

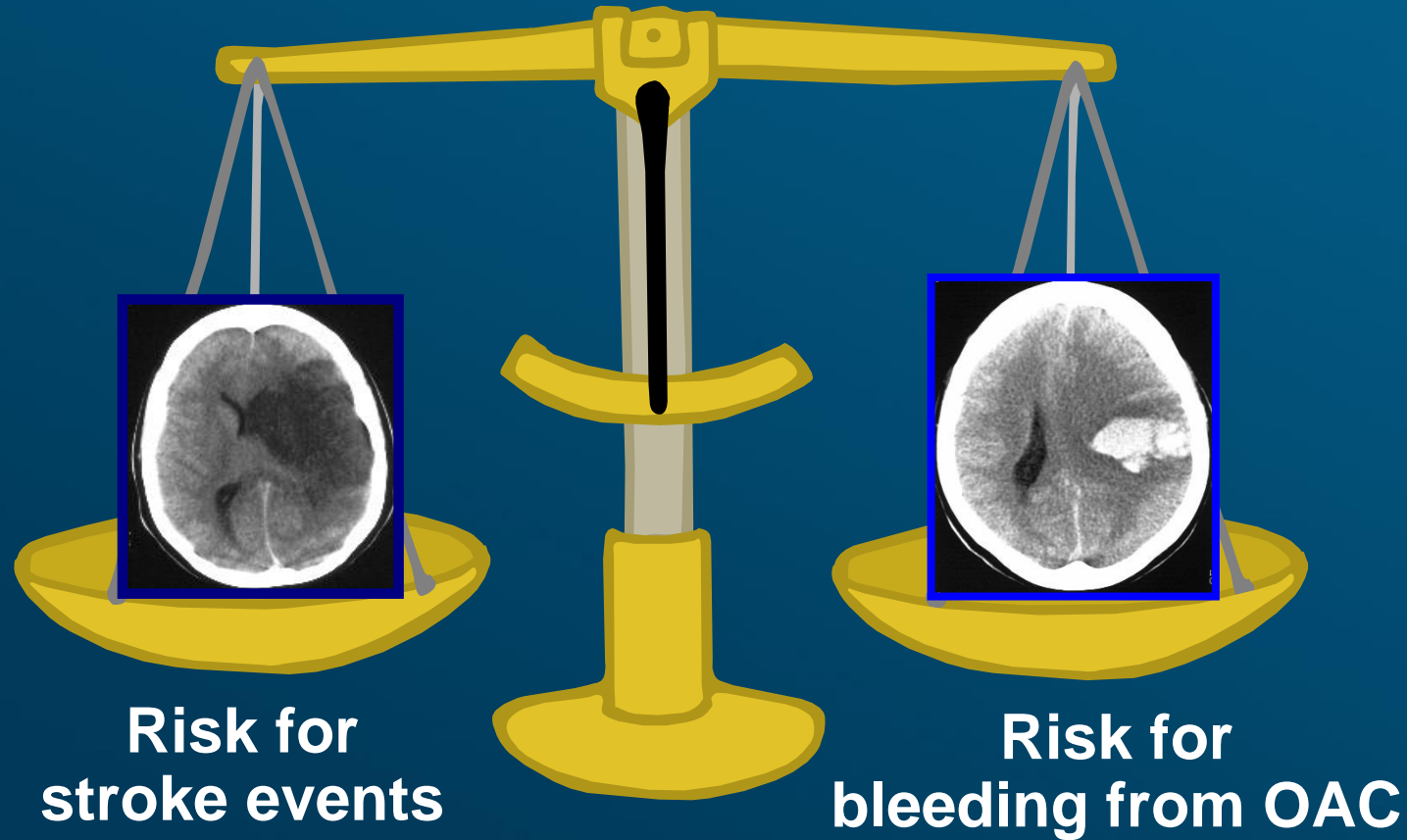
ANTICOAGULATION IN SPAF THE REAL-WORLD DATA

A Sukonthasarn MD. FACP. M FRCP

Professor of Cardiovascular Medicine

**Head of Internal Medicine & Cardiovascular Unit
Deputy Hospital Director @ Bangkok Hospital Chiang Mai**

The **AF** Dilemma



Differences between RCTs and RWD

RCTs

- Optimal for detecting AEs and evaluating outcomes
- Well-characterized cohort and minimal missing data
- Higher cost and complexity
- Limited representativeness

RWDs

- Less reliability of data due to bias and confounders
- Broader representative samples with incomplete & inaccurate data
- Inexpensive
- Provide new insights in a broader groups and confirm RCTs findings

The advantage of RWD



Broader representative samples¹



Data from routine care¹



Less expensive¹



Provide insights beyond those addressed by RCTs²

The French National Health System Claims data

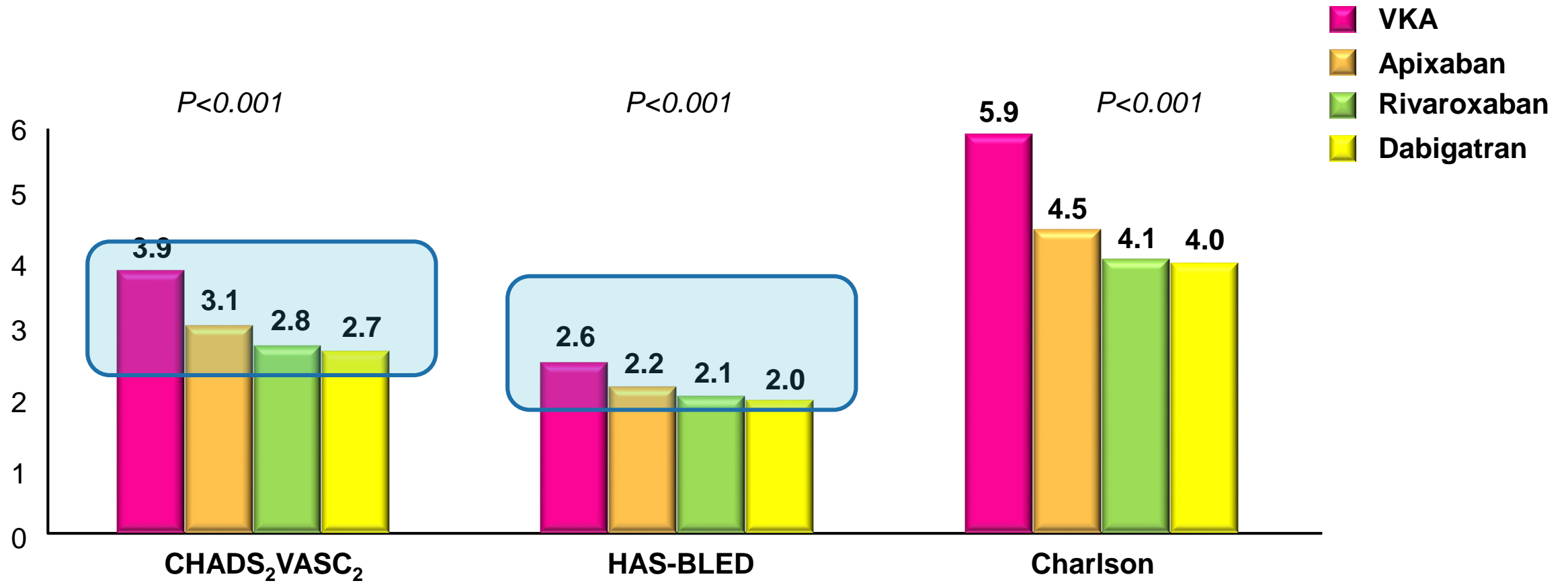


- ◆ France (population 66 million) has nearly universal health coverage
- ◆ The National Health System* claims data cover >90% of the population
- ◆ The NHS claims data collects information about demographics, medical history, hospital admissions, procedures and diagnoses, treatments, outpatient reimbursements and mortality

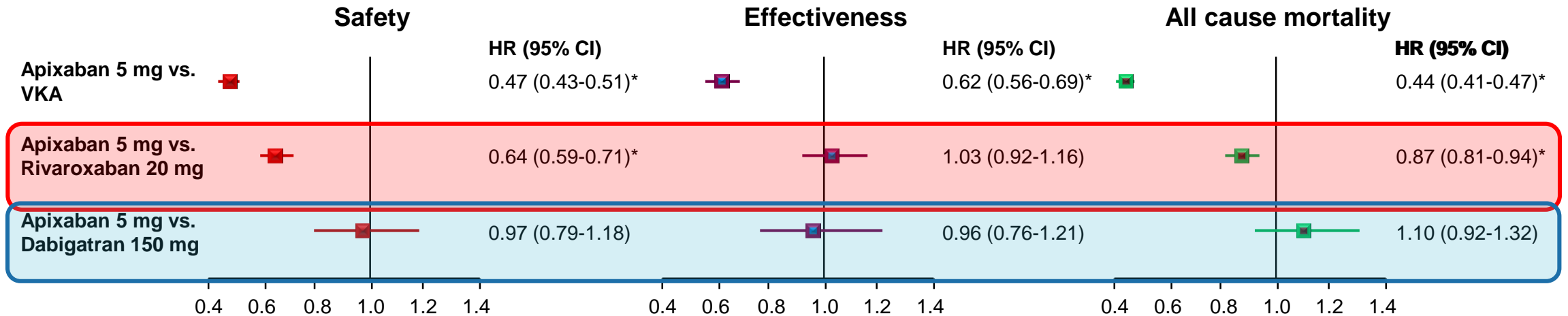
N=321,501

NAXOS

Risk Scores



Comparative safety and effectiveness (propensity score adjusted comparison)



Major bleeding events leading to hospitalization

Stroke and systemic thromboembolism



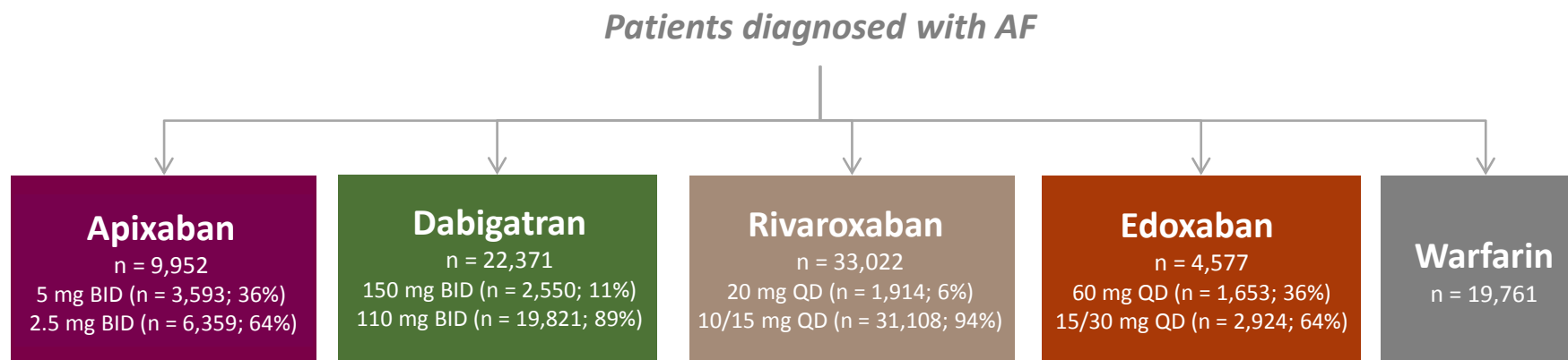
Effectiveness and Safety of Four Direct Oral Anticoagulants in Asian Patients With Nonvalvular Atrial Fibrillation

Chan YH, et al. Chest. 2019

Study design and endpoints



Nationwide retrospective cohort study based on data from Taiwan's NHIRD
To investigate the outcomes associated with four DOACs vs warfarin among Asian patients with NVAF.

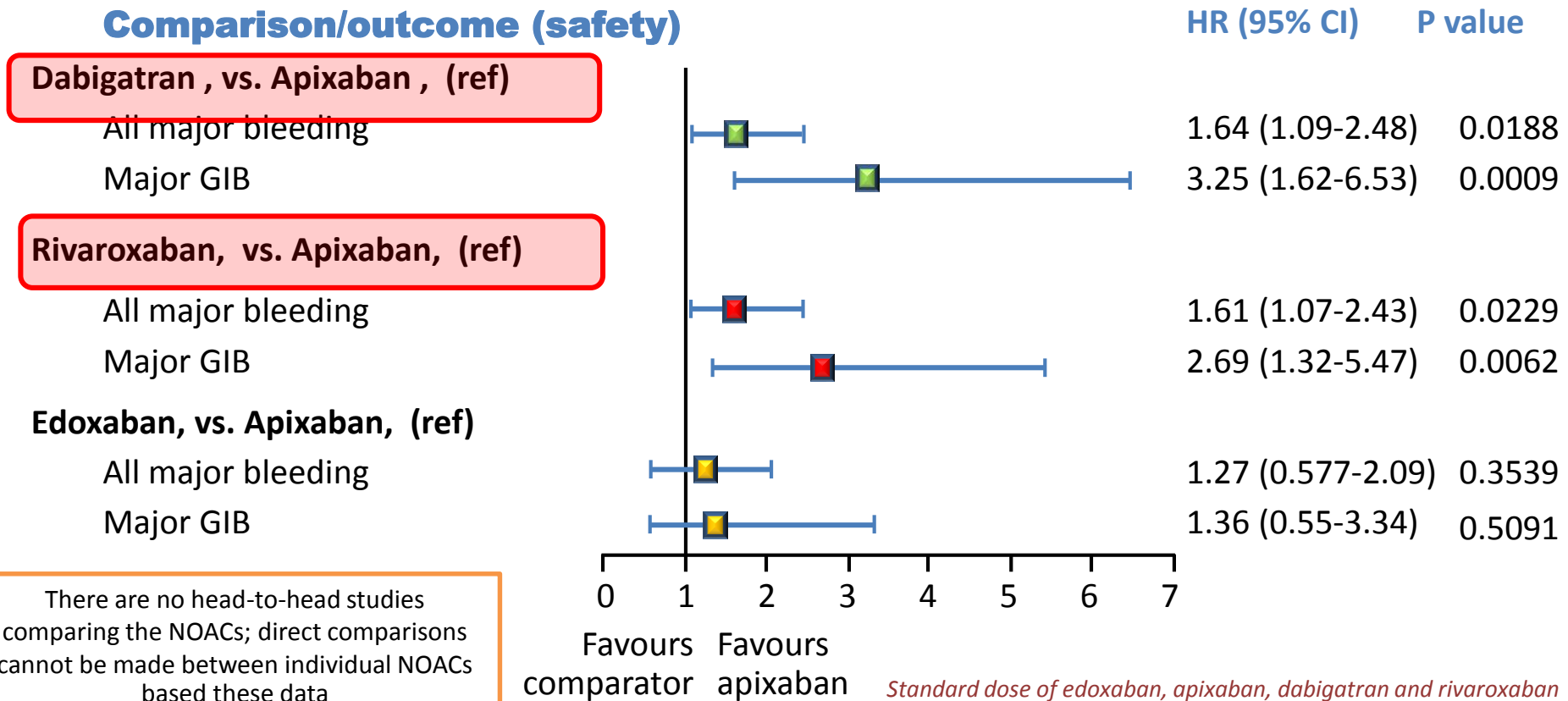


Endpoint:

- IS/SE
- AMI
- ICH
- Major GIB
- Fatal bleeding
- All major bleeding

Taiwan database: Safety outcomes - NOACs vs NOACs

Edoxaban, rivaroxaban and dabigatran showed a comparable risk of IS/SE: or other thromboembolic events with apixaban



HR, hazard ratio

Chan YH, et al. Chest 2019;doi:10.1016/j.chest.2019.04.108.

Standard dose of edoxaban, apixaban, dabigatran and rivaroxaban used in 36%, 36%, 11% and 6% of patients, respectively (post-PSM). Standard (reduced) NOAC doses: edoxaban 60 mg OD (30/15 mg OD), apixaban 5 mg BID (2.5 mg BI), rivaroxaban 20 mg OD (15/10 mg OD), dabigatran 150 mg BID (110 mg BID).

openheart Safety and effectiveness of non-vitamin K oral anticoagulants versus warfarin in real-world patients with non-valvular atrial fibrillation: a retrospective analysis of contemporary Japanese administrative claims data

Shun Kohsaka,¹ Jun Katada ,² Kumiko Saito,³ Aaron Jenkins,⁴ Benjamin Li,⁵ Jack Mardekian,⁵ Yasuo Terayama⁶

Patients eligible for the analysis
(N=73,989)

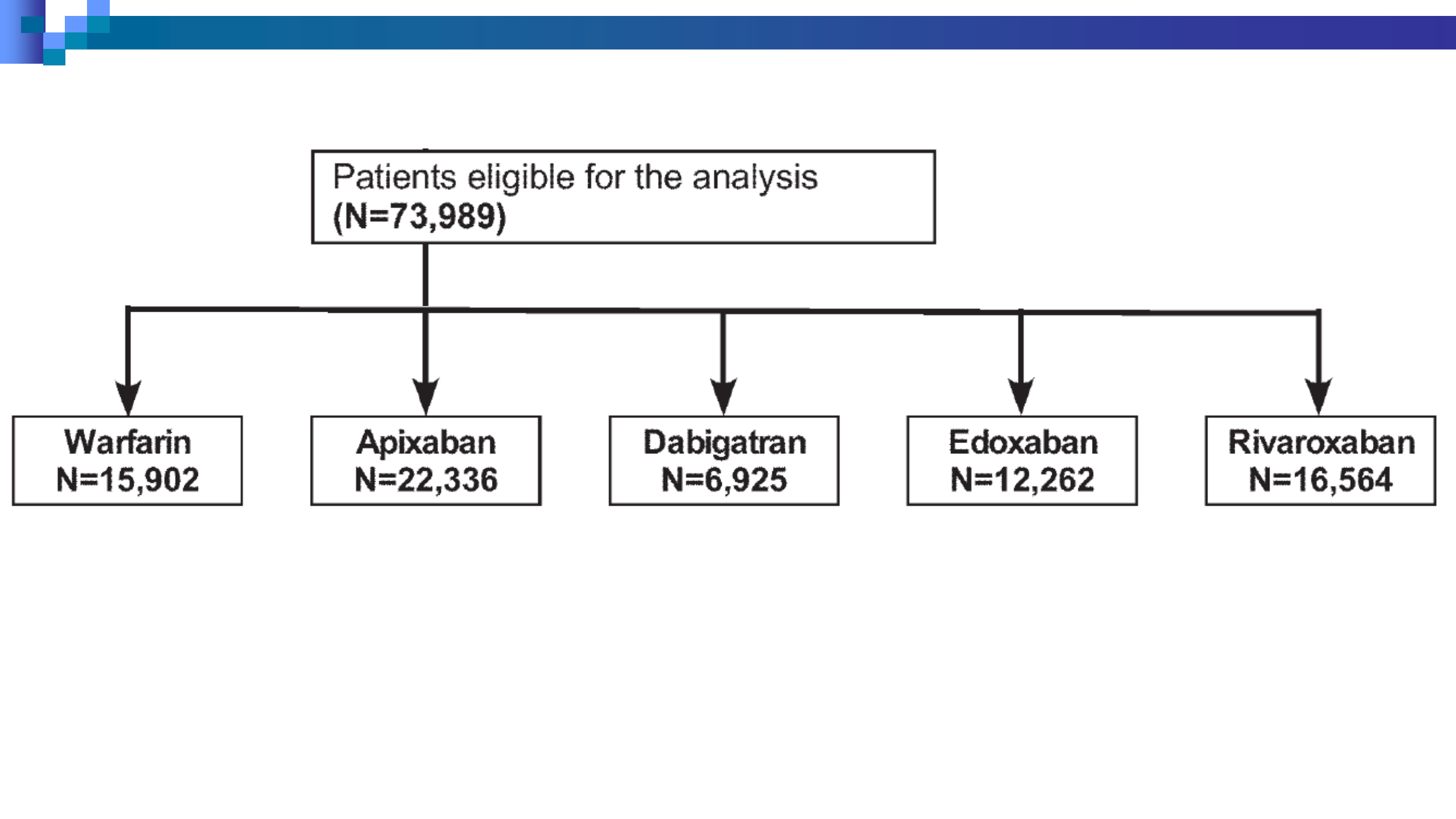
Warfarin
N=15,902

Apixaban
N=22,336

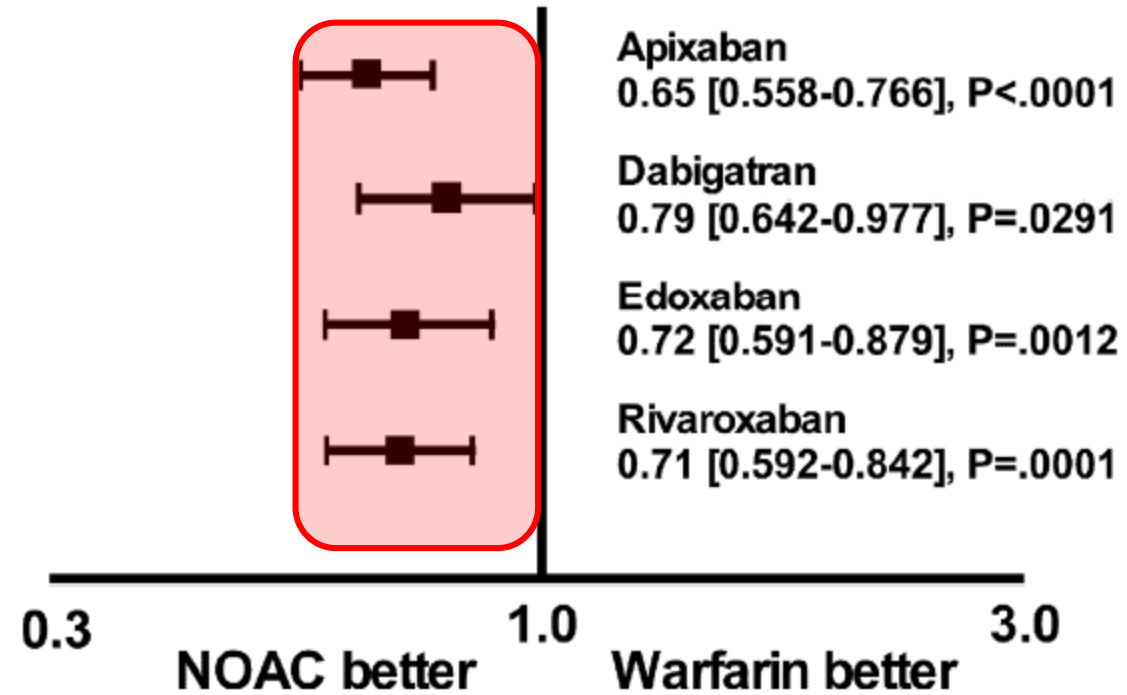
Dabigatran
N=6,925

Edoxaban
N=12,262

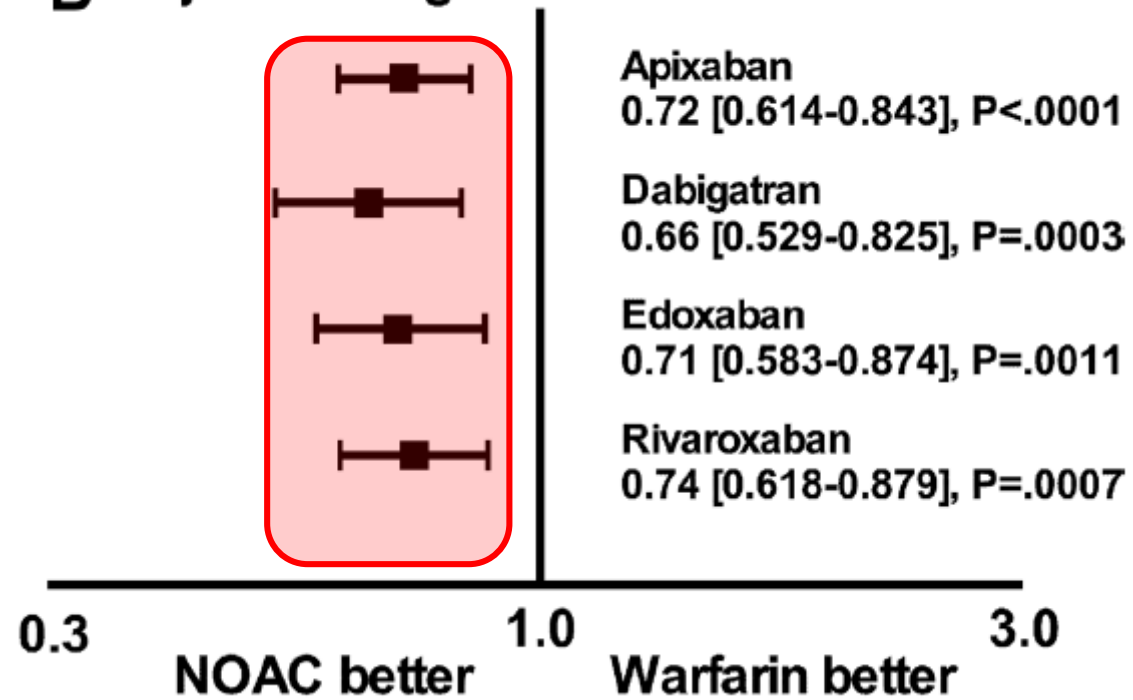
Rivaroxaban
N=16,564



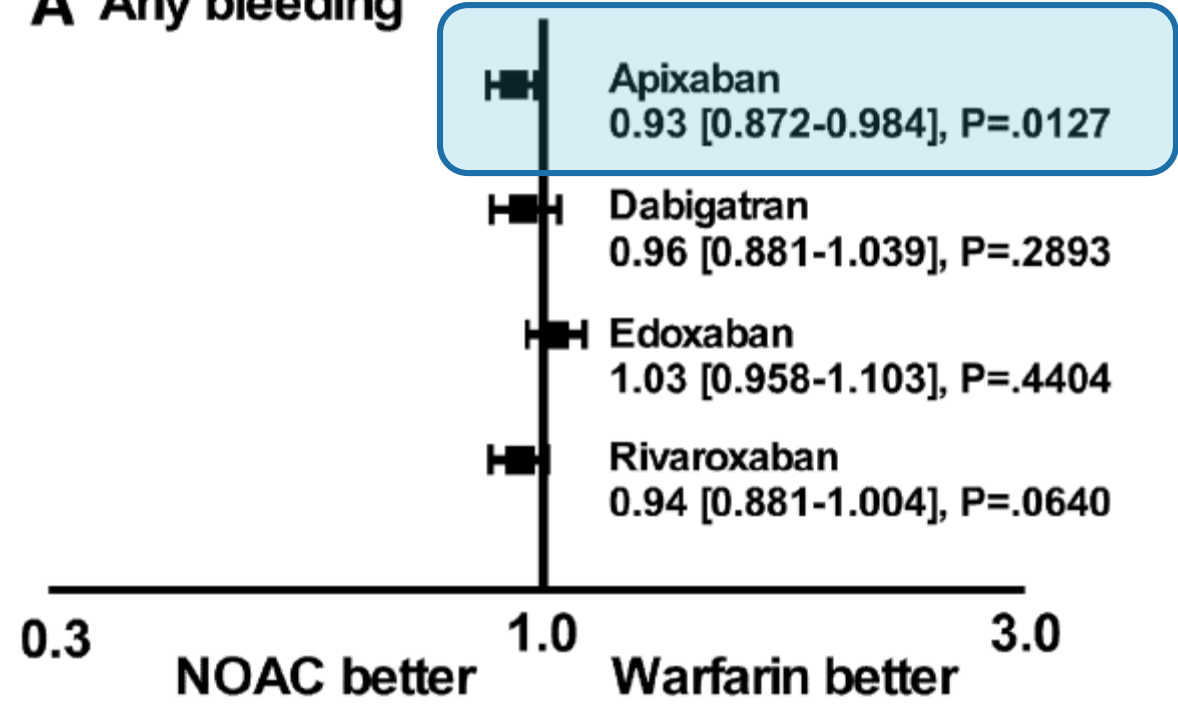
C Stroke/SE



B Major bleeding



A Any bleeding





Effectiveness and safety of contemporary oral anticoagulants among Asians with nonvalvular atrial fibrillation

Lee SR, et al. Stroke. 2019

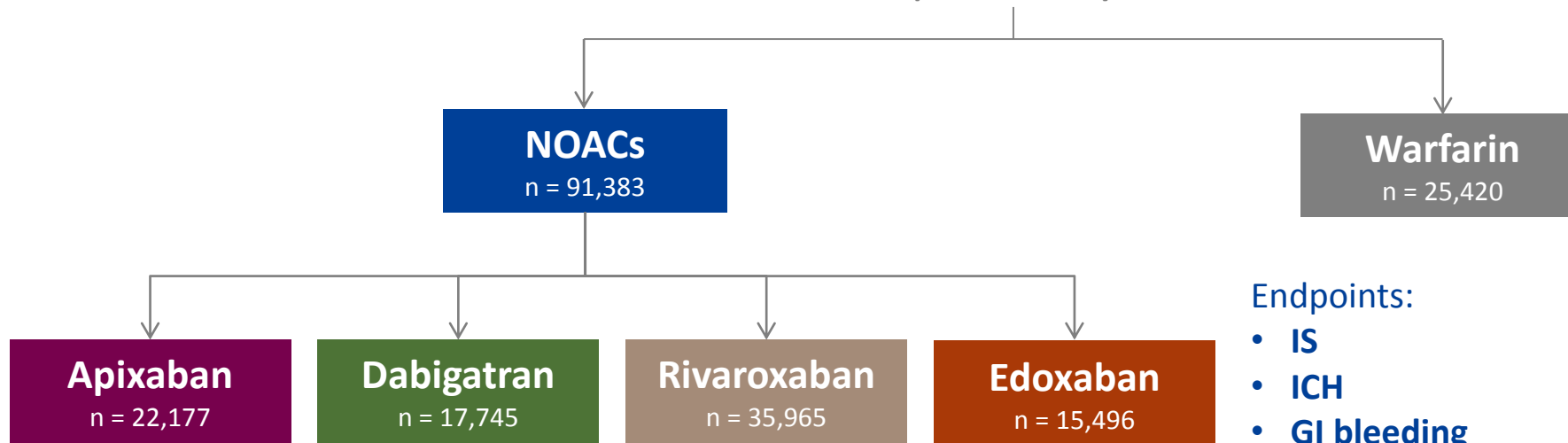
Study design and endpoints



Retrospective nonrandomized observational cohort study

To evaluate the comparative effectiveness and safety of warfarin and 4 NOACs.

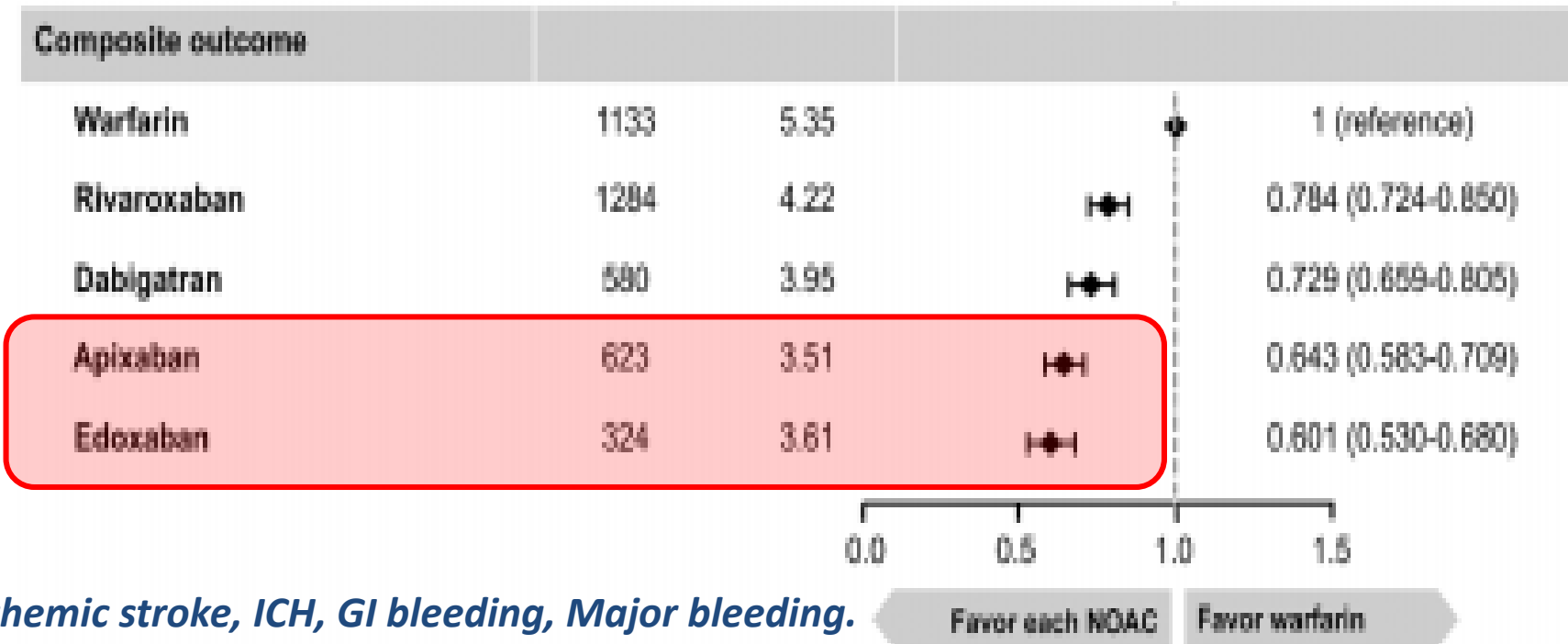
Oral anticoagulant naïve patients with NVAF
(n = 116,804)



Endpoints:

- IS
- ICH
- GI bleeding
- Major bleeding
- Composite clinical outcome

Hazard Ratio of Composite Outcome* in Warfarin vs Each NOAC



Lee SR, et al. Stroke. 2019;50:2245-9

Real-World Comparative Effectiveness and Safety of Non-vitamin K Antagonist Oral Anticoagulants versus Warfarin in a Developing Country

Phatcharin Mitsuntisuk, BS, BCP¹, Surakit Nathisuwan, PharmD, BCPS², Athirat Junpanichjaroen, PharmD¹, Wanwarang Wongcharoen, MD³, Arintaya Phrommintikul, MD³, Phannita

Wattanaruengchai, BS, BCP⁴, Wipharak Rattanaivanon, BS, BCP², Suvatna Chulavatnatol, PhD²,

Nathorn Chaiyakunapruk, PharmD, PhD⁵, Khanchit Likittanasombat, MD⁶, Gregory Y. H. Lip, MD,

FRCP, DFM, FACC, FESC⁷

Clin Pharm Ther 2020. doi:10.1002/CPT.2090

Apixaban was chosen for Thai Patients with highest stroke/SE & highest bleeding risk

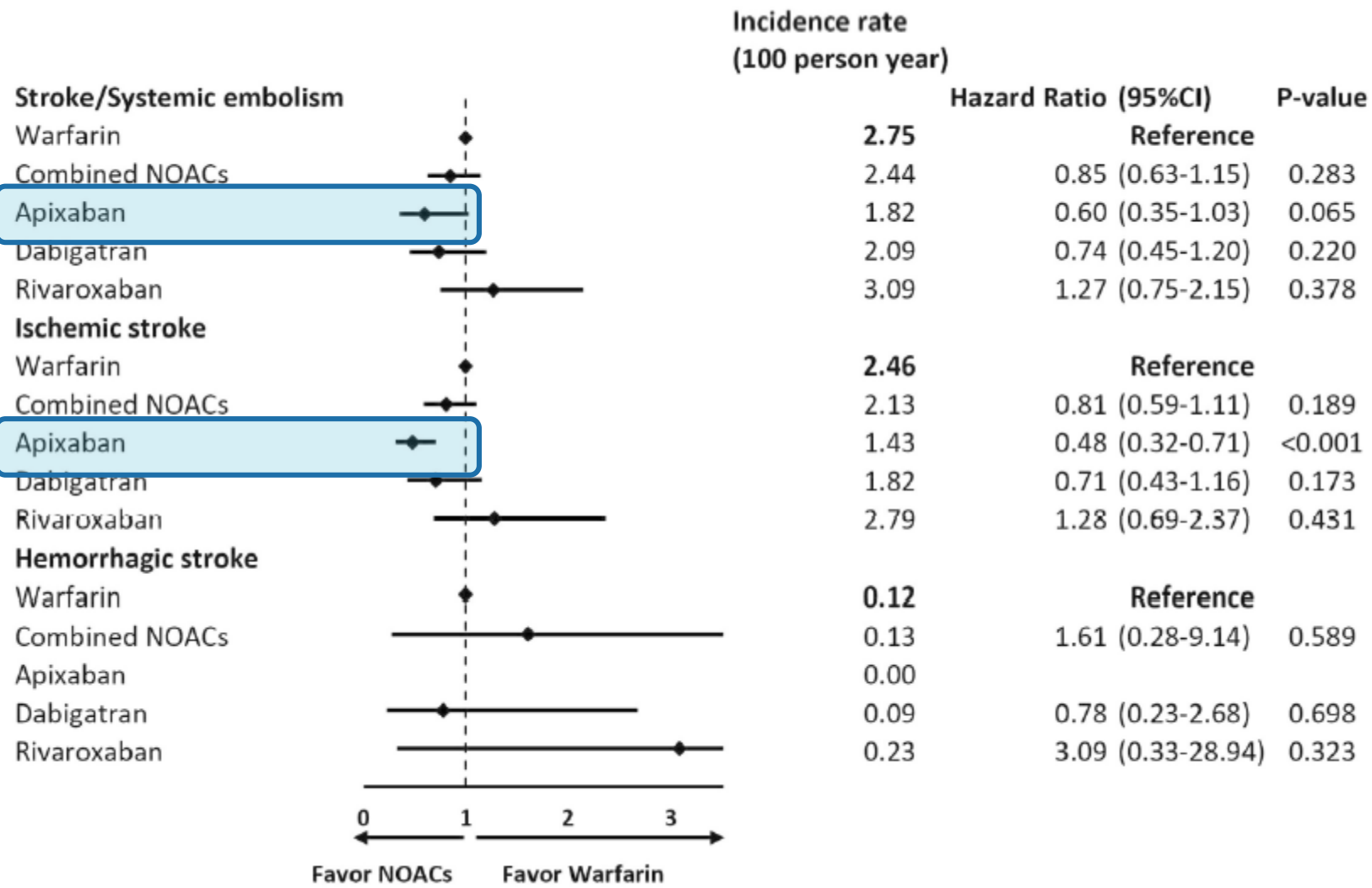
Table 1 Baseline characteristics of study population by type of oral anticoagulants.

Baseline Characteristics	Warfarin (N=605)	Apixaban (N=405)	Dabigatran (N=441)	Rivaroxaban (N=604)	p-value	Adjusted p-value ^a
Age, mean + SD in years	68.40 + 11.40	73.89 + 10.24	70.26 + 11.04	71.12 + 10.84	0.0001	0.7537
Female, n (%)	304 (50.25)	201 (49.63)	205 (46.49)	293 (48.51)	0.663	-
Weight, mean + SD in kgs	65.26 + 14.57	63.30 + 14.39	66.32 + 14.43	65.25 + 13.39	0.0194	0.6310
Follow-up, mean + SD in years	2.82+1.89	1.90+0.97	2.50+1.41	2.19+1.32	0.0001	-
CHA ₂ DS ₂ -VASc score, mean + SD	3.28 + 1.75	3.86 + 1.72	3.25 + 1.74	3.28 + 1.72	0.0001	-
SAMe-TT2R2 score, mean + SD	2.93 + 0.81	2.82 + 0.79	2.82 + 0.79	2.81 + 0.74	0.0257	-
HAS-BLED score, mean + SD	1.27 + 0.91	1.65 + 1.00	1.59 + 1.05	1.39 + 1.00	0.0001	-
Previous ICH	0 (0.00)	7 (1.73)	4 (0.91)	8 (1.32)	0.023	-
Previous GI bleeding	8 (1.32)	29 (7.16)	12 (2.72)	19 (3.15)	0.0001	0.7033

Apixaban related to lowest incidence of stroke & low bleeding risk

Table 2. Primary outcomes and net adverse clinical events (NACE) of warfarin users versus NOACs users

Event	Warfarin (N=605)	Combined NOACs (N=1,450)			Apixaban (N=405)			Dabigatran (N=441)			Rivaroxaban (N=604)		
	Event (Incidence Rate*)	Event (Incidence Rate*)	Adjusted HR (95%CI)	p-value	Event (Incidence Rate*)	Adjusted HR (95%CI)	p-value	Event (Incidence rate*)	Adjusted HR (95%CI)	p-value	Event (Incidence Rate*)	Adjusted HR (95%CI)	p-value
NACE	146 (8.55)	186 (5.82)	0.57 (0.45-0.73)	<0.001	41 (5.33)	0.48 (0.35-0.67)	<0.001	43 (3.90)	0.43 (0.28-0.65)	<0.001	102 (7.69)	0.82 (0.62-1.09)	0.171
Stroke/SE	47 (2.75)	78 (2.44)	0.85 (0.63-1.15)	0.283	14 (1.82)	0.60 (0.35-1.03)	0.065	23 (2.09)	0.74 (0.45-1.20)	0.220	41 (3.09)	1.27 (0.75-2.15)	0.378
Stroke	44 (2.58)	72 (2.25)	0.84 (0.62-1.13)	0.240	11 (1.43)	0.48 (0.33-0.68)	<0.001	21 (1.91)	0.72 (0.46-1.10)	0.132	40 (3.02)	1.35 (0.80-2.28)	0.261
Ischemic	42 (2.46)	68 (2.13)	0.81 (0.59-1.11)	0.189	11 (1.43)	0.48 (0.32-0.71)	<0.001	20 (1.82)	0.71 (0.43-1.16)	0.173	37 (2.79)	1.28 (0.69-2.37)	0.431
Hemorrhagic	2 (0.12)	4 (0.13)	1.61 (0.28-9.14)	0.589	0 (0)	- -	-	1 (0.09)	0.78 (0.23-2.68)	0.698	3 (0.23)	3.09 (0.33-28.94)	0.323
ISTH major bleeding	96 (5.62)	105 (3.29)	0.46 (0.34-0.62)	<0.001	26 (3.38)	0.42 (0.27-0.67)	<0.001	19 (1.72)	0.30 (0.18-0.50)	<0.001	60 (4.53)	0.64 (0.48-0.85)	0.002



Cost-Effectiveness Analysis



Cost-Effectiveness Analysis of Non-Vitamin K Antagonist Oral Anticoagulants Versus Warfarin in Thai Patients With Non-Valvular Atrial Fibrillation

Piyameth Dilokthornsakul, PharmD, PhD ^a,
Surakit Nathisuwan, PharmD, BCPS ^b, Rungroj Kittayaphong, MD ^c,
Aurauma Chutinet, MD ^d, Unchalee Permsuwan, PhD ^{e*}

^aCenter of Pharmaceutical Outcomes Research, Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Naresuan University, Muang, Phitsanulok, Thailand

^bDepartment of Pharmacy, Faculty of Pharmacy, Mahidol University, Bangkok, Thailand

^cDepartment of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

^dChulalongkorn Stroke Center, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

^eDepartment of Pharmaceutical Care, Faculty of Pharmacy, Chiang Mai University, Chiang Mai, Thailand

Received 17 April 2018; received in revised form 1 December 2018; accepted 9 February 2019; online published-ahead-of-print xxx

Price sensitivity analysis

Treatment	Total cost (THB)	Life years	QALYs	Incremental cost	Incremental QALY	ICER (95% CrI) THB	ICER (95% CrI) USD
Scenario analysis using the same NOAC cost (85.8 THB/day)							
Warfarin (INR 2 - 3)	158,814	9.28	6.98	Reference	Reference	Reference	Reference
Dabigatran 150mg	451,118	9.58	7.28	292,304	0.29	997,849 (550,856 - 3,072,617)	31,518 (17,399 - 97,050)
Dabigatran 110mg	453,453	9.57	7.26	294,640	0.27	1,083,174 (550,701 - 5,978,304)	34,213 (17,394 - 188,828)
Apixaban 5 mg	443,159	9.75	7.42	284,345	0.43	657,423 (455,163 - 1,171,122)	20,765 (14,377 - 36,991)
Rivaroxaban 20 mg	455,501	9.49	7.20	296,687	0.22	1,347,650 (727,868 - 5,184,086)	42,566 (22,990 - 63,742)
Edoxaban 60mg	446,869	9.63	7.31	288,056	0.33	877,361 (546,731 - 1,774,085)	27,712 (17,837 - 56,036)
Edoxaban 30mg	439,351	9.63	7.30	280,537	0.32	878,375 (514,894 - 2,557,052)	27,744 (16,263 - 80,766)

At similar price per day (85.8 THB), Apixaban also has the highest potential to be cost-effective strategy among NOACs when comparing with warfarin

Conclusions

- In real world data, there were trend toward prescribing ***Apixaban in NVAF population with higher risk for stroke/SE and bleeding.***
- These trends reflected clinician perception about safety of apixaban in ARISTOTLE.
- Despite the higher baseline risk, there were trends in ***better prevention of stroke/SE and less bleeding in NVAF using Apixaban in real world data .***
- The Real-World Data from ***France, Taiwan, Japan, Korea and Thailand confirm the better efficacy and safety of Apixaban in ARISTOTLE.***



Thank You For Your Attention