Les nouvelles perspectives dans l'anticoagulation orale de la fibrillation atriale

Lyon, 7 Février 2019

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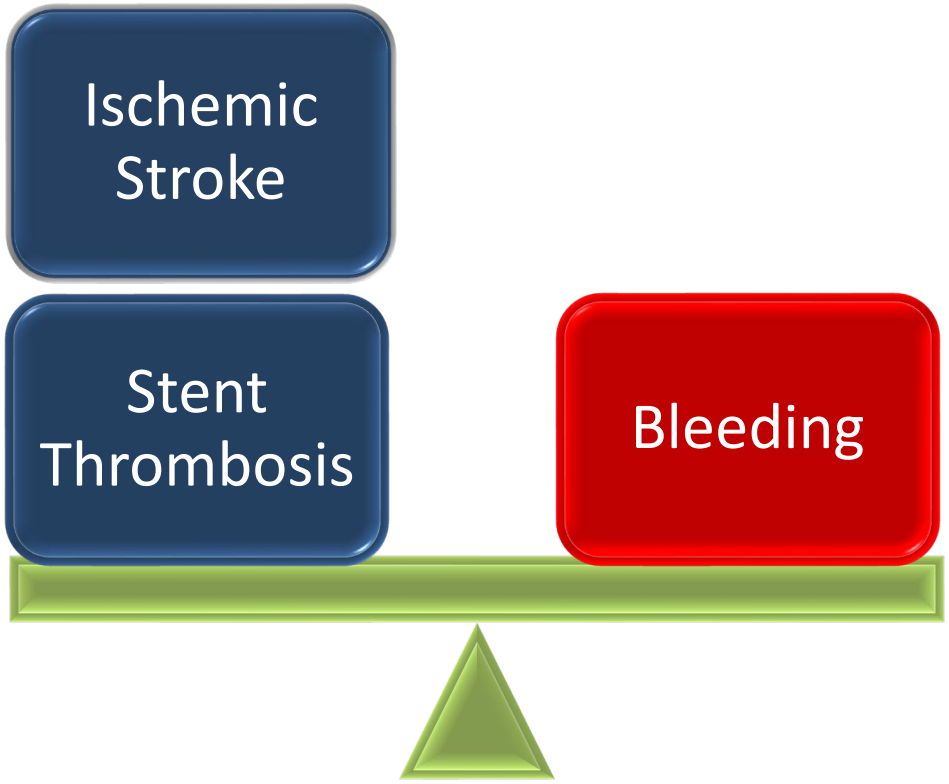
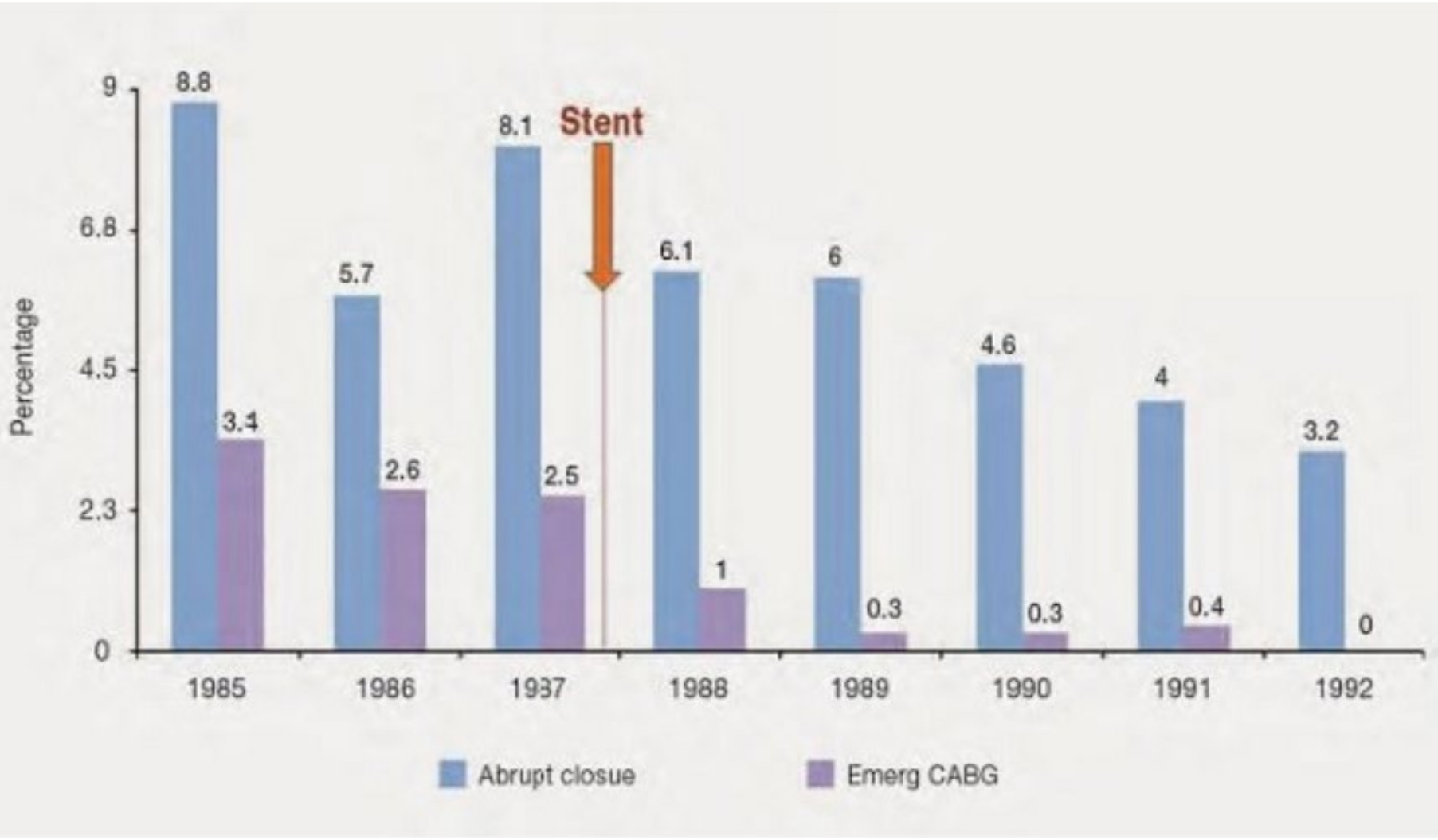
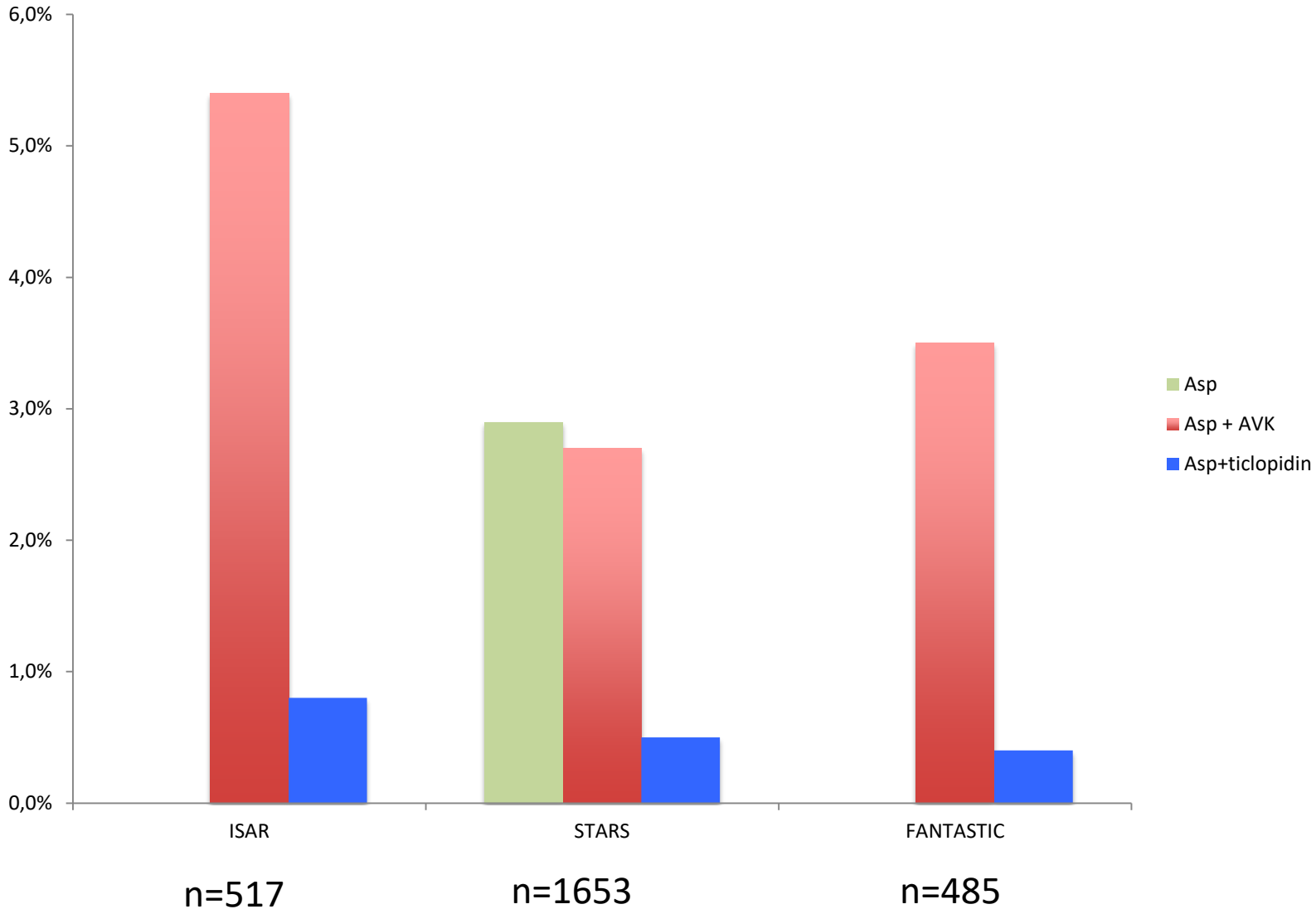
CarMeN LYON

Background

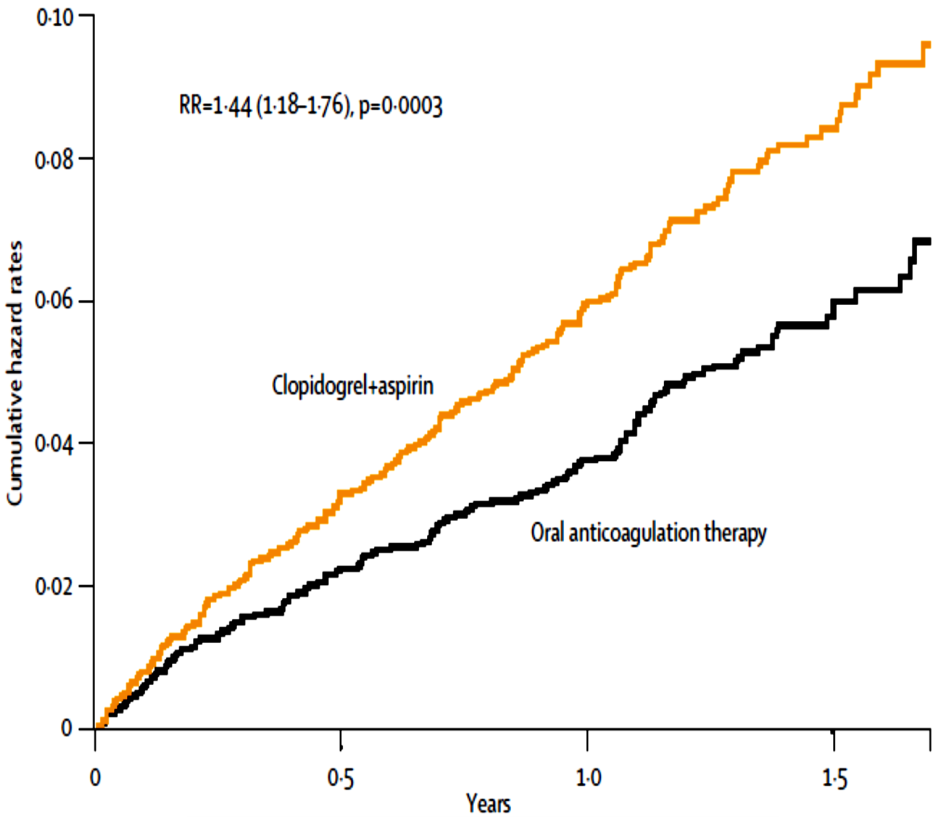
- **5-8%** of patients who undergo percutaneous coronary intervention (PCI) have atrial fibrillation
- **20–30%** of patients with AF and an indication for continuous OAC have coexisting CAD




Percentage
9
6.8
4.5
2.3
0
8.8
3.4
5.7
2.6
8.1
2.5
Stent
6.1
1
6
0.3
4.6
0.3
4
0.4
3.2
0
1985
1986
1987
1988
1989
1990
1991
1992
Abrupt closue
Emerg CABG

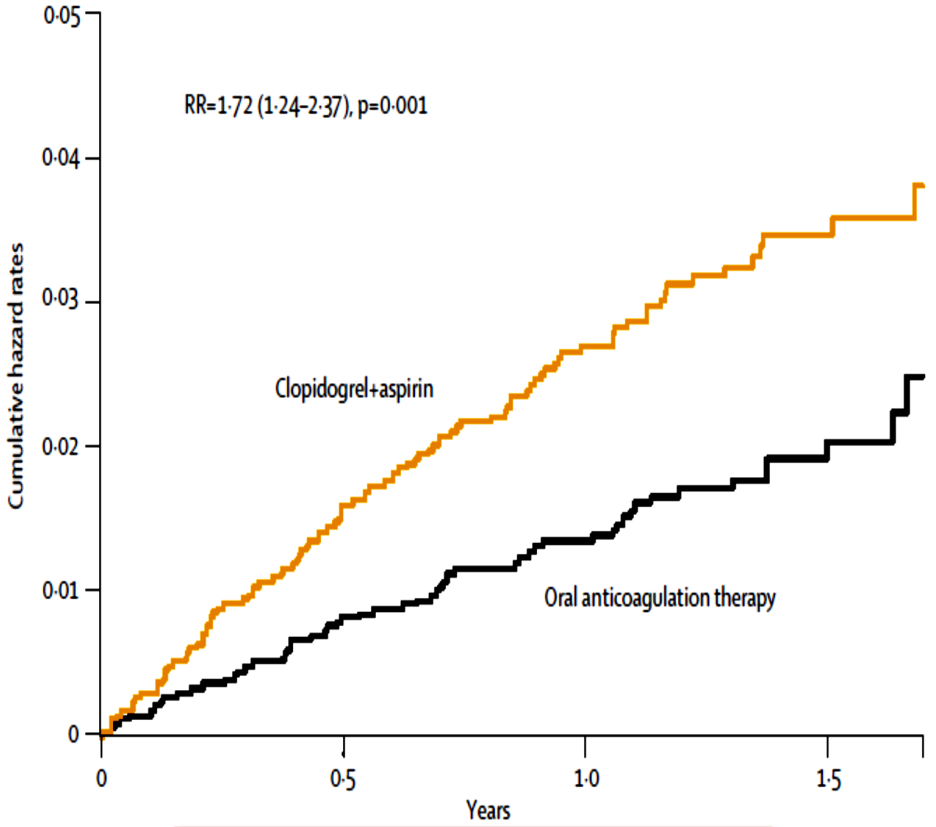

6,0%
5,0%
4,0%
3,0%
2,0%
1,0%
0,0%
ISAR
STARS
FANTASTIC
n=517
n=1653
n=485
Asp
Asp + AVK
Asp+ticlopidin

Stroke Reduction in Atrial Fibrillation



Primary Outcome

First occurrence of stroke, non-CNS systemic embolus, myocardial infarction, or vascular death

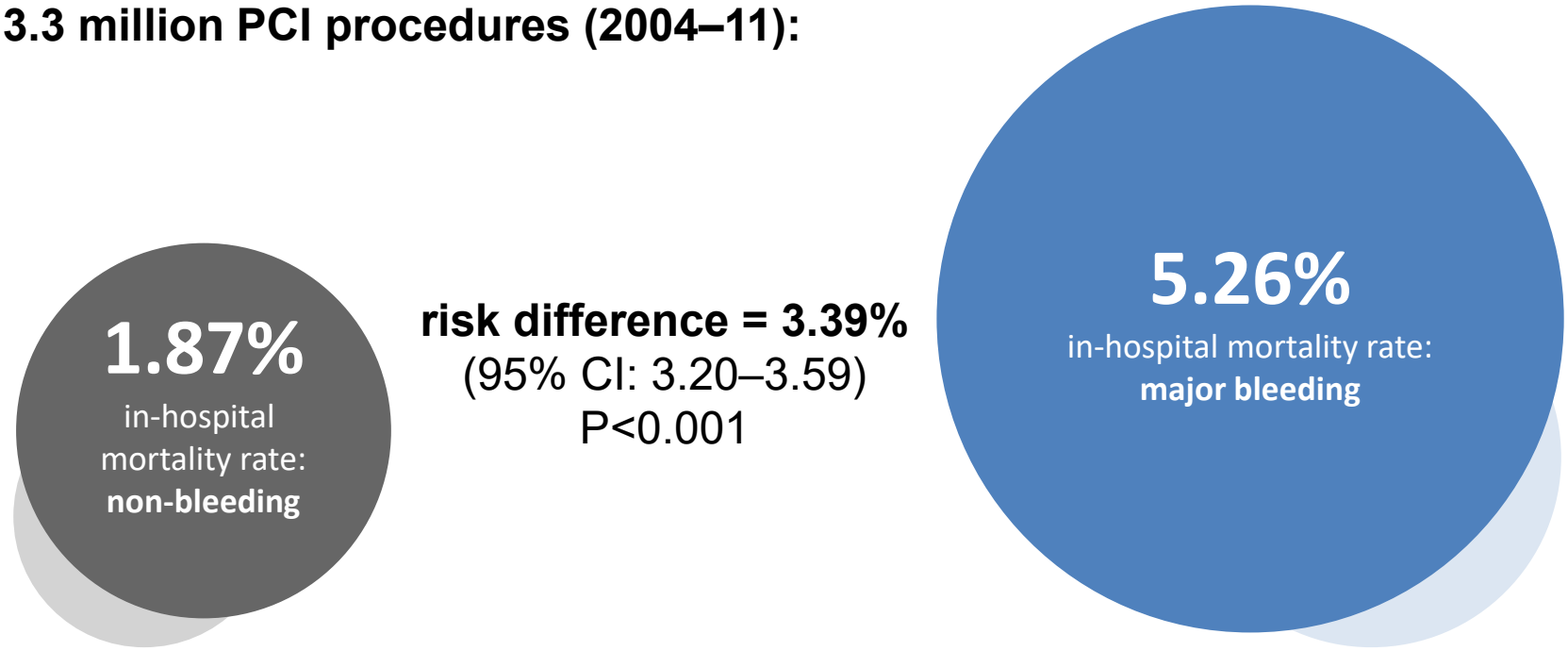


Cumulative Risk of Stroke

Lancet 2006;367:1903-12

Major bleeding was associated with a significant increase in in-hospital mortality, regardless of bleeding site

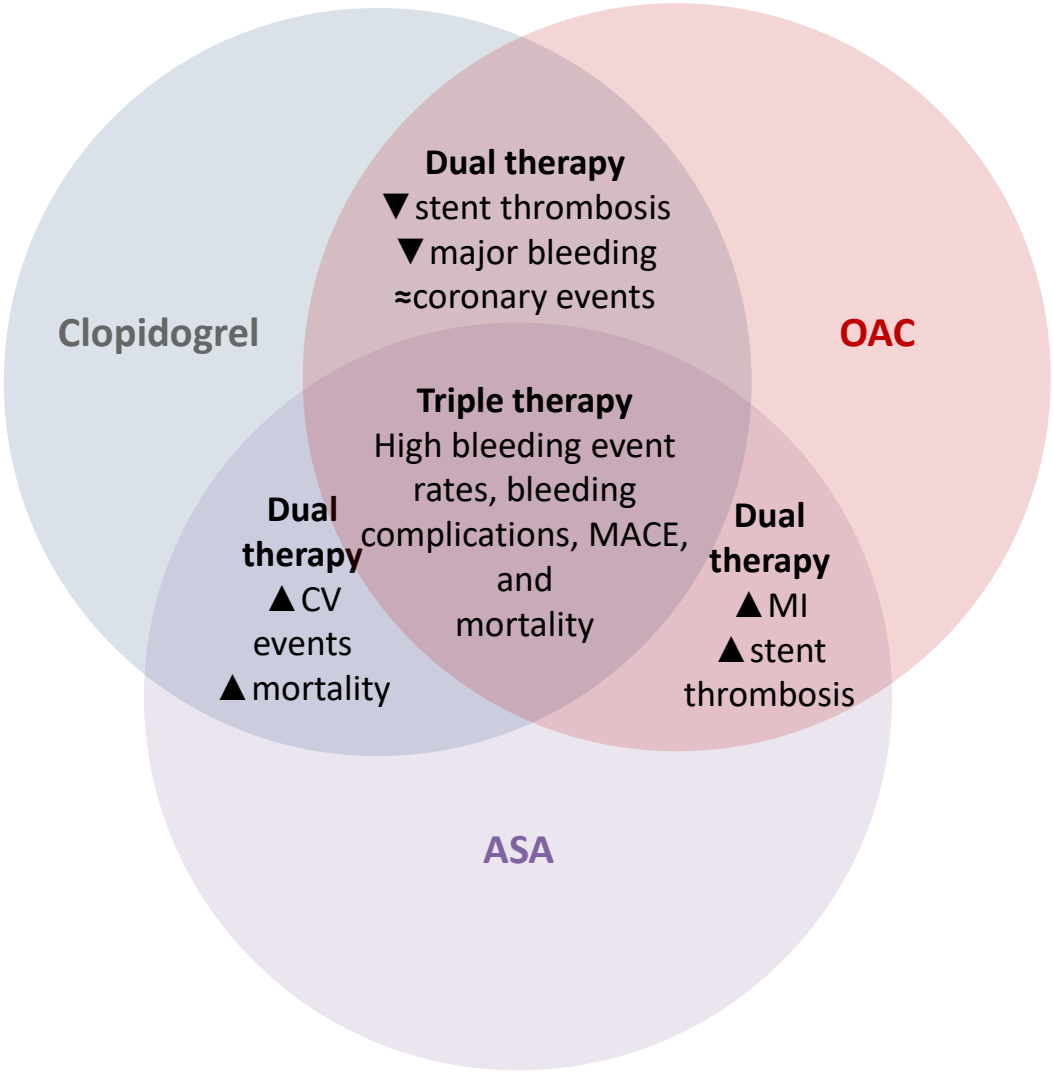
In the CathPCI registry, analysing data from 3.3 million PCI procedures (2004–11):



Bleeding is the most common non-cardiac complication of PCI

Antithrombotic therapy that minimizes the risk of bleeding complications therefore might be expected to result in better short- and long-term clinical outcomes after PCI

PCI, percutaneous coronary intervention; Chhatriwalla et al. JAMA 2013


Clopidogrel
OAC
ASA
Dual therapy
▼stent thrombosis
▼major bleeding
≈coronary events
Triple therapy
High bleeding event rates, bleeding complications, MACE, and mortality
Dual therapy
▲CV events
▲mortality
Dual therapy
▲MI
▲stent thrombosis

WOEST trial

Total number of TIMI bleeding events

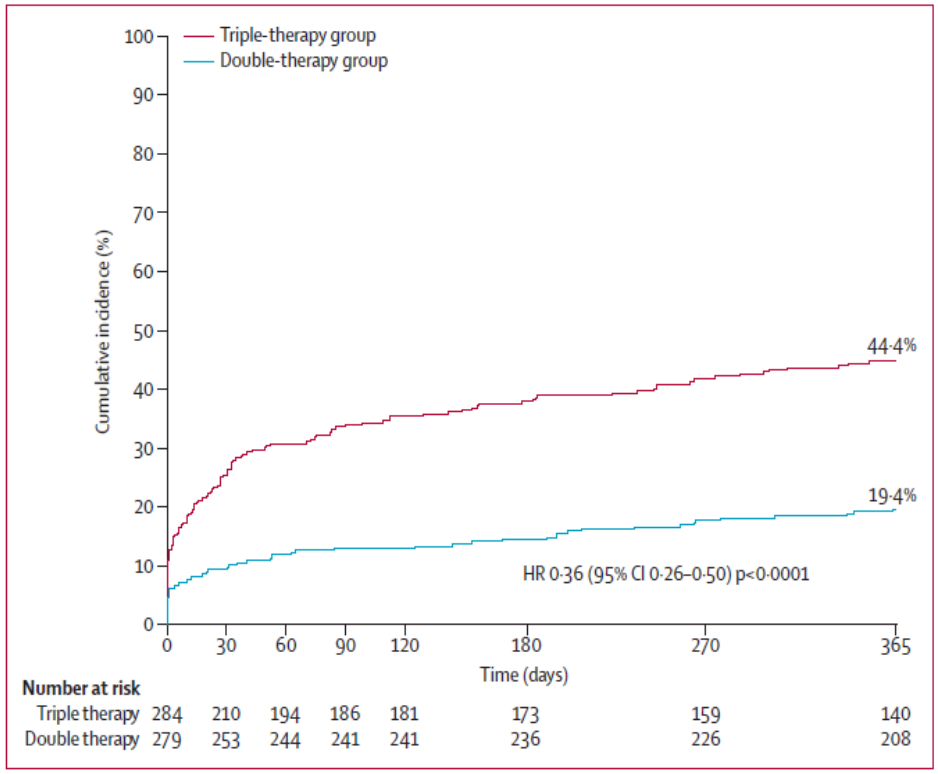


Figure 2: Incidence of the primary endpoint (any bleeding)

Death, MI, TVR, Stroke, ST

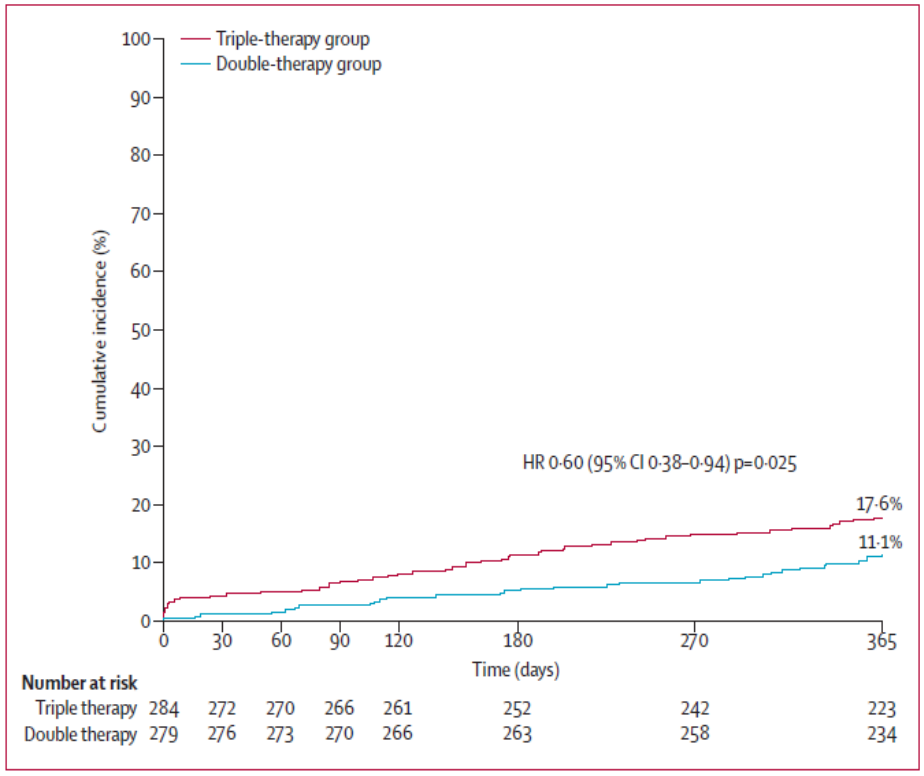


Figure 3: Cumulative incidence of the secondary endpoint (death, myocardial infarction, stroke, target-vessel revascularisation, and stent thrombosis)

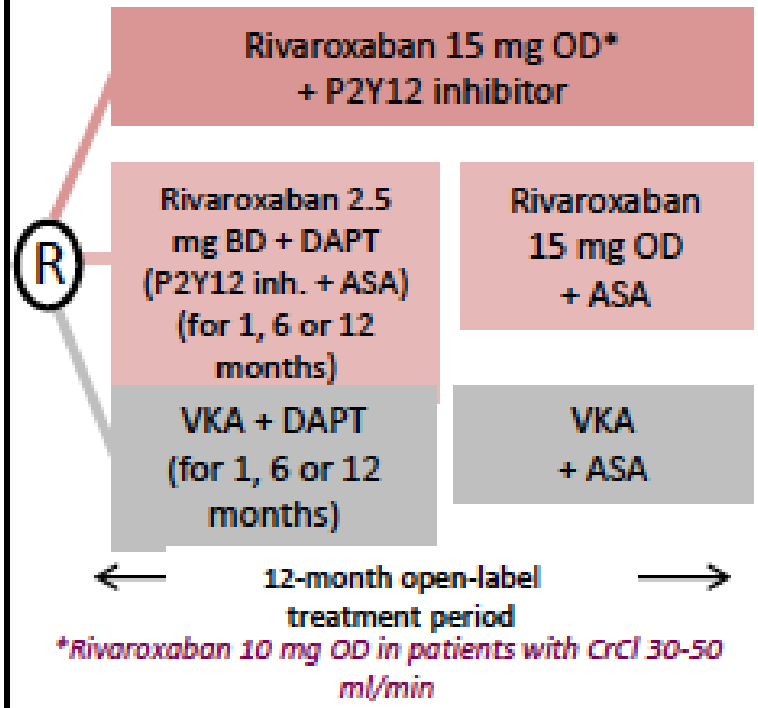
n=573 – Afib 69%

	Double therapy (n=297)	Triple therapy (n=284)	Hazard ratio (95% CI)	p value
Stroke				
Any	3 (1·1%)	8 (2·8%)	0·37 (0·10–1·40)	0·128
Stent thrombosis				
Any	4 (1·4%)	9 (3·2%)	0·44 (0·14–1·44)	0·165

De Wilde Lancet 2013

PIONEER AF-PCI (rivaroxaban)

2,100 NVAF patients with PCI



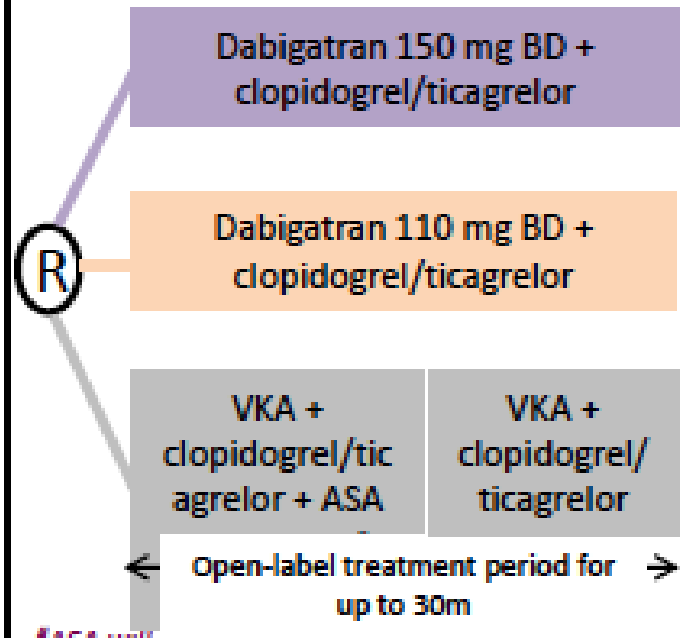
**Rivaroxaban 10 mg OD in patients with CrCl 30-50 ml/min*

Primary objective: To assess the safety of two rivaroxaban treatment strategies vs the combination of VKA with DAPT

Primary endpoint: TIMI major, minor bleeding or bleeding requiring medical attention (through 12 months)

RE-DUAL PCI (dabigatran)

2,500 NVAF patients with ACS or PCI

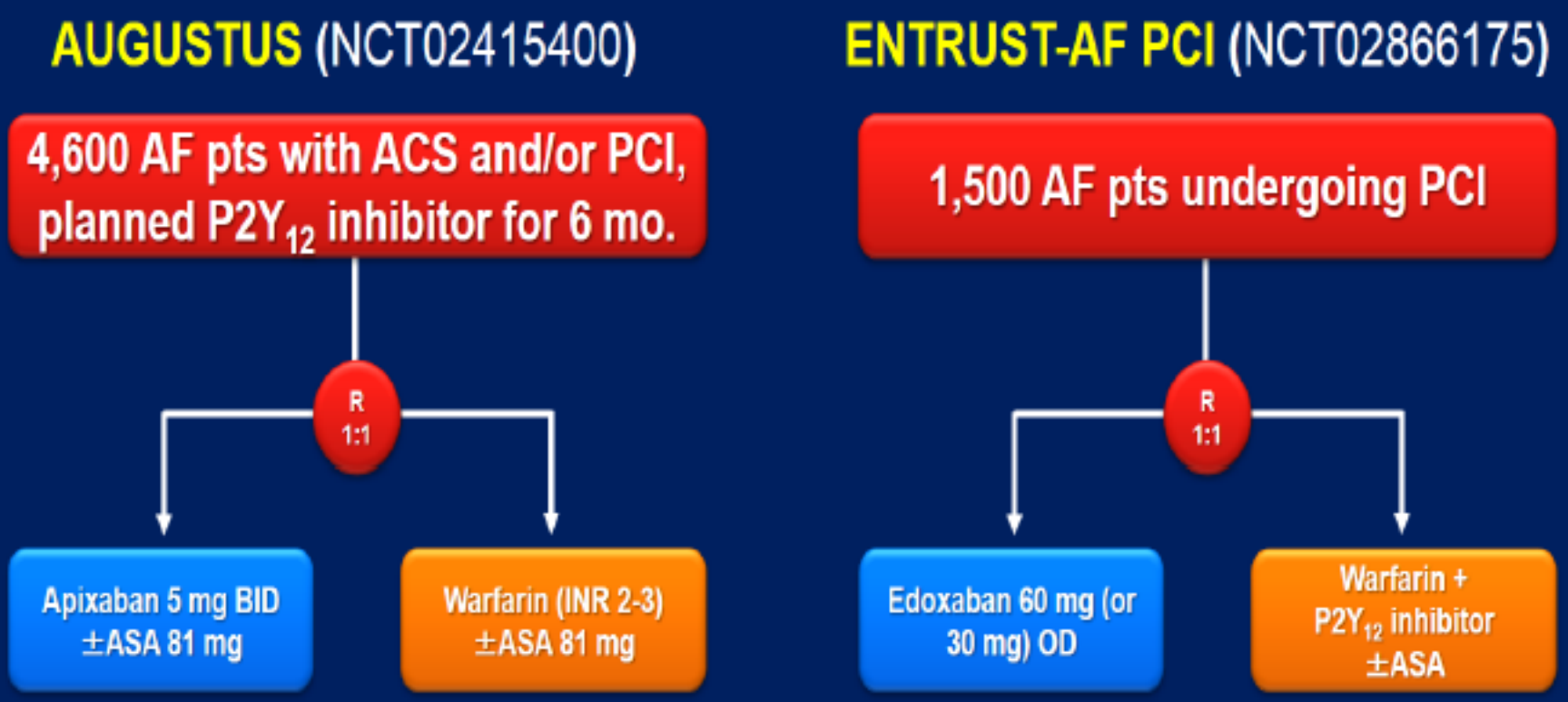


#ASA will be given for 1 month post-BMS and 3 months post-DES

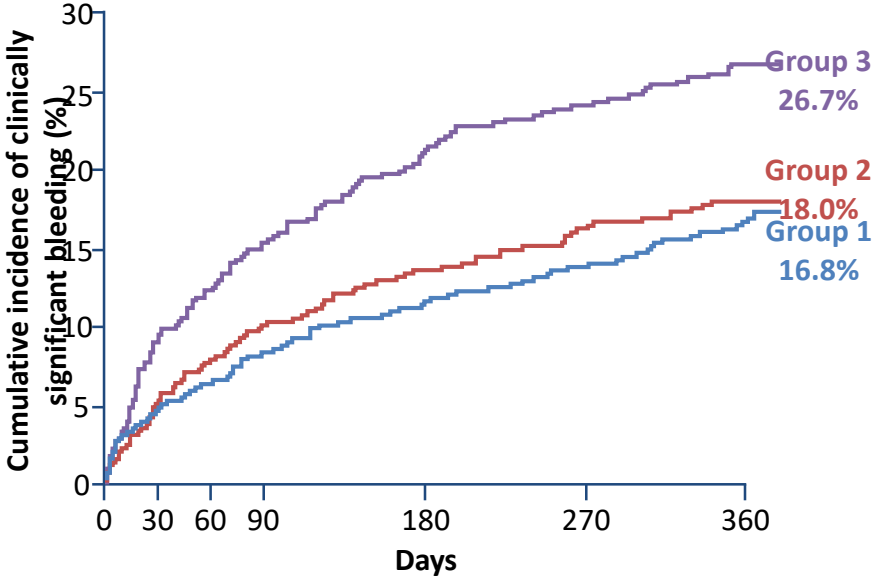
Primary objective: To show non-inferiority of two different doses of dabigatran (150mg BD and 110 mg BD) + single antiplatelet therapy (clopidogrel or ticagrelor) vs the combination of warfarin + DAPT

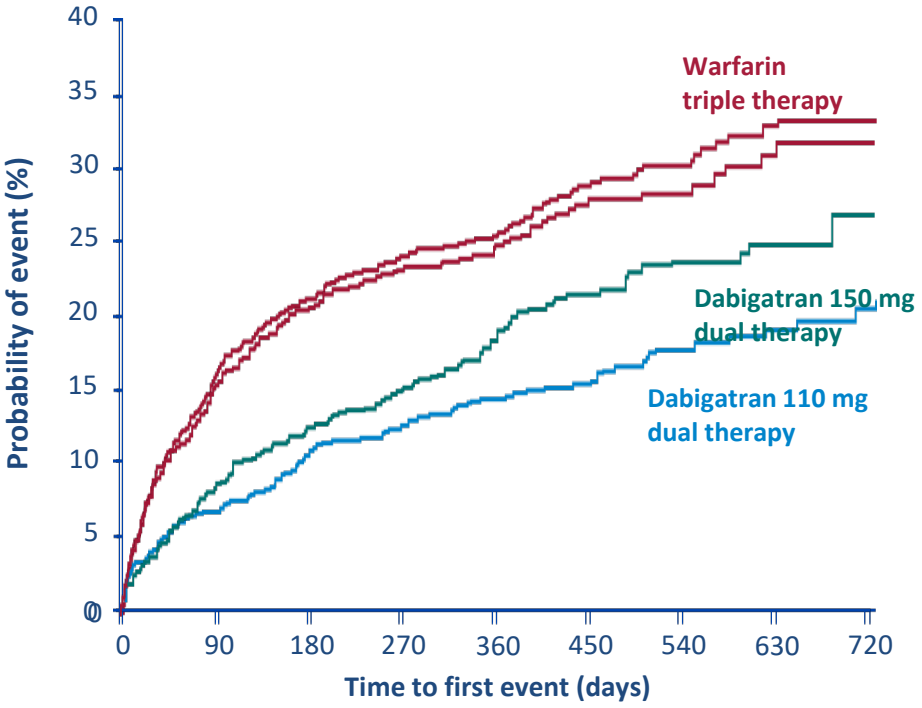
Primary endpoint: ISTH major bleeding (even-driven)

Ongoing Trials of Dropping Aspirin with NOACs (Apixaban and Edoxaban) in AF+PCI



Composite of bleeding events





PIONEER AF-PCI

n=2123

RE-DUAL-PCI

n=2725

Gibson NEJM 2016

Cannon NEJM 2017

Composite of ischaemic events

PIONEER AF-PCI

Cohort and End Point	Group 1	Group 2	Group 3	Group 1 vs. Group 3		Group 2 vs. Group 3	
	No. of Participants with Events (Kaplan–Meier Event Rate)			Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
All participants — no.	694	704	695				
Major adverse cardiovascular event	41 (6.5)	36 (5.6)	36 (6.0)	1.08 (0.69–1.68)	0.75	0.93 (0.59–1.48)	0.76
Stroke	8 (1.3)	10 (1.5)	7 (1.2)	1.07 (0.39–2.96)	0.89	1.36 (0.52–3.58)	0.53
Stent thrombosis	5 (0.8)	6 (0.9)	4 (0.7)	1.20 (0.32–4.45)	0.79	1.44 (0.40–5.09)	0.57

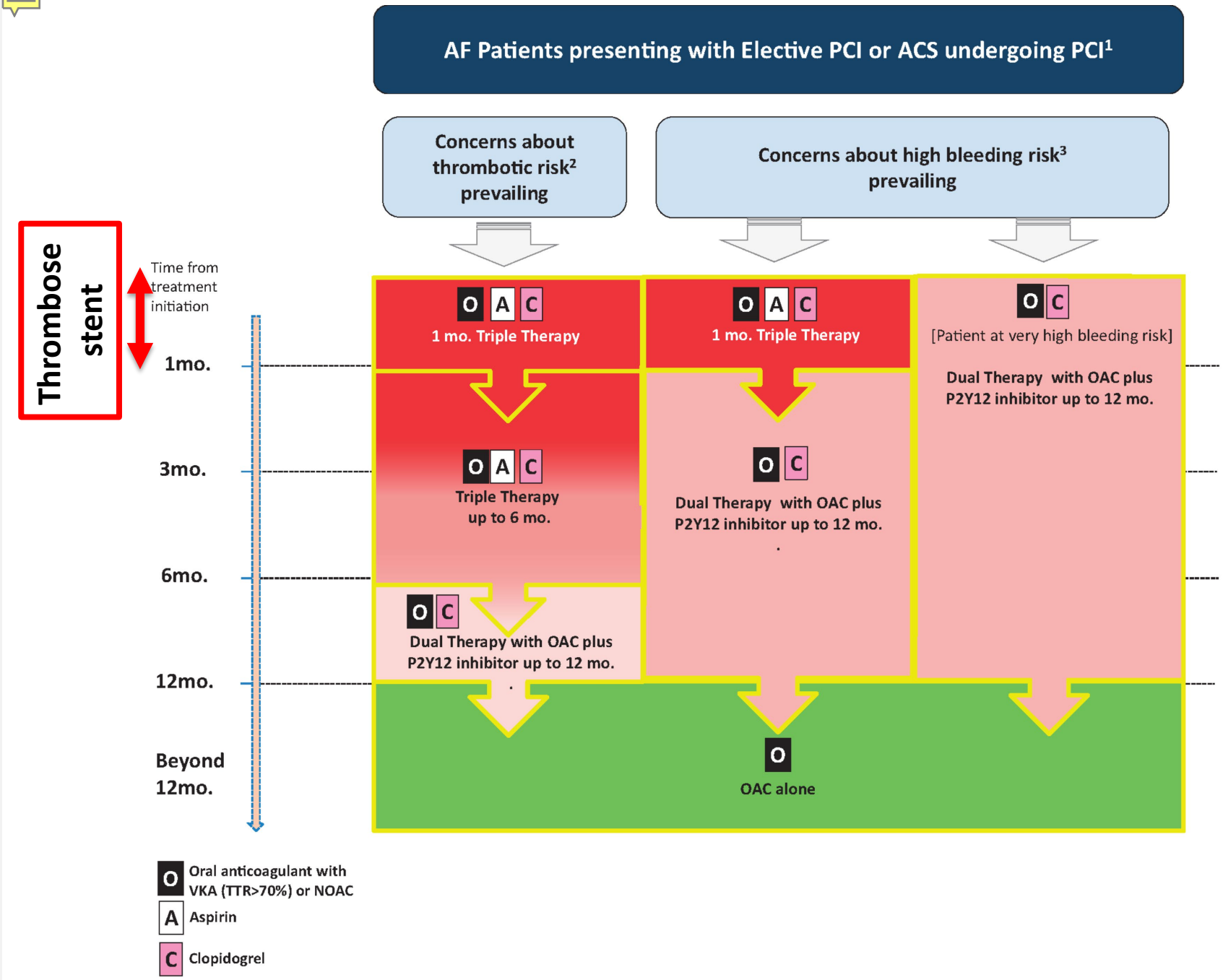
RE-DUAL-PCI

Table 3. Efficacy End Points.*

End Point	Dual Therapy with Dabigatran (Combined) vs. Triple Therapy with Warfarin				Dual Therapy with Dabigatran (110 mg) vs. Triple Therapy with Warfarin				Dual Therapy with Dabigatran (150 mg) vs. Triple Therapy with Warfarin			
	Combined Dual-Therapy Groups (N=1744)	Triple-Therapy Group (N=981)	Hazard Ratio (95% CI)	P Value†	110-mg Dual-Therapy Group (N=981)	Triple-Therapy Group (N=981)	Hazard Ratio (95% CI)	P Value†	150-mg Dual-Therapy Group (N=763)	Corresponding Triple-Therapy Group (N=764)	Hazard Ratio (95% CI)	P Value†
	no. (%)				*no. (%)*				*no. (%)*			
Composite efficacy end point: thromboembolic events, death, or unplanned revascularization	239 (13.7)	131 (13.4)	1.04 (0.84–1.29)	0.74 (0.005 for noninferiority)	149 (15.2)	131 (13.4)	1.13 (0.90–1.43)	0.30	90 (11.8)	98 (12.8)	0.89 (0.67–1.19)	0.44
Stroke					17 (1.7)	13 (1.3)	1.30 (0.63–2.67)	0.48	9 (1.2)	8 (1.0)	1.09 (0.42–2.83)	0.85
Definite stent thrombosis					15 (1.5)	8 (0.8)	1.86 (0.79–4.40)	0.15	7 (0.9)	7 (0.9)	0.99 (0.35–2.81)	0.98

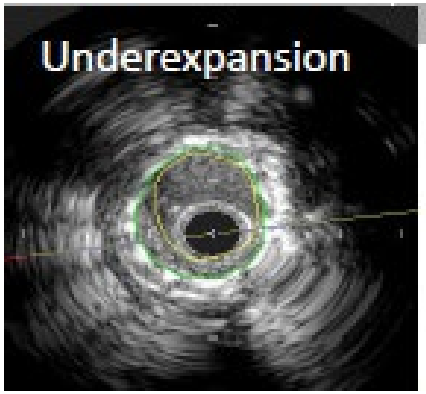
Gibson NEJM 2016

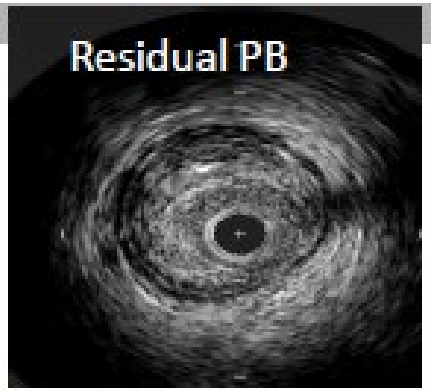
Cannon NEJM 2017

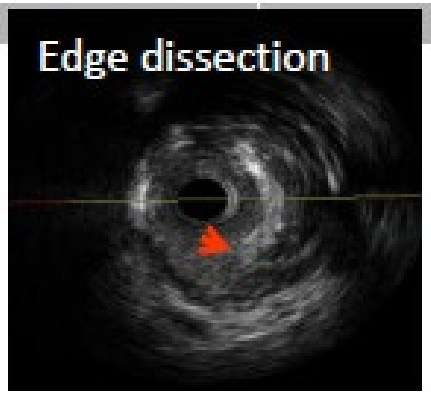


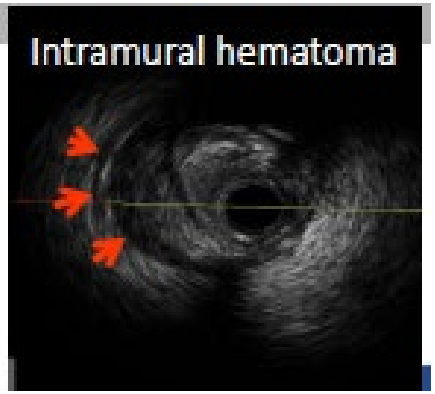
Lip Eur Heart J 2018

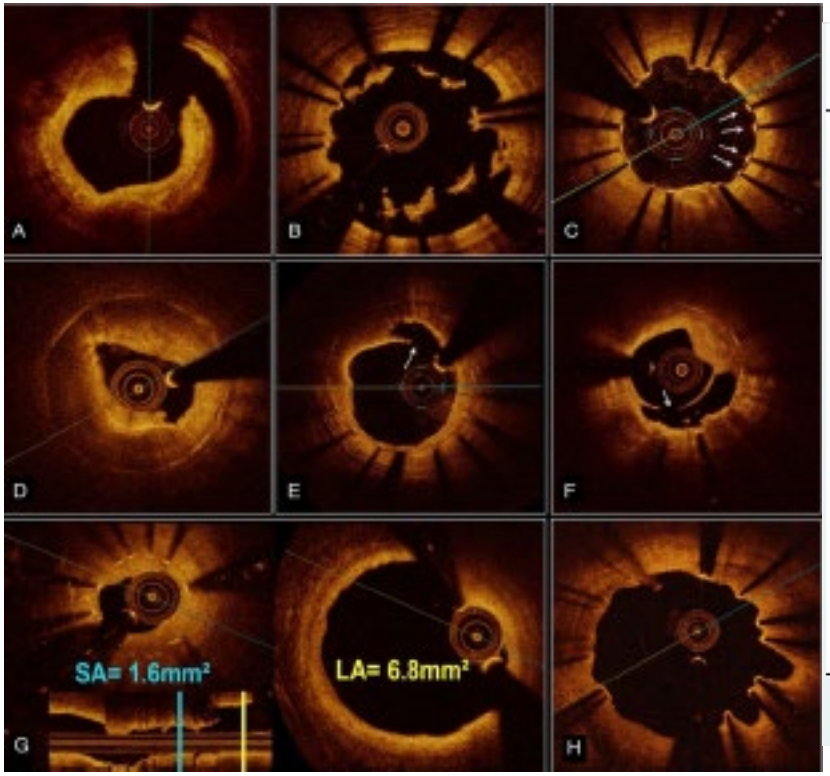
Trend in stent thrombosis (1)

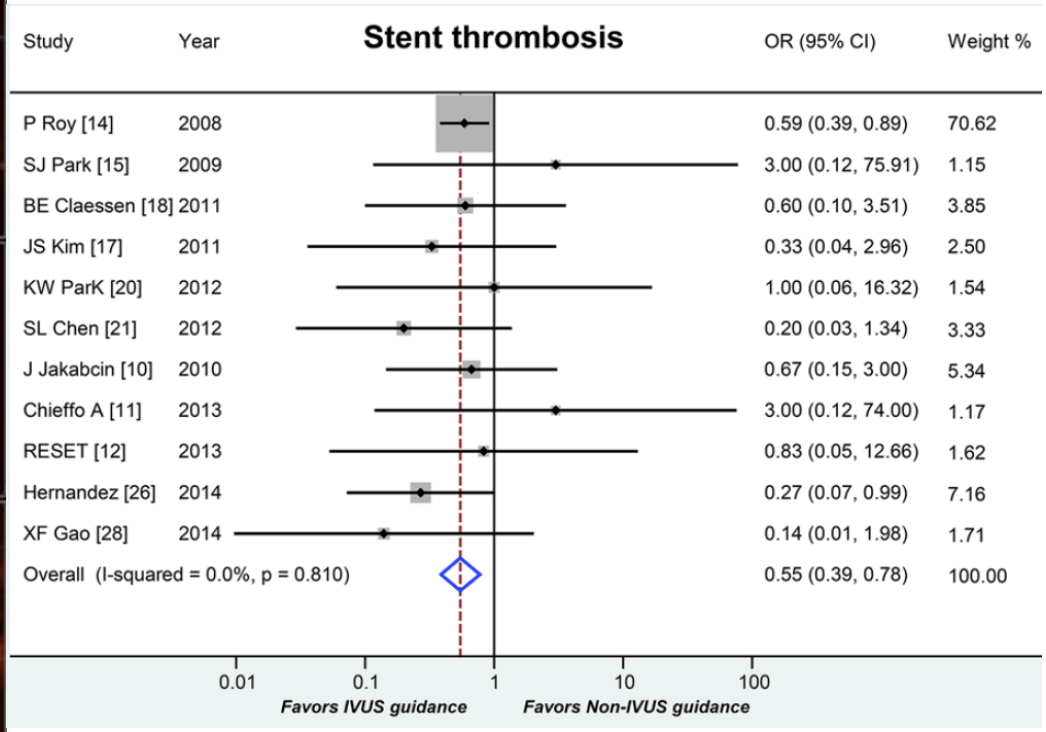






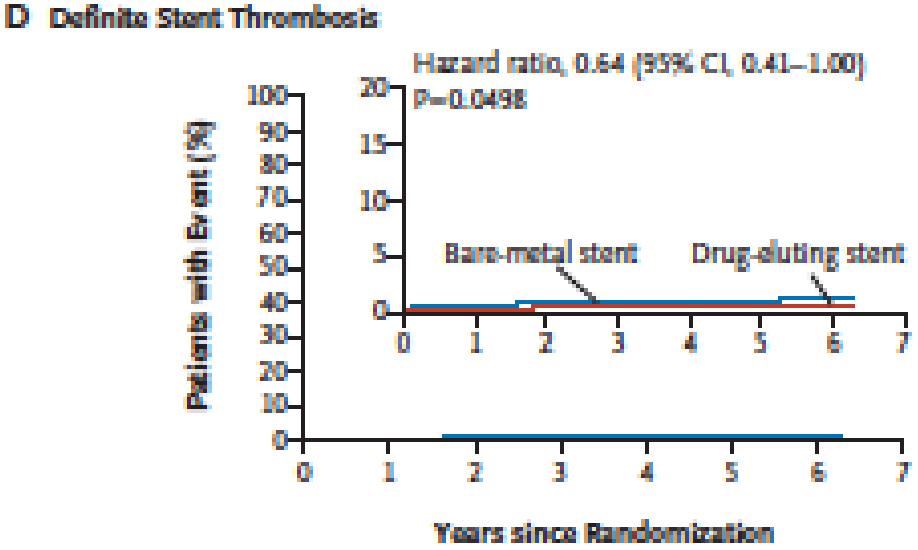


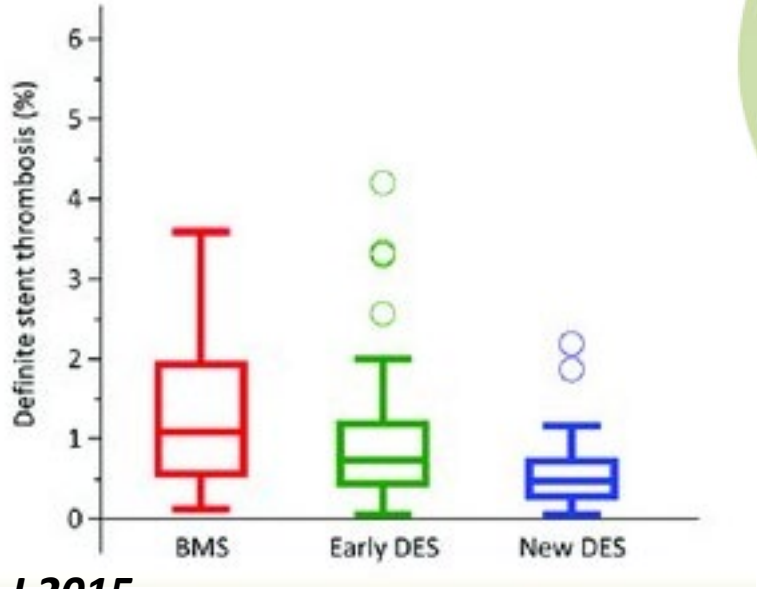


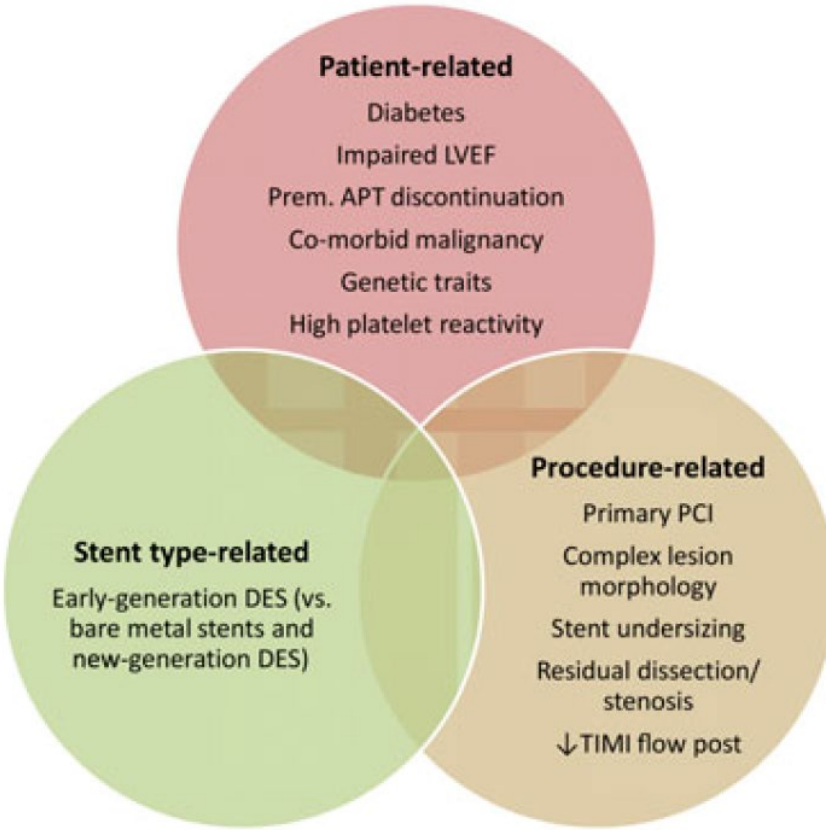


Zhang BMC Cardiovasc Dis 2015

Trend in stent thrombosis (2)

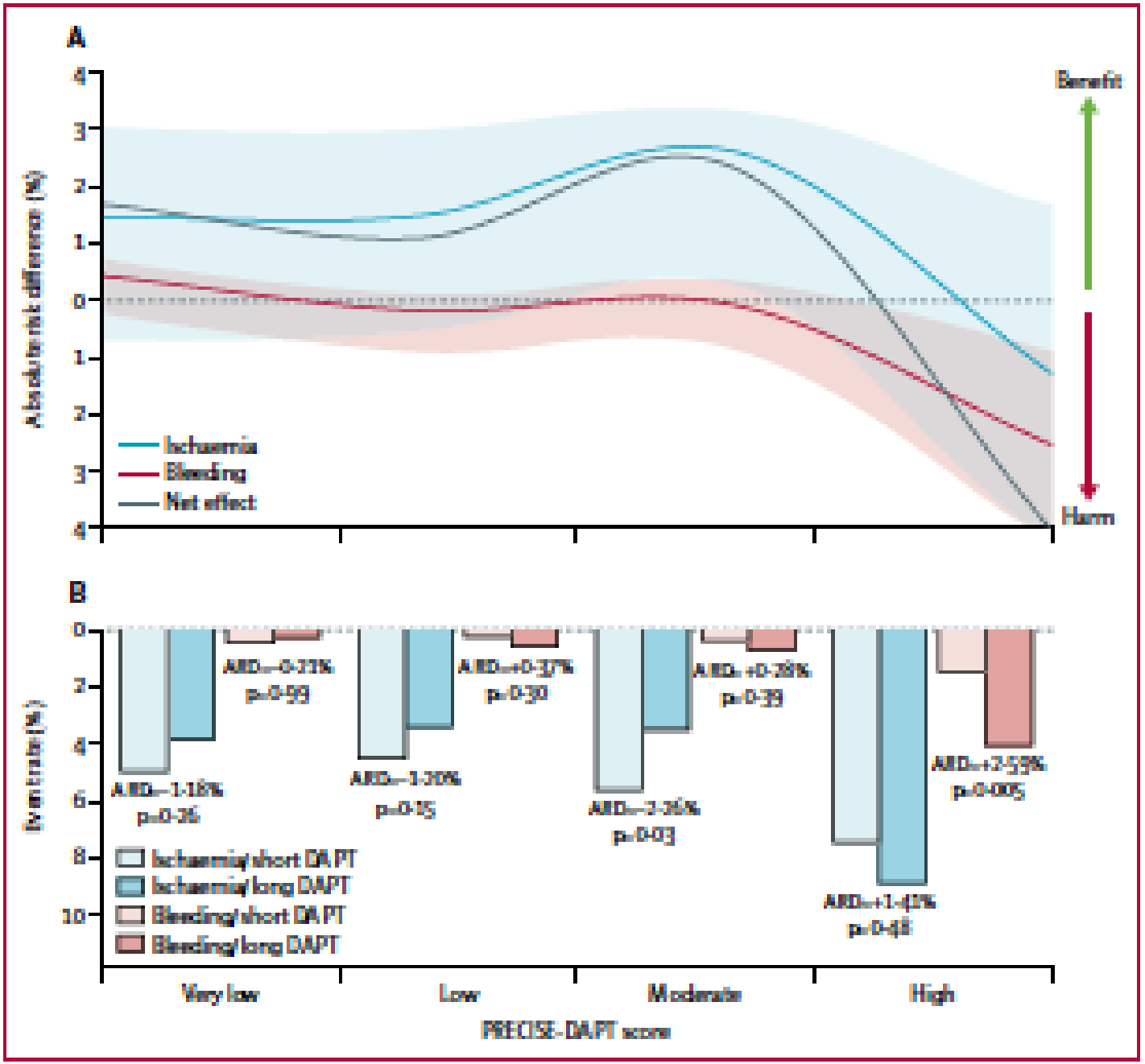




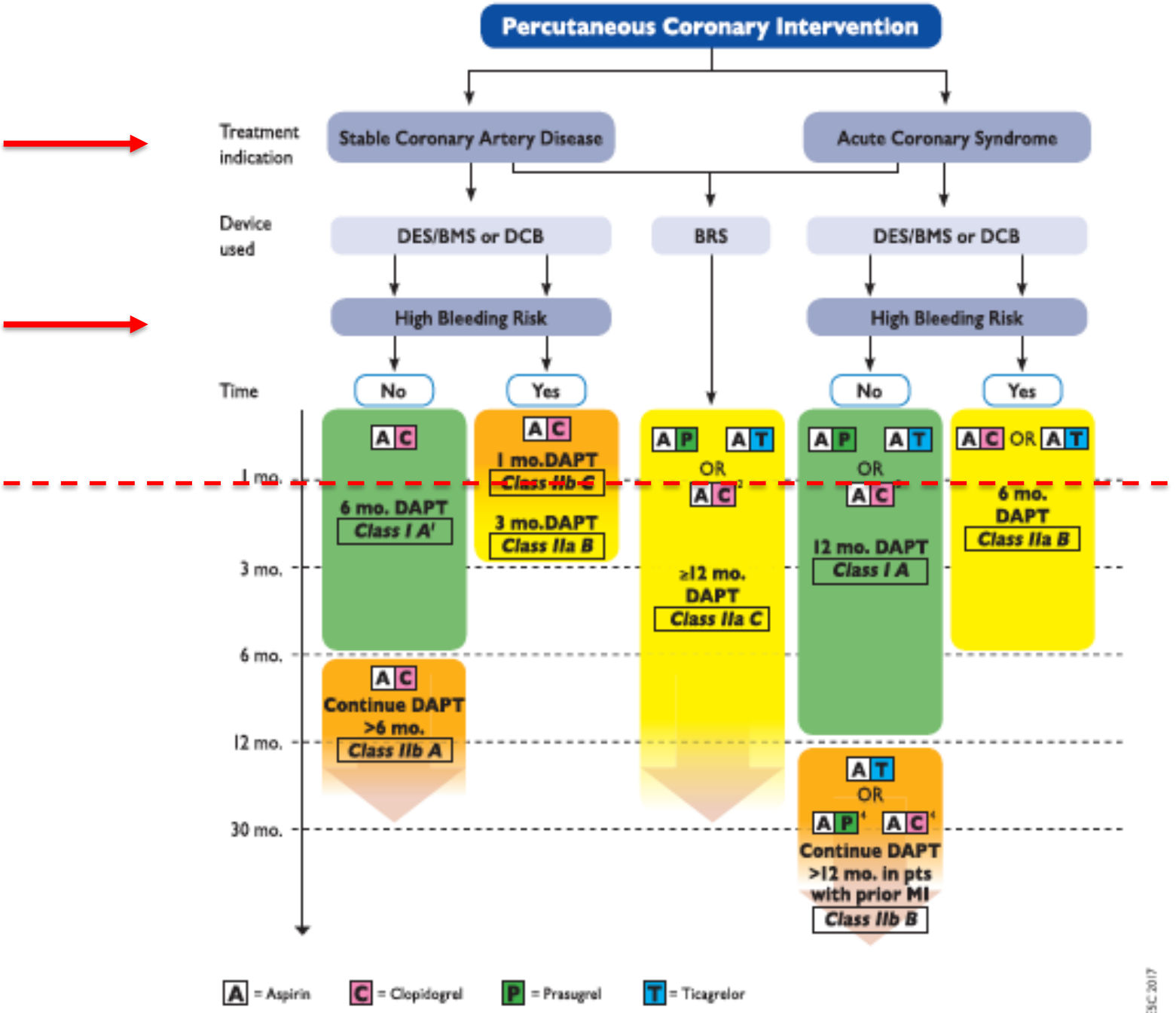


Byrne Eur Heart J 2015

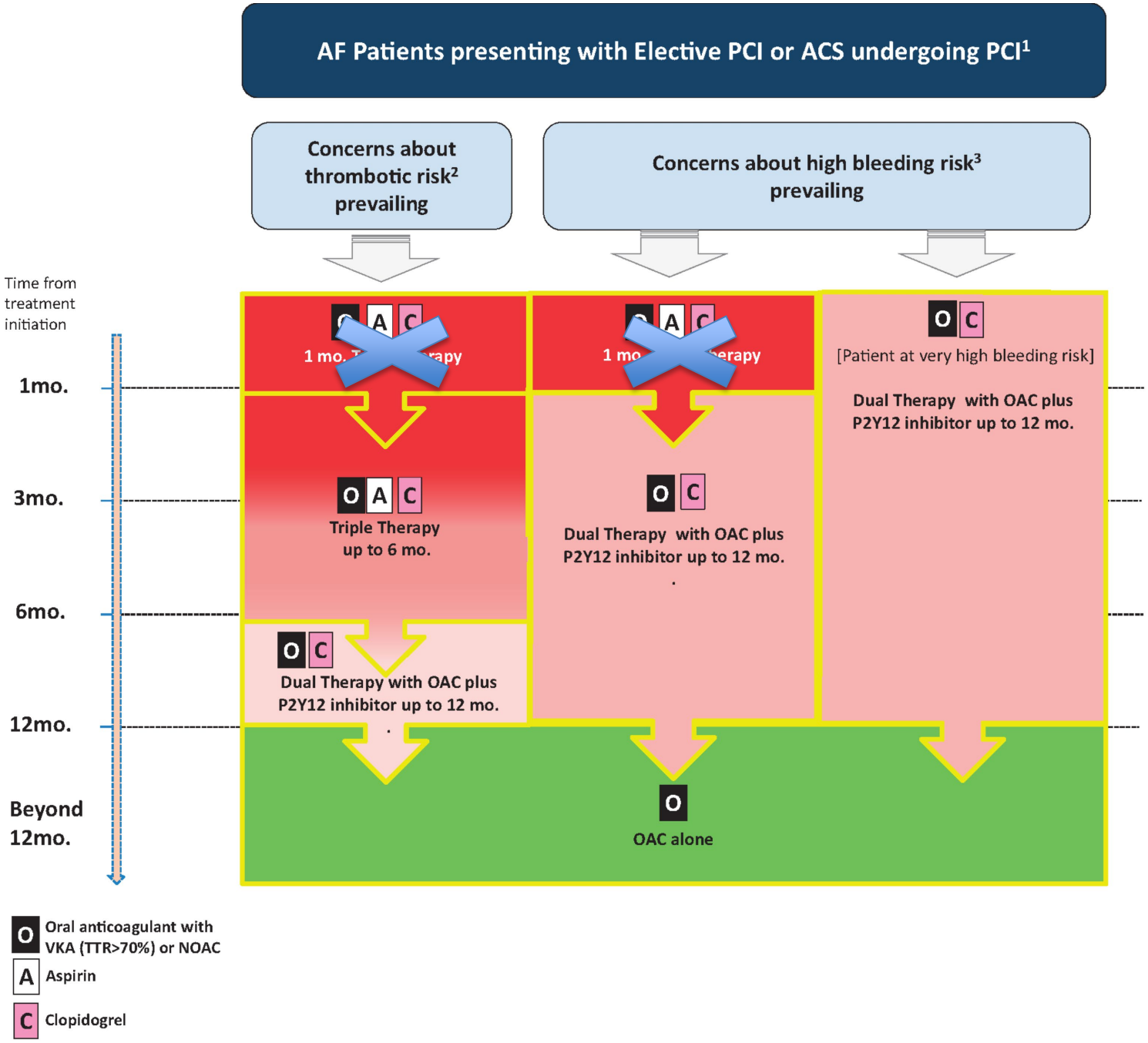
NORSTENT investigators NEJM 2016



Costa Lancet 2017



Valgimigli Eur Heart J 2018



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Conclusions: Anticoagulation orale et PCI

- Diminution du risque hémorragique avec une bithérapie Anticoagulant+Thienopyridine

- Etudes favorisant AOD vs AVK

- Dosage rivaroxaban non formellement évalué pour les AVC

- Puissance insuffisante pour évaluer formellement la thrombose de stent

- Puissance insuffisante pour évaluer formellement les AVC

… Demain uniquement Bithérapie AOD + Thienopyridine ??