Prevention in Stable Post-MI
Aspirin Plus P2Y12 Inhibitor Still Remains as a Key Player

Dominick J. Angiolillo, MD, PhD
Professor of Medicine
Director - Cardiovascular Research
Program Director – Interventional Cardiology Fellowship
University of Florida College of Medicine - Jacksonville

Presenter Disclosure Information

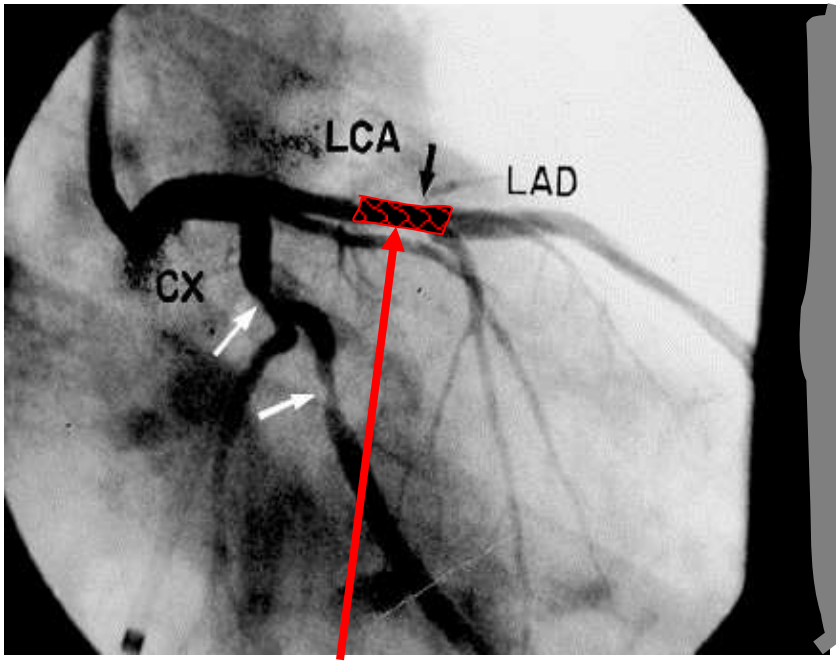
Name: Dominick J Angiolillo

Within the past 12 months, the presenter or their spouse/partner have had a financial interest/arrangement or affiliation with the organization listed below.

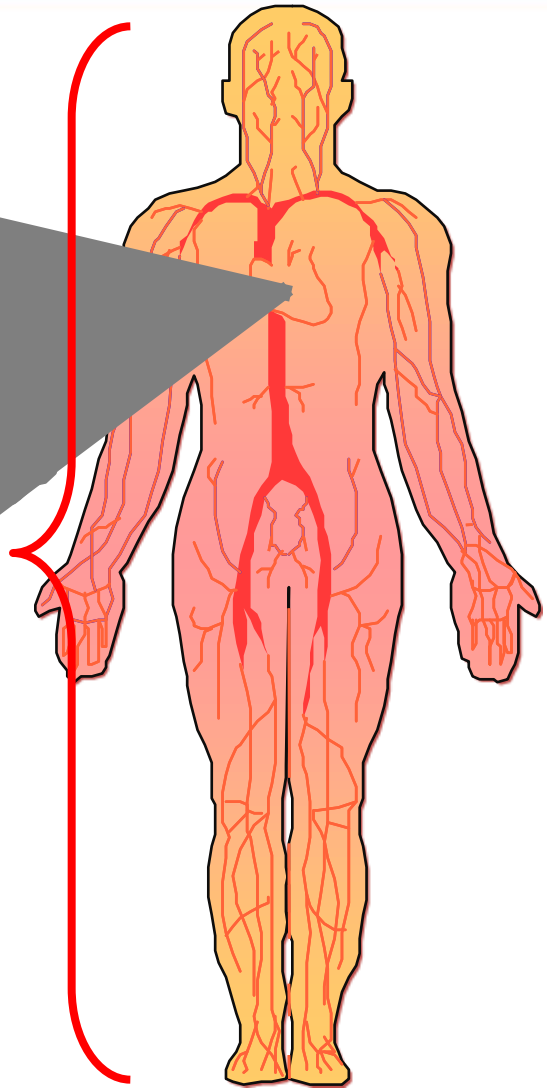
Received payment as an individual for:
a) Consulting fee or honorarium from Amgen, Bayer, Chiesi, Sanofi, Eli Lilly, Daiichi-Sankyo, The Medicines Company, AstraZeneca, Merck, Abbott Vascular, Pfizer, and PLx Pharma;
b) Honorarium for participation in review activities (DSMB member) from CeloNova, Johnson & Johnson, St. Jude, and Sunovion.
c) Honorarium from the American Board of Internal Medicine (Interventional Cardiology Subspecialty Exam Writing Committee Member)

Institutional payments for:
a) Grant support industry: from Amgen, Glaxo-Smith-Kline, Eli Lilly, Daiichi-Sankyo, The Medicines Company, AstraZeneca, Janssen Pharmaceuticals, Inc., Osprey Medical, Inc., Novartis, CSL Behring, and Gilead.
b) Grant in gift: Spartan; Scott R. MacKenzie Foundation
c) Federal agency: NIH

How Much of the Patient Are We Treating?



1000 m^2

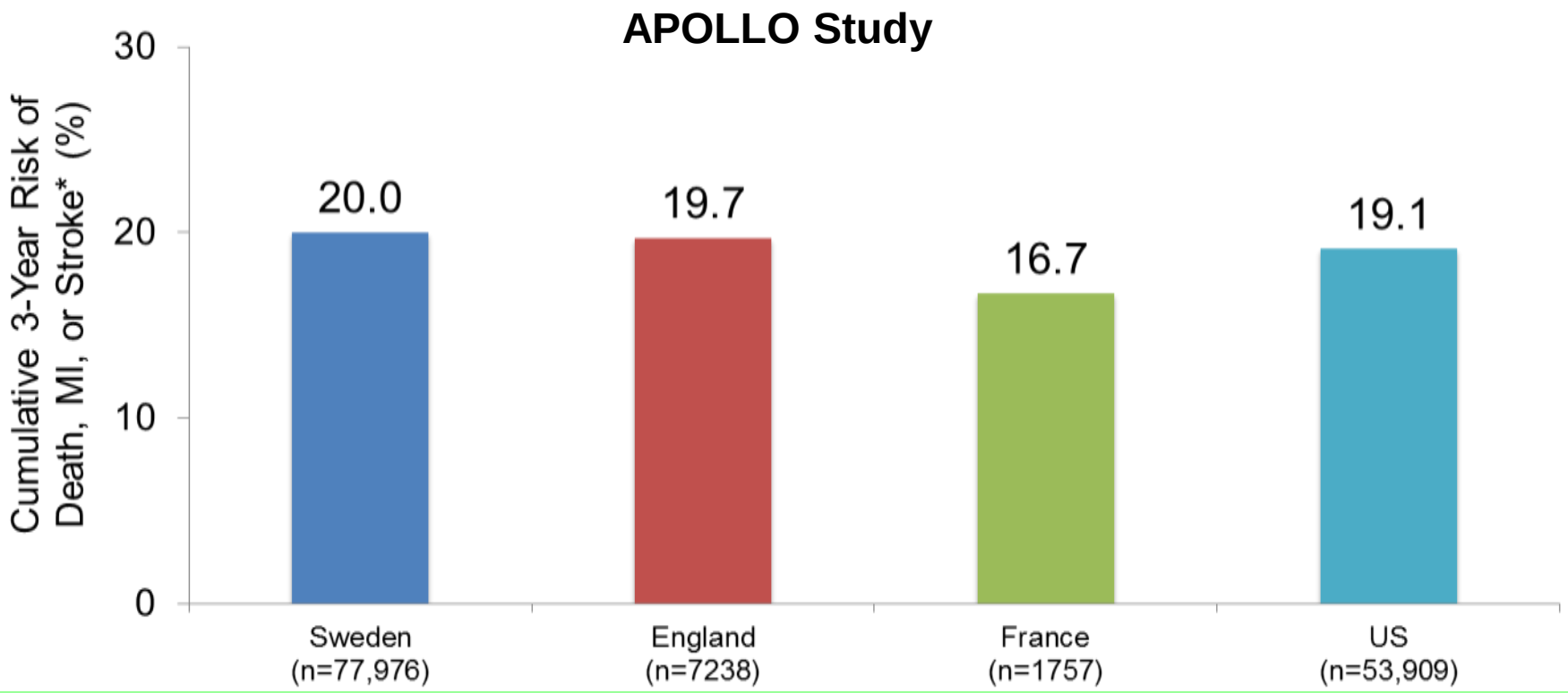


0.0002 m^2

=1/5 000 000

Courtesy of Steven Steinhubl

Patients Free of MI for 1 Year Continued to Be at Risk for CV Events Over the Next 3 Years

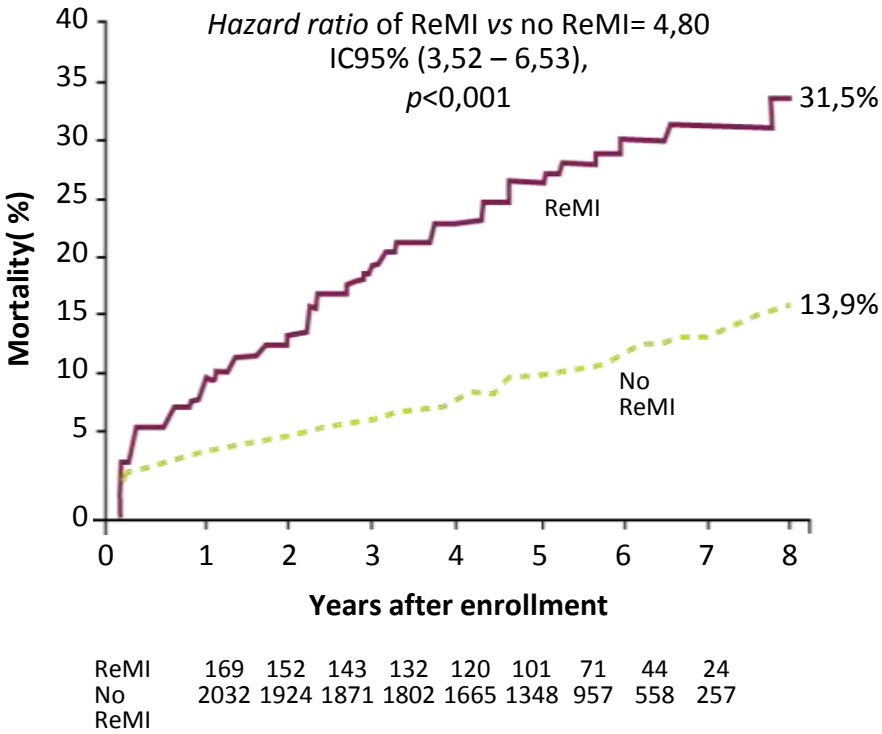


Retrospective 4-country analysis of patients who survived without a further MI for 1 year following hospitalization for MI in 2002 to 2011. Results are based on data from national linked electronic health records and disease registries as well as administrative data

*Adjusted for differences in study populations.

Rapsomaniki E et al. Presented at: European Society of Cardiology Meeting; August 30-September 3, 2014; Barcelona, Spain.

Impact of recurrent MI on long-term mortality



Recurrent MI 28 days after index event:

- Recurrent MI ocurred in 8% of patients at 7 years
- Nearly 5-fold increase in moratlity rate

Mendis S et al. *Int J Epidemiol.* 2011;40:139-146;; Adlbrecht C et al. *Int J Cardiol.* 2014;174(1):90-95.

UNIVERSITY OF FLORIDA
The Cardiovascular Center at SHANDS Jacksonville

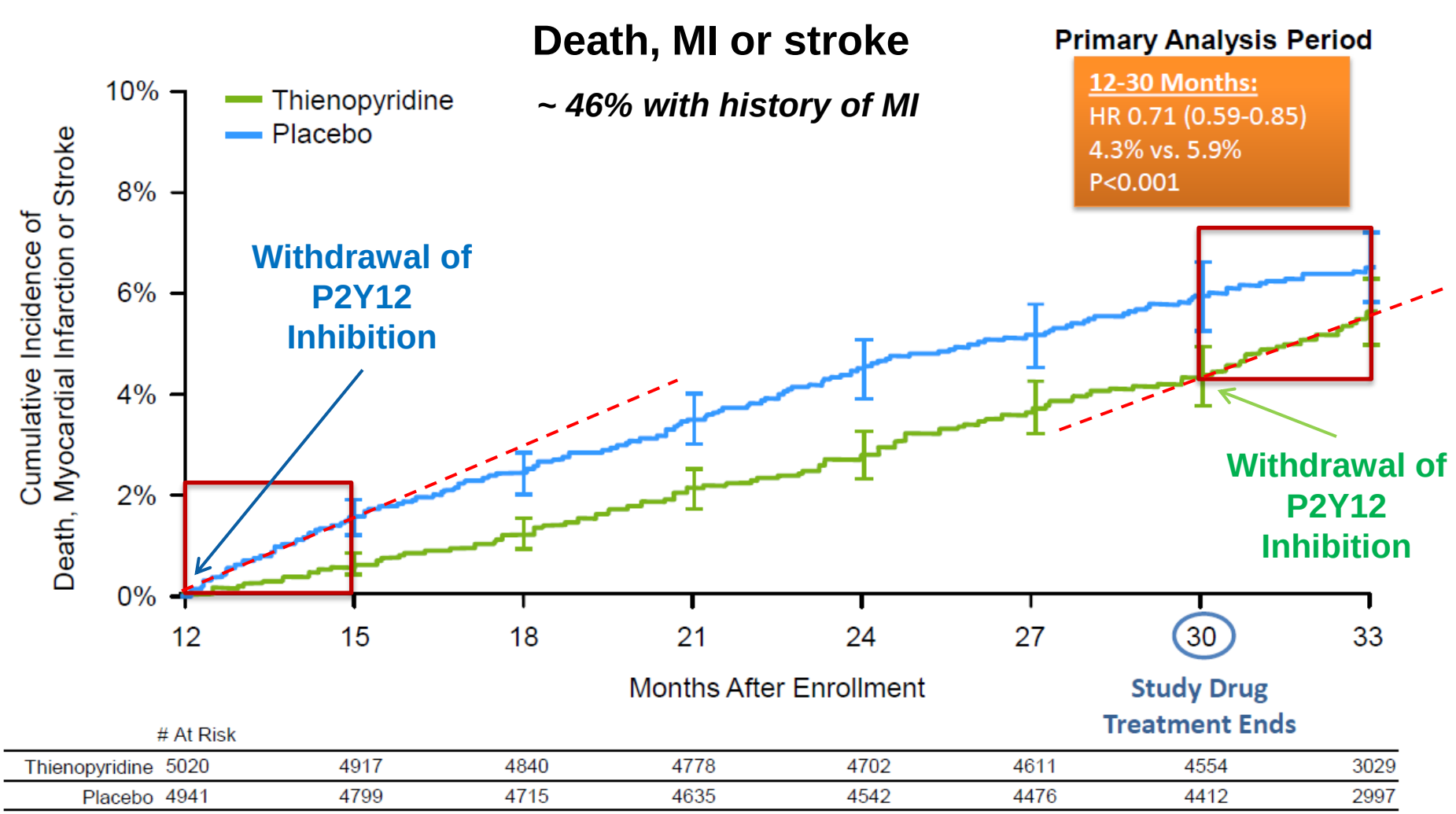
How do we treat post-MI patients?

1. **Revascularize** (if possible)
(to allow adequate tissue perfusion / ischemic relief)

2. **Secondary prevention**
(in order to reduce the risk atherothrombotic recurrences)

Is prolonging (>1-year) DAPT the answer?
YES!!!!

DAPT: Withdrawal of Thienopyridine 12 Months after Coronary Stenting

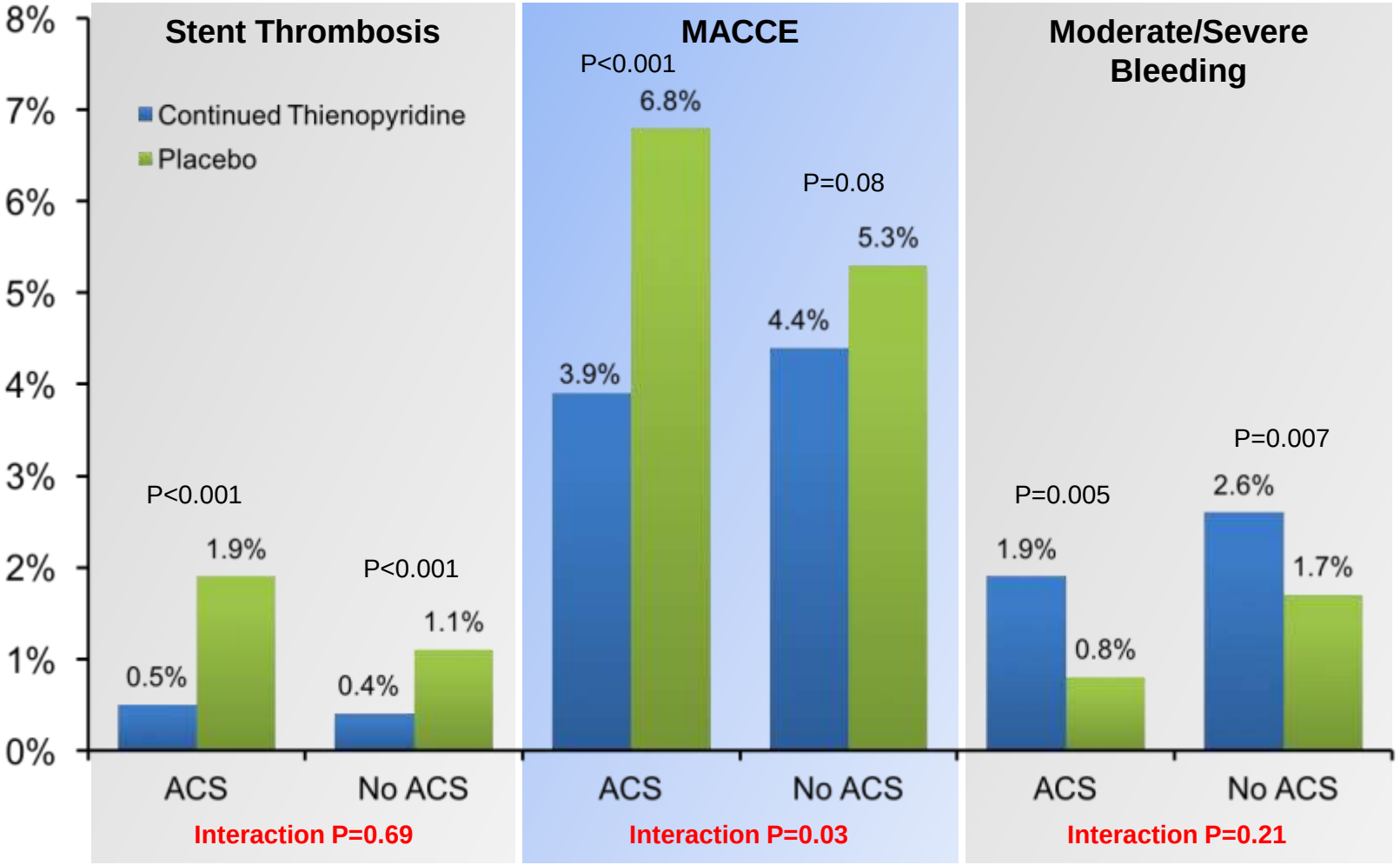


# At Risk								
Thienopyridine	5020	4917	4840	4778	4702	4611	4554	3029
Placebo	4941	4799	4715	4635	4542	4476	4412	2997

Mauri et al. NEJM 2014

DAPT Trial: Treatment Effect According to ACS Status at 12-30 Months: Primary Endpoints

All Randomized Subjects (N=11648)



Yeh RW et al J Am Coll Cardiol.2015;65:2211-21.

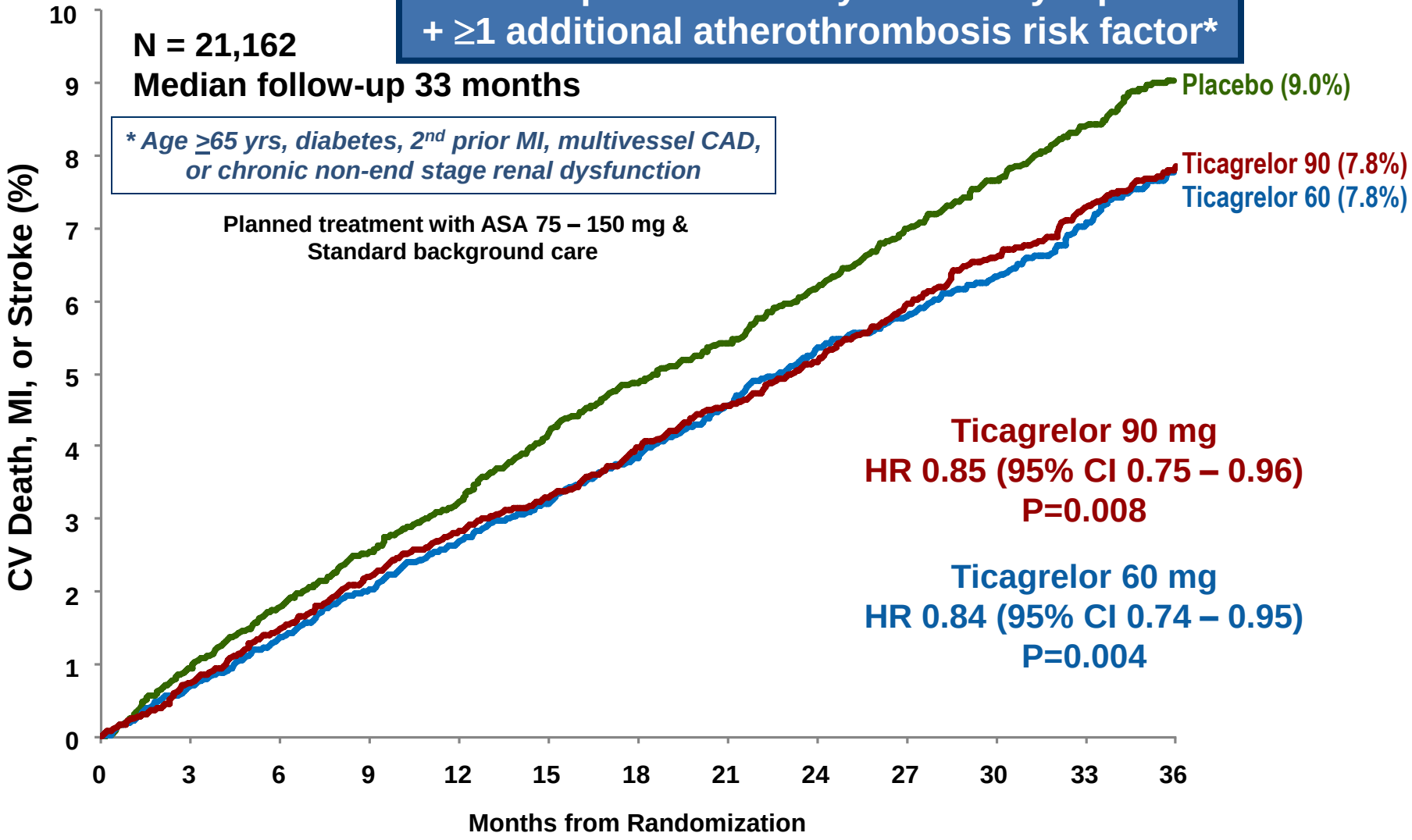
Primary Endpoint

Stable pts with history of MI 1-3 yrs prior + ≥1 additional atherothrombosis risk factor*

N = 21,162
Median follow-up 33 months

** Age ≥65 yrs, diabetes, 2nd prior MI, multivessel CAD, or chronic non-end stage renal dysfunction*

Planned treatment with ASA 75 – 150 mg & Standard background care

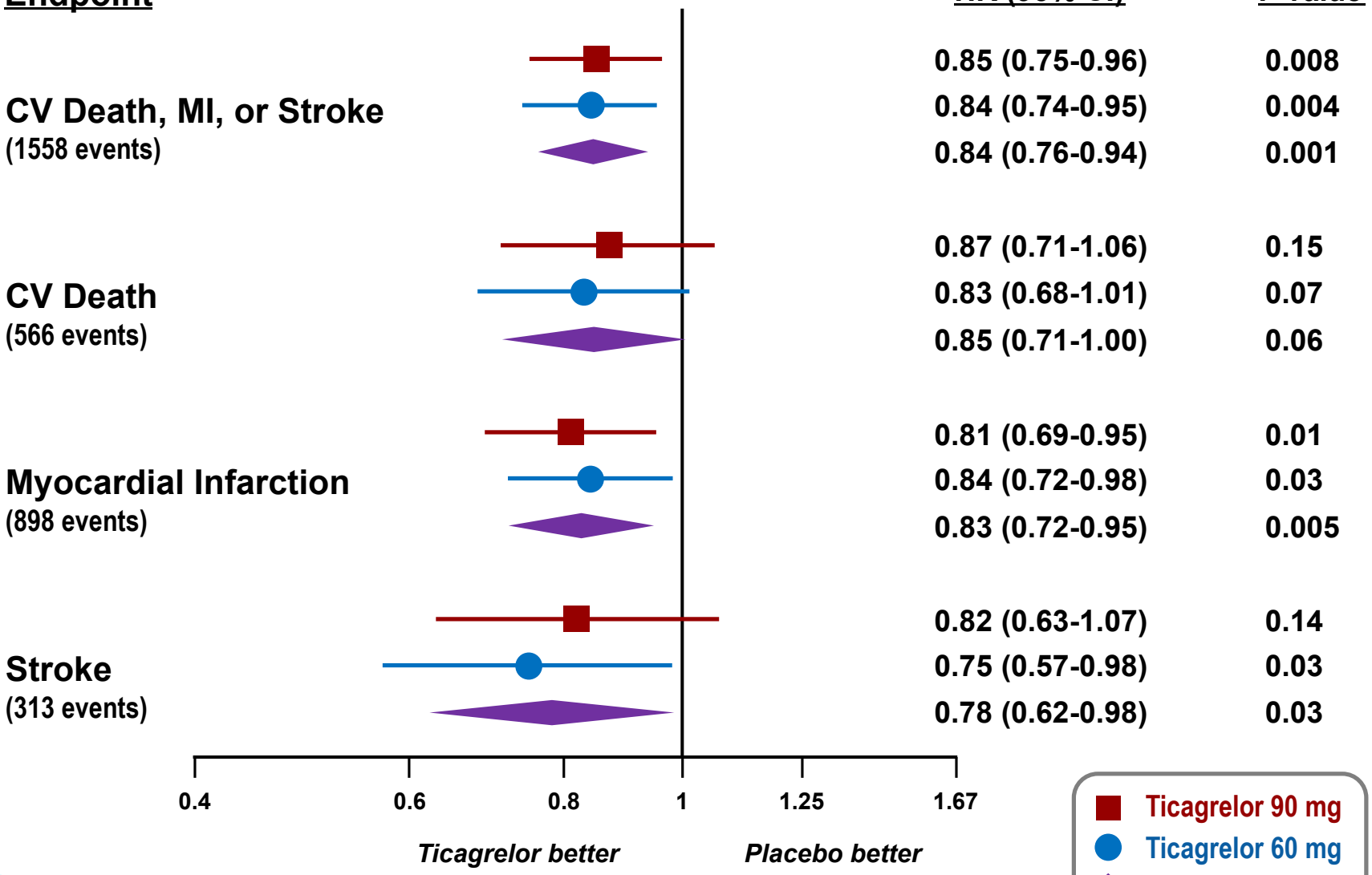


Ticagrelor 90 mg
HR 0.85 (95% CI 0.75 – 0.96)
P=0.008

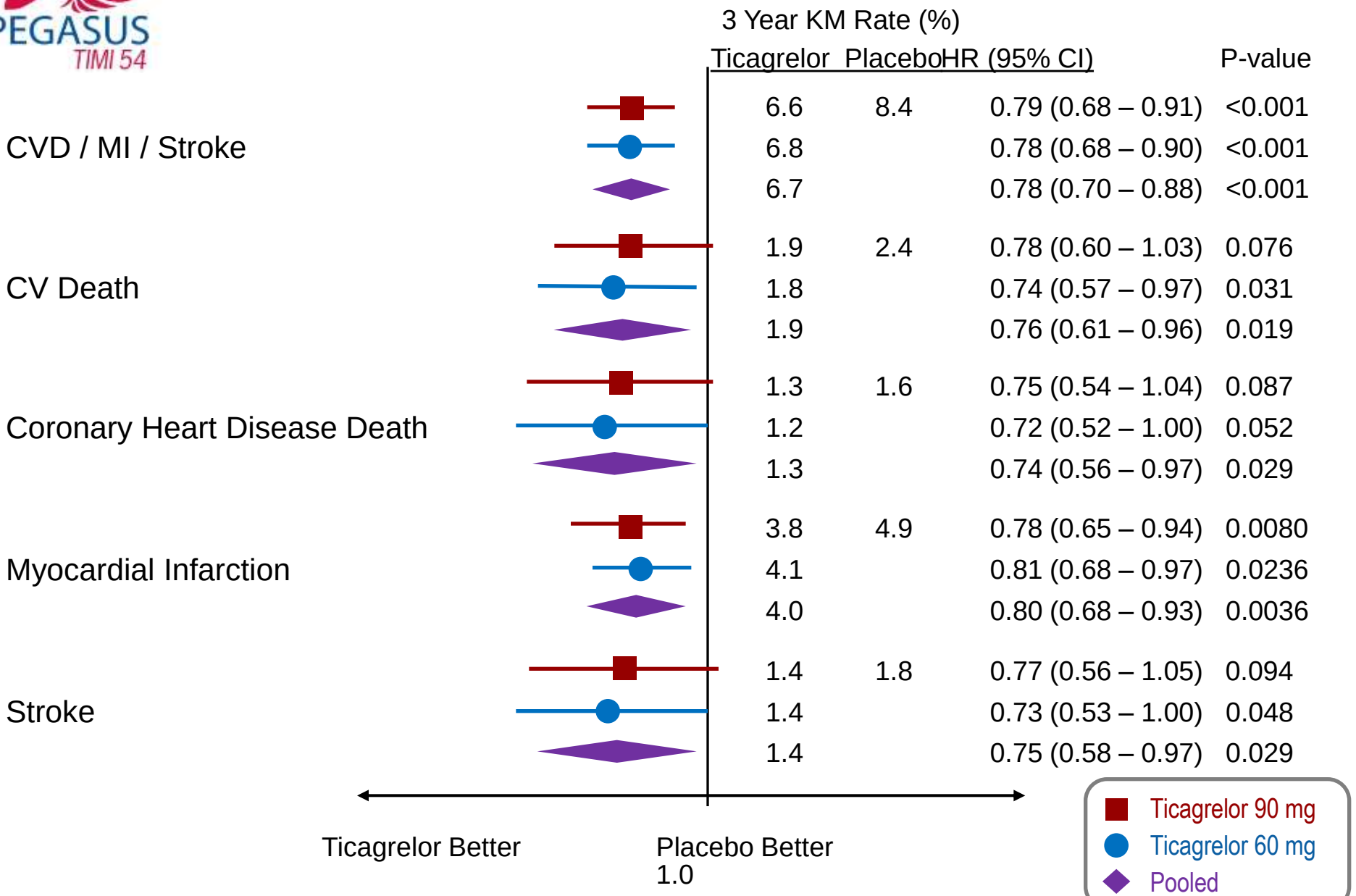
Ticagrelor 60 mg
HR 0.84 (95% CI 0.74 – 0.95)
P=0.004

Bonaca MP et al. NEJM 2015

Components of Primary Endpoint



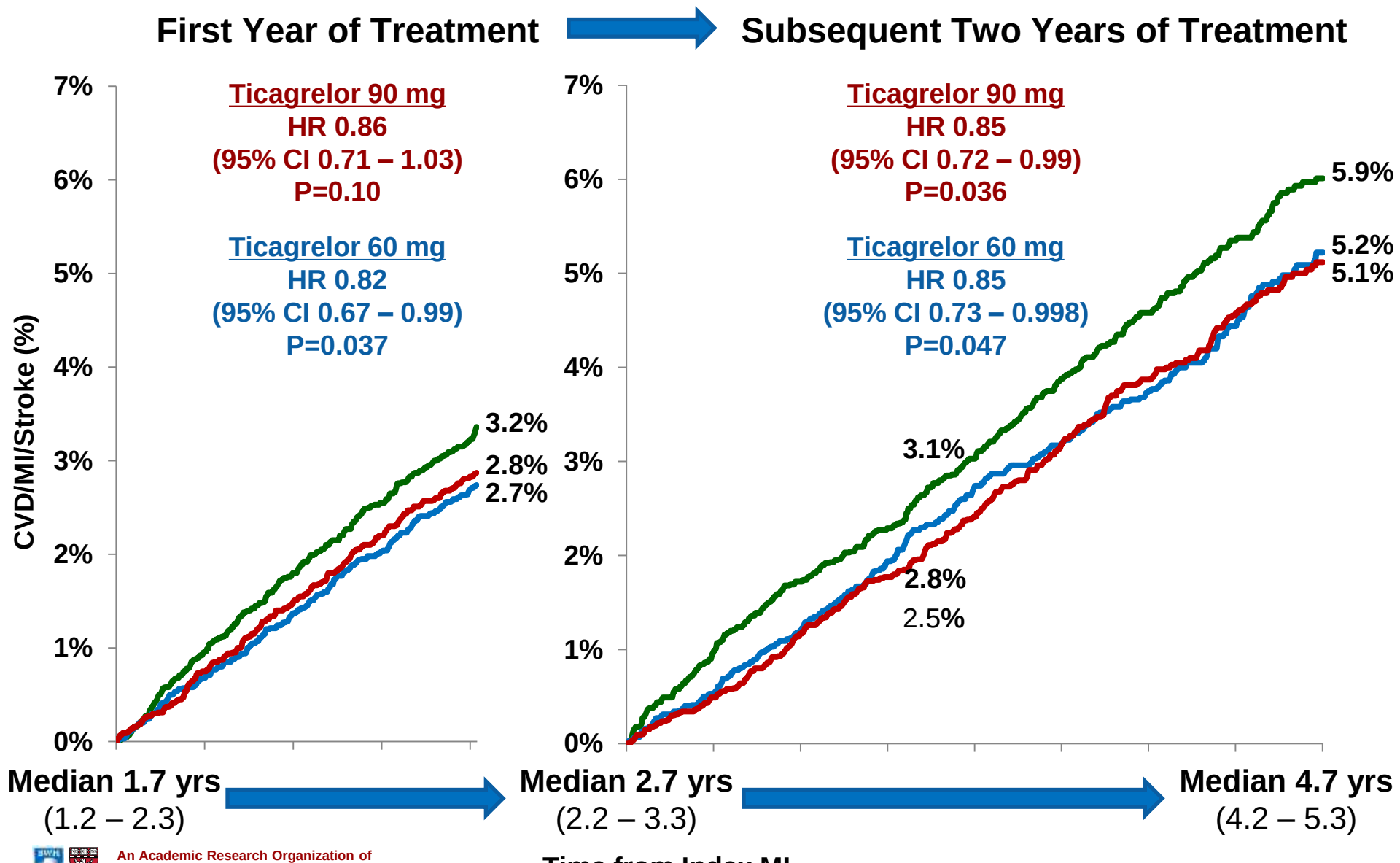
Efficacy of Ticagrelor – On Treatment*



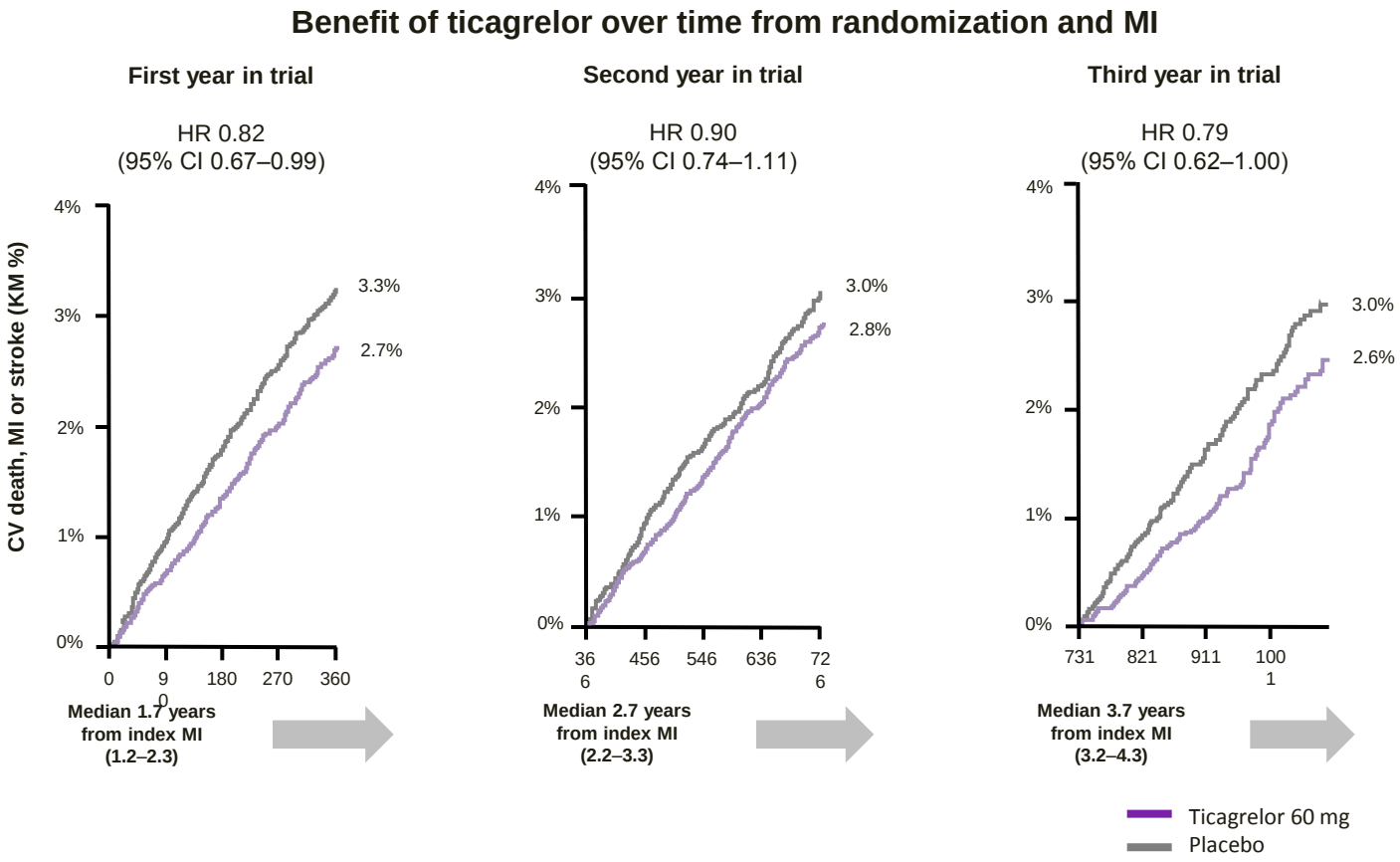
*N=20,942 patients who received at least one dose of study drug including events through 7 days from the last dose of study drug

Bonaca et al. JAMA Cardiology 2016

Primary Endpoint – Landmark (ITT)

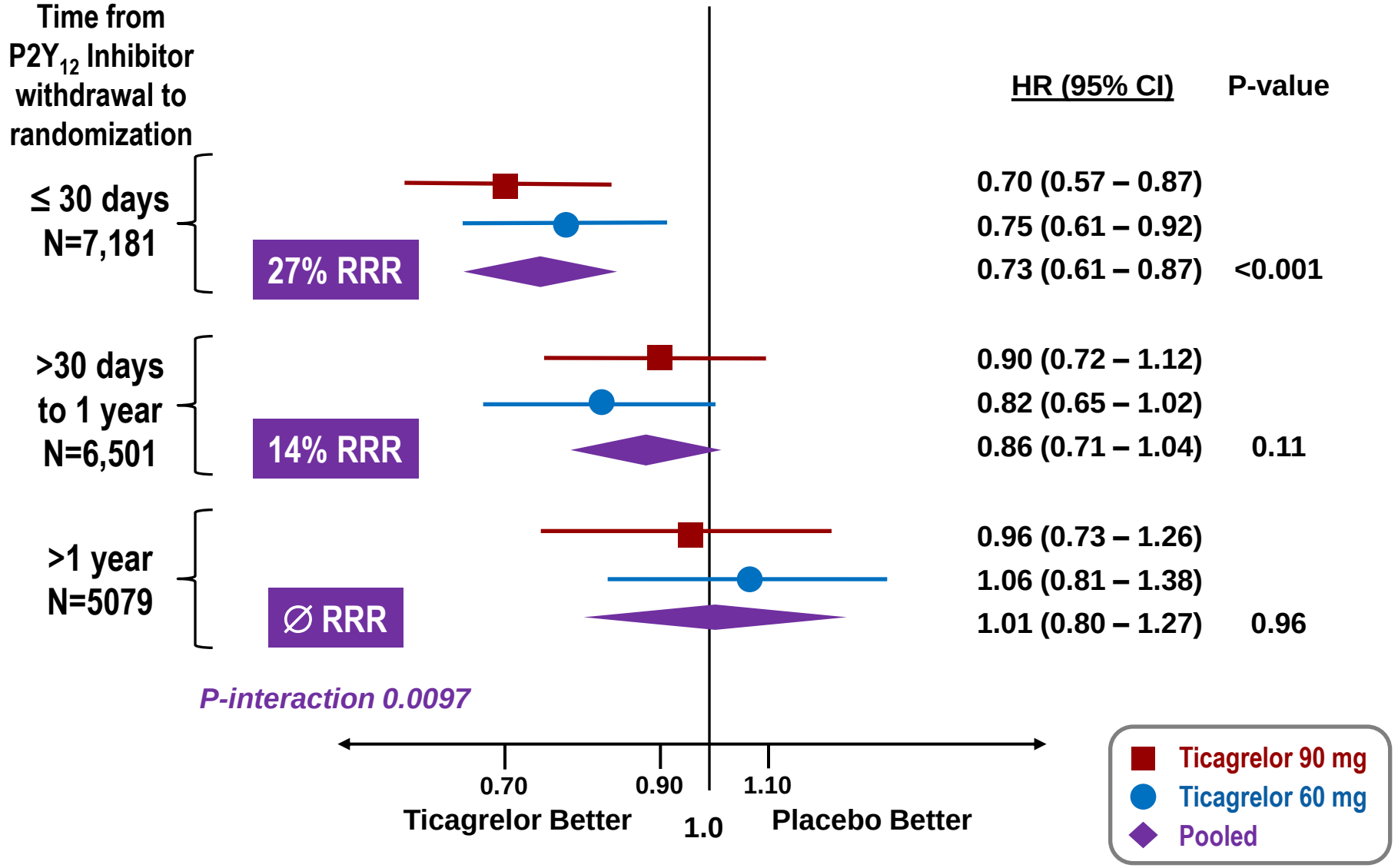


The efficacy of ticagrelor 60 mg (vs placebo) in reducing CV events is consistent over time



1. Bonaca MP, *et al*. Efficacy and Safety of Ticagrelor Over Time in Patients With Prior MI in PEGASUS-TIMI 54. *J Am Coll Cardiol 2017*;**70**:1368–1375. Http://dx.doi.org/10.1016/j.jacc.2017.07.768., online supplementary data.

Reduction in MACE with Ticagrelor by Time from $P2Y_{12}$ Inhibitor Withdrawal



PEGASUS-TIMI 54 Trial:

EU Label post hoc sub-analysis* Patients with ≤2 years from qualifying MI or ≤1 year from prior ADP receptor inhibitor treatment

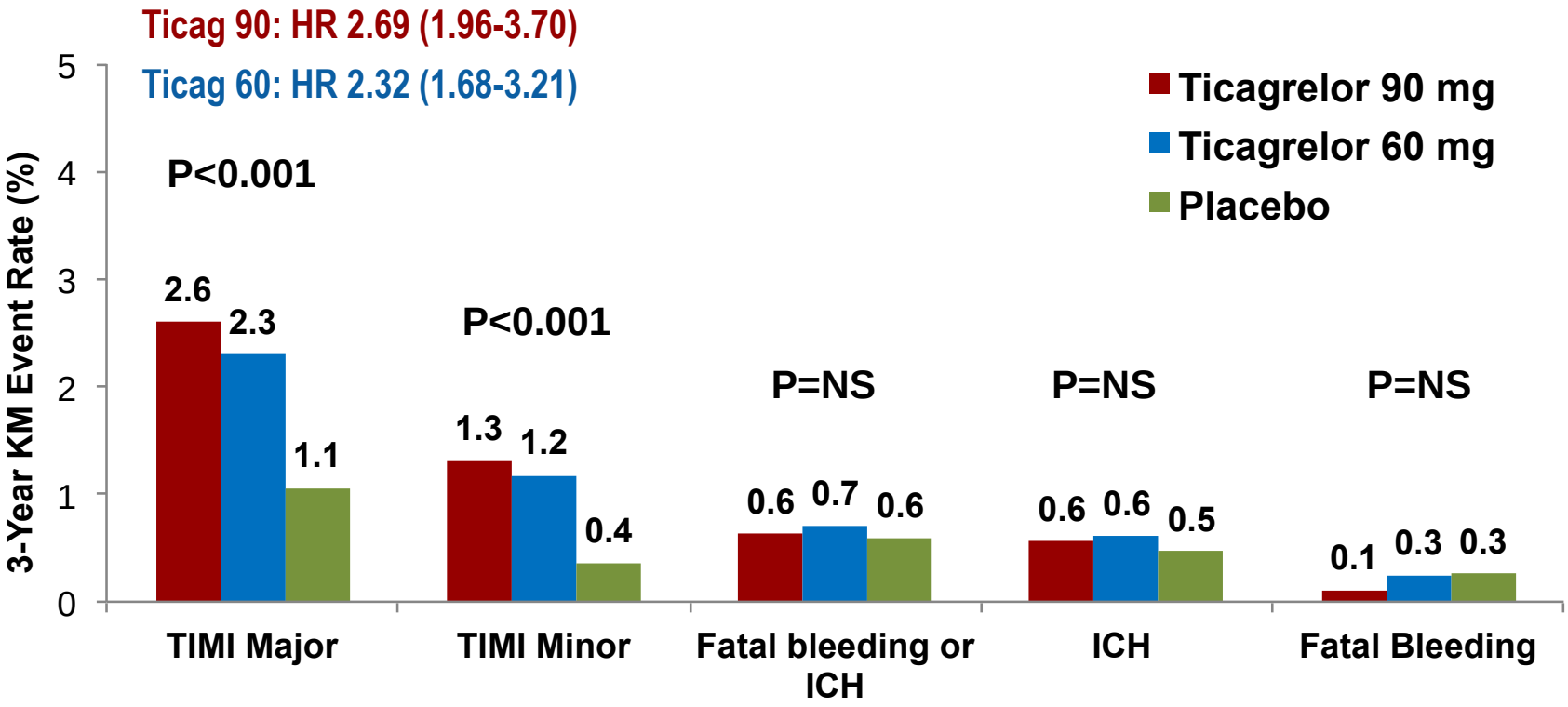
Primary and Secondary Endpoints

Outcome	Ticagrelor 60 mg bd (N=5388)		Placebo (N=5391)		Hazard ratio (95% CI)	P value
	n	3-yr KM%	n	3-yr KM%		
Composite of CV death, MI or stroke	373	7.9	463	9.6	0.80 (0.70–0.91)	0.001
CV death	119	2.6	167	3.6	0.71 (0.56–0.90)	0.0041
MI	230	4.8	274	5.6	0.83 (0.70–0.99)	0.041
Stroke	71	1.5	95	2.0	0.74 (0.55–1.01)	0.058
All-cause mortality	206	4.4	256	5.4	0.80 (0.67–0.96)	0.018

*EU Label sub-analysis was post hoc imposed by European Medicines Agency (EMA).

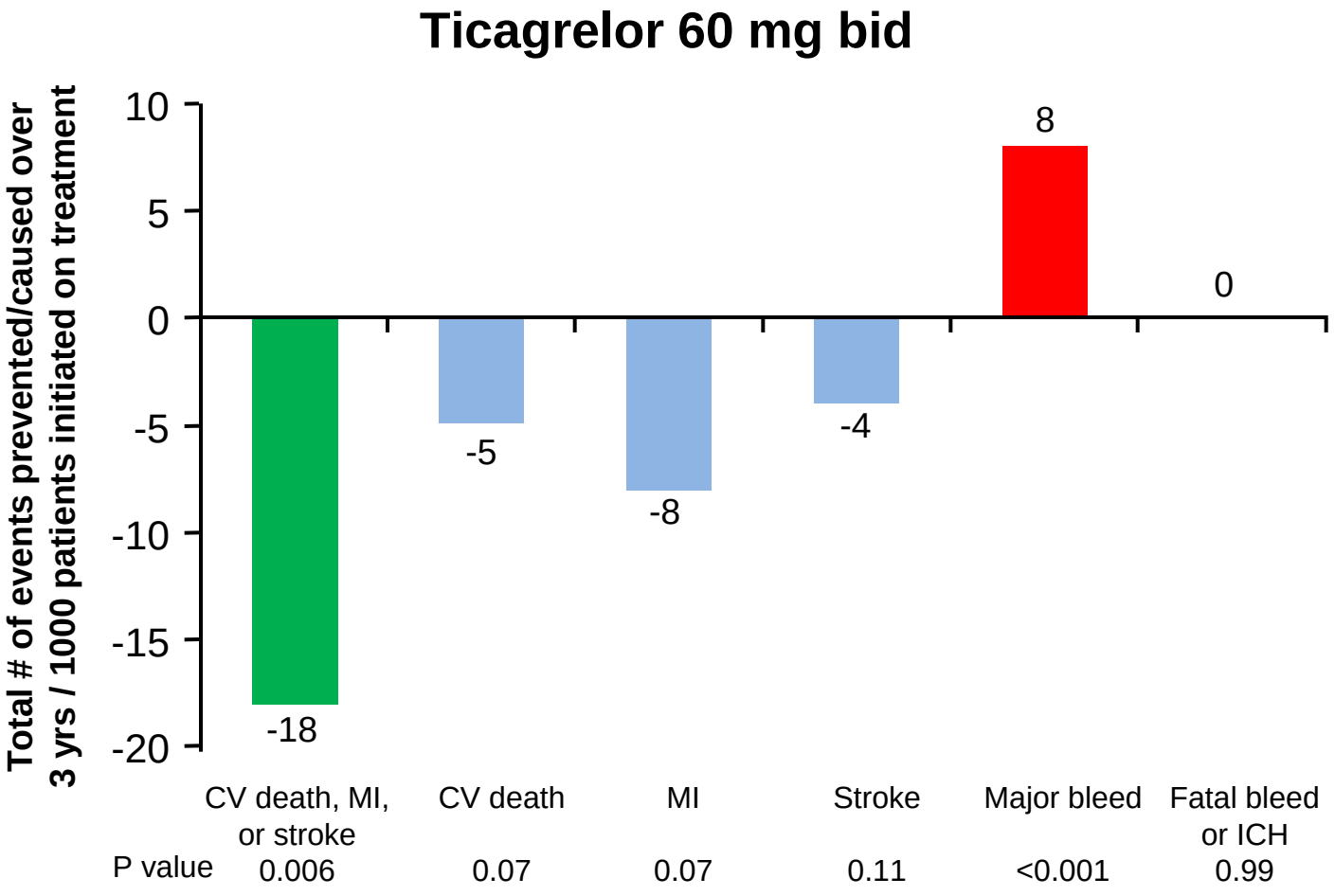
1. Dellborg M, *et al. ESC 2017, Poster P3670.*

Bleeding



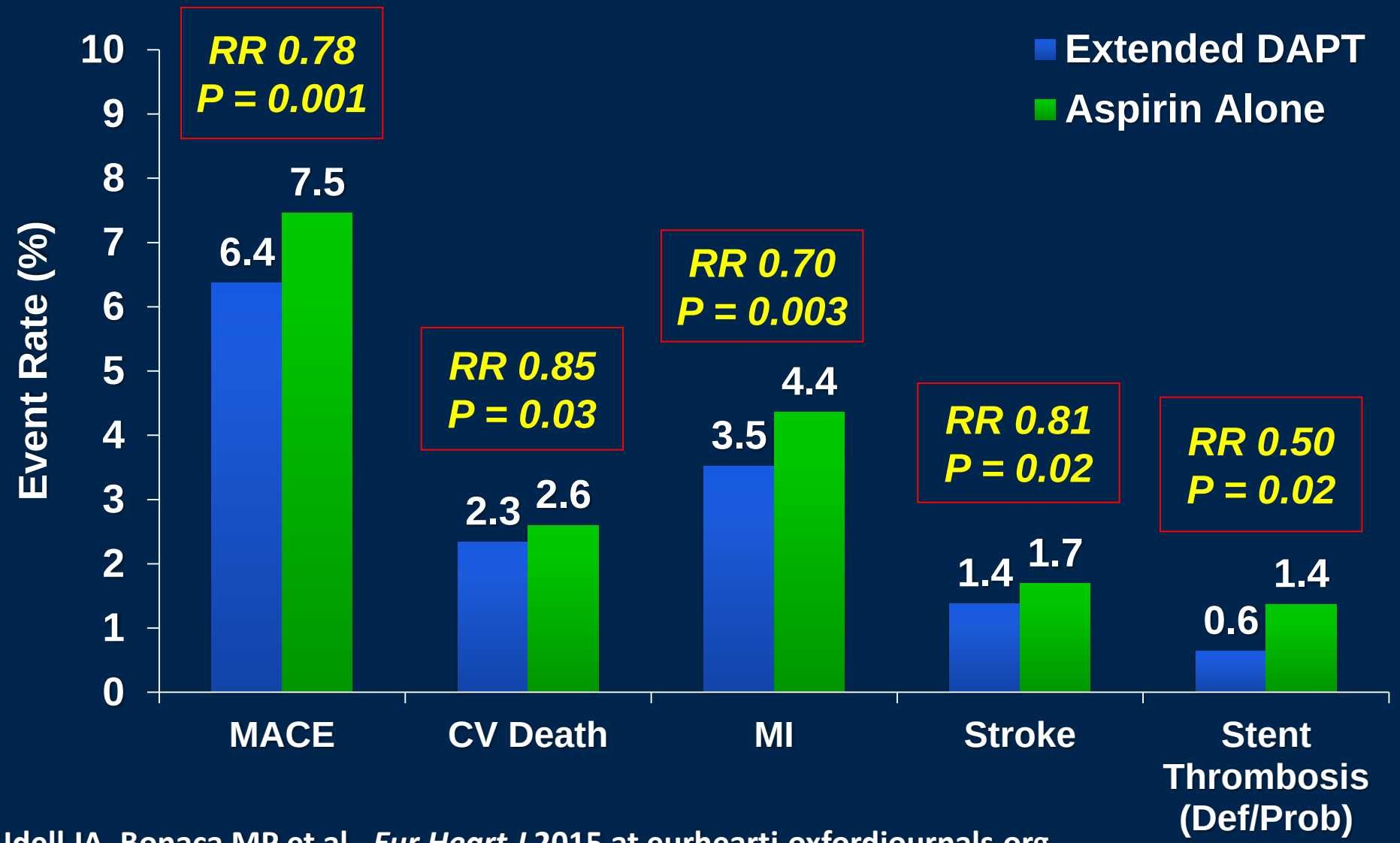
Bonaca MP et al. NEJM 2015

Total events: efficacy and safety



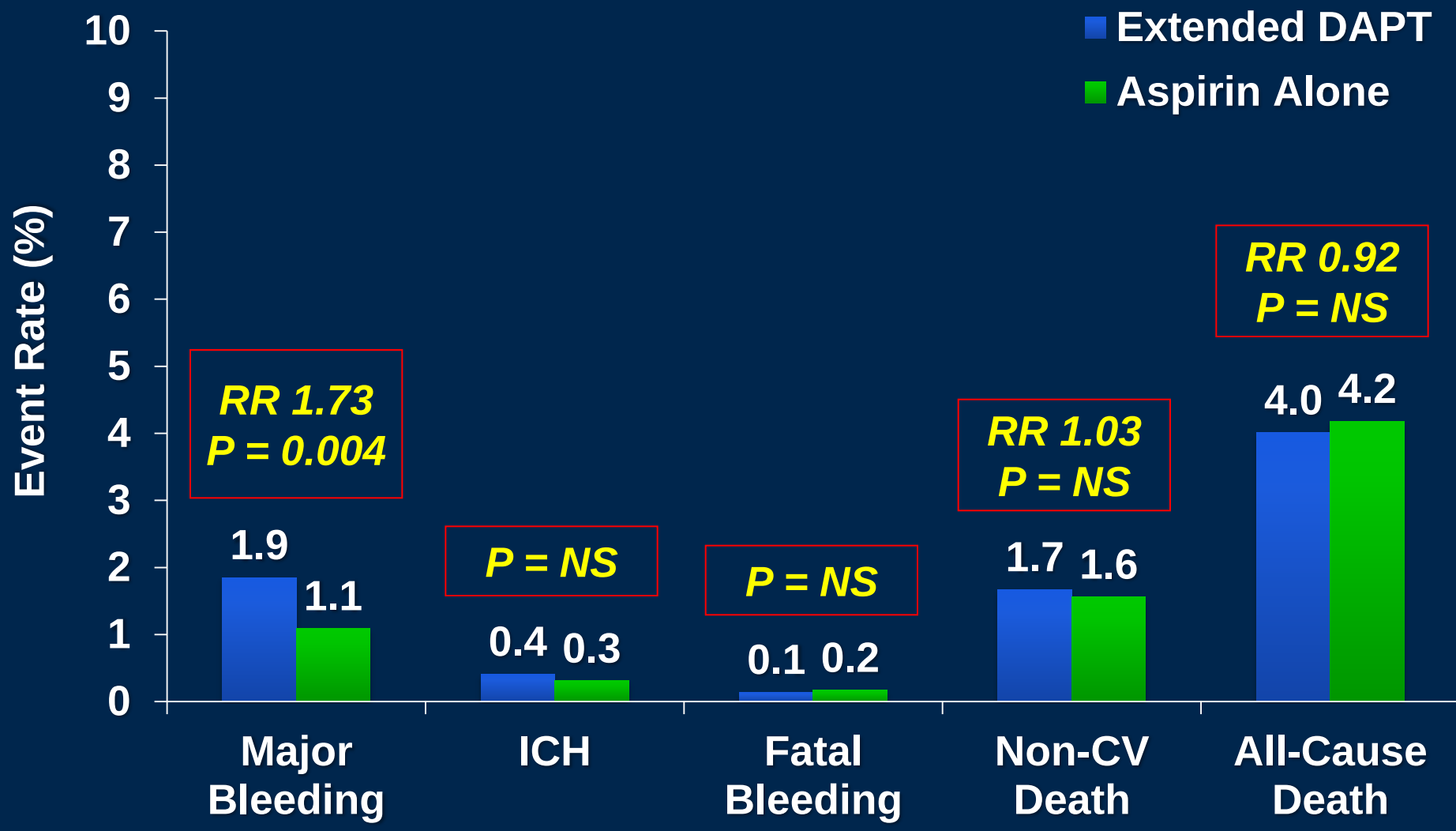
Murphy SA et al. Presented at AHA Congress 2015 (Abstract 742)

Outcomes with Continued DAPT after MI



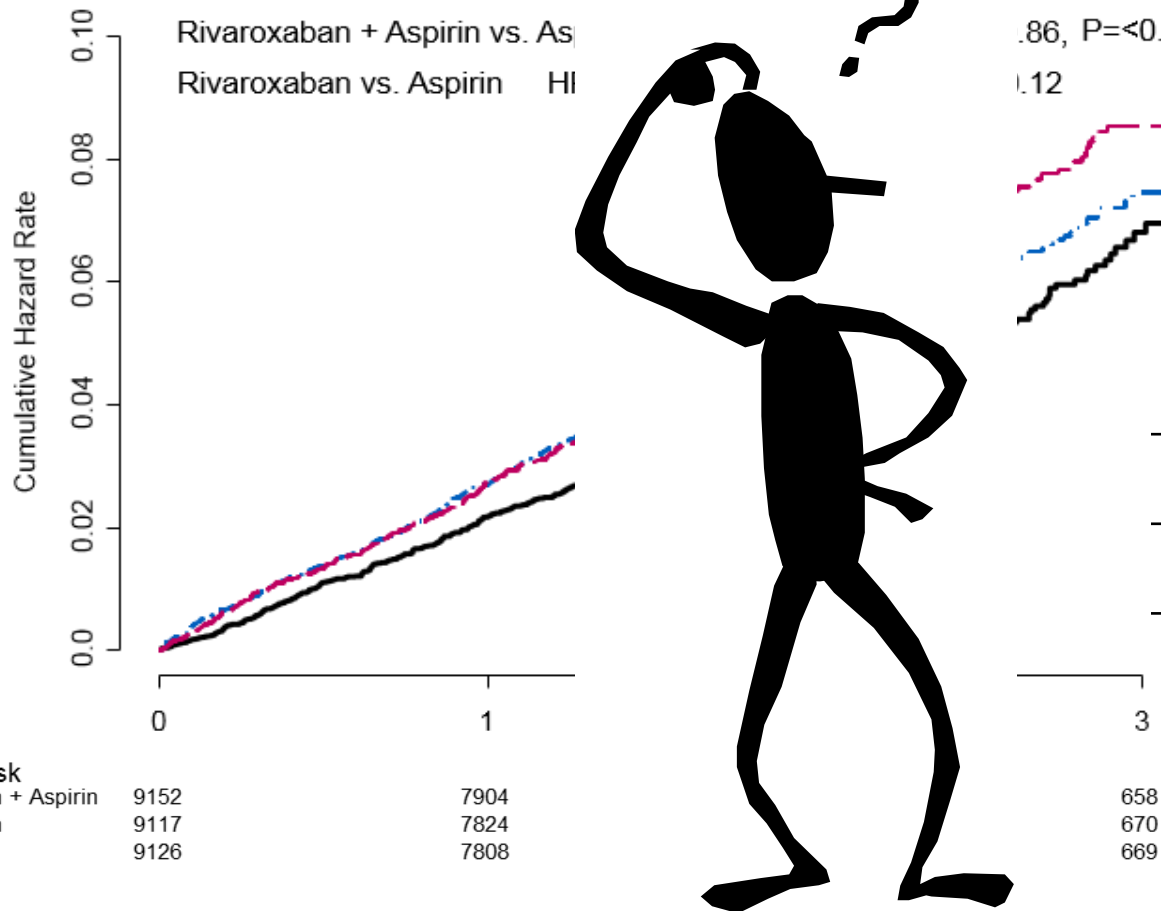
Udell JA, Bonaca MP et al. *Eur Heart J* 2015 at eurheartj.oxfordjournals.org.

Safety of Continued DAPT after MI



Udell JA, et al. *Eur Heart J* 2015 at eurheartj.oxfordjournals.org.

Primary: CV death, stroke, MI



Outcome	Rivaroxaban + Aspirin vs. Aspirin	
	HR (95% CI)	p
CV death	0.78 (0.64-0.96)	0.02
Stroke	0.58 (0.44-0.76)	<0.0001
MI	0.86 (0.70-1.05)	0.14

Eikelboom J et al. NEJM 2017

COMPASS

Primary: CV death, stroke, MI

Outcome	R + A N=9,152	Riva N=9,117	Aspirin N=9,126	Riva + aspirin vs. aspirin		Rivaroxaban vs. aspirin	
	N (%)	N (%)	N (%)	HR (95% CI)	p	HR (95% CI)	p
CV death, stroke, MI	379 (4.1)	448 (4.9)	496 (5.4)	0.76 (0.66-0.86)	<0.0001	0.90 (0.79-1.03)	0.12

Major bleeding

Outcome	R + A N=9,152	R N=9,117	A N=9,126	Rivaroxaban + Aspirin vs. Aspirin		Rivaroxaban vs. Aspirin	
	N (%)	N (%)	N (%)	HR (95% CI)	P	HR (95% CI)	P
Major bleeding	288 (3.1%)	255 (2.8%)	170 (1.9%)	1.70 (1.40-2.05)	<0.0001	1.51 (1.25-1.84)	<0.0001

496 - 379= 117 ischemic events prevented
288 -170= 118 more bleeding events

Eikelboom J, et al. N Engl J Med 2017; 377: 1319-1330.

With advances in antiplatelet therapy we keep adding treatments to aspirin

OR

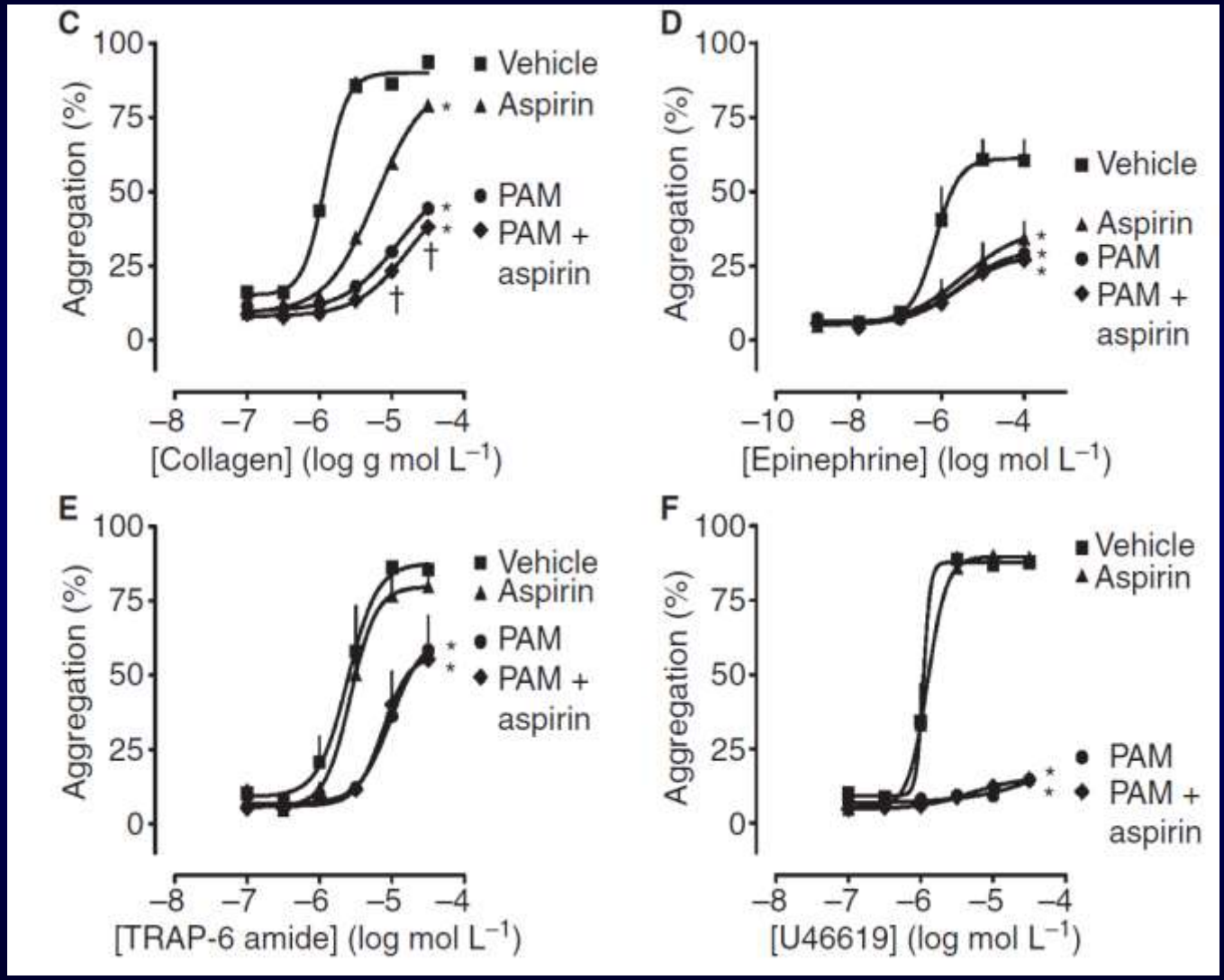
OR

OR

AND

Courtesy of PG Steg

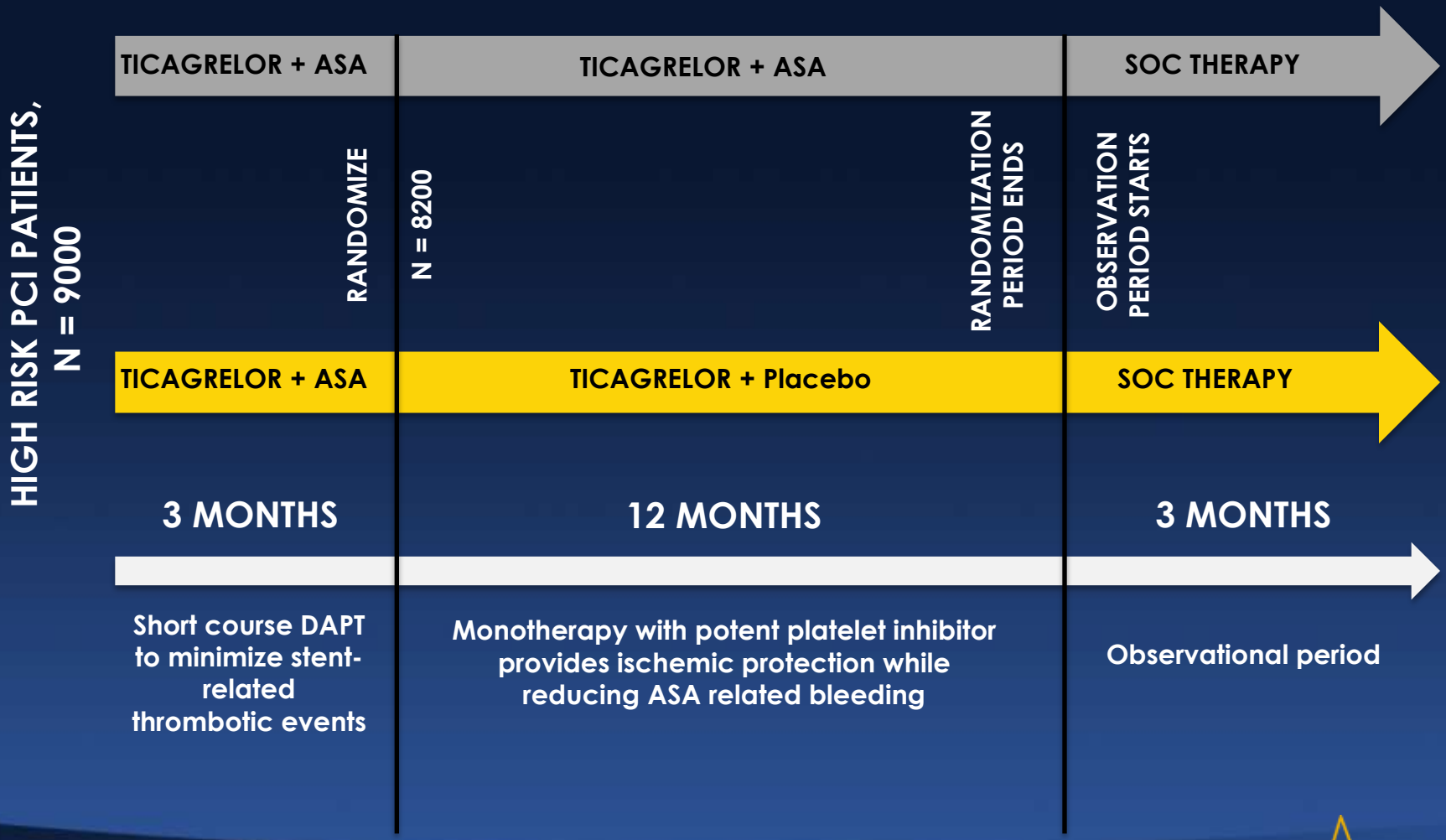
In the presence of strong P2Y12 receptor blockade, aspirin provides little additional platelet inhibition: *in vitro* findings



Armstrong PCJ et al. J Thromb Haemost 2011; 9: 552–61

Study Design

Multicenter, prospective, blinded dual-arm study



Mount Sinai Heart

twilight

Prevention in Stable Post-MI
Aspirin Plus P2Y12 Inhibitor Still Remains as a Key Player

Give to Caesar what belongs to Caesar!

Atherothrombotic complications after an MI are largely platelet mediated and require treatment with antiplatelet therapy. Large scale clinical trial data support a reduction in overall events in a way that makes sense (CV death, MI and stroke).

If you are concerned about bleeding, drop the aspirin, but antiplatelet therapy is the way to go!