Updates in Antithrombotic therapy in Cardiovascular Diseases

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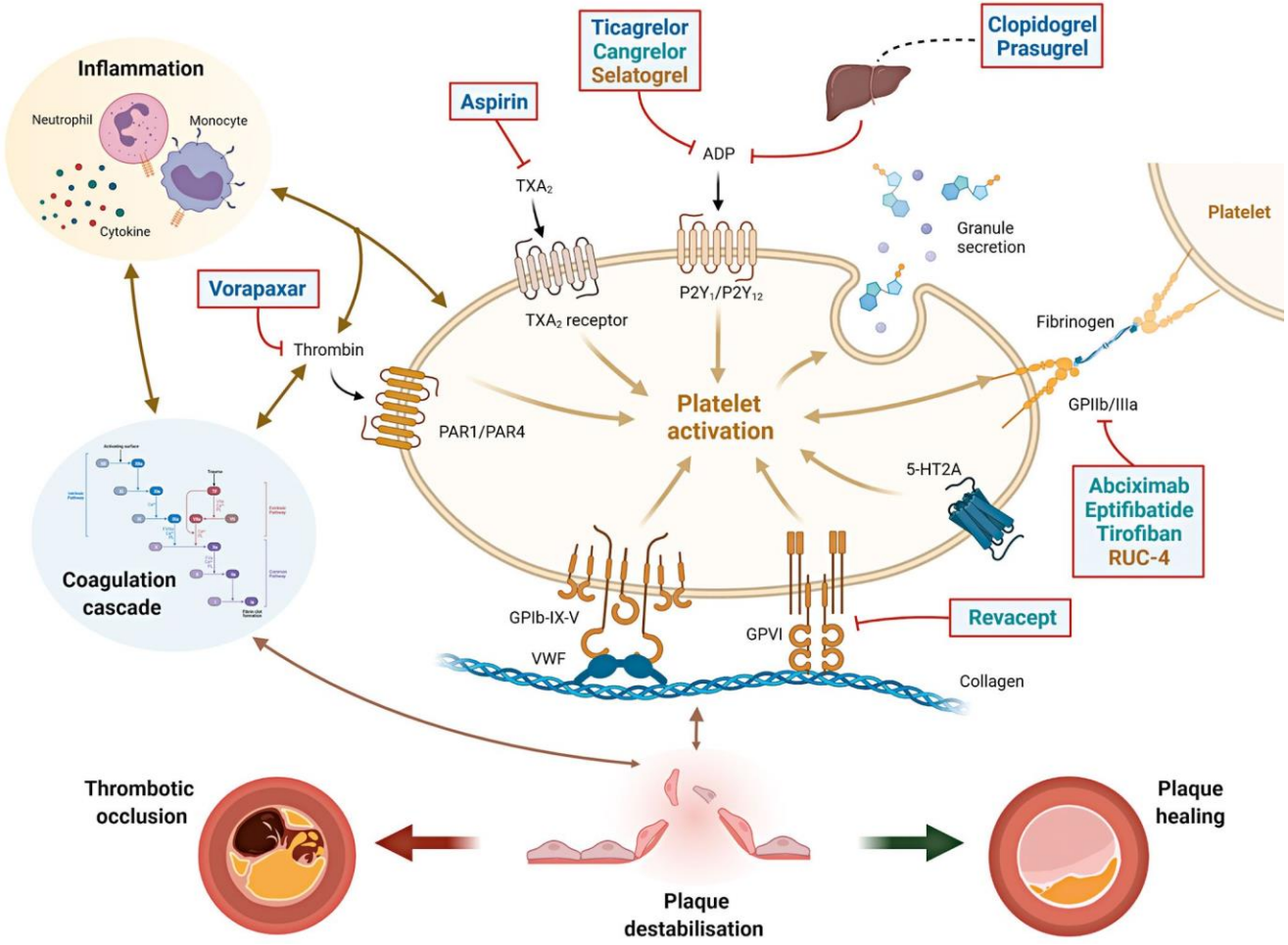
Jeffrey K. Lei, MD
Chief Cardiology Fellow PGY-6

KIRK KERKORIAN SCHOOL OF MEDICINE | UNLV

Learning Objectives

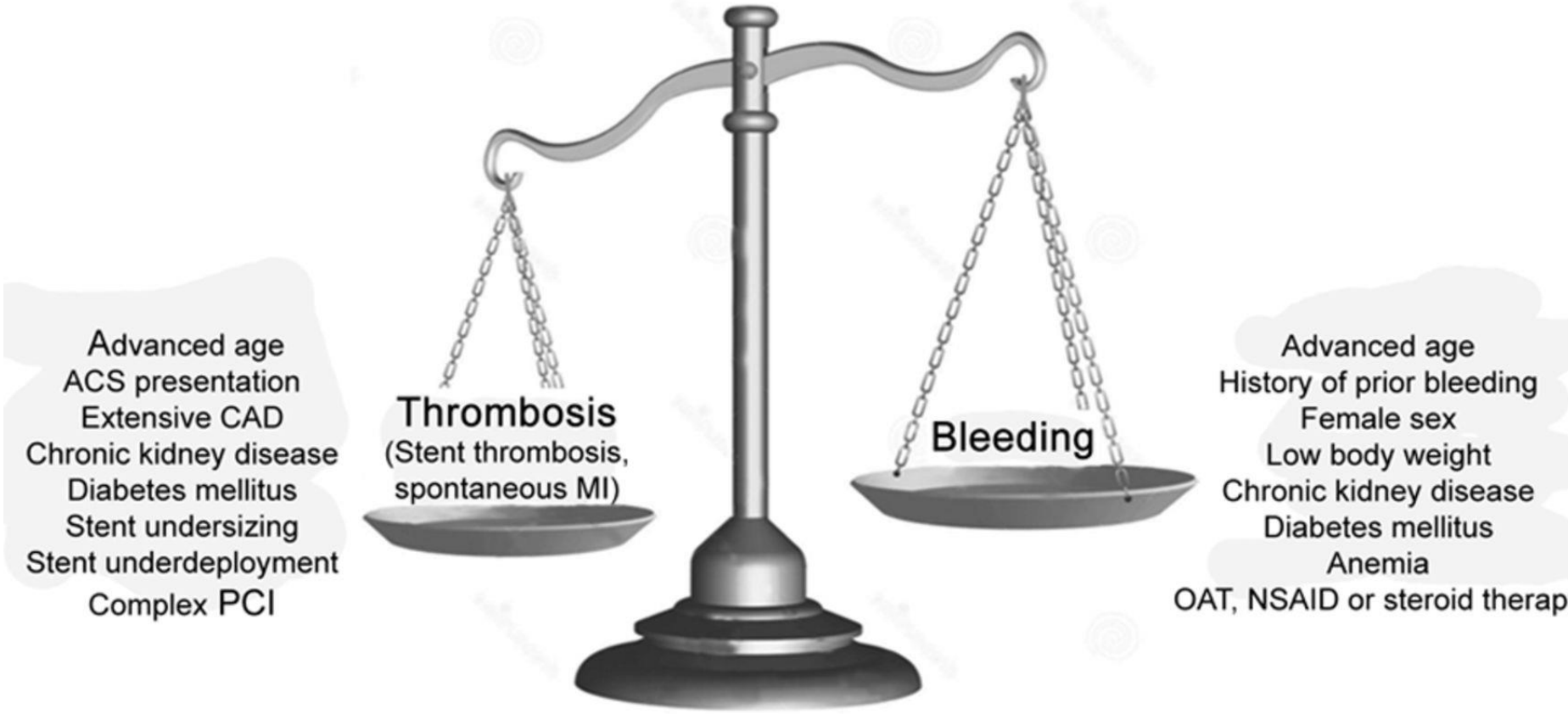
- Review the pharmacology of antithrombotic therapy
- Valvular and non-valvular atrial fibrillation
  - LAAO devices
- Bioprosthetic and mechanical valves
  - TAVR and On-X mechanical valve
- Dual antiplatelet therapy in acute coronary syndrome
- Common scenarios

Back to medical school



Eurointervention. 2022

Balancing the risks and benefits



Levine. Circulation. 2017

Atrial Fibrillation

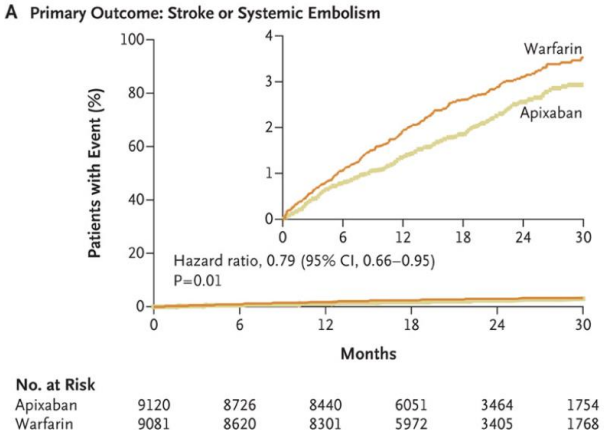
Valvular vs non-valvular Atrial Fibrillation

- Valvular
  - Moderate to severe rheumatic mitral stenosis
  - Mechanical prosthesis
- Non-valvular
  - Men>2; Women >3
- ASA not recommended for stroke prophylaxis

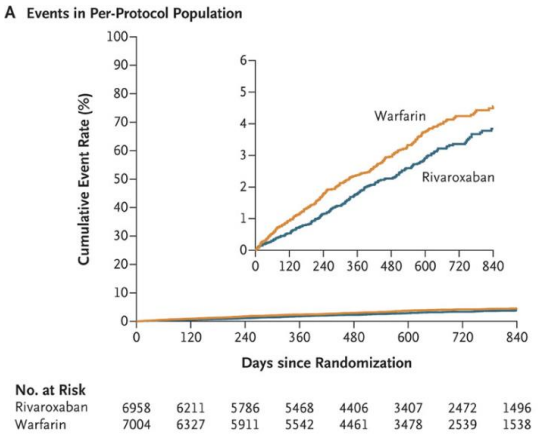
	CHA_2DS_2-VASc risk factor	Points
C	Congestive heart failure	+1
H	Hypertension	+1
A_2	Age 75 years or older	+2
D	Diabetes mellitus	+1
S_2	Previous stroke, transient ischaemic attack or thromboembolism	+2
V	Vascular disease	+1
A	Age 65–74 years	+1
Sc	Sex category (female)	+1

DOACs are preferred over warfarin in non-valvular Afib

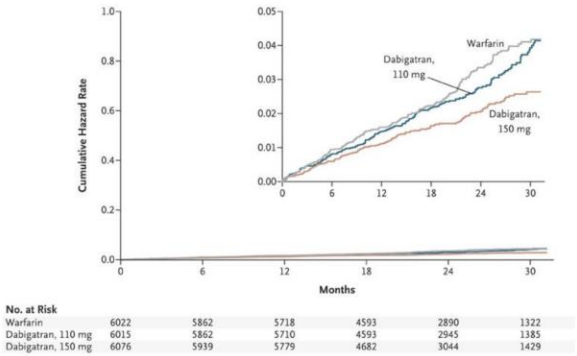
ARISTOTLE



ROCKET-AF



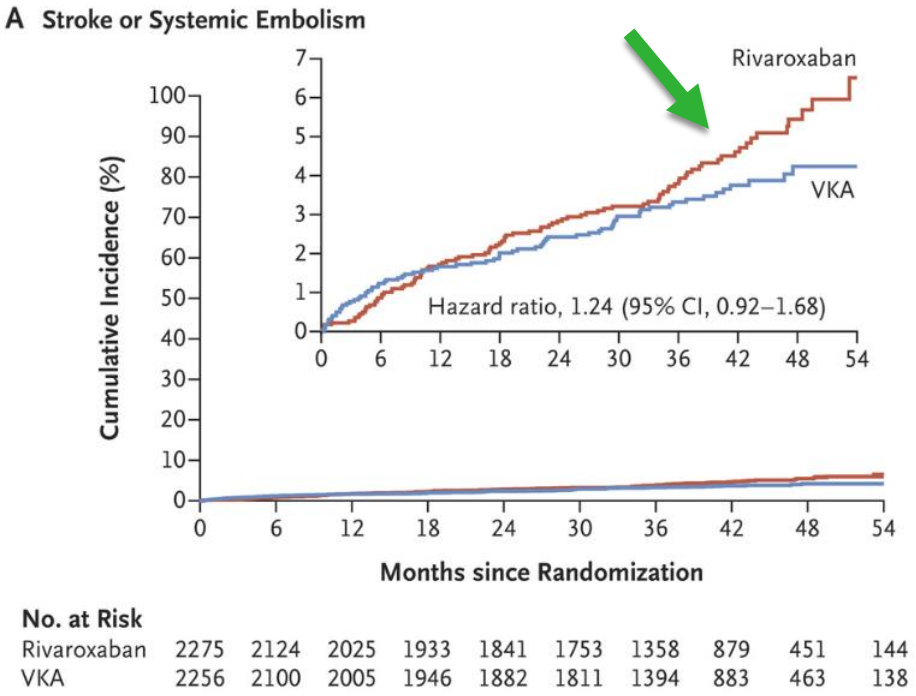
RE-LY

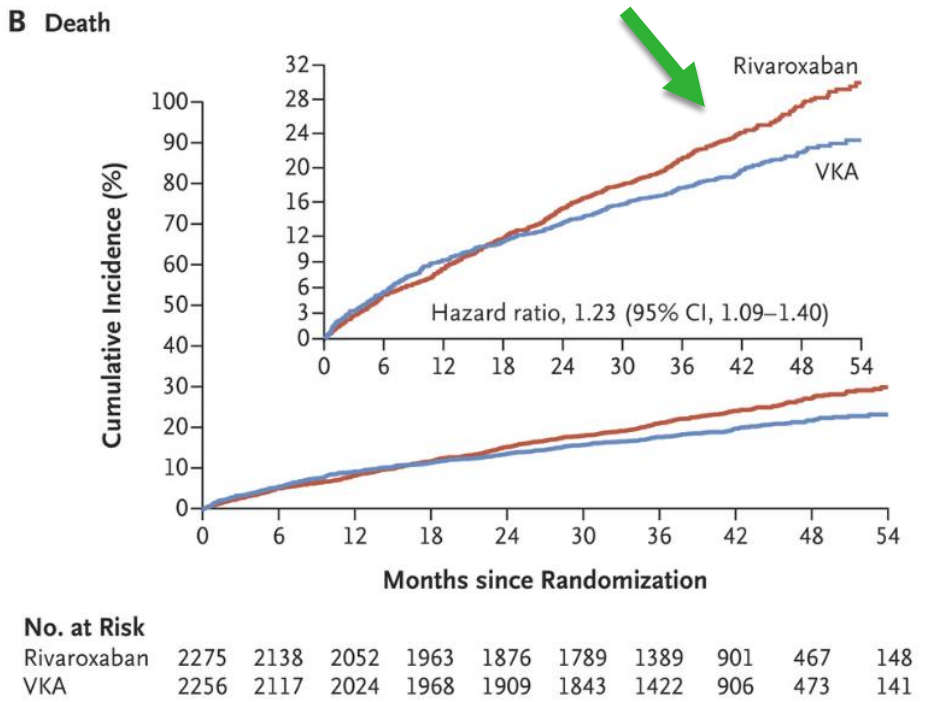


1	B-NR

2. In patients with AF and valve disease other than moderate or greater mitral stenosis or a mechanical heart valve, DOACs are recommended over VKAs.[2-8]

DOACs in mitral stenosis? Not at its prime time





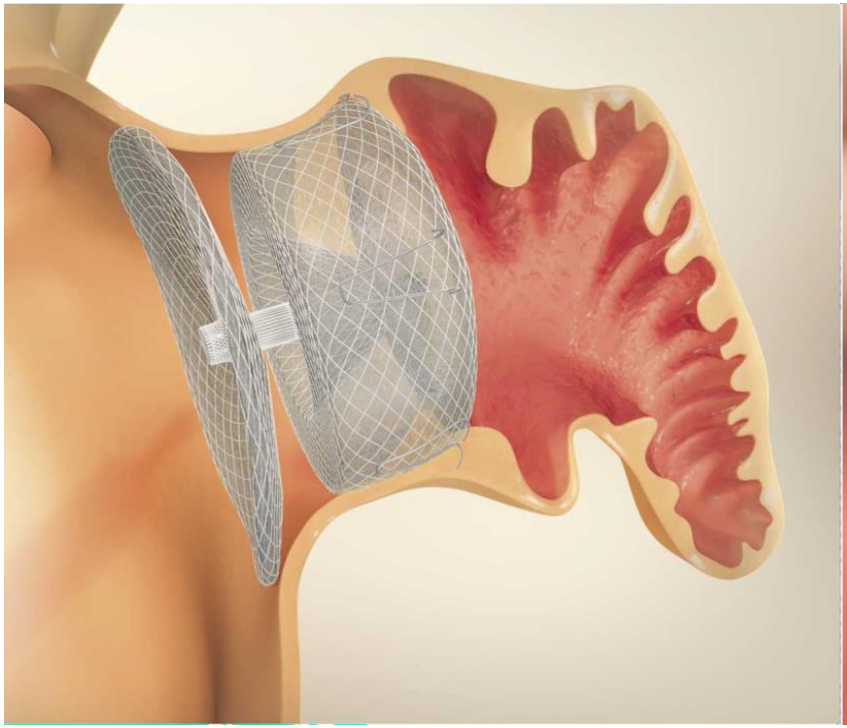
COR	LOE	RECOMMENDATIONS
1	B-R	1. In patients with rheumatic mitral stenosis or mitral stenosis of moderate or greater severity and history of AF, long-term anticoagulation with warfarin is recommended over DOACs, independent of the CHA_2DS_2-VASc score to prevent cardiovascular events, including stroke or death.[1]

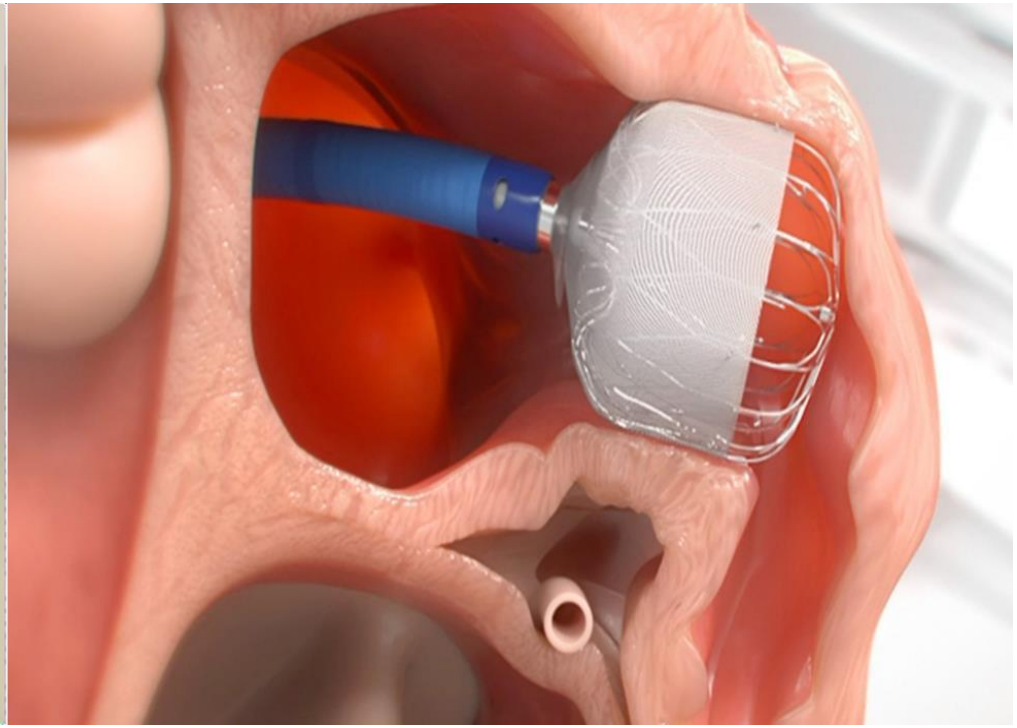
2023 Afib Guideline. ACC; Connolly. NEJM. 2022

Scenarios that you should anticoagulate regardless of CHADSVASC score

- Rheumatic mitral stenosis
- Mechanical prosthesis
- Hyperthyroidism
- Hypertrophic Cardiomyopathy
- After Cardioversion but low CHADSVASC

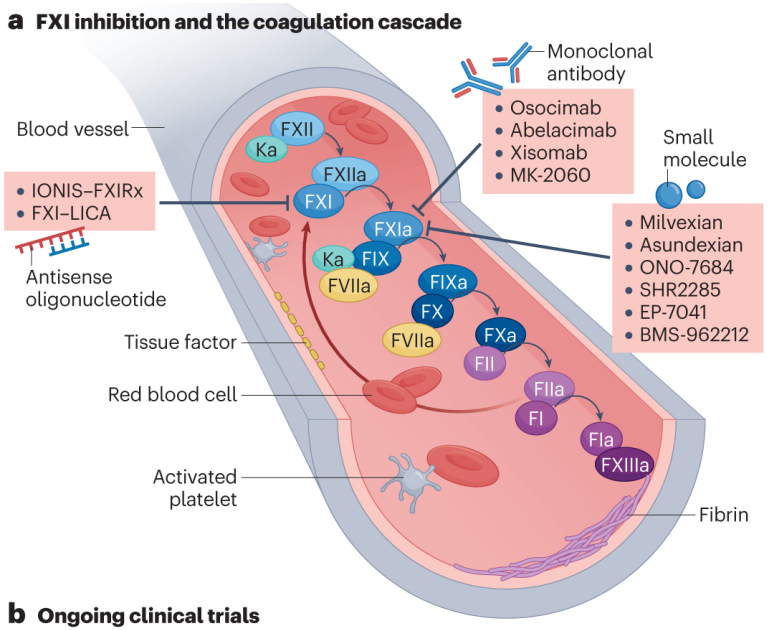
Left Atrial Appendage Closure Devices

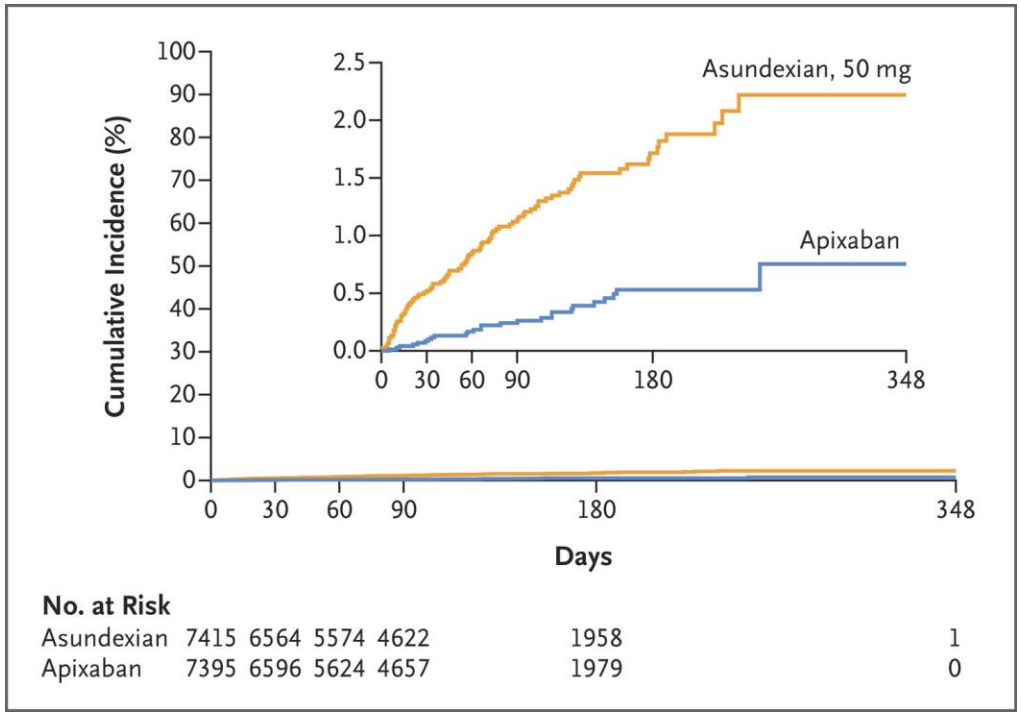




Antithrombotic therapy in LAAO

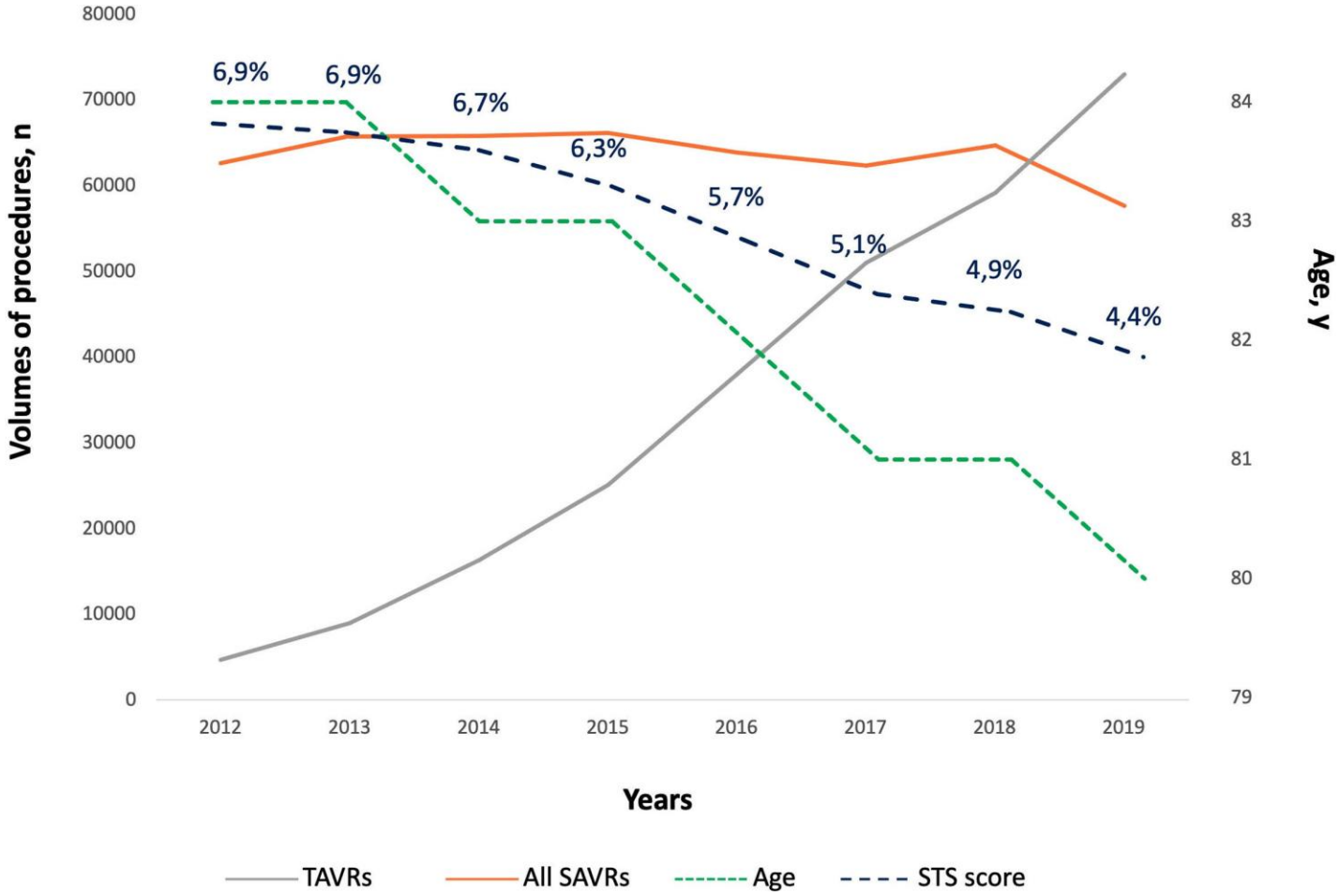
Factor XI did not reduce stroke risk compared to Apixaban





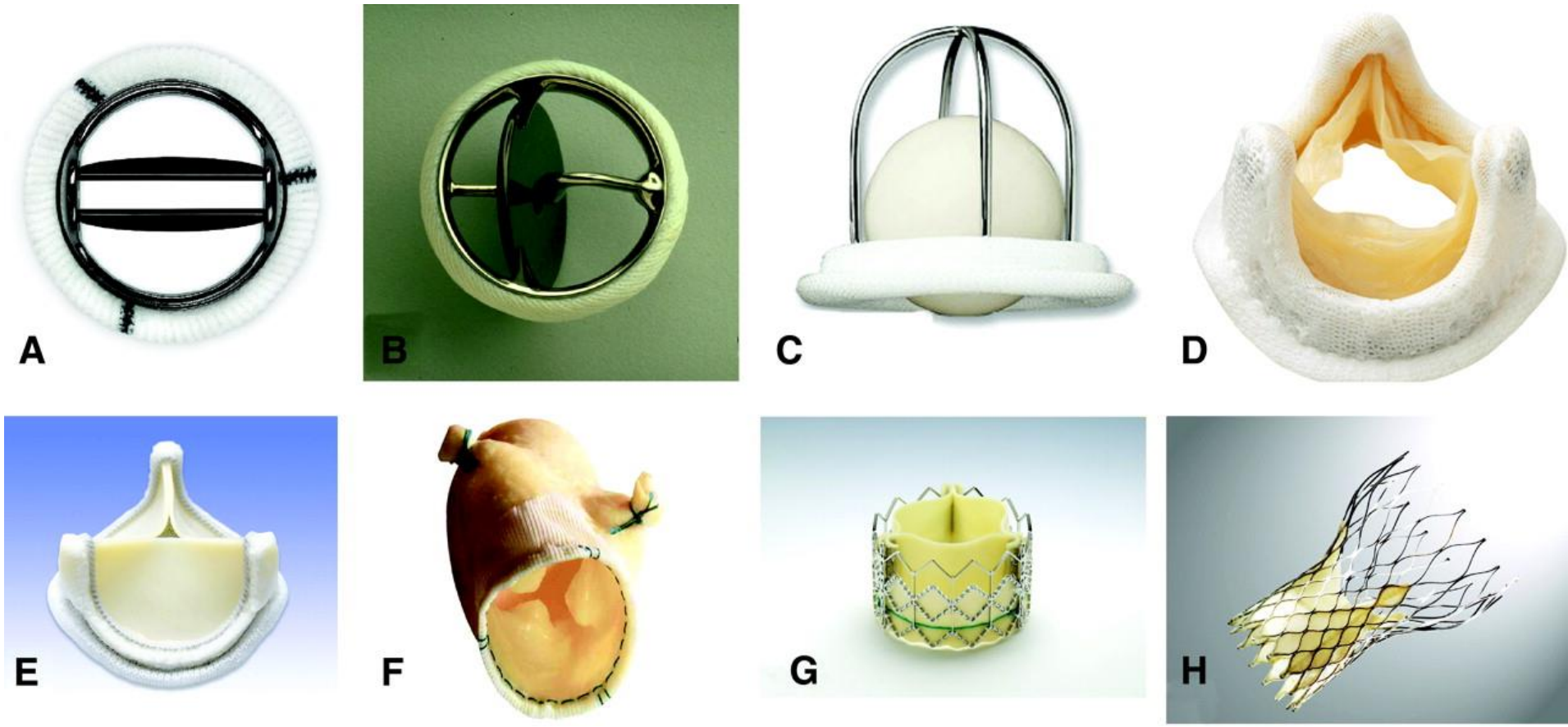
Prosthetic Valves

Less open heart surgery, more catheter based valve replacement



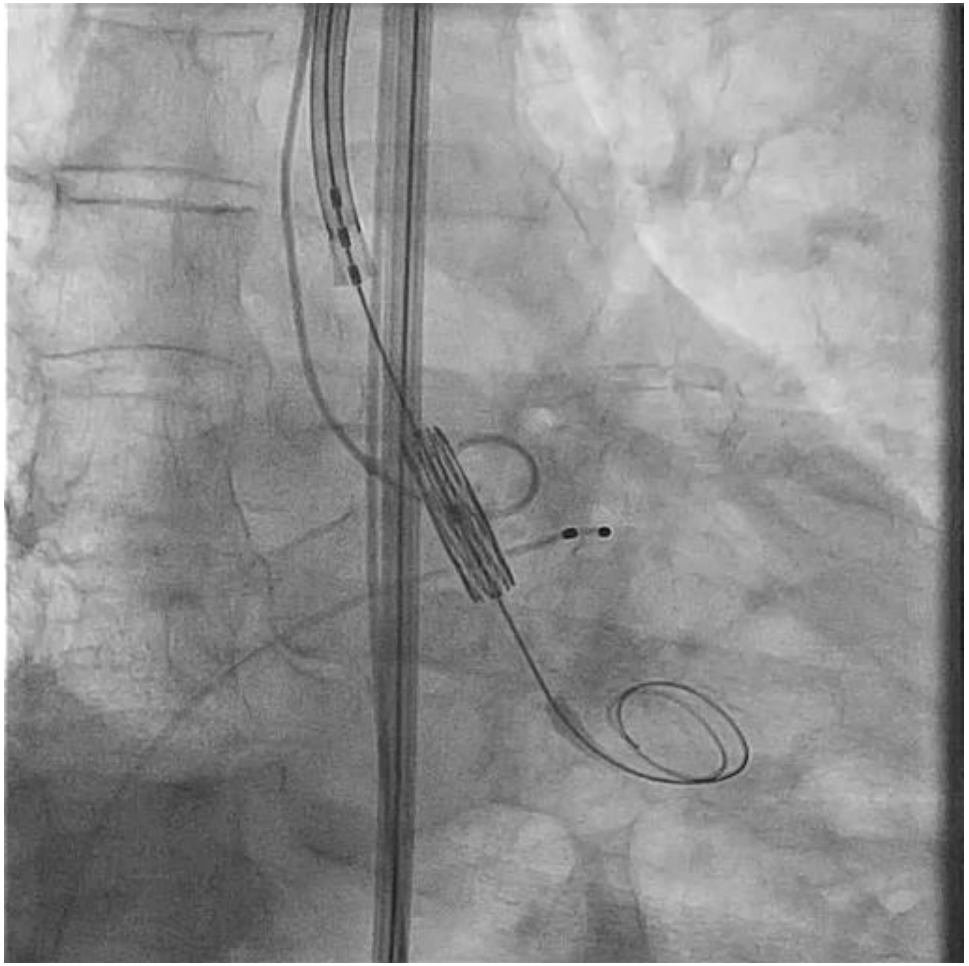
Tang. Lifetime management of AS. Circulation: CI. 2022

Mechanical and bioprosthetic valve replacement



Pibarot. Circulation. 2009

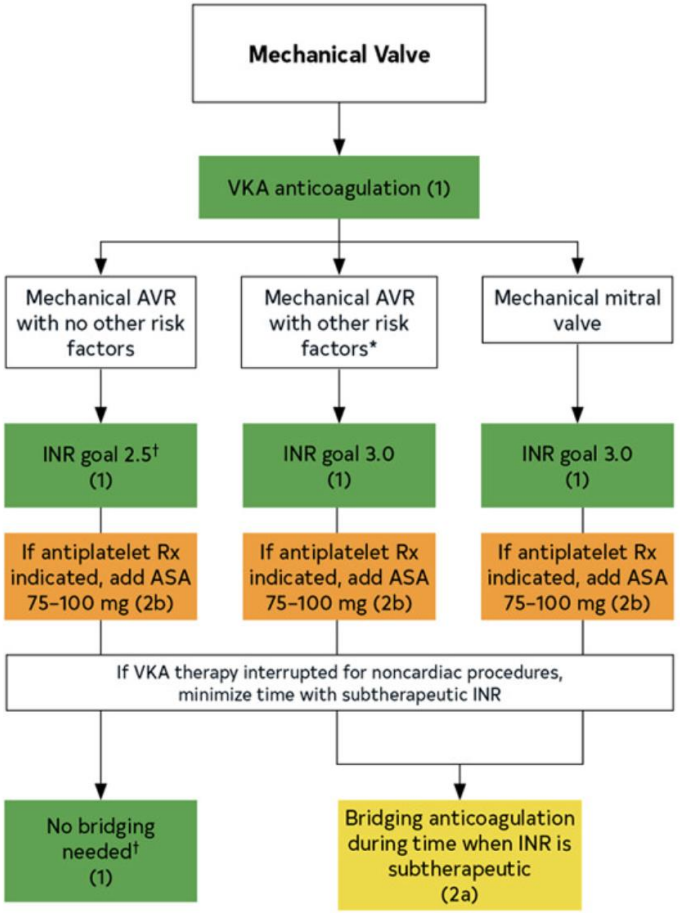
82 years old male with severe AS



Anticoagulation in patients with mechanical prosthesis

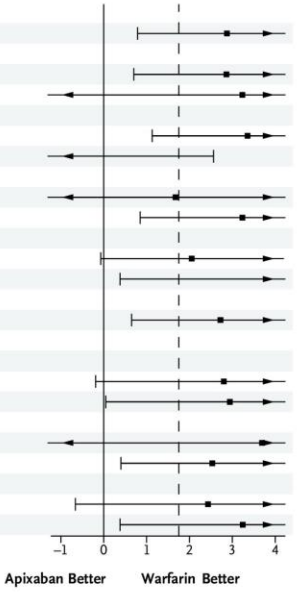
- INR goal typically at 2-3.
- INR goal can be lowered to 1.5-2 for On-X bi-leaflet mechanical aortic valve.
- INR goal for mechanical mitral valve 2.5-3.5
- Bridging can be avoided if patient has no other risk factors for aortic position prosthesis.

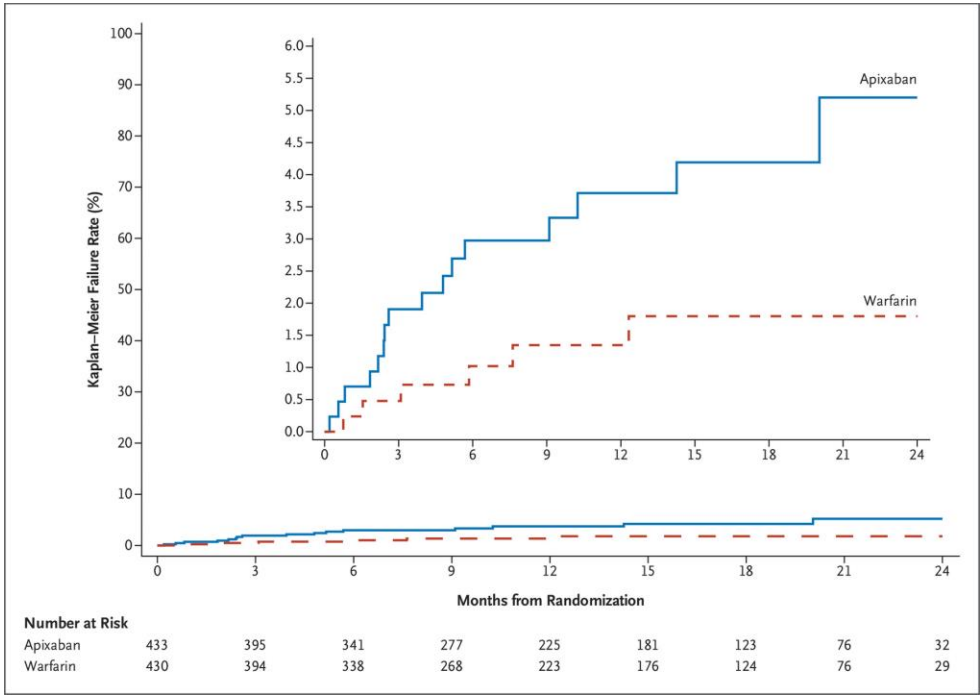
On-X Mechanical valve



DOAC is not better than warfarin in mechanical On-X aortic valves

Group	Apixaban Number of events	Warfarin (%/patient-year)	Apixaban – Warfarin (%/patient-year) Event Rate Difference (95% CI)
Primary efficacy end point	20 (4.17)	6 (1.28)	2.88 (0.79, 4.98)
Age			
≤65 years	16 (3.91)	4 (1.04)	2.87 (0.70, 5.04)
>65 years	4 (5.66)	2 (2.42)	3.24 (–3.25, 9.73)
Race			
White	20 (4.52)	5 (1.16)	3.36 (1.13, 5.59)
Non-White	0 (0.00)	1 (2.67)	–2.67 (–7.90, 2.56)
Sex			
Female	4 (3.56)	2 (1.89)	1.68 (–2.69, 6.04)
Male	16 (4.35)	4 (1.11)	3.24 (0.85, 5.64)
AVR type			
AVR alone	14 (3.40)	5 (1.34)	2.06 (–0.07, 4.20)
AVR with aortic root replacement	6 (8.79)	1 (1.07)	7.72 (0.38, 15.06)
Baseline apixaban dose			
5 mg twice a day	19 (4.01)	6 (1.28)	2.73 (0.65, 4.81)
2.5 mg twice a day	0 (0.00)	NA (NA)	NA
Time from surgery			
≤1 year	8 (3.83)	2 (1.01)	2.81 (–0.19, 5.81)
>1 year	12 (4.43)	4 (1.48)	2.95 (0.05, 5.85)
Valve size			
≤21 mm	8 (6.36)	3 (2.66)	3.70 (–1.64, 9.03)
>21 mm	12 (3.39)	3 (0.85)	2.54 (0.40, 4.69)
Risk of primary event			
High risk*	9 (3.95)	3 (1.51)	2.44 (–0.66, 5.53)
Low risk	11 (4.37)	3 (1.12)	3.25 (0.38, 6.12)

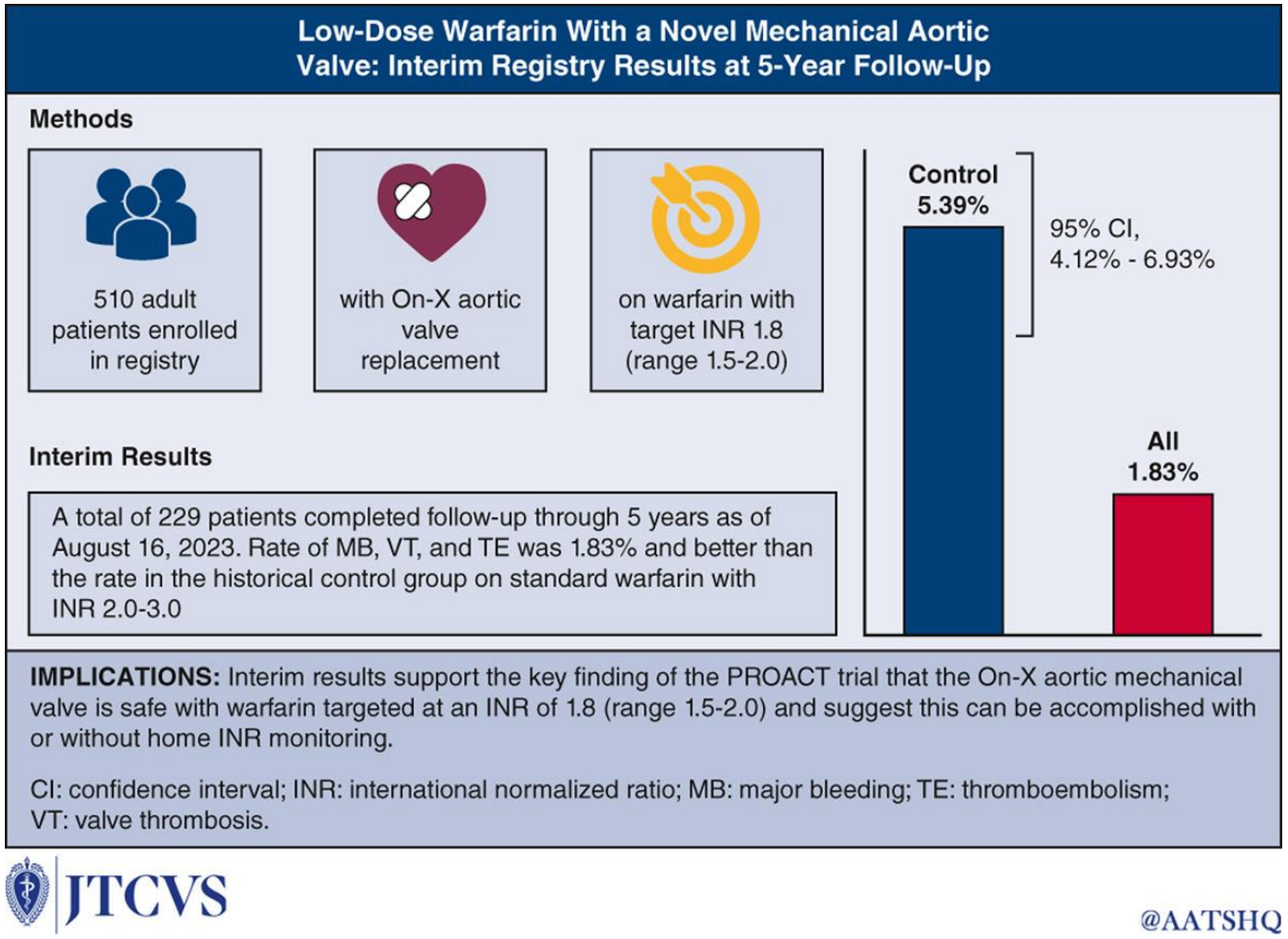




This is also reflected in the Mitral On-X mechanical valve.

PROACT Trial. NEJM. 2023

Lower INR goal (1.5-2) for aortic On-X valve is non-inferior to conventional INR goal 2-3

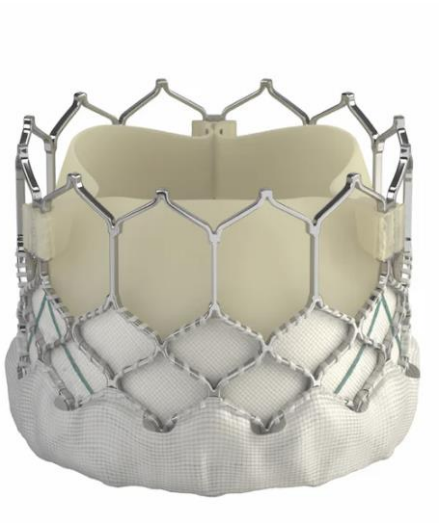


Gerdisch. JTCVS.2024

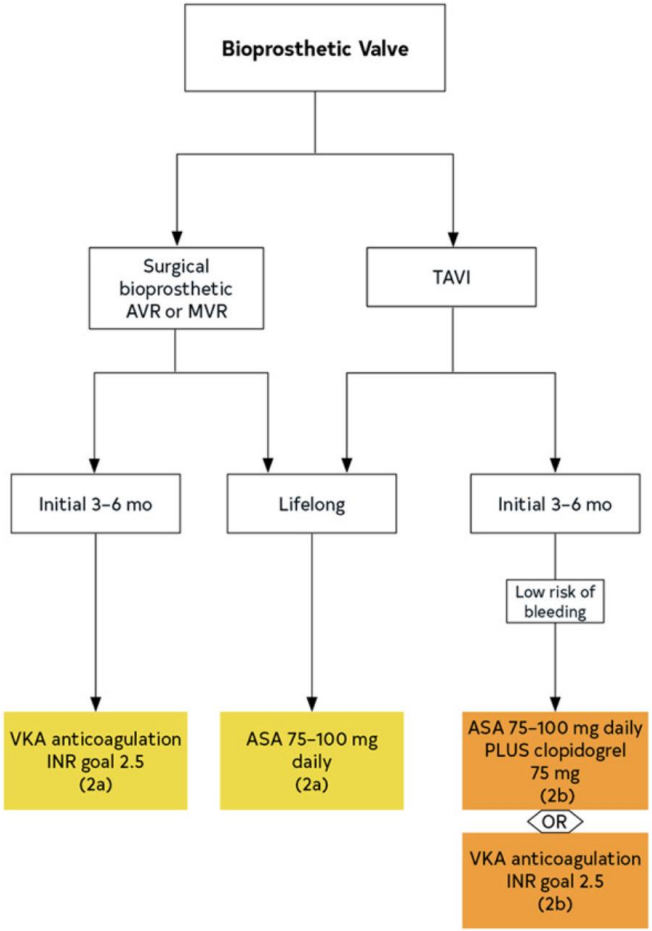
Antithrombotic therapy for bioprosthetic valve

- Historically we give DAPT for 3 months.
- Newer data support SAPT is enough with ASA 81mg.
  - Data also support no antiplatelet therapy for TAVR.

Evolut

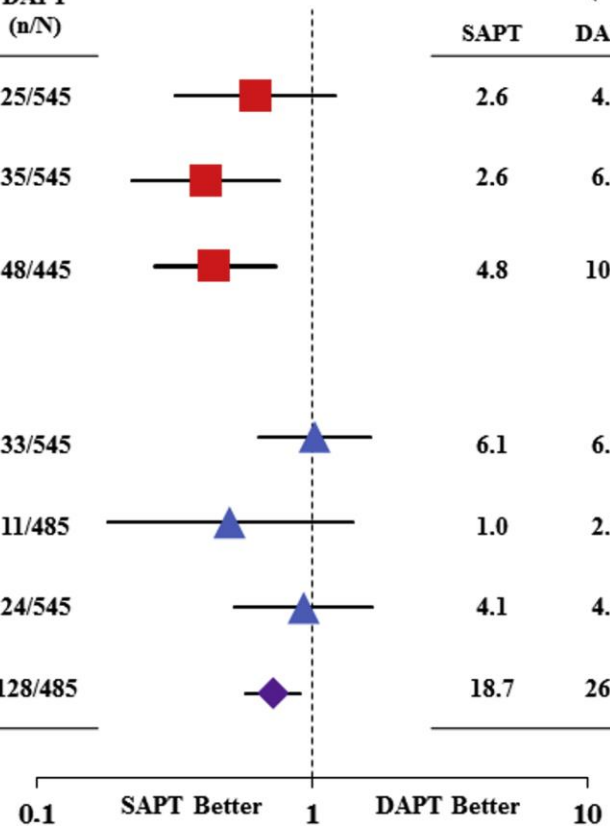


Sapien



SAPT (ASA 81mg) is sufficient and to minimize bleeding risk

Included trials:	POPular TAVI cohort A (n=665 ; 61.2%)		ARTE (n=222 ; 20.4%)		SAT-TAVI (n=120 ; 11.1%)		Ussia et al. (n=79 ; 7.3%)			
SAFETY OUTCOMES	**SAPT (n/N)**	**DAPT (n/N)**	**Event rates (%) SAPT**	**DAPT**	**Risk ratio**	**95%CI**	**I²**	**P-value**		
Life-threatening or disabling bleeding	14/541	25/545	2.6	4.6	0.56	0.30 – 1.07	0%	0.08		
Major bleeding	14/541	35/545	2.6	6.4	0.40	0.22 – 0.74	0%	0.003		
Life-threatening, disabling or major bleeding	21/442	48/445	4.8	10.8	0.44	0.27 – 0.72	0%	0.001		
EFFICACY OUTCOMES										
All-cause death	33/541	33/545	6.1	6.1	1.01	0.63 – 1.61	0%	0.97		
Myocardial infarction	5/481	11/485	1.0	2.3	0.48	0.18 – 1.32	0%	0.16		
Stroke	22/541	24/545	4.1	4.4	0.92	0.53 – 1.63	0%	0.79		
Composite of safety or efficacy outcomes	90/481	128/485	18.7	26.4	0.71	0.56 – 0.90	0%	0.004		

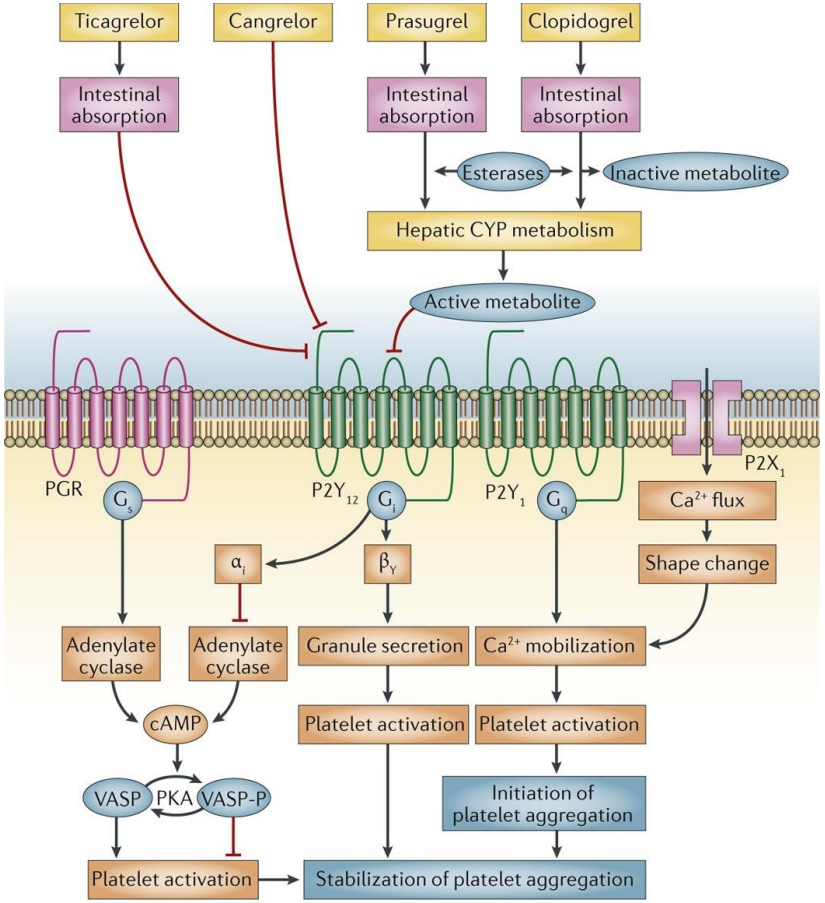


Guedeney. JACC: CI. 2021

Acute Coronary Syndrome

P2Y12 inhibitors

- In general, more potent P2Y12i is better at preventing stent thrombosis.
- Clopidogrel is affected by genetic polymorphism (CYP2C19)

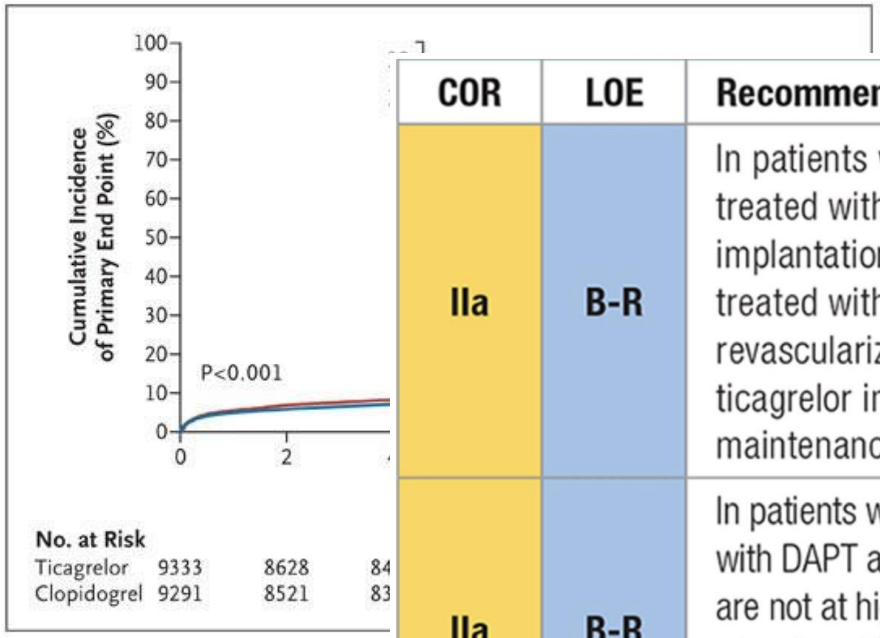


Nature Reviews | Cardiology

Capodanno. Nature. 2022

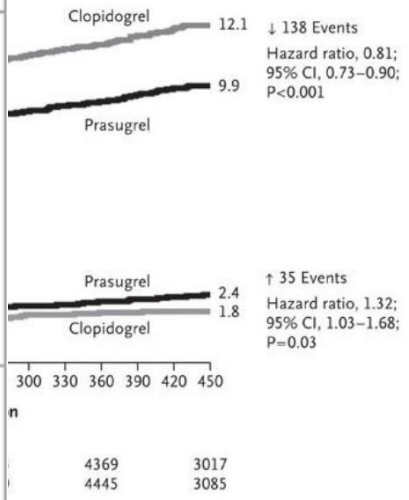
Ticagrelor and Prasugrel are better than clopidogrel to prevent stent thrombosis

PLATO

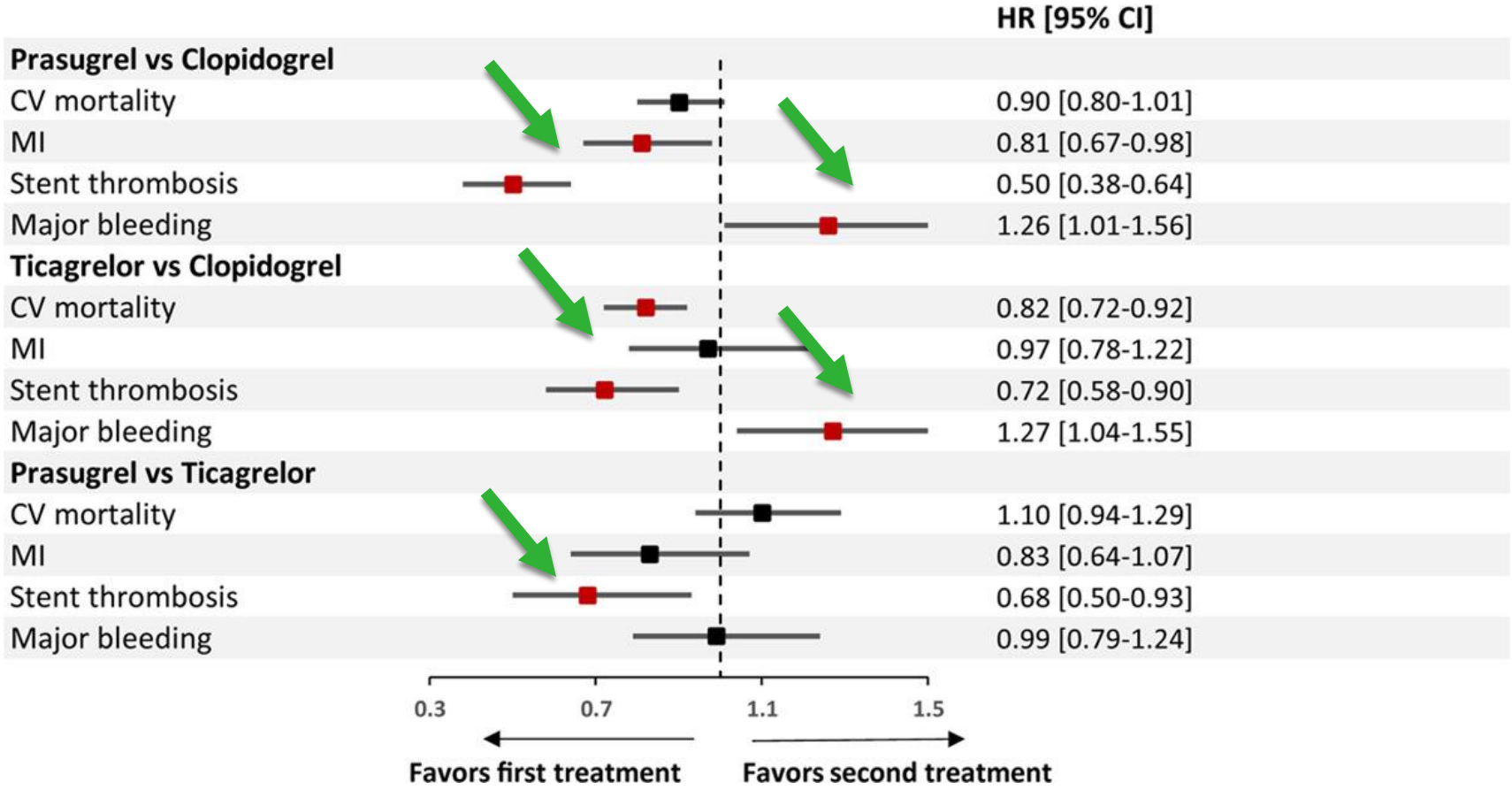


COR	LOE	Recommendations
IIa	B-R	In patients with ACS (NSTE-ACS or STEMI) treated with DAPT after coronary stent implantation and in patients with NSTE-ACS treated with medical therapy alone (without revascularization), it is reasonable to use ticagrelor in preference to clopidogrel for maintenance $P2Y_{12}$ inhibitor therapy.[53,71,72]
IIa	B-R	In patients with ACS (NSTE-ACS or STEMI) treated with DAPT after coronary stent implantation who are not at high risk for bleeding complications and who do not have a history of stroke or TIA, it is reasonable to choose prasugrel over clopidogrel for maintenance $P2Y_{12}$ inhibitor therapy.[54,55]

TRITON TIMI 38



More potent = more bleeding



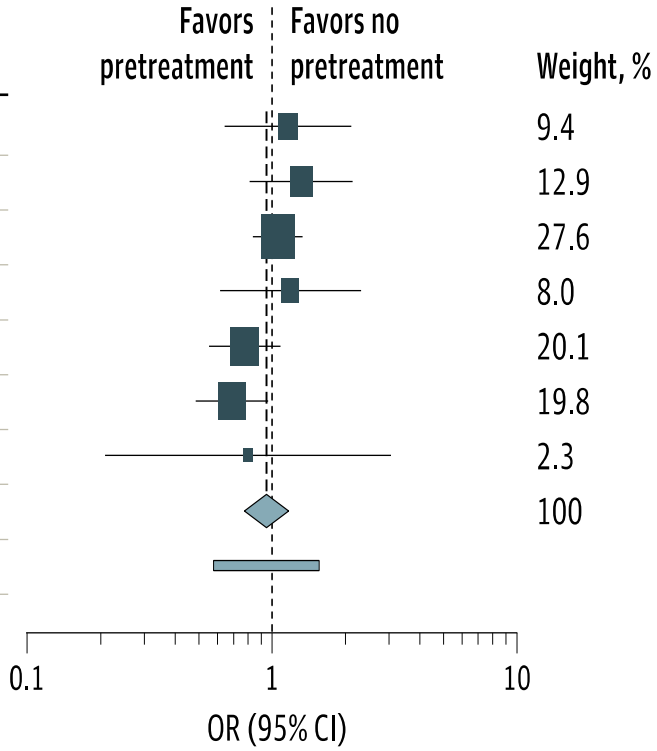
Navaraese. Circulation.2020.

Should we preload P2Y12i before cath?

30-day MACE

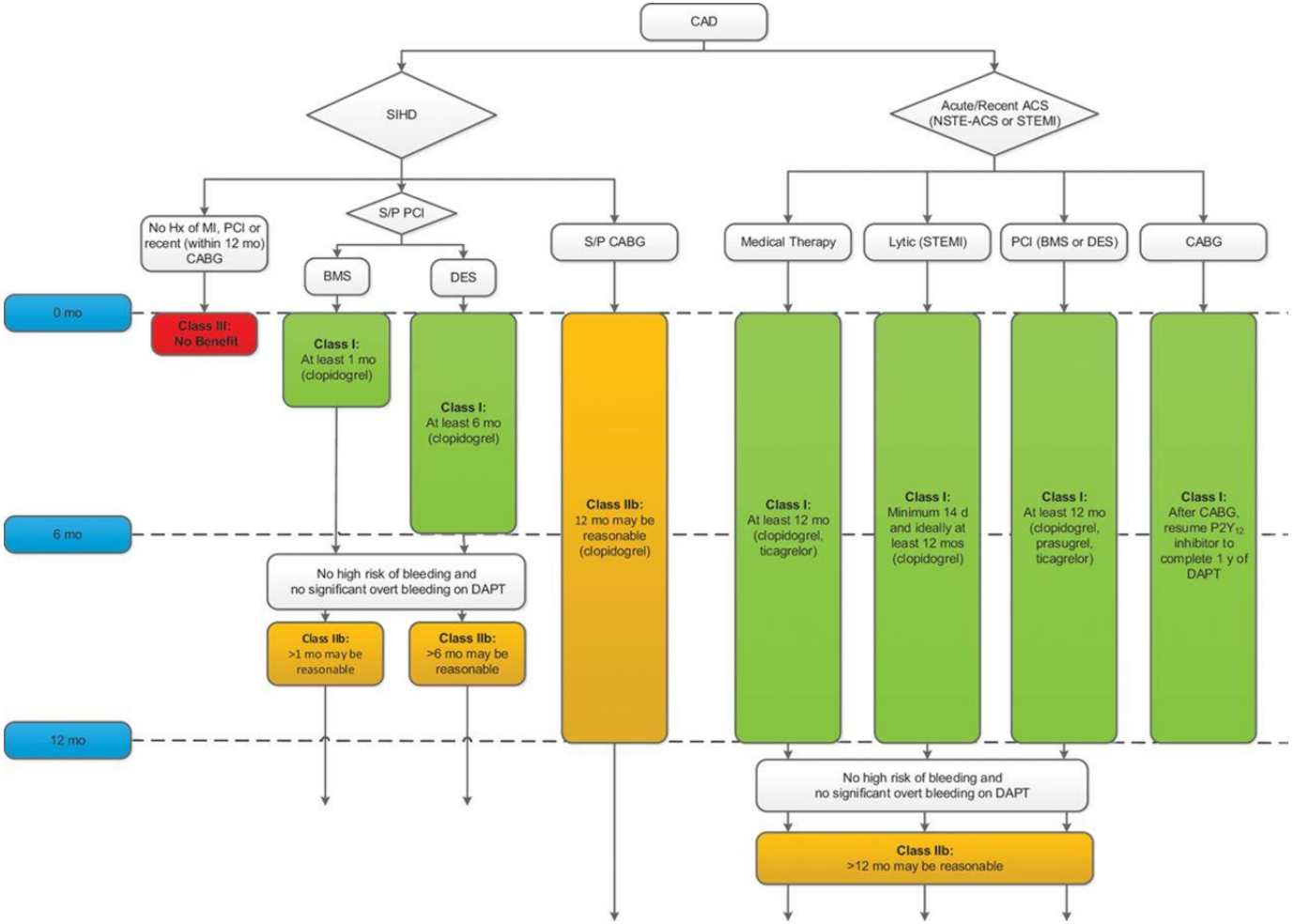
Source	No./total No. Pretreatment	No pretreatment	OR (95% CI)
DUBIUS,[19] 2020	24/711	21/721	1.16 (0.64-2.11)
ISAR-REACT 5,[11] 2020	39/1179	30/1186	1.32 (0.81-2.14)
ACCOAST,[9] 2013	157/2037	146/1996	1.06 (0.84-1.34)
ARMYDA-5,[17] 2010	21/204	18/205	1.19 (0.62-2.31)
CREDO,[18] 2002	65/1053	83/1063	0.78 (0.55-1.09)
PCI CURE,[5] 2001	59/1313	86/1345	0.69 (0.49-0.97)
Bonello et al,[16] 2015	4/106	5/107	0.80 (0.21-3.06)
Overall	369/6603	389/6623	0.95 (0.77-1.17)
Prediction interval			(0.58-1.56)

Random-effects model ($I^2 = 28\%$, $P = .21$)



Answer is NO, it delays surgery with no additional benefit

Dual antiplatelet therapy duration can be confusing..

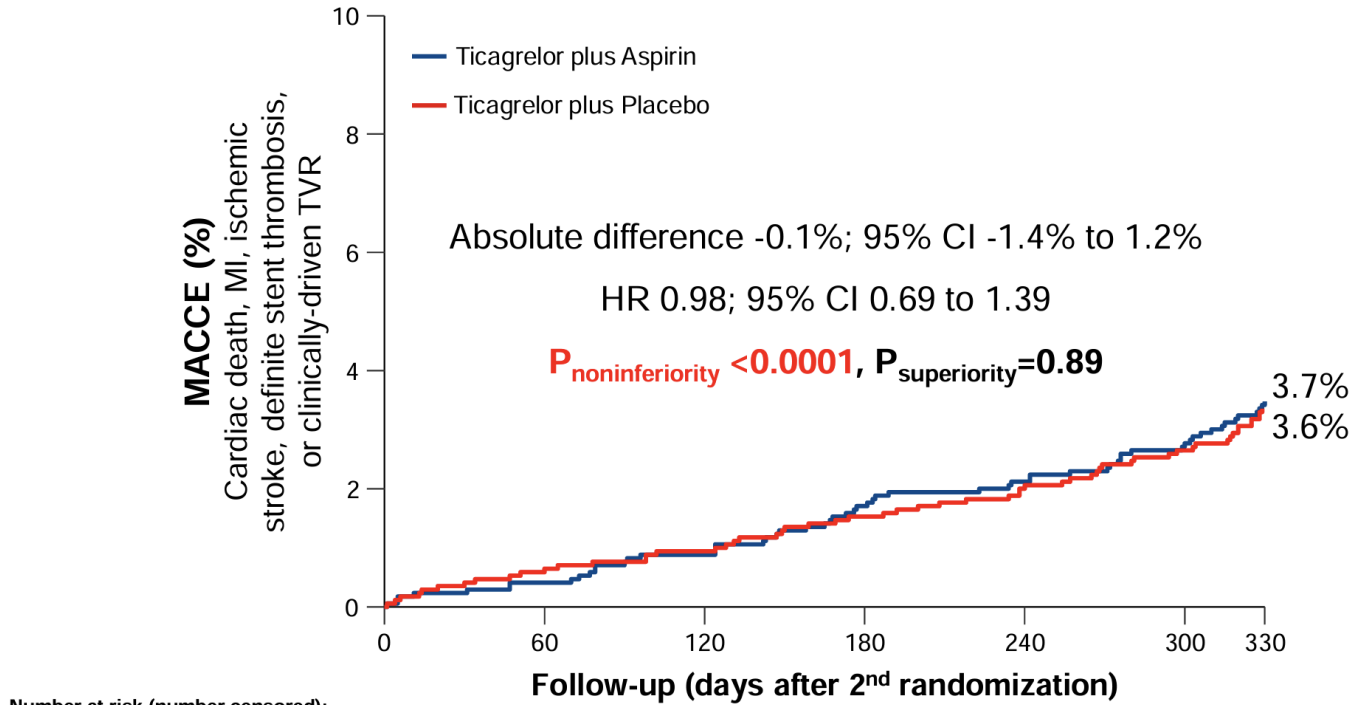


To simplify..

- Acute coronary syndrome
  - DAPT for 1 year (Class 1)
- Stable coronary syndrome
  - DAPT for 6 months (Class 1)
  - ASA can be dropped, in patients with Afib+ SIHD (Class 1)
- Beyond 12 months depends on ischemic risk (Class 2b)

How about shorter DAPT? 1 month!

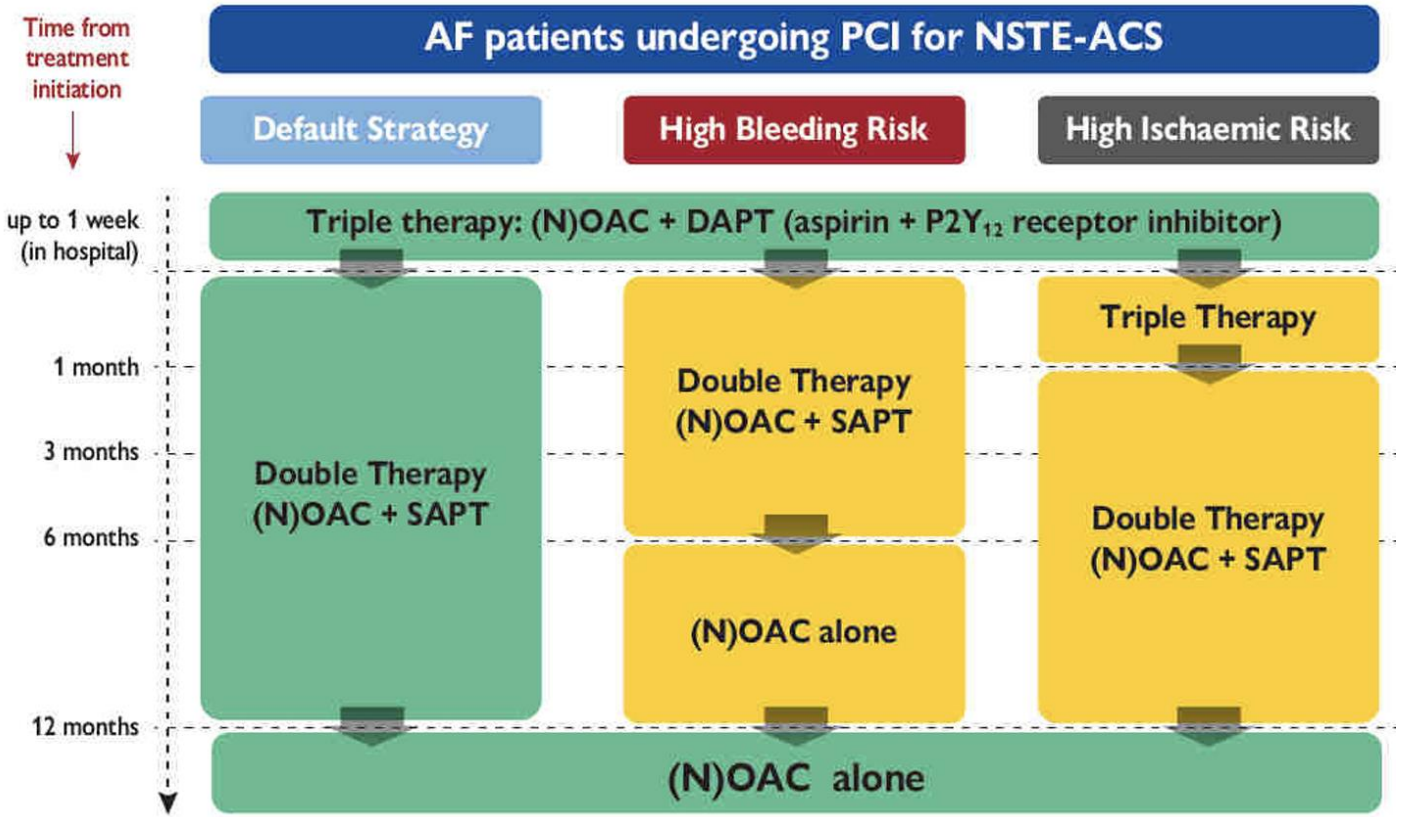
Primary Safety Endpoint: MACCE



Stone, Ge. ULTIMATE DAPT. Lancet. 2024

Triple therapy- 1-2 weeks (ACS+ Afib)

- If bleeding risk is elevated, PPI should be added.



Common anti-thrombotic scenarios

- Patients with rheumatic mitral stenosis and afib
  - Warfarin INR goal 2-3
- Patients with On-X mechanical aortic valve with no risk factors.
  - Warfarin INR goal 1.5-2, no bridging needed.
- Patients with recent DES placement and afib
  - Triple therapy for 1 weeks, then P2Y12i + DOAC
- Patients presented with ACS (STEMI/NSTEMI/UA)
  - ASA 325mg, consult cardiology and do not pre-load P2Y12i

Questions?