AZIENDA
OSPEDALIERA
SAN PIO
BENEVENTO

Unità Operativa Complessa

Cardiologia Interventistica e UTIC

Direttore : Dr Marino Scherillo

Follow up integrato Ospedale Territorio Paziente Cronico post SCA

Marino Scherillo

Congresso CARD, Pisa 24 maggio 2019

Regione Campania
Il Commissario ad Acta per l'attuazione
del Piano di rientro dai disavanzi del SSR campano
(Deliberazione Consiglio dei Ministri 10/07/2017)

DECRETO N. 32 DEL 25.03.2019

OGGETTO: **Approvazione del "Documento Tecnico di indirizzo sulla metodologia di stesura dei PDTA in Regione Campania".**

(Deliberazione del Consiglio dei Ministri del 10.07.2017 *acta vii: "attuazione degli interventi rivolti all'incremento della produttività e della qualità dell'assistenza erogata dagli enti del Servizio Sanitario Regionale").*

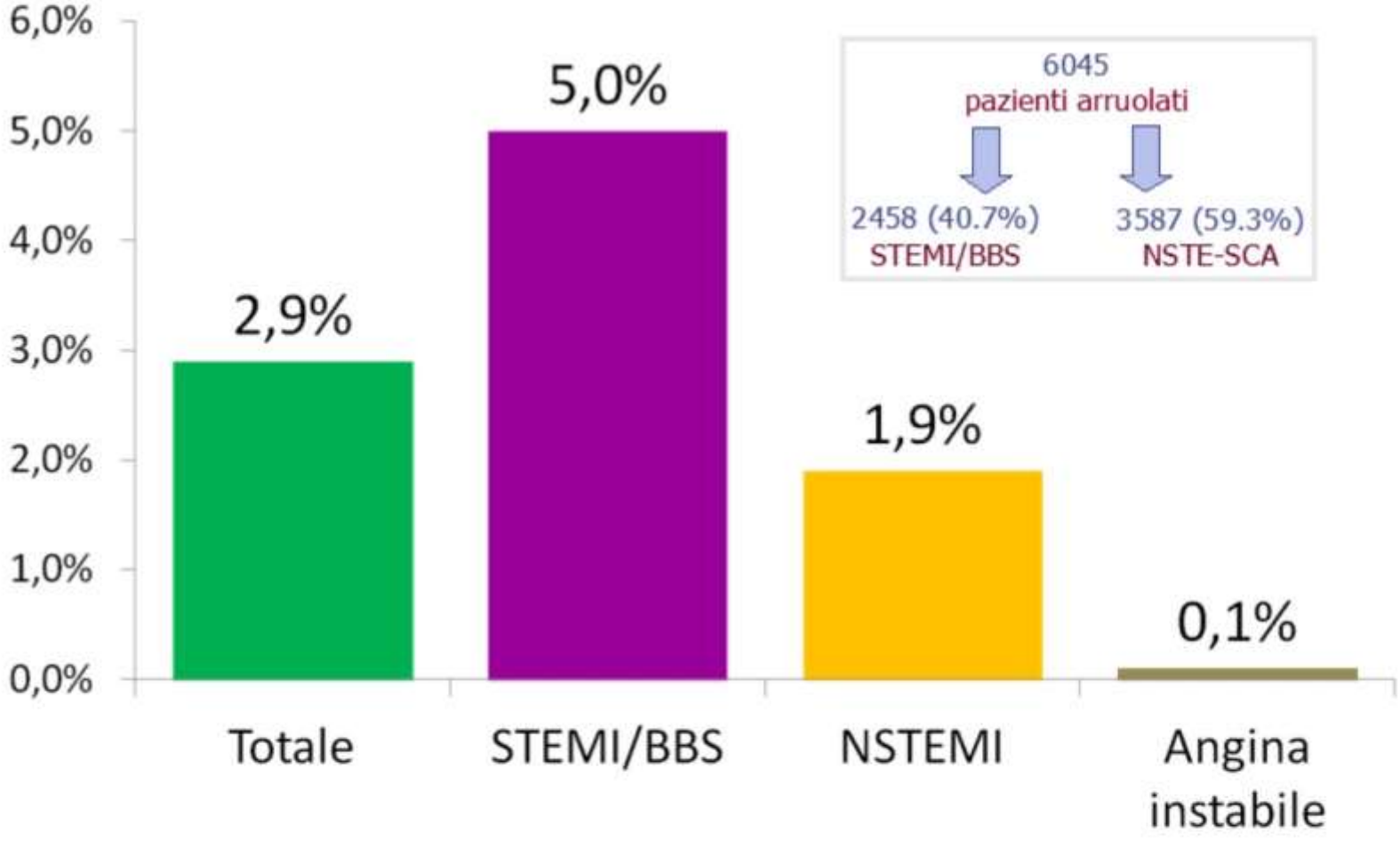
Documento tecnico di indirizzo sulla metodologia di stesura dei PDTA in Regione Campania

INDICE

1

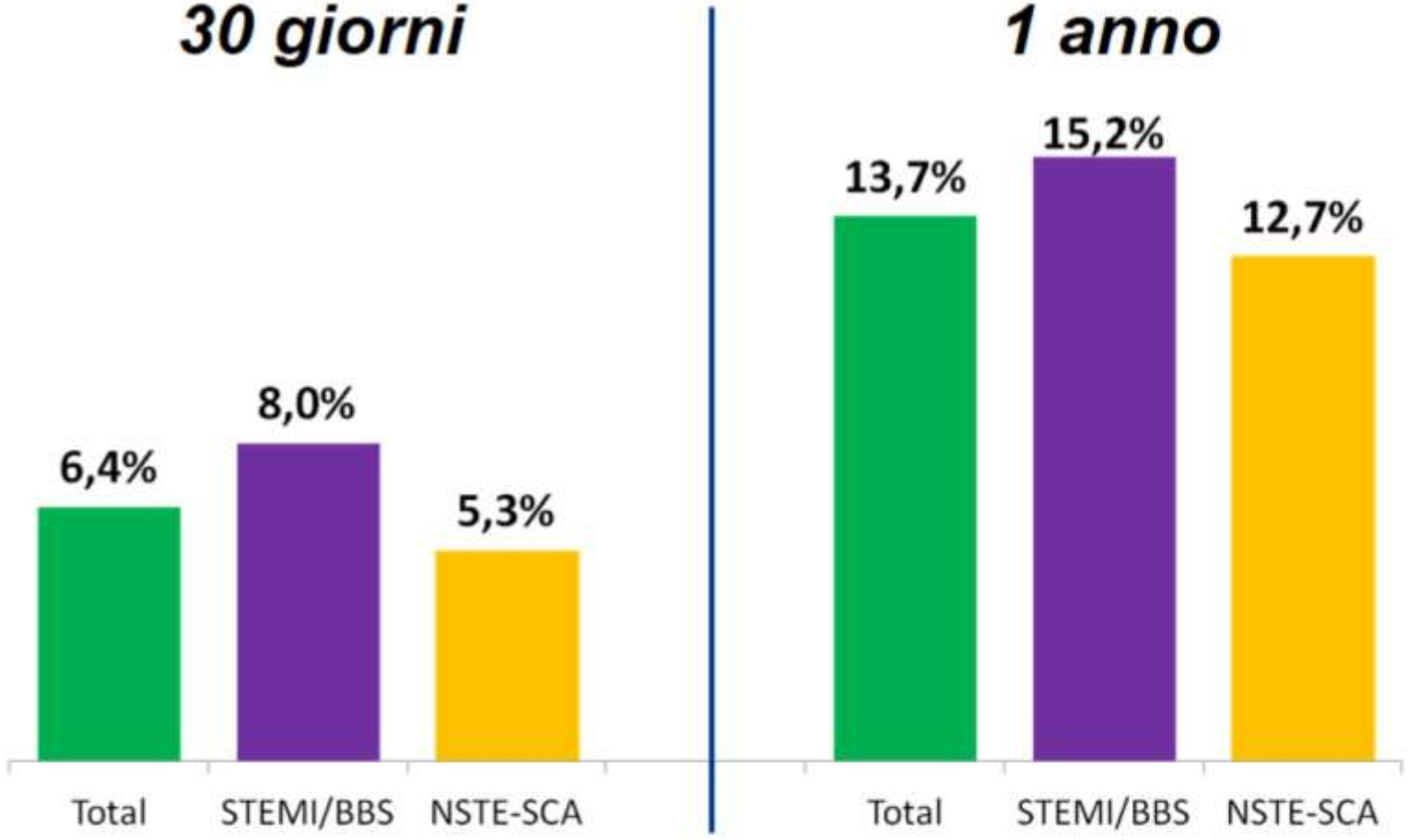
L' Infarto e' una Malattia Cronica con un Esordio Acuto

SCA : MORTALITÀ IN H NEL MONDO REALE:
REGISTRO IN-ACS OUTCOME



SCA : EVENTI 30 GIORNI E UN ANNO

Mortalità & IMA



Ministero della Salute - Agenzia Nazionale per i Servizi Sanitari Regionali

PNE 2017 ITA

INTRODUZIONE FONTI METODI APPENDICE

Programma Nazionale Esiti - PNE

PNE è uno strumento di valutazione a supporto di programmi di audit clinico e organizzativo

"PNE non produce classifiche, graduatorie, giudizi."

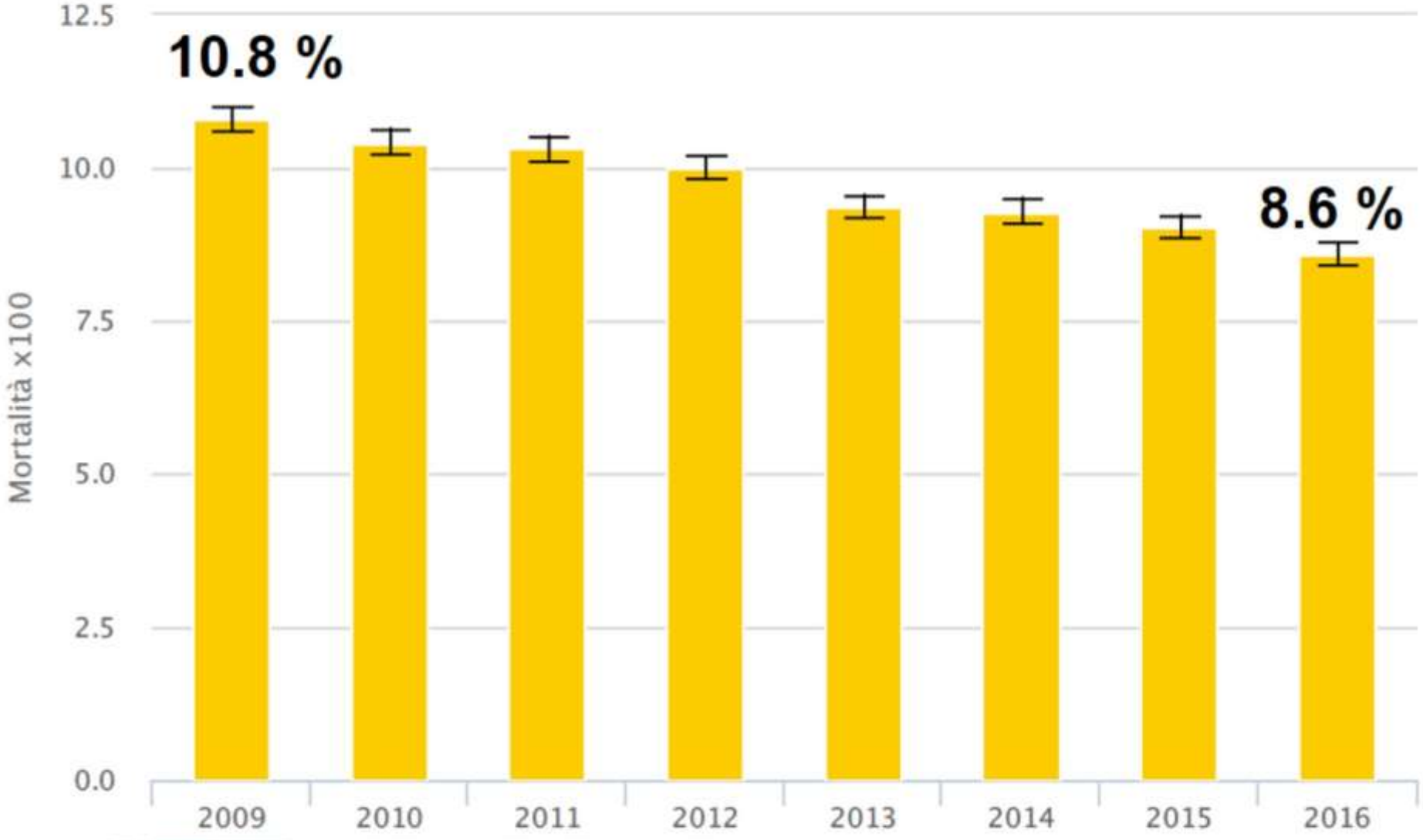
APP

PNE INFORMA

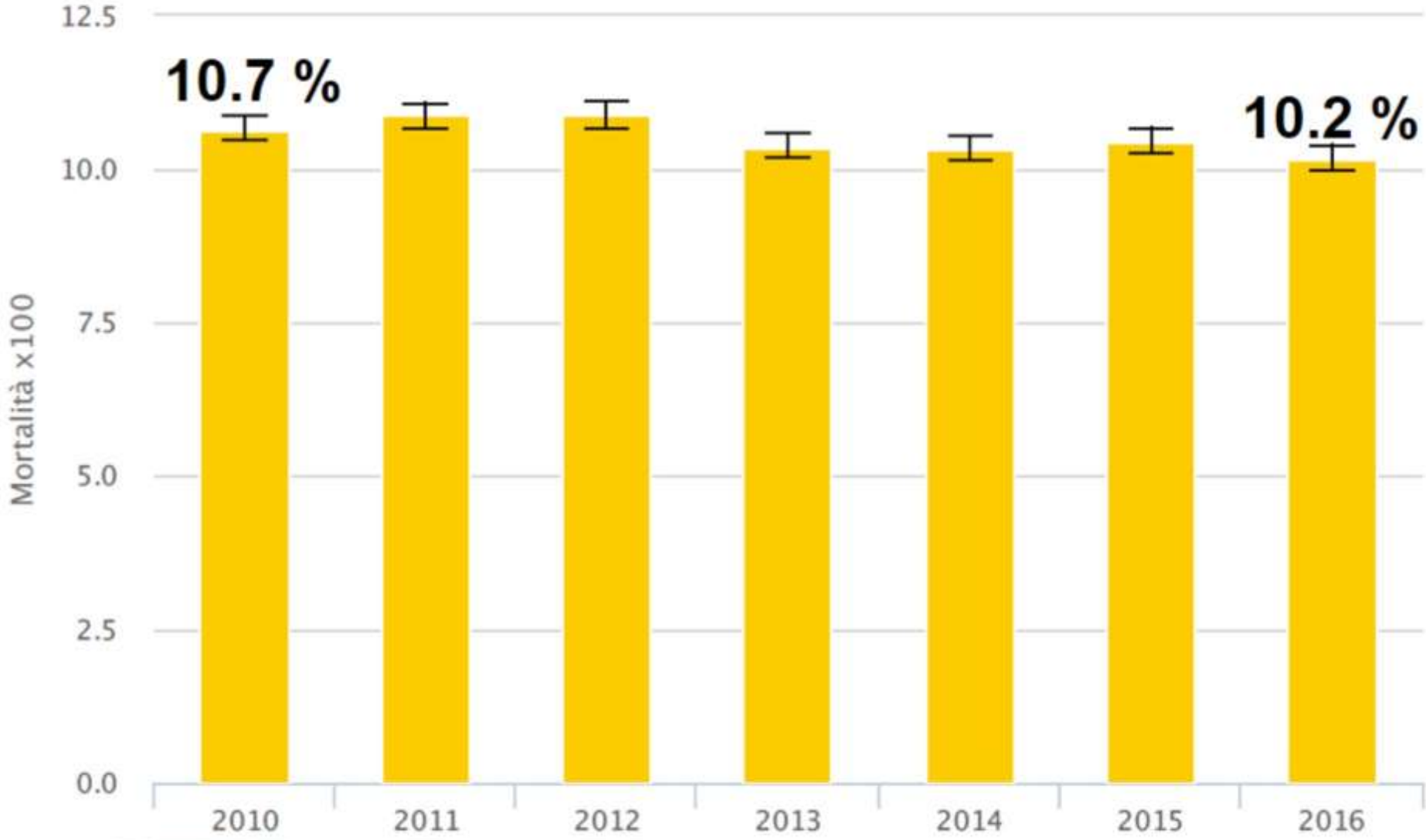
FORMAZIONE

- Formazione ECM
- Tutorial
- Panoramica del sito

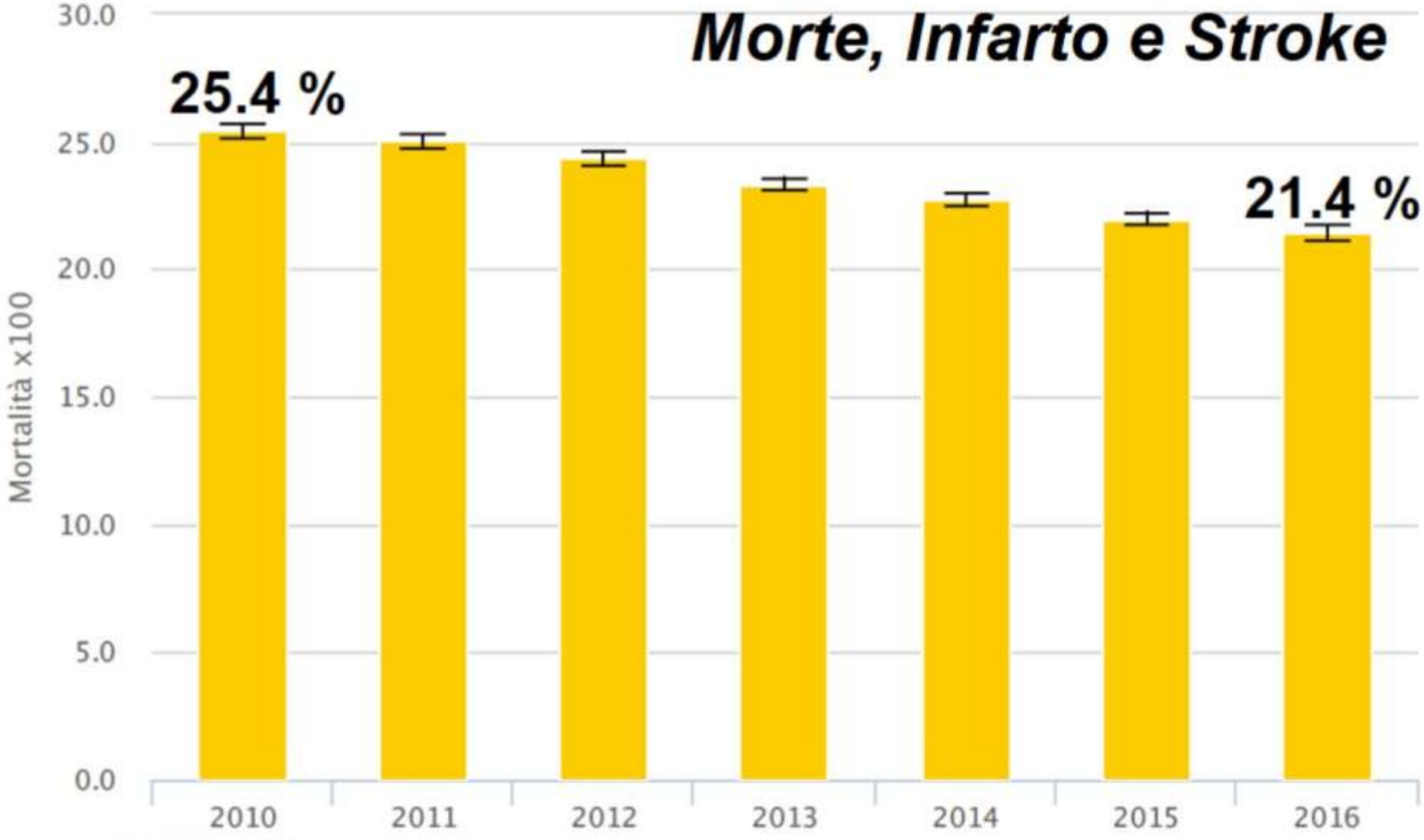
IMA : Mortalità a 30 giorni



IMA : Mortalità a 1 anno



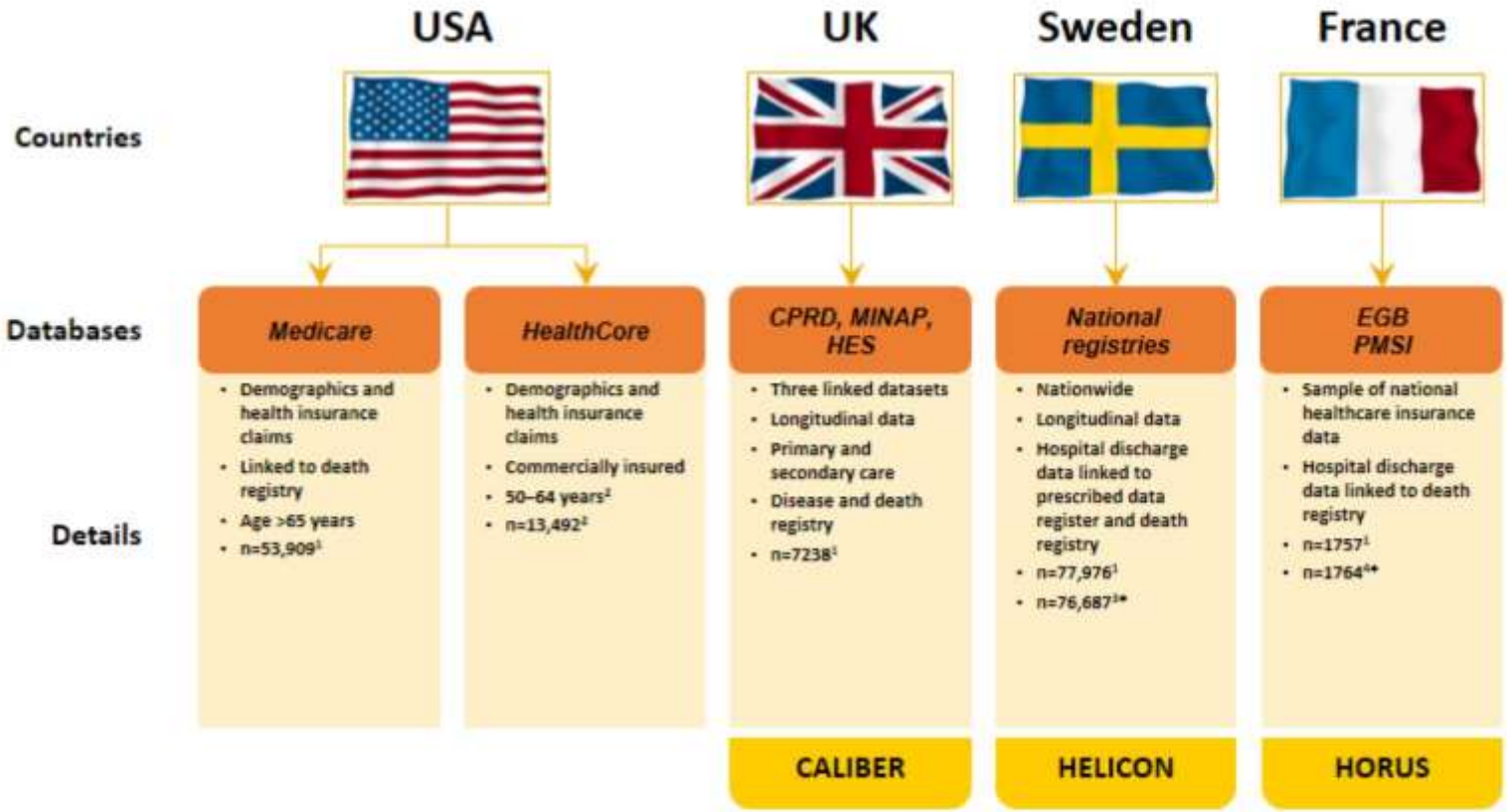
IMA : MACCE ad 1 anno



Programma Nazionale Esiti - PNE

2017

APOLLO: 5 individual studies in 4 countries encompassing > 150,000 patients



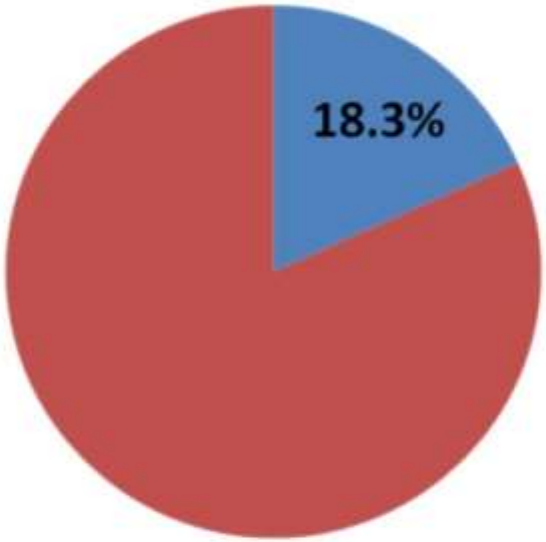
*This differs from the N in the 4-country analysis[1] due to harmonisation of the data.

CPRD, Clinical Practice Research Datalink; EGB, Échantillon Généraliste des Bénéficiaires; HES: hospital episode statistics; MINAP, Myocardial Ischaemia National Audit Project; PMSI, Programme de Médicalisation du Système d'Information.

1. Rapsomaniki E *et al.* ESC Late Breaking Registry abstract 2014: In press; 2. Mellstrom C *et al.* Value in Health 2014;17:A106–A107 (Abstract);
3. Rapsomaniki E *et al.* Eur Heart J 2014;35(Suppl 1):363 (Abstract P2077); 4. Jernberg, T. et al. Eur Heart J 2015: doi:10.1093/eurheartj/ehu505;
5. Blin P *et al.* Eur Heart J 2014;35(Suppl 1):150 (Abstract P790).

~ 1 in 5 patients suffered an MI, Stroke or CV Death within 1 year after an MI

APOLLO HELICON Sweden analysis
Immediate post-MI survivors (n=97,254)[Jernberg 2014]

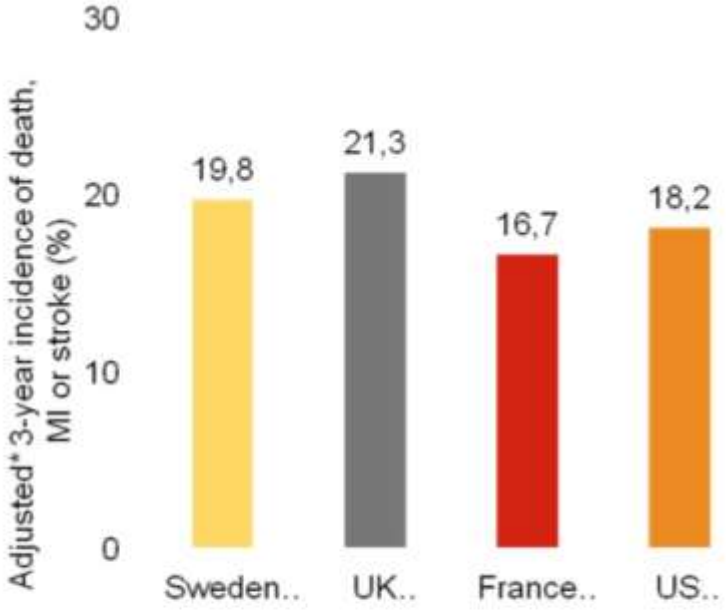


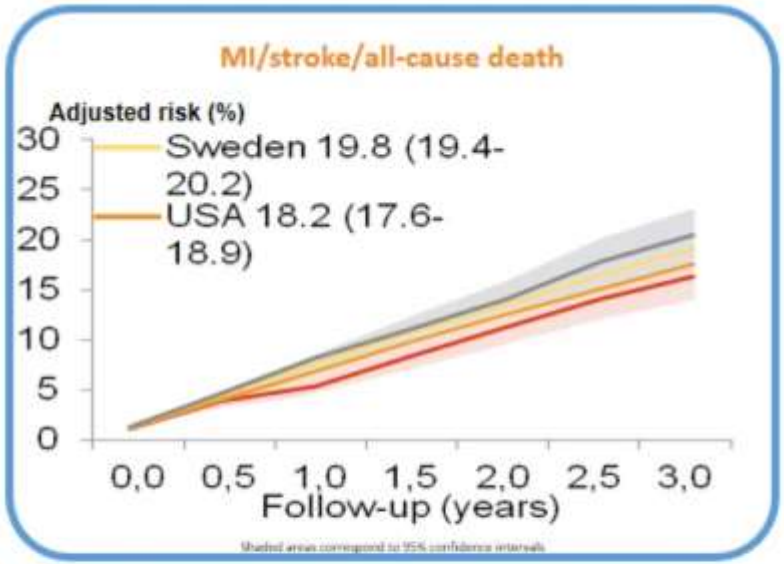
18.3 % Cumulative first year incidence of CV death, MI or stroke (%)

CV, cardiovascular; MI, myocardial infarction.
Jernberg, T. et al. Eur Heart J 2015: doi:10.1093/eurheartj/ehu505

~ 1 in 5 patients were event free for the first year post-MI suffered an MI, Stroke or CV Death within 3 years

APOLLO 4-country analysis: adjusted incidence*[Rapsomaniki 2014]

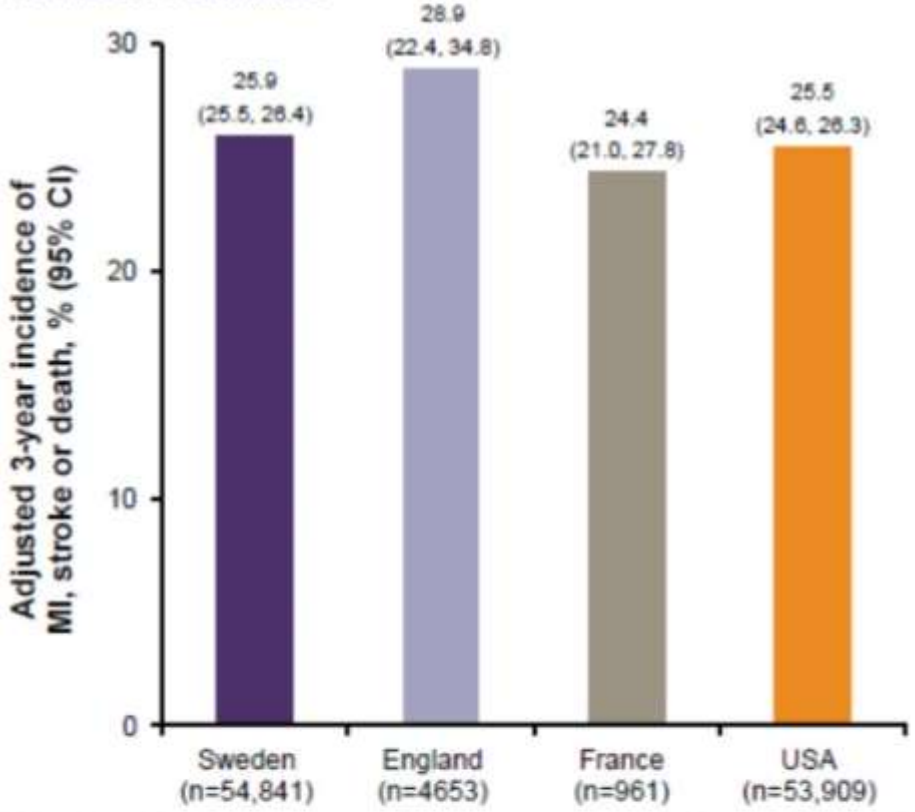


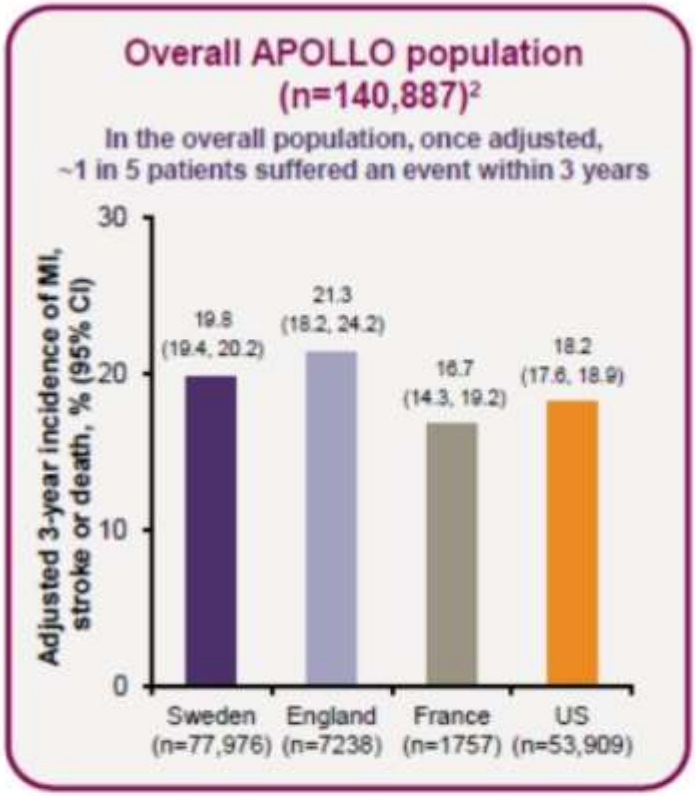


MI, myocardial infarction.
*Adjusted for differences in study populations; MI, myocardial infarction. Shaded areas / figures in brackets [95%CI]
1. Rapsomaniki E *et al.* ESC Late Breaking Registry presentation 2014.

~ 1 in 4 patients aged ≥ 65 years were event free for the first year post-MI suffered an MI, Stroke or CV Death within 3 years

After adjustment*, event rates for the composite of MI, stroke and death were consistent between countries





*Adjusted for differences between countries in age, sex, year of index MI, comorbidities and revascularisation treatments

1. Rapsomaniki E *et al* submitted to *Eur Heart J Qual Care Clin Outcomes*
2. Rapsomaniki E *et al* ESC Late Breaking Registry presentation 2014

APOLLO 4-country subanalysis (Rapsomaniki 2016)

2

Riduzione del Rischio Residuo post IMA : Rivaroxaban 2.5 mg bid + ASA 100 mg od

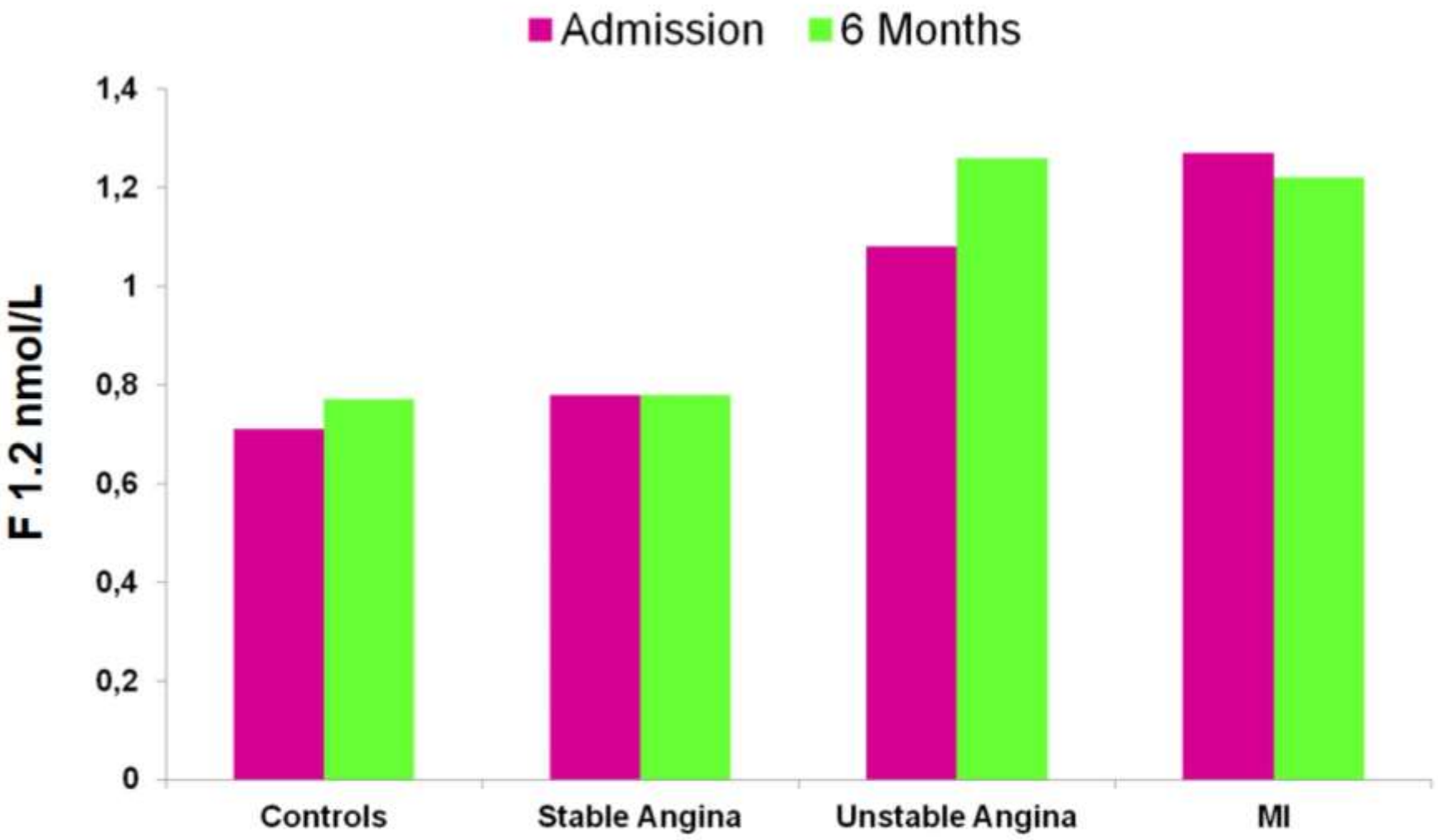
COMPASS Results

A Randomized Controlled Trial of Rivaroxaban for the Prevention of Major Cardiovascular Events in Patients With Coronary or Peripheral Artery Disease

(Cardiovascular OutcoMes for People Using Anticoagulation StrategieS)

Co-PIs: John Eikelboom & Stuart Connolly
SC Chair: Salim Yusuf
SC Co-Chair: Keith Fox

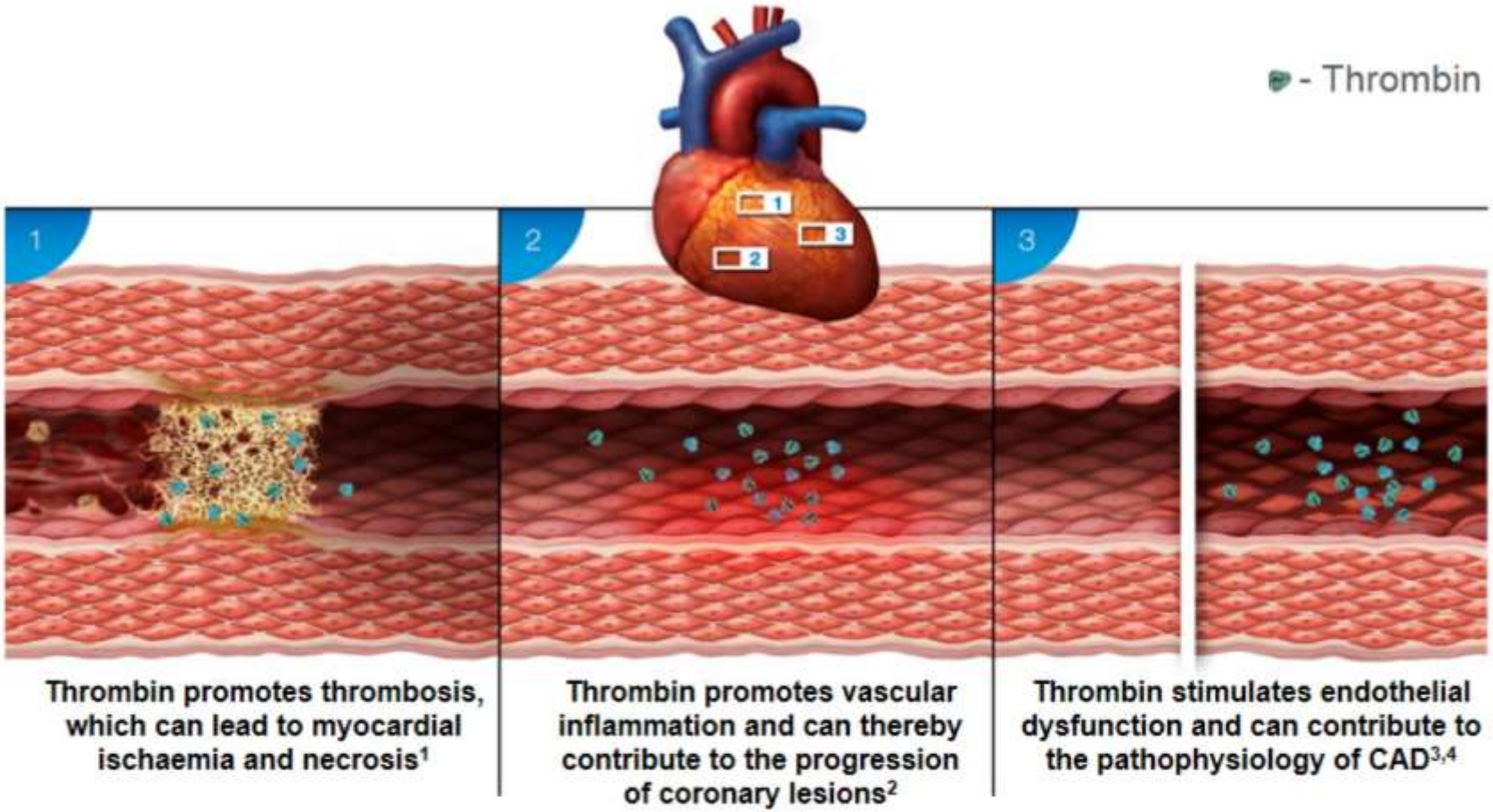
Persistent Elevation of Thrombin Generation in Post-ACS Patients



Merlini et al. Circ 1994;90:61-68

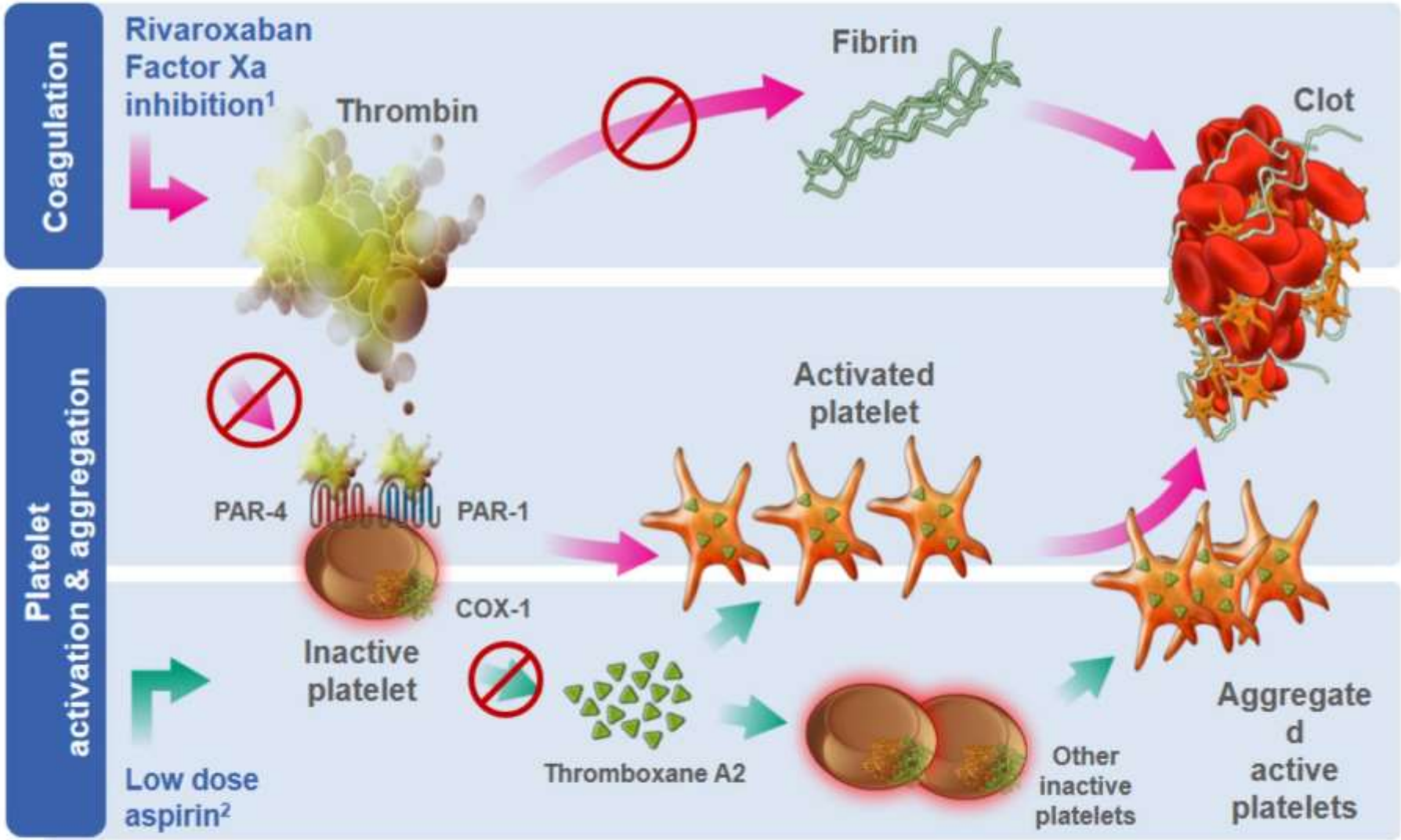
Scientific Evidence Supports Thrombin Involvement in Cardiovascular Pathophysiological Processes

Thrombin promotes myocardial necrosis, inflammation and endothelial dysfunction



1. Hansen CH *et al*, *Thromb J* 2015;13:31; 2. Popović M *et al*, *Mol Cell Biochem* 2012;359:301–313;
3. Ming XF *et al*, *Circulation* 2004;110:3708–3714; 4. Choi BJ *et al*, *Eur Heart J* 2013;34:2047–2054

Rivaroxaban and Aspirin Synergistically Target Essential Components of Atherothrombosis



Rivaroxaban impacts not only fibrin formation, but also platelet activation

1. Adapted from Angiolillo DJ *et al. Eur Heart J* 2010;31:17–28; 2. Adapted from Mitchell JRA. *BMJ* 1981;282:590–594

COMPASS Study: *Rivaroxaban Shows Overwhelming Efficacy and Meets Primary Endpoint Early*

Phase III COMPASS study with Bayer's Rivaroxaban in Patients with Coronary or Peripheral Artery Disease Shows Overwhelming Efficacy and Meets Primary Endpoint Early

Leverkusen, February 08, 2017, 04:35 p.m. CET

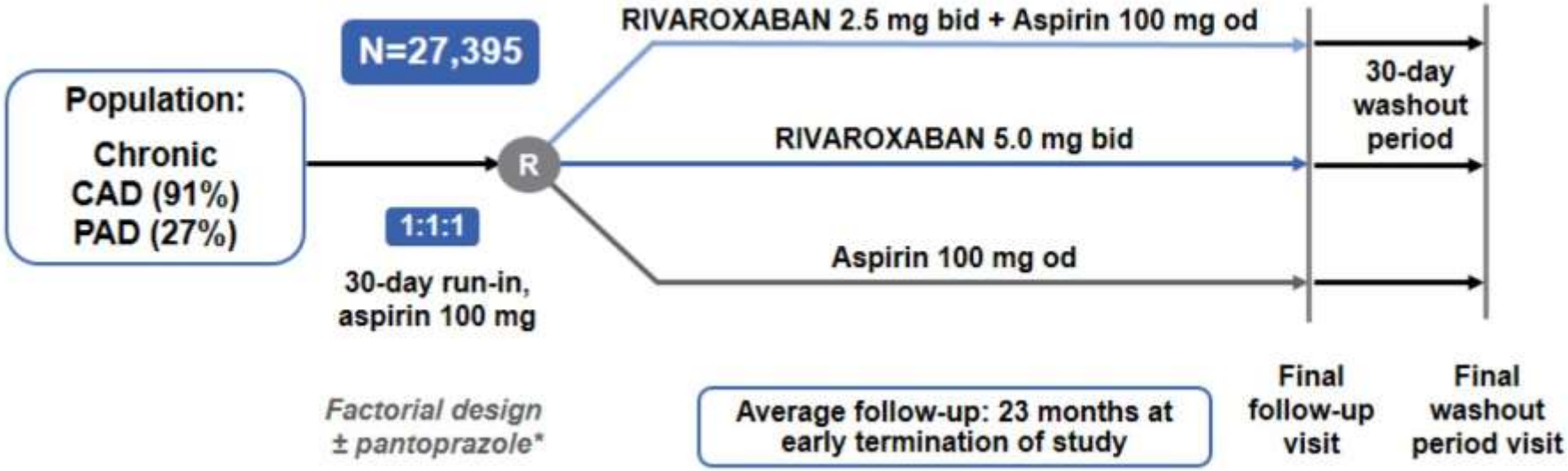
Bayer AG and its cooperation partner Janssen Research & Development, LLC today announced that the Phase III trial COMPASS evaluating the efficacy and safety of rivaroxaban (Xarelto®) for the prevention of major adverse cardiac events (MACE) including cardiovascular death, myocardial infarction and stroke in patients with coronary artery disease (CAD) or peripheral artery disease (PAD) has met its primary endpoint ahead of time. Following a planned interim analysis conducted by the independent Data Monitoring Committee (DMC), the DMC recommended to stop the trial early as the primary MACE endpoint has reached its prespecified criteria for superiority. Owing to the magnitude of effect and the confirmation of the existing safety profile of rivaroxaban, Bayer, Janssen and the Population Health Research Institute (PHRI) will offer rivaroxaban to study participants in an open-label extension trial. The COMPASS study is the largest clinical study of rivaroxaban to date.

The Phase III COMPASS study was conducted in collaboration with the PHRI and has enrolled 27,402 patients from more than 600 sites across more than 30 countries worldwide. In the study, patients were randomized to receive either rivaroxaban 2.5 mg twice daily in addition to aspirin 100 mg once daily, rivaroxaban 5 mg twice daily alone, or aspirin 100 mg once daily alone.

A complete data analysis from this study is expected to be presented at an upcoming medical meeting in 2017.

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

*Patients who were not receiving a proton pump inhibitor (PPI) were randomized to pantoprazole or placebo (partial factorial design); the PPI pantoprazole component of the study is continuing; data will be communicated once complete

1. Eikelboom JW *et al. N Engl J Med* 2017; DOI: 10.1056/NEJMoa1709118;
2. Bosch J *et al. Can J Cardiol* 2017;33(8):1027–1035

COMPASS

Inclusion and Exclusion Criteria Ensure That Patients Are Chronic CAD and PAD Patients

Key INCLUSION criteria*

- PAD
- CAD with ≥1 of:
  - Age ≥65 years
  - Age <65 years plus atherosclerosis in ≥2 vascular beds or ≥2 additional risk factors
    - Current smoker
    - Diabetes mellitus
    - Renal dysfunction (eGFR<60 ml/min)
    - Heart failure
    - Non-lacunar ischemic stroke ≥1 month ago

Key EXCLUSION criteria‡

- Stroke ≤1 month or any haemorrhagic or lacunar stroke
- Severe HF with known ejection fraction <30% or NYHA class III or IV symptoms
- Need for dual antiplatelet therapy, other non-aspirin antiplatelet therapy, or oral anticoagulant therapy
- eGFR <15 ml/min

*Including but not limited to; ‡any other exclusion criteria in conjunction with the local Product Information and any other contraindication listed in the local labelling for rivaroxaban or the comparator have to be considered

www.clinicaltrials.gov/ct2/show/NCT01776424 [accessed 21 Mar 2017];
Bosch J *et al*, *Can J Cardiol* 2017;33:1027–1035

COMPASS

Main Study Outcomes

Primary efficacy outcome

- Composite of MI, stroke or CV death

Secondary efficacy outcomes

- Composite of major thrombotic events
  - Coronary heart disease death, MI, ischaemic stroke, acute limb ischaemia
  - Cardiovascular death, MI, ischaemic stroke, acute limb ischaemia
- Mortality (all cause)

Primary safety outcome

- Modified ISTH major bleeding
  - Fatal bleeding, *and/or*
  - Symptomatic bleeding in a critical area or organ, such as intracranial, *or*
  - Bleeding into the surgical site requiring re-operation, *and/or*
  - Bleeding leading to hospitalization

Eikelboom JW *et al. N Engl J Med* 2017; DOI: 10.1056/NEJMoa1709118

COMPASS

Modified ISTH Major Bleeding Definition Applied at Regulators' Request with the Intent of Capturing all Bleeding that Required Medical Attention

ISTH major bleeding[1]	Modified ISTH major bleeding (COMPASS)
◆ Fatal bleeding, *and/or*	◆ Fatal bleeding, *and/or*
◆ Symptomatic bleeding in a critical area or organ (such as intracranial), *and/or*	◆ Symptomatic bleeding in a critical area or organ (such as intracranial), *or*
◆ ***Bleeding causing a drop in haemoglobin level of ≥20 g/l, or leading to transfusion of ≥2 units of whole blood or red cells***	◆ ***Bleeding into the surgical site requiring re-operation, and/or*** ◆ ***Bleeding leading to hospitalization***

Unlike the standard ISTH criteria, all bleeding that led to presentation to an acute care facility or hospitalization were considered as major compared with the standard ISTH major bleeding definition

1. Schulman S *et al, J Thromb Haemost* 2005;3:692–694

COMPASS

Key Baseline Characteristics Are in Line With Those Usually Seen in Patients With Chronic CAD or PAD

Characteristic	Rivaroxaban 2.5 mg bid + aspirin 100 mg N=9152	Rivaroxaban 5 mg bid N=9117	Aspirin 100 mg N=9126
Age, years	68	68	68
Blood pressure, mmHg	136/77	136/78	136/78
Total cholesterol, mmol/L	4.2	4.2	4.2
CAD, %	91	90	90
PAD, %	27	27	27
Diabetes, %	38	38	38
Lipid-lowering drugs, %	90	90	89
ACE inhibitors/ARB, %	71	72	71

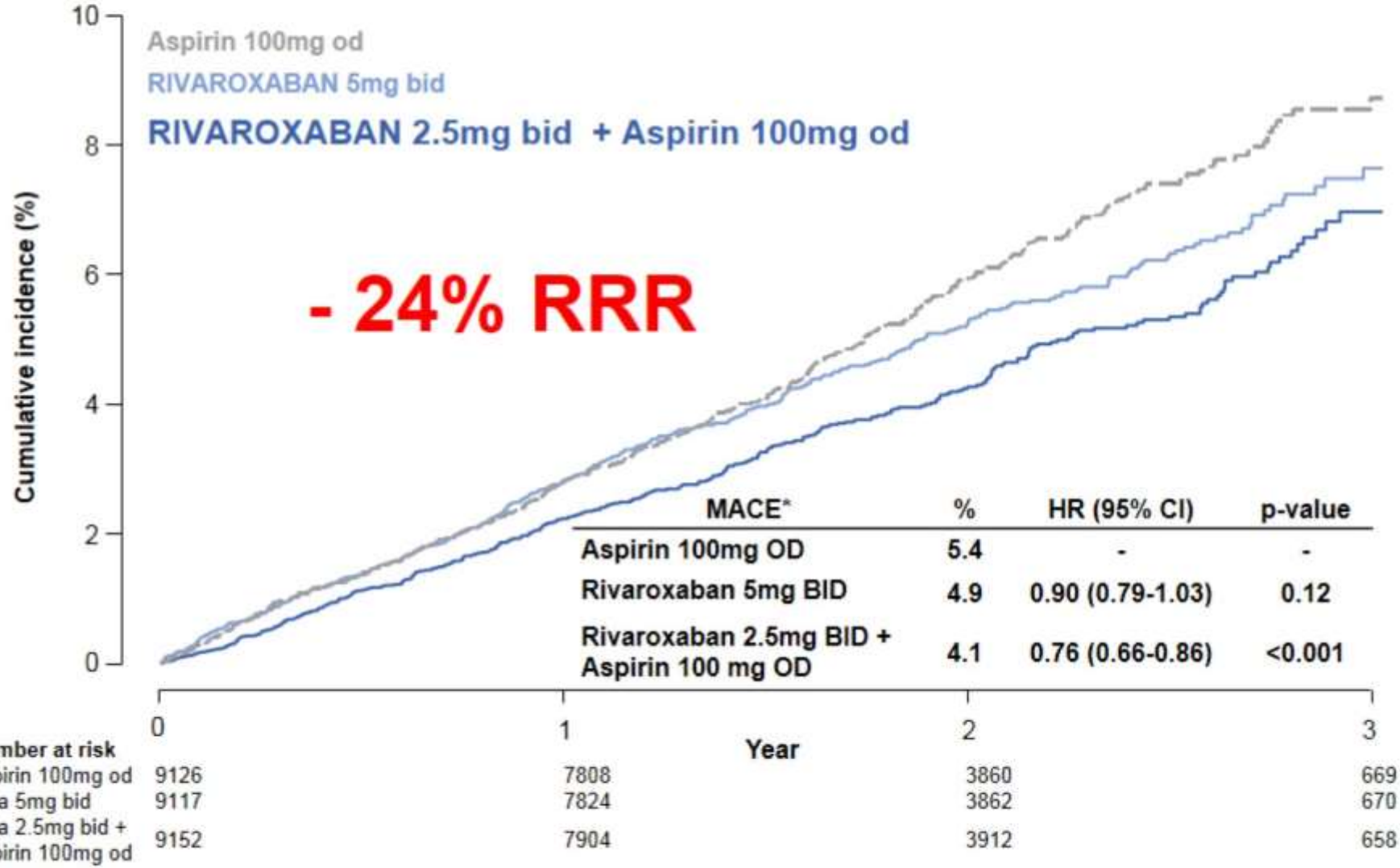
ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker

*Excluding <7 days before randomization

Eikelboom JW *et al. N Engl J Med* 2017; DOI: 10.1056/NEJMoa1709118

COMPASS

Dual Pathway Inhibition with Rivaroxaban Vascular Dose 2.5 mg bid + Aspirin Reduced CV Death, Stroke and MI



MACE*	%	HR (95% CI)	p-value
Aspirin 100mg OD	5.4	-	-
Rivaroxaban 5mg BID	4.9	0.90 (0.79-1.03)	0.12
Rivaroxaban 2.5mg BID + Aspirin 100 mg OD	4.1	0.76 (0.66-0.86)	<0.001

Number at risk				
Aspirin 100mg od	9126	7808	3860	669
Riva 5mg bid	9117	7824	3862	670
Riva 2.5mg bid + Aspirin 100mg od	9152	7904	3912	658

*Rates as at mean follow up of 23 months

Eikelboom JW *et al. N Engl J Med* 2017; DOI: 10.1056/NEJMoa1709118

COMPASS

Dual Pathway Inhibition with Rivaroxaban 2.5 mg bid + Aspirin: Significantly Reduced CV Events by 24% Versus Aspirin

Outcomes, n (%)	Rivaroxaban 2.5 mg bid + aspirin 100 mg N=9152	Aspirin 100 mg N=9126	Rivaroxaban 2.5 mg bid + aspirin 100 mg vs aspirin 100 mg	
			HR (95% CI)	*p*-value
CV death, stroke, or MI	379 (4.1)	496 (5.4)	0.76 (0.66–0.86)	<0.001
CV death	160 (1.7)	203 (2.2)	0.78 (0.64–0.96)	0.02
Stroke	83 (0.9)	142 (1.6)	0.58 (0.44–0.76)	<0.001
MI	178 (1.9)	205 (2.2)	0.86 (0.70–1.05)	0.14

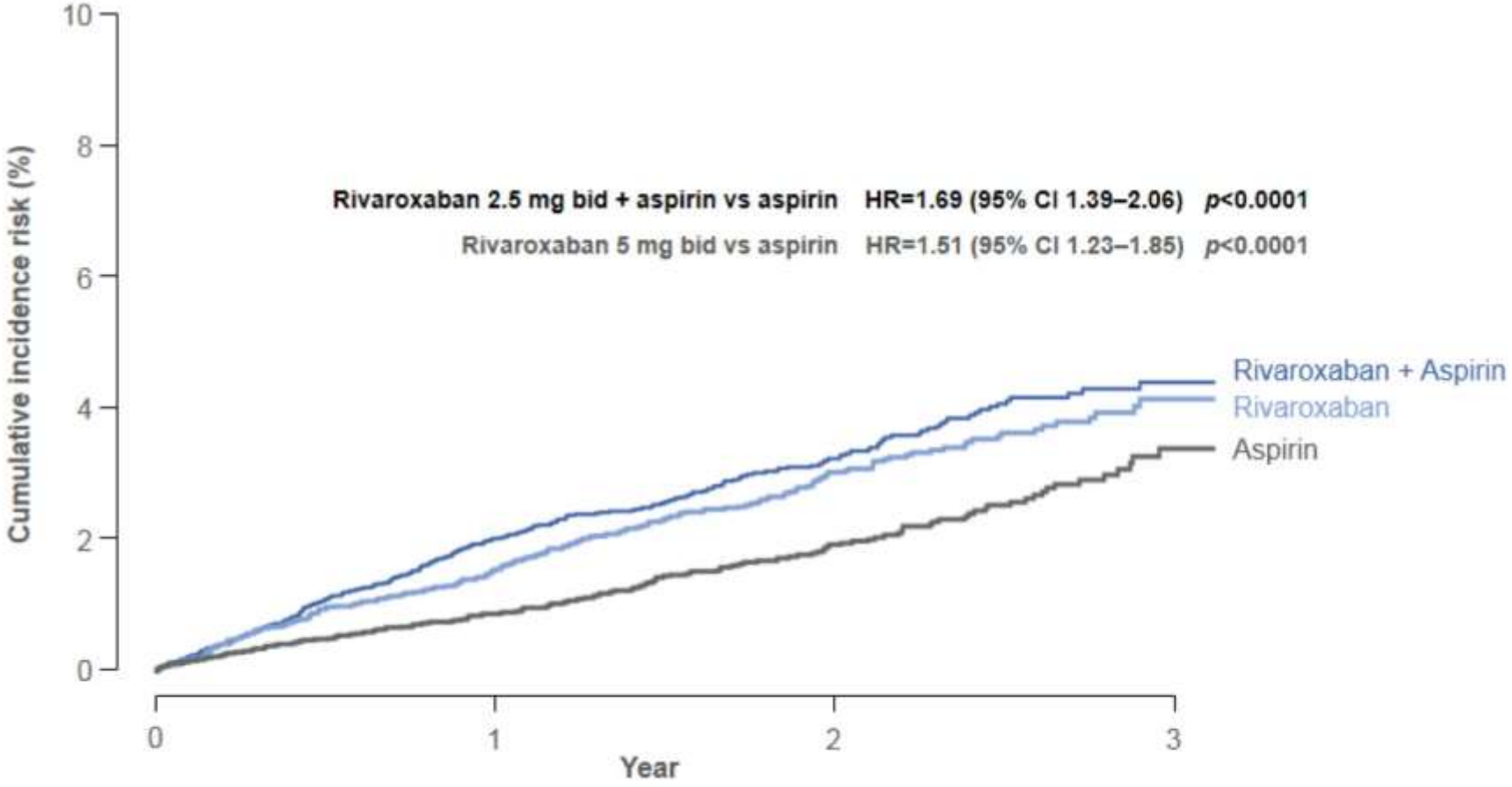
Outcomes, n (%)	Rivaroxaban 5 mg bid N=9117	Rivaroxaban 5 mg bid vs aspirin 100 mg	
		HR (95% CI)	*p*-value
CV death, stroke, or MI	448 (4.9)	0.90 (0.79–1.03)	0.12
CV death	195 (2.1)	0.96 (0.79–1.17)	0.69
Stroke	117 (1.3)	0.82 (0.65–1.05)	0.12
MI	182 (2.0)	0.89 (0.73–1.08)	0.24

Eikelboom JW *et al. N Engl J Med* 2017; DOI: 10.1056/NEJMoa1709118

COMPASS

Bleeding Rates Increased but Low with Rivaroxaban 2.5 mg bid + Aspirin Versus Aspirin Alone

Major bleeding



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

COMPASS

Bleeding Rates Increased but Low with Rivaroxaban 2.5 mg bid + Aspirin Versus Aspirin Alone, with No Differences Seen in Fatal and Intracranial Bleeding

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

The use of the standard ISTH major bleeding definition would have led to approximately one third fewer major bleeding events than with the use of the modified ISTH definition

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. *Symptomatic

Eikelboom JW *et al. N Engl J Med* 2017; DOI: 10.1056/NEJMoa1709118

COMPASS

Bleeding Events

Outcome	Rivaroxaban plus Aspirin (N=9152)	Aspirin Alone (N=9126)	Rivaroxaban plus Aspirin vs. Aspirin Alone	
			Hazard Ratio (95% CI)	P Value
Site of major bleeding				
Gastrointestinal	140 (1.5)	65 (0.7)	2.15 (1.60–2.89)	<0.001
Intracranial	28 (0.3)	24 (0.3)	1.16 (0.67–2.00)	0.60
Skin or injection site	28 (0.3)	12 (0.1)	2.31 (1.18–4.54)	0.01
Urinary	13 (0.1)	21 (0.2)	0.61 (0.31–1.23)	0.16

Eikelboom JW *et al. N Engl J Med* 2017; DOI: 10.1056/NEJMoa1709118

NET CLINICAL BENEFIT: with RIVAROXABAN 2.5 mg bid + Aspirin Versus Aspirin

- **Definition: composite of CV death, stroke, MI, fatal bleeding or symptomatic bleeding into a critical organ**
  - **In other words, net clinical benefit represented the composite of fatal and non-fatal events of irreversible harm**

Outcome	Rivaroxaban 2.5 mg bid + aspirin 100 mg N=9152	Aspirin 100 mg N=9126	Rivaroxaban 2.5 mg bid + aspirin 100 mg vs aspirin 100 mg	
			HR (95% CI)	*p*-value
Net clinical benefit	431 (4.7%)	534 (5.9%)	0.80 (0.70–0.91)	<0.001

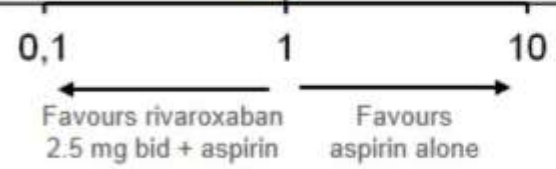
NET CLINICAL BENEFIT: RRR – 20 %

Eikelboom JW *et al. N Engl J Med* 2017; DOI: 10.1056/NEJMoa1709118

COMPASS

Dual Pathway Inhibition with Rivaroxaban 2.5 mg bid + Aspirin Demonstrated a Clear Benefit Across All Subgroups

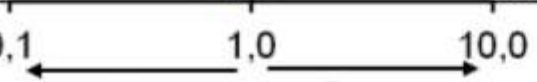
Subgroup	Rivaroxaban 2.5 mg bid + aspirin n/N (%)	Aspirin alone n/N (%)	HR (95% CI)	HR (95% CI)	*p*-value
All participants	379/9152 (4.1)	496/9126 (5.4)		0.76 (0.66–0.86)	
Age					0.20
<65 years	79/2150 (3.7)	126/2184 (5.8)		0.63 (0.48–0.84)	
65–75 years	179/5078 (3.5)	238/5045 (4.7)		0.74 (0.61–0.90)	
≥75 years	121/1924 (6.3)	132/1897 (7)		0.89 (0.69–1.14)	
Sex					0.75
Male	300/7093 (4.2)	393/7137 (5.5)		0.76 (0.66–0.89)	
Female	79/2059 (3.8)	103/1989 (5.2)		0.72 (0.54–0.97)	
Body weight					0.64
≤60 kg	41/901 (4.6)	45/836 (5.4)		0.83 (0.55–1.27)	
>60 kg	335/8241 (4.1)	448/8285 (5.4)		0.75 (0.65–0.86)	
Estimated GFR					0.95
<60 mL/min	132/2054 (6.4)	177/2114 (8.4)		0.75 (0.60–0.94)	
≥60 mL/min	247/7094 (3.5)	319/7012 (4.5)		0.76 (0.64–0.90)	
CAD					0.47
Yes	347/8313 (4.2)	460/8261 (5.6)		0.74 (0.65–0.86)	
No	32/839 (3.8)	36/865 (4.2)		0.89 (0.55–1.43)	
PAD					0.61
Yes	126/2492 (5.1)	174/2504 (6.9)		0.72 (0.57–0.90)	
No	253/6660 (3.8)	322/6622 (4.9)		0.77 (0.66–0.91)	



Eikelboom JW *et al. N Engl J Med* 2017; DOI: 10.1056/NEJMoa1709118

Dual Pathway Inhibition with Rivaroxaban 2.5 mg bid + Aspirin Demonstrated a Clear Benefit Across All Subgroups

Subgroup	Rivaroxaban 2.5 mg bid + aspirin n/N (%)	Aspirin alone n/N (%)	HR (95% CI)	*p*-value
Geographic Region				0.56
North America	63/1304 (4.8)	80/1309 (6.1)	0.78 (0.56–1.08)	
South America	93/2054 (4.5)	111/2054 (5.4)	0.84 (0.63–1.10)	
Western Europe	117/2855 (4.1)	141/2855 (4.9)	0.82 (0.64–1.05)	
Eastern Europe	59/1607 (3.7)	90/1604 (5.6)	0.65 (0.46–0.90)	
Asia-Pacific	47/1332 (3.5)	74/1304 (5.7)	0.62 (0.43–0.89)	
Race or ethnic group				0.37
White	235/5673 (4.1)	306/5682 (5.4)	0.76 (0.64–0.90)	
Black	2/76 (2.6)	8/92 (8.7)	0.30 (0.06–1.46)	
Asian	54/1451 (3.7)	81/1397 (5.8)	0.64 (0.45–0.90)	
Other	88/1952 (4.5)	101/1955 (5.2)	0.87 (0.65–1.16)	
Tobacco use				0.29
Yes	80/1944 (4.1)	122/1972 (6.2)	0.66 (0.50–0.88)	
No	299/7208 (4.1)	374/7154 (5.2)	0.79 (0.68–0.92)	
Diabetes				0.77
Yes	179/3448 (5.2)	239/3474 (6.9)	0.74 (0.61–0.90)	
No	200/5704 (3.5)	257/5652 (4.5)	0.77 (0.64–0.93)	
Hypertension				0.68
Yes	317/6907 (4.6)	409/6877 (5.9)	0.76 (0.66–0.89)	
No	62/2245 (2.8)	87/2249 (3.9)	0.71 (0.51–0.98)	
Dyslipidemia				0.47
Yes	325/8239 (3.9)	428/8158 (5.2)	0.74 (0.64–0.86)	
No	54/913 (5.9)	68/968 (7)	0.85 (0.60–1.22)	



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Consistent Benefit Of Rivaroxaban 2.5 mg bid + Aspirin Supported by Secondary Outcomes, Including All-Cause Mortality

Outcome	Rivaroxaban 2.5 mg bid + aspirin 100 mg N=9152	Aspirin 100 mg N=9126	Rivaroxaban 2.5 mg bid + aspirin 100 mg vs aspirin 100 mg	
			HR (95% CI)	*p*-value*
CHD death, ischaemic stroke, MI, ALI	329 (3.6%)	450 (4.9%)	0.72 (0.63–0.83)	<0.001
CV death, ischaemic stroke, MI, ALI	389 (4.3%)	516 (5.7%)	0.74 (0.65–0.85)	<0.001
Mortality (all-cause)	313 (3.4%)	378 (4.1%)	0.82 (0.71–0.96)	0.01

ALI, acute limb ischaemia; CHD, coronary heart disease; CV, cardiovascular; MI, myocardial infarction;

ALL CAUSE MORTALITY: RRR – 18 %

*pre-specified threshold $p=0.0025$

CHD coronary heart disease death: death due to acute MI, sudden death, or CV procedure

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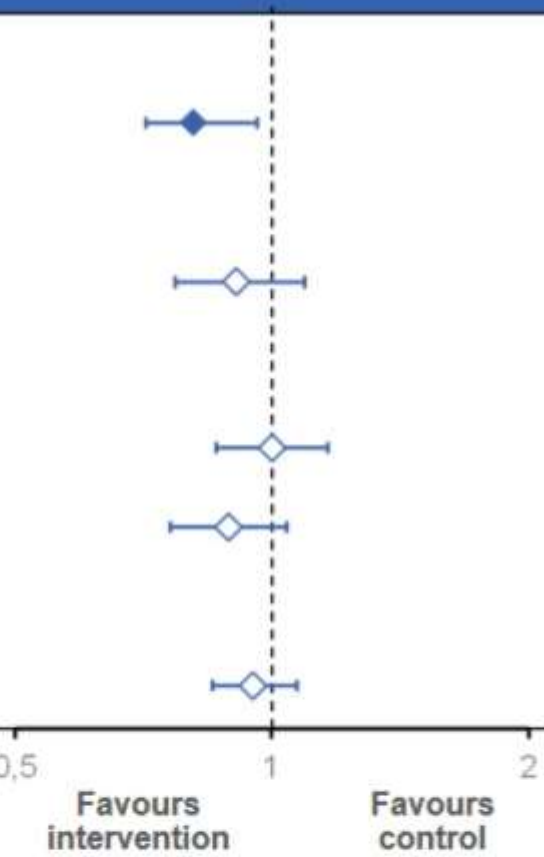
COMPASS

Rivaroxaban 2.5 mg bid + Aspirin Improved Overall Survival in Patients with CAD or PAD

Study / Treatment arm	Control %/year	Intervention %/year	HR	HR (95% CI)	*p*-value
COMPASS[1]					
Rivaroxaban 2.5 mg bid	2.1†	1.8†	0.82		0.01
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; threshold for formal significance p=0.0025* ‡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

COMPASS PAD Analysis

Dual Pathway Inhibition with Rivaroxaban 2.5 mg bid + Aspirin Significantly Reduced MACE by 28% and MALE by 46% Versus Aspirin

Outcome	Rivaroxaban 2.5 mg bid + aspirin N=2492	Rivaroxaban 5 mg bid N=2474	Aspirin N=2,504	Rivaroxaban 2.5 mg bid + aspirin vs. aspirin		Rivaroxaban 5 mg bid vs. aspirin	
	N (%)	N (%)	N (%)	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
MACE	126 (5.1)	149 (6.0)	174 (6.9)	0.72 (0.57–0.90)	0.005	0.86 (0.69–1.08)	0.19
CV death	64 (2.6)	66 (2.7)	78 (3.1)	0.82 (0.59–1.14)	-	0.86 (0.62–1.19)	-
Stroke	25 (1.0)	43 (1.7)	47 (1.9)	0.54 (0.33–0.87)	-	0.93 (0.61–1.40)	-
MI	51 (2.0)	56 (2.3)	67 (2.7)	0.76 (0.53–1.09)	-	0.84 (0.59–1.20)	-
MALE	30 (1.2)	35 (1.4)	56 (2.2)	0.54 (0.35–0.84)	0.005	0.63 (0.41–0.96)	0.03
Major amputation	5 (0.2)	8 (0.3)	17 (0.7)	0.30 (0.11–0.80)	0.01	0.46 (0.20–1.08)	0.07

RIVAROXABAN 2.5 mg bid + ASA
significantly reduced major amputation
by 70% versus ASA

Anand SS *et al.* ESC 2017, Abs 1157; Available at: http://spo.escardio.org/SessionDetails.aspx?eevtid=1220&sessId=22247&subSessId=0;
Anand SS *et al.* *Lancet* 2017;In Press

COMPASS

Low Overall Incidence of Major Bleeding with Rivaroxaban 2.5 mg bid + Aspirin Versus Aspirin Alone, with Similar Fatal and Intracranial Bleeding

Outcome	Rivaroxaban 2.5 mg bid + aspirin N=2492	Rivaroxaban 5 mg bid N=2474	Aspirin N=2504	Rivaroxaban 2.5 mg bid + aspirin vs. aspirin		Rivaroxaban 5 mg bid vs. aspirin	
	N (%)	N (%)	N (%)	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Major bleeding	77 (3.1)	79 (3.2)	48 (1.9)	1.61 (1.1–2.31)	0.009	1.68 (1.17–2.40)	0.004
Fatal	4 (0.2)	5 (0.2)	3 (0.1)	-	-	-	-
Non-fatal ICH*	4 (0.2)	5 (0.2)	8 (0.3)	-	-	-	-
Non-fatal other critical organ*	13 (0.5)	18 (0.7)	8 (0.3)	1.55 (0.64–3.74)	0.33	2.15 (0.94–4.96)	0.06

*Symptomatic

Anand SS *et al.* ESC 2017, Abs 1157; Available at: http://spo.escardio.org/SessionDetails.aspx?eevtid=1220&sessId=22247&subSessId=0;
Anand SS *et al. Lancet* 2017;In Press

COMPASS

Conclusions

RIVAROXABAN 2.5 mg bid plus ASA Improve Outcomes for Patients with Chronic CAD or PAD

In patients with chronic CAD or PAD, dual pathway inhibition with RIVAROXABAN 2.5 mg bid plus ASA :

- **Reduction in CV Death and MI RRR 24%**
- **Reduction in Stroke RRR 42%**
- **Reduction in CV Death RRR 22%**
- **Reduction in All-cause Mortality RRR 18%**
- **As expected, resulted in increased Major Bleeding, however bleeding rates were low and notably, there was no significant increase in intracranial, critical organ or fatal bleeding**
- **Improvement in Net Clinical Benefit of 20%**

Eikelboom JW *et al. N Engl J Med* 2017; DOI: 10.1056/NEJMoa1709118

COMPASS

3

Riduzione del Rischio Residuo post IMA : Si può sin da subito !

Canadian Journal of Cardiology 33 (2017) 1027–1035

Clinical Research

Rationale, Design and Baseline Characteristics of Participants in the Cardiovascular Outcomes for People Using Anticoagulation Strategies (COMPASS) Trial

Table 5. COMPASS participant baseline characteristics

Characteristic	Value
Participant n	27,395
Mean age (SD), years	68.2 (7.94)
Male sex	21,375 (78)
Mean heart rate (SD), beats per minute	67.6 (10.65)
Mean SBP (SD), mm Hg	135.5 (17.57)
Mean DBP (SD), mm Hg	77.6 (9.98)
Body mass index	28.3 (4.74)
ABI < 0.9	3643 (13.3)
Mean cholesterol (SD), mmol/L	4.3 (3.51)
Mean creatinine (SD), µmol/L	90.7 (54.12)
Mean eGFR (SD), mL/min/1.73m^2	73.8 (17.9)
Current smoking	5866 (21.4)
Hypertension	20,627 (75.3)
Diabetes	10,340 (37.7)
CAD history	24,825 (90.6)
Previous MI	[illegible]
Mean time since last MI (SD), years	7.1 (6.46)
Previous CABG surgery	[illegible]
Heart failure history	5900 (21.5)
Stroke history	1033 (3.8)
PAD history	7470 (27.3)
Asymptomatic carotid stenosis > 50%	1917 (7)
Peptic ulcer history	1237 (4.5)
Bleeding requiring transfusion	723 (2.6)
Region	
North America	3918 (14.3)
South America	6144 (22.4)
Western Europe	8555 (31.2)
Eastern Europe	4823 (17.6)
Asia/Pacific	3955 (14.4)

Alla dimissione del paziente con IMA Identifica il

Fenotipo MADRE

almeno uno dei seguenti elementi

Multivessel disease: CAD - PAD

Age ≥ 65 anni

Diabetes

Renal Impairment eGFR ≤ 60

Event recurrent

Scherillo M et al. J Thromb Thrombolysis 26 June 2018

COMING SOON

RIDURRE IL RISCHIO RESIDUO

Post AMI Check Point

Fenotipo MADRE