La sicurezza dei NAO nella fibrillazione atriale: ha ancora un ruolo l'aspirina ?

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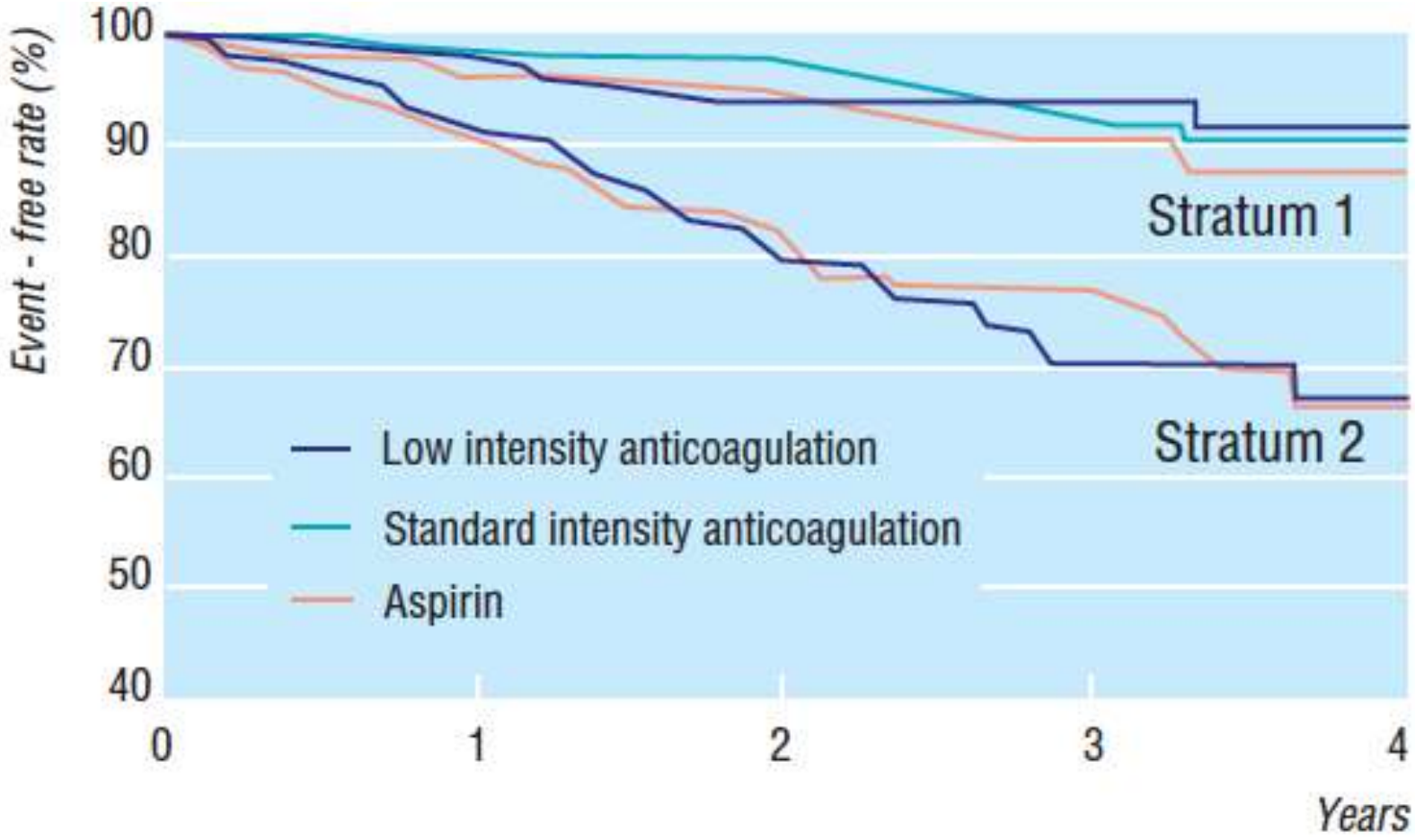
mt

AF in primary care: ASA vs. two intensities of coumarin

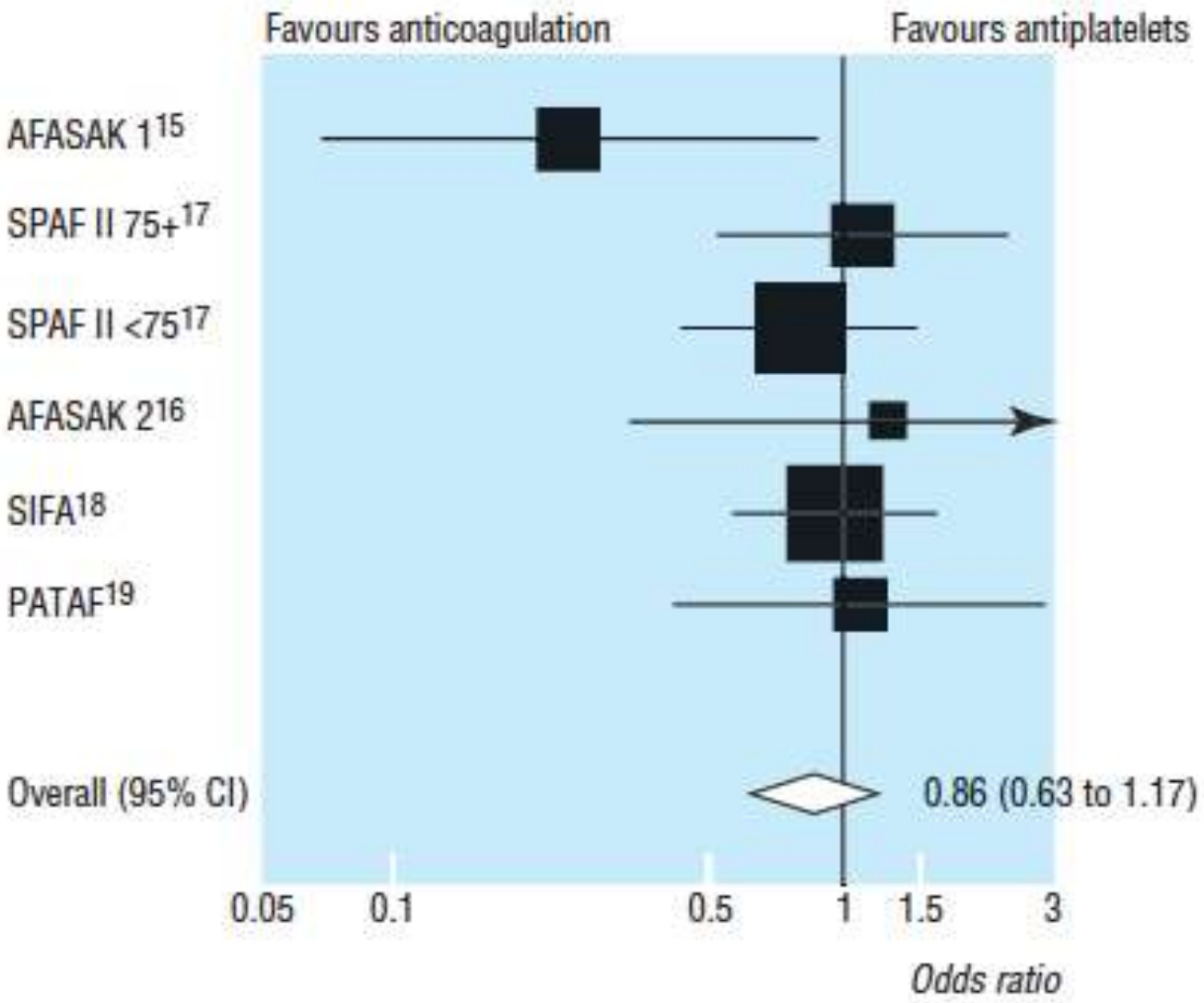


"aspirin may therefore be the first choice in patients with atrial fibrillation in general practice"

Hellemons BSP, BMJ 1999

long term anticoagulation vs. antiplatelet therapy

- non rheumatic AF -



Taylor FC, BMJ 2001;322:321.

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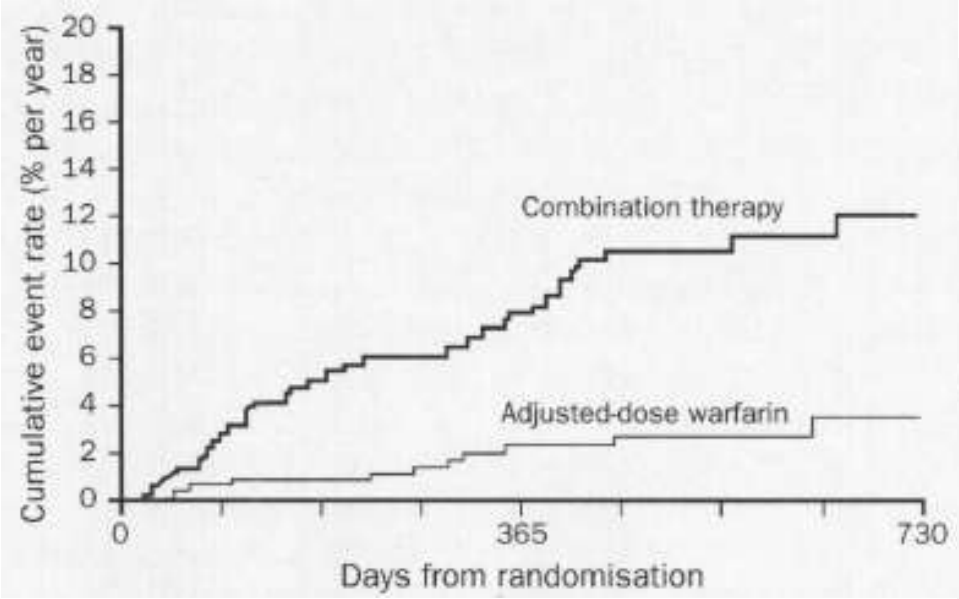
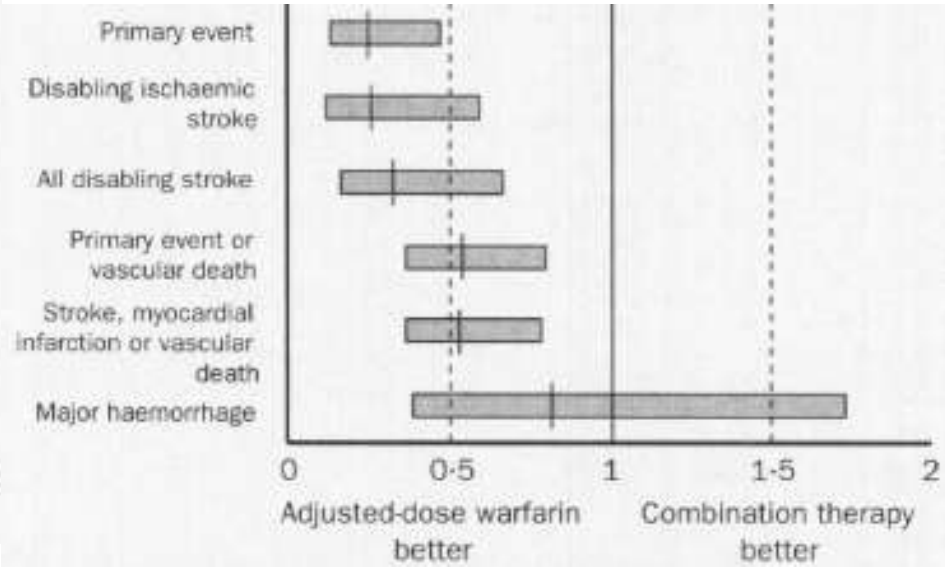
SPAF III: fixed-dose warfarin + ASA vs. adjusted-dose warfarin

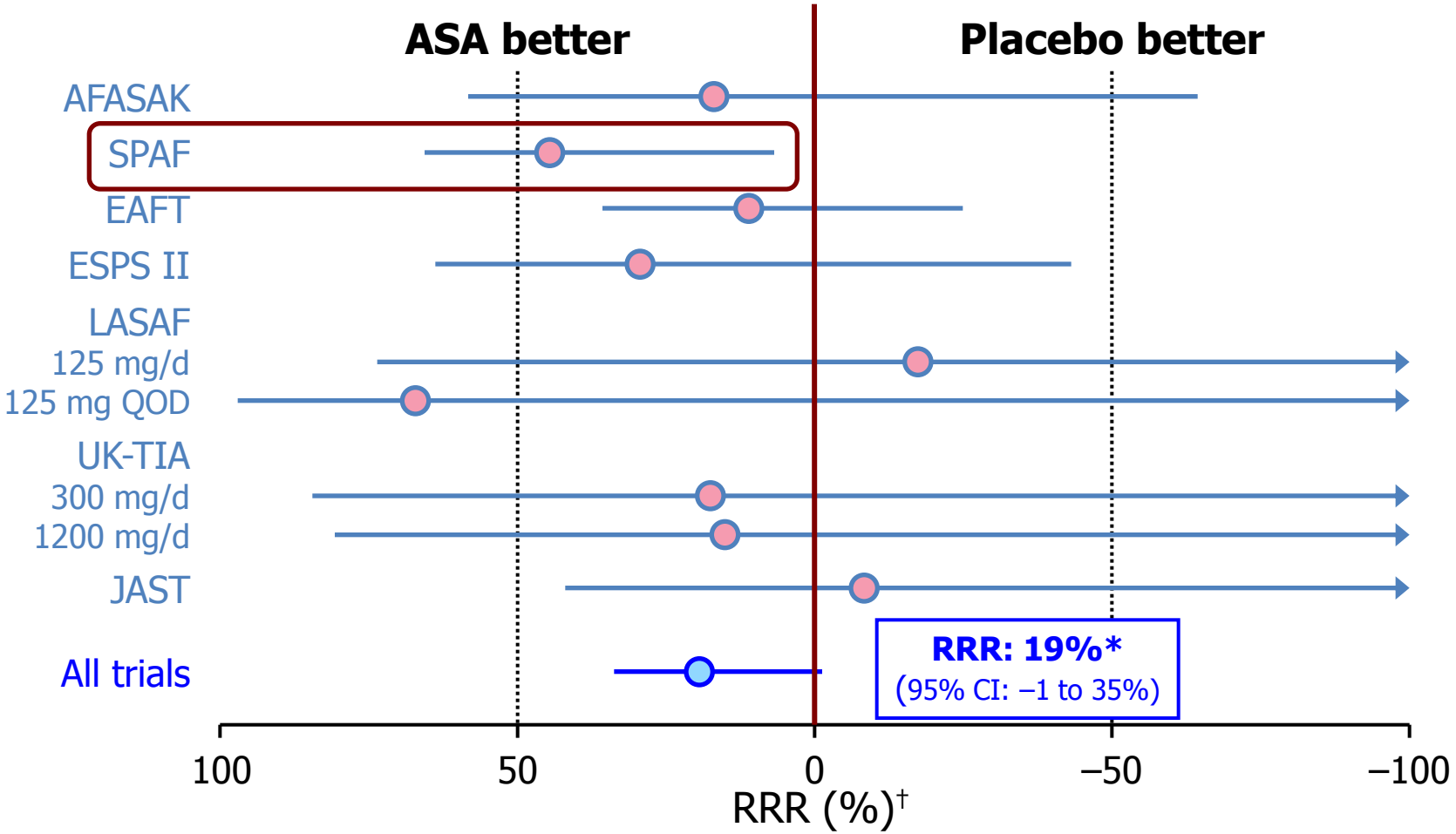
- fixed dose warfarin (INR=1.2-1.5) + ASA 325 mg
- adjusted dose warfarin (INR=2.0-3.0)





Blackshear, J L; Lancet 1996;348: 9028.

Limited efficacy of ASA in reducing the risk of stroke in patients with AF



Random effects model; error bars = 95% CI; *P>0.2 for homogeneity; †Relative risk reduction (RRR) for all strokes (ischaemic and haemorrhagic); for ischaemic stroke only, RRR was 21% (95% CI: −1 to 38%)

ASA = acetylsalicylic acid; QOD = every other day

Hart RG et al. Ann Intern Med 2007;146:857–67

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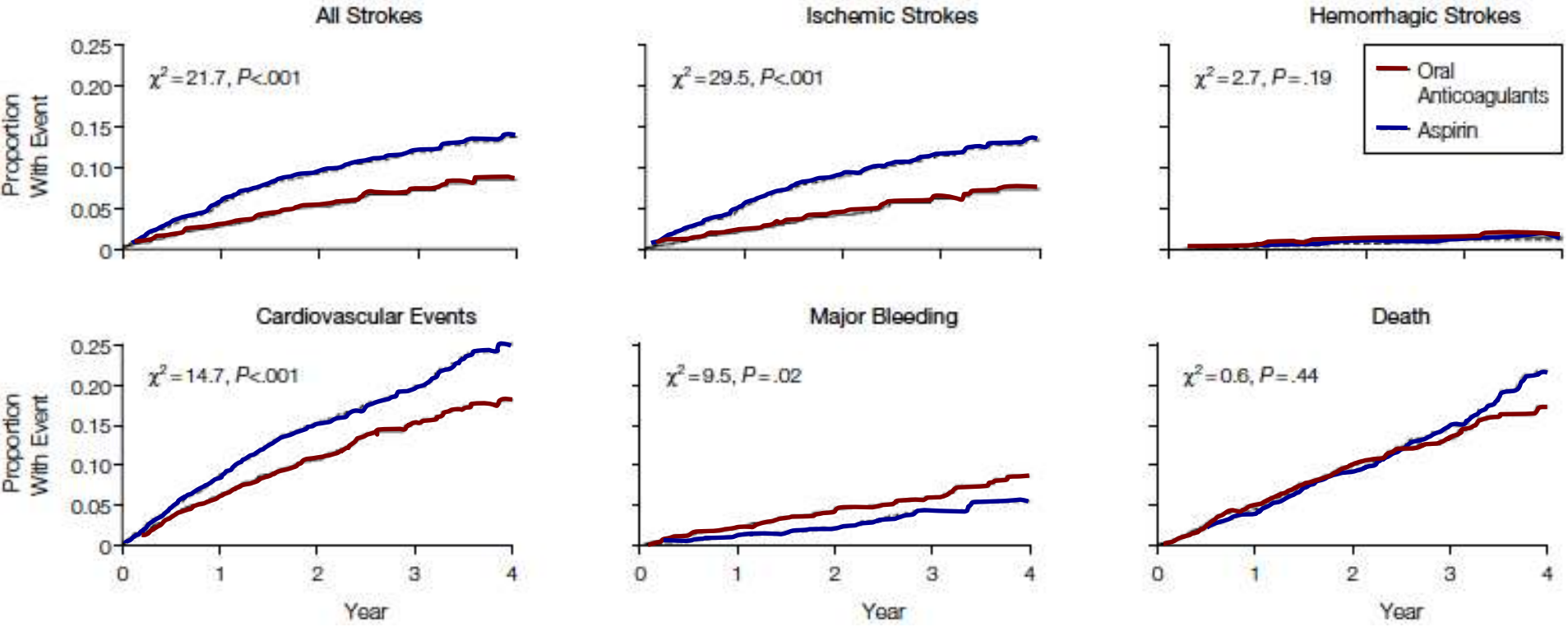
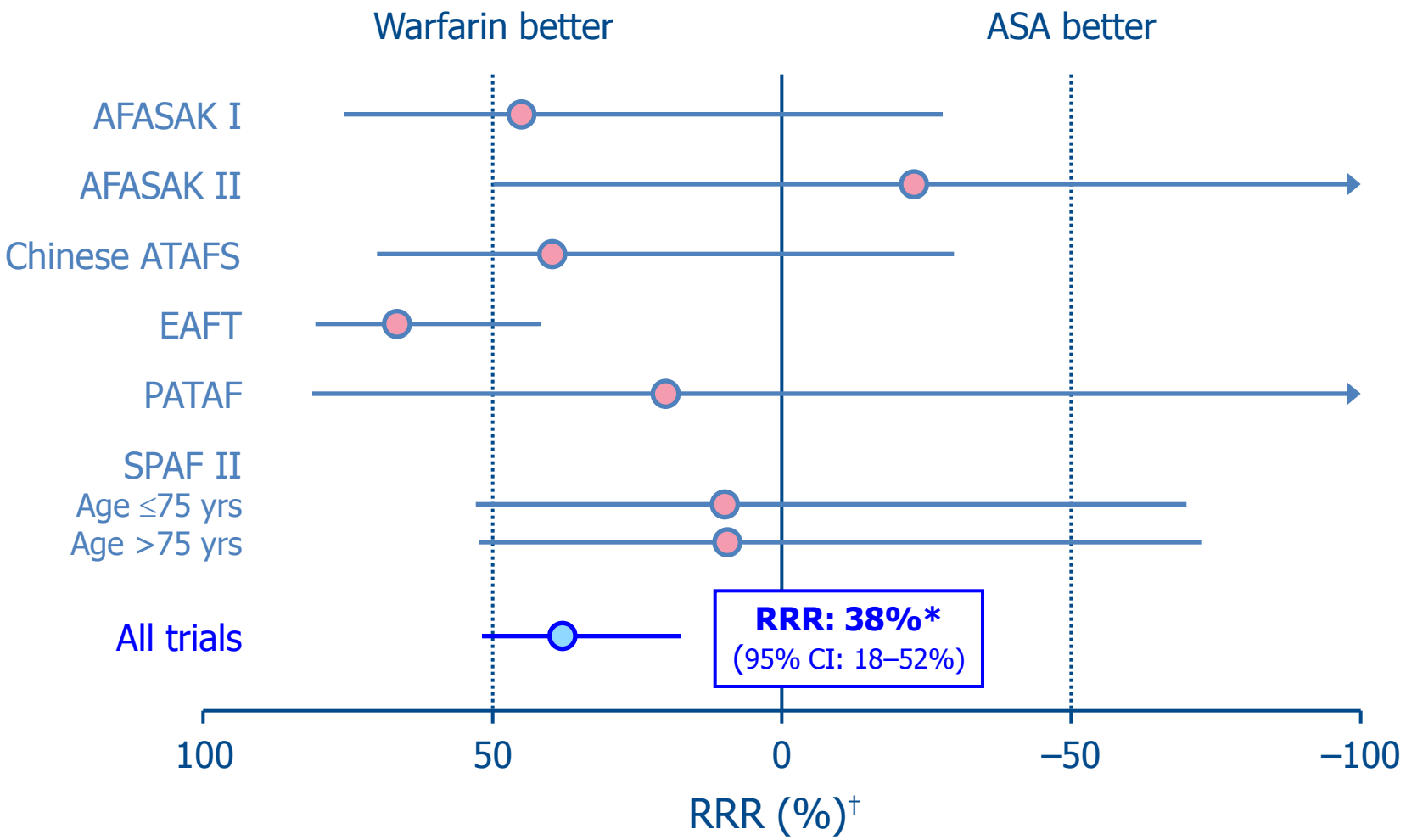
OAC vs ASA in non-valvular AF

individual patient meta-analysis



van Walraven C. JAMA 2002;288:2441.

ASA inferior to warfarin for stroke prevention in AF

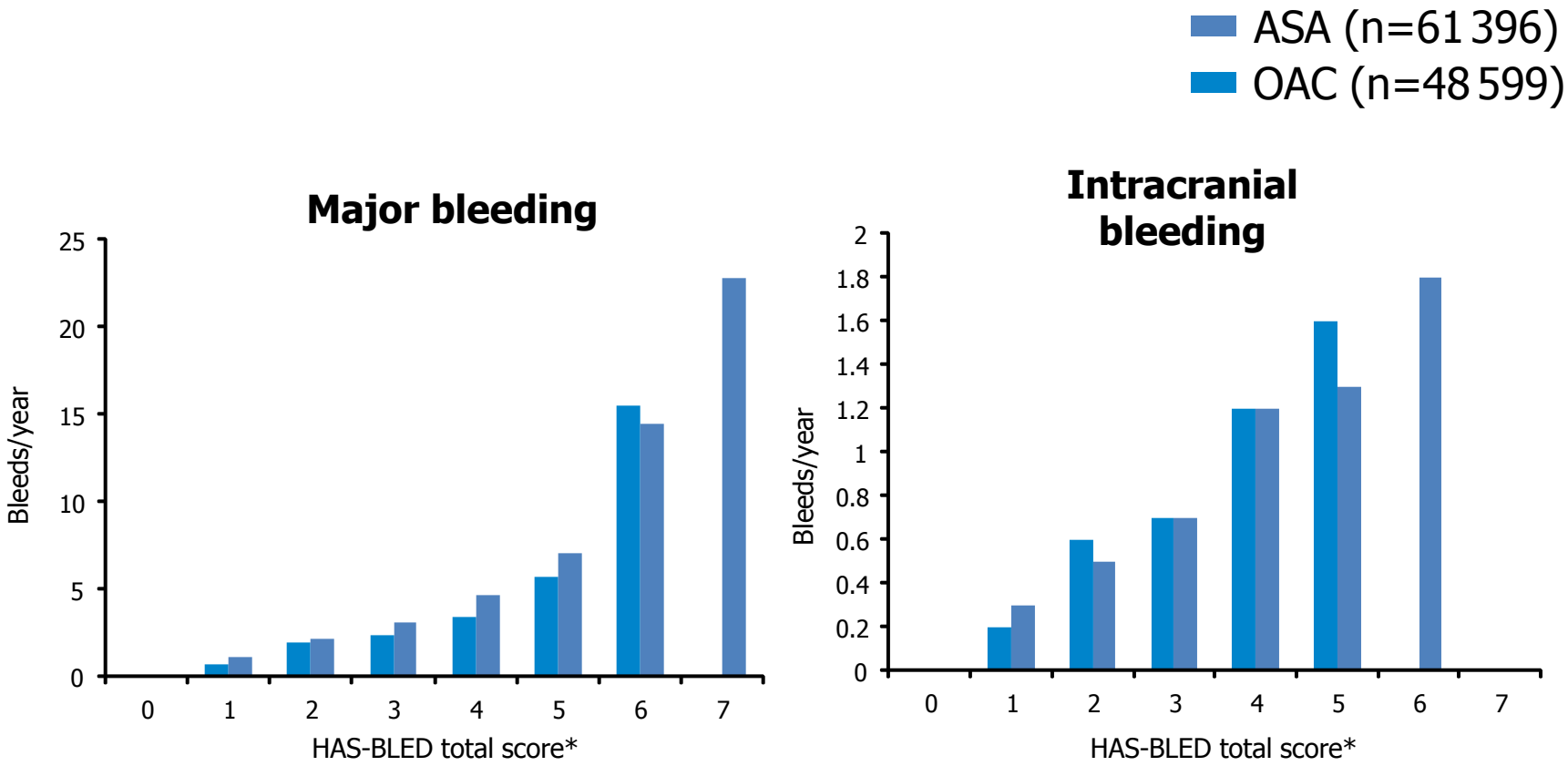


Random effects model; error bars = 95% CI; *P>0.2 for homogeneity;
†Relative risk reduction (RRR) for all strokes (ischaemic and haemorrhagic); ASA = acetylsalicylic acid

Hart RG et al. Ann Intern Med 2007;146:857–67

major and intracranial bleeding risk: OAC vs ASA

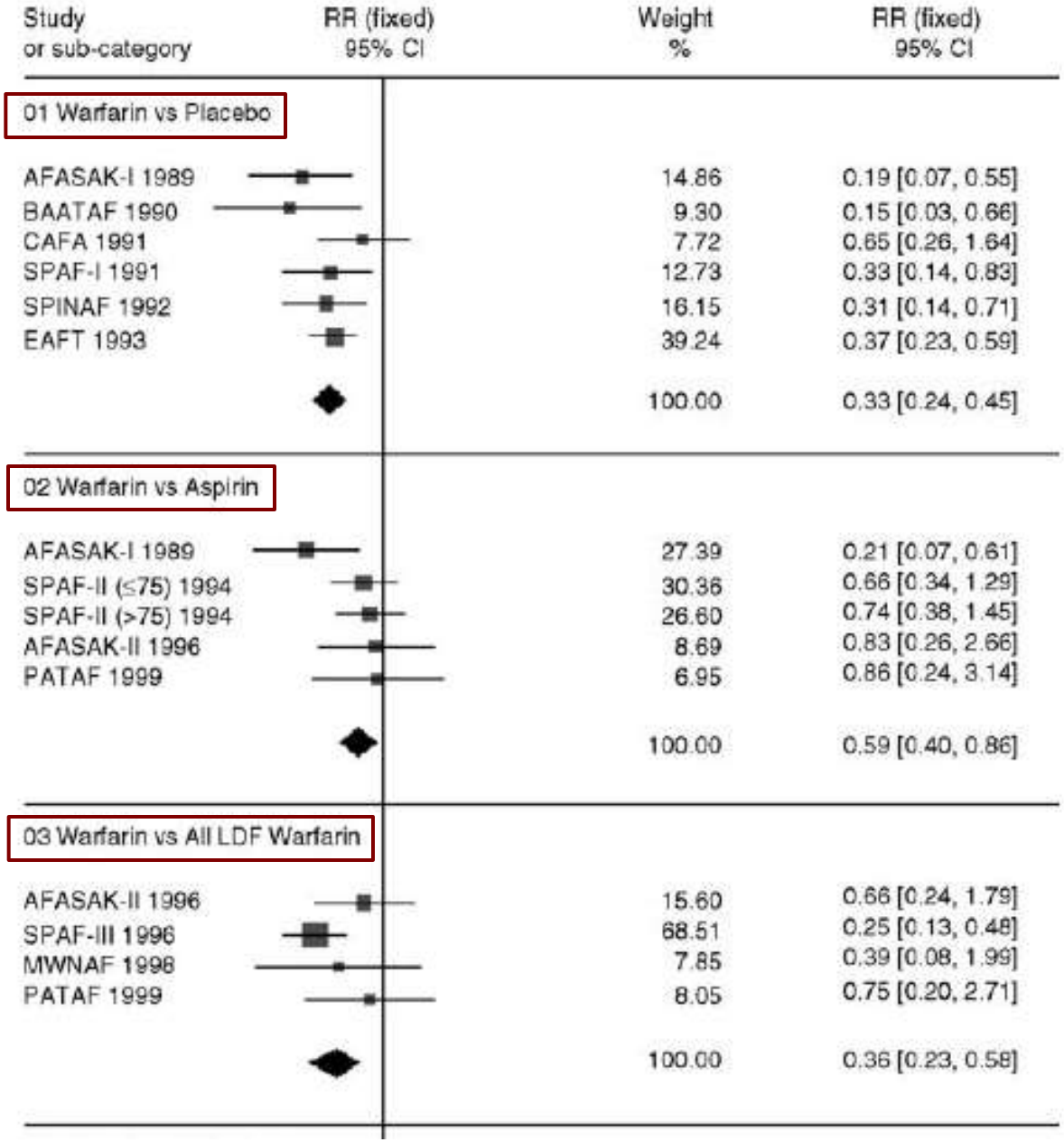
Swedish AF Cohort Study



Friberg L et al. Eur Hear J 2012:33:1500-10; Pisters R et al. Chest 2010;138:1093–100

ASA & warfarin in SPAF (meta-analysis)

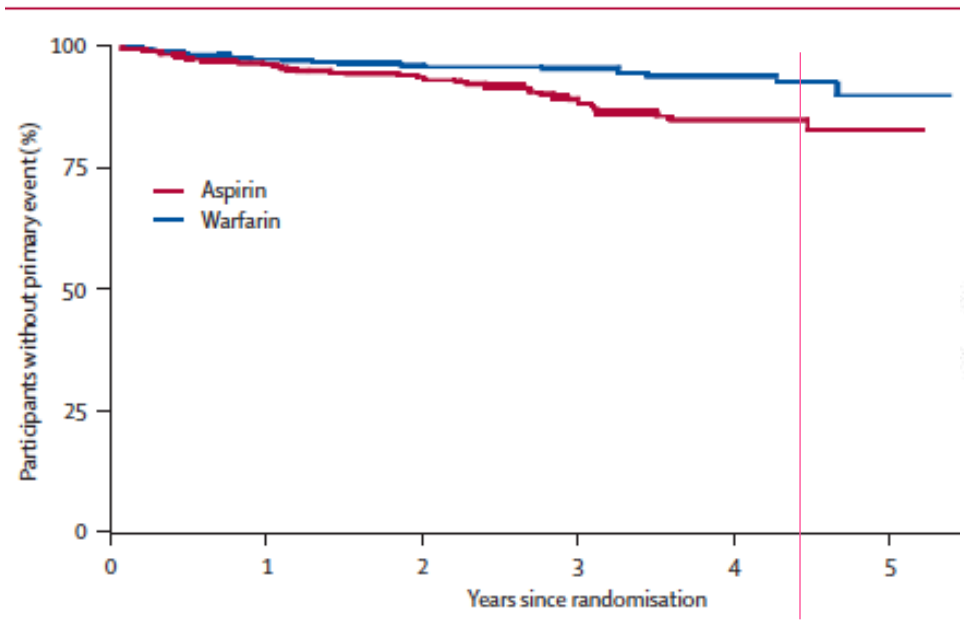
S/SE

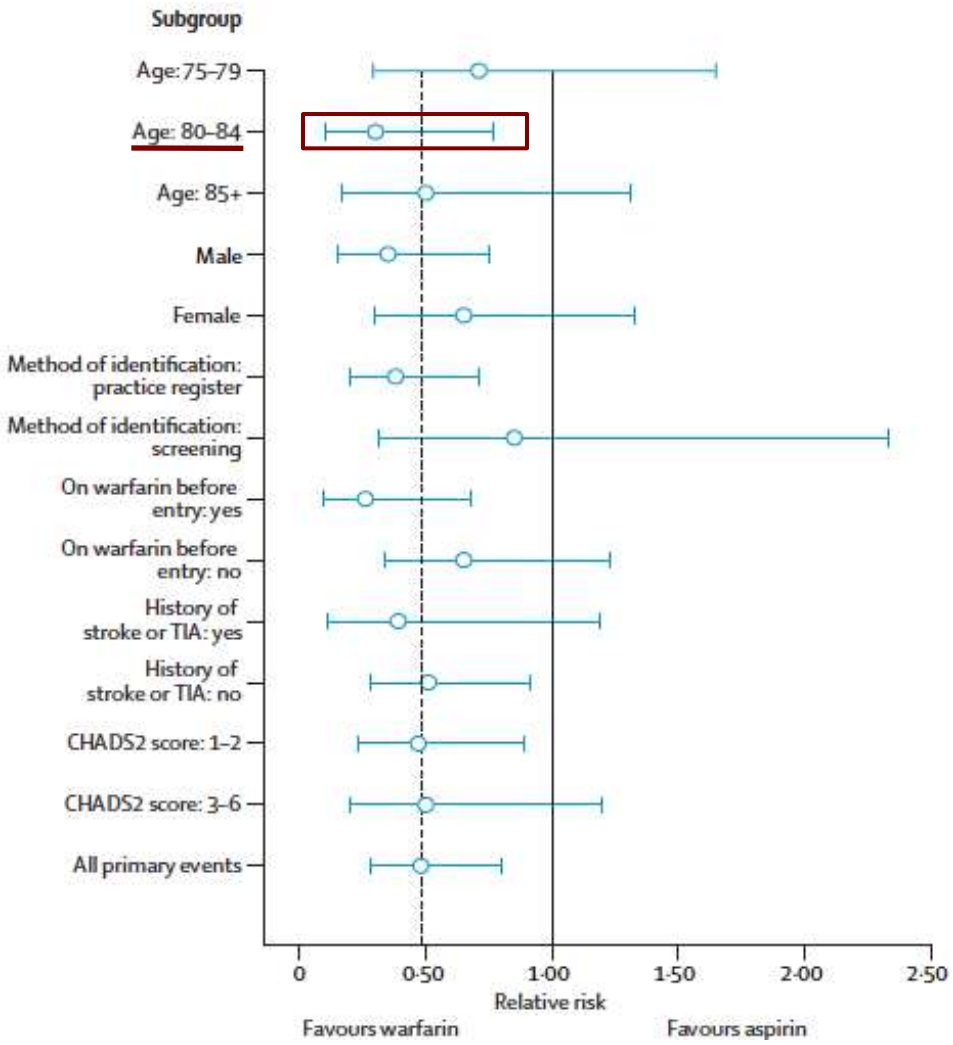


Lip GYH, Thromb Res 2006;118:321.

BAFTA: warfarin vs. ASA in SPAF in elderly

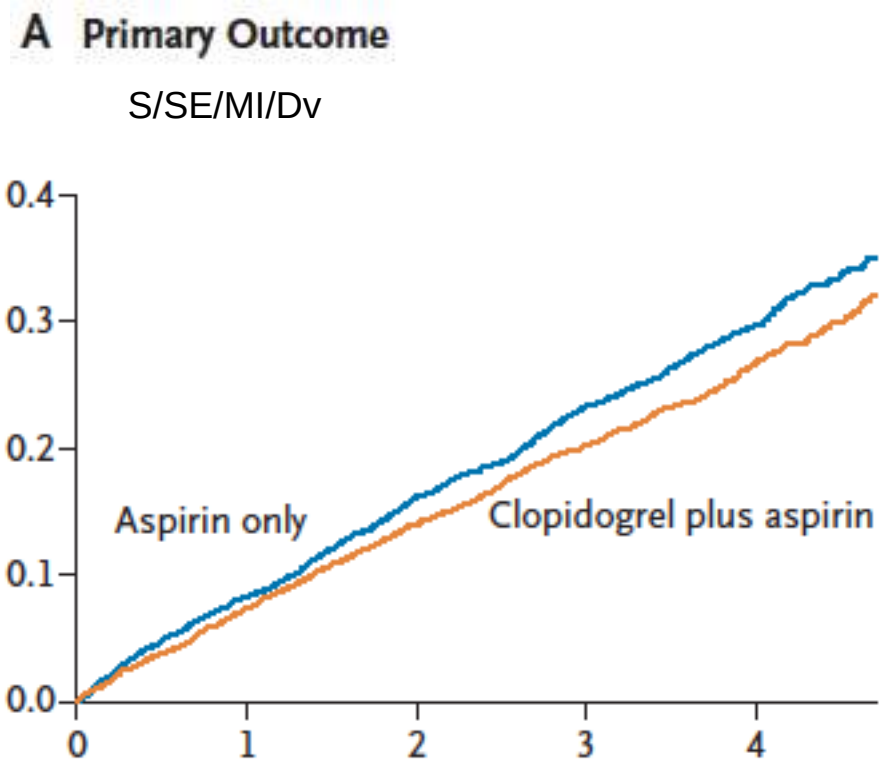
973 pts ≥ 75 yrs (mean 81.5)

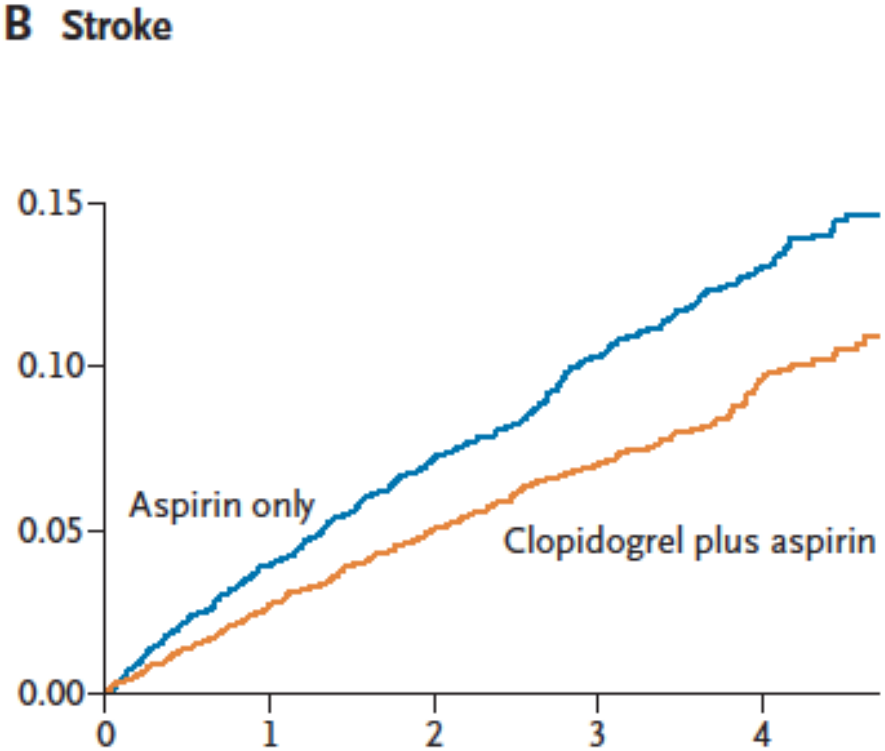




Mant J. Lancet 2007;370:493.

ACTIVE A: ASA + clopidogrel in patients with AF





Bleeding	Relative Risk (95% CI)	P Value
Major bleeding	1.57 (1.29–1.92)	<0.001
Severe	1.57 (1.25–1.98)	<0.001
Fatal	1.56 (0.96–2.53)	0.07
Minor bleeding	2.42 (2.03–2.89)	<0.001

N Engl J Med 2009;360:2066-78

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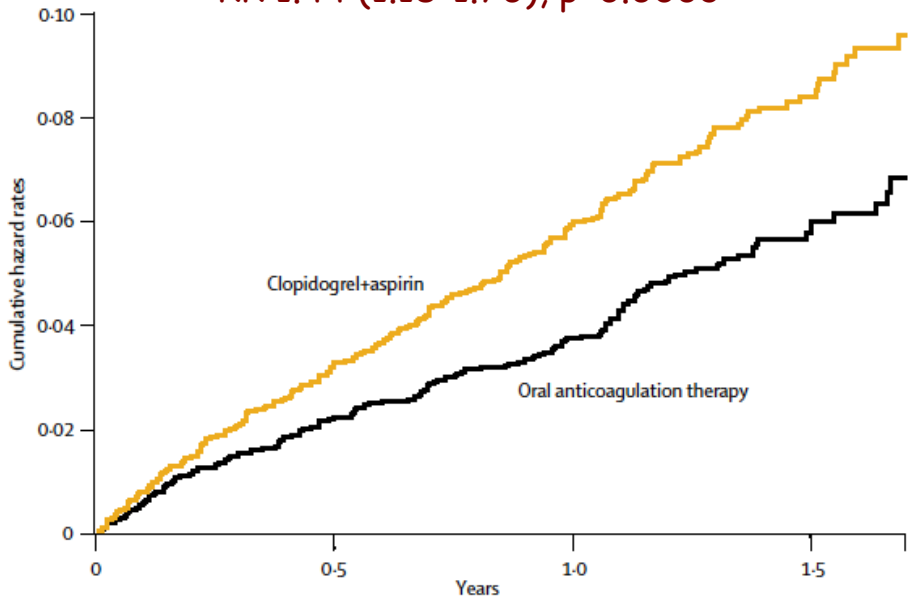
ACTIVE W: ASA + clopidogrel vs. OAC in AF pts

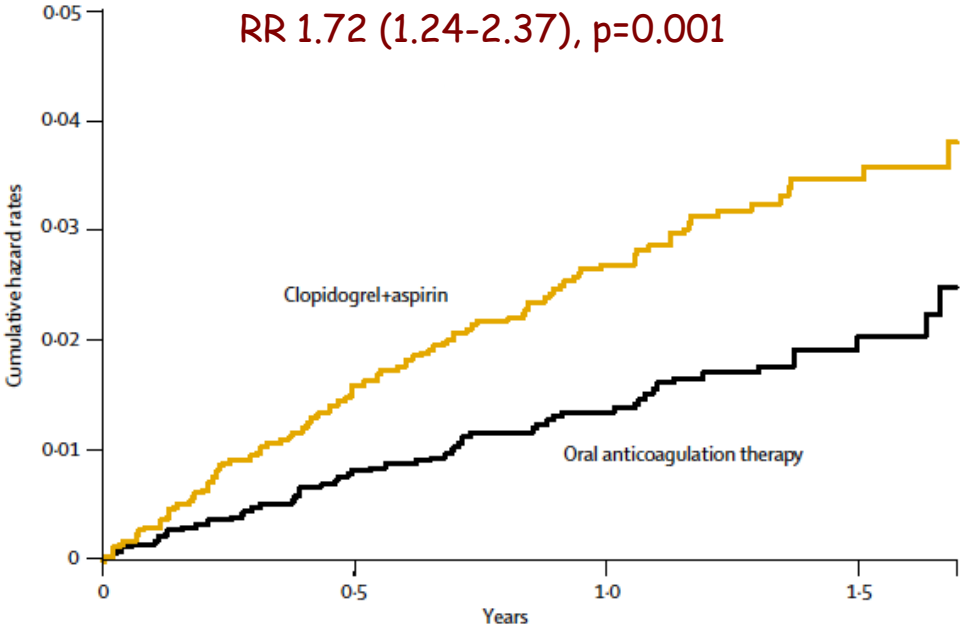
stroke / non-CNS systemic embolus / MI / vascular death

RR 1.44 (1.18-1.76), p=0.0003



stroke

RR 1.72 (1.24-2.37), p=0.001



Lancet 2006; 367: 1903–12

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AVERROES: Apixaban in patients with atrial fibrillation who have failed or are unsuitable for VKA rreatment

N=5,599

Event-driven

Patient Population

- Patients with AF and one or more risk factors for stroke
- Not receiving VKA therapy (demonstrated or expected to be unsuitable for VKA)

Apixaban 5 mg BD (2.5 mg in selected patients)

Aspirin 81–324 mg OD

Primary Outcomes

- Confirmed ischaemic stroke, haemorrhagic stroke, or systemic embolism

Secondary Outcomes

- Confirmed ischaemic stroke, haemorrhagic stroke, systemic embolism, myocardial infarction, or vascular death

522 centres

AVERROES=Apixaban VERsus Acetylsalicylic Acid (ASA) to PRevent StrOkES.

Connolly SJ et al. *N Engl J Med*. 2011;364:806–817
Eikelboom JW et al. *Am Heart J* 2010;159:348–353.e1.

AVERROES: mancata somministrazione di vitamina K

previsione di inadattabilità (60% pz.)

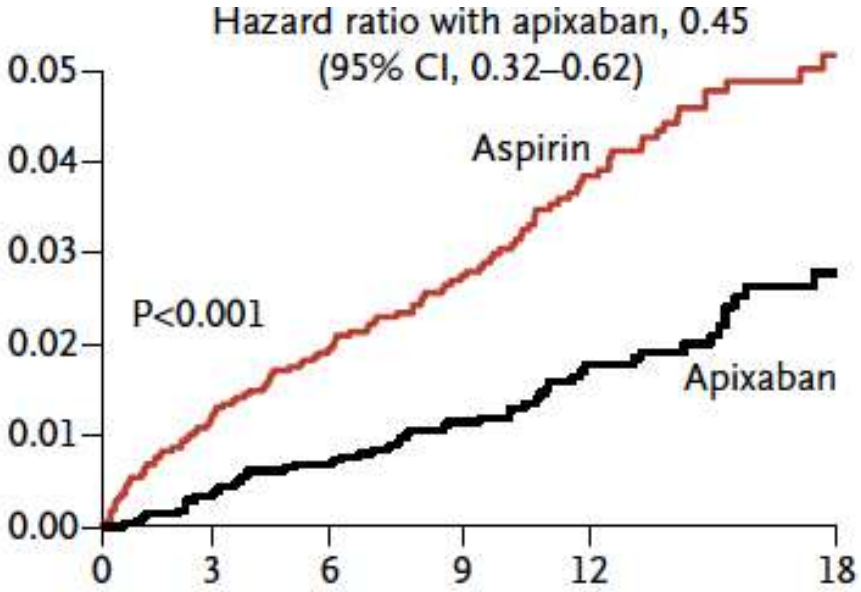
- scarsa aderenza
- interazione con altri trattamenti
- mancata restrizione dietetica
- rischio eccessivo dei VKA
- rifiuto del paziente

sospensione della VKA (40% pz.)

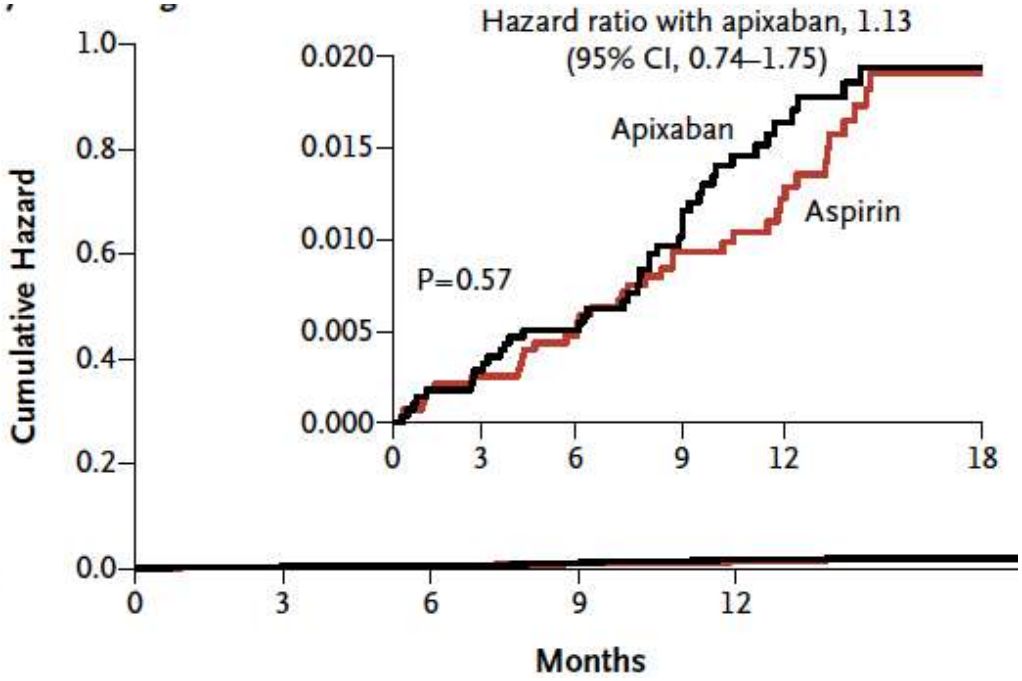
- scarsa aderenza al monitoraggio INR
- controllo inadeguato dell'INR
- eventi avversi
- interazione con altri trattamenti

AVERROES: apixaban vs. ASA in patients with AF

stroke or systemic embolism

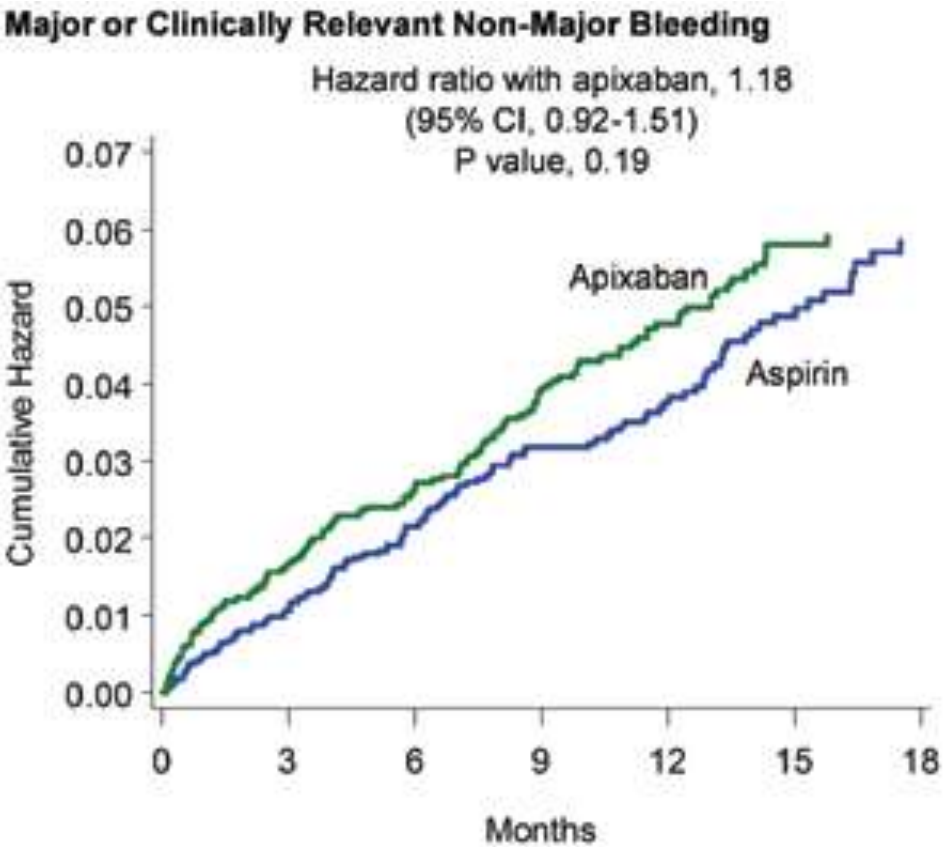


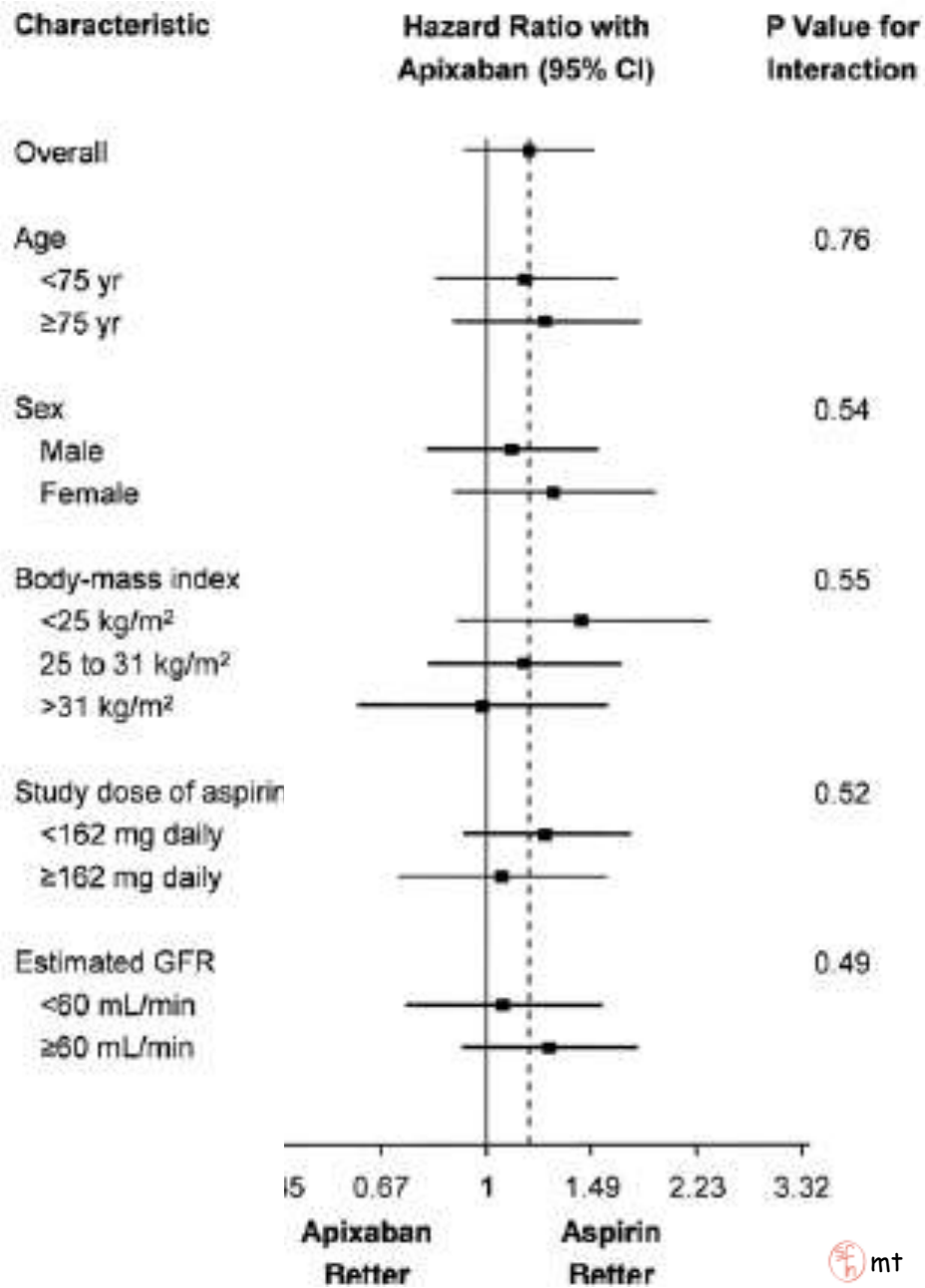
major bleeding



Connolly SJ, N Engl J Med 2011

AVERROES: bleeding analysis



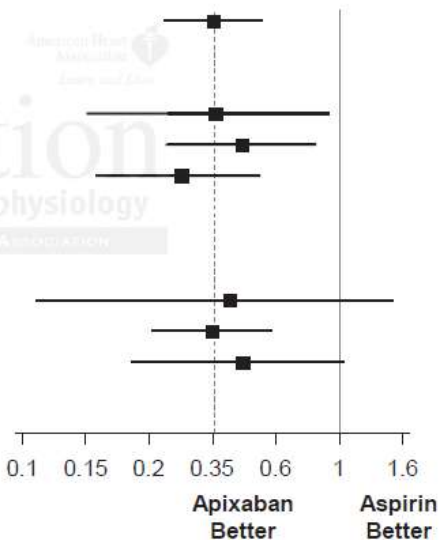


Flaker GC, Stroke 2012;43:3291

AVERROES: apixaban vs. aspirin in relation to stroke risk

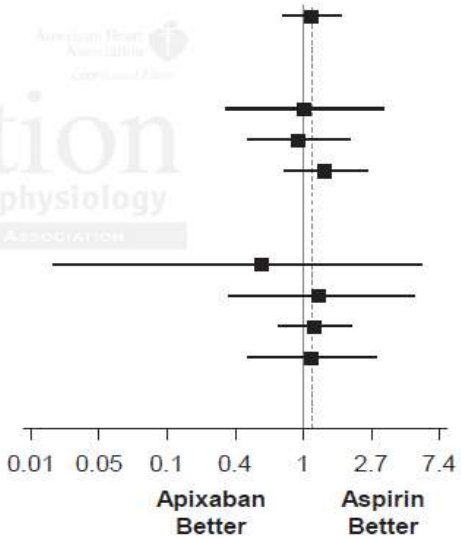
Ischaemic stroke

	Aspirin			Apixaban			P Value for Interaction
	no. of patients / no. of events (%/yr)						
Overall	2788	93	(3.0)	2806	35	(1.1)	
$CHADS_2$ score							0.54
0-1	1022	16	(1.4)	1004	6	(0.5)	
2	954	33	(3.1)	1044	17	(1.4)	
3-6	812	44	(5.0)	758	12	(1.5)	
CHA_2DS_2-VASc score							0.35
0-1	312	5	(1.4)	277	0	(0)	
2	660	7	(0.9)	689	3	(0.4)	
3-5	1616	62	(3.5)	1659	24	(1.3)	
6-8	200	19	(8.6)	181	8	(4.2)	



Major bleeding

Overall	2788	39	(1.3)	2806	44	(1.4)	
$CHADS_2$ score							0.70
0-1	1022	6	(0.5)	1004	6	(0.5)	
2	954	14	(1.3)	1044	14	(1.2)	
3-6	812	19	(2.1)	758	24	(2.9)	
CHA_2DS_2-VASc score							0.94
0-1	312	2	(0.6)	277	1	(0.3)	
2	660	4	(0.5)	689	5	(0.7)	
3-5	1616	24	(1.3)	1659	29	(1.6)	
6-8	200	9	(4.1)	181	9	(4.7)	



Lip GYH. Circ EP 2013;6:31

AVERROES: unsuitable for VKA vs. VKA failure

	Apixaban vs. Aspirin		
	Hazard ratio (95% CI)	***P*-value**	**Interaction *P*-value**
Stroke or systemic embolism			
All	0.45 (0.32–0.62)	<0.001	
Tried and failed VKA therapy	0.32 (0.19–0.56)	<0.001	0.13
Expected to be unsuitable for VKA therapy	0.55 (0.36–0.84)	0.005	
Major bleeding			
All	1.13 (0.74–1.75)	0.57	
Tried and failed VKA therapy	1.06 (0.58–1.93)	0.84	0.74
Expected to be unsuitable for VKA therapy	1.22 (0.66–2.31)	0.52	

Coppens M. Eur Heart J 2014

mt

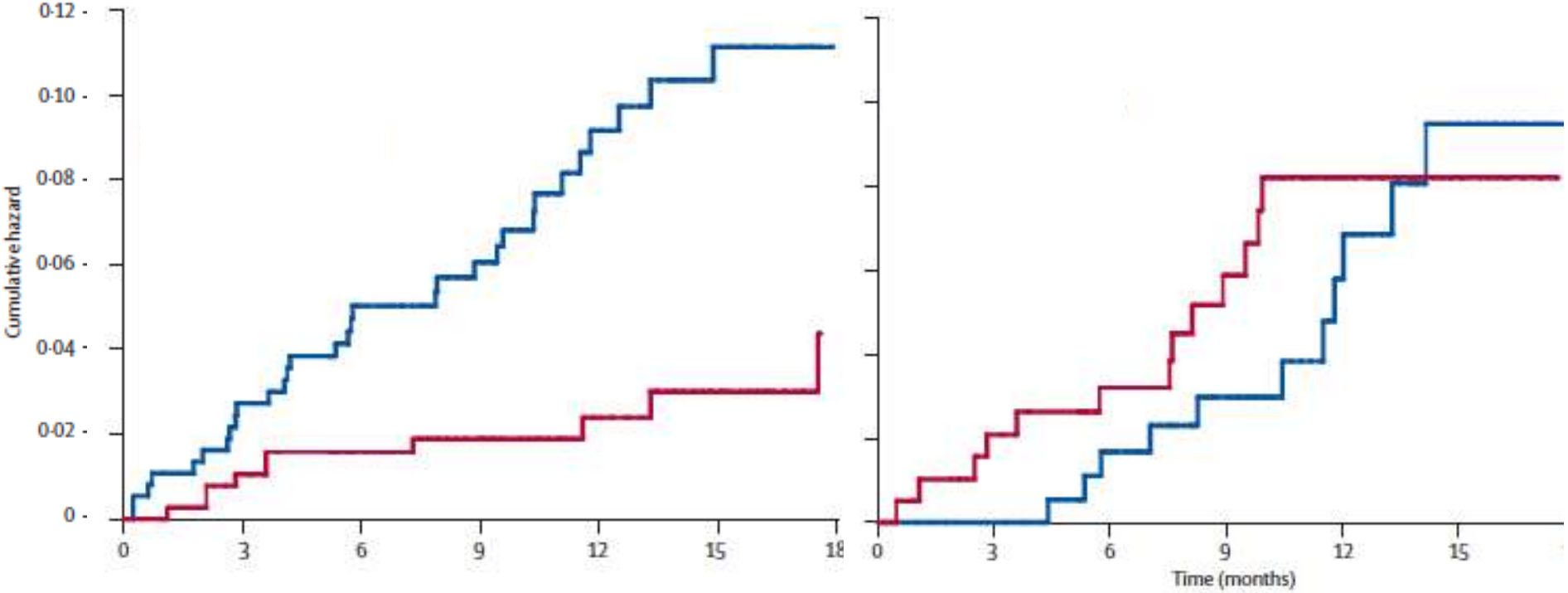
AVERROES: apixaban in pts with previous stroke/TIA

stroke or systemic embolism

HR 0.29 (0-15-0.60)

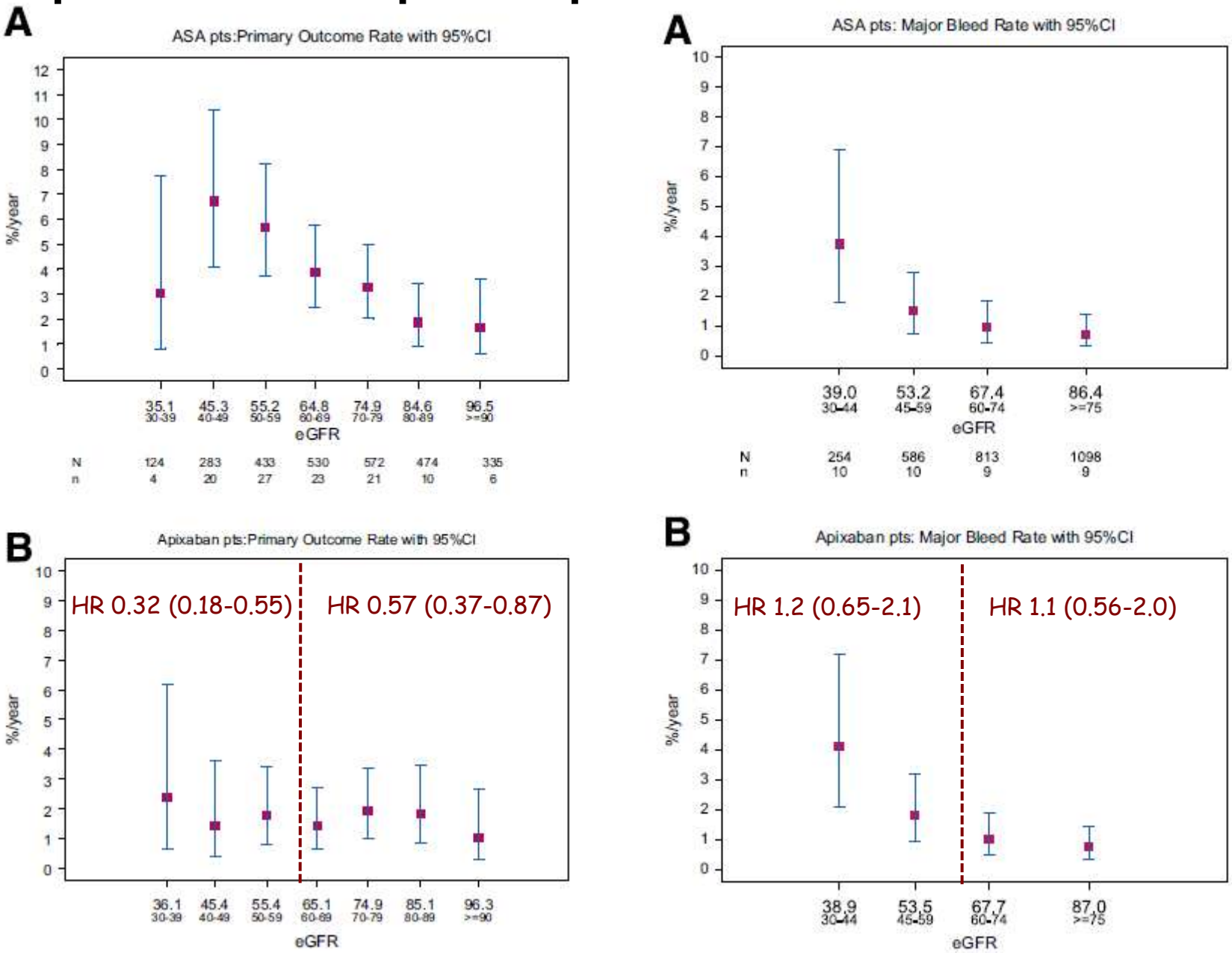
major bleeding

HR 1.28 (0-58-2.82)



Diener H-C, Lancet 2012

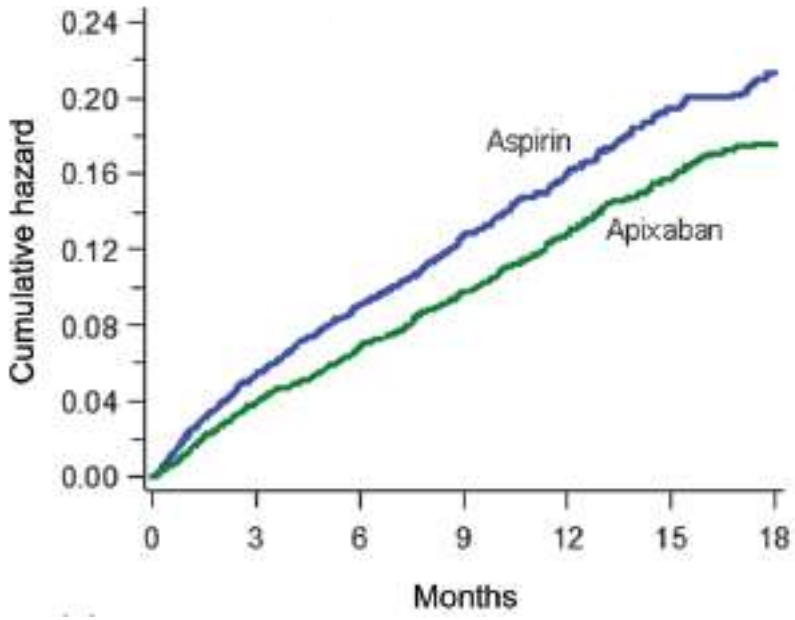
Apixaban and aspirin in patients with moderate CKD



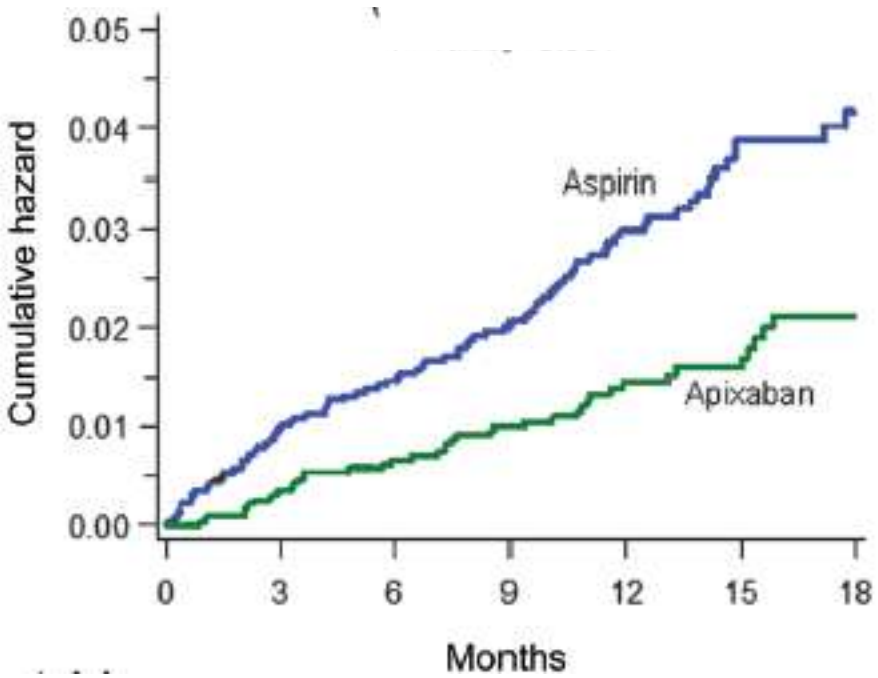
Eikelboom JW. J Stroke Cerebrovasc Dis 2012;21:429

AVERROES: effects of apixaban on hospitalizations

CV hospitalizations
HR 0.80 (0.69-0.92), p=0.002



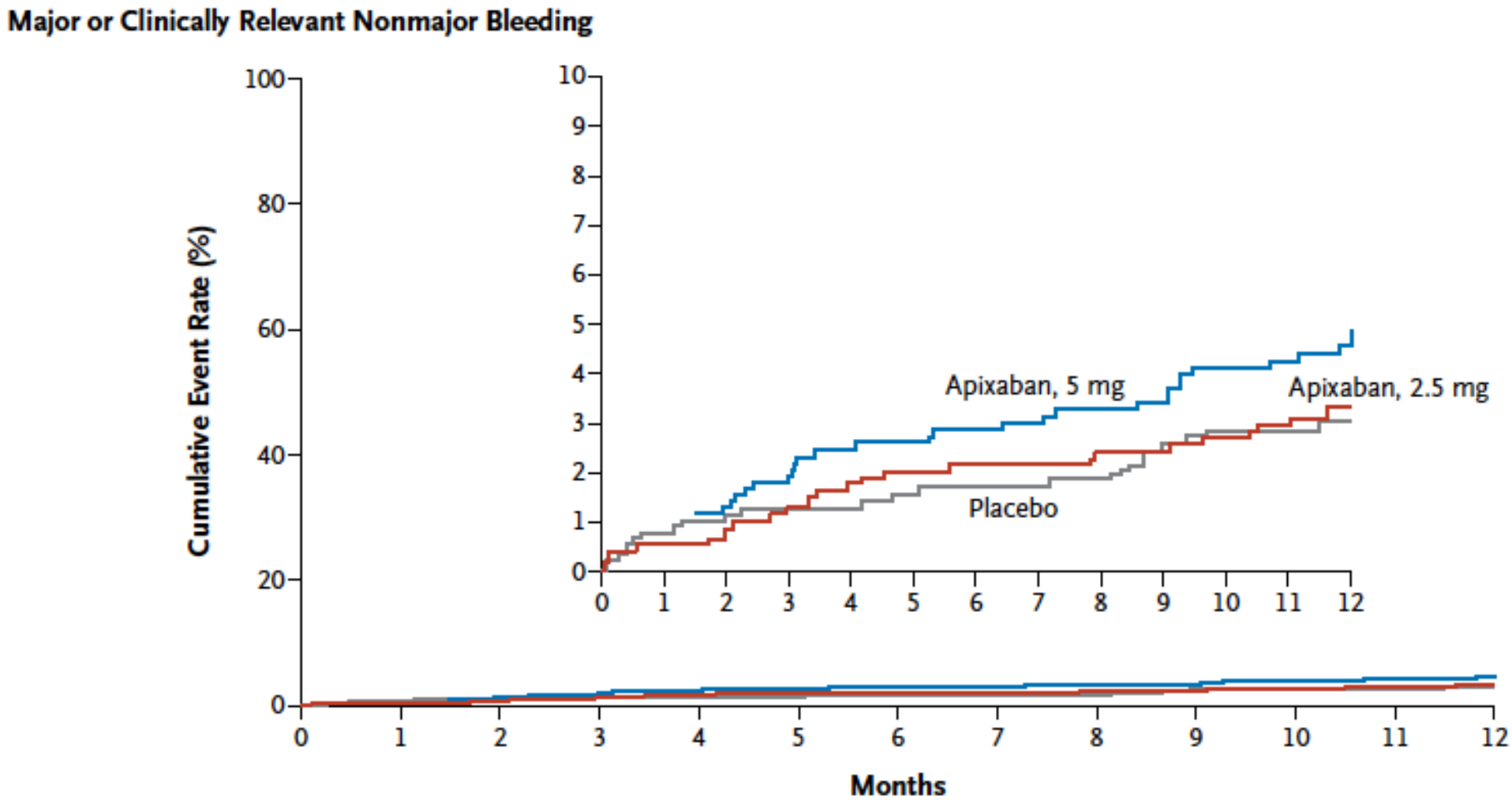
stroke or hospitalizations
HR 0.45 (0.31-0.65), p=0.002



ospedalizzazioni per motivi cardiovascolari → mortalità HR 3.95 (3.06-5.09)

Hohnloser SH, Eur Heart J 2013

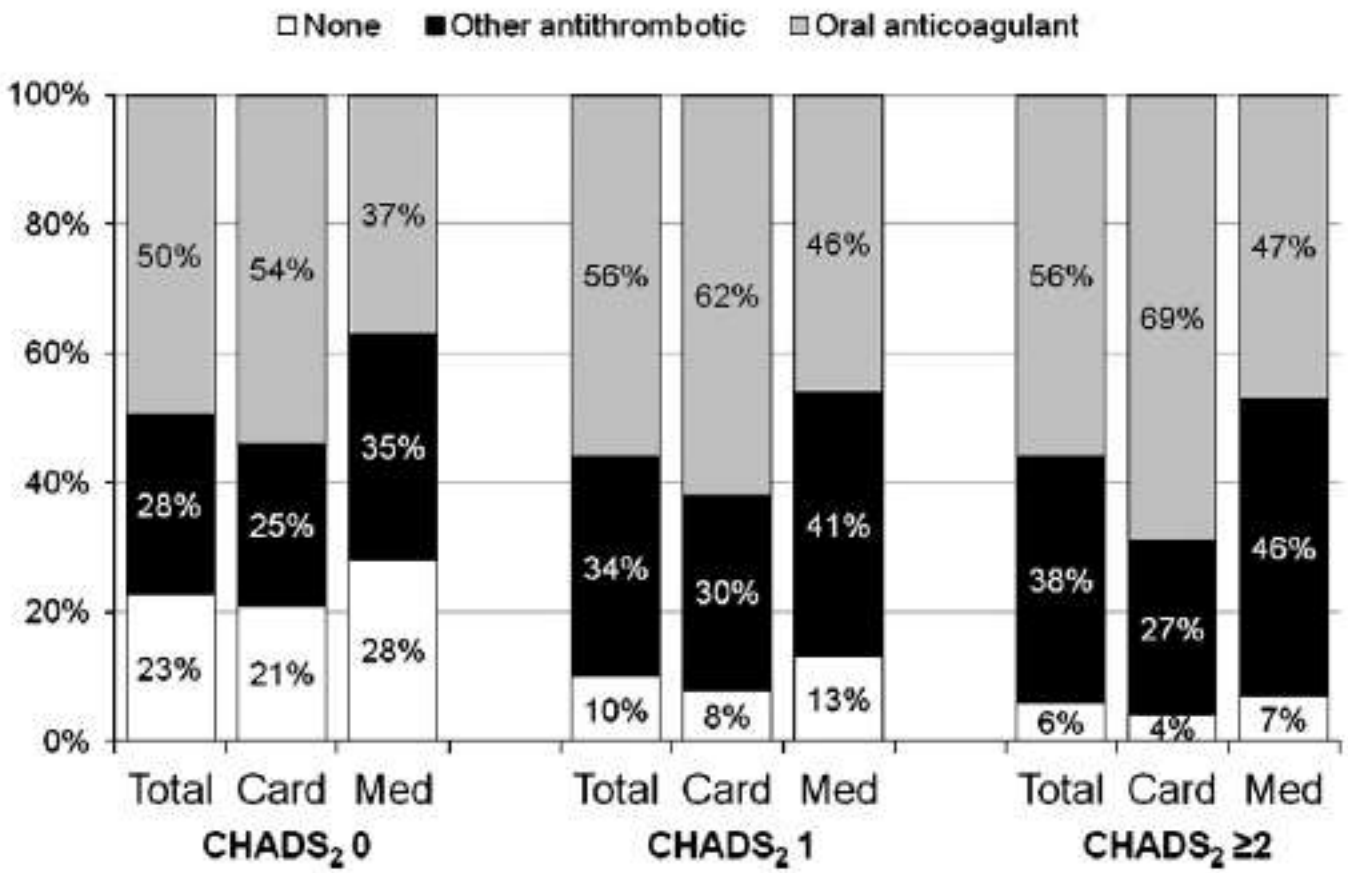
AMPLIFY-EXT: apixaban vs. placebo after VTE



Agnelli G. N Engl J Med 2012

ATA-AF Registry: management of AF in Italy

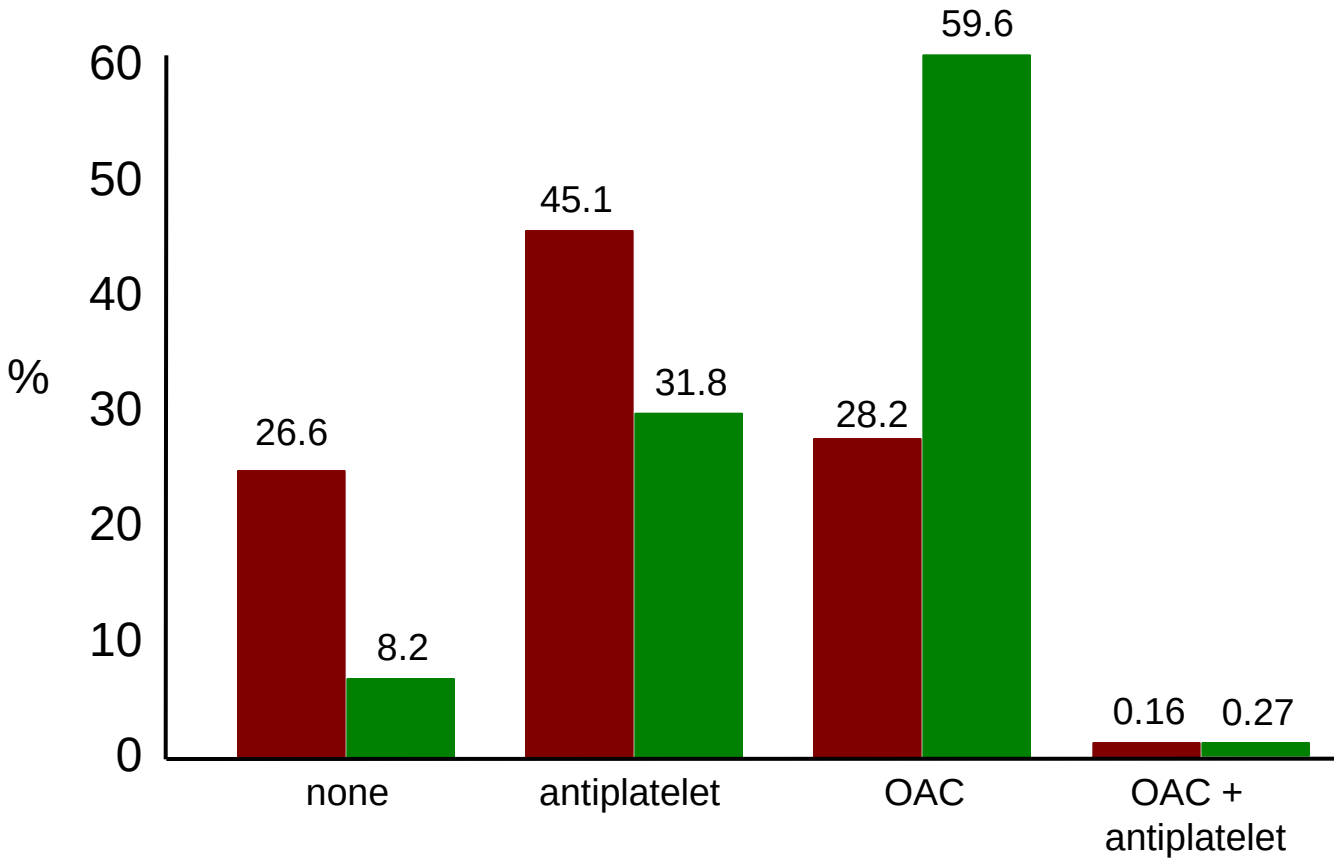
360 centres, 7148 pts, median age 77 yrs



Di Pasquale G. Int J Cardiol 2012

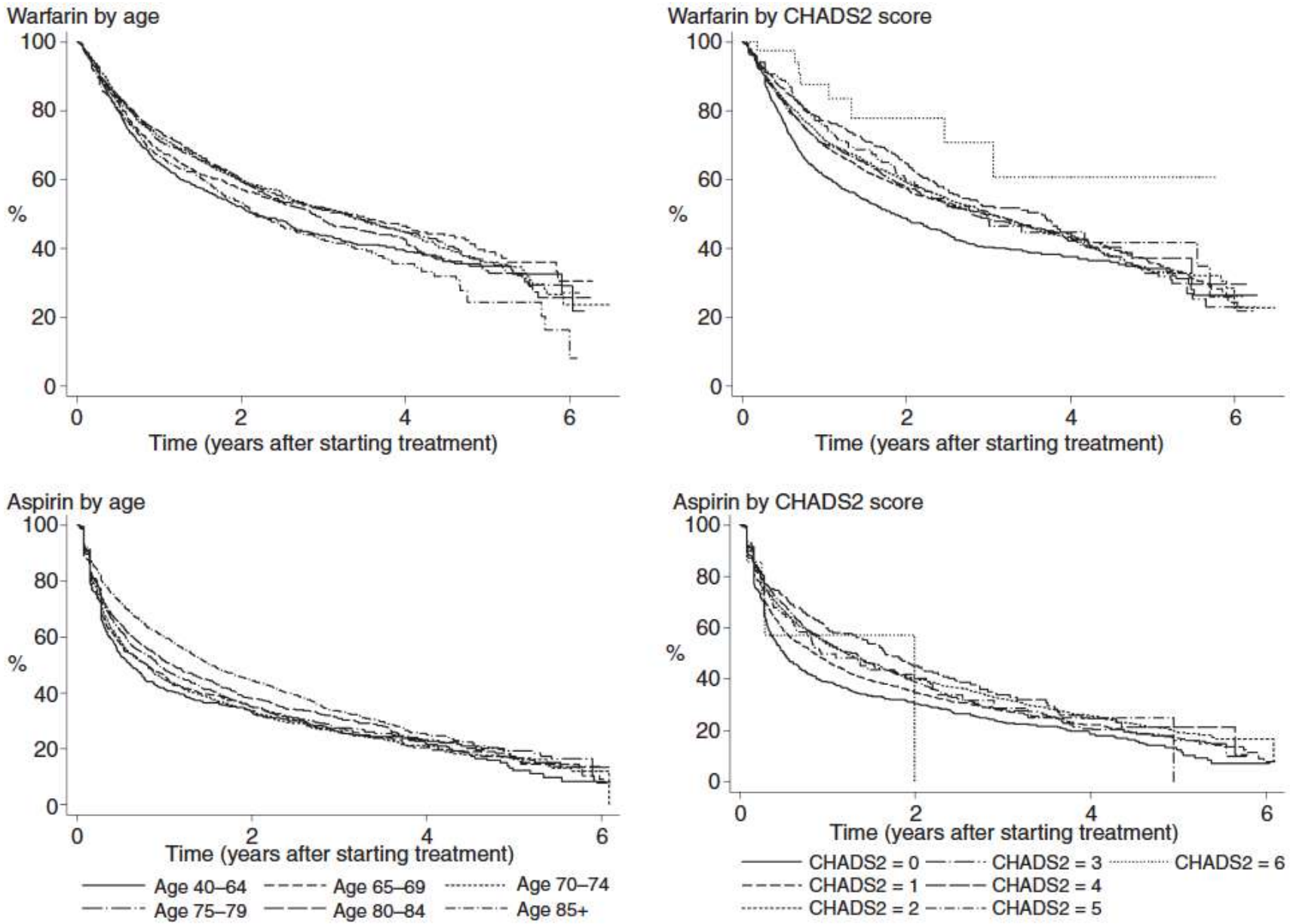
ISAF: Italian Survey of Atrial Fibrillation Management Study

233 practitioners, 6036 pts



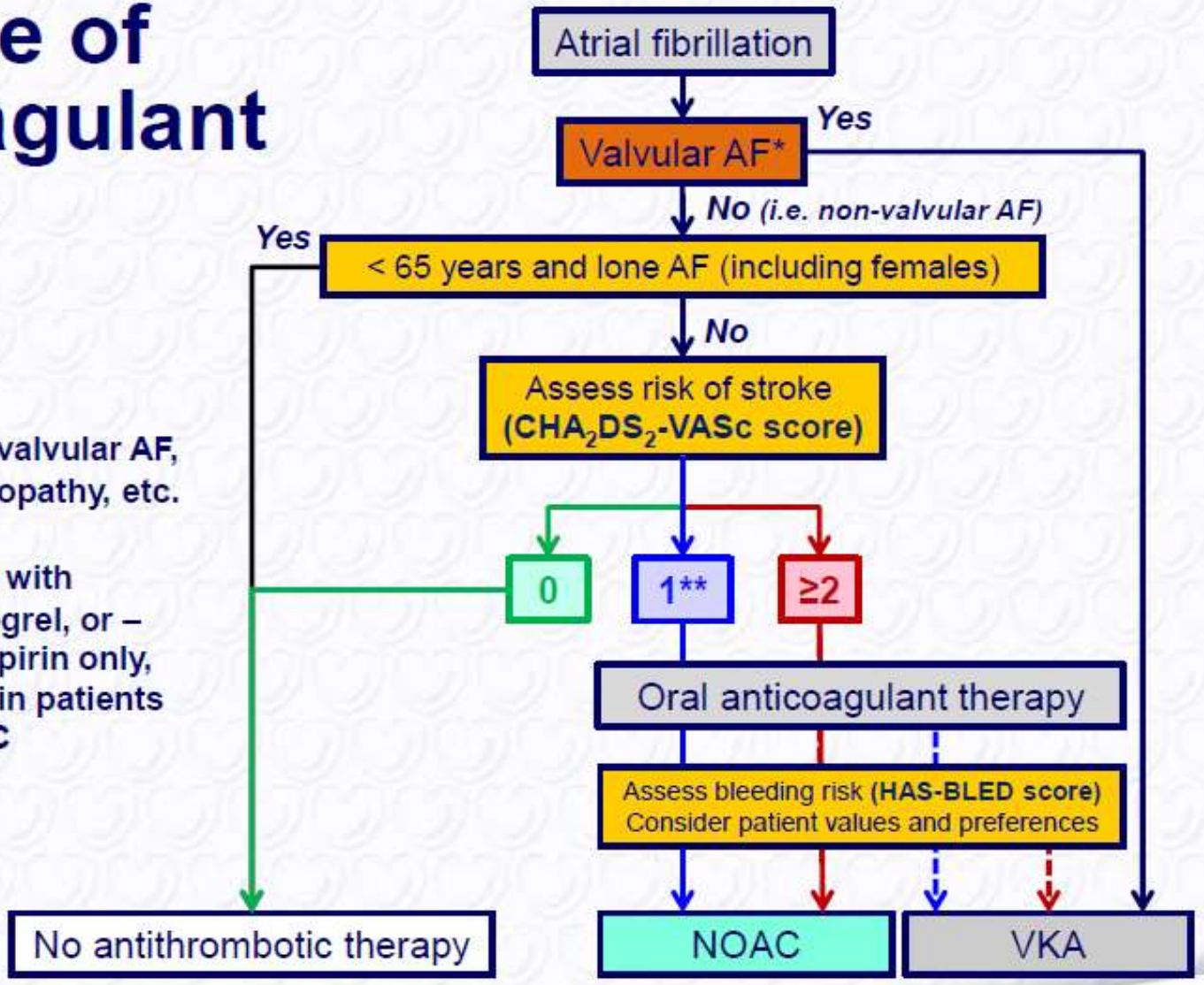
Zoni Berisso M. Am J Cardiol 2013

chronic AF: persistence of warfarin vs. aspirin



Gallagher AM. J thromb Haemost 2008

Choice of Anti-coagulant



* Includes rheumatic valvular AF, hypertrophic cardiomyopathy, etc.

** Antiplatelet therapy with aspirin plus clopidogrel, or – less effectively – aspirin only, may be considered in patients who refuse any OAC

European Heart Journal 2012 · doi:10.1093/eurheartj/ehs253