DAPT Duration and NOAC Selection in the Afib-PCI Patient

Renato D Lopes, MD MHS PhD
Professor of Medicine
Division of Cardiology
Duke Clinical Research Institute
Duke University Medical Center

Duke Clinical Research Institute

From Thought Leadership to Clinical Practice

Disclosures

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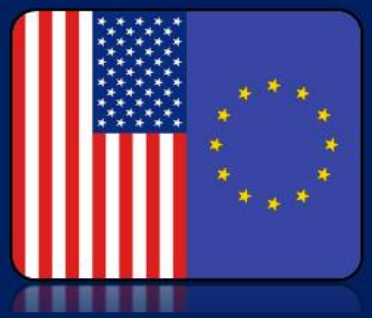
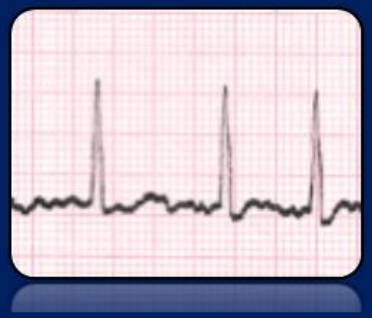
- Funding for consulting or other services from Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Pfizer

Atrial fibrillation and PCI: Epidemiology



People in EU and US[1,2]

~1 billion

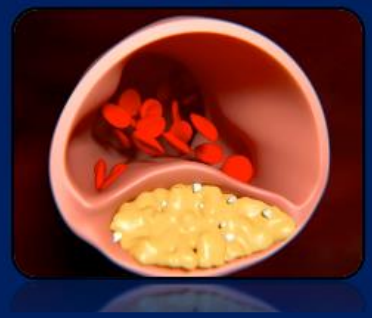


With AF[3,4]

~15–20 million

OAC indicated[3,4]

~16 million



With CAD[4,5]

~4.8 million

Revasc. indicated[3]

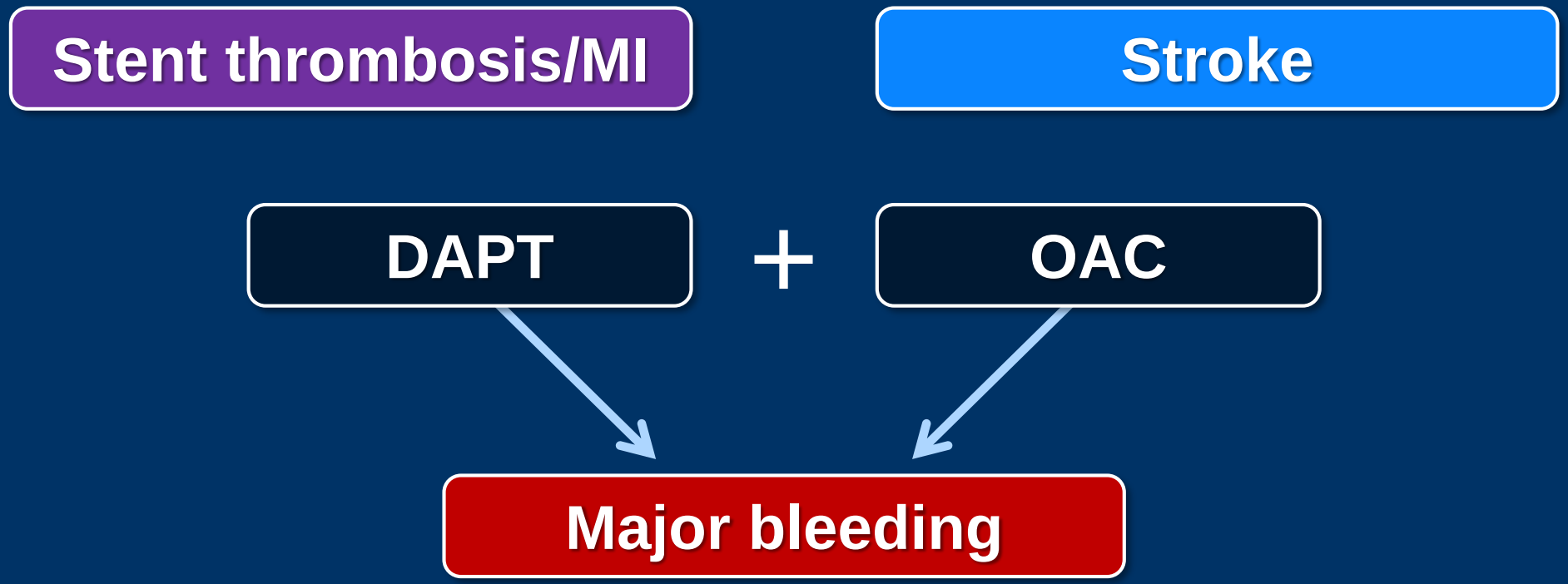
~1–2 million

OAC, oral anticoagulation; Revasc., revascularisation.

1. US population. Available at: www.census.gov/popclock. Accessed Aug 2019; 2. EU population. Available at: europa.eu/european-union/about-eu/figures/living_en. Accessed Aug 2019; 3. Capodanno D, Angiolillo DJ. Circ Cardiovasc Interv 2014;7:113–24; 4. Capodanno D, et al. J Am Coll Cardiol 2019;74:83–99; 5. Verheugt FWA, et al. J Am Coll Cardiol 2019. pii: S0735-1097(19)35400-2.

Coronary stenting in patients with AF and high risk of stroke

The problem: you cannot simultaneously prevent all three!



DAPT, dual antiplatelet therapy; OAC, oral anticoagulant.

Bewildering number of strategies in the ACS patient with atrial fibrillation

ASA dose:	None Low High	2	1+8 = 9
ASA duration (mos):	1 3 6 12	4	ASA
Thienopyridine:	None Clop Ticlid Pras Ticag	4	1+16 = 17
Thienopyridine duration (mos):	1 3 6 12	4	Thieno
AC:	None Warf Dabi Riva Apix Edox	5	1+10 = 11
AC INR/dose:	Low High	2	ACs

Permutations of single, dual or triple therapy as *Early Initial Therapy (0, 1, 3, 6 mos)* following ACS: 9 x 17 x 11 = 1,683

Permutations of single or dual therapy *Late After Early Therapy (0, 1, 3, 6 mos)* following ACS: 1,683

Total Permutations *throughout one year:* 2.8 million

AC, anticoagulant; Apix, apixaban; ASA, acetylsalicylic acid; Clop, clopidogrel; Dabi, dabigatran; Edox, edoxaban; INR, international normalised ratio; mos, months; Pras, prasugrel; Riva, rivaroxaban; Ticag, ticagrelor; Warf, warfarin.

Slide by C. Michael Gibson, M.S., M.D.

1. Data adapted from Gibson CM. J Am Coll Cardiol 2017;69:172–5.

What evidence is there for NOACs in AF + ACS?

None of these trials were powered for efficacy

ACC, American College of Cardiology; AHA, American Heart Association.

1. Gibson CM, et al. N Engl J Med 2016;375:2423–34; 2. Cannon CP, et al. N Engl J Med 2017;377:1513–24; 3. Lopes RD, et al. N Engl J Med 2019;380:1509–24; 4. Vranckx P, et al. Am Heart J 2018;196:105–12; 5. NCT02866175. Available at: clinicaltrials.gov/ct2/show/NCT02866175. Accessed Aug 2019.

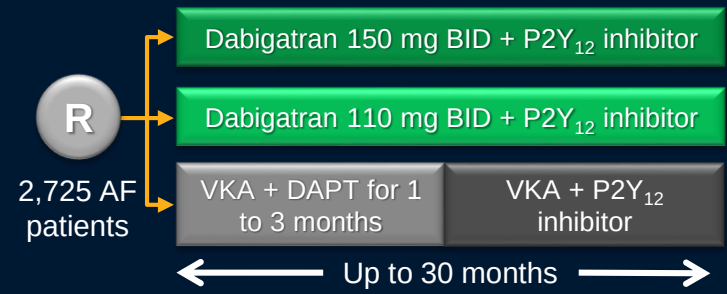
NOAC AF-PCI clinical studies

PIONEER AF-PCI – Rivaroxaban[1]

Primary endpoint:
TIMI major, minor bleeding or bleeding requiring medical attention (for 12 months)

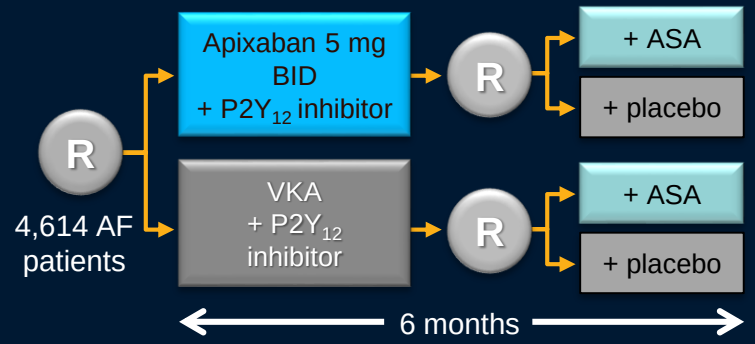
RE-DUAL AF-PCI – Dabigatran[2]

Primary endpoint:
Time to first major or CRNM bleeding (ISTH)



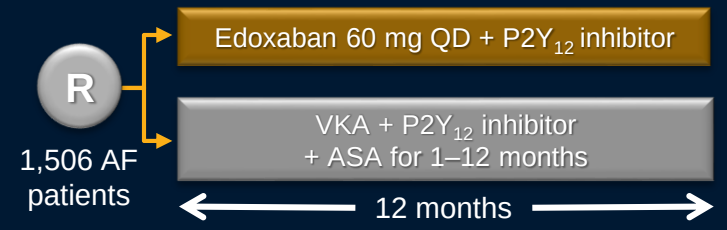
AUGUSTUS AF-PCI – Apixaban[3]

2x2 Factorial design
Primary endpoint:
ISTH major bleeding or CRNM bleeding



ENTRUST AF-PCI – Edoxaban[4]

Primary endpoint:
ISTH major and CRNM bleeding

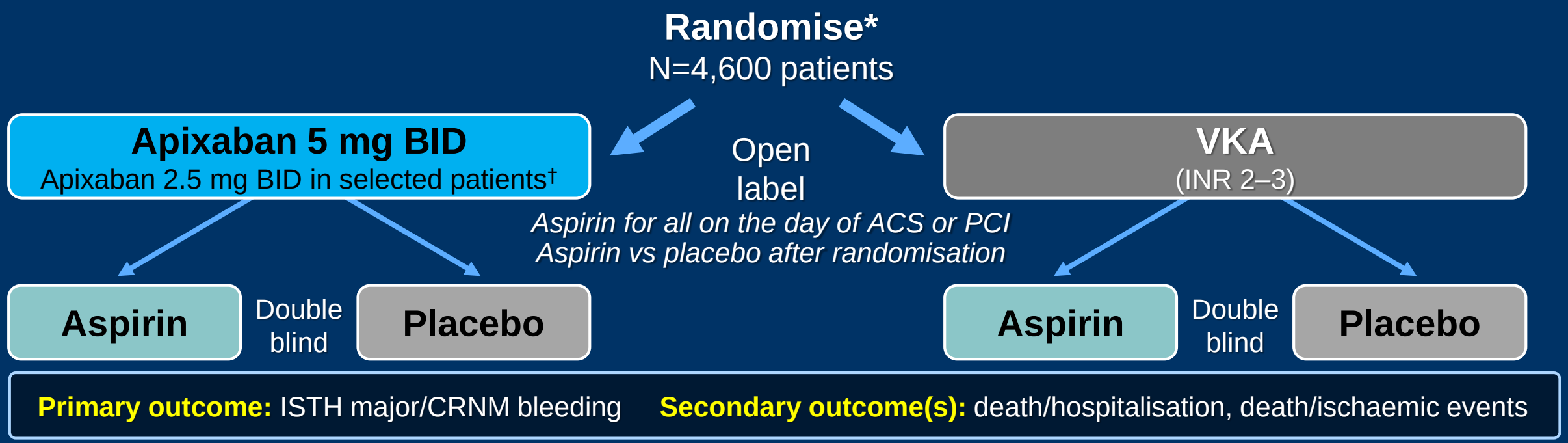


None of these trials were powered for efficacy

CNRM, clinically relevant non-major; DAPT, dual antiplatelet therapy; ISTH, International Society on Thrombosis and Hemostasis; OD, once daily; QD, once daily; riva, rivaroxaban; TIMI, Thrombolysis in Myocardial Infarction.

1. Gibson CM, et al. N Engl J Med 2016;375:2423–34; 2. Cannon CP, et al. N Engl J Med 2017;377:1513–24; 3. Lopes RD, et al. N Engl J Med 2019;380:1509–24; 4. Vranckx P, at al. Lancet 2019;394:1335–43.

AUGUSTUS: Trial design



INCLUSION

- AF (prior, persistent, >6 hours); physician decision for OAC
- ACS or PCI; planned $P2Y_{12}$ inhibitor for ≥6 months

EXCLUSION

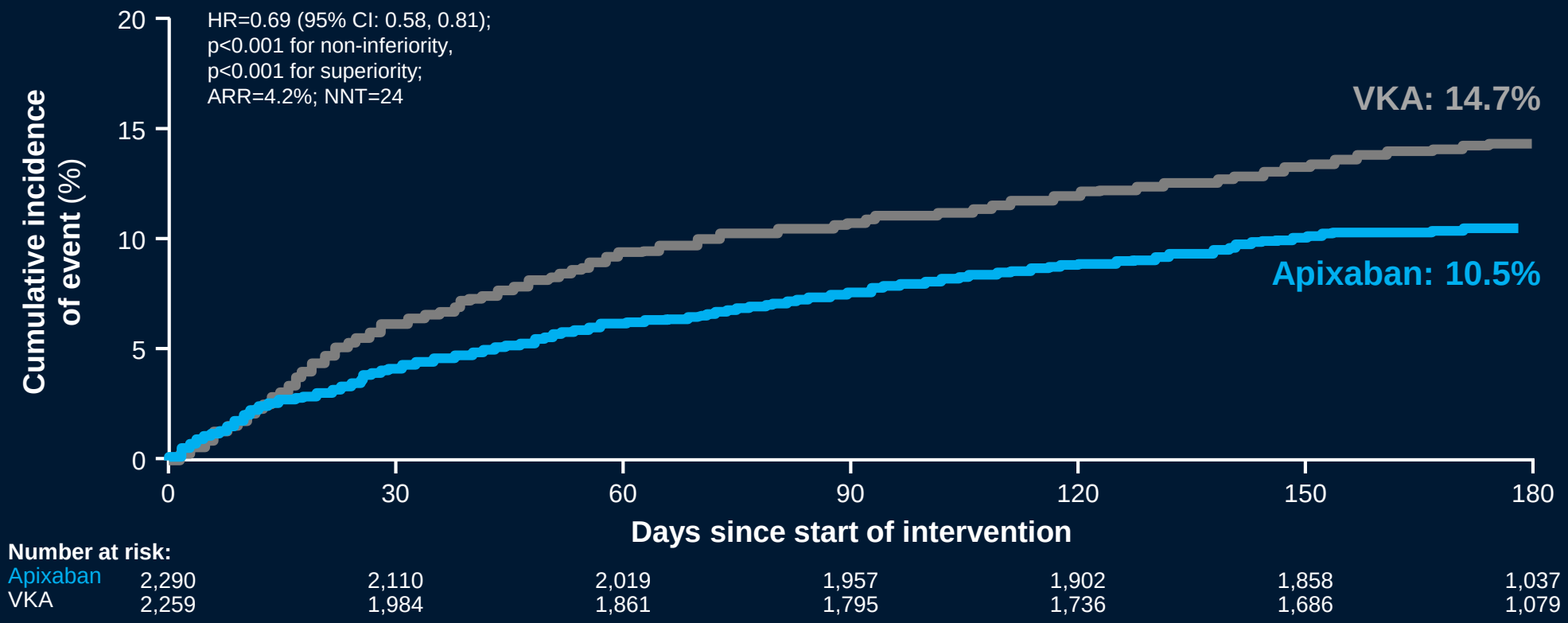
- Contraindication to DAPT
- Other conditions that require OAC (such as prosthetic valves or moderate or severe mitral stenosis), severe renal insufficiency, and history of intracranial haemorrhage
- Recent or planned CABG, coagulopathy or ongoing bleeding, contraindication to VKA, apixaban, all $P2Y_{12}$ inhibitors, or aspirin

*Randomisation was not sequential; at enrolment, eligible patients were randomised simultaneously to apixaban or VKA and to aspirin or aspirin placebo; †2.5 mg BID used in patients with ≥2 of the following criteria: age ≥80 years, weight ≤60 kg, or serum creatinine ≥1.5 mg/dL (133 µmol/L).

Lopes RD, et al. Am Heart J 2018;200:17–23.

Major/CRNM bleeding

Apixaban vs VKA



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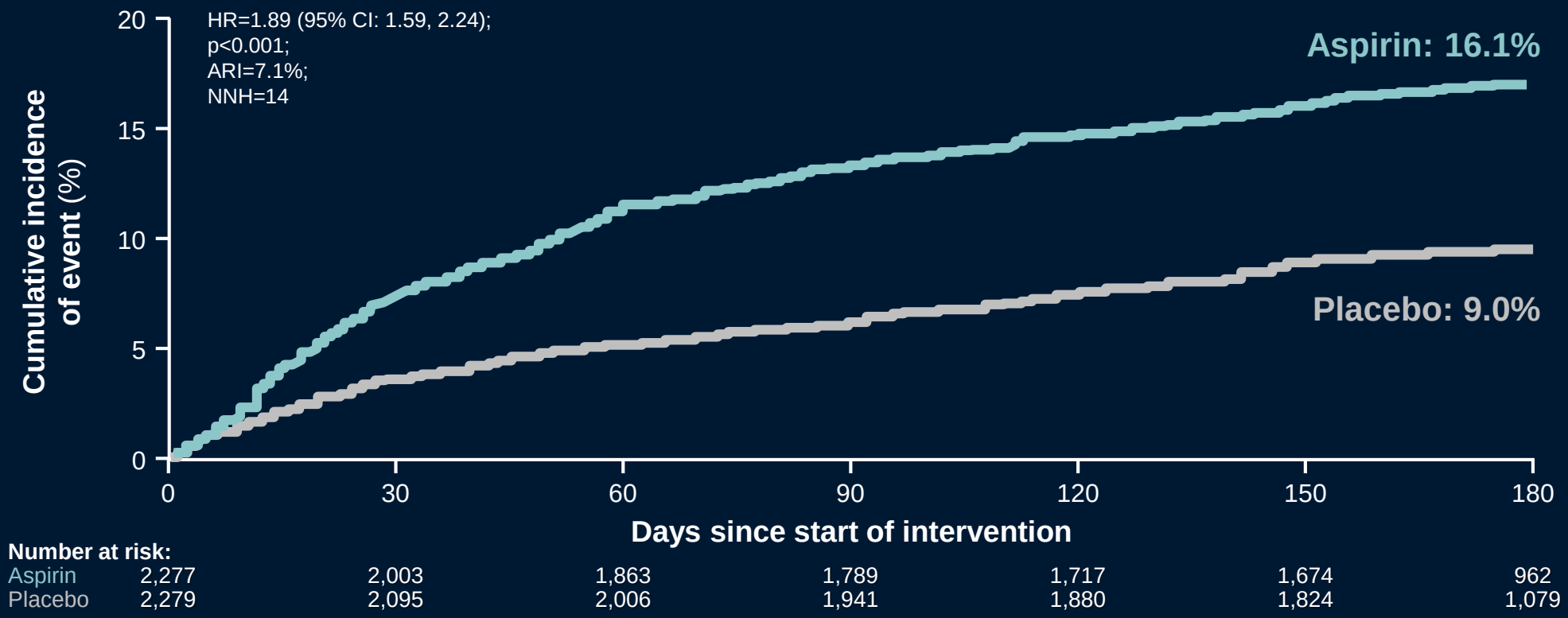
Lopes RD, et al. N Engl J Med 2019;380:1509–24.

Major/CRNM bleeding

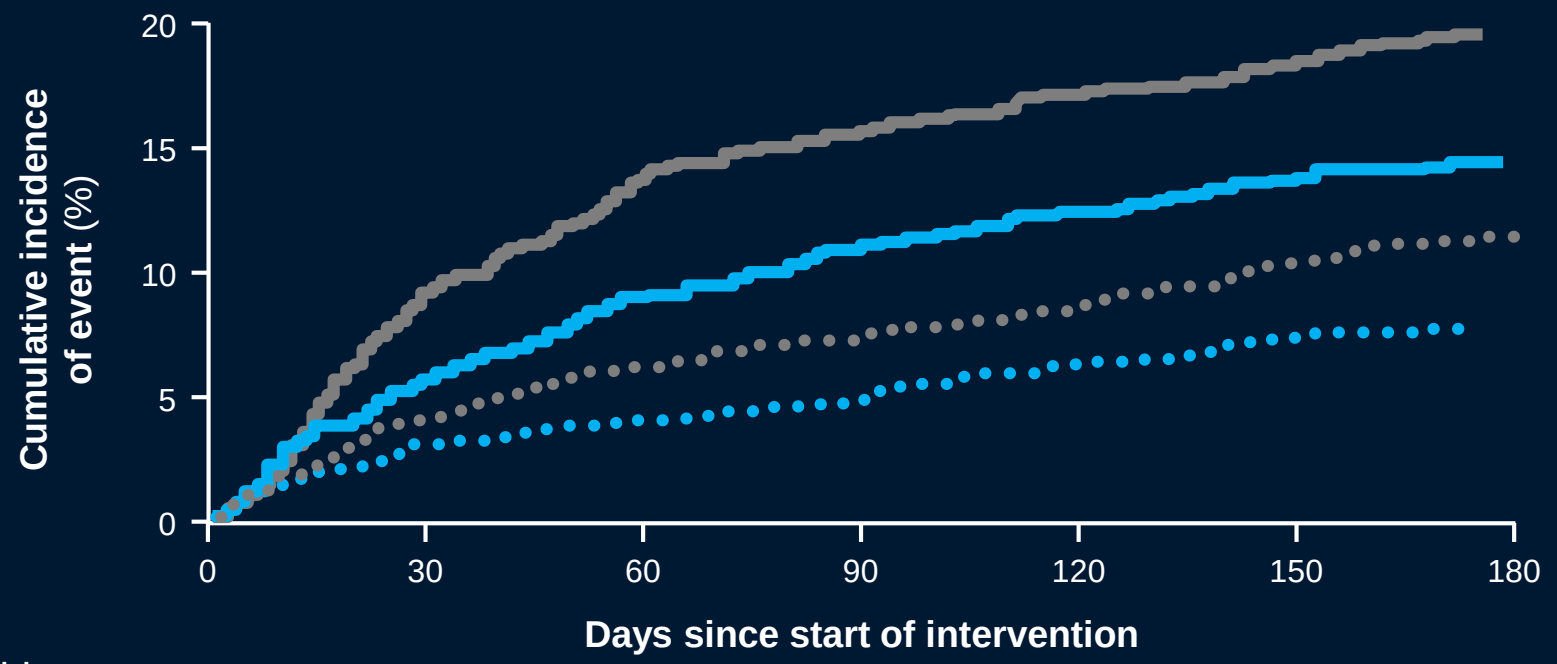
Aspirin vs placebo



ARI, absolute risk increase; NNH, number needed to harm.

Lopes RD, et al. N Engl J Med 2019;380:1509–24.

Major/CRNM bleeding[1]



Number at risk:

Apixaban and aspirin	1,145	1,036	975	937	903	880	485
Apixaban and placebo	1,143	1,075	1,044	1,007	975	947	536
VKA and aspirin	1,123	962	881	838	800	776	467
VKA and placebo	1,126	1,007	947	917	883	851	528

VKA + aspirin: 18.7%[2]

Apixaban + aspirin: 13.8%[2]

VKA + placebo: 10.9%[2]

Apixaban + placebo: 7.3%[2]

Apixaban + placebo vs VKA + aspirin:[2]

11.4% absolute risk reduction (NNT=9)

AUGUSTUS was not powered to compare individual primary outcomes for apixaban + placebo vs VKA + aspirin

1. Lopes RD, et al. N Engl J Med 2019;380:1509–24;
2. Lopes RD, et al. N Engl J Med 2019;380:1509–24. Suppl appendix.

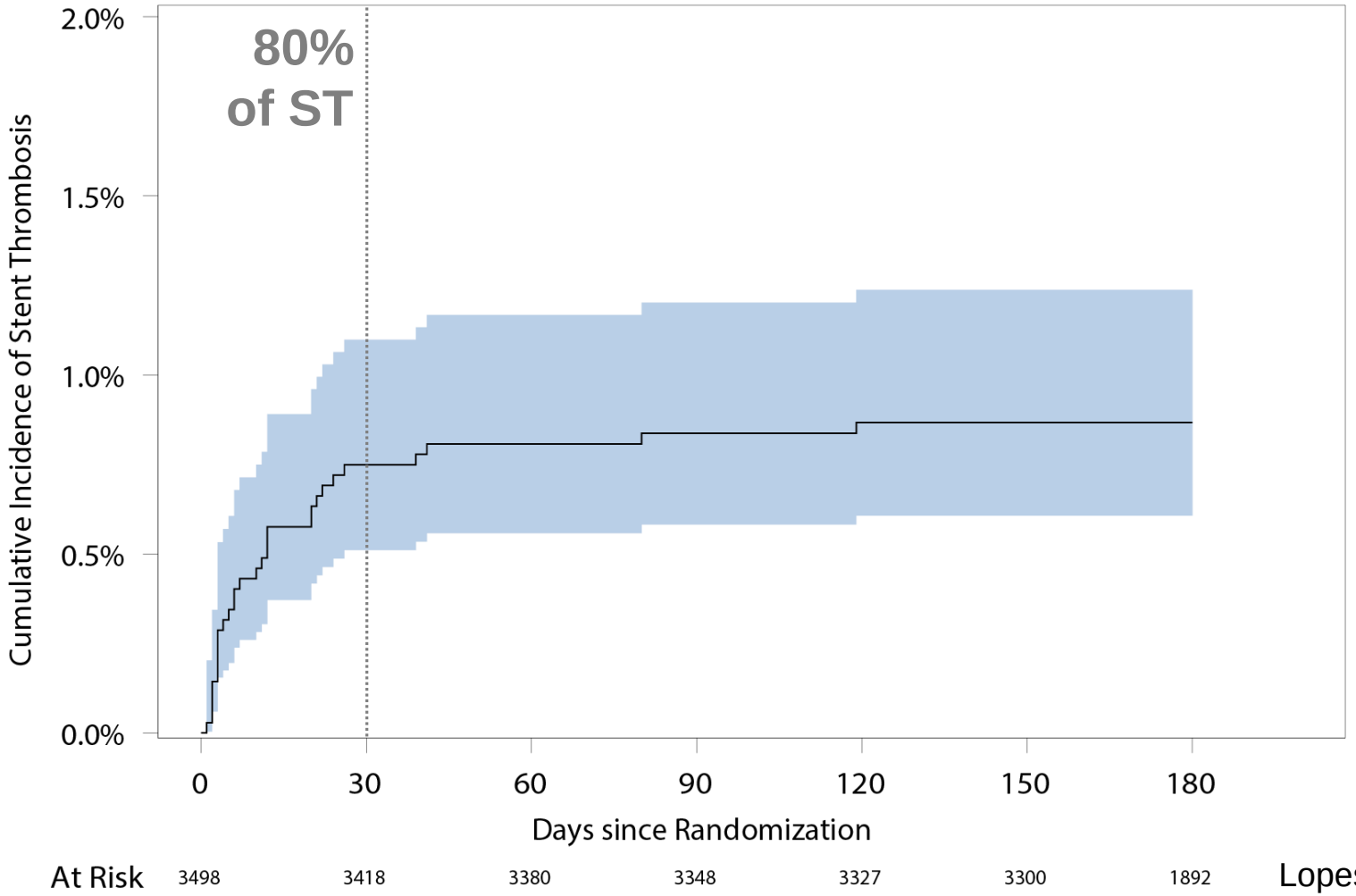
Ischemic outcomes

Aspirin vs placebo

Endpoint	Aspirin (N=2,307)	Placebo (N=2,307)	HR (95% CI)
Death/ischaemic events (%)	6.5	7.3	0.89 (0.71, 1.11)
Death (%)	3.1	3.4	0.91 (0.66, 1.26)
CV death (%)	2.3	2.5	0.92 (0.63, 1.33)
Stroke (%)	0.9	0.8	1.06 (0.56, 1.98)
Myocardial infarction (%)	2.9	3.6	0.81 (0.59, 1.12)
Definite or probable stent thrombosis (%)	0.5	0.9	0.52 (0.25, 1.08)
Urgent revascularisation (%)	1.6	2.0	0.79 (0.51, 1.21)
Hospitalisation (%)	25.4	23.4	1.10 (0.98, 1.24)

Lopes RD, et al. N Engl J Med 2019;380:1509–24.

Overall Incidence of Definite/Probable Stent Thrombosis at 6 Months

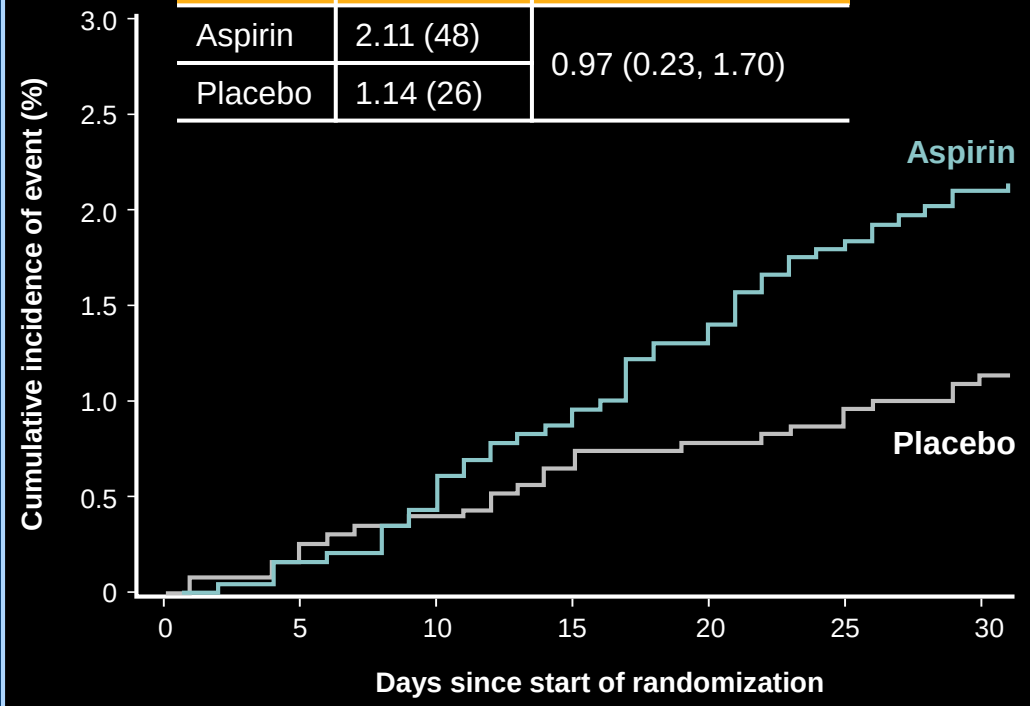


Lopes RD et al. Circulation, 2019

Severe bleeding and ischemic outcomes
Randomization to 30 days[1]

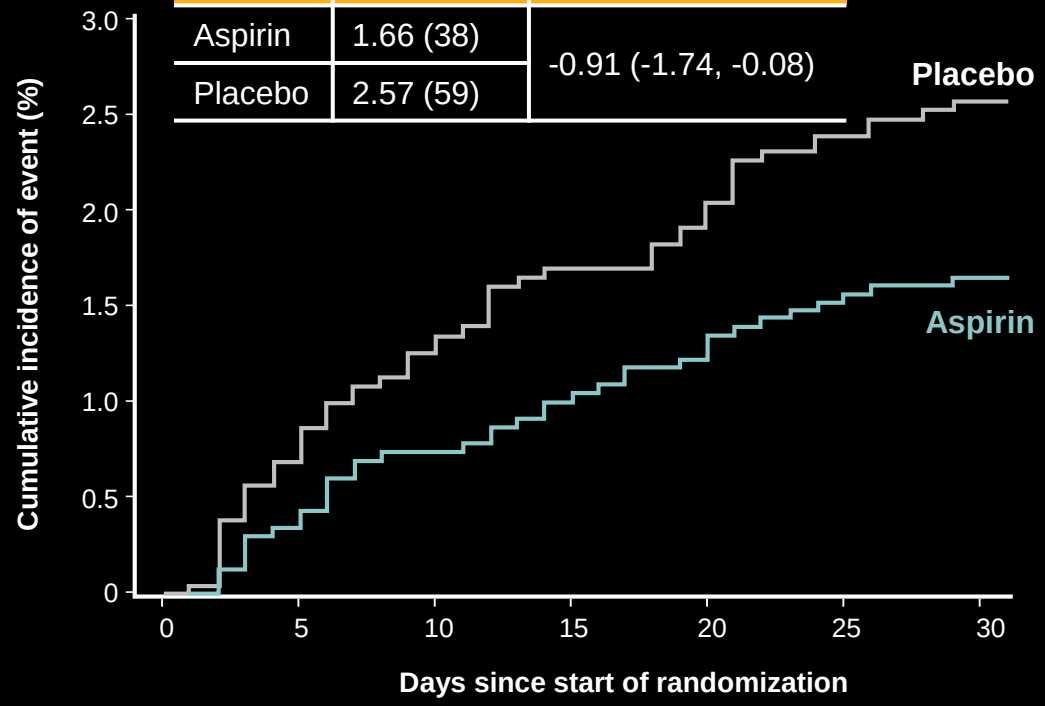
Fatal, ICH, major bleeding

	KM% (events)	Absolute risk difference (95% CI)
Aspirin	2.11 (48)	0.97 (0.23, 1.70)
Placebo	1.14 (26)	



CV death, stroke, MI, stent thrombosis

	KM% (events)	Absolute risk difference (95% CI)
Aspirin	1.66 (38)	-0.91 (-1.74, -0.08)
Placebo	2.57 (59)	



Adapted from Alexander et al. 2020.

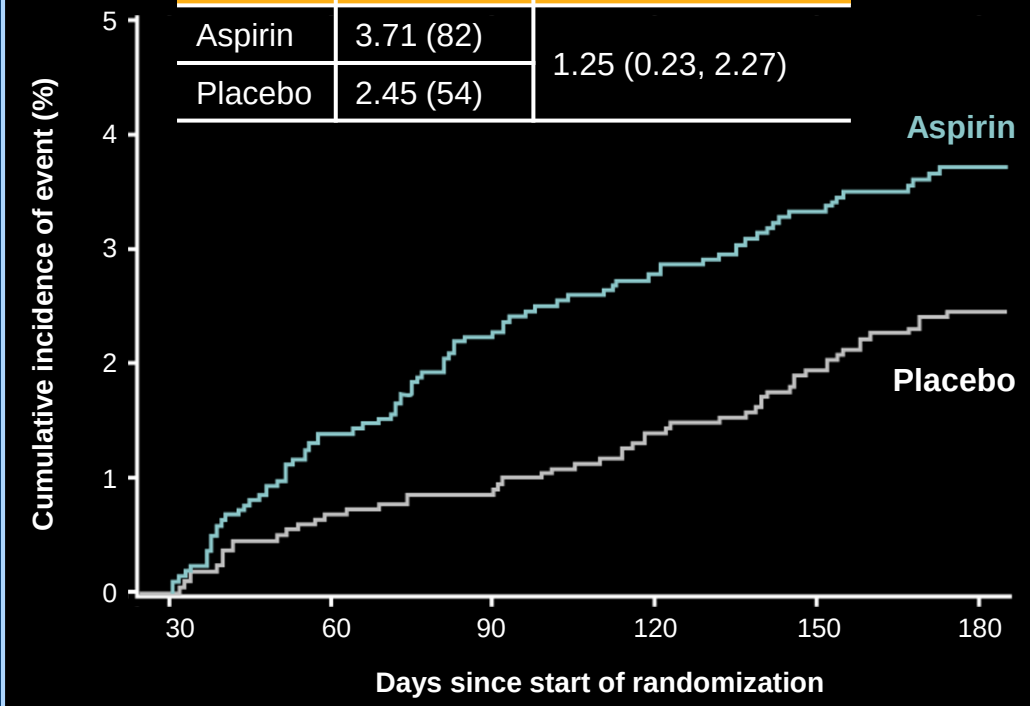
KM, Kaplan Meier.

1. Alexander JH, et al. Circ 2020;141:1618–27.

Severe bleeding and ischemic outcomes 30 days to 6 months[1]

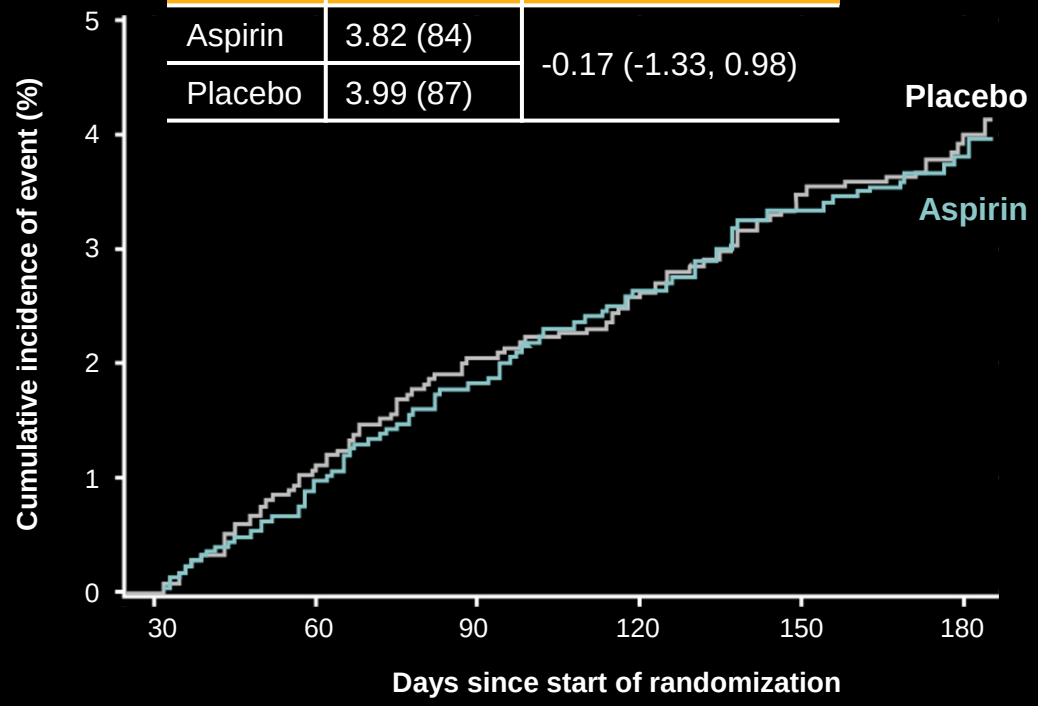
Fatal, ICH, major bleeding

	KM% (events)	Absolute risk difference (95% CI)
Aspirin	3.71 (82)	1.25 (0.23, 2.27)
Placebo	2.45 (54)	



CV death, stroke, MI, stent thrombosis

	KM% (events)	Absolute risk difference (95% CI)
Aspirin	3.82 (84)	-0.17 (-1.33, 0.98)
Placebo	3.99 (87)	



Adapted from Alexander et al. 2020.

1. Alexander JH, et al. Circ 2020;141:1618–27.

Research

JAMA Cardiology | Brief Report

Optimal Antithrombotic Regimens for Patients With Atrial Fibrillation Undergoing Percutaneous Coronary Intervention

An Updated Network Meta-analysis

Renato D. Lopes, MD, PhD; Hwanhee Hong, PhD; Ralf E. Harskamp, MD, PhD; Deepak L. Bhatt, MD, MPH; Roxana Mehran, MD; Christopher P. Cannon, MD; Christopher B. Granger, MD; Freek W. A. Verheugt, MD, PhD; Jianghao Li, MS; Jurriën M. ten Berg, MD, PhD; Nikolaus Sarafoff, MD; Pascal Vranckx, MD; Andreas Goette, MD; C. Michael Gibson, MD; John H. Alexander, MD, MHS

Supplemental content

IMPORTANCE Antithrombotic treatment in patients with atrial fibrillation (AF) and percutaneous coronary intervention (PCI) presents a balancing act with regard to bleeding and ischemic risks.

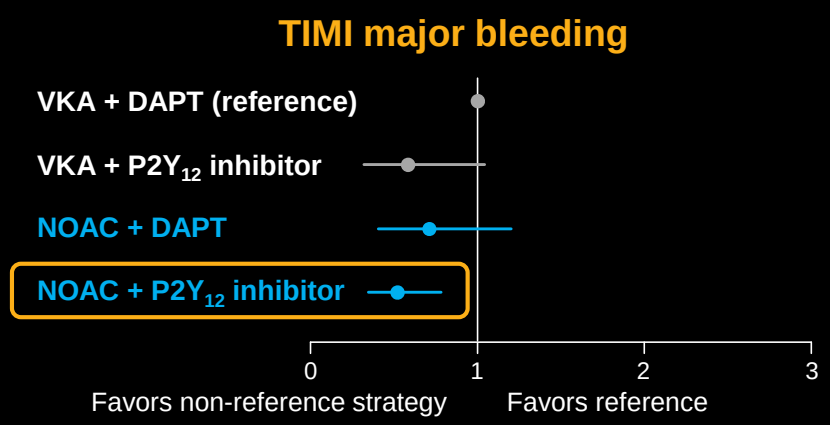
OBJECTIVES To evaluate the safety and efficacy of 4 antithrombotic regimens by conducting an up-to-date network meta-analysis and to identify the optimal treatment for patients with AF undergoing PCI.

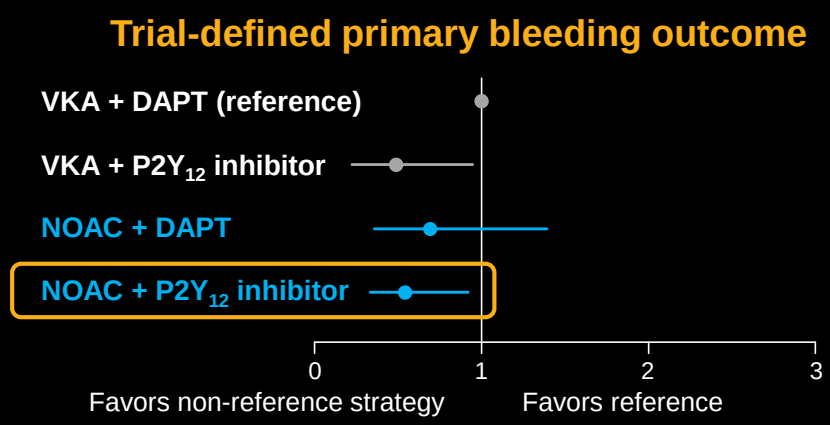
DATA SOURCES Online computerized database (MEDLINE).

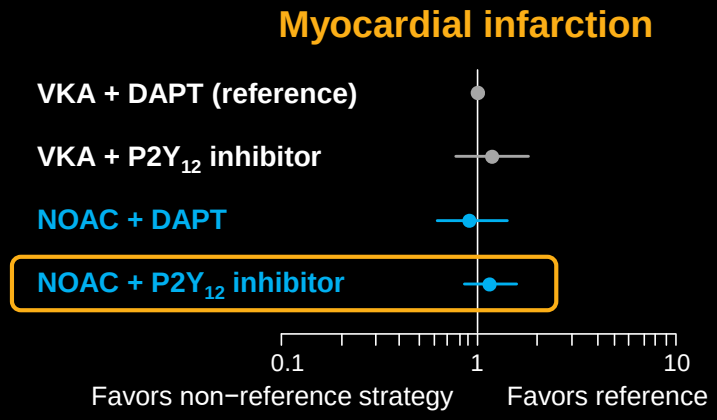
STUDY SELECTION Five randomized studies were included (N = 11 542; WOEST, PIONEER AF-PCI, RE-DUAL PCI, AUGUSTUS, ENTRUST-AF PCI).

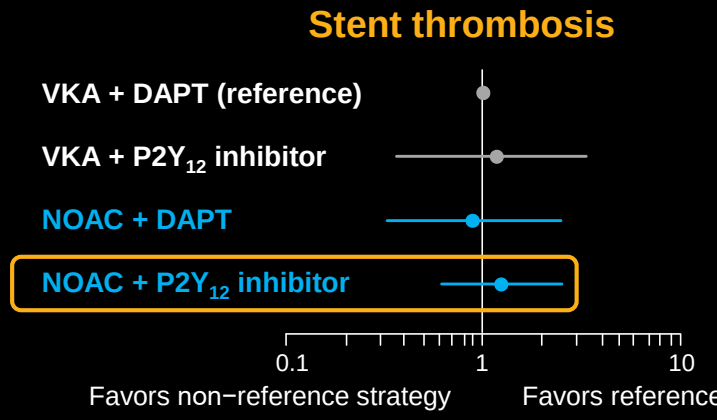
1. Lopes RD, et al. JAMA Cardiol 2020

Updated meta-analysis: Patients with AF undergoing PCI (~12,000 patients)[1]









Adapted from Lopes et al. 2020.

Data show odds ratio (95% CI)

1. Lopes RD, et al. JAMA Cardiol 2020;5:582–9.

A network meta-analysis: The safety and efficacy of different antithrombotic regimens in patients with AF and ACS and/or PCI

In patients with AF undergoing PCI, a regimen of **NOAC plus $P2Y_{12}$ inhibitor was associated with fewer bleeding complications, including intracranial bleeding, without a significant difference in ischemic events vs VKA plus DAPT**[1]

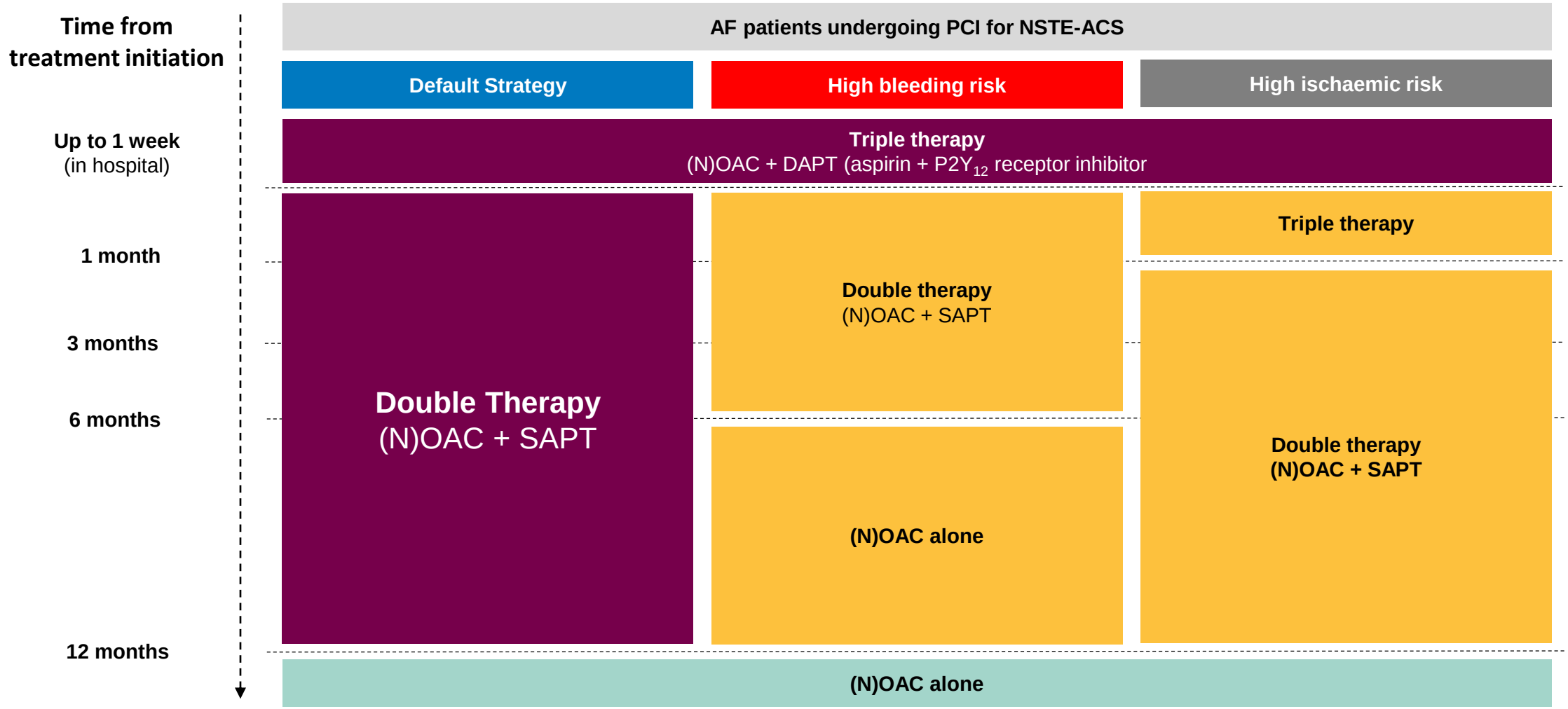
1. Lopes RD, et al. JAMA Cardiol 2019. doi:10.1001/jamacardio.2019.1880.
2. Lopes RD, et al. JAMA Cardiol 2020.

The present/future

- In patients with AF and a recent ACS or PCI, the use of a NOAC at the appropriate dose for stroke prevention plus a $P2Y_{12}$ without aspirin should be the preferred treatment option.
- In General, DAPT duration should be around 1 week after PCI
- If the risk of stent thrombosis and other ischemic events is high, aspirin use for 30 days seems reasonable
- Consistency in guidelines – LOE A
- Patient management options should be tested in randomized trials

Slide Dr. Renato D. Lopes

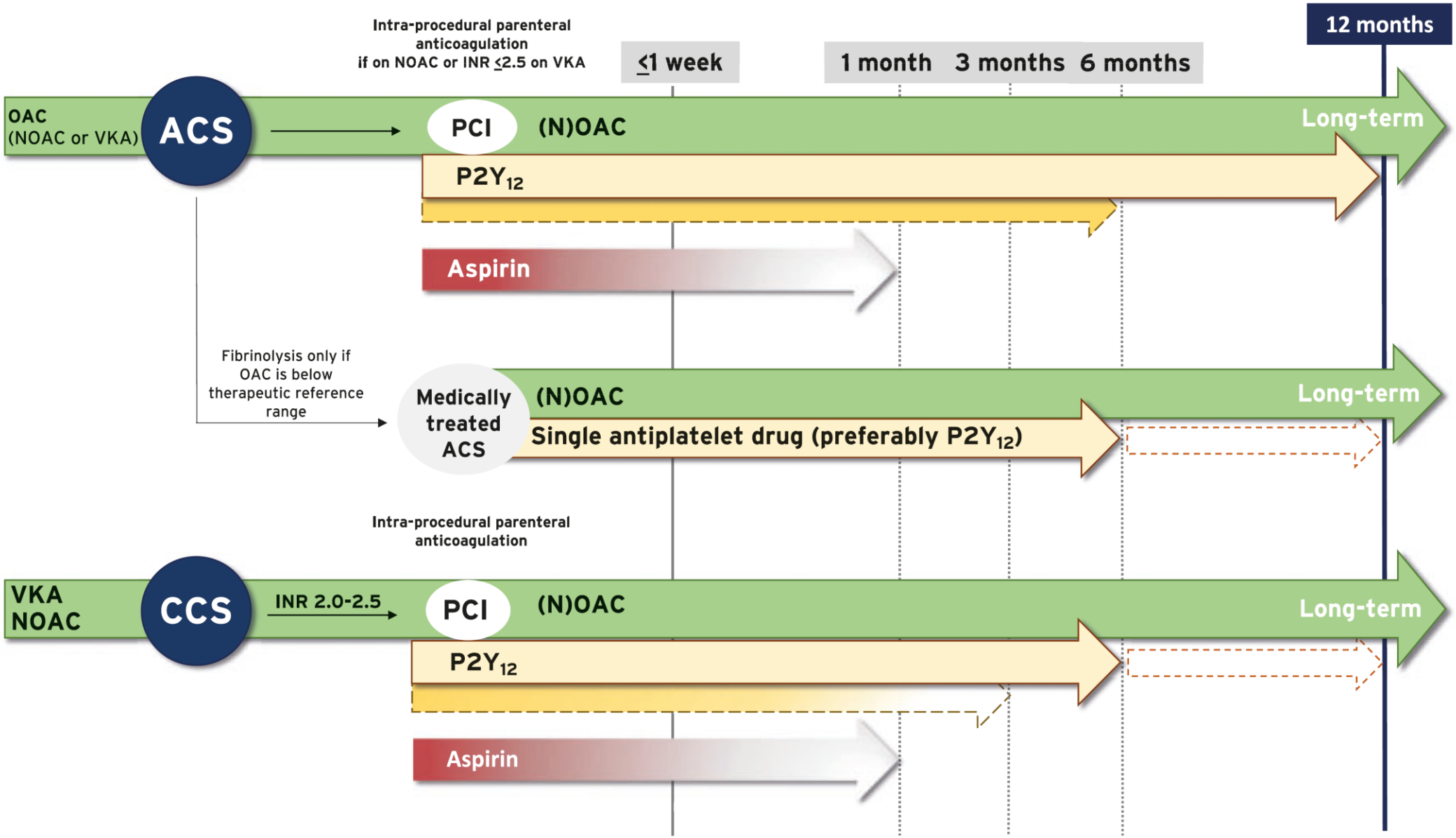
2020 ESC guidelines stratify according to bleeding and ischaemic risk



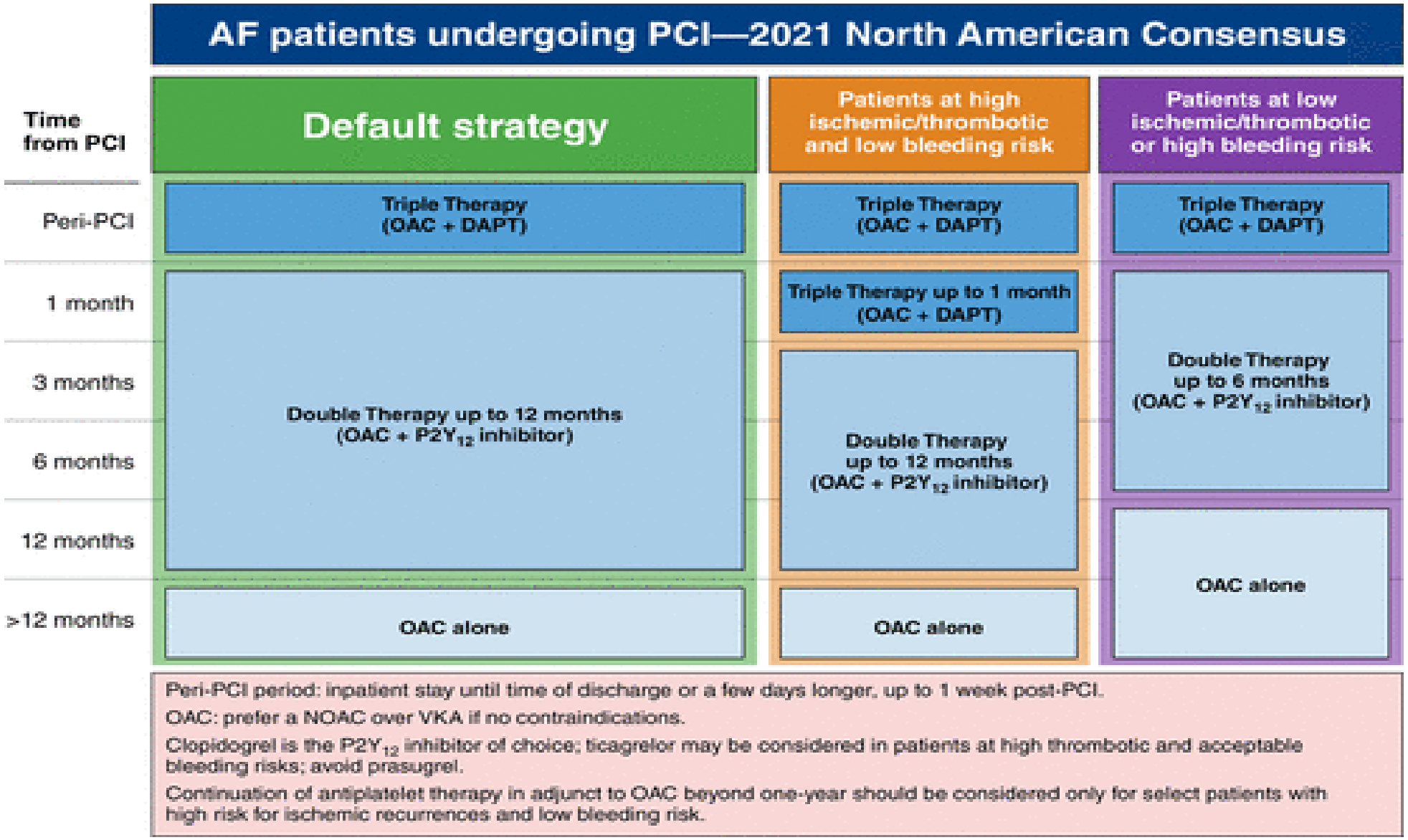
AF: Atrial fibrillation; NSTE-ACS: Non-ST-elevation acute coronary syndrome; (N)OAC: (Non-vitamin C inhibitor) oral anticoagulant; SAPT: Single antiplatelet therapy;

Reference: 1. Collet J-P *et al. EHJ* 2020; **00:** 1-79.

Anticoagulation in AF patients after ACS / PCI (2020 ESC AF Guidelines)



Hindricks et al., European Heart Journal 2020



Dominick J. Angiolillo. Circulation. Antithrombotic Therapy in Patients With Atrial Fibrillation Treated With Oral Anticoagulation Undergoing Percutaneous Coronary Intervention, Volume: 143, Issue: 6, Pages: 583-596, DOI: (10.1161/CIRCULATIONAHA.120.050438)

ESC European Society of Cardiology

European Heart Journal (2019) **0**, 1–3
doi:10.1093/eurheartj/ehz823

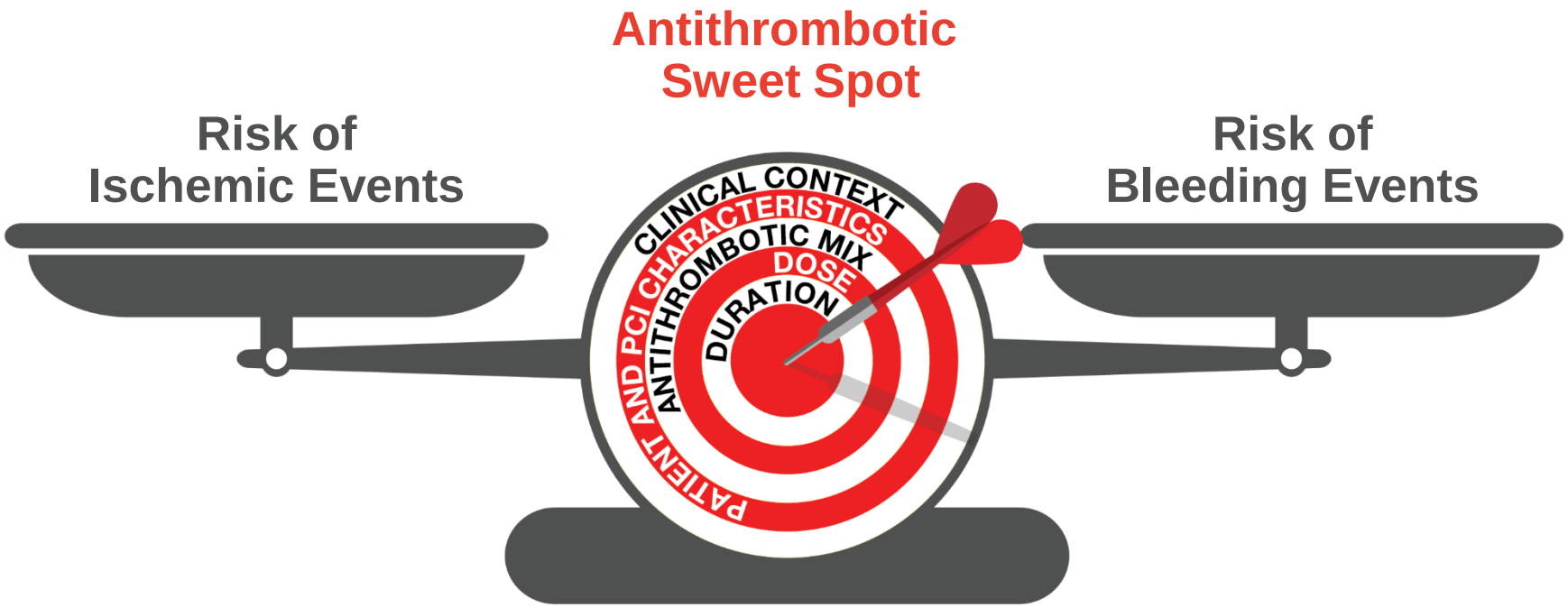
EDITORIAL

Antithrombotic therapy after acute coronary syndrome and/or percutaneous coronary intervention in atrial fibrillation: finding the sweet spot

Renato D. Lopes[1,2]*, Hwanhee Hong [2,3], and John H. Alexander [1,2]

[1]Division of Cardiology, Duke University School of Medicine, Durham, NC, USA; [2]Duke Clinical Research Institute, Duke University School of Medicine, Durham, NC, USA; and [3]Department of Biostatistics and Bioinformatics, Duke University School of Medicine, Durham, NC, USA

Finding the Antithrombotic Sweet Spot



The right combination of antithrombotic agents at the right dose and duration to reduce ischemic events as much as possible at a minimal cost of bleeding

Lopes RD et al. EHJ, 2019

Thank you!

Renato D Lopes, MD MHS PhD
Professor of Medicine
Division of Cardiology
Duke Clinical Research Institute
Duke University Medical Center

Duke Clinical Research Institute

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