

24.25.26
MAGGIO 2019
SORRENTO
HILTON SORRENTO PALACE
Via Sant'Antonio, 13

DOAC 4.0:
IL PAZIENTE
AL CENTRO
E NUOVI
PARADIGMI



Post SCA: Percezione e realtà del rischio residuo

Marco Ferlini, MD,

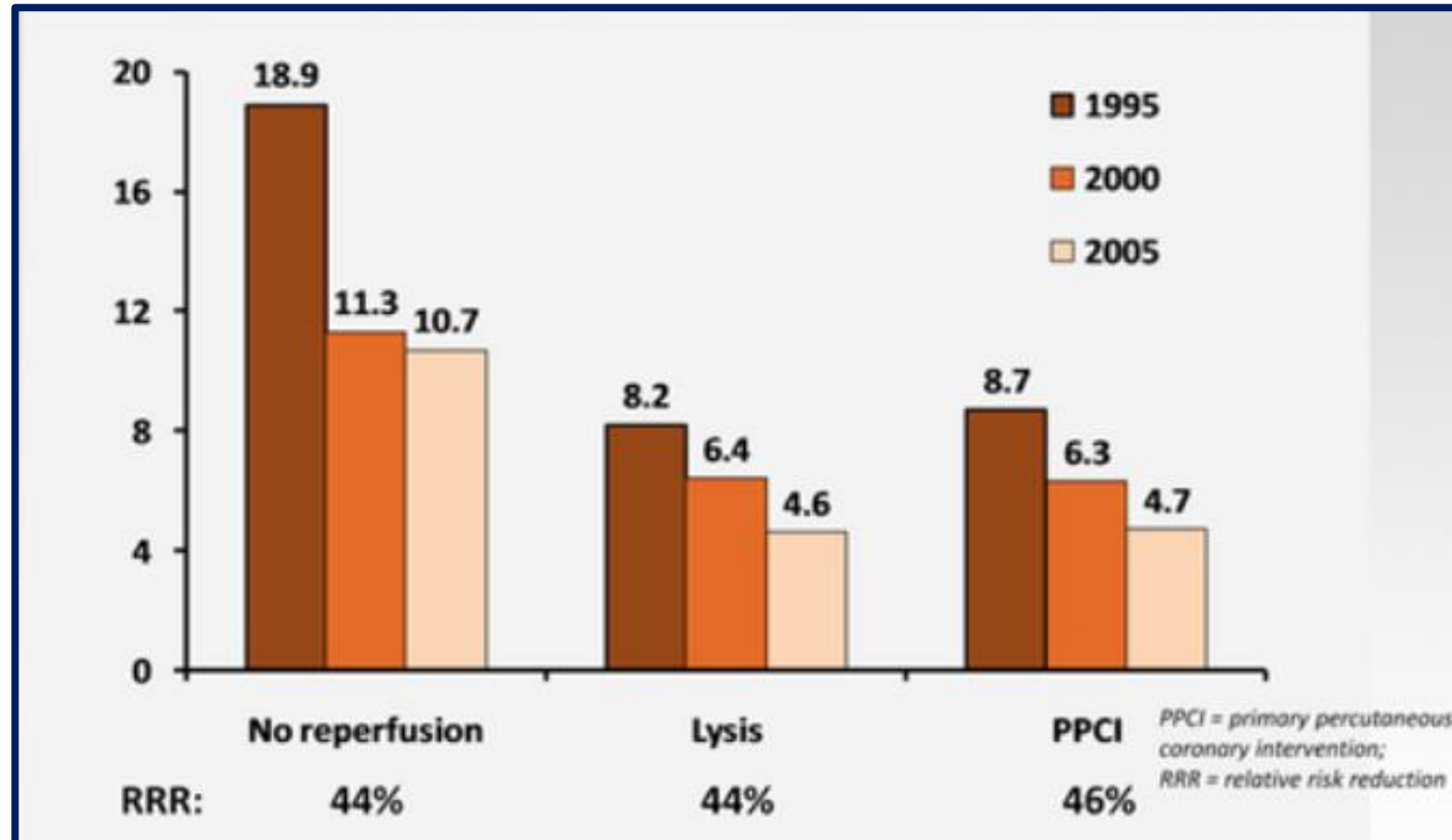
FESC, FANMCO, FSICI-GISE

Disclosures

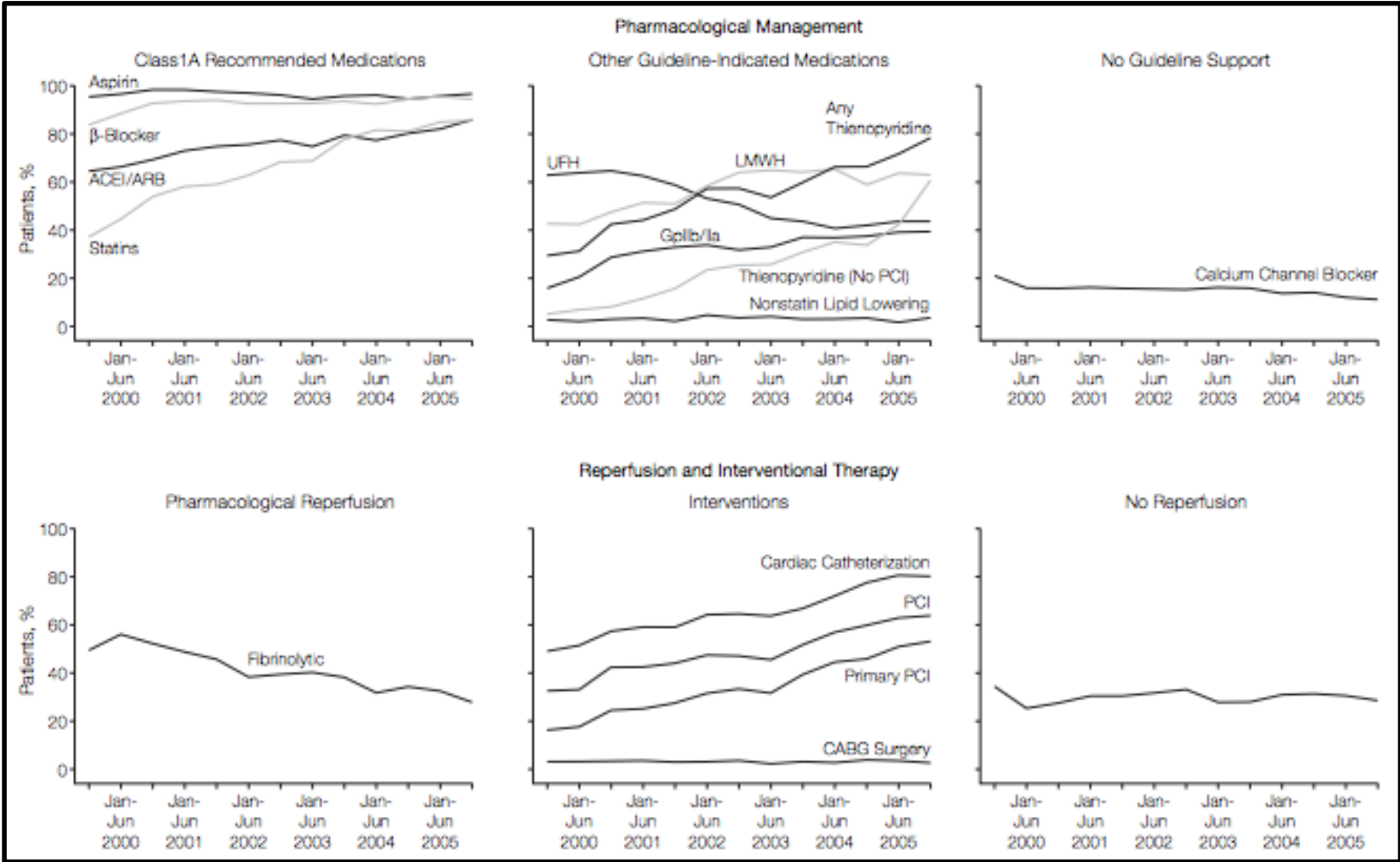
Honoraria as consultant, advisory board or speaker from:

- **Astra Zeneca,**
- **Eli Lilly**
- **Chiesi**
- **Sanofi**
- **Bayer**
- **Boheringer**

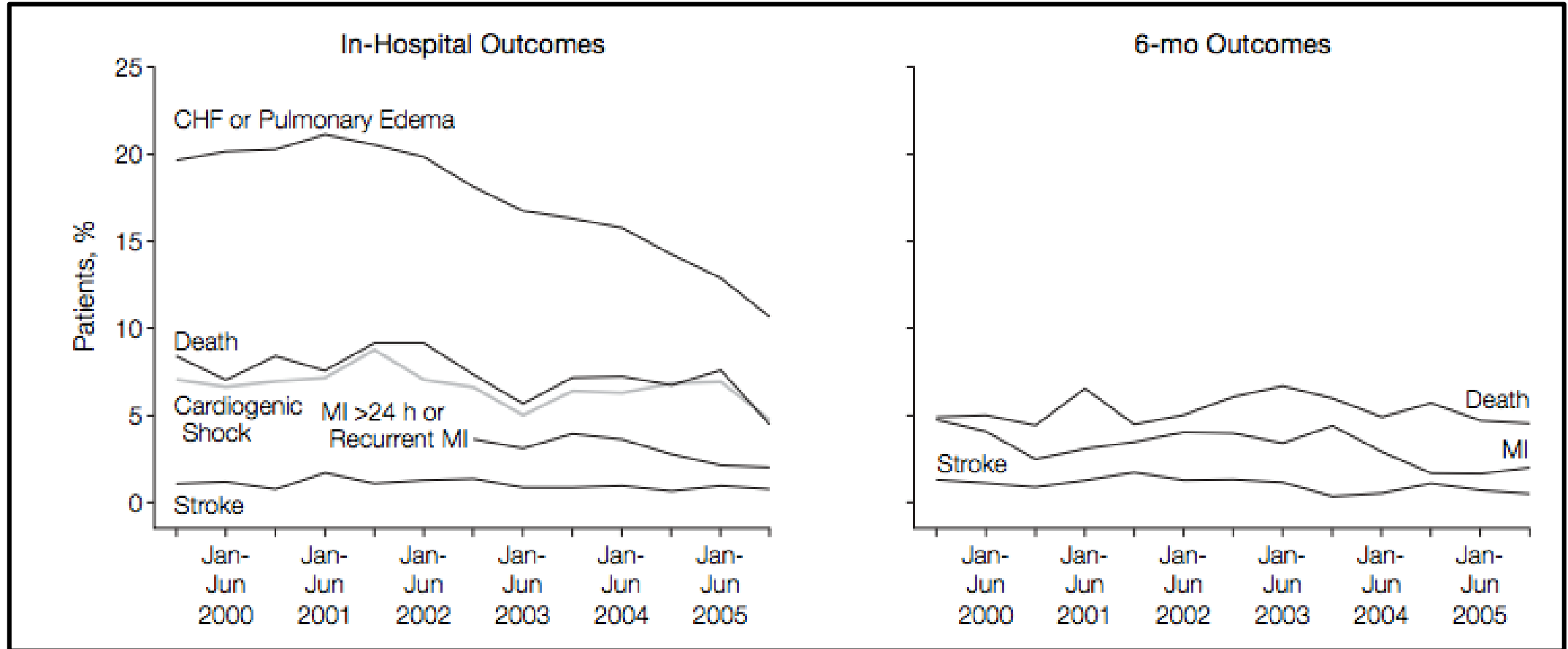
30 days mortality according to reperfusion therapy (STEMI)



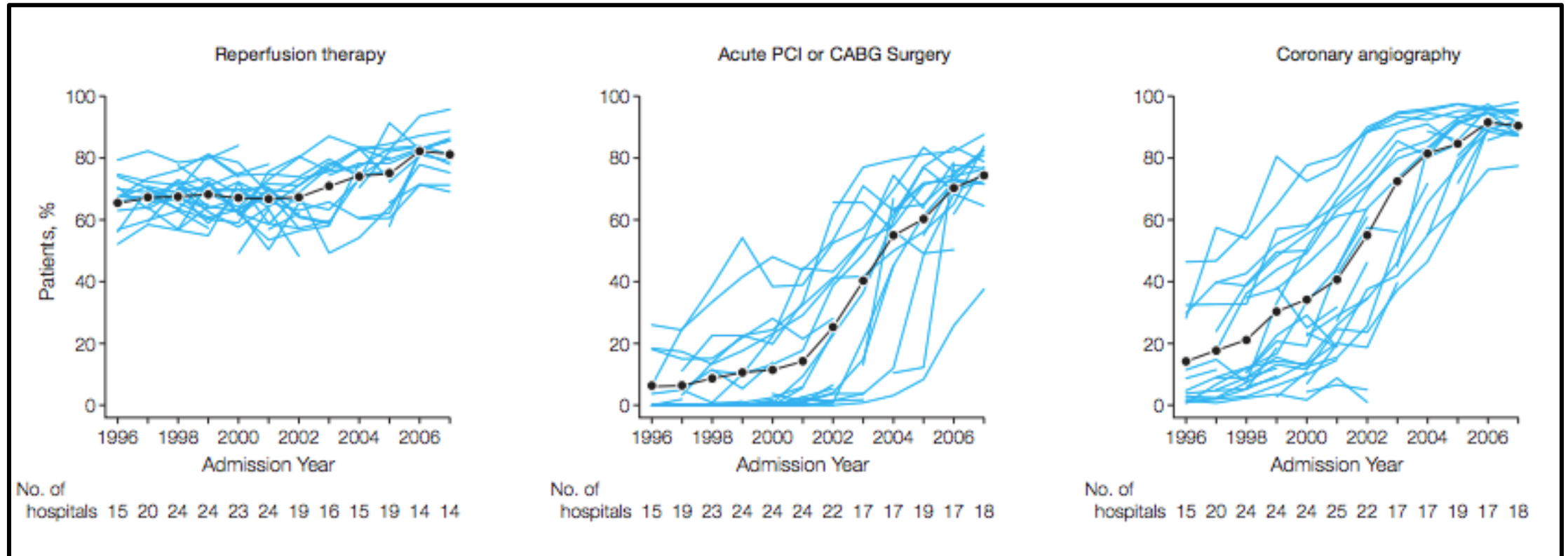
Trends in Management of STEMI in GRACE Registry



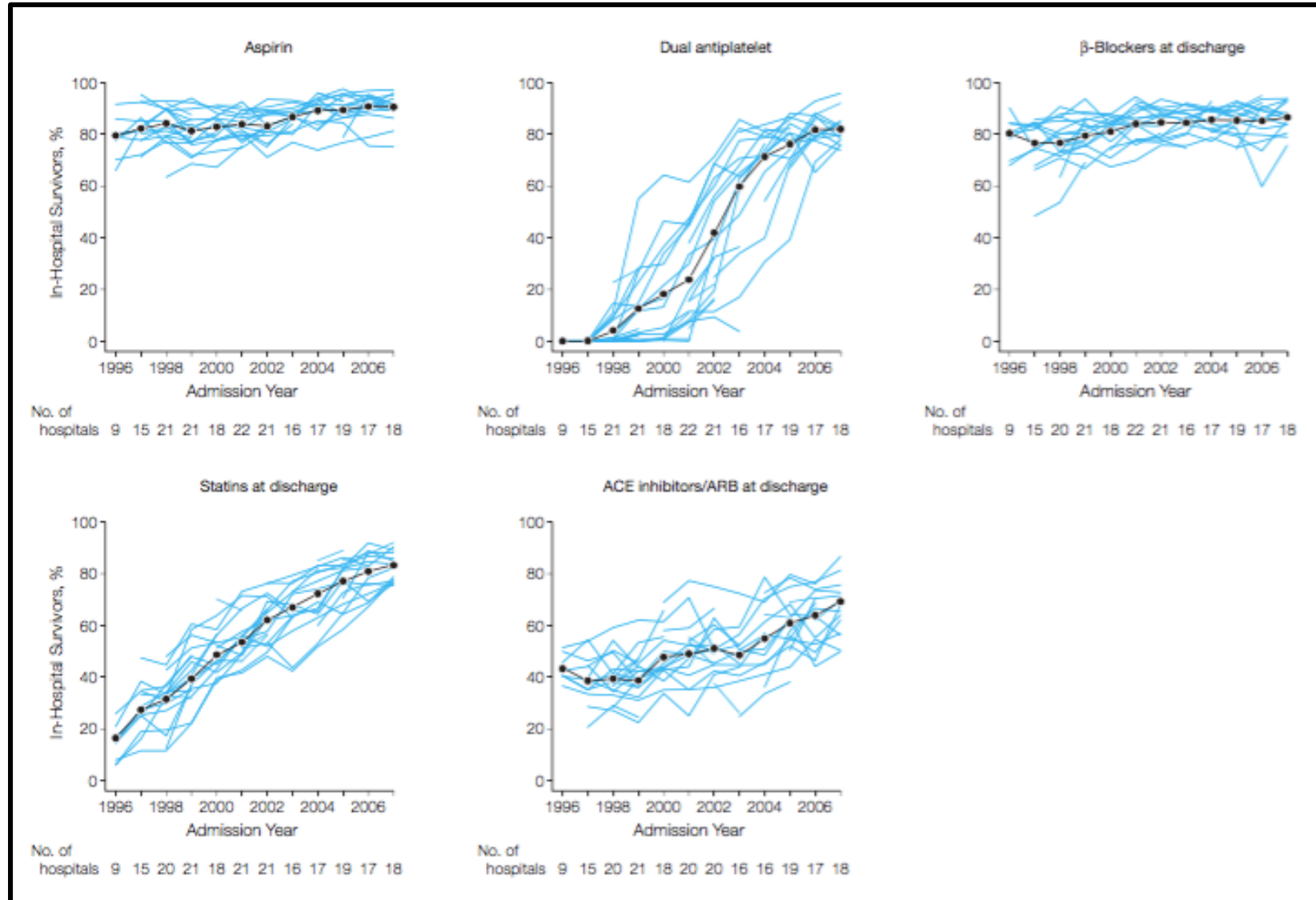
In-Hospital and 6-month outcomes in Patients with STEMI or LBBB



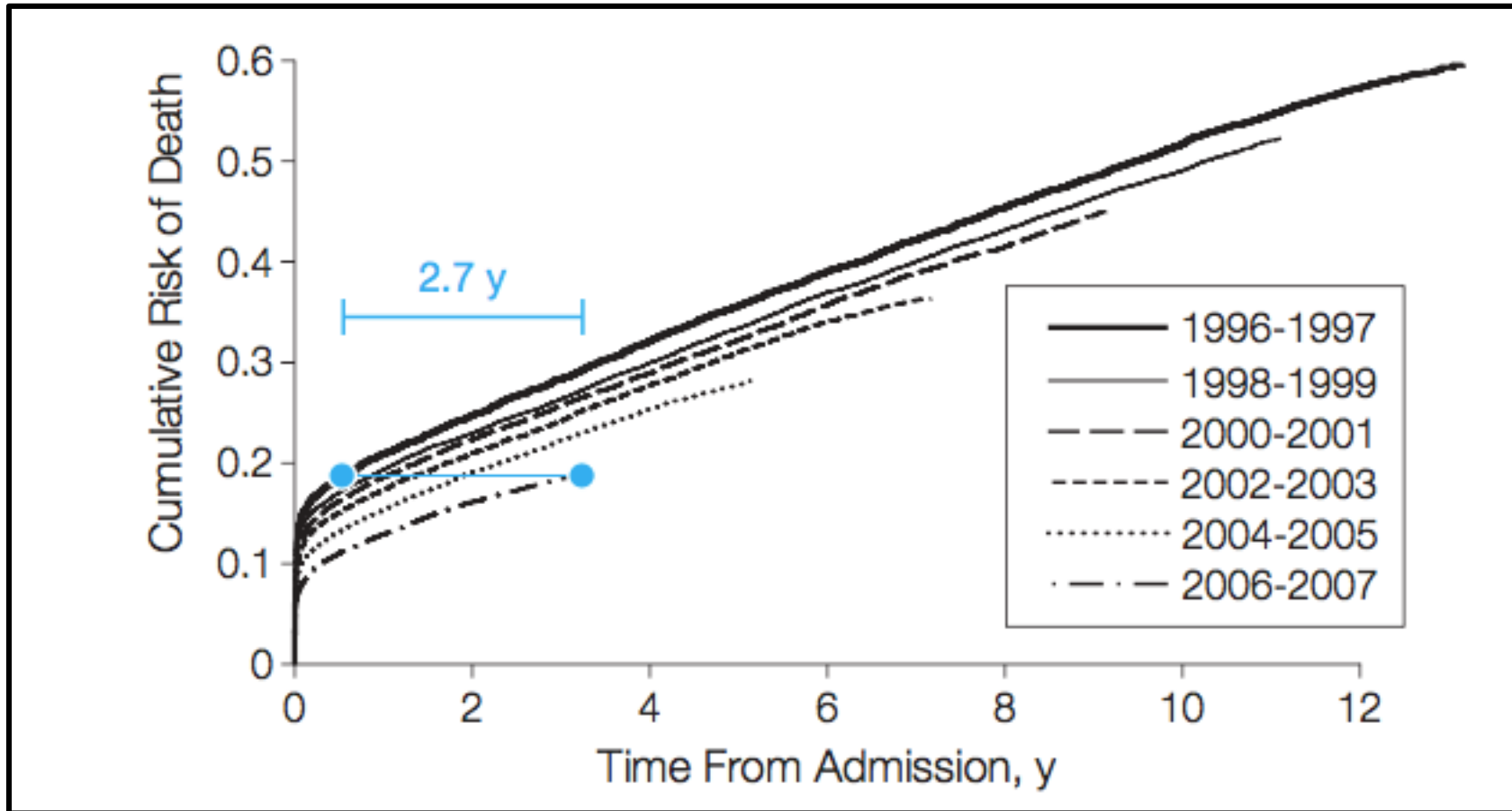
The SwedesHeart/Risk-HIA Data



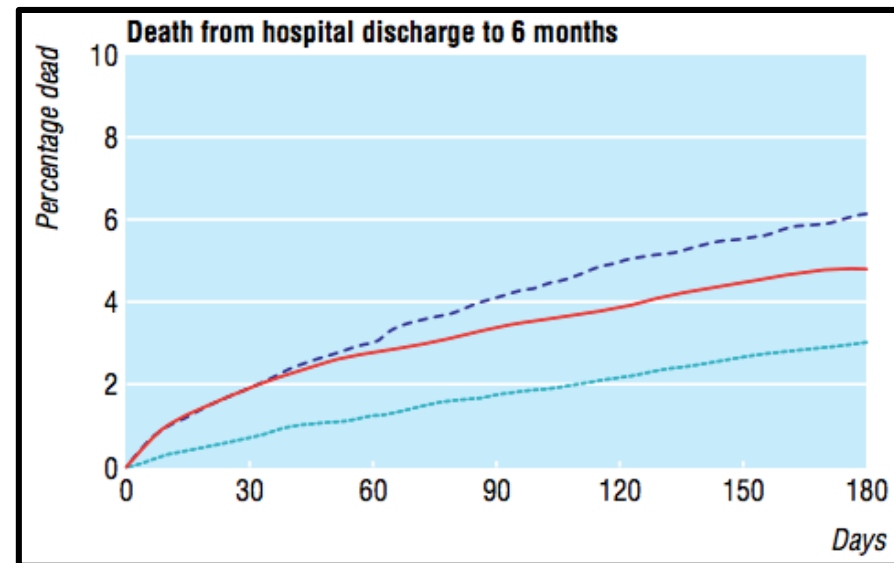
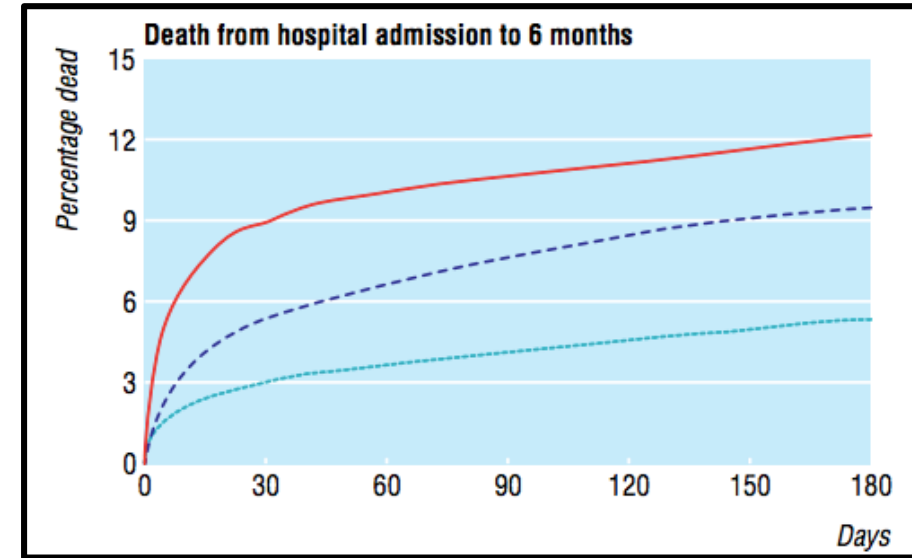
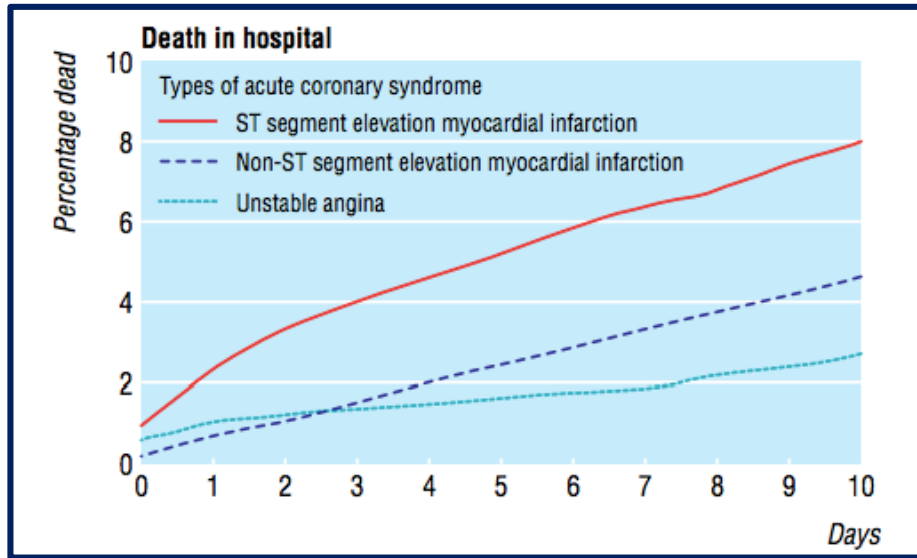
The SwedesHeart/Risk-HIA Data



The SwedesHeart/Risk-HIA Data

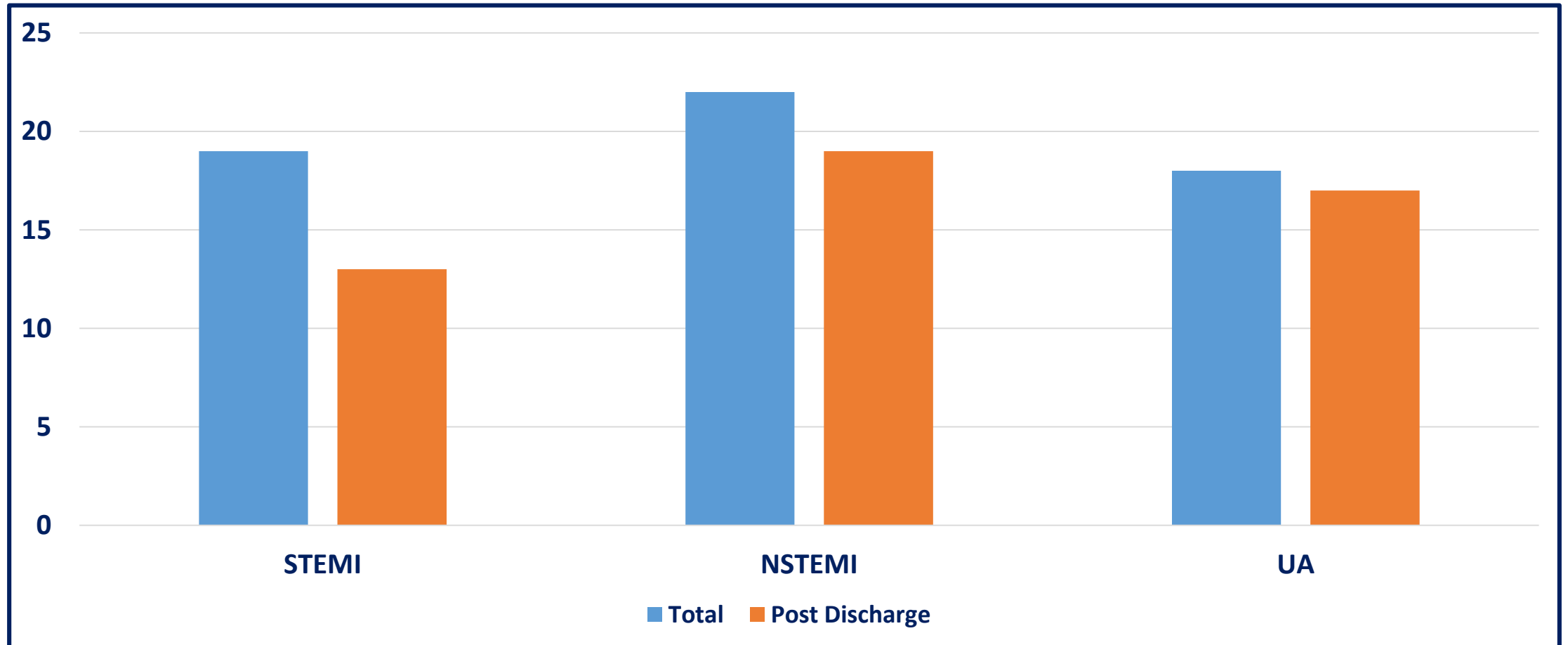


Overall Risk of Death in H, from H-admission to 6 months and from H-discharge to 6 months after ACS

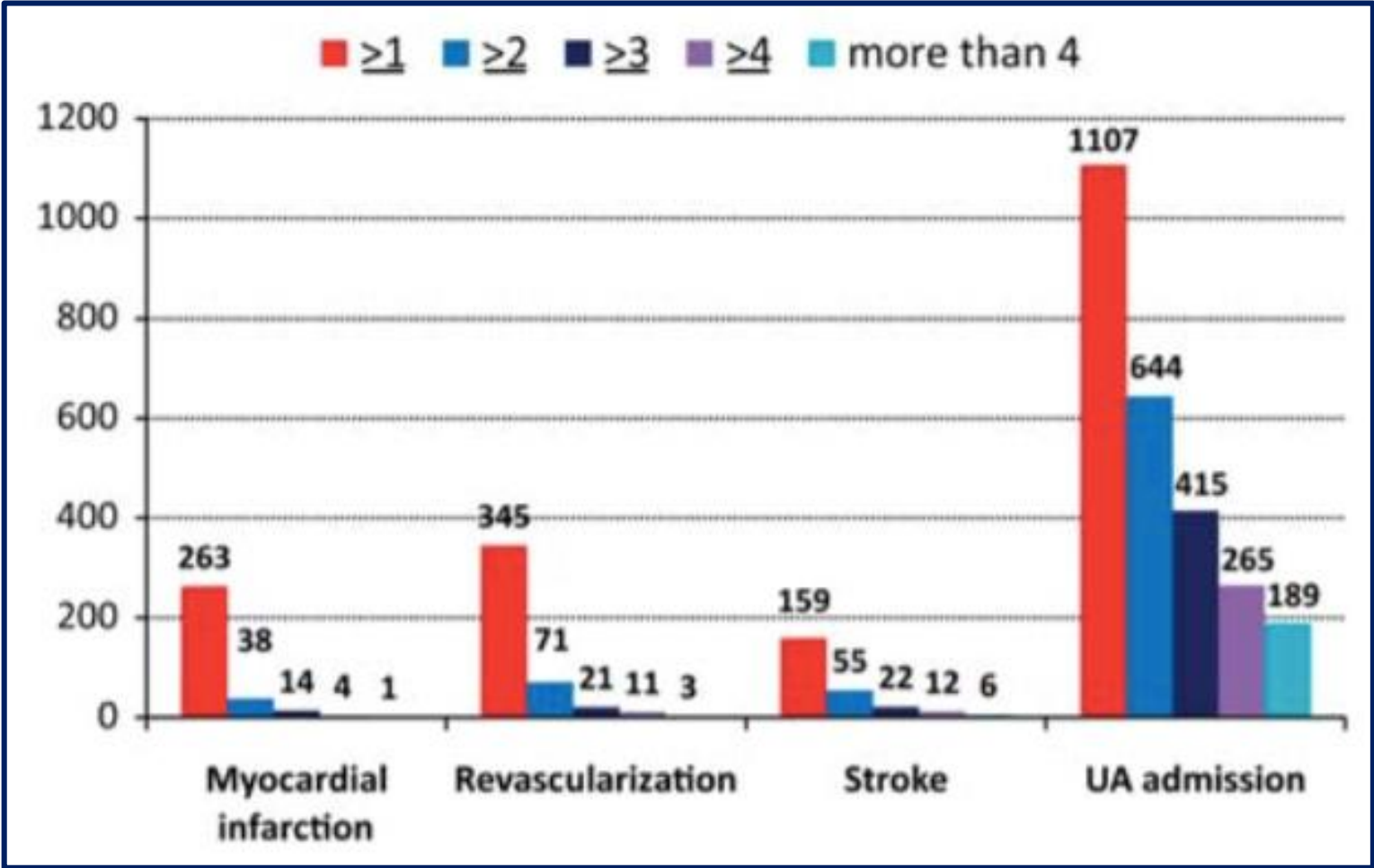


Post ACS events are often fatal!

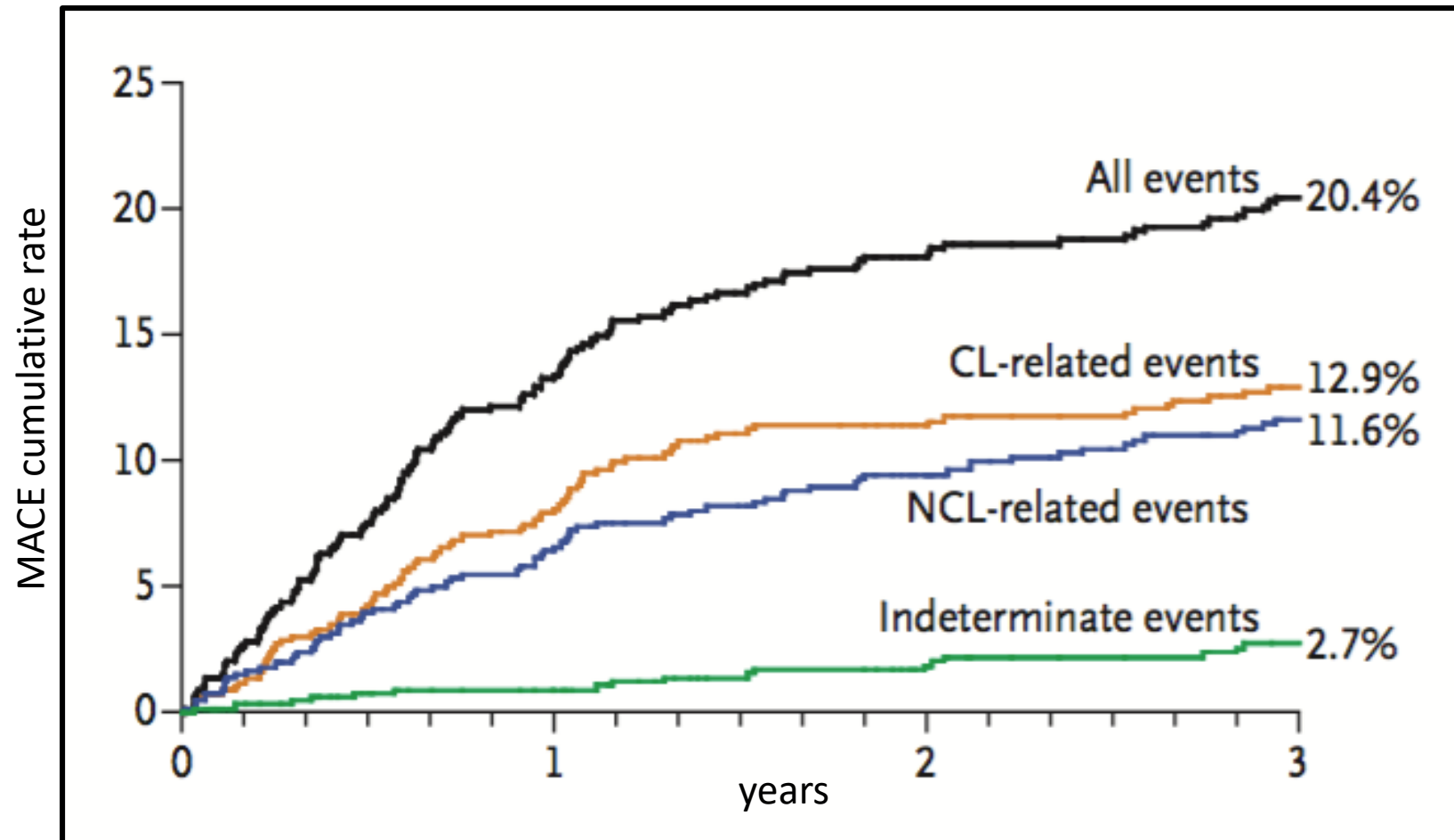
5-years death rates post ACS



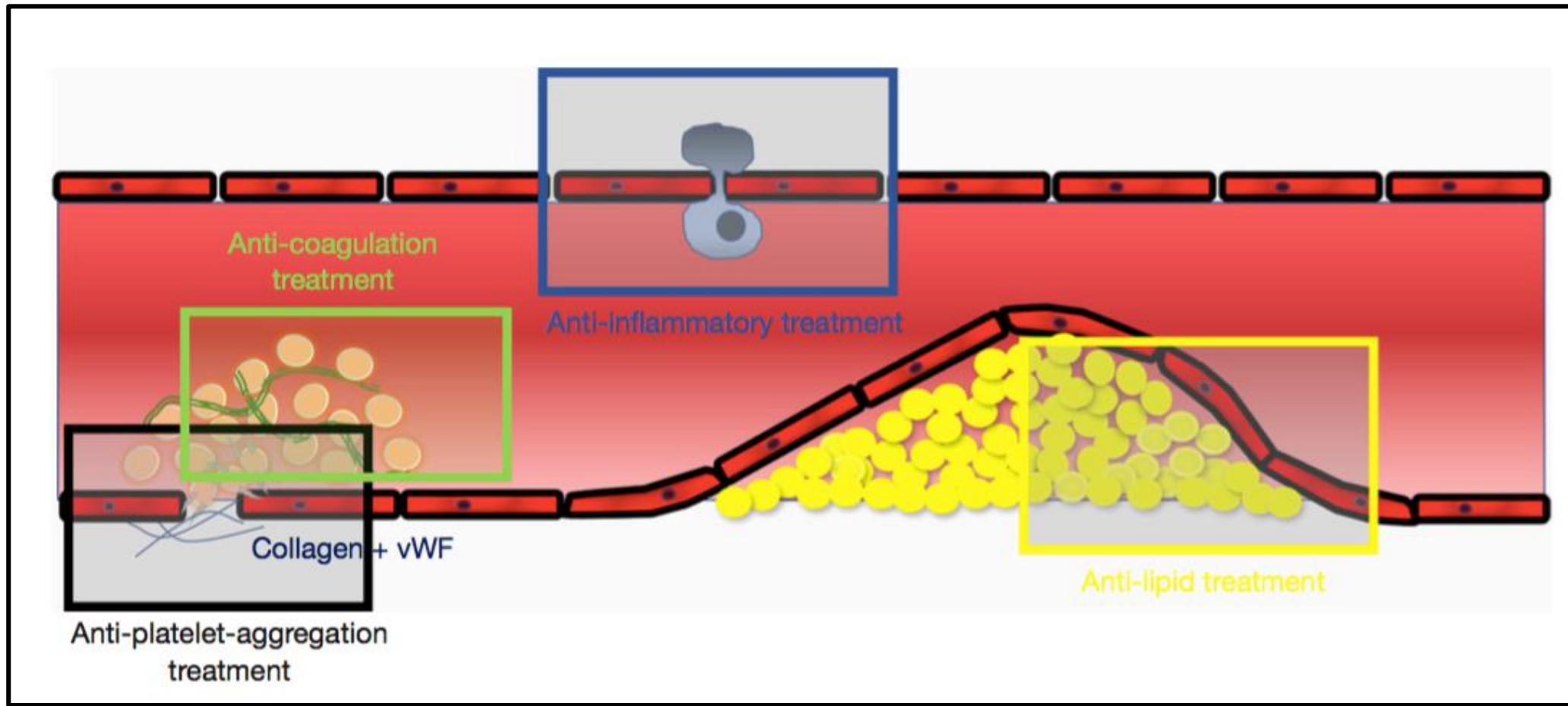
Recurrent Cardiovascular Events following ACS



A Prospective Natural-History Study of Coronary Atherosclerosis



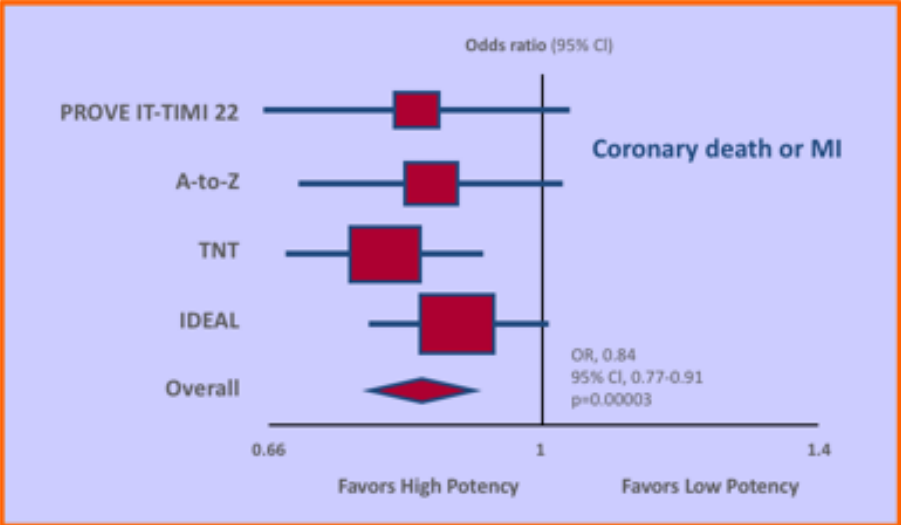
Residual Risk in established cardiovascular disease



Residual cholesterol risk

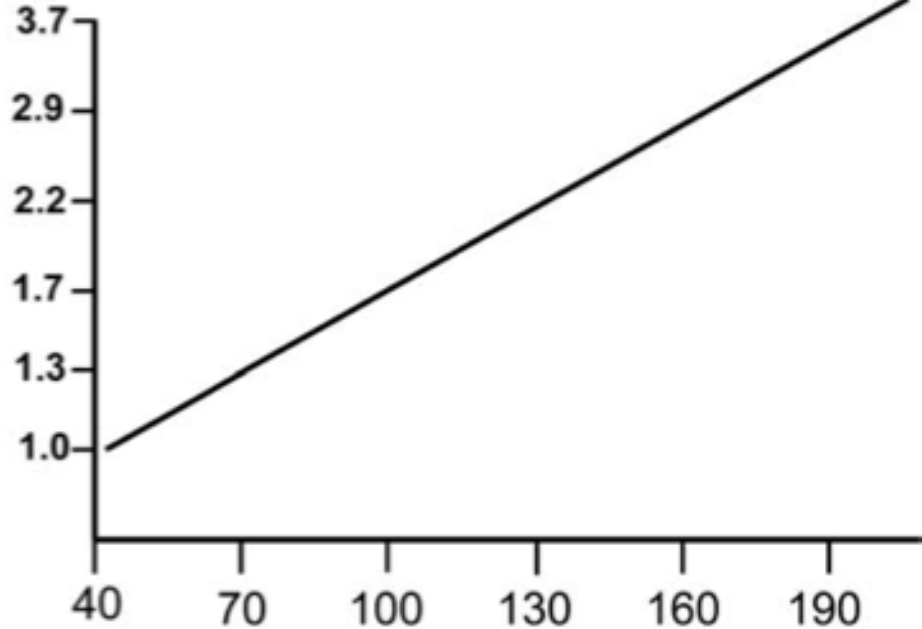
Intensive vs Moderate Statin Therapy

	PROVE IT-TIMI 22	A-to-Z	TNT	IDEAL	Pooled*
Baseline	108	113	152	122	130
Standard	97	101	101	104	101
Intensive	65	69	77	81	75



Cannon CP, JACC 2006

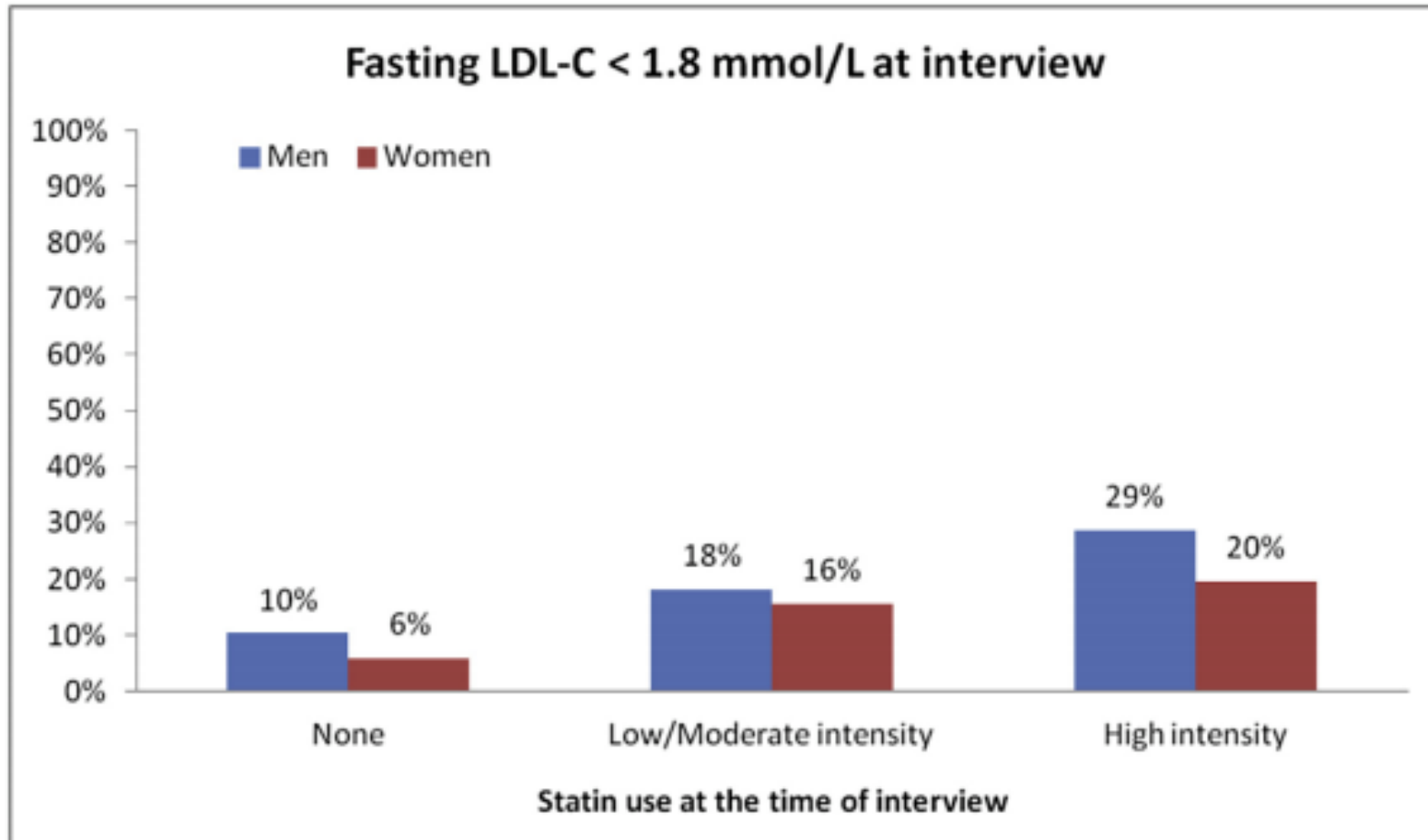
Relative Risk for Coronary Heart Disease (Log Scale)



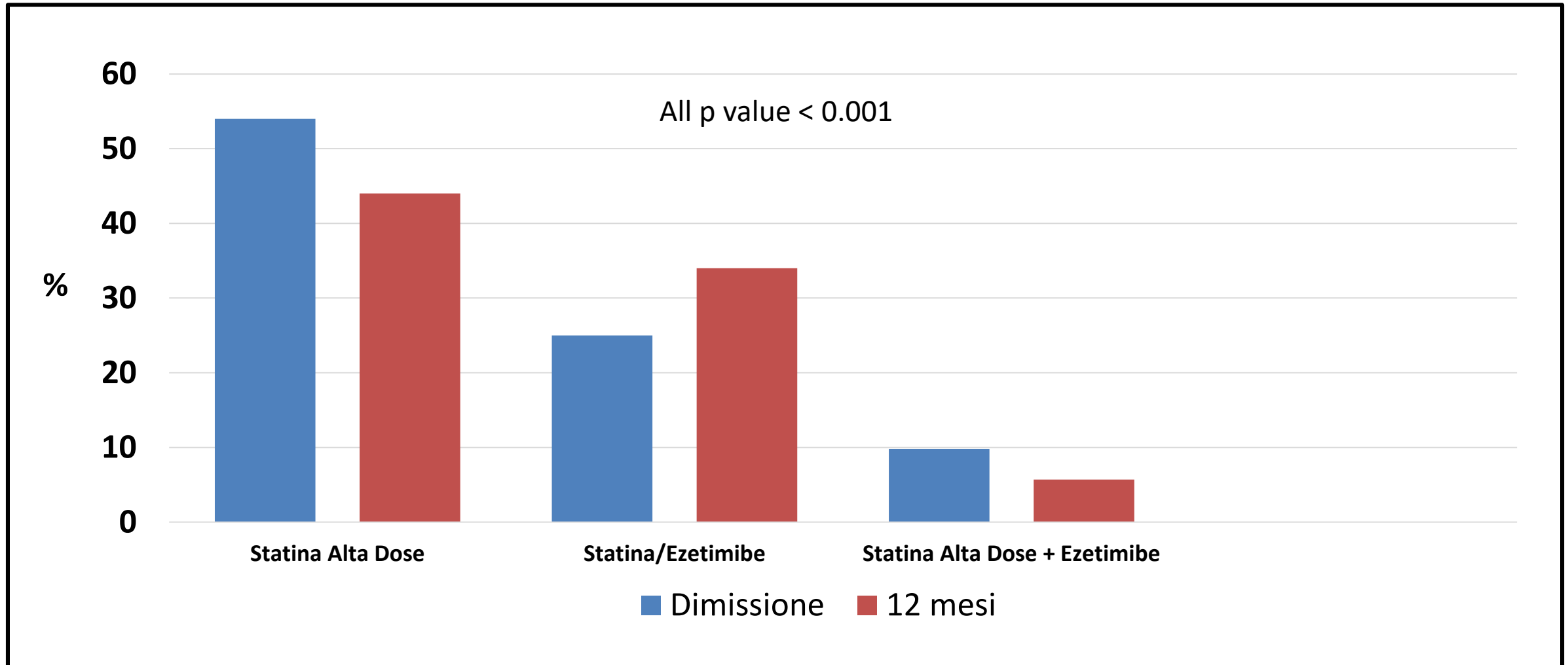
LDL-Cholesterol (mg/dL)

JACC 2004; 44: 720-32

Proportions of patients achieving cLDL target by statin class



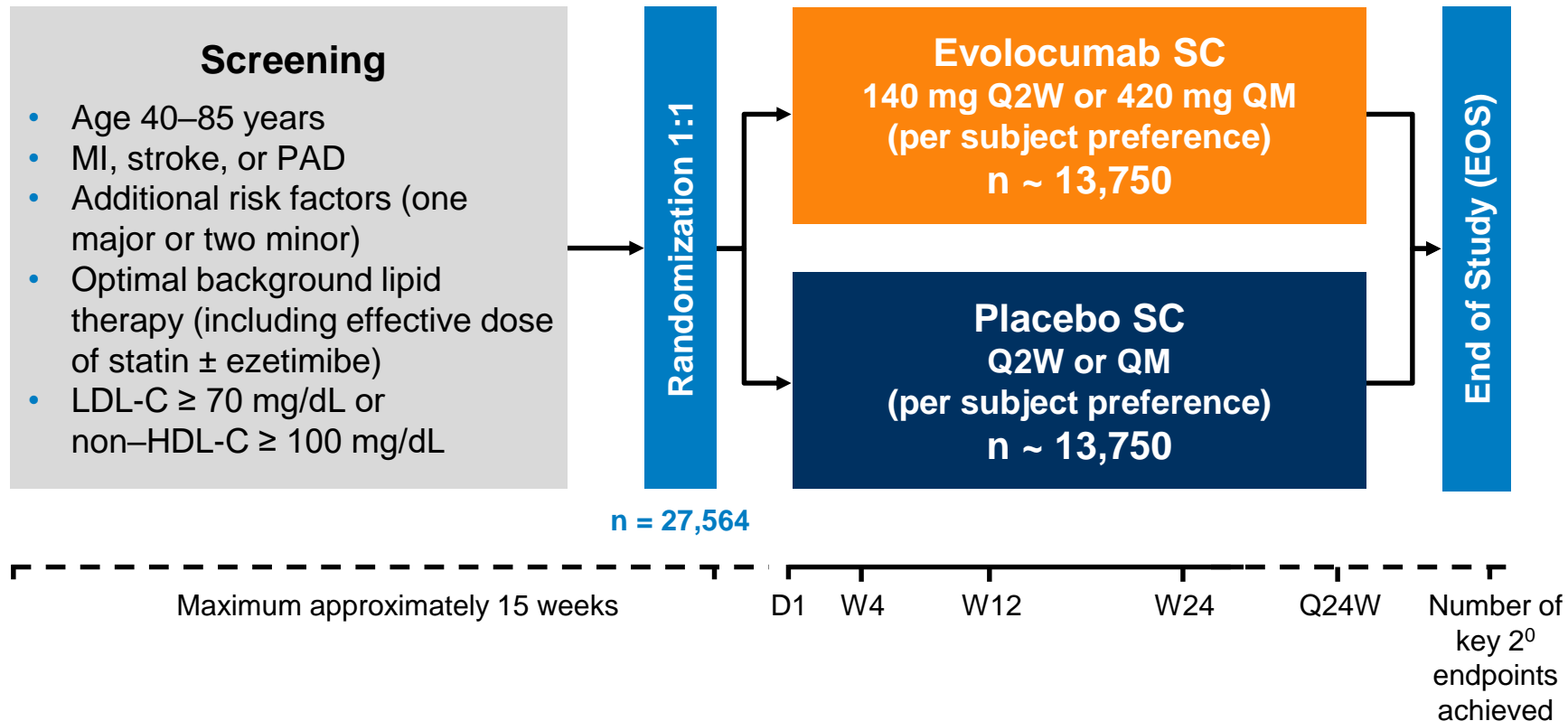
Terapia Ipolimemizzante Registro Post-PCI: Dimissione vs 12 mesi



Evolocumab Outcomes Trial: Study Design Overview



FOURIER: Further cardiovascular **OU**tcomes **R**esearch with PCSK9 **I**nhibition in subjects with **E**levated **R**isk

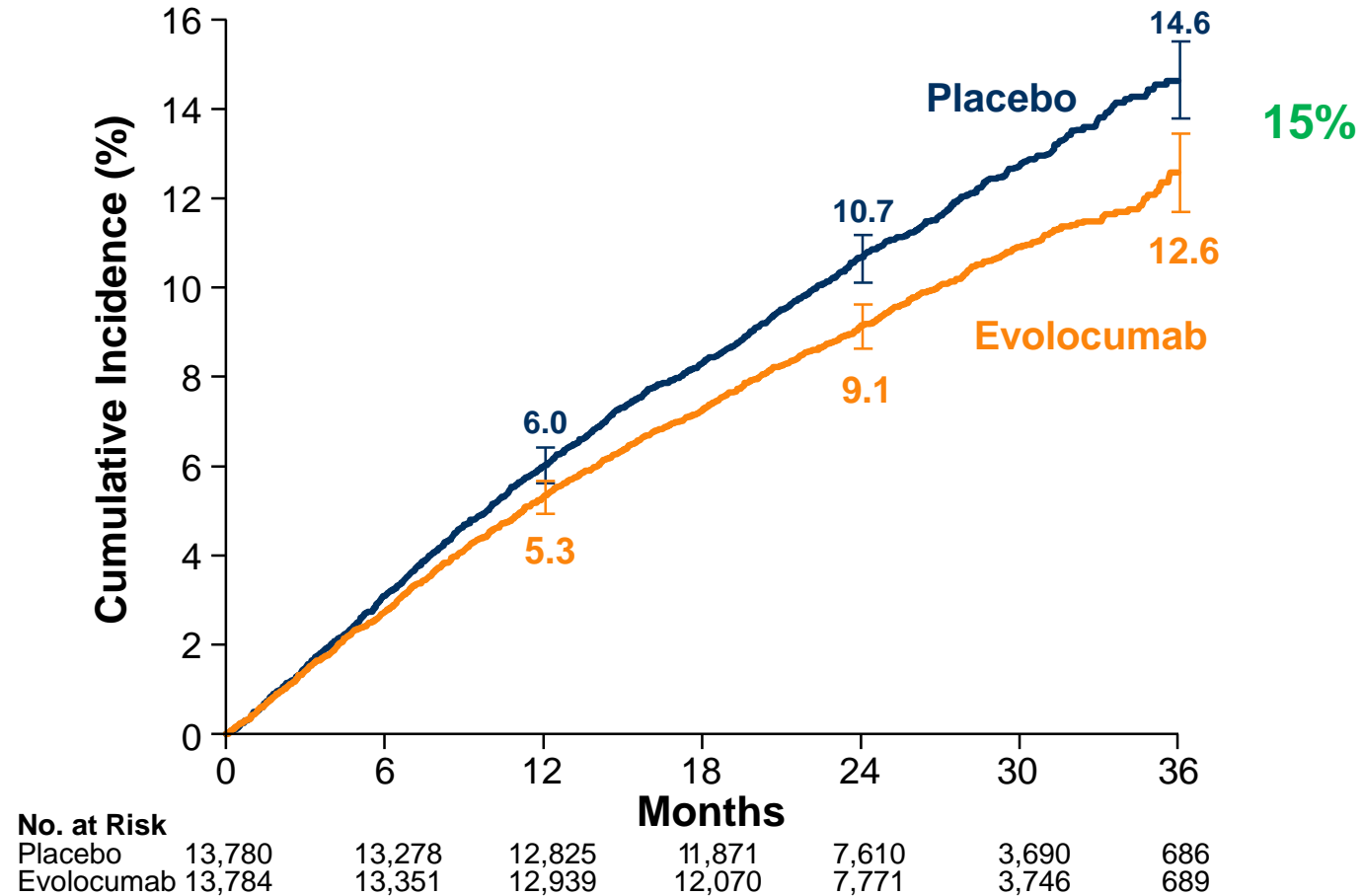


D = day; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol;

MI = myocardial infarction; PAD = peripheral artery disease; Q2W = every 2 weeks; Q24W = every 24 weeks; QM = every month; SC = subcutaneous; W = week.

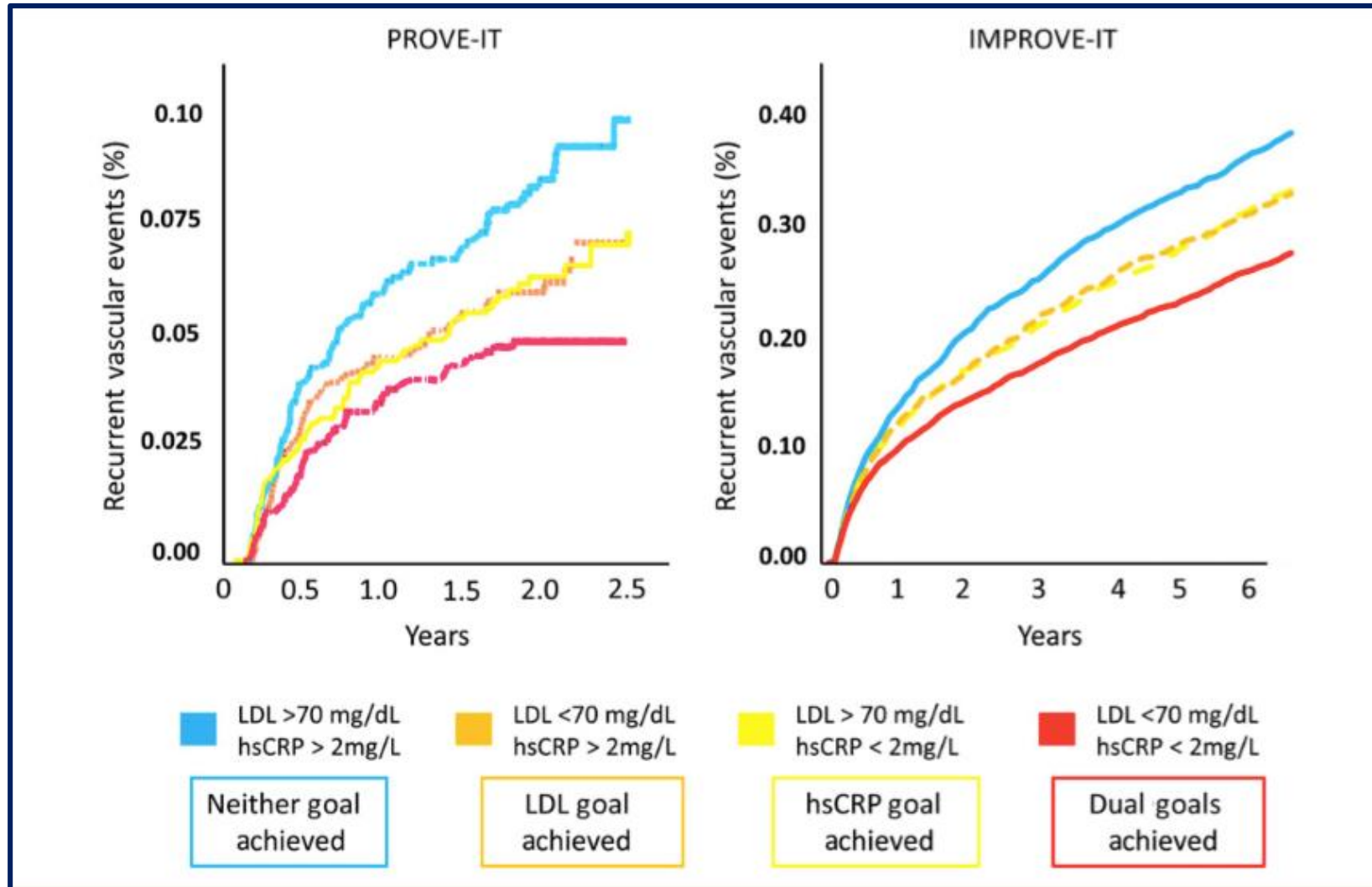
Sabatine MS, et al. *Am Heart J*. 2016;173:94-101. Sabatine MS, et al. *NEJM*. [published online ahead of print March 17, 2017]. doi: 10.1056/NEJMoa1615664

Primary Endpoint: Composite of CV Death, MI, Stroke, Hospitalization for UA, or Coronary Revascularization



HR 0.85 (95% CI 0.79 to 0.92); $P < 0.001$

Residual Risk: the inflammatory pathway



Variable	CANTOS
n	10061
Population	h/o MI, hs-CRP>2 mg/l
FU-time	3.7 years (median)
Concept	Anti-inflammatory
Substance/dosage	Canakinumab 50, 150, 300 mg vs placebo
Adverse Effect	Neutropenia, thrombocytopenia, infection
RRR (mortality)	ns
NNT (mortality)	ns
RRR (PEP: MACCE)	12.4%
NNT (PEP)	50
Treatment cost per year	54160 eur
Treatment cost per avoidance of PEP	2,708,005 eur

- Dose dependent reduction in hsCRP leveles
- Best outcome for 150 mg: HR 0.85, 95% CI 0.74-0.98, p=0.021)
- Greater risk reduction for hsCRP > 2 median
- Significant increase of fatal infections
- Cancer significantly reduced

Perceived risk for cLDL or hsCRP

It's easy.....just look at the value

The risk for antithrombotic therapy

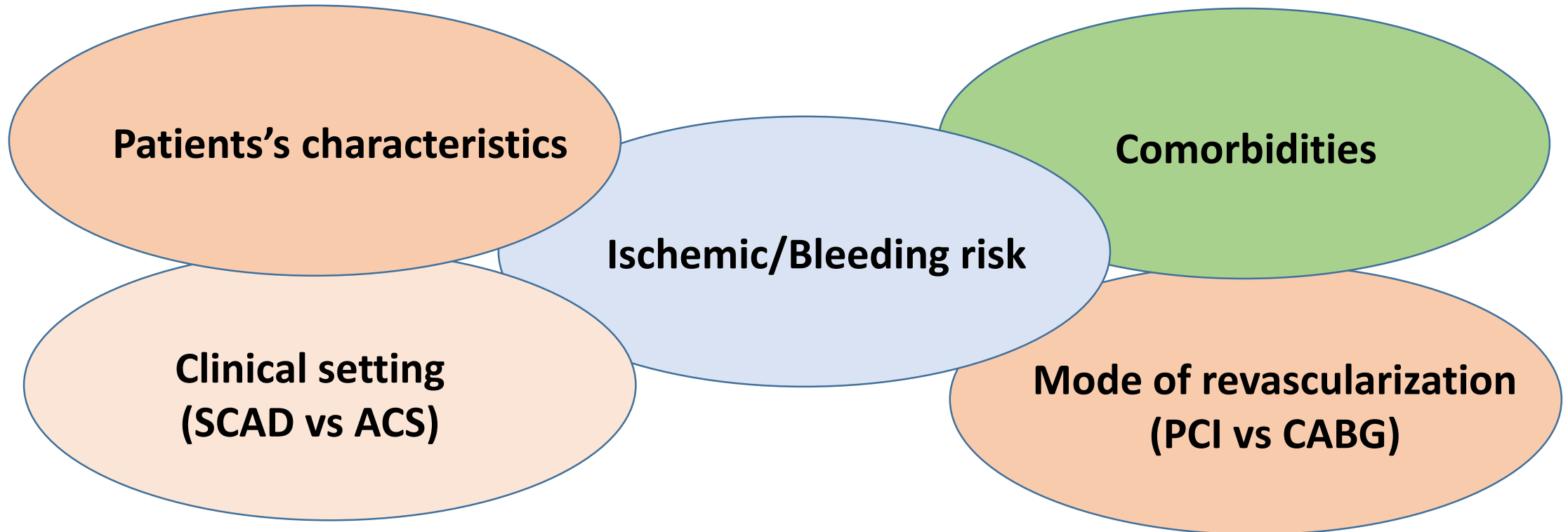


thrombotic risk

haemorrhagic risk

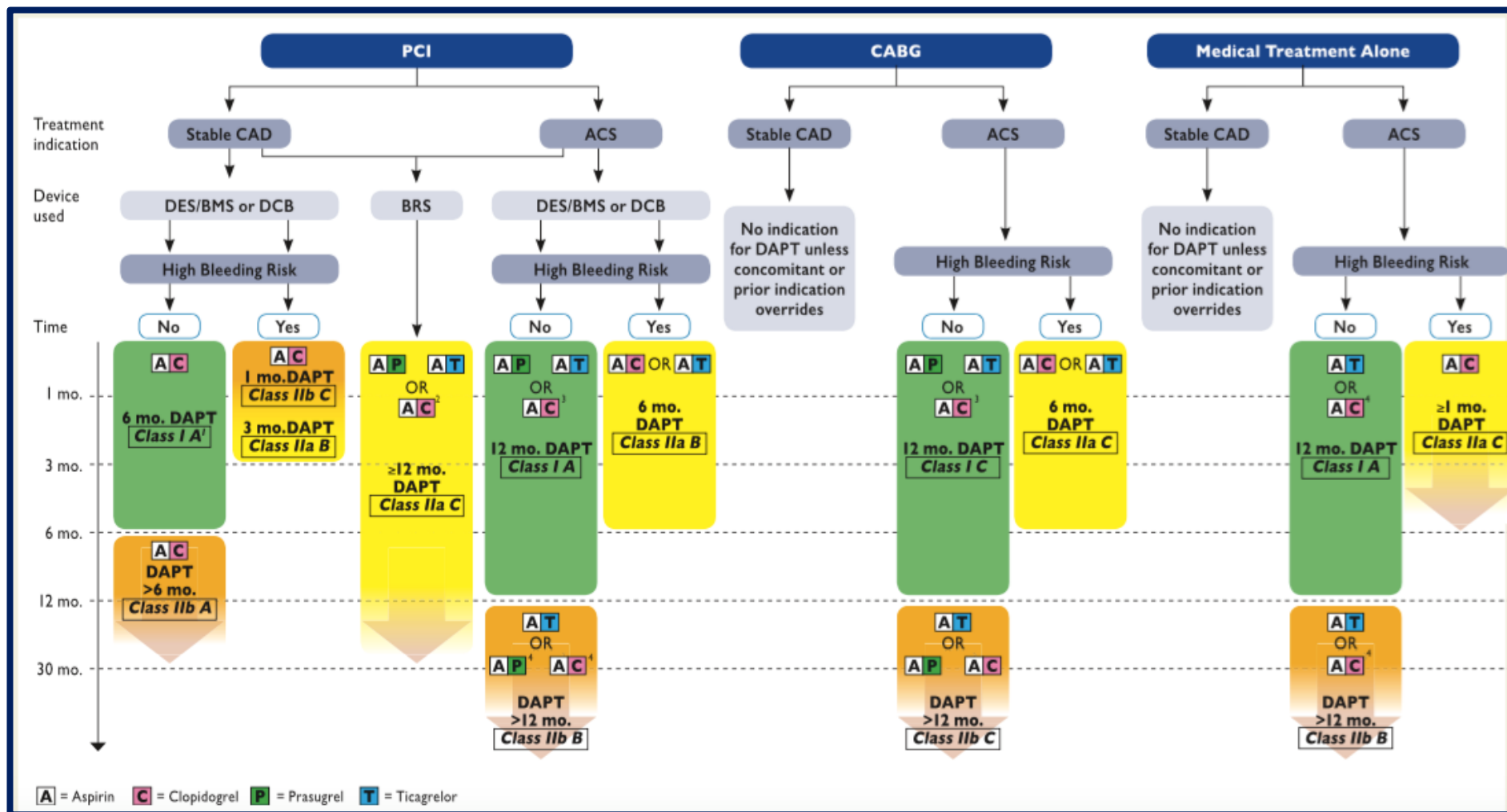
Antithrombotic therapy in CAD

choice, combination, time point of initiation and duration depends on:

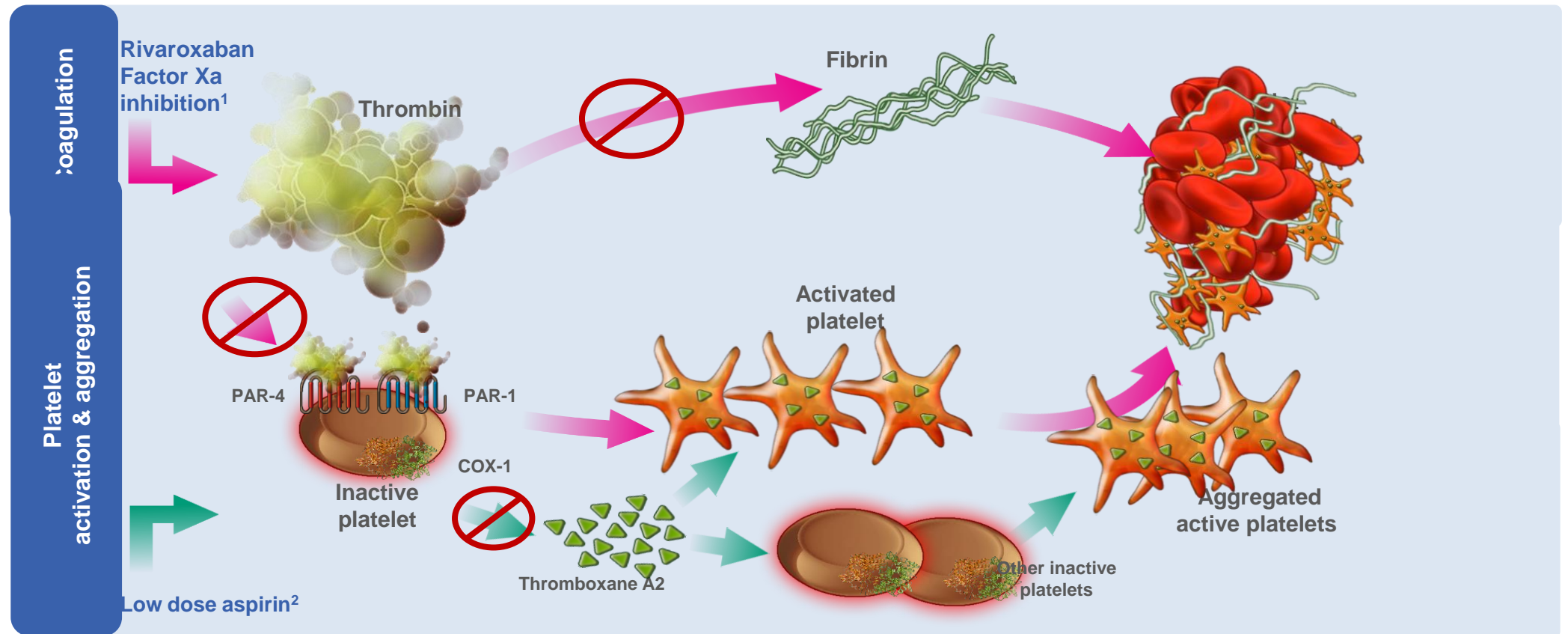




ESC Guidelines



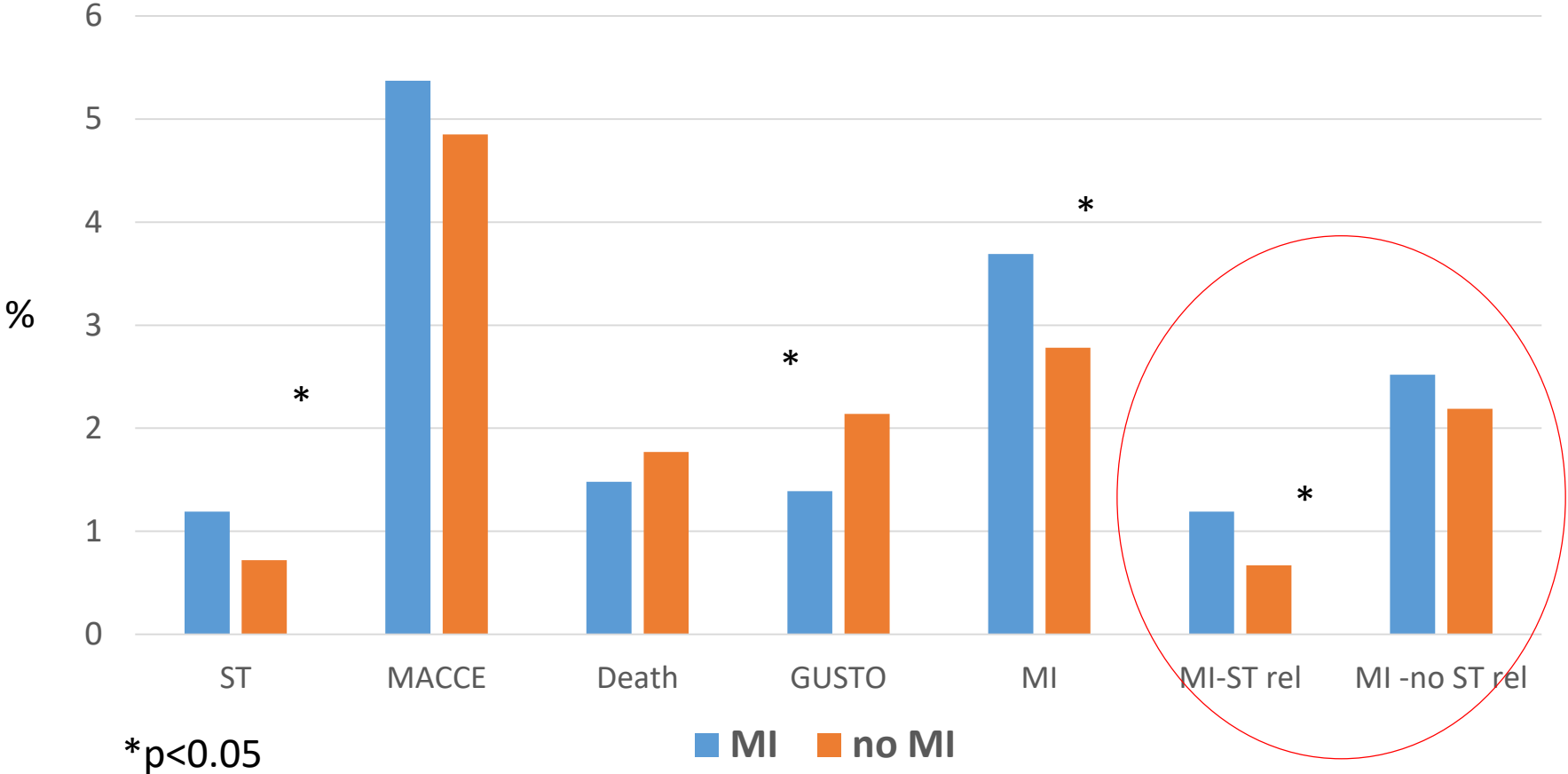
Antithrombotic therapy: a synergistic approach



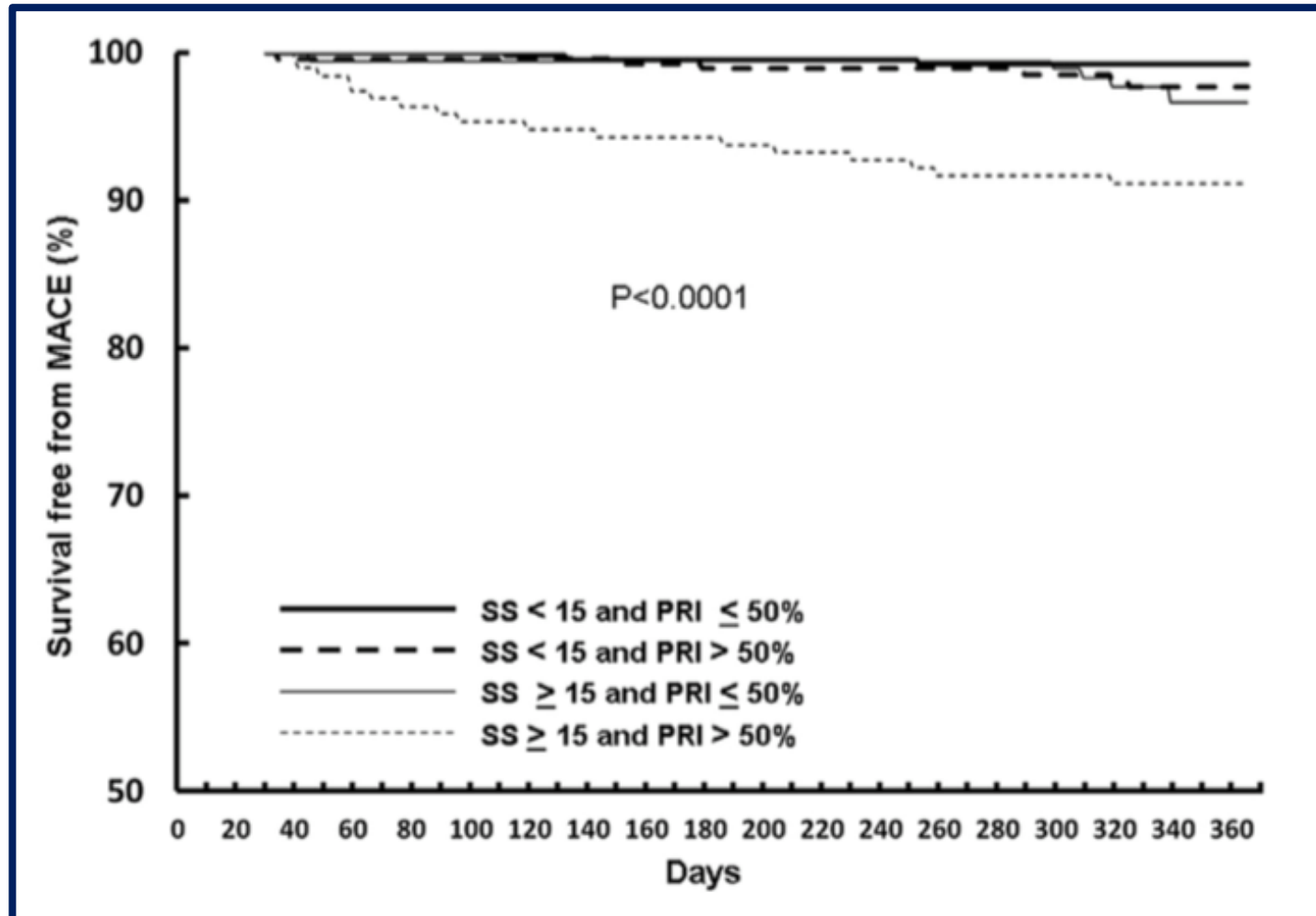
1. Adapted from Angiolillo DJ *et al. Eur Heart J* 2010;31:17–28;

2. Adapted from Mitchell JRA. *BMJ* 1981;282:590–594

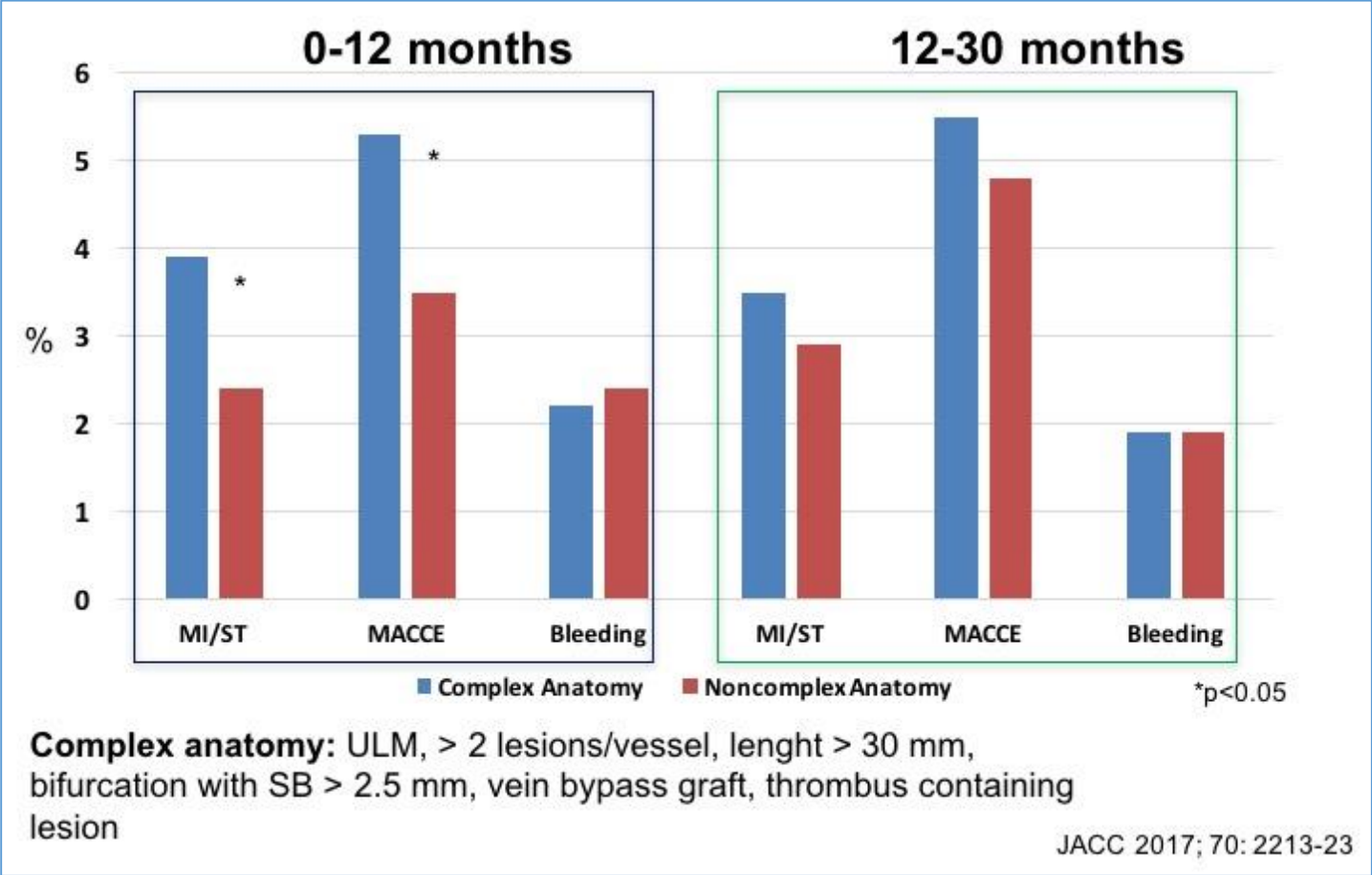
Long-term Ischaemic al bleeding risk according to MI status



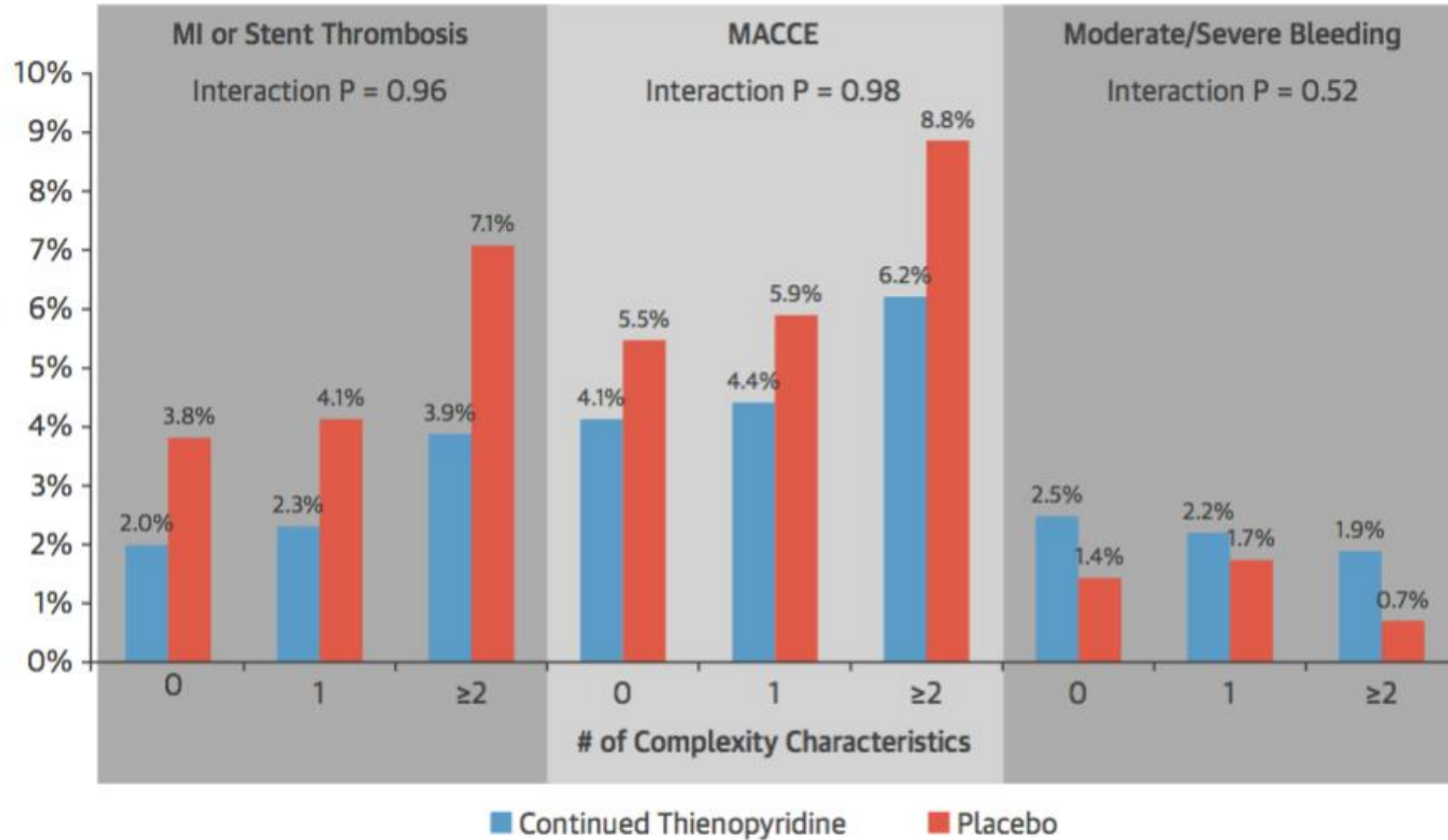
Does coronary anatomy matter?



Does coronary anatomy matter?

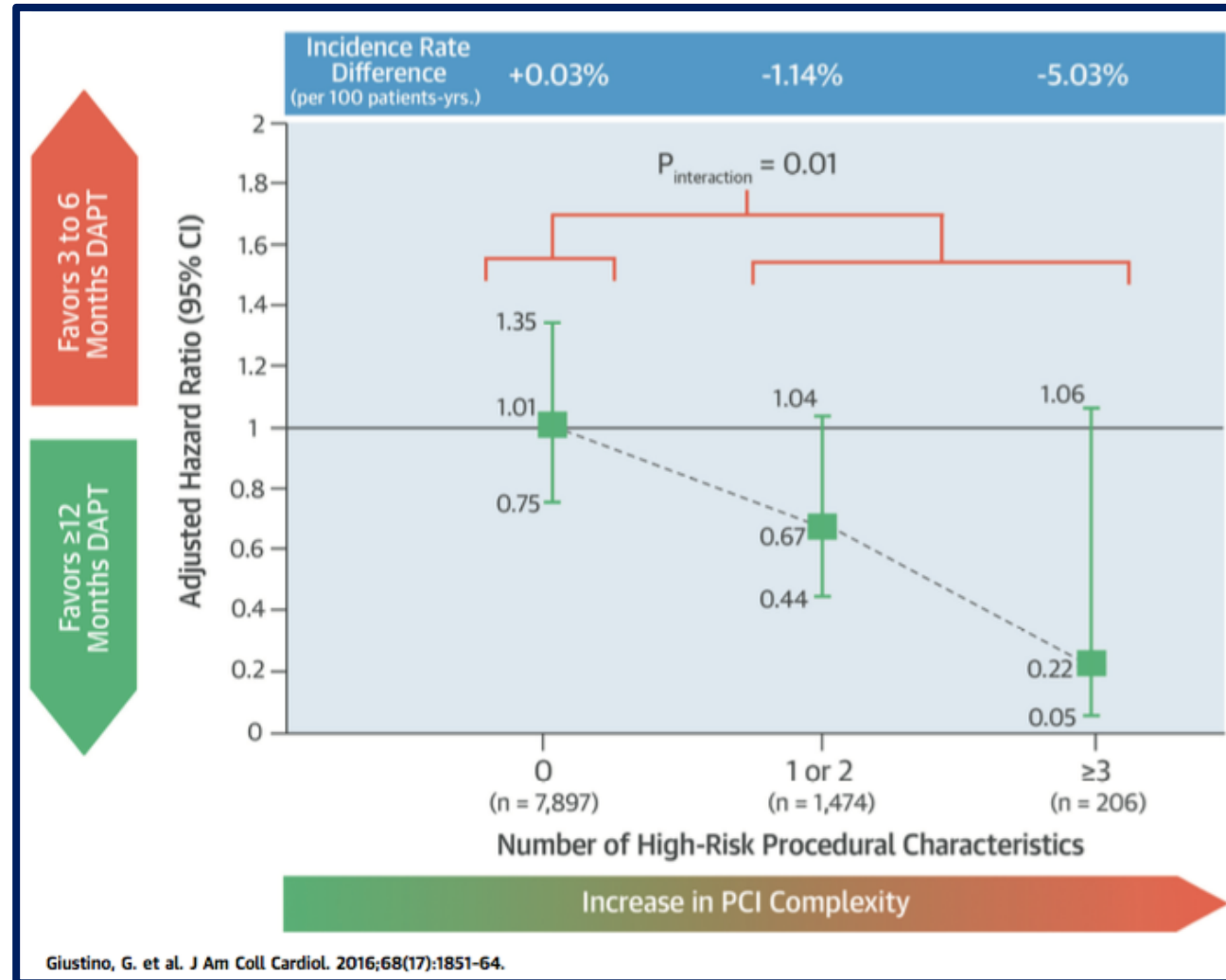


Does coronary anatomy matter?



Does PCI matter?

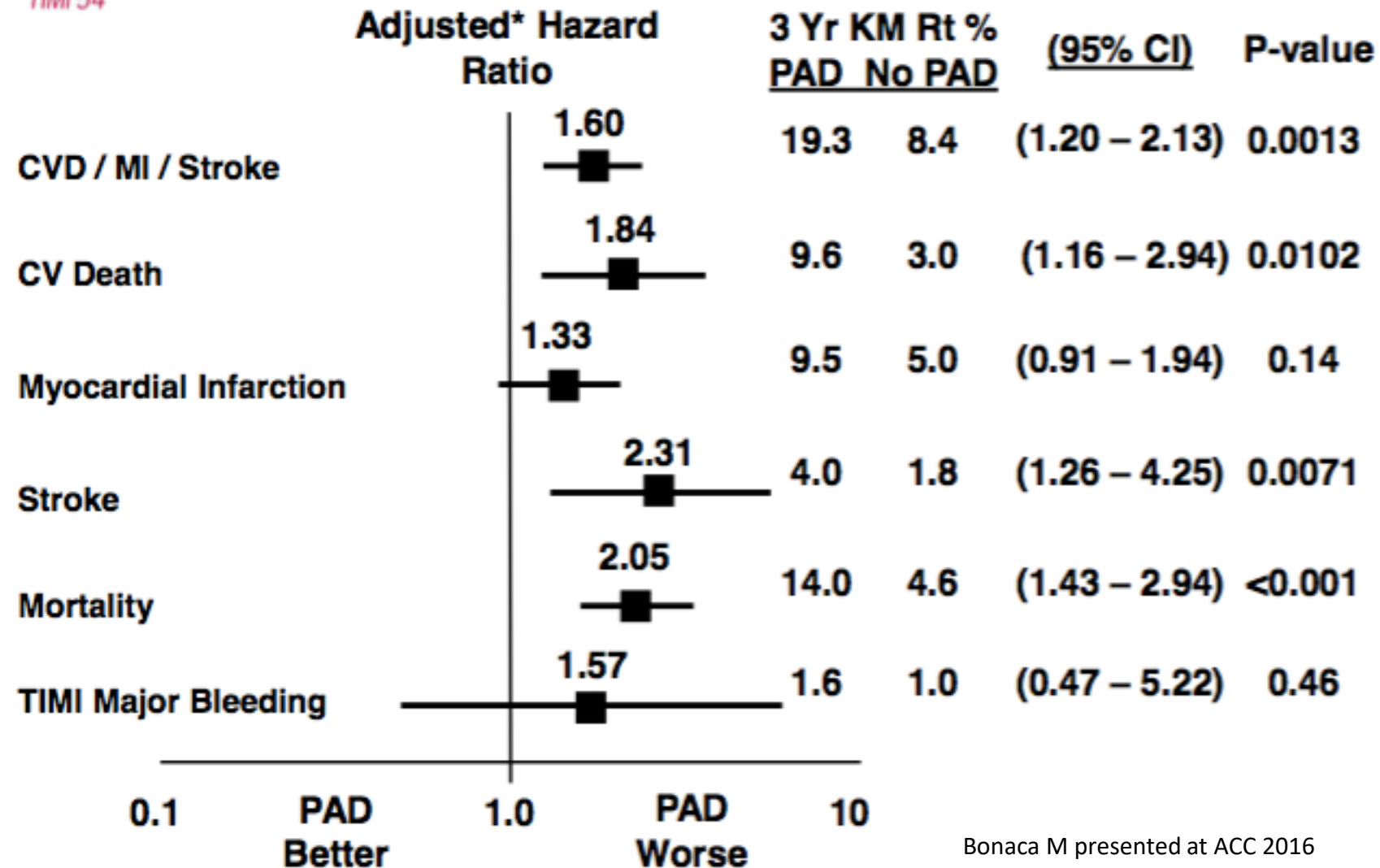
- 3 vessels treated
- ≥ 3 stent implanted
- ≥ 3 lesions treated
- Bifurcation with 2 stent implanted
- Total stent length > 60 mm
- CTO



Cardiac death, MI, ST

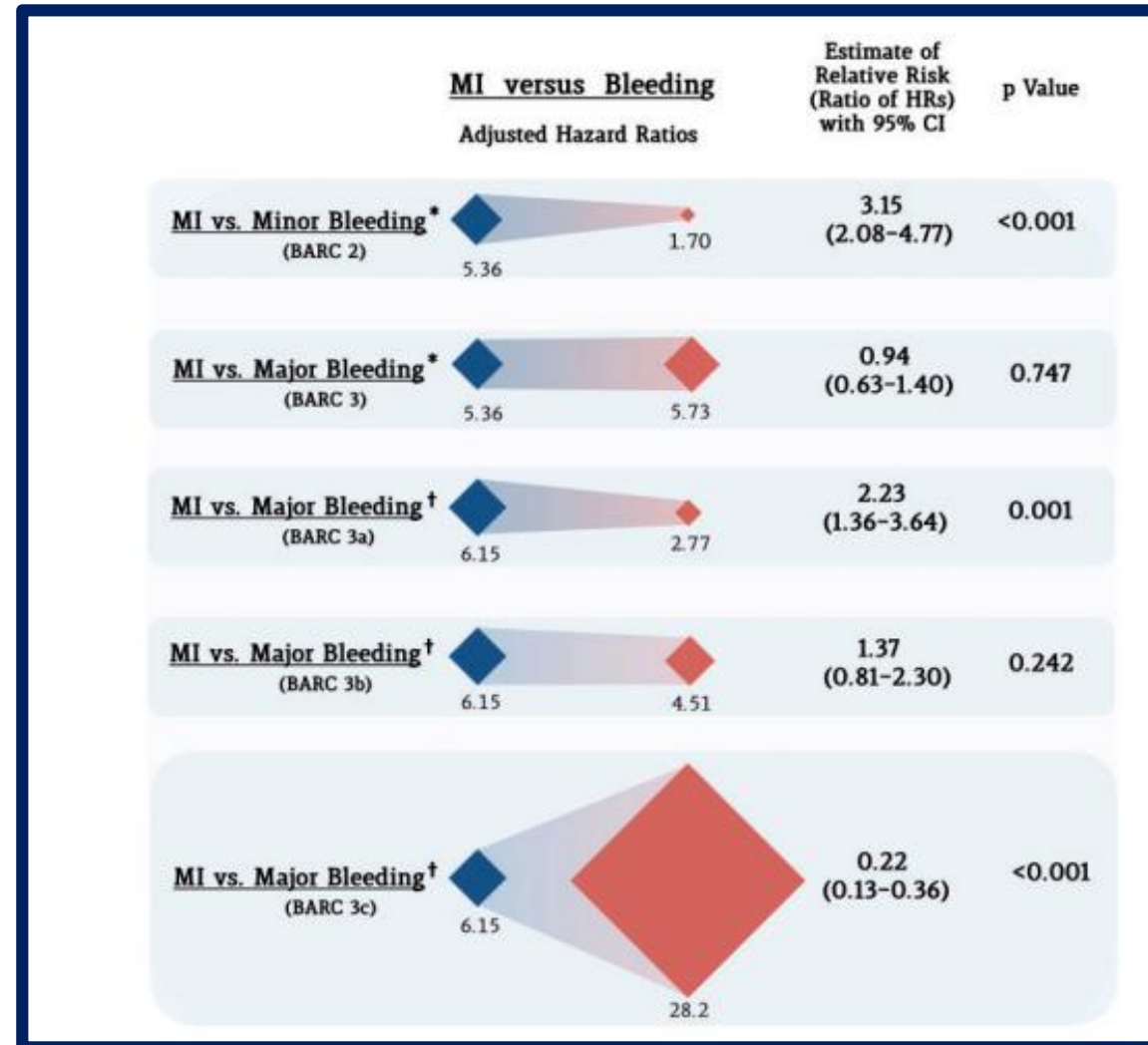
**Complex coronary anatomy and complex PCI help us in detection
of ischemic risk but NOT of bleeding risk!**

Adjusted Risk for Events in Placebo Patients by PAD

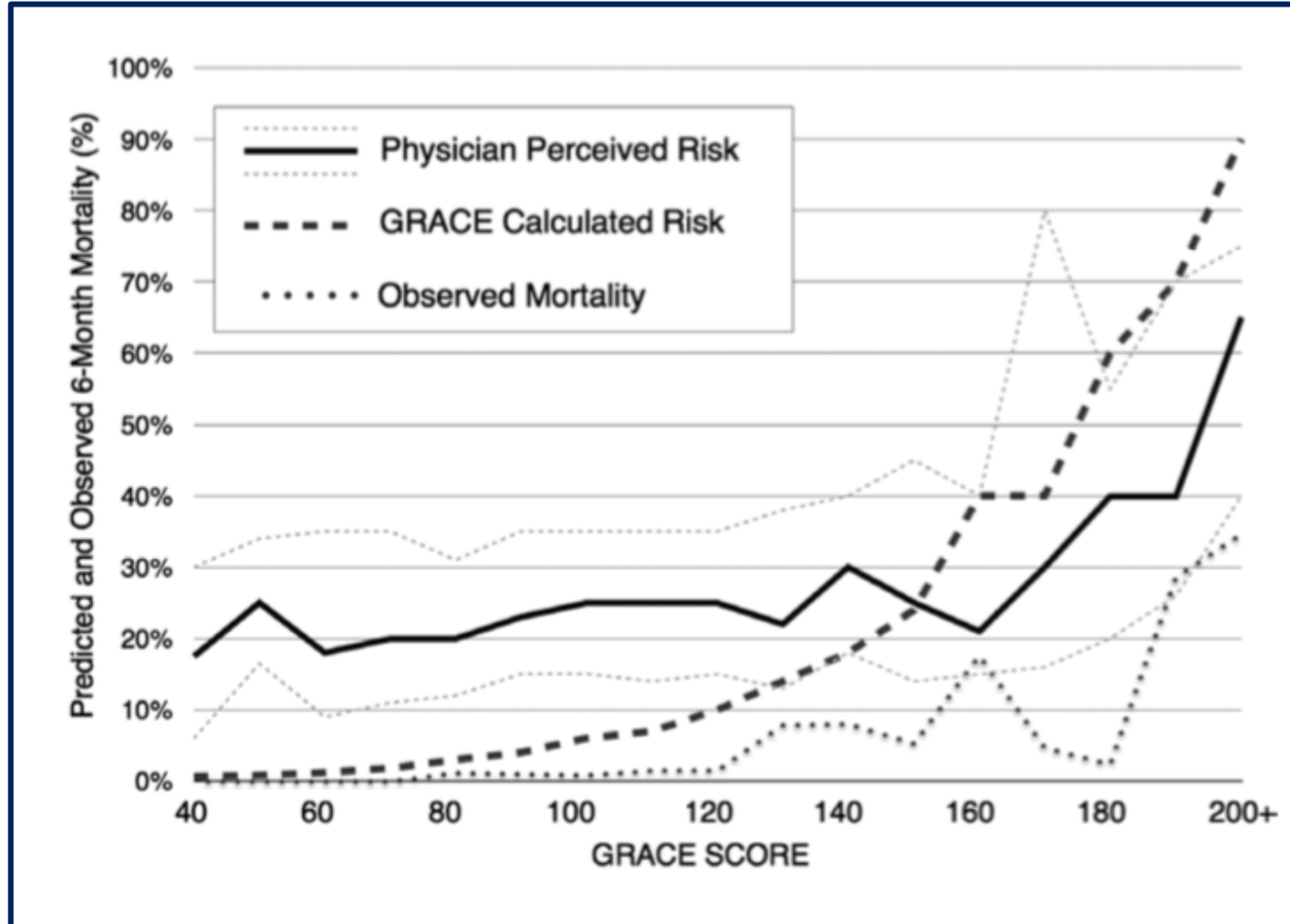


Bonaca M presented at ACC 2016

Bleeding-MI-Mortality



Perceived or calculated risk?



Ischemic/Bleeding risk score

Recommendations	Class ^a	Level ^b
The use of risk scores designed to evaluate the benefits and risks of different DAPT durations ^c may be considered. ^{15,18}	IIb	A

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Coronary Thrombosis and Major Bleeding After PCI With Drug-Eluting Stents

Risk Scores From PARIS

Usman Baber, MD, MS,^a Roxana Mehran, MD,^a Gennaro Giustino, MD,^a David J. Cohen, MD, MSc,^b Timothy D. Henry, MD,^c Samantha Sartori, PhD,^d Cono Ariti, MSc,^d Claire Litherland, MS,^e George Dangas, MD, PhD,^a C. Michael Gibson, MD,^f Mitchell W. Krucoff, MD,^g David J. Moliterno, MD,^h Ajay J. Kirtane, MD, SM,^{h,i} Gregg W. Stone, MD,^{h,j} Antonio Colombo, MD,^k Alaide Chieffo, MD,^l Annapoorna S. Kini, MD,^g Bernhard Witzenbichler, MD,^g Giora Weisz, MD,^h Philippe Gabriel Steg, MD,^m Stuart Pocock, PhD^d

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ISSN 0735-1097/\$36.00
[doi:10.1016/j.jacc.2009.09.076](https://doi.org/10.1016/j.jacc.2009.09.076)

Acute Coronary Syndromes

A Risk Score to Predict Bleeding in Patients With Acute Coronary Syndromes

Roxana Mehran, MD,* Stuart J. Pocock, PhD,† Eugenia Nikolsky, MD, PhD,* Tim Clayton, MSc,‡ George D. Dangas, MD,* Ajay J. Kirtane, MD,* Helen Parise, ScD,* Martin Fahy, MSc,* Steven V. Manoukian, MD,‡ Frederick Feit, MD,§ Magnus E. Ohman, MD,|| Bernard Witzenbichler, MD,¶ Giulio Guagliumi, MD,# Alexandra J. Lansky, MD,* Gregg W. Stone, MD*

New York, New York; London, United Kingdom; Nashville, Tennessee; Durham, North Carolina; Berlin, Germany; and Bergamo, Italy

Research

Original Investigation

Development and Validation of a Prediction Rule for Benefit and Harm of Dual Antiplatelet Therapy Beyond 1 Year After Percutaneous Coronary Intervention

Robert W. Yeh, MD, MSc; Eric A. Secemsky, MD, MSc; Dean J. Kereiakes, MD; Sharon-Lise T. Normand, PhD; Anthony H. Gershlick, MBBS; David J. Cohen, MD, MSc; John A. Spertus, MD, MPH; Philippe Gabriel Steg, MD; Donald E. Cutlip, MD; Michael J. Rinaldi, MD; Edoardo Camenzind, MD; William Wijns, MD, PhD; Patricia K. Apruzzese, MA; Yang Song, MS; Joseph M. Massaro, PhD; Laura Mauri, MD, MSc, for the DAPT Study Investigators

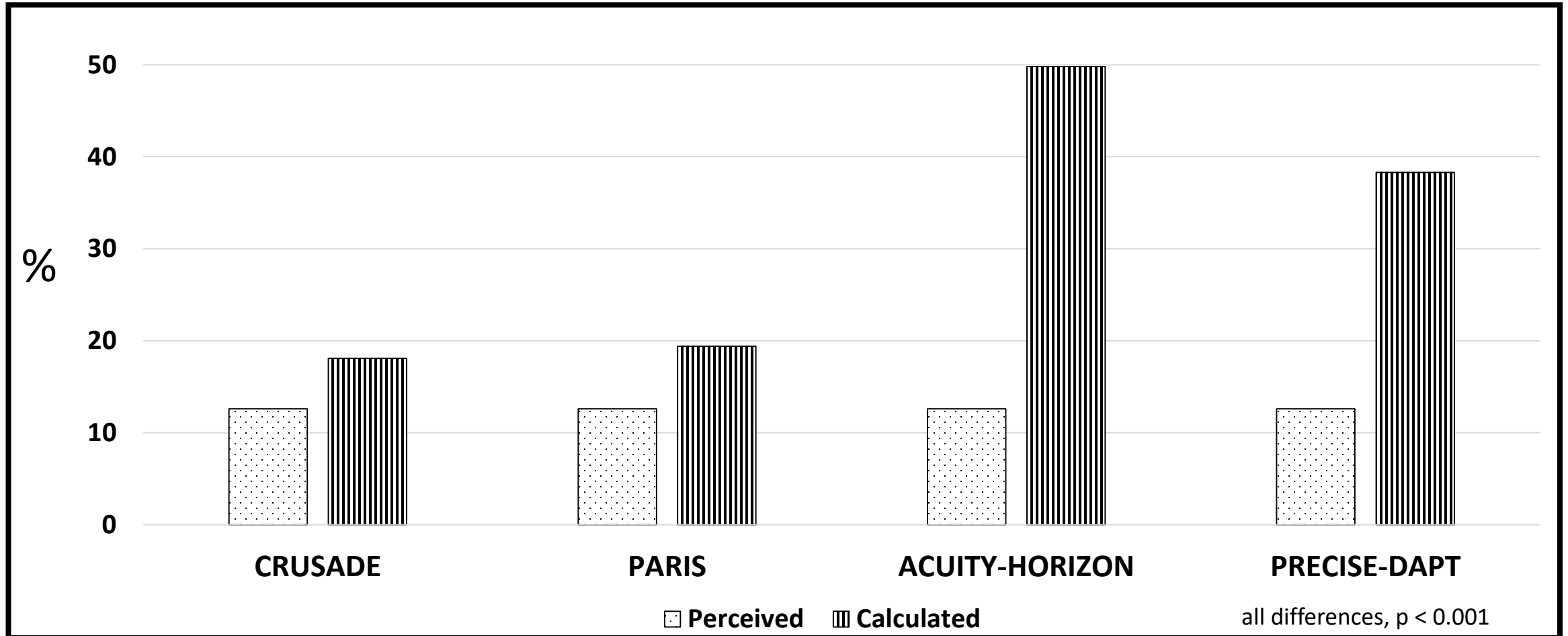
Derivation and validation of the predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy (PRECISE-DAPT) score: a pooled analysis of individual-patient datasets from clinical trials

Francesco Costa*, David van Klaveren*, Stefan James, Dik Heg, Lorenz Raber, Fausto Feres, Thomas Pilgrim, Myeong-Ki Hong, Hyo-Soo Kim, Antonio Colombo, Philippe Gabriel Steg, Thomas Zanchin, Tullio Palmerini, Lars Wallentin, Deepak L. Bhatt, Gregg W. Stone, Stephan Windecker, Ewout W. Steyerberg, Marco Valgimigli, for the PRECISE-DAPT Study Investigators

	Popolazione derivazione	P2Y12	Popolazione validazione	Timing evento emorragico	C-statistic
CRUSADE	NSTEMI	NA	SCA-NSTEMI	intraospedaliero	0.70
PARIS	Stable/ACS	clopidogrel (94%)	Stable/ACS	24 mesi	0.64
Mehran	ACS	NA	NA	30 giorni	NA
PRECISE-DAPT	Stable/ACS	clopidogrel (88%)	ACS	12 mesi	0.70/0.66
DAPT	Stable/ACS	clopidogrel (65%)	Stable/ACS	dal 12 mese	0.64
BleeMACS	ACS	NA	ACS	12 mesi	0.65

Ferlini M et al GIC 2018

Comparison between rate of patients at high bleeding risk perceived vs calculated



Data from Post PCI registry Supported by SICI-GISE with unrestricted grant of Astra Zeneca

Ferlini M et al. Circulation CV Int in press

The DAPT Score

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

Distribution of DAPT Scores among all randomized subjects in the DAPT Study

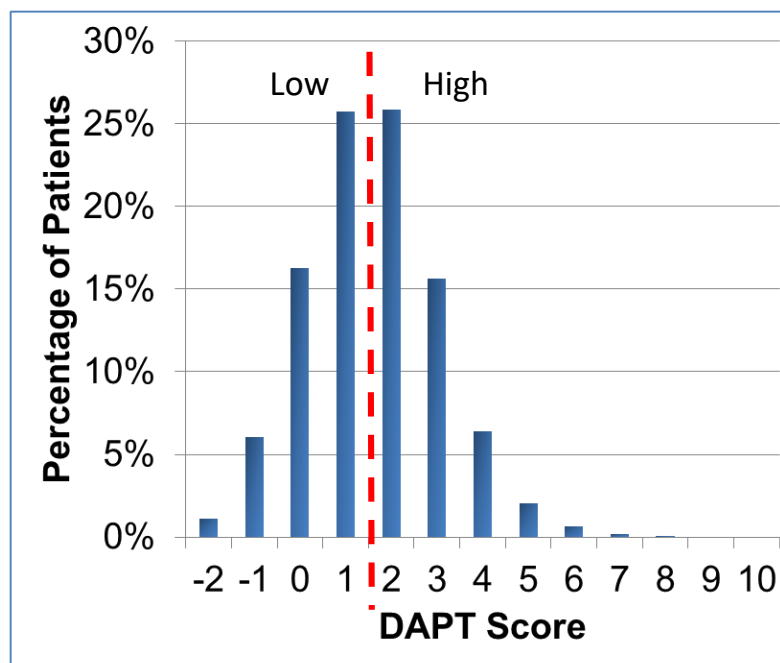


TABLE 3 Discrimination of the DAPT Score for Ischemic and Bleeding Outcomes

	All	New-Generation DES	MI at Index PCI	No MI at Index PCI
MI or stent thrombosis	0.58 (0.56–0.60)	0.57 (0.54–0.59)	0.58 (0.56–0.60)	0.58 (0.55–0.61)
MACCE	0.54 (0.53–0.55)	0.54 (0.52–0.56)	0.54 (0.52–0.55)	0.54 (0.52–0.56)
Fatal or major bleeding*	0.49 (0.45–0.53)	0.51 (0.46–0.57)	0.48 (0.43–0.52)	0.49 (0.42–0.56)
Fatal or major bleeding or bleeding requiring hospitalization*	0.48 (0.46–0.51)	0.48 (0.45–0.51)	0.48 (0.46–0.51)	0.48 (0.45–0.52)

Values are Harrell's C (95% confidence interval). *Discrimination of the DAPT score in analyses where a lower score indicates higher bleeding risk.

MI = myocardial infarction; MACCE = major adverse cardiovascular and cerebrovascular event(s); other abbreviations as in [Table 1](#).

JACC 2018; 72: 1069-78

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VOL. 72, NO. 10, 2018

EDITORIAL COMMENT

A Swing and a Miss for the DAPT Score*

John A. Bittl, MD



Variable	COMPASS	PEGASUS
n	27395	21162
Population	Stable CAD	Prior MI 1-3 year + additional risk
Median time form MI	*79% ≥ 2 yrs	1.7 yrs
FU-time	23 months	33 months
Concept	Anti-thrombotic	Anti-platelet
Substance/dosage	Riv 5 mg bid mono vs Riv 2.5 mg bid + ASA vs ASA mono	Tic 60 or 90 mb bid vs placebo
Adverse Effect	ISTH bleed (HR 1.7; 95% CI 1.4-2.05, p<0.001)	TIMI maj (HR 2.32, 95% CI 1.68-3.21, p<0.001)
NNH	83	80
RRR (mortality)	17.4%	ns
NNT (mortality)	139	212
RRR (PEP)	23.8%	15.5%
NNT (PEP)	77	78
Treatment cost per year	1298 eur	943 eur
Treatment cost per avoidance of PEP	99,87 eur	74.48 eur

*69% ha histoty of prior MI



DANKSCHEEN

BIYAN
SHUKRIA

GRACIAS

ARIGATO

SHUKURIA

JUSPAXAR

GOZAIMASHITA

EFCHARISTO

TASHAKKUR ATU

KOMAPSUMNIDA

YAQHANYELAY

GRAZIE

MEHRBANI

BOLZIN

SUKSAMA

EKHMET

PALDIES

YOU

MERCII

THANK

TINGKI