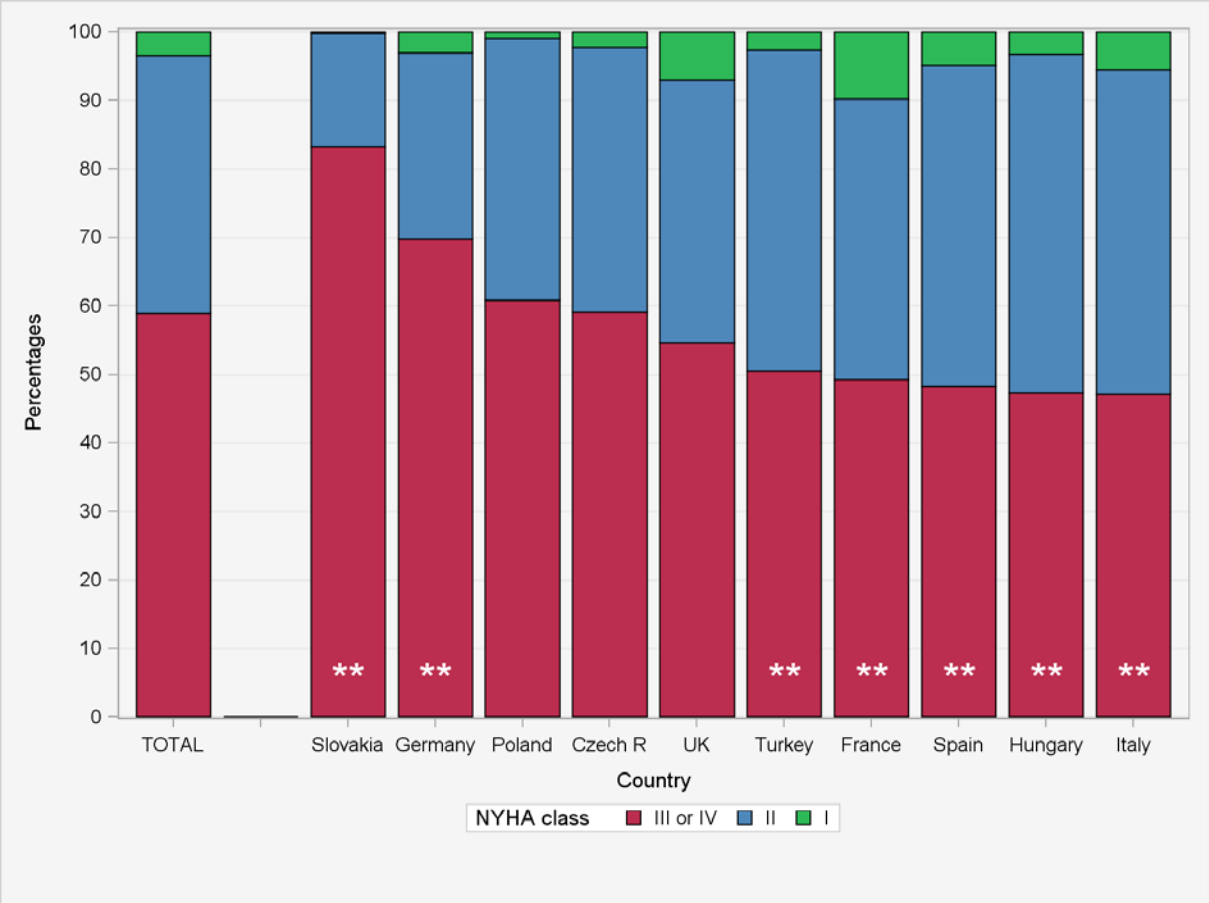


Figure 1, Panel C - QRS Morphology on Pre-Implantation ECG per Country.

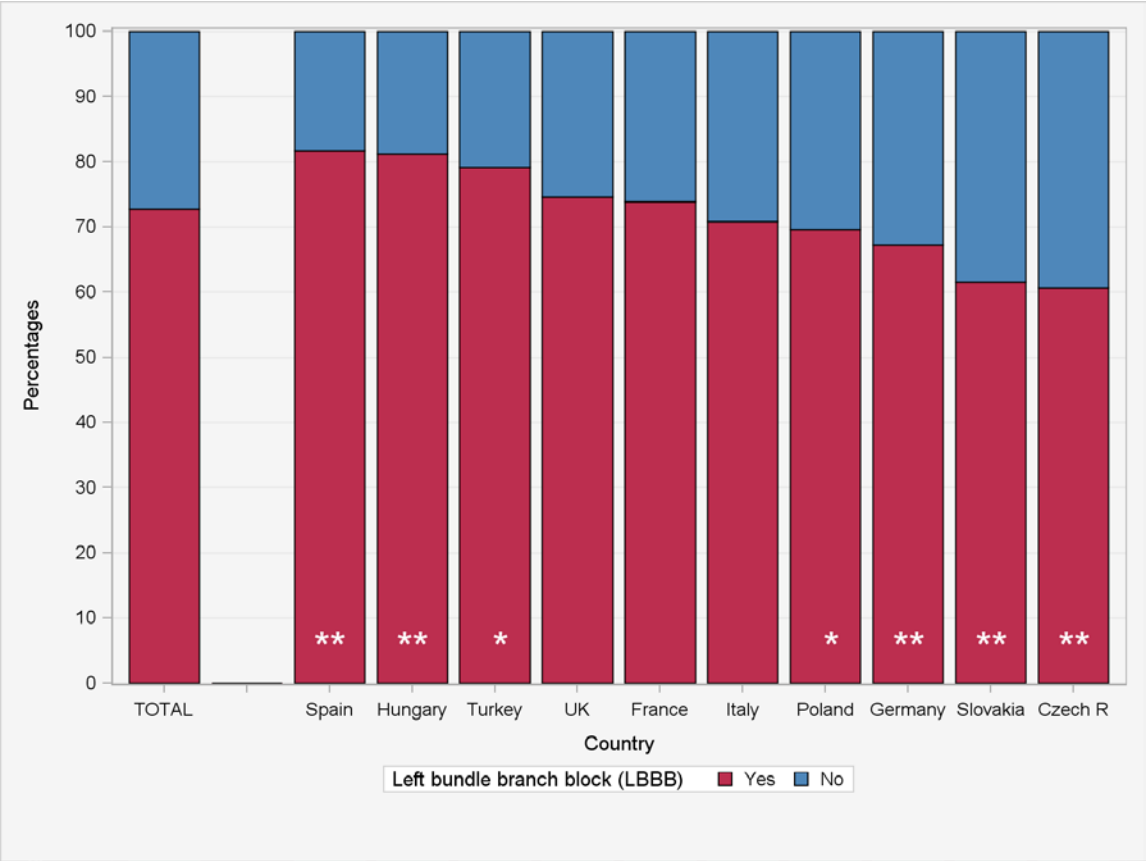


Figure 1, Panel D - QRS Duration on Pre-implantation ECG per Countries

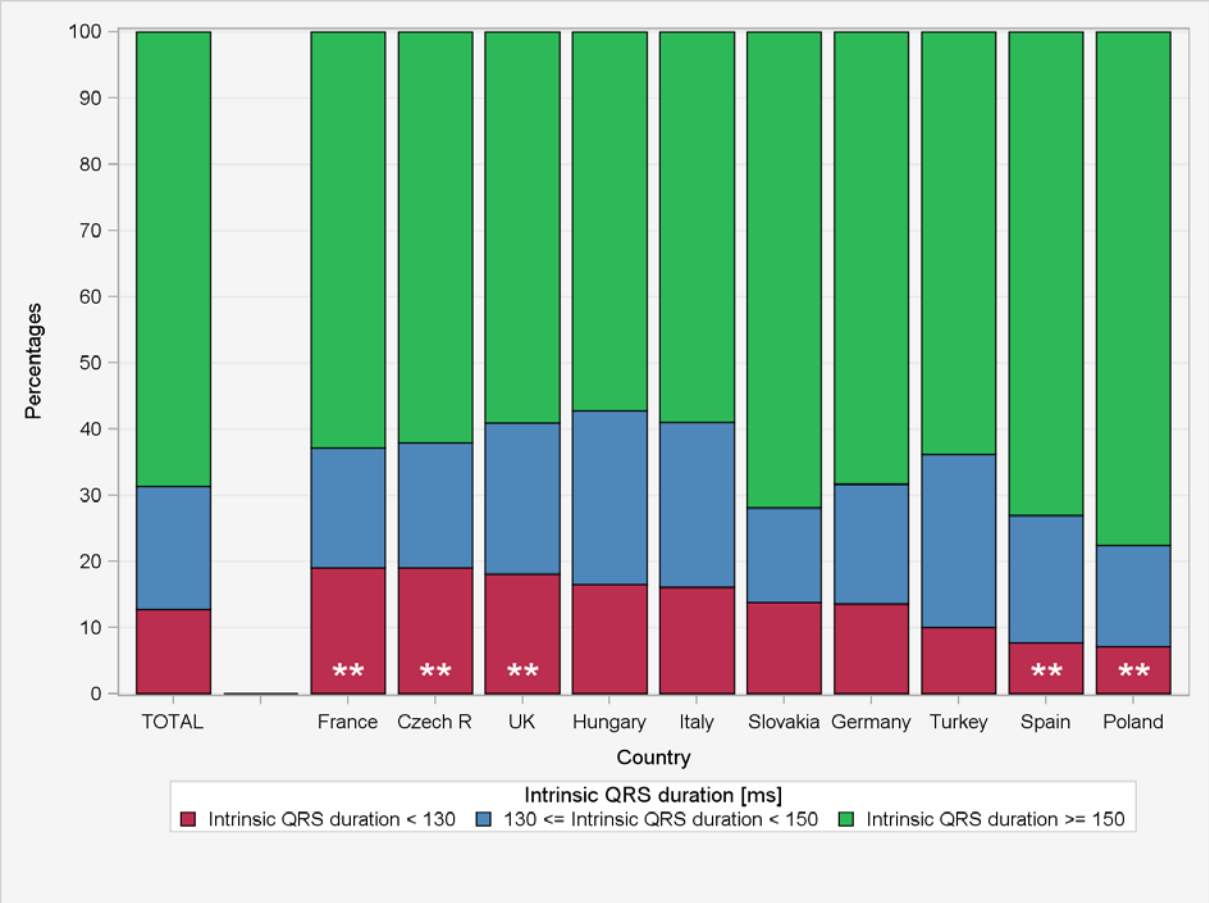


Figure 1, Panel E - Upgrades to CRT from Previous device (PPM or ICD) per Country

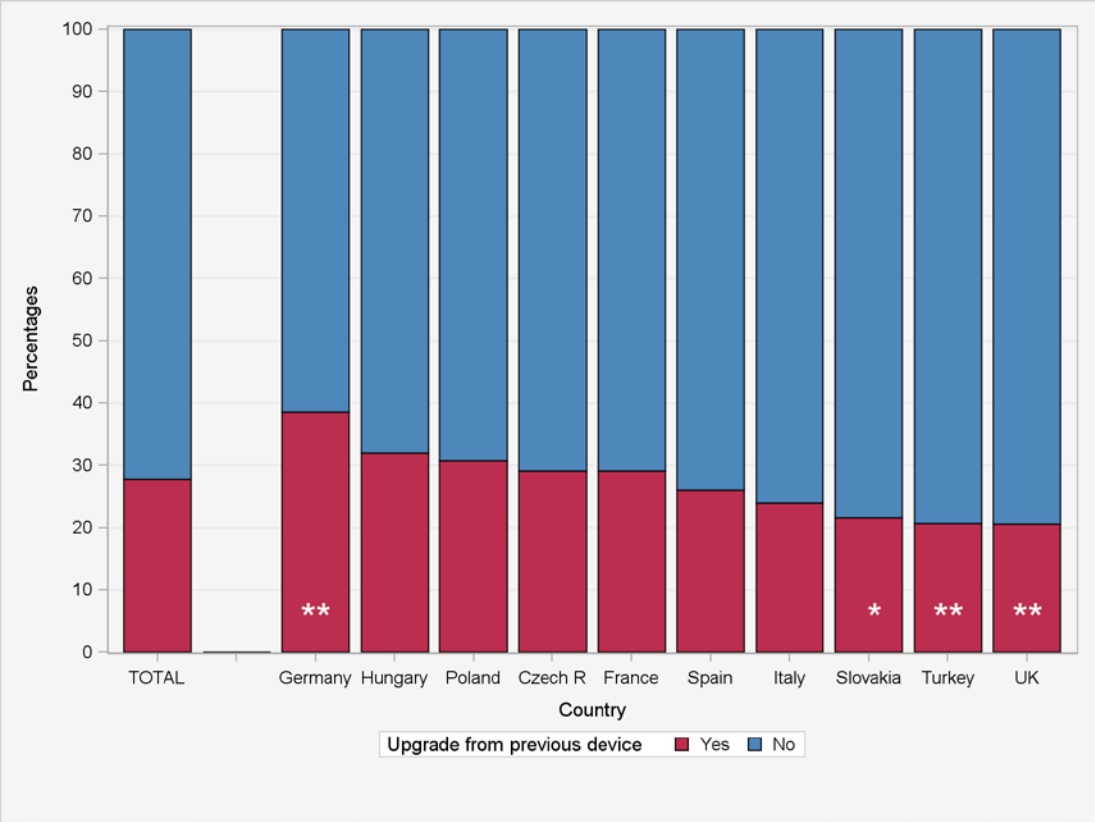


Figure 1, Panel F - Type of Device Implanted (CRT-P vs. CRT-D) per Country

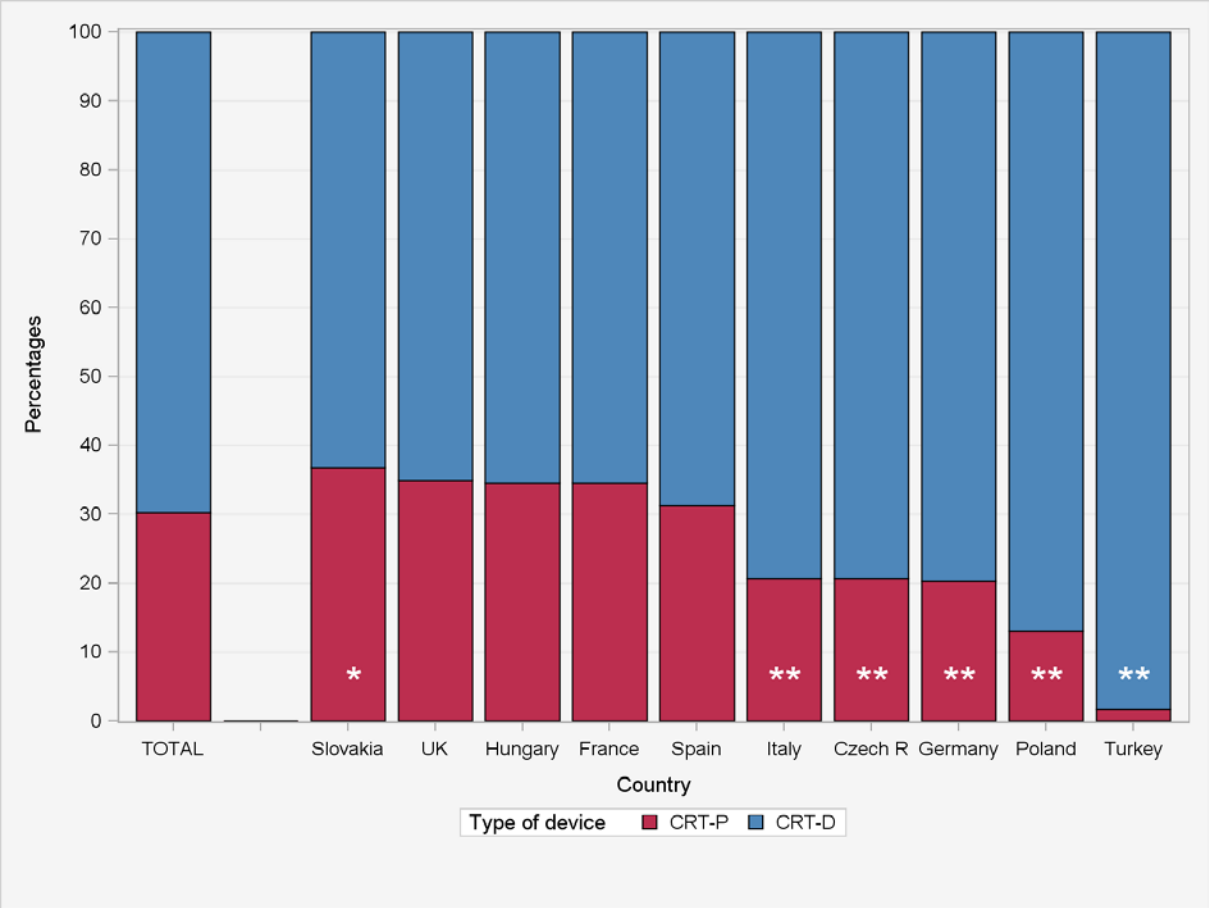
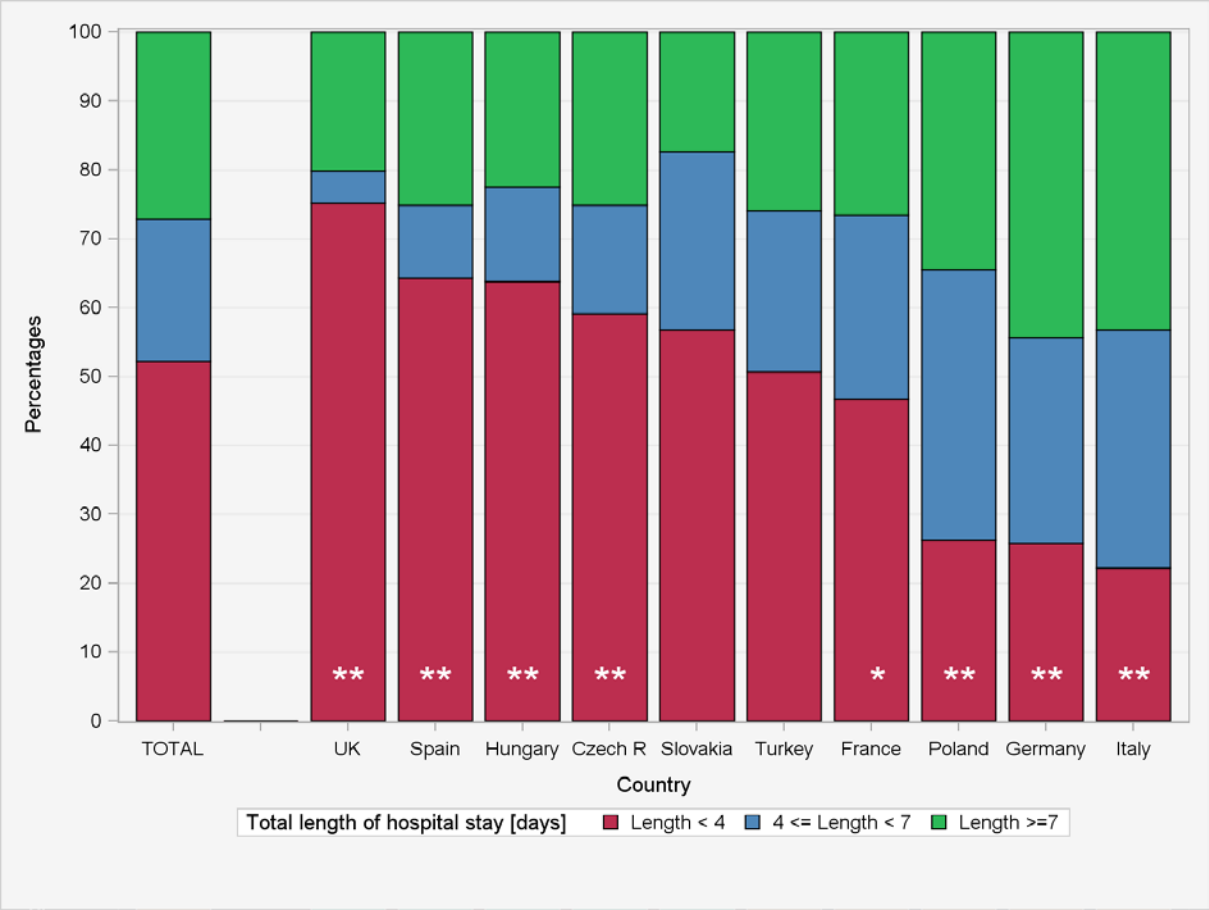


Figure 1, Panel G - Length of Hospital Stay per Country.



## Appendix 1– Implanters

**Algeria**: Seddik Ait-Messaoudene, Djouhri Messaouda, Brahim Kichou. **Armenia**: Svetlana Grigoryan, Hermine Poghosyan. **Austria**: Marianne Gwechenberger, Wolfgang Dichtl, Martin Martinek, Ulrike Neuhold, Günther Prenner, Bernhard Ströhmer, Alexander Teubl, Christian Georg Wollmann. **Belgium:** Jean-Benoît le Polain de Waroux, X. Carryn, Alexandre Delcour, Fabien Dormal, Stefan Liliana, Georges Mairesse, Wilfried Mullens, Yves Vanderkerckhove, Rik Willems. **Bulgaria:** Svetoslav Iovev, B. Borisov, Dobri Hazarbasanov, Nadia Pan, M. Predovski, V. Traykov, Velchev Vasil. **Croatia:** Sandro Brusich, Ante Anic, Ivo Bozic, Sime Manola, R. Matasic. **Czech Republic:** Alan Bulava, J. Chovancik, S. Ipula, Lukas Kryze, Milena Kubickova, Petr Neužil, Pavel Osmancik, Petr Parizek, Rostislav Polasek, Jan Vecera. **Denmark:** Helen Hoegh Pedersen, Jens Gerd, Finn Peter Heath, Christian Joens, Jens Kristensen, Jens Nielsen, Berit Thornvig Philbert, Jesper Hastrup Svendsen, Anna Margrethe Thøgersen. **Egypt:** Mostafa Nawar, Hayam Damnhoury, A. Mokhtar. **Estonia:** Jüri Voitk, Urmet Arus, Indrik Roose. **Finland:** Sami Pakarinen, Ismo Anttila, Tuomas Kerola, Juhani Koistinen, Pentti Korhonen, Annika Lonnberg, Marko Nikkinen, Tuomas Paana, Juha Rantala, Juha Rantonen, Kari Ylitalo, Tuija Vasankari. **France:** Christophe Leclercq, Serge Boveda, Paul Bru, Paul Defaye, Kamila Djouadi, Christine Durand, Jacques Horvilleur, Jacques Mansourati, Isabelle Martel, Beard Ormeau, Philippe Rumeau, Pascal Sagnol, Mathieu Steinbach, Salem Younsi. **Georgia:** Giorgi Papiashvili, Kakhaber Etsadashvili. **Germany:** Carsten Israel, Martin Borggrefe, Ole Breithardt, G. Buchwalsky, Micha Döring, Gerlinde Drexler, Nils Gosau, Andreas Götte, Spyridon Koulouris, Dejan Mijic, Michael Niehaus, K. Oebeju, S. Rolf, Christoph Stellbrink, Carsten Stoepel, Ekrem Uecer, Bernhard Zrenner. **Greece:** Emmannuel Simantirakis, M. Agelaki, Matthaios

Didagelos, Polychronis Dilaveris, Goudevenos Ioannis, Antonios Sideris, Eftihia Simeonidou, Skevos Sideris, Paraskevaidis A. Stylianos. **Hungary:** Gabor Duray, Csaba Foldesi, Bela Merkely, Attila Konyi. **Iceland:** Sigfús Gizurarson. **Ireland:** Ricky Sheahan, Niall Mahon. **Israel:** Michael Geist, Mahmoud Suleiman. **Italy:** Gianlucca Botto, Massimo Zoni Berisso, Card Campana, Bertaglia Ferro, Maurizio Gasparini, G. Mascioli, Erminio Mauro, Porcu Maurizio, Eraldo Occhetta, Renato Pietroricci, Alessandro Proclemer, M. Racheli, Antonio Rapacciuolo, Wer Raubz, C. Tomasi, Cinzia Valzania, Franc Zanon, M. Zardini. **Kazakhstan:** Roin Rekvava, Adil Baimbetov, Ulan Kabayev. **Latvia:** Oskars Kalejs. **Lebanon:** Marwan Refaat. **Lithuania:** Germanas Marinskis, Aras Puodziukynas. **Luxemburg:** Laurent Groben. **Macedonia:** Nikola Gjorgov, V. Boskov, Lidija Poposka. **Malta:** Mark Sammut. **Montenegro:** Ljilja Music. **Morocco:** Salima Abdelali. **The Netherlands:** Alexander Maass, Lucas Boersma, A. E. Borger Van der Burg, Mike Scheffer, Kevin Vernooy. **Norway:** Torkel Steen, Nigussie Bogale, Tor Edvardsen, Geir Heggelund, Finn Tore Gjestvang, Hilde Hellebust Håland, Kari Jonland, Knut Lappegård. **Poland:** Maciej Sterlinski, Szymon Budrejko, Elżbieta Dulak, Tomasz Godlewski, Bogusław M. Grzegorzewski, Bogdan Galar, Marcin Gulaj, Krystian Josiak, Krzysztof Kaczmarek, Lukasz Jan Janusz Kiewicz, Karol Krol, Mateusz Kusmierz, Lidia Michalak, Artur Oreziak, Zbigniew Orski, Jerzy Ozga, Dr. Marmak, Mariusz Nowakowski, Anna Polewczyk, Ryszard Serafin, Grzegorz Skonieczny, Marcin Szczasny, Mateusz Tajstra, Andrzej Tatarczuk , Bartek Topolinski, Sławomir Tłuczek, J. Wilczek, Dariusz Zając. **Portugal:** Francisco Morgado. **Romenia:** Dan Dobreanu, Dragos Constantin Cozma, Alexandru Deutsch, Gabriel Gușetu, Dr. Rosianu, Micu Sorin, Cristian Statescu, Radu Vatasescu. **Russian Federation:** Amiran Revishvili, Dr. Davtyan, Max Didenko, Lebedev Dmitry, Dol Dubrovin, Art Elena. **Slovenia:** Peter Margitfalvi,

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