

Best Management of AMI in 2006

Guidelines Revisited



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The ESC 2003 STEMI Guidelines

Task Force Report

Management of acute myocardial infarction in patients presenting with ST-segment elevation

The Task Force on the Management of Acute Myocardial Infarction of the European Society of Cardiology,

Frans Van de Werf, Chair, Diego Ardissino, Amadeo Betriu, Dennis V. Cokkinos, Erling Falk, Keith A.A. Fox, Desmond Julian, Maria Lengyel, Franz-Josef Neumann, Witold Ruzyllo, Christian Thygesen, S. Richard Underwood, Alec Vahanian, Freek W.A. Verheugt, William Wijns

Eur Heart J 2003;24:28-66

10/11/2006





Changes/Updates Needed

- **Choice between Fibrinolysis or Primary PCI**
- **Antithrombin Therapy**
- **Antiplatelet Therapy**
- **Routine prophylactic treatment in acute phase**
- **Secondary prevention**

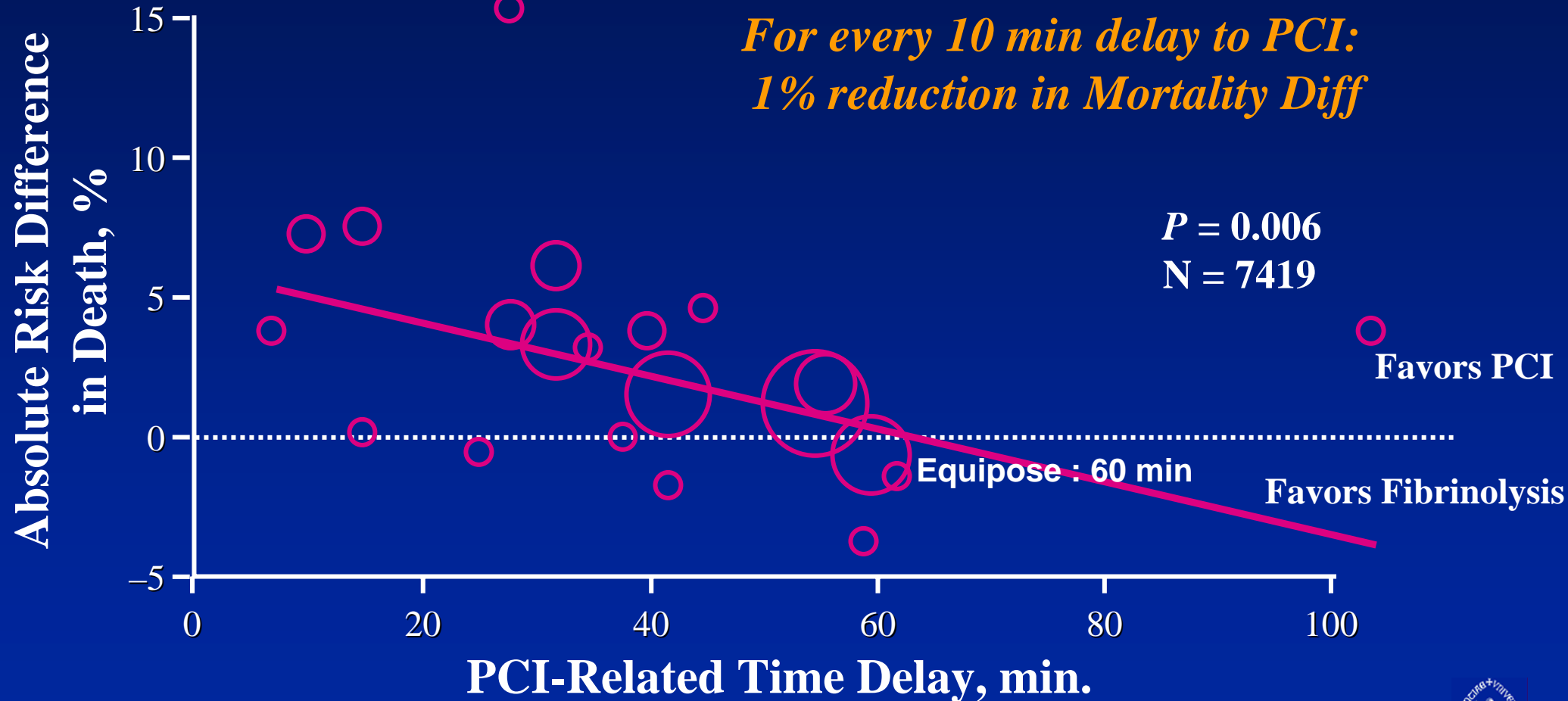


Primary PCI vs. Thrombolysis

| Recommendations | Class I | IIa | IIb | III | Level of Evidence |
|--|---------|-----|-----|-----|-------------------|
| • Preferred treatment if performed by experienced team <90 min after first medical contact / < 120 min ? | X | | | | A |
| • Indicated for patients in shock and those with contraindications to fibrinolytic therapy | X | | | | C |
| • GP IIb/IIIa antagonists and primary PCI | | | | | |
| no stenting | X | | | | A |
| with stenting | | X | | | A |



PCI vs. Lysis: Importance of Timing



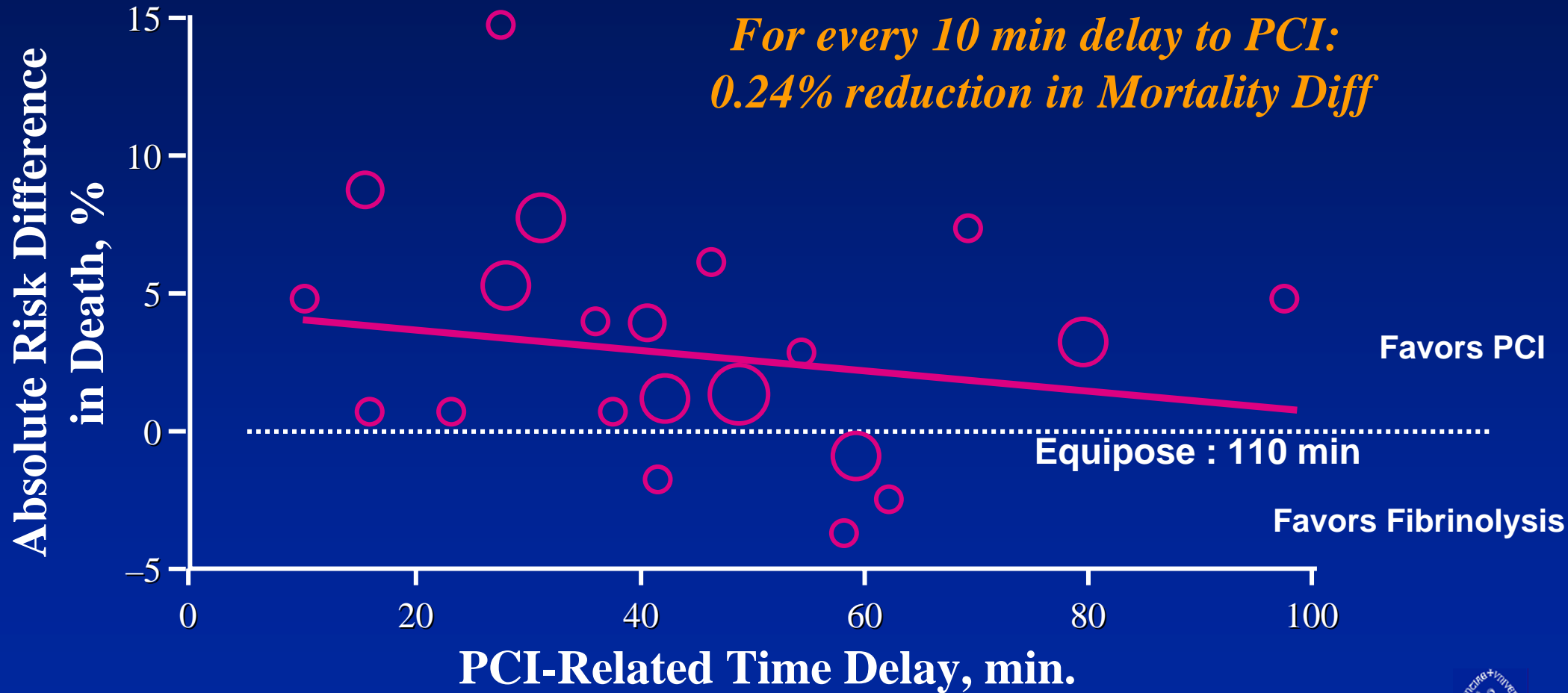
Nallamothu and Bates, AJC, 2003.

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PCI vs. Lysis: Importance of Timing



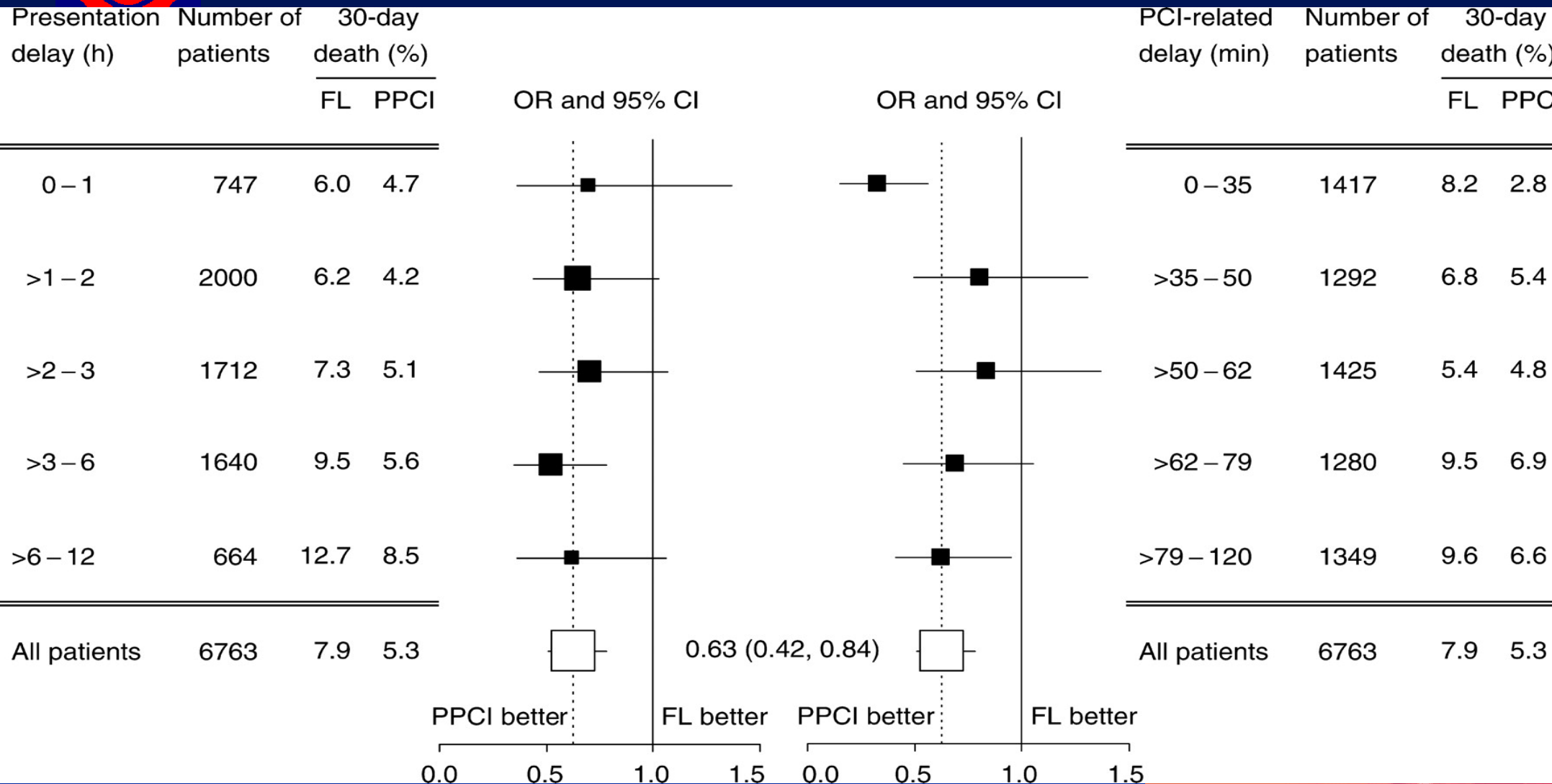
Betriu and Masotti, AJC, 2005.

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30-D Mortality after primary PCI vs Fibrinolysis according to presentation (left) and PCI-related delay (right)





Time delays in Transfer Patients for Primary PCI

**Door of community hospital to first balloon inflation in PCI
hospital (median delay time):**

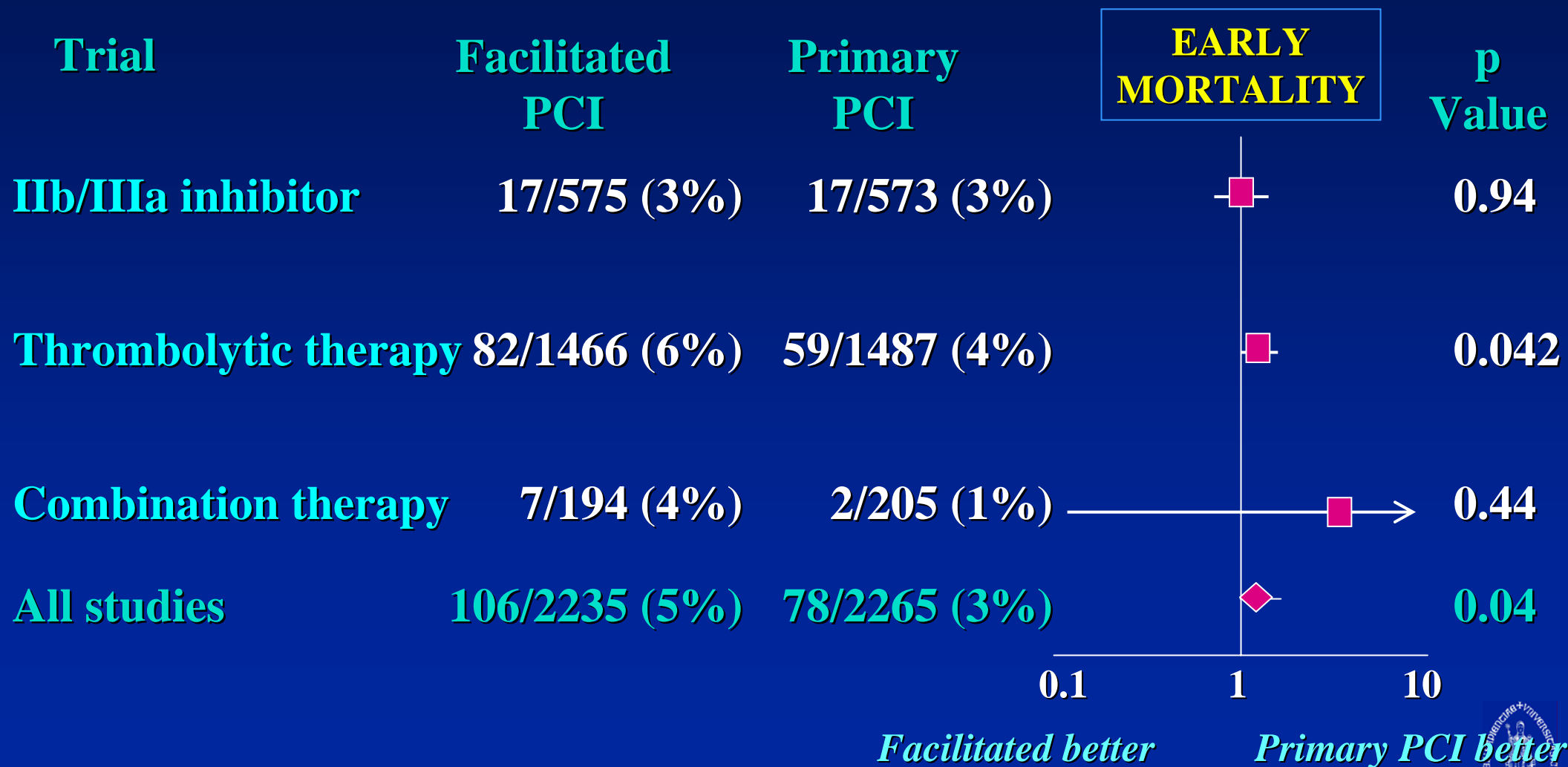
in 103 patients from EHS ACS II: 121 min

in 4278 patients from NRMI 3/4: 180 min

**Pre-PCI pharmacological treatment or
facilitated PCI?**

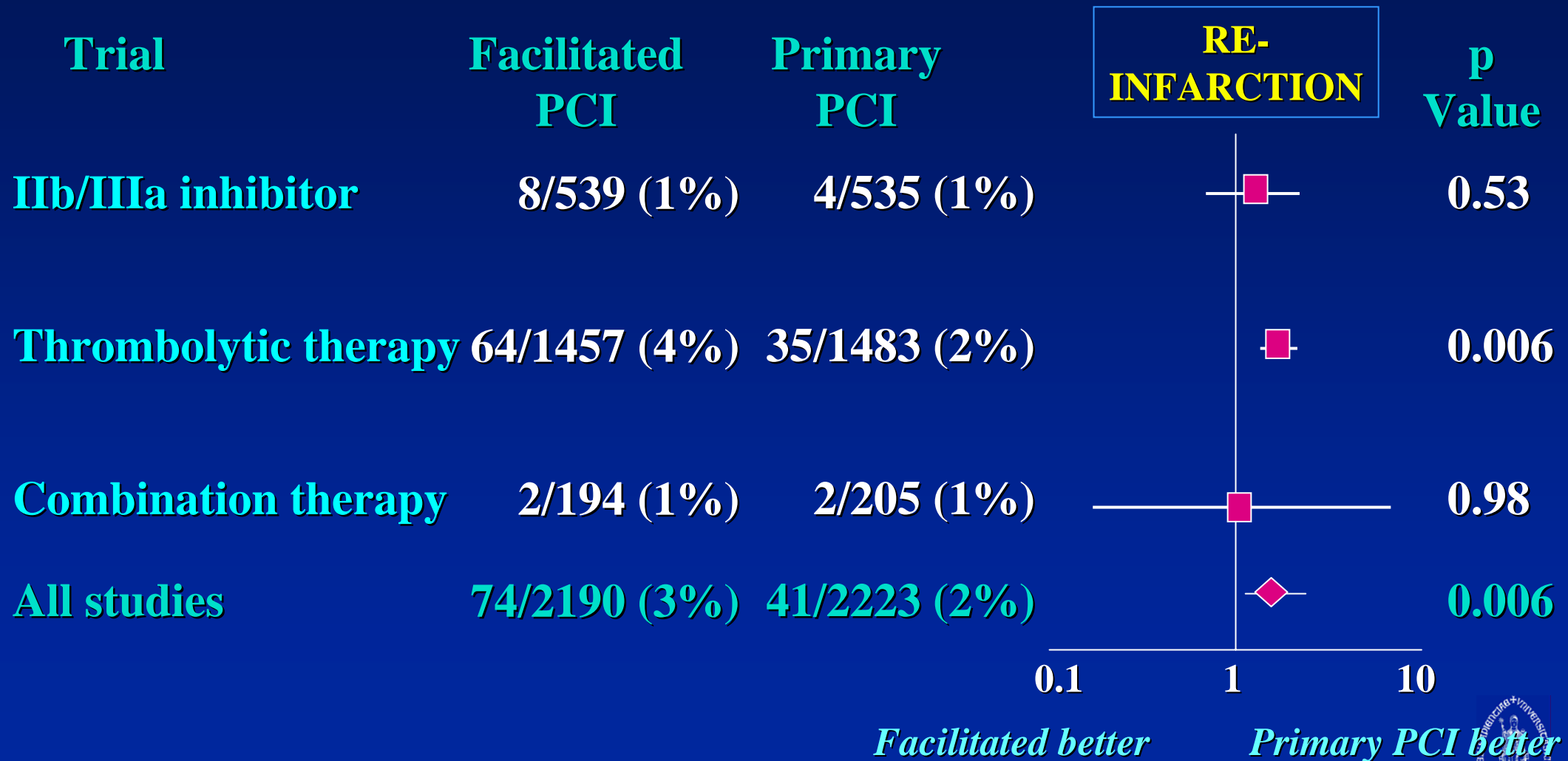


Early Mortality



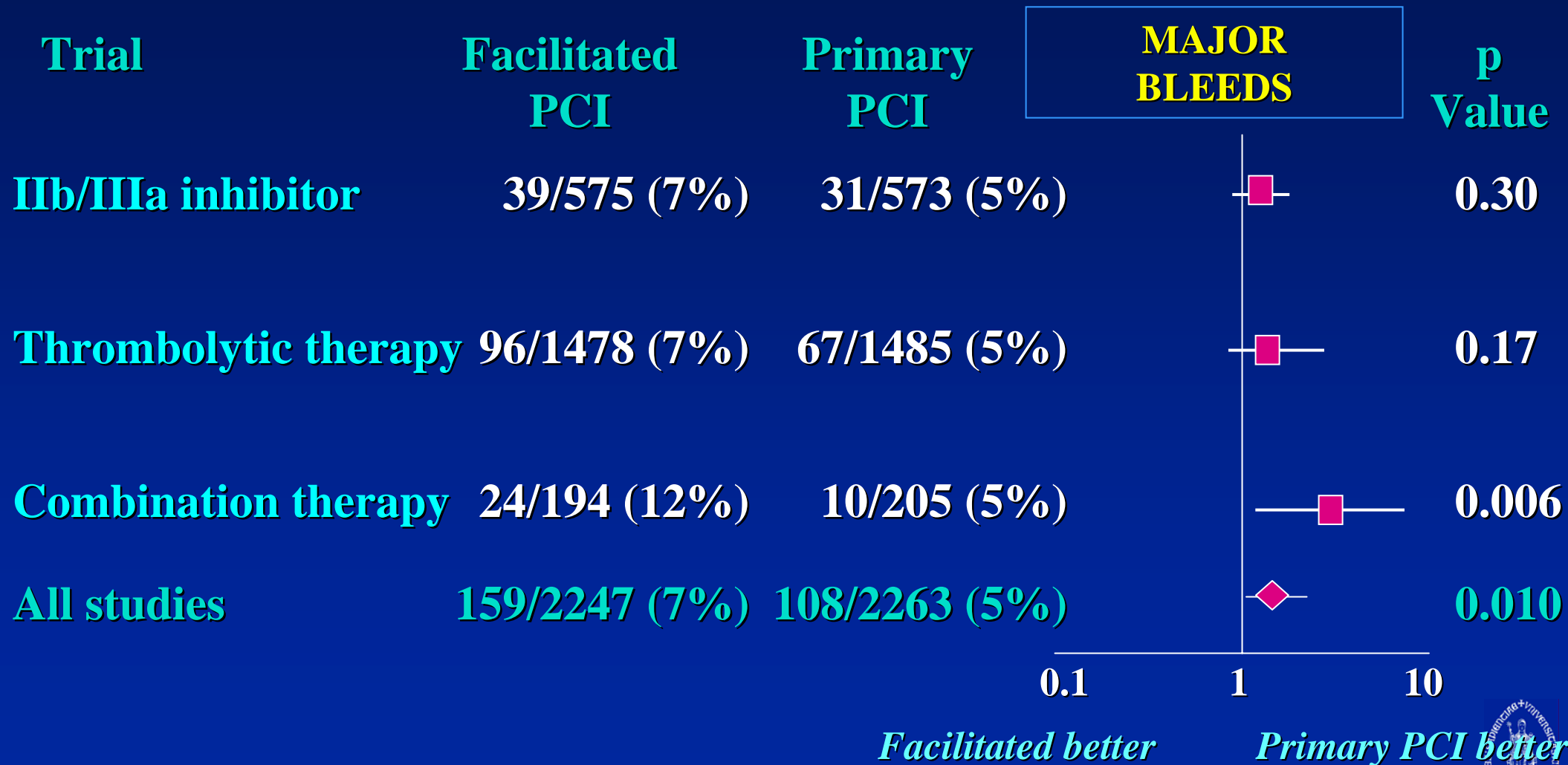


Early Reinfarction





Major Bleeding





Antiplatelet Co-Therapy in Acute Phase

| Recommendations | Class I | IIa | IIb | III | Level of evidence |
|---|---------|-----|-----|-----|-------------------|
| <ul style="list-style-type: none">• If not already on aspirin 150-325 mg chewable aspirin (no enteric-coated tablets)• Clopidogrel to be added? irrespective of age? | X | | | | A |



CLARITY: Study Design

Double-blind, randomized, placebo-controlled trial in
3491 patients, age **18-75 yrs** with STEMI < 12 hours

Fibrinolytic, ASA, Heparin

randomize

**Clopidogrel
300 mg + 75 mg qd**

Placebo

**Coronary Angiogram
(2-8 days)**

30-day clinical follow-up

Study
Drug

Open-label
clopidogrel
per MD in
both groups

Primary endpoint:
*Occluded
artery (TIMI Flow
Grade 0/1)
or D/MI by time
of angio*

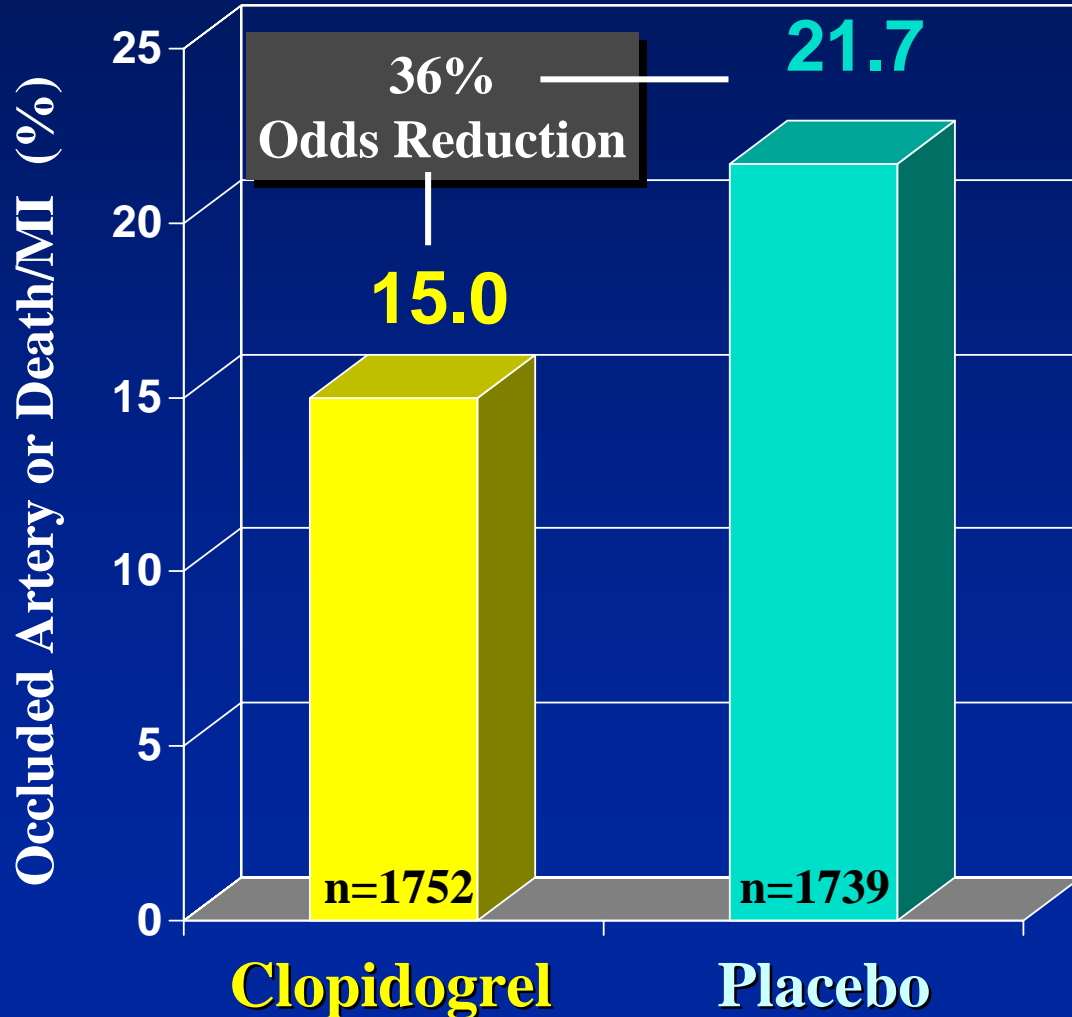
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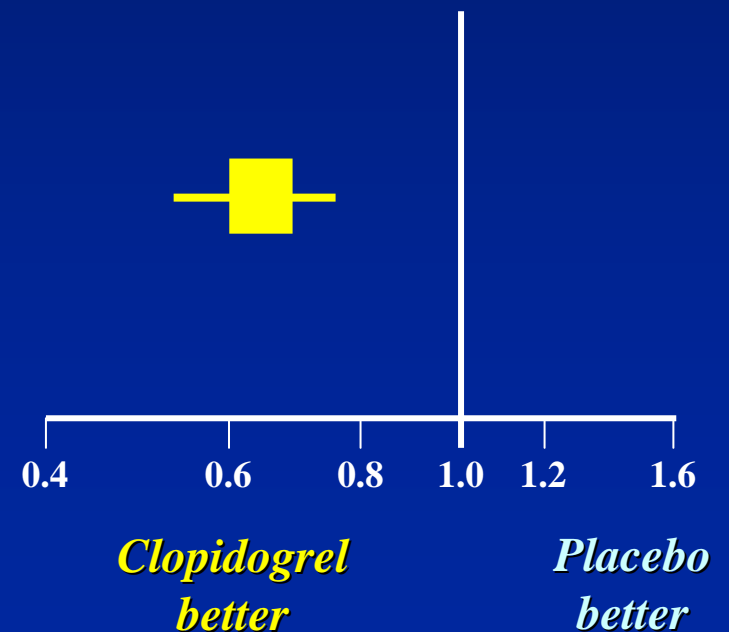
CLARITY: Primary Endpoint

Occluded Artery (or Death/MI before Angio/Discharge)



Odds Ratio 0.64
(95% CI 0.53-0.76)

P=0.00000036





CLARITY: Bleeding

| Outcome | Clopidogrel (%) | Placebo (%) | P value |
|---|----------------------------|------------------------|----------------|
| Through angiography | | | |
| TIMI major (Hgb ↓ >5 g/dL or ICH) | 1.3 | 1.1 | NS |
| TIMI minor (Hgb ↓ 3-5 g/dL) | 1.0 | 0.5 | NS |
| Intracranial hemorrhage | 0.5 | 0.7 | NS |
| Through 30 days | | | |
| TIMI major | 1.9 | 1.7 | NS |
| In those undergoing CABG | 7.5 | 7.2 | NS |
| CABG w/in 5 d of study med | 9.1 | 7.9 | NS |
| TIMI minor | 1.6 | 0.9 | NS |



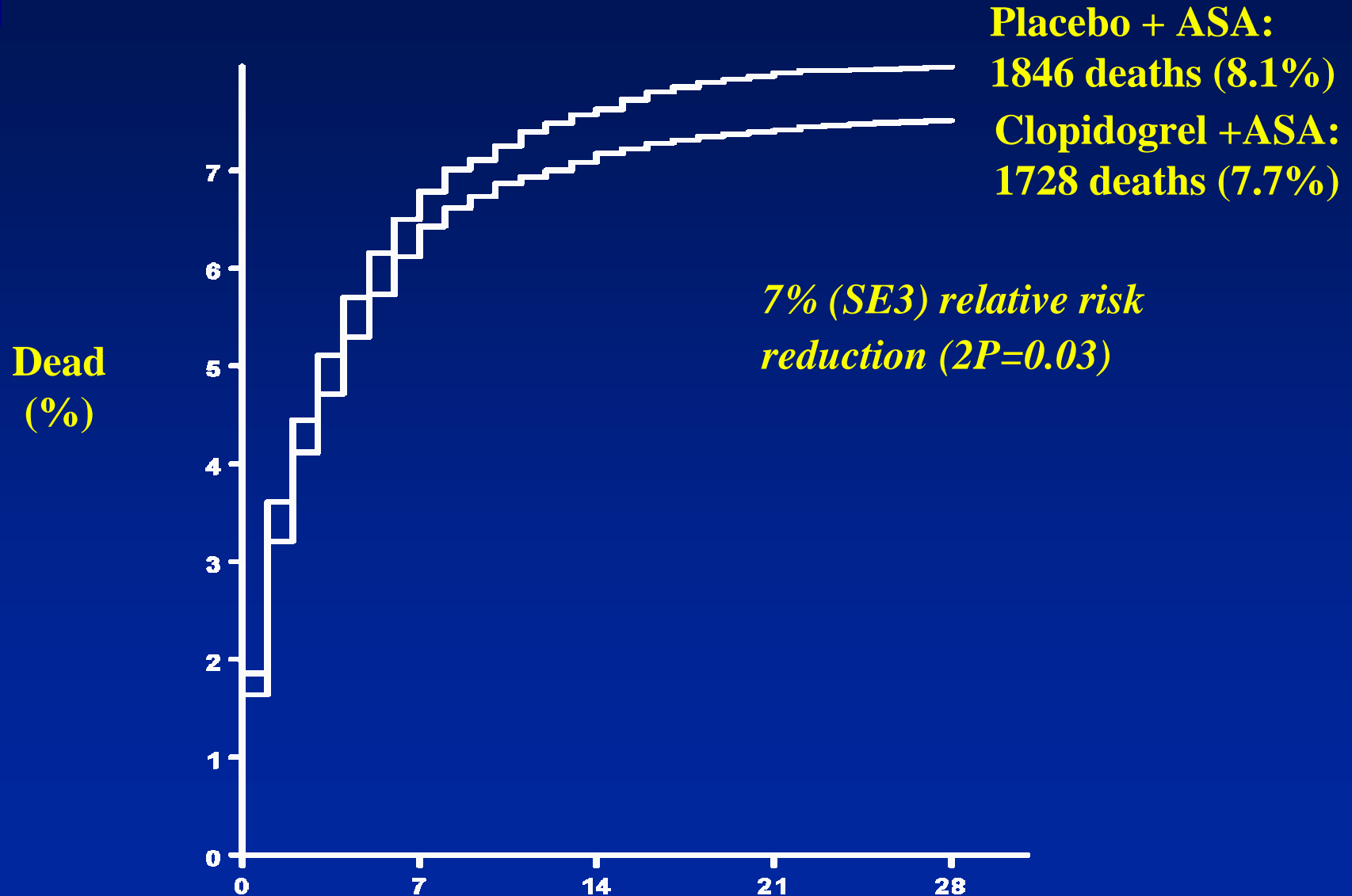
***COMMIT*: Study design**

- **TREATMENT:** Clopidogrel 75 mg daily vs placebo (aspirin 162mg daily in both groups)
- **INCLUSION:** Suspected acute MI (ST change or LBBB) within 24 h of symptom onset
- **EXCLUSION:** Primary PCI or high-risk of bleeding
- **1° OUTCOMES:** Death & death, re-MI or stroke up to 4 weeks in hospital (or prior discharge)

Mean treatment and follow-up: 16 days



COMMIT: Effect of CLOPIDOGREL on Death in Hospital





COMMIT: Major Bleed in Hospital

| Type | Clopidogrel (n=22,958) | Placebo (n=22,891) |
|-------------------|---------------------------|-----------------------|
| • Cerebral | | |
| Fatal | 39 | 40 |
| Non-fatal | 16 | 15 |
| • Non-cerebral | | |
| Fatal | 36 | 37 |
| Non-fatal | 46 | 36 |
| • Any major bleed | 134 (0.58%) | 124 (0.54%) |

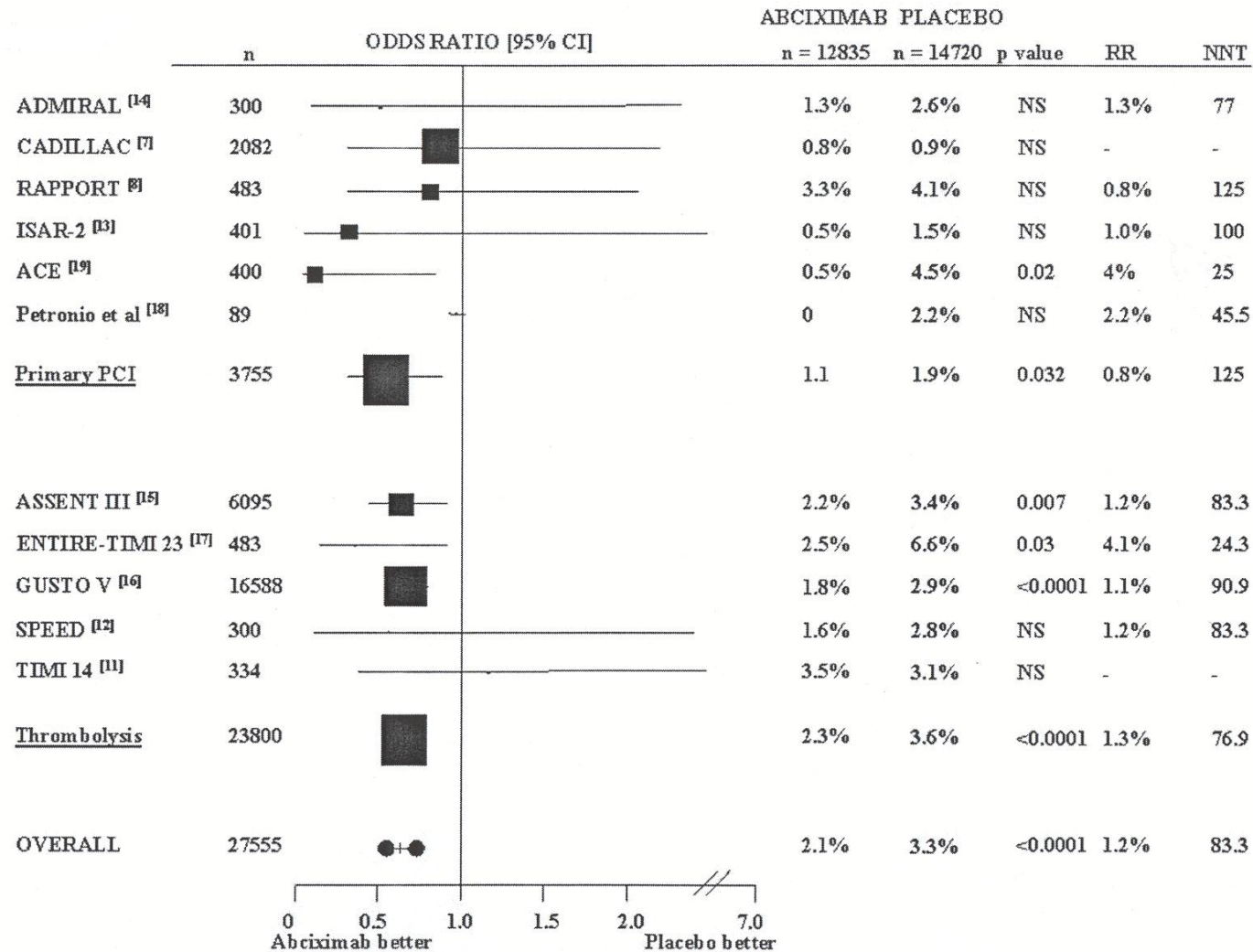


GP IIb/IIIa Antagonists

| Recommendations | Class I | IIa | IIb | III | Level of Evidence |
|--|---------|-----|-----|-----|-------------------|
| • Preferred treatment if performed by experienced team <90 min after first medical contact | X | | | | A |
| • Indicated for patients in shock and those with contraindications to fibrinolytic therapy | X | | | | C |
| • GP IIb/IIIa antagonists and primary PCI | | | | | |
| no stenting | X | | | | A |
| with stenting | | | X? | | A |

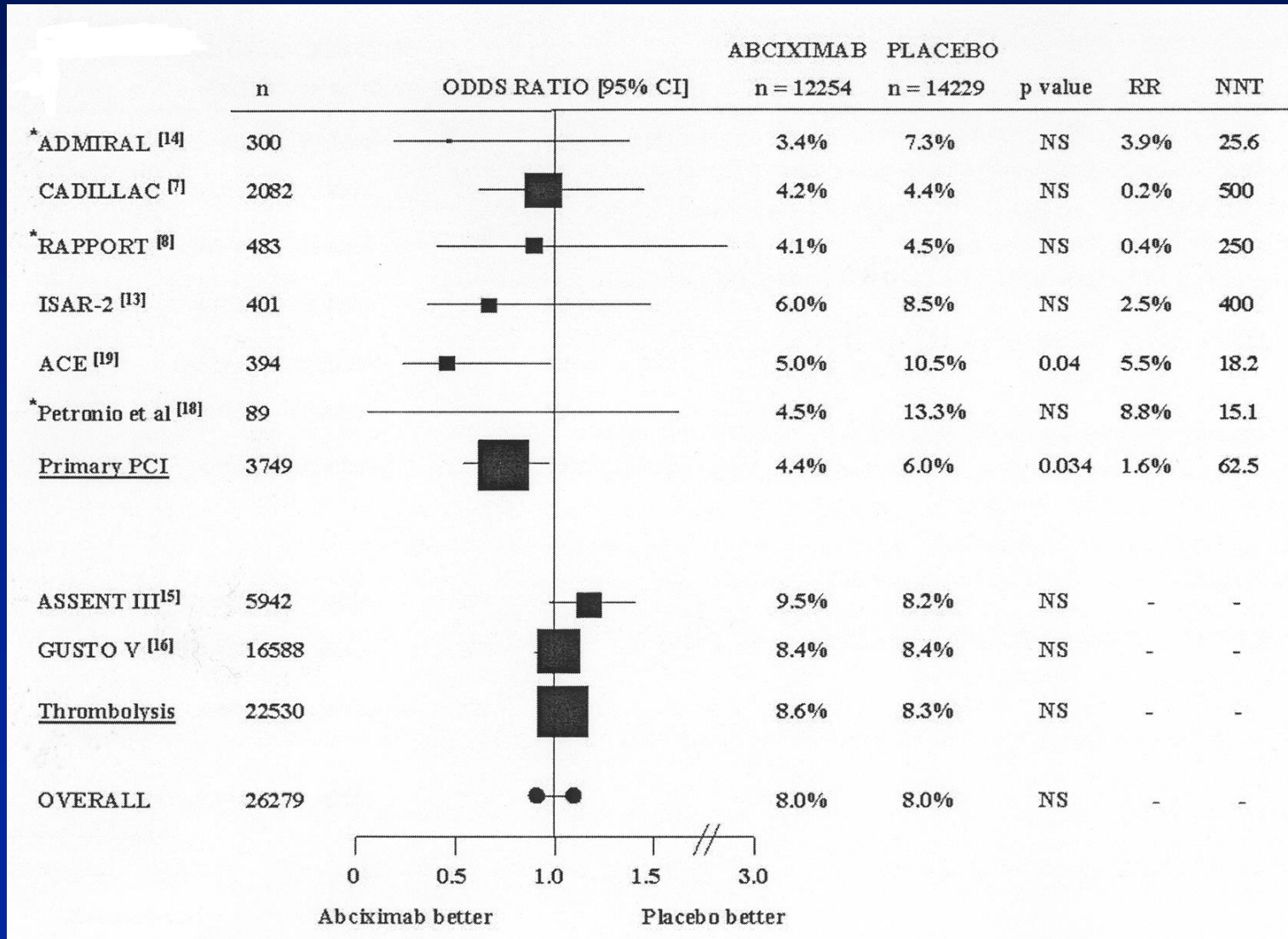


Abciximab vs. Placebo in STEMI: ReMI at 30 Days





Abciximab vs. Placebo in STEMI: 6 or 12 Month Mortality



* 6 Month





Antiplatelet Co-Therapy

- **GPIIb/IIIa antagonists in combination with half-dose lytic:**
 - **No short-term or long-term mortality reduction**
 - **Excess of bleeding complications especially in the elderly**
 - **Increased cost**
 - **As a pre-PCI strategy? Wait for **FINESSE****



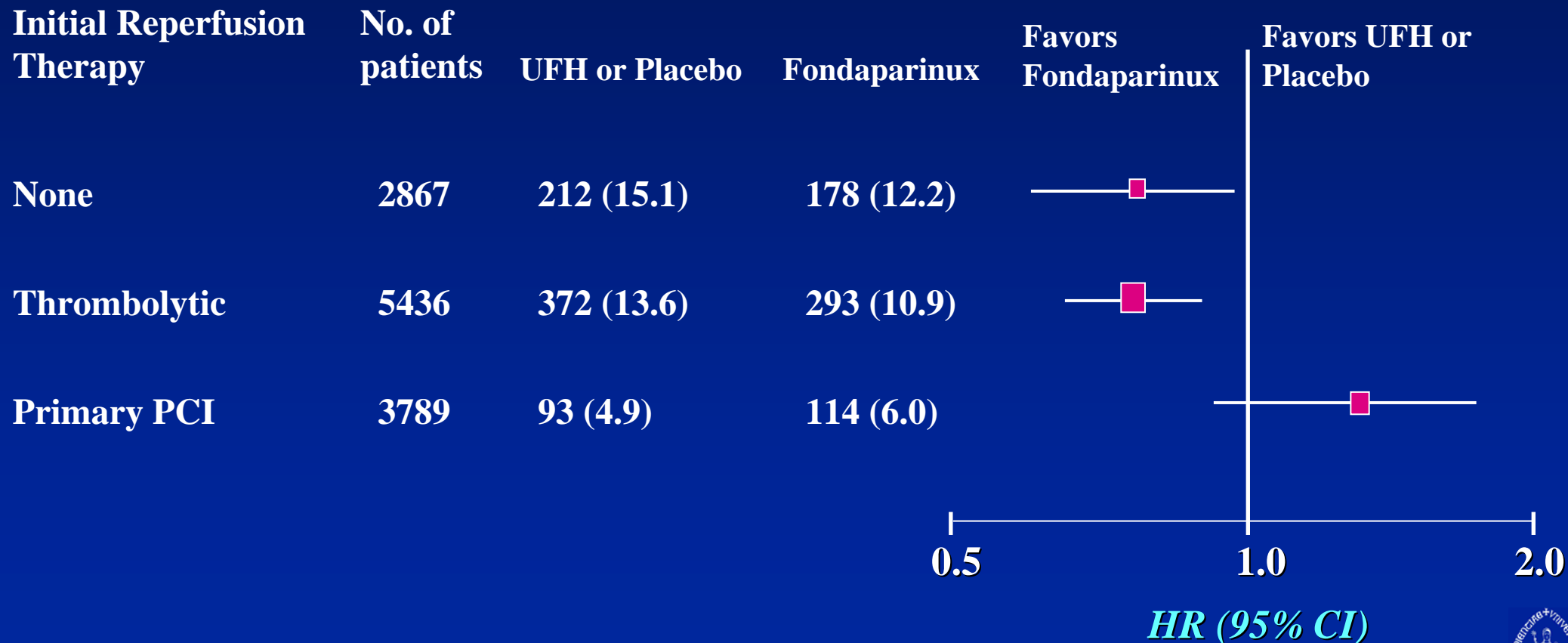
Antithrombin Co-Therapy

- A reduced, weight adjusted, dose of **UFH** with early (3h) aPTT monitoring
- **Fondaparinux**: important new data from **OASIS-6**
- **Enoxaparin**: important new data from **EXTRACT**
- Direct Antithrombins (eg. **bivalirudin**) not recommended (cfr HERO-2)



Rates of Death and reMI in Prespecified Subgroups at 30 Days

The OASIS-6 Trial Group*, JAMA 2006;295:1519-1530.





Protocol Design



**STEMI < 6 h
Lytic Eligible**

ASA

**Lytic Choice by MD
(TNK, tPA, rPA, SK)**

**Double-blind
Double-dummy**

Enoxaparin
< 75 y : 30 mg IV bolus
sc 1.0 mg/kg q 12 h (Hosp DC)
≥ 75 y : No bolus
sc 0.75 mg/kg q 12 h (Hosp DC)

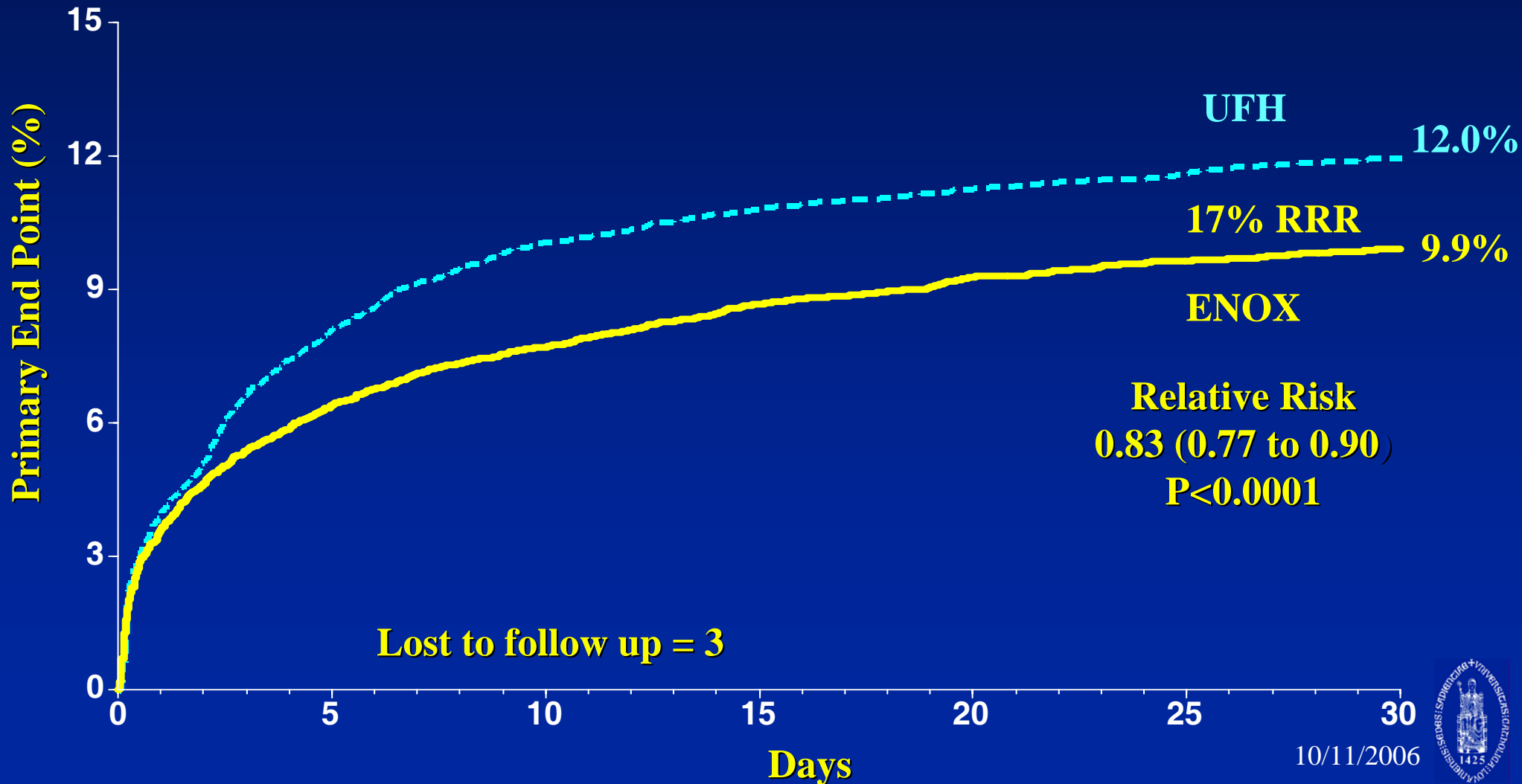
UFH
bolus 60 U/kg
Inf 12 U/kg/h for ≥ 48 h

Day 30
Primary Efficacy Endpoint: Death/MI
Primary Safety Endpoint: TIMI Major Haemorrhage

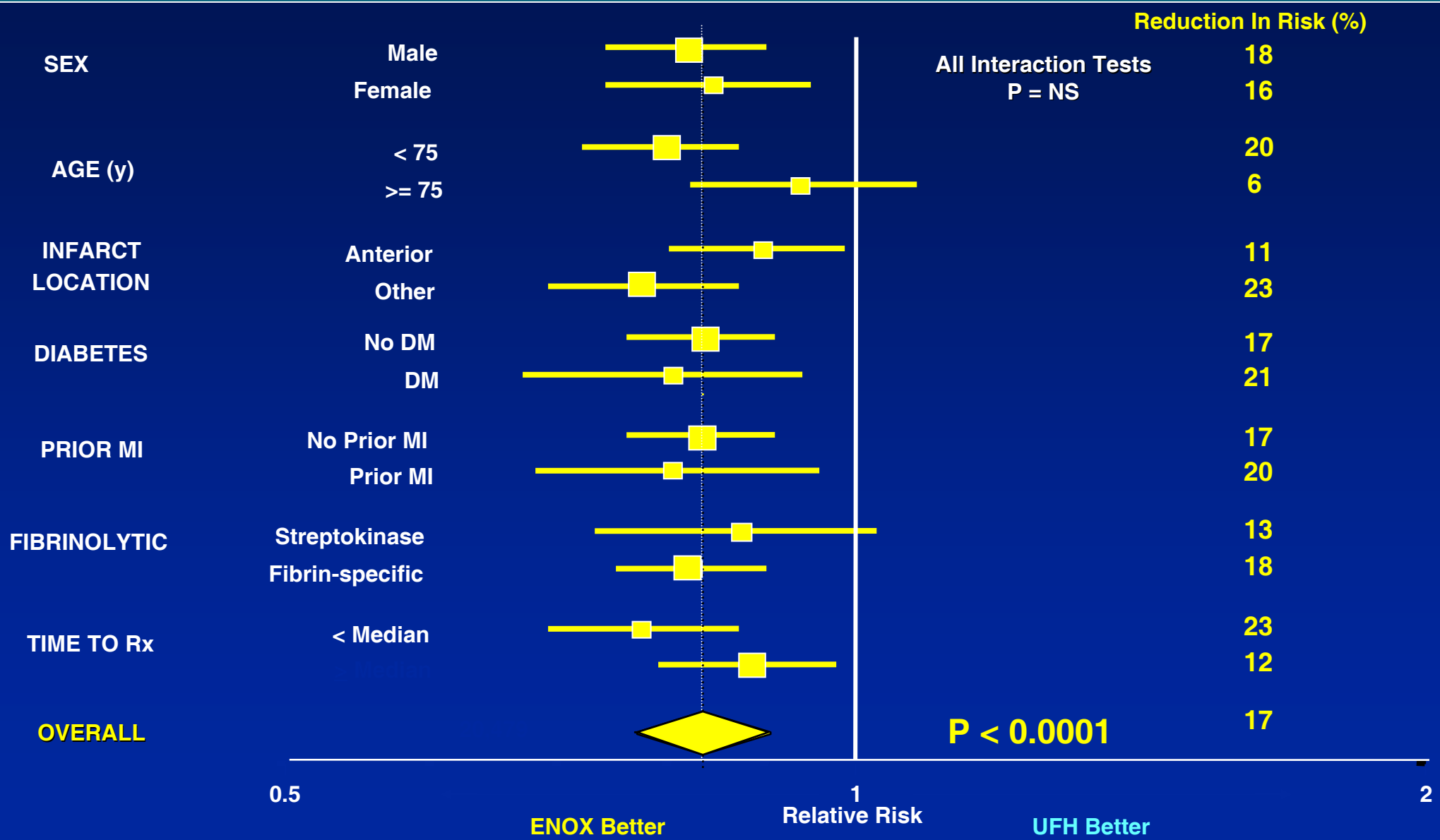




Primary End Point (ITT) Death or Nonfatal MI

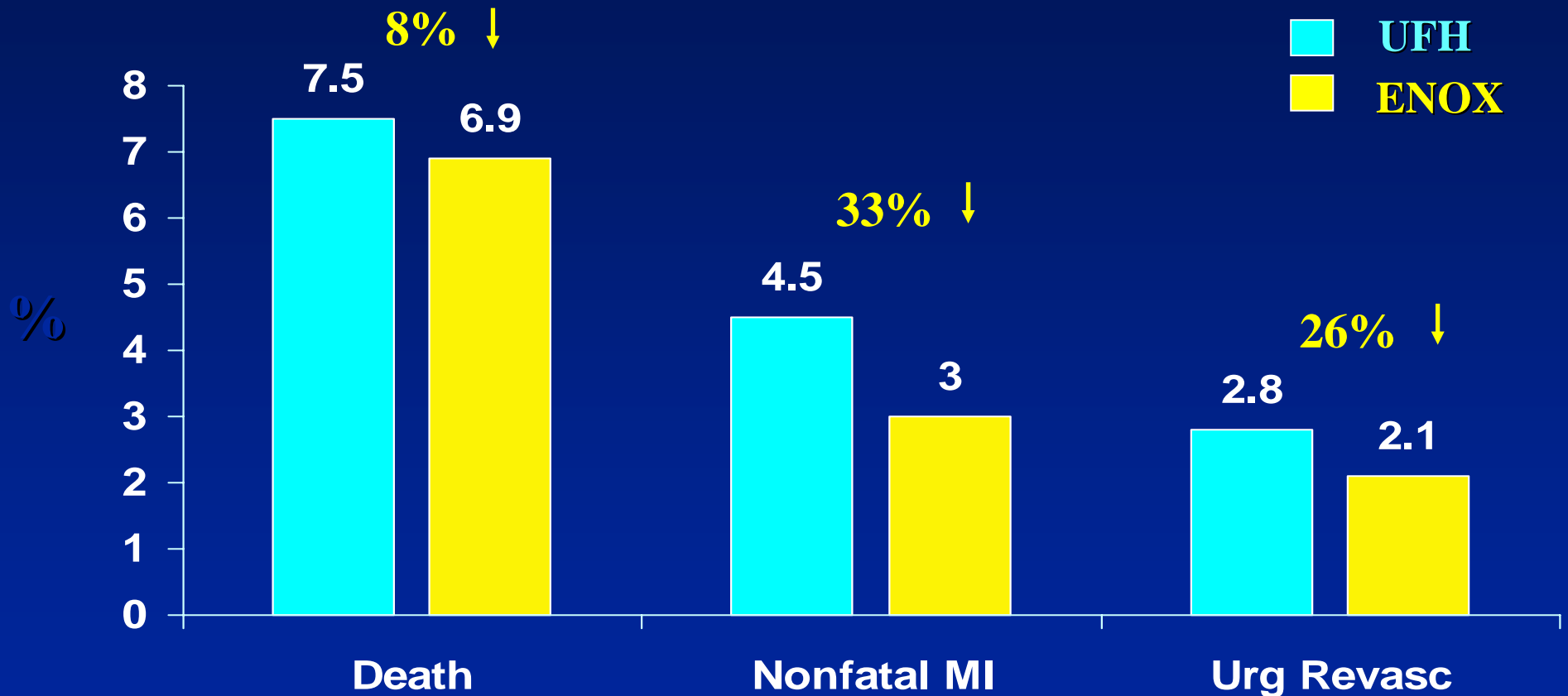


Death or Nonfatal MI - Day 30: Subgroups





EXTRACT: Outcomes at 30 Days (ITT)



RR

0.92

0.67

0.74

P value

0.11

<0.0001

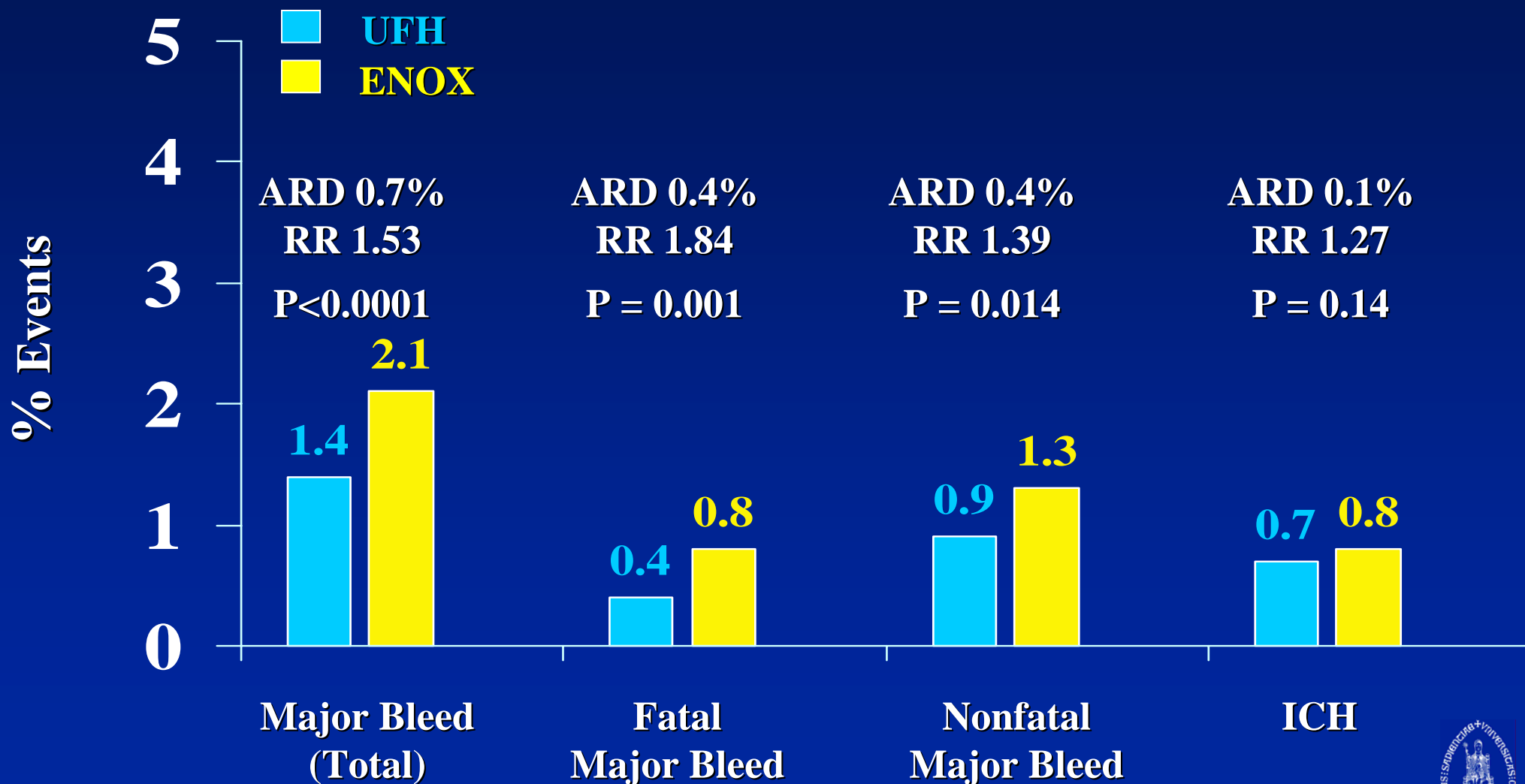
0.0008

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EXTRACT: Bleeding Endpoints (TIMI) 30 Days





Routine Prophylactic Therapies in Acute Phase

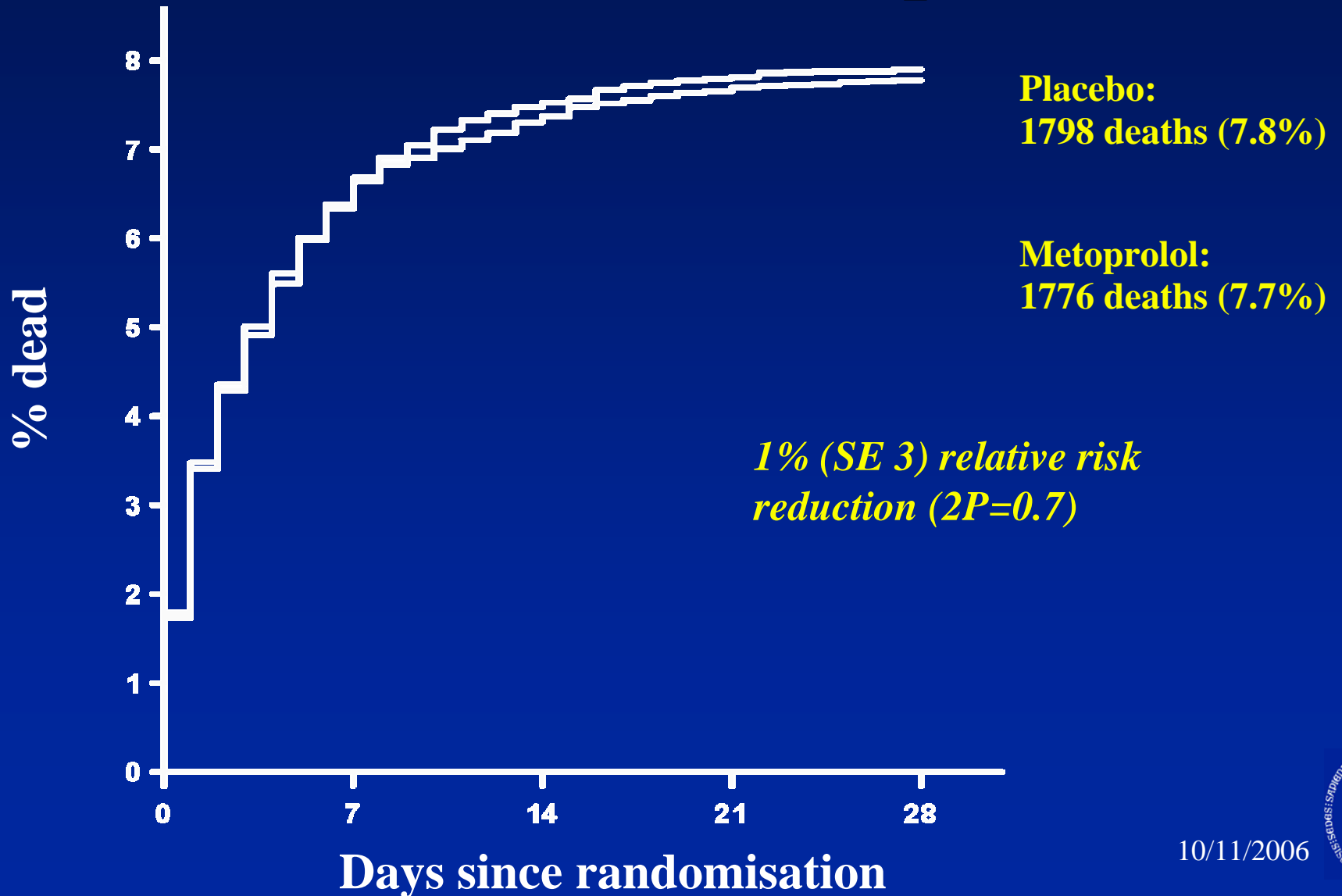
| Recommendations | Class I | IIa | IIb | III | Level of Evidence |
|--|---------|-----|-----|-----|-------------------|
| • Aspirin: 150-325 mg + Clopidogrel? | X | | | | A |
| • IV BB if no contraindication | | | X | | A |
| • ACEI: oral formulation on first day - to all patients if no contraindication - to high-risk patients ARB ? | X | X | | | A |
| • Nitrates | | | X | | A |
| • Calcium antagonists | | | | X | B |
| • Magnesium | | | | X | A |
| • Lidocaine | | | | X | B |

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COMMIT: Effects of METOPROLOL on Death in hospital





Routine Prophylactic Therapies in Acute Phase

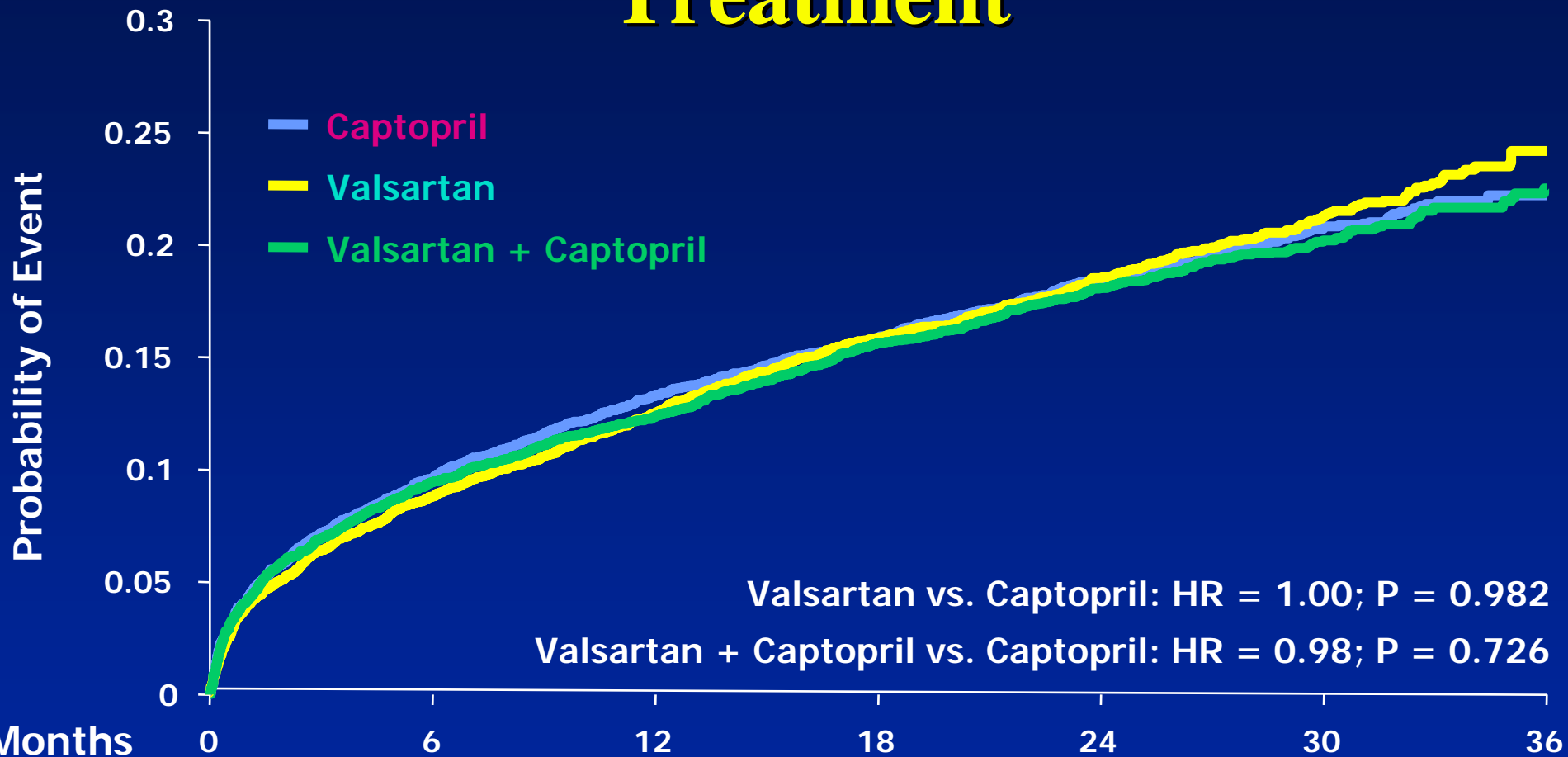
| Recommendations | Class I | IIa | IIb | III | Level of Evidence |
|--|---------|-----|-----|-----|-------------------|
| • Aspirin: 150-325 mg + Clopidogrel? | X | | | | A |
| • IV BB if no contraindication | | | X | | A |
| • ACEI: oral formulation on first day - to all patients if no contraindication - to high-risk patientsARB? | X | X | | | A A |
| • Nitrates | | | X | | A |
| • Calcium antagonists | | | | X | B |
| • Magnesium | | | | X | A |
| • Lidocaine | | | | X | B |

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VALIANT: 30 Day Mortality by Treatment



| | 0 | 6 | 12 | 18 | 24 | 30 | 36 |
|-----------------|------|------|------|------|------|------|-----|
| Captopril | 4909 | 4428 | 4241 | 4018 | 2635 | 1432 | 364 |
| Valsartan | 4909 | 4464 | 4272 | 4007 | 2648 | 1437 | 357 |
| Valsartan + Cap | 4885 | 4414 | 4265 | 3994 | 2648 | 1435 | 382 |



Secondary Prevention (1)

| Recommendations | Class I | IIa | IIb | III | Level of evidence |
|---|---------|-----|-----|-----|-------------------|
| • Stop smoking | X | | | | C |
| • Optimal glycaemic control | X | | | | B |
| • Blood pressure control | X | | | | C |
| • Mediterranean-type diet | X | | | | B |
| • Supplementation with 1 g fish oil n-3 poly-unsaturated fatty acids | X | | | | B |
| • Aspirin: 75 to 160 mg daily | X | | | | A |
| • If aspirin is not tolerated - clopidogrel (75 mg daily) - oral anticoagulant | | X | X | | C B |

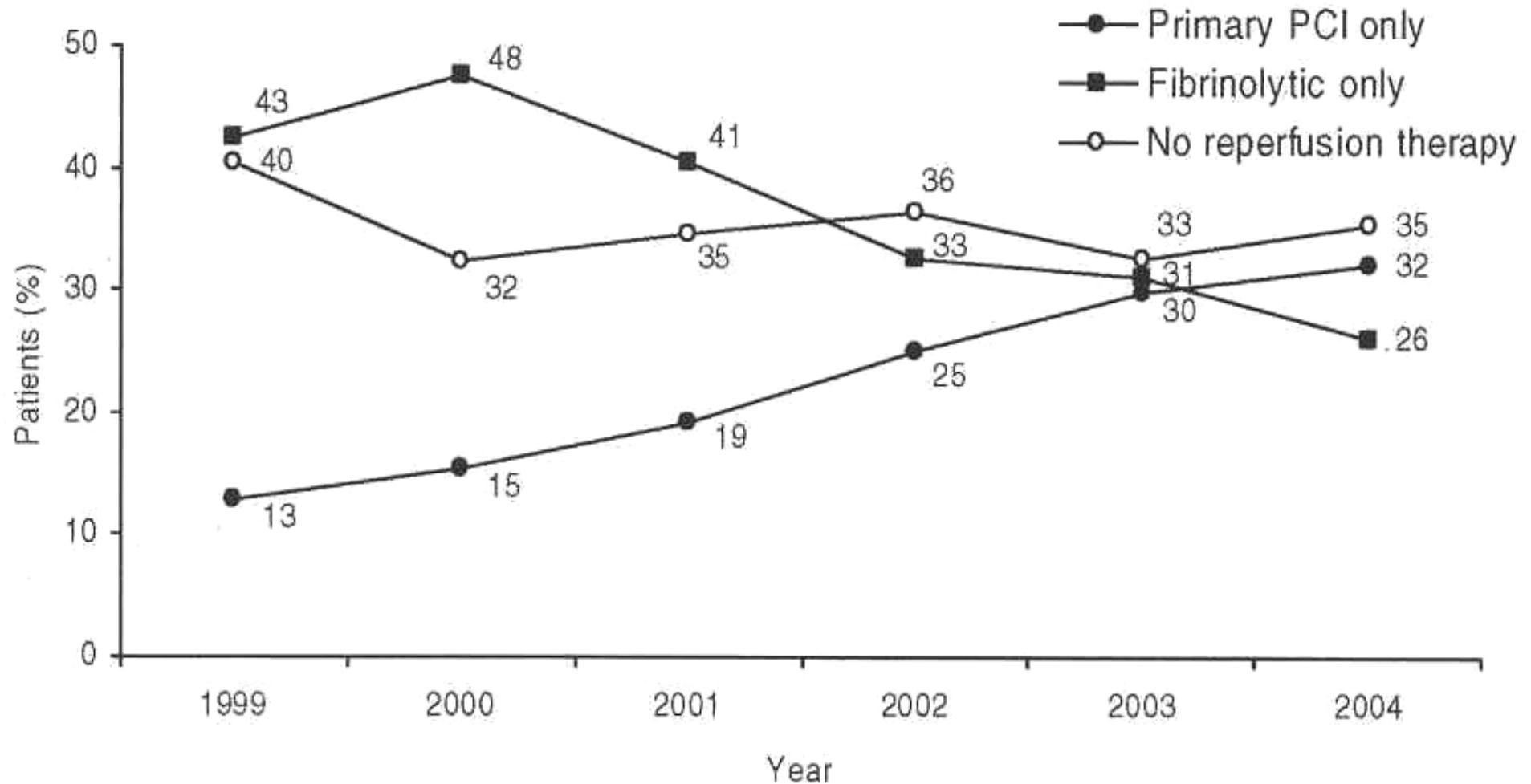


Secondary Prevention (2)

| Recommendations | Class I | IIa | IIb | III | Level of evidence |
|--|---------|-----|-----|-----|-------------------|
| • Oral BB if no contraindications | X | | | | A |
| • Continuation of ACEIor ARB (valsartan)? | X | | | | A |
| • Statins: if in spite of diet TC >190 mg/dl and/or LDL >115 mg/dl | X | | | | A |
| • Fibrates: if HDL cholesterol \leq 45 mg/dl and TG \geq 200 mg/dl | | X | | | A |
| • Calcium antagonists (diltiazem or verapamil) if contraindications to BB and no heart failure | | | X | | B |
| • Nitrates in the absence of angina | | | | X | A |



Use of Reperfusion Therapy (GRACE)





Reperfusion Therapy for STEMI (NRM1 2-4)

