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Dosaggio Vascolare di Rivaroxaban: Possiamo Ridurre gli Eventi Cardiovascolari?

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February 6, 2017
First Interim Analysis

MACE
(CV death, MI, stroke)
RRR 26%

2y EP
(stroke, MI, ALI, CHD death)
RRR 28%

2y EP
(stroke, MI, ALI, CV death)
RRR 26%

STROKE
RRR 42%

CV DEATH
RRR 22%

MALE
RRR 46%

CHD DEATH
RRR 27%

Vascular Amputation
RRR 58%

Non-CV DEATH
RRR 13%

February 6, 2017
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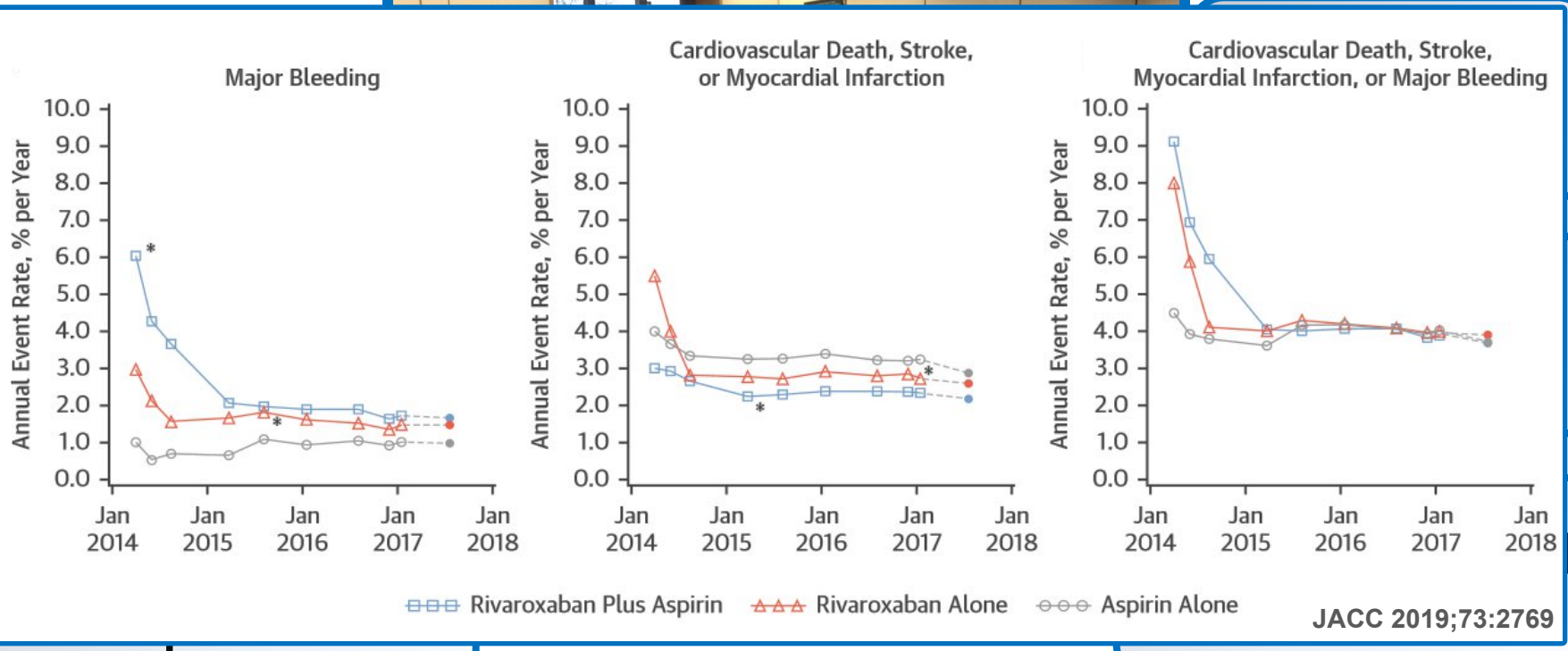

JACC 2019;73:2769

RRR 58%

February 6, 2017
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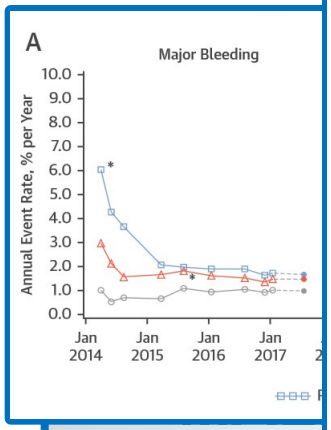
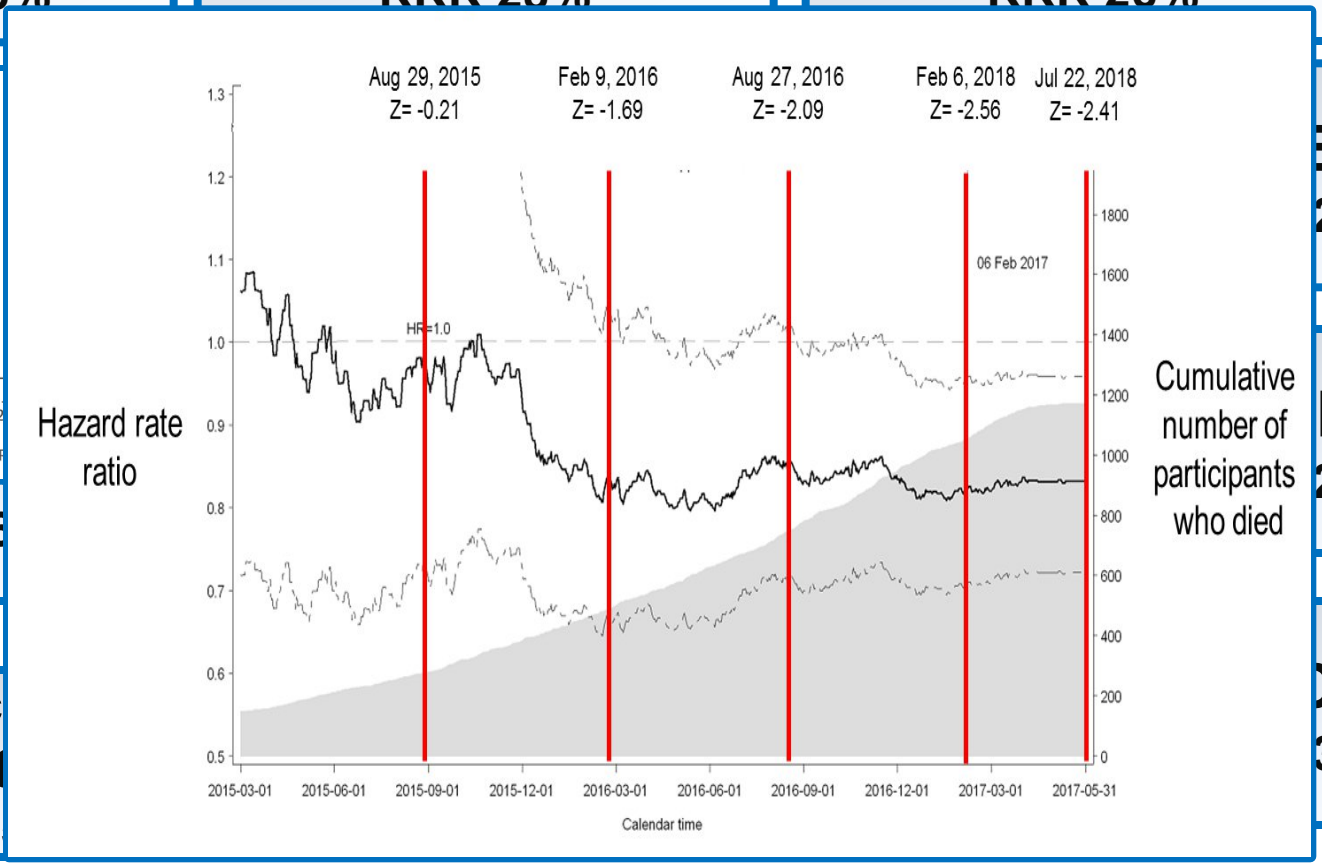


RRR 46

Vasc
Amput
RRR



EATH
22%

EATH
27%

DEATH
3%

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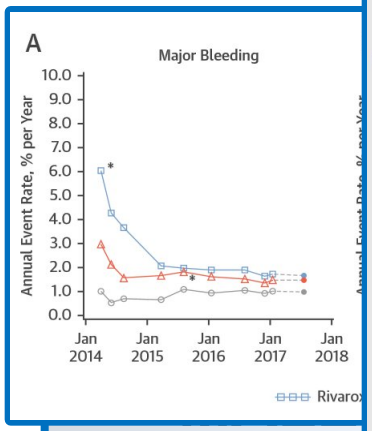


RRR 46%

Vascul
Amputa
RRR 58

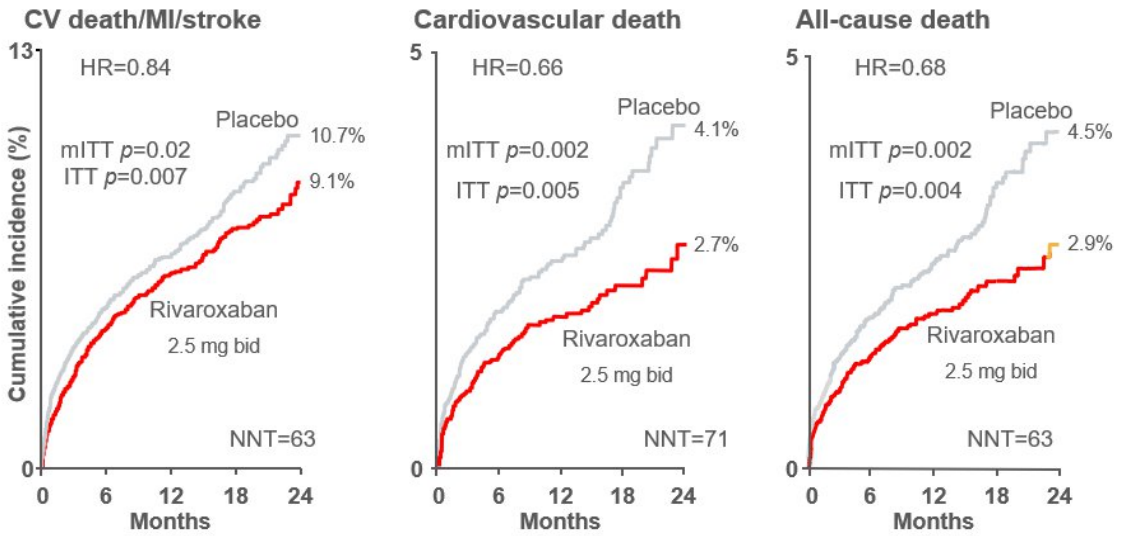
DEATH
R 22%

DEATH
R 27%

DEATH
R 13%

Components of Primary Endpoint
Rivaroxaban 2.5 mg bid, Both Strata

ATLAS ACS 2 TIMI 51



Mega JL et al, N Engl J Med 2012;366:9

February 6, 2017
First Interim Analysis

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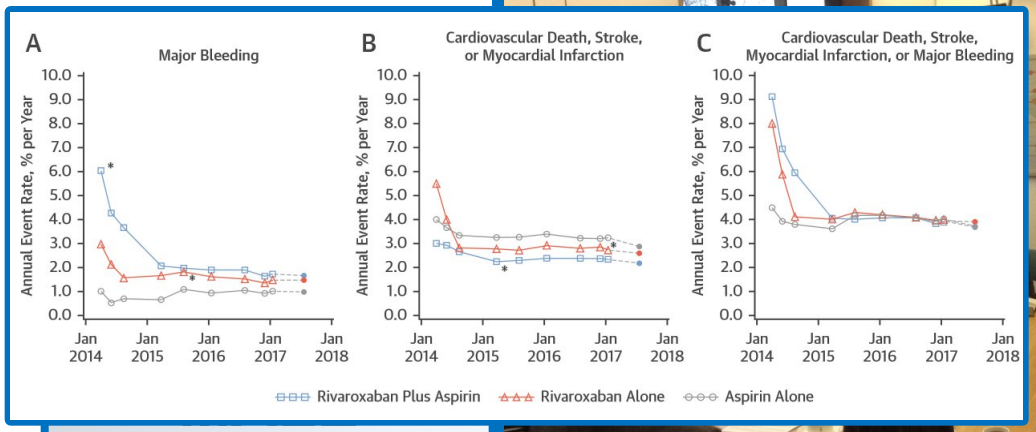
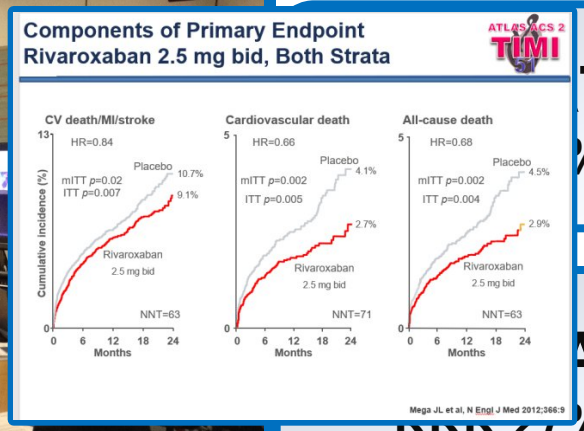
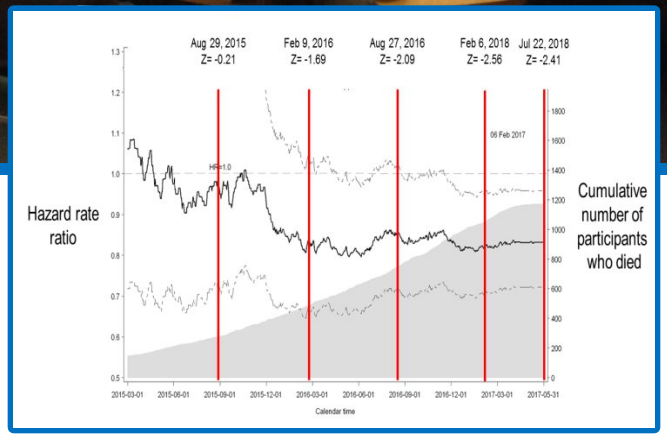




RRR 46%

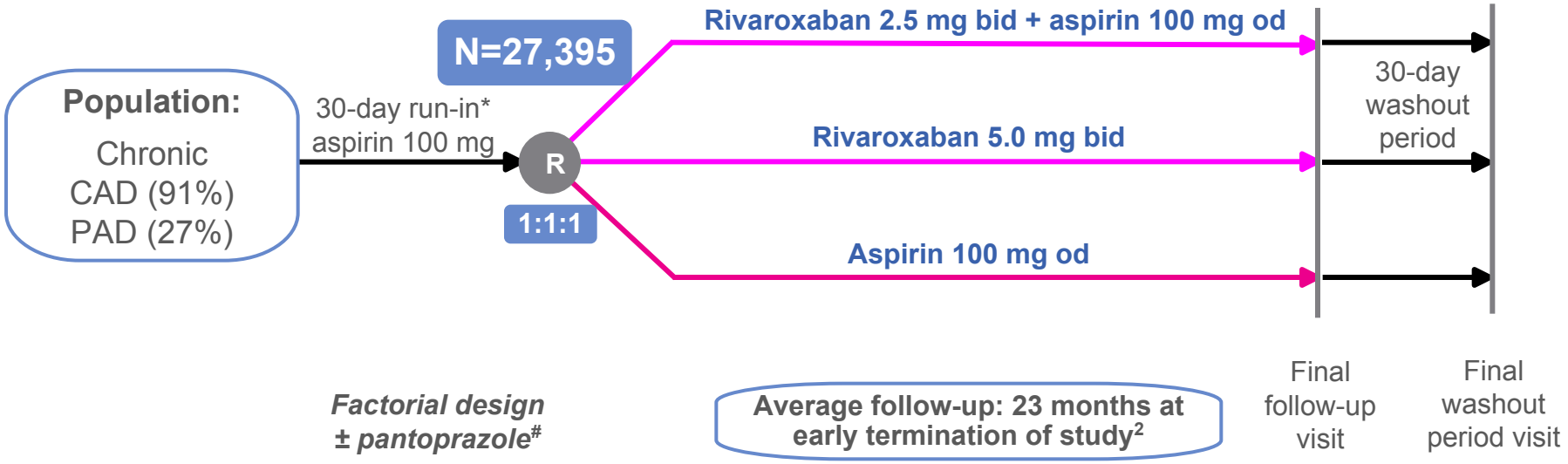


Vascular Amputation
RRR 58%

Non-CV DEATH
RRR 13%

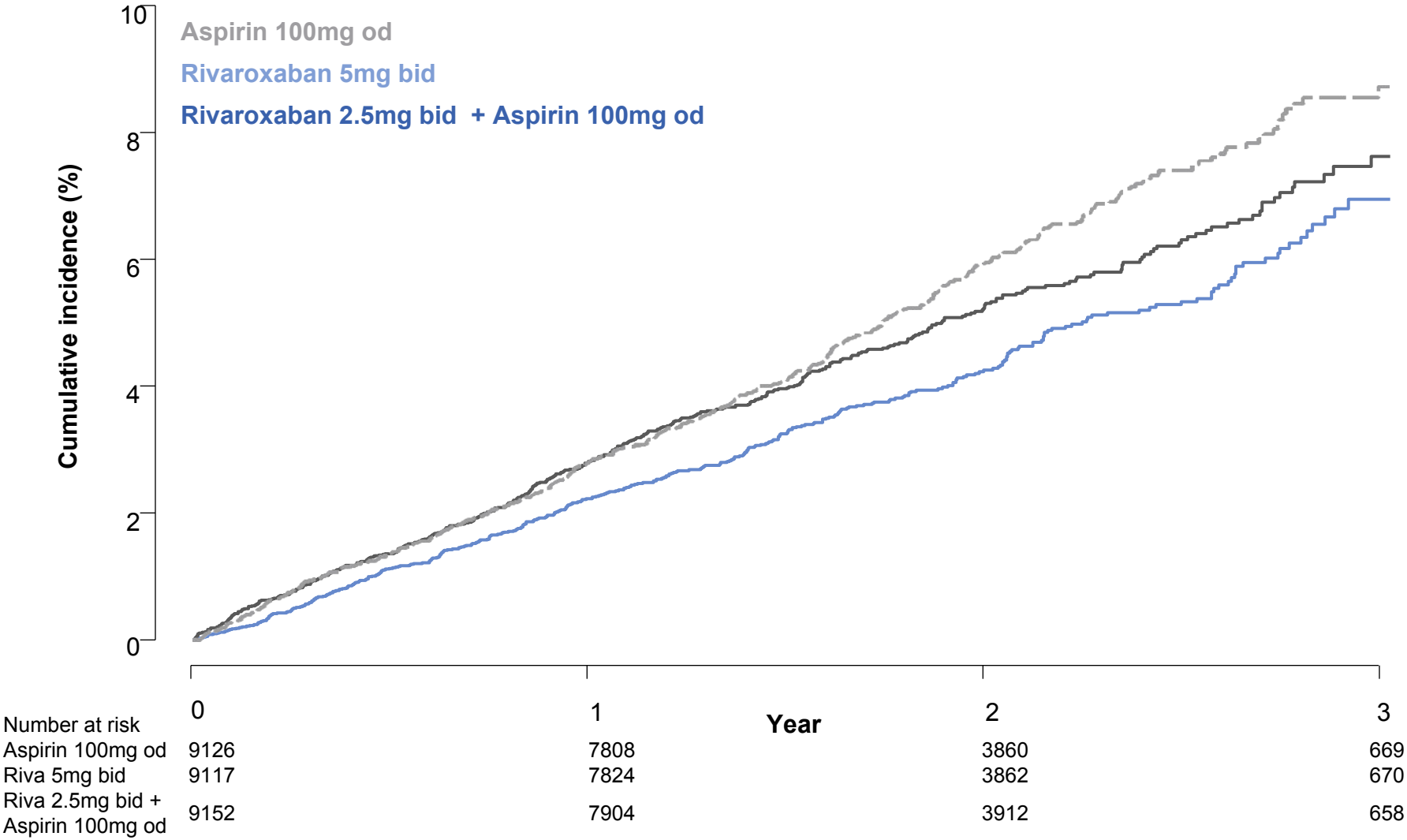
The COMPASS Trial

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



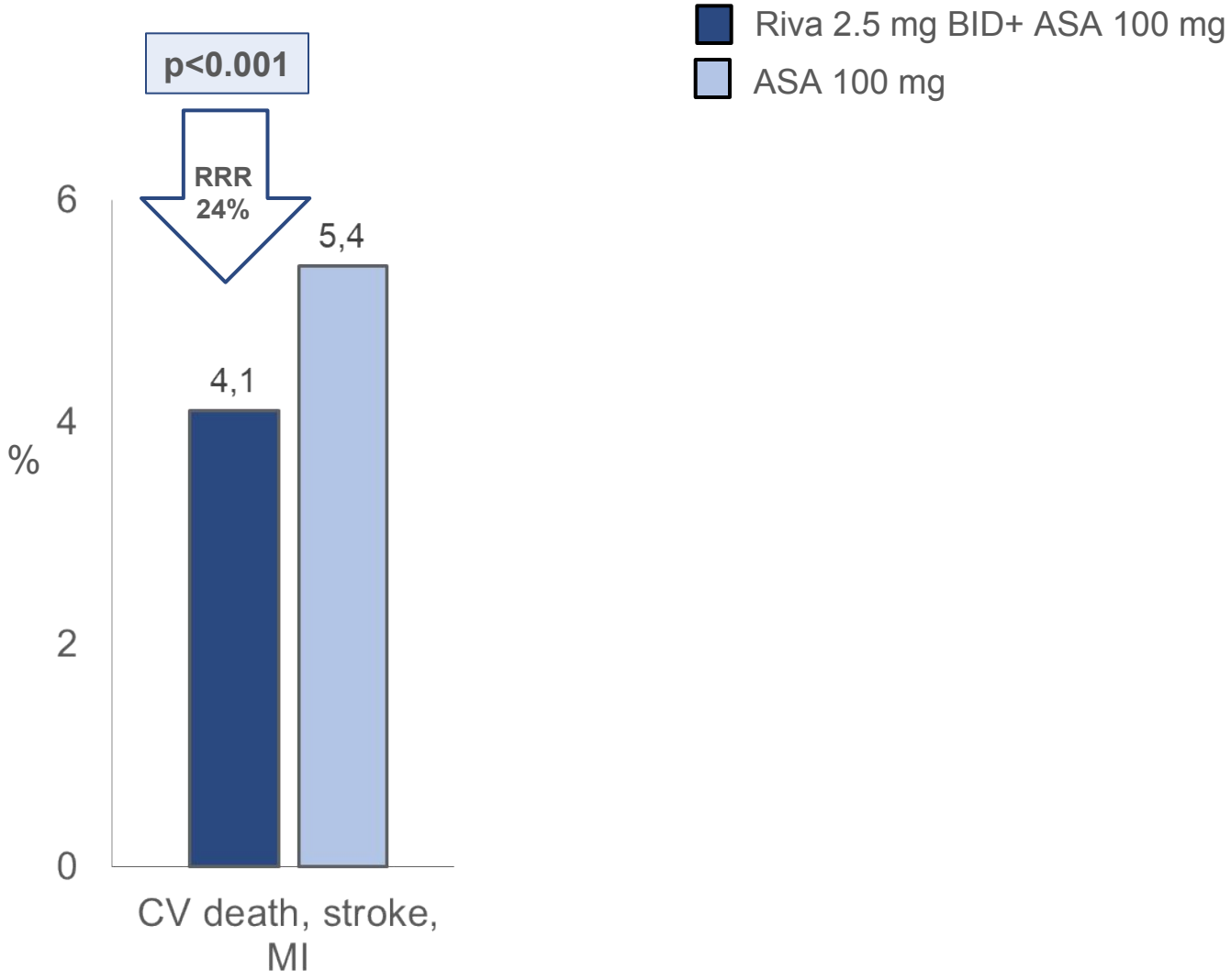
1. **Bosch J et al, Can J Cardiol 2017;33:1027–1035; 2. Eikelboom JW et al, N Engl J Med 2017;377:1319-1330; 3. Connolly SJ et al, Lancet 2017; doi:10.1016/S0140-6736(17)32816-7**

Primary Endpoint
Kaplan Meier Curves



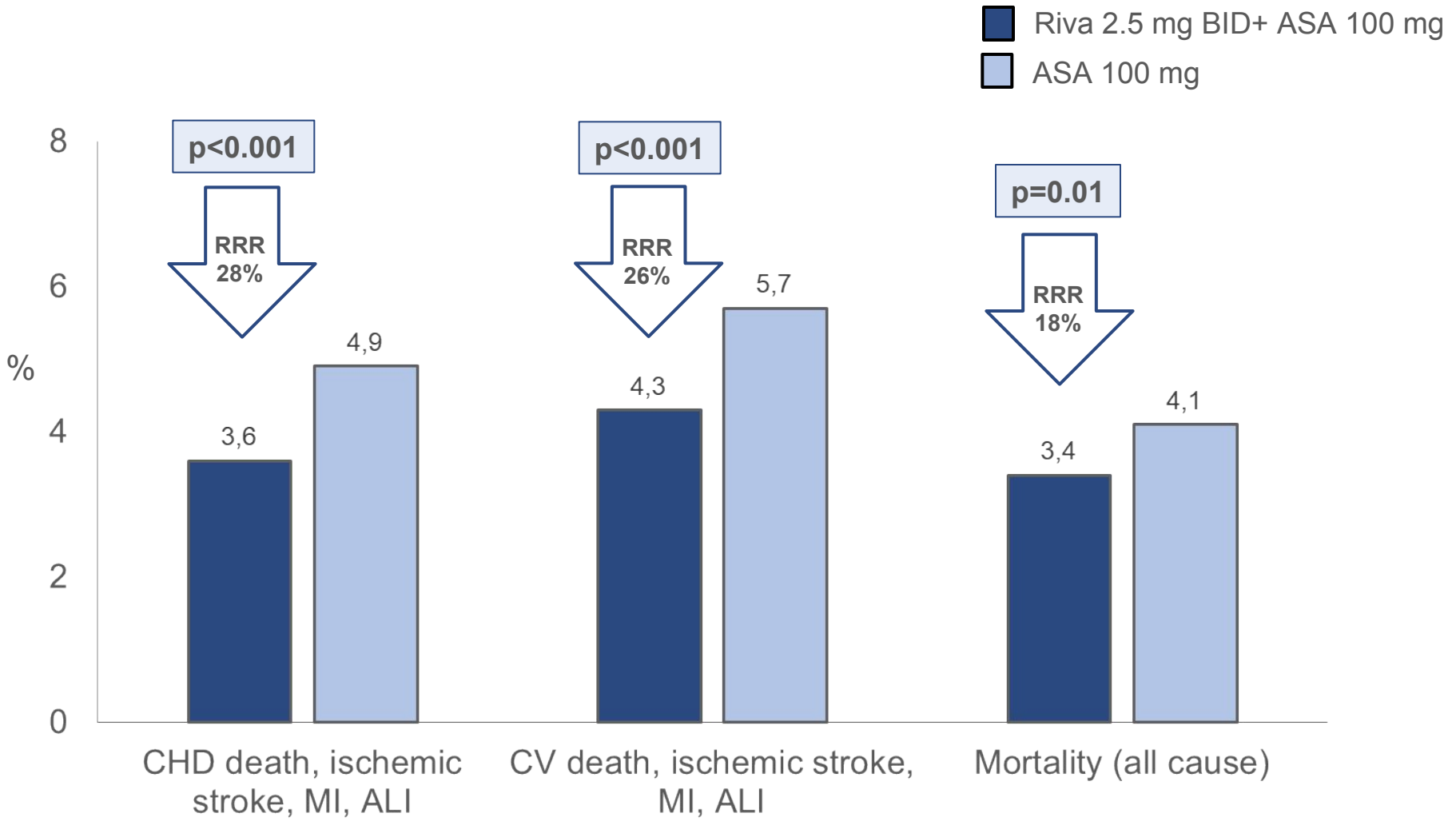
Eikelboom JW et al, N Engl J Med 2017;377:1319

Primary Endpoint and its Single Components



Eikelboom JW et al, N Engl J Med 2017;377:1319

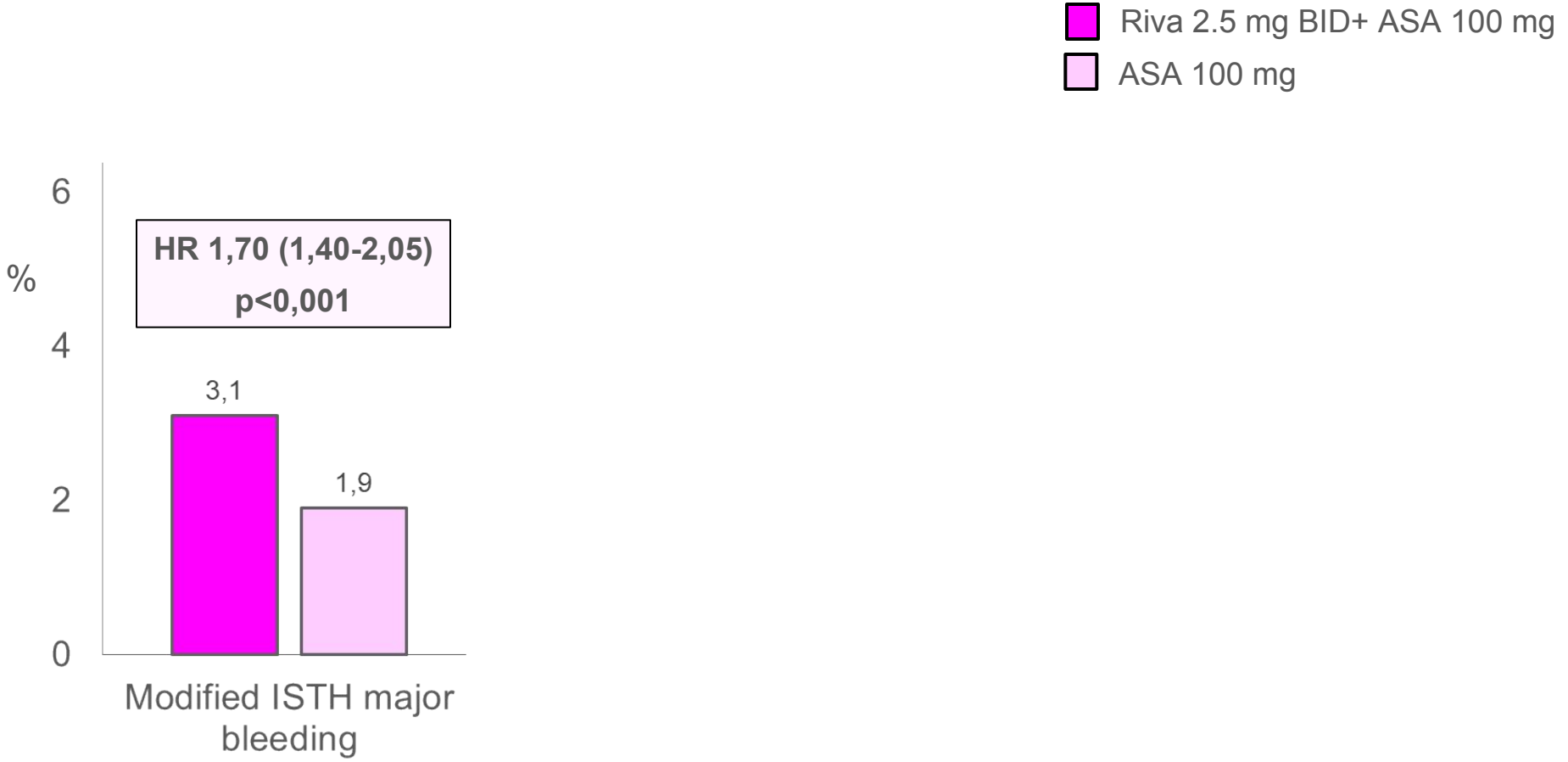
Secondary Outcomes, Including All-Cause Mortality



pre-specified threshold *p*=0.0025

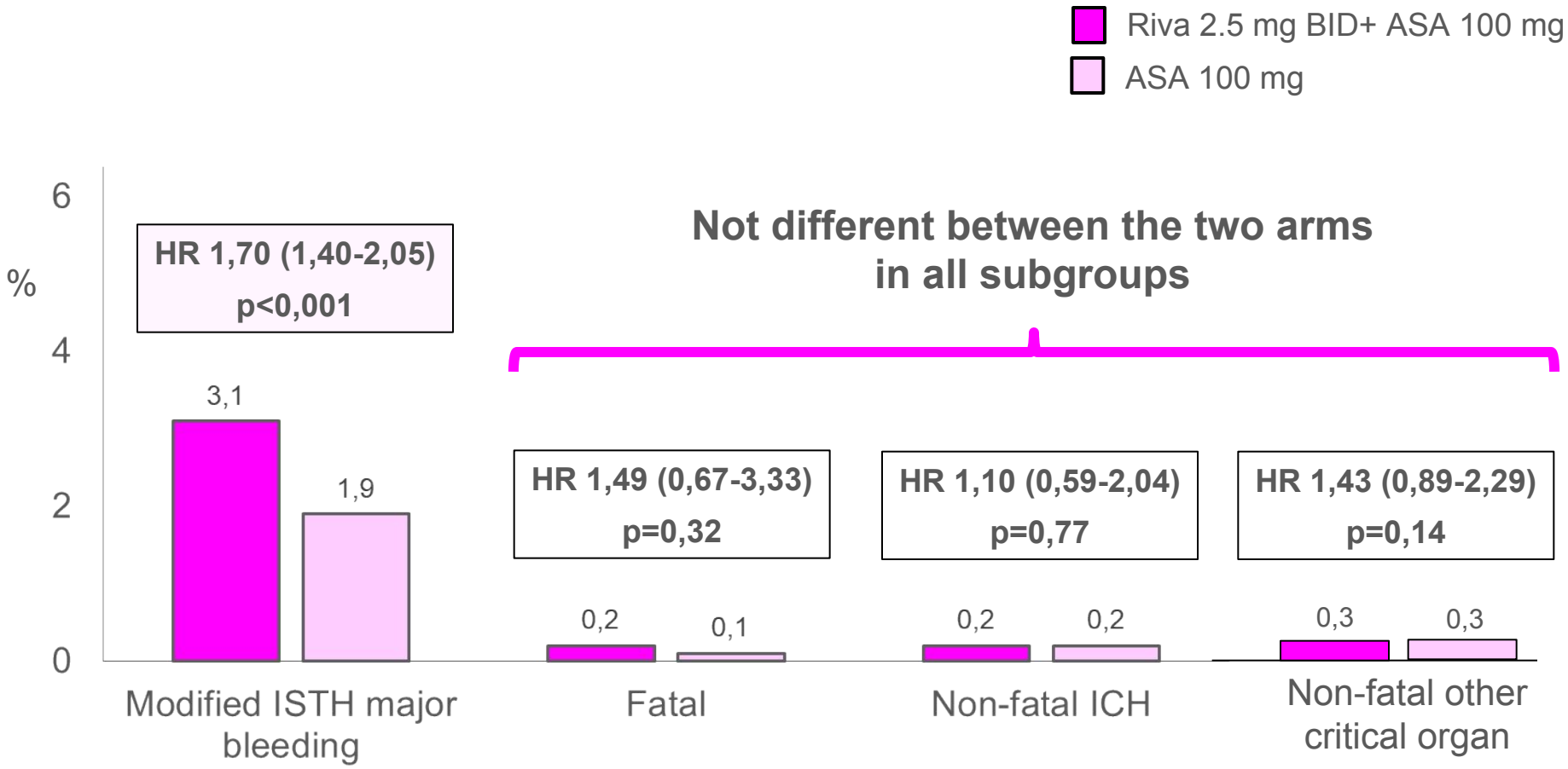
Eikelboom JW et al, N Engl J Med 2017;377:1319

Bleeding Rates



Eikelboom JW et al, N Engl J Med 2017;377:1319

Bleeding Rates



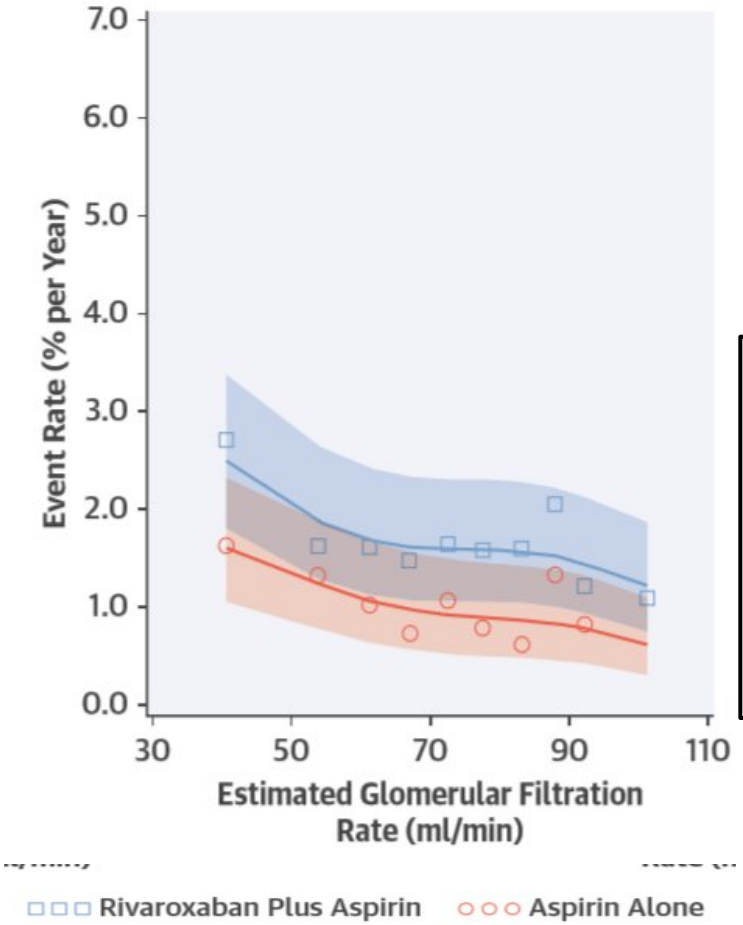
Each event is counted in the most severe hierarchical category (fatal; critical organ bleeding; bleeding into surgical site requiring re-operation; bleeding leading to hospitalization) only. For each outcome, the first event experienced per patient is considered. Subsequent events of the same type are not shown. Therefore subcategories do not necessarily sum up to overall category.

Eikelboom JW et al, N Engl J Med 2017;377:1319

Rivaroxaban+ASA in Patients with Vascular Diseases and Renal Dysfunction

COMPASS

Major Bleeding

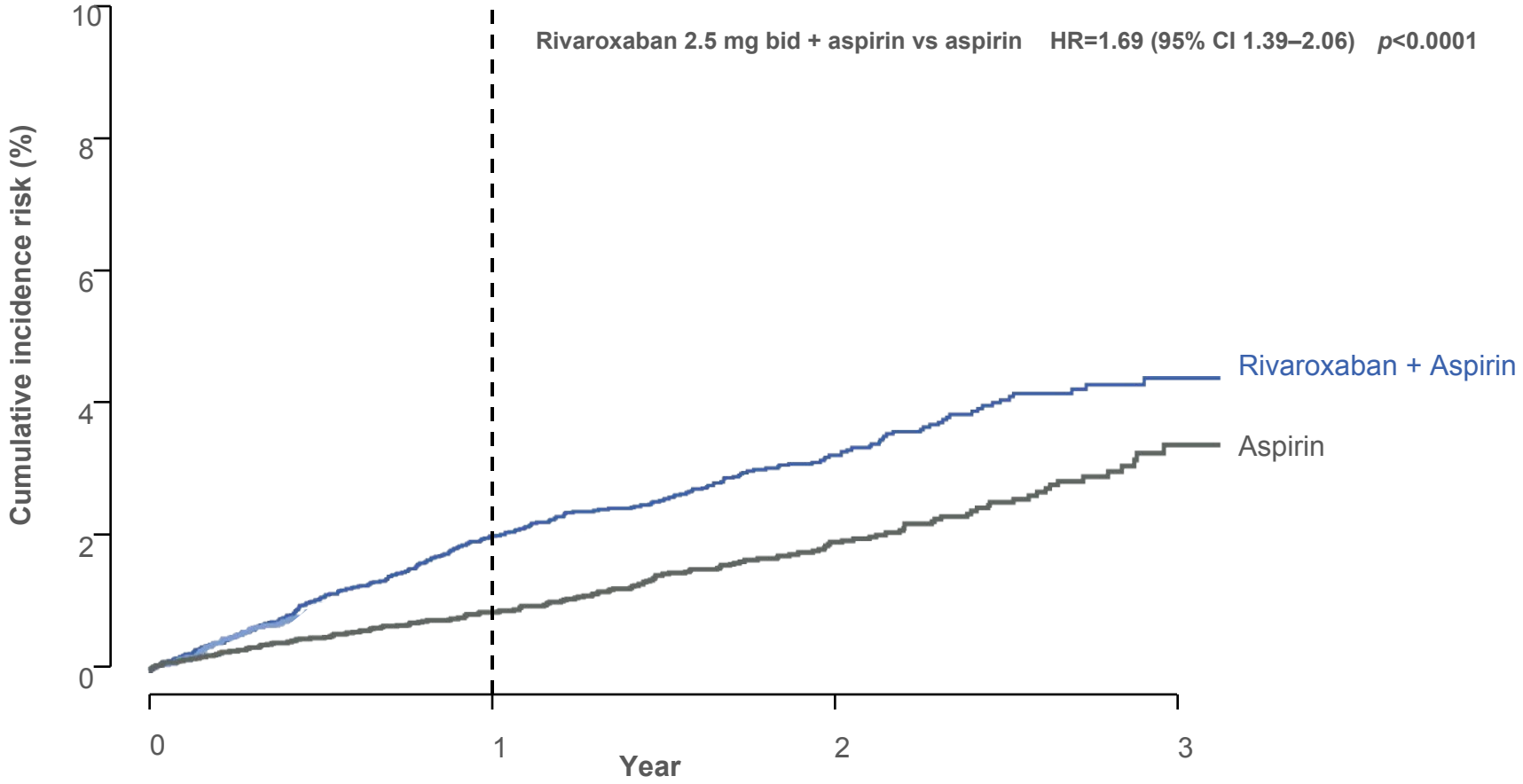


Major Bleeding

		Rivaroxaban Plus Aspirin	Aspirin Alone	HR (95% CI)
		No. of Events / Patients (%)		
eGFR <60 ml/min	13	81/2,054 (3.9)	57/2,114 (2.7)	1.47 (1.05-2.07)
eGFR ≥60 ml/min	24	206/7,094 (2.9)	113/7,012 (1.6)	1.81 (1.44-2.28)

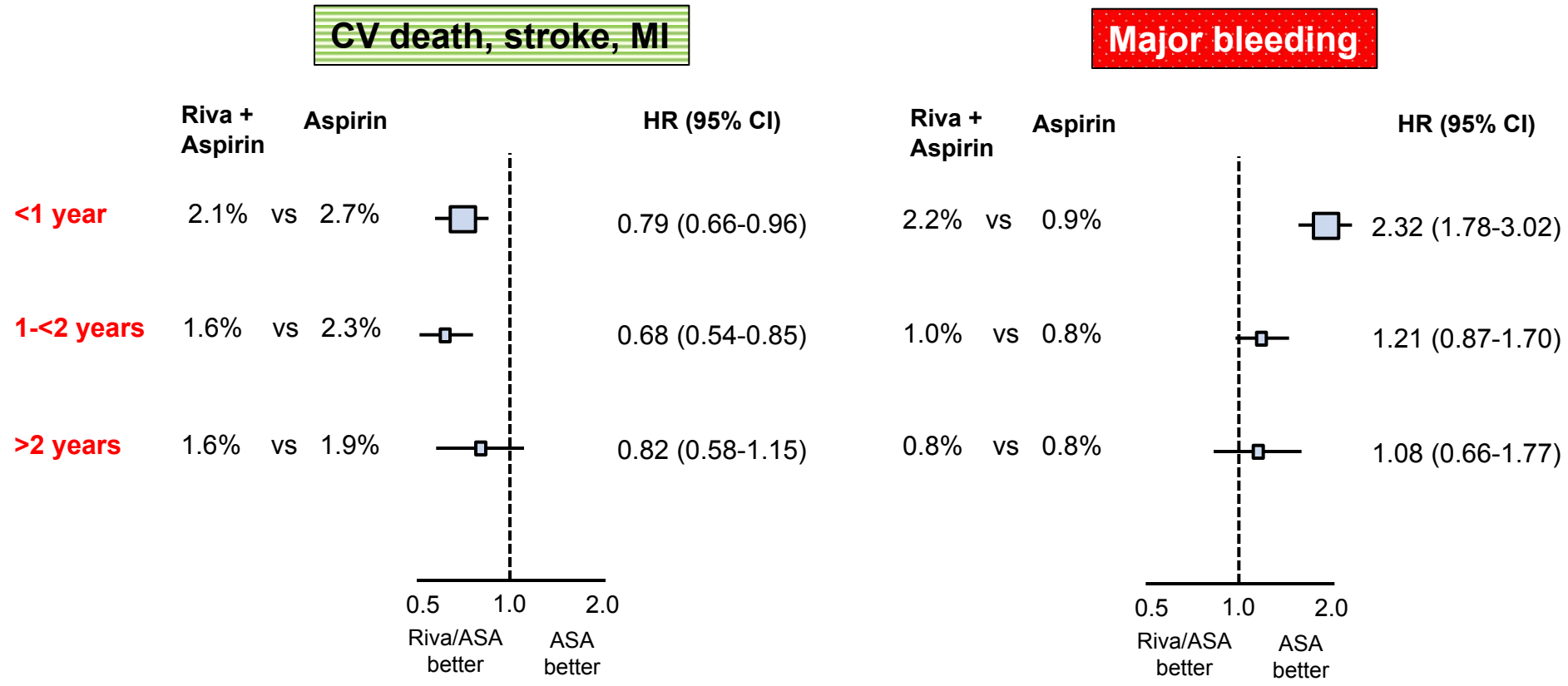
Fox KAA, et al. J Am Coll Cardiol 2019;73:2243

Rate of Major Bleeding in Patients with CAD

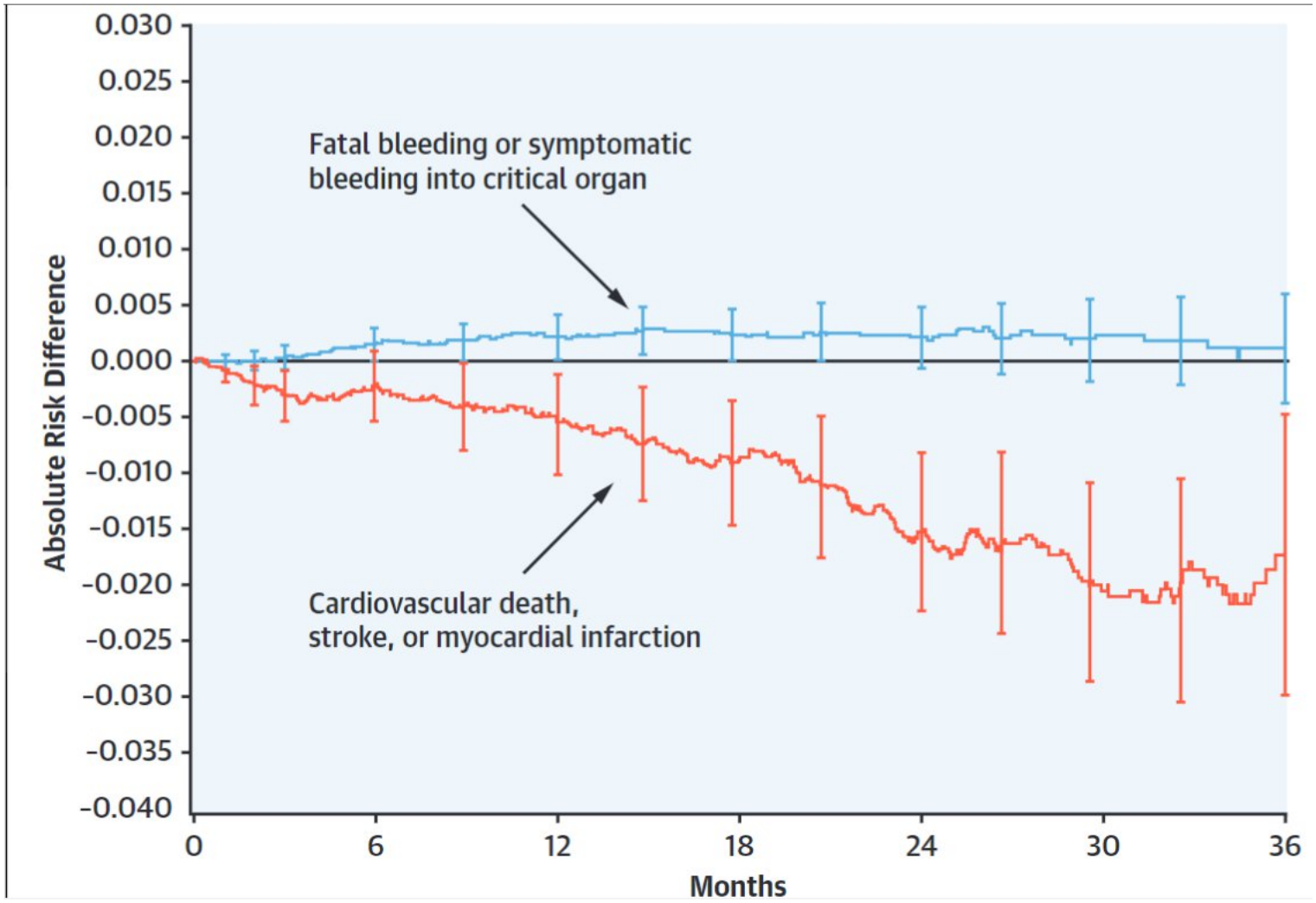


Connolly SJ *et al*, *Lancet* 2017; doi:10.1016/S0140-6736(17)32816-7

Primary Efficacy and Safety Outcomes
Landmark analyses



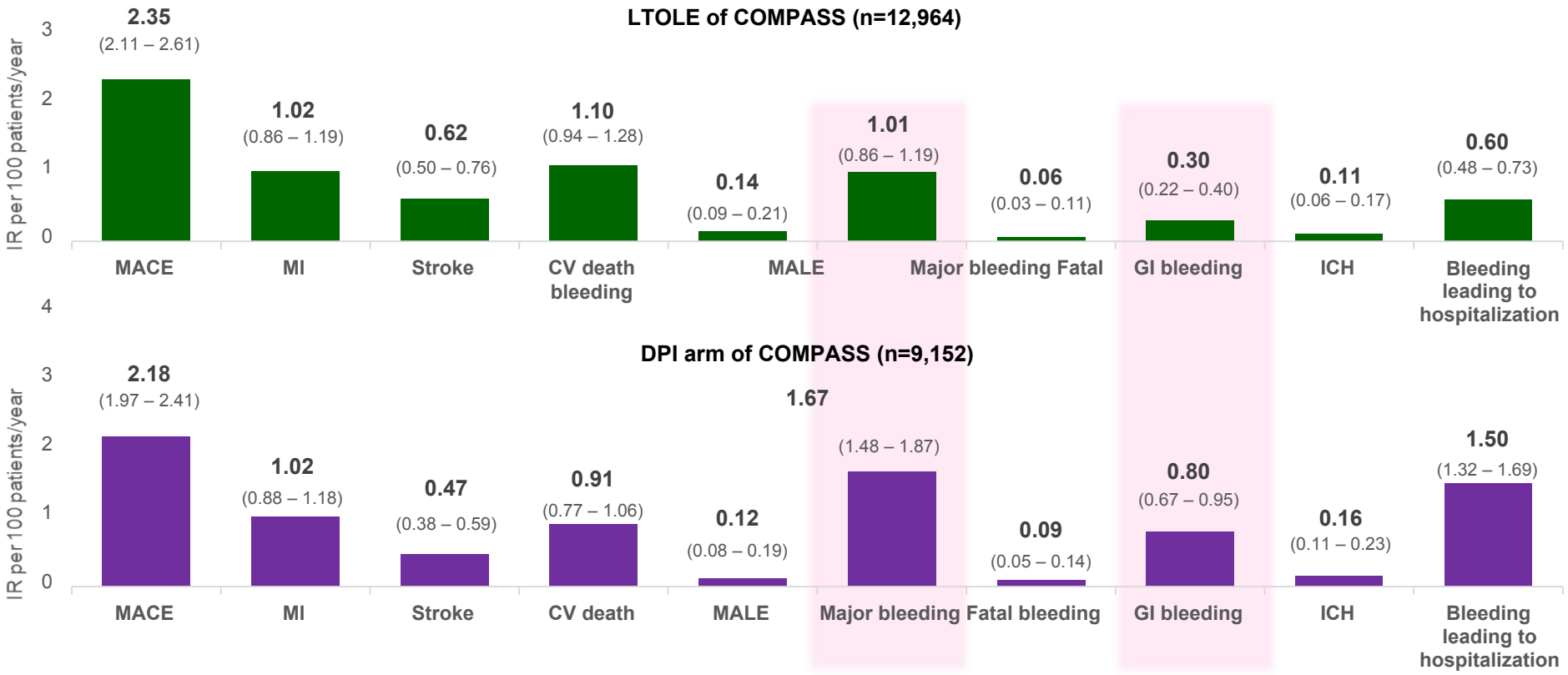
Major Bleeding in the COMPASS Trial



Eikelboom, J.W. et al. J Am Coll Cardiol. 2019;74:1519

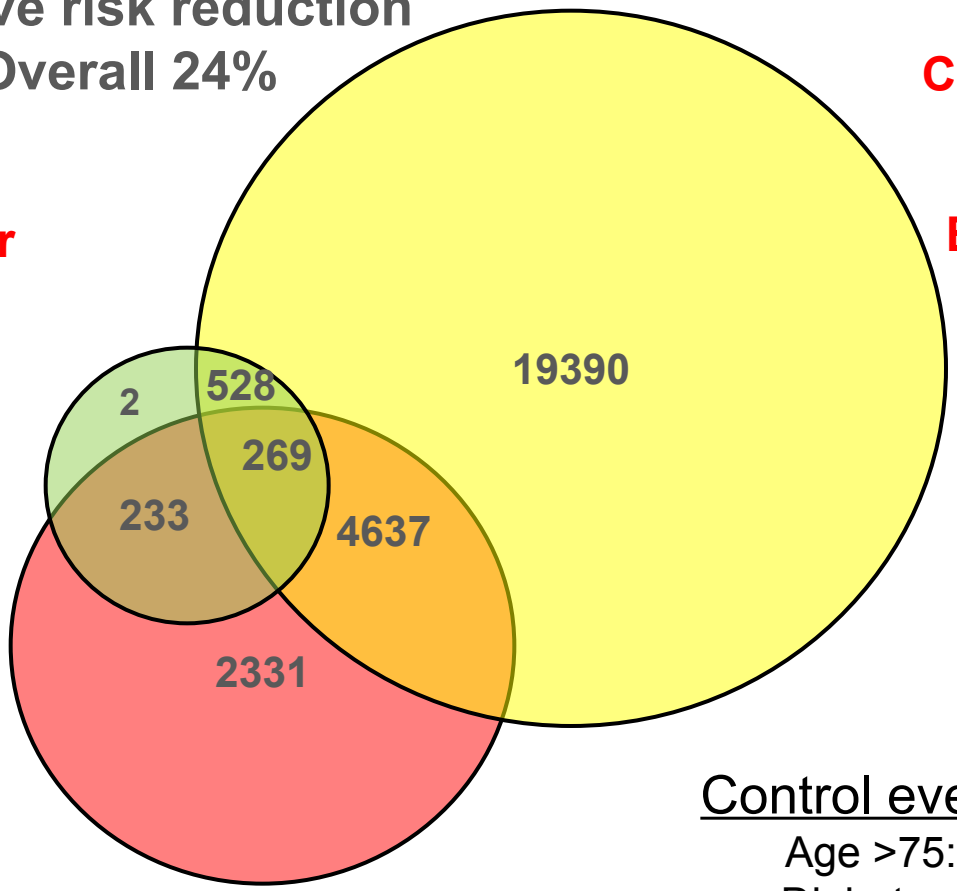
Consistent Efficacy and Lower Bleeding Risk was Seen in COMPASS LTOLE (Long-Term Open Label Extension)

- All participants received **DPI** in LTOLE study regardless of the original treatment assignment in COMPASS
- Mean follow-up of **15.7 months** with up to further 3 years



Eur Heart J Cardiovasc Pharmacother. 2022 Apr 6;pvac023

COMPASS at a Glance



Control event rates

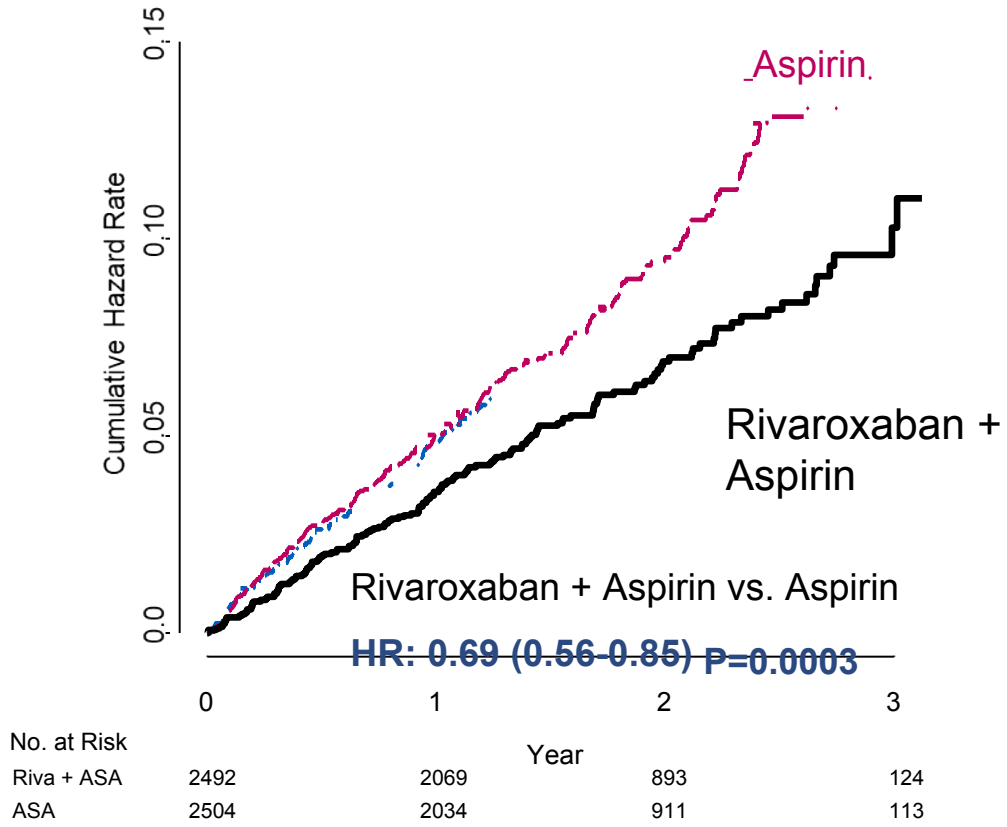
Age >75: 7.3%

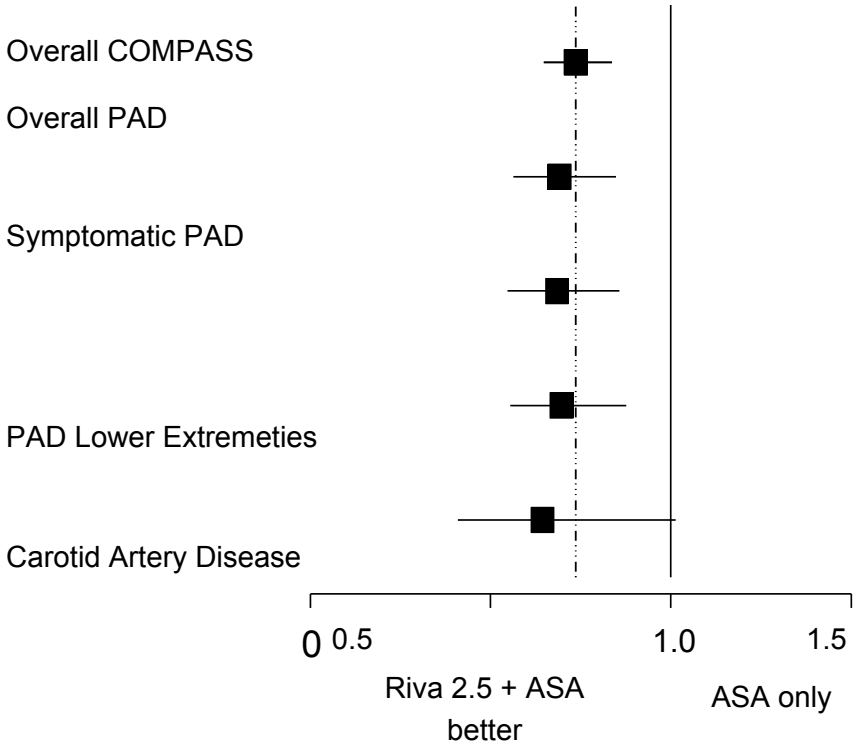
Diabetes: 6.9%

GFR<60: 8.4%

CAD and PAD: 8.4%

PAD Pts in COMPASS: MACE or MALE or Major Amputation

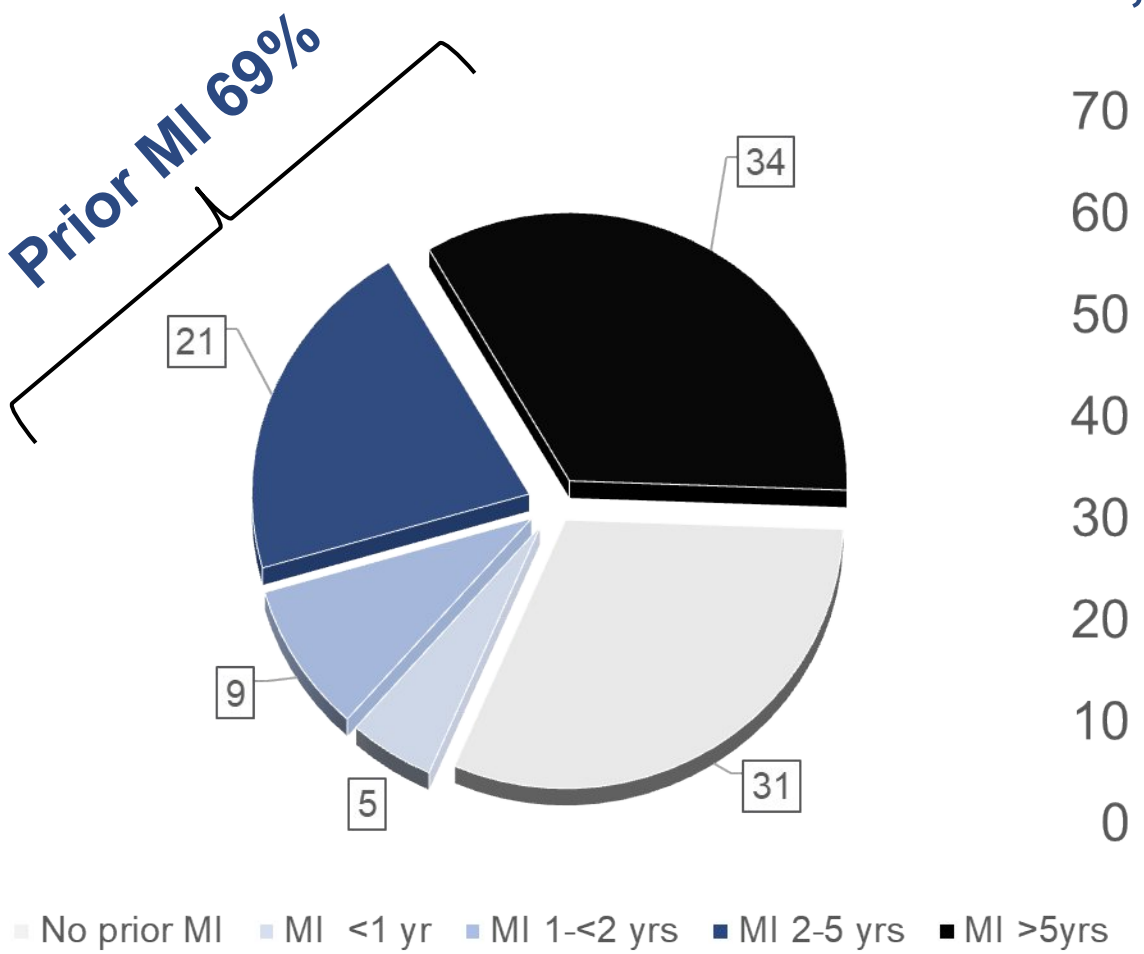


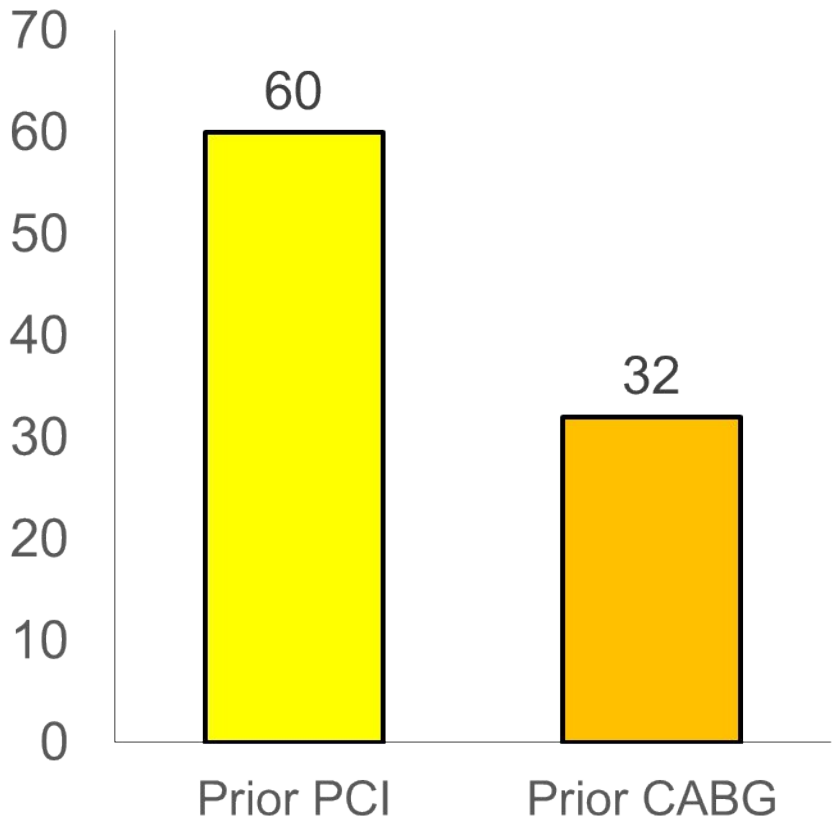


Anand SS, et al. Lancet 2017

Patients with CAD Enrolled in the COMPASS

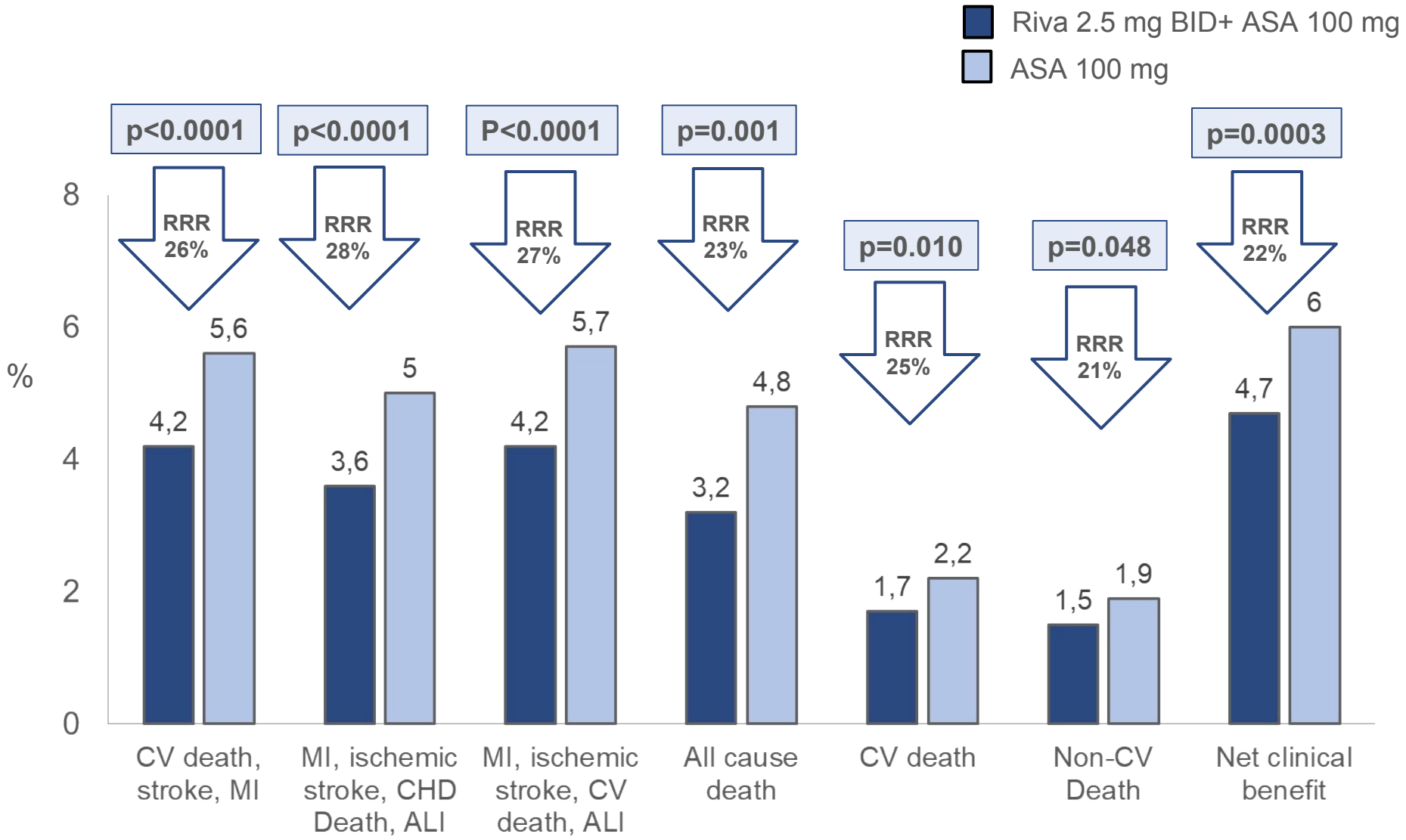
Patients with CAD 24,824 (90,5%)





1. Connolly SJ et al, Lancet 2017; doi:10.1016/S0140-6736(17)32816-7;
2. Bosch J et al, Can J Cardiol 2017;33:1027–1035

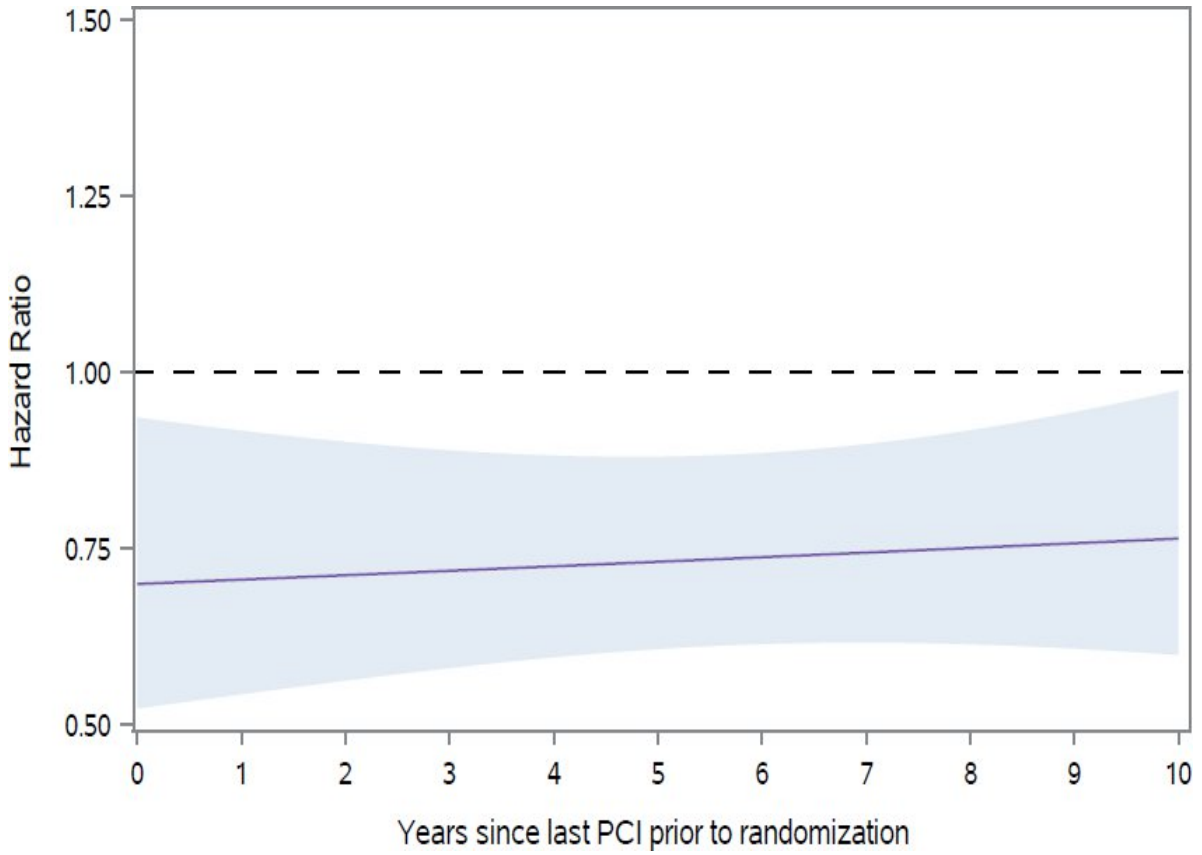
Ischemic Events in COMPASS CAD



Connolly SJ et al, Lancet 2017

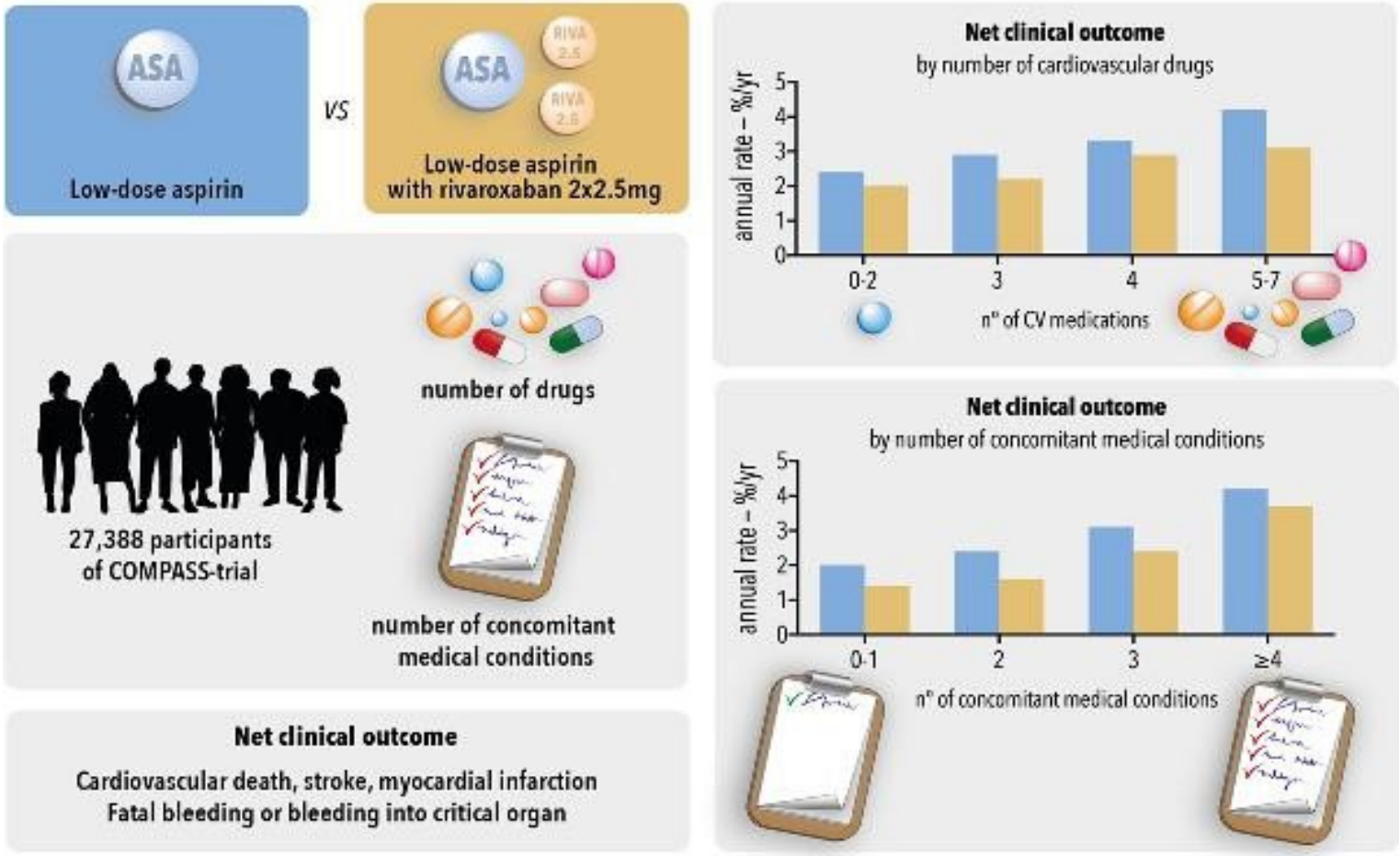
Benefit of Riva+ASA as a Function of Time from Last PCI

CV Death, MI, Stroke



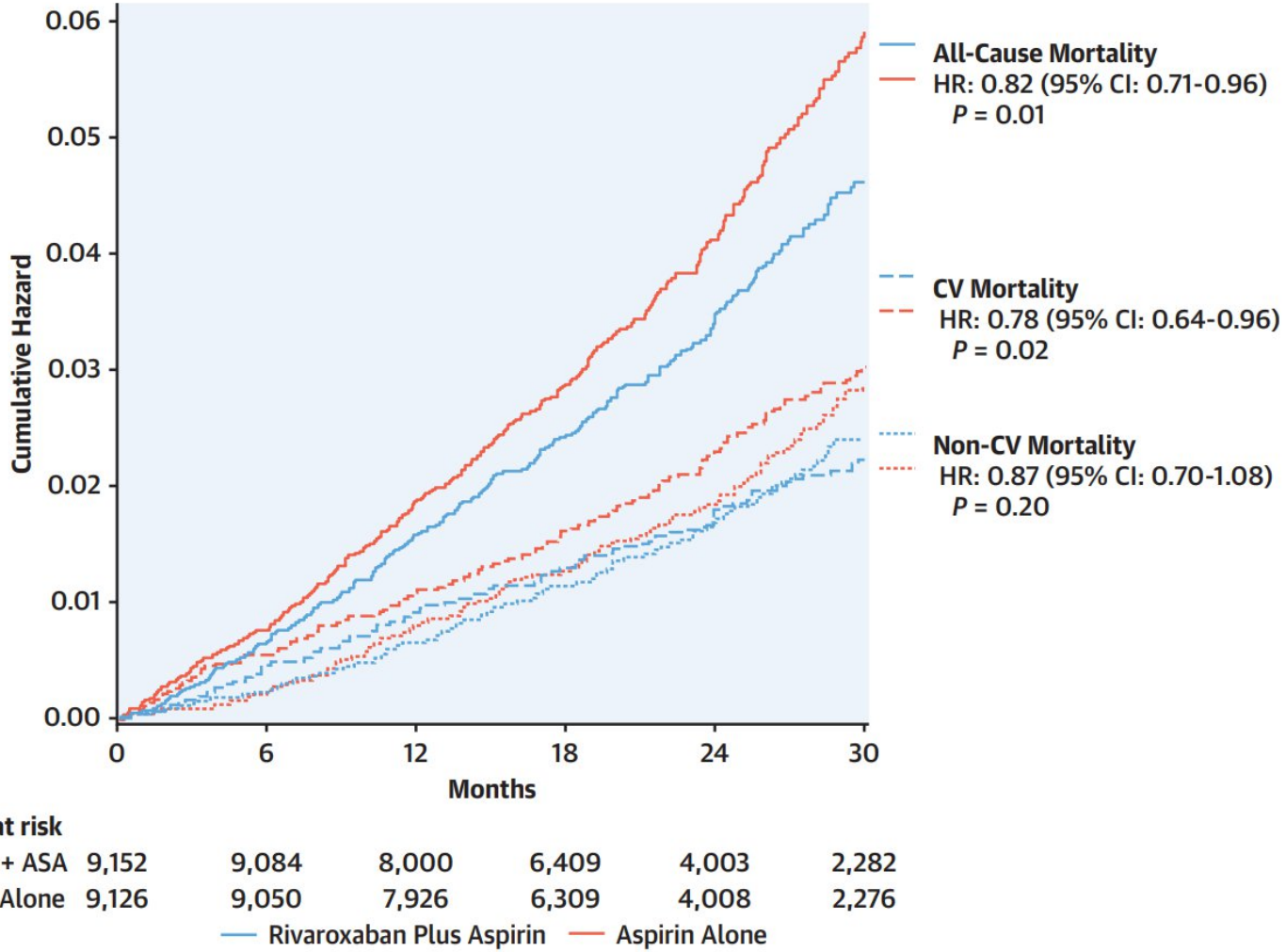
The p-value of interaction between treatment group and time since percutaneous coronary intervention was 0.66

Low-dose rivaroxaban plus aspirin in patients with polypharmacy and multimorbidity



Vanassche T, et al. EHJ: Card Pharmacot 2021

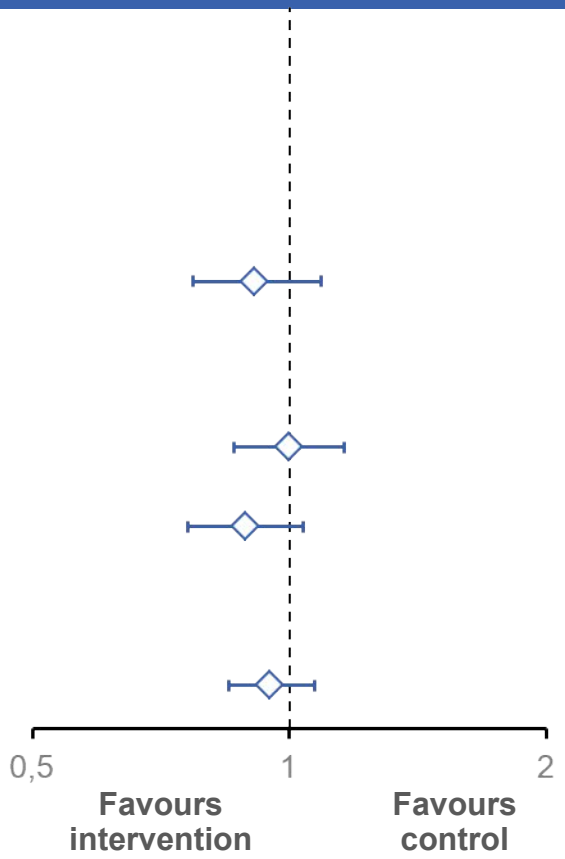
Mortality Benefit of Rivaroxaban Plus Aspirin in Patients With CAD or PAD



Eikelboom JW, et al. J Am Coll Cardiol 2021;78:14

RCTs and Overall Survival in Patients with CAD or PAD

Study / Treatment arm	Control %/year	Intervention %/year	HR	HR (95% CI)	*p*-value
CHARISMA[2]					
Clopidogrel 75 mg od	2.3‡	2.1‡	0.91		0.32
PEGASUS[3]					
Ticagrelor 90 mg bid	1.7¶	1.7¶	1.00		0.99
Ticagrelor 60 mg bid	1.7¶	1.6¶	0.89		0.14
TRA2P-TIMI 50[4]					
Vorapaxar 2.5 mg od	1.8¶	1.7¶	0.95		0.41

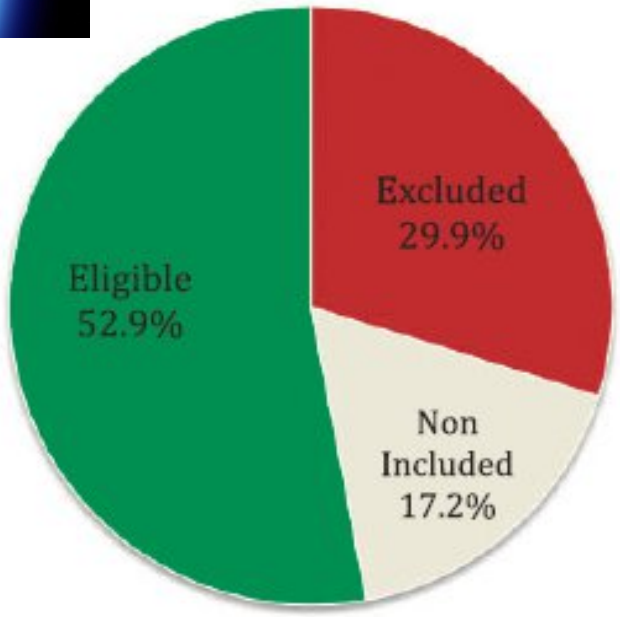


†Estimate calculated from reported overall % across 23 months of mean follow up; *p-value nominally significant because the study was stopped approximately 1 year ahead of schedule due to overwhelming efficacy;* ‡Estimate calculated from reported overall % across 28 months of median follow up; ¶Estimate calculated from reported 3-year Kaplan-Meier event rates

1. Eikelboom JW et al. N Engl J Med 2017; DOI: 10.1056/NEJMoa1709118; 2. Bhatt DL et al. J Am Coll Cardiol 2007;49:1982–1988; 3. Bonaca MP et al. N Engl J Med 2015;372:1791–1800; 4. Morrow DA et al. N Engl J Med 2012;366:1404–1413

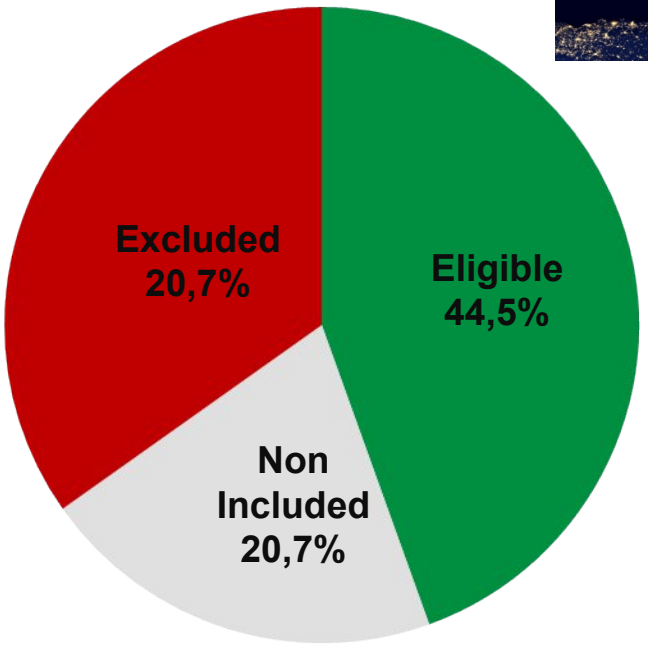
Proportion of COMPASS-Eligible Patients in the REACH and START Registry

COMPASS Evaluable
n = 31,873



Darmon A et al. Eur Heart J 2018;39:750

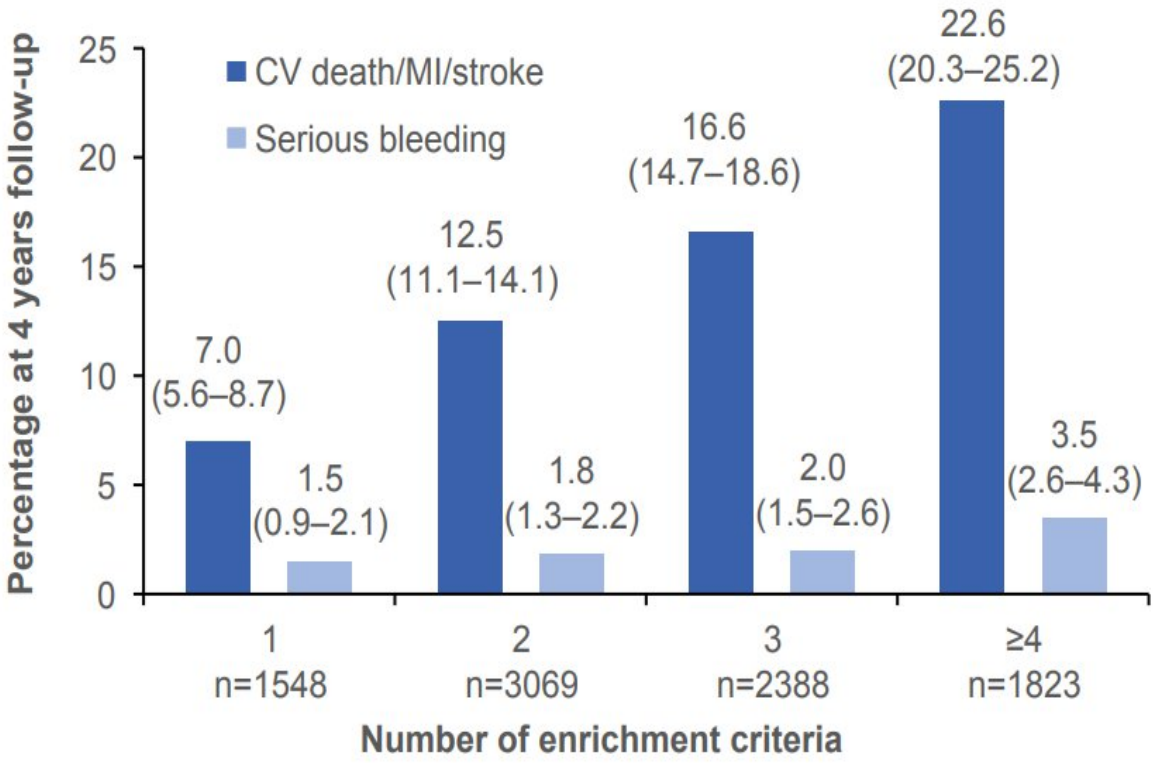
COMPASS Evaluable
N = 4,068



De Luca L, submitted

Identifying High-Benefit Patients for Dual Pathway Inhibition: The REACH Registry

Ischaemic and bleeding outcomes in COMPASS-eligible patients in the REACH registry according to the number of enrichment criteria[1]



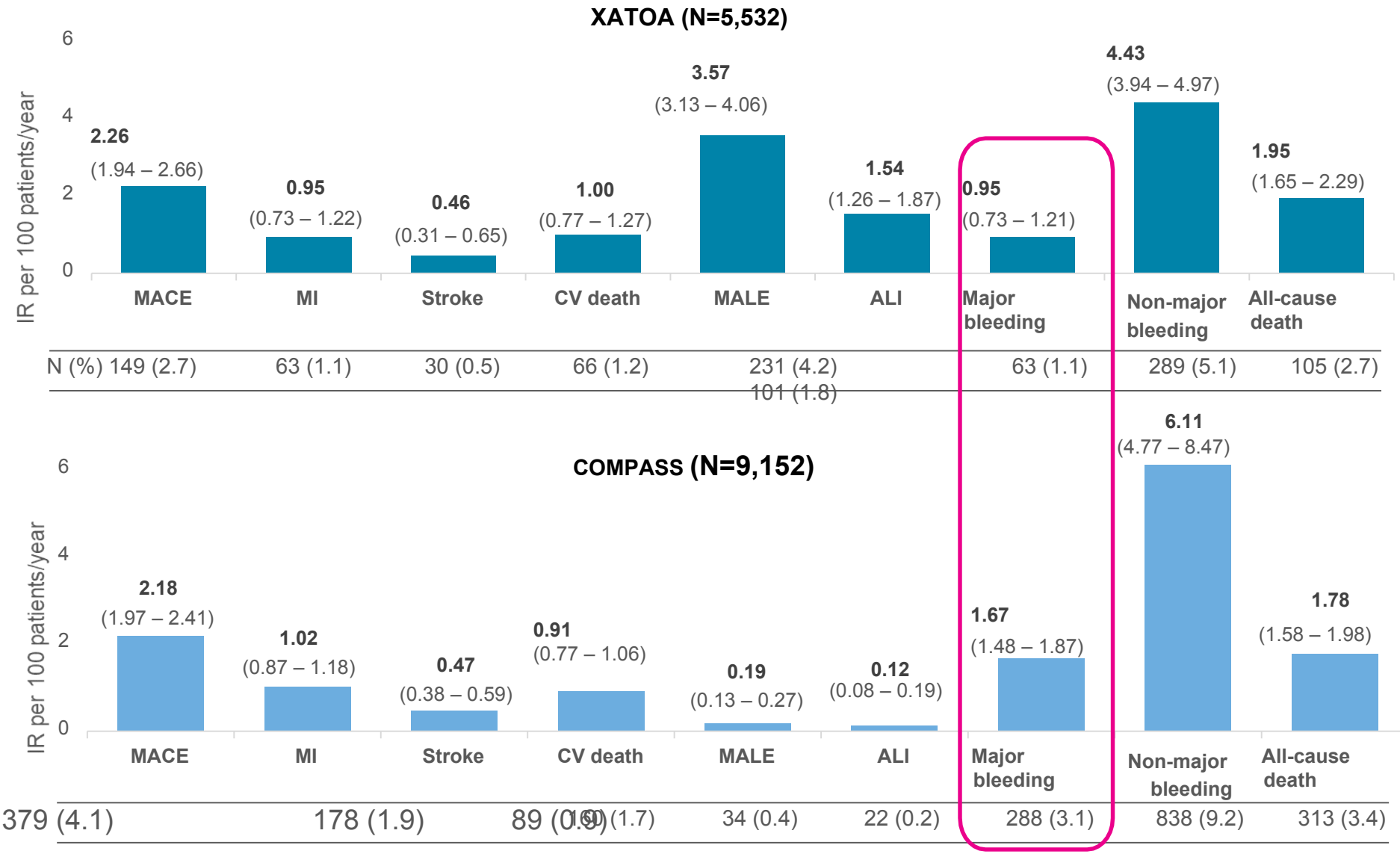
Values show above the bars are % (95% CI)

Enrichment criteria:

- Age >65 years old
- Smoking
- Diabetes
- Renal dysfunction
- HF
- Carotid disease
- PAD
- Prior stroke

Darmon A, et al. J Am Coll Cardiol 2019;73:3281

Consistent MACE Effectiveness with Low Bleeding Risk in Real World Practice



Zeymerl et al, @ ACC 2022 poster presentation

Actual Proven Effective Secondary Prevention Therapies

	Lipid lowering (1 mmol/L)	BP lowering (10 mm Hg)	ACE-I	Riva+ASA (COMPASS)	SGLT2 Inh (Empagliflozin)	PCSK9 Inh (Alirocumab)
MACE	**-21%**	**-20%**	**-18%**	**-24%**	**14%**	**-14%**
Mortality	**-9%**	**-13%**	**-14%**	**-18%**	**-32%**	**-15%***
Stroke	**-15%**	**-27%**	**-23%**	**-42%**	**+18%***	**-27%**
MI	**-24%**	**-17%**	**-18%**	**-14%***	**-13%**	**-12%**

*not formally significant

Yusuf S et al. N Engl J Med 2000;342:145; ATT Collaboration Lancet 2009;373:1849
Ettehad D, et al. Lancet 2016;387:957; CTT Collaboration Lancet 2015;385:1397;
Collins R et al. Lancet 2016;388:2532; Eikeboom et al N Engl J Med 2017;377:1319;
Zimman B et al. N Engl J Med 2015;373:2117; Schwart GG et al. N Engl J Med 2018;379:2097