

Barcelona, novembre 2019

# Continues novetats en anticoagulació

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CONGRÉS SOCIETAT CATALANA  
**XXV GERIATRIA  
GERONTOLOGIA**  
7-8 NOVEMBRE 2019 AUDITORI DE L'ACADÈMIA  
**SUMEM SALUT AMB LES PERSONES GRANS**  
"LET'S COME TOGETHER"



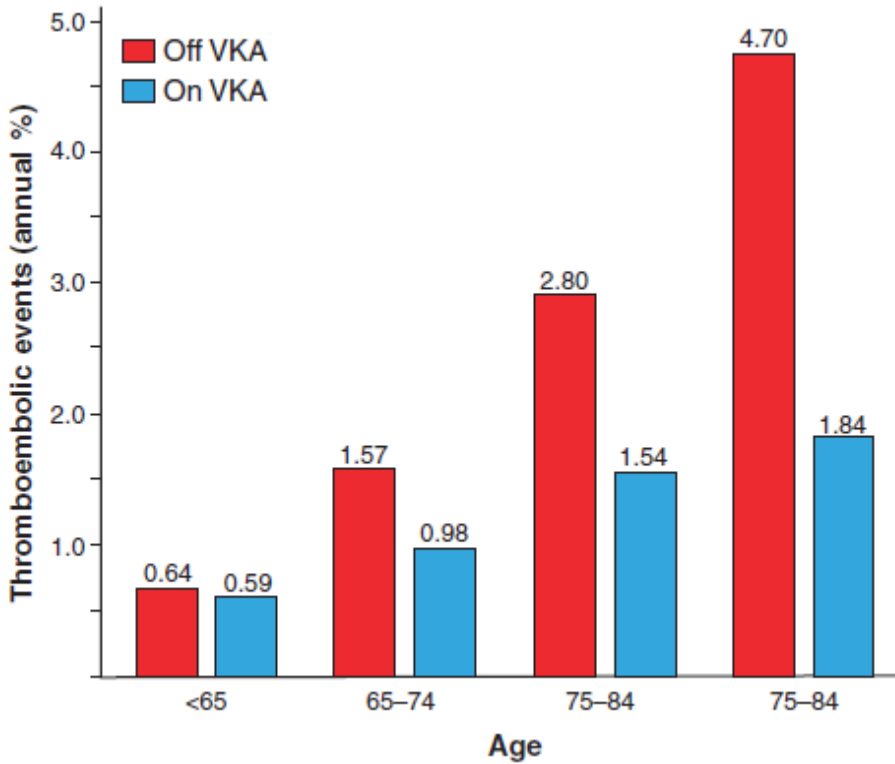
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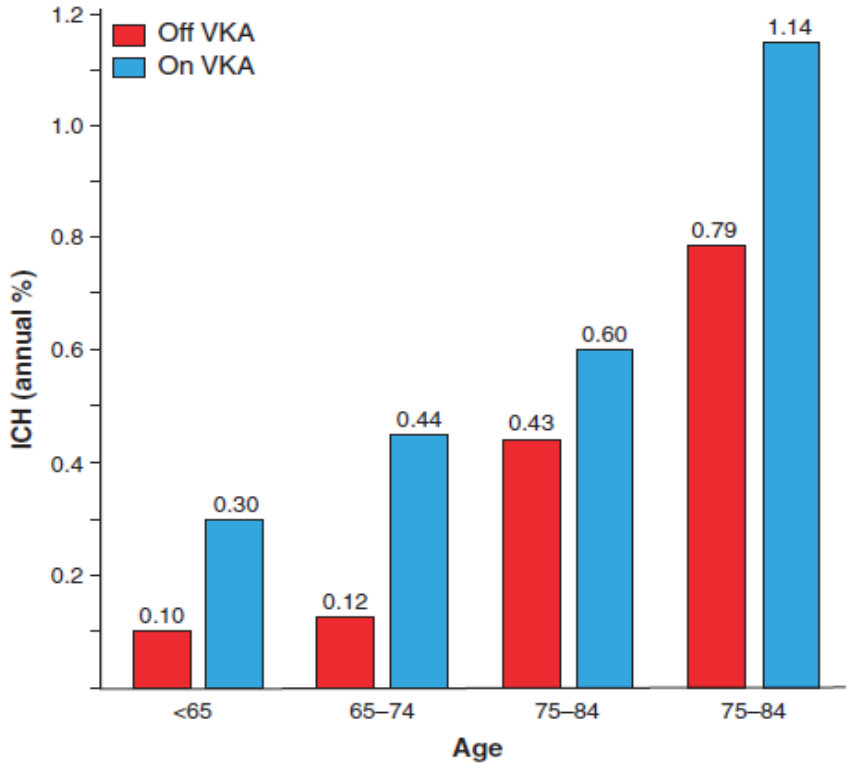
# Cohorte ATRIA:

## Tasa de accidentes tromboembólicos y de hemorragia intracraneal en pacientes con fibrilación auricular en función de la edad

### Tromboembolismos

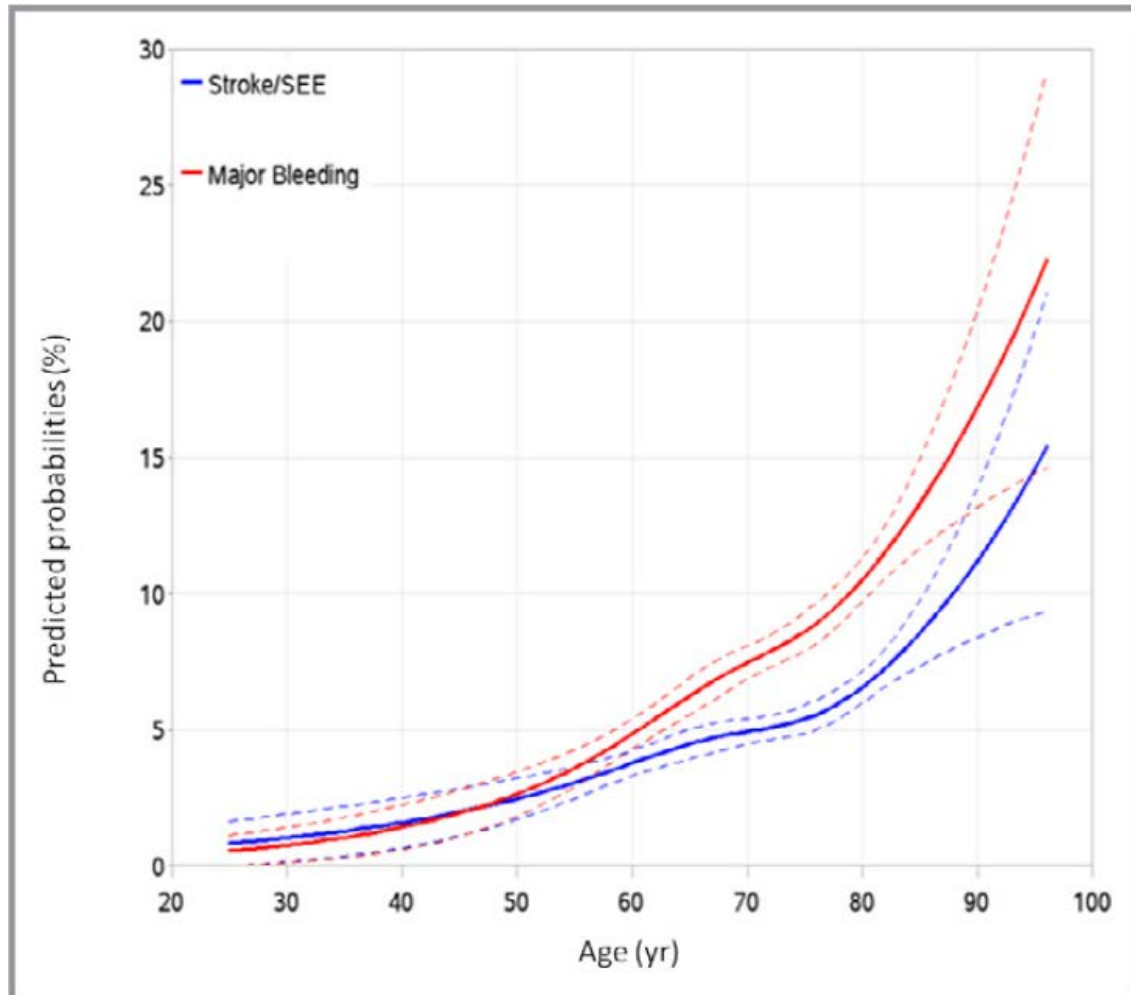


### Hemorragia intracraneal



## ENGAGE AF:

Outcomes by Age in the Warfarin Group analyzed as a continuous variable

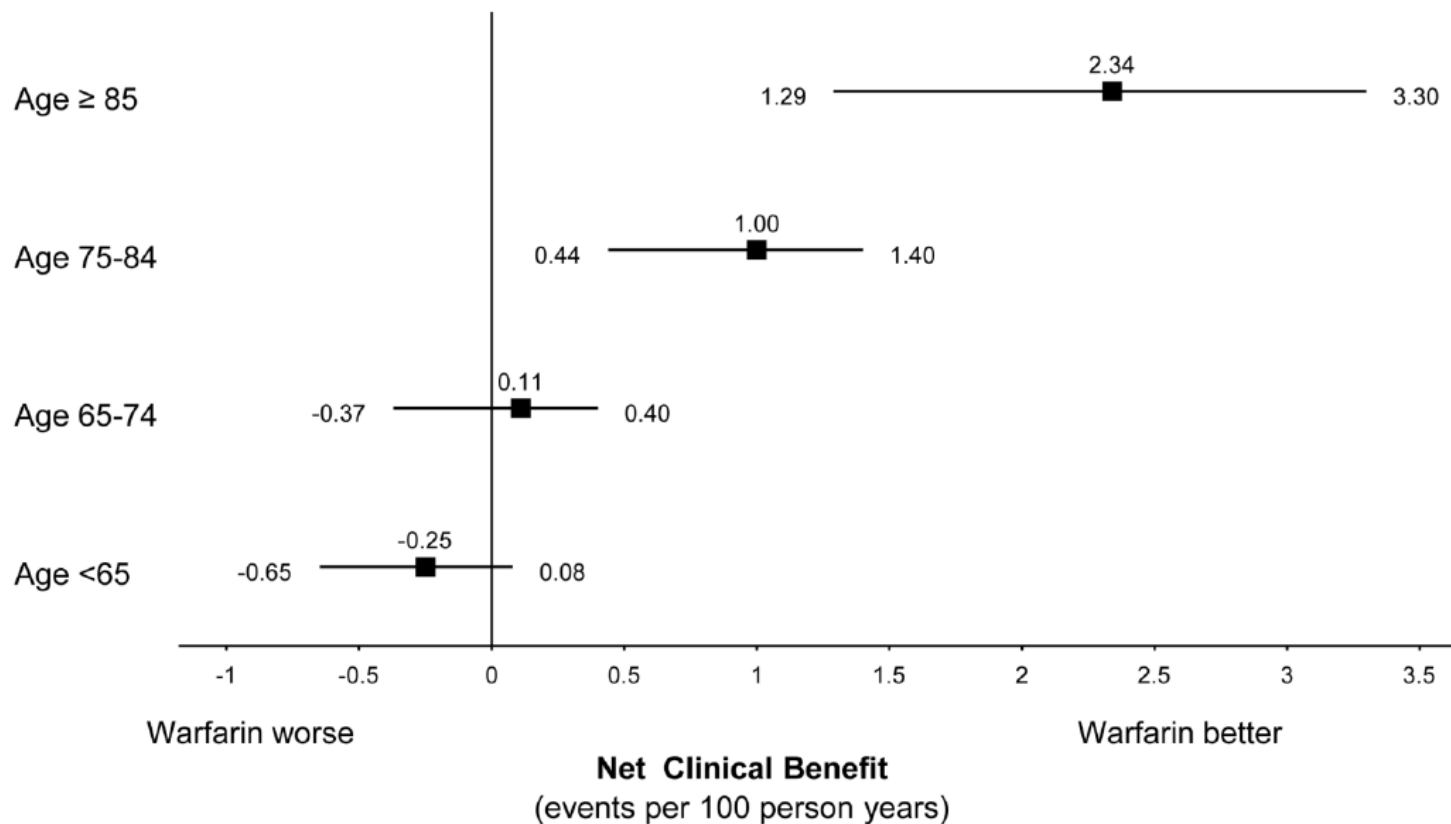


# ATRIA Study Cohort:

13559 pacientes seguidos entre 1996 y 2003 (66000 pacientes-años)

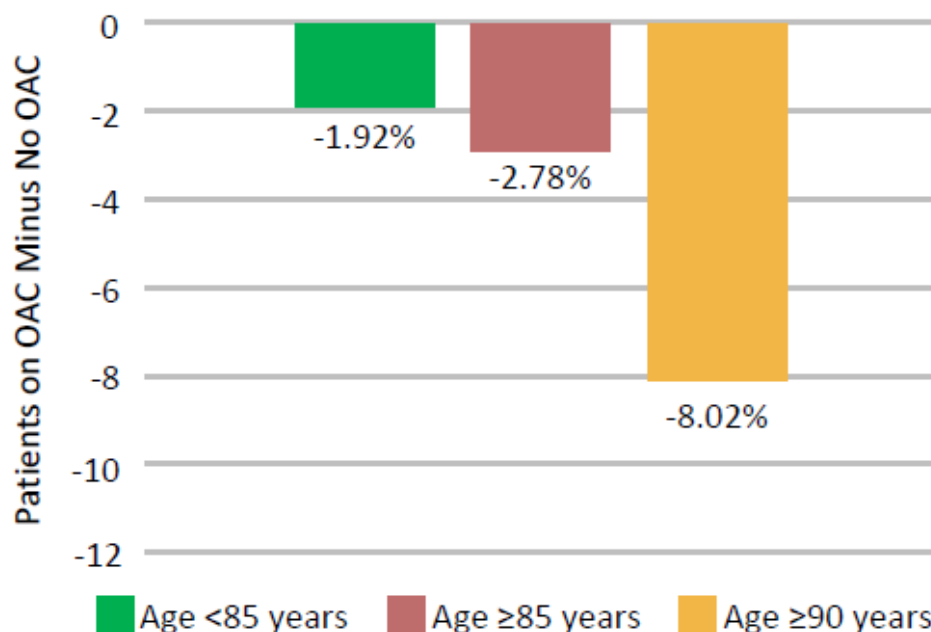
**Eventos adversos (hospitalizaciones embolismo & AVC hemorrágico) ajustados prevenidos por 100 pacientes-años debido a la warfarina en función del CHADS2 y la edad**

*Score: Hemorragia intracraneal=ICTUS isquémico x 1.5*



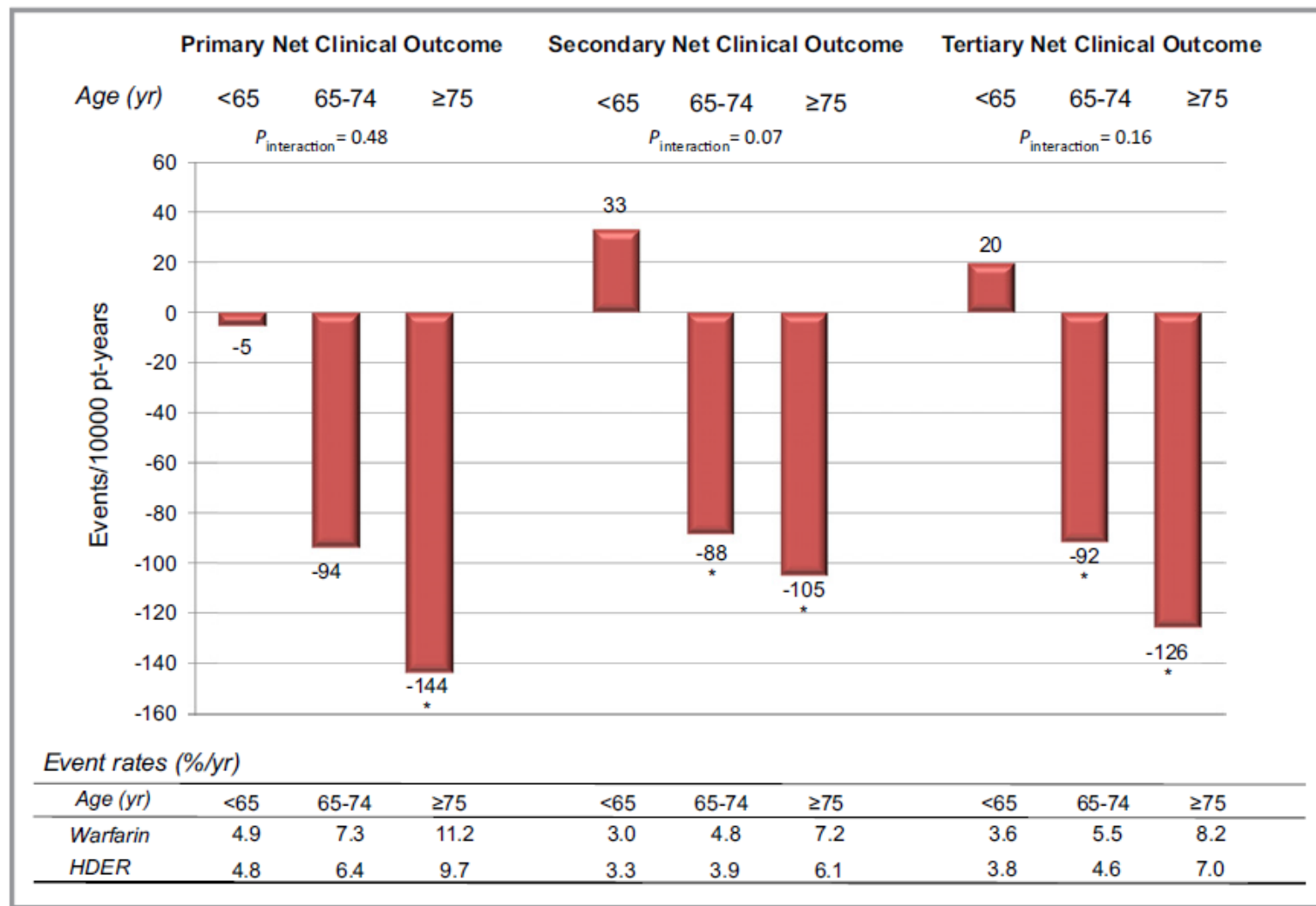
## Net Clinical Benefit Of OAC In Very Elderly Patients With AF: Results From The PREFER in AF Study

Net Clinical Benefit\* Adjusted For Mortality Risk In The Overall Population:  
-2.19%; 95% CI -4.23%,-0.15%; P=0.036



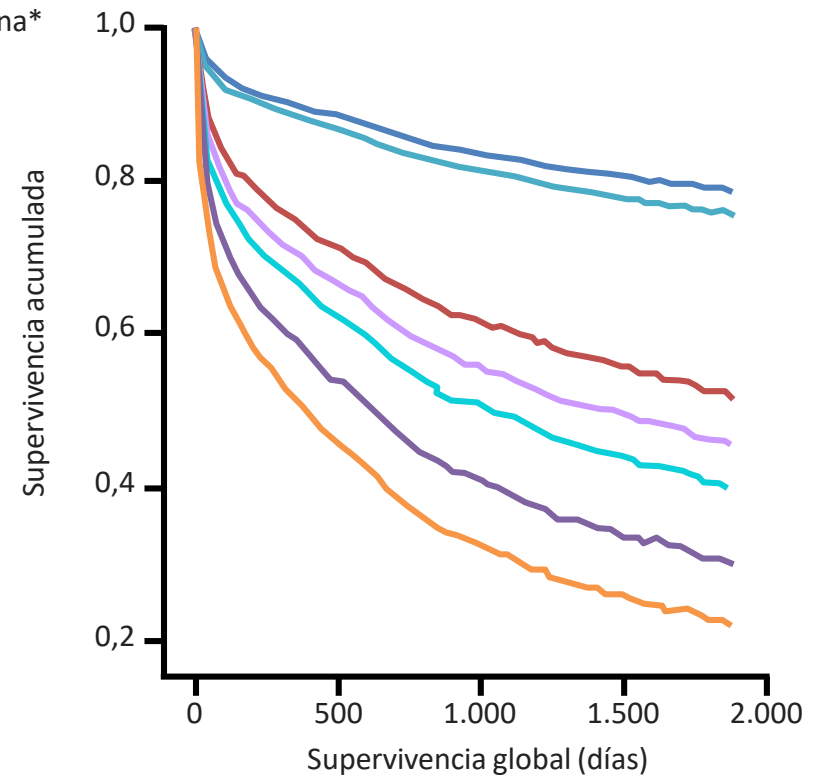
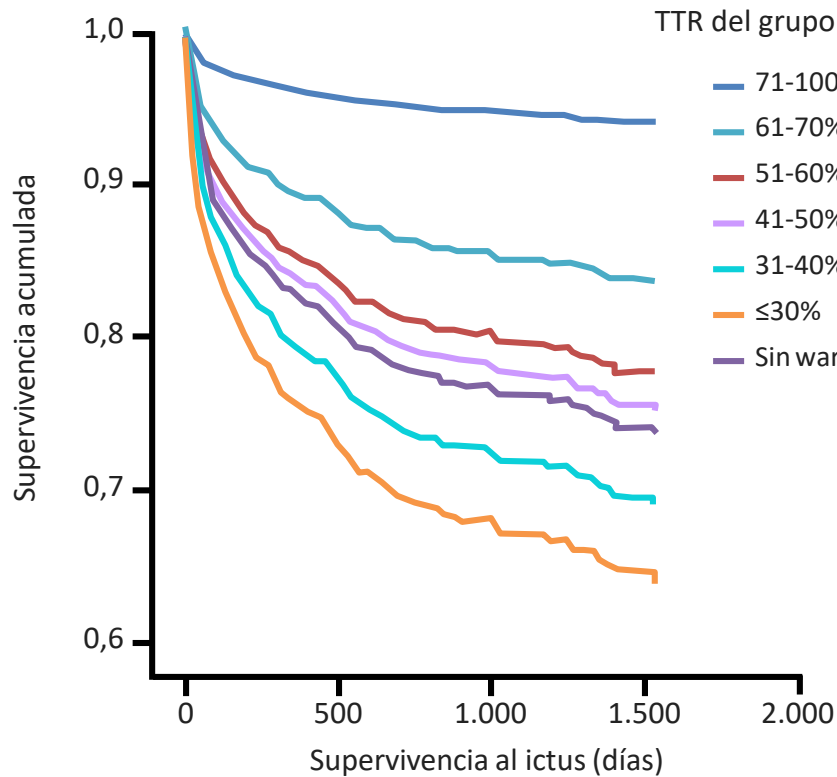
\*Net clinical benefit: includes ischemic stroke, systemic embolism, myocardial infarction, hemorrhagic stroke, major bleeding

# ENGAGE AF: Absolute risk differences in net clinical outcomes with the higher-dose edoxaban regimen as compared to warfarin



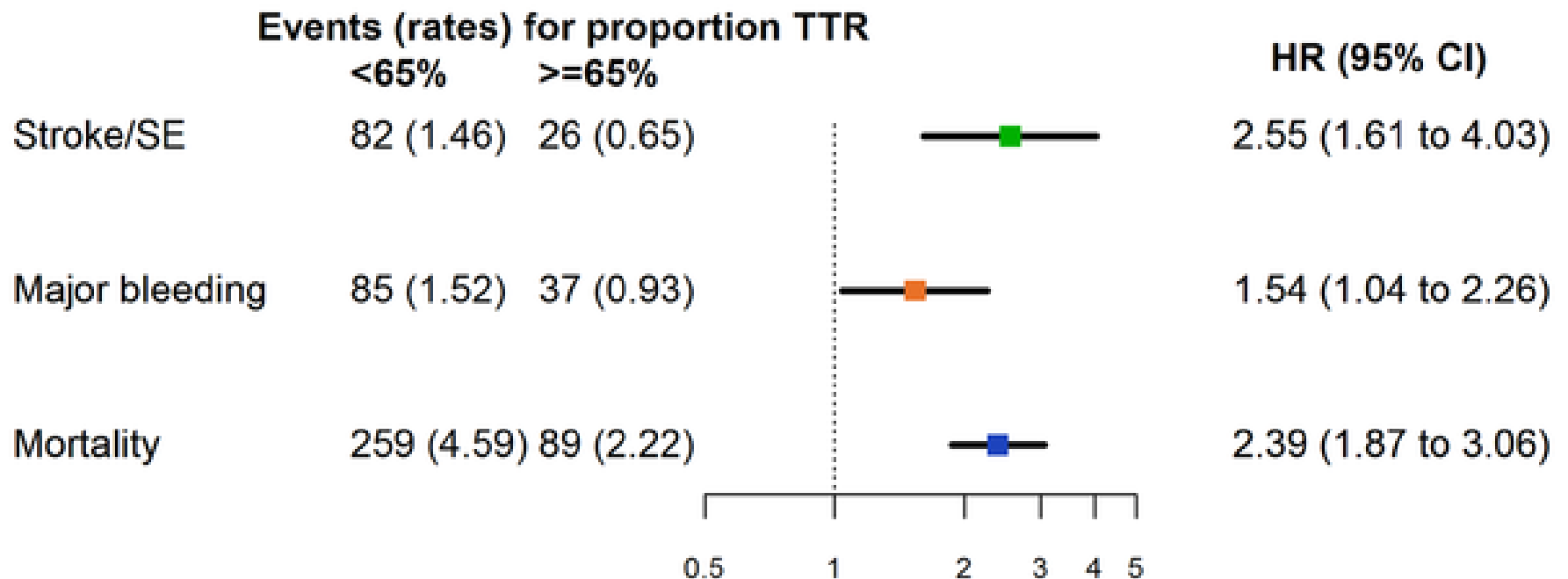
Primary Net Clinical Outcome: stroke, systemic embolic events, major bleeding, or death from any cause. Secondary Net Clinical Outcome: disabling stroke, life-threatening bleeding, or death from any cause. Tertiary Net Clinical Outcome: stroke, systemic embolic events, life-threatening bleeding, or death from any cause.

# Riesgo de ictus y muerte en función del tiempo en rango terapéutico



Morgan et al. Thromb Res. 2009;124:37-41.

# Incidence rates and adjusted hazard ratios for 1-year clinical outcomes according to proportion of time in therapeutic range.

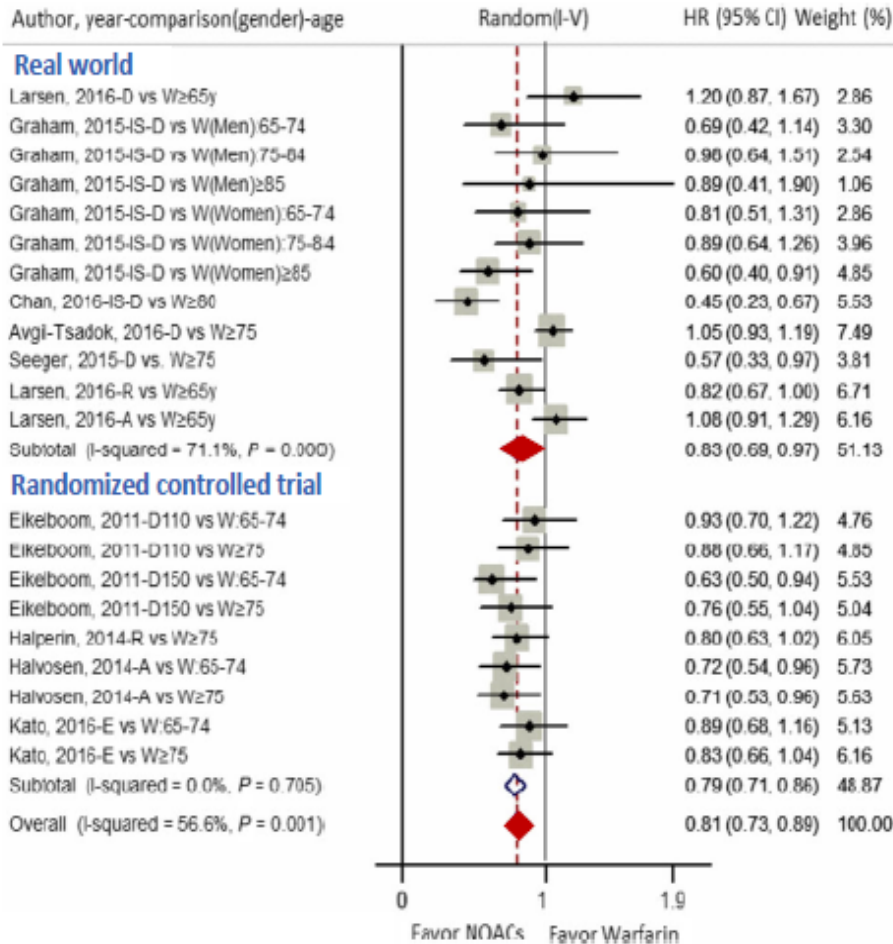


Haas S et al from the GARFIELD-AF Registry. PLoS ONE 11(10): e0164076. doi:10.1371/journal.pone.0164076  
<http://journals.plos.org/plosone/article?id=info:doi/10.1371/journal.pone.0164076>

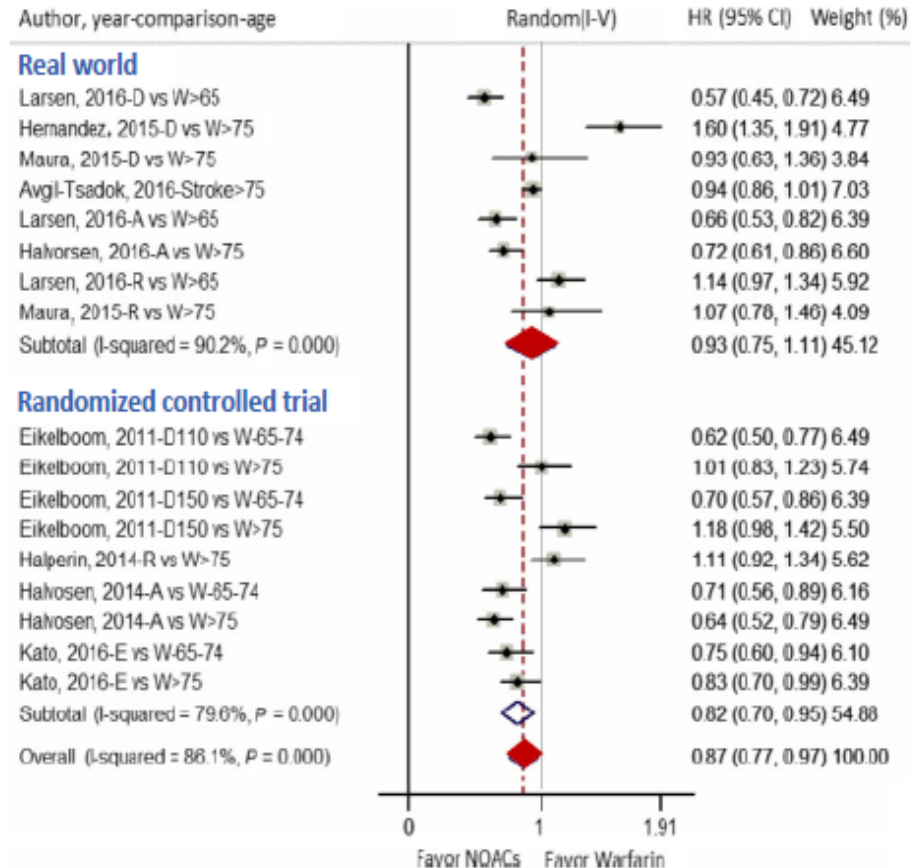


# Effectiveness And Safety Of NOACs In Older Patients With AF: Systematic Review And Meta-Regression Analysis Of Both RCT And RWE

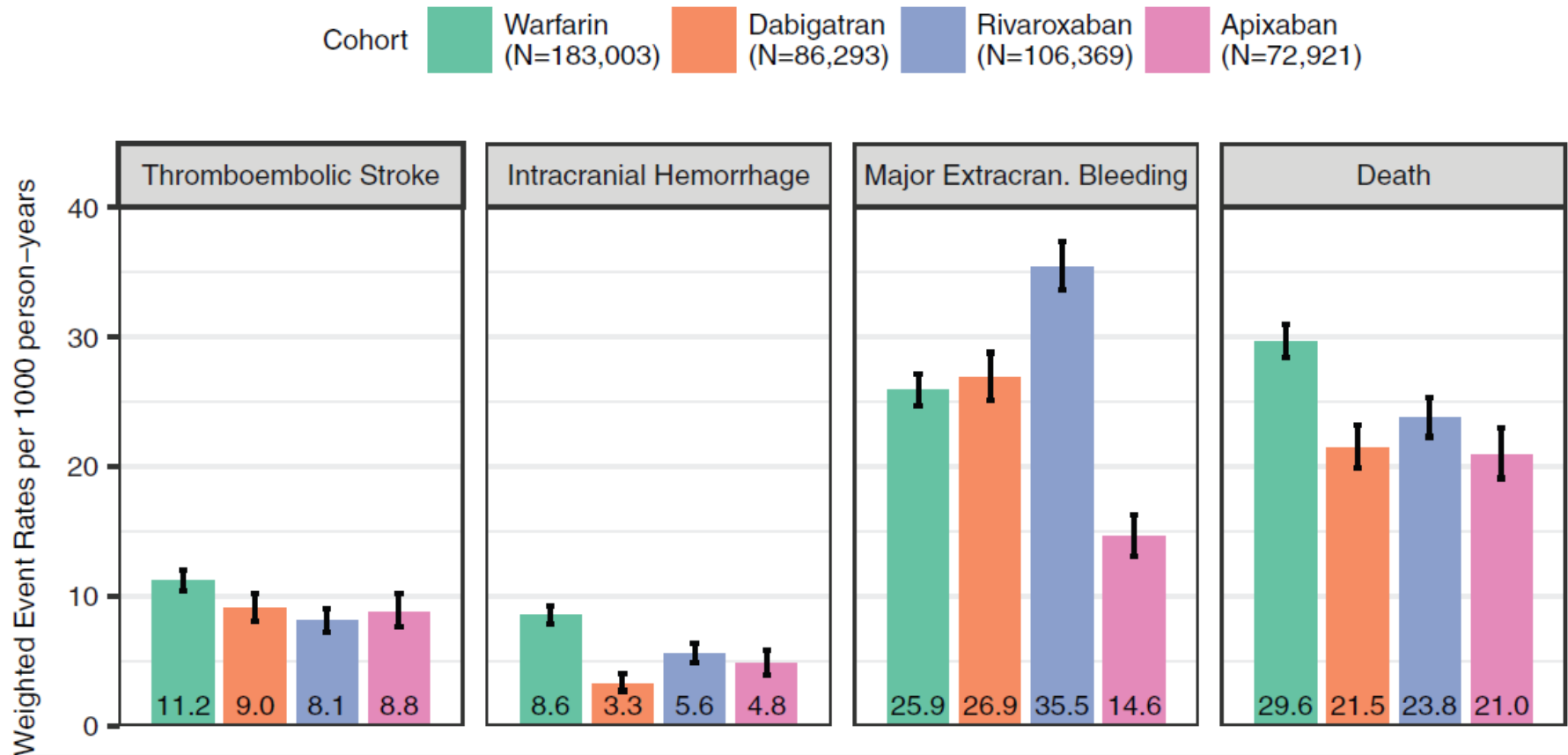
## Risk Of Stroke/TIA



## Risk Of Major Bleeding



# Comparative Stroke, Bleeding, and Mortality Risks in Older Medicare Patients Treated with Oral Anticoagulants for Nonvalvular Atrial Fibrillation

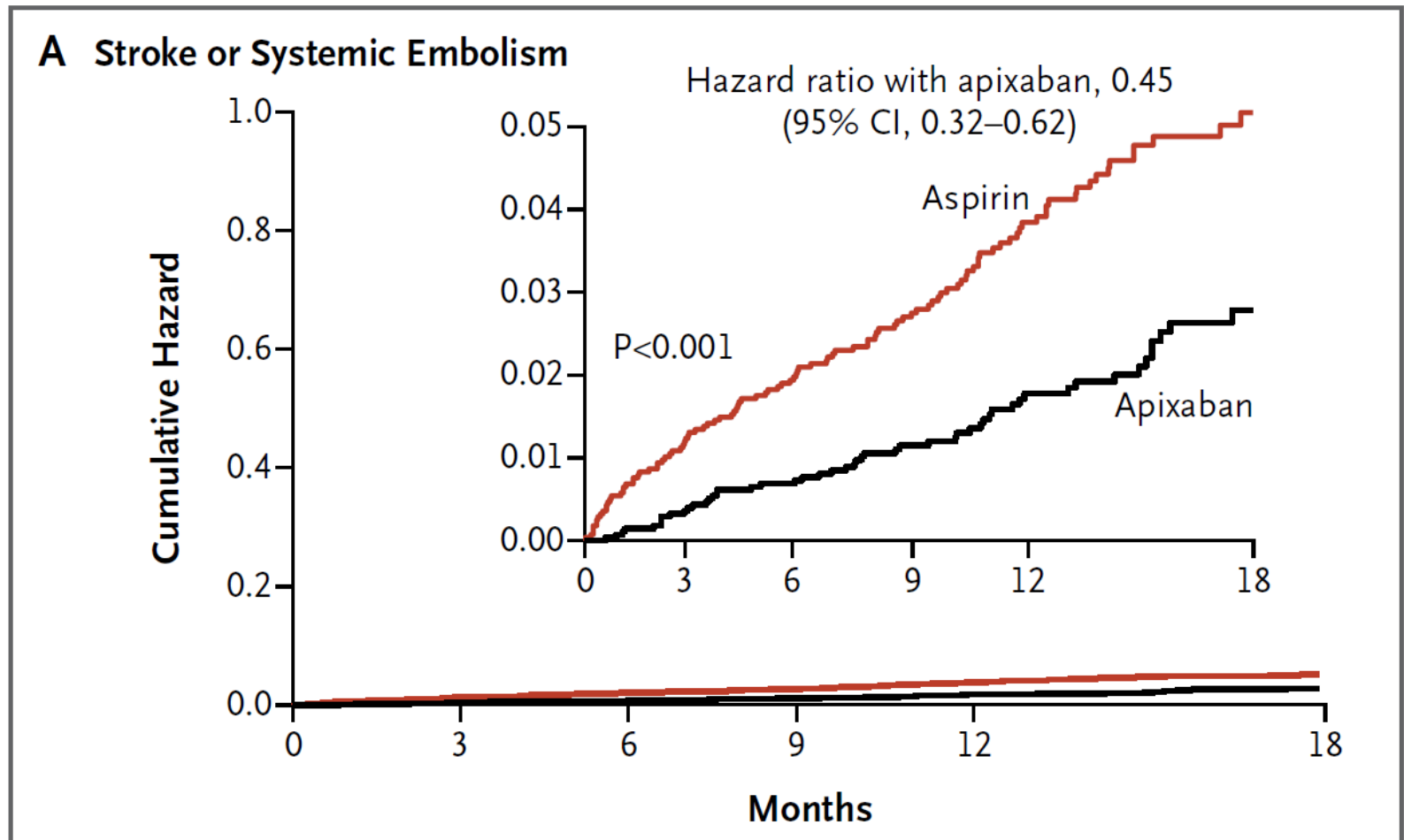


**Figure 1** <sup>\*</sup> Adjusted incidence rates per 1000 person-years of thromboembolic stroke, intracranial hemorrhage, major extracranial bleeding, and all-cause mortality in Medicare beneficiaries with nonvalvular atrial fibrillation treated with warfarin, dabigatran, rivaroxaban, or apixaban. Weighted cohort sizes are shown.

<sup>\*</sup>Propensity score-adjusted Cox proportional hazards regression was used to estimate adjusted hazard ratios

# AVERROES study: apixaban vs aspirin in AF

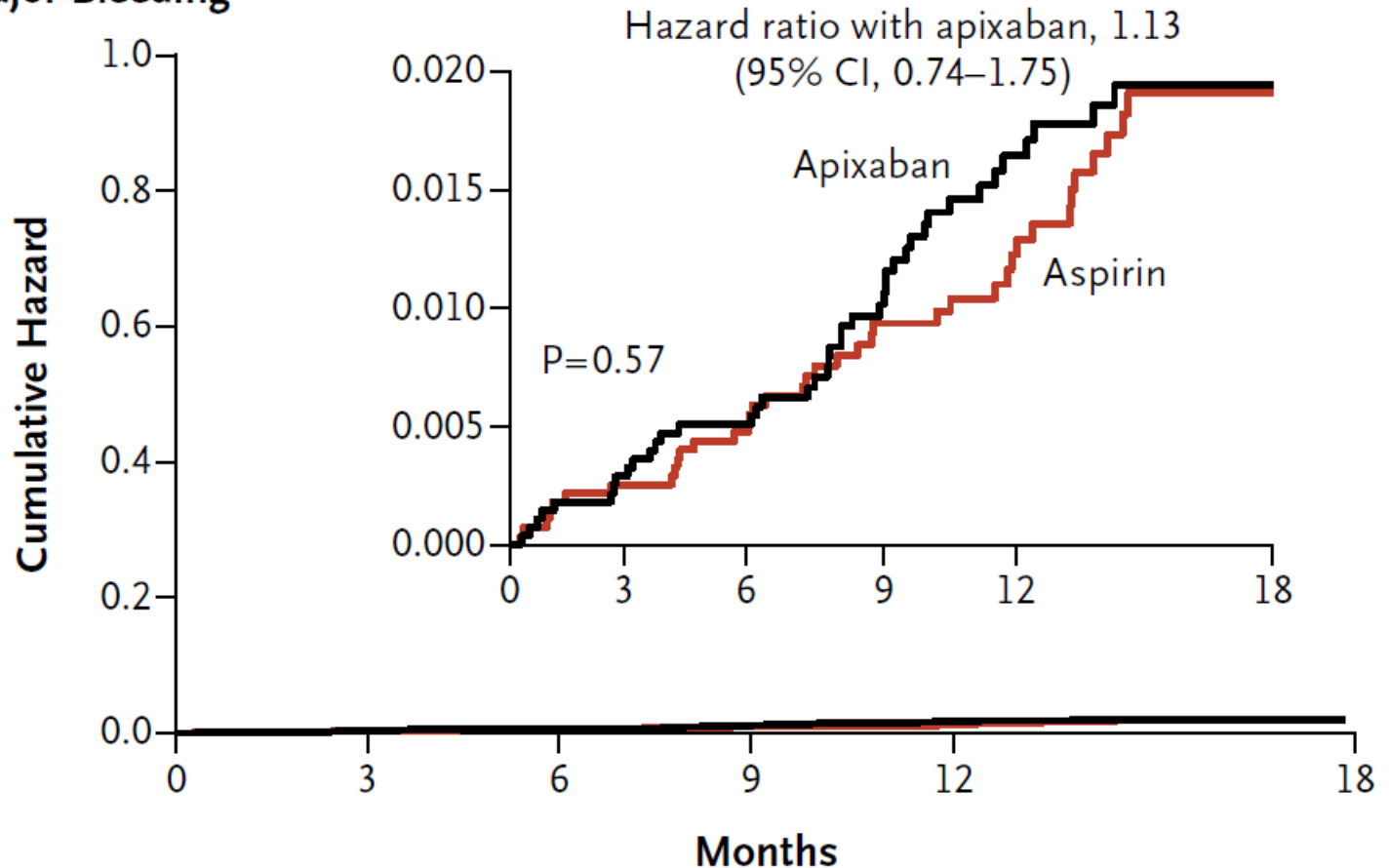
Cumulative Hazard Rates for the Primary Efficacy Outcomes, According to Treatment Group.



# AVERROES study: apixaban vs aspirin in AF

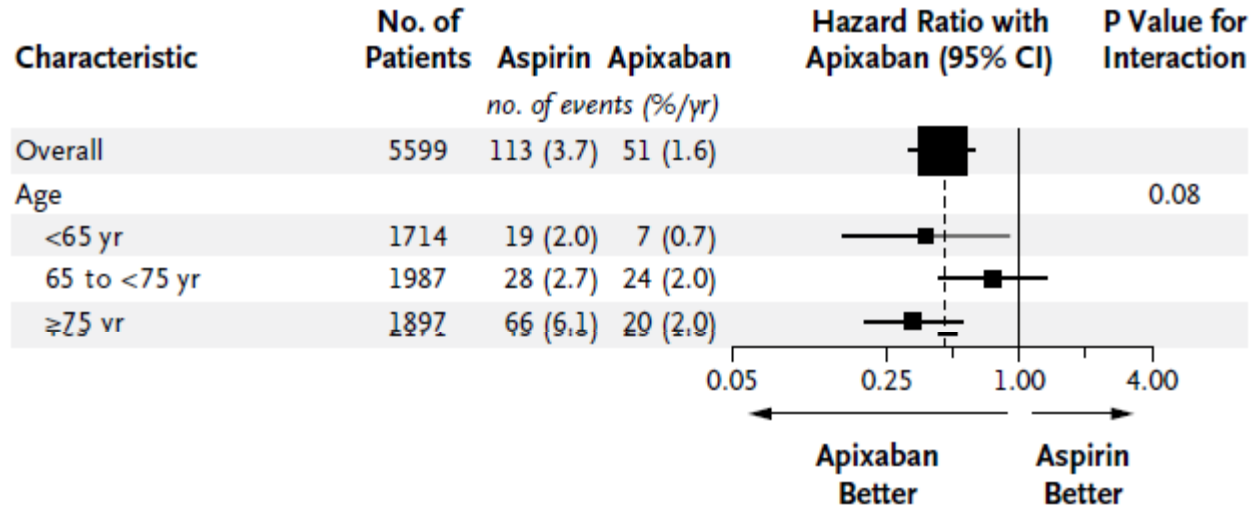
Cumulative Hazard Rates for the Safety Outcomes, According to Treatment Group.

## Major Bleeding

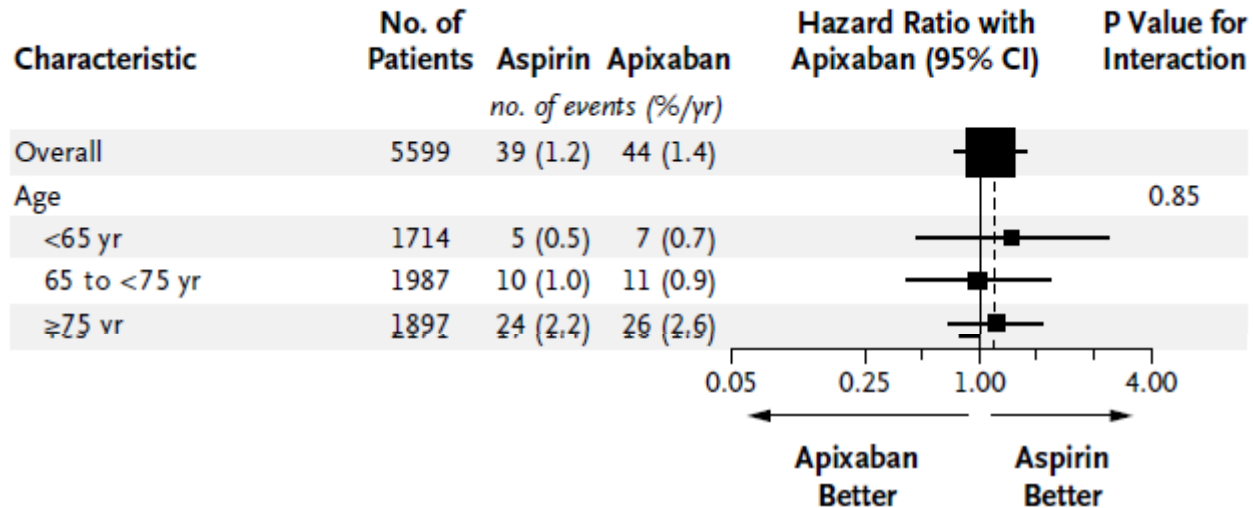


# Estudio AVERROES: apixaban 5mg bid vs aspirina en la fibrilación auricular

## A Stroke or Systemic Embolism

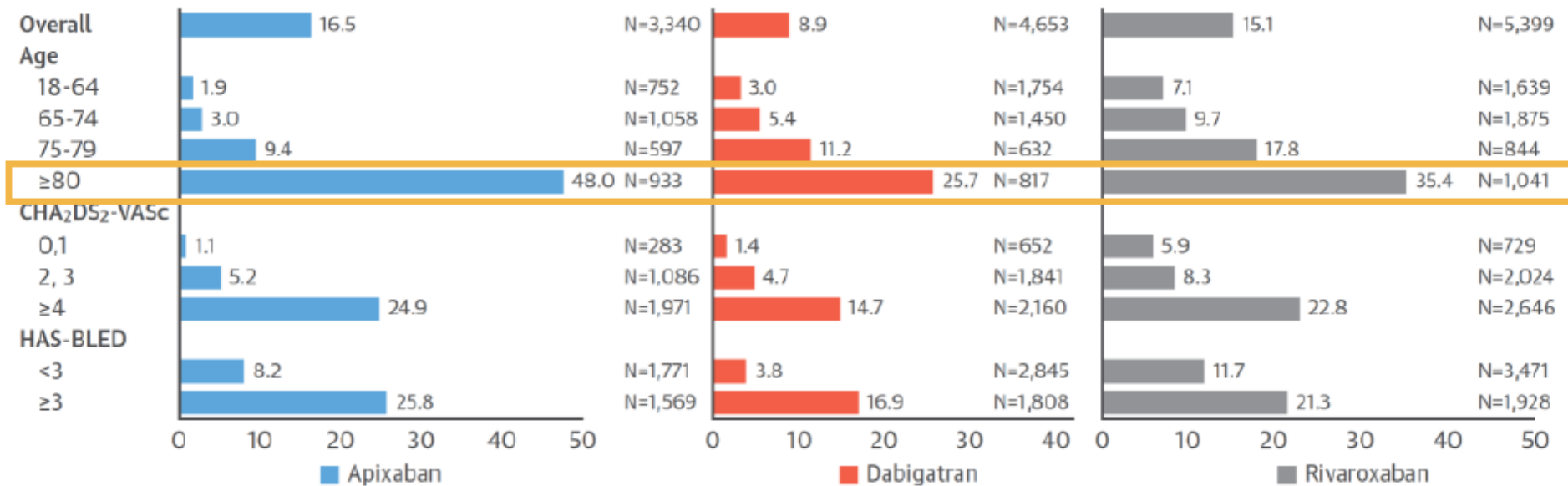


## B Major Bleeding



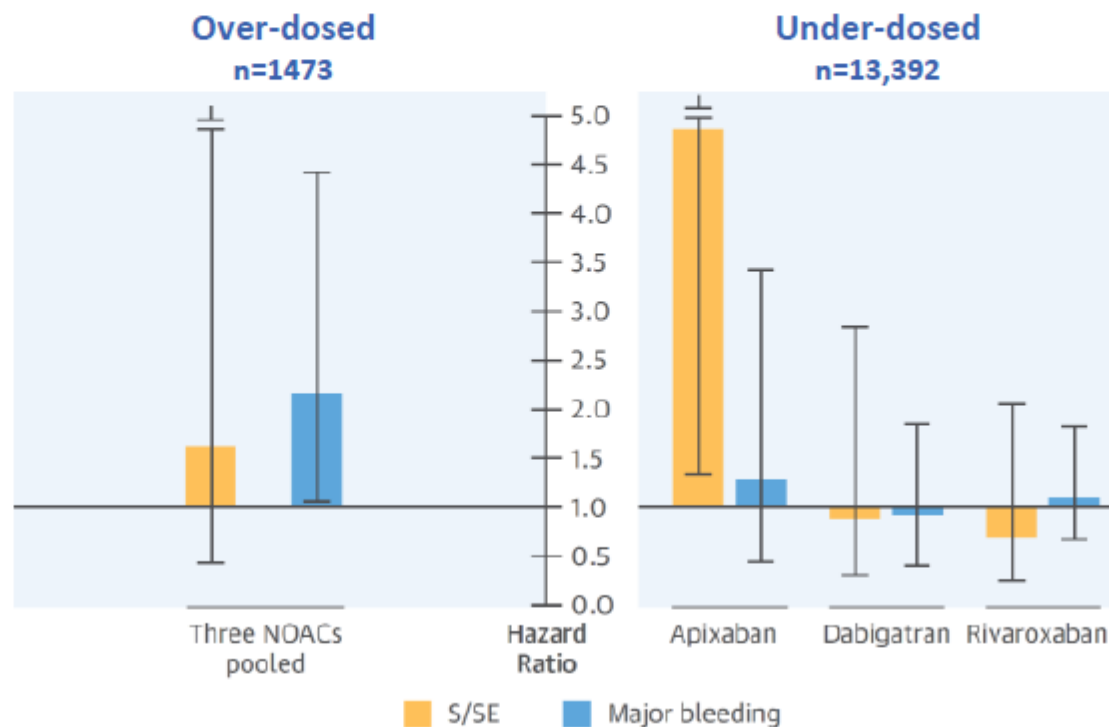
# Current Management Of Frail And Elderly Patients With AF: Age-Related Under-dosing Is Seen Across All NOACs

Inappropriate Under-dosing Of NOAC In 13,392 US Patients With AF And No Renal Indication For A Dose Reduction



# The Clinical Consequences Of NOAC Under-dosing

Outcomes With Inappropriate Under-dosing Of NOAC In 13,392 US Patients With AF And No Renal Indication For A Dose Reduction



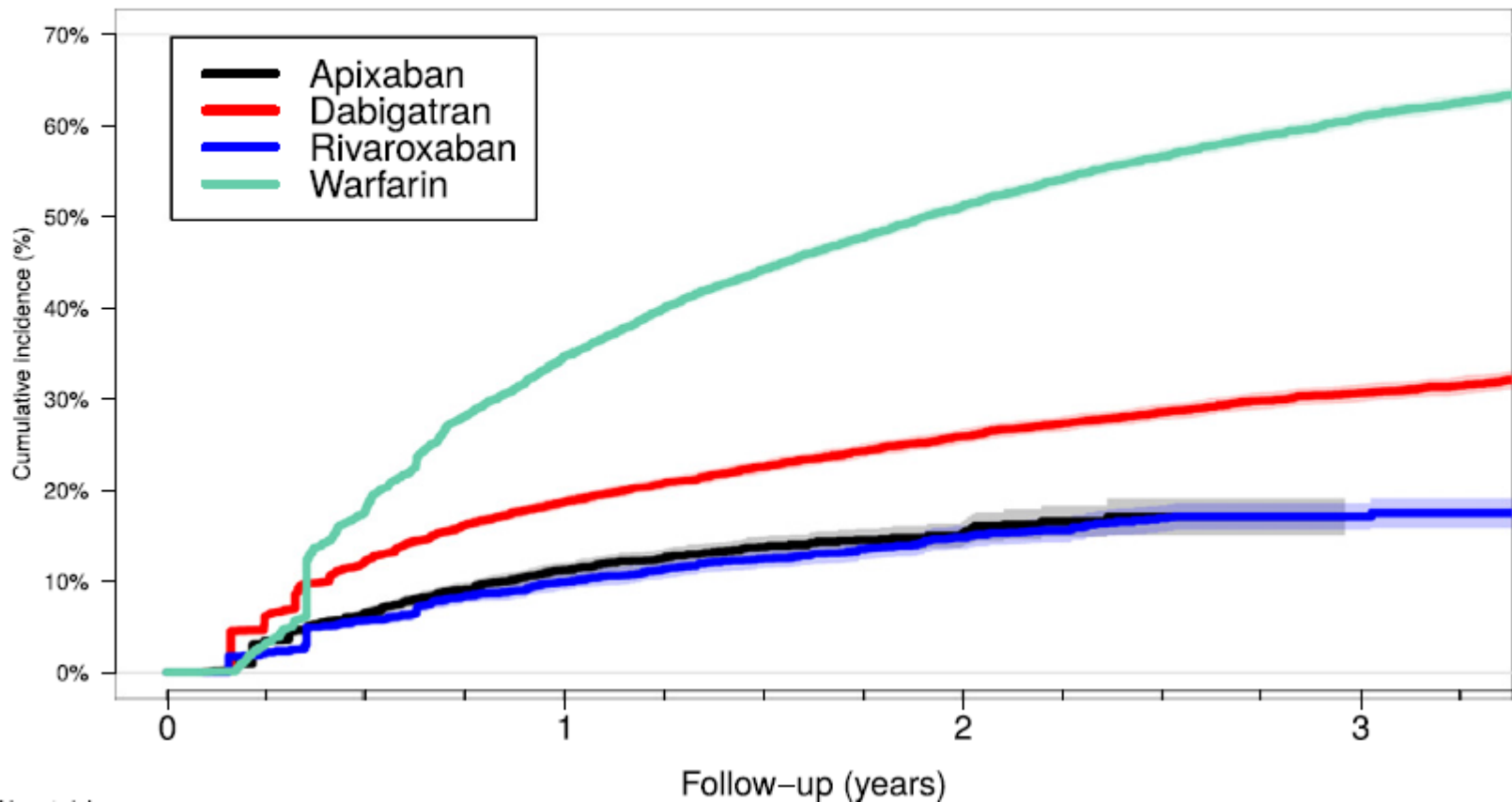
NOAC=non-VKA oral anticoagulant

Yao X, et al. *J Am Coll Cardiol* 2017;69:2779-2790

Results are not intended for direct comparison between NOACs

# Cumulative incidence of nonpersistence

## Non-persistence





## Dosificación de los ACODs en la FA

	Dabigatran	Rivaroxaban	Apixaban		Edoxaban
Dosis	150 mg bid	20 mg qd	5 mg bid		60 mg qd
Criterios de ajuste de dosis	Edad $\geq$ 80 años FG 50-30 ml/min + apreciación RH>RT	FG 50-15 mL/min	2 de 3*	Edad $\geq$ 80 años* Peso $\leq$ 60 kg* Creatinina > 1,5 mg/dl*	Peso $\leq$ 60 kg FG 50-15 ml/min Inhibidores potentes P-gp
			FG 30-15mL/min		
Dosis ajustada	110 mg bid	15 mg qd	2,5 mg bid		30 mg qd

JAMA Internal Medicine | [Original Investigation](#)

# Perioperative Management of Patients With Atrial Fibrillation Receiving a Direct Oral Anticoagulant (The PAUSE study)

James D. Douketis, MD; Alex C. Spyropoulos, MD; Joanne Duncan, BSc; Marc Carrier, MD, MSc; Gregoire Le Gal, MD; Alfonso J. Tafur, MD; Thomas Vanassche, MD; Peter Verhamme, MD; Sudeep Shivakumar, MD; Peter L. Gross, MD, MSc; Agnes Y. Y. Lee, MD, MSc; Erik Yeo, MD; Susan Solymoss, MD; Jeannine Kassis, MD; Geneviève Le Templier, MD; Stephen Kowalski, MD; Mark Blostein, MD; Vinay Shah, MD; Elizabeth MacKay, MD; Cynthia Wu, MD; Nathan P. Clark, PharmD; Shannon M. Bates, MDCM, MSc; Frederick A. Spencer, MD; Eleni Arnaoutoglou, MD, PhD; Michiel Coppens, MD, PhD; Donald M. Arnold, MD, MSc; Joseph A. Caprini, MD; Na Li, PhD; Karen A. Moffat, MLT; Summer Syed, MD, MSc; Sam Schulman, MD, PhD

JAMA Intern Med. 2019 Aug 5. doi: [10.1001/jamainternmed.2019.2431](https://doi.org/10.1001/jamainternmed.2019.2431).

Figure. Perioperative Direct Oral Anticoagulant (DOAC) Management Protocol

DOAC	Surgical Procedure-Associated Bleeding Risk	Preoperative DOAC Interruption Schedule					Day of Surgical Procedure (No DOAC)	Postoperative DOAC Resumption Schedule			
		Day -5	Day -4	Day -3	Day -2	Day -1		Day +1	Day +2	Day +3	Day +4
Apixaban	High	→							→		
	Low	→							→		
Dabigatran etexilate (CrCl ≥50 mL/min)	High	→							→		
	Low	→							→		
Dabigatran etexilate (CrCl <50 mL/min) <sup>a</sup>	High	→							→		
	Low	→							→		
Rivaroxaban	High	→							→		
	Low	→							→		

**Table 3. Primary Study Outcomes**

Outcome	DOAC Cohort		
	Apixaban (n = 1257)	Dabigatran Etexilate (n = 668)	Rivaroxaban (n = 1082)
<b>Primary</b>			
Major bleeding <sup>a</sup>			
No. (%)	17 (1.35)	6 (0.90)	20 (1.85)
1-Sided 95% CI	0-2.00	0-1.73	0-2.65
P value	.051	.02	.36
Arterial thromboembolism <sup>b,c</sup>			
No. (%)	2 (0.16)	4 (0.60)	4 (0.37)
1-Sided 95% CI	0-0.48	0-1.33	0-0.82
P value	<.001	.03	.001

**Table 4. Incidence of Major Bleeding by Elective Surgery or Procedure-Associated Bleeding Risk**

Procedure-Associated Bleeding Risk	Apixaban Cohort (n = 1257)	Dabigatran Etexilate Cohort (n = 668)	Rivaroxaban Cohort (n = 1082)
Low bleeding risk			
No. (%)	851 (67.7)	440 (65.9)	709 (65.5)
30-d Postoperative rate of major bleeding, % (95% CI)	0.59 (0-1.20)	0.91 (0-2.01)	1.27 (0-2.17)
High bleeding risk			
No. (%)	406 (32.3)	228 (34.1)	373 (34.5)
30-d Postoperative rate of major bleeding, % (95% CI)	2.96 (0-4.68)	0.88 (0-2.62)	2.95 (0-4.76)

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