

# Tracing the European course of cardiac resynchronization therapy from 2006 to 2008

Bela Merkely<sup>1\*</sup>, Attila Roka<sup>1</sup>, Valentina Kutya<sup>1</sup>, Lucas Boersma<sup>2</sup>, Antoine Leenhardt<sup>3</sup>, Andrzej Lubinski<sup>4</sup>, Ali Oto<sup>5</sup>, Alessandro Proclemer<sup>6</sup>, Josep Brugada<sup>7</sup>, Panos E. Vardas<sup>8</sup>, and Christian Wolpert<sup>9</sup>

<sup>1</sup>Heart Centre, Semmelweis University, Varosmajor utca 68, Budapest H-1122, Hungary; <sup>2</sup>Cardiology Department, St Antonius Hospital, Heart Lung Centre Utrecht, Utrecht, The Netherlands; <sup>3</sup>Cardiology Department, Lariboisiere University Hospital, Paris, France; <sup>4</sup>Department of Interventional Cardiology, Medical University of Lodz, Lodz, Poland; <sup>5</sup>Department of Cardiology, Hacettepe University, Ankara, Turkey; <sup>6</sup>Division of Cardiology, Department of Cardiovascular Sciences, S. Maria della Misericordia, Hospital, Udine, Italy; <sup>7</sup>Thorax Institute, Hospital Clínic, University of Barcelona, Institut d'Investigació Biomèdica August Pi i Sunyer, Barcelona, Catalonia, Spain; <sup>8</sup>Department of Cardiology, Heraklion University Hospital, Heraklion, Crete, Greece; and <sup>9</sup>Klinikum Ludwigsburg, Klinik für Innere Medizin, Kardiologie, Nephrologie und internistische Intensivmedizin, Ludwigsburg, Germany

Received 20 October 2009; accepted after revision 26 January 2010; online publish-ahead-of-print 2 March 2010

Cardiac resynchronization therapy (CRT) is a highly efficient treatment modality for patients with severe congestive heart failure and intra-ventricular dyssynchrony. However, the high individual cost and technical complexity of the implantation may limit its widespread utilization. The European Heart Rhythm Association (EHRA) launched a project to assess treatment of arrhythmias in all European Society of Cardiology member countries in order to have a platform for a progressive harmonization of arrhythmia treatment. As a result, two EHRA White Books have been published in 2008 and 2009 based on governmental, insurance, and professional society data. Our aim was to analyse the local differences in the utilization of CRT, based on these surveys. A total of 41 countries provided enough data to analyse years 2006–2008. Significant differences were found in the overall number of implantations and the growth rate between 2006 and 2008. Other contributing factors include local reimbursement of CRT, the existence of national guidelines, and a high number of conventional implantable cardioverter-defibrillator implantations, while GDP or healthcare spending has less effect. Focusing on improving these factors may increase the availability of CRT in countries where it is currently underutilized.

## Keywords

Cardiac resynchronization therapy • Europe • Reimbursement • Pacemaker • Implantable cardioverter-defibrillator

## Introduction

The increasing incidence of congestive heart failure (CHF) is one of the major causes for the growing healthcare costs in industrialized countries. The overall CHF prevalence is ~2%, which increases to 6–10% in the elderly population (age >65 years). The lifetime risk of developing CHF is ~20%, regardless of gender,<sup>1</sup> while the age-adjusted incidence of CHF remained stable over the past 20 years in Europe.<sup>2,3</sup> Despite the advances of medical therapy, mortality is still high and quality of life is severely impaired in advanced stages.<sup>4</sup> Using different measurements, the prevalence of mechanical dyssynchrony can reach 70% in patients with severe CHF.<sup>5</sup>

Cardiac resynchronization therapy (CRT) with atrioventricular pacing (CRT-P) was introduced in the mid-90s and became increasingly popular after the promising results of the early

trials.<sup>6,7</sup> From the year 2000 onwards, implantable cardioverter-defibrillators capable of atrioventricular stimulation became available (CRT-D). The convincing results first of large clinical trials and subsequently of meta-analyses formed the basis of evidence-based practice guidelines, published by professional societies, such as the European Society of Cardiology (ESC), European Heart Rhythm Association (EHRA), American Heart Association, American College of Cardiology, and the Heart Rhythm Society.<sup>8–11</sup>

Survey- and registry-based data regarding local pacing and electrophysiological practice, from several European countries are available<sup>12,13</sup> and the EHRA launched a project to assess the treatment of arrhythmias in all ESC member countries in order to have a platform for a progressive harmonization of arrhythmia treatment. As a result, two EHRA White Books were published

\* Corresponding author. Tel: +36 20 8258036; fax: +36 1 458 6842, Email: merkely.bela@kardio.sote.hu

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author 2010. For permissions please email: journals.permissions@oxfordjournals.org.

in 2008 and 2009 based on governmental, insurance, and professional society data.<sup>14,15</sup>

## Methods

### Data gathering

Data were gathered from the EHRA White Book publications.<sup>14,15</sup> A total of 41 countries provided comprehensive data and were included in the analysis (Figure 1). It should be noted that demographic or economical data were dated a few years earlier in a few cases, but did not exceed 3 years. Implantation data from 2006, 2007, and 2008 have been analysed.

To gather data on the specific items a questionnaire was prepared. The questionnaire was presented and explained to the individual national representatives during the annual Spring Summit of the European Heart Rhythm Association in Nice 2007 and 2008. Each chairperson of the national working group of arrhythmias and/or pacing or president of the national society of arrhythmias was asked to provide data for each item. In many of the countries, national registry data, e.g. Spanish registry for catheter ablation were used as data source. In other countries, the president conducted a national survey or used reasonable estimates, if no exact data were available. Whenever estimates were used they were clearly indicated as such. Furthermore, data on ICD and pacemaker implantation were provided in parallel by EUCOMED (European Confederation of Medical Devices Association) for a number of countries. Data from EUCOMED were only used for entry into the White Book if the national chairman authorized the correctness of data for his country and only served as an additional source. In case no valid data were available, the data were not presented. For the presentation of the data of 2007, the most recent updated data were used from the 2009 edition. The same procedure was used both for the 2008 and 2009 edition. After the publication of the White Book, the national chairmen were asked to verify the data and to indicate mistakes. Only two mistakes were found and were immediately corrected in the published web version. The data collection and entry was performed by a Task Force of EHRA consisting of MBA students, EHRA staff, and members of the National Societies Committee.

### Statistical analysis

For comparison, data are shown as mean  $\pm$  standard deviation. Correlation analysis was performed by calculating Pearson's *r*. Stepwise multiple regression analysis was performed to identify independent factors that affect the number of CRT implantations per capita. The variables included were local CRT reimbursement, number of CRT centres per capita, availability of electrophysiology subspecialty, adherence to national or international CRT implantation guidelines, and healthcare spending per capita.

## Results

### Number of implantations

The number of CRT implantations per million capita for each country is shown in Figure 2. Table 1 lists the number of pacemaker, CRT, and ICD implantations in 2008 and the changes from 2006.

Between 2006 and 2008, a comparison between the number of implantations for conventional pacemakers showed a relatively small increase. Only a few countries were able to significantly increase the rate by more than 100/million capita, namely Estonia,

Finland, Israel, Italy, Latvia, Lithuania, Norway, and Poland. The ratio of dual-chamber pacemaker devices shows a great variation from as low as 16% in Bulgaria to as high as 75% in France.

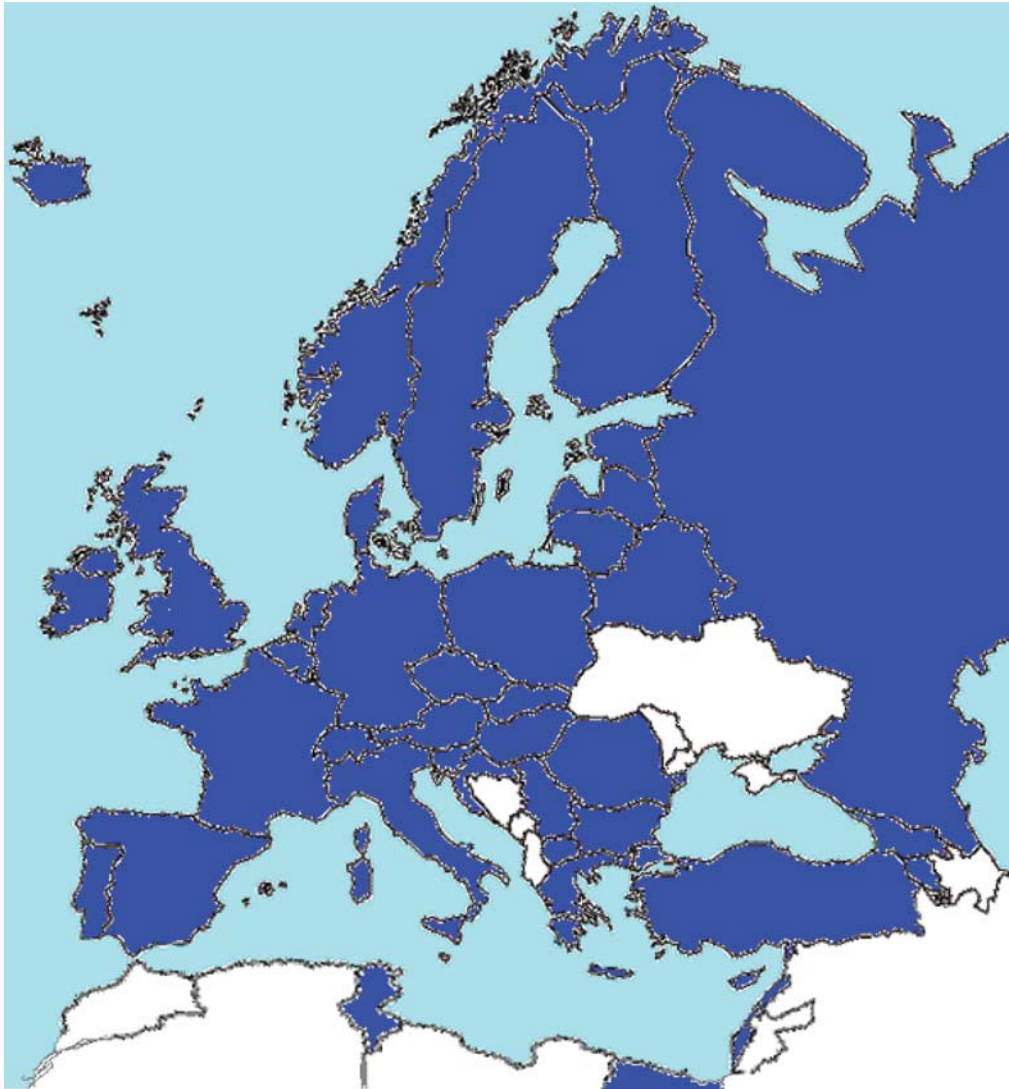
The number of ICD implantations in 2008 also showed great variability: the highest was 310/capita in Italy. The increase in the number of implantations between 2006 and 2008 was more dramatic than for pacemakers, most prominently in Belgium, the Czech Republic, Denmark, Germany, Italy, the Netherlands, and Switzerland.

The highest CRT implantation rate in 2008 was in Italy with 163 CRT devices/million capita (CRT-D only, data on CRT-P are unavailable). The number of implantations grew most dramatically in Italy and Israel: an increase of 60 and 59 implantations/million capita in 2008 compared with 2006. The ratio of CRT-D to total CRT shows great variability between countries. The ratio was 100% only in Georgia, however, the total number of procedures was very low, just 0.4/million capita in 2008 (six implants in total). The ratio in most countries was  $<60\%$ . The average number of CRT implantations/million capita for the 31 ESC countries which had data for all 3 year was 53 in 2006, 65 in 2007, and 76 in 2008, a 43.4% increase in just 2 years (population 518 million, excluded countries: Belgium, Bulgaria, Cyprus, Czech Republic, Egypt, Iceland, Ireland, Norway, Russia, and Turkey). Taking all 41 countries into account, using the last available year, if data from 2008 were missing, the total number of implantations was 42/million capita, total population 782 million, only Belgium excluded. In 2008, 70.9% of implanted devices were CRT-D and 29.1% CRT-P.

## Economical, reimbursement, and medical-professional differences

Table 2 summarizes the gross demographic, economical, and insurance data. The health expenditure generally ranges between 7 and 10% of each country's income, the lowest ratio is in Armenia (4.7%), while the highest is in Switzerland (11.3%). The per capita healthcare expenditure shows great variability, mostly depending on the nation's per capita GDP: the lowest is in Egypt, 133 Euro/capita, the highest is in Luxembourg: 8499 Euro/capita. The proportion of the public insurance for the healthcare costs is generally between 60 and 80%, with several examples on both extremes: Croatia, the Czech Republic, Denmark, Iceland, Luxembourg, the Netherlands, Norway, Sweden, and the UK above 80%, while Armenia, Cyprus, Egypt, Georgia, Greece, Lebanon, and Tunisia significantly below 60%. The availability of general public insurance also shows significant variation. Only a few countries had no reimbursement for pacemakers, ICD, and CRT in 2008: Bulgaria, Croatia, Cyprus, Denmark, Egypt, Iceland, and the Former Yugoslav Republic of Macedonia (FYROM).

The local differences in cardiac electrophysiological practice are significant (Table 3). Only Belarus, the Czech Republic, Egypt, Hungary, Latvia, the Netherlands, Poland, Portugal, Russia, Slovakia, Spain, and Tunisia recognized this field as an individual subspecialty. The number of CRT centres per capita is highest in Austria, 7.9/million capita, while most countries have between 1 and 2. The average number of CRT implantations per year for a centre is usually low, only the Czech Republic, Denmark, France, Israel,



**Figure 1** The 41 countries included in this analysis are Armenia, Austria, Belarus, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Egypt, Estonia, Finland, France, Georgia, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Latvia, Lebanon, Lithuania, Luxembourg, FYROM, Netherlands, Norway, Poland, Portugal, Romania, Russia, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Tunisia, Turkey, and UK (coloured in dark blue).

the Netherlands, Russia, Serbia, and the UK have more than 50 patients implanted per year. Most implants are now performed by cardiologists. Almost each country developed national PM/ICD guidelines and/or adheres to European or American guidelines, with the exception of Israel as of 2008.

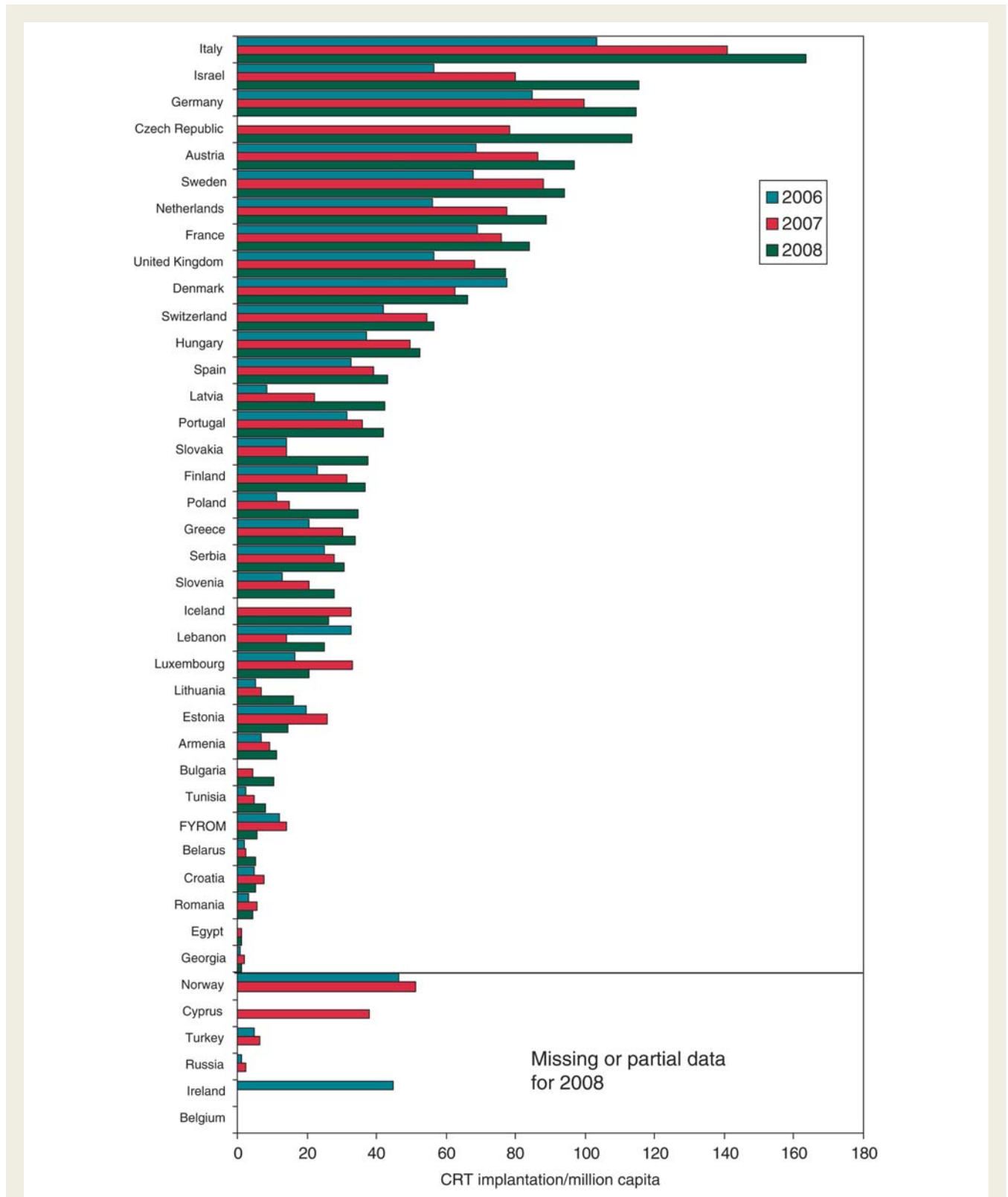
## Factors affecting the number of CRT implantations

The number of CRT implantations and the growth between 2006 and 2008 is higher in countries, where the devices are reimbursed or who adhere to a national guideline (Table 4).

While countries with higher GDP or healthcare spending per capita generally had a higher number of implantations, due to

large variations the correlation between these factors and the number of CRT implantations was weak. There is stronger correlation between per capita CRT implantations and the number of ICD implantations (Figure 3, Table 4). Similarly, the ratio of dual-chamber pacemaker implantations, the general availability of governmental or public insurance, or cardiologist-performed procedures have minimal or no correlation with the number of CRT implantations. Both the growth of CRT implantations and the higher ratio of CRT-D correlated mostly with the number of ICD implantations (Table 4).

Multiple regression analysis showed that the number of CRT implantations per capita was significantly affected by local CRT reimbursement ( $P = 0.023$ ), number of CRT centres per capita



**Figure 2** Number of CRT implantations between 2006 and 2008.

( $P < 0.001$ ), adherence to national guidelines ( $P = 0.002$ ), and adherence to European or US guidelines (negative effect,  $P < 0.001$ ). Accredited electrophysiology subspecialty and healthcare spending per capita were not significant factors ( $P = 0.668$  and

$P = 0.899$ , respectively). As of note, only a very few countries, each one with a high implantation rate, indicated that they follow national guidelines only (Czech Republic, Denmark, UK; Israel denied both).

**Table 1** Pacemaker, ICD, and CRT implantation data 2006–2008

	PM/mil pop 2008	Change 2006– 2008, PM/mil pop	DDD PM 2007 (%)	CRT/mil pop 2008	Change 2006– 2008, CRT/mil pop	CRT-D% 2008	ICD/mil pop 2008	Change 2006– 2008, ICD/mil pop
Armenia	100.4	10.1	n.a.	11.5	4.7	85	34.7	18.5
Austria	922.5	32.2	64	96.9	28.3	70	134.1	25.0
Belarus	161.5	–1.6	n.a.	5.2	3.1	50	4.1	3.6
Belgium	833.1 <sup>a</sup>	–224.1 <sup>a</sup>	n.a.	n.a.	n.a.	n.a.	153.8	28.8
Bulgaria	335.6	32.2 <sup>a</sup>	16	10.6	6.1 <sup>a</sup>	19	1.2	0.0 <sup>a</sup>
Croatia	482.2	57.4	n.a.	5.1	0.2	9	18.5	6.7
Cyprus	378.5	n.a.	n.a.	n.a.	n.a.	n.a.	44.2	n.a.
Czech Republic	821.9	–27.6	55	113.6	35.4 <sup>a</sup>	58	196.9	70.7
Denmark	737.9	–1.3	63	66.2	–11.1	61	228.8	125.8
Egypt	26.9	n.a.	n.a.	1.3	n.a.	31	0.2	n.a.
Estonia	851.2	142.2	71	14.5	–5.4	5	13.8	2.3
Finland	803.5	154.2	n.a.	36.6	13.5	63	31.5	–50.0
France	983.5	46.1	75	84.0	15.1	61	128.0	62.6
Georgia	60.0	12.7	29	1.3	0.4	100	2.4	1.5
Germany	1 193.4	16.9	67	114.6	30.0	89	262.2	69.5
Greece	711.3	70.8	n.a.	33.8	13.2	75	93.1	55.0
Hungary	470.7	20.6	53	52.5	15.2	42	54.3	16.8
Iceland	896.9	n.a.	n.a.	26.3	n.a.	38	141.3	n.a.
Ireland	441.8 <sup>a</sup>	–104.7 <sup>a</sup>	48	n.a.	n.a.	n.a.	79.2 <sup>a</sup>	–45.5 <sup>a</sup>
Israel	456.8	105.9	41	115.6	59.2	85	108.1	23.3
Italy	1 054.3	108.3	n.a.	163.4 <sup>b</sup>	60.2 <sup>b</sup>	100 <sup>b</sup>	309.6	79.1
Latvia	487.2	126.0	n.a.	42.3	33.8	43	16.9	9.4
Lebanon	93.2	17.6	n.a.	25.2	–7.6	90	27.7	–2.5
Lithuania	561.8	157.9	74	16.0	10.9	4	14.3	9.8
Luxembourg	191.4	63.8	n.a.	20.6	4.1	40	84.4	22.6
FYROM	108.7	18.9	n.a.	5.8	–6.3	17	1.5	–1.9
Netherlands	648.8	62.2	n.a.	88.6	32.4	89	194.5	87.7
Norway	587.8 <sup>a</sup>	162.3 <sup>a</sup>	68	51.2 <sup>a</sup>	5.0 <sup>a</sup>	43 <sup>a</sup>	126.8 <sup>a</sup>	56.4 <sup>a</sup>
Poland	707.8	240.3	37	34.8	23.6	61	91.2	56.2
Portugal	739.6	69.8	55	41.8	10.4	74	68.1	23.9
Romania	105.5	15.9	19	4.5	1.3	24	4.8	1.8
Russia	145.0 <sup>a</sup>	36.6 <sup>a</sup>	32	2.3 <sup>a</sup>	1.2 <sup>a</sup>	6 <sup>a</sup>	2.3 <sup>a</sup>	1.1 <sup>a</sup>
Serbia	461.3	2.7	n.a.	30.6	5.7	30	31.3	12.4
Slovakia	490.3	29.5	30	37.6	23.3	80	103.4	64.2
Slovenia	547.9	27.9	n.a.	27.9	14.9	34	47.8	9.0
Spain	790.3	80.5	53	43.1	10.3	71	86.1	30.1
Sweden	917.6	37.7	70	94.0	26.3	41	75.2	34.2
Switzerland	710.7	45.5	64	56.6	14.8	69	155.5	98.4
Tunisia	134.8	37.6	58	7.9	5.5	33	6.1	2.2
Turkey	69.5 <sup>a</sup>	0.0 <sup>a</sup>	n.a.	6.3 <sup>a</sup>	1.4 <sup>a</sup>	33 <sup>a</sup>	12.5 <sup>a</sup>	1.4 <sup>a</sup>
UK	631.7	55.8	n.a.	77.1	20.5	60	73.8	11.5

n.a., no data available.

<sup>a</sup>Data from 2007.<sup>b</sup>CRT-D only, no data for CRT-P.

## Discussion

Cardiac resynchronization therapy with or without a defibrillator is a class I recommendation with a level of evidence 'A' for patients with left ventricular systolic dysfunction (ejection fraction <35%),

symptomatic heart failure despite optimal medical therapy, and a QRS duration of  $\geq 120$  ms, in order to improve survival and reduce morbidity.<sup>10</sup> Based on the great difference in the number of implantations between the countries, it is likely that many patients who would potentially benefit from device therapy do



**Table 2** Demographic, economical, and insurance data

	Pop, million 2008	GDP, Euro/capita	Health expenditure, Euro/capita	Government health expenditure (%)	Public insurance (%)	CRT reimbursement
Armenia	2 968 586	3401	160	41.2	35	Yes
Austria	8 205 533	52 159	5164	77	83	Yes
Belarus	9 658 768	6058	388	74.9	100	Yes
Belgium	10 403 951	49 430	4696	71.1	90	Yes
Bulgaria	7 262 675	6849	473	59.8	63	No
Croatia	4 491 543	14 414	1081	80.1	90	No
Cyprus	792 604	32 195	2028	44.8	70	No
Czech Republic	10 220 911	21 041	1431	87.9	100	Yes
Denmark	5 484 723	67 387	6402	84	100	No
Egypt	81 713 517	2109	133	40.7	54	No
Estonia	1 307 605	18 810	940	74.2	99	Yes
Finland	5 244 749	54 578	4148	78.5	76	Yes
France	64 057 790	48 012	5329	79.7	100	Yes
Georgia	4 630 841	3061	257	21.5	25	Yes
Germany	82 369 548	49 499	5148	76.6	90	Yes
Greece	10 722 816	33 434	3310	42.5	89	Yes
Hungary	9 930 915	16 343	1242	70.8	100	Yes
Iceland	304 367	60 122	5591	83.1	100	No
Ireland	4 156 119	64 660	4849	78.3	32	Yes
Israel	7 112 359	26 536	2070	65.3	94	Yes
Italy	58 145 321	40 450	3640	77.1	100	Yes
Latvia	2 245 423	14 930	896	63.2	90	Yes
Lebanon	3 971 941	7376	656	46.8	60	Yes
Lithuania	3 565 205	14 456	896	70	100	Yes
Luxembourg	486 006	118045	8499	90.6	100	Yes
FYROM	2 061 315	4683	384	71.6	90	No
Netherlands	16 645 313	54 445	5063	81.8	65	Yes
Norway	4 644 457	102525	8920	83.6	100	Yes
Poland	38 500 696	14 893	923	69.9	90	Yes
Portugal	10 676 910	24 031	2403	71.8	85	Yes
Romania	22 246 862	9953	567	71	57	Yes
Russia	140 702 094	12 579	667	63.2	0	Yes
Serbia	7 413 882	7054	536	71	100	Yes
Slovakia	5 455 407	18 585	1301	73.9	75	Yes
Slovenia	2 007 711	28 328	2380	73	85	Yes
Spain	40 491 051	36 970	2995	72.5	100	Yes
Sweden	9 045 389	55 624	4951	81.2	100	Yes
Switzerland	7 581 520	67 379	7614	60.3	34	Yes
Tunisia	10 383 577	4032	214	43.7	80	Yes
Turkey	71 892 807	9629	741	72.3	95	Yes
UK	60 943 912	45 681	3837	87.4	90	Yes

not receive it. On the other hand, there are data that some patients who receive a CRT do not fulfil all the guideline criteria.<sup>16</sup> As guidelines do not necessarily conform strictly to the entry criteria for clinical trials (for instance, the ESC guidelines do not exclude patients with atrial fibrillation), substantial variations in implantation routines may exist, based on economical factors or individual experience. The EHRA and the Heart Failure Association initiated the European CRT survey in 2009 to describe the current

European practice and routines associated with CRT implantations-based sampling in 13 countries. The survey analysed demographics and clinical characteristics, diagnostic criteria, implantation routines and techniques, short-term outcomes, adverse experience, and assessment of adherence to guideline recommendations.<sup>17</sup> It has showed that approximately one-fourth (23%) of the patients had atrial fibrillation and one-fourth of them (26%) had had a device implanted previously. Thirty-one

**Table 3** Local practices in device therapy

	EP subspec	CRT centres/ mil pop, 2008	Average CRT/ centre/year	CRT implantation by cardiologists (%)	National PM/ICD guidelines	US/Euro PM/ICD guidelines
Armenia	No	0.3	34.0	100	No	Yes
Austria	No	7.9	12.2	35	No	Yes
Belarus	Yes	0.2	25.0	0	Yes	Yes
Belgium	No	3.4	n.a.	95	Yes	Yes
Bulgaria	No	0.8	12.8	87.5	No	Yes
Croatia	No	0.9	5.8	80	No	Yes
Cyprus	No	2.5	n.a.	100	No	Yes
Czech Republic	Yes	1.5	77.4	80	Yes	No
Denmark	No	1.3	51.9	100	Yes	No
Egypt	Yes	0.1	18.0	50	Yes	Yes
Estonia	No	1.5	9.5	76	No	Yes
Finland	No	1.5	24.0	95	Yes	Yes
France	No	1.3	63.3	100	Yes	Yes
Georgia	No	0.6	2.0	100	No	Yes
Germany	No	4.0 <sup>a</sup>	28.4 <sup>a</sup>	45	Yes	Yes
Greece	No	1.3	25.9	99	No	Yes
Hungary	Yes	1.2	43.4	93	Yes	Yes
Iceland	No	3.3	8.0	50	No	Yes
Ireland	No	n.a.	n.a.	n.a.	Yes	Yes
Israel	No	1.7	68.5	95	No	No
Italy	No	6.9 <sup>a</sup>	23.8 <sup>a</sup>	99	Yes	Yes
Latvia	Yes	0.9	47.5	60	Yes	Yes
Lebanon	No	2.5	10.0	100	No	Yes
Lithuania	No	0.8	19.0	100	No	Yes
Luxembourg	No	2.1	10.0	100	No	Yes
FYROM	No	0.5	12.0	100	No	Yes
Netherlands	Yes	1.0	86.8	99	Yes	Yes
Norway	No	2.6 <sup>a</sup>	19.8 <sup>a</sup>	100	No	Yes
Poland	Yes	1.4	25.7	99	No	Yes
Portugal	Yes	2.0	21.2	99	No	Yes
Romania	No	0.4	9.9	100	No	Yes
Russia	Yes	0.0	53.3	70	Yes	Yes
Serbia	No	0.5	56.8	100	No	Yes
Slovakia	Yes	1.1	34.2	100	Yes	Yes
Slovenia	No	1.0	28.0	95	No	Yes
Spain	Yes	0.9	47.1	98	Yes	Yes
Sweden	No	2.4	38.6	98	Yes	Yes
Switzerland	No	2.9	19.5	99	Yes	Yes
Tunisia	Yes	0.8	10.3	100	No	Yes
Turkey	No	0.3	18.0	100	No	Yes
UK	No	0.9	88.7	100	Yes	No

The two right columns indicate adherence to local or international device guidelines. In case of missing data the field was left blank.

<sup>a</sup>Data from 2007.

percent of the patients were older than 75 years. Altogether 22% of the patients were in NYHA functional class I or II. In conclusion, the survey data showed that general practice do not adhere to the guidelines strictly and there are major differences with regard to the proportion of elderly patients, presence of atrial fibrillation, or a previous device as compared with the randomized clinical

trials. However, long-term data are needed to evaluate the response to the therapy in this patient population.

There is no easy way to tell what number of CRT implantations would be optimal. With current implantation indications, up to 30% of patients are non-responders, while other patients, who could potentially benefit, may not be included. The surveys

**Table 4** Analysis of factors affecting CRT implantations

	CRT/mil pop 2008	Change 2006–2008, CRT/mil pop	CRT-D of total CRT, 2008
CRT reimbursement			
Yes	48.5 ± 41.2	48.0 ± 80.8	56.6 ± 27.2%
No	19.2 ± 24.6	26.8 ± 24.6	29.0 ± 18.8%
EP subspecialty			
Yes	39.3 ± 34.6	61.3 ± 72.4	53.2% ± 23.8%
No	46.0 ± 43.1	39.4 ± 79.1	51.8% ± 29.9%
National guideline			
Yes	63.5 ± 43.8	25.6 ± 85.2	59.6 ± 23.4%
No	28.0 ± 29.5	63.9 ± 65.5	46.2 ± 30.1%
European or US guideline			
Yes	38.1 ± 37.8	47.2 ± 79.3	50.6 ± 28.7%
No	93.1 ± 25.2	33.2 ± 59.7	65.9 ± 12.9%
% DDD PM	$r = 0.457$	$r = 0.165$	$r = -0.023$
ICD/mil pop	$r = 0.843$	$r = -0.082$	$r = 0.569$
GDP/capita	$r = 0.410$	$r = 0.028$	$r = 0.188$
Health/capita	$r = 0.468$	$r = -0.013$	$r = 0.257$
Gov cost (%)	$r = 0.427$	$r = 0.049$	$r = -0.186$
Publ ins (%)	$r = 0.350$	$r = 0.220$	$r = -0.100$
CRTcentre/mil pop	$r = 0.657$	$r = 0.016$	$r = 0.401$
Avg impl/CRT centre	$r = 0.517$	$r = -0.101$	$r = 0.238$
CRT by cardiologist	$r = 0.023$	$r = 0.093$	$r = 0.111$

Data for dichotomous variables are shown as mean ± standard deviation. Pearson's correlation coefficient ( $r$ ) was calculated for scale variables.

initiated by ESC and its associated organizations will provide detailed data on the epidemiology of CHF and potentially eligible patients.

Clarification of the indications is the subject of several ongoing or recently finished trials.<sup>18,19</sup> The MADIT-CRT trial has shown the effect of CRT in NYHA I, II class patients.<sup>20</sup> Recent publications suggest that patients with a left ventricular ejection fraction of up to 40% and with few or no symptoms may also benefit from CRT.<sup>21</sup> The deleterious effects of chronic right ventricular stimulation have long been identified.<sup>22</sup> Currently a large number of patients with bradycardia indications receive conventional pacemakers and are at risk of developing pacing-induced dyssynchrony and CHF. Initial data are promising that a 'CRT upgrade' in this population can be similarly effective as with patients with conventional CRT indications.<sup>23</sup> The BIOPACE clinical trial investigates the use of CRT in high-degree AV block in a general population.<sup>24</sup> In the case of a positive outcome, the number of patients eligible for CRT may increase significantly, similar to the sudden increase in ICD implantations when the results of primary prevention trials were incorporated into guidelines. However, in addition to the cost, the high complexity of CRT implantation and the relatively low number of procedures per centre, with lack of experience (possibly also because of the low number of EP subspecialists) may also limit the number of implantations.

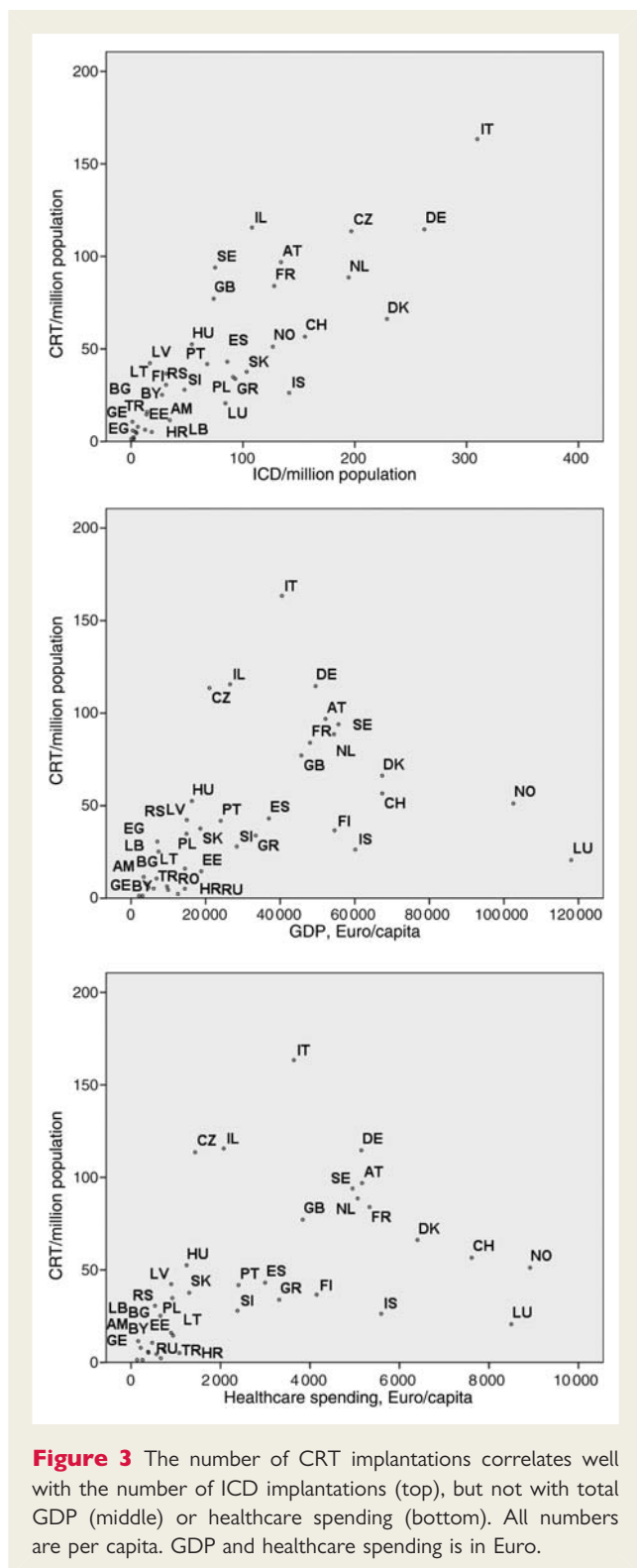
The issue of cost-efficiency of CRT has been addressed in several papers.<sup>18,19</sup> CRT-P appears a highly cost-effective addition to medical therapy among eligible patients. CRT-D is cost-effective when there is a reasonable life expectancy at the time of

implantation. CRT was shown to be cost-effective even in the ninth decade.<sup>19</sup> The question whether CRT-D or CRT-P will be more cost-efficient in a given patient group will need to be determined in future studies. Cost-efficiency data are essential to convince the local healthcare insurers to reimburse CRT, and this seems to be a major factor describing the differences between European countries.

Implantation of a transvenous CRT device is a technically demanding task which requires significant expertise and may require new invasive methods to apply.<sup>25</sup> All the large randomized clinical trials (COMPANION, CARE-HF, REVERSE) showed a failure rate to implant the device of 5–10%.<sup>26–28</sup> European data show that having an accredited electrophysiology subspecialty only has a very modest effect on the number of CRT implantations. This may be due to different requirements for certification or high number of implantations performed by non-electrophysiologists even when such a subspecialty exists in a country. More studies will be needed to investigate this finding.

In addition, the number of CRT devices implanted per centre may highly influence the success rate. Beyond reimbursement, the fact that the number of CRT implantations have a better correlation with ICD implantations than with financial indicators like GDP or healthcare spending, may suggest that the limitations for widespread utilization of CRT are mainly technical and not economical (physicians who can perform ICD implantations may also consider implanting CRT-D when indicated). Therefore, the education of device therapy treatment and the implantation procedure has to be focused upon to increase the number of





**Figure 3** The number of CRT implantations correlates well with the number of ICD implantations (top), but not with total GDP (middle) or healthcare spending (bottom). All numbers are per capita. GDP and healthcare spending is in Euro.

implantations. European standards such as the EHRA individual accreditation in Cardiac Pacing and ICDs (and CRT) may help this process. The aim is to ensure an equal access to this highly efficient and cost-effective treatment and to have CRT devices implanted by qualified electrophysiologists in all European countries.

## Limitations

The EHRA White Book survey was not able to provide complete data for all 51 ESC countries. The data represent a reasonable percentage of the actual procedures but certainly not the absolute reality, since even the best national or international registries do not cover 100% of the interventions. However, the correctness of data were authorized by each national chair or president and in case of estimates, they are very close to what can be expected. Benchmarking testing had not been conducted. There has been no negative feedback over the last 2 years after publication of the White Book, although there is open access to the data. There were no indications of mistakes or changes by national societies during the last 2 years, which makes us confident that the data represent each country's reality at best.

## Conclusion

The joint effort of the ESC and EHRA highlighted the significant variation in local utilization of CRT. These differences might not only be explained by the unequal financial realities of the countries, but also by variations in reimbursement and guideline adherence.

## Funding

The whole EHRA White Book project was made possible by an unrestricted educational grant from Biotronik GMBH, Berlin, Germany. The article has been granted an unrestricted educational grant of TÁMOP (Social Renewal Operative Program) 4.2.2-08/1/KMR (National Development Agency, Hungary).

**Conflict of interest:** Biotronik GMBH provided funding for the project.

## References

- Lloyd-Jones DM, Larson MG, Leip EP, Beiser A, D'Agostino RB, Kannel WB *et al.* Lifetime risk for developing congestive heart failure: the Framingham Heart Study. *Circulation* 2002;**106**:3068–72.
- Levy D, Kenchaiah S, Larson MG, Benjamin EJ, Kupka MJ, Ho KKL *et al.* Long-term trends in the incidence of and survival with heart failure. *N Engl J Med* 2002;**347**: 1397–402.
- Roger VL, Weston SA, Redfield MM, Hellermann-Homan JP, Killian J, Yawn BP *et al.* Trends in heart failure incidence and survival in a community-based population. *JAMA* 2004;**292**:344–50.
- Russell SD, Miller LW, Pagani FD. Advanced heart failure: a call to action. *Congest Heart Fail* 2008;**14**:316–21.
- Kass DA. An epidemic of dyssynchrony: but what does it mean? *J Am Coll Cardiol* 2008;**51**:12–7.
- Cazeau S, Ritter P, Bakdach S, Lazarus A, Limousin M, Heno L *et al.* Four chamber pacing in dilated cardiomyopathy. *Pacing Clin Electrophysiol* 1994;**17**: 1974–9.
- Bakker PF, Meijburg HW, de Vries JW, Mower MM, Thomas AC, Hull ML *et al.* Biventricular pacing in end-stage heart failure improves functional capacity and left ventricular function. *J Interv Card Electrophysiol* 2000;**4**:395–404.
- Swedberg K, Cleland J, Dargie H, Drexler H, Follath F, Komajda M *et al.* Guidelines for the diagnosis and treatment of chronic heart failure: executive summary (update 2005): the Task Force for the diagnosis and treatment of chronic heart failure of the European Society of Cardiology. *Eur Heart J* 2005; **26**:1115–40.
- Dickstein K, Cohen-Solal A, Filippatos G, McMurray JJV, Ponikowski P, Poole-Wilson PA *et al.* ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the diagnosis and treatment of acute and chronic heart failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM). *Eur Heart J* 2008;**29**:2388–442.

10. Vardas PE, Auricchio A, Blanc J, Daubert J, Drexler H, Ector H *et al*. Guidelines for cardiac pacing and cardiac resynchronization therapy: the Task Force for cardiac pacing and cardiac resynchronization therapy of the European Society of Cardiology. Developed in collaboration with the European Heart Rhythm Association. *Eur Heart J* 2007;**28**:2256–95.
11. Epstein AE, DiMarco JP, Ellenbogen KA, Freedman RA, Gettes LS, Gillinov AM *et al*, Estes NAM3. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices) developed in collaboration with the American Association for Thoracic Surgery and Society of Thoracic Surgeons. *J Am Coll Cardiol* 2008;**51**:e1–62.
12. Dickstein K, Bogale N, Priori S, Auricchio A, Cleland JG, Gitt A *et al*. The European cardiac resynchronization therapy survey. *Eur Heart J* 2009;**30**:2450–60.
13. van Veldhuisen DJ, Maass AH, Priori SG, Stolt P, van Gelder IC, Dickstein K *et al*. Implementation of device therapy (cardiac resynchronization therapy and implantable cardioverter defibrillator) for patients with heart failure in Europe: changes from 2004 to 2008. *Eur J Heart Fail* 2009;**11**:1143–51.
14. The EHRA White Book. July 2008. <http://www.escardio.org/communities/EHRA/publications/Documents/ehra-white-book-2008.pdf>.
15. The EHRA White Book. July 2009. <http://www.escardio.org/communities/EHRA/publications/Documents/ehra-white-book-2009.pdf>.
16. Piccini JP, Hernandez AF, Dai D, Thomas KL, Lewis WR, Yancy CW *et al*. Use of cardiac resynchronization therapy in patients hospitalized with heart failure. *Circulation* 2008;**118**:926–33.
17. CRT Survey Scientific Committee. European cardiac resynchronization therapy survey: rationale and design. *Eur J Heart Fail* 2009;**11**:326–30.
18. Calvert MJ, Freemantle N, Yao G, Cleland JGF, Billingham L, Daubert J *et al*. Cost-effectiveness of cardiac resynchronization therapy: results from the CARE-HF trial. *Eur Heart J* 2005;**26**:2681–8.
19. Yao G, Freemantle N, Calvert MJ, Bryan S, Daubert J, Cleland JGF. The long-term cost-effectiveness of cardiac resynchronization therapy with or without an implantable cardioverter-defibrillator. *Eur Heart J* 2007;**28**:42–51.
20. Moss AJ, Hall WJ, Cannom DS, Klein H, Brown MW, Daubert JP *et al*, Estes NAM3. Cardiac-resynchronization therapy for the prevention of heart-failure events. *N Engl J Med* 2009;**361**:1329–38.
21. Cleland JGF, Freemantle N, Daubert J, Toff WVD, Leisch F, Tavazzi L. Long-term effect of cardiac resynchronization in patients reporting mild symptoms of heart failure: a report from the CARE-HF study. *Heart* 2008;**94**:278–83.
22. Wilkoff BL, Cook JR, Epstein AE, Greene HL, Hallstrom AP, Hsia H *et al*. Dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator: the dual chamber and VVI implantable defibrillator (DAVID) trial. *JAMA* 2002;**288**:3115–23.
23. Delnoy PP, Ottervanger JP, Luttikhuis HO, Elvan A, Misier AR, Beukema WP *et al*. Long-term clinical response of cardiac resynchronization after chronic right ventricular pacing. *Am J Cardiol* 2009;**104**:116–21.
24. Funck RC, Blanc J, Mueller H, Schade-Brittinger C, Bailleul C, Maisch B. Biventricular stimulation to prevent cardiac desynchronization: rationale, design, and endpoints of the 'biventricular pacing for atrioventricular block to prevent cardiac desynchronization (BioPace)' study. *Europace* 2006;**8**:629–35.
25. Szilagyi S, Merkely B, Roka A, Zima E, Fulop G, Kutyla V *et al*. Stabilization of the coronary sinus electrode position with coronary stent implantation to prevent and treat dislocation. *J Cardiovasc Electrophysiol* 2007;**18**:303–7.
26. Bristow MR, Saxon LA, Boehmer J, Krueger S, Kass DA, De Marco T *et al*. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. *N Engl J Med* 2004;**350**:2140–50.
27. Cleland JGF, Daubert J, Erdmann E, Freemantle N, Gras D, Kappenberger L *et al*. The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med* 2005;**352**:1539–49.
28. Linde C, Abraham WT, Gold MR, St John Sutton M, Ghio S, Daubert C. Randomized trial of cardiac resynchronization in mildly symptomatic heart failure patients and in asymptomatic patients with left ventricular dysfunction and previous heart failure symptoms. *J Am Coll Cardiol* 2008;**52**:1834–43.