A DEFIBRILLATOR IS INDICATED : SHOULD WE RESYNCHRONISE ?

Michel CHAUVIN
DIU 2007

M.CHAUVIN

Les Hôpitaux Universitaires de STRASBOURG

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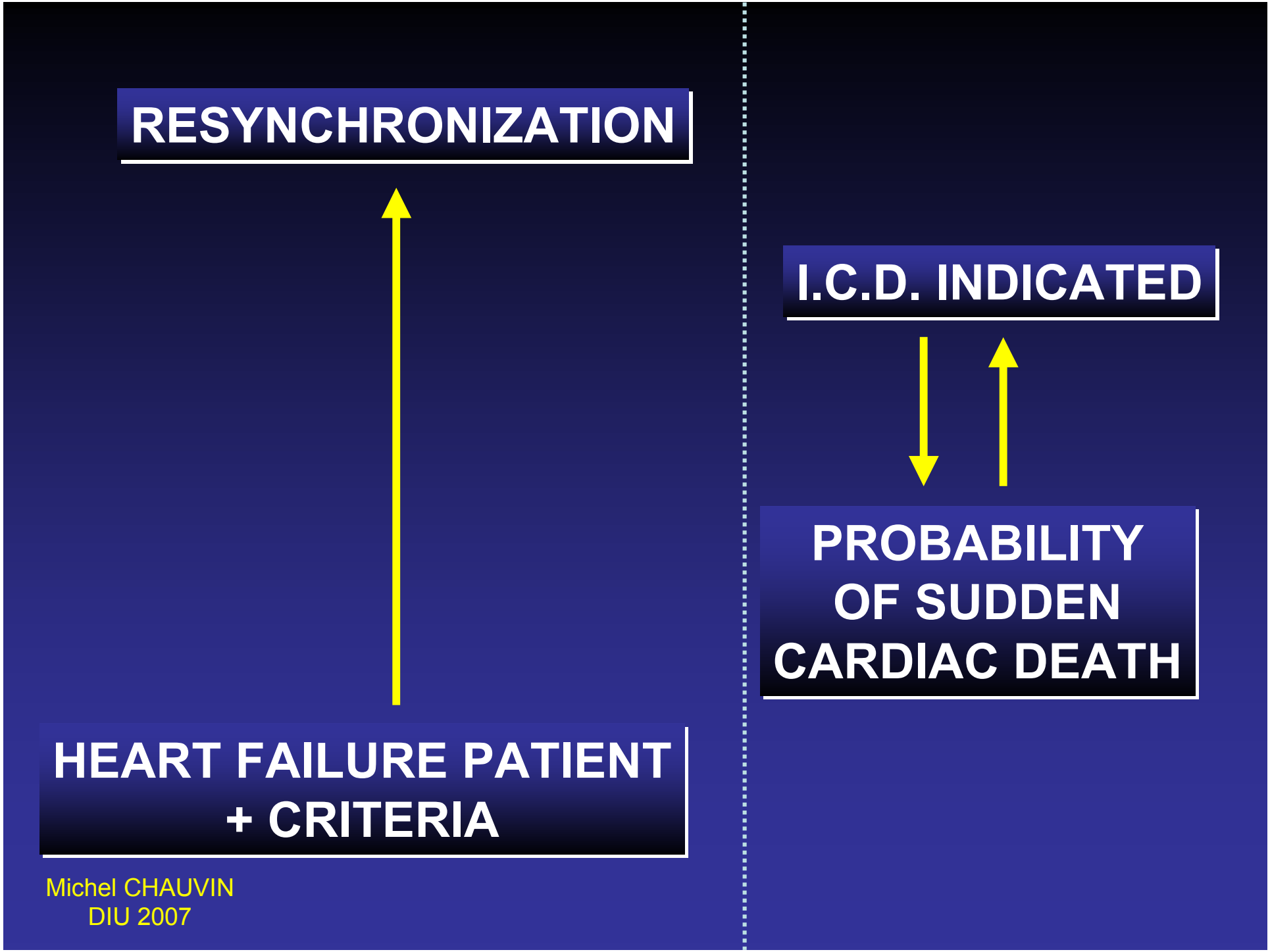
RESYNCHRONIZATION
I.C.D. INDICATED
PROBABILITY OF SUDDEN CARDIAC DEATH
HEART FAILURE PATIENT + CRITERIA
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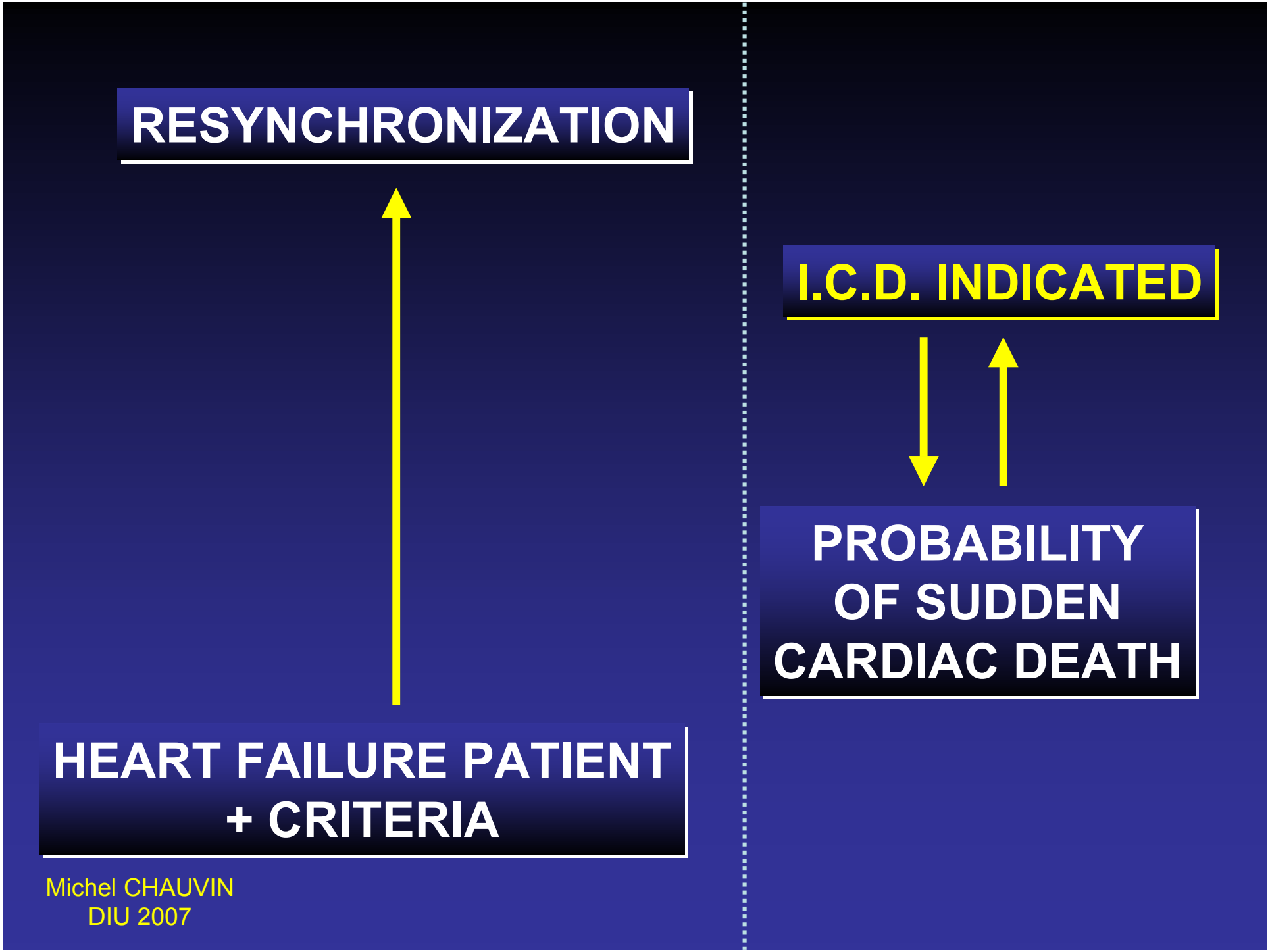
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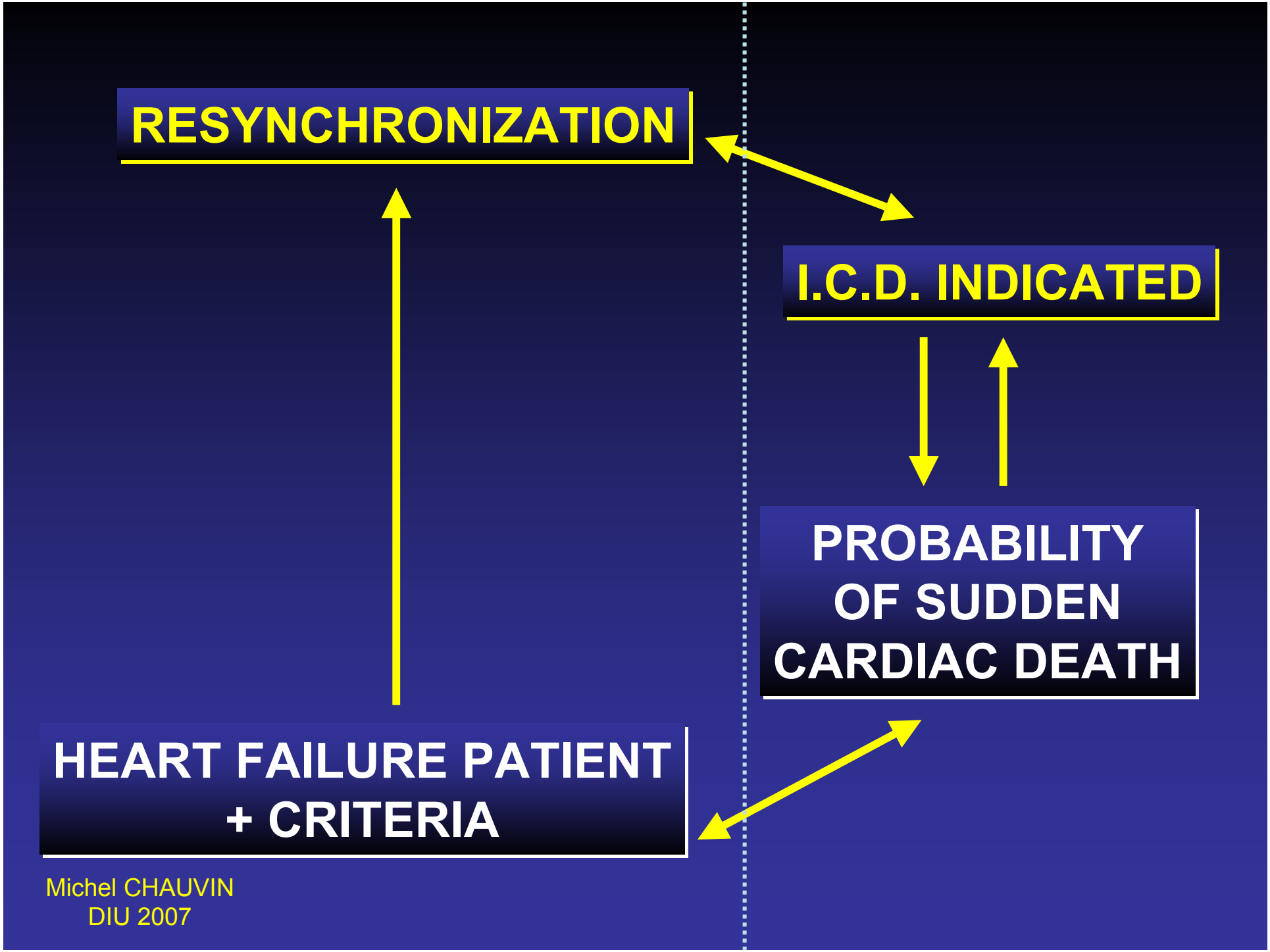
RESYNCHRONIZATION
I.C.D. INDICATED
PROBABILITY OF SUDDEN CARDIAC DEATH
HEART FAILURE PATIENT + CRITERIA
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Cardiac Resynchronization Therapy for the Treatment of Heart Failure in Patients with Intraventricular Conduction Delay and Malignant Ventricular Tachyarrhythmias

SL Higgins et al JACC 2003; 42 : 1454-9

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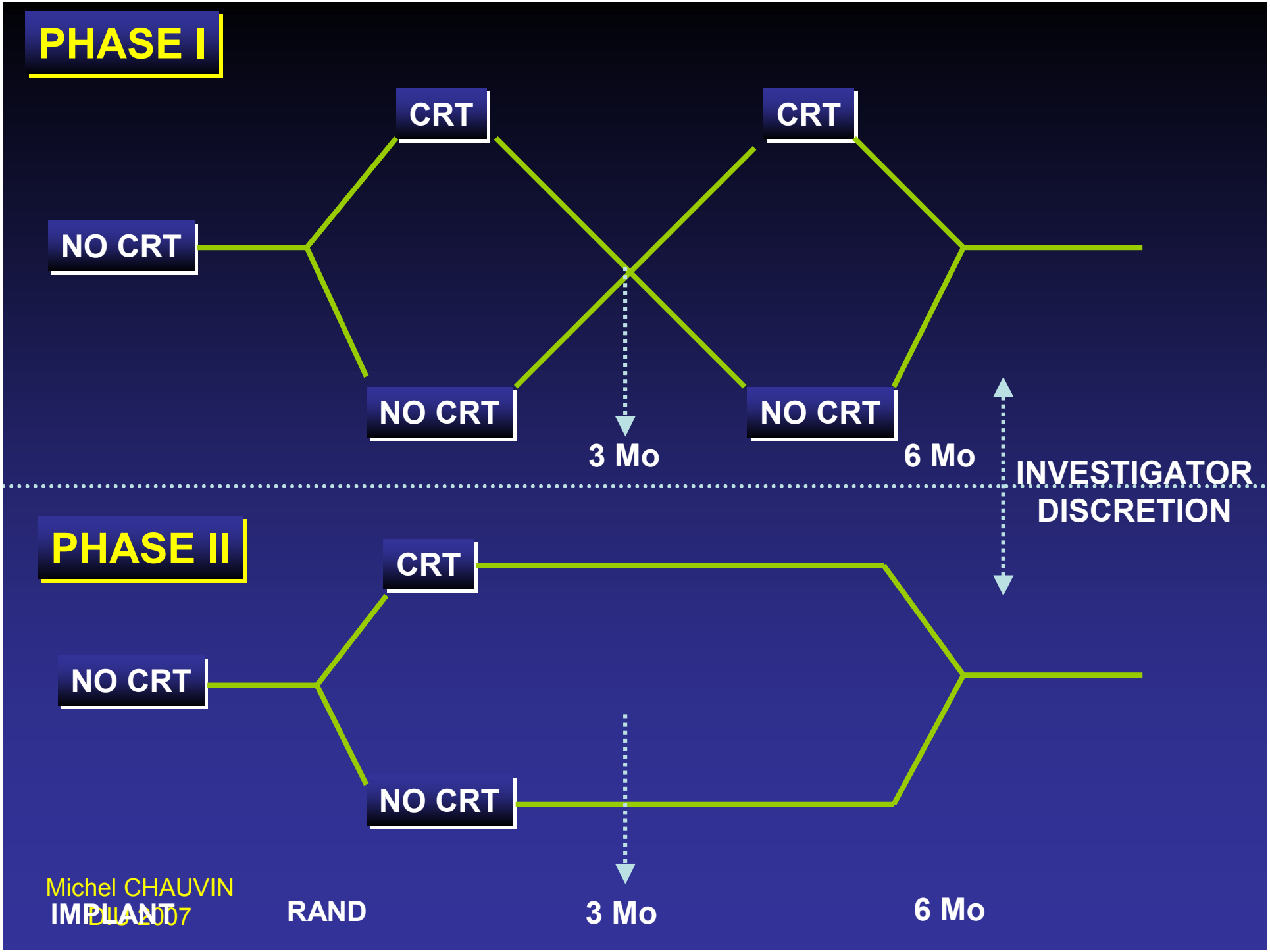
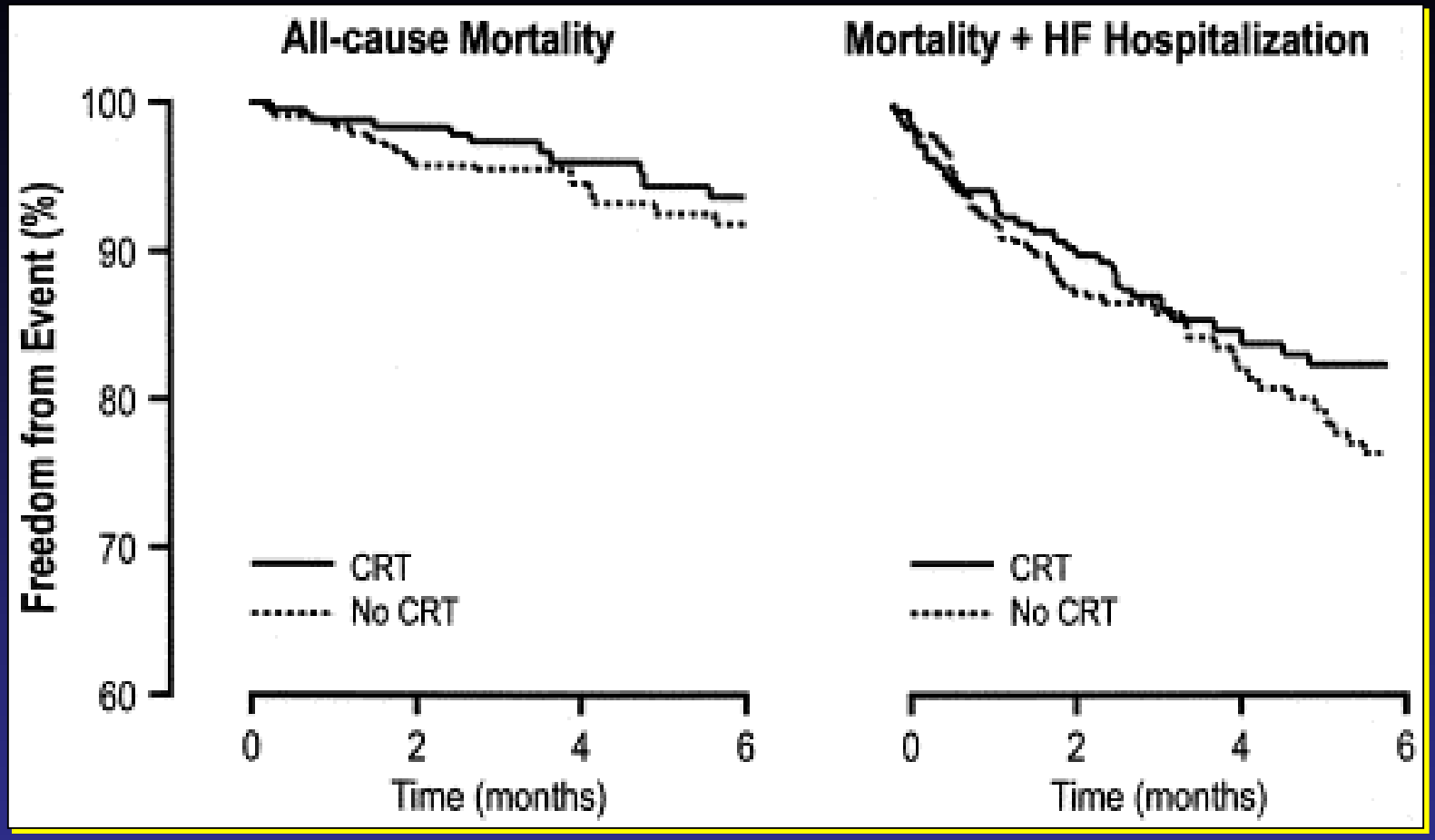

PHASE I
CRT
CRT
NO CRT
NO CRT
NO CRT
3 Mo
6 Mo
INVESTIGATOR
DISCRETION
PHASE II
CRT
NO CRT
NO CRT
RAND
3 Mo
6 Mo



The CRT improved functional status in patients indicated for an ICD who also have symptomatic HF and intraventricular conduction delay

SL Higgins et al JACC 2003; 42 : 1454-9

A DEFIBRILLATOR IS INDICATED : SHOULD WE RESYNCHRONISE ?

YES , WHEN AN I.C.D. IS INDICATED IN A PATIENT WITH « OFFICIAL » CRITERIA OF RESYNCHRONIZATION

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A DEFIBRILLATOR IS INDICATED : SHOULD WE RESYNCHRONISE …

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A DEFIBRILLATOR IS INDICATED : SHOULD WE RESYNCHRONISE …

… WHEN A PATIENT HAS ANY OF THE « OFFICIAL » CRITERIA FOR A RESYNCHRONIZATION ?

NYHA CLASSES I AND II

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A DEFIBRILLATOR IS INDICATED : SHOULD WE RESYNCHRONISE …

THE NATURAL HISTORY OF MILD SYMPTOMATIC HEART FAILURE

DOES RESYNCHRONIZATION PREVENT DISEASE WORSENING ?

DOES RESYNCHRONIZATION PREVENT REMODELING ?

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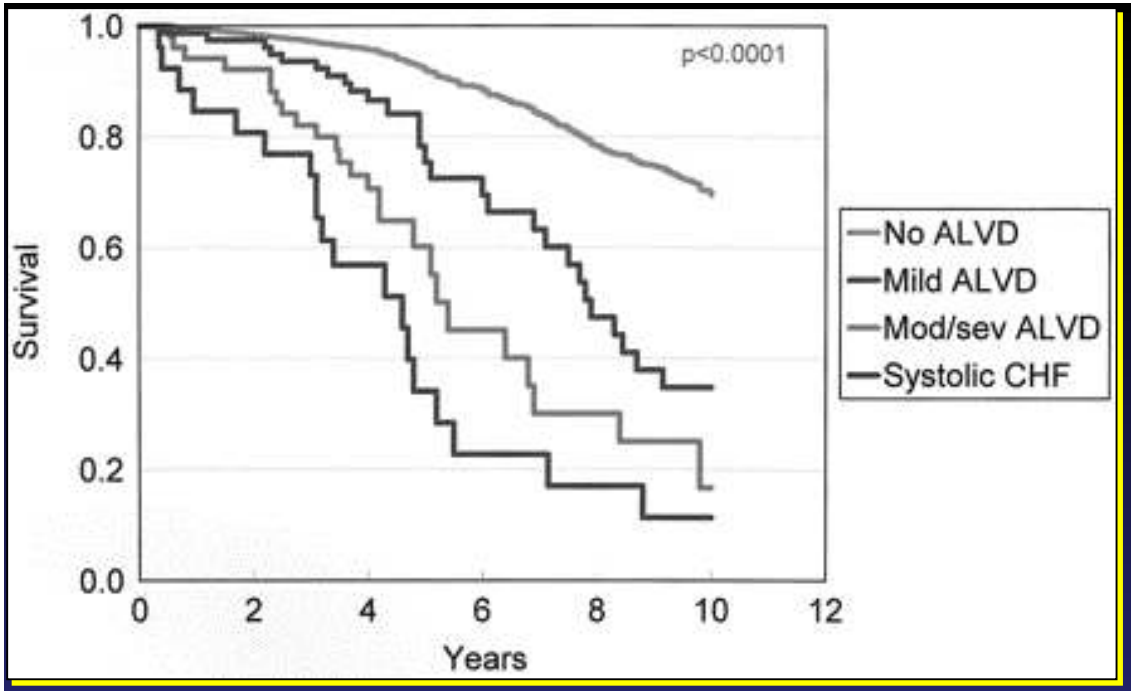
Natural History of Asymptomatic Left Ventricular Systolic Dysfunction (ALVD) in the Community

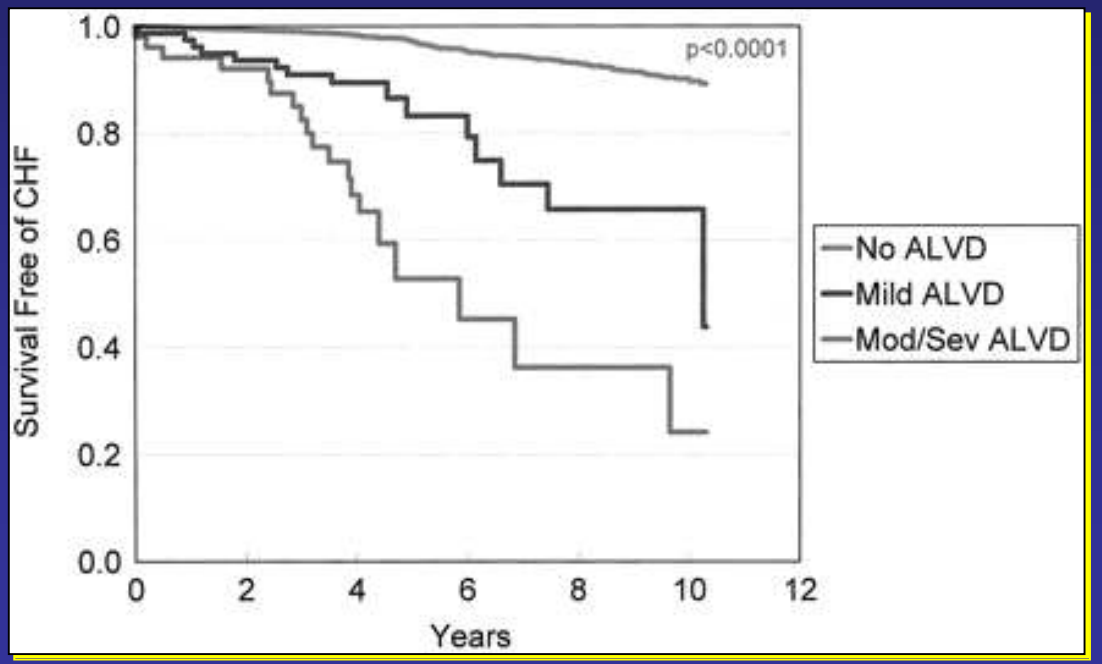
Thomas J. Wang, et al
Circulation. 2003;108:977

Natural History of ALVD

- FRAMINGHAM STUDY
- MILD ALVD (0.4 ≤ LVEF ≤ 0.5)
- MODER./SEVERE ALVD (LVEF < 0.4)
- NO HISTORY OF C.H.F.
- 12 YEARS FOLLOW UP



KAPLAN-MEIER CURVES FOR SURVIVAL



KAPLAN-MEIER CURVES FOR SURVIVAL FREE OF CHF

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CONCLUSIONS

- Individuals with ALVD in the community are at high risk of CHF and death, even when only mild impairment of EF is present.
- Additional studies are needed to define optimal therapy for mild ALVD.

Causes and Consequences of Heart Failure After Prophylactic Implantation of a Defibrillator in the Multicenter Automatic Defibrillator Implantation Trial II

MADIT II Investigators
I. Goldenberg et al
Circulation 2006; 113: 2810-17

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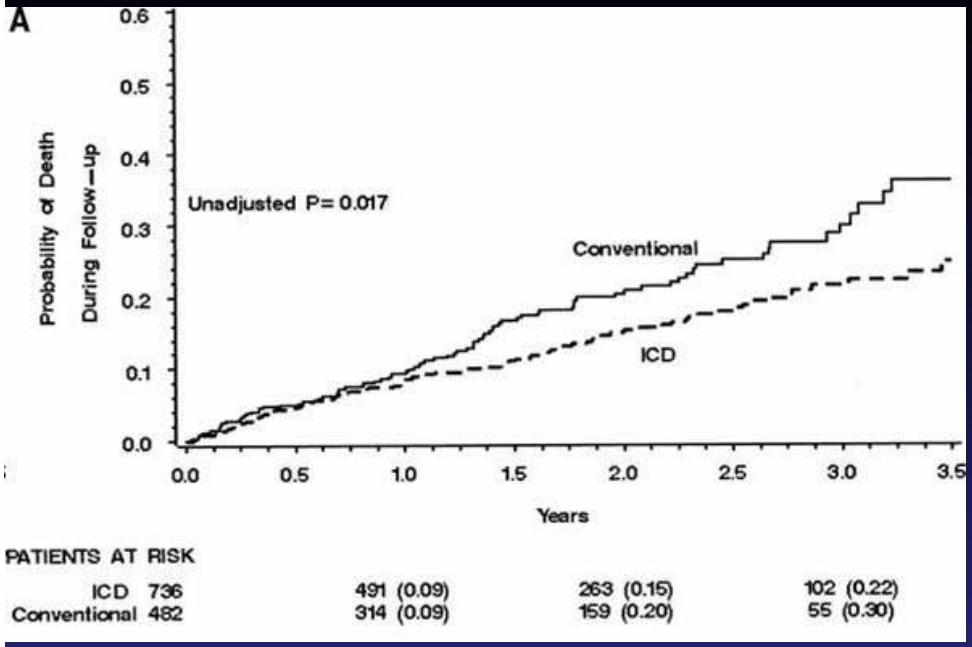
TABLE 1. Clinical Characteristics of Patients in the Conventional-Therapy Group and in the Defibrillator Group by Device Type

		Defibrillator	
	Conventional (n=482)	Single Chamber (n=402)	Dual Chamber (n=313)
Age ≥65 y, %	53	47	61§
Female sex, %	15	16	14
NYHA functional class ≥2, %*	60	61	72§
I	40	39	28§
II	34	35	37
III	22	22	30
IV	4	4	5

MADIT II Investigators

I. Goldenberg et al Circulation 2006; 113: 2810-17



KAPLAN-MEIER ESTIMATES OF ALL-CAUSE MORTALITY (A)

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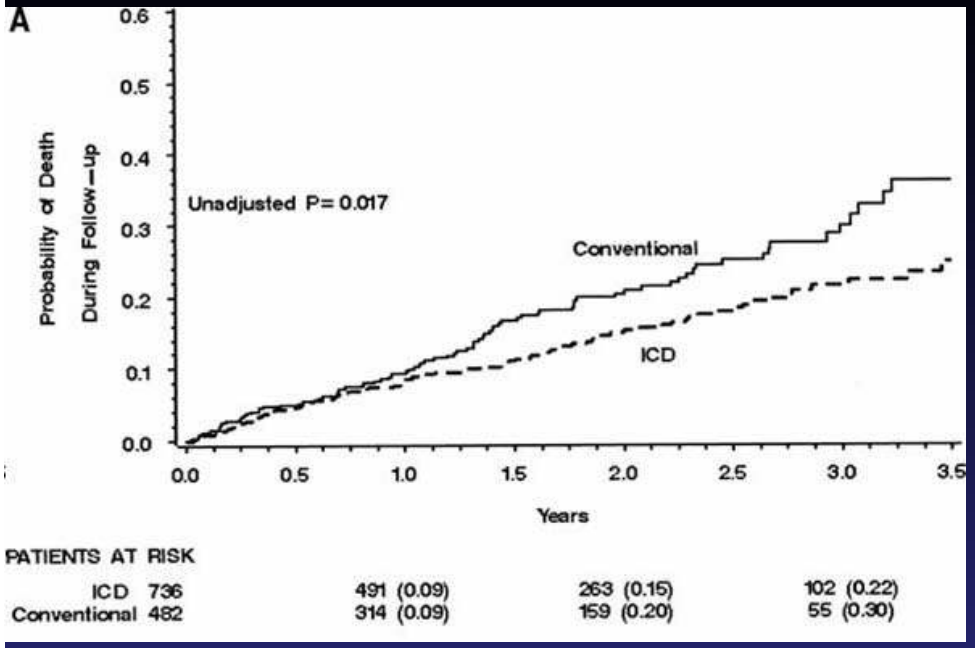

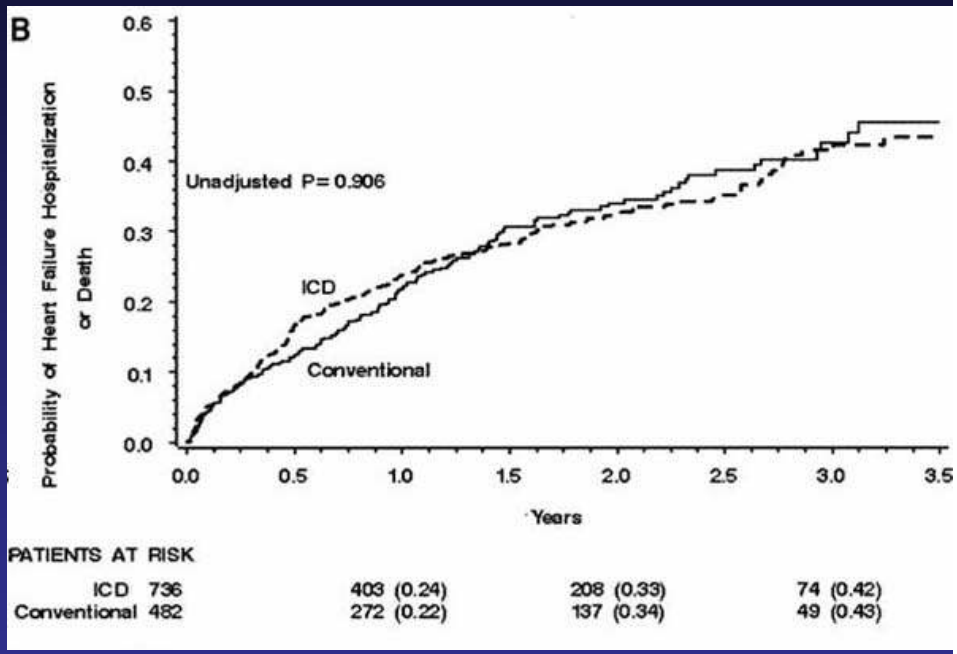

KAPLAN-MEIER ESTIMATES OF ALL-CAUSE MORTALITY (A)

(B) ALL-CAUSE MORTALITY OR FIRST HOSPITALIZATION FOR HF

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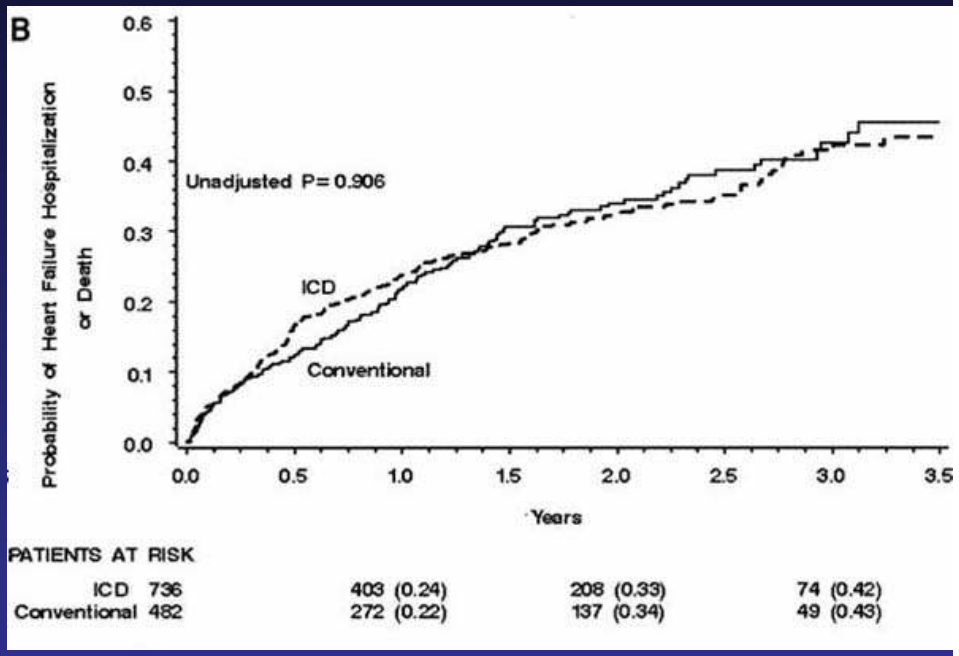
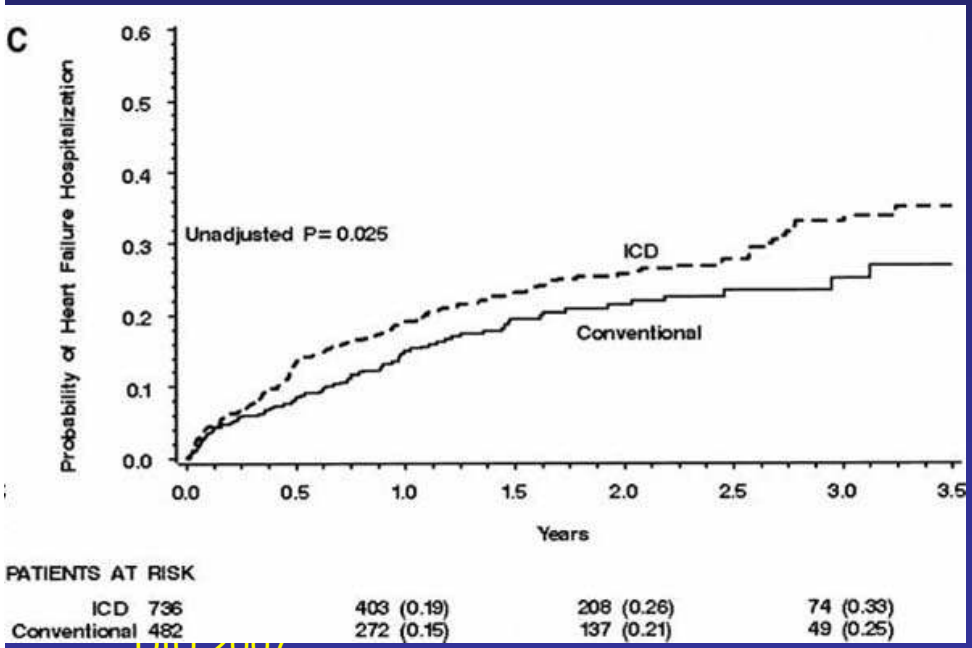
(B) ALL-CAUSE MORTALITY OR FIRST HOSPITALIZATION FOR HF

(C) FIRST HOSPITALIZATION FOR HF WITH CENSORING ON DEATH





MADIT II CONCLUSION

- ICD THERAPY TRANSFORMS SUDDEN DEATH RISK TO A SUBSEQUENT HF RISK.
- THESE FINDINGS SHOULD DIRECT MORE ATTENTION TO THE PREVENTION OF HF IN PATIENTS WHO RECEIVE AN ICD

Multicenter InSync Randomized Clinical Evaluation (MIRACLE) Study Group. Effect of Cardiac Resynchronization Therapy on Left Ventricular Size and Function in Chronic Heart Failure

SJ SUTTON et al
Circulation 2003; 107 : 1985-90

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STUDY ENDPOINTS

- **Primary Efficacy:**
  - **NYHA Functional Class**
  - **Quality of life (Minnesota Living with Heart Failure)**
  - **6-minute Walk Distance**
- **Secondary Efficacy Included:**
  - **Peak VO_2, Exercise Time, LVEF, LVEDD, MR, QRS Duration, Clinical Composite Response**
- **Other Protocol Specified Endpoints:**
  - **Death or Worsening Heart Failure (Safety)**
  - **# Days Spent in Hospital (Health Care Utilization)**

PATIENTS CARACTERISTICS

	Control N=225	CRT N=228
Age (years)	65 ± 11	64 ± 11
Gender (% male)	68%	68%
Heart Failure Etiology (% ischemic)	58%	50%
NYHA (% Class III)	91%	90%
QRS duration (ms)	165 ± 20	167 ± 21
LVEF (%)	22 ± 6	22 ± 6
LVEDD, mm	69 ± 10	70 ± 10

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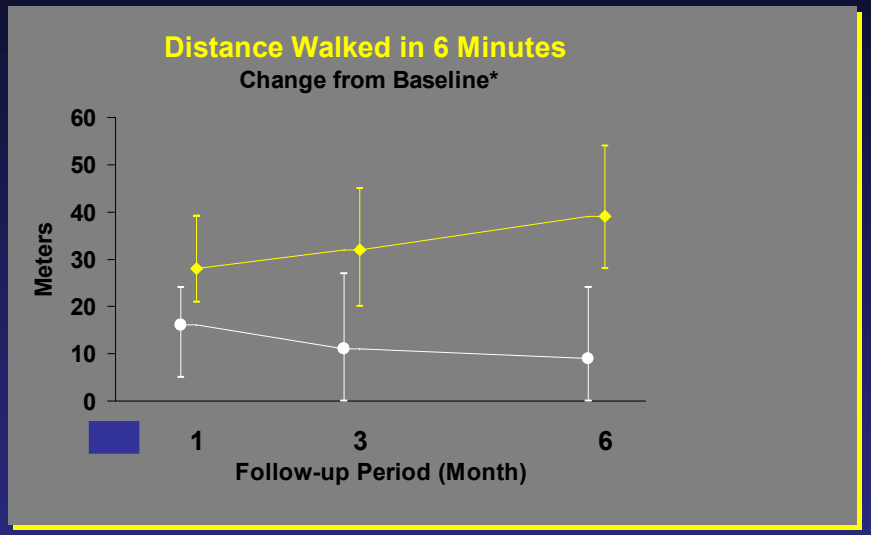
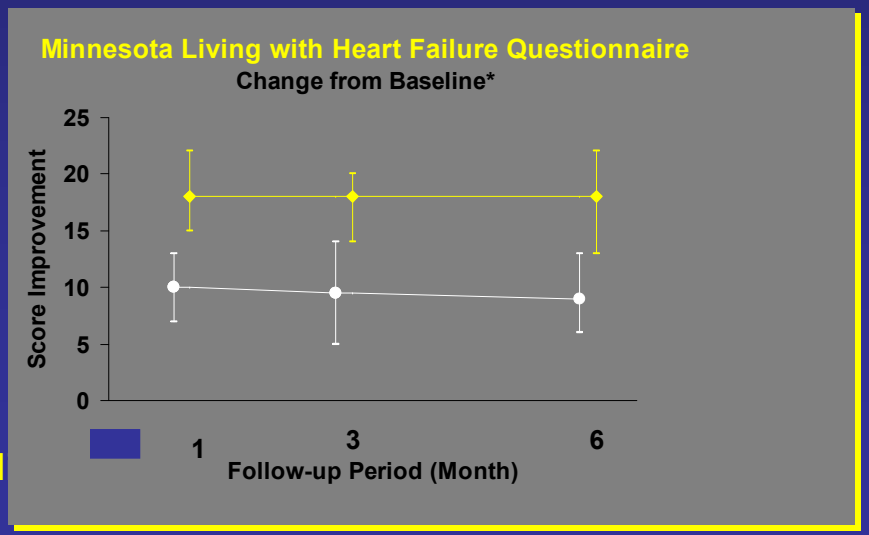
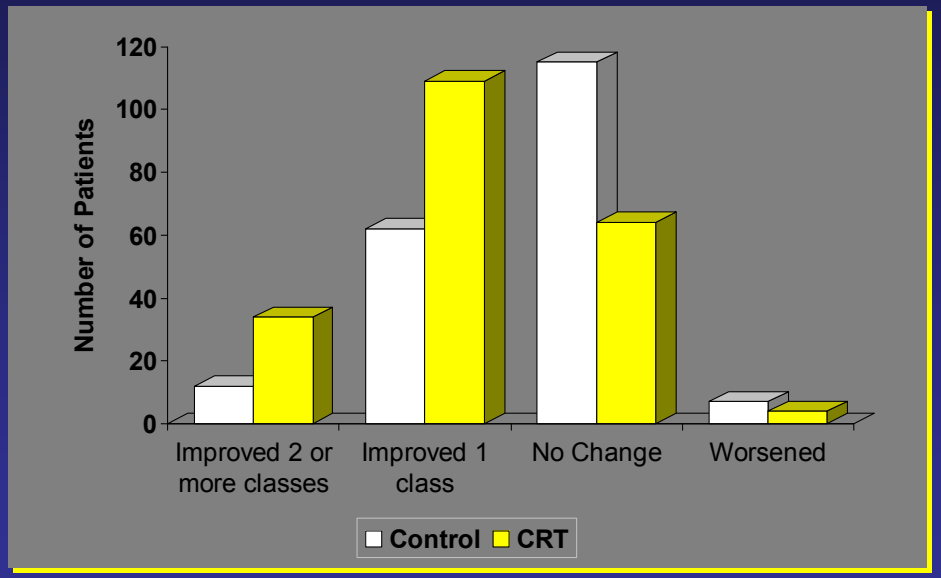
RESULTS





CRT IMPROVES NYHA FUNCTIONAL CLASS



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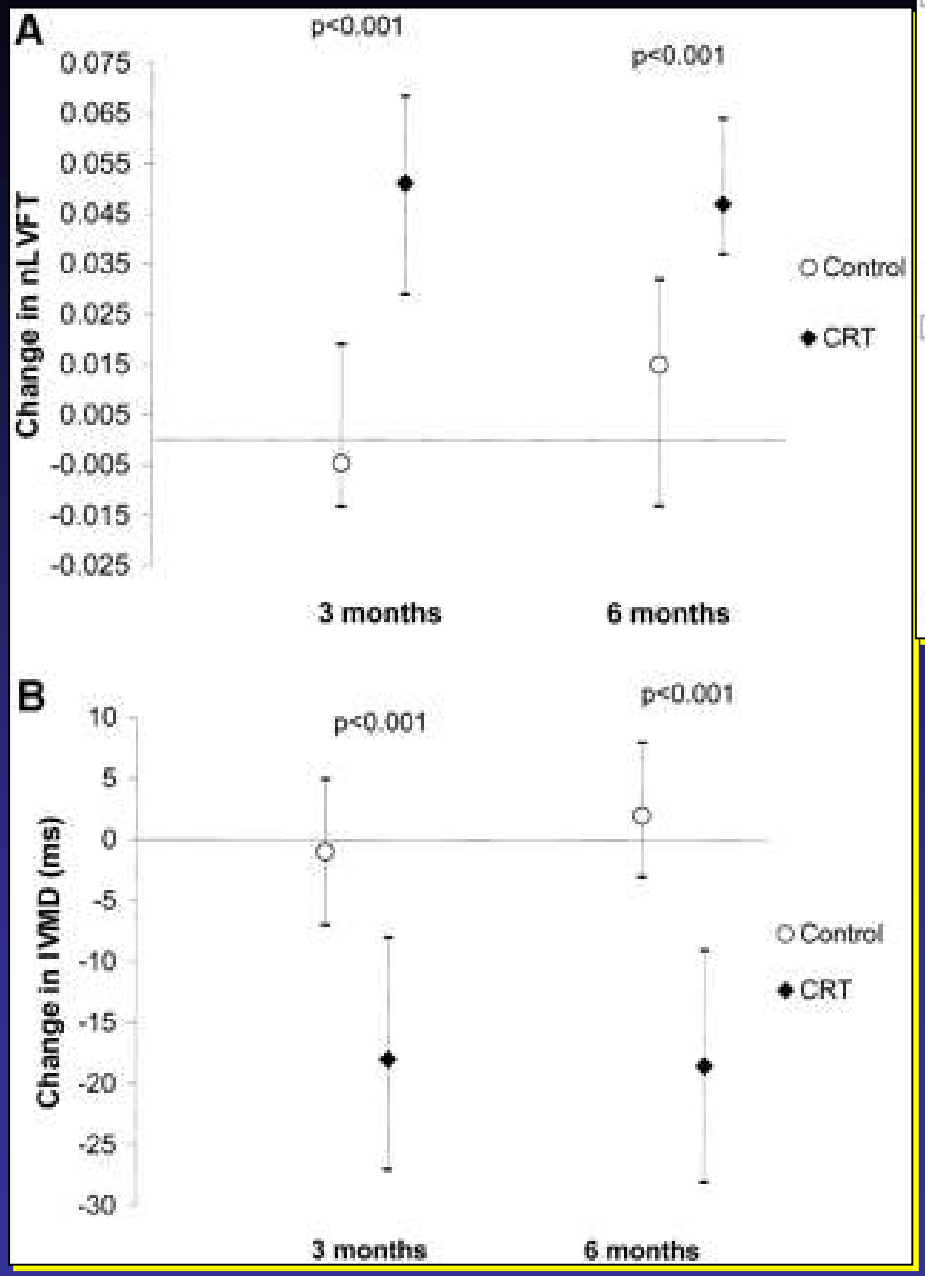

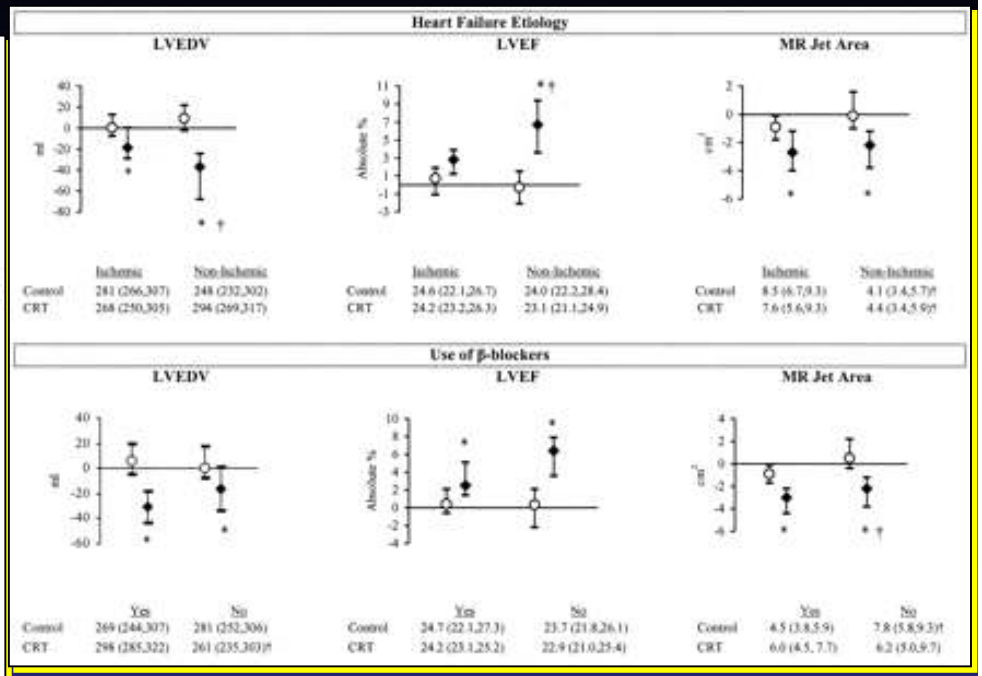

SJ SUTTON et al
Circulation 2003; 107 : 1985-90

The Multicenter InSync ICD II Study (MIRACLE ICD II)

Effects of Cardiac Resynchronization on Disease Progression in Patients with Left Ventricular Systolic Dysfunction, an Indication for an Implantable Cardioverter-Defibrillator and Mildly Symptomatic Chronic Heart Failure

Abraham WT et al
Circulation 2004; 110 : 2864-8

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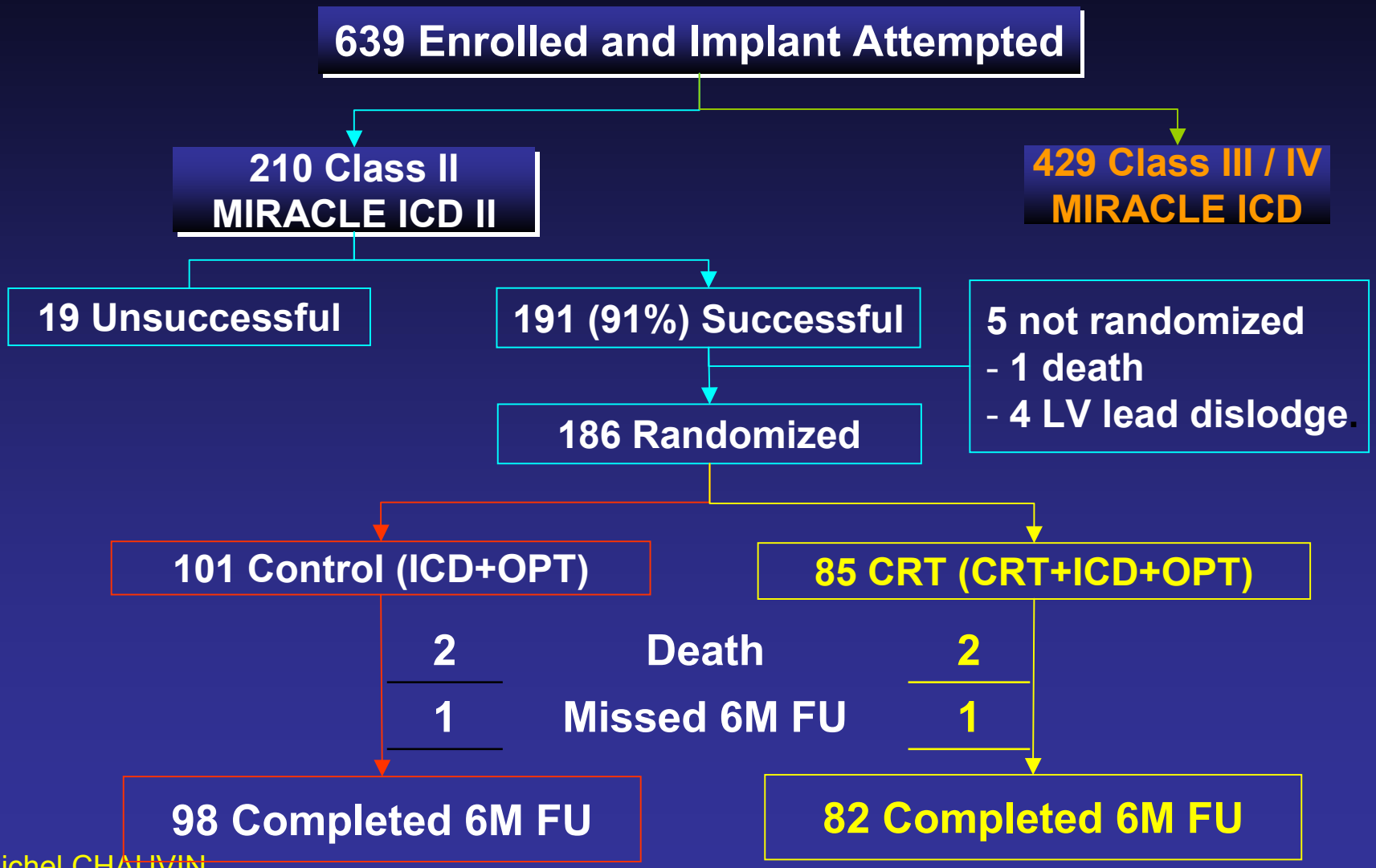
ENROLLMENT AND FOLLOW-UP



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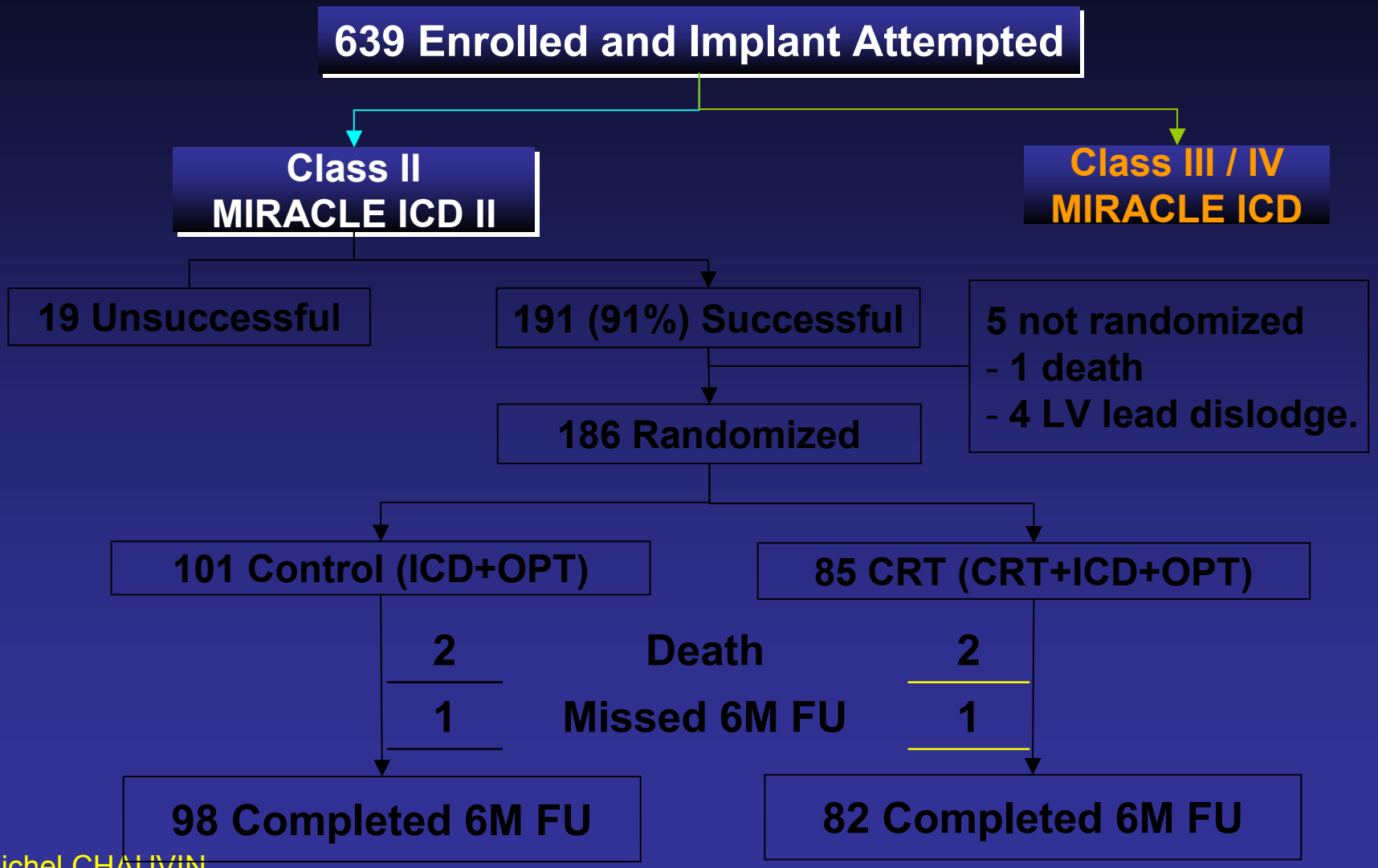
ENROLLMENT AND FOLLOW-UP



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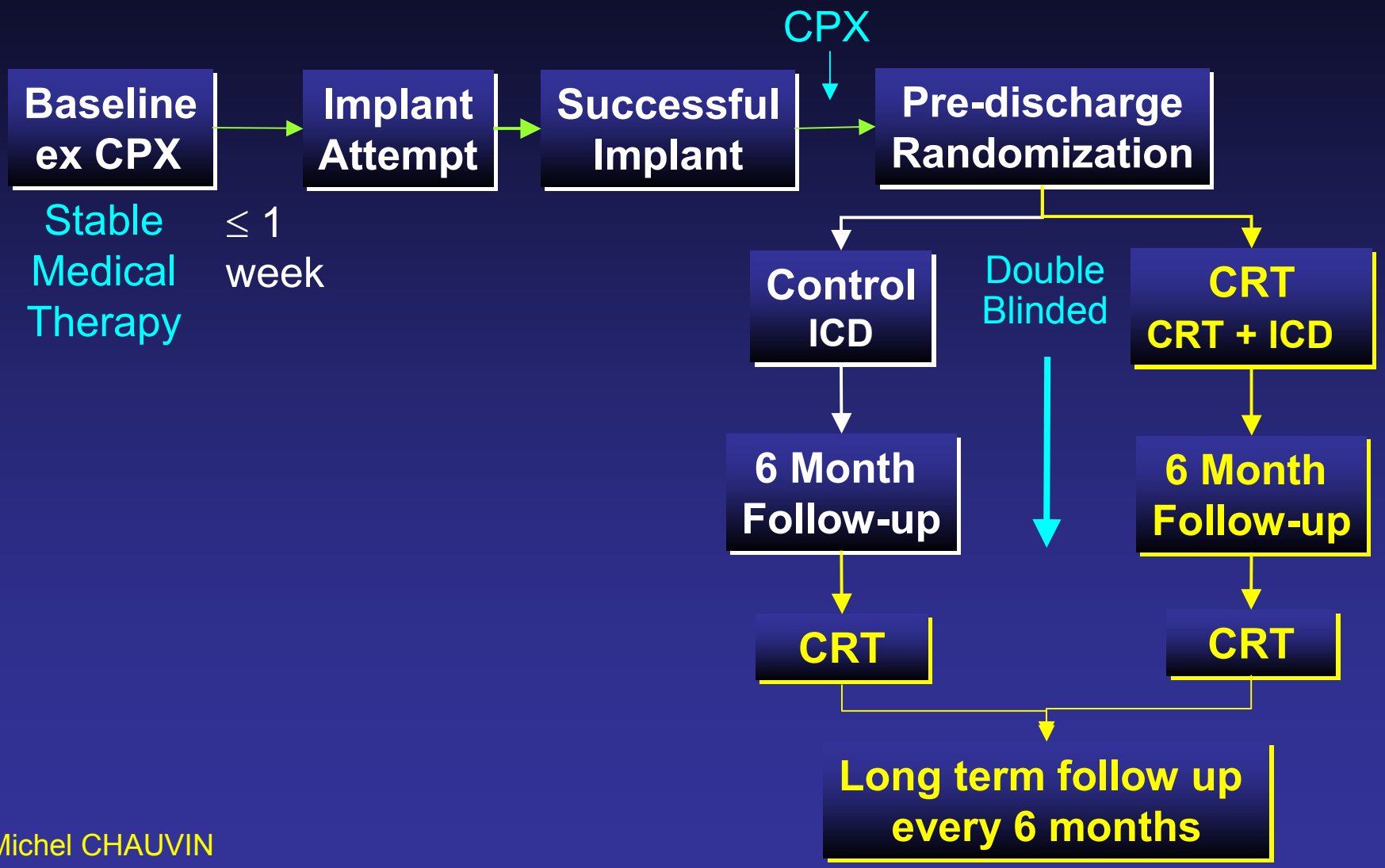
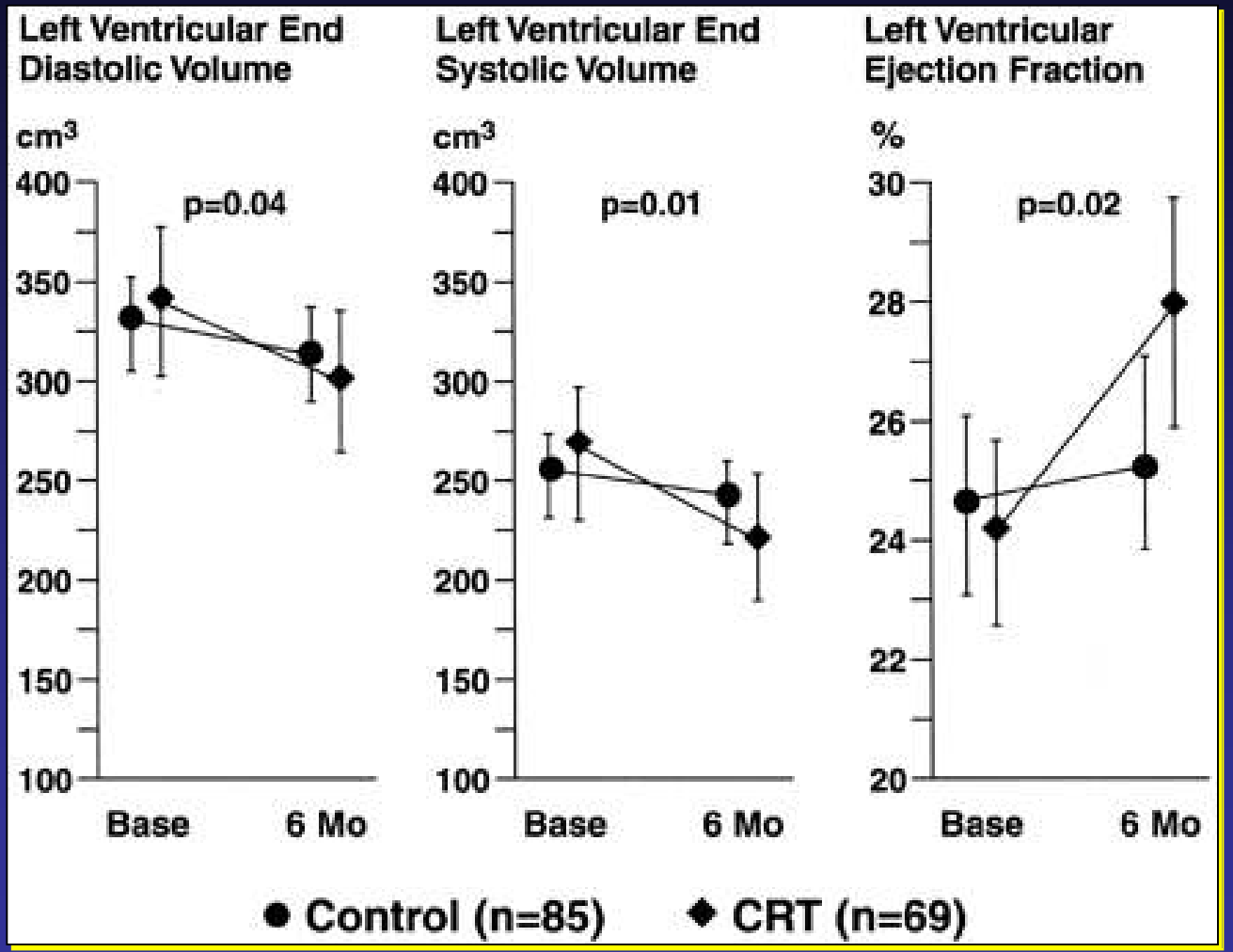
STUDY DESIGN



IMPROVEMENTS IN CARDIAC VOLUMES AND DIMENSIONS



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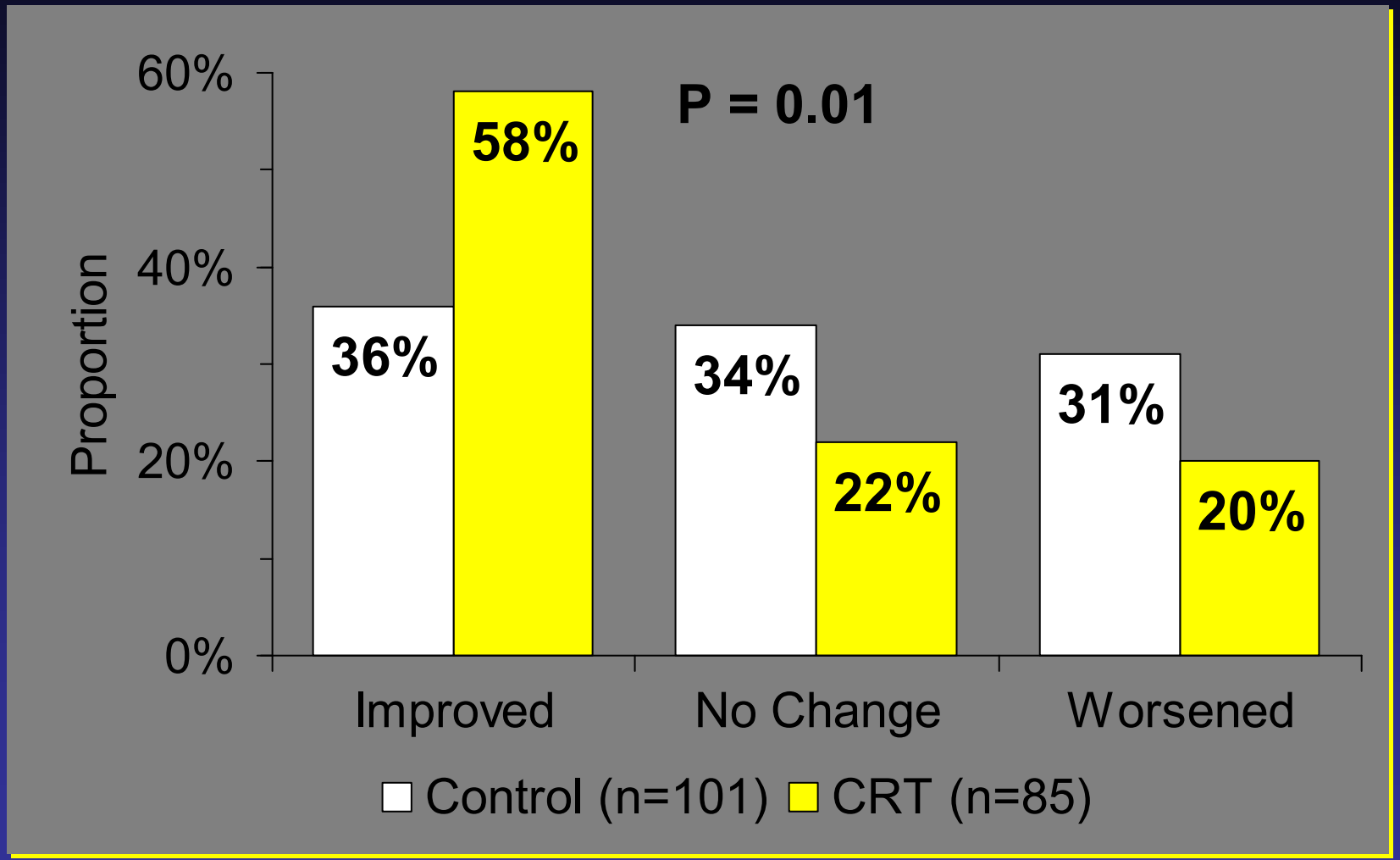
Abraham WT et al Circulation 2004; 110 : 2864-8

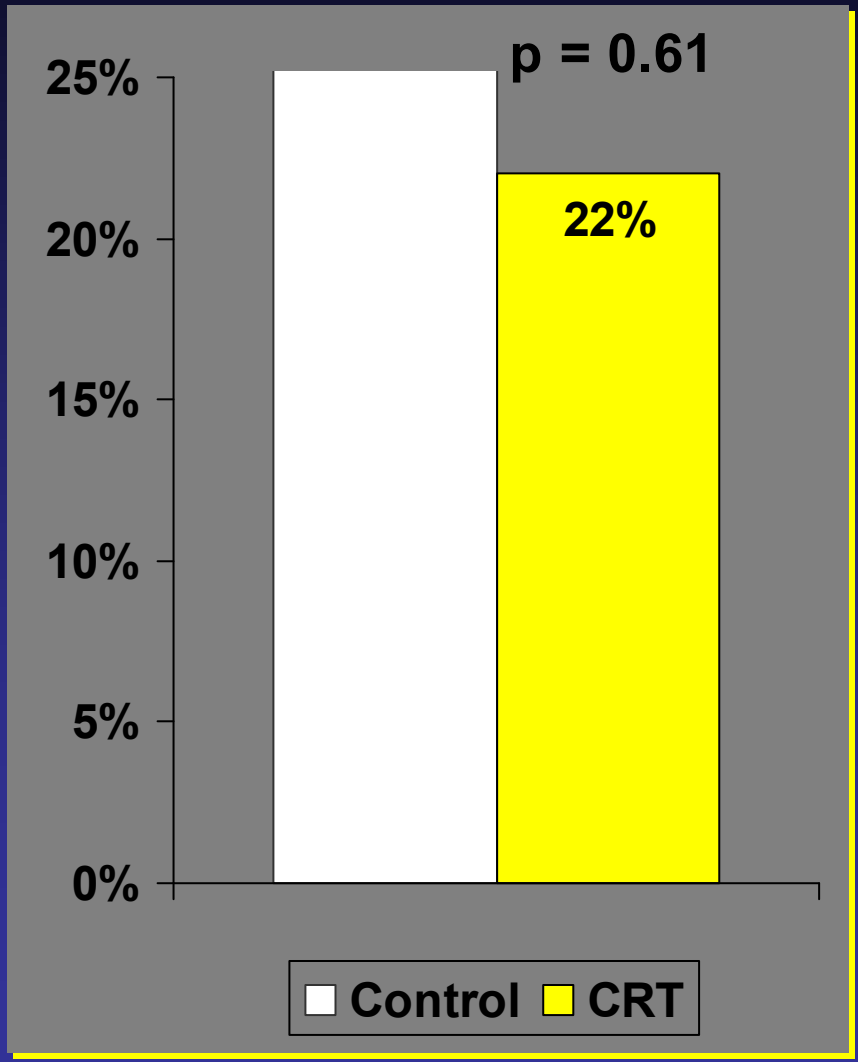
EFFECTS OF CRT ON COMPOSITE RESPONSES



Abraham WT et al
Circulation 2004; 110 : 2864-8

CRT EFFECTS ON VENTRICULAR ARRHYTHMIAS

During 6 Month Randomization Period



The REsynchronization reVErses Remodeling in Systolic left vEntricular dysfunction (REVERSE) study

Rationale and Design of a Randomized Controlled Trial to Assess the Safety and Efficacy of Cardiac Resynchronization Therapy in Patients with Asymptomatic Left Ventricular Dysfunction with Previous Symptoms or Mild Heart Failure

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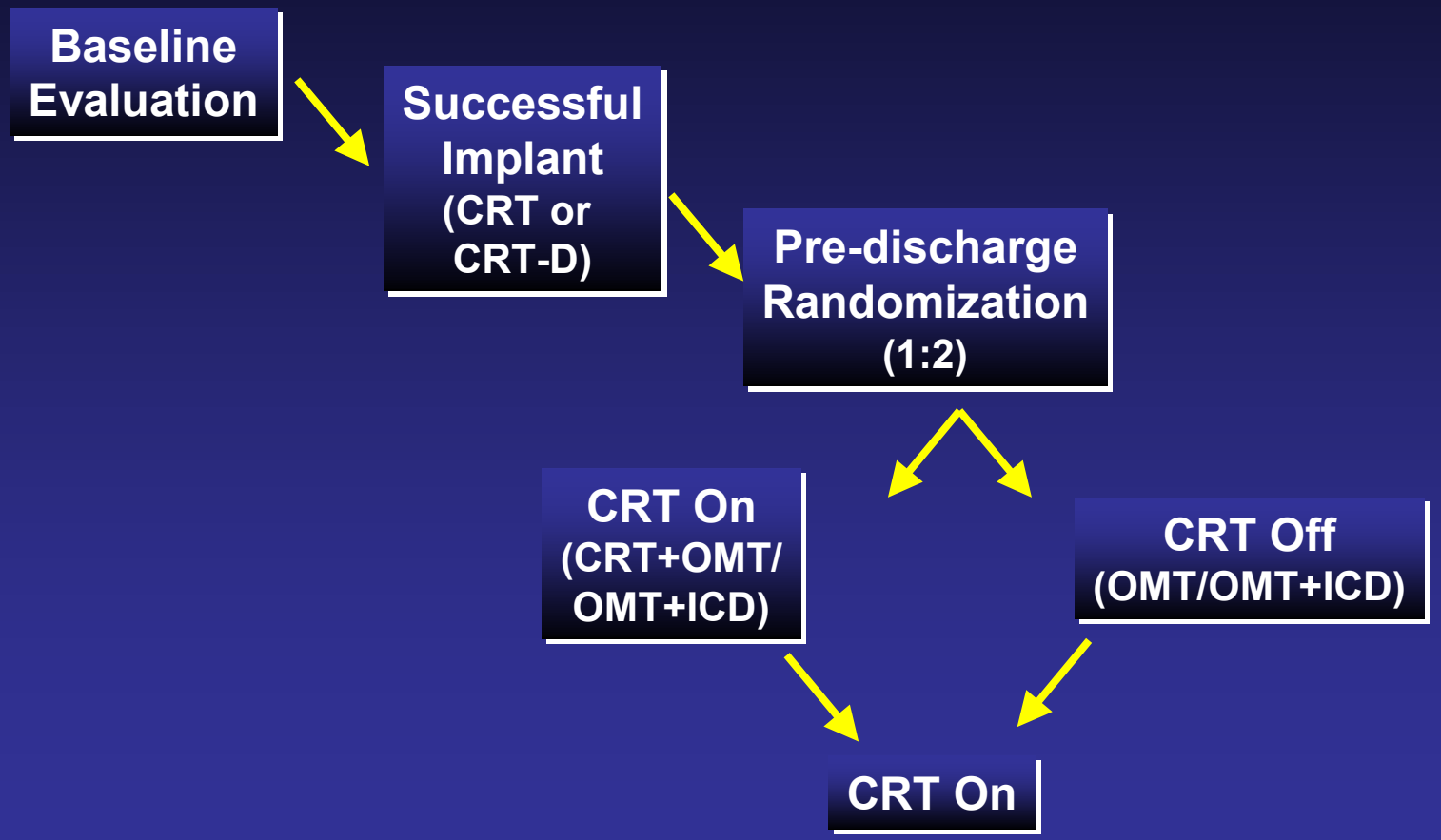
LINDE C et al
Am Heart J 2006; 151: 288-94

The REsynchronization reVErses Remodeling in Systolic left vEntricular dysfunction (REVERSE) study

Patients	NYHA Class I-II, QRS ≥ 120 ms, LVEF ≤ 40%, LVEDD ≥ 55 mm, w/o bradycardia, with or without ICD indication, on OMT
Objective	Assess whether CRT will limit the clinical progression of HF
Primary EP	Clinical Composite Response[1]
Key Secondary	Left Ventricular End Systolic Volume index
Size, Locations	683 patients in 115 centers in US, Europe, Canada
Sponsor	Medtronic

LINDE C et al
Am Heart J 2006; 151: 288-94

The REsynchronization reVErses Remodeling in Systolic left vEntricular dysfunction (REVERSE) study



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MADIT-CRT:
Automatic Defibrillator Implantation With Cardiac Resynchronization Therapy

PURPOSE

The MADIT-CRT trial is designed to determine if combined ICD - CRT-D will reduce the risk of mortality and heart failure (HF) events by approximately 25%, in subjects who are in NYHA Class II with non-ischemic or ischemic cardiopathy and subjects who are in NYHA Class I with ischemic cardiopathy, left ventricular dysfunction (LVEF < or = 0.30), and QRS duration > or = 130 ms.

MADIT-CRT

Patients	NYHA Class I / II, QRS ≥ 130 ms, LVEF ≤ 30%, post MI > 3 months or dilated cardiomyopathy with or without non-sustained VT, on optimal medical therapy (OMT)
Objective	Evaluate effect of CRT on the clinical progression of heart failure
Primary EP	Reduction in all-cause mortality + heart failure event
Key Secondary	Left-ventricular end-systolic volume index
Size, Locations	1,820 patients in multiple centers in US
Sponsor	Guidant

MADIT-CRT: Automatic Defibrillator Implantation With Cardiac Resynchronization Therapy

PRIMARY OUTCOMES

To determine whether CRT-D in high-risk coronary subjects will significantly reduce the combined endpoint of all-cause mortality or HF events when compared to ICD-only therapy, whichever comes first

MADIT-CRT:
Automatic Defibrillator Implantation With Cardiac Resynchronization Therapy

SECONDARY OUTCOMES

Evaluate the effects of CRT-D, relative to ICD-only, on the changes from baseline to one year on echocardiogram (ECHO)-determined left ventricular internal volume at end systole with CRT turned off during the one year echocardiogram;

MADIT-CRT:
Automatic Defibrillator Implantation With Cardiac Resynchronization Therapy

SECONDARY OUTCOMES

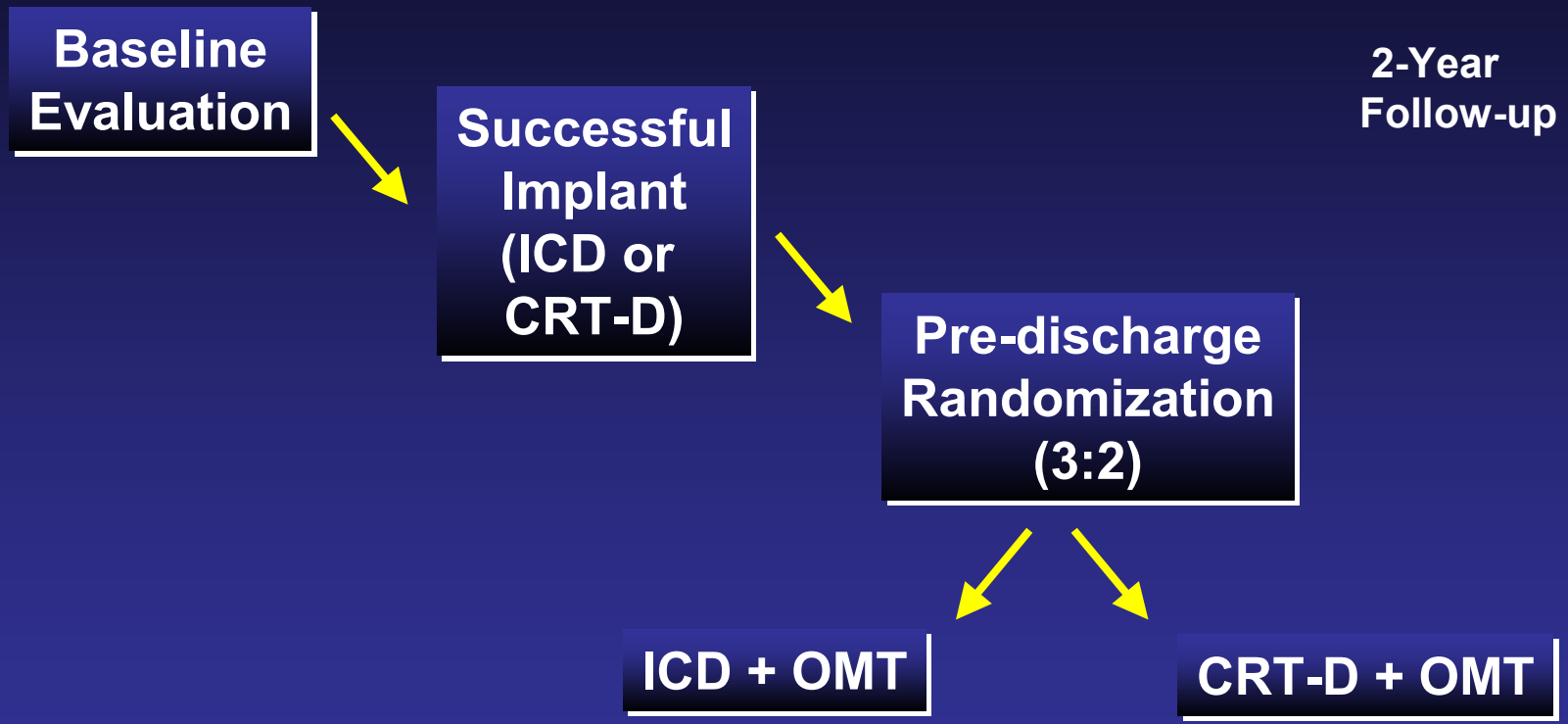
Evaluate the effects of CRT-D, relative to ICD-only, on the changes from baseline to one year on ECHO-determined left ventricular internal volume at end diastole with CRT turned off during the one year echocardiogram;

MADIT-CRT: Automatic Defibrillator Implantation With Cardiac Resynchronization Therapy

SECONDARY OUTCOMES

Evaluate the effects of CRT-D, relative to ICD-only, on the subject-specific rates of multiple HF events over the full study period

MADIT-CRT


Baseline Evaluation
Successful Implant (ICD or CRT-D)
Pre-discharge Randomization (3:2)
2-Year Follow-up
ICD + OMT
CRT-D + OMT

IN CONCLUSION …

A DEFIBRILLATOR IS INDICATED : SHOULD WE RESYNCHRONISE ?

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