Antiplatelet Strategy for Complex PCI

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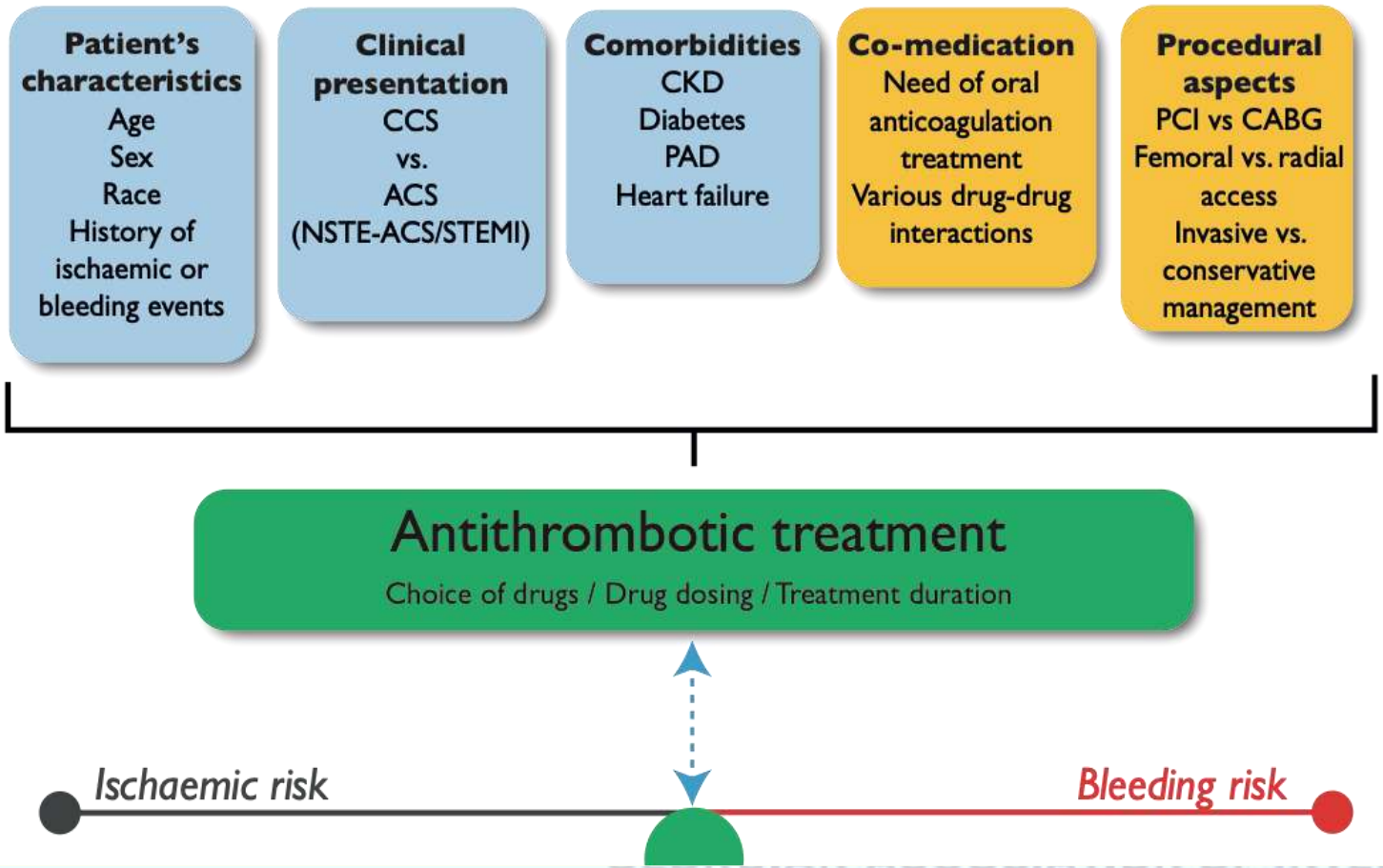
Determinants of antithrombotic treatment

2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (European Heart Journal 2020 - doi/10.1093/eurheartj/ehaa575)

ESC European Society of Cardiology

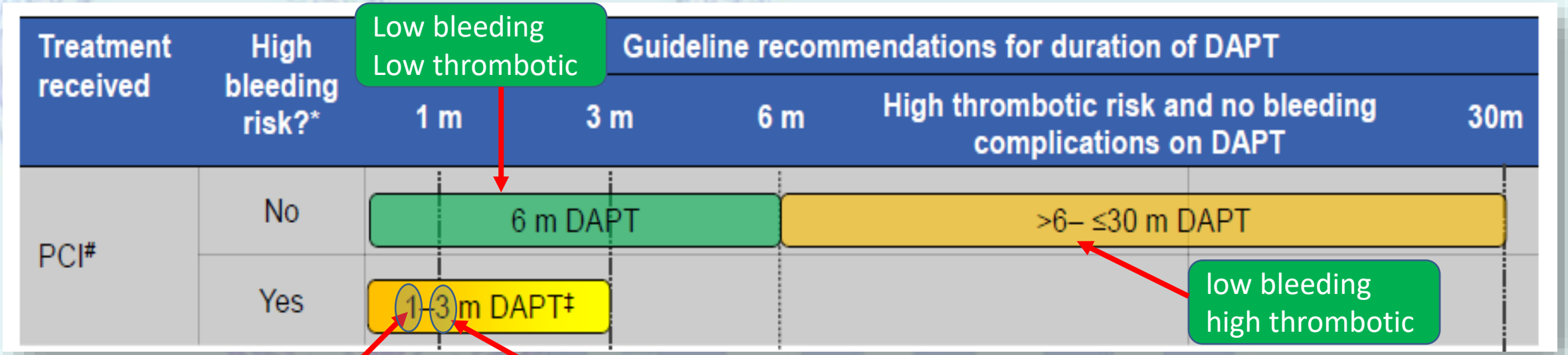


What is Complex PCI? EuroIntervention definition

Multivessel PCI

- ≥3 stents or ≥3 lesions
- Stent length ≥60 mm
- Bifurcation with 2-stent technique
- Left main, CTO, SVG

In a CCS – chronic coronary syndrome setting



Low bleeding
Low thrombotic

low bleeding
high thrombotic

high bleeding
Low thrombotic

high bleeding
High thrombotic

CCS: Aspirin+Clopidogrel
Default regimen

ESC Guideline on Complex-high risk PCI for CCS

European Heart Journal

JOURNAL ARTICLE GUIDELINES

2024 ESC Guidelines for the management of chronic coronary syndromes: Developed by the task force for the management of chronic coronary syndromes of the European Society of Cardiology (ESC) *Endorsed by the European Association for Cardio-Thoracic Surgery (EACTS)* FREE

In CCS patients undergoing high-thrombotic risk stenting (e.g. complex left main stem, 2-stent bifurcation, suboptimal stenting result, prior stent thrombosis, previously known CYP2C19 *2/*3 polymorphisms), prasugrel or ticagrelor (in addition to aspirin) may be considered instead of clopidogrel, for the first month, and up to 3–6 months.	IIb	C

In an Acute coronary syndrome setting

Low bleeding
Low thrombotic

low bleeding
high thrombotic

Treatment received*	High bleeding risk?*	Guideline recommendations for duration of DAPT				
		1 m	3 m	6 m	12 m	Prior MI and no bleeding complications on DAPT
PCI#	No	12 m DAPT‡				>12 m DAPT§
	Yes	6 m DAPT				

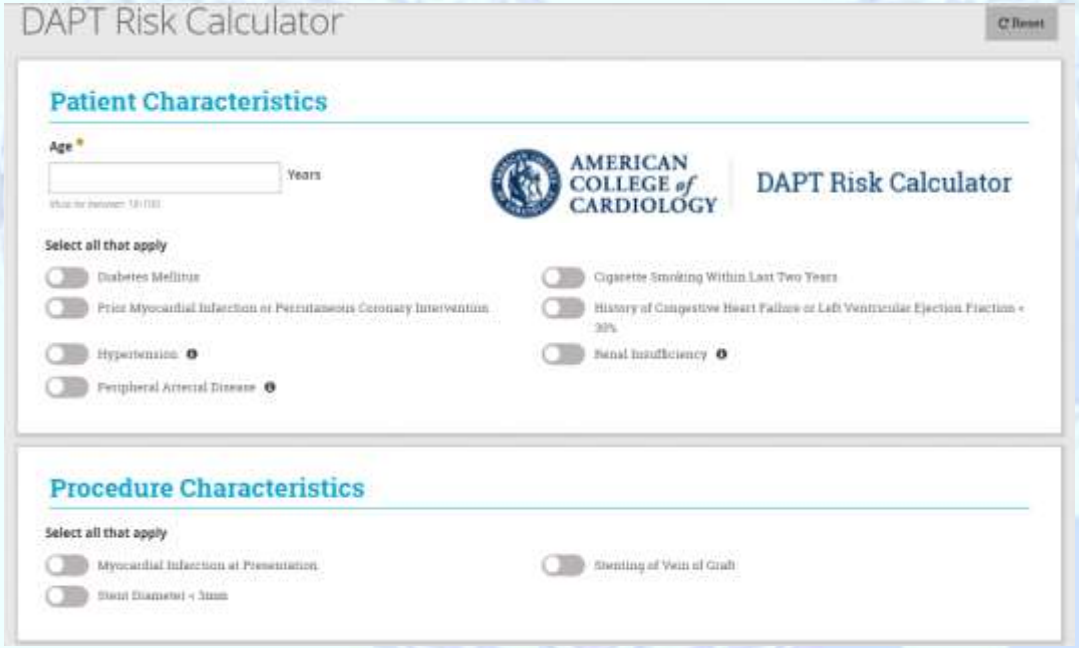
high bleeding
Low thrombotic

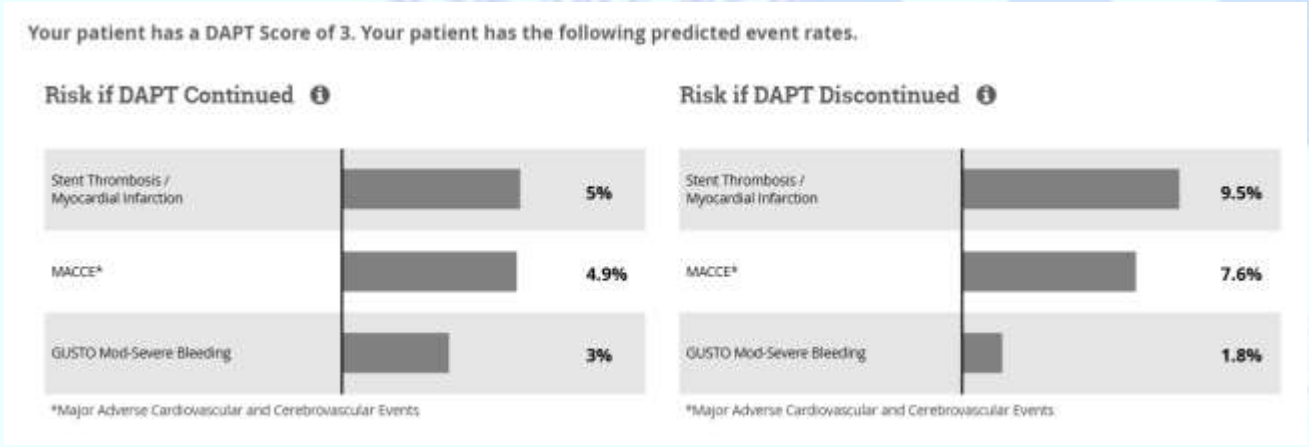
high bleeding
High thrombotic

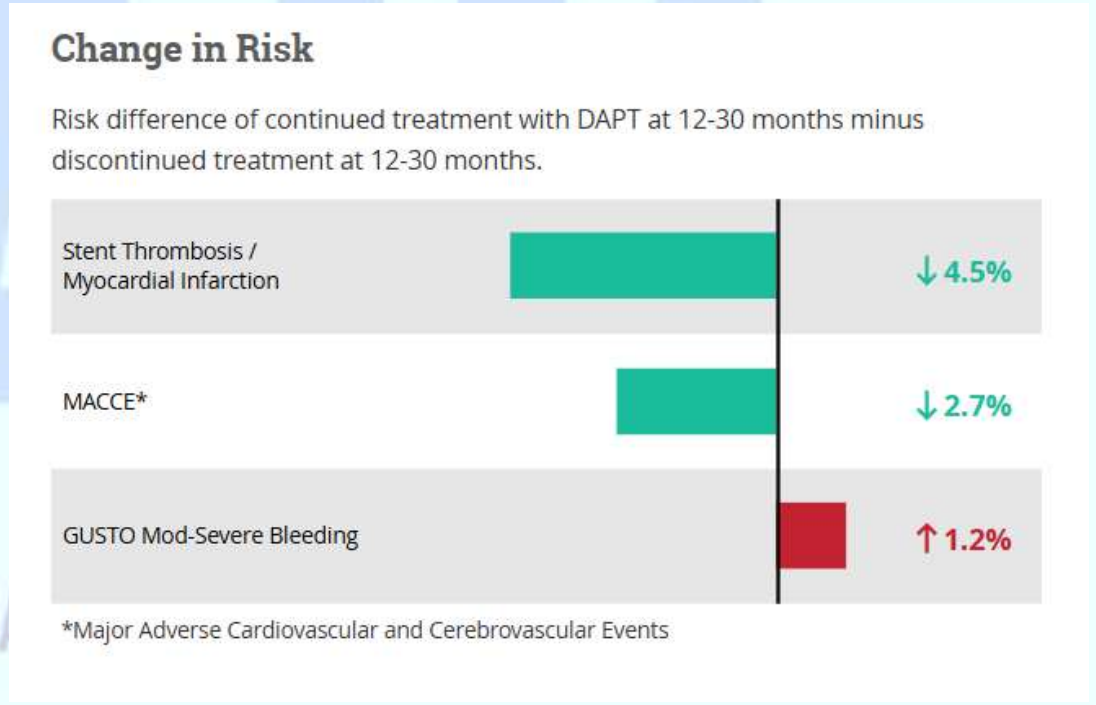
ACS: Aspirin+Prasigrel/Ticagrelor
Default regimen

DAPT Score for extension dual APT in pts w/out high bleeding risk

https://tools.acc.org/daptriskapp/#!/content/calculator/







ESC Guideline on extended DAPT approach

European Heart Journal

2023 ESC Guidelines for the management of acute coronary syndromes

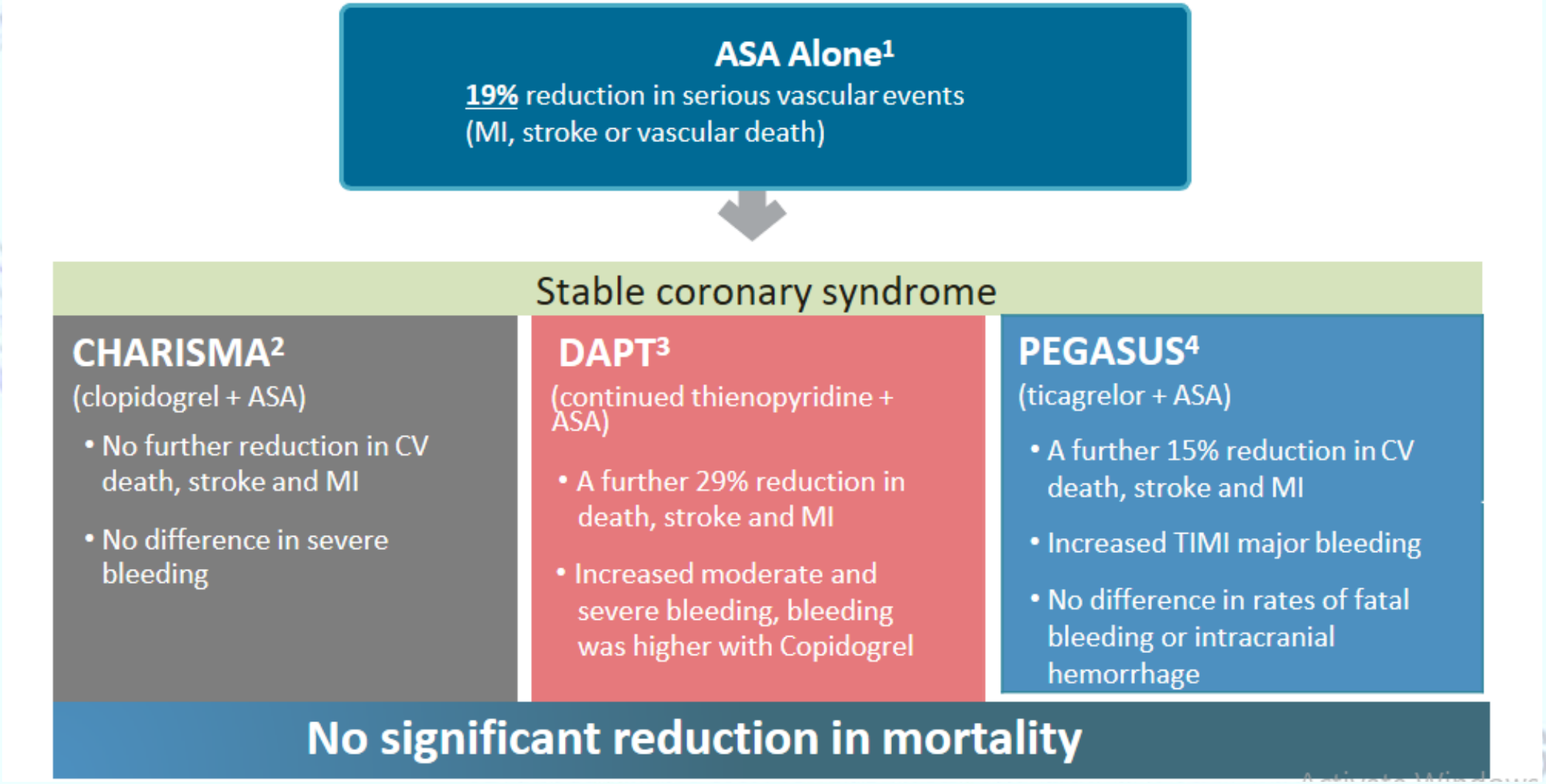
ESC European Society of Cardiology

European Heart Journal (2023) **44**, 3720–3826
https://doi.org/10.1093/eurheartj/ehad191

Prolonging antithrombotic therapy		
Discontinuation of antiplatelet treatment in patients treated with an OAC is recommended after 12 months.[324,325]	I	B
Adding a second antithrombotic agent to aspirin for extended long-term secondary prevention should be considered in patients with high ischaemic risk and without HBR[c].[314–318]	IIa	A
Adding a second antithrombotic agent to aspirin for extended long-term secondary prevention may be considered in patients with moderate ischaemic risk and without HBR[c].[314–318]	IIb	A
$P2Y_{12}$ inhibitor monotherapy may be considered as an alternative to aspirin monotherapy for long-term treatment.[326,327]	IIb	A

? Second antithrombotic

Evidence on Extended APT



Comparative Evidence Strength for Extended DAPT (>12 Months)

P2Y12 Inhibitor	Key Trials	Evidence for >12 Months	ESC/EAPCI Recommendation	Comment
Clopidogrel	DAPT, OPTIDUAL, DES-LATE, PRODIGY	✅ Supported (modest benefit, ↑ bleeding)	May extend if high ischemic / low bleeding risk	Most data available
Ticagrelor	PEGASUS-TIMI 54, THEMIS-PCI	✅ Supported (esp. prior MI, diabetes)	Consider extended therapy in selected patients	Clear net benefit in THEMIS-PCI subgroup
Prasugrel	— (no dedicated RCTs)	❌ Not established	12-month duration standard (ACS)	Evidence extrapolated from other agents

ESC/EAPCI 2023 Guideline Perspective in CCS:

– Standard DAPT duration: 6 months after elective DES in CCS.

– May shorten to 3 months in HBR patients.

– May extend >12 months in prior MI, multivessel disease, or diabetic post-PCI (THEMIS-PCI).

– Extension only if bleeding risk is low (PRECISE-DAPT <25).

In CCS, extended DAPT >12 months is the exception — justified mainly in prior MI or THEMIS-PCI–like diabetic patients.

References: Mauri et al., NEJM 2014 (DAPT); Bonaca et al., NEJM 2015 (PEGASUS-TIMI 54); Steg et al., Lancet 2019 (THEMIS-PCI); ESC/EAPCI DAPT Guidance 2023.

Extended APT – COMPAS Trial *(Riva 2.5 mg BID)

In stable CAD patients on guideline-recommended therapy,
rivaroxaban vascular dose 2.5 mg BID + ASA 100 mg QD vs. ASA 100 mg QD resulted in:

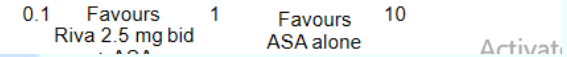
EFFICACY:

- ↓ CV death, stroke or MI by 24%
- ↓ Ischemic stroke by 49%
- ↓ CV mortality by 22%, all-cause mortality by 18%
- Clear net clinical benefit of 20%

SAFETY:

- ↑ Major bleeding by 70% (absolute increase 1.2%)
  - Mainly GI bleeding, concentrated in the first year
- Did not significantly increase fatal bleeding, intracranial hemorrhage or bleeding into a critical organ

Time from Randomization	Rivaroxaban vascular dose 2.5 mg BID + ASA n/N (%)		ASA Alone n/N (%)		HR (95% CI)
MACE					
<1 year	176/8313	(2)	221/8261	(3)	0.79 (0.65–0.96)
1–<2 years	113/7228	(2)	169/7125	(2)	0.66 (0.52–0.83)
>2 years	58/3655	(2)	70/3621	(2)	0.82 (0.58–1.16)
Major bleeding					
<1 year	163/8313	(2)	70/8261	(1)	2.32 (1.75–3.07)
1–<2 years	70/7189	(1)	59/7183	(1)	1.19 (0.84–1.68)
>2 years	30/3626	(1)	29/3694	(1)	1.05 (0.63–1.75)
All deaths					
<1 year	117/8313	(1)	145/8261	(2)	0.80 (0.63–1.02)
1–<2 years	93/7323	(1)	120/7242	(2)	0.77 (0.59–1.01)
>2 years	52/3743	(1)	74/3762	(2)	0.70 (0.49–1.00)



Bleeding Risk Assessment

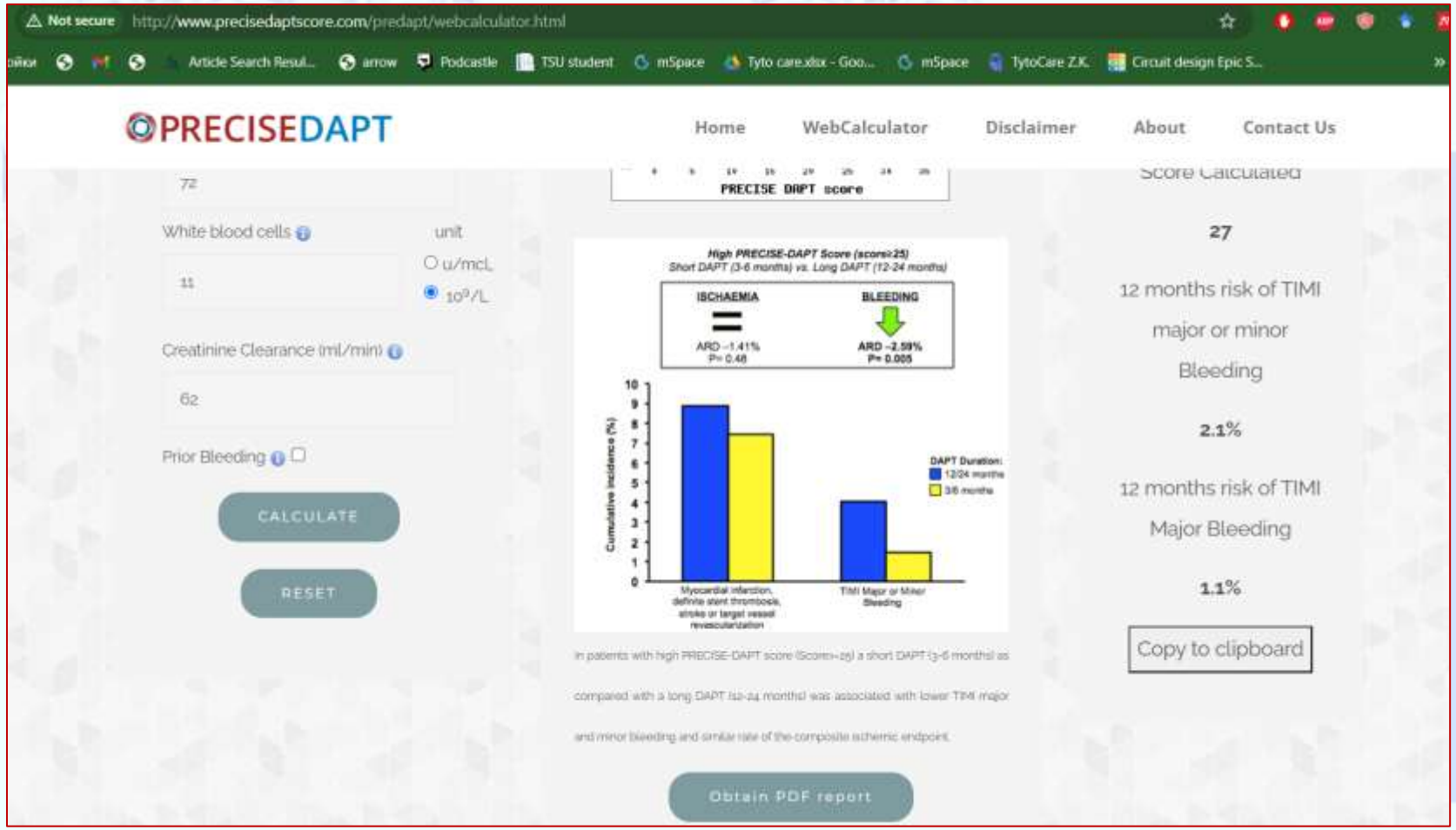
- Complex anatomy ↑ ischemic events
- Risk scores:
  - **PRECISE-DAPT (bleeding prediction)**
  - DAPT Score (benefit from prolonged DAPT)

PRICESE-DAPT Score

- Haemoglobin: 11.9 (g/dl)
- Age: 72 (years)
- White Blood Cell: 11 (10^9/L)
- Creatinine clearance: 62 (ml/min)
- Prior Bleeding: no

PRECISE-DAPT Score: 27 (high risk >25)

http://www.precisedaptscore.com



Shorter DAPT strategies

DAPT abbreviation strategy

- shortening the duration of DAPT followed by single antiplatelet therapy
- 1-6 month DAPT followed by monotherapy (aspirin or a single P2Y12 inhibitor)

DAPT de-escalation strategy

- moving from potent P2Y12 inhibitor-based DAPT and changing to aspirin and clopidogrel

Shorter DAPT trials

TWILIGHT

- Benefit for TICA monotherapy after 3 month of DAPT

GLOBAL-LEADERS

- The experimental strategy appeared to reduce bleeding risk in patients with ACS but not in patients with SCAD.

TOPIC

- A switched DAPT is superior to an unchanged DAPT strategy to prevent bleeding complications without increase in ischaemic events following ACS

STOPTDAPT-2 ACS

- Net clinical benefit of Clopidogrel monotherapy after 1 month of DAPT

STOPDAPT-3

- Not seen benefit from Aspirin free strategy within 1 month from PCI

MASTER DAPT

- In HBR patients free from recurrent ischaemic events at 1 month, DAPT discontinuation was associated with similar MACCE and lower bleeding rates compared with standard DAPT, regardless of PCI or patient complexity

Short-DAPT Strategies in High Bleeding-Risk (HBR) PCI Patients

Trial	Primary Population	Comment	Complex PCI Inclusion	$P2Y_{12}$ Inhibitor(s) Used
LEADERS FREE (NEJM 2015)	High bleeding-risk, any anatomy	Complex cases not excluded; DCS (BioFreedom) maintained low ST even in complex anatomy	**≈25 % complex** (bifurcation, ≥2 stents, long lesions)	**Clopidogrel only**
MASTER-DAPT (NEJM 2021)	HBR patients, contemporary DES (Ultimaster)	Subgroup analysis → 1-month DAPT **safe even in complex PCI** (HR 1.00 [0.73–1.37] for NACE)	**≈40 % complex PCI** (multivessel, long lesions, bifurcations)	**Clopidogrel ≈ 92 %, Ticagrelor ≈ 8 %**
ONYX ONE (JACC Intv 2020)	HBR population (Resolute Onyx vs BioFreedom)	Non-inferiority preserved across complexity strata; ST 1.3 % vs 2.1 %	**≈45 % complex** (mean 1.6 stents; 25 % bifurcation; 14 % CTO)	**Clopidogrel only**

ESC Guideline on De-escalating after PCI in ACS

European Heart Journal

2023 ESC Guidelines for the management of acute coronary syndromes

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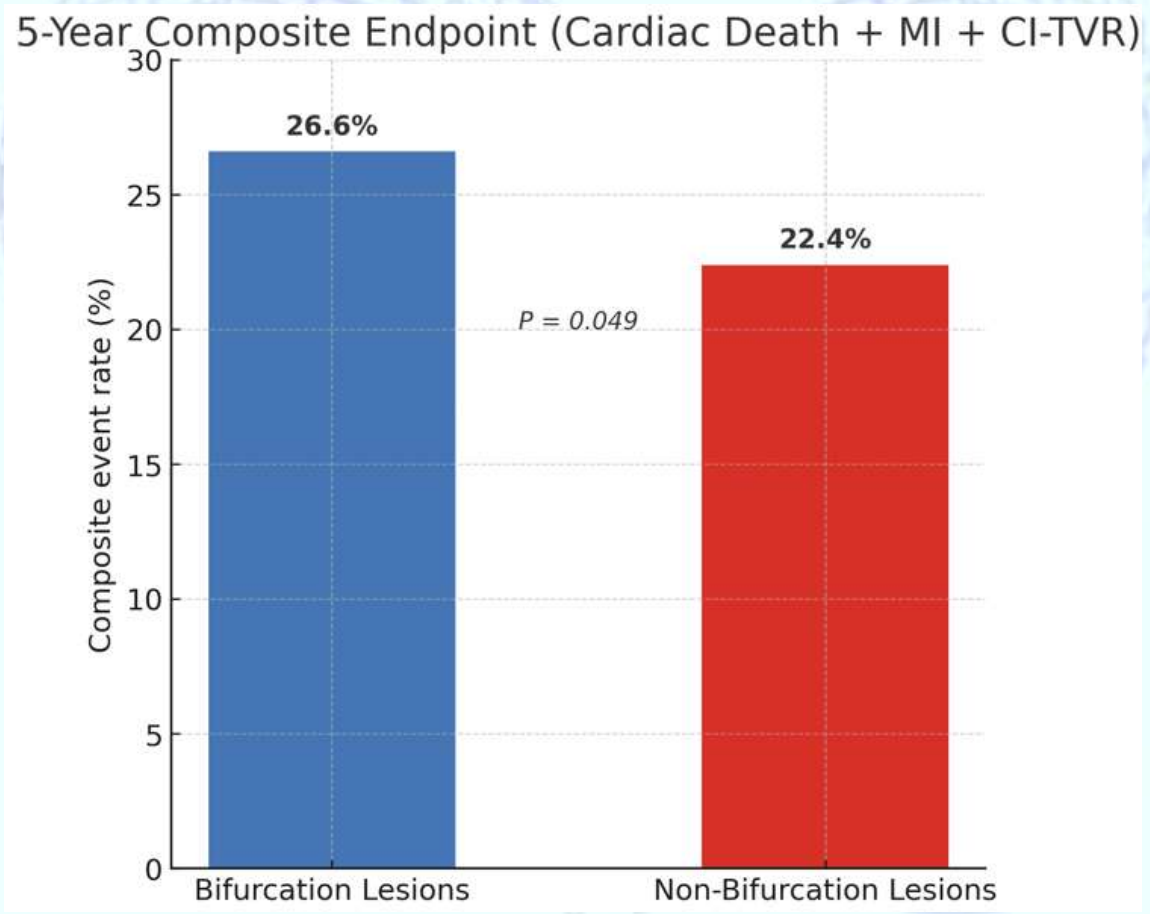
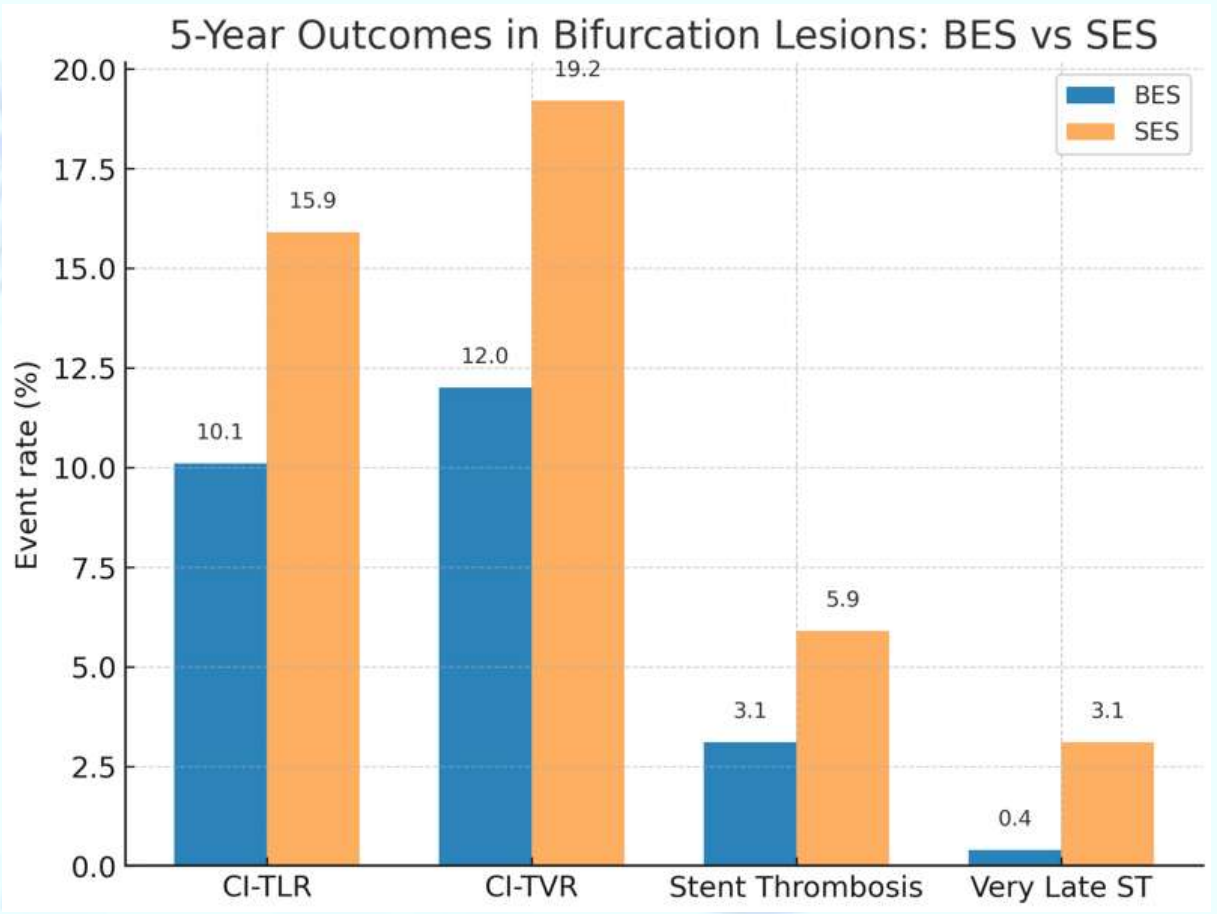
Recommendation Table 6 — Recommendations for alternative antithrombotic therapy regimens

Recommendations	Class[a]	Level[b]
Shortening/de-escalation of antithrombotic therapy		
In patients who are event-free after 3–6 months of DAPT and who are not high ischaemic risk, single antiplatelet therapy (preferably with a $P2Y_{12}$ receptor inhibitor) should be considered.[264,268–271,273,274,276,313,320]	IIa	A
De-escalation of $P2Y_{12}$ receptor inhibitor treatment (e.g. with a switch from prasugrel/ticagrelor to clopidogrel) may be considered as an alternative DAPT strategy to reduce bleeding risk.[279–282,321,322]	IIb	A
In HBR patients, aspirin or $P2Y_{12}$ receptor inhibitor monotherapy after 1 month of DAPT may be considered.[276,313]	IIb	B
De-escalation of antiplatelet therapy in the first 30 days after an ACS event is not recommended.[238,323]	III	B

CCI Catheterization & Cardiovascular Interventions

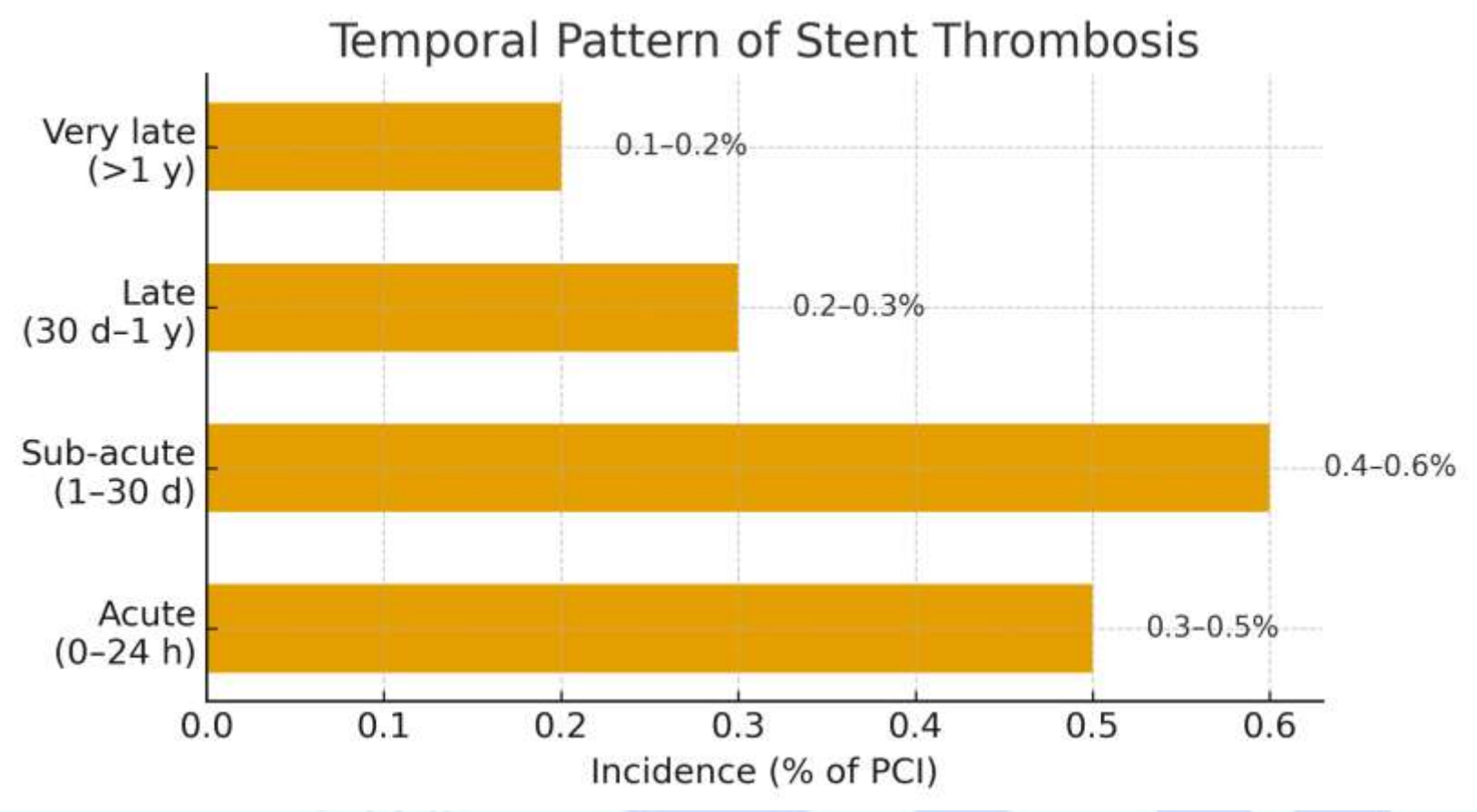
First generation versus second generation drug-eluting stents for the treatment of bifurcations: 5-year follow-up of the LEADERS all-comers randomized trial





Grundeken, Maik J., et al. "First generation versus second generation drug-eluting stents for the treatment of bifurcations: 5-year follow-up of the LEADERS all-comers randomized trial." *Catheterization and Cardiovascular Interventions* 87.7 (2016): E248-E260.

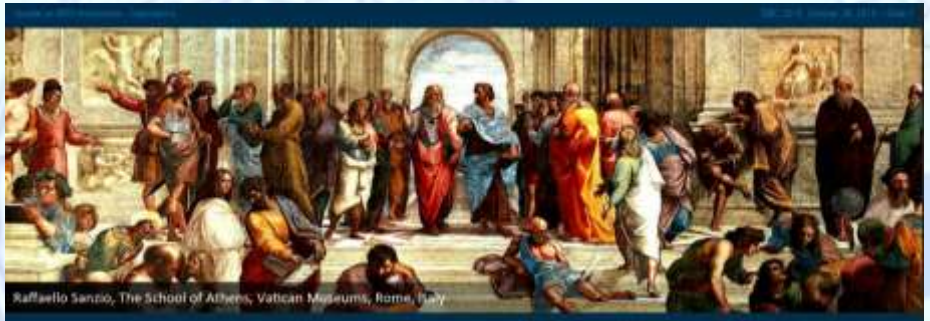
Temporal Pattern of Stent Thrombosis



Take-home: Early events dominate overall incidence, but vigilance remains essential beyond 1 year.

References: Cutlip DE et al., Circulation 2011; Bangalore S et al., JACC 2017; SCAAR Registry 2021.

B-SEARCH Registry - stent thrombosis data



B-SEARCH Registry

			Patient related		Lesion related	Procedure related			Device related
Case	Type	Days	ACS	DAPT cessation	Bifurcation	Incomplete coverage	ISA	Poor expansion	Loss of integrity
#1	Acute	0	Yes	No	No	Yes	N/A	No	No
#2	Acute	0	Yes	No	No	Yes	Yes	No	No
#3	Acute	1	Yes	No	No	Yes	N/A	No	No
#4	Acute	1	Yes	No	No	No	Yes	No	No
#5	Subacute	2	No	No	No	No	No	No	No
#6	Subacute	17	Yes	No	No	No	Yes	Yes	No
#7	Late	47	Yes	No	Yes	No	Yes	No	No
#8	Late	112	No	No	No	No	Yes	Yes	No
#9	Late	129	No	Yes	Yes	No	No	No	No
#10	Late	142	Yes	No	Yes	Yes	No	No	No
#11	Late	161	No	Yes	No	No	Yes	Yes	Yes
#12	Very Late	371	Yes	No	No	No	Yes	No	No
#13	Very Late	478	Yes	No	No	No	Yes	No	Yes
#14	Very late	675	No	No	No	No	Yes	No	Yes

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Karanasos A, et al. Circ Cardiovasc Interv. 2015
[Data Supplement, ePub Ahead of print]

UNIVERSITÀ degli STUDI di CATANIA

Capodanno, Davide, Michael Joner, and Marco Zimarino. "What about the risk of thrombosis with bioresorbable scaffolds." *EuroIntervention* 11.Suppl V (2015): V181-V184.

IVUS/OCT, MACE and stent thrombosis (ST)

Trial	Imaging	Population focus	MACE/TVF result	ST result
RENOVATE-COMPLEX PCI	IVUS±OCT (IVUS 74%)	Anatomically complex (bifurcation, long, CTO)	**7.7% vs 12.3%** (HR **0.64**, P=0.008)	—
OCTOBER	**OCT**	True bifurcation lesions	**10.1% vs 14.1%** (HR **0.70**, P=0.035)	—
ILUMIEN IV	**OCT**	Clinical ± anatomical complexity	TVF 7.4% vs 8.2% (NS)	**0.5% vs 1.4%** (HR **0.36**, P=0.02)

In complex PCI, **IVUS/OCT reduces MACE by ~30–35%** (RENOVATE, OCTOBER) and **cuts stent thrombosis by ~60%** (ILUMIEN IV). Use imaging **by default** in LM/bifurcation/long/CTO work and to de-risk HBR strategies.

Factors Influencing Stent Thrombosis Risk

Procedural factors:

- under-expansion/malapposition,
- edge dissection,
- residual stenosis,
- incomplete coverage,
- lack of IVUS/OCT optimization.

Pharmacologic factors:

- premature DAPT discontinuation,
- non-adherence,
- drug–drug interactions.

Clinical factors:

- ACS presentation,
- diabetes,
- CKD,
- bifurcation/long/small-vessel lesions,
- high bleeding risk leading to early DAPT stop.

References: ESC 2023 ACS/CCS guidance; EAPCI consensus 2022; ADAPT-DES Registry (JACC 2013).

Take-home: Stent thrombosis is multifactorial — meticulous technique, optimized DAPT, and adherence minimize risk.

High Ischemic and low Bleeding risk patient

- In **ACS** potent P2Y12 inhibitors with Aspirin at least 12 month,
  - Think about the prolongation of DAPT with:
    - Tigatrelor 60 mg BID (PEGASUS trial), or Clopodogrel (CHARISMA trial), or Rivaroxaban 2.5 mg BID (COMPAS trial)
- Think to prolong DAPT till 12 months in CCS patients and more than 12 months in ACS patients

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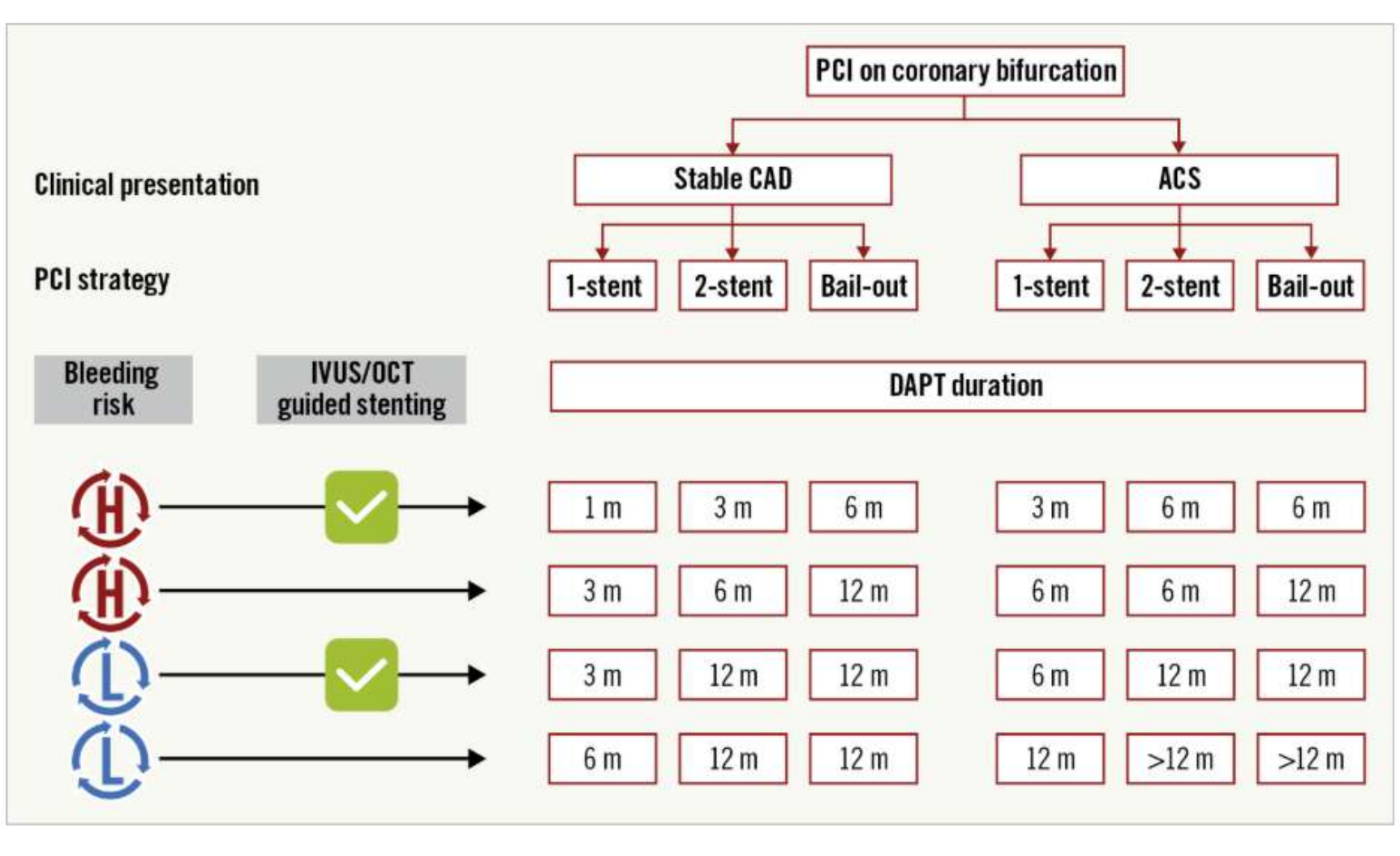
- In **CCS** potent P2Y12 inhibitors with Aspirin 1-3 month would be acceptable aproach - followed by de-escalation strategy of DAPT with ASA/Clopidogrel within 3-9 month
  - Evidence in Complex Coronary Intervention is missing

In all cases of high risk PCI or high Bleeding risk

- Avoid Complexity of technique by choose provisional technique
- Use newer Generation DES (dedicated to higher BR patients)
- Use imaging IVUS/OCT to reduce the device related acute thrombosis
- Think about using DCB (avoid full metal jacket)
- Think about how to individualize the case and develop a tailored antiplatelet strategy
  - First month to keep DAPT therapy is crucial
    - **Aspirin + Clopidogrel** remains the recommended standard approach, but consider a more potent $P2Y_{12}$ inhibitor during the first month after PCI
  - Think about SAPT strategy or de-escalation strategy after 1-3 month
  - Longer DAPT (≥12 mo) ↓ MI, But ↑ major bleeding
    - Net benefit only in non-HBR complex PCI

Expert consensus EuroIntervention



Zimarino, Marco, et al. "Antithrombotic therapy after percutaneous coronary intervention of bifurcation lesions: Antithrombotic drugs in bifurcation PCI." *EuroIntervention* 17.1 (2021): 59.

Evidence guides us — patients inspire us