

Surgical Left Atrial Appendage Occlusion and Rationale for design of LAAOS IV

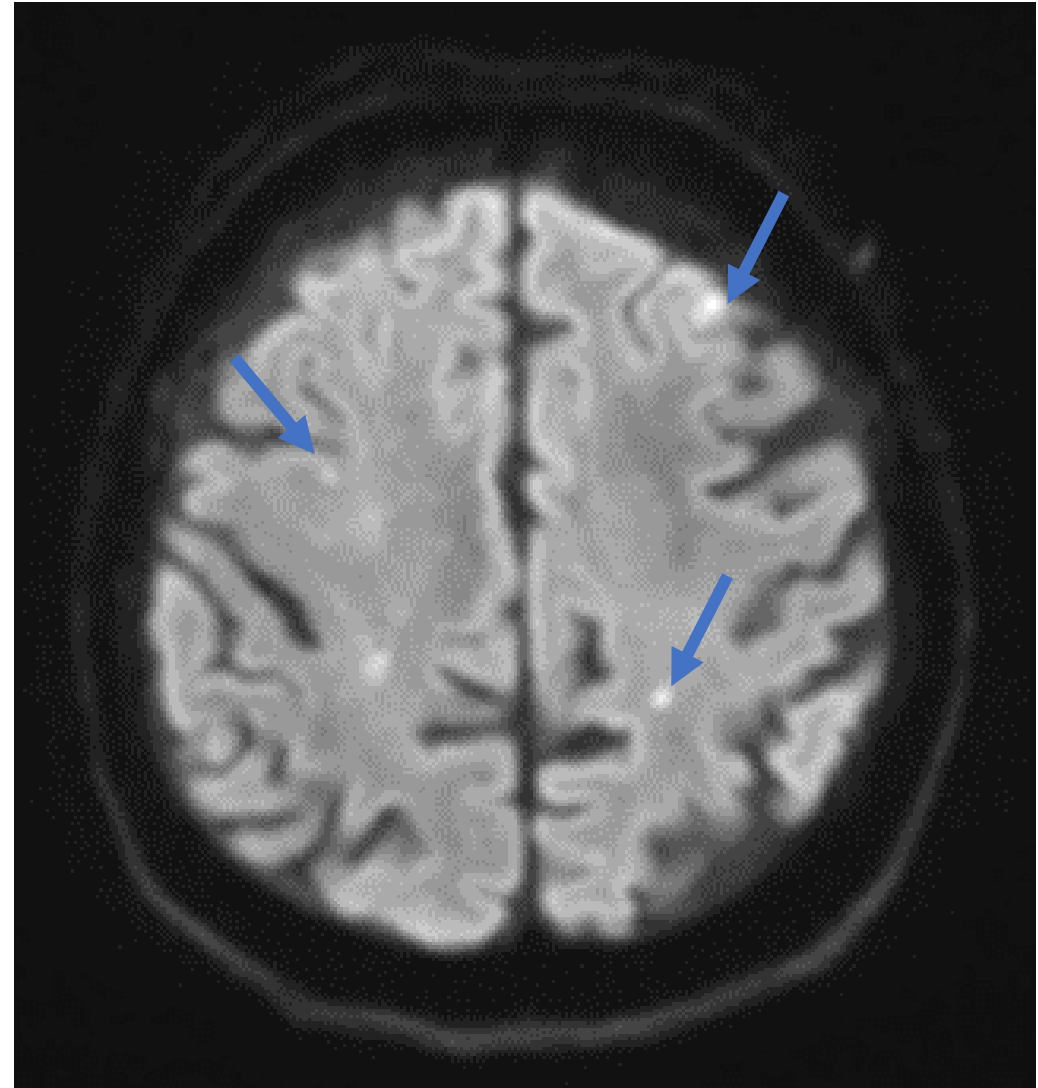
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CRT 2023*

Disclosures

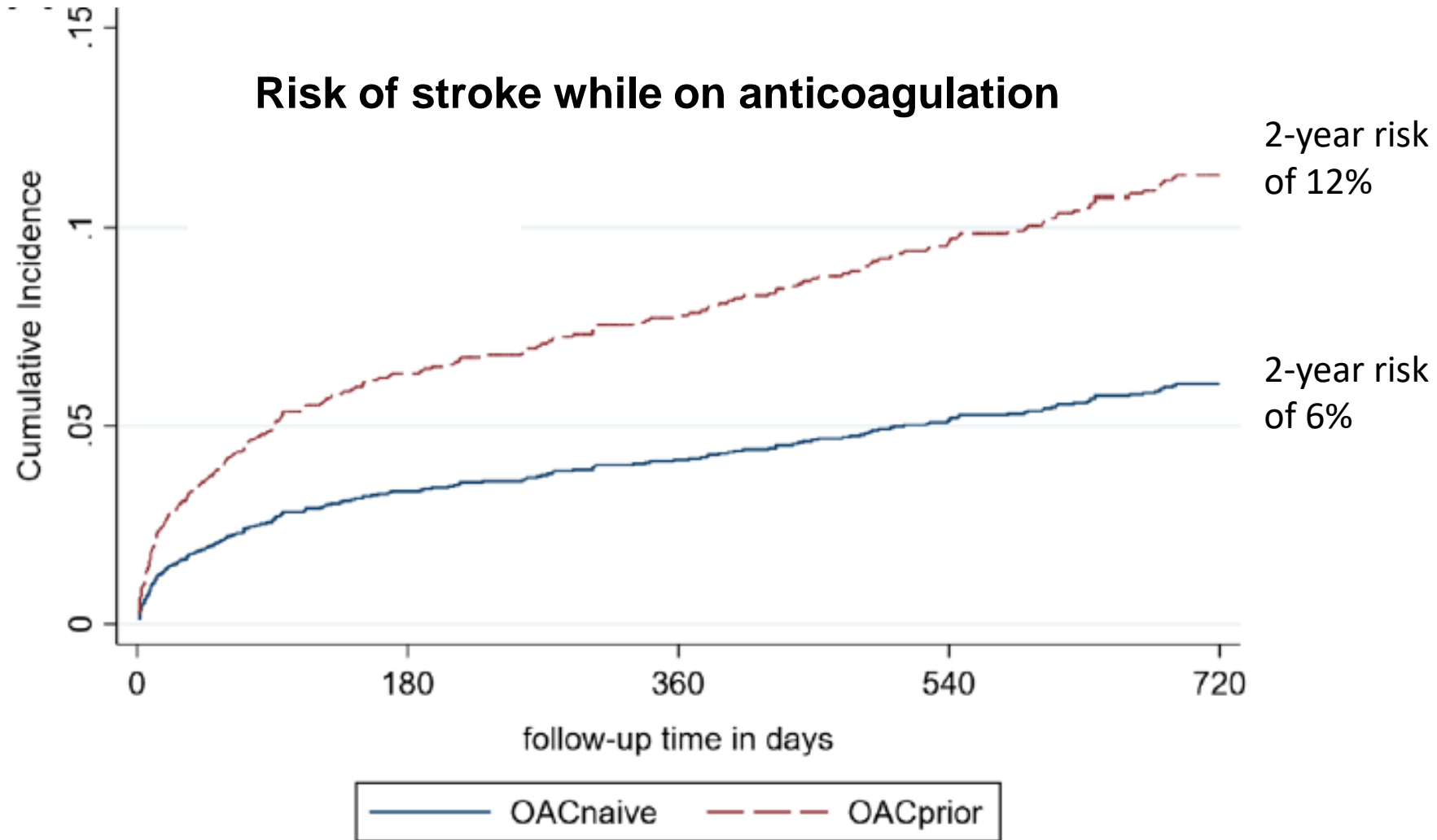
- Institutional Grants from Boston Scientific
- Speakers fees Penumbra

Case 1: Minor Stroke,

- 64 yo male with AF, On Rivaroxaban 20 mg, **had minor** stroke 2 weeks ago **(symptoms resolve completely)**
- History of HTN and Diabetes
- **Is there a rationale for LAAO?**



Two-year Follow up After Acute Ischemic Stroke in AF Patients receiving Anticoagulation during follow up



Case 2

- 72 yo female with CHADSVASC5, permanent AF, Apixaban 5 mg bid, GFR 35.
- Estimated 5 year stroke rate 10% **on continued apixaban**
- Is there a **rationale** for LAAO in addition to OAC?

Reasons why DOAC does not prevent all strokes

- Temporary and permanent discontinuation
 - Permanent discontinuation remains 40-50% at 2-3 years
 - 25% of all patients interrupt DOAC for surgery/procedures within 2 years (RELY)
 - DOACs often interrupted due to bleeding

- Compliance/adherence

Does LAA occlusion reduce stroke
on top of anticoagulation?

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Left Atrial Appendage Occlusion during Cardiac Surgery to Prevent Stroke

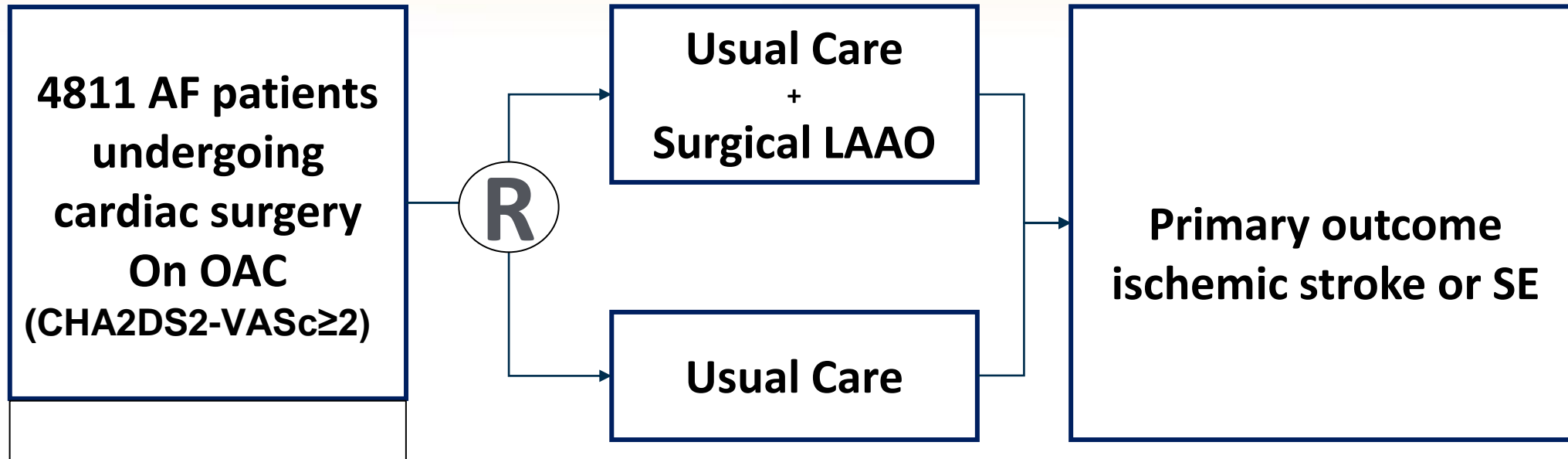
R.P. Whitlock, E.P. Belley-Cote, D. Paparella, J.S. Healey, K. Brady, M. Sharma, W. Reents, P. Budera, A.J. Baddour, P. Fila, P.J. Devereaux, A. Bogachev-Prokophiev, A. Boening, K.H.T. Teoh, G.I. Tagarakis, M.S. Slaughter, A.G. Royse, S. McGuinness, M. Alings, P.P. Punjabi, C.D. Mazer, R.J. Folkeringa, A. Colli, Á. Avezum, J. Nakamya, K. Balasubramanian, J. Vincent, P. Voisine, A. Lamy, S. Yusuf, and S.J. Connolly, for the LAAOS III Investigators*



**Population Health
Research Institute**
HEALTH THROUGH KNOWLEDGE



LAAOS III Design



Blinding of patient, treating team and research team

Whitlock, R, et al. NEJM. 2021; 348:2081.



Patient Characteristics

	LAAO (n=2379)	No LAAO (n=2391)
Age, mean (SD)	71.3 (8.4)	71.1 (8.3)
CHA₂DS₂-VASc, mean (SD)	4.2 (1.5)	4.2 (1.5)
Permanent atrial fibrillation (%)	692 (29.1%)	707 (29.6%)
Male (%)	1617 (68.0%)	1601 (67.0%)
Myocardial infarction (%)	567 (23.8%)	583 (24.4%)
History of stroke (%)	214 (9.0%)	219 (9.2%)
History of heart failure (%)	1348 (56.7%)	1372 (57.4%)
Peripheral arterial disease (%)	236 (9.9%)	256 (10.7%)
Diabetes mellitus (%)	770 (32.4%)	765 (32.0%)
Hypertension (%)	1960 (82.4%)	1941 (81.2%)

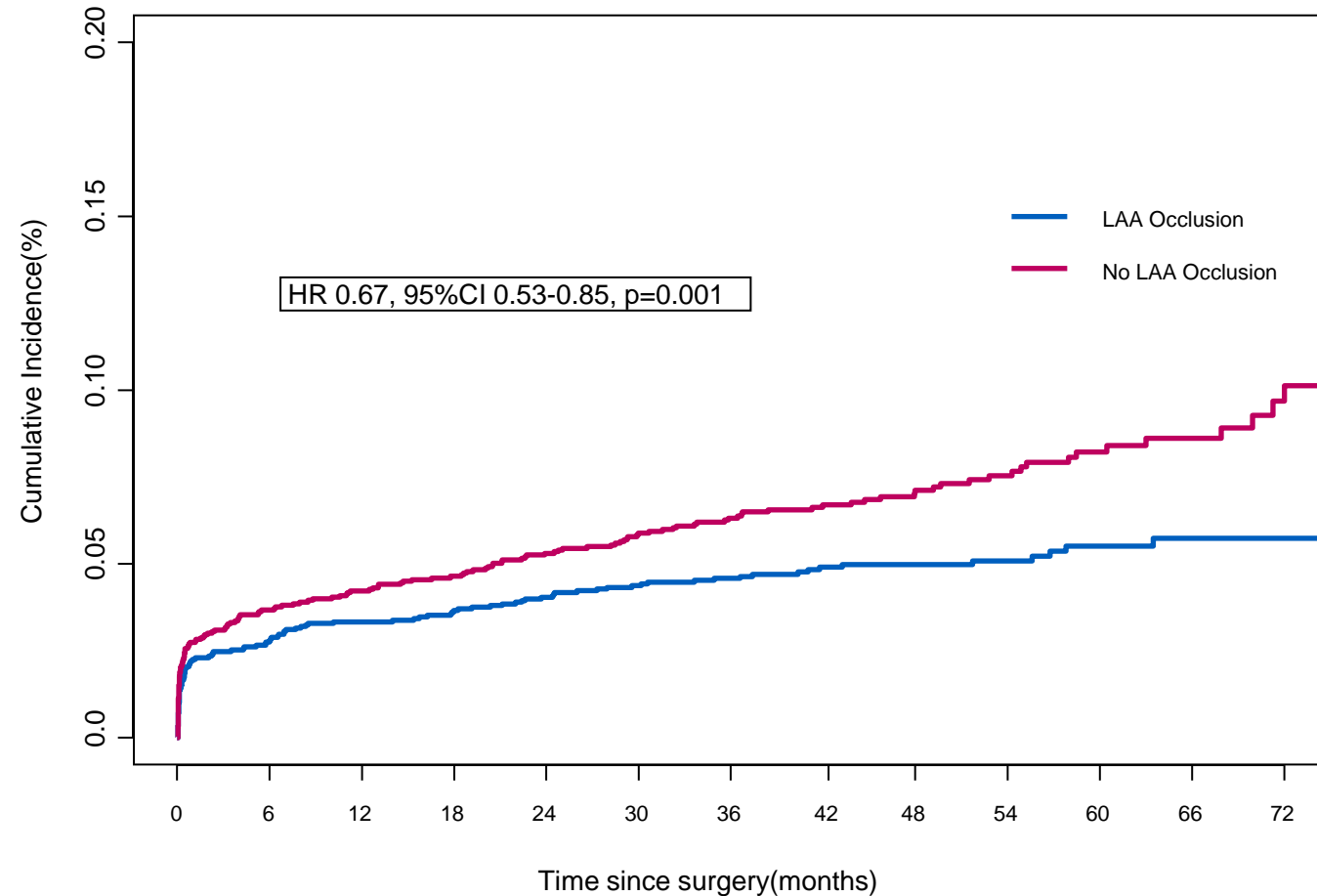
Oral Anticoagulation Use During Follow-up

	LAAO	No LAAO
Discharge	83%	81%
1 year	80%	79%
2 years	77%	78%
3 years	75%	78%



LAAOS-III: Stroke or Systemic Embolism

RP Whitlock,
NEJM 2021



# at Risk	0	6	12	18	24	30	36	42	48	54	60	66	72
LAA Occlusion	2379	2163	2105	2059	2020	1948	1642	1322	1046	781	550	349	199
No LAA Occlusion	2391	2134	2081	2030	1981	1897	1607	1291	1016	751	540	348	205

LAAOS-III: Primary Outcome at 3.8 Years

	LAAO (%)	No LAAO (%)	HR (95% CI)	p-value
Ischemic stroke or systemic embolism	4.8	7.0	0.67 (0.53-0.85)	0.001
Landmark analysis				
Before 30 days	2.2	2.7	0.82 (0.57-1.18)	
After 30 days	2.7	4.6	0.58 (0.42-0.80)	

Adjusted Cox proportional hazard analysis with OAC use as a time dependent covariate

	LAA occlusion		No LAA occlusion		HR (95% CI)
	Events	Incidence / 100 Person Years	Events	Incidence / 100 Person Years	
On OAC	56	0.82	85	1.264	0.63 (0.45-0.89)
Not on OAC	14	0.752	22	1.219	0.63 (0.322-1.232)

New Paradigm for Stroke Prevention in Atrial Fibrillation

Combination systemic and mechanical therapy

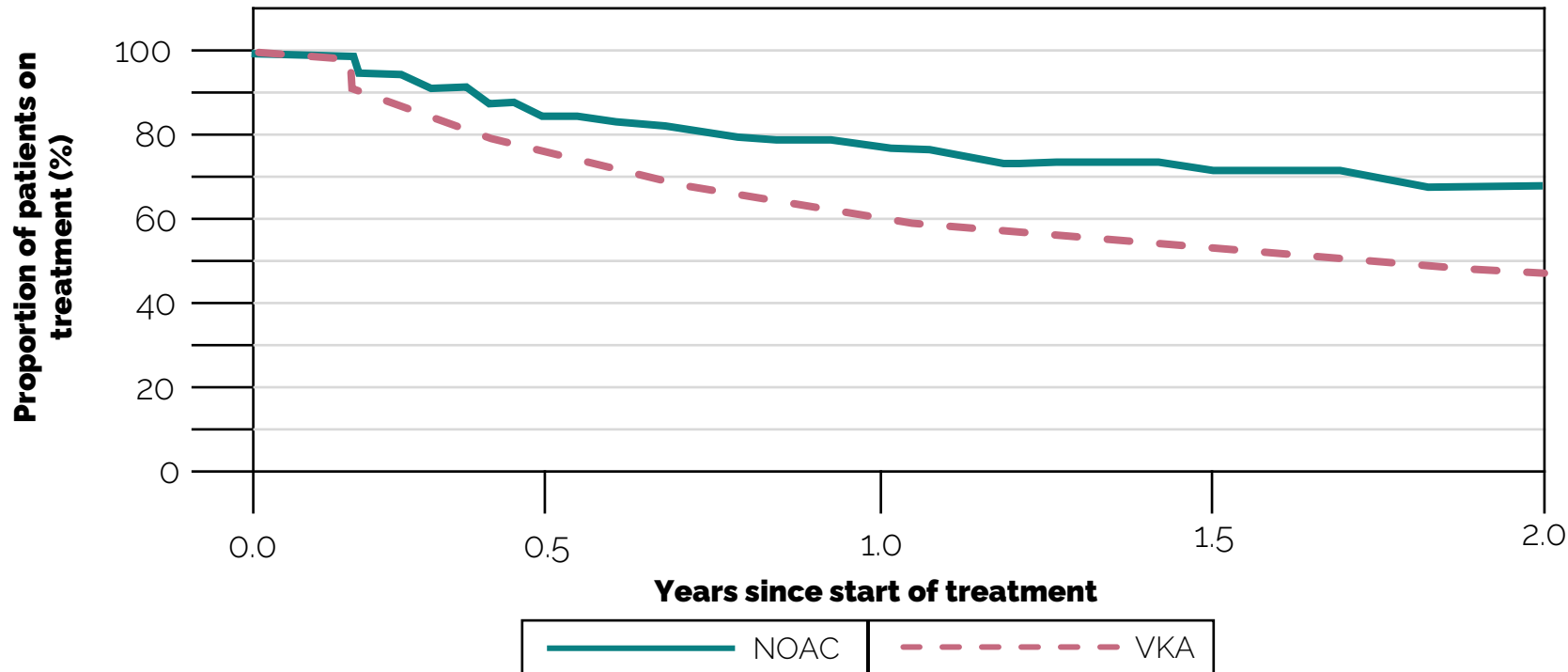
Similar to how we approach coronary artery disease, cerebrovascular disease, etc.

New way of thinking about SPAF for most physicians (stroke neurologists are early adopters)



Despite NOAC Adoption and Ability to Switch NOACs, Adherence to Anticoagulation Remains a Challenge

~**30%** of NOAC patients stop taking any drug at **2 years**



NOAC	914	651	342	139	41
VKA	12307	8453	5762	3915	2506

US Perspective:

- Total AF Population
5 Million Patients
- NVAF (95%)
4.75 Million Patients
- CHA₂DS₂VASc ≥2 (75%)
3.56 Million Patients
- OAC Intolerant (35%)
1.25 Million Patients

AF: atrial fibrillation; CHA₂DS₂VASc: congestive heart failure, hypertension, age ≥75 (doubled), diabetes, stroke (doubled), vascular disease, age 65 to 74 years and sex category (female); DOAC: direct oral anticoagulation; OAC: oral anticoagulant; INR: international normalized ratio; NOAC: novel oral anticoagulant; NVAF: non valvular AF; VKA: vitamin K antagonist. Martinez C et al. Thromb Haemost. 2015;115(1):31-39. doi:10.1160/TH15-04-0350.

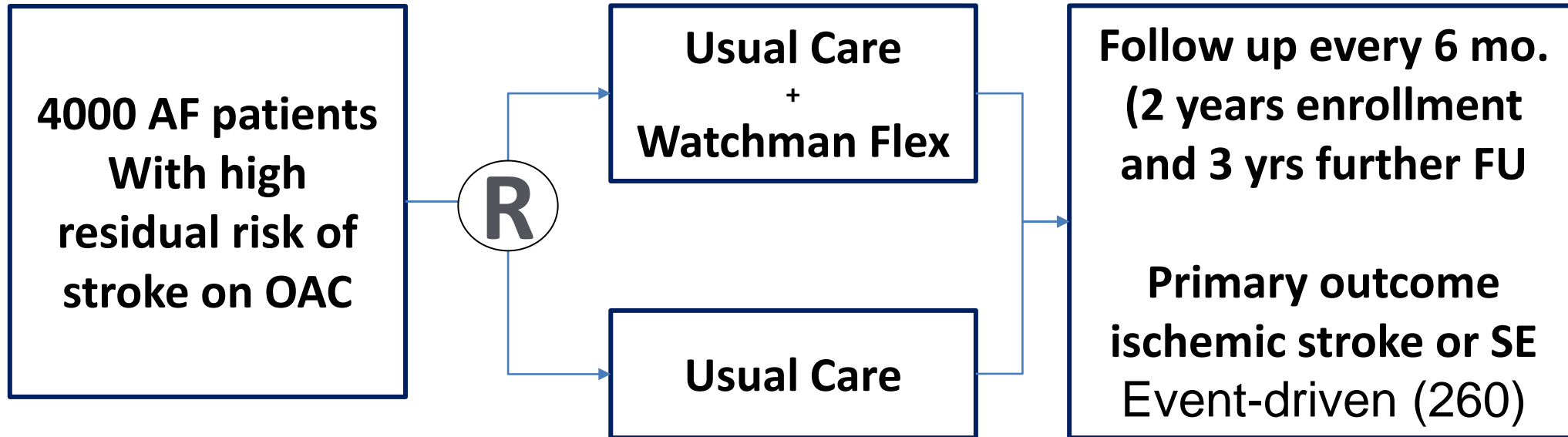
LAAOS-4:

Randomized trial of Watchman on top of OAC in AF patients at high risk of stroke despite OAC

Rationale for LAAOS-4 (combination therapy)

- Surgical LAAO shown to reduce stroke on top of OAC, but does endovascular LAAO do the same?
- We can identify a large group of AF patients with sufficient residual risk, despite OAC, to justify testing if LAAO further reduces stroke.
 - ~30% of AF patients have CHA₂DS₂-VASc score of ≥ 4
 - Residual stroke risk is 2.0% per year (10% at 5 years)
 - AF patients with prior stroke have much higher risk

LAAOS-4



Patients must have all of

1. CHA₂DS₂-VASc score of ≥ 4
2. Plan to treat with OAC
3. Permanent/persistent AF
 - or paroxysmal AF with stroke history

Summary

- Surgical LAAO reduces stroke on top of OAC
- New paradigm of combined device and medical Rx similar to CAD
- LAAOS-4 trial will be akin to PARTNER trial for LAAO and is starting soon