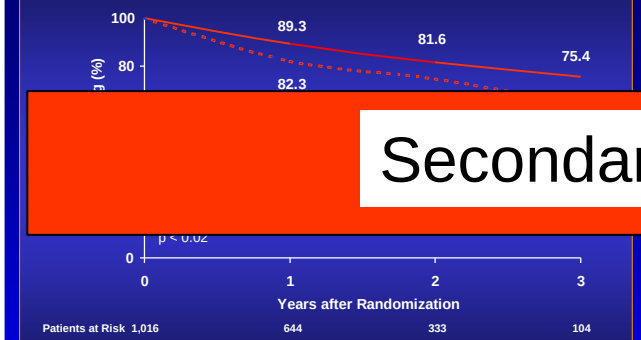
Et comment ?

Bordeaux, le 20 Novembre 2010.
Dr Sylvain Reuter. Dr Stéphane Garrigue.
Clinique Saint Augustin, Bordeaux.

Pour QUI ?

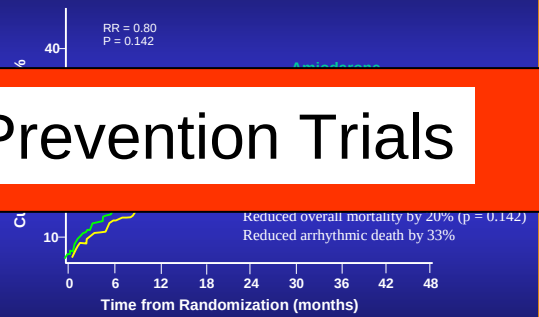
Secondary Prevention Trials

AVID Overall Survival Results



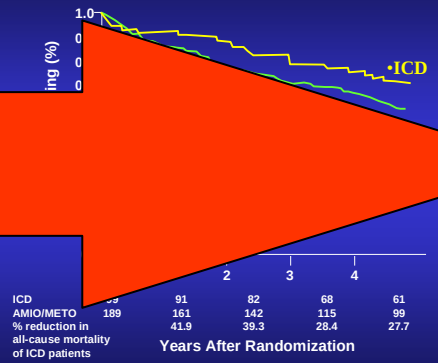
The AVID Investigators. *N Engl J Med*. 1997;337(22):1576-1583.

CIDS Overall Mortality Results



Connolly SJ. *Circulation*. 2000;101:1297-1302.

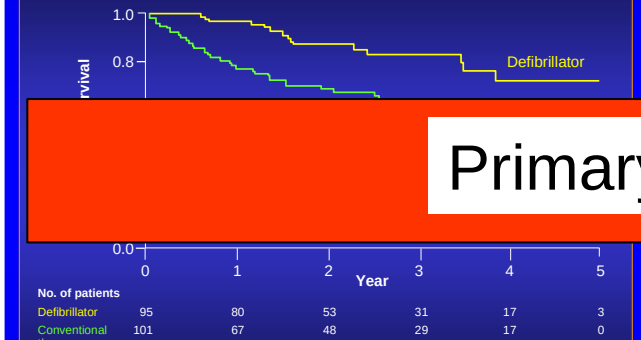
CASH Survival Results



Kuck K. *Circulation*. 2000;102:748-754.

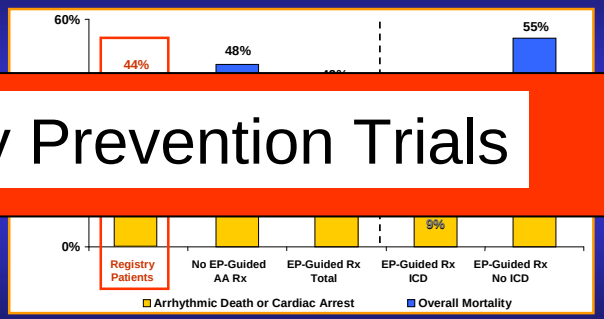
Primary Prevention Trials

MADIT Survival Results



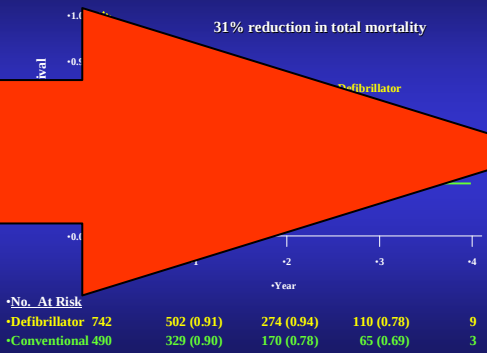
Moss AJ. *N Engl J Med*. 1996;335:1933-40.

MUSTT Mortality/5 Years



Buxton AE. *N Engl J Med*. 1999;341:1882-90.
Buxton AE. *N Engl J Med*. 2000;342:1937-45.

MADIT-II Survival Results

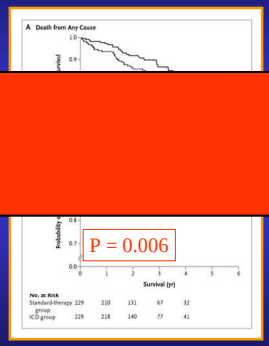


Moss AJ. *N Engl J Med*. 2002;346:877-83.

ICD in HF patients

DEFINITE

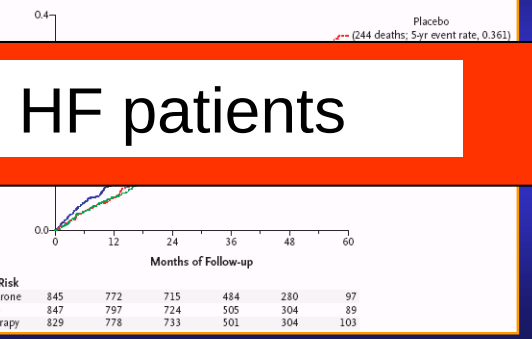
Defibrillators **i**n **N**on-**I**schemic Cardiomyopathy **T**reatment **E**valuation



Kadish, A. et al. N Engl J Med 2004;350:2151-2158

SCD-HeFT: Kaplan-Meier mortality (all-cause) *

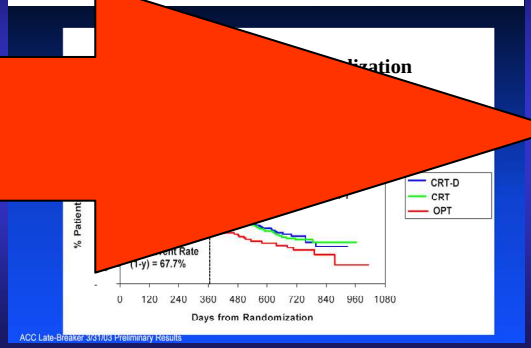
	Hazard Ratio (97.5% CI)	P Value
Amiodarone vs. placebo	1.06 (0.86–1.30)	0.53
ICD therapy vs. placebo	0.77 (0.62–0.96)	0.007



* Rules of Evidence; PACE 2005, Editorial; 28: 81-88; Sweeney MO & al (Boston, MA)

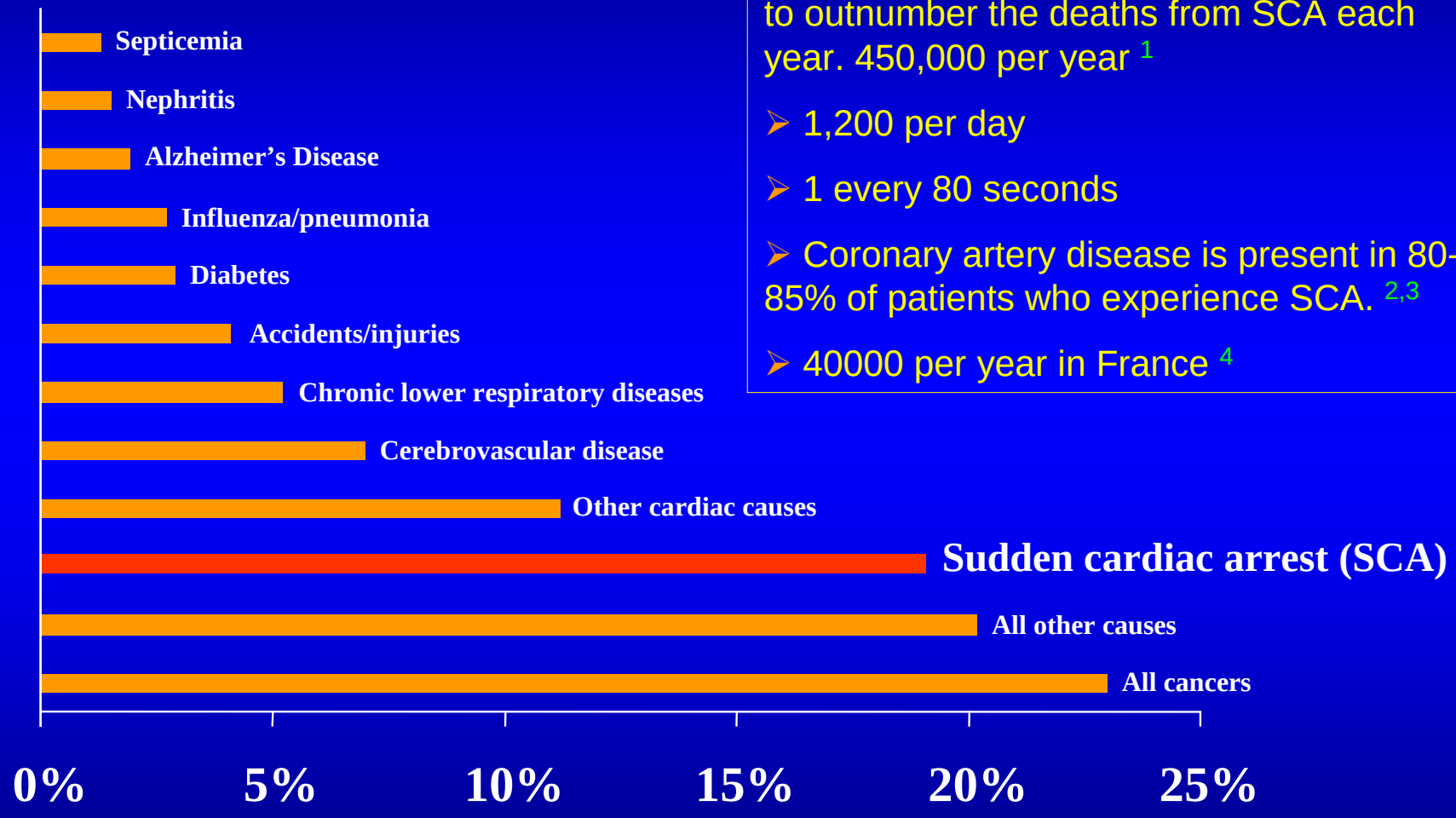
COMPANION

Comparison of **M**edical Therapy, **P**acing **an**d Defibrillat**ion** in Heart Failure Trial



Bristow, M. R. et al. N Engl J Med 2004;350:2140-2150

Leading Causes of Death in the U.S.

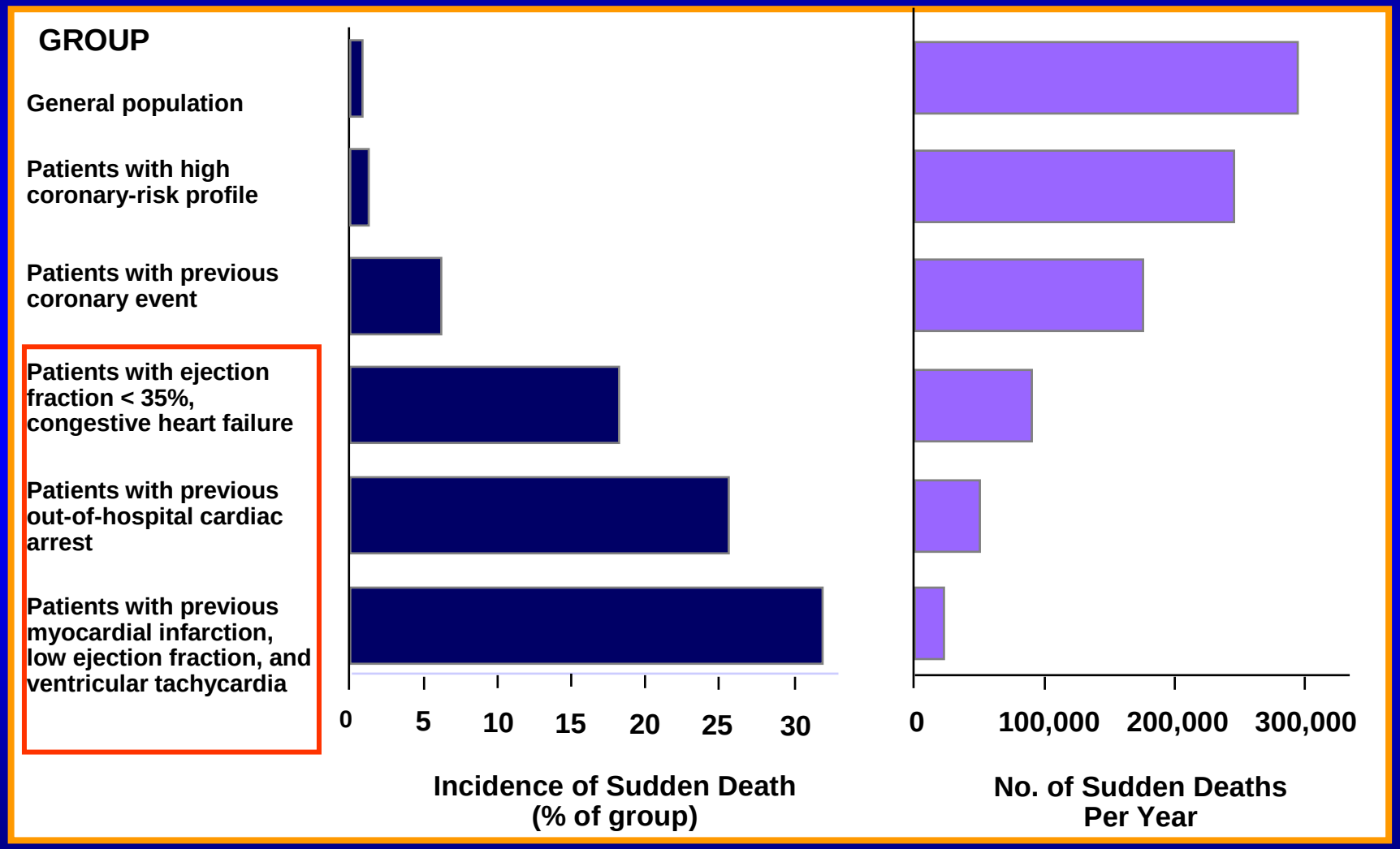


- You must combine deaths from all cancers to outnumber the deaths from SCA each year. 450,000 per year [1]
- 1,200 per day
- 1 every 80 seconds
- Coronary artery disease is present in 80-85% of patients who experience SCA. [2,3]
- 40000 per year in France [4]

National Vital Statistics Report. Oct. 12, 2001;49(11). *MMWR*. State-specific mortality from sudden cardiac death – US 1999. Feb 15, 2002;51:123-1261.
[1] Zheng Z. *Circulation*. 2001;104:2158-2163.
[2] Myerburg RJ, Heart Disease, *A Textbook of Cardiovascular Medicine*. 6th ed. W.B. Saunders, Co. 2001.
[3] Cobb LA. *Circulation*. 1975;51(III):223.
[4] Chauvin M et al. Recommandations concernant l'implantation et la surveillance des défibrillateurs automatiques implantables. *Arch Mal Coeur & Vx* 2004 ; 97 (9) : 915-9.

Interpretation of Outcomes of Antiarrhythmic Clinical Trials

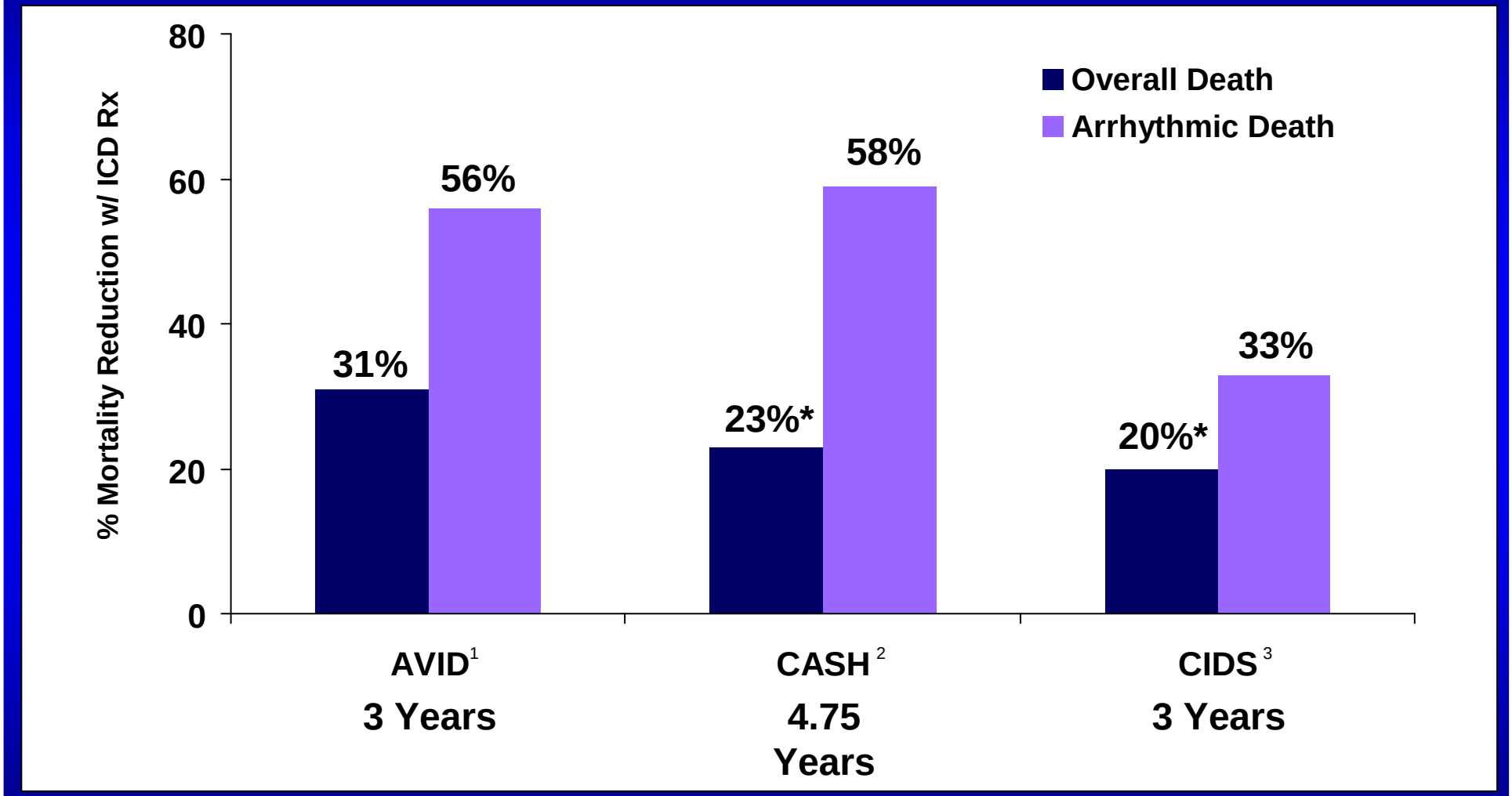
Design Features and Population Impact



Incidence of SCD in Specific Populations and Annual SCD Numbers

Myerburg RJ et al. *Circulation*.1998;97:1514-1521.

Secondary Prevention Trials: Reduction in Mortality with ICD Therapy



* Non-significant results.

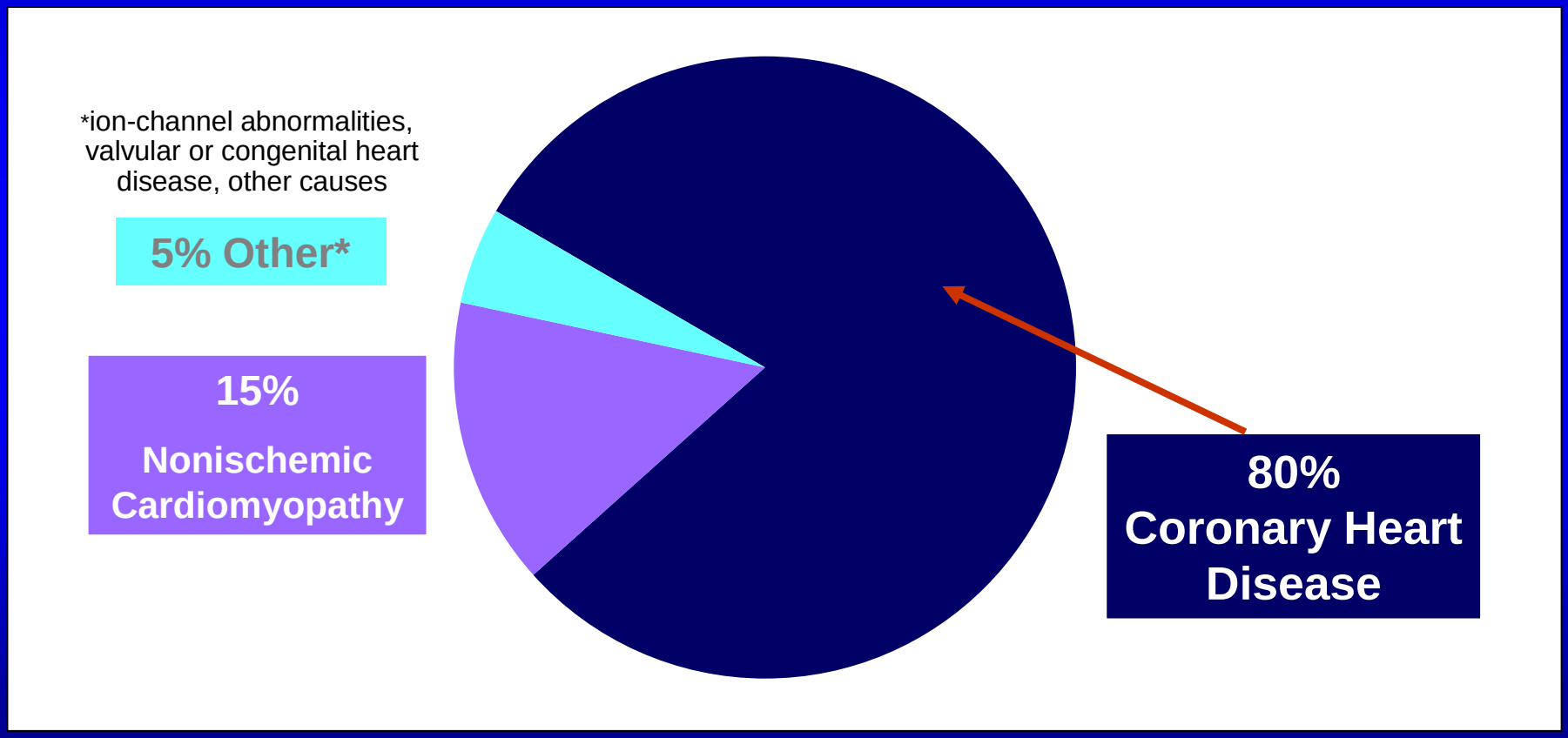
[1] The AVID Investigators. *N Engl J Med*. 1997;337:1576-1583.

[2] Kuck K. *Circulation*. 2000;102:748-754.

[3] Connolly S. *Circulation*. 2000;101:1297-1302.

Coronary Heart Disease

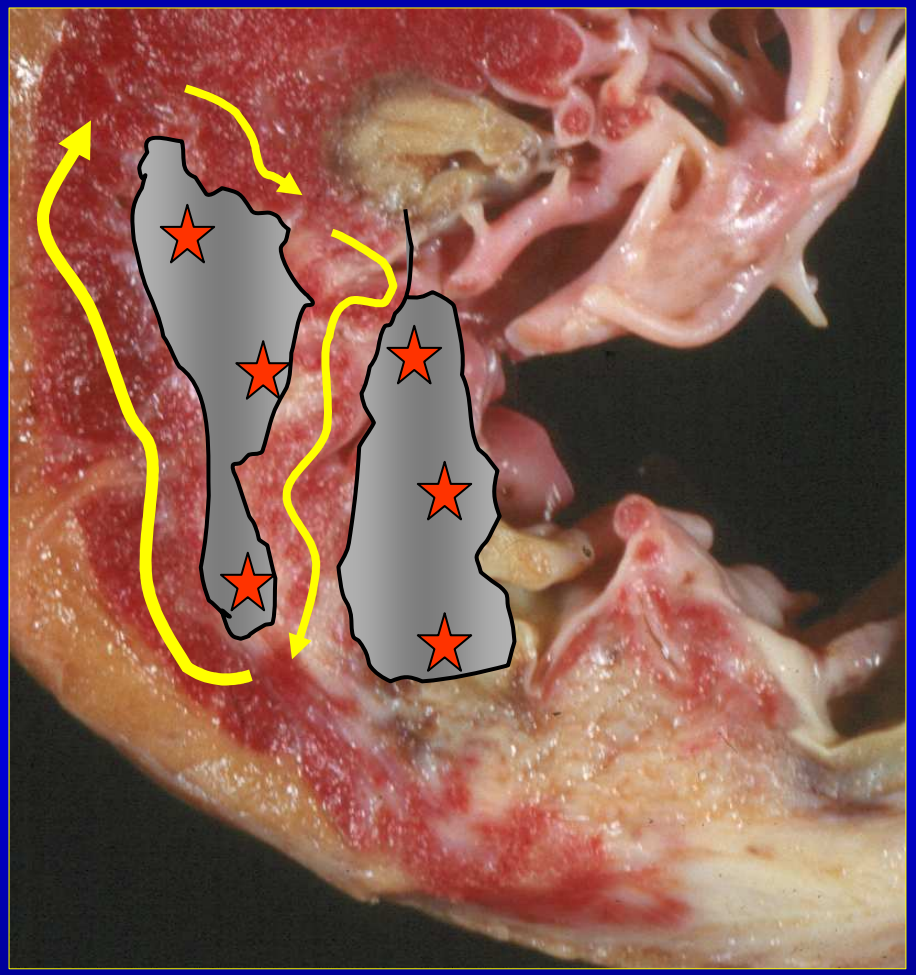
Coronary heart disease and its consequences account for the majority of sudden cardiac deaths in Western cultures.

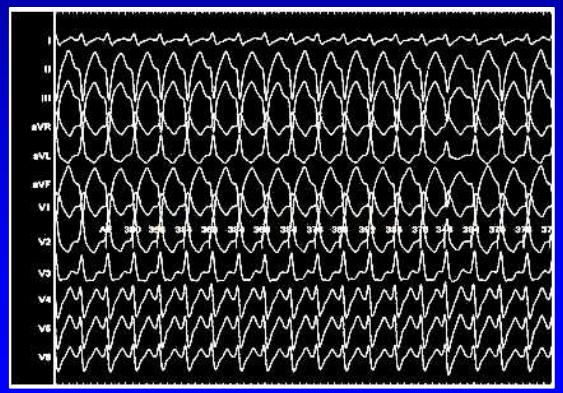


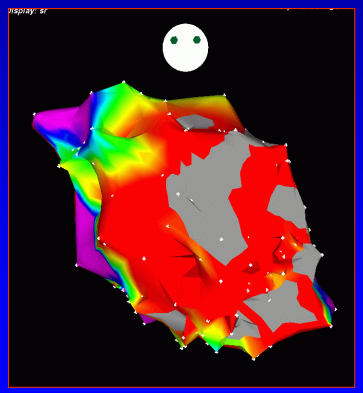
Huikuri HV. *N Engl J Med*. 2001;345:1473-1482.

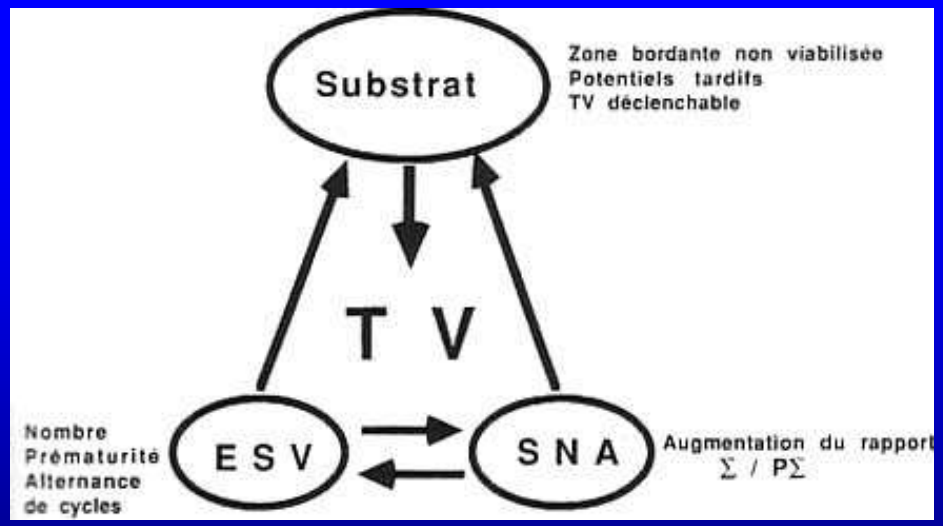
Myerburg RJ. Heart Disease, *A Textbook of Cardiovascular Medicine*. 6th ed. W.B. Saunders, Co. 2001.

Coronary Heart Disease



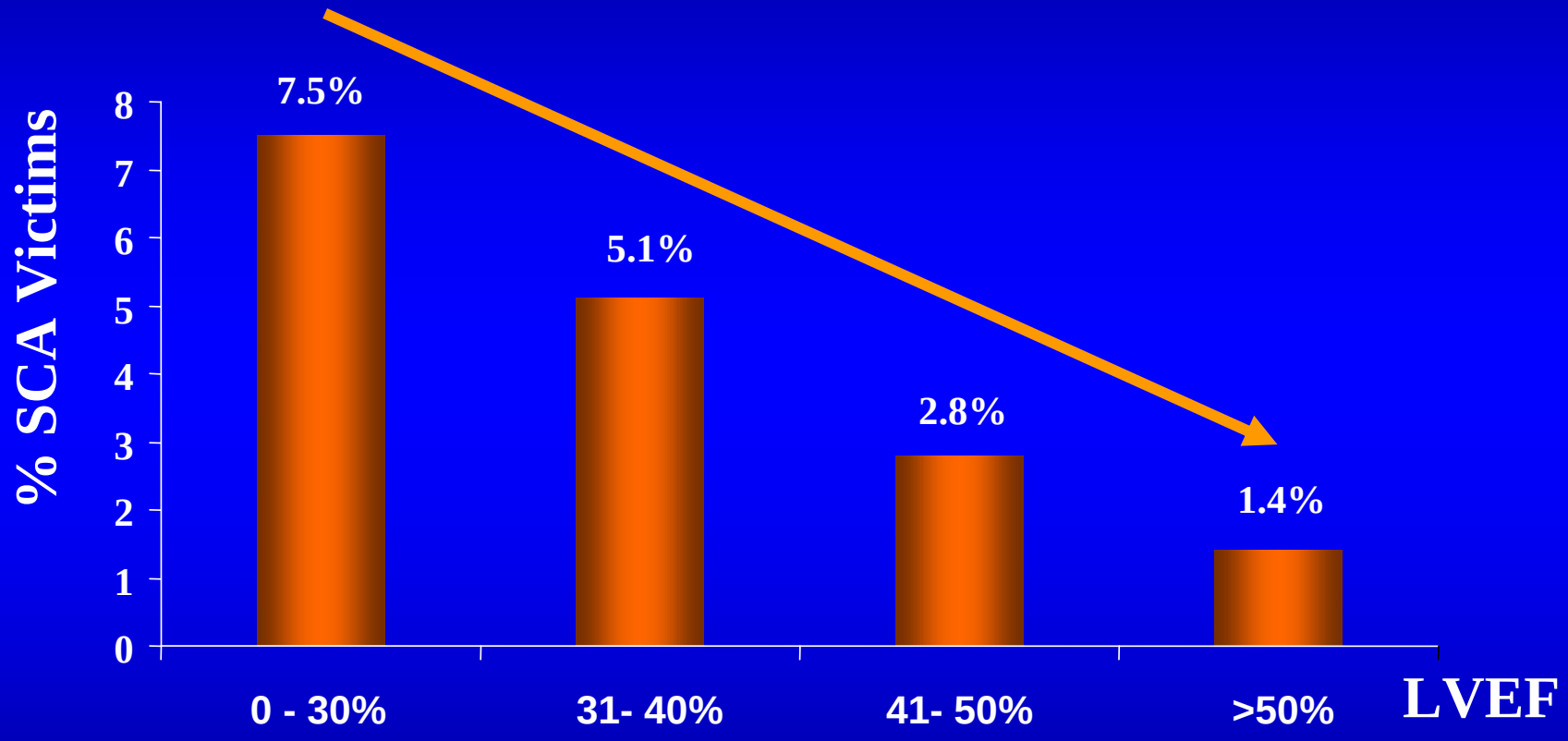






Courtesy of *N Derval*.

Out-of-Hospital Cardiac Arrest in the 1990s: A Population-Based Study in the Maastricht Area on Incidence, Characteristics and Survival



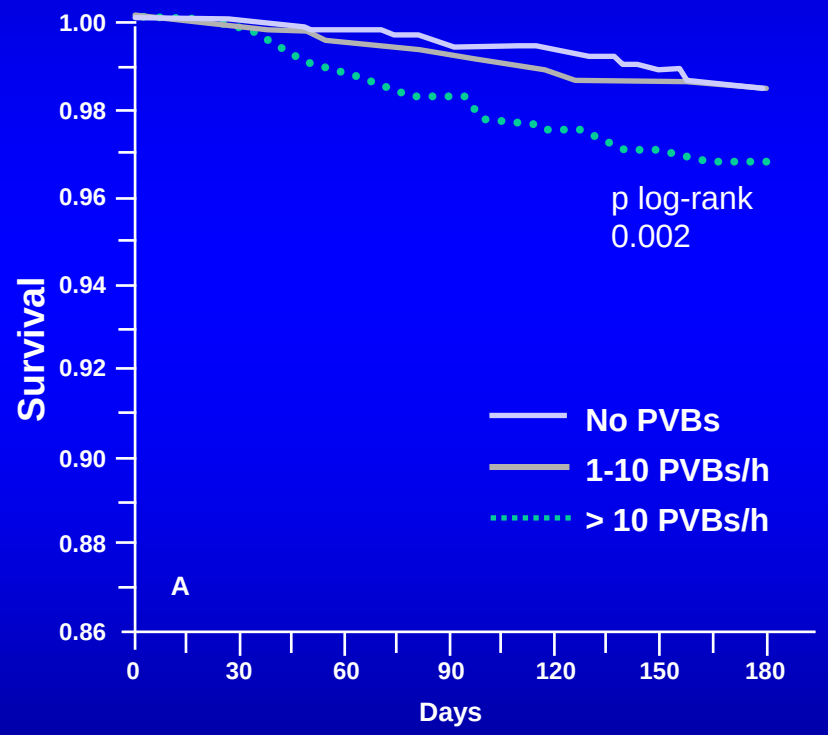
LVEF and SCA Incidence

Vreede-Swagemakers JJ et al. *J Am Coll Cardiol*. 1997;30:1500-1505.

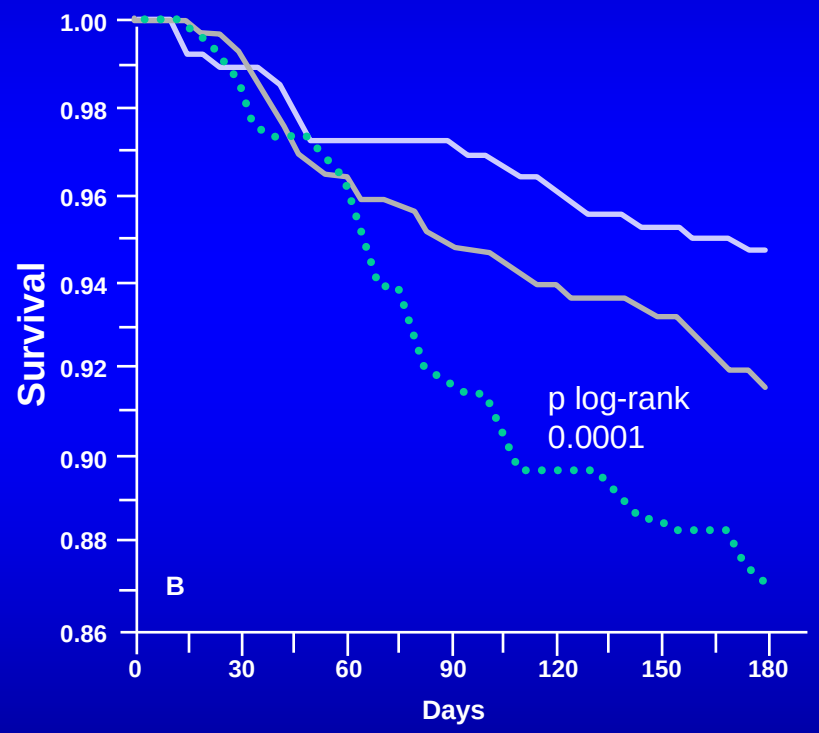
Prevalence and Prognostic Significance of Ventricular Arrhythmias After Acute Myocardial Infarction in the Fibrinolytic Era

GISSI-2 Results

Patients ***without*** LV Dysfunction



Patients ***with*** LV Dysfunction



Role of Ventricular Ectopy and LV Dysfunction in SCD Risk – GISSI-2 Trial

Maggioni AP et al. *Circulation*. 1993;87:312-322.

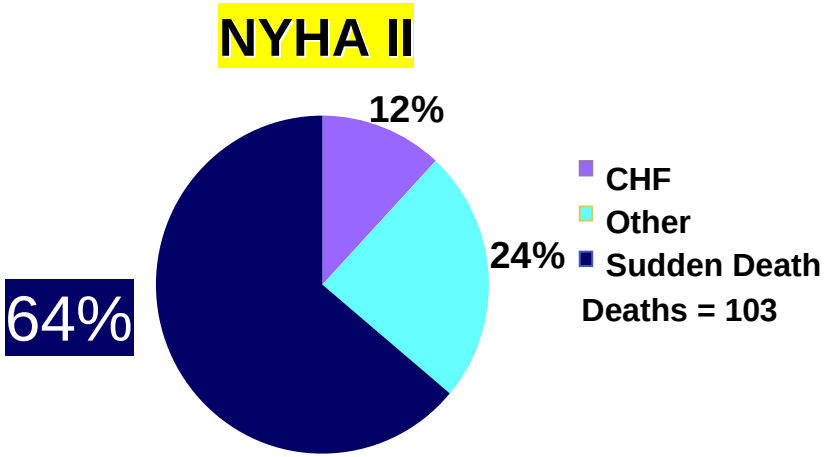
Proportion of Sudden Cardiac Death Among All-Cause Mortality in Heart Failure Patients

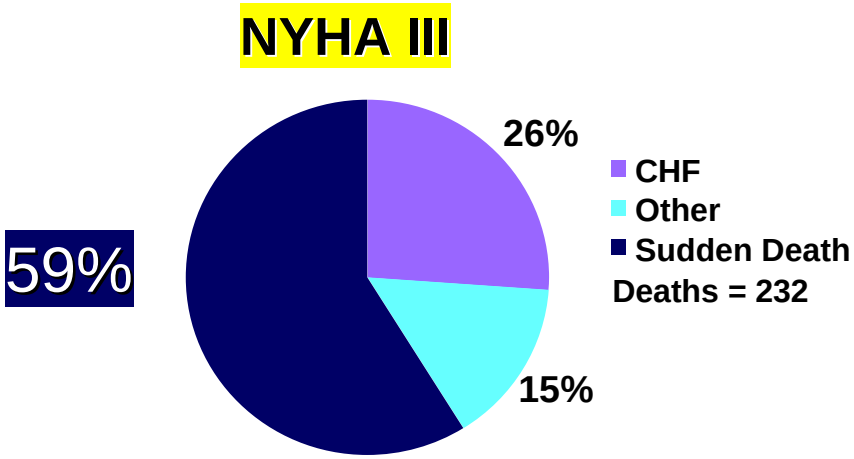
Controlled studies / Control groups

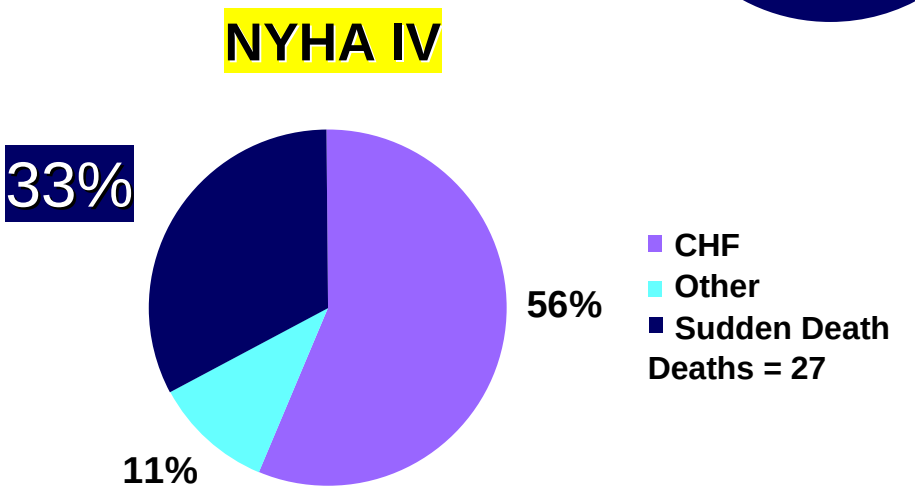
Study	year	n	grade	1-year mortality	SCD %
V-HEFT (1)	1986	642	II-III	12%	45%
V-HEFT (2)	1991	804	II-III	15%	50%
CHF-STAT	1995	674	II-III	15%	49%
RALES	1999	822	III-IV	23%	35%
CIBIS II	1999	1320	III-IV	14%	36%
MERIT-HF	1999	2001	II-IV	11%	35%
COPERNICUS	2001	2289	IIIb-IV	18%	36%

THE LANCET

Effect of metoprolol CR/XL in chronic heart failure: Metoprolol CR/XL Randomised Intervention Trial in-Congestive Heart Failure (MERIT-HF)







Modes of Death in HF

MERIT-HF Study Group. Effect of metoprolol CR/XL in chronic heart failure. *Lancet* 1999;353:2001-07.

RECOMMANDATIONS

Indications du défibrillateur automatique implantable ventriculaire.
Mise à jour de la version française

Classe I: Traitement bénéfique prouvé
Classe IIa: Traitement bénéfique suggéré
Classe IIb: Traitement bénéfique incertain

Cas du Patient Coronarien

Syncope	TV soutenue spontanée symptomatique	FEVG ≤30%	FEVG ≤35% QRS >120ms	FEVG entre 31 et 35%	FEVG entre 31 et 35%
↓	↓	↓	↓	↓	↓
TV ou FV inductible			NYHA III ou IV	TV ou FV inductible	
↓	↓	↓	↓	↓	↓
DEF [1-3] Classe I	DEF [1-3] Classe I	DEF [4-6] Classe I	DEF + CRT [7-10] Classe IIa	DEF [6,11] Classe IIa	DEF [6,11] Classe IIb

1. AVID Investigators. *N Engl J Med 1997;337:1576-83*
2. Conolly SJ, et al. CIDS study. *Circulation 2000;101:1297-302*
3. Kuck KH, et al. CASH study. *Circulation 2000;102:748-54*
4. Moss AJ, et al. MADIT-II. *N Engl J Med 1996;335:33-40*
5. Moss AJ, et al. Long-term MADIT-II. *N Engl J Med 2002;346:877-83*
6. Bardy GH, et al. SCD-HeFT study. *N Engl J Med 2005;352:225-37*
7. Cazeau S, et al. MUSTIC study. *N Engl J Med 2001;344:873-80*
8. Abraham WT, et al. MIRACLE study. *N Engl J Med 2002;346:1845-53*
9. Bristow MR, et al. COMPANION study. *N Engl J Med 2004;350:2140-50*
10. Cleland JG, et al. CARE-HF study. *N Eng J Med 2005;352:1539-49*
11. Buxton AE, et al. MUSTT study. *N Engl J Med 1999;341:1882-90*

Courtesy of SORIN Group

FEVG < 35%, QRS > 150 ms et NYHA II: CRT-D, Classe I_A

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

RECOMMANDATIONS

Indications du défibrillateur automatique implantable ventriculaire.
Mise à jour de la version française

Cas du patient avec Altération de la FEVG + Absence d'IDM

Syncope	TV soutenue spontanée non syncopale	FEVG ≤30%	FEVG ≤35% QRS >120ms	FEVG entre 31 et 35%
TV ou FV inductible		NYHA II ou III	NYHA III ou IV	NYHA II ou III
DEF [1-3] Classe I	DEF [1-3] Classe I	DEF [4-5] Classe IIa	DEF + CRT [6-9] Classe IIa	DEF [4-5] Classe IIb

1. AVID Investigators. *N Engl J Med 1997;337:1576-83*
2. Conolly SJ, et al. CIDS study. *Circulation 2000;101:1297-302*
3. Kuck KH, et al. CASH study. *Circulation 2000;102:748-54*
4. Kadish A, et al. DEFINITE study. *N Engl J Med 2004 ;350 :2151-8*
5. Bardy GH, et al. SCD-HeFT study. *N Engl J Med 2005;352:225-37*
6. Cazeau S, et al. MUSTIC study. *N Engl J Med 2001;344:873-80*
7. Abraham WT, et al. MIRACLE study. *N Engl J Med 2002;346:1845-53*
8. Bristow MR, et al. COMPANION study. *N Engl J Med 2004;350:2140-50*
9. Cleland JG, et al. CARE-HF study. *N Eng J Med 2005;352:1539-49*

Courtesy of SORIN Group

FEVG < 35%, QRS > 150 ms et NYHA II: CRT-D, Classe I_A

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

QUAND ?

JACC

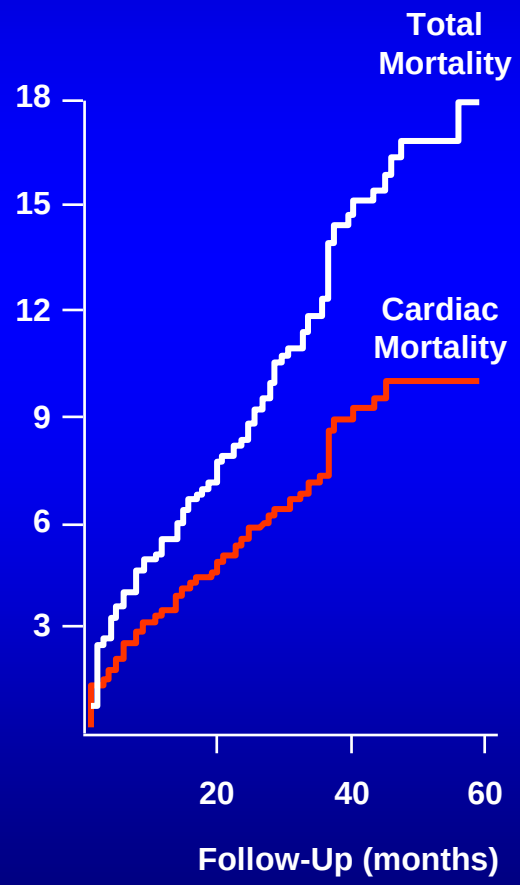
Prediction of Sudden Cardiac Death After Myocardial Infarction in the Beta-Blocking Era

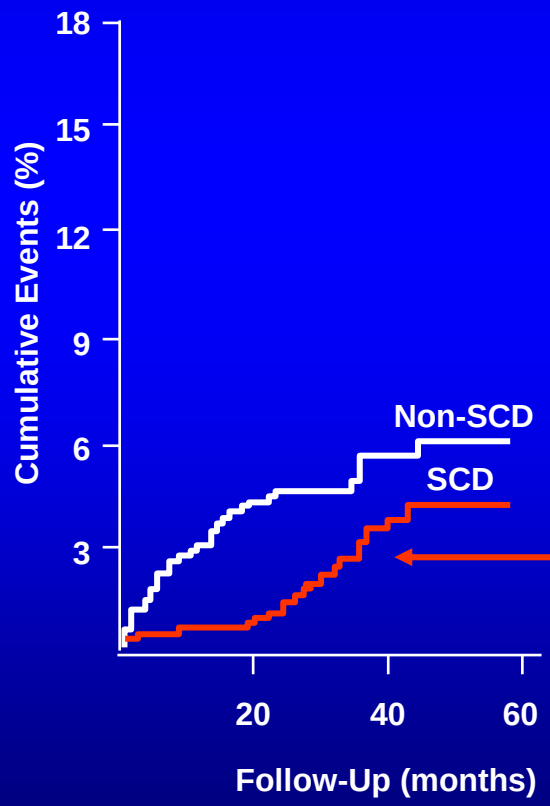
Heikki V. Huikuri, MD, FACC,* Jari M. Tapanainen, MD,* Kai Lindgren, MD,* Pekka Raatikainen, MD,* Timo H. Mäkikallio, MD,* K. E. Juhani Airaksinen, MD,* Robert J. Myerburg, MD, FACC†

Oulu, Finland; and Miami, Florida

Time Dependence of Mortality Risk Post-MI

Prediction of Sudden Cardiac Death After Myocardial Infarction in the Beta-Blocking Era[1]





- 700 post-MI patients; ~ 95% on beta-blockers 2 years after discharge.
- The epidemiologic pattern of SCD was different from that reported in previous studies.

Arrhythmia events did not concentrate early after the index event; most occurred > 18 months post-MI.

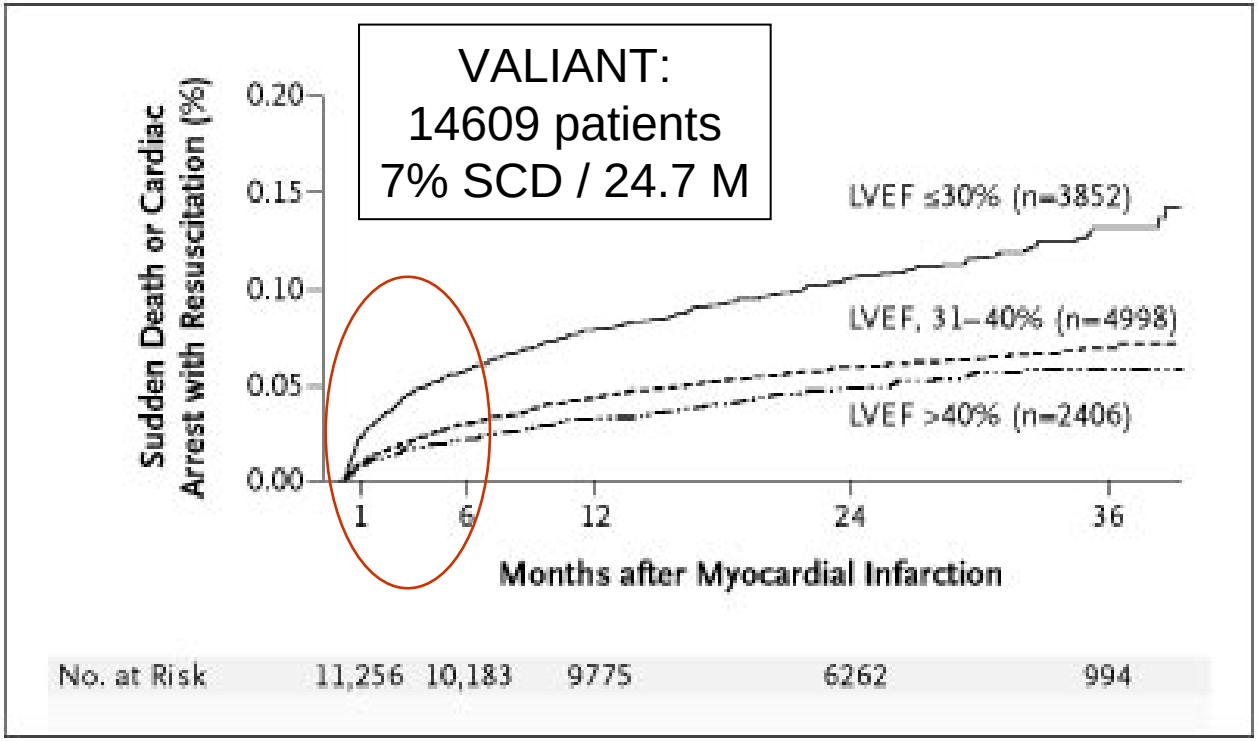
Timing of Implantation

[1] Huikuri HV. *J Am Coll Cardiol*. 2003;42:652-658.

NEJM

Sudden Death in Patients with Myocardial Infarction and Left Ventricular Dysfunction, Heart Failure, or Both

Scott D. Solomon, M.D., Steve Zelenkofske, D.O., John J.V. McMurray, M.D., Peter V. Finn, M.D., Eric Velazquez, M.D., George Ertl, M.D., Adam Harsanyi, M.D., Jean L. Rouleau, M.D., Aldo Maggioni, M.D., Lars Kober, M.D., Harvey White, D.Sc., Frans Van de Werf, M.D., Ph.D., Karen Pieper, M.S., Robert M. Califf, M.D., and Marc A. Pfeffer, M.D., Ph.D., for the Valsartan in Acute Myocardial Infarction Trial (VALIANT) Investigators



Kaplan-Meier Estimates of the Rates of Sudden Death or Cardiac Arrest with Resuscitation, According to the Left Ventricular Ejection Fraction (LVEF)

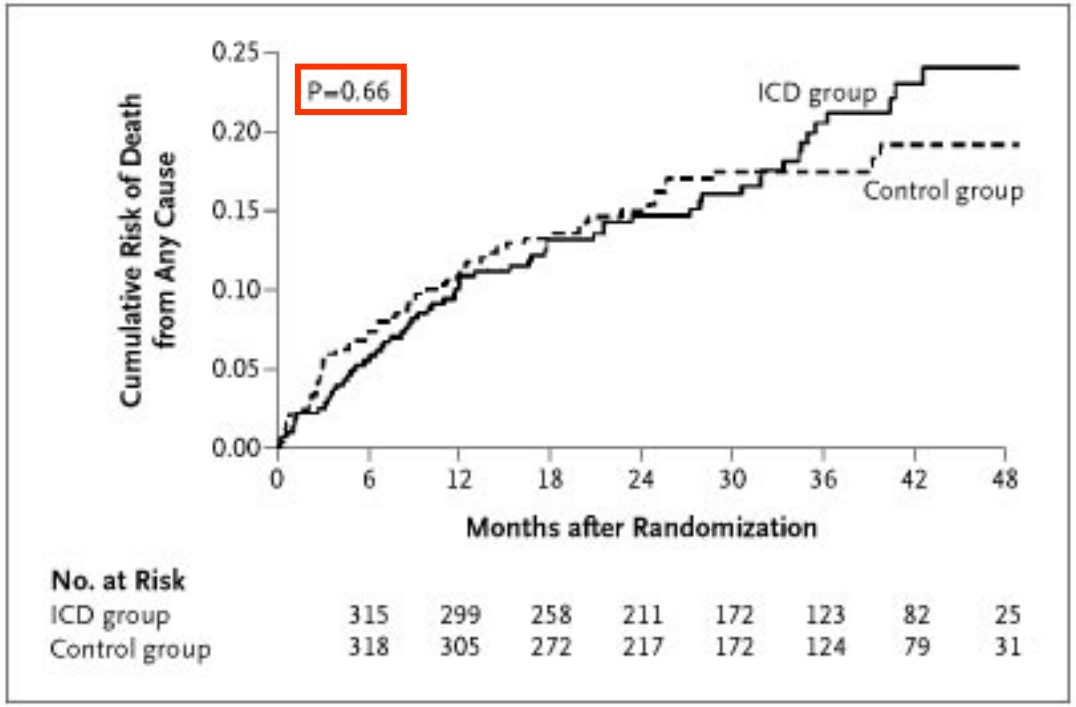
Timing of Implantation

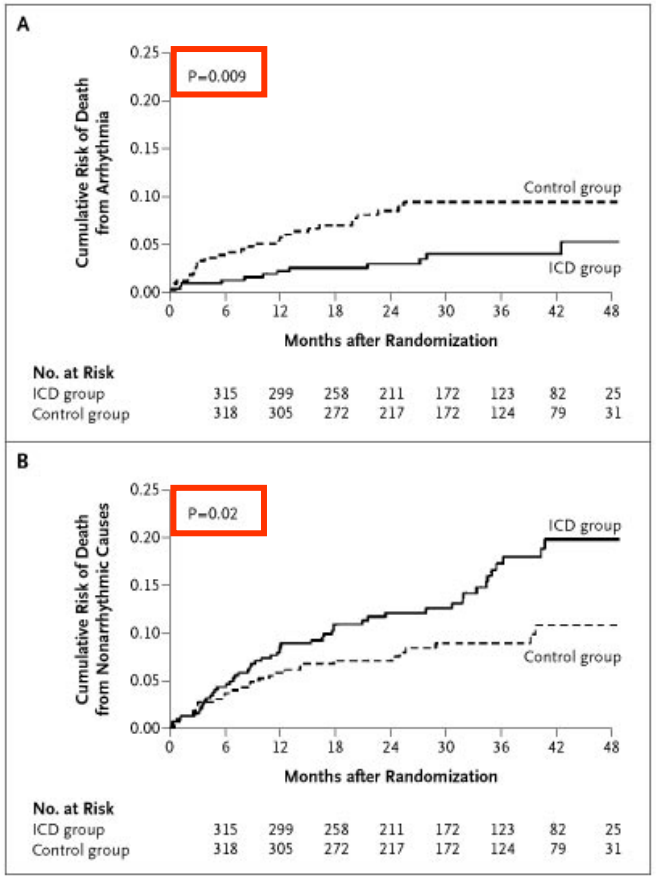
Solomon, S. et al. *N Engl J Med* 2005;352:2581-2588

NEJM

Prophylactic Use of an Implantable Cardioverter–Defibrillator after Acute Myocardial Infarction

Stefan H. Hohnloser, M.D., Karl Heinz Kuck, M.D., Paul Dorian, M.D., Robin S. Roberts, M.Tech., John R. Hampton, M.D., Robert Hatala, M.D., Eric Fain, M.D., Michael Gent, D.Sc., and Stuart J. Connolly, M.D., on behalf of the DINAMIT Investigators*





Timing of Implantation

DINAMIT Hohnloser, S. H. et al. *N Engl J Med* 2004;351:2481-2488

RECOMMANDATIONS

Indications du défibrillateur automatique implantable ventriculaire.
Mise à jour de la version française

1 mois après un IDM

Patients coronariens sans ou avec symptômes d'insuffisance cardiaque légère ou modérée (classe NYHA II ou III), une FEVG ≤ 30 % mesurée au moins 1 mois après un IDM et 3 mois après un geste de revascularisation (chirurgie ou angioplastie)	I	B
Patients coronariens avec dysfonction ventriculaire gauche (FE de 31 à 35 %) mesurée au moins 1 mois après un IDM et 3 mois après une procédure de revascularisation (chirurgie ou angioplastie) avec une arythmie ventriculaire (TV, FV) déclenchable	IIa	B

3 mois après une procédure de revascularisation

Timing of Implantation

E. Aliot et al.ARCHIVES DES MALADIES DU COEUR ET DES VAISSEAUX, tome 99, n°2, février 2006

NYHA function class III/IV

European Heart Journal
doi:10.1093/eurheartj/ehq337

ESC GUIDELINES

NYHA function class II

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

Recommendation in patients with heart failure in New York Heart Association function class III/IV

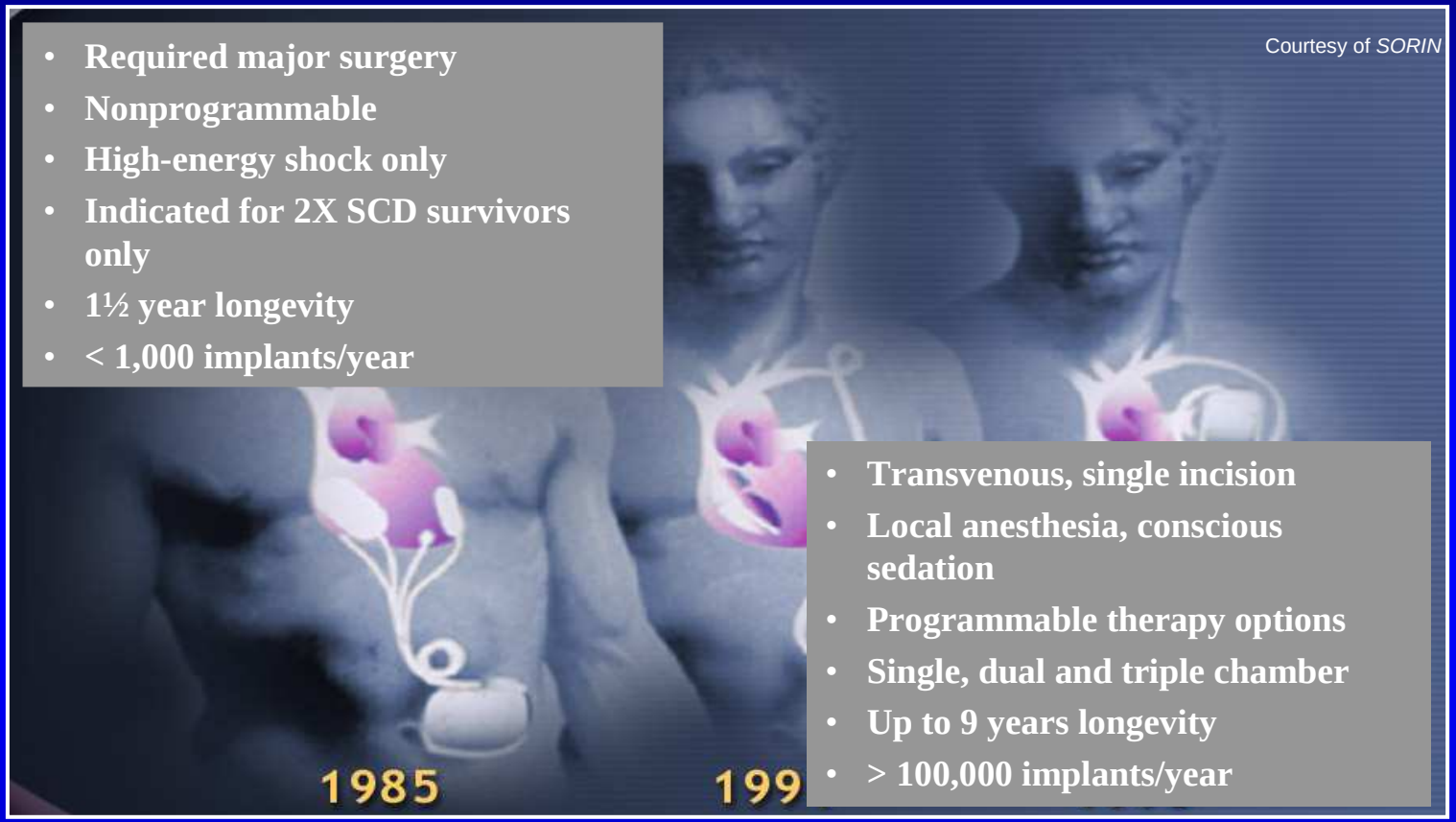
Recommendation	Patient population	Class[a]	Level[b]	Ref.[c]
CRT-P/CRT-D is recommended to reduce morbidity and mortality[d]	NYHA function class III/IV LVEF ≤35%, QRS ≥120 ms, SR Optimal medical therapy Class IV patients should be ambulatory[e]	I	A	5–19

Recommendation in patients with heart failure in New York Heart Association function class II

Recommendation	Patient population	Class[a]	Level[b]	Ref.[c]
CRT preferentially by CRT-D is recommended to reduce morbidity or to prevent disease progression[d]	NYHA function class II LVEF ≤35%, QRS ≥150 ms, SR Optimal medical therapy	I	A	9, 20–22

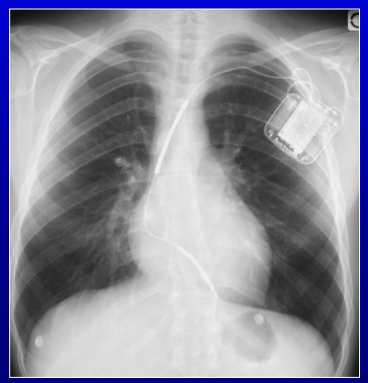
COMMENT ?

DAI: Principes de fonctionnement

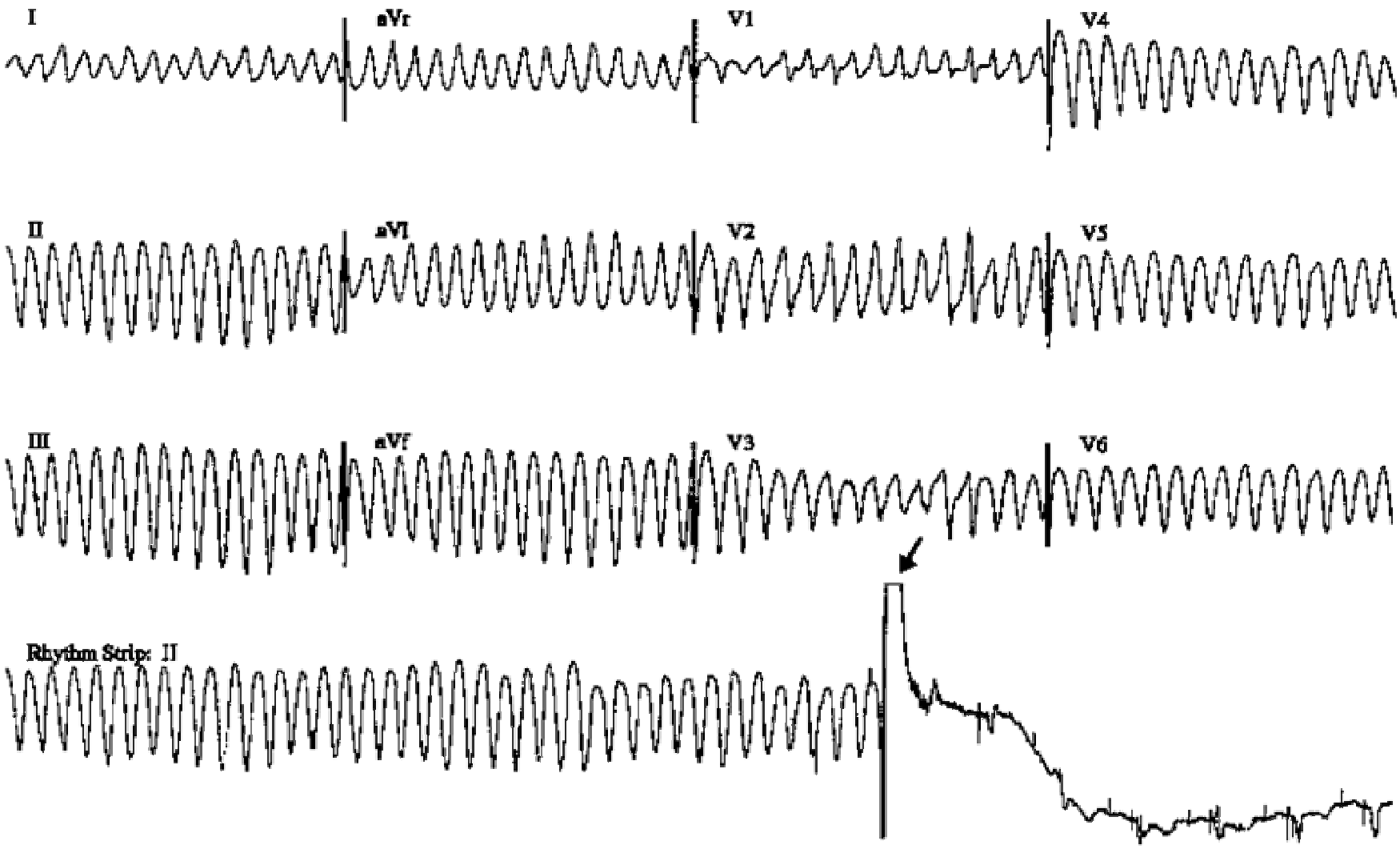


- **Required major surgery**
- **Nonprogrammable**
- **High-energy shock only**
- **Indicated for 2X SCD survivors only**
- **1½ year longevity**
- **< 1,000 implants/year**

- **Transvenous, single incision**
- **Local anesthesia, conscious sedation**
- **Programmable therapy options**
- **Single, dual and triple chamber**
- **Up to 9 years longevity**
- **> 100,000 implants/year**



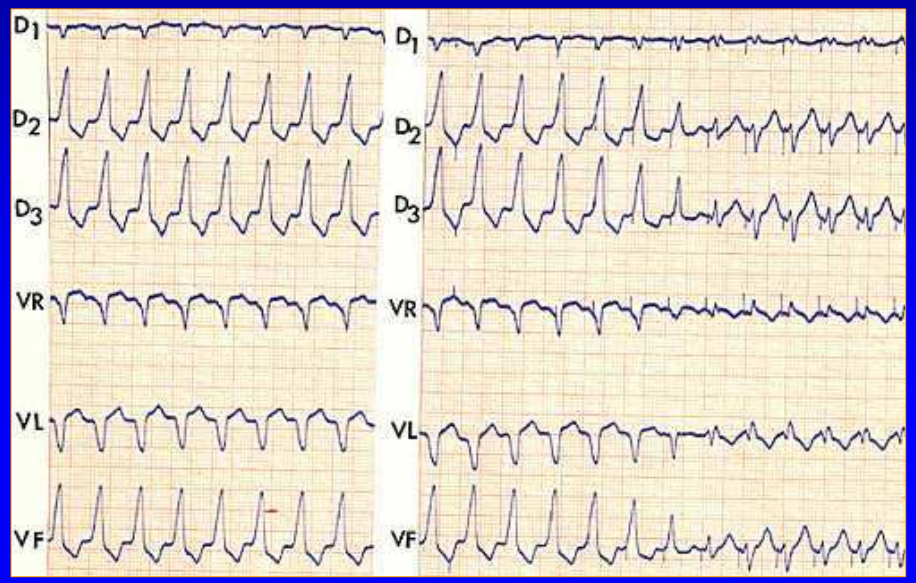
DAI: Principes de fonctionnement

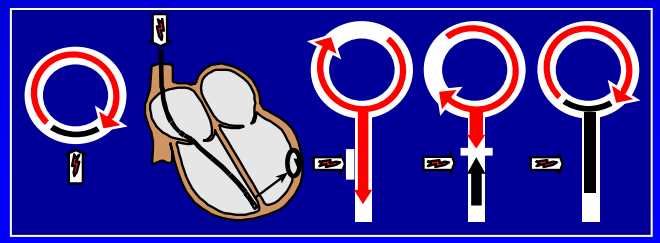


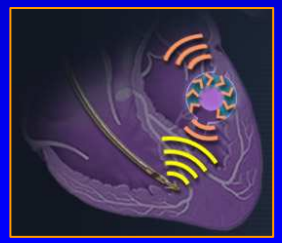
DAI: Principes de fonctionnement

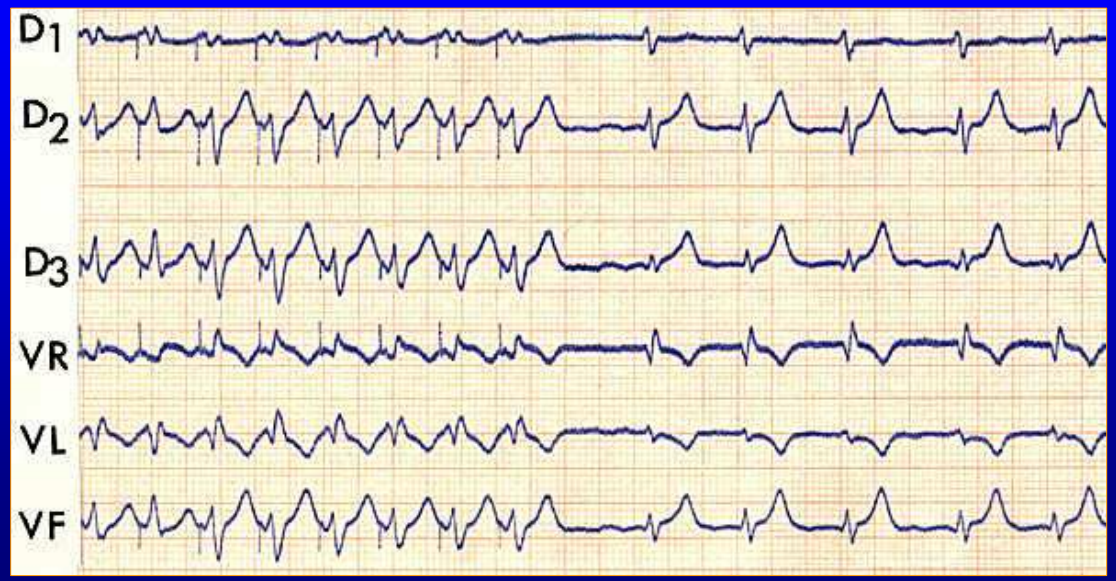
DAI: Principes de fonctionnement

Stimulation Anti Tachycardique









Adaptated from Dr Briand, CHU Besançon.

DAI comment: VVI ?

Chronotropic Incompetence in Patients with an Implantable Cardioverter Defibrillator: Prevalence and Predicting Factors

CHRISTOPH MELZER,* MARCO BÖHM,* HANS JOACHIM BONDKE,* WILLIAM COMBS,† GERT BAUMANN,* and HEINZ THERES*

From the *Med. Klinik mit Schwerpunkt Kardiologie, Angiologie, Pneumologie; Charité University Medical Center, Berlin, Germany, and †Medtronic, Inc., Minneapolis, Minnesota

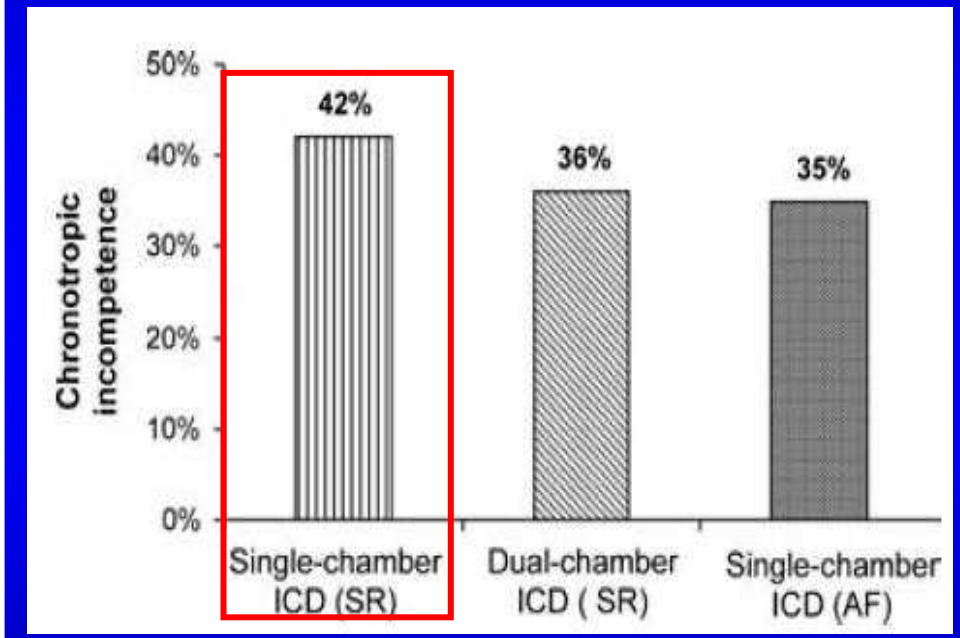
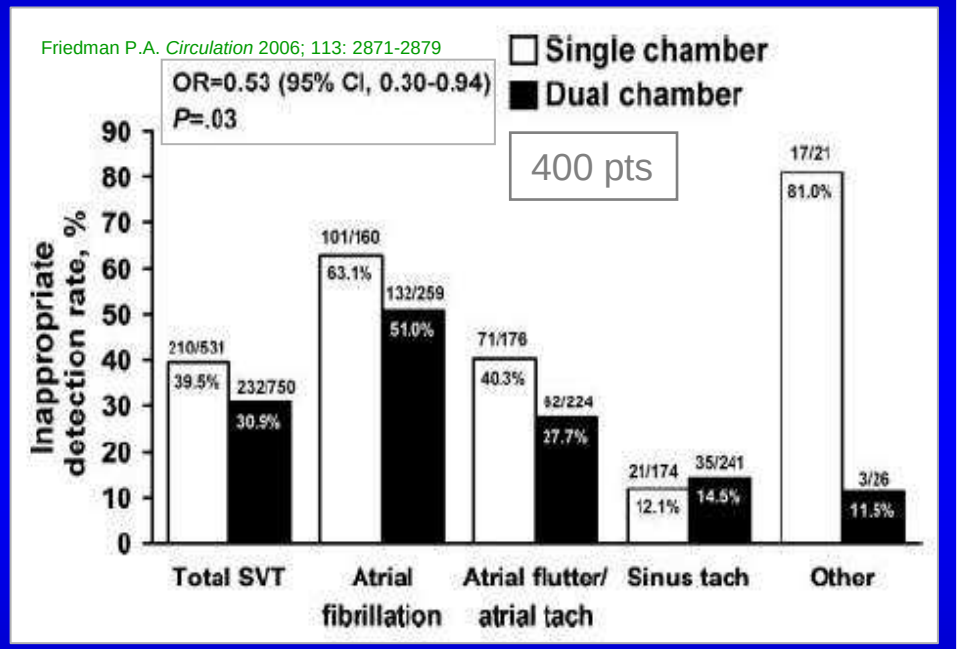


Figure 2. *Percentages of chronotropic incompetence for patient subgroups—38% of the patients studied (47 of 123) were found to be chronotropically incompetent.*

Dual-Chamber Versus Single-Chamber Detection Enhancements for Implantable Defibrillator Rhythm Diagnosis

The Detect Supraventricular Tachycardia Study



"The odds of inappropriate detection were decreased by almost half with the use of the dual-chamber detection enhancements"

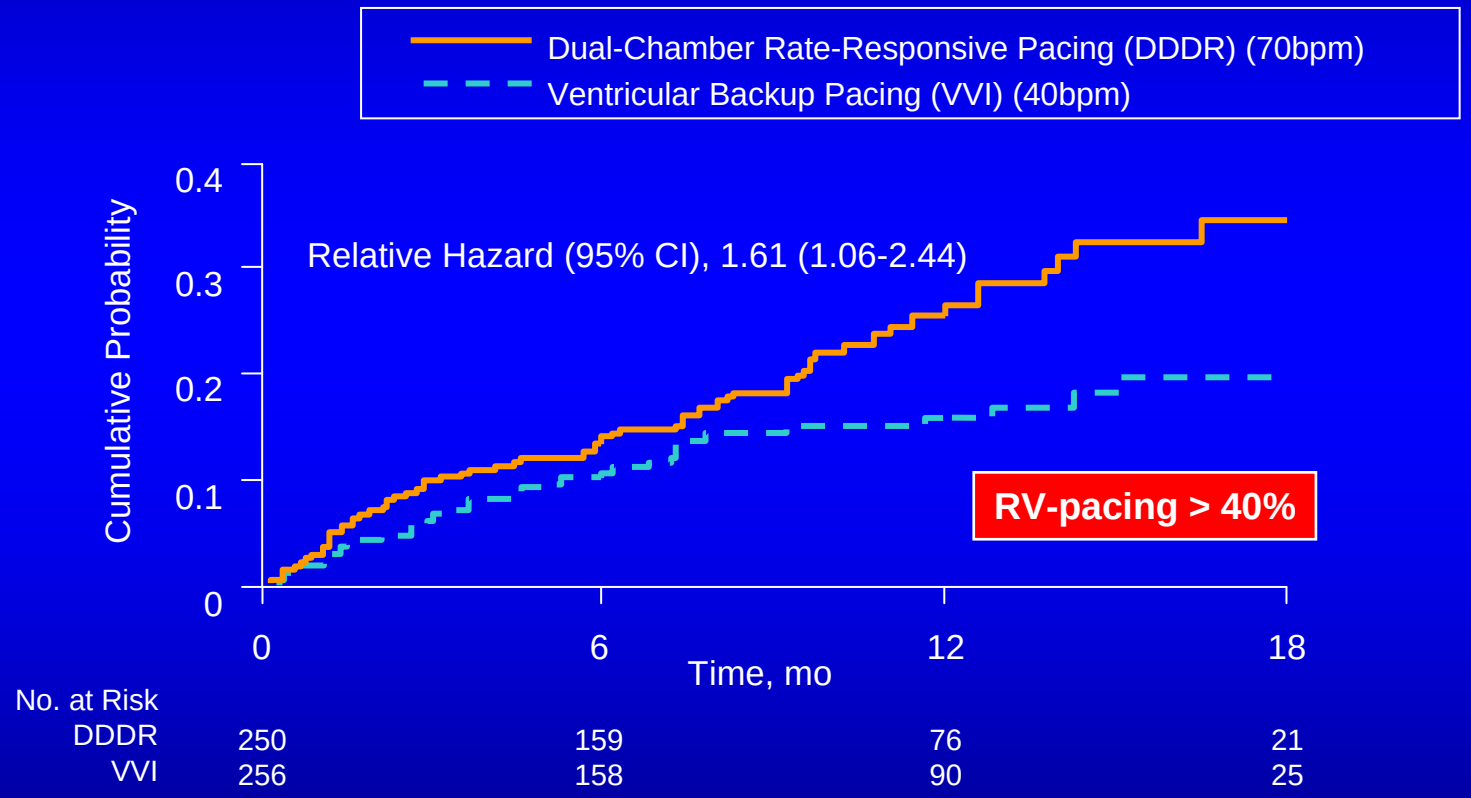
Friedman PA et al. *Circulation* 2006; 113: 2871-2879
Melzer C et al. *PACE* 2005;28:1025-31.

Implantation: *La prothèse (VVI /DDD/CRT)*

JAMA® The Journal of the American Medical Association

Dual-Chamber Pacing or Ventricular Backup Pacing in Patients With an Implantable Defibrillator
The Dual Chamber and VVI Implantable Defibrillator (DAVID) Trial

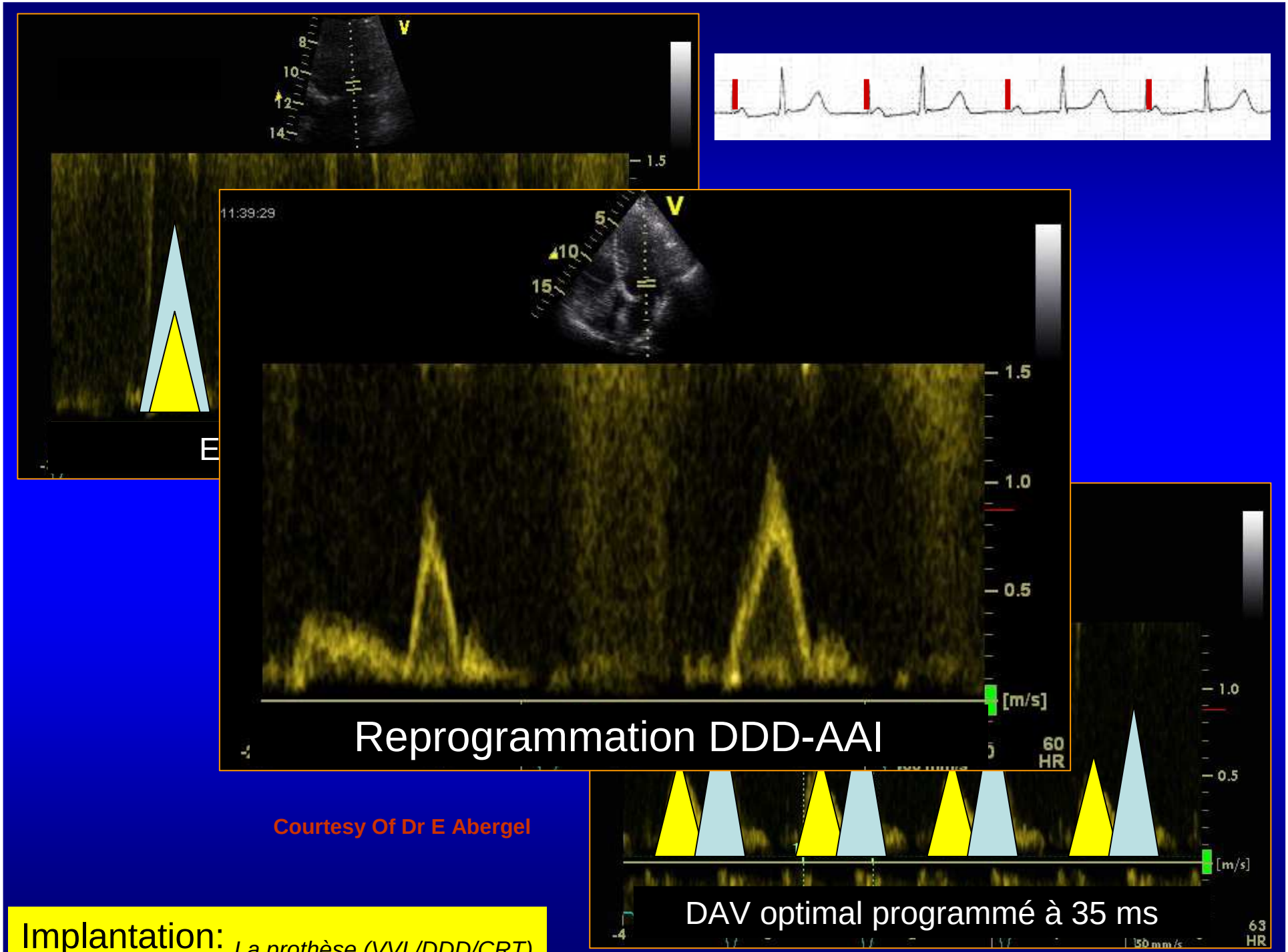
DAI comment: DDD ?



Death or New/Worsening Heart Failure Hospitalization

Implantation: *La prothèse (VVI /DDD/CRT)*

Wilkoff BL et al. *JAMA* 2002; 288:3115



Courtesy Of Dr E Abergel

Implantation: *La prothèse (VVI /DDD/CRT)*

DAI comment: CRT ?

Patients en insuffisance cardiaque qui restent symptomatiques en classe NYHA III ou IV sous traitement médical optimal, avec FE ≤ 35 % et durée de QRS > 120 ms : indication d'un défibrillateur triple-chambre * ** Il n'existe pas à cette date d'évidence actuelle de la supériorité du DAI biventriculaire sur le stimulateur de resynchronisation seul, dans cette indication*	IIa	B

Les non répondeurs…

- ***Pré-implantation***
  - **- sélection des patients**
  - •Absence de substrat favorable:
    - –Critères de désynchronisation: ECG vs Echo.
    - – Présence d'une quantité insuffisante de myocarde viable à resynchroniser.

    Hummel JP, et al. 2006 *Heart rhythm* Da Costa A, et al. 2006 Heart rhythm
- ***Implantation***
  - **- position des sondes**
- ***Post-implantation***
  - **- réglage et suivi de la prothèse**

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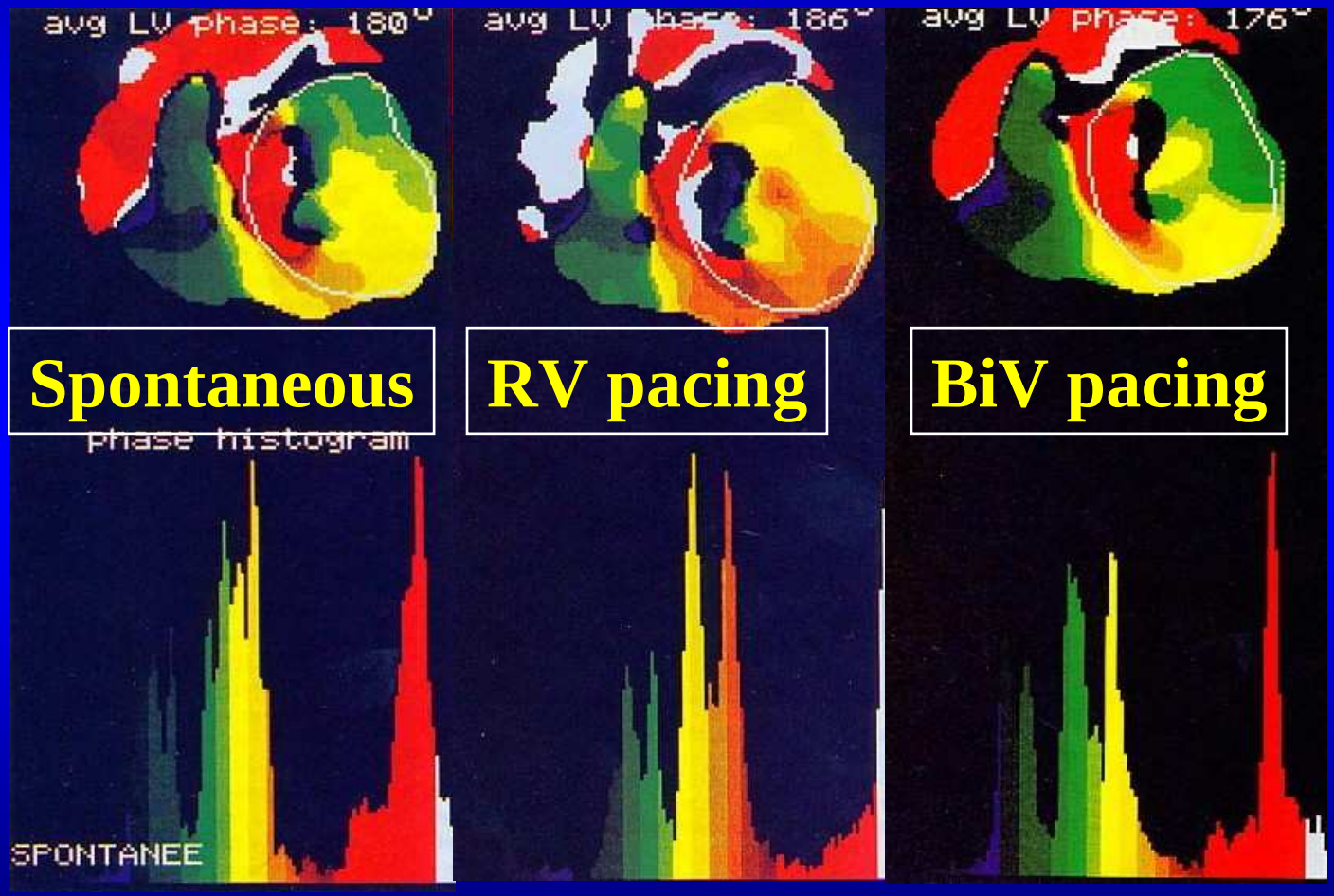
Pacing Clin Electrophysiol. 1994 Nov;17(11 Pt 2):1974-9.

Four chamber pacing in dilated cardiomyopathy.

Cazeau S, Ritter P, Bakdach S, Lazarus A, Limousin M, Henao L, Mundler O, Daubert JC, Mugica J.
Val d'Or Surgical Centre, St. Cloud, France.



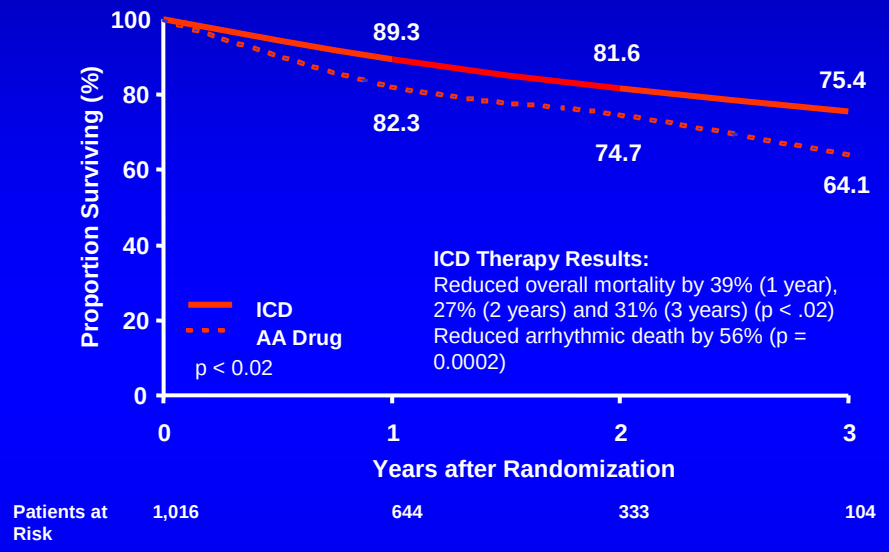
Cazeau S et al. *Pacing Clin Electrophysiol*. 1994 Nov;17(11 Pt 2):1974-9

POURQUOI ?

NEJM
The New England Journal of Medicine

A COMPARISON OF ANTIARRHYTHMIC-DRUG THERAPY WITH IMPLANTABLE DEFIBRILLATORS IN PATIENTS RESUSCITATED FROM NEAR-FATAL VENTRICULAR ARRHYTHMIAS

THE ANTIARRHYTHMICS VERSUS IMPLANTABLE DEFIBRILLATORS (AVID) INVESTIGATORS*



	3 Mo	12 Mo	24 Mo	36 Mo
VT	36%	68%	81%	85%
VF	15%	39%	53%	69%

The cumulative percentage of patients with any activation of the defibrillator, either antitachycardia pacing or shock, was as follows: for the patients with ventricular tachycardia, 36 percent at three months, 68 percent at one year, 81 percent at two years, and 85 percent at three years; for the patients with ventricular fibrillation, 15 percent, 39 percent, 53 percent, and 69 percent, respectively ($P<0.001$ for patients with ventricular tachycardia vs. those with ventricular fibrillation).

In patients implanted in secondary prevention, supposed to have a high proportion of recurrence of VT_VF episodes, HM is useful to provide a closer follow up.

The AVID Investigators. *N Engl J Med*. 1997;337(22):1576-1583.

Annals of Internal Medicine

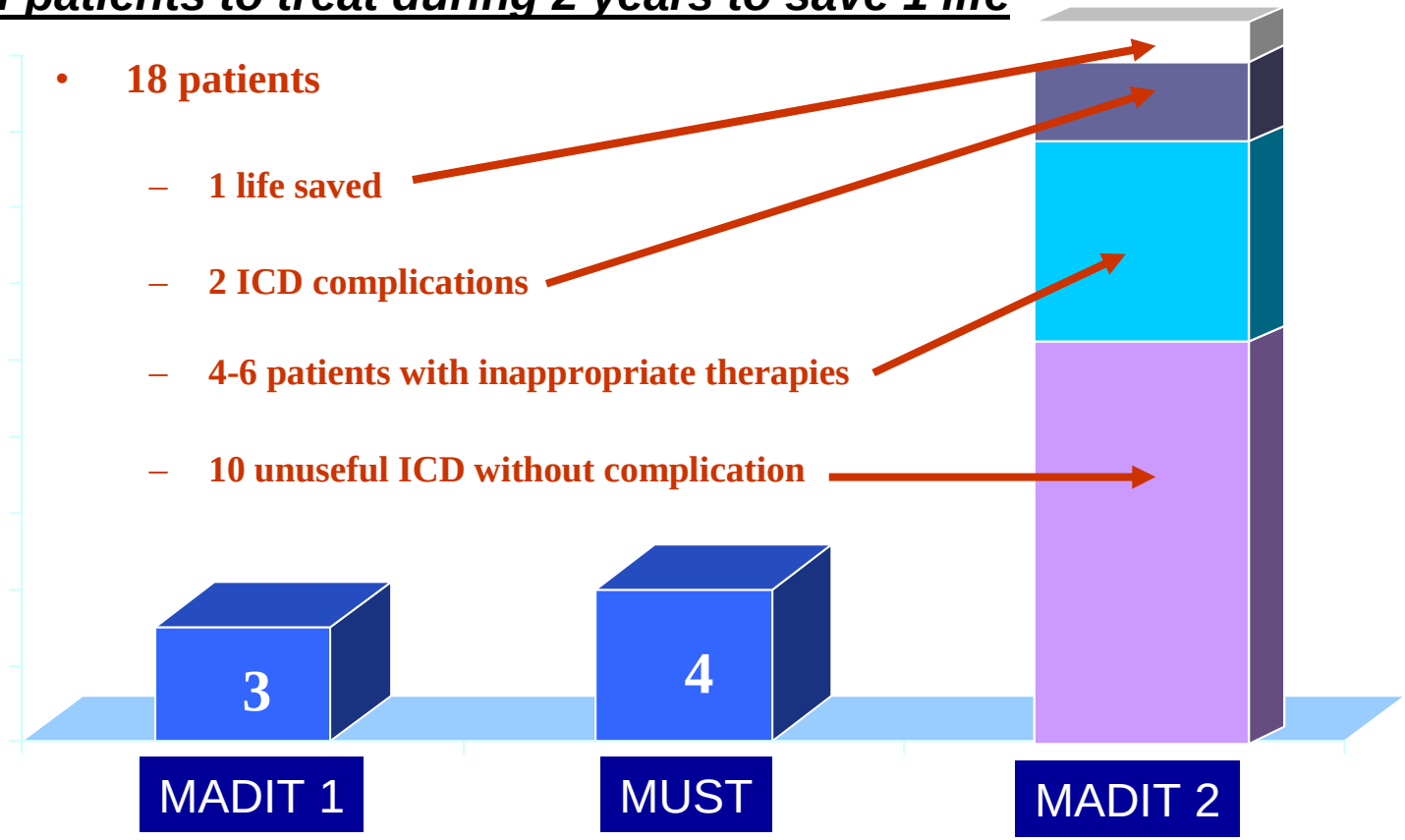
ARTICLE

Implantable Cardioverter Defibrillators in Primary and Secondary Prevention: A Systematic Review of Randomized, Controlled Trials

Justin A. Ezekowitz, MB, BCh; Paul W. Armstrong, MD, FRCPC; and Finlay A. McAlister, MD, MSc, FRCPC

Nb of patients to treat during 2 years to save 1 life

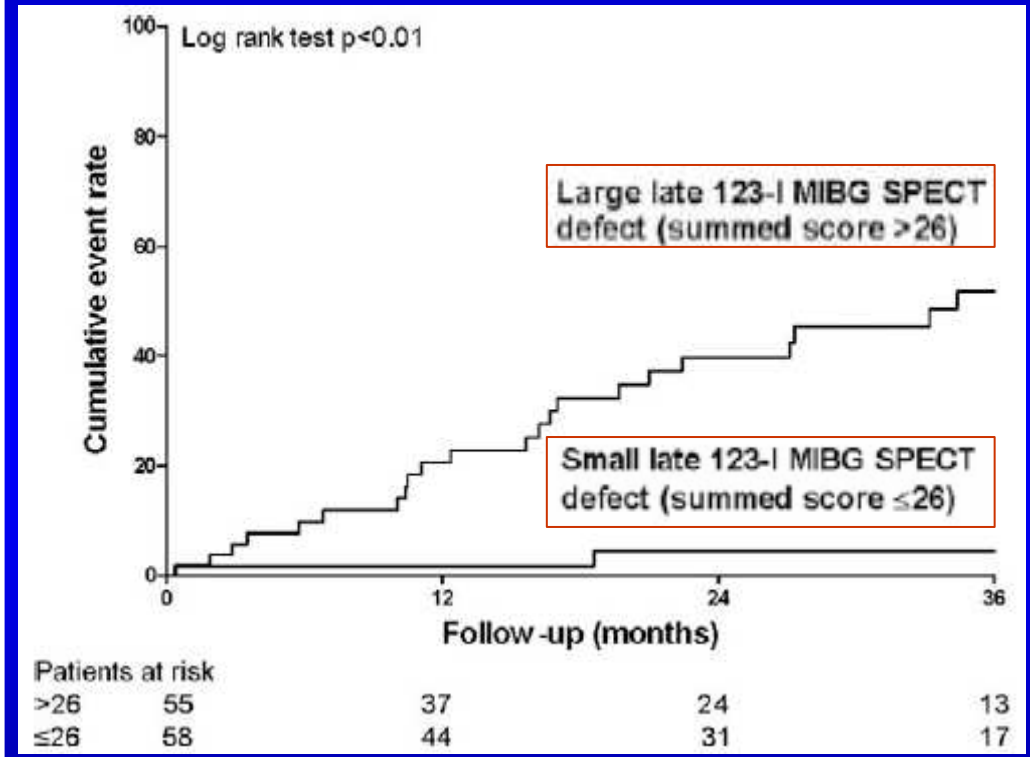
- **18 patients**
  - **1 life saved**
  - **2 ICD complications**
  - **4-6 patients with inappropriate therapies**
  - **10 unuseful ICD without complication**

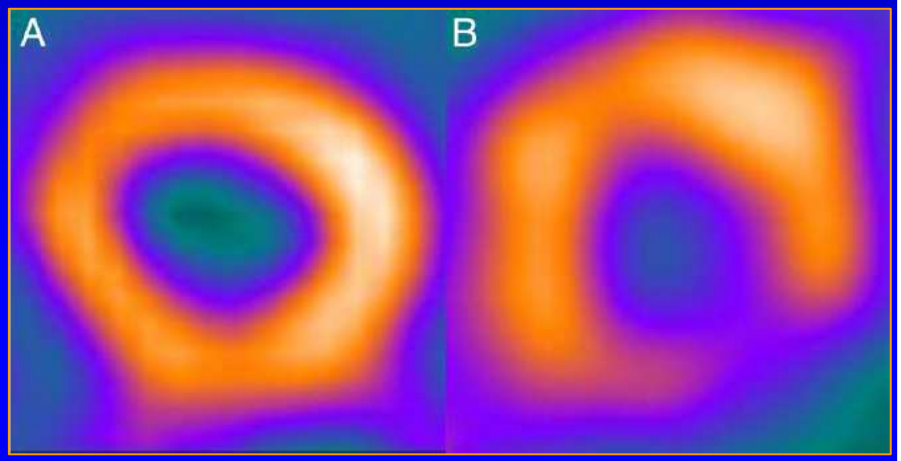


400 ICD/Million to save 22 pts/Million

Ezekowitz AJ et al. *Ann Intern Med* 2003;138:445-452

Cardiac Sympathetic Denervation Assessed With 123-Iodine Metaiodobenzylguanidine Imaging Predicts Ventricular Arrhythmias in Implantable Cardioverter-Defibrillator Patients





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Conclusions Cardiac sympathetic denervation predicts ventricular arrhythmias causing appropriate ICD therapy as well as the composite of appropriate ICD therapy or cardiac death. (J Am Coll Cardiol 2010;55:2769–77) © 2010 by the

Boogers MJ et al. *J Am Coll Cardiol* 2010; 55: 2769-77.