

## Long-term DAPT after STEMI : What do the guidelines say ?

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### Agenda

- Background
- Case study
- What is the evidence (clinical trials) ?
- What do the ESC 2017 guidelines say ?

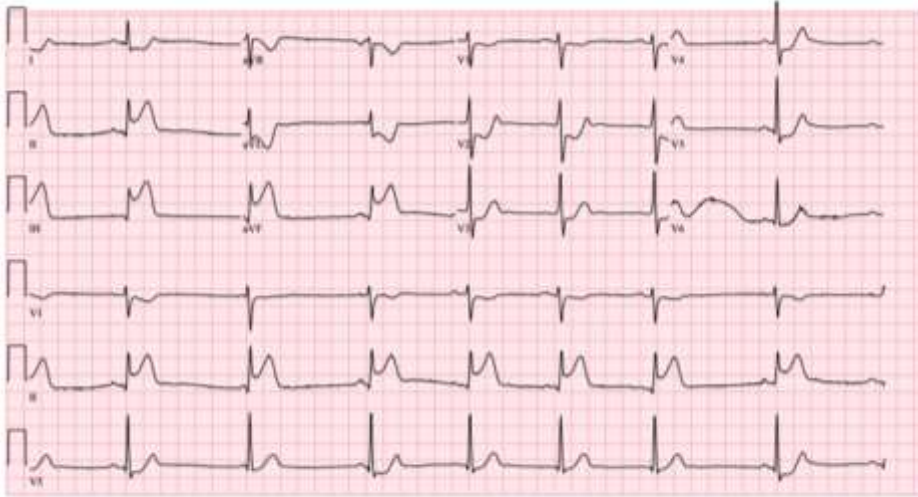
## Background

- Dual antiplatelet therapy (DAPT) with aspirin and a P2Y12 receptor inhibitor is standard therapy in patients with acute coronary syndrome (ACS) and in those undergoing drug-eluting stent (DES) implantation
- There is emerging evidence that DAPT reduces the long-term risk of non-stent-related MI as well as stroke
- DAPT has moved from a local (i.e. stent-related) to a systemic treatment strategy (i.e. capable of preventing thrombotic arterial vessel occlusion), conveying global patient protection
- The potential benefit of DAPT beyond 1 year after a MI has

## Case study

- 44 year old male
- Type 2 DM
- Dyslipidemia on atorvastatin 20 mg /d
- Obesity
- Smoker
- FH of CAD
- C/O : prolonged chest pain & sweating

## ECG



- Troponin I = 20 ng/ml
- Hb = 14 gm/dl
- WBCs = 7000 units/mcL
- Creatinine clearance = 90 ml/min

- Inferior STEMI
- Transferred to the Cath Lab after giving :
  - ASA 300mg
  - Ticagrelor 180 mg
  - Heparin 5000 U IV

## Coronary Angiography

- Normal LMT
- LAD & diagonals are normal
- Cx : normal & non dominant

## 1 Year post STEMI

- Most control of risk factors
- Kept on ticagrelor and aspirin for 12 months
- Compliant on medications without events (MI or bleeding )
- Asymptomatic
- Dual antiplatelet therapy considerations beyond 12 months ?

## Dual antiplatelet therapy considerations beyond 12 months ?

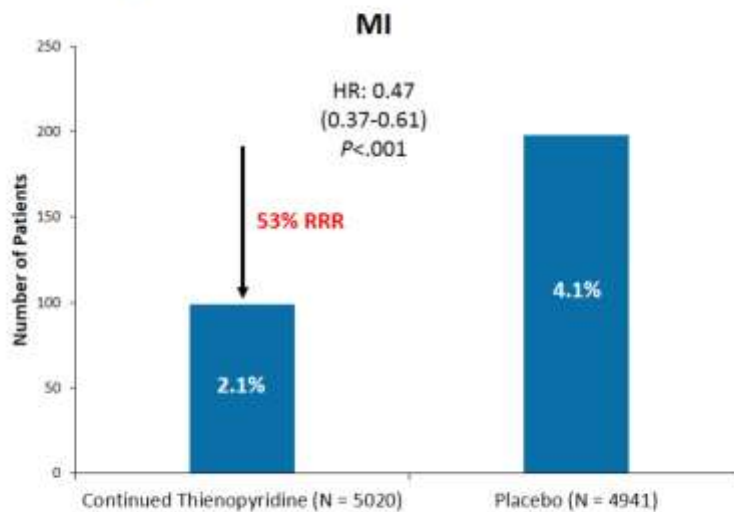
### Rationale

- In patients presenting with ACS, the cardiovascular risk remains substantially elevated beyond the first year, even if successful revascularization has been achieved
- Intensified antiplatelet therapy on top of aspirin has been shown to be an effective therapeutic strategy to prevent recurrent ischemic events but with associated bleeding risk

### Randomized controlled trials of extended dual antiplatelet therapy after stent placement

Trial (No. of patients)	Design	Follow-up	Stent thrombosis (study vs control)	MACE (study vs control)	Bleeding events (study vs control)	Conclusion
<b>DAPT</b> <sup>®</sup> (9,961)	DAPT vs aspirin alone beyond 12 months	18 months	0.4% vs 1.4% <sup>†</sup>	4.3% vs 5.9% <sup>†</sup>	2.5% vs 1.6% <sup>†</sup>	DAPT > 1 year decreased risk of stent thrombosis and MACE
<b>ARCTIC-Interruption</b> <sup>®</sup> (1,259)	DAPT vs aspirin alone beyond 12 months	17 months	0% vs 1%	4% vs 4%	1% vs < 0.5%	No benefit of DAPT beyond 12 months
<b>DES-LATE</b> <sup>®</sup> (5,045)	DAPT vs aspirin alone beyond 12 months	24 months	0.5% vs 0.3%	2.4 vs 2.6%	1.1% vs 1.4%	No benefit of DAPT for 24 more months at end of 1 year
<b>CREDO</b> <sup>®</sup> (2,116)	DAPT vs aspirin and placebo up to 12 months	12 months	Not reported	8.5% vs 11.5% <sup>†</sup>	8.8% vs 6.7% <sup>†</sup>	Significant benefit of DAPT vs placebo at 1 year
<b>OPTIMIZE</b> <sup>®</sup> (3,118)	DAPT for 3 vs 12 months	12 months	0.3% vs 0.1%	2.6% vs 2.6%	0.2% vs 0.4%	Noninferiority of 3 vs 12 months of DAPT
<b>RESET</b> <sup>®</sup> (2,117)	DAPT for 3 vs 12 months	12 months	0.2% vs 0.3%	4.7% vs 4.7%	0.5% vs 1%	Noninferiority of 3 vs 12 months DAPT
<b>EXCELLENT</b> <sup>®</sup> (1,493)	DAPT for 6 vs 12 months	12 months	0.9% vs 0.1%	8% vs 8.5%	0.3% vs 0.6%	Noninferiority of 6 vs 12 months of DAPT
<b>PRODIGY</b> <sup>®</sup> (1,970)	DAPT for 6 vs 12 months	12 months	3.9% vs 4.7%	10.1% vs 10%	1.6% vs 0.6% <sup>†</sup>	No significant benefit of 24 vs 6 months of DAPT with clopidogrel
<b>SECURITY</b> <sup>®</sup> (1,399)	DAPT for 6 vs 12 months	24 months	0.3% vs 0.4%	4.5% vs 3.7%	0.2% vs 0.3%	Noninferiority of 6 vs 12 months of DAPT

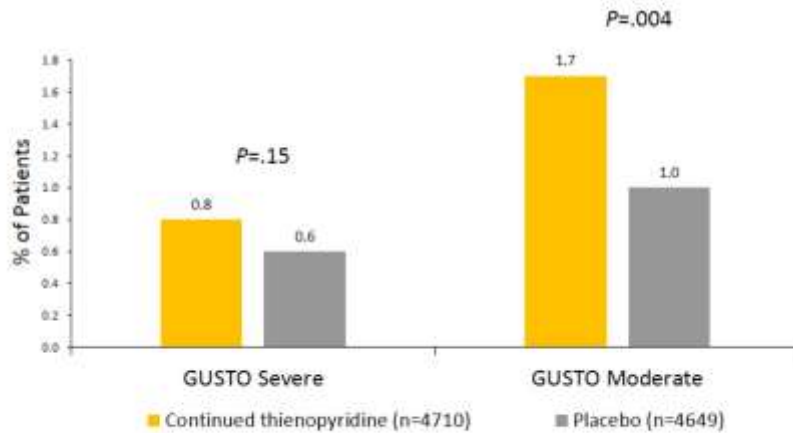
## DAPT: Long-term DAPT in DES Patients, Months 12-30



Mauri L, et al. *N Engl J Med*. 2014;371:2155-2166.

## DAPT: GUSTO Bleeding, Severe or Moderate, Months 12-30

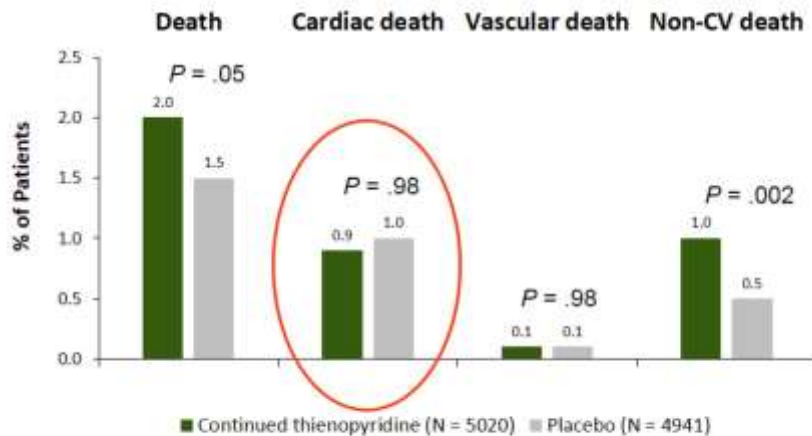
### Bleeding Complications



Mauri L, et al. *N Engl J Med.* 2014;371:2155-2166.

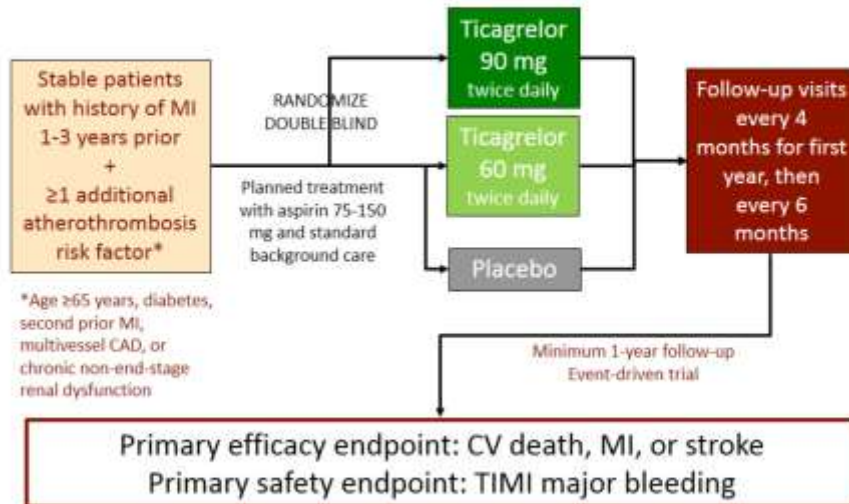
## DAPT: Mortality Outcomes

### Months 12-30



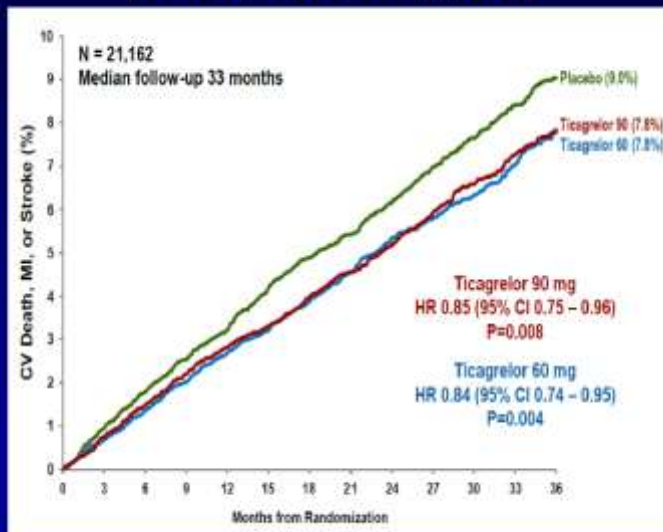
Mauri L, et al. *N Engl J Med.* 2014;371:2155-2166.

## PEGASUS-TIMI 54: Trial Design



Bonaca MP, et al. *Am Heart J.* 2014;167:437-444.

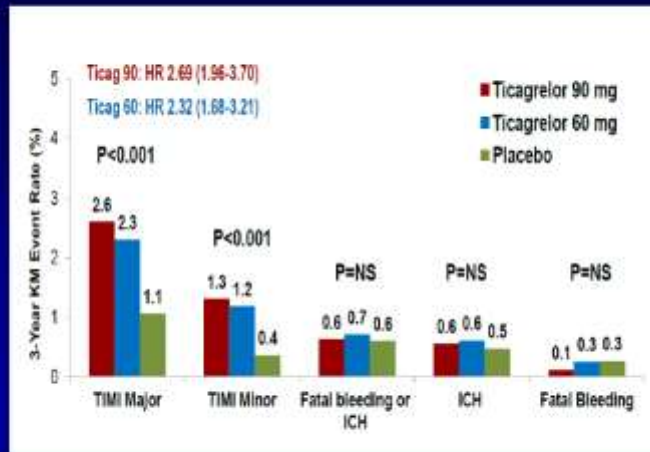
## PEGASUS – TIMI 54



Bonaca MP, Bhatt DL, Cohen M, et al. *NEJM.* 2015.

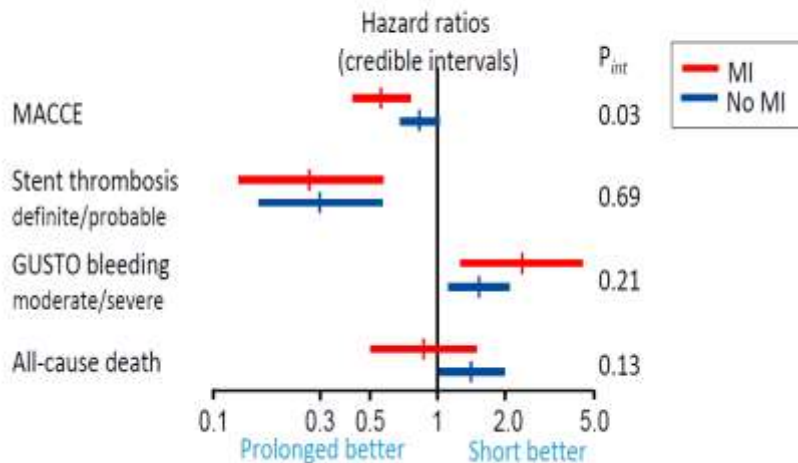


## PEGASUS – TIMI 54

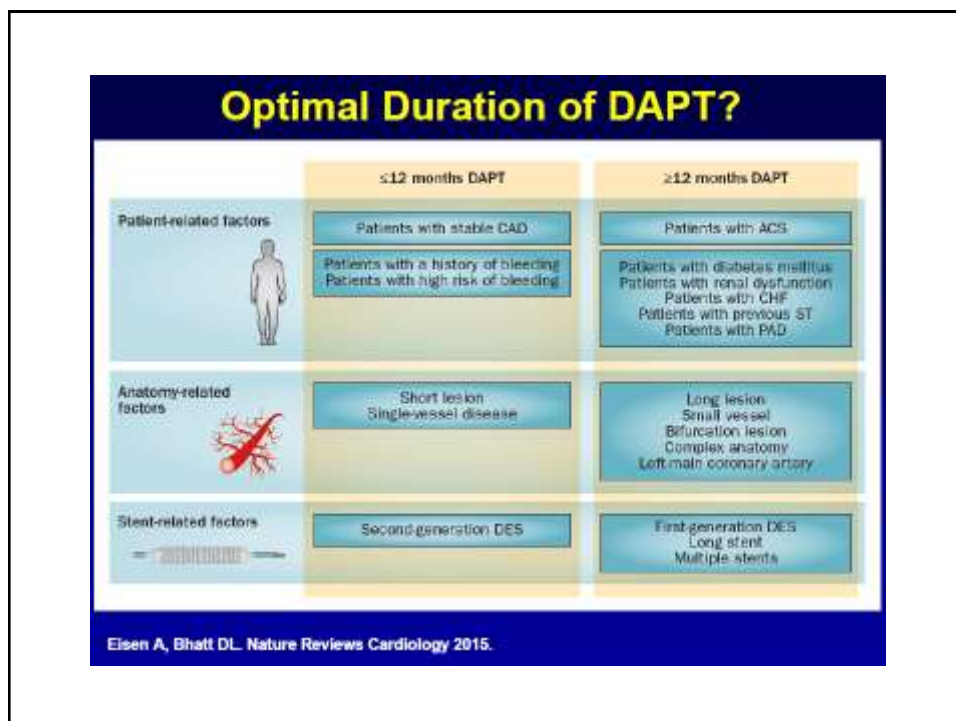
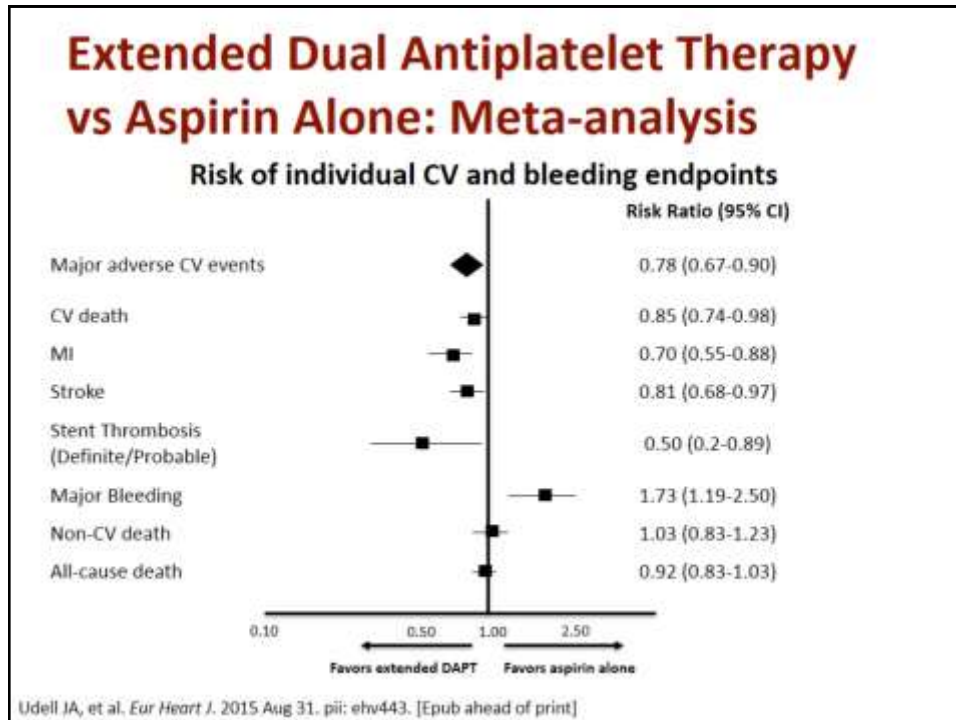


Bonaca MP, Bhatt DL, Cohen M, et al. NEJM. 2015.


## Prolonged DAPT after myocardial infarction - Benefit/risk ratio in DAPT -



Yeh RW et al., J Am Coll Cardiol 2015



## What is new in the 2017 ESC focussed update on DAPT?



### New recommendations 2017

- The occurrence of a life-threatening bleed while on DAPT should prompt reconsideration of type and duration of DAPT regimen.
- The decision for DAPT duration should be dynamic and reassessed during the course of the initially selected DAPT regimen.
- Discontinuation of P2Y<sub>12</sub> inhibitor therapy after 6 months when stenting ACS patients with PRECISE DAPT ≥ 25
- 6-month DAPT regimen in patients with SCAD treated with drug-coated balloon
- Early administration of ticagrelor/clopidogrel in NSTEMI ACS with invasive approach
- Ticagrelor 60 mg b.i.d. preferred over other oral P2Y<sub>12</sub> inhibitors for DAPT continuation >12 months in post-MI

I
  IA
  IB
  III

### New/revised concepts

- Metallic stent and DAPT duration**
- Switch between P2Y<sub>12</sub> inhibitors**
- Risk scores to guide DAPT duration**
  - PRECISE DAPT score
  - DAPT score
- Specific profiling**
  - Definition of complex PCI
  - Unfavourable profile for DAC and APT
  - Gender considerations and special populations
- DAPT duration without stenting**
  - Medical management
  - CABG or cardiac surgery
- Anticoagulation and DAPT**
  - Acute and chronic setting
  - Opening regimen

**Table 3** Risk scores validated for dual antiplatelet therapy duration decision-making

	PRECISE-DAPT score <sup>18</sup>	DAPT score <sup>18</sup>
Time of use	At the time of coronary stenting	After 12 months of uneventful DAPT
DAPT duration strategies assessed	Short DAPT (3–6 months) vs. Standard/long DAPT (12–24 months)	Standard DAPT (12 months) vs. Long DAPT (30 months)
Score calculation <sup>a</sup>	HB $\frac{100}{110} \frac{110}{120} \frac{120}{130} \frac{130}{140}$ WBC $\frac{10}{11} \frac{11}{12} \frac{12}{13} \frac{13}{14} \frac{14}{15} \frac{15}{16}$ Age $\frac{10}{20} \frac{20}{30} \frac{30}{40} \frac{40}{50}$ CrCl $\frac{100}{80} \frac{80}{60} \frac{60}{40} \frac{40}{20}$ Prior Bleeding $\frac{No}{Yes}$ Score Points $0 \ 1 \ 2 \ 4 \ 8 \ 8 \ 12 \ 14 \ 18 \ 20 \ 22 \ 24 \ 28 \ 30$	Age $\frac{<65}{65 \text{ to } <75} \frac{\geq 75}{-2 \text{ pt}}$ Cigarette smoking $\frac{+1 \text{ pt}}$ Diabetes mellitus $\frac{+1 \text{ pt}}$ MI at presentation $\frac{+1 \text{ pt}}$ Prior PCI or prior MI $\frac{+1 \text{ pt}}$ Paclitaxel-eluting stent $\frac{+1 \text{ pt}}$ Stent diameter <3 mm $\frac{+1 \text{ pt}}$ CHF or LVEF <30% $\frac{+2 \text{ pt}}$ Vein graft stent $\frac{+2 \text{ pt}}$
Score range	0 to 100 points	-2 to 10 points
Decision making cut-off suggested	Score $\geq 25 \rightarrow$ Short DAPT Score $<25 \rightarrow$ Standard/long DAPT	Score $\geq 2 \rightarrow$ Long DAPT Score $<2 \rightarrow$ Standard DAPT
Calculator	<a href="http://www.precisedaptscore.com">www.precisedaptscore.com</a>	<a href="http://www.daptscore.org">www.daptscore.org</a>

**PRECISEDAPT**

Stent implanted (type): DES  
 Stent implanted (brand):  
 Total number of stent implanted: 1  
 Intended DAPT duration: 24  
 Antiplatelet agents implemented: ASA+Ticagrelor  
 Did score calculation change your treatment duration strategy? Yes

Hemoglobin value	14.0 (g/dl)
Age	38 (years)
White blood cell count	7900 (units/mL)
Creatinine clearance	90 (ml/min)
Prior Bleeding	No
<b>PRECISE-DAPT Score</b>	<b>5</b>
<b>Risk category</b>	<b>Very Low</b>

**PRECISEDAPT**      Home   WebCalculator   Disclaimer   About   Contact Us

Hemoglobin  g/dl

Age (years)

White blood cells  units/mL

Creatinine Clearance (ml/min)

Prior Bleeding

**CALCULATE**

**12-month risk of TIMI major or minor bleeding**

PRECISE-DAPT score: 5

**RESULT**

Class of risk: **Very low**

Score Calculated: **5**

12 months risk of TIMI major or minor Bleeding: **0.4%**

12 months risk of TIMI Major Bleeding: **0.3%**


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**Also High PRECISE-DAPT Score (score 6)**

Category	Score
Major Bleeding	0.3%
Minor Bleeding	0.3%

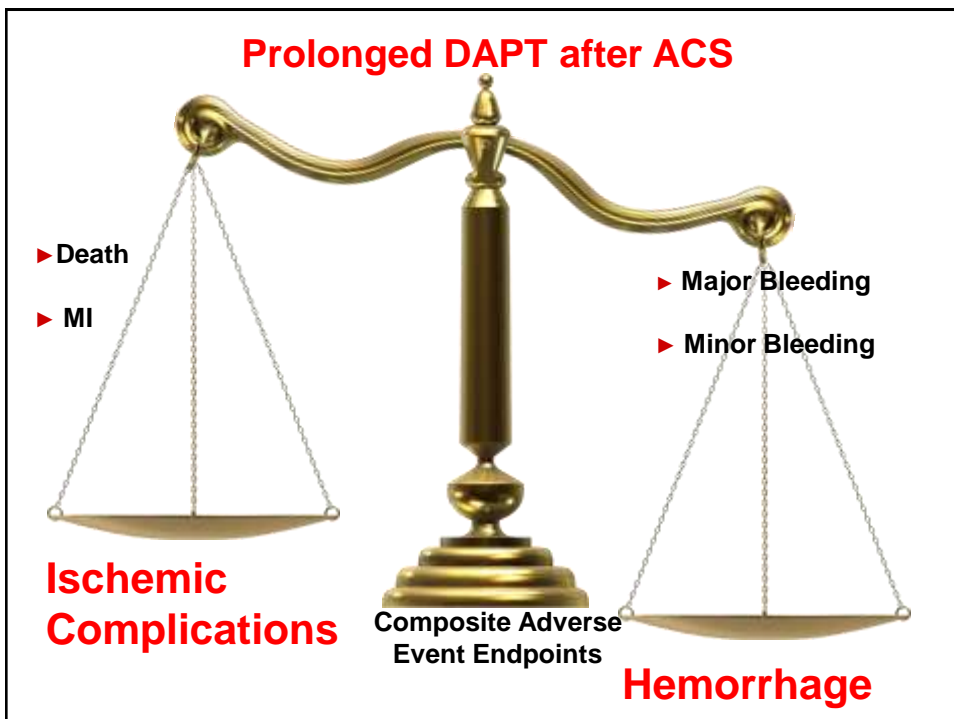
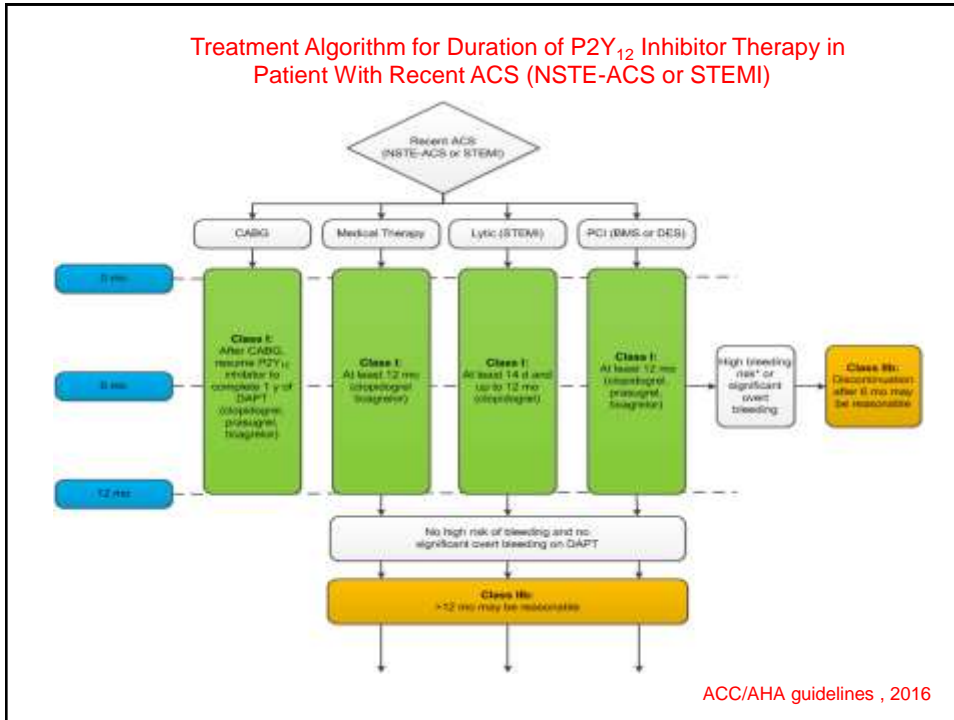
PRECISE-DAPT score 5 vs 6 comparison bar chart showing risk reduction for major and minor bleeding.

## Long-term DAPT after STEMI : What do the guidelines say ?

**DAPT Type and Duration in ACS Patients: Treatment duration after PCI** 

Recommendation	Class	Level
In patients with ACS treated with coronary stent implantation, DAPT with a P2Y <sub>12</sub> inhibitor on top of aspirin is recommended for 12 months unless there are contraindications such as excessive risk of bleeding (e.g. PRECISE-DAPT $\geq$ 25)	I	A
In patients with ACS and stent implantation who are at high risk of bleeding (e.g. PRECISE-DAPT $\geq$ 25), discontinuation of P2Y <sub>12</sub> inhibitor therapy after 6 months should be considered.	IIa	B
In patients with ACS who have tolerated DAPT without a bleeding complication, continuation of DAPT for longer than 12 months may be considered.	IIb	A
In patients with MI and high ischaemic risk who have tolerated DAPT without a bleeding complication, ticagrelor 60 mg b.i.d. for longer than 12 months on top of aspirin may be preferred over clopidogrel or prasugrel.	IIb	A

[www.escardio.org/guidelines](http://www.escardio.org/guidelines) 2017 ESC Focused Update on DAPT in Coronary Artery Disease, developed in collaboration with EACTS (European Heart Journal 2017 - doi:10.1093/eurheartj/ehx415)



## Take Home Message

- Dual antiplatelet therapy indicated for at least 1 year after ACS
- Likely benefit > 1 year in patients w/ prior MI – CHARISMA subgroup
- PEGASUS showed a significant reduction in CV death/MI/stroke but at the cost of excess bleeding
- Important to individualize therapy based on ischemic/bleeding risk

