Short DAPT Strategy in the Contemporary PCI Era: Routine or Selective?

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#TCTAP2020

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Industry Funding and Disclosures

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To Individualize or Not to Individualize

Individualizing treatment (”selective”) is favored over one-size-fits all (“routine”) approaches in current guidelines

Antiplatelet therapy after stenting			
DAPT is indicated for at least 1 month after BMS implantation.	I	A	791,799–801
DAPT is indicated for 6 months after DES implantation.	I	B	799,802,803
Shorter DAPT duration (<6 months) may be considered after DES implantation in patients at high bleeding risk.	IIb	A	804,805
Life-long single antiplatelet therapy, usually ASA, is recommended.	I	A	776,794
Instruction of patients about the importance of complying with antiplatelet therapy is recommended.	I	C	-
DAPT may be used for more than 6 months in patients at high ischaemic risk and low bleeding risk.	IIb	C	-

IIb A SR	In patients with ACS treated with coronary stent implantation who have tolerated DAPT without bleeding complication and who are not at high bleeding risk (e.g., prior bleeding on DAPT, coagulopathy, oral anticoagulant use) continuation of DAPT for longer than 12 months may be reasonable (16,22–26,28,30,40,41,43,53,54,72).
IIb C-LD	In patients with ACS treated with DAPT after DES implantation who develop a high risk of bleeding (e.g., treatment with oral anticoagulant therapy), are at high risk of severe bleeding complication (e.g., major intracranial surgery), or develop significant overt bleeding, discontinuation of $P2Y_{12}$ therapy after 6 months may be reasonable (17–21,34,36,37).

2014 ESC/EACTS Guidelines on Myocardial Revascularization

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Reframing the Question

What constitutes a “short DAPT strategy” in 2020?

- DAPT for < 6 months (e.g. 1-3 months) for elective
- DAPT < 12 months (e.g 1-6 months) for ACS
- Stopping DAPT means moving to either ASA **or** P2Y12-inhibitor monotherapy

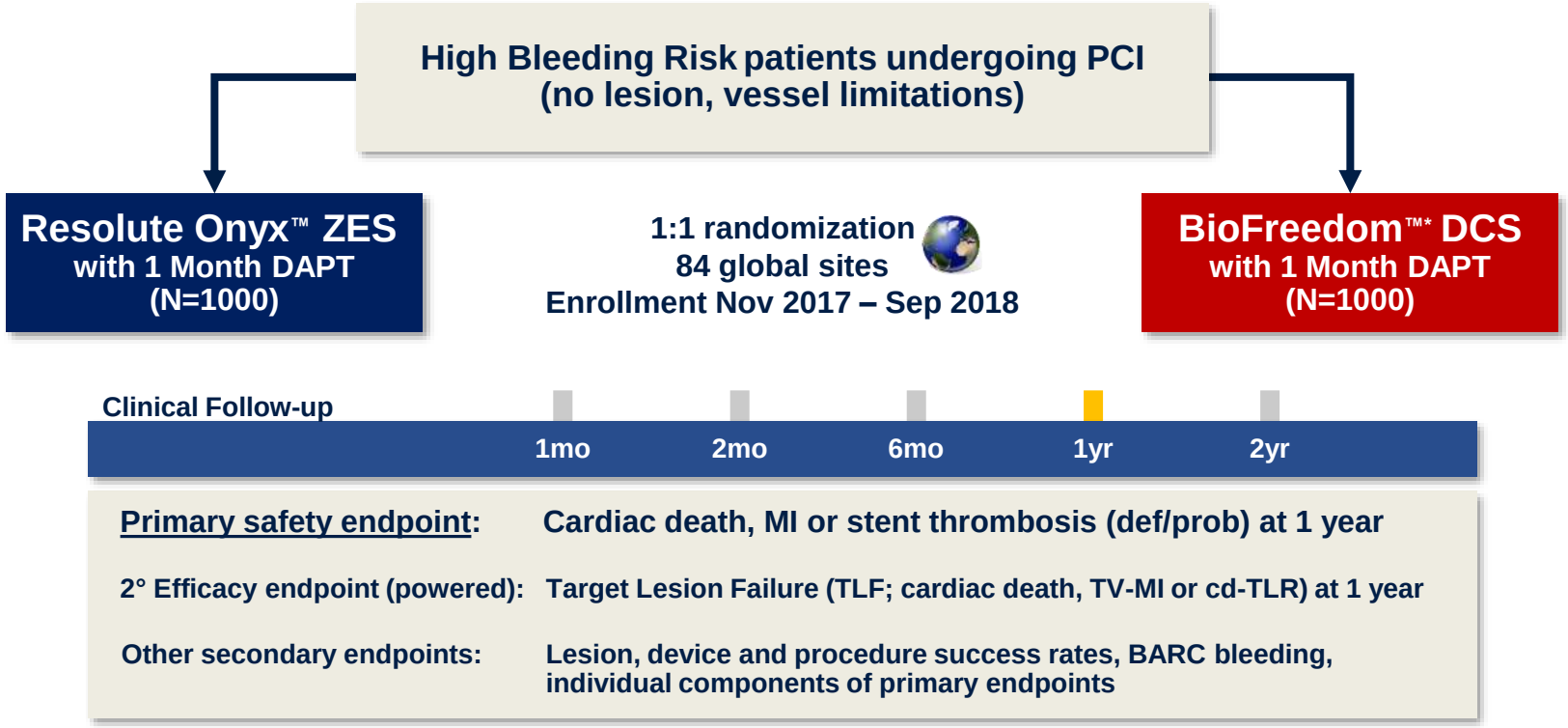
Two relevant questions:

1) Should the default DAPT strategy (6 months elective, 12 months ACS) be shortened?

2) How do I implement a selective approach to short DAPT duration?

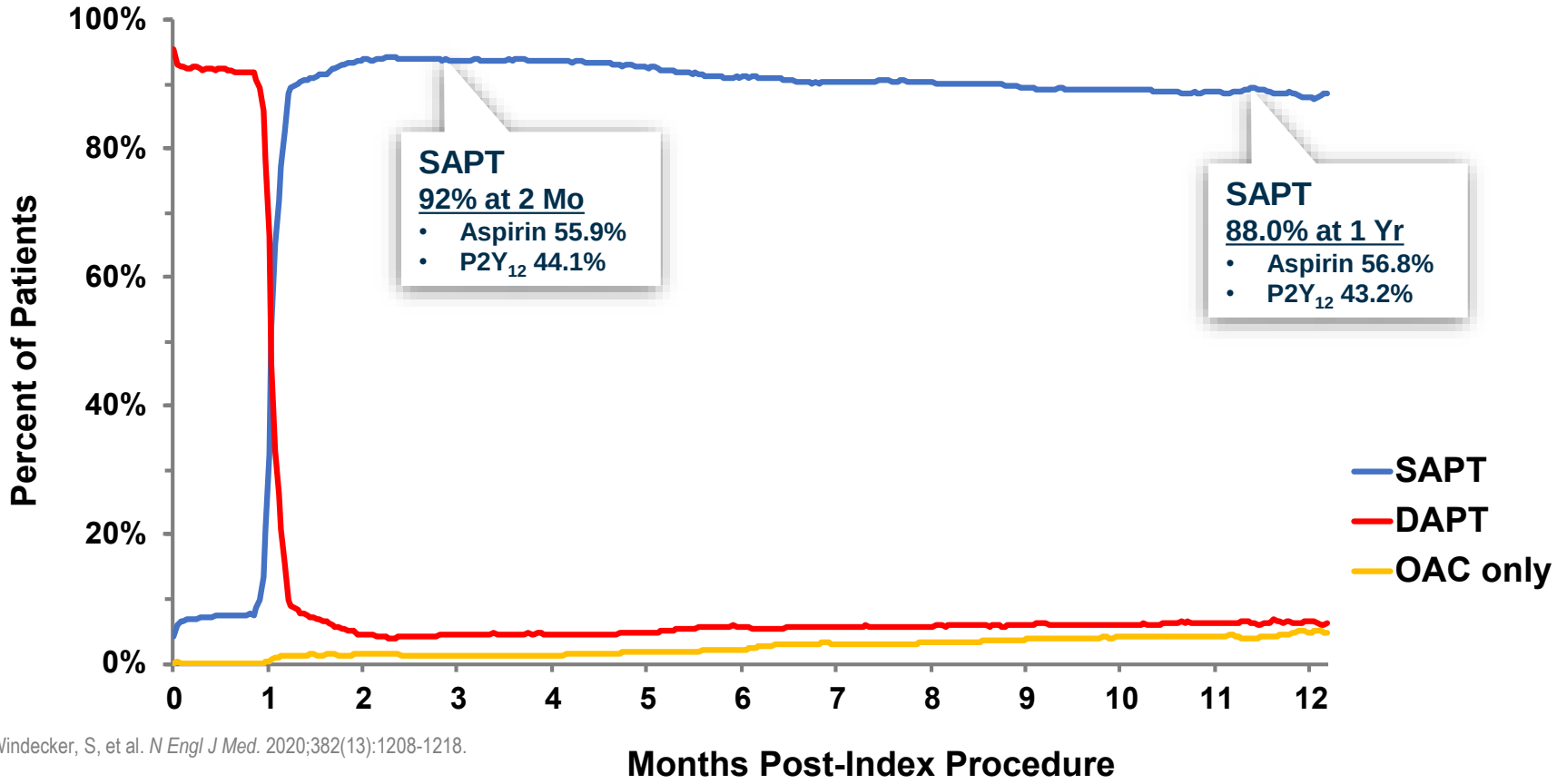
Onyx ONE Global Study Design

Prospective, Multicenter, Single-blind Randomized Trial



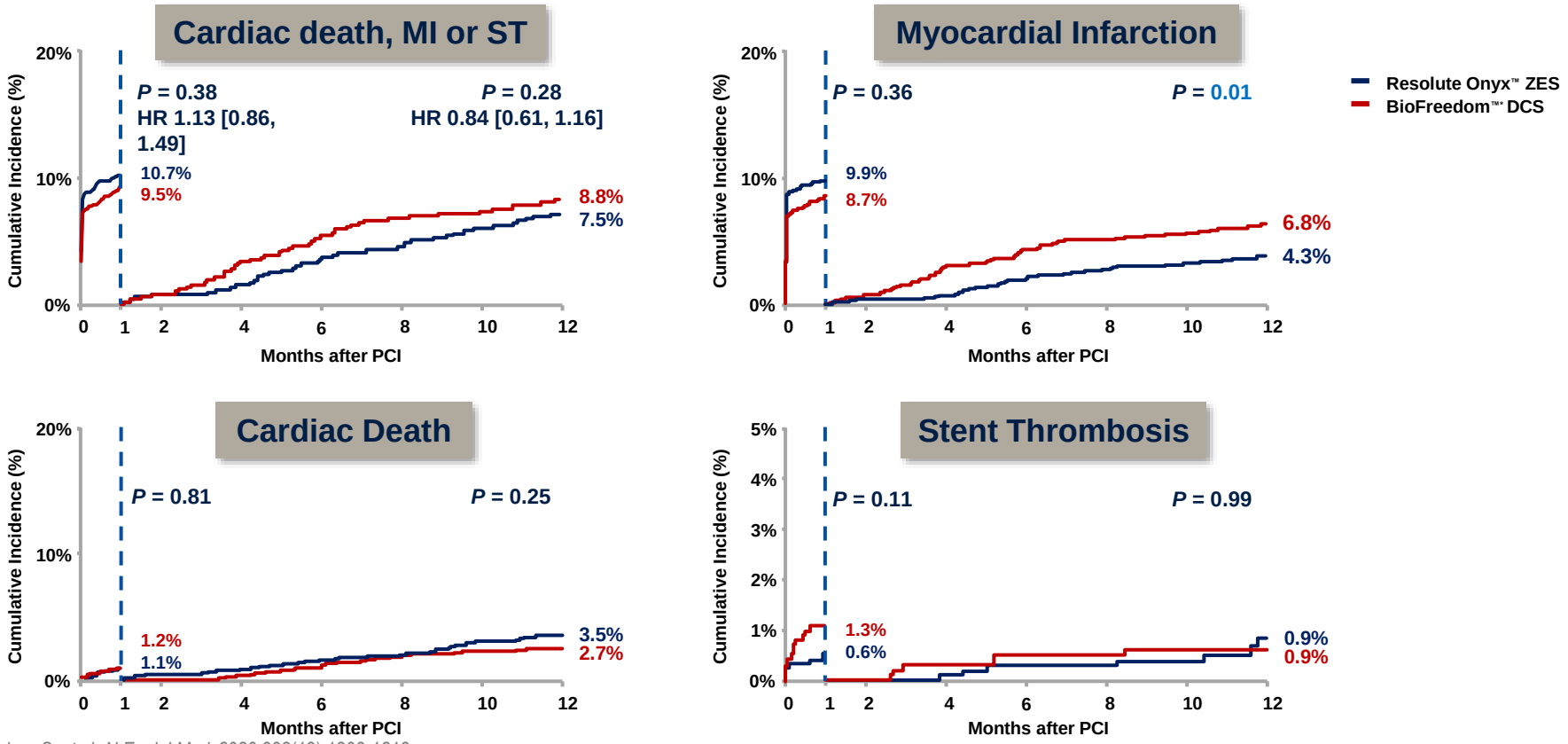
Windecker, S, et al. *N Engl J Med.* 2020;382(13):1208-1218.

Onyx ONE Global Program
Antithrombotic Therapy Transition After PCI



Windecker, S, et al. *N Engl J Med.* 2020;382(13):1208-1218.

One-Month Landmark Analyses (Time of DAPT Discontinuation)



Windecker, S, et al. *N Engl J Med.* 2020;382(13):1208-1218.

EVOLVE Short DAPT Study Design

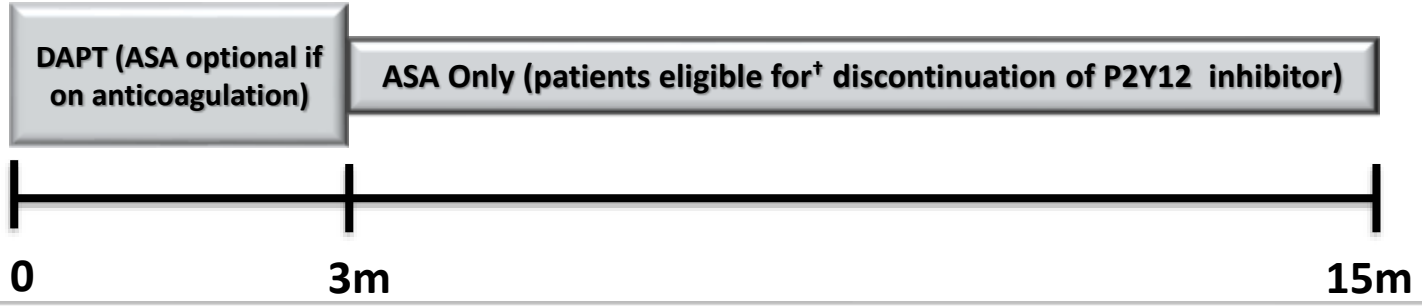
Prospective, N=2009 patients, 110 global sites

Key Inclusion Criteria

Patients considered by the treating physician to be at high risk for bleeding:

i) ≥75 years of age and high bleeding risk; ii) History of major bleeding; iii) Anticoagulation therapy; iv) History of stroke or renal insufficiency/failure; v) Platelet count ≤100,000/µL

(excluded LM disease, ostial lesions, >2 vessels, >3 lesions, CTO, SVG, ISR, NSTEMI or STEMI)



Co-primary Endpoints: (1) Death or MI, and (2) ARC definite/probable ST between 3-15 months

Secondary Endpoint: Rate of major bleeding (BARC bleeding classification 2,3,5) between 3-15 months

†Eligible to discontinue $P2Y_{12}$ inhibitor at 3 months if they receive 3 months of $P2Y_{12}$ inhibitor/ASA and are free from events (stroke, MI, revascularization, or ST)

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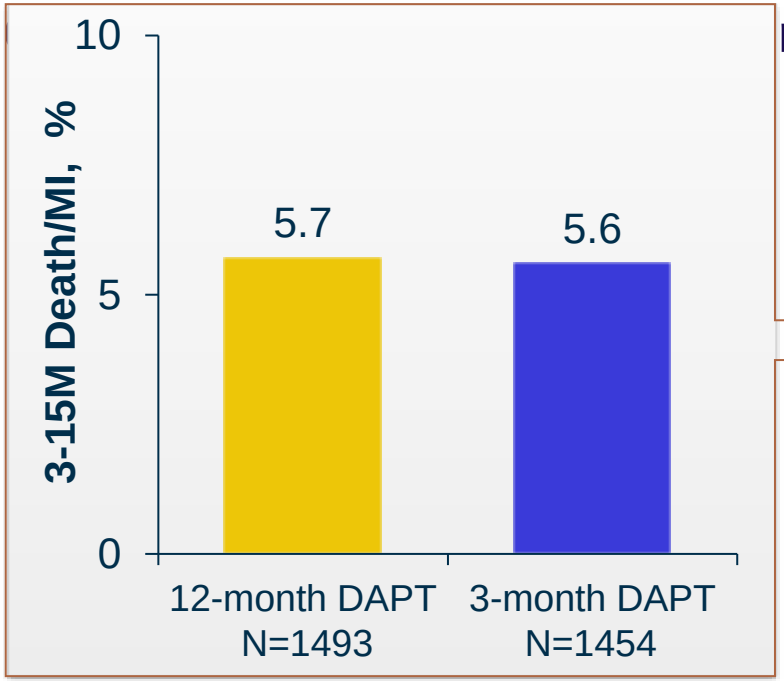
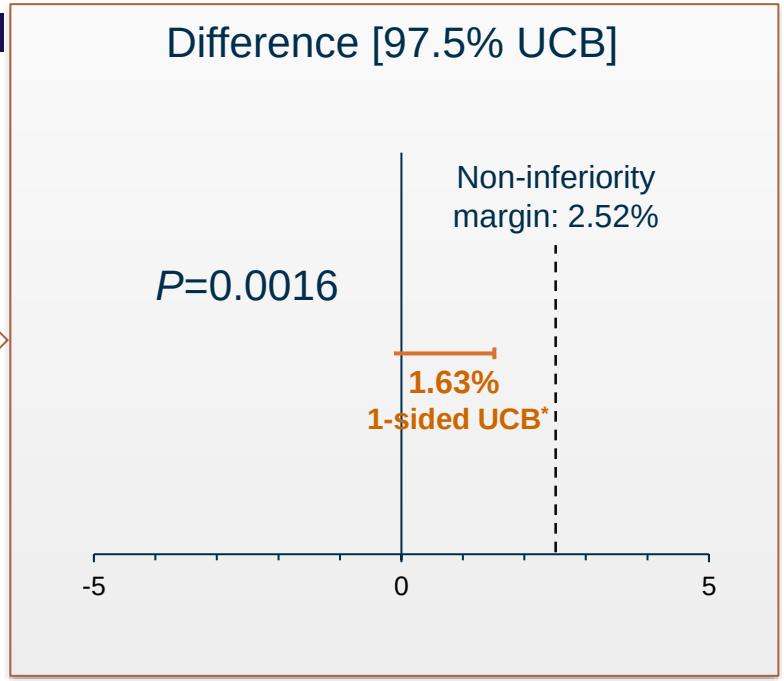
Presented by Dr. Ajay Kirtane, MD., at TCT 2019; Mauri, et al. Am Heart J 2018;205:110-117.

EVOLVE Short DAPT Co-Primary Endpoint: Adjusted Death/MI between 3-15 months with 3-Month DAPT

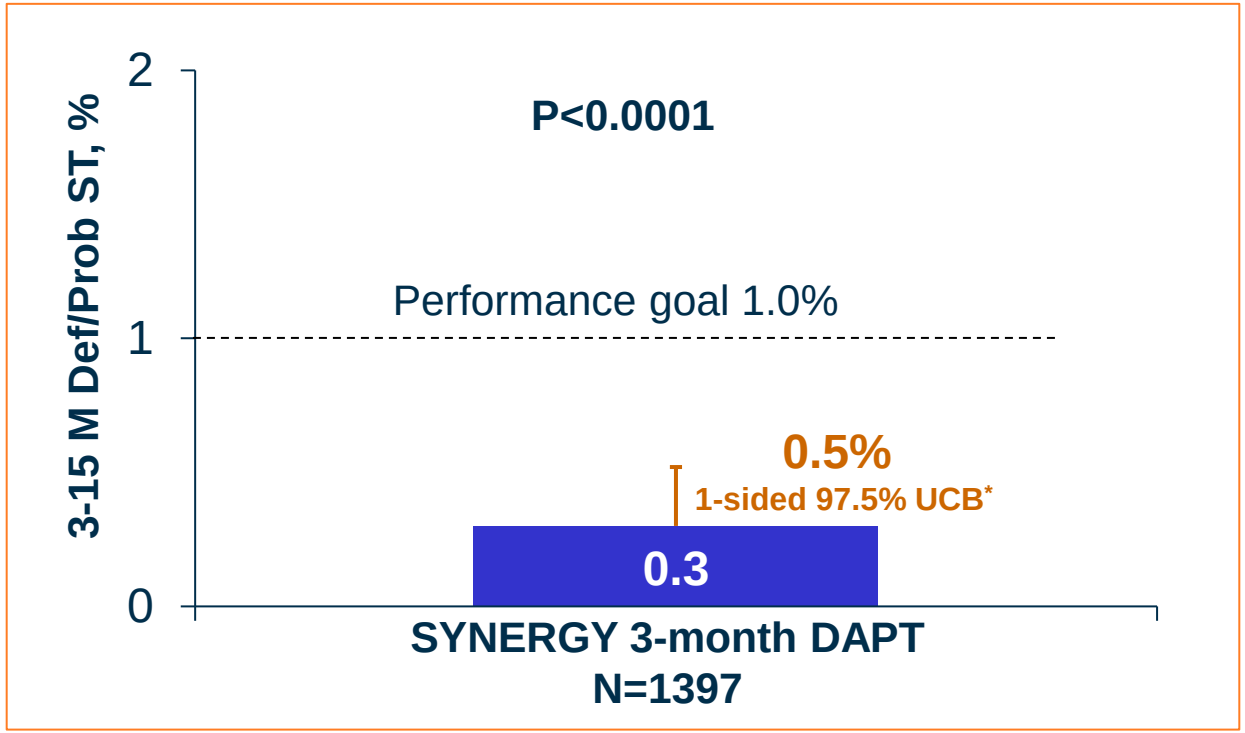




Patients with respective event or sufficient follow-up included in the denominator

Kirtane et al.

Co-Primary Endpoint: ARC Definite/Probable ST between 3-15 months



Patients with respective event or sufficient follow-up included in the denominator

Kirtane et al. TCT19.

JAMA | Original Investigation

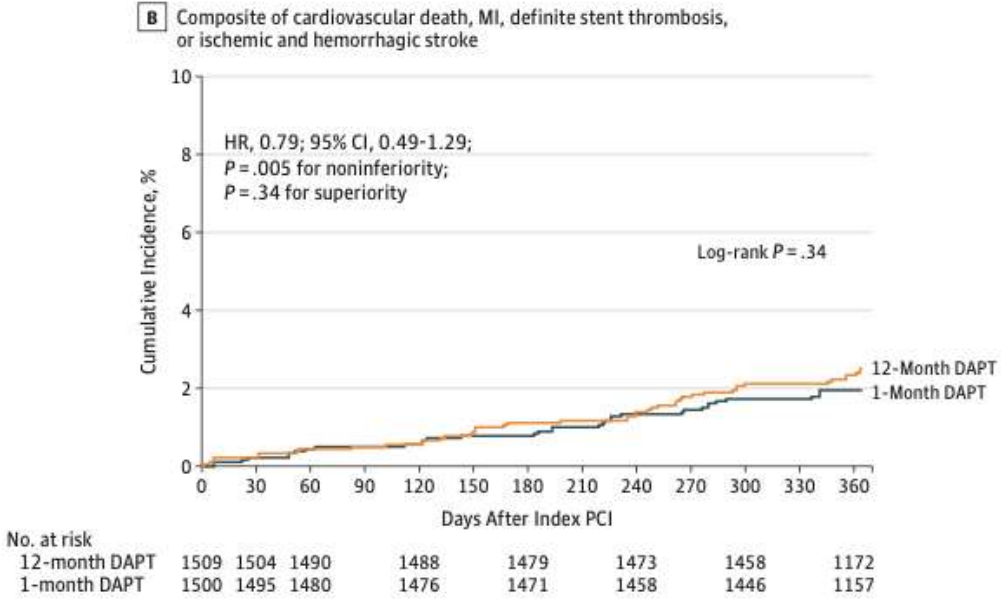
Effect of 1-Month Dual Antiplatelet Therapy Followed by Clopidogrel vs 12-Month Dual Antiplatelet Therapy on Cardiovascular and Bleeding Events in Patients Receiving PCI

The STOPDAPT-2 Randomized Clinical Trial

Pts randomized to
1 month DAPT followed by
clopidogrel monotherapy
vs. 12 months DAPT

PCI with Xience EES

2/3 stable CAD, 1/3 ACS
4 vs. 1 def/prob stent thrombosis (< 0.3%)



Watanabe et al. JAMA 2019.

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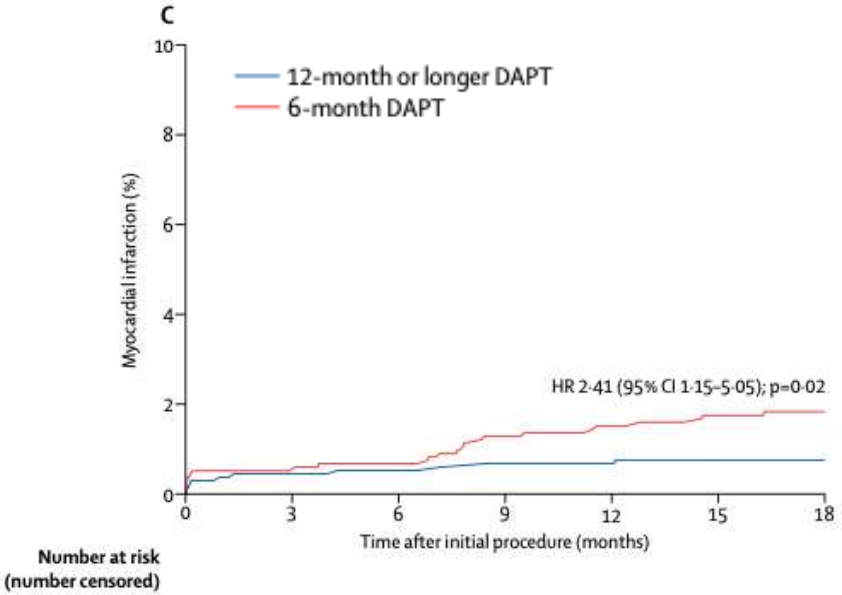
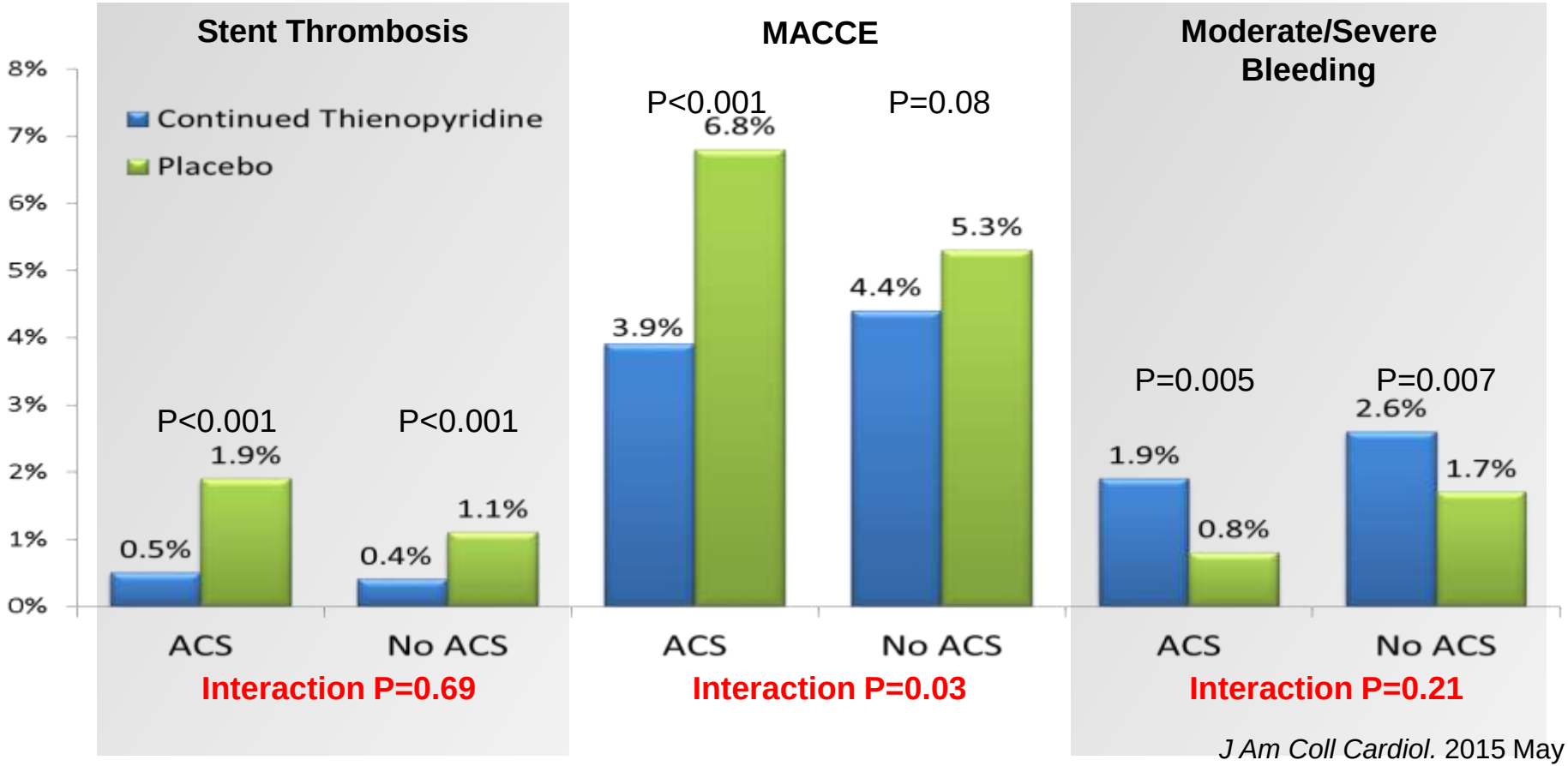
Going too short in ACS

- SMART-DATE: 6 vs. 12+ months DAPT after ACS (2700 pts). SAPT regimen = ASA monotherapy



Hahn et al. Lancet 2018.

DAPT Study Results Among Patients with vs. without Myocardial infarction



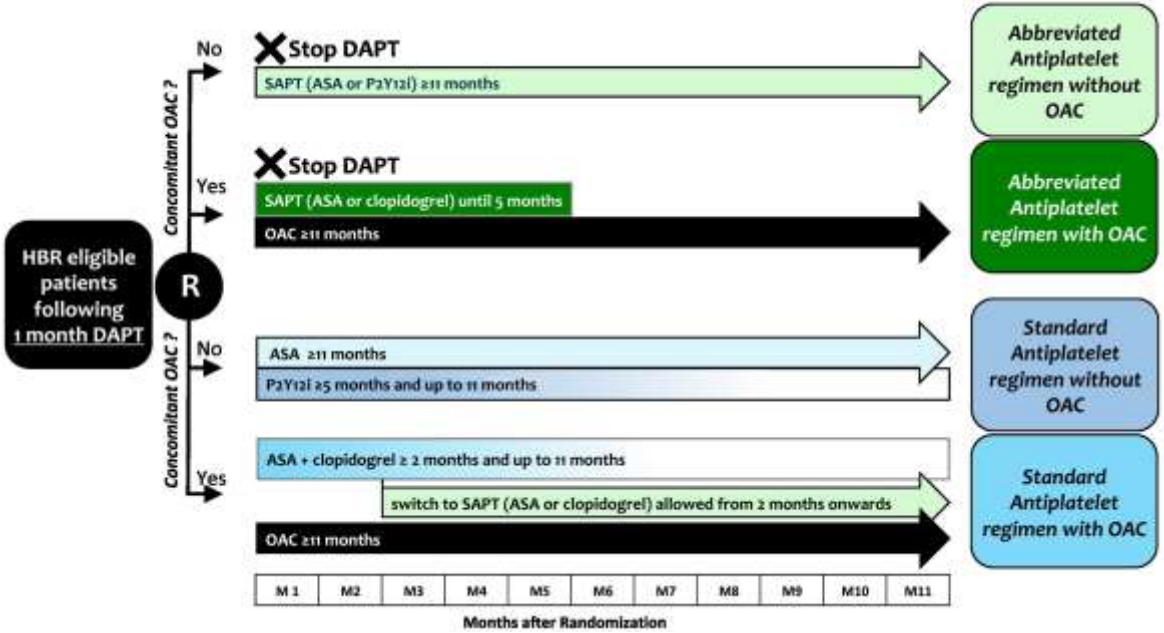
J Am Coll Cardiol. 2015 May 26.

Should our default durations be changed?

If SAPT = aspirin monotherapy, then default strategy should remain.

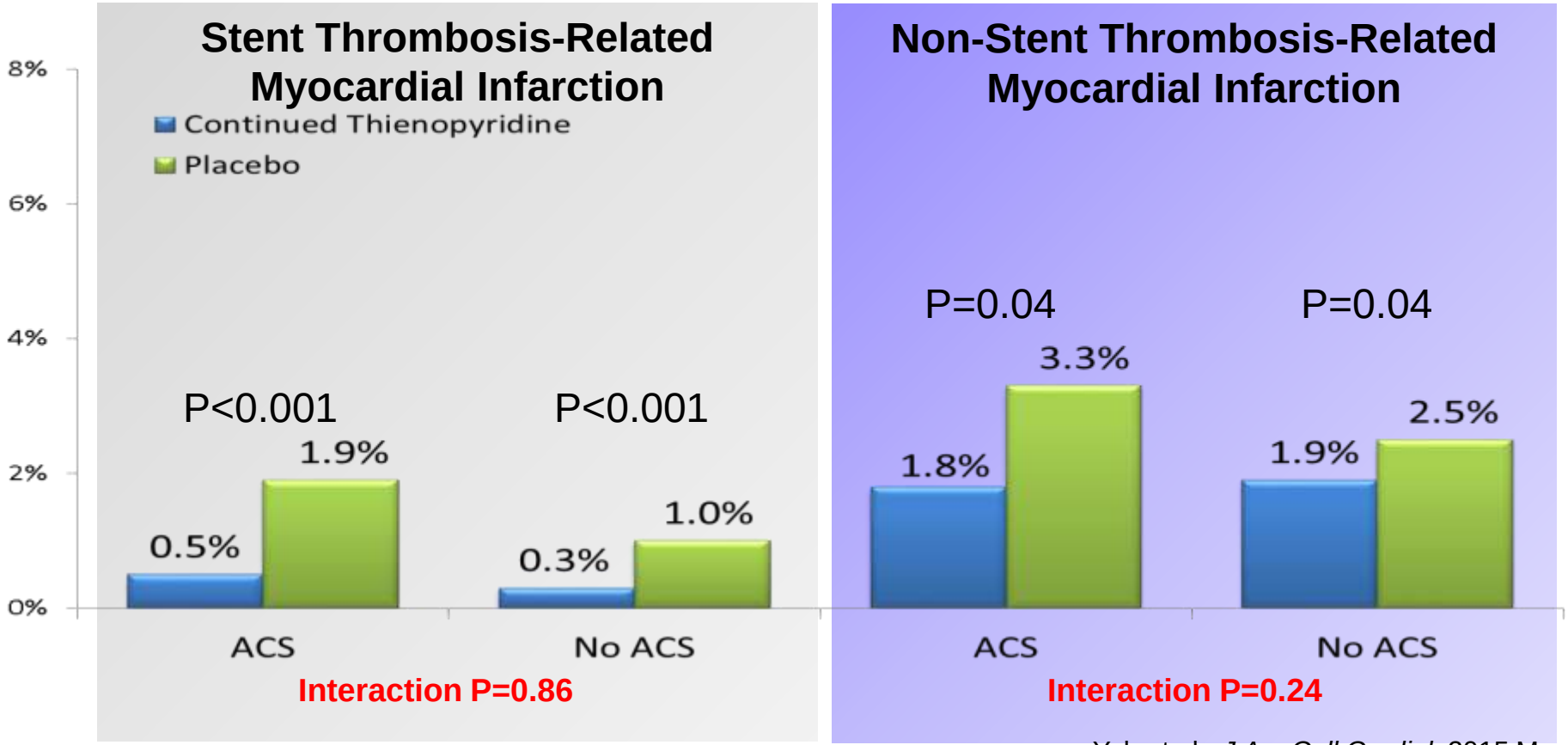
- Growing evidence that short DAPT durations result in few **stent-related** events with modern DES.
- No evidence that 1-3 month DAPT followed by ASA monotherapy is better than the current 6 month default in stable CAD, even among HBR patients.
- Suggestion that shorter duration followed by ASA monotherapy is harmful compared to current 12 month standard for high risk ACS patients. Older data which shows benefit for > 12 month duration for ACS patients without bleeding in the 1st year.

MASTER-DAPT will test shorter DAPT duration as a default strategy for HBR patients



Frigoli, Valgimigi et al. American Heart Journal 2019.

Treatment Effect According to MI Status
Myocardial Infarction Type, 12-30 M follow-up



Yeh et al., *J Am Coll Cardiol.* 2015 May 26.

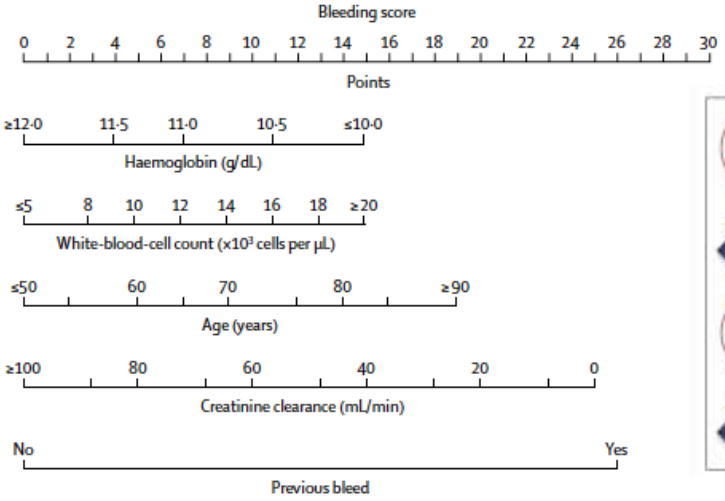
How Do I Implement a Selective Strategy?

- Is my patient at high bleeding risk? Limit very short durations to these patients.

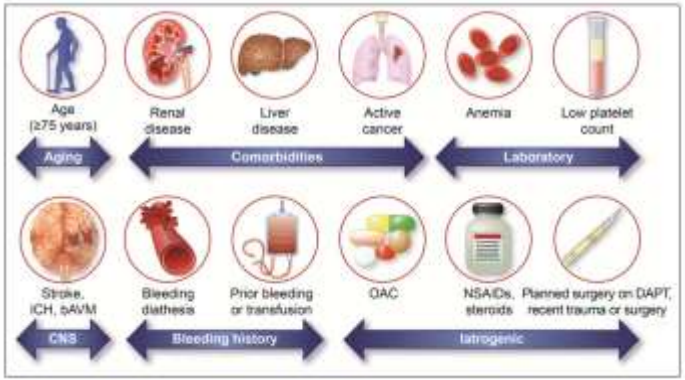
TABLE 4 Integer Risk Score for Major Bleeding

Parameter	Score
Age, yrs	
<50	0
50-59	+1
60-69	+2
70-79	+3
≥80	+4
BMI, kg/m²	
<25	+2
25-34.9	0
≥35	+2
Current smoking	
Yes	+2
No	0
Anemia	
Present	+3
Absent	0
CrCl <60 mL/min	
Present	+2
Absent	0
Triple therapy on discharge	
Yes	+2
No	0

PARIS Bleeding Risk

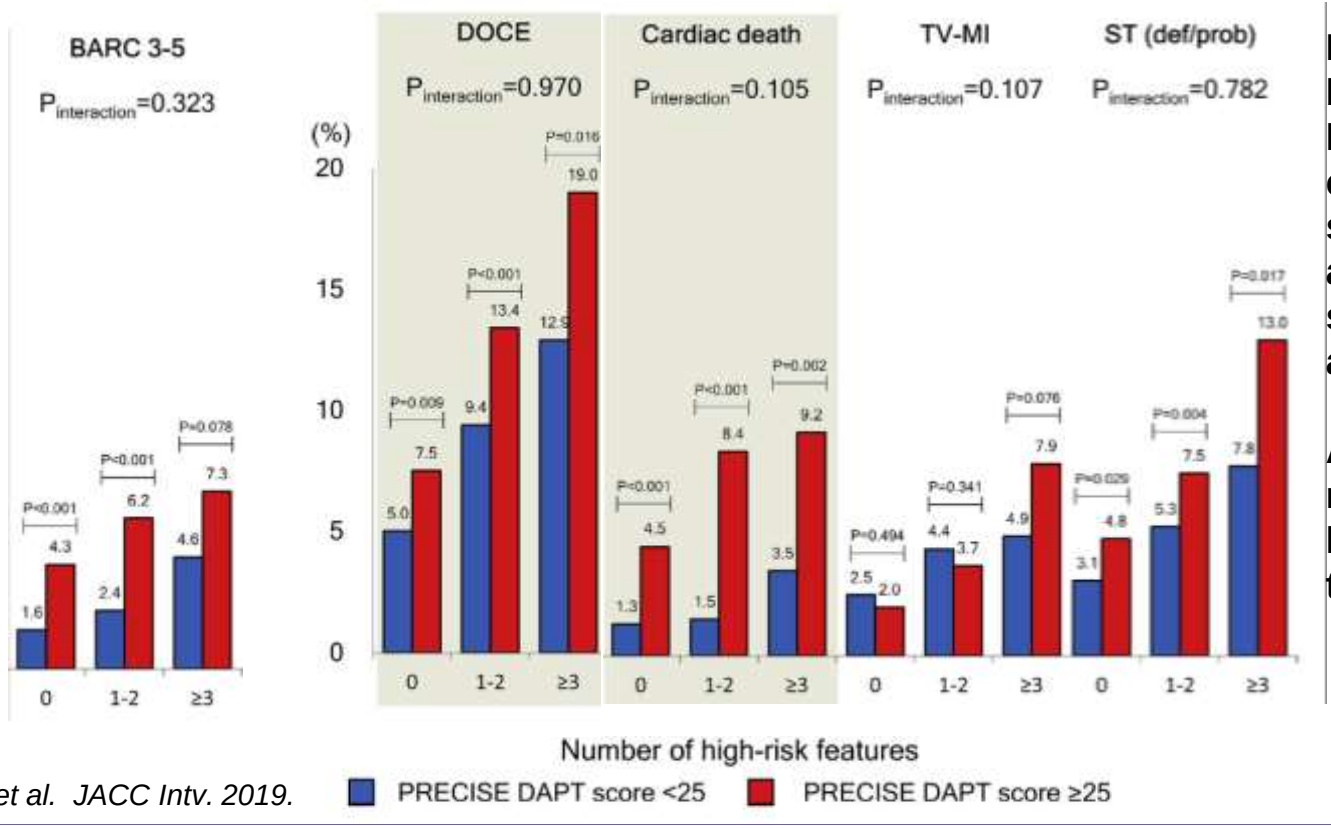


PRECISE DAPT Score



HBR criteria

Assessing Bleeding Risk is Important, But Not Enough



Patients with higher bleeding scores have higher rates of cardiac death, MI and stent thrombosis across the entire spectrum of anatomical disease.

Assessing bleeding risk alone does NOT help assess the tradeoff of risks.

Ueki et al. JACC Intv. 2019.

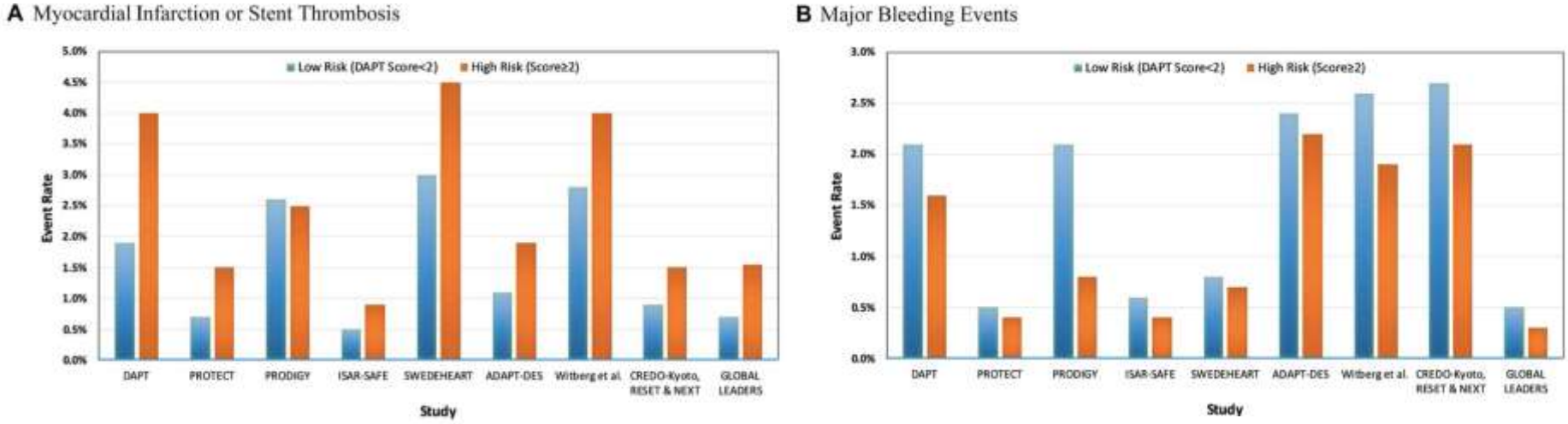
Among these HBR patients, are there some who are at high ischemic risk?

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

- Not a bleeding risk score – but a treatment benefit/harm score
- Validated in more than 90,000 patients in 9 different populations

Yeh, Secemsky, Kereiakes et al. JAMA 2016

High DAPT score identifies elevated ischemic risk but lower bleeding risk



Across multiple studies, high DAPT score patients have 60% higher ST/MI risk, 20% lower bleeding risk compared with low DAPT score patients

Yeh, Mihatov. JACC Intv 2020.

Additional considerations for a selective strategy: What happened during the procedure?

1) Intravascular imaging?
2) Vessel preparation for optimal expansion?
3) High pressure post-dilation?
4) Post-stent imaging?

Conclusions

- The cliché holds true: there is no one size fits all for DAPT strategies.
  - Caveat: P2Y12 monotherapy strategies may prove to be the optimal middle ground for a large swatch of patients.
- Shortening duration in stable PCI likely does not meaningfully increase ischemic events, nor decrease bleeding events in low risk patients
- Use tools to identify HBR patients most likely to benefit from short duration
- Consider that some HBR patients may still likely benefit from longer duration, particularly those with high ischemic risk (high DAPT score, complex or suboptimal procedure etc).