Atrial Fibrillation & Stroke Prevention

Risk Stratification, Prevention Strategies, Emerging Evidence, & Knowledge Gaps
(Neurologist Perspective)

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Objectives

1. Evaluate stroke risk stratification tools including performance metrics & limitations

2. Understand stroke prevention strategies: anticoagulation, timing after stroke, alternatives

3. Introduce emerging approaches and select knowledge gaps in AF-related stroke prevention

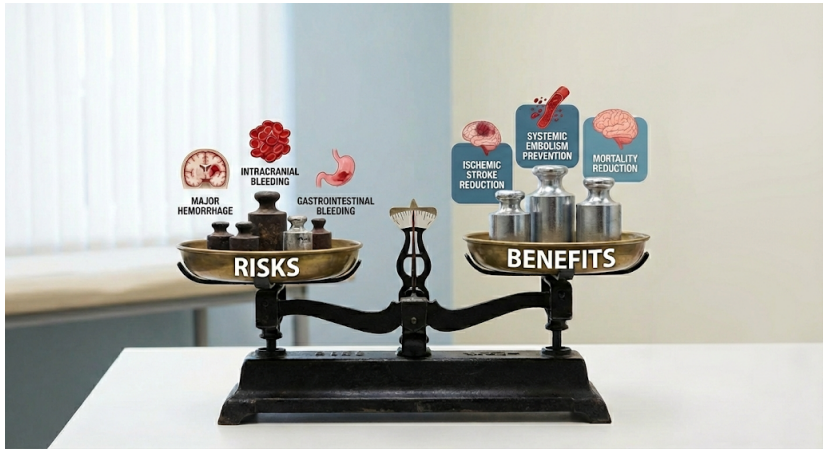
Clinical Risk Stratification

AF & Stroke Risk

AF ↑ stroke risk ~5X

- Absolute risk varies widely

Anticoagulation ↓ stroke risk ~60-70%, but ↑ bleeding



Decision Framework & Treatment Threshold

Net Clinical Benefit = stroke risk reduction – major hemorrhage risk increase

Circulation. 2023 Dec 5;148(23):e1-e125.
Image generated with Google Gemini

CHA_2DS_2-VASc Risk Score

TABLE 4 CHA_2DS_2-VASc Score for Prediction of Stroke in Atrial Fibrillation Patients

C	Congestive heart failure	1
H	Hypertension (>140/90 mm Hg)	1
A	Age ≥75 yrs	2
D	Diabetes mellitus	1
S_2	Prior TIA or stroke	2
V	Vascular disease (MI, aortic plaque, and so on)	1
A	Age 65-74 yrs	1
Sc	Sex category (female = 1 point)	1

MI = myocardial infarction; TIA = transient ischemic attack.

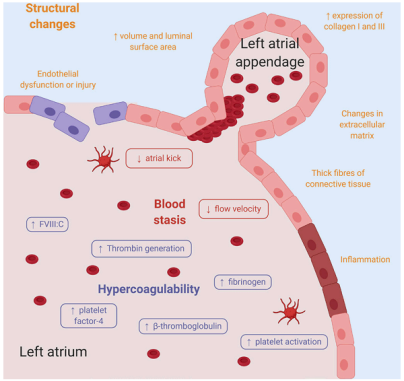
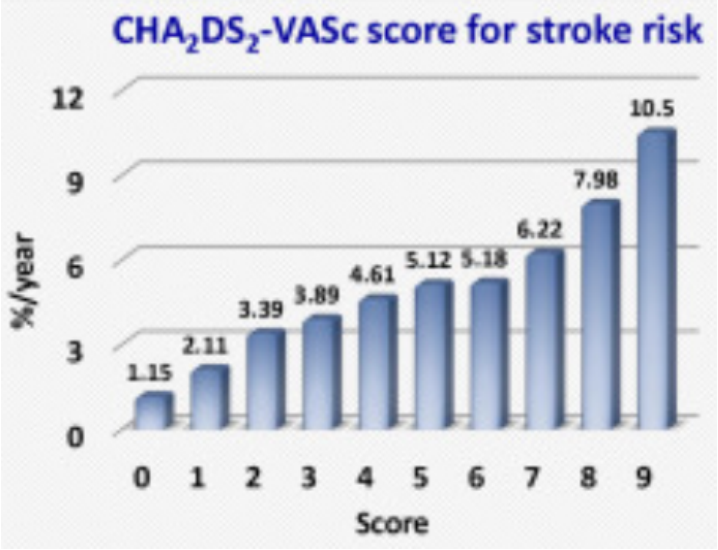


Figure 1 Effects of atrial fibrillation on the various elements of Virchow's triad (hypercoagulability, structural changes and blood stasis).



J Am Coll Cardiol. 2020 Apr 14;75(14):1689-1713.
Eur Heart J. 2012 Jun;33(12):1500-1510.
Circulation. 2023 Dec 5;148(23):e1-e125.
Heart. 2020 Oct;106(19):1463-1468.

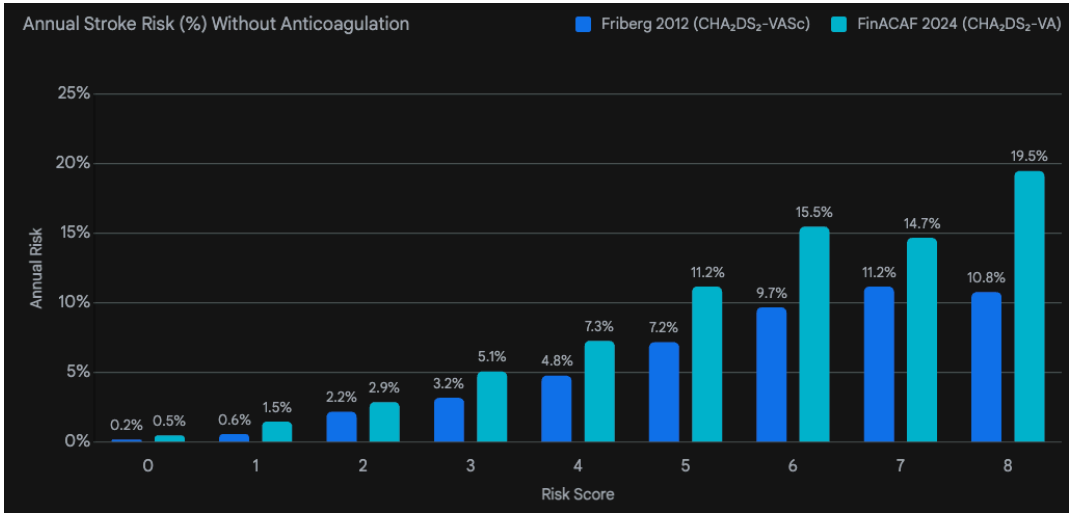
CHA_2DS_2-VASc: Performance Characteristics

Discrimination & Calibration

- C-statistic: ~0.65 (modest)
- Variable across populations
- Overestimates in certain subgroups

Limitations

- Binary variables (loss of granularity)
- No AF burden/type or renal function



Why is it clinically useful?

- High negative predictive value (identifies true "low risk" from "not low risk") → is risk low enough to avoid anticoagulation?
- Simplicity → clinical factors, reproducible, scalable

2024 ESC: CHA_2DS_2-VA

- Female sex is modifier (not independent risk factor)

Circulation. 2012 May 15;125(19):2298-307.
Lancet Reg Health Eur. 2024 Jun 10;43:100967.

Bleeding Risk

HAS-BLED Score

Score ≥3 = High hemorrhage risk

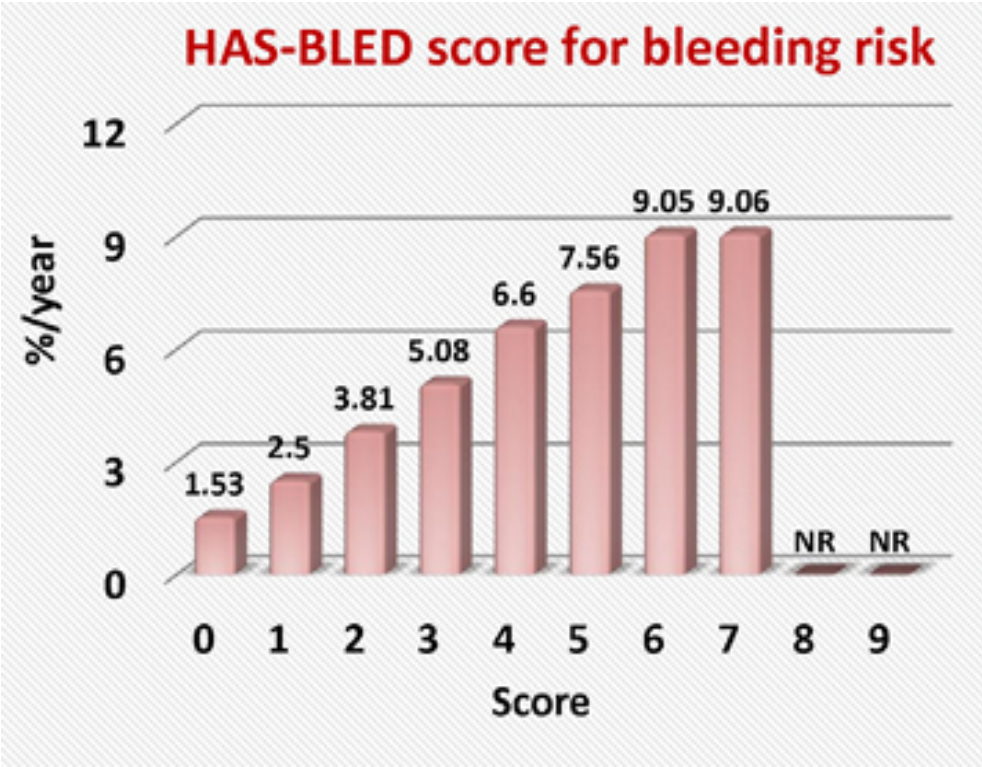
C-index ~0.6

High hemorrhage risk ≠ "Don't anticoagulate"
- Identify & address modifiable risk factors
- Guide monitoring intensity

Often hemorrhage risk < stroke risk

* Developed in warfarin treatment era

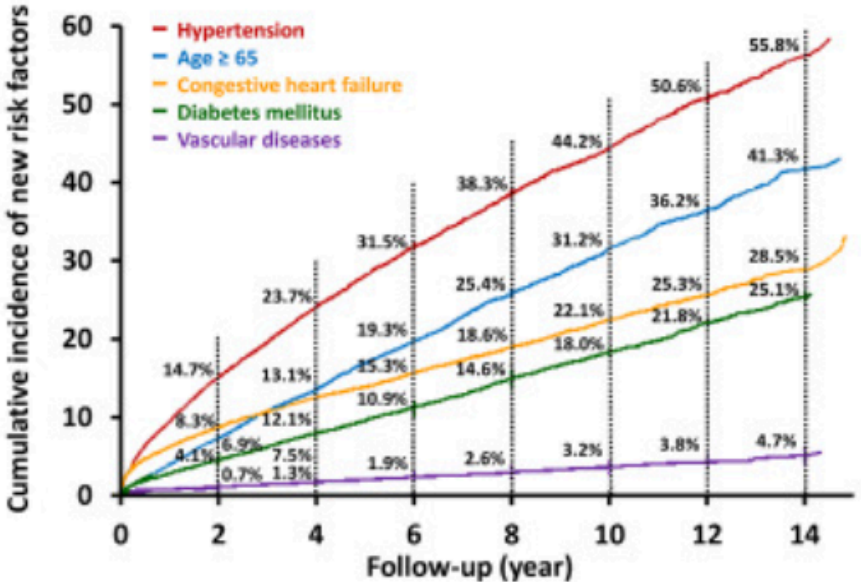
Condition	Points
H – Hypertension	1
A – Ab(N) liver/renal	1 point each
S – Stroke	1
B – Bleeding	1
L – Labile INRs	1
E – Elderly (>65)	1
D – Drugs or ETOH	1 point each



Am J Med. 2020 Oct;133(10):1195-1202.e2.
Lancet Reg Health Eur. 2024 Feb 1;37:100797.
Chest. 2010 Nov;138(5):1093-1100.
Eur Heart J. 2012 Jun;33(12):1500-1510.

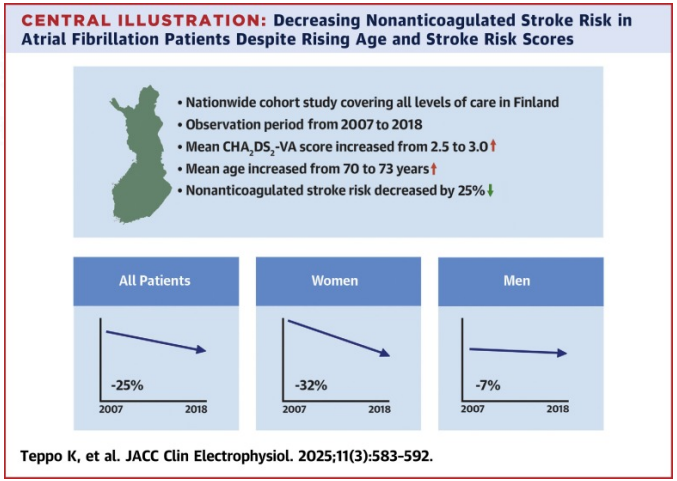
Risk is Dynamic

Cumulative incidence of new stroke risk factors for patients with a baseline CHA_2DS_2-VASc score of 0 (M) or 1 (F)



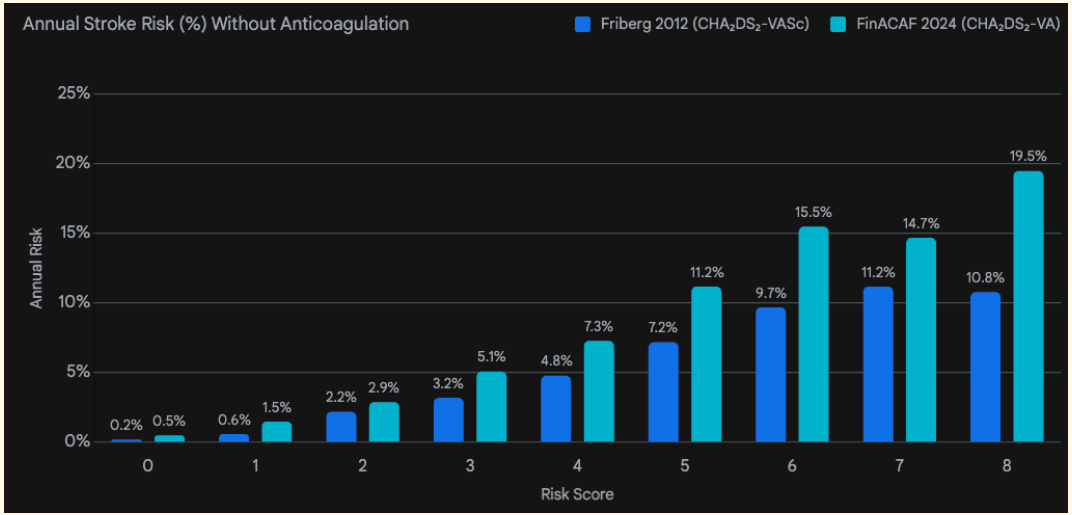
Multimorbidity → Δ net clinical benefit of treatment

- Age
- Accumulation risk factors for stroke & hemorrhage



J Am Coll Cardiol. 2018;71(2):122-132.
Thromb Haemost. 2018 Jul;118(7):1296-1304.
Eur Heart J. 2024 May 27;45(20):1819-1827.

💬 Discussion Question



FinACAF 2024 cohort shows higher stroke rates at each score compared to Friberg 2012 - what factors contribute to temporal shift?

1. Competing risks from AC uptake
2. Survivor bias
3. AF detection changes
4. Comorbidity burden shift
5. Methodological differences

Lancet Reg Health Eur. 2024 Jun 10;43:100967.

Anticoagulation

- DOACs > warfarin
- Among DOACs → no direct comparative trials
- Apixaban preferred (↓ hemorrhage risk)
- Warfarin → mechanical valves, mitral stenosis

* Aspirin alone NOT recommended

DOACs vs. Warfarin

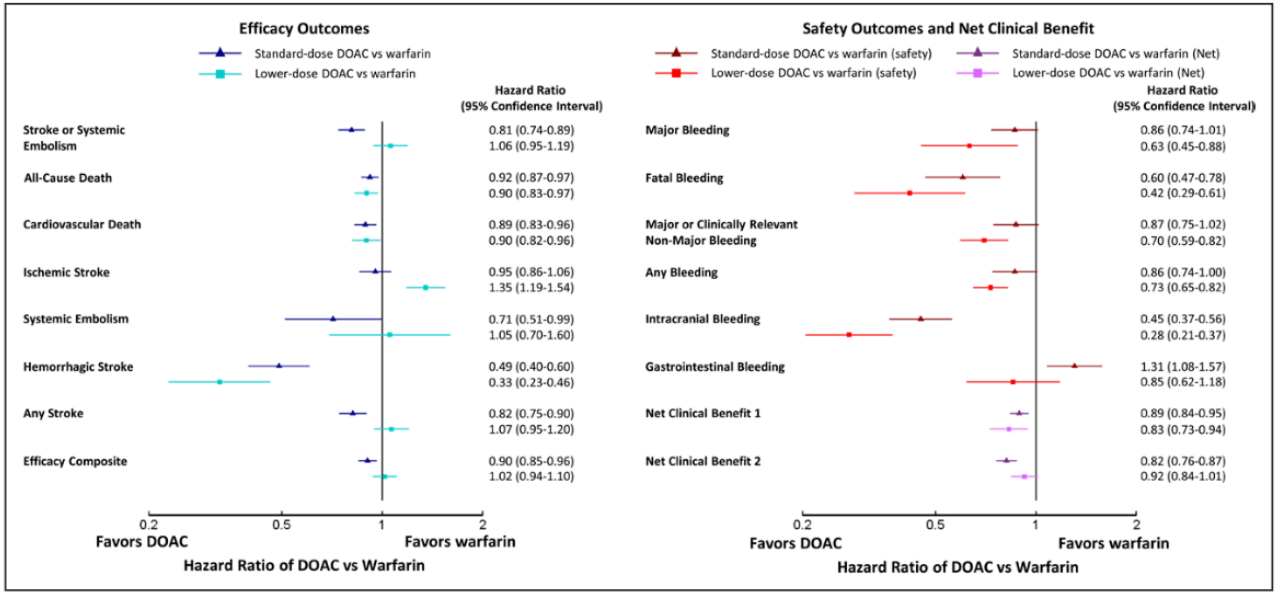
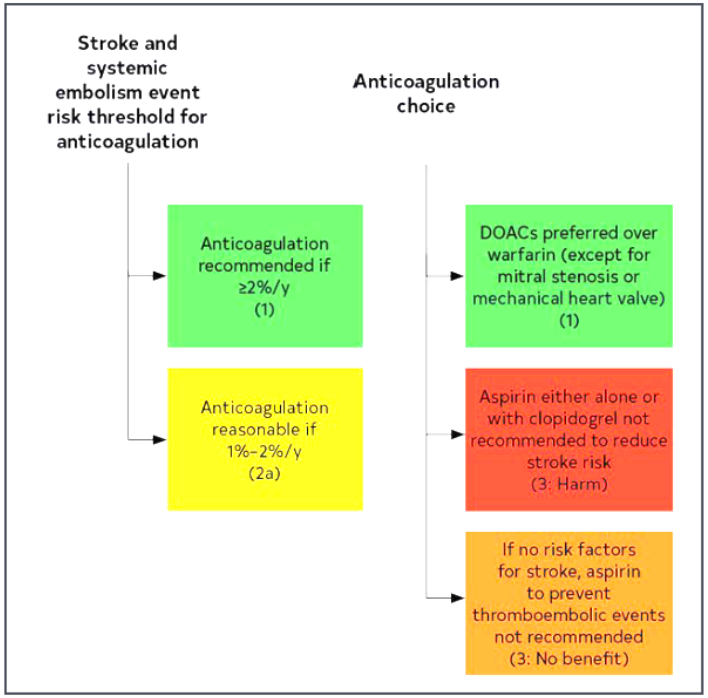


Figure 1. Comparison of standard-dose and lower-dose direct oral anticoagulants vs warfarin for efficacy, safety, and net clinical benefit outcomes.

Circulation. 2022 Jan 25;145(4):242-255.
Eur J Epidemiol. 2021 Aug;36(8):793-812.

Comprehensive Atrial Fibrillation Management



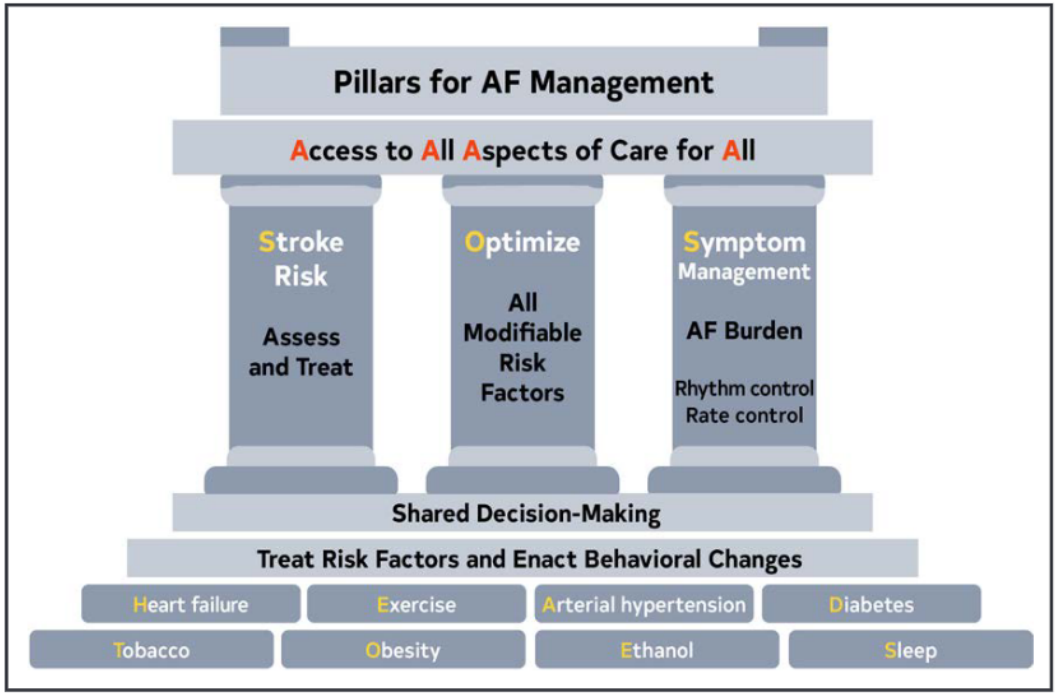


Figure 10. Antithrombotic Options in Patients With AF.

Timing After Acute Ischemic Stroke

CATALYST meta-analysis

Individual participant data meta-analysis of 4 trials (TIMING, ELAN, OPTIMAS, START)

- Population: acute ischemic stroke + AFib
- Treatment/Comparator: DOAC initiation ≤4 days (early) or ≥5 days (late)
- Outcome: (composite) recurrent ischemic stroke or symptomatic ICH in ≤ 30 days

→ Early DOAC initiation reduced risk
  - Limited generalizability to severe stroke, hemorrhagic transformation

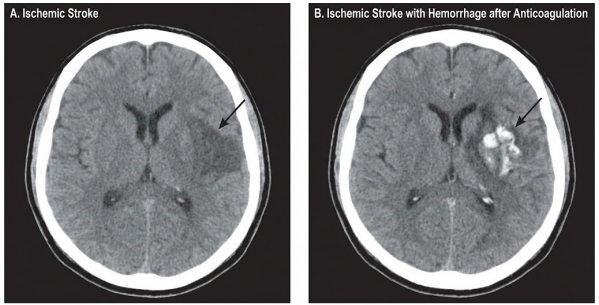


Figure 1. Comparison of head CTs: (A) Acute ischemic stroke showing hypodensity. (B) Hemorrhagic transformation within the ischemic region following anticoagulation therapy, indicated by hyperdense blood

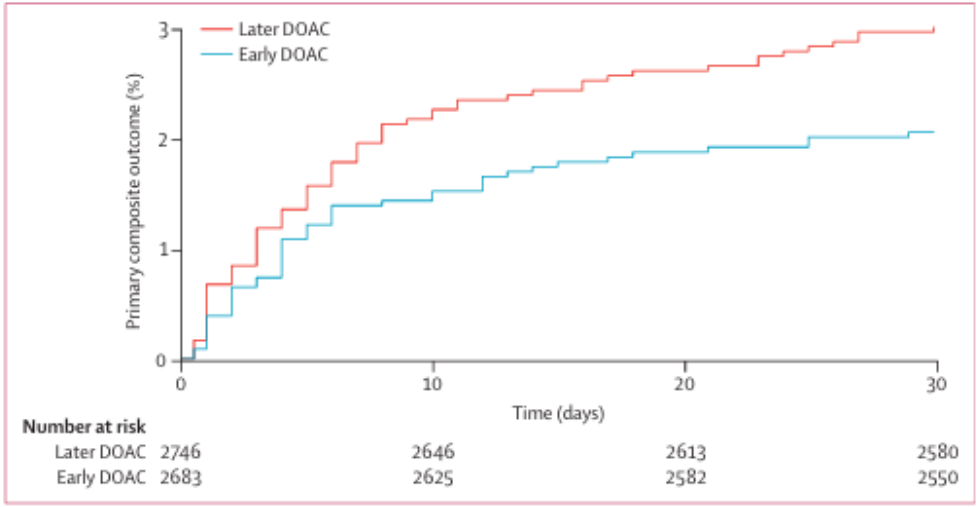


Figure 2: **Primary composite outcome at 30 days by DOAC initiation timing (cumulative hazard)**
Log-rank p value: 0·034. DOAC=direct oral anticoagulant.

- Small-moderate infarct → ≤ 2-4 days
- Large infarct → 1-2 weeks

Lancet. 2025 Jul 5;406(10498):43-51.
Lancet Neurol. 2024 Apr;23(4):404-417.
Image generated with Google Gemini

Low-Burden AF

- Asymptomatic
- Device-detected
- 6 minutes – 24 hours

- Lower stroke risk than clinical AF
- AC decisions require more nuanced shared decision-making

Table. Comparison of DOAC vs No Anticoagulation in Randomized Clinical Trials

Characteristic	AVERROES[7,8]	NOAH-AFNET 6[2]	ARTESIA[3]
Mean age, y	70	78	77
AF classification	Paroxysmal (27%) Persistent (20%) Permanent (52%)	>6 min Atrial high-rate event	6 min to 24 h of Subclinical AF
CHA_2DS_2Vasc score	3.2[a]	4[b]	3.9[a]
Treatment arm	Apixaban	Edoxaban	Apixaban
Control arm	Aspirin	Placebo	Aspirin
Annualized risk of stroke or systemic embolism without DOAC, %	3.7%[c]	1.07[c]	1.02[c]
Annualized risk of stroke or systemic embolism with DOAC, %	1.6[c]	0.86[c]	0.64[c]
No. needed to treat	48	476	263
Annualized risk of major bleeding without DOAC, %	3.8[c]	1.00[c]	0.94[d]
Annualized risk of major bleeding on DOAC, %	4.5[c]	2.09[c]	1.71[d]
No. needed to harm	143	92	130

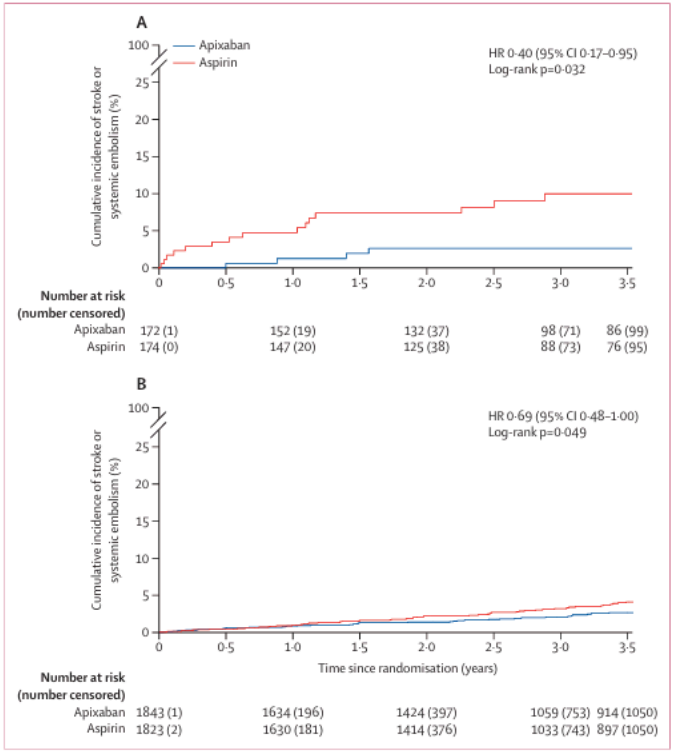


Figure 2: **Time to stroke or systemic embolism during 3·5 years of follow-up in participants with a history of stroke or transient ischaemic attack (A) and those without (B) according to treatment assignment (apixaban *vs* aspirin)**

HR=hazard ratio.

JAMA Neurol. 2024 Jun 1;81(6):573-574.
Lancet Neurol. 2025 Feb;24(2):140-151.

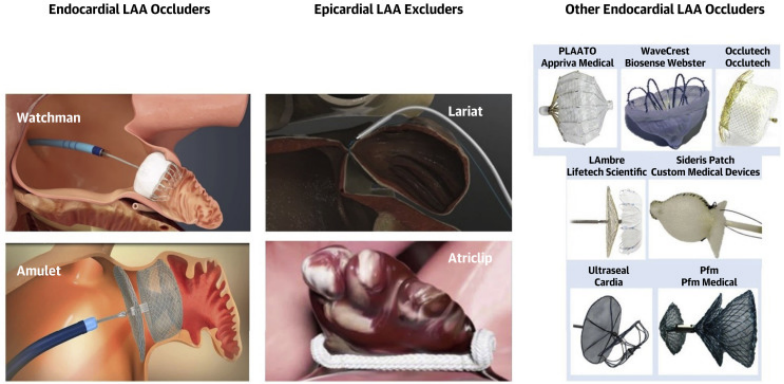
Left Atrial Appendage Occlusion (LAAO) - Percutaneous

Rationale

~80-90% of AF thrombi form in the LAA

Occlude LAA → eliminate source of most thromboembolism → Avoid long-term anticoagulation

- Considered for ABSOLUTE contraindication to long-term AC → NOT first-line alternative to DOACs
- Non-inferiority of LAAO to DOACs uncertain (high-risk groups)
- Requires post-procedure anticoagulation (or dual AP treatment)



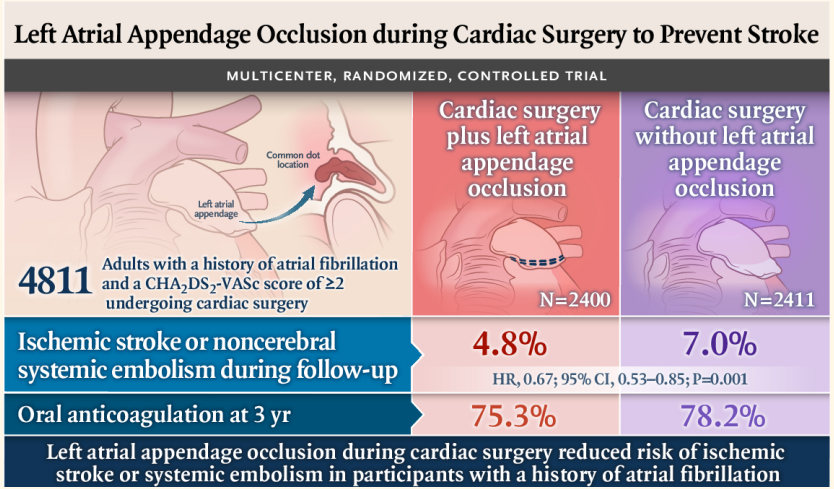
Summary Plot of Clinical Outcomes

	LAAC	OAC	Risk Ratio	95% CI	p Value
All Stroke or SE	6.1% (57/933)	5.8% (34/583)	0.98	0.65–1.48	0.92
Ischemic Stroke or SE	5.6% (52/933)	3.6% (21/583)	1.48	0.89–2.46	0.13
Ischemic Stroke or SE >7 days	4.7% (44/933)	3.6% (21/583)	1.27	0.76–2.14	0.37
Hemorrhagic Stroke	0.5% (5/933)	2.4% (14/583)	0.22	0.08–0.58	0.002
Cardiovascular Mortality	5.4% (50/933)	8.2% (48/583)	0.65	0.44–0.95	0.03
All-Cause Mortality	14.3% (133/933)	17.8% (104/583)	0.78	0.62–0.99	0.04
Major Bleeding	10.5% (98/933)	11% (64/583)	0.89	0.66–1.20	0.46
Nonprocedure-Related Major Bleeding	6.2% (58/933)	11.1% (65/583)	0.53	0.38–0.74	0.0002

J Am Coll Cardiol. 2020 Apr 14;75(14):1689-1713.
J Am Heart Assoc. 2021 Nov 2;10(21):e022274
J Am Coll Cardiol. 2022 Jan 4;79(1):1-14.

💬 Discussion Question

Left Atrial Appendage Occlusion (LAAO) - Surgical



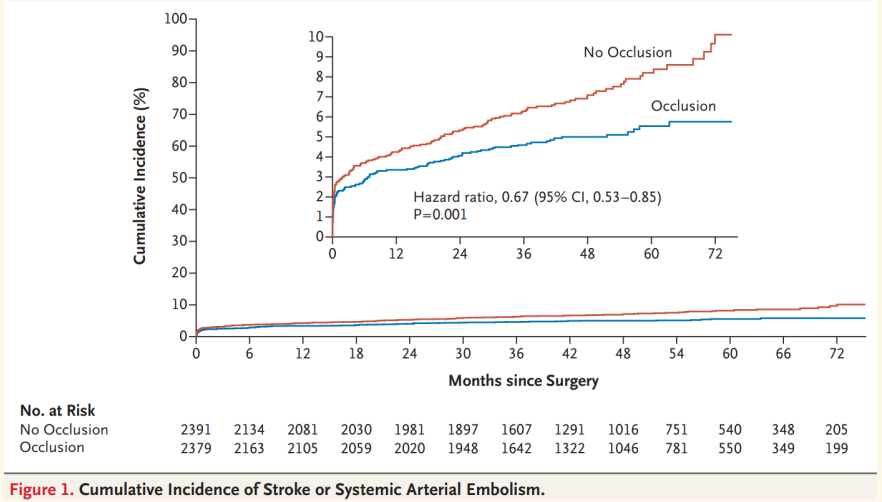


Figure 1. Cumulative Incidence of Stroke or Systemic Arterial Embolism.

Mean $CHADS_2VASc$ ~4

~77% on AC @ 3 y

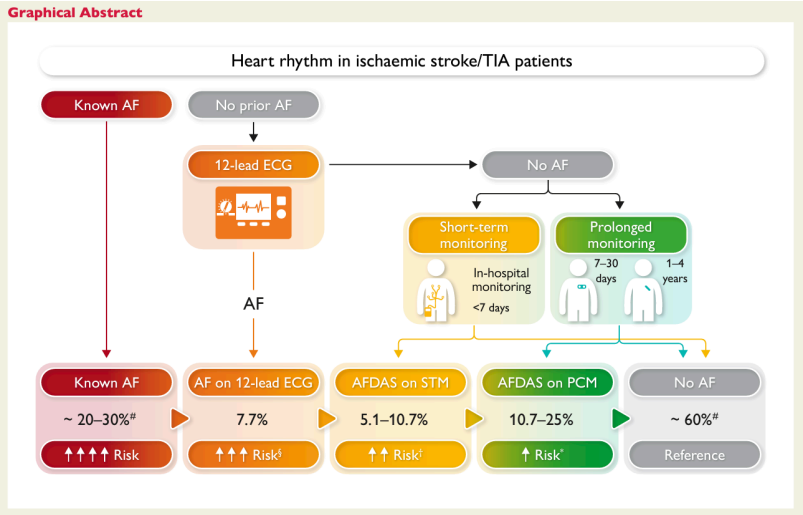
Why was AC continued in most?
How should findings be interpreted?

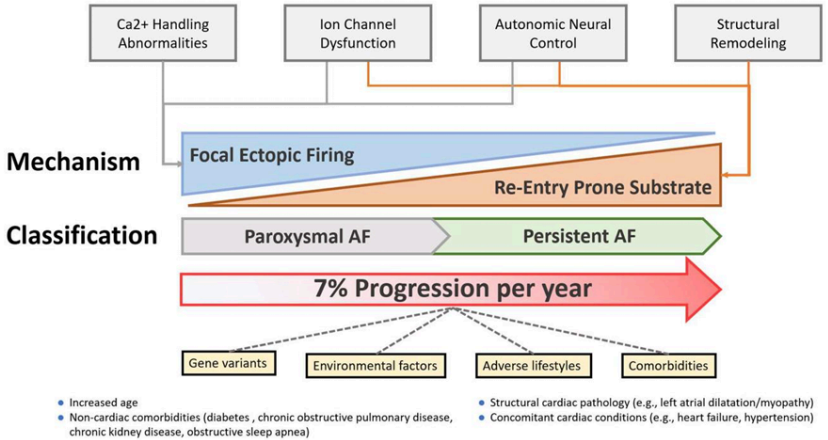
- Lack of clinical equipoise
- Real-world uncertainty
- How were 23% that stopped AC different?

→ Supports LAAO + AC may further reduce stroke risk

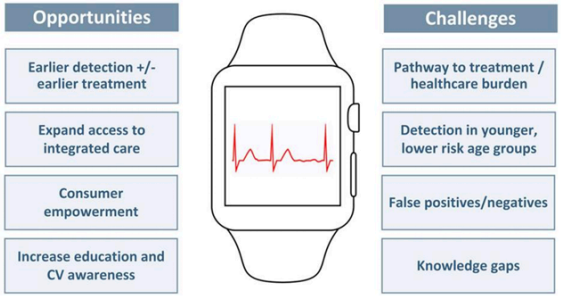
N Engl J Med. 2021 Jun 3;384(22):2081-2091.

Knowledge Gap: Detection – Outcome Disconnect



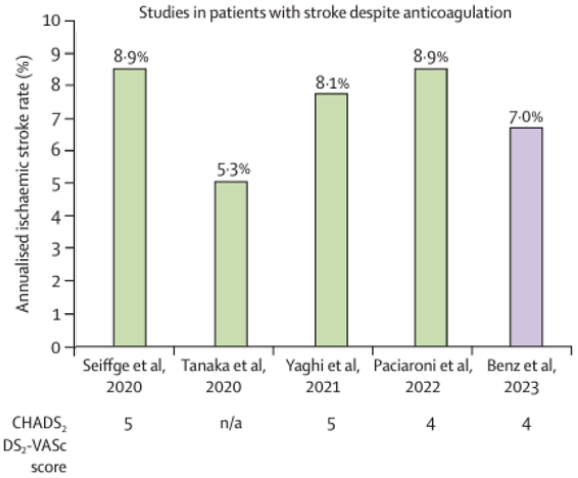


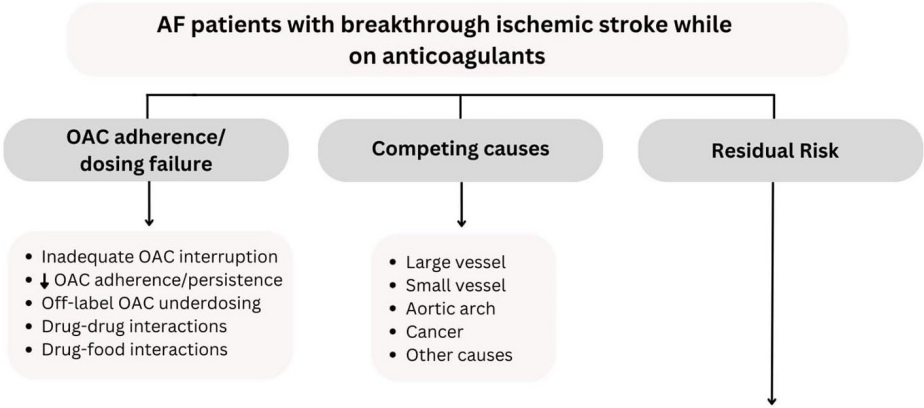
- Screening ↑ detection, BUT early detection ≠ ↓ stroke/mortality
- Low-burden → higher burden
- Treatment threshold uncertain

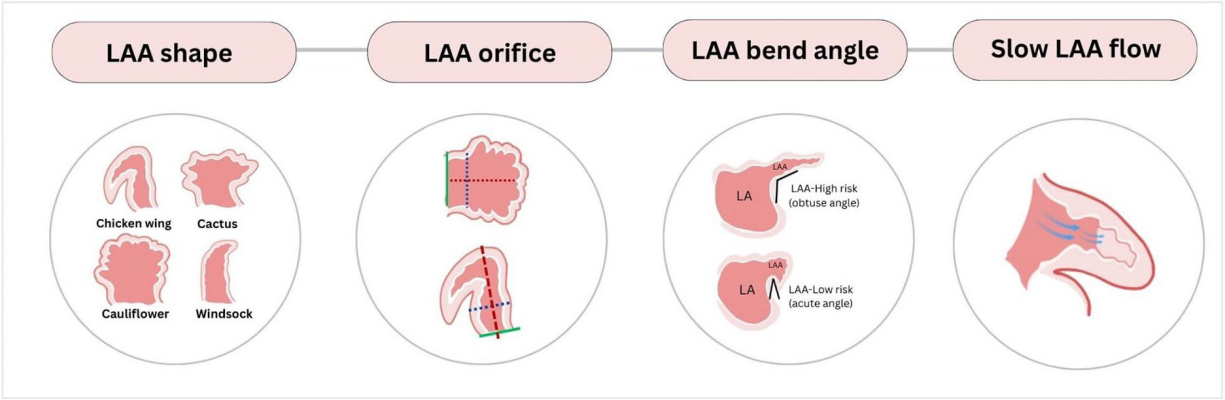


Eur Heart J. 2026 Jan 7;47(2):170-187.
Eur Heart J. 2024 Feb 1;45(5):396-398.

Knowledge Gap: Recurrent Stroke Despite AC





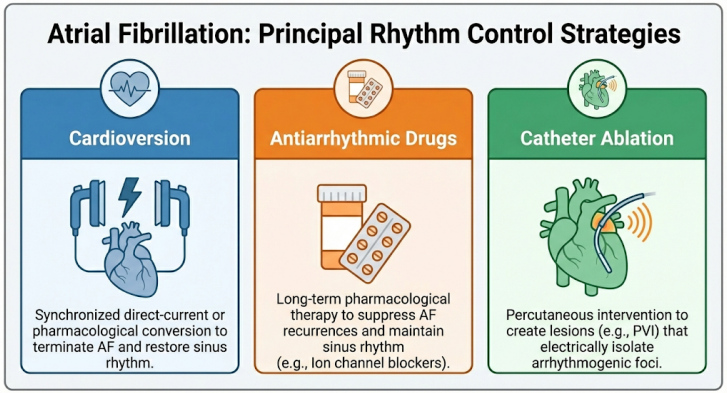


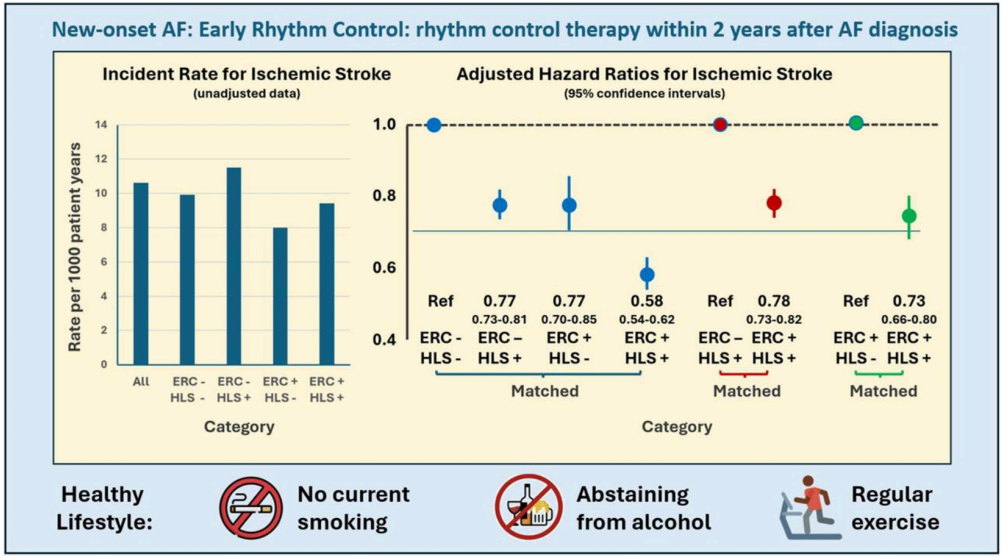
🛑 Switching DOACs or addition of aspirin 🖐️

- LAAO + AC
- Factor XI inhibitors

Lancet Neurol. 2024 Apr;23(4):404-417.
Int J Stroke. 2025 Apr;20(4):385-400.

Knowledge Gap: Early Rhythm Control





- ↓ stroke risk (by ↓ AF burden)
- Successful restoration of sinus rhythm ≠ discontinuation of AC
  - High risk of recurrence
  - Subgroup? – early onset, low-burden, low CHA_2DS_2VASC

Int J Stroke. 2025 Apr;20(4):385-400.
Eur Heart J. 2026 Jan 7;47(2):170-187.
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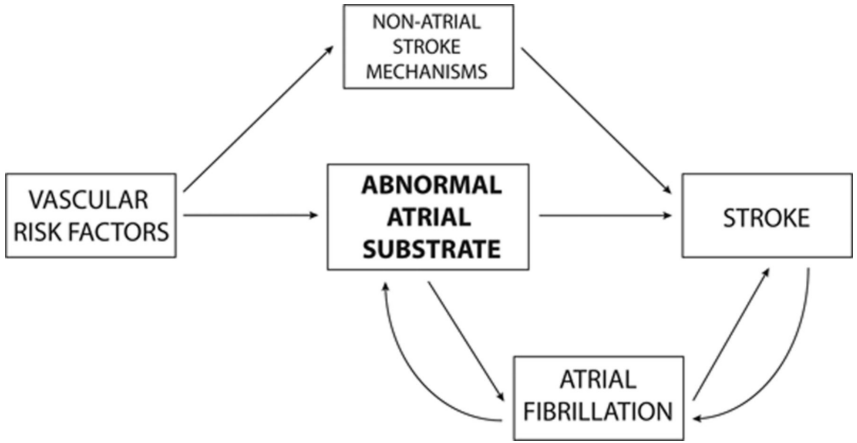
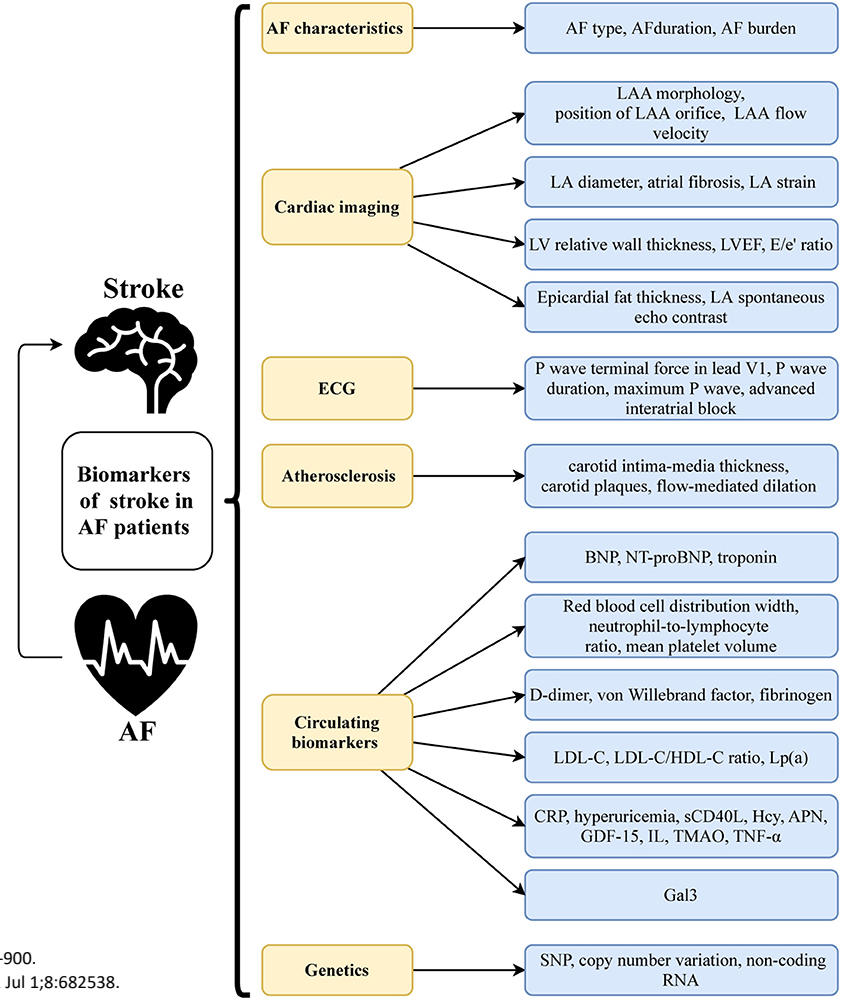
Knowledge Gap: Risk (& Therapeutic) Biomarkers



- Cardiac Structural
- Electrophysiologic (EKG markers)
- Circulating (proteins, metabolites)



Stroke. 2016 Mar;47(3):895-900.
Front Cardiovasc Med. 2021 Jul 1;8:682538.

Questions?