Optimal medical therapy in patients with stable CAD

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Disclosures

Company name	Relationship
• AstraZeneca	Research grant, honoraria, consultant
• Avacta	Consultant
• Bayer	Consultant
• BMS/Pfizer	Consultant
• PlaqueTec	Research grant, consultant
• Aspen	Consultant
• ThermoFisher Scientific	Consultant
• The Medicines Company	Consultant

Preventive strategies in stable CAD

Antithrombotic
Aspirin, $P2Y_{12}$i, OACs

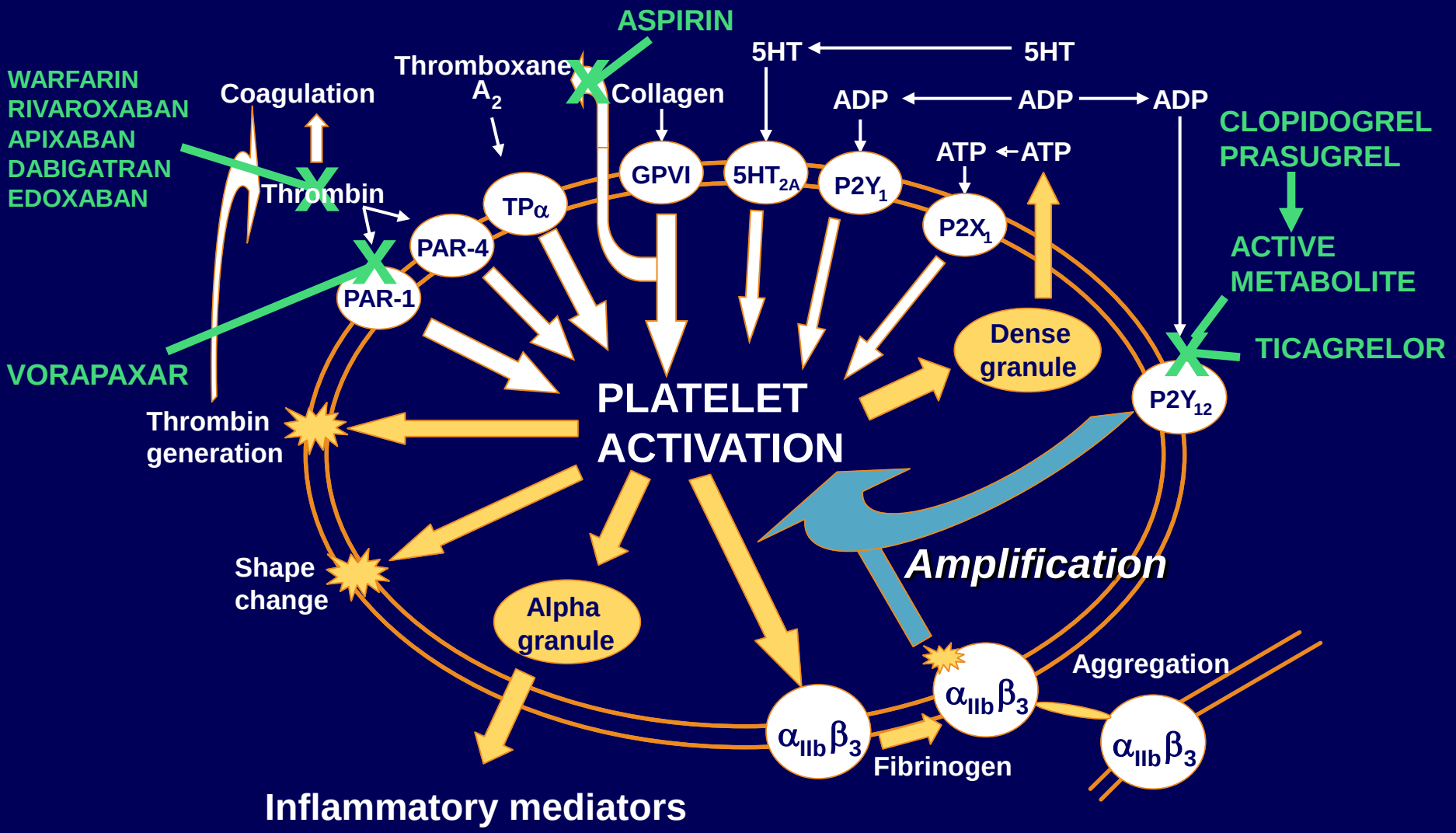
Lipid lowering
Statins, PCSK9i, ezetimibe

Antihypertensive
ACEi/ARBs, amlodipine etc.

Lifestyle modification
Smoking cessation, diet & weight optimisation, exercise

Revascularisation
PCI, CABG

Mechanisms of oral platelet inhibitors



ADP, adenosine diphosphate; ATP, adenosine triphosphate; GP = glycoprotein; PAR = protease-activated receptor; TP = thromboxane A2 / prostaglandin H2
Storey RF. Curr Pharm Des 2006

Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients

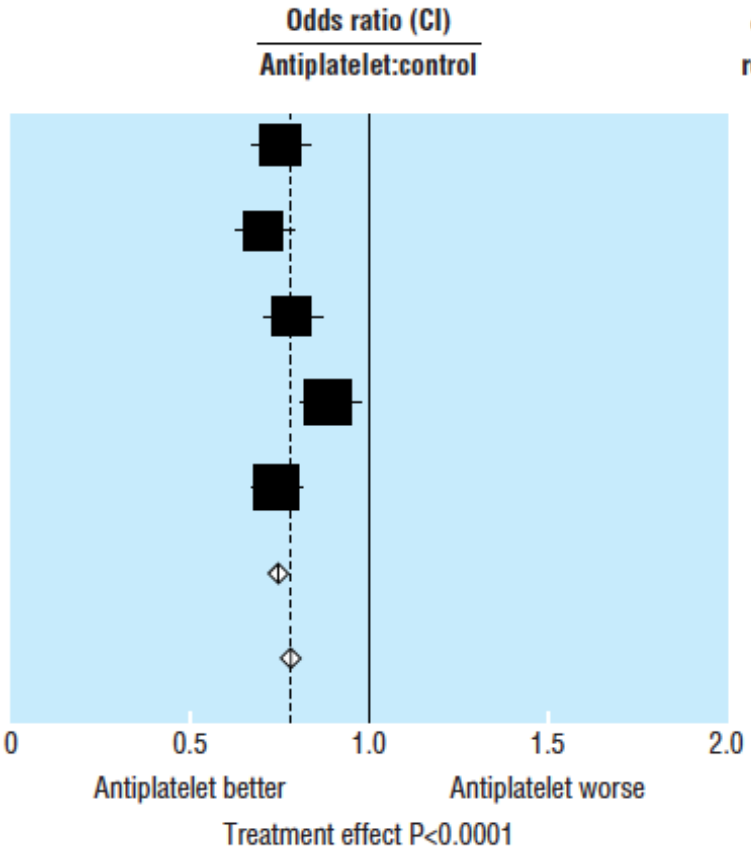
Antithrombotic Trialists' Collaboration

Category of trial	No of trials with data	No (%) of vascular events: Allocated antiplatelet	No (%) of vascular events: Adjusted control	Observed-expected	Variance	% Odds reduction (SE)
Previous myocardial infarction	12	1345/9984 (13.5)	1708/10 022 (17.0)	-159.8	567.6	25 (4)
Acute myocardial infarction	15	1007/9658 (10.4)	1370/9644 (14.2)	-181.5	519.2	30 (4)
Previous stroke/transient ischaemic attack	21	2045/11 493 (17.8)	2464/11 527 (21.4)	-152.1	625.8	22 (4)
Acute stroke	7	1670/20 418 (8.2)	1858/20 403 (9.1)	-94.6	795.3	11 (3)
Other high risk	140	1638/20 359 (8.0)	2102/20 543 (10.2)	-222.3	737.0	26 (3)
Subtotal: all except acute stroke	188	6035/51 494 (11.7)	7644/51 736 (14.8)	-715.7	2449.6	25 (2)
All trials	**195**	**7705/71 912 (10.7)**	**9502/72 139 (13.2)**	**-810.3**	**3244.9**	**22 (2)**

Heterogeneity of odds reductions between:

5 categories of trial: χ^2=21.4, df=4; P=0.0003

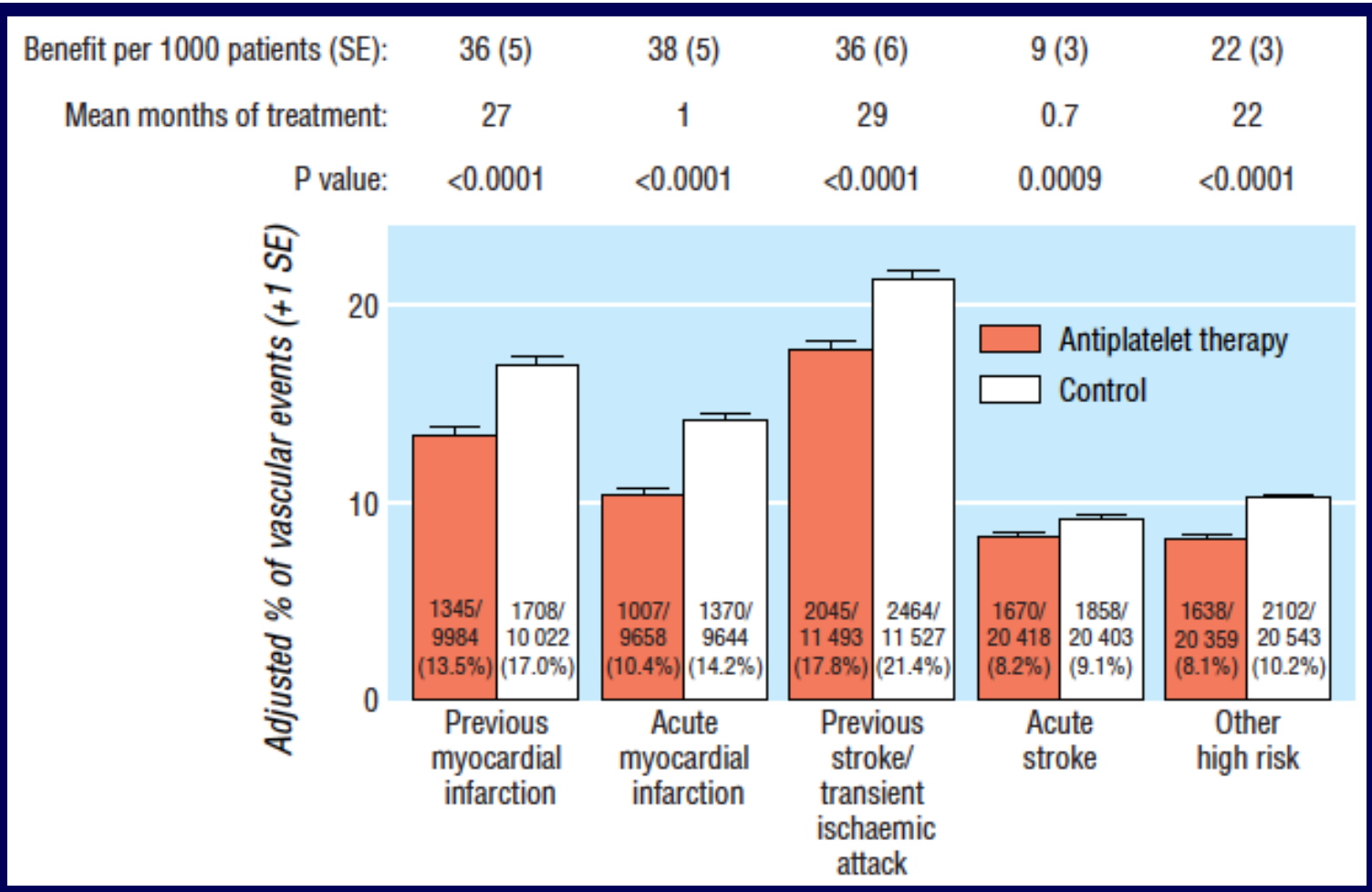
Acute stroke *v* other: χ^2=18.0, df=1; P=0.00002



Antithrombotic trialists' collaboration. BMJ 2002

Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients

Antithrombotic Trialists' Collaboration



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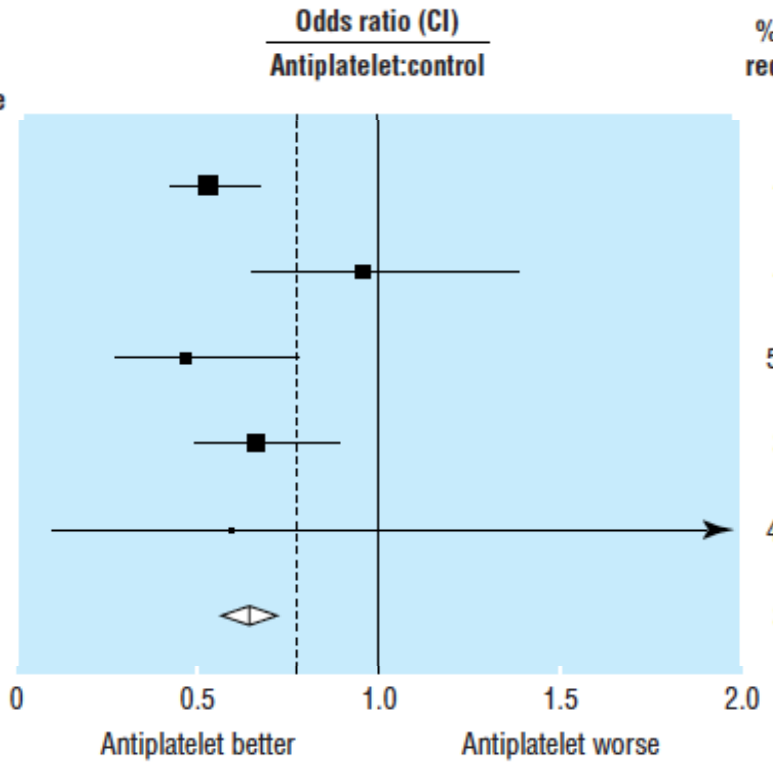
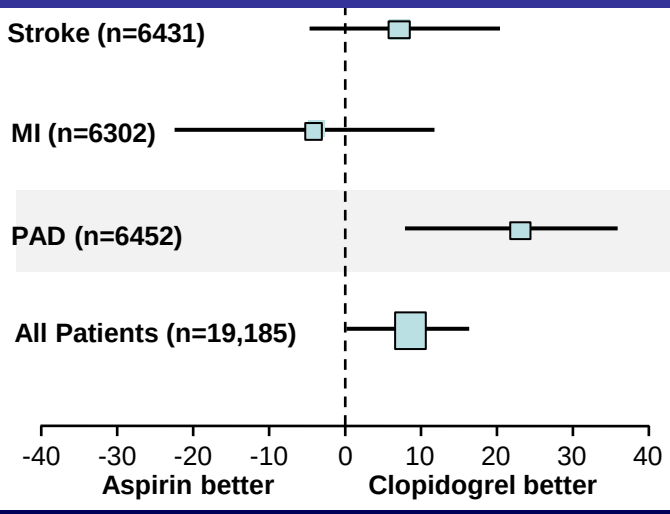
Coronary artery disease:						
Unstable angina	12	199/2497 (8.0)	336/2534 (13.3)	-64.8	104.6	46 (7)
Coronary artery bypass	25	149/3105 (4.8)	146/3126 (4.7)	-1.9	47.4	4 (14)
Coronary angioplasty	9	43/1592 (2.7)	89/1620 (5.5)	-18.7	24.6	53 (14)
Stable angina/coronary artery disease	7	144/1448 (9.9)	208/1472 (14.1)	-30.7	76.3	33 (9)
Heart failure	2	4/66 (6.1)	7/68 (10.3)	-1.0	1.9	41 (56)
Subtotal	55	539/8708 (6.2)	786/8820 (8.9)	-117.1	254.8	37 (5)



Antithrombotic trialists' collaboration. BMJ 2002

CAPRIE: Clopidogrel Monotherapy in Recent Ischaemic Stroke, MI or Symptomatic PAD

CV Risk in Overall Cohort and Subgroups



	Average Event Rate/Year*		RRR (95% CI)	p-value
	Clopidogrel	Aspirin		
Stroke (n=6431)	7.15%	7.71%	7.3% (-5.7 to 18.7)	0.26
MI (n=6302)	5.03%	4.84%	-3.7% (-22.1 to 12.0)	0.66
PAD (n=6452)	3.71%	4.86%	23.8% (8.9 to 36.2)	0.0028
All Patients (n=19,185)	5.32%	5.83%	8.7% (0.3 to 16.5)	0.043

Randomized, multinational, double-blind, 1-3 year trial of clopidogrel 75 mg/day versus aspirin 325 mg/day in 19,185 patients with recent ischemic stroke, recent MI, or symptomatic PAD (mean follow up 1.9 years). Subgroup analysis included 6452 patients with PAD

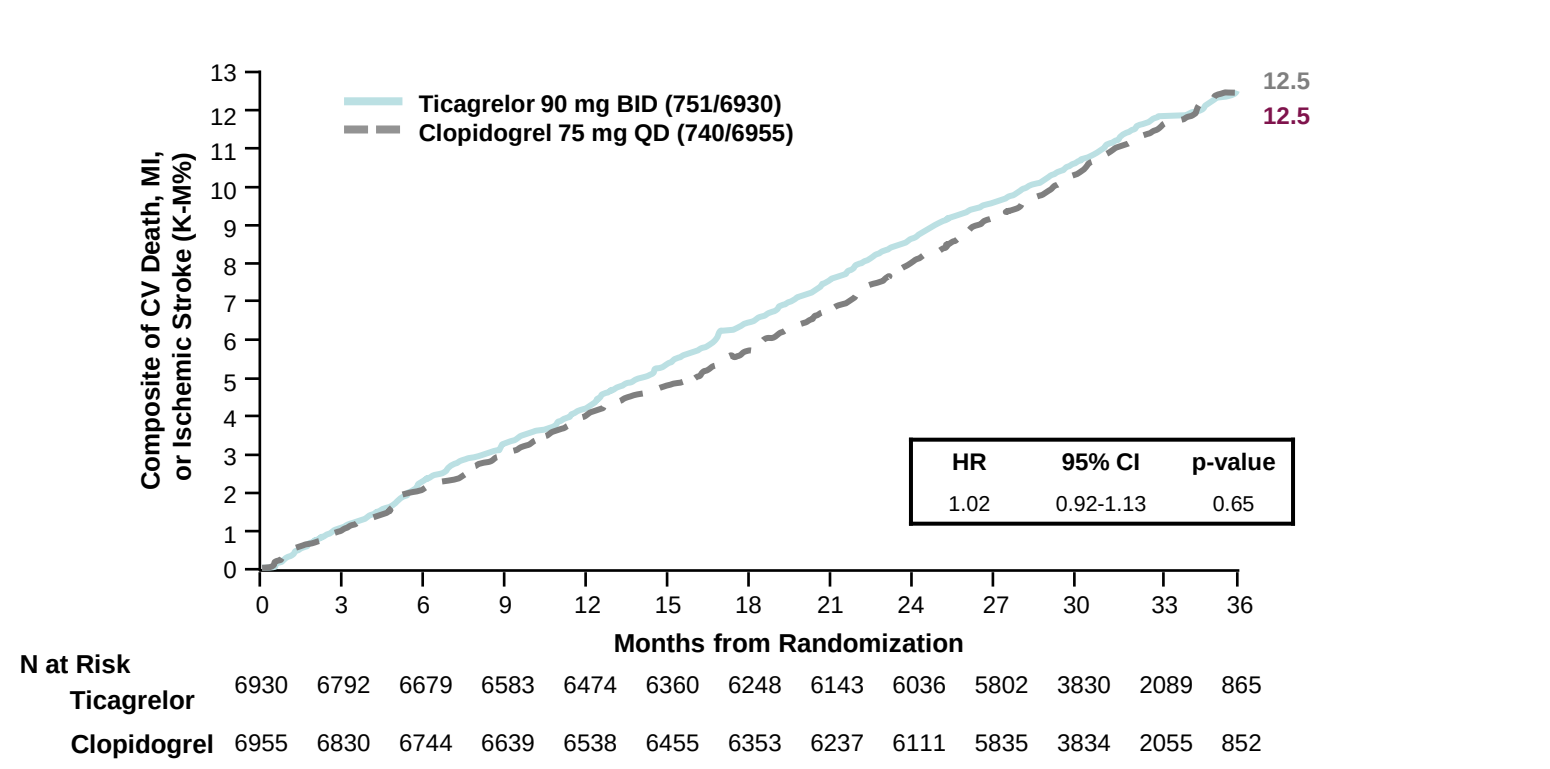
*Cumulative risk of CV death, MI, or ischemic stroke.

CAPRIE = Clopidogrel versus Aspirin in Patients at Risk of Ischaemic Events; CI = confidence interval; CV = cardiovascular; MI = myocardial infarction; PAD = peripheral artery disease; RRR = relative risk reduction.

CAPRIE steering committee. *Lancet.* 1996;348:1329-1339.

EUCLID: Primary Efficacy Endpoint in patients with PAD

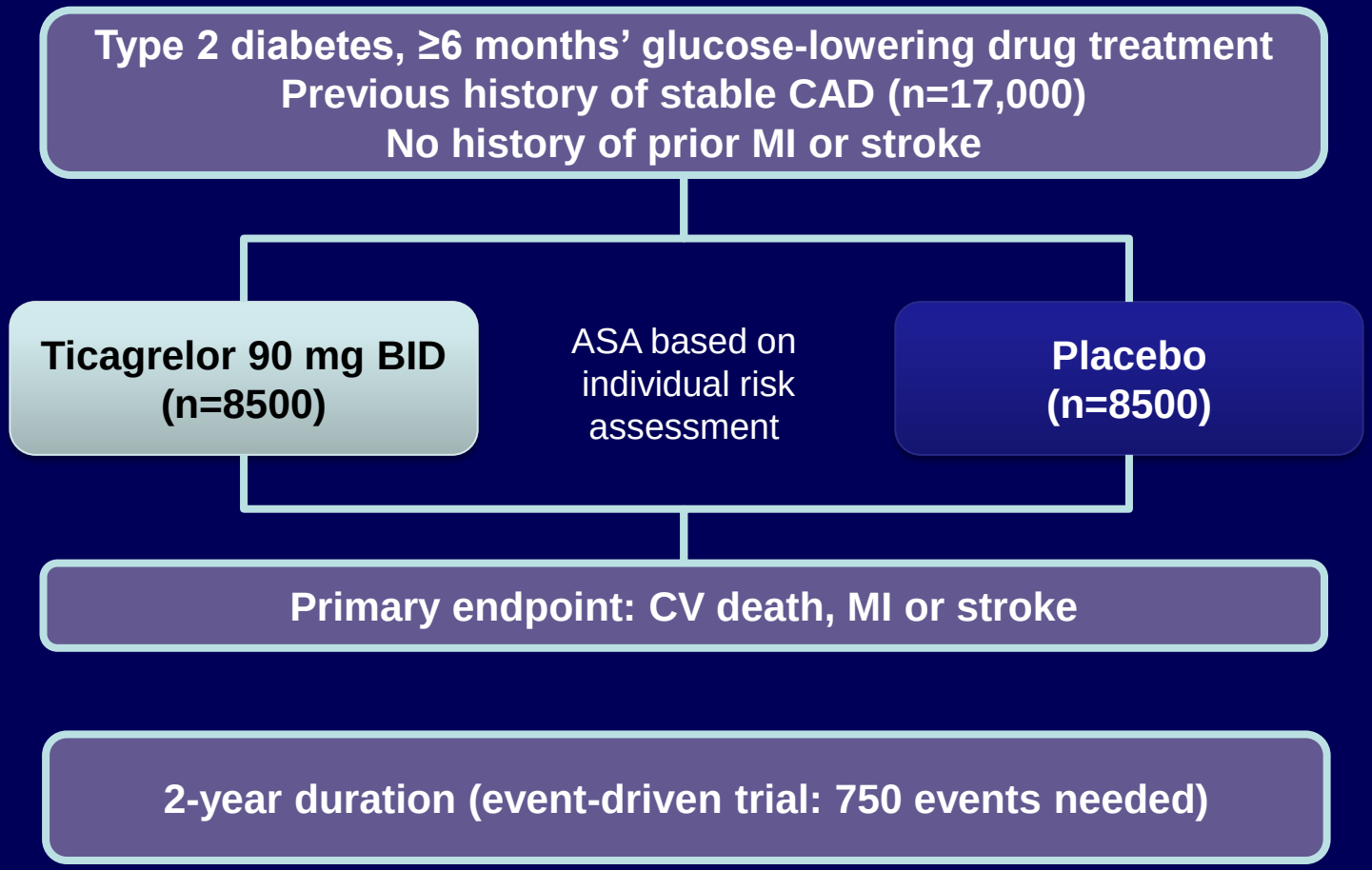
Composite of CV Death, MI, or Ischemic Stroke



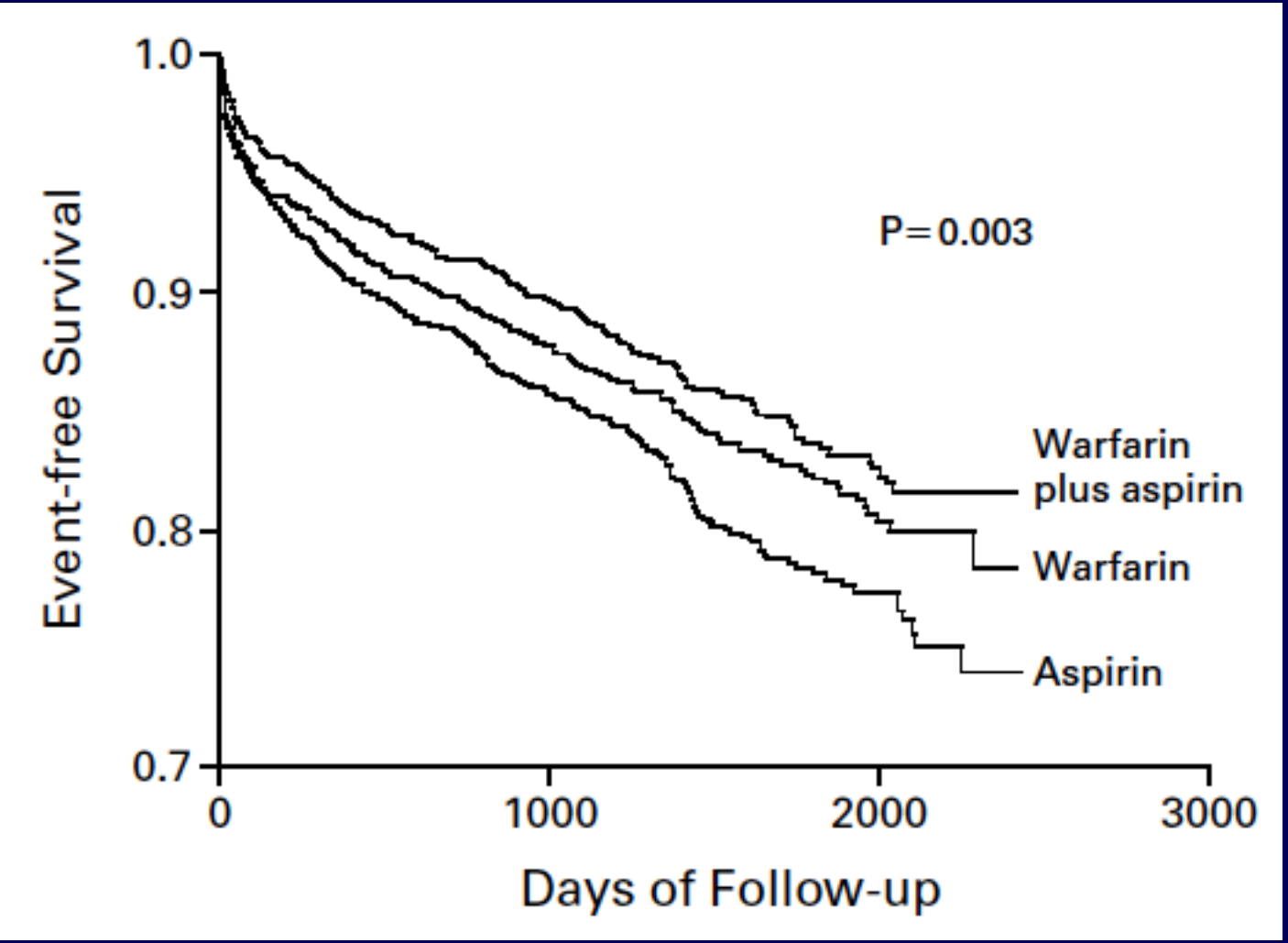
BID = twice daily; CI = confidence interval; CV = cardiovascular; HR = hazard ratio; K-M = Kaplan-Meier; MI = myocardial infarction; QD = once daily

Hiatt WR et al. Article online ahead of print. *N Engl J Med.* 2016

THEMIS study design

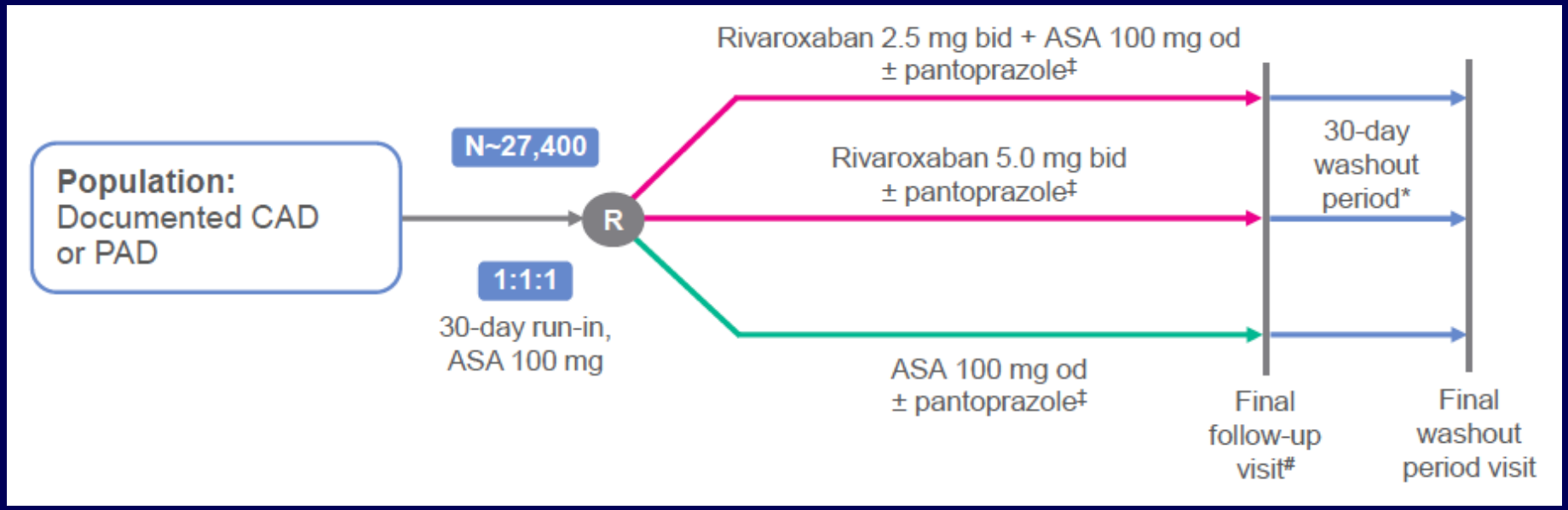


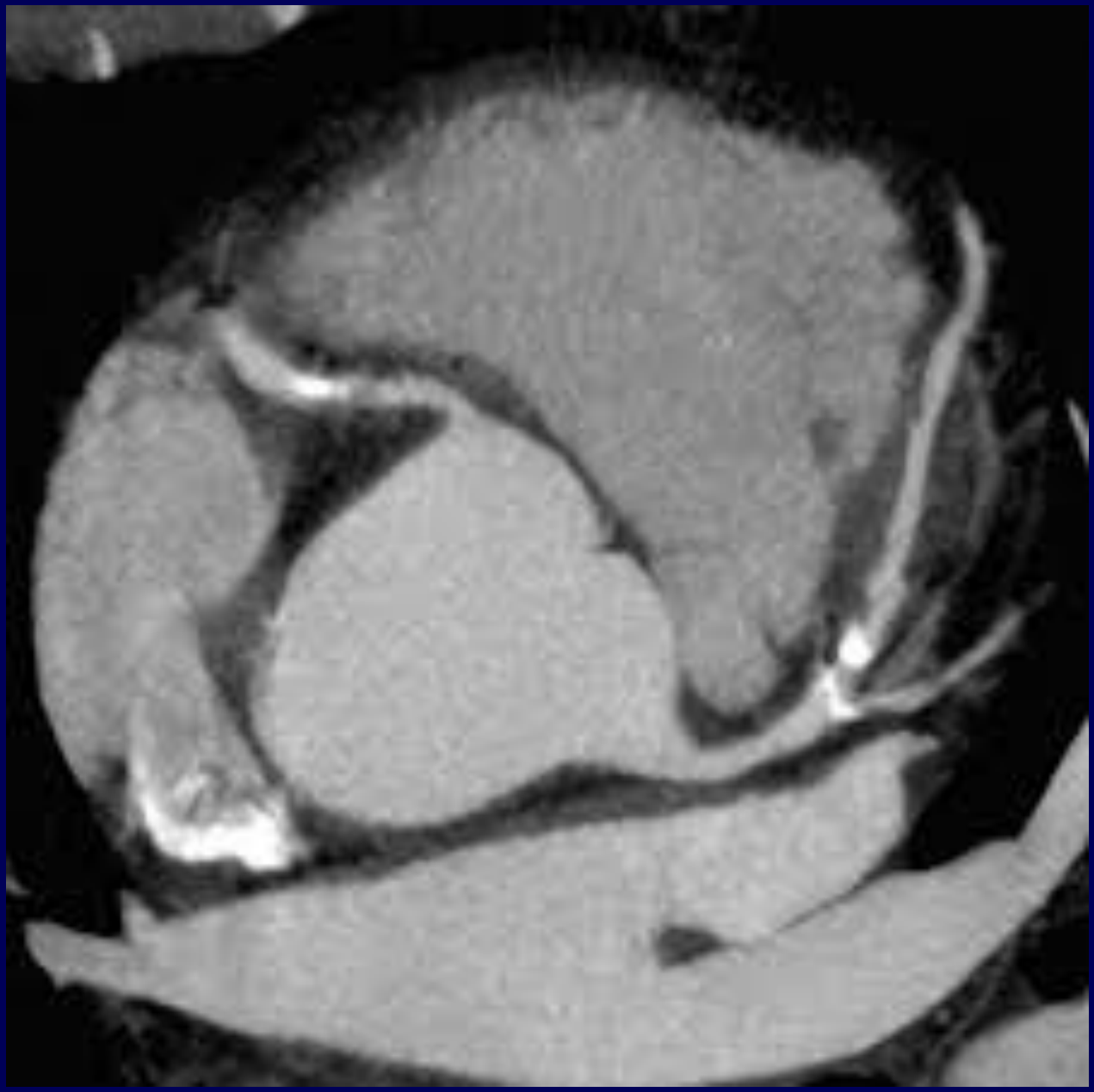
WARIS II: warfarin, aspirin or both following myocardial infarction



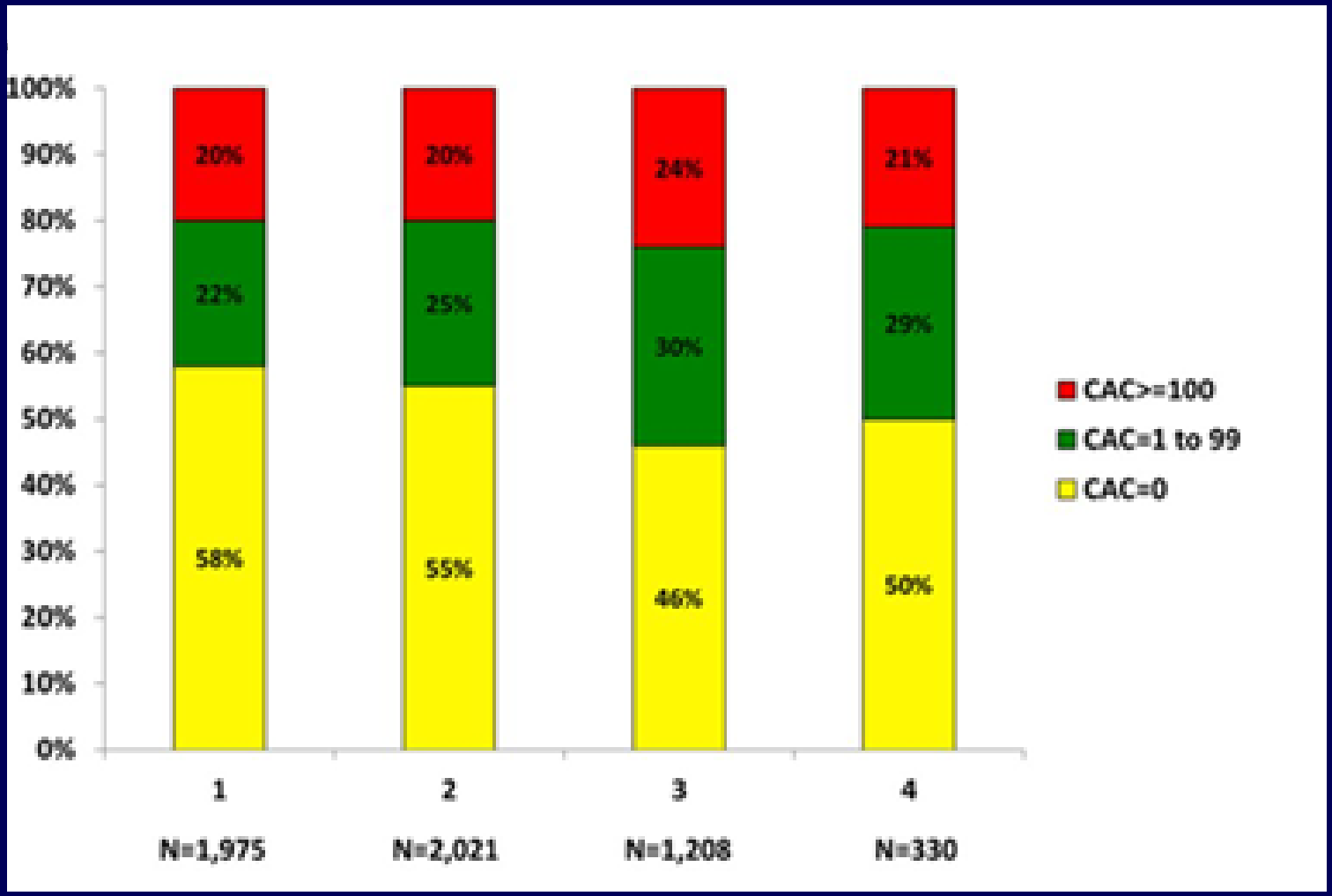
Hurlen M et al. *N Engl J Med.* 2002

COMPASS: randomised controlled trial of rivaroxaban for the prevention of major cardiovascular events in patients with coronary or peripheral artery disease



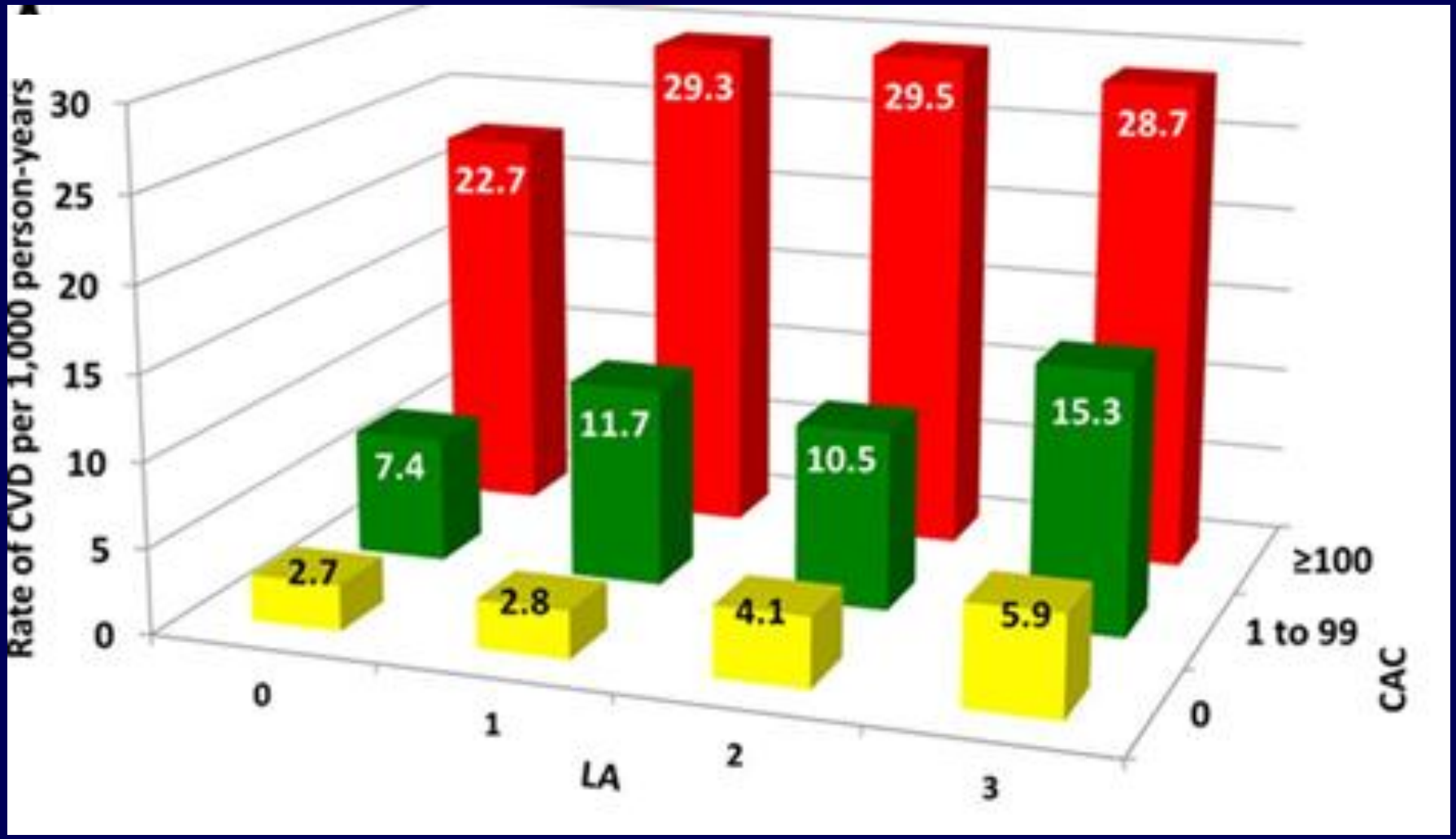


Multi-Ethnic Study of Atherosclerosis Distribution of coronary artery calcium score by number of lipid abnormalities



Martin S S et al. Circulation. 2014;129:77-86

CV events per 1000 person-years by strata of coronary artery calcium score (CAC) and number of lipid abnormalities (LA)



Martin S S et al. Circulation. 2014;129:77-86

Role of CT coronary artery calcium score in predicting benefit from aspirin

Adjusted* Hazard Ratios (95% CI) by CAC Burden vs CAC=0 in Nondiabetic, Nonaspirin MESA Cohort

CAC Score Range	Population (%)	CHD HR (95% CI)	CVD HR (95% CI)
0	55.8	1.00	1.00
1–99	25.8	2.09 (1.18–3.70)	1.88 (1.21–2.92)
≥ 100	18.3	4.19 (2.36–7.43)	2.85 (1.81–4.50)

*Adjusted for age, sex, race, MESA site, smoking status, cigarette pack-years, body-mass index, LDL cholesterol, HDL cholesterol, dyslipidemia medication use, hypertension, antihypertensive medication use, MI family history, education level, and Framingham risk score

"For the primary prevention of CHD, Multi-Ethnic Study of Atherosclerosis participants with CAC≥100 had favorable risk/benefit estimations for aspirin use while participants with zero CAC were estimated to receive net harm from aspirin"

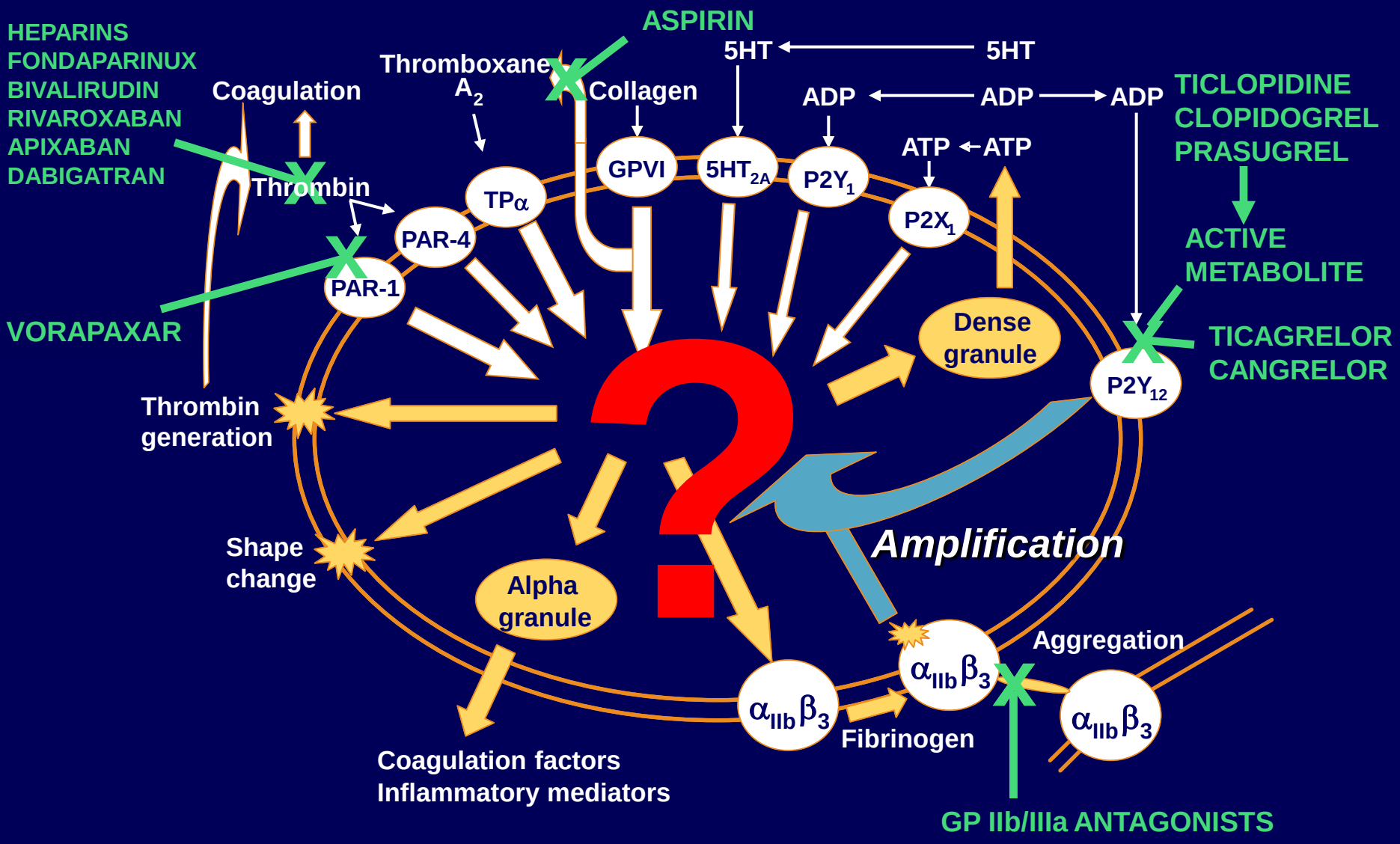
Miedema MD et al. Circ Cardiovasc Qual Outcomes 2014

Medscape. Stiles S. http://www.medscape.com/viewarticle/824686

Conclusions

- Aspirin remains indicated in stable CAD
- Clopidogrel may be considered as an alternative to aspirin, including in those with prior history of PAD or stroke
- Combination of aspirin with another antithrombotic is likely to become an option in stable CAD patients at higher risk of atherothrombotic events e.g. diabetes, coexistent PAD, renal failure, severe multivessel CAD
- CTCA may guide indication for antithrombotic therapy as well as other preventive medication (lipid-lowering, BP-lowering)

Discussion



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Storey RF. *Curr Pharm Des.* 2006.