Update on Antithrombotic Therapy After ACS/PCI: Recent Advances and Innovations in Drugs and Strategy

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BRIGHAM AND WOMEN'S HOSPITAL
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Disclosures

Dr. Deepak L. Bhatt discloses the following relationships - Advisory Board: Cardax, Cereno Scientific, Elsevier Practice Update Cardiology, Medscape Cardiology, PhaseBio, Regado Biosciences; Board of Directors: Boston VA Research Institute, Society of Cardiovascular Patient Care, TobeSoft; Chair: American Heart Association Quality Oversight Committee; Data Monitoring Committees: Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute, for the PORTICO trial, funded by St. Jude Medical, now Abbott), Cleveland Clinic (including for the ExCEED trial, funded by Edwards), Duke Clinical Research Institute, Mayo Clinic, Mount Sinai School of Medicine (for the ENVISAGE trial, funded by Daiichi Sankyo), Population Health Research Institute; **Honoraria**: American College of Cardiology (Senior Associate Editor, Clinical Trials and News, ACC.org; Vice-Chair, ACC Accreditation Committee), Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute; RE-DUAL PCI clinical trial steering committee funded by Boehringer Ingelheim; AEGIS-II executive committee funded by CSL Behring), Belvoir Publications (Editor in Chief, Harvard Heart Letter), Duke Clinical Research Institute (clinical trial steering committees, including for the PRONOUNCE trial, funded by Ferring Pharmaceuticals), HMP Global (Editor in Chief, Journal of Invasive Cardiology), Journal of the American College of Cardiology (Guest Editor; Associate Editor), Medtelligence/ReachMD (CME steering committees), **Population Health Research Institute (for the COMPASS operations committee, publications committee, steering committee, and USA national co-leader, funded by Bayer)**, Slack Publications (Chief Medical Editor, Cardiology Today's Intervention), Society of Cardiovascular Patient Care (Secretary/Treasurer), WebMD (CME steering committees); Other: Clinical Cardiology (Deputy Editor), NCDR-ACTION Registry Steering Committee (Chair), VA CART Research and Publications Committee (Chair); **Research Funding**: Abbott, Afimmune, Amarin, Amgen, **AstraZeneca**, **Bayer**, Boehringer Ingelheim, Bristol-Myers Squibb, Chiesi, CSL Behring, Eisai, Ethicon, Ferring Pharmaceuticals, Forest Laboratories, Idorsia, Ironwood, Ischemix, Lilly, Medtronic, **PhaseBio**, Pfizer, PLx Pharma, Regeneron, Roche, Sanofi Aventis, Synaptic, The Medicines Company; Royalties: Elsevier (Editor, Cardiovascular Intervention: A Companion to Braunwald's Heart Disease); Site Co-Investigator: Biotronik, Boston Scientific, St. Jude Medical (now Abbott), Svelte; Trustee: American College of Cardiology; Unfunded Research: FlowCo, Fractyl, Merck, Novo Nordisk, Takeda.

This presentation discusses off label and investigational uses of drugs.

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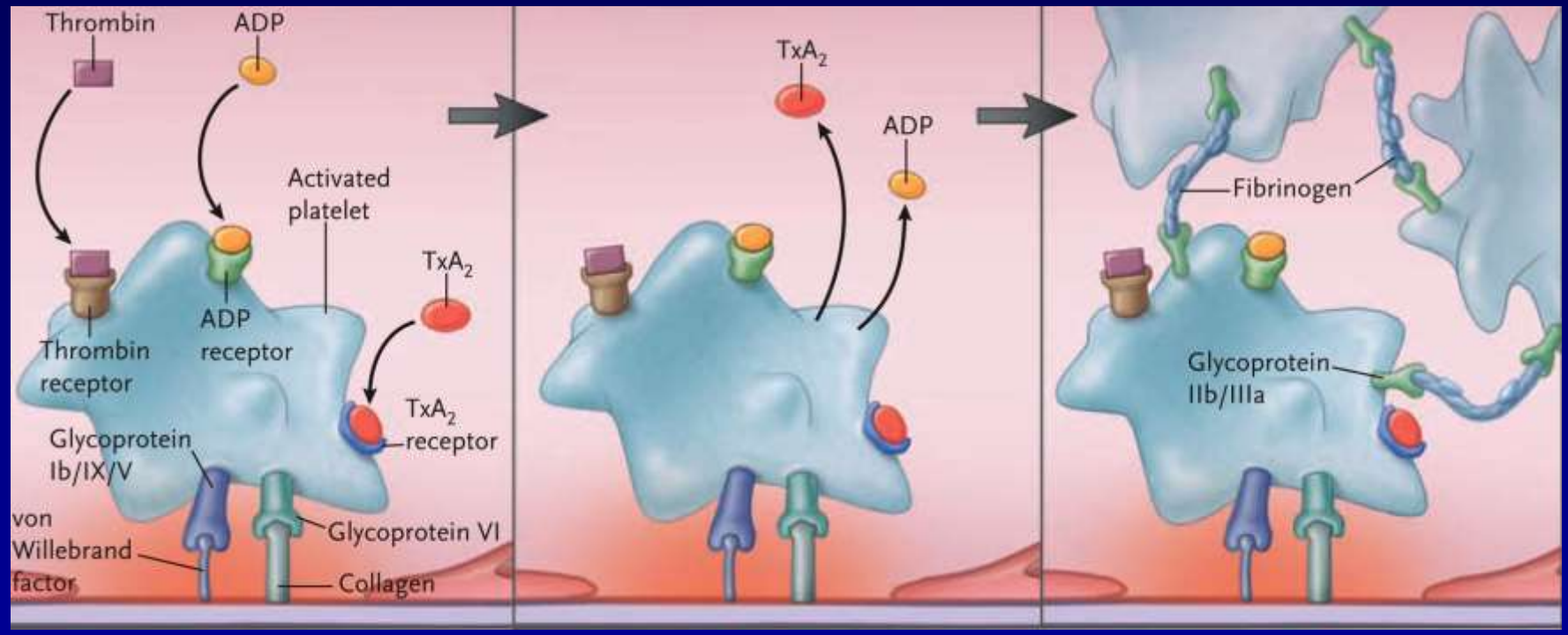
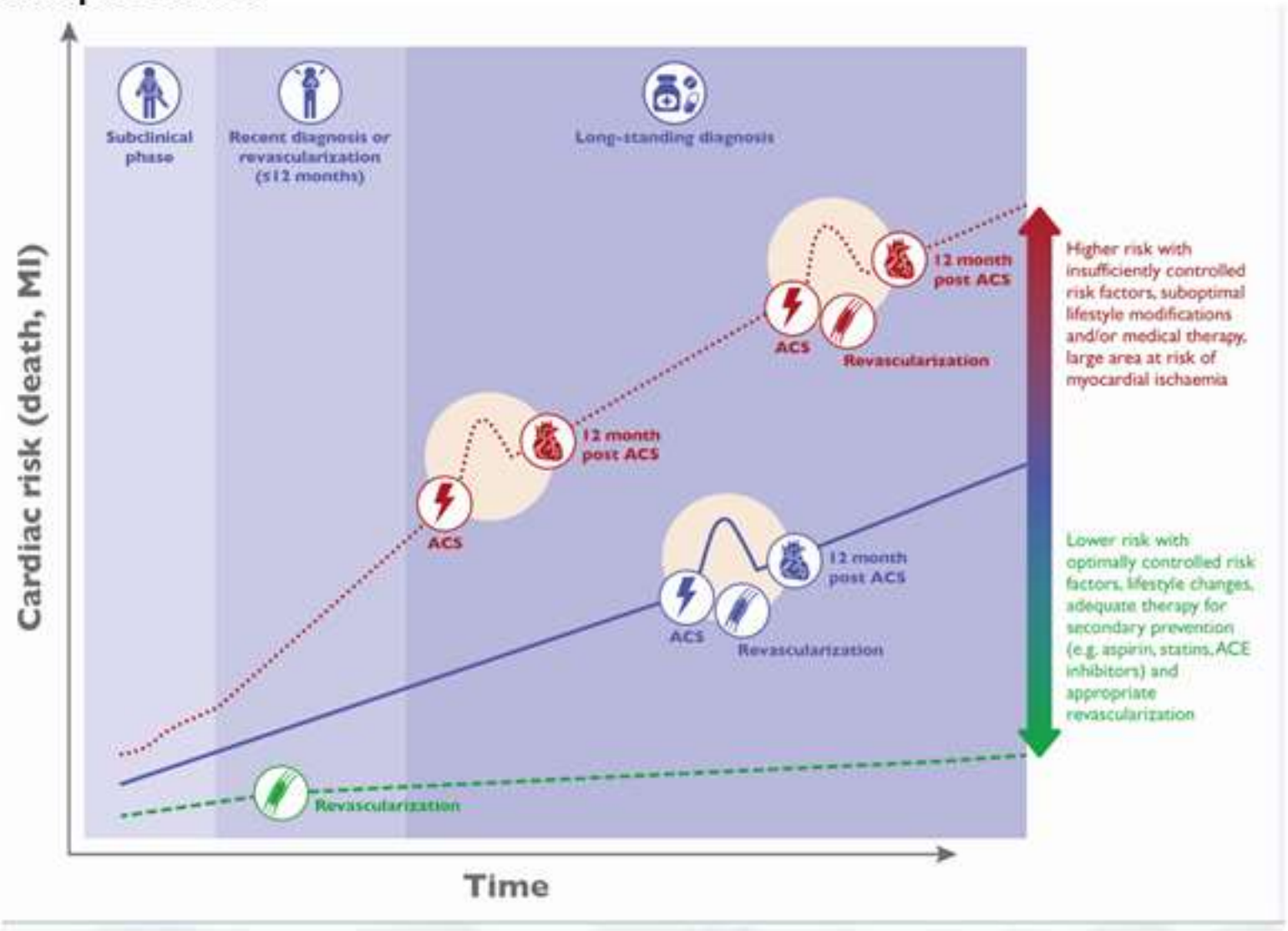
Role of Platelet Activation and Aggregation



Bhatt DL. N Engl J Med 2007;357:2078-81.

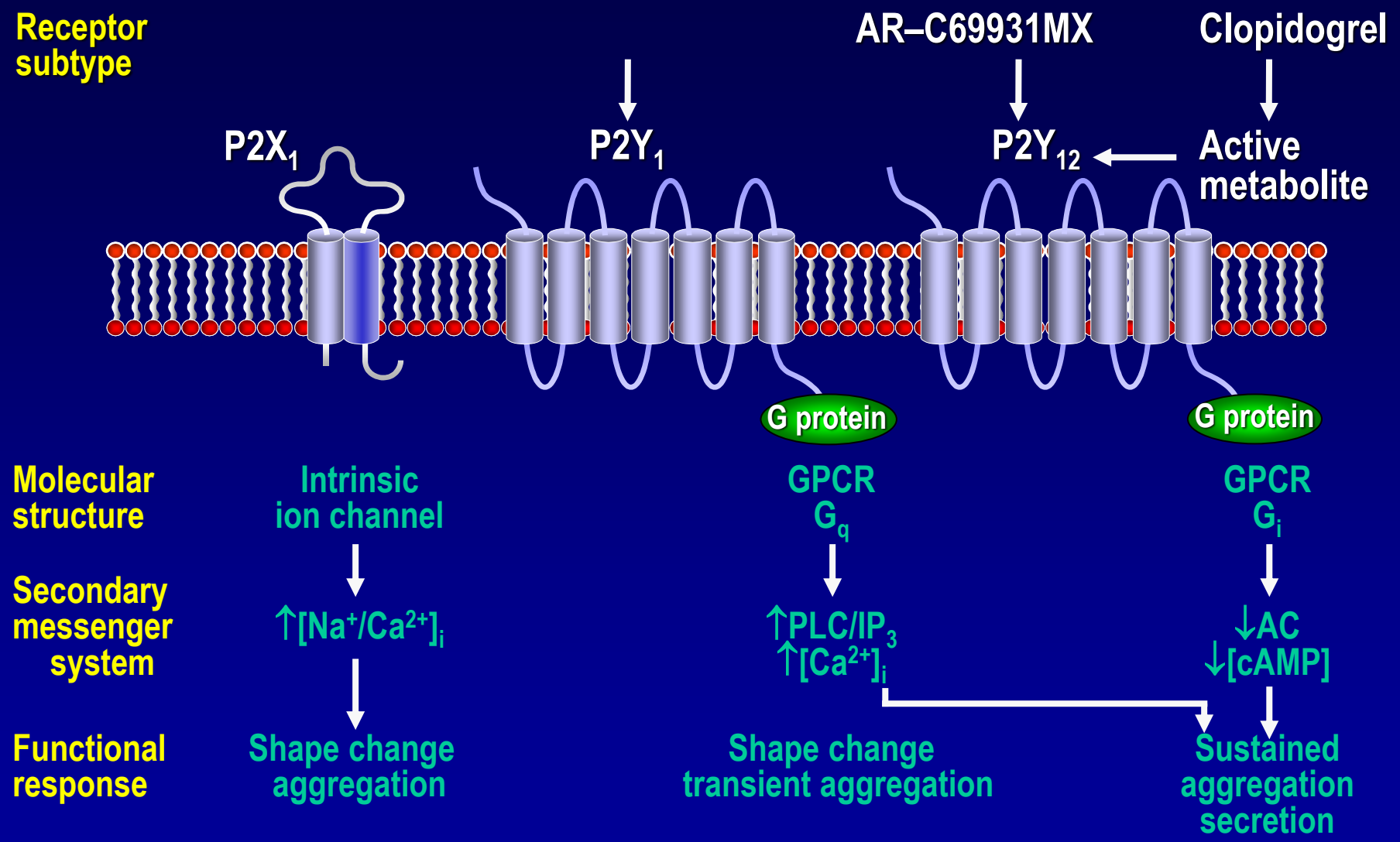
Natural history of chronic coronary syndromes

A dynamic process



ESC Guidelines on the diagnosis and management of chronic coronary syndromes (European Heart Journal 2019; 10.1093/eurheartj/ehz425)

ADP Receptors



Bhatt DL et al. *Nat Rev Drug Discov*. 2003;2:15-28.

European Heart Journal

doi: 10.1093/eurheartj/ehv443

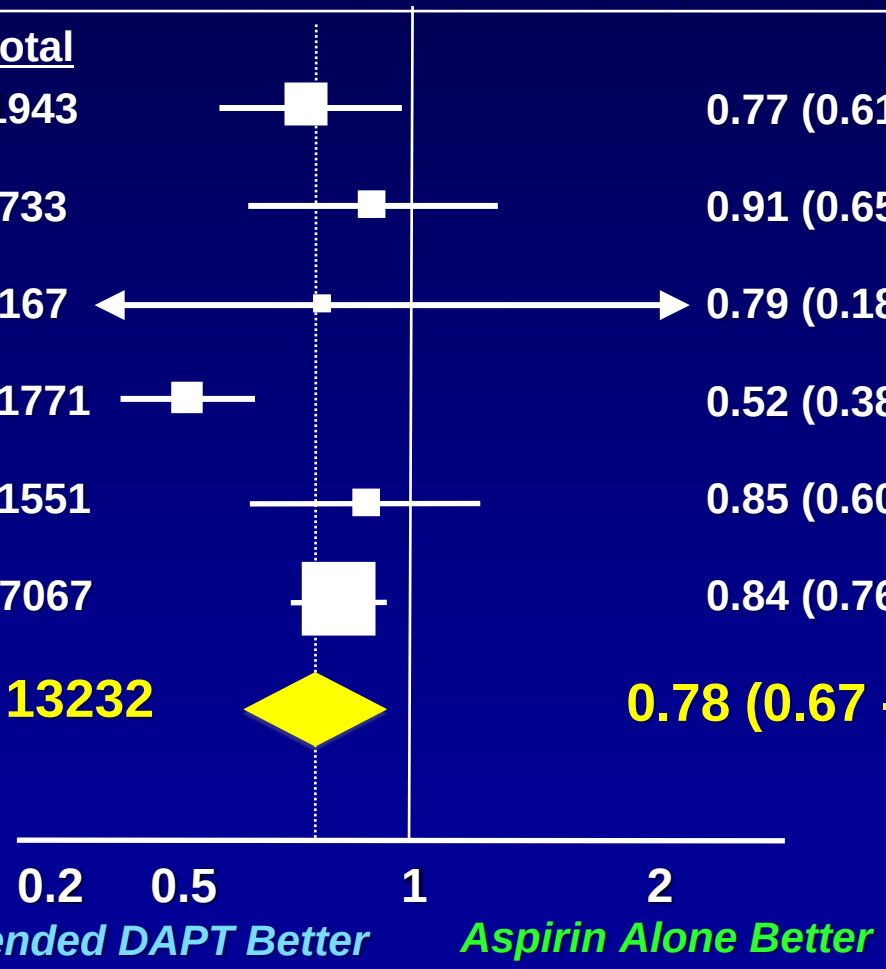
FASTTRACK CLINICAL RESEARCH
Coronary artery disease

Long-term dual antiplatelet therapy for secondary prevention of cardiovascular events in the subgroup of patients with previous myocardial infarction: a collaborative meta-analysis of randomized trials

Jacob A. Udell[1,2*], Marc P. Bonaca[3], Jean-Philippe Collet[4], A. Michael Lincoff[5], Dean J. Kereiakes[6], Francesco Costa[7], Cheol Whan Lee[8], Laura Mauri[9], Marco Valgimigli[7], Seung-Jung Park[8], Gilles Montalescot[4], Marc S. Sabatine[3], Eugene Braunwald[3], and Deepak L. Bhatt[3*]

Primary Endpoint – CV Death, MI, or Stroke

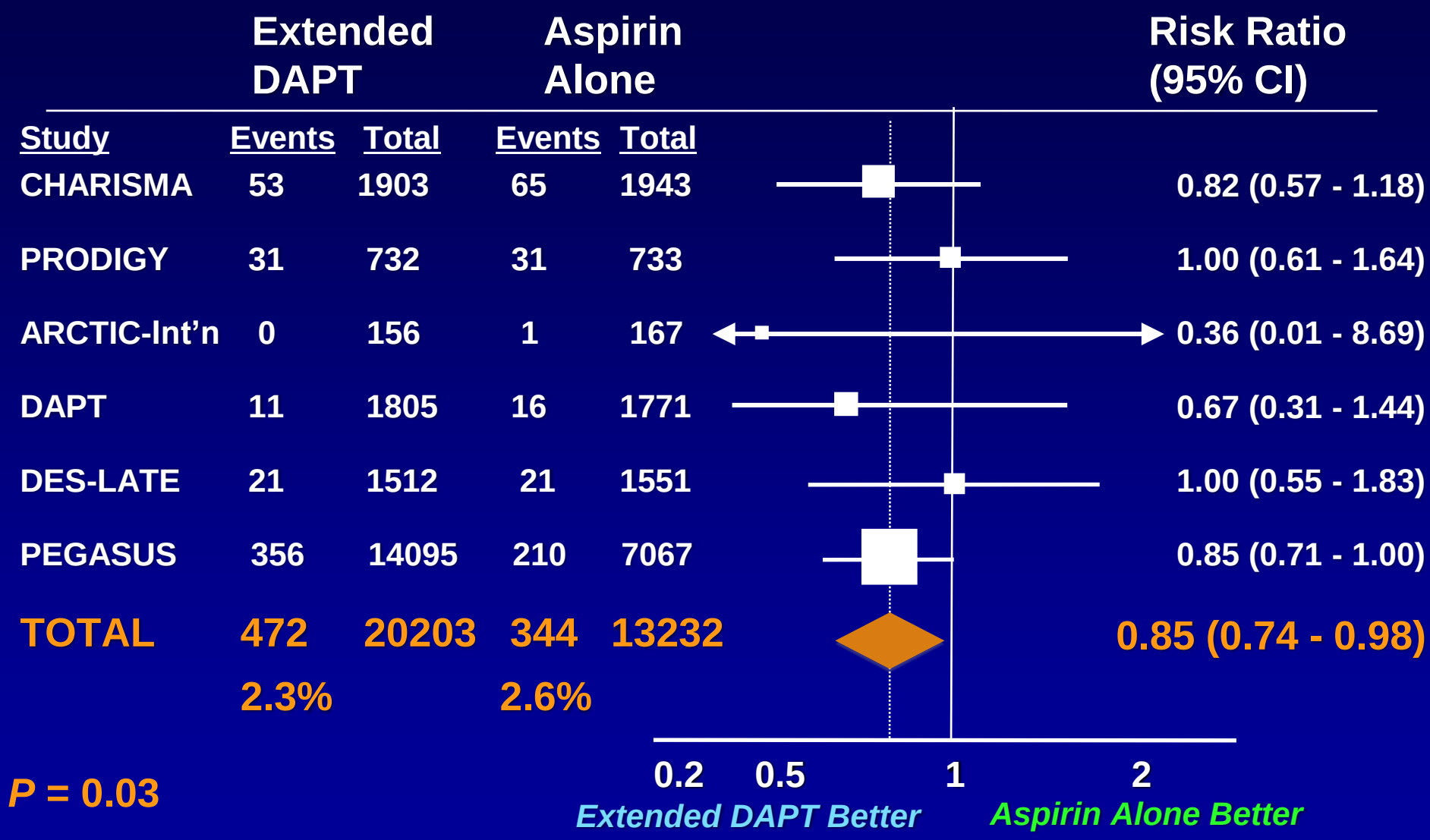
Study	Extended DAPT Events	Extended DAPT Total	Aspirin Alone Events	Aspirin Alone Total	Risk Ratio (95% CI)
CHARISMA	125	1903	162	1943	0.77 (0.61 - 0.98)
PRODIGY	63	732	69	733	0.91 (0.65 - 1.28)
ARCTIC-Int'n	3	156	4	167	0.79 (0.18 - 3.51)
DAPT	59	1805	108	1771	0.52 (0.38 - 0.72)
DES-LATE	56	1512	66	1551	0.85 (0.60 - 1.21)
PEGASUS	980	14095	578	7067	0.84 (0.76 - 0.94)
TOTAL	1286	20203	987	13232	0.78 (0.67 - 0.90)
	6.4%		7.5%		



P = 0.001

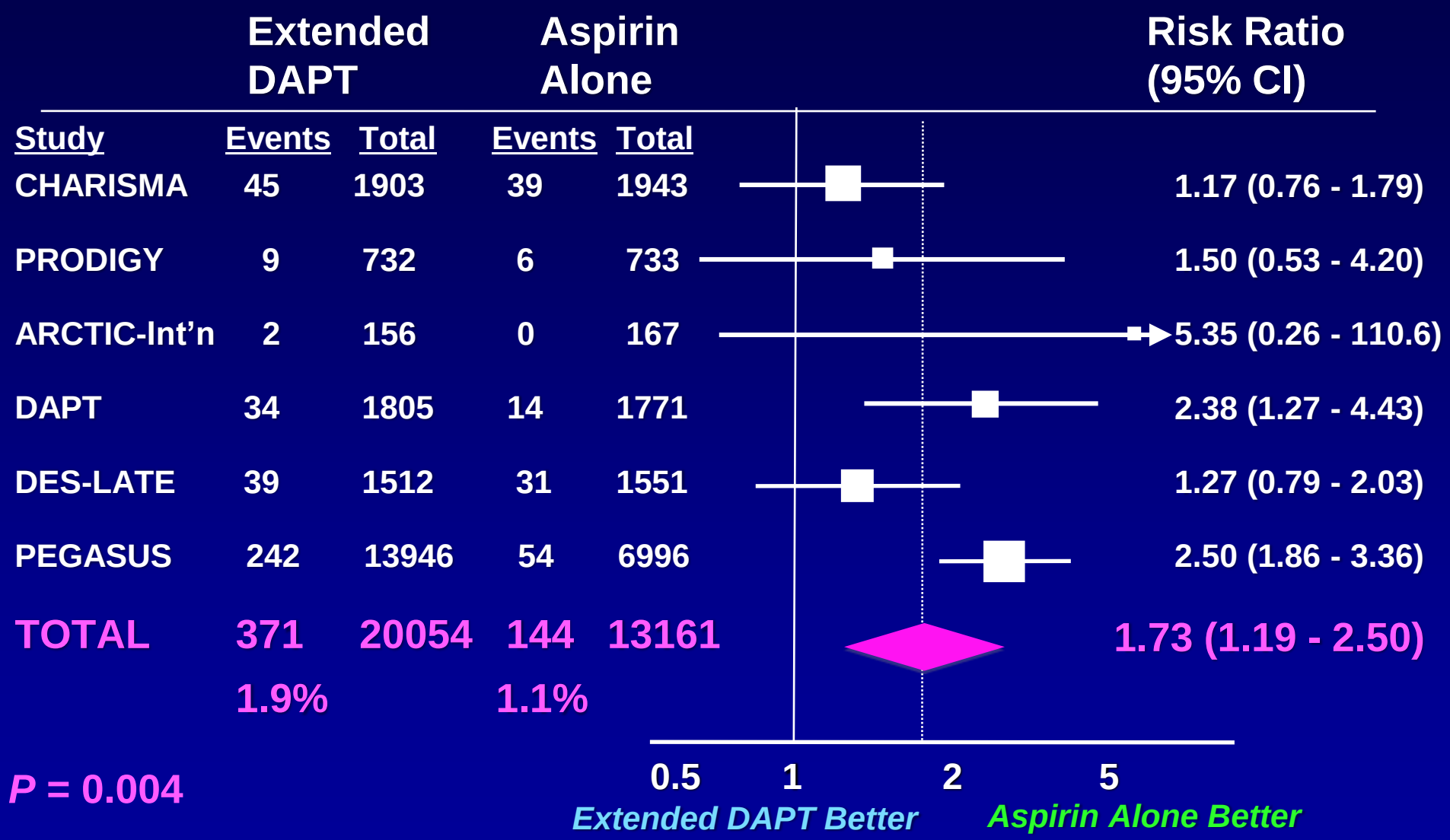
Udell JA, et al. *Eur Heart J* 2015 at eurheartj.oxfordjournals.org.

Cardiovascular Death



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

Major Bleeding



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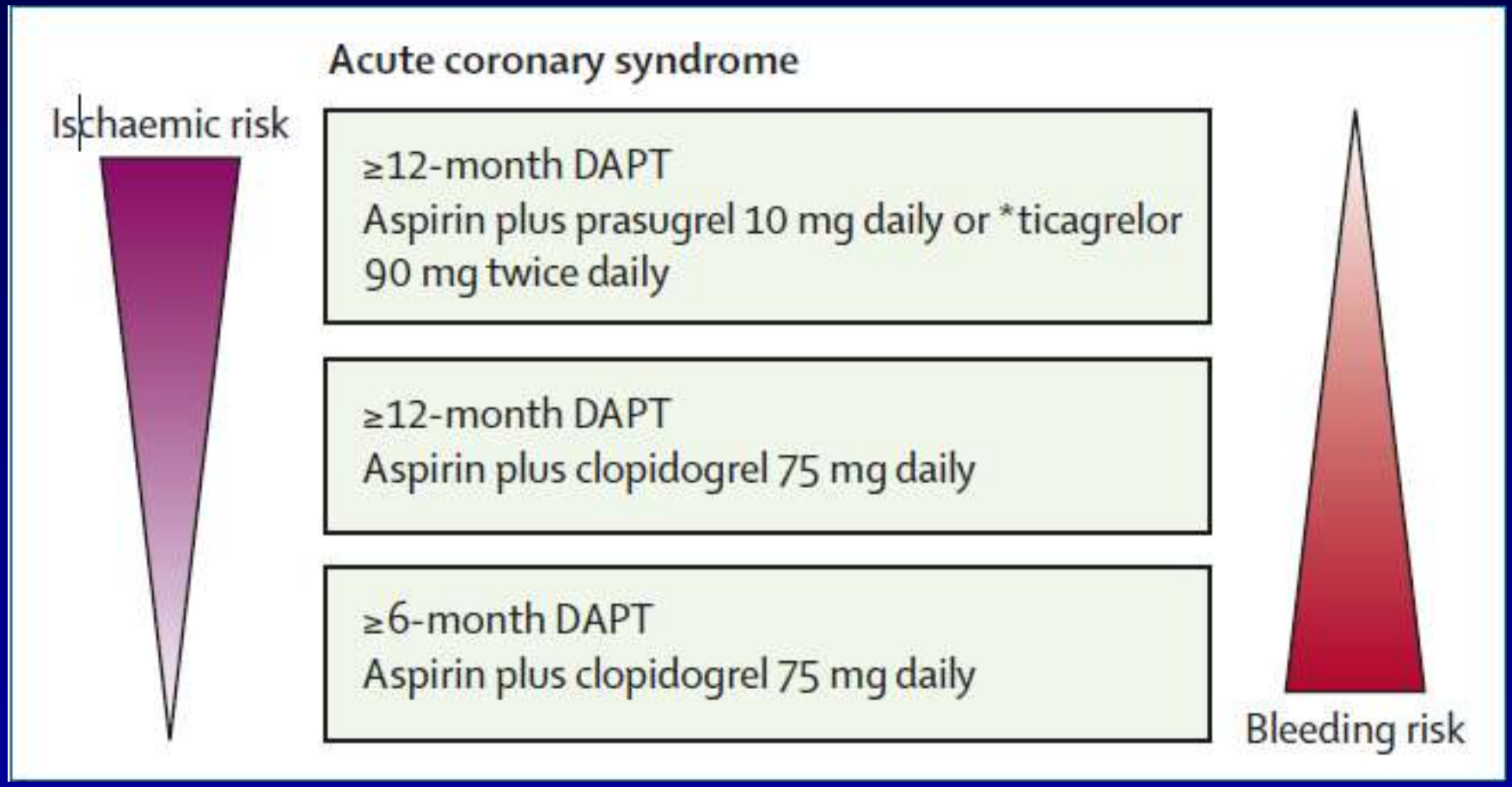
Udell JA, et al. *Eur Heart J* 2015 at eurheartj.oxfordjournals.org.

SMART DATE



Motovska Z and Bhatt DL. Lancet 2018.

THEMIS:
Ticagrelor Added to Aspirin in Patients with Stable Coronary Disease and Diabetes

Presented by Deepak L. Bhatt, MD, MPH

Philippe Gabriel Steg,* Deepak L Bhatt,*

Tabassome Simon, Kim M. Fox, Shamir R. Mehta, Robert A. Harrington, Claes Held, Marielle Andersson, Anders Himmelmann, Wilhelm Ridderstråle, Maria Leonsson-Zachrisson, Yuyin Liu, Grzegorz Opolski, Dmitry Zateyshchikov, Junbo Ge, José Carlos Nicolau, Ramón Corbalán, Jan Hein Cornel, Petr Widimský, Lawrence A. Leiter

on behalf of the THEMIS Steering Committee and Investigators

*co-Chairs and co-Principal Investigators of THEMIS

European Society of Cardiology 2019

ClinicalTrials.gov registration: NCT01991795

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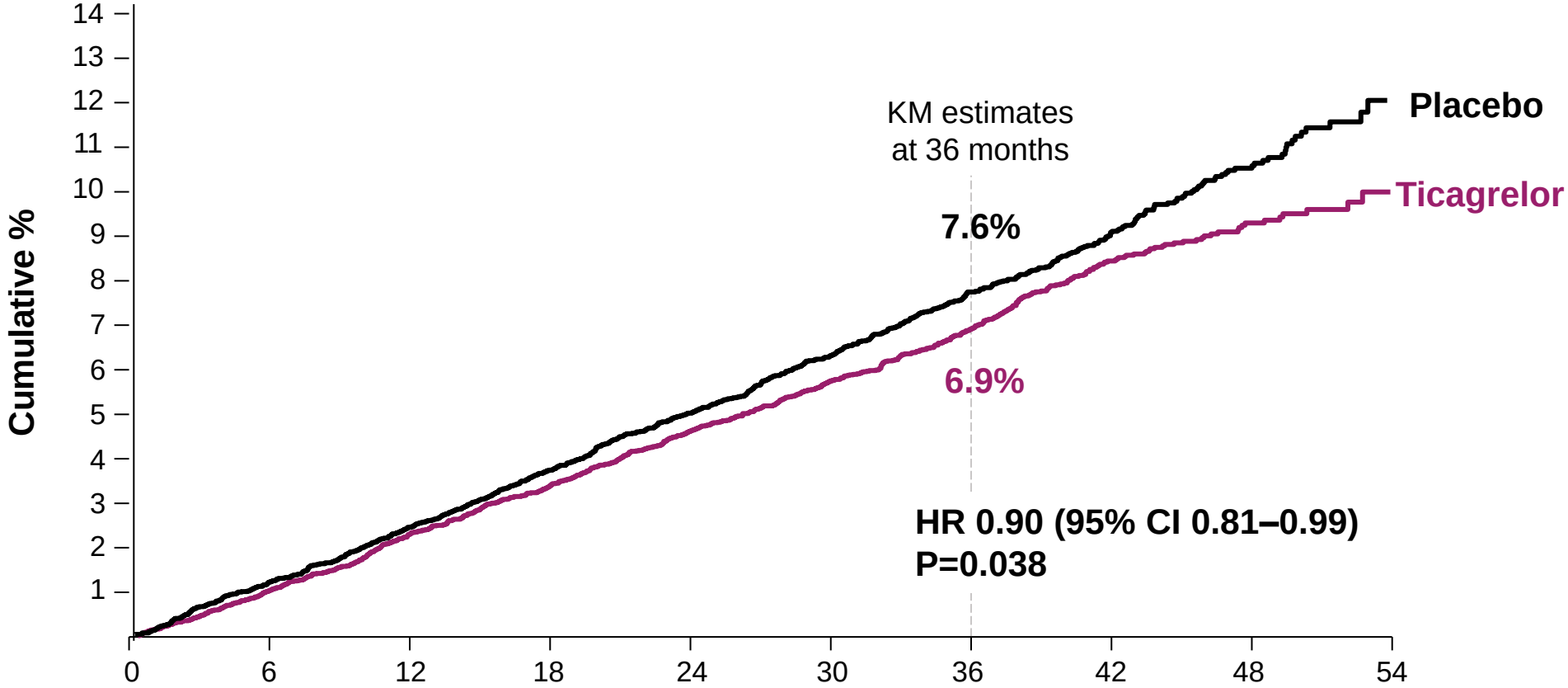
TICAGRELOR IN STABLE CAD AND T2D TREATED WITH ASA

PARTNERS THEMIS

Primary Composite Endpoint

Cardiovascular death/MI/stroke



N at Risk										
Ticagrelor	9619	9416	9237	9074	8909	8692	5974	3664	1684	170
Placebo	9601	9414	9246	9076	8909	8692	5934	3682	1685	174

CI=confidence interval; HR=hazard ratio; KM=Kaplan-Meier; MI=myocardial infarction; N=number of patients

Steg PG, Bhatt DL, et al. NEJM 2019 DOI: 10.1056/NEJMoa1908077.

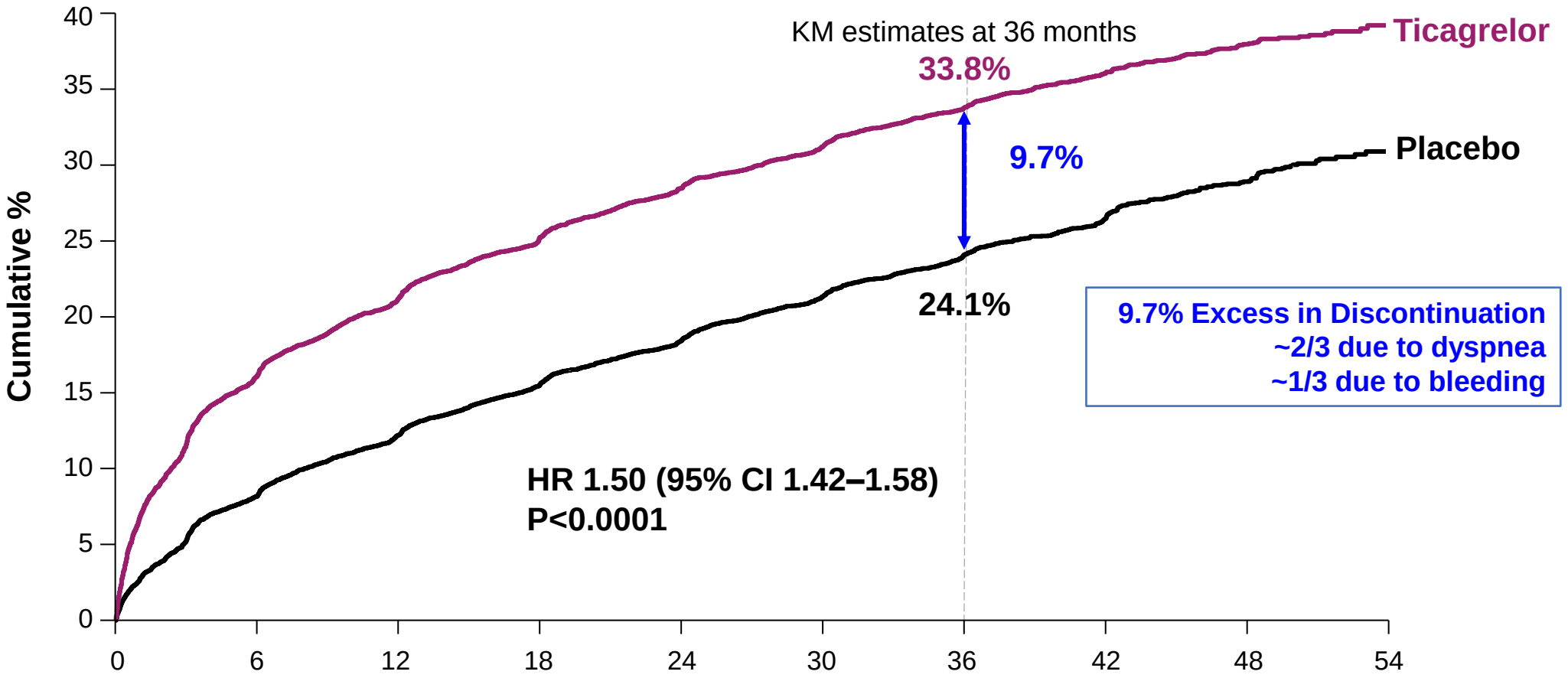
Bleeding Outcomes

	Ticagrelor (N=9562)		Placebo (N=9531)			
	Patients with events (%)	Event rate/ 100 patient years)	Patients with events (%)	Event rate/ 100 patient years)	Hazard Ratio (95% CI)	p-value
TIMI major bleeding	206 (2.2%)	0.89	100 (1.0%)	0.38	2.32 (1.82–2.94)	<0.001
TIMI major or minor bleeding	285 (3.0%)	1.23	129 (1.4%)	0.49	2.49 (2.02–3.07)	<0.001
TIMI major, minor, or requiring medical attention	1072 (11.2%)	4.61	485 (5.1%)	1.85	2.51 (2.26–2.80)	<0.001
PLATO major bleeding	310 (3.2%)	1.33	145 (1.5%)	0.55	2.41 (1.98–2.93)	<0.001
BARC bleeding						
5 (fatal bleeding)	17 (0.2%)	0.07	10 (0.1%)	0.04	1.90 (0.87–4.15)	0.11
5 or 4	17 (0.2%)	0.07	11 (0.1%)	0.04	1.73 (0.81–3.69)	0.16
5, 4 or 3	341 (3.6%)	1.47	163 (1.7%)	0.62	2.36 (1.96–2.84)	<0.001
Intracranial hemorrhage	70 (0.7%)	0.30	46 (0.5%)	0.18	1.71 (1.18–2.48)	0.005
Spontaneous	28 (0.3%)	0.12	27 (0.3%)	0.10	1.17 (0.69–1.98)	0.57
Procedural	1 (0.0%)	0.00	3 (0.0%)	0.01		
Traumatic	41 (0.4%)	0.18	16 (0.2%)	0.06	2.87 (1.61–5.12)	<0.001

Includes events with onset from randomization up to 7 days after last dose. BARC bleeding was defined according to a score of 3 to 5 as follows: type 3, bleeding with a decrease in the hemoglobin of more than 3 g per deciliter, any transfusion, cardiac tamponade, or intracranial or ocular involvement; type 4, CABG-related bleeding; and type 5, fatal bleeding. Traumatic ICH: 27 (66%) on ticagrelor and 6 (38%) on placebo reported as subdural bleeding by investigators.

BARC=Bleeding Academic Research Consortium, CABG=coronary artery bypass grafting; CI=confidence interval; N=number of patients; PLATO=PLATelet inhibition and patient outcomes; TIMI=Thrombolysis in Myocardial Infarction

Permanent Treatment Discontinuation



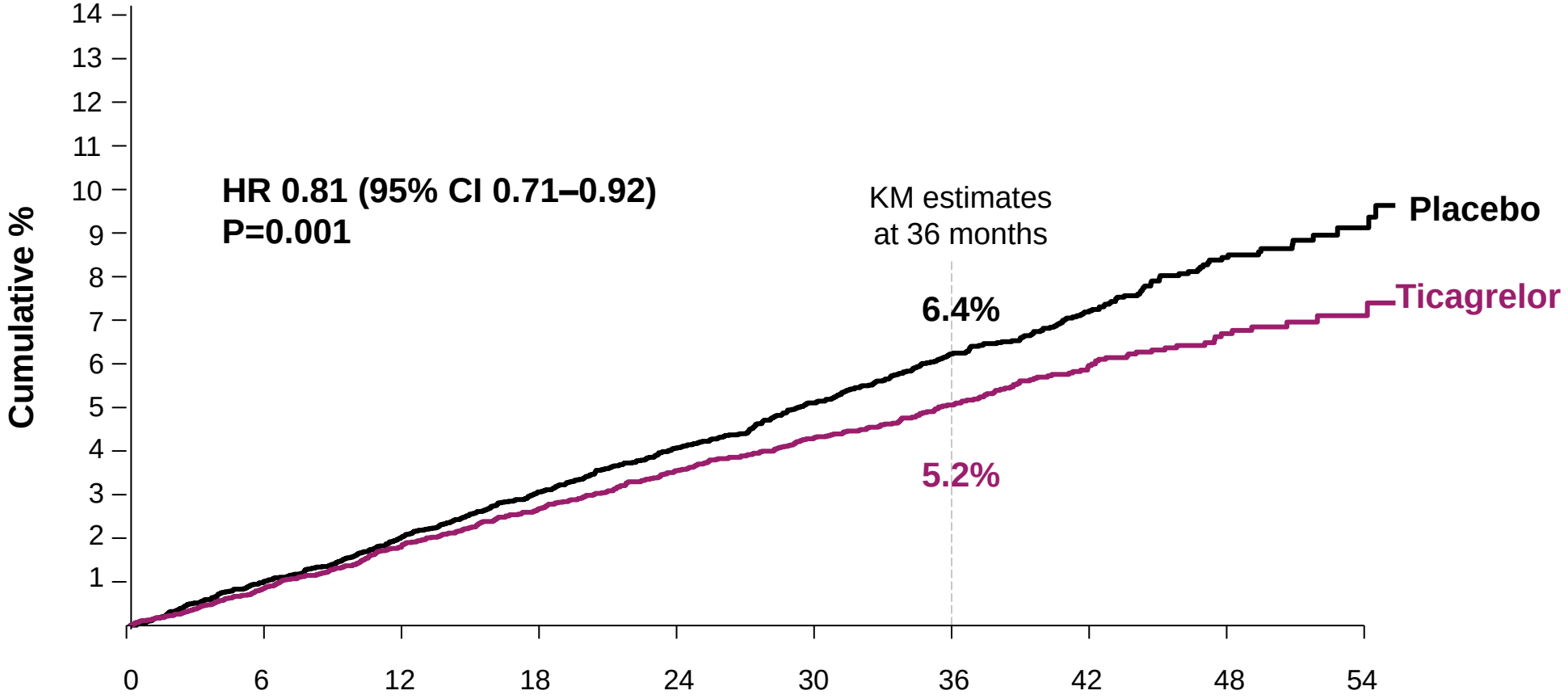
Number at risk										
Ticagrelor	9562	7904	7316	6831	6414	6029	4105	2483	1172	173
Placebo	9531	8660	8179	7772	7367	6974	4786	2959	1362	218

Discontinuation due to dyspnea 6.9% on ticagrelor vs. 0.8% on placebo (HR 9.27 [7.30-11.77] p <0.001); due to bleeding 4.9% vs 1.3% (HR 4.04 [3.32-4.92] p<0.001). CI=confidence interval; HR=hazard ratio; KM=Kaplan-Meier

Steg PG, Bhatt DL, et al. NEJM 2019 DOI: 10.1056/NEJMoa1908077.

Primary Composite Endpoint

Cardiovascular death/MI/stroke – on treatment*



Number at Risk

Ticagrelor	9562	7891	7291	6799	6343	5962	4040	2431	1137	168
Placebo	9531	8639	8136	7702	7373	6875	4712	2904	1333	213

*Prespecified analysis with patients censored 3 days after the last dose; CI=confidence interval; HR=hazard ratio; KM=Kaplan-Meier; MI=myocardial infarction; N=number of patients

Steg PG, Bhatt DL, et al. NEJM 2019 DOI: 10.1056/NEJMoa1908077.

THEMIS-PCI: Ticagrelor Added to Aspirin in Patients with Diabetes and Stable Coronary Artery Disease with a History of Prior Percutaneous Coronary Intervention

Presented by Ph. Gabriel Steg, MD

Deepak L. Bhatt,* Philippe Gabriel Steg,*

Shamir R. Mehta, Lawrence A. Leiter, Tabassome Simon, Kim Fox, Claes Held, Marielle Andersson, Anders Himmelmann, Wilhelm Ridderstråle, Jersey Chen, Yang Song, Rafael Diaz, Shinya Goto, Stefan K James, Kausik K. Ray, Alexander Parkhomenko, Mikhail N. Kosiborod, Darren K. McGuire, Robert A. Harrington,

on behalf of the THEMIS Steering Committee and Investigators

*co-Chairs and co-Principal Investigators of THEMIS

European Society of Cardiology 2019

ClinicalTrials.gov registration: NCT01991795

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TICAGRELOR IN STABLE CAD AND T2D TREATED WITH ASA

THEMIS

Efficacy Endpoints

ITT Population

	Subgroup	Ticagrelor (N=9619) N	Ticagrelor (N=9619) Patients with events (%)	Placebo (N=9601) N	Placebo (N=9601) Patients with events (%)	Hazard Ratio (95% CI)	P-value	P-interaction
CV death/MI/stroke (Primary)	History of PCI	5558	404 (7.3%)	5596	480 (8.6%)	0.85 (0.74–0.97)	0.013	0.16
	No history of PCI	4061	332 (8.2%)	4005	338 (8.4%)	0.98 (0.84–1.14)	0.76	
All-cause death/MI/stroke	History of PCI	5558	494 (8.9%)	5596	603 (10.8%)	0.82 (0.73–0.93)	0.0014	**0.021**
	No history of PCI	4061	425 (10.5%)	4005	415 (10.4%)	1.02 (0.89–1.17)	0.80	
All-cause death/MI/stroke/ ALI/ major amputation, vascular etiology	History of PCI	5558	500 (9.0%)	5596	616 (11.0%)	0.82 (0.72–0.92)	0.0007	**0.023**
	No history of PCI	4061	427 (10.5%)	4005	423 (10.6%)	1.00 (0.88–1.15)	0.97	

Hazard ratios, p-values calculated for ticagrelor vs placebo from a Cox proportional hazards model with treatment as the only explanatory variable. * Includes deaths based on publicly available vital status data in patients who withdrew consent. ALI=acute limb ischemia; CI=confidence interval; CV=cardiovascular; ITT=intention to treat; MI=myocardial infarction; N=number of patients; PCI=percutaneous coronary intervention; STEMI=ST segment elevation MI

Bhatt DL, Steg PG, et al. *Lancet* 2019 http://dx.doi.org/10.1016/ S0140-6736(19)31887-2.

Efficacy Endpoints

ITT Population

	Subgroup	Ticagrelor (N=9619) N	Ticagrelor (N=9619) Patients with events (%)	Placebo (N=9601) N	Placebo (N=9601) Patients with events (%)	Hazard Ratio (95% CI)	P-value	P-interaction
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	No history of PCI	4061	332 (8.2%)	4005	338 (8.4%)	0.98 (0.84–1.14)	0.76	
All-cause death/MI/stroke	History of PCI	5558	494 (8.9%)	5596	603 (10.8%)	0.82 (0.73–0.93)	0.0014	**0.021**
	No history of PCI	4061	425 (10.5%)	4005	415 (10.4%)	1.02 (0.89–1.17)	0.80	
All-cause death/MI/stroke/ ALI/ major amputation, vascular etiology	History of PCI	5558	500 (9.0%)	5596	616 (11.0%)	0.82 (0.72–0.92)	0.0007	**0.023**
	No history of PCI	4061	427 (10.5%)	4005	423 (10.6%)	1.00 (0.88–1.15)	0.97	
CV death	History of PCI	5558	174 (3.1%)	5596	183 (3.3%)	0.96 (0.78–1.18)	0.68	0.41
	No history of PCI	4061	190 (4.7%)	4005	174 (4.3%)	1.08 (0.88–1.33)	0.44	
All-cause death*	History of PCI	5558	282 (5.1%)	5596	323 (5.8%)	0.88 (0.75–1.03)	0.11	0.059
	No history of PCI	4061	297 (7.3%)	4005	269 (6.7%)	1.09 (0.93–1.29)	0.29	
MI	History of PCI	5558	171 (3.1%)	5596	216 (3.9%)	0.80 (0.65–0.97)	0.027	0.42
	No history of PCI	4061	103 (2.5%)	4005	112 (2.8%)	0.91 (0.70–1.19)	0.51	
STEMI	History of PCI	5558	16 (0.3%)	5596	51 (0.9%)	0.32 (0.18–0.55)	<0.0001	0.85
	No history of PCI	4061	6 (0.1%)	4005	21 (0.5%)	0.28 (0.11–0.70)	0.007	
Stroke	History of PCI	5558	96 (1.7%)	5596	131 (2.3%)	0.74 (0.57–0.96)	0.024	0.26
	No history of PCI	4061	84 (2.1%)	4005	90 (2.2%)	0.93 (0.69–1.25)	0.62	
ALI /major amputation of vascular etiology	History of PCI	5558	7 (0.1%)	5596	15 (0.3%)	0.47 (0.19–1.15)	0.099	0.88
	No history of PCI	4061	6 (0.1%)	4005	14 (0.3%)	0.43 (0.16–1.11)	0.080	

Hazard ratios, p-values calculated for ticagrelor vs placebo from a Cox proportional hazards model with treatment as the only explanatory variable. * Includes deaths based on publicly available vital status data in patients who withdrew consent. ALI=acute limb ischemia; CI=confidence interval; CV=cardiovascular; ITT=intention to treat; MI=myocardial infarction; N=number of patients; PCI=percutaneous coronary intervention; STEMI=ST segment elevation MI

Bhatt DL, Steg PG, et al. *Lancet* 2019 http://dx.doi.org/10.1016/ S0140-6736(19)31887-2.

Primary and Secondary Efficacy Endpoints

On treatment

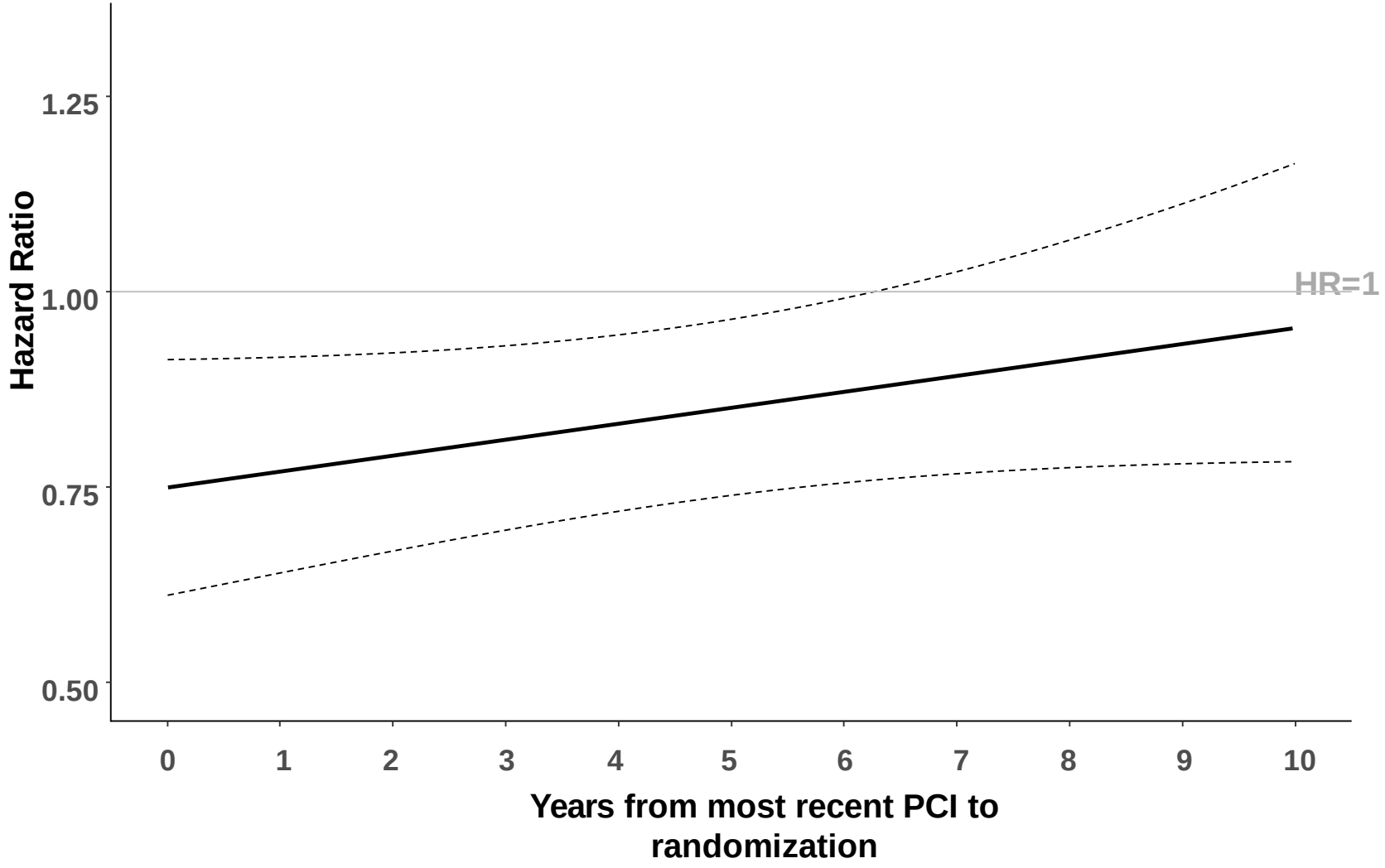
		Ticagrelor (N=9562)		Placebo (N=9531)				
	Subgroup	N	Patients with events (%)	N	Patients with events (%)	Hazard Ratio (95% CI)	p-value	p-interaction
CV death/ MI/stroke	History of PCI	5536	225 (4.1%)	5564	347 (6.2%)	0.73 (0.62–0.87)	0.0003	**0.036**
	No history of PCI	4026	200 (5.0%)	3967	233 (5.9%)	0.96 (0.80–1.16)	0.70	
All-cause death/ MI/ stroke	History of PCI	5536	242 (4.4%)	5564	378 (6.8%)	0.73 (0.62–0.85)	<.0001	**0.01**
	No history of PCI	4026	222 (5.5%)	3967	250 (6.3%)	1.00 (0.83–1.20)	0.99	
All-cause death/ MI/ stroke/ ALI/ major amputation of vascular etiology	History of PCI	5536	244 (4.4%)	5564	387 (7.0%)	0.71 (0.61–0.84)	<.0001	**0.011**
	No history of PCI	4026	224 (5.6%)	3967	258 (6.5%)	0.98 (0.82–1.17)	0.78	
CV death	History of PCI	5536	60 (1.1%)	5564	85 (1.5%)	0.81 (0.58–1.12)	0.20	0.15
	No history of PCI	4026	86 (2.1%)	3967	87 (2.2%)	1.11 (0.83–1.50)	0.48	
All-cause death*	History of PCI	5536	77 (1.4%)	5564	118 (2.1%)	0.74 (0.56–0.99)	0.044	**0.021**
	No history of PCI	4026	110 (2.7%)	3967	105 (2.6%)	1.18 (0.90–1.54)	0.22	
MI	History of PCI	5536	109 (2.0%)	5564	177 (3.2%)	0.70 (0.55–0.88)	0.003	0.21
	No history of PCI	4026	69 (1.7%)	3967	86 (2.2%)	0.90 (0.66–1.24)	0.51	
STEMI	History of PCI	5536	9 (0.2%)	5564	39 (0.7%)	0.26 (0.13–0.54)	0.0003	0.76
	No history of PCI	4026	3 (0.1%)	3967	16 (0.4%)	0.21 (0.06–0.73)	0.014	
Stroke	History of PCI	5536	65 (1.2%)	5564	99 (1.8%)	0.74 (0.54–1.02)	0.062	0.38
	No history of PCI	4026	62 (1.5%)	3967	76 (1.9%)	0.91 (0.65–1.28)	0.59	
ALI/major amputation of vascular etiology	History of PCI	5536	3 (0.1%)	5564	9 (0.2%)	0.38 (0.10–1.39)	0.14	0.65
	No history of PCI	4026	5 (0.1%)	3967	10 (0.3%)	0.55 (0.19–1.61)	0.27	

Hazard ratios and P-values calculated for ticagrelor vs placebo from a Cox proportional hazards model with treatment as the only explanatory variable. Includes events with onset date at or after randomization day up to 7 days after the last dose; only patients who took at least 1 dose of study drug are included. The number of first events for the components are the actual number of first events for each component and do not add up to the number of events in the composite endpoint. Includes deaths based on publicly available vital status data in patients who have withdrawn consent.
ALI= acute limb ischemia; CI=confidence interval; CV=cardiovascular; MI=myocardial infarction; PCI=percutaneous coronary intervention; STEMI=ST-segment elevation MI

Bhatt DL, Steg PG, et al. *Lancet* 2019 http://dx.doi.org/10.1016/ S0140-6736(19)31887-2.

Benefit of Ticagrelor vs Placebo

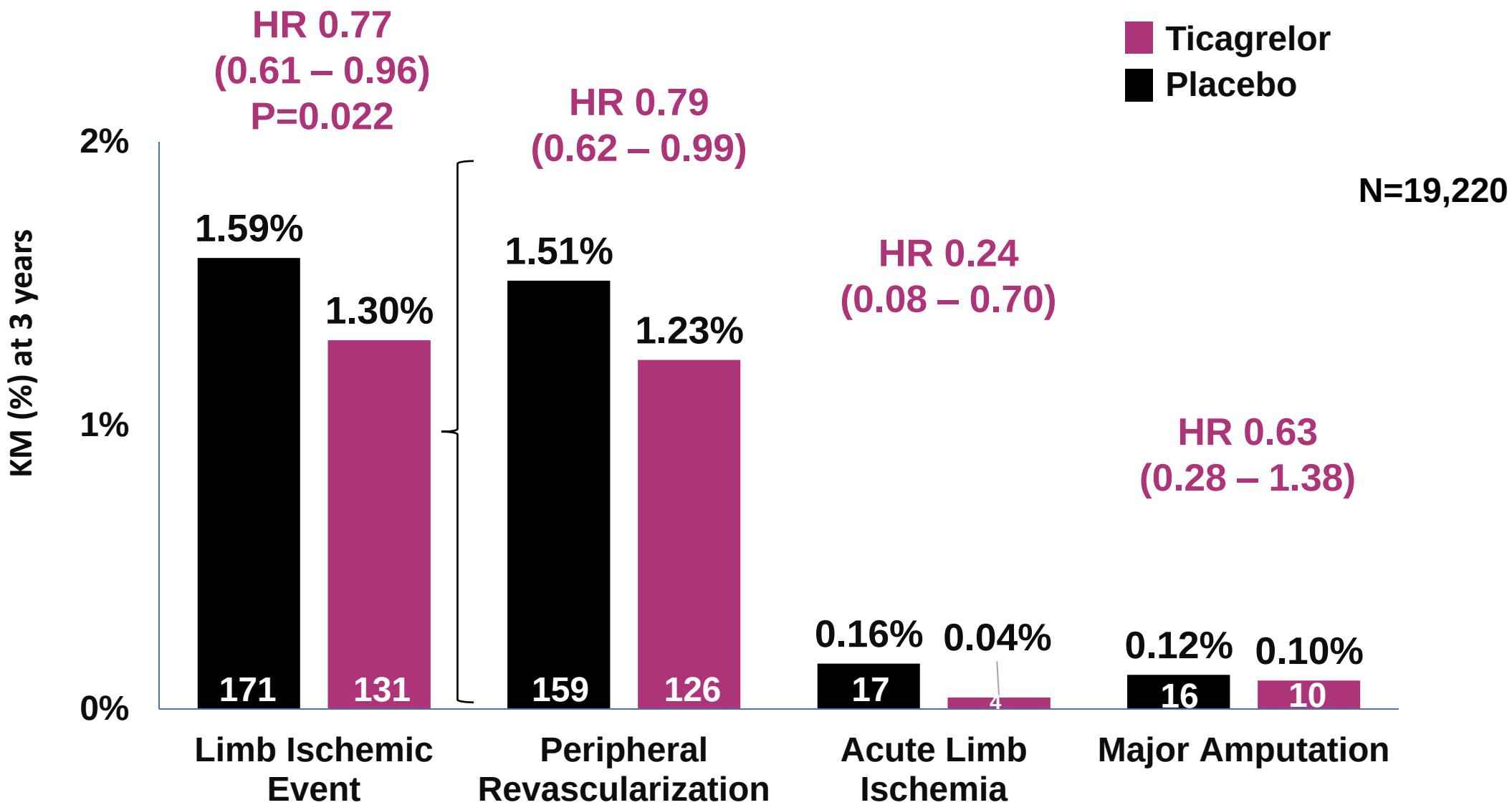
as a Function of Time between PCI and randomization



Dotted lines signify 95% confidence interval; HR=hazard ratio; PCI=percutaneous coronary intervention

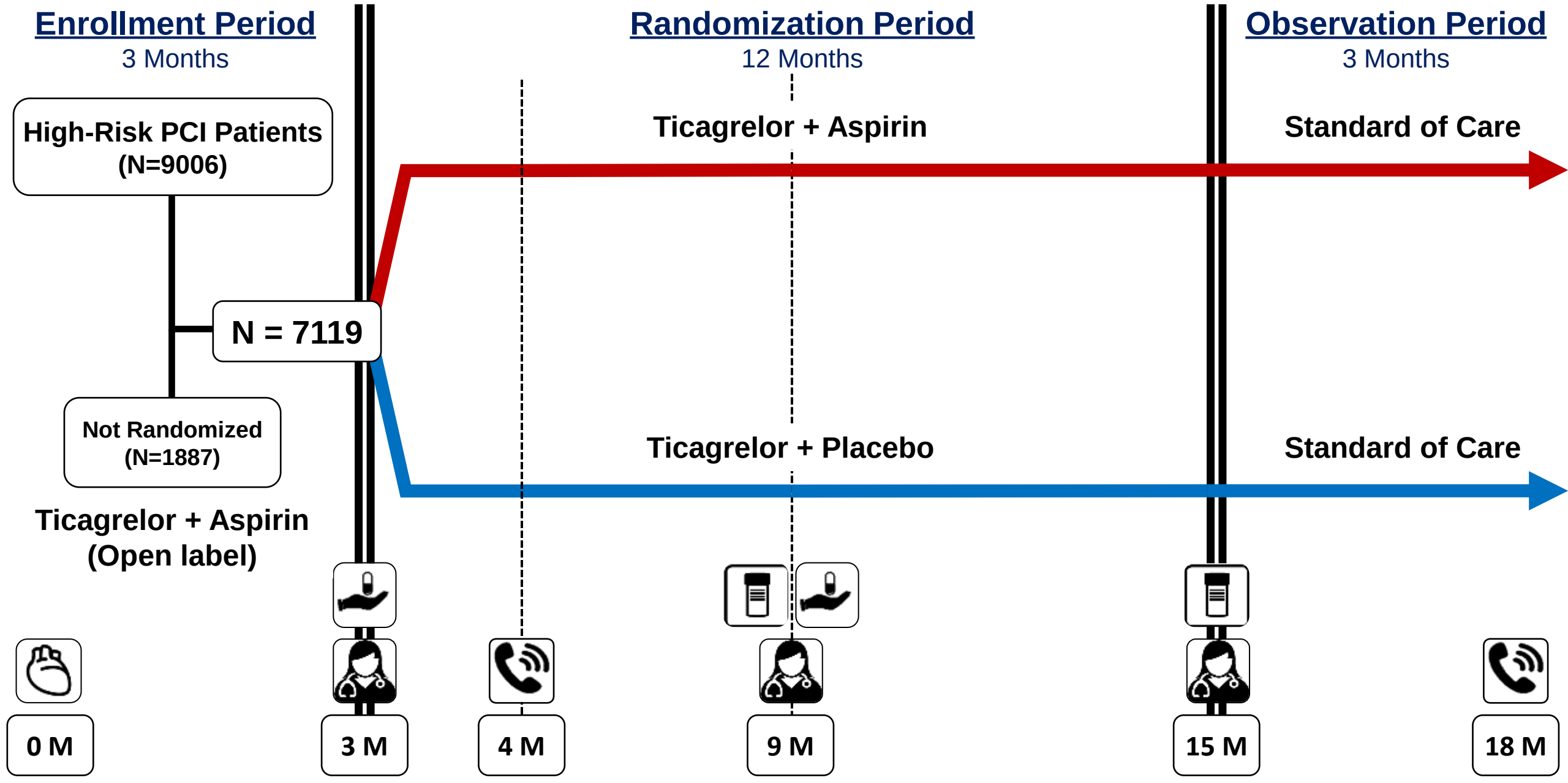
Bhatt DL, Steg PG, et al. *Lancet* 2019 http://dx.doi.org/10.1016/ S0140-6736(19)31887-2.

Limb Outcomes by Type with Ticagrelor versus Placebo



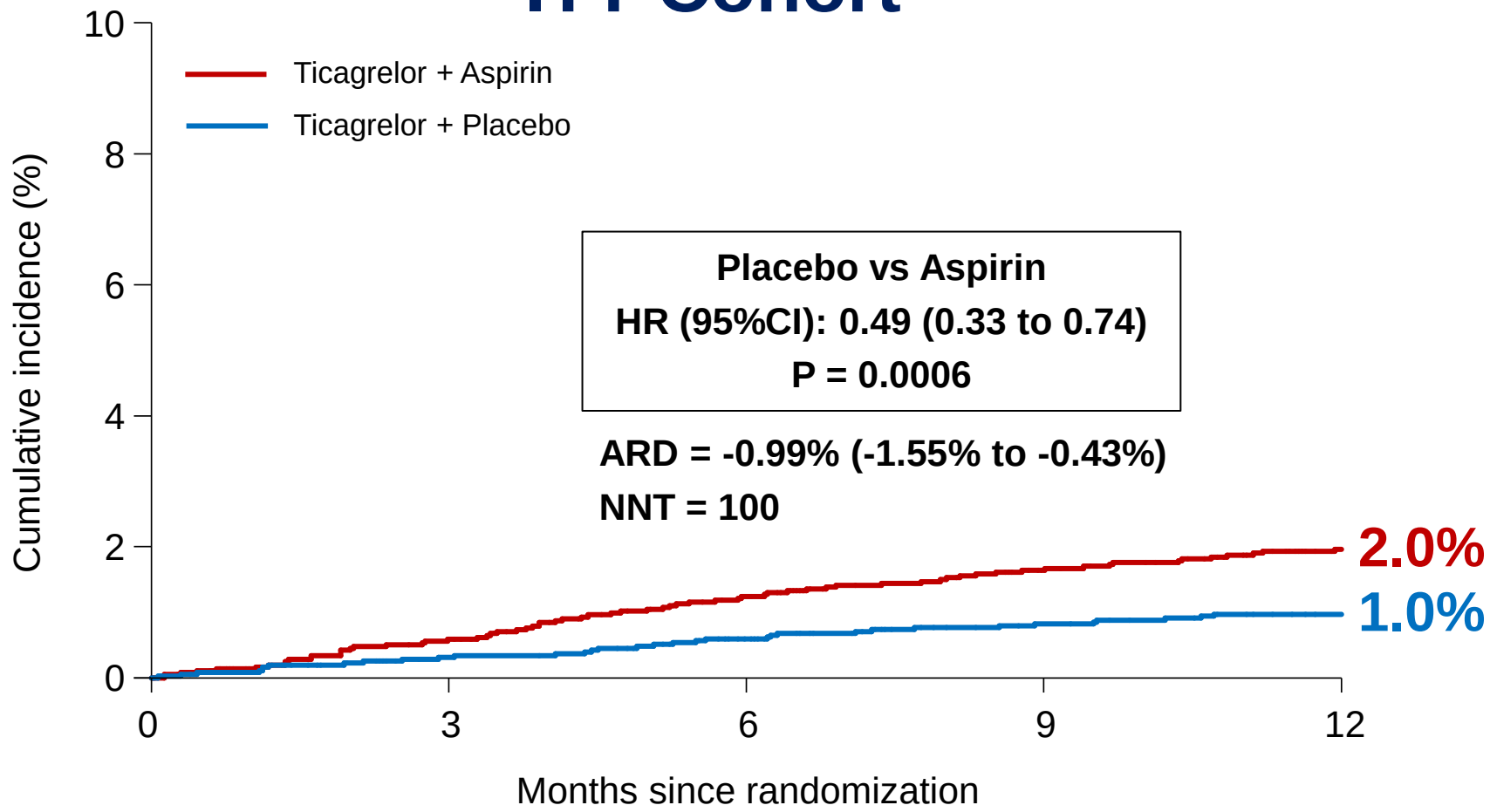
Bonaca MP, Bhatt DL, Steg PG, et al. ESC LBS 2020

TWILIGHT Study Design



BARC 3 or 5 Bleeding

ITT Cohort



No. at risk					
Ticagrelor + Aspirin	3564	3516	3470	3426	3390
Ticagrelor + Placebo	3555	3504	3475	3440	3423

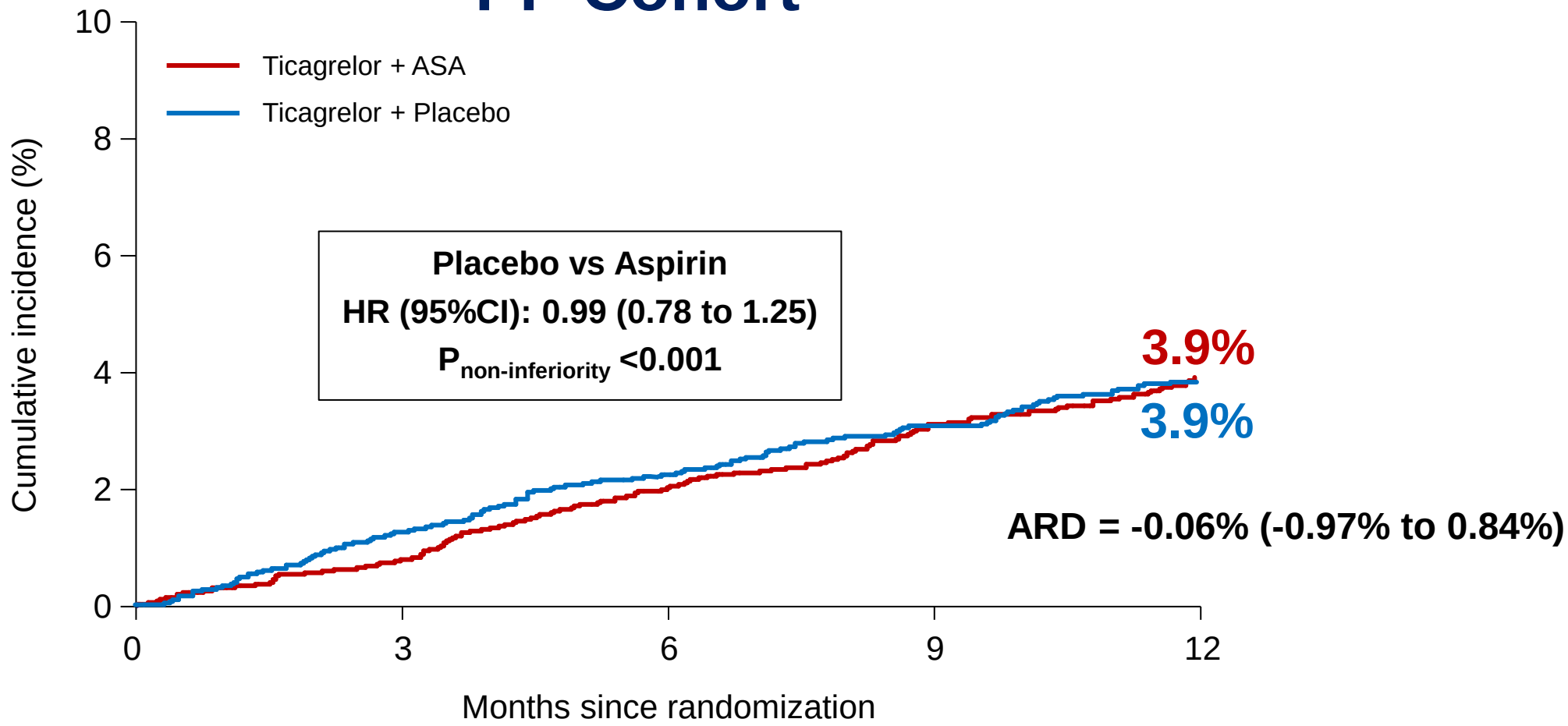
Mount Sinai

twilight

Mehran et al. *NEJM* 2019.

Key Secondary Endpoint: Death, MI or Stroke

PP Cohort



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

Mount Sinai

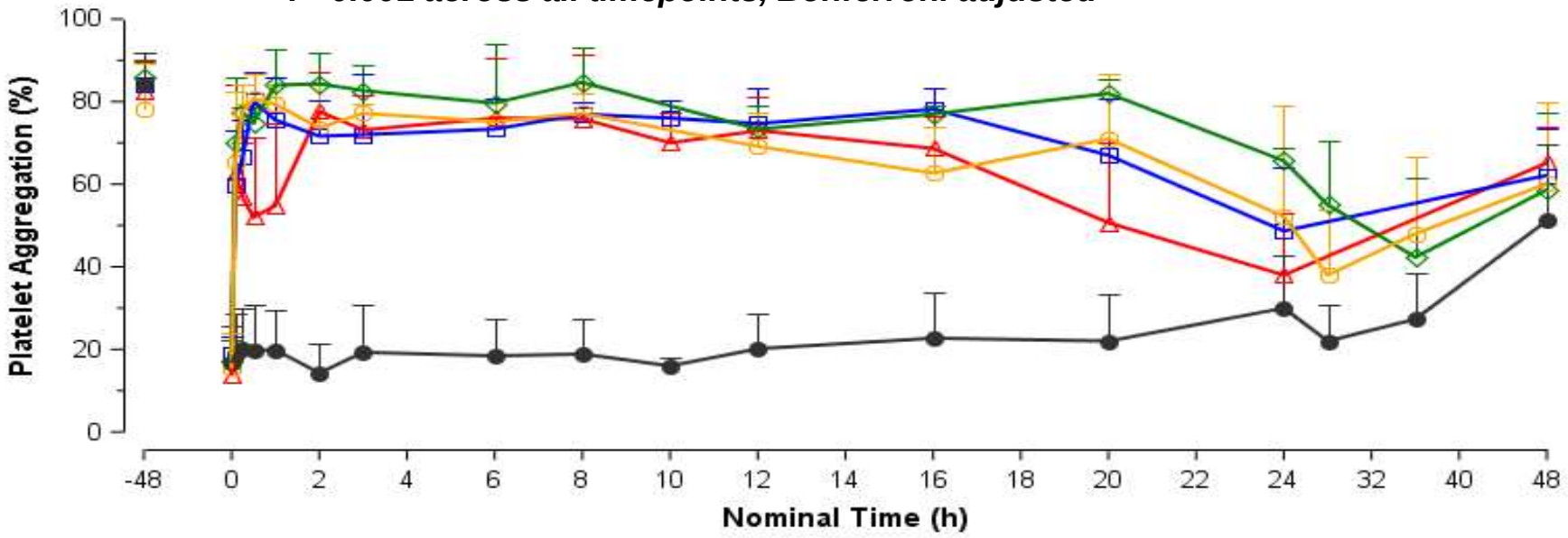
twilight

Mehran et al. *NEJM* 2019.

Onset and Duration of Ticagrelor Reversal - LTA

Volunteers in Cohorts 7-10 were given fixed 18-g doses of PB2452 for 8, 12, and 16 hours in Cohorts 7, 8, and 9/10, respectively

P<0.001 across all timepoints, Bonferroni adjusted

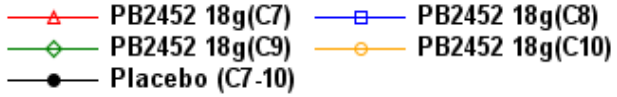


1. **Immediate and sustained ticagrelor reversal with bolus + prolonged infusion of 18 g PB2452.**
2. **Significant reversal was observed 5 minutes after initiation of PB2452 infusion.**
3. **Duration of reversal was infusion-time dependent, lasting 20-24 hours with a 16-hour infusion**.

P values by timepoint for each cohort

Cohort	5min	0.25h	0.5h	1h	2h	3h	6h	8h	10h	12h	16h	20h
7	0.040	0.040	0.131	0.037	0.040	0.019	0.019	0.019	0.152	0.019	0.019	0.224
8	0.019	0.019	0.019	0.019	0.019	0.019	0.019	0.019	0.152	0.019	0.019	0.019
10	0.043	0.020	0.020	0.020	0.020	0.020	0.020	0.020	N/A	0.020	0.020	0.020

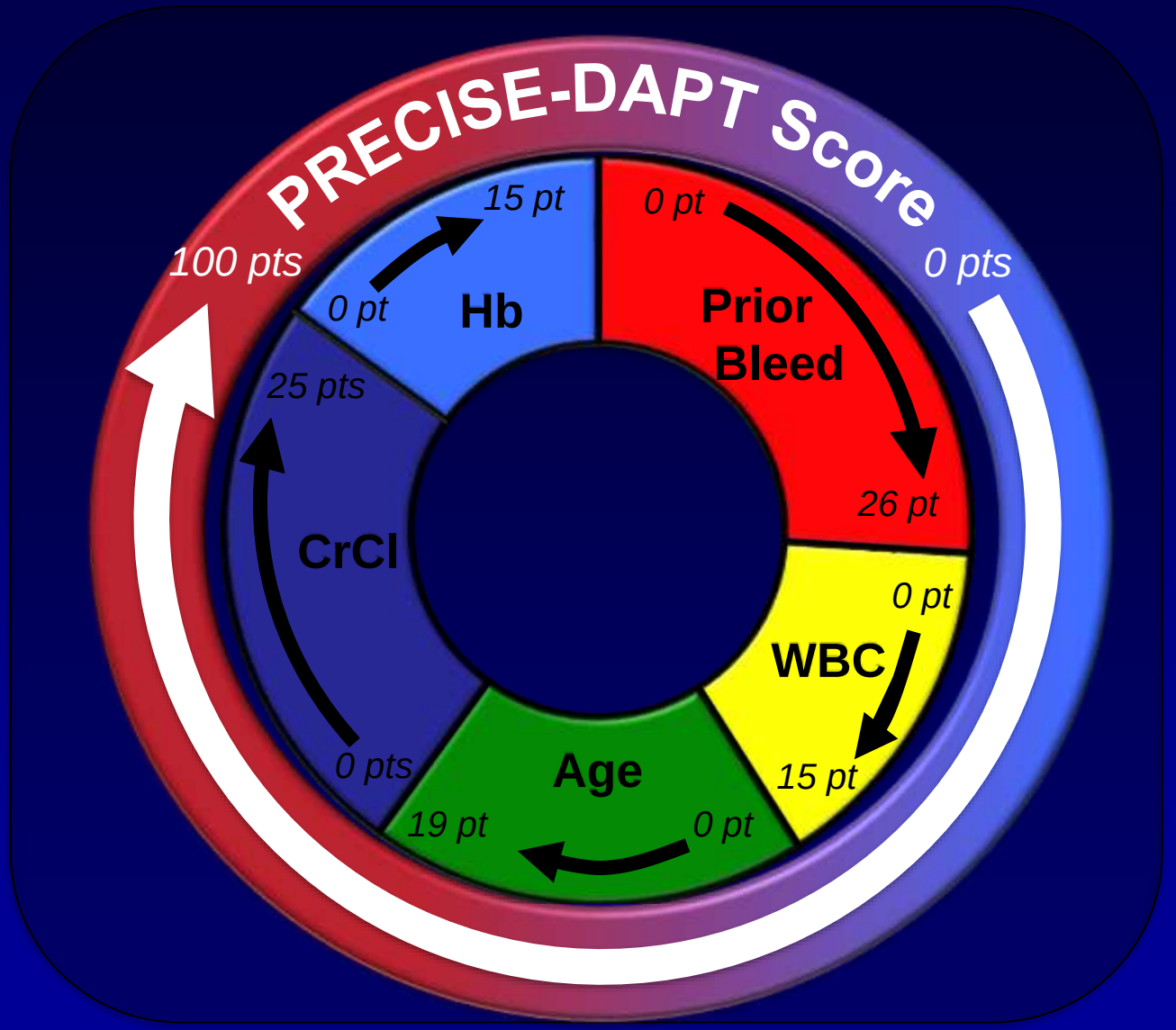
Due to the small sample size for cohort 9 (n=3), statistical testing was not performed. For Cohorts 9 and 10, no 10-hour timepoint was collected. P-values for time point 24 hours or above are not significant.

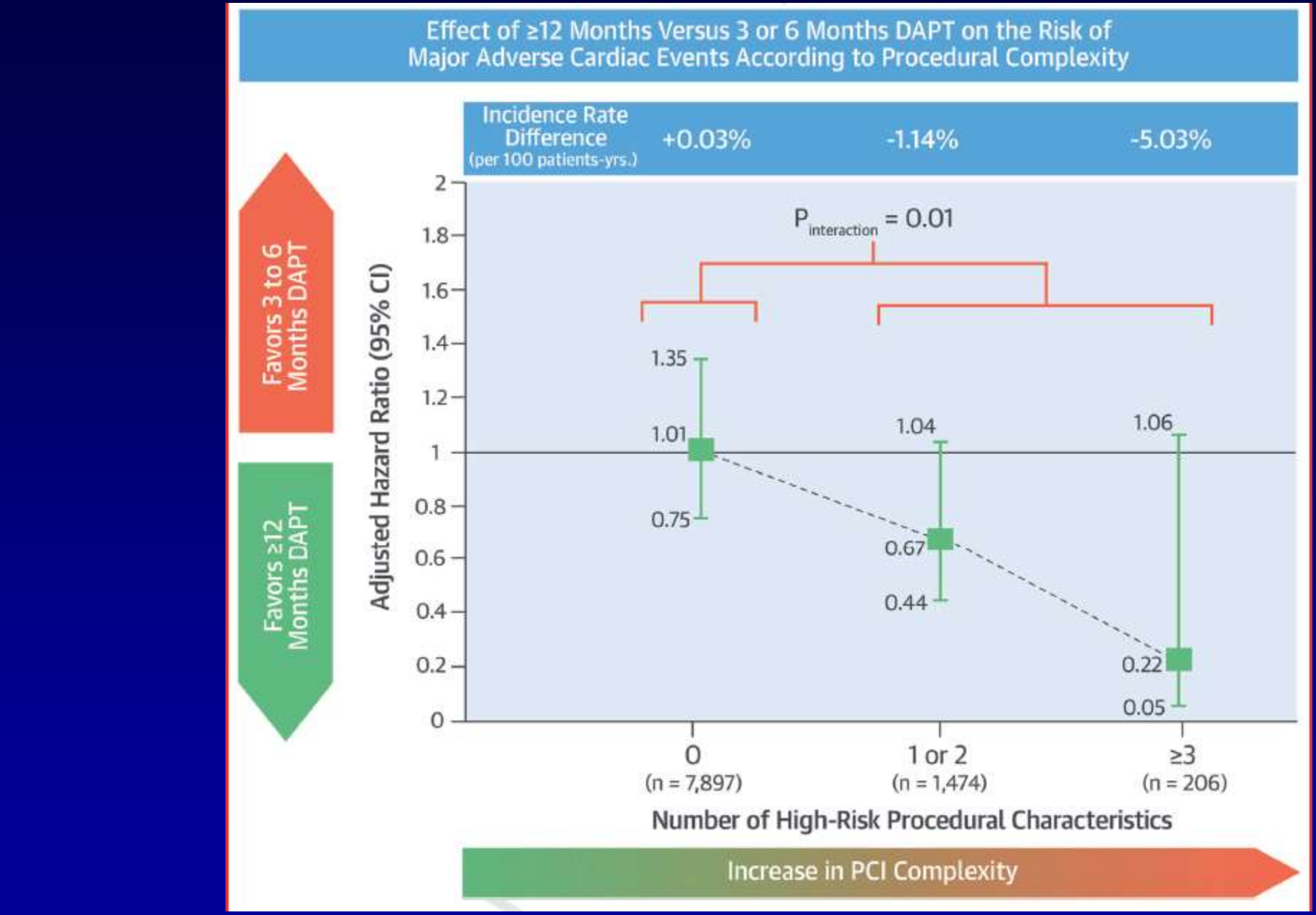


LTA= light transmittance aggregometry; ADP is the agonist

Bhatt DL, Pollack CV, Weitz JI, et al. *N Engl J Med*. 2019.

PRECISE DAPT Score





Giustino G, Chieffo A, Palmerini T, et al... Colombo A. JACC. 2016.

Optimal Duration of DAPT?

	≤12 months DAPT	≥12 months DAPT
Patient-related factors 	Patients with stable CAD Patients with a history of bleeding Patients with high risk of bleeding	Patients with ACS Patients with diabetes mellitus Patients with renal dysfunction Patients with CHF Patients with previous ST Patients with PAD
Anatomy-related factors 	Short lesion Single-vessel disease	Long lesion Small vessel Bifurcation lesion Complex anatomy Left-main coronary artery
Stent-related factors 	Second-generation DES	First-generation DES Long stent Multiple stents

Eisen A, Bhatt DL. Nature Reviews Cardiology 2015.

Breaking Update: US FDA Approval

Current FDA Approvals

Agent	ACS + PCI	ACS (Medical)	Prior MI	CAD (No Event)
Clopidogrel	✓	✓	✓	
Ticagrelor	✓	✓	✓	
Prasugrel	✓			

Steg PG, Bhatt DL et al. *N Engl J Med* 2019. Bhatt DL, Steg PG, et al. *Lancet* 2019.

Breaking Update: US FDA Approval

Ticagrelor approved by FDA June 1, 2020 “to reduce the risk of a first MI or stroke in patients with coronary artery disease at high risk for such events”

Agent	ACS + PCI	ACS (Medical)	Prior MI	CAD (No Event)
Clopidogrel	✓	✓	✓	
Ticagrelor	✓	✓	✓	✓
Prasugrel	✓			

Steg PG, Bhatt DL et al. *N Engl J Med* 2019. Bhatt DL, Steg PG, et al. *Lancet* 2019.

ORIGINAL RESEARCH ARTICLE

Dual Antiplatelet Therapy After Percutaneous Coronary Intervention and Drug-Eluting Stents

A Systematic Review and Network Meta-Analysis

BACKGROUND: The optimal duration of dual antiplatelet therapy (DAPT) after percutaneous coronary intervention with drug-eluting stents remains uncertain. We compared short-term (<6-month) DAPT followed by aspirin or P2Y12 inhibitor monotherapy; midterm (6-month) DAPT; 12-month DAPT; and extended-term (>12-month) DAPT after percutaneous coronary intervention with drug-eluting stents.

METHODS: Twenty-four randomized, controlled trials were selected using Medline, Embase, Cochrane library, and online databases through September 2019. The coprimary end points were myocardial infarction and major bleeding, which constituted the net clinical benefit. A frequentist network meta-analysis was conducted with a random-effects model.

RESULTS: In 79 073 patients, at a median follow-up of 18 months, extended-term DAPT was associated with a reduced risk of myocardial infarction in comparison with 12-month DAPT (absolute risk difference, –3.8 incident cases per 1000 person-years; relative risk, 0.68 [95% CI, 0.54–0.87]), midterm DAPT (absolute risk difference, –4.6 incident cases per 1000 person-years; relative risk, 0.61 [0.45–0.83]), and short-term DAPT followed by

Safi U. Khan, MD
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Muhammad U. Khan, MD
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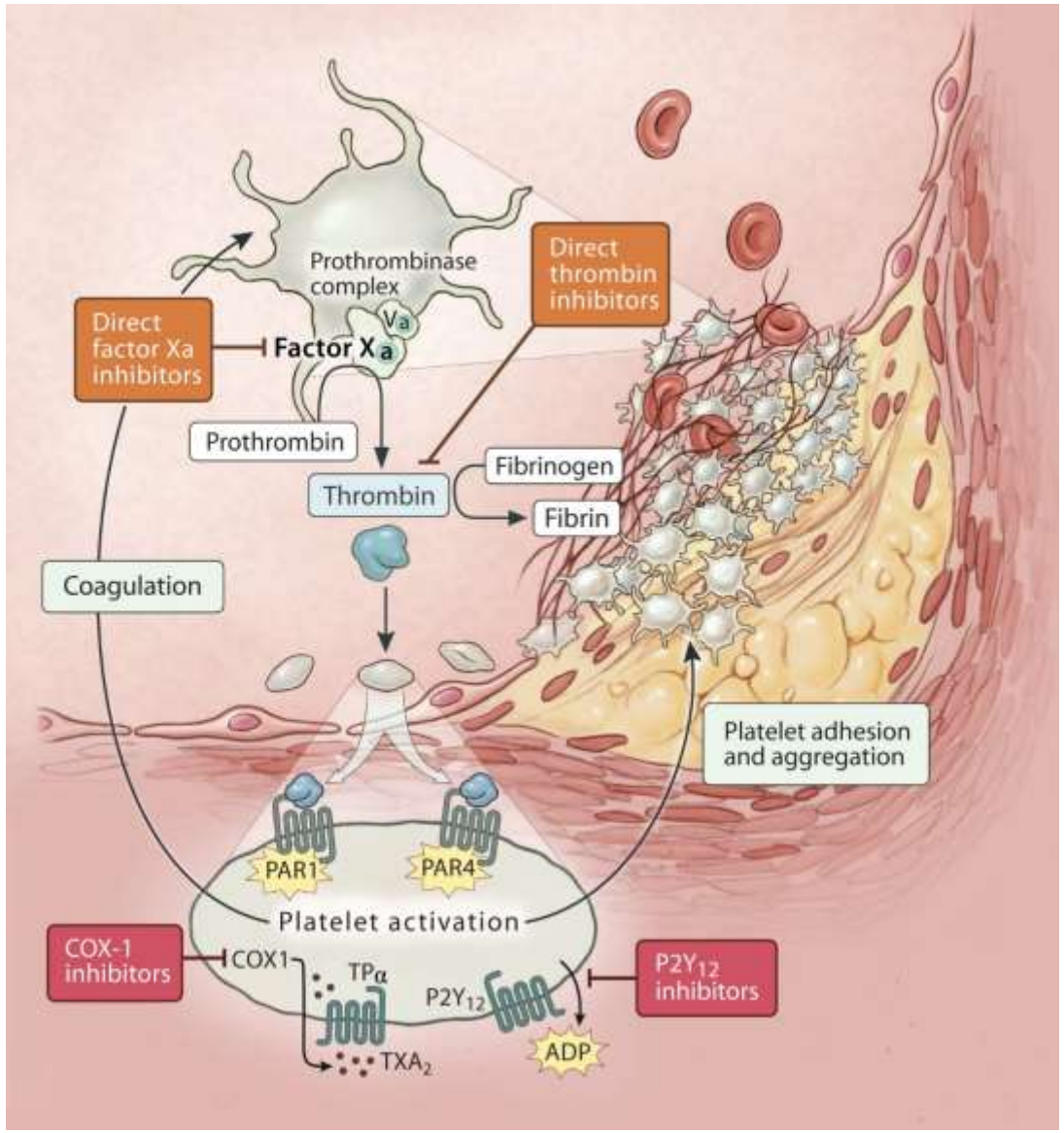
Gregg W. Stone, MD
Ankur Kalra, MD*
Deepak L. Bhatt, MD, MPH*

Dual Pathway Inhibition



Verma S, Eikelboom JW, Al-Omran M, Choi R, Heffernan M, Teoh H, Bhatt DL. *Med* 2020. https://doi.org/10.1016/j.medj.2020.05.003

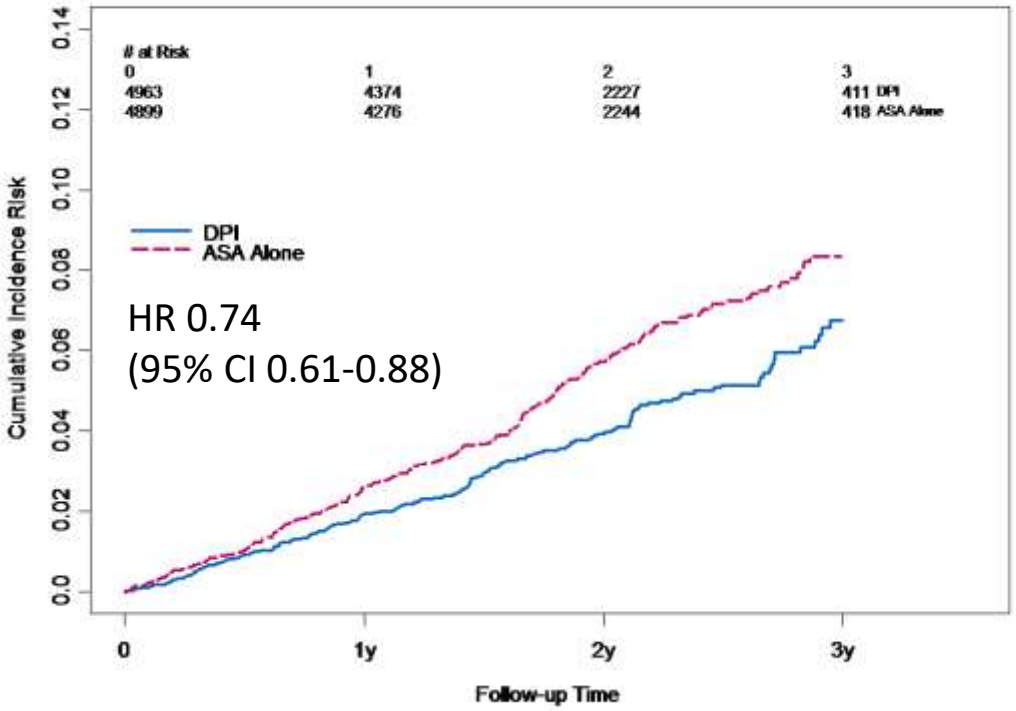
Primary Efficacy Endpoint: CV death, MI or stroke (ITT)

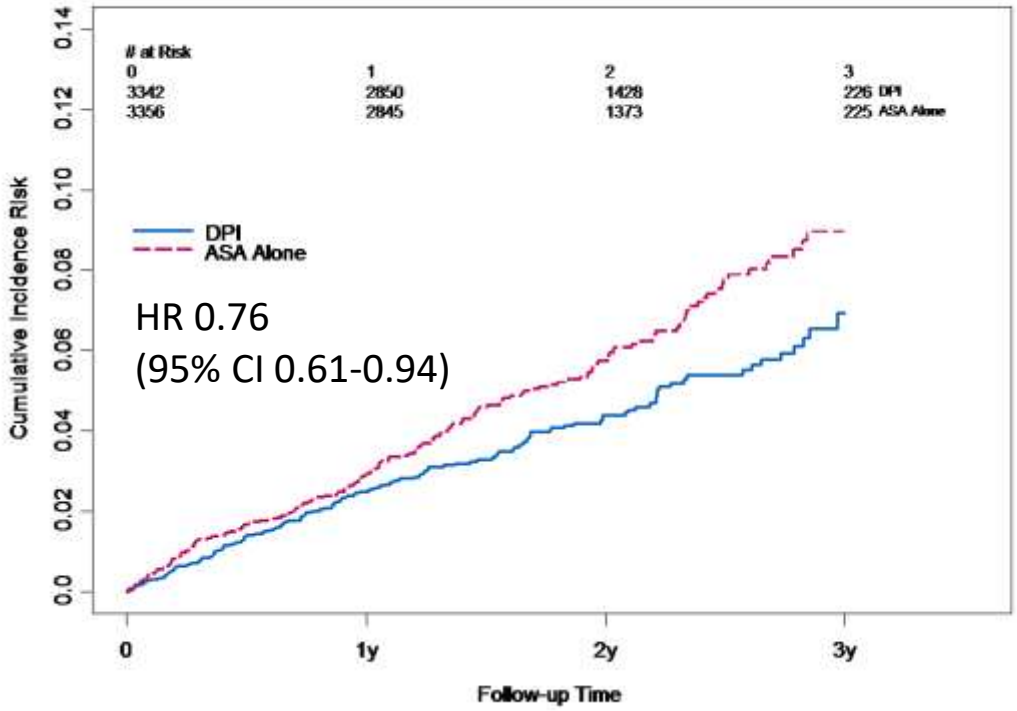
COMPASS PCI

Prior PCI

Interaction p=0.85

No Prior PCI





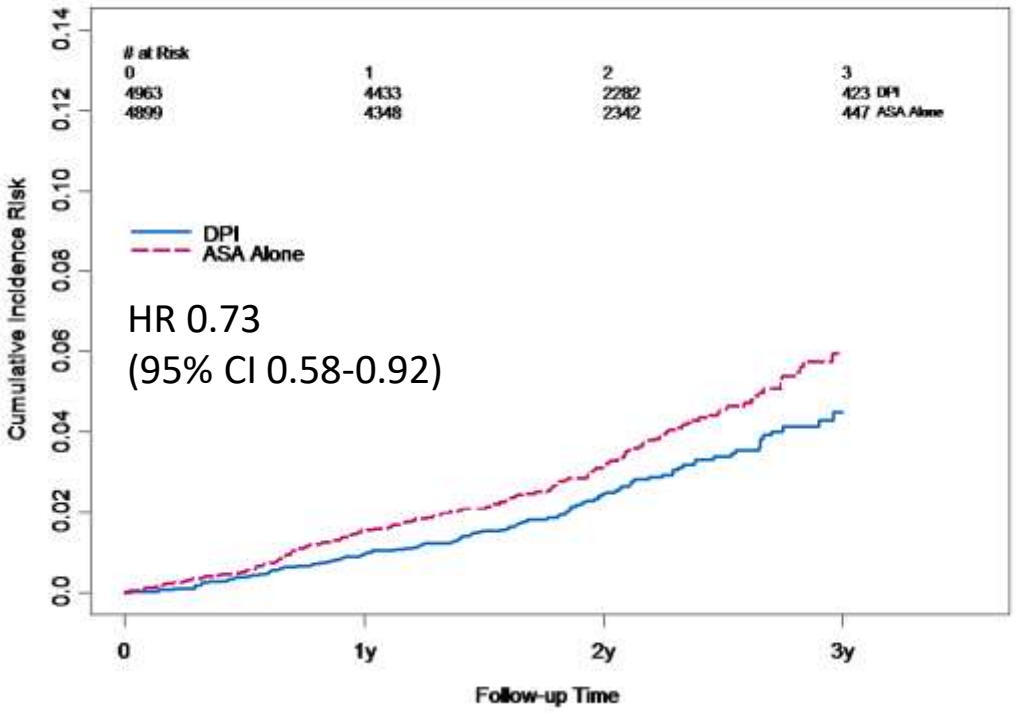
Bainey KR, Welsh RC, Connolly SJ, et al… Bhatt DL. *Circulation*. 2020.

Secondary Efficacy Endpoint: All-Cause Death (ITT)

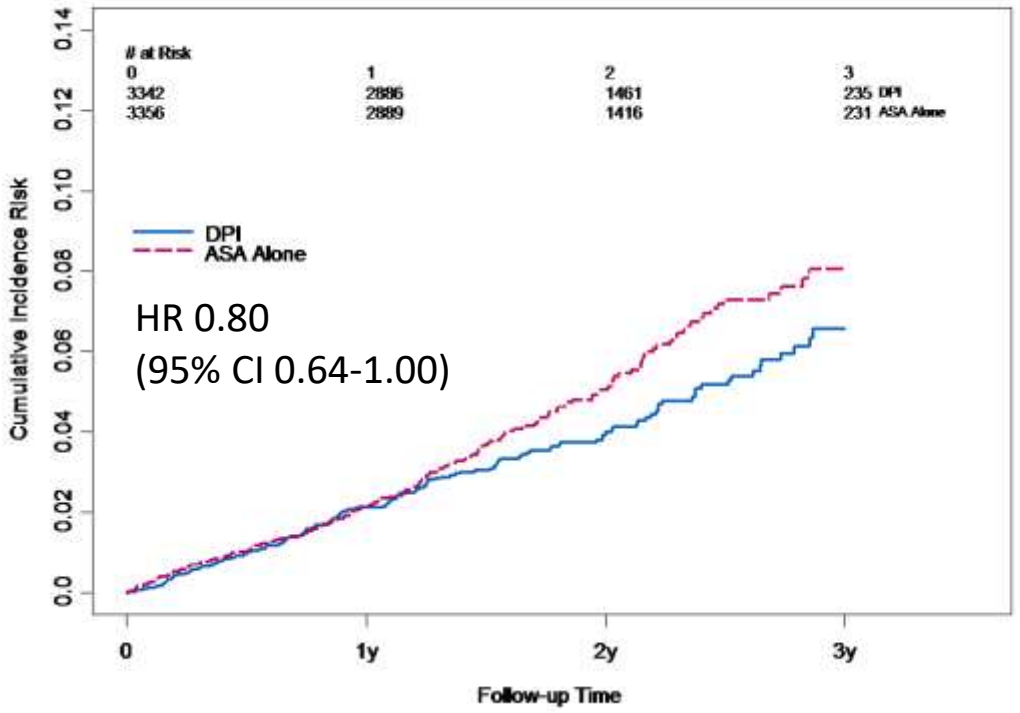
COMPASS PCI

Interaction p=0.59

Prior PCI



No Prior PCI



Bainey KR, Welsh RC, Connolly SJ, et al… Bhatt DL. *Circulation*. 2020.

Conclusions

- In ACS, at least 12 months of DAPT if no bleeding
- If high bleeding risk post PCI, can abbreviate DAPT at 3 months
  - At that point ticagrelor (preferred) or clopidogrel monotherapy is an option in select patients
- If post-MI, diabetes, complex stenting/disease, consider longer
  - Ticagrelor US label updated based on THEMIS, THEMIS PCI for CAD

BRIGHAM AND WOMEN'S HOSPITAL

Heart & Vascular Center

Thank You!

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