KNUH 경북대학교병원
KYUNGPOOK NATIONAL UNIVERSITY HOSPITAL

Management of Atrial Fibrillation in Myocardial infarction

경북의대 배명환

AF incidence in AMI

Study	Pts, n	Design	Inclusion criteria	Treatment	Trial Period	Any AF, %	Prior AF, %	New-Onset/In-Hospital AF, %
GUSTO I[2]	40891	RCT	STEMI	Thrombolysis streptokinase vs alteplase	1 year	10.4%	2.5%	7.9%
GUSTO III[8]	13858	RCT	STEMI	Thrombolysis alteplase vs reteplase	1 year	-	-	6.5%
GISSI[9]	17944	RCT	STEMI	Thrombolysis 72% lisinopril/lisinopril+nitrates/nitrates	4 years	-	-	7.8%
TRACE[10]	6776	RCT Pre-enrolment	STEMI LV dysfunction	Thrombolysis 75% of patients	5 years	-	3.9%	21%
OPTIMAAL[11]	5477	RCT	STEMI HF and LV dysfunction (EF<40% or LVED>=65)	Thrombolytics- 54.4% Captopril vs losartan	3 years	-	12%	7.2%
VALIANT[12]	14703	RCT	STEMI Radiological or clinical HF and/or LV dysfunction	Thrombolytics 35.1%, primary PCI 14.8% Captorpil, valsartan or both	3 years	-	2.3%	12.3%
OACIS[4]	2475	Observa-tional co-hort study	STEMI	Primary PCI	1 year	12%	4.3%	7.7%
APEX-MI[15]	5745	Observa-tional co-hort	STEMI	Primary PCI, dual and triple anti-thrombotic therapy		11%	4.8%	6.3%

Current Cardiology Reviews, 2012, 8, 281-289

AMI incidence in AF

- Systemic review in 1965~2015-

- **Annual rate of AMI in AF**

  - 21 observation studies: 0.4%~2.5%

  - 10 clinical trials: 0.4%~1.3%

  ; improved control of atherosclerotic risk factors

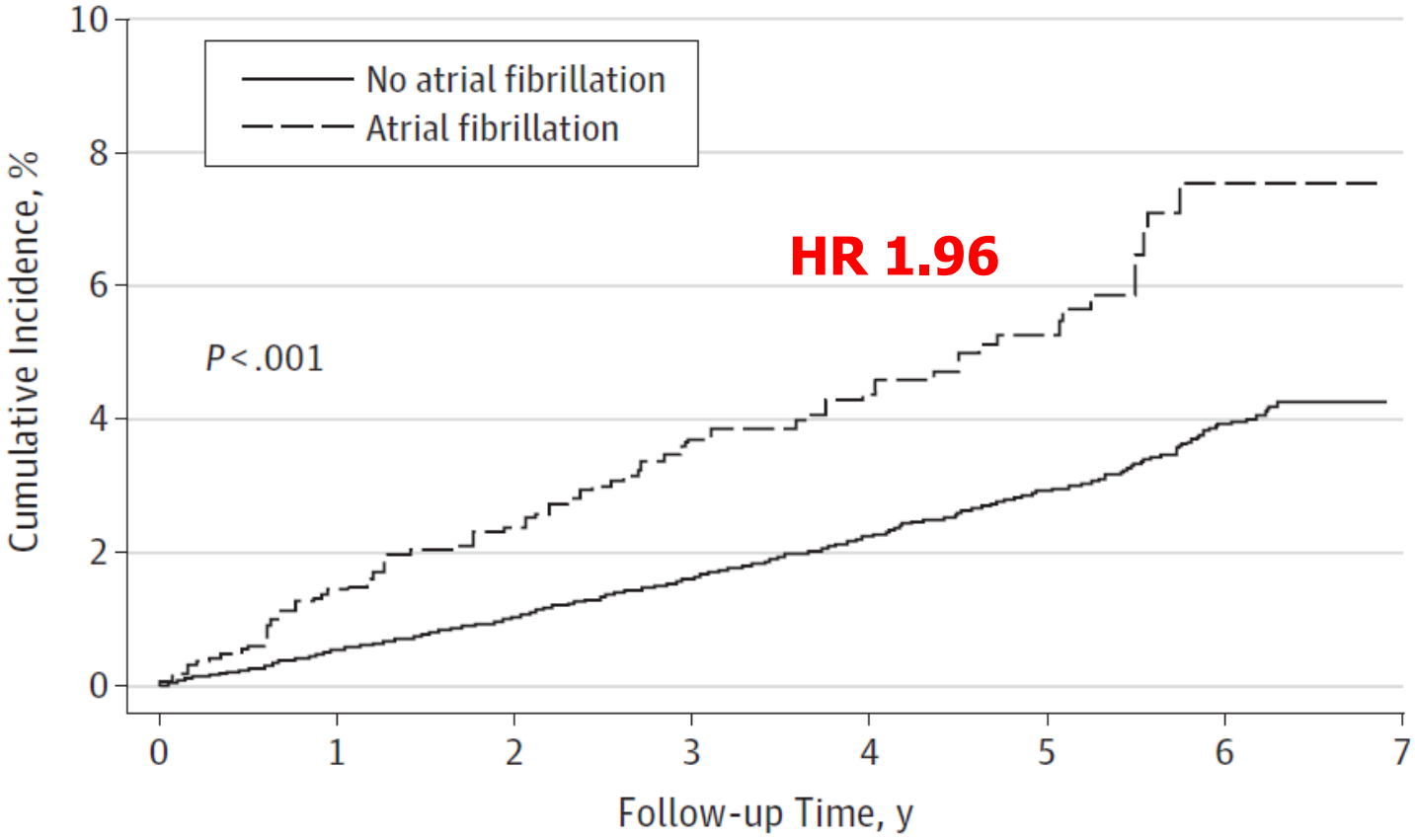
  ; inadequate prevention of thromboembolism in real world

  - Eastern countries: 0.2~0.3%

J Am Heart Assoc. 2016

MI incidence in AF vs. no AF

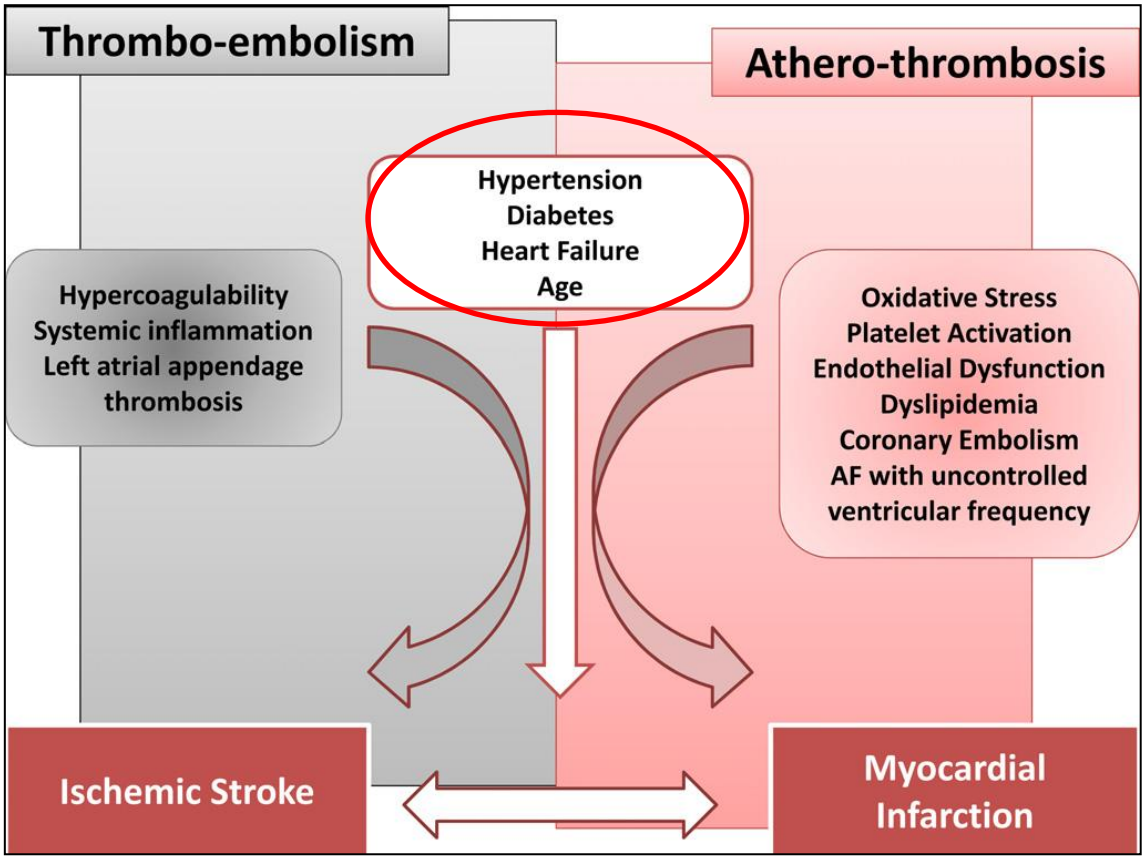
- REGARDS study, 23,928명, 6.9yrs F/U



AMA Intern Med. 2014;174:107–114.

AF and AMI

- AF and MI often occur together because of the strong association of both conditions with **aging** and **overlapping risk factors**.



J Am Heart Assoc. 2016

Prognostic implication of AF in AMI

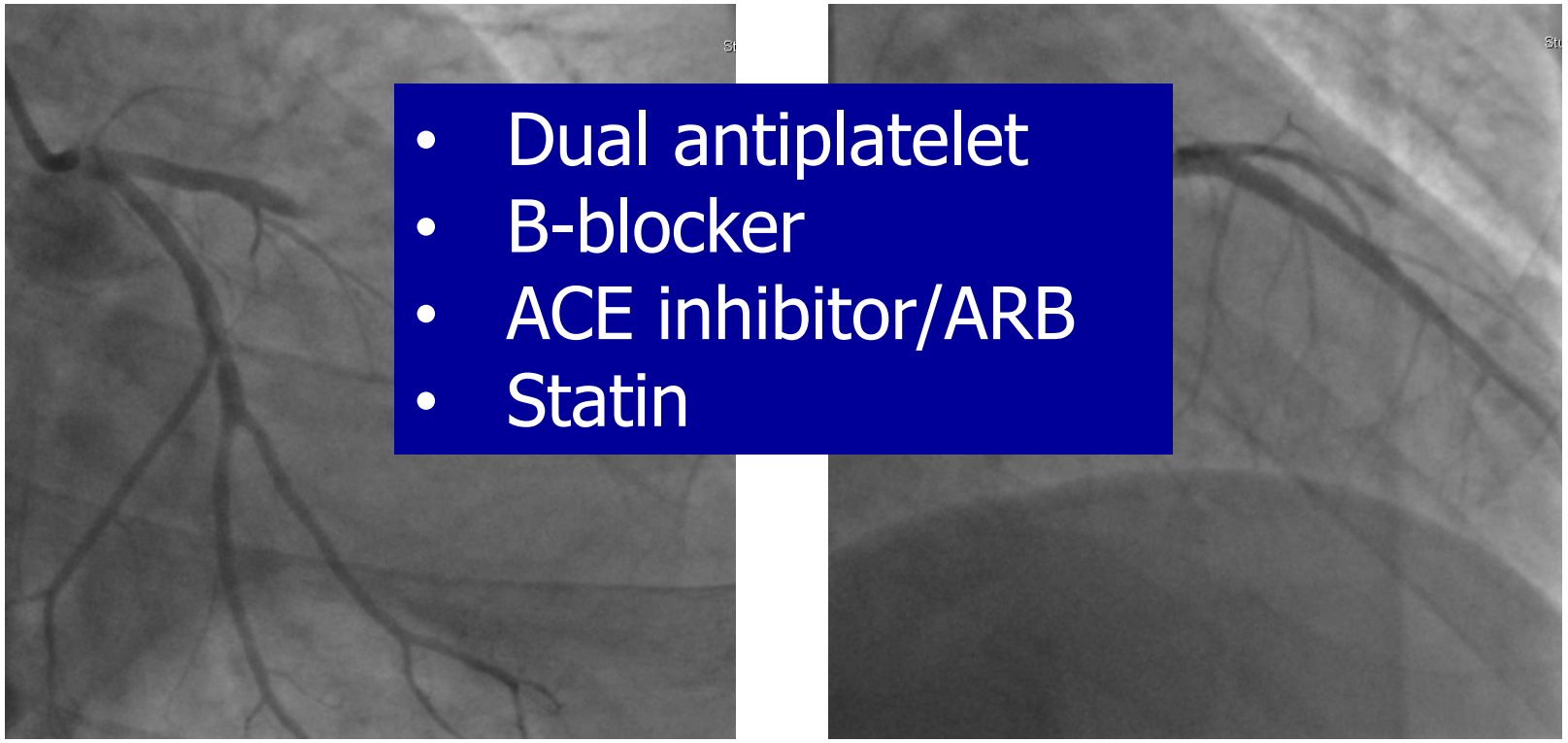
Table 3 Prognostic implication of atrial fibrillation in acute myocardial infarction (in-hospital and long-term)

Study/author	OR [95% CI]	
	In-hospital mortality	Long-term mortality
Behar/Sprint Prognosis[20]	no	1.28 [1.12–1.46]
Madias[37]	no	n.a.
Crenshaw/GUSTO I[19]	1.3 [1.2–1.4]	n.a.
Eldar/Sprint[18]	1.32 [0.92–1.87]	1.33 [1.05–1.68]
Pedersen/TRACE[33]	1.5 [1.2–1.8]	1.3 [1.2–1.4]
Rathore[10]	1.21 [0.99–1.10]	1.34 [1.30–1.39]
Wong/GUSTO III[17]	1.63 [1.31–2.02]	1.64 [1.35–2.01]
Pizzetti/GISSI III[28]	yes	yes
Goldberg[21]	1.71 [1.27–2.31]	1.23 [0.99–1.52]
Kinjo/OACIS[22]	no	1.64 [1.05–2.55]
Lehto/OPTIMAAL[34]	3.83 [1.97–7.43]	1.82 [1.39–2.39]
Pedersen/TRACE CHF[43]	n.a.	n.a.
Stenestrand/RIKS-HIA[46]	n.a.	n.a.
McMurray/ CAPRICORN[35]	n.a.	n.a.
Pedersen/TRACE SCD[44]	n.a.	1.33 [1.19–1.49]
Kober/VALIANT[36]	n.a.	1.32 [1.20–1.45]

European Heart Journal (2009) 30, 1038–1045

CASE 1

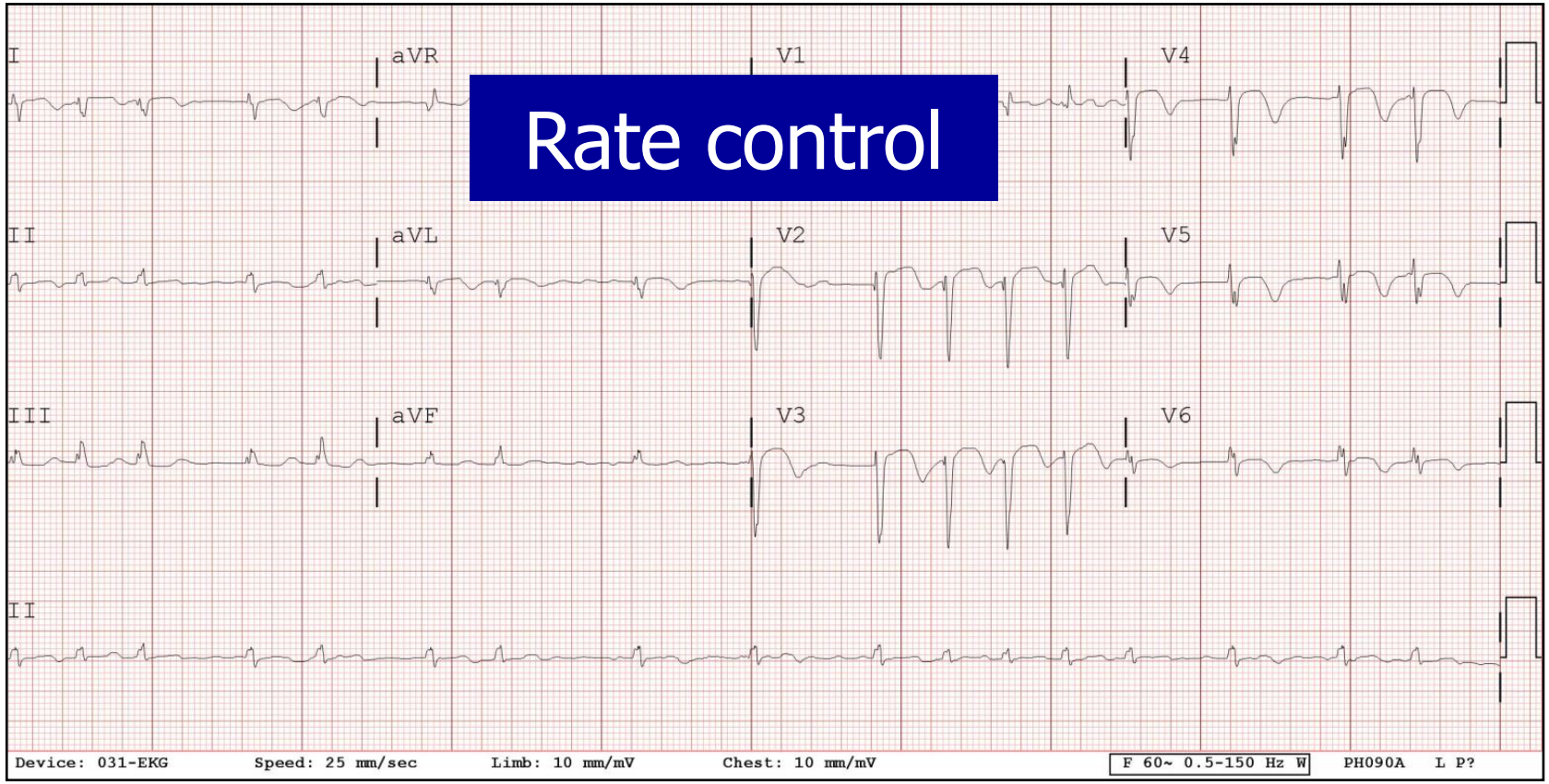
- M/67
- HTN/DM (+/-)
- Chest pain → STEMI



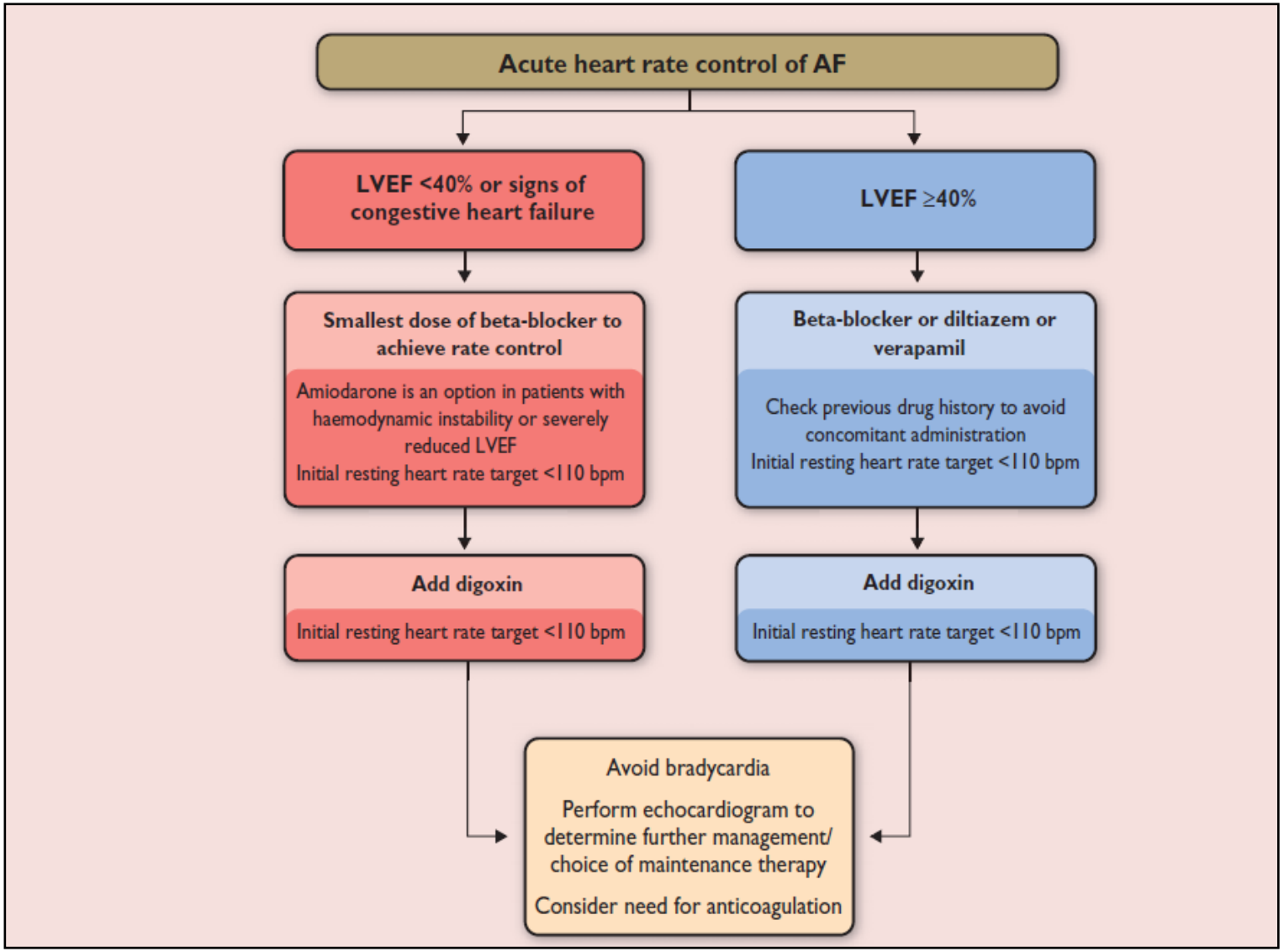
- Dual antiplatelet
- B-blocker
- ACE inhibitor/ARB
- Statin

Rate vs. Rhythm control of AF in AMI

- M/67
- HTN/DM (+/-)
- STEMI (pLAD stent #1 insertion), LVEF 38%, LA 3.8cm

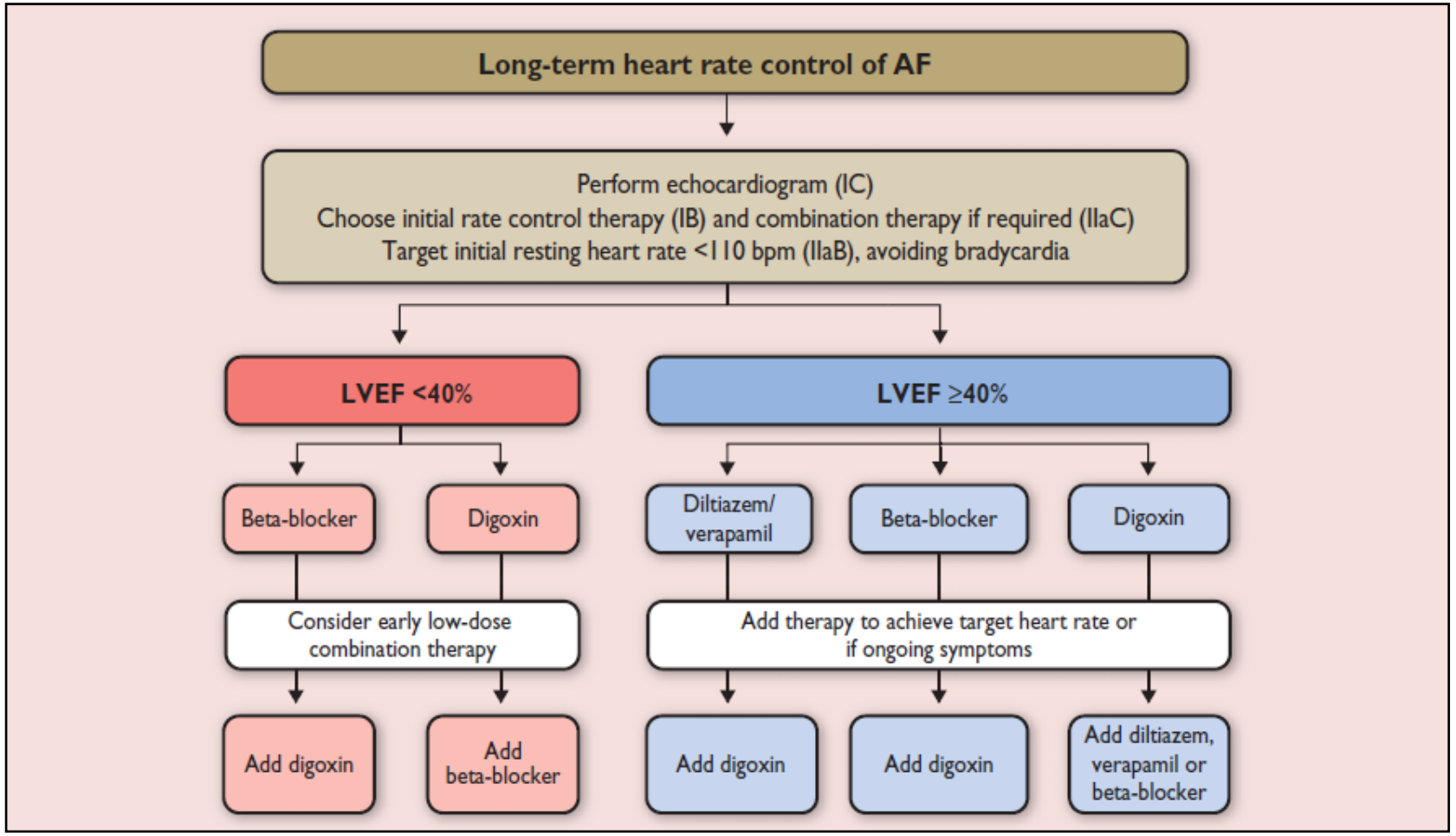


Acute heart rate control of AF



2016 ESC Guideline. European Heart Journal (2016) 37, 2893–2962

Long-term heart rate control of AF



2016 ESC Guideline. European Heart Journal (2016) 37, 2893–2962

Rate vs. Rhythm control of AF in AMI

- M/67
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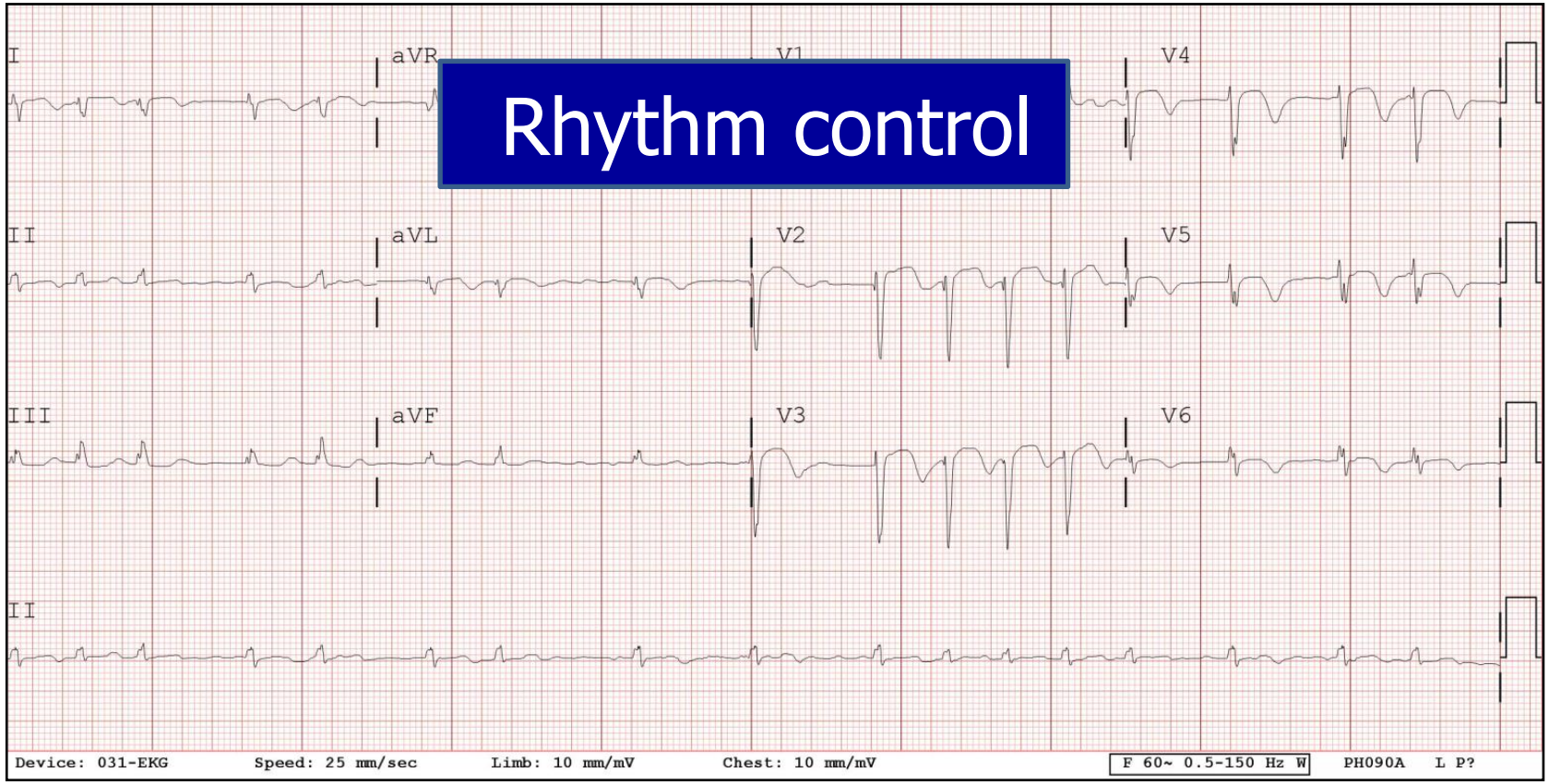
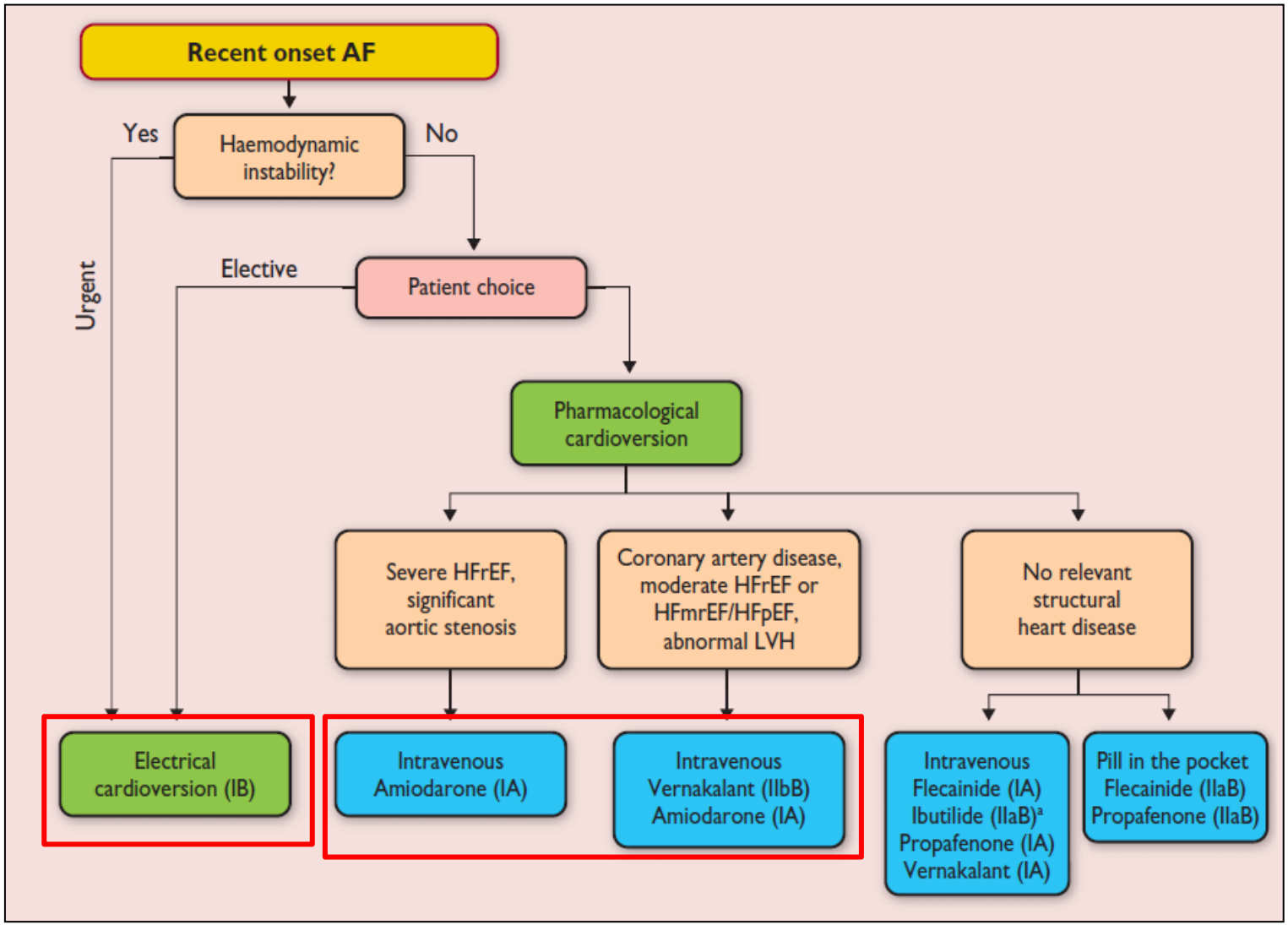
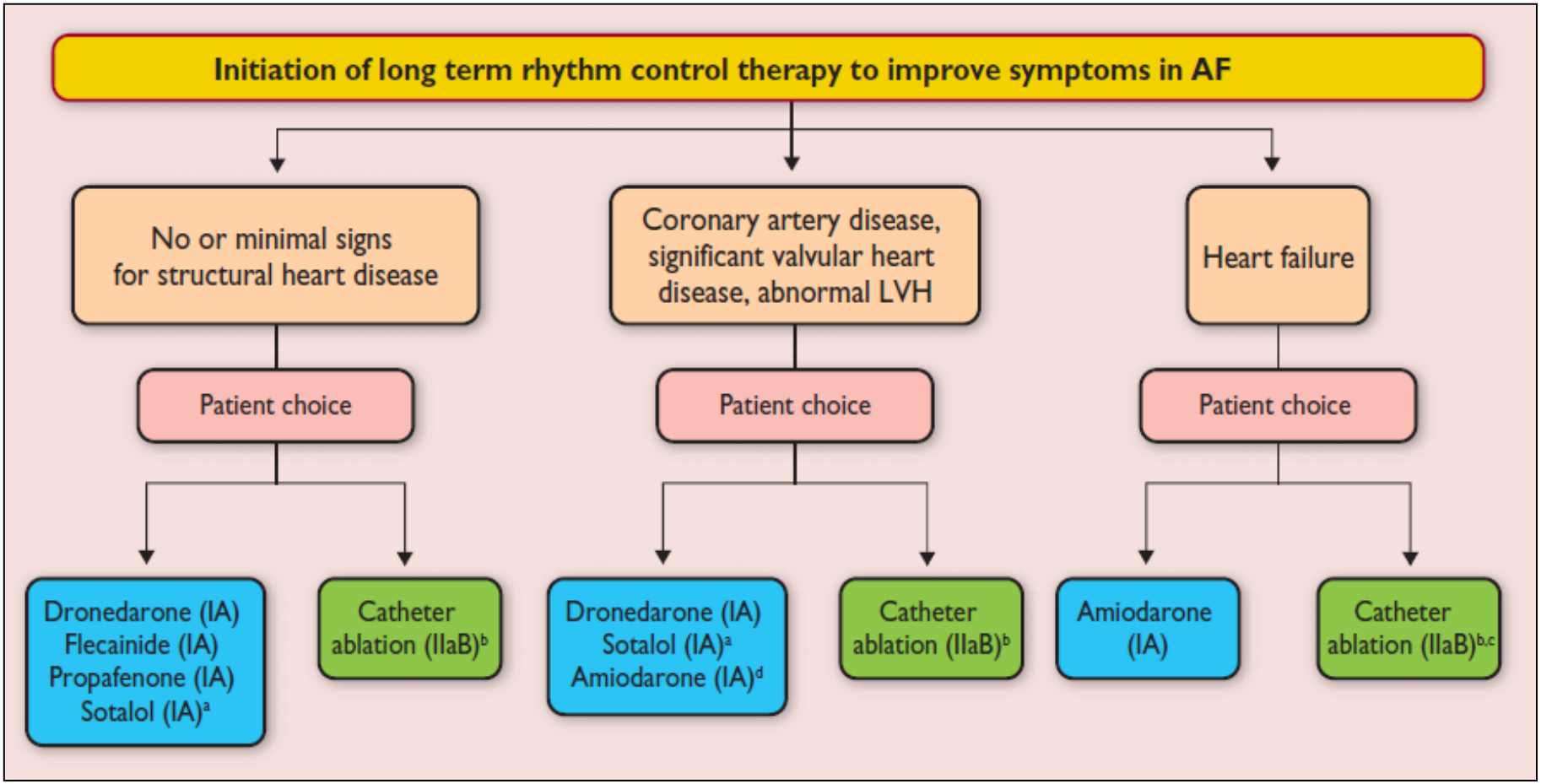


Rhythm control of recent onset AF



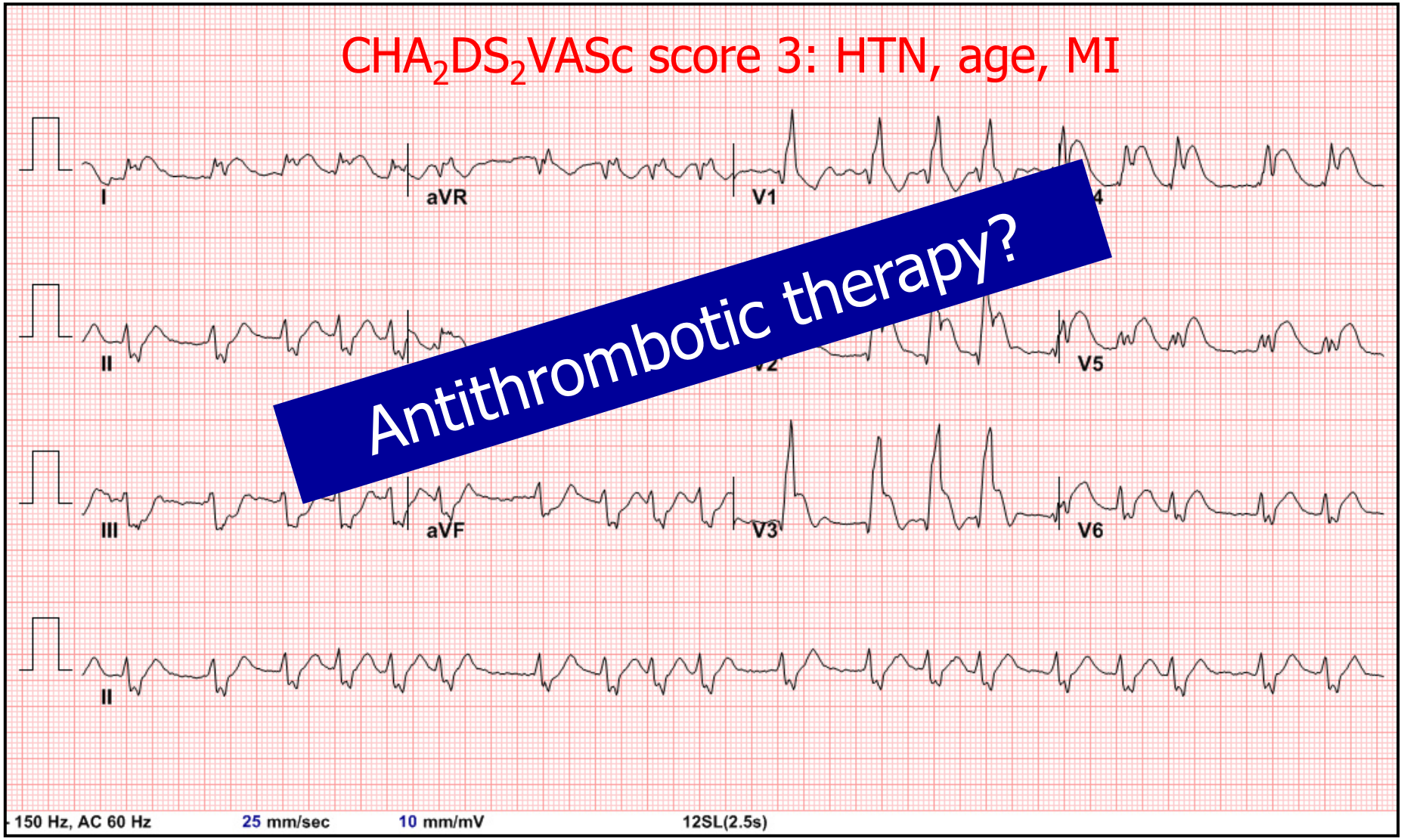
2016 ESC Guideline. European Heart Journal (2016) 37, 2893–2962

Long-term Rhythm control of AF



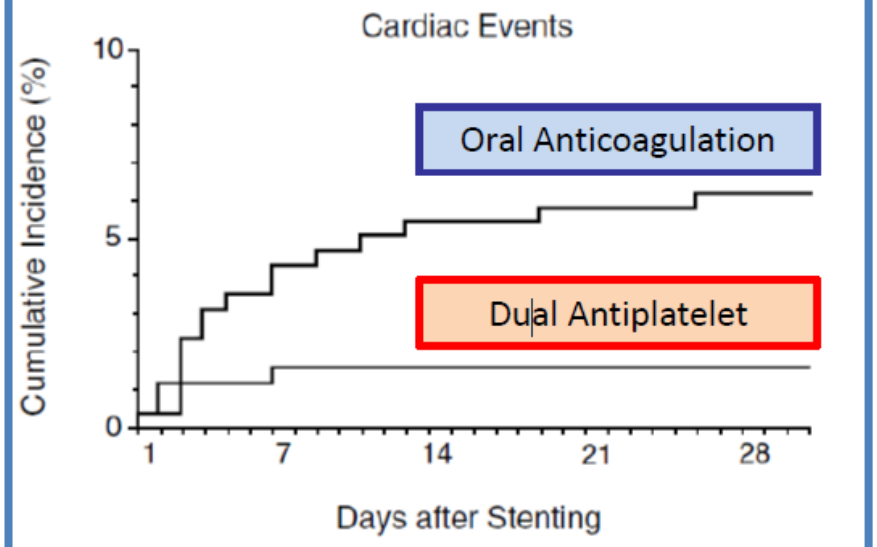
2016 ESC Guideline. European Heart Journal (2016) 37, 2893–2962

Antithrombotic therapy of AF in AMI



Dual antiplatelet vs. anticoagulation

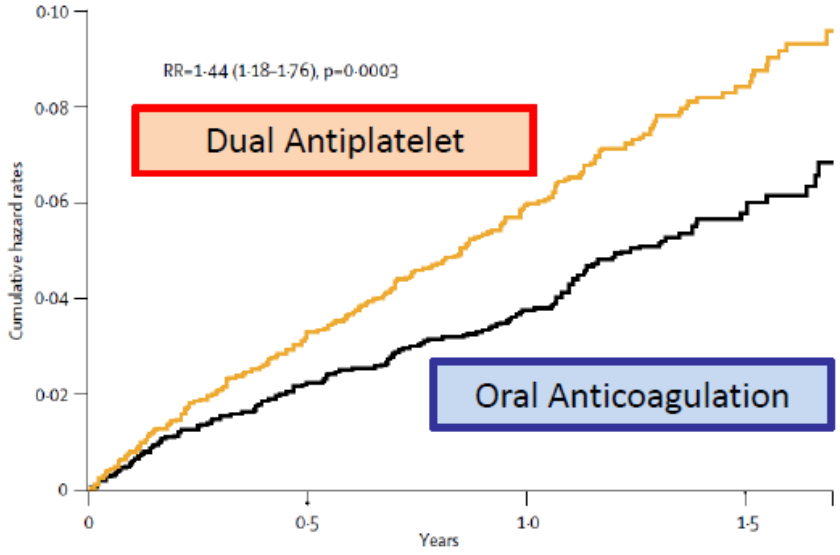
Coronary stent implantation



ISAR, NEJM 1996

+

Atrial fibrillation



ACTIVE-W Lancet 2006

CAD + AF
Dual antiplatelet +anticoagulation

Schömig et al. NEJM 1996;334:1084-9.
Connolly et al. Lancet 2006;367:1903-12.

Concomitant Use of Antiplatelet Therapy with Dabigatran or Warfarin in the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) Trial

- N=18,113, 6,952 (**38.4%**) received concomitant aspirin or clopidogrel

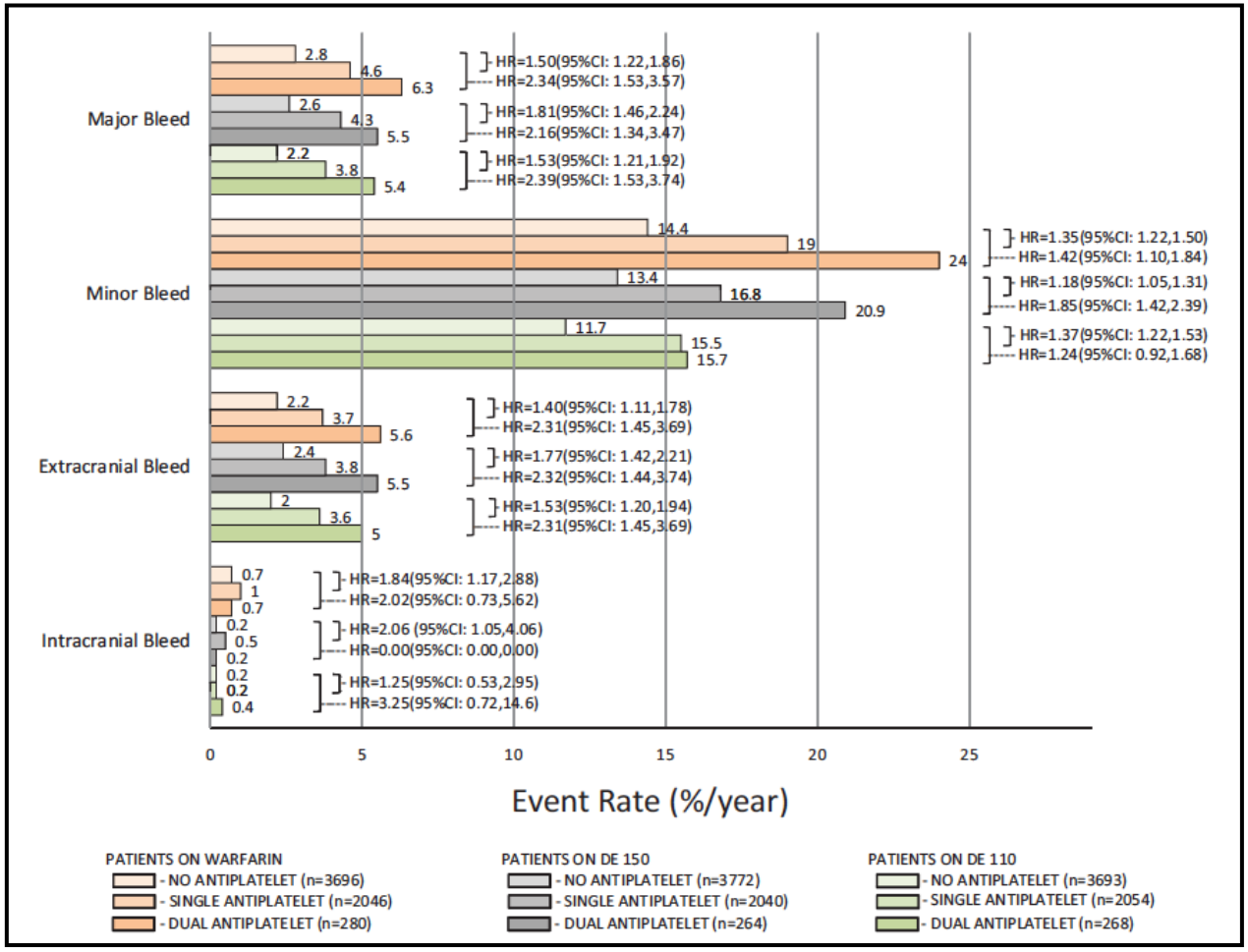
Table 2. Concomitant Use of ASA in Different Regions of the World

Region	Concomitant ASA Used	%
North America/western Europe	4120	39.3
Central/South America	410	42.9
Eastern/southern Europe	885	31.3
Southeast/East Asia	1232	44.3
Others	548	51.12

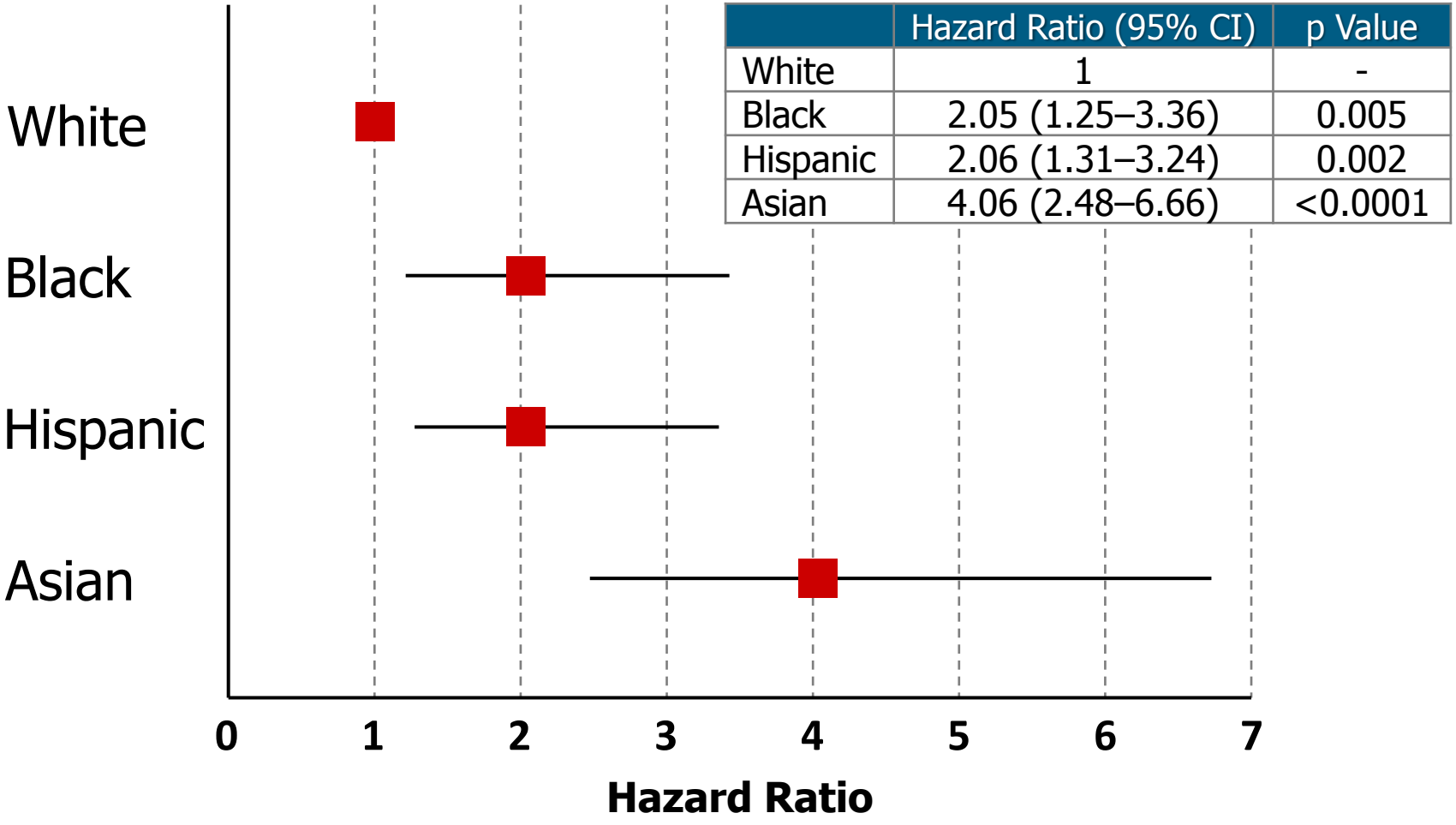
KUDMCDansAL, et al. Circulation 2013;127:634

Concomitant Use of Antiplatelet Therapy with Dabigatran or Warfarin in the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) Trial

- Major bleeding 1.6↑ in SAPT and 2.31 ↑ DAPT



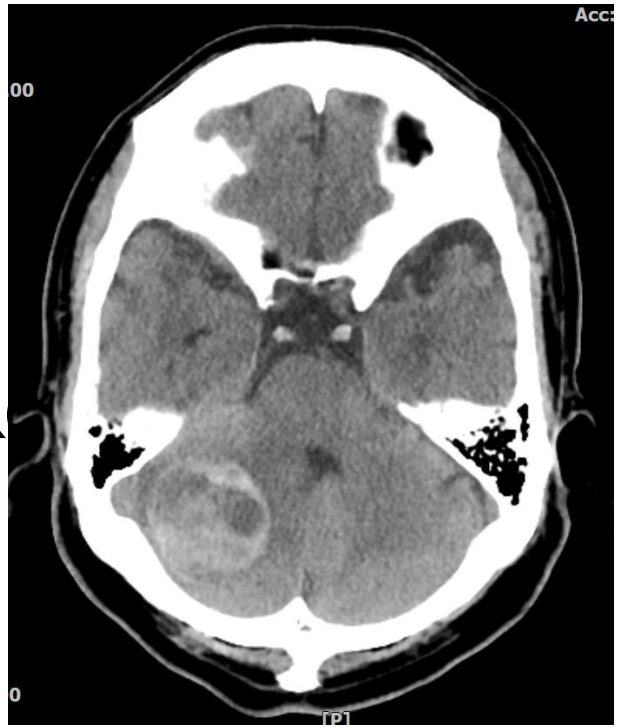
Ethnic difference of ICH on warfarin therapy



	Hazard Ratio (95% CI)	p Value
White	1	-
Black	2.05 (1.25–3.36)	0.005
Hispanic	2.06 (1.31–3.24)	0.002
Asian	4.06 (2.48–6.66)	<0.0001

Shen AY, et al: J Am Coll Cardiol 50: 309-315, 2007

Case 2



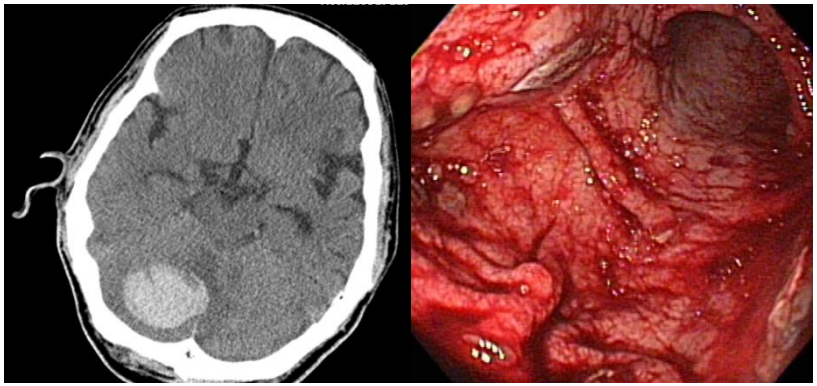
- M/59
- HTN/DM (-/-), HF (+), OMI (+), AF (+)
- 2017.1.16 타 병원 unstable angina (mR
  #2)
- 2017.1.21 dysarthria로 본원 내원

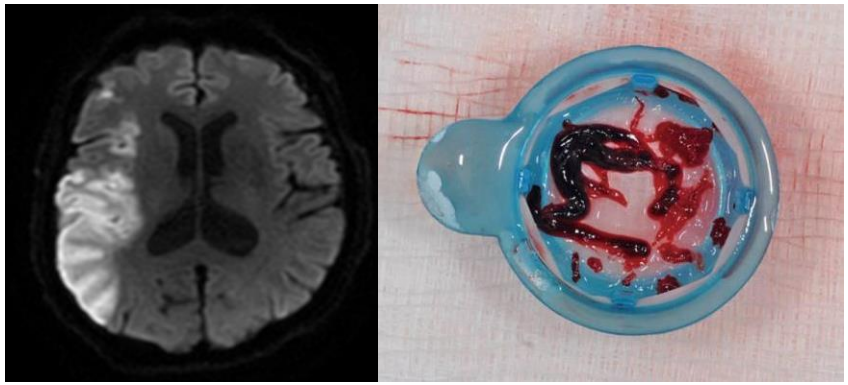
- Current medication
  - Aspirin 100mg, clopidogrel 75mg, rivaroxaban 15mg
    amiodarone 200mg, telmisartan 40mg, carvedilol 12.5mg,
    rosuvastatin 10mg, spironolactone 25mg, torsemide 5mg

AMI & AF

Bleeding

Stent thrombosis
Stroke





Possible combinations of anti-thrombotic therapy

- OAC + Aspirin + Clopidogrel
  ; efficacy ↑, **bleeding ↑**

- Aspirin + Clopidogrel
  ; **stroke ↑**

- OAC
  ; **stent thrombosis ↑**

- OAC + Aspirin

- OAC + Clopidogrel

The WOEST Study

What is the **O**ptimal antiplat**E**let and anticoagulant therapy in patients with oral anticoagulation and coronary **S**ten**T**ing

- 573 patients, OAC undergoing PCI; 68% AF

1:1 Randomisation:

Double therapy group:	Triple therapy group
OAC + 75mg Clopidogrel qd	OAC + 75mg Clopidogrel qd + 80mg Aspirin qd
1 month minimum after BMS	1 month minimum after BMS
1 year after DES	1 year after DES

Follow up: 1 year

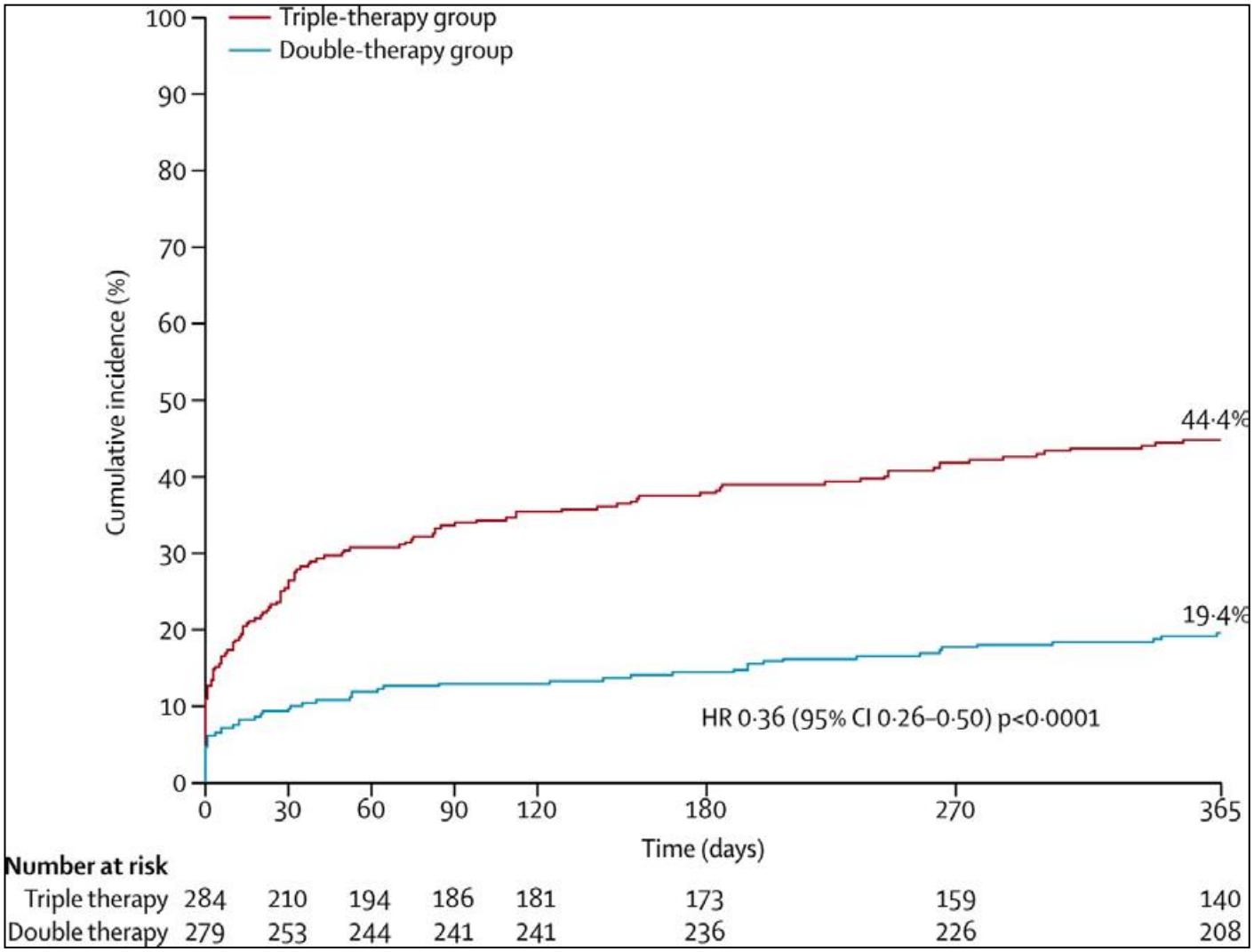
Primary Endpoint: The occurence of all bleeding events (TIMI criteria)

Secondary Endpoints:
- Combination of stroke, death, myocardial infarction, stent thrombosis and target vessel revascularisation
- All individual components of primary and secondary endpoints

De Wilde et al. Lancet 2013;381:1107-15

The WOEST Study

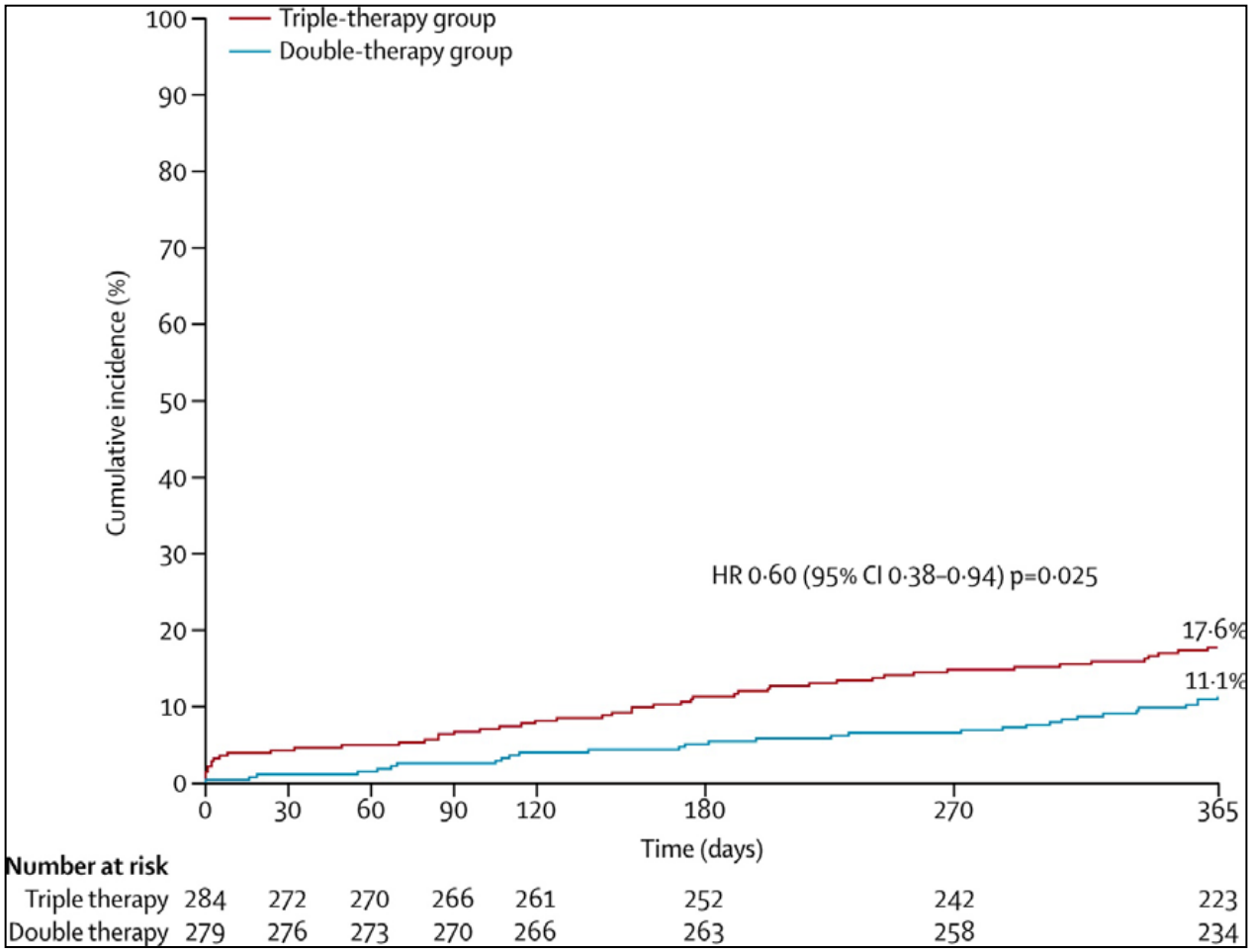
Primary Endpoint (Any Bleeding)



De Wilde et al. Lancet 2013;381:1107-15

The WOEST Study

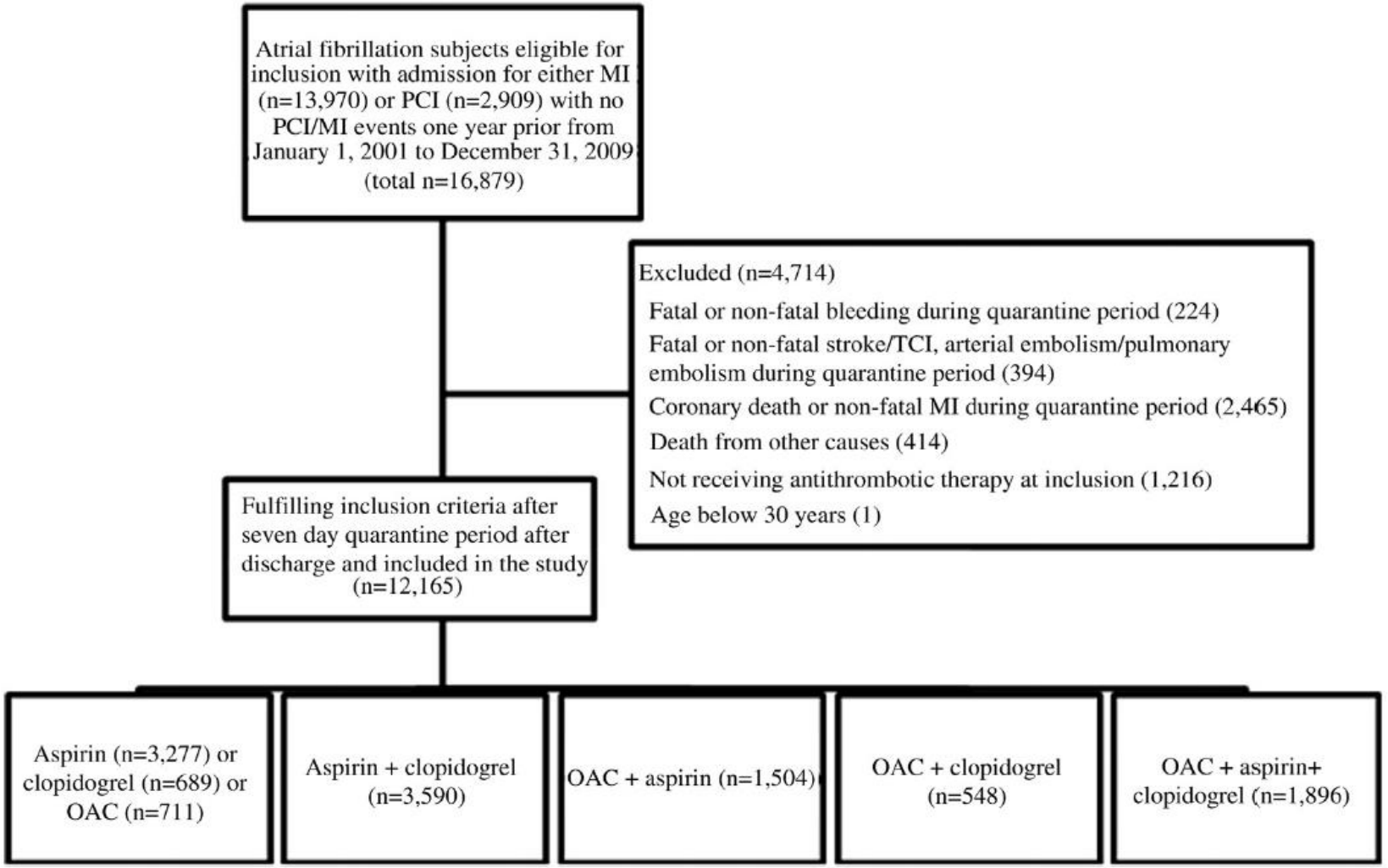
Secondary Endpoint: Death, MI, Stroke, Target Vessel Revascularization, Stent Thrombosis



De Wilde et al. Lancet 2013;381:1107-15

Antithrombotic therapy in AF & MI or PCI

Danish Nationwide Observational Cohort



Lamberts et al. J Am Coll Cardiol 2013;62:891-9

Antithrombotic therapy in AF & MI or PCI

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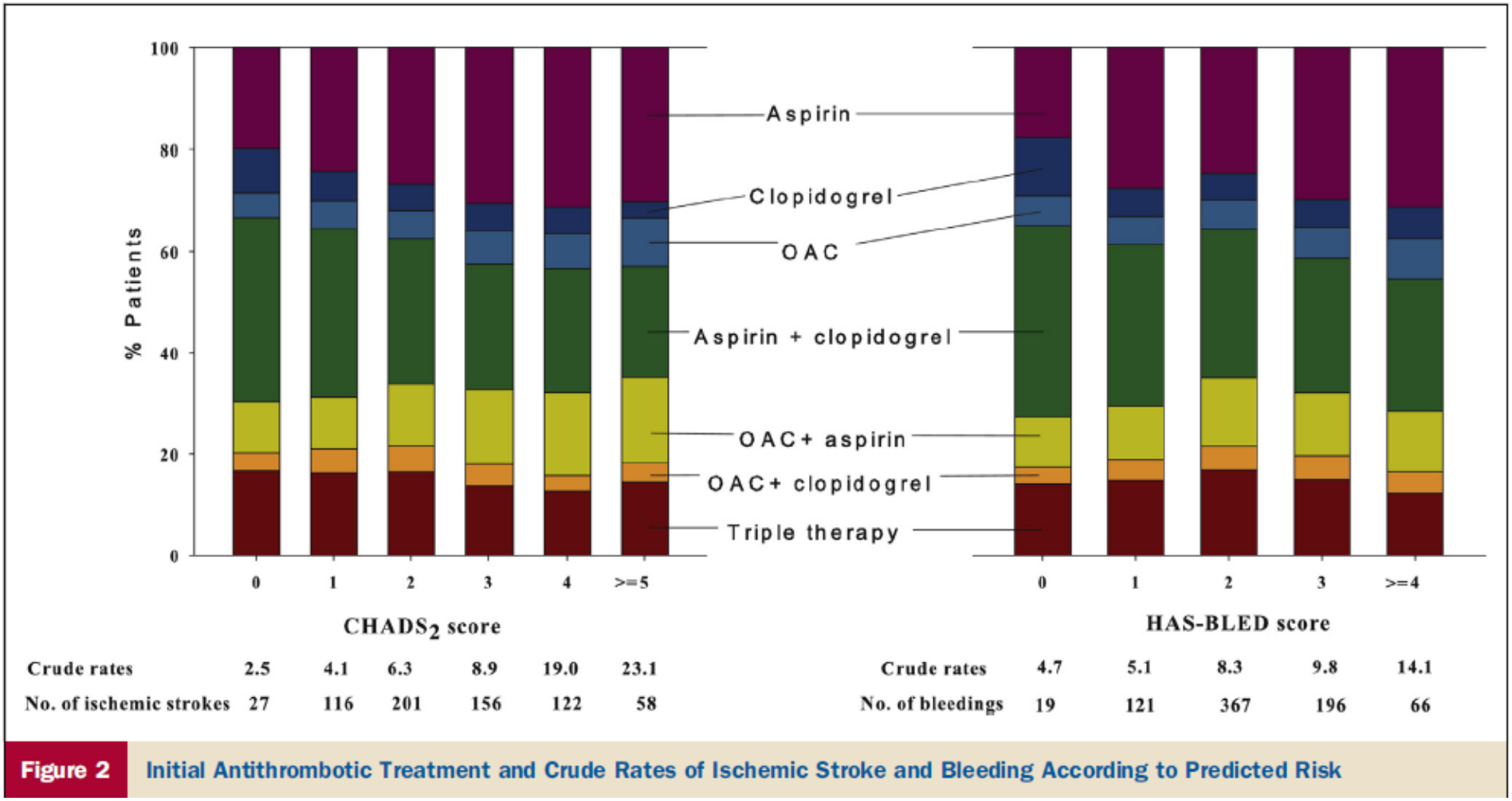
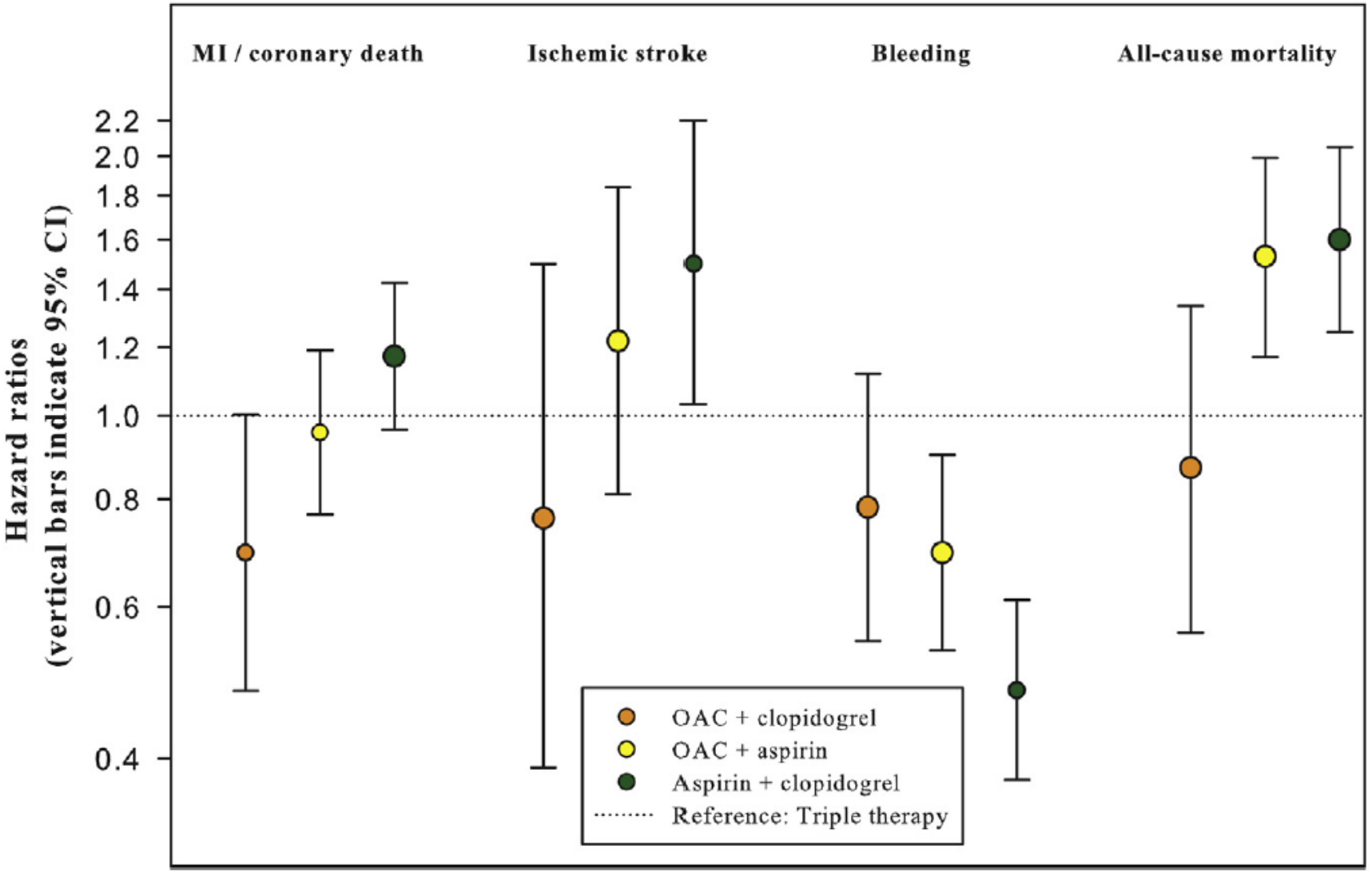


Figure 2 Initial Antithrombotic Treatment and Crude Rates of Ischemic Stroke and Bleeding According to Predicted Risk

Lamberts et al. J Am Coll Cardiol 2013;62:891-9

Antithrombotic therapy in AF & MI or PCI



Lamberts et al. J Am Coll Cardiol 2013;62:891-9

Results of WOEST & Danish registry

Clopidogrel + OAC ≥

dual antiplatelet + OAC

: Efficacy in CAD (WOEST ↑, Danish registry ↔)

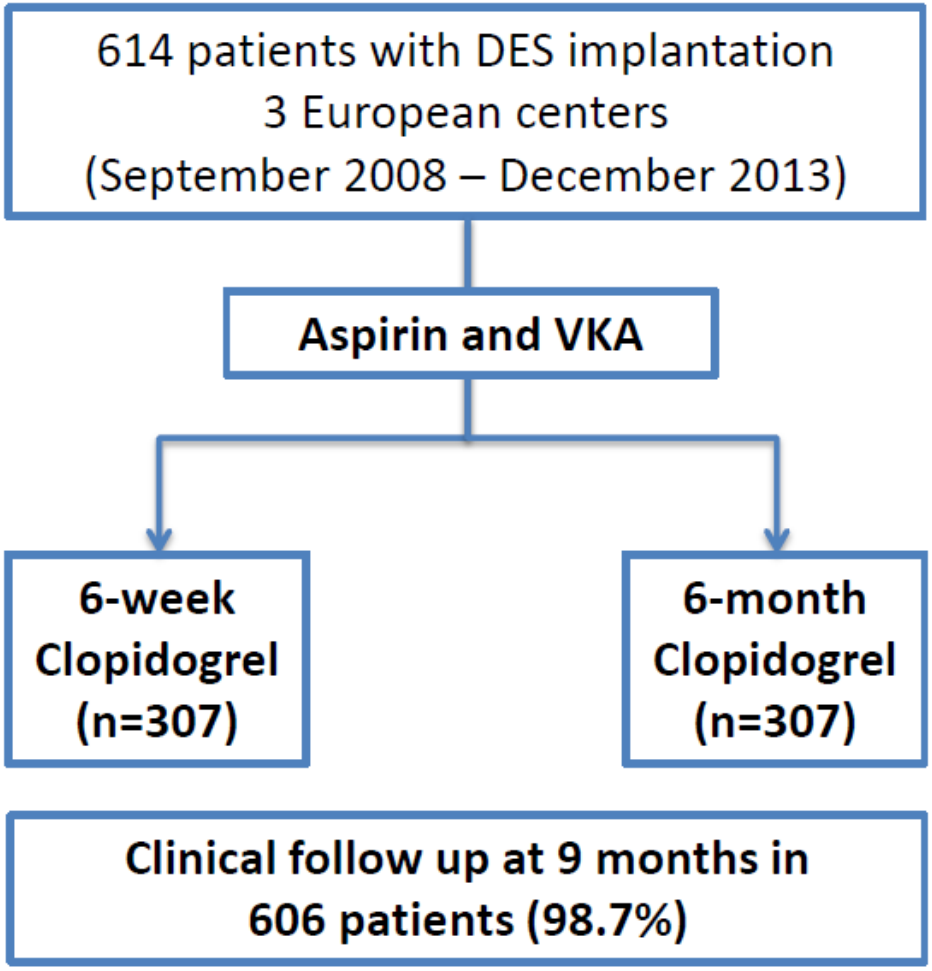
Stroke prevention (WOEST ↔, Danish registry ↔)

Bleeding (WOEST ↓, Danish registry ↔)

ISAR-TRIPLE Trial

Duration of triple therapy in patients requiring oral anticoagulation after drug-eluting stent implantation

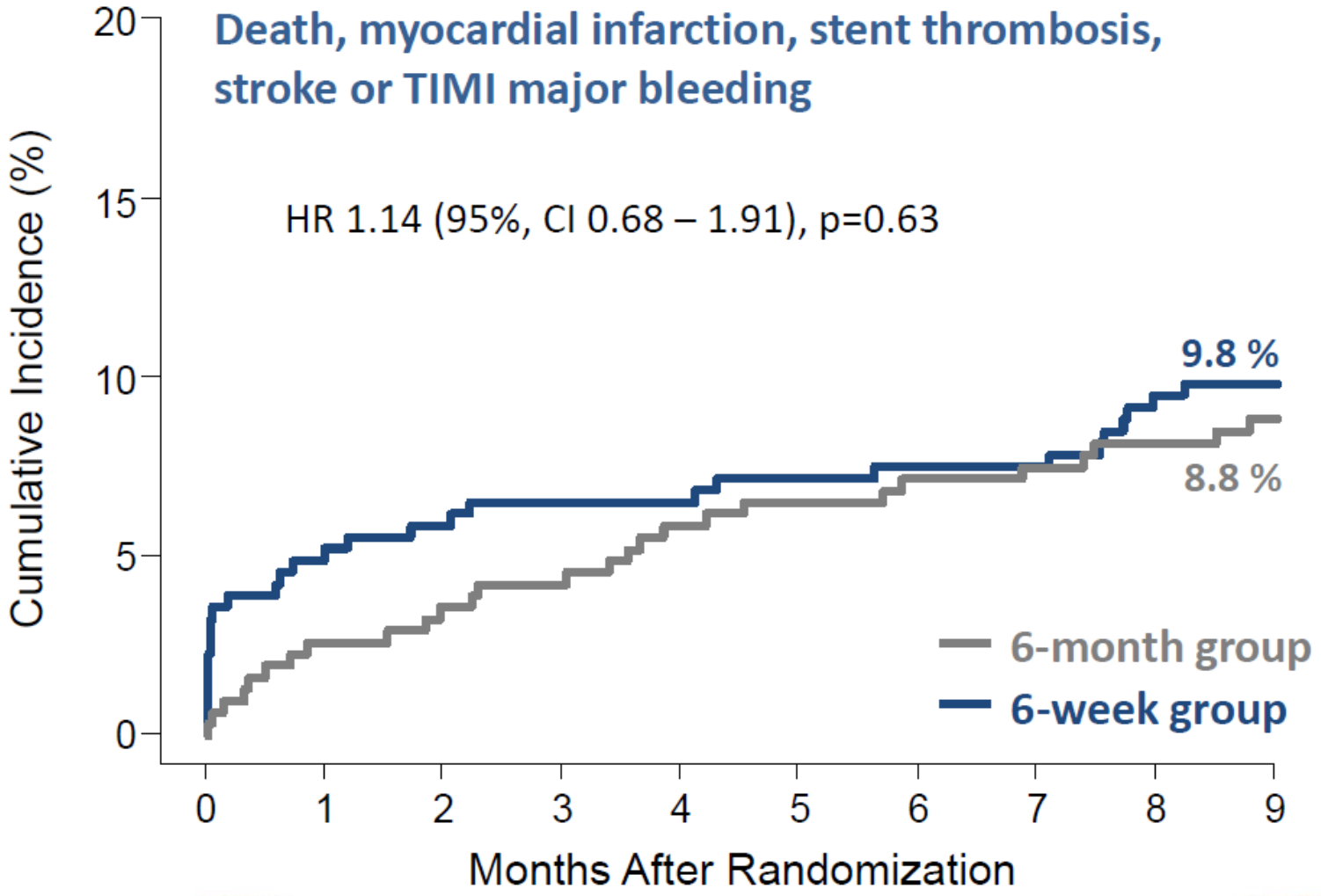
- N=614
- ACS 32%
- AF 84%



Fiedler KA, et al. J Am Coll Cardiol. 2015;65:1619-29.

ISAR-TRIPLE Trial

Primary Endpoint

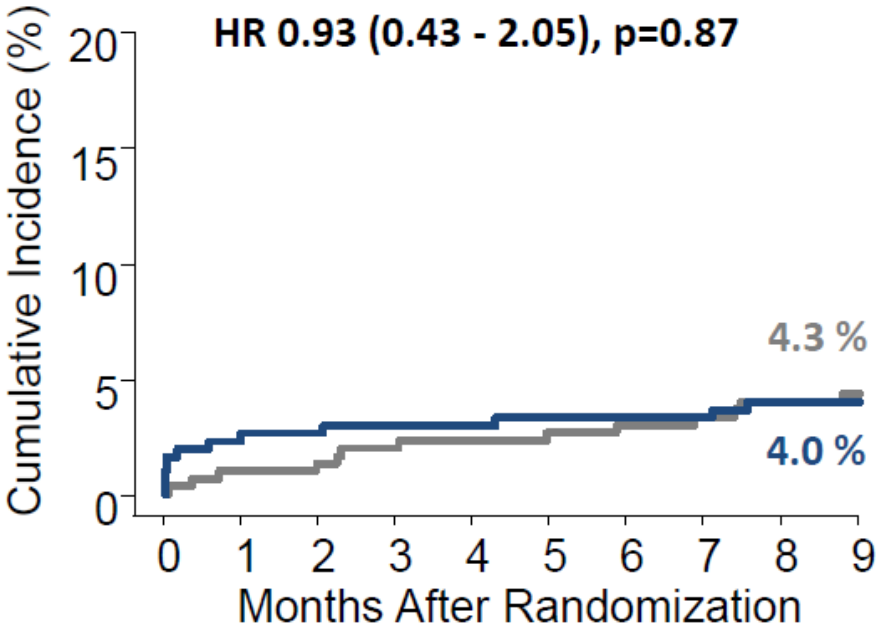


Fiedler KA, et al. J Am Coll Cardiol. 2015;65:1619-29.

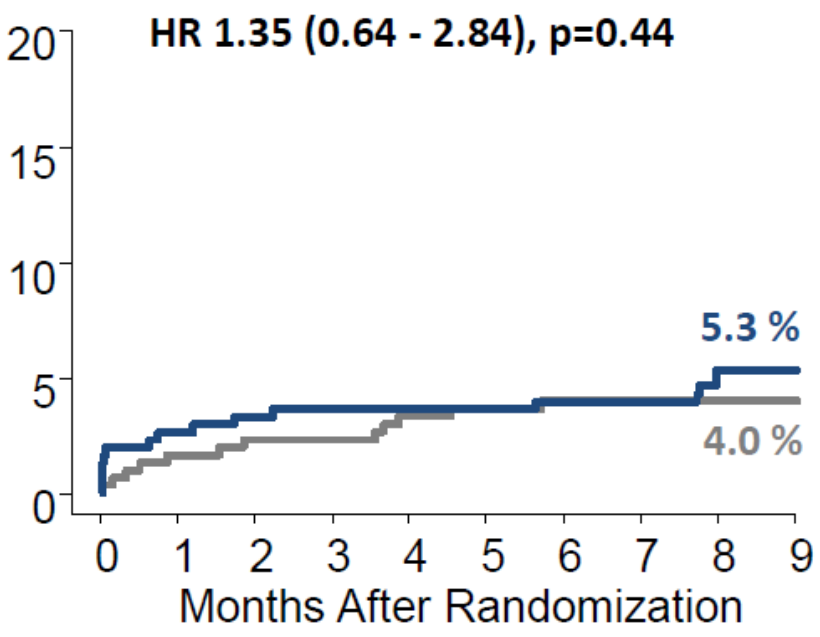
ISAR-TRIPLE Trial

Secondary Endpoint

Cardiac death, myocardial infarction, stent thrombosis or ischemic stroke

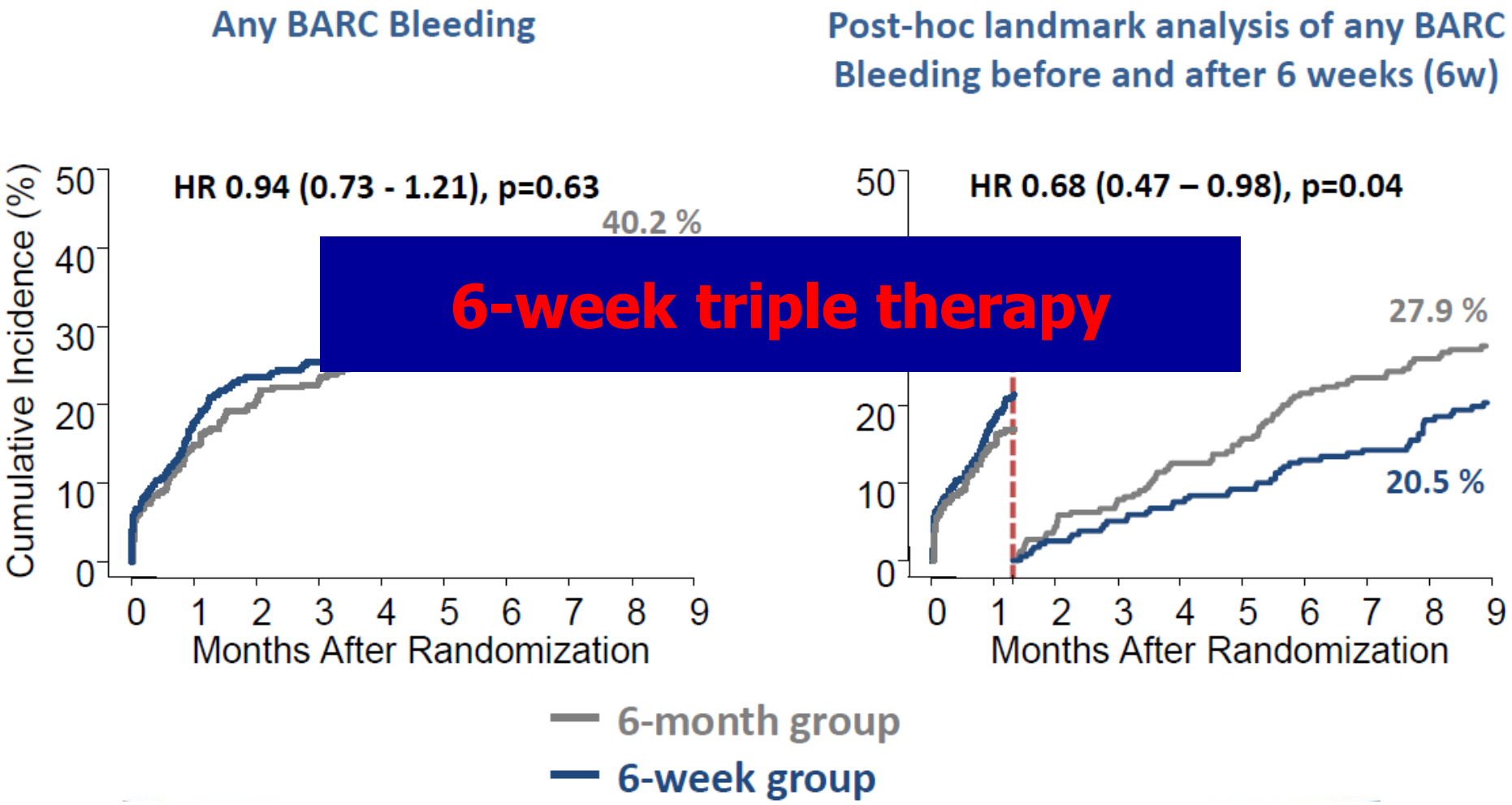


TIMI major bleeding



ISAR-TRIPLE Trial

Any BARC Bleeding



Non-vitamin K antagonist oral anticoagulant (NOAC) in AF and ACS

Comparison of NOAC : Meta-Analysis

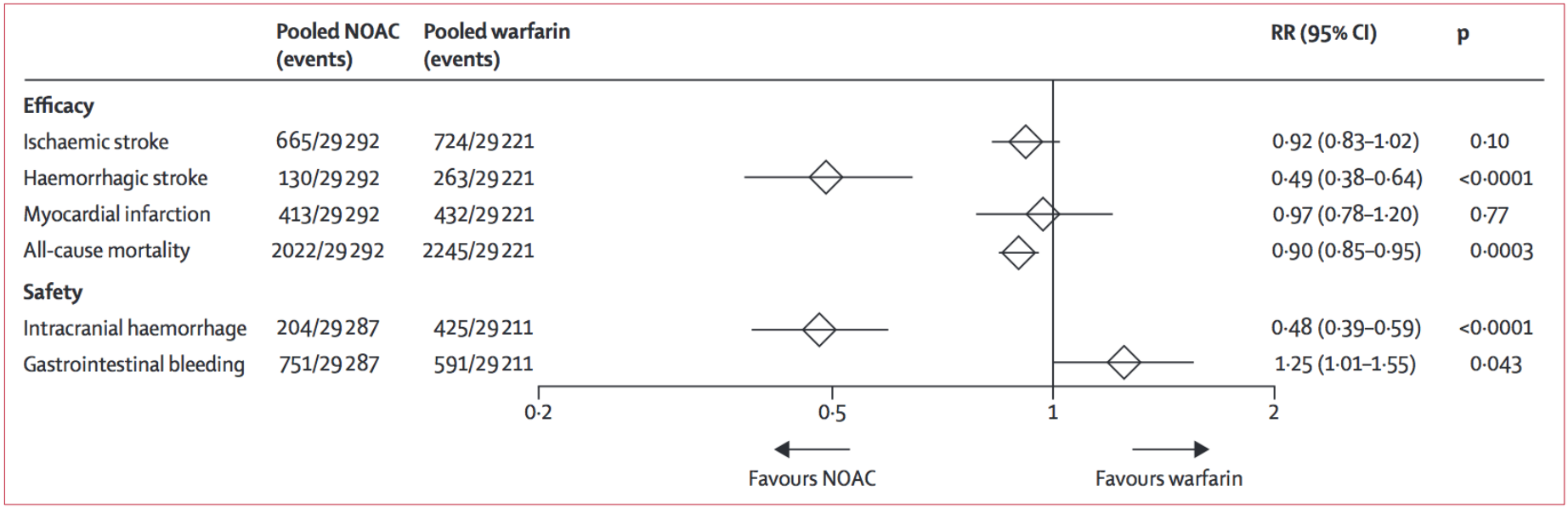


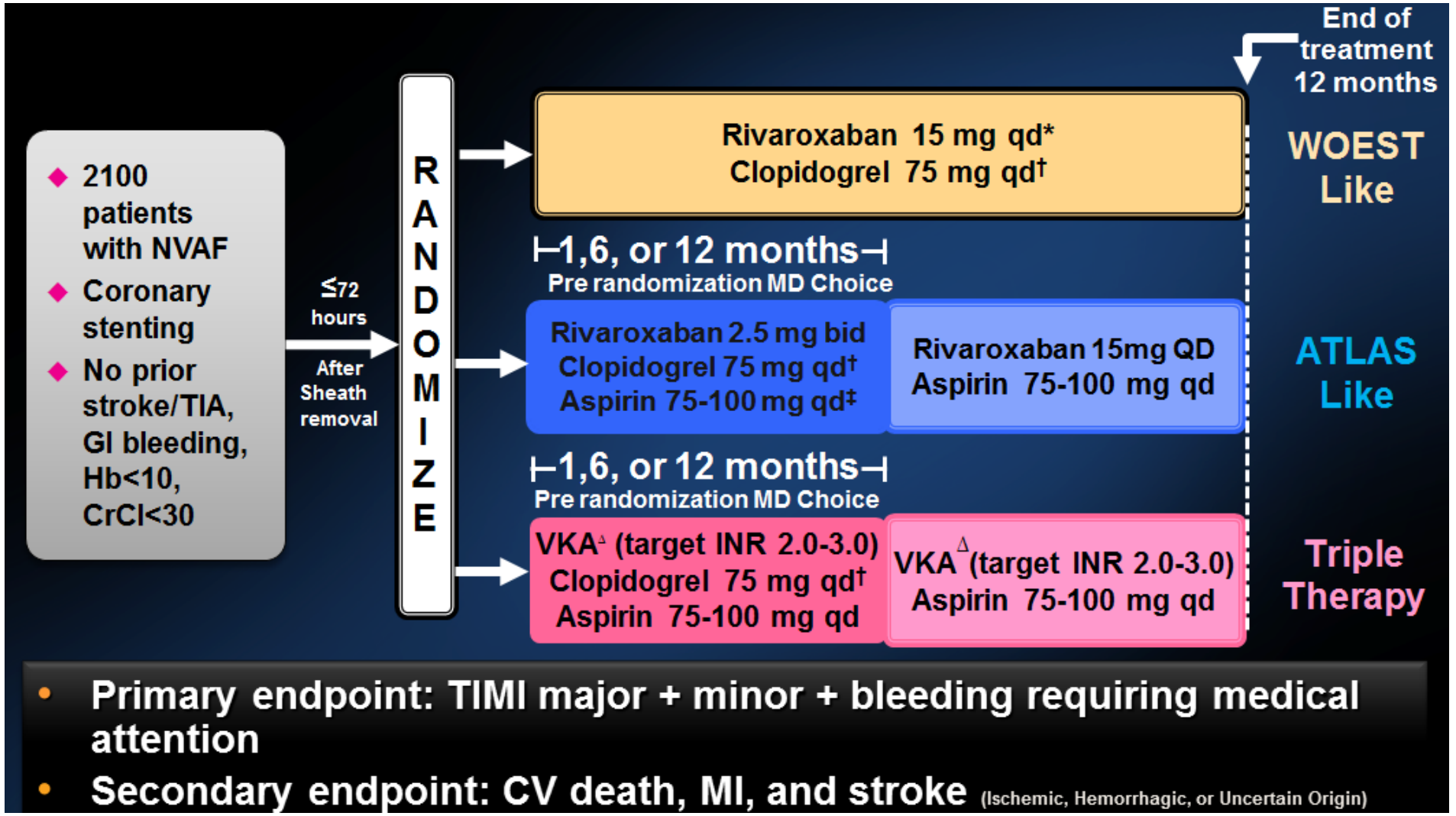
***Figure 2*: Secondary efficacy and safety outcomes**

Data are n/N, unless otherwise indicated. Heterogeneity: ischaemic stroke I^2=32%, p=0·22; haemorrhagic stroke I^2=34%, p=0·21; myocardial infarction I^2=48%, p=0·13; all-cause mortality I^2=0%, p=0·81; intracranial haemorrhage I^2=32%, p=0·22; gastrointestinal bleeding I^2=74%, p=0·009. NOAC=new oral anticoagulant. RR=risk ratio.

Ruff CT et al. Lancet. 2014;383:955-62

PIONEER AF-PCI

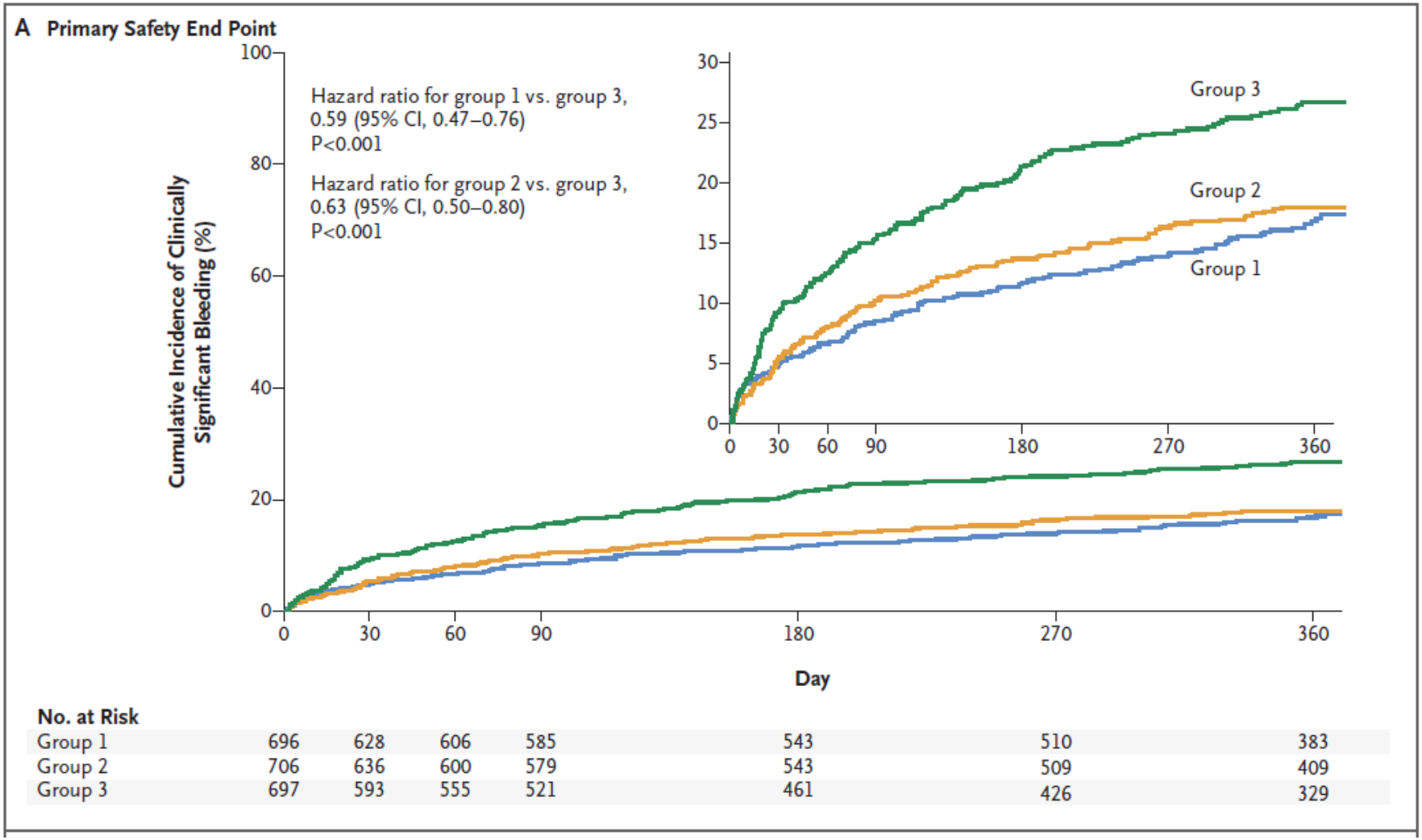
- N=2,124, AF & PCI with stent



N Engl J Med. 2016;375:2423-2434

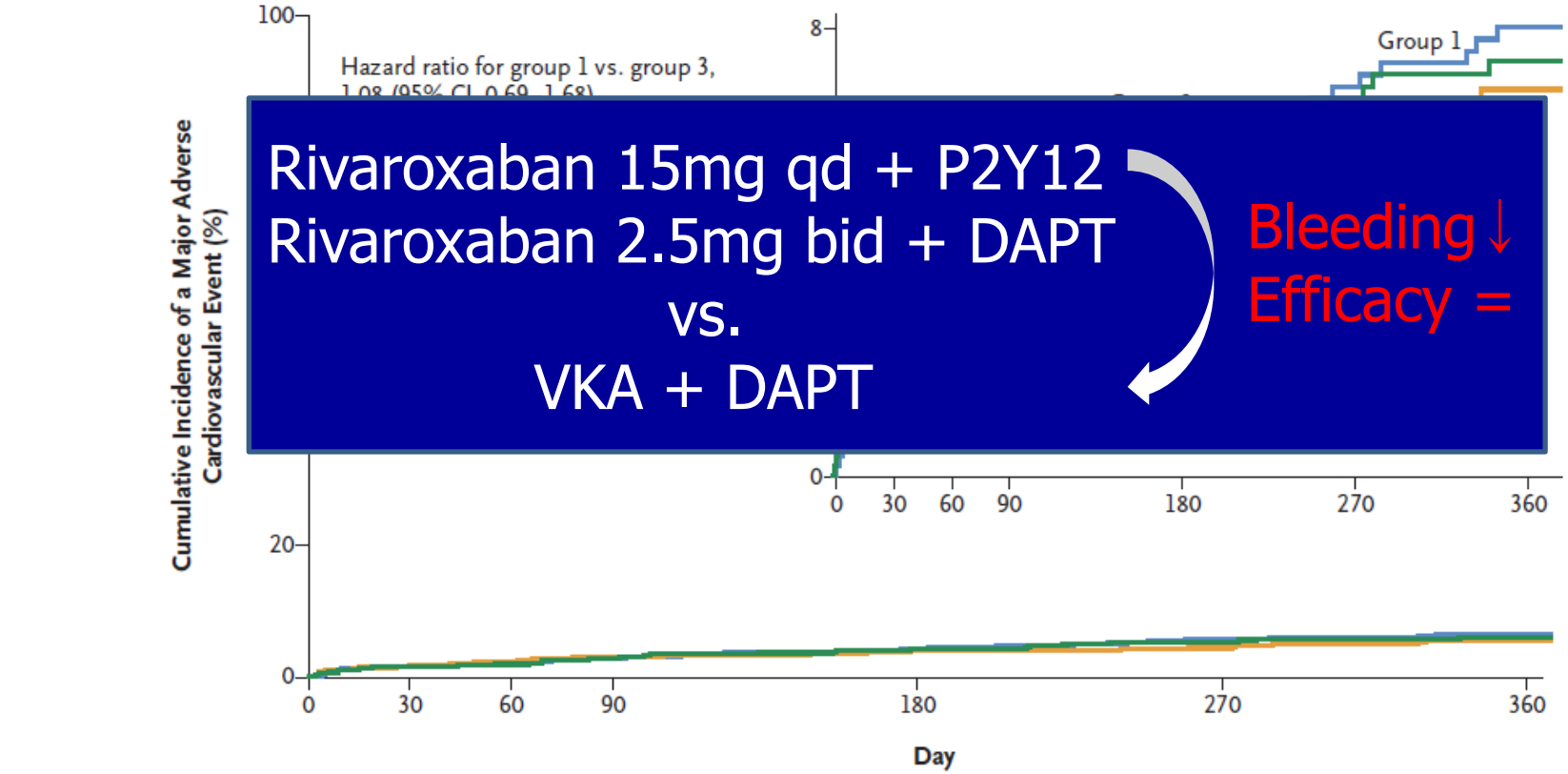
PIONEER AF-PCI

Primary Safety End Point



PIONEER AF-PCI

Secondary Efficacy End Point

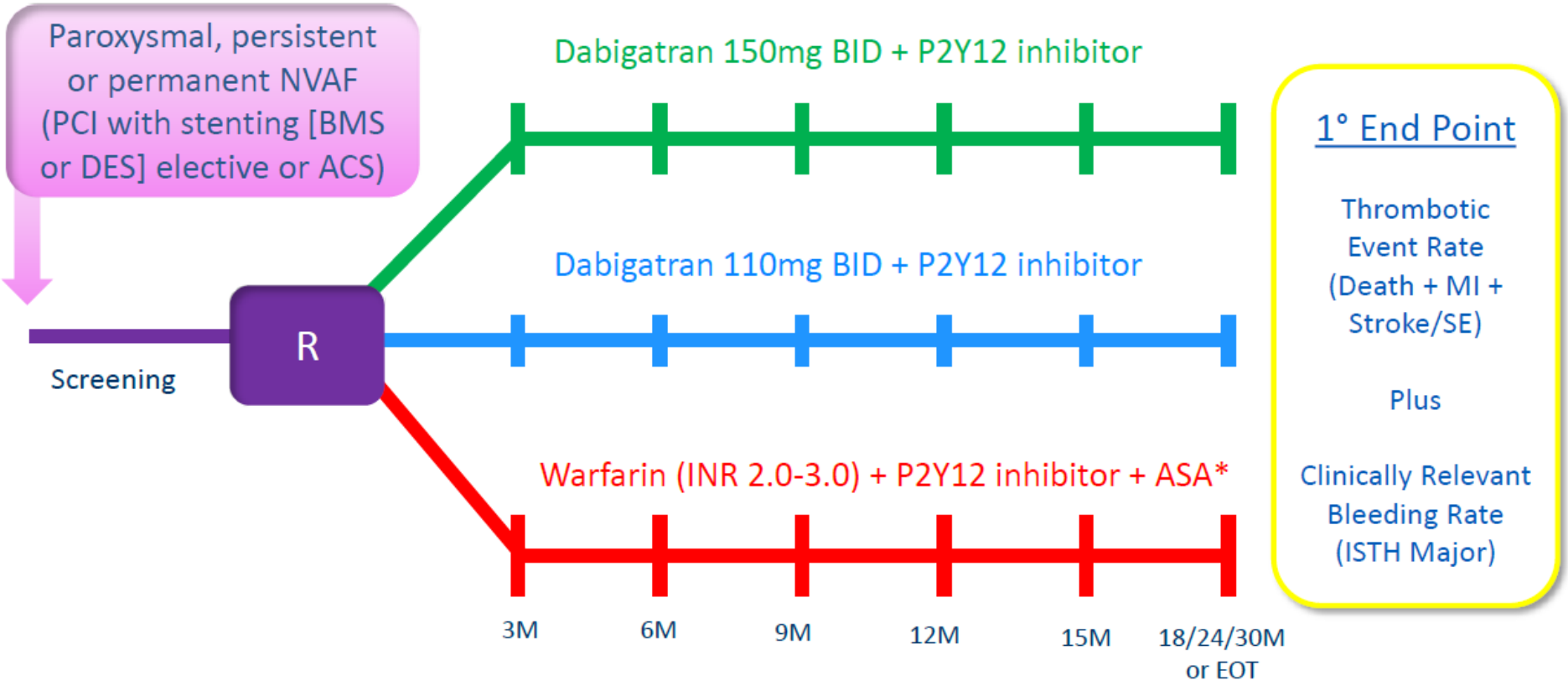


No. at Risk							
Group 1	694	648	633	621	590	562	430
Group 2	704	662	640	628	596	570	457
Group 3	695	635	607	579	543	514	408

RE-DUAL PCI

Ongoing randomized trials

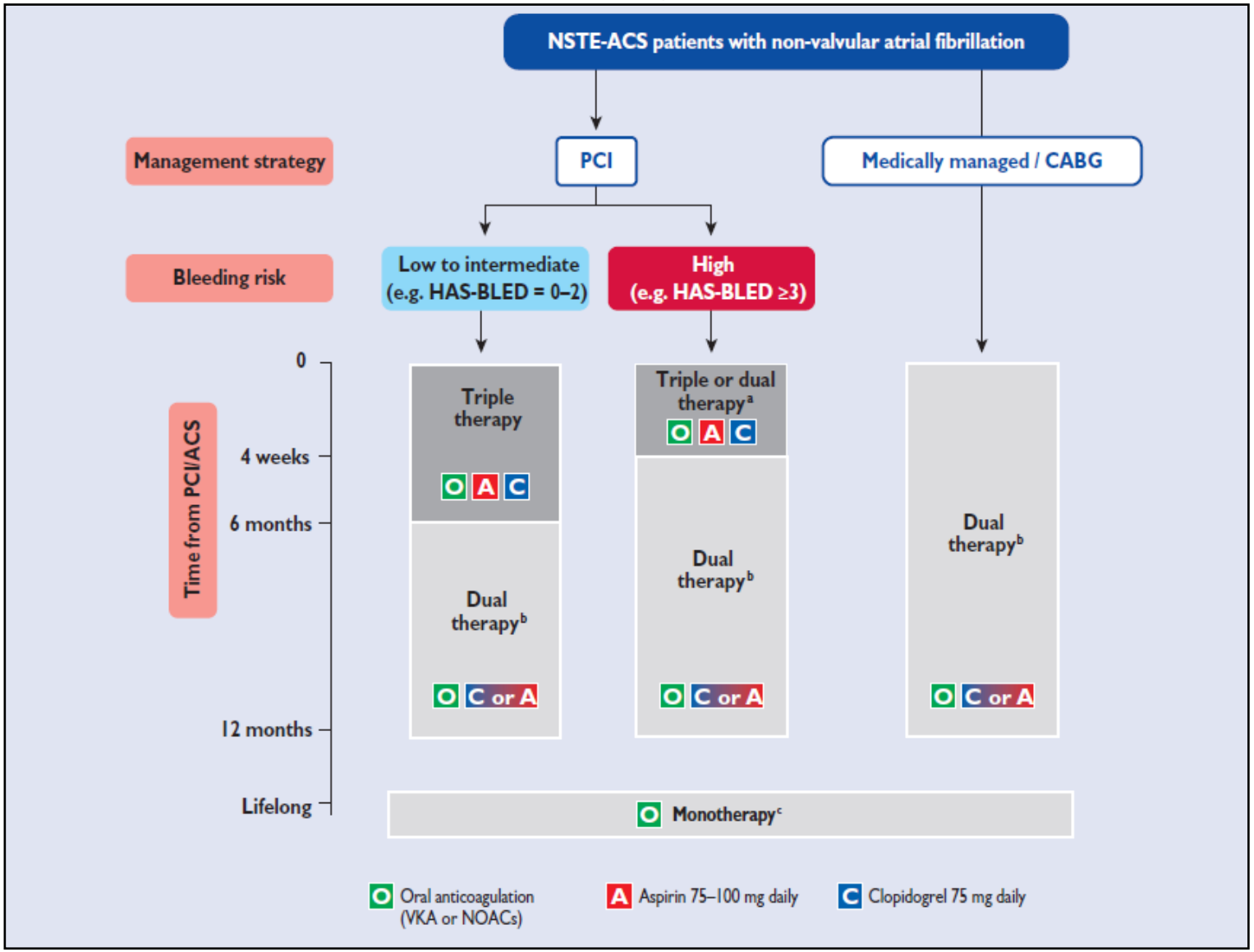
Worldwide event-driven trial with 2840 patients per arm
(Total = 8520 patients)



*ASA will be given for 1 month post BMS and 3 months post DES

Antithrombotic therapy in AF with NSTEMI

-2015 ESC guideline-



2015 ESC Guideline. Eur Heart J. 2016;37(3):267-315

Antithrombotic therapy in AF with AMI

EHRA/EAPCI/ACCA/HRS/APHRS

- When VKA is given in combination with clopidogrel and/or low-dose aspirin, the dose intensity of VKA should be carefully regulated, with a target INR range of 2.0 – 2.5 *(Class IIa, level of evidence C)*.

- Novel P2Y12 receptor inhibitors (prasugrel and ticagrelor) should not be part of a triple therapy regimen in patients with AF *(Class III, level of evidence C).*

- Where a NOAC is used in combination with clopidogrel and/or low-dose aspirin, the lower tested dose for stroke prevention in AF (that is, dabigatran 110 mg b.i.d., rivaroxaban 15 mg o.d. or apixaban 2.5 mg b.i.d.) may be considered *(Class IIb, level of evidence C)*.

Lip GY et al., Eur Heart J. 2014;35(45):3155-79.

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경청해 주셔서 감사합니다.