Fibrillazione Atriale ed Ictus Cardioembolico. Roma, 15 Maggio 2013

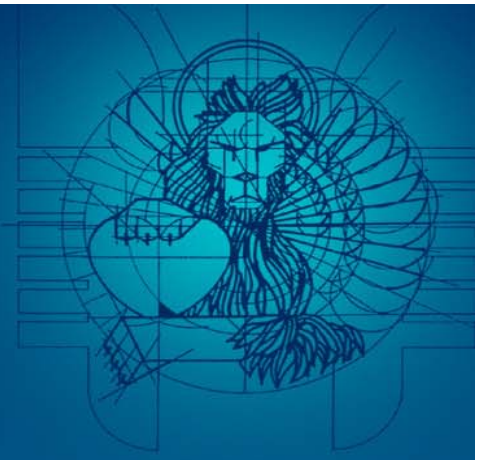
Epidemiologia e prognosi della fibrillazione atriale: dimensioni del problema

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Definizione

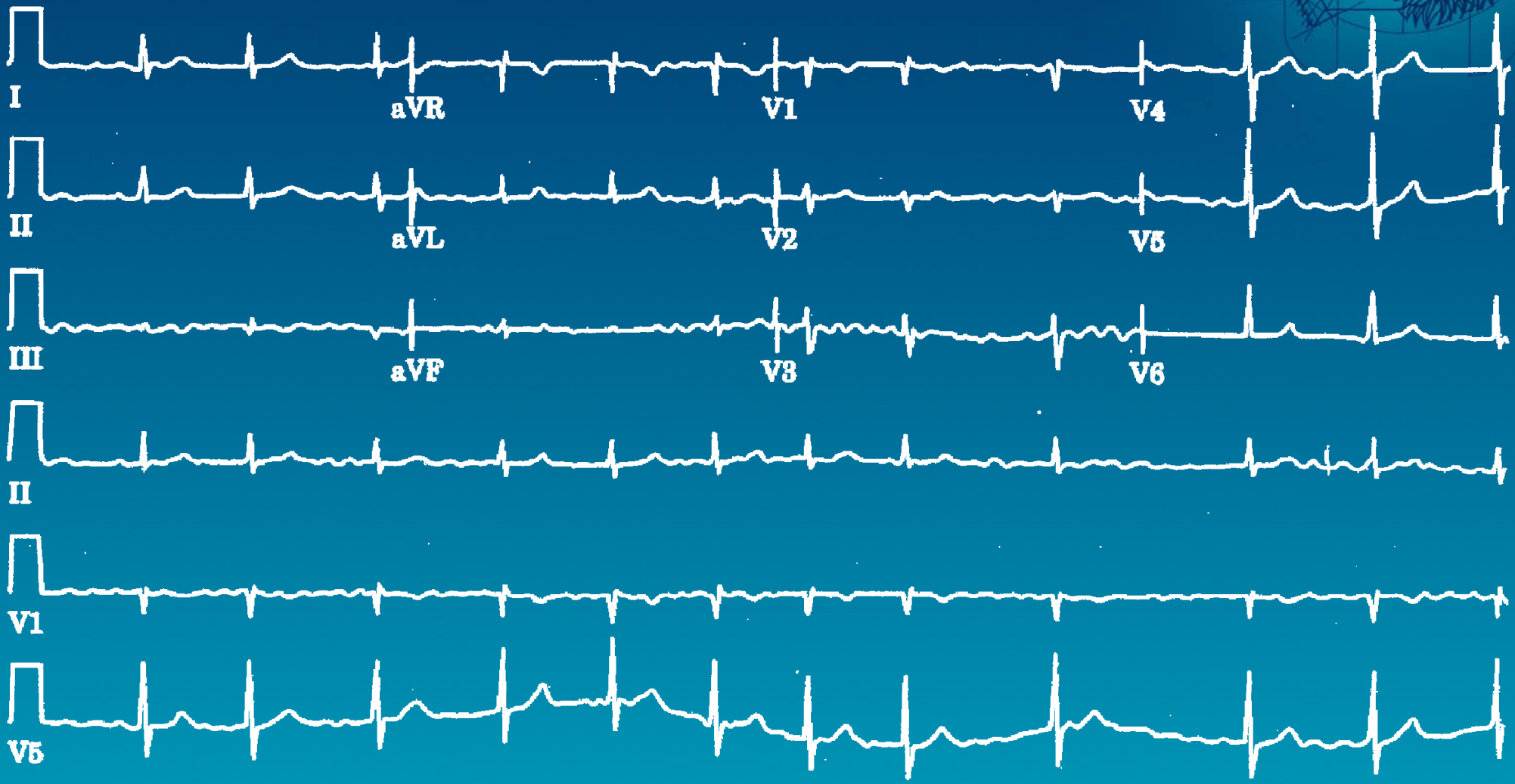


La ***Fibrillazione Atriale*** è una tachiaritmia sopraventricolare caratterizzata da un'attivazione atriale caotica che determina una perdita della funzione meccanica atriale

Fibrillazione Atriale



ECG



Prevalenza

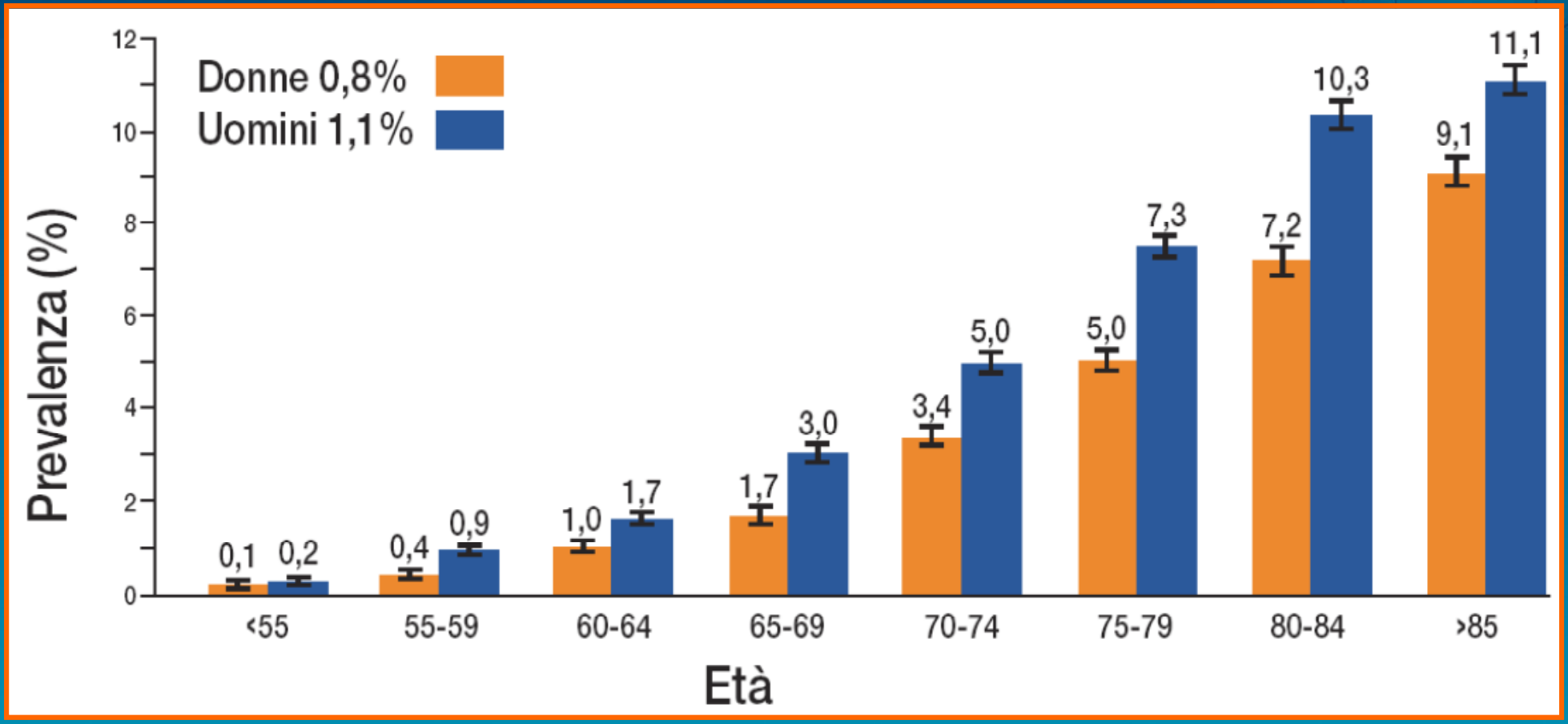
FA nella popolazione generale:

Europa	USA	Olmsted County
0,90%*	0,95%**	2,5%***

* Stewart S et al. *Heart* 2004; 90: 286-292;
** Go AS et al. *JAMA* 2001; 285: 2370-2375;
*** Miyasaka Y et al. *Circulation* 2006; 114: 119-125

Prevalenza

Stratificata per età e sesso:



Go AS et al. *JAMA* 2001; 285: 2370-75

Incidenza

FA nella popolazione generale:

Europa	USA	Olmsted County
0,18%*	0,2%**	0,34%***

* Stewart S et al. *Heart* 2004; 90: 286-292;
** Go AS et al. *JAMA* 2001; 285: 2370-2375;
*** Miyasaka Y et al. *Circulation* 2006; 114: 119-125

Rischio di comparsa di fibrillazione atriale

FA nella popolazione generale con età > 40-55 anni:

	ETÀ > 40 ANNI (Framingham Study)	ETÀ > 55 ANNI (Rotterdam Study)
Uomini	26%*	23,8%**
Donne	23%*	22,2%**
	1 su 4	1 su 4

*Lloyd-Jones DM et al. *Circulation* 2004; 110: 1042-1046;
**Heeringa J et al. *Eur Heart J* 2006; 27: 949-953

Epidemiologia della Fibrillazione Atriale

Prevalenza: 0.9-2.5%

Incidenza: 0.2-0.34%

Soggetti con FA
(milioni)

- USA ~ 3-7.6
- EU ~ 5-12.5

Nuovi casi di FA per anno
(milioni)

- USA ~ 0.6-1
- EU ~ 1-1.7

Prevalenza della FA in Italia per età diverse

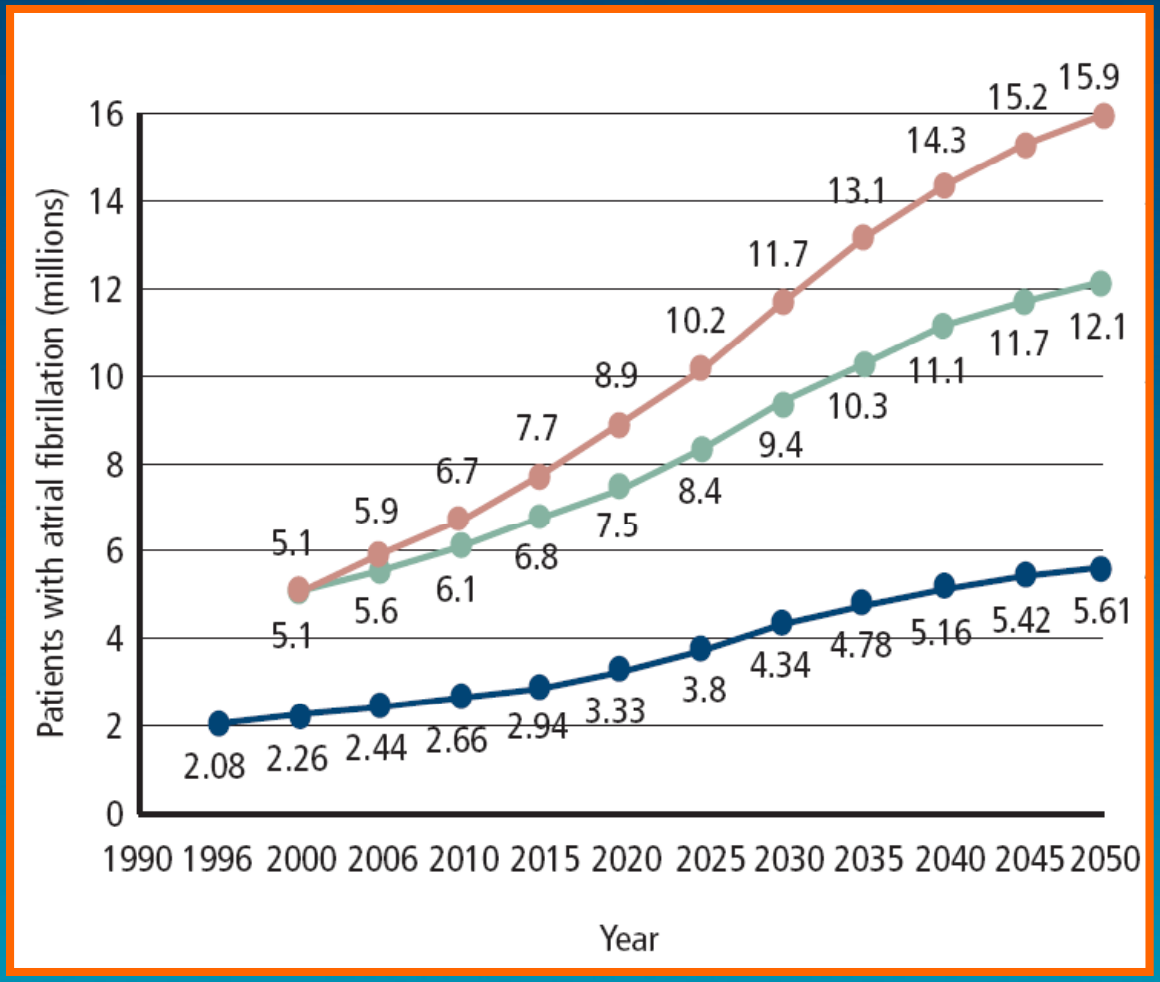
(Anni 2011-2051)

Età	Popolazione Italiana (dati ISTAT)					Prevalenza FA	N. pazienti con FA				
	(2011)	(2021)	(2031)	(2041)	(2051)	%	(2011)	(2021)	(2031)	(2041)	(2051)
55-59	3.714.610	4.710.457	4.813.096	3.843.489	3.593.178	0,7	26.002	32.973,2	33.692	26.904	25.152
60-64	3.815.181	4.005.263	4.801.497	4.196.544	3.636.034	1,7	64.858	68.089,5	81.625	71.341	61.813
65-69	3.045.131	3.520.074	4.498.131	4.633.189	3.733.189	4,0	121.805	140.803	179.925	185.328	149.327
70-74	3.085.299	3.451.837	3.687.660	4.472.028	3.951.576	6,0	185.118	207.110	221.260	268.322	237.095
75-79	2.524.660	2.557.450	3.038.507	3.963.404	4.144.782	9,0	227.219	230.171	273.466	356.706	373.030
80-84	1.947.783	2.276.051	2.652.205	2.941.603	3.655.219	13,5	262.951	307.267	358.048	397.116	493.455
85-	1.709.555	2.427.646	2.903.393	3.675.619	4.835.515	17,8	304.301	432.121	516.804	654.260	860.722
Totale	**60.468.034**	**61.706.810**	**62.157.325**	**62.225.183**	**61.611.498**		**1.192.254**	**1.418.534**	**1.664.819**	**1.959.978**	**2.200.594**
Scostamento	-	2.0 %	0.7 %	0.1%	-1.0%		-	19.0%	17.4%	17,7%	12.3%
Prevalenza della FA nella popolazione gnerale							1,97%	2,30%	2,68%	3,15%	3,57%

Themistoclakis S. et al. *G Ital Cardiol* 2011;12:726-76

Proiezione dell'incremento dei casi di FA

Studi ATRIA e Olmsted County:



Olmsted County
(assumendo un incremento continuo dell'incidenza di FA)

Olmsted County
(non assumendo ulteriori incrementi di incidenza della FA)

ATRIA

Go AS et al. *JAMA* 2001; 285: 2370-75

Miyasaka Y et al. *Circulation* 2006; 114: 119-125

Cause dell'aumento della prevalenza e dell'incidenza della fibrillazione atriale

Invecchiamento rapido della popolazione con considerevole aumento del numero delle persone anziane che sono a rischio elevato di sviluppo di fibrillazione atriale

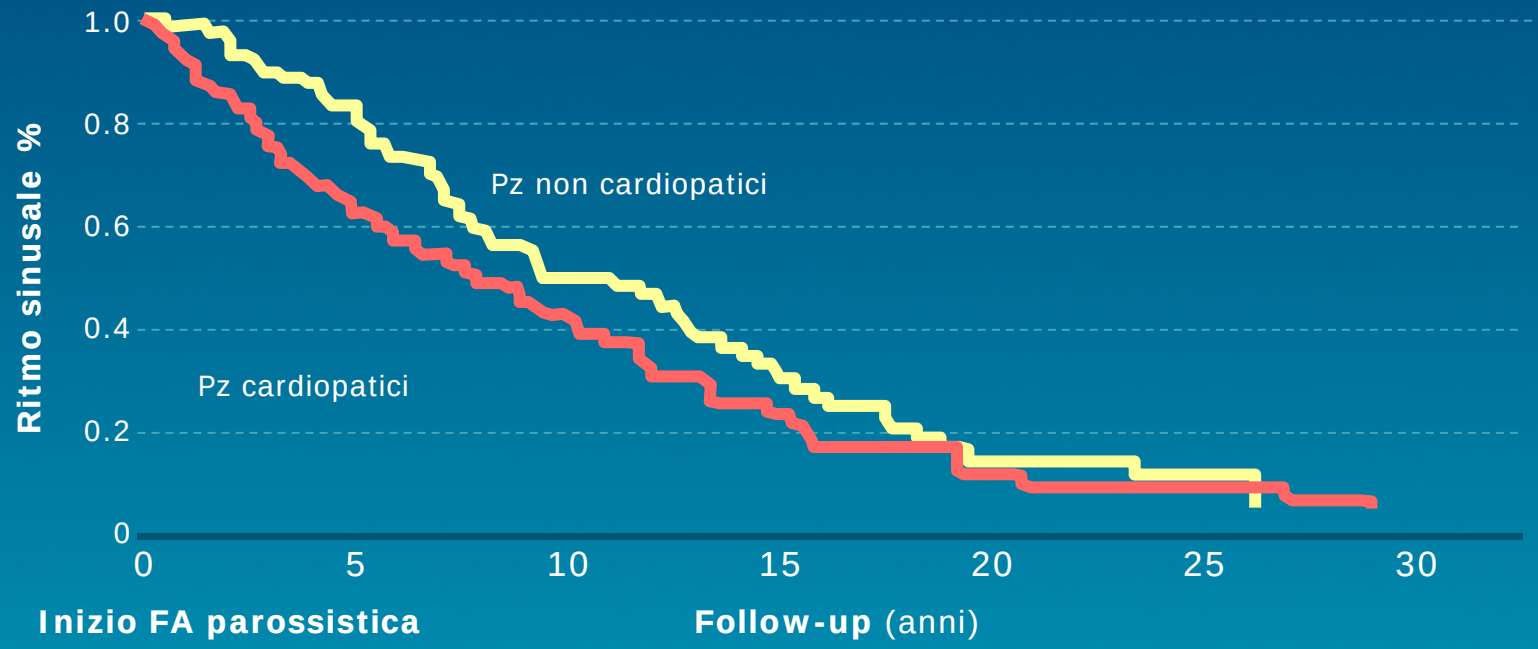
Crescita della popolazione

Aumento della sopravvivenza di soggetti affetti da condizioni cliniche strettamente associate alla fibrillazione atriale, come ipertensione arteriosa, malattia coronarica e insufficienza cardiaca

Miyasaka Y et al. *Circulation* 2006; 114: 119-125
Steinberg JS et al. *Heart* 2004; 90: 239-240

Progressione da FA Parossistica a Persistente

Trasformazione da FA parossistica a persistente: 5.5% pazienti per anno



Kato et al. *Circ J* 2004; 68: 568

Predictors of Progression of Recently Diagnosed Atrial Fibrillation in REgistry on Cardiac Rhythm DisORDers Assessing the Control of Atrial Fibrillation (RecordAF)—United States Cohort

Yuan-Yuan Zhang, MD, PhD[a], Chunfu Qiu, PhD[b], Pamela J. Davis, MD[c], Mehul Jhaveri, PharmD, MPH[b], Eric N. Prystowsky, MD[d], Peter Kowey, MD[e], and William S. Weintraub, MD[a,*]

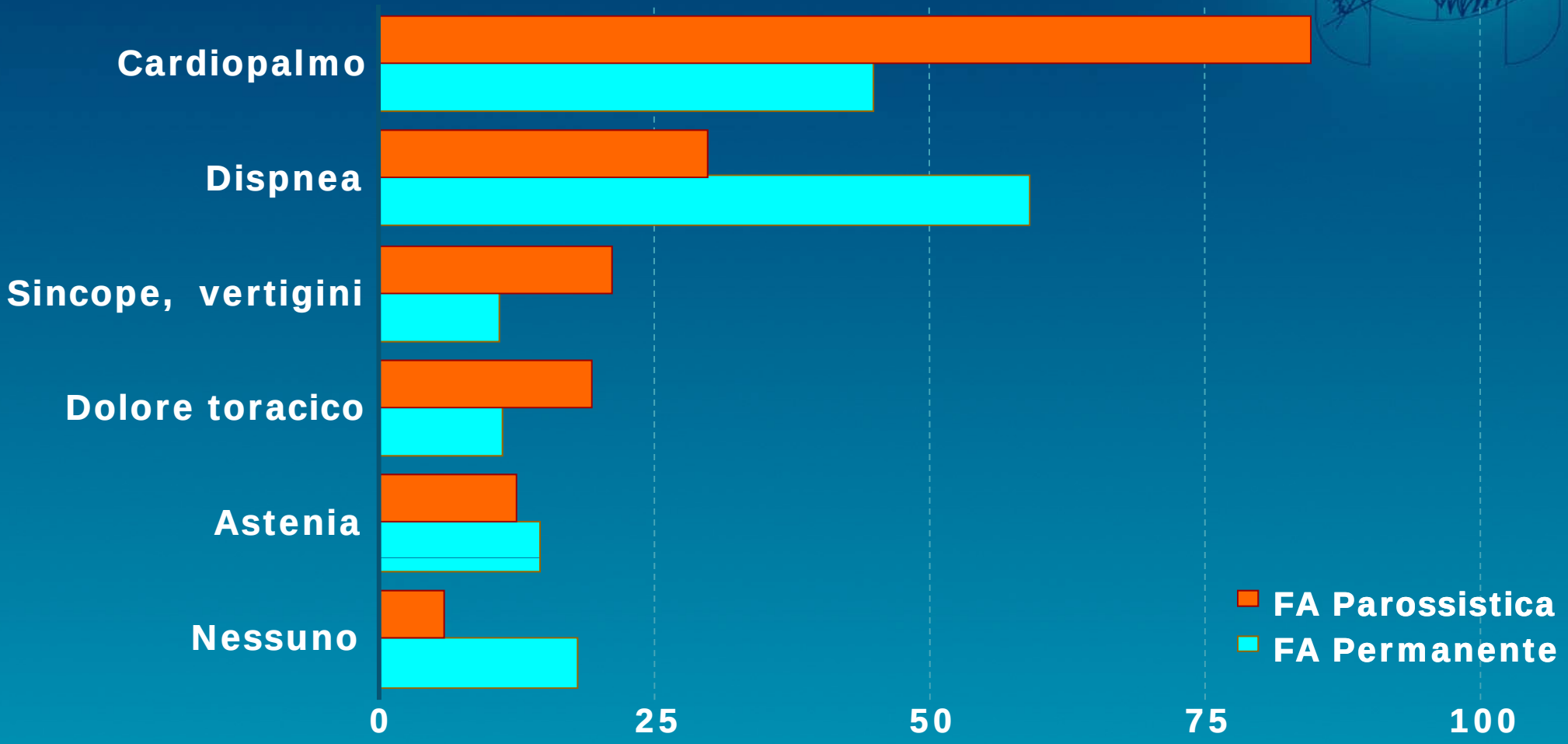
AF progression occurred in 18.6% of patients at 12 months

AF Status	Treatment Strategy at Baseline				p Value
	Rate-Control (n = 546)		Rhythm-Control (n = 370)		
	Paroxysmal at Baseline	Persistent at Baseline	Paroxysmal at Baseline	Persistent at Baseline	
Patients at baseline (n)	334 (61.2%)	212 (38.8%)	298 (80.5%)	72 (19.5%)	<0.001*
Patients at 12 mo (n)	265	159	238	57	
Paroxysmal	227 (85.7%)	38 (23.9%)	231 (97.1%)	27 (47.4%)	
Persistent	15 (5.7%)	42 (26.4%)	1 (0.4%)	20 (35.1%)	
Permanent	23 (8.7%)	79 (49.7%)	6 (2.5%)	10 (17.5%)	<0.001†
AF progression	38 (14.3%)	79 (49.7%)	7 (2.9%)	10 (17.5%)	<0.001‡; <0.001§
Total progression	117 (27.6%)		17 (5.8%)		<0.001‖

Zhang et al. *Am J Cardiol* 2013

Sintomi della fibrillazione atriale

Studio ALFA: FA parossistica n=167; permanente/cronica n=389



Levy S et al. *Circulation* 1999; 99. 3028-35

Incidenza della FA asintomatica

	(%)
Riscontro occasionale/ ECG*	**16 - 25**
Durante terapia AA / TTEM^	**56 - 70**
Portatori di PM – ICD / Memorie device°	**51 - 74**

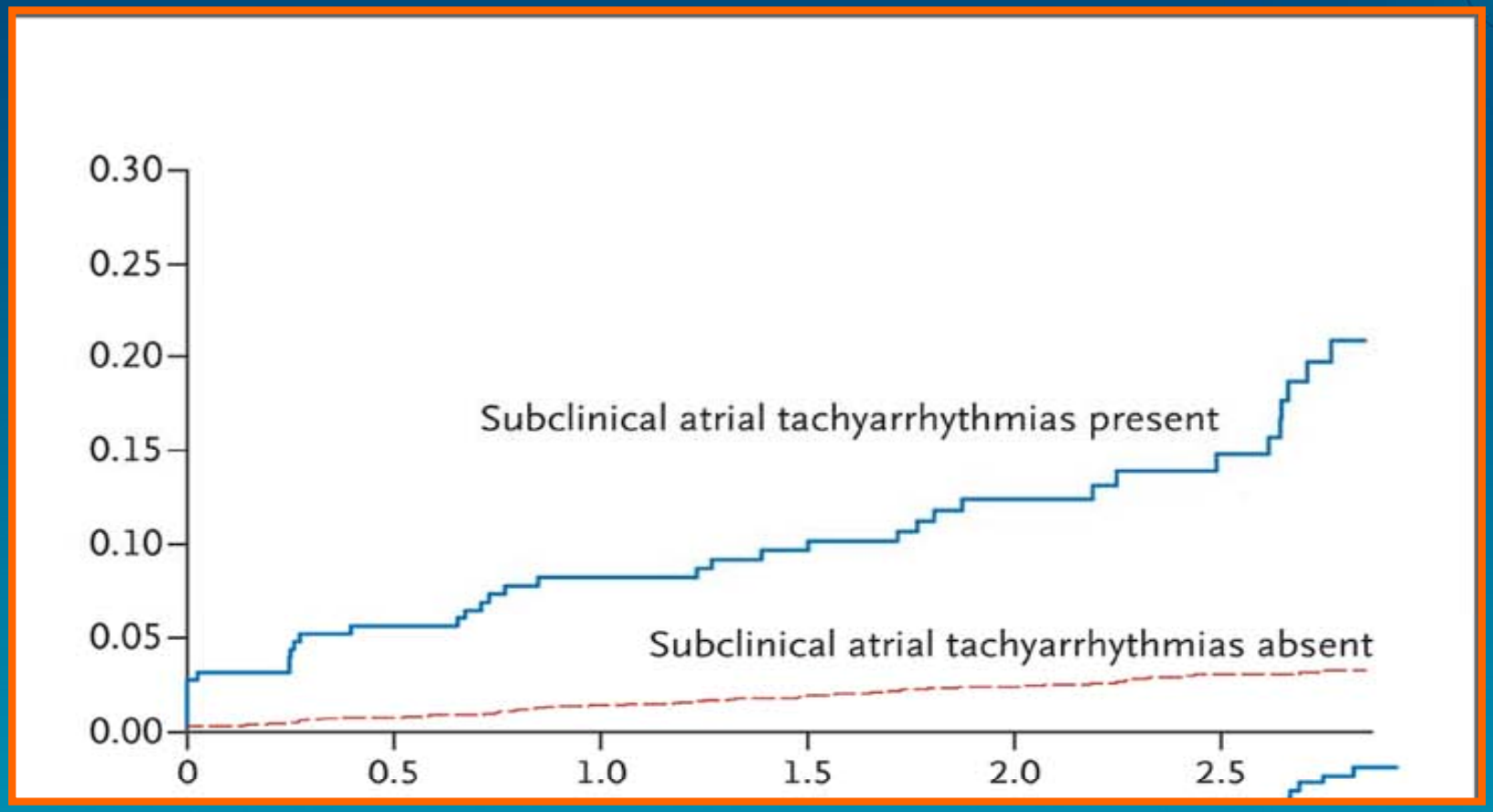
*Kerr CR et al. Eur Heart J 1996; 17 (suppl C): 48-51; Nieuwlaat R et al. Eur Heart J 2005; 26: 1422-34; Miyasake Y et al. Circulation 2006; 114: 119-25

^Fetsch T et al. Eur Heart J 2005; 26: 1422-34; Patten M et al. Eur Heart J 2004; 25: 1395-404

° Israel CW et al J Am Coll Cardiol 2004; 43:47-5; Glotzer TV et al. Circulation 2003; 107: 1614-9 ; Capucci A et al. J Am Coll : Cardiol 2005; 26: 1913-20

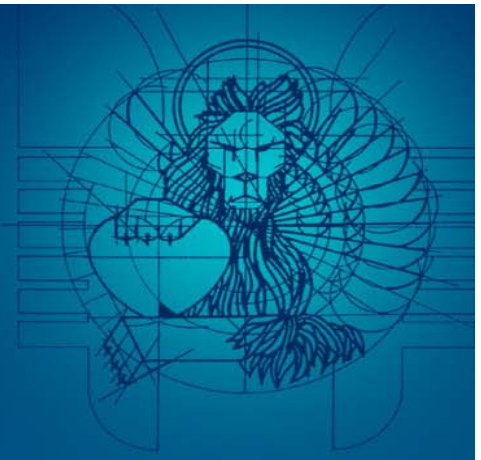
Rischio di tachiartmie atriali cliniche in pazienti con o senza forme subcliniche rilevate da PM/ICD

Studio ASSERT:



Healey JS et al. N Engl J Med 2012;366:120-9

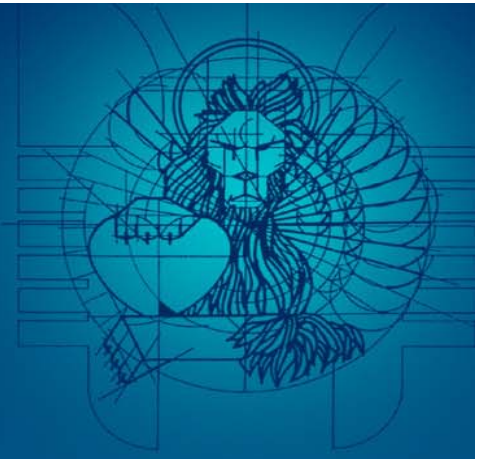
Fibrillazione Atriale



Influenza sulla prognosi:

- ⬇ Qualità della vita
- ⬆ Complicanze tromboemboliche
- ⬆ Scompenso cardiaco
- ⬆ Mortalità cardiovascolare

Fibrillazione Atriale



Influenza sulla prognosi:

- ⬇ Qualità della vita
- ⬆ Complicanze tromboemboliche
- ⬆ Scompenso Cardiaco
- ⬆ Mortalità cardiovascolare

AFib has an Impact on All Aspects of QoL

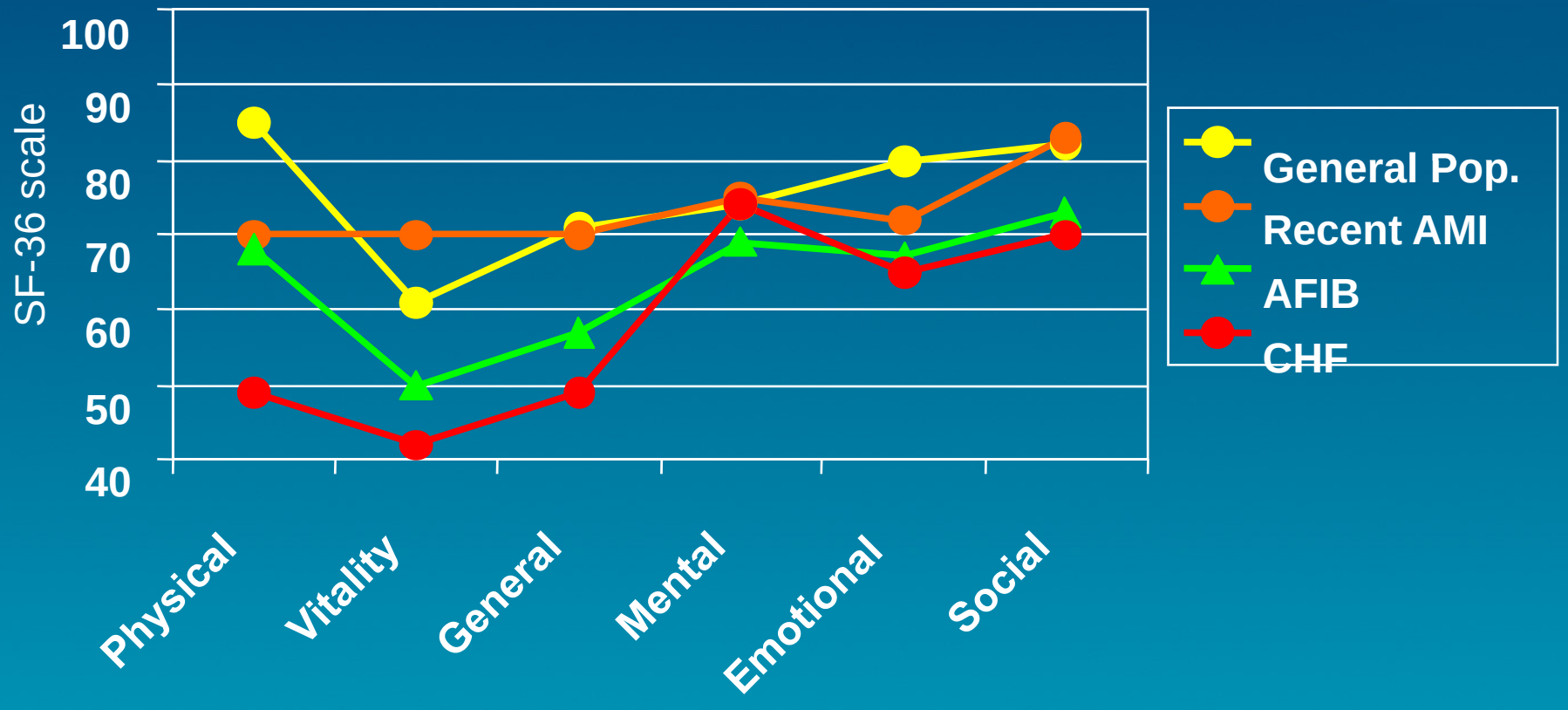
SF-36 quality of life scores in AF patients and healthy subjects:

SF-36 scale	AF patients (n=152)	Healthy controls (n=47)
General health	54 ± 21	78 ± 17*
Physical functioning	68 ± 27	88 ± 19*
Role physical	47 ± 42	89 ± 28*
Vitality	47 ± 21	71 ± 14*
Mental health	68 ± 18	81 ± 11*
Role emotional	65 ± 41	92 ± 25*
Social functioning	71 ± 28	92 ± 14*
Bodily pain	69 ± 19	77 ± 15*

* $p<0.001$

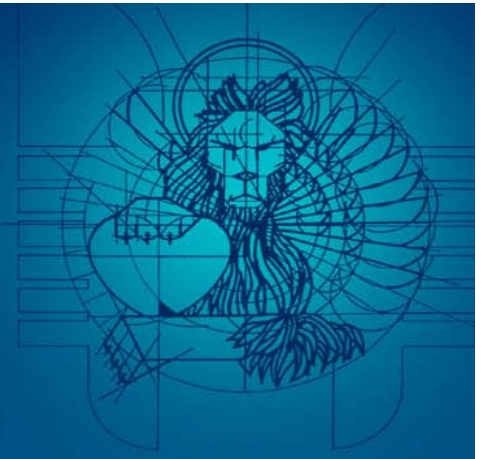
Dorian P et al. *J Am Coll Cardiol* 2000; 36: 1303

Qualità della vita in pazienti con FA rispetto ad altre condizioni cliniche



Jung W *JACC* 1999; 33:104A

Fibrillazione Atriale

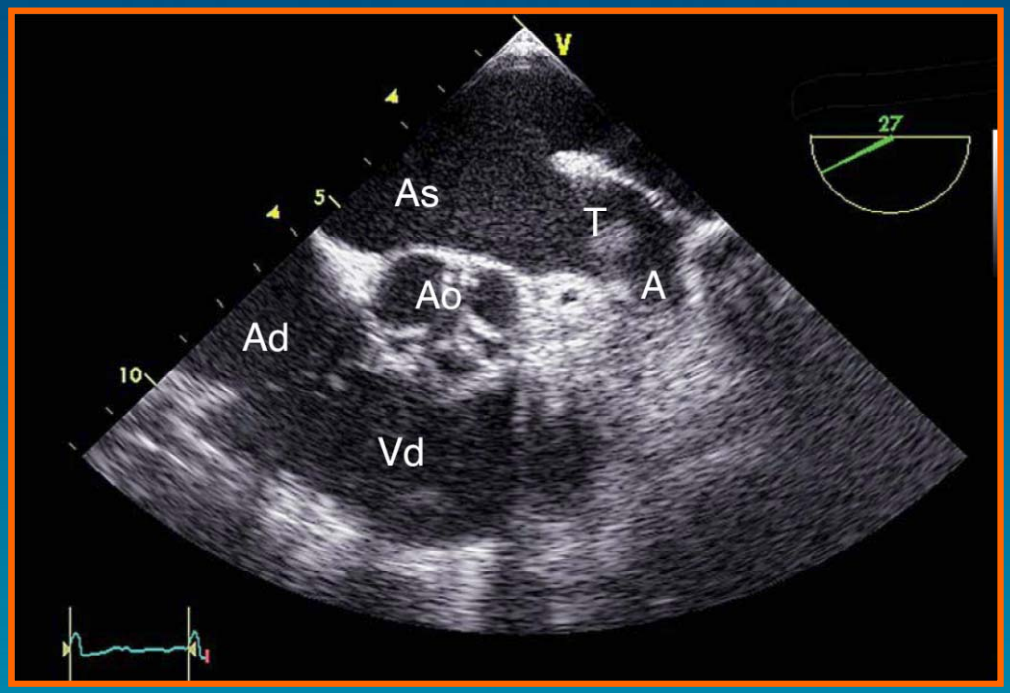


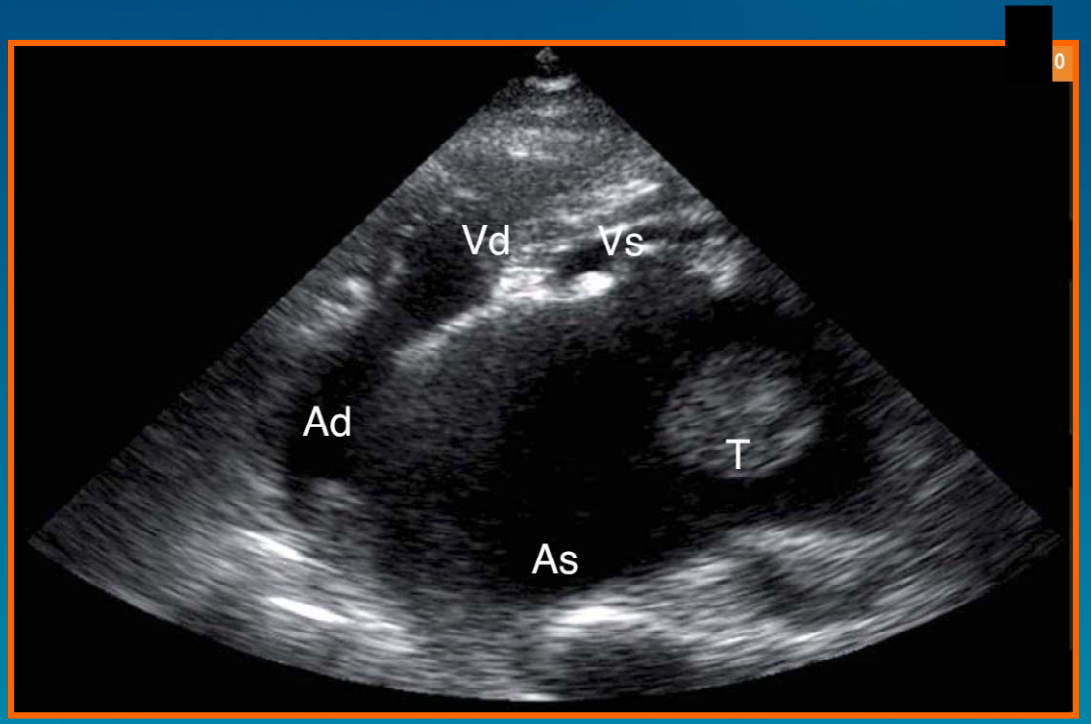
Influenza sulla prognosi:

- ⬇ Qualità della vita
- ⬆ Complicanze tromboemboliche
- ⬆ Scompenso Cardiaco
- ⬆ Mortalità cardiovascolare

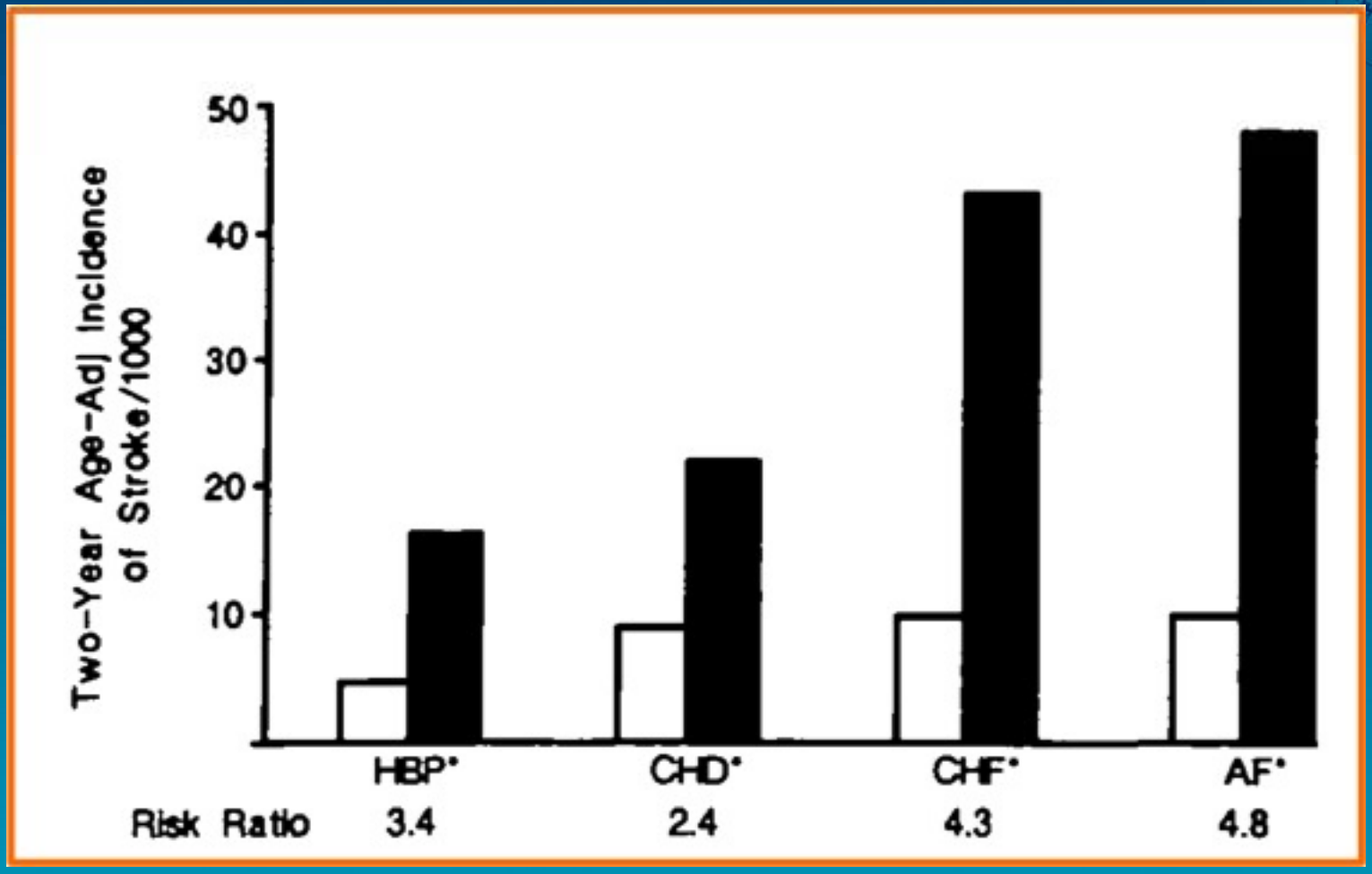
Trombo in auricola/atrio sinistro

Ecografia Transesofagea:





Incidenza di stroke in presenza o meno di patologie cardiovascolari



PA Wolf, et al. Stroke 1991;22: 983-988

Incidenza di stroke in pazienti con cardiopatia con fibrillazione atriale associata

TABLE 3. Attributable Risk of Stroke for Hype Fibrillation by Age

Cardiovascular condition	50–59 ye stroke ev
Hypertension	
Attributable risk (%)	48.8
Events occurring with condition (%)	72.8
Coronary heart disease	

Man
Woman

PA Wolf, et al. Stroke 1991;22: 983-988

Incidenza annuale di complicanze tromboemboliche nella Fibrillazione Atriale

FA → 4,5%

Controlli → 0,2% - 1,4%

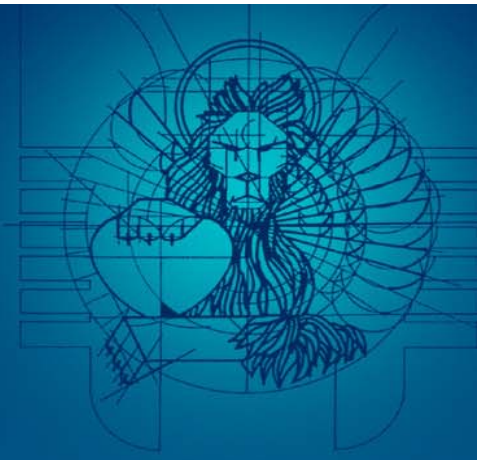
The SPAF Investigators. AIM 1992; 116: 1 – 5

Incidenza di stroke nei pazienti con Fibrillazione Atriale

Tromboembolia cerebrale	Incidenza (%/anno)
Stroke invalidanti	2,5
Stroke ischemici complessivi	5
Stroke + TIA	7
Stroke + TIA + infarti cerebrali silenti	>7

AFASAK, BAATAF, SPAF, CAFA, SPINAF

Prevalence of AF in Stroke



18% - 31%

Higher Mortality and More Severe Stroke in Patients with AF



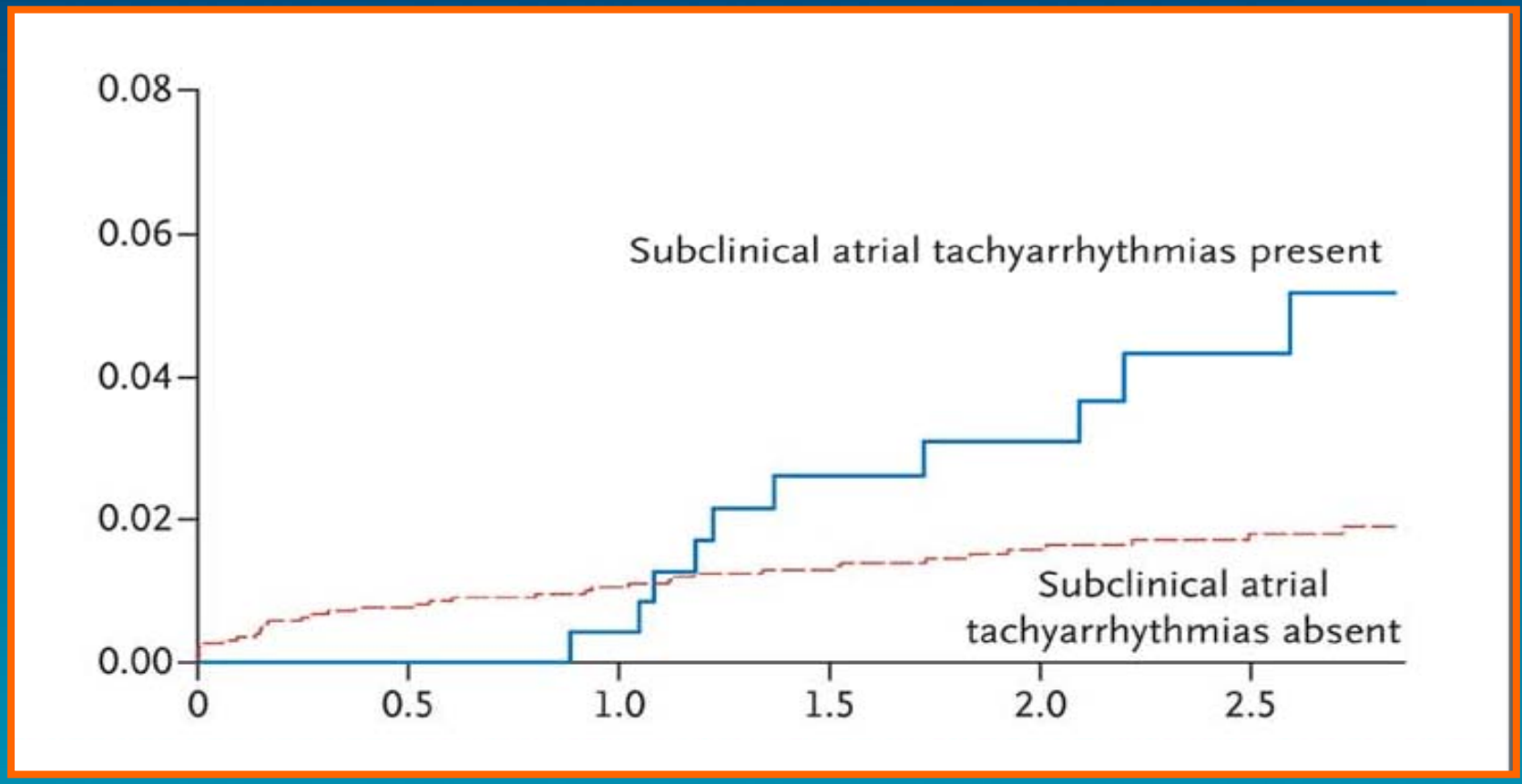
The European Community Stroke Project:

- Multi-centre, multi-national hospital-based registry involving 4462 patients hospitalized for first stroke
- AFib diagnosed in 803 stroke patients (18%)
- **At 3 months, 32.8% of stroke patients with AFib were dead vs 19.9% of stroke patients without AFib**
- **AFib increased by approximately 50% the probability of remaining disabled**

Lamassa M et al. *Stroke* 2001; 32: 392-8

Rischio di stroke in pazienti con o senza forme subcliniche rilevate da device

Studio ASSERT:



Healey JS et al. *N Engl J Med* 2012;366:120-9

Fattori di rischio per stroke ischemico/TIA ed embolia sistemica in pazienti con FA

Swedish Cohort Atrial Fibrillation study:

Hypertension	1.17 (1.11–1.22)
Diabetes mellitus	1.19 (1.13–1.26)
Thyroid disease Thyrotoxicosis	1.00 (0.92–1.09) 1.03 (0.83–1.28)

Camm AJ et al. *Eur Heart J 2012*

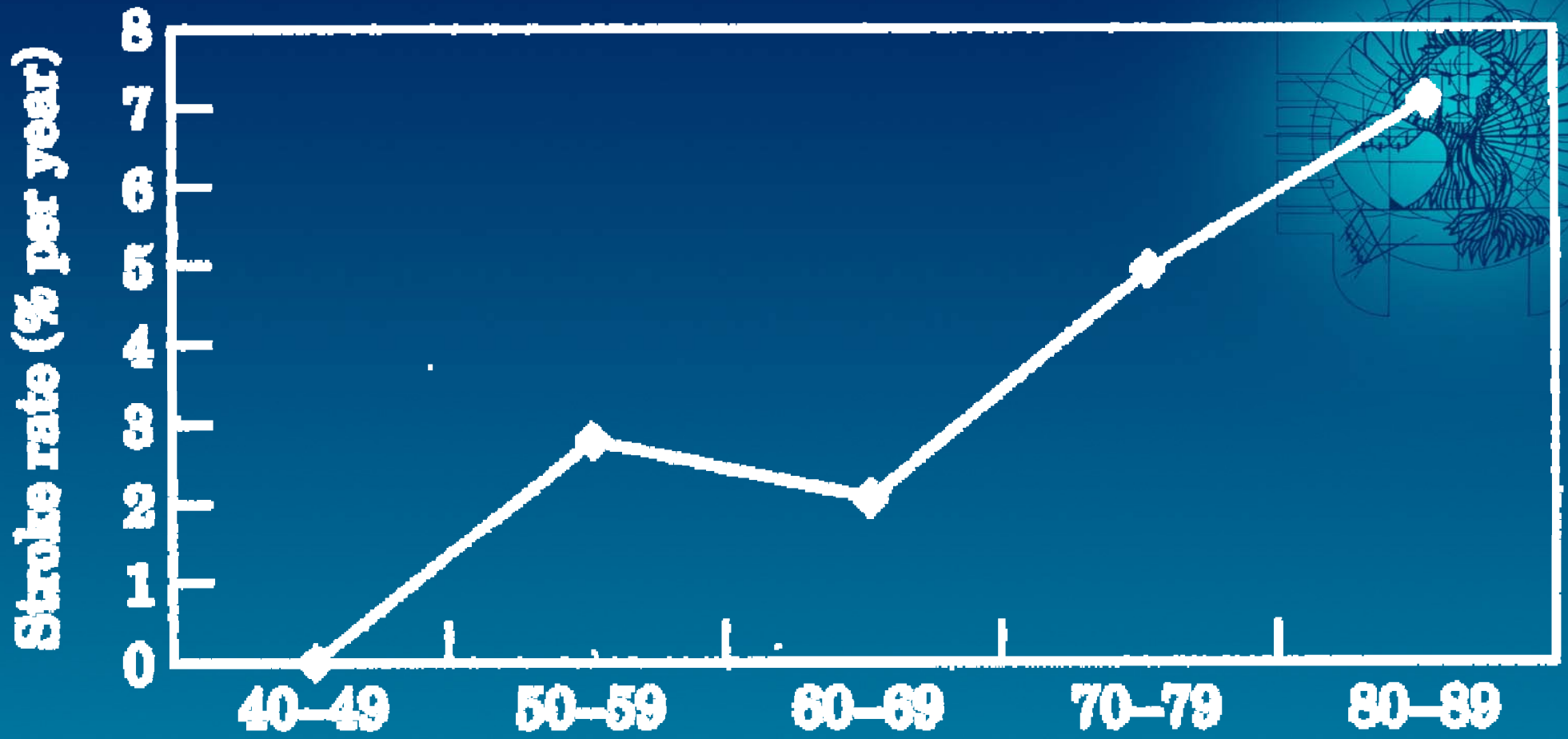


Figure 15. Stroke rates in relation to age among patients with atrial fibrillation in the Framingham Heart Study.

Wolf PA et al. Arch Intern Med 1987;147:1561-4

Increasing Age as a Risk Factor For Stroke

Inoue et al., 2000 (23)	740	Age >65 yrs	RR: 3.33 (1.92–5.81)	0.0001
Wang et al., 2003 (15)	705	Incremental risk per decade	*	<0.05
Stollberger et al., 2004 (10)	409	Correlation with increasing age	RR: 1.06 (1.04–1.08)	0.0006

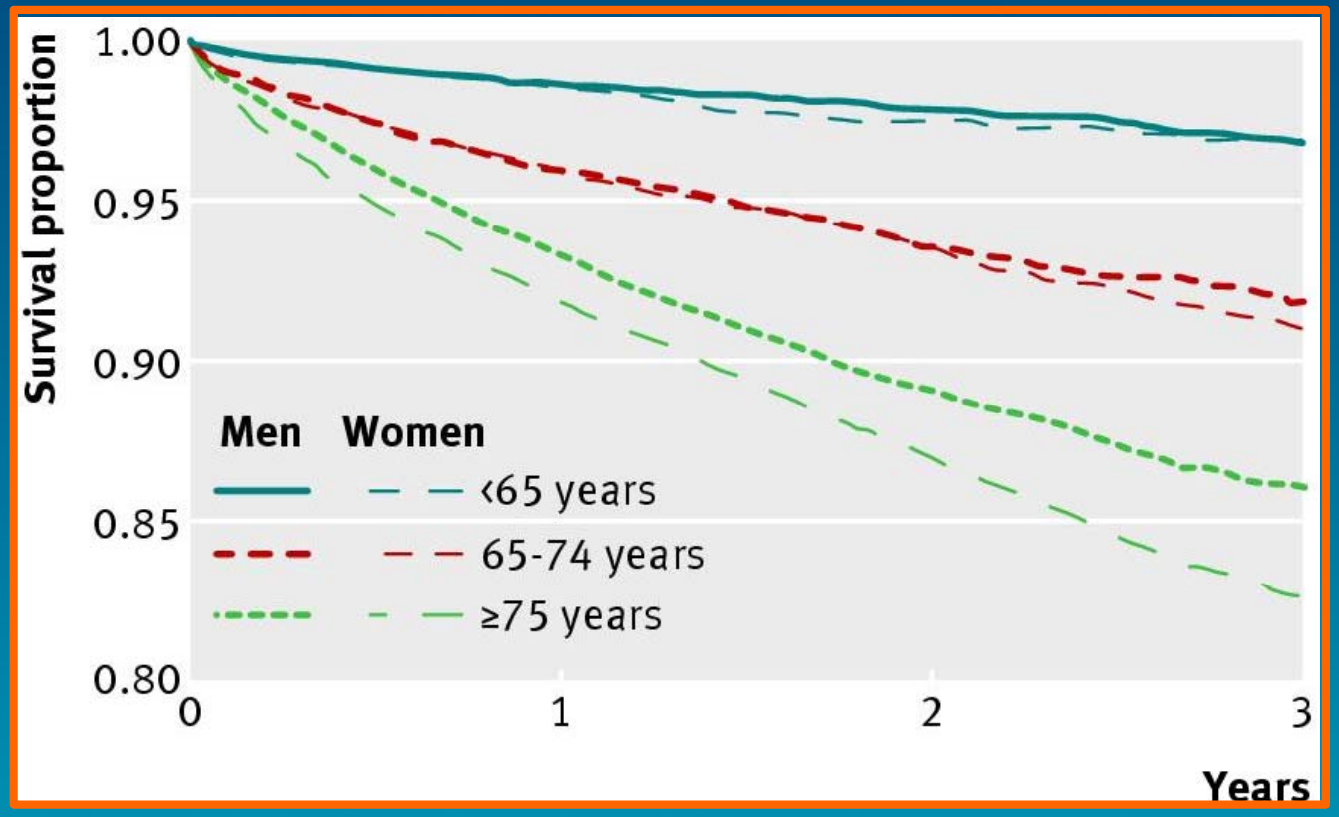
Marinigh R et al. J Am Coll Cardiol 2010; 56:827–37

2012 focused update of the ESC Guidelines for the management of atrial fibrillation

A history of ‘any heart failure’ per se is not consistently defined as a risk factor and is considered as risk factor the documentation of moderate-to-severe systolic dysfunction or patients with recent decompensated heart failure requiring hospitalization, irrespective of ejection fraction

Camm AJ et al. *Eur Heart J 2012*

Assessment of female sex as a risk factor in atrial fibrillation in Sweden: nationwide retrospective cohort study

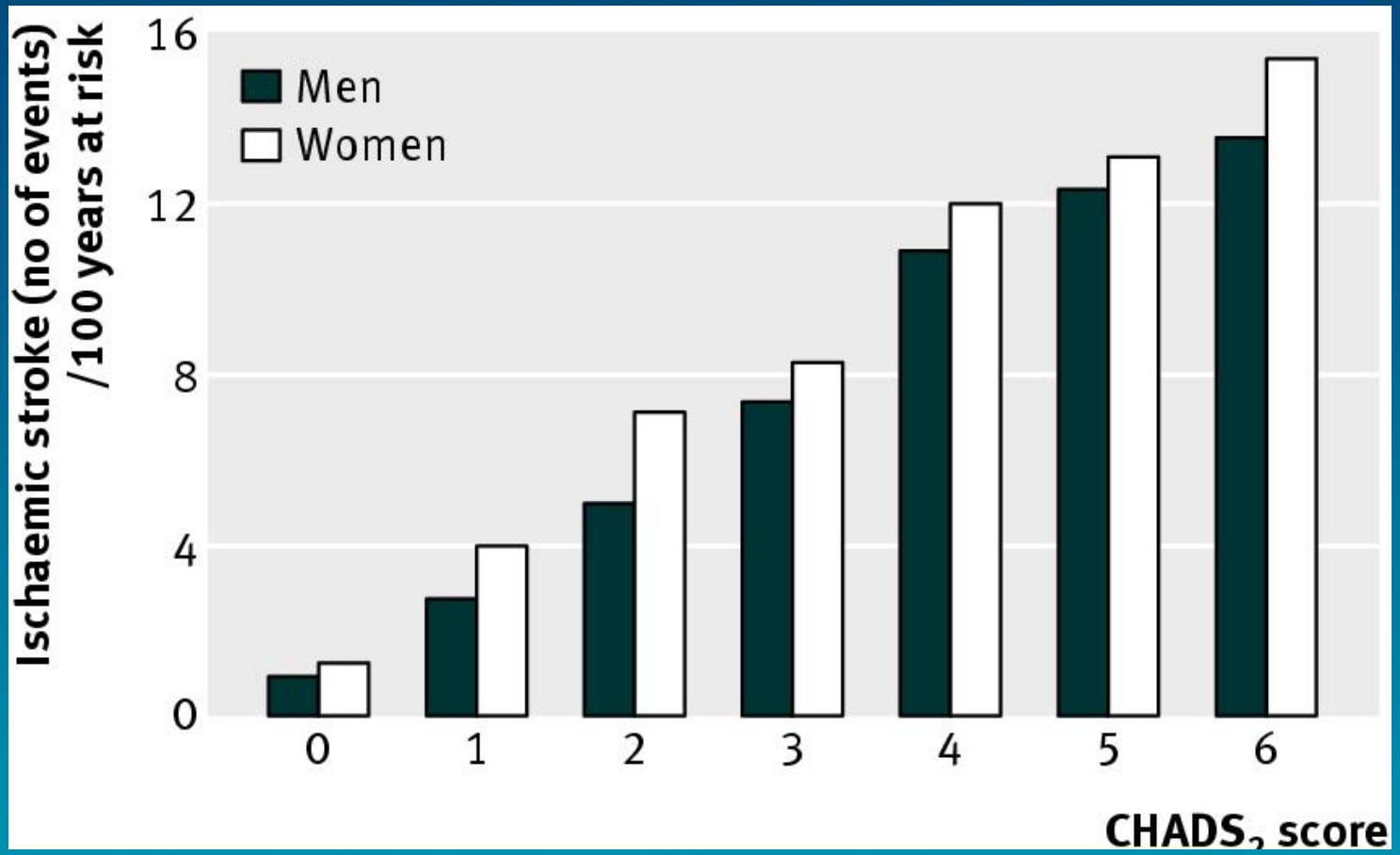


Friberg L et al. *BMJ* 2012;344:e3522

Ejection fraction and outcomes in patients with atrial fibrillation and heart failure: the Loire Valley Atrial Fibrillation Project

HFPEF, heart failure with preserved ejection fraction; HFREF, heart failure with reduced ejection fraction; TE, thrombo-embolism.
*P-value for two-sided χ^2 test using Fisher's exact test using patients with normal ejection fraction (EF $\geq$50%) as the reference group.

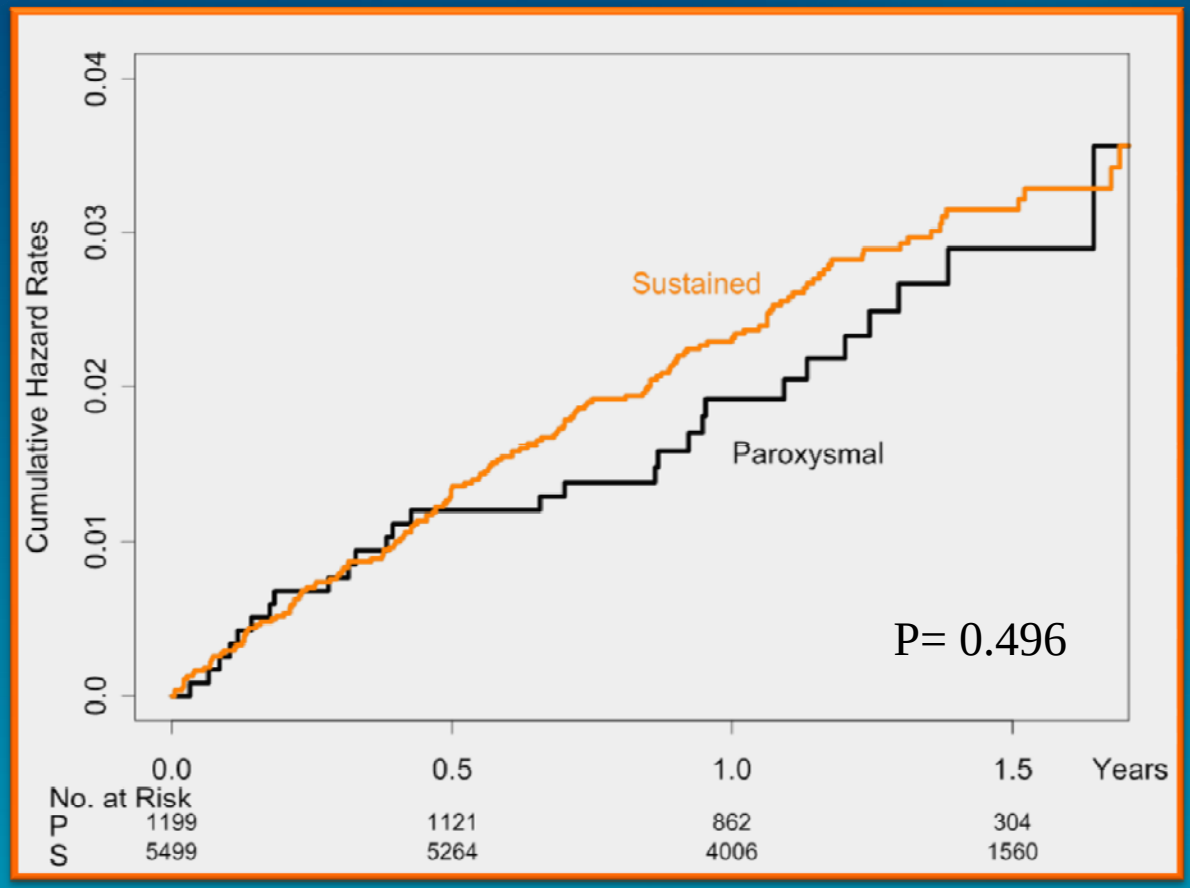
Banerjee A et al. *Eur J Heart Fail 2012; 14: 295–301*


Ischaemic stroke (no of events) /100 years at risk
16
12
8
4
0
Men
Women
0
1
2
3
4
5
6
CHADS2 score

Incidenza di eventi tromboembolici in pazienti con FA parossistica e non-parossistica

Rischio annuo di eventi TE:

- *FA parossistica: 2.0*
- *FA non-parossistica: 2.2*



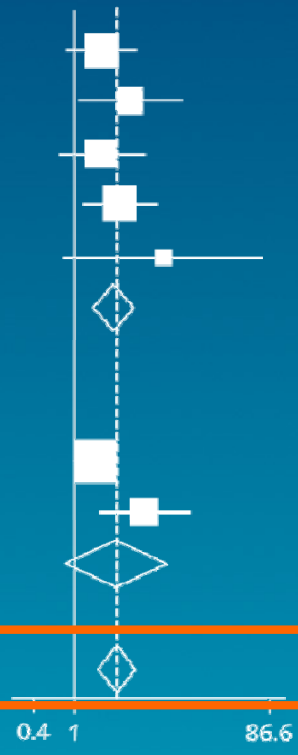
Hohnloser SH et al. *J Am Coll Cardiol* **2007;50:2156–61**

Fattori di rischio tromboembolico

Fattori di rischio	Rischio relativo
Precedente stroke o TIA	2,5
Diabete mellito	1,7
Ipertensione arteriosa	1,6
Scompenso cardiaco	1,4
Età avanzata (per decennio)	1,4

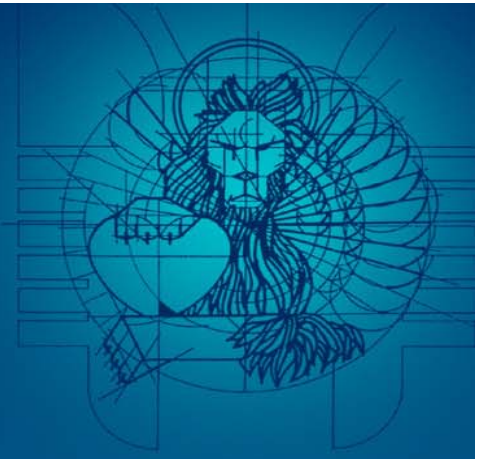
Association between AF and cognitive impairment independent of stroke history

Study, Year (Reference)	End Point	AF Events/ Patients, *n/N*	No AF Events/ Patients, *n/N*	Relative Risk (95% CI)	Weight, %*	Adjustment
Prospective cohort						
Inzitari et al, 1998 (37)	Dementia after stroke	16/56	41/282	2.33 (1.09–4.98)	17.05	Multivariate
Barba et al, 2000 (38)	Dementia after stroke	19/33	56/218	4.40 (1.40–13.83)	9.43	Multivariate
Altieri et al, 2004 (39)	Dementia after stroke	61/14	35/177	2.30 (0.90–5.88)	12.79	Multivariate
Zhou et al, 2004 (40)	Dementia after stroke	31/56	87/378	3.45 (1.58–7.51)	16.53	Multivariate
Tang et al, 2006 (41)	Cognitive impairment after stroke	4/8	35/171	9.36 (1.01–86.62)	2.93	Multivariate
Subtotal (I^2 = 0.0%; P = 0.682)				3.01 (1.96–4.61)	58.73	
Cross-sectional						
Mizrahi et al, 2011 (42)	Cognitive impairment after stroke	NR/126	NR/581	1.60 (1.03–2.49)	29.48	Multivariate
Khan et al, 2012 (43)	Dementia after stroke	NR/37	NR/272	5.12 (1.90–13.80)	11.79	Multivariate
Subtotal (I^2 = 77.4%; P = 0.036)				2.62 (0.85–8.09)	41.27	
Overall (I^2 = 32.3%; P = 0.182)				2.70 (1.82–4.00)	100	



Kalantarian S et al. *Ann Intern Med.* 2013;158:338-46

Fibrillazione Atriale

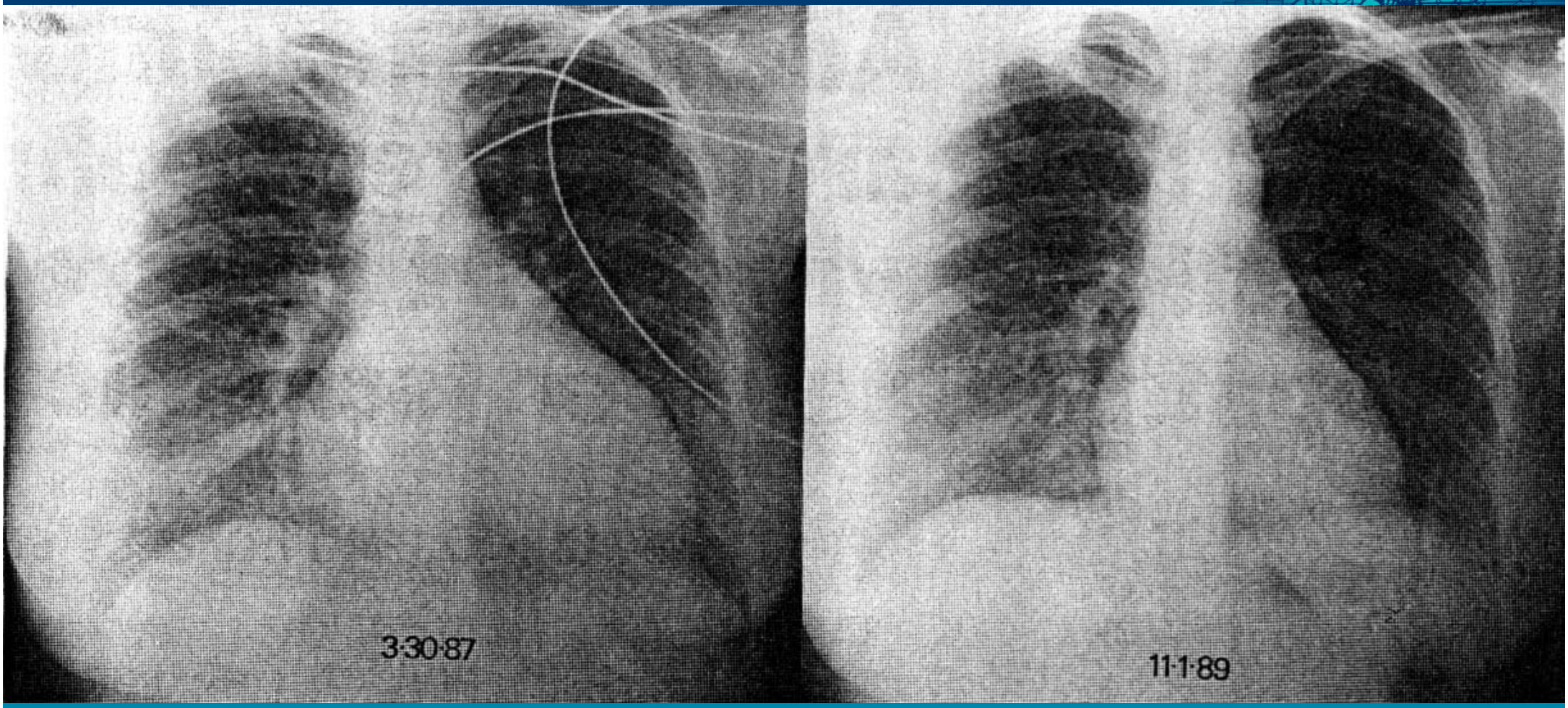


Influenza sulla prognosi:

- ⬇ Qualità della vita
- ⬆ Complicanze tromboemboliche
- Scompenso Cardiaco/ Tachicardiomiopatia
- ⬆ Mortalità cardiovascolare

ATRIA Study

Characteristic	(n = 17 974)
Age, mean (SD), y	71.2 (12.2)
≥80 y	25.4
Women	43.4
Race†	
White	84.7
Black	3.6
Hispanic or Latino	2.5
Other or multiple	9.1
Known valvular heart disease	4.9
Previous ischemic stroke	8.9
Diagnosed heart failure	29.2
Hypertension	49.3
Diabetes mellitus	17.1
Previous coronary heart disease	34.6
Angina	21.8
Myocardial infarction	9.4



Grogan M et al Am J Cardiol 1992; 69: 1570-73

Studio ATRIA

Caratteristiche dei pazienti con Fibrillazione Atriale:

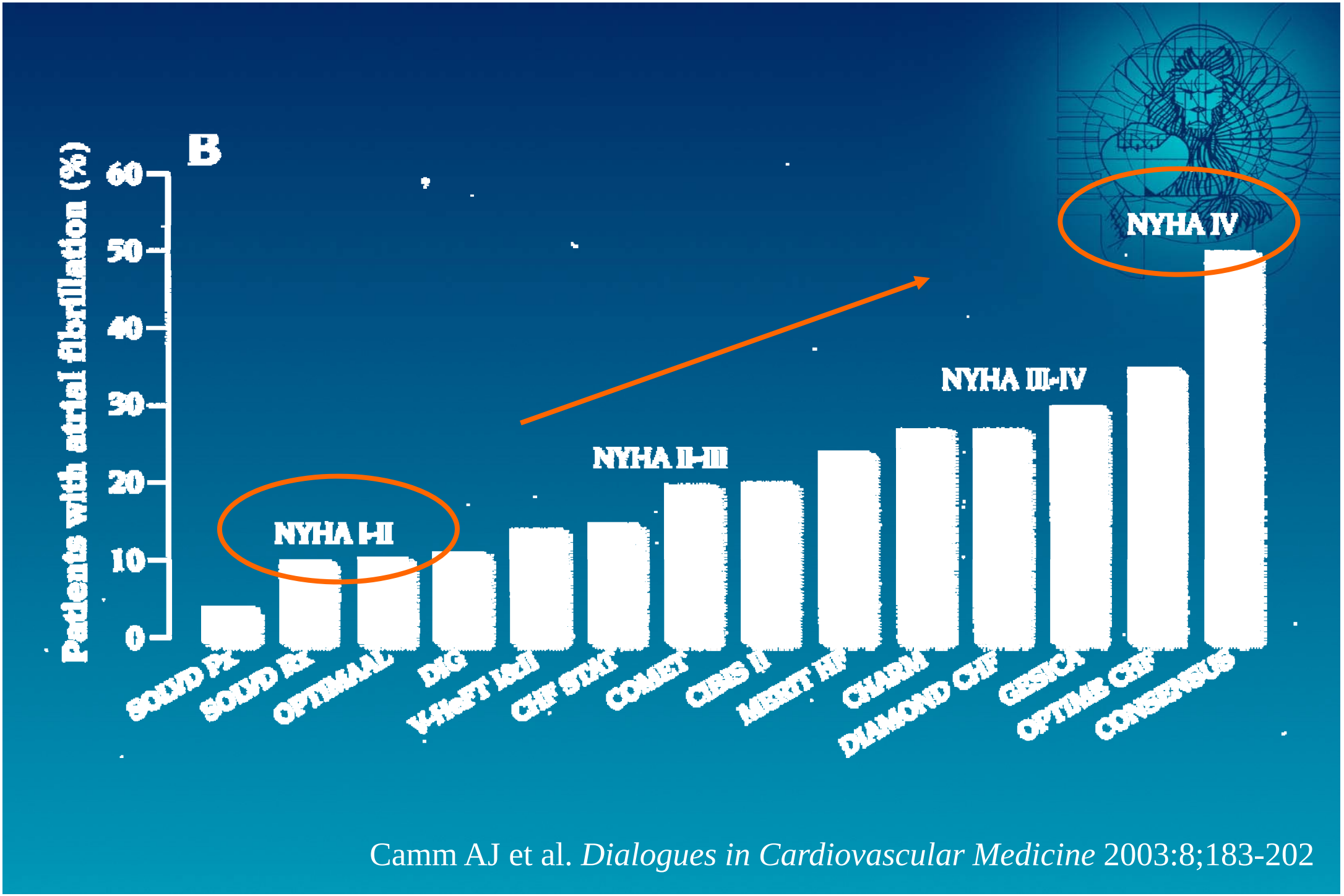
Characteristic	ATRIA Cohort (n = 17 974)
Age, mean (SD), y	71.2 (12.2)
≥80 y	25.4
Women	43.4
Race†	
White	84.7
Black	3.6
Hispanic or Latino	2.5
Other or multiple	9.1
Known valvular heart disease	4.9
Previous ischemic stroke	8.9
Diagnosed heart failure	29.2
Hypertension	49.3
Diabetes mellitus	17.1
Previous coronary heart disease	34.6
Angina	21.8
Myocardial infarction	9.4

Go AS et al. *JAMA* 2001;285:2370-5

Prevalenza della FA in pazienti con Scompenso cardiaco

Predominant NYHA Class	Prevalence of AF (%)	Study
I	4	SOLVD–Prevention (1992)[14a]
II-III	10 to 26	SOLVD–Treatment (1991)[14b] CHF-STAT (1995)[14c] MERIT-HF (1999)[14d] DIAMOND-CHF (1999)[501]
II-IV	12 to 27	CHARM (2003) Val-HeFT (2003)[848]
III-IV	20 to 29	Middlekauff (1991)[14e] Stevenson (1996) GESICA (1994)[14f]
IV	50	CONSENSUS (1987)[14g]

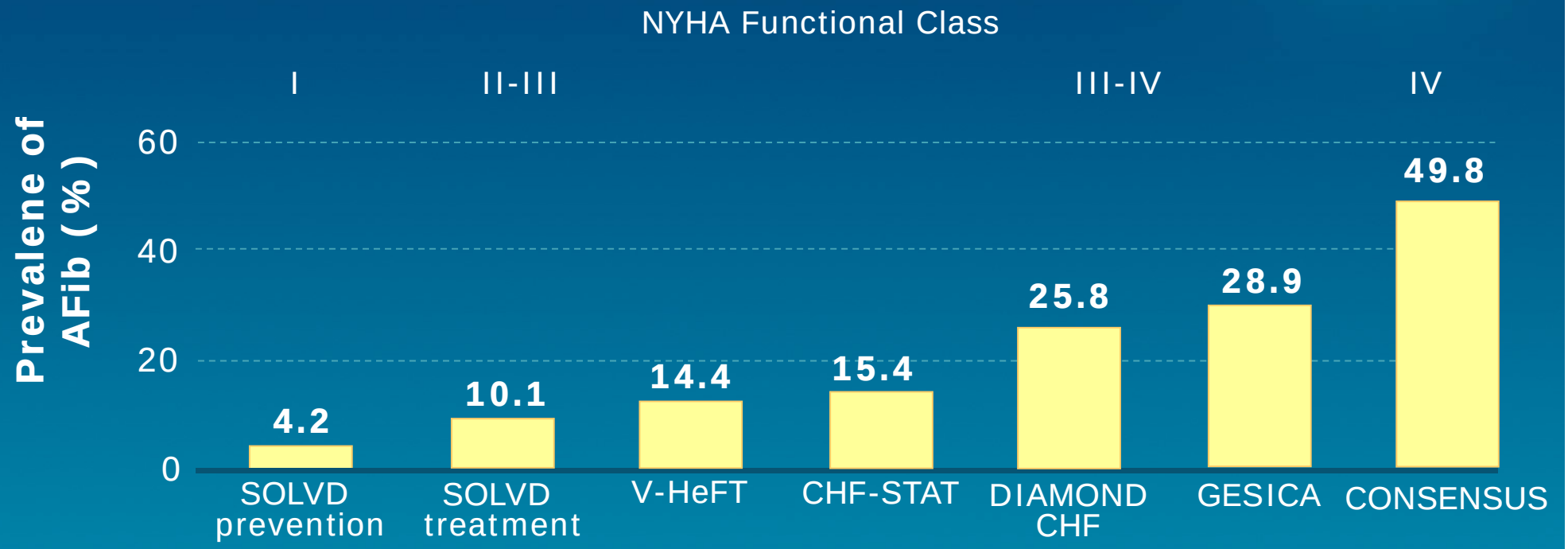
Fuster V et al. *Circulation. 2006;114:e257-e354.*



Camm AJ et al. *Dialogues in Cardiovascular Medicine* 2003:8;183-202

Prevalence of AFib in Major Heart Failure Trials

2-fold excess risk of mortality compared with healthy control



Maisal WH, Stevenson LW. *Am J Cardiol* (2003) 91: 2D-8D

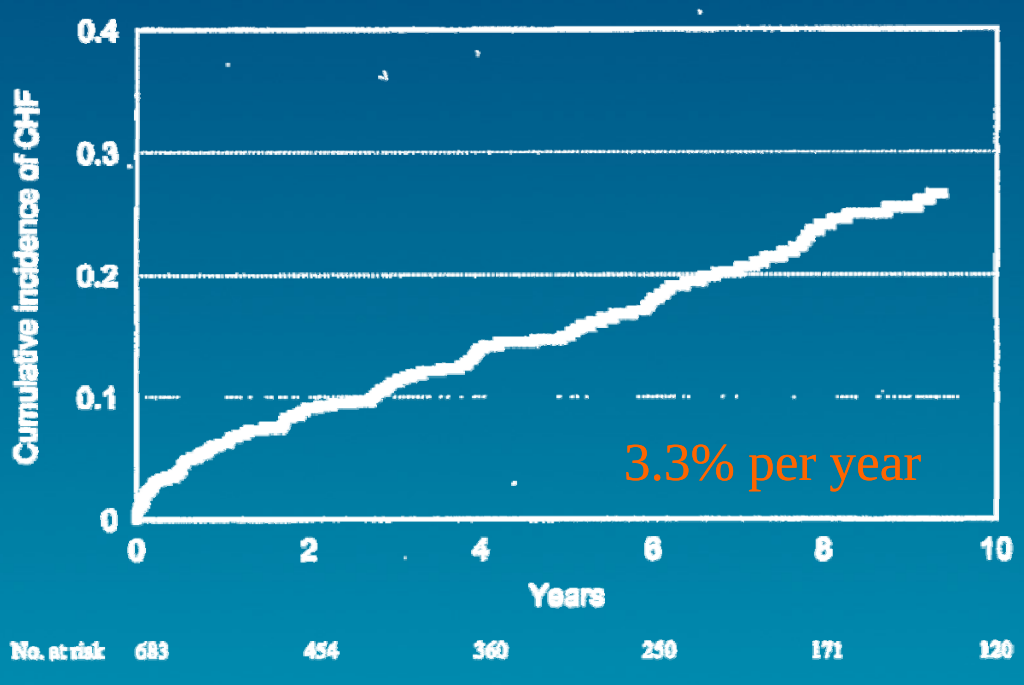
Table 1 Prevalence of atrial fibrillation in patients with heart failure

Predominant NYHA type	Prevalence of AF, %	Study, year
I	4	SOLVD-prevention (1992)
II–III	10–26	SOLVD-treatment (1991)
		CHF-STAT (1995)
		MERIT-HF (1999)
		Diamond (1999)
III–IV	20–29	Middlekauff (1991)
		Stevenson (1996)
		GESICA (1994)
IV	50	CONSENSUS (1987)

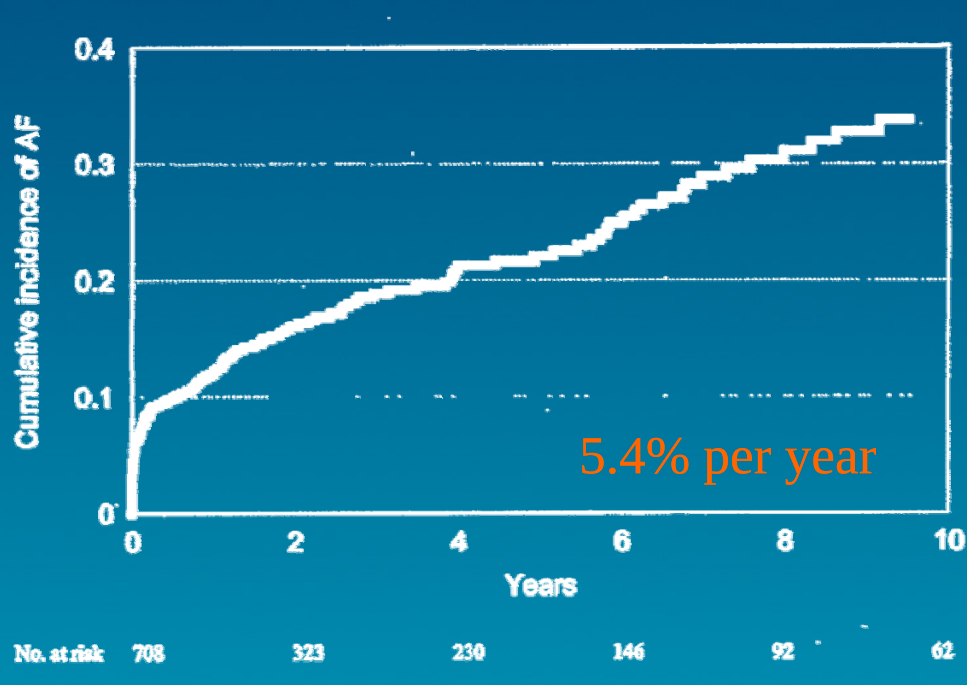
AHA / ACC / ESC Guidelines Circulation 2001; 104: 2118-2150

Scompenso cardiaco e fibrillazione atriale

Unadjusted cumulative incidence of 1st CHF in individuals with AF



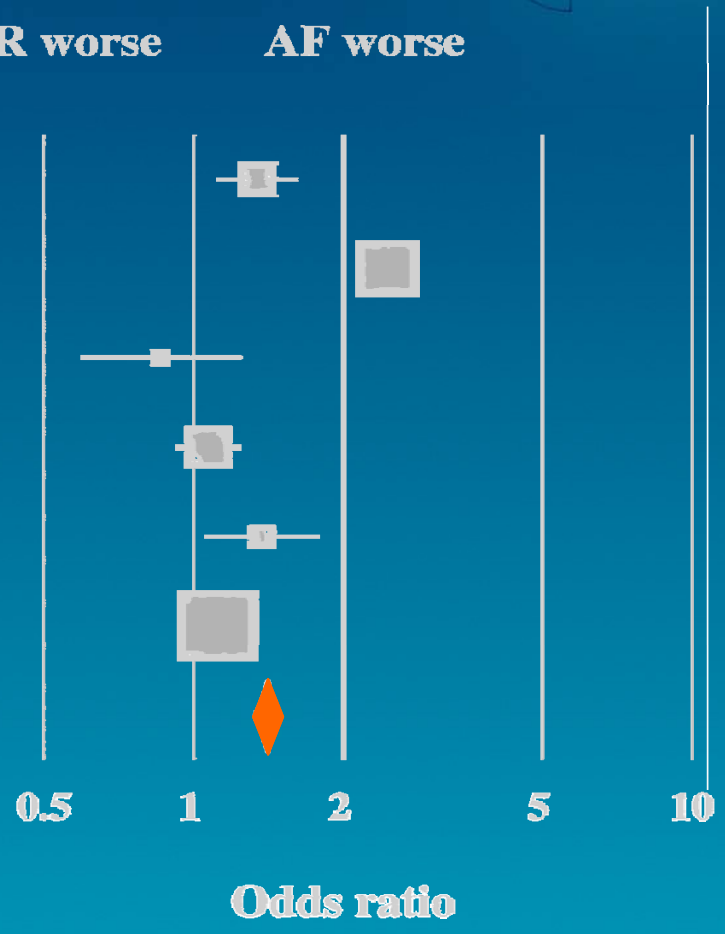
Unadjusted cumulative incidence of 1st AF in individuals with CHF



Wang TJ et al. *Circulation* 2003; 107: 2920-25

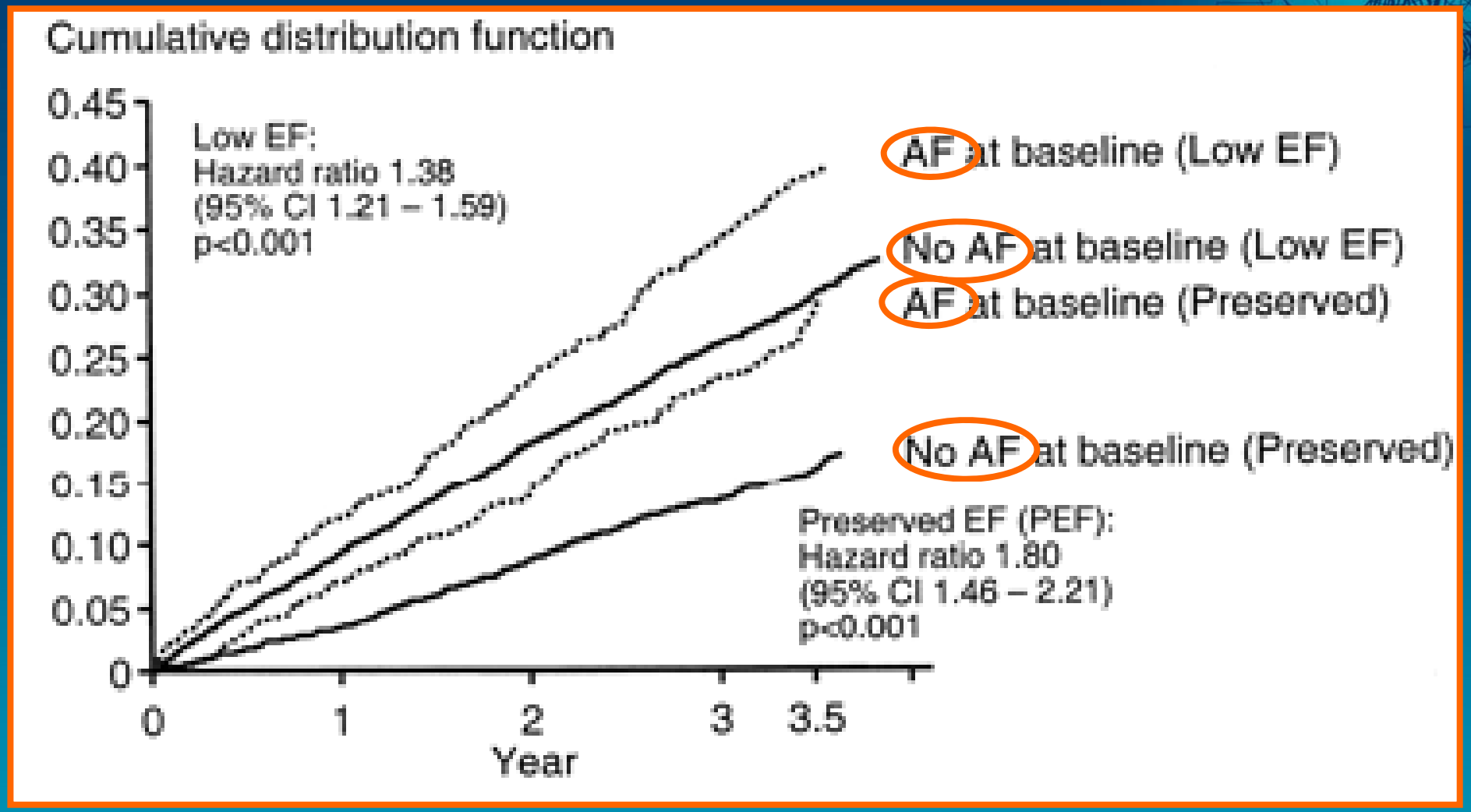
Adjusted mortality outcomes following multivariate analysis from randomized studies in chronic heart failure patients in sinus rhythm and atrial fibrillation.

Study name	Adjusted OR (95% CI)
SOLVD 1998	1.34 (1.11–1.61)
DIG 2000	2.45 (2.19–2.74)
PRIME II 2000	0.86 (0.59–1.25)
COMET 2005	1.07 (0.92–1.24)
CHARM 2006	1.37 (1.05–1.78)
DIAMOND 2007	1.12 (1.02–1.16)
POOLED	1.40 (1.32–1.48)



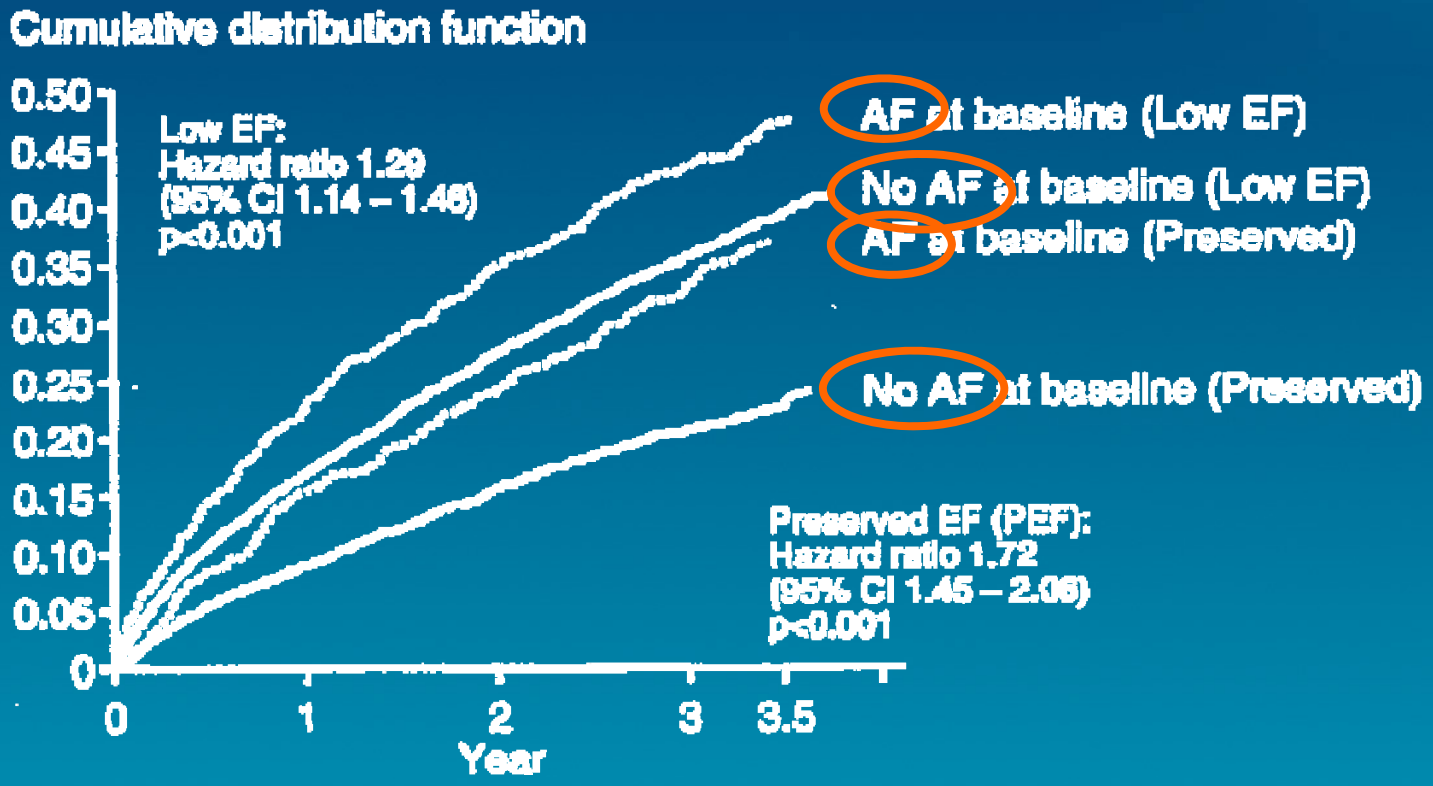
Mamas M A et al. *Eur J Heart Fail* 2009;11:676-683

All-cause mortality in CHF patients with & without AF



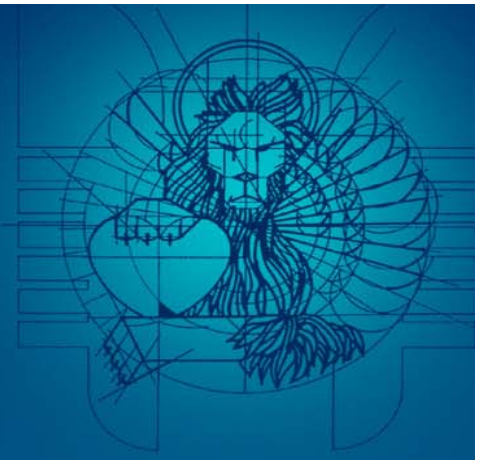
Olsson LJ et al. *J Am Coll Cardiol* 2006; 47: 1997-2004

Time to CV Death or Hospitalization for HF in AF pts



Olsson et al. JACC (2006); 47: 1997-2004

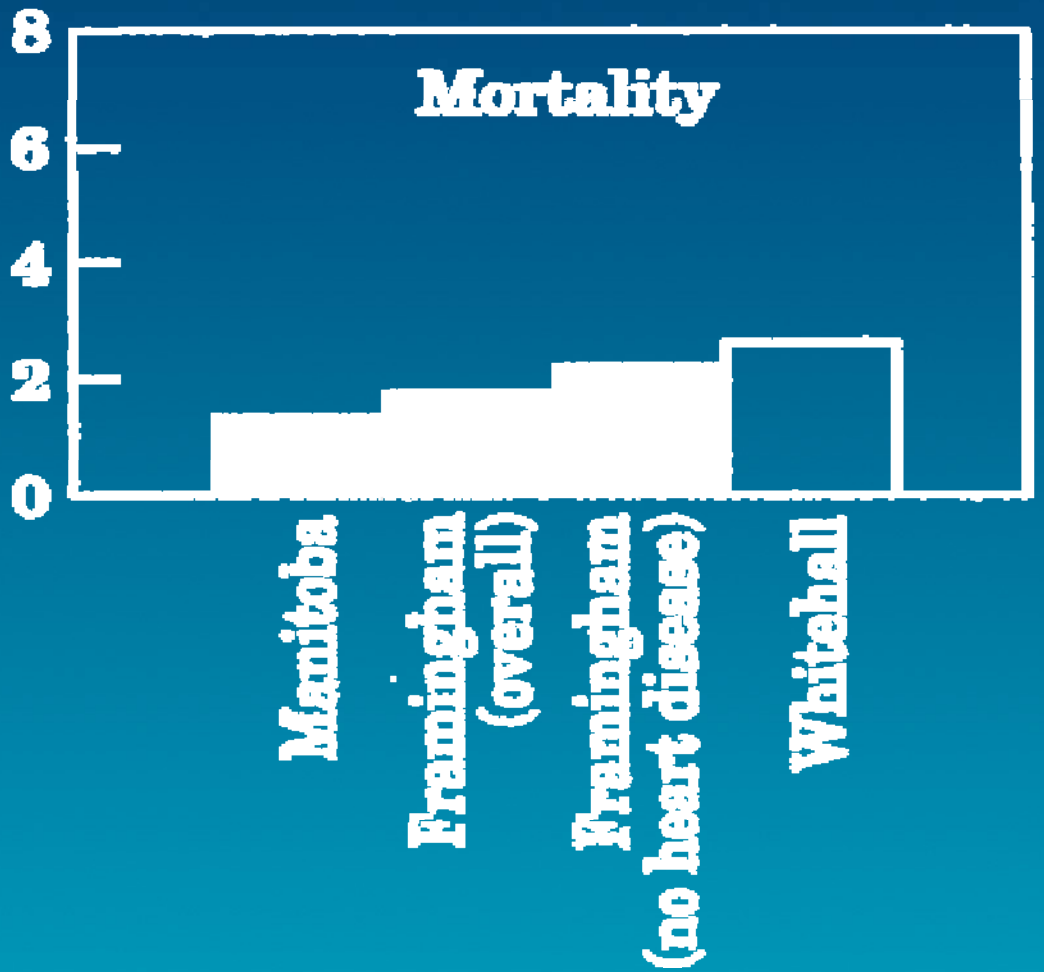
Fibrillazione Atriale



Influenza sulla prognosi:

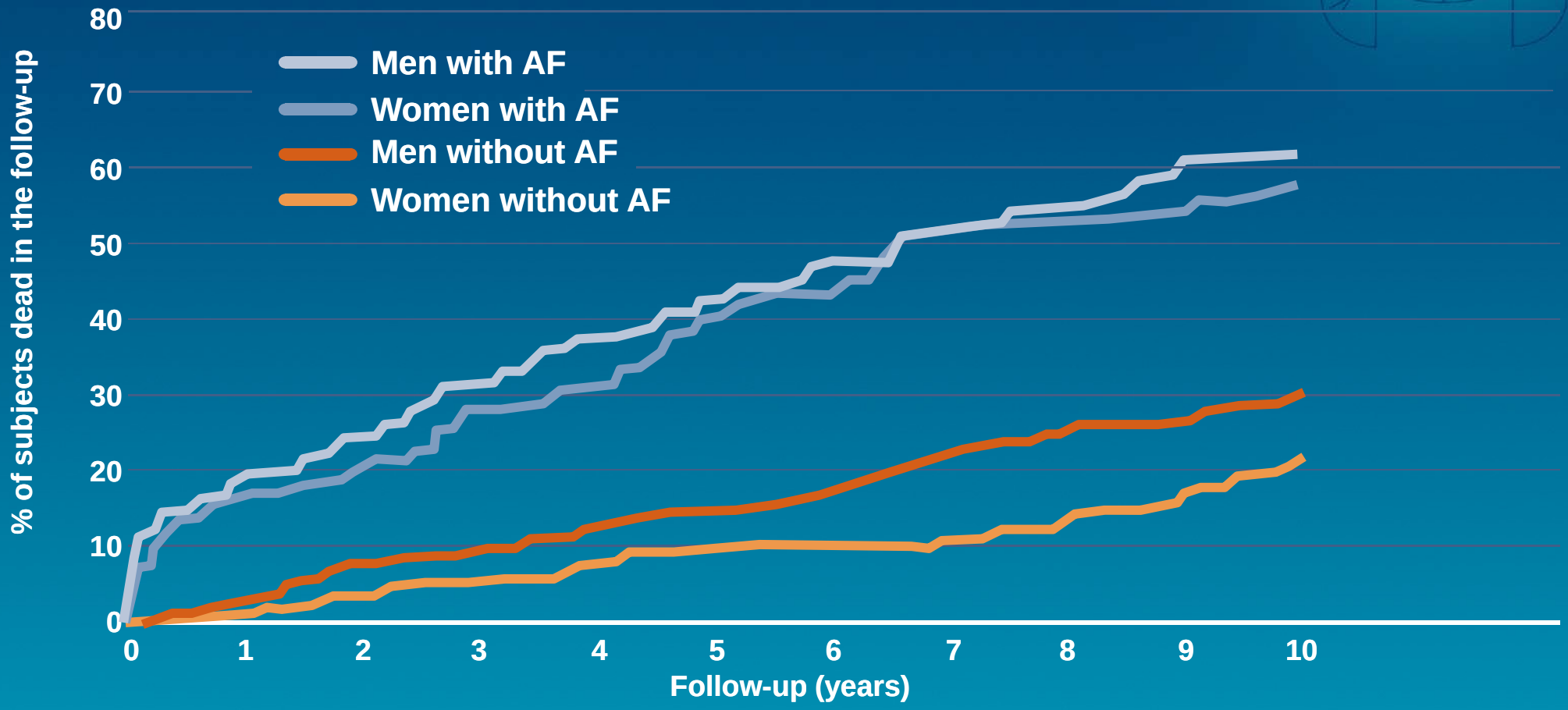
- ⬇ Qualità della vita
- ⬆ Complicanze tromboemboliche
- Scompenso Cardiaco/ Tachicardiomiopatia
- ⬆ Mortalità cardiovascolare

Relative risk of mortality in pts with AF compared with pts without AF



Impact of AF on the risk of death: the Framingham study

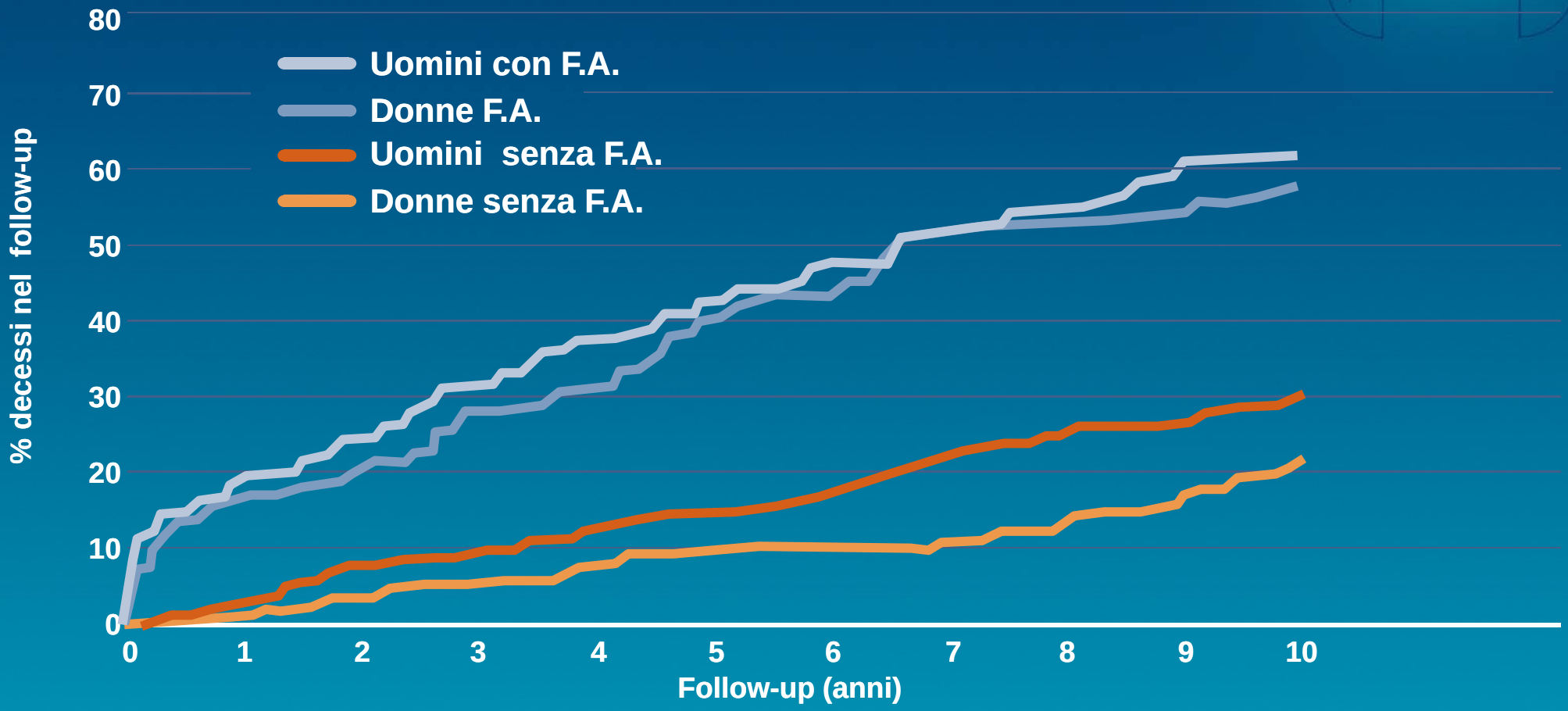
N = 5209; follow-up: 40 years



Benjamin EJ et al. Circulation 1998; 98: 946-952

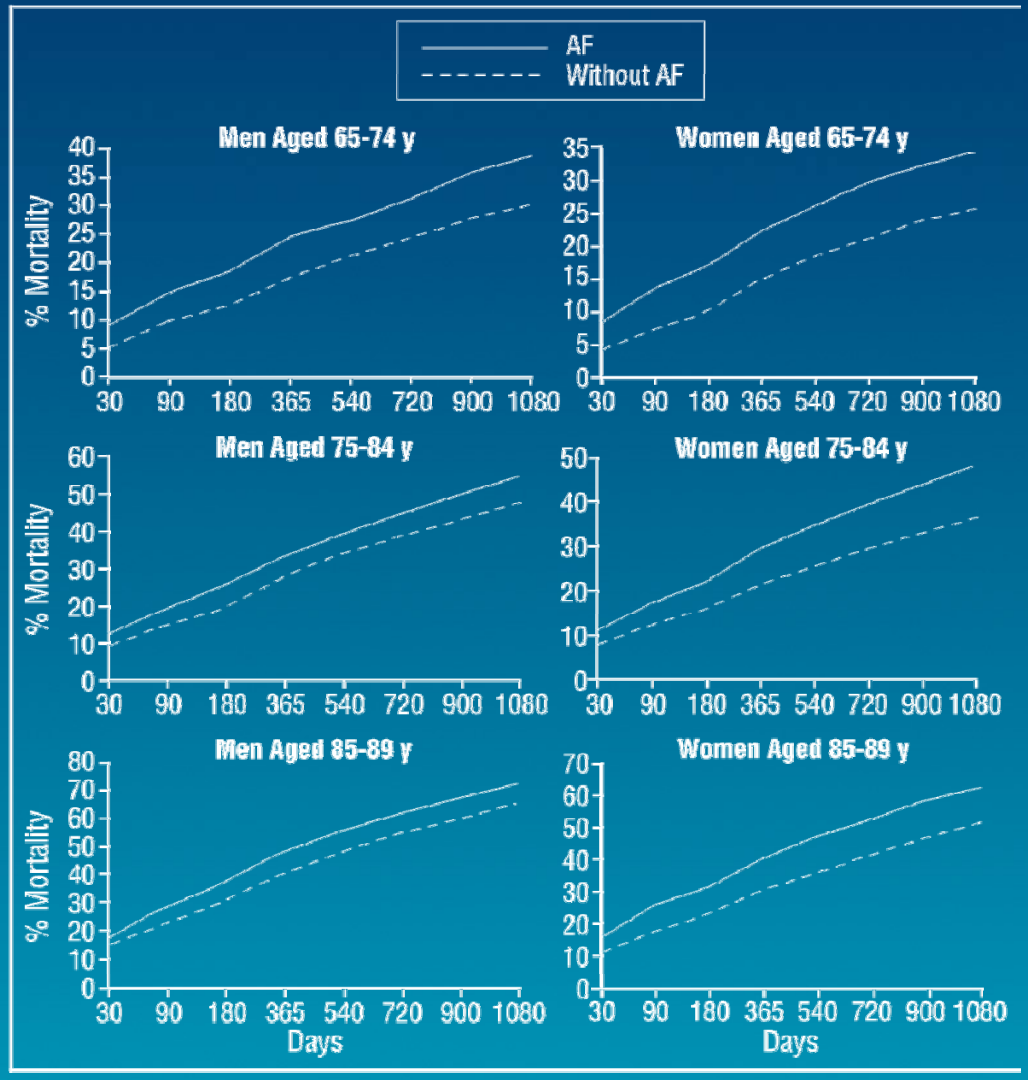
Fibrillazione atriale e rischio di morte: Studio Framingham

N = 5209; follow-up: 40 anni



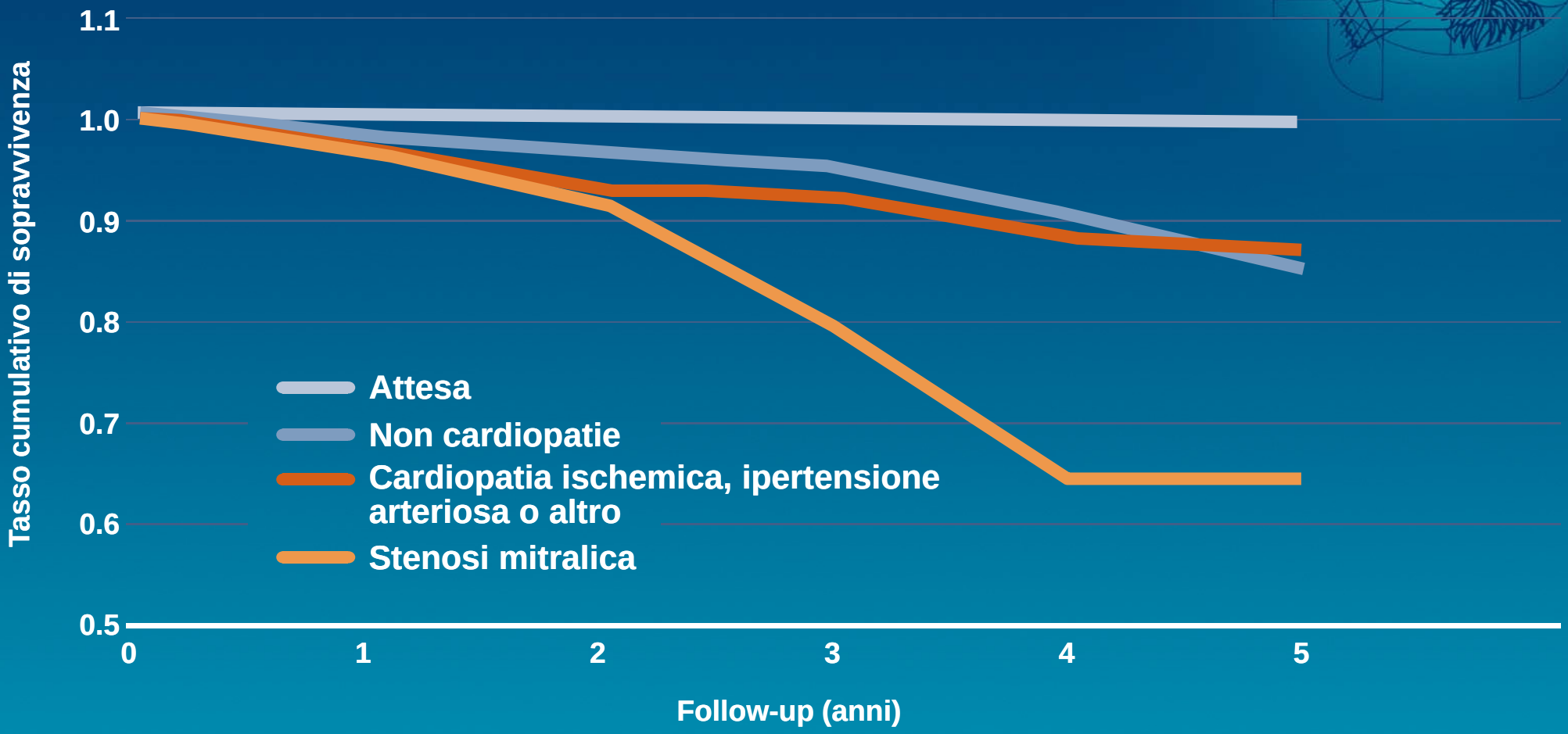
Benjamin EJ et al. *Circulation* 1998; 98: 946-952

Cumulative mortality in Medicare patients with a diagnosis of cardiovascular disease with and without AF



Wolf et al. Arch Intern Med 1998; 158: 229-34

Mortalità in rapporto alla causa di Fibrillazione Atriale



(Capucci A et al. La Fibrillazione Atriale. Ed. McGraw-Hill 1996)

Rischio di mortalità totale e cardiovascolare

Paris Prospective Study 1:

Variabile	RR mortalità totale (IC 95%)	p	RR mortalità cardiovascolare (IC 95%)	p
Fibrillazione Atriale idiopatica	1,95 [1,13-3,37]	0,02	4,31 [2,14-8,68]	0,0001
Età all'arruolamento	1,03 [1,01-1,11]	0,04	1,08 [0,98-1,19]	ns
Pressione arteriosa sistolica	1,44 [1,38-1,51]	0,0001	1,51 [1,39-1,63]	0,0001
Colesterolo	1,00 [0,96-1,04]	ns	1,24 [1,14-1,35]	0,0001
Indice massa corporea	0,89 [0,85-0,94]	0,0001	1,00 [0,92-1,10]	ns
Abitudine al fumo	1,40 [1,34-1,45]	0,0001	1,31 [1,22-1,41]	0,0001

Jouven X et al. *EHJ* 1999; 20: 896-9

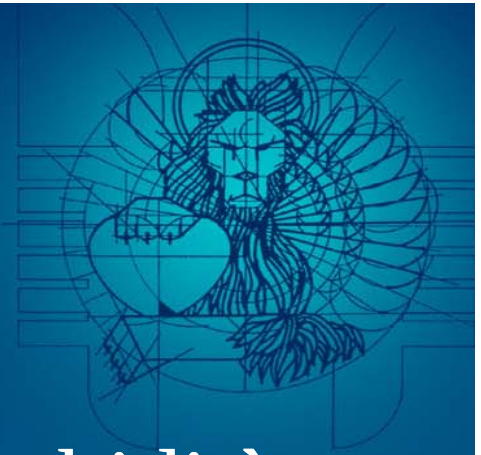
Fibrillazione atriale e mortalità cardiovascolare

The Atherosclerosis Risk in Communities Study (ARIC) and Cardiovascular Health Study CHS):



Chen LY et al. *JAMA Intern Med*. 2013;173:29-35

Fibrillazione atriale



Considerata la sua epidemiologia, morbidità e mortalità, rappresenta un significativo problema sanitario ed ha un importante impatto sociale che richiede più attenzione e risorse rispetto a quelle destinate finora

The New England Journal of Medicine

Special Article

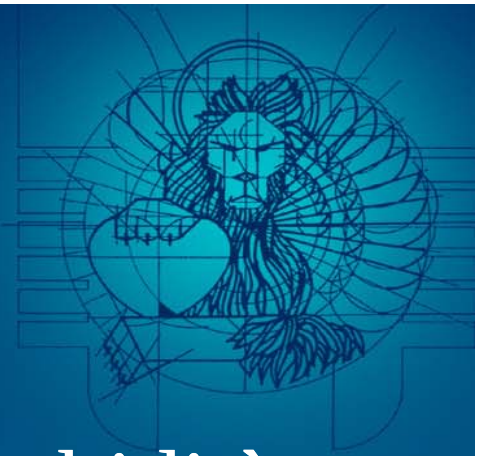
SHATTUCK LECTURE — CARDIOVASCULAR MEDICINE AT THE TURN OF THE MILLENNIUM: TRIUMPHS, CONCERNS, AND OPPORTUNITIES

EUGENE BRAUNWALD, M.D.

"Two new epidemics of cardiovascular disease are emerging: heart failure and atrial fibrillation."

N Engl J Med 1997; 337:1360-1369

Fibrillazione atriale



Considerata la sua epidemiologia, morbidità e mortalità, la FA ha un significativo impatto socio-sanitario che richiede più attenzione e risorse rispetto a quelle destinate finora.

Adeguata organizzazione per gestirla….

