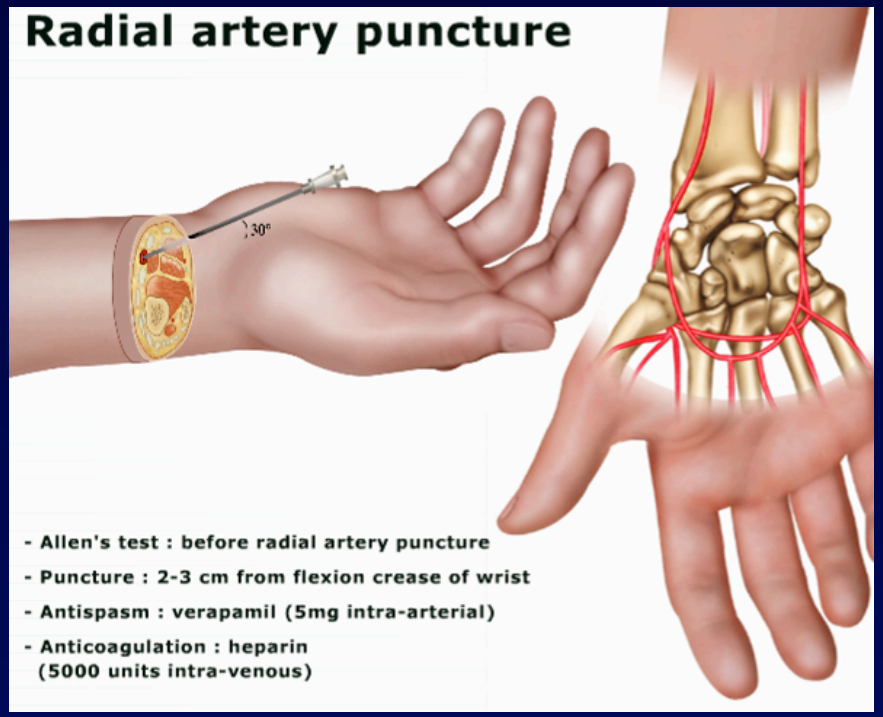
Comment réduire le risque hémorragique dans l'infarctus avec sus-décalage de ST ?

Pr Pierre Coste
Hôpital Cardiologique du Haut Lévêque
Université de Bordeaux 2

APPAC
Actualisations et Perspectives en PAthologie Cardiovasculaire

Qui sont les responsables des hémorragies ?

- Le patient (risque individuel variable)
- Les anti-thrombotiques : anti-agrégants plaquettaires et antithrombines
- Le cardiologue interventionnel

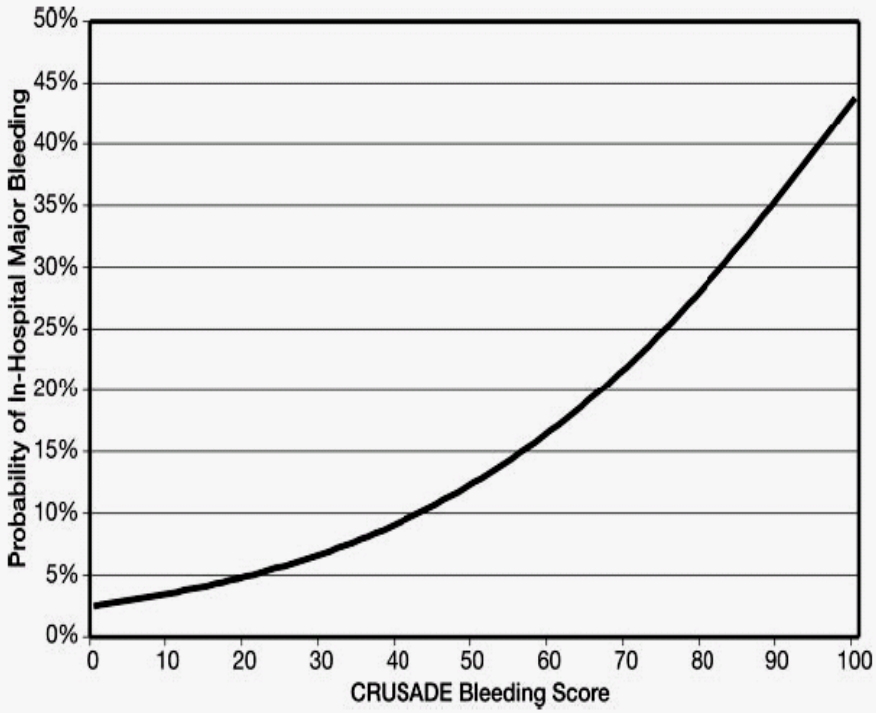


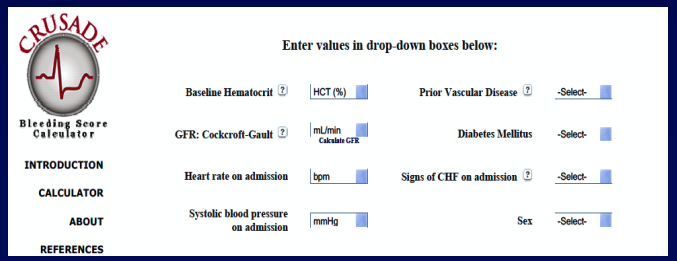
CRUSADE registry : multivariate predictors of in-hospital bleedings

N = 71 277 patients

Table 4. Multivariate Predictors of In-Hospital Major Bleeding

Variable	χ^2	Derivation Cohort OR (95% CI)	Validation Cohort OR (95% CI)
Baseline hematocrit <36% (vs ≥36%)	434.6	2.28 (2.11–2.46)	2.17 (1.92–2.44)
CrCl (per 10-mL/min decrease)*	433.2	1.12 (1.10–1.13)	1.11 (1.09–1.13)
Heart rate (per 10-bpm increase)	159.2	1.08 (1.07–1.10)	1.09 (1.07–1.12)
Female sex	77.8	1.31 (1.23–1.39)	1.33 (1.19–1.50)
Signs of CHF at presentation	37.7	1.23 (1.15–1.31)	1.13 (1.01–1.28)
SBP ≤110 mm Hg (vs 110–180 mm Hg)	33.6	1.26 (1.16–1.36)	1.27 (1.10–1.47)
SBP ≥180 mm Hg (vs 110–180 mm Hg)		1.24 (1.14–1.35)	1.18 (1.02–1.37)
Prior vascular disease†	30.4	1.19 (1.12–1.27)	1.10 (0.98–1.24)
Diabetes mellitus	26.6	1.16 (1.10–1.23)	1.25 (1.12–1.40)
c Statistic		0.72	0.71

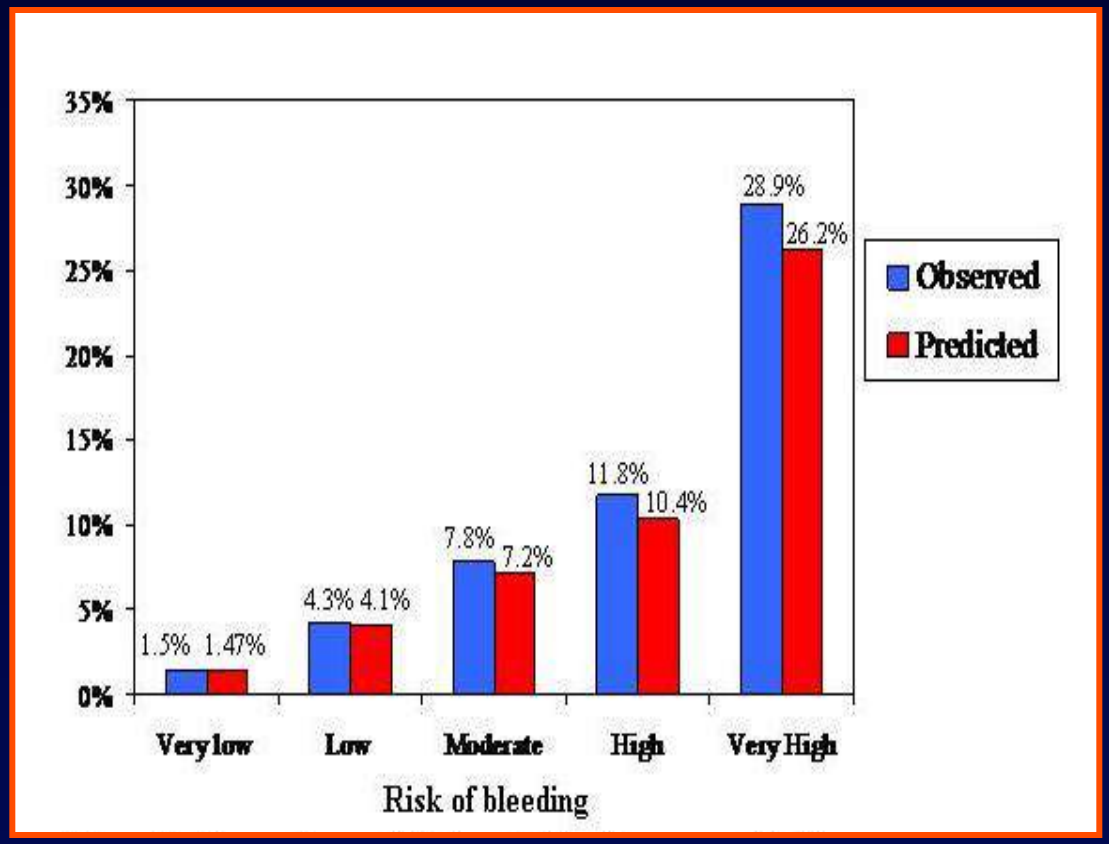




http://www.crusadebleedingscore.org

Subherwall S Circulation 2009;119:1873

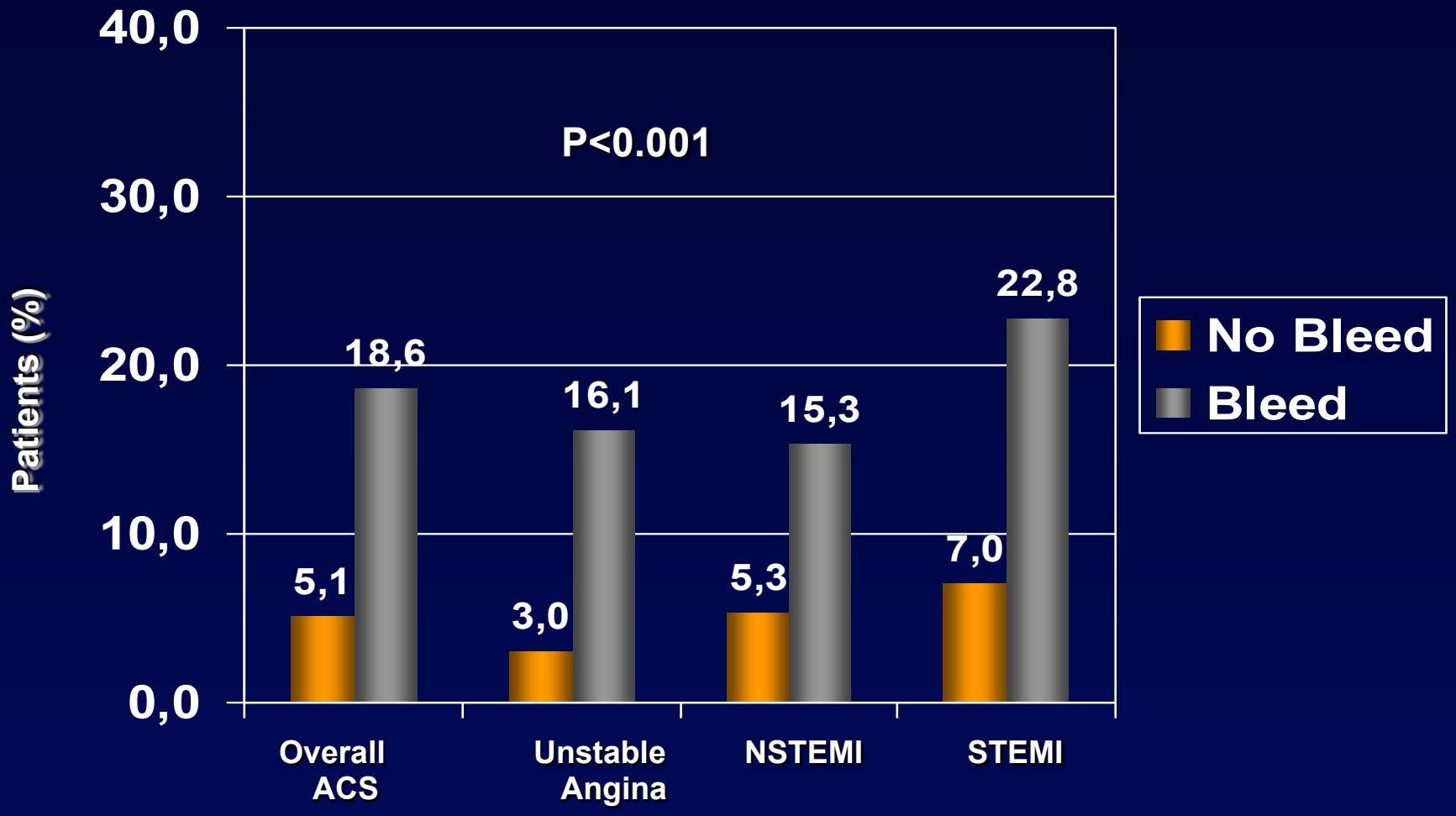
Validation of CRUSADE score in Europe



Abu-Asi E, González-Juanatey JR Circulation 2010

Major bleeding predicts mortality in acute coronary syndromes

24,045 ACS patients in the GRACE registry, in-hospital death



Moscucci M Eur Heart J 2003;24:1815-23.

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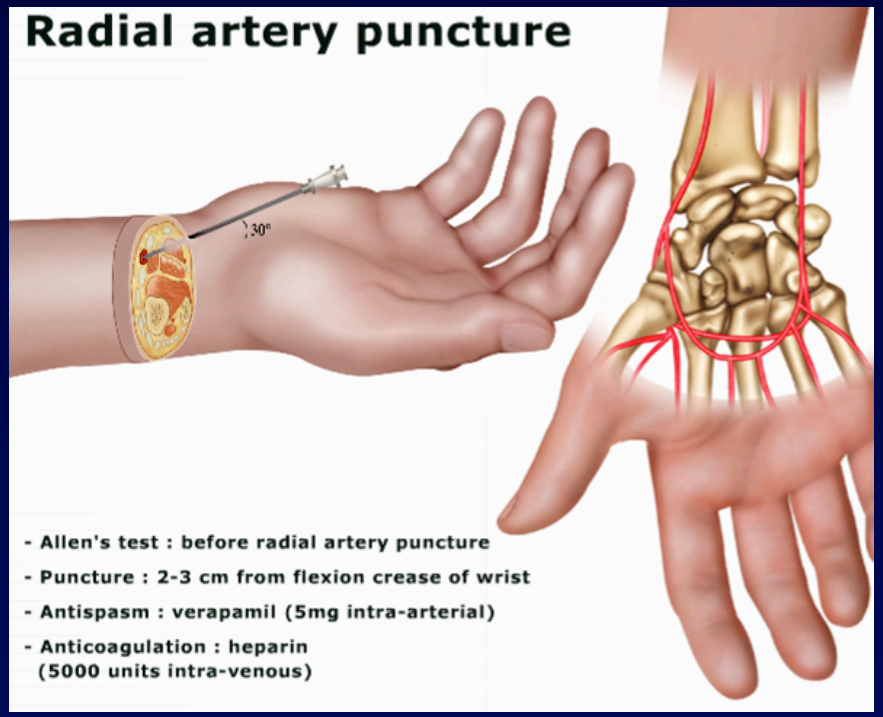
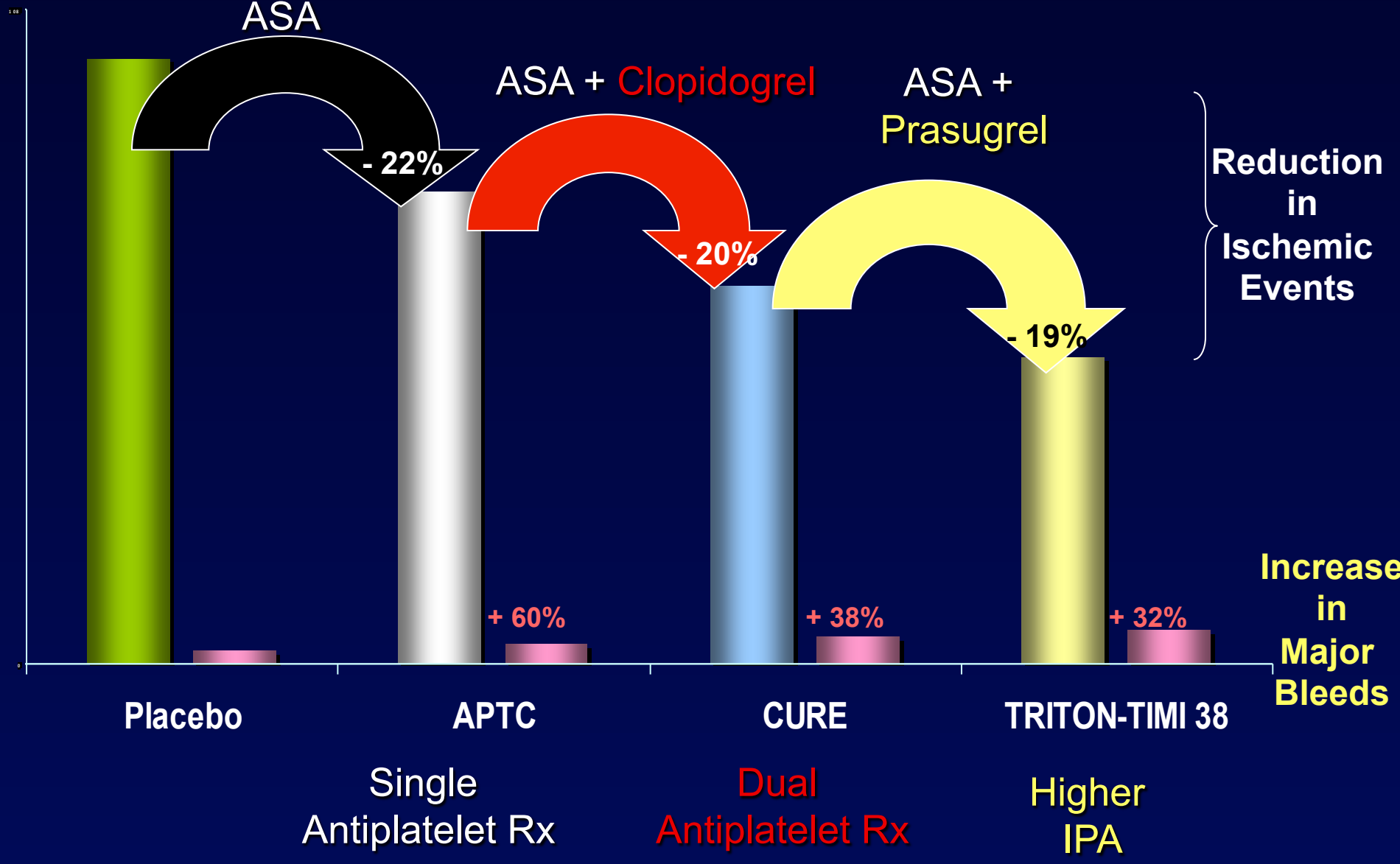
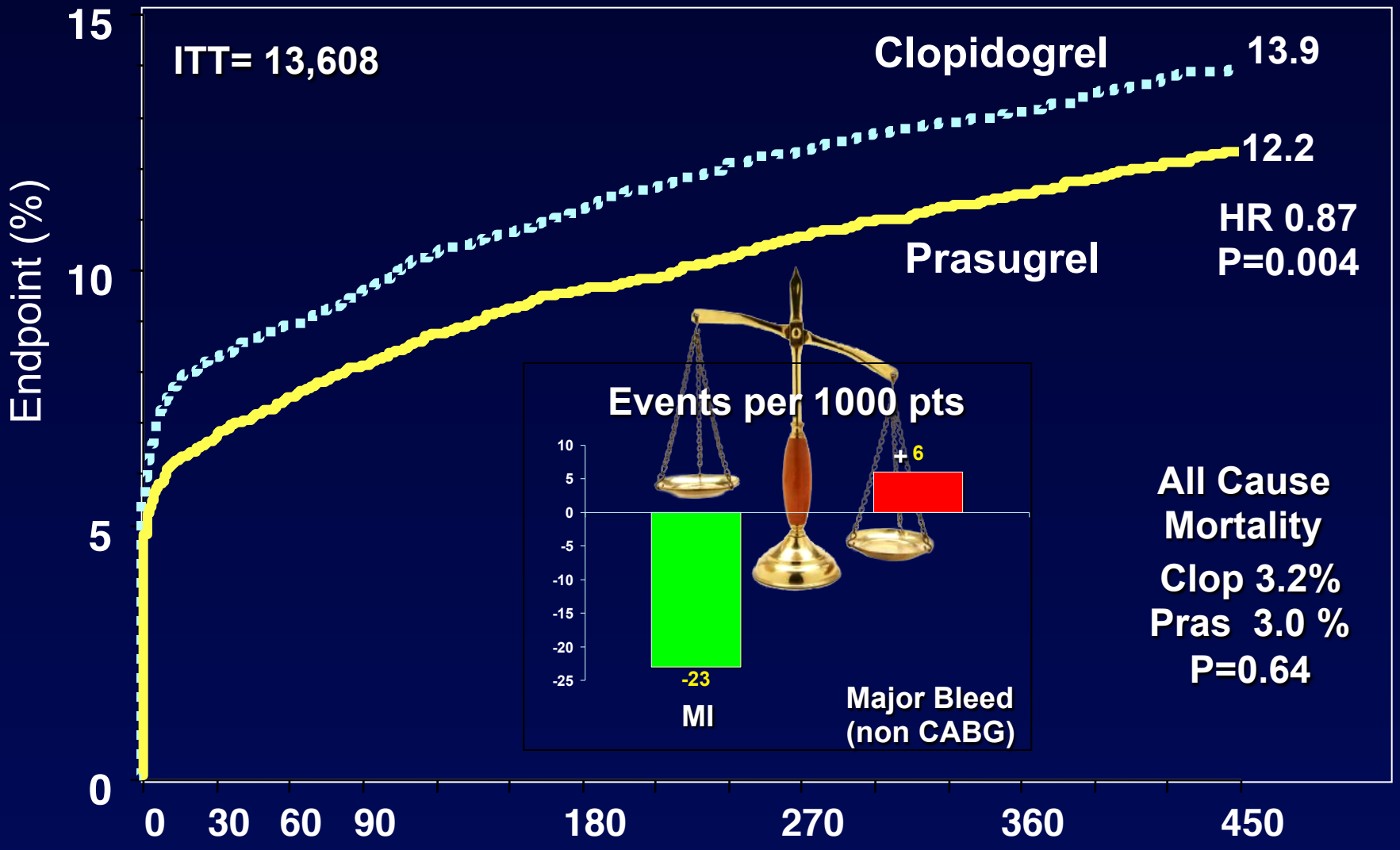


Antiplatelet Therapy in ACS

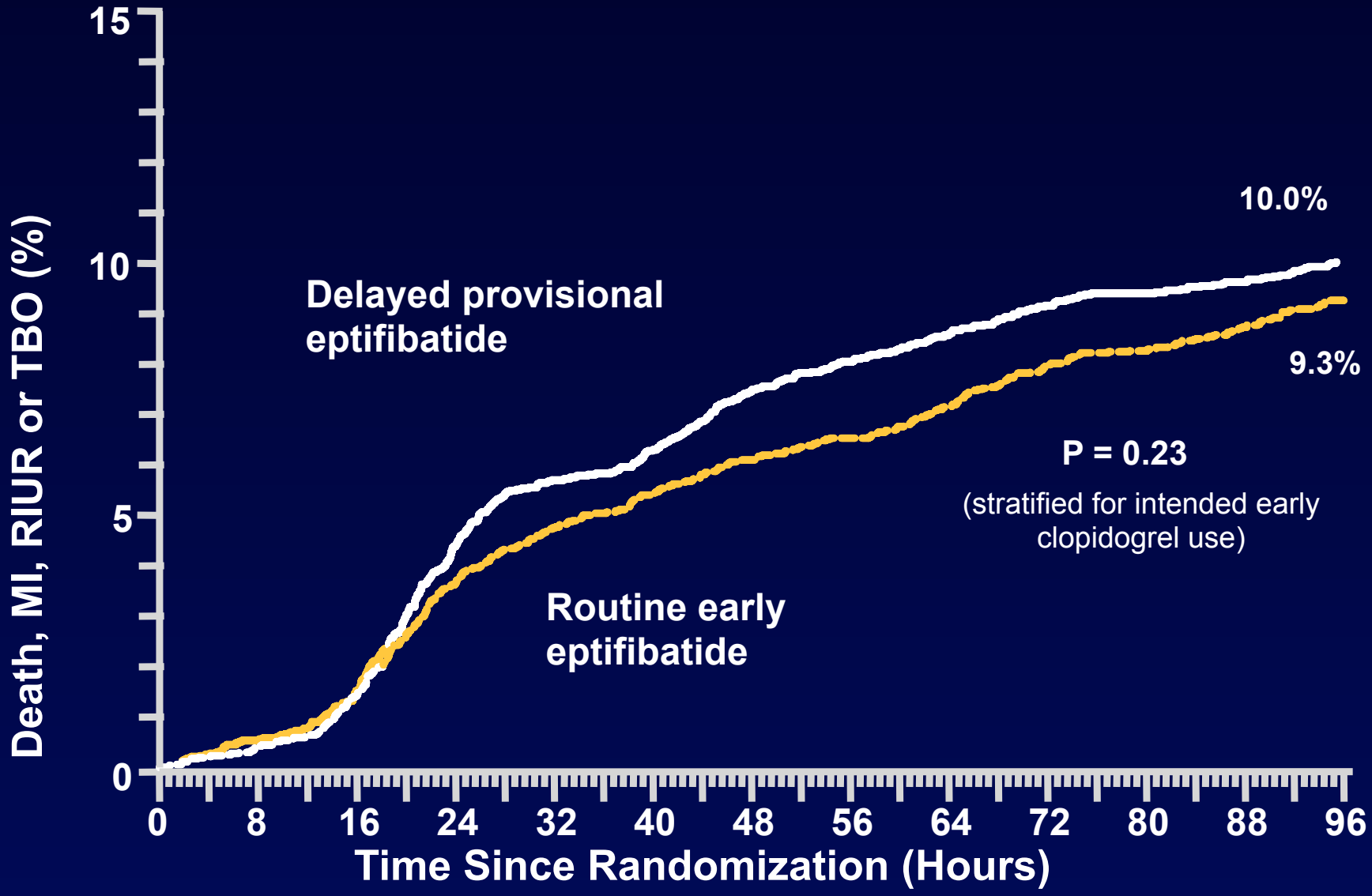


Net Clinical Benefit : Death, MI, Stroke, Major Bleed (non CABG)



Wiviott N Engl J Med 2007;357:2001

EARLY-ACS trial : Primary Endpoint



Giugliano N Engl J Med 2009;360:2176

EARLY-ACS trial : Safety Results (through 120 hours)

	Routine Early Eptifibatide (n=4686)	Delayed Provisional Eptifibatide (n=4643)	OR (95% CI)	P
Bleeding (all patients, %)				
TIMI major	2.6	1.8	1.42 (1.07-1.89)	0.015
TIMI major or minor	5.8	3.4	1.75 (1.43-2.14)	<0.001
GUSTO severe	0.8	0.9	0.99 (0.64-1.55)	0.97
GUSTO moderate or severe	7.6	5.1	1.52 (1.28-1.80)	<0.001
PRBC transfusion	8.6	6.7	1.31 (1.12-1.53)	0.001
Bleeding (CABG)				
Re-operation for bleeding (%)	6.0	8.4	0.70 (0.39-1.27)	0.24
Chest tube output (mL/24 H)	720	770	--	0.41
Thrombocytopenia (<100K, %)	3.3	2.8	1.19 (0.93-1.51)	0.17
Stroke (total, %)	0.6	0.8	0.79 (0.48-1.30)	0.36

Bleeding Within 30 Days is a Powerful and Independent Predictor of 1-year Death After PCI

5,384 patients from 4 RCT on the value of abciximab after pretreatment with 600 mg of clopidogrel: ISAR-REACT, SWEET, SMART-2 and REACT-2

Variable	Hazard Ratio (95% CI)	P Value
Bleeding within 30 days	**2.96(1.96-4.48)**	<0.001
Myocardial infarction within 30 days	2.29(1.52-3.46)	<0.001
Urgent revascularization within 30 days	2.49(1.16-5.35)	0.019
Age (years)*	2.27(1.78-2.89)	<0.001
Diabetes	1.47(1.11-1.96)	0.008
Multivessel coronary disease	2.72(1.56-4.67)	<0.001
Elevated troponin	1.77(1.27-2.47)	<0.001
Left ventricular ejection fraction	0.71(0.60-0.85)	<0.001
Creatinine level	1.10(1.06-1.14)	<0.001

"Our study demonstrates a strong relationship between the 30-day frequency of bleeding and 1-year mortality after PCI and supports the inclusion of periprocedural bleeding in a 30-day quadruple endpoint for the assessment of outcome after PCI."

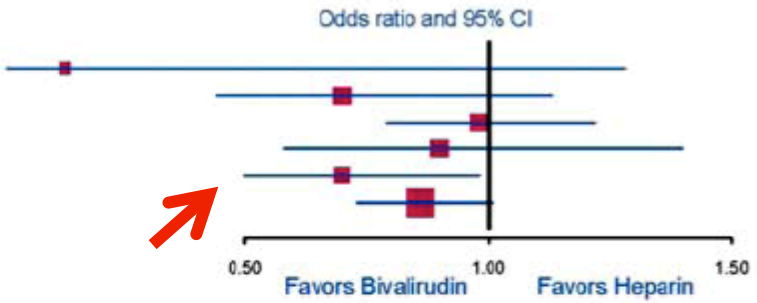
Ndrepepa G. JACC 2008;51:690-7 * Calculated for a 10-year increase in age.

Which anticoagulant to use during PCI ?

A Bivalirudin vs. Heparin

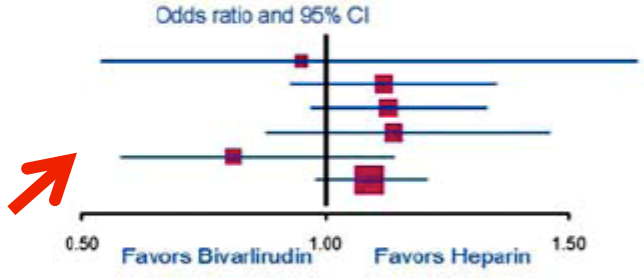
i) Death

Study name	Dead/Total		Odds ratio (95% CI)
	Bivalirudin	Heparin	
REPLACE 1	0/532(0%)	3/524(0.6%)	0.13(0.01-1.28)
REPLACE 2	28/2994(0.9%)	40/3008(1.3%)	0.70(0.44-1.13)
ACUITY	169/4612(3.7%)	172/4603(3.7%)	0.98(0.79-1.22)
ISAR REACT 3	43/2289(1.9%)	39/2281(1.7%)	1.10(0.71-1.70)
HORIZONS AMI	61/1800(3.4%)	86/1802(4.8%)	0.70(0.50-0.98)
OVERALL	301/12227(2.5%)	340/12218(2.8%)	0.88(0.75-1.03)



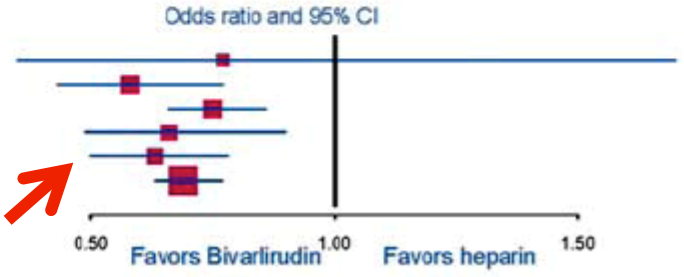
ii) MI

Study name	MI/Total		Odds ratio (95% CI)
	Bivalirudin	Heparin	
REPLACE 1	26/532(4.9%)	27/524(5.2%)	0.95(0.54-1.64)
REPLACE 2	243/2994(8.1%)	220/3008(7.3%)	1.12(0.93-1.35)
ACUITY	349/4612(7.6%)	310/4603(6.7%)	1.13(0.97-1.33)
ISAR REACT 3	137/2289(6.0%)	121/2281(5.3%)	1.14(0.88-1.46)
HORIZONS AMI	62/1800(3.4%)	76/1802(4.2%)	0.81(0.58-1.14)
OVERALL	817/12226(6.7%)	754/12218(6.2%)	1.09(0.98-1.21)



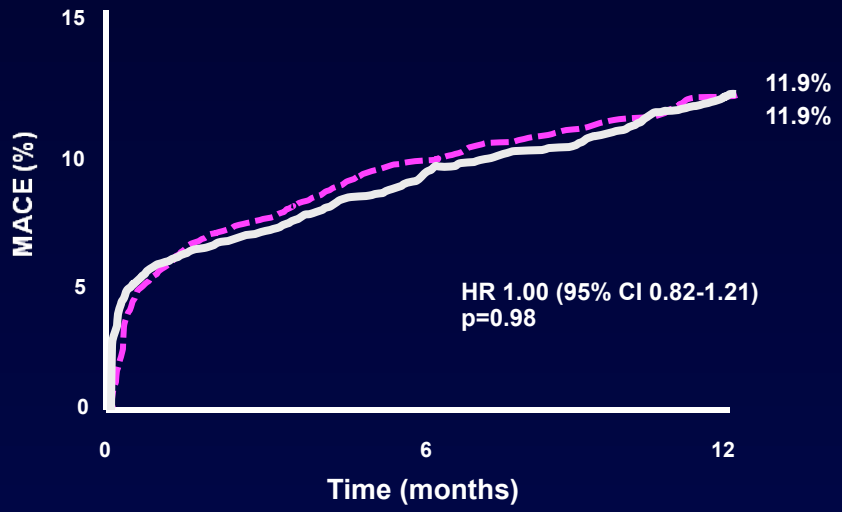
iii) Major Bleed

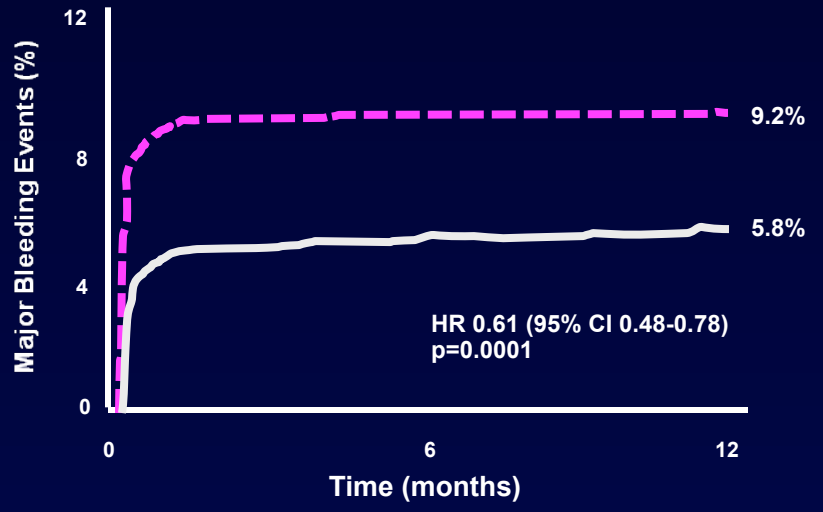
Study name	Major Bleed/Total		Odds ratio (95% CI)
	Bivalirudin	Heparin	
REPLACE 1	11/532(2.1%)	14/524(2.7%)	0.77(0.35-1.70)
REPLACE 2	71/2994(2.4%)	123/3008(4.1%)	0.58(0.43-0.77)
ACUITY	421/4612(9.1%)	543/4603(11.8%)	0.75(0.66-0.86)
ISAR REACT 3	70/2289(3.1%)	104/2281(4.6%)	0.66(0.49-0.90)
HORIZONS AMI	137/1800(7.6%)	210/1802(11.7%)	0.63(0.50-0.78)
OVERALL	710/12226(5.8%)	994/12218(8.1%)	0.69(0.63-0.77)

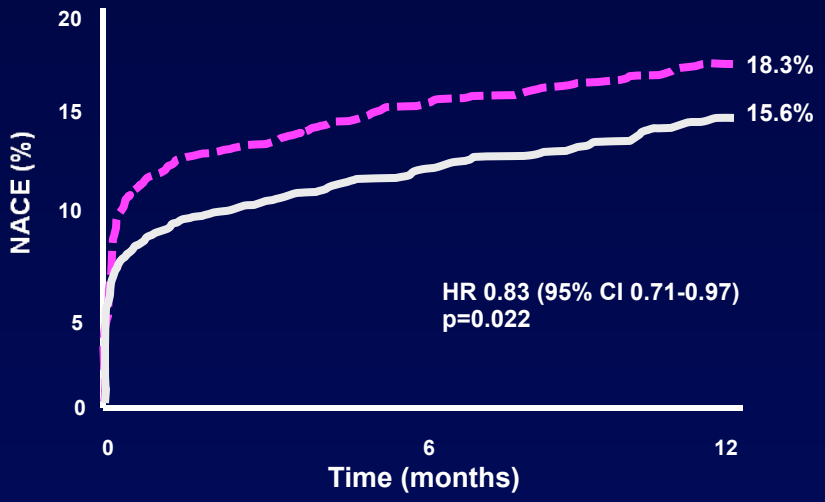


Jolly SS, Yusuf S Eur Heart J 2010, 31 : 522-524

Bivalirudin in Primary PCI. 1-Year Results of the HORIZONS-AMI







Bivalirudin (n=1800)

Control (n=1802)

Mehran R, et al. *Lancet* 2009;374:1149

Qui sont les responsables des hémorragies ?

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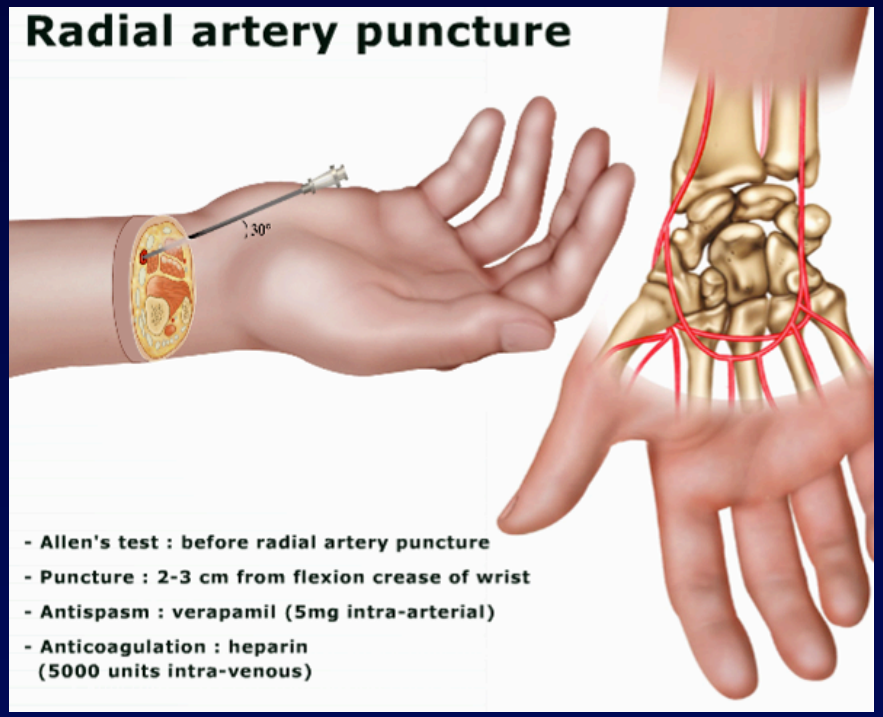
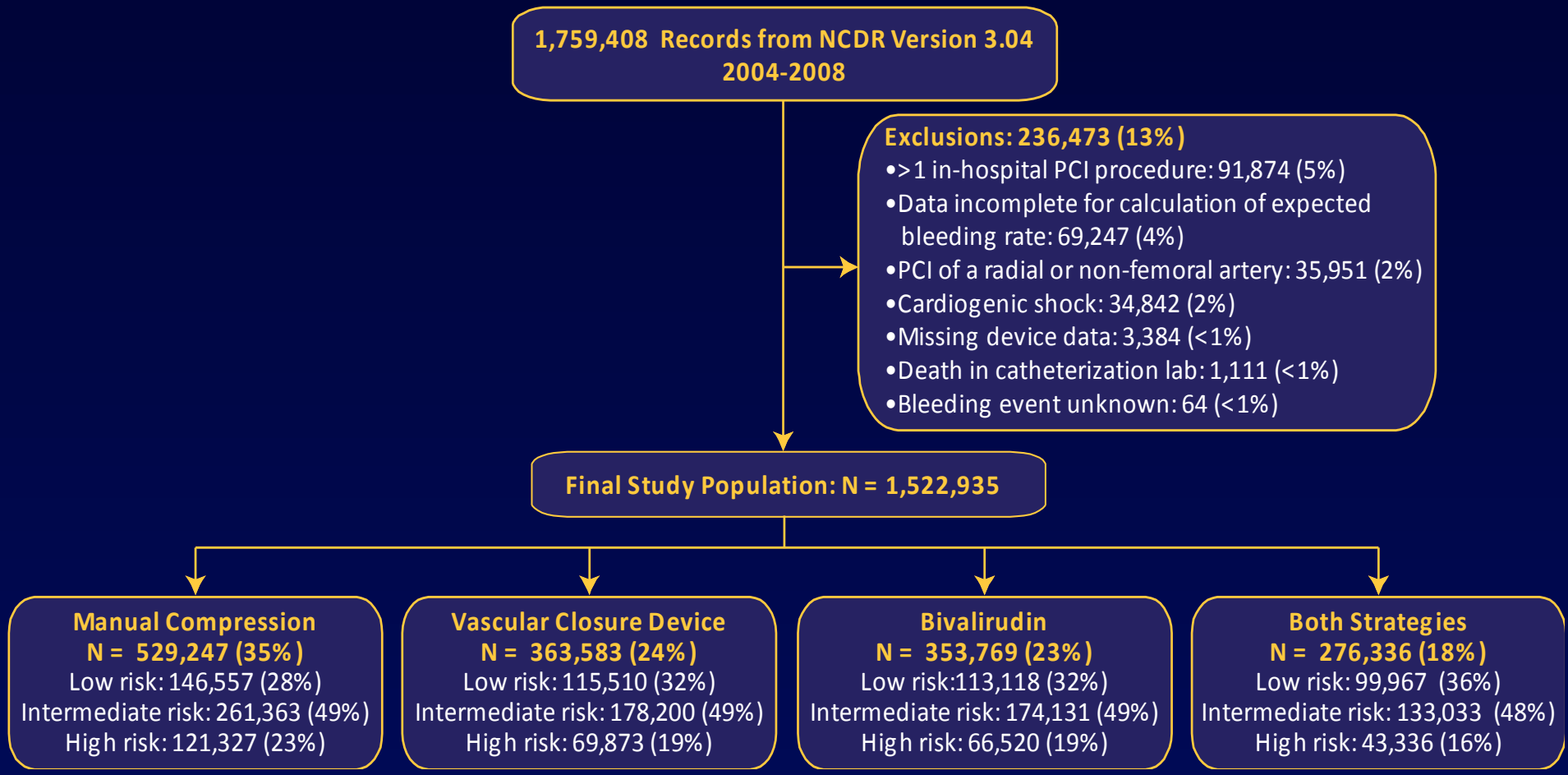


Association Between Use of Bleeding Avoidance Strategies and Risk of Periprocedural Bleeding Among Patients Undergoing PCI



Marso et al. JAMA 2010;303:2156-2164

Admission Characteristics

	Total (N=1,522,935)	Manual Compression (N = 529,247)	Vascular Closure Devices (N=363,583)	Bivalirudin (N = 353,769)	Both (N = 276,336)
No symptoms	196,190 (12.88)	55,961 (10.57)	42,224 (11.61)	54,346 (15.36)	43,659 (15.80)
Atypical chest pain	113,339 (7.44)	32,570 (6.15)	27,031 (7.44)	27,758 (7.85)	25,980 (9.40)
Stable angina	260,582 (17.11)	73,109 (13.81)	57,179 (15.73)	69,093 (19.53)	61,201 (22.15)
Unstable angina	527,624 (34.65)	168,813 (31.90)	113,413 (31.19)	142,473 (40.27)	102,925 (37.25)
Non-STEMI	238,305 (15.65)	98,866 (18.68)	64,921 (17.86)	43,239 (12.22)	31,279 (11.32)
STEMI	186,810 (12.27)	99,900 (18.88)	58,796 (16.17)	16,843 (4.76)	11,271 (4.08)
PCI type					
Elective	758,110 (49.79)	220,576 (41.68)	157,348 (43.28)	212,562 (60.09)	167,624 (60.67)
Urgent	553,524 (36.35)	196,634 (37.16)	140,023 (38.52)	121,995 (34.49)	94,872 (34.34)
Emergency	209,465 (13.76)	110,990 (20.97)	65,758 (18.09)	19,011 (5.37)	13,706 (4.96)
Salvage	1,662 (0.11)	968 (0.18)	422 (0.12)	172 (0.05)	100 (0.04)

All data are N (%)

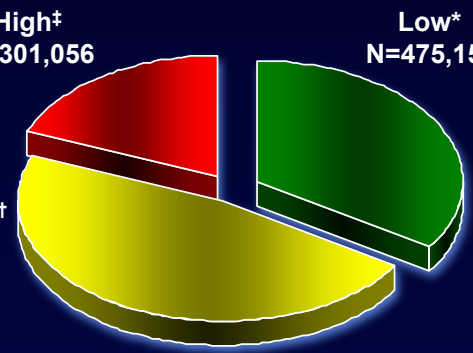
All P<0.001

Study Outcomes

- In-hospital bleeding according to NCDR data definition:
  - Requiring transfusion *and/or*
  - Prolonged hospital stay *and/or*
  - Decrease in hemoglobin >3 g/dL

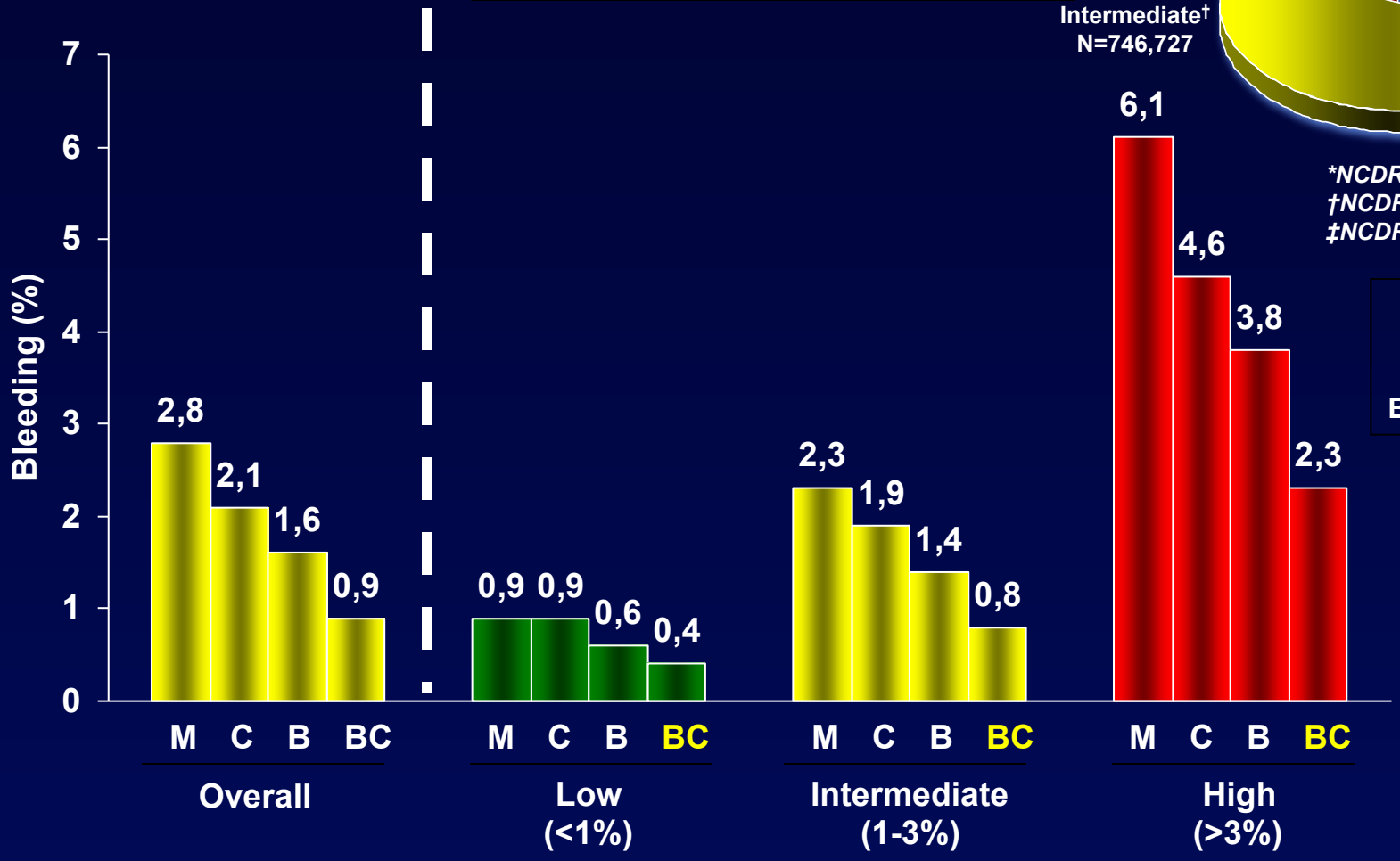
Bleeding Rates

Overall bleeding = 30,429 (2%)



*NCDR bleeding risk <1%
†NCDR bleeding risk 1-3%
‡NCDR bleeding risk ≥3%

M = Manual comp.
C = Closure only
B = Bival only
BC = Bival+closure



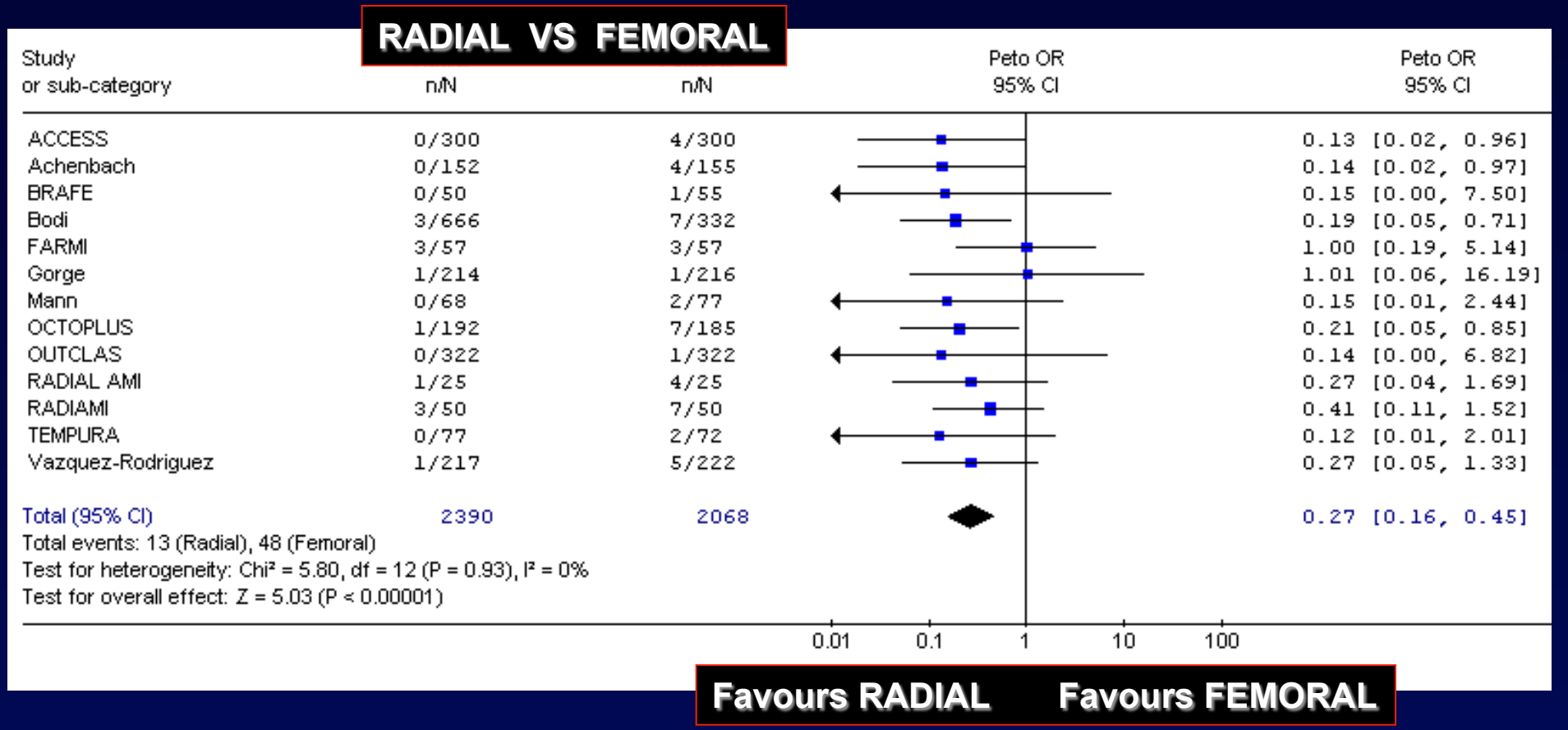
P<0.001 all intra-risk group comparisons

Estimated Bleeding Reductions (Propensity Adjusted)

	Treatment (N)	Bleeding N (%)	Odds Ratio (95% CI)	NNT (95% CI)	Reduction in Bleeding Events per 1,000 Patients Treated (95% CI)
Low Risk, <1%					
Manual compression	144,594	1,320 (0.9)	1 [Reference]		
Vascular closure devices	54,217	532 (1.0)	1.07 (0.93-1.22)	NS	NS
Bivalirudin	48,378	296 (0.6)	0.65 (0.56-0.77)	315 (247-470)	3.2 (2.1-4.0)
Both	41,999	166 (0.4)	0.42 (0.34-0.51)	188(167-222)	5.3 (4.5-6.0)
Total	289,188	2,314 (0.8)			
Intermediate Risk, 1-3%					
Manual compression	252,898	5,722 (2.3)	1 [Reference]		
Vascular closure devices	103,095	2,077 (2.0)	0.76 (0.71-0.81)	169 (141-217)	5.9 (4.6-7.1)
Bivalirudin	85,800	1,311 (1.5)	0.69 (0.63-0.74)	153 (131-187)	6.5 (5.3-7.6)
Both	64,003	573 (0.9)	0.39 (0.35-0.44)	80 (75-86)	12.5 (11.6-13.3)
Total	505,796	9,683 (1.9)			
High Risk, >3%					
Manual compression	110,963	6,555 (5.9)	1 [Reference]		
Vascular closure devices	48,294	2,441 (5.1)	0.79 (0.75-0.82)	81 (66-109)	12.3 (9.2-15.3)
Bivalirudin	38,293	1,617 (4.2)	0.67 (0.62-0.73)	56 (49-66)	17.9 (15.1-20.6)
Both	24,376	622 (2.6)	0.42 (0.38-0.47)	33 (31-36)	30.5 (27.9-32.8)
Total	221,926	11,235 (5.1)			

Radial vs Femoral Access : Impact on Major Bleeding

Meta-analysis of 18 Randomized Trials



Jolly S et al. Am Heart J 2009

Beyond Access Site Bleeding: Incidence, Sources, and Impact of Antithrombotic Therapy in the PCI Patient

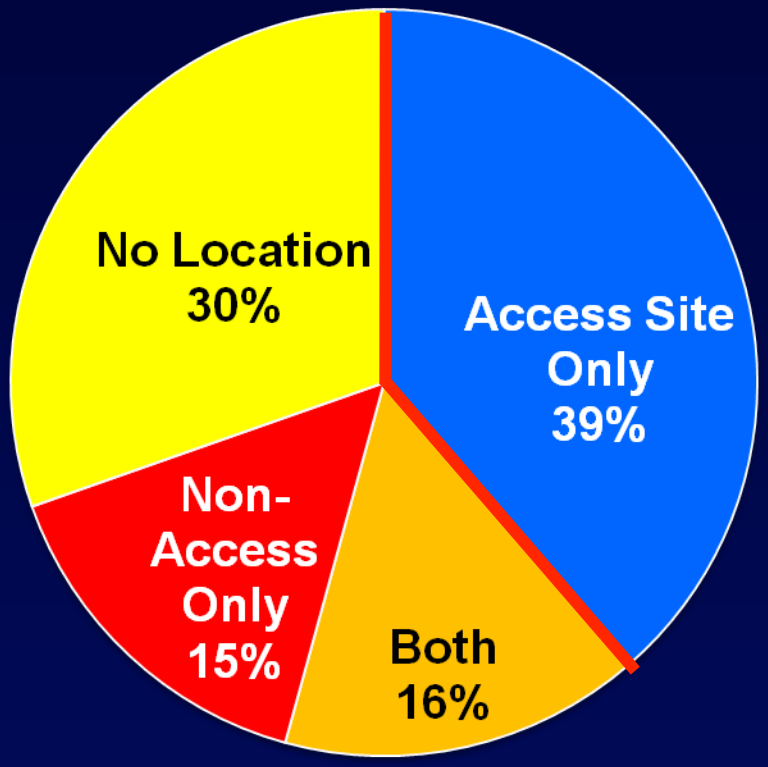
A Combined Analysis of 17,393 Patients REPLACE-2, ACUITY and HORIZONS-AMI

Freek W.A. Verheugt, Steven R. Steinhubl, Martial Hamon, Harald Darius, Ph. Gabriel Steg, Marco Valgimigli, Steven P. Marso, Sunil V. Rao, Anthony H. Gershlick.

Onze Lieve Vrouwe Gasthuis, Amsterdam

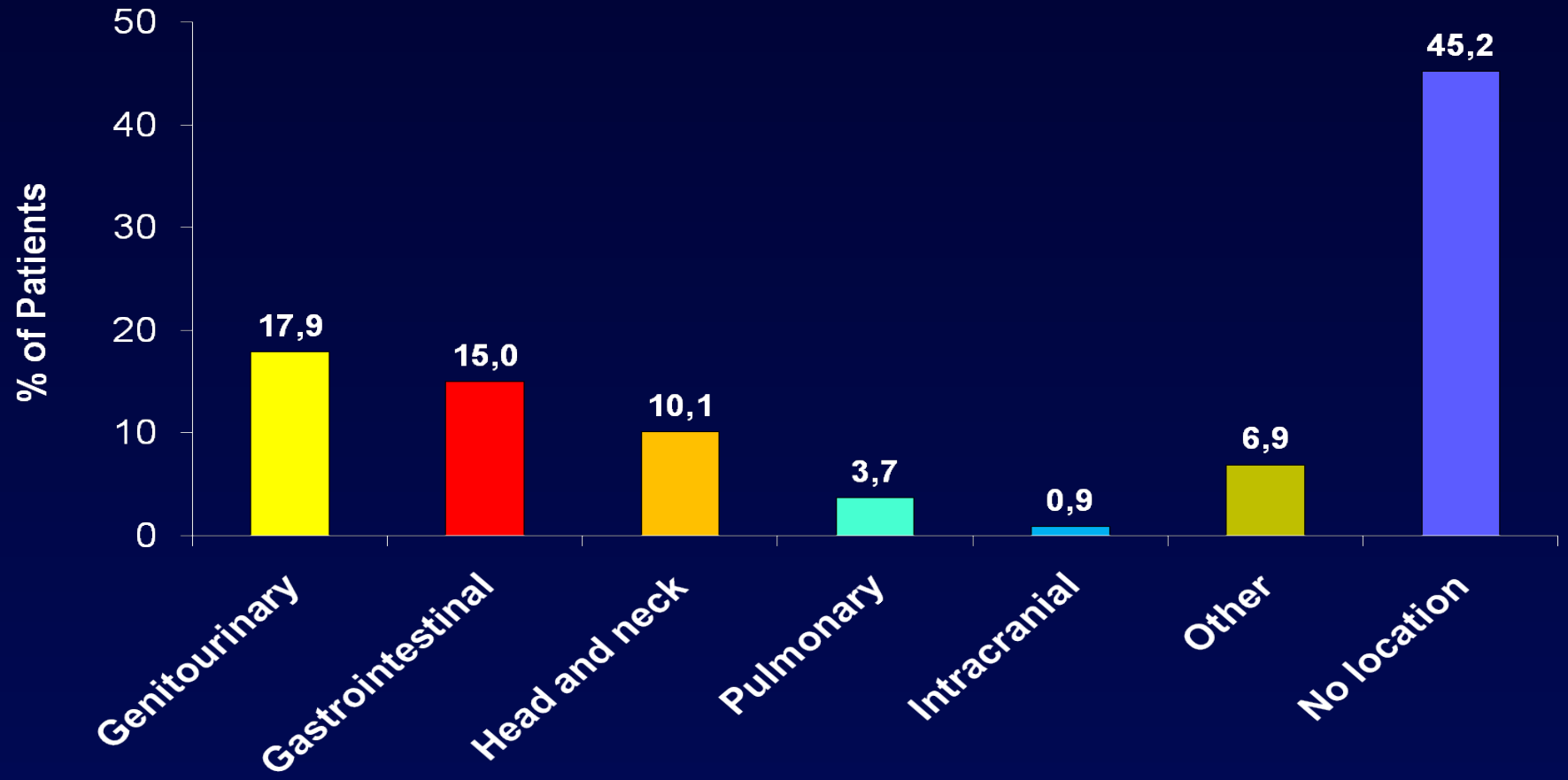
Sources and Incidence of TIMI Bleeding Among 17,393 PCI Patients

5.3% (n=925) of the study population experienced a TIMI (Major + Minor) bleeding event.

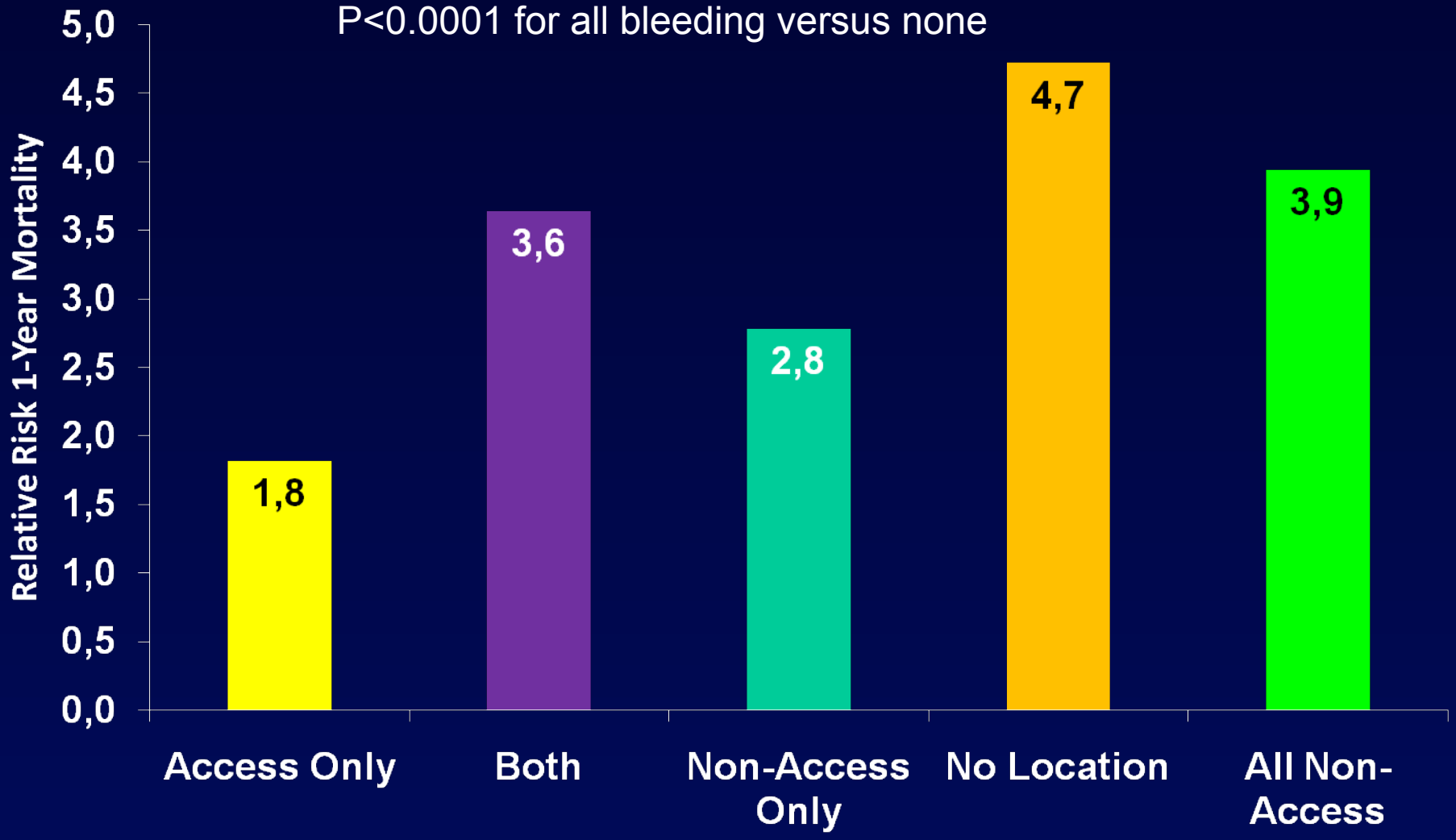


Access-site only bleeds occurred in 357 (39.6%) of patients.

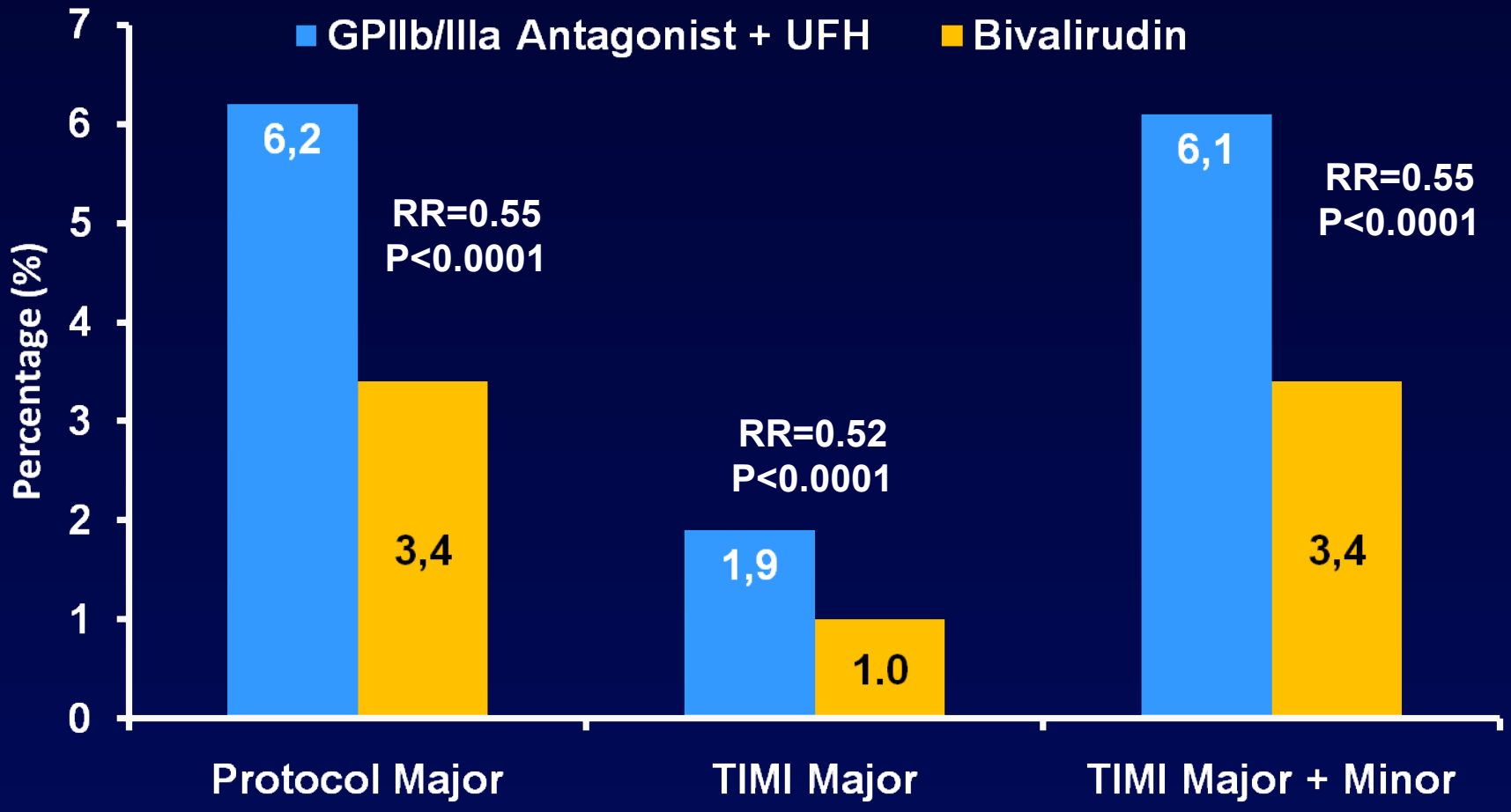
Incidence and Location of Bleeding Events Excluding Access Site



Adjusted Relative Risk of 1-Year Mortality Based on TIMI Bleeding Source Compared to No Bleeding



Impact of Randomized Antithrombotic Therapy: All Bleeding Sources



En conclusion

- Le risque hémorragique pénalise lourdement le pronostic des patients avec syndrome coronarien aigu
- Le cardiologue doit l'intégrer dans la stratégie de prise en charge
- Le choix de la voie d'abord et des anti thrombotiques influence le risque hémorragique
- La bivalirudine réduit les évènements hémorragiques indépendamment de la voie d'abord