The implantable cardiac defibrillator in octagenarian patients: indications, exceptions and caveats

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Background

- Increase in life expectancy and heart failure management has led to higher rate of ICD implantation in older patients.

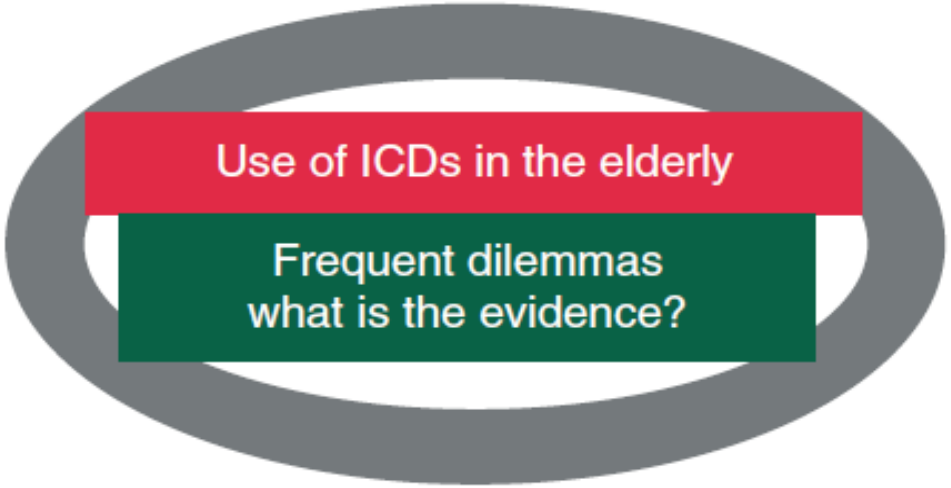
- Limited resources, major attention to costs and no current formal recommendations in the GL led to assess the true effectiveness of ICD in elderly pts.

Can we extrapolate the results of trials supporting the guidelines to this population?

Possibly: weak evidence[48]

Are there specific elderly groups with higher benefit?

Some risk classifications have been proposed[49–55], but an ultimate score providing strong support for implanting in some patients while excluding others is still lacking



What is the risk of peri- and post-procedural complications?

Similar or only slightly higher for peri-procedural: strong evidence[12,24,28,32,33–37]
Not clear in the mid/long-term: lacking evidence

Does it improve survival?

Mortality is higher in elderly: strong evidence[24,26,34,43,44]
However, there may be a survival benefit in selected individuals: weak evidence[12–14]

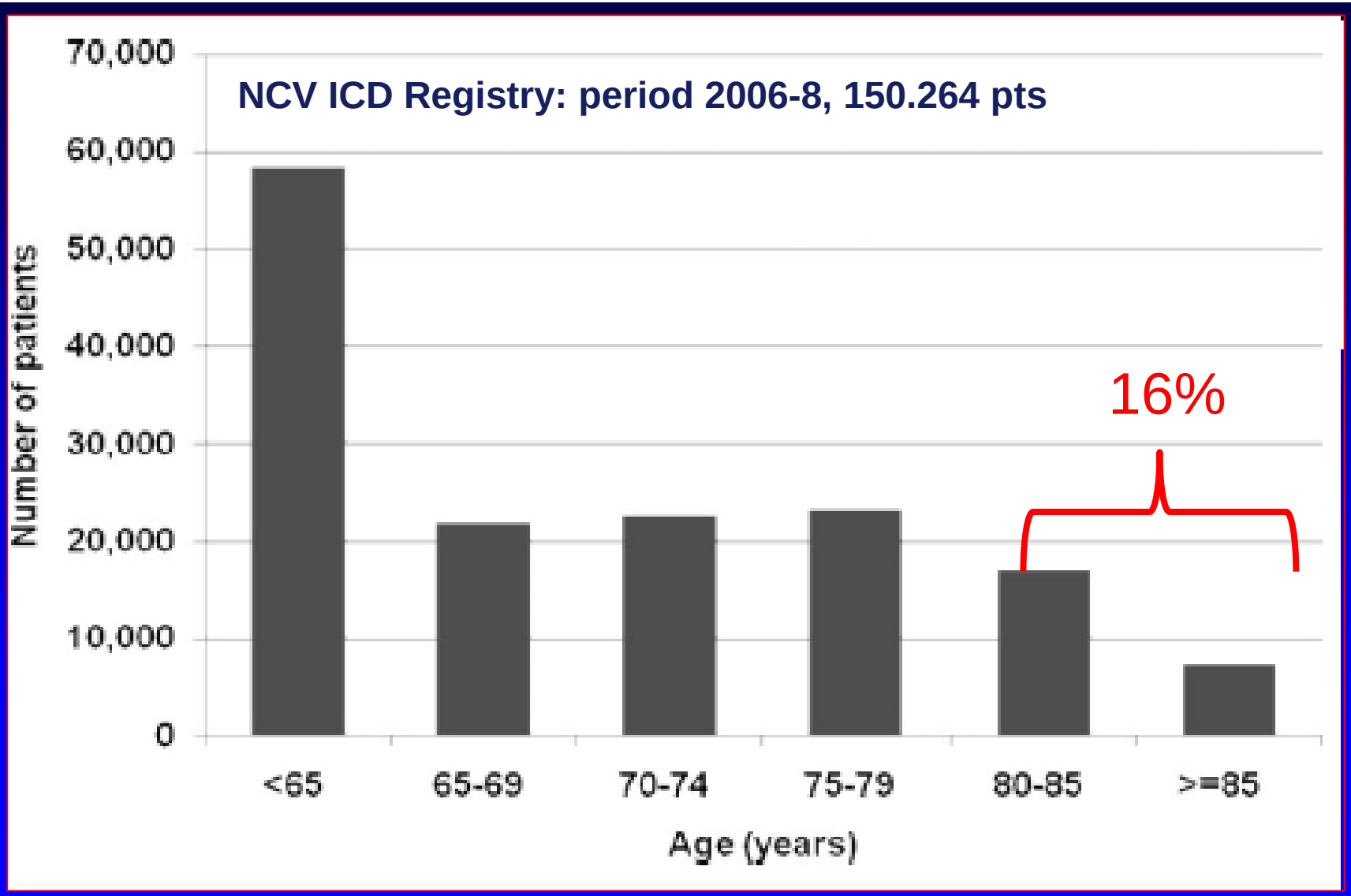
When should therapies be disabled?

This should occur after a combined patient and/or family (if the patient is unable to decide) decision
Consensus / Not evidence-based

Table I Studies evaluating rates of ICD implantation in the elderly

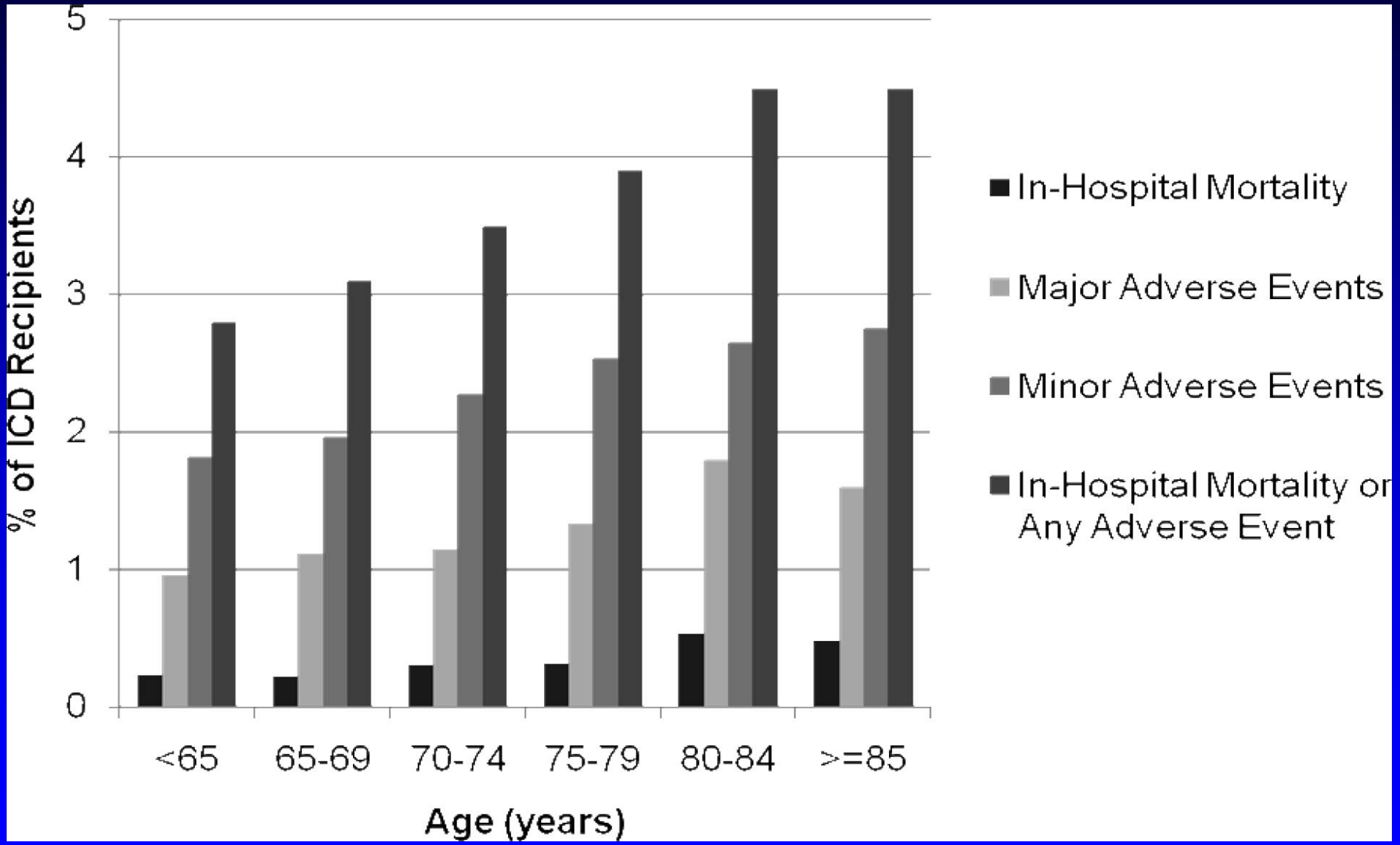
Study	Study Design	Percentage of elderly patients
United States National ICD Registry[22]	• National registry 2006–08 • 339 076 ICD patients	>70 years old/42% >80 years old/12.4%
Advancements in ICD Therapy Registry[8]	• Prospective 2-year study of largely community-based practice and reporting data from 264 centres in the USA between November 2004 and March 2006 • 4566 ICD/CRT-D patients	70–79 years old/29% ≥80 years old/12%
Ontario ICD Database[23]	• Population-based prospective registry, February 2007–September 2010 • 5399 ICD patients	70–79 years old/31.6% ≥80 years old/8.0%
Italian ICD Registry[24]	• Prospective ICD registry for the years 2005–07 • Number of ICDs per million of inhabitants: 180.6 in the year 2005, 192.5 in the year 2006, and 220.6 in the year 2007	≥75 years old/25%
Papworth Hospital ICD Registry[25]	• Prospective ICD registry, November 1991–May 2012 • 1428 patients admitted for ICD implantation or generator replacement	5.3% octogenarians

Influence of Age on Perioperative Complications Among Patients Undergoing Implantable Cardioverter-Defibrillators for Primary Prevention in the United States



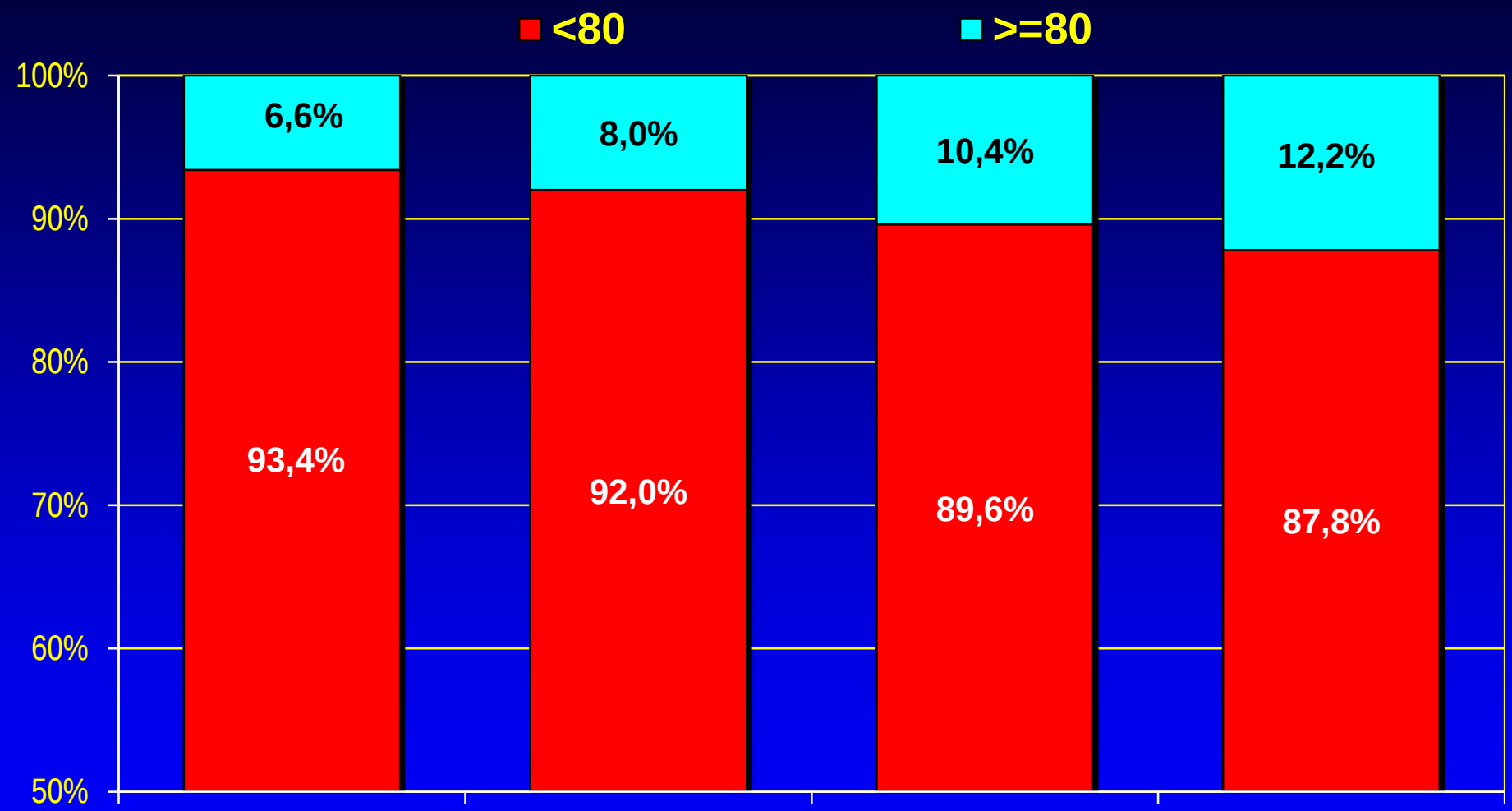
Tsai et al., Circ Cardiovasc Qual Outcomes. 2011;4:549-56

In-hospital adverse events and mortality by age



Tsai et al, Circ Cardiovasc Qual Outcomes. 2011;4:549-56

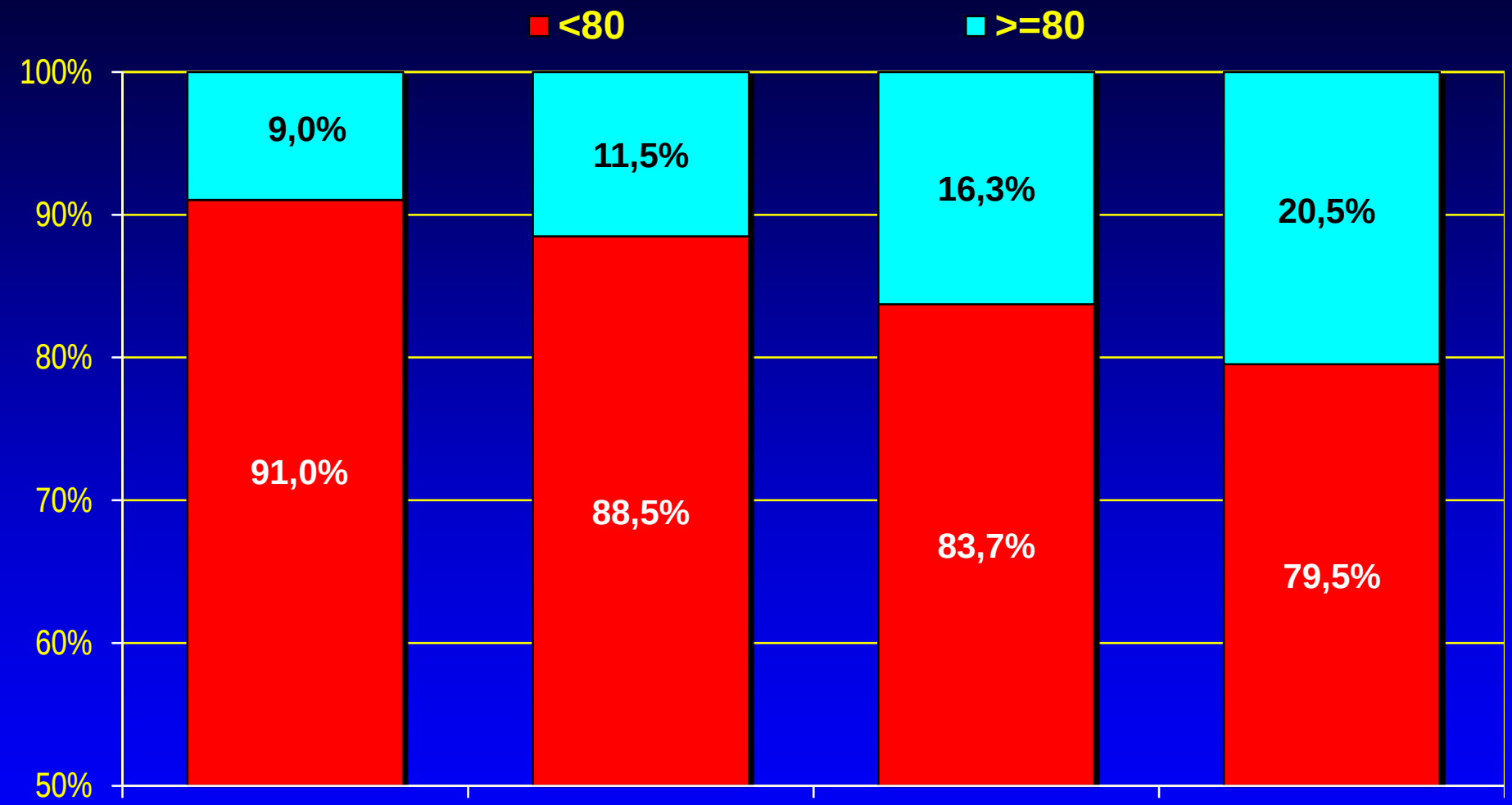
First ICD implants by age: 2003-14 (93470 pts)



	2003-5	2006-8	2009-11	2012-4
<80 y	15479	26836	27233	24005
≥80 y	1093	2330	3159	3335

A.I.A.C. Italian ICD Registry

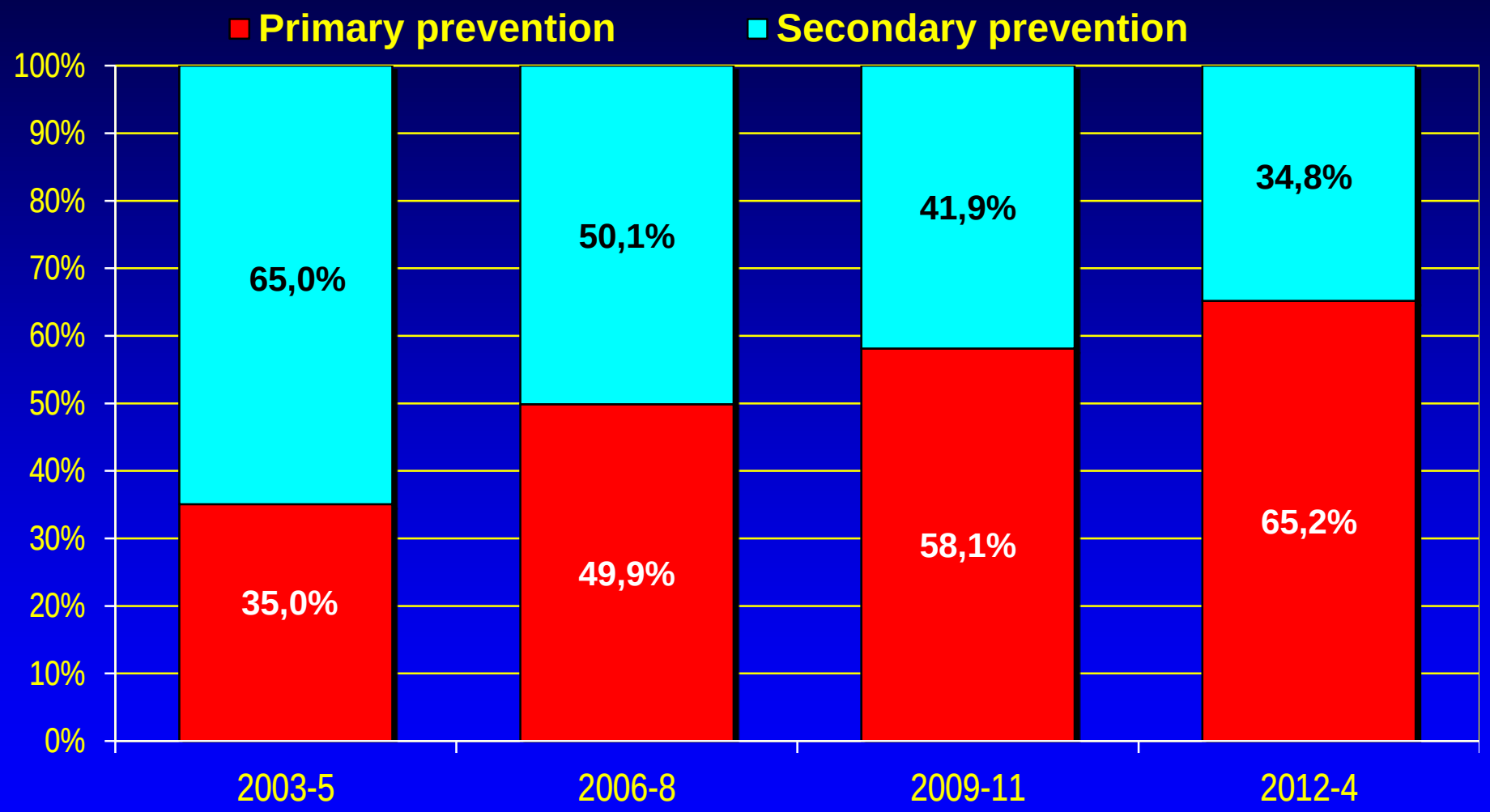
ICD replacements by age: 2003-14 (41454 pts)



	2003-5	2006-8	2009-11	2012-4
<80 y	5229	8004	11697	10892
≥80 y	515	1042	2272	2803

A.I.A.C. Italian ICD Registry

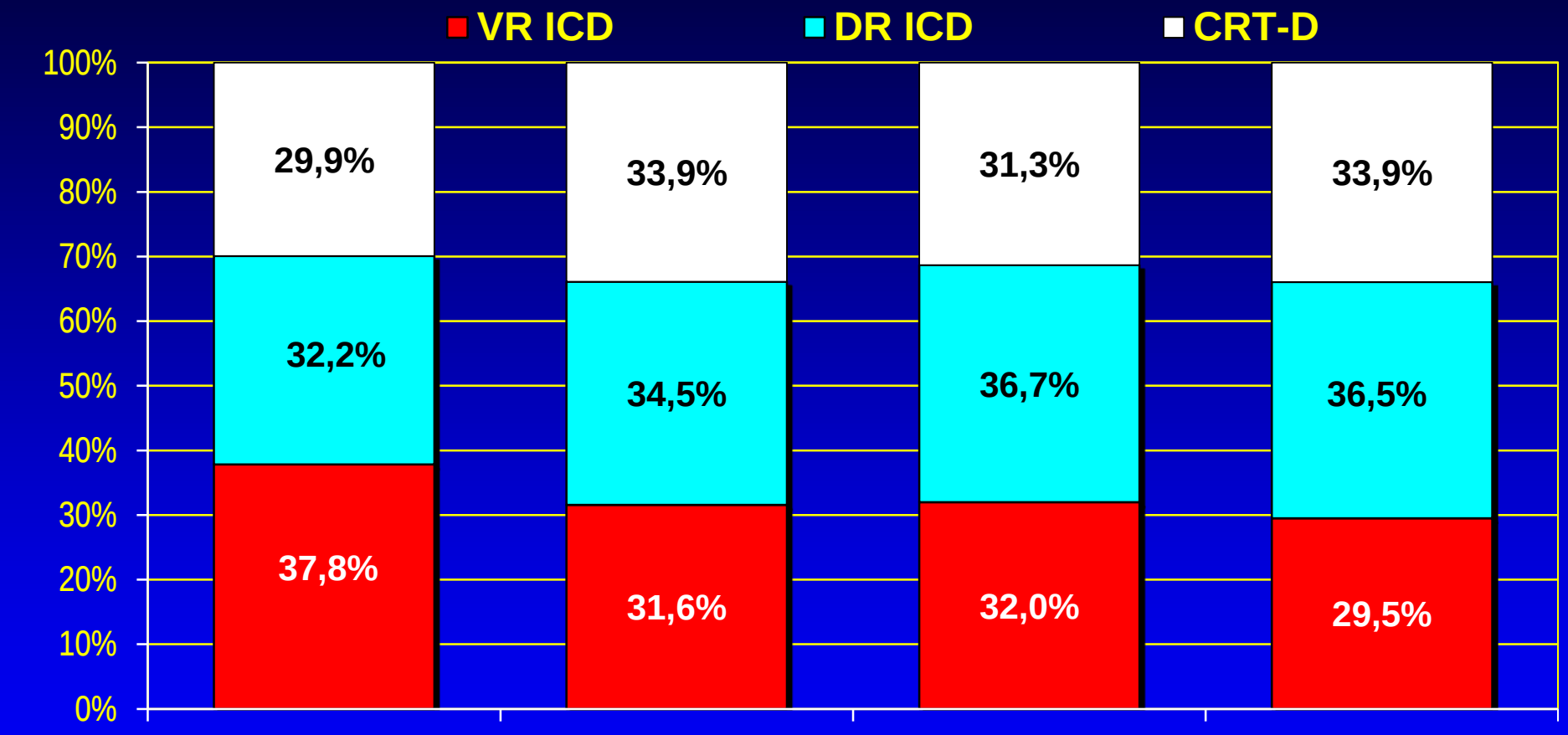
First ICD implants over 80: 2003-14



	2003-5	2006-8	2009-11	2012-4
PP	383	1162	1836	2173
SP	710	1168	1323	1162

A.I.A.C. Italian ICD Registry

First ICD implants over 80: 2003-14



	2003-5	2006-8	2009-11	2012-4
VR	413	735	1009	413
DR	352	804	1157	352
CRT-D	327	790	989	327

A.I.A.C. Italian ICD Registry

Use of implantable cardioverter-defibrillators for primary prevention in older patients: A systematic literature review and meta-analysis

Melissa H. Kong, Sana M. Al-Khatib, Gillian D. Sanders,
Vic Hasselblad, Eric D. Peterson

Duke Clinical Research Institute, Duke University Medical Center, Durham, NC, USA

- **Meta-analysis on efficacy in reducing all-cause mortality in older patients**
- **3562 pts >65 y; 579 pts> 75y**
- **No difference in ICD related complications and benefit among older patients compared to younger.**

Cardiol J 2011; 18, 5: 503–14

Older primary prevention patients in trials

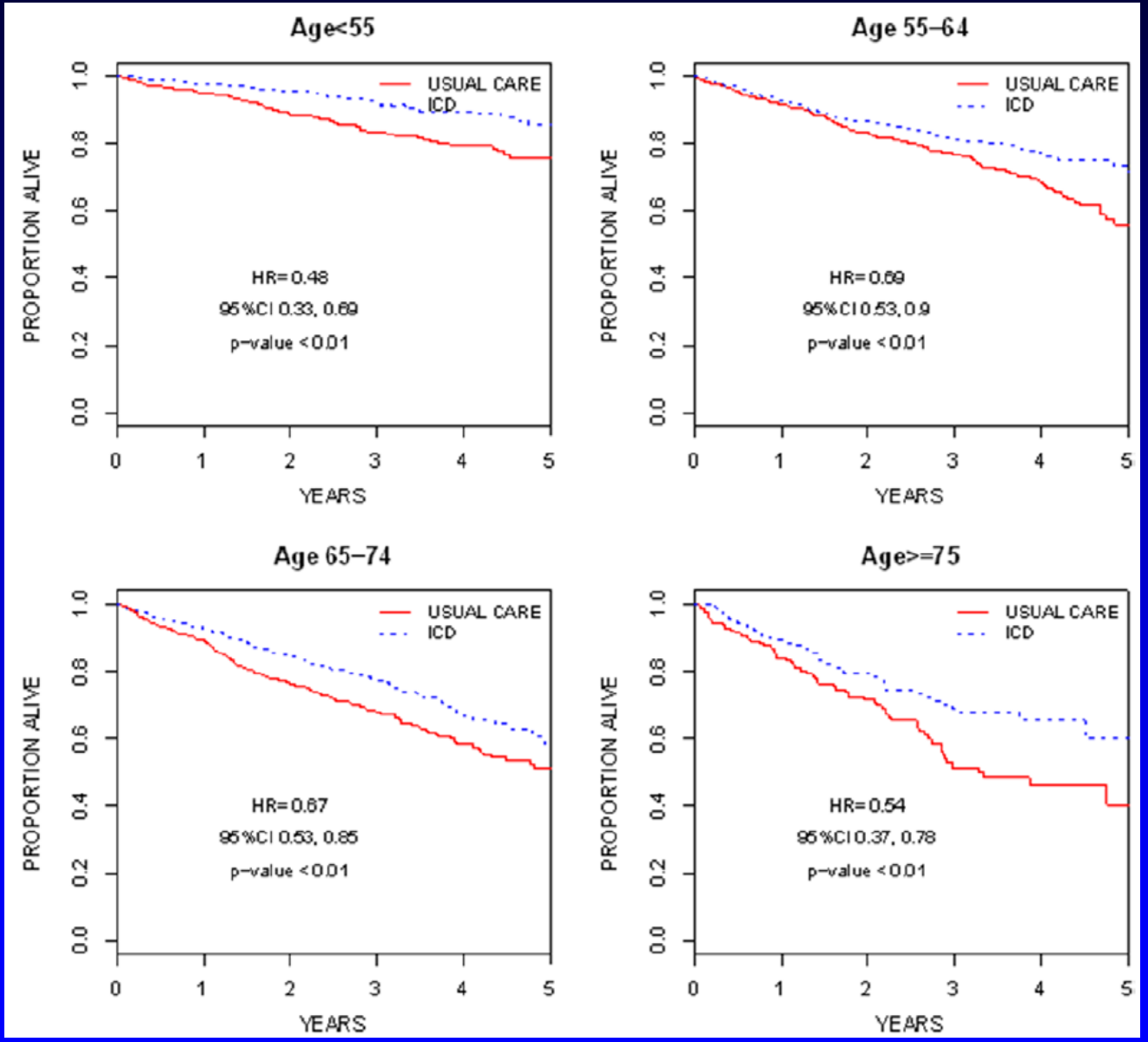
Trial	Patients	Patients >75 y	% Patients >75y	HR for effect of ICD therapy on all-cause mortality
MADIT-I	196	18	9.18	NO death in ICD treatment arm
MUSTT	704	96	13.6	1(0.58-1.75)
MADIT-II	1232	204	16.6	0.71(0.42-1.19)
DEFINITE	458	43	9.4	0.29(0.09-0.97)
SCD-HeFT	2521	236	9.4	0.65(0.39-1.05)

Survival Benefit of the Primary Prev. ICDs in Older Pts

Data from:

MADIT-I, MUSTT, MADIT-II, DEFINITE and SCD-HeFT

Unadjusted K–M survival by age groups



Hess et al, 2015 Circ Cardiovasc Qual Outcomes;8:179-186

Survival Benefit of the Primary Prev. ICDs in Older Pts

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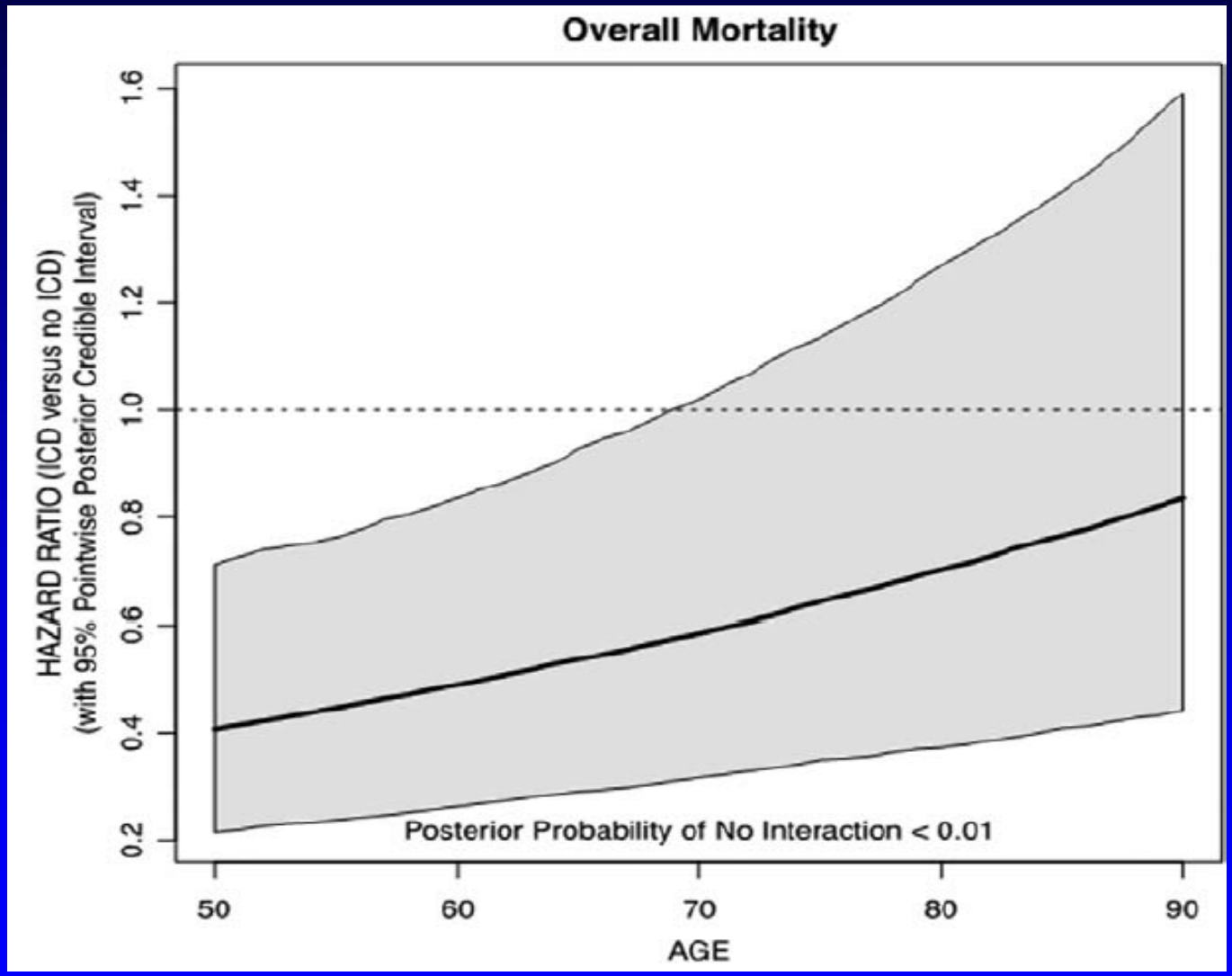


Hess et al, 2015 Circ Cardiovasc Qual Outcomes;8:179-186

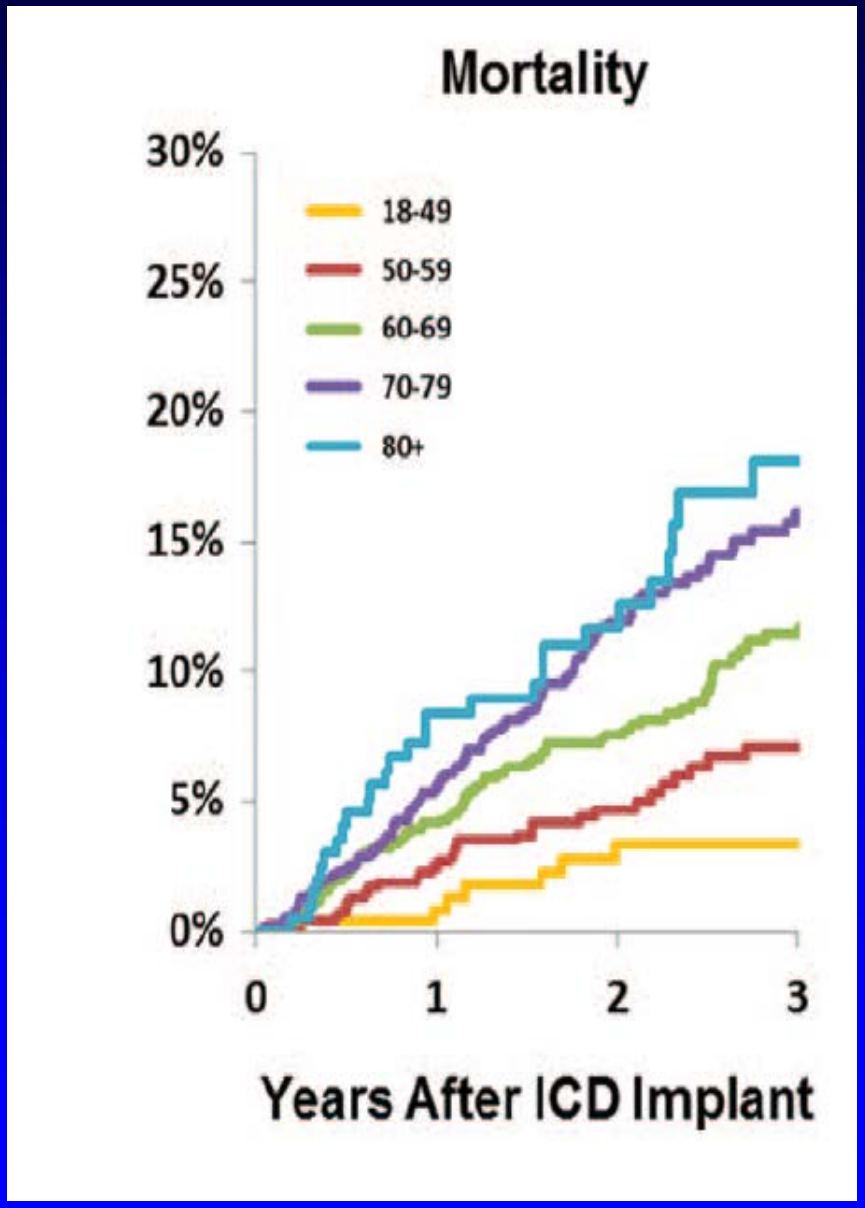
Survival After Implantable Cardioverter-Defibrillator Implantation in the Elderly

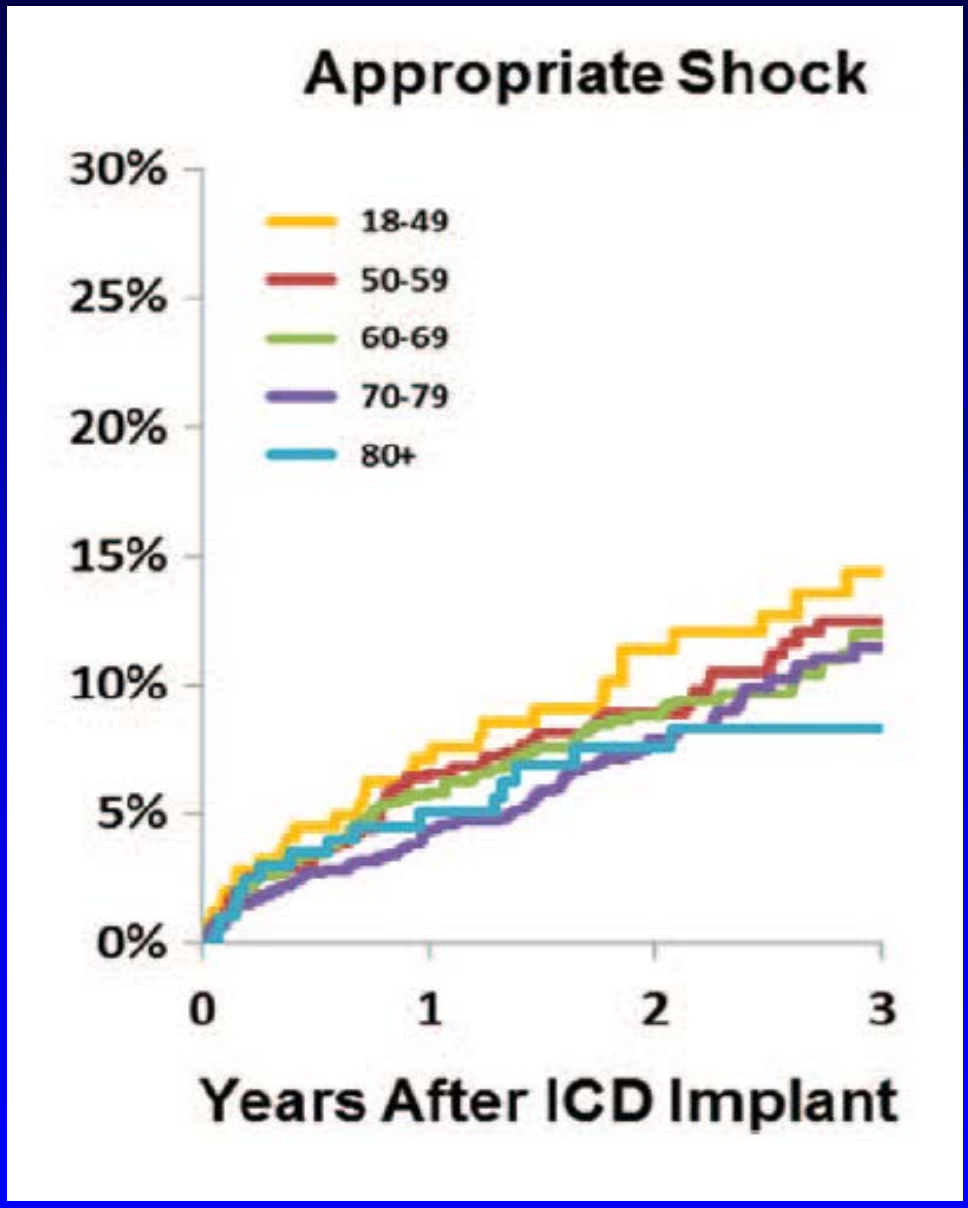
Derek Yung, MD; David Birnie, MBChB; Paul Dorian, MD; Jeffrey S. Healey, MD, MSc; Christopher S. Simpson, MD; Eugene Crystal, MD; Andrew D. Krahn, MD; Yaariv Khaykin, MD; Douglas Cameron, MD; Zhongliang Chen, MD; Douglas S. Lee, MD, PhD

- **Prospective registry on 5399 ICD & CRTD patients in Ontario (Canada)**
- **Both primary & secondary prevention**
- **Evaluation of mortality, appropriate shock rate**

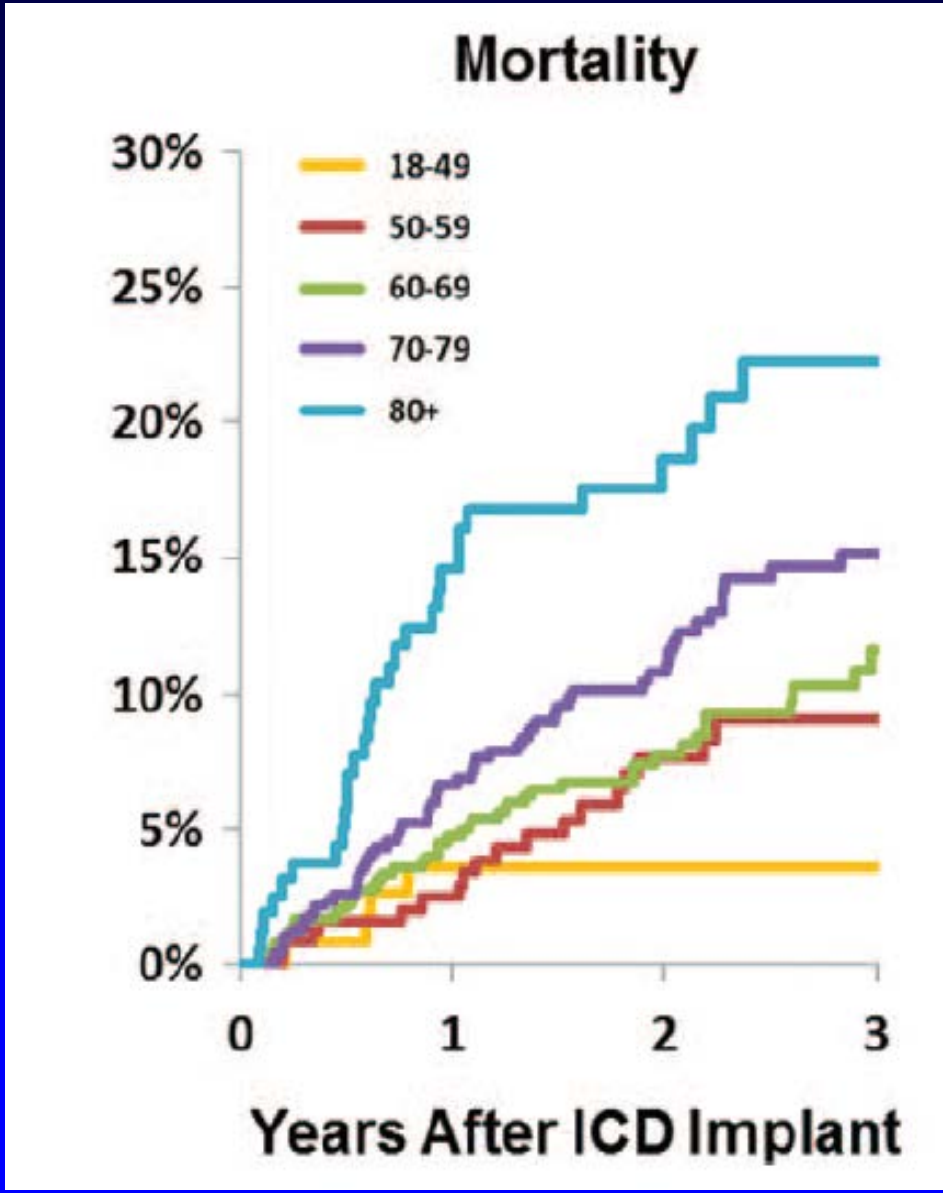
Circulation 2013;127:2383-92

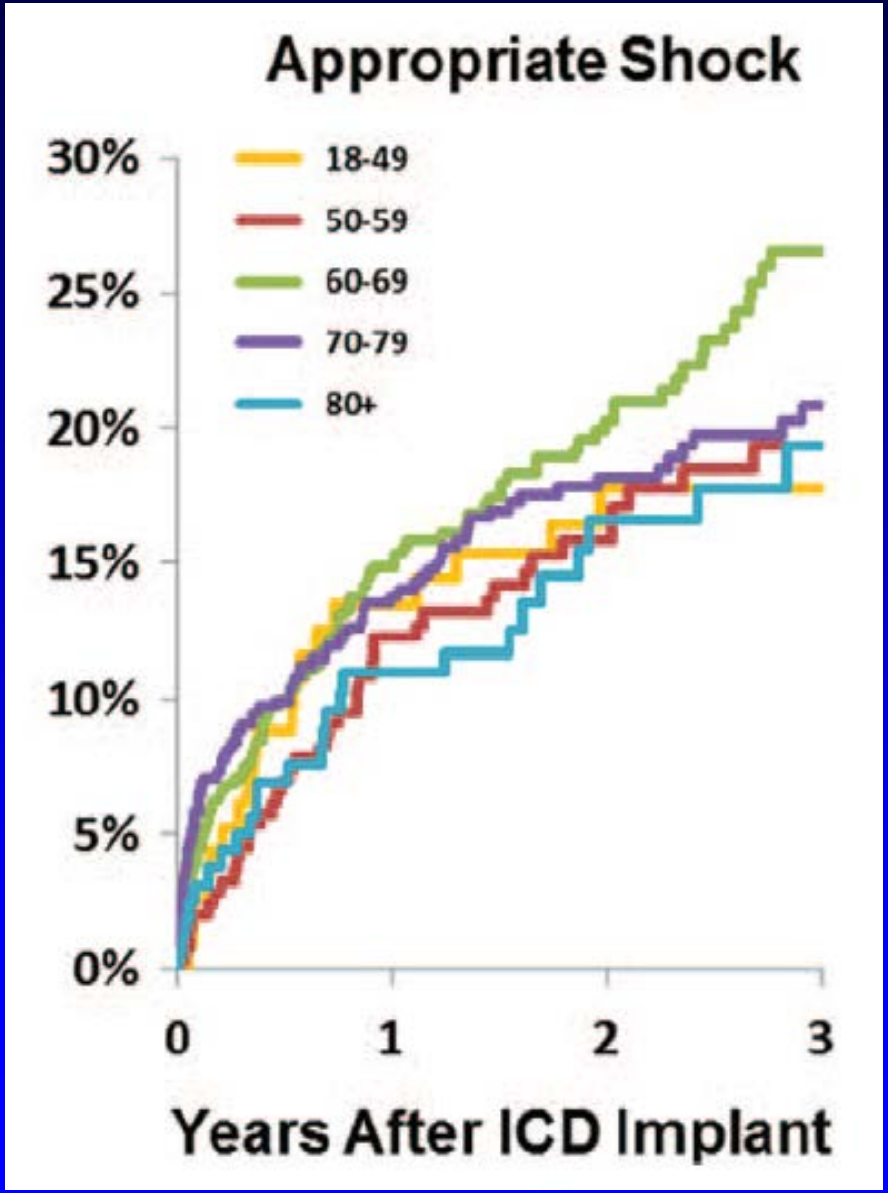
Primary Prevention





Secondary Prevention





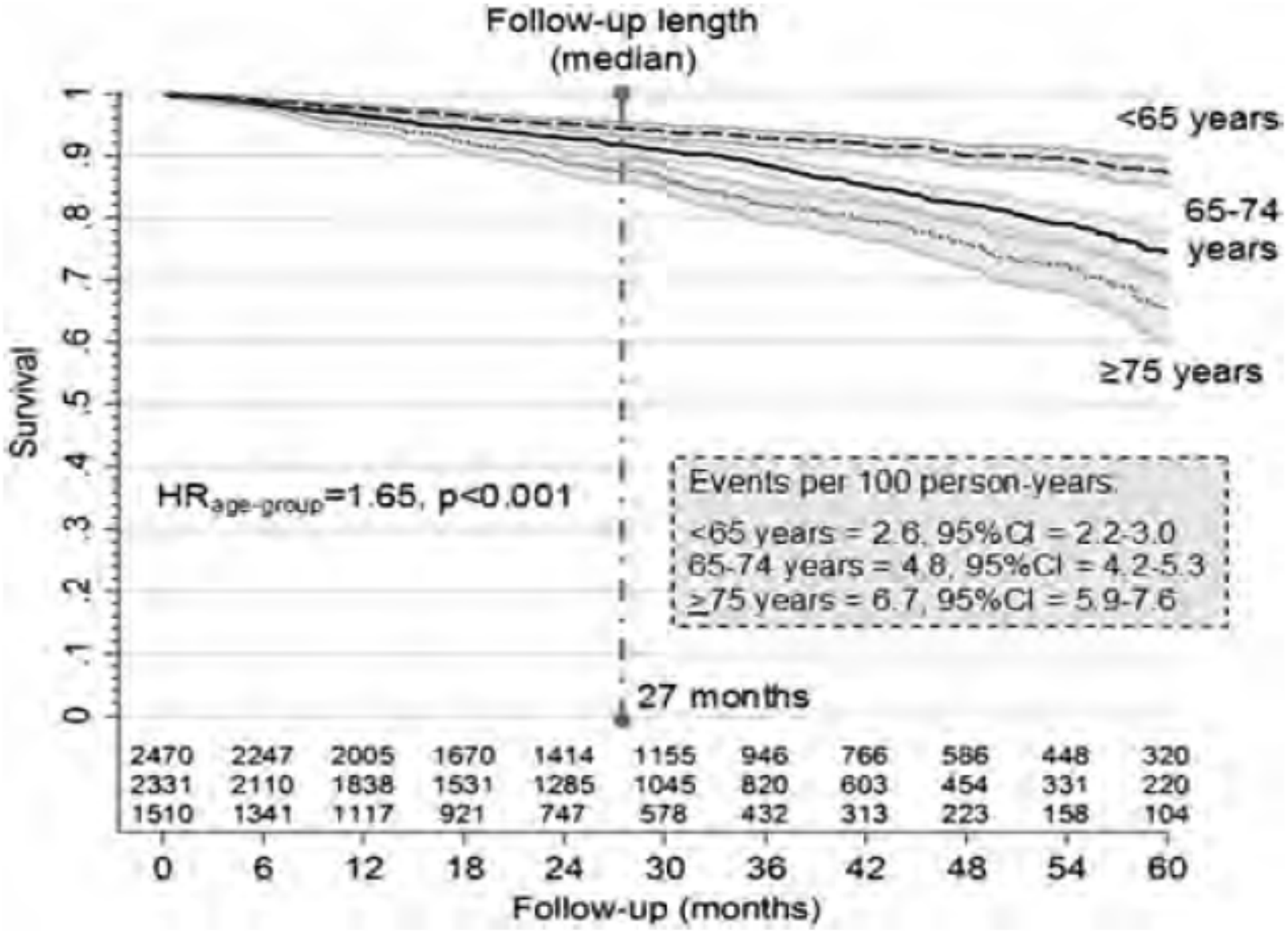
Determinants of All-Cause Mortality in Different Age Groups in Patients With Severe Systolic Left Ventricular Dysfunction Receiving an Implantable Cardioverter Defibrillator (from the Italian ClinicalService Multicenter Observational Project)

Stefano Fumagalli, MD, PhD[a,*], Maurizio Gasparini, MD[b], Maurizio Landolina, MD[c], Maurizio Lunati, MD[d], Giuseppe Boriani, MD, PhD[e], Alessandro Proclemer, MD[f], Massimo Santini, MD[g], Lorenza Mangoni, MSc[h], Margherita Padeletti, MD[a], Niccolò Marchionni, MD[a], and Luigi Padeletti, MD[i,j], on behalf of the Italian ClinicalService Project Centers

- 6311 ICD patients (CRT-ICD: 66.7 %)
- 1510 pts >75 y (24%)
- Prevalence of co-morbidities increases with age

Am J Cardiol 2014;113:1691-6

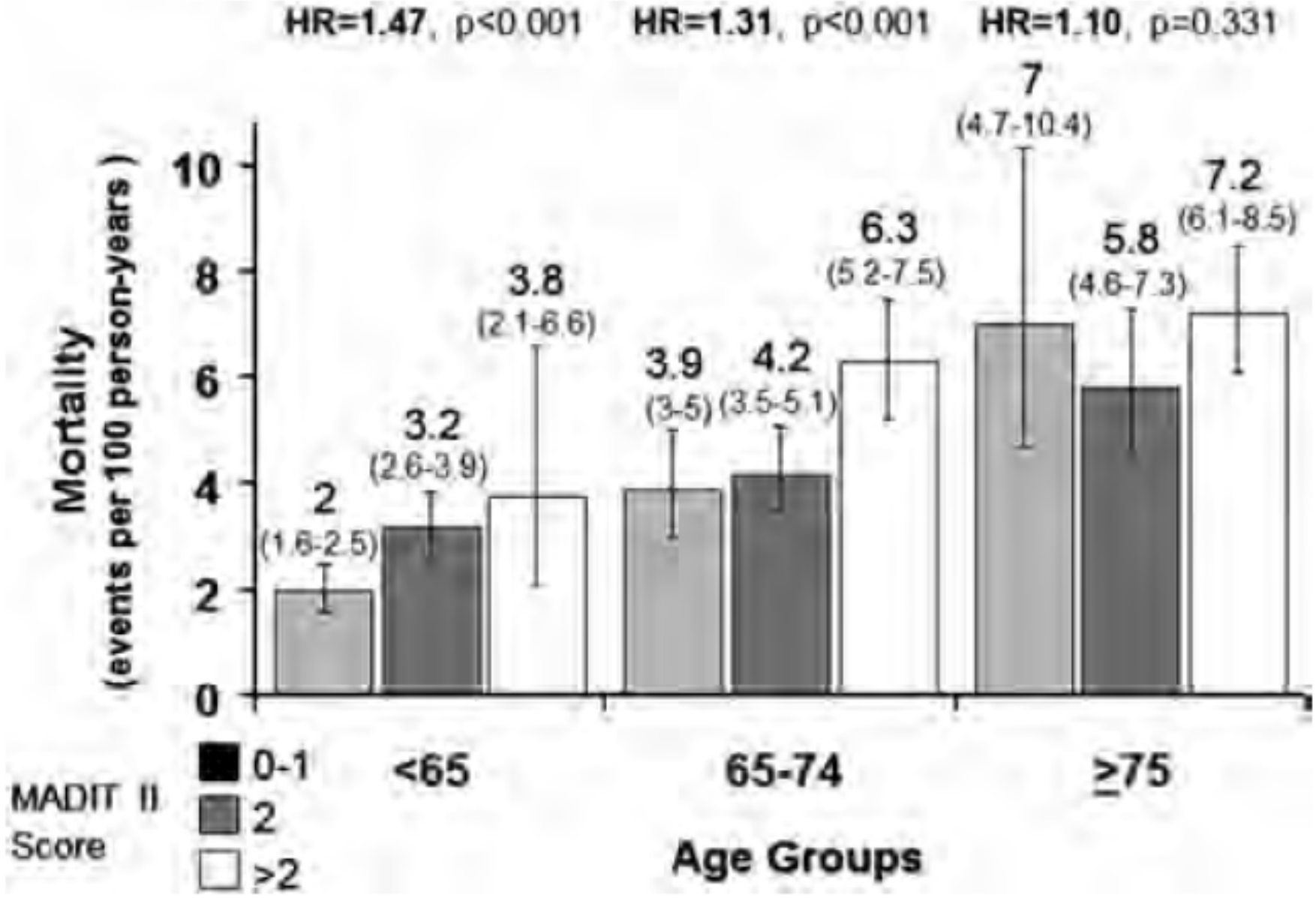
All cause mortality by age groups



Association of clinical characteristics with mortality (>75 y only age)

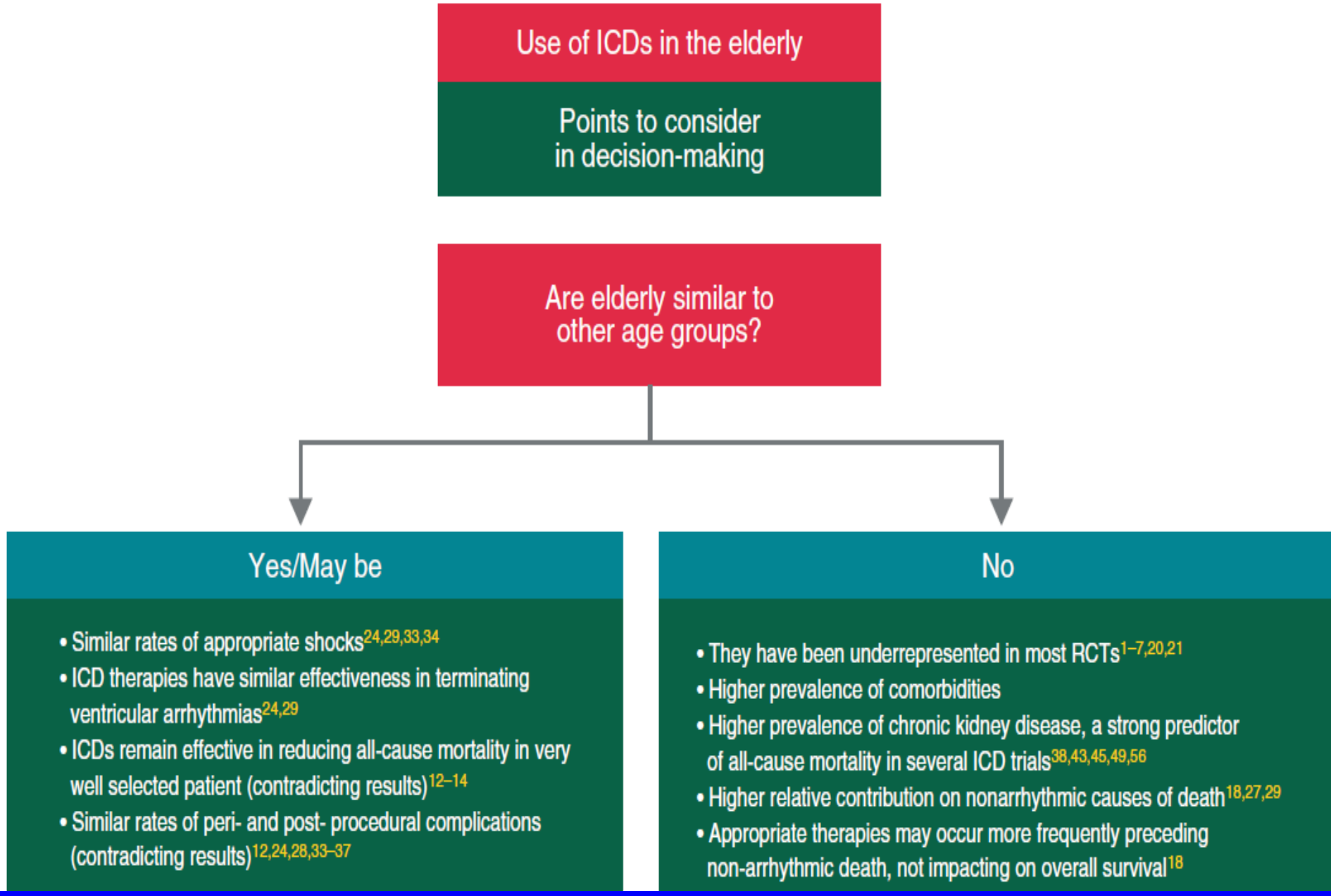
b. Multivariate analysis	HR	95% CI	p Value
Age group (delta·group)	1.58	1.38–1.80	<0.001
CAD (yes vs no)	1.67	1.67–1.35	<0.001
Chronic obstructive pulmonary disease (yes vs no)	1.55	1.18–2.04	0.001
Diabetes mellitus (yes vs no)	1.34	1.06–1.68	0.013
Renal failure (yes vs no)	1.63	1.23–2.18	<0.001
Ventricular arrhythmias (yes vs no)	1.43	1.16–1.77	<0.001
LVEF (delta·%)	0.97	0.96–0.98	<0.001

All cause mortality by age groups



Conclusions

- ***Indications:*** **The ICD registries indicate a progressive increase of over 80 y old ICD recipients.**
- ***Exceptions:*** **Biological age and minimum comorbidities should be the decisive factors in selection of best ICD candidates in the elderly.**
- ***Caveats:*** **In the elderly termination of VT/VF could prevent SCD, but results in a marginal prolongation of life for high non-SCD risk.**



Barra Europace doi:10.1093/europace/euu296

Trial & patient age

Trial (year)	Treatment group	Patients	Mean age (years)	Patients ≥ 65 y/o (%)	Hazard ratio for effect of ICD therapy on all-cause mortality (95% CI)
MADIT-I (1996) [5]	Total	196	63 ± 9*	53.5	0.46 (0.26–0.82)
	ICD	95	62 ± 9	53.5	
	Control	101	64 ± 9	53.5	
CABG-PATCH (1997) [4]	Total	900	64 ± 9*	49.89	1.07 (0.81–1.42)
	ICD	446	64 ± 9	50.0	
	Control	454	63 ± 9	50.0	
MUSTT (1999) [7]	Total	704	66.5*†	55.97	0.45 (0.32–0.63)
	ICD	161	65.4 (8.52)‡	56.9	
	Control	543	64.9 (9.65)‡	54.1	
CAT (2002) [14]	Total	104	52 ± 11	NR	0.83 (0.45–1.52)
	ICD	50	52 ± 12	NR	
	Control	54	52 ± 10	NR	
MADIT-II (2002) [6]	Total	1,232	64 ± 10*	48.0	0.69 (0.51–0.93)
	ICD	742	64 ± 10	44.2	
	Control	490	65 ± 10	51.4	
AMIOVIRT (2003) [15]	Total	103	NR	NR	NR
	ICD	51	58 ± 11	NR	
	Control	52	60 ± 12	NR	
DINAMIT (2004) [3]	Total	674	62 ± 11*	NR	1.08 (0.76–1.55, p = 0.66)
	ICD	332	61.5 ± 10.9	NR	
	Control	342	62.1 ± 10.6	NR	
DEFINITE (2004) [8]	Total	458	58.3	34.28	0.65 (0.40–1.06, p = 0.08)
	ICD	229	58.4	35.4	
	Control	229	58.1	33.2	
SCD-HeFT (2005) [9]	Total	2,521	60*†	34.49	0.77 (0.62–0.96, p = 0.007)§
	ICD	829	60.1†	35.5	
	Control (amiodarone)	845	60.4†	33.5	
	Control (placebo)	847	59.7†		

Non randomized studies of the effect of age on ICD efficacy

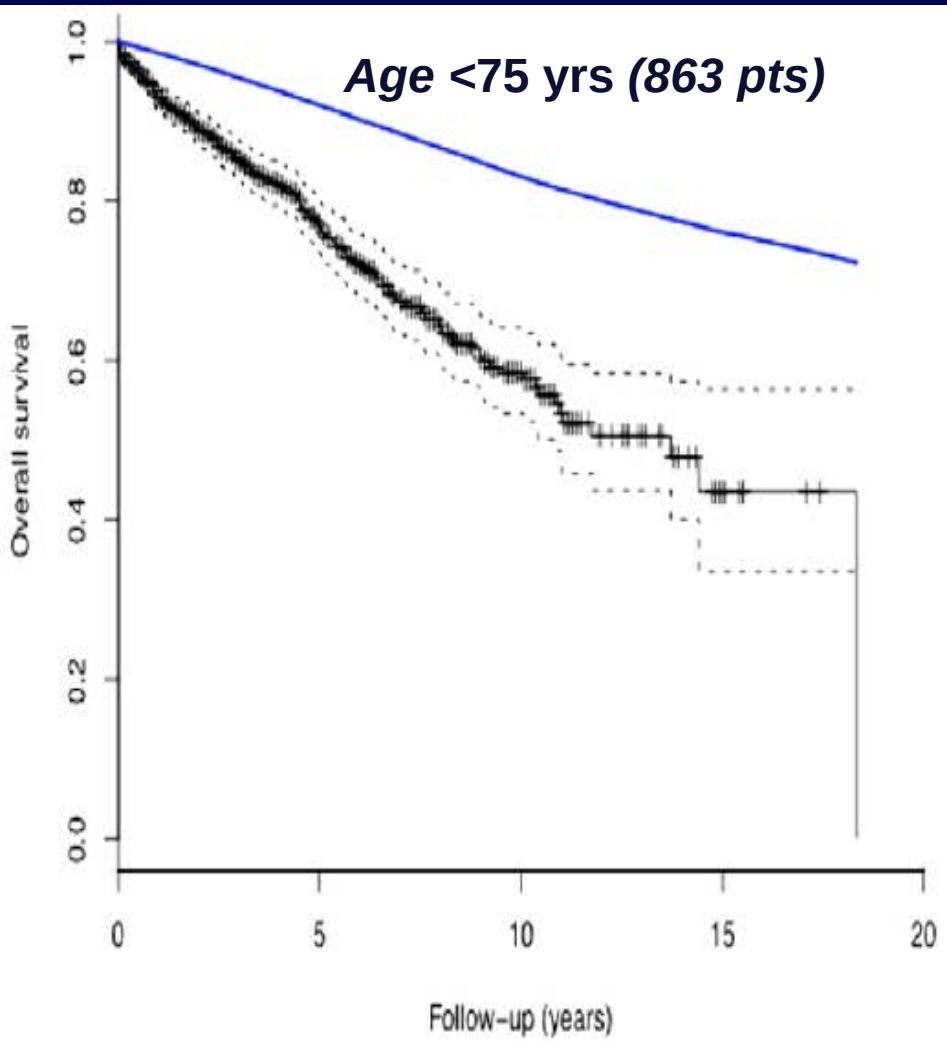
Author (year)	Inclusion criteria	Study type	Groups	Patients	Mean age (years ± SD)	Primary endpoint	Findings
Primary prevention							
Chan (2009) [25]	965 consecutive patients enrolled from seven outpatient cardiology clinics at two centers from March 2001 to June 2005	Prospective cohort in which 494 patients received an ICD	Total	965	67.3*	Long-term mortality	Comparable absolute and relative mortality risk reductions with ICD use among older patients despite higher annual mortality rates
			< 65	383			HR 0.74 (95% CI 0.43–1.28, p = 0.43)
			65–74	313			HR 0.76 (95% CI 0.45–1.29, p = 0.43)
			≥ 75	269			HR 0.59 (95% CI 0.39–0.90, p = 0.43)
Primary and secondary prevention							
Noseworthy (2004) [20]	Patients aged > 70 selected from database of 637 patients who underwent ICD implantation at single center from December 1985 to March 2002	Prospective case series	Total	637	63 ± 13	Actuarial survival	No difference in actuarial survival between 70–79 years age group and ≥ 80 years group (p = NS)
			70–79	183	73.6 ± 2.9		
			≥ 80	29	83.3 ± 2.3		
Duray (2005) [22]	375 consecutive ICD recipients with structural heart disease at single center	Retrospective case series	Total	375	63.6 ± 10.0	Time to death from any cause	No significant difference in average time to death among the two groups (28.4 ± 16.7 *vs* 30.4 ± 22.1 months, p = NS)
			< 70	273	59.7 ± 8.9		
			≥ 70	102	74.0 ± 3.1		

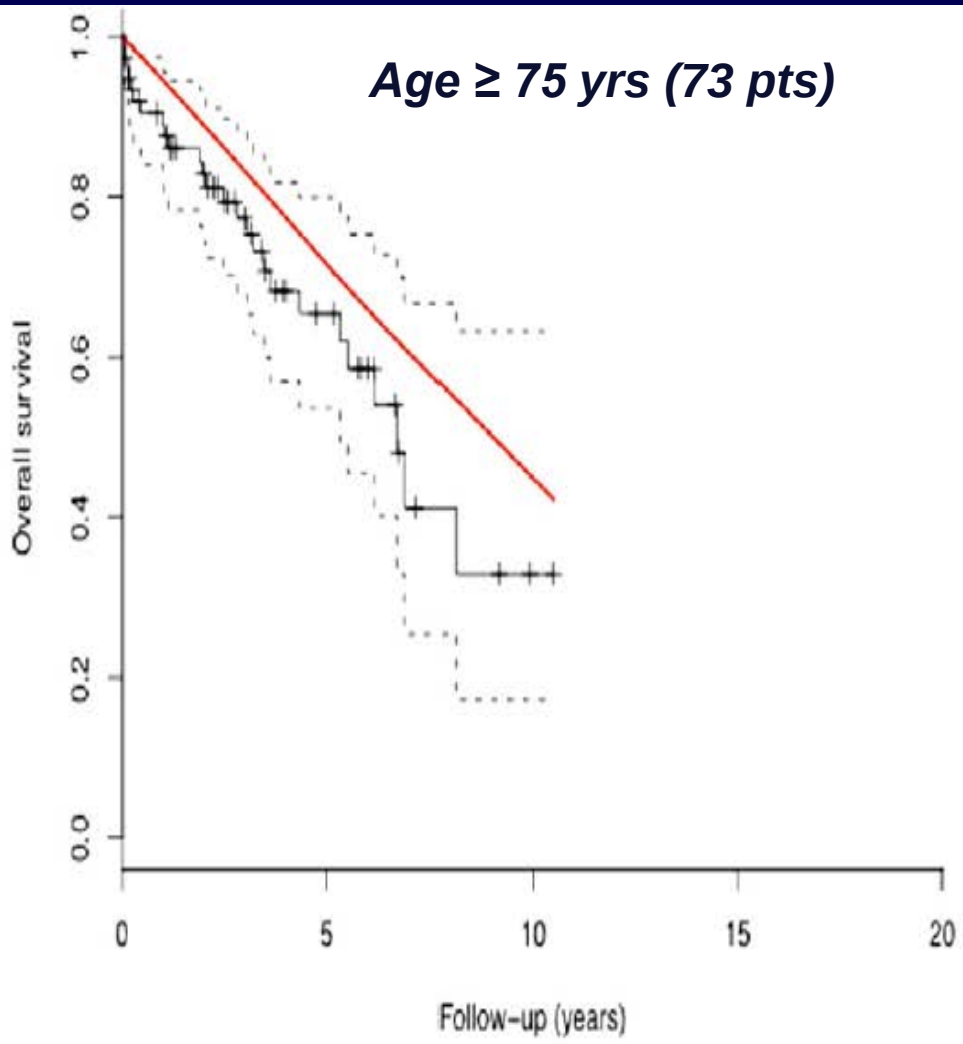
Non randomized studies of the effect of age on ICD efficacy

Author (year)	Inclusion criteria	Study type	Groups	Patients	Mean age (years ± SD)	Primary endpoint	Findings
Koplan (2006) [21]	Consecutive patients ≥ 80 years of age at ICD implantation from July 1995 to September 2003 and consecutive nonelderly patients aged 60–70 years who underwent ICD implantation over same time period	Retrospective case series	Total	348	NR	Median survival	Median survival was 4.2 years after implantation in the older group *vs* seven years in the younger group ($p < 0.01$)
			60–70	241	65 ± 3		
			≥ 80	107	82 ± 2		
Ermis (2007) [24]	250 consecutive patients who underwent ICD implantation at single center	Prospective case series	Total	208	NR	Ventricular tachy-arrhythmia burden	Total ventricular tachyarrhythmia burden (calculated as the number of VT and VF episodes per patient per month) based on total patient population at risk was 0.3 ± 2.3 (median: 0) and 0.4 ± 1.9 (median: 0) for Group 1 and Group 2, respectively ($p = 0.74$)
			< 75	159	59 ± 12		
			≥ 75	49	79 ± 3		
Grimm (2007) [23]	500 consecutive patients from the Marburg Defibrillator database who underwent ICD implantation at single center from January 1994 to February 2006	Retrospective case series; indications for ICD implantation were not reported	Total	500	58 ± 14	Overall mortality	Five-year overall mortality rate was higher in patients age ≥ 75 than in patients < 75 years (55% *vs* 21%, $p = 0.001$)
			< 75	460	56 ± 14		
			≥ 75	40	77 ± 4		

Benefit and Mortality of ICD in Pts ≥75 vs <75 yrs

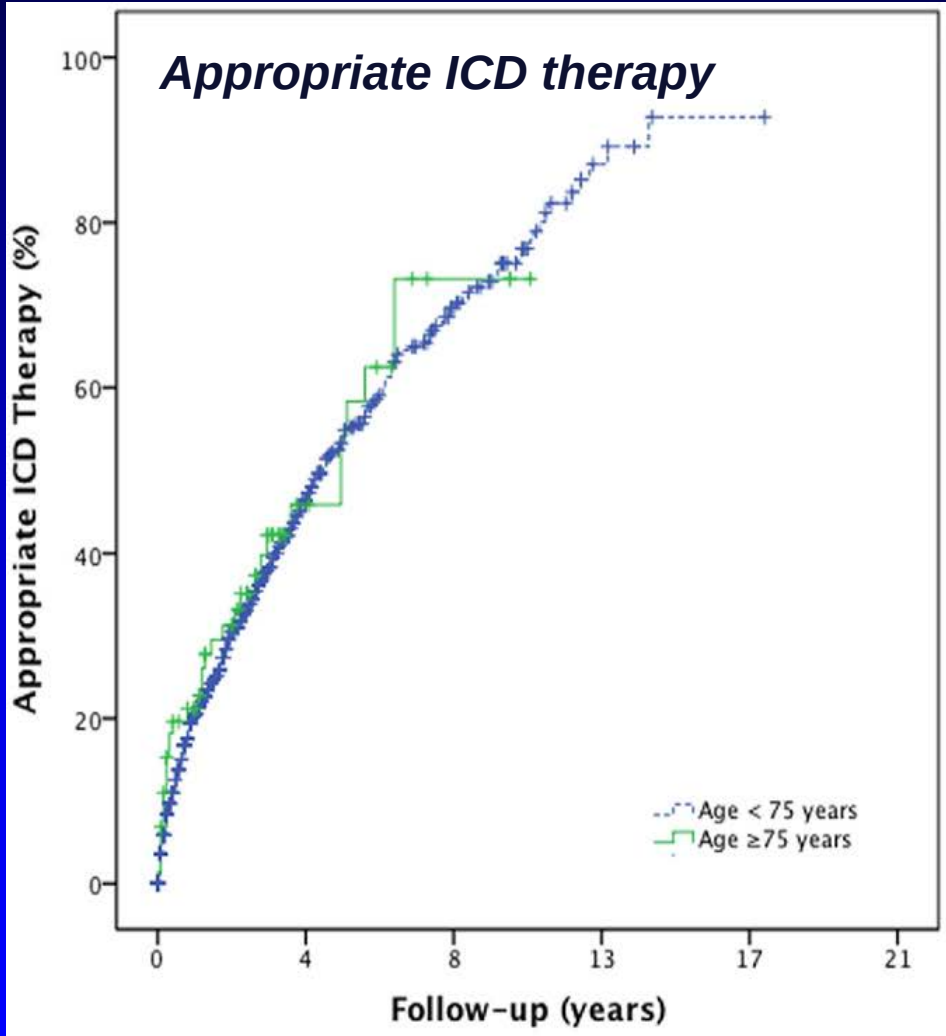
Survival of ICD recipients and age-matched overall population (straight lines)

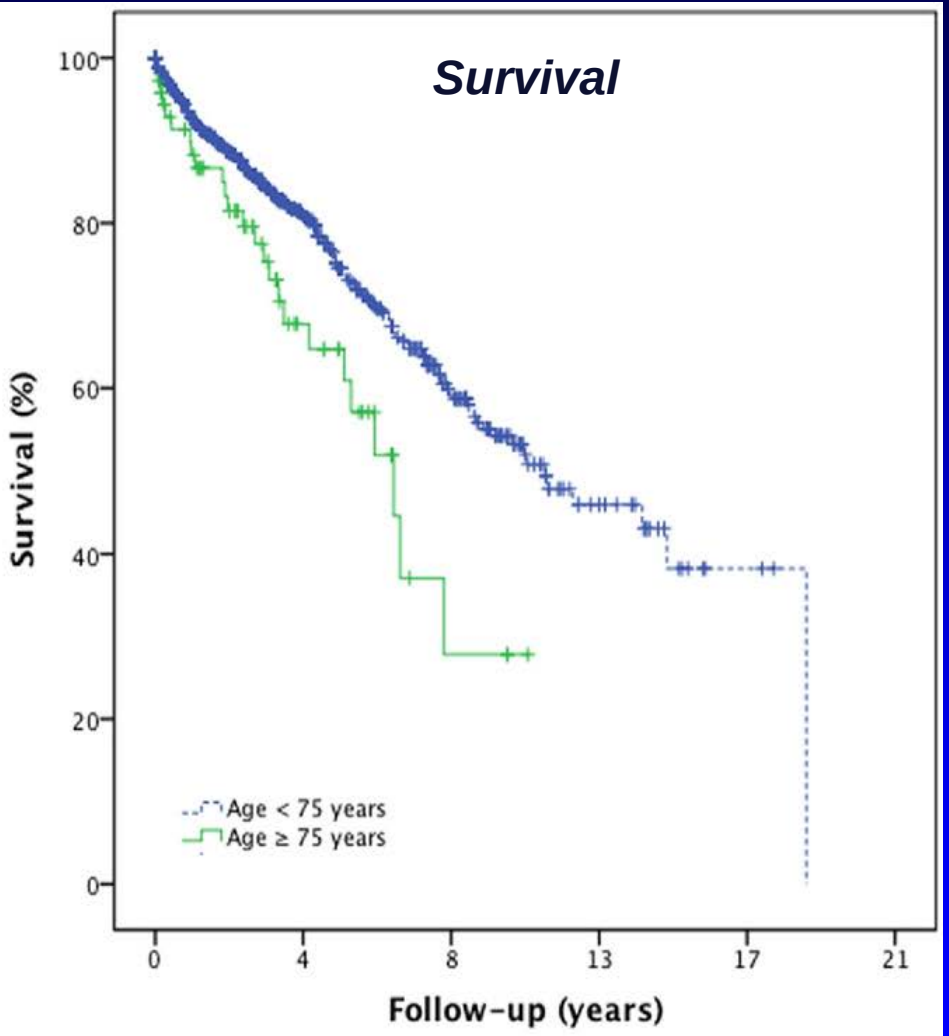




Brullmann et al, Am J Cardiol 2012 ;109:712–717

Benefit and Mortality of ICD in Pts ≥75 vs <75 yrs

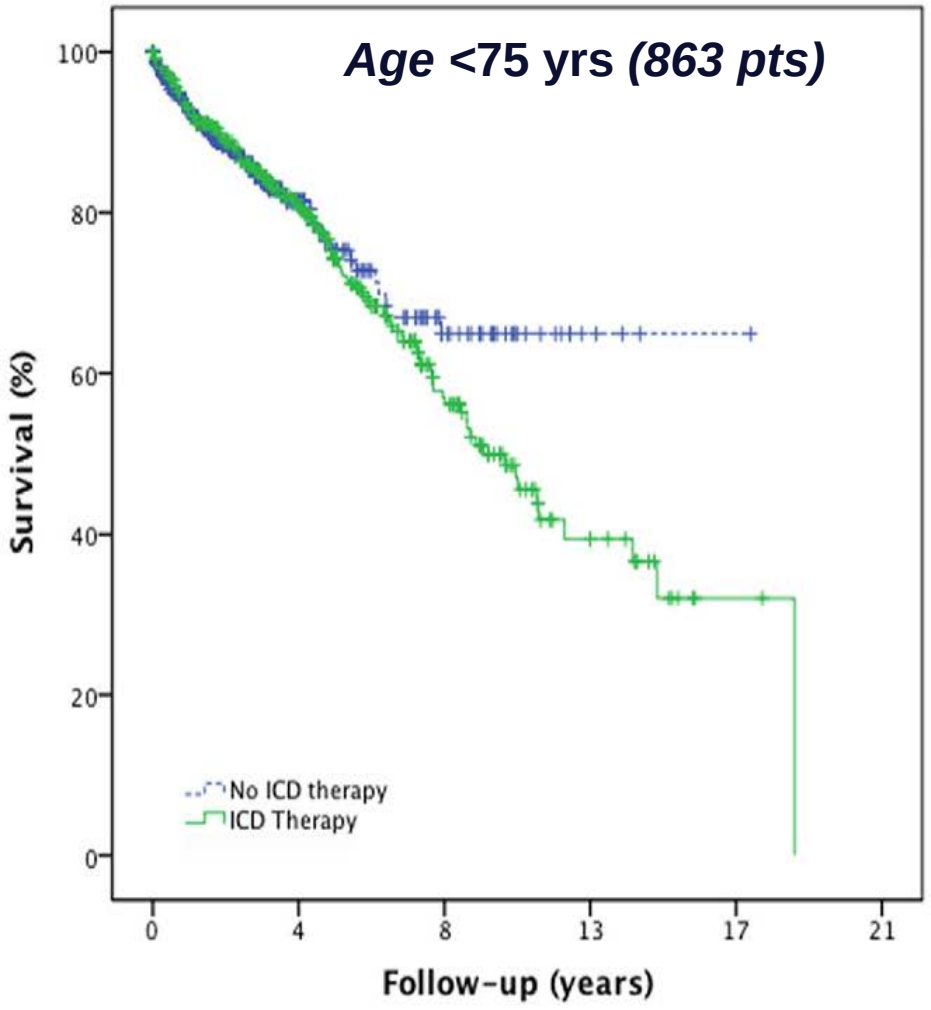


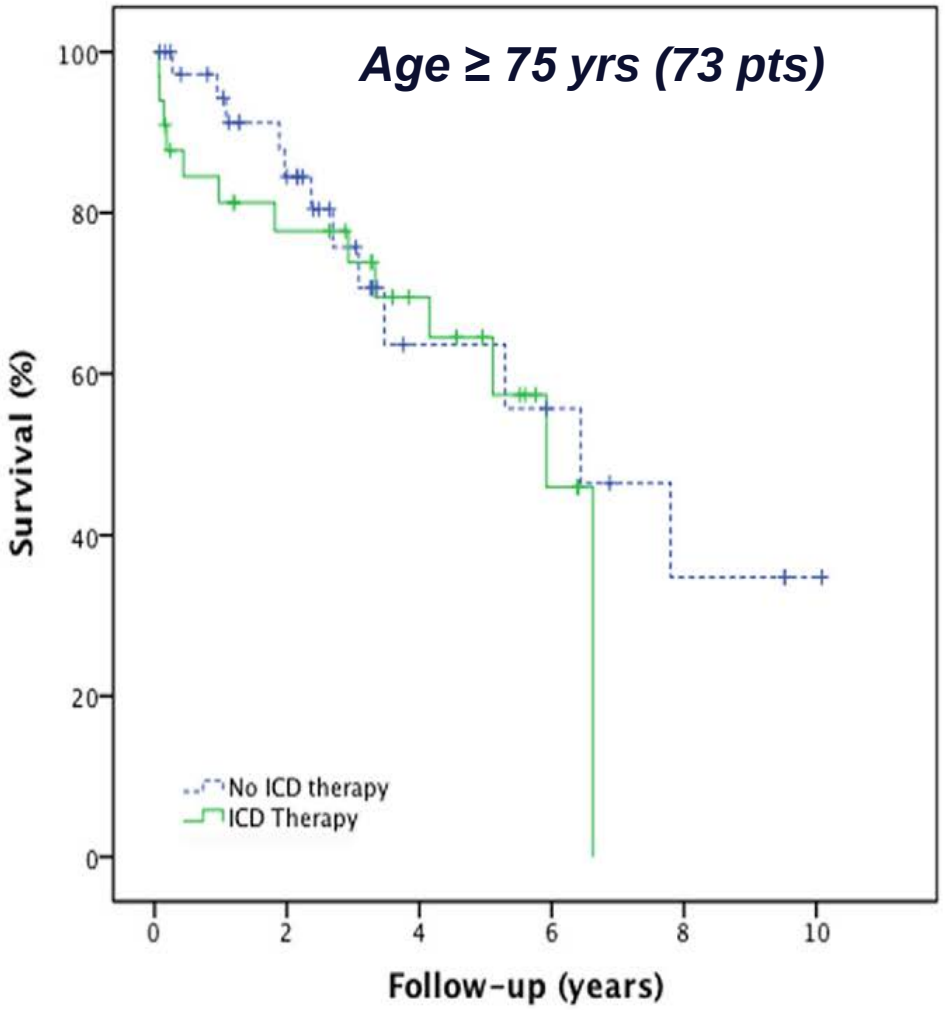


Brullmann et al, Am J Cardiol 2012;109:712–717

Benefit and Mortality of ICD in Pts ≥75 vs <75 yrs

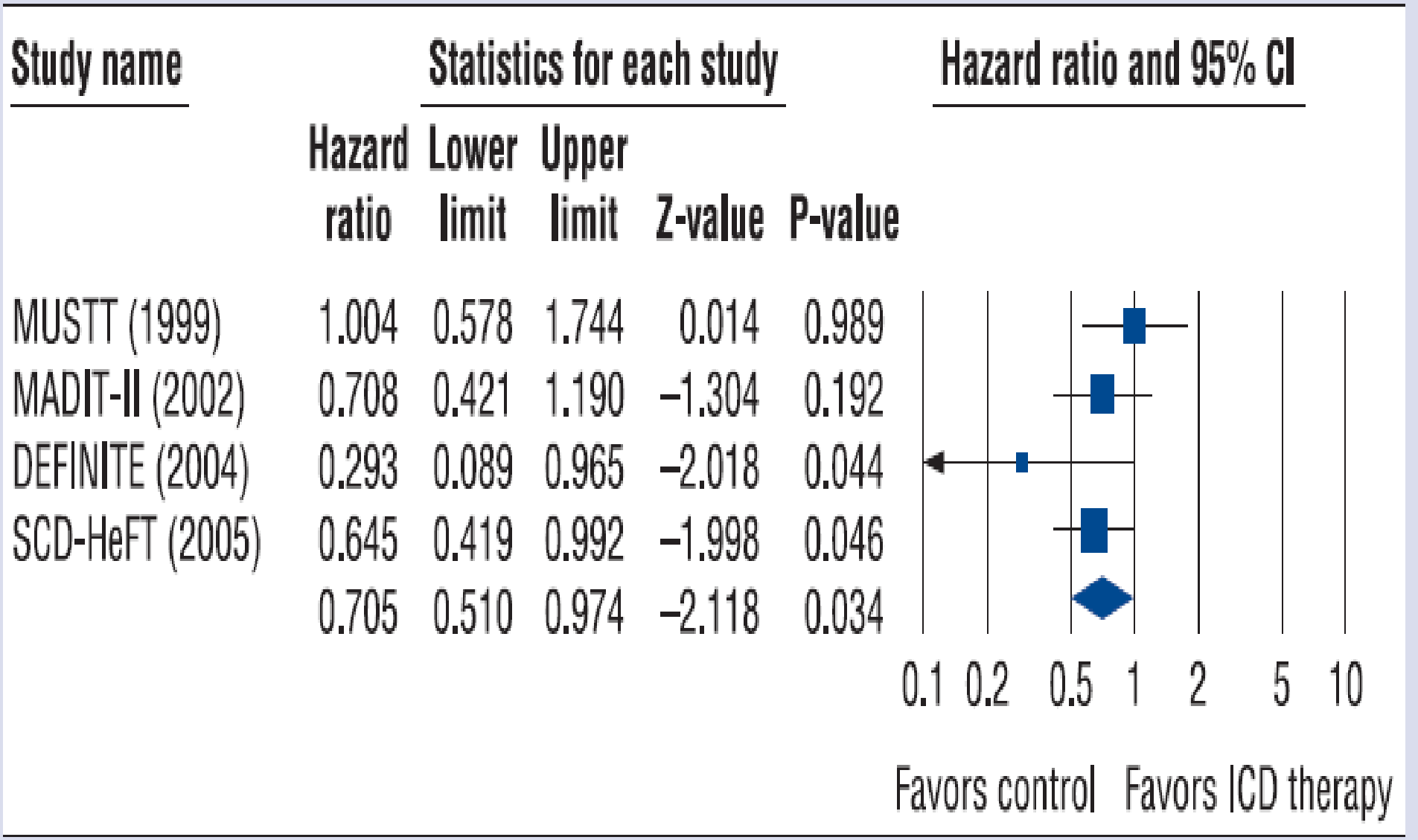
Survival curves according to delivery of ICD therapy





Brullmann et al, Am J Cardiol 2012 ;109:712–717

HR for all-cause mortality in patients ≥ 75 yrs



Primary Prevention

	Hazard Ratio	95% CI	P_{trend} Value
Competing risk analysis: primary prevention*			
Death			
Age 18–49 y	Reference	Reference	
Age 50–59 y	1.56	0.71–3.39	
Age 60–69 y	2.10	1.01–4.39	<0.001
Age 70–79 y	2.42	1.16–5.06	
Age ≥80 y	3.01	1.36–6.68	
Appropriate shock			
Age 18–49 y	Reference	Reference	
Age 50–59 y	0.83	0.54–1.29	
Age 60–69 y	0.77	0.50–1.18	0.130
Age 70–79 y	0.68	0.44–1.07	
Age ≥80 y	0.71	0.38–1.34	

Secondary Prevention

Competing risk analysis: secondary prevention†

Death			
Age 18–49 y	Reference	Reference	
Age 50–59 y	1.41	0.51–3.89	
Age 60–69 y	1.56	0.59–4.08	<0.001
Age 70–79 y	1.88	0.72–4.93	
Age ≥80 y	3.61	1.35–9.67	
Appropriate shock			
Age 18–49 y	Reference	Reference	
Age 50–59 y	0.91	0.55–1.50	
Age 60–69 y	1.15	0.73–1.82	0.810
Age 70–79 y	0.89	0.55–1.45	
Age ≥80 y	0.79	0.43–1.44	