How Long Patietns Will Be on Dual Antiplatelet Therapy?

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- Educational Grant Support for CRT from variety of device and drug companies
- You will find this presentation on

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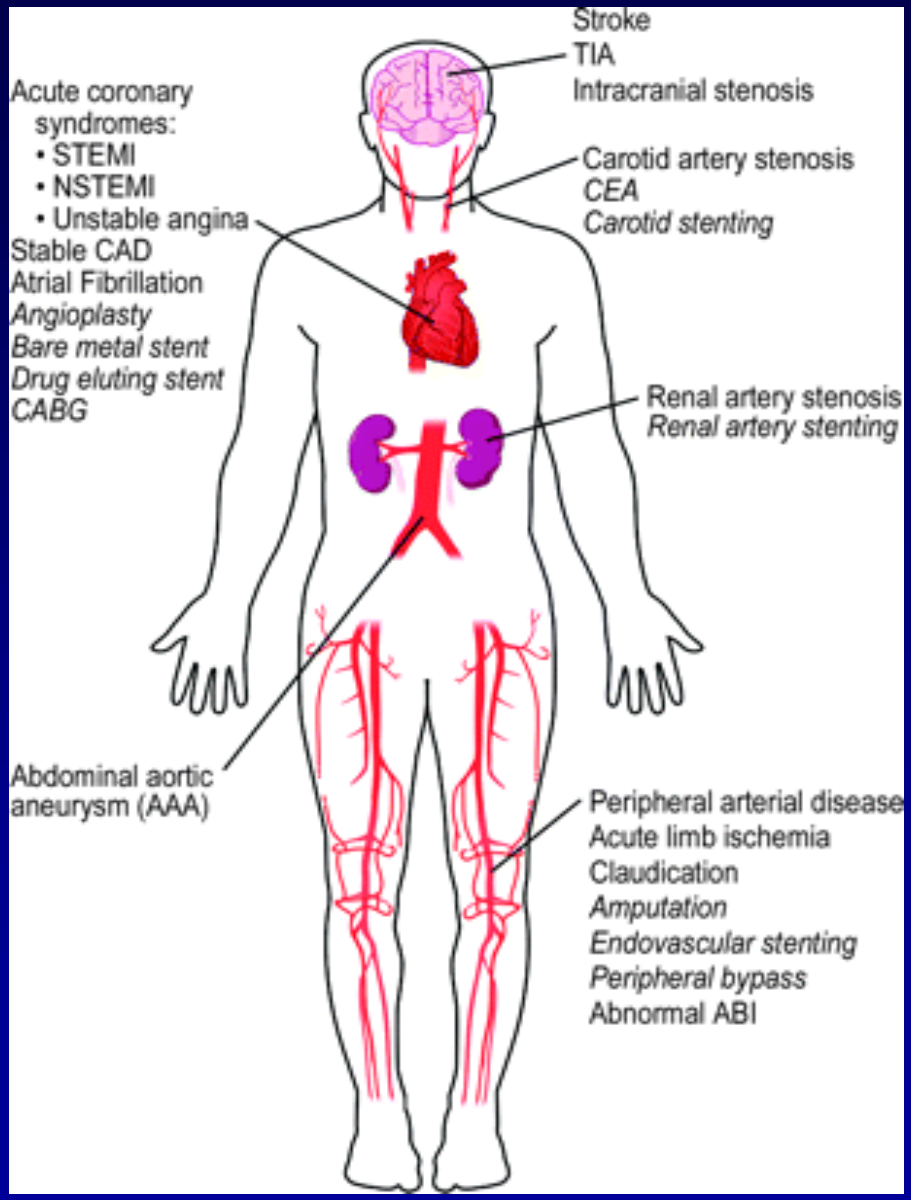
Atherothrombosis: Clinical Manifestations



Meadows TA, Bhatt DL. *Circ Res*. 2007;100:1261-1275

Disease in any vascular bed increases the lifetime risk of multiple atherothrombotic events

History	Increased risk of MI	Increased risk of stroke
MI	5-7 X **greater risk** (includes death)	3-4 X **greater risk** (includes TIA)
Ischemic Stroke	2-3 X **greater risk** (includes angina and sudden death)	9 X **greater risk**
PAD	4 X **greater risk** (includes only fatal MI and other coronary heart disease death)	2-3 X **greater risk** (includes TIA)

Circulation 1994; 89: 1333-1363; J Cardiovasc Risk 1994; 1:333-339; Arch Neurol 1992; 42:857-863; NEJM 1992; 326: 381-386

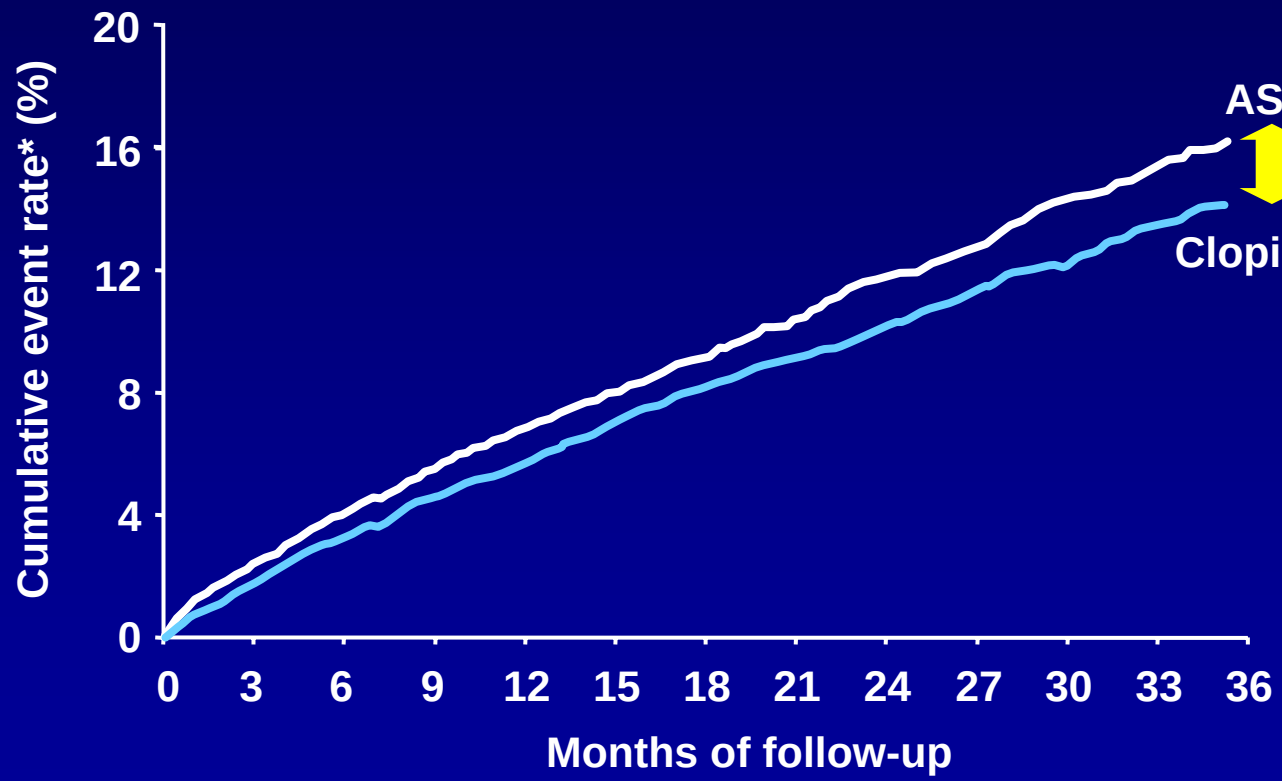
CAPRIE

- In the Clopidogrel versus Aspirin in Patients at Risk for Ischemic Events (CAPRIE) trial ; 19.185 patients with atherosclerotic vascular disease (recent ischemic stroke , recent MI , or symptomatic peripheral vascular disease) were randomized to aspirin 325 mg daily or clopidogrel 75 mg daily .

- At 1.9 years there was an 8.7% reduction in the composite endpoint of ischemic stroke , MI or vascular death with clopidogrel .

CAPRIE: Superior Efficacy of Clopidogrel versus ASA

Patients with recent ischemic stroke, recent MI or symptomatic PAD

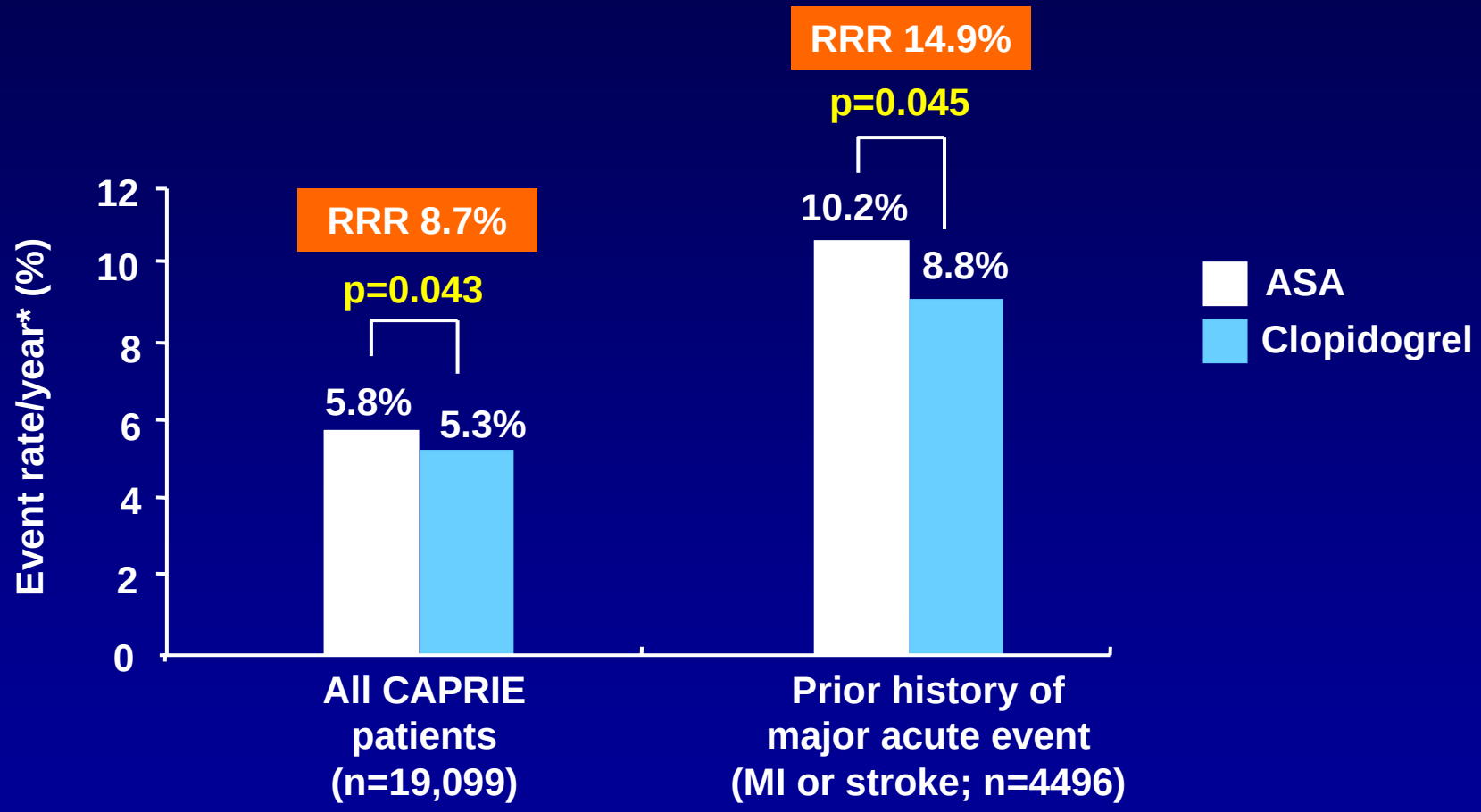


*MI, ischemic stroke or vascular death

†Intent-to-treat analysis (n=19,185)

CAPRIE Steering Committee. *Lancet* 1996; 348(9038): 1329–1339.

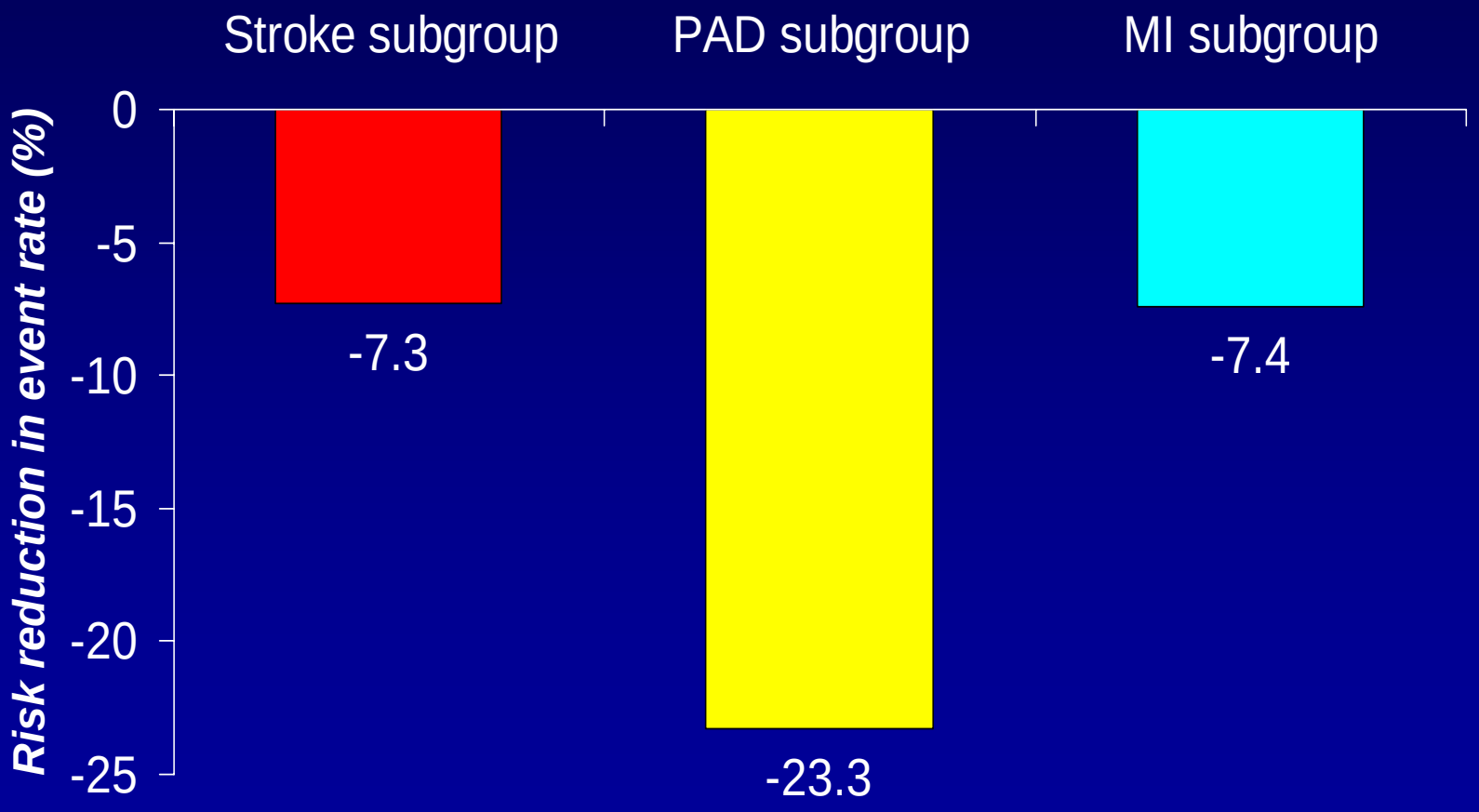
CAPRIE: Clopidogrel Provides Amplified Benefit in Patients with High Vascular Risk



*MI, ischemic stroke or vascular death; mean duration of treatment was 1.6 years

Ringleb PA, Bhatt DL, Hirsch AT, et al. *Stroke* 2004;35: 528–532.

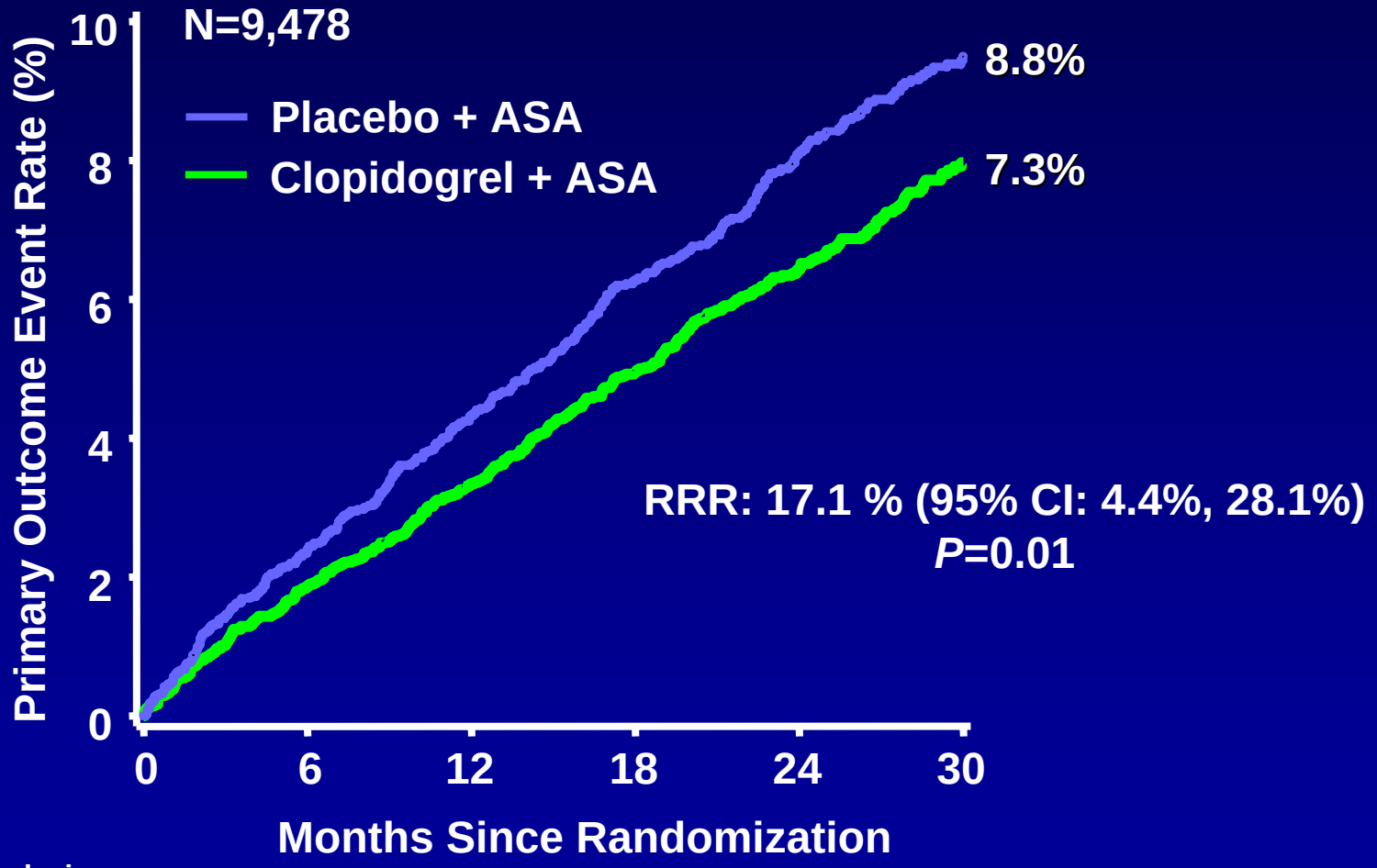
CAPRIE trial: Risk reduction in specific subgroups



Lancet 1996; 348: 1329-1339

Primary Endpoint (MI/Stroke/CV Death) in Patients With Previous MI, IS, or PAD*

"CAPRIE-like Cohort"



* Post hoc analysis.

Bhatt DL, Flather MD, Hacke W, et al. *J Am Coll Cardiol.* 2007;49(19):1982-1988.

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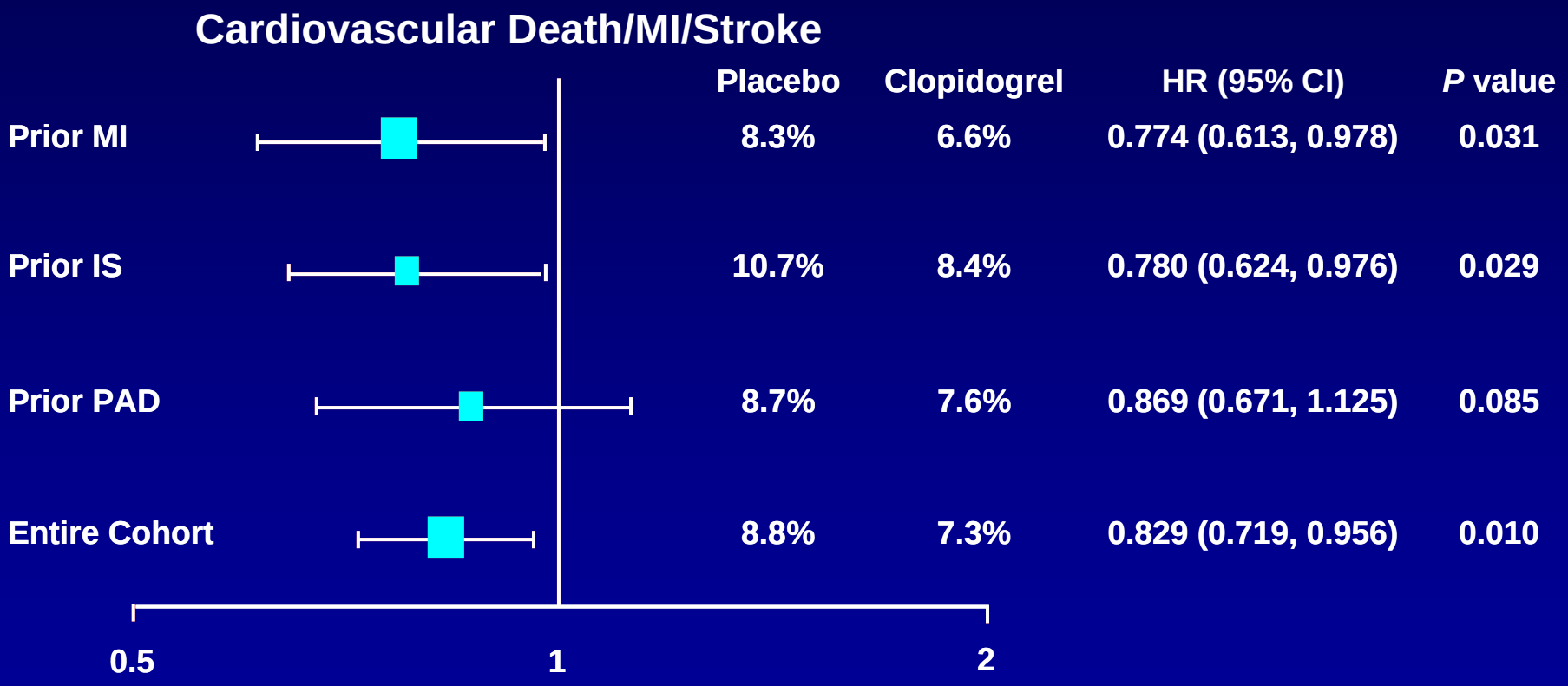

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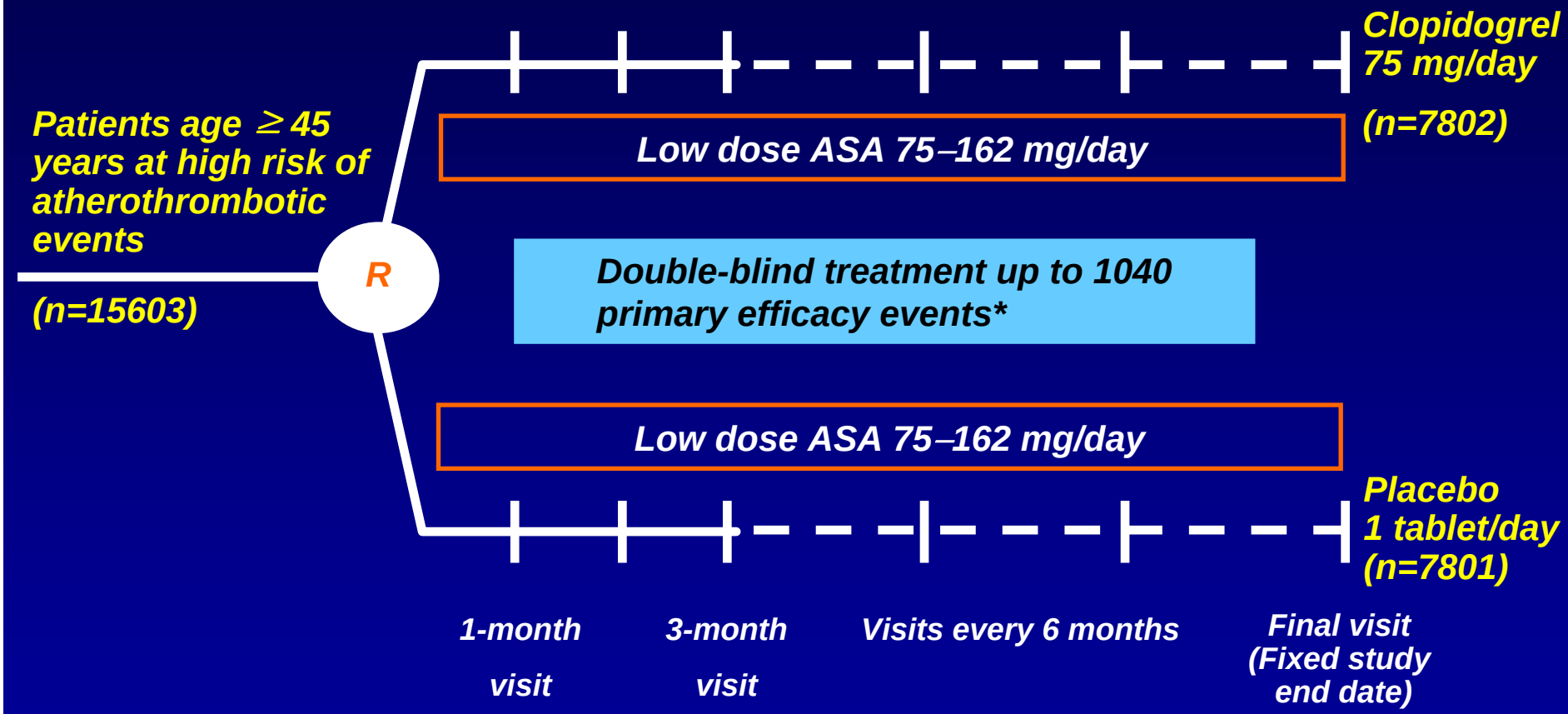
CHARISMA Trial Design



* MI (fatal or non-fatal), stroke (fatal or non-fatal), or cardiovascular death; event-driven trial

Bhatt DL et al. Am Heart J 2004; 148: 263–268.

Inclusion Criteria

Patients aged ≥45 years

with

at least one of the following:

1A) Documented coronary disease

and/or

1B) Documented cerebrovascular disease

and/or

1C) Documented symptomatic PAD

and/or

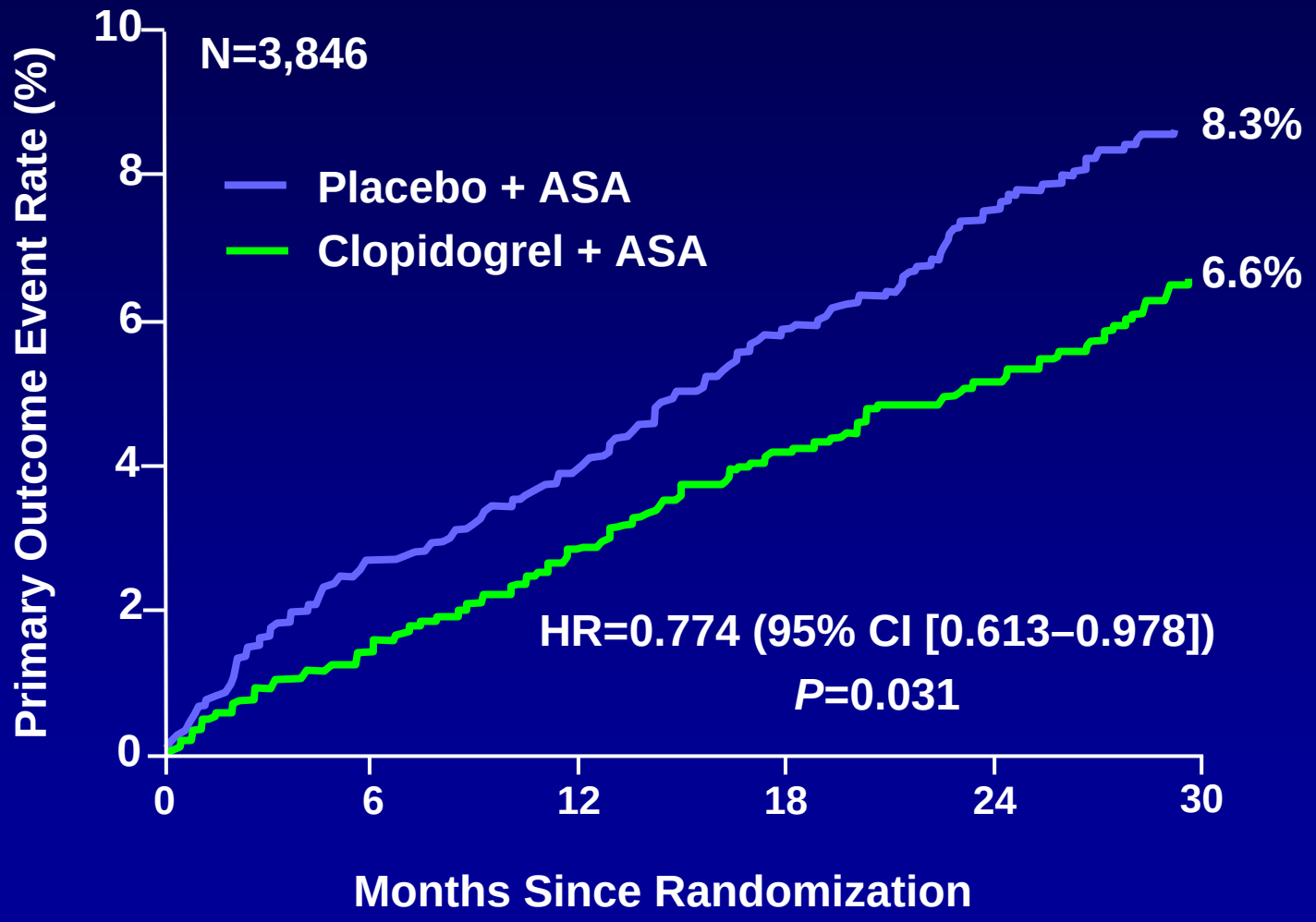
2) Two major or one major and two minor or three minor risk factors

With written informed consent

Without exclusion criteria

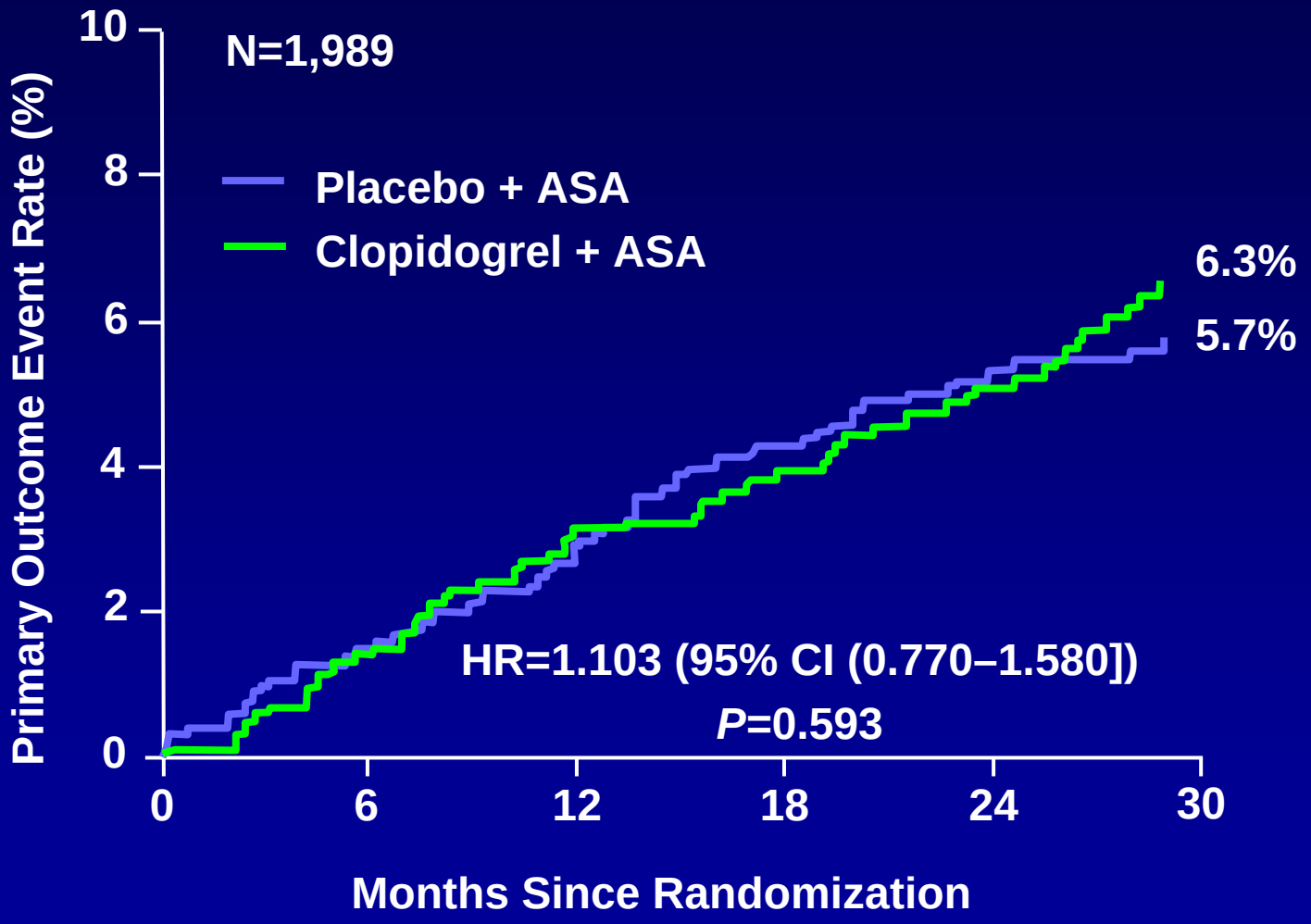
Bhatt DL et al. Am Heart J 2004; 148: 263–268.

CHARISMA—Prior MI



Bhatt DL, Flather MD, Hacke W, et al. *J Am Coll Cardiol.* 2007;49(19):1982-1988.

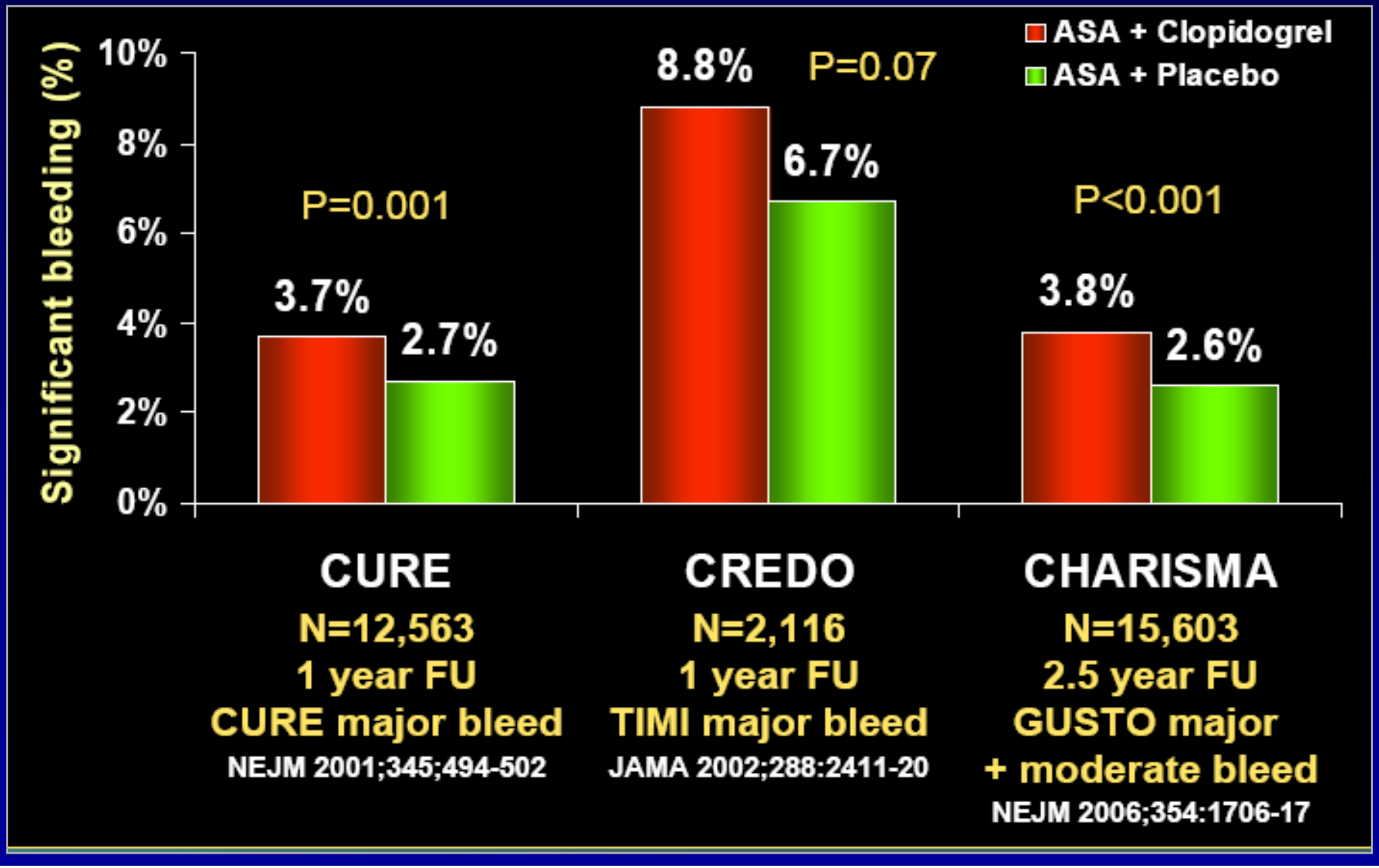
CHARISMA—CAD Without Prior MI



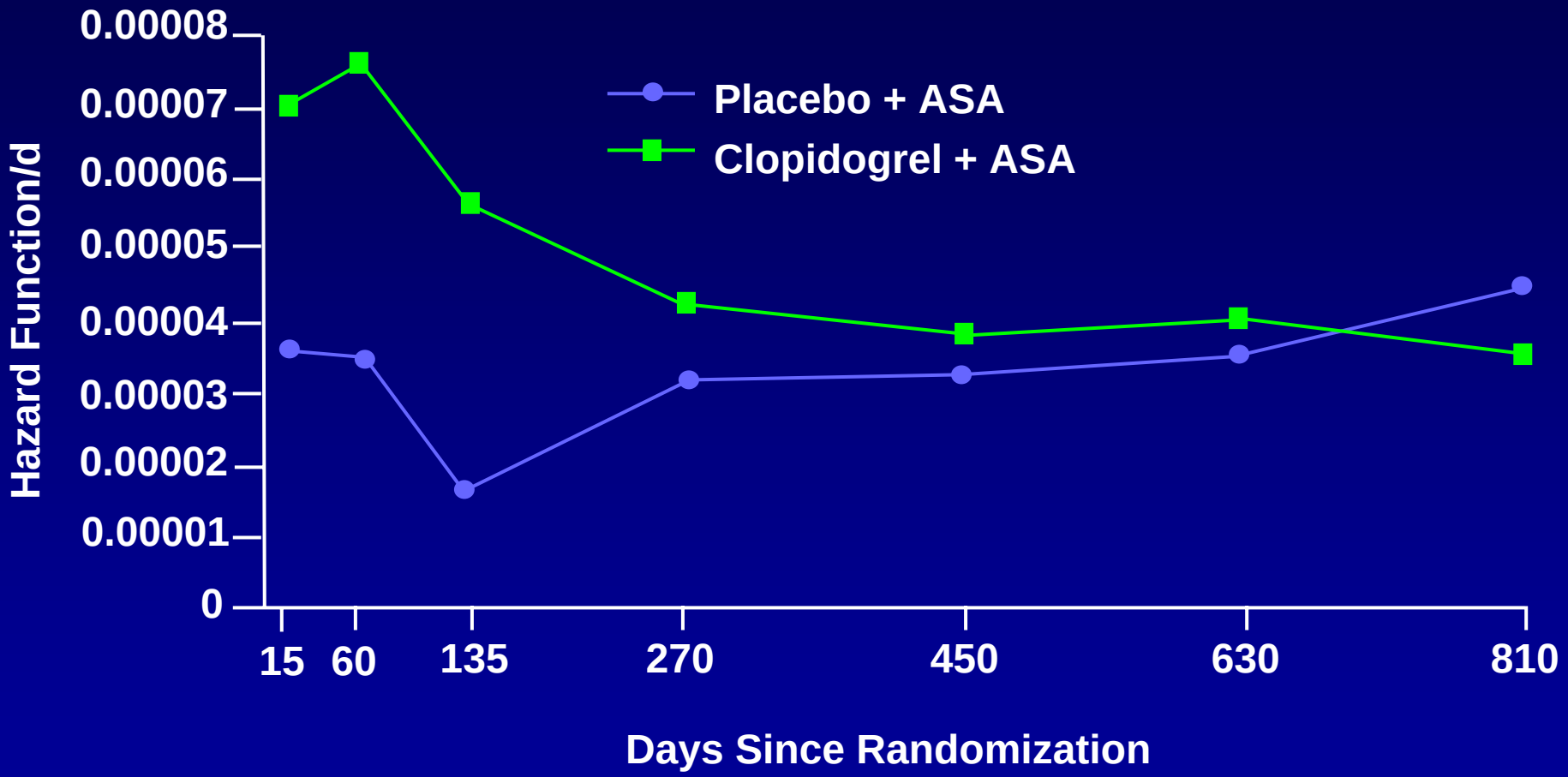
Bhatt DL, Flather MD, Hacke W, et al. *J Am Coll Cardiol.* 2007;49(19):1982-1988.

Safety of Long-Term Clopidogrel

3 Placebo Controlled Trials

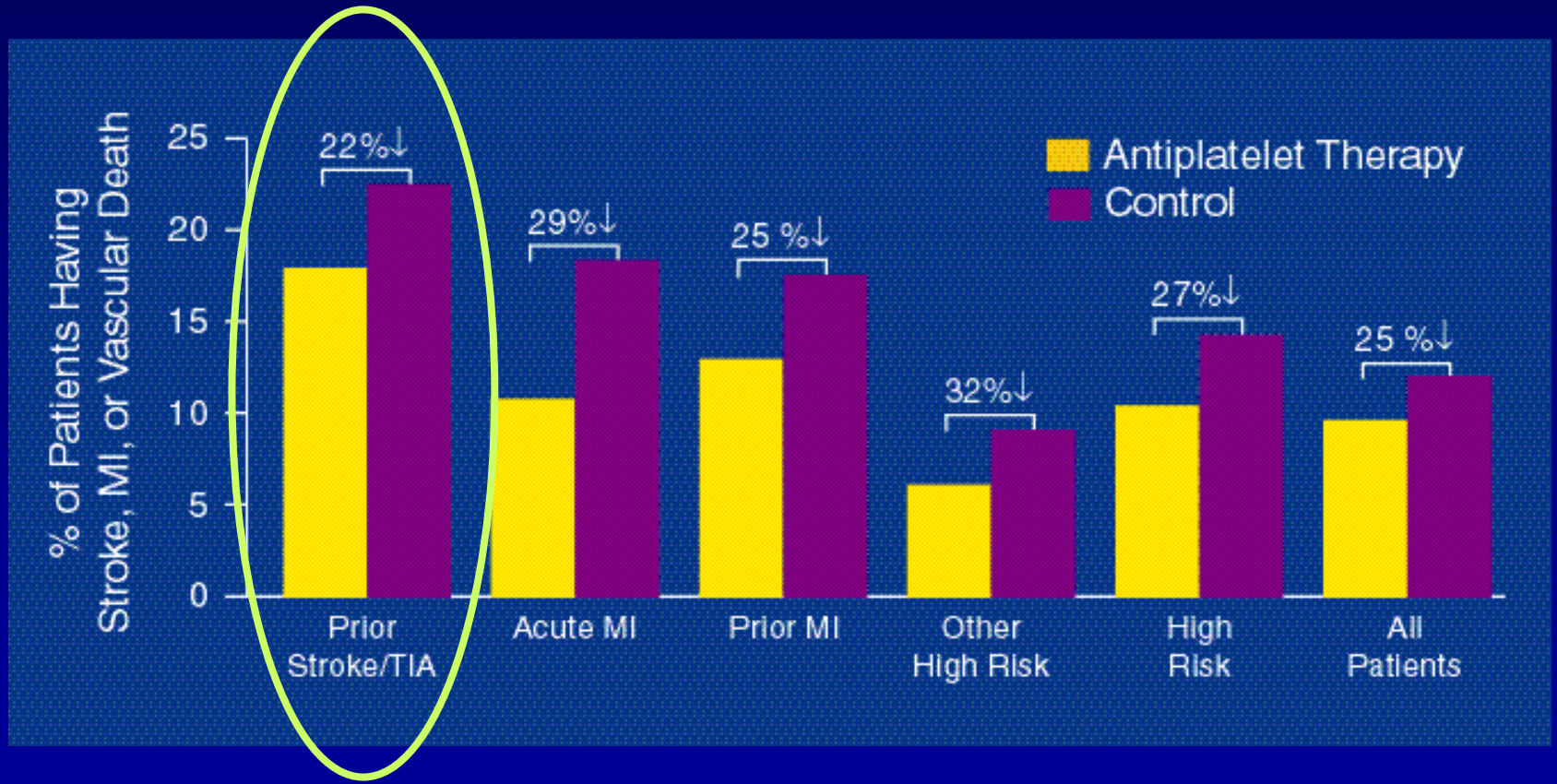


Timing of Severe or Moderate Bleeding



Bhatt DL, Flather MD, Hacke W, et al. *J Am Coll Cardiol.* 2007;49(19):1982-1988.

Antiplatelet Trialists' Collaboration
Efficacy in Prevention of Ischemic Events



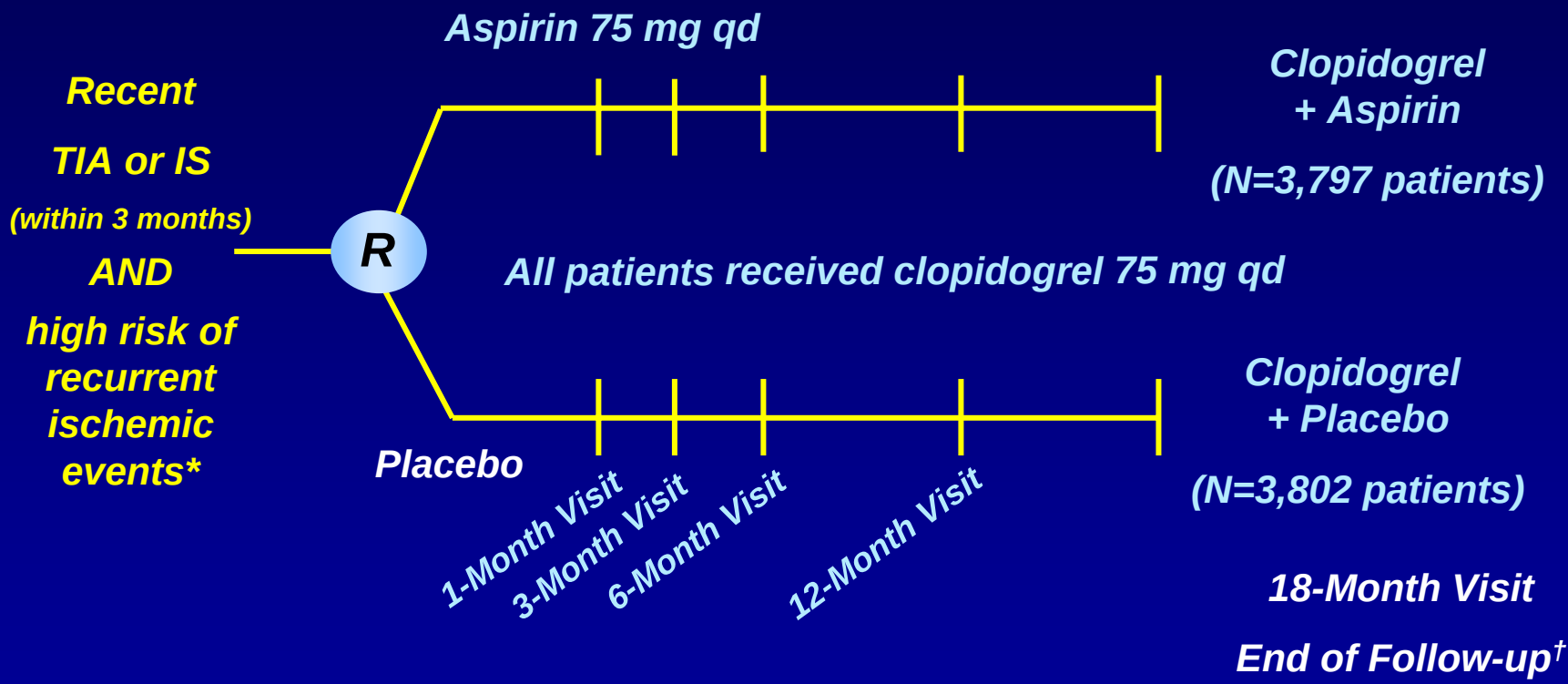
Antiplatelet Trialists' Collaboration. BMJ. 1994;308:81–106.

MATCH

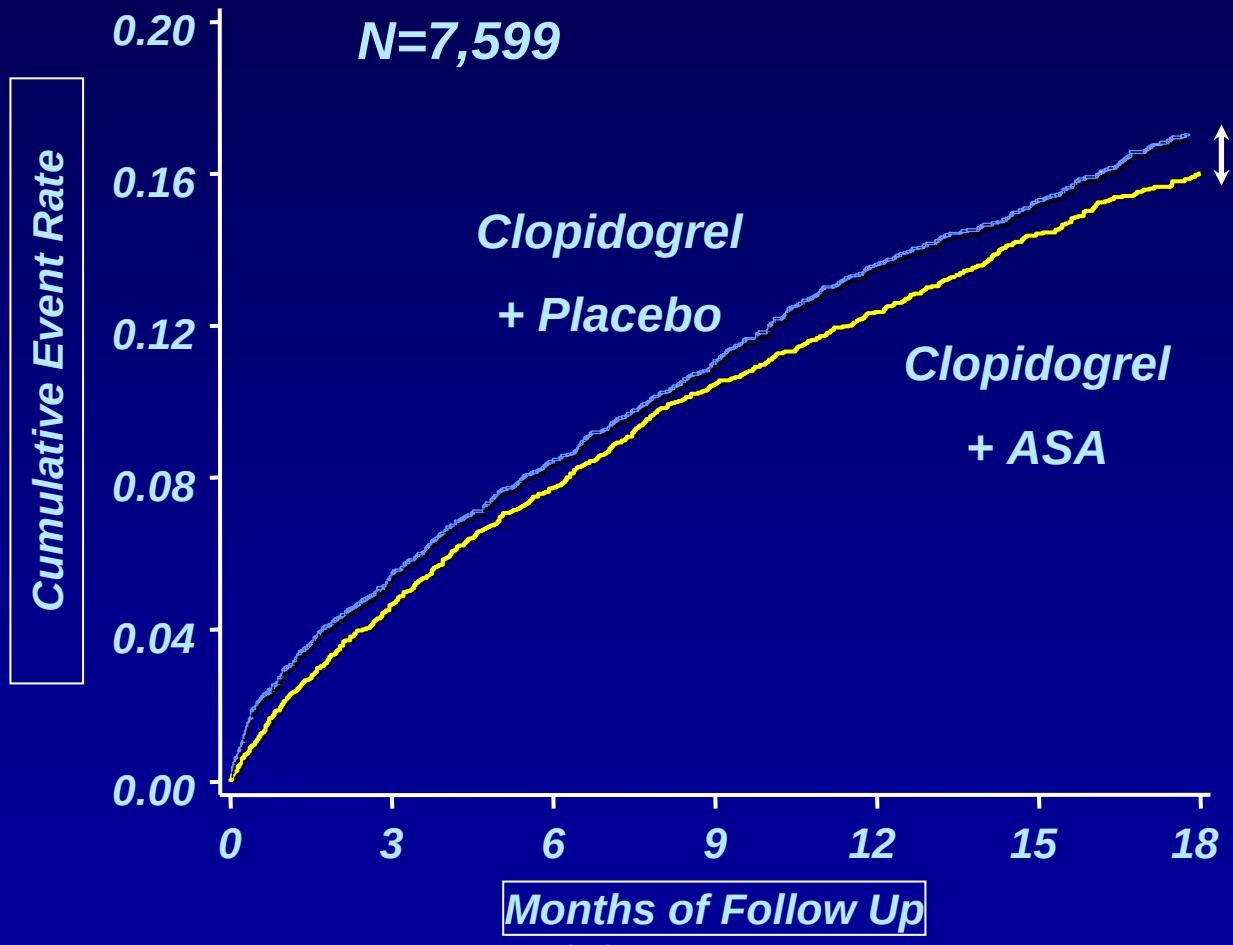
Management of ATherothrombosis With Clopidogrel in High-risk Patients With Recent Transient Ischemic Attack or Ischemic Stroke

PLAVIX backup slide.

MATCH Study Design



MATCH: Primary End Point: MI, IS, Vascular Death, or Rehospitalization for an Acute Ischemic Event



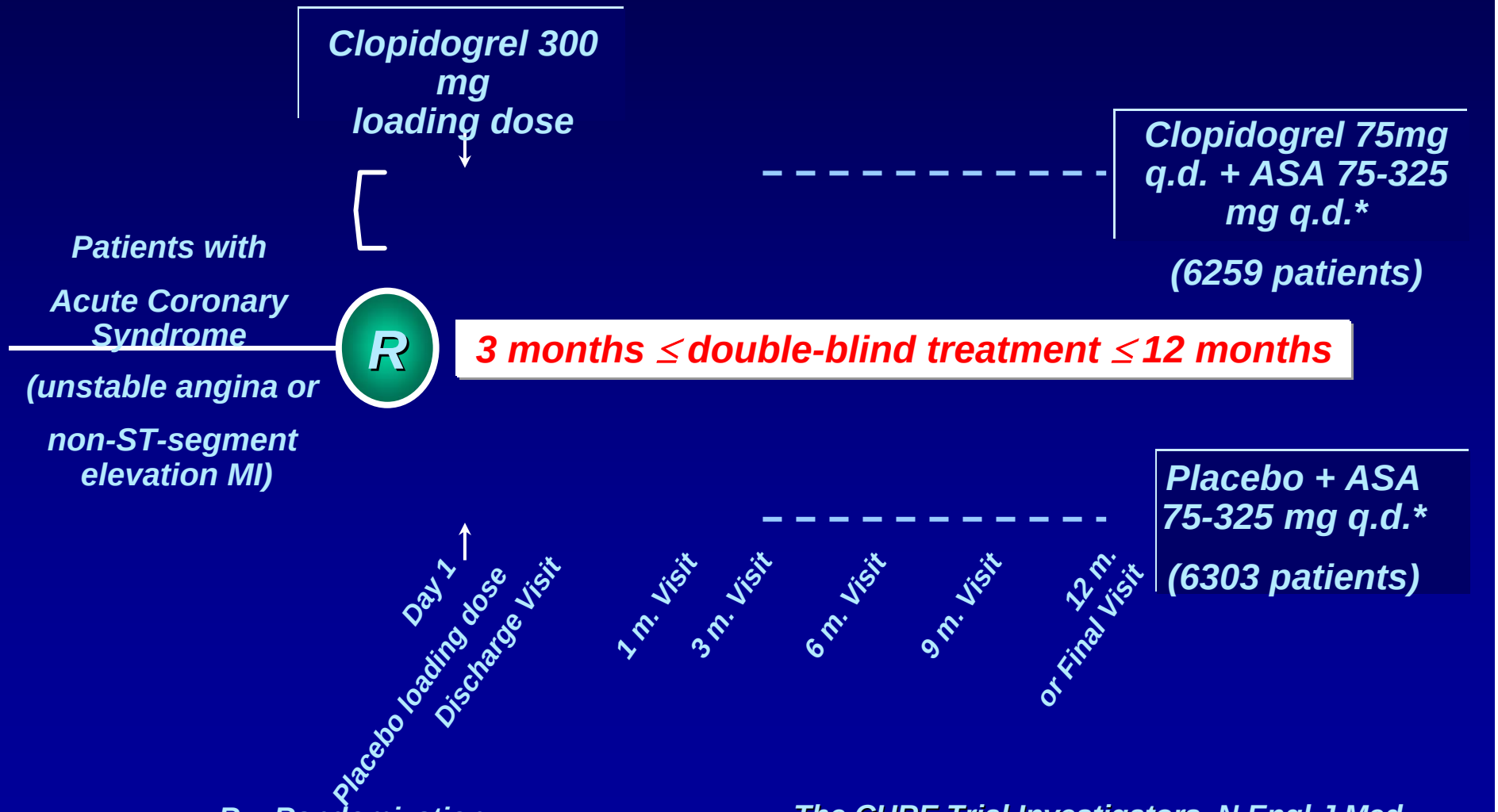
• ITT analysis.

MI=myocardial infarction; IS=ischemic stroke.

Diener C. 13th European Stroke Conference. Mannheim, Germany. May 2004
PLAVIX backup slide.

CURE

Study Design

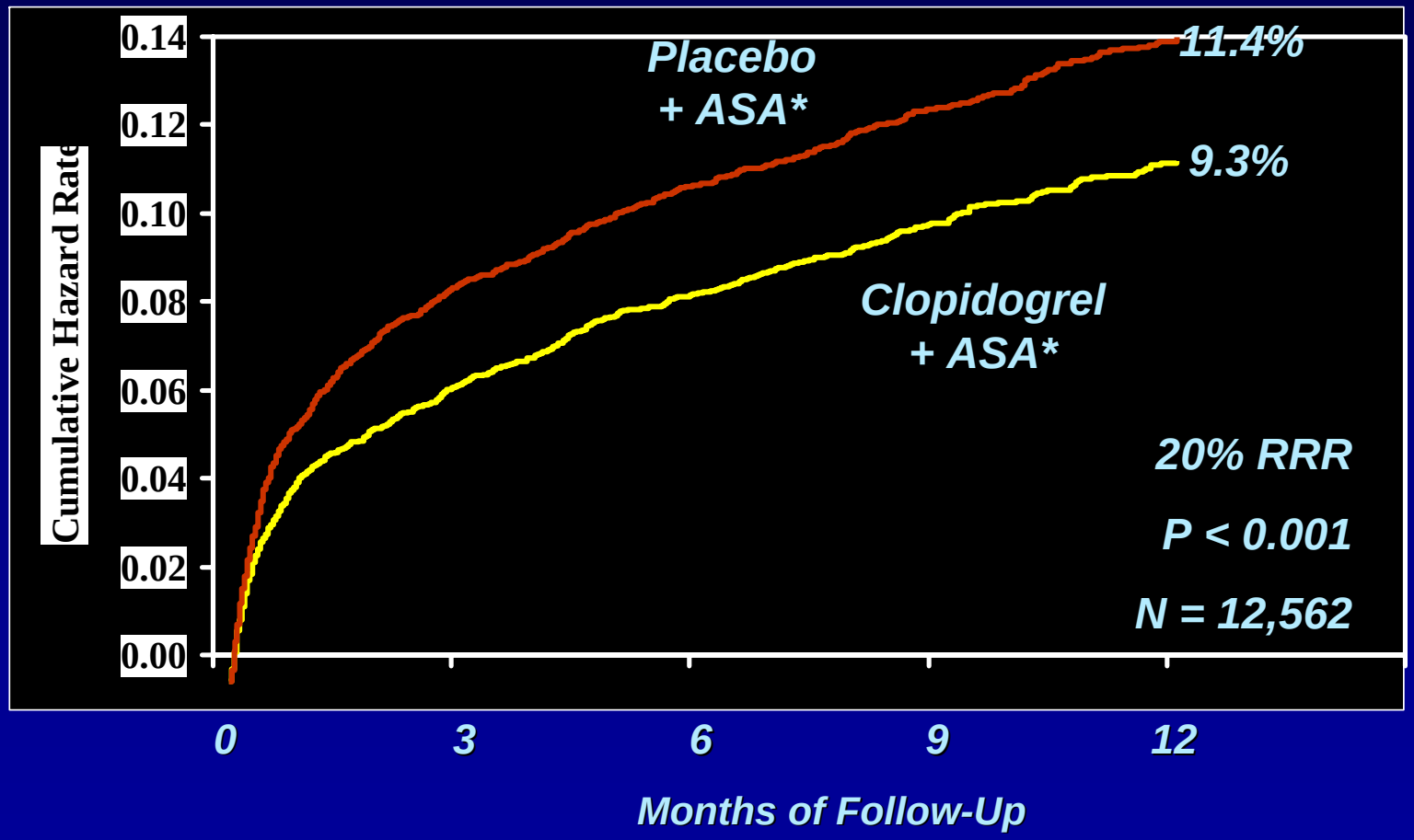


R = Randomization
* In combination with other standard therapy

The CURE Trial Investigators. N Engl J Med. 2001;345:494-502.

CURE

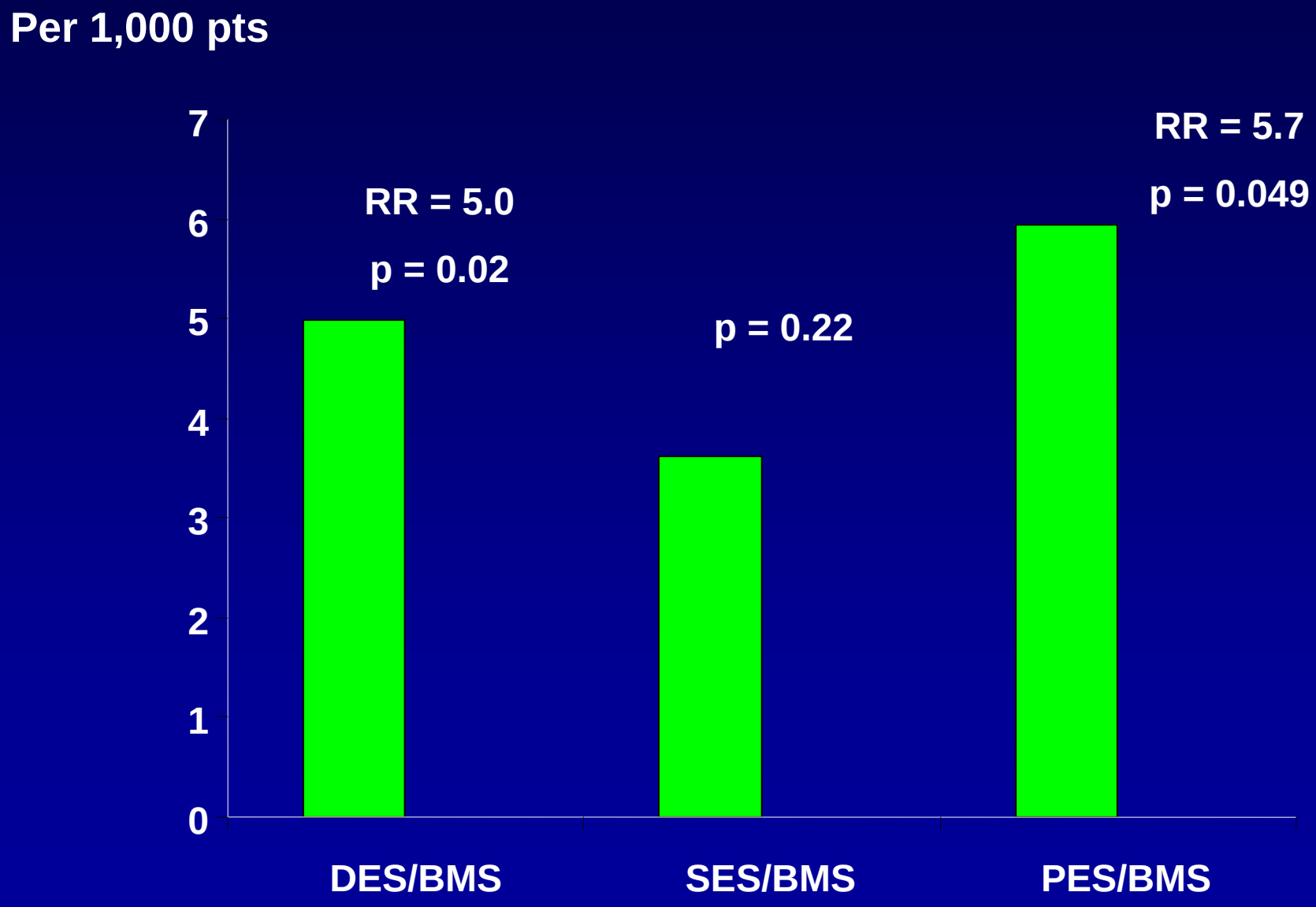
Primary End Point - MI/Stroke/CV Death



* In combination with standard therapy

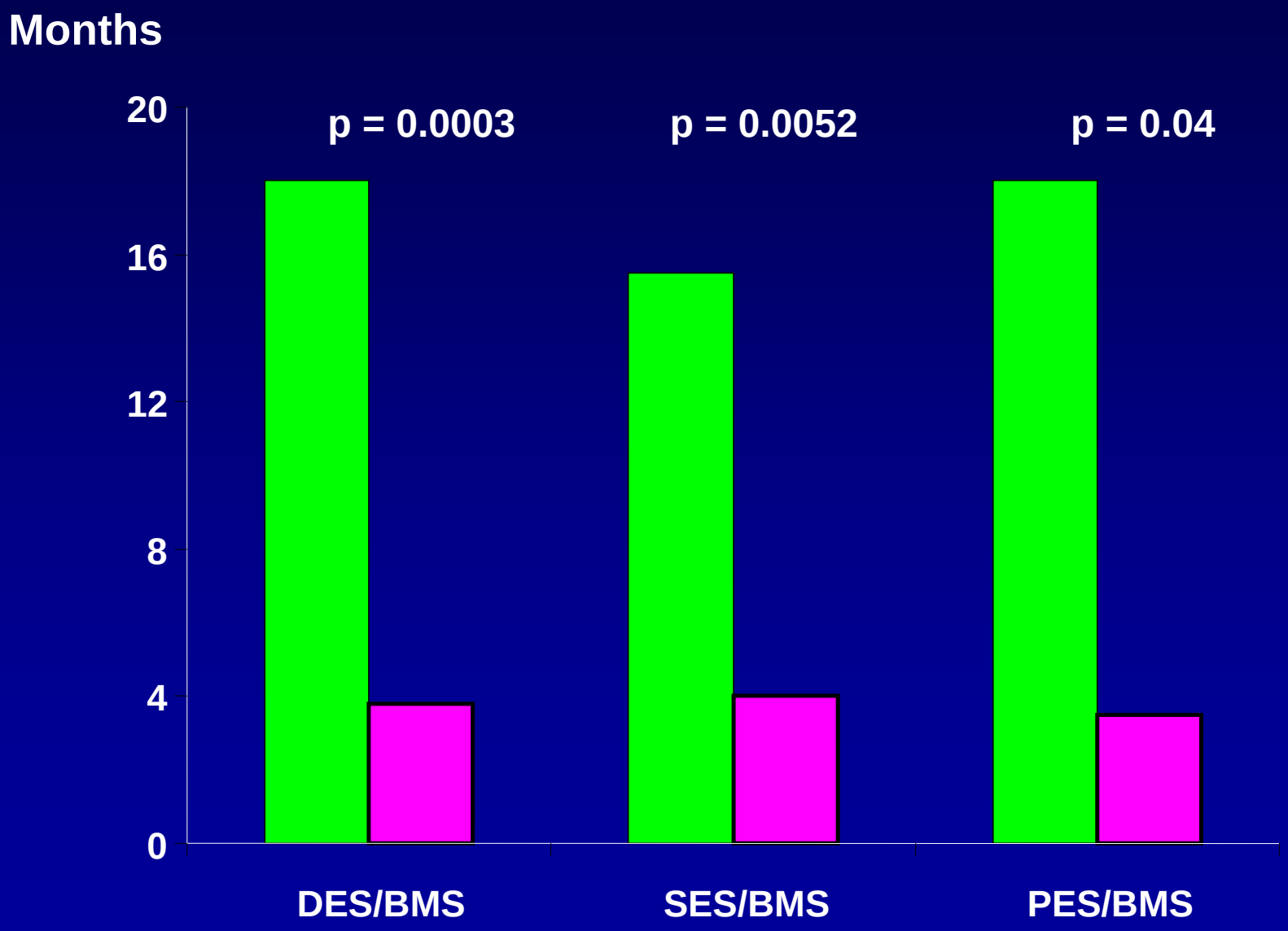
The CURE Trial Investigators. N Engl J Med. 2001;345:494-502.

Incidence of Late Stent Thrombosis: > 1 Year



Bavry, Kumbhani, Helton, Borek, Mood, Bhatt. Am J Med. 2006;119:1056-1061.

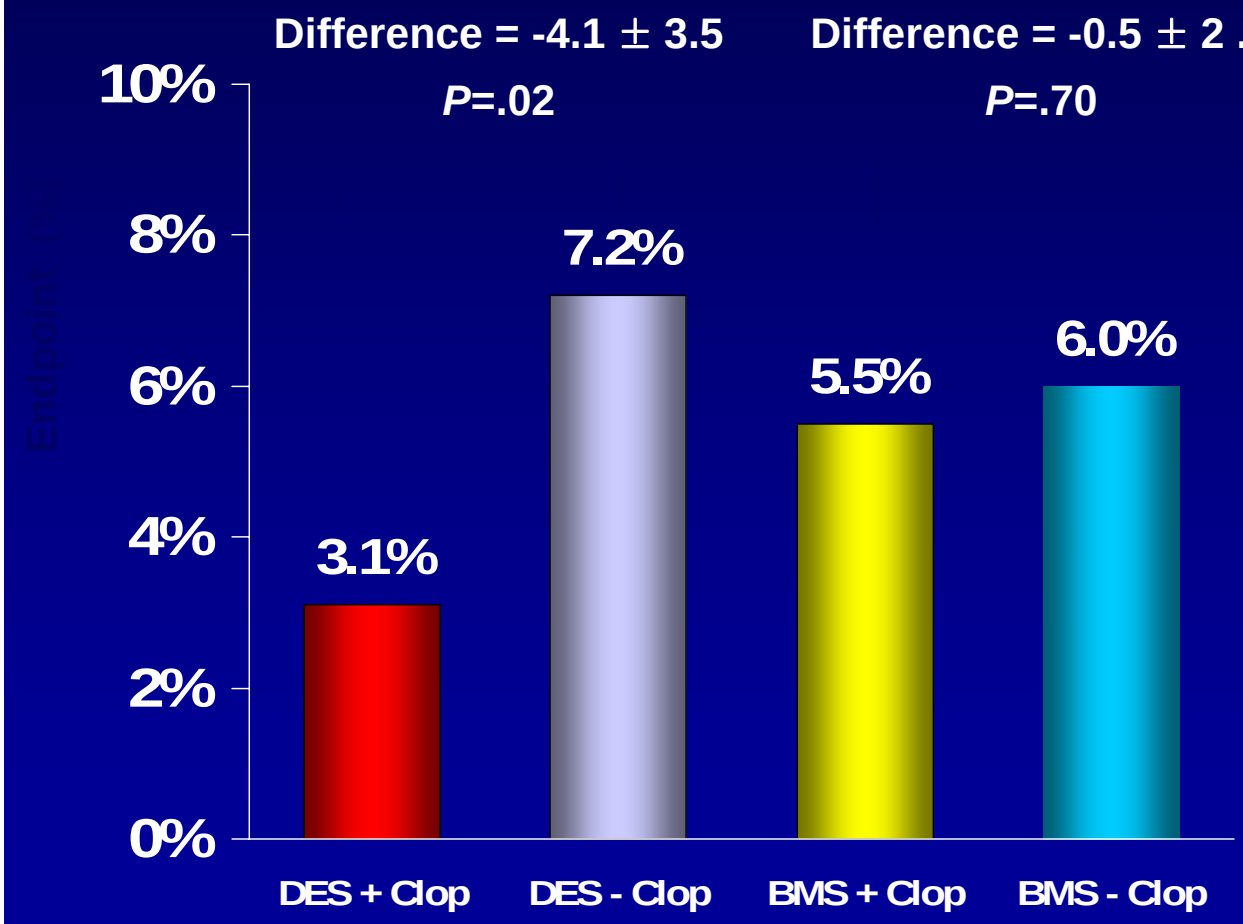
Median Time of Late Stent Thrombosis



Bavry, Kumbhani, Helton, Borek, Mood, Bhatt. Am J Med. 2006;119:1056-1061.

Clopidogrel Use and Long-term Clinical Outcomes after DES - Duke Registry

Adjusted rates of death or MI starting at 6 months

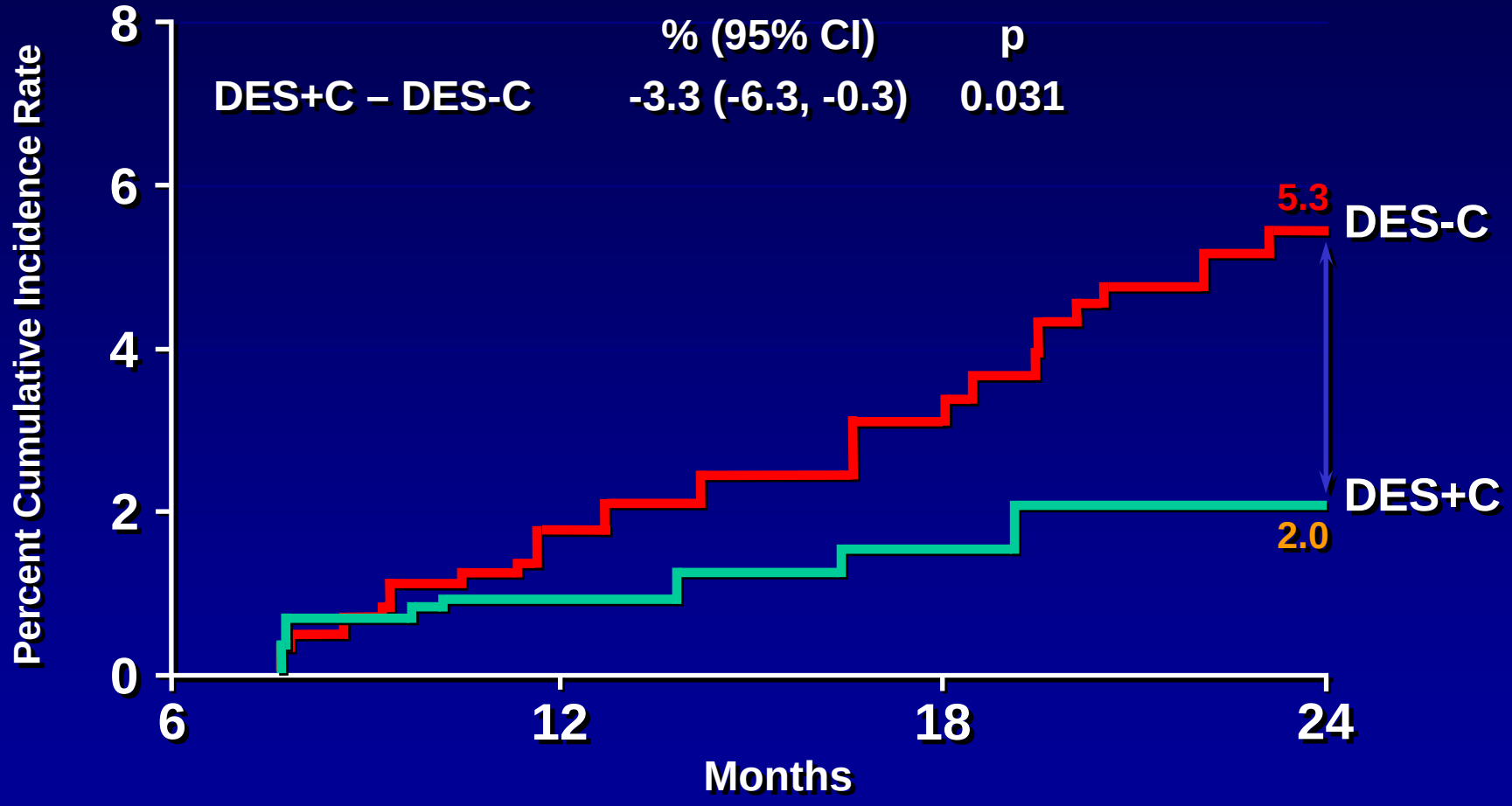


- Adjusted outcomes were analyzed at 24 months
- Patients in the DES with clop. group had significantly lower rates of death or MI than did patients in the DES without clopidogrel group
- Among BMS patients, there were no differences in death or MI

Eisenstein EL, et al. *JAMA*. 2007;10;297(2):159-168.

6-Month Landmark Analysis

Adjusted Cumulative Mortality Rates



Eisenstein et al. JAMA 2006

Independent Predictors of Late Stent Thrombosis

Variables	Hazard ratio (95% CI)	*P*-value
Premature antiplatelet therapy discontinuation	57.13 (14.84-219.96)	<.001
Bifurcation lesion	8.11 (2.50-26.26)	.001
LVEF per 10% decrease	1.06 (1.01-1.12)	.03

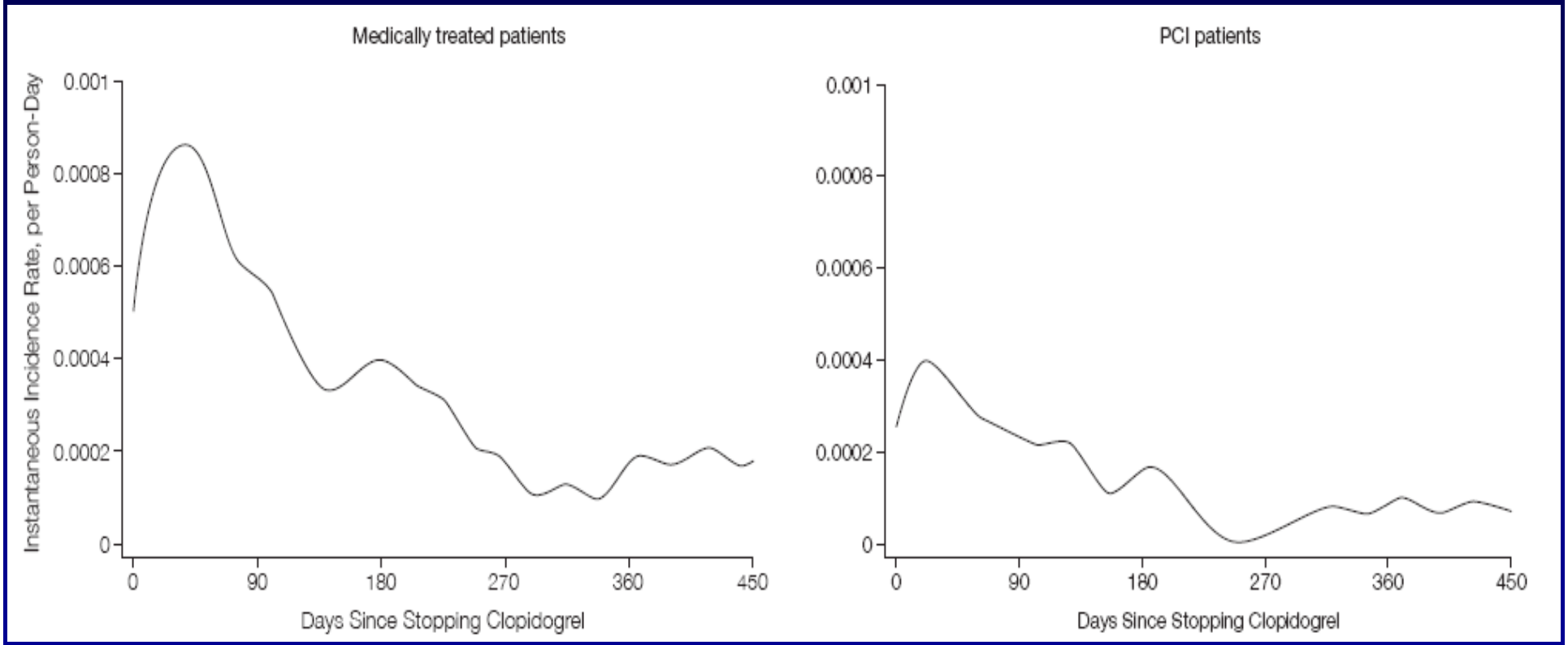
Iakovou I, et al. *JAMA*. 2005;293(17):2126-2130.

Antiplatelet Therapy

Summary of FDA Circulatory Panel Findings

- Premature discontinuation (before labeled duration) of dual anti-platelet therapy is associated with increased risk of ST
- Dual antiplatelet therapy is recommended for at least 12 months post DES implant
- Ideal duration of dual antiplatlet therapy is uncertain
- Cypher and Taxus labels should carry AHA/ACC/SCAI recommendation re: APT 12 months for patients that can tolerate DAP

Clopidogrel Rebound vs Withdrawal of Protection



Events post Clopidogrel Cessation:

Is it due to lack of antiplatelet therapy lose protection or to rebound?

Ho PM, et al. *JAMA*. 2008;10;299:532-539.

Conclusions

- Dual antiplatelet therapy indicated for at least 1 year after ACS and/or PCI – CURE, PCI CURE, CREDO
- Potential benefit beyond 1 year in patients with prior ischemic events – CHARISMA subgroup
- Potential benefit beyond 1 year in patients with DES – registry data
- Trials of novel antiplatelet agents indirectly support longer therapy