PATIENT SELECTION FOR ICD AFTER MI BEYOND EJECTION FRACTION

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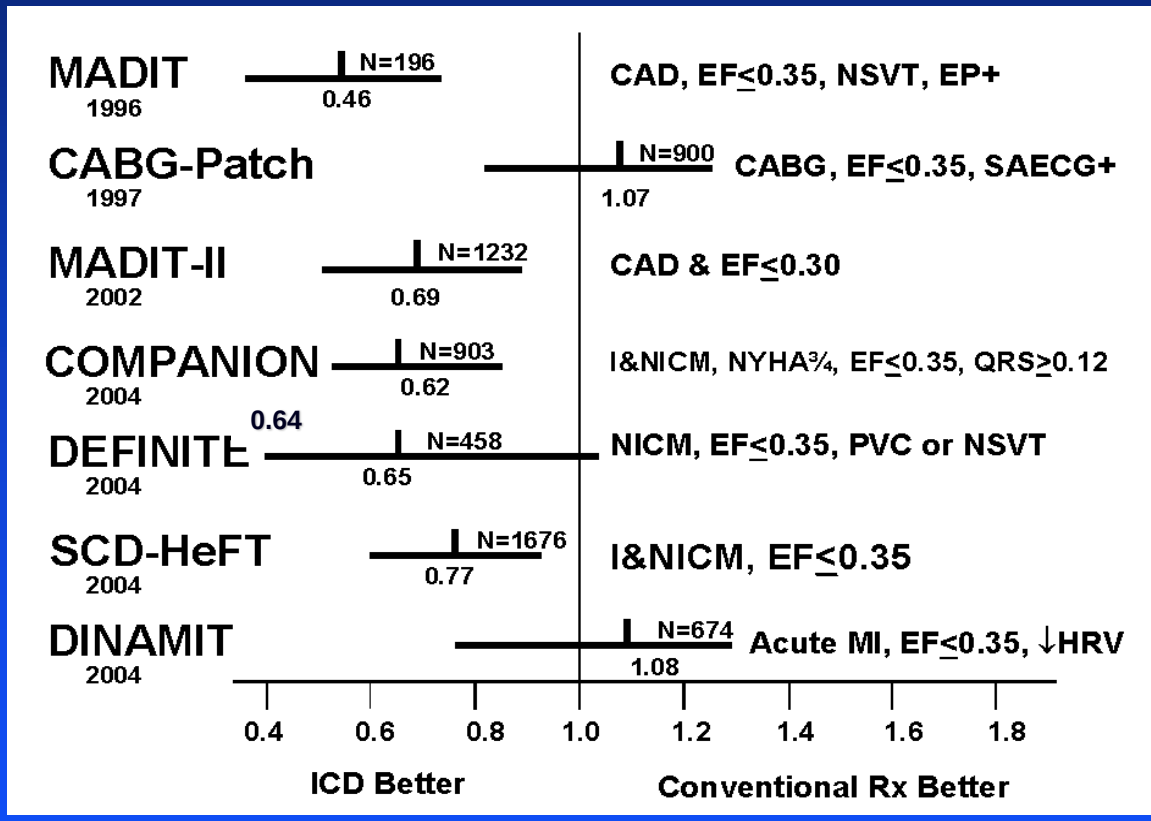
BACKGROUND: CURRENT GUIDELINES FOR PRIMARY ICD THERAPY

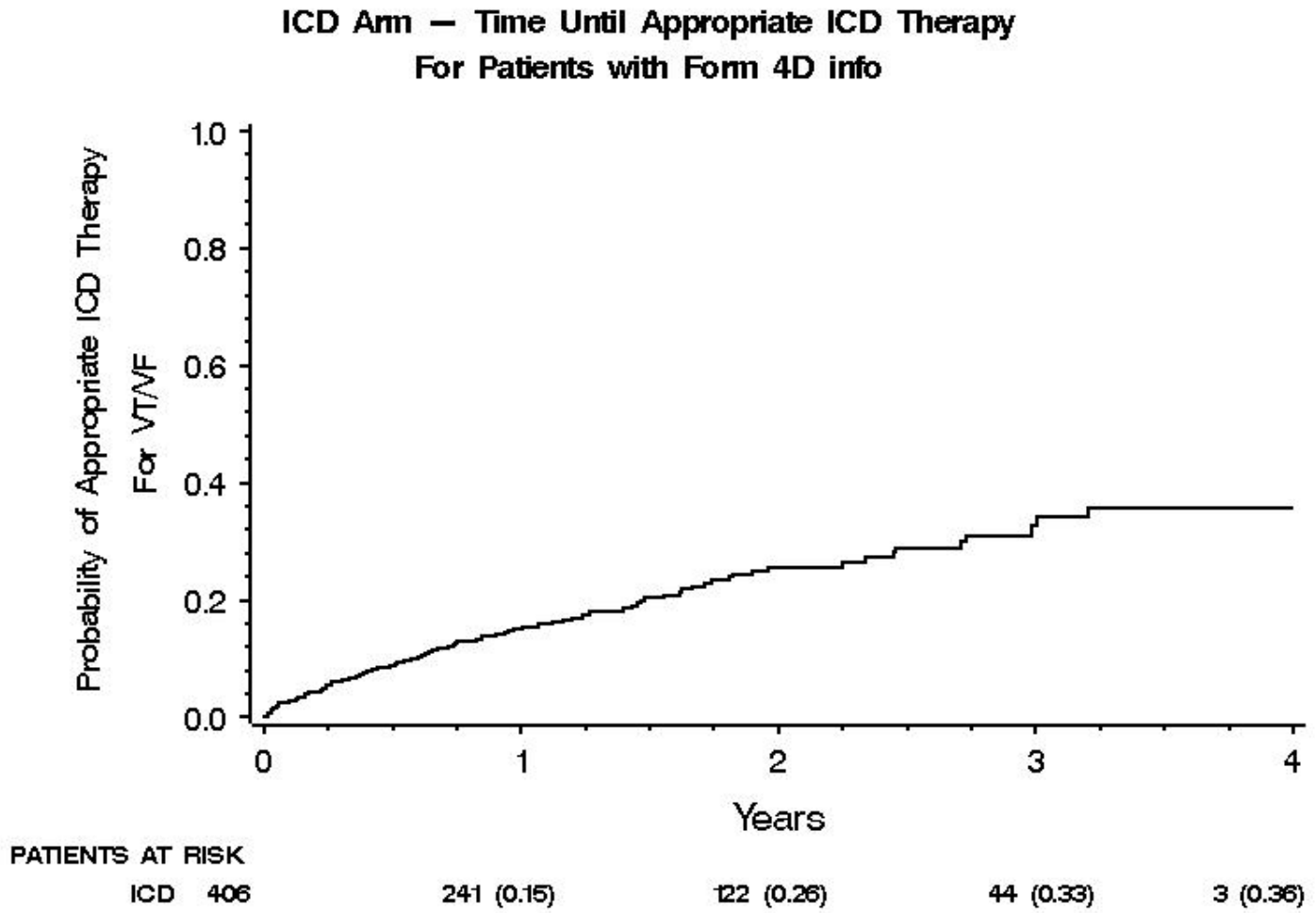
- Class I indication in pts with EF ≤ 35%

  AHA/ACC/HRS 2012 Guidelines

- Not all patients derive a survival benefit from primary device Rx



APPROPRIATE THERAPY FOR VT/VF IN MADIT-II



DINAMIT NEJM, 2004

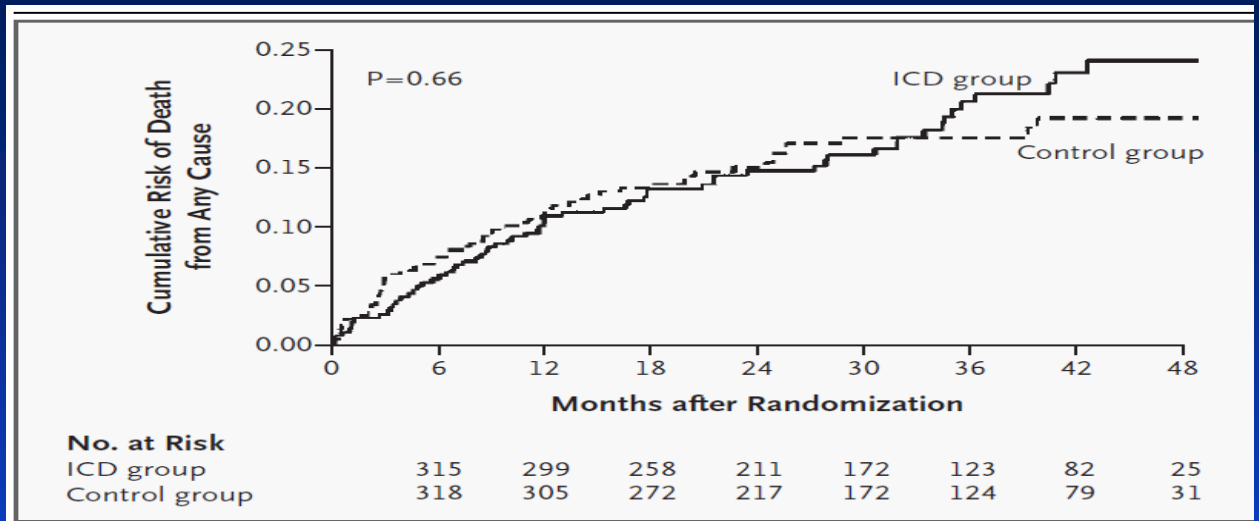
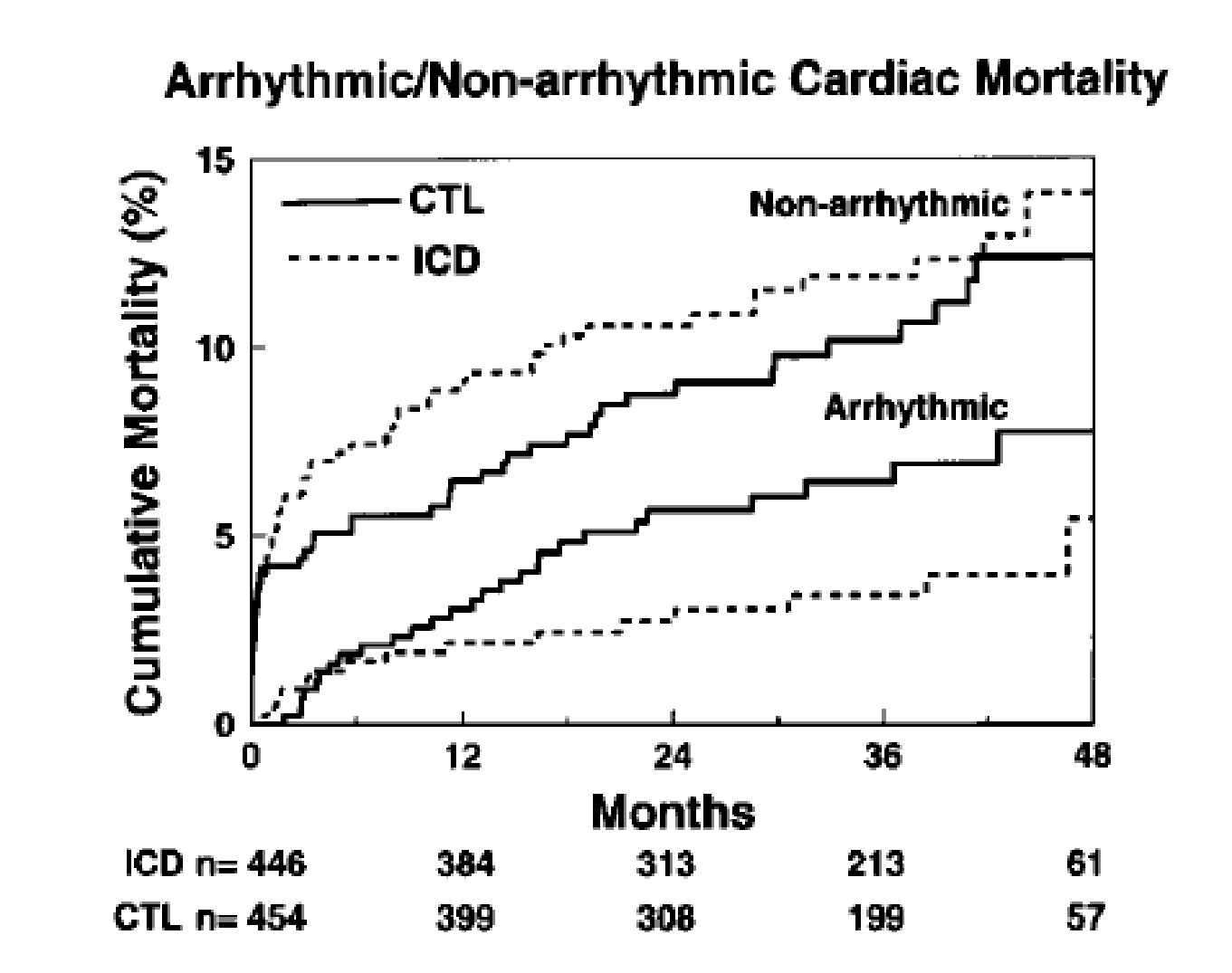


Table 2. Mortality Rates.*

Cause of Death	ICD Group		Control Group		Hazard Ratio (95% CI)†	P Value‡
	No. of Deaths	Rate %/yr	No. of Deaths	Rate %/yr		
Any cause	62	7.5	58	6.9	1.08 (0.76–1.55)	0.66
Arrhythmia	12	1.5	29	3.5	0.42 (0.22–0.83)	0.009
Nonarrhythmic causes	50	6.1	29	3.5	1.75 (1.11–2.76)	0.02
Cardiac, nonarrhythmic	34	4.1	20	2.4	1.72 (0.99–2.99)	0.05
Vascular, noncardiac	5	0.6	3	0.4	1.69 (0.40–7.06)	0.47
Nonvascular	11	1.3	6	0.7	1.85 (0.68–5.01)	0.22

MECHAISM OF DEATH IN CABG-PATCH

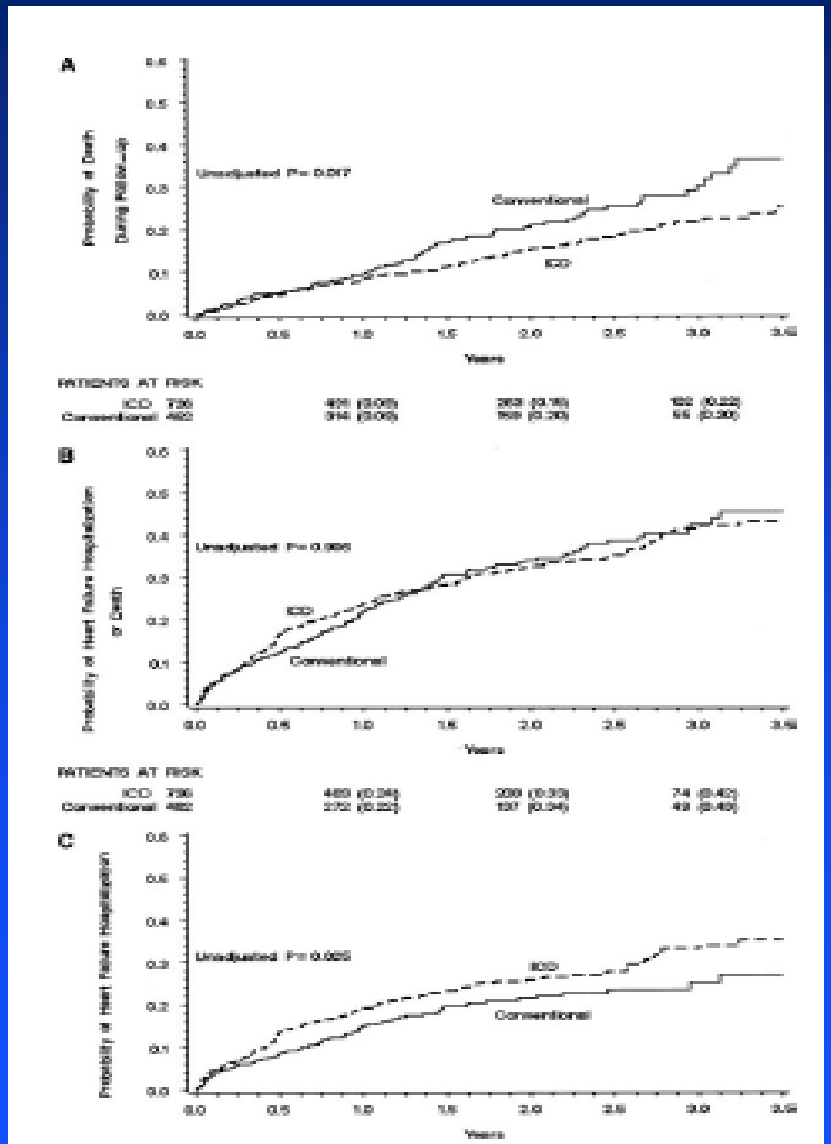


Bigger JT Jr, et al. Circulation, 1999

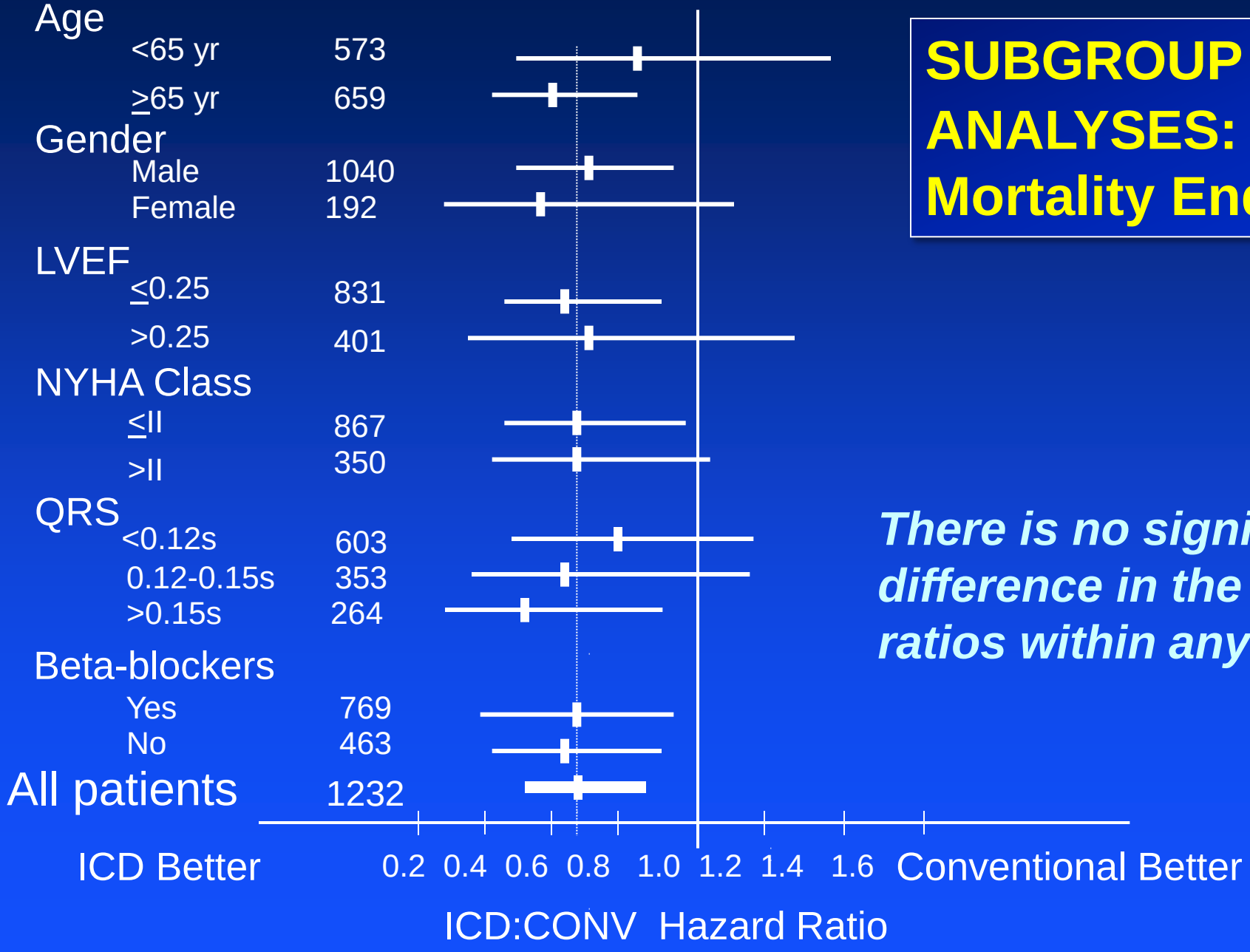
RISK OF HEART FAILURE

Reduction in the risk of SCD with ICD may be transformed into increased risk for subsequent HF events

Goldenberg et al. Circulation 2006



MADIT-II



SUBGROUP ANALYSES: Mortality Endpoint

There is no significant difference in the hazard ratios within any subgroup

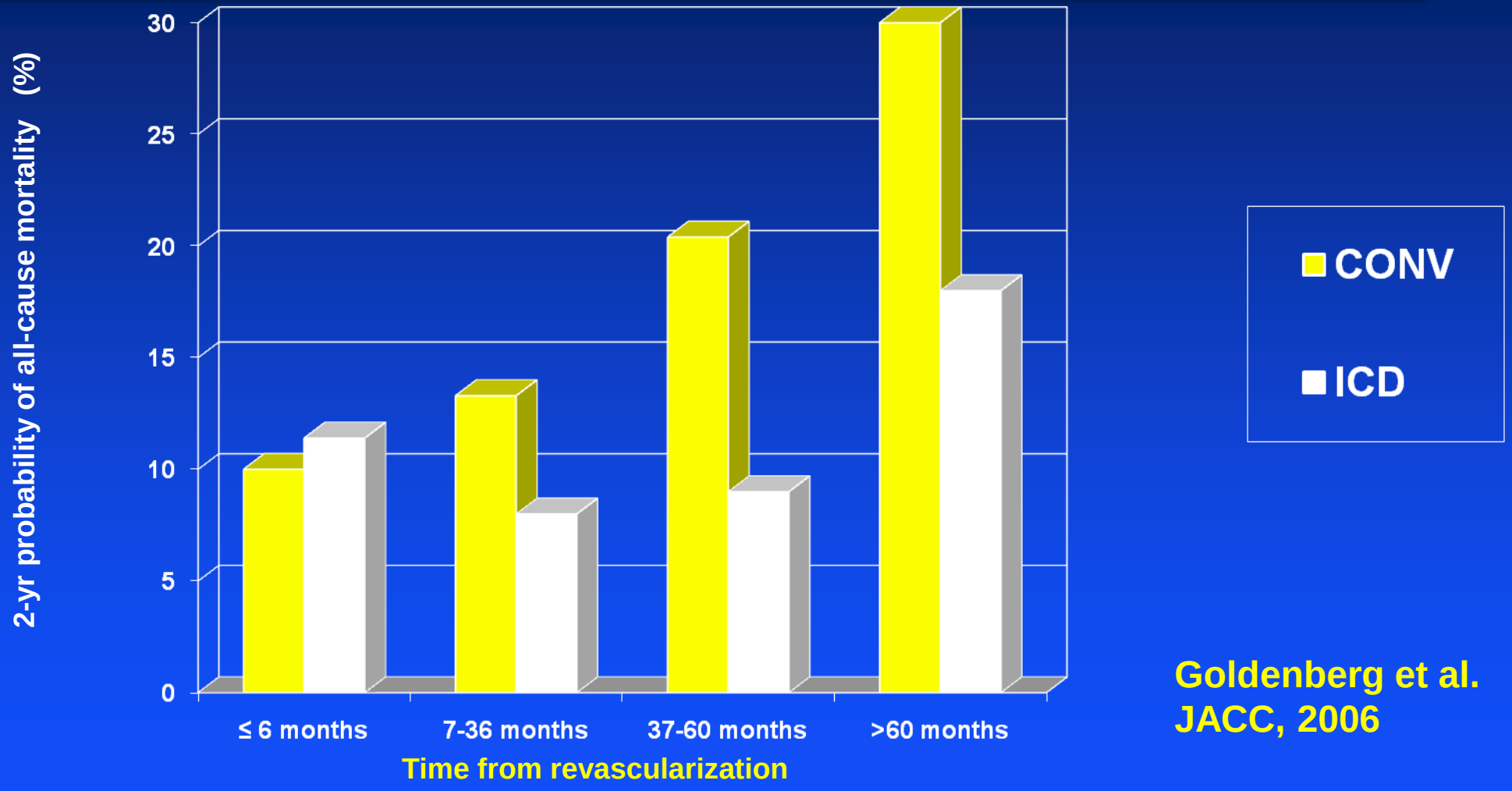
Factors NOT Associated with Prediction of ICD Benefit

- Predict arrhythmic risk
  - SAECG
  - EPS inducibility
  - HRV
  - HRT
  - MTWA
- Do no account for competing risk of non-arrhythmic mortality

ICD EFFICACY IN RISK SUBSETS

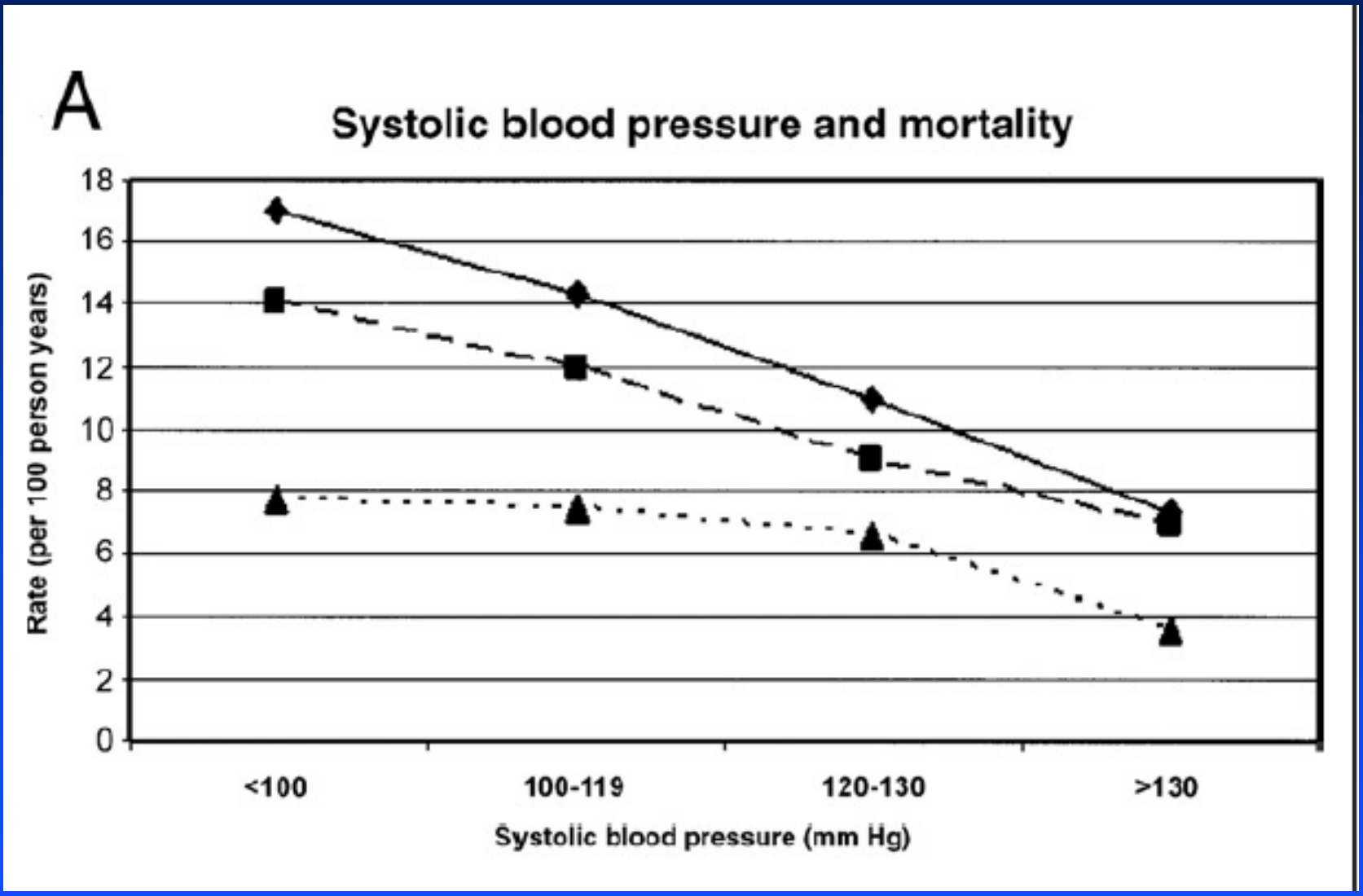
- **Subanalyses of MADIT-II suggest:**
  - **Attenuated efficacy in a lower-risk subsets:**
    Relatively low mortality rates preclude a meaningful ICD benefit within a reasonable time horizon
  - **Attenuated efficacy in pts with major comorbidities:**
    Short-term risk of non-arrhythmic mortality may predominate despite ICD therapy

MADIT-II:
TIME FROM REVASCULARIZATION



Goldenberg et al.
JACC, 2006

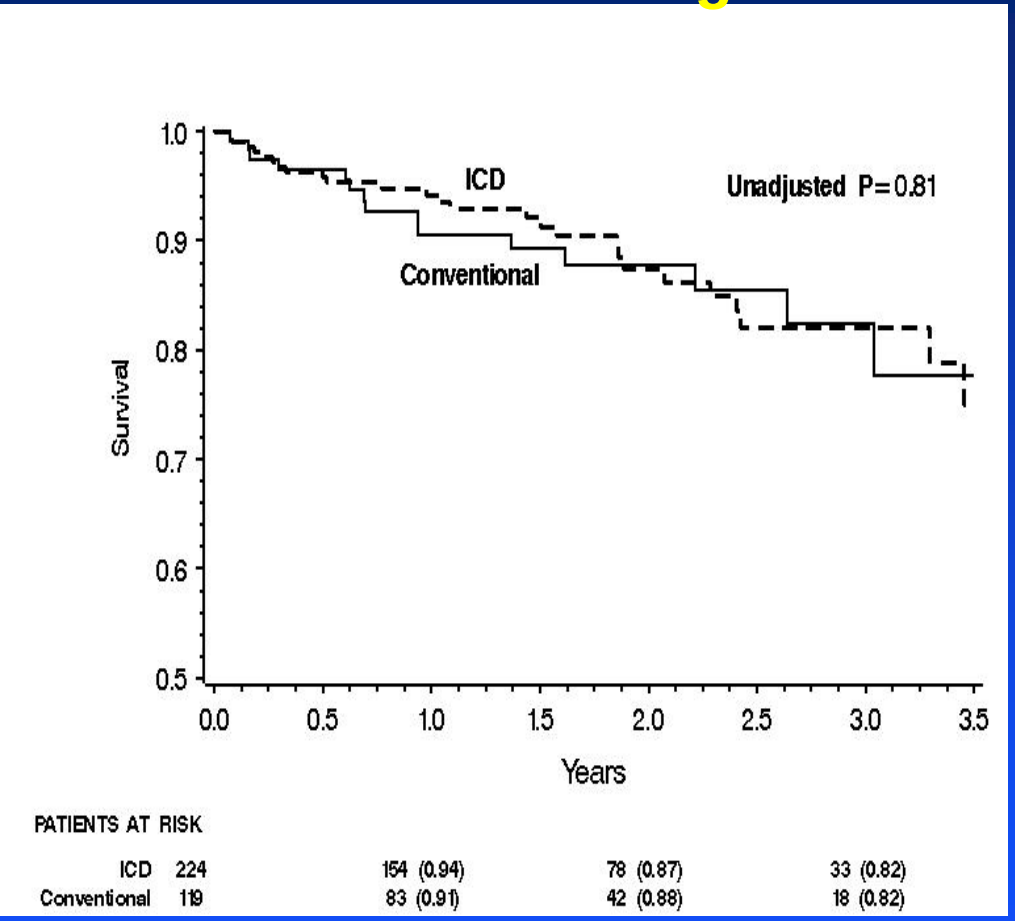
MADIT-II: BLOOD PRESSURE



Goldenberg et al. JACC 2007

MADIT-II: BLOOD PRESSURE

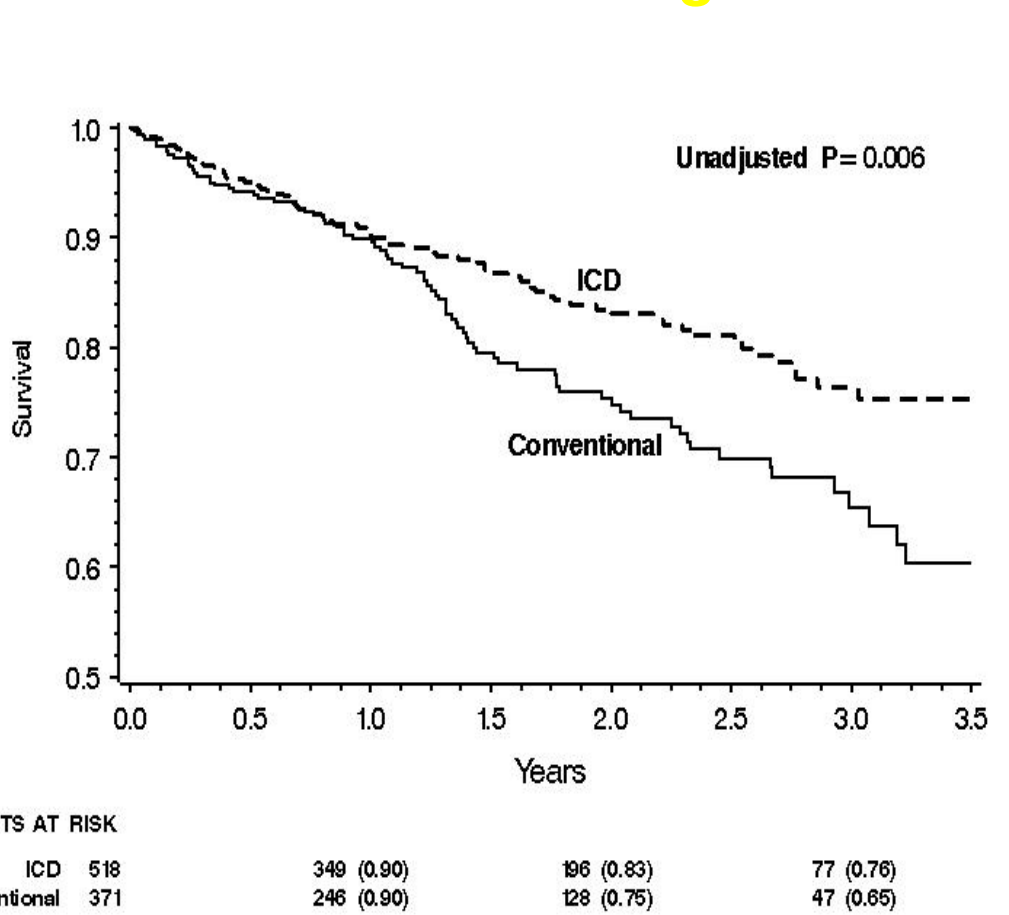
SPB > 130 mm Hg



PATIENTS AT RISK

ICD	224	154 (0.94)	78 (0.87)	33 (0.82)
Conventional	119	83 (0.91)	42 (0.88)	18 (0.82)

SPB ≤ 130 mm Hg

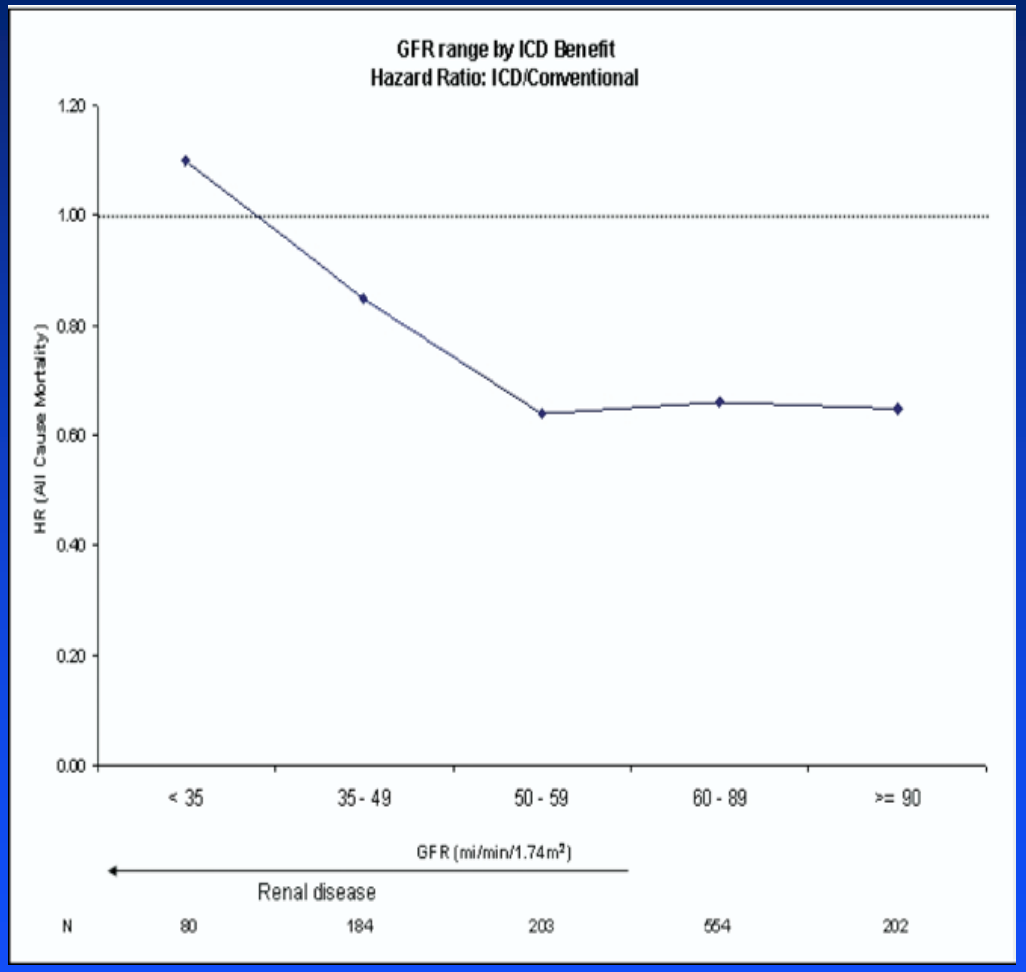


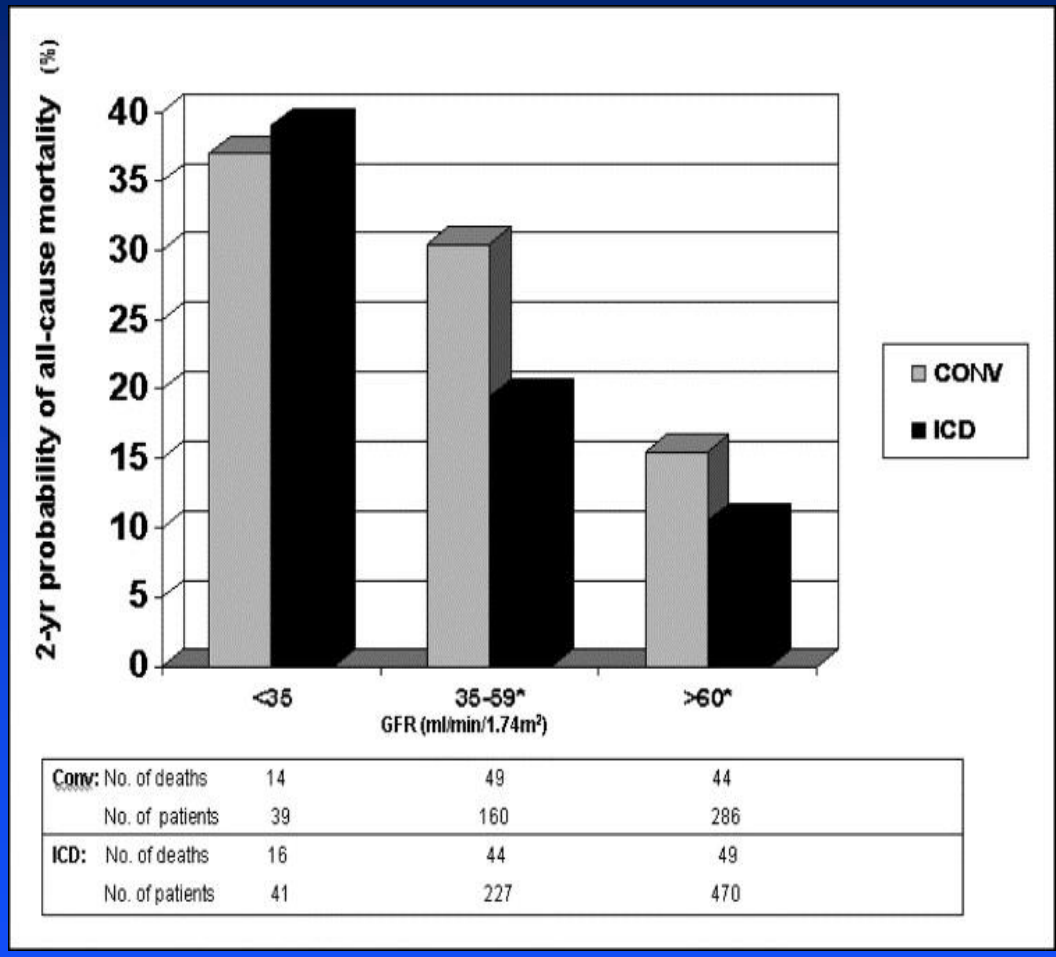
PATIENTS AT RISK

ICD	518	349 (0.90)	196 (0.83)	77 (0.76)
Conventional	371	246 (0.90)	128 (0.75)	47 (0.65)

Goldenberg et al. JACC 2007

MADIT-II: RENAL FUNCTION





Conv:	No. of deaths	14	49	44
	No. of patients	39	160	286
ICD:	No. of deaths	16	44	49
	No. of patients	41	227	470

Goldenberg et al. Am J Cardiol 2006;

CLINICAL RISK STRATIFICATION

- Individual risk markers have limited ability to identify pts who should receive an ICD
- We hypothesized that assessment of multiple risk factors can more clearly delineate risk groups with different ICD efficacy

Goldenberg, Moss, et al. JACC 2008

MADIT-II: CLINICAL RISK STRATIFICATION APPROACH

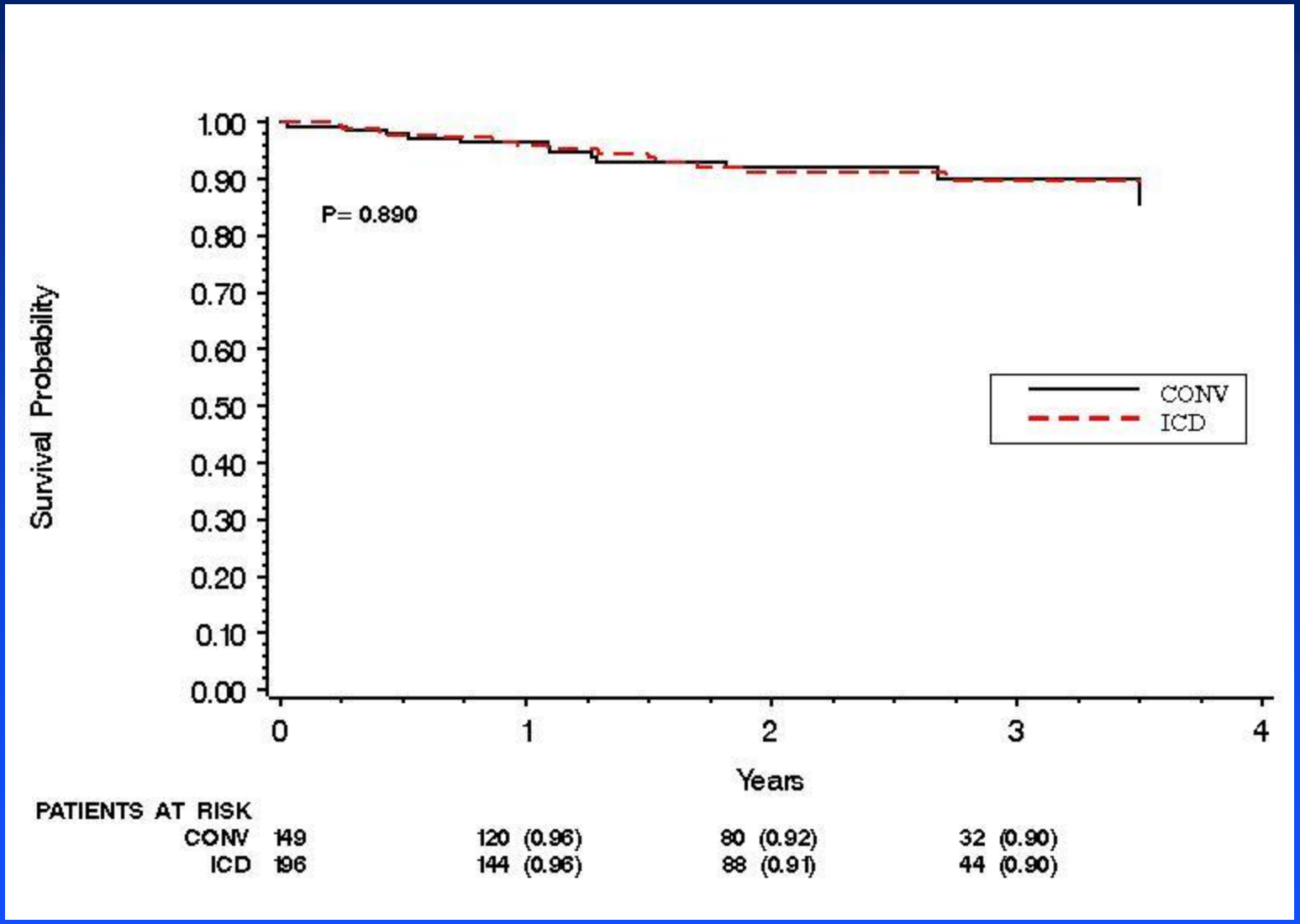
- Risk score developed in the CONV group using simple clinical factors
- ICD vs. CONV benefit assessed in risk score subgroups
- Very high-risk pts (BUN ≥50mg/dL and/or SCr ≥2.5 mg/dL) assessed separately

RISK OF ALL-CAUSE MORTALITY IN THE CONVENTIONAL THERAPY GROUP FOR PRESPECIFIED RISK FACTORS*

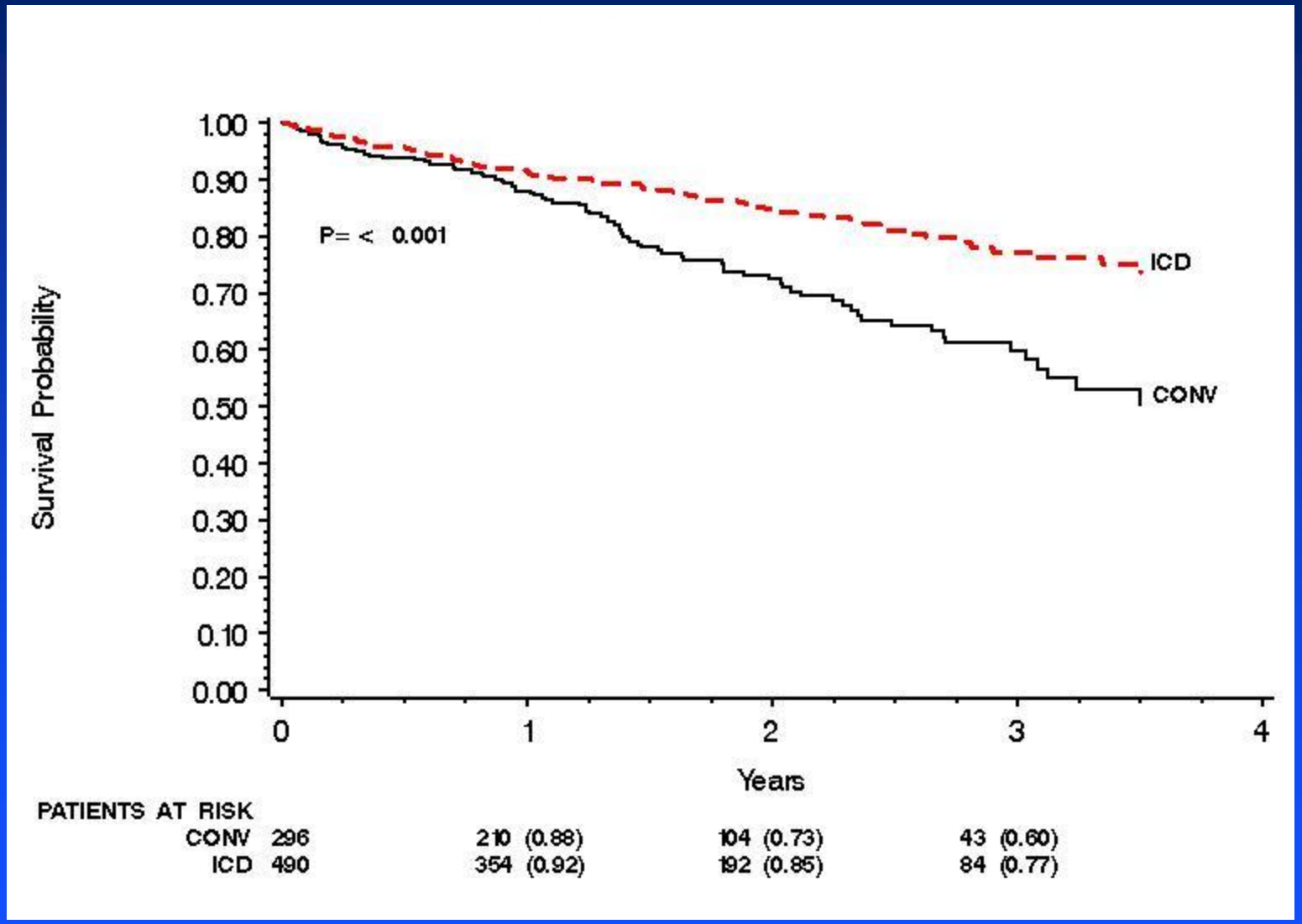
RISK FACTOR	HAZARD RATIO	P-VALUE
NYHA >II	1.87	0.004
ATRIAL FIB	1.87	0.03
QRS >120ms	1.65	0.02
AGE >70yr	1.57	0.04
BUN 27- 49mg/dL	1.56	0.04

*After excluding the VHR group with BUN>50mg/dL

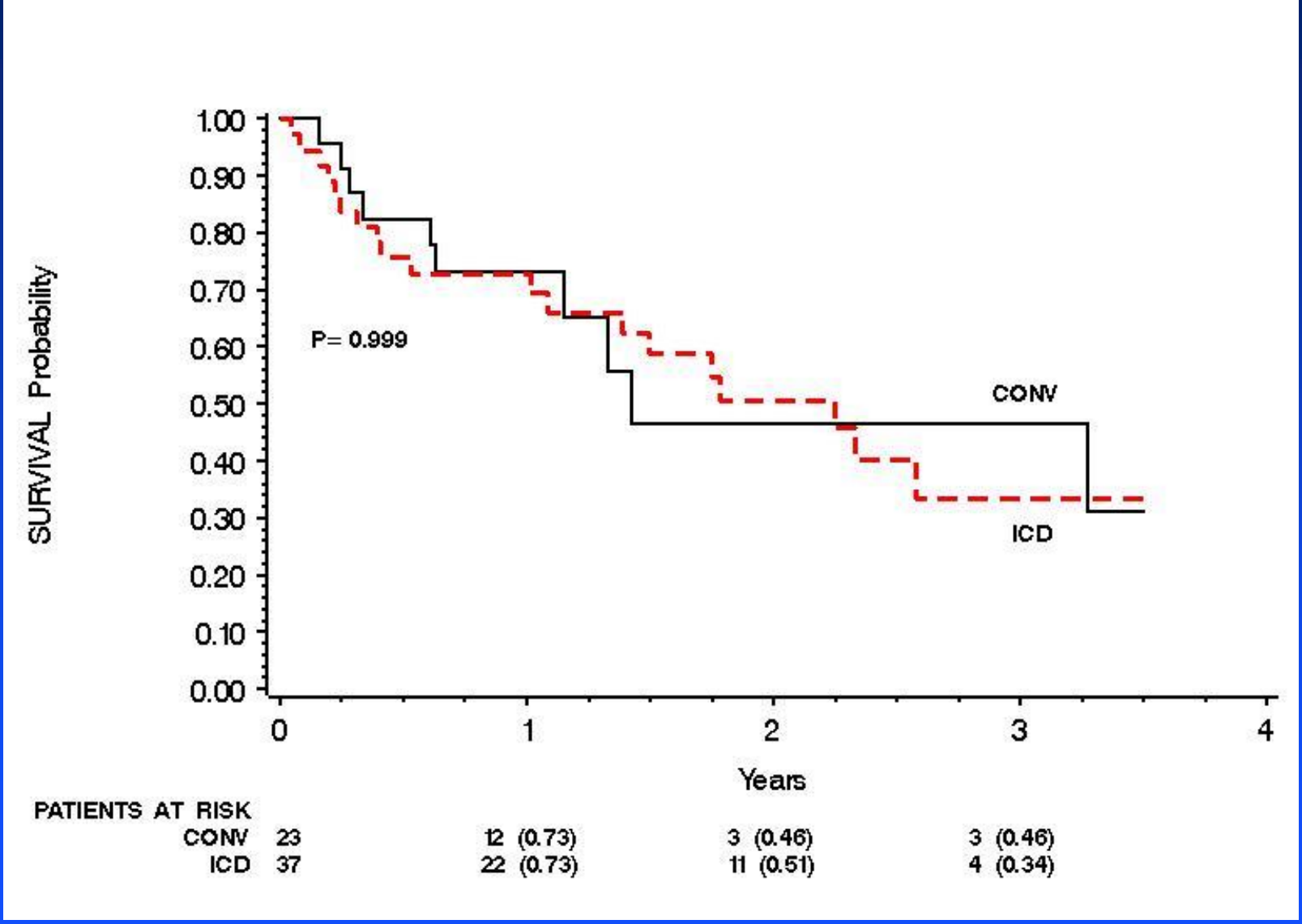
RISK SCORE = 0, CONV. VS. ICD



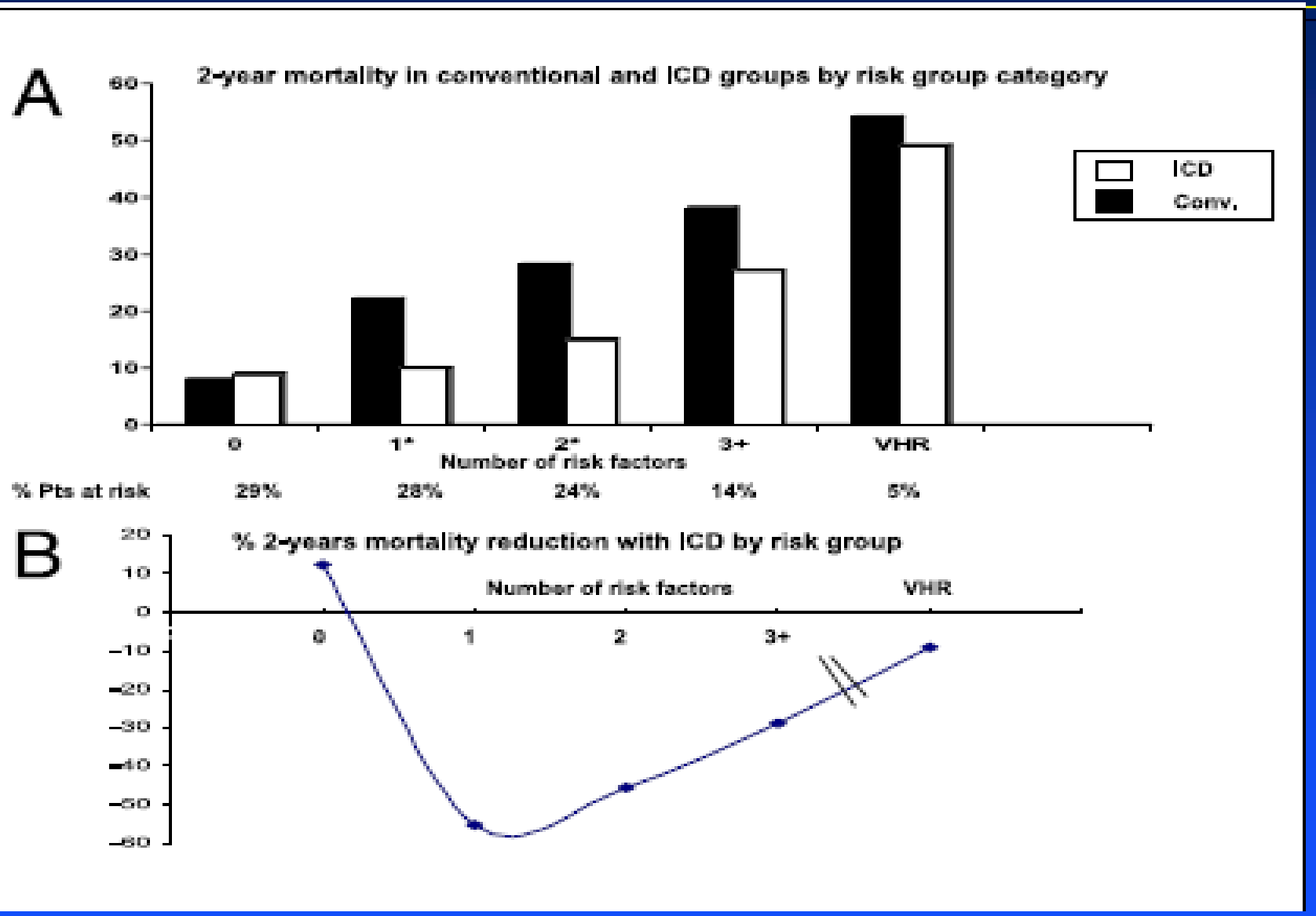
RISK SCORE ≥ 1, CONV. VS. ICD



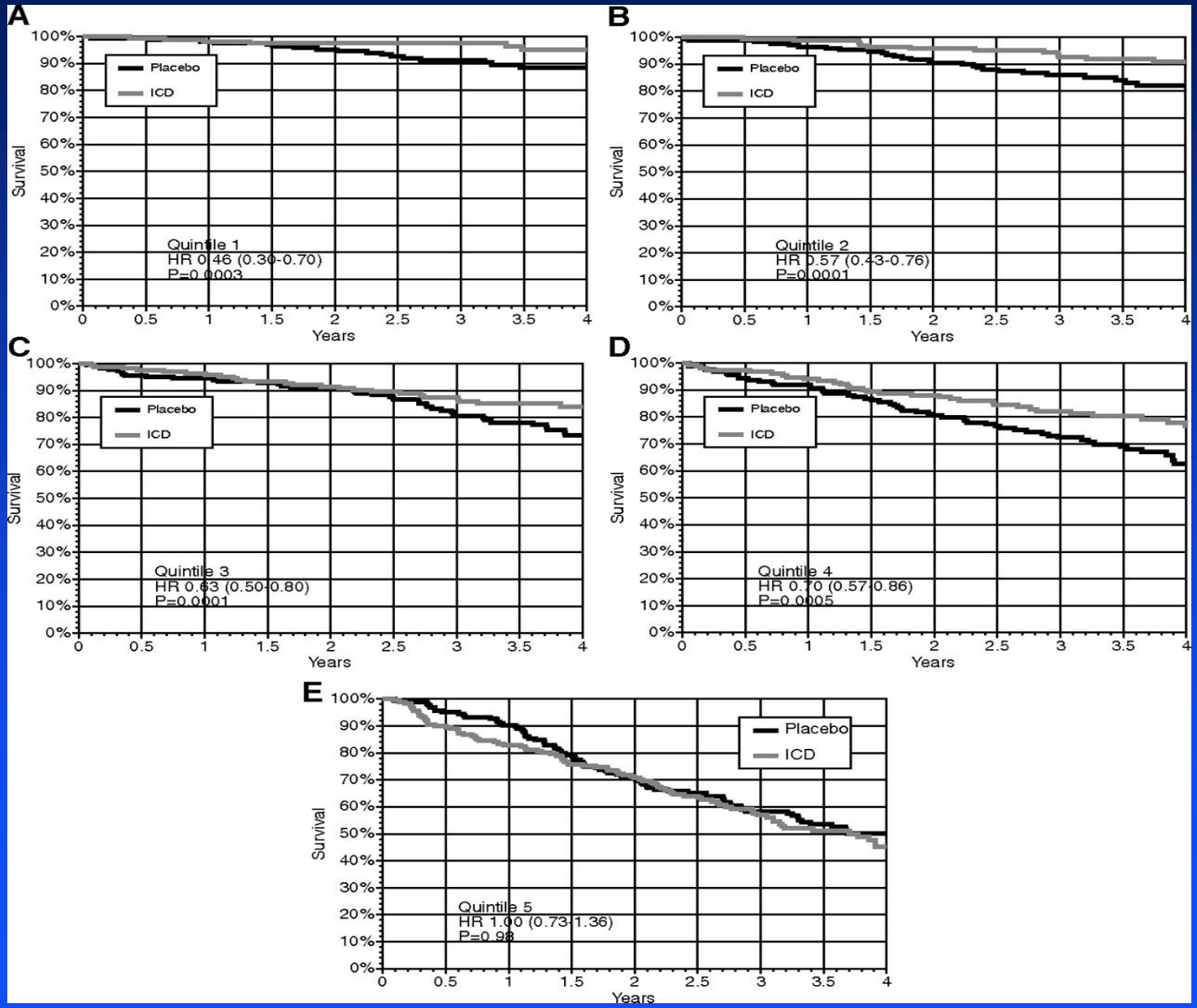
VHR: CONV. VS. ICD



U-SHAPED CURVE FOR ICD BENEFIT



RISK STRATIFICATION IN SCD-HeFT



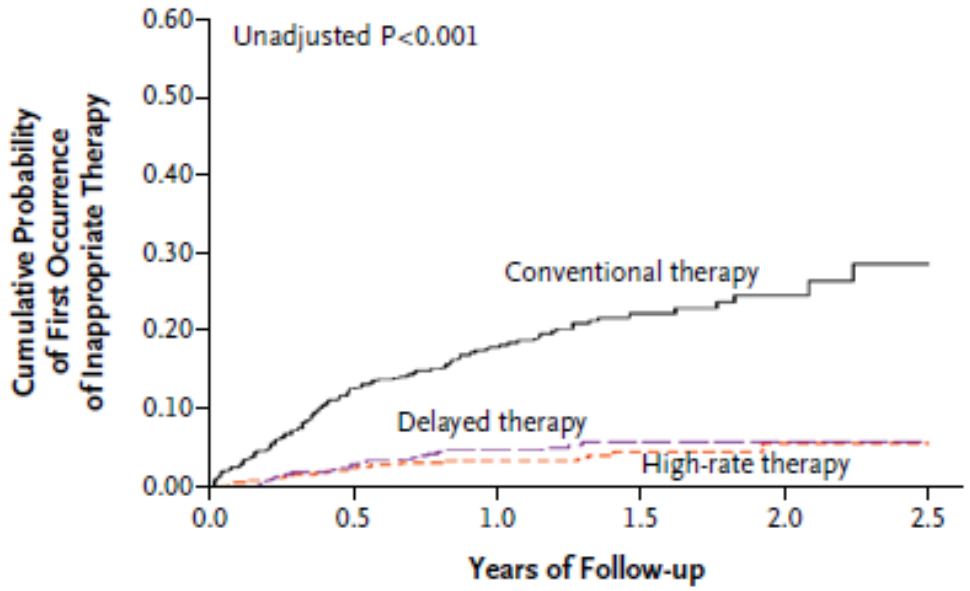
Levy, W. C. et al.
Circulation, 2009

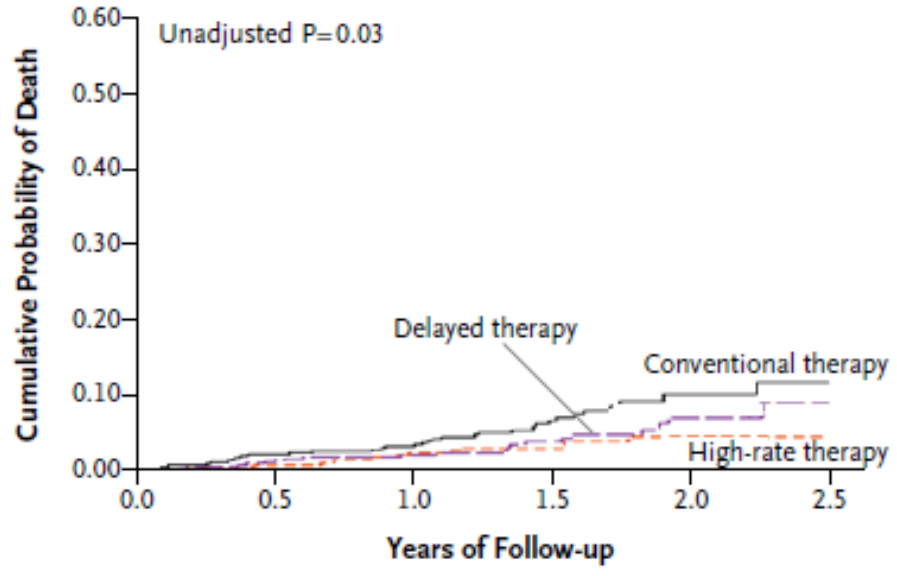
CONTEMPORARY CHARACTERISTICS OF PRIMARY ICD PATIENTS

CONTEMPORARY CHARACTERSITICS: MADIT-RIT

Variable	Conventional Therapy (N = 514)	High-Rate Therapy (N = 500)	Delayed Therapy (N = 486)
Age — yr	63±11	63±12	62±12
Male sex — no. (%)	357 (69.5)	354 (70.8)	353 (72.6)
Race — no./total no. (%)†			
White	393/509 (77.2)	371/493 (75.3)	355/483 (73.5)
Black	84/509 (16.5)	91/493 (18.5)	97/483 (20.1)
Asian	23/509 (4.5)	27/493 (5.5)	26/483 (5.4)
Other	9/509 (1.8)	4/493 (0.8)	5/483 (1.0)
Cardiac history — no./total no. (%)			
Ischemic heart disease	271/514 (52.7)	268/499 (53.7)	252/485 (52.0)
Nonischemic heart disease	243/514 (47.3)	231/499 (46.3)	233/485 (48.0)
Cardiac risk factors — no./total no. (%)			
Hypertension	346/513 (67.4)	359/497 (72.2)	324/485 (66.8)
Diabetes mellitus	166/510 (32.5)	159/491 (32.4)	160/482 (33.2)
Current cigarette smoking	86/483 (17.8)	83/472 (17.6)	78/463 (16.8)
Atrial fibrillation	47/508 (9.3)	57/495 (11.5)	49/483 (10.1)
NYHA class II or III — no./total no. (%)	495/507 (97.6)	482/495 (97.4)	474/484 (97.9)
Body-mass index‡	29.4±7.1	28.9±6.5	29.5±6.9
Cardiac findings at enrollment			
Blood pressure — mm Hg			
Systolic	124±20	123±19	124±19
Diastolic	73±11	73±12	73±12
Resting heart rate — beats/min	72±12	72±12	73±13
Ejection fraction — %	26±6	26±7	26±7
Defibrillator type — no./total no. (%)			
ICD	258/514 (50.2)	248/499 (49.7)	236/486 (48.6)
CRT-D	256/514 (49.8)	251/499 (50.3)	250/486 (51.4)

MADIT-RIT: OUTCOMES





Variable	Conventional Therapy (N=514)	High-Rate Therapy (N=500)	Delayed Therapy (N=486)
First occurrence of therapy — no. of patients (%)			
Appropriate therapy	114 (22)	45 (9)	27 (6)
Shock	20 (4)	22 (4)	17 (3)
Antitachycardia pacing	94 (18)	23 (5)	10 (2)

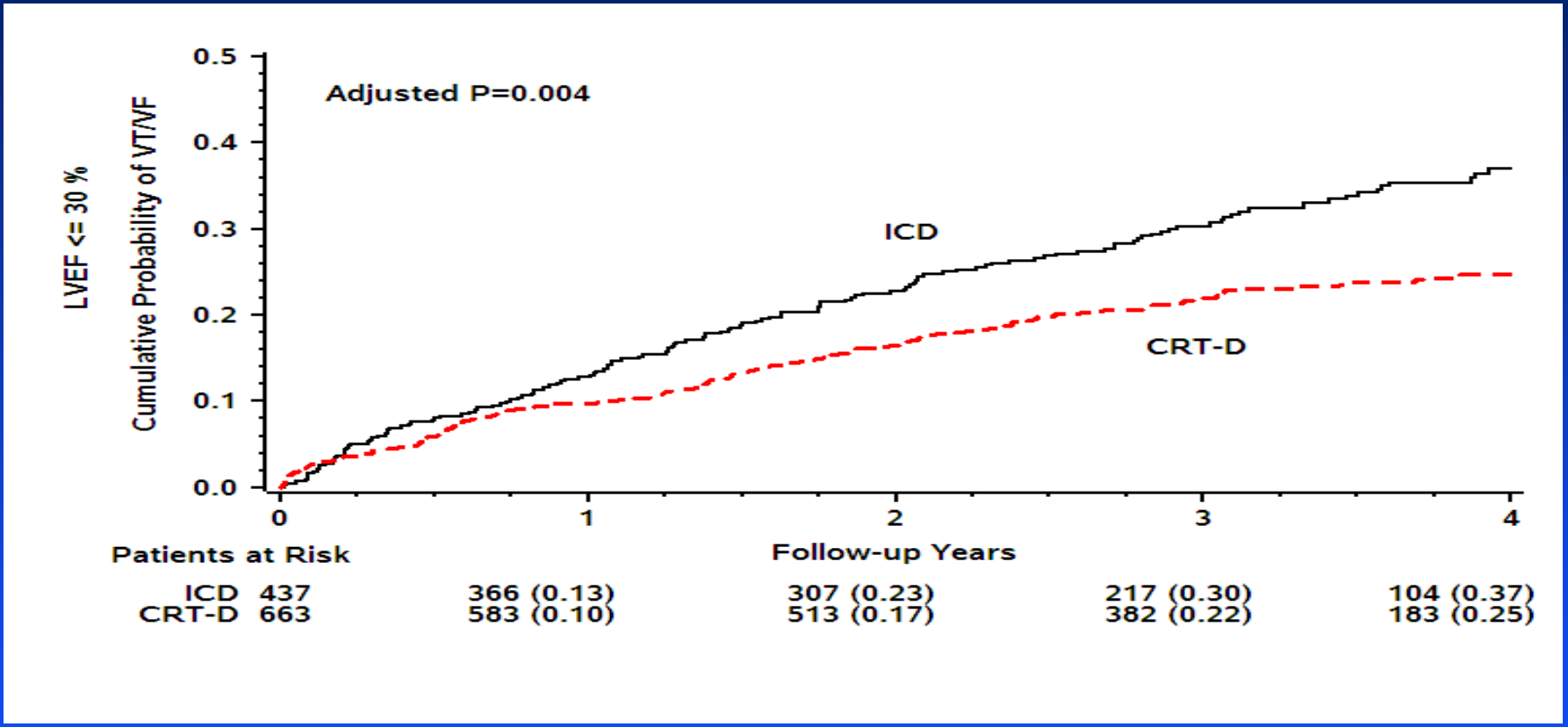
Characteristics of Trial vs. Registry Data

Characteristic	MADIT-II	Israeli ICD Registry: Primary Prevention
	N=1232	N = 1550
Age, yrs	64 ± 10	63 ± 15
Female	20%	16%
NYHA > 2	53%	30%
Diabetes	42%	33%
BUN > 25 mg/dl	30%	29%
LVEF	26%	25%
Nonischemic CMP	0%	21%
QRS > 120 msec	51%	50%
CRT-D	0%	51%

Israeli ICD Registry Primary: Prevention Cohort

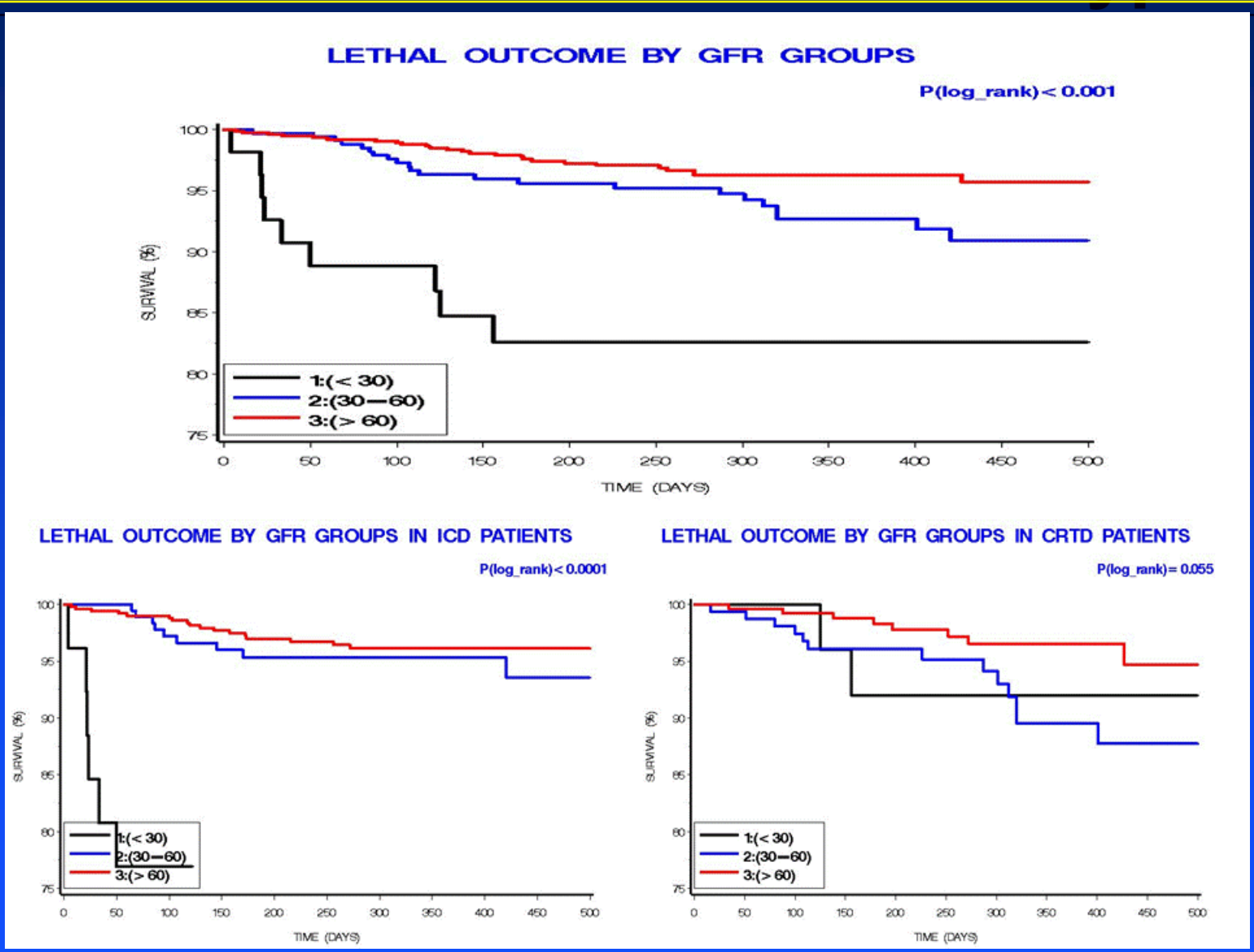
Endpoint	Primary prevention (n=1131)	Secondary Prevention (n=405)	P-value
Any appropriate therapy for VT/VF	6%	19%	<0.001
Appropriate shocks	1%	3%	<0.001
Appropriate ATPs	5%	16%	<0.001
Any inappropriate therapy	4%	4%	0.91
Inappropriate shocks	2%	1%	0.85
Inappropriate ATPs	2%	3%	0.99
Death	5%	14%	0.001

MADIT-CRT: effect of CRT-D on the risk of VT or VF in pts with EF ≤ 30%

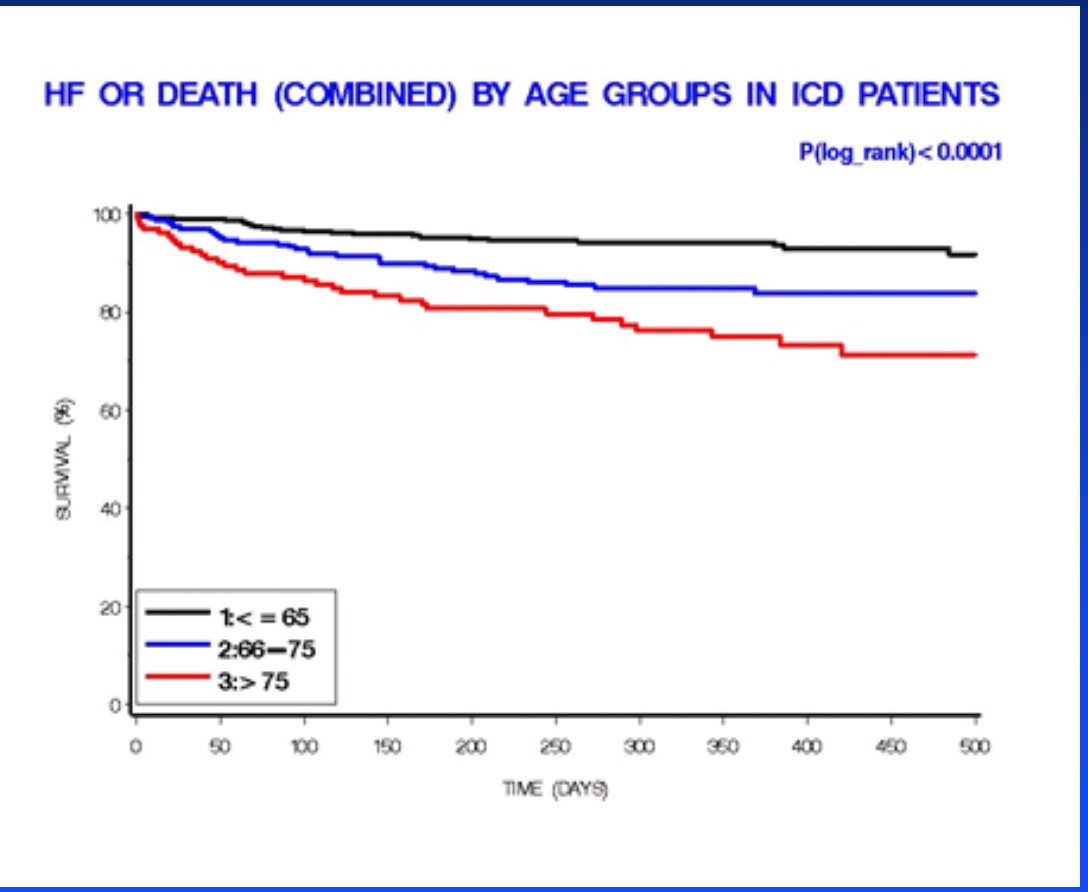


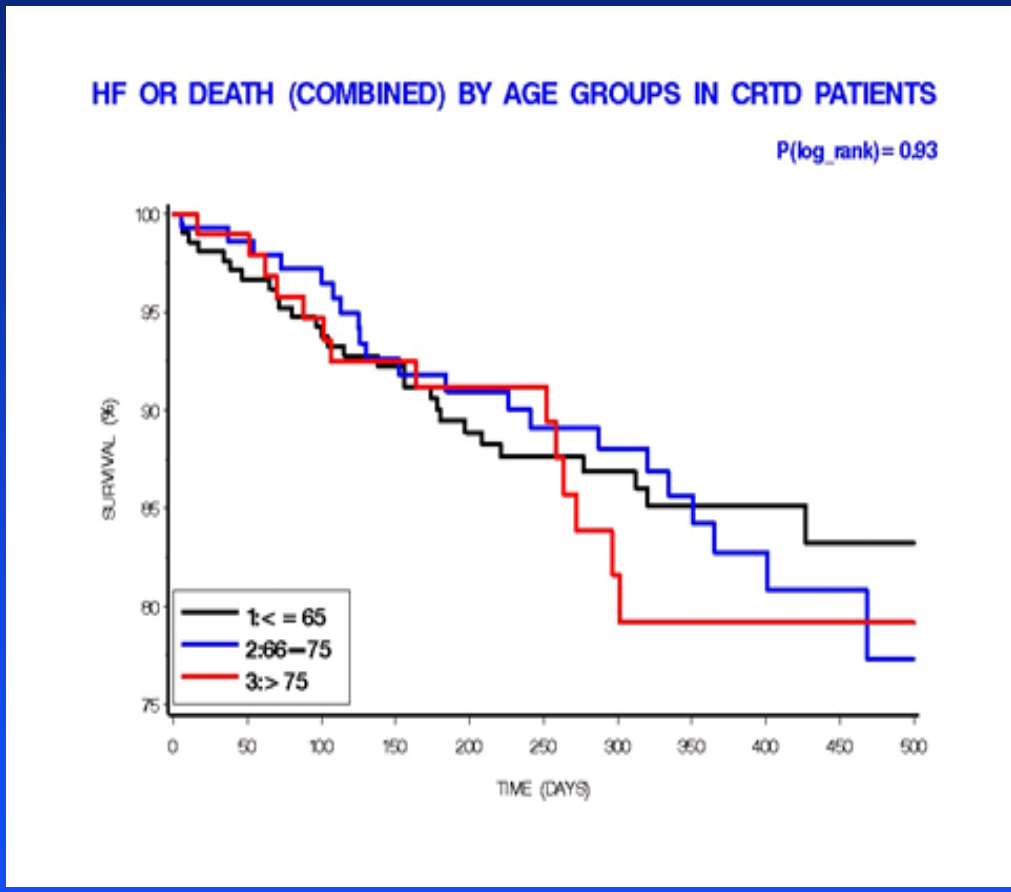
Adjusted HR= 0.70, 95% CI: 0.55-0.88, =0.002

Israeli ICD Registry: Effect of Renal Function on Outcomes BY Device Type

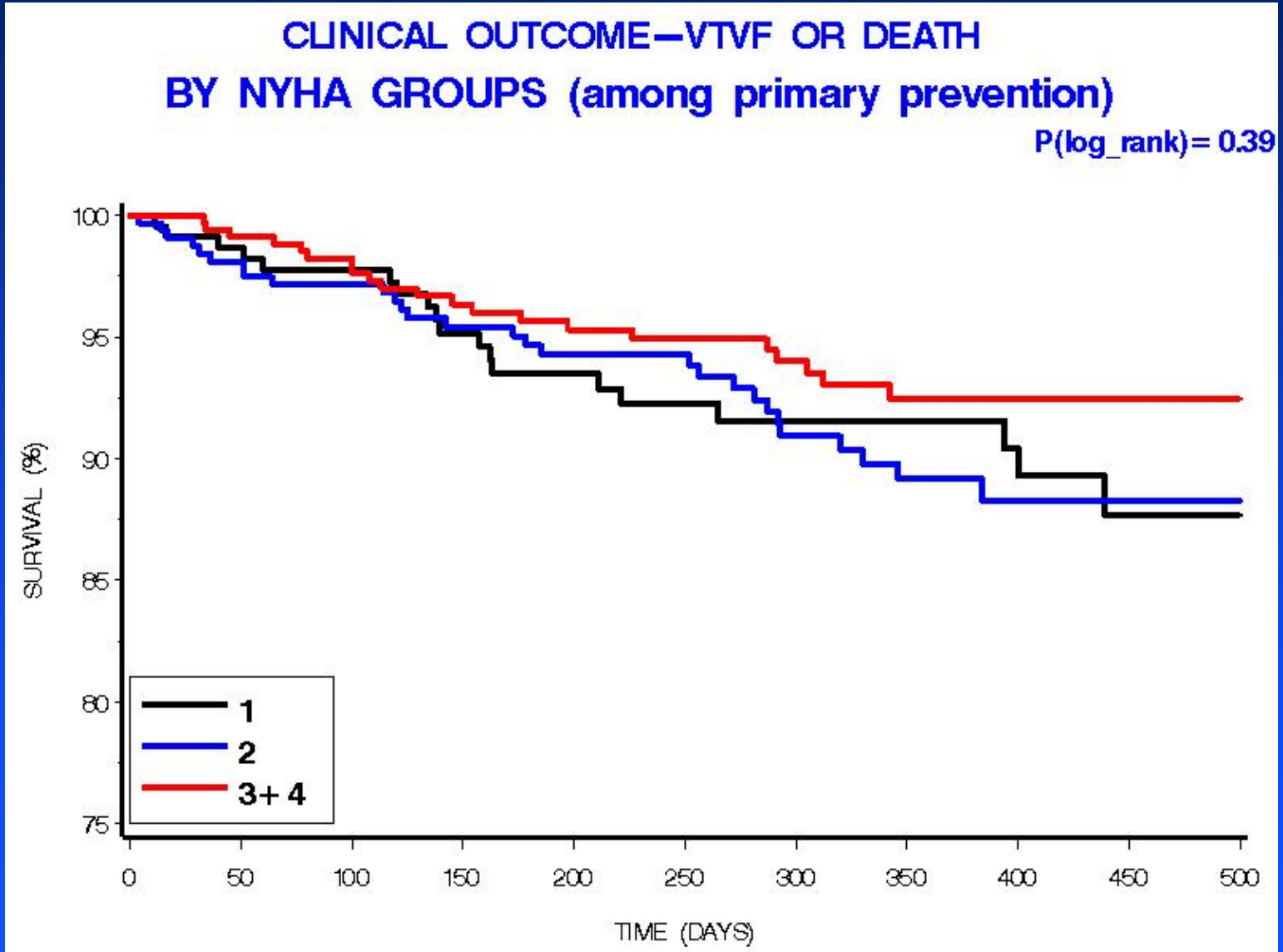


Israeli ICD Registry: Effect of Age on Outcomes BY Device Type





Israeli ICD Registry: Effect of NYHA on Arrhythmias in CRT-D Patients



CONCLUSIONS

- Effective risk stratification for ICD therapy can be achieved using combined assessment of simple, readily available, parameters

- Risk stratification approaches need to be updated and validated in contemporary studies with long-term follow-up:
  - Due to ongoing changes in target populations, ICD programming, device-types, and medical therapies

Thank You