

Venerdì 17 febbraio 2012

**Gestione appropriata dei pazienti con ICD/CRT**

**Terapia di resincronizzazione cardiaca nello  
scompenso cardiaco dell'anziano**

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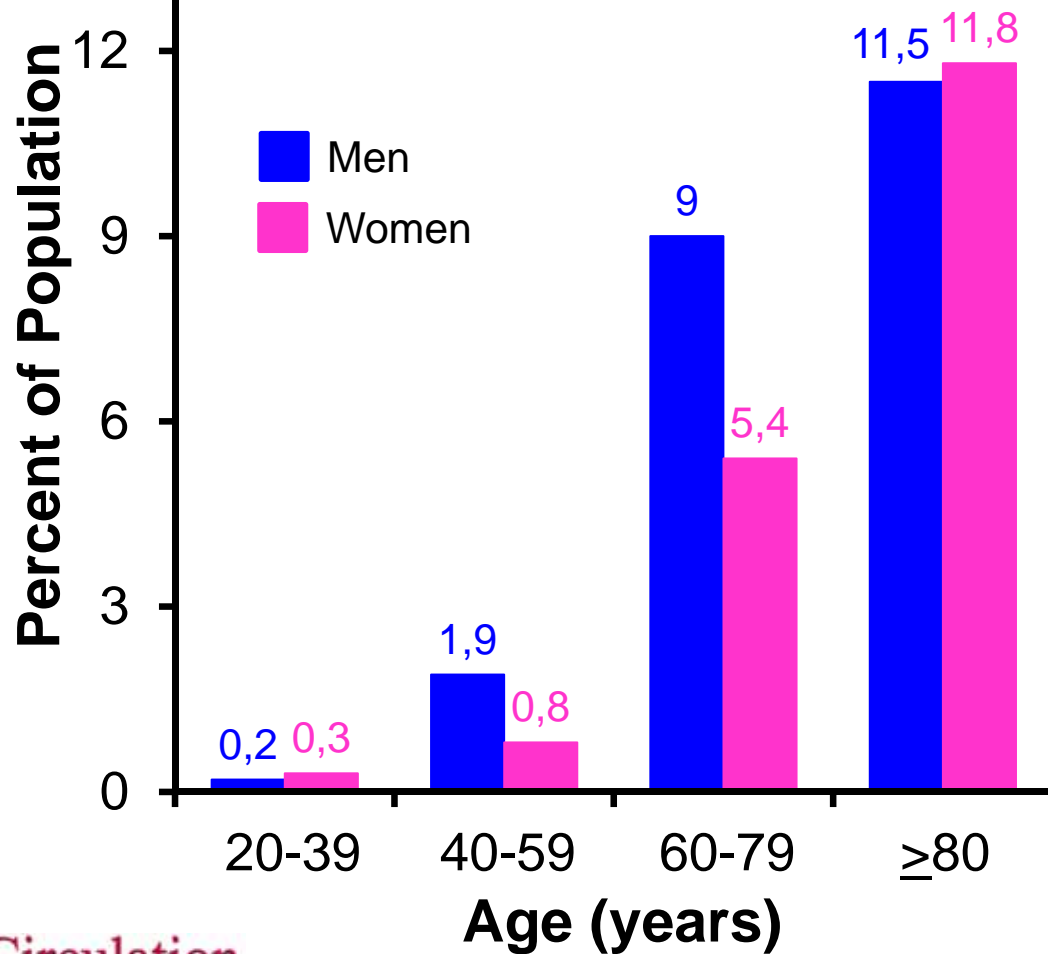


# Heart Disease and Stroke Statistics—2012 Update

## A Report From the American Heart Association

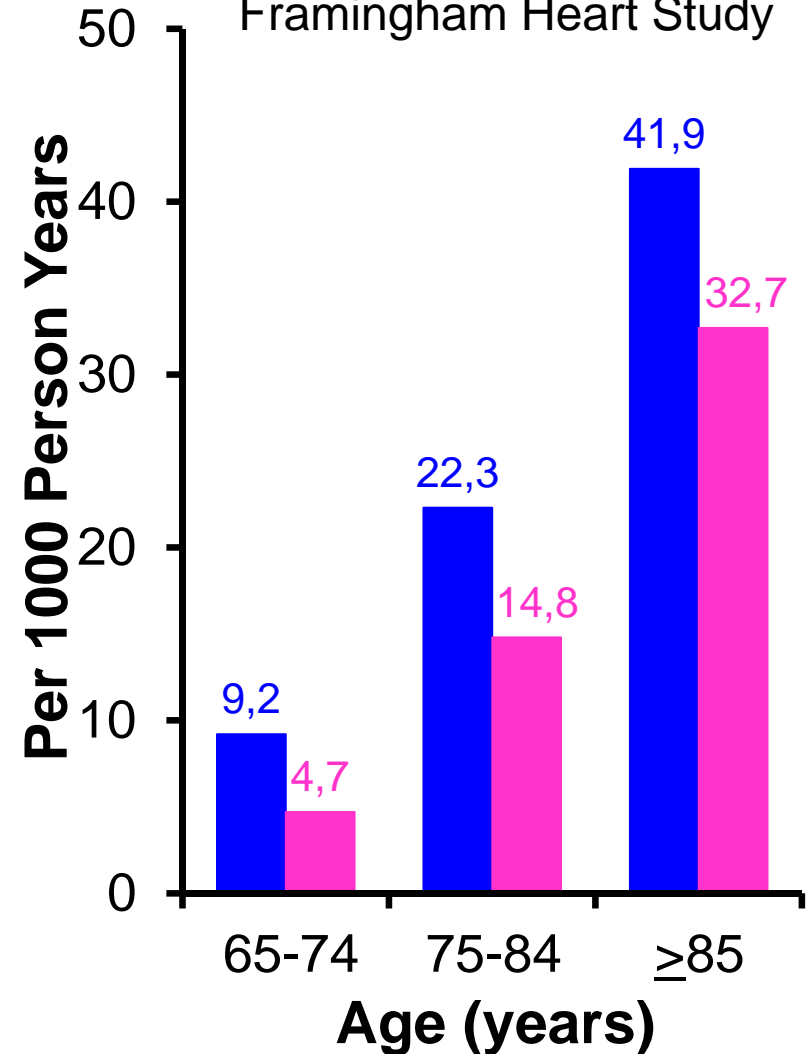
### Prevalence of HF

National Health and Nutrition Examination Survey



### Incidence of HF

Framingham Heart Study



## STATE-OF-THE-ART PAPER

# Integrating Quality Into the Cycle of Therapeutic Development

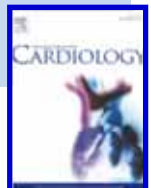
**The Great Circle** - a model to integrate quality measures into the development cycle for therapeutics



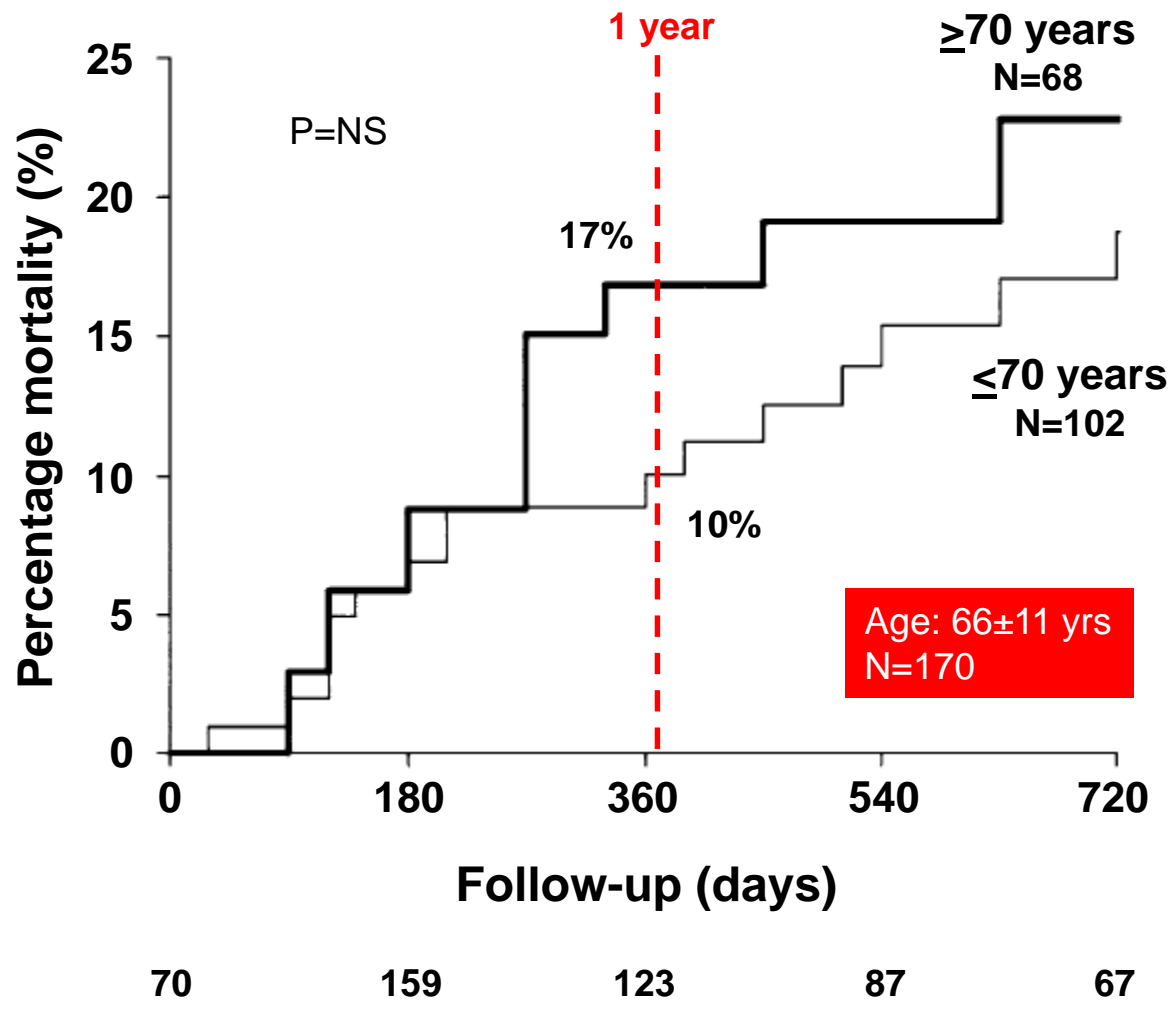
## Device therapy in patients with heart failure and advanced age: Too much too late?

Raymond Cutro<sup>a</sup>, Michael W. Rich<sup>b</sup>, Paul J. Hauptman<sup>c,\*</sup>

- Despite the compelling findings from several CRT trials, it must be recognized that patients enrolled in these studies were **highly selected**
- Specifically, **few patients >75** were enrolled ...
- Thus, **RCT evidence** for efficacy of CRT in patients >75 years **is lacking** and, as previously noted, **extrapolation** of data from trials in much younger patients to the very elderly may not be justified due to age-related alterations in both **the risks (higher)** and **benefits (potentially lower)** in older patients



# Comparison of Effectiveness of Cardiac Resynchronization Therapy in Patients <70 Versus ≥70 Years of Age





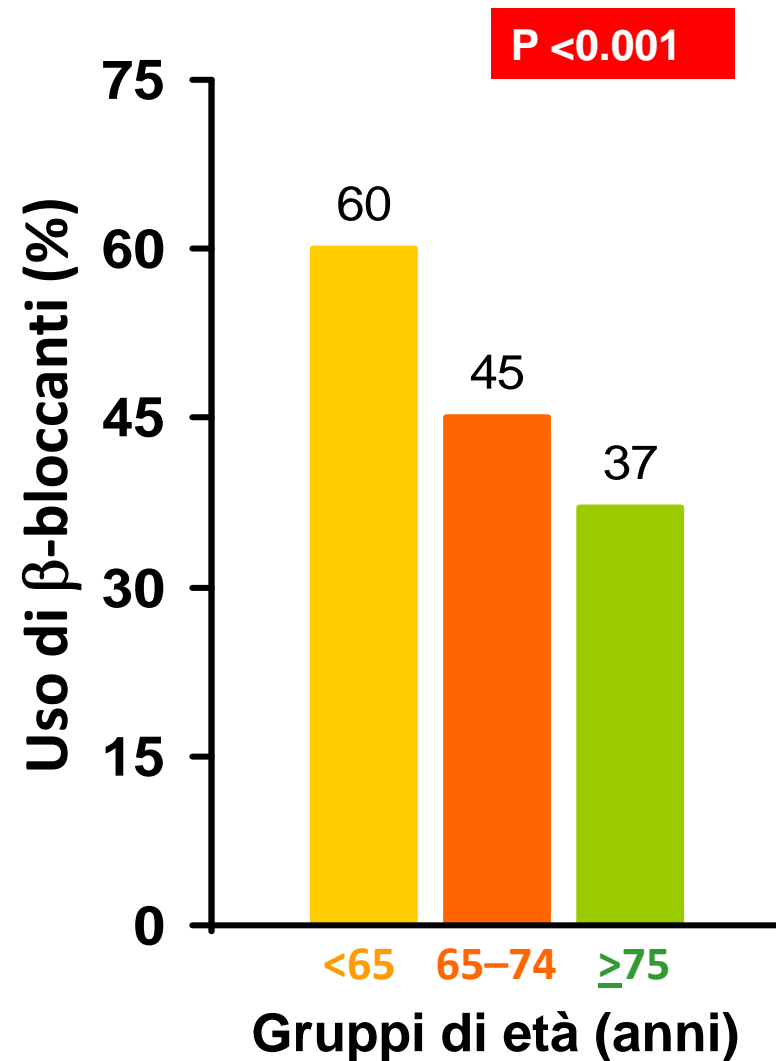
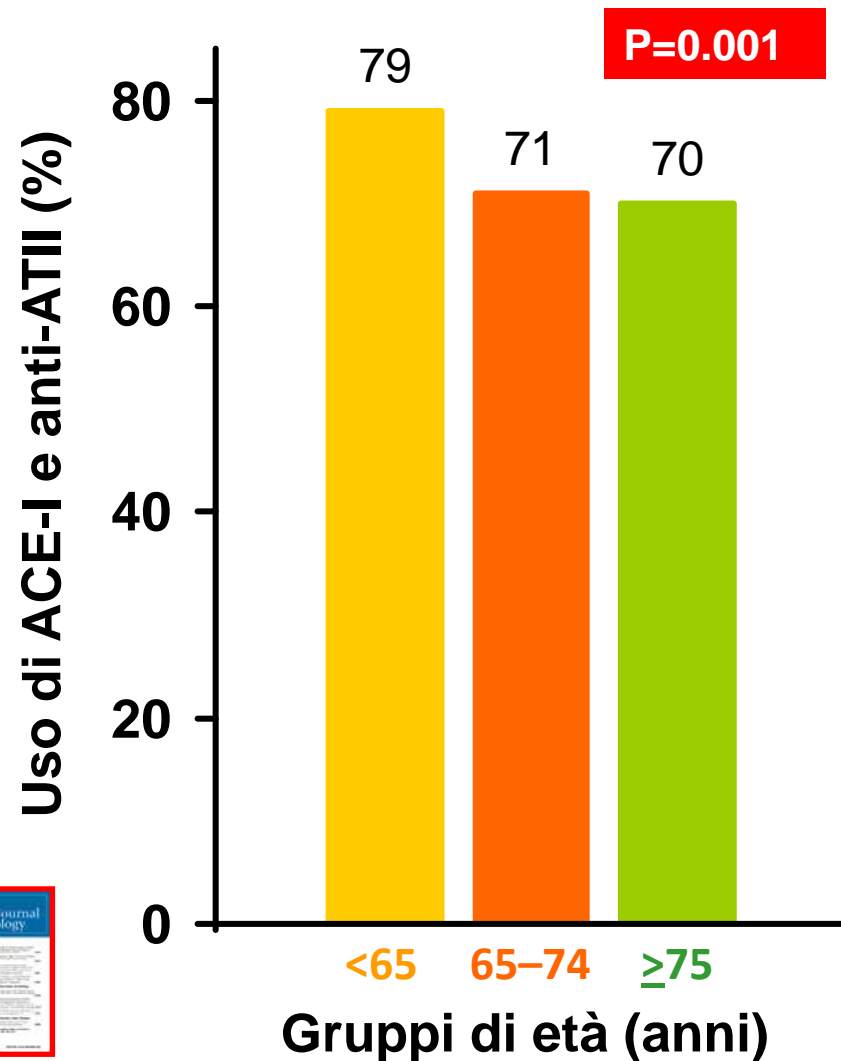
# Caratteristiche cliniche della popolazione del Registro Italiano InSync / InSync ICD, per gruppi di età

N=1787	Gruppi di età (anni)			P
	<65 (N=571)	65-74 (N=740)	≥75 (N=476)	
Età (anni)	57 ± 7	70 ± 3	78 ± 3	/
Uomini (%)	84	81	76	0.003
BPCO (%)	5	7	6	0.088
Diabete (%)	8	9	6	0.312
IRC (%)	3	8	4	0.001
≥2 patologie (%)	2	4	3	0.099
CAD (%)	39	50	50	<0.001
LVEDD (mm)	70 ± 10	69 ± 9	68 ± 9	0.015
LVESD (mm)	60 ± 12	58 ± 10	57 ± 11	0.016
FE (%)	26 ± 8	26 ± 7	27 ± 8	0.123
Durata QRS (ms)	167 ± 33	165 ± 31	162 ± 32	0.136
Ricoveri (n)	1.6 ± 1.4	1.6 ± 1.5	1.7 ± 1.4	0.256
FA permanente (%)	11	18	21	<0.001
Diuretici (%)	87	89	88	0.415
Nitrati (%)	17	23	46	0.001
AA Classe III (%)	34	38	34	0.312

**IRC:** insufficienza renale cronica; **CAD:** cardiopatia ischemica;  
**Ricoveri:** ricoveri per CHF nei 12 mesi precedenti; **AA:** antiaritmici



# Terapia con $\beta$ -bloccanti e ACE-inibitori o sartani, per gruppo di età. I risultati del Registro Italiano InSync / InSync ICD

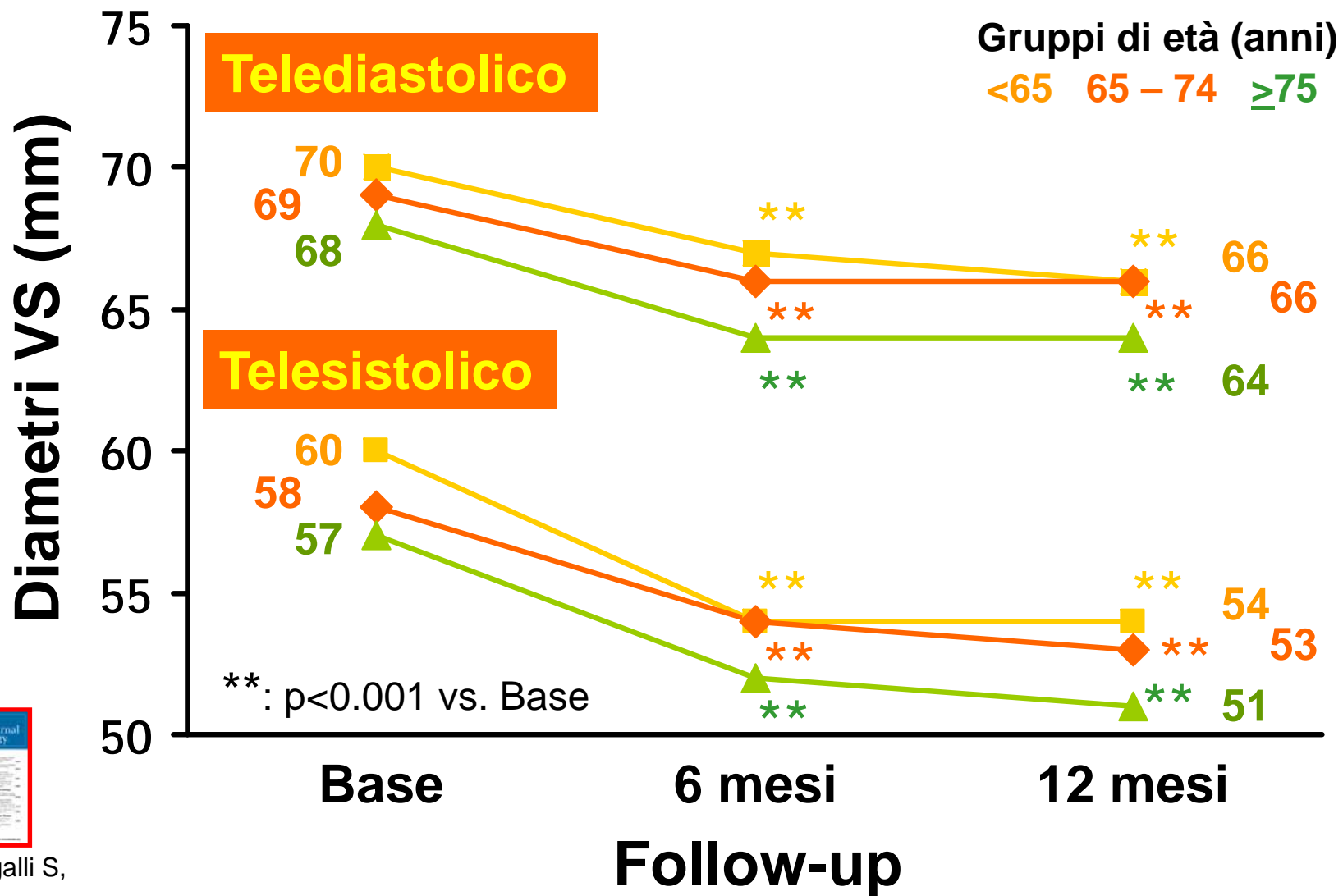


Fumagalli S,  
2011



# Variazioni dei diametri del ventricolo sinistro (VS) con CRT durante il follow-up, per gruppo di età

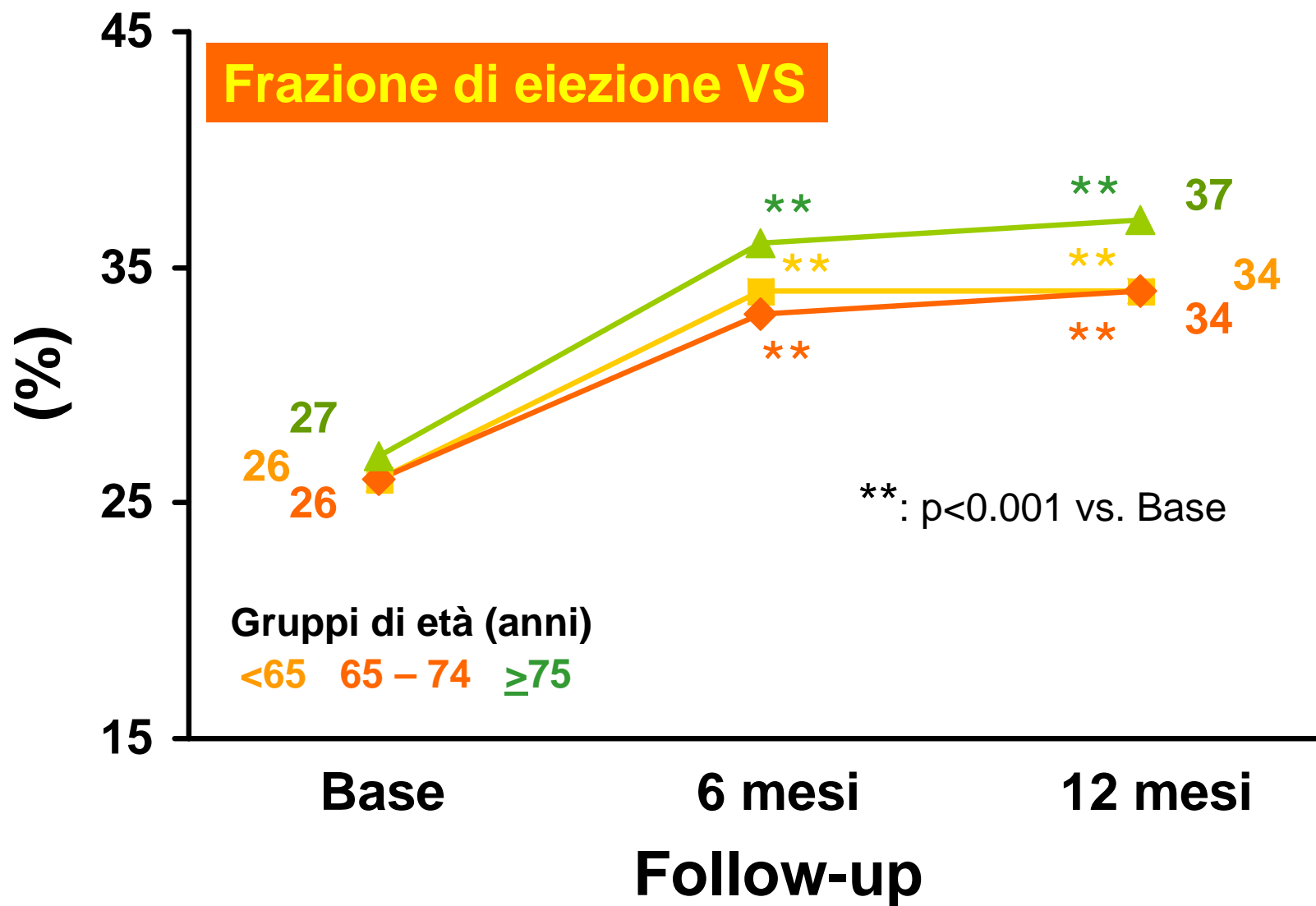
*I risultati del Registro Italiano InSync / InSync ICD*



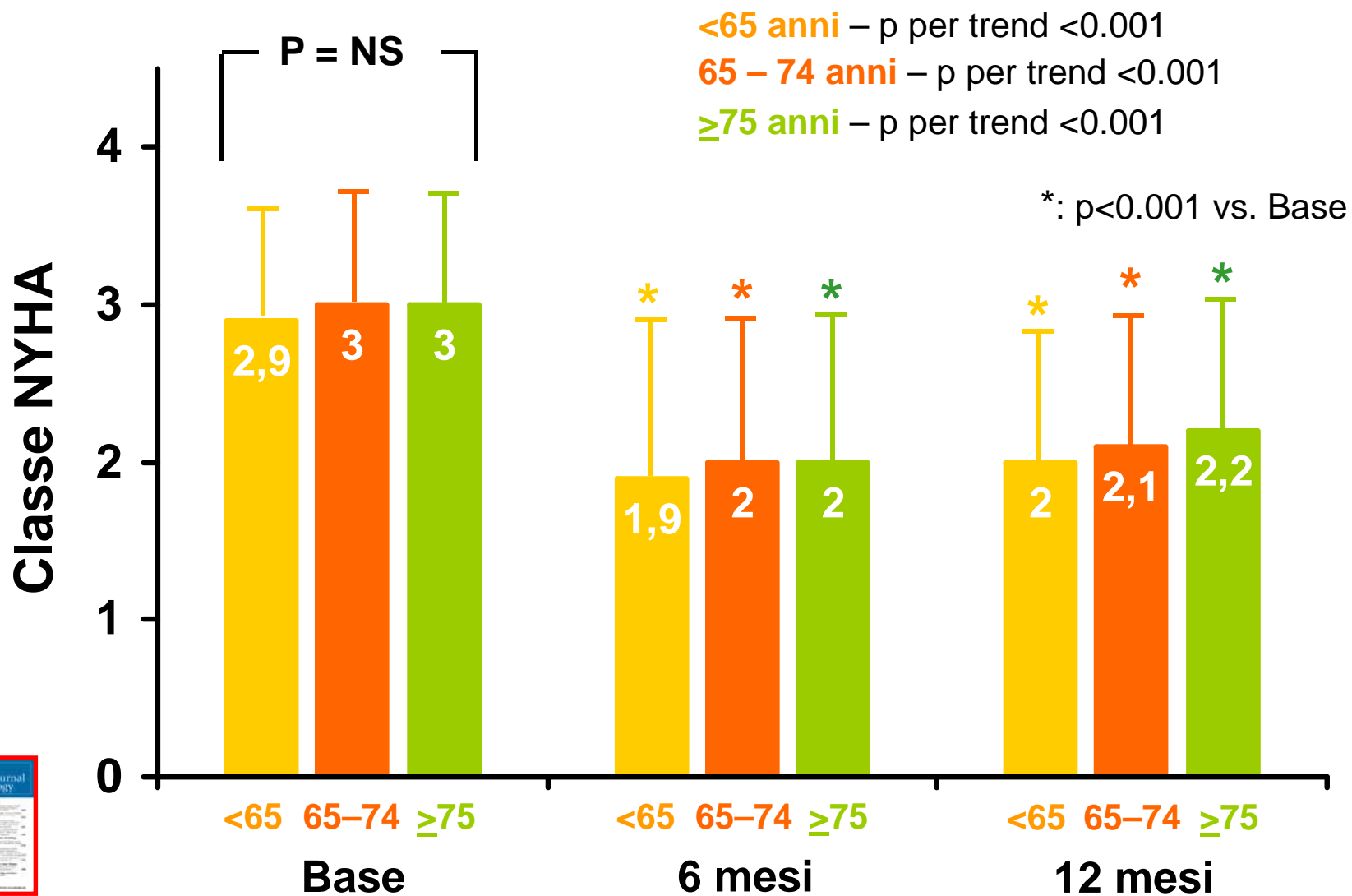


# Variazioni della frazione di eiezione del VS con CRT durante il follow-up, per gruppo di età

*I risultati del Registro Italiano InSync / InSync ICD*



# Classe NYHA in condizioni di base e durante il follow-up, per gruppo di età. I risultati del Registro Italiano InSync / InSync ICD

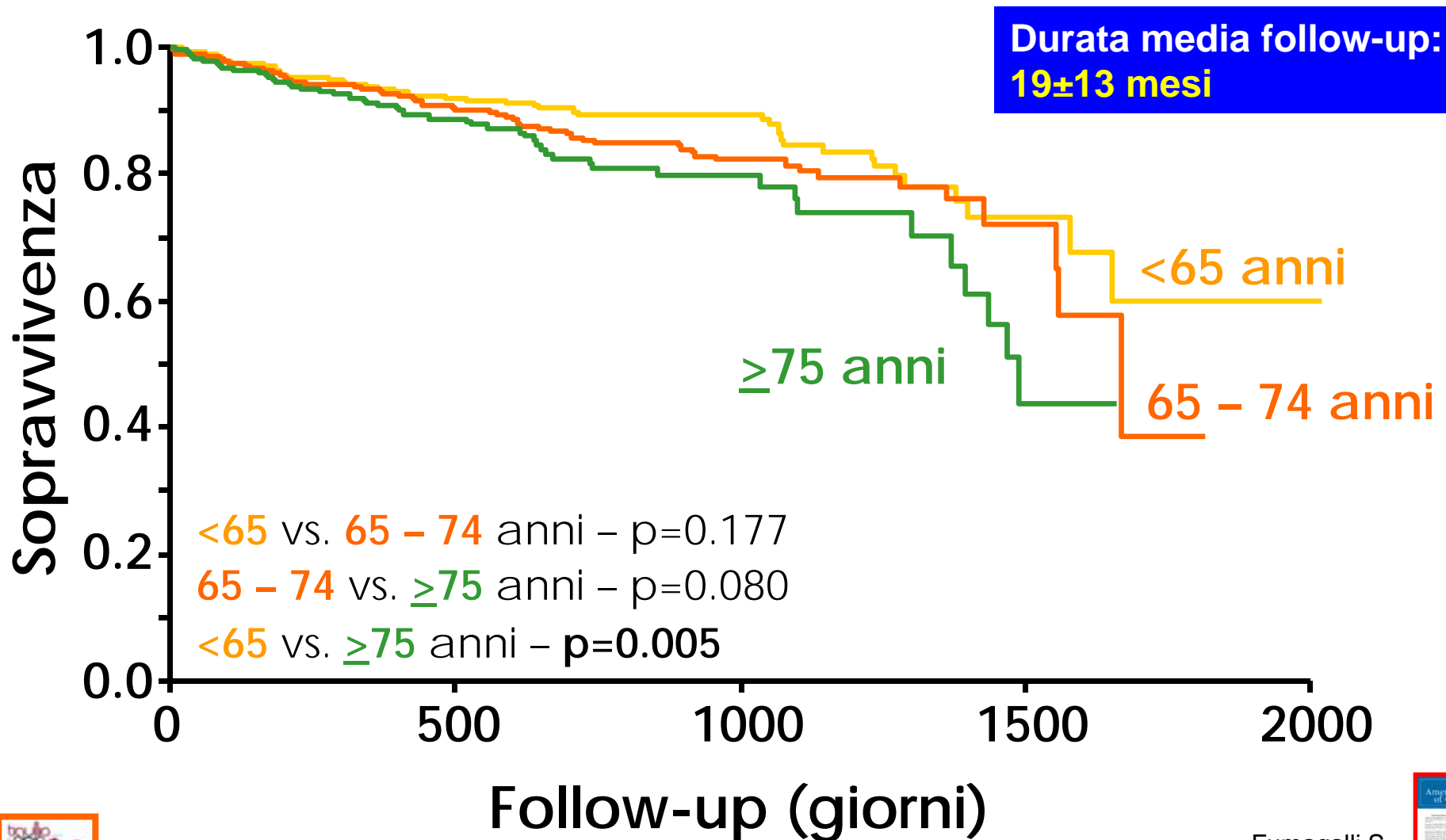


Fumagalli S,  
2011

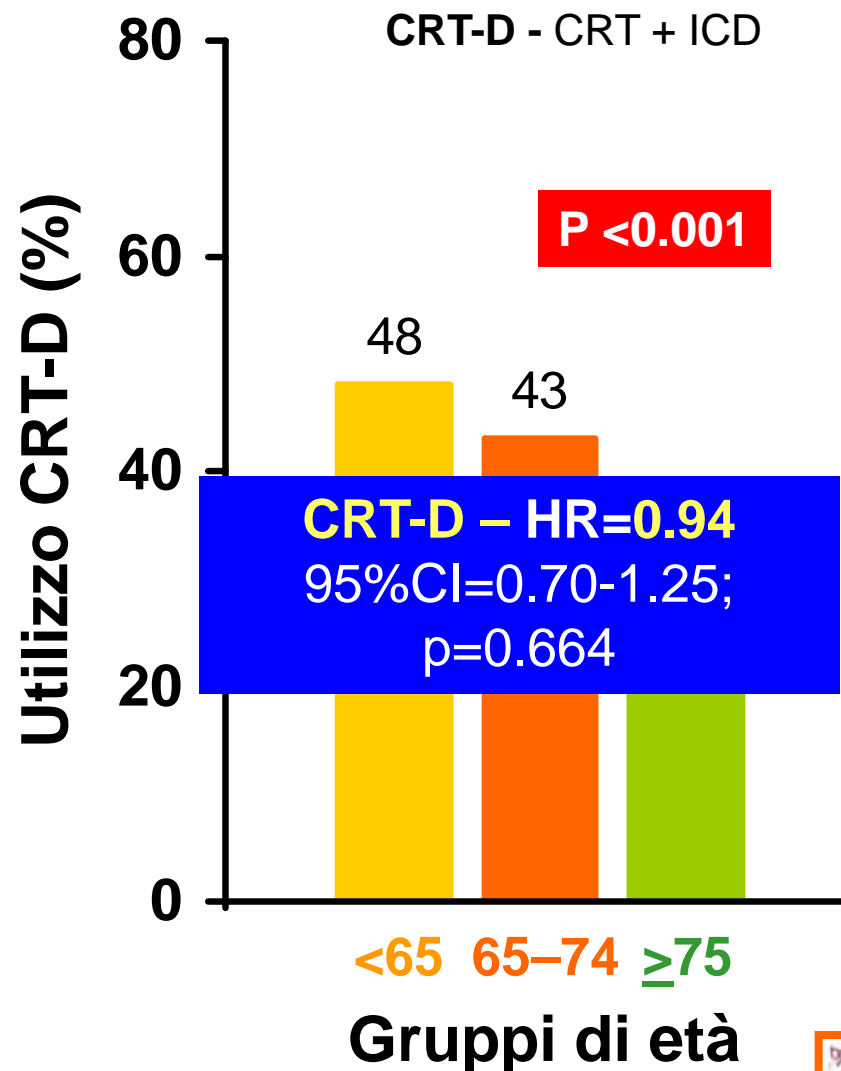
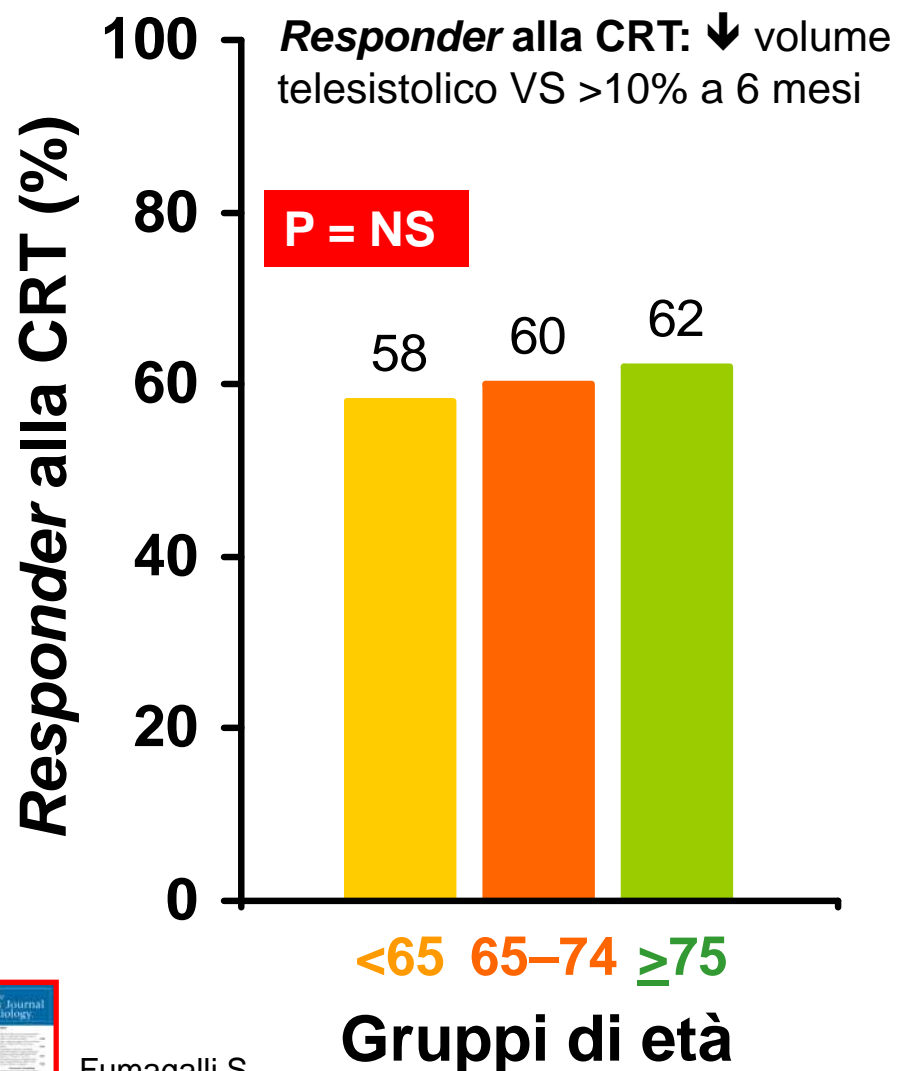


# Sopravvivenza nel registro InSync per gruppo di età

## Risultati dell'analisi di Kaplan-Meier



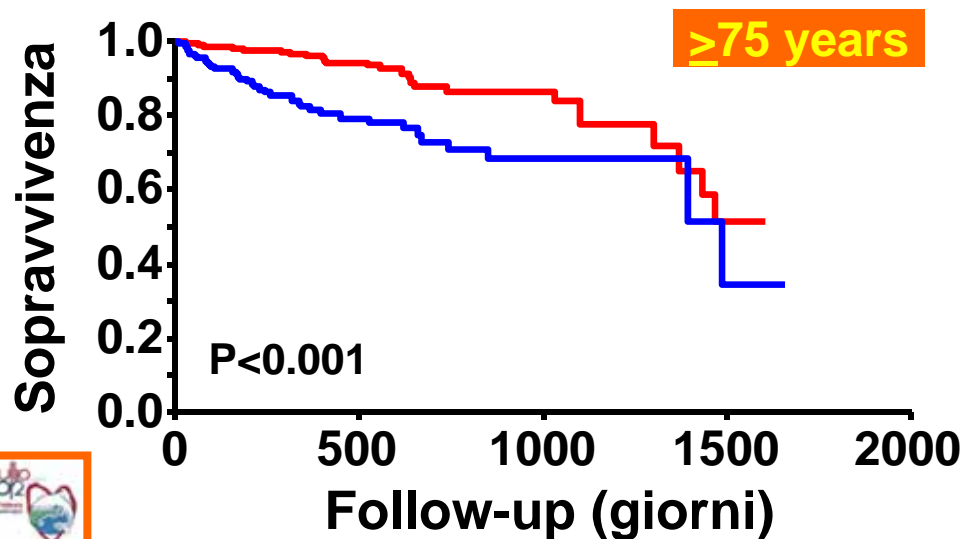
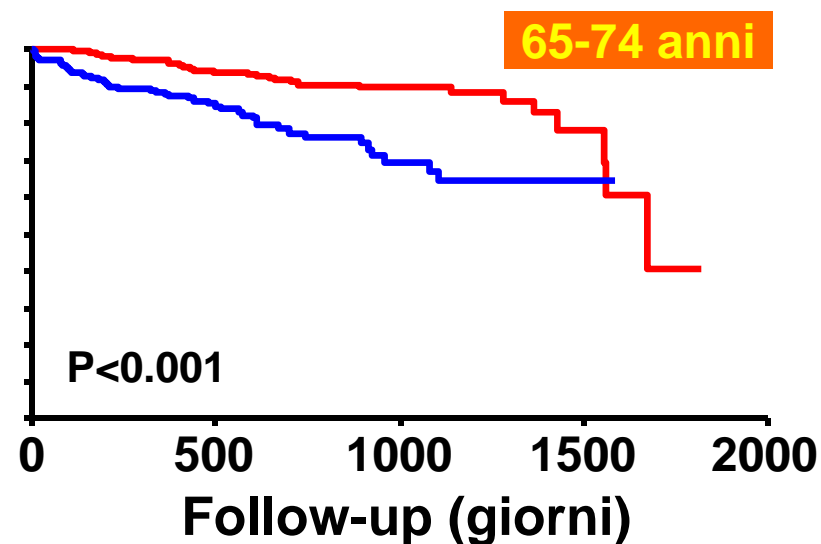
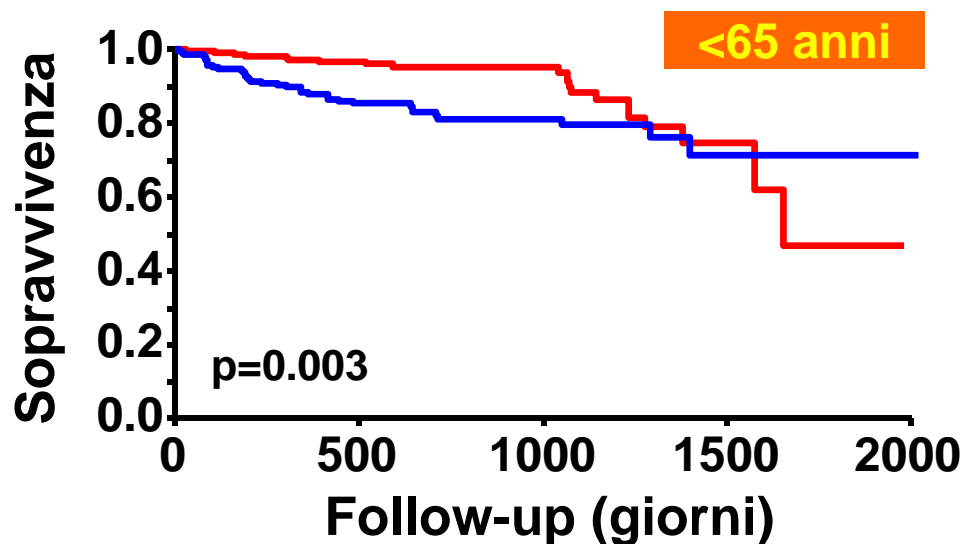
# Responder alla CRT ed utilizzo della CRT-D, per gruppo di età. I risultati del Registro Italiano InSync / InSync ICD



Fumagalli S,  
2011



# Sopravvivenza durante il follow-up, per risposta alla CRT & gruppo di età. I risultati del Registro Italiano InSync / InSync ICD



- *Responder alla CRT*
- *Non Responder alla CRT*

***Responder alla CRT:*** riduzione del volume telesistolico del VS >10% nella valutazione a 6 mesi





# Variabili cliniche correlate alla prognosi durante CRT nel Registro Italiano InSync / InSync ICD. Risultati del modello di Cox

	HR (95% CI)	p Value
Età <65 anni	1	/
65-74 anni	1.17 (0.80-1.69)	NS
<u>≥75 anni</u>	<b>1.57</b> (1.06-2.35)	0.026
Uomini	1.38 (0.90-2.12)	NS
Insufficienza renale	1.29 (0.75-2.22)	NS
Cardiopatía ischemica	1.18 (0.87-1.60)	NS
<u>FE VS, per Δ %</u>	<b>0.96</b> (0.94-0.98)	<0.001
<u>FA permanente</u>	<b>1.63</b> (1.16-2.30)	0.005
<u>ACE-I / ARB</u>	<b>0.72</b> (0.52-0.98)	0.038
<u>β-bloccanti</u>	<b>0.49</b> (0.35-0.67)	<0.001
<u>Responder CRT</u>	<b>0.37</b> (0.27-0.51)	<0.001

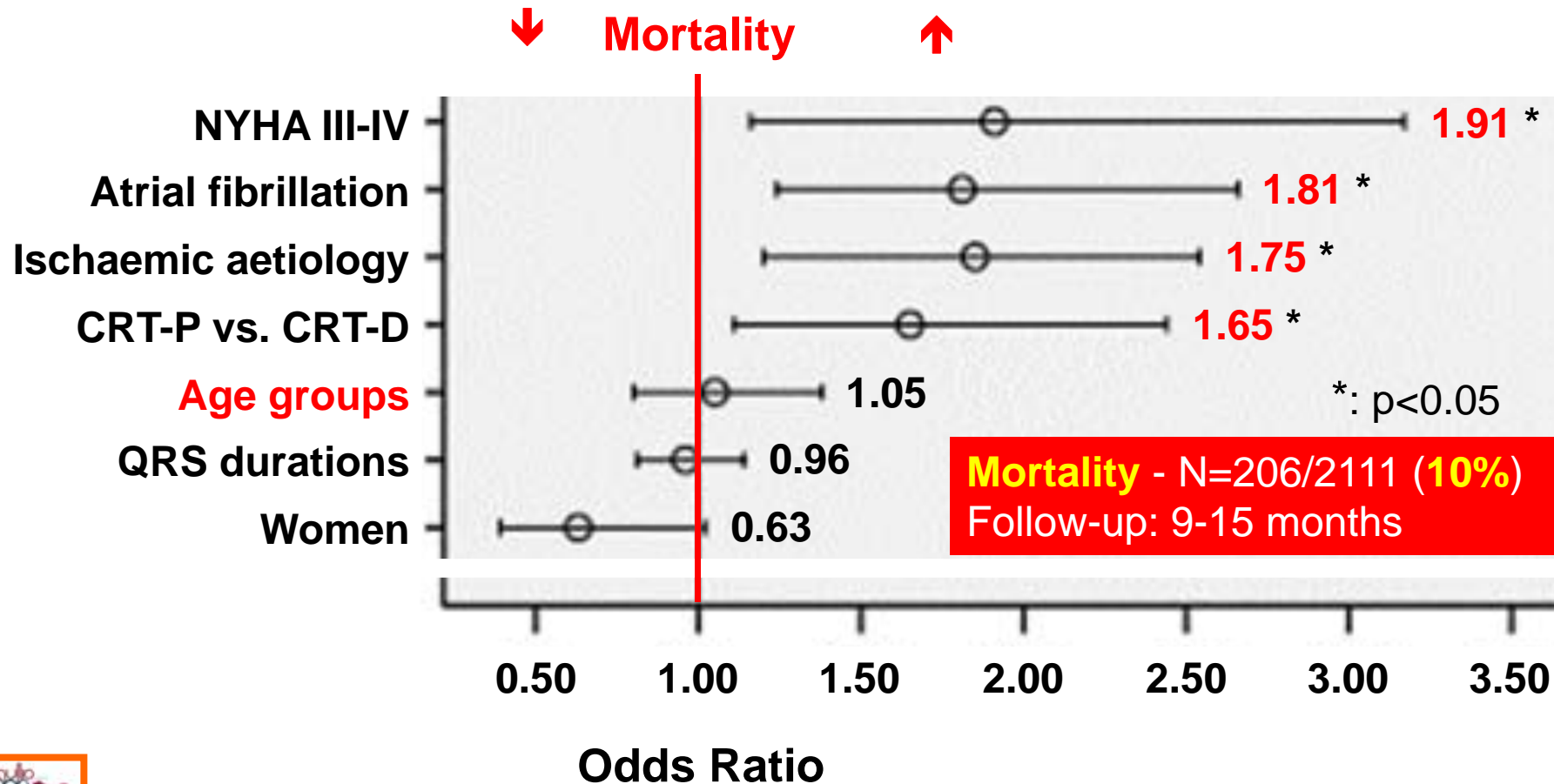


# The European CRT Survey: 1 year (9–15 months) follow-up results



Centres - N=141, Countries – N=13  
 Enrollment: November 2008 – June 2009

N=2111 (median age: 70 years)  
 >75 years: 30.6%



# The European CRT Survey: 1 year (9–15 months) follow-up results

## Device-related complications during 1 year (9-15 months, N=1648)

<b>Device-related complications</b>	<b>170 (10.3)</b>
<i>Lead displacement</i>	<i>55 (3.3)</i>
Lead malfunction	13 (0.8)
<i>Device-related arrhythmias</i>	<i>18 (1.1)</i>
<i>Phrenic nerve stimulation</i>	<i>51 (3.1)</i>
Device replacement	6 (0.4)
<i>Infection</i>	<i>27 (1.6)</i>



Bogale N  
et al., 2012

## The InSync / InSync ICD Registry

Device implantation complications – N = 190/1787 (**11%**)

No age-related trend - <65: 10%, 65 - 74: 11%, ≥75 years: 10%; p=NS



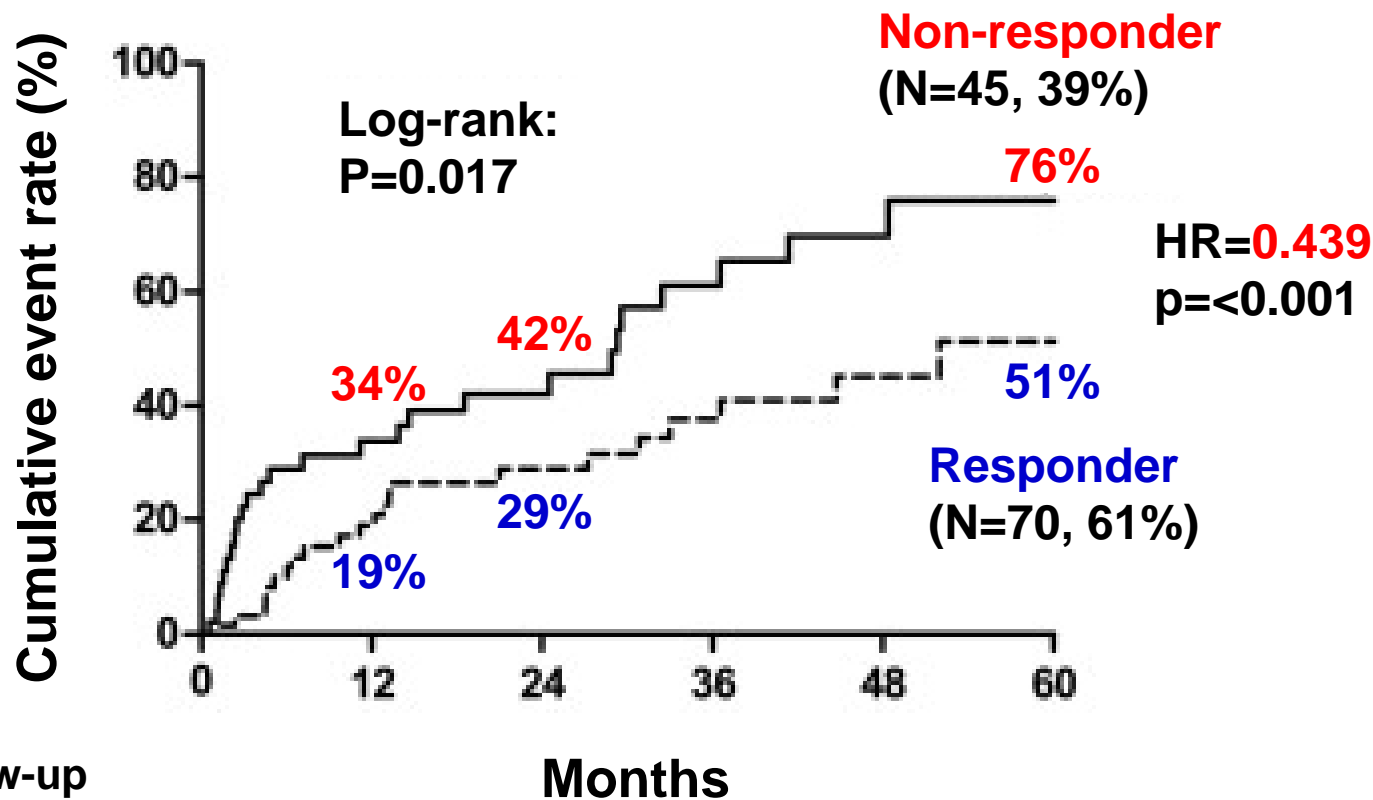
Fumagalli S  
et al, 2011





# Implantable Cardioverter-Defibrillator Patients Who Are Upgraded and Respond to Cardiac Resynchronization Therapy Have Less Ventricular Arrhythmias Compared With Nonresponders

N=115 (age: 65±12 years) – 1996-2010



**Follow-up**

After upgrade: **37** months

Before upgrade: **54** months

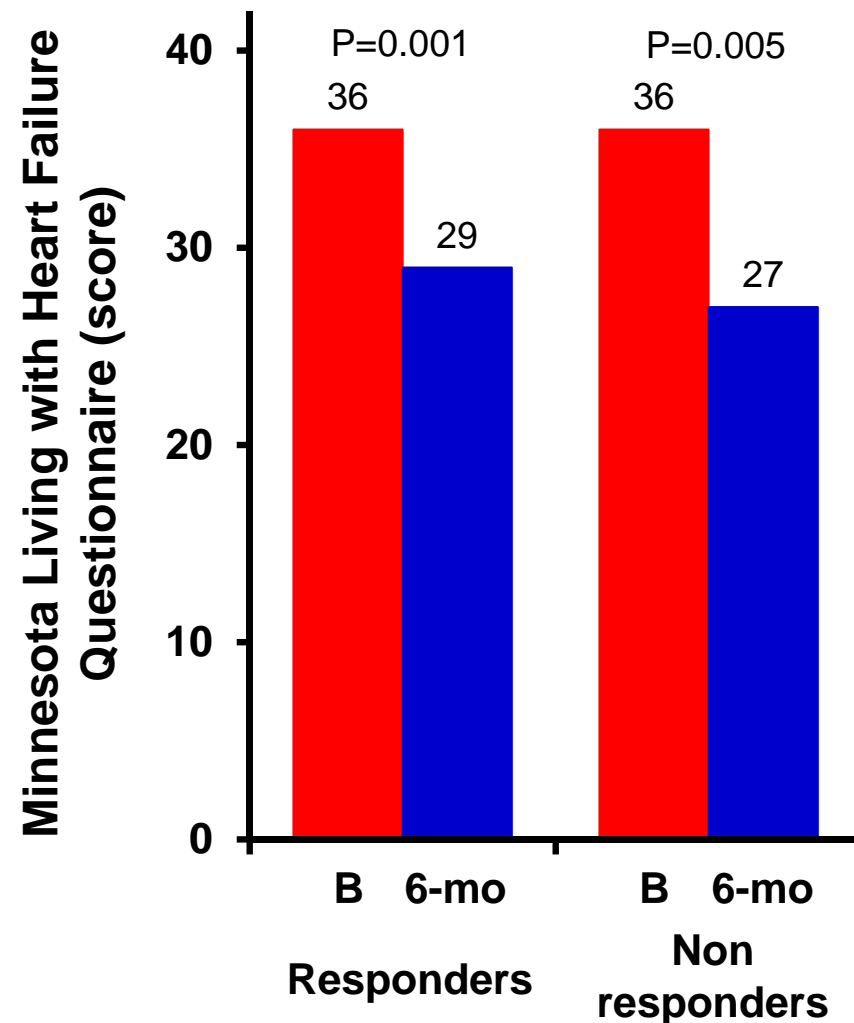
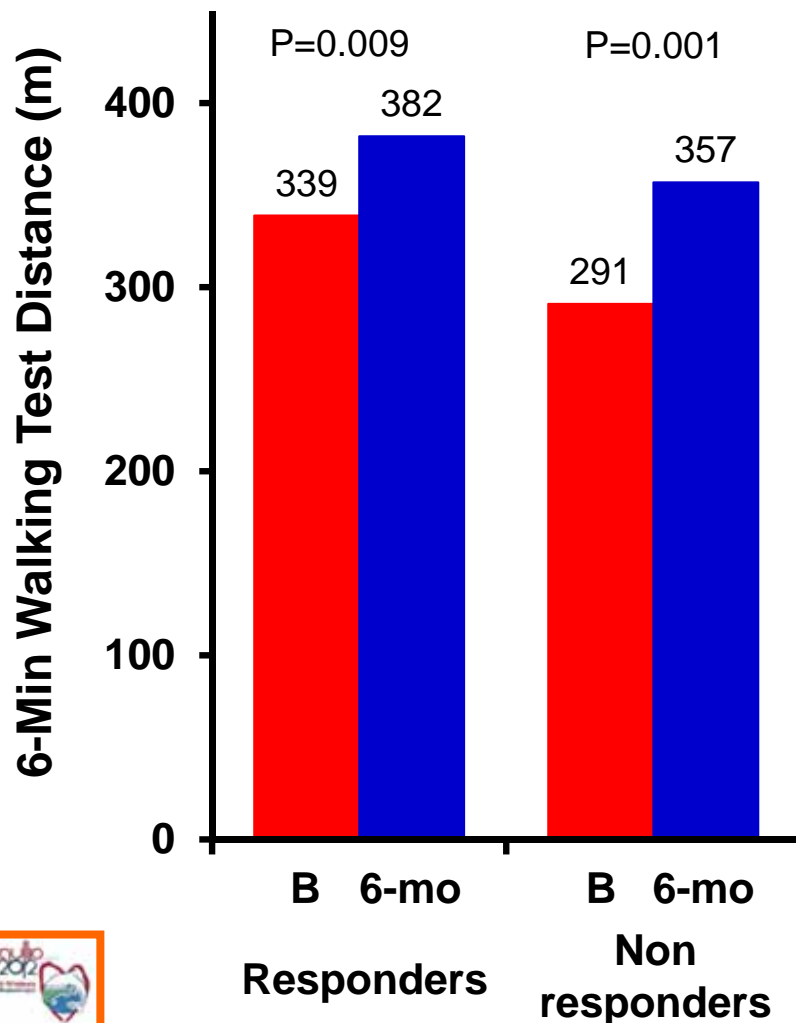
**Responder – LVESV ↓ ≥15% (6 months)**



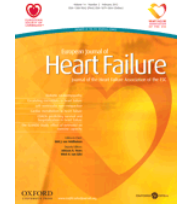
# Implantable Cardioverter-Defibrillator Patients Who Are Upgraded and Respond to Cardiac Resynchronization Therapy Have Less Ventricular Arrhythmias Compared With Nonresponders



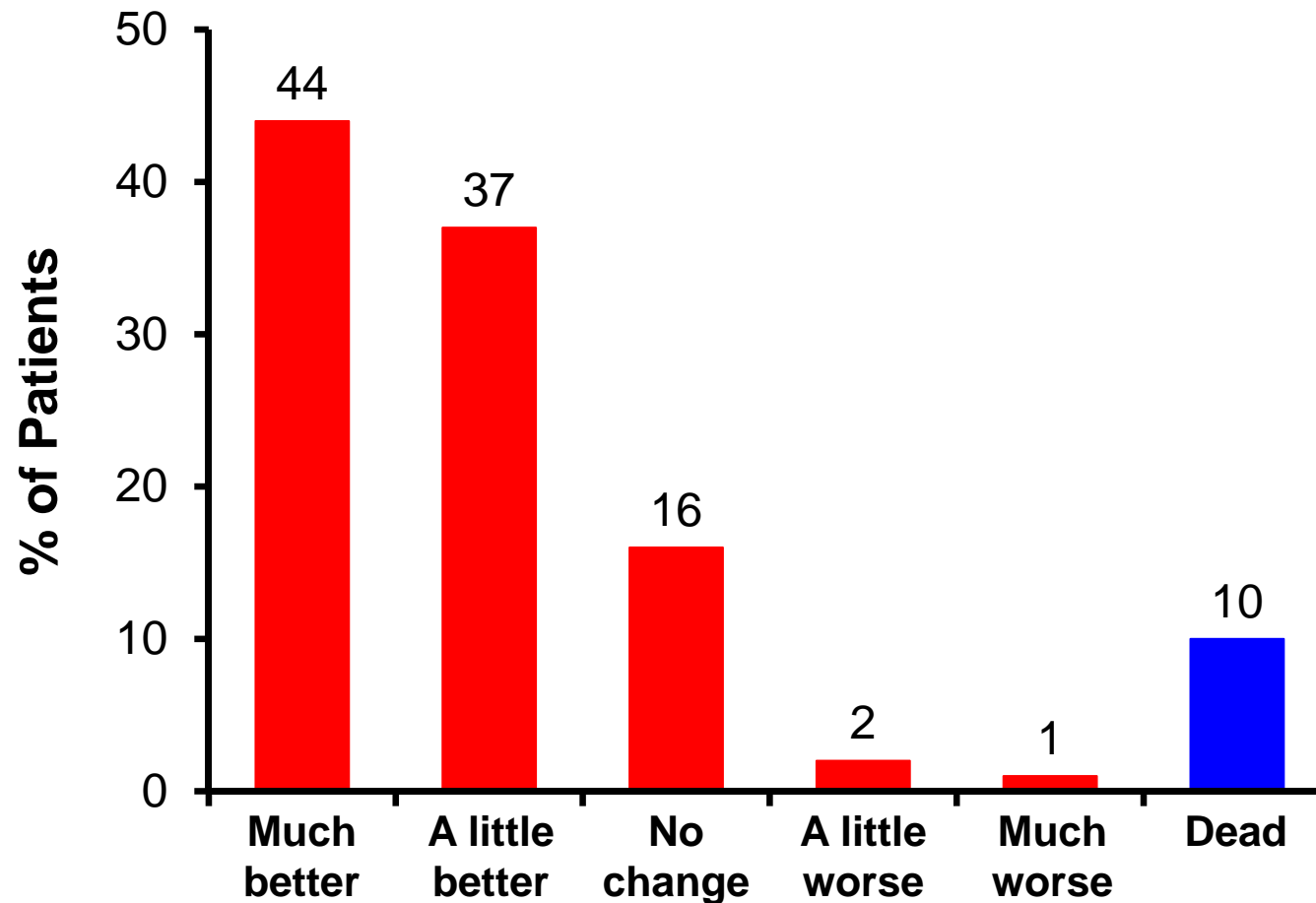
Thijssen J et al., 2011



# The European CRT Survey: 1 year (9–15 months) follow-up results



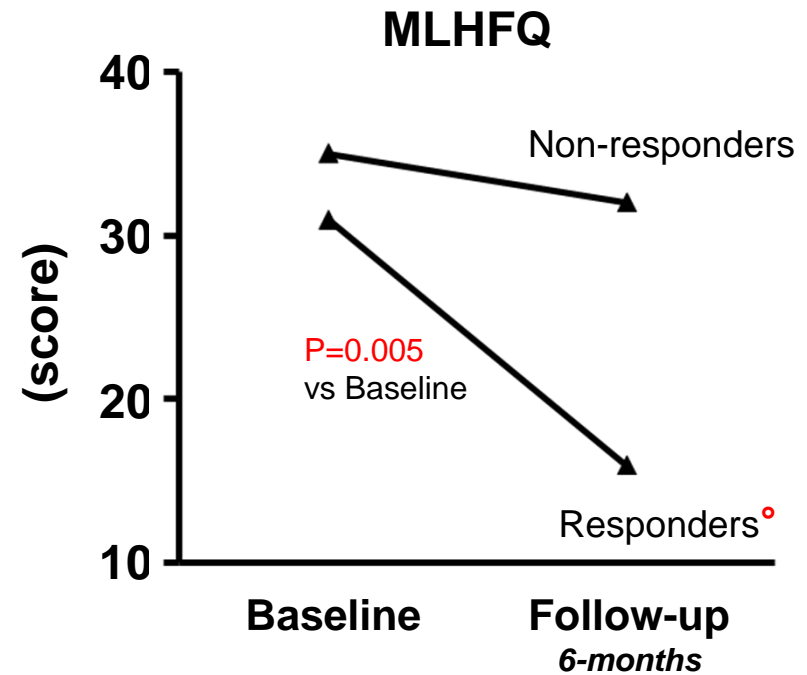
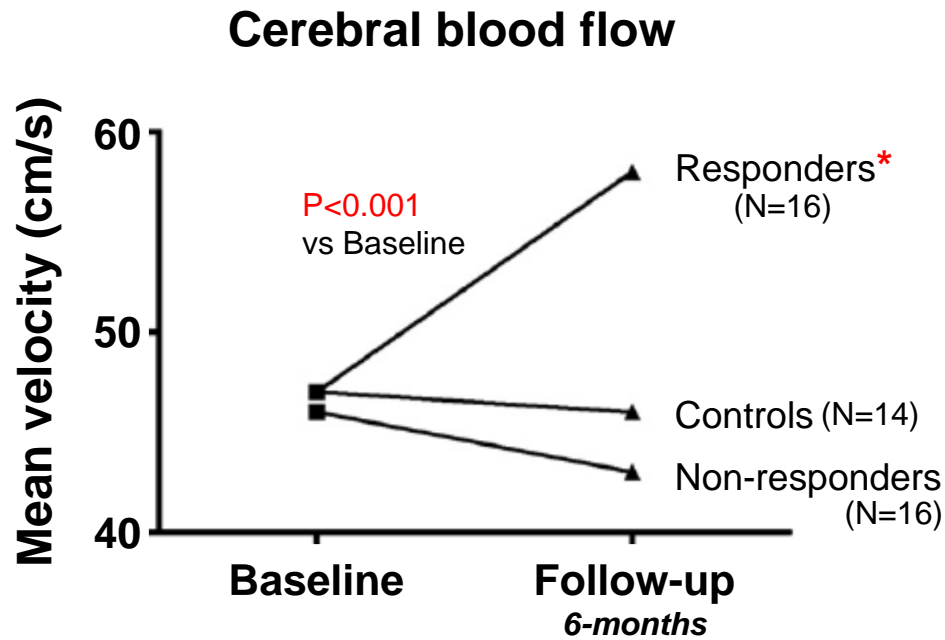
## Patient self-reported global assessment and rate of death during follow-up



# Effect of Cardiac Resynchronization Therapy on Cerebral Blood Flow

**Patients** - Age: 68 yrs; LVEF: 29%; QRS: 152 ms  
**Controls** - Age: 66 yrs; LVEF: 32%; QRS: 110 ms

**Responders** – 6-month reduction  $\geq 15\%$  of LV end-systolic volume



**Cerebral blood flow** - Transcranial Doppler of the right middle cerebral artery

**MLHF** – Minnesota Living with Heart Failure Questionnaire

\*/<sup>o</sup>: *p* < 0.01 / *p* < 0.05 vs Controls & Non-responders



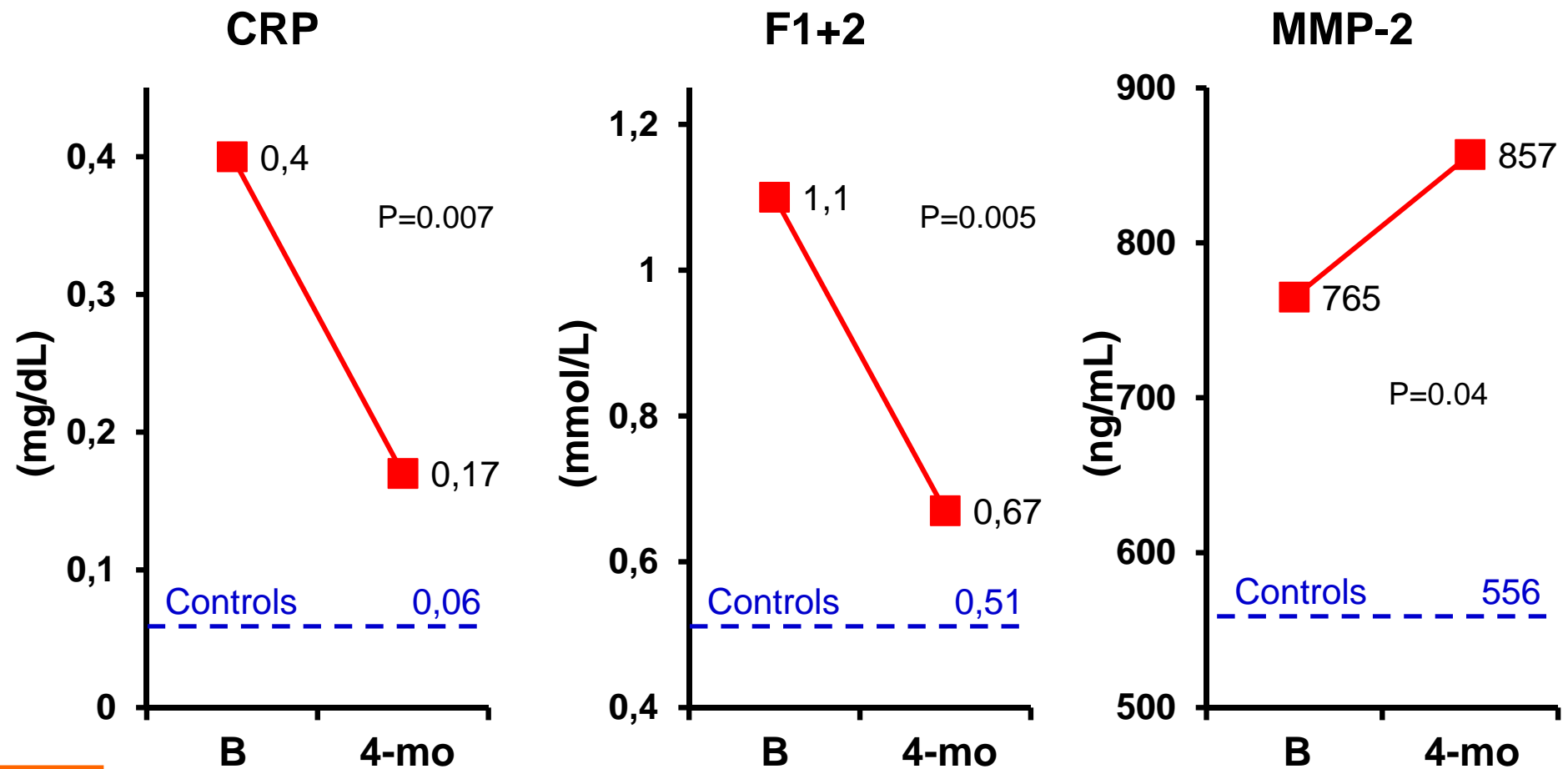
# Influence of cardiac resynchronization therapy on indices of inflammation, the prothrombotic state and tissue remodeling in systolic heart failure: A pilot study

**Patients** - N=36, Age: 70 years, EF: 28%

**Controls** - N=49, Age: 69 years, EF: 69%

**CRP:** C-reactive protein; **F1+2:** prothrombin fragment 1+2;

**MMP-2:** matrix metalloproteinase-2



B: baseline  
4-mo: 4 months

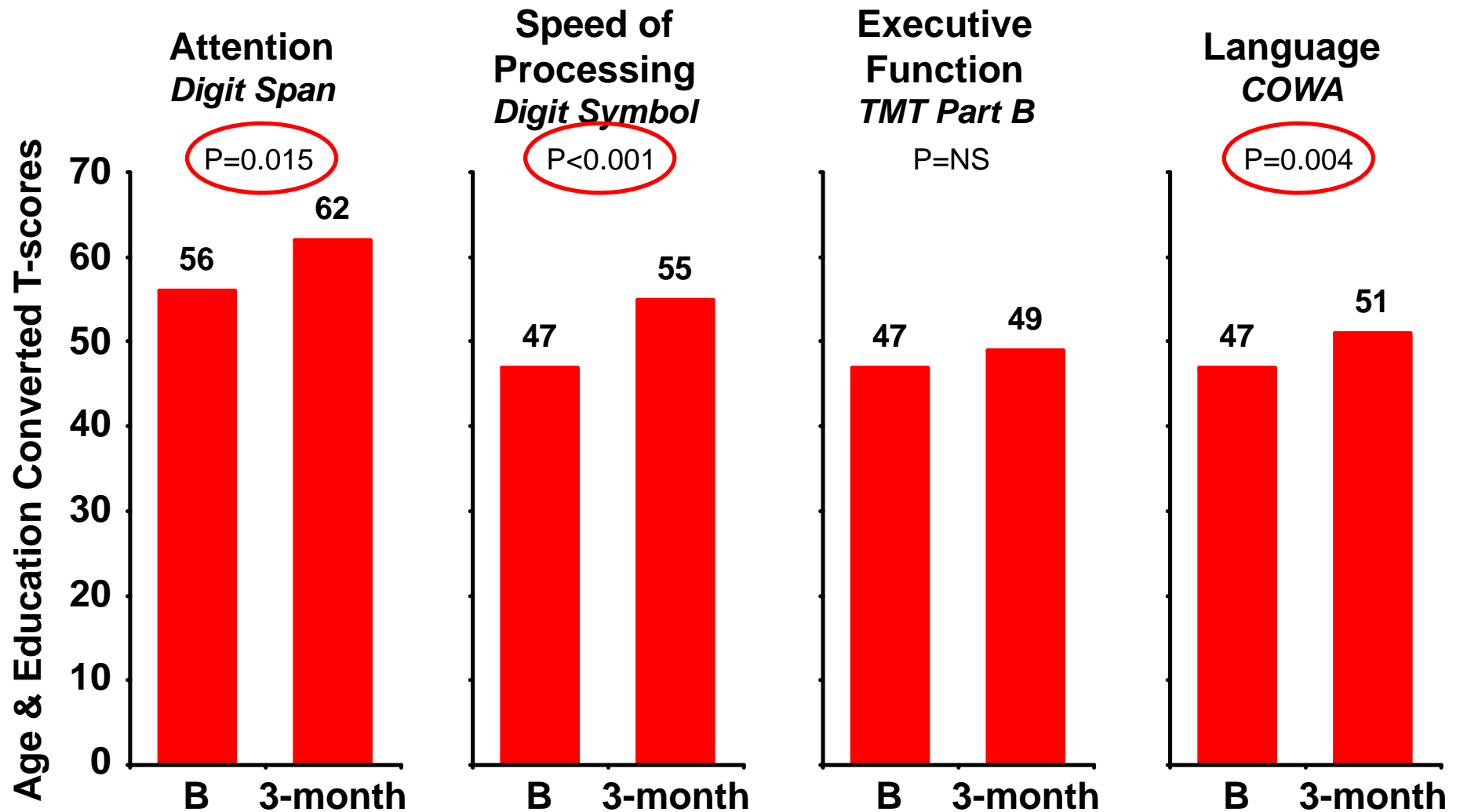




# Cardiac Resynchronization Therapy: A Pilot Study Examining Cognitive Change in Patients Before and After Treatment

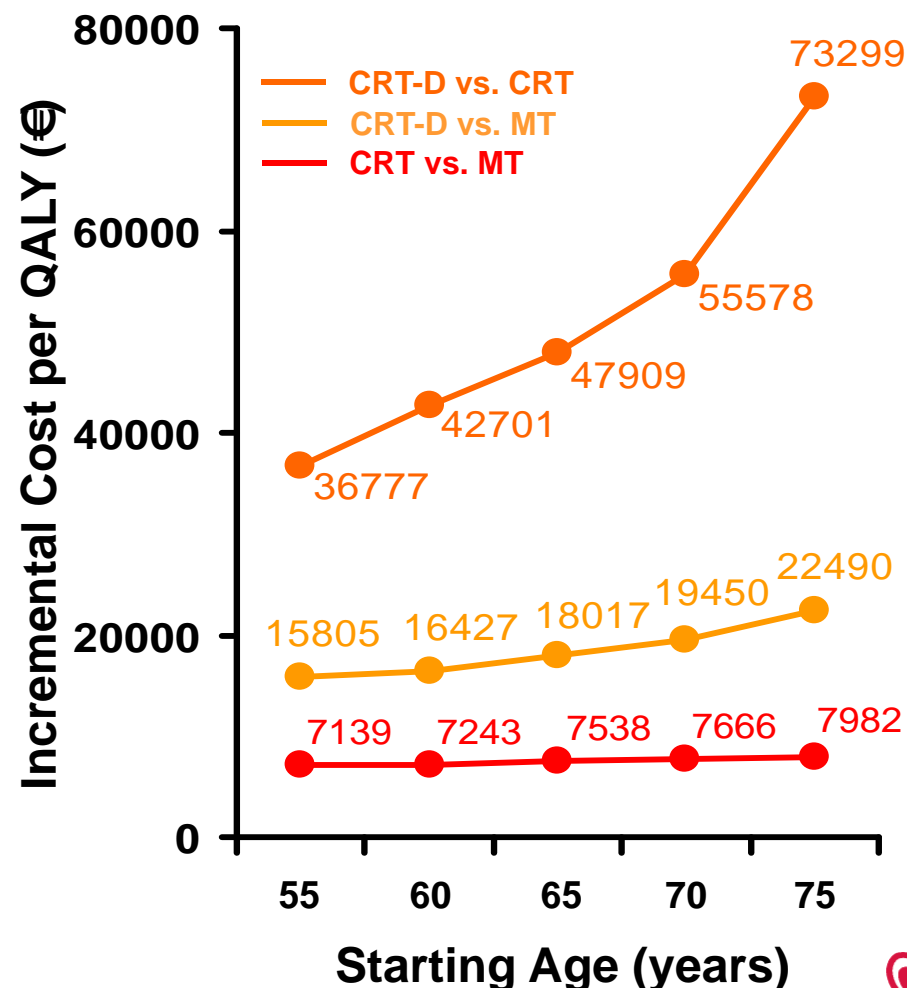
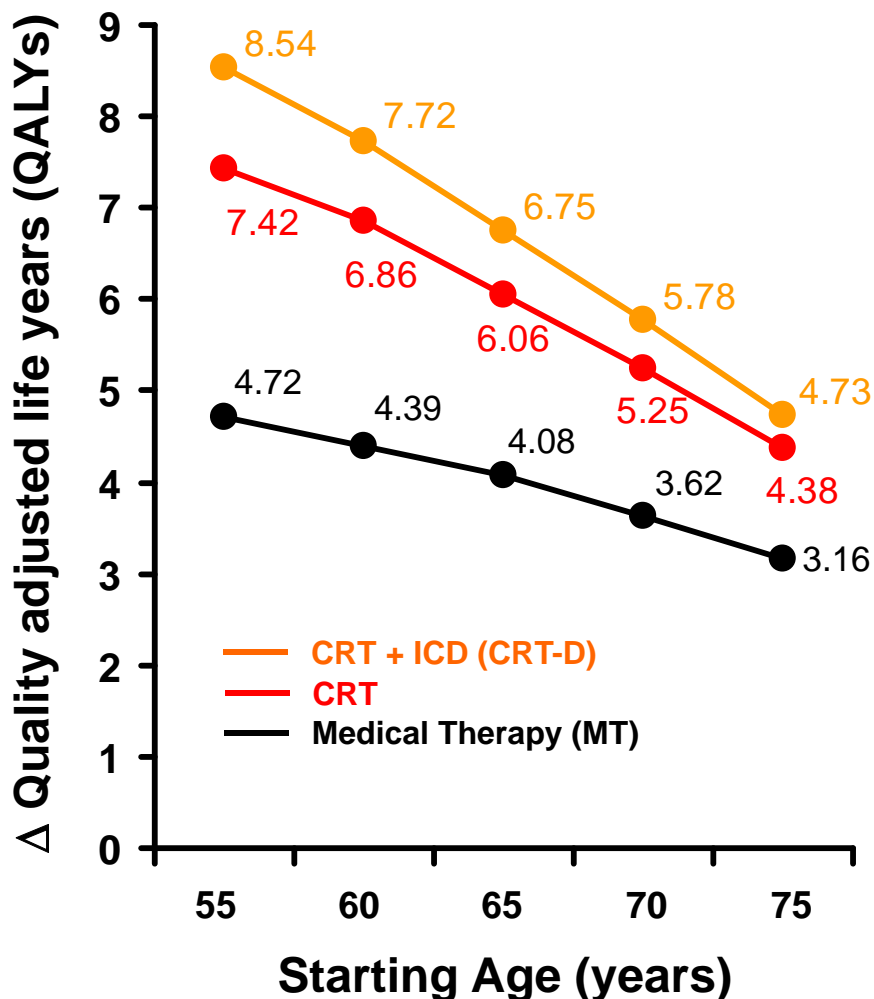
Dixit NK, Clin Cardiol, 2010

Age:  $55 \pm 12$  – N=20  
Baseline (B) EF: 17%  
3-month EF: 30%



# The long-term cost-effectiveness of cardiac resynchronization therapy with or without an implantable cardioverter-defibrillator

Estimates from individual patient data from the CARE-HF & the COMPANION trials



## EHRA Expert Consensus Statement on the management of cardiovascular implantable electronic devices in patients nearing end of life or requesting withdrawal of therapy



Padeletti L, Arnar DO,  
Boncinelli L. Europace,  
2010

CONSENSUS STATEMENT

- Terminally ill patients are more likely to develop conditions such as hypoxia, sepsis, pain, HF and electrolyte disturbances, ... thus increasing the frequency of shock therapy
- Shocks can be **physically painful** and **psychologically stressful**, without prolonging a life of acceptable quality
- When a patient dies after ICD deactivation, the cause of death may be deemed to be the underlying disease. ICD deactivation in dying patients may be ethically permissible

Pacing **is not** perceptible and **is painless**. Pacemakers are not life-support devices. But, by preventing symptomatic bradycardia and the failure of major organs, it will provide **a better HRQL**, therefore meeting the goals of palliative care. The same applies to CRT





## Conclusioni

- La CRT determina il miglioramento della geometria e della funzione del VS in pazienti di tutte le età
- I benefici della CRT sono apprezzabili anche in termini di capacità funzionale e qualità della vita
- L'aumento della perfusione cerebrale e il miglioramento del quadro umorale indotti dalla CRT potrebbero rallentare lo sviluppo di deterioramento cognitivo in scompensati anziani
- L' undertreatment farmacologico costituisce un problema reale in gran parte correlato all'età
- L'uso della CRT in età avanzata non è svantaggioso in termini economici
- Sono necessari studi clinici per confermare questi risultati ottenuti da registri di ampie proporzioni

# Effects of cardiac resynchronization therapy on health-related quality of life in older adults with heart failure

Age: 68±8 yrs (range: 56-84)– N=21  
 EF: B=30% - 3m=39%, p<0.01  
 6-mWT : B=351 m - 3m=381 m, p<0.05

