Newark Beth Israel Medical Center | RWJBarnabas HEALTH

201 Lyons Avenue, Newark, N.J. 07112

Anti-platelet Conundrums and Confusions: Electives, Emergencies, and the Elderly

Marc Cohen, M.D, FACC, FSCAI

Chairman, Dept. of Medicine; Newark Beth Israel Med Ctr,

Professor of Medicine, Rutgers-New Jersey Medical School

Cors at the Shore 2023

Presenter Disclosure Information

DR. MARC COHEN has the following relationships that might materially affect this presentation:

Grant/Research Support: Edwards

Consultant: Getinge

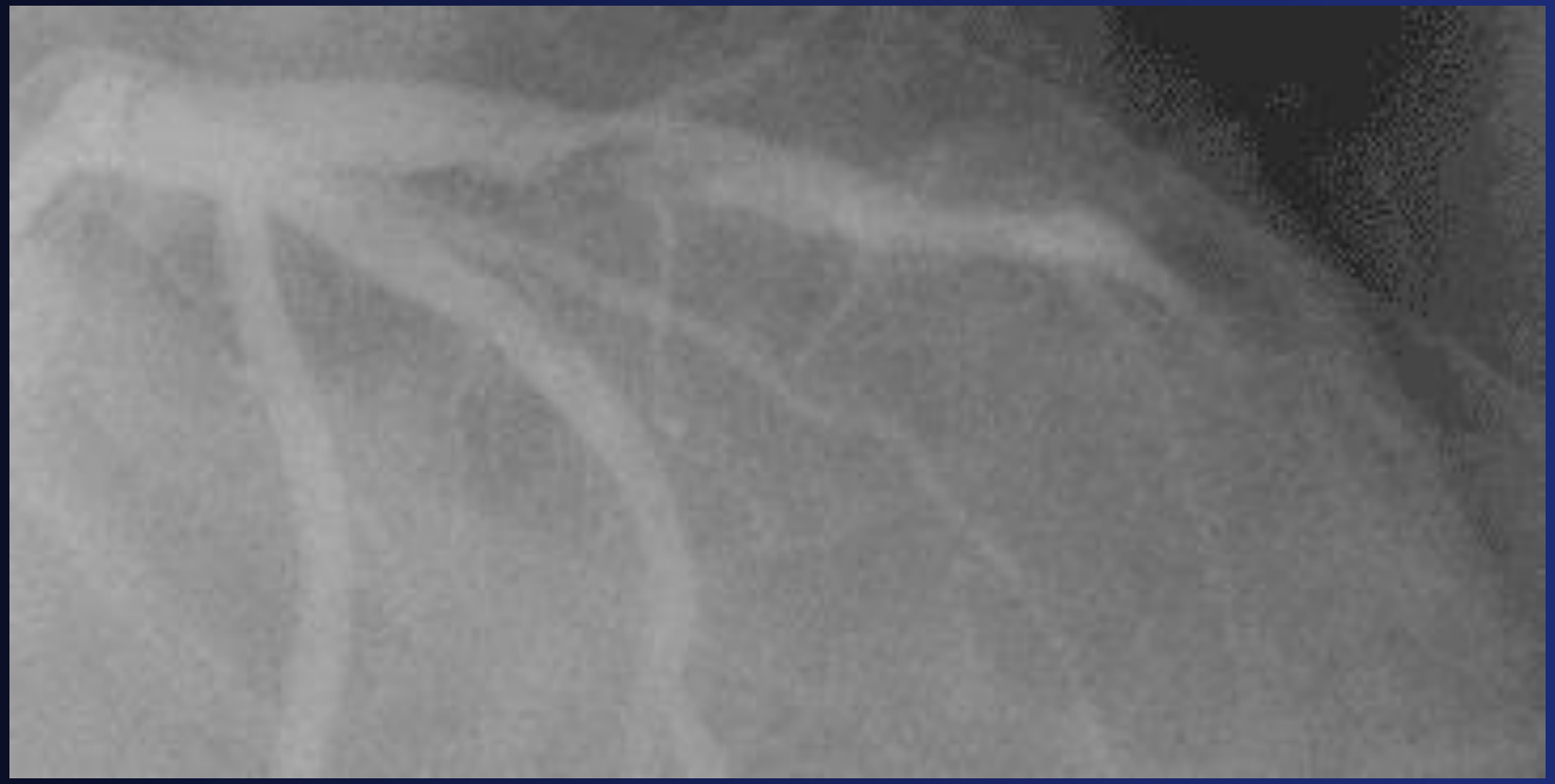
Speakers Bureau: BI, Janssen, AZ, Lilly

Major Stock Shareholder: NONE

2023 Cors at the Shore

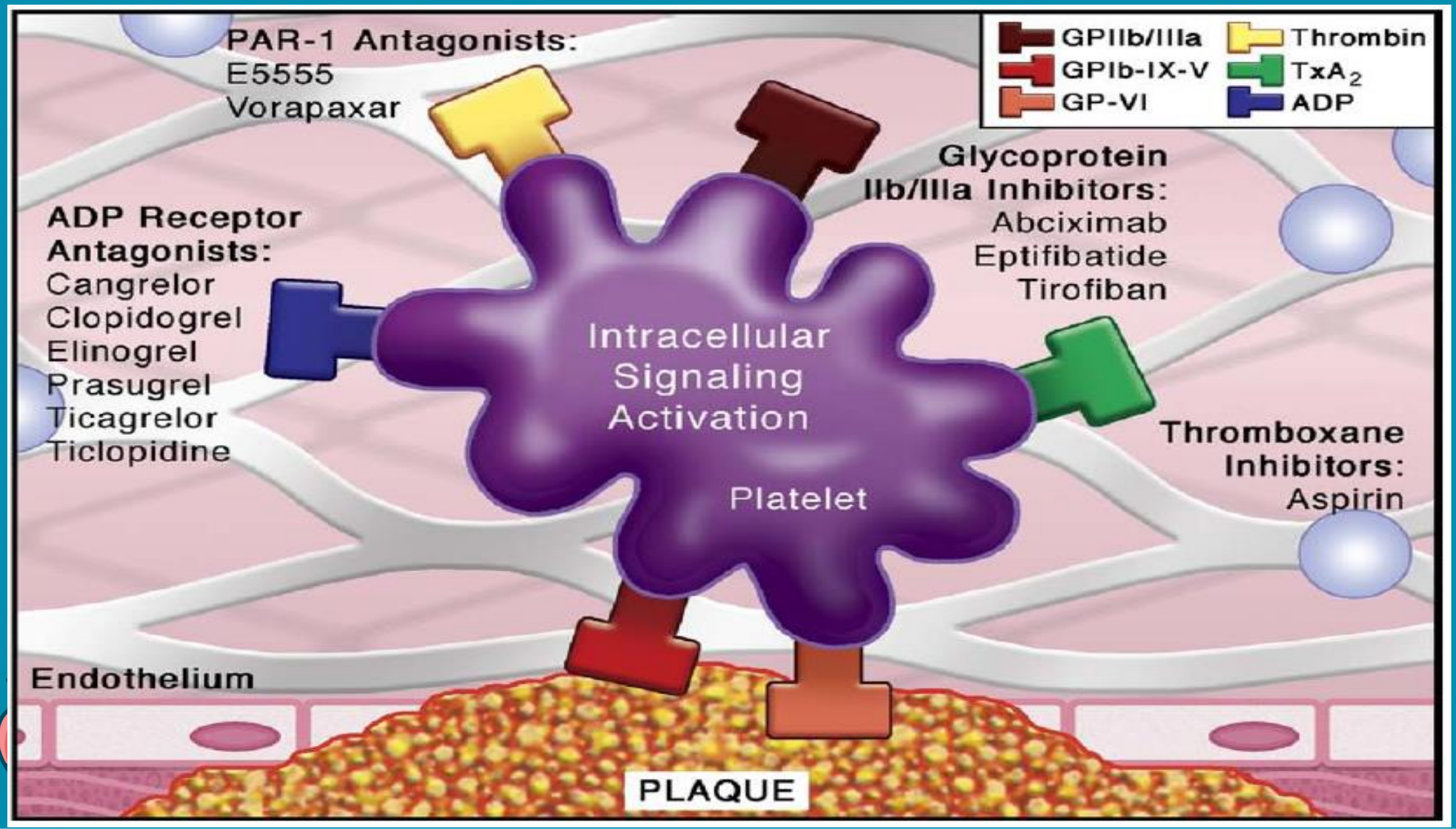
Microembolization in ACS

The KEY is platelet aggregation

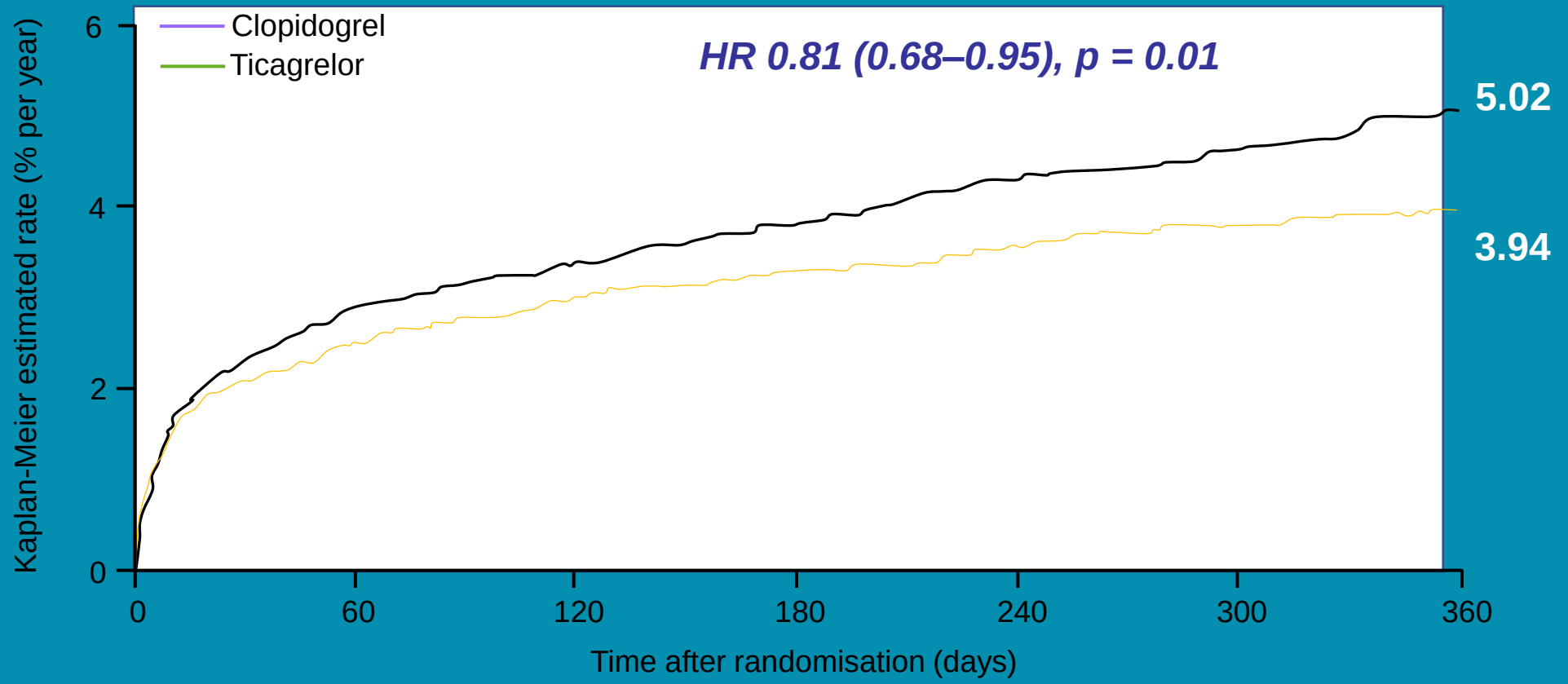


Courtesy of C. Michael Gibson, MS, MD, Director TIMI Data Coordinating Center, Brigham & Women's Hospital, Associate Chief of Cardiology, Interventional Cardiologist, Beth Israel Deaconess Medical Center, Harvard Medical School.

JACC Cardiovascular Interventions 2010; Bhatt D.



ALL Cause Mortality PLATO: Invasive Cohort



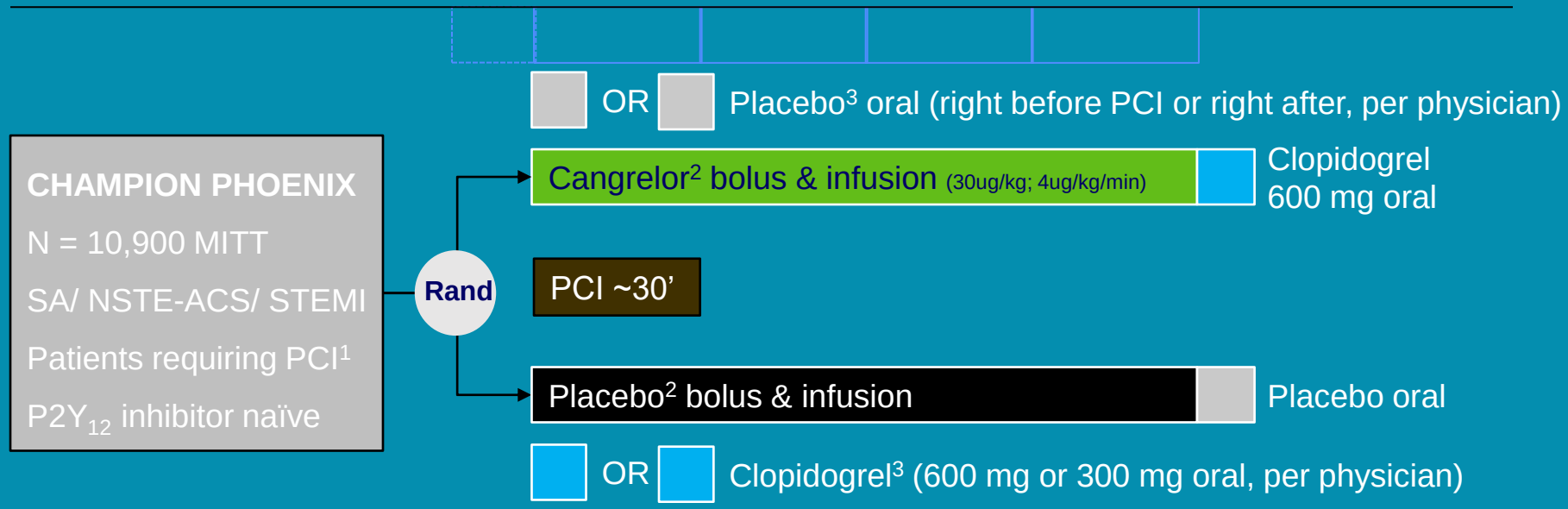
Number at risk

Clopidogrel	6676	6376	6331	6209	5114	3917	3164
Ticagrelor	6732	6439	6375	6241	5141	3951	3233

Cors at the Shore 2022

Cannon CP, et al. Lancet 2010;375:283–293

CHAMPION PHOENIX Study Design



[1]Randomization occurred once suitability for PCI was confirmed either by angiography or STEMI diagnosis. Double blind study medication was administered as soon as possible following randomization.

[2]Study drug Infusion (cangrelor or matching placebo) was continued for 2-4 hours at the discretion of the treating physician. At the end of the infusion patients received a loading dose of clopidogrel or matching placebo and were transitioned to maintenance clopidogrel therapy.

[3]Clopidogrel loading dose (or matching placebo) was administered as directed by the investigator. At the time of patient randomization, a clopidogrel loading dose of 600 mg or 300 mg was specified by the investigator.

MITT=modified intent-to-treat; NSTE-ACS=non-ST-elevation acute coronary syndrome; PCI=percutaneous coronary intervention; SA=stable angina; STEMI=ST-elevation MI.

Primary Efficacy Outcomes at 48 Hours, MITT

	Cangrelor (N=5472)	Clopidogrel (N=5470)	OR (95% CI)	P-value
Primary Analysis Adjusted[1]				
Death/MI/IDR/ST	257/5470 (4.7%)	322/5469 (5.9%)	0.78 (0.66, 0.93)	0.005

Secondary Efficacy Outcomes at 48 Hours, MITT

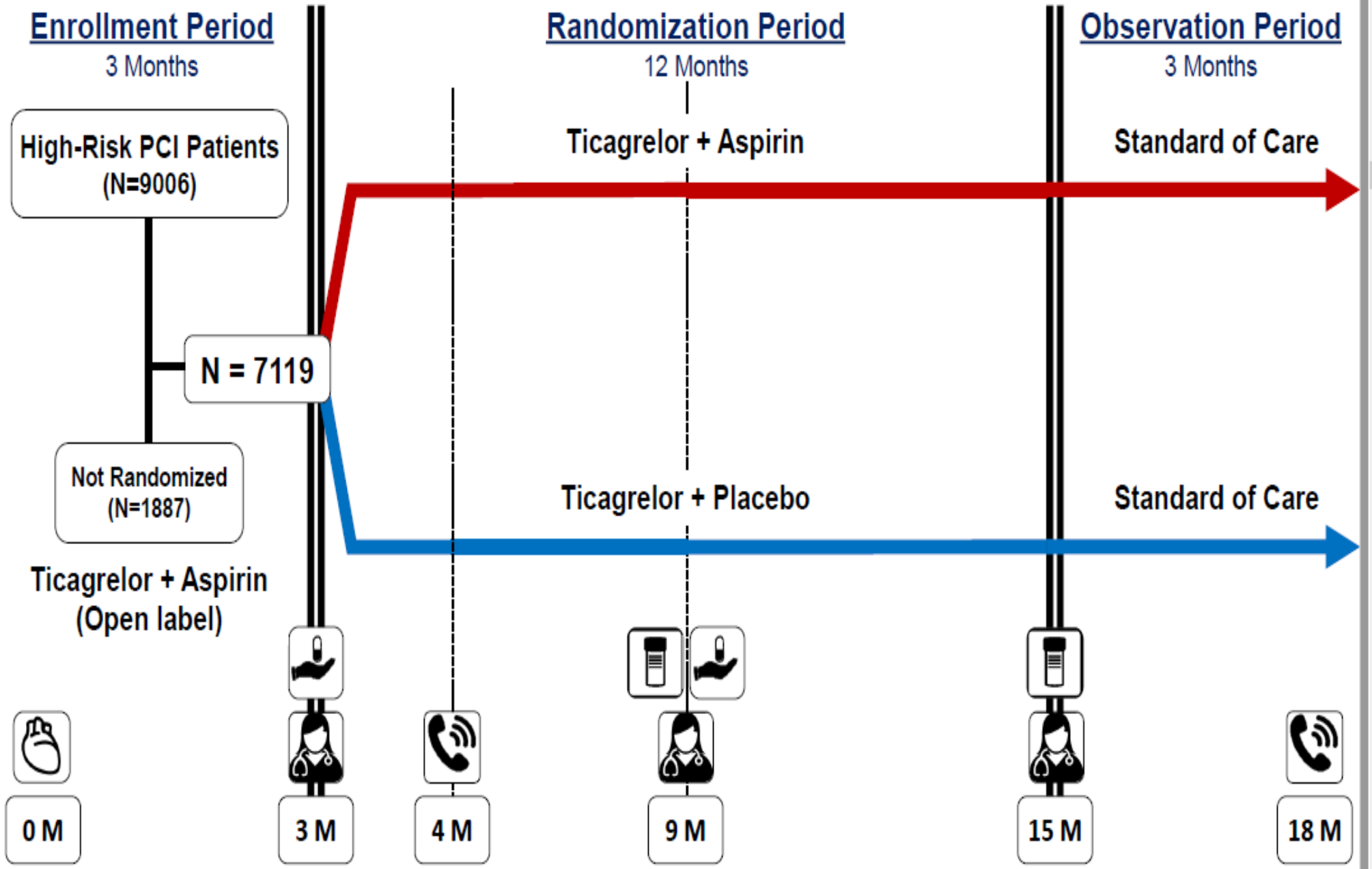
Stent thrombosis (key secondary endpoint)	46/5470 (0.8%)	74/5469 (1.4%)	0.62 (0.43,0.90)	0.01
MI	207/5470 (3.8)	255/5469 (4.7)	0.80 (0.67,0.97)	0.02
Q-wave MI	11/5470 (0.2)	18/5469 (0.3)	0.61 (0.29,1.29)	0.19
IDR	28/5470 (0.5)	38/5469 (0.7)	0.74 (0.45,1.20)	0.22
Death	18/5470 (0.3)	18/5469 (0.3)	1.00 (0.52,1.92)	>0.99
CV Death	18/5470 (0.3)	18/5469 (0.3)	1.00 (0.52,1.92)	>0.99

[1]The logistic model was adjusted for baseline status and clopidogrel dose. P value of 0.006 shown on the KM curve is log rank p value.

Bhatt DL, Stone GW, Mahaffey KW, et al…. Harrington RA. NEJM 2013 at www.nejm.org

TWILIGHT

Study Design

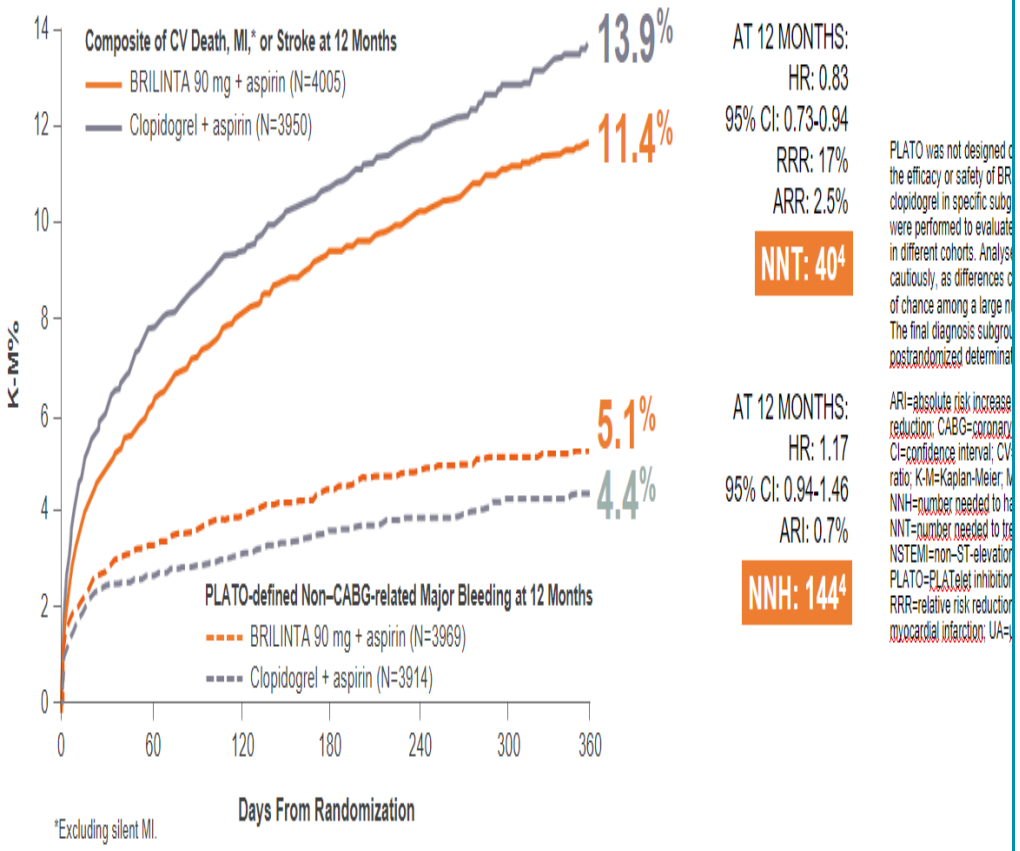


Cors at the Shore 2023

NSTEMI Subgroup Analyses

Primary Efficacy Endpoint And Non–CABG-related Major Bleeding[1-4]

PLATO



AT 12 MONTHS:
HR: 0.83
95% CI: 0.73-0.94
RRR: 17%
ARR: 2.5%
NNT: 40[4]

AT 12 MONTHS:
HR: 1.17
95% CI: 0.94-1.46
ARI: 0.7%
NNH: 144[4]

PLATO was not designed
the efficacy or safety of BR
clopidogrel in specific subg
were performed to evaluat
in different cohorts. Analys
cautiously, as differences
of chance among a large n
The final diagnosis subgrou
postrandomized determinat

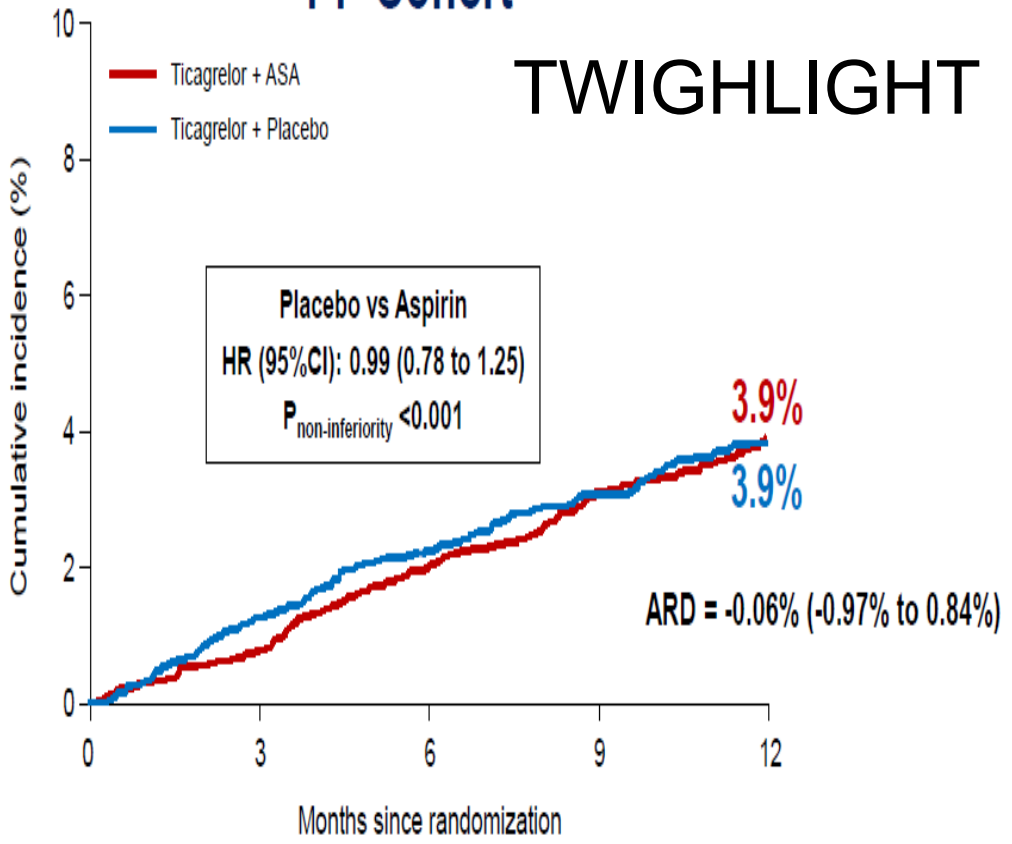
ARI=absolute risk increase
reduction; CABG=coronary
CI=confidence interval; CV
ratio; K-M=Kaplan-Meier;
NNH=number needed to ha
NNT=number needed to tre
NSTEMI=non–ST-elevation
PLATO=PLATelet inhibition
RRR=relative risk reduction
myocardial infarction; UA=

- Composite efficacy end point K-M% at 12 months in additional final diagnosis subgroups.[2] BRILINTA 90 mg plus aspirin vs clopidogrel plus aspirin,
  - STEMI 8.5% (N=3496) vs 10.1% (N=3530), HR: 0.84, 95% CI: 0.72-0.98;
  - UA 8.6% (N=1549) vs 9.1% (N=1563), HR: 0.96, 95% CI: 0.75-1.22

Key Secondary Endpoint: Death, MI or Stroke

PP Cohort

TWIGHLIGHT



No. at risk					
Ticagrelor + Aspirin	3515	3466	3415	3361	3320
Ticagrelor + Placebo	3524	3457	3412	3365	3330

Mount Sinai

twilight

DAPT STUDY: RESULTS - 1° Efficacy Analysis

- The two groups had similar rates of death from cardiac causes (0.9% and 1.0%, respectively; P = 0.98), death from vascular causes (0.1% in each group, P = 0.98), and stroke (0.8% and 0.9%, respectively; P = 0.32).

- ***The rate of death from any cause was <u>2.0%</u> with continued thienopyridine therapy and <u>1.5%</u> with placebo (hazard ratio, 1.36 [95% CI, 1.00 to 1.85]; P = 0.05)***

Cors at the Shore 2023

Expert Consensus Recommendations on Switching: *Bridging*

- Cangrelor may be used as a bridging strategy.
- The BRIDGE trial showed that among patients who discontinue thienopyridine therapy before cardiac surgery, the use of cangrelor compared with placebo resulted in a higher rate of maintenance of platelet inhibition.
- The dose of cangrelor used for bridging (0.75µg/kg/min infusion without a bolus) derives from a dose-finding study that
- The PD results from the BRIDGE study do not suggest any type of DDI, likely because there are still unoccupied receptors in patients treated with oral $P2Y_{12}$ inhibitors that can be bound and inhibited by cangrelor.

US Preventive Services Task Force (USPSTF)

1. Use of primary prevention ASPIRIN for pts aged 50-59 yrs at elevated CVD risk without bleeding: GRADE B

2. Individual decision making for pts aged 60-69 at elevated CV risk and NO bleeding: GRADE C

Cors at the Shore 2023

Thrombosis is MULTIFACETED

Find Synergy in Our Therapeutic Efforts

Cors at the Shore 2023

Cohen M, et al. Circulation 1994;89:81
ASA + Heparin, followed by ASA + Warfarin

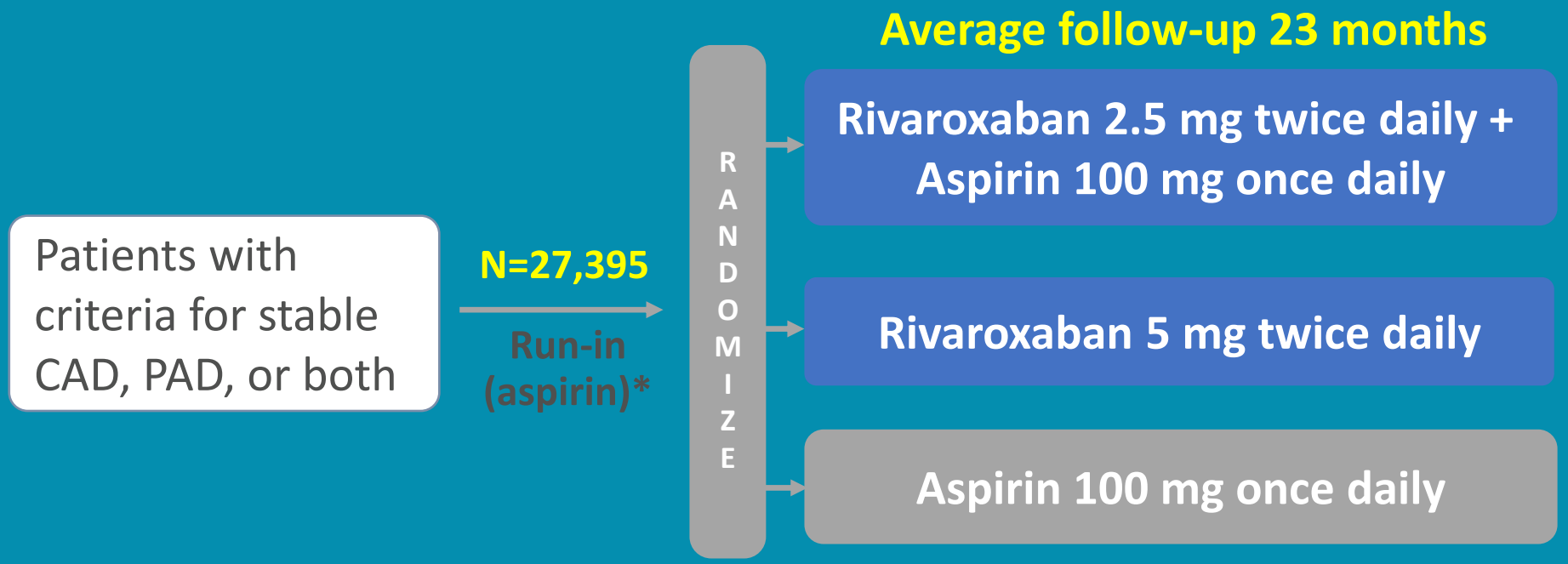
Pooled Analysis of Relative Risk of Combination Therapy Versus Aspirin Alone

	ATACS		RISC[8]		Theroux et al[11]		
	Aspirin (n=109)	Aspirin + Heparin (n=105)	Aspirin (n=189)	Aspirin + Heparin (n=210)	Aspirin (n=121)	Aspirin + Heparin (n=122)	RR_{mh} (CI)
infarction/death	9 (8.3%)	4 (3.8%)	7 (3.7%)	3 (1.4%)	4 (3.3%)	2 (1.6%)	.44 (.21-.93)

Eikelboom et al. NEJM 2017;377:1319

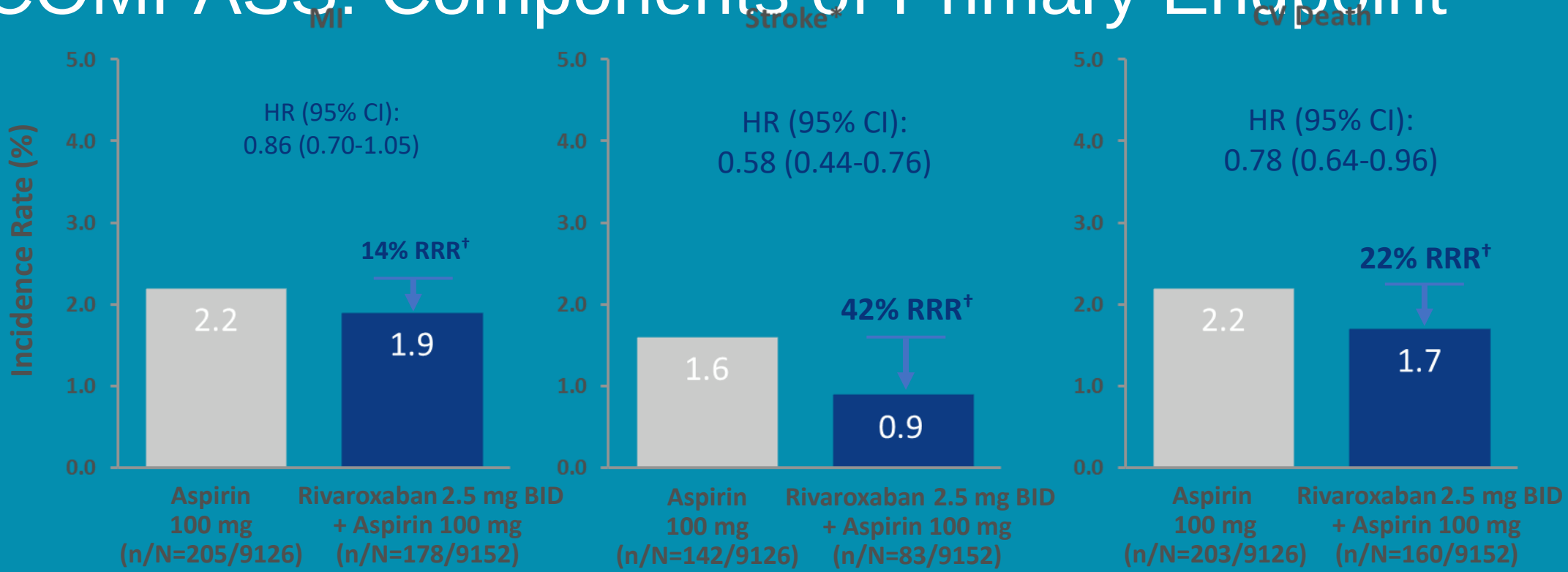
COMPASS Trial

Cardiovascular ***O***utco***M***es for ***P***eople using ***A***nticoagulation ***S***trategie***S***



Cors at the Shore 2023

COMPASS: Components of Primary Endpoint

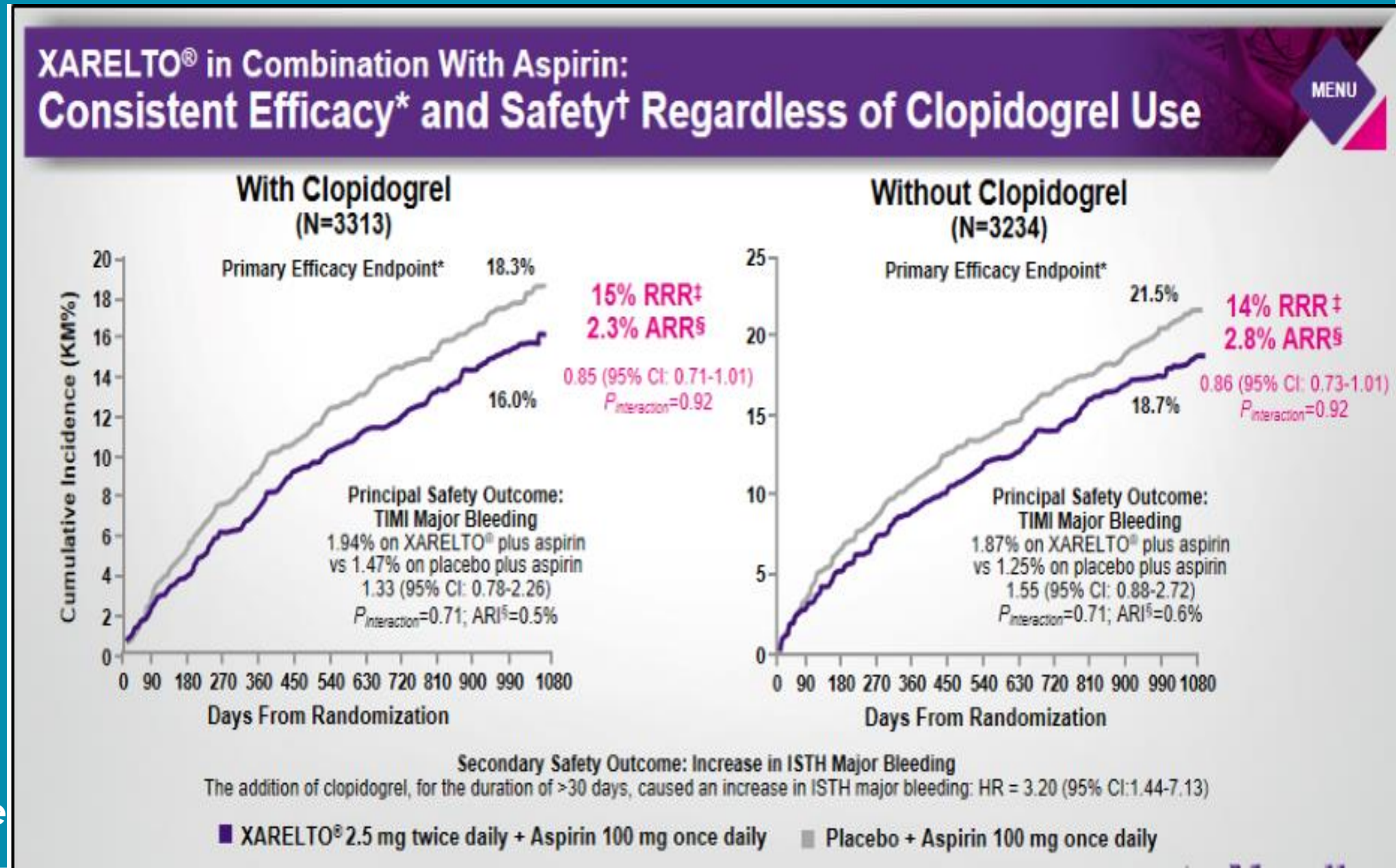


These endpoints were not adjusted for multiplicity

*A total of 7 participants in the rivaroxaban-plus-aspirin group and 11 participants in the aspirin-alone group who were reported to have atrial fibrillation had a stroke. †RRR calculated using one minus the HR.

Eikelboom JW, et al. *N Engl J Med*. 2017;377(14):1319-1330.

VOYAGER PAD Trial



Cors at the Shore 2023

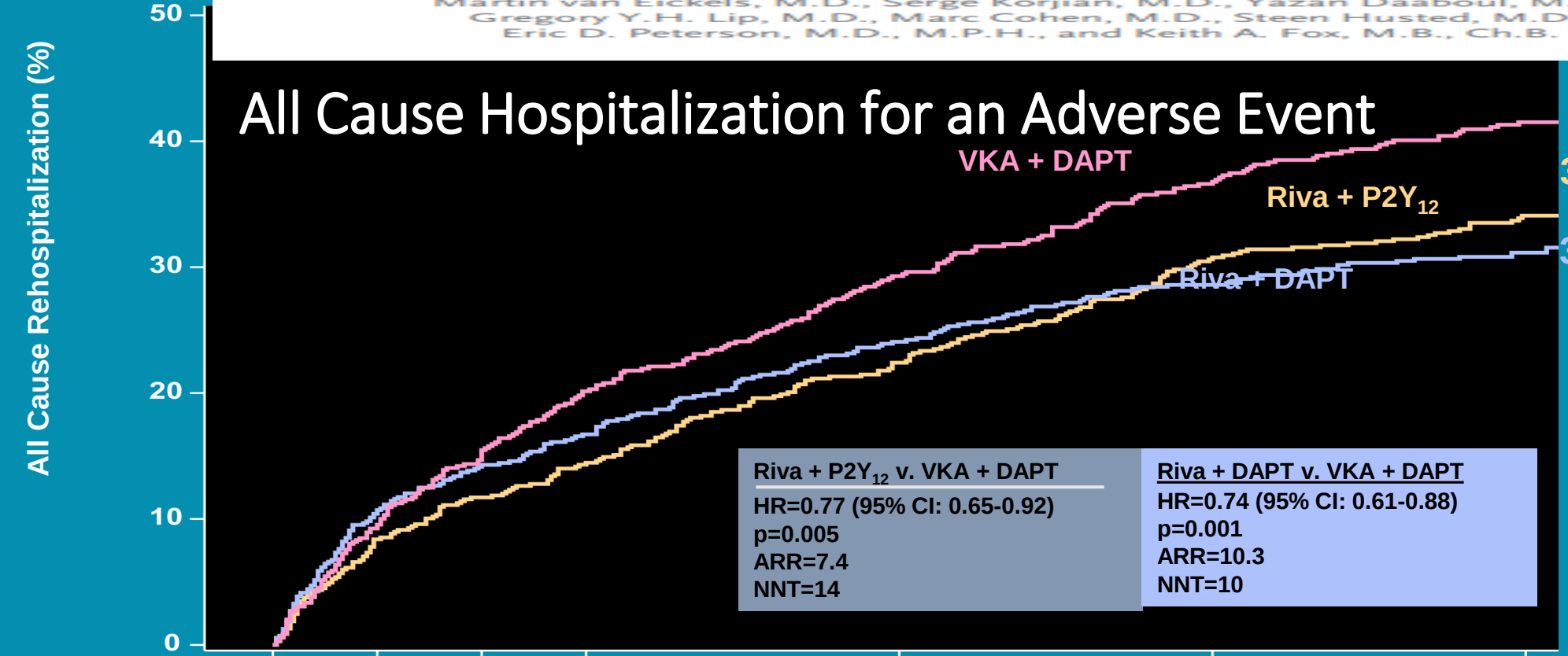
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Prevention of Bleeding in Patients with Atrial Fibrillation Undergoing PCI

C. Michael Gibson, M.D., Roxana Mehran, M.D., Christoph Bode, M.D., Jonathan Halperin, M.D., Freek W. Verheugt, M.D., Peter Wildgoose, Ph.D., Mary Birmingham, Pharm.D., Juliana Ianus, Ph.D., Paul Burton, M.D., Ph.D., Martin van Eickels, M.D., Serge Korjian, M.D., Yazan Daaboul, M.D., Gregory Y.H. Lip, M.D., Marc Cohen, M.D., Steen Husted, M.D., Eric D. Peterson, M.D., M.P.H., and Keith A. Fox, M.B., Ch.B.

All Cause Hospitalization for an Adverse Event



Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.
Rehospitalizations did not include the index event and include the first rehospitalization after the index event.
Hazard ratios as compared to the VKA group are based on the Cox proportional hazards model.
Log-Rank P-values as compared to VKA group are based on the two-sided log rank test.

Gibson et al. AHA 2016