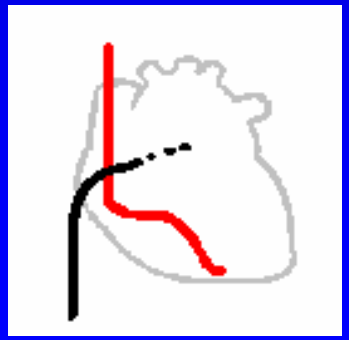
Longevidade dos geradores e análises de custo eficácia em CDI e CRT

João de Sousa

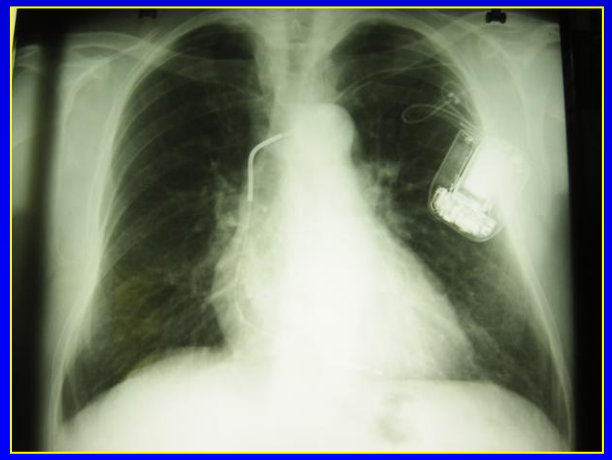
Unidade Electrofisiologia e Pacing
Serviço de Cardiologia
Hospital de Santa Maria, CHLN
Lisboa

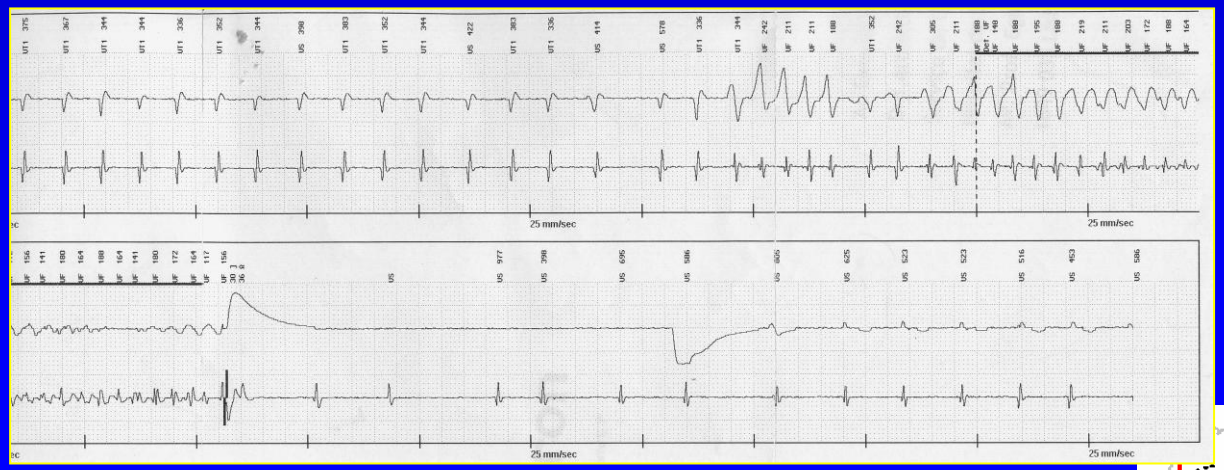


Cardioversor-Desfibrilhador Implantável

Características clínicas

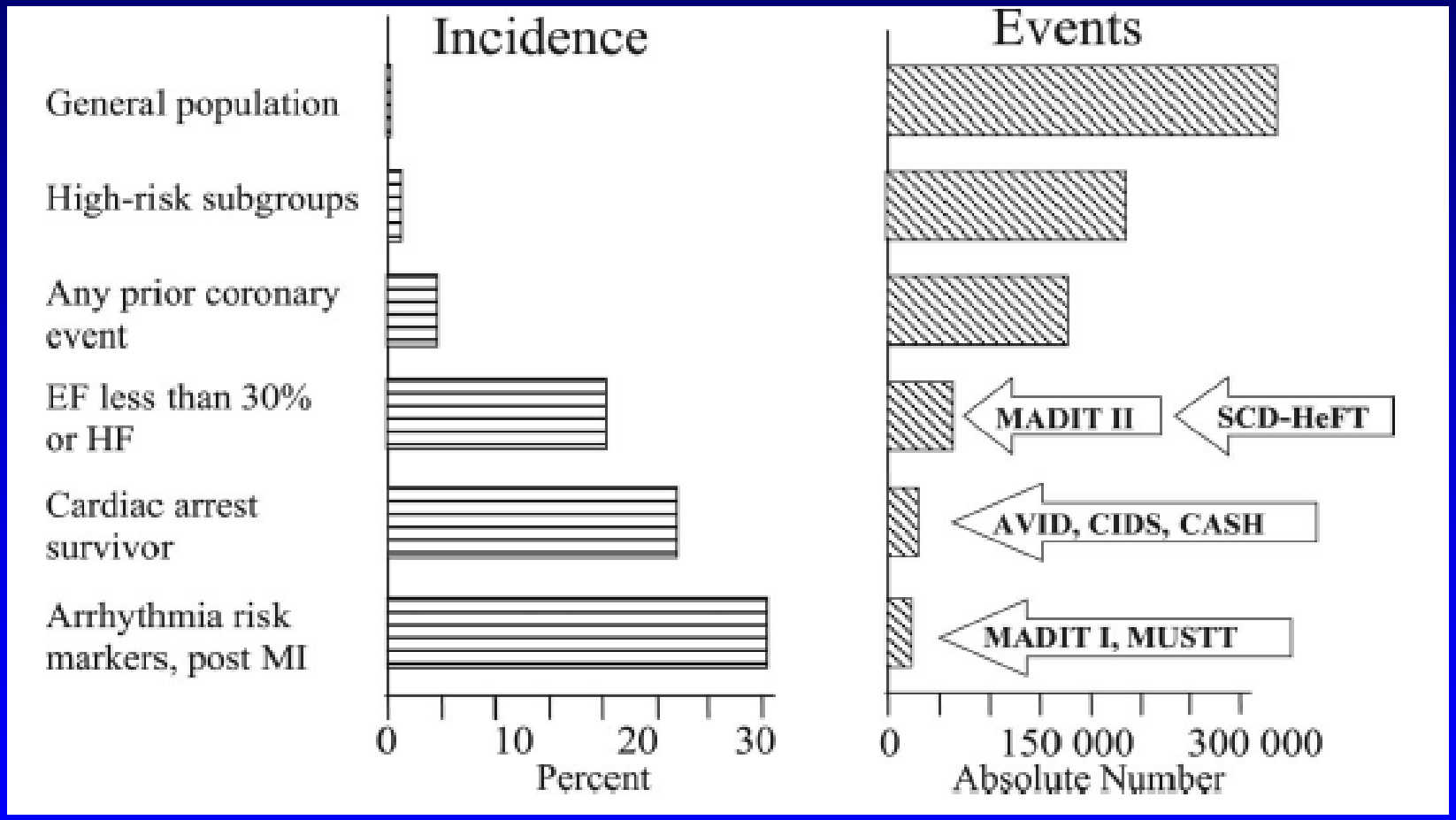
- Múltiplas funções: pacing (VVI, DDD, CRT), cardioversão, desfibrilhação, PAT, memória
- Mortalidade implantação: 0.5-0.8%
- 99% eficácia terminação FV
- Terapêutica não-apropriada em 5-10% (FA)
- Taxa morte súbita 1-2%/ano





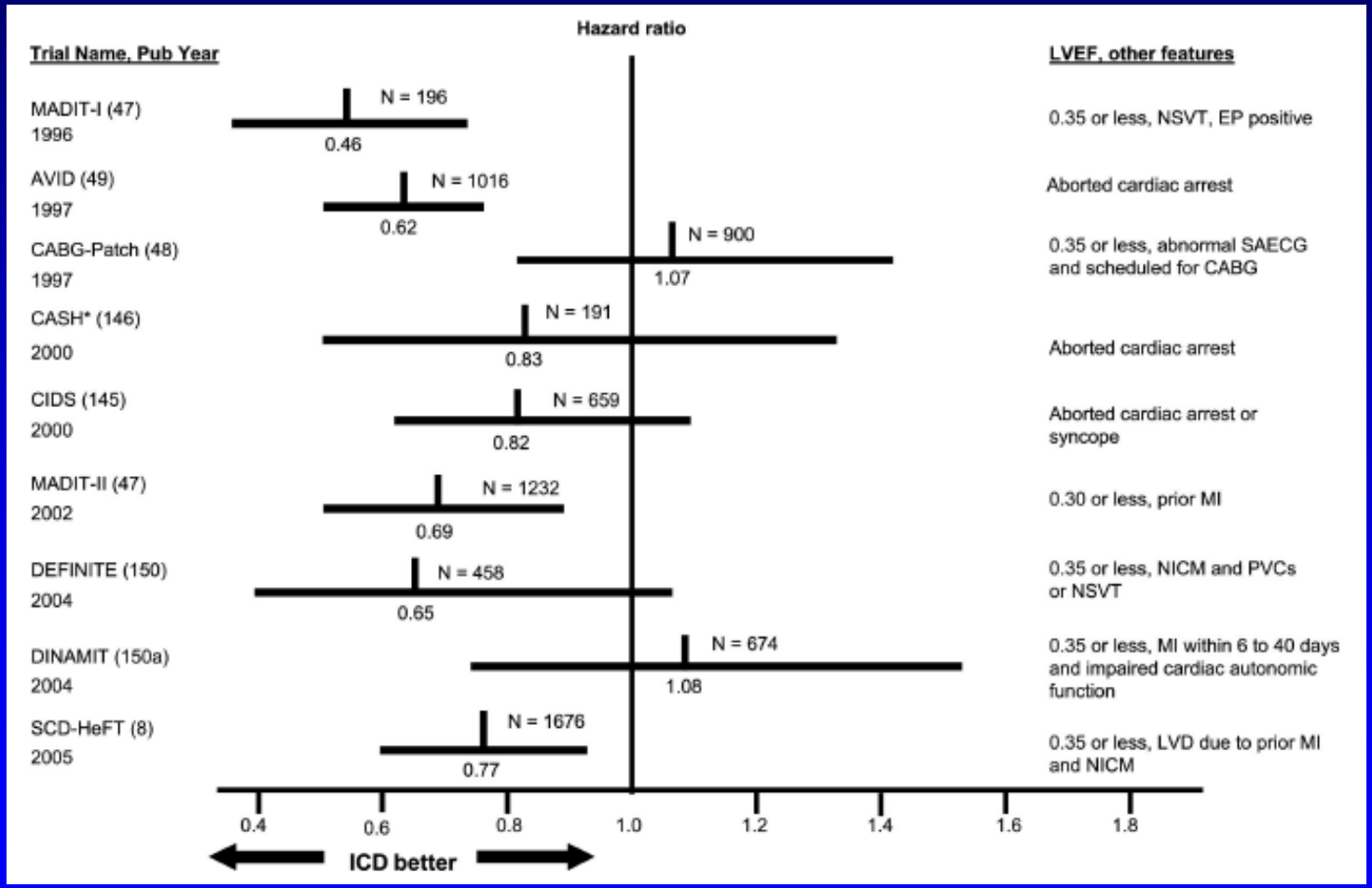
Morte súbita

Sub-grupos de risco e estudos randomizados



Europace 2006;8:746-837

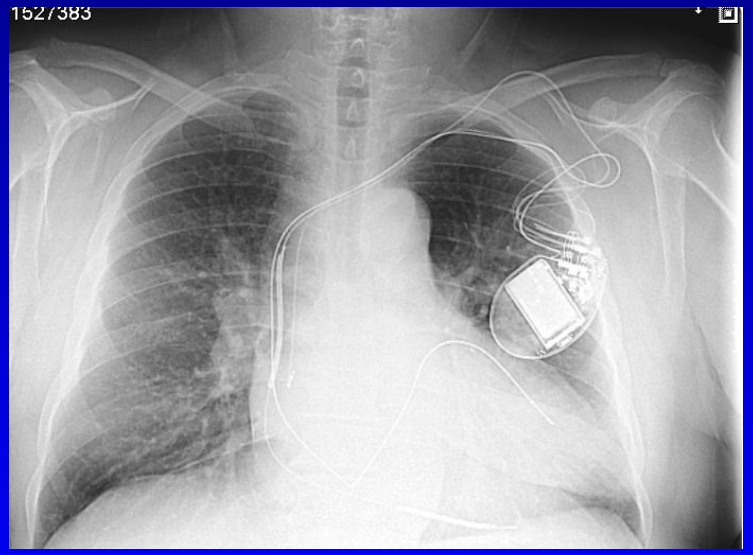
Ensaios CDI
Resultados mortalidade



Europace 2006;8:746-837

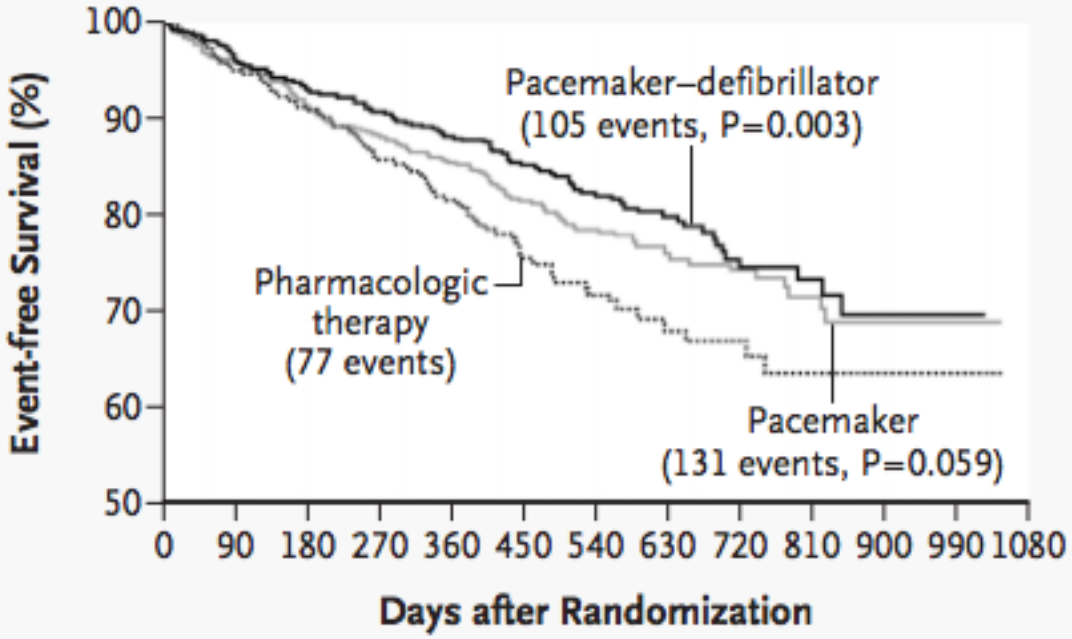
Benefício CRT: Efeitos morbilidade e mortalidade

- Meta-análise: 18 estudos, 3701 dts
- Companion, CARE-HF
- “Respondedores”: 75-80%
- Resultados:
  - ↑ FEVE (3.5%)
  - ↓ mortalidade (21% - NNT 24)
  - ↓ hospitalização (32% - NNT 8)
  - ↑ estado funcional (redução 1 classe funcional em 58%)
  - ↑ QOL



F McAlister: Ann Intern Med 2004;141:381-390
J Cleland et al: NEJM 2005;352:1539-49

Estudo COMPANION
Mortalidade total

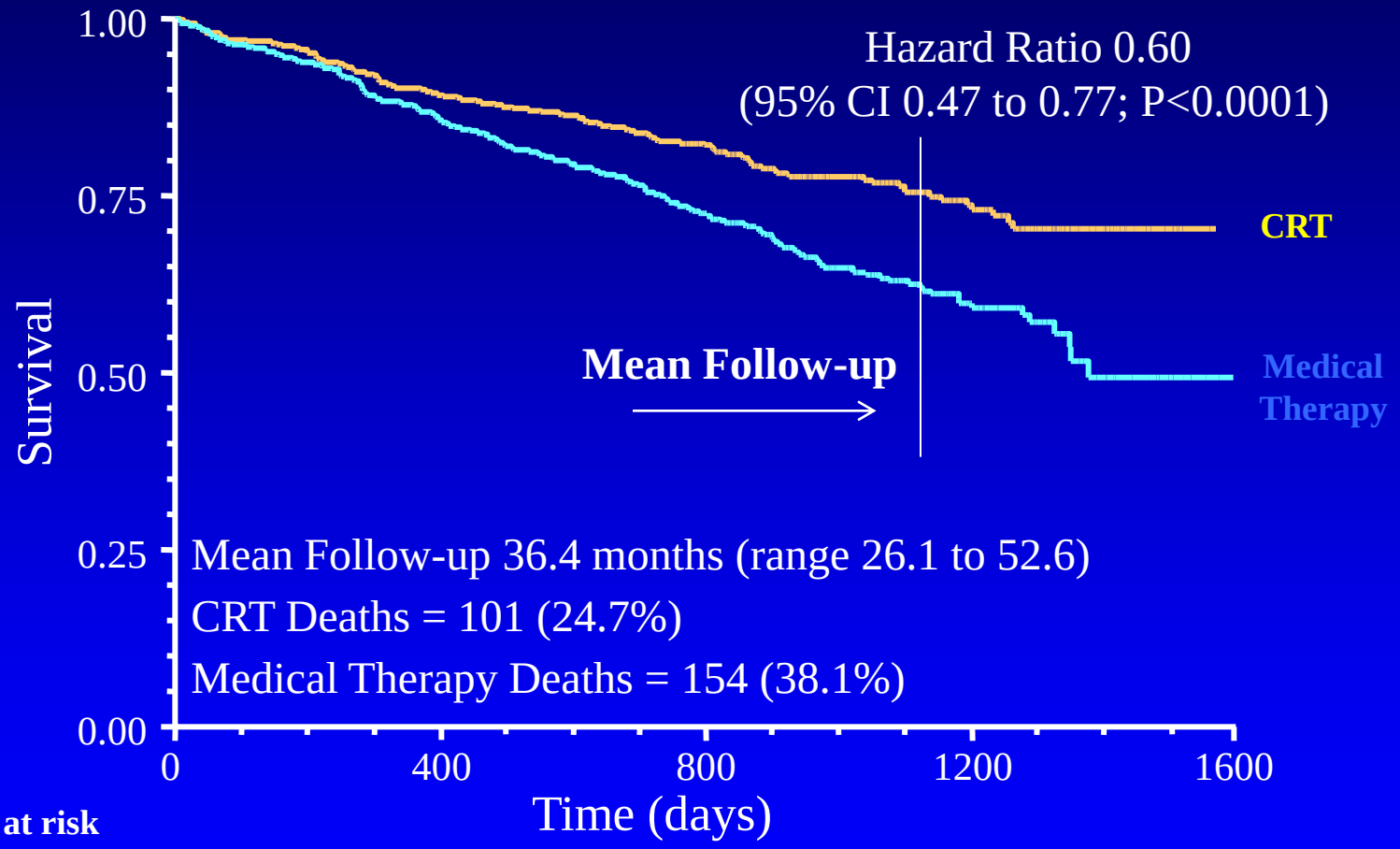


No. at Risk

Pharmacologic therapy	308	284	255	217	186	141	94	57	45	25	4	2
Pacemaker	617	579	520	488	439	355	251	164	104	60	25	5
Pacemaker–defibrillator	595	555	517	470	420	331	219	148	95	47	21	1

Bristov MR. *N Engl J Med* 2004;350:2140-50

CARE-HF Extension Study
Mortalidade total

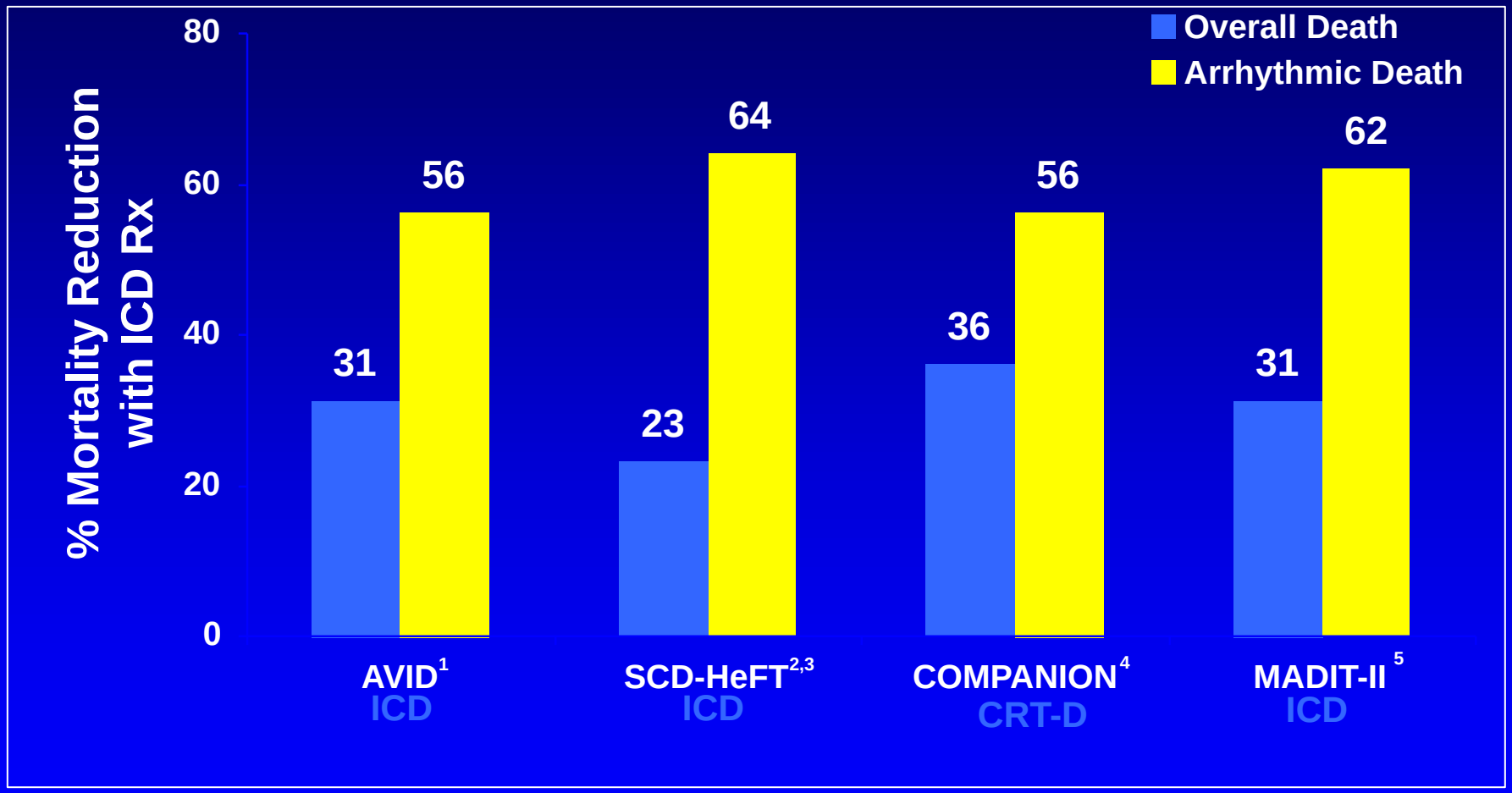


Number at risk

CRT	**409**	**383**	**358**	**338**	**209**	**85**	**9**
Medical therapy	**404**	**372**	**331**	**298**	**178**	**63**	**6**

Cleland JG. *N Engl J Med* 2005;352:1539-49

Redução mortalidade: CDI e CRT-D



[1] The AVID Investigators. *N Engl J Med.* 1997;337:1576-1583.

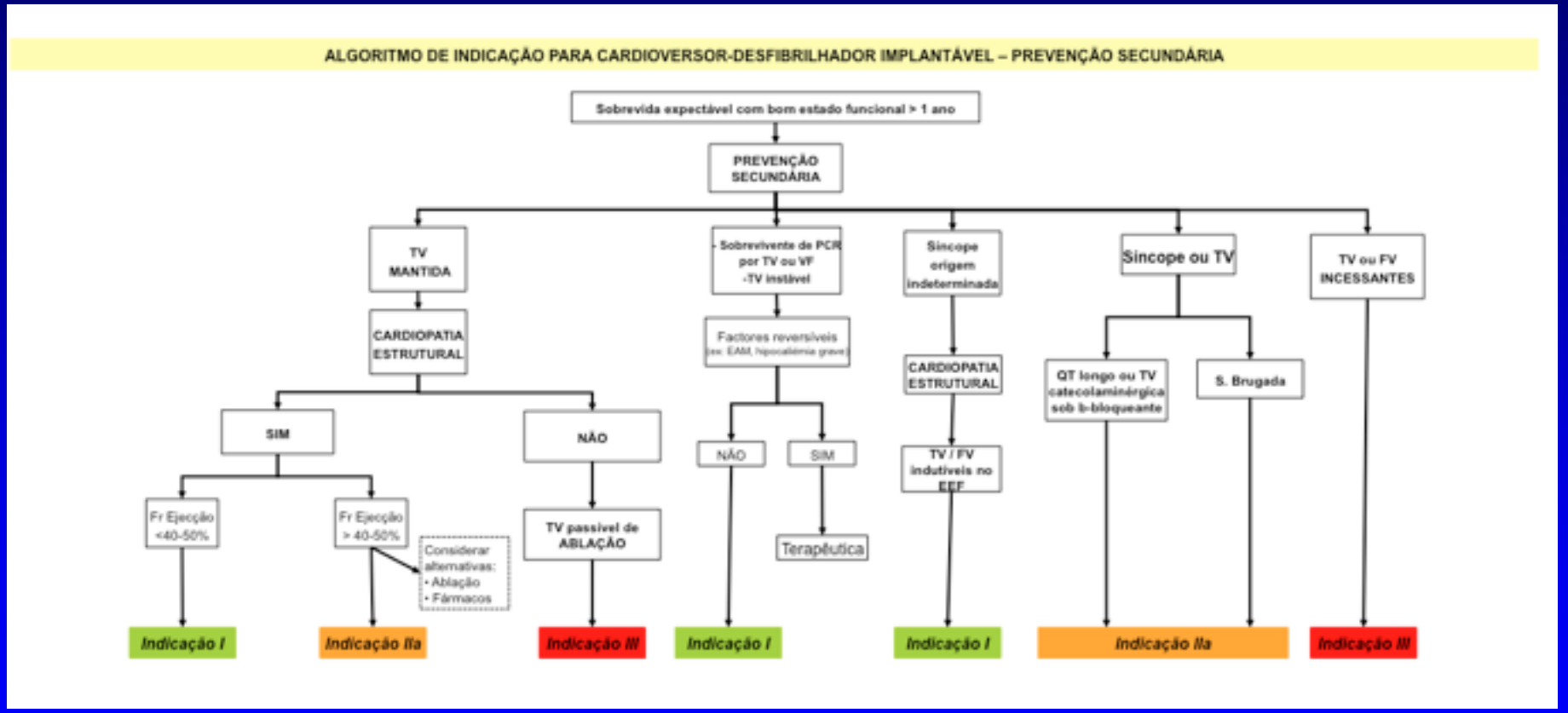
[2] Bardy GH, et al. *N Engl J Med*. 2005;352:225-237.

[3] Packer DL. *Heart Rhythm.* 2005;2:S38-S39.

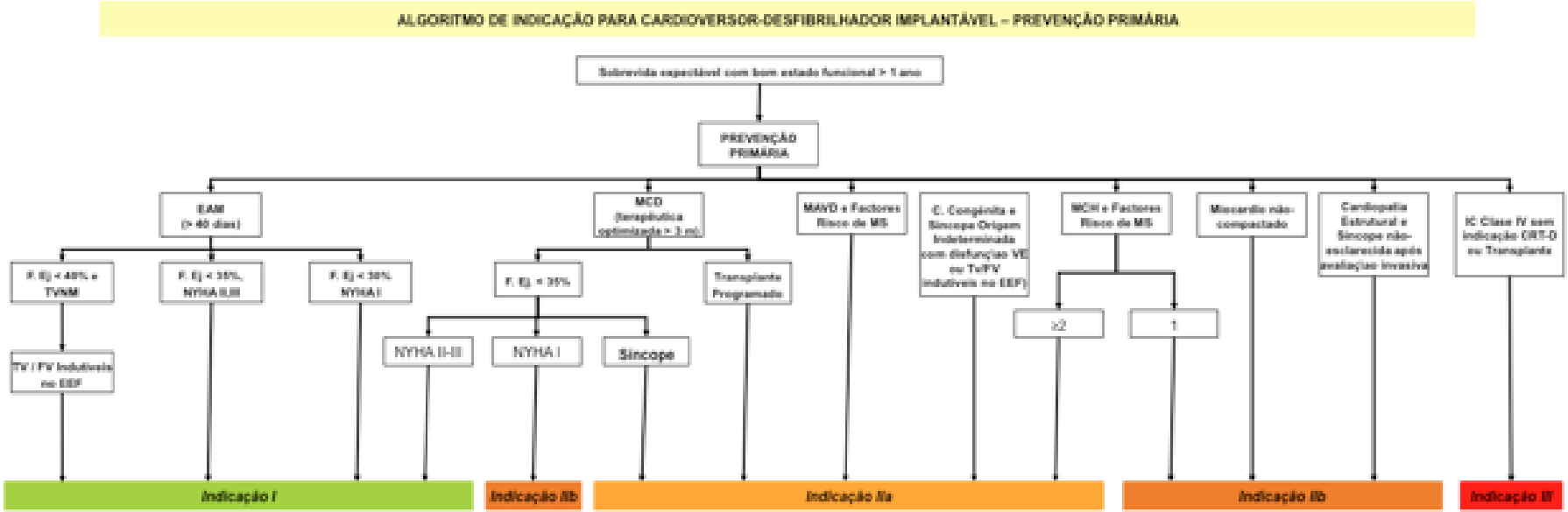
[4] Bristow MR, et al. *N Engl J Med*. 2004;350:2140-2150.

[5] Moss AJ, et al. *N Engl J Med.* 2002;346:877-8

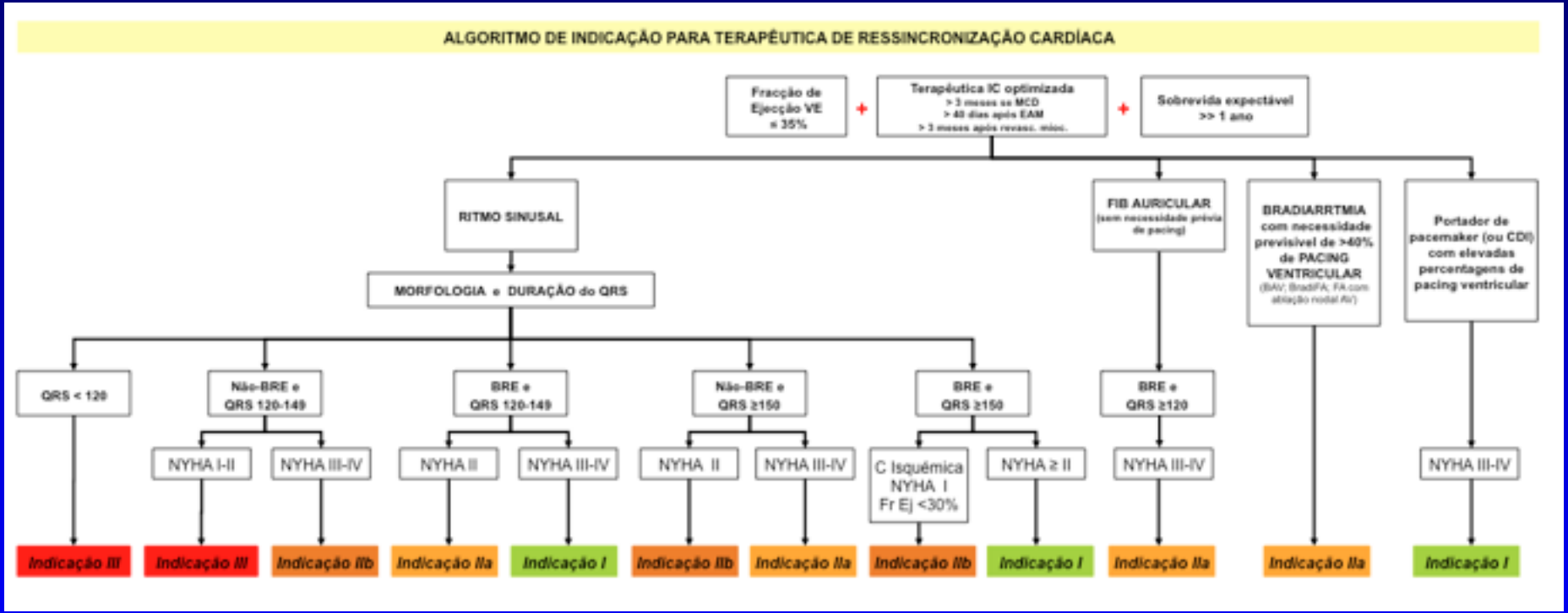
Indicações para CDI – Prevenção secundária



Indicações para CDI – Prevenção Primária

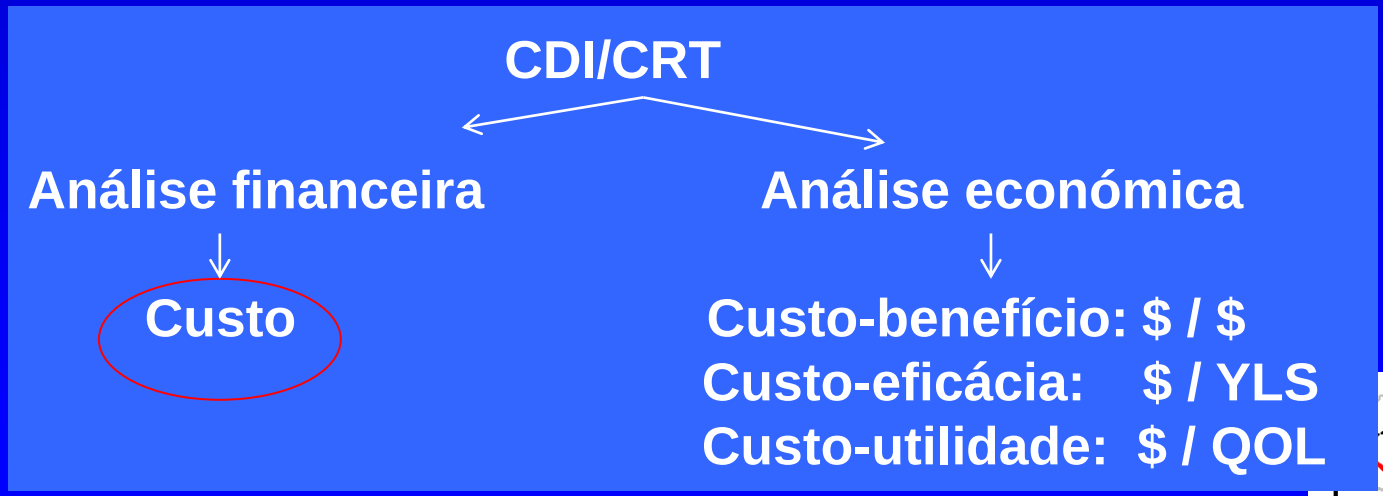


Indicações para Ressincronização

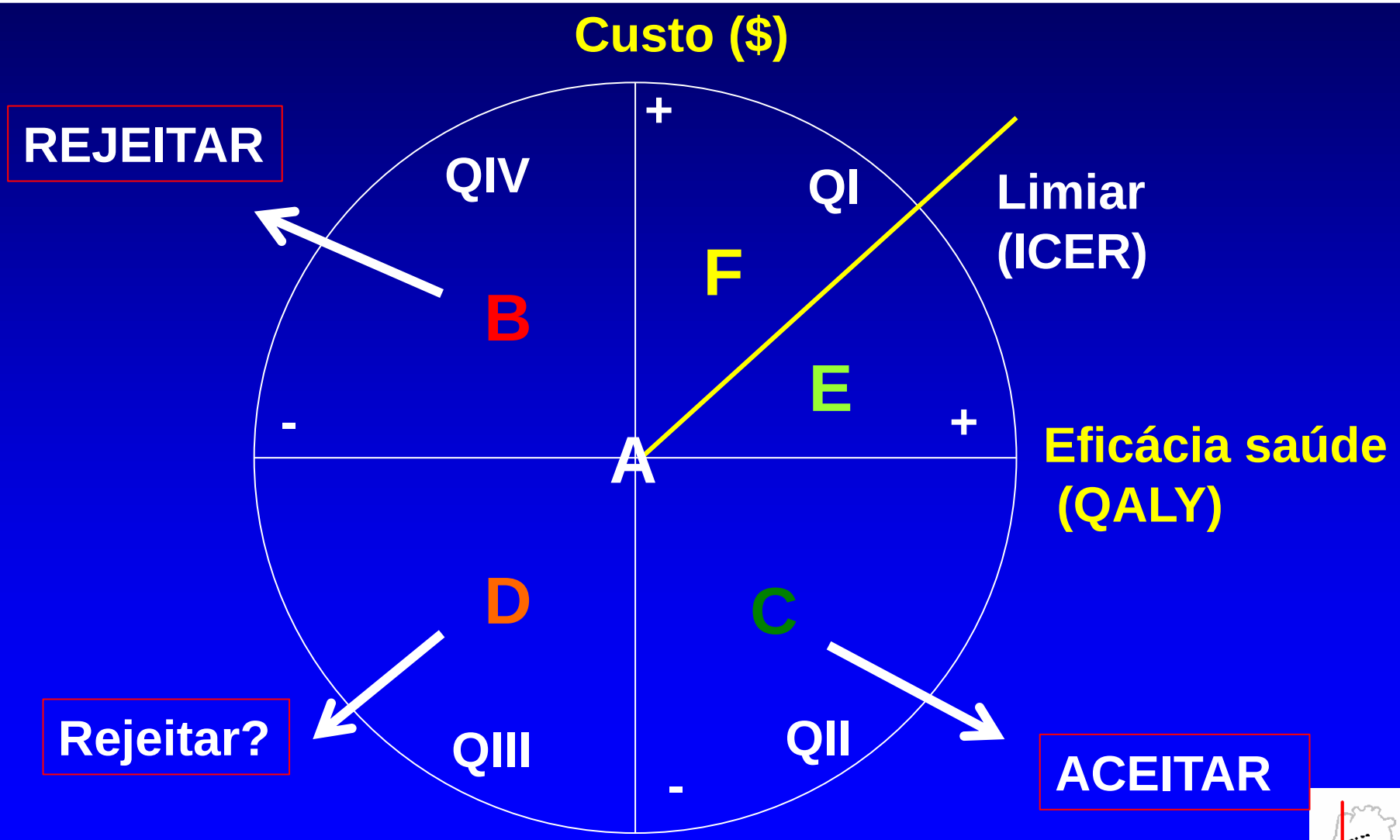


CDI e CRT são eficazes, mas serão rentáveis?

- ECONOMIA SAÚDE
  - Elevados custos iniciais de implantação de CDIs ou CRT
  - Modalidade de tratamento “cara” para “todos”
  - Os recursos económicos são escassos, sendo necessário alocá-los em tecnologias que maximizam o beneficio da população em geral
  - Modelos de avaliação económica com análise custo-eficácia:
    - Estudos randomizados
    - Modelos de decisão (Markov)



Análises Custo-Eficácia

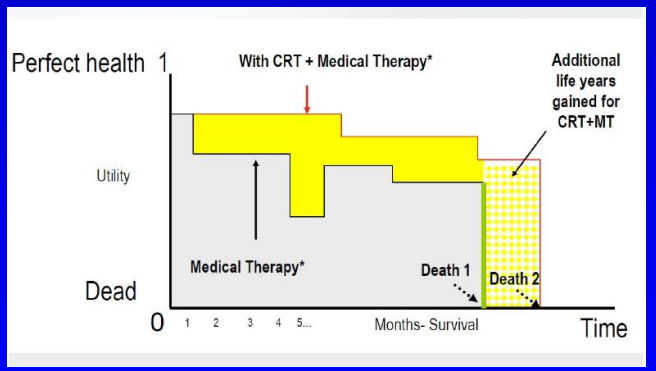


Avaliação Custo-Eficácia

- ICER: Incremental cost-effectiveness ratio
  - difference between the mean costs of each strategy divided by the difference in mean health outcome

Atractivo:	< €20.000/QALY
Aceitável:	€20-40.000/QALY
Borderline:	€40-60.000/QALY
Excessivo:	€60 -100,000/QALY

- Quantificação ganho em saúde
  - QALY – anos de vida ajustados à qualidade de vida
  - YLS – anos de vida ganhos
- Limiares aceitáveis de custo-eficácia
  - EUA: < US$ 50,000 / YLS
  - NICE: < £30.000 / QALY
  - WHO: < 2-3 x PIB / QALY
    - Portugal: PIB – US$20,182 ou €15.702



Avaliação Custo-Eficácia CDI
Prevenção secundária

- 11 estudos publicados entre 1990 e 2002
  - 6 modelos de decisão
  - 4 ensaios randomizados
  - 1 estudo observacional
- Comparação com amiodarona ou outros AA ou terapêutica guiada por EEF
- CDI trans-venoso apenas em 4 estudos
- ICER:
  - Modelos: US$17,100-US$56,000/YLS
  - AVID: US$68,378/YLS
  - CIDS: Can$99,420-Can$213,543/YLS

Gialama et al: The cost-effectiveness of implantable cardioverter-defibrillators: A systematic review of economic evaluations. Appl Health Policy 12:41-49, 2014

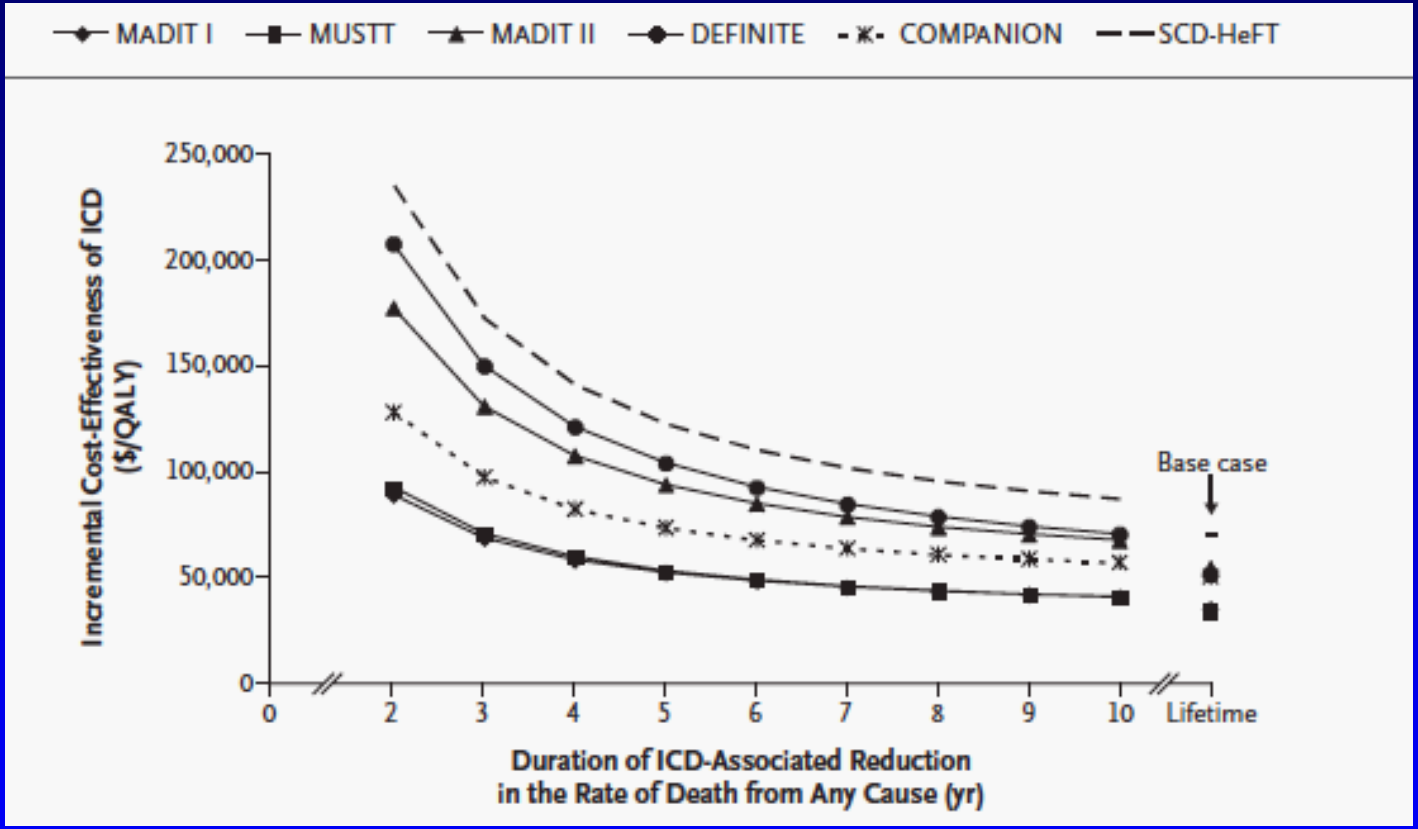
Avaliação Custo-Eficácia CDI
Prevenção primária

Table 1. Health and Economic Outcomes of the Prophylactic Implantation of an ICD as Compared with Control Therapy.*

Trial and Strategy	Cost	Increase in Cost Related to ICD	Life Expectancy	Increase in Life Expectancy Related to ICD	QALY	Increase in QALY Related to ICD	Incremental Cost-Effectiveness of ICD†			
							$/Life-Yr	Baseline Efficacy	High Efficacy	Low Efficacy
	$			year					$/QALY	
MADIT I										
Control	38,300		4.06		2.98					
ICD	130,400	92,100	7.70	3.64	5.62	2.64	25,300	34,900	27,000	96,600
CABG Patch										
Control	78,600		8.41		6.13					
ICD	134,400	55,700	8.01	(0.40)	5.84	(0.29)	Dominated	Dominated	84,200	Dominated
MUSTT										
Control	44,300		4.72		3.46					
ICD	145,800	101,500	8.86	4.14	6.45	2.99	24,500	34,000	28,800	47,600
MADIT II										
Control	57,500		6.16		4.51					
ICD	136,900	79,400	8.20	2.03	5.98	1.47	39,000	54,100	37,200	213,900
DEFINITE										
Control	84,400		9.03		6.57					
ICD	184,900	100,500	11.75	2.73	8.53	1.96	36,800	51,300	34,500	Dominated
DINAMIT										
Control	88,300		9.44		6.87					
ICD	147,200	58,800	8.96	(0.48)	6.53	(0.34)	Dominated	Dominated	70,900	Dominated
COMPANION										
Control	37,800		4.01		2.95					
ICD	106,100	68,300	5.88	1.87	4.31	1.36	36,500	50,300	36,100	123,800
SCD-HeFT										
Control	57,800		6.19		4.53					
ICD	128,800	71,000	7.59	1.40	5.54	1.01	50,700	70,200	45,600	368,800

Sanders et al. Cost-effctiveness of Implabntable Cardioverter-Defibrillator: NEJM 2005;353:1471-80

Avaliação Custo-Eficácia CDI
Prevenção primária



ICER de $34,000-$70,200 / QALY com terapêutica > 7 anos

Sanders et al. Cost-effctiveness of Implabntable Cardioverter-Defibrillator: NEJM 2005;353:1471-80

Avaliação Custo-Eficácia CRT-P

Table 7 | Cost-effectiveness analyses of CRT-P versus pharmacological therapy for heart failure

Study (year)	Study type and country	NYHA class evaluated	Time period	Source of efficacy estimate	ICER per QALY gained
Nichol et al. (2004)[139]	Markov model with Monte Carlo simulation Public Health System USA	III–IV	Lifetime	Systematic review	US$107,800
Feldman et al. (2005)[131]	Trial-based Medicare and Medicaid USA	III–IV	7 years	COMPANION	US$19,600
Fox et al. (2007)[94]	Markov model Public health system UK	III–IV	Lifetime	Meta-analysis	£16,700
Yao et al. (2007)[138]	Markov model with Monte Carlo simulation Public health system UK	III–IV	Lifetime	CARE-HF COMPANION	€7,500
Blomstrom et al. (2008)[95]	Trial-based with extrapolation Health-care system Denmark, Finland, Sweden	III–IV	Lifetime	CARE-HF	€4,800 (Denmark) €3,600 (Finland) €6,700 (Sweden)
Callejo et al. (2010)[97]	Markov model Public health system Spain	III–IV	Lifetime	Meta-analysis	€28,600
Maniadakis et al. (2011)[99]	Trial-based with extrapolation Health-care system Greece	III–IV	Lifetime	CARE-HF	€8,000
Bertoldi et al. (2011)[100]	Markov model Public health system Brazil	II–IV	20 years	Meta-analysis	Int$15,700*
Neyt et al. (2011)[101]	Markov model Health-care payer Belgium	III–IV	Lifetime	COMPANION	€11,200

Rhode et al. Cost-effectiveness of heart failure therapies. Nat Rev Cardiol 10:338-354, 2013

Avaliação Custo-Eficácia CRT-D

Table 8 | Cost-effectiveness analyses of CRT-D for heart failure

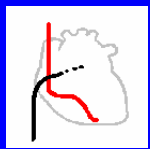
Study (year)	Study type and country	Comparison	Patients	Time period	Source of efficacy estimate	ICER per QALY gained
Callejo *et al.* (2002)[87]	Markov model Health-care system Spain	CRT-D vs CRT-P	Heart failure reduced LVEF; NYHA III–IV	Lifetime	Meta-analysis	€53,500
Feldman *et al.* (2005)[111]	Trial-based Medicare and Medicaid USA	CRT-D vs OMT	Heart failure LVEF ≤35%; NYHA III–IV	7 years	COMPANION	US$43,000
Fox *et al.* (2007)[88]	Markov model Public health system UK	CRT-D vs CRT-P	Heart failure LVEF ≤35%; NYHA III–IV	Lifetime	Meta-analysis	£40,200
Yao *et al.* (2007)[139]	Markov model with Monte Carlo simulation Public health system UK	CRT-D vs CRT-P	Heart failure LVEF ≤35%; NYHA III–IV	Lifetime	CARE-HF COMPANION	€47,900
Aidelsburger *et al.* (2008)[102]	Markov model Health-care system Germany	CRT-D vs OMT	Heart failure LVEF ≤35%; NYHA III–IV	2 years	COMPANION	€24,600
Noyes *et al.* (2009)[132]	Trial-based Health-care system USA	CRT-D vs ICD	Heart failure LVEF ≤30%; NYHA I–II	4 years	MADIT-CRT	US$58,300
Bertoldi *et al.* (2011)[116]	Markov model Health-care system Brazil	CRT-D vs CRT-P	Heart failure LVEF ≤35%; NYHA II–IV	20 years	Meta-analysis	Int$84,300*
Neyt *et al.* (2011)[131]	Markov model Health-care payer Belgium	CRT-D vs CRT-P	Heart failure LVEF ≤35%; NYHA III–IV	Lifetime	COMPANION	€57,000

Rhode et al. Cost-effectiveness of heart failure therapies. Nat Rev Cardiol 10:338-354, 2013

Análises de custo-eficácia
CDI e CRT: Resumo

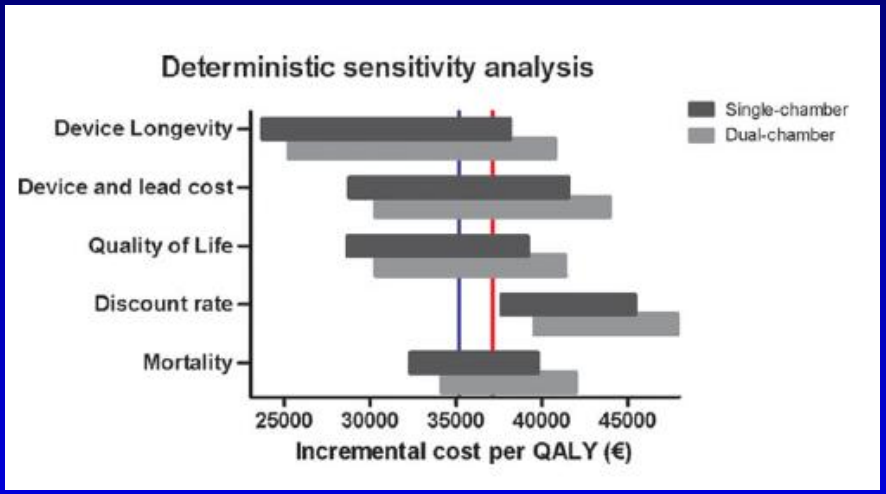
- CDI têm perfil vantajoso
  - Prevenção primária melhor que secundária
  - Perfil melhora com adição de factores de risco para morte súbita (disfunção VE, inducibilidade no EEF, QRS alargados)

- Terapêutica de Ressincronização
  - CRT-P: Perfil muito vantajoso
  - CRT-D: Perfil borderline
    - Aumento de tempo F/U estudos
    - Redução de custos: preço/longevidade bateria



Factores determinantes do custo-eficácia dos CDI / CRT

- Eficácia (efeito mortalidade)
- Segurança (complicações)
- Impacto qualidade de vida
- Custo implantação dispositivo
- Duração bateria
- Demografia doentes e perfil de risco
  - % mortalidade súbita/não-súbita
- Duração efeito terapêutico



Longev. 4 anos: ICER €38,123/QALY
Longev. 10 anos: ICER €23,744/QALY
25% redução preço – melhoria ICER em 19%

Thijssen et al. Cost-effectiveness of primary prevention implantable cardioverter defibrillator treatment. Data from a large clinical registry. PACE 2014; 37:25-34

Redução significativa dos custos CDI e CRT

Diário da República, 2.ª série — N.º 6 — 9 de janeiro de 2013

Designação do produto	Preço unitário máximo (€)
Sistema de stent dedicado para bifurcações coronárias	1.000€
Sistema de cardioversor desfibrilhador implantável de câmara única (CDI-VVI)	14.000€
Sistema de cardioversor desfibrilhador implantável de dupla câmara (CDI-DDD)	18.000€
Sistema de cardioversor desfibrilhador implantável com ressincronização (CDI CRT-D)	21.000€
Sistema de pacemaker de uma câmara (SSI)	1.000€
Sistema de pacemaker de uma câmara com resposta FC (SSI-R)	1.500€
Sistema de pacemaker dupla câmara (DDD)	2.000 €
Sistema de pacemaker dupla câmara com resposta a FC (DDD-R)	2.500€
Sistema de pacemaker dupla câmara e eletrocatéter único (VDD-R)	1.900€
Sistema de pacemaker tripla câmara (CRT-P)	5.500€

Redução significativa dos custos CDI e CRT

Ministério da Saúde publicou hoje despacho que impõe uma corte de 15% nos preços dos dispositivos médicos, como "pacemakers", praticados às unidades do SNS.

Ana Sofia Santos | **20:21** Quarta feira, 24 de abril de 2013

JORGE SIMÃO

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O Ministério da Saúde decretou a redução dos preços dos dispositivos médicos que são vendidos a todas as unidades do Serviço Nacional de Saúde (SNS), de acordo com um despacho publicado hoje em 'Diário da República'.

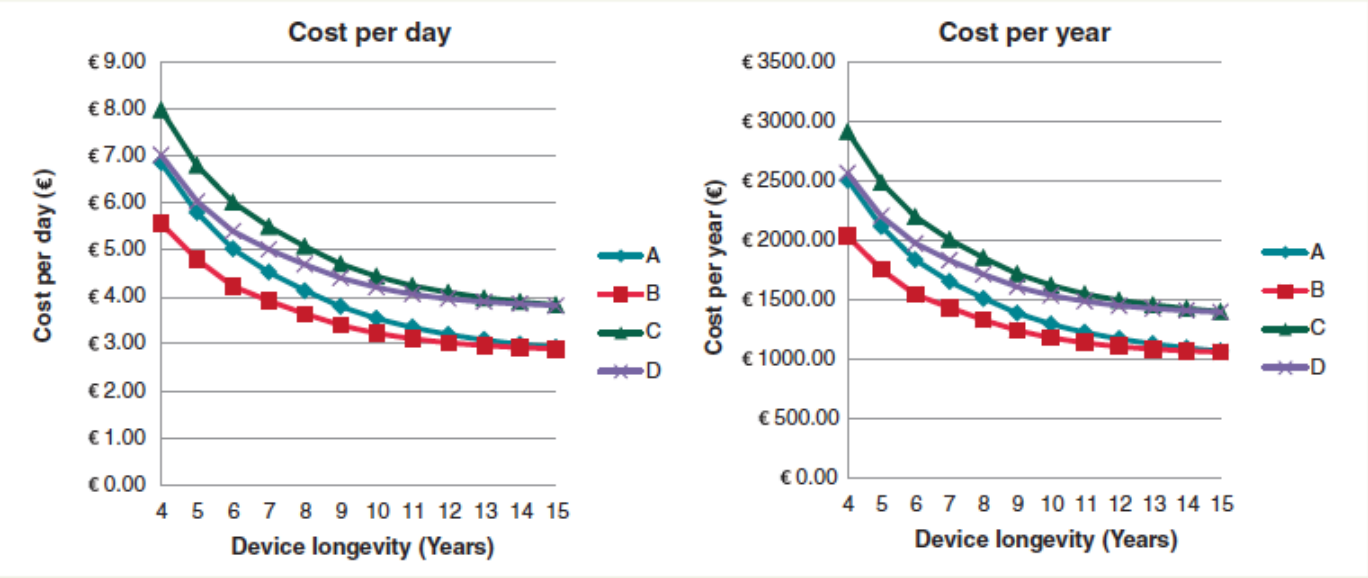
Depois das reduções administrativas nos preços dos medicamentos, o Governo ataca outra das rubricas de maior despesa do Estado com a Saúde.

Em nome da "sustentabilidade financeira do SNS", o ministério de paulo Macedo assina um despacho em que

Longevidade CDI / CRT-D

Importância na avaliação custo-eficácia

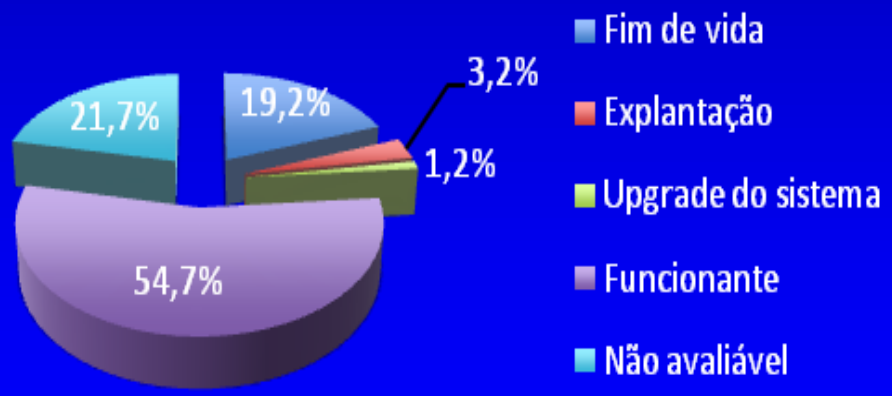
- Modelo teórico
- Impacto de aumento de longevidade de CDI / CRT-D
  - CDI: de 5 para 9 anos
  - CRT-D: de 4 para 7 anos
- Seguimento 15 anos
- Redução de custos de 29-34%
- Redução de substituições representou 46-62% da poupança

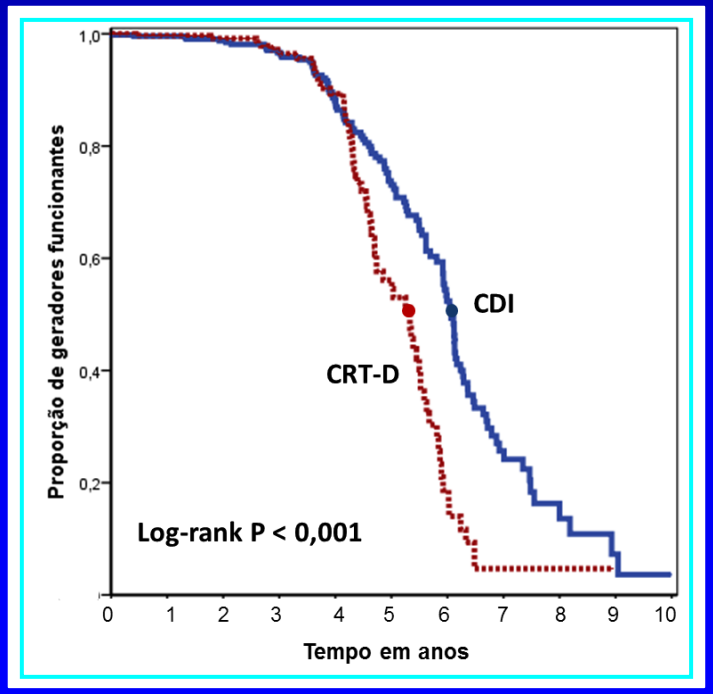


Boriani et al. Europace 15:1453-1462, 2013

Longevidade CDI e CRT-D
A realidade: HSM/CHLN

- Novembro 95-Dezembro 2012: 525 CDI e 377 CRT-D
- A longevidade mediana dos geradores de CDI foi de 6,1 anos (IC 95% 5,9-6,2), enquanto dos CRT-D foi de 5,3 anos (IC 95% 4,8-5,8)

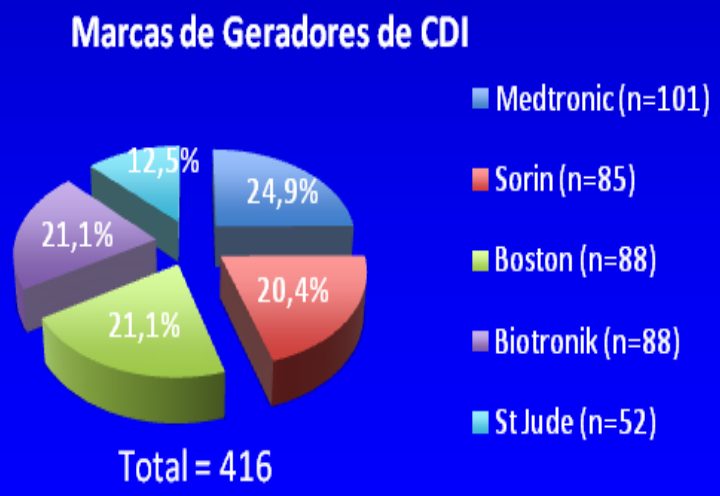


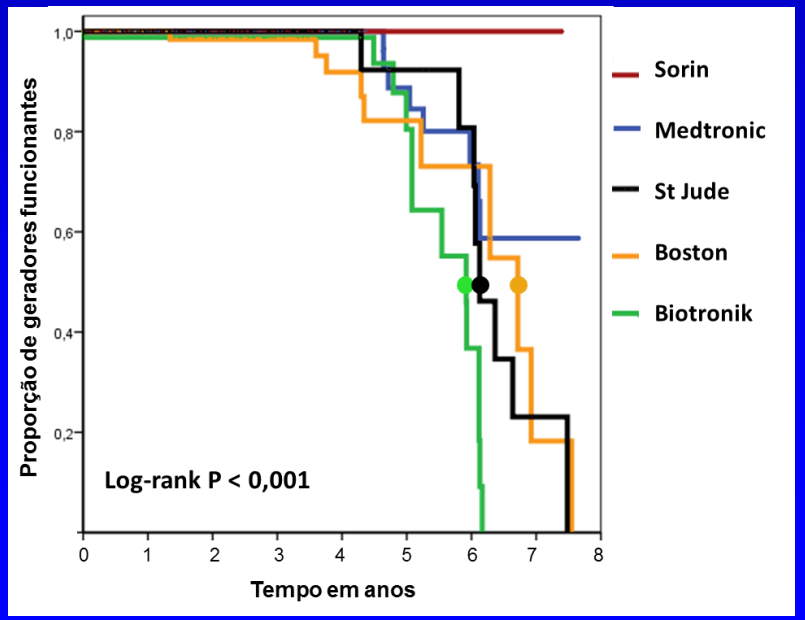


Existe diferença entre as marcas?

CDI entre Setembro de 2005 e Dezembro de 2012 no HSM

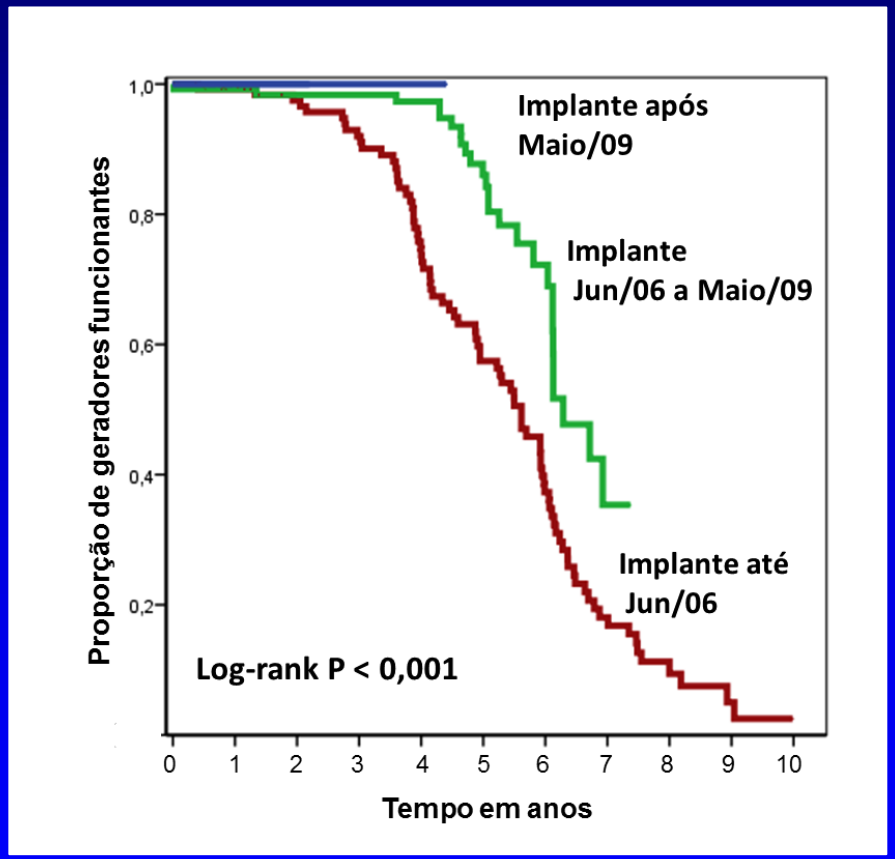
- 416 geradores, 76% em implantação inicial
- 36 geradores foram substituidos por exaustão de bateria (9,4%)
- A longevidade média dos geradores CDI foi de 6,2 anos e diferiu significativamente em função da marca (log-rank p <0,001)





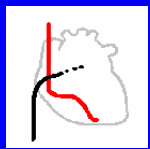
Melhoria da longevidade dos CDI com evolução tecnológica

- Implantação de CDI entre Novembro de 1995 e Dezembro de 2012: 401 doentes (85,3% do sexo masculino, 65±12 anos) no HSM
- A longevidade mediana dos geradores de CDI foi de 6,1 anos e diferiu significativamente em função do período de implantação (Log-rank P <0,001)
- Longevidade
  - Antes de Junho de 2006 : 5,6 anos
  - Junho de 2006 a Maio de 2009 – 6,3 anos
  - Todos os dispositivos implantados após Maio de 2009 mantêm geradores ainda funcionantes



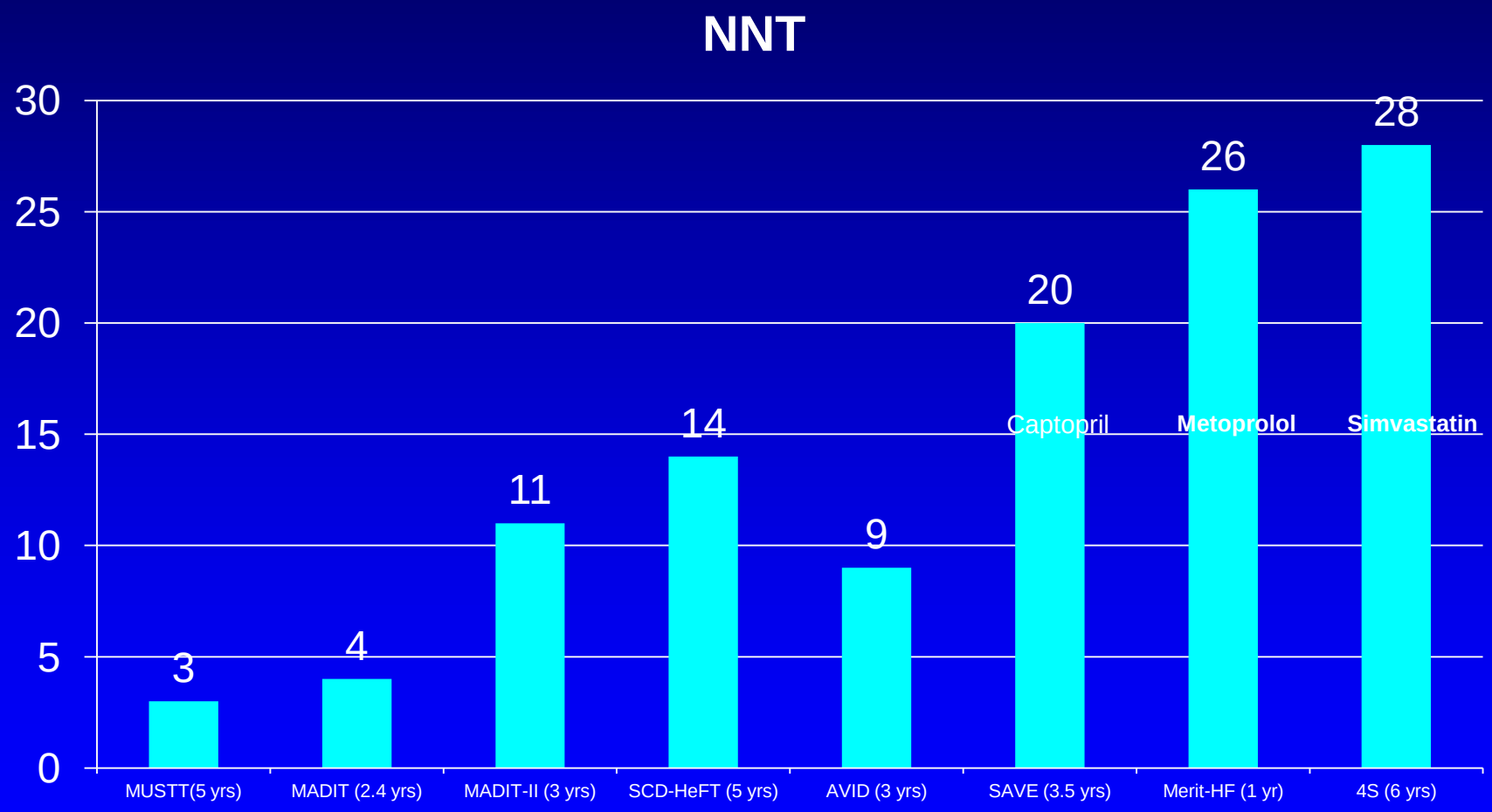
Conclusões

- A terapêutica com dispositivos CDI / CRT tem elevada eficácia na redução da mortalidade e morbilidade
- A sua avaliação económica deve basear-se em estudos de custo-eficácia, os quais demostraram um perfil comparável ao de terapêuticas médicas universalmente aceites
- A redução de custo dos dispositivos e o seu previsivel aumento de longevidade irão tornar estas terapêuticas muito atrativas e permitir o seu crescimento



Autor	Ano	Nº	Dispositivos	Longevidade
Shafat	2013	275	CDI	5 a 29% abaixo previsto
Thijssen	2012	4673	CDI e CRT-D	5,5 a VVI- 5,5 DDD- 5,8 CRT-D – 4,7 > Longevidade após 2002
Biffi	2008	153	2000-2002 com seguimento até 2007	Substituições Medtronic 42% Boston 95% SJM 97%
Horlbeck	2012	1502	CDI/CRT-D	Biot 4,3 Sorin 4,5 Boston 4,7 SJM 5 Medtronic 5,8
Alam	2013	646	CRT-D	Sobrevida sem ERI Boston 67% Medtronic 92% SJM 98%

ICD: Custo / Eficácia



Avaliação Custo-Eficácia da TRC

Table 2 Studies from the literature reporting estimates of costs, cost utility, or cost effectiveness of cardiac resynchronization therapy (with devices with or without defibrillation capabilities)

Author, year	Setting, patients	Methods	Results		
			Notes	Incremental cost-utility and cost-effectiveness estimates	
				Per QALY gained	Per LY gained
Nichol *et al.*, 2004[24]	Systematic review of studies on CRT	Markov model with Monte Carlo simulation in a lifetime horizon from a US perspective		$107 800 for CRT-P vs. control	
Feldman *et al.*, 2005[25]	1520 HF patients (NYHA III–IV) enrolled in COMPANION trial and randomized to CRT-P or CRT-D vs. control	Assessment of costs at 2-year follow-up and modelling to predict CE at 7 years	Hospitalizations in a 2-year follow-up	$19 600 for CRT-P vs. control $43 000 for CRT-D vs. control	$28 100 for CRT-P vs. control $46 700 for CRT-D vs. control
Calvert *et al.*, 2005[26]	813 HF patients (NYHA III–IV) enrolled in CARE HF trial and randomized to CRT-P vs. control	Assessment of post-implant cost during a mean follow-up of 29.4 months	CRT-P associated with increased costs, survival and QALYs	€19 319	€43 596
Banz *et al.*, 2005[27]	Modelling study on a decision analytic model	Decision analytic model, based on data from data sets, trials, and expert opinion. Estimates at 1 year from a German perspective	At 1 year	€36 600 for CRT-P vs. control	
Fattore *et al.*, 2005[28]	Modelling study on a decision analytic model	Decision analytic model, based on data from data sets, trials, and expert opinion. Estimates at 1, 2 and 3 years from an Italian perspective	At 1 year At 2 years At 3 years	€63 225 for CRT-P vs. control €30 343 for CRT-P vs. control €21 720 for CRT-P vs. control	€306 545 for CRT-P vs. control €71 986 for CRT-P vs. control €43 628 for CRT-P vs. control
Caro *et al.* 2006[29]	Simulation of 1000 HF patients (NYHA III–IV) receiving CRT-P vs. 1000 control patients with a similar profile, on the basis of CARE HF data	Discrete event simulation model for a 5-year time horizon from a UK perspective	5-year perspective	£15 247 for CRT-P vs. control	
Yao *et al.*, 2007[30]	Economic model based on HF patients (NYHA III–IV) enrolled in CARE HF trial. Survival data for CRT-D from the COMPANION trial	Markov model with Monte Carlo simulation to assess CE of CRT-P and CRT-D for a lifetime horizon from a UK perspective	In a 65-year-old patient	€7538 for CRT-P vs. control €47 909 for CRT-D vs. control	€7011 for CRT-P vs. control €35 864 for CRT-D vs. control
Fox *et al.*, 2007[31]	Systematic review and meta-analysis of clinical trials on CRT	Markov model on the basis of a meta-analysis from five RCTs (3434 patients). Estimate of CE of CRT-P and CRT-D for a lifetime horizon	Estimates for a mixed age cohort	£16 735 for CRT-P vs. control £40 160 for CRT-D vs. CRT-P	
Bentkover *et al.*, 2007[32]	72 HF patients (NYHA III–IV) randomized to ICD vs. CRT-D in Canada	Assessment of post-implant costs during a 6-month follow-up	Post-implant cost for CRT-D lower than ICD with a mean saving of Canadian $2000–2400 in a 6-month follow-up		
Aidelsburger *et al.*, 2008[33]	HF patients (NYHA III–IV), similar to COMPANION patients, implanted with CRT-D	Decision analytic model, based on cost and resources utilized in Germany in 2005, and on CRT-D effectiveness derived from COMPANION for a 2-year perspective	2-year perspective with a device longevity of 2 years 2-year perspective with a device longevity of 5 years	€88 143 vs. control €24 650 vs. control	€193 996 vs. control €33 116 vs. control
Blomström *et al.*, 2008[34]	Simulation of HF patients (NYHA III–IV) in Scandinavian University Hospitals, on the basis of data from CARE HF	Bootstrap resampling of data from CARE HF in a time horizon equal to patient's expected lifetime, considering costs in Denmark, Finland, and Sweden	No CRT benefits assumed after 6 years. Device longevity of 6 years	€3600–6700 vs. control	

Indicação CDI
ACC/AHA/ESC Guidelines

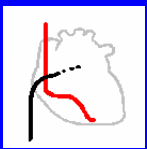
(Optimal medical therapy, good survival expectation and functional status > 1 year)

- Class I
  - Secondary prevention of SCD in patients who survived VF or hemodinamicaly unstable VT with syncope, with EF < 40% (Level A)
  - Primary prevention, ischemic heart disease, > 40 days after MI, EF < 30-40%, functional class II-III (Level A)
  - Primary prevention, nonischemic heart disease, EF < 30-35%, functional class II-III (Level B)

- Class IIA
  - ICD combined with biventricular pacing, functional class III-IV, optimal therapy, sinus rhythm, QRS > 120 msecs (Level B)
  - Primary prevention, ischemic heart disease, > 40 days after MI, EF < 30-35%, functional class I (Level B)
  - Biventricular pacing without ICD in class III-IV, EF < 35%, QRS > 160 msecs or > 120 msec and other evidence of dyssynchrony (Level B)
  - Heart failure, recurrent stable VT, near normal EF (Level C)

- Class IIB
  - Primary prevention, nonischemic heart disease, EF < 30-35%, functional class I (Level B)

Zipes et al: Europace 2006



Indicações CDI

ACC / AHA / HRS 2008 Guidelines

- Prevenção secundária
  - Classe I
    - Sobreviventes de paragem cardíaca devida a FV ou TV instável
    - Cardiopatia estrutural e TV mantida (estável ou instável)
    - Síncope de etiologia não esclarecida e TV/FV indutível no EEF
  - Classe IIA
    - TV mantida e função ventricular normal ou ligeiramente comprometida

Epstein et al: JACC 2008; 53

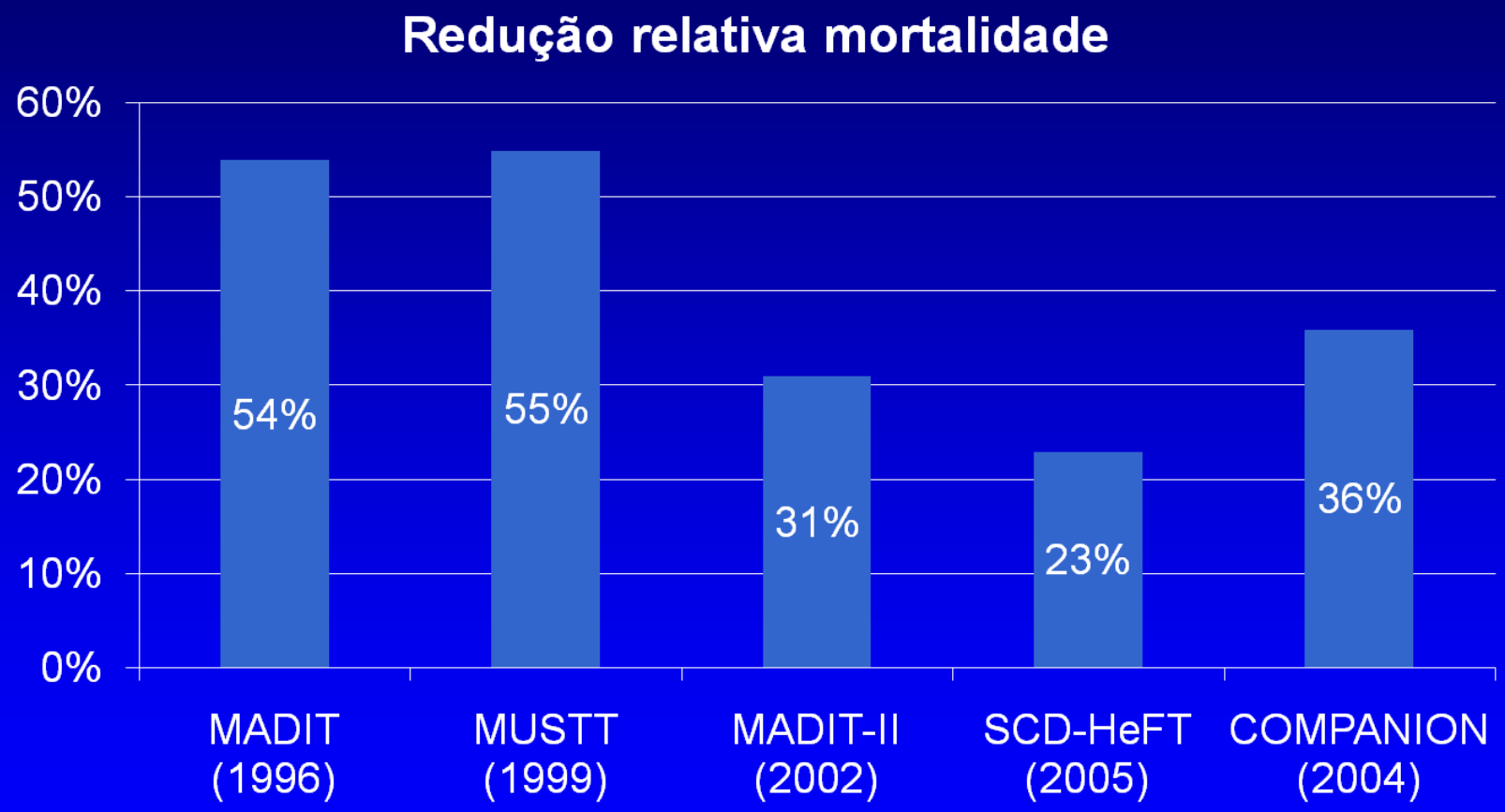
Indicação CDI

2010 Focused Update of ESC Guidelines on device therapy in heart failure

- Class I, nível A: CRT-D / CRT-P
  - ICC classes III/IV (ambulatória) com FE < 35%, QRS > 120 msegs, em ritmo sinusal, sob terapia médica optimizada
  - ICC classe II, FE < 35%, QRS > 150 msegs, em ritmo sinusal, sob terapêutica médica optimizada
- Class IIA, nível B: CRT-D / CRT-P
  - ICC classe III/IV, fibrilhação auricular, com FE < 35%, QRS > 130 msegs, sob dependência de pacing pós-ablação NAV
- Class IIA, nível C: CRT-D / CRT-D
  - ICC classes III/IV, fibrilhação auricular, FE < 35%, QRS > 130, > 95% ritmo > 95% pacing
  - Indicação para PMK, ICC classes III/IV, FE < 35%, QRS < 120

Dickstein et al: Eur Heart J: 2010

CDI: Eficácia



	COMPANION 2004			CARE-HF 2005		REVERSE 2008		MADIT-CRT 2009		RAFT 2010	
Desenho	**CRT-D vs CRT-P vs OMT**			**CRT-P vs. OMT**		**CRT (D/P) vs No CRT**		**CRT-D vs. CDI**		**CRT-D vs. CDI**	
NYHA	III / IV ambult.			III/IV		II / I (sintomática)		II / I (isquémica)		II / III	
FEj	FEj ≤35%			FEj ≤35%		FEj ≤40%		FEj ≤30%		FEj ≤30%	
Ritmo QRS	RS / ≥120ms			RS / ≥150ms (120-149 + dess)		RS / ≥120ms		RS / ≥130ms		RS ≥120 (pacing >200)	
Duração FUp	**16m**			**29m**		**12m (extensão 24m)**		**28m**		**40m**	
População	**1520 dts**			**813 dts**		**610 dts**		**1.820 dts**		**1.798 dts**	
NYHA	**III 86%** / IV 14%			**III 94%** / IV 6%		**II 82%** / I 18%		**II 85%** / I 15%		**II 80%** / III 20%	
FEj média	21%			26%		27%		24%		23%	
QRS	159 ms			160 ms		153 ms		158 ms		158 ms	
Endpoint	**CRT-D**	**CRT-P**	**OMT**	**CRT-P**	**OMT**	**CRT-D/P**	**No CRT**	**CRT-D**	**CDI**	**CRT-D**	**CDI**
Morte	**12%**	15%	19%	**20%/2a**	30%/2a	5,7%	8,6%	6,8%	7,3%	**20,8%**	**26,1%**
Hospitaliz. IC	**36%**	**33%**	46%			7,8%	18,4%	**13,9%**	**22,8%**	**19,5%**	**26,1%**
Morte ou IC	**29%**	**31%**	45%	**39%/2a**	55%/2a	12%	24%	**17,2%**	**25,3%**	**33,2%**	**40,3%**

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Cardiac-Resynchronization Therapy for the Prevention of Heart-Failure Events

Arthur J. Moss, M.D., W. Jackson Hall, Ph.D., David S. Cannom, M.D., Helmut Klein, M.D., Mary W. Brown, M.S., James P. Daubert, M.D., N.A. Mark Estes III, M.D., Elyse Foster, M.D., Henry Greenberg, M.D., Steven L. Higgins, M.D., Marc A. Pfeffer, M.D., Ph.D., Scott D. Solomon, M.D., David Wilber, M.D., and Wojciech Zareba, M.D., Ph.D., for the MADIT-CRT Trial Investigators*

ABSTRACT

BACKGROUND

This trial was designed to determine whether cardiac-resynchronization therapy (CRT) with biventricular pacing would reduce the risk of death or heart-failure events in patients with mild cardiac symptoms, a reduced ejection fraction, and a wide QRS complex.

METHODS

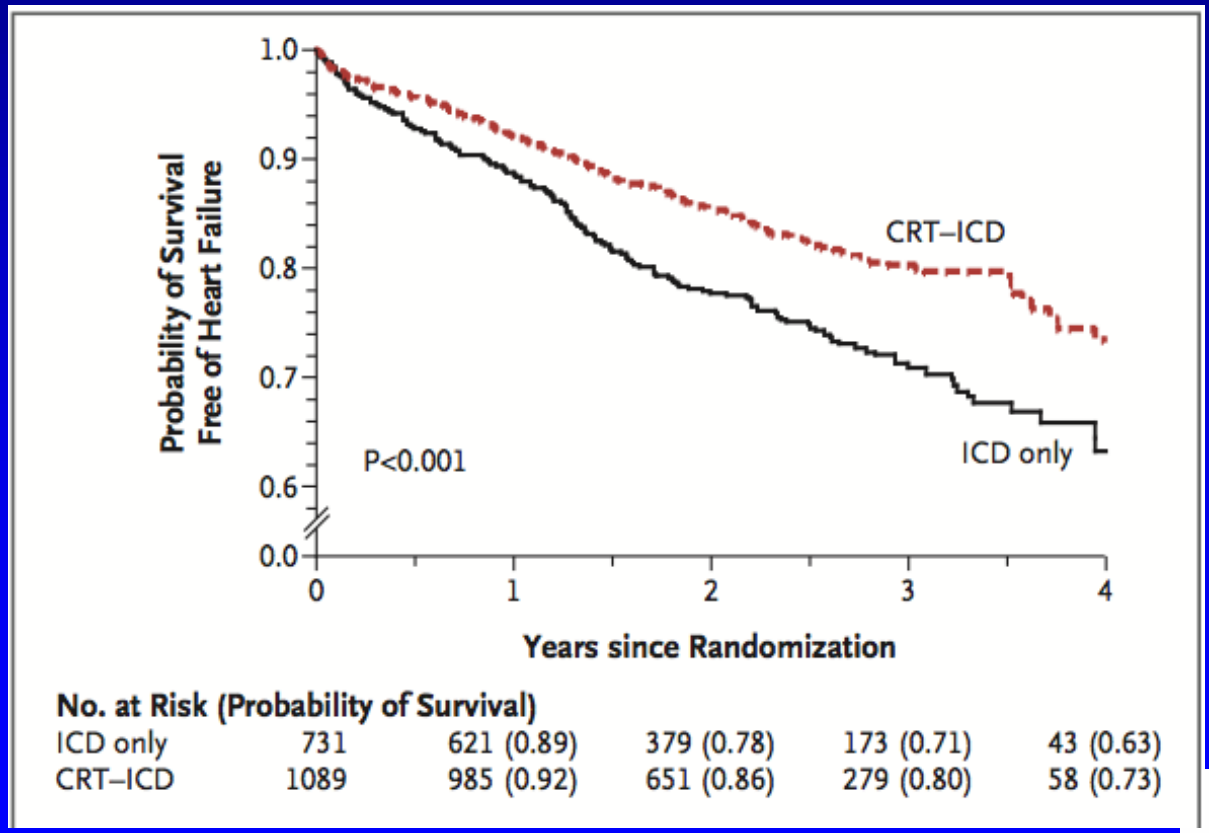
During a 4.5-year period, we enrolled and followed 1820 patients with ischemic or nonischemic cardiomyopathy, an ejection fraction of 30% or less, a QRS duration of 130 msec or more, and New York Heart Association class I or II symptoms. Patients were randomly assigned in a 3:2 ratio to receive CRT plus an implantable cardioverter–defibrillator (ICD) (1089 patients) or an ICD alone (731 patients). The primary end point was death from any cause or a nonfatal heart-failure event (whichever came first). Heart-failure events were diagnosed by physicians who were aware of the treatment assignments, but they were adjudicated by a committee that was unaware of assignments.

RESULTS

During an average follow-up of 2.4 years, the primary end point occurred in 187 of 1089 patients in the CRT–ICD group (17.2%) and 185 of 731 patients in the ICD-only group (25.3%) (hazard ratio in the CRT–ICD group, 0.66; 95% confidence interval [CI], 0.52 to 0.84; P=0.001). The benefit did not differ significantly between patients with ischemic cardiomyopathy and those with nonischemic cardiomyopathy. The superiority of CRT was driven by a 41% reduction in the risk of heart-failure events, a finding that was evident primarily in a prespecified subgroup of patients with a QRS duration of 150 msec or more. CRT was associated with a significant reduction in left ventricular volumes and improvement in the ejection fraction. There was no significant difference between the two groups in the overall risk of death, with a 3% annual mortality rate in each treatment group. Serious adverse events were infrequent in the two groups.

CONCLUSIONS

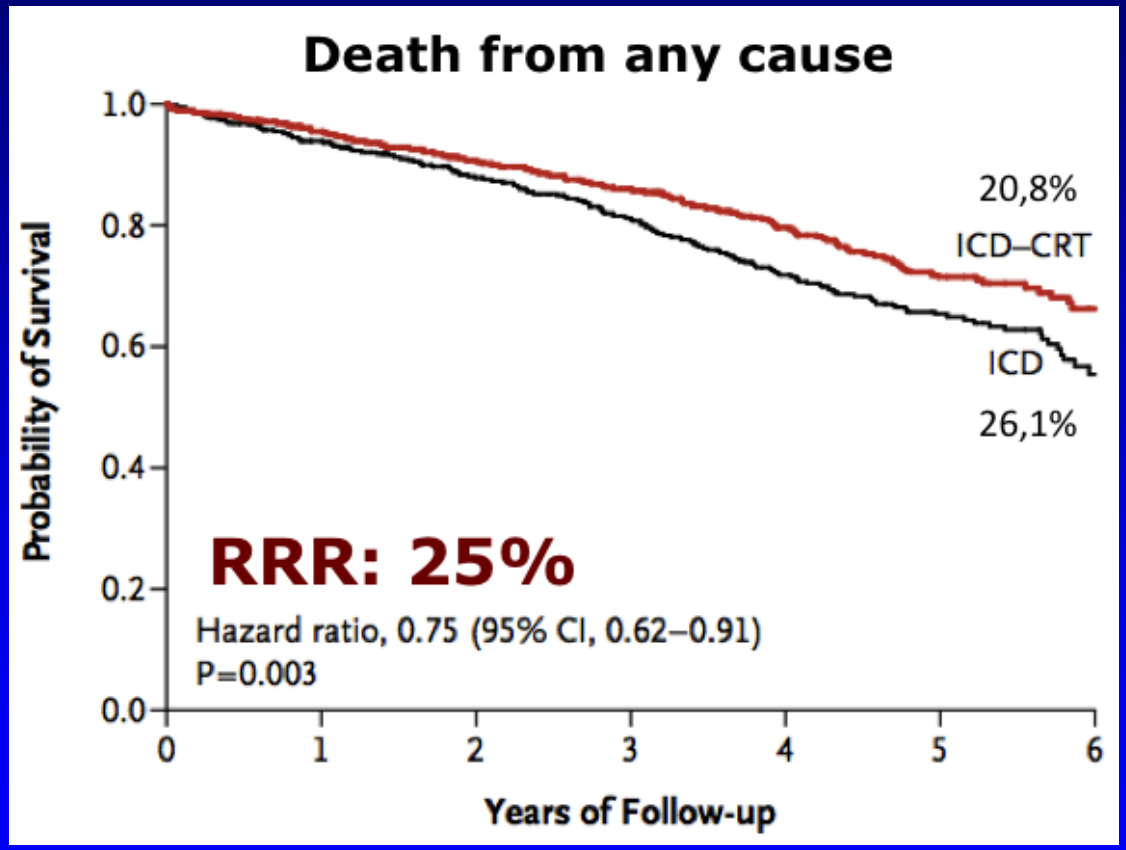
CRT combined with ICD decreased the risk of heart-failure events in relatively asymptomatic patients with a low ejection fraction and wide QRS complex. (ClinicalTrials.gov number, NCT00180271.)



No. at Risk (Probability of Survival)

ICD only	731	621 (0.89)	379 (0.78)	173 (0.71)	43 (0.63)
CRT–ICD	1089	985 (0.92)	651 (0.86)	279 (0.80)	58 (0.73)

Estudo RAFT



Tang A. *N Engl J Med* 2010;363:2385-95

Razão Incremento Custo-Eficácia (ICER)

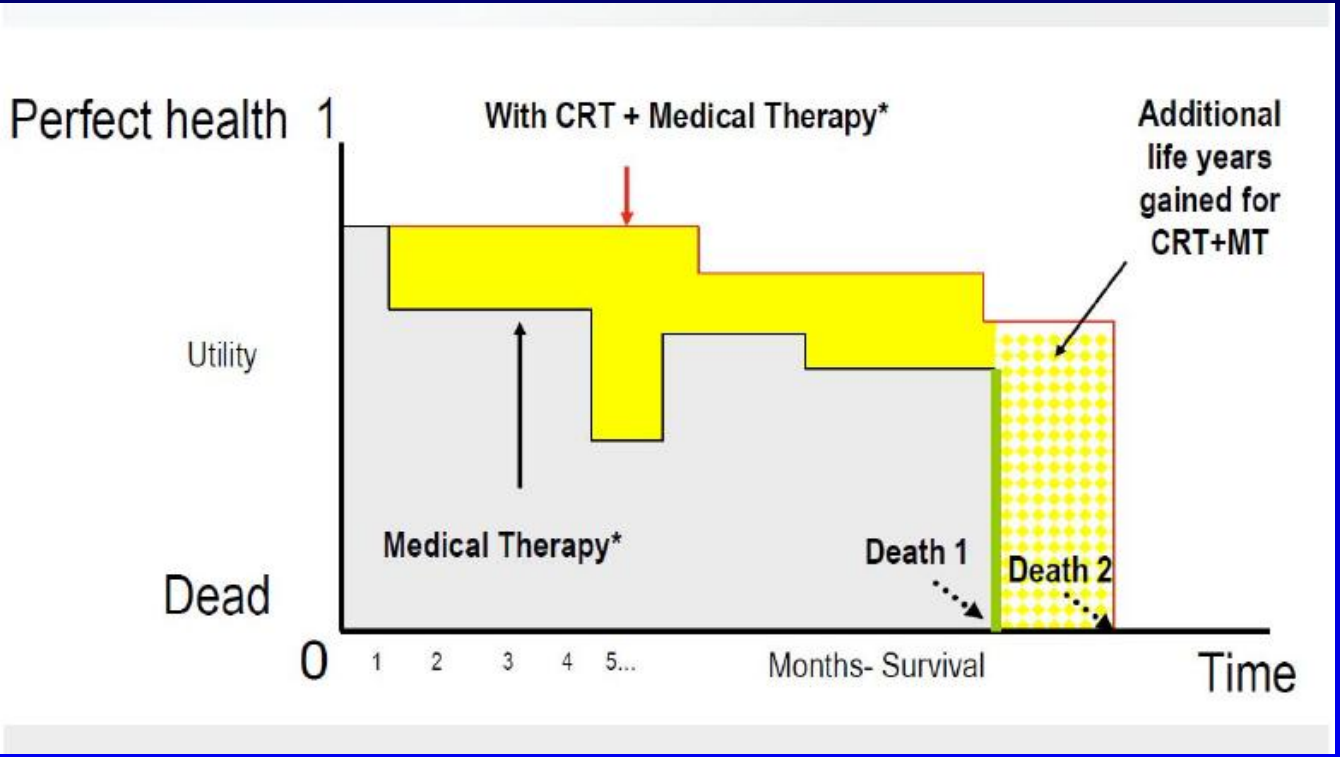
$$\frac{\text{CUSTO (nova terapeutica – tratamento actual)}}{\text{Eficácia (nova terapeutica – tratamento actual)}}$$

Atractivo: < €20.000/QALY
Aceitável: €20-40.000/QALY
Borderline: €40-60.000/QALY
Desfavorável: €60 -100,000/QALY

Porquê usar QALY

- Medida mais genérica que combina sobrevida com morbilidade
- Utilizado em estudos com end-point combinado, em que tanto a sobrevida como a Qol são importantes
- Permite a comparação de terapeuticas
- Uma só medida permite caracterizar os efeitos de um tratamento

QALY



Exemplo: Se a utility index (QOL) for 0.5 para a IC então + 2 anos de sobrevida são 1QALY. Se o device melhorar para 0.75 o index então a prazo de 5 anos ganha-se 1,25 QALY.

Avaliação Custo-Eficácia CDI Insuficiência cardíaca

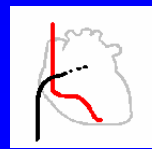
Table 6 | Cost-effectiveness analyses of ICDs for heart failure

Study (year)	Study type and country	Patients	Time period	Source of efficacy estimate	ICER
Mushlin et al. (1998)[19]	Trial-based Third party payer USA	Ischaemic heart failure, NSVT, and inducible VT in EPT	4 years	MADIT-I	US$27,000/LYG
Sanders et al. (2005)[20]	Markov model Societal USA	Heart failure (varied with trial)	Lifetime	Various trials	US$34,000–70,200/QALY
Al-Khatib et al. (2005)[21]	Registry-based with extrapolation Societal USA	Ischaemic heart failure LVEF ≤30%	Lifetime	Registry	US$50,500/LYG
NICE (2006)[22]	Markov model Public health system UK	Ischaemic heart failure LVEF <30%	Lifetime	Meta-analysis	£30,300/QALY
Caro et al. (2007)[128]	Discrete event simulation Health-care system UK, France	Heart failure LVEF ≤35%	5 years	SCD-HeFT	Cost–benefit ratio 1:6 (UK), 1:7 (France)
Neyt et al. (2008)[127]	Markov model Health insurance system Belgium	Heart failure LVEF ≤35%	Lifetime	SCD-HeFT	€71,400/QALY
Deniz et al. (2009)[129]	Microsimulation Health-care system Canada	Heart failure LVEF ≤35%	5 years	SCD-HeFT	Cost–benefit ratio 1:20
Ribeiro et al. (2010)[23]	Markov model Health-care system Brazil	Hear failure NYHA class II–III	20 years	Meta-analysis	Int$50,300/QALY*
Gandjour et al. (2011)[41]	Markov model Statutory health insurance Germany	Ischaemic heart failure LVEF ≤30%	Lifetime	MADIT-II	€44,700/QALY
Smith et al. (2013)[44]	Markov model Societal Europe	Heart failure LVEF ≤40%	Lifetime	Meta-analysis	€44,000/QALY

Custo-eficácia CDI / CRT
Perspectiva global

Cost-effectiveness (from G. Boriani, G. Larsen in ESC book 2006)

Treatment	Cost per year of life saved ($/YLS) or QUALY
PM for complete AV block	1,400
Valve replacement for aortic stenosis	2,200
Neonatal intensive care	7,400
CABG for left main stenosis	9,200
Aspirin	11,000
Enalapril post MI	10,200
CABG for 3-v disease	18,500
Beta-blockers in low-risk MI	20,200
ICD for VT/VF with EPS	25,700
Primary Stent in PTCA	26,800
ICD for MADIT I profile	27,000
Clopidogrel in ineligible to ASA	31,000
ICD for SCD-HeFT profile	33,192
ICD for MADIT II profile	36,700
CRT-D in COMPANION	38,200
Anti-hypertensive tx (PAD 95-104)	41,900
ICD for MADIT II profile	50,500
Hospital hemodialysis	59,500
CABG in 2-v disease	72,900
PTCA in 1-v disease	109,000
Clopidogrel in ACS	130,000
Neurosurgery for malignant tumor	320,000



CRT in COMPANION Trial: Estimated cost-effectiveness of device therapy over 7 years compared with optimal medical therapy only

Parameter	CRT-P	CRT-D
Cost per life-year saved ($)	28 100	38 200
Cost per QALY saved ($)	19 600	35 200

CRT-P= CRT with pacing only
CRT-D= CRT with defibrillator

Feldman AM. American College of Cardiology 2005 Scientific Sessions; March 6-9, 2005; Orlando, FL.

Análise de Markov

CARE-HF

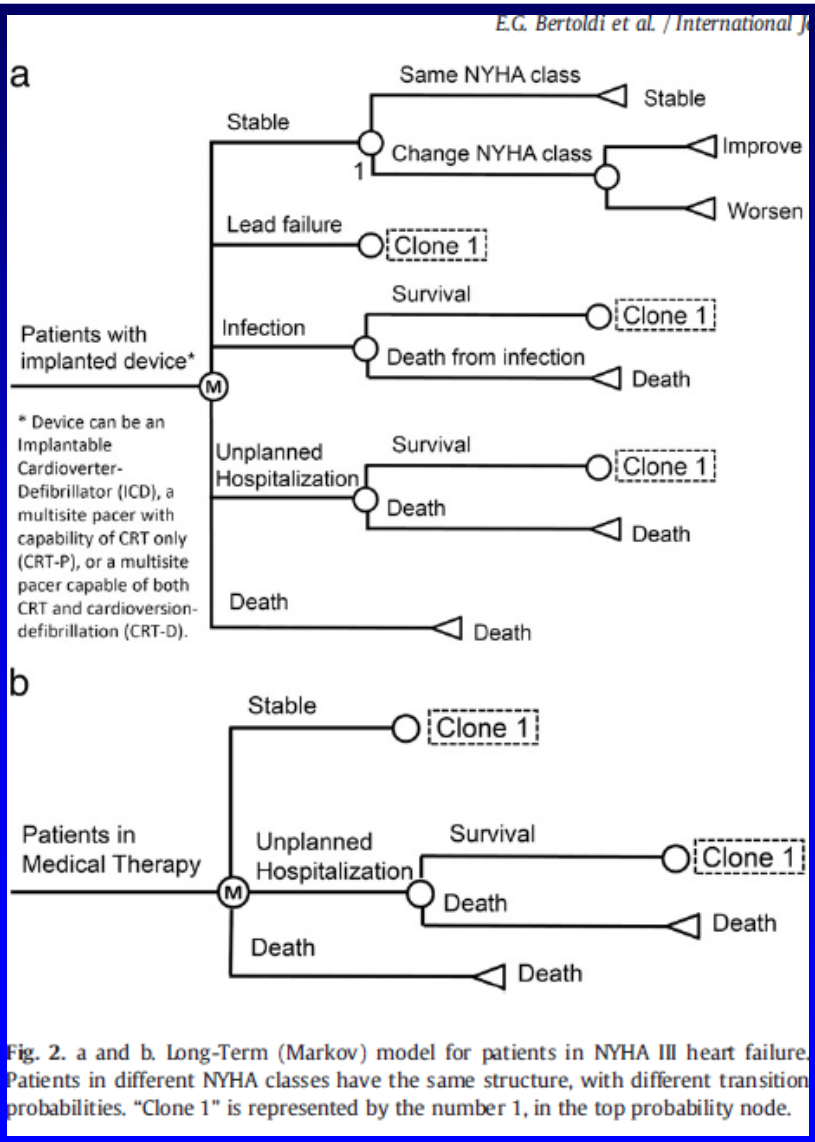


Fig. 2. a and b. Long-Term (Markov) model for patients in NYHA III heart failure. Patients in different NYHA classes have the same structure, with different transition probabilities. "Clone 1" is represented by the number 1, in the top probability node.