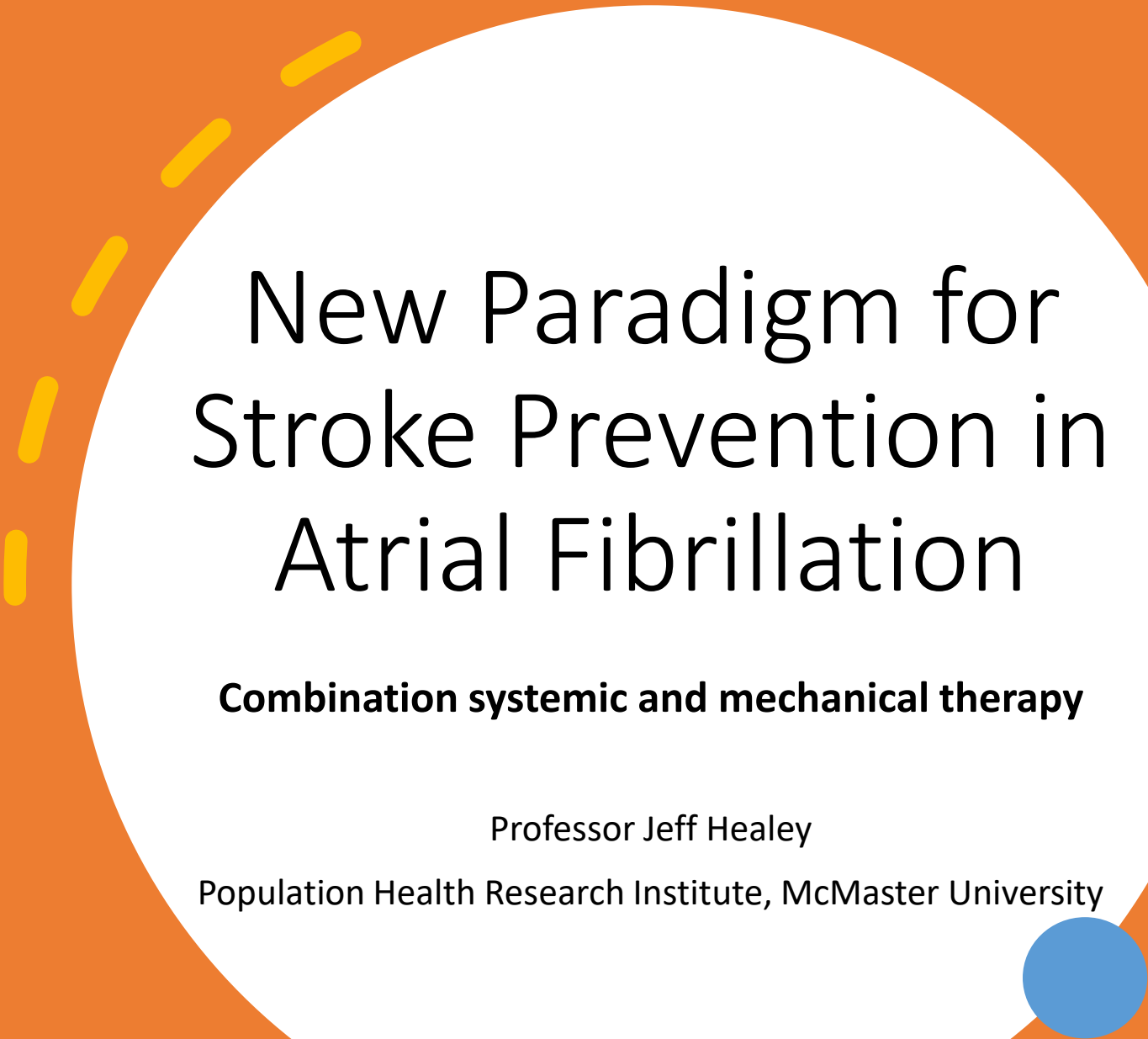




New Paradigm for Stroke Prevention in Atrial Fibrillation

Combination systemic and mechanical therapy

Professor Jeff Healey

Population Health Research Institute, McMaster University

Declaration of Interests: Jeff Healey

- Research grants and speaking fees from
 - Medtronic, Boston Scientific
 - BMS/Pfizer
- Scientific advisory board
 - Boston Scientific



Stroke Prevention in AF: The Present

- Oral anticoagulants can prevent >65% of strokes in individuals with AF
 - Limited by 30-50% permanent discontinuation by 2-3 years
 - Medication often stopped due to minor bleeding
- Additional stroke prevention through BP reduction and treatment of other CV conditions
- Emerging evidence that rhythm control may further reduce stroke risk

Stroke Prevention in AF: The Future?

- **1. New approaches to stroke prevention with less bleeding**
 - New OAC drugs with less bleeding and greater persistence OAC (fXIIa inhibitors)
 - LAA closure Devices (CLOSURE-AF, CHAMPION, AMULET)
- **2. Rhythm control and risk factor clinical trials**
 - EAST-HIGH, EAST-STROKE, OCEAN, etc.
 - RASTA
- **3. Combination stroke-prevention therapy in the highest risk individuals**
 - LAA closure, carotid filters
 - ELAPSE, LAAOS-4, Intercept

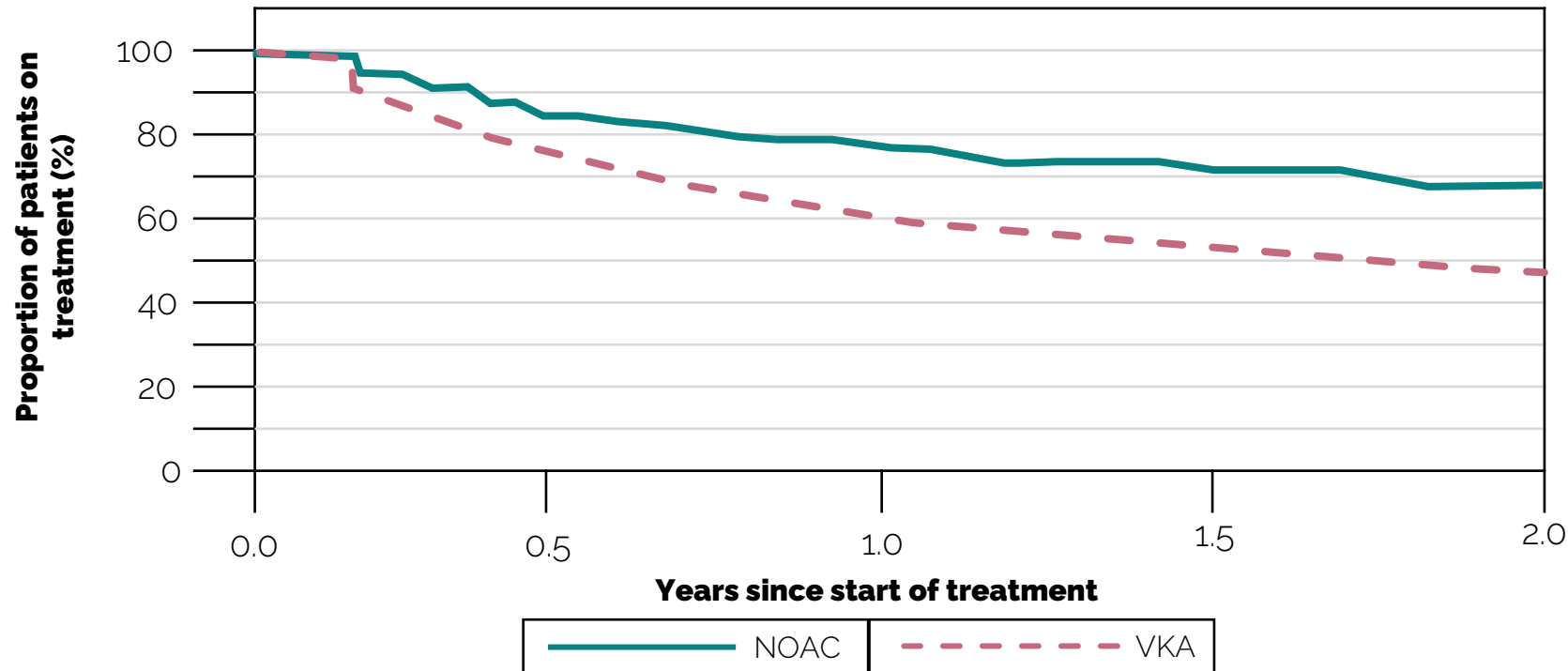
Reasons why DOAC does not prevent all strokes

- Temporary and permanent discontinuation
 - Permanent discontinuation remains 30-50% at 2-3 years
 - 25% of all patients interrupt DOAC for surgery/procedures within 2 years (RELY)
- Compliance/adherence
 - Must take all dose, as directed (e.g. with food), at indicated dose
- Some strokes not prevented by DOAC (e.g. lacunar infarcts, atheroemboli)



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

RESIDUAL RISK Ischemic Stroke/SE on DOAC

Persistent and Permanent AF

N=54,857, COMBINE-AF Meta-Analysis

LB Johnson, JAHA 2024

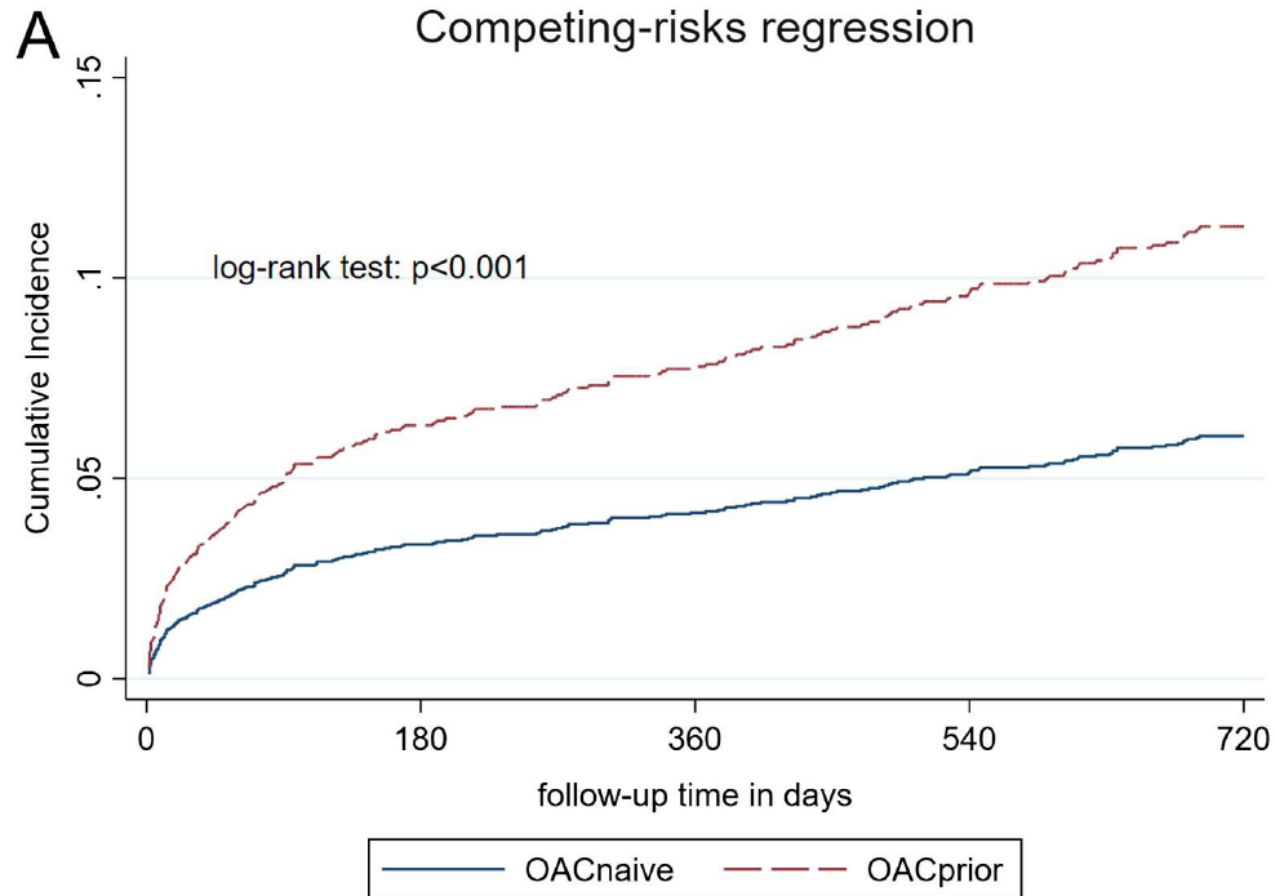
CHA ₂ DS ₂ -VASc score	
2 (n=7,978)	0.61 (0.50-0.74)
3 (n=13,062)	1.06 (0.95-1.19)
4 (n=14,169)	1.51 (1.38-1.66)
5 (n=10,682)	2.04 (1.86-2.23)
6 (n=5,773)	2.71 (2.43-3.02)
7 (n=2,420)	2.90 (2.46-3.02)

25% of all AF patients have persistent/permanent AF
and CHA₂DS₂-VASc score of ≥ 4

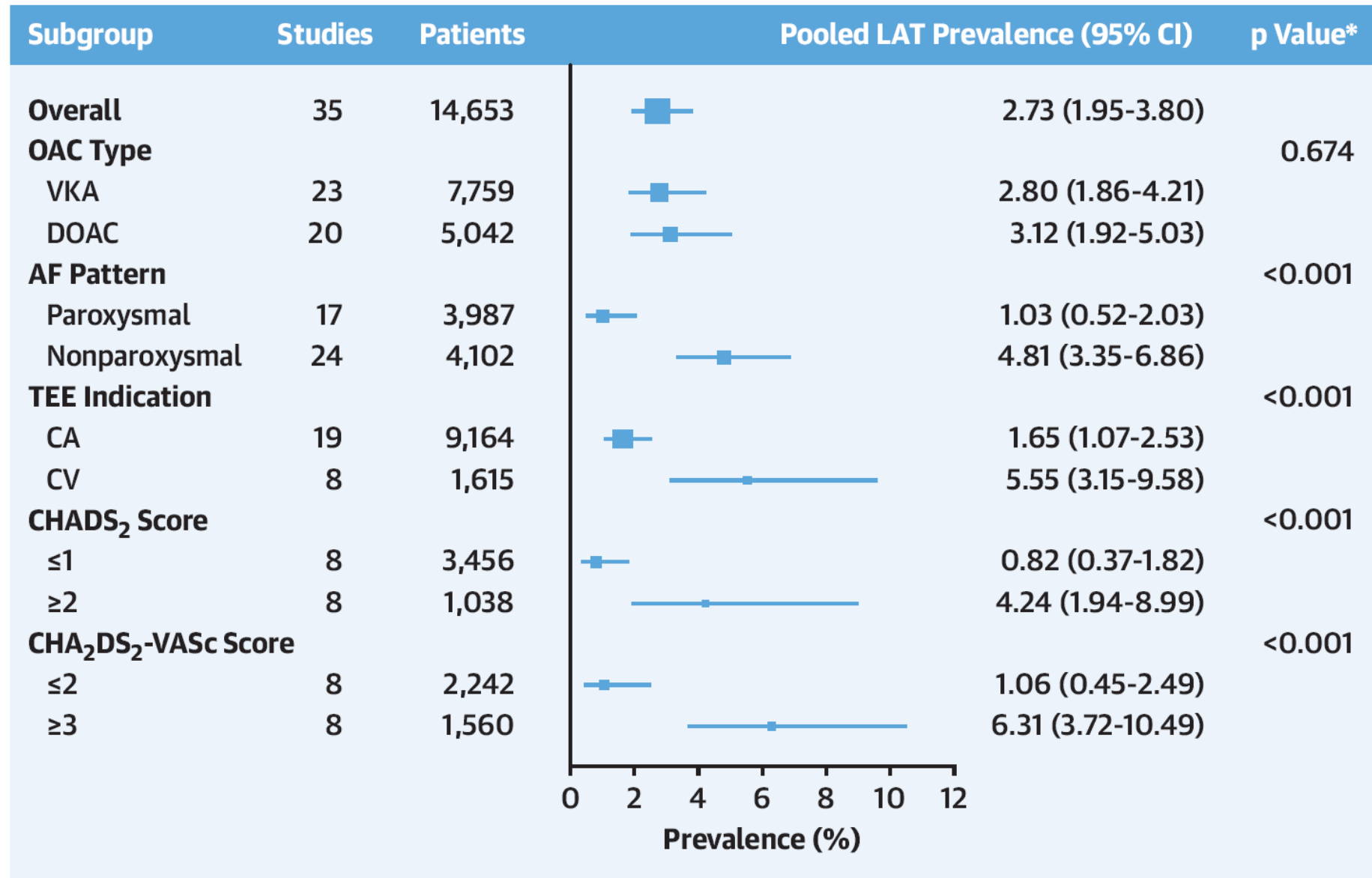
Their residual stroke risk is about 2% per year

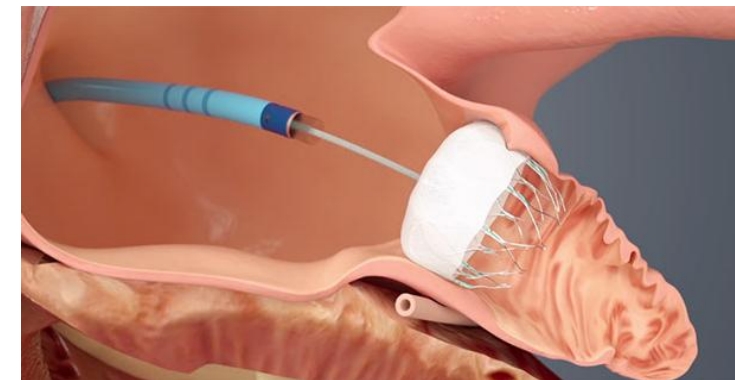
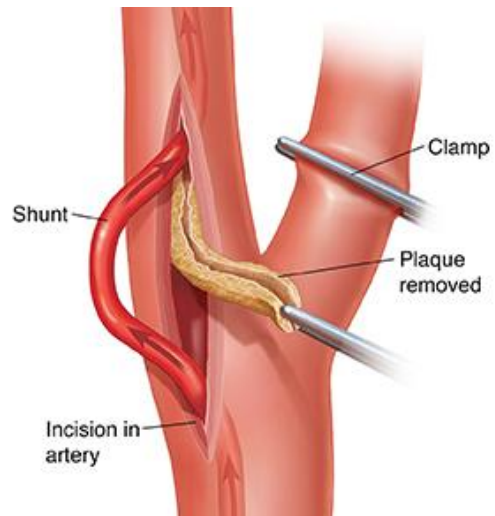
Stroke risk very high in AF patients with prior stroke

Both Groups had
Median CHADS-
VASc
Score of 5 (4-6)



CENTRAL ILLUSTRATION Subgroup Analyses for Left Atrial Thrombus Prevalence in Anticoagulated Patients With Atrial Fibrillation/Atrial Flutter

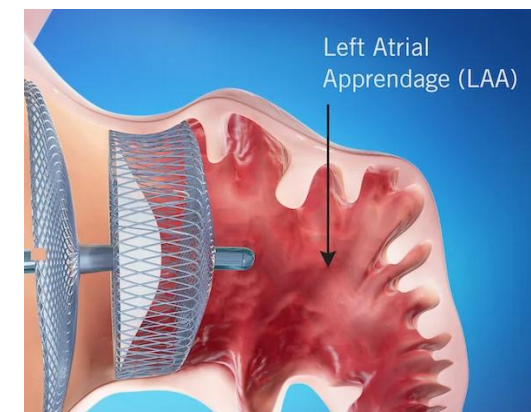
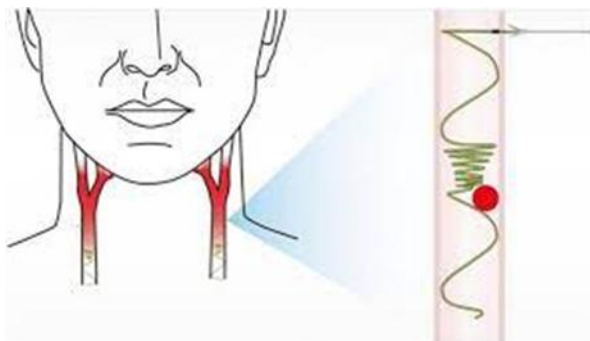




LAAOS

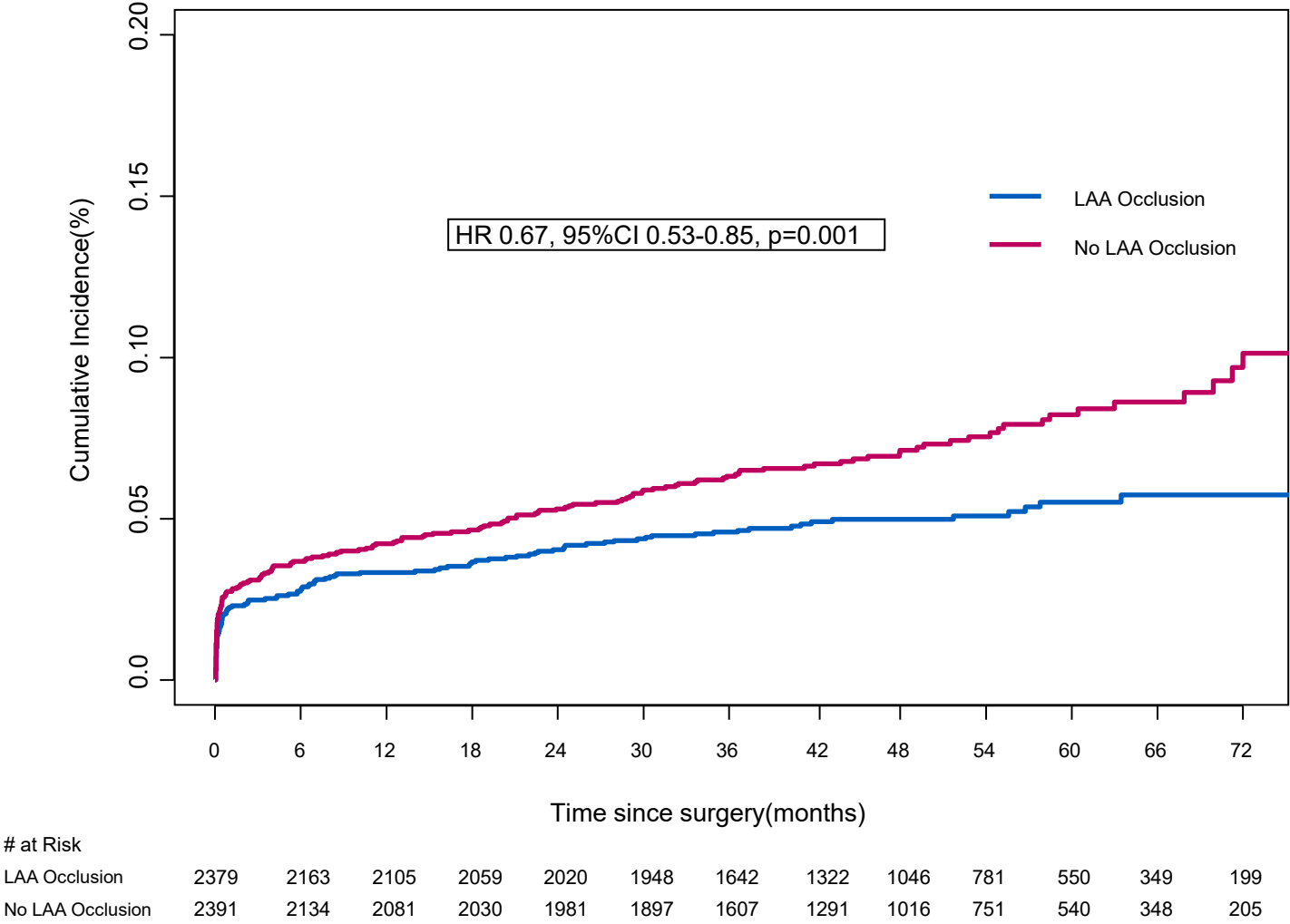
Left Atrial Appendage Occlusion Study 4

Combination Medical and Mechanical Therapy



LAAOS-3: Stroke or Systemic Embolism

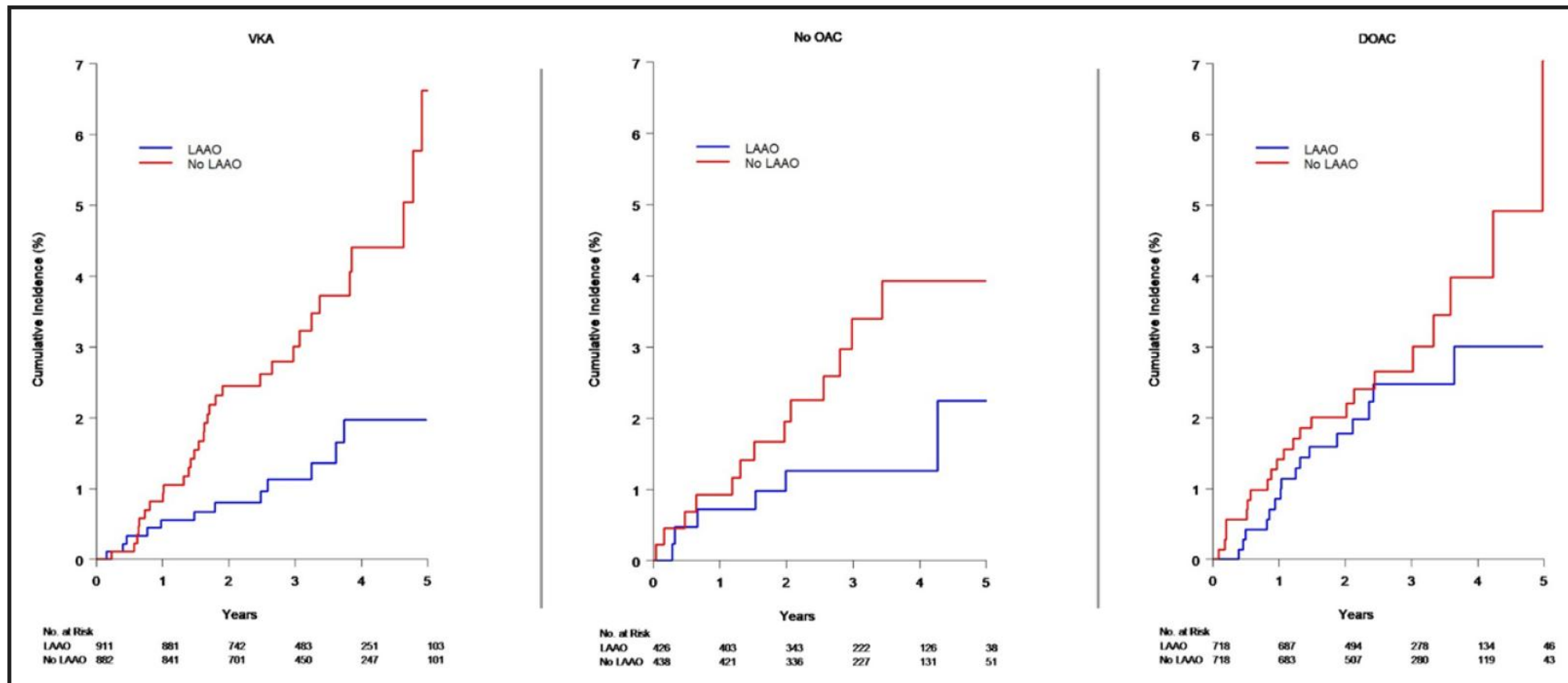
RP Whitlock,
NEJM 2021



Oral Anticoagulation Use and Left Atrial Appendage Occlusion in LAAOS III

Stuart J. Connolly^{ID}, MD; Jeff S. Healey^{ID}, MD; Emilie P. Belley-Cote^{ID}, MD, PhD; Kumar Balasubramanian, MSc; Domenico Paparella^{ID}, MD; Kathryn Brady^{ID}; Wilko Reents^{ID}, MD; Bernhard C. Danner, MD; P.J. Devereaux^{ID}, MD, PhD; Mukul Sharma^{ID}, MD; Chinthanie Ramasundarahettige; Salim Yusuf^{ID}, DPhil; Richard P. Whitlock^{ID}, MD, PhD

Circulation 2023



Rationale for LAAOS-4: Overview of Key Points

1. About **25%** of all AF patients have non-paroxysmal AF and CHA₂DS₂-VASc score of ≥ 4
2. Their residual stroke risk is **2.0%** per year; approximately 10% at 5 years
3. Based on LAAOS-3, LAAO with Watchman-FLX is likely to reduce this risk by **30-40%**

LAAOS-4 Design

