The European CRT Survey: 1 year (9–15 months) follow-up results

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Aims
The European CRT Survey is a joint initiative of the Heart Failure Association (HFA) and the European Heart Rhythm Association (EHRA) of the European Society of Cardiology evaluating the contemporary implantation practice of cardiac resynchronization therapy (CRT) in Europe.

Methods and results
Patients who had a successful CRT implantation were enrolled from 141 centres in 13 countries between November 2008 and June 2009. Baseline demographics, clinical and implantation data were collected, with a follow-up of ≈1 year (9–15 months). The current report describes clinical outcomes including symptom severity, cardiovascular (CV) hospitalization, and survival. A total of 2438 patients were enrolled, and follow-up data were acquired from 2111 patients (87%). The population included important groups of patients poorly represented in randomized controlled trials, including very elderly patients and those with prior device implantation, atrial fibrillation, and/or QRS duration >120 ms. Investigators reported substantial improvement in New York Heart Association (NYHA) functional class at follow-up. Patient self-assessment indicated that 81% of the patients felt improved, 16% reported no change, and 4% reported deterioration. During follow-up, 207 (10%) patients died, 346 (16%) had a CV hospitalization, and 501 (24%) died or had CV hospitalization. Worse NYHA functional class, atrial fibrillation, ischaemic aetiology, and device type (CRT-P, i.e. CRT alone) were associated with poorer survival. Women had a better outcome, as did patients who had a CRT-D (with an implantable cardioverter defibrillator function) device.

Conclusions
Outcomes including death and hospitalization in this European CRT survey were consistent with results from clinical trials of CRT. At 1 year follow-up, most patients who received a CRT device considered their symptoms improved compared with their pre-implant assessment. Although prospective, this is an observational study of successful CRT implantations, and outcomes in subgroup analyses must be interpreted with appropriate conservatism.

Clinical study no: NCT 01185392

Keywords
Cardiac resynchronization therapy (CRT) • Survey • Heart failure • 1 year (9–15 months) follow-up

Introduction
Cardiac resynchronization therapy (CRT) improves symptoms and reduces morbidity and mortality.1–7 The 2007 ESC/EHRA Guidelines for Cardiac Pacing,8 the 2008 ESC Heart Failure Guidelines,7 and the 2008 ACC/AHA/HRS Guidelines for Device Therapy10 provide class I A recommendation for CRT treatment with or without an implantable cardioverter defibrillator (ICD)
function in patients with New York Heart Association (NYHA) functional class III and IV, QRS width $\geq 120$ ms. and left ventricular ejection fraction (LVEF) $\leq 35\%$ in order to improve symptoms and reduce mortality. More recent studies have explored the effect of CRT in patients with mild symptoms and markers of cardiac dys-synchrony most of whom were already indicated for an ICD,\textsuperscript{5}–\textsuperscript{7} resulting in a focused ESC guideline update on device therapy.\textsuperscript{11} Meanwhile, there has been a substantial increase in implantation rates for CRT across Europe, although with marked differences amongst countries.\textsuperscript{12,13}

Surveys and registries differ from randomized controlled trials (RCTs) in several ways, and both approaches have their strengths and limitations. RCTs are designed to evaluate the response to interventions, but also measure outcomes,\textsuperscript{14} by scientifically validated methods. However, they often exclude patients with co-morbidities and rely on statistical precision and consistency across subgroups.\textsuperscript{15} Surveys capture data from a much more heterogeneous population and are closer to actual clinical practice.\textsuperscript{16–18} However, they are subject to selection bias and missing data, and only measure outcomes rather than the response to therapy.\textsuperscript{19}

We performed a survey to evaluate contemporary European practice related to CRT implantations with or without an ICD as a joint initiative of the Heart Failure Association (HFA) and the European Heart Rhythm Association (EHRA) of the European Society of Cardiology (ESC). The first publications, describing the patients and implant procedures, provided important information on clinical characteristics, diagnostic criteria, adverse events, in-hospital course, status at discharge, physician adherence to guideline recommendations, and the influence of the volume of implants at a centre.\textsuperscript{19,20} These reports show major differences between guidelines and clinical practice. Substantial numbers of patients had milder symptoms, narrow QRS width, and had a previous device (permanent pacemakers and ICDs). This publication reports the 1 year (9–15 months) follow-up results of patients included into this survey.

**Methods**

**Design**

The rationale and design of the CRT Survey have been published previously.\textsuperscript{21} All centres implanting CRT with or without an ICD were invited to participate. Centres were asked to enrol consecutive successful implantations performed between 1 November 2008 and 30 June 2009. The variables captured at 1 year follow-up included survival, hospitalization, patient global assessment (self-reported), NYHA functional class, electrocardiogram (ECG), key echocardiographic data, and device-related complications.

**Participating countries and centres**

A total of 141 centres from the following 13 ESC countries participated: Austria, Belgium, France, Germany, Ireland, Israel, Italy, The Netherlands, Norway, Spain, Sweden, Switzerland, and the UK. The number of patients from each is shown in Appendix 3.

**Data collection**

Data were collected using electronic case report forms (eCRFs). The contents for both index hospitalization and follow-up variables have been reported.\textsuperscript{21} A follow-up assessment was planned 9–15 months post-implantation. The window of 6 months was allowed in order to give enough time to capture data from routine device follow-ups.

Two national co-ordinators, one each from the fields of heart failure and electrophysiology, were selected and given the responsibility of facilitating recruitment and follow-up in their respective countries (Appendix 1). Germany and Sweden have ongoing device registries in most of their centres which includes CRT which capture most of the information contained in the CRT Survey eCRF. With permission from both of the Steering Committees (Appendix 2), CRT follow-up data were merged into the CRT Survey database.

A central database was created at the data management centre, Institut für Herzinfarktforschung in Ludwigshafen an der Universität Heidelberg, Germany which also maintained and interrogated the database and performed analyses. A website, www.crt-survey.org, supported by the ESC Web department provided all the relevant documents and permitted online data entry. Ethical approval and written informed consent were obtained according to the rules for clinical investigations in each participating country at the initiation of the study.

**Statistical methodology**

Absolute numbers and percentages are shown for categorical variables to describe the patient population, and means (with standard deviations (SD)) or medians (with quartiles) for continuous variables. Categorical variables were compared between subgroups by the Pearson $\chi^2$ test and continuous variables (numeric values) by the Mann–Whitney–Wilcoxon test. Descriptive statistics were calculated for the available cases. Logistic regression analysis was performed for selected variables. Kaplan–Meier survival estimates were performed for age, gender, aetiology, rhythm, QRS durations, and device type. A significance level of $P < 0.05$ was assumed for the statistical tests, and all $P$-values are results of two-tailed tests. All statistical analyses were performed using SAS\textsuperscript{25} statistical software, version 9.1 (Cary, North Carolina, USA).

**Results**

This survey enrolled 2438 patients during the 8 month inclusion period. One-year follow-up data (9–15 months), including vital status, were available for 2111 (87%) patients. Most patients received CRT with an ICD function (CRT-D) rather than CRT alone (CRT-P). The characteristics of patients who did not have follow-up data were similar to those of the overall population. During follow-up, 207 (10%) patients died, 346 (16%) were hospitalized for cardiovascular causes, and 501 (24%) were hospitalized or died.

**Mortality (Table 1)**

Patients who died were slightly older, were likely to be men, were more likely to have ischaemic heart disease, diabetes mellitus, chronic lung disease, and atrial fibrillation, had lower LVEF, were less likely to be prescribed beta-blockers and more likely to be prescribed diuretics, had worse NYHA functional class, and were more likely to be hospitalized for heart failure the previous year, as shown by unadjusted description of baseline characteristics in the table.

Patients with narrow QRS complex, left bundle branch block (LBBB), or paced ventricular rhythm had similar survival rates, but those with right bundle branch block (RBBB) had a worse
Table 1  Baseline characteristics of survivors vs. dead patients, patients with and without cardiovascular hospitalization, and the composite of both with follow-up data (n = 2111)

<table>
<thead>
<tr>
<th></th>
<th>Dead</th>
<th>Alive</th>
<th>P-value</th>
<th>CV hospitalization</th>
<th>No CV hospitalization</th>
<th>P-value</th>
<th>Death or CV hospitalization</th>
<th>No death or CV hospitalization</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n, %)</td>
<td>207 (9.8)</td>
<td>1904 (90.2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>501 (20.7)</td>
<td>1621 (66.8)</td>
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</tr>
<tr>
<td>Demographics</td>
<td></td>
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<tr>
<td>Age (years, median)</td>
<td>71 (65–76)</td>
<td>70 (62–76)</td>
<td>&lt;0.01</td>
<td>69 (61–75)</td>
<td>70 (62–76)</td>
<td>0.32</td>
<td>70 (63–76)</td>
<td>70 (62–76)</td>
<td>0.44</td>
</tr>
<tr>
<td>Age &gt;75</td>
<td>71 (34)</td>
<td>575 (30)</td>
<td>0.22</td>
<td>100 (29)</td>
<td>446 (31)</td>
<td>0.50</td>
<td>156 (31)</td>
<td>491 (30)</td>
<td>0.76</td>
</tr>
<tr>
<td>Women</td>
<td>32 (16)</td>
<td>456 (24)</td>
<td>&lt;0.01</td>
<td>68 (20)</td>
<td>363 (25)</td>
<td>&lt;0.05</td>
<td>92 (18)</td>
<td>400 (25)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>HF aetiology</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischaemic</td>
<td>118 (61)</td>
<td>888 (50)</td>
<td>&lt;0.01</td>
<td>170 (53)</td>
<td>702 (52)</td>
<td>0.51</td>
<td>258 (56)</td>
<td>750 (50)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Non-ischaemic</td>
<td>53 (28)</td>
<td>725 (41)</td>
<td>&lt;0.001</td>
<td>126 (40)</td>
<td>503 (41)</td>
<td>0.77</td>
<td>164 (36)</td>
<td>614 (41)</td>
<td>0.05</td>
</tr>
<tr>
<td>Other</td>
<td>22 (11)</td>
<td>157 (9)</td>
<td>0.25</td>
<td>17 (5)</td>
<td>88 (7)</td>
<td>0.46</td>
<td>37 (8)</td>
<td>142 (9)</td>
<td>0.37</td>
</tr>
<tr>
<td>Past medical history</td>
<td></td>
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</tr>
<tr>
<td>HF hospitalization last year</td>
<td>119 (69)</td>
<td>914 (54)</td>
<td>&lt;0.001</td>
<td>215 (63)</td>
<td>764 (53)</td>
<td>&lt;0.01</td>
<td>296 (64)</td>
<td>740 (52)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>78 (45)</td>
<td>479 (28)</td>
<td>&lt;0.0001</td>
<td>106 (31)</td>
<td>409 (28)</td>
<td>0.38</td>
<td>165 (35)</td>
<td>394 (28)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>48 (28)</td>
<td>265 (16)</td>
<td>&lt;0.001</td>
<td>67 (20)</td>
<td>230 (16)</td>
<td>0.12</td>
<td>99 (21)</td>
<td>216 (15)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>3 (2)</td>
<td>27 (2)</td>
<td>0.91</td>
<td>2 (1)</td>
<td>22 (2)</td>
<td>0.17</td>
<td>4 (1)</td>
<td>26 (2)</td>
<td>0.17</td>
</tr>
<tr>
<td>II</td>
<td>21 (11)</td>
<td>364 (21)</td>
<td>&lt;0.01</td>
<td>48 (14)</td>
<td>316 (22)</td>
<td>&lt;0.001</td>
<td>66 (14)</td>
<td>320 (21)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>III</td>
<td>119 (65)</td>
<td>1251 (71)</td>
<td>0.09</td>
<td>243 (72)</td>
<td>969 (69)</td>
<td>0.24</td>
<td>330 (70)</td>
<td>1050 (70)</td>
<td>0.91</td>
</tr>
<tr>
<td>IV</td>
<td>41 (22)</td>
<td>127 (7)</td>
<td>&lt;0.0001</td>
<td>45 (13)</td>
<td>105 (7)</td>
<td>&lt;0.001</td>
<td>71 (15)</td>
<td>97 (7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LVEF %</td>
<td>24 ± 7</td>
<td>27 ± 8</td>
<td>&lt;0.0001</td>
<td>26 ± 8</td>
<td>27 ± 8</td>
<td>&lt;0.05</td>
<td>26 ± 8</td>
<td>27 ± 8</td>
<td>0.21</td>
</tr>
<tr>
<td>Sinus</td>
<td>133 (65)</td>
<td>1391 (74)</td>
<td>&lt;0.01</td>
<td>220 (65)</td>
<td>1063 (74)</td>
<td>&lt;0.001</td>
<td>320 (65)</td>
<td>1209 (76)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>64 (31)</td>
<td>410 (22)</td>
<td>&lt;0.001</td>
<td>106 (31)</td>
<td>305 (21)</td>
<td>&lt;0.001</td>
<td>154 (31)</td>
<td>323 (20)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Other</td>
<td>9 (4)</td>
<td>71 (4)</td>
<td>0.68</td>
<td>13 (4)</td>
<td>61 (4)</td>
<td>0.72</td>
<td>20 (4)</td>
<td>63 (4)</td>
<td>0.92</td>
</tr>
<tr>
<td>QRS complex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>28 (14)</td>
<td>240 (74)</td>
<td>0.76</td>
<td>45 (13)</td>
<td>170 (12)</td>
<td>0.49</td>
<td>66 (13)</td>
<td>205 (13)</td>
<td>0.78</td>
</tr>
<tr>
<td>LBBB</td>
<td>126 (61)</td>
<td>1270 (68)</td>
<td>0.05</td>
<td>233 (69)</td>
<td>1020 (72)</td>
<td>0.31</td>
<td>324 (66)</td>
<td>1079 (68)</td>
<td>0.37</td>
</tr>
<tr>
<td>RBBB</td>
<td>21 (10)</td>
<td>108 (6)</td>
<td>&lt;0.05</td>
<td>23 (7)</td>
<td>96 (7)</td>
<td>0.97</td>
<td>39 (8)</td>
<td>91 (6)</td>
<td>0.08</td>
</tr>
<tr>
<td>Other</td>
<td>34 (17)</td>
<td>246 (13)</td>
<td>0.18</td>
<td>36 (11)</td>
<td>139 (10)</td>
<td>0.63</td>
<td>66 (13)</td>
<td>214 (13)</td>
<td>0.97</td>
</tr>
<tr>
<td>Ventricular paced rhythm</td>
<td>38 (18)</td>
<td>341 (18)</td>
<td>0.94</td>
<td>51 (15)</td>
<td>241 (17)</td>
<td>0.39</td>
<td>81 (16)</td>
<td>300 (19)</td>
<td>0.22</td>
</tr>
<tr>
<td>QRS durations</td>
<td>162 ± 33</td>
<td>157 ± 31</td>
<td>0.13</td>
<td>156 ± 33</td>
<td>157 ± 31</td>
<td>0.50</td>
<td>158 ± 32</td>
<td>157 ± 31</td>
<td>0.86</td>
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<tr>
<td>QRS durations</td>
<td></td>
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<td></td>
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<tr>
<td>&lt;130 ms</td>
<td>22 (14)</td>
<td>286 (18)</td>
<td>0.15</td>
<td>54 (18)</td>
<td>247 (18)</td>
<td>0.07</td>
<td>69 (16)</td>
<td>240 (18)</td>
<td>0.39</td>
</tr>
<tr>
<td>130 to &lt;160 ms</td>
<td>53 (33)</td>
<td>455 (29)</td>
<td>0.30</td>
<td>100 (32)</td>
<td>387 (29)</td>
<td>0.22</td>
<td>134 (32)</td>
<td>379 (29)</td>
<td>0.23</td>
</tr>
<tr>
<td>160–180 ms</td>
<td>51 (32)</td>
<td>532 (34)</td>
<td>0.57</td>
<td>101 (33)</td>
<td>454 (34)</td>
<td>0.70</td>
<td>140 (33)</td>
<td>446 (34)</td>
<td>0.82</td>
</tr>
</tbody>
</table>

Follow-up results of the European CRT Survey

[63] Downloaded from https://eurjhf.oxfordjournals.org/ on February 2, 2021
<table>
<thead>
<tr>
<th></th>
<th>Dead</th>
<th>Alive</th>
<th>( P )-value</th>
<th>CV hospitalization</th>
<th>No CV hospitalization</th>
<th>( P )-value</th>
<th>Death or CV hospitalization</th>
<th>No death or CV hospitalization</th>
<th>( P )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>( &gt; 180 ) ms</td>
<td>35 (22)</td>
<td>297 (19)</td>
<td>0.39</td>
<td>54 (18)</td>
<td>254 (19)</td>
<td>0.55</td>
<td>79 (19)</td>
<td>255 (19)</td>
<td>0.79</td>
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<tr>
<td>Device type(^a)</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
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</tr>
<tr>
<td>CRT-D</td>
<td>129 (63)</td>
<td>1365 (72)</td>
<td>&lt;0.01</td>
<td>264 (77)</td>
<td>1088 (76)</td>
<td>0.51</td>
<td>357 (72)</td>
<td>1146 (71)</td>
<td>0.78</td>
</tr>
<tr>
<td>CRT-P</td>
<td>77 (37)</td>
<td>521 (28)</td>
<td>&lt;0.01</td>
<td>77 (23)</td>
<td>349 (24)</td>
<td>0.51</td>
<td>139 (28)</td>
<td>461 (29)</td>
<td>0.78</td>
</tr>
<tr>
<td>Medical treatment(^b)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>123 (73)</td>
<td>1426 (85)</td>
<td>&lt;0.0001</td>
<td>293 (86)</td>
<td>1193 (84)</td>
<td>0.40</td>
<td>379 (82)</td>
<td>1181 (84)</td>
<td>0.34</td>
</tr>
<tr>
<td>Diuretics</td>
<td>159 (94)</td>
<td>1456 (87)</td>
<td>&lt;0.01</td>
<td>309 (90)</td>
<td>1227 (86)</td>
<td>&lt;0.05</td>
<td>421 (91)</td>
<td>1205 (86)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>106 (63)</td>
<td>1135 (67)</td>
<td>0.22</td>
<td>223 (65)</td>
<td>962 (68)</td>
<td>0.45</td>
<td>296 (64)</td>
<td>955 (68)</td>
<td>0.15</td>
</tr>
<tr>
<td>ARB</td>
<td>31 (18)</td>
<td>410 (24)</td>
<td>0.08</td>
<td>81 (24)</td>
<td>345 (24)</td>
<td>0.77</td>
<td>105 (23)</td>
<td>337 (24)</td>
<td>0.54</td>
</tr>
<tr>
<td>Aldosterone antagonist</td>
<td>80 (47)</td>
<td>755 (45)</td>
<td>0.54</td>
<td>171 (50)</td>
<td>623 (44)</td>
<td>&lt;0.05</td>
<td>225 (49)</td>
<td>614 (44)</td>
<td>0.07</td>
</tr>
</tbody>
</table>

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CRT-D and CRT-P, cardiac resynchronization with or without an implantable cardioverter defibrillator function, respectively; CV, cardiovascular; HF, heart failure; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; RBBB, right bundle branch block.

Patient information available in the six rows, respectively (dead/alive, CV hospitalization/no CV hospitalization and death or CV hospitalization/no death or CV hospitalization):
\(^a\)459/1506, 313/1343, and 193/1770.
\(^b\)466/1419, 344/1439, and 173/1701.
\(^c\)471/1493, 338/1412, and 184/1769.
\(^d\)494/1595, 339/1429, and 206/1872.
\(^e\)616/1570, 309/1342, and 422/1320.
\(^f\)496/1607, 341/1437, and 206/1886.
\(^g\)461/1403, 342/1422, and 169/1685.
outcome. Survivors were more likely to have received a CRT-D. Unadjusted Kaplan–Meier survival estimates suggested a better prognosis in patients who received a CRT-D than patients with a CRT-P (P < 0.0002, Figure 1A).

Cardiovascular hospitalization and cardiovascular hospitalization or death (Table 1)
Women were hospitalized less frequently than men (25% vs. 20%, P < 0.05). Age, aetiology of disease, and prevalence of co-morbidities, with the exception of atrial fibrillation, and the proportion of patients that received a CRT-D was similar in patients who did or did not have a CV hospitalization. QRS duration and morphology were similar amongst patients who were or were not hospitalized.

Patients who were hospitalized had a slightly lower LVEF, were more likely to be prescribed diuretics and aldosterone antagonists, had more severe symptoms, and were more likely to be hospitalized for heart failure in the year before implantation.

The characteristics of patients who did or did not reach the composite outcome of cardiovascular hospitalization or death were similar to the pattern shown for survival.

Aetiology (Table 2, Figure 1)
Patients with ischaemic heart disease were older (71 vs. 68 years, P < 0.0001), more likely to be men, more likely to have a QRS duration <130 ms (20% vs. 16%, P < 0.05), and less likely to have a QRS duration of between 130 and <160 ms (31% vs. 36%, P < 0.05) compared with patients who did not have ischaemic heart disease.
were allocated to a CRT-P rather than a CRT-D (39% vs. 29%, 0.0001), and more patients in this category had QRS durations, which were independently associated with poorer survival.

Table 1

Multivariable analyses were performed using the variables listed in Table 4. These showed that NYHA functional class III–IV, atrial fibrillation, ischaemic aetiology, and allocation to device type CRT-P were independently associated with poorer survival.

Table 2 Selected variables for ischaemic and non-ischaemic aetiology (n, %)

<table>
<thead>
<tr>
<th></th>
<th>Ischaemic</th>
<th>Non-ischaemic</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years, median)</td>
<td>71 (65–77)</td>
<td>68 (60–75)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Women</td>
<td>168 (15)</td>
<td>339 (32)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>QRS durationa</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;130 ms</td>
<td>188 (20)</td>
<td>132 (16)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>130 to &lt;160 ms</td>
<td>282 (30)</td>
<td>241 (28)</td>
<td>0.23</td>
</tr>
<tr>
<td>160–180 ms</td>
<td>286 (31)</td>
<td>304 (36)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>&gt;180 ms</td>
<td>175 (19)</td>
<td>172 (20)</td>
<td>0.44</td>
</tr>
<tr>
<td>Device typeb</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRT-D</td>
<td>842 (77)</td>
<td>671 (63)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CRT-P</td>
<td>251 (23)</td>
<td>391 (37)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

CRT-D and CRT-P, cardiac resynchronization with or without an implantable cardioverter defibrillator function, respectively.

Table 3 Selected variables for atrial fibrillation and sinus rhythm or other (n, %)

<table>
<thead>
<tr>
<th></th>
<th>Atrial fibrillation</th>
<th>Sinus rhythm or other</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years, median)</td>
<td>71 (65–77)</td>
<td>69 (61–76)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Women</td>
<td>112 (21)</td>
<td>441 (25)</td>
<td>0.06</td>
</tr>
<tr>
<td>RBBBa</td>
<td>50 (9)</td>
<td>104 (6)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>QRS durationb</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;130 ms</td>
<td>107 (28)</td>
<td>481 (31)</td>
<td>0.38</td>
</tr>
<tr>
<td>130 to &lt;160 ms</td>
<td>111 (29)</td>
<td>538 (34)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>160–180 ms</td>
<td>80 (21)</td>
<td>294 (19)</td>
<td>0.44</td>
</tr>
<tr>
<td>Device typec</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRT-D</td>
<td>338 (62)</td>
<td>1340 (75)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CRT-P</td>
<td>207 (38)</td>
<td>442 (25)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

CRT-D and CRT-P, cardiac resynchronization with or without an implantable cardioverter defibrillator function, respectively; RBBB, right bundle branch block.

Table 4 Selected variables for CRT-D and CRT-P recipients (n, %)

<table>
<thead>
<tr>
<th></th>
<th>CRT-D</th>
<th>CRT-P</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>Age (years, median)</td>
<td>68 (61–74)</td>
<td>75 (68–80)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age ≥75</td>
<td>396 (23)</td>
<td>337 (22)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Women</td>
<td>363 (21)</td>
<td>194 (30)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RBBBc</td>
<td>120 (7)</td>
<td>34 (5)</td>
<td>0.10</td>
</tr>
<tr>
<td>QRS durationb</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;130 ms</td>
<td>269 (18)</td>
<td>75 (8)</td>
<td>0.37</td>
</tr>
<tr>
<td>130 to &lt;160 ms</td>
<td>450 (30)</td>
<td>137 (30)</td>
<td>0.82</td>
</tr>
<tr>
<td>160–180 ms</td>
<td>493 (33)</td>
<td>155 (33)</td>
<td>0.86</td>
</tr>
<tr>
<td>&gt;180 ms</td>
<td>277 (19)</td>
<td>95 (21)</td>
<td>0.35</td>
</tr>
<tr>
<td>Previous VF/sustained VT</td>
<td>295 (20)</td>
<td>15 (2)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

CRT-D and CRT-P, cardiac resynchronization with or without an implantable cardioverter defibrillator function, respectively; RBBB, right bundle branch block; VF, ventricular fibrillation; VT, ventricular tachycardia.

Predictors of death and cardiovascular hospitalization (Table 5, and Figure 1 and 2)

Multivariable analyses were performed using the variables listed in Table 4. These showed that NYHA functional class III–IV, atrial fibrillation, ischaemic aetiology, and allocation to device type CRT-P were independently associated with poorer survival.

Atrial fibrillation (Table 3, Figure 1)

Patients with atrial fibrillation were older (72 vs. 69 years, P < 0.0001), and more patients in this category had QRS durations <130 ms (22% vs. 17%, P < 0.05), RBBB (9% vs. 6%, P < 0.01), and were allocated to a CRT-P rather than a CRT-D (39% vs. 29%, P < 0.0001). Patients with atrial fibrillation had a worse outcome on both unadjusted and multivariable analyses.

QRS durations

Except for a slightly higher mortality in patients with RBBB, outcomes were similar regardless of QRS morphology or duration or presence of paced ventricular rhythm. Patients with QRS <130 ms were more likely to have ischaemic heart disease and be in atrial fibrillation.

Device type (Table 4)

CRT-D recipients were substantially younger (68 vs. 75 years, P < 0.0001), more likely to be women, and had significantly more previous ventricular fibrillation/sustained ventricular tachycardia (20% vs. 2%, P < 0.0001). The proportions of patients with different QRS morphology and durations were similar regardless of device type implanted.

Upgraded patients vs. de novo implantations

A recent report from this database shows that outcomes in patients upgraded to CRT from permanent pacemakers and ICDs were similar to those who received de novo implantations.
Clinical status (Figure 3A and B)

Investigators reported a substantial improvement in NYHA functional class. At the time of implant, 1902 (78%) patients were in NYHA III–IV of whom 160 (8%) died. At follow-up 976 (50%) patients were in NYHA III–IV. Of 536 (22%) patients who were in NYHA I–II at the time of implant, only 1% died. The proportion in NYHA I–II had risen to 995 (50%) patients at follow-up. For patients' self-reported assessment of their global condition, 81% felt much better/a little better, 16% reported no change, and 4% reported worsening.

Complications

Table 6 reports device-related complications during the course of follow-up, with an overall rate of 10%. Lead displacement and phrenic nerve stimulation were the most common adverse events at ~ 3%. Infection was reported in 1.6% of cases.

Discussion

This survey suggests that implanting a CRT-P or a CRT-D device is associated with broadly similar impact on symptoms and rates of hospitalization and survival as observed in landmark RCTs of patients with predominantly NYHA functional class III–IV heart failure, despite embracing a far broader range of patients that were also older and with more co-morbidity than in the landmark trials. Comparison of baseline characteristics and outcomes of the survey cohort with selected RCTs is provided in Table 7. In CARE-HF, the 1-year mortality in patients assigned to CRT was 9.7% and ~ 25% of patients had been hospitalized for a major cardiovascular event or died and by 18 months 62% were alive and in NYHA I–II.23 A further analysis of CARE-HF that imputed the additional effect of adding an ICD function to CRT suggests that this would have provided an additional mortality benefit.24 This survey suggests that implanting CRT devices into a broader population of patients who do not meet the inclusion criteria of the landmark trials is associated with a favourable outcome. However, this is no substitute for information from a RCT, and the data must be interpreted with caution.

The population included important groups of patients poorly represented or excluded from RCTs, including women, very elderly patients, and those with prior device implantation, atrial fibrillation, and/or narrow QRS durations.19 Women had a lower mortality than men despite being older and more likely to receive a CRT-P than a CRT-D. Lower mortality may reflect a lower prevalence of ischaemic disease in women, but randomized trials comparing ICD with CRT-D have suggested greater benefit in women. However, the effect of a CRT-P or a CRT-D on

<table>
<thead>
<tr>
<th>Table 5 Multivariate analysis for death, hospitalization, and death and hospitalization during the 1-year (9–15 months) follow-up period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variables</td>
</tr>
<tr>
<td>死亡</td>
</tr>
<tr>
<td>艾畅性心律</td>
</tr>
<tr>
<td>Ischaemic aetiology</td>
</tr>
<tr>
<td>Device type: CRT-P</td>
</tr>
<tr>
<td>年龄分组a</td>
</tr>
<tr>
<td>QRS durationsb</td>
</tr>
<tr>
<td>女性</td>
</tr>
<tr>
<td>心血管住院</td>
</tr>
<tr>
<td>艾畅性心律</td>
</tr>
<tr>
<td>Ischaemic aetiology</td>
</tr>
<tr>
<td>Device type: CRT-P</td>
</tr>
<tr>
<td>年龄分组a</td>
</tr>
<tr>
<td>QRS durationsb</td>
</tr>
<tr>
<td>女性</td>
</tr>
<tr>
<td>死亡或心血管住院</td>
</tr>
<tr>
<td>艾畅性心律</td>
</tr>
<tr>
<td>Ischaemic aetiology</td>
</tr>
<tr>
<td>Device type: CRT-P</td>
</tr>
<tr>
<td>年龄分组a</td>
</tr>
<tr>
<td>QRS durationsb</td>
</tr>
<tr>
<td>女性</td>
</tr>
</tbody>
</table>

CI, confidence interval; CRT-P, cardiac resynchronization without an implantable cardioverter defibrillator function; NYHA, New York Heart Association; OR, odds ratio.

aAge groups divided as <62, 62–76, and >76 based on quartiles (the oldest group as reference).
bQRS durations divided as <130, 130–160, 160–180, and >180 ms based on quartiles (the widest group as reference).
mortality was similar in men and women in both CARE-HF and COMPANION. This survey cannot determine whether the better outcome in women reflects a better outcome to CRT or a better intrinsic prognosis amongst women. This survey suggests that age is not a strong determinant of 1-year outcome in patients who receive a CRT-P or CRT-D device, which is surprising since age is usually a strong predictor of survival in patients with heart failure. This could reflect a greater benefit of CRT in older patients, although randomized trials suggest a similar response in younger and older patients.

Many more CRT-D than CRT-P devices are implanted in all ESC countries, although a substantial minority receive a CRT-P in some countries. The COMPANION study\(^3\) and an imputed analysis of CARE-HF\(^{25}\) suggest a modest additional survival benefit from a CRT-D. Patients who received a CRT-D device had a substantially lower mortality in both univariate and multivariate analysis, as has been reported in large patient series reported by others.\(^{26}\) However, these findings should be interpreted cautiously since CRT-P recipients were older and had more atrial fibrillation. Moreover statistical analyses cannot correct for unrecorded confounders, hence the need for RCTs. The reasons for selecting a CRT-D in preference to a CRT-P device may account for much of the difference in outcome, although the inconclusive data from randomized trials support an additional therapeutic effect.

Our survey included 544 patients (23 %) with atrial fibrillation. These patients were older, more likely to receive a CRT-P,
had higher morbidity and mortality. Clinical trials provide conflicting evidence regarding whether prevalent atrial fibrillation carries independent prognostic information after correction for differences for age and symptoms, although new-onset atrial fibrillation is associated with a sharp increase in mortality, suggesting that patients with chronic atrial fibrillation are a survivor subgroup.27

The RAFT trial included 115 patients (13%) with atrial fibrillation or flutter.7 No benefit of CRT-D compared with ICD was observed in this population. Information on the percentage of cumulative biventricular pacing, the extent of AV node ablation post-device implantation, or up-titration of medical treatment to ensure adequate pacing was not captured in this survey, which can potentially explain the observation of poorer outcome of patients with atrial fibrillation and the disparity with other observational data sets.28–33

Landmark RCTs comparing CRT-P and CRT-D against medical therapy included few patients with a QRS duration <140 ms but did not identify a marked interaction between QRS duration and the effect of CRT on mortality. Patients with RBBB have a worse overall prognosis than those with LBBB, and may benefit less from CRT, although many patients who have additional left-sided fascicular blocks may still benefit.2,4,34 More recently, trials comparing ICD and CRT-D have suggested that only patients with either QRS >150 ms or LBBB benefit from a CRT-D,6,7 although controversy surrounds which is more important. We found similar outcomes regardless of QRS duration. However, as patients with longer QRS duration would be expected to have a worse prognosis, the similar outcome could still be interpreted as a greater response in those with longer QRS duration. A substantial long-term trial to confirm or refute a benefit from implanting a CRT-P or CRT-D device compared with no device in patients regardless of QRS duration is required. Information from trials comparing ICD and CRT-D do not adequately address this

### Table 6

<table>
<thead>
<tr>
<th>Parameters</th>
<th>(n, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device-related complications</td>
<td>170 (10.3)</td>
</tr>
<tr>
<td>Lead displacement</td>
<td>55 (3.3)</td>
</tr>
<tr>
<td>Lead malfunction</td>
<td>13 (0.8)</td>
</tr>
<tr>
<td>Device-related arrhythmias</td>
<td>18 (1.1)</td>
</tr>
<tr>
<td>Phrenic nerve stimulation</td>
<td>51 (3.1)</td>
</tr>
<tr>
<td>Device replacement</td>
<td>6 (0.4)</td>
</tr>
<tr>
<td>Infection</td>
<td>27 (1.6)</td>
</tr>
</tbody>
</table>

*aInformation available for 1648 patients.*

### Table 7

<table>
<thead>
<tr>
<th>Parameters</th>
<th>COMPANION3</th>
<th>CARE-HF4,38</th>
<th>REVERSE5,39</th>
<th>MADIT-CRT6</th>
<th>RAFT7</th>
<th>CRT Survey</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients (CRT-P/CRT-D)</td>
<td>1212</td>
<td>409</td>
<td>419</td>
<td>1089</td>
<td>894</td>
<td>2438</td>
</tr>
<tr>
<td>Control groups</td>
<td>308</td>
<td>404</td>
<td>191</td>
<td>731</td>
<td>904</td>
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<tr>
<td>Mean follow-up (months)</td>
<td>14.8–16.5</td>
<td>37.4</td>
<td>12</td>
<td>28.8</td>
<td>40</td>
<td>12</td>
</tr>
<tr>
<td>Baseline characteristics (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Mean age (years)</td>
<td>67</td>
<td>66</td>
<td>62</td>
<td>65</td>
<td>66</td>
<td>68</td>
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<tr>
<td>Men</td>
<td>67</td>
<td>74</td>
<td>79</td>
<td>75</td>
<td>83</td>
<td>76</td>
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<td>Ischaemic heart disease</td>
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<td>38</td>
<td>55</td>
<td>55</td>
<td>67</td>
<td>51</td>
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<tr>
<td>Atrial fibrillation</td>
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<td>0</td>
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<tr>
<td>Previous device</td>
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<td>0</td>
<td>0</td>
<td>0</td>
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</tr>
<tr>
<td>Ventricular paced rhythm</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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</tr>
<tr>
<td>RBBB</td>
<td>10</td>
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<td>10</td>
<td>13</td>
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<td>6</td>
</tr>
<tr>
<td>QRS duration (ms)</td>
<td>160</td>
<td>165</td>
<td>153</td>
<td>65% &gt;150</td>
<td>158</td>
<td>160</td>
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<tr>
<td>Mean LVEF</td>
<td>22</td>
<td>24.8</td>
<td>27</td>
<td>24</td>
<td>23</td>
<td>26</td>
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<td>NYHA class</td>
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<td>I–II</td>
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<td>100</td>
<td>100</td>
<td>80</td>
</tr>
<tr>
<td>III–IV</td>
<td>100</td>
<td>100</td>
<td>0</td>
<td>0%</td>
<td>0%</td>
<td>80%</td>
</tr>
<tr>
<td>Outcomes in the CRT-D/P treated group (n, %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality during follow-up</td>
<td>246 (20.3)</td>
<td>101 (24.7)</td>
<td>9 (2.2)</td>
<td>74 (6.8)</td>
<td>186 (20.8)</td>
<td>207 (9.8)</td>
</tr>
<tr>
<td>Death or hospitalization for HF</td>
<td>449 (37.1)</td>
<td>118 (28.9)</td>
<td>26 (6.2)</td>
<td>187 (17.2)</td>
<td>297 (33.2)</td>
<td>501 (23.7)*</td>
</tr>
</tbody>
</table>

**Notes:** CRT-D and CRT-P, cardiac resynchronization with or without an implantable cardioverter defibrillator function, respectively; HF, heart failure; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; RBBB, right bundle branch block.

*aThese were exclusion criteria in the trials.
*bPrevious ICDs were exclusion criteria in RAFT and only paced rhythm is reported.
*cFollow-data available for 2111 (86.6% of the total cohort).
*dCombined mortality and hospitalization data from CARE-HF 2005 publication.
*eHospitalization data available for 1797 (73.7% of the total cohort).
question. A large trial, Echo-CRT, is addressing the question of whether dyssynchrony measured by echocardiography can identify a group of patients with shorter QRS duration who benefit from CRT-D rather than ICD implantation, but will not answer the question of the impact of CRT compared with no device nor the impact of devices in patients with narrow QRS who do not have dyssynchrony.

Ischaemic heart disease predicts a worse outcome amongst patients with heart failure, and patients with ischaemic heart disease had a worse outcome in this survey. Randomized trials confirm that patients with ischaemic heart disease have a worse prognosis and less benefit from CRT in terms of ventricular remodelling but, in terms of benefits on morbidity and mortality, the relative benefits in patients with and without ischaemic heart disease is similar and therefore the absolute reduction in mortality may be somewhat greater in patients with ischaemic heart disease.

The lack of insight into the mechanism of benefits of CRT is frustrating and may reflect the fact that the main mechanism of benefit varies from one patient to the next and from one time and situation to another. Mitrval regurgitation, prevention of tachy- and bradyarrhythmias, ventricular remodelling, as well as atrioventricular and biventricular resynchronization may all play different roles at different times in this patient population. Like many successful interventions in heart failure, the lack of specificity is its secret of success.

Limitations
Surveys are important sources of information on how evidence acquired through RCTs, usually on highly selected patients managed according to detailed protocols, are adopted in clinical practice. However, surveys also have many limitations. Centre participation was voluntary and, among ~ 800 invited implanting centres in the 13 participating ESC countries, 141 centres responded and recruited patients during the 8 months inclusion period. The 2009 EHRA white Book reports ~ 30 000 annual CRT implantations in the participating countries (primary implants and replacements). Although the importance of consecutive inclusion was emphasized, we cannot confirm that all patients were included consecutively, and there are several sources for potential investigator selection bias. Importantly, only successful implantations were entered into the database which selects the patient population, and could lead to an under-reporting of adverse experience in connection with implantation. The accuracy of the data has not been audited. NYHA functional class was investigator reported and the length of follow-up is short. There is a considerable variation in volume of participating centres and the sample size for some of the eCRI variables due to incomplete data entry and lack of appropriate data fields in two device registries. However, the most important limitation of surveys is their inability to distinguish between outcome and response.

Conclusions
This survey suggests that a group of patients representative of those encountered in routine clinical practice who received a CRT device considered their symptoms had improved compared with their pre-implant assessment. Overall survival was >90. These favourable outcomes suggest that the benefits of CRT observed in RCTs can be replicated in routine clinical practice. However, further randomized trials comparing CRT-Ps with CRT-Ds would be desirable in patients with atrial fibrillation and in patients who do not have a substantial increase in QRS duration.

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Stavanger University Hospital; HFA and EHRA of the ESC; EUCOMED (Biotronik, Boston Scientific, Medtronic, Sorin, and St. Jude Medical—members of the European Medical Device Trade Organization); Roche Diagnostics Ltd.

Conflict of interest: N.B., none to declare. S.P. is a consultant for Medtronic, Boston Scientific, and Biotronik. J.G.F.C. has received research grants from Medtronic and honoraria for speaking and consultation from Medtronic, St Jude, and Biotronik. J.B. has received research grants from Medtronic, Boston Scientific, St Jude Medical, Biotronik, and Sorin. C.L. is a consultant to Medtronic, a member of the Advisory Board for St Jude, and has received a research grant from Medtronic. A.A. is a consultant for Biotronik, St Jude EBR, Medtronic, Merck, and Philips. D.J.v.V has received consultancy fees from Medtronic. T.L., none to declare. A.G., none to declare. D.G. is a consultant to St Jude Medical, Medtronic, and Biotronik. C.S. has been sponsored by Medtronic, Biotronik, Boston Scientific, and SJM in the past. M.G. is a member of the advisory board to Medtronic and Boston Scientific. M.M. has received honoraria for participation in advisory board meetings and speeches from Corthera, Daiichi, Novartis, Servier, Sorin, and Stroder pharmaceuticals. G.D. has received travel support for scientific meetings from Actelion, Astra Zeneca, Boehringer Ingelheim, Medtronic, Pfizer, Sanofi, and Servier, and grants paid to the institution from Astra Zeneca, Actelion, Bayer, Brahms, General Electrics, Medtronic, Pfizer, Servier, Toshiba, and Trophos. F.G., none to declare. L.B., none to declare. K.D. has received speaker’s honoraria from Medtronic and Biotronik.

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Appendix 1. Members of the European CRT Survey Scientific Committee and National Co-ordinators

Scientific Committee
Kenneth Dickstein (HFA Co-ordinator)
Silvia Priori (EHRA Co-ordinator)
Angelo Auricchio
Nigussie Bogale
Josep Brugada
John G.F. Cleland
Appendix 2. Steering Committee members of the Swedish Device registry and the German device registry

Sweden
Cecilia Linde
Fredrik Gadler
Johan Brant

Germany
Dietrich Andresen
Christian Butter
Bernd Gonska
Werner Jung
Karl-Heinz Kuck
Jochen Senges
Christoph Stellbrink

Appendix 3. List of contributing countries and centres (numbers of patients contributed)

Austria (156)
A. ö. Landeskrankenhaus, Universitätsklinikum Graz
Landeskrankenhaus-Innsbruck-Universitätskliniken
Krankenhaus der Elisabethinen Linz
Landesklinikum Thermenregion Mödling
Landesklinikum Salzburg
Landesklinikum St. Pölten
Krankenhaus Hietzing mit Neurologischem Zentrum am Rosenhügel
Wilhelminenspital der Stadt Wien
A. ö. Krankenhaus Wiener Neustadt

Belgium (43)
Clinique St Jean
Cliniques Universitaires Ucl
UZ Gent
Virga Jesse Ziekenhuis

France (160)
Hôpital du Bocage
Saint Etienne
Nouvelles Cliniques Nantaises
Hôpital Louis Pradel
Hôpital Princesse Grace

Germany (291)
Städtisches Klinikum Dessau
Städt. Klinikum Brandenburg GmbH
Krankenhaus Reinbek
Universitätsklinikum Aachen-UKA
Klinik Rotes Kreuz
Saarland-Heilstätten GmbH Kliniken Völklingen
Universitätskliniken des Saarlandes Kreiskliniken Altötting-Burghausen
Klinikum St. Marien Amberg
Hufeland Krankenhaus GmbH
Städt. Klinikum Frankfurt
Städt. Klinikum München Klinik Bogenhausen
Krankenhaus St. Franziskus Mönchengladbach
St. Josefs-Krankenhaus Potsdam
Klinikum Lippe-Detmold
Städt. Kliniken Bielefeld-Klinikum Mitte
Krankenhaus München-Neuperlach (Kardiologie)
Klinikum der Universität München-Großhadern
Universitätsklinikum Heidelberg
Universitätsklinikum Münster (Kardiologie)
Klinikum Coburg
Herzzentrum Ludwigshafen
Herzzentrum Brandenburg
Allgemeines Krankenhaus Celle
Klinikum Ernst von Bergmann Potsdam
Herzzentrum Coswig

Ireland (47)
Mater Misericordia University Hospital
South Infirmary Victoria University Hospital
St Vincent’s University Hospital

Israel (195)
Sheba Medical Center
Barzilai Medical Center
Wolfson Medical Center
Kaplan Medical Center
Rabin Medical Center
Haemek Medical Center

Italy (571)
Ospedale Moriggia-Pelascini
Ospedale Fatebenefratelli Sgc
Ospedale S. Giovanni di Dio Fatebenefratelli
P.O. Frosinone Ceccano
Ospedale S.Maria Misericordia-Perugia
Presidio Ospedaliero di Rivol
Sweden (321)
Danderyds Sjukhus AB
P.O. Genova-Ponente P.A. Micone
A.O. Ospedale S.Gerardo Monza
Policlinico Di Monza-Monza
IRCCS Instituo Clinico Humanitas Rozzano
IRLCS Multimedica
A.O. Ospedale Treviglio Caravaggio Trev-Treviglio
A.O. Desenzano Del Garda
Spedali Civili Di Brescia
Fondazione Poliambulatoria Iast. Osp.
A.O. Maggiore Della Cantit Novara
Presidio Ospedaliero Di Montebelluna
Azienda Ospedaliero S. Maria Miseric Udine
Presidio Ospedaliero Di Camposampiero
Presidio Ospedaliero Di Cittadella
Azienda Ospedaliera Di Padova
Presidio Ospedaliero Di Vicenza
Ospedale Civile Destra Sciechia
Osp. Le S.M. Annunziata Bagno A Rip-Bagno A Ripoli
Stabilimento Di Cisanello
Istituto Fisiologia Clinica
Pia Fondazione (Tricase)-Tricase
Ospedale S.Maria Di Loreto Mare
Azienda Ospedaliero S. Giovanni Di Dio
Clinica Sant’Anna
Ospedale ‘Umberto I’
Clinica Mediterranea

The Netherlands (114)
Academisch Medisch Centrum
Amphia Ziekenhuis
Catharina Ziekenhuis
Isala Klinieken Zwolle
Medisch Centrum Alkmaar
Medisch Spectrum Twente
Erasmus MC
Kennemer Gasthuis
University Medical Center Groningen

Norway (126)
Ålesund Hospital
Haukeland University Hospital
Kristiansand Hospital
Oslo University Hospital, Rikshospitalet
Oslo University Hospital, Ullevål
Stavanger University Hospital
St. Olavs Hospital

Spain (131)
Hosp. De Cruces
Hospital Gregorio Maranon, Madrid
Hosp. Virgen de la Victoria
Hospital Universitario De Tenerife
Hospital Dr. Peset, Valencia
Centro Medico Salus Baleares S.l. – Benidorm, Alicante
Hospital Clinico Y Provincial, Barcelona
Hospital Sta. Creu Y St. Pau, Barcelona
Hospital General U. De Alicante, Alicante

Sweden (321)
Danderyds Sjukhus AB
Länsjukhuset, Kalmar
Karolinska Universitetssjukhuset, Solna
Akademiska sjukhuset
Blekingesjukhuset
Centrallasarettet Västerås
Falu lasarett
Hudiksvalls sjukhus
Kärnsjukhuset Skövde
Lässjukhuset Gävle
Länsjukhuset Kalmar
Norrlands Universitetssjukhus
Sahlgrenska Universitetssjukhuset
St Görans sjukhus
Sundsvalls sjukhus
Universitetssjukhuset Örebro
Universitetssjukhuset Lund
Varbergs sjukhus

Switzerland (83)
Cardiocentro Ticino
HCF Hospital Cantonal Fribourg
Hopitaux Universitaires de Geneve, Geneve 14
Universitatsspital Basel

UK (201)
Southampton General Hospital
Kings College Hospital
Queen Elizabeth Hospital
Leeds General Infirmary
Hull Royal Infirmary
Papworth Hospital
University Hospital of Wales

References


