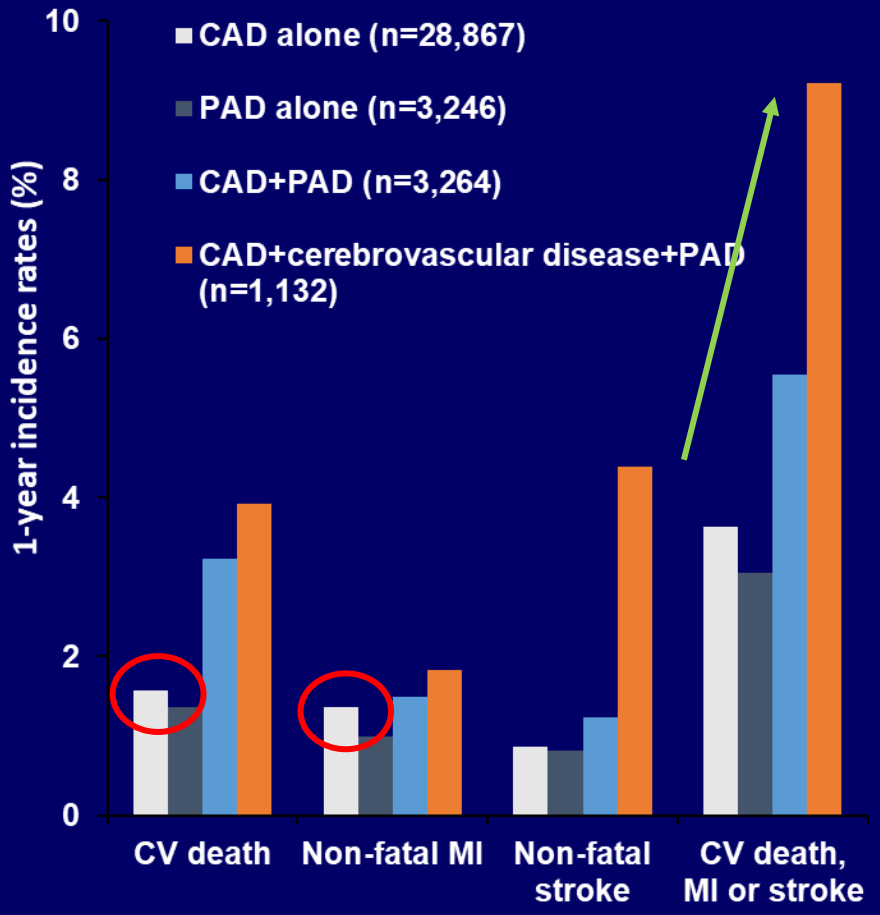
SABATO 9 OTTOBRE

Prevenzione degli eventi ischemici nei soggetti con arteriopatia polidistrettuale

Giuseppe Patti, *Novara*

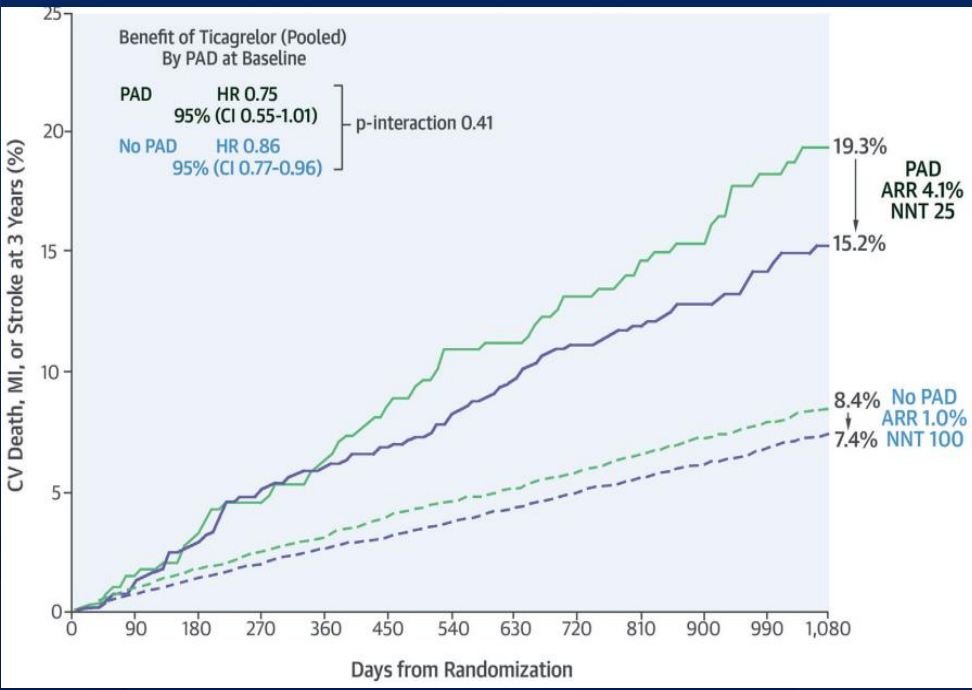
Atherothrombosis is an Unpredictable and Life-Threatening Consequence of Chronic, Progressive Atherosclerosis

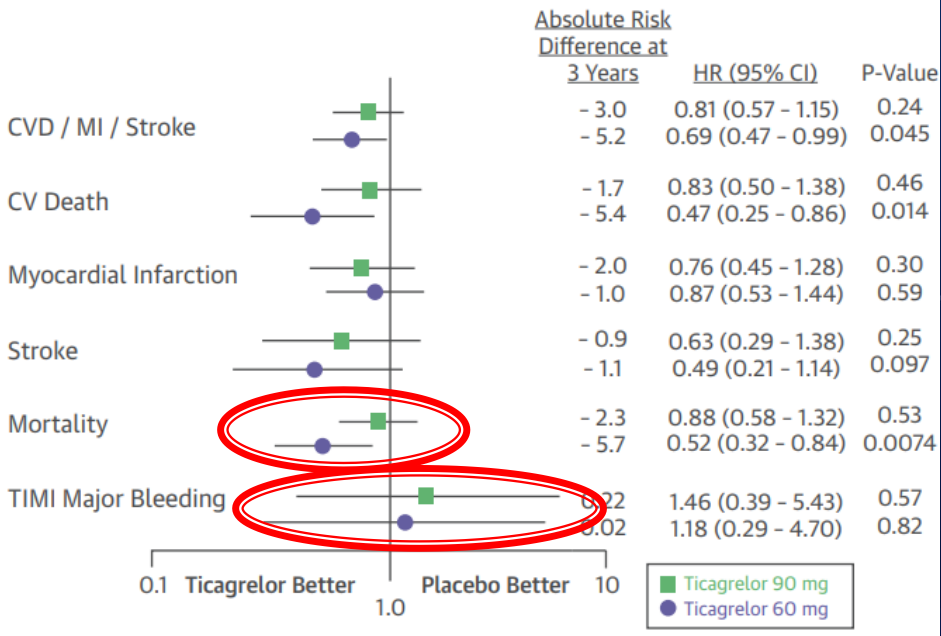
- 1-year outcomes in patients with atherosclerotic disease[1]



Steg P *et al*. *JAMA* 2007;297:1197–1206

Outcome with ticagrelor + aspirin vs aspirin alone in pts with PAD included in the PEGASUS trial



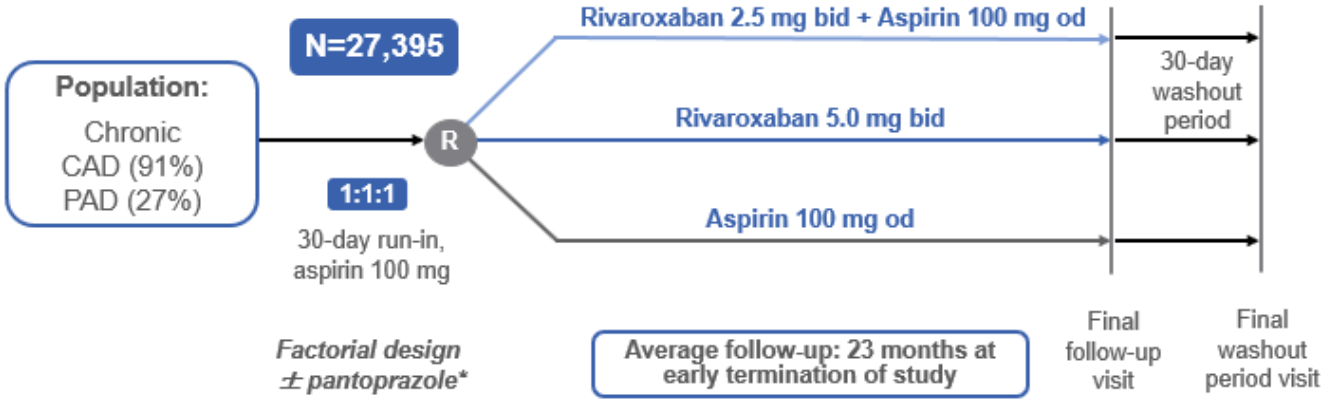


Bonaca MP, et al. J Am Coll Cardiol 2016

COMPASS: TRIAL DESIGN

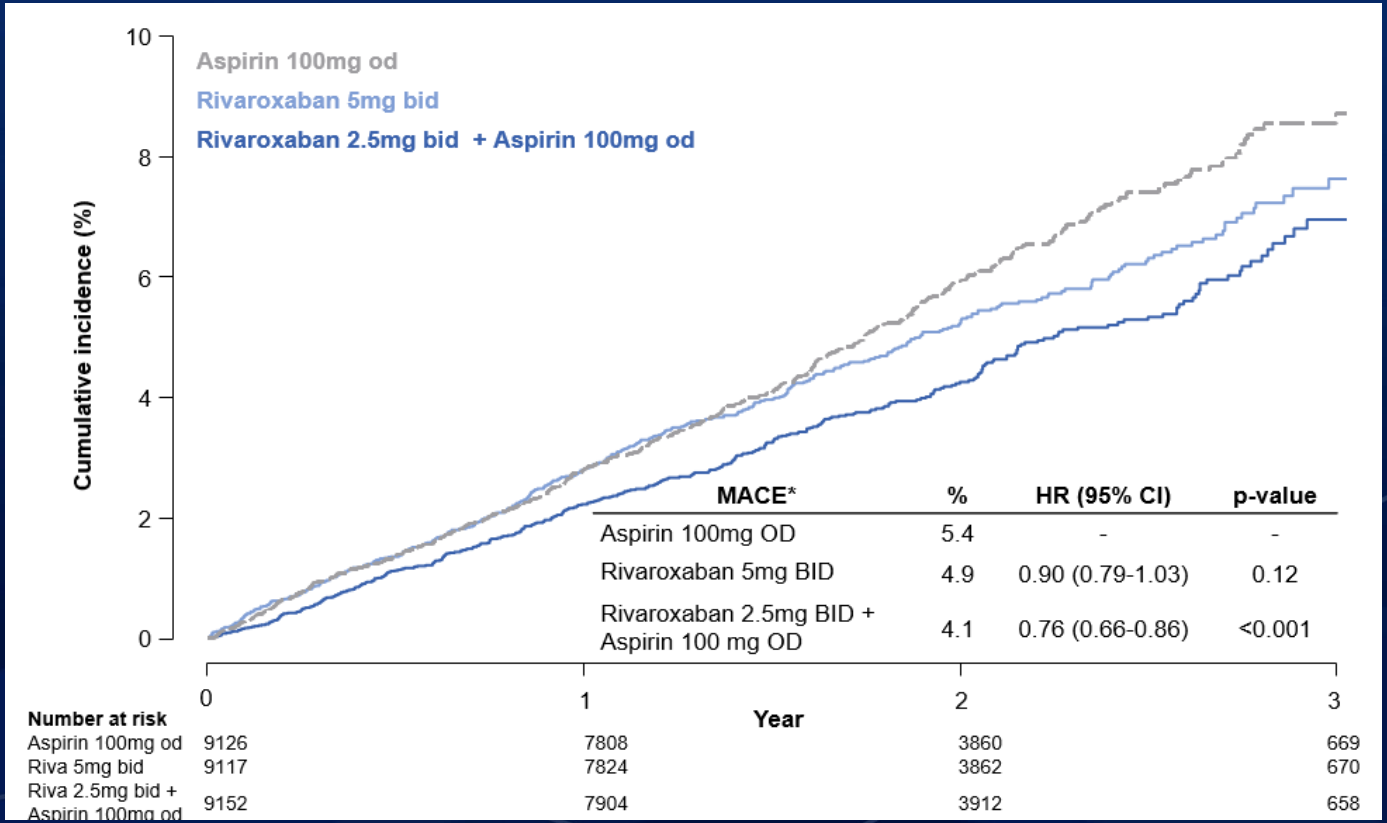
A Dual Pathway Approach Targeting Chronic Patients with CAD or PAD was Investigated in COMPASS

Objective: To determine the efficacy and safety of rivaroxaban, vascular dose of rivaroxaban plus aspirin or aspirin alone for reducing the risk of MI, stroke and cardiovascular death in CAD or PAD



Antithrombotic investigations* were stopped 1 year ahead of expectations in Feb 2017 due to overwhelming efficacy in the rivaroxaban 2.5 mg bid + aspirin arm

COMPASS: Events for the primary ischemic endpoint



Eikelboom JW, et al. N Engl J Med 2017

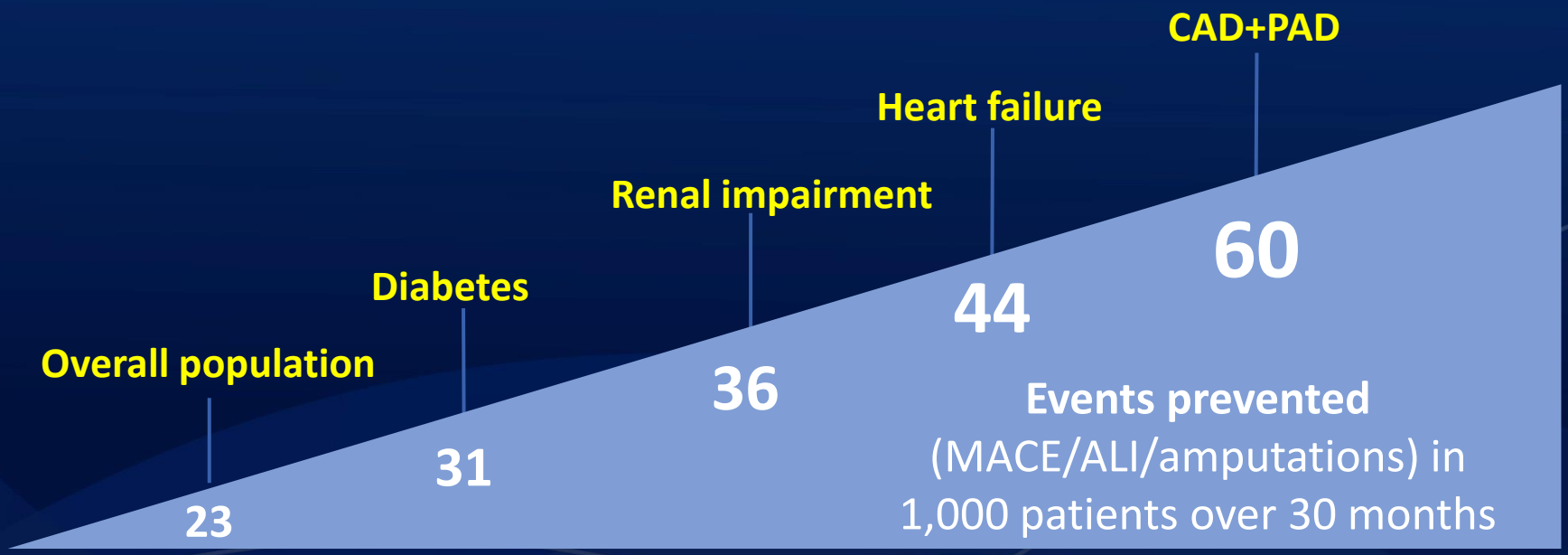
COMPASS: SAFETY RESULTS

Rates at mean follow-up of 23 months	Rivaroxaban 2.5 mg bid + aspirin 100 mg N=9152	Rivaroxaban 5 mg bid N=9117	Aspirin 100 mg N=9126
Modified major ISTH bleeding	288 (3.1%)	255 (2.8%)	170 (1.9%)
Fatal	15 (0.2%)	14 (0.2%)	10 (0.1%)
Non-fatal ICH*	21 (0.2%)	32 (0.4%)	19 (0.2%)
Non-fatal other critical organ*	42 (0.5%)	45 (0.5%)	29 (0.3%)

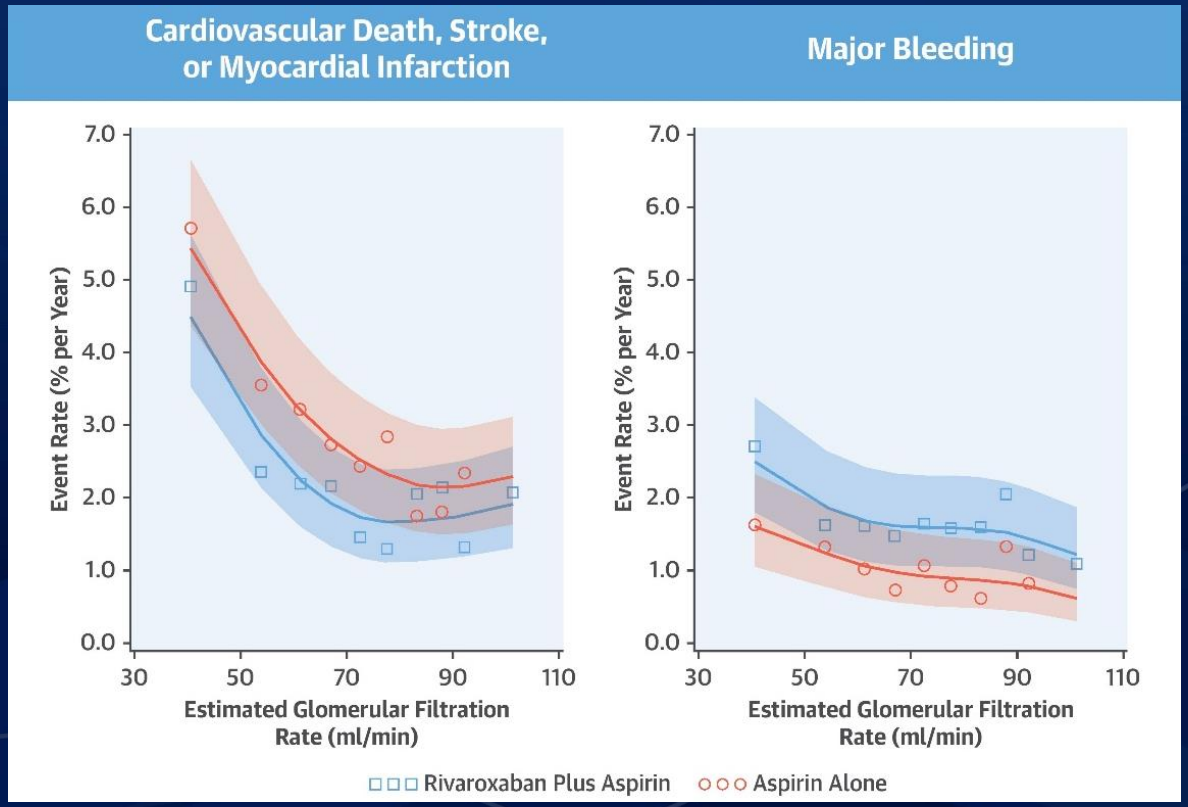
Rates at mean follow-up of 23 months	Rivaroxaban 2.5 mg bid + aspirin 100 mg vs aspirin 100 mg		Rivaroxaban 5 mg bid vs aspirin 100 mg	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Modified ISTH major bleeding	1.70 (1.40–2.05)	<0.001	1.51 (1.25–1.84)	<0.001
Fatal	1.49 (0.67–3.33)	0.32	1.40 (0.62–3.15)	0.41
Non-fatal ICH*	1.10 (0.59–2.04)	0.77	1.69 (0.96–2.98)	0.07
Non-fatal other critical organ*	1.43 (0.89–2.29)	0.14	1.57 (0.98–2.50)	0.06

Eikelboom JW, et al. N Engl J Med 2017

Patients at Higher CV Risk Benefit More from Rivaroxaban Vascular Dose Plus Aspirin



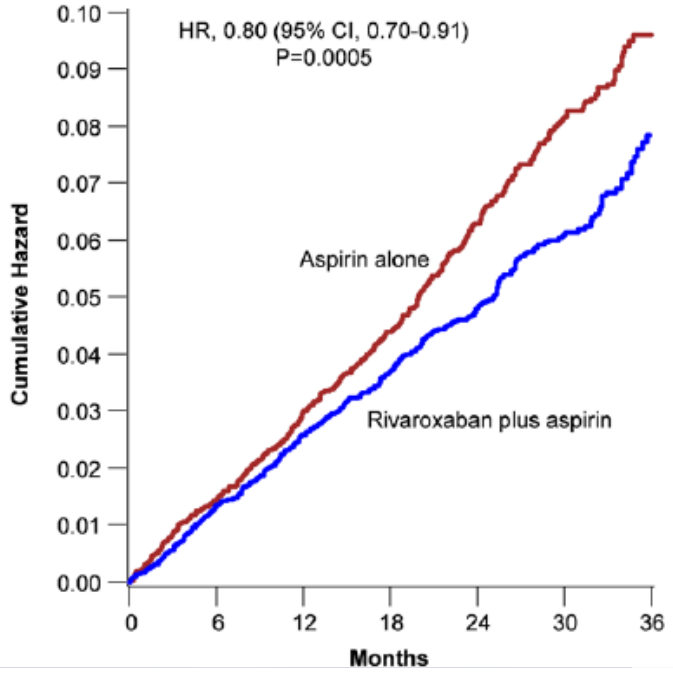
Continuous plot over the range of eGFR for the primary outcome (left) and for bleeding (right) in COMPASS patients with highest rates (for MACE and bleeding) in patients with renal impairment

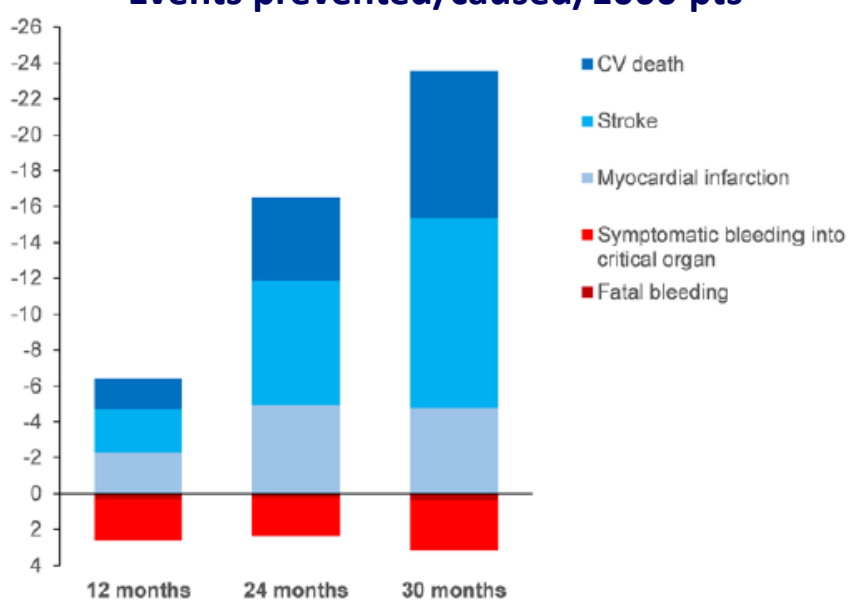


Fox KAA *et al*, *JACC* 2019;73:2243–2250

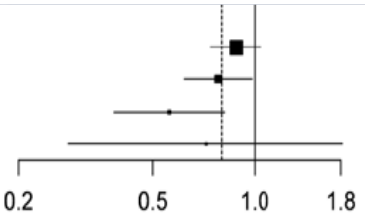
Net clinical benefit (NCB) with vascular dose rivaroxaban in COMPASS

NCB
- CV death
- MI
- Stroke
- Fatal bleeding
- Bleeding into a critical organ





Polyvascular, renal dysfunction, heart failure, diabetes					
None or 1 out of 4	252 / 6612	2	283 / 6553	2.3	0.88 (0.74-1.04)
2 out of 4	129 / 1936	3.6	164 / 1941	4.7	0.78 (0.62-0.98)
3 out of 4	43 / 548	4.4	75 / 557	7.7	0.56 (0.38-0.81)
4 out of 4	7 / 56	7	12 / 75	10.3	0.71 (0.28-1.83)



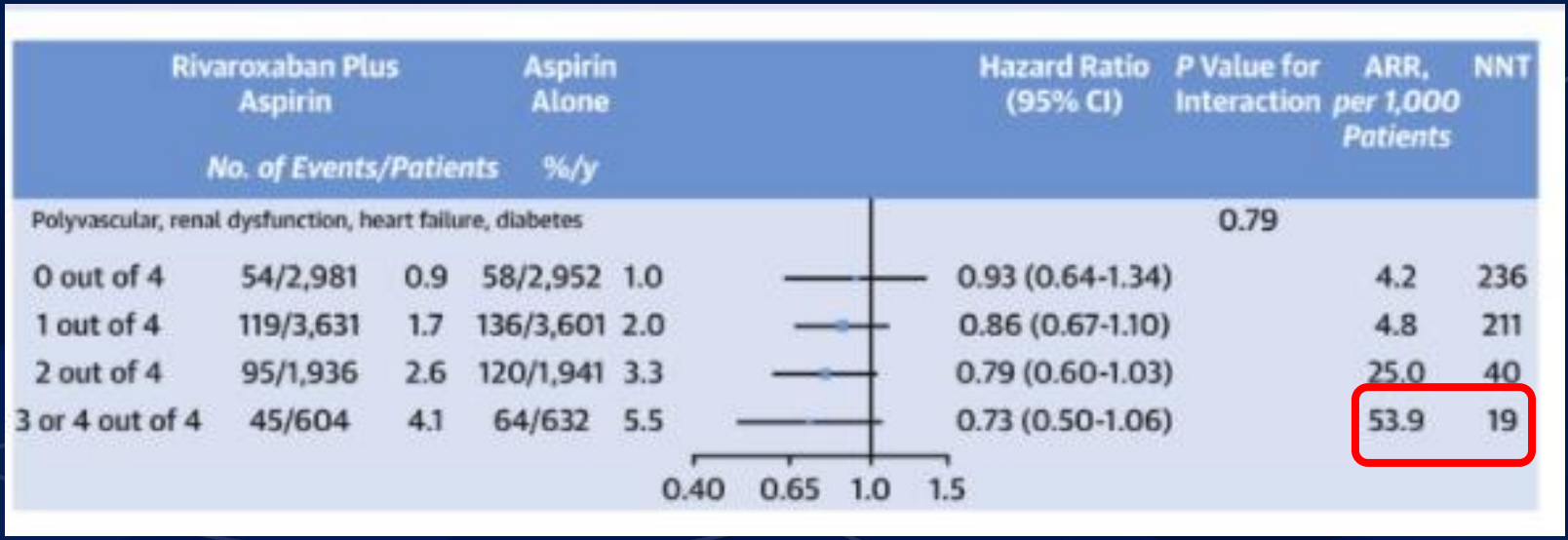
Steffel J, et al. Circulation 2020

Mortality benefit of rivaroxaban plus aspirin vs aspirin alone across different high-risk features in COMPASS

All-cause death: 3.4% vs 4.1%, HR: 0.82, 95% CI 0.71-0.96, P = 0.01
CV death: 1.7% vs 2.2%, HR: 0.78; 95% CI: 0.64-0.96 P = 0.02

High-risk features:

- DM
- PAD + CAD
- CRF
- CHF

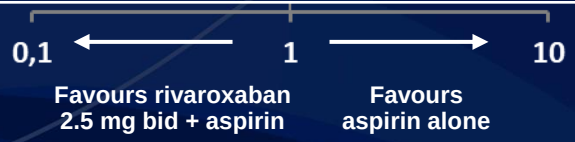


Eikelboom JW. et al. J Am Coll Cardiol 2021

Efficacy outcomes in the PAD population: MACE and MALE

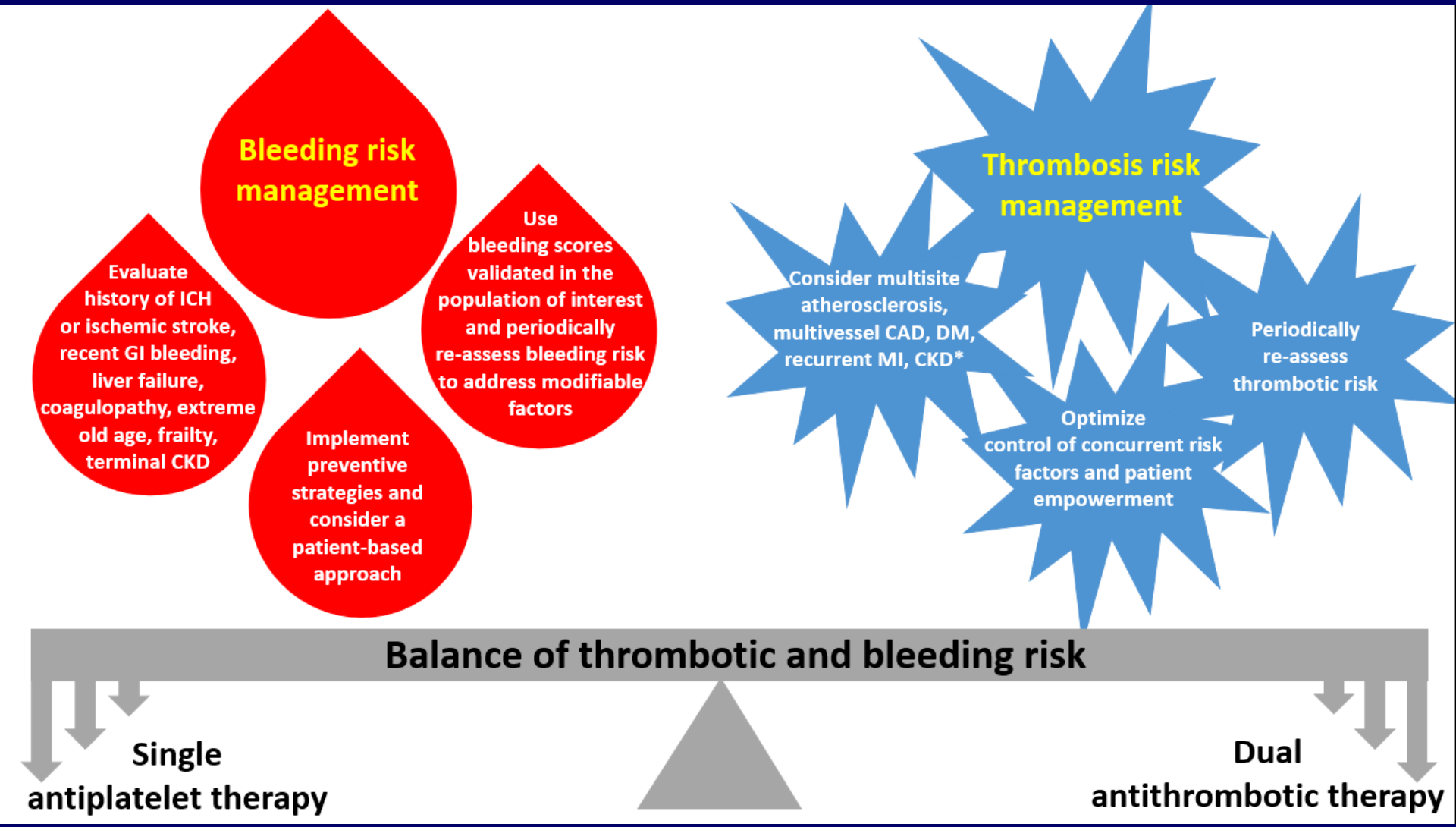
28% MACE reduction – 46% MALE reduction – 70% MAJOR AMPUTATION reduction

	Rivaroxaban 2.5 mg bid + aspirin n (%)	Aspirin n (%)	HR	HR (95% CI)	*p*-value
CV death, stroke, MI (MACE)	126 (5.1)	174 (6.9)	0.72		<0.005
Acute limb ischaemia or chronic limb ischaemia (MALE)	30 (1.2)	56 (2.2)	0.54		0.005
Major amputation	5 (0.2)	17 (0.7)	0.30		0.01
MACE, MALE or major amputation	157 (6.3)	225 (9.0)	0.69		0.0003



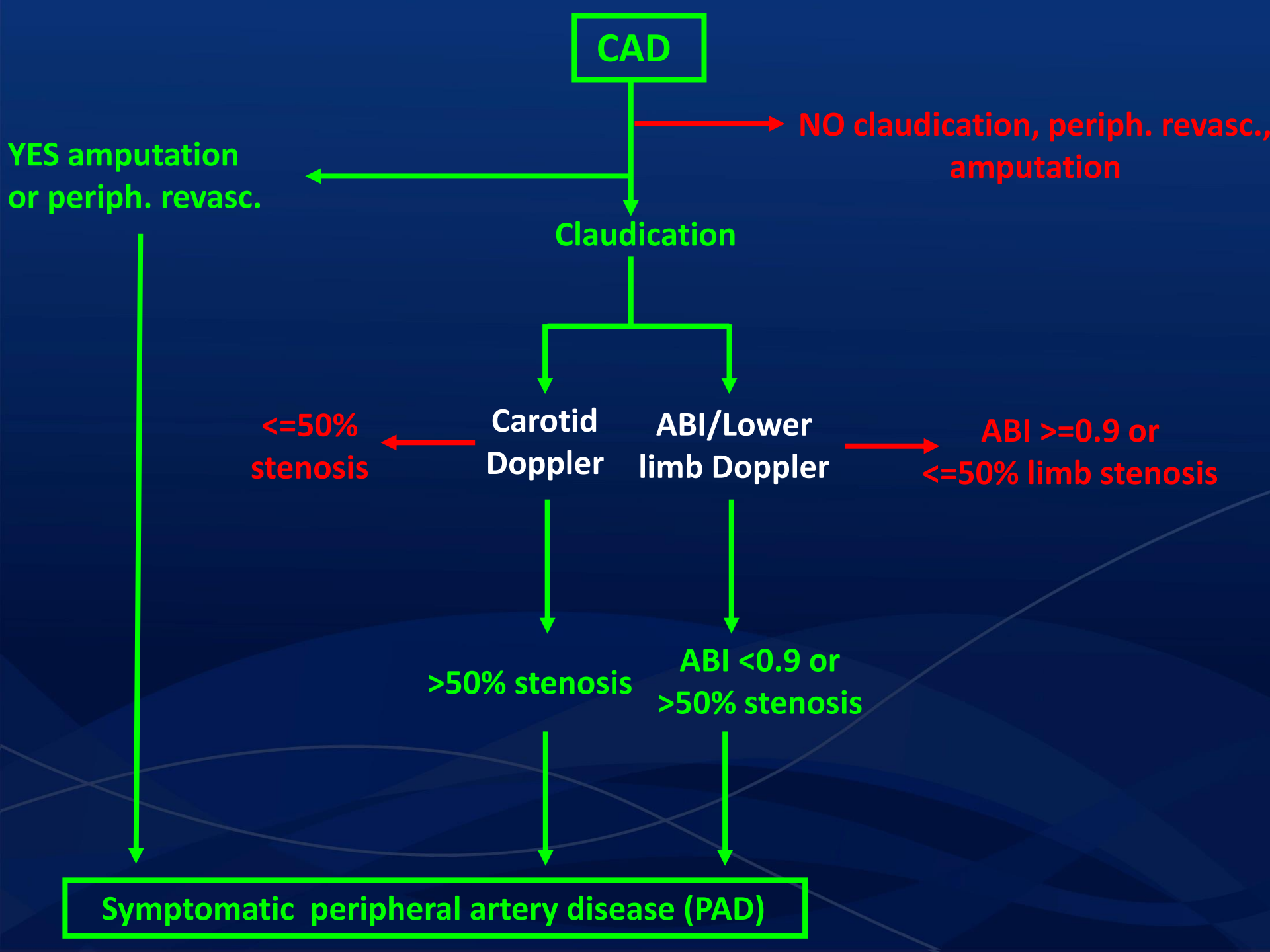
Anand S *et al*, *Lancet* 2018;391:219–229

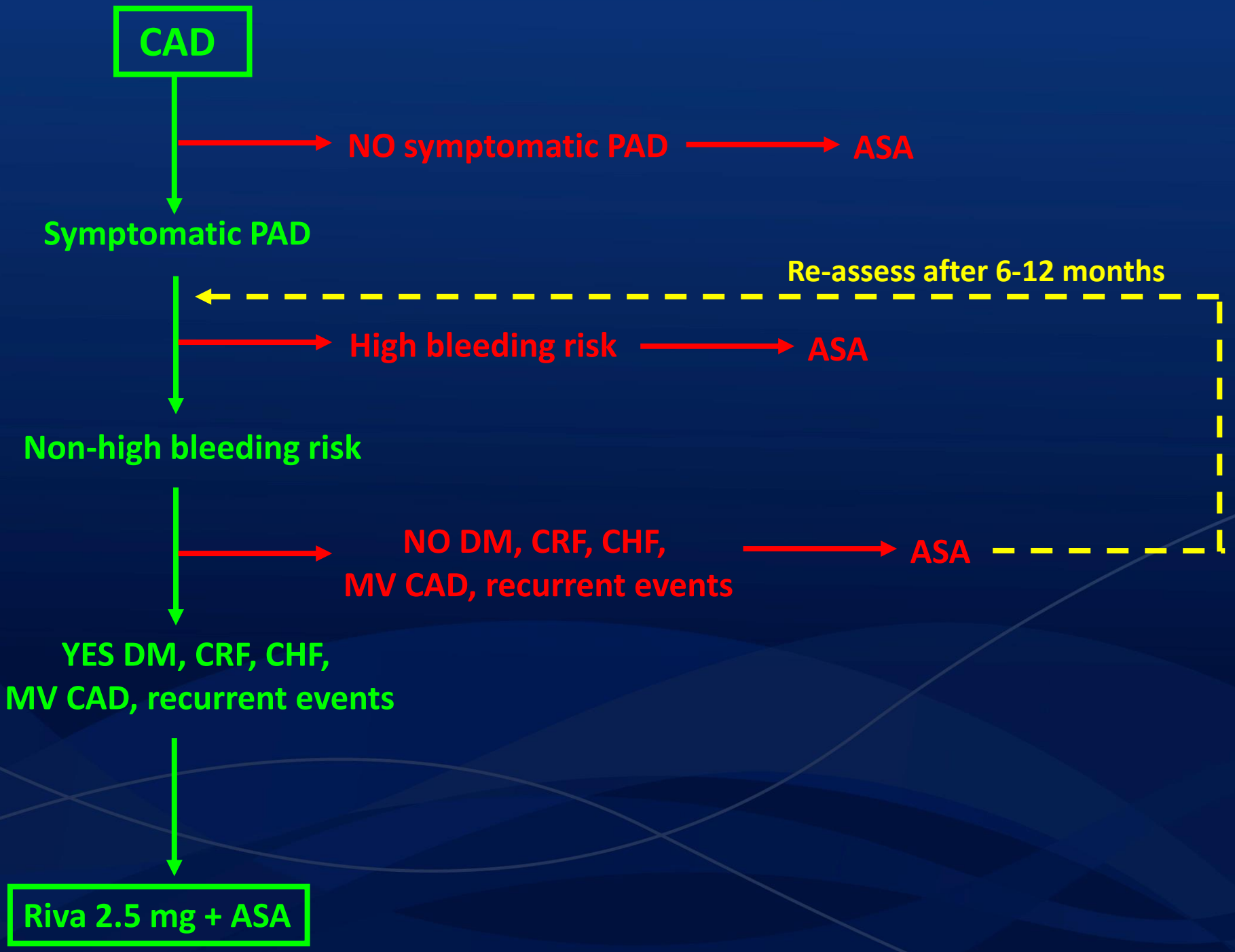
Dual vs Single antithrombotic therapy in CCS



Patti G, et al. Biomed Pharmacother. 2021 Aug;140:111783

Fattori clinici di rischio ischemico	SI	NO
Diabete mellito		
Cr Cl <30 ml/min		
Arteriopatia periferica sintomatica		
Eventi coronarici ricorrenti		
Scompenso cardiaco		
Fattori coromarici di rischio ischemico	**SI**	**NO**
Coronaropatia multivasale		
>= 3 stent / lunghezza stent >60 mm		
Biforcazione con 2 stent		
Occlusione coronarica cronica		
Pregressa trombosi di stent		
Fattori di rischio emorragico	**SI**	**NO**
Età > 75 aa o peso corporeo < 60 Kg		
Anemia e/o storia di sanguinamento maggiore		
Terapia anticoagulante + antiaggregante		
Cr Cl <30 ml/min o diabete mellito		
Uso di cortisone/FANS/alcool		


CAD
NO claudication, periph. revasc., amputation
YES amputation or periph. revasc.
Claudication
<=50% stenosis
Carotid Doppler
ABI/Lower limb Doppler
ABI >=0.9 or <=50% limb stenosis
>50% stenosis
ABI <0.9 or >50% stenosis
Symptomatic peripheral artery disease (PAD)


CAD
NO symptomatic PAD
ASA
Symptomatic PAD
Re-assess after 6-12 months
High bleeding risk
ASA
Non-high bleeding risk
NO DM, CRF, CHF,
MV CAD, recurrent events
ASA
YES DM, CRF, CHF,
MV CAD, recurrent events
Riva 2.5 mg + ASA