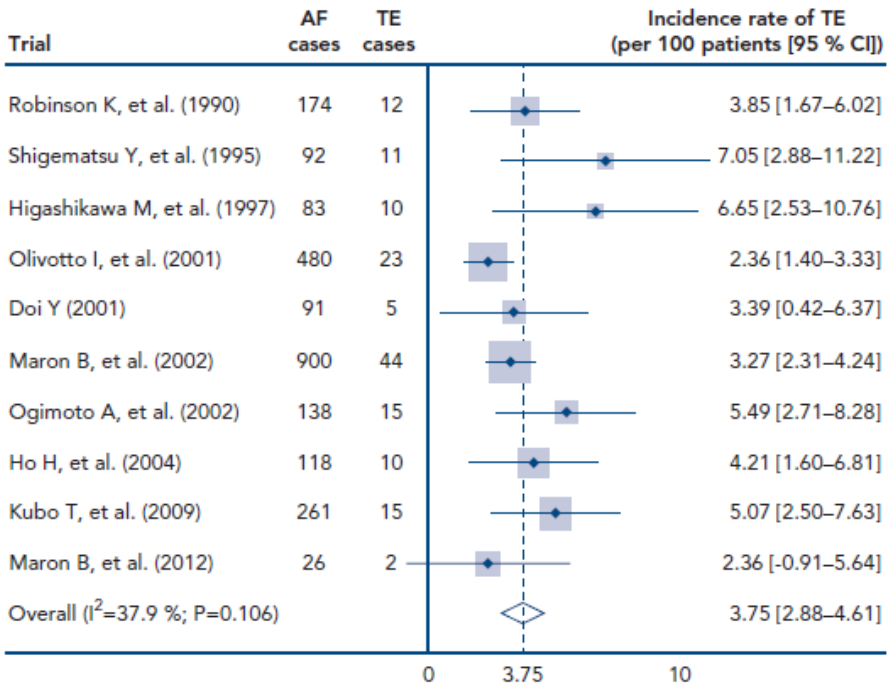
EFFICACIA DEI NUOVI ANTICOAGULANTI ORALI NELLA PREVENZIONE DI ICTUS NEI PAZIENTI CON CARDIOMIOPATIA IPERTROFICA E FIBRILLAZIONE ATRIALE

BACKGROUND

- Atrial fibrillation (AF) is the most common arrhythmia in patient with hypertrophic cardiomyopathy (prevalence 22%)
- Incident rates of stroke in HCM, irrespective of AF diagnosis, have been estimated as 2.5 %/year
- Compared with patients with HCM in sinus rhythm, those in AF were shown to have an eightfold increase in stroke risk

BACKGROUND

Figure 2: Incidence of Thromboembolism in Patients with Hypertrophic Cardiomyopathy and Atrial Fibrillation



Forest plot From random effect meta-analysis shows study specific incidence and pooled incidence of thromboembolism (TE). Source: modified from Guttmann et al., 2014.[21]
HCM = hypertrophic cardiomyopathy.

Arrhythmia & Electrophysiology Review 2017;6(2):63–8.

BACKGROUND

- Guidelines for AF recommend non–vitamin K antagonist oral anticoagulants (NOACs) more strongly than warfarin in the general population, but data for patients with HCM are limited.

ESC guidelines for the management of hypertrophic cardiomyopathy, 2014

As patients with HCM tend to be younger than other high risk groups and have not been included in clinical trials of thromboprophylaxis, use of the CHA_2DS_2-VASc score to calculate stroke risk is not recommended.

Given the high incidence of stroke in patients with HCM and paroxysmal, persistent or permanent AF, it is recommended that all patients with AF should receive treatment with VKA. In general, lifelong therapy with oral anticoagulants is recommended, even when sinus rhythm is restored.

Unless contraindicated, oral anticoagulation with VKA (target INR 2.0–3.0) is recommended in patients who develop persistent, permanent or paroxysmal AF, to prevent thromboembolism.	I	B	223,352

Novel Oral Anticoagulants for Primary Stroke Prevention in Hypertrophic Cardiomyopathy Patients With Atrial Fibrillation

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Stroke 2019; 50(9): 2582-6

METHODS

- Korean Health Insurance Review and Assessment Service database
- 2397 patients with HCM and nonvalvular AF on oral anticoagulation from 2013 to 2016
- No history of ischemic stroke, intracranial hemorrhage (ICH), or gastrointestinal bleeding
- 992 on warfarin and 1405 on NOACs
- Inverse probability of treatment weighting with propensity scores was used to balance covariates between treatment groups.
- Risk for ischemic stroke, ICH, gastrointestinal bleeding, death, and their composite outcome associated with NOAC use was assessed with warfarin use as the reference.

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BASELINE CHARACTERISTICS

- NOAC group:
  - Rivaroxaban 38.0%
  - Dabigatran 21.6%
  - Apixaban 26.6%
  - Edoxaban 3.8%

- After IPTW, the 2 treatment groups were well balanced in all variables (all absolute standardized differences <0.1)

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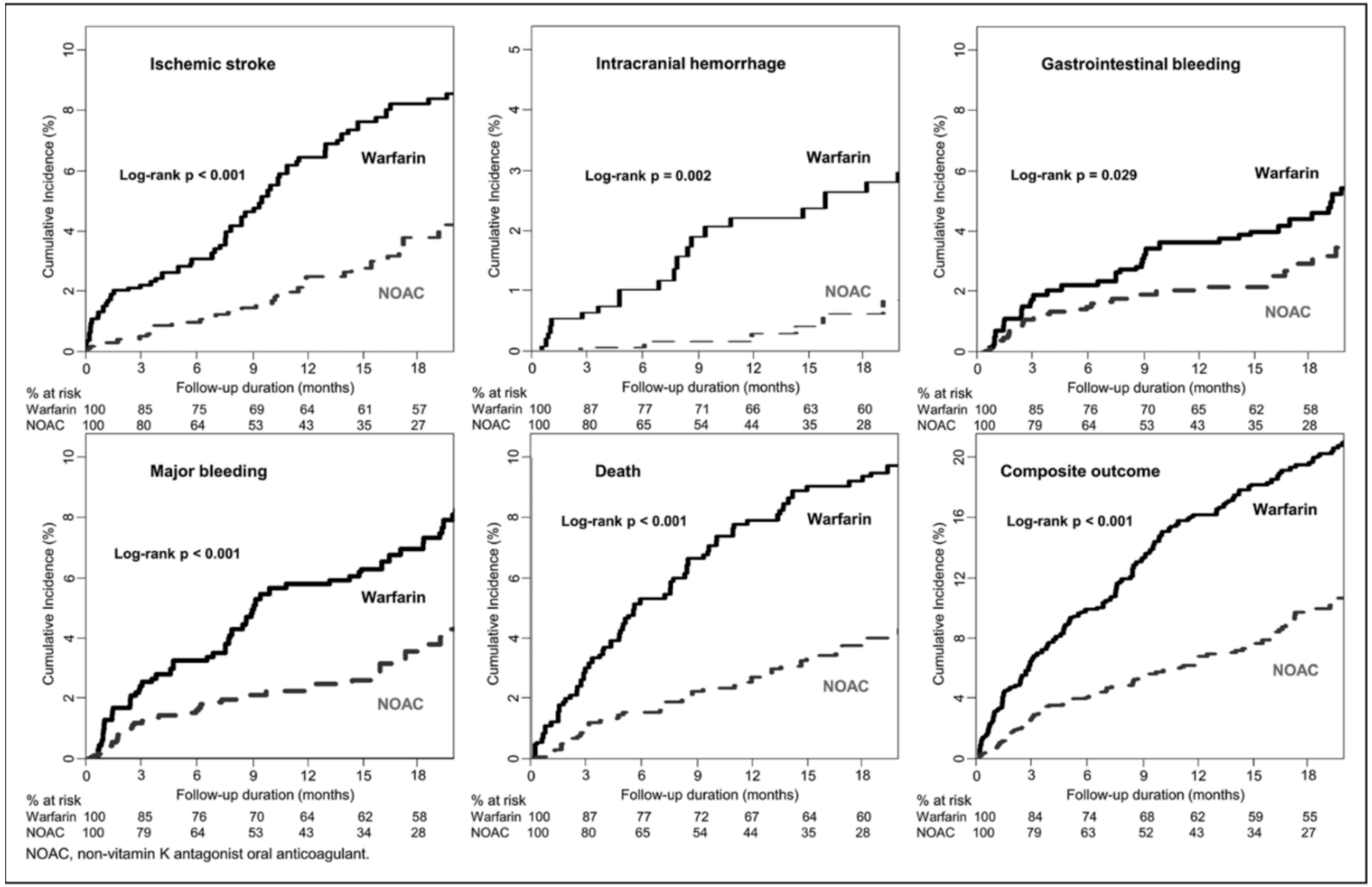
WEIGHTED CUMULATIVE INCIDENCE CURVES FOR POOLED NOAC AND WARFARIN

Mean follow-up of 1.6±1.4 years (2.4±1.7 years for warfarin and 1.0±0.8 years for NOAC)



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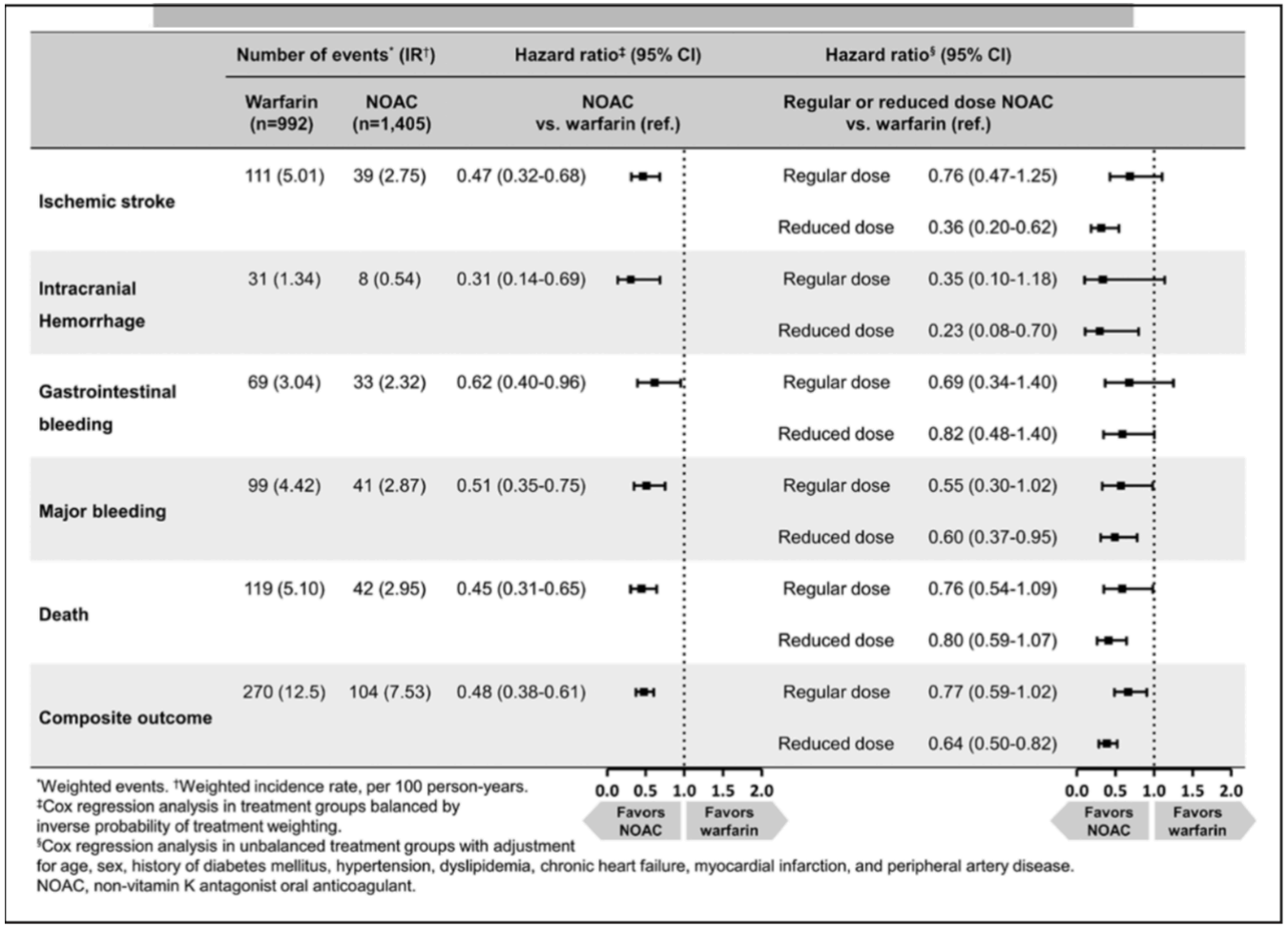
RISK OF STROKE, BLEEDING, OR DEATH FOR POOLED NOAC VS WARFARIN, WITH SUBANALYSIS FOR NOAC DOSE



	Number of events* (IR†)		Hazard ratio‡ (95% CI)	Hazard ratio§ (95% CI)	
	Warfarin (n=992)	NOAC (n=1,405)	NOAC vs. warfarin (ref.)	Regular or reduced dose NOAC vs. warfarin (ref.)	
Ischemic stroke	111 (5.01)	39 (2.75)	0.47 (0.32-0.68)	Regular dose	0.76 (0.47-1.25)
				Reduced dose	0.36 (0.20-0.62)
Intracranial Hemorrhage	31 (1.34)	8 (0.54)	0.31 (0.14-0.69)	Regular dose	0.35 (0.10-1.18)
				Reduced dose	0.23 (0.08-0.70)
Gastrointestinal bleeding	69 (3.04)	33 (2.32)	0.62 (0.40-0.96)	Regular dose	0.69 (0.34-1.40)
				Reduced dose	0.82 (0.48-1.40)
Major bleeding	99 (4.42)	41 (2.87)	0.51 (0.35-0.75)	Regular dose	0.55 (0.30-1.02)
				Reduced dose	0.60 (0.37-0.95)
Death	119 (5.10)	42 (2.95)	0.45 (0.31-0.65)	Regular dose	0.76 (0.54-1.09)
				Reduced dose	0.80 (0.59-1.07)
Composite outcome	270 (12.5)	104 (7.53)	0.48 (0.38-0.61)	Regular dose	0.77 (0.59-1.02)
				Reduced dose	0.64 (0.50-0.82)

*Weighted events. †Weighted incidence rate, per 100 person-years.
‡Cox regression analysis in treatment groups balanced by inverse probability of treatment weighting.
§Cox regression analysis in unbalanced treatment groups with adjustment for age, sex, history of diabetes mellitus, hypertension, dyslipidemia, chronic heart failure, myocardial infarction, and peripheral artery disease.
NOAC, non-vitamin K antagonist oral anticoagulant.

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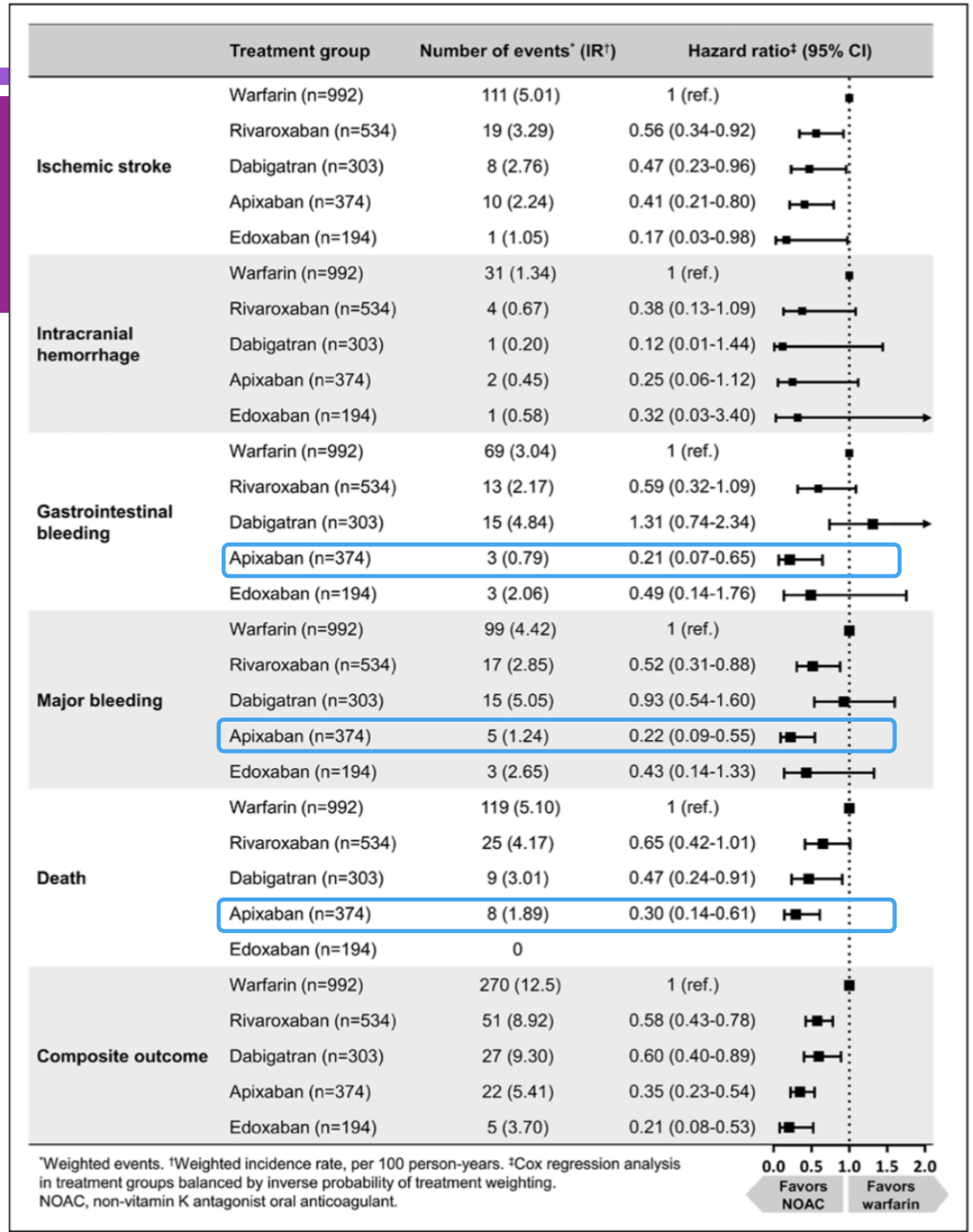
RISK OF STROKE, BLEEDING, OR DEATH FOR INDIVIDUAL NOAC VS WARFARIN

Only apixaban was associated with a significantly lower risk of gastrointestinal bleeding versus warfarin and showed the greatest risk reduction for major bleeding and death



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NOAC IN HCM

1. Noseworthy

- U.S. commercial insurance database
- 2198 pts with HCM and AF
  - NOACs (579)
  - warfarin (1,619)
- Mean follow-up: 0.56 years

TABLE 1 Event Rates Per 100 Person-Years and Hazard Ratios in Propensity Score-Matched NOACs Versus Warfarin Users

Outcomes	Event Rate (Per 100 Person-Years)		Hazard Ratio (95% CI)
	NOACs	Warfarin	
Stroke or systemic embolism	1.93	2.03	0.92 (0.32-2.63)
Ischemic stroke	1.61	1.12	1.37 (0.40-4.67)
Hemorrhagic stroke	0.32	0.91	0.35 (0.04-3.36)
Major bleeding	4.18	5.38	0.75 (0.36-1.57)
Intracranial	0.32	1.22	0.26 (0.03-2.25)
Gastrointestinal	3.22	4.06	0.77 (0.33-1.82)

CI = confidence interval; NOAC = non-vitamin K antagonist oral anticoagulants.

Noseworthy, JACC 2016

NOAC IN HCM

2. Dominiguez

9 inherited cardiac diseases units:

- NOACs (n=99)
- VKA (n=433)

Median follow-up: 63 months

	NOAC (n=99)	VKA (n = 433)	VKA < 2011 (n = 381)	HR/SHR NOAC vs. VKA	95%CI NOAC vs. VKA	p-value NOAC vs. VKA	HR/SHR NOAC vs. VKA<2011	95%CI NOAC vs. VKA<2011	p-value NOAC vs. VKA<2011
TIA (per 100 pts/y)	0	0.25	0.26	-	-	-	-	-	-
Stroke (per 100 pts/y)	0.62	1.06	1.10	0.46*	0.06–3.62	0.46	0.41*	0.05–3.29	0.40
Peripheral embolism (per 100 pts/y)	0	0.35	0.36	-	-	-	-	-	-
Thromboembolic event (per 100 pts/y)	0.62	1.59	1.65	0.32*	0.04–2.45	0.27	0.29*	0.04–2.21	0.23
Major/clinically relevant bleeding on AC (per 100 pts/y)	0.62	0.60	0.56	1.28*	0.18–9.30	0.85	1.98*	0.32–12.49	0.47
• Gastrointestinal (%)	100	68.4	68.8						
• Intracranial (%)	0	0	0						
• Genitourinary (%)	0	15.8	18.7						
• Others (%)	0	15.8	12.5						
Death (per 100 pts/y)	1.26	3.81	3.72	0.55	0.13–2.30	0.41	0.69	0.16–2.93	0.61

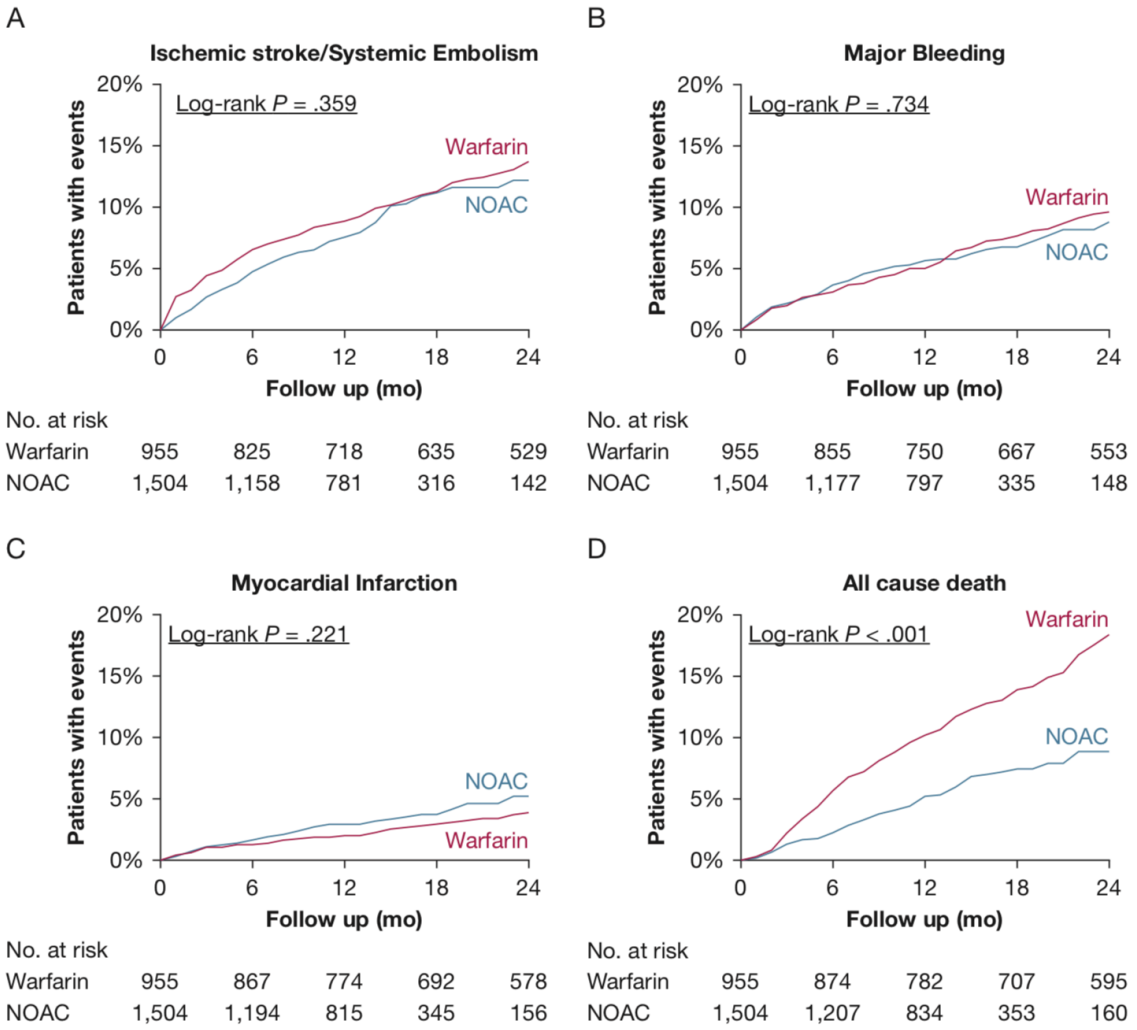
Dominiguez, IJC 2017

NOAC IN HCM

3. Jung

Pts with HCM and AF compared with a 1:2 propensity-matched
- Warfarin (n=955)
- NOAC (n=1504)

Median follow-up:16 months



Jung, Chest 2019

LIMITATIONS

- Severity of symptoms and echocardiography results were unavailable
- Prothrombin time or time in the therapeutic range were unavailable.
- Patients with HCM on NOACs had shorter follow-up duration than those on warfarin.
- Data comparing stroke and bleeding risks with a non-anticoagulated control group or according to concomitant antiplatelet use were unavailable.

CONCLUSIONS

- In a real-world, sizable Asian population with HCM and AF, NOACs showed superior effectiveness and safety for primary prevention of stroke over warfarin

- Confirmation in future studies required.