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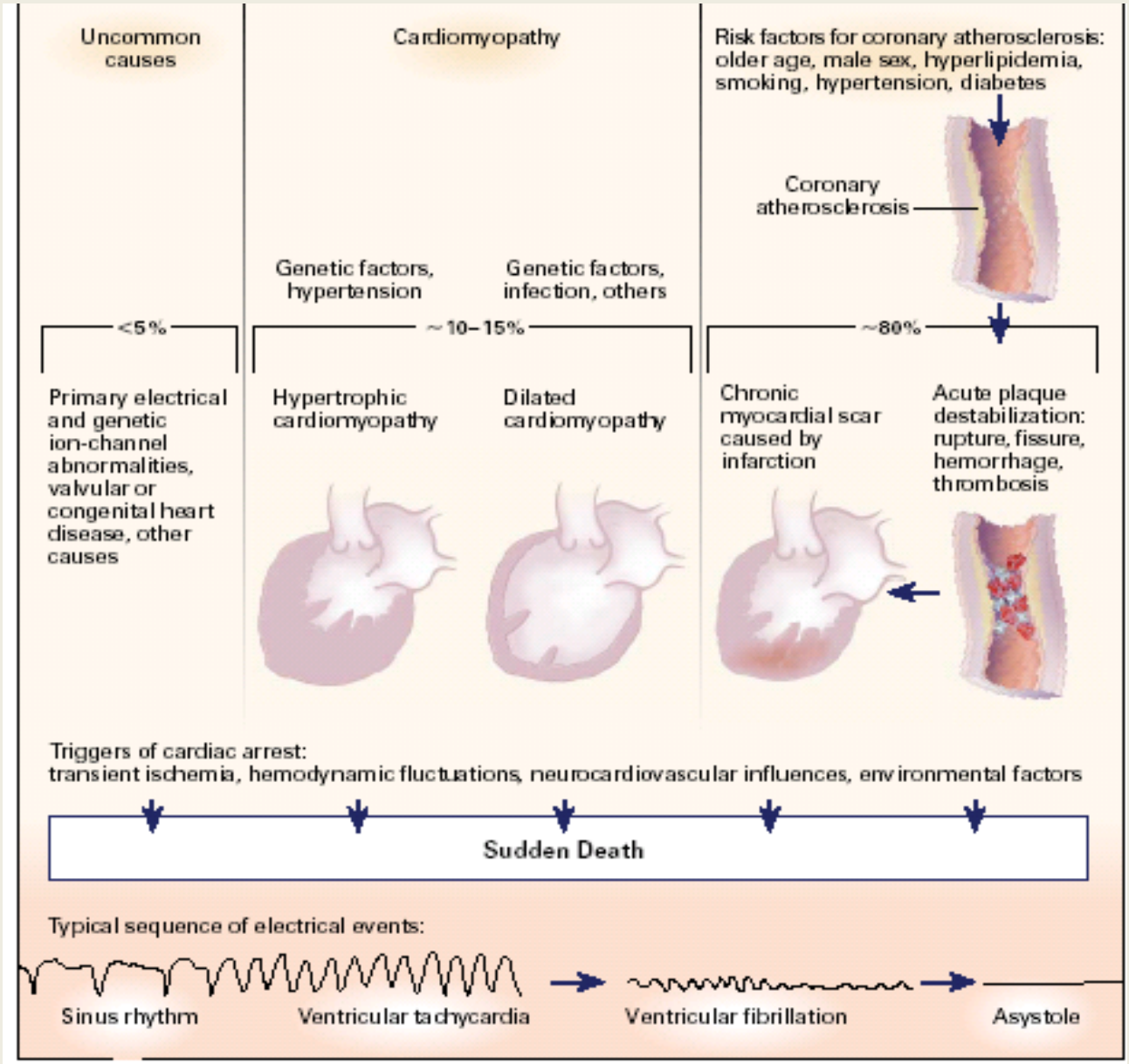
Primary Prevention of Sudden death:
Guidelines and critical review of the trials

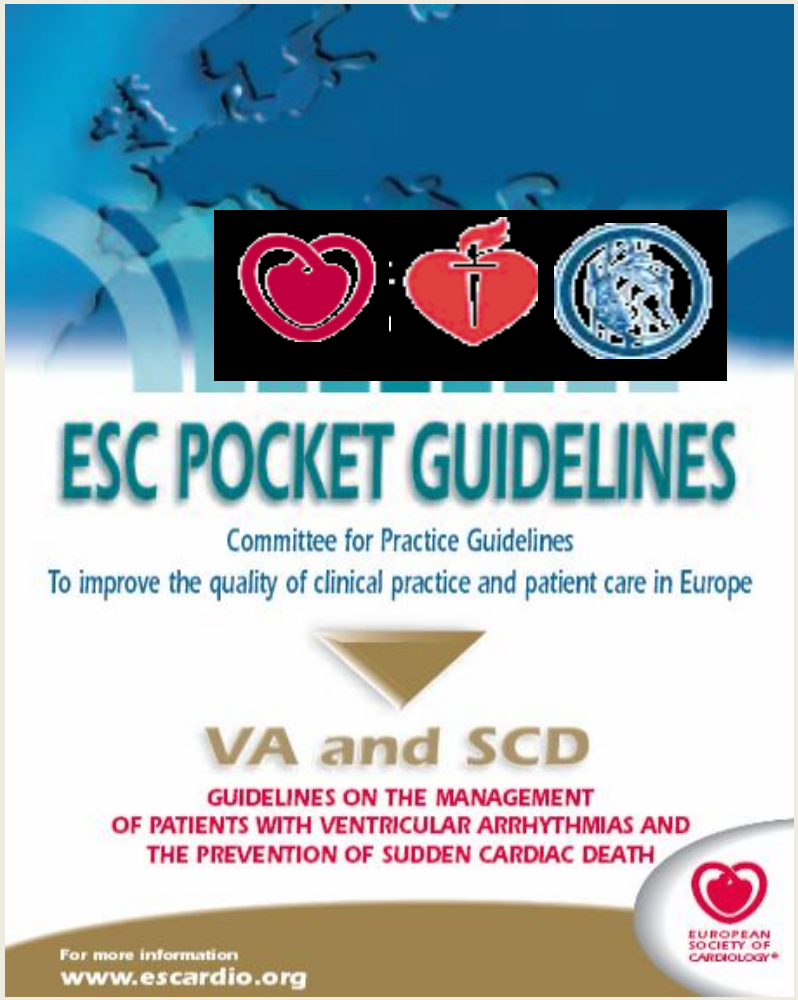
Prof. Dr. Martin Borggrefe
Mannheim

Advances in Cardiovascular Arrhythmias
and Great Innovations in Cardiology
Turin, October 20-22, 2011

Pathophysiology and Epidemiology of SCD



Huikuri et al.
N Engl J Med, 2001; 345:1473-1482



Ventricular Arrhythmias and Sudden Cardiac Death Guidelines

ACC/AHA/ESC

Zipes et al. Circulation 2006; 114: e385 - e484.

ACC/AHA/ESC 2006

Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death

Douglas P. Zipes, MD, MACC, FAHA, FESC, *Co-Chair*

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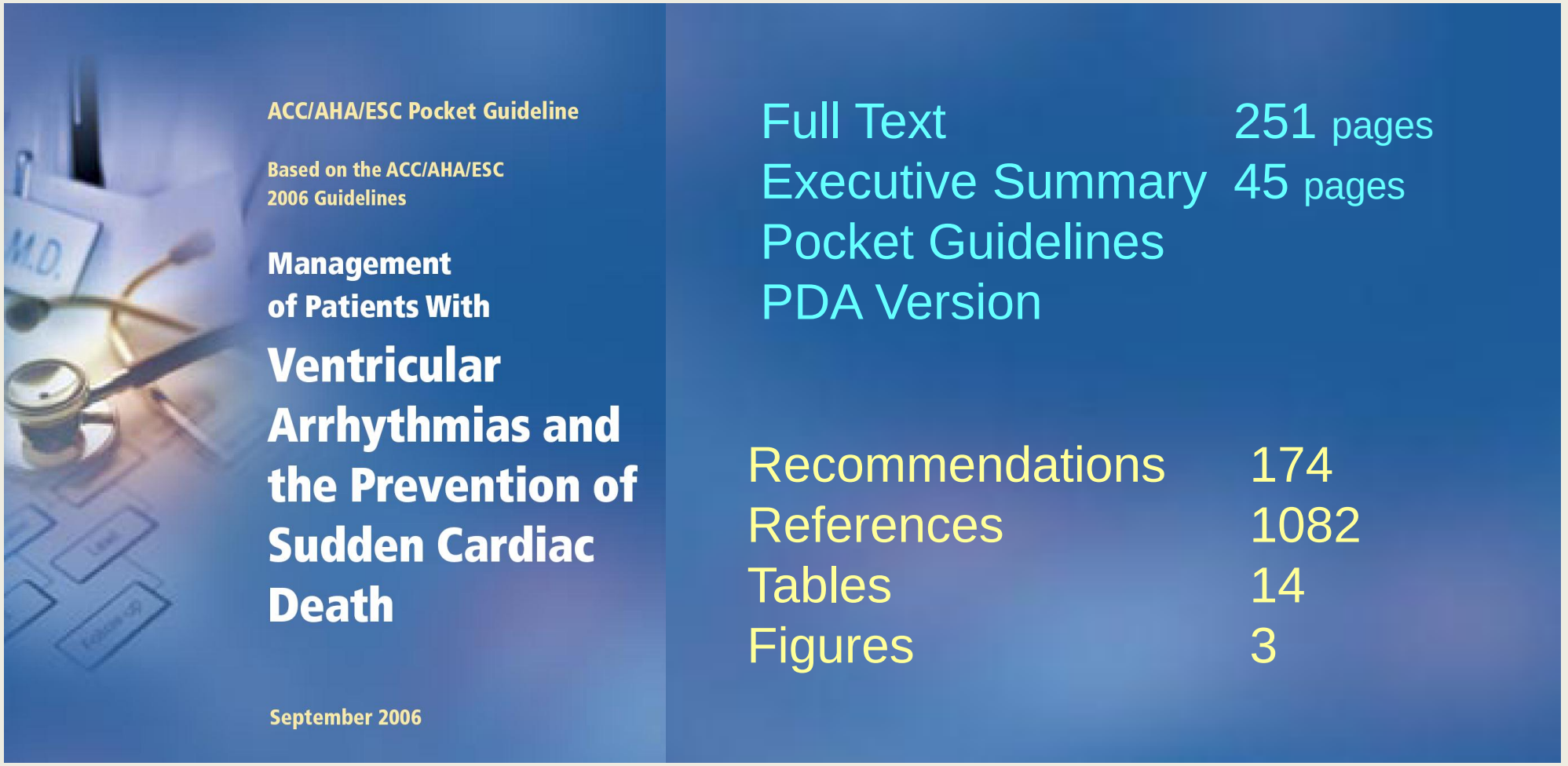
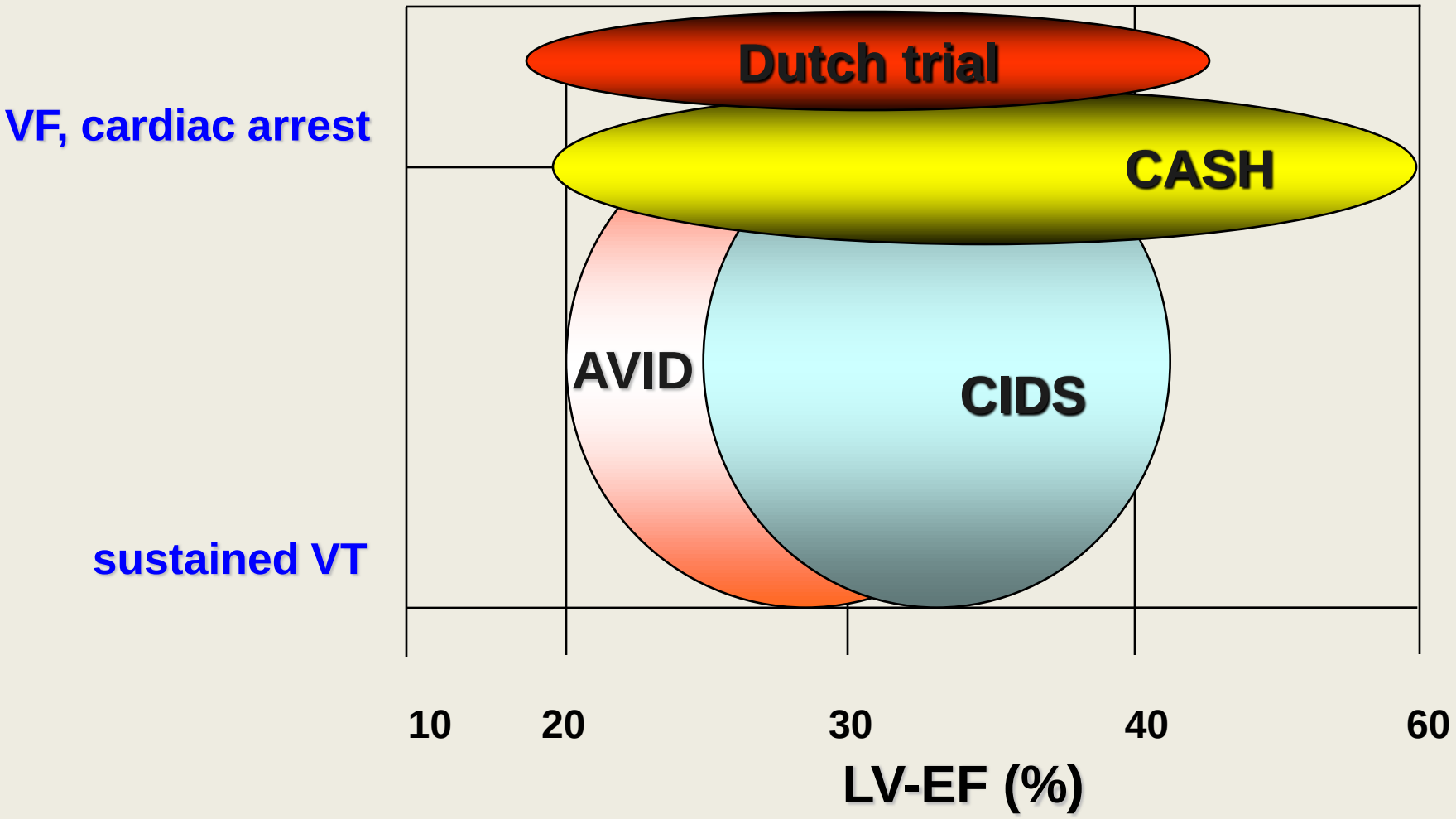
Guideline Statistics



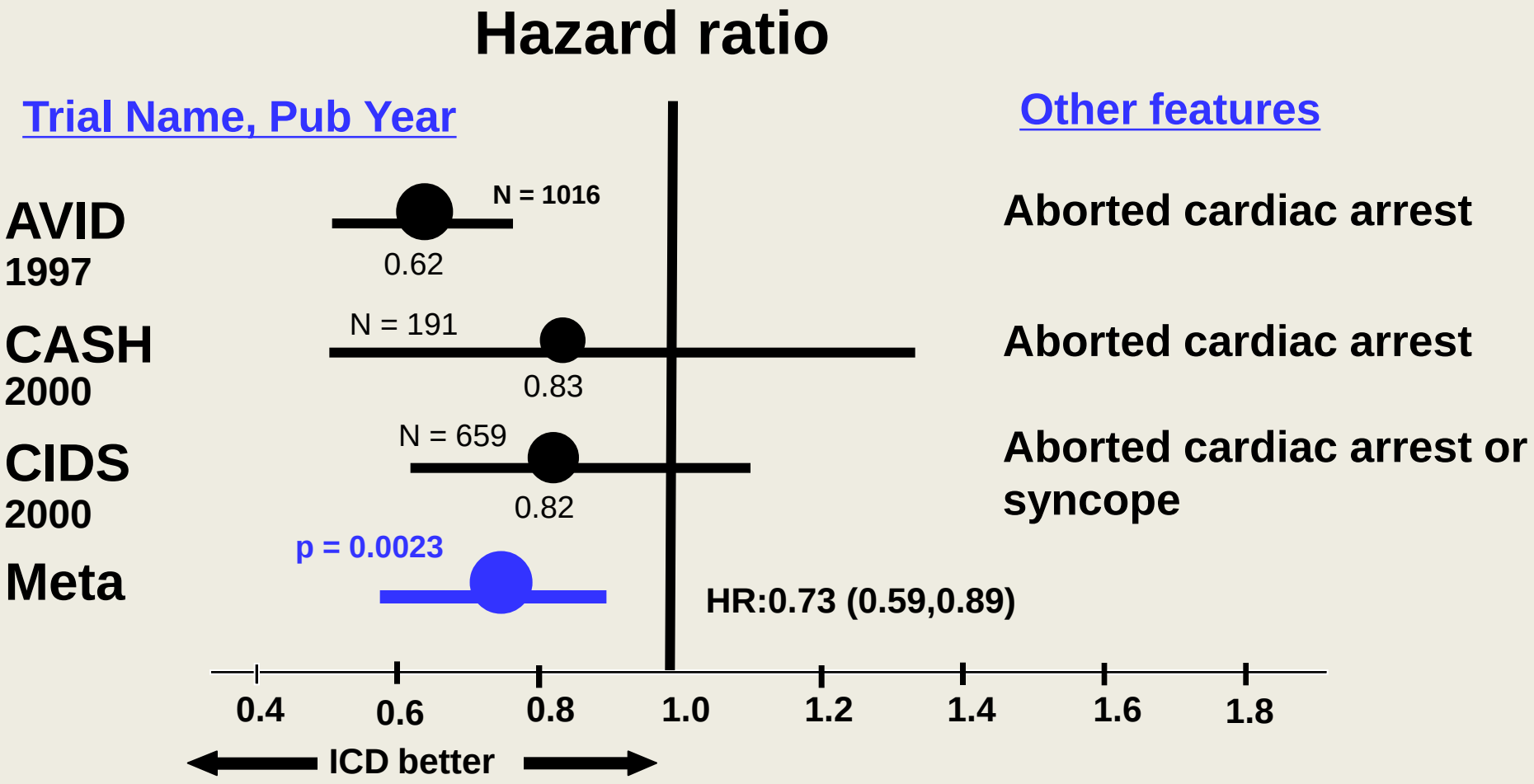
Full Text	251 pages
Executive Summary	45 pages
Pocket Guidelines	
PDA Version	

Recommendations	174
References	1082
Tables	14
Figures	3

ICD Trials - Secondary prophylaxis



Summary of 2^0 Prevention Trials



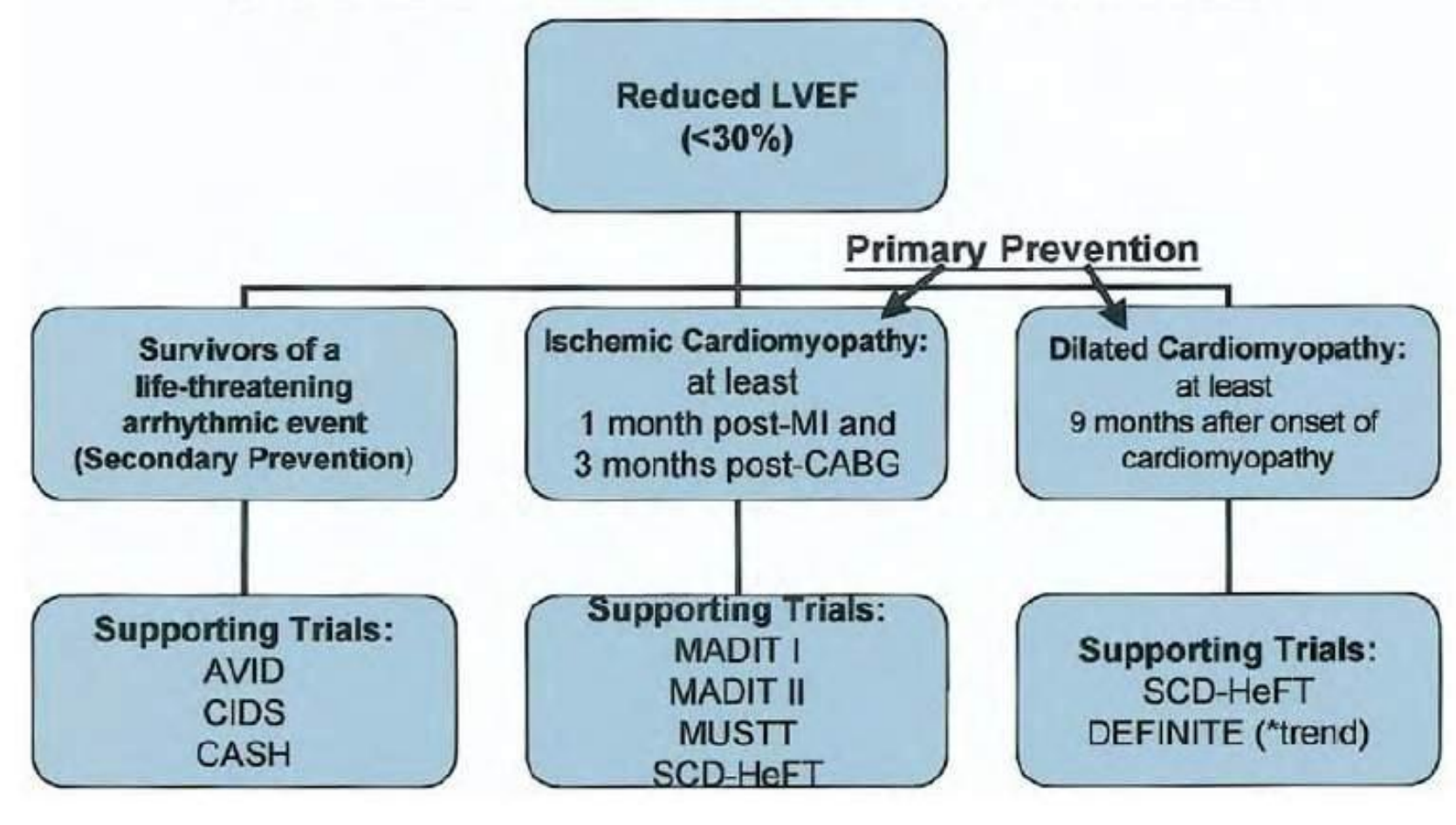
Recommendations for 2^0 Prevention

- Class I Recommendations

  The ICD is effective therapy to reduce mortality by a reduction in SCD in patients with LVD due to prior MI who present with ***hemodynamically unstable sustained VT***, who are receiving chronic optimal medical therapy, and who have reasonable ***expectation of survival with a good functional status for more than 1 year*** (Level of Evidence: A)

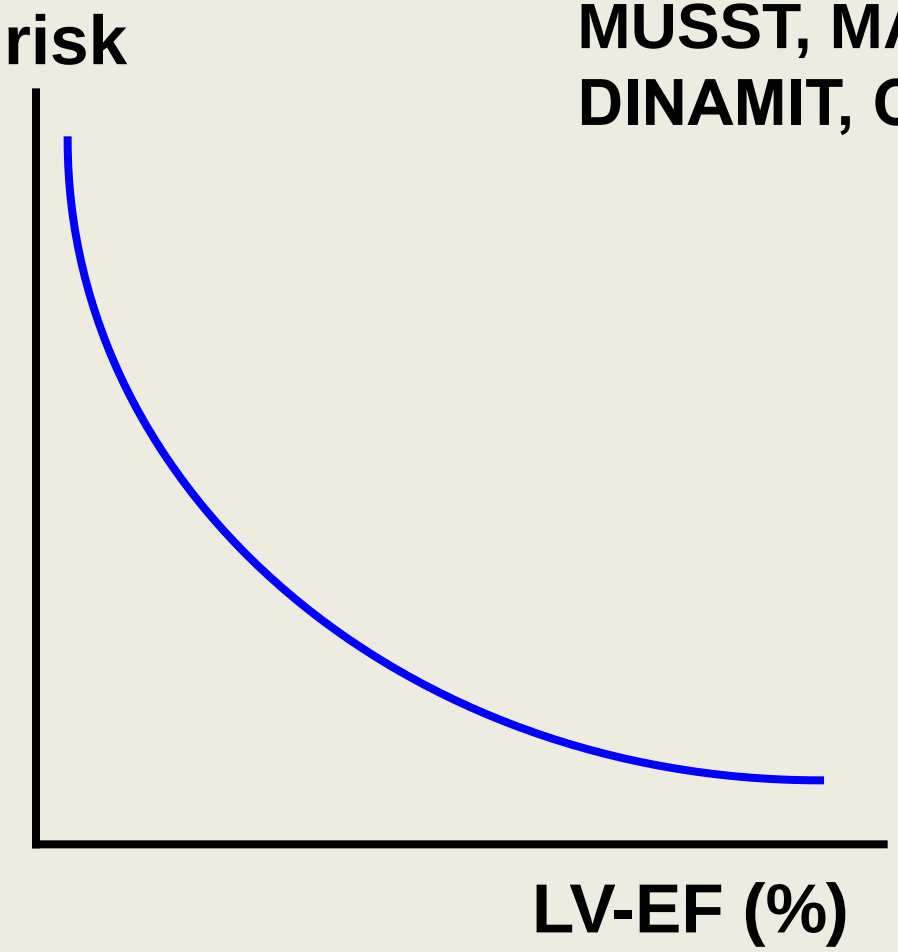
  An ICD should be implanted in patients with ***non-ischemic DCM and significant LVD who have sustained VT or VF***, who are receiving chronic optimal medical therapy, and who have reasonable expectation of survival with a good functional status for more than 1 year (Level of Evidence: A)

Reduced EF and ICD Indications



Cesario and Dec, J Am Coll Cardiol 2006;47:1507–17

LV-function as predictor of SCD

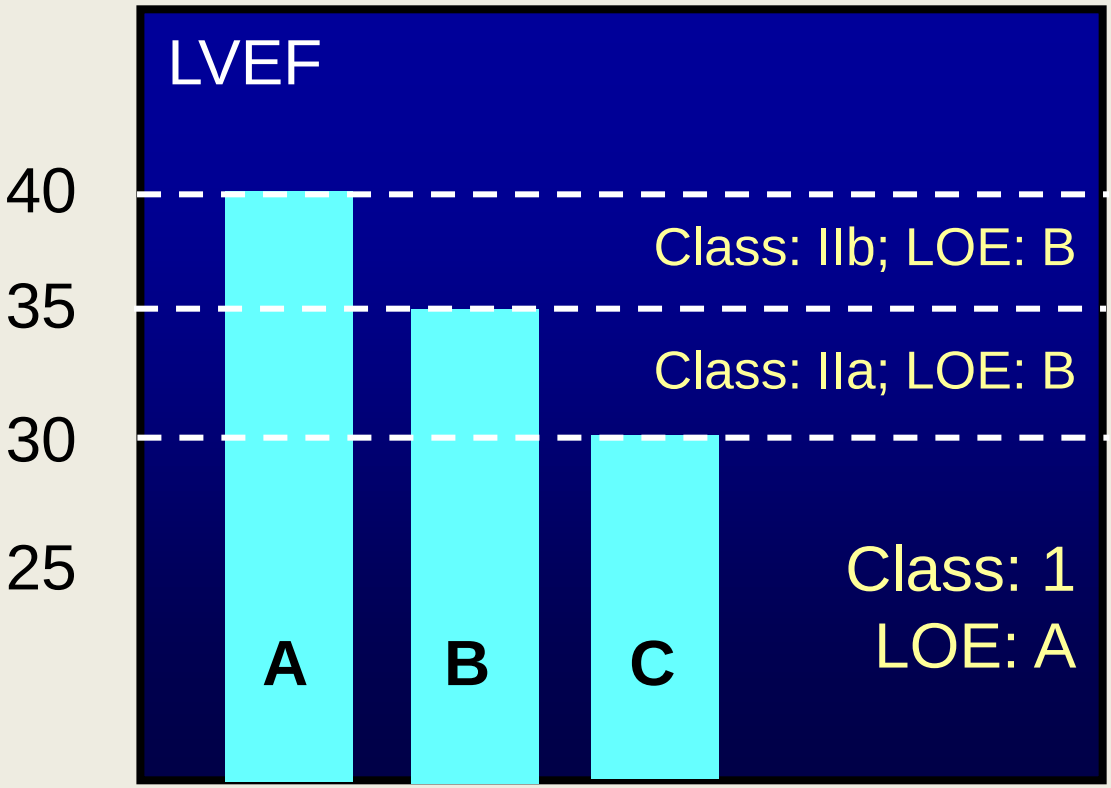


MUSST, MADIT, MADIT-2, SCD-HeFT
DINAMIT, COMPANION, ……

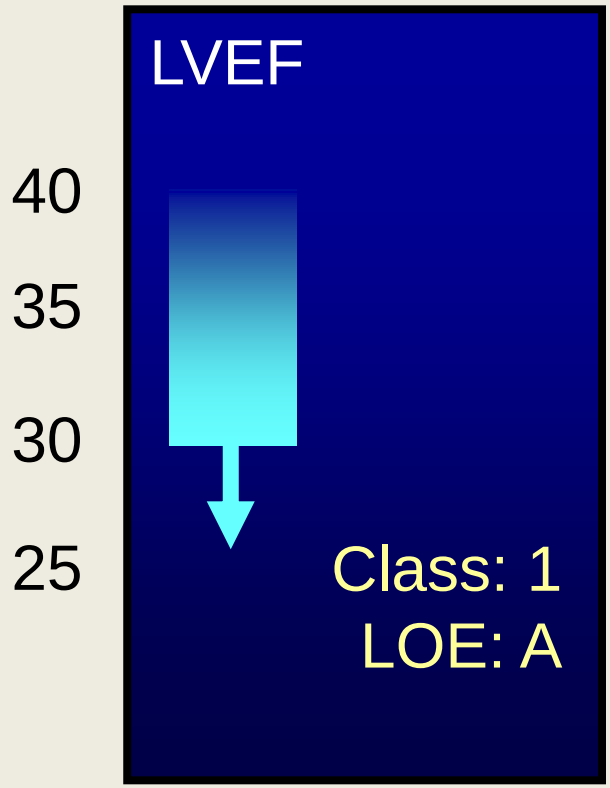
LV-EF is considered as the best parameter for risk stratification after MI

exponential increase of risk of SCD below EF 35-40%

Principle of Guidelines



- Multiple trials with EF < 30%
- No trials of EF 30-35% or 35-40%



- EF difficult to measure

ICD Therapy in CHF

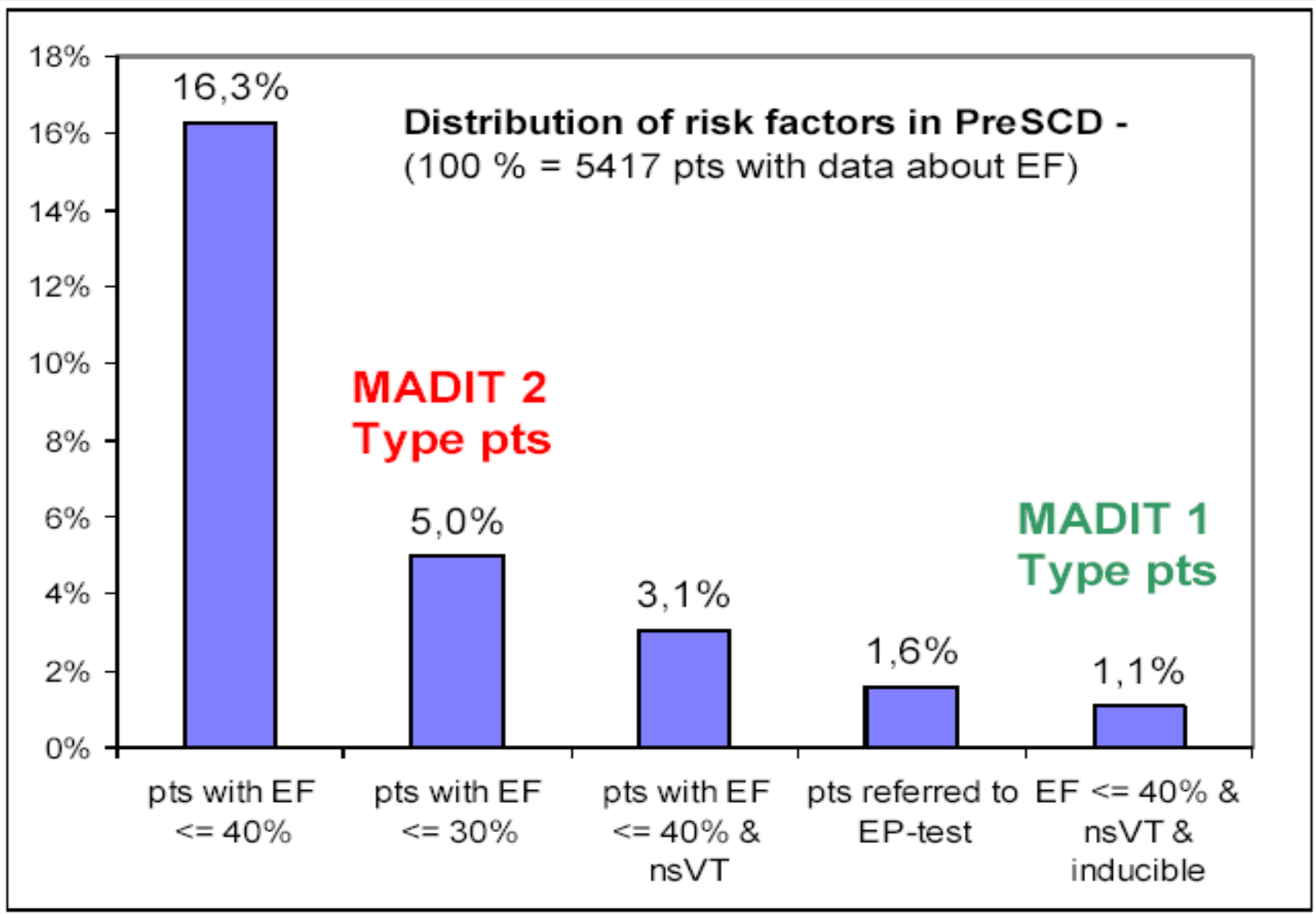
Concerns

- Therapy is expensive
- Burden of painful shocks
- Modest benefit in chronically ill patients (advanced heart disease)
- Relevant complications (late lead failure, replacement of ICD, safety advisories from the manufacturer)

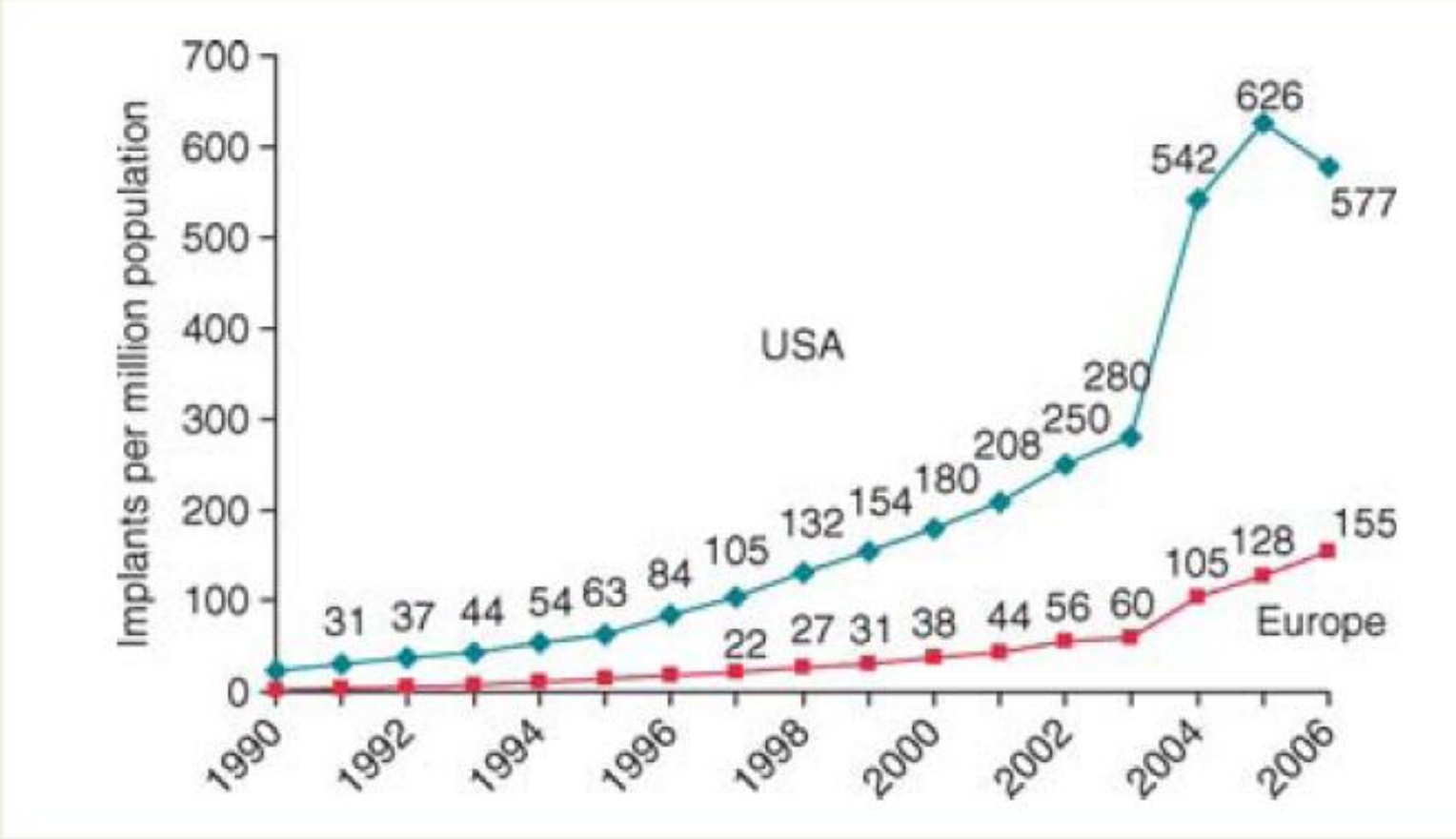
German PreSCD Registry

- **Screening of 5417 Post-MI patients at 41 cardiologists in a private practice or rehabilitation centers spread all over Germany**
- **Screening cascade according to MADIT 1 / MUSTT – criteria**
  - MI > 21 days
  - EF ≤ 40%
  - Holter-ECG (nsVT ≥ 3 beats
  - Exclusion of ischemia
- **Referral to tertiary centres for EP-testing**

MADIT 2 patients outnumber MADIT 1 patients by a factor of 5



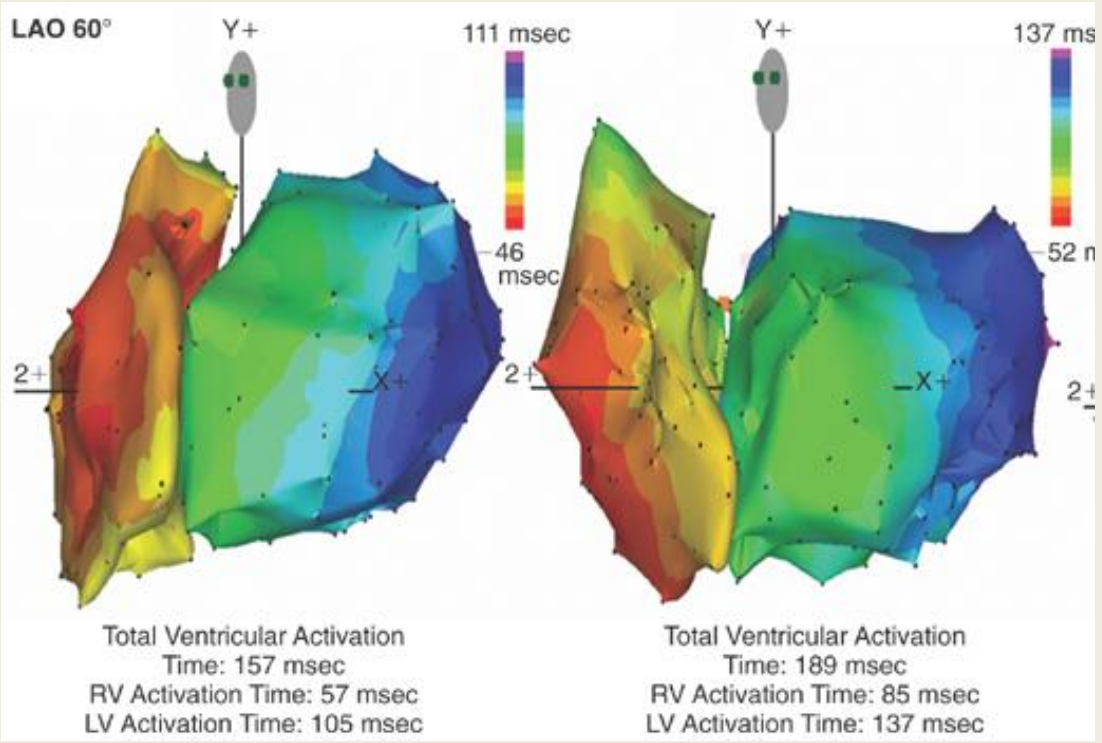
ICD/CRT-D implantations per million of population in Europe and the USA in 1990 - 2006



Camm and Nisam, Europace 2010; 12:1063-1069

Left Bundle Brunch Block

Left Bundle Brunch Block

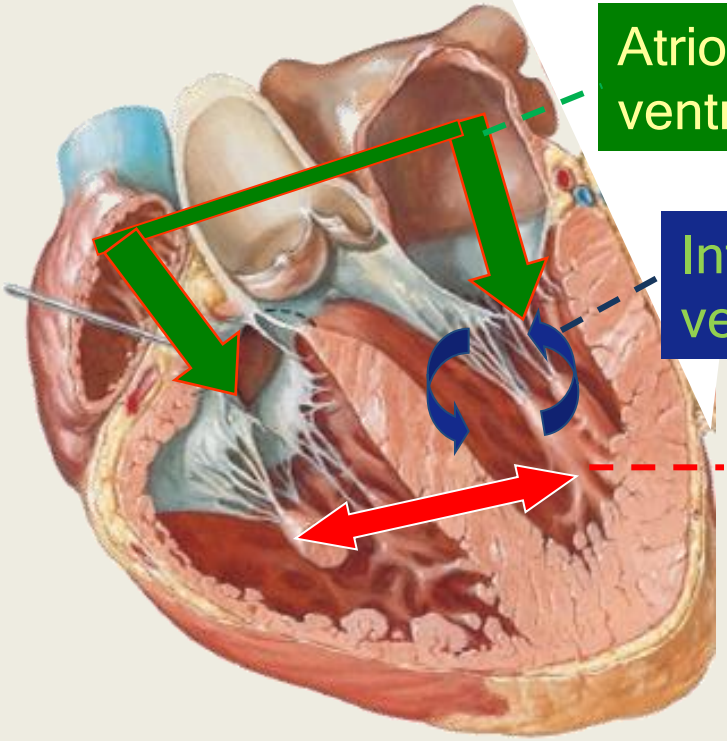


Color coded electroanatomic isochromal maps

Aproximately 30% of heart failure patients

Cardiac Resynchronization Therapy (CRT)

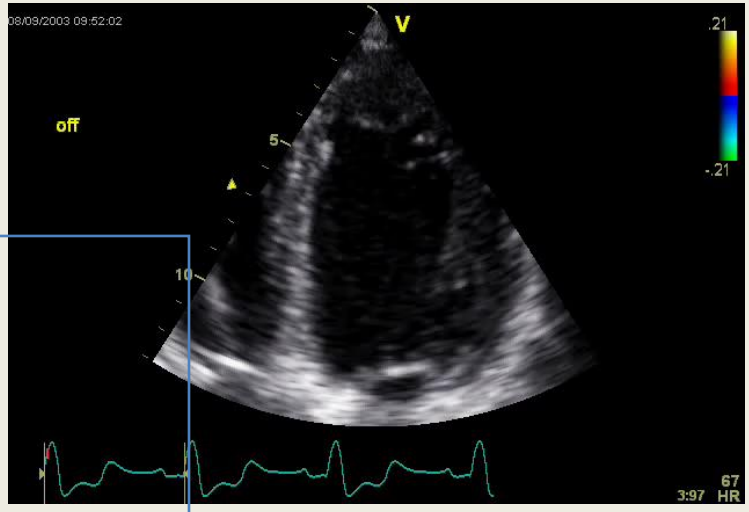
Elements of Cardiac Dyssynchrony

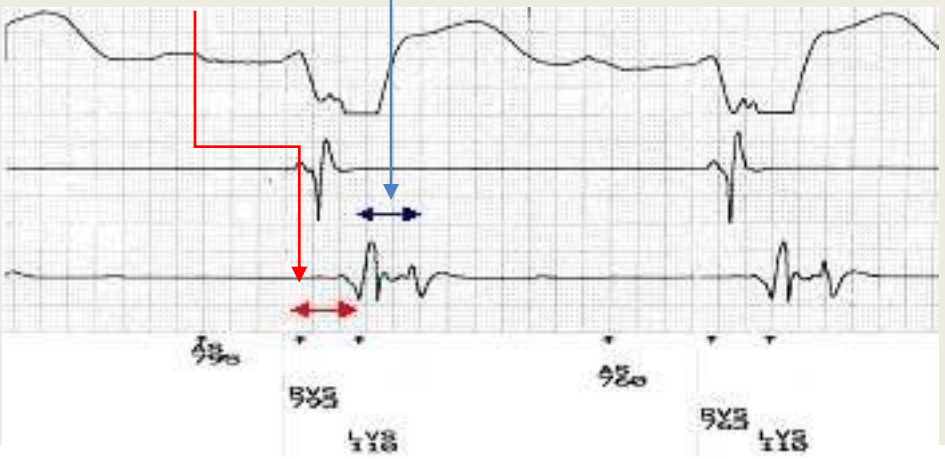


Atrio-ventricular

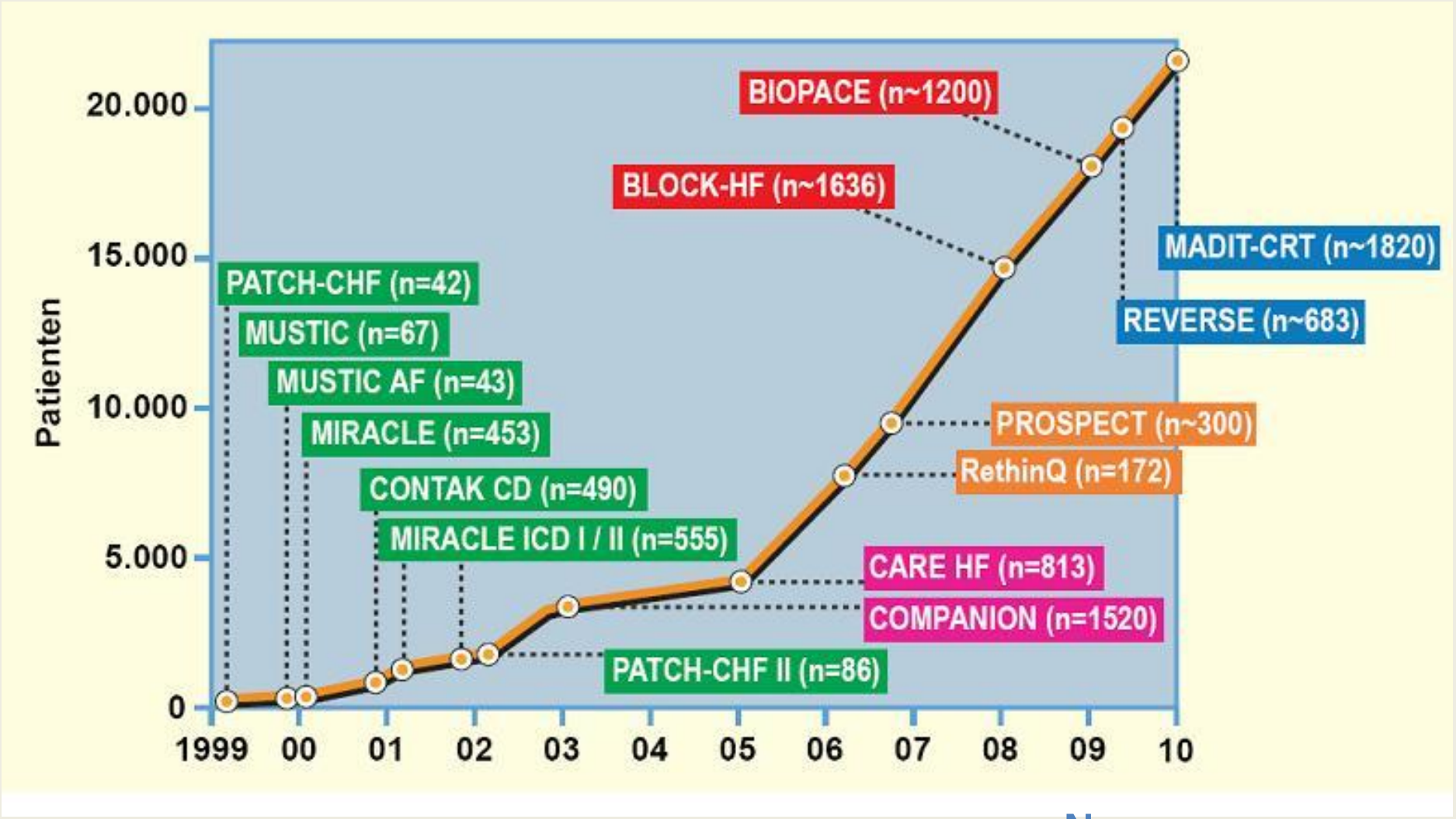
Intra-ventricular

Inter-ventricular





CRT – Clinical Trials



Symptoms | Mortality | New Indikations

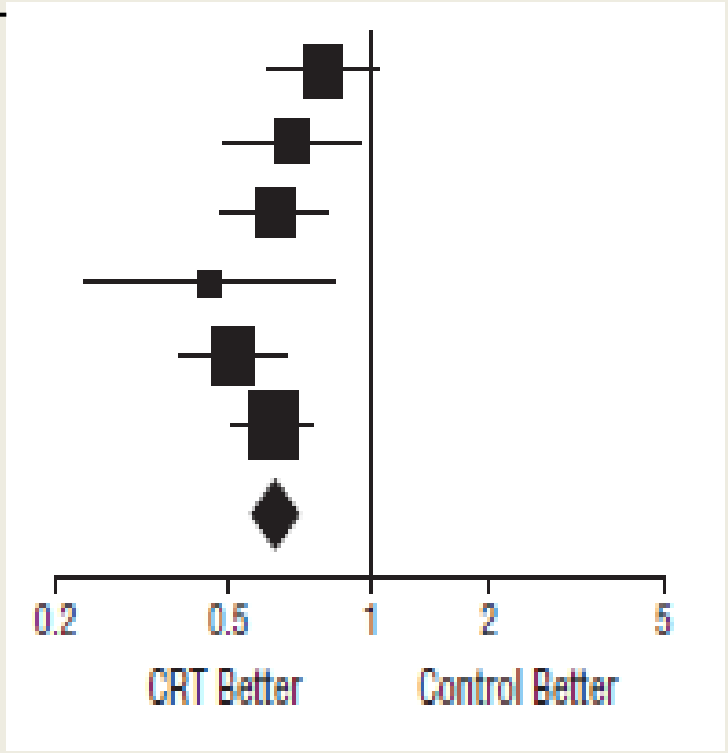
Effects of CRT

- Mortality ↓
- Hospitalization ↓
- Functional Status ↑
- Quality of Life ↑
- Reverse Remodeling

Cardiac Resynchronization Therapy (CRT)

Outcome and QRS duration

	Statistics for each study		
	RR (95% CI)	*z* Value	*P* Value
COMPANION (QRS, 148-168 ms, n=314)	0.78 (0.59-1.04)	-1.70	.09
COMPANION (QRS, >168 ms, n=287)	0.66 (0.47-0.93)	-2.35	.02
CARE-HF (QRS,>159 ms, n=505)	0.60 (0.46-0.79)	-3.70	<.001
REVERSE (QRS,>151 ms, n=307)	0.42 (0.22-0.81)	-2.61	.009
MADIT-CRT (QRS,>149 ms, n=1175)	0.48 (0.37-0.63)	-5.41	<.001
RAFT (QRS, >149 ms, n=1036)	0.59 (0.48-0.73)	-4.93	<.001
Meta-analysis	0.60 (0.53-0.67)	-8.67	<.001

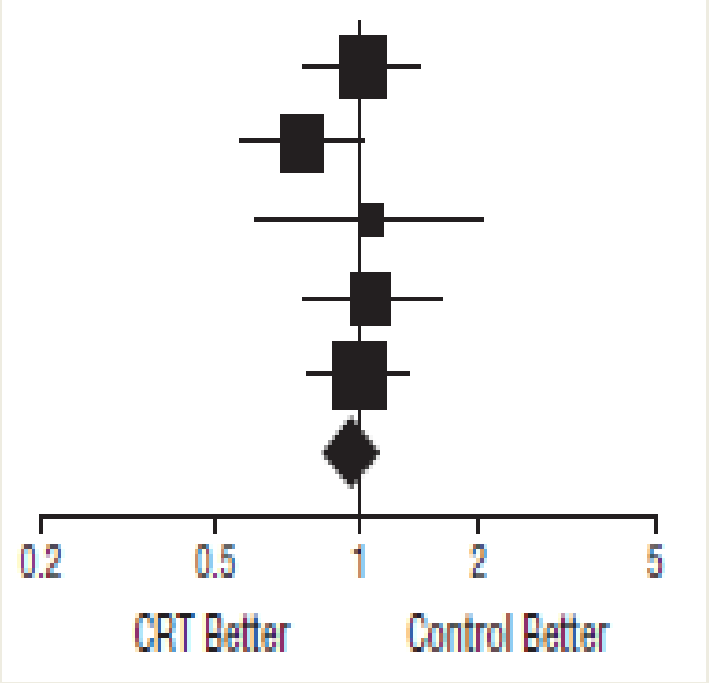


Sipahi et al. Arch Intern Med., Published online June 13, 2011.; doi:10.1001/archinternmed.2011.247

Cardiac Resynchronization Therapy (CRT)

Outcome and QRS duration

	Statistics for each study		
	RR (95% CI)	*z* Value	*P* Value
COMPANION (QRS, 120-147 ms, n=324)	1.01 (0.76-1.35)	0.07	.95
CARE-HF (QRS, 120-159 ms, n=290)	0.74 (0.54-1.02)	-1.86	.06
REVERSE (QRS,120-151ms, n=303)	1.05 (0.58-1.89)	0.16	.87
MADIT-CRT (QRS, 130-149 ms, n=645)	1.06 (0.74-1.52)	0.32	.75
RAFT (QRS, 120-149 ms, n=627)	0.99 (0.77-1.27)	-0.08	.94
Meta-analysis	0.95 (0.82-1.10)	-0.68	.49



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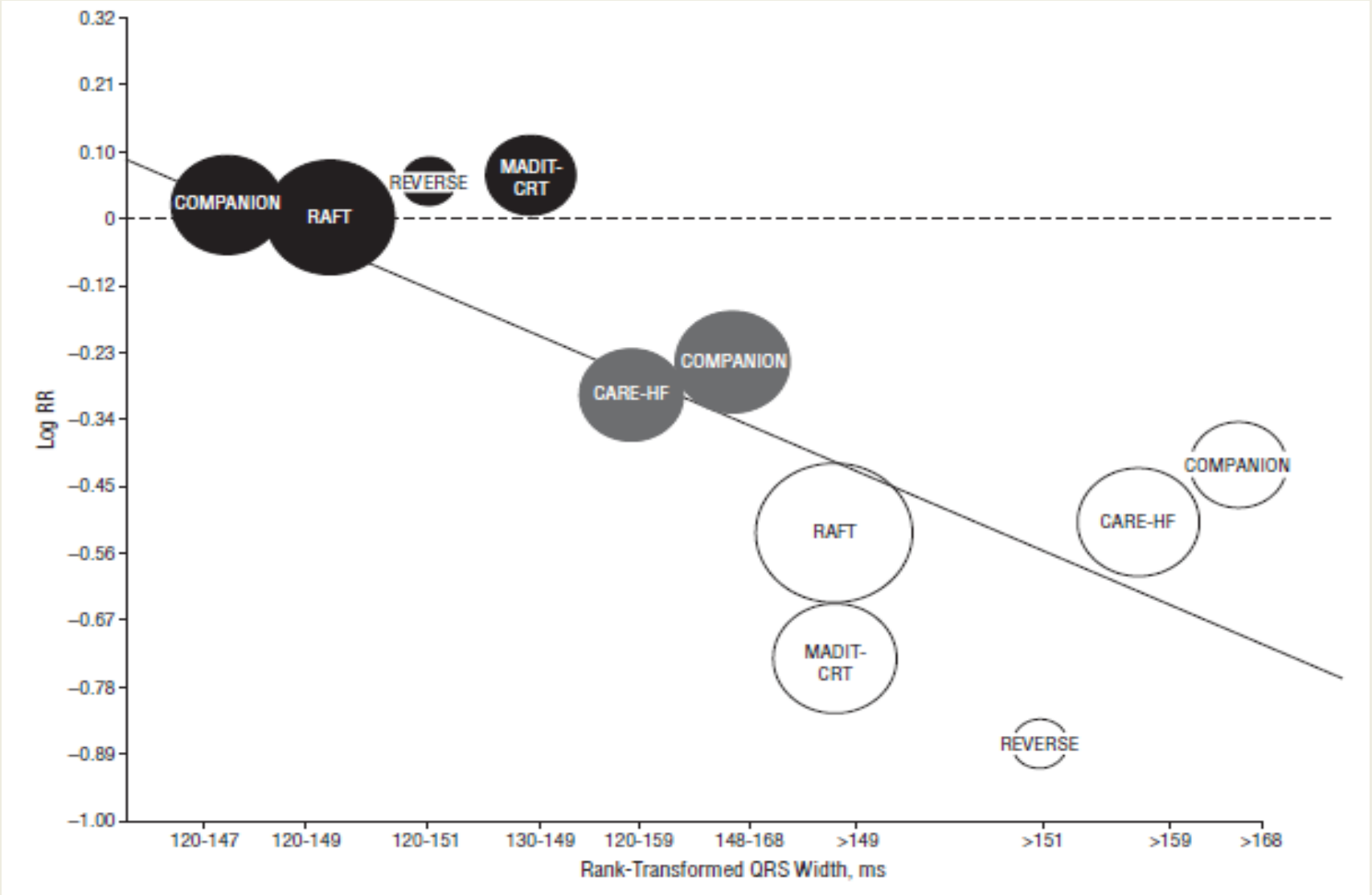
Cardiac Resynchronization Therapy (CRT)



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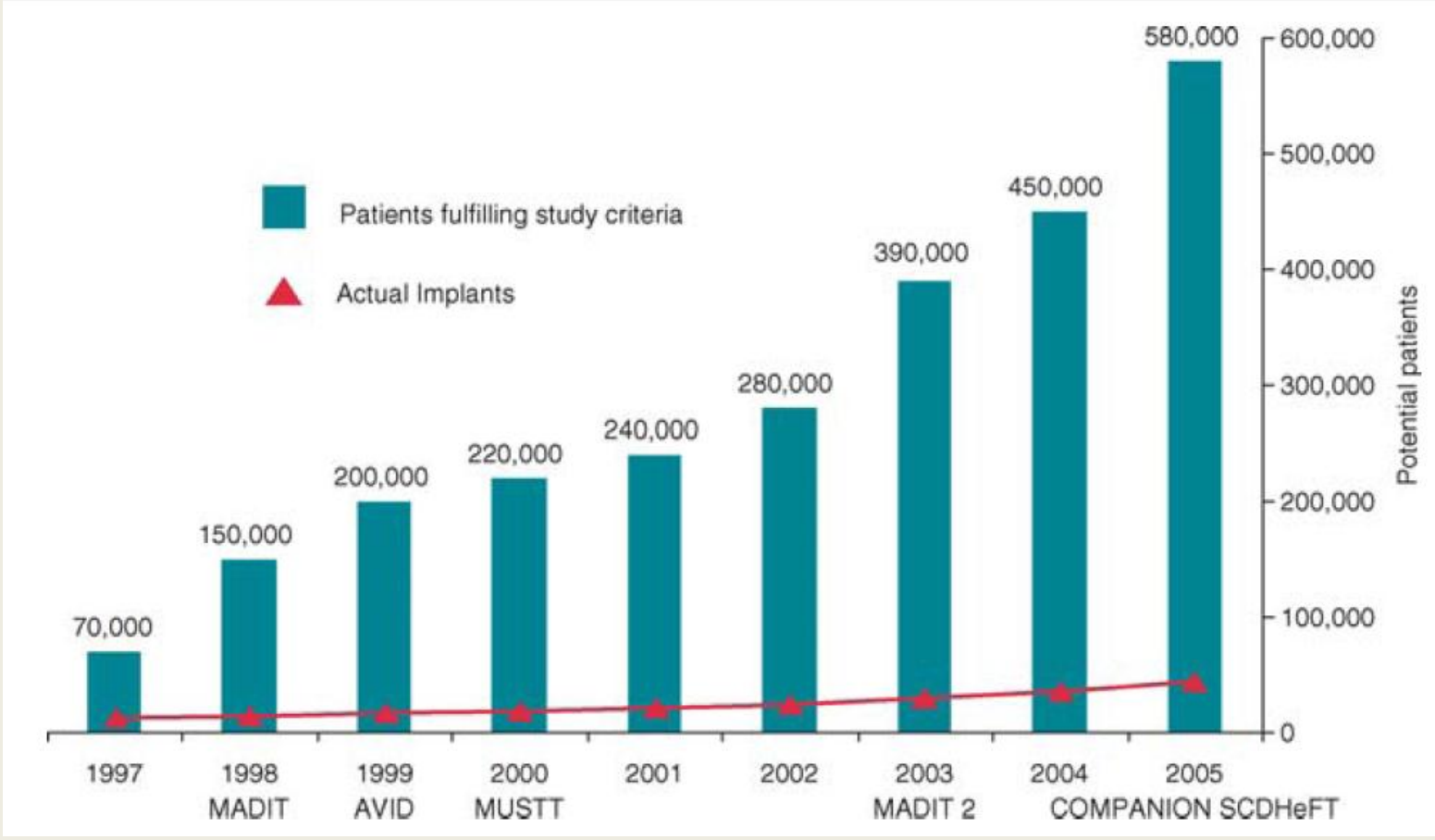
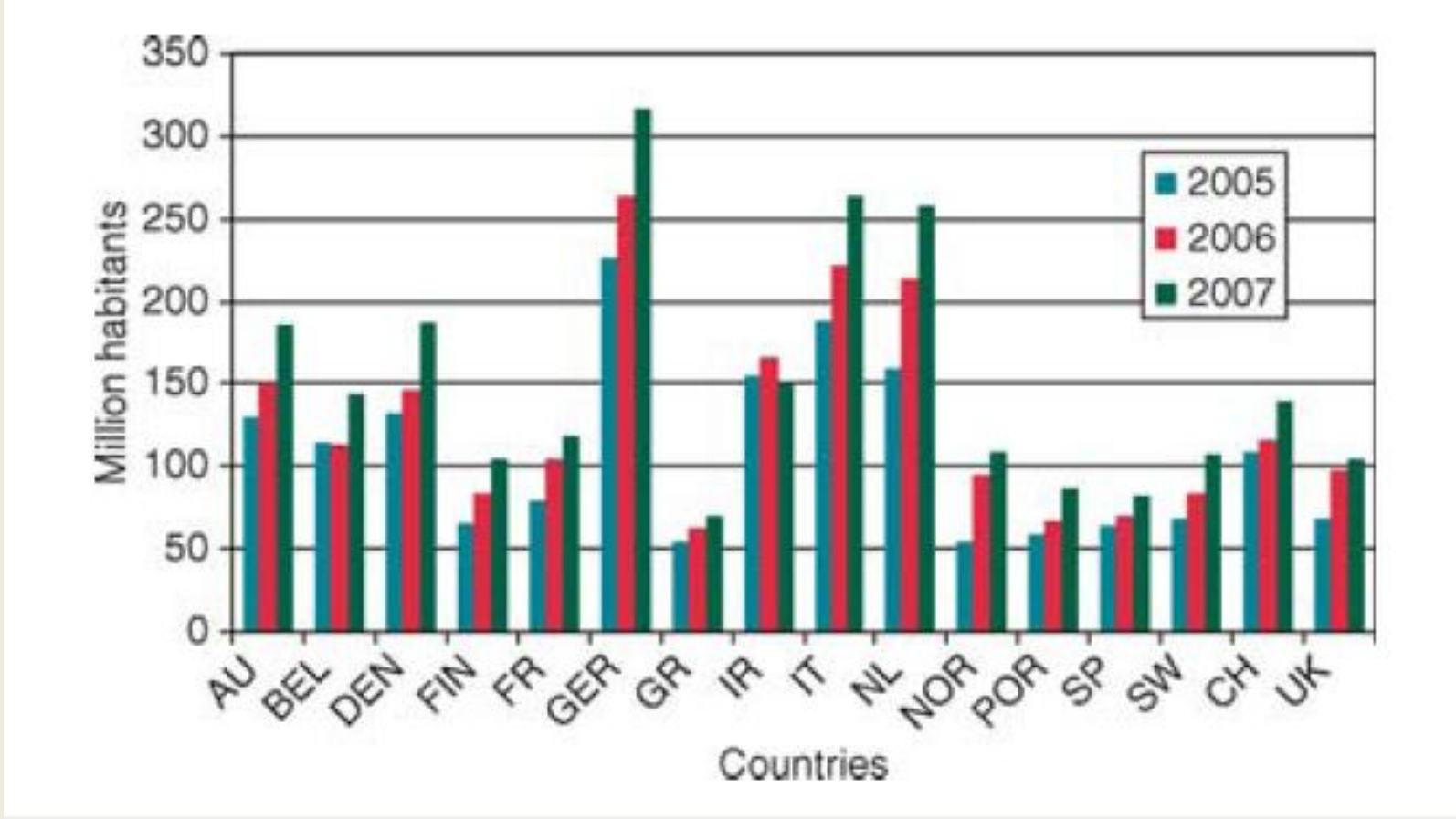
Percentage of patients fulfilling the criteria for the major randomized ICD trials



Camm and Nisam, Europace 2010; 12:1063-1069

ICD and CRT-D European implant rates implantations per million inhabitants between 2005 and 2007



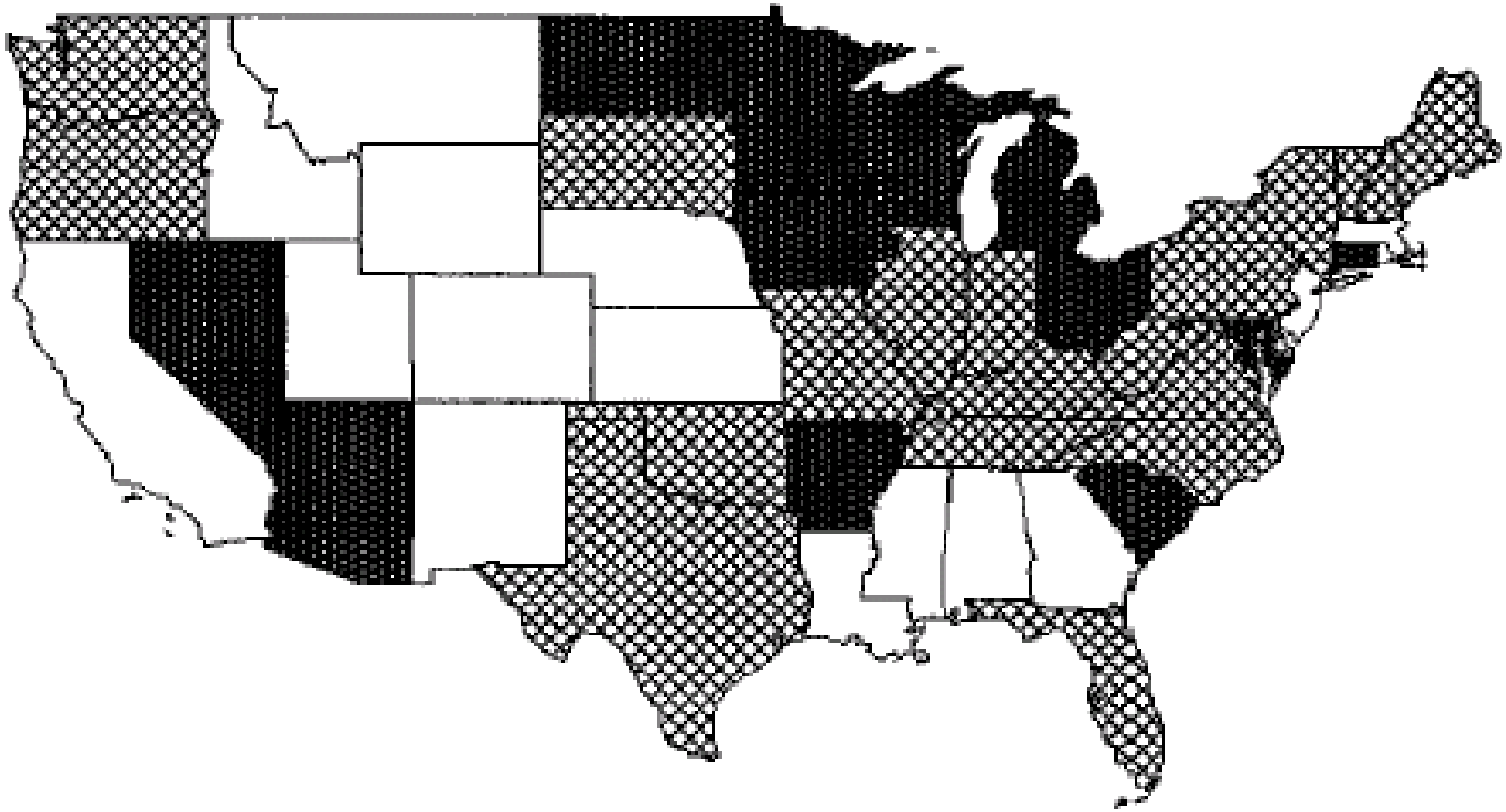
Camm and Nisam, Europace 2010; 12:1063-1069

ICD/CRT-D implantations per million and centres implanting (per million population)

	Implants per million	ICD/ CRT-D centres per million	Index implants per million	Index ICD/ CRT-D centres per million
Germany	226	4.4	100	65
Italy	192	6.8	85	100
France	83	1.4	37	21
UK	69	0.7	31	10

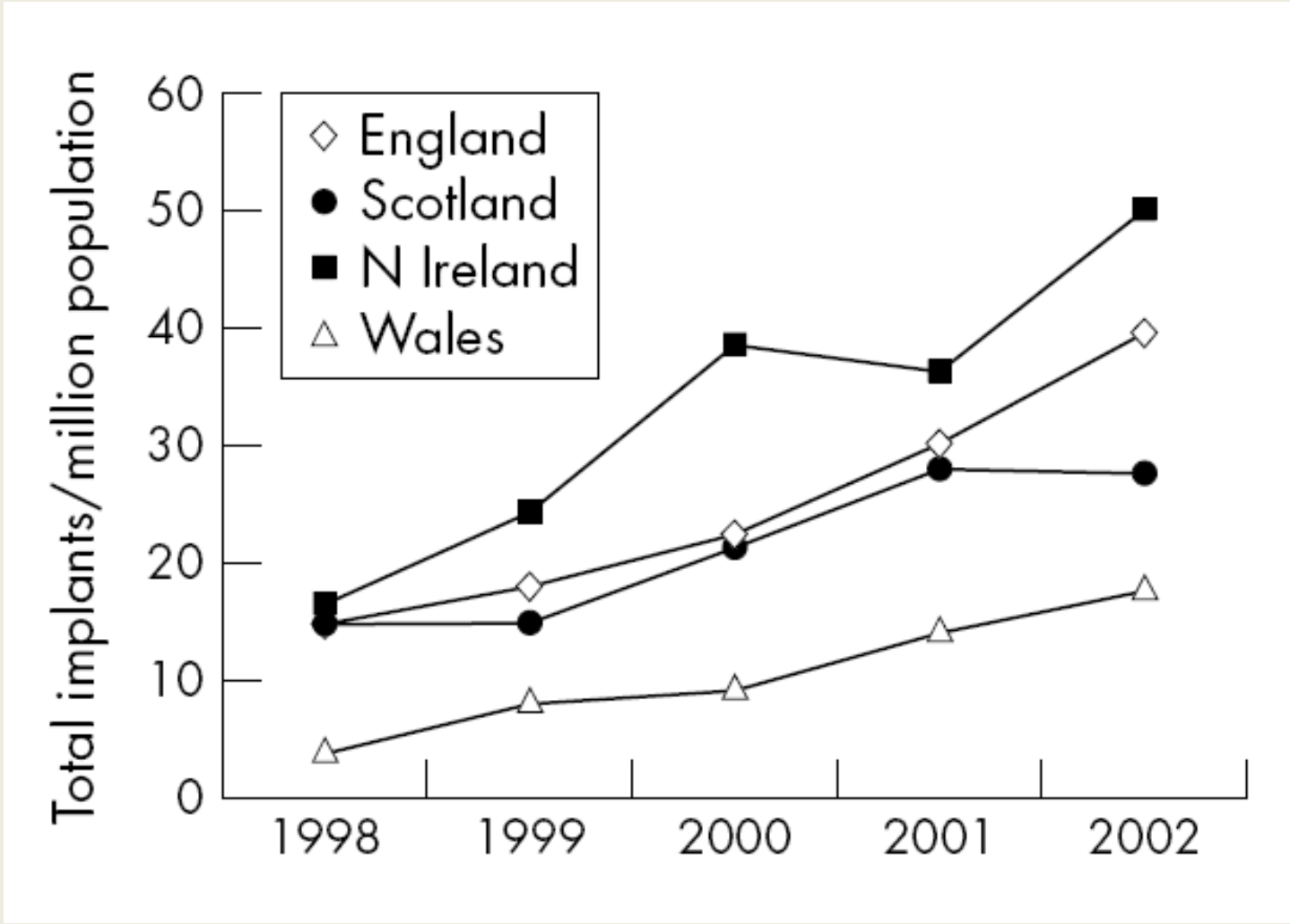
Camm and Nisam, Europace 2010; 12:1063-1069

ICD implantation by state



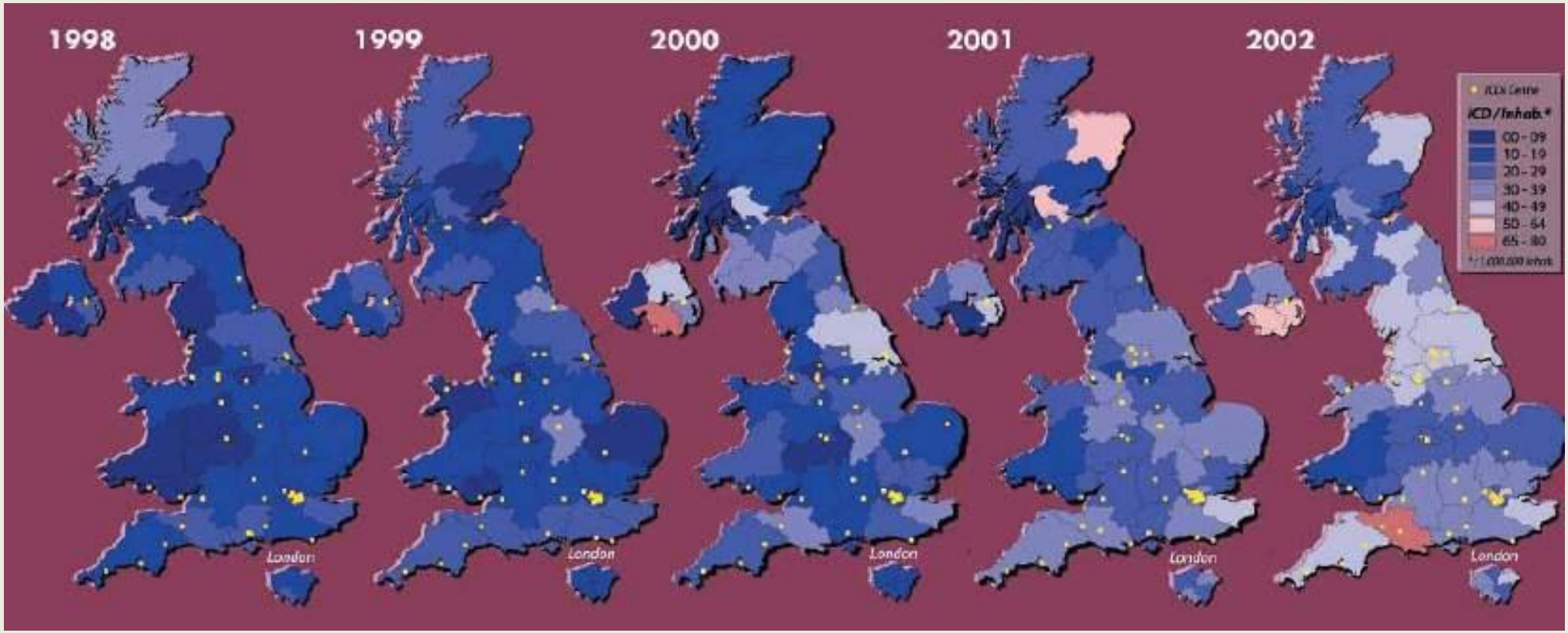
Hlatky et al, Am Heart J, 2002; 144:397-403

ICD implantation rate per million population in the countries of the UK in 1998 - 2002



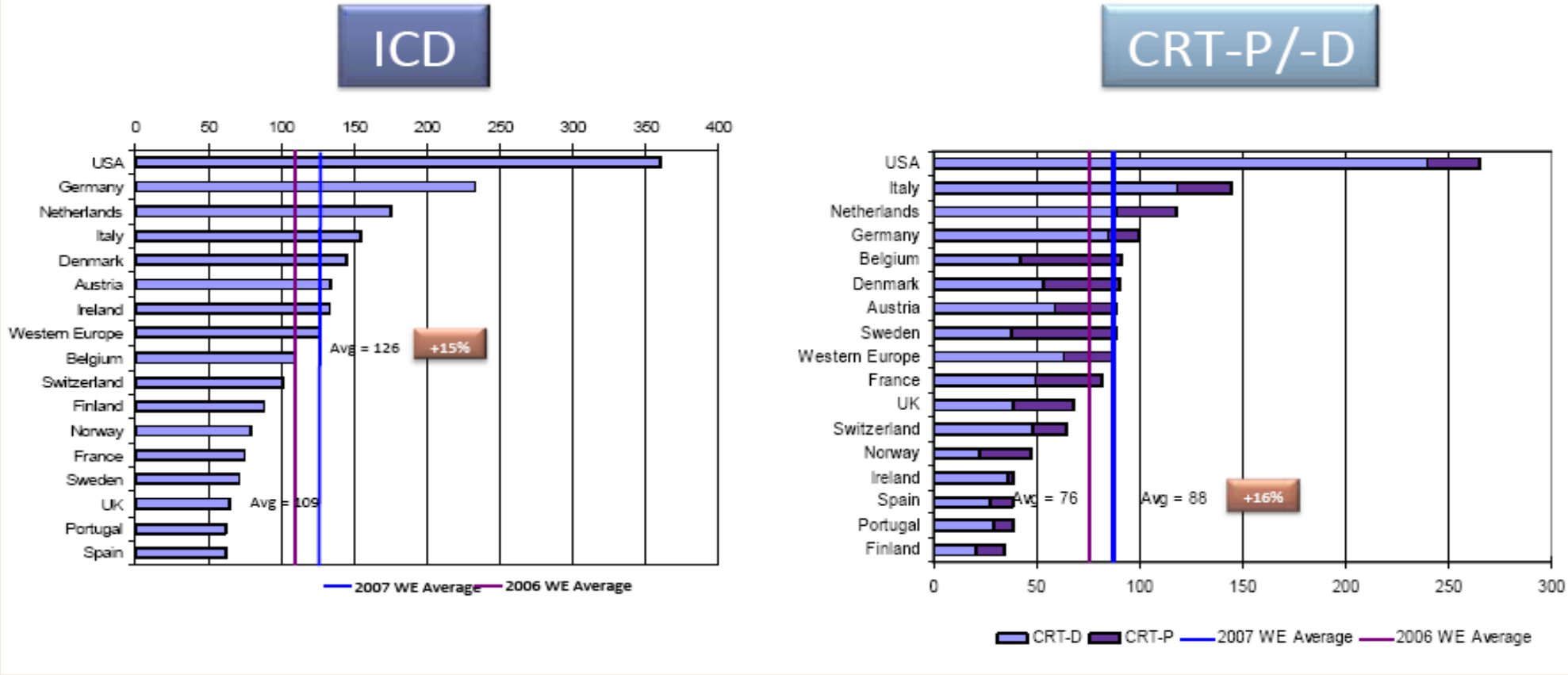
Cunningham et al. Heart 2005; 91: 1280 - 1283

ICD implantation rate per million population in UK in 1998 - 2002



Cunningham et al. Heart 2005; 91: 1280 - 1283

ICD & CRT implant rates per million 2007



EUCOMED Database

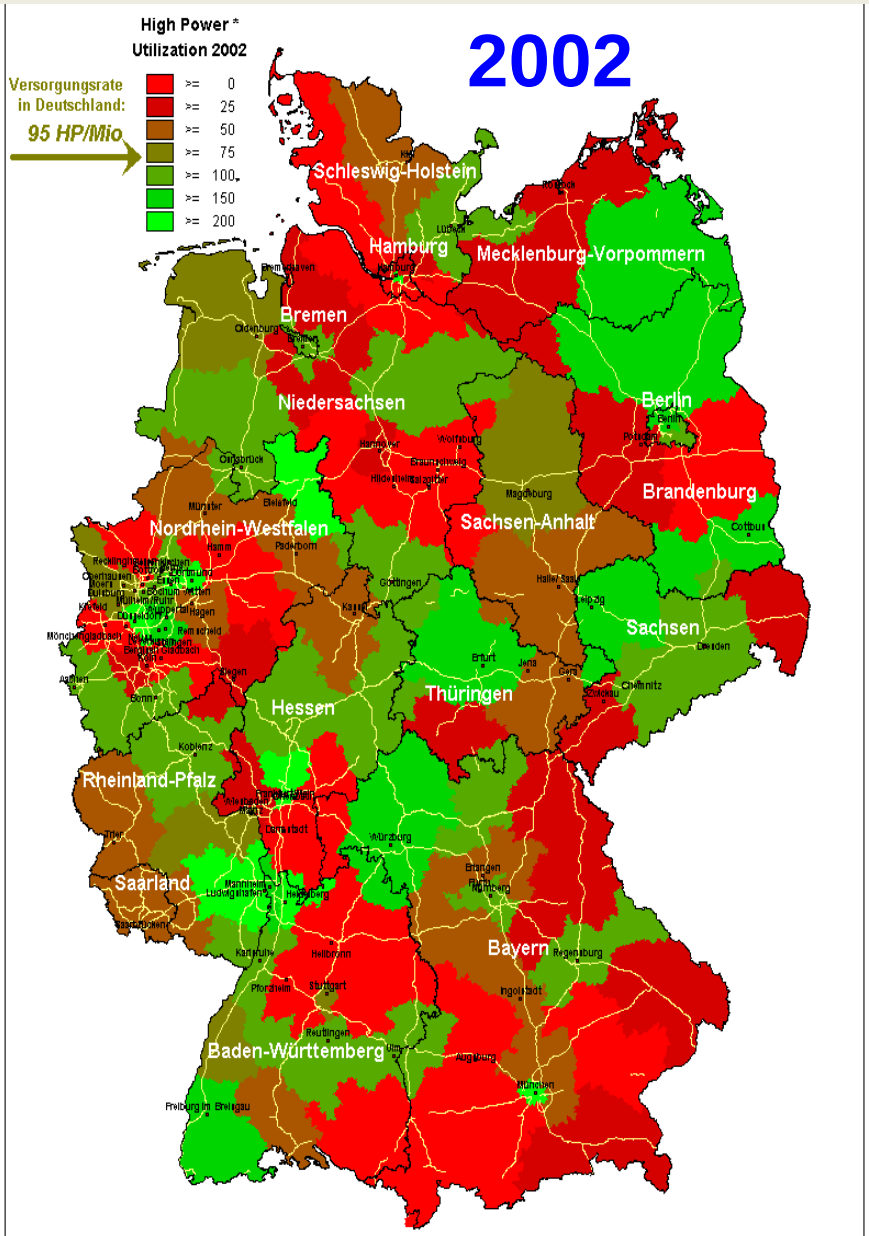
Brugada J, Vardas P, Wolpert C. The EHRA White Book 2008

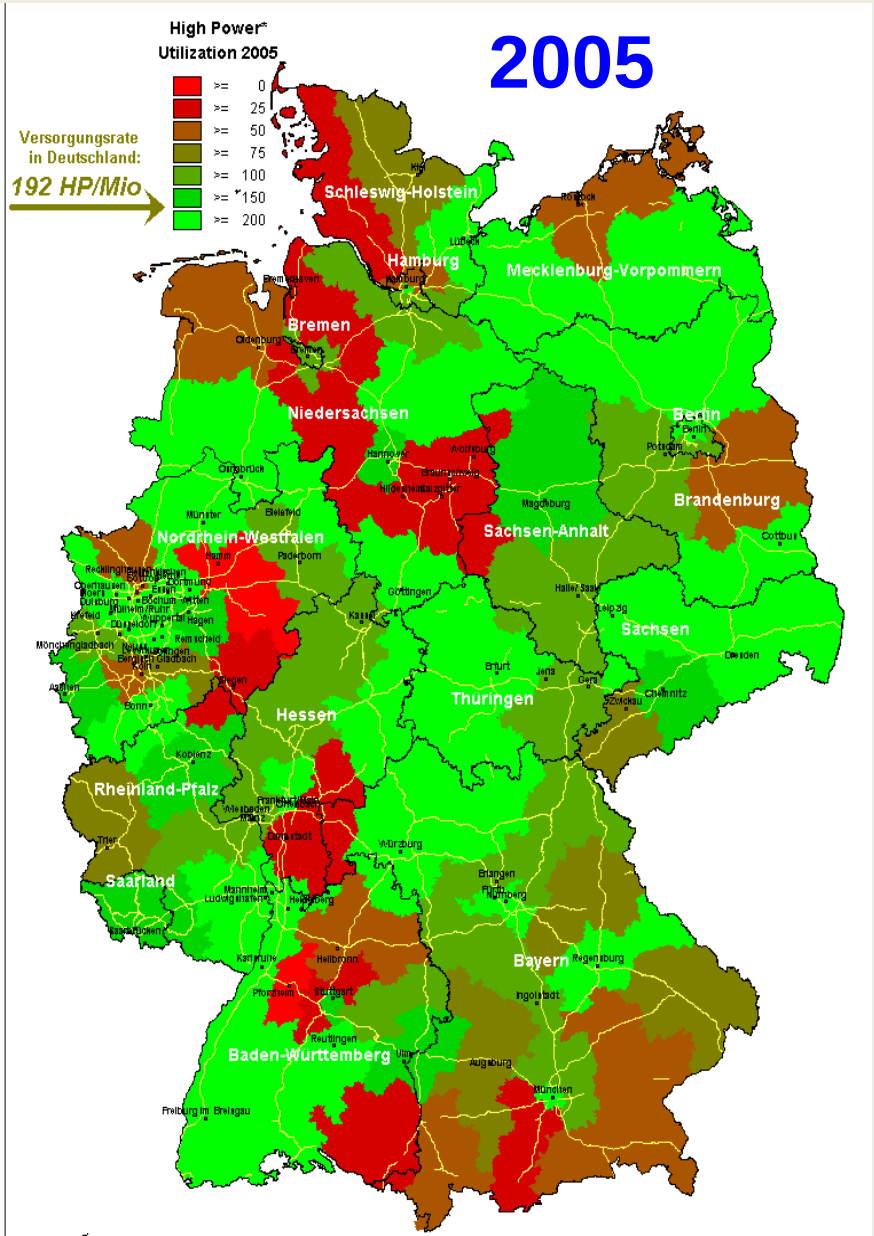
EU differences in ICD use

	GDP / Health expenditure %	Life expectancy at birth	No. Implanting Center / mil	ICD/CRT-D Implanted Units		
				2006	2007	2007
Countries	2004	2006	ICD	CRT-D	Absolute		/mil
Switzerland	11.5	81.4	3.33	3.6	657	823	139
Germany	10.6	79.4	4.37	2.42	21609	26016	316
France	10.5	80.5	NA	1.9	6598	7472	117
Netherlands	9.2	79.4	0.96	0.96	2574	4218	255
Sweden	9.1	80.6	1.67	1.33	538	982	109
Italy	8.7	80.4	6.87	5.16	17400	20635	355
Spain	8.1	80.4	1.96	1.10	3093	3635	80
UK	8.1	79.3	0.88	0.88	5850	6260	103
Greece	7.9	79.8	1.74	2.01	525	874	80
Poland	6.2	75.1	1.16	1.26	1420	1735	49

Auricchio A, EHRA Summit 2009

ICD - Utilization





Reasons for ICD “underuse” in VT / VF survivors

- **Financial resources**
- **Awareness of ICD Tx – physician compliance / education (guidelines)**
- **Patient compliance / education**
- **General awareness of the sudden death problem:**
  Cancer – AIDS – – – awareness of sudden death
- **Perception: sudden death = “nice ”**

Heart ONLINE

Regional variation in ICD implantation rates: the shocking truth?

C C Lang

Heart 2005;91;1251-1253
doi:10.1136/hrt.2004.056754

European Heart Journal (2006) 27, 882–885
doi: 10.1093/eurheartj/ehi794

EUROPEAN SOCIETY OF CARDIOLOGY®

ESC workshop report

Improving patient access to novel medical technologies in Europe

Peter Kearney[1*], Graham Stokoe[2], Günter Breithardt[3], Carole Longson[4], Jean Marco[5], John Morgan[6], Silvia Priori[7], Alric Ruether[8], Rod Taylor[9] and Michaël Hertog[10] on behalf of the Taskforce 2 of the ESC-Cardiovascular Round Table