17° MEETING CARDIOLUCCA 2023
22-24 Giugno 2023

Guida al trattamento antiaggregante personalizzato nelle SCA: rischi definiti ed obiettivi mutevoli

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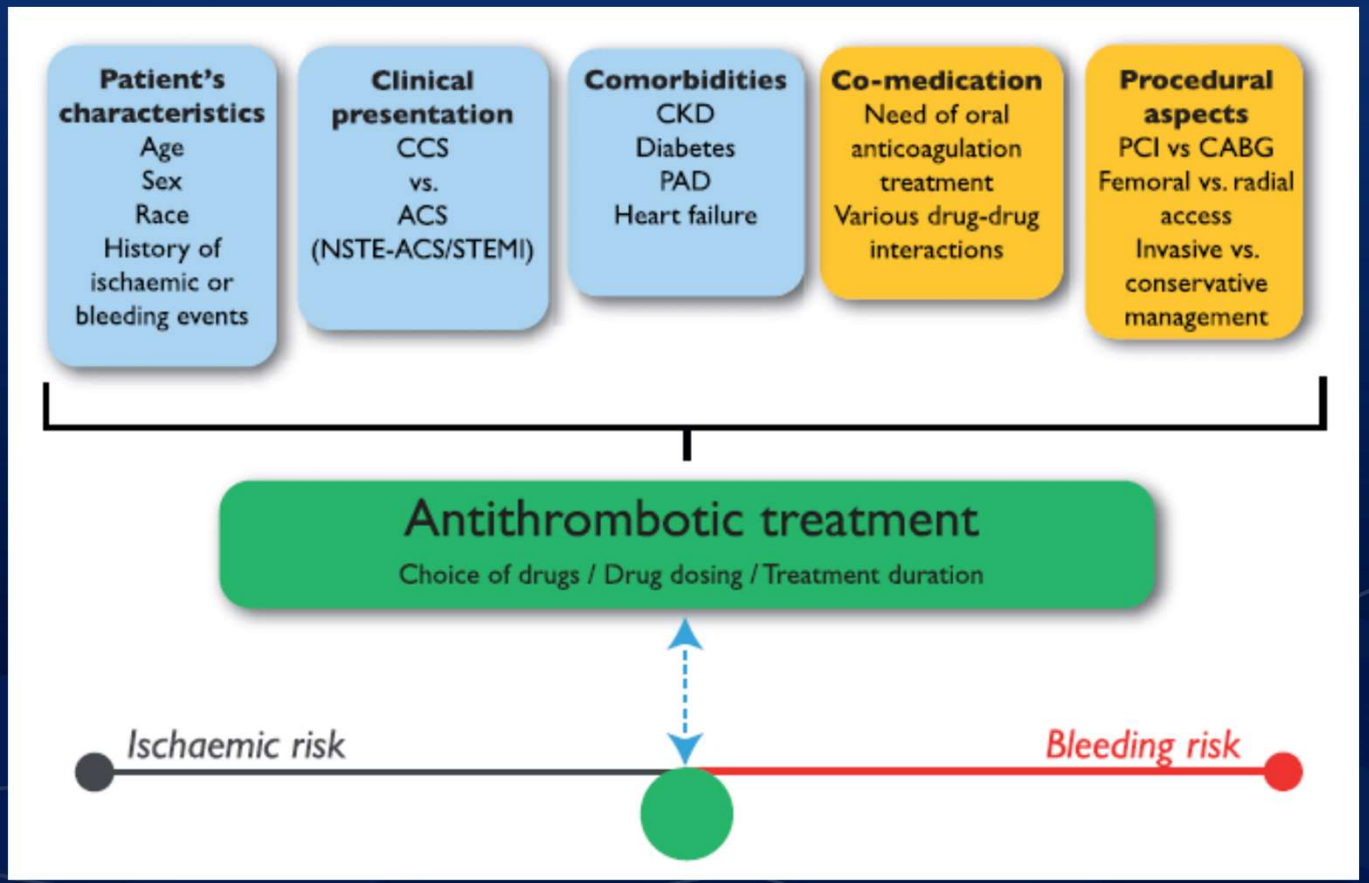
2020 ESC guidelines on ACS



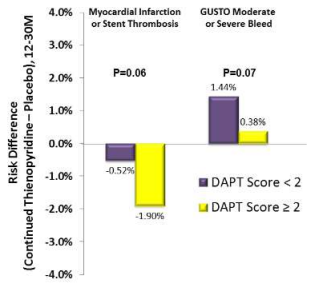
Ischemic risk scores

Score	Clinical setting	Variables included	Events included in outcome	Timing of outcome
Ischemic risk				
TIMI	**NSTE-ACS**	- Age ≥65 years - ≥3 CAD risk factors* - Known CAD (stenosis ≥50%) - ASA use in past 7 days - Severe angina (≥2 episodes in 24 hours) - EKG ST changes ≥0.5 mm - Positive cardiac markers	**All-cause death, new or recurrent MI, severe recurrent ischemia requiring urgent revascularization**	**14 days**
TIMI	**STEMI**	- Age - Diabetes mellitus, hypertension or angina - Systolic BP <100 mmHg - Heart rate >100 bpm - Killip class II-IV - Weight <67 kg - Anterior ST elevation or LBBB - Time to treatment >4 hours	**All-cause death**	**30 days**
GRACE	**ACS**	- Age - Heart rate - Systolic BP - Serum creatinine - Cardiac arrest at admission - ST-segment deviation - Abnormal cardiac markers - Killip class	**All-cause death**	**6 months**

Ischemic and bleeding risk				
DAPT score	**At least one year from STEMI/NSTE-ACS**	**- Age - Heart failure/LV dysfunction - Venous graft bypass - MI at the time of acute event - Previous MI or PCI - Diabetes mellitus - Stent diameter <3 mm - Current smoking - Paclitaxel stent**	**MI or stent thrombosis; GUSTO moderate or severe bleeding**	**30 months after the index event**
Bleeding risk				
PRECISE-DAPT	**At the time of coronary stenting**	**- Haemoglobin - White blood cells - Age - CrCl - Prior bleeding**	**TIMI major bleeding; any TIMI bleeding**	**1 year**
CRUSADE	**MI**	**- Heart rate - Systolic BP - Haematocrit - CrCl - Gender - Signs of CHF - History of vascular disease - Diabetes mellitus**	**CRUSADE major bleeding**	**In-hospital**
ACUITY	**ACS**	**- Gender - Age - Serum creatinine - White blood cell count - Anemia - Clinical presentation - Antithrombotic drugs**	**Major bleeding ****	**30 days**

Bleeding and ischemic scores

	DAPT score[15]	PRECISE-DAPT score[18]
Time of use	After 12 months of uneventful DAPT	At the time of coronary stenting
DAPT duration strategies assessed	Standard DAPT (12 months) vs. Long DAPT (30 months)	Short DAPT (3–6 months) vs. Standard/long DAPT (12–24 months)
Score calculation[a]	Age ≥75: −2 pt; 65 to <75: −1 pt; <65: 0 pt Cigarette smoking: +1 pt Diabetes mellitus: +1 pt MI at presentation: +1 pt Prior PCI or prior MI: +1 pt Paclitaxel-eluting stent: +1 pt Stent diameter <3 mm: +1 pt CHF or LVEF <30%: +2 pt Vein graft stent: +2 pt	HB ≥12 11-5 11 10-5 ≤10 WBC ≤5 8 10 12 14 16 18 ≥20 Age ≤50 60 70 80 ≥90 CrCl ≥100 80 60 40 20 0 Prior Bleeding No Yes Score Points 0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30
Score range	−2 to 10 points	0 to 100 points
Decision making cut-off suggested	Score ≥2 → Long DAPT Score <2 → Standard DAPT	Score ≥25 → Short DAPT Score <25 → Standard/long DAPT
Calculator	www.daptstudy.org	www.precisedaptscore.com

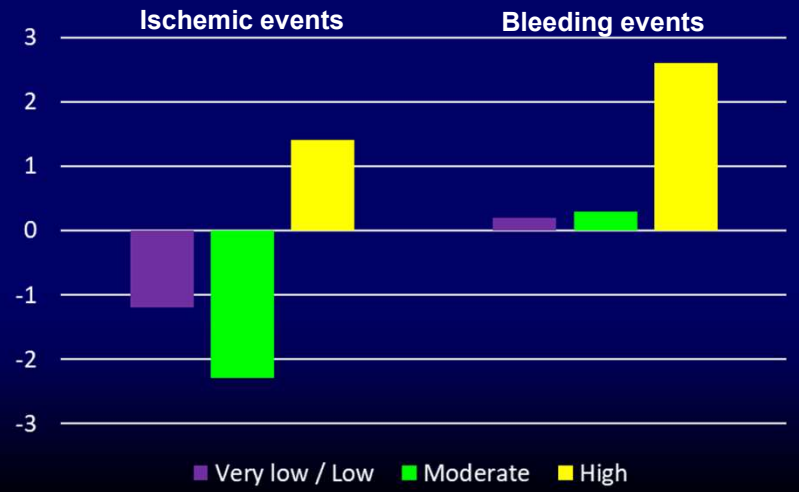


P values are for comparison of risk differences across DAPT Score category (interaction).

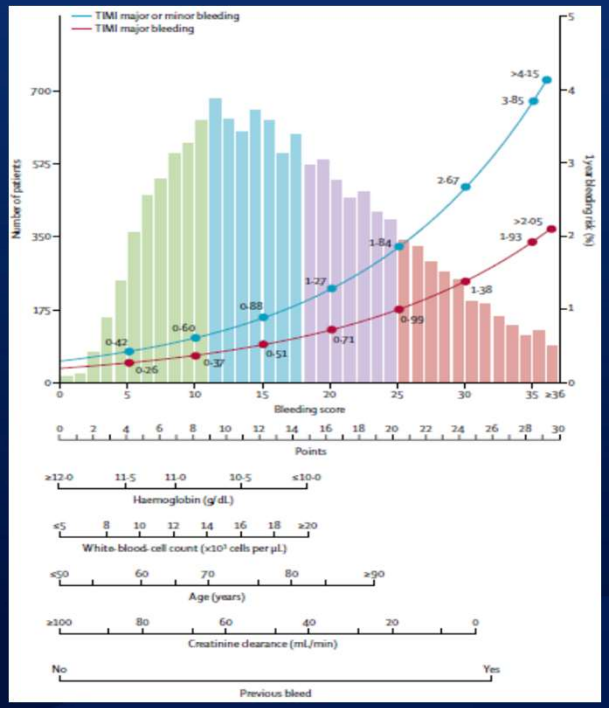
this analysis suggests that patients with DAPT score ≥ 2 gets more CV benefits with DAPT with relatively lower risk of bleedings, so they are candidates for extended DAPT.

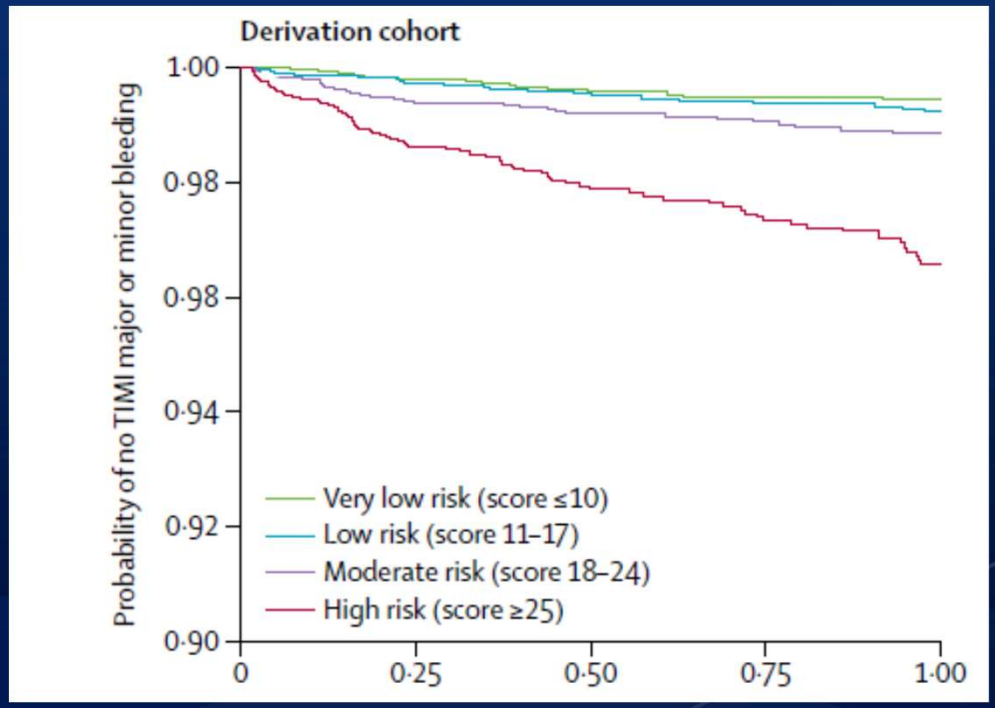
Low DAPT Score (< 2)
NNT to prevent ischemia = 153
NNH to cause bleeding = 64

High DAPT Score ≥ 2
NNT to prevent ischemia = 34
NNH to cause bleeding = 272



PRECISE DAPT: c-index 0.70 (0.65-0.74)





- High-risk score: 97% probability to have no any bleeding at 1 year
- Low predictive role for major bleeding (c-index 0.65) in ACS patients undergoing PCI and treated with prasugrel or ticagrelor

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	DAPT score[15]		PRECISE-DAPT score[18]
Time of use	After 12 months of uneventful DAPT		At the time of coronary stenting
DAPT duration strategies assessed	Standard DAPT (12 months) vs. Long DAPT (30 months)		Short DAPT (3–6 months) vs. Standard/long DAPT (12–24 months)
Score calculation[a]	Age		HB ≥12 11-5 11 10-5 ≤10
	≥75	−2 pt	WBC ≤5 8 10 12 14 16 18 ≥20
	65 to <75	−1 pt	Age ≤50 60 70 80 ≥90
	<65	0 pt	CrCl ≥100 80 60 40 20 0
	Cigarette smoking	+1 pt	Prior Bleeding No Yes
	Diabetes mellitus	+1 pt	Score Points 0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30
	MI at presentation	+1 pt	
	Prior PCI or prior MI	+1 pt	
	Paclitaxel-eluting stent	+1 pt	
	Stent diameter <3 mm	+1 pt	
	CHF or LVEF <30%	+2 pt	
	Vein graft stent	+2 pt	
Score range	−2 to 10 points		0 to 100 points
Decision making cut-off suggested	Score ≥2 → Long DAPT Score <2 → Standard DAPT		Score ≥25 → Short DAPT Score <25 → Standard/long DAPT
Calculator	www.daptstudy.org		www.precisedaptscore.com

Considerations on the risk scores

- Underestimation of the ischemic risk in elderly patients
- Underestimation of the bleeding risk in the low risk score
- No mention on frailty
- No validation in prospective studies
- No accuracy in the individual patient, especially for the bleeding risk

An individual patient……..

- ❑ Hb 11.5 g/dL
- ❑ Age 70 yrs
- ❑ Normal renal function
- ❑ No prior bleeding

PRECISE DAPT 15 !!!!!

- ❑ Need for OAC
- ❑ Inflammatory bowel disease or bowel angiodysplasia

More comprehensive ischemic risk stratification

High thrombotic risk (Class IIa)	Moderate thrombotic risk (Class IIb)
Complex CAD and at least 1 criterion	**Non-complex CAD and at least 1 criterion**
Risk enhancers	
Diabetes mellitus requiring medication	Diabetes mellitus requiring medication
History of recurrent MI	History of recurrent MI
Any multivessel CAD	Polyvascular disease (CAD plus PAD)
Polyvascular disease (CAD plus PAD)	CKD with eGFR 15–59 mL/min/1.73 m^2
Premature (<45 years) or accelerated (new lesion within a 2-year time frame) CAD	
Concomitant systemic inflammatory disease (e.g. human immunodeficiency virus, systemic lupus erythematosus, chronic arthritis)	
CKD with eGFR 15–59 mL/min/1.73 m^2	
Technical aspects	
At least 3 stents implanted	
At least 3 lesions treated	
Total stent length >60 mm	
History of complex revascularization (left main, bifurcation stenting with ≥2 stents implanted, chronic total occlusion, stenting of last patent vessel)	
History of stent thrombosis on antiplatelet treatment	

More comprehensive bleeding risk stratification

Major	Minor
• Anticipated use of long-term OAC[a]	• Age ≥ 75 years
• Severe or end-stage CKD (eGFR <30 mL/min)	• Moderate CKD (eGFR 30–59 mL/min)
• Haemoglobin <11 g/dL	• Haemoglobin 11–12.9 g/dL for men or 11–11.9 g/dL for women
• Spontaneous bleeding requiring hospitalization and/or transfusion in the past 6 months or at any time, if recurrent	• Spontaneous bleeding requiring hospitalization and/or transfusion within the past 12 months not meeting the major criterion
• Moderate or severe baseline thrombocytopenia[b] (platelet count <100 × 10^9/L)	• Chronic use of oral non-steroidal anti-inflammatory drugs or steroids
• Chronic bleeding diathesis	• Any ischaemic stroke at any time not meeting the major criterion
• Liver cirrhosis with portal hypertension	
• Active malignancy[c] (excluding non-melanoma skin cancer) within the past 12 months	
• Previous spontaneous intracranial haemorrhage (at any time) • Previous traumatic intracranial haemorrhage within the past 12 months • Presence of a brain arteriovenous malformation • Moderate or severe ischaemic stroke[d] within the past 6 months	
• Recent major surgery or major trauma within 30 days prior to PCI • Non-deferrable major surgery on DAPT	

PRAISE score

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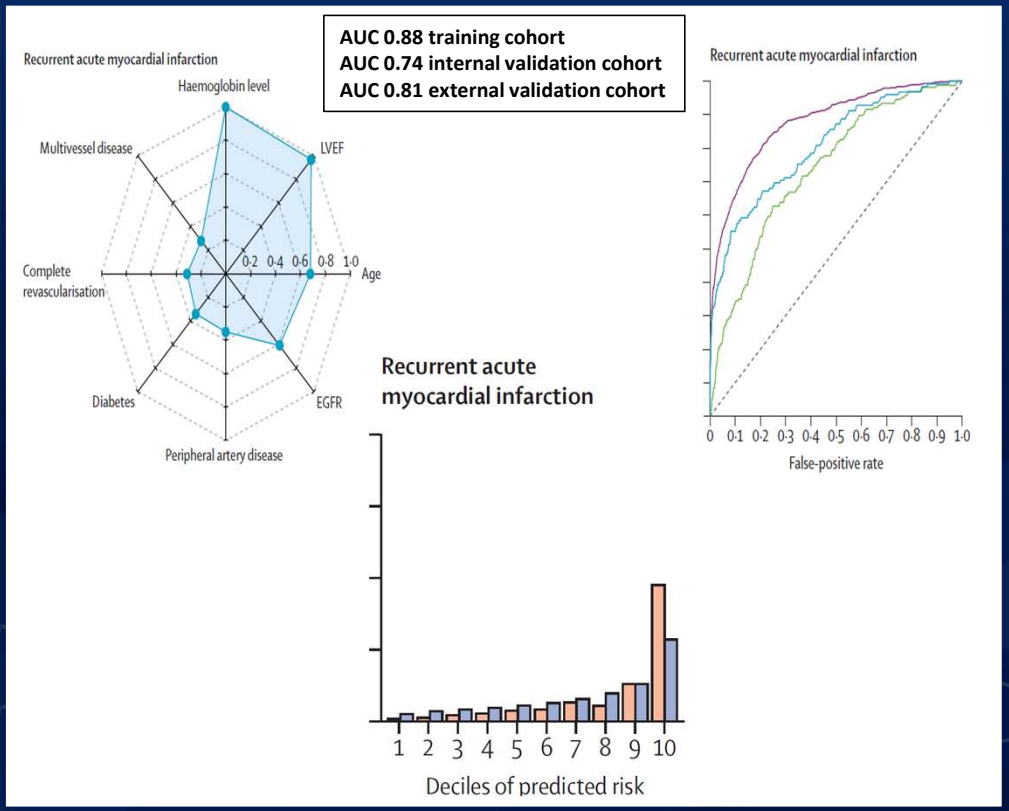
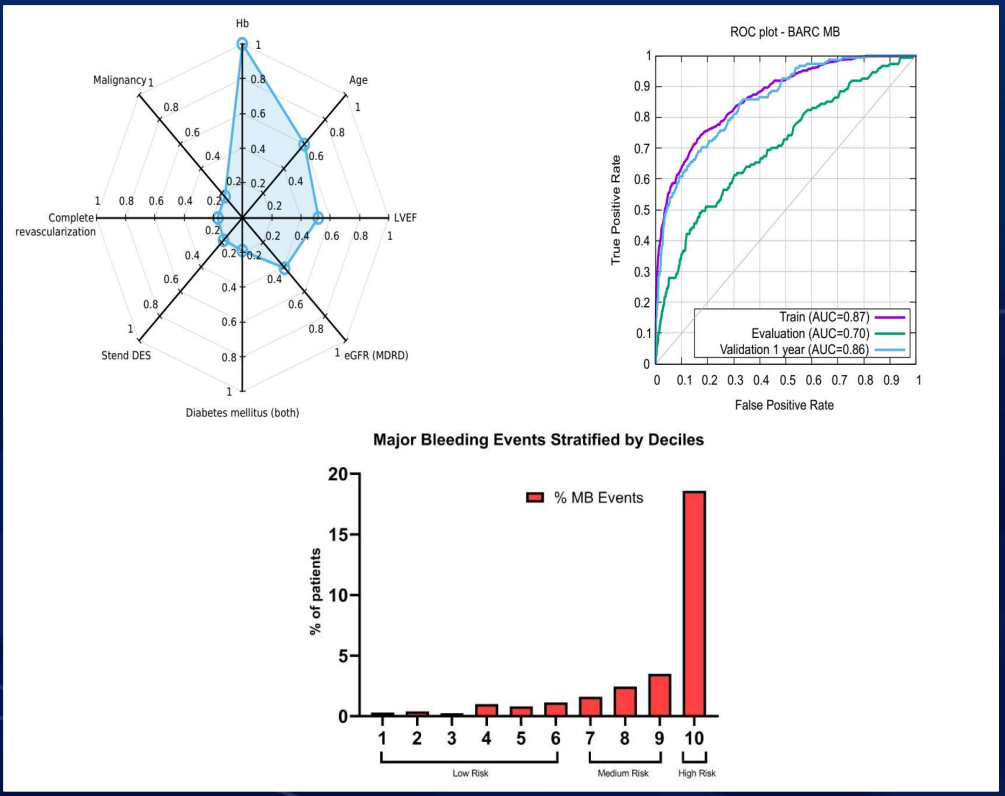
Myocardial infarction



Major bleeding



D'Ascenzo F, Patti G, De Ferrari GM, et al. The Lancet 2021

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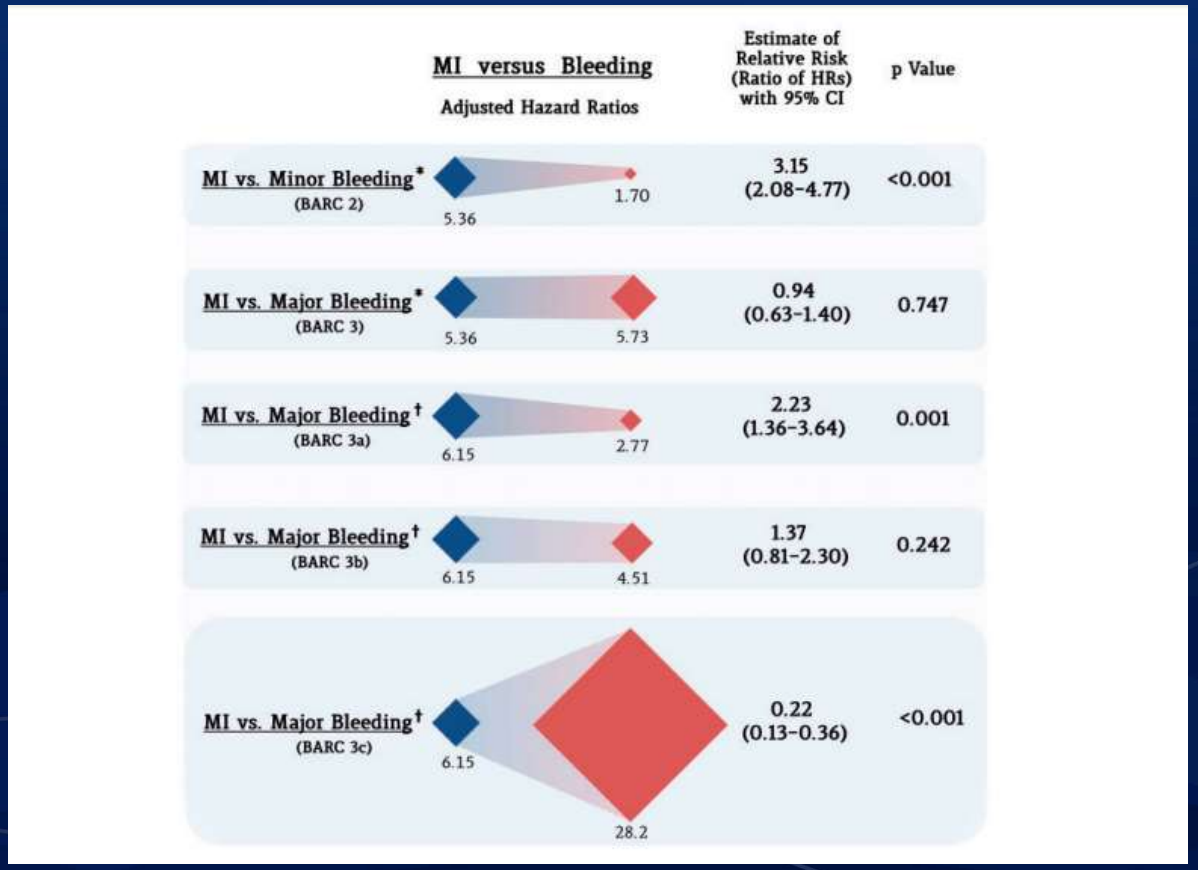
The bleeding side of the moon….

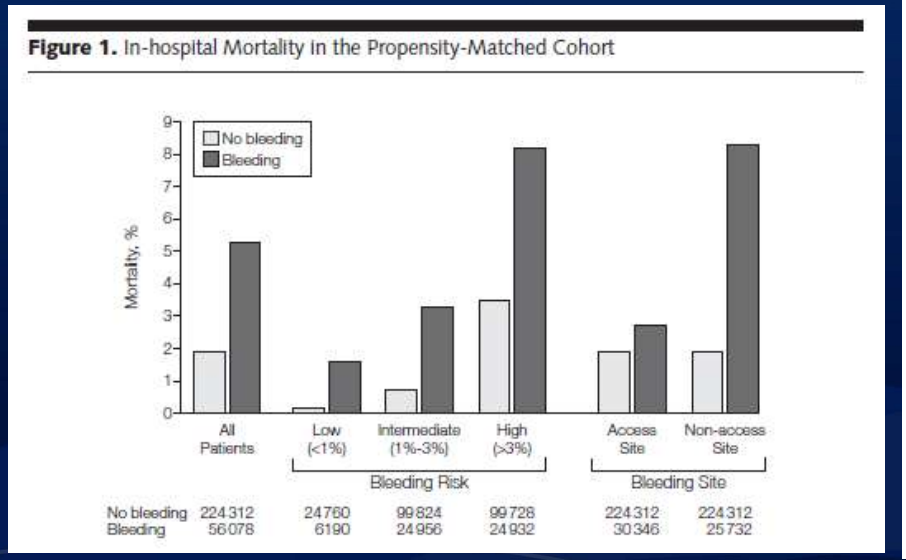
Impact of mortality of MI vs bleeding event

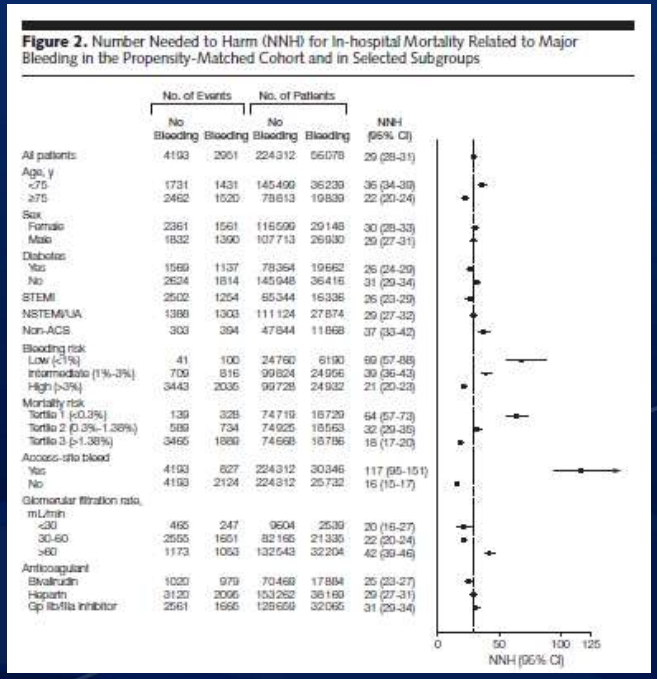


Eur Heart J 2017;38:804-810

Association between bleeding events and in-hospital mortality after PCI

N=3 386 688 procedures and 57 246 bleedings (1.7%)





The attributable risk for mortality related to major bleed was 12%

Chhatriwalla AK et al. JAMA 2013

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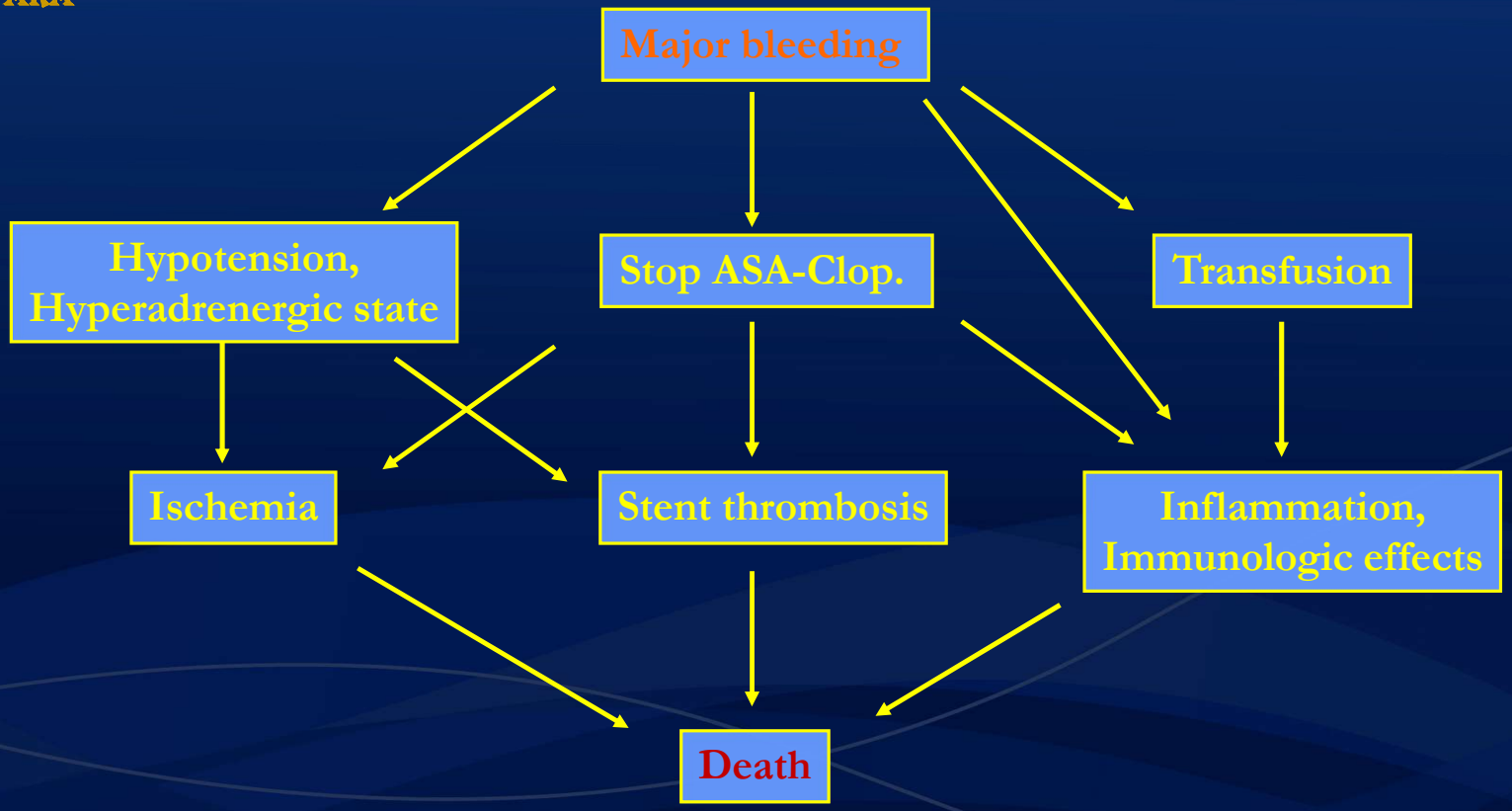
Relationship between major bleeding and mortality in CAD patients (especially in ACS)

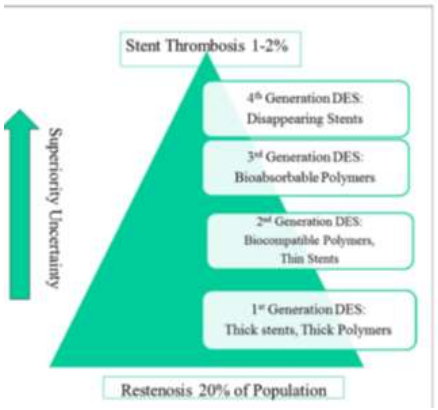


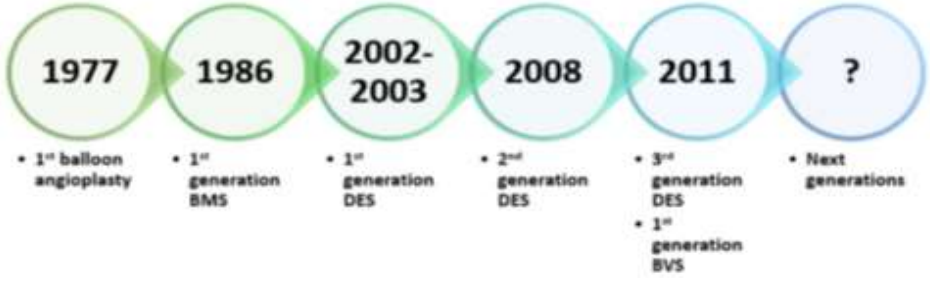
Weight of different predictors of bleeding

The ischemic side of the moon……

Innovations in coronary stents

Bare Metal Stents	First-generation drug-eluting Stents	Durable Polymer-Coated Stents	Biodegradable Polymer-oated Stents	Polymer-free Drug-Coated Stents
Early: Palmaz-Schatz Modern BMS: Multilink, Coroflex, Rebel, Integrity	Cypher Taxus	Xience Resolute Onyx	BioMatrix Synergy Ultimaster Orsiro Supraflex Cruz	BioFreedom
STRUT THICKNESS 55/162microm	132/140microm	80/90micrm	60/120microm	112 microm
DRUG None	Sirolimus or paclitaxel	Everolimus, zotarolimus or sirolimus	Biolimus, sirolimus or everolimus	Biolimus





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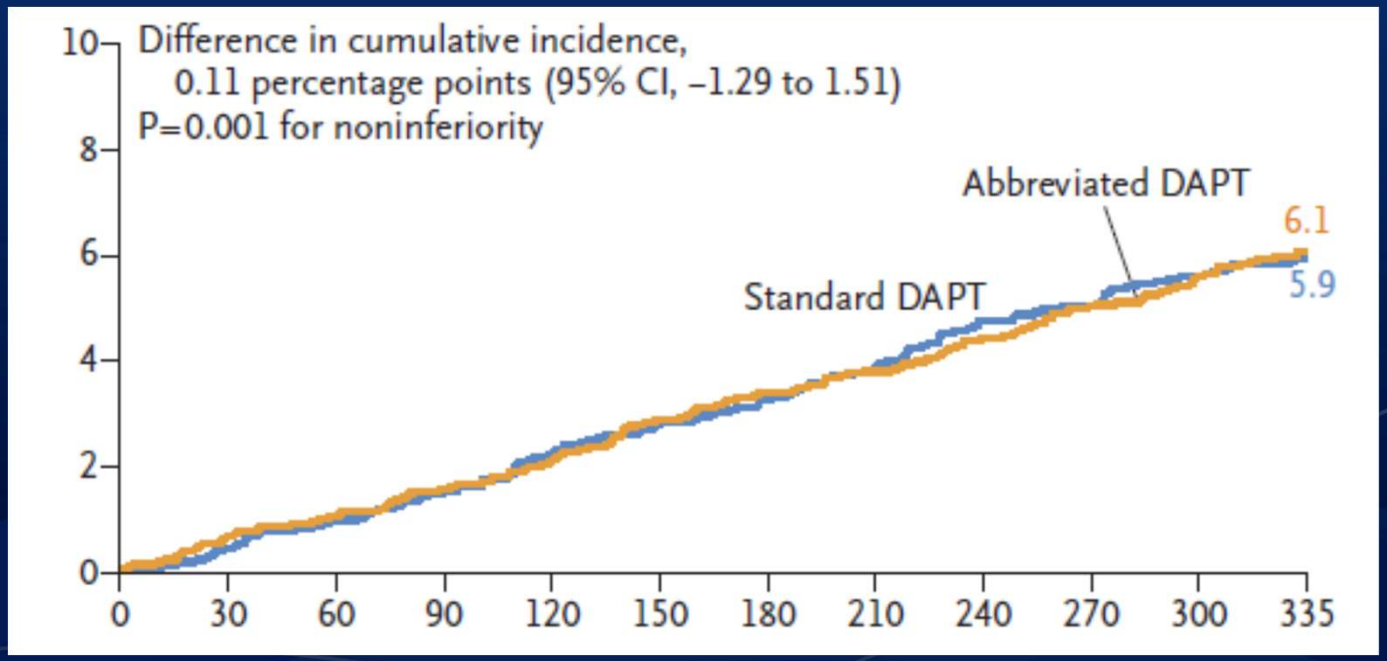
DAPT duration after implantation of last-generation coronary stents

MACE



Stent thrombosis incidence: 0.5%

N Engl J Med October 28, 2021

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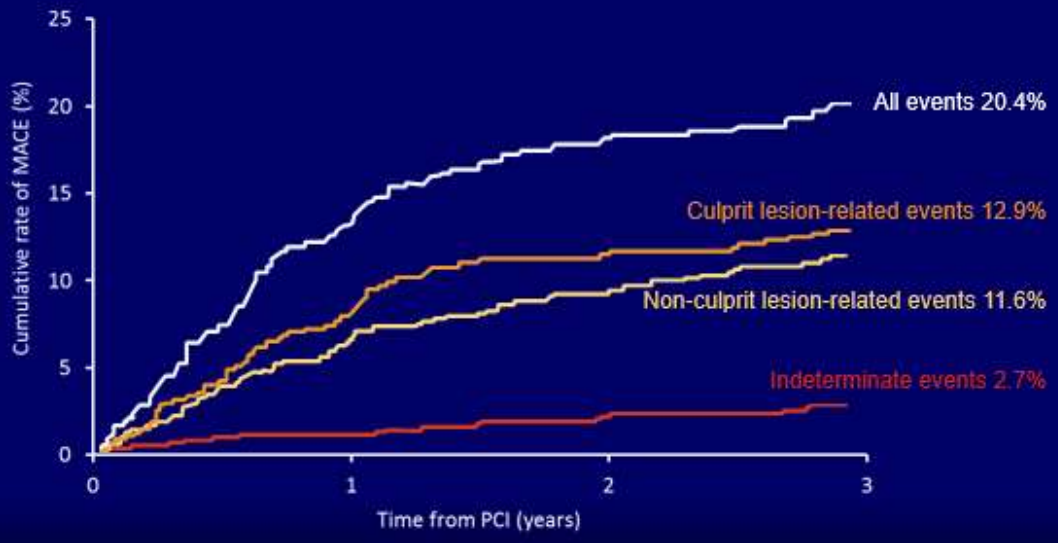
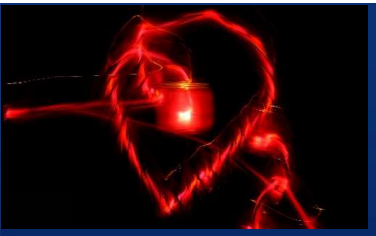
Recurrent events are as likely to originate from a new atherosclerotic plaques

PROSPECT study (N=697 ACS pts undergoing PCI)



Stone GW *et al.* N Engl J Med 2011;364:226–235.



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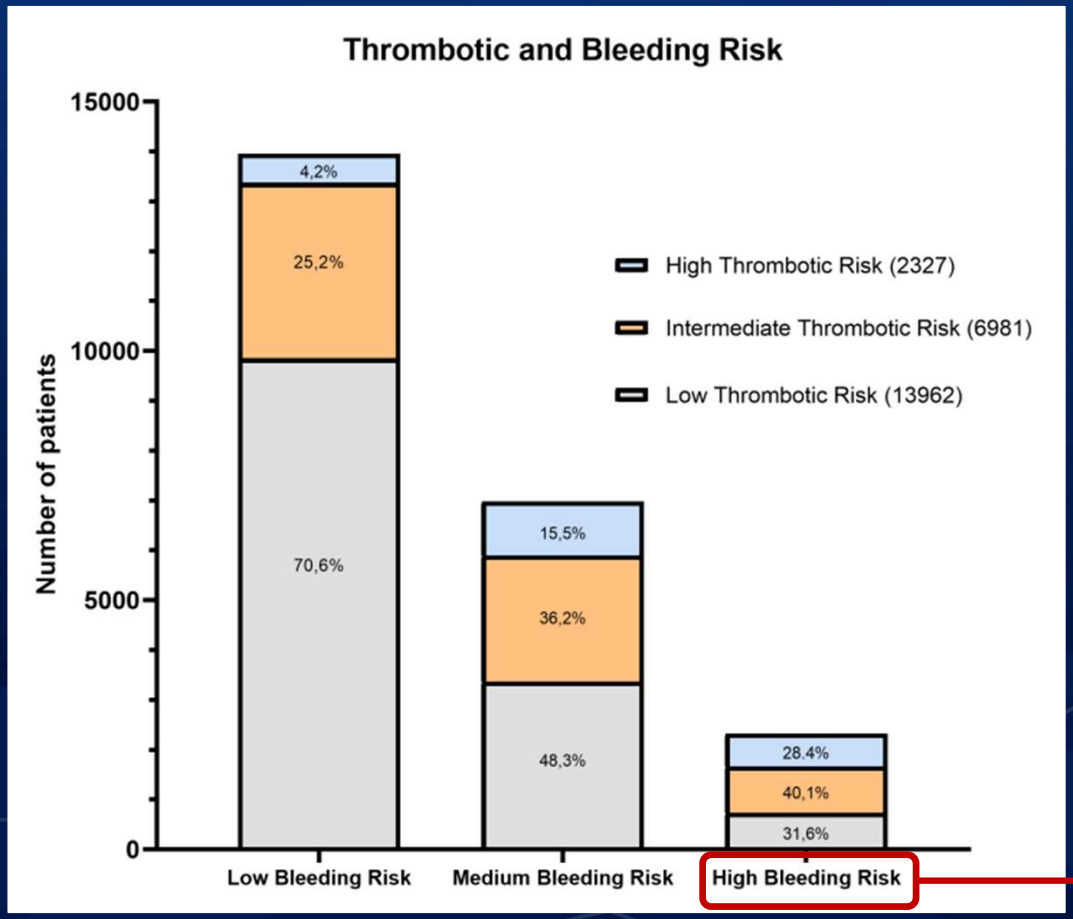
Fattori clinici di rischio ischemico	Fattori di rischio emorragico
Età >75 aa	Età > 75 aa o peso corporeo < 60 Kg
Cr Cl <30 ml/min	Anemia e/o storia di sanguinamento maggiore
Diabete mellito	Terapia anticoagulante + antiaggregante
Arteriopatia periferica sintomatica	Cr Cl <30 ml/min
Eventi coronarici ricorrenti	Diabete mellito
Scompenso cardiaco	Uso di cortisone/FANS/alcool

Fattori coromarici di rischio ischemico
Coronaropatia multivasale
>= 3 stent / lunghezza stent >60 mm
Biforcazione con 2 stent
Occlusione coronarica cronica
Pregressa trombosi di stent

Patti G, et al. Biomed Pharmacother. 2021 Aug;140:111783

PRAISE score



10%

D'Ascenzo F, Patti G, De Ferrari GM, et al. The Lancet 2021

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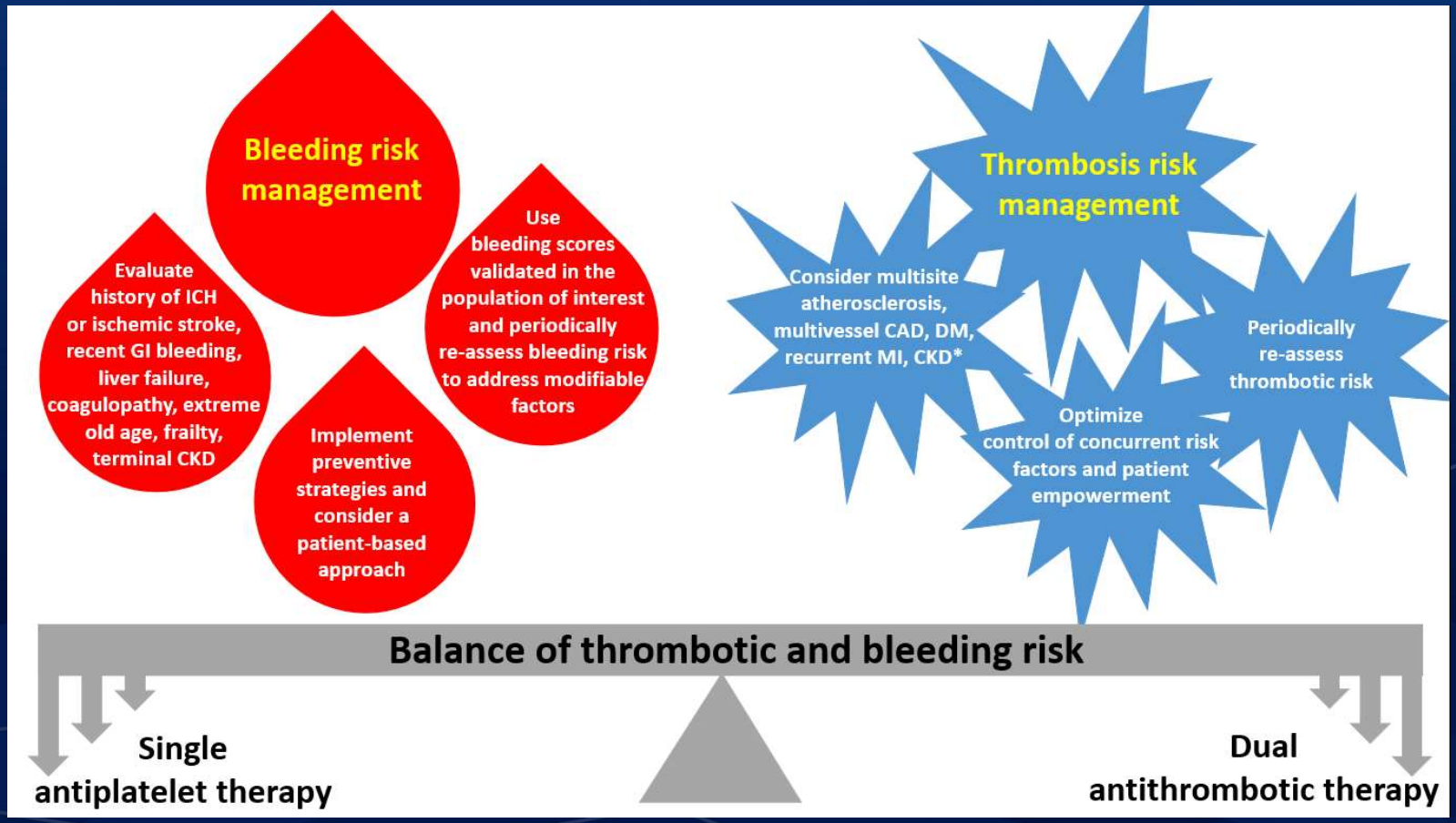
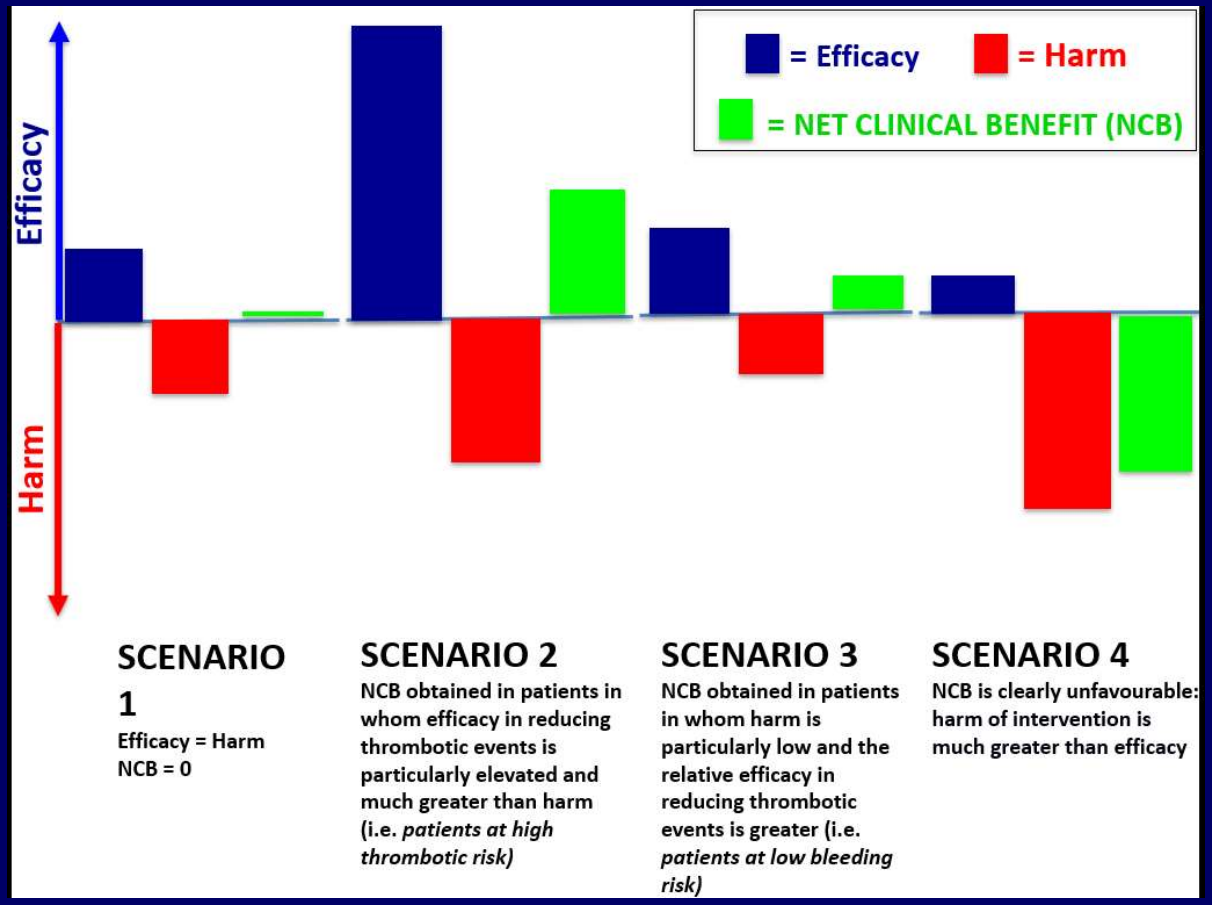
Dual vs Single antithrombotic therapy in CCS

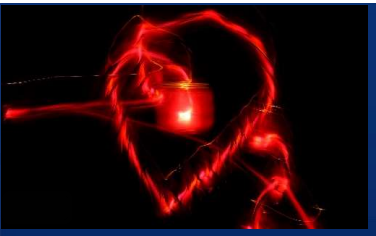


Patti G, et al. Biomed Pharmacother. 2021 Aug;140:111783

Less aggressive vs more aggressive therapies in CAD



Patti G, et al. Biomed Pharmacother. 2021 Aug;140:111783



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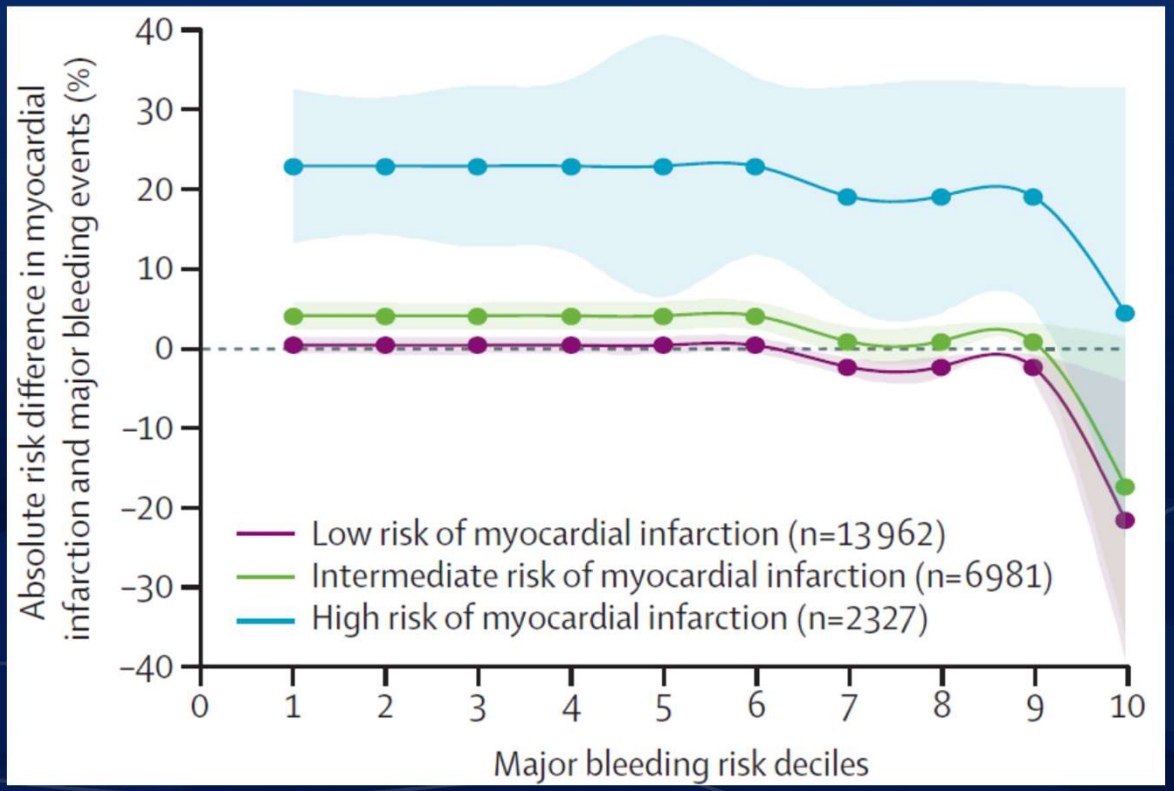
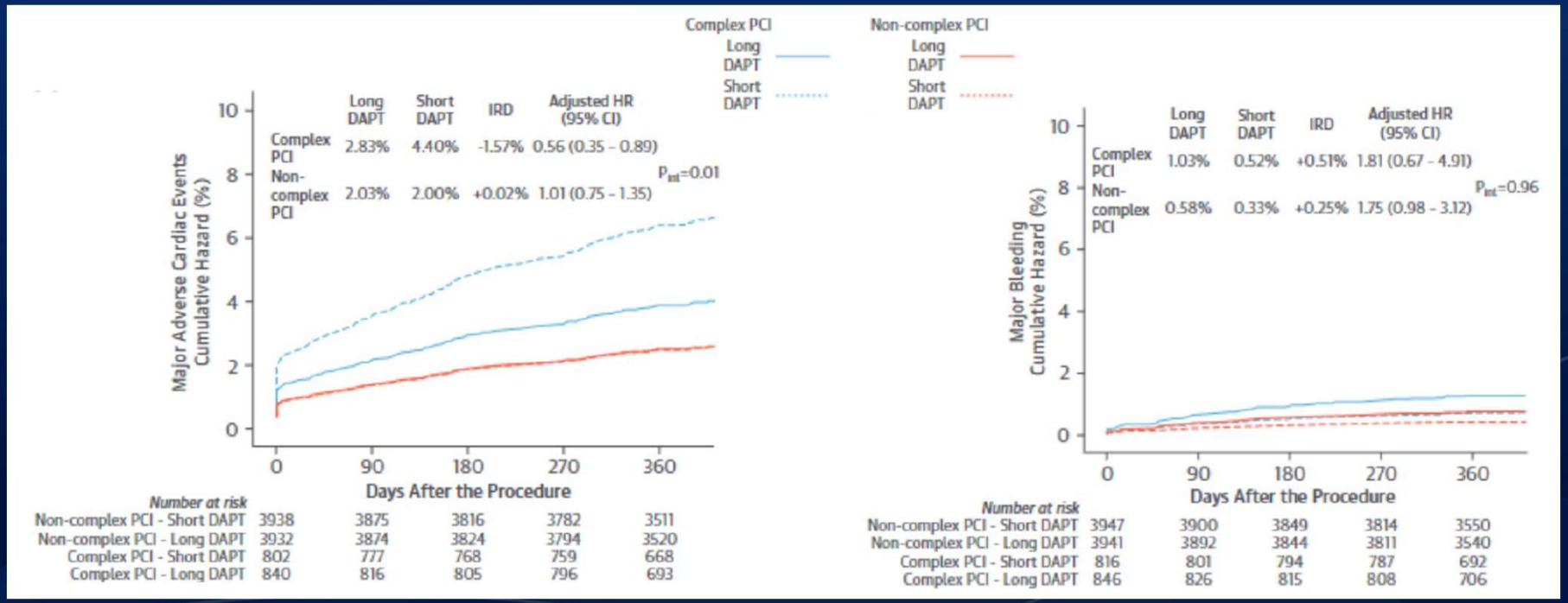
Machine learning-based prediction of adverse events after ACS: PRAISE score

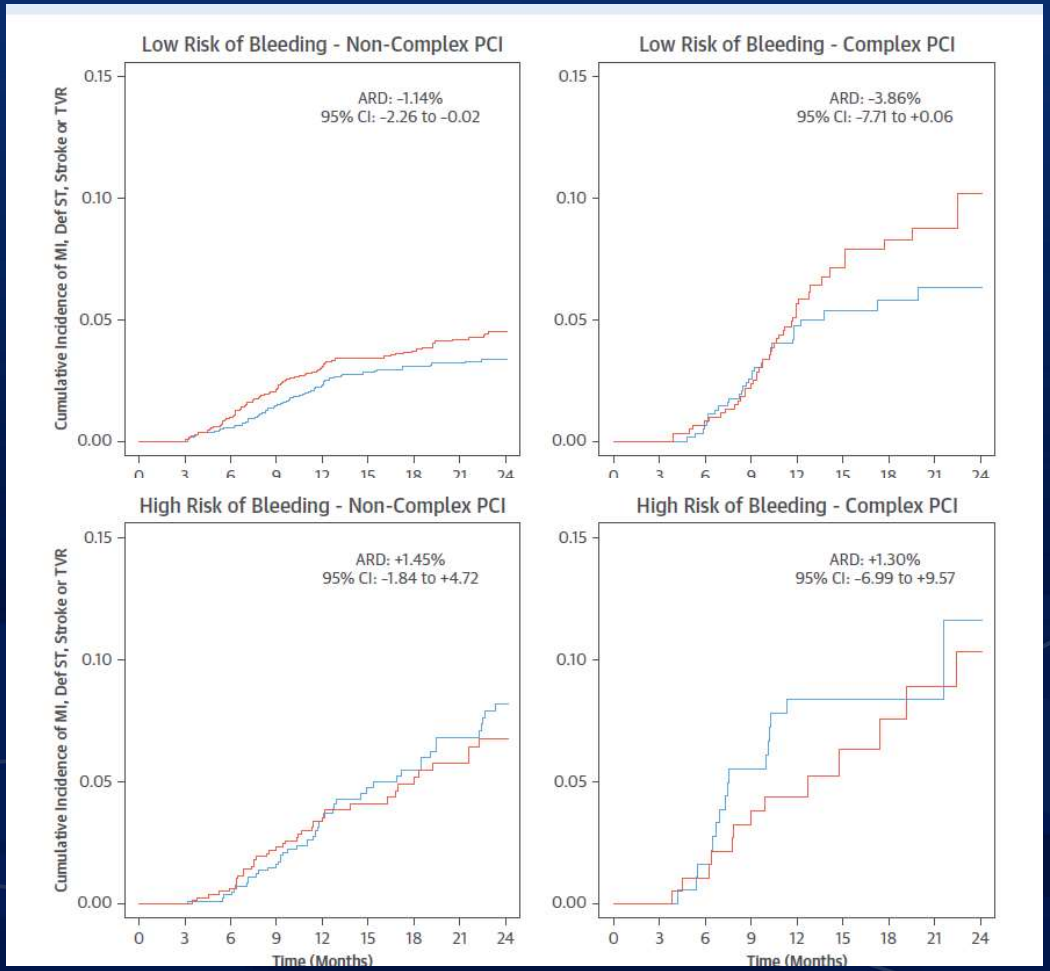


D'Ascenzo F, Patti G, De Ferrari GM, et al. The Lancet 2021

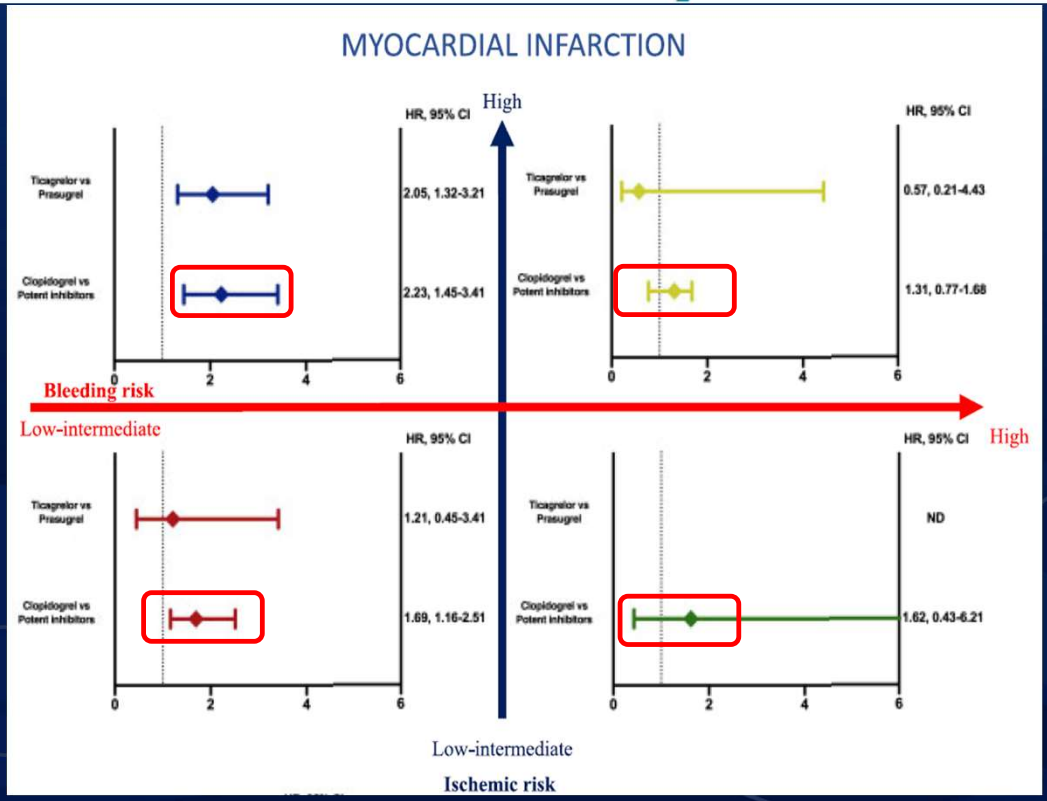
Patient-level meta-analysis on outcome with DAPT prolungation according to PCI complexity



Incidence of ischemic events according to bleeding risk and PCI complexity (Costa et al. J Am Coll Cardiol 2019)



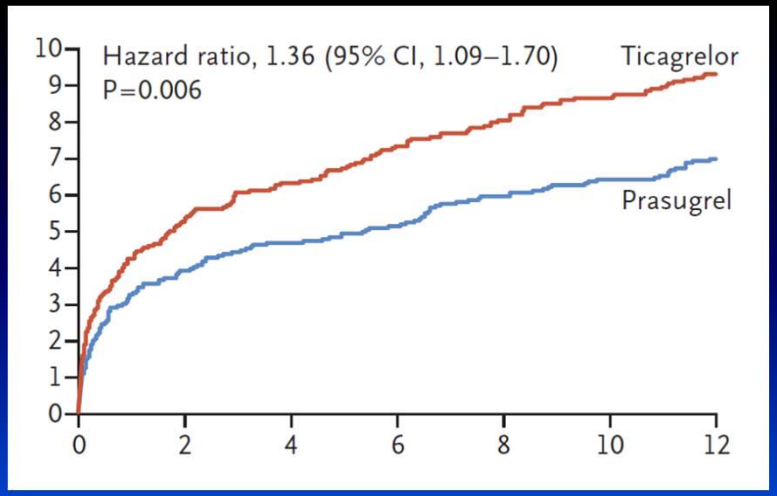
Safety and efficacy of different P_2Y_{12} inhibitors in patients with acute coronary syndromes stratified by the PRAISE risk score: a multicentre study



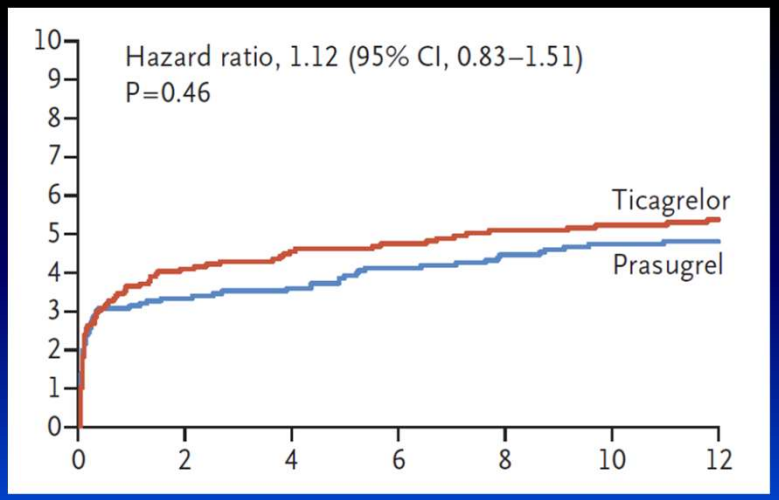
Patti G, D'Ascenzo F, De Ferrari G, et al. European Heart Journal - Quality of Care and Clinical Outcomes 2022

NSTE-ACS: oral antiplatelet drugs
Prasugrel vs Ticagrelor (ISAR-REACT 5, N Engl J Med 2019)

Death/MI/Stroke



BARC 3-5 bleeding



Prasugrel should be considered in preference to ticagrelor for NSTE-ACS patients who proceed to PCI.[174] **IIa** **B**

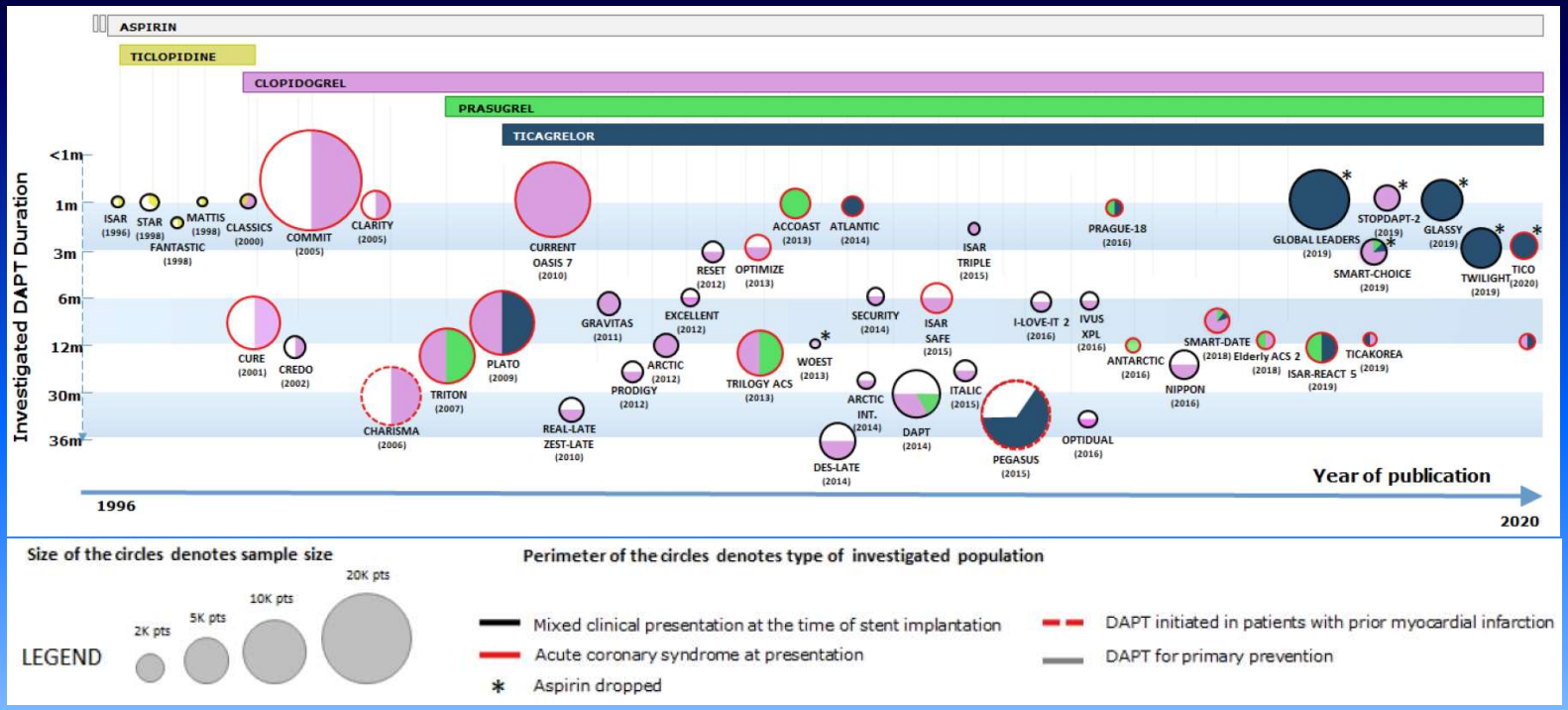
Strengths

- Adequate size (N=4018)
- Reduction of MI (both ppMI and 1- 2)

Limitations

- Not blinded
- Prasu 5 mg, if age >75 yrs
- Phone-call f-up 83%
- Drug discontinuation 15% Tica, 12% Prasu

HISTORY OF DUAL ANTIPLATELET THERAPY IN PATIENTS WITH CORONARY ARTERY DISEASE



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Antithrombotic strategies in high bleeding risk patients with ACS

- Stop P2Y12 and continue with aspirin alone
- Stop aspirin and continue with clopidogrel alone (STOP-DAPT 2))
- Stop aspirin and continue with ticagrelor alone (TWILIGHT)
- De-escalation

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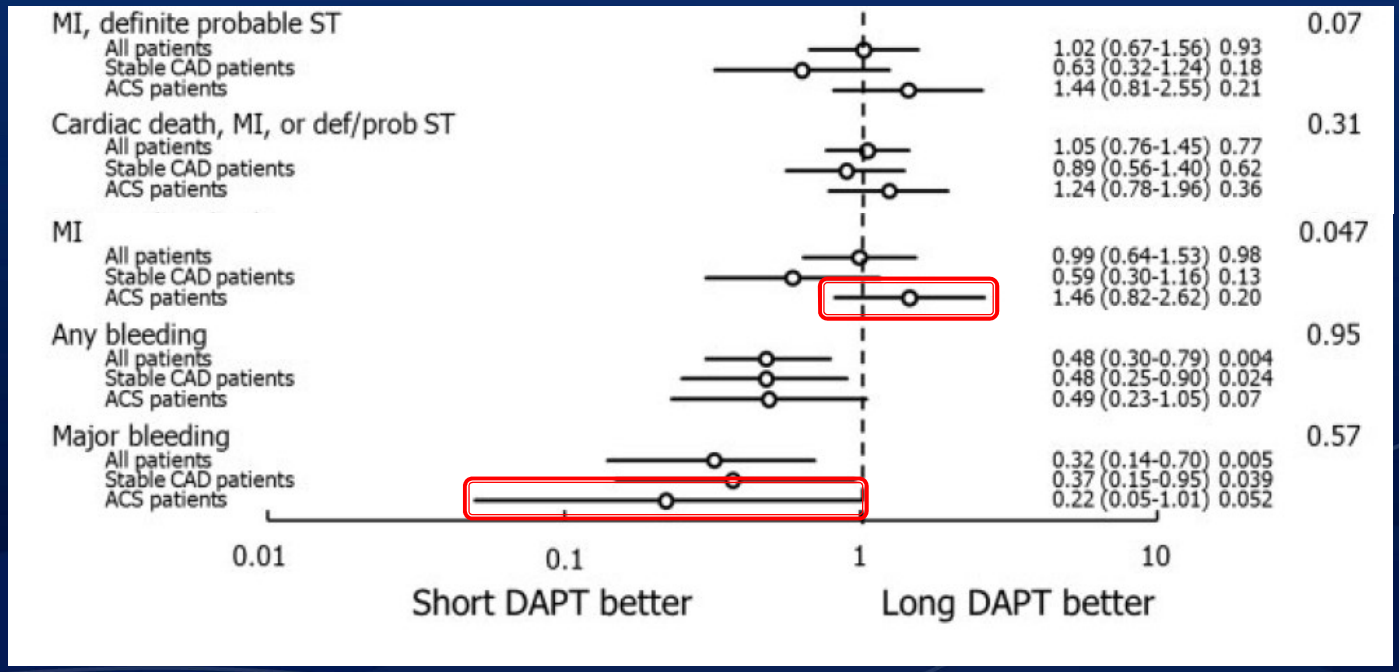
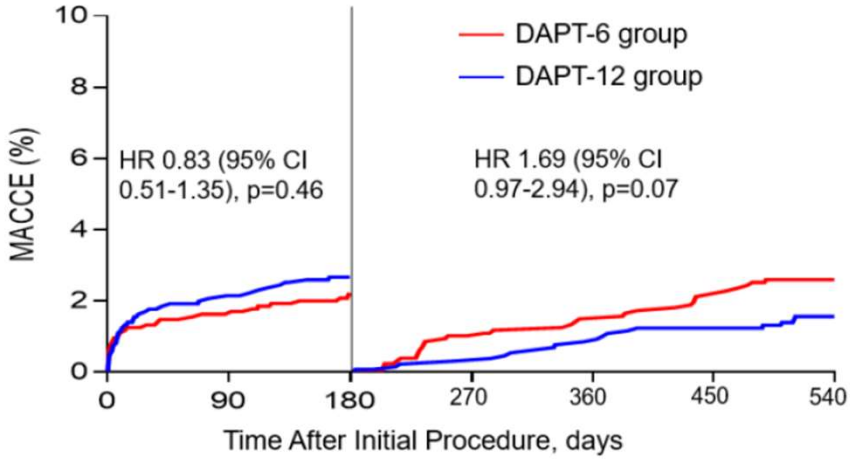
≤6 months vs 1-year DAPT duration in patients undergoing PCI in the contemporary era of new-generation DES N=6 CRTs and 11,473 patients



- Incidence of MI or ST was 7-fold higher than incidence of MB
- ARR of MI or ST with longer DAPT: 1%
- ARI of MB with longer DAPT: 0.4%

Palmerini T, et al. Eur Heart J 2017

SMART-DATE trial:
Landmark analysis of Primary Endpoint (MACCE)



No. at risk							
Long-term	1355	1312	1299	1290	1283	1278	1043
Short-term	1357	1318	1296	1271	1264	1255	1032

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Antithrombotic strategies in high bleeding risk patients with ACS

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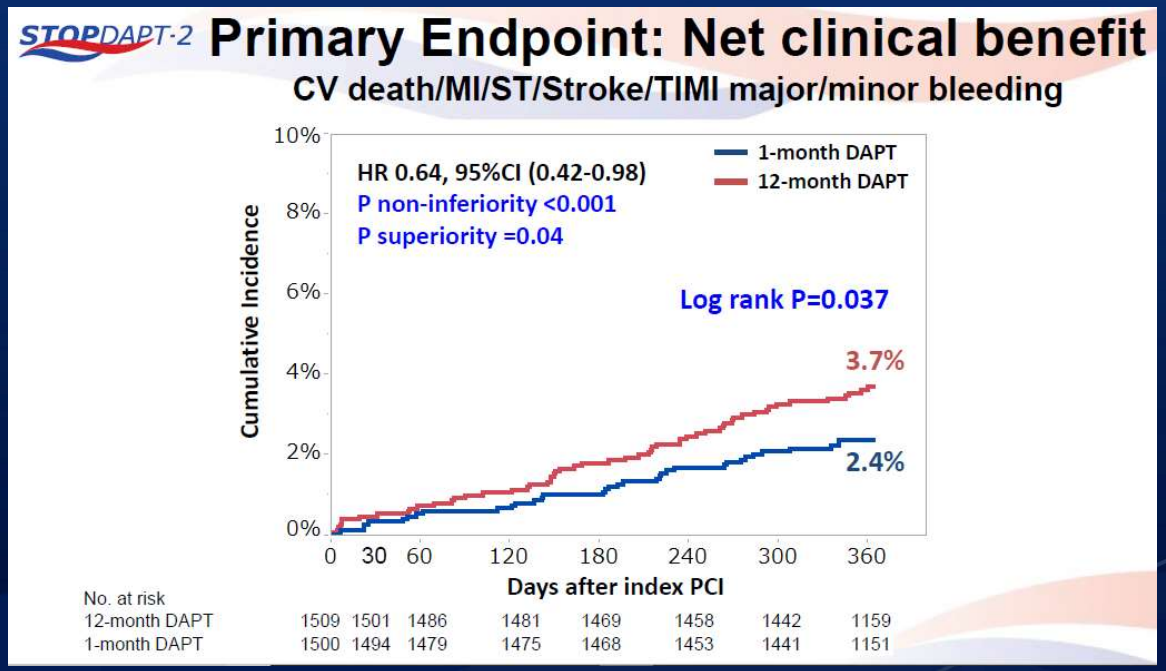
STOPDAPT-2: Randomized trial of 1-mo. DAPT (ASA+Clop, then Clop) Vs 12-mo. DAPT (ASA+Clop) in PCI (N=3009)



Issues related to STOPDAPT-2:

- Eastern Asian population
- 60% stable CAD
- Low SINTAX score
- >95% imaging

Watanabe H. ACC Congress 2019

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Antithrombotic strategies in high bleeding risk patients with ACS

- Stop P2Y12 and continue with aspirin alone
- Stop aspirin and continue with clopidogrel alone (STOP-DAPT 2)
- **Stop aspirin and continue with ticagrelor alone (TWILIGHT)**
- De-escalation

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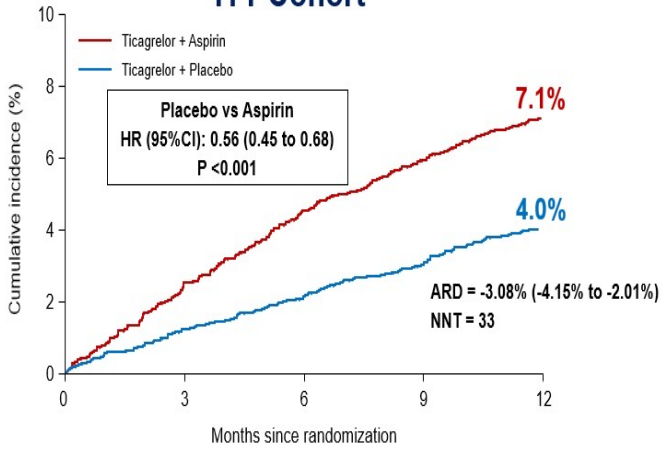
TWILIGHT: Randomized trial of 3-mo. DAPT (ASA+Tica, then Tica) vs 12-mo. DAPT (ASA+Tica) in *HIGH-RISK PCI* (N=7119)

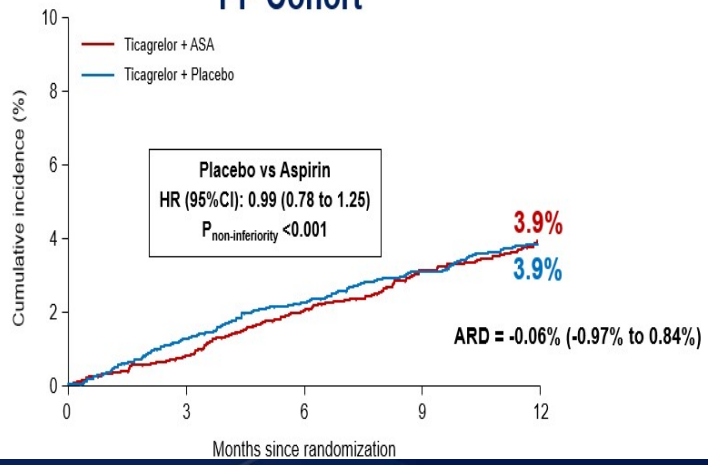
Primary Endpoint: BARC 2, 3 or 5 Bleeding

ITT Cohort



Key Secondary Endpoint: Death, MI or Stroke

PP Cohort



Issues related to TWILIGHT:

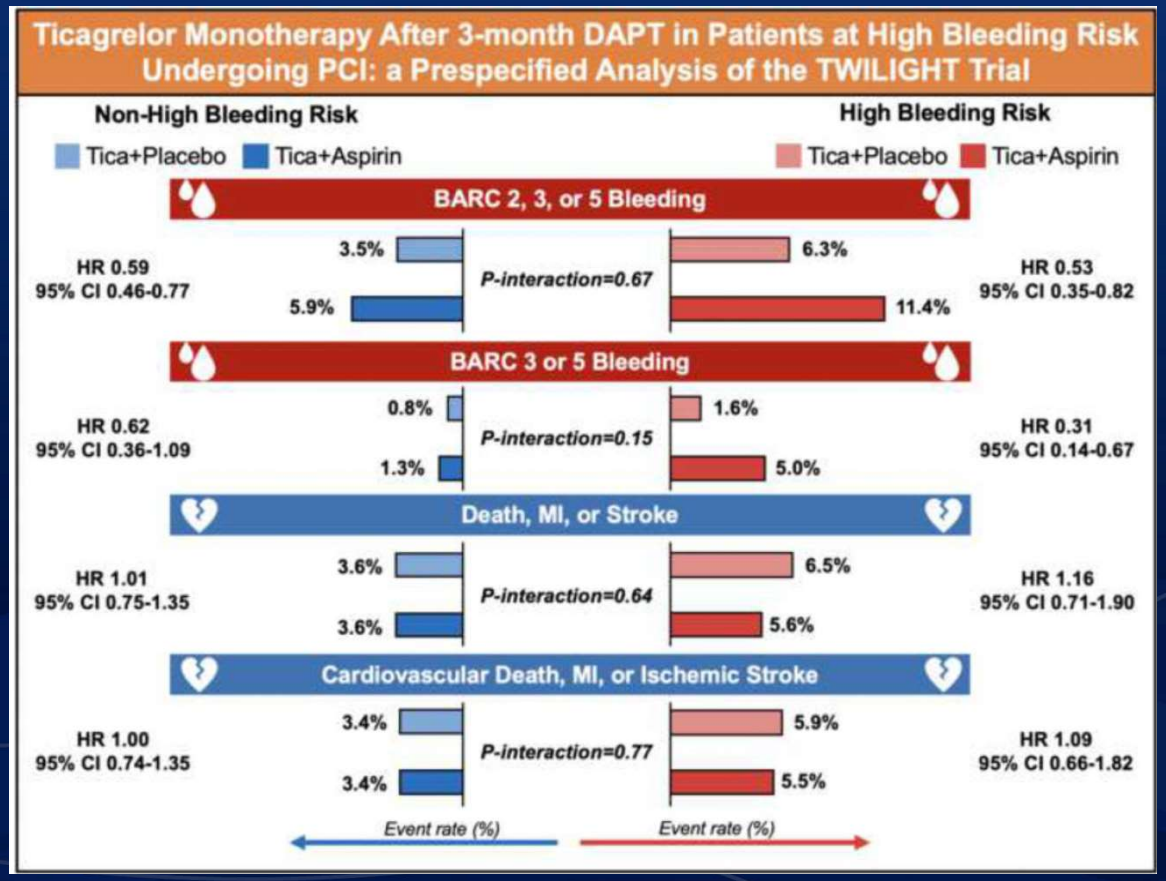
- High angiographic/clinical risk
- Powered for ischemic events
- No data on the bleeding risk at baseline

Mehran R, et al. N Engl J Med 2019

TWILIGHT results according to bleeding risk

NNT 42

NNT 200

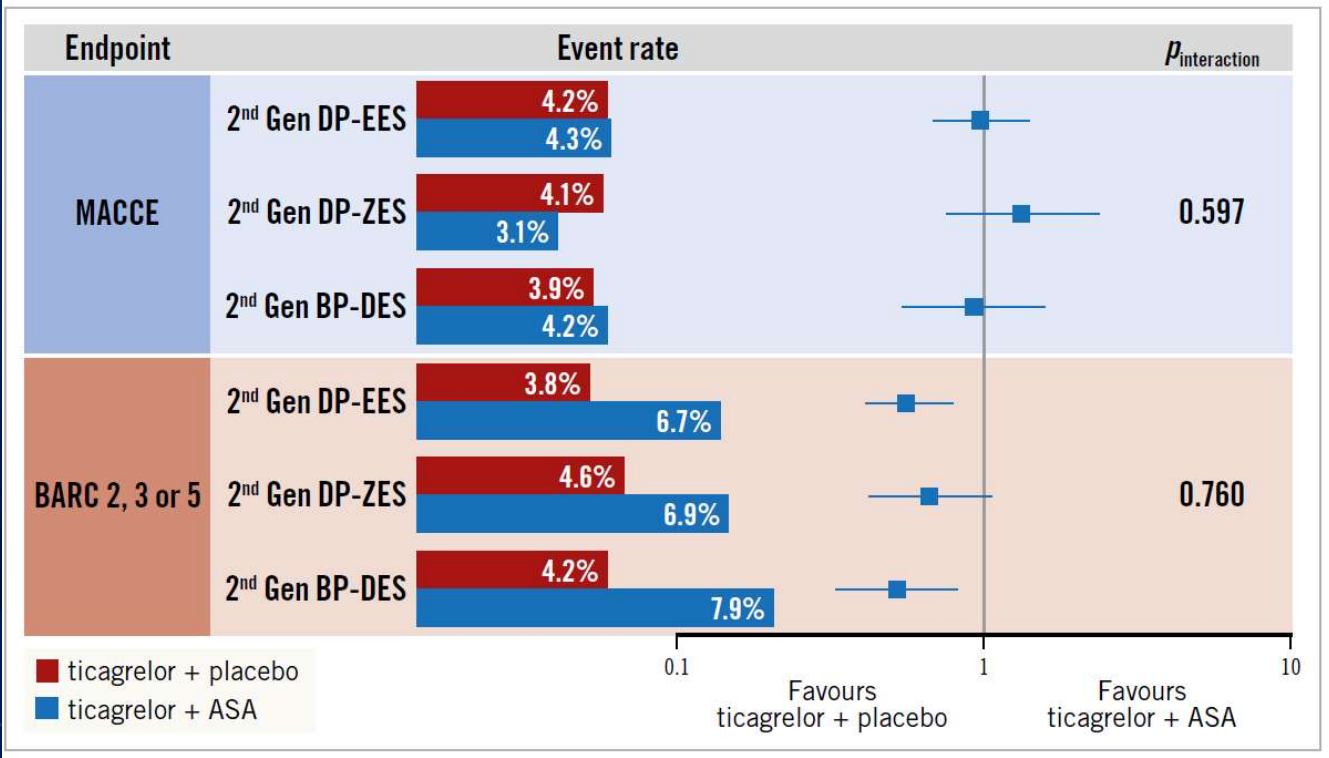


NNT 19

NNT 29

Escaned J. et al. Eur Heart J 2021

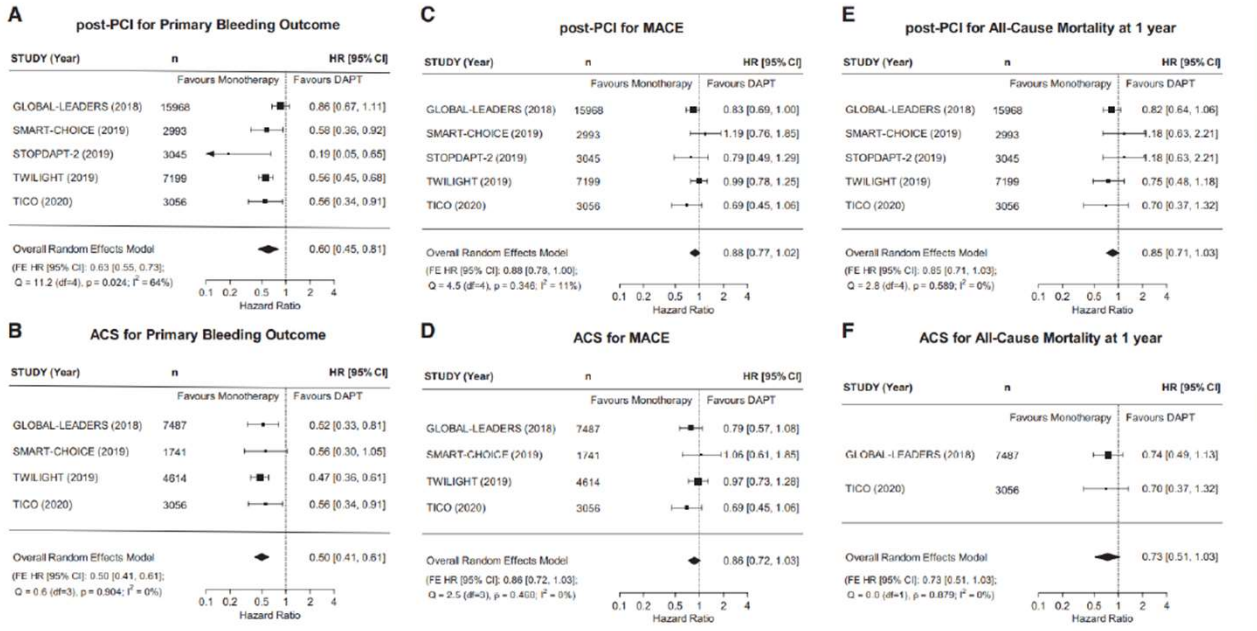
TWILIGHT results according to type of DES



Dangas G, et al. EuroIntervention 2022

Pooled Analysis of Clinical Trials of Time-Constrained DAPT After PCI

John D. McClure, et al. J Am Heart Assoc. 2020



Trials
Testing Monotherapy

Trial	Pts enrolled	Masking	n	Primary Endpoint	Main outcome	Durantion of DAPT in mono arm	Monotherapy	Ref
GLOBAL LEADERS 	Elective or urgent PCI	Open Label	15968	All-cause mortality or non-fatal MI at 2 yrs	Negative	1 month	Ticagrelor	Lancet 2018
SMART-CHOICE 	Elective or urgent PCI	Open Label	2993	Major adverse cardiac and cerebrovascular events at 1 y	Non-inferior	3 months	Clopidogrel (76%) Prasu/Tica (24%)	JAMA 2019
STOPDAPT-2 	Elective PCI	Open Label	3045	NACE at 1 y	Non-inferior/ superior	1 month	Clopidogrel	JAMA 2019
TWILIGHT 	Elective or urgent PCI (high risk pts)	Double blind	9000	Bleeding events: BARC 2,3 or 5 at 1 y	Positive	3 months	Ticagrelor	NEJM 2019
TICO 	PCI for ACS	Open Label	3056	NACE at 1 y	Positive	3 months	Ticagrelor	JAMA 2020

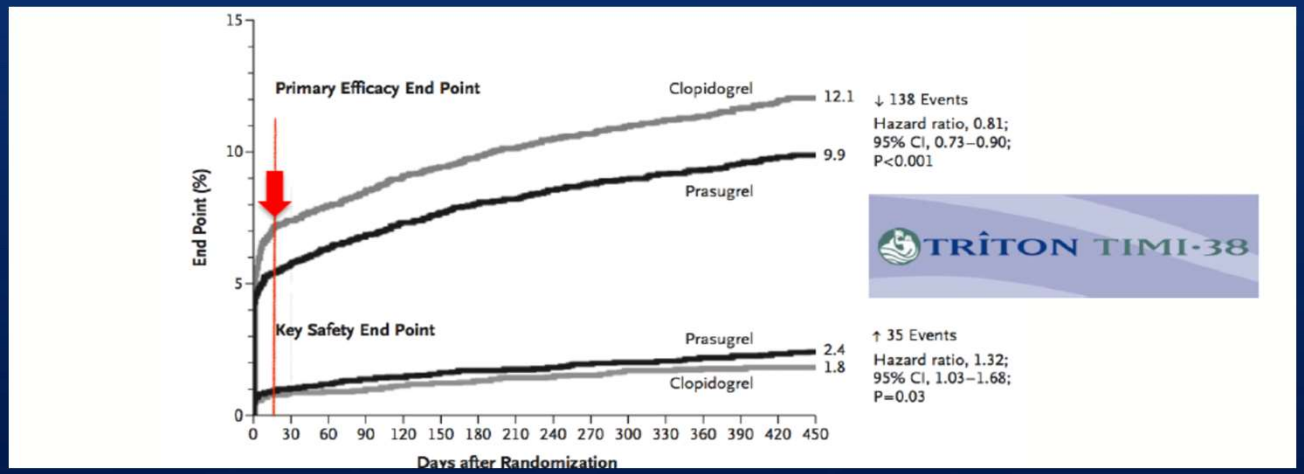
CARDIOLOGIA NOVARA

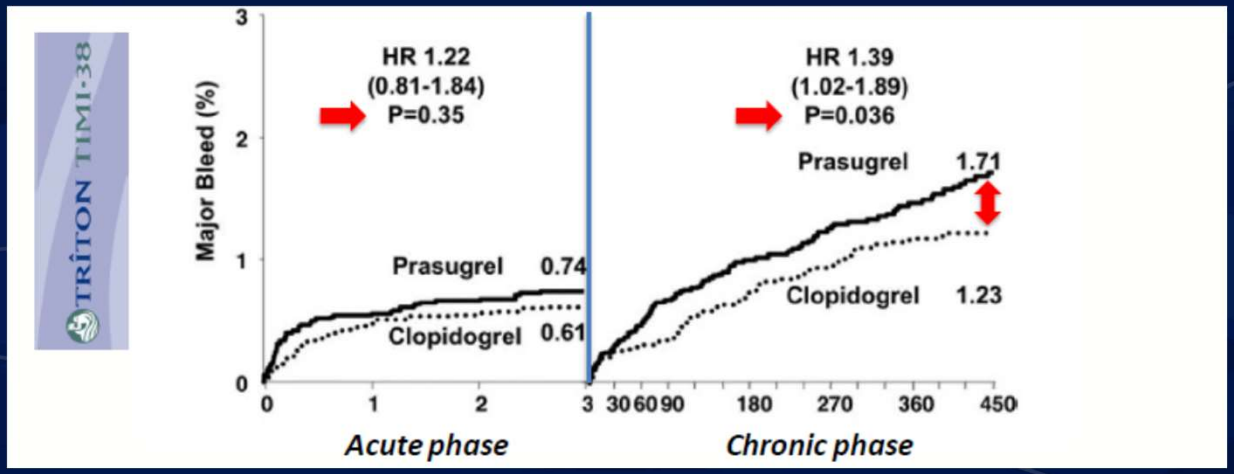
Antithrombotic strategies in high bleeding risk patients with ACS

- Stop P2Y12 and continue with aspirin alone
- Stop aspirin and continue with clopidogrel alone (STOP-DAPT 2)
- Stop aspirin and continue with ticagrelor alone (TWILIGHT)
- **De-escalation**

CARDIOLOGIA NOVARA

Rationale for de-escalation from the newer, more potent P2Y12 inhibitors to clopidogrel

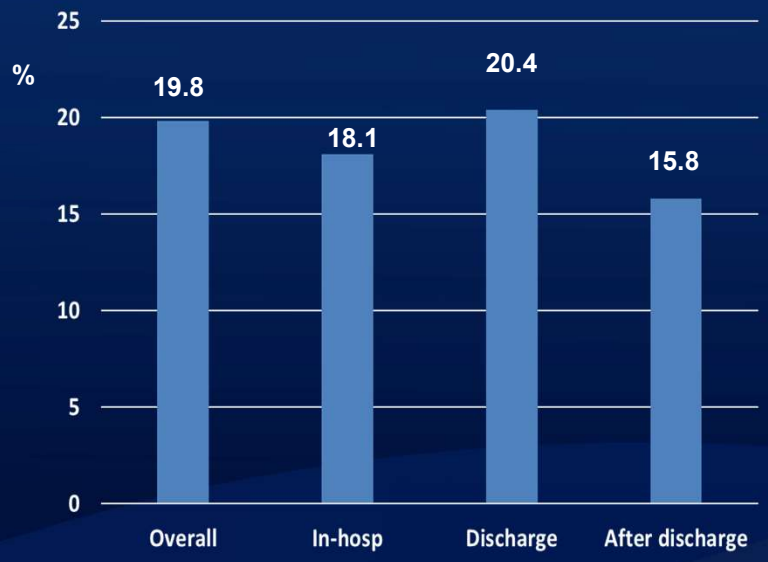


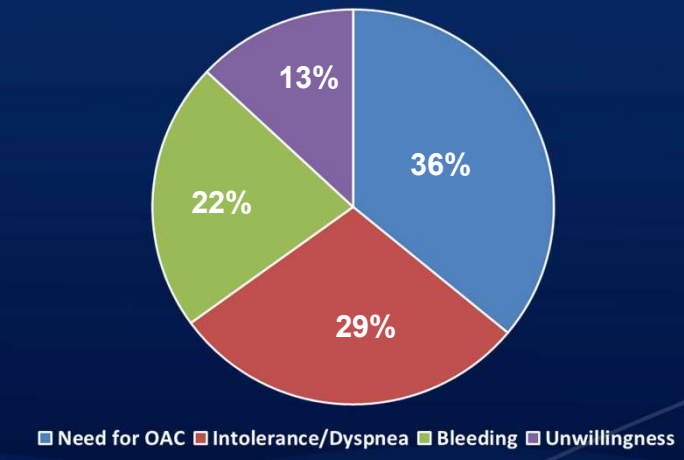


Prevalence of de-escalation in the real world

Meta-analysis of 12 observational studies

N=15,535 patients on Ticagrelor





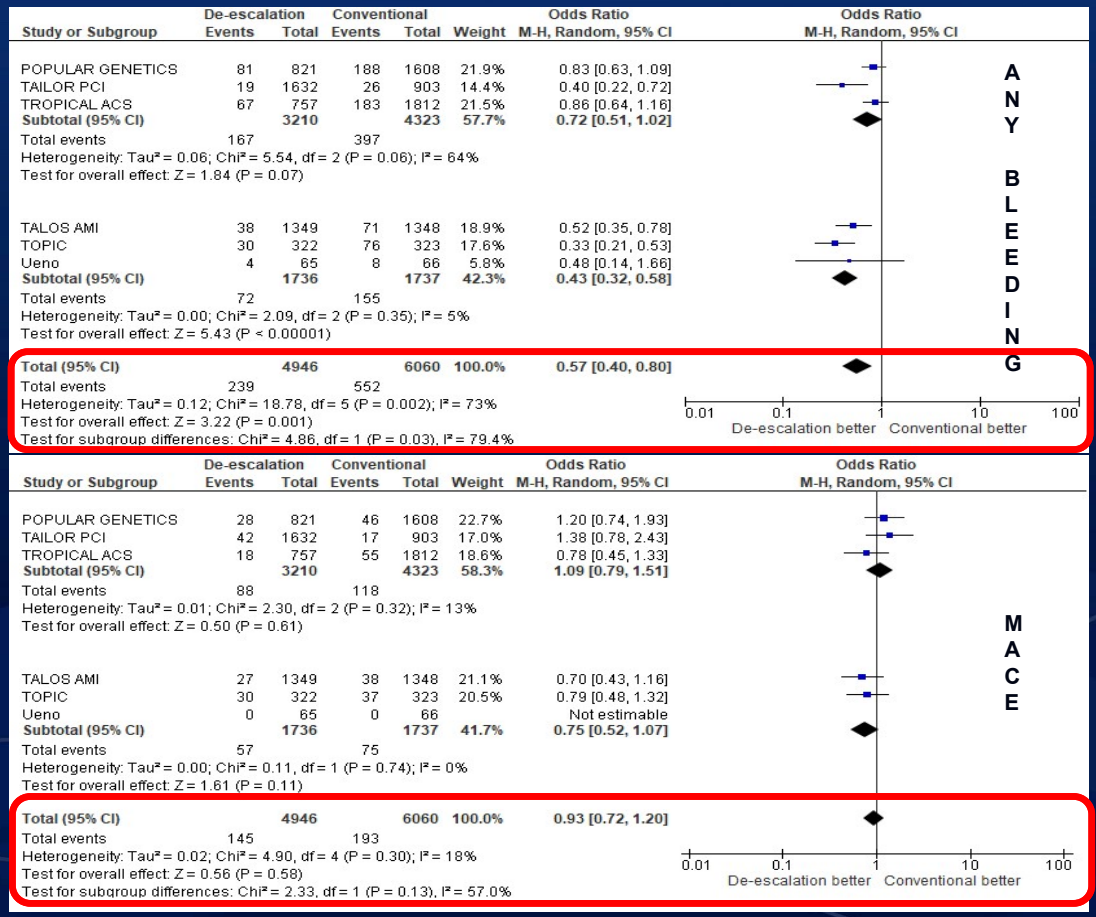
Timing of de-escalation: mean 115 days

Predictors:

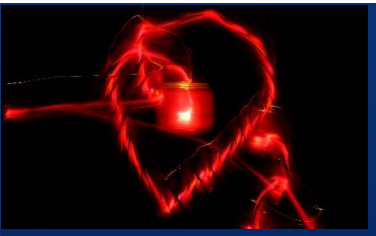
- Older age
- Female gender
- Previous bleeding
- NSTEMI/UA

Angiolillo D, Patti G, et al. J Thromb Thrombol 2019

De-escalation vs standard Rx with ticagrelo/prasugrel in ACS patients undergoing PCI: a meta-analysis of 6 CRTs and approximately 11,000 pts



Patti G, et al. Thrombosis Haemostasis 2022

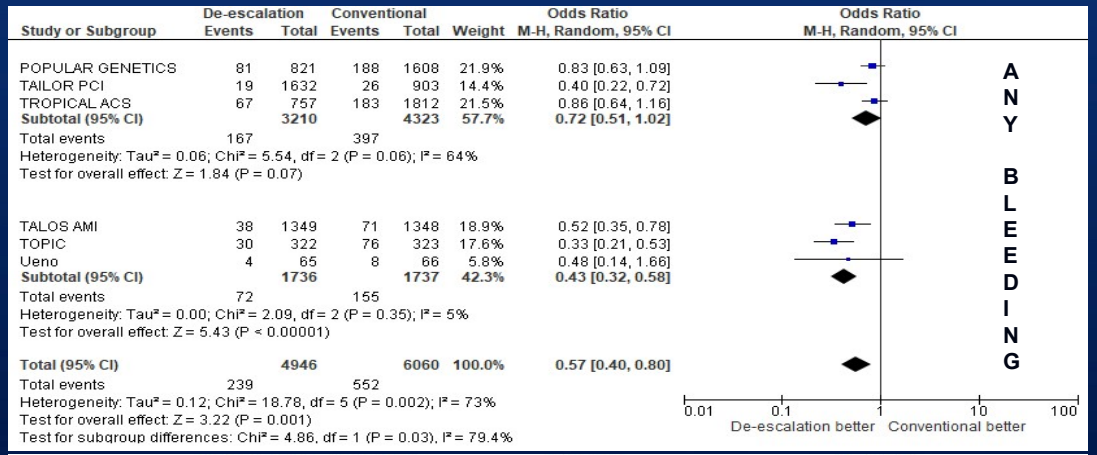


CARDIOLOGIA NOVARA

Guided versus unguided de-escalation in ACS patients undergoing PCI: a meta-analysis of 6 CRTs and approximately 11,000 pts

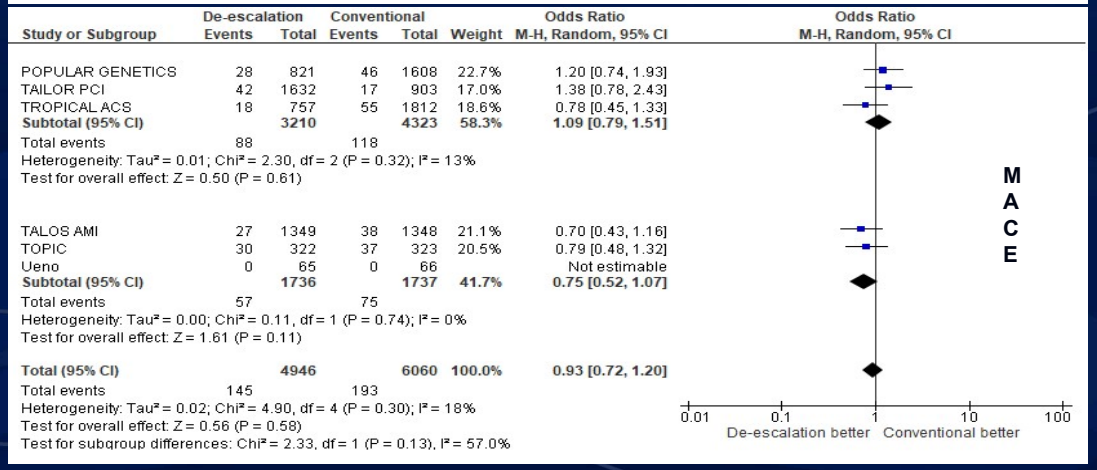
Studies on guided clopidogrel therapy

Studies on unguided de-escalation to clopidogrel

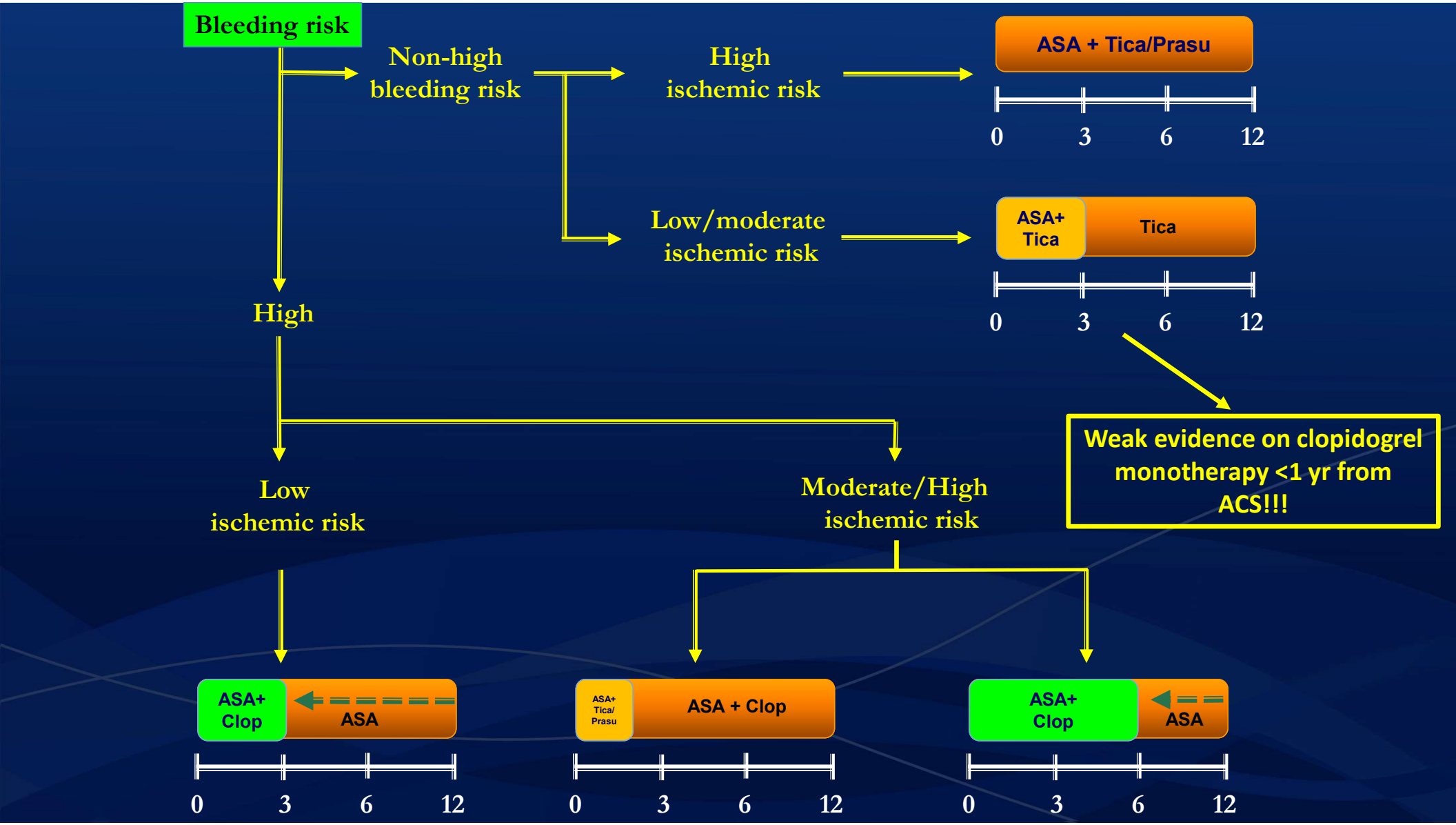


Studies on guided clopidogrel therapy

Studies on unguided de-escalation to clopidogrel



Patti G, et al. Thrombosis Haemostasis 2022


Bleeding risk
Non-high bleeding risk
High ischemic risk
ASA + Tica/Prasu
0 3 6 12
Low/moderate ischemic risk
ASA+ Tica
Tica
0 3 6 12
High
Weak evidence on clopidogrel monotherapy <1 yr from ACS!!!
Low ischemic risk
Moderate/High ischemic risk
ASA+ Clop
ASA
0 3 6 12
ASA+ Tica/ Prasu
ASA + Clop
0 3 6 12
ASA+ Clop
ASA
0 3 6 12

2019 ESC guidelines on CCS

Recommendations	Class	Level
Antithrombotic therapy in patients with CCS and in sinus rhythm		
Adding a second antithrombotic drug to aspirin for long-term secondary prevention should be considered in patients with high risk of ischaemic events[a] and without high bleeding risk.[b]	IIa	A
Adding a second antithrombotic drug to aspirin for long-term secondary prevention may be considered in patients with at least a moderately increased risk of ischaemic events[c] and without high bleeding risk.[b]	IIb	A

[a] Diffuse multivessel CAD with at least one of the following: diabetes mellitus requiring medication, recurrent MI, PAD, or CKD with eGFR 15-59 mL/min/1.73 m^2.

[b] Prior history of intracerebral haemorrhage or ischaemic stroke, history of other intracranial pathology, recent gastrointestinal bleeding or anaemia due to possible gastrointestinal blood loss, other gastrointestinal pathology associated with increased bleeding risk, liver failure, bleeding diathesis or coagulopathy, extreme old age or frailty, or renal failure requiring dialysis or with eGFR <15 mL/min/1.73 m^2.

[c] At least one of the following: multivessel/diffuse CAD, diabetes mellitus requiring medication, recurrent MI, PAD, HF, or CKD with eGFR 15-59 mL/min/1.73 m2

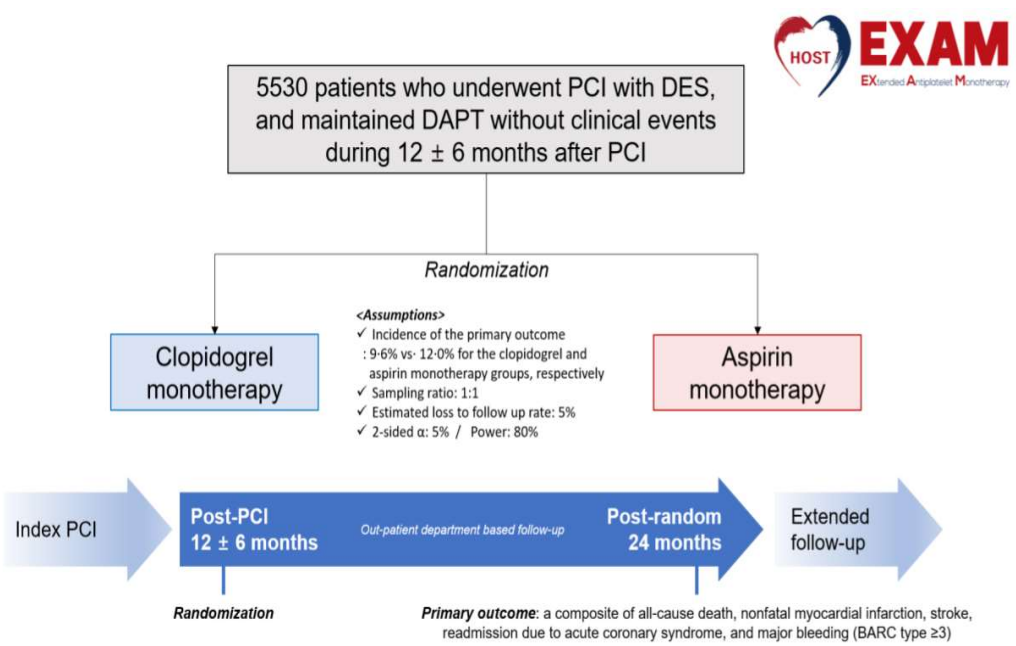
2019 ESC guidelines on chronic coronary syndromes

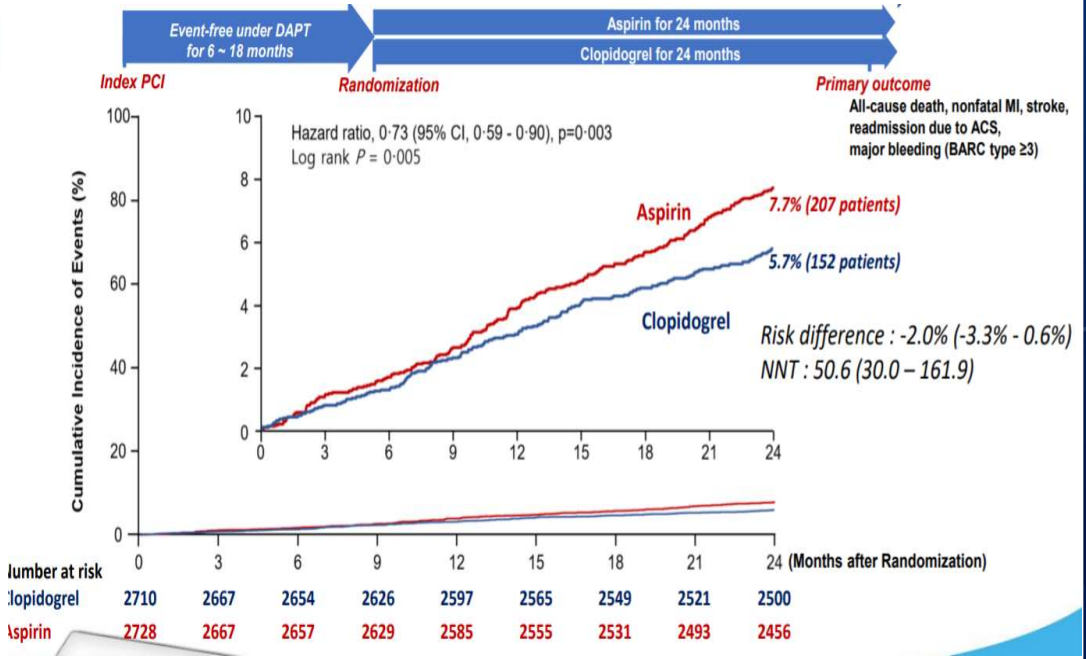
Recommendations	Class[a]	Level[b]
Antithrombotic therapy in patients with CCS and in sinus rhythm		
Aspirin 75–100 mg daily is recommended in patients with a previous MI or revascularization.[270]	I	A
Clopidogrel 75 mg daily is recommended as an alternative to aspirin in patients with aspirin intolerance.[273]	I	B
Clopidogrel 75 mg daily may be considered in preference to aspirin in symptomatic or asymptomatic patients, with either PAD or a history of ischaemic stroke or transient ischaemic attack.[273]	IIb	B
Aspirin 75–100 mg daily may be considered in patients without a history of MI or revascularization, but with definitive evidence of CAD on imaging.	IIb	C
Adding a second antithrombotic drug to aspirin for long-term secondary prevention should be considered in patients with a **high risk** of ischaemic events[c] and without high bleeding risk[d] (see *Table 9* for options).[289,296,297,307]	IIa	A
Adding a second antithrombotic drug to aspirin for long-term secondary prevention may be considered in patients with at least a **moderately increased risk** of ischaemic events[e] and without high bleeding risk[d] (see *Table 9* for options).[289,296,297,307]	IIb	A

Drug option	Dose	Indication	Additional cautions	References
Clopidogrel	75 mg o.d.	Post-MI in patients who have tolerated DAPT for 1 year		289,290
Prasugrel	10 mg o.d or 5 mg o.d.; if body weight <60 kg or age >75 years	Post-PCI for MI in patients who have tolerated DAPT for 1 year	Age >75 years	289,290,313
Rivaroxaban	2.5 mg b.i.d.	Post-MI >1 year or multivessel CAD	Creatinine clearance 15 - 29 mL/min	297
Ticagrelor	60 mg b.i.d.	Post-MI in patients who have tolerated DAPT for 1 year		291–293,307,314

Treatment options are presented in alphabetical order.
b.i.d. = bis in die (twice a day); CAD = coronary artery disease; CKD = chronic kidney disease; DAPT = dual antiplatelet therapy; eGFR = estimated glomerular filtration rate; HF = heart failure; MI = myocardial infarction; o.d. = omni die (once a day); PAD = peripheral artery disease; PCI = percutaneous coronary intervention.
[a]High risk of ischaemic events is defined as diffuse multivessel CAD with at least one of the following: diabetes mellitus requiring medication, recurrent MI, PAD, or CKD with eGFR 15 - 59 mL/min/1.73 m^2.
[b]Moderately increased risk of ischaemic events is defined as at least one of the following: multivessel/diffuse CAD, diabetes mellitus requiring medication, recurrent MI, PAD, HF, or CKD with eGFR 15 - 59 mL/min/1.73 m^2.
[c]High bleeding risk is defined as history of intracerebral haemorrhage or ischaemic stroke, history of other intracranial pathology, recent gastrointestinal bleeding or anaemia due to possible gastrointestinal blood loss, other gastrointestinal pathology associated with increased bleeding risk, liver failure, bleeding diathesis or coagulopathy, extreme old age or frailty, or renal failure requiring dialysis or with eGFR <15 mL/min/1.73 m^2.

HOST EXAM trial (Lancet 2021)





HOST EXAM trial (Lancet 2021)

HOST EXAM
EXtended Antiplatelet Monotherapy

5530 patients who underwent PCI with DES, and maintained DAPT without clinical events during 12 ± 6 months after PCI

Randomization

Clopidogrel monotherapy

Aspirin monotherapy

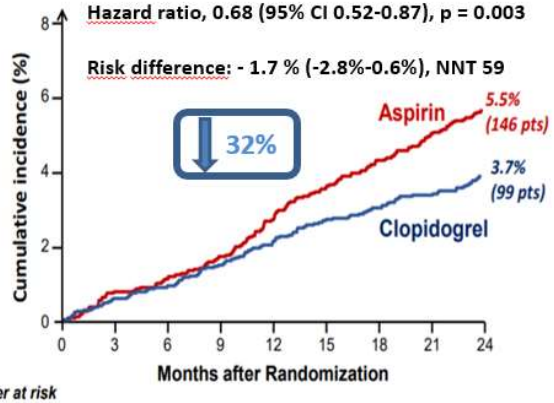
<Assumptions>
- ✓ Incidence of the primary outcome : 9·6% vs· 12·0% for the clopidogrel and aspirin monotherapy groups, respectively
- ✓ Sampling ratio: 1:1
- ✓ Estimated loss to follow up rate: 5%
- ✓ 2-sided α: 5% / Power: 80%

Index PCI → **Post-PCI 12 ± 6 months** (*Out-patient department based follow-up*) → **Post-random 24 months** → Extended follow-up

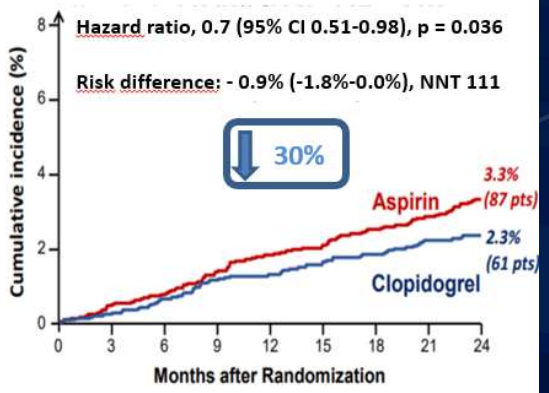
Randomization

Primary outcome: a composite of all-cause death, nonfatal myocardial infarction, stroke, readmission due to acute coronary syndrome, and major bleeding (BARC type ≥3)

Thrombotic composite outcome
(cardiac death, non-fatal MI, ischemic stroke, readmission due to ACS, and definite or probable stent thrombosis)



Any bleeding
(BARC type ≥2 bleeding)



Number at risk

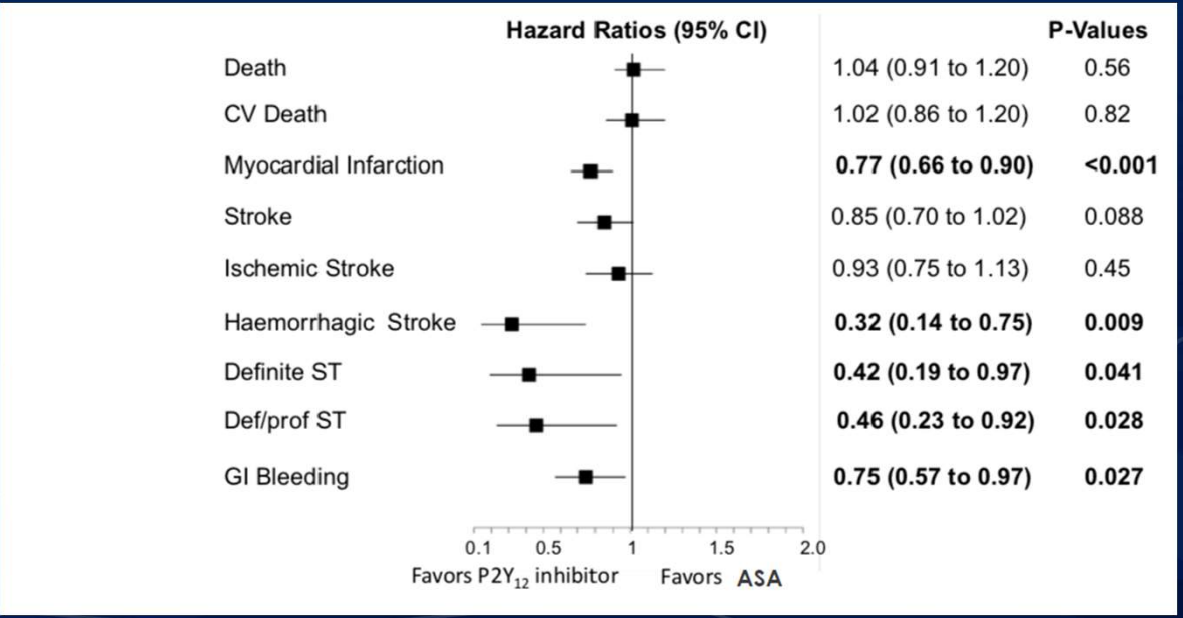
Clopidogrel	2710	2661	2612	2569	2524	2710	2664	2621	2585	2542
Aspirin	2728	2670	2608	2557	2495	2728	2677	2626	2595	2547

HOST-EXAM
Component of Outcomes for 2 Years

	Clopidogrel (n=2710)	ASA (n=2728)	Hazard Ratio (95% CI)	P value
	No. of patients (%)			
All-cause death	1.9% (51)	1.3% (36)	1.43 (0.93-2.19)	0.101
Cardiac death	0.7% (19)	0.5% (14)	1.37 (0.69-2.73)	0.374
Non-cardiac death	1.2% (32)	0.8% (22)	1.47 (0.85-2.52)	0.167
Non-fatal myocardial infarction	0.7% (18)	1.0% (28)	0.65 (0.36-1.17)	0.150
Stroke	0.7% (18)	1.6% (43)	0.42 (0.24-0.73)	0.002
Ischemic stroke	0.5% (14)	1.0% (26)	0.54 (0.28-1.04)	0.064
Hemorrhagic stroke	0.2% (4)	0.6% (17)	0.24 (0.08-0.70)	0.010
Readmission due to ACS	2.5% (66)	4.1% (109)	0.61 (0.45-0.82)	0.001
Major bleeding (BARC type ≥3)	1.2% (33)	2.0% (53)	0.63 (0.41-0.97)	0.035
Any revascularization	2.1% (56)	2.6% (69)	0.82 (0.57-1.16)	0.261
Target lesion revascularization	0.9% (24)	1.4% (36)	0.67 (0.40-1.12)	0.130
Target vessel revascularization	1.4% (37)	1.8% (48)	0.78 (0.50-1.19)	0.245
Definite or probable stent thrombosis	0.4% (10)	0.6% (16)	0.63 (0.29-1.39)	0.251
Any minor GI complaints	10.2% (272)	11.9% (320)	0.85 (0.72-1.00)	0.048

PANTHER meta-analysis
(J Am Coll Cardiol 2023)

7 trials and 24,325 participants (12,147 on aspirin vs 12,178 on P2Y12i - 62% clop, 38% ticagrelor 90 mg x 2)



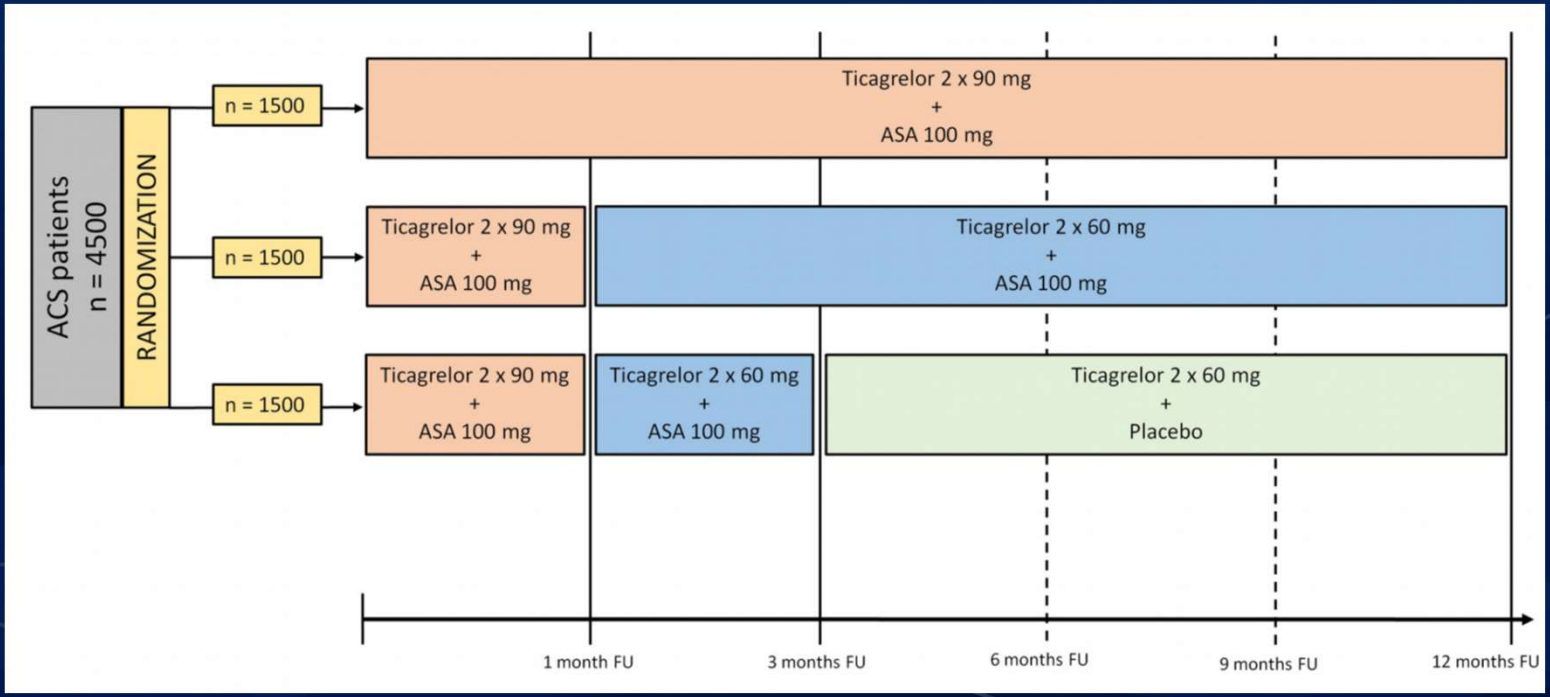
P2Y12i vs ASA in pts with chronic coronary syndrome

Conclusions

- In pts with CCS, P2Y12 monotherapy may reduce MI events vs aspirin, without survival benefit
- NNT for MACE >100
- Major bleeding reduction (ICH) with P2Y12 monotherapy in individual trials may depend on aspirin dose
- Consistency of data for ticagrelor and clopidogrel, but more robust evidence with the latter
- Reduction of GI bleeding appears consistent with clopidogrel use
- Unclear efficacy to safety ratio, especially for ticagrelor
- Selective CCS patients possibly candidates to clopidogrel monotherapy:
  - with PAD
  - with stroke/TIA o
  - with high ischemic risk and high bleeding risk
  - with AF and high coronary complexity (+ NOAC)

Low-dose ticagrelor with or without acetylsalicylic acid in patients with acute coronary syndrome: ELECTRA-SIRIO 2 trial

Jacek Kubica, Diana A. Gorog, Paul A. Gurbel, Dimitrios Alexopoulos, Dariusz Dudek, Giuseppe Patti, Eliano P. Navarese



Future perspectives: aspirin-free post-PCI antiplatelet therapies

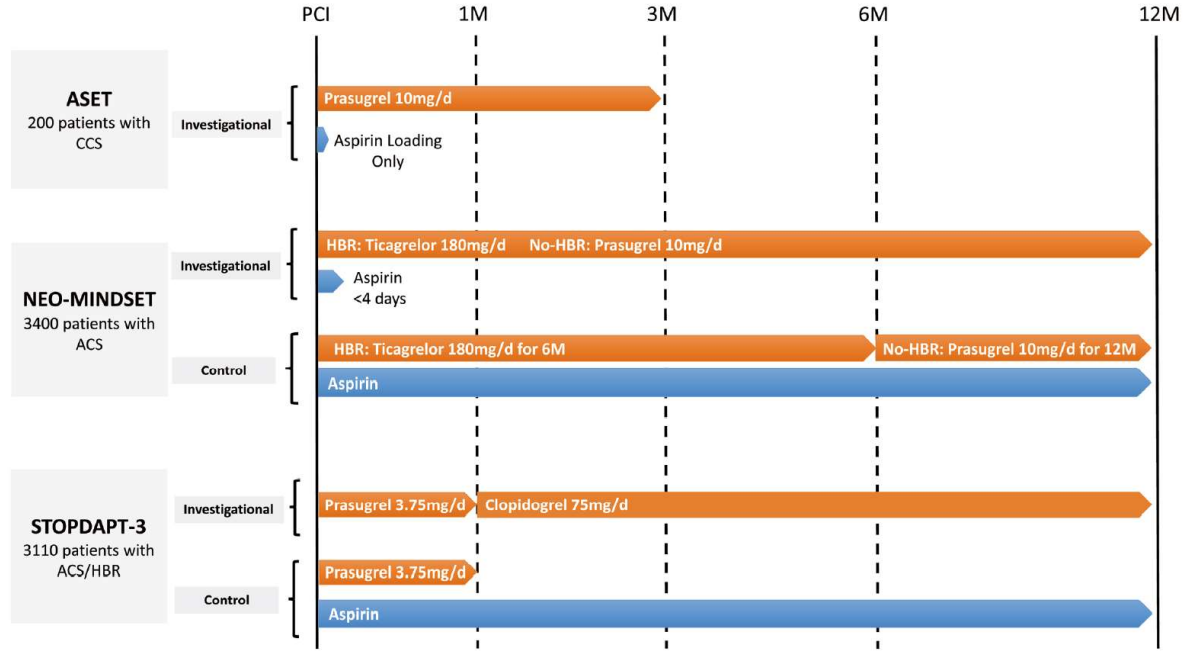
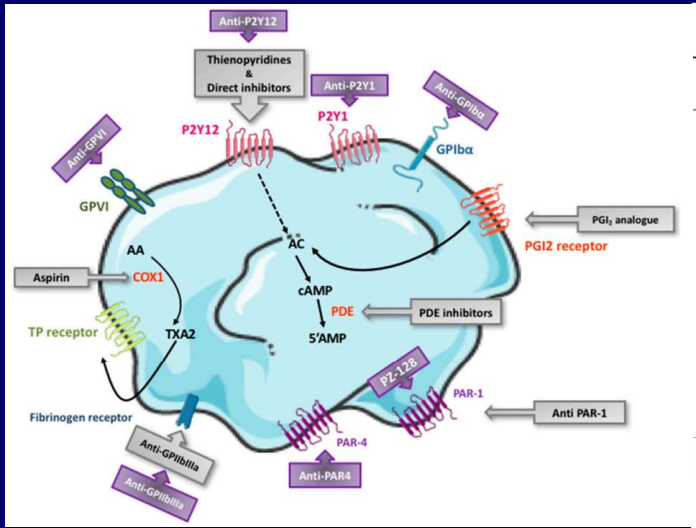


Figure 3. Clinical trials evaluating an aspirin-free strategy in patients undergoing PCI. ACS, acute coronary syndrome; CCS, chronic coronary syndrome; DAPT, dual-antiplatelet therapy; DES, drug-eluting stent; HBR, high bleeding risk; PCI, percutaneous coronary intervention.

NOVEL ANTIPLATELET AGENTS UNDER CLINICAL DEVELOPMENT



Name	Company	Type	Route of Administration	Target	Completed Clinical Trial
PZ-128	Tufts Medical Center	Pepducin	IV	PAR1	Phase I
BMS-986120	Bristol-Myers Squibb	Small molecule	oral	PAR4	Phase I
BMS-986141	Bristol-Myers Squibb	Small molecule	oral	PAR4	Phase I Phase II
Revacept	Advance Cor	Fusion protein	IV	GPVI ligand	Phase I Phase II
ACT017	Acticor Biotech	Antibody	IV	GPVI	Phase I
ARC1779	Archemix	DNA aptamer	IV	VWF	Phase I Phase II
AZD6482	AstraZeneca	Small molecule	IV	PI3Kβ	Phase I Phase I
Isoquercetin	Beth Israel NHLBI	Small molecule Small molecule	oral oral	PDI PDI	Phase I Phase II/III

GP: glycoprotein; IV: intravenous; PAR: protease-activated receptor; PDI: protein disulfide isomerase; PI3Kβ: phosphoinositide 3-kinase-β; VWF: von Willebrand factor.

Jourdi, G. et al. Current and Novel Antiplatelet Therapies for the Treatment of Cardiovascular Diseases. Int J Mol Sci 2021, 22, 13079