

Summit TCT Asia Pacific 2008

Management of ACS: New Guidelines and New Data

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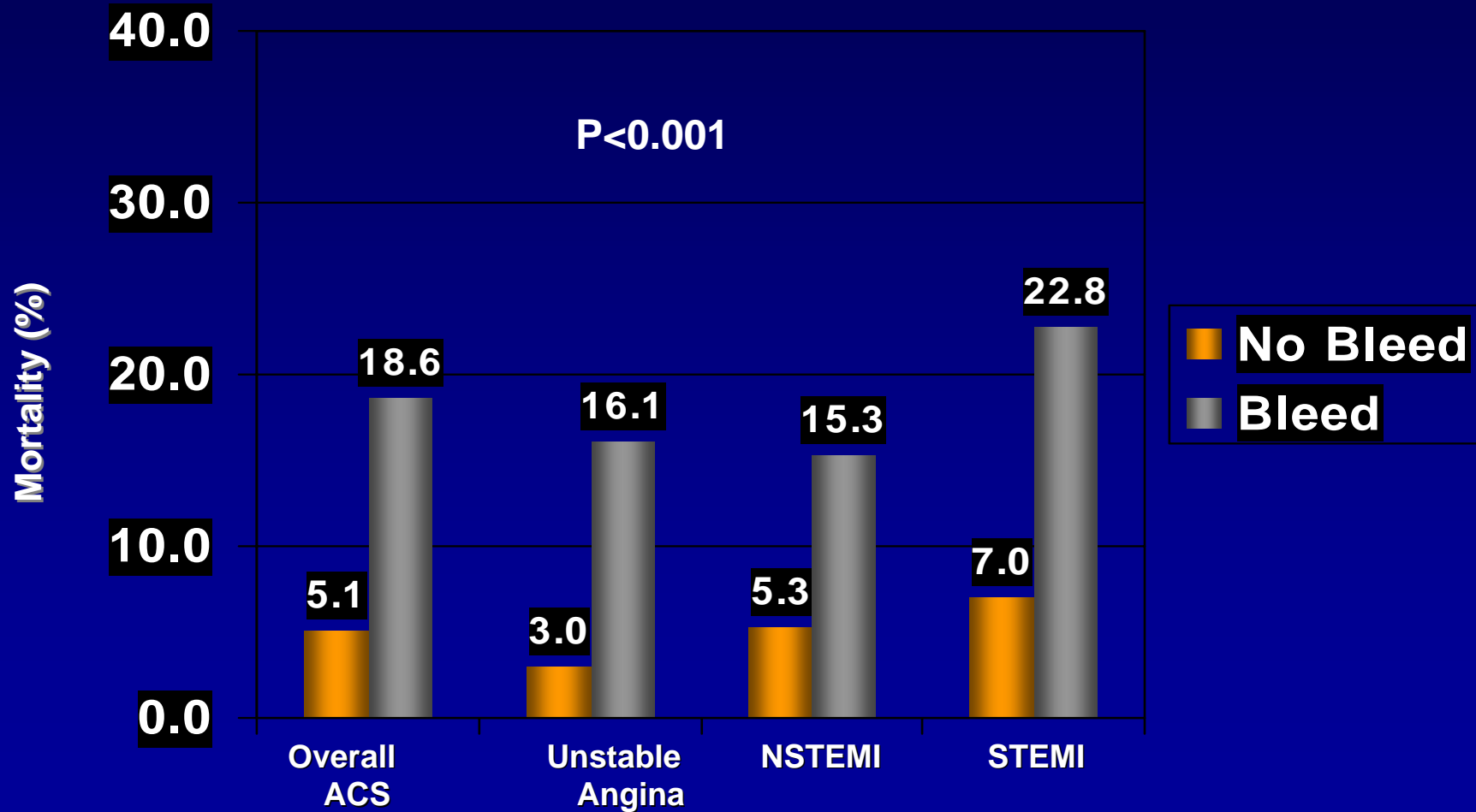


I have no conflicts of interest with regard to industry or for-profit organizations that are relevant to this presentation.

**New Data Relevant to
UAP/NSTEMI 2007 Guidelines**

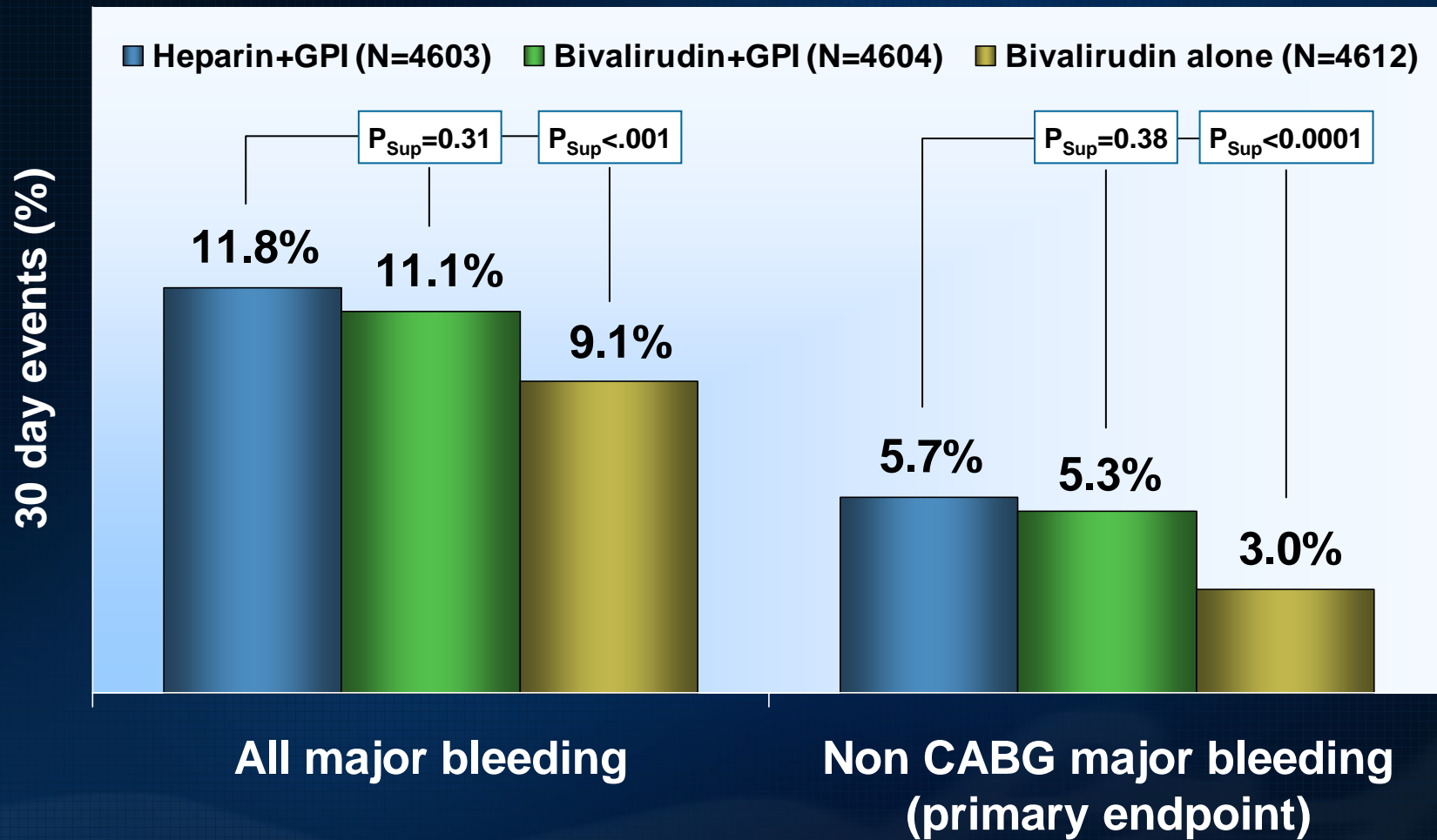
Background: The GRACE Registry

Major Bleeding is Associated with Increased Mortality in ACS

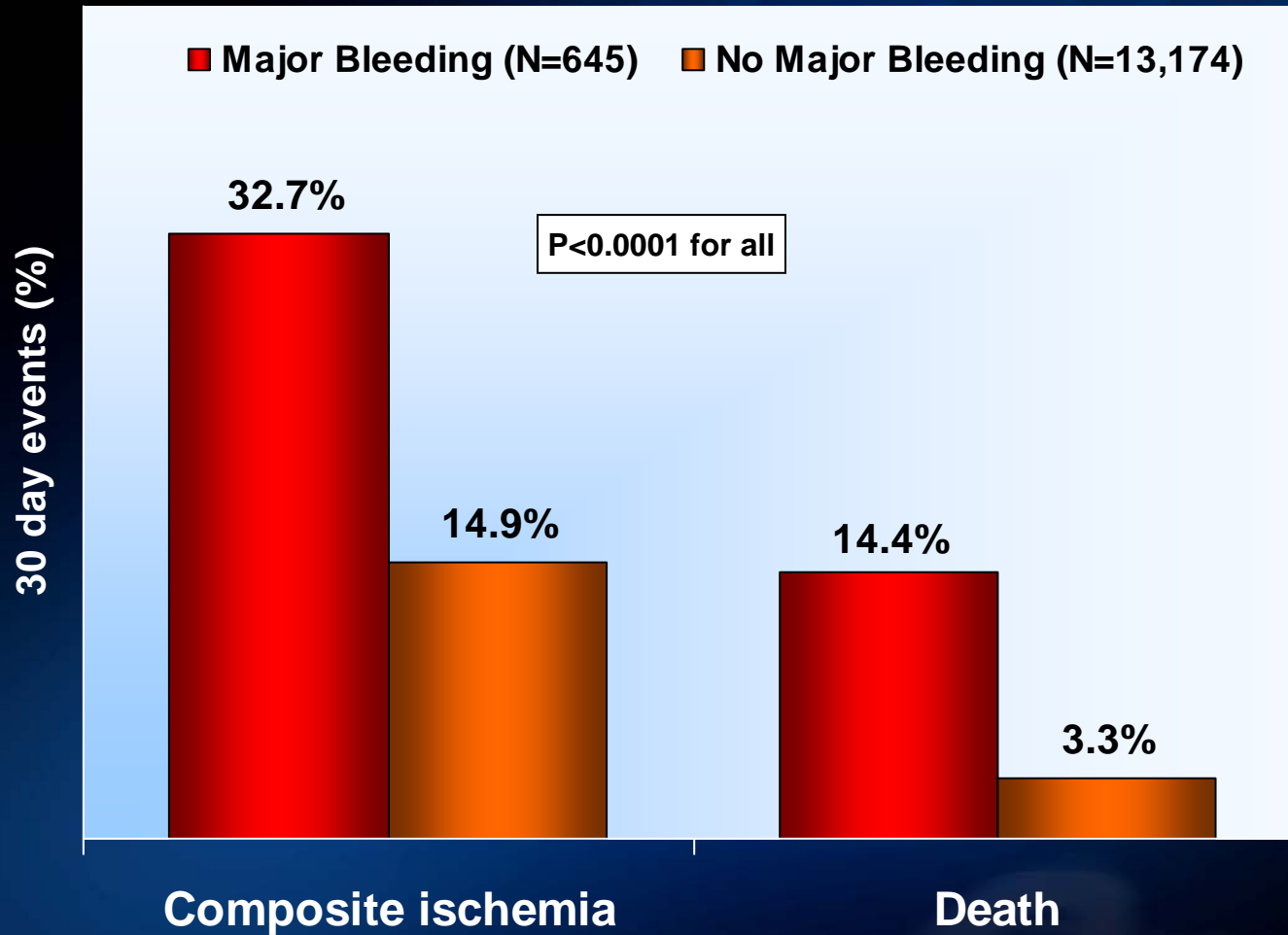


Major Bleeding Endpoints

UFH/Enoxaparin + GPI vs. Bivalirudin + GPI vs. Bivalirudin Alone



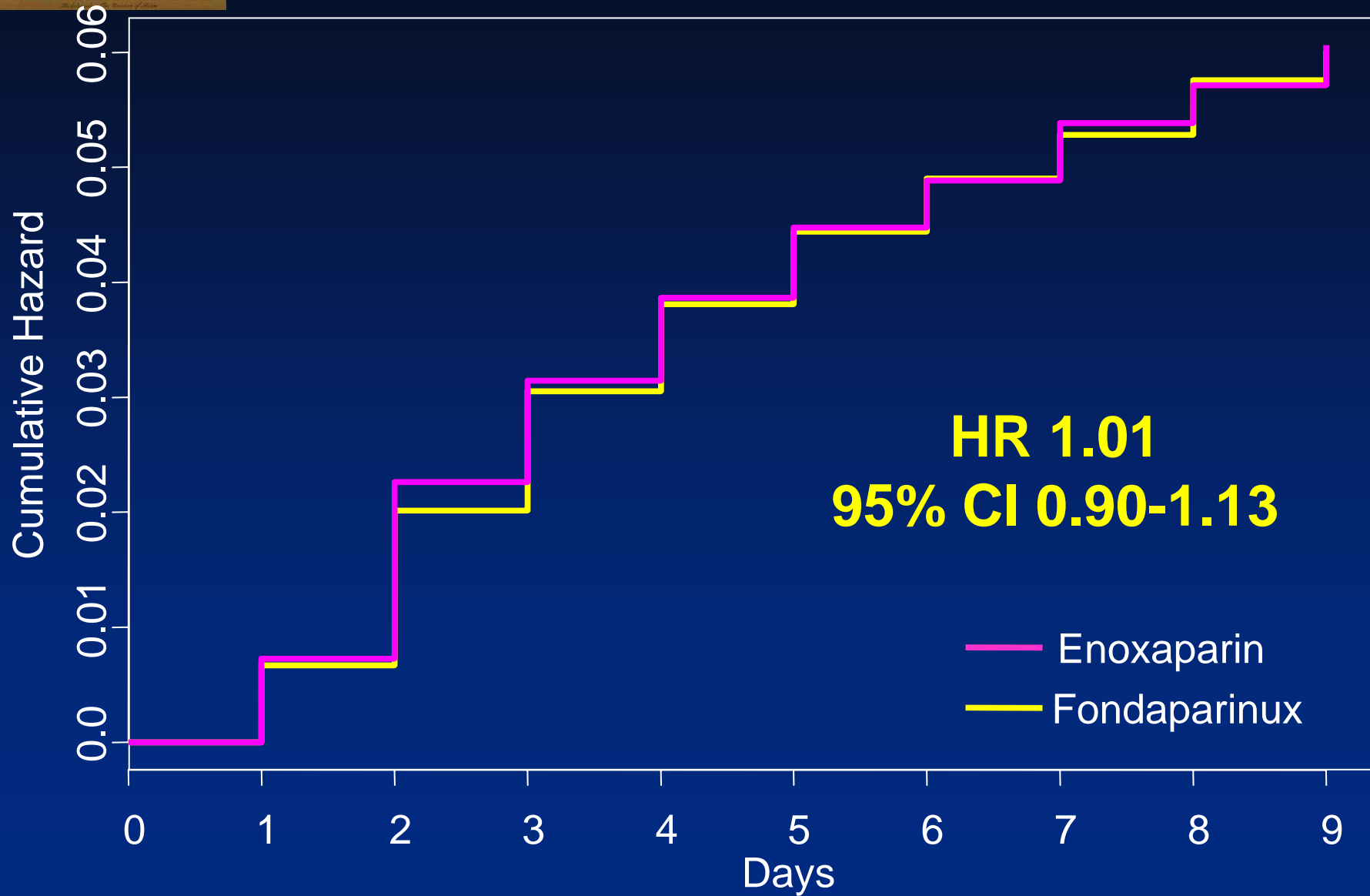
Major Bleeding and 1-Year Event Rates



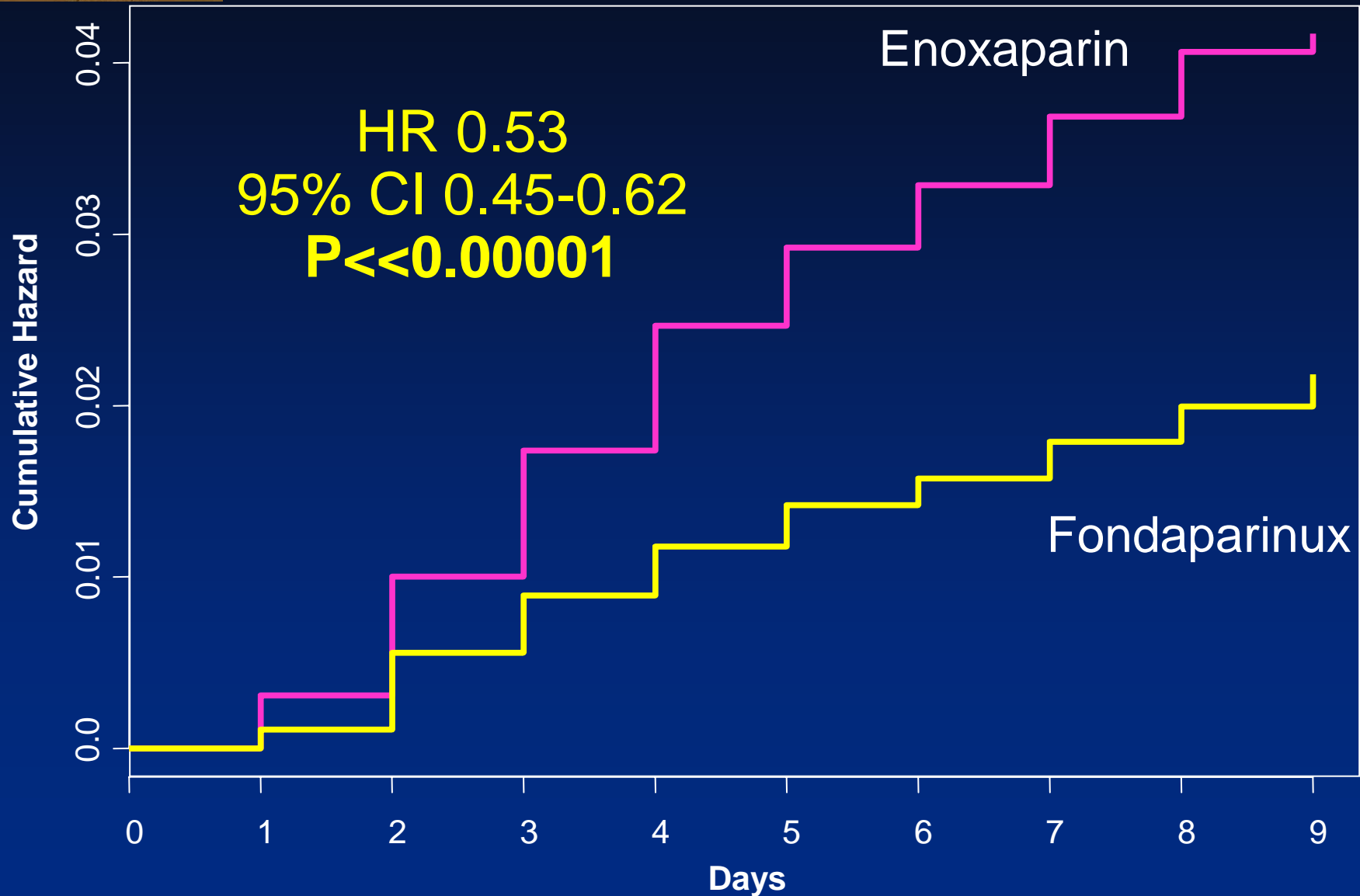


Death/MI/RI: Day 9

OASIS 5



Major Bleeding: 9 Days



ACC/AHA GUIDELINE REVISION

ACC/AHA 2007 Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction)

Developed in Collaboration with the American College of Emergency Physicians, the Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons

Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation and the Society for Academic Emergency Medicine

Guideline Classes

- **Class I**
 - Benefit >>>Risk
 - Procedure/treatment **should be** performed
- **Class IIa**
 - Benefit>>Risk-additional studies needed
 - **It is reasonable** to perform/administer treatment
- **Class IIb**
 - Benefit \geq Risk
 - Procedure/treatment **may be considered**
- **Class III**
 - Risk \geq Benefit
 - Procedure/treatment **should not** be performed as it may be not helpful or harmful

Guidelines Levels of Evidence (LOE)

- **LOE A**

- Multiple RCTs or meta-analyses
- General consistency of direction and magnitude of effect

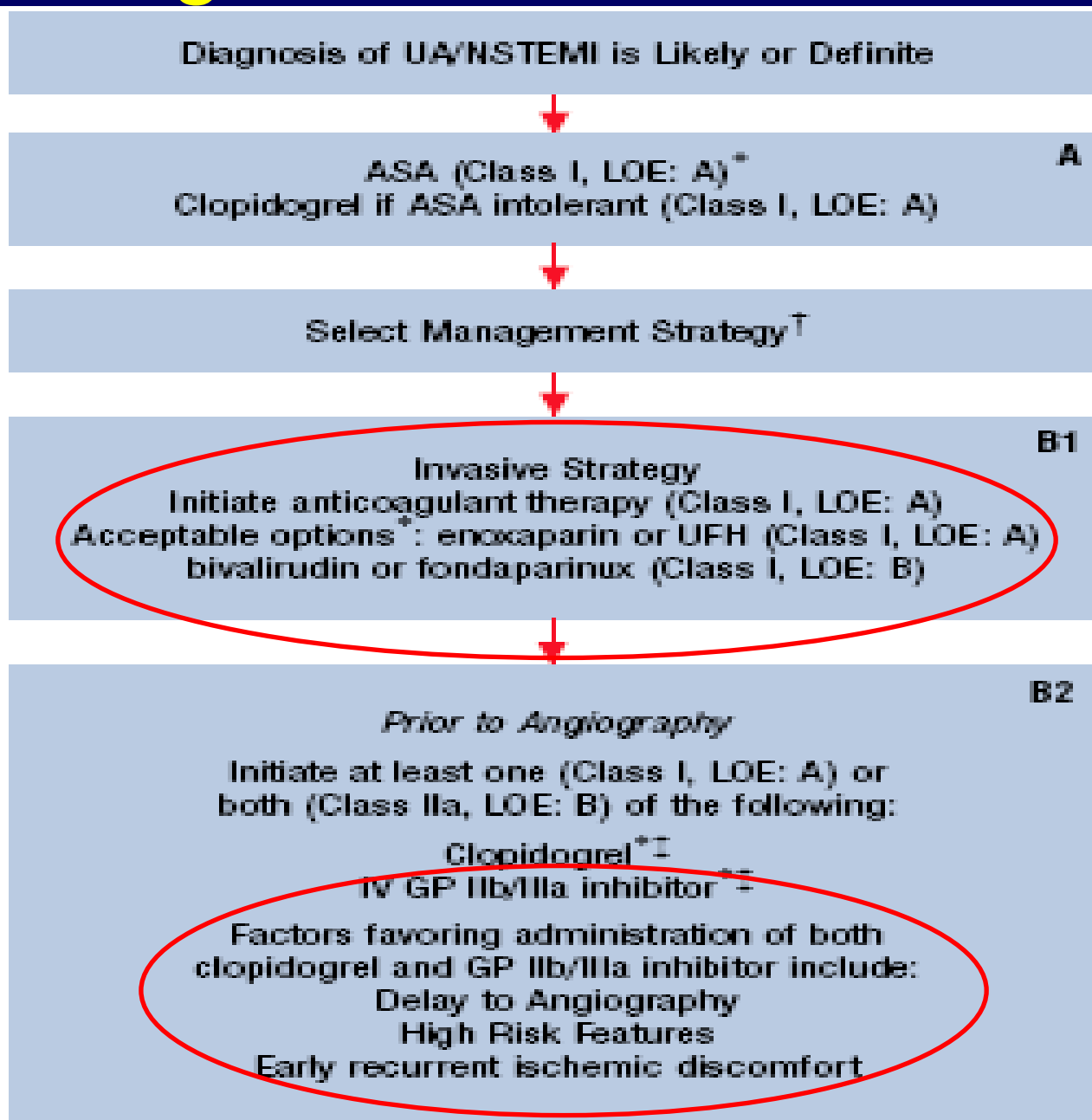
- **LOE B**

- Single randomized trial or non-randomized studies

- **LOE C**

- Only expert opinion, case studies, or standard of care exist as data

Management 2007 Guidelines



Early Conservative vs. Invasive Strategies

- **Class I**

- Early invasive strategy with any of the following high risk indicators (A)
 - **Recurrent ischemia at rest or with minimal activity on intensive anti-ischemic therapy**
 - **Elevated troponin (I or T)***
 - **New or presumably new ST depression***
 - **Recurrent ischemia with CHF, S3, pulmonary edema, worsening rales, or worsening MR**
 - **High risk stress test findings**
 - **Depressed LVEF (<0.40) on noninvasive testing**
 - **Hemodynamic instability**
 - **Sustained VT**
 - **PCI within 6 months or prior CABG**
 - **High risk score (TIMI or GRACE)**
- Absent these findings, either approach in patients without contraindications for revascularization (B)

TIMI RISK SCORE for UA/NSTEMI

HISTORICAL

Age ≥ 65

1

≥ 3 CAD risk factors

(FHx, HTN, \uparrow chol, DM, active smoker)

1

Known CAD (stenosis $\geq 50\%$)

1

ASA use in past 7 days

1

PRESENTATION

Recent (≤ 24 H) severe angina

1

\uparrow cardiac markers

1

ST deviation ≥ 0.5 mm

1

RISK SCORE = Total Points (0 - 7)

RISK OF CARDIAC EVENTS (%) BY 14 DAYS IN TIMI 11B*

RISK SCORE	DEATH OR MI	DEATH, MI OR URGENT REVASC
0/1	3	5
2	3	8
3	5	13
4	7	20
5	12	26
6/7	19	41

*Entry criteria: UA or NSTEMI defined as ischemic pain at rest within past 24H, with evidence of CAD (ST segment deviation or +marker)

Grace Risk Profile

Medical History

① Age in Years	Points
≤29	0
30-39.....	0
40-49.....	18
50-59.....	36
60-69.....	55
70-79.....	73
80-89.....	91
≥90.....	100

② History of Congestive Heart Failure.....	24
③ History of Myocardial Infarction	12

Findings at Initial Hospital Presentation

④ Resting Heart Rate, beats/min	Points
≤49.9.....	0
50-69.9.....	3
70-89.9.....	9
90-109.9.....	14
110-149.9.....	23
150-199.9.....	35
≥200.....	43

⑤ Systolic Blood Pressure, mm HG	Points
≤79.9.....	24
80-99.9.....	22
100-119.9.....	18
120-139.9.....	14
140-159.9.....	10
160-199.9.....	4
≥200.....	0

⑥ ST-Segment Depression ..	11
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Findings During Hospitalization

⑦ Initial Serum Creatinine, mg/dL	Points
0-0.39.....	1
0.4-0.79.....	3
0.8-1.19.....	5
1.2-1.59.....	7
1.6-1.99.....	9
2-3.99.....	15
≥4.....	20

⑧ Elevated Cardiac Enzymes	15
⑨ No In-Hospital Percutaneous Coronary Intervention	14

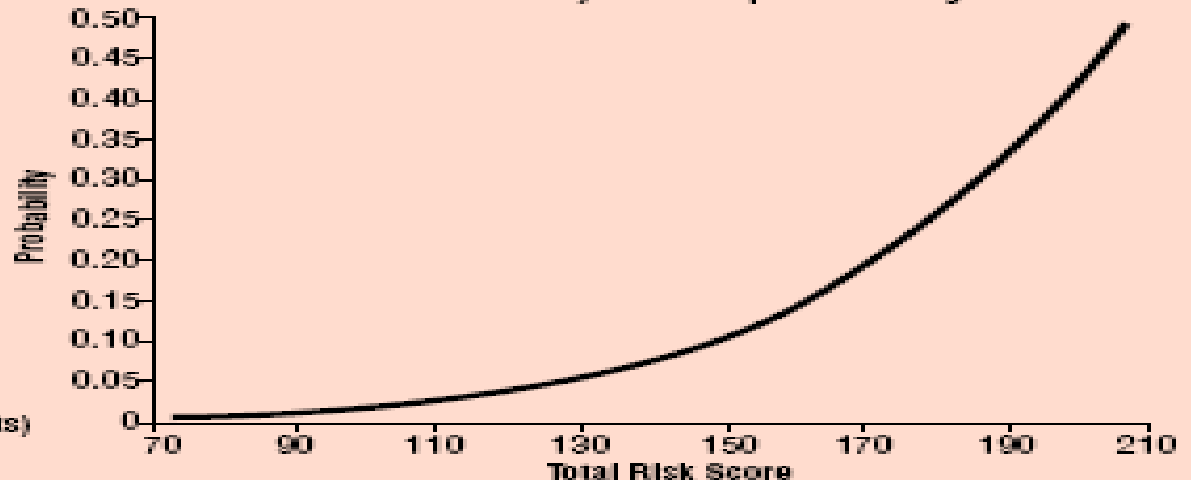
Points

- ① _____
- ② _____
- ③ _____
- ④ _____
- ⑤ _____
- ⑥ _____
- ⑦ _____
- ⑧ _____
- ⑨ _____

Total Risk Score _____ (Sum of Points)

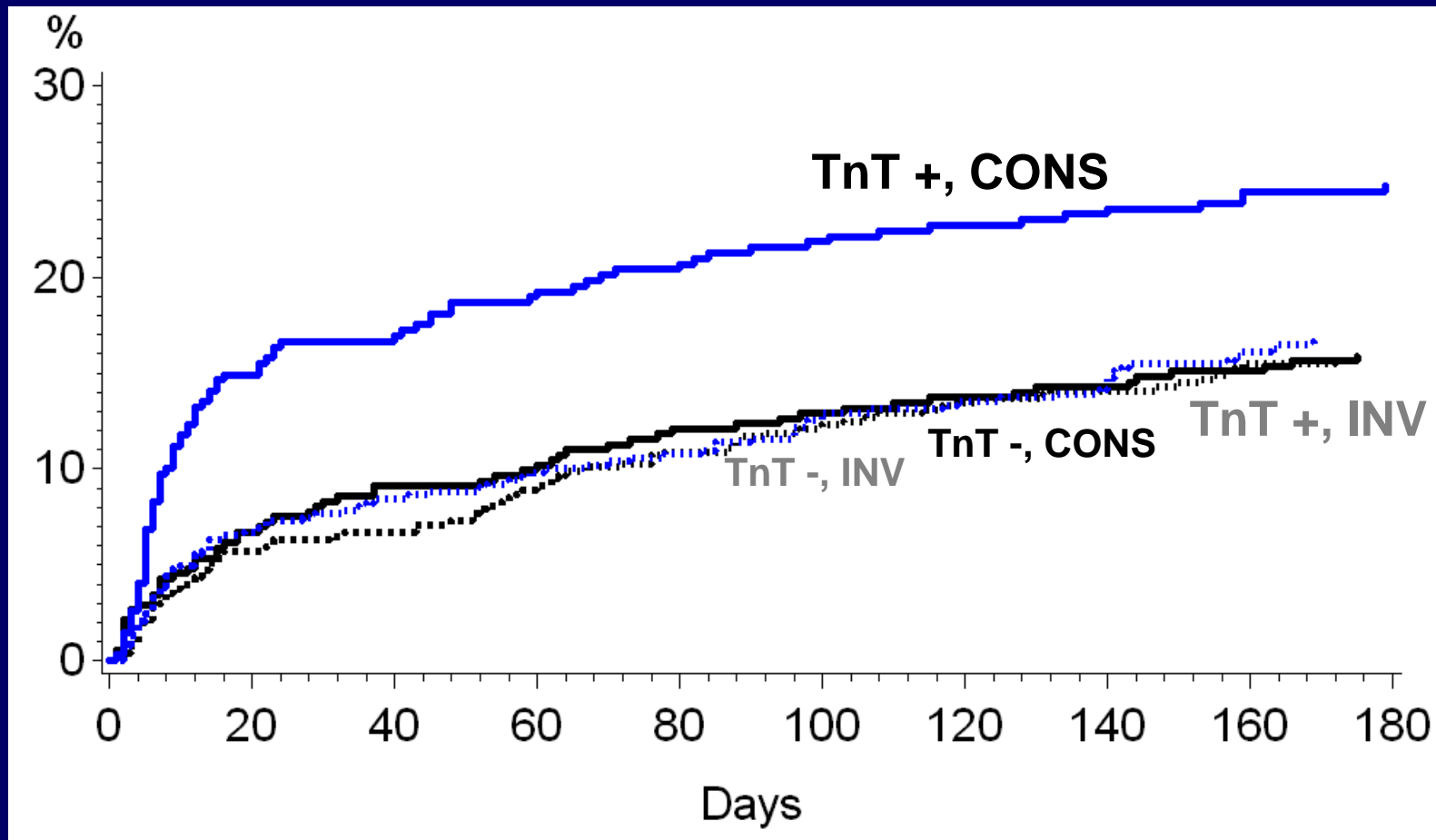
Mortality Risk _____ (From Plot)

Predicted All-Cause Mortality From Hospital Discharge to 6 Months



Troponin T > 0.1 ng/dl: 6 Months

Death/MI/Rehosp ACS



ACS PCI Guidelines

- Class I
 - Early invasive strategy for high risk patients (criteria presented) with lesions amenable to PCI
 - PCI (or CABG) recommended for 1 or 2 vessel CAD with a large area of viable myocardium and high risk features on non-invasive testing. (B)
 - PCI is recommended with multivessel CAD, normal LV function and no diabetes (A)
 - IV Gp 2b/3a agents generally recommended (A)

ACS PCI Guidelines

- Class IIa

- PCI is reasonable for SVG lesions or multiple stenoses in patients who are poor candidates for reoperation (C)
- PCI (or CABG) reasonable for 1-2 vessel CAD with moderate area of viable myocardium and ischemia (B)
- PCI (or CABG) can be beneficial compared to medical Rx with **1 vessel disease of proximal LAD** (B)
- PCI is reasonable with significant MLCAS who are not eligible for CABG or require emergent intervention (B)

ACS PCI Guidelines

- Class IIb

- In absence of high risk features PCI may be considered with single or multi-vessel CAD on medical Rx and who have 1 or more lesion to be dilated with a **reduced likelihood of success** (B)
- PCI may be considered in patients on medical Rx with 2 or 3 vessel CAD, significant proximal LAD disease, diabetes or abnormal LV function (B)

ACS PCI Guidelines

- Class III
 - PCI is not recommended for patients with 1 or 2 vessel disease **without** proximal LAD disease with no recurrent ischemic symptoms and without ischemia on non-invasive testing (C)
 - In the absence of high risk features PCI is not recommended without a trial of medical Rx and 1 or more of the following:
 - Small area at risk (C)
 - All lesions have a low likelihood of success (C)
 - High risk or procedure related morbidity/mortality (C)
 - Insignificant disease (C)
 - Significant MLCAS and a candidate for CABG (B)

Post Hospital Management

A Aspirin and Anticoagulants

B Beta blockers and Blood Pressure

C Cholesterol and Cigarettes

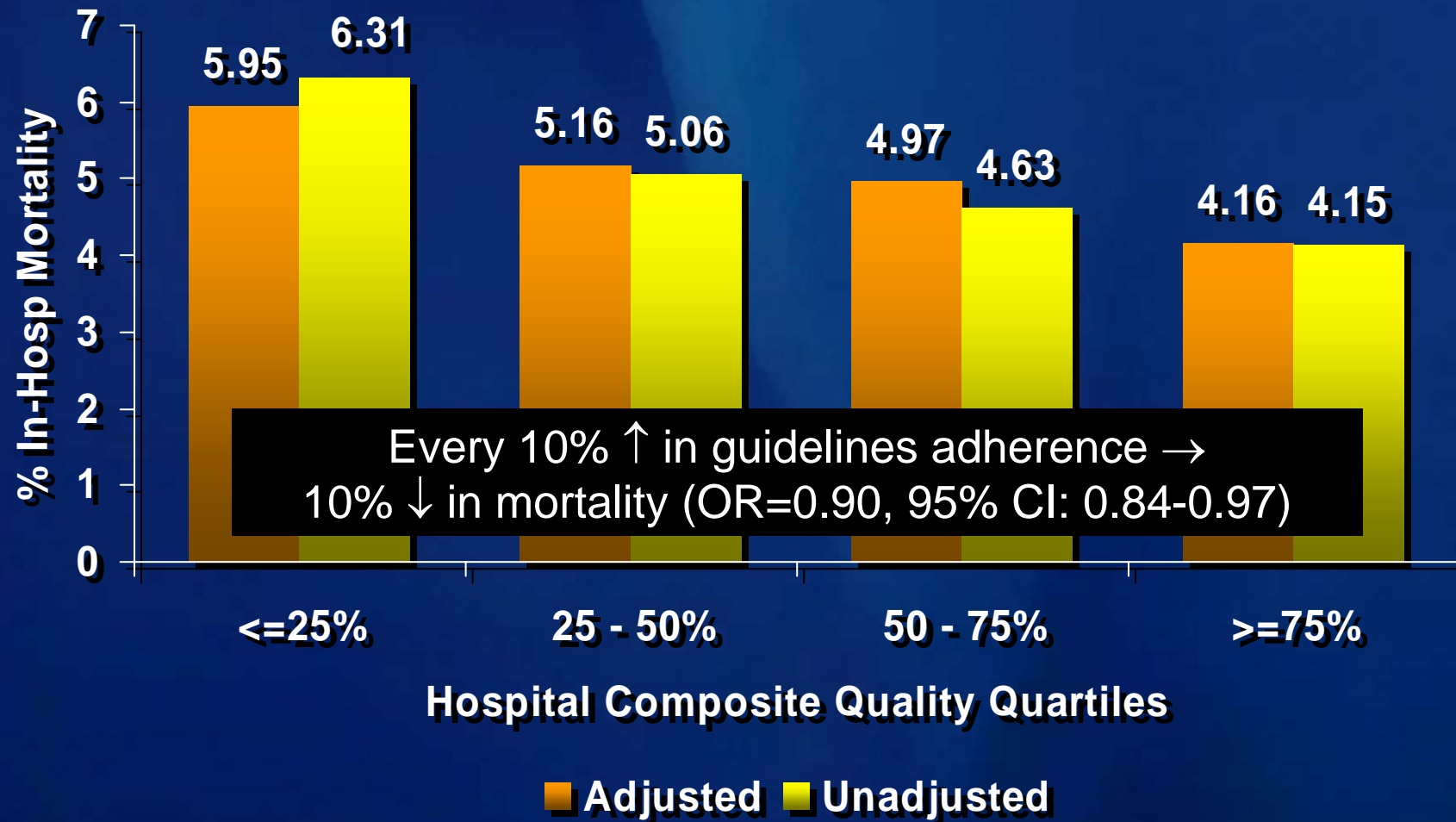
D Diet and Diabetes

E Education and Exercise

How useful is guideline adherence?



Hospital Link Between Overall Guidelines Adherence and Mortality



Peterson et al, JAMA 2006;295:1863-1912

More Recent Data

Discontinuance of Clopidogrel after ACS and Subsequent Death and MI Events

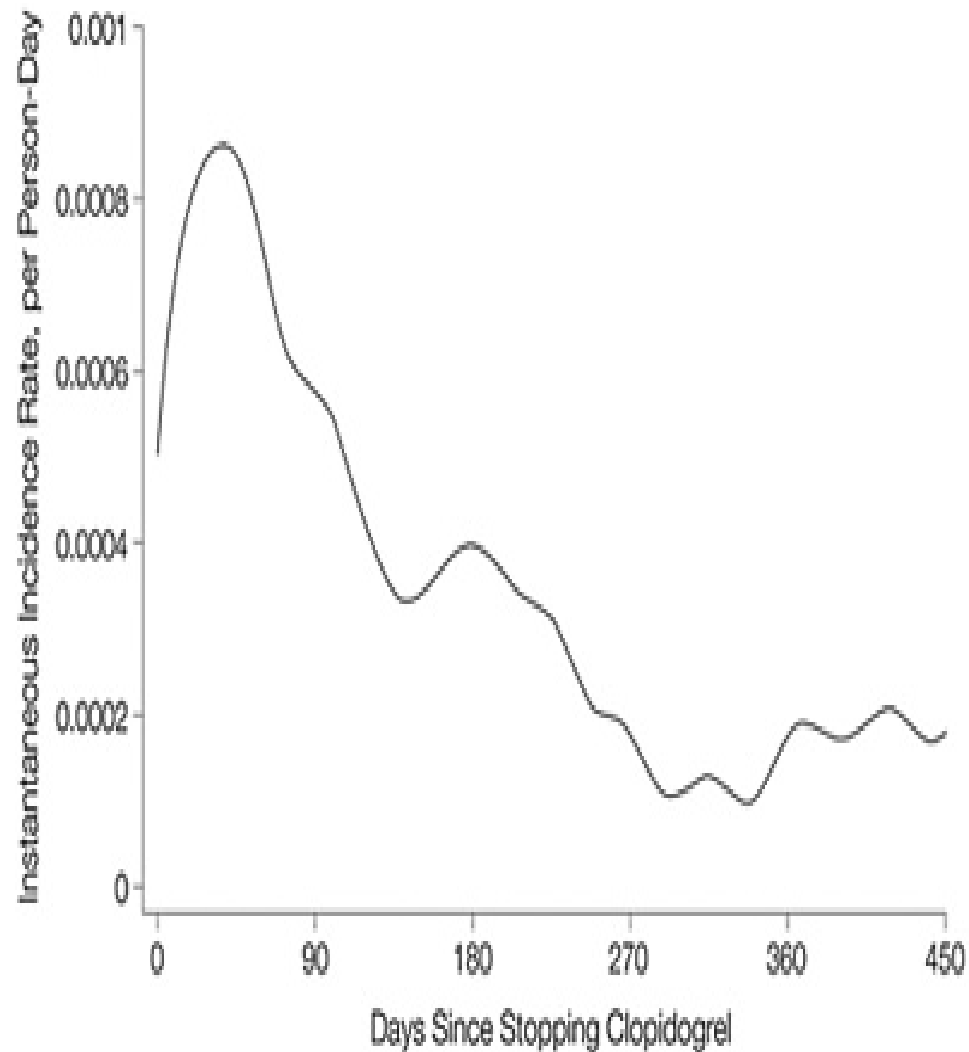
Ho PM et. al., Journal of the American Medical Association 2008; 299(5):532-539.

Design of Study

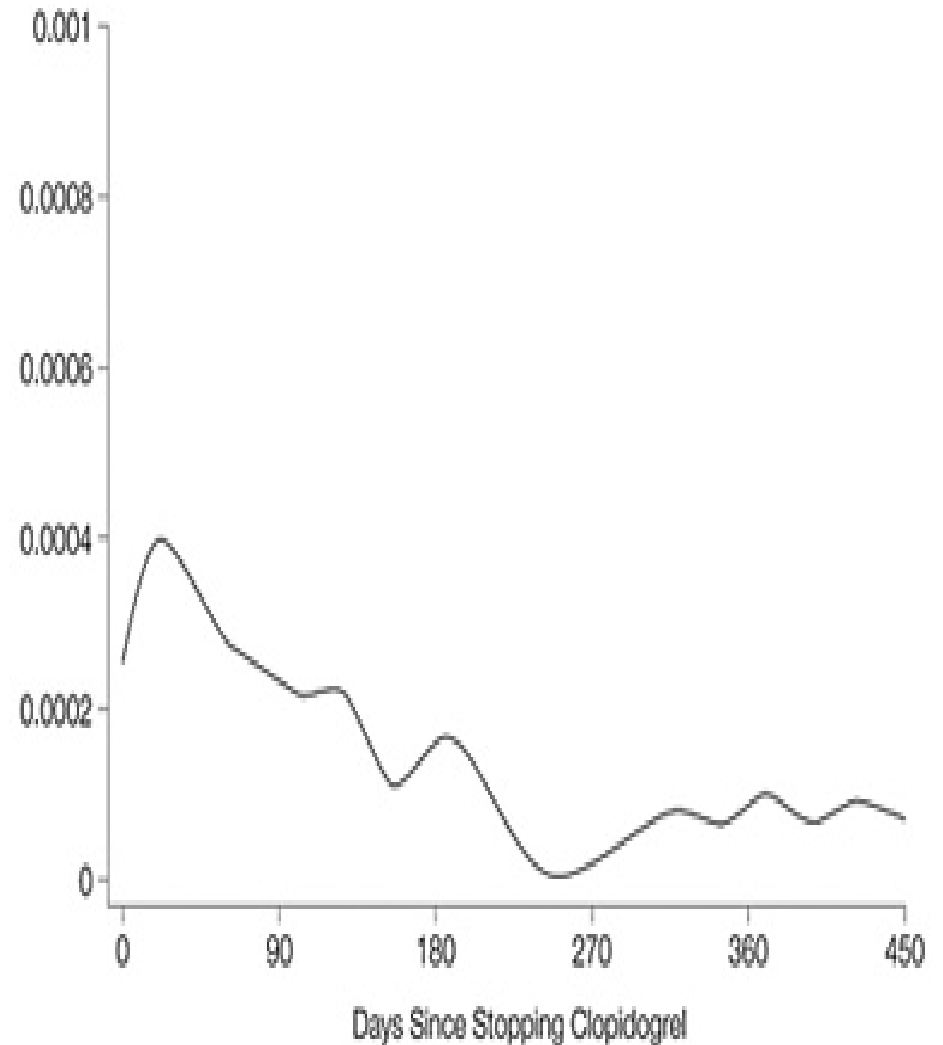
- Retrospective cohort study of 3137 patients with ACS discharged from 127 Veterans Affairs hospitals between October 2003 and March 2005.
- All patients had post hospital treatment with clopidogrel.
- Main outcome measure was all-cause mortality or acute myocardial infarction (AMI) after stopping clopidogrel.

Risk Adjusted Rates Death or AMI after D/C Clopidogrel

Medically treated patients



PCI patients



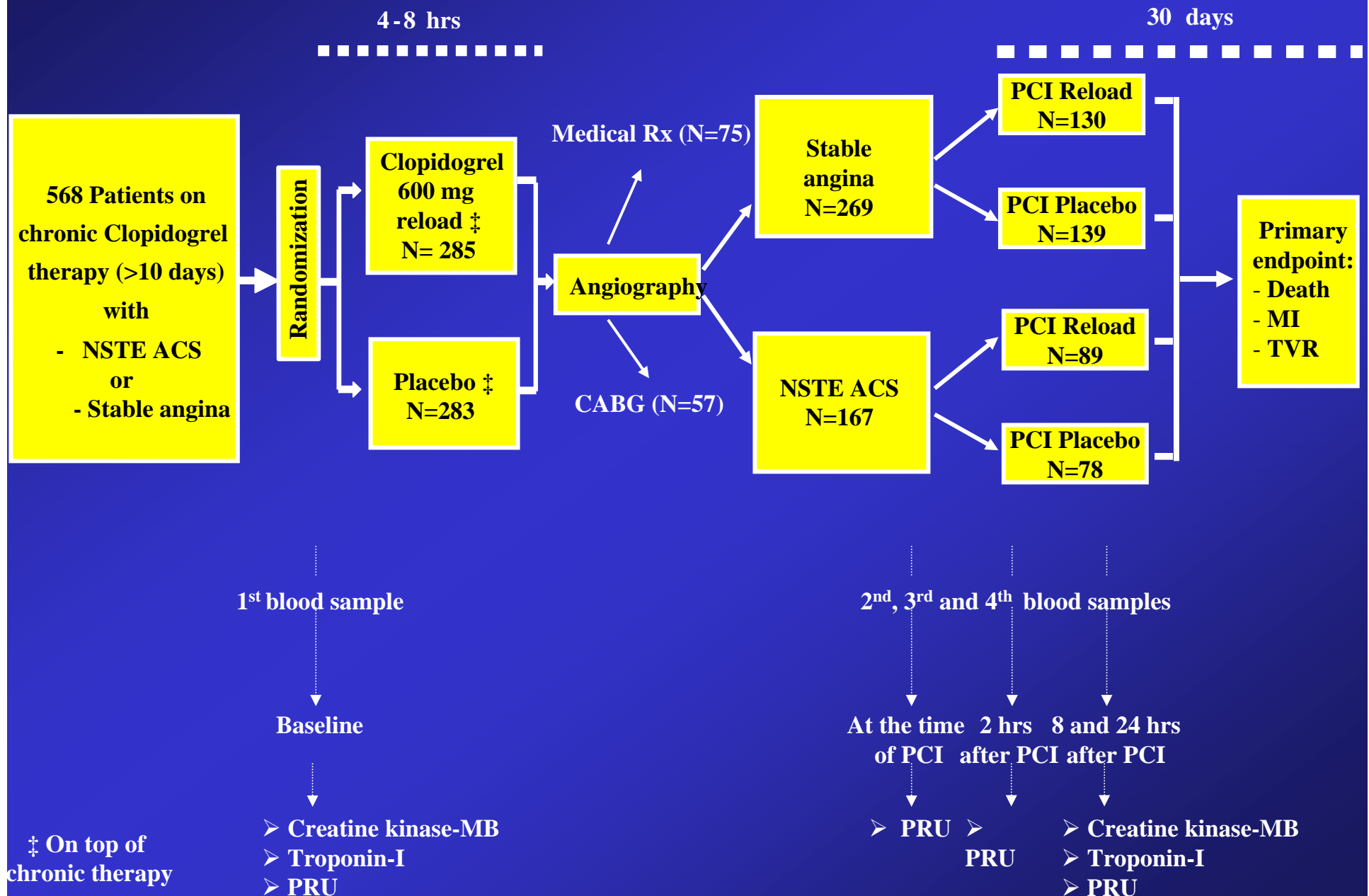
Conclusions of Clopidogrel Discontinuance in ACS Patients Data

- Data support the hypothesis of a possible rebound hyperthrombotic period after stopping clopidogrel
- Adds to the existing literature supporting a rebound effect after stopping aspirin.
- Data support observations of the STRATEGY study which reported a clustering of death or nonfatal MI in the first month after stopping a thienopyridine in stented (BMS and DES) STEMI patients
- N.B.: This is not late stent thrombosis as it occurred most prominently in the medical treatment group.

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

ARMYDA-RELOAD
SCAI-ACC i2 March 2008

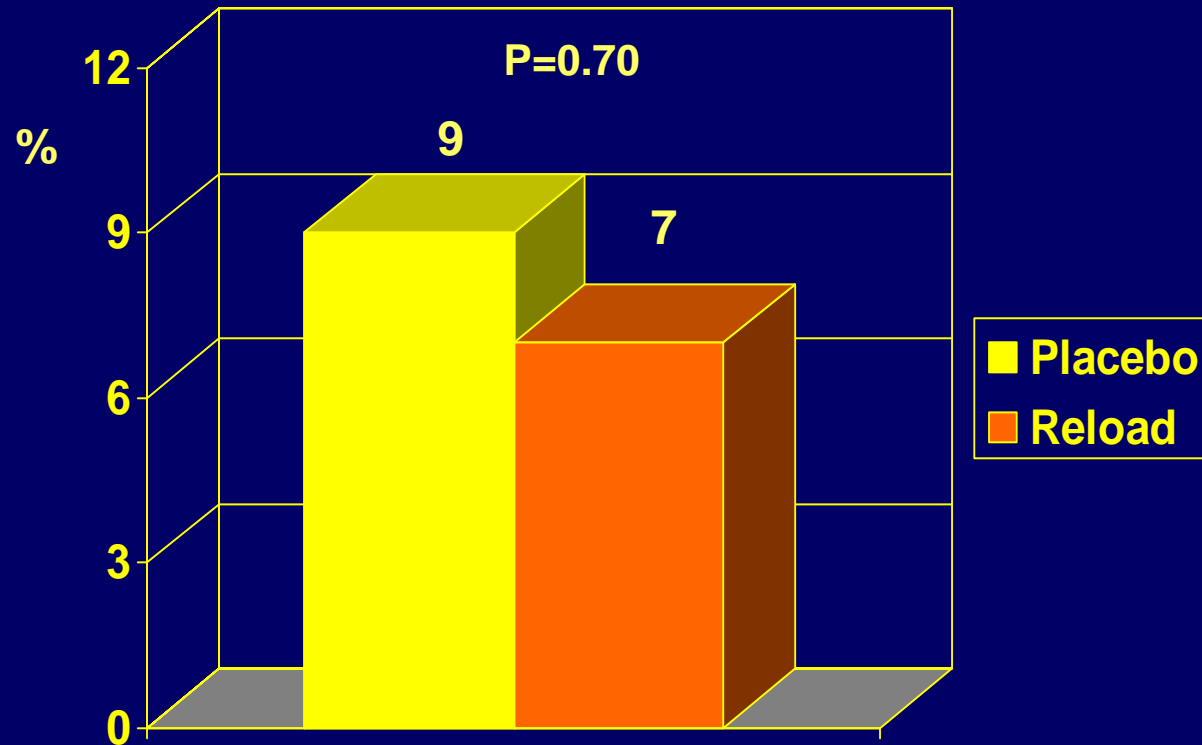
ARMYDA-RELOAD: Study design



ARMYDA-RELOAD Trial

Composite primary endpoint (30-day death, MI, TVR)

Overall population N=436

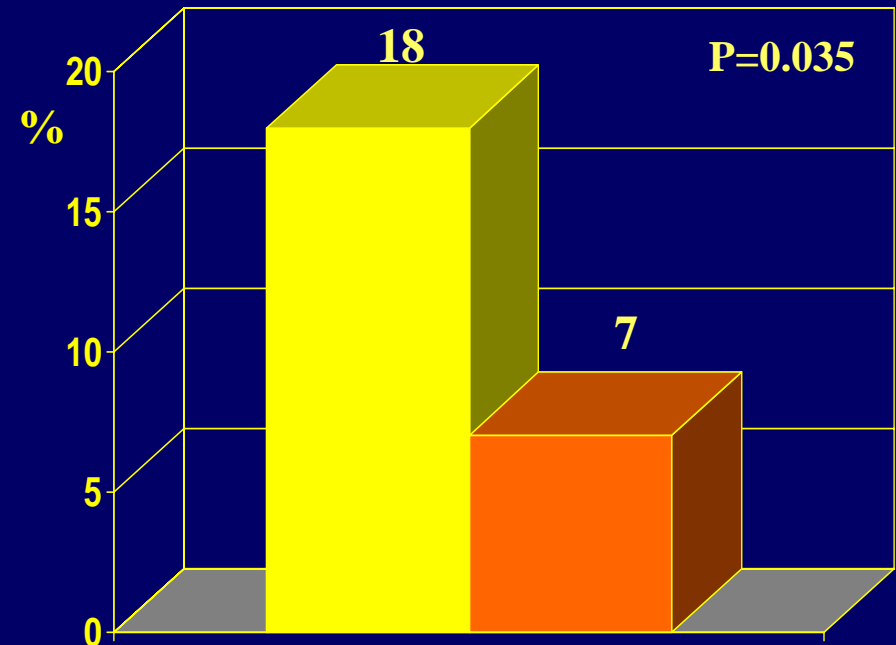
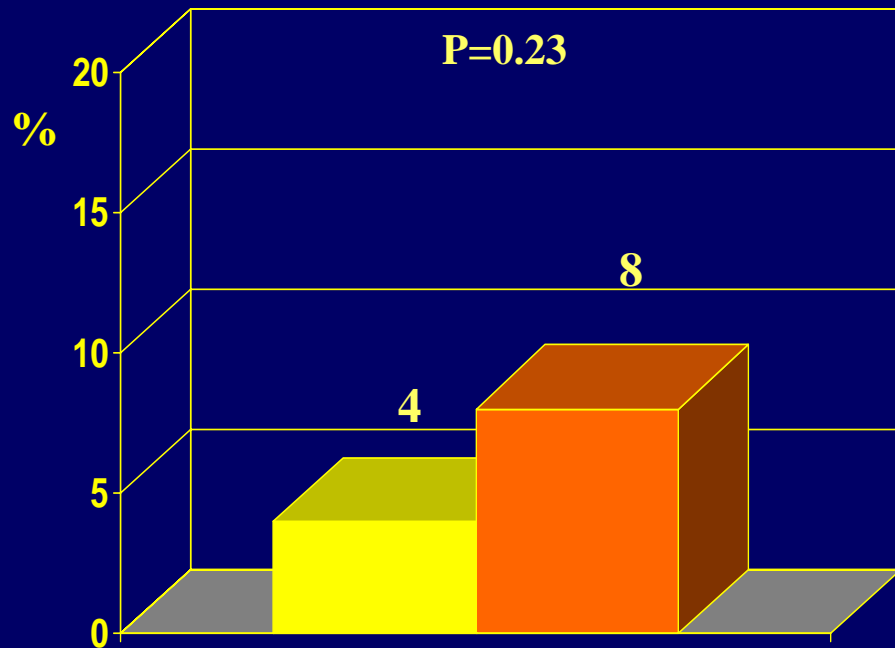


ARMYDA-RELOAD Trial

Composite primary endpoint (30-day death, MI, TVR)

Stable

ACS



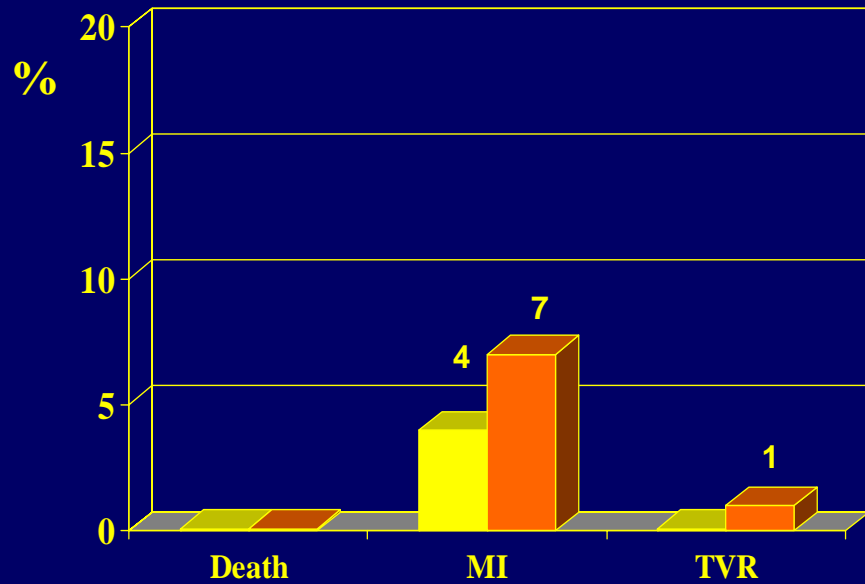
■ Placebo

■ 600 mg Clopidogrel reload

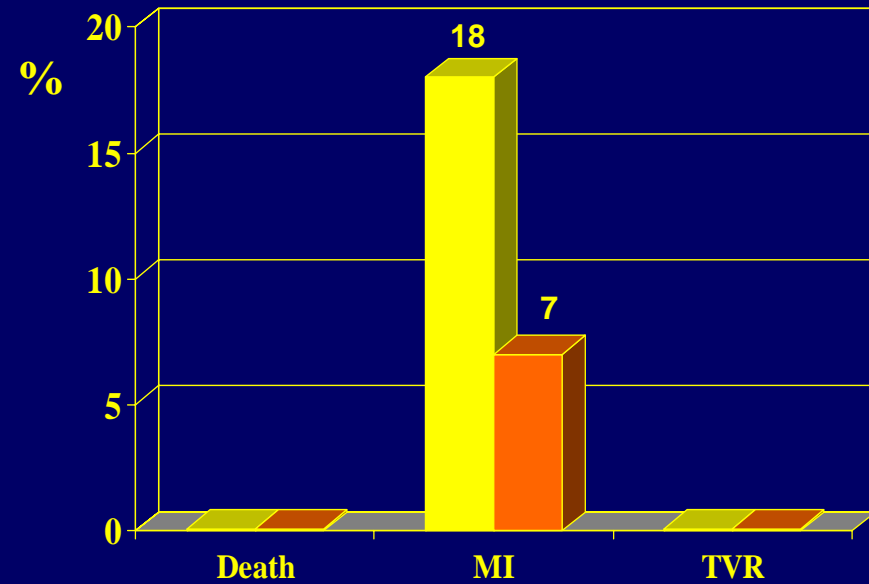
ARMYDA-RELOAD Trial

Individual components of primary endpoint

Stable



ACS



■ Placebo

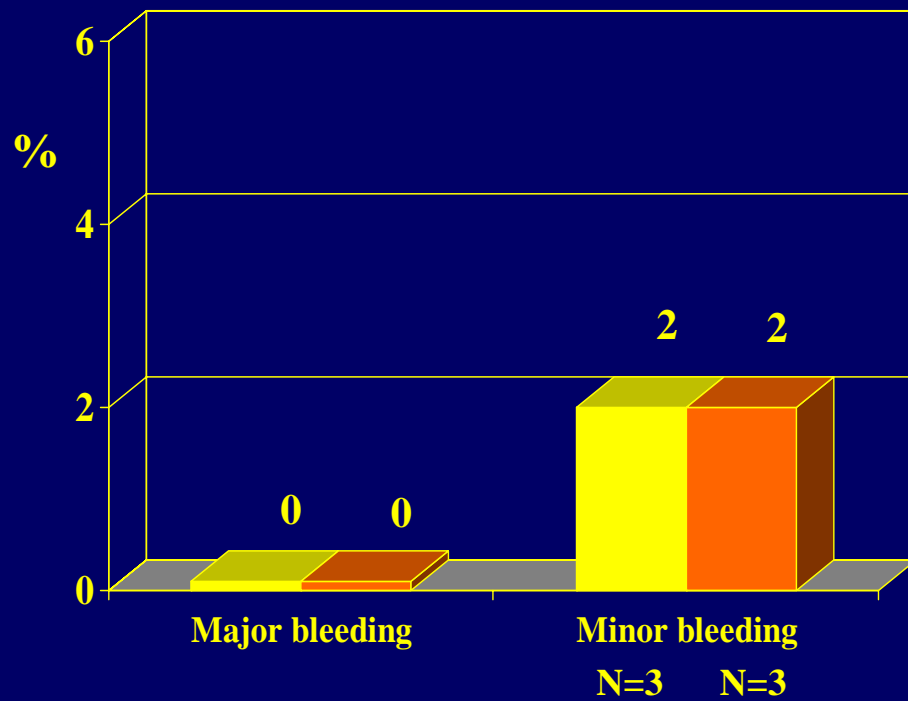
■ 600 mg Clopidogrel reload

ARMYDA-RELOAD Trial

Secondary endpoint:

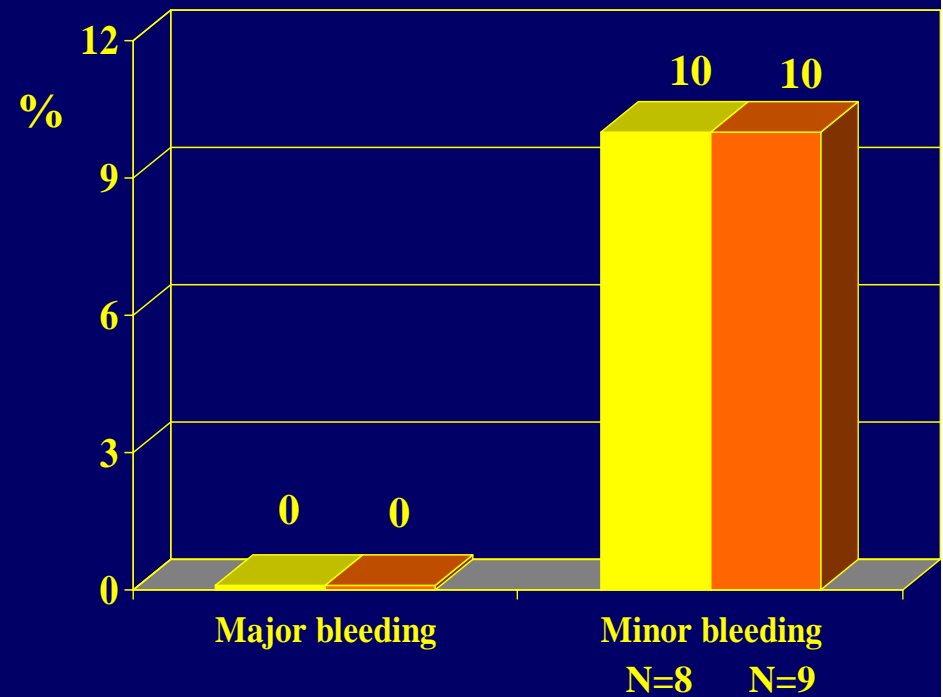
Bleeding rates

Stable



■ Placebo

ACS



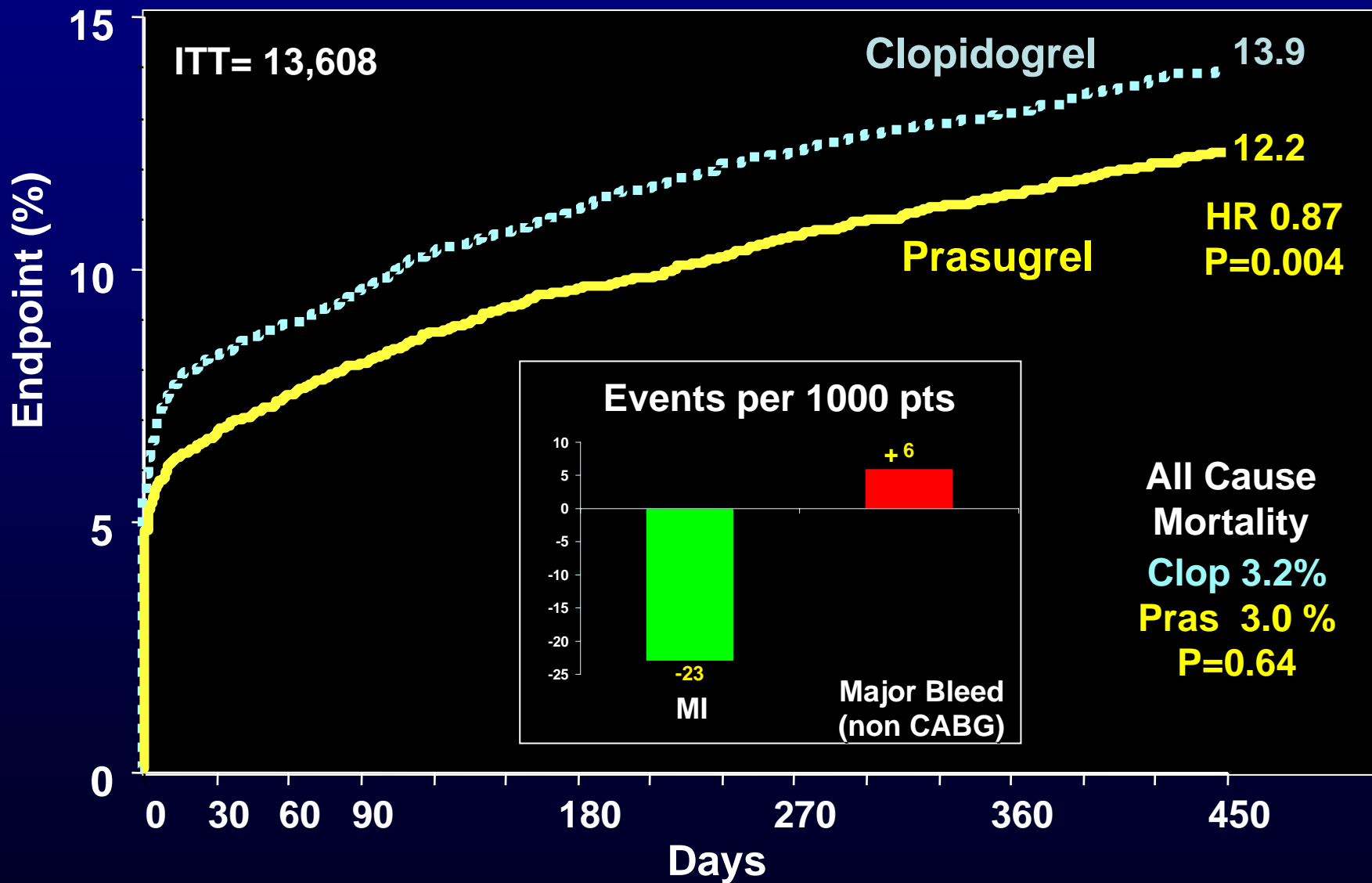
■ 600 mg Clopidogrel reload

Conclusion ARMYDA RELOAD

- Patients with stable angina who are on clopidogrel can safely undergo PCI without reloading
- Patients with ACS who are on clopidogrel have improved outcomes when reloaded with 600 mgm of clopidogrel
- No major bleeding was observed with the reload strategy.

Net Clinical Benefit

Death, MI, Stroke,
Major Bleed (non CABG)



Summary

- There is more to competent management of ACS patients than being technically proficient in the cath lab!
 - Knowledge of and adherence to guidelines results in improved patient outcomes and reduced mortality
- More aggressive utilization of antiplatelet agents results in improved outcomes
 - Aggressive reloading of clopidogrel in ACS patients appears to result in improved outcomes
- Newer antiplatelet agents show promise for improved outcomes but with some increased bleeding.
- Abrupt discontinuance of clopidogrel is not without consequence and needs further study
- The underlying disease, atherosclerosis, is chronic and currently incurable and requires aggressive management!