Apixaban for the Reduction of Thrombo-Embolism in Patients with Device-Detected Subclinical Atrial Fibrillation (ARTESiA)

Top 4 Arrhythmia Trials 2023-2025

ARTESiA

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QUEBEC CITY

OCTOBER 2025

Population Health Research Institute
HEALTH THROUGH KNOWLEDGE

Heart & Stroke™

CIHR IRSC

McMaster University

Canadian Cardiovascular Society

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CASE PRESENTATION

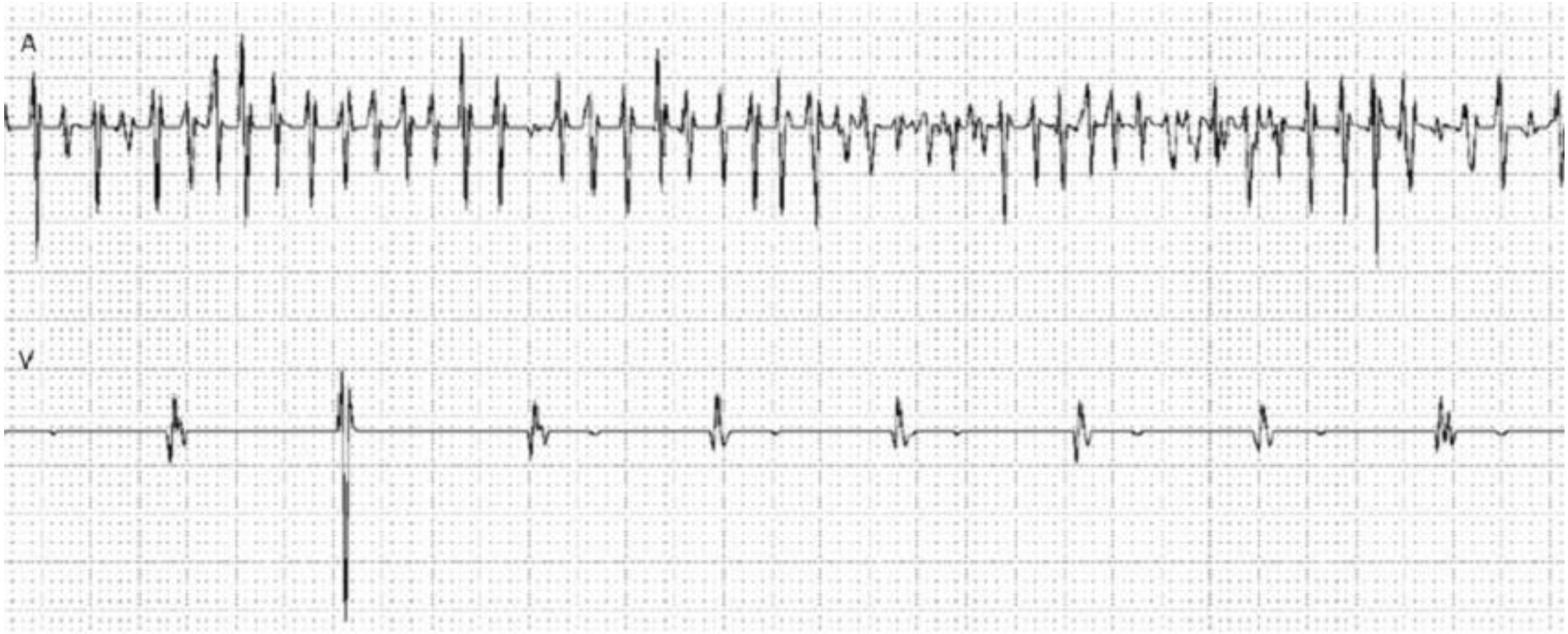
You are asked to see a 78-year-old male in your office.

As you review his chart notes you note that the patient has:

- Controlled hypertension on candesartan,
- Type 2 diabetes on oral antihyperglycemics
- A dual chamber pacemaker inserted 5 years ago for intermittent high-grade AV block and syncope.

On review of his last device interrogation, you note that they had an episode of atrial fibrillation which lasted 12 hours.

The patient was asymptomatic during this episode but is concerned and asks you if anything should be done.



https://www.researchgate.net/figure/Example-of-atrial-high-rate-episode_fig1_365346251

A 78 YEAR OLD MALE
CHA_2DS_2-VASC = 4
UP TO 12 HOURS OF DEVICE-DETECTED AF

Which is true with respect to Direct Oral Anticoagulants (DOACs) for your patient:

a) They reduce the risk of stroke, but increase the risk of bleeding

b) They have no effect on risk of stroke, but increase the risk of bleeding

c) They reduce the risk of stroke, and have no effect on the risk of bleeding

d) No effect on either

CASE PRESENTATION

You are called to see a patient in pacemaker clinic.

This is an 82-year-old female with a dual chamber pacemaker implanted for syncope and bifascicular block.

Her history is notable for hypertension, coronary artery disease with a prior stent (taking ASA 81 mg daily), remote stroke without any sequalae, and chronic lower back pain for which she requires a walker to mobilize.

You note several episodes of atrial fibrillation over the past month, some lasting as little as 6 minutes, and others up to 6 hours.

What is your anti-thrombotic plan for this patient?

AN 82 YEAR OLD FEMALE
CHA_2DS_2-VASC = 7, PRIOR STROKE + PCI
UP TO 6 HOURS OF DEVICE-DETECTED AF

What would you do

a) Continue them on ASA 81 mg alone

b) Stop ASA, start apixaban

c) Continue ASA, start apixaban

d) Stop ASA

e) I don’t know, go Blue Jays!

DR MCINTYRE

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PROGRAM DISCLOSURE OF COMMERCIAL SUPPORT

I have relationships with for-profit and not-for-profit organizations over the past 2 years:

Nature of Relationship	Name of the for-profit of not-for-profit organization	Description of Relationship
Any direct financial payments including receipt of honoraria	Heart and Stroke, PHRI	
Membership on advisory boards or speakers' bureaus	Atricure iRhythm	Consulting Speaking
Funded grants of clinical trials	Heart and Stroke, CIHR	
Patents on a drug, product or device		
All other investments/relationship that could be seen as having the potential to influence the content of the educational activity	Author and Steering Committee, ARTESiA Trial	

OAC for device-detected AF? The Issues

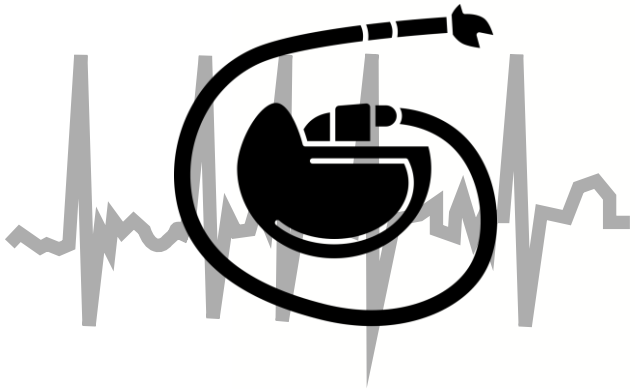
1. Are patients with device-detected AF at risk of stroke?

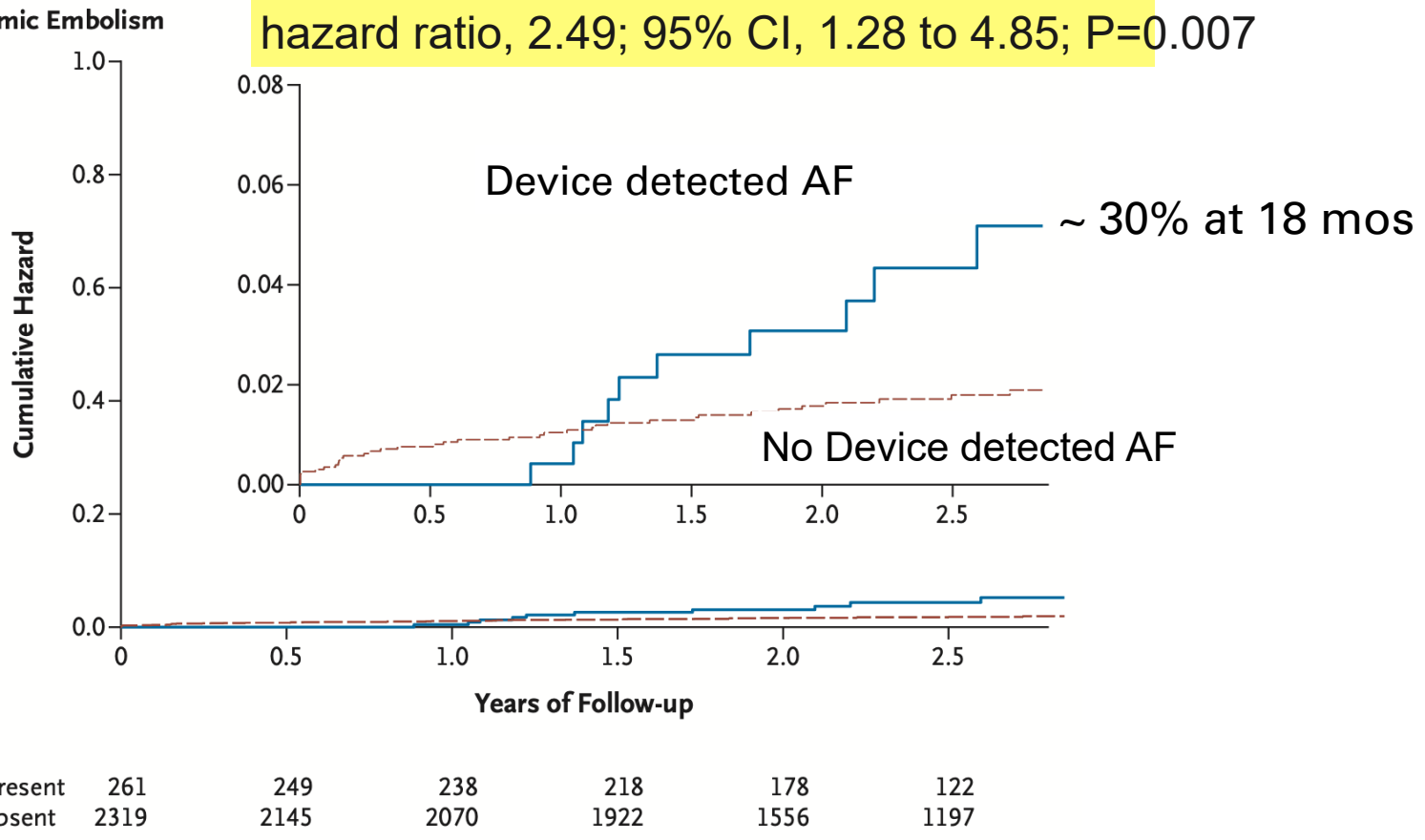
2. Does OAC reduce stroke in these patients?

3. Is the risk of stroke sufficiently high to justify OAC?

4. Is the bleeding risk acceptable?

Device-detected AF increases the risk of stroke





Healey JS et al NEJM 2012

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OAC for device-detected AF? The Issues

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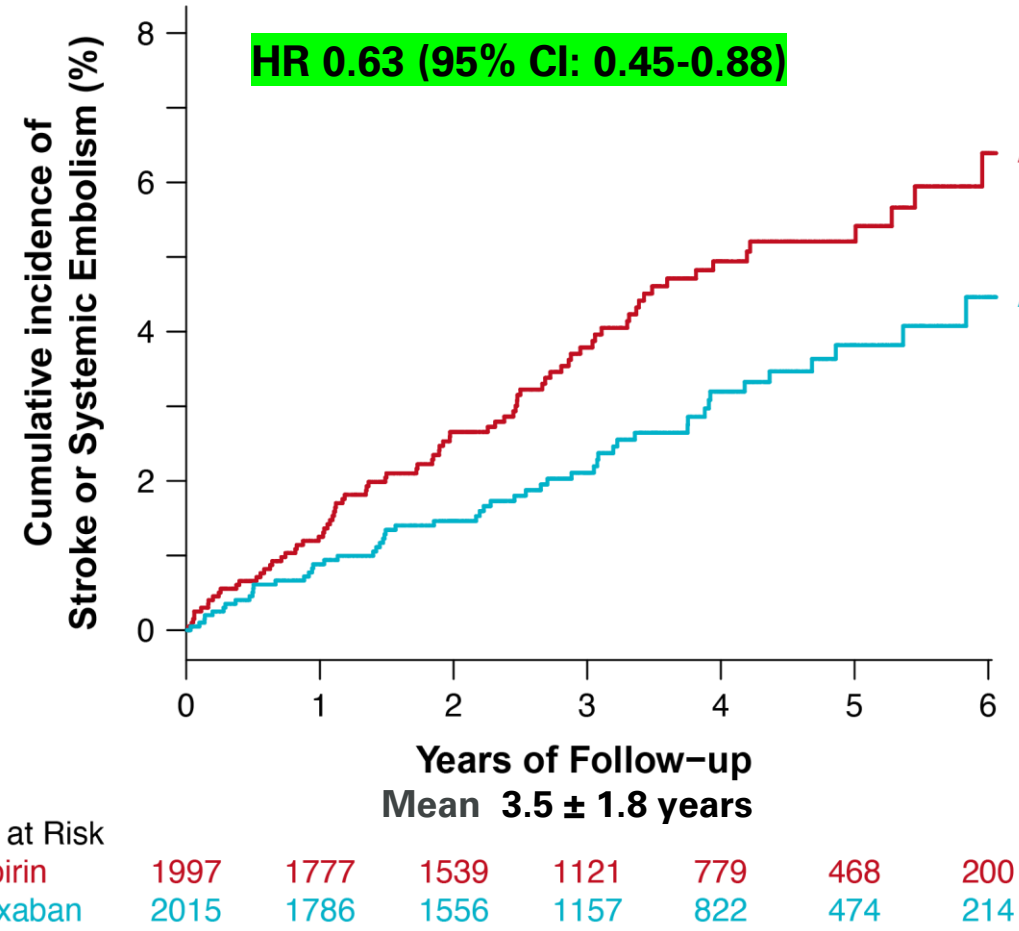
APIXABAN REDUCES STROKE IN DEVIE-DETECTED AF



Aspirin 1.24% per year

Apixaban 0.78% per year

Healey JS et al NEJM 204

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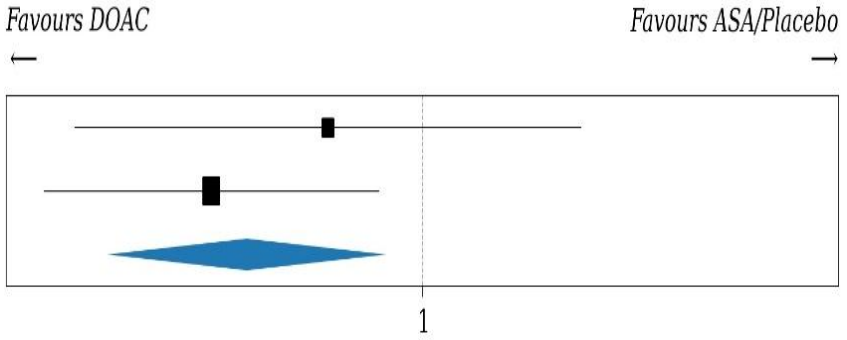
Direct Oral Anticoagulants for Stroke Prevention in Patients With Device-Detected Atrial Fibrillation: A Study-Level Meta-Analysis of the NOAH-AFNET 6 and ARTESiA Trials

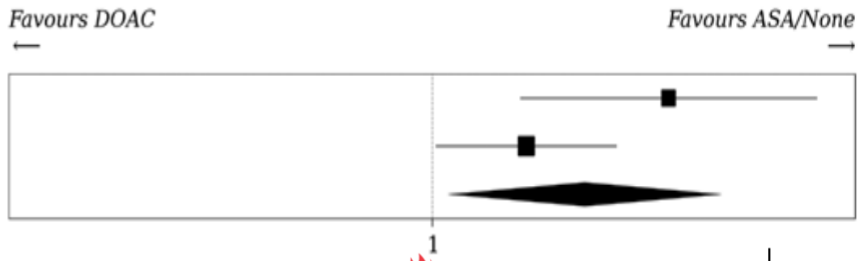
Ischemic Stroke

Study	DOAC	(%)	ASA/Placebo	(%)	Weight	RR [95% CI]
NOAH-AFNET 6	22/1,270	(1.7%)	27/1,266	(2.1%)	30.4%	0.81 [0.47, 1.42]
ARTESiA	45/2,015	(2.2%)	71/1,997	(3.6%)	69.6%	0.63 [0.43, 0.91]
Pooled Estimate	67/3,285	(2.0%)	98/3,263	(3.0%)	I^2: 0%	0.68 [0.5, 0.92]
Mantel-Haenszel, DerSimonian-Laird Random Effects	*p=0.01, z=2.47 τ^2=0.00*					*RR: Risk Ratio CI: Confidence Interval*



Major Bleeding

Study	DOAC	(%)	ASA/None	(%)	Weight	RR [95% CI]
NOAH-AFNET 6	53/1,270	(4.2%)	25/1,266	(2.0%)	41.1%	2.11 [1.32, 3.38]
ARTESiA	106/2,015	(5.3%)	78/1,997	(3.9%)	58.9%	1.35 [1.01, 1.79]
Pooled Estimate	159/3,285	(4.8%)	103/3,263	(3.2%)	I^2: 61%	1.62 [1.05, 2.5]
Mantel-Haenszel, DerSimonian-Laird Random Effects	*p=0.03, z=2.18 τ^2=0.06*					*RR: Risk Ratio CI: Confidence Interval*



McIntyre WF et al Circulation. 2024;149:981–988.

OAC for device-detected AF? The Issues

1. Are patients with device-detected AF at risk of stroke?

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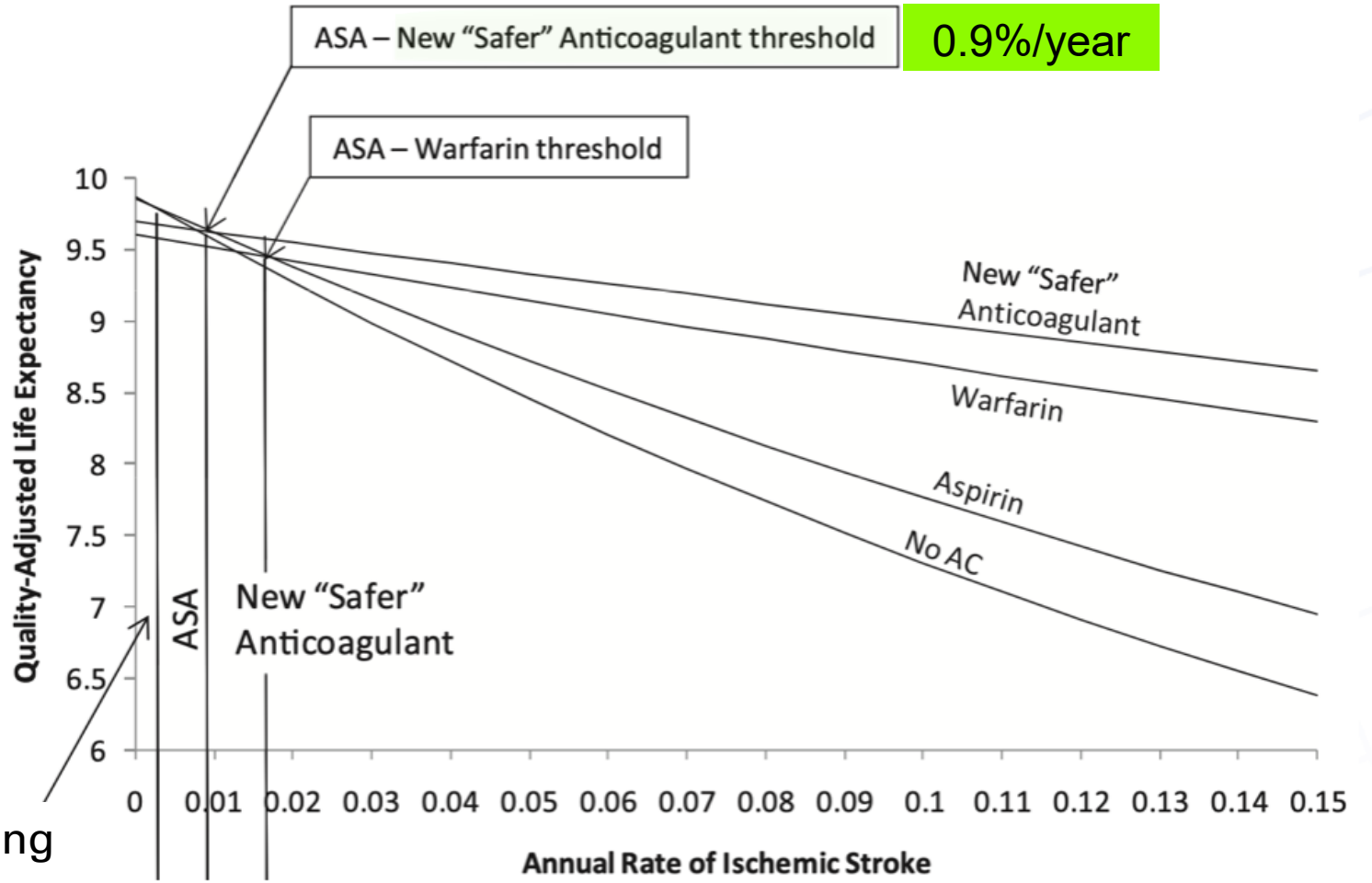
What annual rate of stroke justifies OAC?



- Basis for CCS "CHADS-65"
- IIA ESC 2024
- IIA AHA/ACC 2023

Eckman MH et al. Circulation Cardiovasc Qual Outcomes 2011;4:14–21

Stroke Rates in Device-Detected AF Exceed 1%/year
A Threshold at Which Bleeding Risk is Generally Justified

ARTESiA

Outcome	Apixaban (N=2015)		Aspirin (N=1997)		Hazard Ratio (95% CI)	P Value
	no. of patients with event	*%/patient-yr*	*no. of patients with event*	*%/patient-yr*		
Stroke or systemic embolism	55	0.78	86	1.24	0.63 (0.45–0.88)	0.007
Stroke	55	0.78	84	1.21	0.64 (0.46–0.90)	
Ischemic or unknown type†	45	0.64	71	1.02	0.62 (0.43–0.91)	
Hemorrhagic	10	0.14	13	0.18	0.76 (0.33–1.73)	

≥1%

NOAH-AFNET 6

Outcome	Edoxaban (N=1270)	Placebo (N=1266)	Adjusted Hazard Ratio (95% CI)
	no. of patients with event/patient-yr (% per patient-yr)		
Primary composite efficacy outcome†	83/2557 (3.2)	101/2495 (4.0)	0.81 (0.60 to 1.08)‡
Ischemic stroke	22/2573 (0.9)	27/2519 (1.1)	0.79 (0.45 to 1.39)
Systemic embolism	14/2579 (0.5)	28/2515 (1.1)	0.51 (0.27 to 0.96)

≥1%

ARTESIA SHOWED A REDUCTION IN FATAL/DISABLING STROKE AT THE EXPENSE OF NON-FATAL MAJOR BLEEDS

	Apixaban (N = 2015)	Aspirin (N = 1997)	Hazard Ratio (95% CI)
Total Stroke	55 (0.78)	84 (1.21)	0.64 (0.46-0.90)
Modified Rankin Score 0-2	31 (0.44)	45 (0.65)	0.68 (0.43-1.07)
Modified Rankin Score 3-6	19 (0.27)	37 (0.53)	0.51 (0.29-0.88)
Major bleeding (ISTH)	*106 (1.53)*	*78 (1.12)*	*1.36 (1.01-1.82)*

	Apixaban (N = 2015)	Aspirin (N = 1997)
Clinical course	n (% of major bleeds)	
1 - *conservative measures*	21 (22.6)	16 (32.7)
2 - *supportive care, transfusion*	54 (58.1)	22 (44.9)
3 - *immediate measures needed to avoid death*	9 (9.7)	4 (8.2)
4 - *death unavoidable*	3 (3.2)	6 (12.2)

Healey JS et al NEJM 204

Many Patients Value Stroke Prevention Over Bleeding Risk

"Patients at high risk for AF placed more value on the avoidance of stroke and less value on the avoidance of bleeding than did physicians who treat patients with AF."

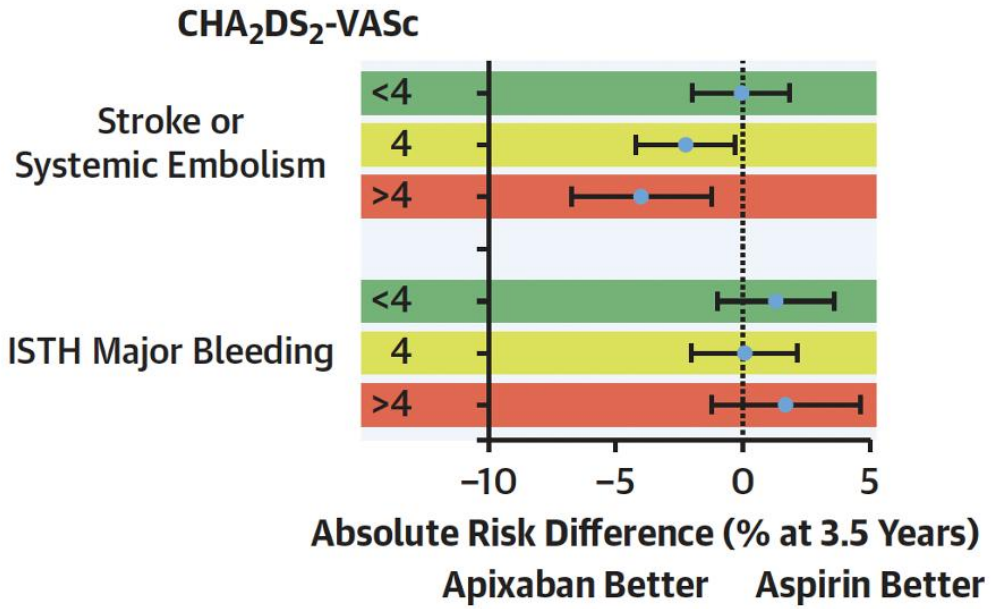
"Patients were willing to endure 4.4 major bleeds in order to prevent one stroke."

Devereaux PJ et al BMJ 2001;323:1–7
SA LaHaye et al Thromb Haemost 2014 111(3):465-73.

Subgroups of Patients with Device-detected AF With a High Baseline Risk of Stroke

CHA_2DS2-VASc Score > 4: 2.25%/year on Aspirin

Patients With Device-Detected Subclinical Atrial Fibrillation in the ARTESiA Trial



CHA_2DS_2-VASc <4	CHA_2DS_2-VASc =4	CHA_2DS_2-VASc >4
Low risk of stroke	Intermediate risk of stroke	High risk of stroke
Bleeding risk outweighs benefit	Similar risk and benefit	Stroke benefit outweighs risk

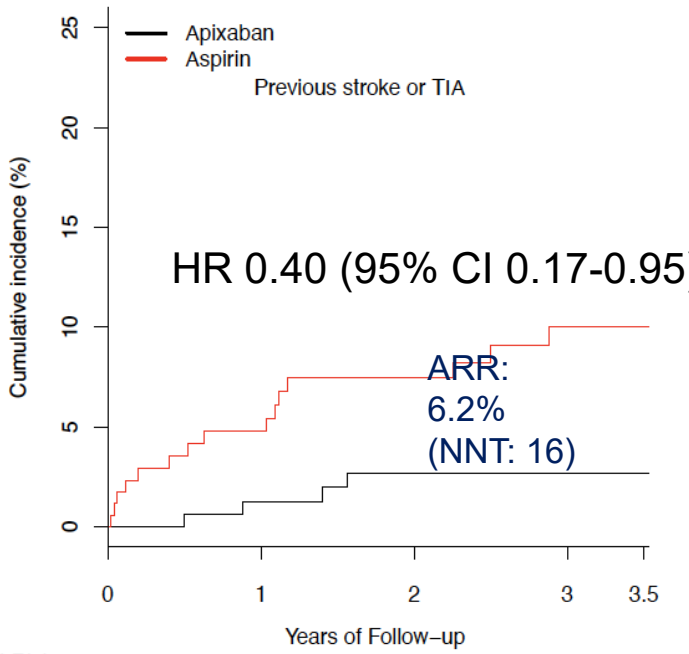
Lopes RD, et al. J Am Coll Cardiol. 2024;84(4):354-364.

Lopes et al JACC 2024

Subgroups of Patients with Device-detected AF With a High Baseline Risk of Stroke

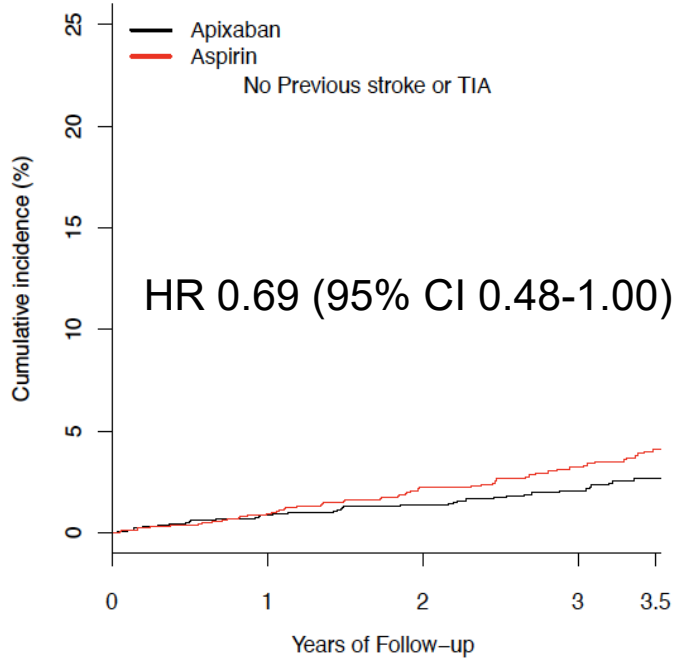
Prior Stroke: 3.4%/year on Aspirin

Patients with Previous stroke or TIA (n=346)



No. at Risk					
Apixaban	172	152	132	98	86
Aspirin	174	147	125	88	76

No Previous stroke or TIA (n=3666)



No. at Risk					
Apixaban	1843	1634	1424	1059	914
Aspirin	1823	1630	1414	1033	897

P-interaction for absolute risk =0.03

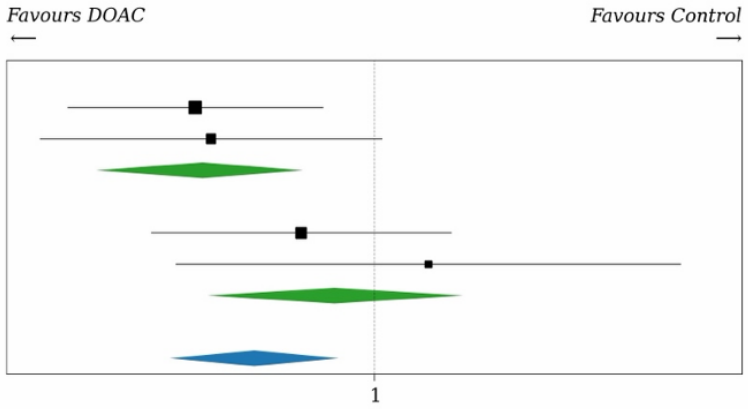
Shoamanesh A et al Lancet Neurol 2025

Subgroups of Patients with Device-detected AF With a High Baseline Risk of Stroke

Vascular Disease: 1.9%/year on Aspirin/Placebo

Study	DOAC	(%)	Control	(%)	Weight	RR [95% CI]
Vascular Disease						
ARTESiA	30/3,140	(1.0%)	54/3,030	(1.8%)	38.1%	0.54 [0.34, 0.84]
NOAH-AFNET 6	17/1,371	(1.2%)	29/1,325	(2.2%)	22.5%	0.57 [0.31, 1.03]
Subgroup Estimate	47/4,511	(1.0%)	83/4,355	(1.9%)	I^2: 0%	0.55 [0.38, 0.78]
No Vascular Disease						
ARTESiA	25/3,919	(0.6%)	32/3,888	(0.8%)	28.6%	0.78 [0.46, 1.31]
NOAH-AFNET 6	11/1,116	(1.0%)	9/1,101	(0.8%)	10.8%	1.21 [0.5, 2.9]
Subgroup Estimate	36/5,035	(0.7%)	41/4,989	(0.8%)	I^2: 0%	0.87 [0.56, 1.36]
					I^2: 8%	0.66 [0.49, 0.88]

RR: Risk Ratio
CI: Confidence Interval



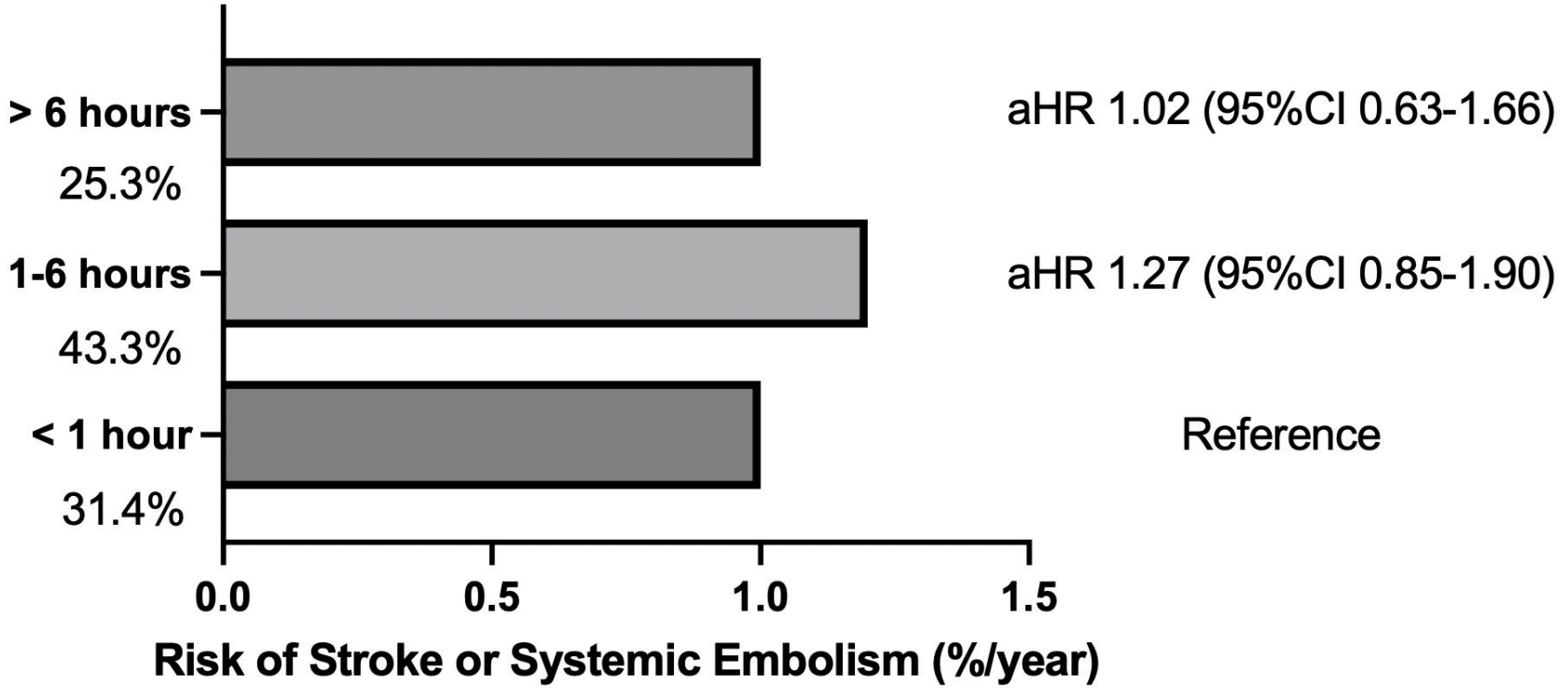
Stroke or systemic embolism

Incidence Rate Ratio

$p_{interaction}$=0.13

Schnabel R et al European Heart Journal 2024

AF Episode Duration < 24 h
• Does Not Affect Stroke Risk



Note:

Episodes > 24 h previously shown as high risk, censored in ARTESiA

McIntyre WF et al Circulation. 2024

Net Benefit:
Apixaban is Cost –Effective for Device-Detected AF

Lifetime Cost




	Canada	United Kingdom	Germany		United States	
Costs	Dominant Strategy	Dominant Strategy	$4937	$7560	$9314	$18424
Incremental Cost			**$2623**		**$9110**	
Incremental Cost (Discounted)			$2319		$8032	
QALYs			4.888	4.995	4.888	4.995
Incremental QALYs			**0.107**		**0.107**	
Incremental QALYs (Discounted)			0.086		0.086	
ICER			**$24,514/QALY**		**$85,140/QALY**	
ICER (Discounted)			$26,965/QALY		$93,395/QALY	

- cost-effective

- cost-effective at $4.35/day
- cost-saving at $3.59/day

Europace Lamy et al Europace 2025

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Device-Detected AF: Take Home Points

1. Patients with Device-Detected AF $\geq$ 24 hours
   - Risk stratify like usual clinical AF

2. Patients with device-detected AF 6 min – 24 h
   - Clear Benefit to OAC if
     - Prior Stroke
     - CHA_2DS_2-VASc Score > 4
     - Vascular disease (ie ASA indication)

Questions and Discussion

Roary
? 2011 – Oct 20, 2025