Optimal Dual Antiplatelet therapy (DAPT) in ACS - shorter, longer?

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Optimal DAPT in ACS - shorter, longer?

- Why do we use antiplatelet therapy?
- What are the risks and benefits?
- What is the evidence base for treatment duration?
- What has changed over time that the duration of therapy has become an important clinical questions?

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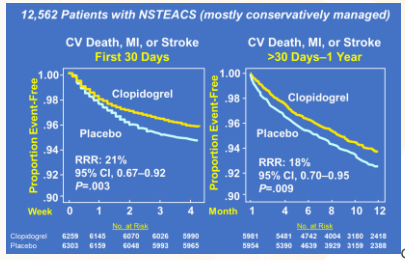
Cure: Long-term benefit of clopidogrel



Yusuf S et al. NEJM 2001

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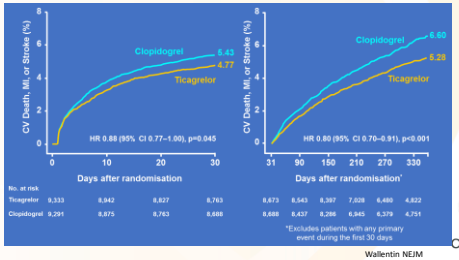
PLATO: Efficacy of ticagrelor vs clopidogrel over time

18,624 patients w/in 24 hrs of onset of ACS (64% underwent PCI)



Wallentin NEJM

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Recommendations on DAPT duration in ACS: combined ESC/ACC/AHA guidelines

- Based on CURE and its PCI-CURE substudy duration should be “at least 12 months”
- DAPT prolongation for longer than 12 months may be considered in patients who have tolerated DAPT without a bleeding complication (COR IIb, LOE A)

Capodanno D et al. JACC 2018; 72:2915-31

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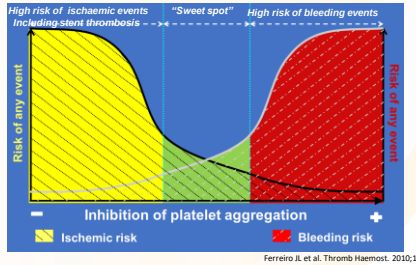
Balance safety and efficacy



Ferreiro JL et al. Thromb Haemost. 2010;103(6):1128

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DAPT: Assessment of risks and benefits

- Stent thrombosis
- Bleeding
- Recurrent ischaemia / myocardial infarction/ death
- Patient preference

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Clinical characteristics comprising the HAS-BLED bleeding risk score

Letter	Clinical characteristics	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g.: age >65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

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Multivariable analysis for out-of-hospital major or minor bleeding: PRECISE-DAPT Score

	Hazard ratio (95% CI)	P value
Age (for each increase of 10 years)	1.34 (1.11-1.48)	0.005
Previous bleeding	4.14 (1.22 – 14.02)	0.023
White-blood-cell count (for each increase of 10^3 cells per µL)	1.06 (0.99-1.13)	0.078
Haemoglobin at baseline (for each increase of 1g/dL)	0.67 (0.53-0.84)	0.001
Creatinine clearance (for each increase of 10 mL/min)	0.90 (0.82-0.99)	0.004

Costa F. et al. Lancet 2017; 389:1025-34

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Why use prolonged DAPT

- Atherothrombosis is a progressive disease
  - Continued plaque rupture in non-stented arteries
- Even with current generation DES, there is still a small risk of stent thrombosis (0.3%/year)

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Issues with longer duration of DAPT

- Bleeding is an independent predictor of 1-year mortality[1] Longer duration is associated with more bleeding and more bleeding related deaths[1]
- Longer duration results in lower rates of major adverse cardiovascular event (predominantly MI) and decreased stent thrombosis

Palmerini T et al. JACC 2017;69:2011-22

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Issues with longer duration of DAPT

- Increased mortality (2.0 vs 1.5%, p=0.05) in DAPT Trial[2]
- In trials with DES numerical increases[3] or statistical increase in mortality including non-cardiac mortality[4]
- Hypothesis that increased non-cardiac mortality is related to bleeding

[2]Mauri L et. N Engl J Med. 2014;371:2155-66 ; [3]Gustino JACC; 65:1298-310;
[4]Palmerini T et al. JACC. 2015; 65;1092-102

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Factors favouring longer DAPT

Patient-related
- ACS as initial indication for PCI/stent
- History of diabetes, renal dysfunction, heart failure, previous stent thrombosis, peripheral artery disease

Anatomy related
- Characteristics of the lesions
- Extent of atherosclerotic burden

Stent related
- First generation DES
- Long stent
- Multiple stents

Patient preference

Adapted: Eisen A, Bhatt DL. Nature Rev Cardiol. 2015;12:445-6

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DAPT: Design

Enrolled: Subjects treated with FDA-approved DES or BMS. Subjects on oral anticoagulant therapy or with life expectancy < 3 years excluded.

Randomized: Free from MI, stroke, repeat revascularization, and moderate or severe bleeding, and adherent with thienopyridine (80% to 120% of doses taken and no interruption > 14 days).

Mauri, et al. AHJ 2010;160:1035-41

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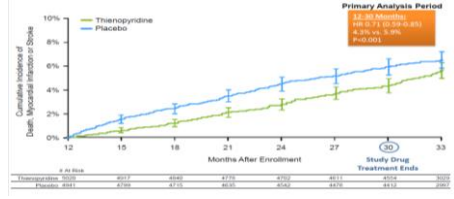
DAPT: Continuation or withdrawal of Thienopyridine 12 months after coronary stenting



Mauri, N Engl J Med 2014; 371 (23) 2155-66

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DAPT: Stent Thrombosis and Major Adverse Cardiovascular and Cerebrovascular events

Outcome	Continued Thienopyridine (N=5020)	Placebo (N=4941)	Hazard Ratio, Thienopyridine vs. Placebo (95% CI)	P Value
Stent thrombosis	No of patients (%)			
Definite	15 (0.3)	58 (1.2)	0.26 (0.14-0.45)	<0.001
Major adverse cardiovascular and cerebrovascular events	211 (4.3)	285 (5.9)	0.71 (0.59-0.85)	<0.001
Death	98 (2.0)	74 (1.5)	1.36 (1.00-1.85)	0.05
Cardiac	45 (0.9)	47 (1.0)	1.00 (0.66-1.52)	0.98
Vascular	5 (0.1)	5 (0.1)	0.98 (0.28-3.39)	0.98
Non-cardiovascular	48 (1.0)	22 (0.5)	2.23 (1.32-3.78)	0.002
Myocardial infarction	99 (2.1)	198 (4.1)	0.47 (0.37-0.61)	<0.001
Stroke	37 (0.8)	43 (0.9)	0.80 (0.51-1.25)	0.32
Ischaemic	24 (0.5)	34 (0.7)	0.68 (0.40-1.17)	0.16
Hemorrhagic	13 (0.3)	9 (0.2)	1.20 (0.50-2.9)	0.68

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DAPT: Bleeding End Point during Month 12 to Month 30

Bleeding Complications	Continued Thienopyridine (N=4710)	Placebo (N=4649)	Difference	Two-sided P Value for difference
	No of patients (%)		Percentage points (95% CI)	
GUSTO severe or moderate	119 (2.5)	73 (1.6)	1.0 (0.4 to 1.5)	0.001
Severe	38 (0.8)	26 (0.6)	0.2 (-0.1 to 0.6)	0.15
Moderate	81 (1.7)	48 (1.0)	0.7 (0.2 to 1.2)	0.004
BARC type 2, 3, or 5	263 (5.6)	137 (2.9)	2.6 (1.8 to 3.5)	<0.001
Type 2	145 (3.1)	72 (1.5)	1.5 (0.9 to 2.1)	<0.001
Type 3	122 (2.6)	68 (1.5)	1.1 (0.6 to 1.7)	<0.001
Type 5	7 (0.1)	4 (0.1)	0.1 (-0.1 to 0.2)	0.38

Mauri, N Engl J Med 2014; 371 (23) 2155-66

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Calculation of a DAPT Score

Variable	Points
Age ≥ 75 y	-2
Age 65 to < 75 y	-1
Age < 65 y	0
Current cigarette smoking	1
T2D	1
MI at presentation	1
Prior PCI	1
Stent diameter < 3 mm?	1
Paclitaxel-eluting stent	1
HF or LVEF < 30%	2
SVG PCI	2

- A score of ≥ 2 is associated with a favorable benefit/risk ratio for prolonged DAPT while a score of < 2 is associated with an unfavorable benefit to risk ratio

Yeh RW et al. JAMA 2016;315:1735-49

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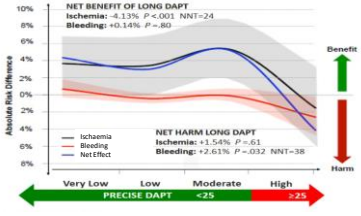
Effect of long (12 to 24 month) vs short (3 to 6 month) DAPT (ACS subgroup)



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

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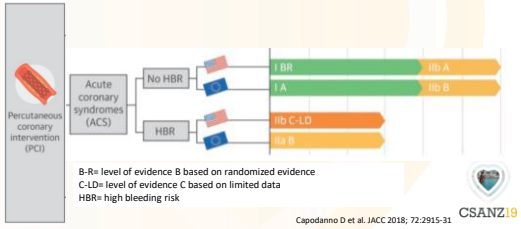
Recommendations for Dual Antiplatelet Therapy in Patients undergoing PCI



B-R= level of evidence B based on randomized evidence
C-LD= level of evidence C based on limited data
HBR= high bleeding risk

Capodanno D et al. JACC 2018; 72:2915-31

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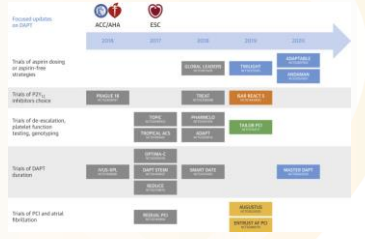
New evidence and ongoing studies in the field of DAPT



Capodanno D et al. JACC 2018; 72:2915-31

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Major differences between the ACC/AHA and ESC updates on DAPT

Topic	2016 ACC/AHA update	2017 ESC update
Risk stratification	DAPT score to assess the risk/benefit of prolonging DAPT	Use of both DAPT and PRECISE-DAPT scores recommended
Type of P2Y12 inhibitor in ACS	Class IIa recommendation for ticagrelor or prasugrel preferred to clopidogrel	Class I recommendadation for ticagrelor or prasugrel preferred to clopidogrel
Proton pump inhibitors	Class I in patients on DAPT with a history of gastrointestinal bleeding and those at increased risk of gastrointestinal bleeding	Class I in patients on DAPT
DAPT duration after PCI for ACS	Extended therapy recommended as class IIb for selected patients at low bleeding risk	Extended therapy, preferentially with ticagrelor, recommended as class IIb for selected patients with prior myocardial infarction

Capadanno et al. JACC 2018; 72:2915-31

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Additional recommendations for ACS after PCI

Rec ESC/EACTS guidelines on myocardial revascularization	Class	Level
In patients with ACS and stent implantation who are at high risk of bleeding (eg PRECISE-DAPT ≥25), discontinuation of P2Y12 inhibitor therapy after 6 months should be considered	IIa	B
De-escalation of P2Y12 inhibitor treatment (eg with a switch from ticagrelor to clopidogrel) guided by platelet function testing may be considered as an alternative DAPT strategy, especially for ACS patients deemed unsuitable for 12-month potent platelet inhibition	IIb	B
In ACS patients with no prior stroke/TIA, and at high ischaemic risk as well as low bleeding risk, receiving aspirin and clopidogrel, low-dose rivaroxaban (2.5 b.i.d. for approximately 1 year) may be considered	IIb	B

Neumann FJ et al. Eur Heart J. 2019;40:87-165

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Combined ishaemic and bleeding risk

- In patients with myocardial infarction, risk factors for bleeding and ischaemic events tend to overlap, but the combined effects have been little studied in contemporary real-world settings

Lindholm D et al. Heart 2019;0:1-7

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SWEDE-HEART

- Patients with invasively managed MI from 2006-2014
- 100,879 patients, of whom 20,831 (20.6%) experienced CVD/MI/stroke and 5,939 (5.9%) major bleeding, during 3.6 years median follow-up: illustrating continued unmet need

Lindholm D et al. Heart 2019;0:1-7

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SWEDE-HEART

Six factors were assessed in relation to cardiovascular death, MI, stroke, and major bleeding:

- age ≥65,
- chronic kidney disease,
- diabetes,
- multivessel disease,
- prior bleeding,
- prior MI

Lindholm D et al. Heart 2019;0:1-7

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SWEDE-HEART: Risk factors for CV death, MI, stroke, and bleeding

	CVD/MI/stroke	Major bleeding
Age ≥65 years	1.74 (1.68 to 1.79)	2.07 (1.94 to 2.20)
MVD	1.52 (1.48 to 1.56)	1.09 (1.03 to 1.15)
CKD	1.81 (1.76 to 1.87)	1.43 (1.35 to 1.52)
Diabetes	1.44 (1.40 to 1.49)	1.21 (1.14 to 1.29)
Prior MI	1.71 (1.66 to 1.76)	1.06 (0.99 to 1.12)
Prior bleeding	1.35 (1.29 to 1.41)	2.24 (2.08 to 2.40)

Adjusted* HR(95% CI)

Lindholm D et al. Heart 2019;0:1-7

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Ischaemic and bleeding risk assessment after myocardial infarction: SWEDE-HEART

- The novelty here is the different impact of the addition of risk factors on ischaemic and bleeding risks
- A limitation of risk scores is the complexity of using them in clinical practice (eg, the PRECISE-DAPT score requires a web calculator)

Darmon A & Ducrocq G. Heart 2019 doi: 10.1136/heartjnl-2019-315050

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Importance of secondary prevention

- Due to the improvement in PCI procedures, stents, and postprocedural management, the risk of a recurrent event is now more associated with a non-culprit lesion than with the stented segment
- The need for risk evaluation has moved to overall secondary prevention

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SMART-DATE: 6-month versus 12-month or longer DAPT after PCI in patient with ACS

- 2712 patients; 1357 to 6-month DAPT
- 1355 to the 12-month or longer DAPT group
- DES stents: Allocated 1: 1:1 to Resolute Integrity (zotarolimus), Xience Prime (everolimus), or BioMatrix Flex (biolimus)
- Clopidogrel was used as a P2Y12 inhibitor for DAPT in 80%
- Predefined non-inferiority margin of 2.0%

Hahn et al. Lancet 2018;391:1274-84

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SMART-DATE: Clinical primary and secondary outcomes at 18 months

	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
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

Data are n (%), unless otherwise stated. Percentages are Kaplan-Meier estimates. We defined major adverse cardiac and cerebrovascular events as a composite of all-cause mortality, myocardial infarction, and stroke. DAPT=dual antiplatelet therapy. HR=hazard ratio. BARC=Bleeding Academic Research Consortium. *Net adverse clinical and cerebral events were defined as major adverse cardiac and cerebrovascular events plus BARC type 2–5 bleeding.

Hahn et al. Lancet 2018;391:1274-84

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SMART-DATE: 6-month versus 12-month or longer DAPT after PCI in patient with ACS

- The increased risk of MI with 6-month DAPT and the wide-non-inferiority margin prevent us from concluding that short-term DAPT is safe in patients with ACS undergoing PCI with current generation DES stents (Resolute Integrity, X
- Prolonged DAPT in patients with ACS without excessive risk of bleeding should remain the standard of care

Hahn et al. Lancet 2018;391:1274-84

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What is different about ACS?

- Acute coronary syndromes reflect a systemic thromboinflammatory state, and multiple plaque ruptures, and vulnerable plaques likely require longer DAPT to prevent future ischaemic events in non-stented regions

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Optimal DAPT in ACS - shorter, longer?

From a patient's perspective

- Preventing an ischaemic event with an optimised antithrombotic strategy will be under-appreciated from the patient's point of view
- While causing a major bleed (or even minor bleeding), would be attributed to treatment

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Optimal DAPT in ACS - shorter, longer?

- Prolonged DAPT (12 months) should remain the standard of care after ACS in patients undergoing PCI
- Provided bleeding risk is not high

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Optimal DAPT in ACS - shorter, longer?

- Prolonged DAPT (12 months) should remain the standard of care after ACS in patients undergoing PCI
- Provided bleeding risk is not high
- Attention to adherence is very important
- Additionally other *risk* factors should be treated (quit smoking, BP < 130mmHg, exercise) including getting LDL < 1.4mmol/L

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Meta-analysis of extended DAPT trials

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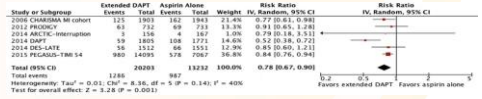
Meta-analysis: Risk of major adverse cardiovascular events DAPT vs. aspirin



Udell JA. et al. Eur Heart J. 2016;37:390-9

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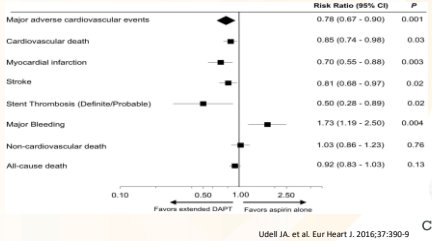
Meta-analysis: Risk of individual cardiovascular and bleeding endpoints comparing extended DAPT vs. aspirin



Udell JA. et al. Eur Heart J. 2016;37:390-9

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ACC / AHA vs ESC guidelines

- The rapid evolution of the field of antithrombotic pharmacotherapy, in an ever-changing landscape of safer stents, bleeding avoidance strategies, and newer drugs for secondary prevention, requires regular updates of recommendations for DAPT
- A common and important theme in both updates is the shift from a population-based treatment approach to one that is more “patient-centred”

Capodanno D et al. JACC 2018; 72:2915-31

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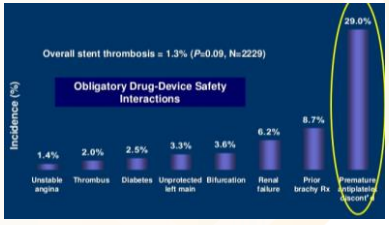
DES introduced 2003 Recommendations: 3-6 months of DAPT



Lakovou L et al. JAMA. 2005;293:2126

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More recent trials of DAPT

- Hong SJ(Everolimus) JACC Cardiovasc Intv 2016;9:1438-46
- Optima EuroIntervention 2018;13:1923-30
- Giustino G(Complex PCI) JACC 2016;68:1851-64
- DAPT-STEMI (6 vs 12 months): Non Inferior (few events)
- REDUCE (3 vs 12 months) non inferior
- SMART-DATE Non inferior (↑ MI) Lancet 2018;391:1274-84)

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Risk score for stent thrombosis

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Risk score for 1-year definite/probable stent thrombosis in patients with ACS

Variable	Integer Assignment for ST Risk Score Calculation			Add to Score
Type of ACS	NSTE-ACS w/o ST-segment changes: +1	NSTE-ACS with ST-segment deviation: +2	STEMI: +4	
Current smoking	Yes: +1	No: +0		
Insulin-treated diabetes mellitus	Yes: +2	No: +0		
History of PCI	Yes: +1	No: +0		
Baseline platelet count, K/μl	<250: +0	250–400: +1	>400: +2	
Absence of early (pre-PCI) heparin*	Yes: +1	No: 0		
Aneurysm or ulceration	Yes: +2	No: 0		
Baseline TIMI flow grade 0/1	Yes: +1	No: 0		
Final TIMI flow grade <3	Yes: +1	No: 0		
Number of vessels treated	1: +0	2: +1	3: +2	
ST risk score:				

*Includes parenteral heparin or low molecular weight heparin.
ACS = acute coronary syndrome; (a) NSTE-ACS = Non-ST-segment elevation acute coronary syndrome; STEMI = ST-segment elevation myocardial infarction; other abbreviations as in Tables 1 and 2.

Dangas, White et al. JACC 2012;11:1097-105

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Choice of stent

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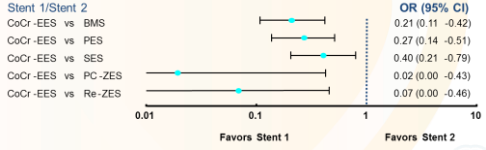
Network meta-analysis (n>50,000) Early (≤30 days) definite stent thrombosis



CoCr-EES denotes cobalt-chromium everolimus-eluting stents; PtCr-EES denotes platinum-chromium everolimus-eluting stents; PES denotes paclitaxel-eluting stents; SES denotes sirolimus-eluting stents; BMS denotes bare metal stents; Re-ZES denotes the Resolute zotarolimus-eluting stents; PC-ZES denotes phosphorylcholine polymer-based zotarolimus-eluting stents.

Palmerini T. et al., Lancet 2012. 379:1393-402

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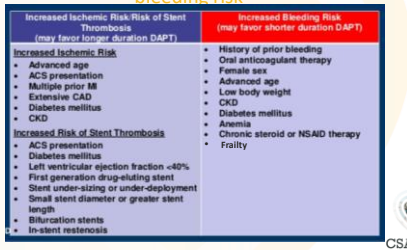
Factors associated with increased ischaemic risk or increased bleeding risk



Increased Ischemic Risk/Risk of Stent Thrombosis (may favor longer duration DAPT)	Increased Bleeding Risk (may favor shorter duration DAPT)
Increased Ischemic Risk • Advanced age • ACS presentation • Multiple prior MI • Extensive CAD • Diabetes mellitus • CKD	• History of prior bleeding • Oral anticoagulant therapy • Female sex • Advanced age • Low body weight • CKD • Diabetes mellitus • Anemia • Chronic steroid or NSAID therapy • Frailty
Increased Risk of Stent Thrombosis • ACS presentation • Diabetes mellitus • Left ventricular ejection fraction <40% • First generation drug-eluting stent • Stent under-sizing or under-deployment • Small stent diameter or greater stent length • Bifurcation stents • In-stent restenosis	

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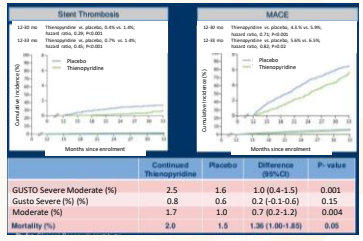
DAPT Trial



	Continued Thienopyridine	Placebo	Difference (95%CI)	P- value
GUSTO Severe Moderate (%)	2.5	1.6	1.0 (0.4-1.5)	0.001
Gusto Severe (%) (%)	0.8	0.6	0.2 (-0.1-0.6)	0.15
Moderate (%)	1.7	1.0	0.7 (0.2-1.2)	0.004
Mortality (%)	2.0	1.8	1.36 (1.00-1.85)	0.05

Mauri L et. N Engl J Med. 2014;371:2155-66

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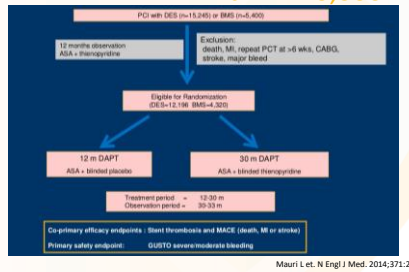
DAPT Trial: N=20,000



Mauri L et. N Engl J Med. 2014;371:2155-66

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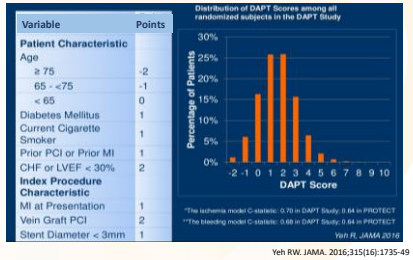
The DAPT Score – risk of ischaemia vs. bleeding



Variable	Points
Patient Characteristic	
Age	
≥ 75	-2
65 - <75	-1
< 65	0
Diabetes Mellitus	1
Current Cigarette Smoker	1
Prior PCI or Prior MI	1
CHF or LVEF < 30%	2
Index Procedure Characteristic	
MI at Presentation	1
Vein Graft PCI	2
Stent Diameter < 3mm	1

Yeh RW. JAMA. 2016;315(16):1735-49

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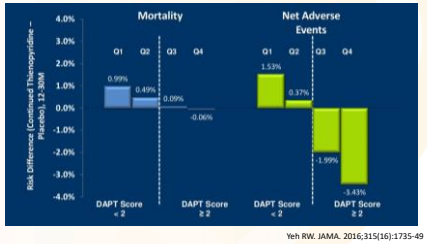
Clopidogrel beyond 1 year vs. Placebo

Treatment effect by DAPT Score Quartile (N = 11,648)



Yeh RW. JAMA. 2016;315(16):1735-49

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Guideline recommendations

- ACS
  - Use **12 months** of DAPT
  - Can use longer if no issues
  - Can use shorter if bleeding or high risk for bleeding

Yeh RW. JAMA. 2016;315(16):1735-49

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Studies of Dual Antiplatelet Duration

ACC/AHA *	ESC *	Trial	Comparison (Months)	Design
Yes	Yes	RESET (N = 2,217)	3 vs. 12	Noninferiority
Yes	Yes	OPTIMIZE (N = 2,199)	3 vs. 12	Noninferiority
Yes	Yes	EXCELLENT (N = 1,443)	6 vs. 12	Noninferiority
Yes	Yes	SECURITY (N = 1,399)	6 vs. 12	Noninferiority (halted)
Yes	Yes	ISAR-SAFE (N = 4,000)	6 vs. 12	Noninferiority (halted)
No	No	I-LOVE-IT-2 (N = 1,829)	6 vs. 12	Noninferiority
No	No	IVUS-XPL (N = 1,400)	6 vs. 12	Noninferiority
No	No	OPTIMA-C (N = 1,368)	6 vs. 12	Noninferiority
No	No	NIPPON (N = 2,772)	6 vs. 24	Noninferiority (halted)
Yes	Yes	PRODIGY (N = 1,970)	6 vs. 24	Superiority
Yes	Yes	ITALIC (N = 1,822)	6 vs. 24	Noninferiority (halted)
Yes	Yes	ARCTIC (N = 1,259)	12 vs. 18	Superiority
Yes	Yes	DAPT (N = 9,961)	12 vs. 30	Superiority
Yes	Yes	DES-LATE (N = 5,045)	12 vs. 36	Superiority
Yes	No	OPTIDUAL (N = 1,385)	12 vs. 48	Superiority (halted)

* The availability status at the time of the ACC/ AHA and ESC guidelines publication is indicated

Capodanno D et al. JACC 2018; 72:2915-31

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Studies of Dual Antiplatelet Duration

ACC/AHA *	ESC *	Trial	Comparison (Months)	Design
ACS-PCI				
No	No	DAPT-STEMI (N = 870)	6 vs. 12	Noninferiority
No	No	REDUCE (N = 1,496)	3 vs. 12	Noninferiority
No	No	SMART-DATE (N = 2,172)	6 vs. 12	Noninferiority

* The availability status at the time of the ACC/ AHA and ESC guidelines publication is indicated

Capodanno D et al. JACC 2018; 72:2915-31

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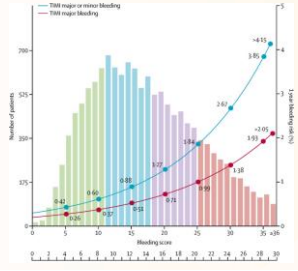
PRECISE-DAPT Score



Costa F. et al. Lancet 2017; 389:1025-34

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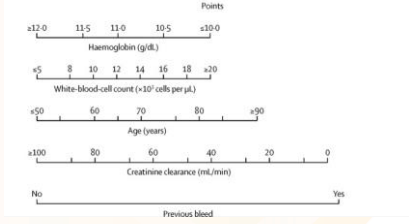
PRECISE-DAPT Score



Costa F. et al. Lancet 2017; 389:1025-34

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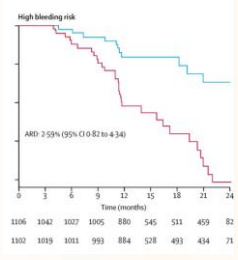
PRECISE-DAPT Score



Costa F. et al. Lancet 2017; 389:1025-34

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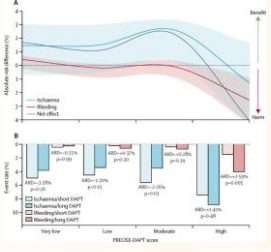
Absolute risk difference (ARD) for a long as compared with a short dual antiplatelet therapy (DAPT)



Costa F. et al. Lancet 2017; 389:1025-34

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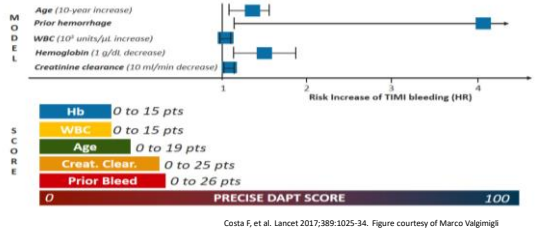
Multivariable prediction model and derivation of the score



Costa F, et al. Lancet 2017;389:1025-34. Figure courtesy of Marco Valgimigli

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Prevention of Cardiovascular Events in Patients With Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin

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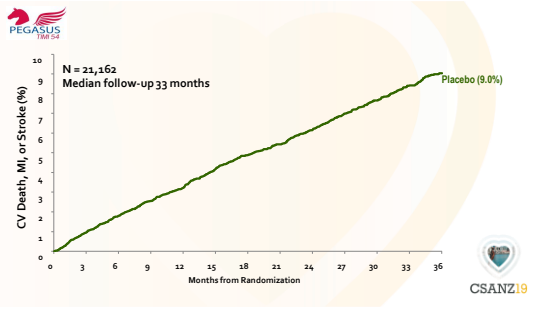
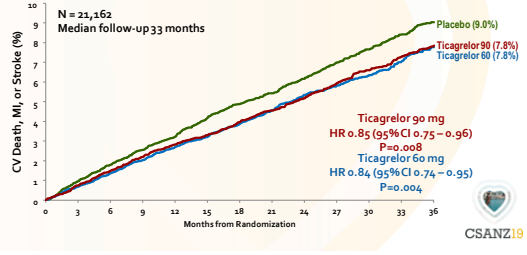


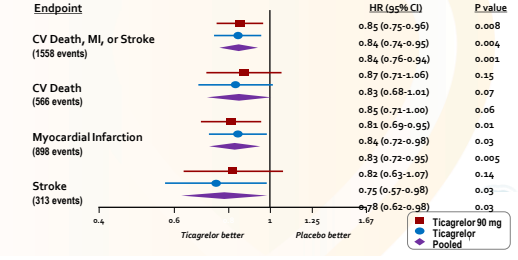
63

Components of Primary Endpoint



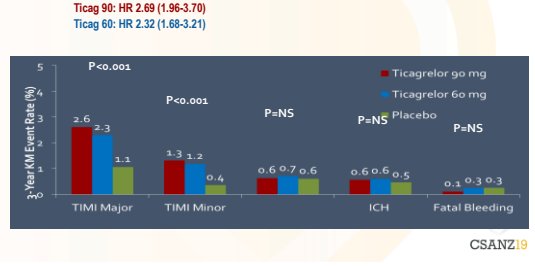
64

Components of Primary Endpoint



65

Bleeding



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Summary

- Adding ticagrelor to low-dose aspirin in stable patients with a history of MI reduced the risk of CV death, MI or stroke
- The benefit of ticagrelor was consistent
  - For both fatal & non-fatal components of primary endpoint
  - Over the duration of treatment
  - Among major clinical subgroups
- Ticagrelor increased the risk of TIMI major bleeding, but not fatal bleeding or ICH
- The two doses of ticagrelor had similar overall efficacy, but bleeding and other side effects tended to be less frequent with 60 mg bid dose

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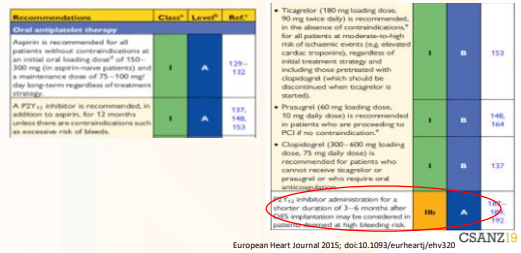
2015 ESC NSTE-ACS Guidelines

Recommendations for platelet inhibition in NSTE-ACS



European Heart Journal 2015; doi:10.1093/eurheartj/ehv320

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2015 ESC NSTE-ACS Guidelines

Recommendations for platelet inhibition in NSTE-ACS

Long-term $P2Y_{12}$ inhibition			
$P2Y_{12}$ inhibitor administration in addition to aspirin beyond 1 year may be considered after careful assessment of the ischaemic and bleeding risks of the patient.	IIb	A	184, 186

'In conclusion, while a 1-year duration of DAPT in NSTE-ACS patients is recommended, based on individual patient ischaemic and bleeding risk profiles, DAPT duration may be shortened (i.e. 3–6 months) or extended (i.e. up to 30 months) in selected patients if required.'

European Heart Journal 2015; doi:10.1093/eurheartj/ehv320

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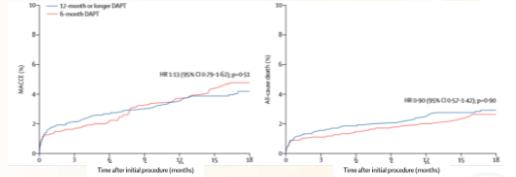
SMART-DATE: Death, MI or Stroke



Hahn et al. Lancet 2018;391:1274-84

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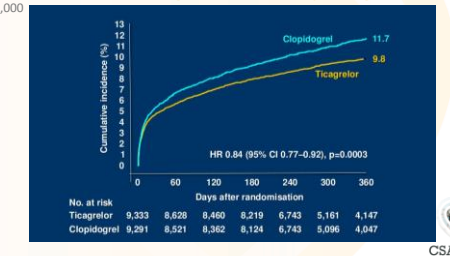
PLATO Trial – ticagrelor vs. clopidogrel in ACS

N = 18,000



Wallentin L et al. NEJM

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Duration of DAPT: Conclusion

- Patient-specific assessment for ischaemic risk
- Patient-specific assessment for bleeding risk
- Patient-specific assessment for stent thrombosis
- Need consideration of adherence issues
- Need consideration of patient preferences
- Careful clinical judgement is required

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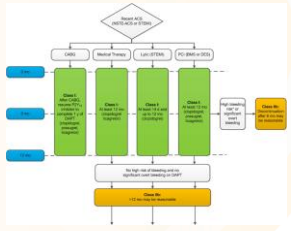
Treatment algorithm for duration of P2Y12 inhibitor therapy in patients with recent ACS (NSTE-ACS or STEMI)



Circulation. 2016 134 (10): e123-e155

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Duration of DAPT: Conclusion

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- Patient-specific assessment for bleeding risk
- Patient-specific assessment for stent thrombosis
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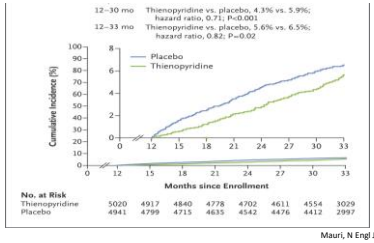
DAPT: Major Adverse Cardiovascular and Cerebrovascular Events



Mauri, N Engl J Med 2014; 371 (23) 2155-66

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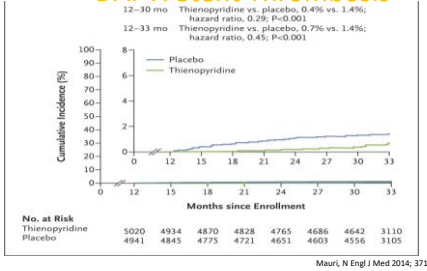
DAPT: Stent Thrombosis



Mauri, N Engl J Med 2014; 371 (23) 2155-66

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Why use shorter duration DAPT?

- DAPT increases the risk of bleeding, particularly in patients requiring oral anticoagulants
- The longer you treat with DAPT the higher the risk of bleeding (and ? mortality)
- Current generation DES, have a very very low risk of stent thrombosis, thus prolonged therapy may not be needed

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When is it safe to stop DAPT

- Not in situations where longer therapy may be needed
  - Complex PCI, prior stent thrombosis
- Situations where shorter therapy may be needed
  - Those requiring oral anticoagulants
  - Those requiring non-cardiac surgery
  - Those at high risk for bleeding

Yeh RW. JAMA. 2016;315(16):1735-49

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Ischaemic and bleeding risk assessment after myocardial infarction

- 20.6% of patients had cardiovascular death, MI, or stroke, and 5.9% major bleeding over 3.6 years, high-lighting that there is still much room for improvement in the management of this population
- All Ischaemic risk factors except 'prior MI' were associated with an increased risk of major bleeding
- 'Prior bleeding' had the highest association with increased bleeding risk

Darmon A & Ducrocq G. Heart 2019 doi: 10.1136/heartjnl-2019-315050

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Ischaemic and bleeding risk assessment after myocardial infarction

- The fact that the risk of ischaemic events increased when patients had several risk factors is not surprising
- However, the relatively small increase in bleeding risk is more unexpected

Darmon A & Ducrocq G. Heart 2019 doi: 10.1136/heartjnl-2019-315050

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SWEDE-HEART

- The majority of patients with MI had two or more established risk factors. Increasing number of risk factors was associated with higher rate of ischaemic events
- When excluding patients with prior major bleeding, bleeding incidence rate increased only minimally with increasing number of risk factors

Lindholm D et al. Heart 2019;0:1-7

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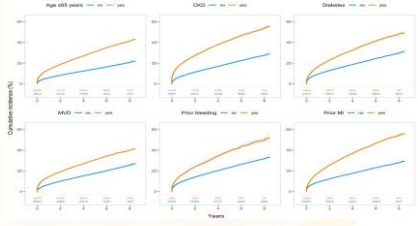
SWEDE-HEART: CVD/MI /stroke



Lindholm D et al. Heart 2019;0:1-7

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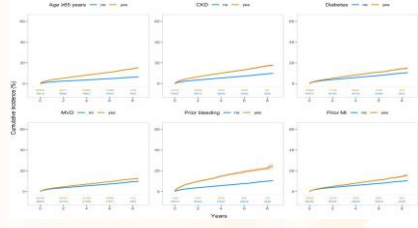
SWEDE-HEART: Major Bleeding



Lindholm D et al. Heart 2019;0:1-7

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