

IL CONTINUUM CARDIOLOGIA D'URGENZA - UTIC PARTE I

Strategie di rivascularizzazione nel paziente con infarto miocardico anziano e/o ad alto rischio emorragico

Mattia Galli



Disclosures

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Paid editorial roles: Associate Editor at European Heart Journal.

Revascularization in Elderly: Key considerations

1. Technically more challenging procedures associated with higher complication rates (arterial tortuosity, extensive coronary calcium or tortuosity)
2. Comorbidity (particularly kidney disease)

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Revascularization in Elderly: Key considerations

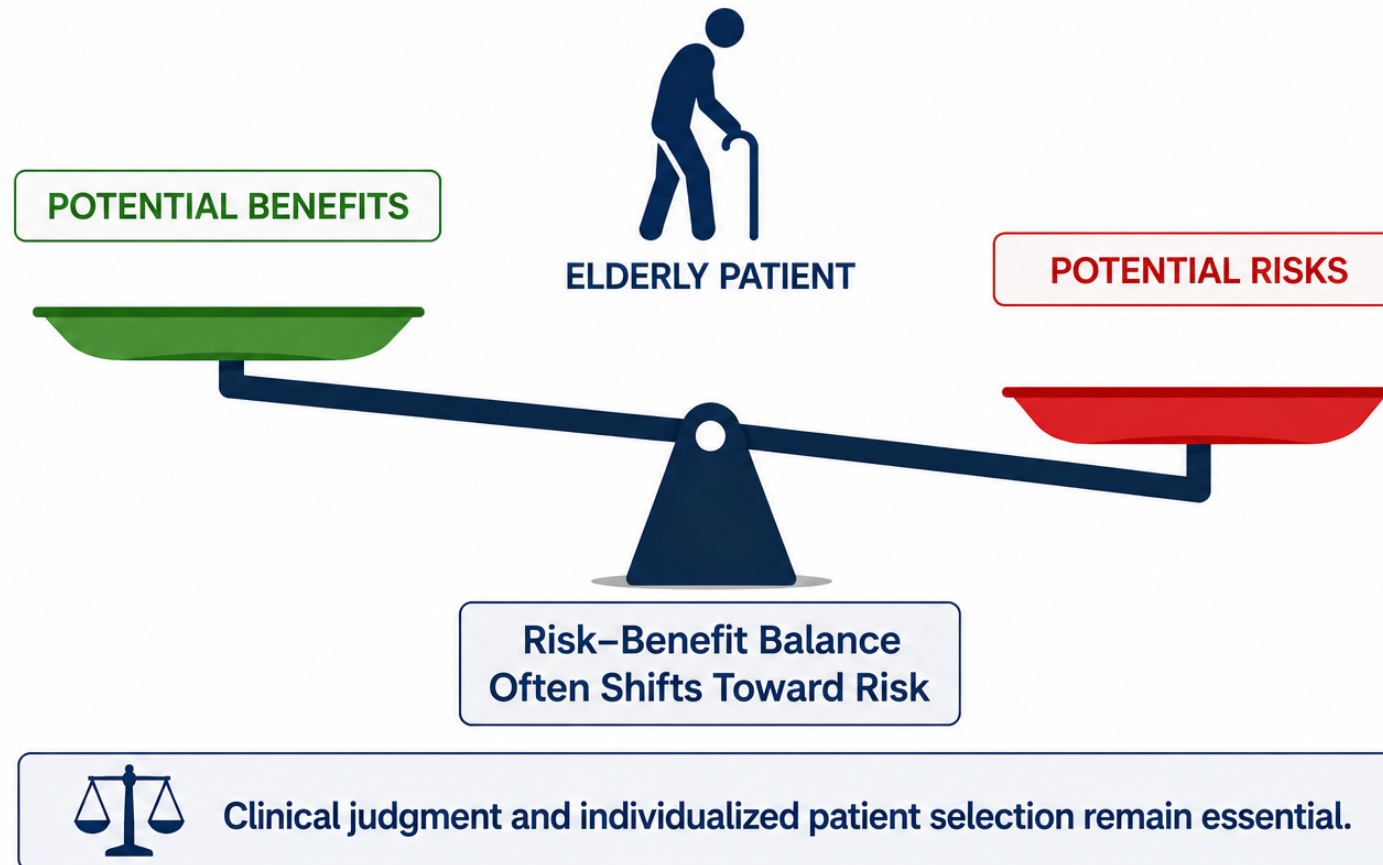
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2. Comorbidity (particularly kidney disease)
3. Life expectancy/frailty/functional status
4. Risk/benefit ratio → strictly depending on clinical presentations (STEMI vs NSTEMI)
5. Increased bleeding risk (periprocedural and associated with antithrombotic therapy)

Revascularization in the Elderly: A Less Balanced Risk–Benefit Ratio



Revascularization Strategy in the Elderly According to Clinical Setting

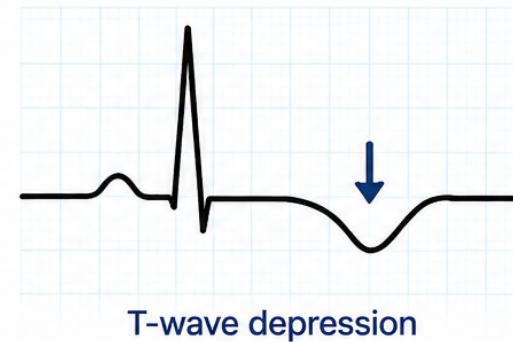
STEMI PRESENTATION



**URGENT
REVASCULARIZATION**
should be performed



NSTEMI PRESENTATION



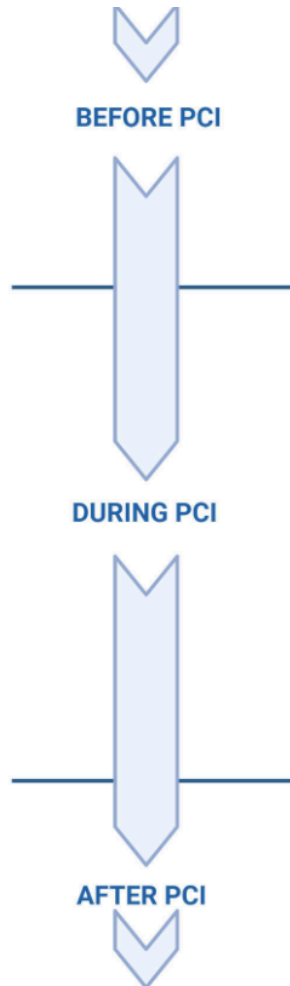
REVASCULARIZATION
should be considered
after careful assessment



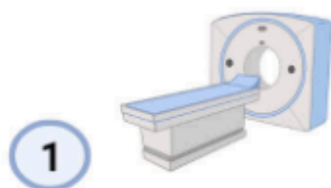
Individualized decision-making is essential,
balancing ischemic benefit and bleeding risk in the elderly.

Bleeding reduction strategies

in patients undergoing percutaneous coronary intervention



Pre-PCI



1

Consider **non-invasive testing** (i.e. stable patients or low risk NSTEMI-ACS)



- Is coronary angiography really needed?
- Is CCTA available?



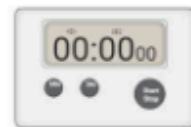
2

Bleeding risk stratification



- Consider using scores (alternatively use clinical sense)

3



Optimal timing of PCI according to the clinical setting and concomitant ATT (i.e. OAC or fibrinolysis)



- Avoid overlaps in antithrombotic therapies

4



Anticoagulation according to the clinical setting and time to PCI (i.e. UFH or fondaparinux)



- Use the best anticoagulant agent

5

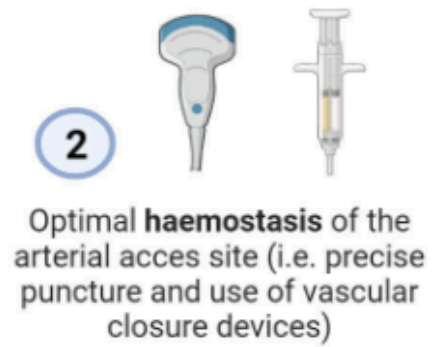


Antiplatelet according to clinical setting and time to PCI (i.e. pre-test PCI probability)



- Use the best antiplatelet agent

During-PCI



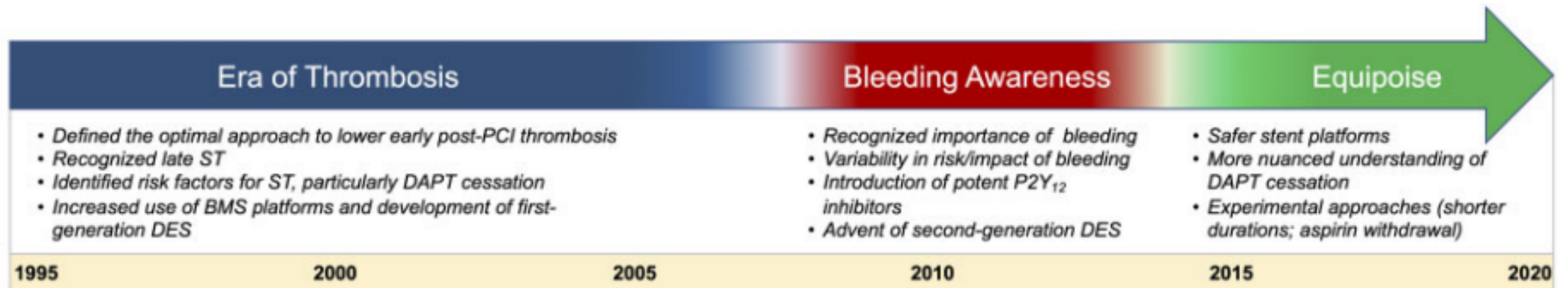
After-PCI

1 
Periodic assessment of
bleeding risk

2 
Consider DAPT **shortening**
or **de-escalation** of P2Y12
inhibitors

3 
Use **proton pump**
inhibitors

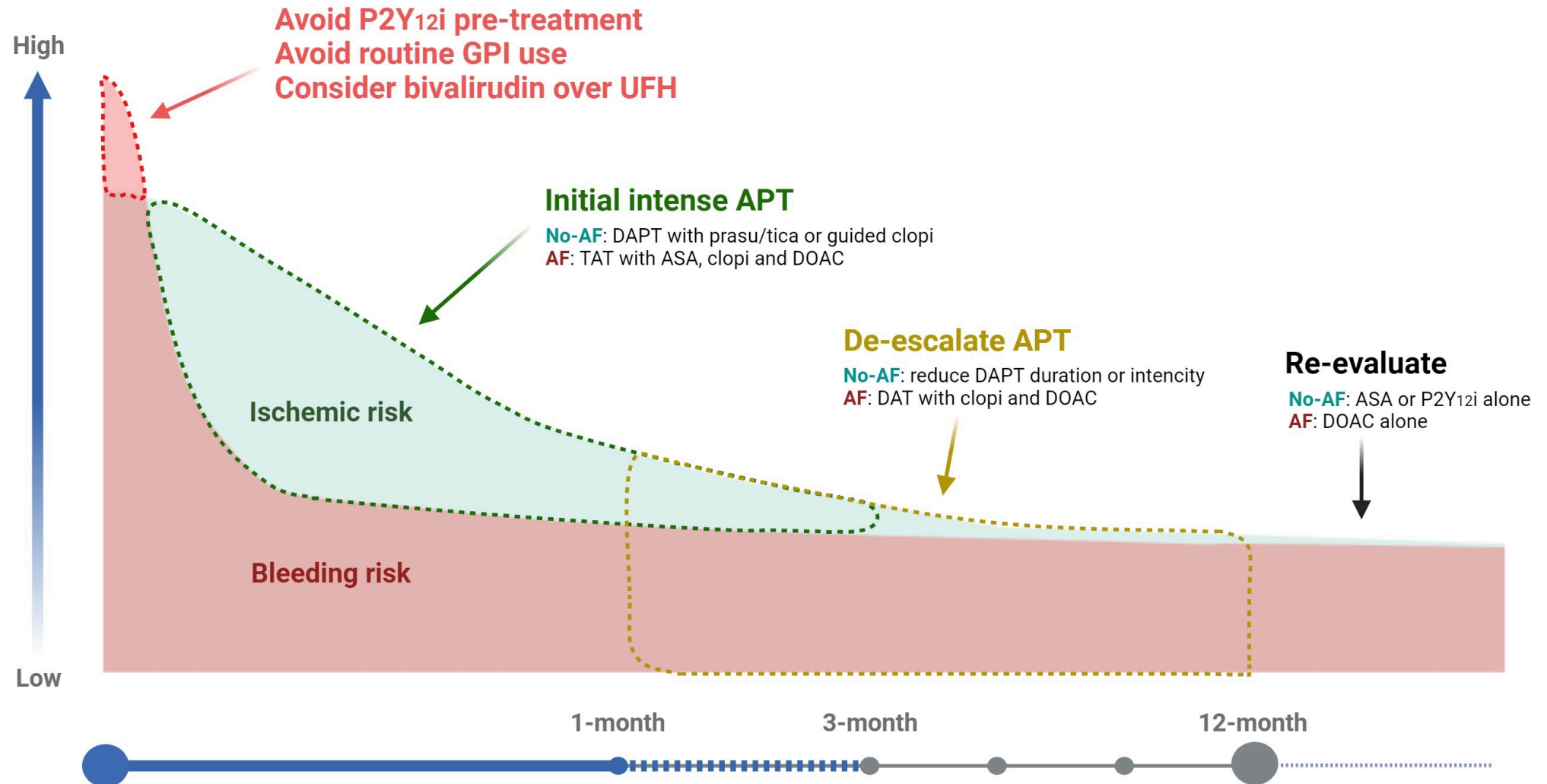
4 
Consider using **platelet**
function or **genetic**
testing

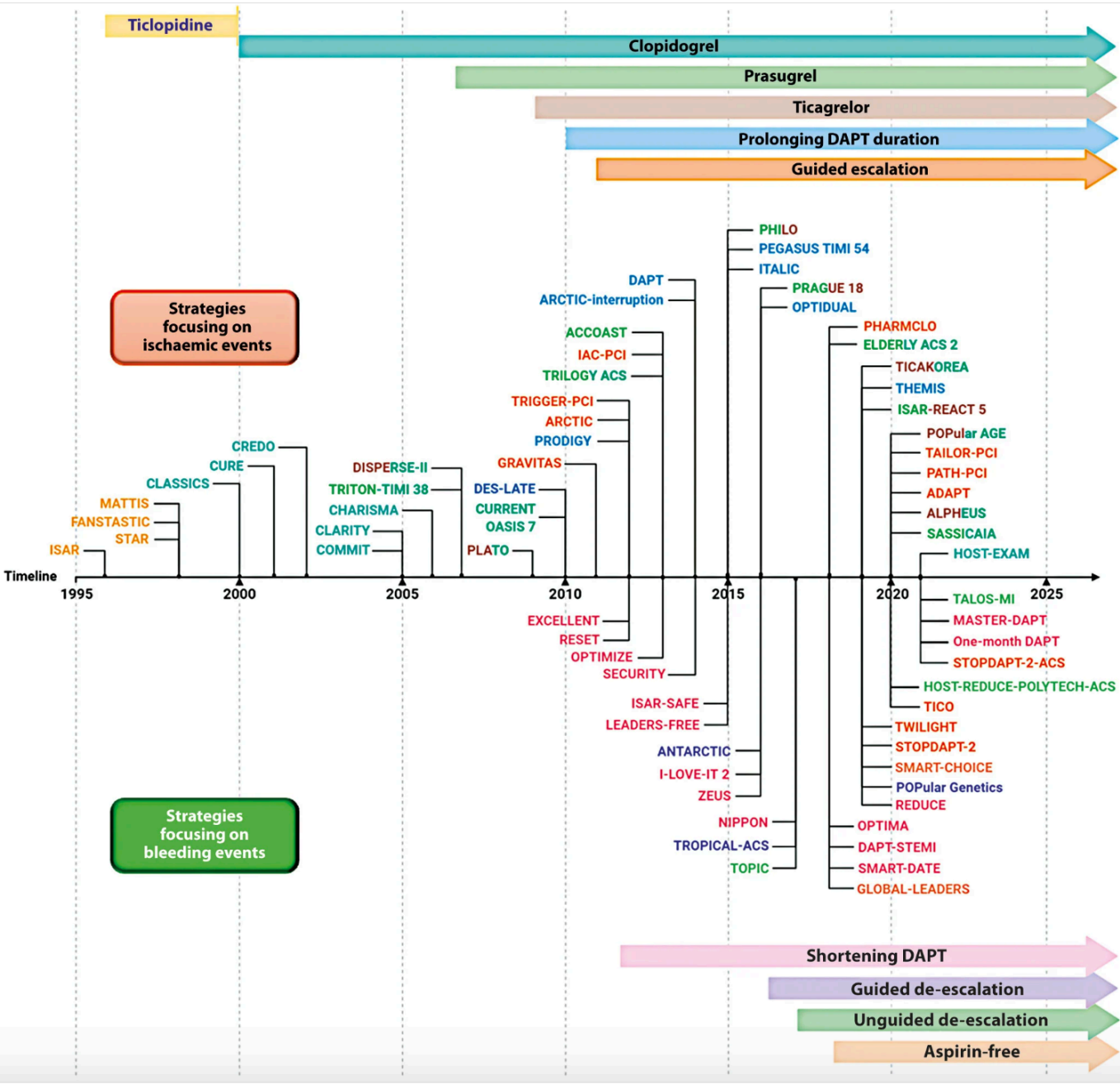


1. Prognostic relevance of bleeding
2. Availability of stent platforms with low thrombogenicity
3. Understanding that ischemic risk varies over time

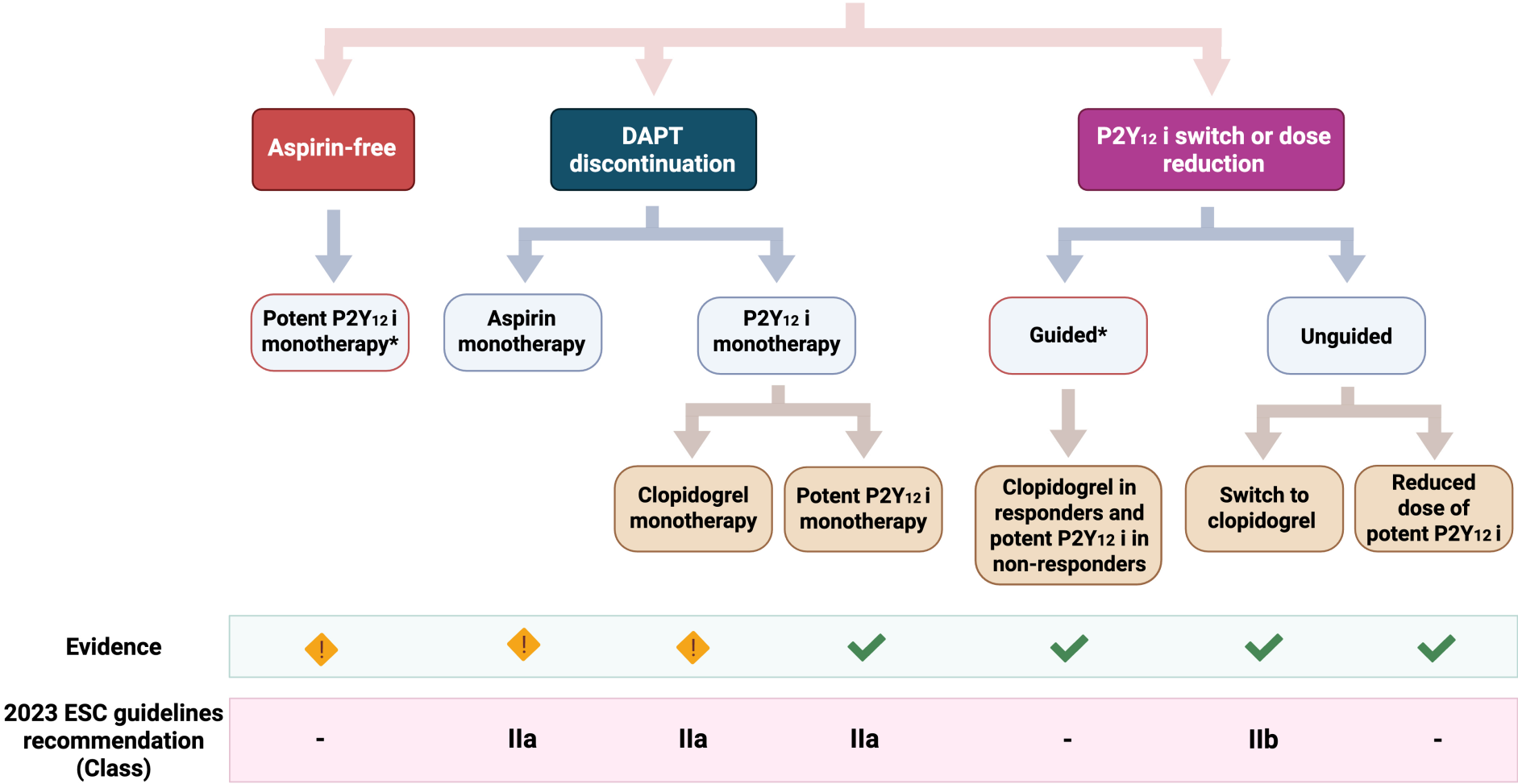


Modulation of antiplatelet therapy over time





De-escalation strategies in patients with acute coronary syndromes



6-month versus 12-month or longer dual antiplatelet therapy after percutaneous coronary intervention in patients with acute coronary syndrome (SMART-DATE): a randomised, open-label, non-inferiority trial



Joo-Yong Hahn*, Young Bin Song*, Ju-Hyeon Oh, Deok-Kyu Cho, Jin Bae Lee, Joon-Hyung Doh, Sang-Hyun Kim, Jin-Ok Jeong, Jang-Ho Bae, Byung-Ok Kim, Jang Hyun Cho, Il-Woo Suh, Doo-il Kim, Hoon-Ki Park, Jong-Seon Park, Woong Gil Choi, Wang Soo Lee, Jihoon Kim, Ki Hong Choi, Taek Kyu Park, Joo Myung Lee, Jeong Hoon Yang, Jin-Ho Choi, Seung-Hyuk Choi, Hyeon-Cheol Gwon, for the SMART-DATE investigators†

- **2712 patients with ACS from South Korea**
- **DAPT with clopidogrel in 80% of patients**
- **37% STEMI, 31% NSTEMI, 31% Unstable angina**
- **Mean age= 62**
- **Diabetes mellitus= 27%**
- **Multivessel intervention= 20%**
- **Stent per patient= 1.4**

	6-month DAPT group (n=1357)	12-month or longer DAPT group (n=1355)	HR (95% CI)	p value
Major adverse cardiac and cerebrovascular events	63 (4.7%)	56 (4.2%)	1.13 (0.79–1.62)	0.51
Death	35 (2.6%)	39 (2.9%)	0.90 (0.57–1.42)	0.90
Myocardial infarction	24 (1.8%)	10 (0.8%)	2.41 (1.15–5.05)	0.02
Target vessel myocardial infarction	14 (1.1%)	7 (0.5%)	2.01 (0.81–4.97)	0.13
Non-target vessel myocardial infarction	10 (0.8%)	3 (0.2%)	3.35 (0.92–12.18)	0.07
Cerebrovascular accident (stroke)	11 (0.8%)	12 (0.9%)	0.92 (0.41–2.08)	0.84
Stent thrombosis	15 (1.1%)	10 (0.7%)	1.50 (0.68–3.35)	0.32
BARC type 2–5 bleeding	35 (2.7%)	51 (3.9%)	0.69 (0.45–1.05)	0.09
Major bleeding	6 (0.5%)	10 (0.8%)	0.60 (0.22–1.65)	0.33



Original Investigation

March 2, 2022

Comparison of Clopidogrel Monotherapy After 1 to 2 Months of Dual Antiplatelet Therapy With 12 Months of Dual Antiplatelet Therapy in Patients With Acute Coronary Syndrome
The STOPDAPT-2 ACS Randomized Clinical Trial

Hirotoishi Watanabe, MD¹; Takeshi Morimoto, MD²; Masahiro Natsuaki, MD³; [et al](#)

» Author Affiliations

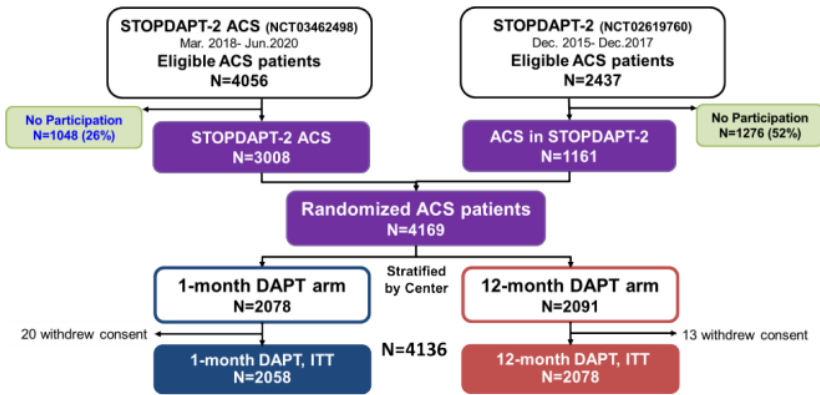
JAMA Cardiol. 2022;7(4):407-417. doi:10.1001/jamacardio.2021.5244

	1 month DAPT	12 months DAPT	Hazard ratio
Primary Endpoint CV death/MI/ST/Stroke/TIMI major/minor bleeding	3.20%	2.83%	1.14 (95%CI 0.80-1.62)
Major Secondary CV Endpoint CV death/MI/ST/Stroke	2.76%	1.86%	1.50 (95%CI 0.99-2.26)
Myocardial Infarction	1.59%	0.85%	1.91 (95% 1.06-3.44)
Major Secondary Bleeding Endpoint TIMI major/minor bleeding	0.54%	1.17%	0.46 (95%CI 0.23-0.94)
BARC 3-5 Bleeding	0.54%	1.31%	0.41 (95%CI 0.20-0.83)



STOPDAPT-2 ACS | Study Design

Prospective, open-label, investigator-initiated randomized controlled trial



ORIGINAL ARTICLE

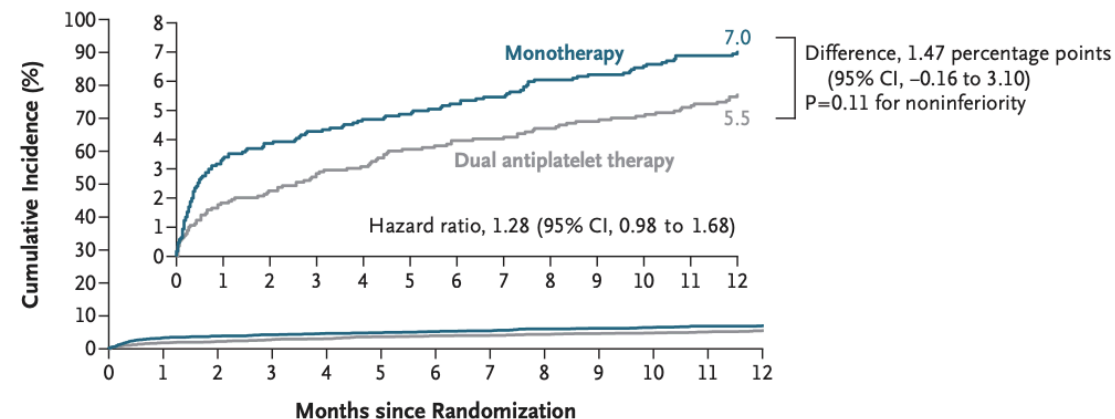
Early Withdrawal of Aspirin after PCI in Acute Coronary Syndromes

P.O. Guimarães,¹ M. Franken,¹ C.A.M. Tavares,^{1,2} M.O. Antunes,^{2,3} F.S. Silveira,⁴ P.B. Andrade,⁵ R.R. Bergo,⁶ R.M. Joaquim,⁷ J.E. Tinoco de Paula,⁸ B.R. Nascimento,⁹ F.G. Pitta,^{1,2} J.A. Arruda,¹⁰ R.G. Serpa,¹¹ L.N. Ohe,¹² F.M. Mangione,¹³ R.H.M. Furtado,^{2,14} E. Ferreira,¹⁵ F.B.A. Sampaio,¹⁶ C. T. do Nascimento,¹⁷ L.O.O. Genelhu,¹⁸ C.G. Bezerra,¹⁹ R. Sarmiento-Leite,²⁰ L.N. Maia,²¹ F.R.A. Oliveira,²² M.V. Wainstein,²³ F.T.C. Dall'Orto,⁶ F. Monfardini,¹ S.R.L. Assis,¹ J.C. Nicolau,² A.C. Sposito,²⁴ R.D. Lopes,²⁵ Y. Onuma,²⁶ M. Valgimigli,²⁷ D.J. Angiolillo,²⁸ P.W.J.C. Serruys,²⁶ O. Berwanger,^{29,30} F. Bacal,^{1,2} and P.A. Lemos,¹ for the NEO-MINDSET Trial Investigators*

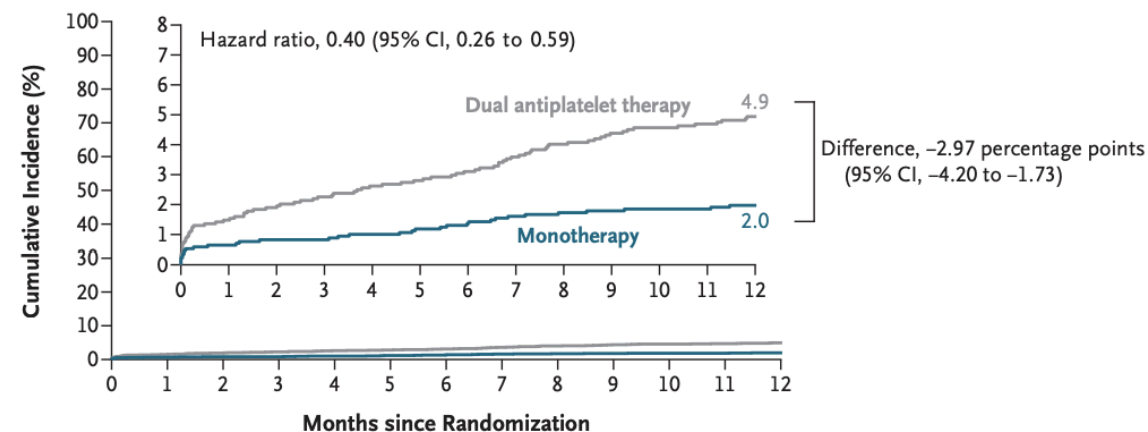
- **3410 patients with ACS from Brazil**
- **Stop aspirin within 4 days of hospitalization and continue P2Y12 inhibitor monotherapy (prasugrel 70%; ticagrelor 28%) or standard 12-months DAPT (same P2Y12 inhibitors)**
- **62% STEMI, 31% NSTEMI, 7% Unstable angina**
- **Mean age= 60**
- **Diabetes mellitus= 27%**



A Death, Myocardial Infarction, Stroke, or Urgent Target-Vessel Revascularization



B Major or Clinically Relevant Nonmajor Bleeding





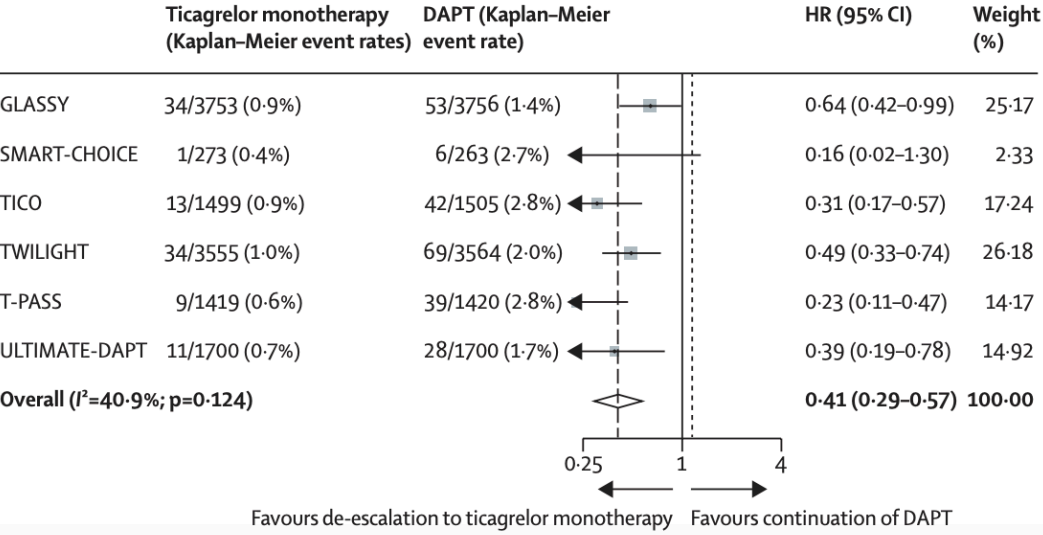
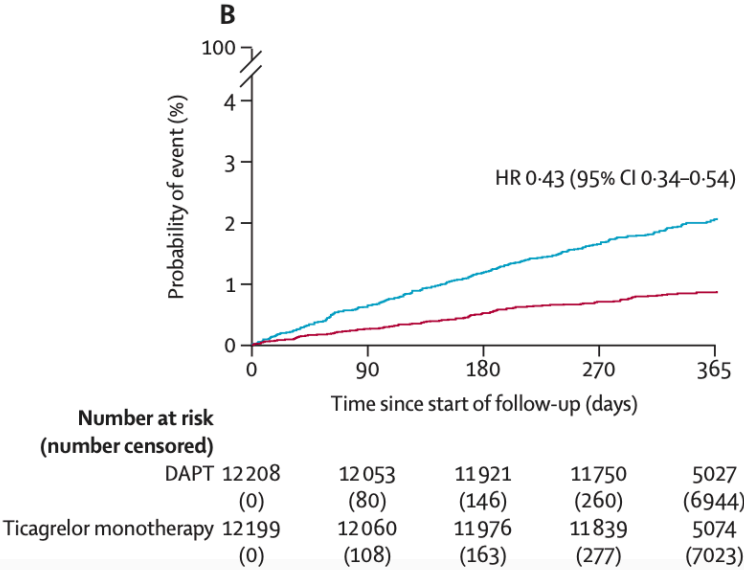
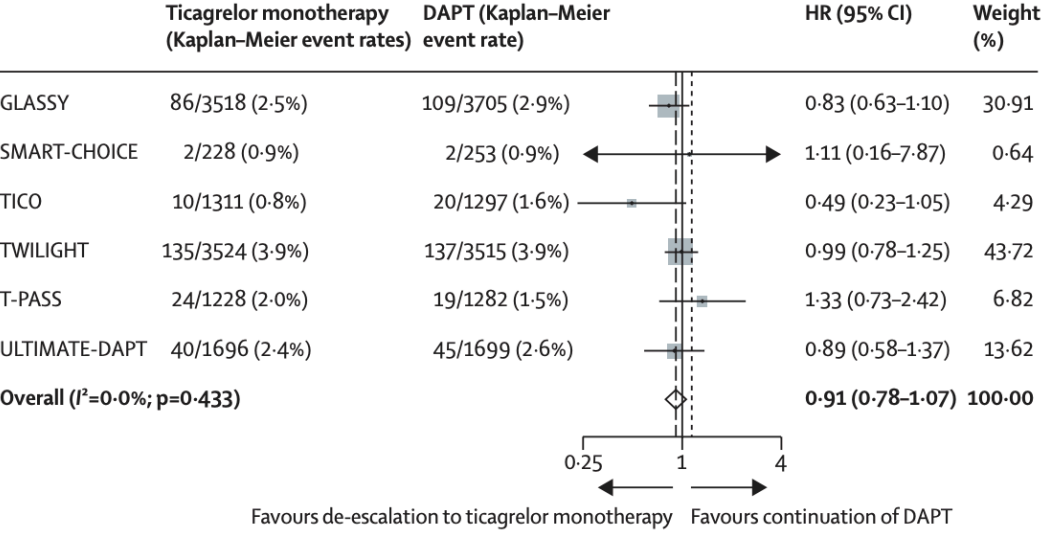
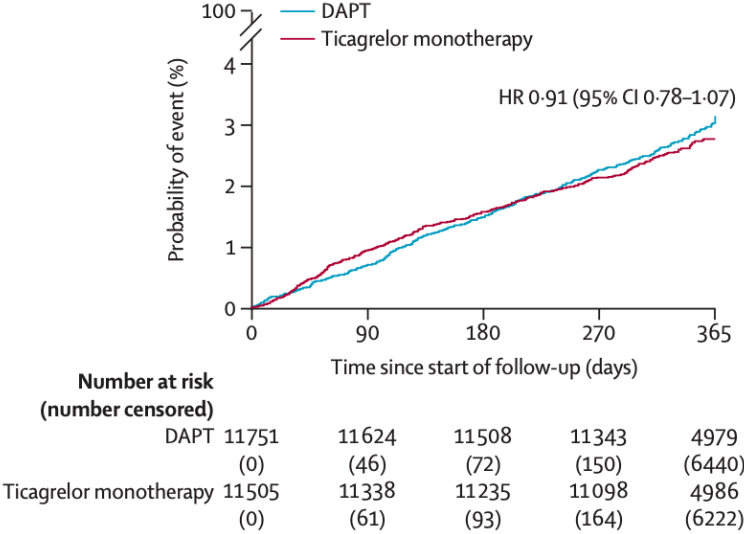
Unguided-de-escalation after 1-month DAPT

Unguided de-escalation								
TOPIC	2017	646	100	0	Clopidogrel-based DAPT versus standard DAPT	CV death, urgent revascularisation, stroke and BARC 2-5 bleeding	Yes	12
HOST-REDUCE-POLYTHEC-ACS	2020	3,429	100	0	Prasugrel 5 mg-based DAPT versus prasugrel 10 mg-based DAPT	All death, MI, ST, repeat revascularisation, stroke and BARC 2-5 bleeding	Yes	12
TALOS-MI	2021	2,697	100	0	Clopidogrel-based DAPT versus ticagrelor-based DAPT	CV death, MI, stroke and BARC 2-5 bleeding	Yes	12





Ticagrelor monotherapy 1-3 months after DAPT



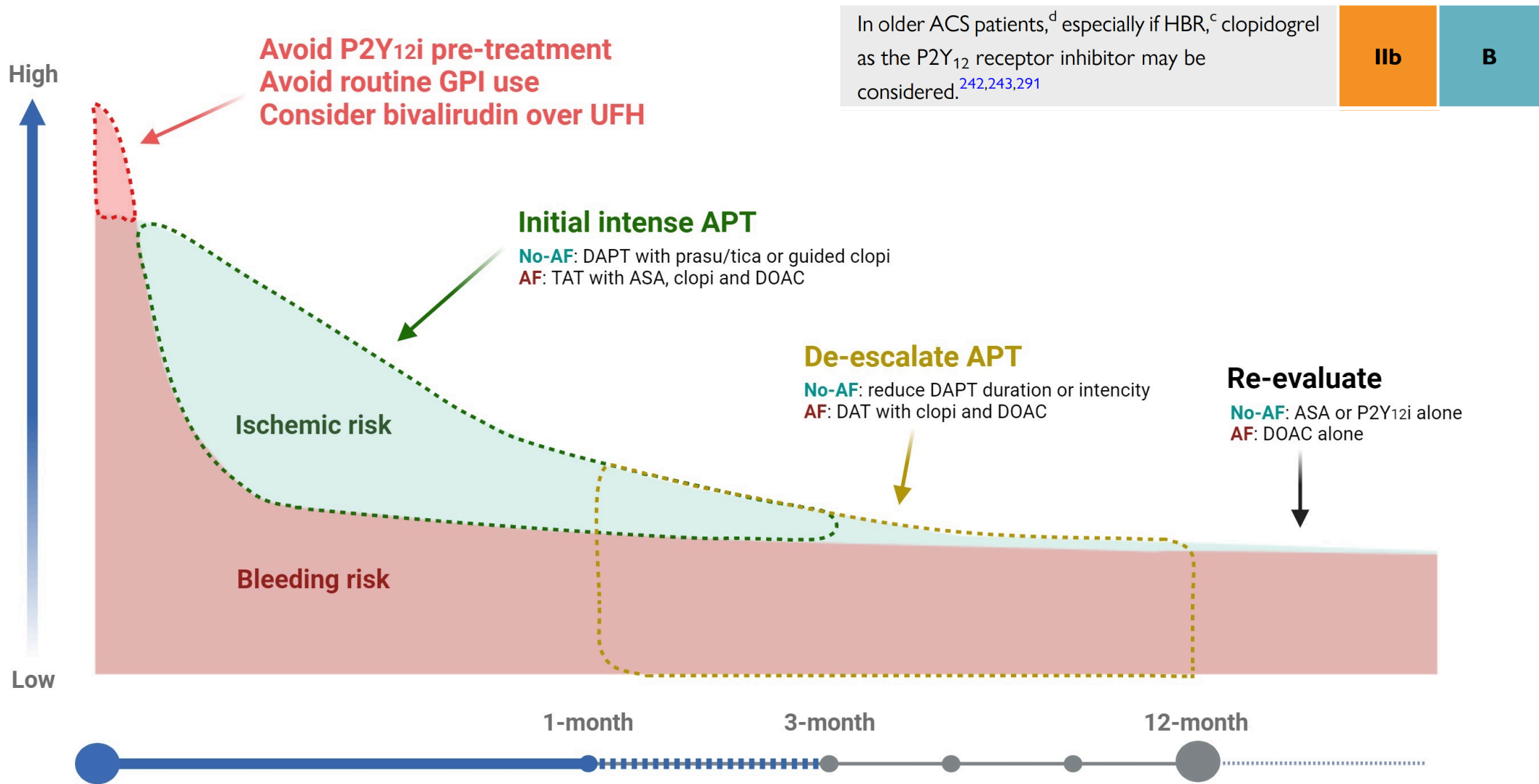


Why can't we just de-escalate to DAPT with clopidogrel or ticagrelor monotherapy 1-3 months after ACS/PCI?

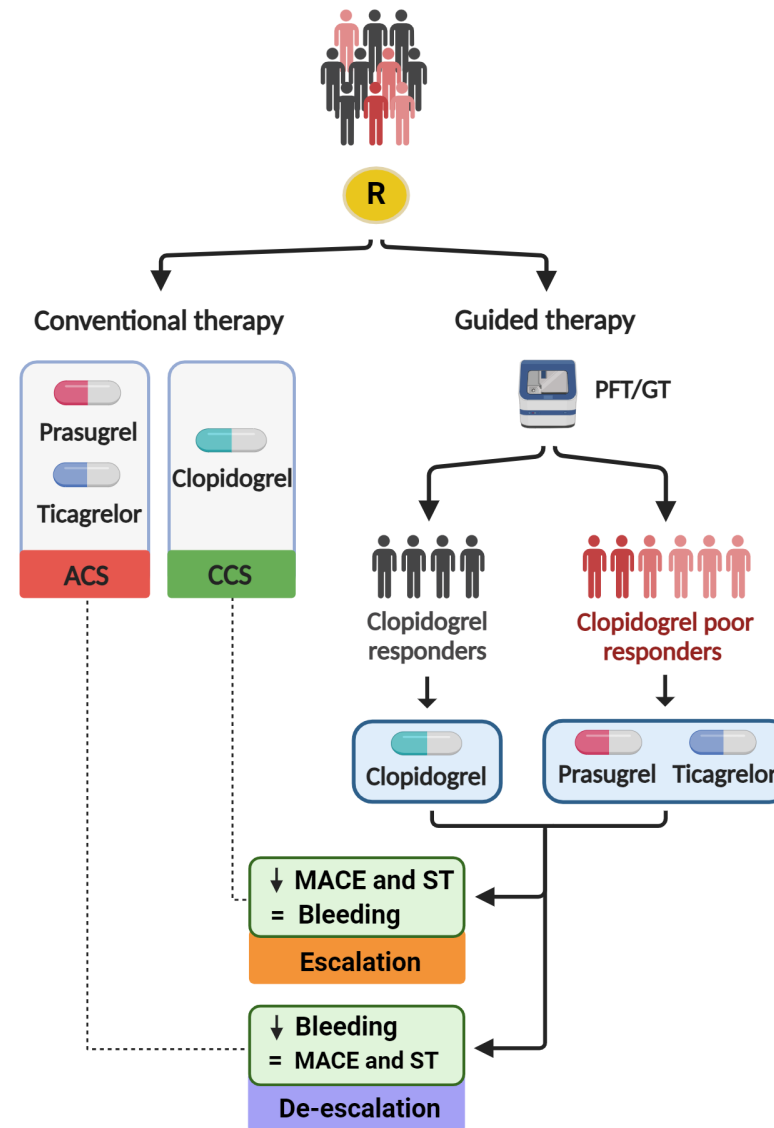
- 1) Precision medicine (is the opposite of evidence based medicine)
- 2) Clopidogrel is the most commonly used P2Y₁₂ inhibitor worldwide
- 3) Ticagrelor 90 mg monotherapy is not approved for use 12 months after ACS
- 4) Reduced dose of ticagrelor (60 mg bid) or prasugrel (5 mg od) are not approved for use
- 5) Unguided de-escalation occurs 1-3 months after ACS/PCI!



Modulation of antiplatelet therapy over time

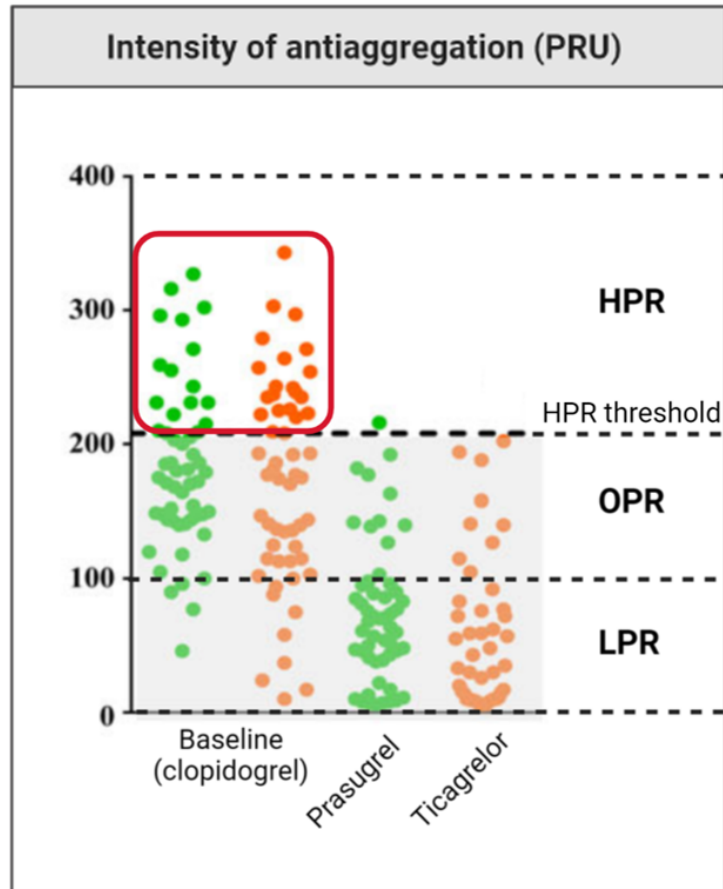


PFT and GT in clinical practice: III Clinical Framework



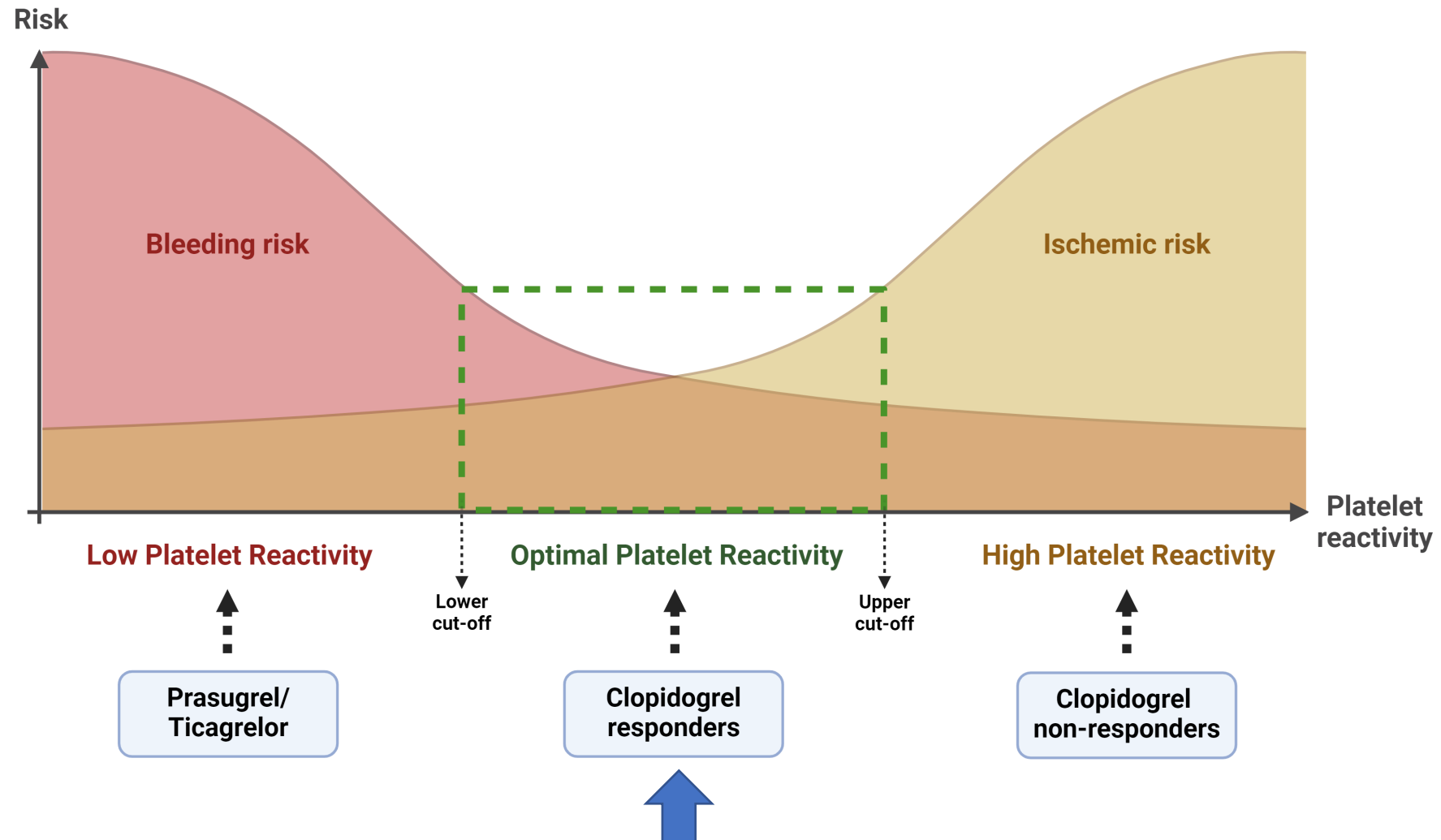
Background and rationale

Analogy between antiplatelet and anticoagulation intensity and clinical events





Background and rationale





ORIGINAL ARTICLE

A Genotype-Guided Strategy for Oral P2Y₁₂ Inhibitors in Primary PCI

Daniel M.F. Claassens, M.D., Gerrit J.A. Vos, M.D., Thomas O. Bergmeijer, M.D., Renicus S. Hermanides, M.D., Ph.D., Arnoud W.J. van 't Hof, M.D., Ph.D., Pim van der Harst, M.D., Ph.D., Emanuele Barbato, M.D., Ph.D., Carmine Morisco, M.D., Ph.D., Richard M. Tjon Joe Gin, M.D., Folkert W. Asselbergs, M.D., Ph.D., Arend Mosterd, M.D., Ph.D., Jean-Paul R. Herrman, M.D., Ph.D., Willem J.M. Dewilde, M.D., Ph.D., Paul W.A. Janssen, M.D., Ph.D., Johannes C. Kelder, M.D., Ph.D., Maarten J. Postma, Ph.D., Anthonius de Boer, M.D., Ph.D., Cornelis Boersma, Pharm.D., Ph.D., Vera H.M. Deneer, Pharm.D., Ph.D., and Jurriën M. ten Berg, M.D., Ph.D.

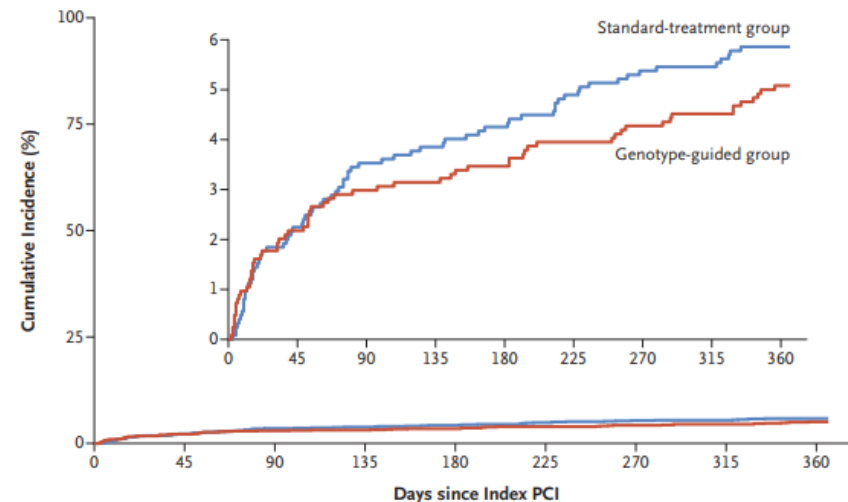


Red flags:

- Non-inferiority design
- Primary endpoint including both ischemic and bleeding outcome

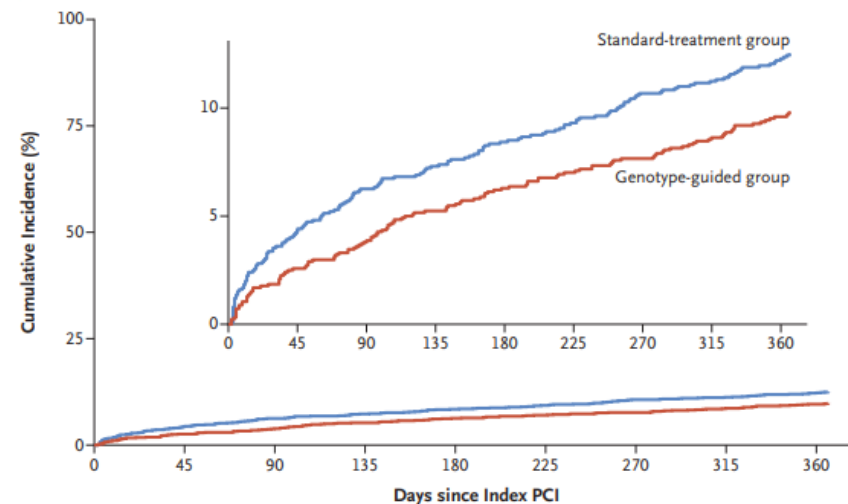
Outcome	Genotype-Guided Group (N=1242)	Standard-Treatment Group (N=1246)	Absolute Difference (95% CI)†	Hazard Ratio (95% CI)	P Value
	no. of patients (%)		percentage points		
Primary combined outcome‡					
Noninferiority analysis	63 (5.1)	73 (5.9)	-0.7 (-2.0 to 0.7)		<0.001§
Superiority analysis	63 (5.1)	73 (5.9)		0.87 (0.62 to 1.21)	0.40
Secondary outcomes					
Primary bleeding outcome: PLATO major or minor bleeding		122 (9.8)	156 (12.5)	0.78 (0.61–0.98)	0.04†
Major or minor bleeding according to other criteria					
BARC type 2–5 bleeding		126 (10.1)	163 (13.1)	0.77 (0.61–0.97)	

A Primary Combined Outcome



No. at Risk	1246	1218	1202	1198	1193	1185	1179	1178	1173
Standard-treatment group	1246	1218	1202	1198	1193	1185	1179	1178	1173
Genotype-guided group	1242	1213	1203	1201	1197	1191	1187	1184	1177

B Primary Bleeding Outcome



Meta-analyses may increase statistical power

Limitations of individual trials:

- Non-inferiority design
- Primary endpoint including both ischemic and bleeding outcome
- Low statistical power for hard endpoints

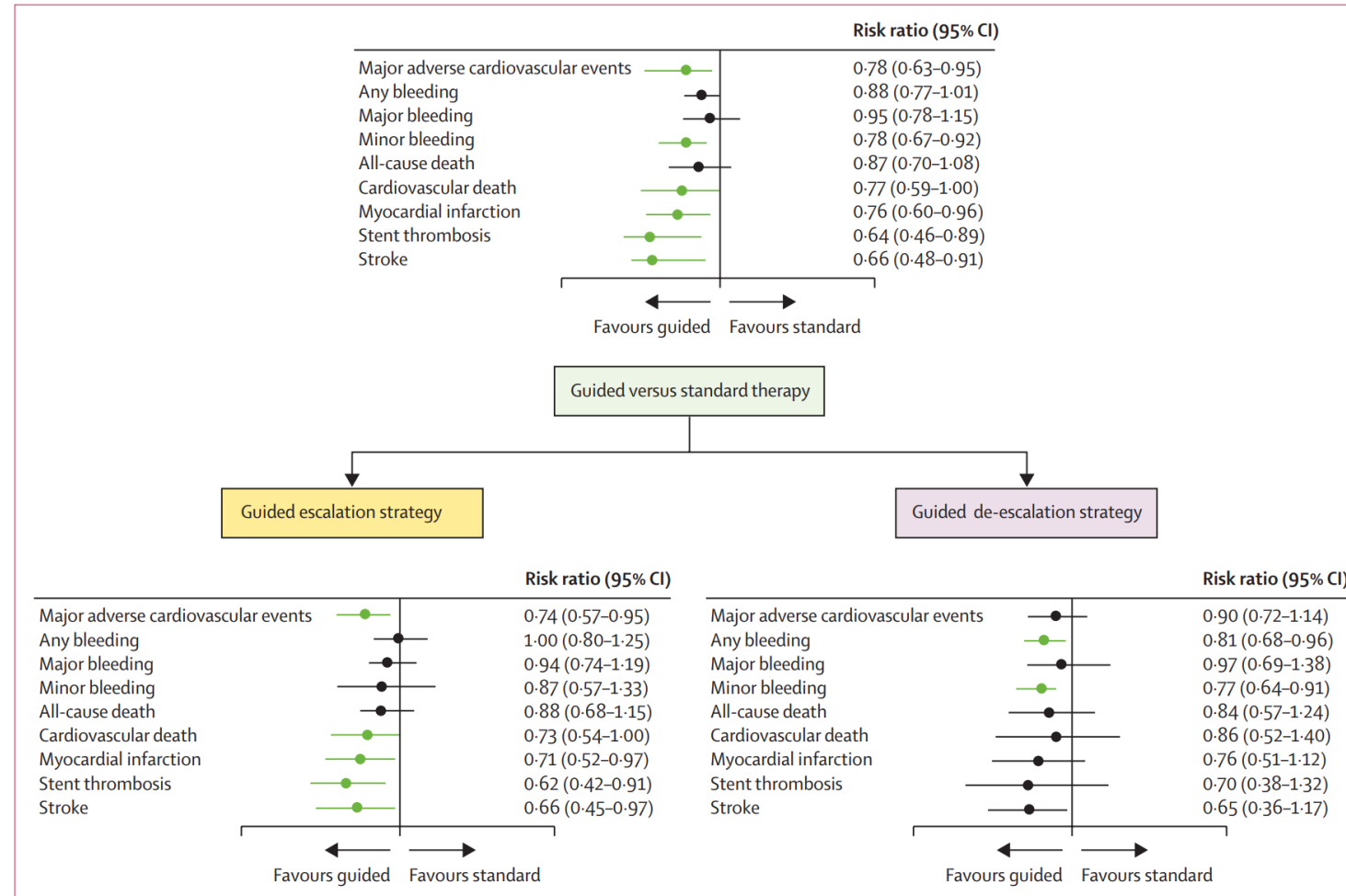


Figure 4: Summary effect estimates for overall guided versus standard therapy, guided de-escalation strategy versus standard therapy, and guided escalation strategy versus standard therapy

Results consistent at secondary analyses according to:

- RCTs vs observational studies
- PFT vs genetic testing
- Proportion of ACS
- Proportion of DES
- Exclusion of cilostazol or double dose clopidogrel
- Duration of follow-up

Comparative effects of guided vs. potent P2Y₁₂ inhibitor therapy in acute coronary syndrome: a network meta-analysis of 61 898 patients from 15 randomized trials

Mattia Galli^{1,2}, Stefano Benenati³, Francesco Franchi¹, Fabiana Rollini¹, Davide Capodanno⁴, Giuseppe Biondi-Zoccai^{5,6}, Giovanni Maria Vescovo⁷, Larisa H. Cavallari⁸, Behnood Bikdeli^{9,10,11}, Jurrien ten Berg¹², Roxana Mehran¹³, Charles Michael Gibson¹⁴, Filippo Crea², Naveen L. Pereira¹⁵, Dirk Sibbing^{16,17,18}, and Dominick J. Angiolillo^{1*}

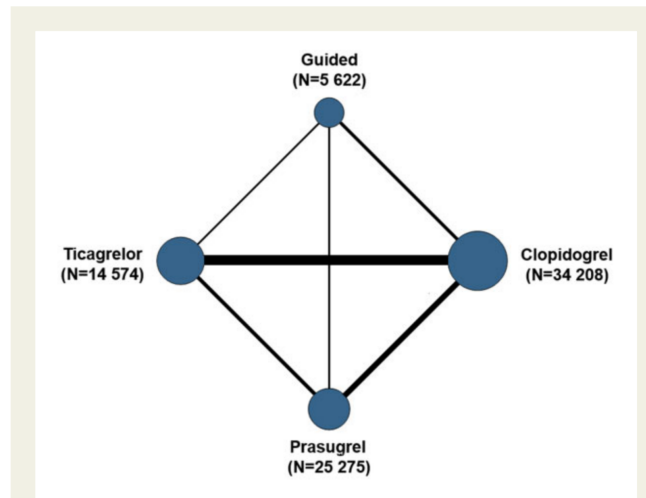
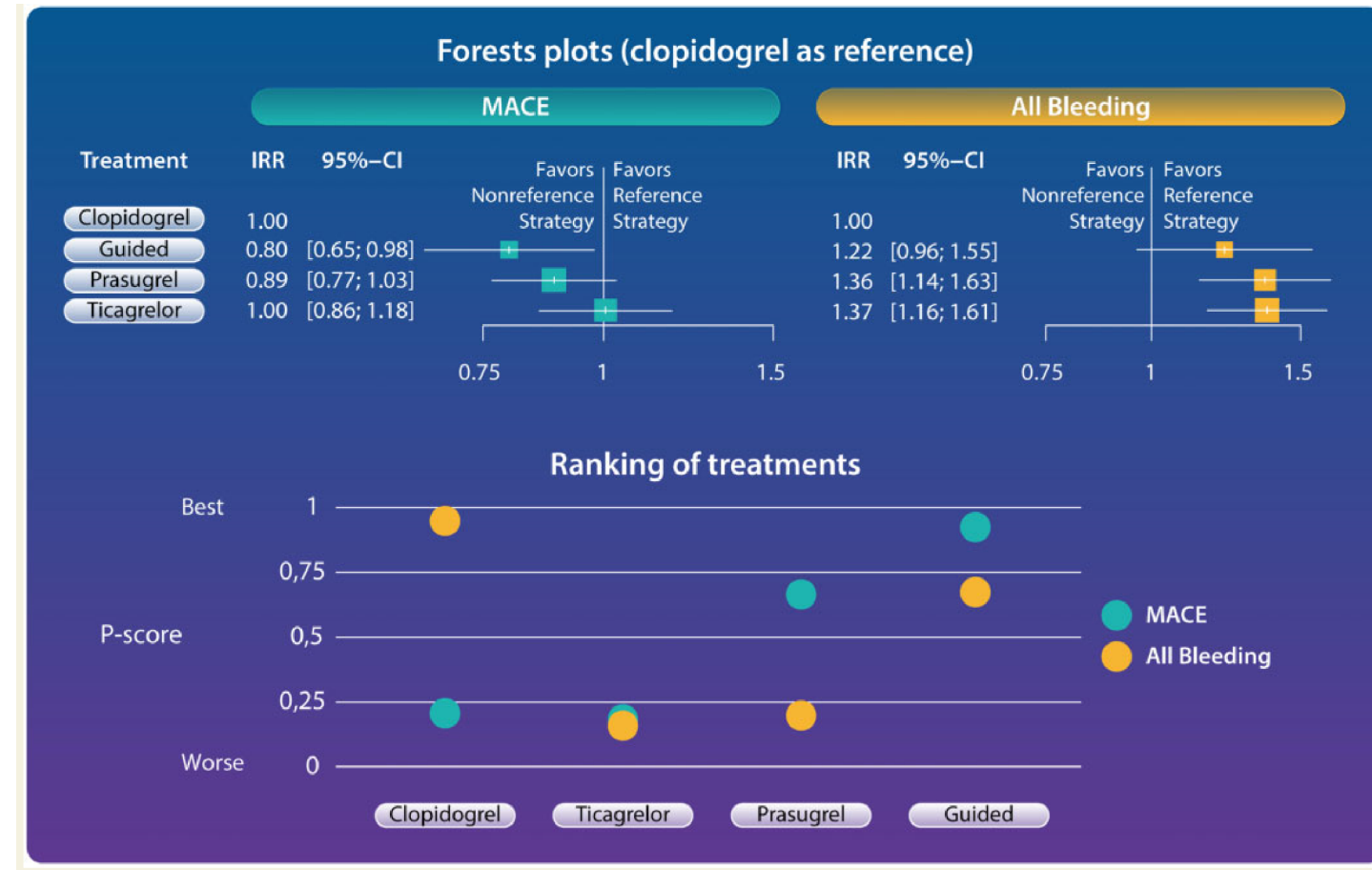


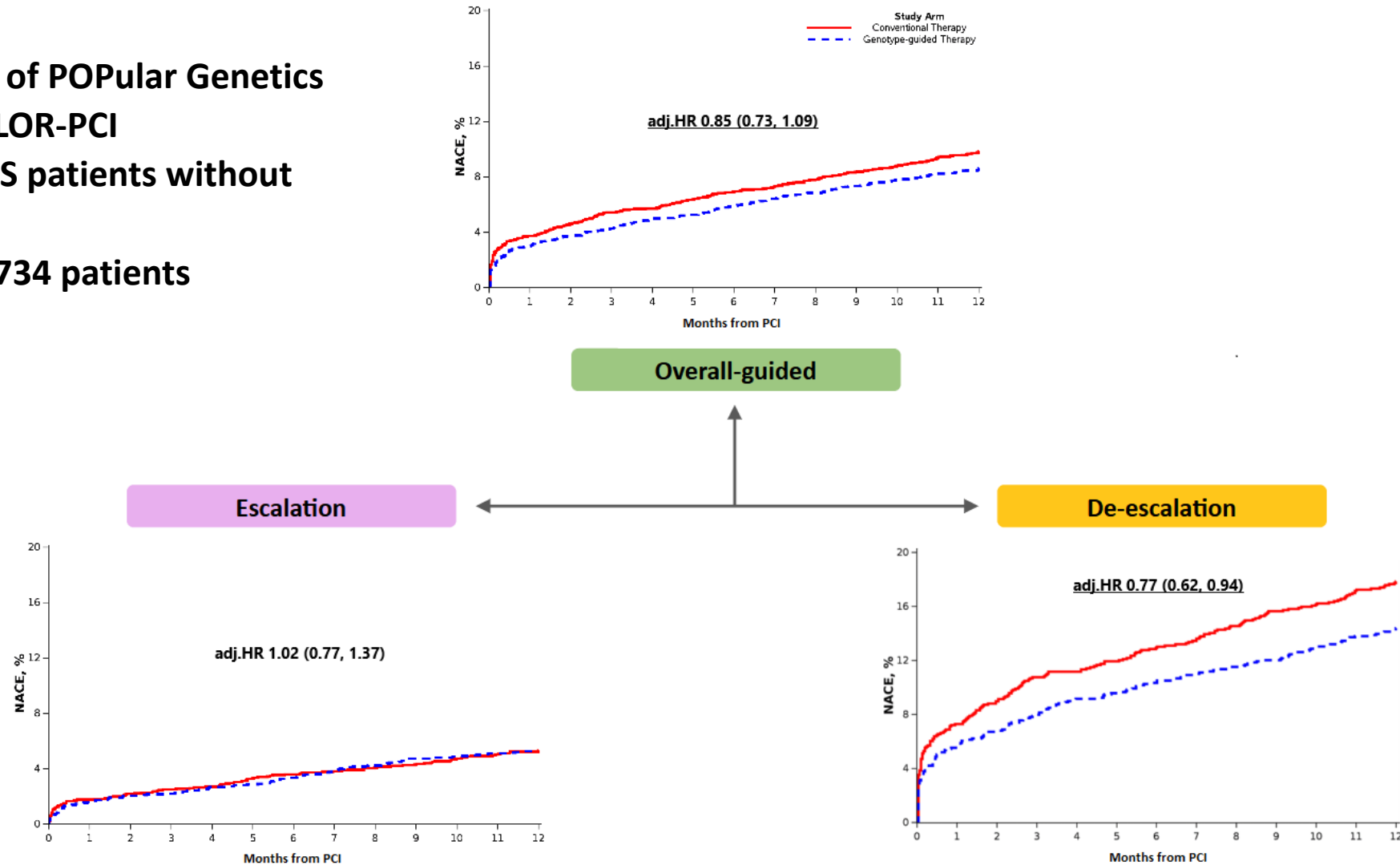
Figure 1 Treatment network. Numbers refer to patient/year.





IPD-Meta-analyses are the highest level of evidence

- IPD-MA of POPular Genetics and TAILOR-PCI
- Only ACS patients without AF
- TOT= 6,734 patients

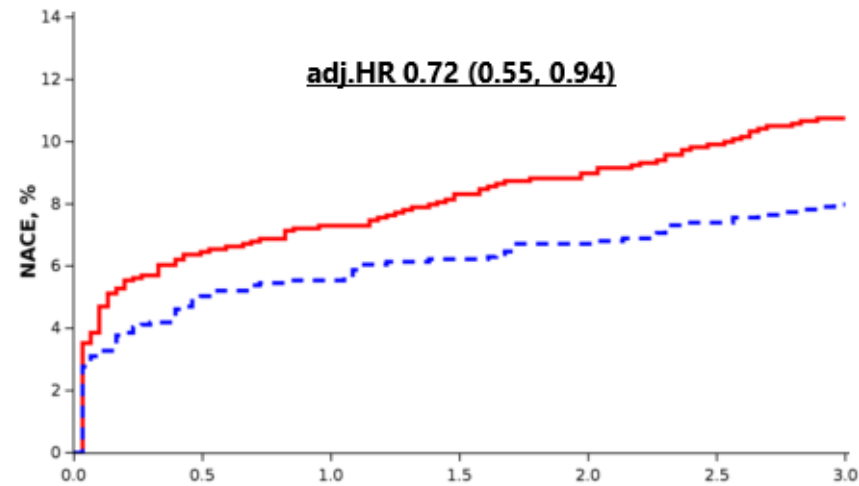


IPD-Meta-analyses are the highest level of evidence

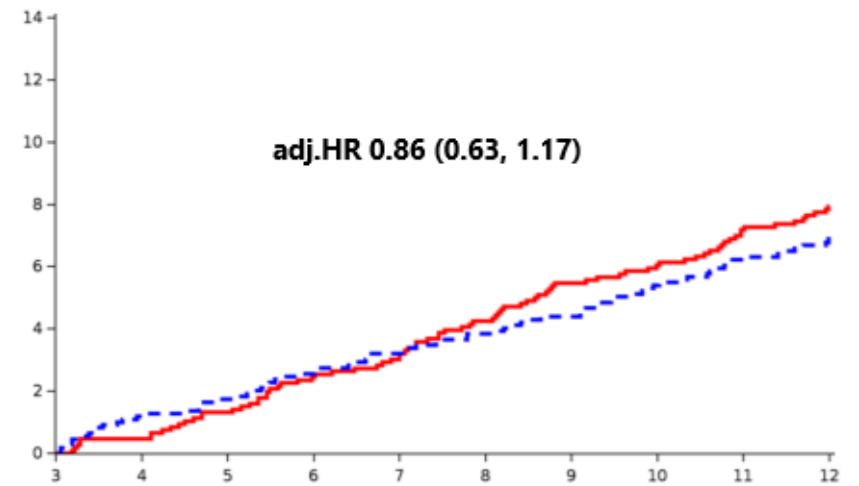
- IPD-MA of POPular Genetics and TAILOR-PCI
- Only ACS patients without AF
- TOT= 6,734 patients

De-escalation

0-3 months



3-12 months



Overview of supporting evidence

YES

BUT

**RCTs meeting their primary endpoints
(NEJM 2019 and JAMA 2020)**



- Non-inferiority design
- Primary endpoint including both ischemic and bleeding outcomes
- Low statistical power for hard endpoints



Study level meta-analysis (Lancet 2021)



- High baseline heterogeneity
- Pivotal RCTs provide more solid evidence



Network meta-analysis (EHJ 2022)



- Evidence from indirect comparisons is weak



**Patient-level meta-analysis
(JACC Cardio Int 2026)**



????????????????

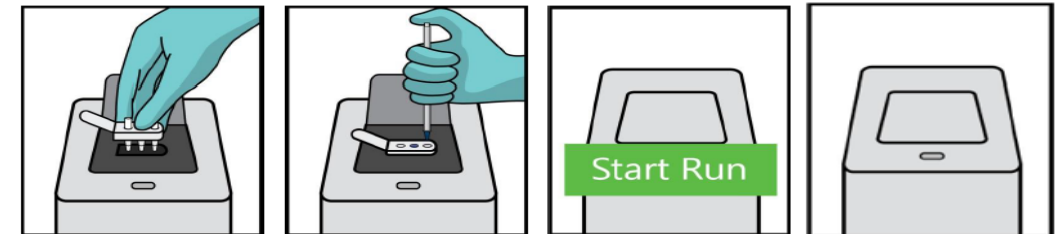
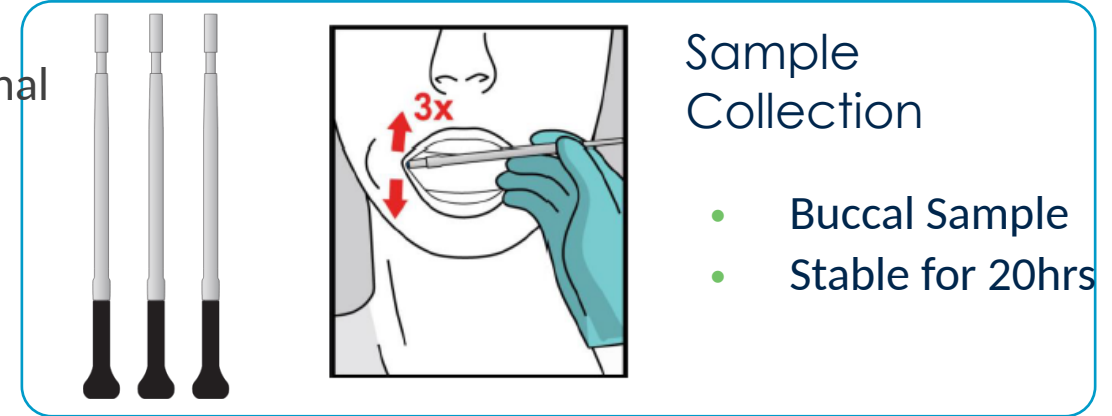
4. Availability of rapid and easy to use tools

Fast

- ~1 hour turnaround time
- Direct PCR results
- Alleles *1, *2, *3, and *17

Accurate

- 99.1% accuracy vs. bidirectional sequencing
- Irreversible tube sealing prevents contamination





2023 European GL

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

2025 North American GL

COR	LOE	Recommendations
Default Duration of DAPT		
1	A	1. In patients with ACS who are not at high bleeding risk, DAPT with aspirin and an oral P2Y ₁₂ inhibitor should be administered for at least 1 year to reduce MACE. ^{1–6}
Bleeding Reduction Strategies		
1	A	2. In patients with ACS who have tolerated DAPT with ticagrelor, transition to ticagrelor monotherapy ≥1 month post PCI is useful to reduce bleeding risk. ^{7–11}
1	A	3. In patients at high risk of gastrointestinal bleeding, a proton pump inhibitor (PPI) is recommended in combination with DAPT, oral anti-coagulants, or both to reduce risk of bleeding. ^{12–15}
2b	B-R	4. In patients with ACS undergoing PCI, de-escalation of DAPT (switching from ticagrelor or prasugrel to clopidogrel) after 1 month may be reasonable to reduce bleeding risk. ^{16–20}
2b	B-R	5. In patients with ACS undergoing PCI who are at high bleeding risk, transition to single antiplatelet therapy (aspirin or P2Y ₁₂ inhibitor) after 1 month may be reasonable to reduce bleeding risk. ²¹

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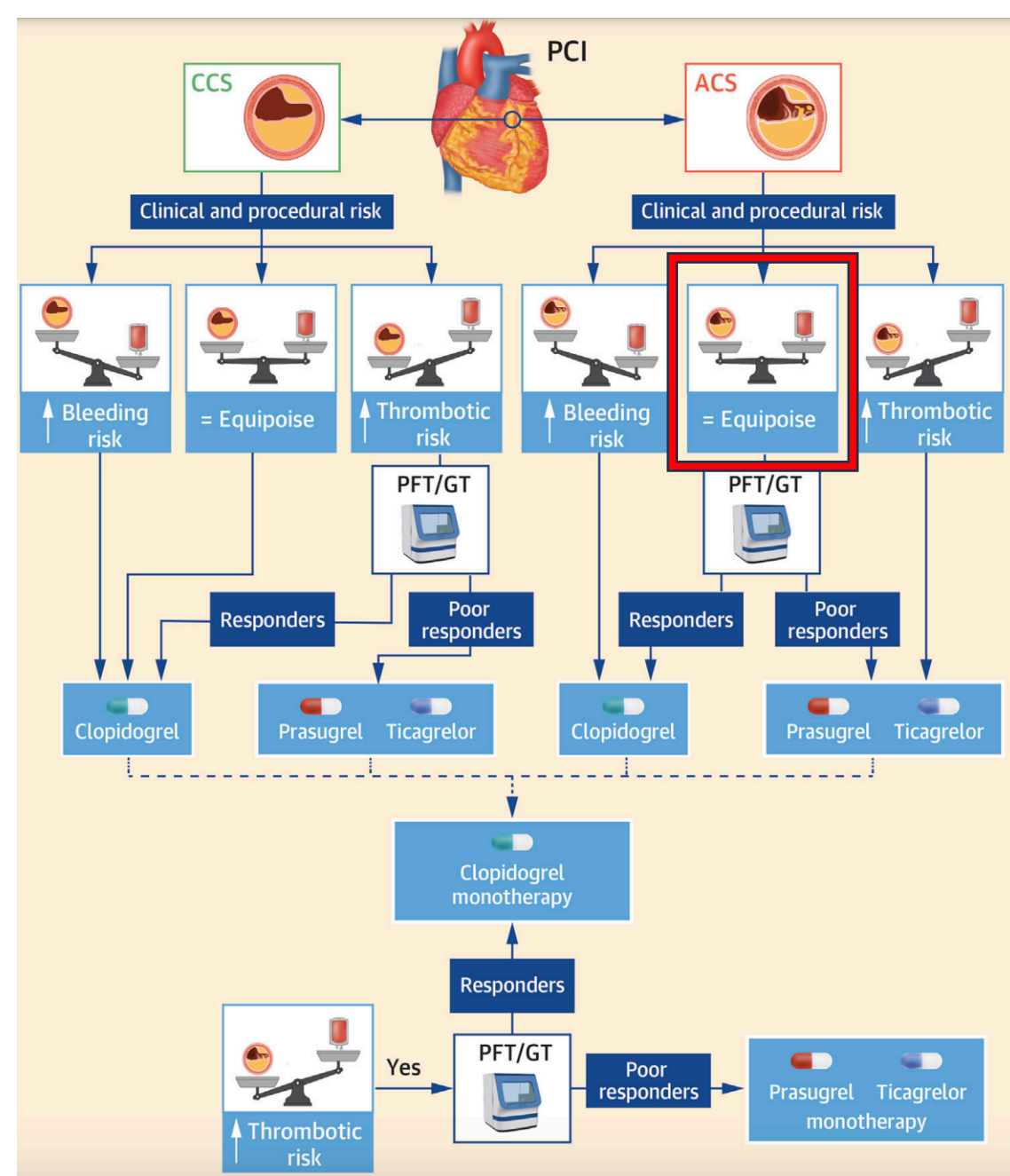
CYP2C19 Genetic Testing for Oral P2Y12 Inhibitor Therapy: A Scientific Statement From the American Heart Association

Naveen L. Pereira, MD, FAHA, Chair, Sharon Cresci, MD, FAHA, Vice Chair, Dominick J. Angiolillo, MD, PhD, Wayne Batchelor, MD, MHS, Quinn
Capers IV, MD, Larisa H. Cavallari, PharmD, Dana Leifer, MD, FAHA, Jasmine A. Luzum, PharmD, PhD, FAHA, Dan M. Roden, MD, FAHA,
Konstantinos Stellos, MD, FAHA, Stephanie L. Turrise, PhD, RN, FAHA, and Sony Tuteja, PharmD, MS, FAHA on behalf of the American Heart
Association Professional/Public Education and Publications Committee of the Council on Genomic and Precision Medicine; Council on
Arteriosclerosis, Thrombosis and Vascular Biology; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on
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International Consensus Statement on Platelet Function and Genetic Testing in Percutaneous Coronary Intervention

2024 Update

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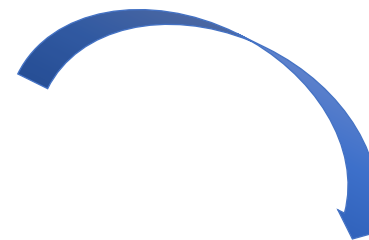


1) Clopidogrel monotherapy

a) after short course of DAPT;

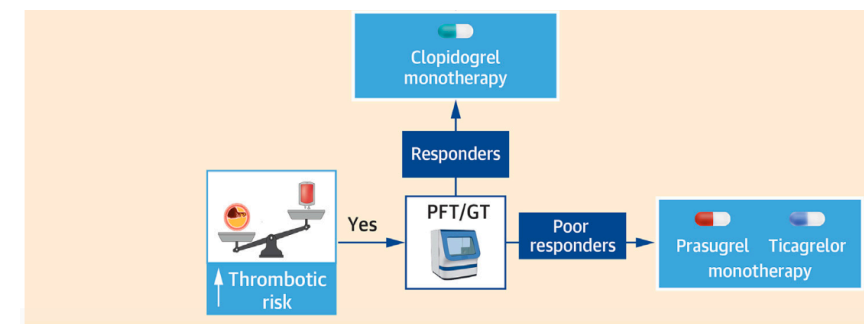
b) long term therapy (also in PAD and stroke patients);

c) DAT with clopidogrel in those with concomitant OAC



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IS ASPIRIN BETTER THAN CLOPIDOGREL?



ESC

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META-ANALYSIS

Thrombosis and antithrombotic treatment

Aspirin vs clopidogrel in chronic coronary syndromes: a meta-analysis of ethnic differences

Claudio Laudani ^{1,2}, Giovanni Occhipinti ³, Francesco Costa ^{4,5}, Domenico D'Amario⁶,
Tullio Palmerini ^{7,8}, Sebastiano Sciarretta^{9,10}, Charles Michael Gibson ¹¹,
Behnood Bikdeli ^{12,13,14,15}, Felicita Andreotti ^{16,17}, Young-Hoon Jeong ^{18,19},
Takeshi Kimura ²⁰, Diana A. Gorog ^{21,22}, Dirk Sibbing ^{23,24,25}, Davide Capodanno ²,
Jurrien ten Berg ²⁶, Raffaele De Caterina ²⁷, and Mattia Galli ^{9,28,*}

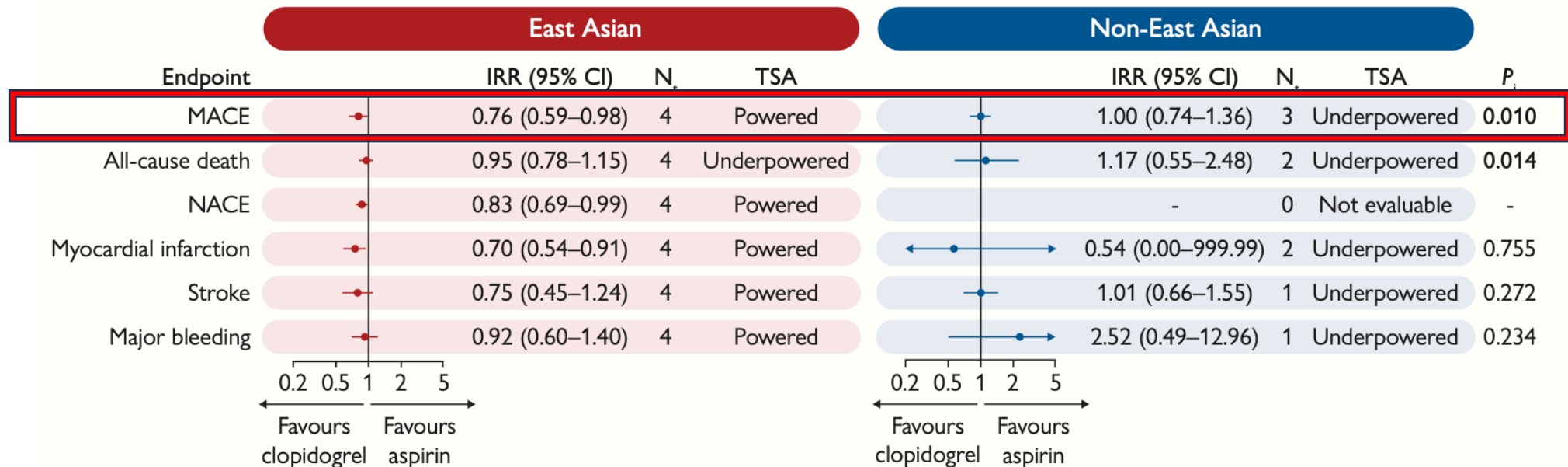
IS ASPIRIN BETTER THAN CLOPIDOGREL?

Random-effect meta-analysis from 7 trials encompassing 30 165 patients

Timeline of included studies



Subgroup analysis according to region of enrolment



Conclusions

- **Elderly patients are characterized by increased bleeding but also thrombotic risk.**
- **Bleeding reduction strategies may be implemented pre-, intra- or post-procedurally.**
- **Clinical judgment and common sense remain paramount and should prevail over risk scores. The goal is to provide the necessary treatment while avoiding overtreatment and the risk of potentially serious adverse events.**
- **Antithrombotic therapy should be intensive during the early high-risk phase and progressively de-escalated thereafter.**
- **Guided strategies are the only approach that can reduce bleeding risk from the early phase after ACS.**

Thanks