In che paziente oggi preferisco usare i NAO

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Varese

Attuali indicazioni ai farmaci anticoagulanti orali diretti

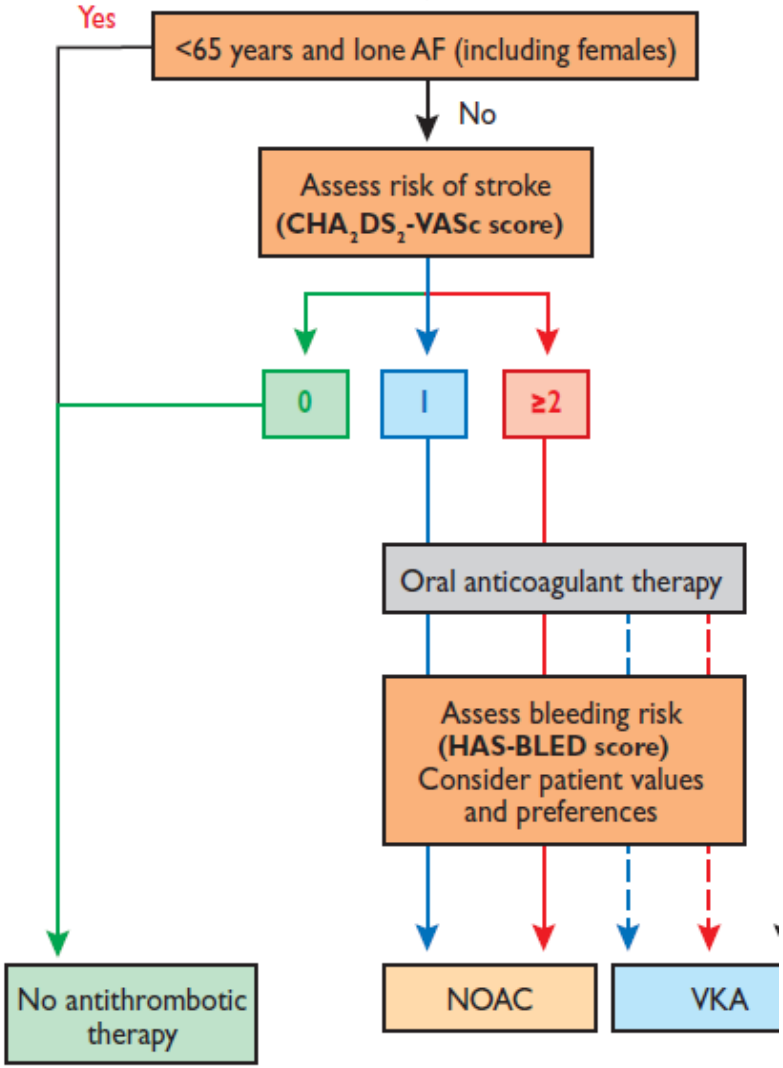
- Prevenzione dell'ictus nei pazienti con fibrillazione atriale non valvolare (tutti)
- Sindromi coronariche acute (rivaroxaban)

- Prevenzione del tromboembolismo venoso in pazienti sottoposti a chirurgia protesica di anca e ginocchio (apixaban, dabigatran, rivaroxaban)
- Terapia acuta e prevenzione secondaria di TVP ed embolia polmonare (tutti)

Indicazioni in corso di studio (e non rimborsabili)

- Prevenzione secondaria dopo ictus criptogenico
- Prevenzione primaria nello scompenso cardiaco
- Prevenzione secondaria del cardioembolismo nella cardiopatia dilatativa
- Terapia dell'arteriopatia periferica

ESC update guidelines for AF



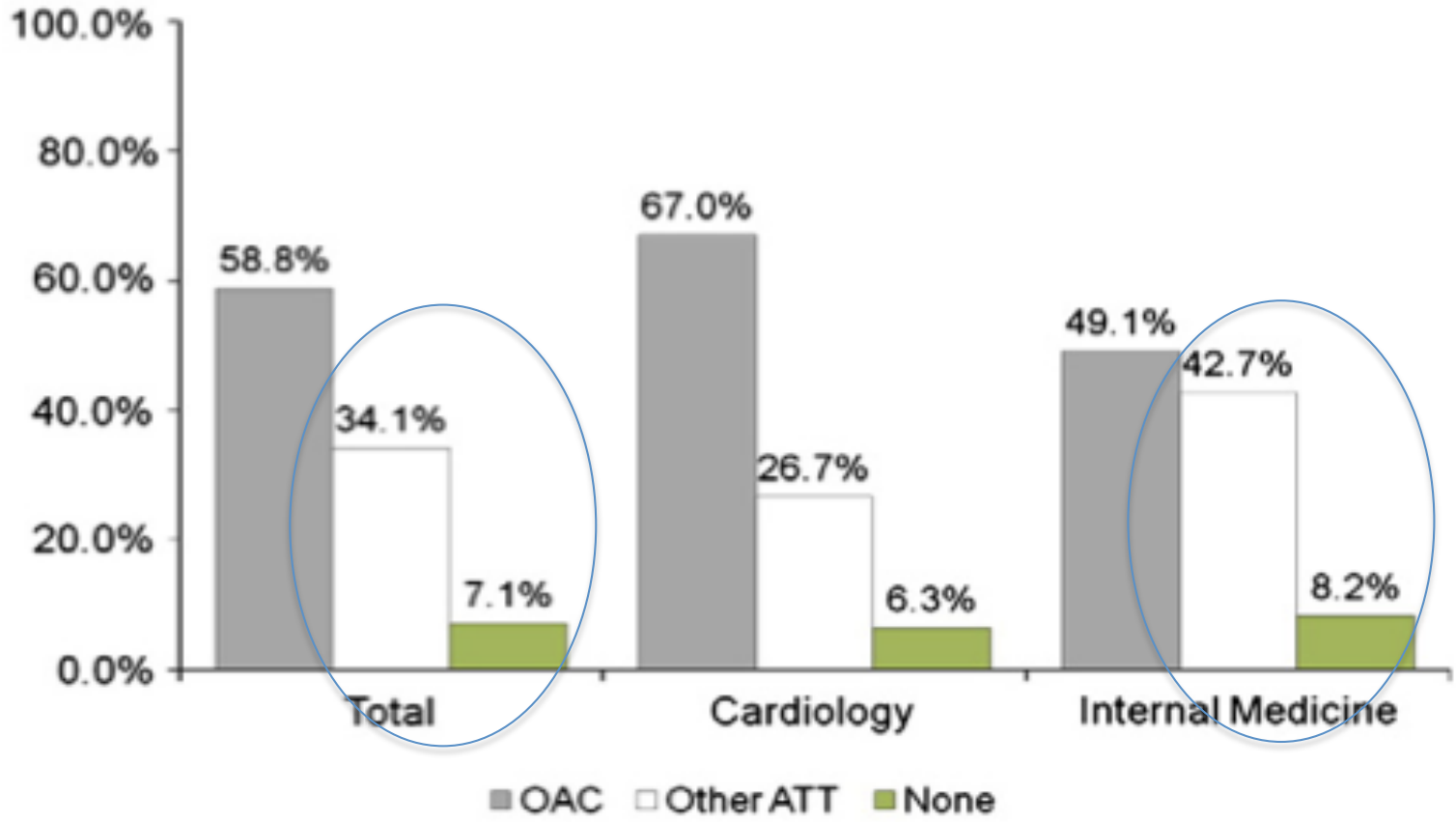
ESC = European Society of Cardiology

Camm J et al. Eur Heart J 2012;33:2719–47

Current presentation and management of 7148 patients with atrial fibrillation in cardiology and internal medicine hospital centers: The ATA AF study☆

Giuseppe Di Pasquale [a], Giovanni Mathieu [b], Aldo Pietro Maggioni [c,*], Gianna Fabbri [c], Donata Lucci [c], Giorgio Vescovo [d], Salvatore Pirelli [e], Francesco Chiarella [f], Marino Scherillo [g], Michele Massimo Gulizia [h], Gualberto Gussoni [i], Fabrizio Colombo [j], Domenico Panuccio [k], Carlo Nozzoli [l], Massimo Zoni Berisso [m] on behalf of ATA-AF Investigators [1]

International Journal of Cardiology 167 (2013) 2895–2903



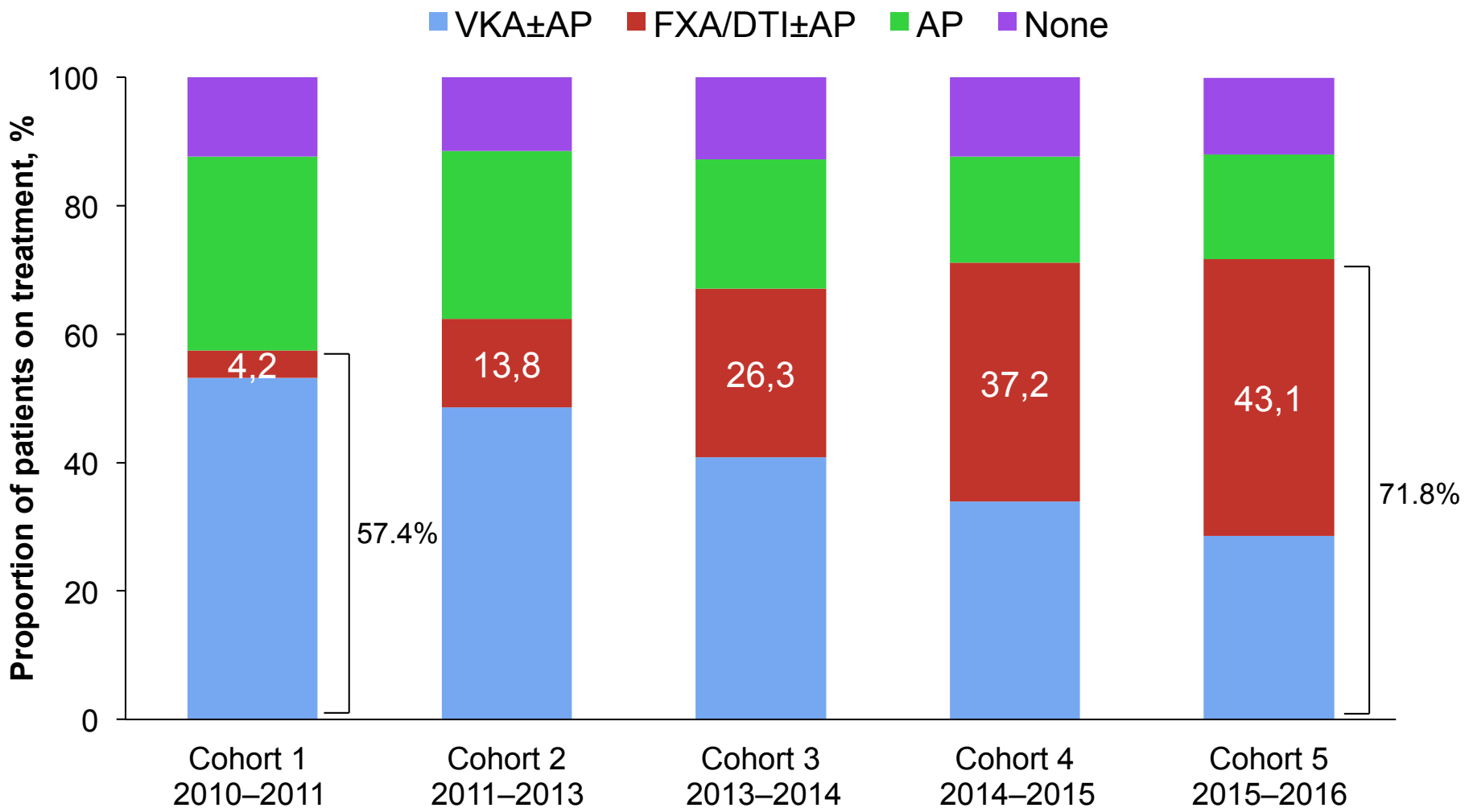
OAC= Oral Anticoagulant; ATT= Antithrombotic Treatment

Current presentation and management of 7148 patients with atrial fibrillation in cardiology and internal medicine hospital centers: The ATA AF study☆

Giuseppe Di Pasquale [a], Giovanni Mathieu [b], Aldo Pietro Maggioni [c,*], Gianna Fabbri [c], Donata Lucci [c], Giorgio Vescovo [d], Salvatore Pirelli [e], Francesco Chiarella [f], Marino Scherillo [g], Michele Massimo Gulizia [h], Gualberto Gussoni [i], Fabrizio Colombo [j], Domenico Panuccio [k], Carlo Nozzoli [l], Massimo Zoni Berisso [m] on behalf of ATA-AF Investigators [1]

Characteristics	Total (n. 7148)	Cardiology (n. 3862)	Internal medicine (n. 3286)	p
Age (years), median [IQR]	77 [70–83]	74 [66–80]	80 [74–86]	<.0001
Females, %	47.0	43.4	51.3	<.0001
Hypertension, %	75.2	74.7	75.8	0.27
Hypercholesterolemia, %	28.9	33.9	22.9	<.0001
Heart failure, %	27.7	24.5	31.5	<.0001
Diabetes, %	24.3	21.4	27.8	<.0001
Coronary artery disease, %	19.9	19.9	20.0	0.91
Valvular heart disease, %	33.1	36.2	29.5	<.0001
Prior stroke/TIA, %	14.6	9.7	20.5	<.0001
Peripheral embolism, %	2.0	1.4	2.8	<.0001
Peripheral artery disease, %	10.9	7.3	15.1	<.0001
Renal dysfunction, %	18.5	14.0	23.7	<.0001
COPD, %	20.8	16.0	26.6	<.0001
Anemia, %	15.8	7.7	25.3	<.0001
Cognitive deficit/Dementia, %	10.4	3.2	18.8	<.0001
Need of assistance				
No assistance, %	65.9	80.0	49.3	<.0001
Partial assistance, %	24.1	16.6	32.8	
24 h-assistance, %	6.2	2.4	10.7	
In bed, %	3.9	1.0	7.2	

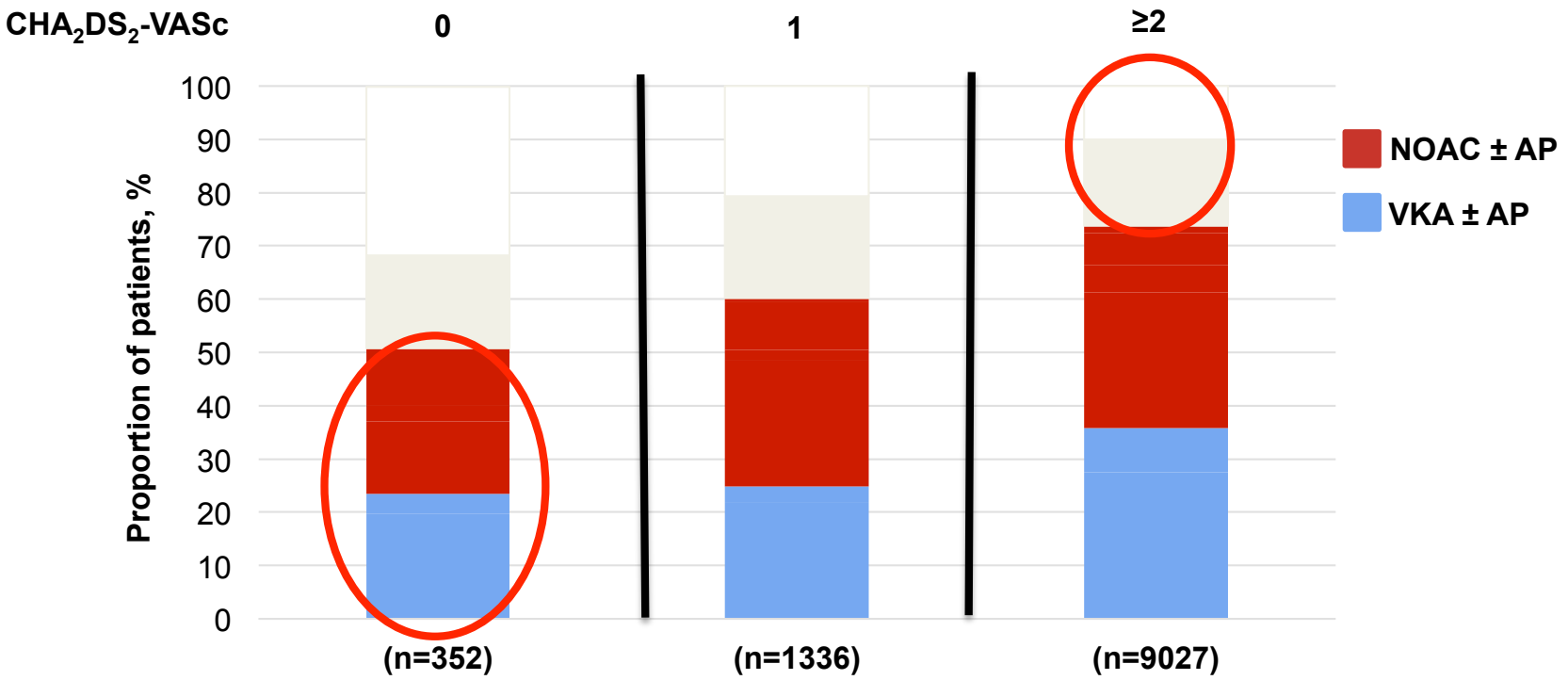
Evolution in baseline treatment for patients enrolled in sequential cohorts of GARFIELD-AF



Cohorts 1–5, N=51,270

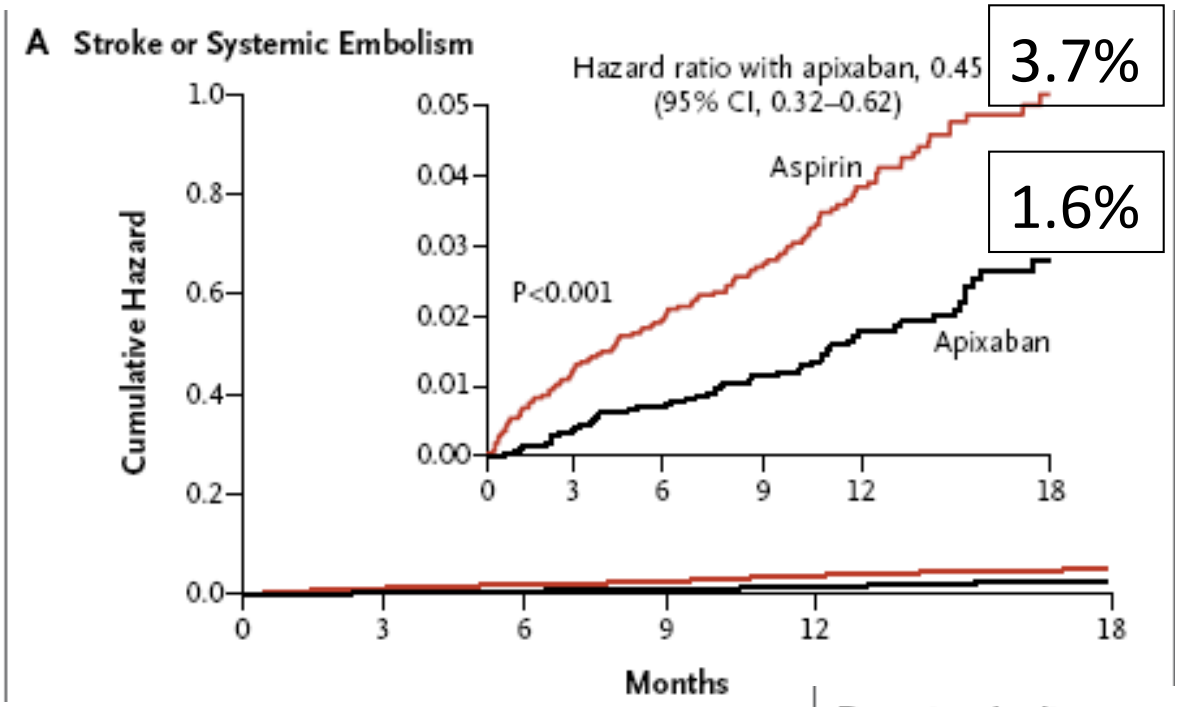
How are low and high risk AF patients managed in practice?

- Contrary to international guideline recommendations,
  - 28% high-risk patients (CHA_2DS_2-VASc ≥2) are not anticoagulated
  - 51% of very low-risk patients (CHA_2DS_2-VASc 0) are anticoagulated



Camm AJ *et al*. Heart 2016 (in press)

AVERROES: efficacy and safety results

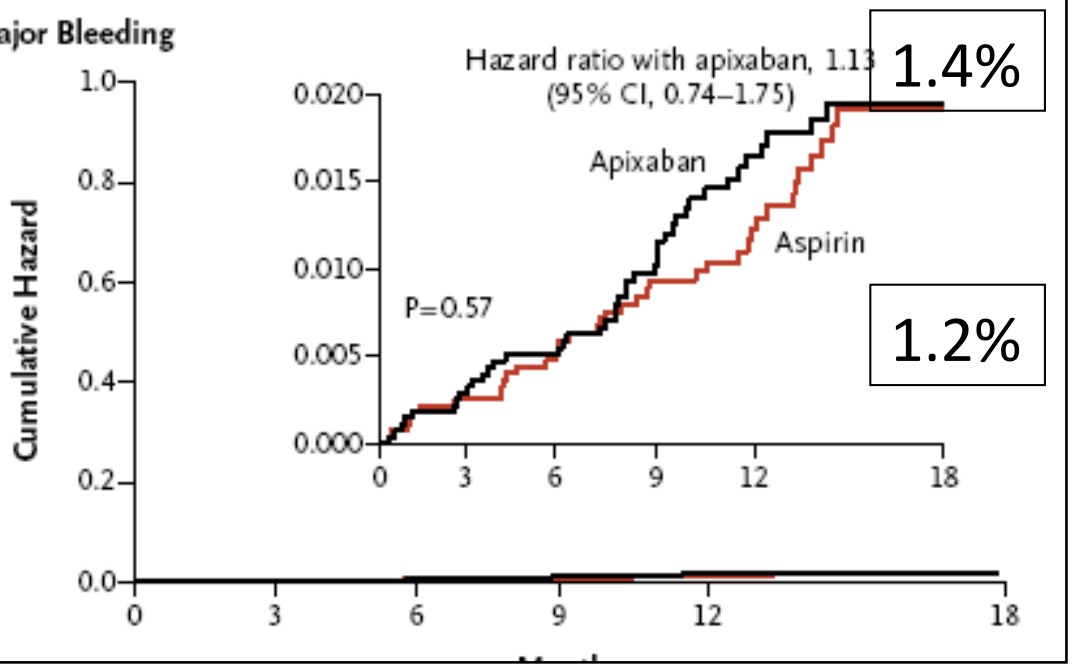


3.7%

1.6%

Stroke or systemic embolism

Major bleeding

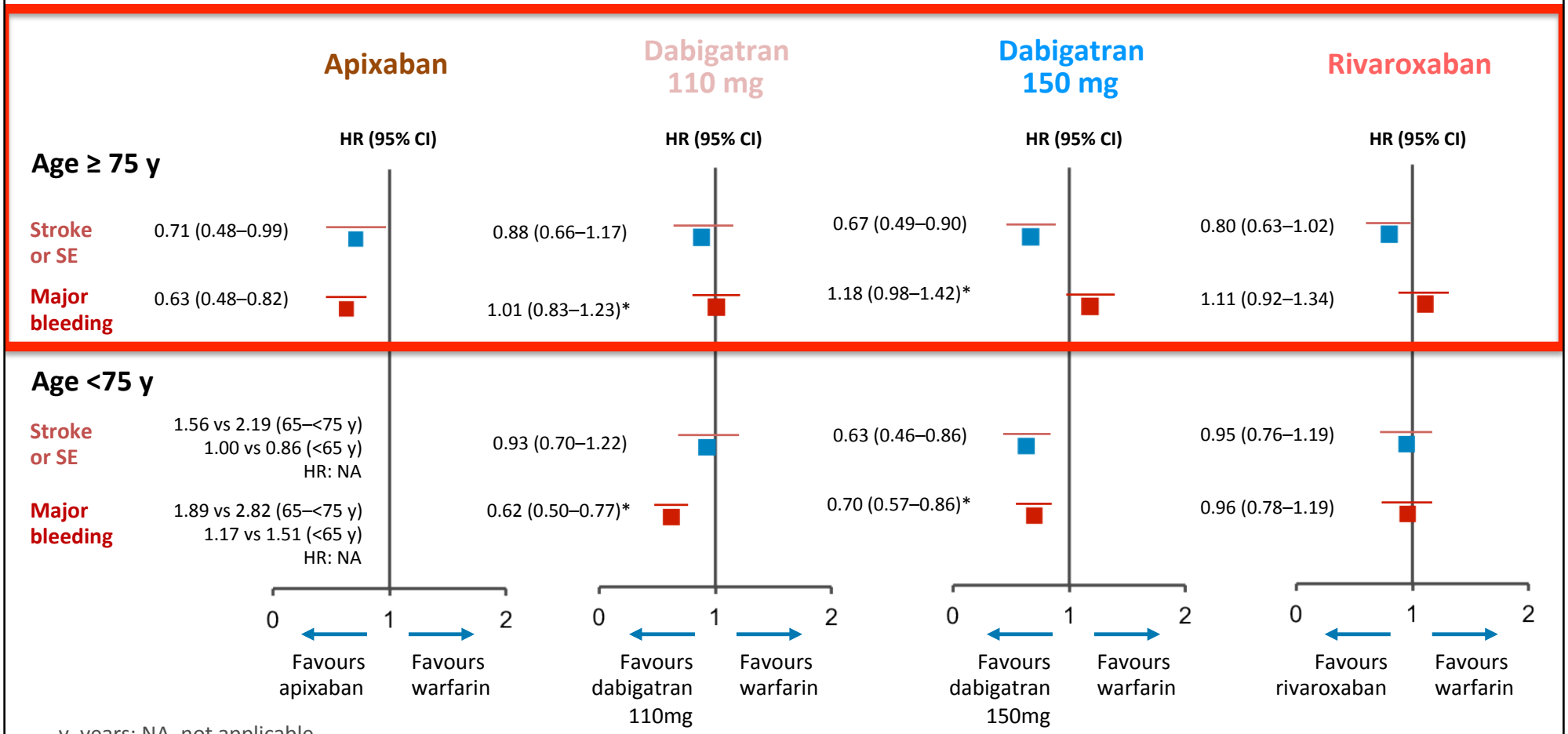


1.4%

1.2%

Connolly et al NEJM 2011

Efficacia e sicurezza degli anticoagulanti orali diretti vs warfarin per gruppi di età



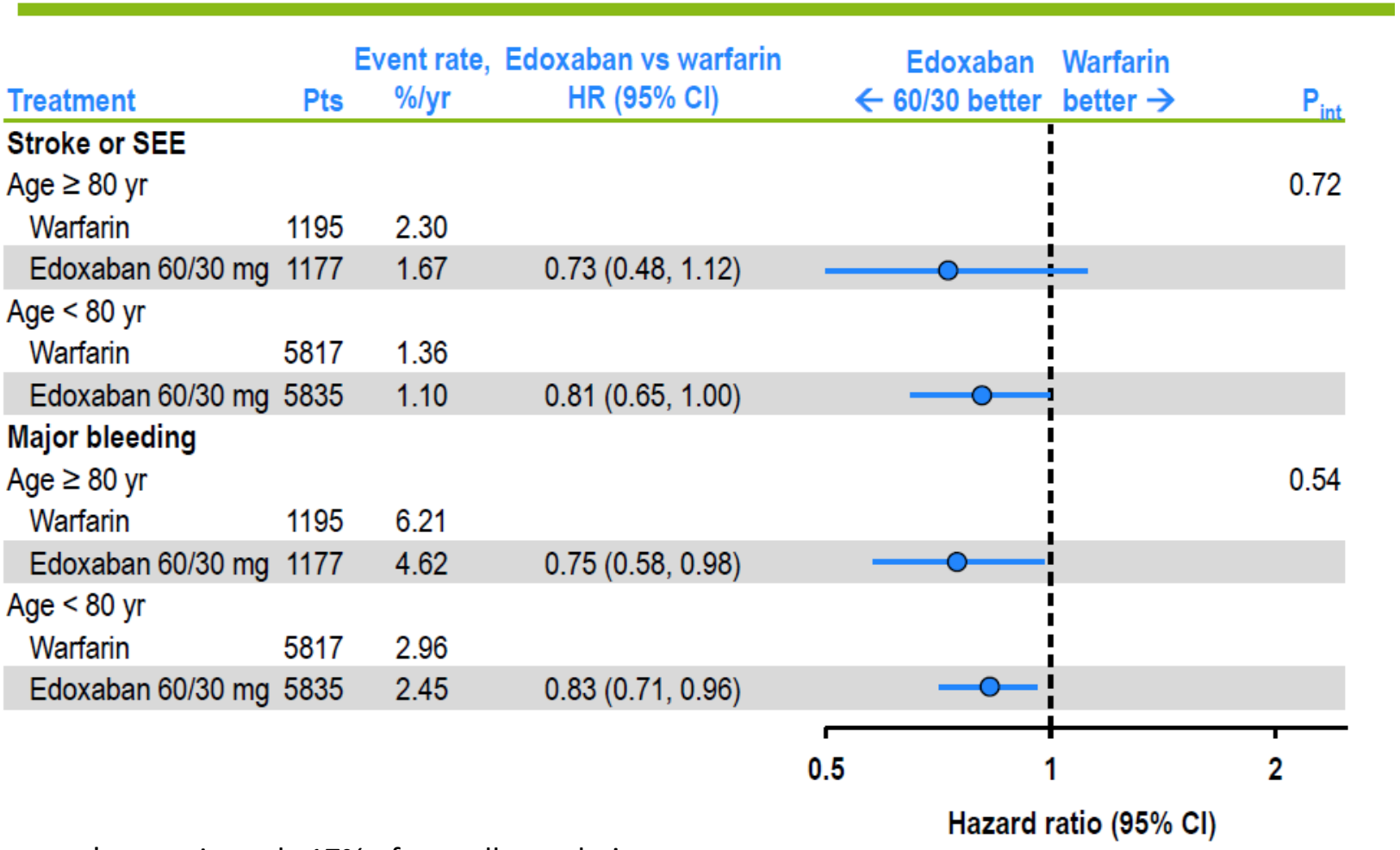
y, years; NA, not applicable

** Significant interaction p<0.001 for both dabigatran doses*

Non esistono studi head-to-head e confronti diretti non sono attuabili

Adapted from Capranzano *et al. Expert Rev Cardiovasc Ther* 2013;11:959-73

Edoxaban: Efficacy and safety in elderly patients (≥80 years)



†approximately 17% of overall population

www.fda.gov Last accessed November 2014

Anticoagulanti orali diretti nella fibrillazione atriale non valvolare

- Sì:
  - Nei pazienti mai trattati (soprattutto anziani?)
  - nei pazienti in terapia dicumarolica con controllo INR inadeguato (salvo pazienti con chiari problemi di aderenza)

- No:
  - Nei pazienti con controindicazioni specifiche (incluse insufficienza renale stadio IV, insufficienza epatica)
  - Nei pazienti con recente/pregressa emorragia digestiva (?)
  - Nei pazienti in terapia dicumarolica ben condotta

  (salvo richiesta del paziente?)

ACCP 2016 Treatment of VTE

In patients with DVT of the leg or PE we suggest

dabigatran, rivaroxaban, apixaban, or edoxaban

over

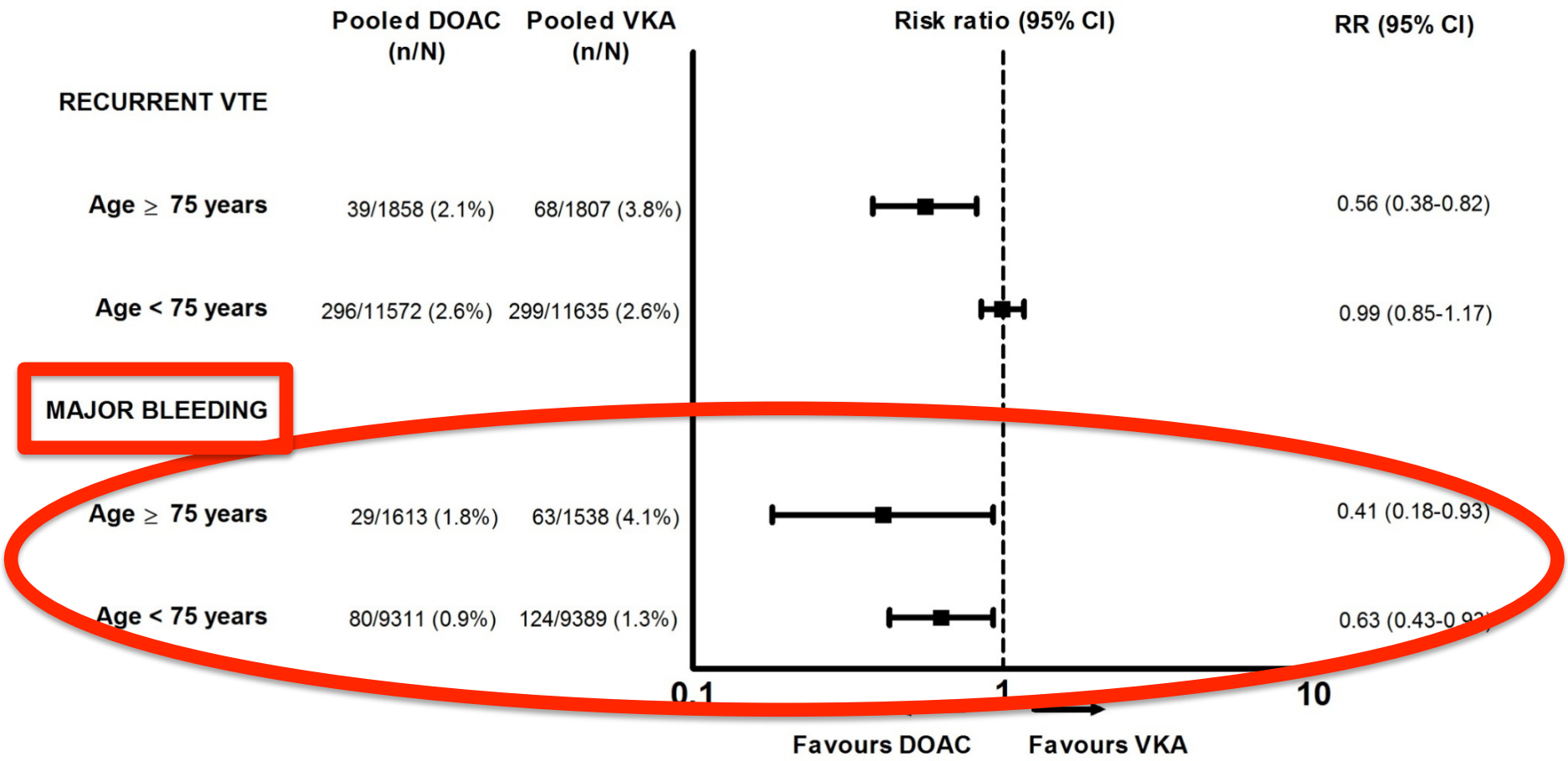
vitamin K antagonists (Grade 2B)

- Adapted from ACCP guidelines. Kearon C et al. Chest 2016

Anticoagulanti orali diretti nel tromboembolismo venoso

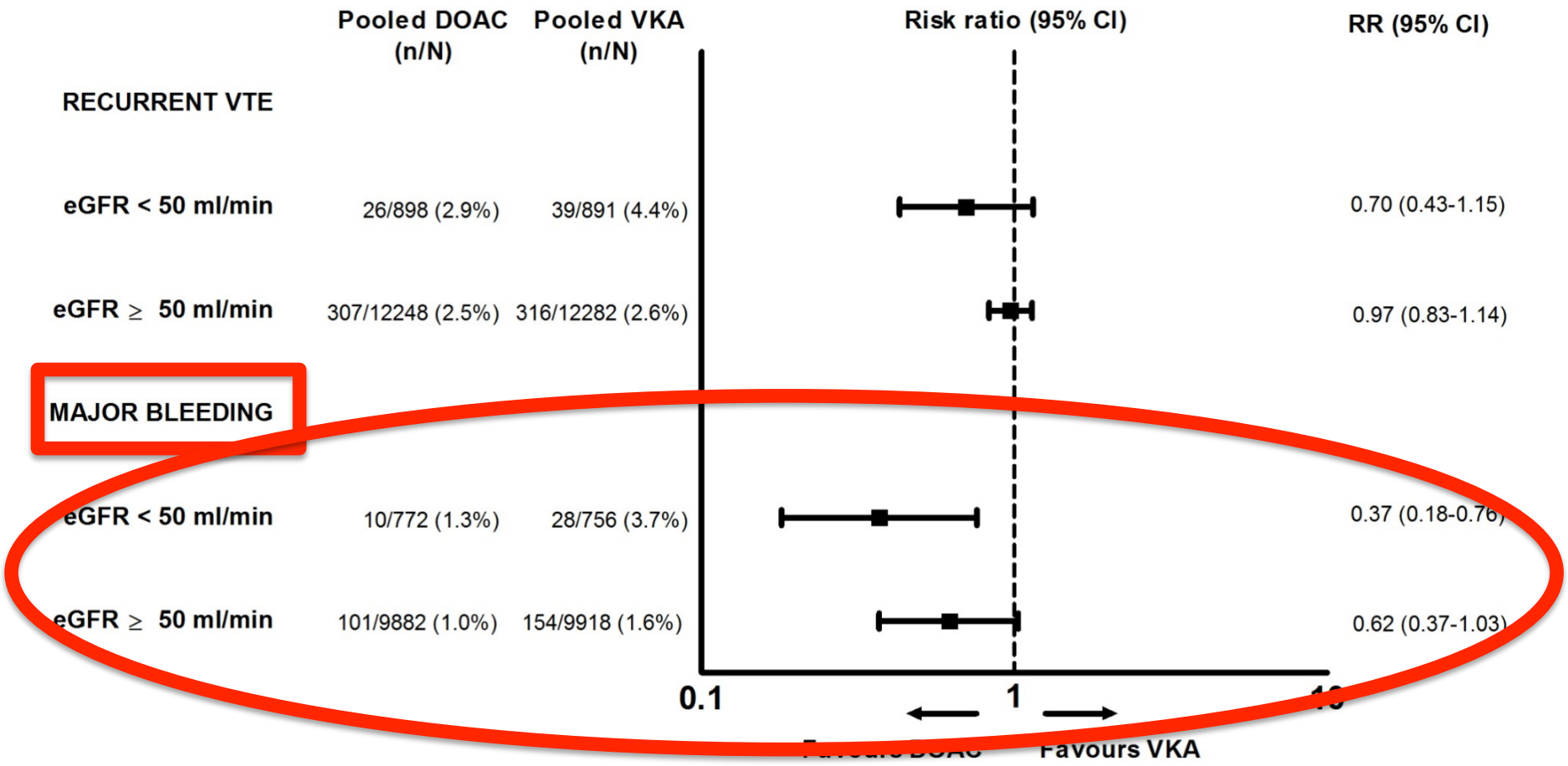
- Sì:
  - In (quasi) tutti i pazienti
- No:
  - Nei pazienti con controindicazioni specifiche (incluse insufficienza renale IV stadio, insufficienza epatica)
  - Nei pazienti con recente/pregressa emorragia digestiva (?)
  - In alcuni particolari sottogruppi

Clinical outcomes in VTE trials in patients aged ≥ 75 years



van Es et al Blood 2014

Clinical outcomes in VTE trials in patients with moderate renal failure



van Es et al Blood 2014

XALIA: Baseline Demographics and Clinical Characteristics

Age, years, mean (SD)	57.3 (16.7)	63.0 (16.9)
<60 years, n (%)	1366 (52.2)	824 (38.8)
≥60 years, n (%)	1253 (47.8)	1325 (61.7)
Male sex, n (%)	1428 (54.5)	1116 (51.9)
Weight, kg, mean (SD)	82.4 (18.0)	80.6 (18.0)
BMI, kg/m^2, mean (SD)	28.0 (5.2)	28.4 (6.9)
Index diagnosis, n (%)		
DVT without PE	2399 (91.6)	1894 (88.1)
DVT with PE	220 (8.4)	255 (11.9)

Ageno W et al Lancet Haematol 2015

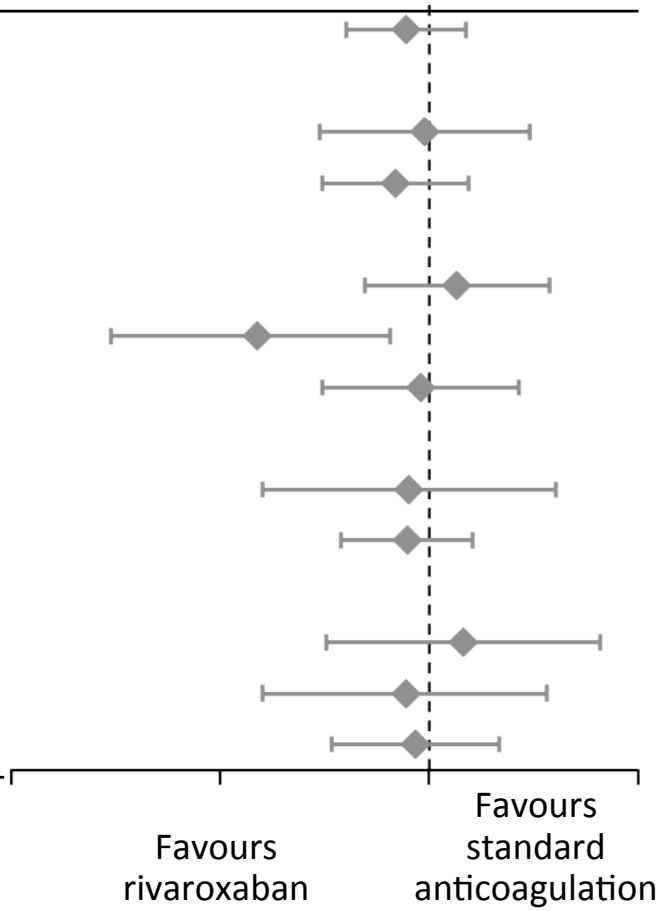
XALIA: Baseline Demographics and Clinical Characteristics (2)

First available CrCl, n (%)		
≥80 ml/min	1125 (43.0)	797 (37.1)
≥50–<80 ml/min	419 (16.0)	398 (18.5)
≥30–<50 ml/min	88 (3.4)	157 (7.3)
<30 ml/min	13 (0.5)	61 (2.8)
Not recorded	974 (37.2)	736 (34.2)
Previous VTE, n (%)	630 (24.1)	481 (22.4)
Previous major bleeding episode, n (%)	37 (1.4)	64 (3.0)
Active cancer, n (%)	146 (5.6)	411 (19.1)

Ageno W et al Lancet Haematol 2015

Treatment-Emergent Major Bleeding Across Subgroups

	Rivaroxaban		Standard anticoagulation		HR (95% CI)
	n/N	(%)	n/N	(%)	
All patients	19/2505	(0.8)	43/2010	(2.1)	
Age					
<60 years	8/1286	(0.6)	11/785	(1.4)	
≥60 years	11/1219	(0.9)	32/1225	(2.6)	
Weight					
≤70 kg	7/522	(1.3)	14/495	(2.8)	
>70–<90 kg	3/843	(0.4)	14/663	(2.1)	
≥90 kg	6/599	(1.0)	12/482	(2.5)	
Active cancer at baseline					
Yes	2/144	(1.4)	13/338	(3.8)	
No	17/2361	(0.7)	30/1672	(1.8)	
First available CrCl					
<50 ml/min	3/98	(3.1)	9/194	(4.6)	
≥50–<80 ml/min	3/410	(0.7)	10/366	(2.7)	
≥80 ml/min	12/1047	(1.1)	16/757	(2.1)	

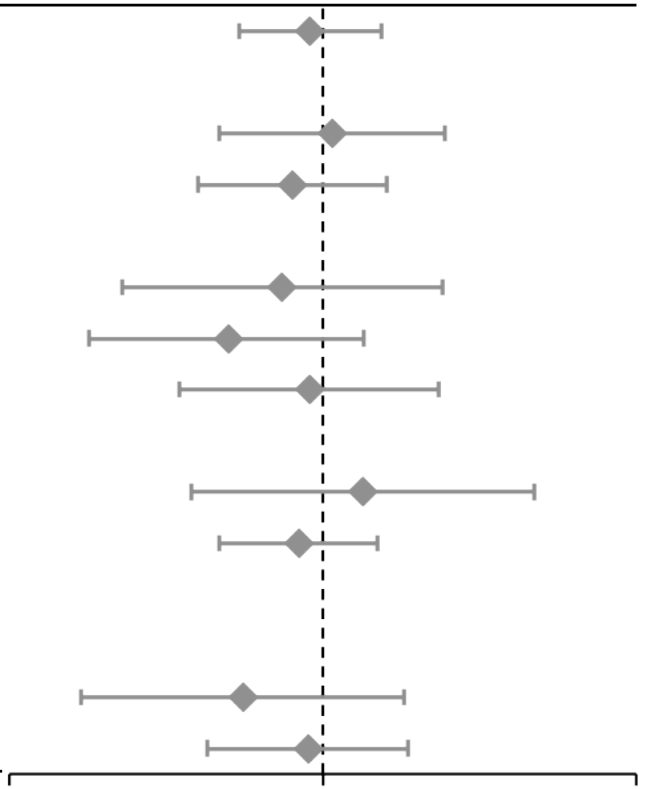


Note: some demographic parameters have data missing
Propensity score-adjusted population

Ageno W et al Lancet Haematol 2015

Recurrent Venous Thromboembolism Across Subgroups

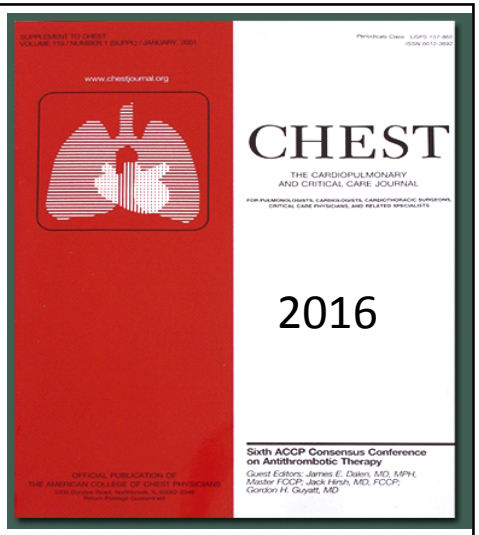
	Rivaroxaban		Standard anticoagulation		HR (95% CI)
	n/N	(%)	n/N	(%)	
All patients	36/2505	(1.4)	47/2010	(2.3)	
Age					
<60 years	17/1286	(1.3)	16/785	(2.0)	
≥60 years	19/1219	(1.6)	31/1225	(2.5)	
Weight					
≤70 kg	8/522	(1.5)	13/495	(2.6)	
>70–<90 kg	8/843	(0.9)	18/663	(2.7)	
≥90 kg	11/599	(1.8)	12/482	(2.5)	
Active cancer at baseline					
Yes	5/144	(3.5)	14/338	(4.1)	
No	31/2361	(1.3)	33/1672	(2.0)	
First available CrCl					
<50 ml/min*	1/98	(1.0)	3/194	(1.5)	
≥50–<80 ml/min	6/410	(1.5)	11/366	(3.0)	
≥80 ml/min	20/1047	(1.9)	21/757	(2.8)	



Note: some demographic parameters have data missing;
* HR not calculated because of too few events
Propensity score-adjusted population

Ageno W et al Lancet Haematol 2015

ACCP 2016 Treatment of VTE in Cancer Patients



- In patients with VTE and cancer, as long-term (first 3 months) anticoagulant therapy, we suggest

LMWH

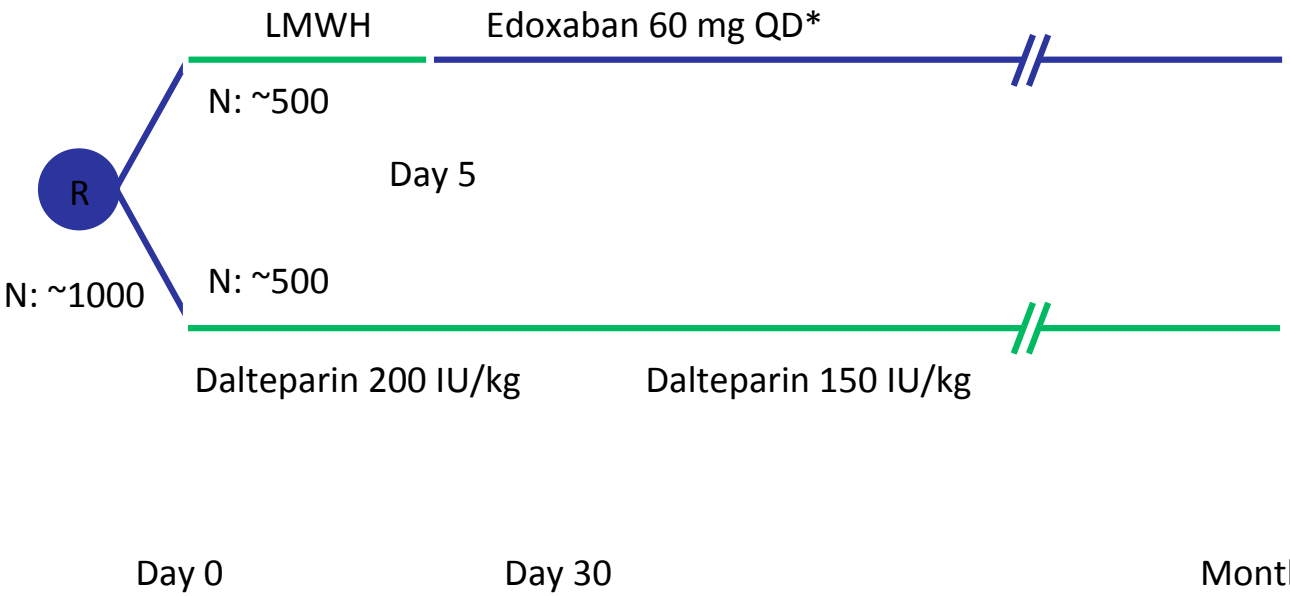
over

VKA therapy (Grade 2C), **dabigatran, rivaroxaban, apixaban, or edoxaban** (Grade 2C).

The Hokusai VTE Cancer study

Objectively confirmed VTE
Straftified randomization for
- Bleeding Risk
- Dose adjustment

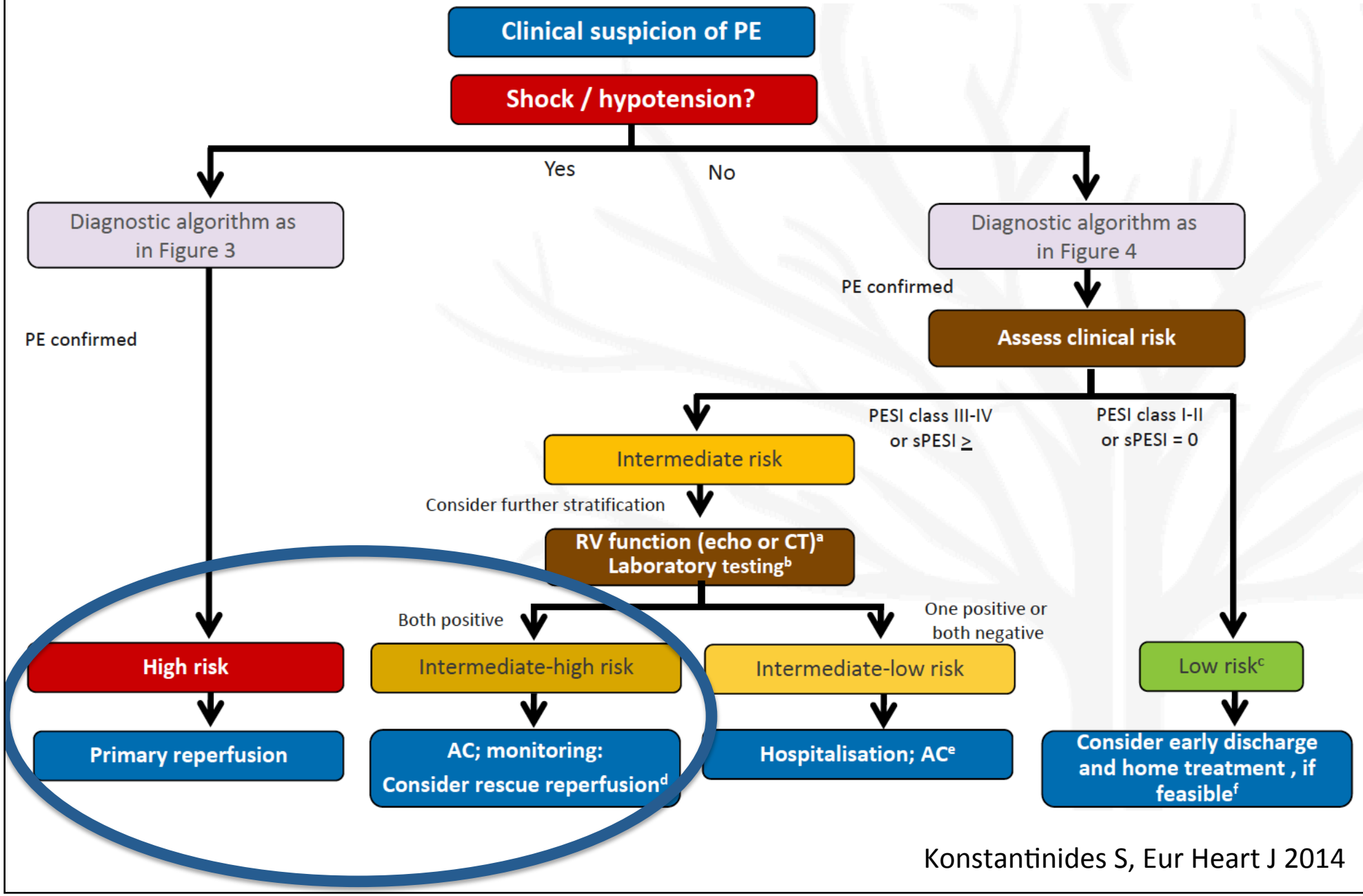
PROBE design



12 months of treatment or shorter (intention for at least 6 months) ~ mitigating factors in subject's clinical status

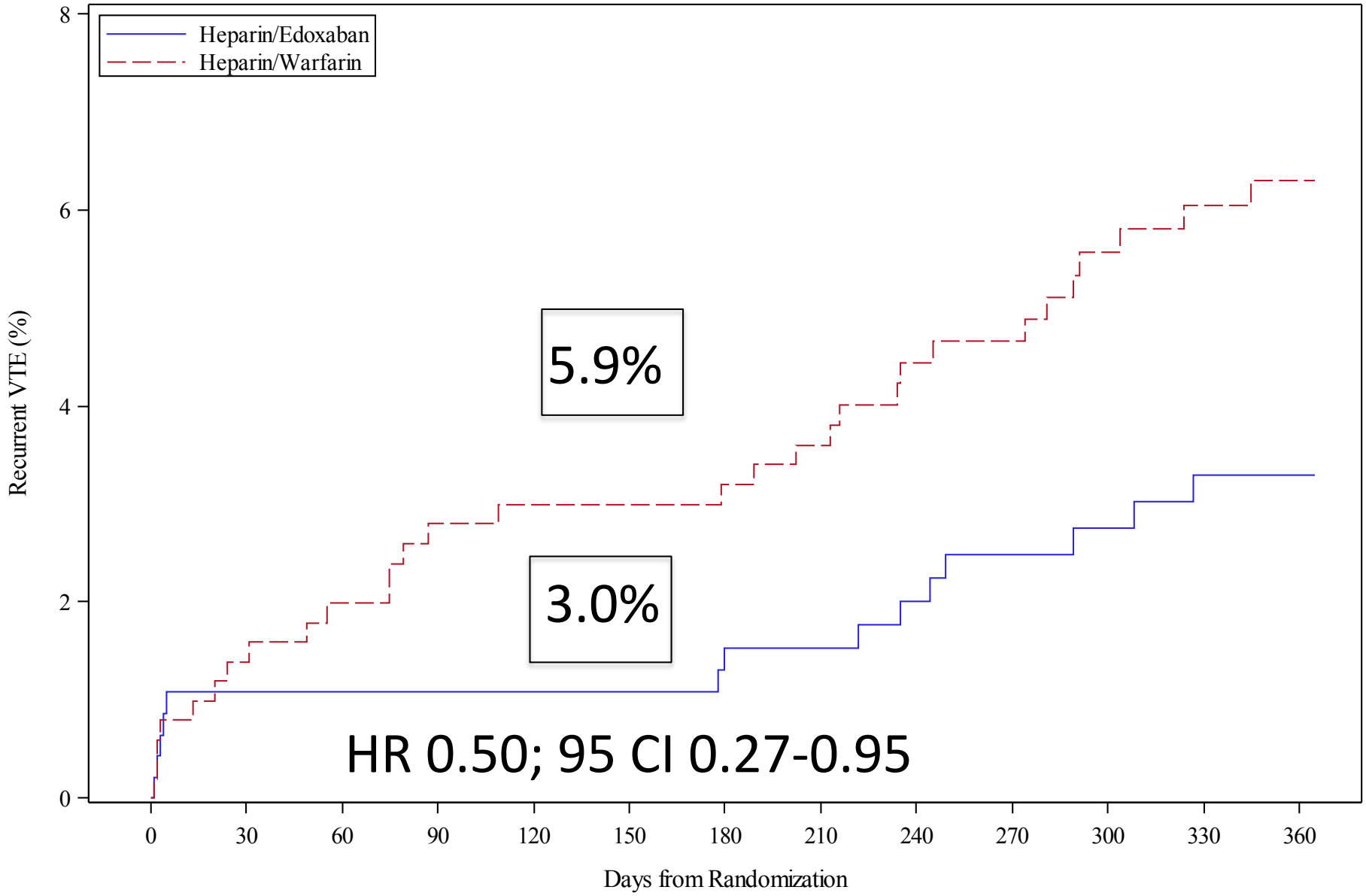
Efficacy and safety data will need to be collected during the entire 12 month study period

PE risk stratification



Konstantinides S, Eur Heart J 2014

Hokusai study: Subgroup analysis in PE patients with NT-proBNP ≥500 pg/mL



Quando non impiego gli anticoagulanti orali diretti?

- Insufficienza renale stadio IV – V
- Cirrosi o epatite acuta
- Neoplasia attiva in CHT
- Bambini (al di fuori di protocolli di studio)
- Donne in gravidanza/puerperio
- Trombosi in sedi venose inusuali (al di fuori di protocolli di studio)
- Embolia polmonare a rischio elevato (successivamente?)