When Enough is Enough: Redefining the Optimal Duration of Dual Antiplatelet Therapy

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DISCLOSURE

I have no potential conflicts of interest to disclose.

Learning Objectives

- Discuss current recommendations for duration of dual antiplatelet therapy.
- Compare and contrast shortened (<6 months) vs long (≥12 months) durations of dual antiplatelet therapy.
- Develop a construct for evaluating ischemic and bleeding risk during dual antiplatelet therapy.
- Recommend a duration of dual antiplatelet therapy for a given patient case based on ischemic and bleeding risks.

CASE

WW is a 59 y/o Asian F who presented to the hospital with chest pain found to have NSTEMI now s/p PCI with DES (Xience [everolimus eluting stent]) to the L circumflex placed on dual antiplatelet therapy with aspirin and ticagrelor.

- PMH: HTN, NIDDM, iron deficiency anemia
- Objective data:
  - Ht: 5'6" Wt: 60kg BMI: 21.3 kg/m^2
  - BP 127/72 mmHg HR 75 RR 14 T 37.1^{o}C

Na	142
K	4.1
Cl	103
CO2	24
BUN	21
SCr	1.1
Glu	223

WBC	8.2
Hgb	11.2
Hct	34.3
Plt	278
Trop (initial)	1.42

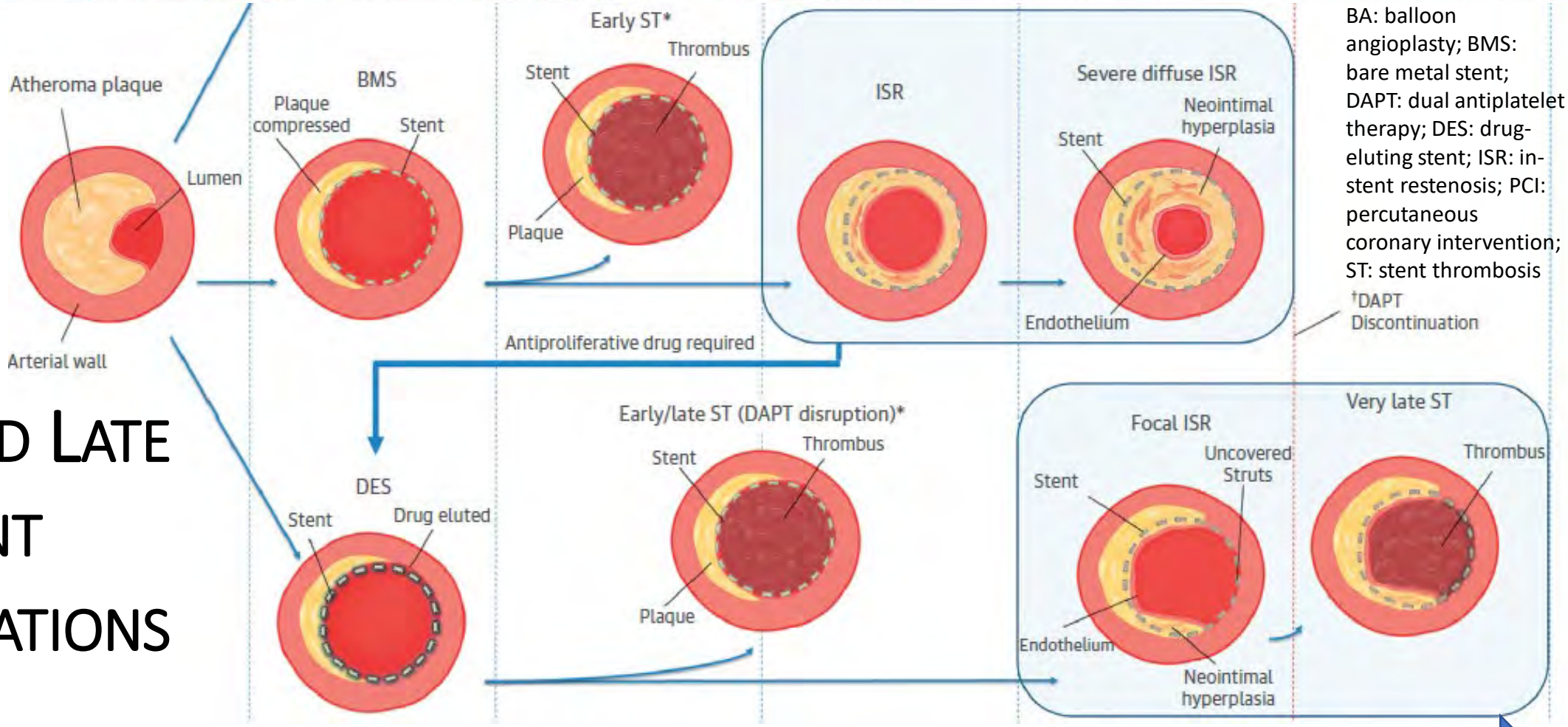
WW is worried about bleeding as her friend had a GI bleed while on dual antiplatelet therapy. Is she an appropriate candidate for shortened duration of therapy?

Dual Antiplatelet Therapy

- Dual antiplatelet therapy (DAPT) consists of aspirin and a second antiplatelet, typically a P2Y12 inhibitor
- Vital in treatment of coronary disease:
  - Acute coronary syndromes (ACS) treated with percutaneous coronary intervention (PCI) with stent placement
  - Medically managed ACS
  - Stable ischemic heart disease (SIHD) treated with PCI with stent placement
- Reduces ischemic complications after PCI with stenting

1. Levine GN, et al. *J Am Coll Cardiol* 2016; 68:1082-115.
2. Valgimigli M, et al. *Eur J Cardiothorac Surg* 2018; 53:34-78

Early and Late Stent Complications



BA: balloon angioplasty; BMS: bare metal stent; DAPT: dual antiplatelet therapy; DES: drug-eluting stent; ISR: in-stent restenosis; PCI: percutaneous coronary intervention; ST: stent thrombosis

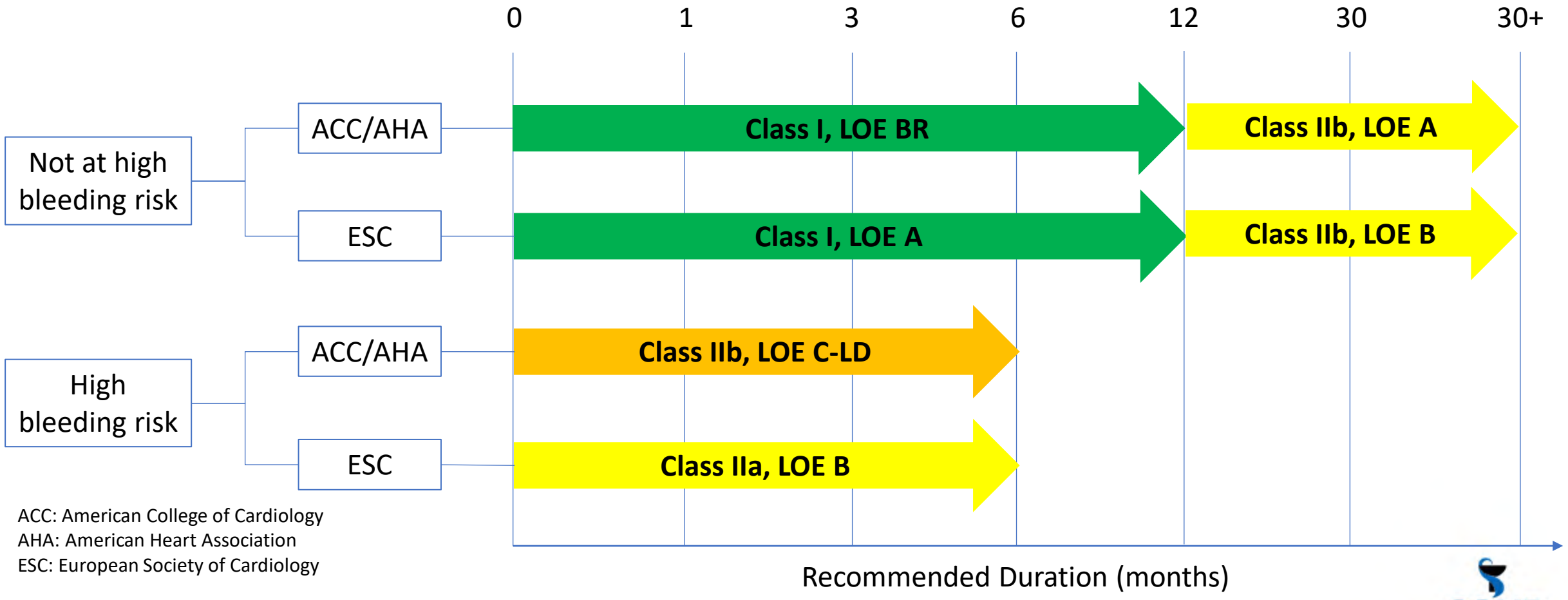
3. Torrado J, et al. *J Am Coll Cardiol* 2018; 71:1676-95.

Benefit of Long Term DAPT

- DAPT reduces major adverse cardiovascular events (MACE), particularly stent thrombosis (ST), but increases risk of bleeding
  - Continue for as long as ischemic benefits outweigh bleeding risks
- Many default to 12 months, but one size may not fit all

1. Levine GN, et al. *J Am Coll Cardiol* 2016; 68:1082-115.
2. Valgimigli M, et al. *Eur J Cardiothorac Surg* 2018; 53:34-78

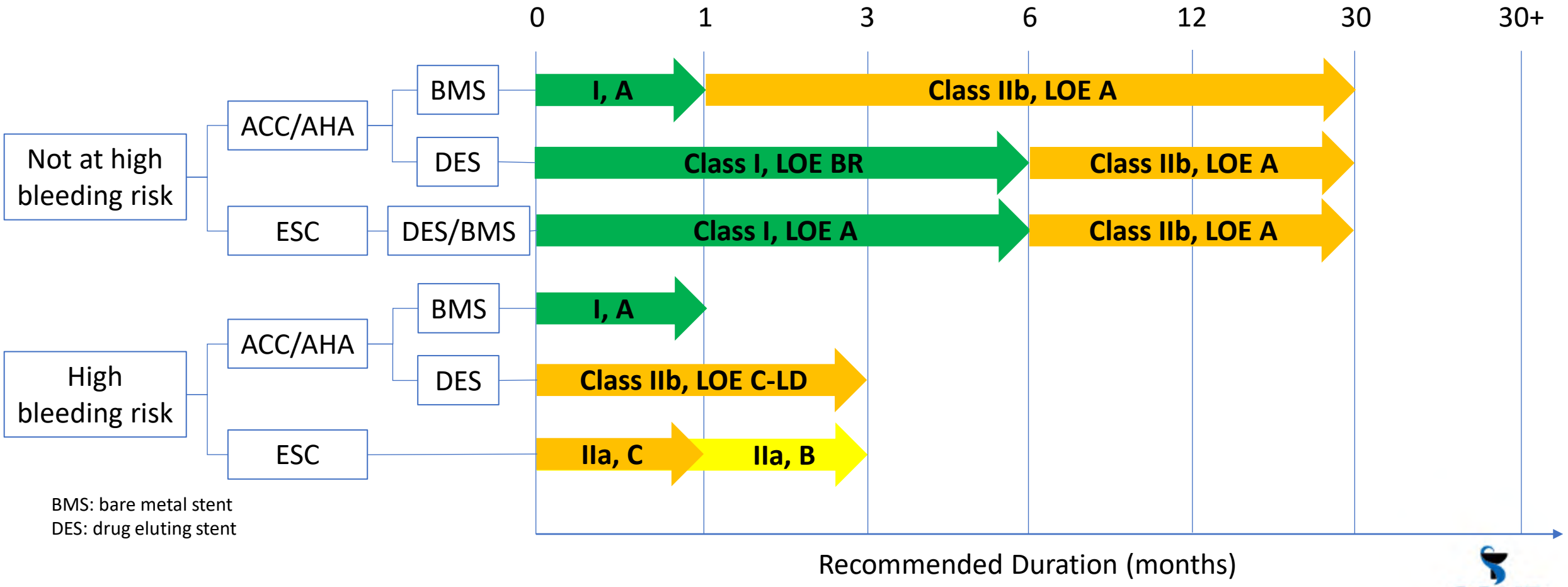
DURATION OF DAPT AFTER PCI FOR ACS



ACC: American College of Cardiology
AHA: American Heart Association
ESC: European Society of Cardiology

1. Levine GN, et al. *J Am Coll Cardiol* 2016; 68:1082-115.
2. Valgimigli M, et al. *Eur J Cardiothorac Surg* 2018; 53:34-78
4. Capodanno D, et al. *J Am Coll Cardiol* 2018; 72:2915-31.

DURATION OF DAPT AFTER PCI FOR SIHD



BMS: bare metal stent
DES: drug eluting stent

1. Levine GN, et al. *J Am Coll Cardiol* 2016; 68:1082-115.
2. Valgimigli M, et al. *Eur J Cardiothorac Surg* 2018; 53:34-78
4. Capodanno D, et al. *J Am Coll Cardiol* 2018; 72:2915-31.

But Why 12 Months?

- Early standard of care with DAPT initially set at 4 weeks
- Seminal PCI-CURE study demonstrated ≤12 months of clopidogrel in addition to aspirin reduced cardiovascular death and MI
  - Further supported by CREDO study

- Notably, these early studies were conducted before the introduction of drug-eluting stents (DES)
  - Stent type impacts risk of in-stent restenosis (ISR) and stent thrombosis

5. Mehta SR, et al. *Lancet* 2001; 358:527-33.
6. Steinhubl SR, et al. *JAMA* 2002; 288:2411-20.

Evolution of Stents

BMS

First BMS implanted in 1986

↓restenosis rates: 20% - 30% at 12 months

1st Generation DES

Introduced in 2003 – 2004

↓ ISR: 5% - 15% at 12 months

↑ late and very late ST

2nd Generation DES

Introduced 2008

↓ ISR: ≤5% at 12 months

↓ late and very late ST

3. Torrado J, et al. *J Am Coll Cardiol* 2018; 71:1676-95.

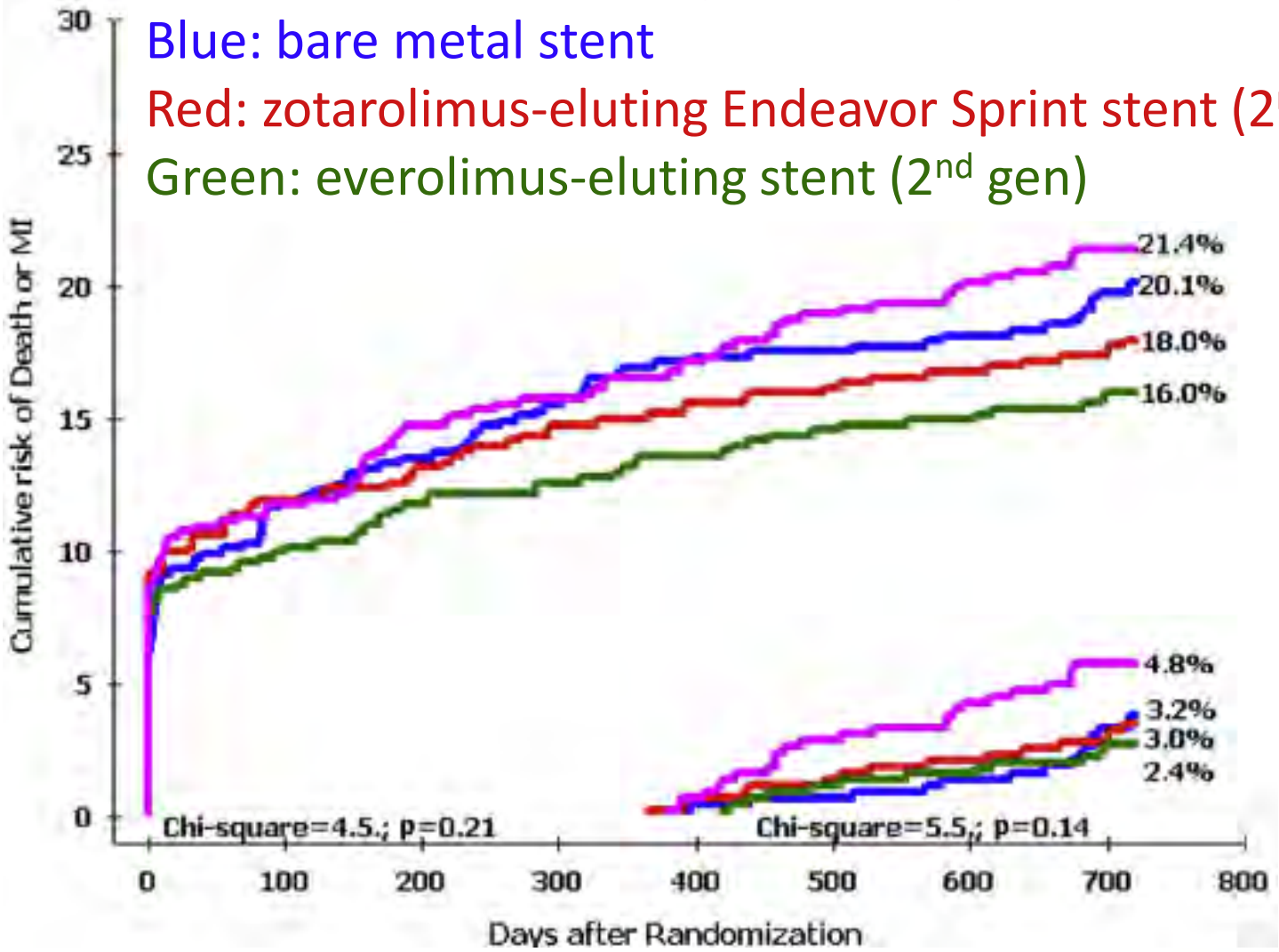
Cumulative Risk of Death or MI Among Different Stents

Purple: paclitaxel-eluting stent (1st gen)

Blue: bare metal stent

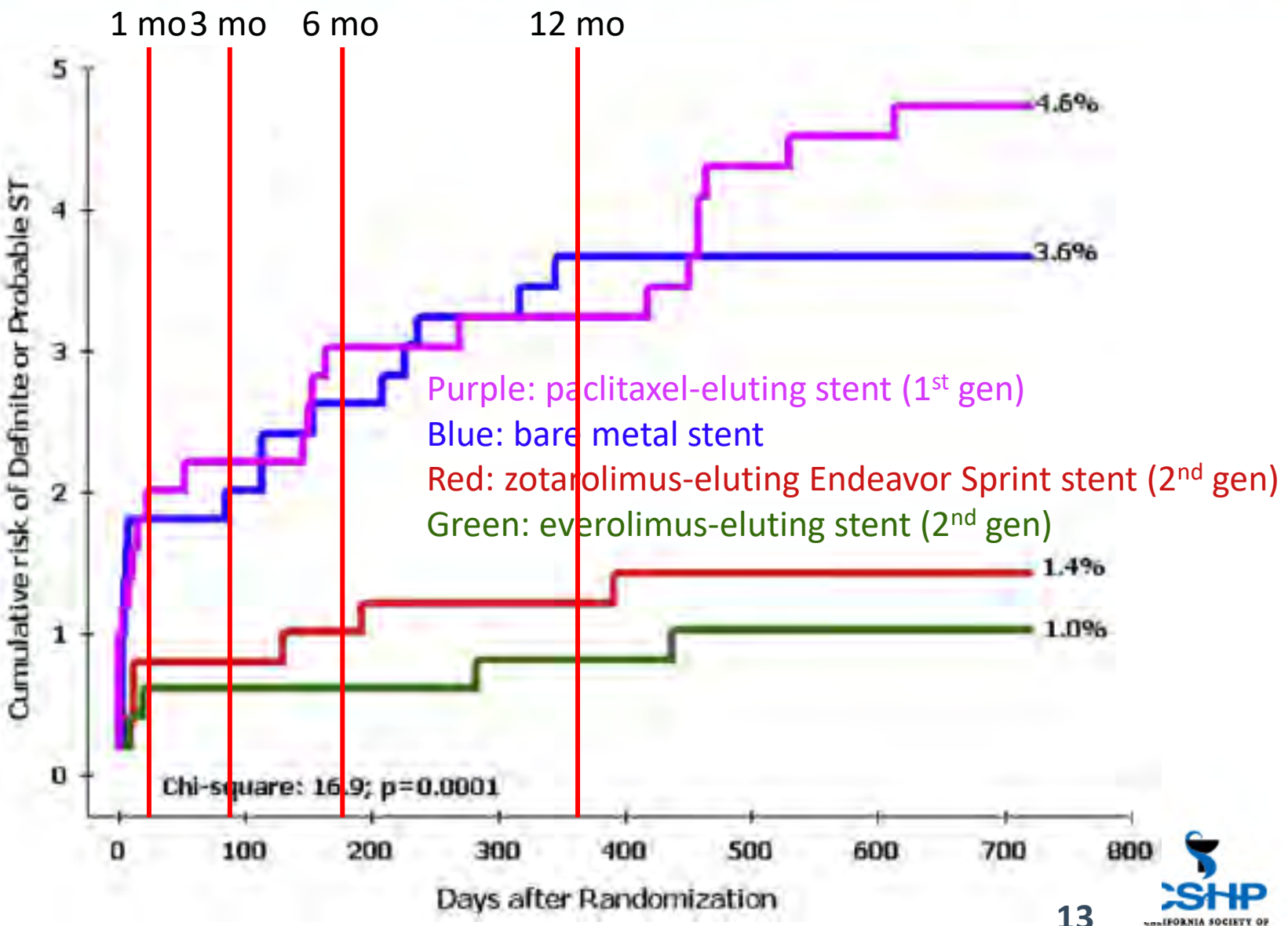
Red: zotarolimus-eluting Endeavor Sprint stent (2nd gen)

Green: everolimus-eluting stent (2nd gen)



7. Valgimigli M, et al. *JACC Cardiovasc Interv* 2014; 7:20-8.

Cumulative Risk of Definite or Probable ST Among Different Stents



7. Valgimigli M, et al. *JACC Cardiovasc Interv* 2014; 7:20-8.

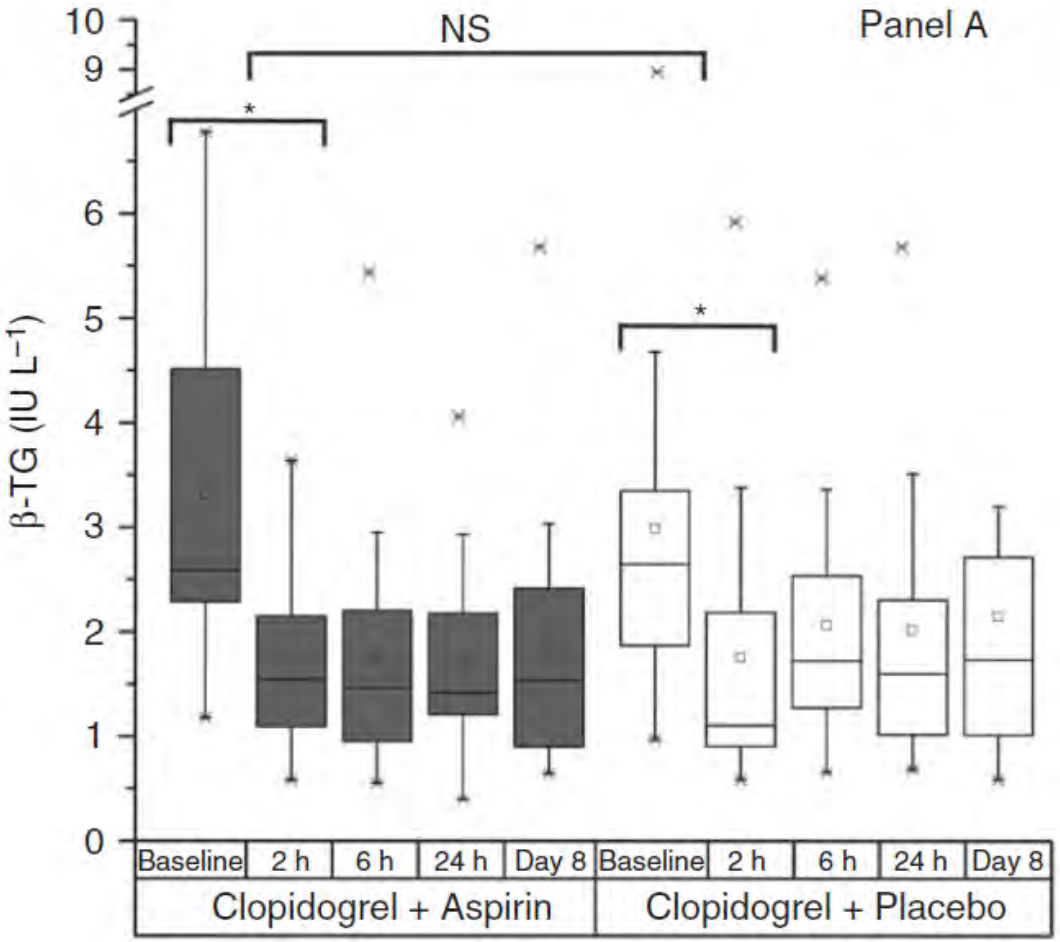
THE CASE FOR SHORTENED DAPT

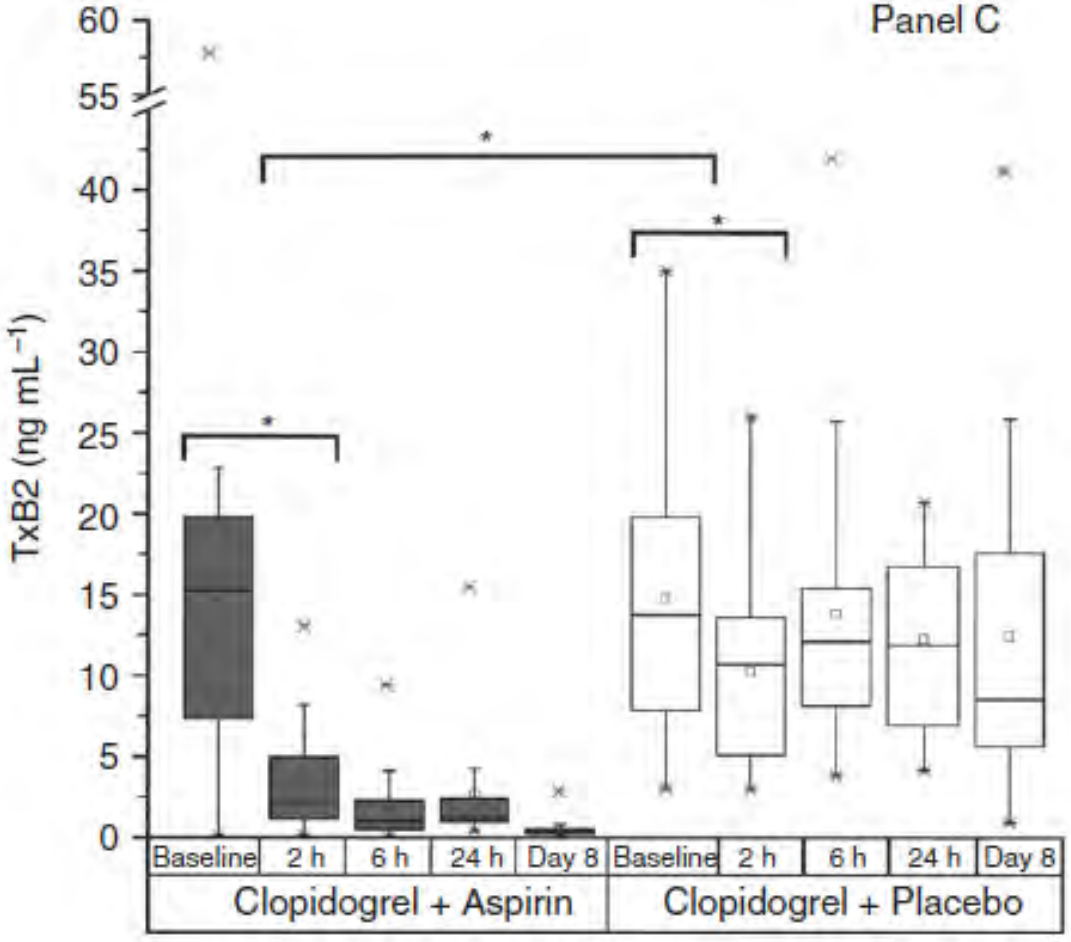
- Given lower rates of ST with newer generation stents, 12 months may not best balance ischemic and bleeding risks in every patient

- Earlier studies suggest shortened DAPT (≤6 mo) followed by aspirin monotherapy reduces bleeding at the expense of increased MI/ST
  - Is aspirin or the P2Y12 inhibitor more important for preventing ST?
  - Is this treatment effect seen with P2Y12 inhibitor monotherapy?
  - Does a reduction in bleeding justify a potential increase in cardiovascular events?

8. Palmerini T, et al. *Lancet* 2015; 385:2371-82.

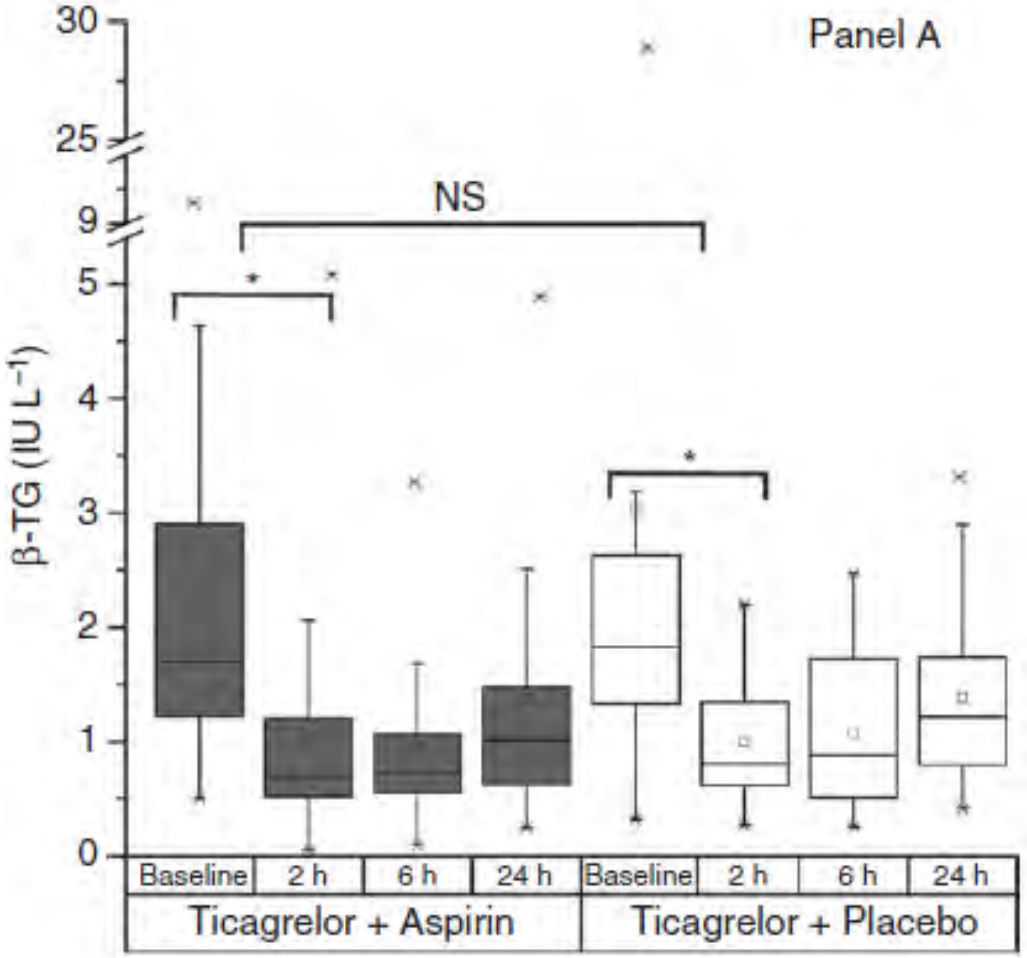
LIMITED EFFECT OF ADDED ASPIRIN

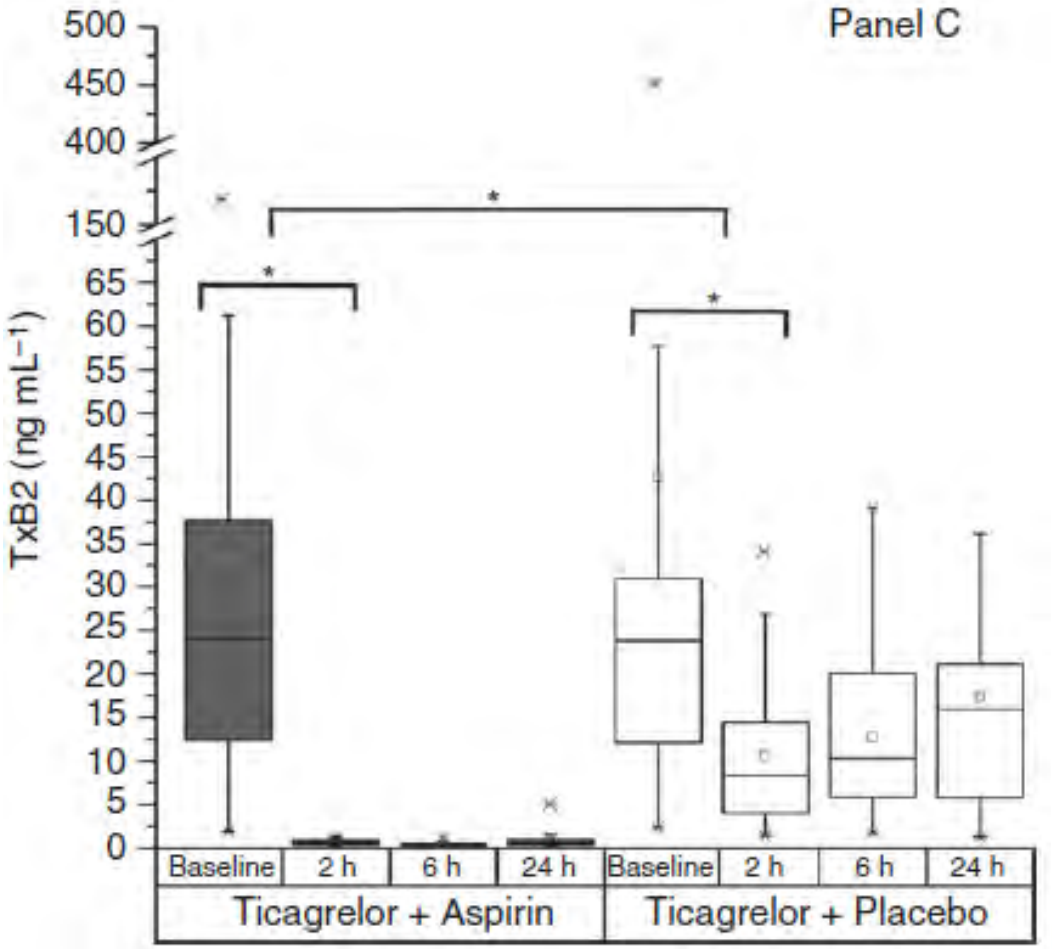




9. Traby L, et al. *J Thromb Haemost* 2016; 14:273-81.

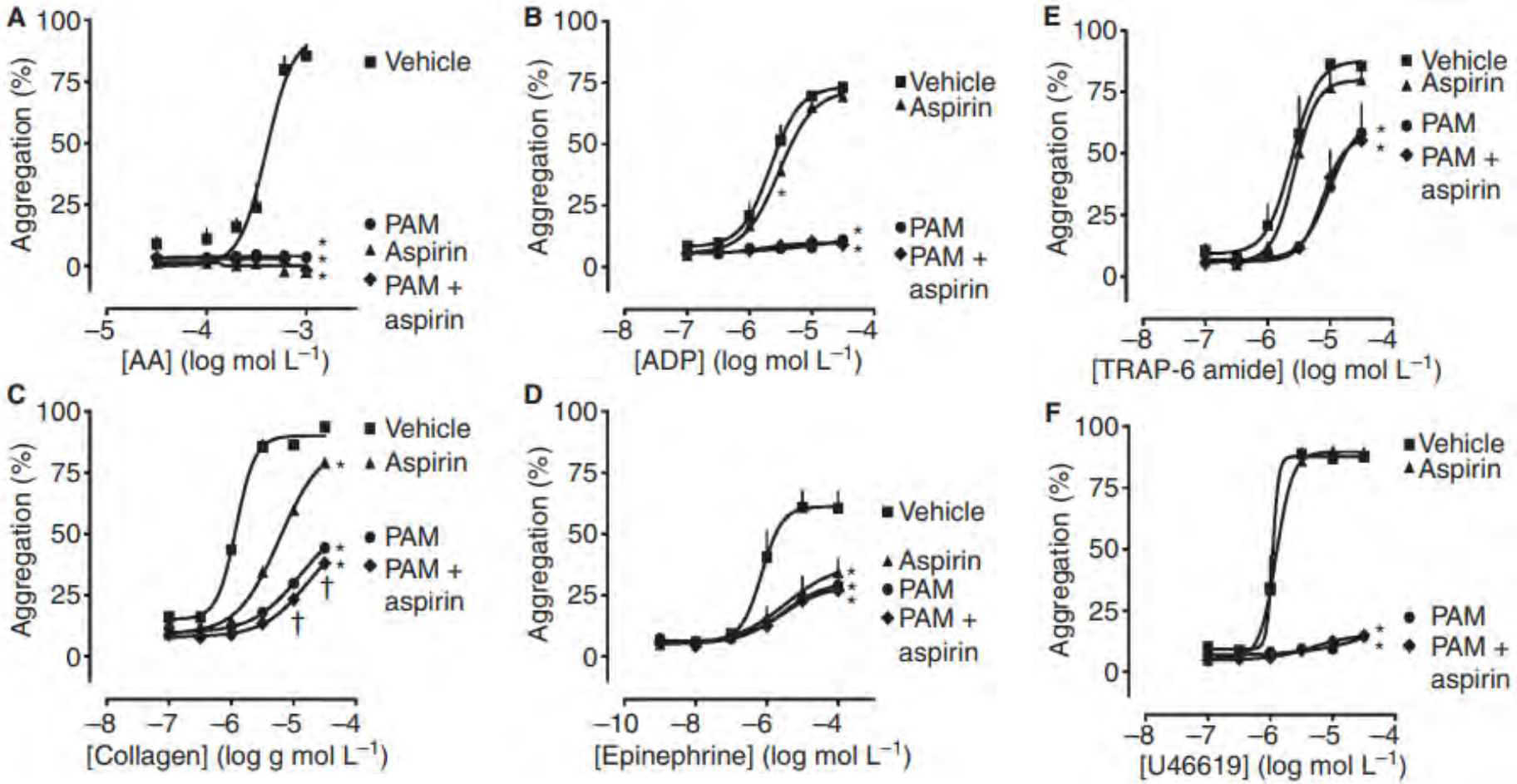
LIMITED EFFECT OF ADDED ASPIRIN





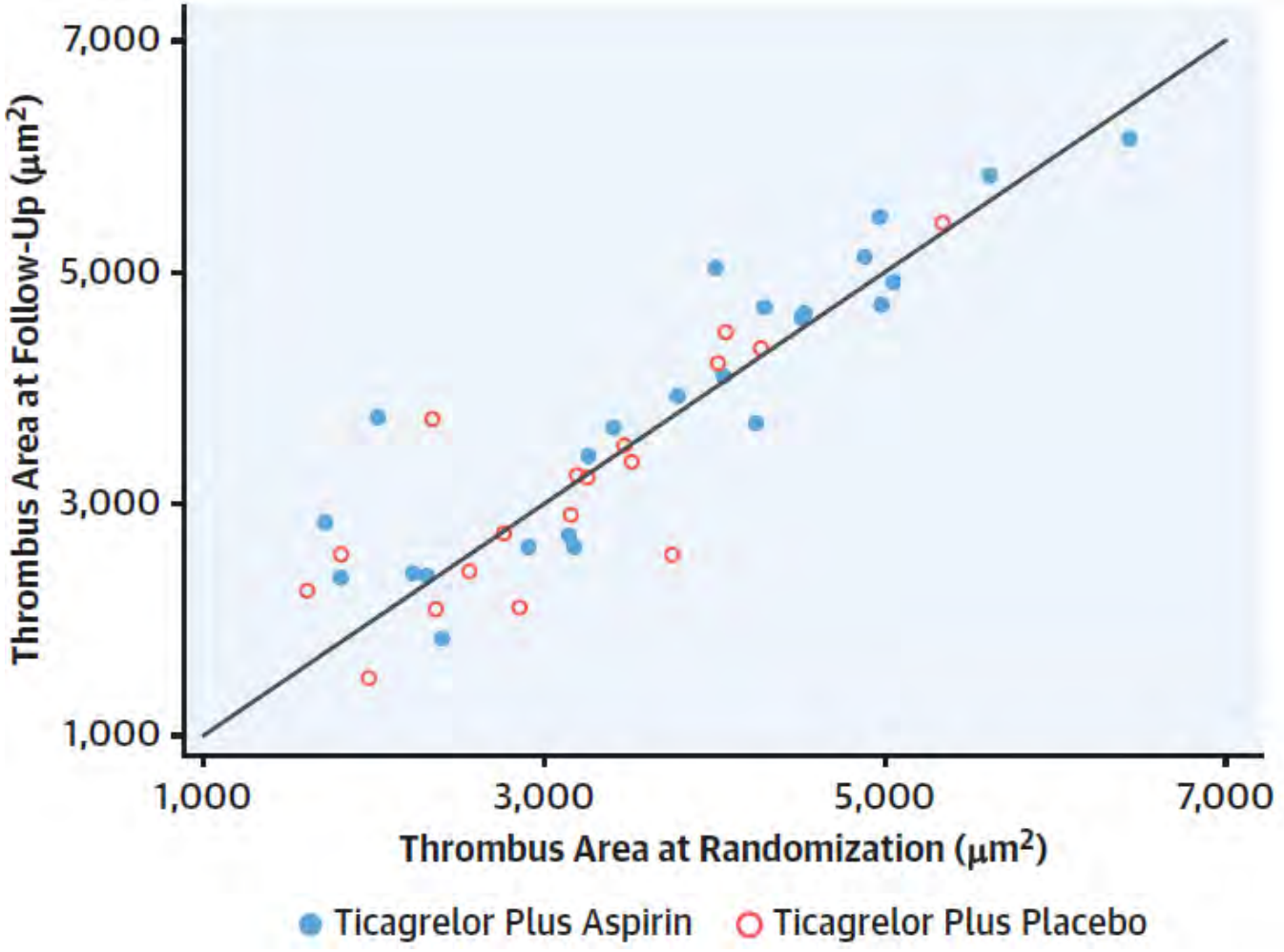
9. Traby L, et al. *J Thromb Haemost* 2016; 14:273-81.

LIMITED EFFECT OF ADDED ASPIRIN



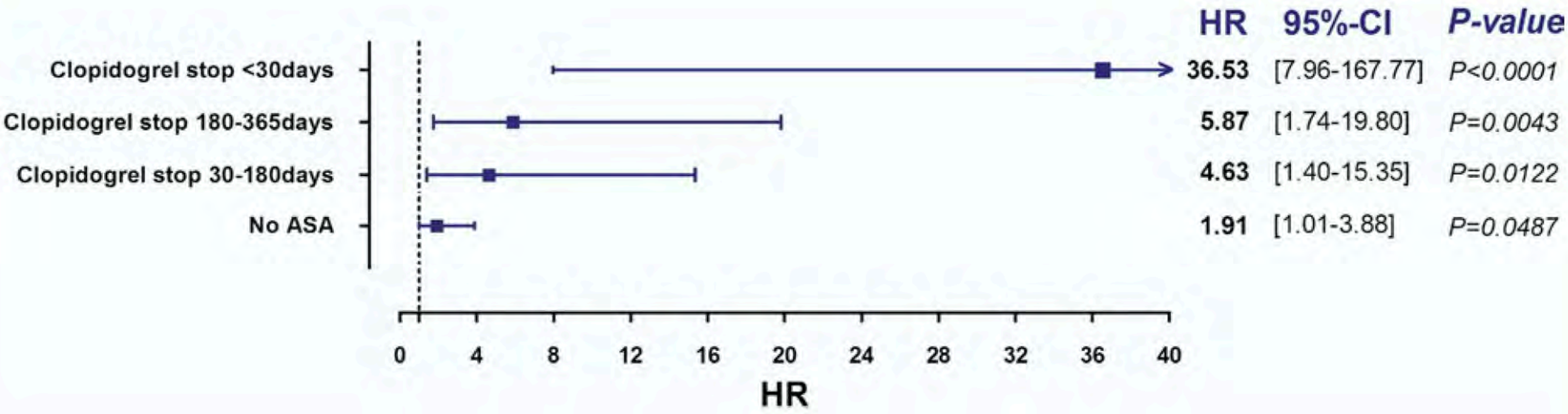
10. Armstrong PCJ, et al. *J Thromb Haemost* 2011; 9:552-61.

ASPIRIN DOESN'T IMPROVE THROMBUS RESOLUTION



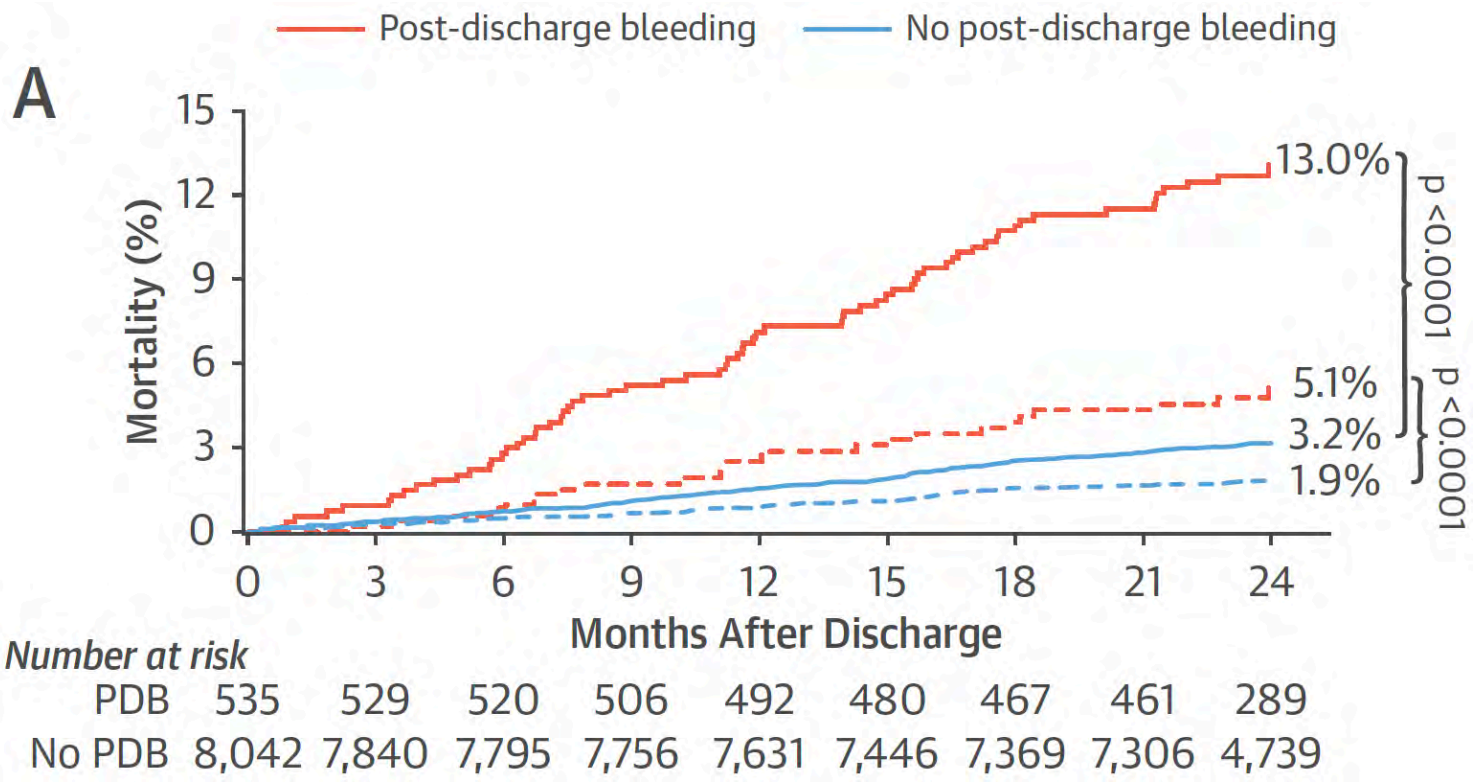
11. Baber U, et al. *J Am Coll Cardiol* 2020; 75:578-86.

CLOPIDOGREL DISCONTINUATION PREDICTS ST



12. van Werkum JW, et al. *J Am Coll Cardiol* 2009; 53:1399-409.

PICK YOUR POISON: BLEEDING OR ISCHEMIA



PDB: post-discharge bleeding
PDMI: post-discharge myocardial infarction

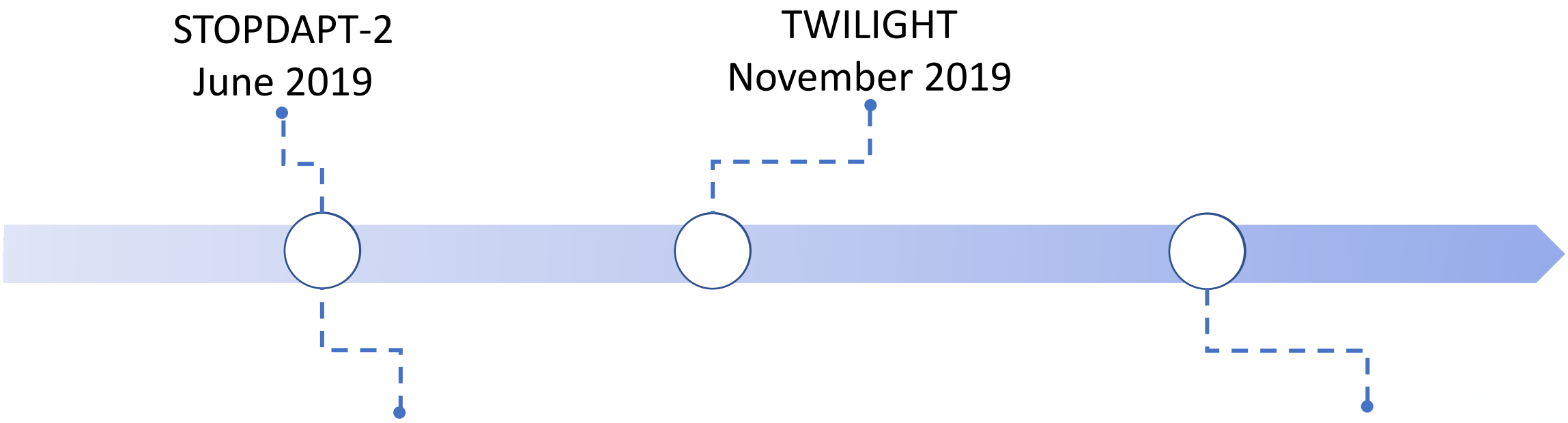
Independent Predictors of All-Cause Mortality

Variable	Adjusted HR (95% CI)	p value
PDB	5.03 (3.29 – 7.66)	<0.0001
PDMI	1.92 (1.18 – 3.12)	0.009

PDB had ~2.6-fold greater effect on all-cause mortality compared to PDMI

13. Genereux P, et al. *J Am Coll Cardiol* 2015; 66:1036-45.

Literature Updates



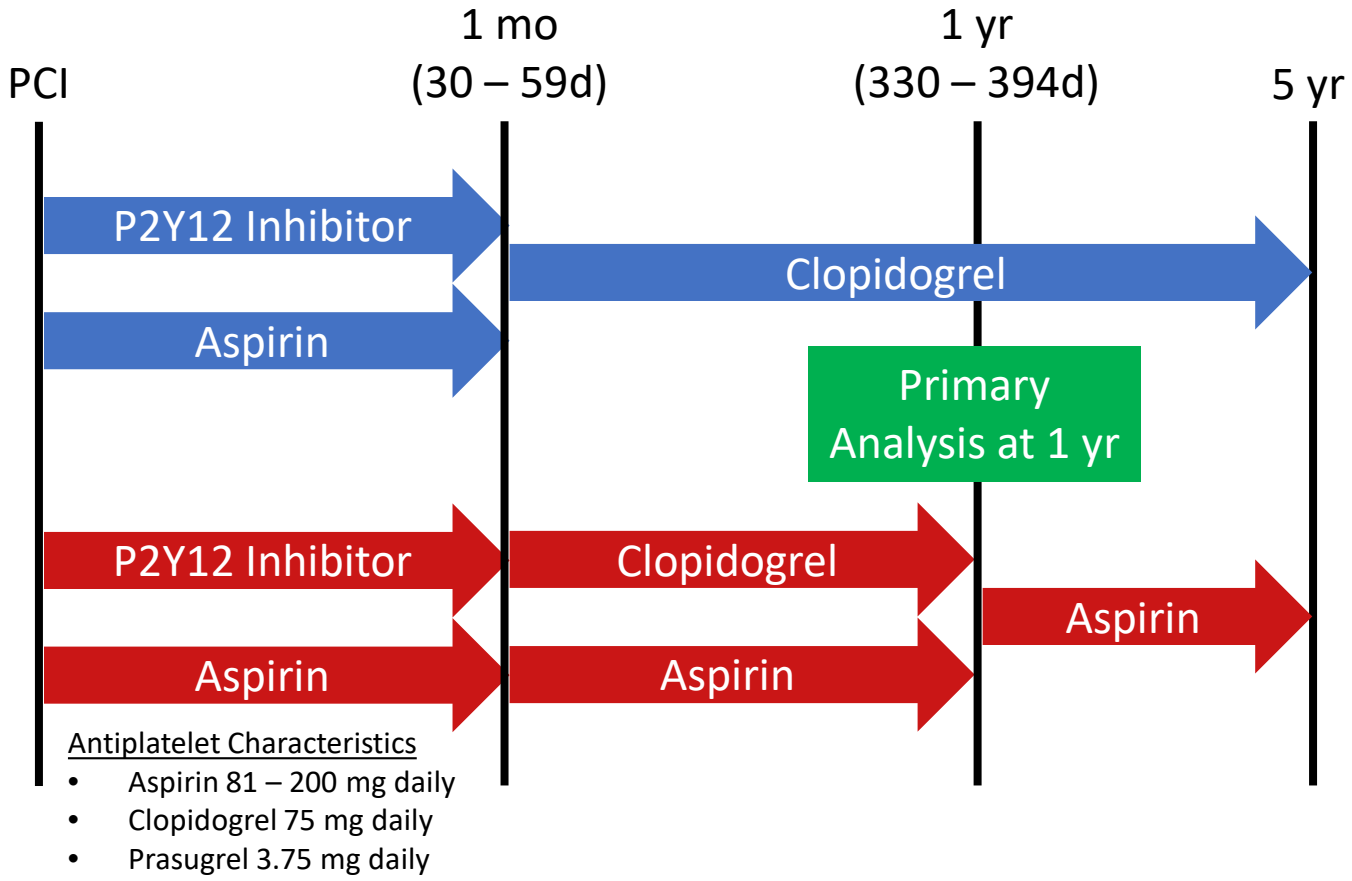
14. Watanabe H, et al. *JAMA* 2019; 321:2414-27.
15. Hahn, JY, et al. *JAMA* 2019; 321:2428-37.
16. Mehran R, et al. *N Engl J Med* 2019; 381:2032-42.
17. Kim BK, et al. *JAMA* 2020; 323:2407-16.

Definitions of Bleeding Outcomes

TIMI	BARC	GUSTO
Major bleeding: • Intracranial bleeding • Clinically overt hemorrhage with >5 g/dL decrease in Hgb • Fatal bleeding (within 7d) Minor bleeding: • Clinically overt hemorrhage with 3 to <5 g/dL decrease in Hgb • Any clinically overt hemorrhage not meeting above criteria but requiring medical intervention	Type 3a: • Overt bleeding with Hgb drop between 3 – 5 g/dL (a) • Overt bleeding with Hgb drop >5 g/dL (b) • Cardiac tamponade (b) • Bleeding requiring surgical intervention and/or vasoactive drugs (b) • Intracranial or intraocular (c) Type 5: • Fatal	Severe or life-threatening: • Intracranial bleeding • Bleeding leading to hemodynamic compromise requiring treatment Moderate: • Bleeding requiring blood transfusion but not leading to hemodynamic compromise

14. Watanabe H, et al. *JAMA* 2019; 321:2414-27.
15. Hahn, JY, et al. *JAMA* 2019; 321:2428-37.
16. Mehran R, et al. *N Engl J Med* 2019; 381:2032-42.
17. Kim BK, et al. *JAMA* 2020; 323:2407-16.

STOPDAPT-2: Overview



Antiplatelet Characteristics

- Aspirin 81 – 200 mg daily
- Clopidogrel 75 mg daily
- Prasugrel 3.75 mg daily

Characteristics	1-Month DAPT (n = 1500)	12-Month DAPT (n = 1509)
ACS, no. (%)	565 (37.7)	583 (38.6)
STEMI	291 (19.4)	270 (17.9)
NSTEMI	81 (5.4)	99 (6.6)
UA	193 (12.9)	214 (14.2)
SIHD, no. (%)	935 (62.3)	926 (61.4)
Medications at Discharge, no. (%)		
Aspirin	1497 (99.8)	1509 (100)
P2Y12 Inhibitor	1499 (99.9)	1508 (99.9)
Clopidogrel	903 (60.2)	949 (62.9)
Prasugrel	594 (39.6)	557 (37.0)
Anticoagulants	7 (0.5)	6 (0.4)
Statin	1318 (87.9)	1318 (87.3)
PPI	1190 (79.3)	1193 (79.1)

14. Watanabe H, et al. *JAMA* 2019; 321:2414-27.

STOPDAPT-2: Ischemic and Bleeding Risks

Thrombotic Risk Scores

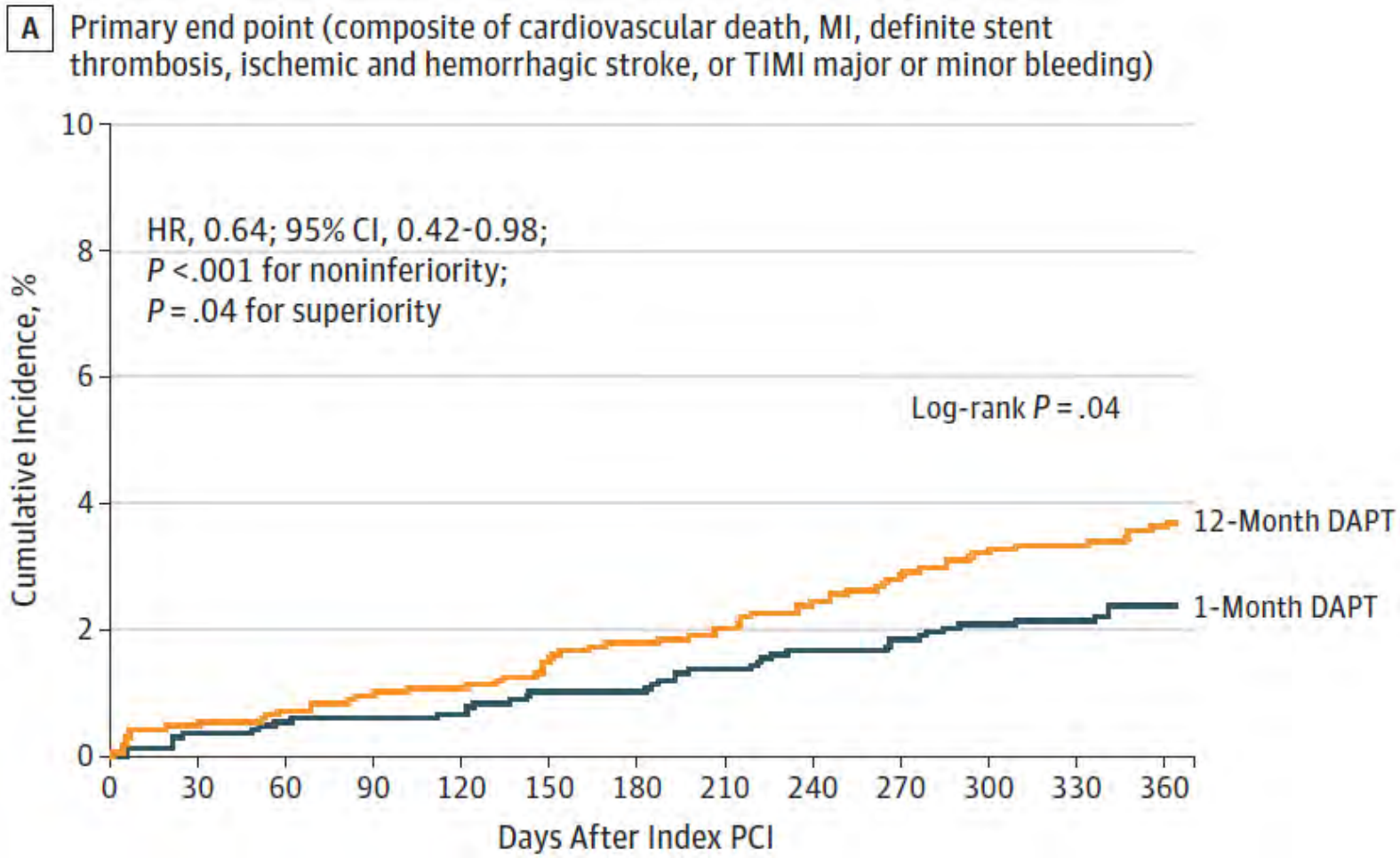
Risk Score	1-Month DAPT (n = 1500)	12-Month DAPT (n = 1509)
PARIS, median (IQR)	3 (1-4)	2 (2-4)
High (≥5), no. (%)	211 (14.1)	215 (14.3)
Intermediate (3-4), no. (%)	560 (37.3)	536 (35.5)
Low (0-2), no. (%)	729 (48.6)	758 (50.2)
CREDO-Kyoto, median (IQR)	1 (0-2)	1 (0-2)
High (≥4), no. (%)	113 (7.5)	122 (8.1)
Intermediate (2-3), no. (%)	318 (21.2)	358 (23.7)
Low (0-1), no. (%)	1069 (71.3)	1029 (68.2)

Bleeding Risk Scores

Risk Score	1-Month DAPT (n = 1500)	12-Month DAPT (n = 1509)
PARIS, median (IQR)	5 (3-7)	5 (3-7)
High (≥8), no. (%)	302 (20.1)	291 (19.3)
Intermediate (4-7), no. (%)	757 (50.5)	801 (53.1)
Low (0-3), no. (%)	441 (29.4)	417 (27.6)
CREDO-Kyoto, median (IQR)	0 (0-1)	0 (0-1)
High (≥3), no. (%)	106 (7.1)	112 (7.4)
Intermediate (1-2), no. (%)	398 (26.5)	401 (26.6)
Low (0), no. (%)	996 (66.4)	996 (66.0)

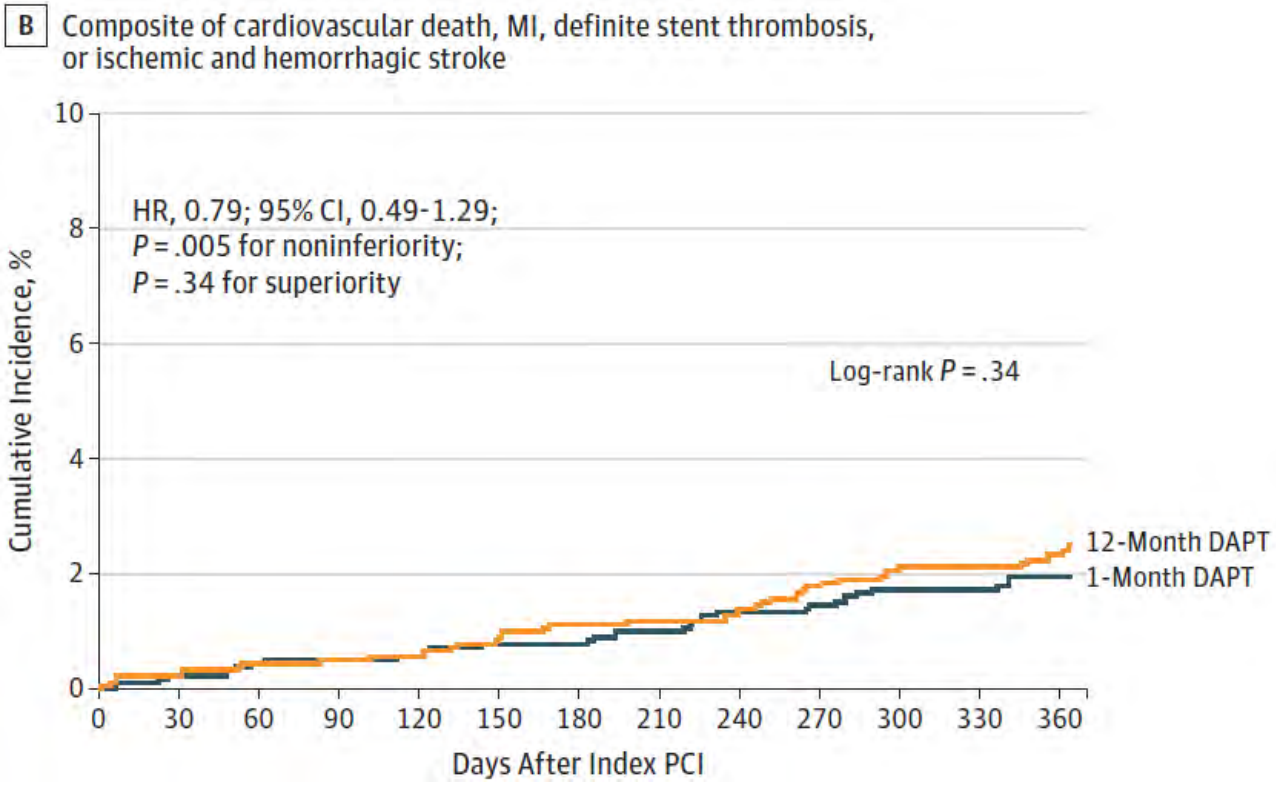
14. Watanabe H, et al. *JAMA* 2019; 321:2414-27.

STOPDAPT-2: PRIMARY ENDPOINT RESULTS



14. Watanabe H, et al. *JAMA* 2019; 321:2414-27.

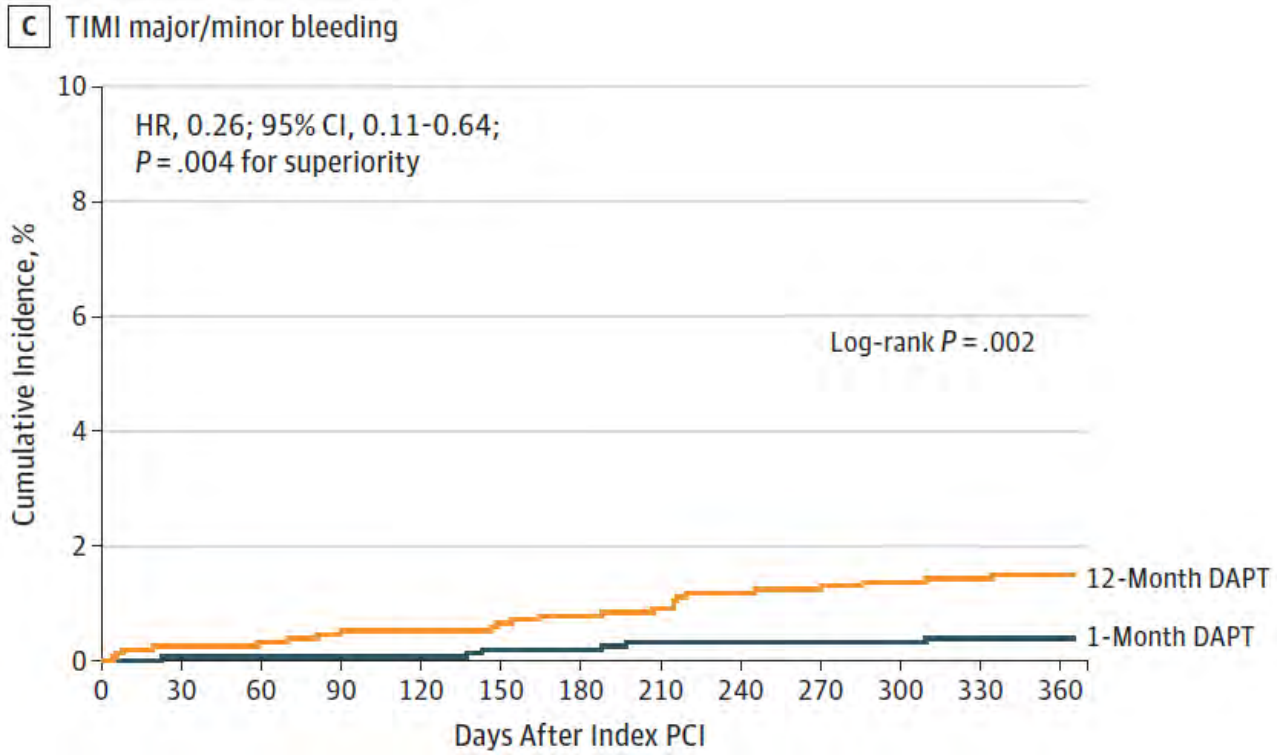
STOPDAPT-2: ISCHEMIC OUTCOMES



Outcome	1-Month, no. (%) (n = 1500)	12-Month, no. (%) (n = 1509)	Hazard Ratio (95% CI)
CV death	9 (0.61)	11 (0.74)	0.83 (0.34 – 1.99)
MI	13 (0.88)	11 (0.75)	1.19 (0.54 – 2.67)
Definite ST	2 (0.13)	1 (0.07)	2.02 (0.18 – 22.26)
Stroke (ischemic or hemorrhagic)	8 (0.54)	16 (1.09)	0.50 (0.22 – 1.18)

14. Watanabe H, et al. *JAMA* 2019; 321:2414-27.

STOPDAPT-2: BLEEDING OUTCOMES

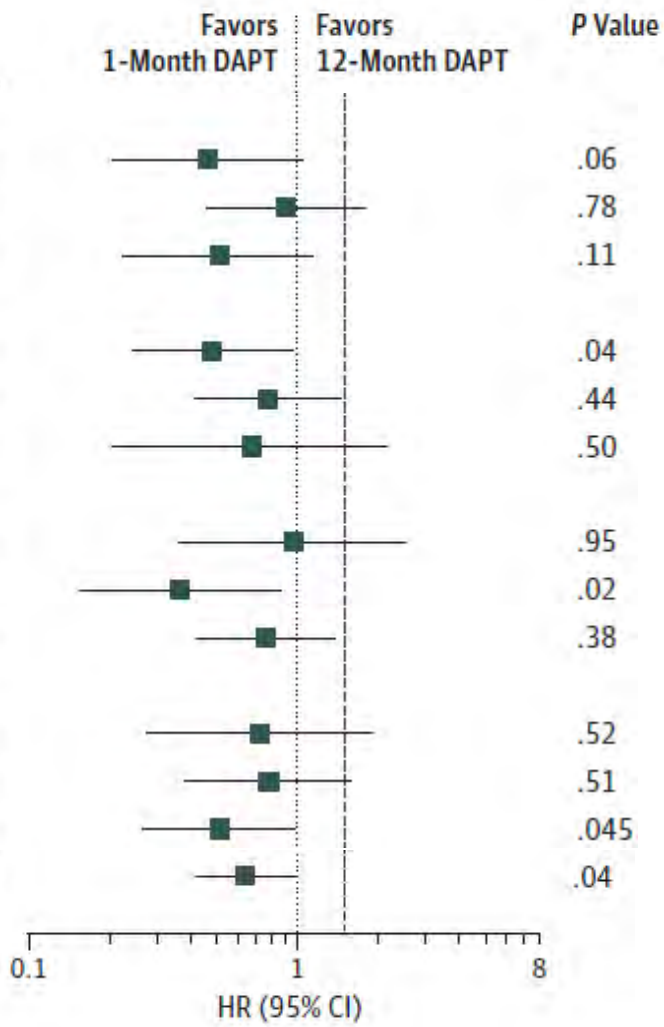


Outcome	1-Month, no. (%) (n = 1500)	12-Month, no. (%) (n = 1509)	Hazard Ratio (95% CI)
TIMI major	3 (0.20)	16 (1.07)	0.19 (0.05 – 0.65)
TIMI minor	3 (0.20)	7 (0.47)	0.43 (0.11 – 1.67)
BARC type 3 or 5	8 (0.54)	27 (1.81)	0.30 (0.13 – 0.65)
GUSTO moderate or severe	6 (0.40)	23 (1.54)	0.26 (0.11 – 0.64)
Gastrointestinal	6 (0.40)	19 (1.27)	0.32 (0.13 – 0.79)

14. Watanabe H, et al. *JAMA* 2019; 321:2414-27.

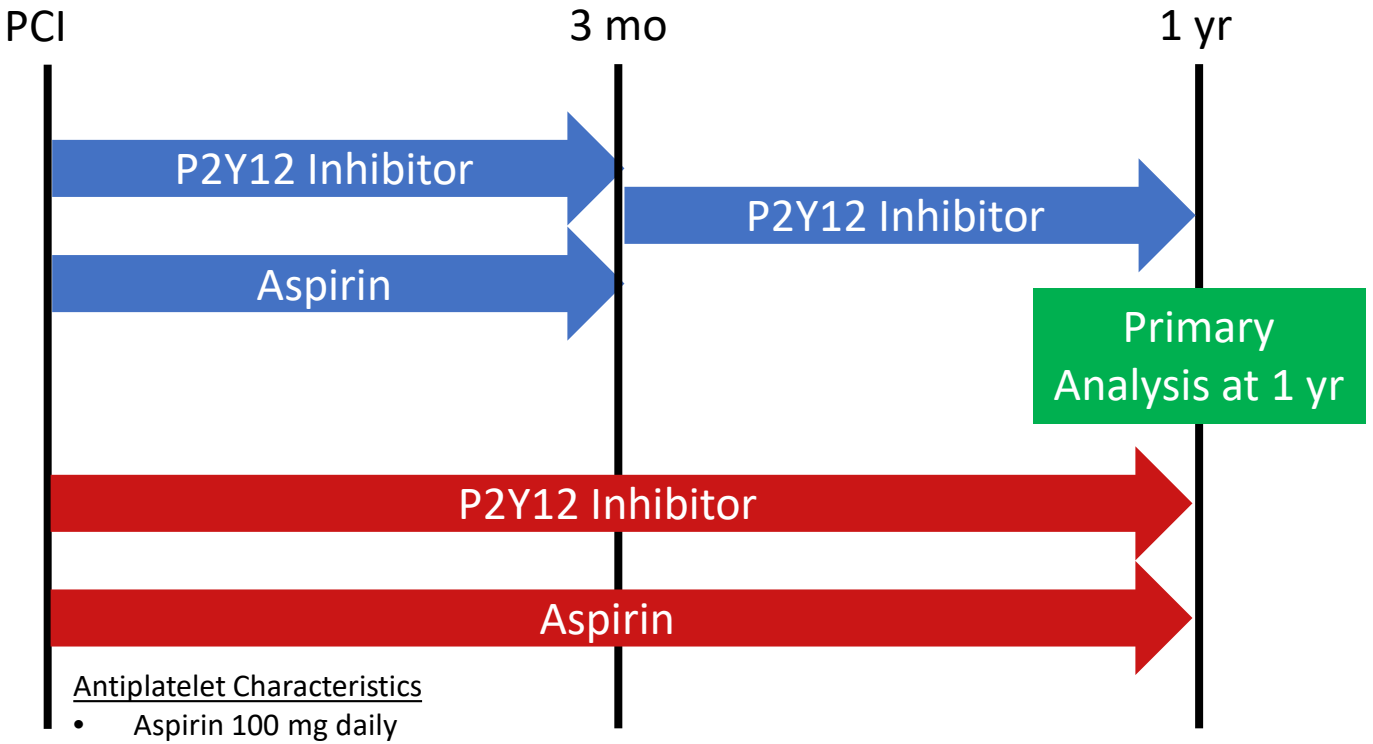
STOPDAPT-2: Outcomes Based on Risk Scores

	No./Total (%)			
	1-Month DAPT (n = 1500)	12-Month DAPT (n = 1509)	HR (95% CI)	*P* Value
PARIS thrombotic risk score				
High	9/211 (4.39)	19/215 (8.90)	0.47 (0.21-1.05)	.06
Intermediate	17/560 (3.07)	18/536 (3.42)	0.91 (0.47-1.77)	.78
Low	9/729 (1.24)	18/758 (2.40)	0.52 (0.23-1.15)	.11
PARIS bleeding risk score				
High	13/302 (4.37)	25/291 (8.62)	0.49 (0.25-0.96)	.04
Intermediate	17/757 (2.27)	23/801 (2.93)	0.78 (0.42-1.46)	.44
Low	5/441 (1.15)	7/417 (1.72)	0.68 (0.21-2.13)	.50
CREDO-Kyoto thrombotic risk score				
High	8/113 (7.24)	9/122 (7.41)	0.97 (0.37-2.51)	.95
Intermediate	7/318 (2.25)	21/358 (5.94)	0.37 (0.16-0.87)	.02
Low	20/1069 (1.89)	25/1029 (2.47)	0.77 (0.43-1.39)	.38
CREDO-Kyoto bleeding risk score				
High	7/106 (6.70)	10/112 (8.93)	0.73 (0.28-1.91)	.52
Intermediate	14/398 (3.58)	18/401 (4.57)	0.79 (0.39-1.59)	.51
Low	14/996 (1.42)	27/996 (2.75)	0.52 (0.27-0.99)	.045
Overall	35/1500 (2.36)	55/1509 (3.70)	0.64 (0.42-0.98)	.04



14. Watanabe H, et al. *JAMA* 2019; 321:2414-27.

SMART-CHOICE: OVERVIEW



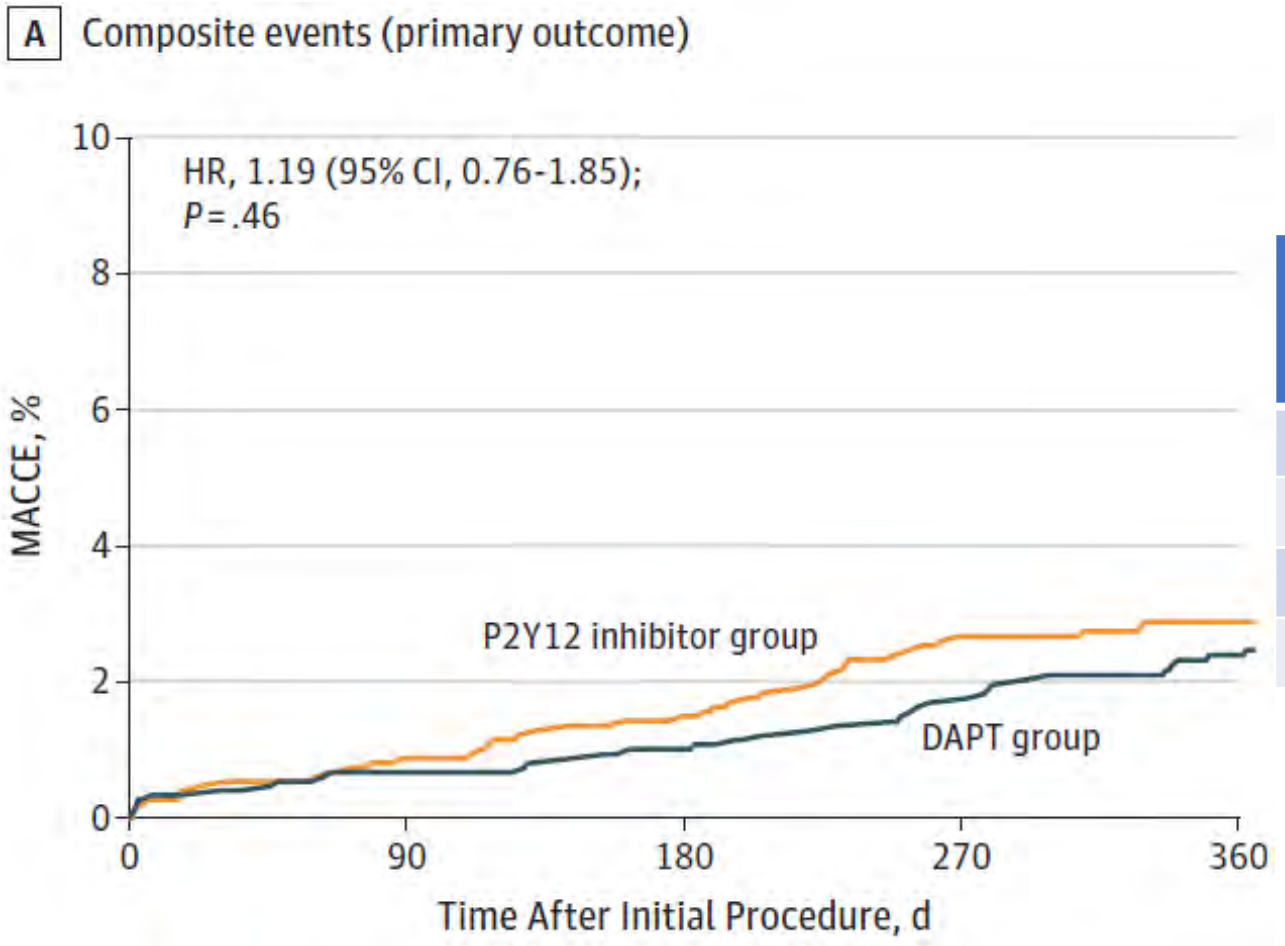
Antiplatelet Characteristics

- Aspirin 100 mg daily
- Clopidogrel 75 mg daily
- Prasugrel 10 mg daily
- Ticagrelor 90mg BID

Characteristics	3-Month DAPT (n = 1495)	12-Month DAPT (n = 1498)
SIHD, no. (%)	625 (41.8)	625 (41.8)
UA, no. (%)	467 (31.2)	491 (32.8)
NSTEMI, no. (%)	239 (16.0)	230 (15.4)
STEMI, no. (%)	164 (11.0)	150 (10.0)
Medications at Discharge, no. (%)		
Aspirin	1492 (99.8)	1496 (99.9)
P2Y12 Inhibitor	1493 (99.9)	1496 (99.9)
Clopidogrel	1149 (76.9)	1163 (77.6)
Prasugrel	62 (4.1)	67 (4.5)
Ticagrelor	284 (19.0)	268 (17.9)
Statin	1416 (94.7)	1408 (94.1)

15. Hahn, JY, et al. *JAMA* 2019; 321:2428-37.

SMART-CHOICE: ISCHEMIC OUTCOMES

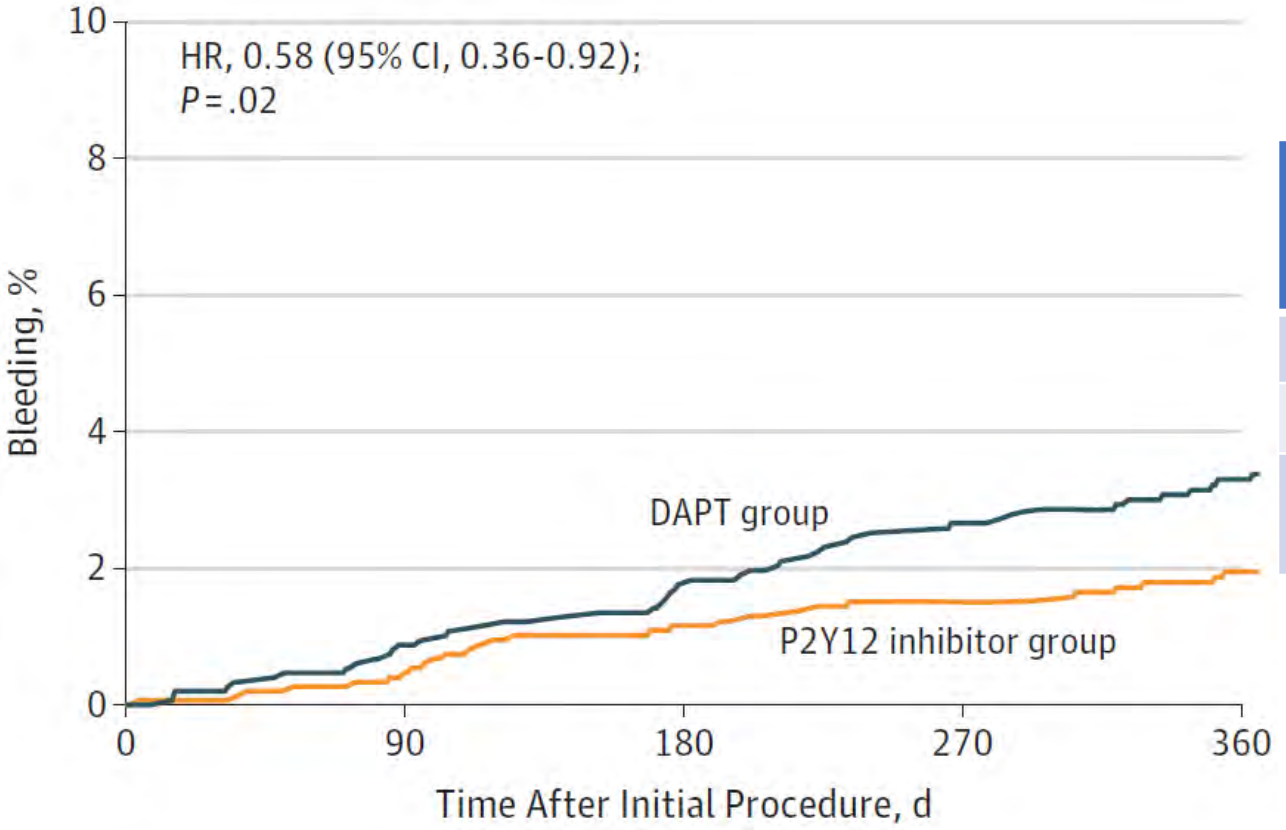


Outcome	3-Month, no. (%) (n = 1495)	12-Month, no. (%) (n = 1498)	Hazard Ratio (95% CI)
All-cause death	21 (1.4)	18 (1.2)	1.18 (0.63 – 2.21)
MI	11 (0.8)	17 (1.2)	0.66 (0.31 – 1.40)
Stroke	11 (0.8)	5 (0.3)	2.23 (0.78 – 6.43)
ST	3 (0.2)	2 (0.1)	1.51 (0.25 – 9.02)

15. Hahn, JY, et al. *JAMA* 2019; 321:2428-37.

SMART-CHOICE: BLEEDING OUTCOMES

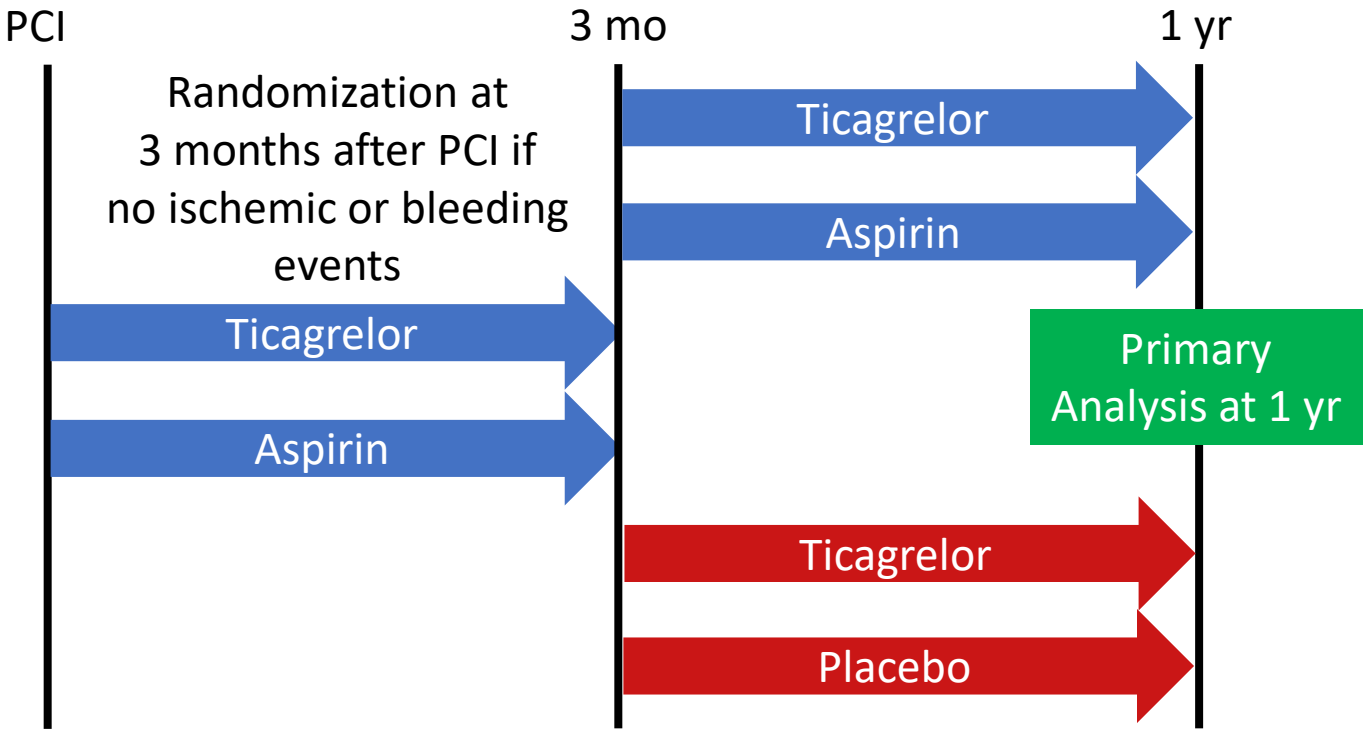
A Bleeding (secondary end point)



Outcome	3-Month, no. (%) (n = 1495)	12-Month, no. (%) (n = 1498)	Hazard Ratio (95% CI)
BARC type 2-5	28 (2.0)	49 (3.4)	0.58 (0.36 to 0.92)
BARC type 3-5	12 (0.8)	14 (1.0)	0.87 (0.40 to 1.88)
Net adverse clinical and cerebral events	65 (4.5)	81 (5.6)	0.81 (0.58 to 1.12)

15. Hahn, JY, et al. *JAMA* 2019; 321:2428-37.

TWILIGHT: OVERVIEW



Characteristics	Ticagrelor Alone (n = 3555)	Ticagrelor + ASA (n = 3564)
Asymptomatic, no. (%)	234 (6.6)	223 (6.3)
Stable angina, no. (%)	1047 (29.5)	999 (28.0)
UA, no. (%)	1249 (35.1)	1245 (34.9)
NSTEMI, no. (%)	1024 (28.8)	1096 (30.8)

Antiplatelet Characteristics

- Aspirin 81-100 mg daily
- Ticagrelor 90mg BID

16. Mehran R, et al. *N Engl J Med* 2019; 381:2032-42.

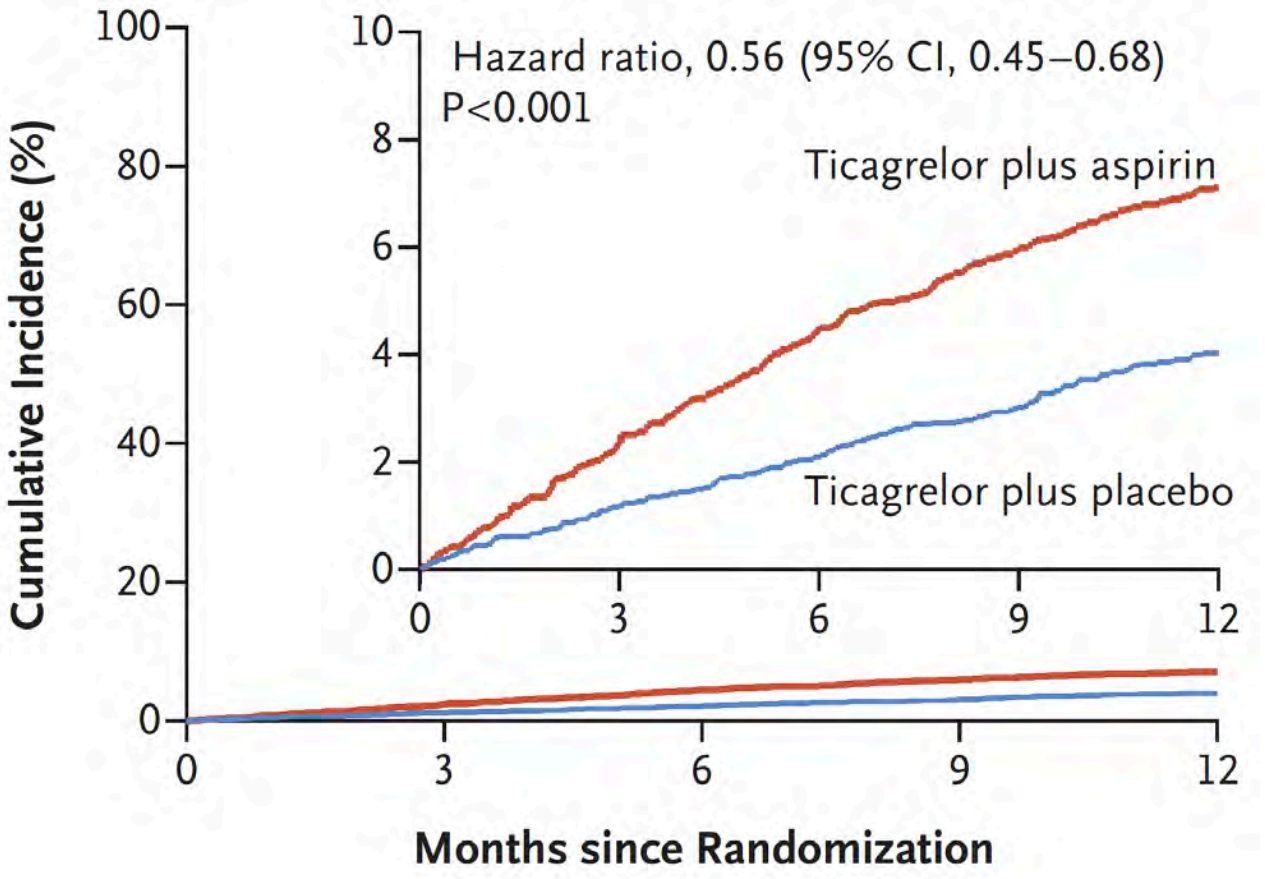
TWILIGHT: High Risk Criteria

Clinical Criteria	Angiographic
• Age ≥65[I,B] • Female sex[B] • Troponin-positive ACS[I,B] • Established vascular disease[I,B] • Diabetes mellitus treated with medication[I] • Chronic kidney disease (eGFR or CrCl <60)[I,B]	• Multivessel coronary artery disease[I] • Total stent length ≥30mm[I] • Thrombotic target lesion[I] • Bifurcation lesions treated with two stents[I,B] • Obstructive left main or proximal LAD lesion[I] • Calcified target lesion treated with atherectomy[I,B]

I: ischemic risk factor
B: bleeding risk factor

16. Mehran R, et al. *N Engl J Med* 2019; 381:2032-42.

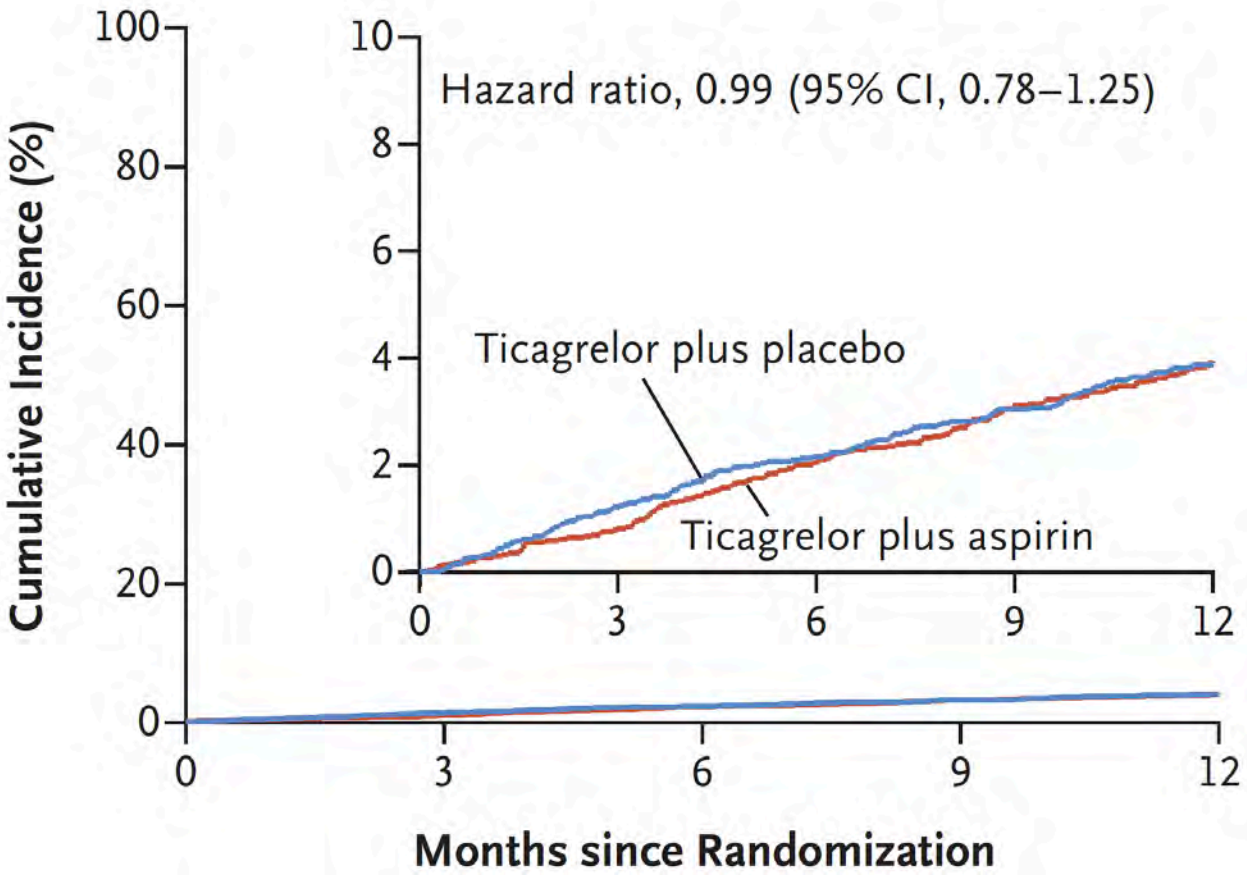
TWILIGHT: BLEEDING OUTCOMES



Outcome	Ticagrelor Alone (n = 3555)	Ticagrelor + ASA (n = 3564)	Hazard Ratio (95% CI)
BARC type 2, 3, or 5	141 (4.0)	250 (7.1)	0.56 (0.45 – 0.68)
BARC type 3 or 5	34 (1.0)	69 (2.0)	0.49 (0.33 – 0.74)
TIMI minor or major	141 (4.0)	250 (7.1)	0.56 (0.45 – 0.68)
GUSTO moderate or severe	26 (0.7)	49 (1.4)	0.53 (0.33 – 0.85)
ISTH major	39 (1.1)	72 (2.1)	0.54 (0.37 – 0.80)

16. Mehran R, et al. *N Engl J Med* 2019; 381:2032-42.

TWILIGHT: ISCHEMIC OUTCOMES

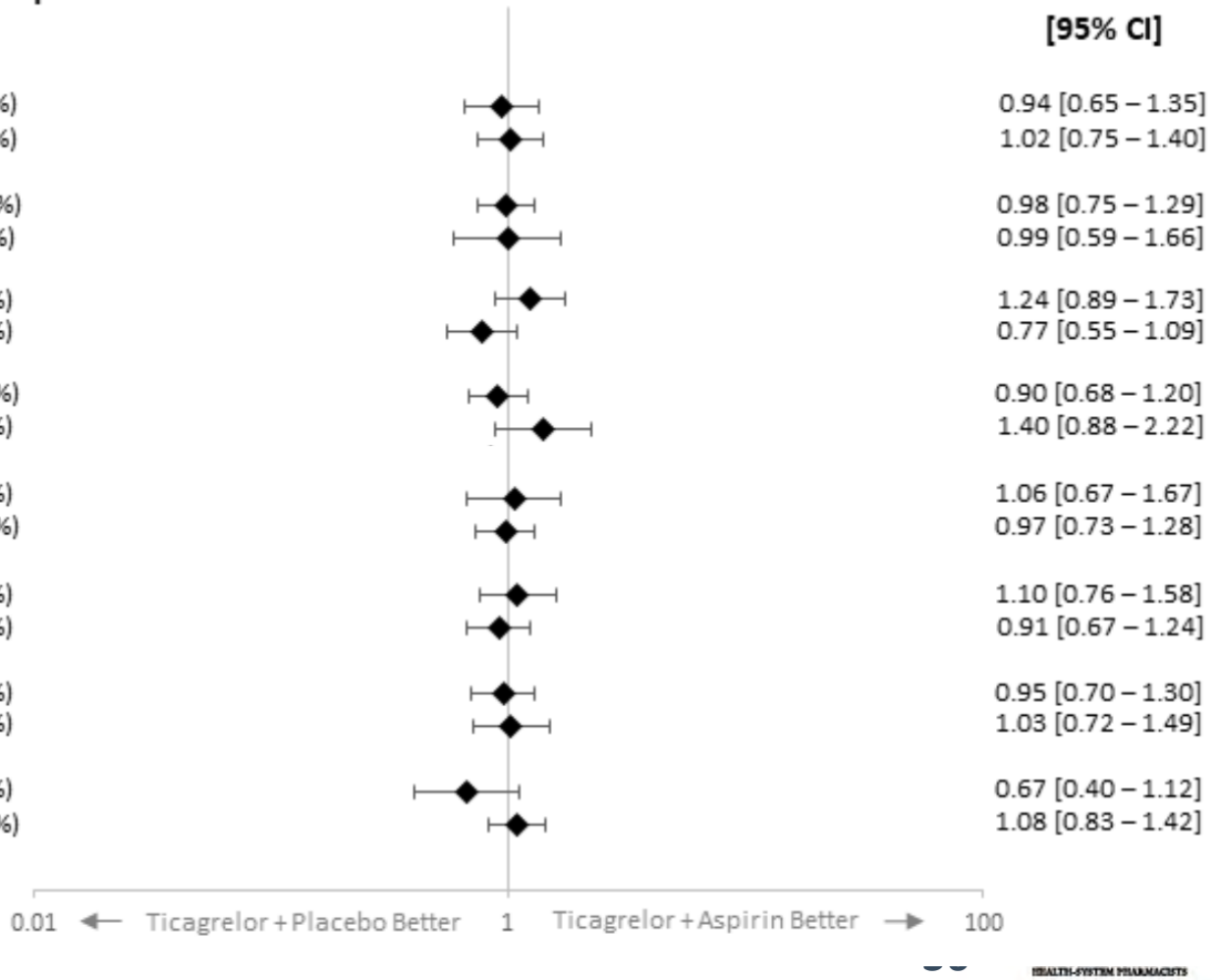


Outcome	Ticagrelor Alone (n = 3555)	Ticagrelor + ASA (n = 3564)	Hazard Ratio (95% CI)
Death from any cause, nonfatal MI, nonfatal stroke	135 (3.9)	137 (3.9)	0.99 (0.78 – 1.25)
Death from CV cause, nonfatal MI, nonfatal ischemic stroke	126 (3.6)	130 (3.7)	0.97 (0.76 – 1.24)
Death from any cause	34 (1.0)	45 (1.3)	0.75 (0.48 – 1.18)
Death from CV cause	26 (0.8)	37 (1.1)	0.70 (0.43 – 1.16)
MI	95 (2.7)	95 (2.7)	1.00 (0.75 – 1.33)
Ischemic stroke	16 (0.5)	8 (0.2)	2.00 (0.86 – 4.67)
Definite/probable ST	14 (0.4)	19 (0.6)	0.74 (0.37 – 1.47)

16. Mehran R, et al. *N Engl J Med* 2019; 381:2032-42.

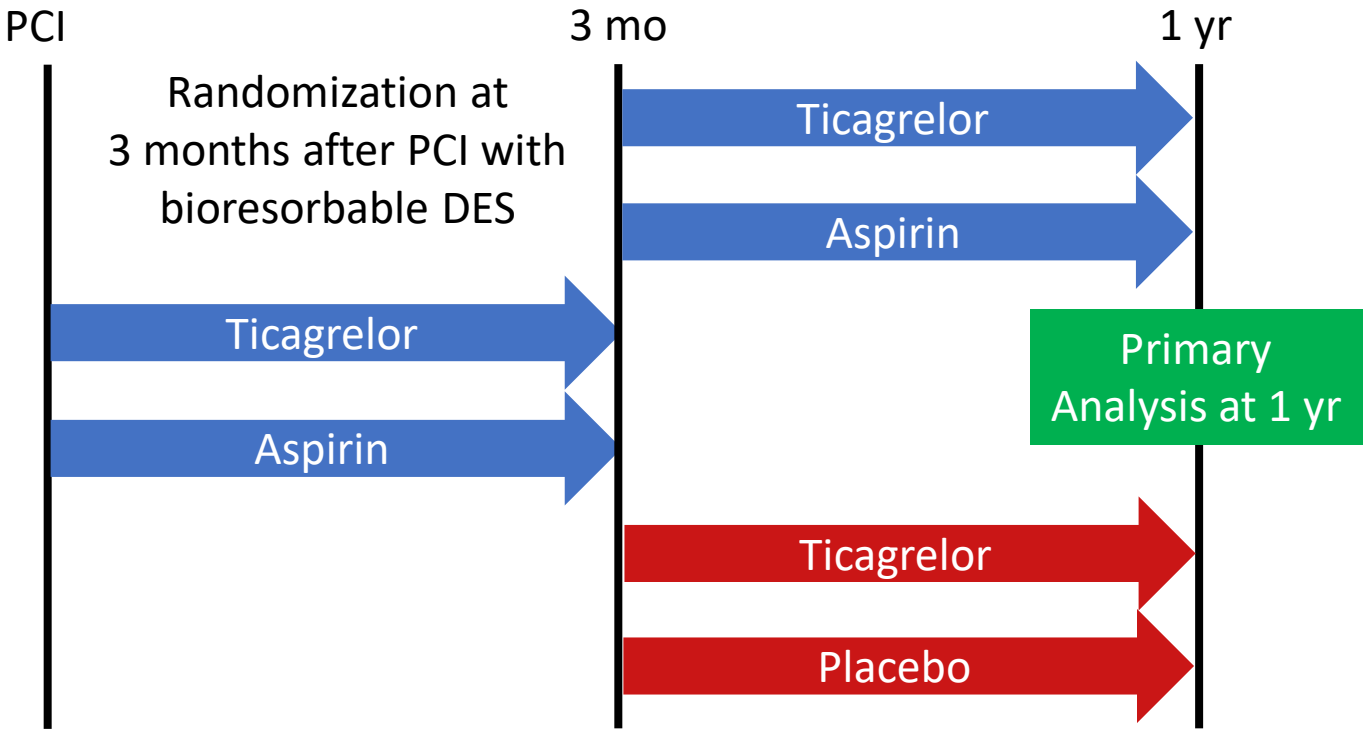
TWILIGHT: Subgroup Analysis of Ischemic Outcomes

Subgroups	No. of patients	Ticagrelor + Placebo	Ticagrelor + Aspirin	HR [95% CI]
		no. of events (% of patients)		
Age (years)				
<65	3362	56 (3.4%)	60 (3.6%)	0.94 [0.65 – 1.35]
≥65	3677	79 (4.3%)	77 (4.2%)	1.02 [0.75 – 1.40]
Sex				
Male	5363	106 (4.0%)	108 (4.1%)	0.98 [0.75 – 1.29]
Female	1676	29 (3.5%)	29 (3.5%)	0.99 [0.59 – 1.66]
Diabetes Mellitus				
No	4446	76 (3.5%)	62 (2.8%)	1.24 [0.89 – 1.73]
Yes	2593	59 (4.6%)	75 (5.9%)	0.77 [0.55 – 1.09]
CKD (eGFR <60 ml/min)				
No	5629	90 (3.2%)	100 (3.6%)	0.90 [0.68 – 1.20]
Yes	1133	43 (7.7%)	31 (5.5%)	1.40 [0.88 – 2.22]
Indication for PCI				
Stable	2472	39 (3.1%)	35 (2.9%)	1.06 [0.67 – 1.67]
ACS	4565	96 (4.3%)	102 (4.5%)	0.97 [0.73 – 1.28]
Total stent length (mm)				
<30	3003	59 (4.0%)	56 (3.7%)	1.10 [0.76 – 1.58]
≥30	4036	76 (3.8%)	81 (4.1%)	0.91 [0.67 – 1.24]
Prior MI				
No	5020	77 (3.1%)	81 (3.3%)	0.95 [0.70 – 1.30]
Yes	2019	58 (5.8%)	56 (5.6%)	1.03 [0.72 – 1.49]
Multivessel Disease				
No	2392	23 (2.0%)	37 (3.0%)	0.67 [0.40 – 1.12]
Yes	4647	112 (4.8%)	100 (4.4%)	1.08 [0.83 – 1.42]



16. Mehran R, et al. *N Engl J Med* 2019; 381:2032-42.

TICO: OVERVIEW



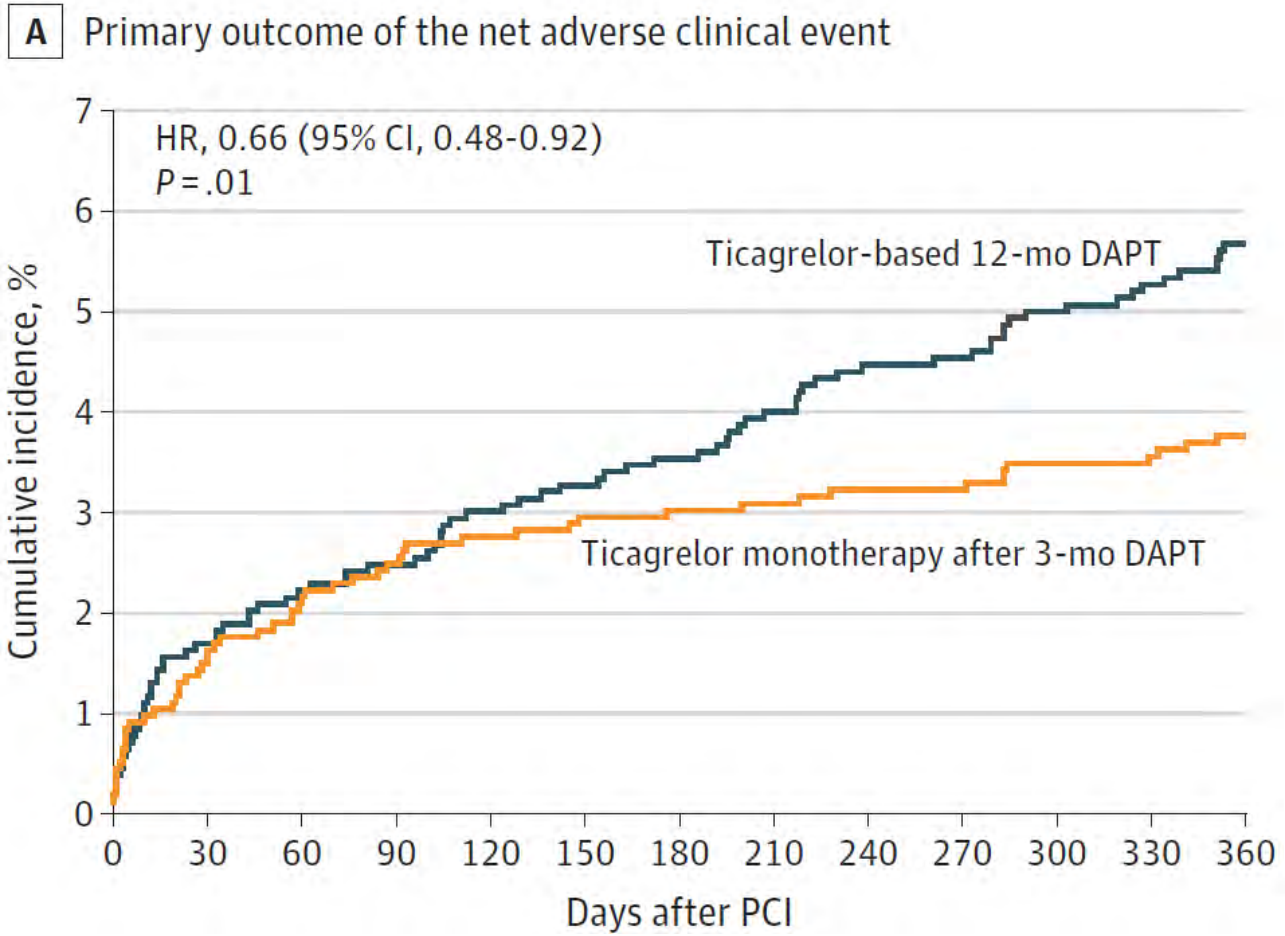
Characteristics	3-Month DAPT (n = 1527)	12-Month DAPT (n = 1529)
UA, no. (%)	442 (29)	484 (32)
NSTEMI, no. (%)	539 (35)	488 (32)
STEMI, no. (%)	546 (36)	557 (36)
Medications at Discharge, no. (%)		
Statin	1494 (97.8)	1499 (98.0)

Antiplatelet Characteristics

- Aspirin 81-100 mg daily
- Ticagrelor 90mg BID

17. Kim BK, et al. *JAMA* 2020; 323:2407-16.

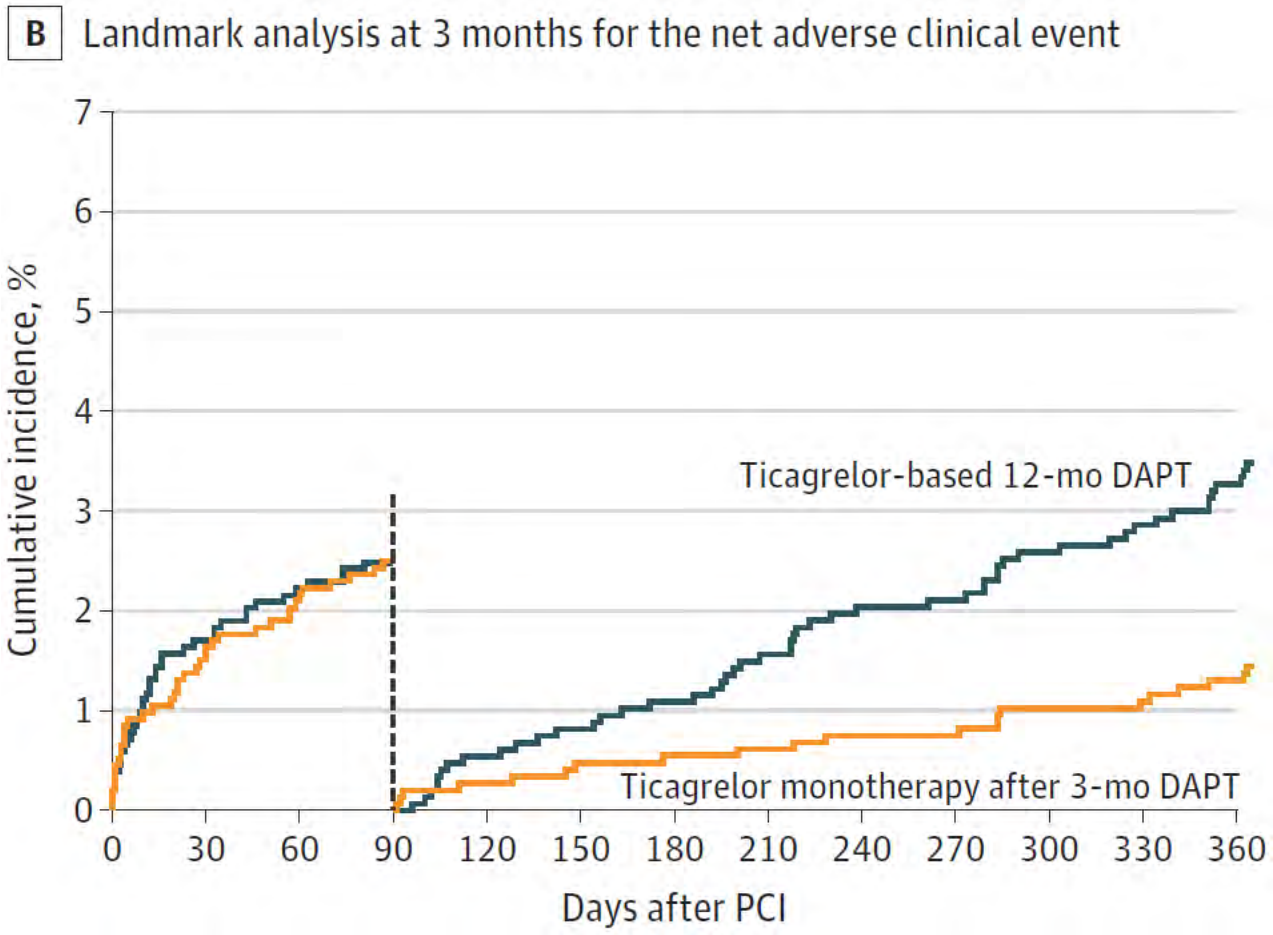
TICO: Net Adverse Clinical Events



Outcome	Ticagrelor Alone (n = 1527)	Ticagrelor + ASA (n = 1529)	Hazard Ratio (95% CI)
TIMI major bleeding, no. (%)	25 (1.7)	45 (3.0)	0.56 (0.34 – 0.91)
TIMI major or minor bleeding, no. (%)	53 (3.6)	83 (5.5)	0.64 (0.45 – 0.90)
Major adverse cardiac and cerebrovascular events, no. (%)	35 (2.3)	51 (3.4)	0.69 (0.45 – 1.06)
Death, no. (%)	16 (1.1)	23 (1.5)	0.70 (0.37 – 1.32)
Acute MI, no. (%)	6 (0.4)	11 (0.7)	0.55 (0.20 – 1.48)
ST, no. (%)	6 (0.4)	4 (0.3)	1.51 (0.43 – 5.33)
Stroke, no. (%)	8 (0.5)	11 (0.7)	0.73 (0.29 – 1.81)

17. Kim BK, et al. *JAMA* 2020; 323:2407-16.

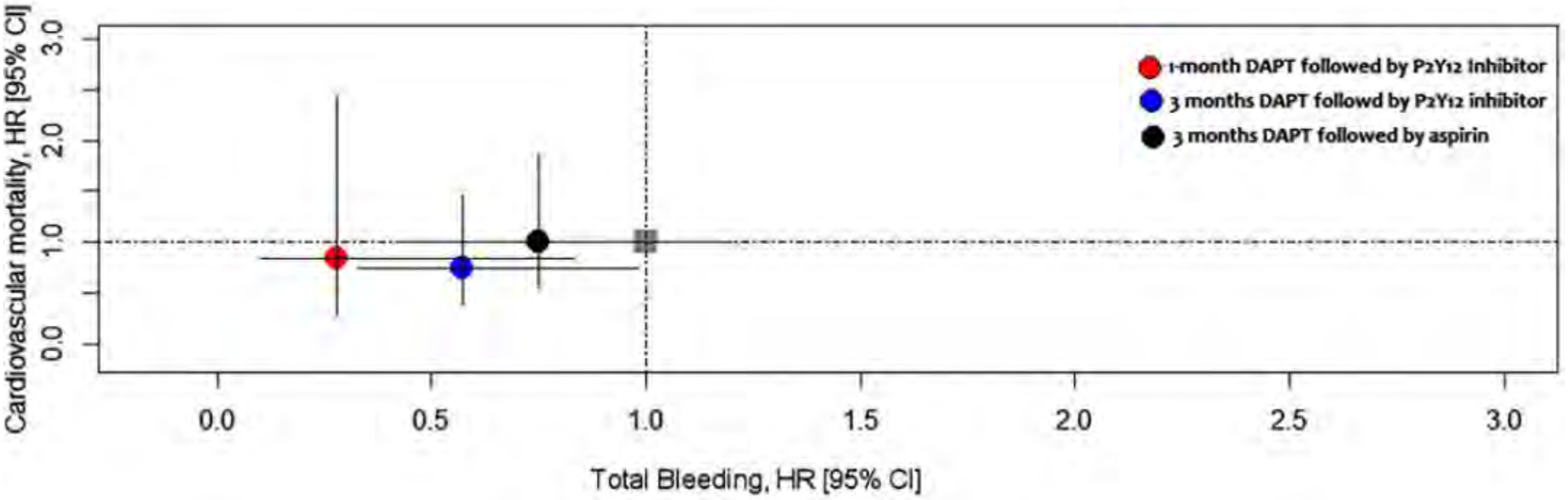
TICO: 3 Month Landmark Analysis



Outcome, Months 3 – 12	Ticagrelor Alone (n = 1527)	Ticagrelor + ASA (n = 1529)	Hazard Ratio (95% CI)
TIMI major bleeding, no. (%)	3 (0.2)	23 (1.6)	0.13 (0.04 – 0.44)
TIMI major or minor bleeding, no. (%)	13 (0.9)	42 (2.9)	0.31 (0.17 – 0.57)
Major adverse cardiac and cerebrovascular events, no. (%)	18 (1.2)	31 (2.1)	0.58 (0.33 – 1.04)
Death, no. (%)	7 (0.5)	11 (0.7)	0.64 (0.25 – 1.65)
Acute MI, no. (%)	3 (0.2)	10 (0.7)	0.30 (0.08 – 1.09)
ST, no. (%)	2 (0.1)	1 (0.1)	2.00 (0.18 – 22.14)
Stroke, no. (%)	3 (0.2)	5 (0.3)	0.60 (0.13 – 2.52)

17. Kim BK, et al. *JAMA* 2020; 323:2407-16.

NET CLINICAL BENEFIT OF SHORTENED DAPT



18. Khan SU, et al. *Eur Heart J Cardiovasc Pharmacother* 2020; doi:10.1093/ehjcvp/pvaa025.

The Dilemma of Shortened DAPT

- Shortened DAPT reduces bleeding compared to longer durations without impacting ischemic event rates
  - Heterogeneous patient population with varying ischemic and bleeding risk
    - Generally low ischemic risk patients evaluated
  - Limited data with ACS, specifically STEMI, patients
  - Much lower than anticipated ischemic event rates

- The benefit of shortened DAPT may be overestimated

14. Watanabe H, et al. *JAMA* 2019; 321:2414-27.
15. Hahn, JY, et al. *JAMA* 2019; 321:2428-37.
16. Mehran R, et al. *N Engl J Med* 2019; 381:2032-42.
17. Kim BK, et al. *JAMA* 2020; 323:2407-16.

Identifying Patients for Shortened DAPT

Increased Ischemic Risk	Increased Risk of ST	Increased Bleeding Risk
• **Advanced age** • ACS presentation • Multiple prior MIs • Extensive CAD • **Diabetes mellitus** • **CKD**	• ACS presentation • **Diabetes mellitus** • LVEF <40% • 1st gen DES • Stent undersizing • Stent underdeployment • Small stent diameter • Greater stent length • Bifurcation stents • In-stent restenosis	• History of prior bleeding • Oral anticoagulant therapy • Female sex • **Advanced age** • Low body weight • **CKD** • **Diabetes mellitus** • Anemia • Chronic steroid or NSAID therapy

May favor longer duration of DAPT

May favor shorter duration of DAPT

1. Levine GN, et al. *J Am Coll Cardiol* 2016; 68:1082-115.
2. Valgimigli M, et al. *Eur J Cardiothorac Surg* 2018; 53:34-78

Applying Risk Stratification Scores

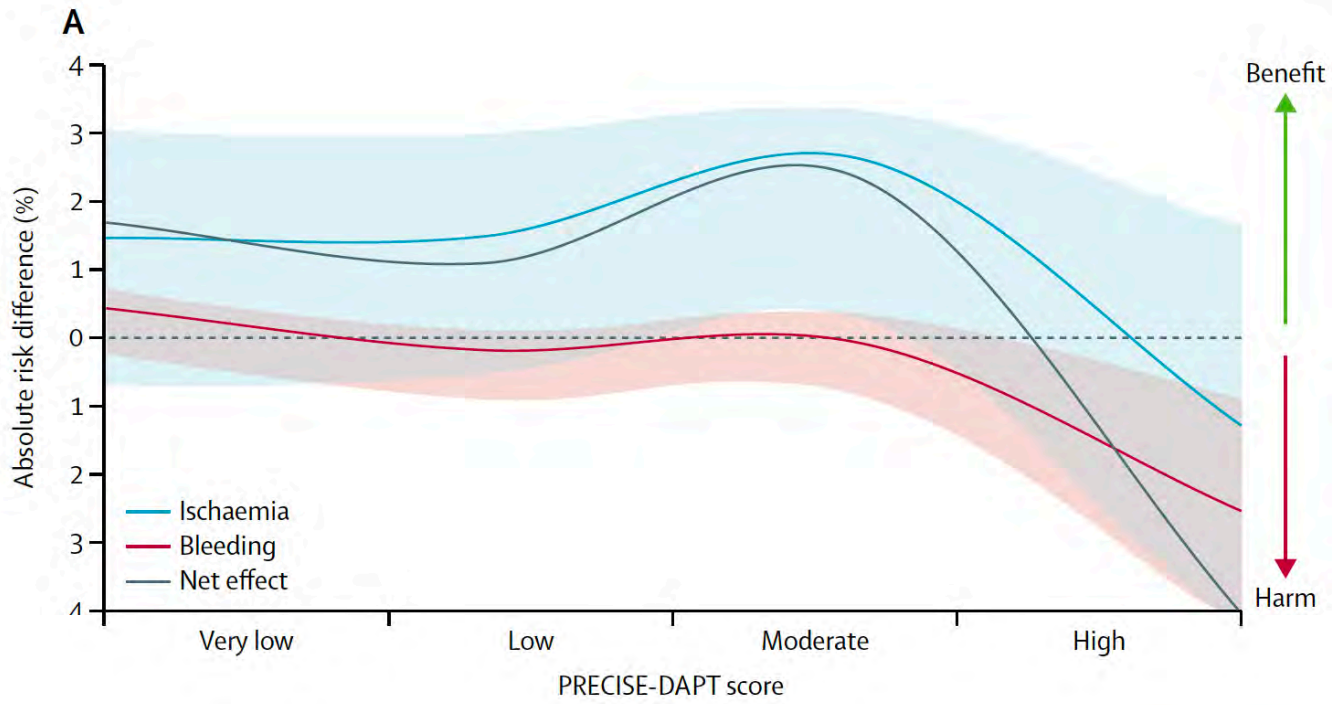
- Risk stratification scores may guide clinicians in weighing the risks of bleeding against risks of ischemic complications
  - Several risk scores generated from clinical trial and registry data
  - Validated against data from other clinical trials or registries

- ESC supports the use of the PRECISE-DAPT and DAPT scores
  - PRECISE-DAPT: Short (3 – 6 mo) vs Standard/long (12 – 24 mo)
  - DAPT: Standard (12 mo) vs. Long (30 mo)

1. Levine GN, et al. *J Am Coll Cardiol* 2016; 68:1082-115.
2. Valgimigli M, et al. *Eur J Cardiothorac Surg* 2018; 53:34-78

PRECISE-DAPT Score

	PRECISE-DAPT score[18]
Time of use	At the time of coronary stenting
DAPT duration strategies assessed	Short DAPT (3–6 months) vs. Standard/long DAPT (12–24 months)
Score calculation[a]	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	0 to 100 points
Decision making cut-off suggested	Score ≥25 → Short DAPT Score <25 → Standard/long DAPT
Calculator	www.precisedaptscore.com



19. Costa F, et al. *Lancet* 2017: 389:1025-34.

PARIS THROMBOTIC AND BLEEDING RISK SCORES

Integer Risk Score for Coronary Thrombotic Events

Parameter	Score
Diabetes mellitus	
None	0
Non-insulin-dependent	+1
Insulin-dependent	+3
Acute coronary syndrome	
No	0
Yes, Tn-negative	+1
Yes, Tn-positive	+2
Current smoking	
Yes	+1
No	0

Parameter	Score
CrCl <60 mL/min	
Present	+2
Absent	0
Prior PCI	
Yes	+2
No	0
Prior CABG	
Yes	+2
No	0

Low: 0 – 2
Intermediate: 3 – 4
High: ≥5

Integer Risk Score for Major Bleeding

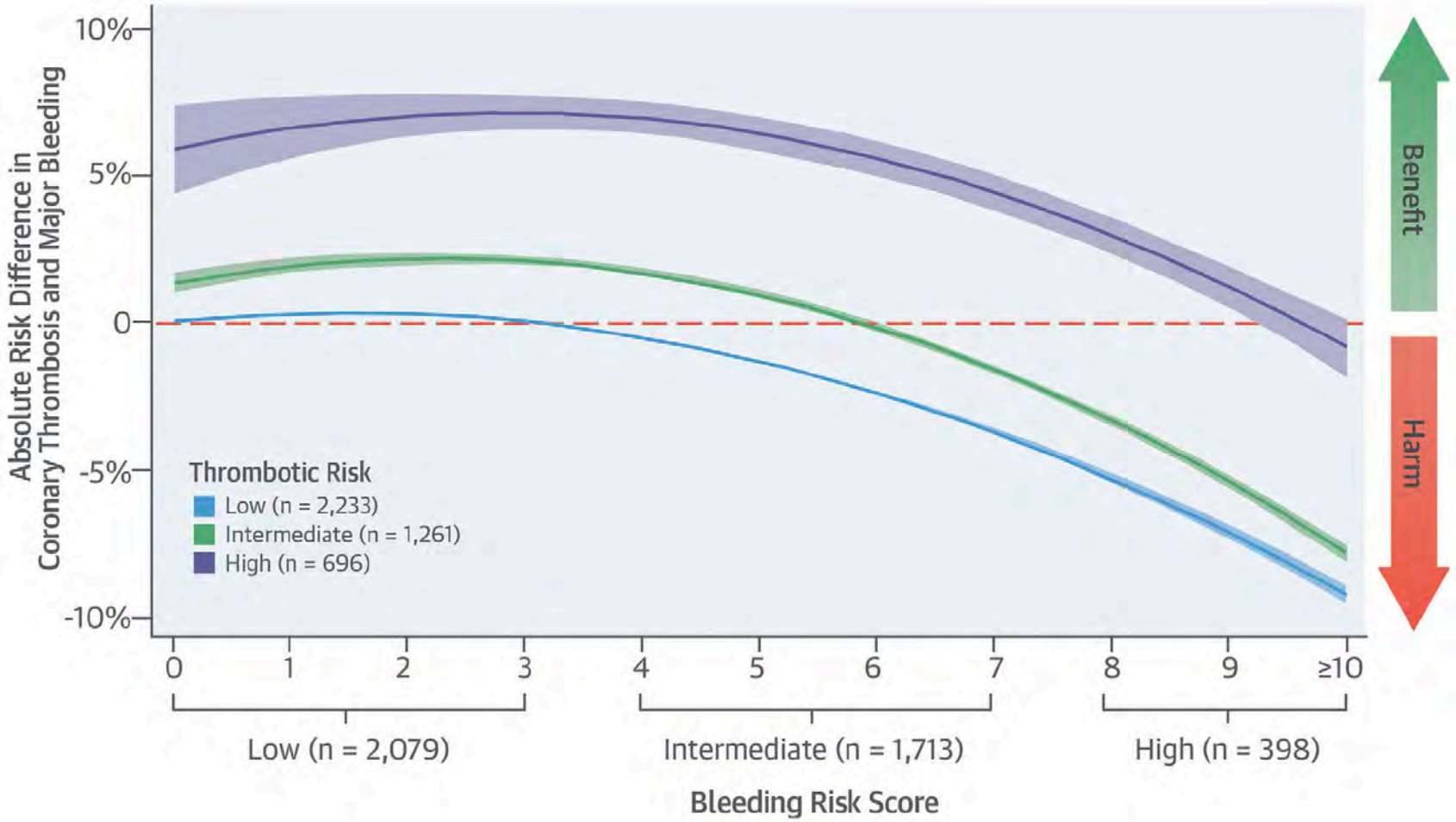
Parameter	Score
Age, yrs	
<50	0
50 – 59	+1
60 – 69	+2
70 – 79	+3
≥80	+4
BMI, kg/m^2	
<25	+2
25 – 34.9	0
≥35	+2
Current smoking	
Yes	+2
No	0

Parameter	Score
Anemia	
Present	+3
Absent	0
CrCl <60 mL/min	
Present	+2
Absent	0
Triple therapy on discharge	
Yes	+2
No	0

Low: 0 – 3
Intermediate: 4 – 7
High: ≥8

20. Usman B, et al. *J Am Coll Cardiol* 2016; 67:2224-34.

PARIS THROMBOTIC AND BLEEDING RISK SCORES



20. Usman B, et al. *J Am Coll Cardiol* 2016; 67:2224-34.

Utility of Risk Scores in Real-World

- Risk scores may not be reflective of real-world patients and external validation may be lacking
  - Application to real-world patients in retrospective datasets suggest that predictive ability may be moderate at best

PARIS Registry	Bianco, et al.	Abu-Assi, et al.	Song, et al.
MB: 0.72 (derivation) 0.64 (validation) **CTE:** 0.70 (derivation) 0.65 (validation)	**MB:** 0.56 **CTE:** 0.64	**MB:** 0.73 **CTE:** N/A	**MB:** 0.56 **CTE:** 0.57

MB: major bleeding
CTE: coronary thrombotic event

21. Ko SQ, et al. *Am J Cardiol* 2018; 122:1843-52.
22. Bianco M, et al. *Int J Cardiol* 2020; 301:200-6.
23. Song L, et al. *Catheter Cardiovasc Interv* 2018; 91:573-81
24. Abu-Assi E, et al. *EuroIntervention* 2018; 13:1914-22.

Bringing It All Together

- Shortened (≤6 mo) duration of DAPT may be appropriate
  - Evaluate for ischemic and bleeding risk factors
  - Consider stent and procedural characteristics
  - Utilize risk stratification scores (while appreciating limitations)

- Further research is needed to clarify the optimal approach to reducing the duration of DAPT

Case Revisited

WW is a 59 y/o Asian F who presented to the hospital with chest pain found to have NSTEMI now s/p PCI with DES (Xience [everolimus eluting stent]) to the L circumflex placed on dual antiplatelet therapy with aspirin and ticagrelor.

- PMH: HTN, NIDDM, iron deficiency anemia
- Objective data:
  - Ht: 5'6" Wt: 60kg BMI: 21.3 kg/m^2
  - BP 127/72 mmHg HR 75 RR 14 T 37.1^{o}C

Na	142
K	4.1
Cl	103
CO2	24
BUN	21
SCr	1.1
Glu	223

WBC	8.2
Hgb	11.2
Hct	34.3
Plt	278
Trop (initial)	1.42

WW is worried about bleeding as her friend had a GI bleed while on dual antiplatelet therapy. Is she an appropriate candidate for shortened duration of therapy?

Emerging Data

- Multiple ongoing studies

Study	Comparison	Anticipated Completion Date
T-PASS	Very short DAPT (<1 mo) followed by ticagrelor monotherapy vs standard duration DAPT	July 2021
STOPDAPT-2 ACS	1-month DAPT followed by P2Y12 monotherapy vs standard duration DAPT	March 2026

- Evolving stent technology (e.g. bioresorbable stents) will change the bleeding and ischemic risk profile
- Updated guidelines should incorporate recent literature into recommendations regarding shortened DAPT

QUESTION 1

Compared to 1st generation stents, 2nd generation stents have a _____ risk of stent thrombosis.

a) Lower
b) Similar
c) Higher

QUESTION 1

Compared to 1st generation stents, 2nd generation stents have a _____ risk of stent thrombosis.

a) **Lower**
b) Similar
c) Higher

QUESTION 2

Compared to standard/long (≥12 months) durations of DAPT, a shortened (≤6 month) duration of DAPT followed by P2Y12 inhibitor monotherapy appears to:

a) Reduce both the risk of bleeding and ischemic complications
b) Reduce the risk of bleeding complications without increasing ischemic complications
c) Reduce the risk of ischemic complications without changing bleeding complications
d) Increase both the risk of bleeding and ischemic complications

QUESTION 2

Compared to standard/long (≥12 months) durations of DAPT, a shortened (≤6 month) duration of DAPT followed by P2Y12 inhibitor monotherapy appears to:

a) Reduce both the risk of bleeding and ischemic complications
b) Reduce the risk of bleeding complications without increasing ischemic complications
c) Reduce the risk of ischemic complications without changing bleeding complications
d) Increase both the risk of bleeding and ischemic complications

QUESTION 3

Risk stratification scores, such as the PRECISE-DAPT, can definitively determine which patients should be treated with a shortened (≤6 month) duration of DAPT.

a) True
b) False

QUESTION 3

Risk stratification scores, such as the PRECISE-DAPT, can definitively determine which patients should be treated with a shortened (≤6 month) duration of DAPT.

a) True
b) False

REFERENCE LIST

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Session Code: