ANCORA SPAZIO PER I VECCHI ANTICOAGULANTI ORALI?

UP TO DATE DELLA TERAPIA CON DOAC NEL 2022

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Cardiologia

Ospedale San Giovanni Bosco

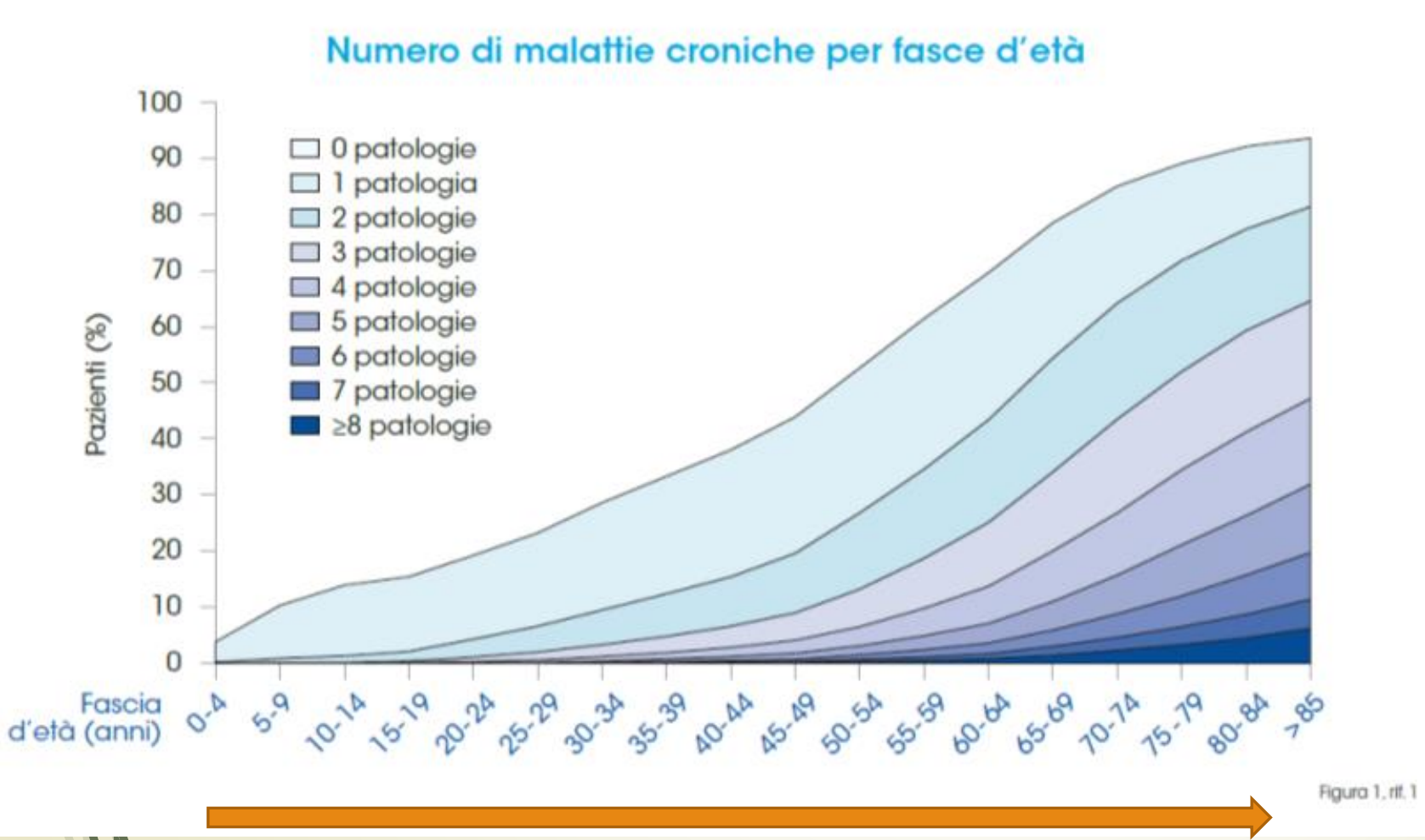
Torino

FIBRILLAZIONE ATRIALE

- ✓ La prevalenza della fibrillazione atriale (FA) è ***in aumento*** con l'invecchiamento della popolazione globale e l'aumento della longevità.
- ✓ Dal 1990 al 2019 la prevalenza è raddoppiata a livello globale a 59,7 milioni nel 2019
- ✓ Sebbene la prevalenza riportata di FA sia del 10% nelle persone di età >80 anni, ciò esclude i pazienti non diagnosticati.
- ✓ Le complicanze del trattamento della FA aumentano notevolmente nei pazienti di età ≥75 anni

Virani SS, Alonso A, Aparicio HJ, et al. Heart disease and stroke statistics-2021 update: a report from the American Heart Association. Circulation. 2021;143(8):e254–e743.

Dopo i 75 anni, il paziente è affetto da almeno altre 5 patologie[1]



Comorbidità		
Scompenso cardiaco/disfunzione ventricolare sinistra	272.776	28,4
Ipertensione arteriosa	826.695	86,2
Diabete mellito	188.095	19,6
Pregresso Ictus	167.311	17,4
Malattie vascolari	259.215	27,0
Alterata funzionalità renale	53.034	5,5

1.Barnett K et al. Lancet 2012; 380: 37-43

Circulation

ACC/AHA/HRS GUIDELINE

2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society

ESC European Society of Cardiology

European Heart Journal (2020) **42**, 373–498
doi:10.1093/eurheartj/ehaa612

ESC GUIDELINES

2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS)

- ✓ FA aumenta rischio STROKE EMBOLICO E TROMBOEMBOLISMO SISTEMICO
- ✓ Avvio di OAC è RACCOMDATA DALLE LINEE GUIDA sulla base del CHA2DS2-VASC

CHA2DAS2-VASC e HAS-BLED

Table 8 CHA_2DS_2-VASc score[334]

CHA_2DS_2-VASc score Risk factors and definitions		Points awarded
C	**Congestive heart failure** Clinical HF, or objective evidence of moderate to severe LV dysfunction, or HCM	1
H	**Hypertension** or on antihypertensive therapy	1
A	**Age 75 years or older**	2
D	**Diabetes mellitus** Treatment with oral hypoglycaemic drugs and/or insulin or fasting blood glucose >125 mg/dL (7 mmol/L)	1
S	**Stroke**Previous stroke, TIA, or thromboembolism	2
V	**Vascular disease** Angiographically significant CAD, previous myocardial infarction, PAD, or aortic plaque	1
A	**Age 65 – 74 years**	1
Sc	**Sex category (female)**	1
Maximum score		**9**

Table 10 Clinical risk factors in the HAS-BLED score[395]

Risk factors and definitions		Points awarded
H	**Uncontrolled hypertension** SBP >160 mmHg	1
A	**Abnormal renal and/or hepatic function** Dialysis, transplant, serum creatinine >200 µmol/L, cirrhosis, bilirubin > × 2 upper limit of normal, AST/ALT/ALP >3 × upper limit of normal	1 point for each
S	**Stroke** Previous ischaemic or haemorrhagic[a] stroke	1
B	**Bleeding history or predisposition** Previous major haemorrhage or anaemia or severe thrombocytopenia	1
L	**Labile INR**[b] TTR <60% in patient receiving VKA	1
E	**Elderly** Aged >65 years or extreme frailty	1
D	**Drugs or excessive alcohol drinking** Concomitant use of antiplatelet or NSAID; and/or excessive[c] alcohol per week	1 point for each
Maximum score		**9**

ESC European Society of Cardiology
European Heart Journal (2020) 42, 373–498
doi:10.1093/eurheartj/ehaa612

ESC GUIDELINES

2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS)

CHA2DAS2-VASC e HAS-BLED

Recommendations	Class[a]	Level[b]
For stroke prevention in AF patients who are eligible for OAC, NOACs are recommended in preference to VKAs (excluding patients with mechanical heart valves or moderate-to-severe mitral stenosis).[423,424]	I	A
For stroke risk assessment, a risk-factor-based approach is recommended, using the CHA_2DS_2-VASc clinical stroke risk score to initially identify patients at 'low stroke risk' (CHA_2DS_2-VASc score = 0 in men, or 1 in women) who should not be offered antithrombotic therapy.[334,388]	I	A
For bleeding risk assessment, a formal structured risk-score-based bleeding risk assessment is recommended to help identify non-modifiable and address modifiable bleeding risk factors in all AF patients, and to identify patients potentially at high risk of bleeding who should be scheduled for early and more frequent clinical review and follow-up.[388,395,404,406]	I	B

European Heart Journal (2014) **35**, 250–256
doi:10.1093/eurheartj/eht483

Clinical course of atrial fibrillation in older adults: the importance of cardiovascular events beyond stroke

Jonathan P. Piccini[1,2*], Bradley G. Hammill[1], Moritz F. Sinner[3], Adrian F. Hernandez[1,2], Allan J. Walkey[4], Emelia J. Benjamin[4,5], Lesley H. Curtis[1,2], and Susan R. Heckbert[6]

Con l'aumento dell'età incrementano sia il rischio tromboembolico sia quello emorragico

Rischio tromboembolico in età superiore a 75 aa va dal 7 al 9%

Rischio emorragico dal 5,4 al 6,6%

TABLE 1 Cumulative Incidence Rate Over 5 Years After AF Diagnosis, By Age

Age Group, y	n	Mortality	Heart Failure	Stroke	GI Bleeding
75-79	44,396	40.1	13.3	6.9	5.9
80-84	41,450	52.1	15.1	8.1	6.4
85-89	28,657	67.0	15.8	8.9	6.6
≥90	18,511	84.3	13.7	6.9	5.4

Values are n or %. Adapted with permission from Piccini et al (62).
AF = atrial fibrillation; GI = gastrointestinal.

ORIGINAL RESEARCH

American Heart Association | American Stroke Association

Thromboembolic Risk, Bleeding Outcomes and Effect of Different Antithrombotic Strategies in Very Elderly Patients With Atrial Fibrillation: A Sub-Analysis From the PREFER in AF (*PREvention oF* Thromboembolic Events–*E*uropean *R*egistry in *A*trial *F*ibrillation)

Giuseppe Patti, MD; Markus Lucerna, PhD; Ladislav Pecen, PhD; Jolanta M. Siller-Matula, MD; Ilaria Cavallari, MD; Paulus Kirchhof, MD; Raffaele De Caterina, MD, PhD

Rischio tromboembolico

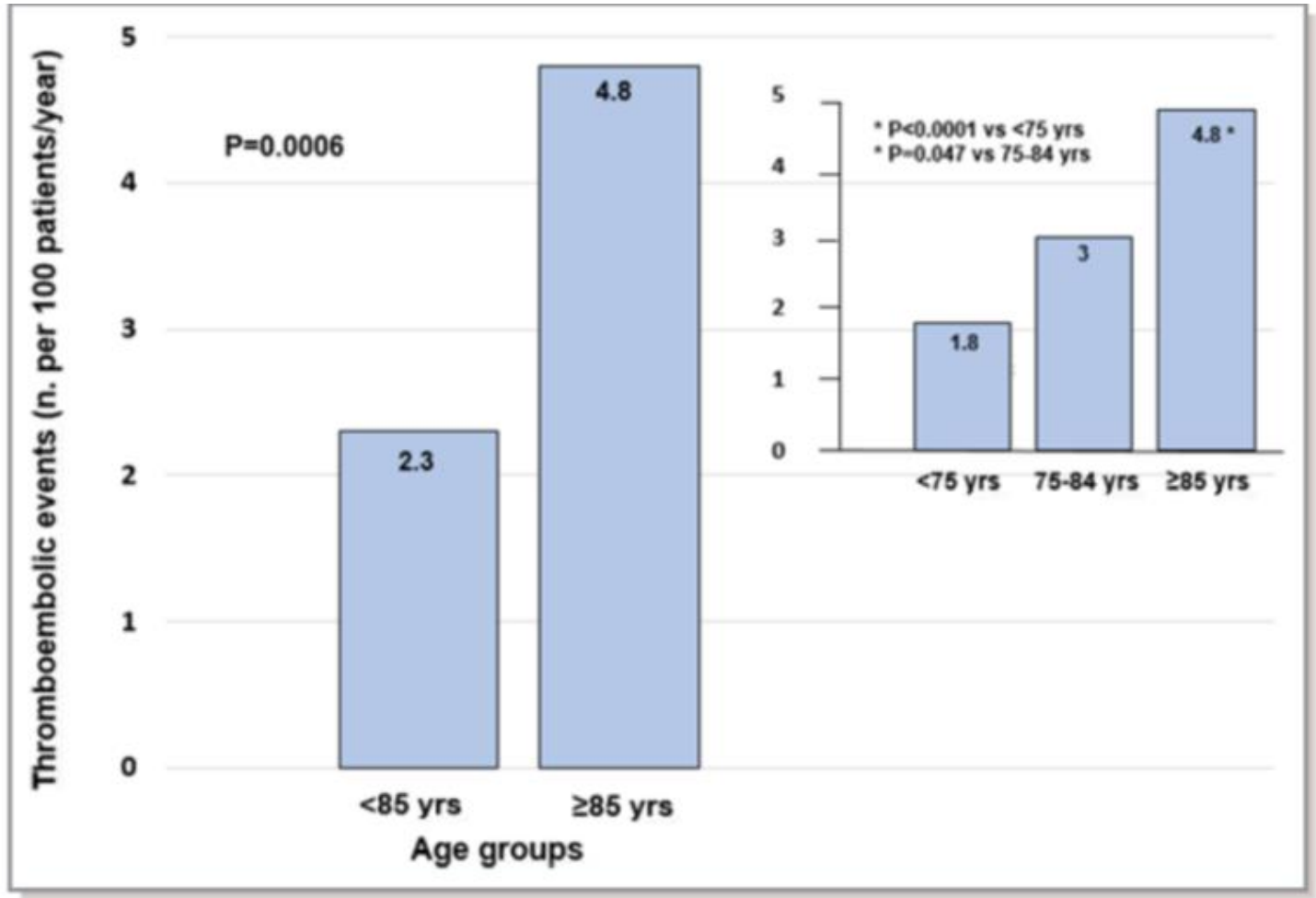


Figure 1. Incidence of thromboembolic events (stroke/TIA/systemic embolism) at 1 year in patients aged <85 and ≥85 years. Rates of thromboembolic events according to 3 age strata (<75, 75–84, and ≥85 years) are also depicted. TIA indicates transient ischemic attack.

Rischio emorragico

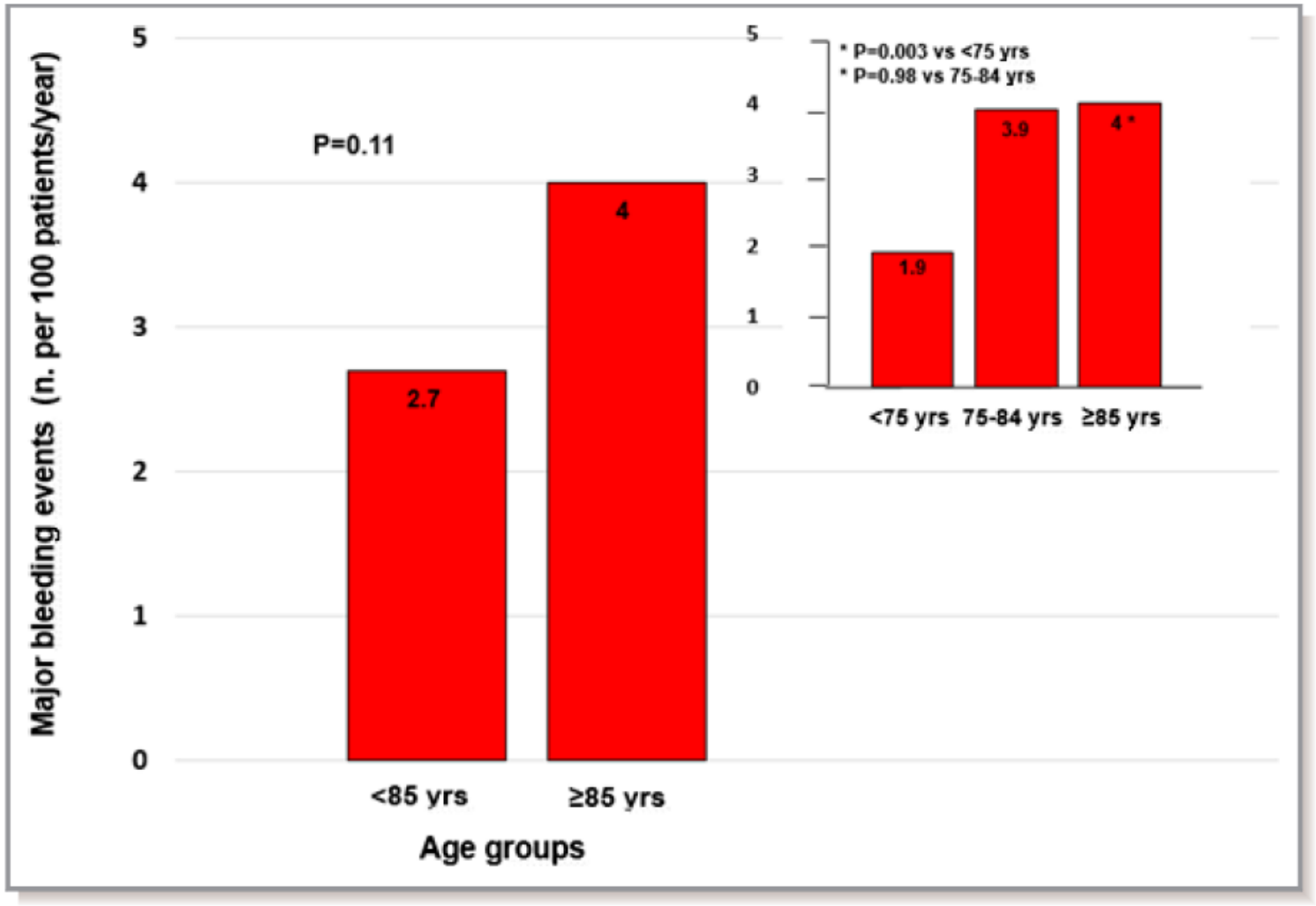
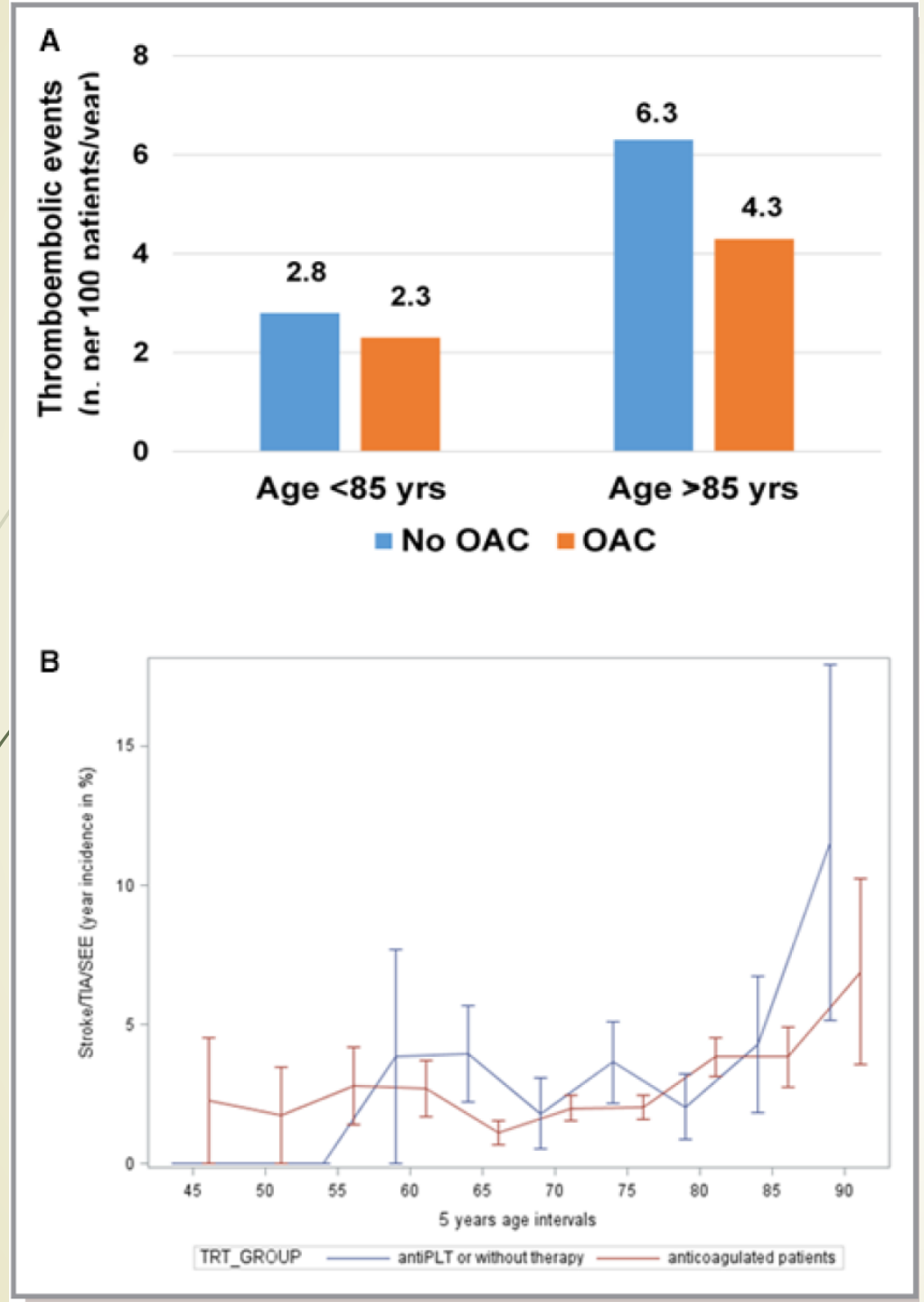
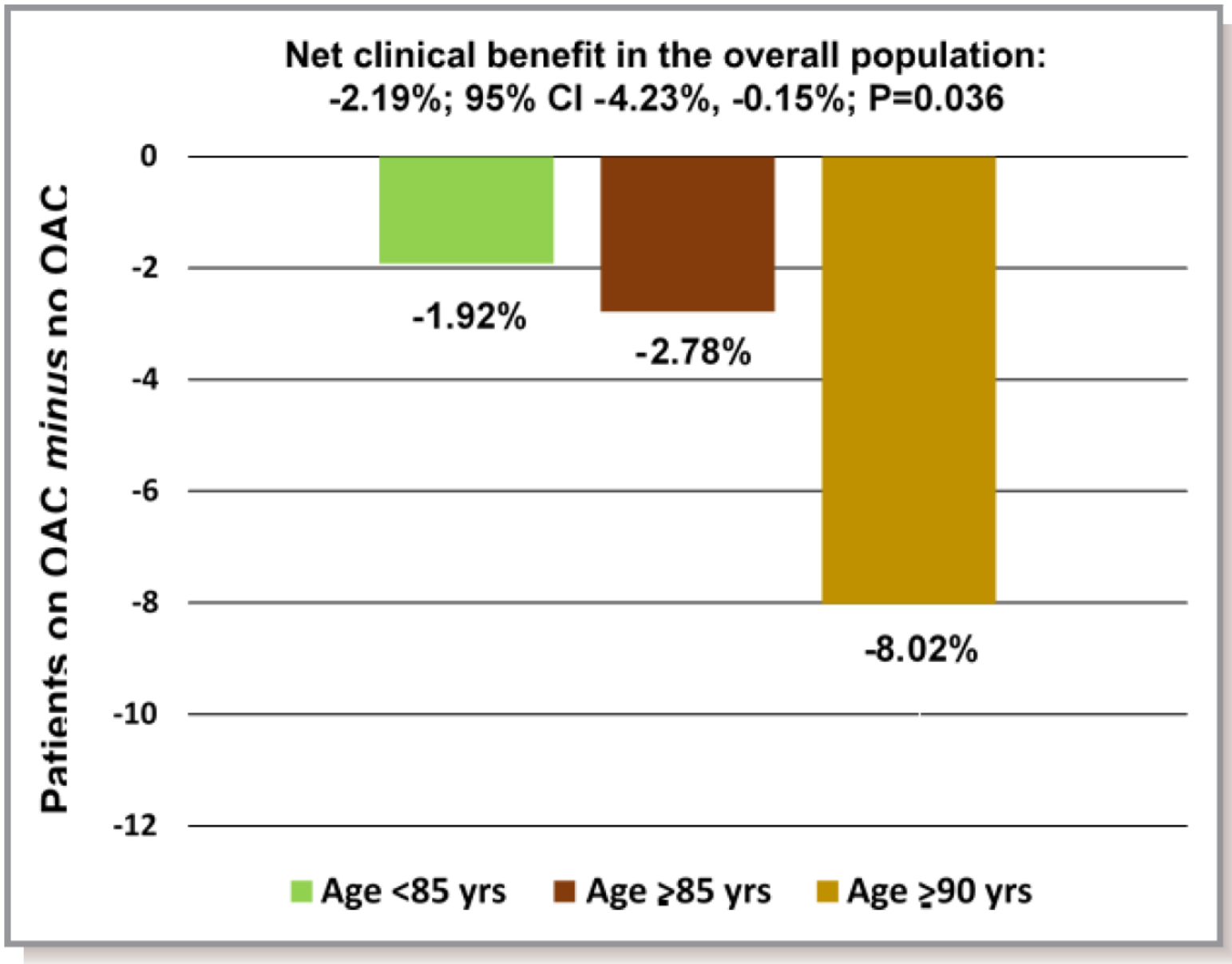


Figure 2. Incidence of major bleeding at 1 year in patients aged <85 and ≥85 years. Rates of major bleeding according to 3 age strata (<75, 75–84, and ≥85 years) are also depicted.



Rischio tromboembolico dei pazienti anziani che non ricevono OAC è superiore rispetto a quelli in terapia anticoagulante orale



Netto beneficio della terapia ANTICOAGULANTE ORALE NEI PAZIENTI CON Età > 85 ANNI

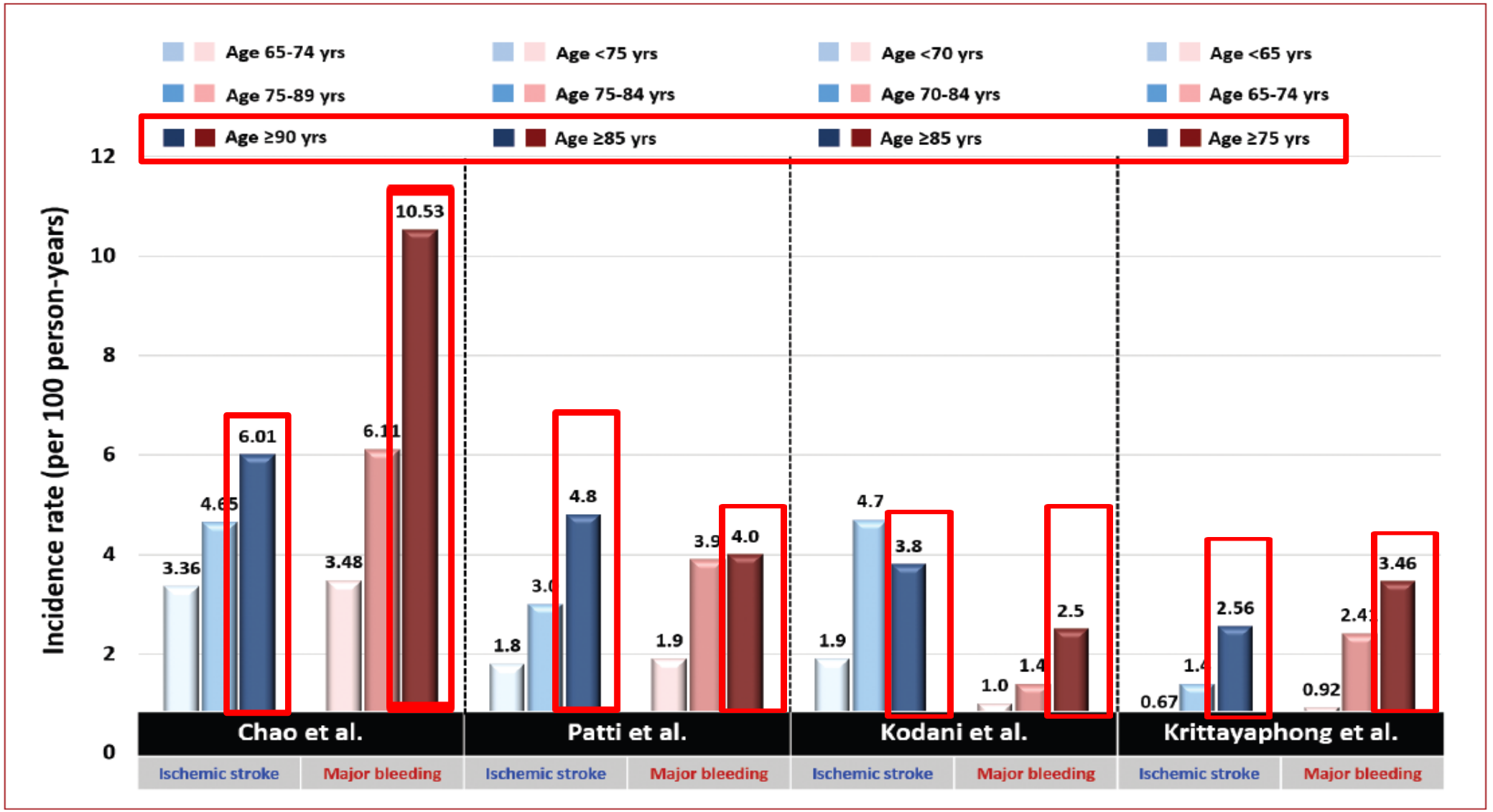


Figure 1. Risks of ischemic stroke and major bleeding in elderly patients with AF. Elderly patients are at increased risks of ischemic stroke and major bleeding, and the risks continues to rise at even advanced age. Data used in the figure were adapted from the papers by Chao et al., Patti et al., Kodani et al., and Krittayaphong et al. [10–13]

Abbreviations: AF, atrial fibrillation

"Old age" should not be the only reason to withhold oral anticoagulants for AF patients

Optimal anticoagulation in elderly patients with atrial fibrillation: Which drug at which dose?

Jo-Nan Liao[1,2]*, Yi-Hsin Chan[3–5]*, Ling Kuo[1,2], Chuan-Tsai Tsai[1,2], Su-Shen Lim[1,2], Tze-Fan Chao[1,2]

11.13 The elderly and frail with atrial fibrillation

patients.[339,390,391,1220–1223] Evidence from RCTs,[441,1224] meta-analyses[423,1225] and large registries[339,433,1209,1226] support the use of OAC in this age group. Antiplatelets are neither more effective nor safer than warfarin and may even be harmful,[433] whereas NOACs appear to have a better overall risk–benefit profile compared with warfarin.[423,433,441,1035,1225,1227–1236] Prescribing a reduced dose of OAC is less effective in preventing AF adverse outcomes.[1107,1211,1237,1238]

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European Heart Journal (2020) **42**, 373–498
doi:10.1093/eurheartj/ehaa612

JAFIB
Featured Review
Journal of Atrial Fibrillation
www. jafib.com

What is the Impact of Frailty on Prescription of Anticoagulation in Elderly Patients with Atrial Fibrillation? A Systematic Review and Meta-Analysis

Zardasht Oqab[1], Payam Pournazari[1], Robert S Sheldon[1]

[1]*Libin Cardiovascular Institute of Alberta, University of Calgary, Calgary, Alberta, Canada .*

REAL WORLD:

PAZIENTI ANZIANI FRAGILI SONO MENO TRATTATI DEI PAZIENTI ANZIANI NON FRAGILI

Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Perera (2009)	0.236	0.078	0.707	-2.578	0.010
Nguyen (2015)	0.665	0.422	1.048	-1.758	0.079
Lefebvre (2015)	0.452	0.315	0.648	-4.319	0.000
	0.487	0.322	0.738	-3.396	0.001

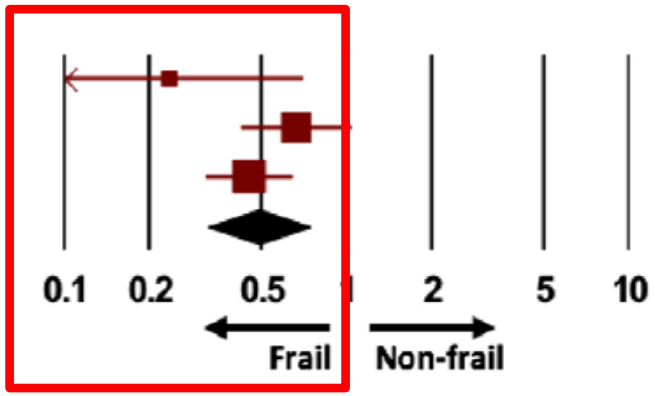

Figure 2: Random effects model meta-analysis of prescription of anticoagulation in frail versus non-frail elderly. Frail elderly subjects were less likely to receive anticoagulation compared to non-frail elderly subjects.

American Journal of Cardiovascular Drugs (2021) 21:419–433
https://doi.org/10.1007/s40256-020-00457-3

REVIEW ARTICLE

Non-adherence to Thromboprophylaxis Guidelines in Atrial Fibrillation: A Narrative Review of the Extent of and Factors in Guideline Non-adherence

Eyob Alemayehu Gebreyohannes[1] · Sandra Salter[1] · Leanne Chalmers[2] · Luke Bereznicki[3] · Kenneth Lee[1,3]

Cause :

- *Cadute frequenti*
- *Anemia*
- *Severa fragilità*
- *Elevato rischio di sanguinamento*
- *Età avanzata*

WARFARIN AND DIRECT ORAL ANTICOAGULANTS PRACTICE RESEARCH REPORTS

Trends in utilization of warfarin and direct oral anticoagulants in older adult patients with atrial fibrillation

Journal of the American Heart Association

ORIGINAL RESEARCH

Management of Atrial Fibrillation in Older Patients by Morbidity Burden: Insights From Get With The Guidelines-Atrial Fibrillation

Frederik Dalgaard, MD, PhD; Haolin Xu, MS; Roland A. Matsouaka, PhD; Andrea M. Russo, MD; Anne B. Curtis, MD; Peter Vibe Rasmussen, MD; Martin H. Ruwald, MD, PhD; Gregg C. Fonarow, MD; Angela Lowenstern, MD; Morten L. Hansen, MD, PhD; Jannik L. Pallisgaard, MD, PhD; Karen P. Alexander, MD; John H. Alexander, MD, MHS; Renato D. Lopes, MD, PhD; Christopher B. Granger, MD; William R. Lewis, MD; Jonathan P. Piccini, MD, MHS; Sana M. Al-Khatib, MD, MHS

Table 5. Documented Reasons for Those Not Receiving OAC at Discharge, Stratified by Morbidity Burden

Variable	Overall N=4935	Low Comorbidity Burden (0–2) N=1890	Moderate Comorbidity Burden (3–5) N=2484	High Comorbidity Burden (≥6) N=561	*P* Value	SD: 3–5 vs 0–2	SD: ≥6 vs 0–2
OAC relative contraindications							
Any contraindications to anticoagulation therapy	3523 (71.4)	1263 (66.8)	1856 (74.7)	404 (72.0)	<0.0001	17.4	11.3
OAC relative contraindication categories							
Unable to adhere/monitor	157 (3.2)	58 (3.1)	81 (3.3)	18 (3.2)	0.9370	1.1	0.8
Occupational risk	4 (0.1)	2 (0.1)	1 (0.0)	1 (0.2)	0.5200	2.4	1.9
High bleeding risk	941 (19.1)	268 (14.2)	535 (21.5)	138 (24.6)	<0.0001	19.3	26.6
Frequent falls/frailty	1411 (28.6)	463 (24.5)	774 (31.2)	174 (31.0)	<0.0001	14.9	14.6
Patient refusal/preference	862 (17.5)	363 (19.2)	432 (17.4)	67 (11.9)	0.0004	4.7	20.1
Physician preference	744 (15.1)	327 (17.3)	355 (14.3)	62 (11.1)	0.0004	8.3	18.0
Need for dual antiplatelet therapy	54 (1.1)	10 (0.5)	34 (1.4)	10 (1.8)	0.0076	8.7	11.7
Transient or reversible causes of atrial fibrillation	63 (1.3)	28 (1.5)	30 (1.2)	5 (0.9)	0.5007	2.4	5.5
Physician preference only	485 (9.8)	218 (11.5)	230 (9.3)	37 (6.6)	0.0010	7.5	17.3
Moderate contraindications*	1982 (40.2)	697 (36.9)	1056 (42.5)	229 (40.8)	0.0008	11.5	8.1

Cadute e anticoagulanti orali

- Il numero di cadute che controindica l'avvio di terapia anticoagulante orale è stato ben definito dalla letteratura (VKA)
- I pazienti anziani e fragili che cadono hanno media di cadute annuali di 1,81
- Dato che il rischio di ematoma subdurale deve essere ≥ 535 volte affinchè i rischi della terapia con warfarin superino i benefici, i pazienti in TAO devono cadere 295 volte/anno (535/1.81) per essere dichiarati non elegibili alla terapia con TAO.

Man-Son-Hing M, Nichol G, Lau A, Choosing antithrombotic therapy for elderly patients with atrial fibrillation who are at risk for falls. Arch Intern Med. 1999;159:677–685.)

Drugs & Aging (2021) 38:713–723
https://doi.org/10.1007/s40266-021-00870-6

ORIGINAL RESEARCH ARTICLE

Impact of Fall Risk and Direct Oral Anticoagulant Treatment on Quality-Adjusted Life-Years in Older Adults with Atrial Fibrillation: A Markov Decision Analysis

Wenfei Wei[1] · Rafia S. Rasu[2] · José J. Hernández-Muñoz[1,3] · Renee J. Flores[4] · Nahid J. Rianon[5] · Genesis A. Hernández-Vizcarrondo[6] · Adam T. Brown[1,7]

- Pazienti con FA ,età > 75 anni nell'ambito di cadute
- 5 sottogruppi: - *non assumeva terapia antitrombotica*
  - *assumeva TAO*
  - *-rivaroxaban*
  - *-apixaban*
  - *-ASA*
- Scopo: 1. valutare beneficio in differenti trattamenti

  2. valutare qualità di vita misurata in anni di vita (QALY, misura dell'aspettativa di vita che sconta proporzionalmente anni vissuti con una qualità inferiore della vita).

Drugs & Aging (2021) 38:713–723
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ORIGINAL RESEARCH ARTICLE

Impact of Fall Risk and Direct Oral Anticoagulant Treatment on Quality-Adjusted Life-Years in Older Adults with Atrial Fibrillation: A Markov Decision Analysis

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Abstract

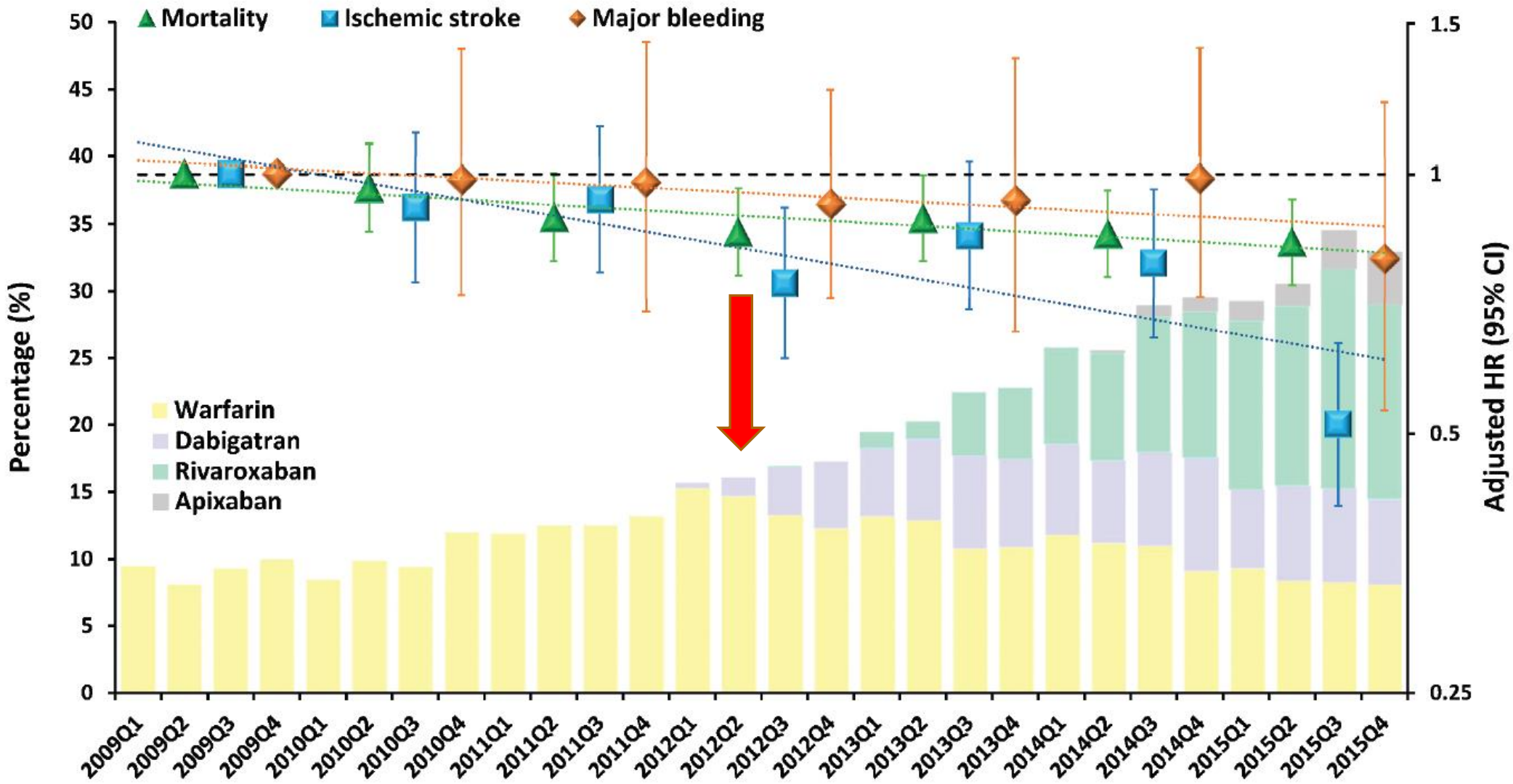
Background and Objective The decision to initiate anticoagulation in older adults with atrial fibrillation is complicated by the benefit of ischemic stroke prevention vs the risk of falls resulting in major bleeds. The objective of this study was to assess the impact of different treatments including direct oral anticoagulants on quality-adjusted life-years (QALYs) in patients aged 75 years and older with atrial fibrillation in the context of falls.

Methods A Markov decision process was constructed for older patients with atrial fibrillation taking no anti-thrombotic, aspirin, warfarin, rivaroxaban, and apixaban. Input probabilities for clinical events were estimated from the available literature. One-way and two-way sensitivity analyses were performed by measuring the impact of varying input probabilities of clinical events on QALY outcomes.

Results The base-case scenario estimated that older adults treated with no anti-thrombotic, aspirin, warfarin, rivaroxaban, and apixaban had QALYs of 8.03, 8.69, 10.38, 11.02, and 11.56, respectively. The sensitivity analysis estimated that an older adult would need to fall over 45 (rivaroxaban) and 458 (apixaban) times per year for the QALY of a direct oral anticoagulant to be lower than that of aspirin.

Conclusions Older adults with atrial fibrillation benefit from stroke protection of anticoagulants, especially direct oral anticoagulants, even if they are at high risk of falls. Clinicians should not consider fall risk as a deciding factor for withholding anticoagulation in this population of patients.

QUALE ANTICOAGULANTE?


Mortality
Ischemic stroke
Major bleeding
Warfarin
Dabigatran
Rivaroxaban
Apixaban
Percentage (%)
Adjusted HR (95% CI)
50
45
40
35
30
25
20
15
10
5
0
1.5
1
0.5
0.25
2009Q1
2009Q2
2009Q3
2009Q4
2010Q1
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2014Q4
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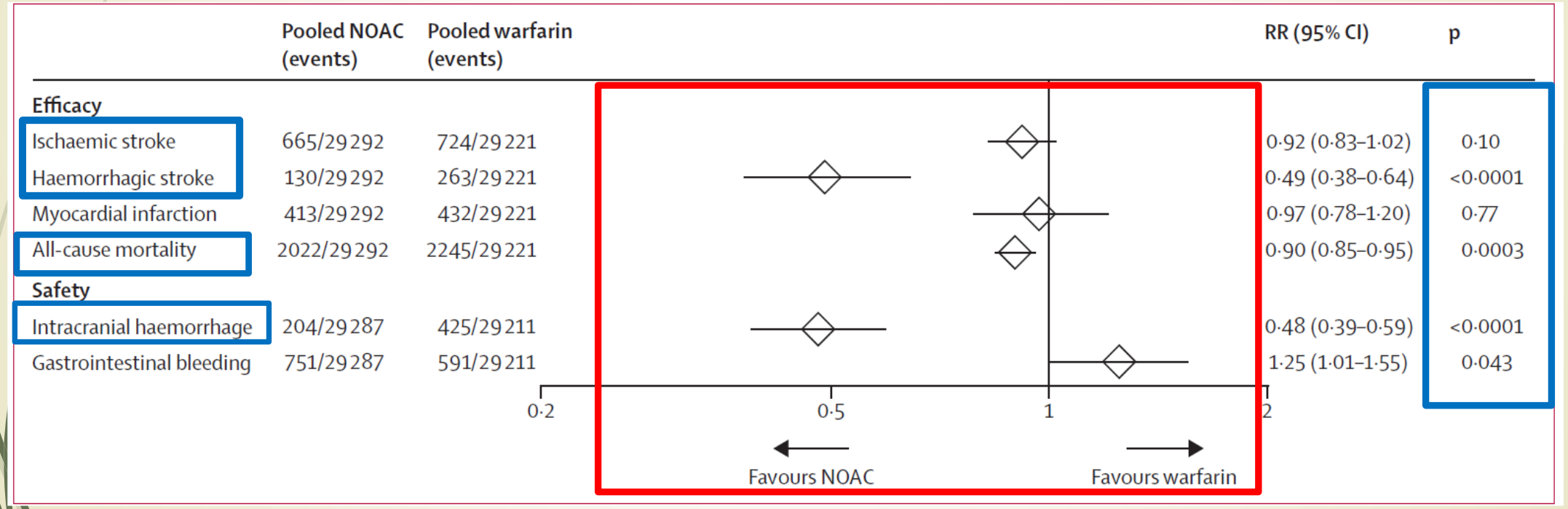
2015Q2
2015Q3
2015Q4

Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials

Christian T Ruff, Robert P Giugliano, Eugene Braunwald, Elaine B Hoffman, Naveen Deenadayalu, Michael D Ezekowitz, A John Camm, Jeffrey I Weitz, Basil S Lewis, Alexander Parkhomenko, Takeshi Yamashita, Elliott M Antman

VKA vs NAO

- SIGNIFICATIVA RIDUZIONE di ICTUS ischemico , EMORRAGIE INTRACRANICHE, E MORTALITA'



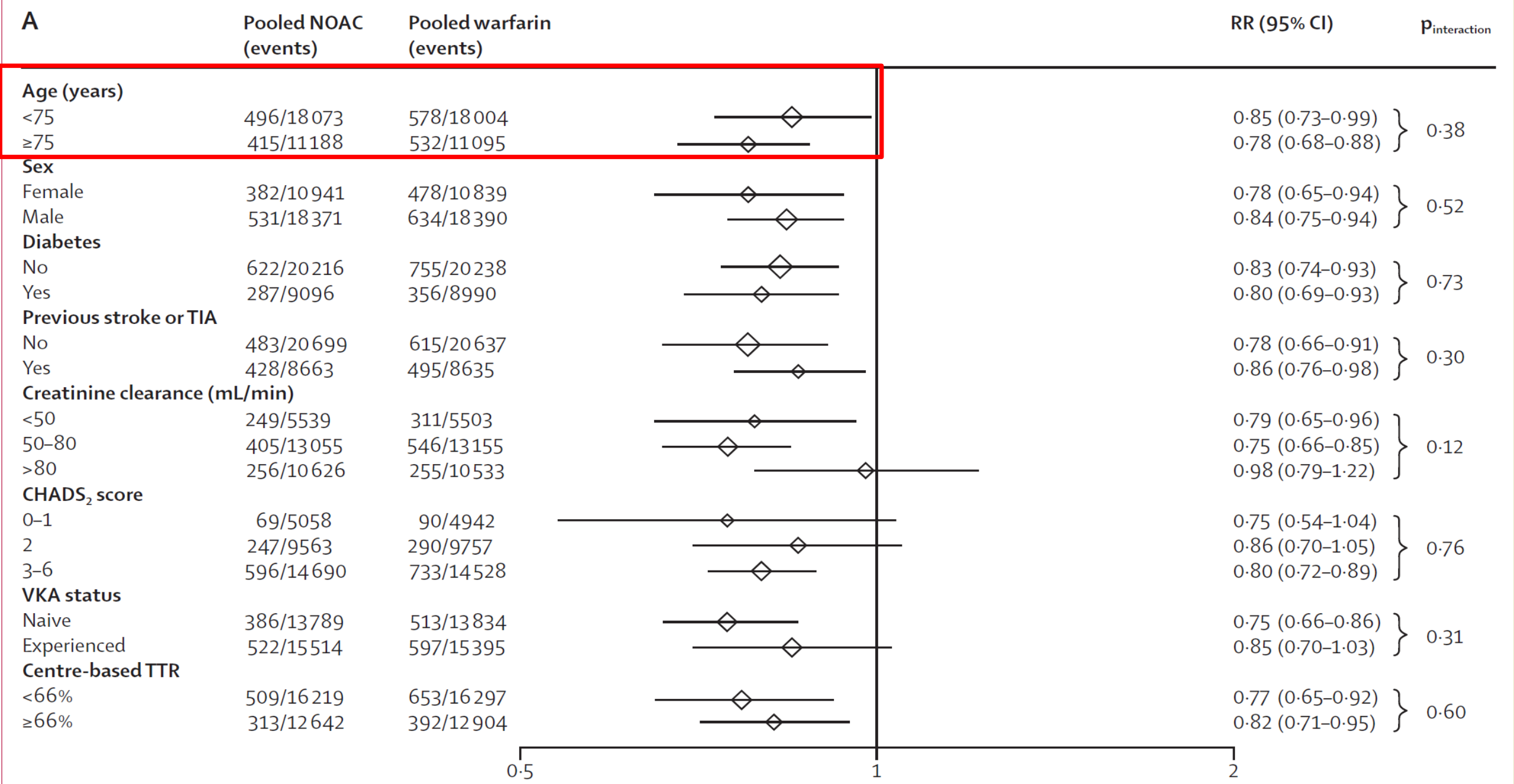


Figure 4: Stroke or systemic embolic events subgroups (A) and major bleeding subgroups (B)

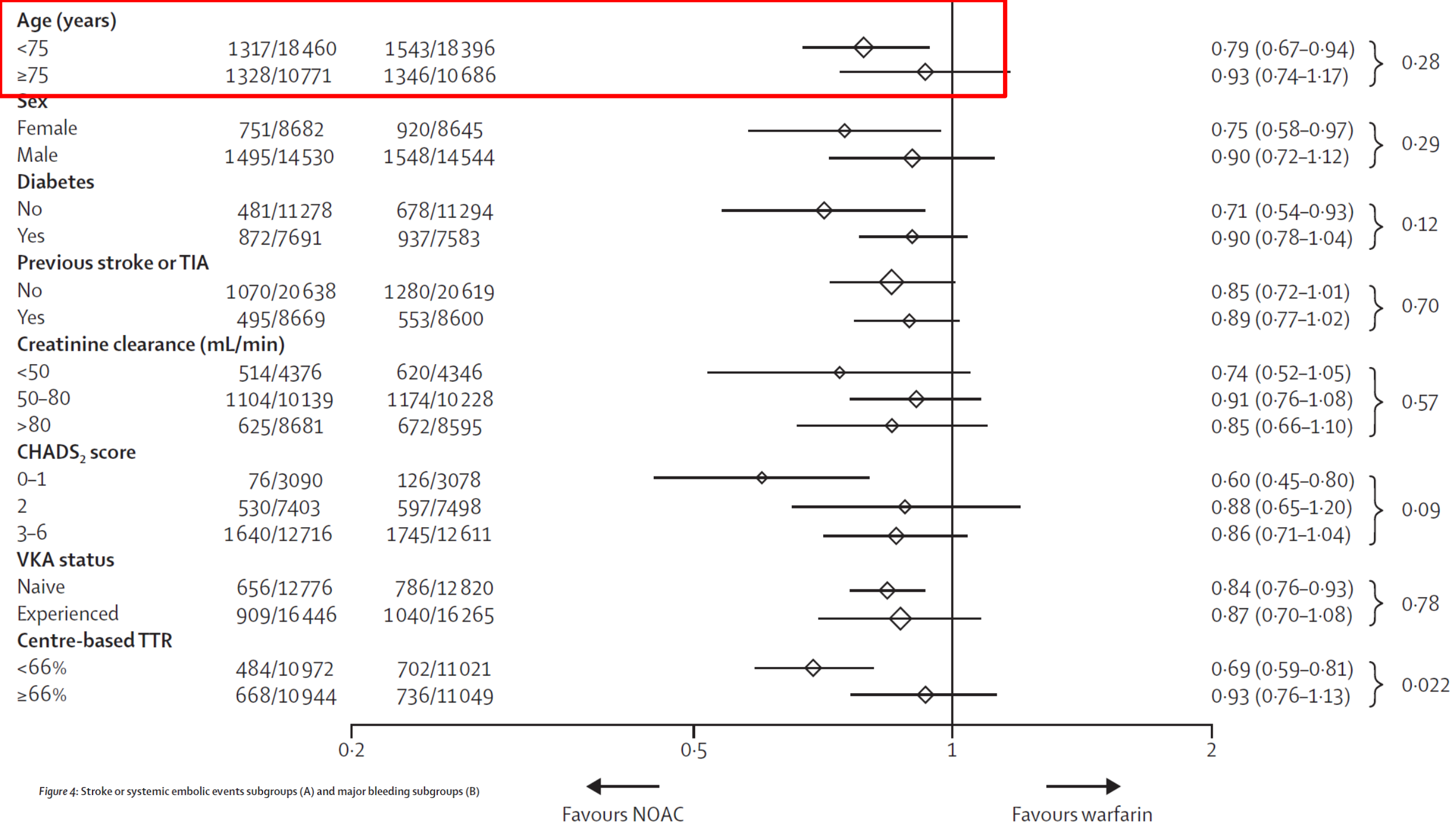


Figure 4: Stroke or systemic embolic events subgroups (A) and major bleeding subgroups (B)

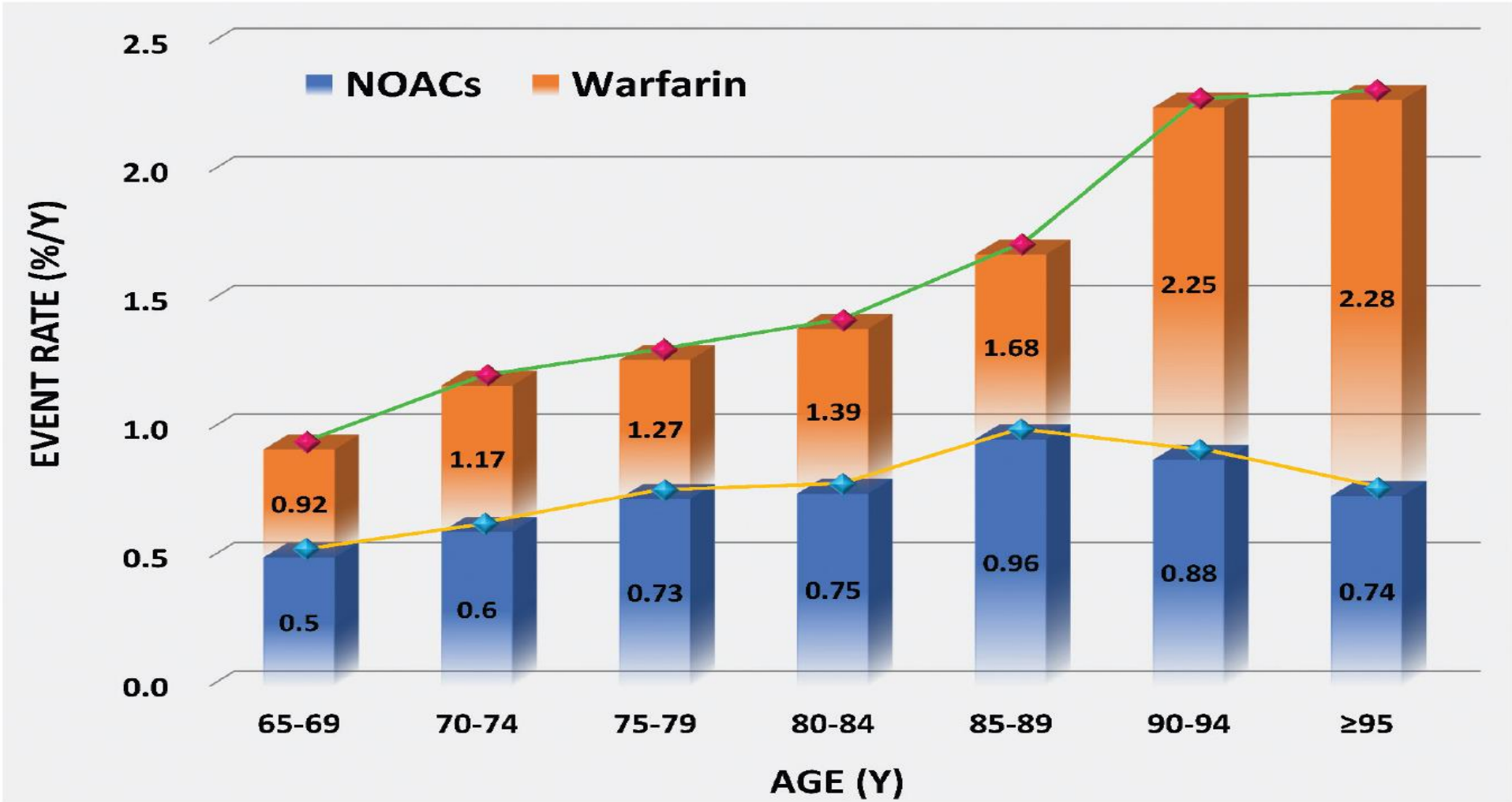
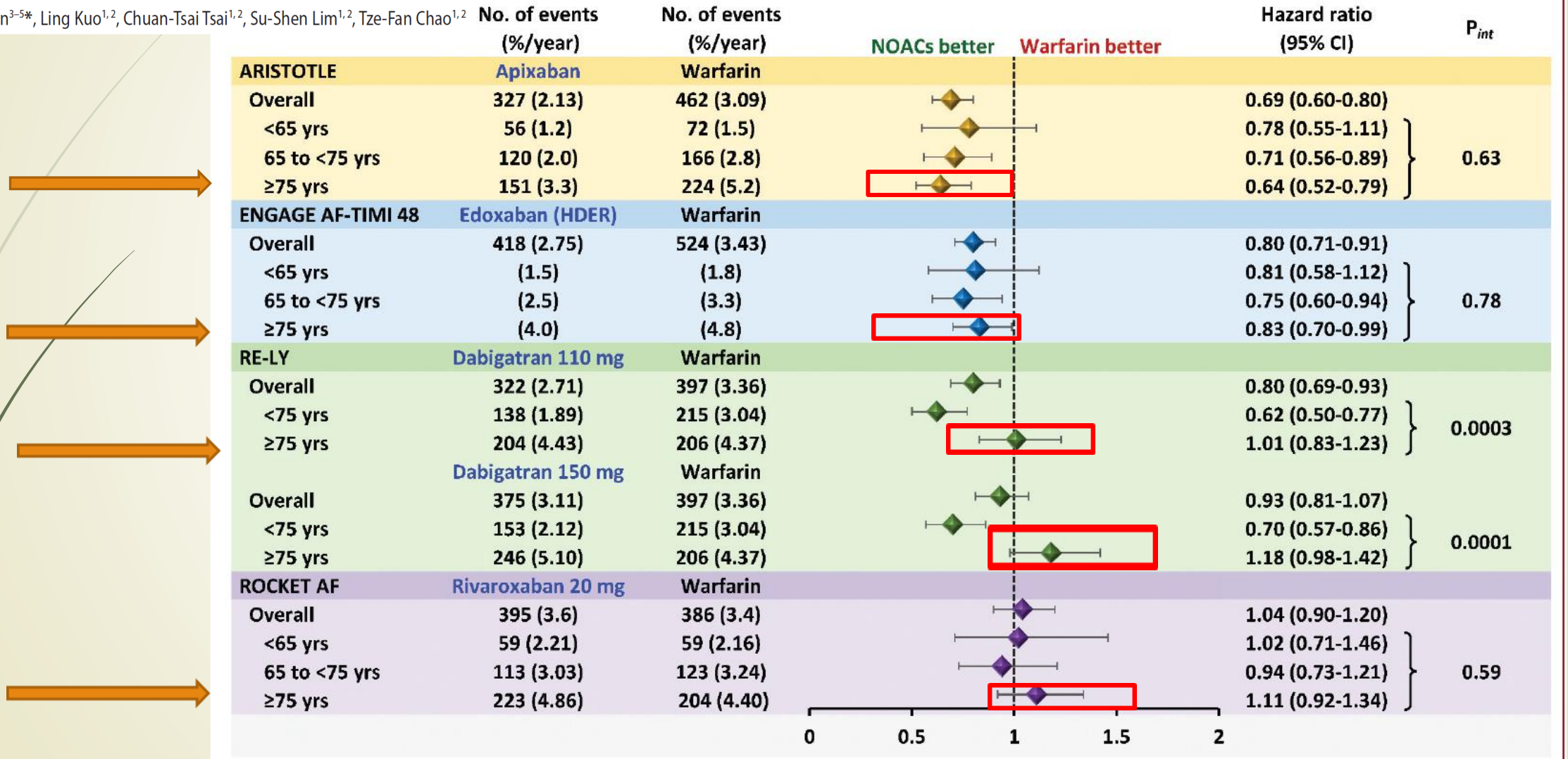


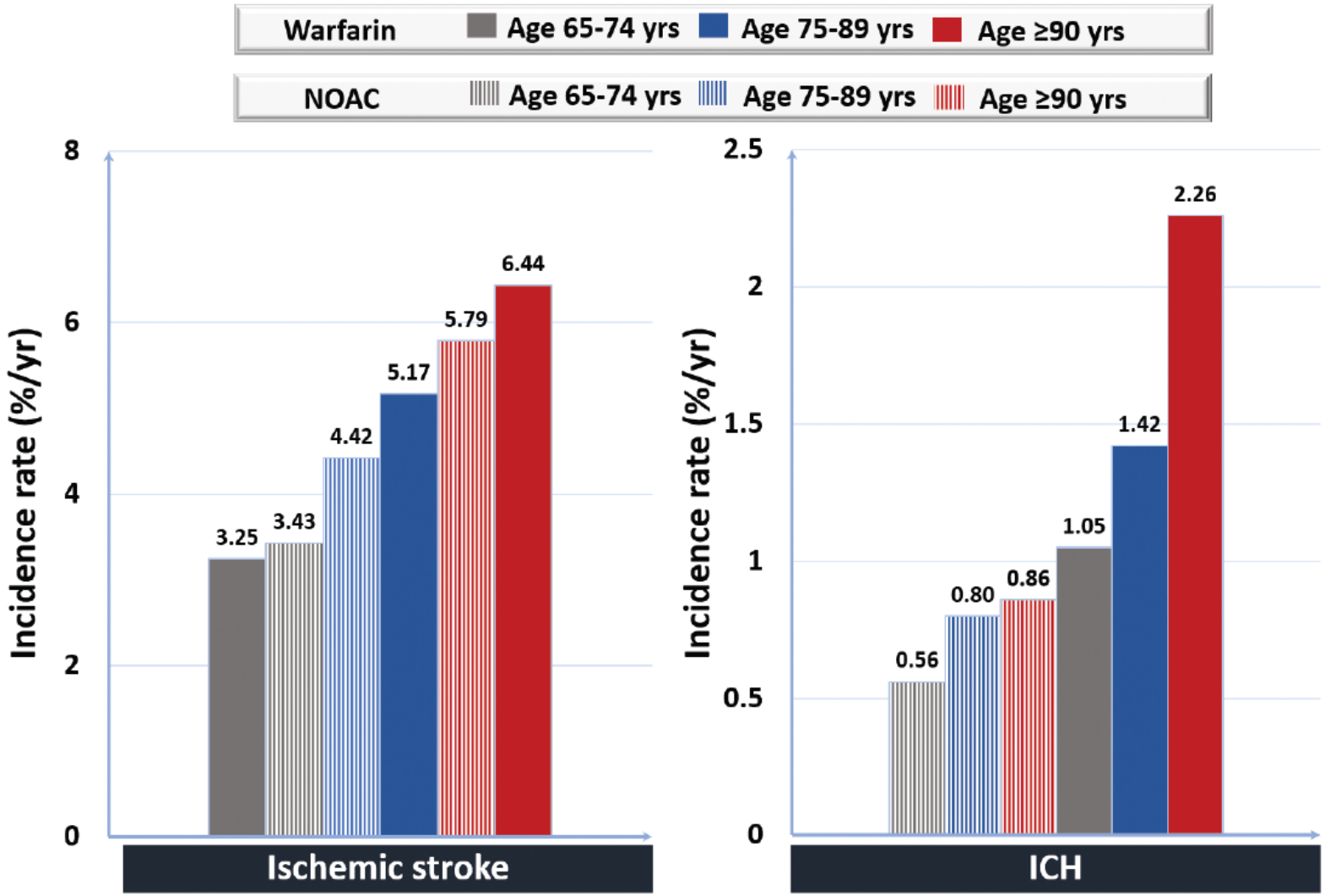
Figure 4. The differences of the risk of ICH between NOACs and warfarin in different age strata. The patterns of the associations between risk of ICH and age seem to be different for warfarin and NOACs. For warfarin, the risk of ICH increased in parallel to the increase in age, while the curve of ICH risk seemed to be relatively flat with NOACs when age increased. Therefore, the absolute risk reductions in ICH with NOACs, compared with warfarin, would be more evident in the elderly AF population. Data used in the figure were adapted from the papers by Chao et al. [10]

Optimal anticoagulation in elderly patients with atrial fibrillation: Which drug at which dose?

Jo-Nan Liao[1,2]*, Yi-Hsin Chan[3–5]*, Ling Kuo[1,2], Chuan-Tsai Tsai[1,2], Su-Shen Lim[1,2], Tze-Fan Chao[1,2]

Figure 2. Risks of major bleeding of NOACs compared to warfarin across different age strata in landmark RCTs. Sub-analyses from landmark trials demonstrated a lower (apixaban and edoxaban) or similar (dabigatran and rivaroxaban) risks of major bleeding with NOACs compared to warfarin for AF patients aged ≥75 years. Data used in the figure were adapted from the papers by Kato et al., Eikelboom et al., Halvorsen et al., and Goodman et al. [22–25].





Jo-Nan Liao et al., Anticoagulation in elderly AF patients

Comparative Safety and Effectiveness of Direct-Acting Oral Anticoagulants Versus Warfarin: a National Cohort Study of Nursing Home Residents

Matthew Alcusky, PharmD, PhD[1], Jennifer Tjia, MD, MS[1], David D. McManus, MD, ScM[1,2], Anne L. Hume, PharmD[3], Marc Fisher, MD[4], and Kate L. Lapane, PhD[1]

[1]Department of Population and Quantitative Health Sciences , University of Massachusetts Medical School, Worcester, MA, USA; [2]Department of Medicine, Division of Cardiovascular Medicine, University of Massachusetts Medical School, Worcester, MA, USA; [3]Department of Pharmacy Practice, College of Pharmacy, University of Rhode Island, Kingston, RI, USA; [4]Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA.

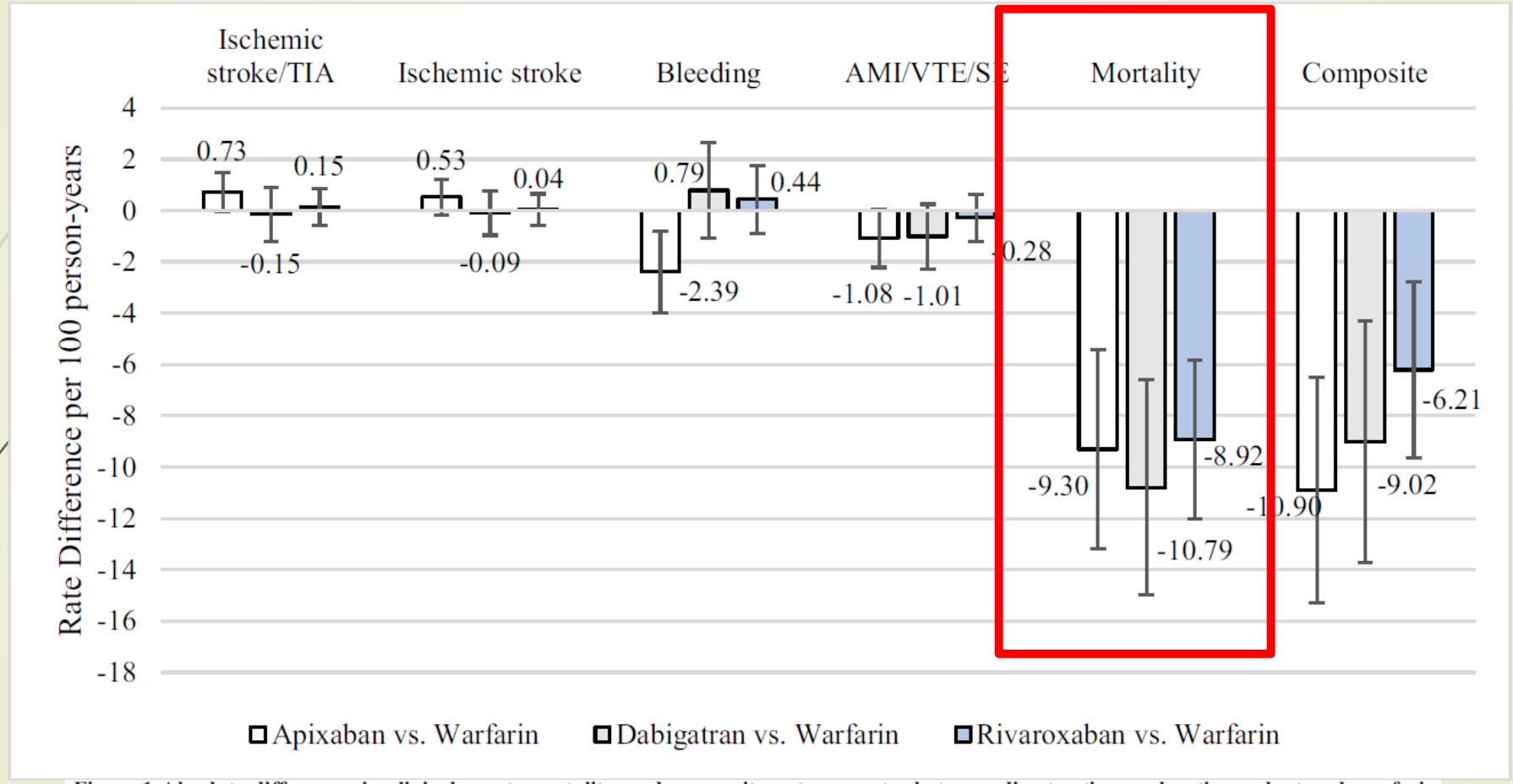
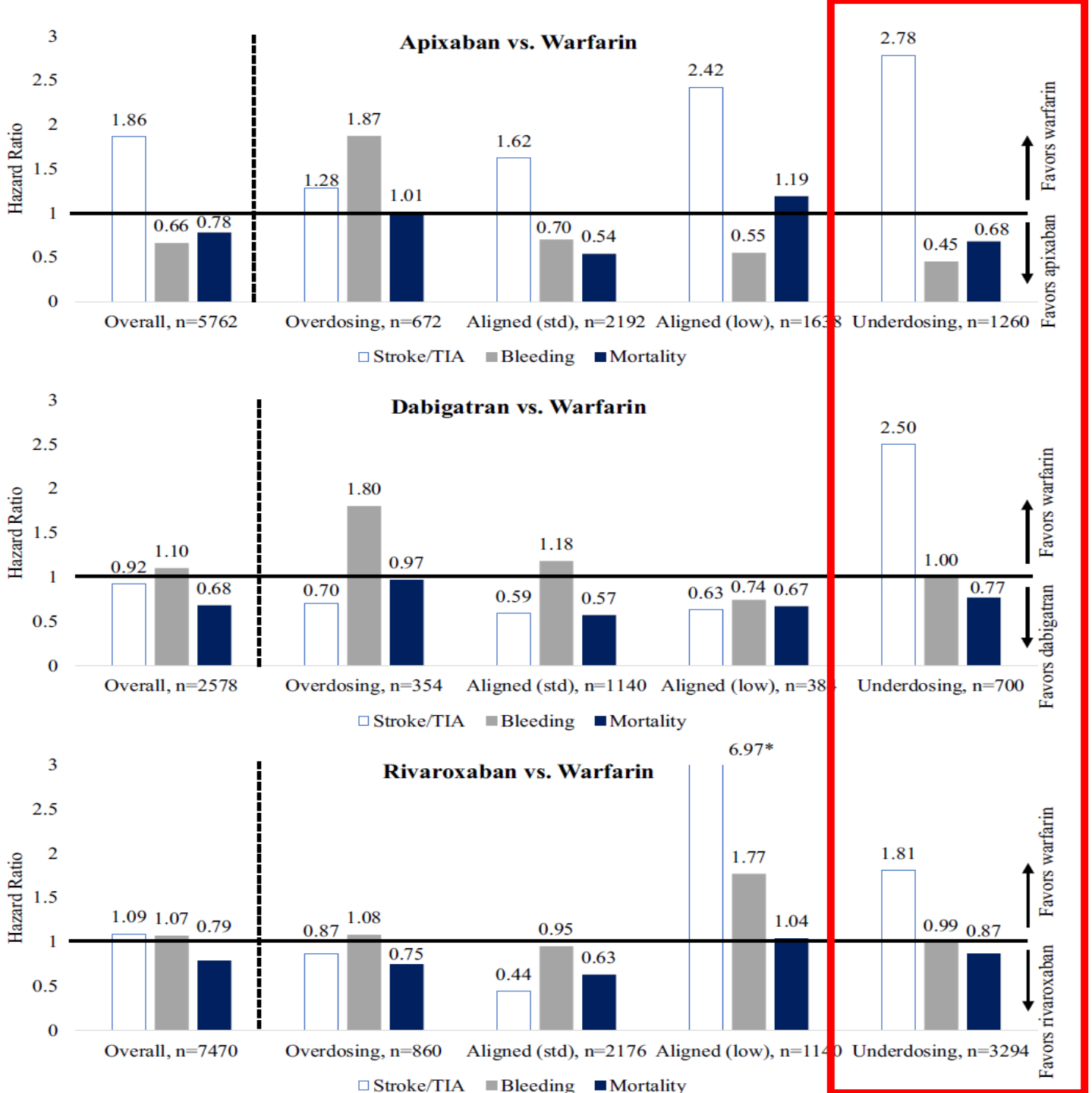


Figure 1 Absolute differences in clinical event, mortality, and composite outcome rates between direct-acting oral anticoagulant and warfarin users. TIA, transient ischemic attack; AMI, acute myocardial infarction; VTE, venous thromboembolism; SE, systemic embolism.



DOSAGGIO INAPPROPRIATO

- 33,5>% APIXABAN
- 40,9% DABIGATRAN
- 55,6% RIVAROXABAN

Alcusky et al.: Comparative safety and effectiveness of anticoagulants

Optimal anticoagulation in elderly patients with atrial fibrillation: Which drug at which dose?

Jo-Nan Liao[1,2]*, Yi-Hsin Chan[3–5]*, Ling Kuo[1,2], Chuan-Tsai Tsai[1,2], Su-Shen Lim[1,2], Tze-Fan Chao[1,2]

ESC European Society of Cardiology
European Heart Journal (2020) 42, 373–498
doi:10.1093/eurheartj/ehaa612

2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS)

Table 11 Dose selection criteria for NOACs

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Standard dose	150 mg b.i.d.	20 mg o.d.	5 mg b.i.d.	60 mg o.d.
Lower dose	110 mg b.i.d.			
Reduced dose		15 mg o.d.	2.5 mg b.i.d.	30 mg o.d.
Dose-reduction criteria	Dabigatran 110 mg b.i.d. in patients with: • Age ≥80 years • Concomitant use of verapamil, or • Increased bleeding risk	CrCl 15 - 49 mL/min	At least 2 of 3 criteria: • Age ≥80 years, • Body weight ≤60 kg, or • Serum creatinine ≥1.5 mg/dL (133 μmol/L)	If any of the following: • CrCl 15 - 50 mL/min, • Body weight ≤60 kg, • Concomitant use of dronedarone, ciclosporine, erythromycin, or ketoconazole

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Frailty and Clinical Outcomes of Direct Oral Anticoagulants versus Warfarin In a Cohort Study of Older Adults with Atrial Fibrillation

Dae Hyun Kim, MD, M
ScD[1,*], Lily G. Besset
Schneeweiss, MD, Sc

Drugs & Aging (2021) 38:713–723
https://doi.org/10.1007/s40266-021-00870-6

ORIGINAL RESEARCH ARTICLE

Impact of Fall Risk and Direct Oral Anticoagulant Treatment on Quality-Adjusted Life-Years in Older Adults with Atrial Fibrillation: A Markov Decision Analysis

Wenfei Wei[1] · Rafia S. Rasu[2] · José J. Hernández-Muñoz[1,3] · Renee J. Flores[4] · Nahid J. Rianon[5] · Genesis A. Hernández-Vizcarrondo[6] · Adam T. Brown[1,7]

Meta-Analysis of Direct-Acting Oral Anticoagulants Compared With Warfarin in Patients >75 Years of Age

Aaqib H. Malik, MD, MPH[a,*], Srikanth Yandrapalli, MD[b], Wilbert S. Aronow, MD[b], Julio A. Panza, MD[b], and Howard A. Cooper, MD[b]

JIM Original Article
doi: 10.1111/joim.13140

Oral anticoagulants for nonvalvular atrial fibrillation in frail elderly patients: insights from the ARISTOPHANES study

G. Y. H. Lip[1,2], A. V. Keshishian[3,4], A. L. Kang[5], A. D. Dhamane[5], X. Luo[6], X. Li[5], N. Balachander[5], L. Rosenblatt[5], J. Mardekian[7], X. Pan[5], M. Di Fusco[7], A. B. Garcia Reeves[5,8], H. Yuce[4] & S. Deitelzweig[9,10]

RESEARCH ARTICLE

Effectiveness and safety of oral anticoagulants in older adults with non-valvular atrial fibrillation and heart failure

Alpesh Amin[1]*, Alessandra B. Garcia Reeves[2,3], Xiaoyan Li[3], Amol Dhamane[3], Xuemei Luo[4], Manuela Di Fusco[5], Anagha Nadkarni[3], Keith Friend[3], Lisa Rosenblatt[3], Jack Mardekian[5], Xianying Pan[6], Huseyin Yuce[7], Allison Keshishian[7,8]

1 University of California, Irvine, California, United States of America, **2** University of North Carolina, Chapel Hill, North Carolina, United States of America, **3** Bristol-Myers Squibb Company, Lawrenceville, New Jersey, United States of America, **4** Pfizer, Inc., Groton, Connecticut, United States of America, **5** Pfizer Inc., New York, New York, United States of America, **6** Bristol-Myers Squibb Company, Wallingford, Connecticut, United States of America, **7** New York City College of Technology, City University of New York, New York, New York, United States of America, **8** SIMR, Inc, Ann Arbor, Michigan, United States of America

ESC European Society of Cardiology
European Heart Journal - Cardiovascular Pharmacotherapy (2021) **7**, f11–f19
doi:10.1093/ehjcvp/pvab002

ORIGINAL ARTICLE
Thrombosis and antithrombotic therapy

Real-world safety and efficacy of direct oral anticoagulants in atrial fibrillation: a systematic review and meta-analysis of 605 771 patients

Danilo Menichelli[1†], Francesco Del Sole[1†], Arianna Di Rocco[2†], Alessio Farcomeni[3], Annarita Vestri[2], Francesco Violi[1], Pasquale Pignatelli[1], Gregory Y.H. Lip[4,5†], and Daniele Pastori[1,4*‡]

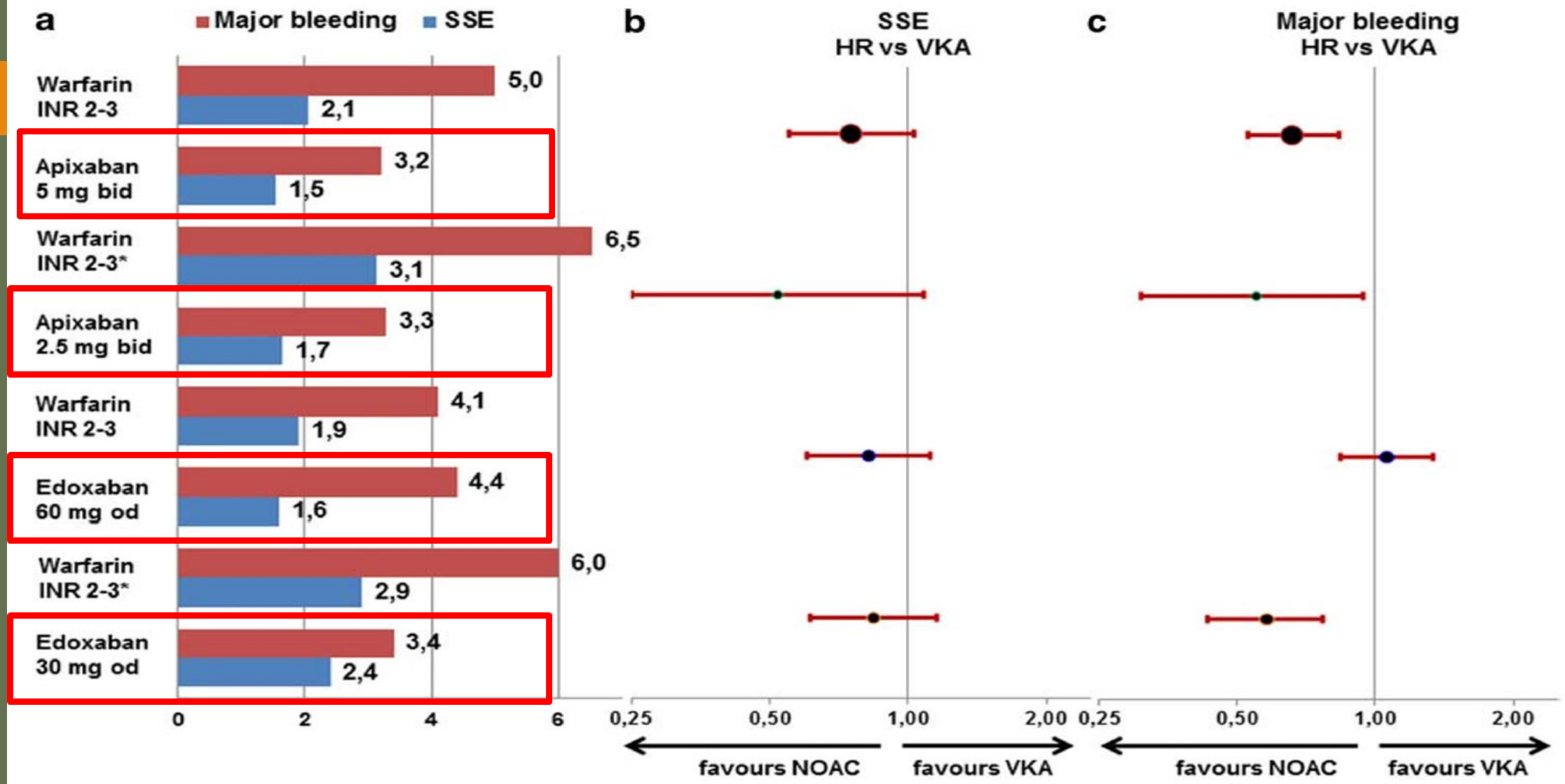
Cardiovascular Drugs and Therapy (2020) 34:555–568
https://doi.org/10.1007/s10557-020-06981-3

REVIEW ARTICLE

Anticoagulants for Stroke Prevention in Atrial Fibrillation in Elderly Patients

Andreas Schäfer[1] · Ulrike Flierl[1] · Dominik Berliner[1] · Johann Bauersachs[1]

Published online: 29 April 2020



HR vs VKA	Apixaban 5.0 mg bid	Apixaban 2.5 mg bid	Edoxaban 60 mg od	Edoxaban 30 mg od
SSE	0.75 (0.55-1.03)	0.52 (0.25-1.08)	0.82 (0.60-1.12)	0.84 (0.61-1.15)
Major bleeding	0.66 (0.53-0.83)	0.55 (0.31-0.94)	1.06 (0.84-1.33)	0.58 (0.43-0.77)

ESC European Society of Cardiology
European Heart Journal - Cardiovascular Pharmacotherapy (2021) 7, f11–f19
doi:10.1093/ehjcvp/pvab002
ORIGINAL ARTICLE
Thrombosis and antithrombotic therapy

Real-world safety and efficacy of direct oral anticoagulants in atrial fibrillation: a systematic review and meta-analysis of 605 771 patients

Table 3 Rankograms (%) values for treatments in bleeding (*A*) and ischaemic (*B*) outcomes

Panel A—safety endpoints				Panel B—efficacy endpoints			
Treatment	**First choice**	**Second choice**	**Third choice**	**Treatment**	**First choice**	**Second choice**	**Third choice**
Any bleeding				All-cause death			
Apixaban	65%	21%	15%	Apixaban	53%	32%	15%
Dabigatran	24%	46%	29%	Dabigatran	46%	52%	2%
Rivaroxaban	11%	33%	56%	Rivaroxaban	1%	16%	83%
Major bleeding				IS			
Apixaban	100%	0%	0%	Apixaban	97%	3%	0%
Dabigatran	0%	100%	0%	Dabigatran	0%	2%	98%
Rivaroxaban	0%	0%	100%	Rivaroxaban	3%	95%	2%
GI bleeding				IS-SE			
Apixaban	100%	0%	0%	Apixaban	96%	4%	1%
Dabigatran	0%	99%	1%	Dabigatran	3%	62%	35%
Rivaroxaban	0%	1%	99%	Rivaroxaban	1%	35%	64%
ICH				SE			
Apixaban	55%	41%	4%	Apixaban	61%	23%	16%
Dabigatran	44%	53%	2%	Dabigatran	12%	27%	61%
Rivaroxaban	1%	6%	94%	Rivaroxaban	27%	50%	23%
HS				Myocardial infarction			
Apixaban	48%	51%	1%	Apixaban	47%	17%	36%
Dabigatran	52%	45%	3%	Dabigatran	9%	36%	55%
Rivaroxaban	1%	4%	96%	Rivaroxaban	44%	47%	9%

GI, gastrointestinal; HS, haemorrhagic stroke; ICH, intracranial haemorrhage; IS, ischaemic stroke; SE, systemic embolism.

Apixaban associato a minori sanguinamenti maggiori e gastrointestinali rispetto a rivaroxaban ed al dabigatran

Apixaban e dabigatran minori emorragie intracraniche e minore stroke emorragico

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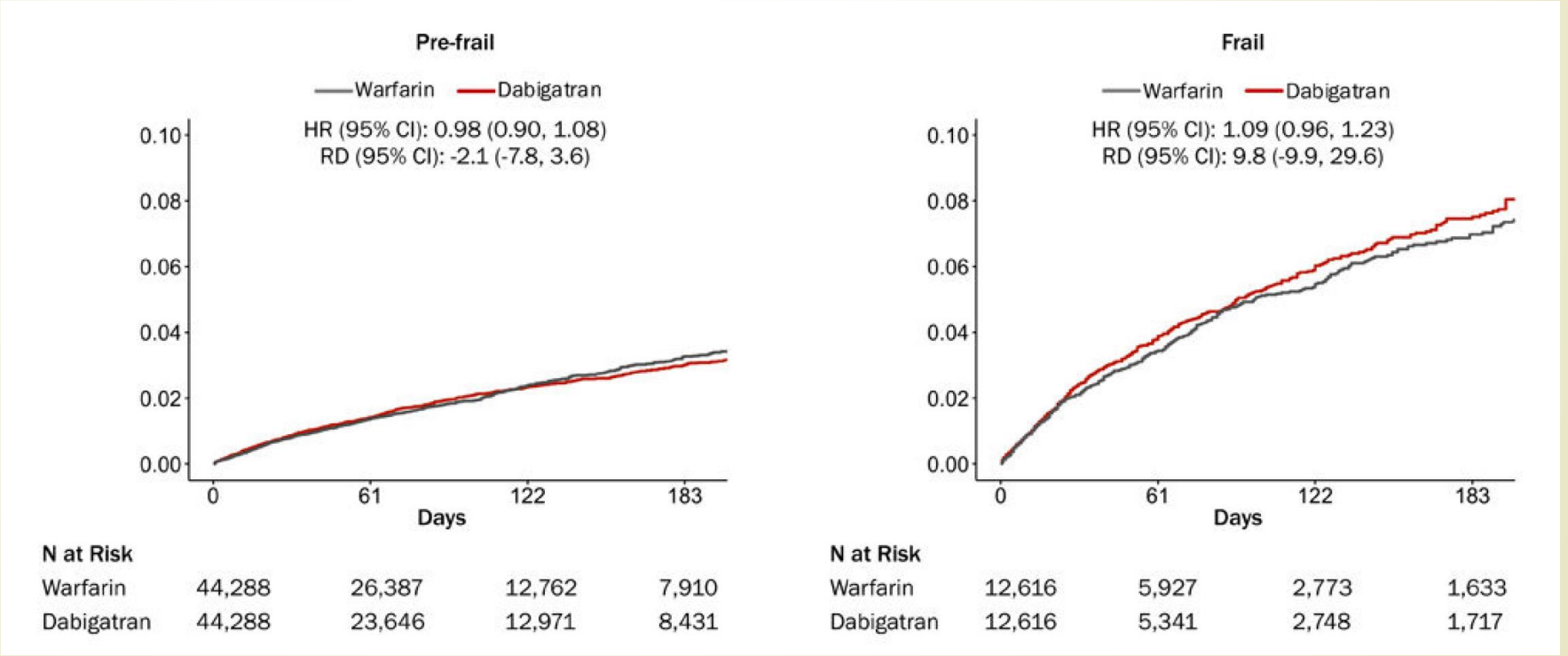
Frailty and Clinical Outcomes of Direct Oral Anticoagulants versus Warfarin In a Cohort Study of Older Adults with Atrial Fibrillation

Dae Hyun Kim, MD, MPH, ScD[1,2,3], Ajinkya Pawar, PhD[1,*], Joshua J. Gagne, PharmD, ScD[1,*], Lily G. Bessette, BS[1], Hemin Lee, MD, MPH[1], Robert J. Glynn, ScD, PhD[1], Sebastian Schneeweiss, MD, ScD[1]

- DABIGATRAN SIMILE EFFICACIA E SICUREZZA IN PAZIENTI PREFRAGILI O FRAGILI

Figure 1. Frailty and Cumulative Incidence Plots of a Composite Endpoint of Death, Ischemic Stroke, or Major Bleeding in Older Adults with Atrial Fibrillation Newly Treated with Direct Oral Anticoagulants vs Warfarin.



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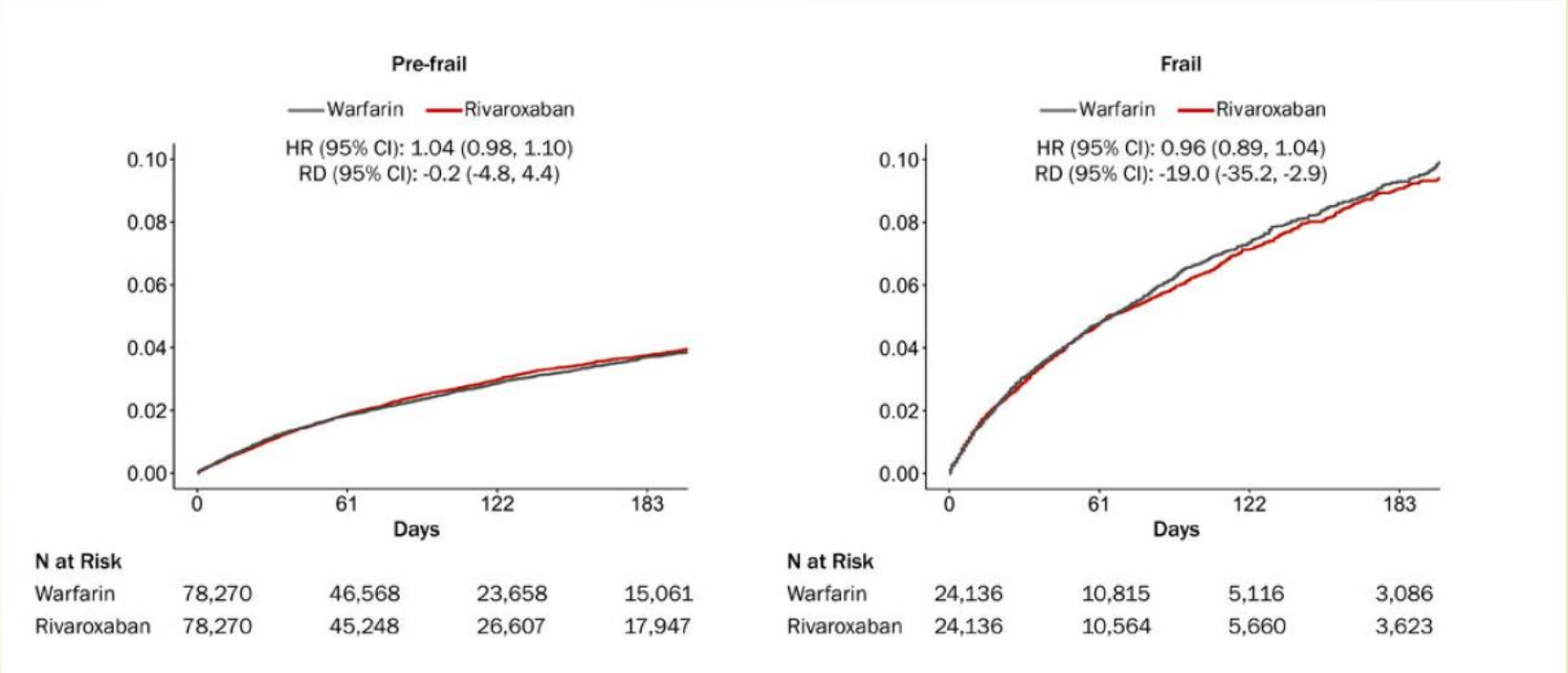
RIVAROXABAN RIDUCE IL RISCHIO ISCHEMICO MA AUMENTA IL RISCHIO DI SANGUINAMENTO



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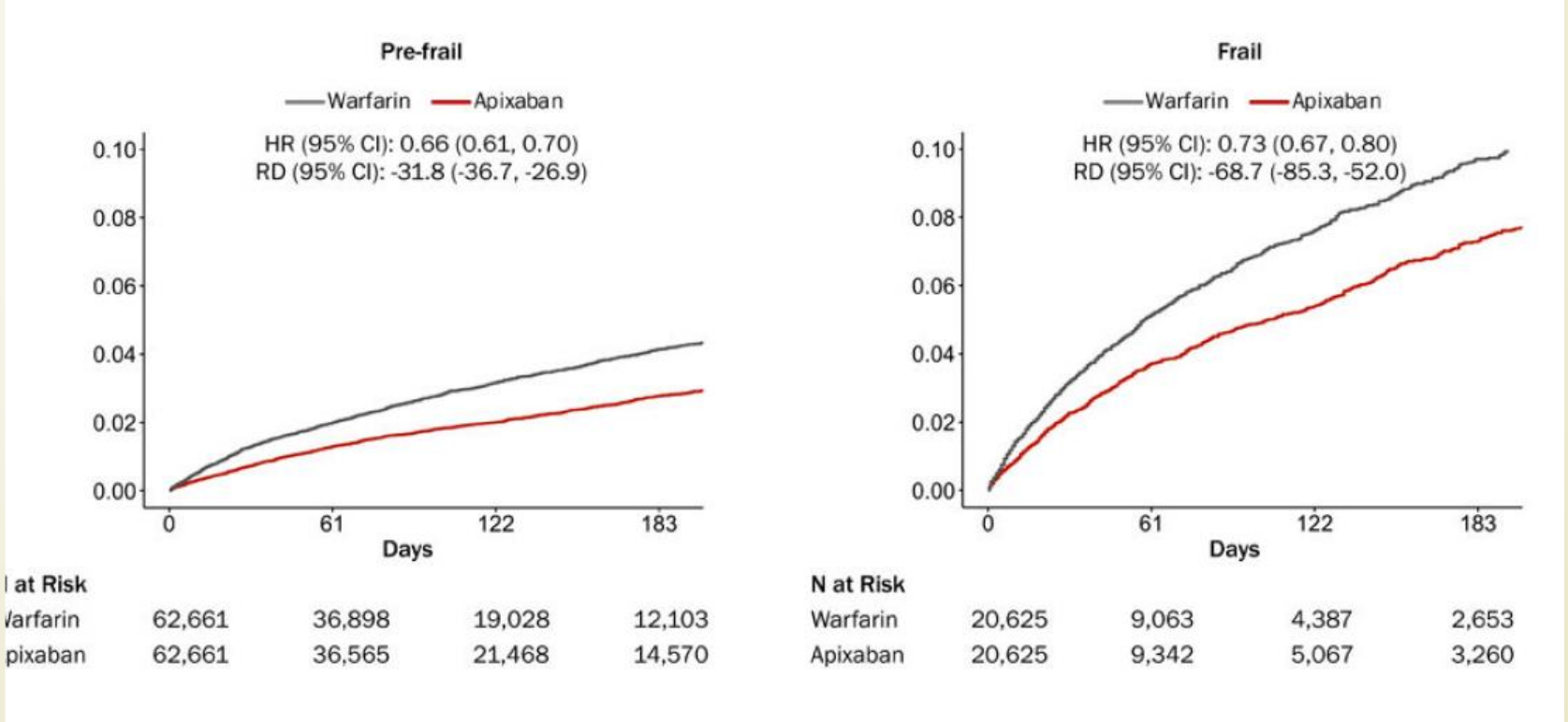
APIXABAN RIDUCE TUTTI GLI OUTCOME



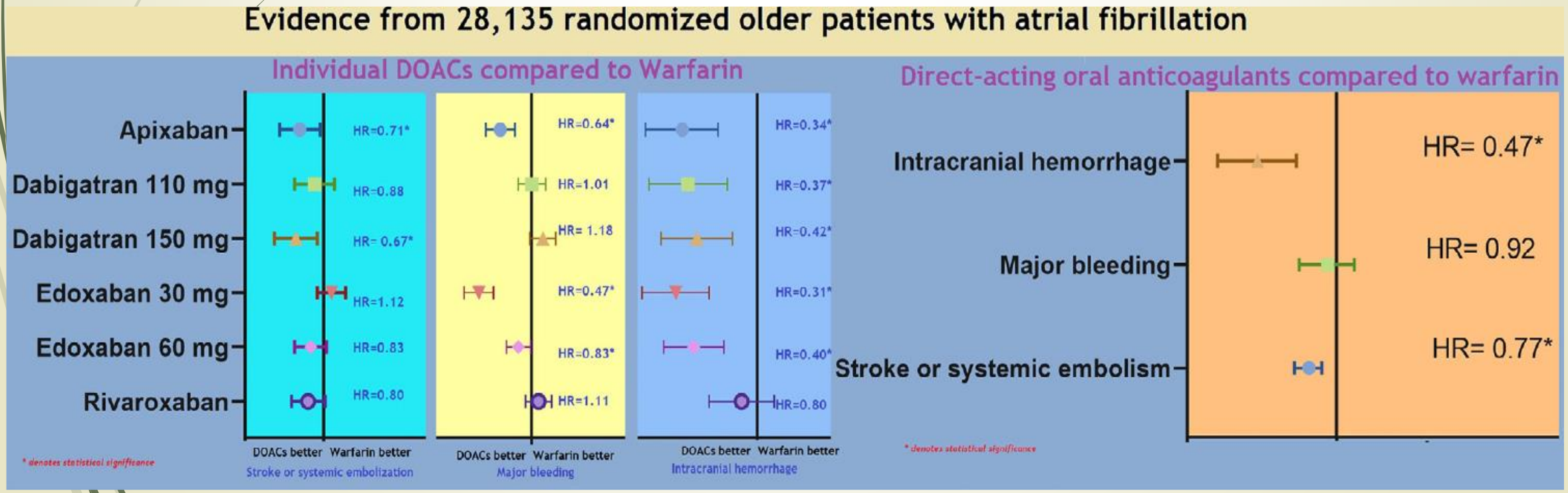
at Risk				
Warfarin	62,661	36,898	19,028	12,103
pixaban	62,661	36,565	21,468	14,570

N at Risk				
Warfarin	20,625	9,063	4,387	2,653
Apixaban	20,625	9,342	5,067	3,260

Meta-Analysis of Direct-Acting Oral Anticoagulants Compared With Warfarin in Patients >75 Years of Age

Aaqib H. Malik, MD, MPH[a,*], Srikanth Yandrapalli, MD[b], Wilbert S. Aronow, MD[b], Julio A. Panza, MD[b], and Howard A. Cooper, MD[b]

(Am J Cardiol 2019;123:2051–2057)



JIM Original Article

doi: 10.1111/joim.13140

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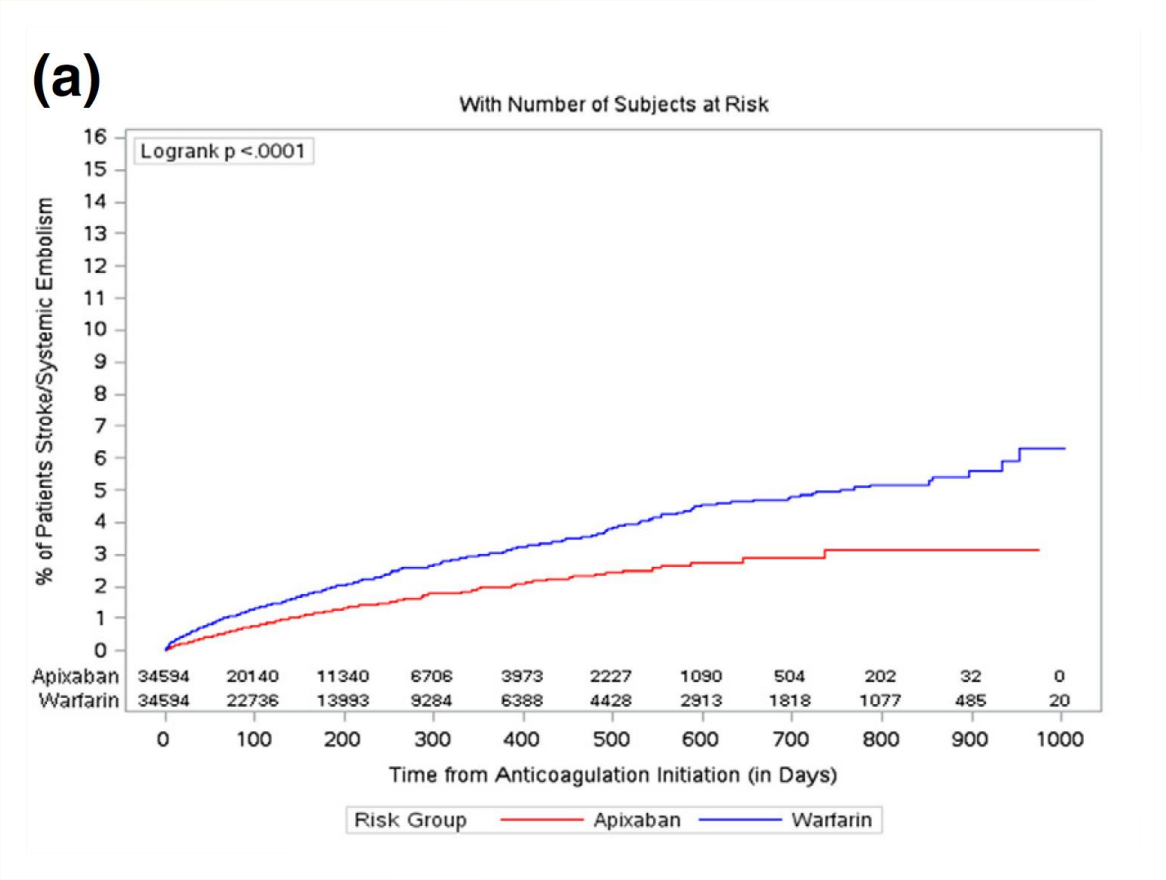
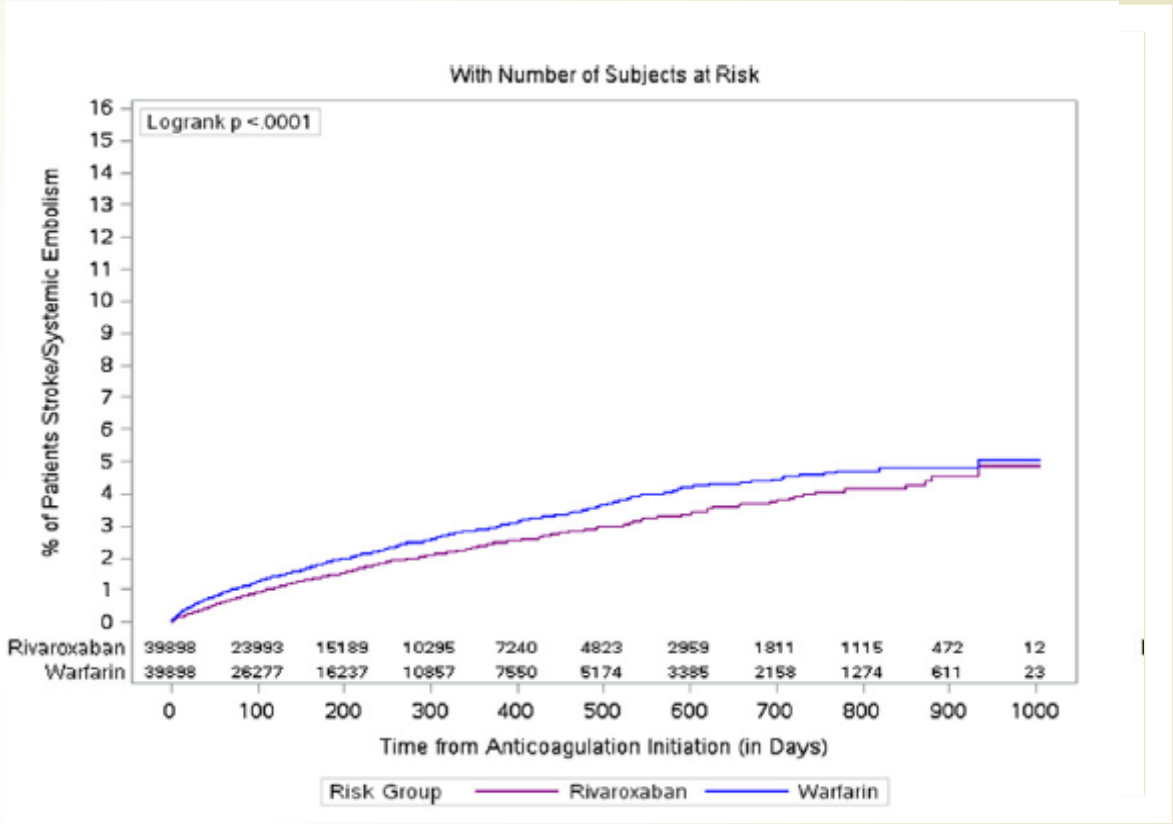
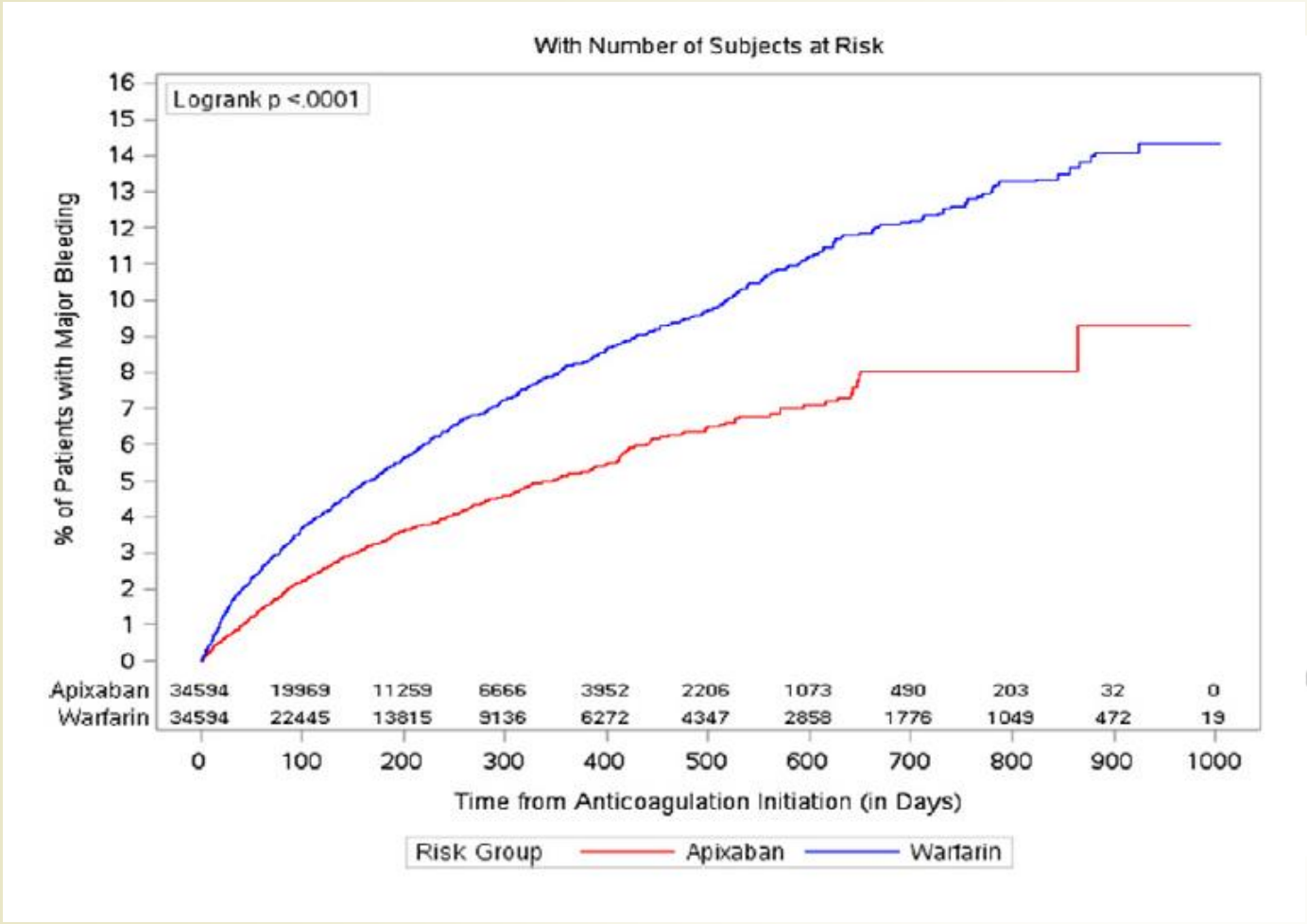
From the [1]Liverpool Centre for Cardiovascular Science, University of Liverpool and Liverpool Heart & Chest Hospital, Liverpool, UK; [2]Aalborg Thrombosis Research Unit, Department of Clinical Medicine, Aalborg University, Aalborg, Denmark; [3]STATinMED Research, Ann Arbor, MI; [4]New York City College of Technology (CUNY), New York, NY; [5]Bristol-Myers Squibb Company, Lawrenceville, NJ; [6]Pfizer, Inc., Groton, CT; [7]Pfizer, Inc., New York, NY; [8]University of North Carolina, Chapel Hill, NC; [9]Department of Hospital Medicine, Ochsner Clinic Foundation; and [10]Ochsner Clinical School, The University of Queensland School of Medicine, New Orleans, LA, USA

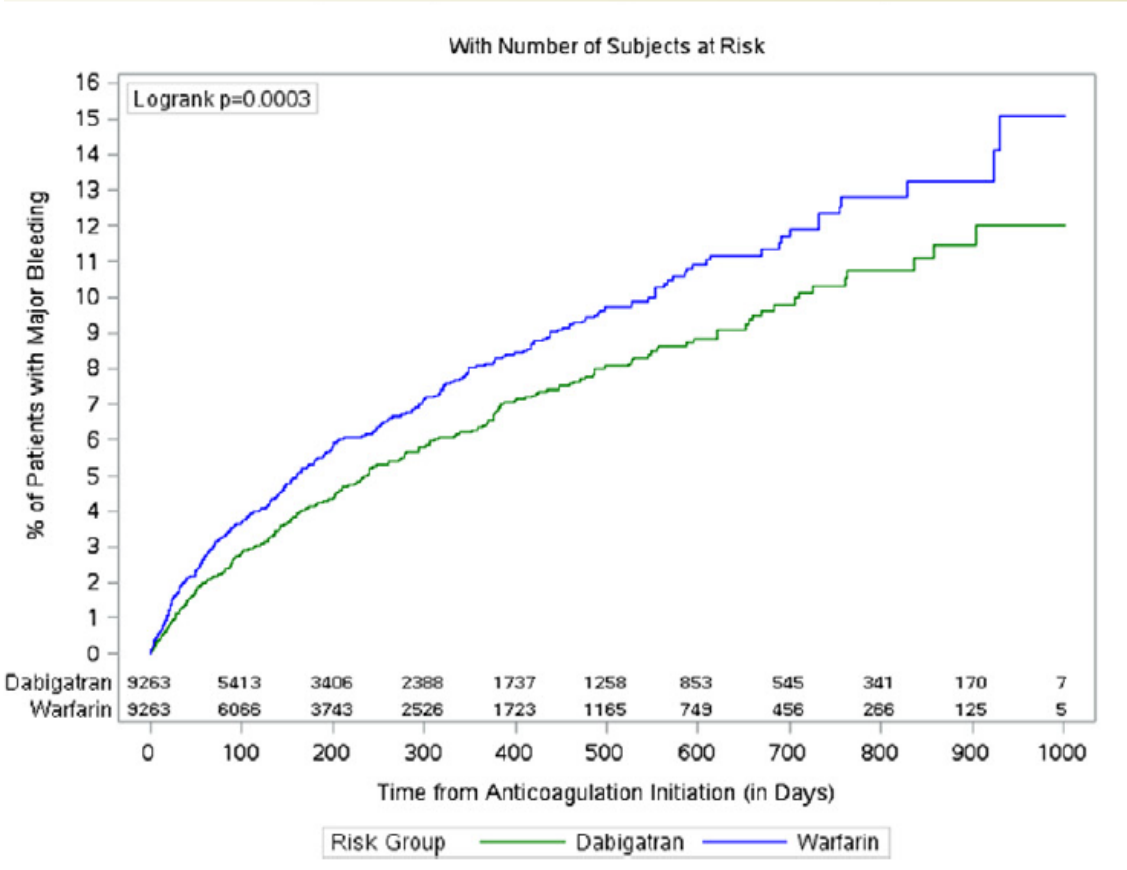
- Popolazione fragile dello studio ARISTOPHANES (34%)
- VKA vs NAO





APIXABAN E RIVAROXABAN ASSOCIATI A MINOR RISCHIO TROMBOEMOLICO RISPETTO AL WARFARIN





APIXABAN E DABIGATRAN ASSOCIATI A MINOR RISCHIO DI SANGUINAMENTO MAGGIORE RISPETTO AL WARFARIN

Journal of *Personalized Medicine*

MDPI

Viewpoint

Use and Prescription of Direct Oral Anticoagulants in Older and Frail Patients with Atrial Fibrillation: A Multidisciplinary Consensus Document

Marco Proietti [1,2,3], Marina Camera [4,5], Maurizio Gallieni [6,7], Luigi Gianturco [8], Antonio Gidaro [7], Carlo Piemontese [9], Giuseppe Pizzetti [10], Franco Redaelli [11], Barbara Scimeca [12], Carlo Sebastiano Tadeo [13], Matteo Cesari [1,2,†], Giuseppe Bellelli [14,15,†] and Laura Adelaide Dalla Vecchia [16,*,†]

Elderly AF patients (high risk of bleeding and stroke)

NOACs (preferred) or Warfarin

Sub-analysis from RCTs
- Lower risk of major bleeding (apixaban and edoxaban)

Real-world cohort studies
- Lower or similar risk of ischemic stroke for all NOACs
- Lower risk of ICH for all NOACs
- Similar or lower risk of major bleeding

Renal function
- Frequent monitoring
- Dose reduction criteria according to CG-derived eGFR

Adherence
- Related to altered cognitive function, depression, social isolation, adverse reaction to treatment, regimen complexity

Fragile features
- NOACs should still be considered based on shared-decision making
- Very low dose NOACs better than no treatment (ELDERCARE-AF)

Risk of falls
- History of falling increased risks of major bleeding, ICH, but not IS/SE and hemorrhagic stroke
- NOACs (preferred)

Polypharmacy
- Drug-drug interaction

Jo-Nan Liao et al., Anticoagulation in elderly AF patients

TAKE HOME MESSAGE

- I pazienti fragili con FA presentano plurime comorbilità che comportano un aumento del rischio ***sia tromboembolico sia di sanguinamento***

- ***La fragilità e le frequenti cadute non dovrebbero scoraggiare dalla prescrizione*** di anticoagulanti considerato il netto beneficio della terapia anticoagulante nella prevenzione dell'ictus.
- ***I NAO rispetto al warfarin*** hanno dimostrato un miglior profilo di efficacia (prevenzione rischio tromboembolico) e maggior profilo di sicurezza (riduzione del rischio emorragico), soprattutto se ***somministrati alla GIUSTA DOSE***.
- I pazienti fragili necessitano pertanto di una ***valutazione multidisciplinare*** che tenga conto delle interazioni farmacologiche, della funzione renale, delle comorbilità e delle capacità cognitive del paziente al fine di ridurre le complicanze e implementare l'aderenza terapeutica

- Non esistono studi comparativi diretti ma dalle metanalisi e dagli studi retrospettici apixaban ha dimostrato riduzione di tutti gli outcome nel mondo reale in tale popolazione