

# **ESC Guidelines for the Management of Non-ST Segment Elevation Acute Coronary Syndromes**

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*ESC Guidelines for the Management of NSTEMI-ACS (1)*




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ESC Guidelines

 † **Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes**

**The Task Force for the Diagnosis and Treatment of Non-ST-Segment Elevation Acute Coronary Syndromes of the European Society of Cardiology**

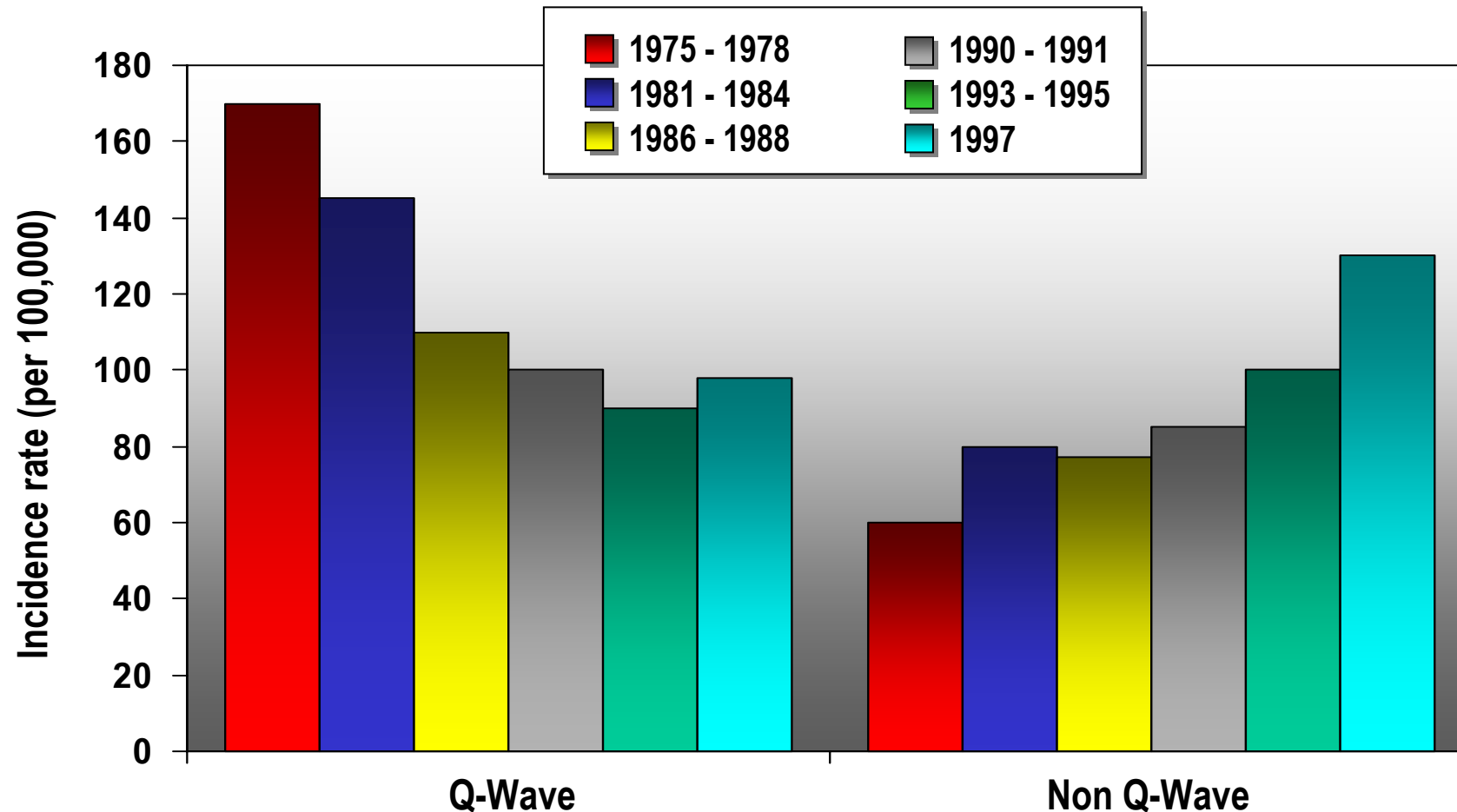
Authors/Task Force Members, Jean-Pierre Bassand\* (Chair) (France), Christian W. Hamm\* (Co-Chair) (Germany), Diego Ardissino (Italy), Eric Boersma (The Netherlands), Andrzej Budaj (Poland), David Hasdai (Israel), Francisco Fernandez-Aviles (Spain), Keith A.A. Fox (UK), Eric Magnus Ohman (USA), Lars Wallentin (Sweden), William Wijns (Belgium)

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# Trends and Prognosis in NSTEMI-ACS



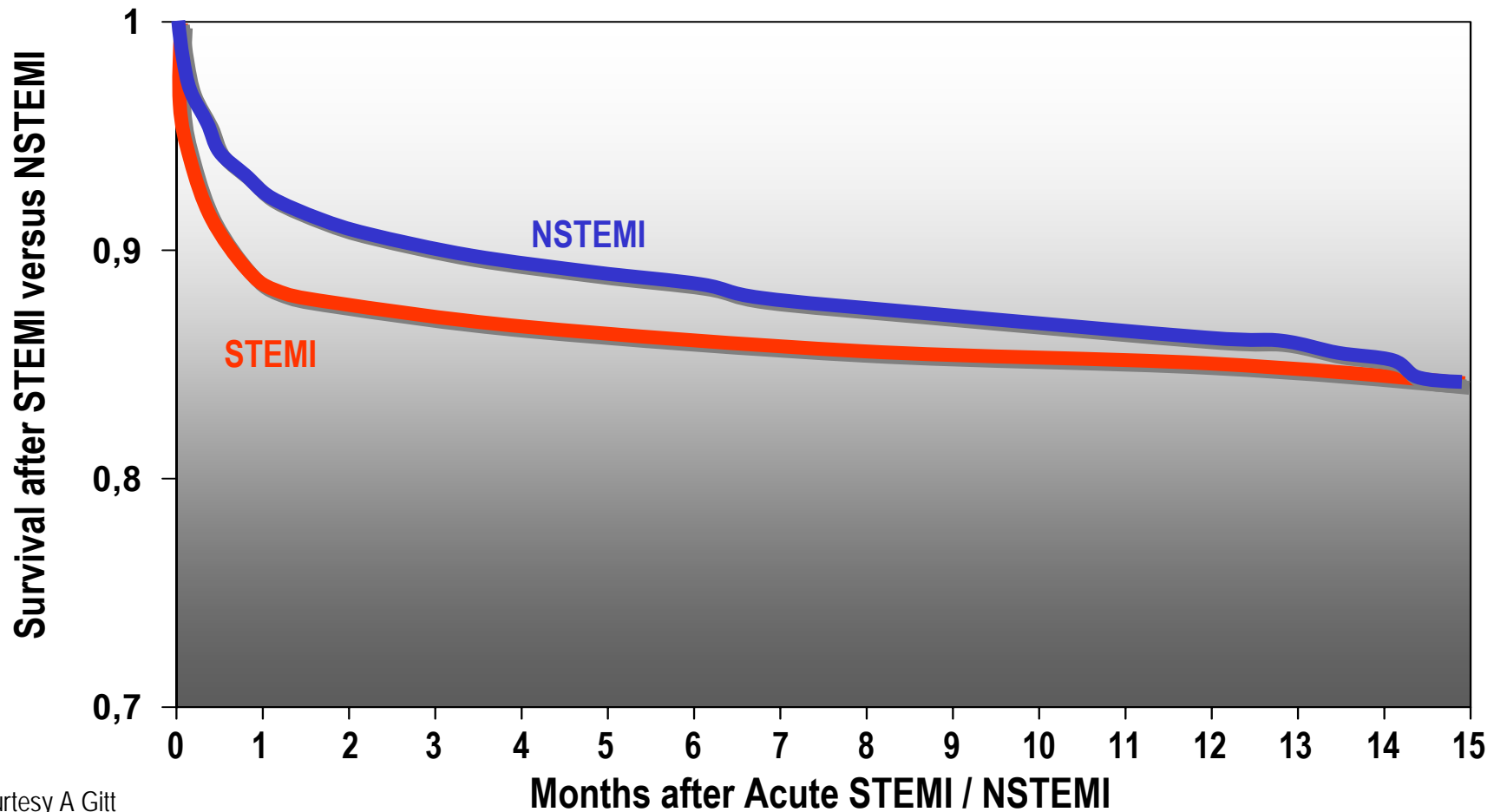
Furman MI. et al JACC 2001; 37: 1571-80

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# Trends and Prognosis in NSTEMI-ACS

## STEMI versus NSTEMI - Cumulative 1 Year Mortality



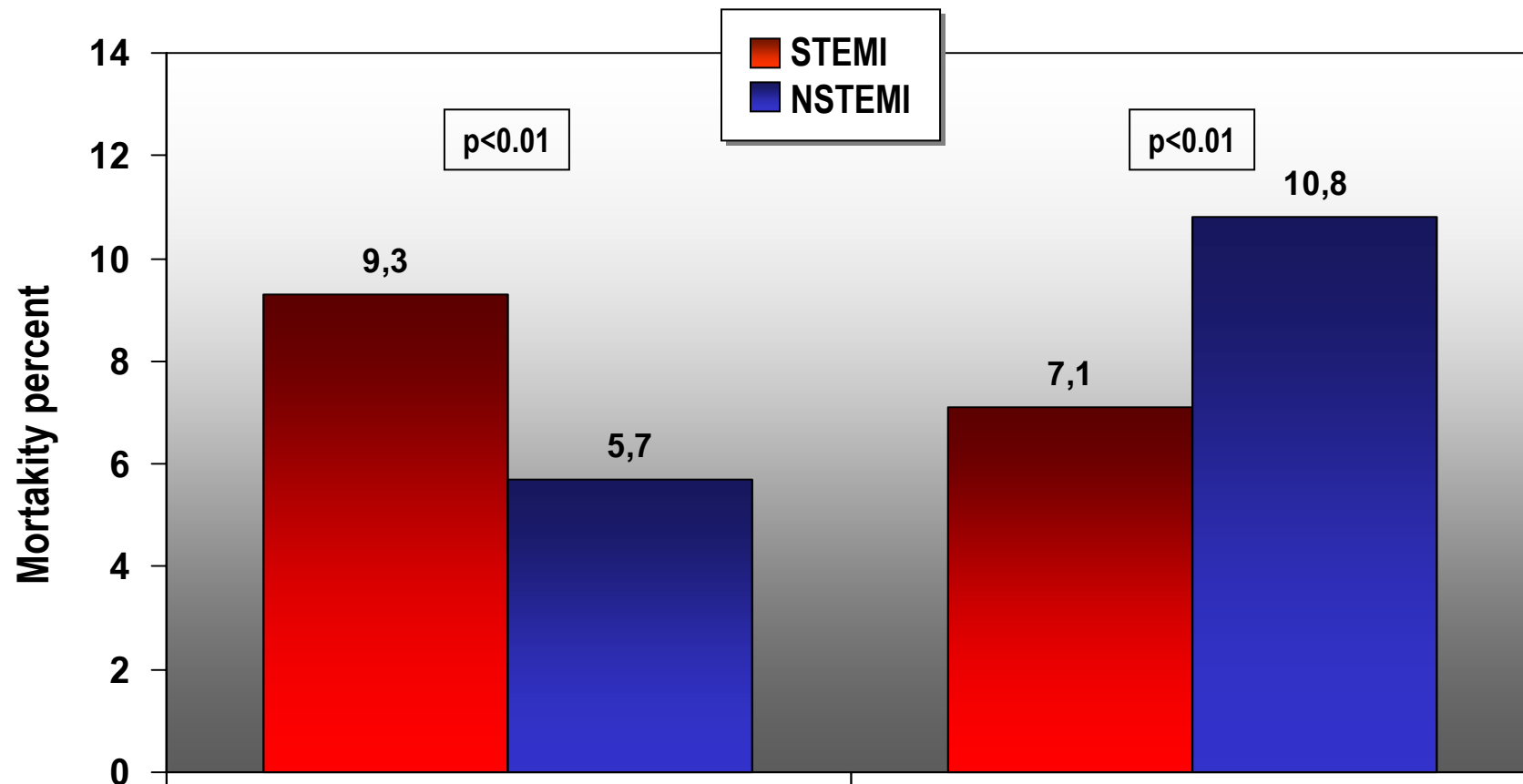
Courtesy A Gitt

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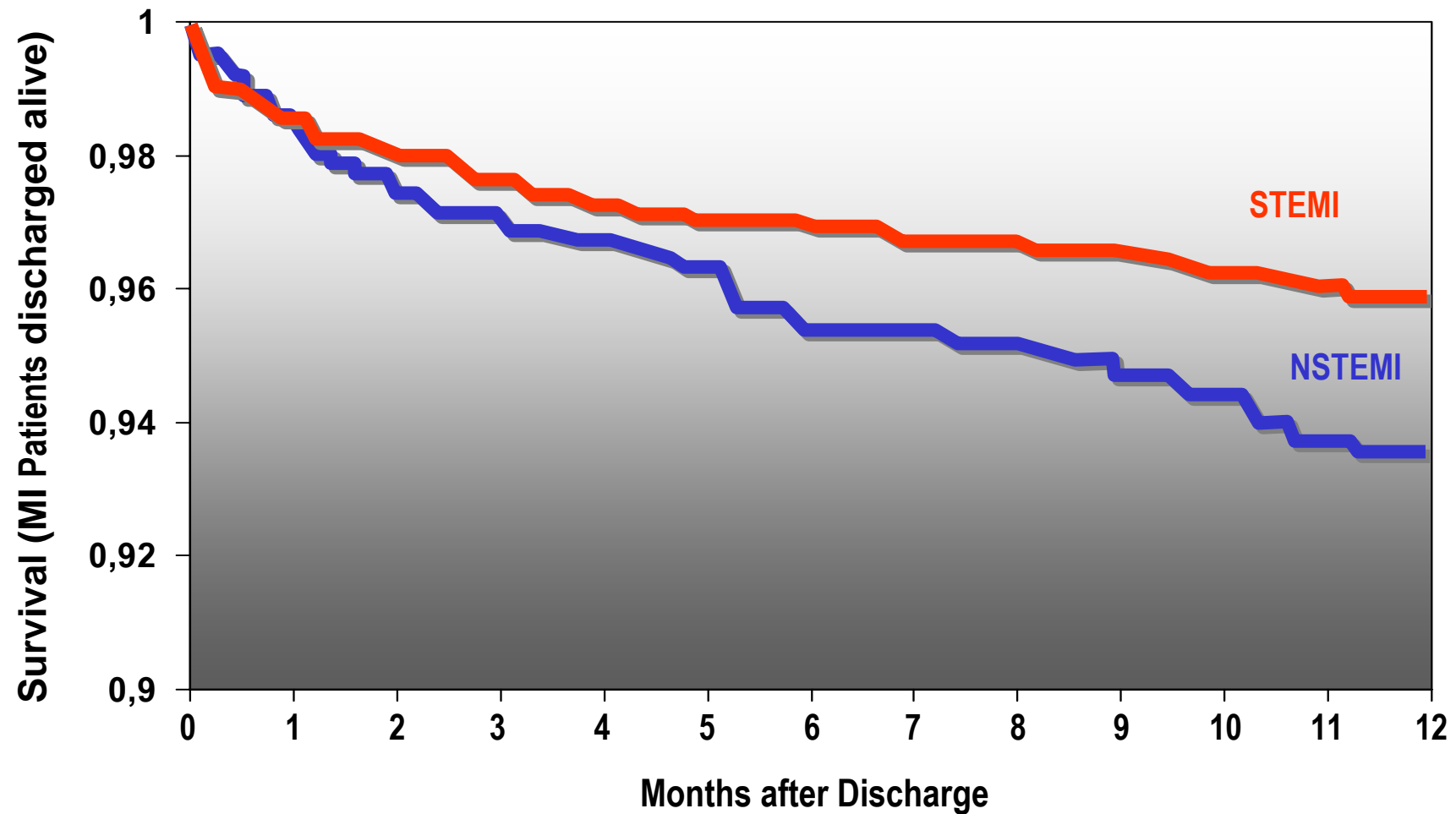
# STEMI versus NSTEMI

## *Hospital vs 1-Year-Mortality*



# STEMI versus NSTEMI

## *Mortality after Discharge*



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# Methods

# Methods

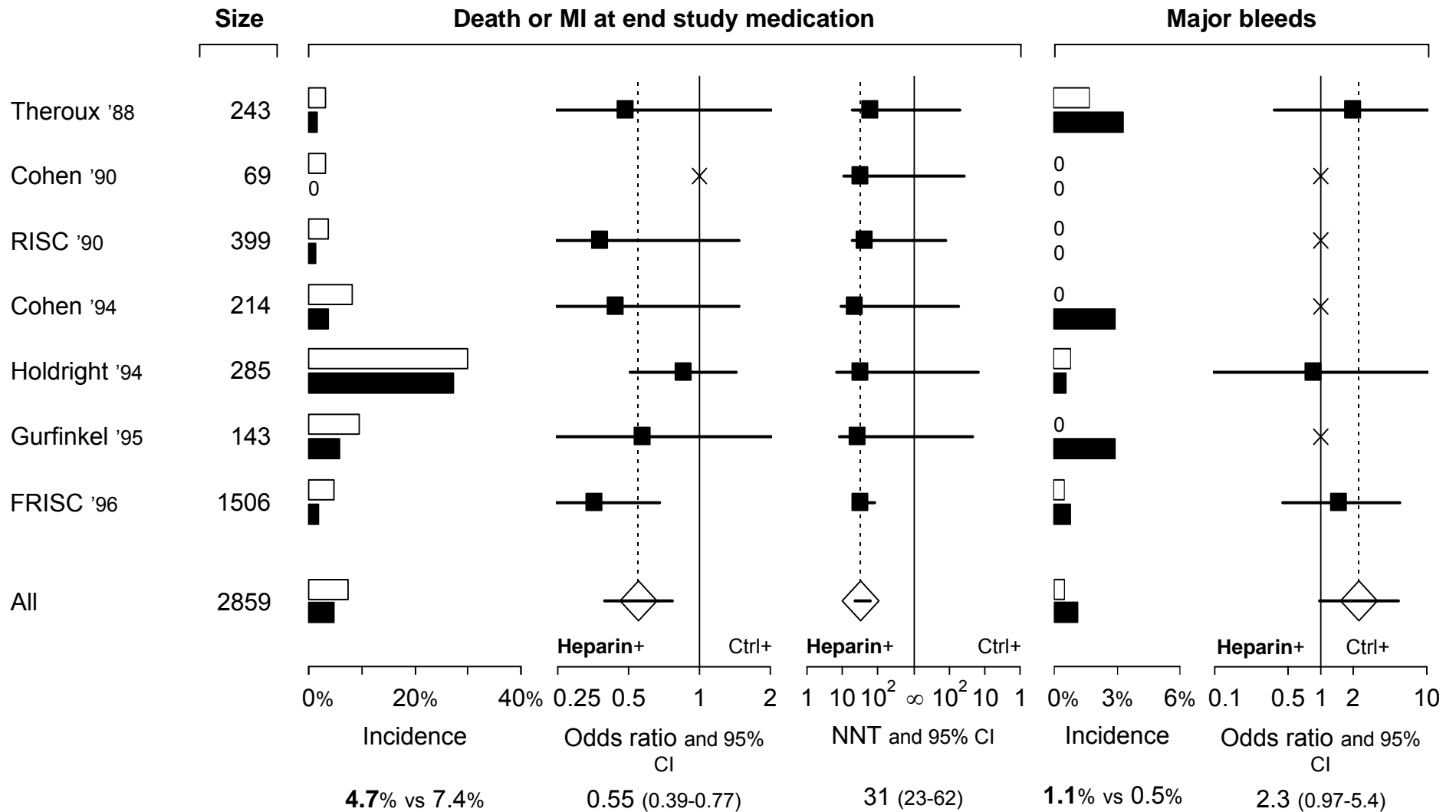
## 1- Cost/benefit and cost/risk ratios in the terms of

- Number Needed to Treat

## 2 - Class III re-introduced in the level of recommendations

- Class III = contra-indication (it goes without saying, but it's better to say it !)

# Randomized trials of UFH/LMWH (dark bars) vs Control (open bars)



# Methods

1- Cost/benefit and cost/risk ratios in the form of

- Number Needed to Treat

2 - **Class III re-introduced** in the level of recommendations

- **Class III = contra-indication (it goes without saying, but it's better in saying !)**

# Methods

## 3- Quality level of trials taken into account

- Double blind, randomised design
- Use of hard endpoints in the primary endpoint
  - death and MI
  - death / MI / stroke and bleeding as net clinical benefit
- Adequate sample size calculations
- Contemporary adjunctive treatments (stents, clopidogrel, IIb/IIIa inhibitors...)

## 4- Efficacy / safety profile of drugs / treatments taken into account for the gradation of recommendations

# Classes of Recommendations

<b>Class I</b>	<b>Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective</b>
<b>Class II</b>	<b>Conflicting evidence and/or a divergence of opinion about the usefulness / efficacy of the given treatment or procedure</b>
<b>Class IIa</b>	<b>Weight of evidence / opinion is in favour of usefulness / efficacy</b>
<b>Class IIb</b>	<b>Usefulness / efficacy is less well established by evidence / opinion</b>
<b>Class III</b>	<b>Evidence or general agreement that the given treatment or procedure is not useful / effective, and in some cases may be harmful.</b>

# Levels of Evidence

<b>Level of Evidence A</b>	<b>Data derived from multiple randomized clinical trials or meta-analyses.</b>
<b>Level of Evidence B</b>	<b>Data derived from a single randomized clinical trial or large non-randomized studies.</b>
<b>Level of Evidence C</b>	<b>Consensus of opinion of the experts and/or small studies, retrospective studies, registries.</b>

# Table of Contents (1)

- **Epidemiology and Natural History**
- **Pathophysiology**
- **Diagnosis & Risk Assessment**
- **Treatment**
  - **Anti-ischaemic agents**
  - **Anti-coagulants**
  - **Anti-platelet agents**
  - **Resistance to antiplatelet agents/drug interactions**
  - **Withdrawal of antiplatelet agents**
  - **Coronary revascularisation**
  - **Long-term management and rehabilitation**

# Table of Contents (2)

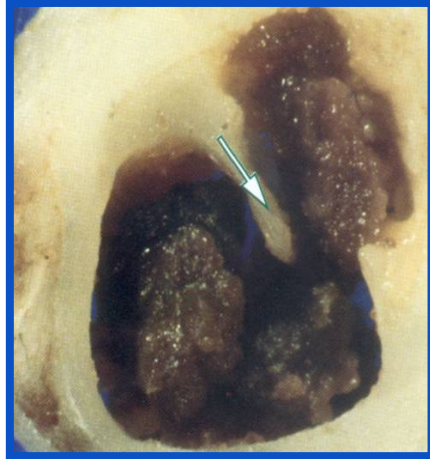
- **Complications and their management**
  - Bleeding
  - Thrombocytopenia
- **Special Conditions & Populations**
  - Elderly
  - Diabetes
  - Impact of Gender
  - Anaemia
  - Chronic Kidney Disease
- **Management Strategy**
- **Performance Measures**

# Pathophysiology

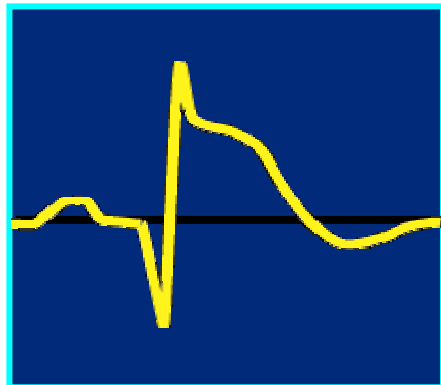
*ESC Guidelines for the Management of NSTEMI-ACS (17)*



## ACS with persistent ST-segment elevation



Adapted from Michael Davies

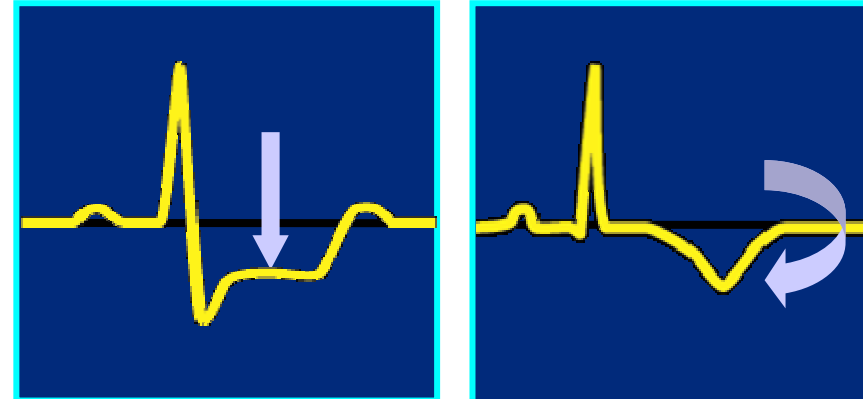


Troponin elevated

## ACS without persistent ST-segment elevation



Adapted from Michael Davies



Troponins elevated or not

# Diagnosis & Risk Assessment

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# Chest Pain

Admission

Working diagnosis

ECG

Bio-chemistry

Risk stratification

Diagnosis

Treatment

Suspicion of **Acute Coronary Syndrome**

Persistent ST – elevation

ST/T – Abnormalities

Normal or Undetermined ECG

Troponin positive

Troponin 2 x negative

*High Risk*

*Low Risk*

STEMI

**NSTEMI**

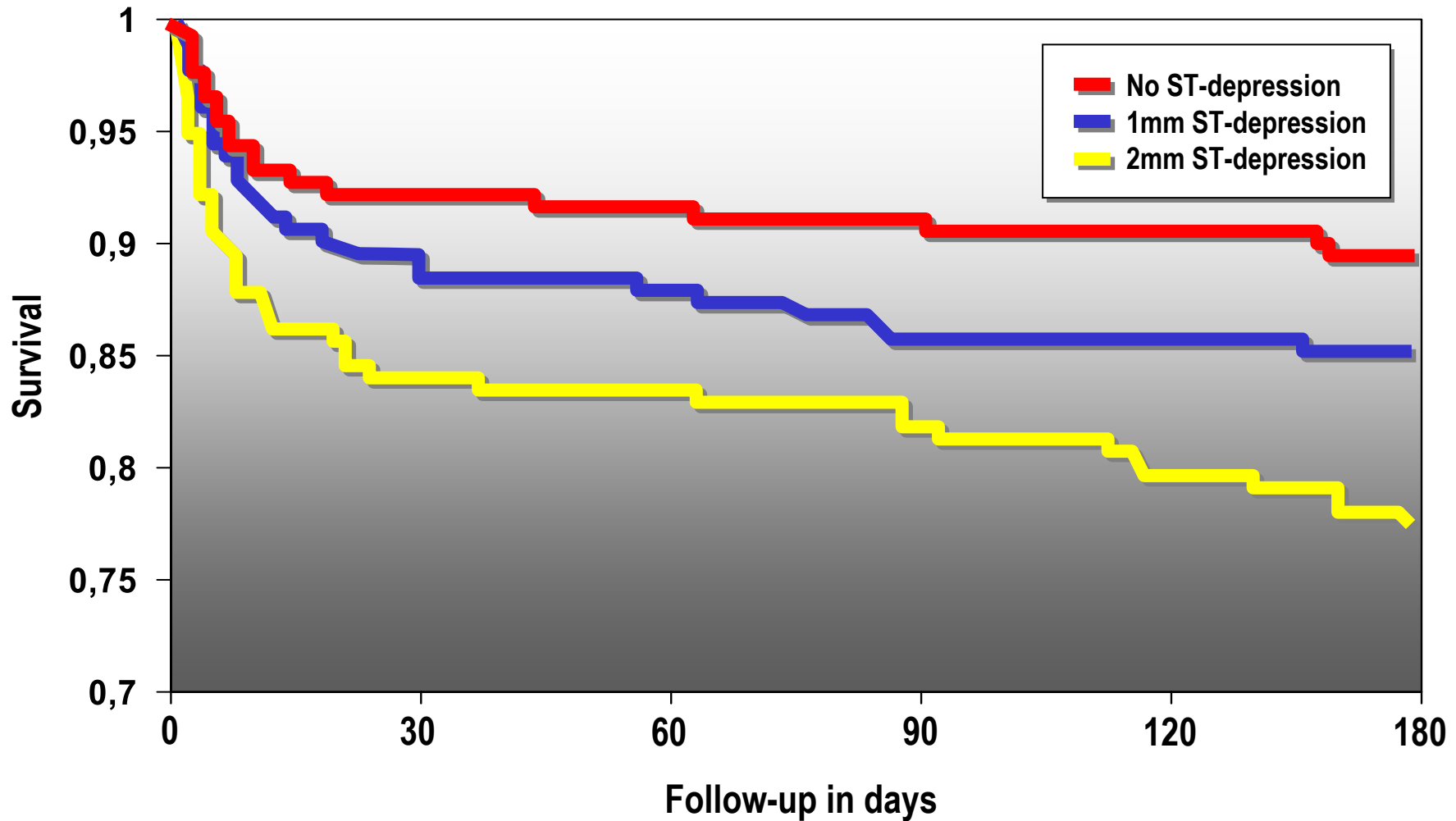
**Unstable Angina**

Reperfusion

Invasive

Non-invasive

# Predictive Value of ST Depression

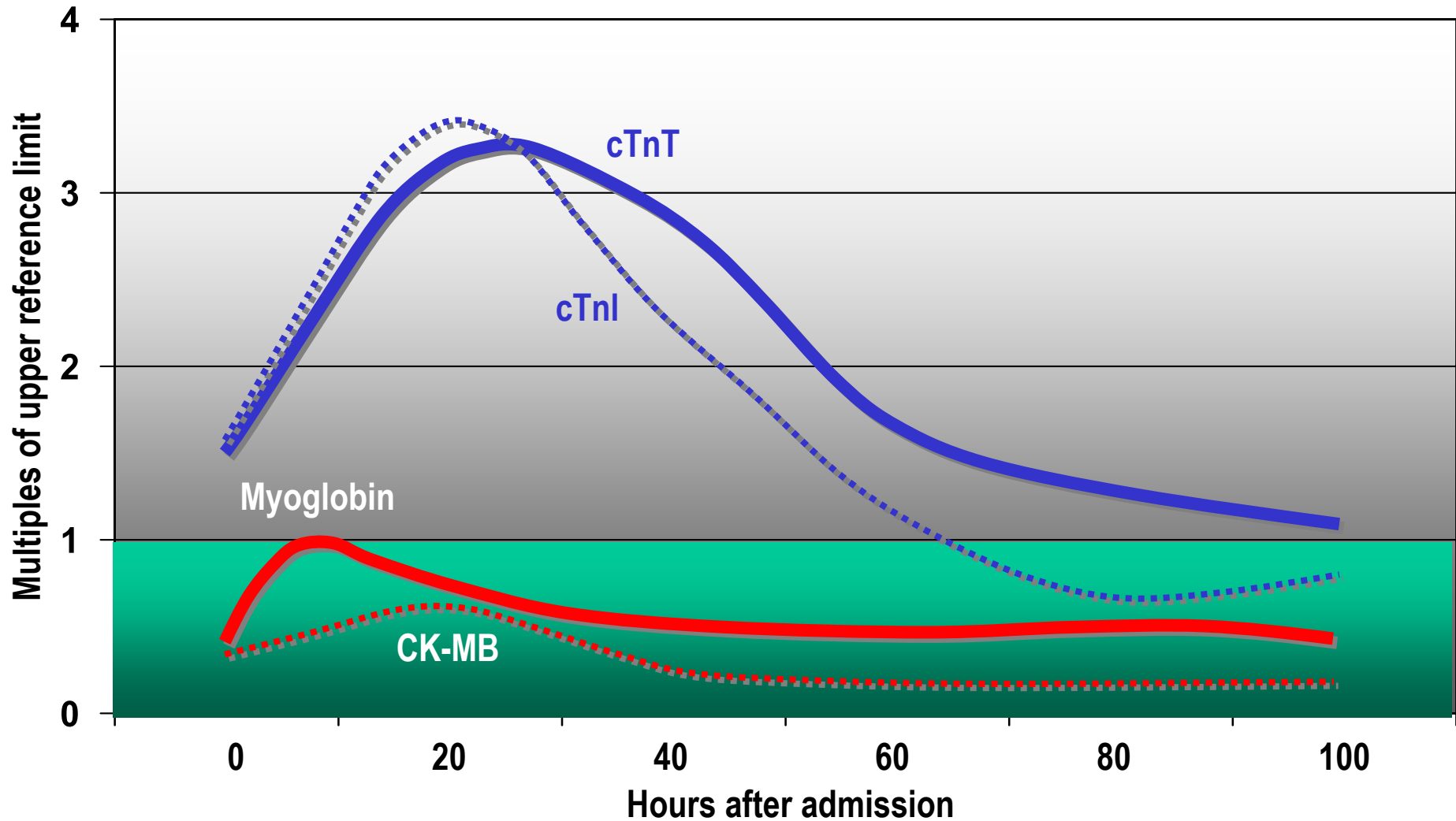


Kaul et al. PARAGON Study. JACC 2003

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## Example of Release of Cardiac Markers in a Patient with NSTEMI-ACS (Shaded Area Indicates Normal Range).



# Non-coronary Conditions with Troponin Elevation

- Severe congestive heart failure – acute and chronic
- Aortic dissection, aortic valve disease or hypertrophic cardiomyopathy
- Cardiac contusion, ablation, pacing, cardioversion, or endomyocardial biopsy
- Inflammatory diseases, e.g., myocarditis, or myocardial extension of endo-/pericarditis
- Hypertensive crisis
- Tachy- or bradyarrhythmias
- Pulmonary embolism, severe pulmonary hypertension
- Hypothyroidism
- .../...

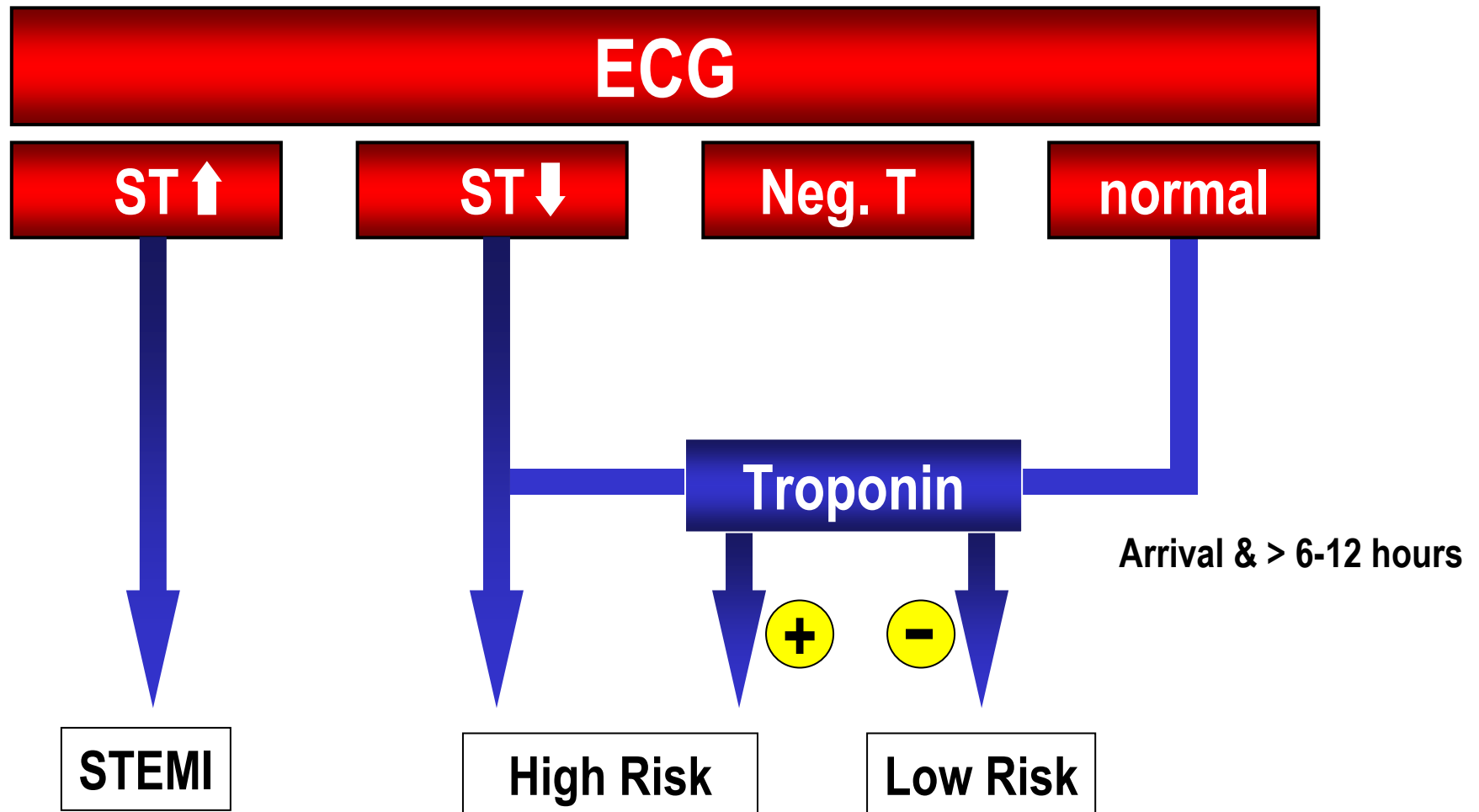
# Non-coronary Conditions with Troponin Elevation

- .../...
- **Apical ballooning syndrome**
- **Chronic or acute renal dysfunction**
- **Acute neurological disease, including stroke, or subarachnoid haemorrhage**
- **Infiltrative diseases, e.g., amyloidosis, haemochromatosis, sarcoidosis, scleroderma**
- **Drug toxicity, e.g., adriamycin, 5-fluorouracil, herceptin, snake venoms**
- **Burns, if affecting >30% of body surface area**
- **Rhabdomyolysis**
- **Critically ill patients, especially with respiratory failure, or sepsis**

# Cardiac and non cardiac conditions that can mimic NSTEMI-ACS

Cardiac	Pulmonary	Haematological	Vascular	Gastro-intestinal	Orthopedic
Myocarditis Pericarditis Myopericarditis Cardiomyopathy Valvular disease Apical ballooning (Tako-Tsubo syndrome)	Pulmonary embolism Pulmonary infarction Pneumonia Pleuritis Pneumothorax	Sickle cell anaemia	Aortic dissection Aortic aneurysm Aortic coarctation Cerebrovascular disease	Esophageal spasm Esophagitis Peptic ulcer Pancreatitis Cholecystitis	Cervical discopathy Rib fracture Muscle injury/inflammation Costochondritis

# ACS Initial Decision-making Algorithm



# Recommendations for Diagnosis and Risk Stratification (1)

- **Diagnosis and short-term risk stratification of NSTEMI-ACS should be based on a combination of clinical history, symptoms, ECG, biomarkers and risk score results (I-B).**

# GRACE ACS Risk Model

The screenshot shows the GRACE ACS Risk Model calculator interface. At the top, the logo for GRACE (Global Registry of Acute Coronary Events) is displayed next to the title 'ACS Risk Model'. Below the title, there are two tabs: 'At Admission (in-hospital/to 6 months)' and 'At Discharge (to 6 months)'. The 'At Admission' tab is active. The interface includes input fields for Age (Years), HR (bpm), SBP (mmHg), Creat. (µmol/l), and CHF (Killip Class). There are also checkboxes for 'Cardiac arrest at admission', 'ST-segment deviation', and 'Elevated cardiac enzymes/markers'. A table shows the 'Probability of' 'Death' and 'Death or MI' for 'In-hospital' and 'To 6 months' periods. The table cells contain dashes. At the bottom, there are buttons for 'US Units' and 'Reset'. A footer bar contains links for 'Calculator', 'Instructions', 'GRACE Info', 'References', and 'Disclaimer'.

**GRACE** ACS Risk Model  
Global Registry of Acute Coronary Events

At Admission (in-hospital/to 6 months) | At Discharge (to 6 months)

Age:

HR:

SBP:

Creat.:

CHF:

Cardiac arrest at admission  
 ST-segment deviation  
 Elevated cardiac enzymes/markers

Probability of	Death	Death or MI
In-hospital	--	--
To 6 months	--	--

Calculator | Instructions | GRACE Info | References | Disclaimer

**Mortality in hospital and at 6 months in low, intermediate and high risk categories in registry populations according to the GRACE Risk score <http://www.outcomes.org/grace>**

<b>Risk category (tertiles)</b>	<b>GRACE Risk Score</b>	<b>In-hospital deaths (%)</b>
<b>Low</b>	<b>≤108</b>	<b>&lt;1</b>
<b>Intermediate</b>	<b>109-140</b>	<b>1-3</b>
<b>High</b>	<b>&gt;140</b>	<b>&gt;3</b>
<b>Risk category (tertiles)</b>	<b>GRACE Risk Score</b>	<b>Post-discharge to 6 months deaths (%)</b>
<b>Low</b>	<b>≤88</b>	<b>&lt;3</b>
<b>Intermediate</b>	<b>89-118</b>	<b>3-8</b>
<b>High</b>	<b>&gt;118</b>	<b>&gt;8</b>

# Recommendations for Diagnosis and Risk Stratification (2)

- The evaluation of the individual risk is a dynamic process that is to be updated as the clinical situation evolves.
  - A 12-lead ECG should be obtained within 10 minutes after first medical contact and immediately read by an experienced physician. (I-C) Additional leads (V3<sub>R</sub> and V4<sub>R</sub>, V7-V9) should be recorded. ECG should be repeated in case of recurrence of symptoms, and at 6, 24 hours and before hospital discharge (I-C).
  - Blood must be drawn promptly for troponin (cTnT or cTnI) measurement. The result should be available within 60 minutes. (I-C) The test should be repeated after 6-12 hours if the initial test is negative (I-A).
  - .../...

# Recommendations for Diagnosis and Risk Stratification (3)

- The evaluation of the individual risk is a dynamic process that is to be updated as the clinical situation evolves.
  - .../...
  - Established risk scores (such as GRACE) should be implemented for initial and subsequent risk assessment (I-B)
  - An echocardiogram is recommended to rule out differential diagnoses (I-C).
  - In patients without recurrence of pain, normal ECG findings, and negative troponins tests, a non-invasive stress test for inducible ischaemia is recommended before discharge (I-A).

## Recommendations for Diagnosis and Risk stratification (4)

### Long Term Risk

- The following predictors of long-term death or MI should be considered in risk stratification (I-B):
  - Clinical indicators: age, heart rate, blood pressure, Killip class, diabetes, previous MI/CAD
  - ECG markers: ST-segment depression
  - Laboratory markers: troponins, GFR/ CrCl/ Cystatin C, BNP/NT-proBNP, hsCRP
  - Imaging findings: low ejection fraction, main stem lesion, 3- vessel disease.
  - Risk score result

# Treatment

# Therapeutic Options

- **Anti-ischæmic agents**
- **Anti-coagulants**
  - UFH or LMWHs
  - Fondaparinux
  - Bivalirudin
- **Anti-platelet agents**
  - ASA
  - Clopidogrel
  - IIb/IIIa Inhibitors
- **Revascularisation**

# Treatment



## Anti-ischaemic agents

# Recommendations for Anti-ischaemic Drugs

- **Beta-blockers are recommended in the absence of contraindications, particularly in patients with hypertension or tachycardia (I-B).**
- **Intravenous or oral nitrates are effective for symptom relief in the acute management of anginal episodes (I-C).**
- **Calcium channel blockers provide symptom relief in patients already receiving nitrates and beta-blockers; they are useful in patients with contraindications to beta-blockade, and in the subgroup of patients with vaso-spastic angina (I-B).**
- **Nifedipine, or other dihydropyridines, should not be used (III-B), unless combined with beta-blockers (IIa-B)**

# Treatment

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# Anti-coagulants

# What's New with Anti-coagulants

## 1 - Pharmacological Treatment

- Superior efficacy with equivalent safety of enoxaparin over UFH (Petersen meta-analysis)
- Fondaparinux non-inferior to enoxaparin in OASIS-5
- Fondaparinux reduced bleeding rate by ~ 50% in OASIS-5
- Reduction in bleeding impacts on outcome (significant risk reduction for death, MI and stroke)

## 2 - Anti-coagulants in the Setting of PCI

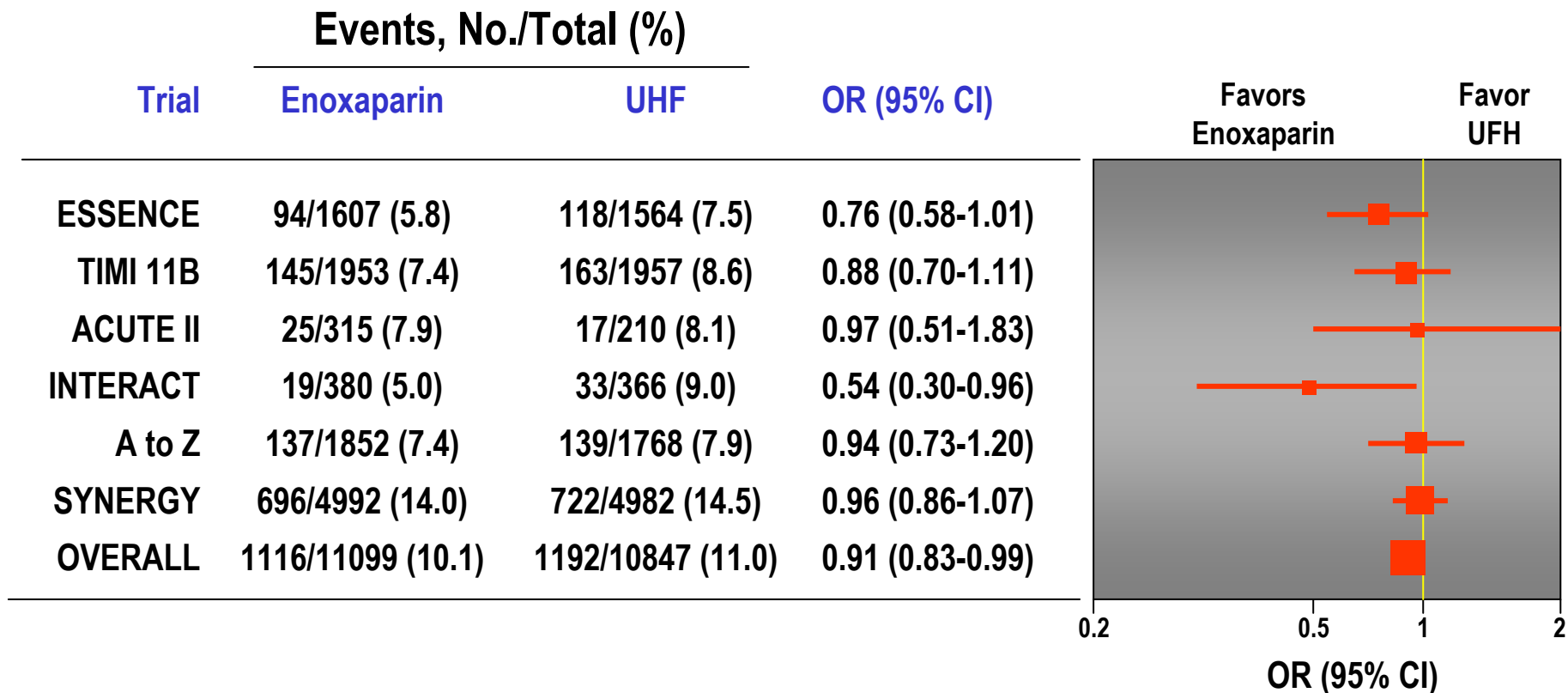
- Enoxaparin is not superior to UFH in SYNERGY
- Bivalirudin superior to UFH/LMWH + GPIIb/IIIa inhibitors in ACUITY

# Anticoagulants – New Comers

- **Fondaparinux**
  - Unequivocal benefit over enoxaparin
  - Significant RR of both bleeding and ischaemic risks
  - Closes the loop – Shift in the paradigm
  - Catheter thrombi issue
  - Bleeding risk issue with UFH ‘on top’ of fonda. in PCI patients
- **Bivalirudin**
  - Not double blind trial
  - Non inferiority margin issue
  - Biased comparison of the different regimens
  - No impact of bleeding risk reduction on outcome at short and long term FU

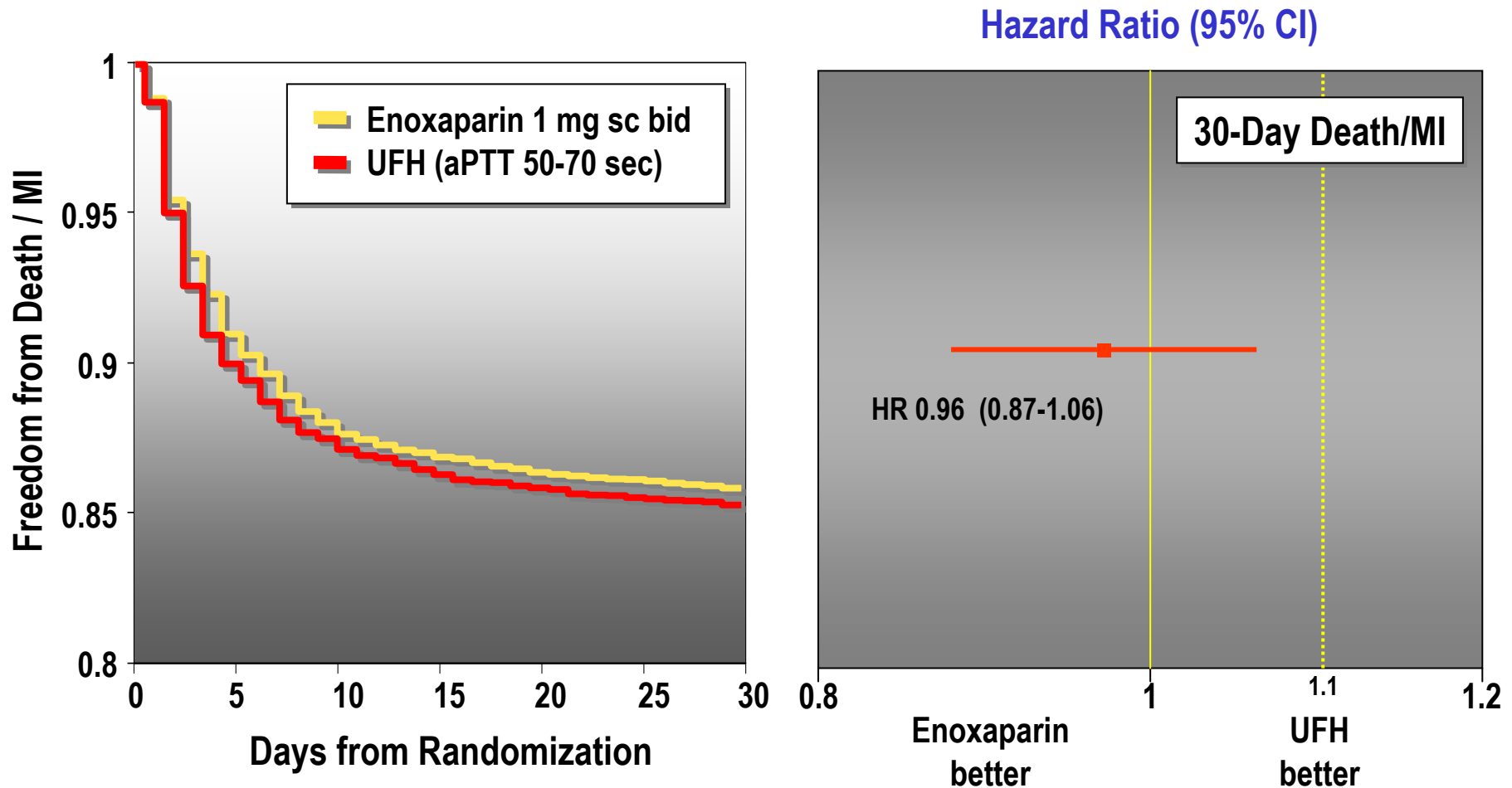
# Efficacy and Bleeding Complications Among Patients Randomized to Enox or UFH in NSTEMI-ACS

## Death or MI at 30 Days



Petersen. JAMA 2004;292:89-96

# Enoxaparin Was Non-Inferior to UFH in Reducing Death or MI in the SYNERGY Trial



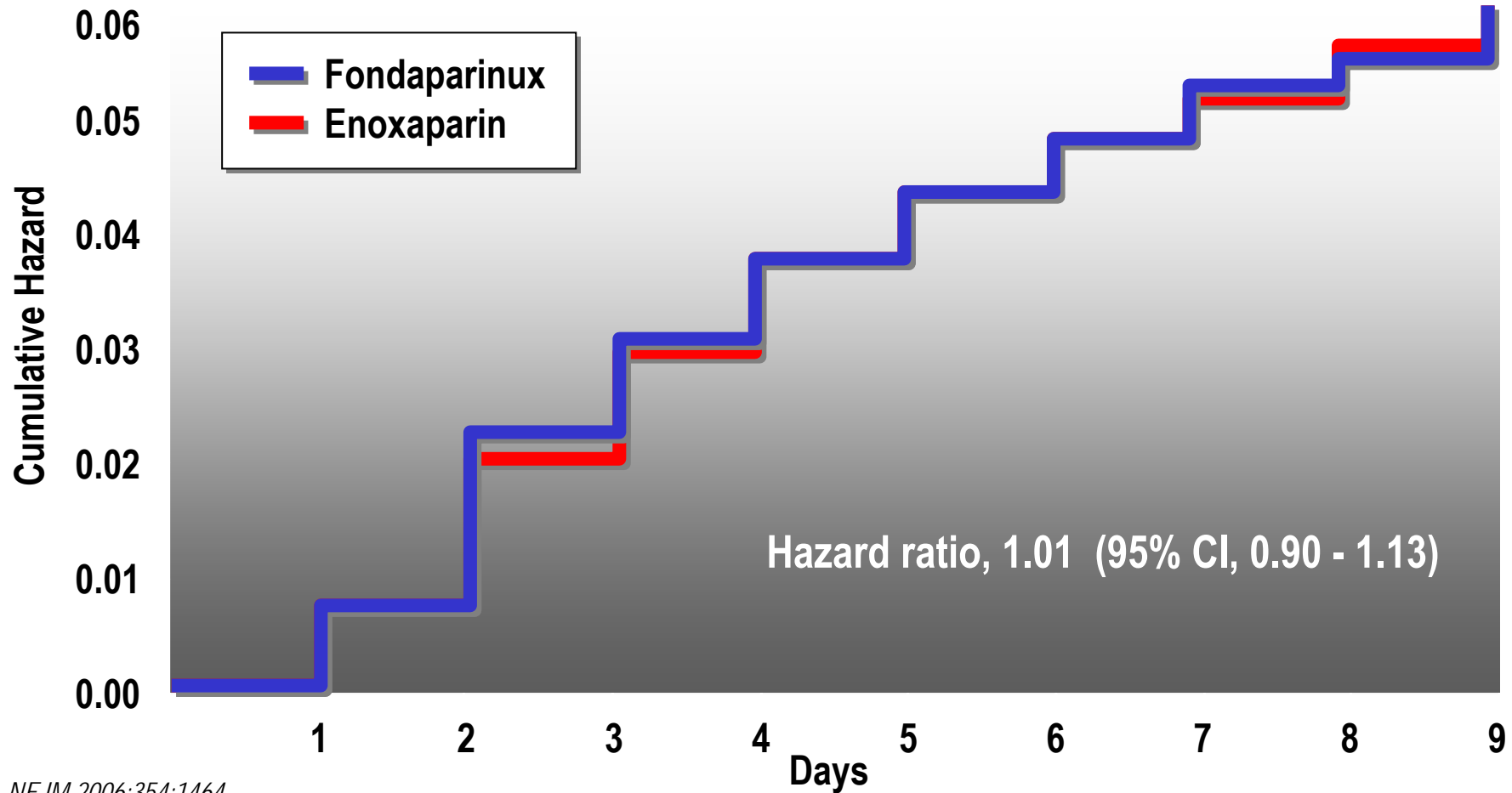
JAMA 2004;292:45-54 Am Heart J 2005;149:581-90

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# OASIS 5 Trial

Death, myocardial infarction or refractory ischemia through day 9



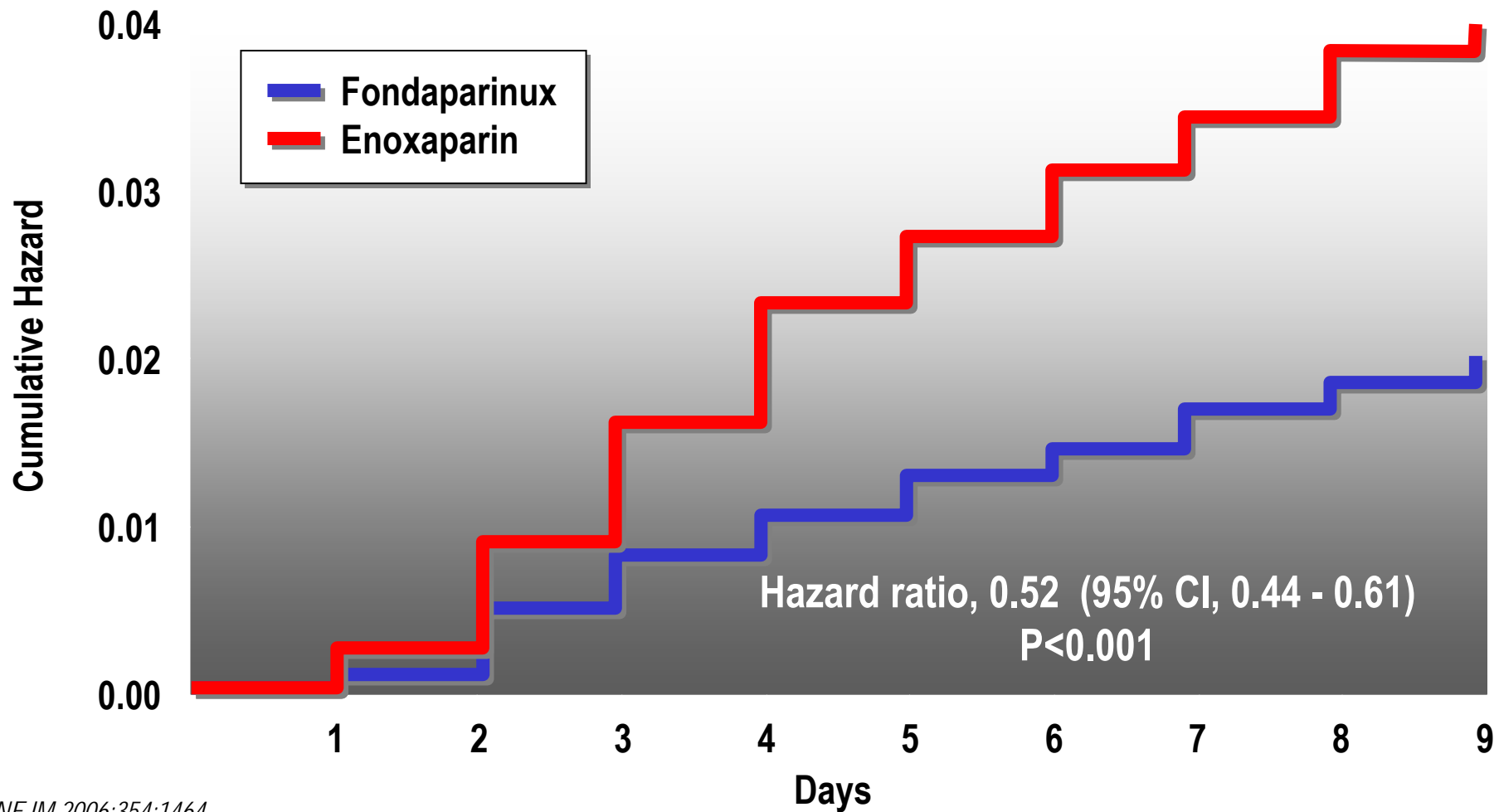
NEJM 2006;354:1464

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# OASIS 5 Trial

Major bleeding through day 9



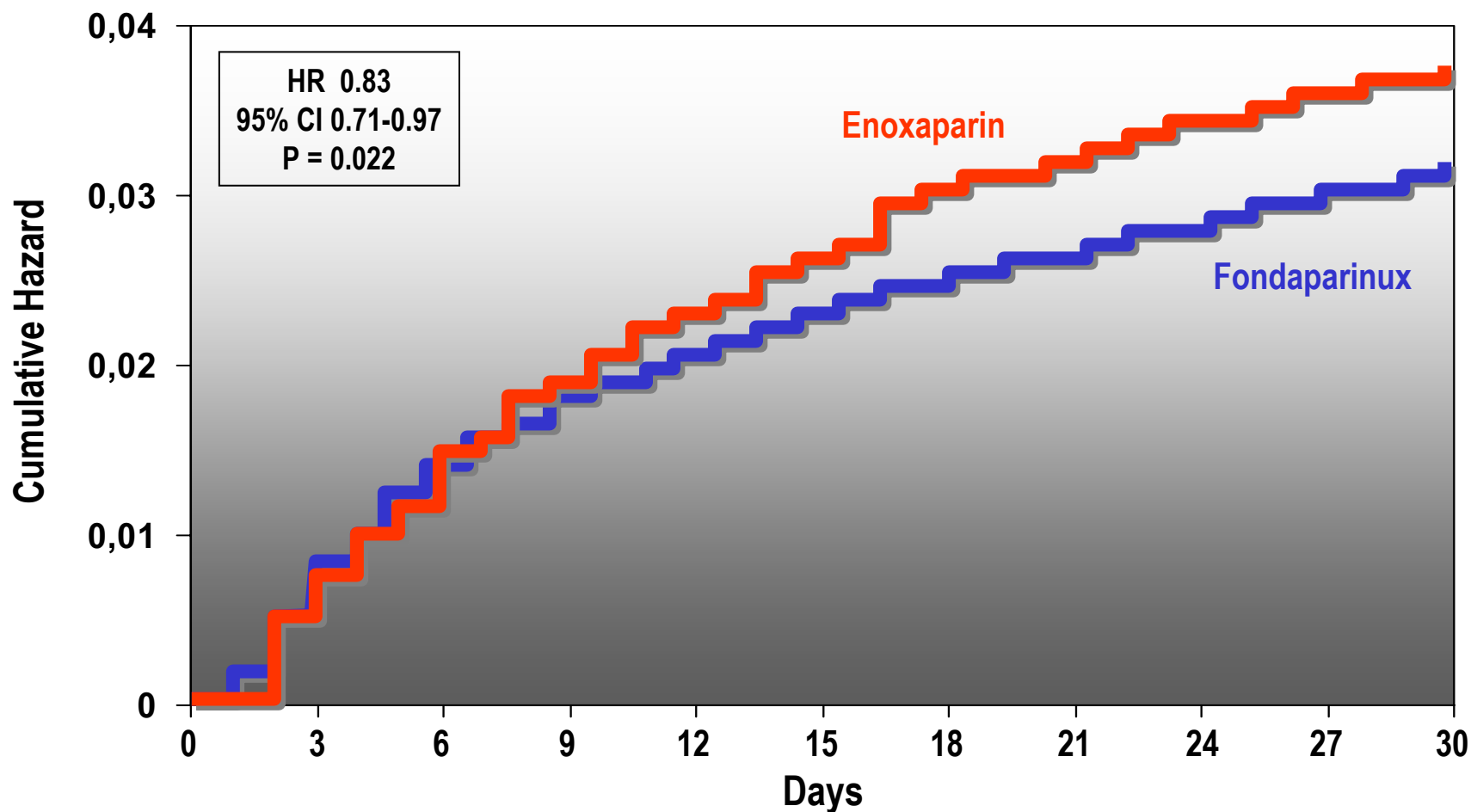
NEJM 2006;354:1464

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# Relation Between Bleeding and Mortality in OASIS-5

Mortality: Day 30



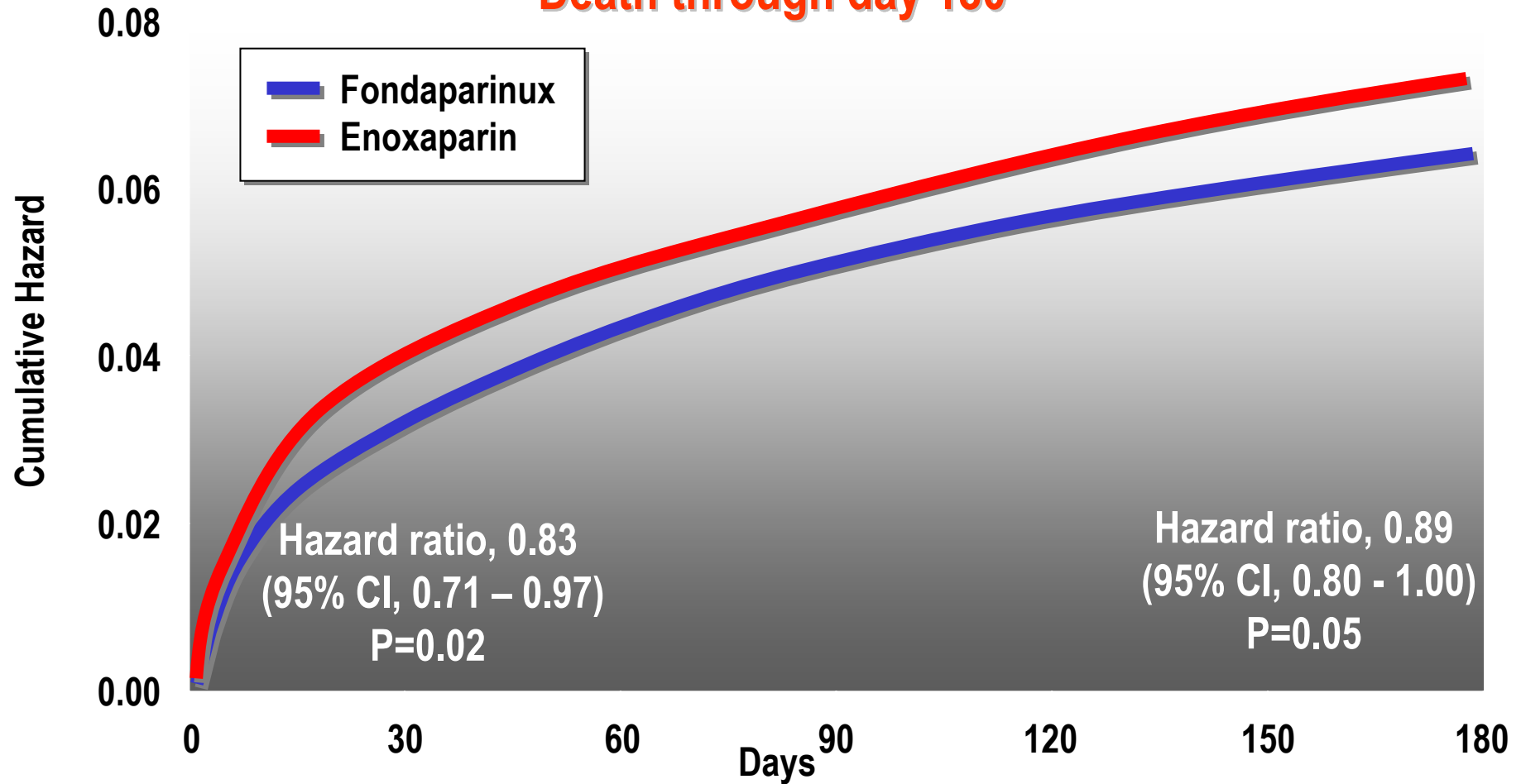
NEJM 2006;354:1464

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# OASIS 5 Trial

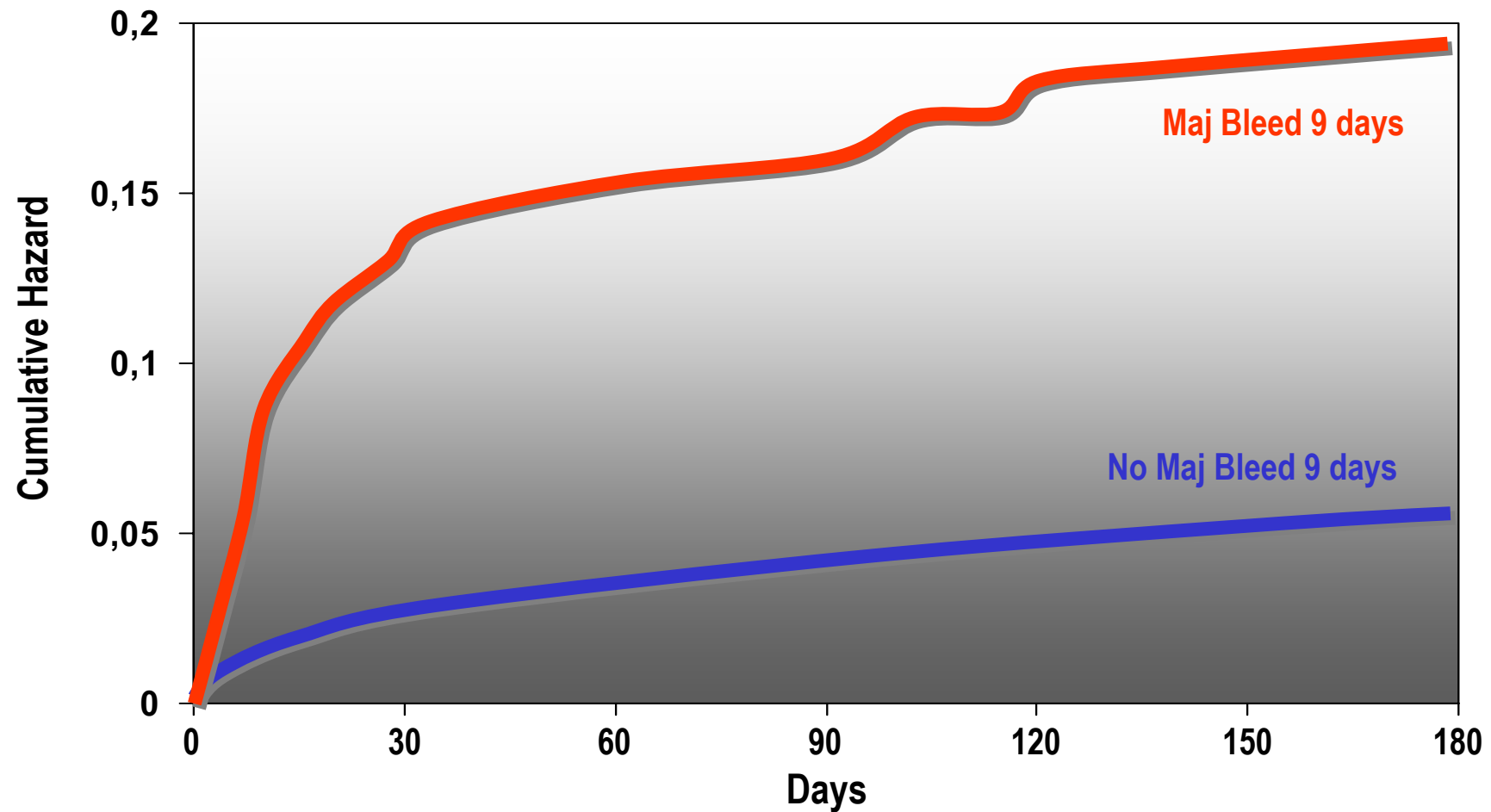
## Death through day 180



NEJM 2006;354:1464

# Relation Between Bleeding and Mortality in OASIS-5

## Mortality at Days 30/180 in Patients with Major Bleeds



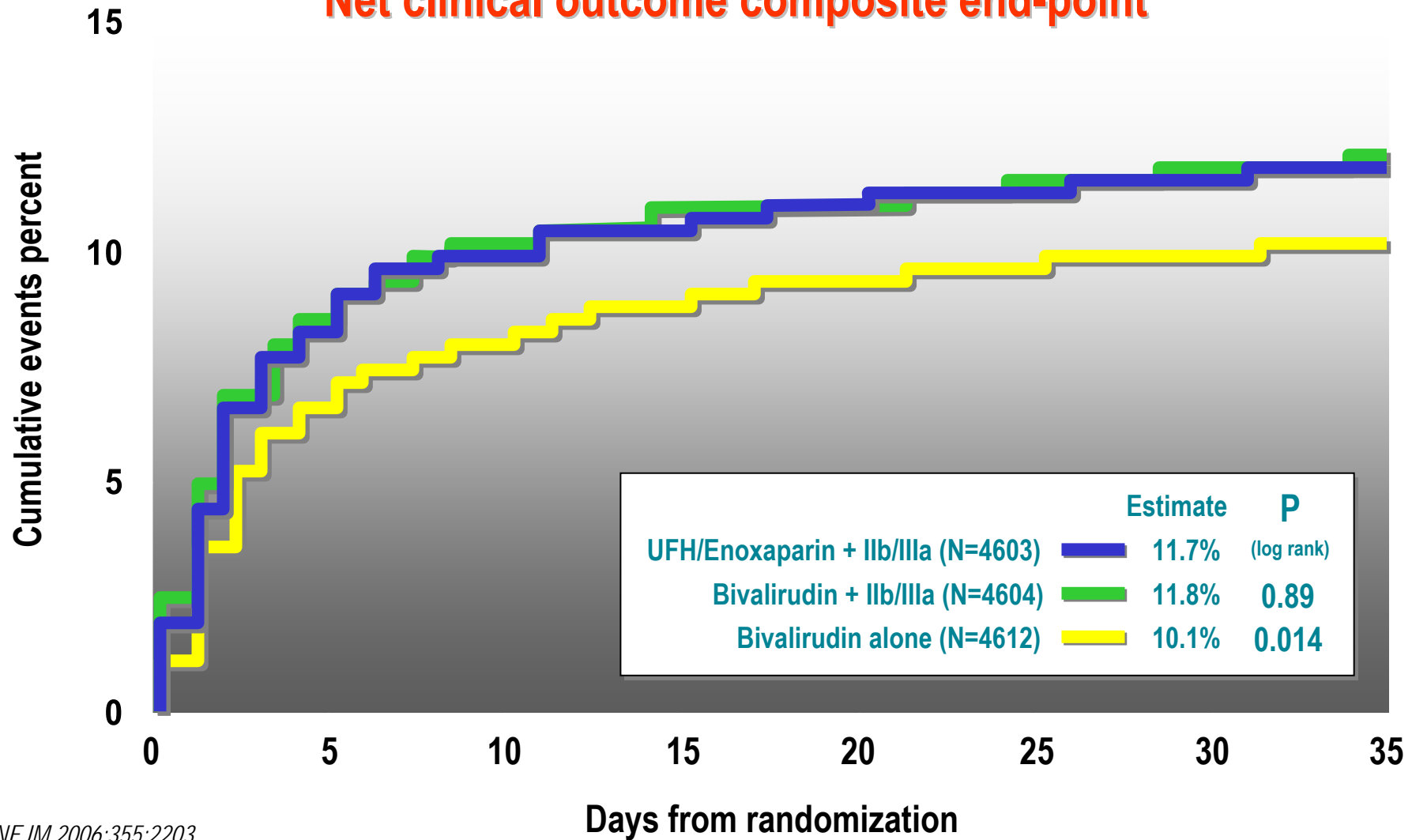
NEJM 2006;354:1464

# A New Concept is Born

1. **Bleeding carries a high risk of death, MI and stroke**
2. **Rate of major bleeding is as high as the rate of death at the acute phase of NSTEMI-ACS**
3. **Prevention of bleeding is equally as important as prevention of ischemic events and results in a significant risk reduction for death, MI and stroke**
4. **Risk stratification for bleeding should be part of the decision making process**

# Acuity Trial

Net clinical outcome composite end-point



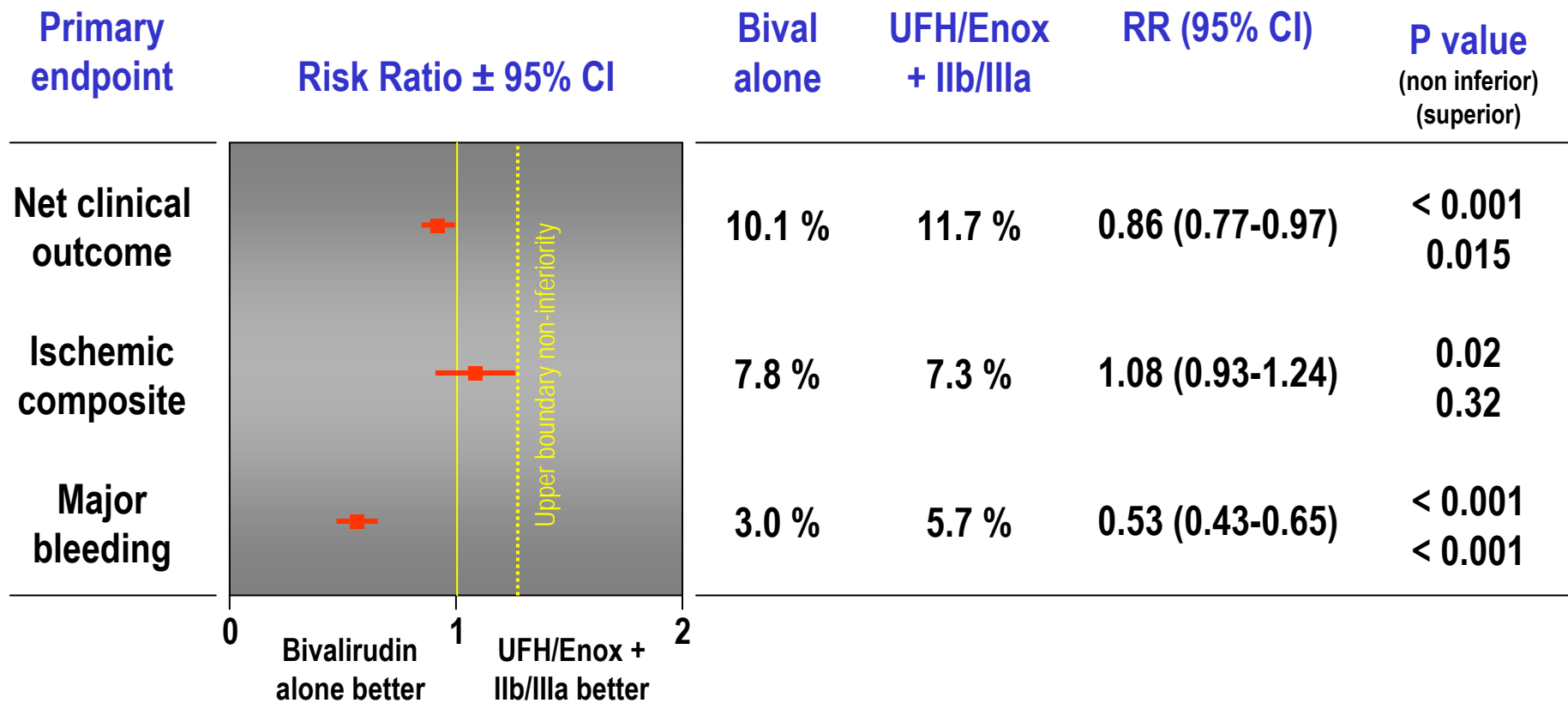
NEJM 2006;355:2203

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# Acuity – Primary Endpoint Measures

## UFH/Enoxaparin + GPI vs. Bivalirudin Alone



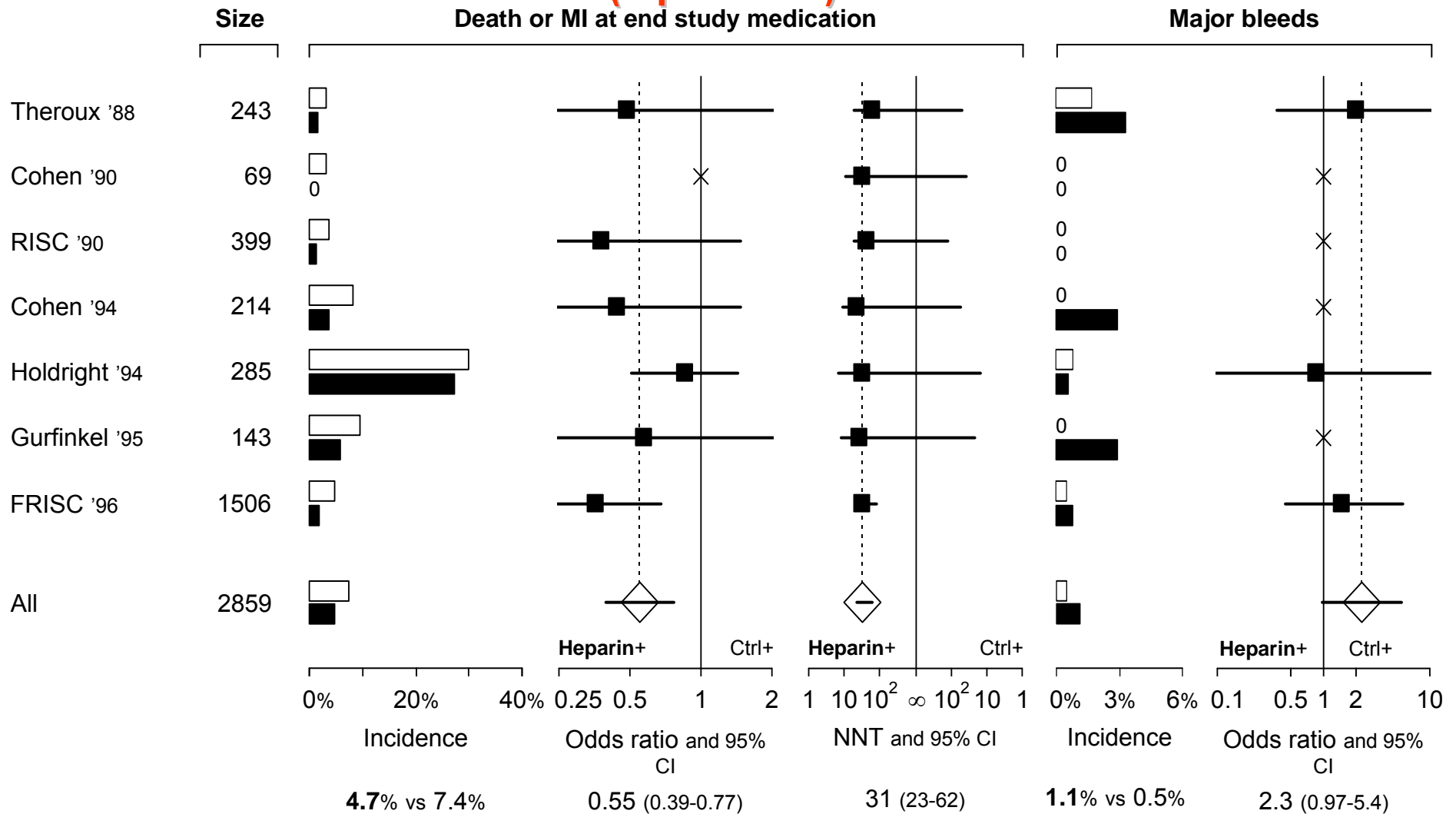
NEJM 2006;355:2203

ESC Guidelines for the Management of NSTEMI-ACS (49)



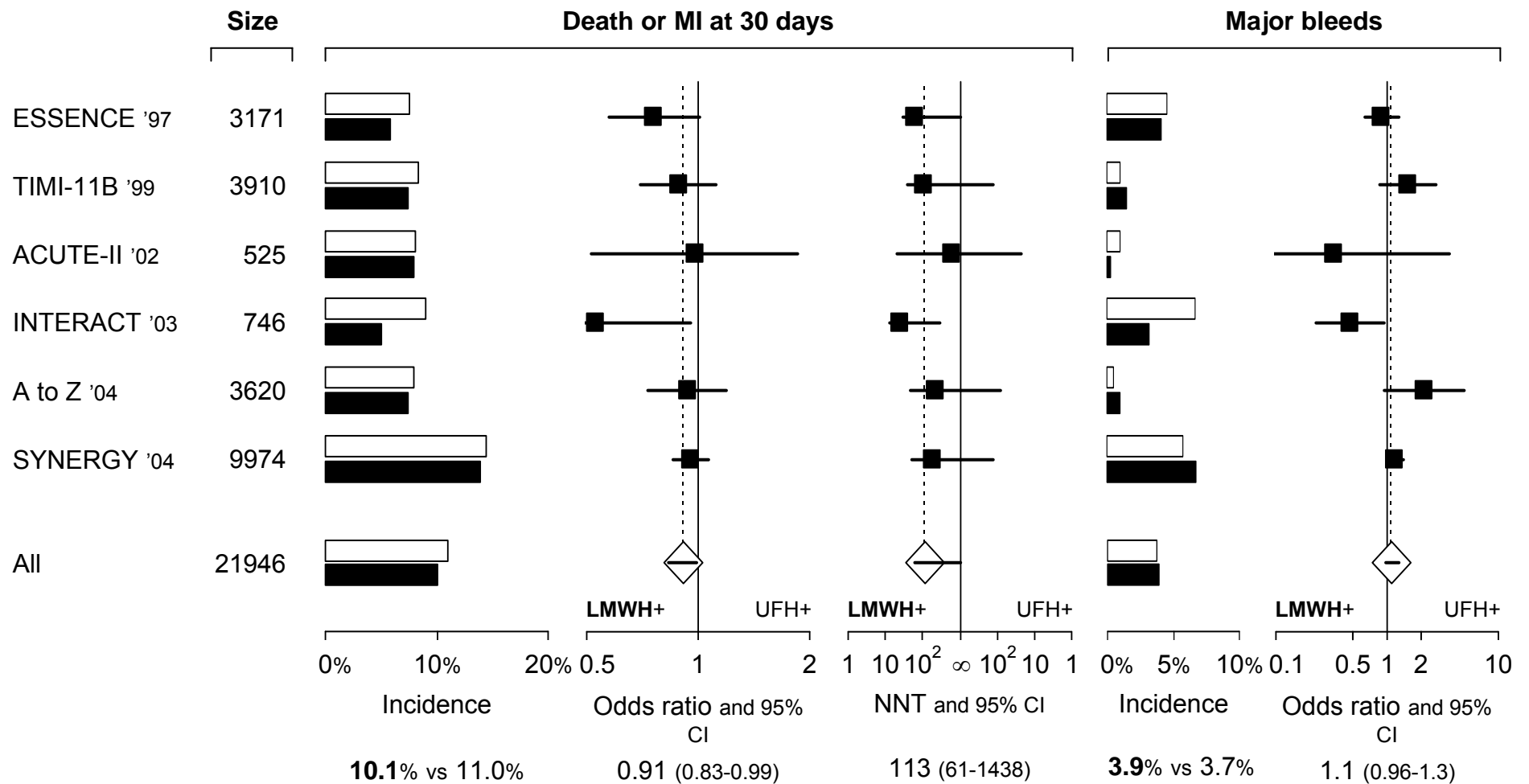
# Randomized trials of UFH/LMWH (dark bars) vs Control

( open bars)



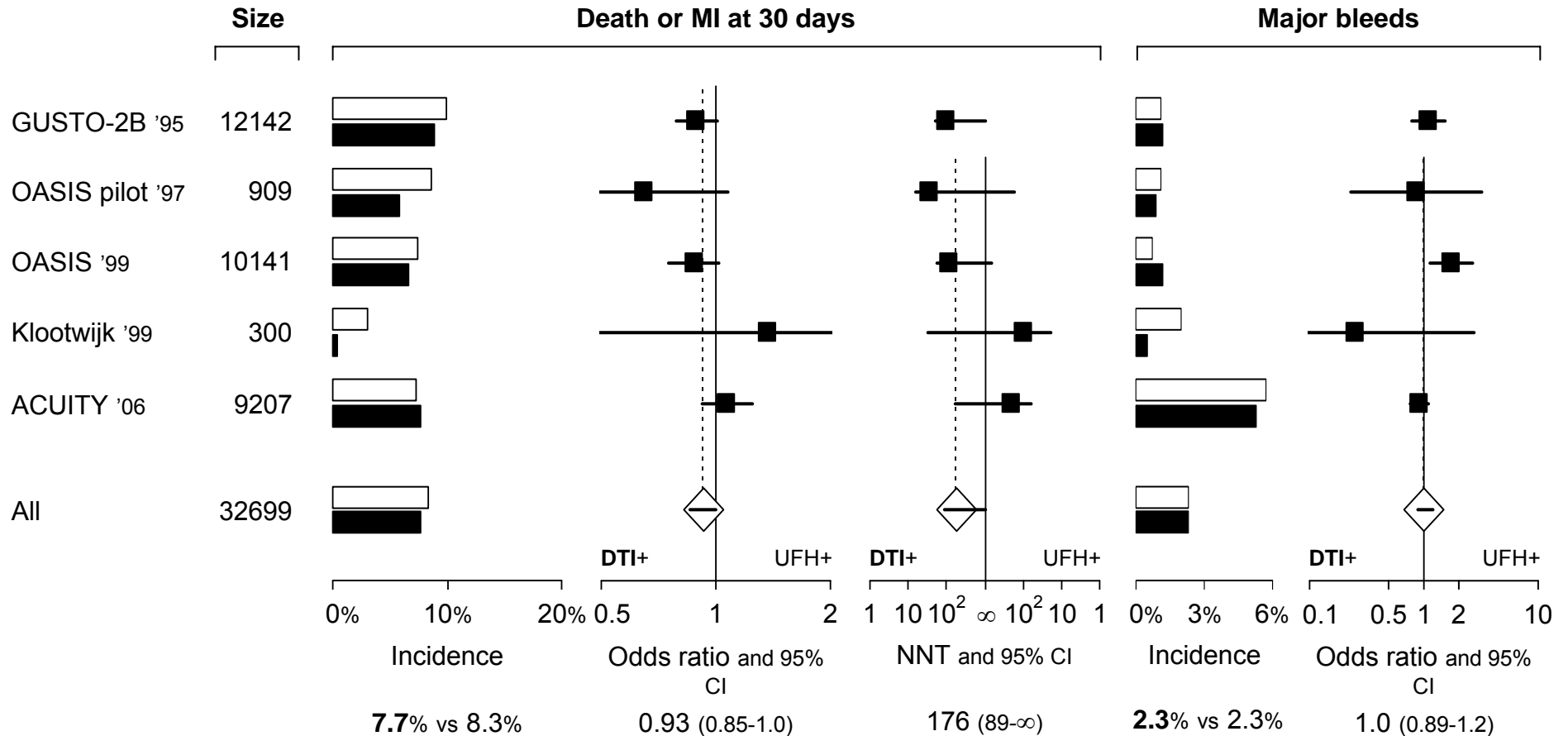
# Randomized trials

## Enoxaparin (dark bars) vs UFH (open bars)



# Randomized trials

## Direct thrombin inhibitors (DTIs) (dark bars) vs UFH/LMWH (open bars)



# Recommendations for Anticoagulation (1)

- Anticoagulation is recommended for all patients in addition to antiplatelet therapy (I-A).
- Anticoagulation should be selected according to the risk of both ischaemic and bleeding events (I-B). Several anticoagulants are available, namely UFH, LMWH, fondaparinux, bivalirudin. The choice depends on the initial strategy, urgent invasive, early invasive, or conservative (I-B) (see section Management Strategy).
- In an urgent invasive strategy UFH (I-C), or enoxaparin (IIa-B) or bivalirudin (I-B) should be immediately started.

# Recommendations for Anticoagulation (2)

- In a non-urgent situation, as long as decision between early invasive or conservative strategy is pending :
  - Fondaparinux is recommended on the basis of the most favorable efficacy/safety profile. (I-A)
  - Enoxaparin with a less favourable efficacy/safety profile than fondaparinux should be used only if the bleeding risk is low (IIa-B)
  - As efficacy/safety profile of LMWH (other than enoxaparin) or UFH relative to fondaparinux is unknown; these anticoagulants cannot be recommended over fondaparinux (IIa-B)

# Recommendations for Anticoagulation (3)

- At PCI procedures the initial anticoagulant should be maintained also during the procedure regardless whether this treatment is UFH (I-C), enoxaparin (IIa-B) or bivalirudin (I-B), while additional UFH in standard dose (50-100 IU/kg bolus) is necessary in case of fondaparinux (IIa-C).
- Anticoagulation can be stopped within 24 hours after invasive procedure (IIa-C). In a conservative strategy, fondaparinux, enoxaparin or other LMWH may be maintained up to hospital discharge (I-B).

# Treatment



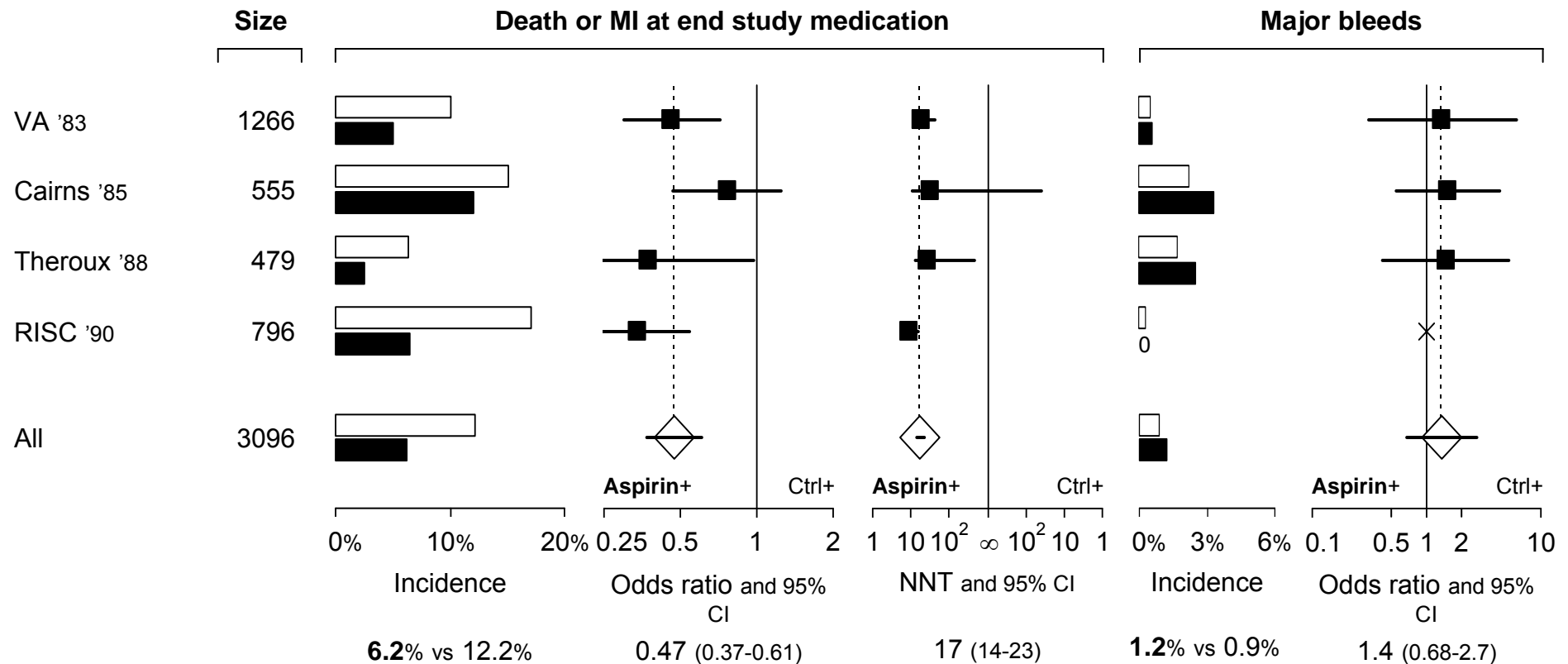
## Anti-platelet agents

# Anti-Platelet Treatment

## Pharmacological Treatment

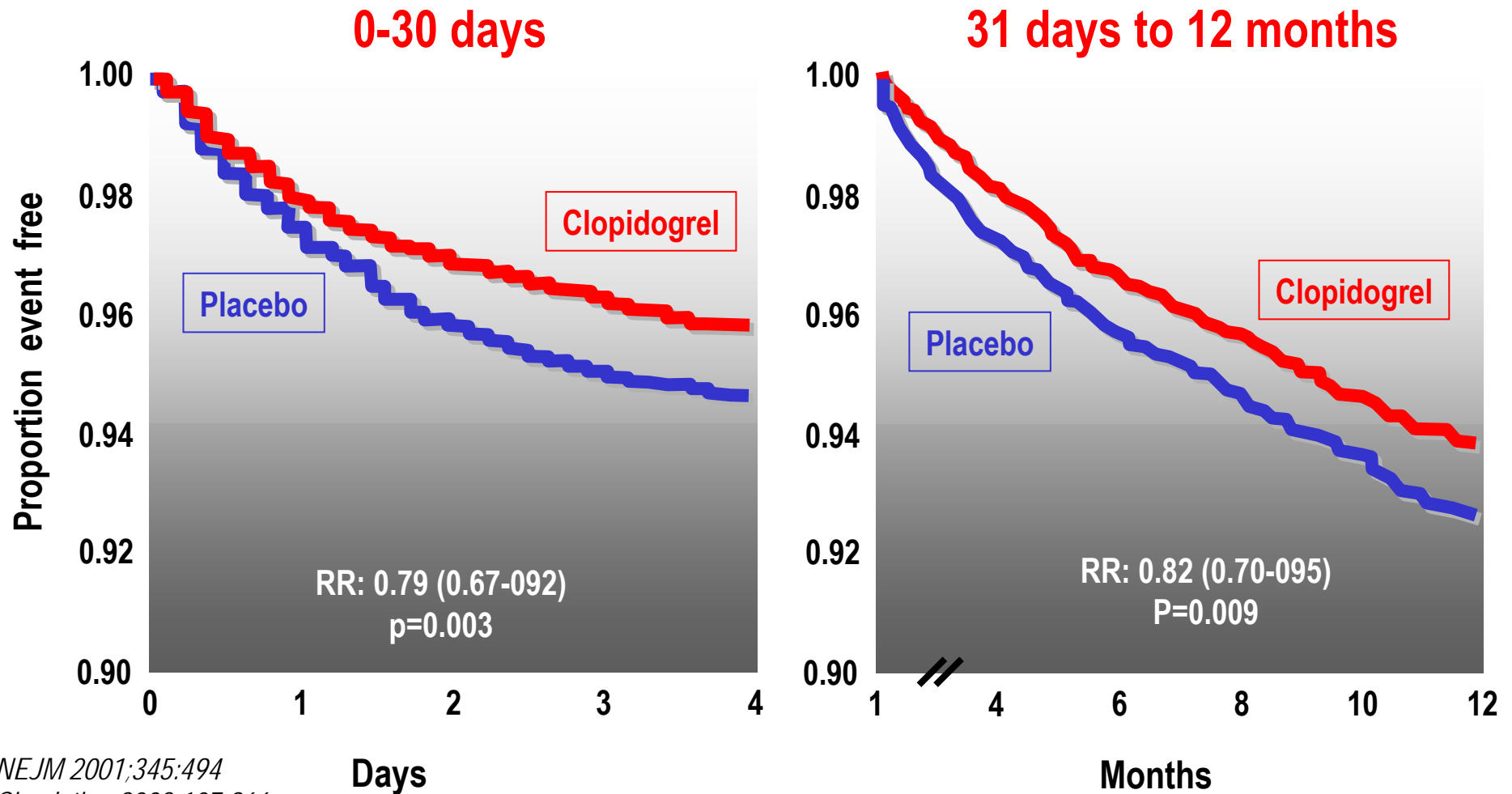
- **Loading dose 600mg vs 300mg clopidogrel : unsettled issue**
- **New ADP receptor antagonists under development (TRITON, PLATO, CHAMPION: ongoing studies)**
- **GP IIb/IIIa inhibitors**
  - **Upstream or deferred**
  - **ACUITY Timing – No unequivocal results**

# Four randomised trials of aspirin (dark bars) VS control (open bars)



# CURE Trial

## Early and late effects of Clopidogrel



NEJM 2001;345:494  
Circulation 2003;107:966

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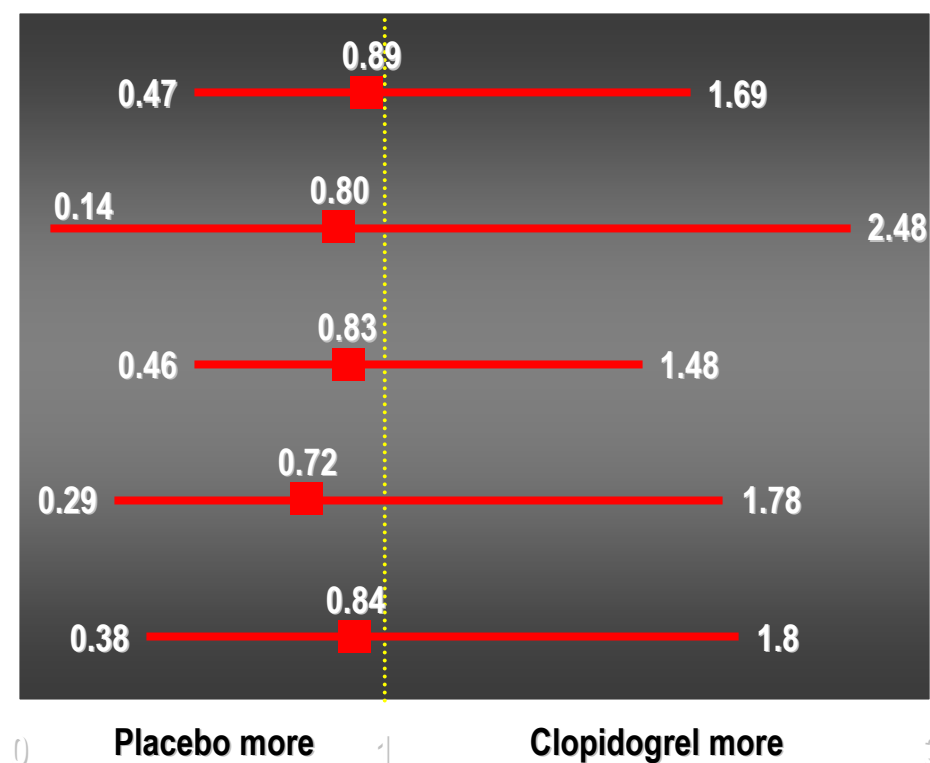
# CURE Trial

## Bleeding Within 7 Days After CABG Surgery

Drug stopped > 5 days prior to CABG

	P	C
Life threatening	4.2	3.7
Other major	1.1	0.7
Life threatening or major	5.3	4.4
TIMI major	2.4	1.8
GUSTO severe/life-threatening	2.9	2.4

OR and 95% CI



*Circulation* 2004;110:1202

ESC Guidelines for the Management of NSTEMI-ACS (60)



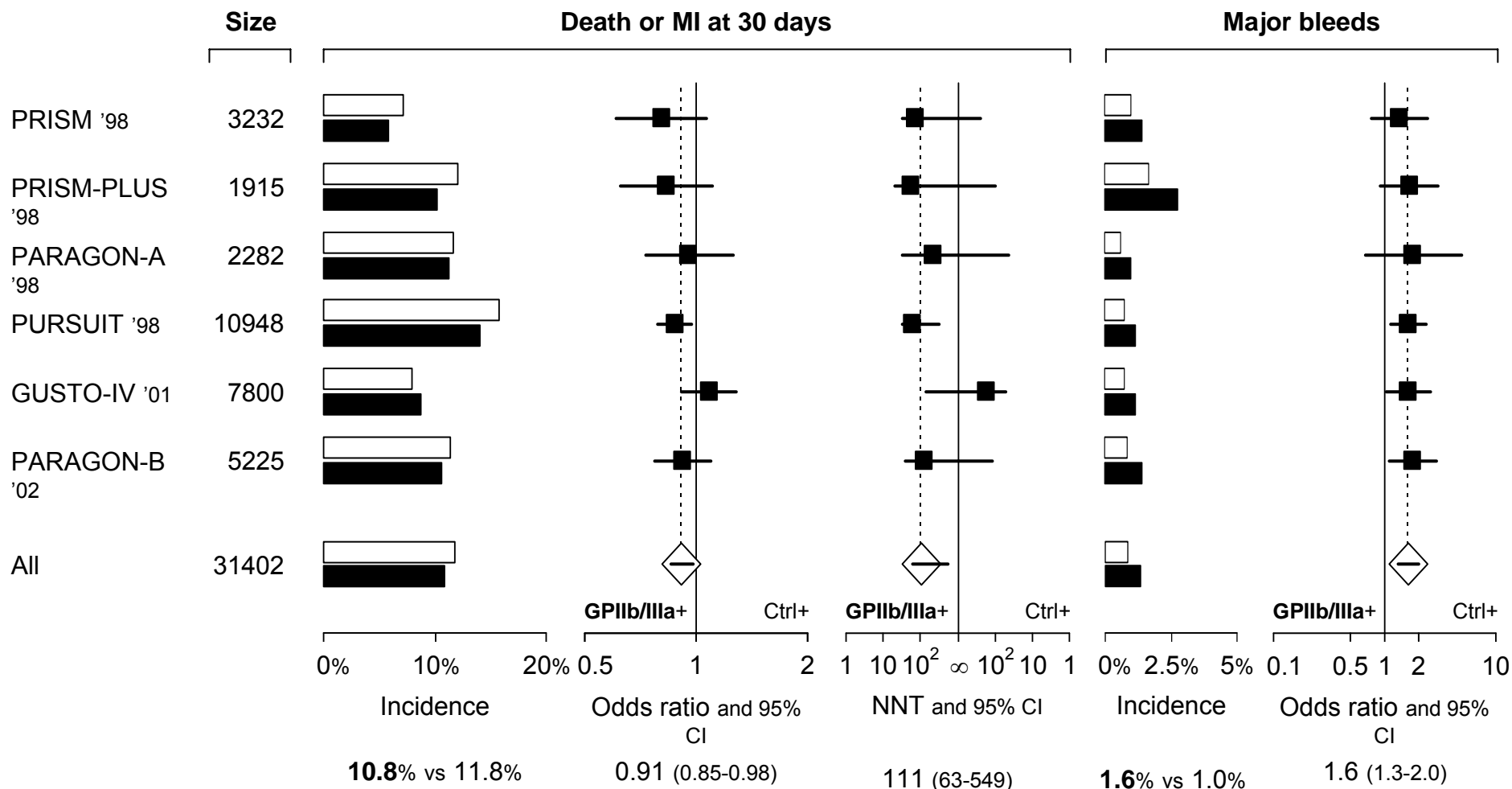
# Recommendations for Oral Antiplatelet Drugs (1)

- Aspirin is recommended for all patients presenting with NSTEMI-ACS without contraindication at an initial loading dose of 160 - 325mg (non-enteric) (I-A), and at a maintenance dose of 75 to 100mg long-term (I-A).
- For all patients, immediate 300mg loading dose of clopidogrel is recommended, followed by 75mg clopidogrel daily (I-A). Clopidogrel should be maintained for 12 months unless there is an excessive risk of bleeding (I-A).
- For all patients with contraindication to aspirin, clopidogrel should be given instead (I-B).

## Recommendations for Oral Antiplatelet Drugs (2)

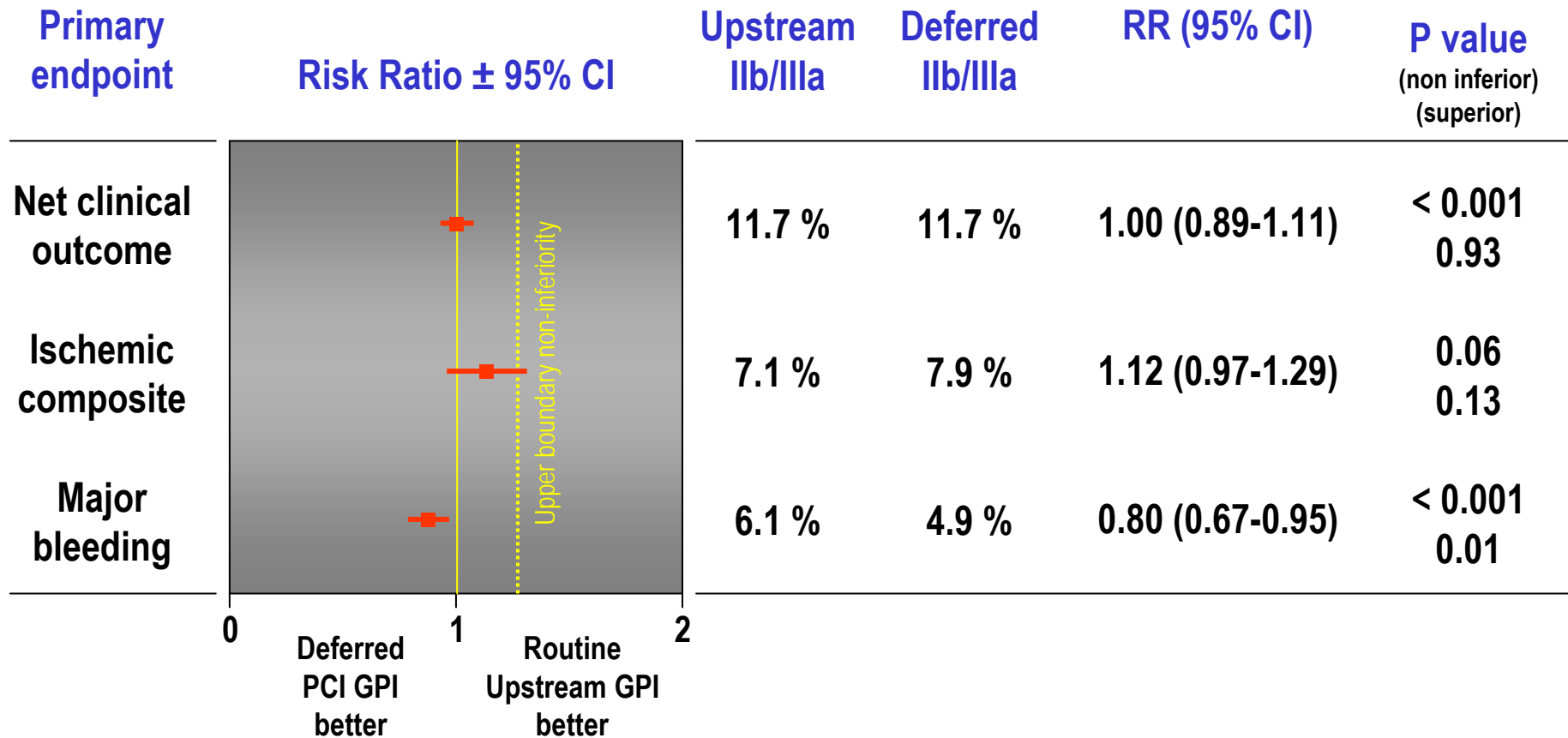
- In patients considered for an invasive procedure/PCI, a loading dose of 600mg of clopidogrel may be used to achieve more rapid inhibition of platelet function (IIa-B).
- In patients pretreated with clopidogrel who need to undergo CABG, surgery should be postponed for 5 days for clopidogrel withdrawal if clinically feasible (IIa-C).

# Randomised trials of GP IIb/IIIa inhibitors (dark bars) VS control (open bars)



# ACUITY Timing - Primary Endpoint Measures

## Routine Upstream IIb/IIIa vs. Deferred PCI IIb/IIIa



JAMA 2007; 297:591

ESC Guidelines for the Management of NSTEMI-ACS (64)



# Recommendations for GP IIb/IIIa Inhibitors (1)

- In patients at intermediate to high risk, particularly patients with elevated troponins, ST-depression, or diabetes, either eptifibatide or tirofiban for initial early treatment are recommended in addition to oral antiplatelet agents (IIa-A).
- The choice of combination of antiplatelet agents and anticoagulants should be made in relation to risk of ischaemic and bleeding events. (I-B)
- Patients who received initial treatment with eptifibatide or tirofiban prior to angiography, should be maintained on the same drug during and after PCI (IIa-B)

## Recommendations for GP IIb/IIIa Inhibitors (2)

- In high risk patients not pretreated with GP IIb/IIIa inhibitors and proceeding to PCI, abciximab is recommended immediately following angiography. (I-A) The use of eptifibatid or tirofiban in this setting is less well established (IIa-B).
- GP IIb/IIIa inhibitors must be combined with an anticoagulant (I-A).
- Bivalirudin may be used as an alternative to GP IIb/IIIa inhibitors plus UFH/LMWH. (IIa-B)
- When anatomy is known and PCI planned to be performed within 24 hours with GP IIb/IIIa inhibitors, most secure evidence is for abciximab (IIa-B)

# Resistance to Antiplatelet Agents & Drug interactions

*ESC Guidelines for the Management of NSTEMI-ACS (67)*



# Recommendations for Resistance to Antiplatelet Treatment/Drugs Interactions

- Routine assessment of platelet aggregation inhibition in patients submitted to either aspirin or clopidogrel therapy, or both, is not recommended (IIb-C).
- NSAID (selective COX 2 inhibitors and non-selective NSAID) should not be administered in combination with either aspirin or clopidogrel (III-C).
- Clopidogrel can be administered with all statins (I-B).
- The triple association of aspirin, clopidogrel and VKA should only be given if compelling indication exists, in which case, the lowest efficacious INR and shortest duration for the triple association should be targeted (IIa-C).

# Withdrawal of antiplatelet agents

# Recommendations for Withdrawal of Antiplatelet Treatment

- Temporary interruption of dual antiplatelet therapy (aspirin and clopidogrel) within the first 12 months after the initial episode is discouraged (I-C).
- Temporary interruption for major or life-threatening bleeding or for surgical procedures where even minor bleeding may result in severe consequences (brain or spinal surgery) is mandatory (IIa-C).
- Prolonged or permanent withdrawal of aspirin, clopidogrel or both is discouraged unless clinically indicated. Consideration should be given to the risk of recurrence of ischaemic events which depends (among other factors), on initial risk, on presence and type of stent implanted, and on time window between proposed withdrawal and index event and/or revascularisation (I-C).

# Clinical Use of Antithrombotic Therapy.

## Oral Antiplatelet Therapy

- Aspirin initial dose: 160–325 mg nonenteric formulation, followed by 75–100mg daily
- Clopidogrel 75 mg/d after a loading dose of 300mg (600mg when rapid onset of action is wanted)

## Anticoagulants

- Fondaparinux\* 2.5mg subcutaneously daily
- Enoxaparin\* 1mg/kg subcutaneously every 12 h
- Dalteparin\* 120 IU/kg every 12 h
- Nadroparin\* 86 IU/kg every 12 h
- UFH intravenous Bolus 60–70 U/kg (maximum 5000 IU) followed by infusion of 12–15 IU/kg/h (maximum 1000 U/h) titrated to aPTT 1.5–2.5 times control
- Bivalirudin\* intravenous bolus of 0.1 mg/kg and infusion of 0.25 mg/kg/hr. Additional intravenous bolus 0.5 mg/kg and infusion increased to 1.75 mg/kg/hour before PCI

## GP IIb/IIIa inhibition\*

- Abciximab 0.25 mg/kg intravenous bolus followed by infusion of 0.125 µg/kg/min (maximum 10 µg/min) for 12 to 24 h
- Eptifibatide 180 µg/kg intravenous bolus (second bolus after 10 min for PCI) followed by infusion of 2.0 µg/kg/min for 72 to 96 h
- Tirofiban 0.4 µg/kg/min intravenously for 30 minutes followed by infusion of 0.10 µg/kg/min for 48 to 96 h. A high dose regimen (bolus 25µg/kg + 0.15µg/kg/min infusion for 18 hours) is tested in clinical trials.

# Treatment



## Coronary revascularisation

# Invasive vs. Conservative Strategies

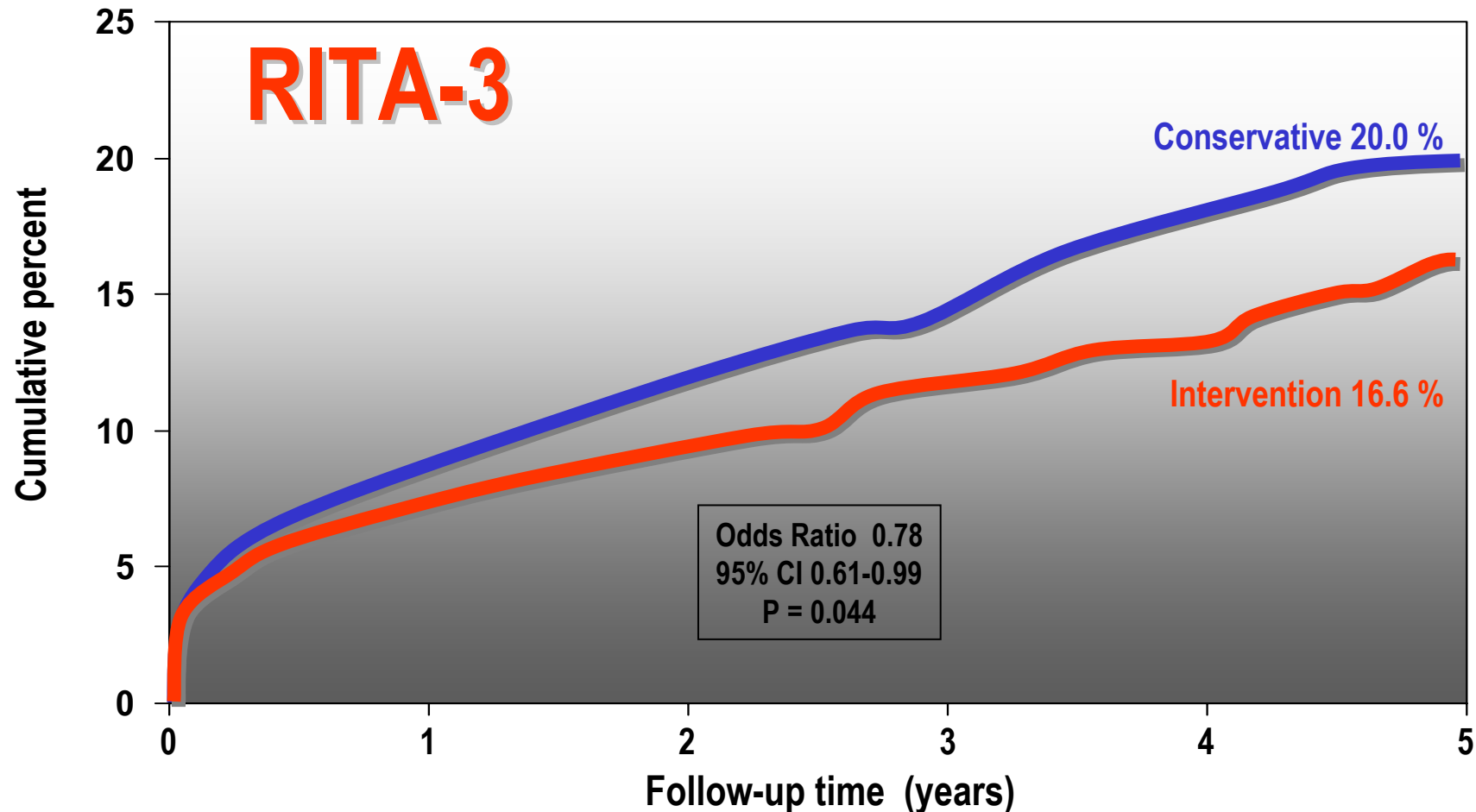
1. New data coming from **long-term follow-up of RITA-3, FRISC-2 and Mehta meta-analysis** show significant risk reduction for death and death & MI at long-term follow-up
2. **Early hazard** shown in **ICTUS trial** (excess of death & MI observed within 1<sup>st</sup> month after revascularisation in immediate invasive group)
3. **Early hazard** shown in **Mehta meta-analysis**

*ICTUS Lancet 2007;369:827*  
*RITA-3 Lancet 2005;366:914*

*FRISC 2 Lancet 2000;356:9-16*  
*Mehta JAMA 2005;293:2908*

# Invasive vs Conservative Strategies

## Death, MI, Rehospitalization for ACS



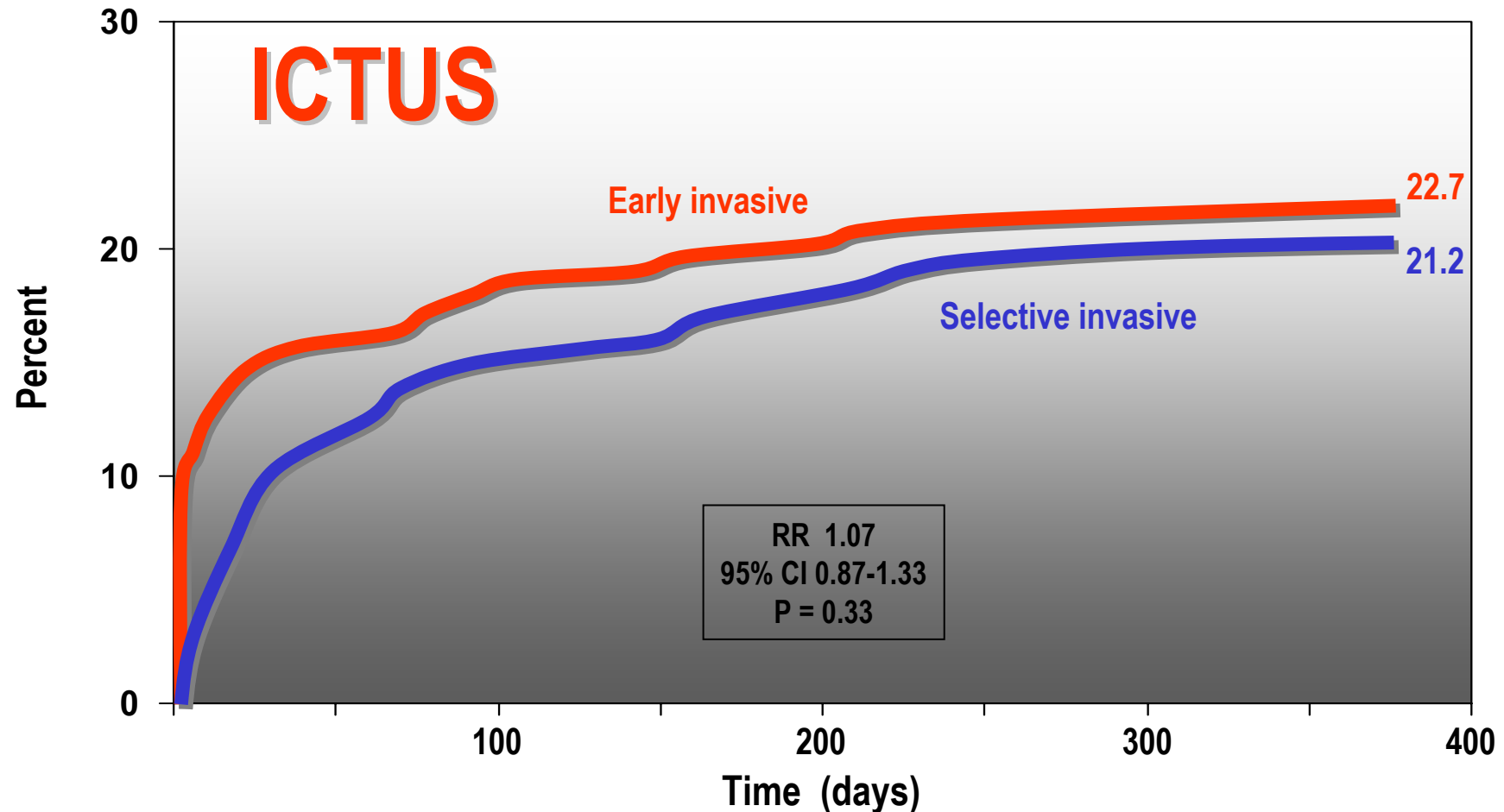
Lancet 2005;366:914

ESC Guidelines for the Management of NSTEMI-ACS (74)



# Invasive vs Conservative Strategies

Death, MI, Rehospitalization for ACS

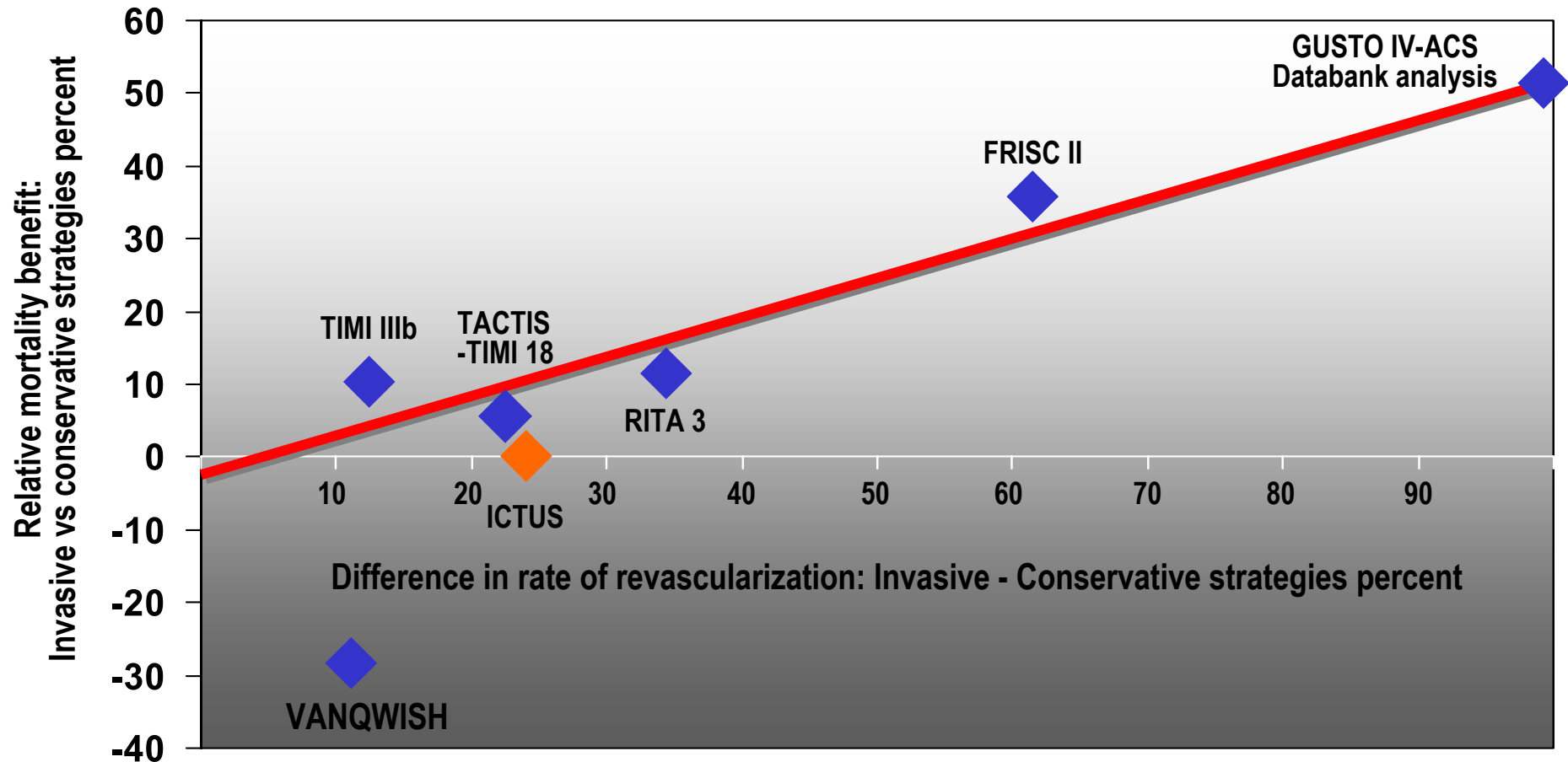


Lancet 2007;369:827

ESC Guidelines for the Management of NSTEMI-ACS (75)



## Relative Mortality Benefit with the Revascularisation vs Gradient in Rates of Revascularisation Between both Randomisation Arms

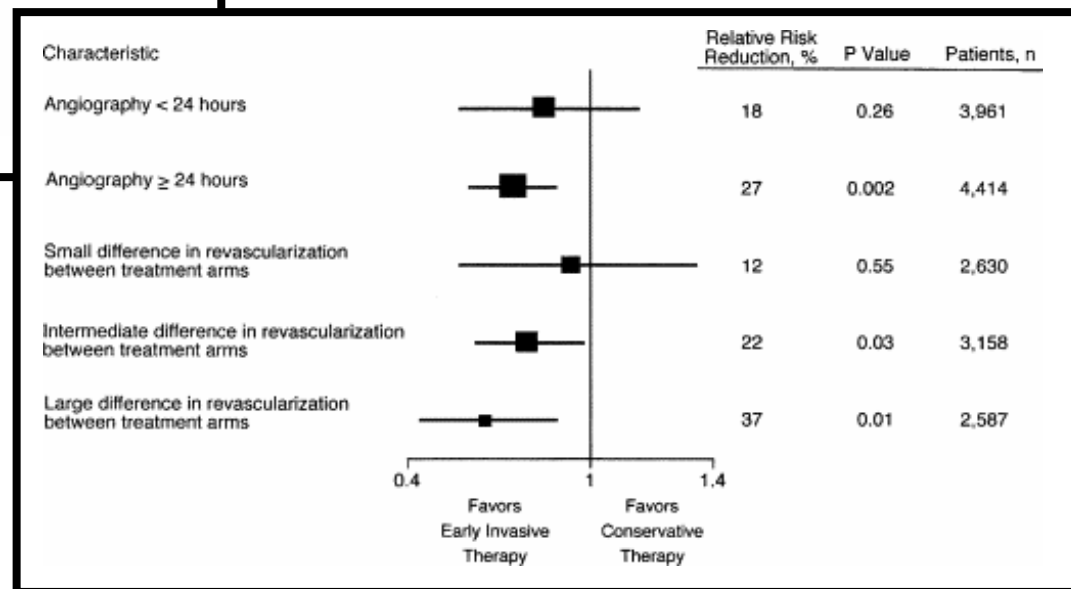
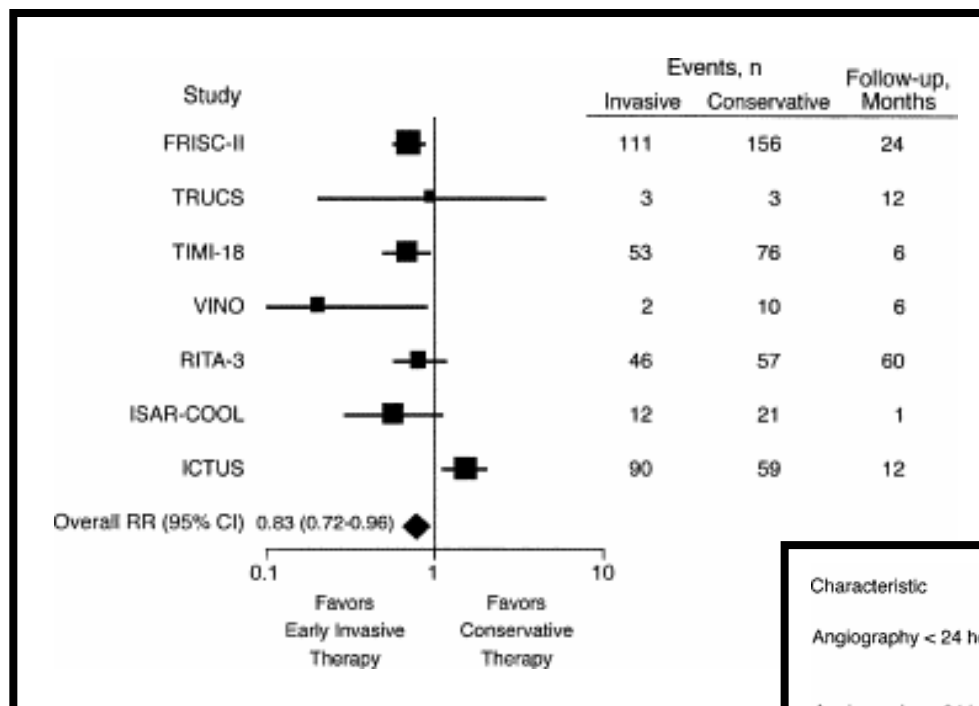


*Eur Heart J* 2004; 25: 1471-1472

*ESC Guidelines for the Management of NSTEMI-ACS (76)*



# Meta-Analysis: Invasive Therapy



Bavry et al. JACC 2006

*ESC Guidelines for the Management of NSTEMI-ACS (77)*

# Timing of Intervention

- 1. Few studies have shown superiority of very early intervention vs deferred intervention.**
  - ISAR-COOL (small sample size) *JAMA 2003;290:1593*
- 2. Many trials, registries and meta-analysis have shown early hazard with early intervention vs deferred intervention**
  - ICTUS trial *NEJM 2005;353:1095*
  - Mehta Meta-analysis *JAMA 2005;293:2908*
  - GRACE & CRUSADE registries *Heart 2007;93:177*  
*Arch Intern Med 2006;166:2027*
- 3. Timing of intervention recommended on the basis of risk stratification**

# Pharmacological Environment of PCI

## 1. Loading dose of clopidogrel

- 300 vs 600mg
- pre-treatment vs no pre-treatment

## 2. Anti-coagulants in the cathlab

- UFH
- Bivalirudin
- Enoxaparin if started in the ward (no cross-over)
- Fondaparinux cannot be used stand-alone

## 3. Triple antiplatelet therapy

- Recommended on the basis of ISAR-REACT-2

*JAMA 2006;295:1531*

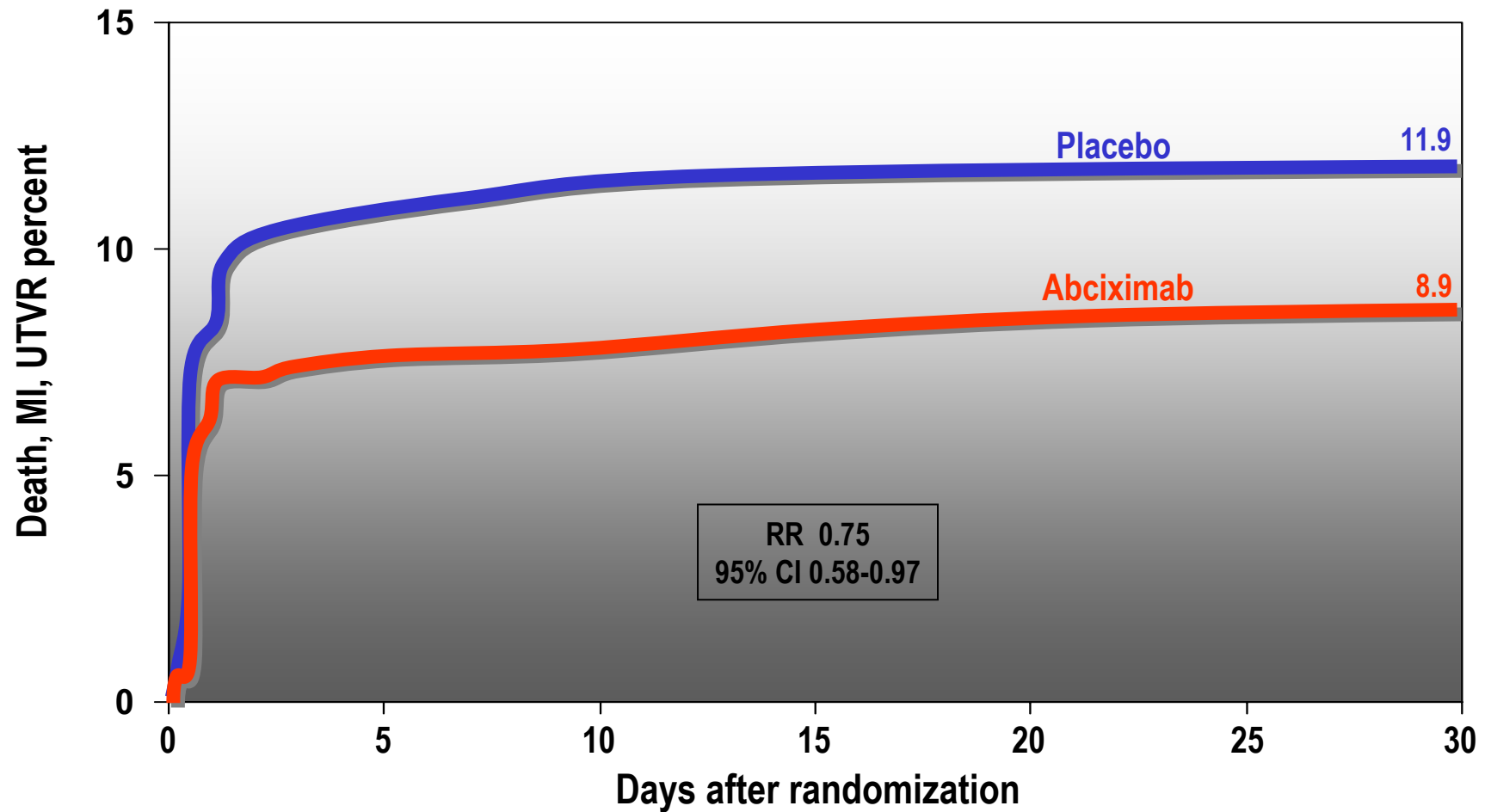
# Glycoprotein IIb/IIIa inhibitors: II B or Not II B?

- **ISAR-REACT 2 : triple antiplatelet Rx superior to double antiplatelet Rx in moderate to high risk patients submitted to PCI**
- ACUITY\* better net clinical outcome (death+MI+urgent revasc+bleeding) with bivalirudin alone vs UFH/LMWH + GPIIb/IIIa inhibitors
  - BUT, trends towards higher ischemic risk with bivalirudin alone (significant in patients not pretreated with clopidogrel)
  - Beneficial effect in ACUITY\* entirely driven by risk reduction for bleeding (no impact on outcome)
  - Liberal non-inferiority margin
  - No impact of bleeding risk reduction on short and long term outcome

***\*Randomised but not double blind study***

# Double vs Triple Antiplatelet Therapy in the Cathlab – ISAR-REACT-2

## Primary End Point



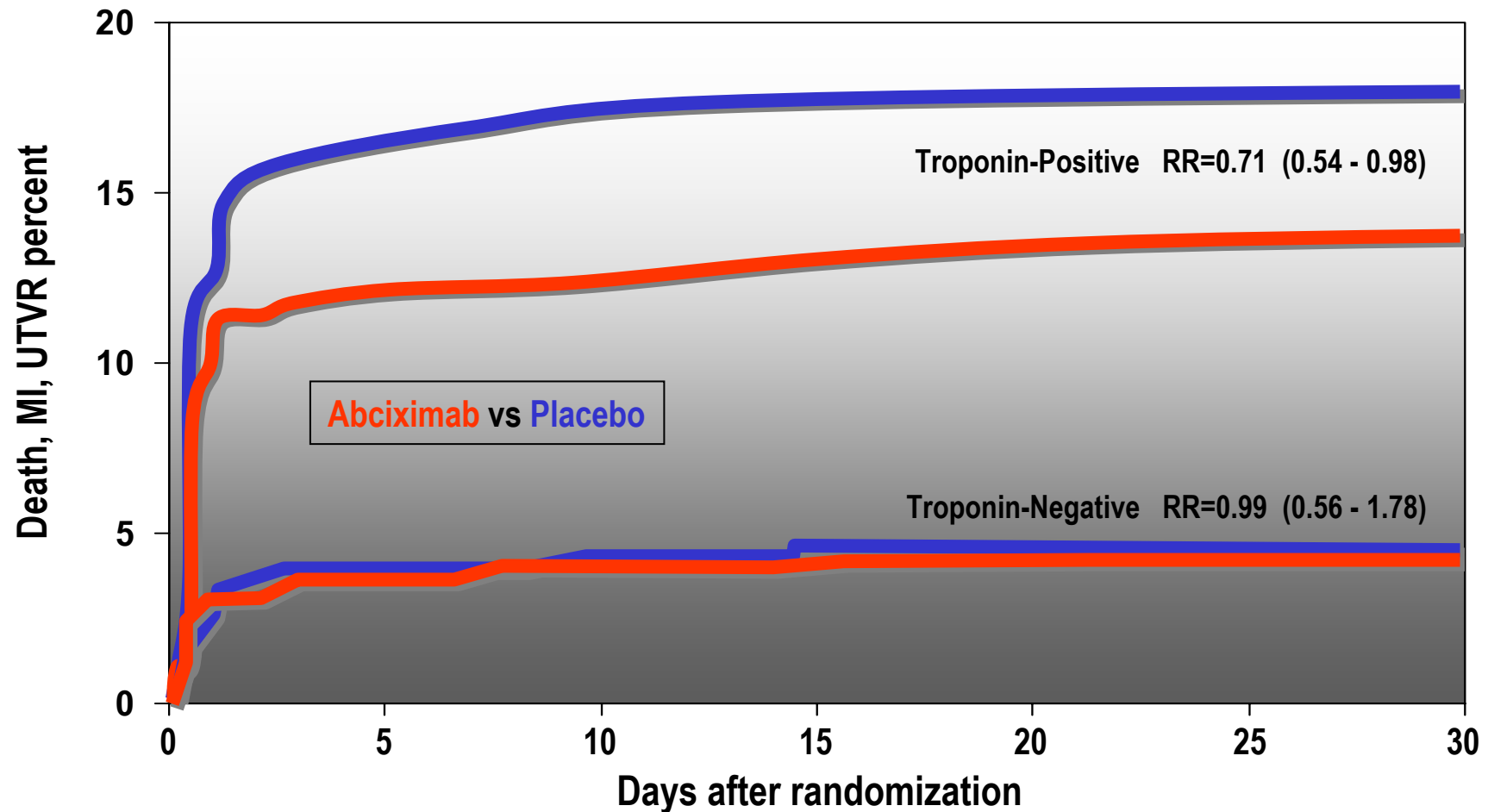
JAMA 2006;295:1531

ESC Guidelines for the Management of NSTEMI-ACS (81)



# Double vs Triple Antiplatelet Therapy in the Cathlab – ISAR-REACT-2

## Troponin Level and Benefit with Abciximab



JAMA 2006;295:1531

ESC Guidelines for the Management of NSTEMI-ACS (82)



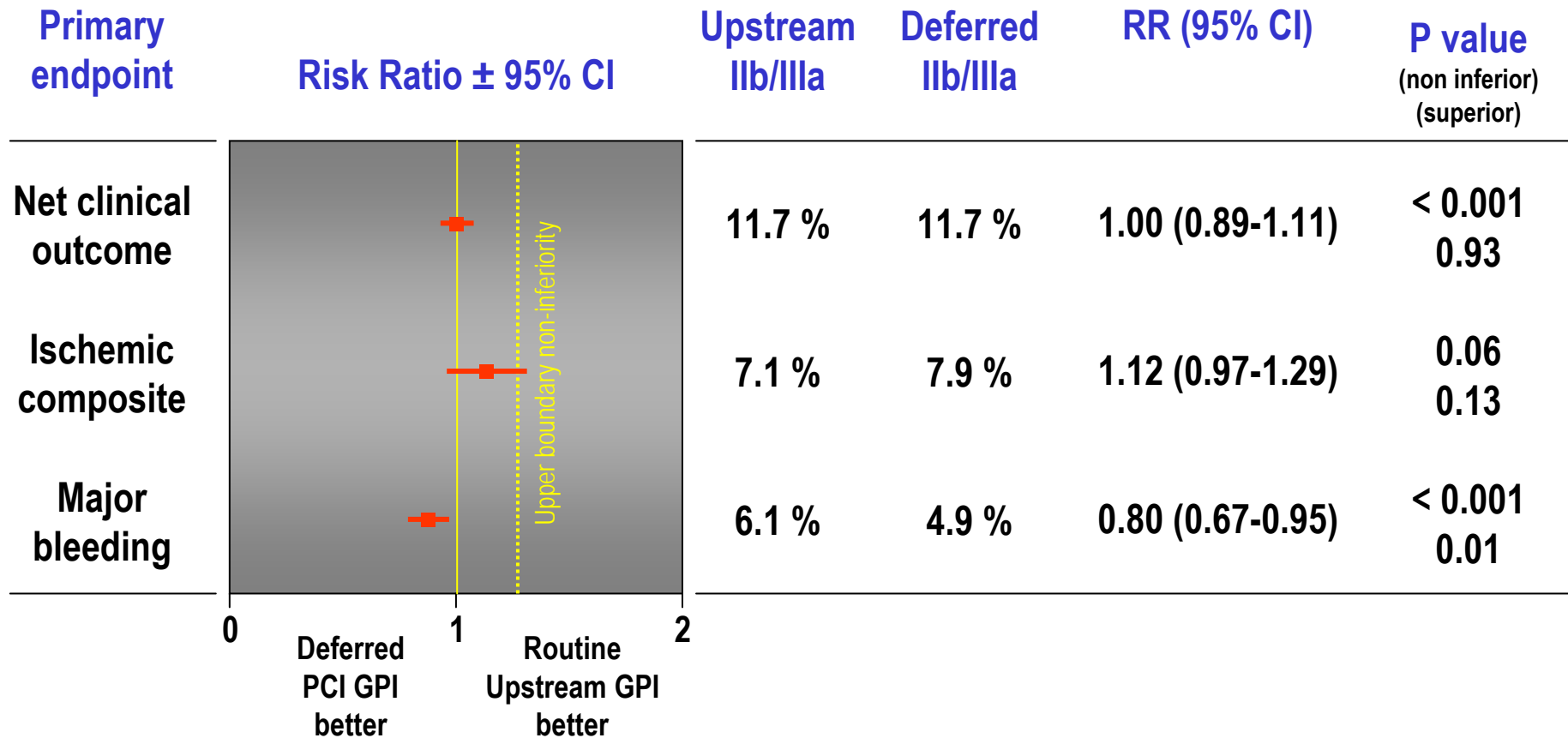
# Glycoprotein IIb/IIIa inhibitors: II B or Not II B?

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  - BUT, trends towards higher ischemic risk with bivalirudin alone (significant in patients not pretreated with clopidogrel)
  - Beneficial effect in ACUITY\* entirely driven by risk reduction for bleeding (no impact on outcome)
  - Wide non-inferiority margin
  - No impact of bleeding risk reduction on short and long term outcome
  - ACUITY Timing – Upstream vs deferred IIB/IIIA inhibitors equivocal results

*\*Randomised but not double blind study*

# ACUITY Timing - Primary Endpoint Measures

## Routine Upstream IIb/IIIa vs. Deferred PCI IIb/IIIa

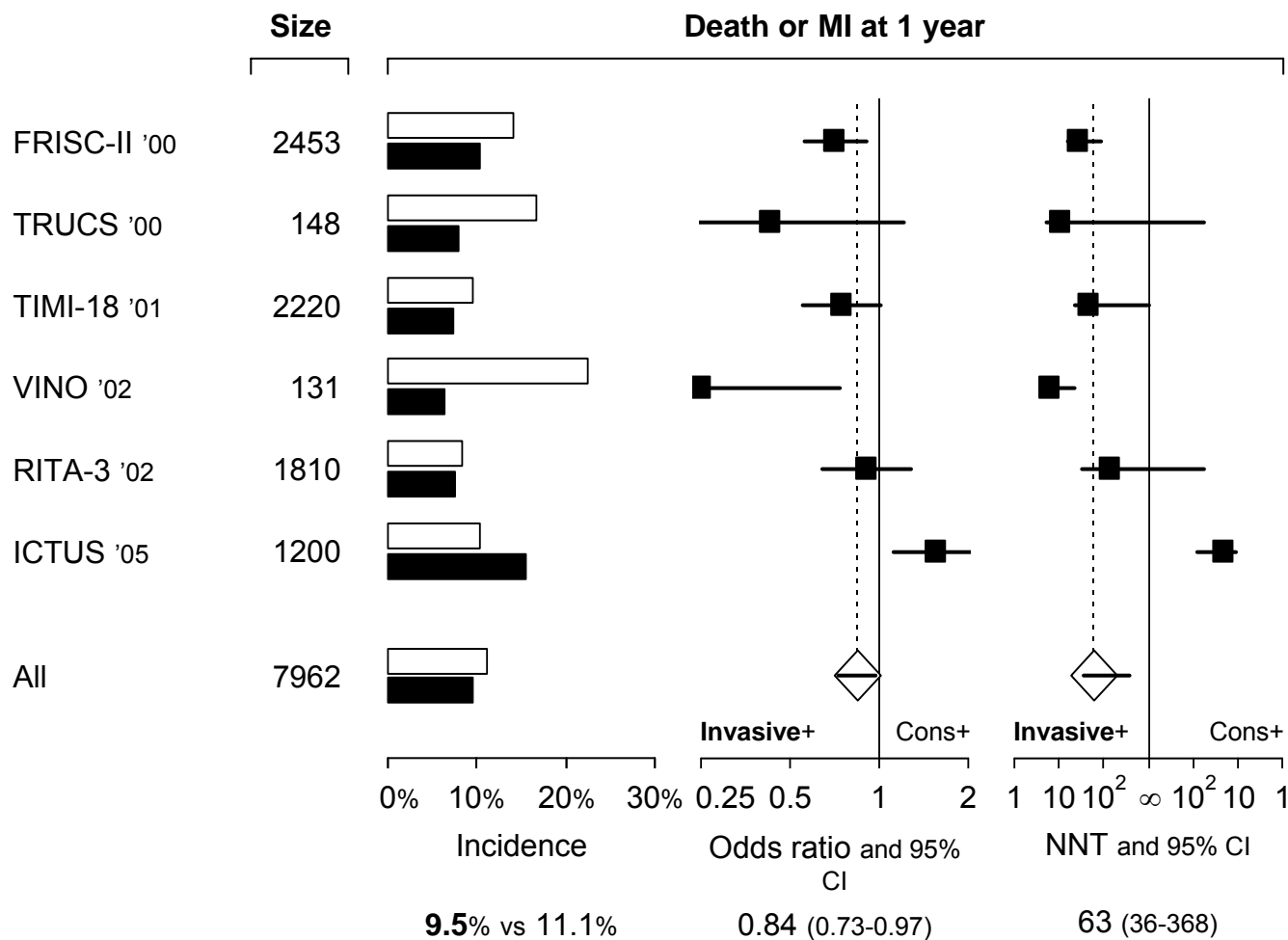


JAMA 2007; 297:591

ESC Guidelines for the Management of NSTEMI-ACS (84)



# Randomised trials comparing early invasive (dark bars) VS conservative strategy (open bars)



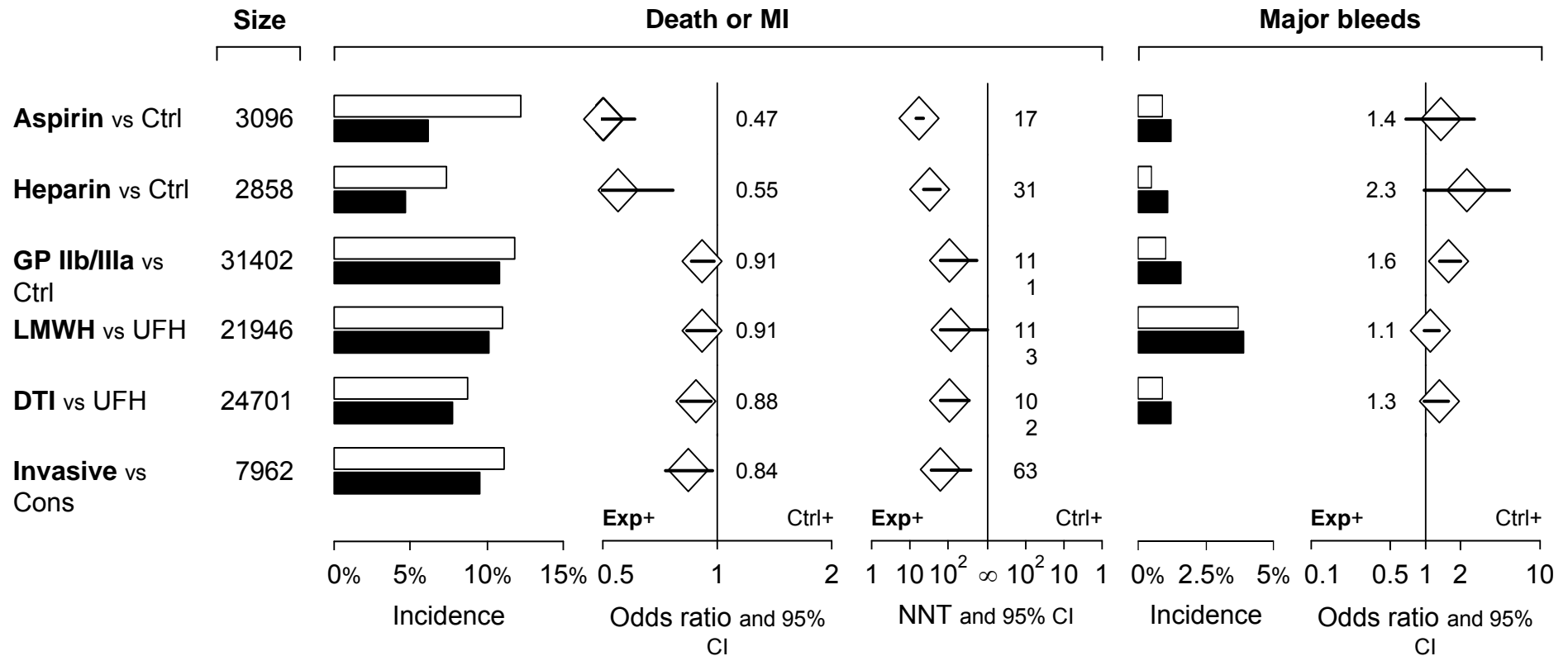
# Recommendations for invasive evaluation and revascularisation (1)

- Urgent coronary angiography is recommended in patients with refractory or recurrent angina associated with dynamic ST deviation, heart failure, life threatening arrhythmias or haemodynamic instability (I - C).
- Early (< 72 hours) coronary angiography followed by revascularisation (PCI or CABG) in patients with intermediate to high-risk features is recommended (I - A).
- Routine invasive evaluation of patients without intermediate to high risk features is not recommended (III-C), but non-invasive assessment of inducible ischaemia is advised (I - C).

# Recommendations for invasive evaluation and revascularisation (2)

- **PCI of non-significant lesions by angiography is not recommended (III - C).**
- **After critical evaluation of the risk to benefit ratio, and depending on known co-morbidities and potential need for non-cardiac surgery in the short/medium term (e.g. planned intervention or other conditions) requiring temporary withdrawal of dual antiplatelet therapy, consideration should be given to the type of stent to be implanted (BMS or DES) (I-C).**

# NSTE-ACS – Summary of Treatment Approaches



# Treatment

## Long-term management & rehabilitation

# Recommendations for Long Term Drug Therapy (1)

## Lipid lowering therapy

- **Statins are recommended for all NSTEMI-ACS patients (in the absence of contraindications), irrespective of cholesterol levels, initiated early (within 1-4 days) after admission, in the aim of achieving LDLc levels <100mg/dL (< 2.6 mmol/L) (I-B).**
- **Intensive lipid-lowering therapy with target LDLc levels <70 mg/dL (< 1.81 mmol/L) initiated within 10 days after admission, is advisable (IIa-B).**

# Recommendations for Long Term Drug Therapy (2)

## Beta-blockers

- Beta-blockers should be given to all patients with reduced LV function (I-A).

## ACE Inhibitors

- ACE inhibitors are indicated long-term in all patients with LVEF  $\leq 40\%$  and in patients with diabetes, hypertension or CKD, unless contraindicated (I-A).
- ACE inhibitors should be considered for all other patients to prevent recurrence of ischaemic events (IIa-B). Agents and doses of proven efficacy are recommended (IIa-C).

# Recommendations for Long Term Drug Therapy (3)

## Angiotensin-Receptor Blockers

- Angiotensin-Receptor Blockers should be considered in patients who are intolerant to ACE inhibitors and/ or who have heart failure or MI with LVEF <40% (I-B).

## Aldosterone receptor antagonists:

- Aldosterone blockade should be considered in patients after MI who are already treated with ACE inhibitors and beta-blockers, and who have a LVEF <40% and either diabetes or heart failure, without significant renal dysfunction or hyperkalemia (I-B).

# Recommendations for Rehabilitation and Return to Physical Activity

- After NSTEMI-ACS, assessment of functional capacity is recommended (I-C).
- Every patient after NSTEMI-ACS should undergo an ECG-guided exercise test (if technically feasible), or an equivalent non-invasive test for ischemia, within 4-7 weeks after discharge (IIa-C)
- Based on cardiovascular status and on the results of functional physical capacity assessment, patients should be informed about the timing of resumption and the recommended level of physical activity, including leisure, work and sexual activities (I-C).

# Complications and their management

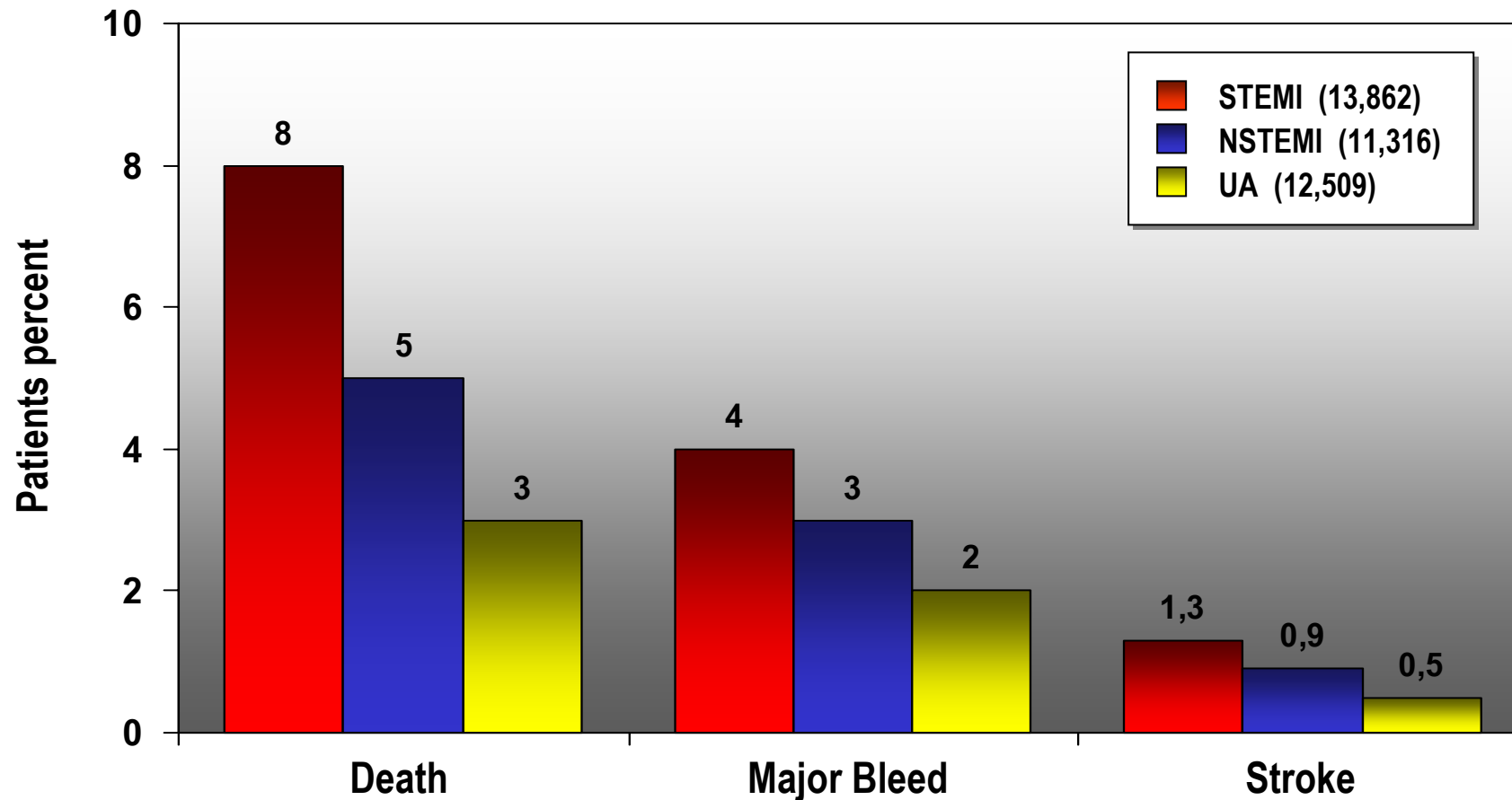
## Bleeding

## Thrombocytopenia

# TIMI and GUSTO Bleeding Definitions

TIMI Bleeding Classification	
Major	Intracranial haemorrhage or clinically overt bleeding (including imaging) $\geq 5$ g/dL decrease in the haemoglobin concentration
Minor	Clinically overt bleeding (including imaging) with 3 to $< 5$ g/dL decrease in the haemoglobin concentration
Minimal	Clinically overt bleeding (including imaging) with a $< 3$ g/dL decrease in the haemoglobin concentration
GUSTO Bleeding Classification	
Severe or life threatening	Either intracranial haemorrhage or bleeding that causes haemodynamic compromise and requires intervention
Moderate	Bleeding that requires blood transfusion but does not result in haemodynamic compromise
Mild	Bleeding that does not meet criteria for either severe or moderate bleeding

# Hospital Outcome by Final Diagnosis



Am J Cardiol 2002; 90: 358

# Multivariate Model for Major Bleeding in Patients with NSTEMI-ACS

Variable	Adjusted OR	95%CI	P-value
Age (per 10-year increase)	1.22	1.10-1.35	0.0002
Female sex	1.36	1.07-1.73	0.0116
History of renal insufficiency	1.53	1.13-2.08	0.0062
History of bleeding	2.18	1.14-4.08	0.014
Mean arterial pressure (per 20mmHg decrease)	1.14	1.02-1.27	0.019
Diuretics	1.91	1.46-2.49	<0.0001
LMWH only	0.68	0.50-0.92	0.012
LMWH and UFH*	0.72	0.52-0.98	0.035
GP IIb/IIIa inhibitors only	1.86	1.43-2.43	<0.0001
Thrombolytics and GP IIb/IIIa inhibitors	4.19	1.68-10.4	0.002
IV inotropic agents	1.88	1.35-2.62	0.0002
Right-heart catheterisation	2.01	1.38-2.91	0.0003

Moscucci. Eur Heart J 2003;24:1815

*ESC Guidelines for the Management of NSTEMI-ACS (97)*



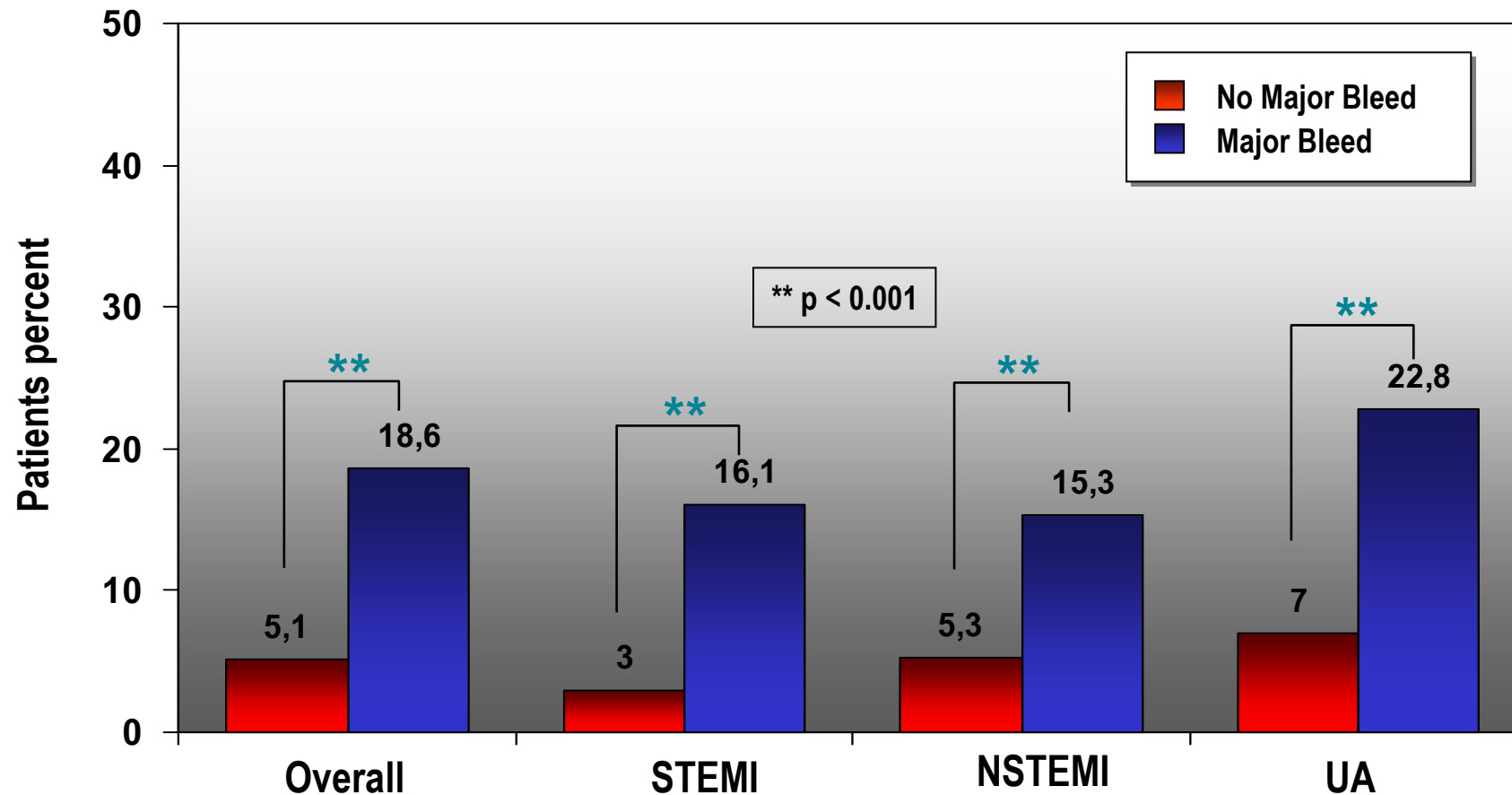
# Multivariate Model for Major Bleeding in Patients with NSTEMI



Variable	Adjusted OR	P-value
Age (per 10y increase)	1.22	0.0002
Female sex	1.36	0.0116
History of renal insufficiency	1.53	0.0062
History of bleeding	2.18	0.014
GPIIb/IIIa blockers	1.86	<0.001
Percutaneous interventions	2.24	<0.0001

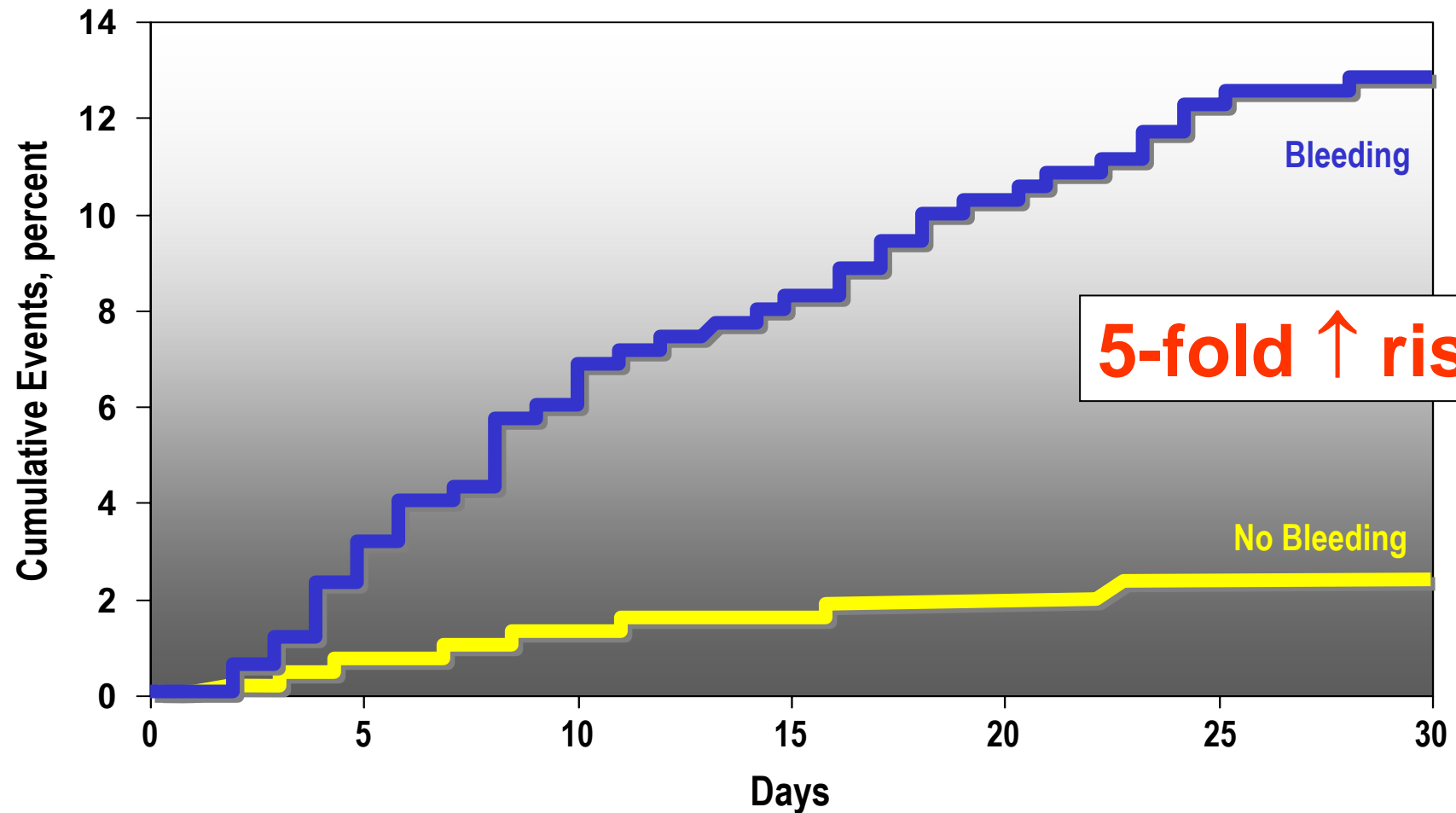
**Moscucci. Eur Heart J 2003;24:1815**

# In-Hospital Death Rates in Patients According to Major Bleeding



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

# 30 Day Death According to Bleeding OASIS Registry, OASIS-2, CURE

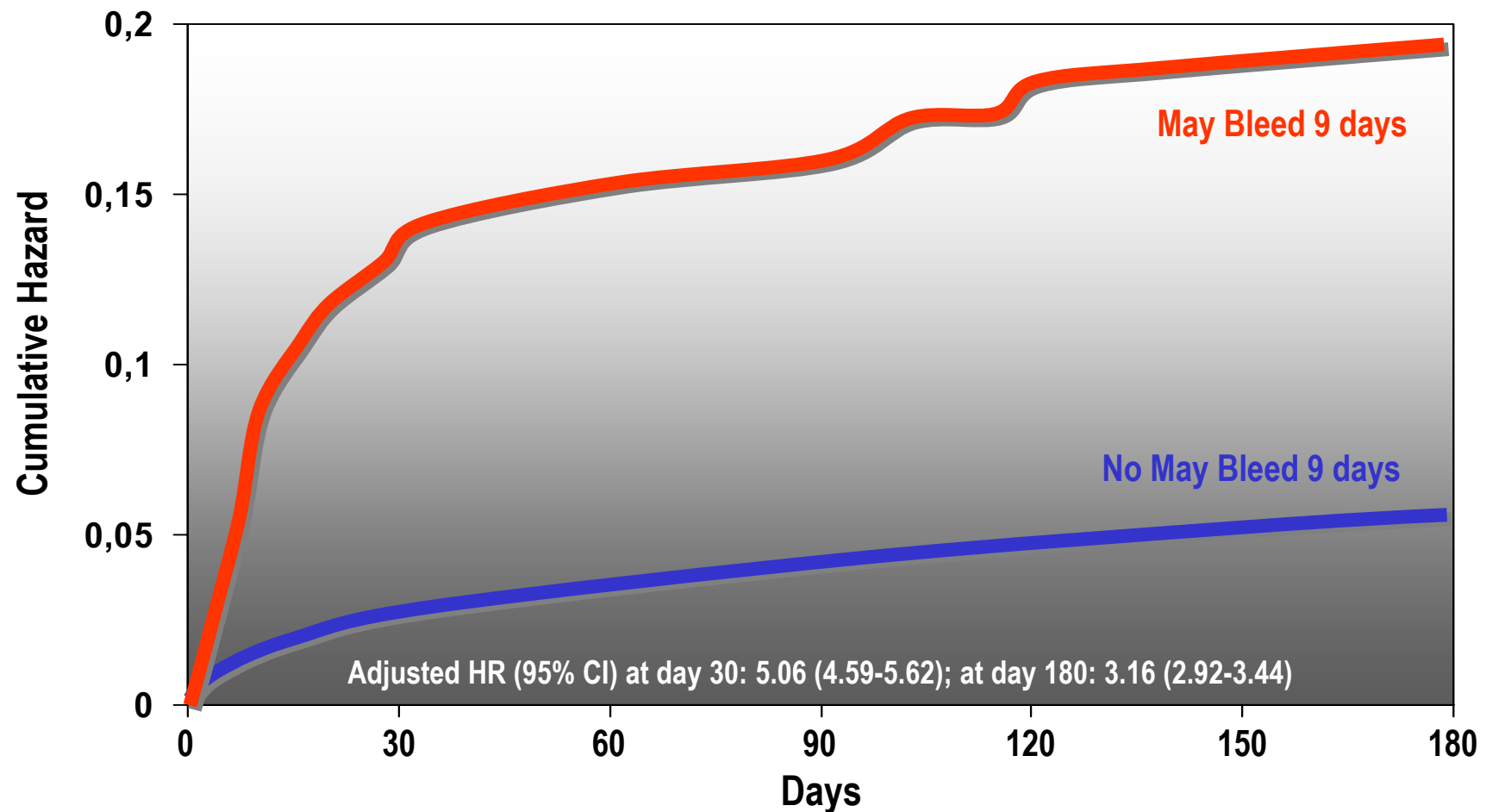


Eikelboom *Circulation* 2006;114: 774 - 782

*ESC Guidelines for the Management of NSTEMI-ACS (100)*



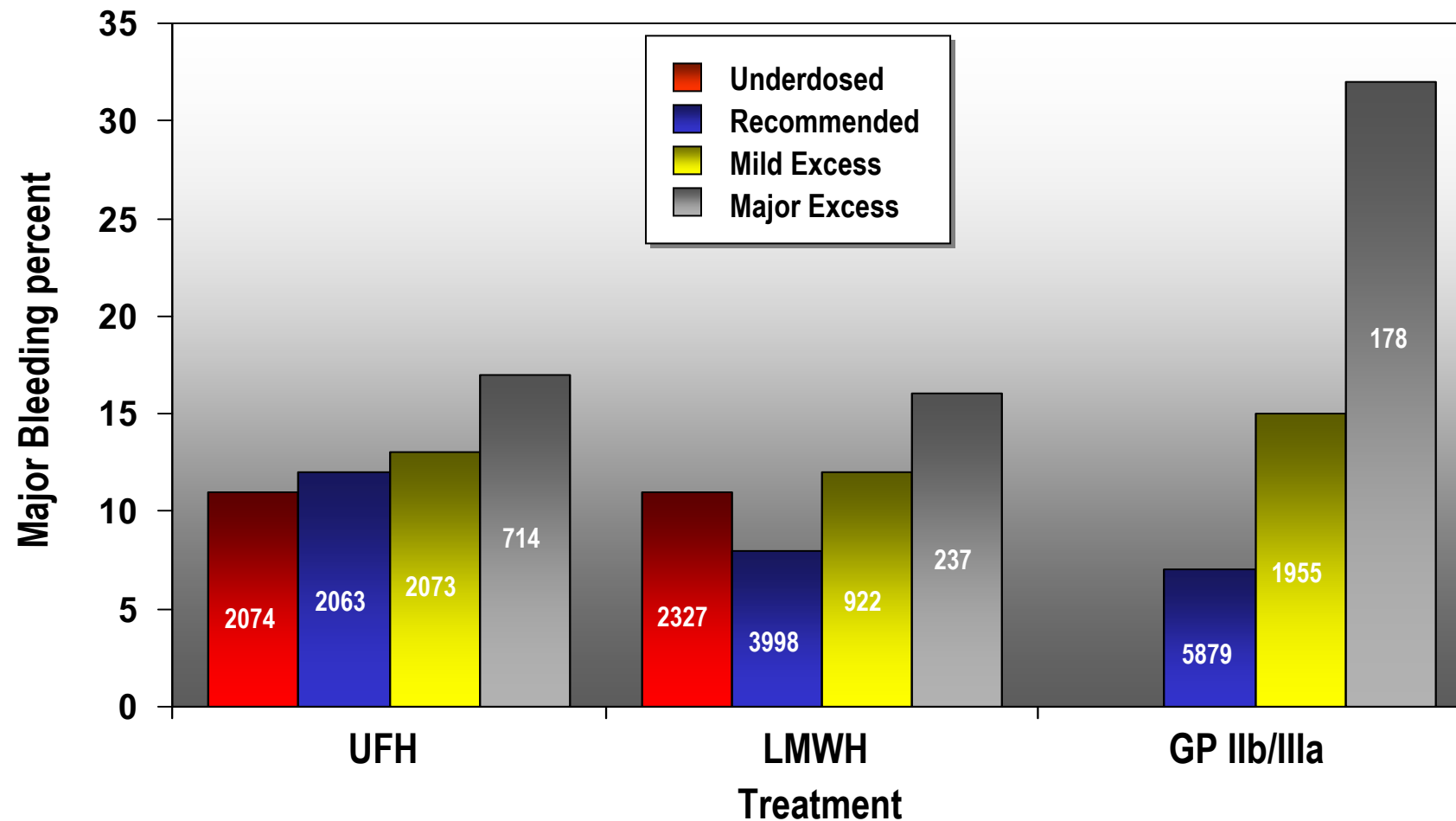
# Increased Mortality at Days 30/180 in Patients with Major Bleeds by Day 9 in OASIS 5



Budaj et al. JACC 2006;abstract 972-224

# Dosage of Drugs and Major Bleeding

## *Dose Group*



Alexander JAMA 2004;294:3108

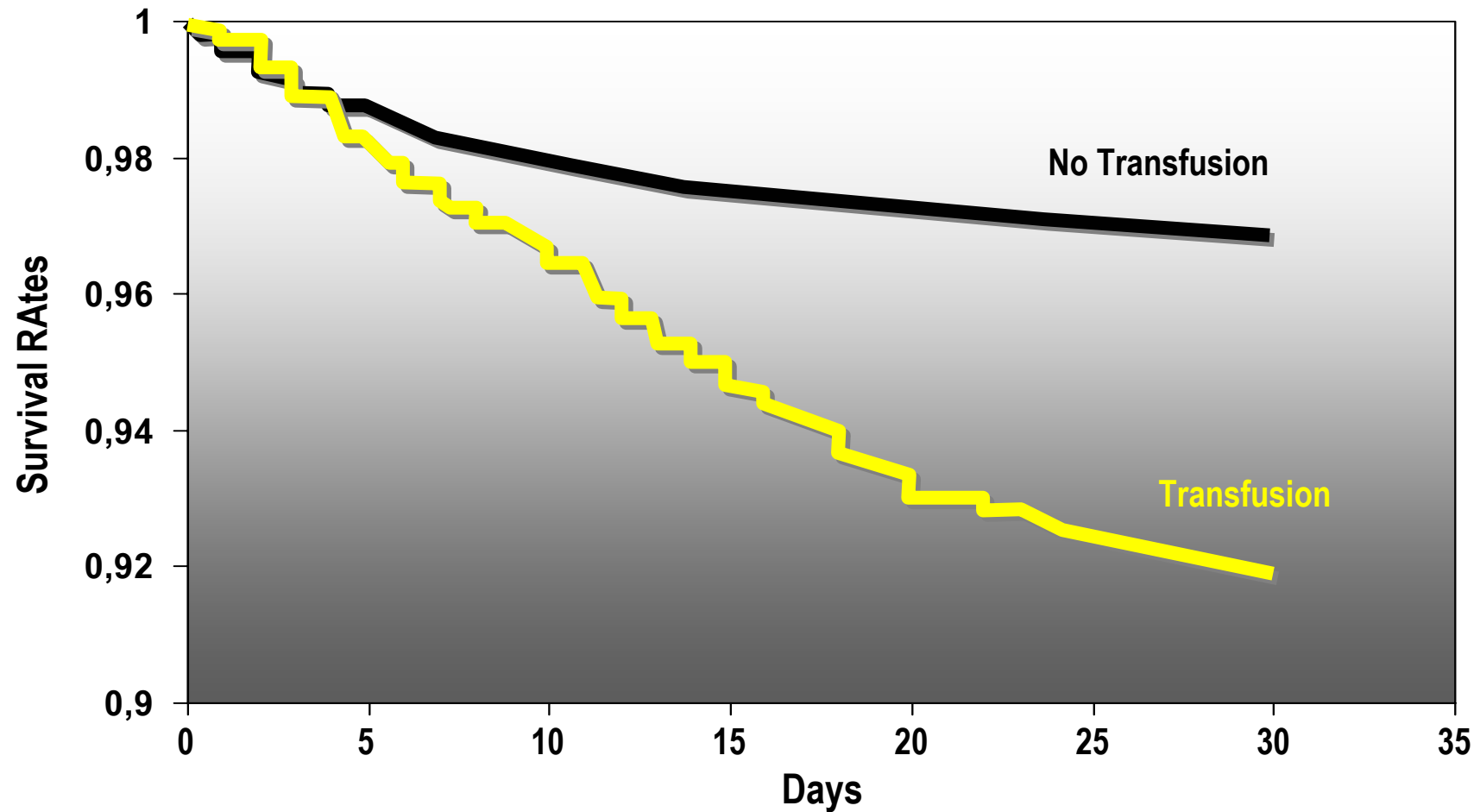
*ESC Guidelines for the Management of NSTEMI-ACS (102)*



# 30 Day Survival by Transfusion Group

## GUSTO IIb, PURSUIT, PARAGON B

(n=24,000 10% transfused)



Rao SV, JAMA 2004;292:1555

ESC Guidelines for the Management of NSTEMI-ACS (103)



# Recommendations for Bleeding Complications (1)

- **Assessment of bleeding risk is an important component of the decision making process. Bleeding risk is increased with higher or excessive doses of anti-thrombotic agents, length of treatment, combinations of several anti-thrombotic drugs, switch between different anticoagulant drugs, as well as with older age, reduced renal function, low body weight, female gender, baseline haemoglobin and invasive procedures (I-B).**
- **Bleeding risk should be taken into account when deciding for a treatment strategy. Drugs, combination of drugs and non-pharmacological procedures (vascular access) known to carry a reduced risk of bleeding should be preferred in patients at high risk of bleeding (I-B)**

# Recommendations for Bleeding Complications (2)

- **Minor bleeding should preferably be managed without interruption of active treatments (I-C).**
- **Major bleeding requires interruption and/or neutralisation of both anticoagulant and antiplatelet therapy, unless bleeding can be adequately controlled by specific haemostatic intervention (I-C).**
- **Blood transfusion may have deleterious effects on outcome, and should therefore be considered individually, but withheld in haemodynamically stable patients with haematocrit >25% or haemoglobin level > 8g/L (I-C).**

# Recommendations for Thrombocytopenia

- Significant thrombocytopenia ( $<100,000/\mu\text{L}$  or  $>50\%$  drop in platelet count) occurring during treatment with GP IIb/IIIa inhibitors and/or heparin (LMWH or UFH) requires the immediate interruption of these drugs. (I-C)
- Severe thrombocytopenia ( $<10,000/\mu\text{L}$ ) induced by GP IIb/IIIa inhibitors requires platelet transfusion with or without fibrinogen supplementation with fresh frozen plasma or cryoprecipitate in case of bleeding. (I-C)
- Interruption of heparin (UFH or LMWH) is warranted in case of documented or suspected HIT. In case of thrombotic complications, anticoagulation can be achieved with DTI (I-C).
- Prevention of HIT can be achieved with use of anticoagulants devoid of risk of HIT, such as fondaparinux or bivalirudin, or by brief prescription of heparin (UFH or LMWH) in case these compounds are chosen as anticoagulant (I-B).

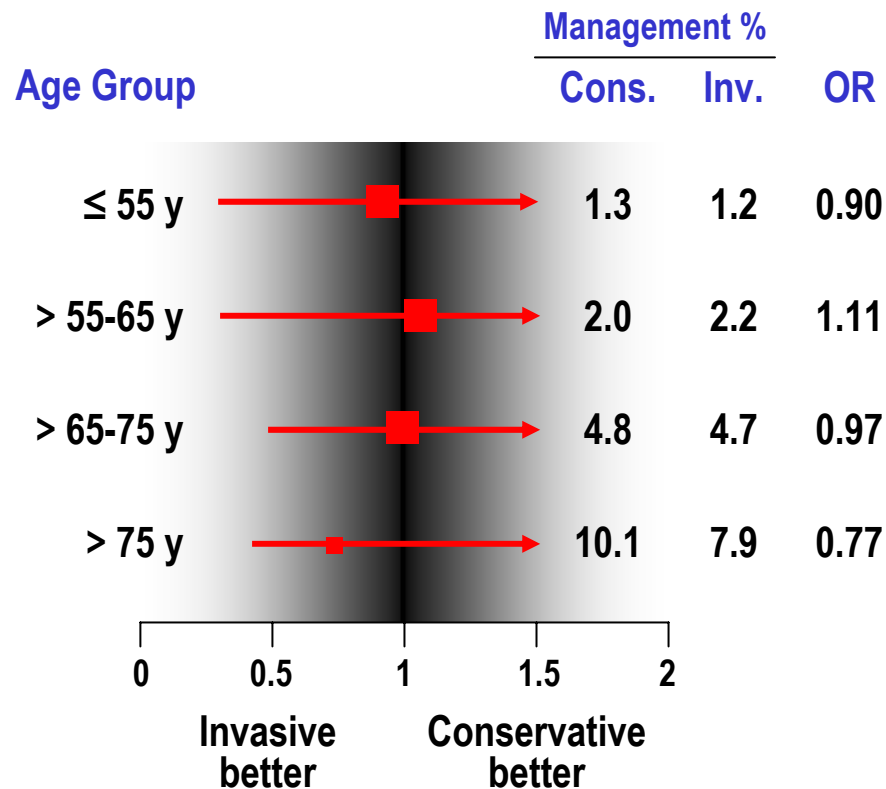
# Special Conditions & Populations

## Elderly

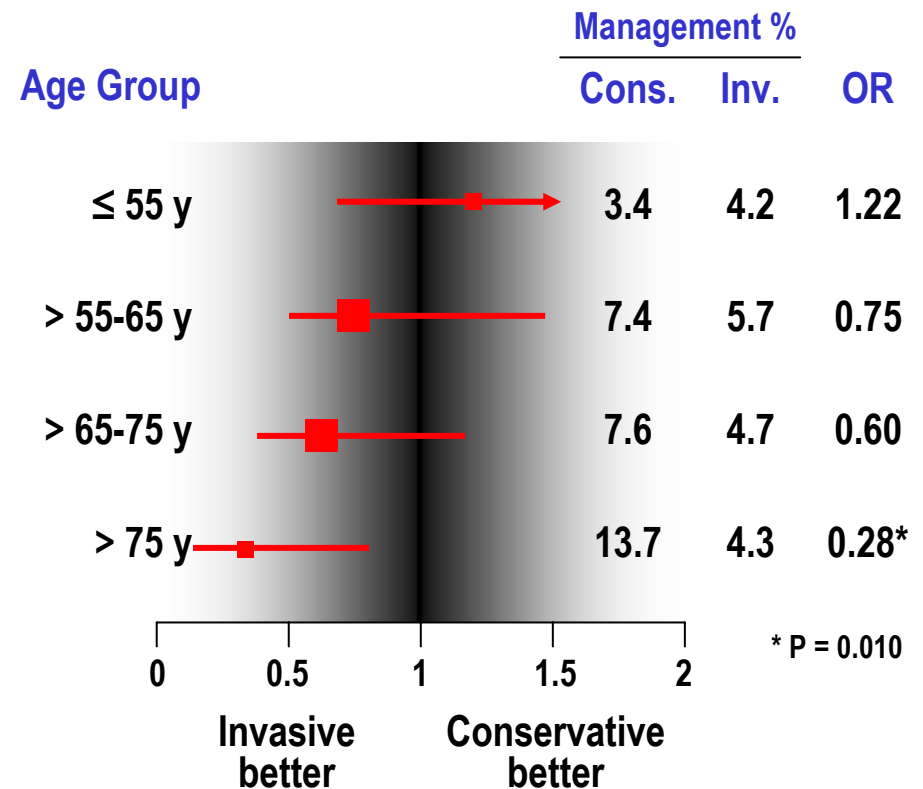
### Impact of Gender

# Clinical Outcomes for Patients Stratified by Age (Invasive Vs Conservative Strategies) from TACTICS-TIMI-18 Trial

## Death



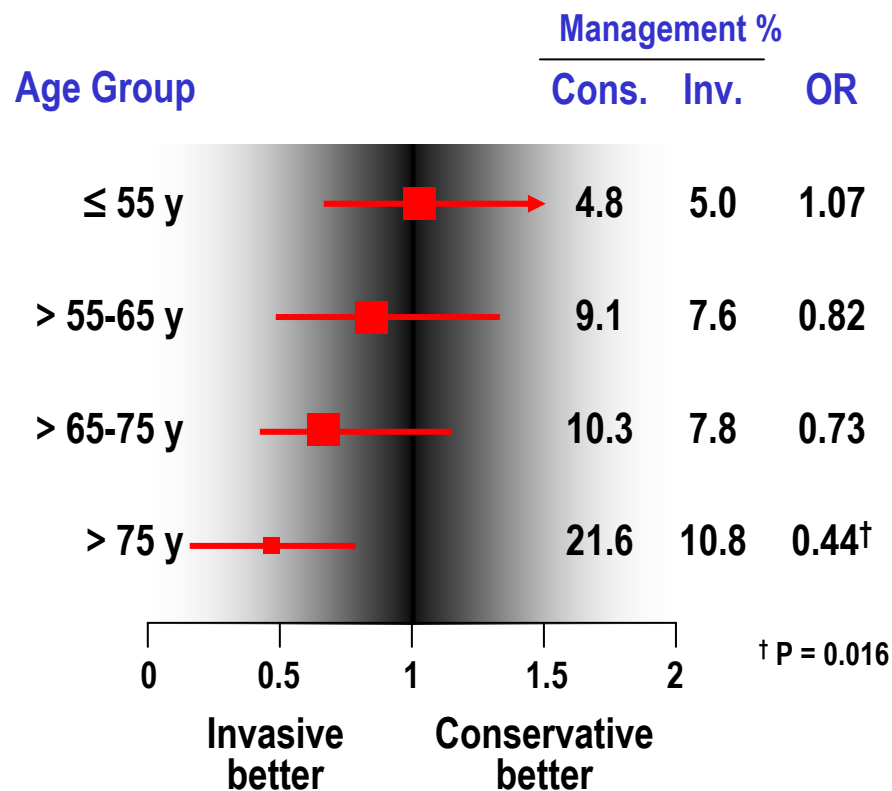
## Nonfatal MI



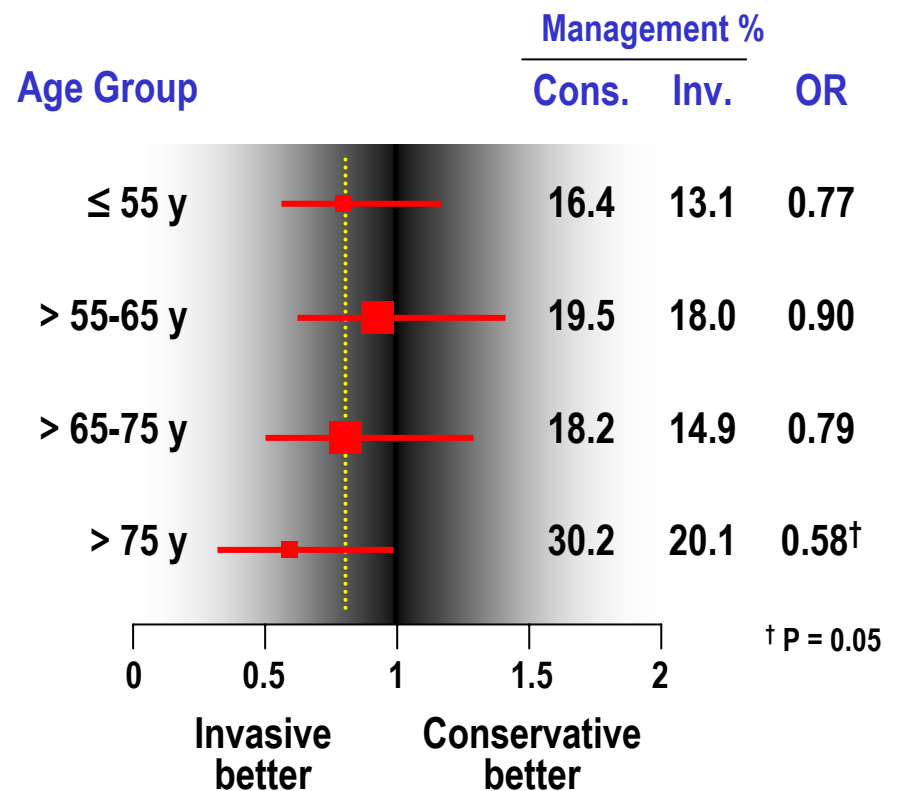
*Am J Cardiol* 2003;91:1466

# Clinical Outcomes for Patients Stratified by Age (Invasive Vs Conservative Strategies) from TACTICS-TIMI-18 Trial

## Death or Nonfatal MI



## Death, MI or Rehospitalization



*Am J Cardiol 2003;91:1466*

# Recommendations for Special Populations

## Elderly

- **Elderly patients (>75 years) often have atypical symptoms. Active screening for NSTEMI-ACS should be initiated at lower levels of suspicion than among younger (<75 years) patients (I-C).**
- **Treatment decisions in the elderly should be tailored according to estimated life expectancy, patient wishes and co-morbidities to minimize risk and improve morbidity and mortality outcomes in this frail but high-risk population. (I – C)**
- **Elderly patients should be considered for routine early invasive strategy, after careful evaluation of their inherent raised risk of procedure-related complications, especially during CABG (I – B).**

## Women

- **Women should be evaluated and treated in the same way as men, with special attention to co-morbidities (I-B).**

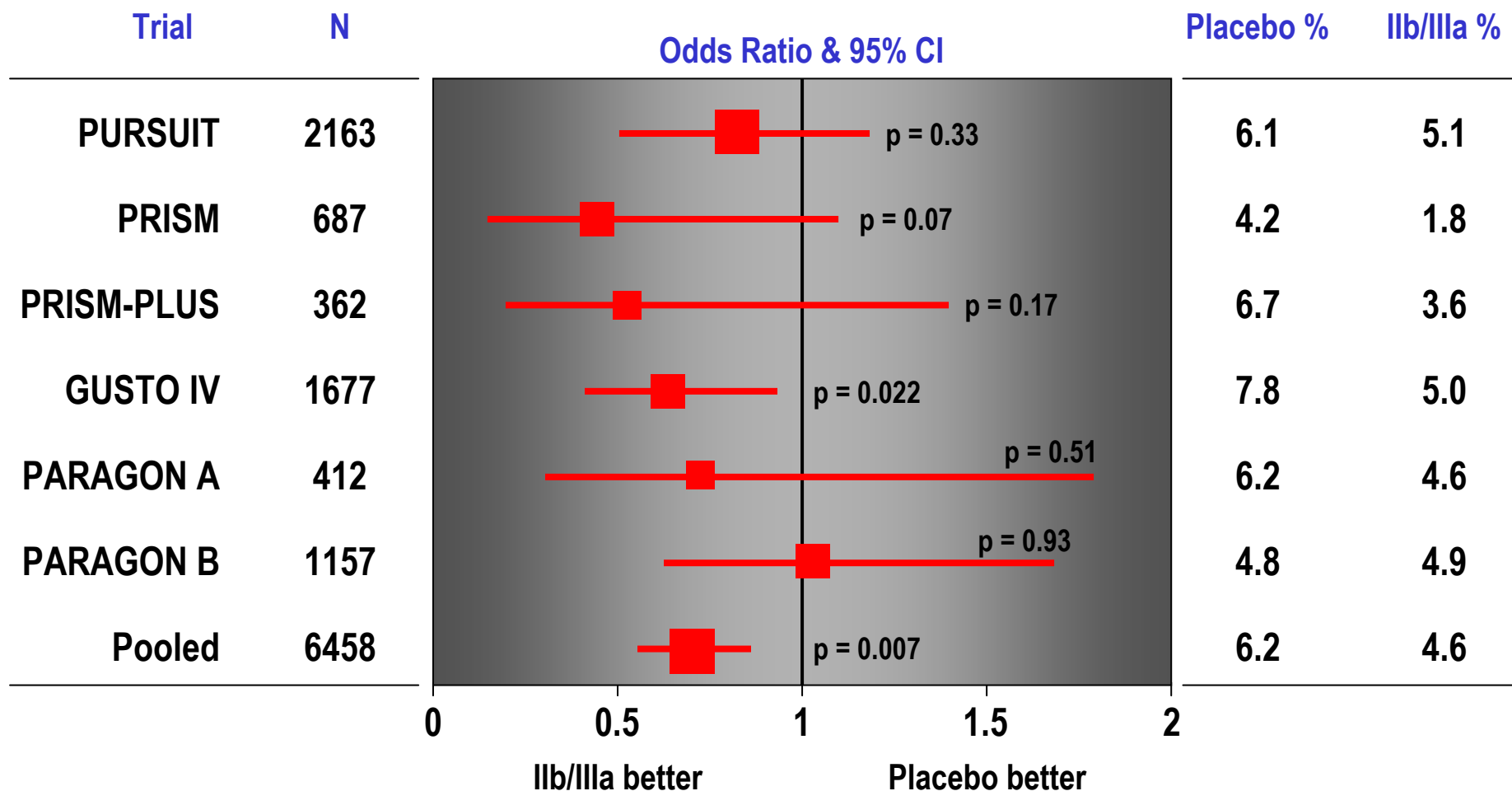
# Special Conditions & Populations

## Diabetes

*ESC Guidelines for the Management of NSTEMI-ACS (111)*



## Treatment Effect on 30-day Mortality Among Diabetic Patients with NSTEMI ACS from Six Randomised Clinical Trials



*Circulation* 2001;104:2767

# Recommendations for Diabetes

- **Tight glycaemic control to achieve normoglycaemia as soon as possible is recommended in all diabetic patients with NSTEMI-ACS in the acute phase (I-C).**
- **Insulin infusion may be needed to achieve normoglycaemia in selected NSTEMI-ACS patients with high blood glucose levels at admission (IIa-C)**
- **Early invasive strategy is recommended for diabetic patients with NSTEMI-ACS (I – A).**
- **Diabetic patients with NSTEMI-ACS should receive intravenous GP IIb/IIIa inhibitors as part of the initial medical management which should be continued through the completion of PCI (IIa-B).**

# Special Conditions & Populations

## Anaemia

*ESC Guidelines for the Management of NSTEMI-ACS (114)*



# Recommendations for Anaemia

- **Low baseline haemoglobin is an independent marker of the risk of ischaemic and bleeding events at 30 days. It should be taken into consideration in assessing initial risk (I-B).**
- **All necessary measures should be taken during the course of initial management to avoid worsening of anaemia by bleeding (I-B).**
- **Well tolerated anaemia at baseline in patients with NSTEMI-ACS should not lead to systematic blood transfusion which should be considered only in case of compromised haemodynamic status (I-C).**

# Special Conditions & Populations

## Chronic Kidney Disease

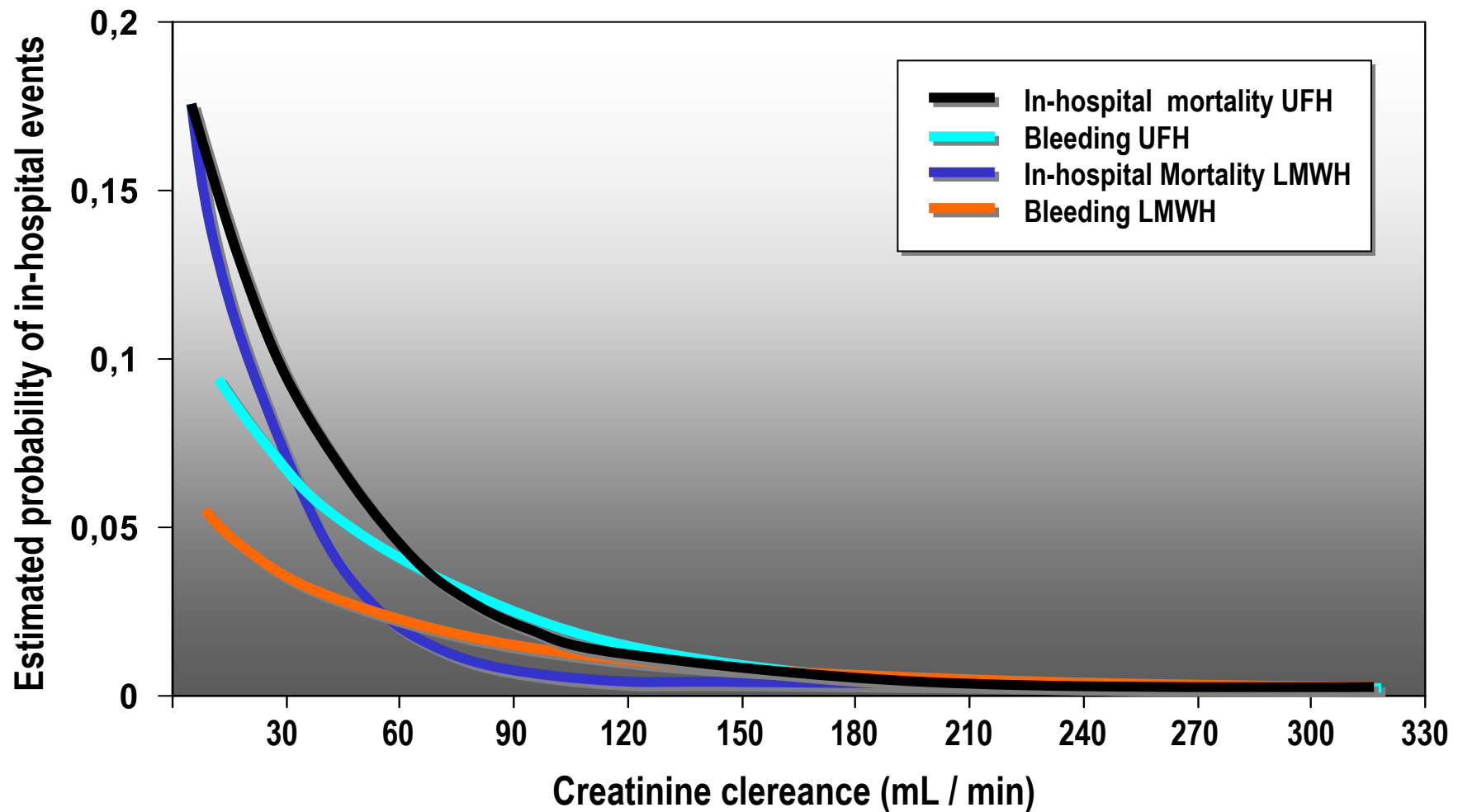
*ESC Guidelines for the Management of NSTEMI-ACS (116)*



# Stages of CKD, according to the National Kidney Foundation

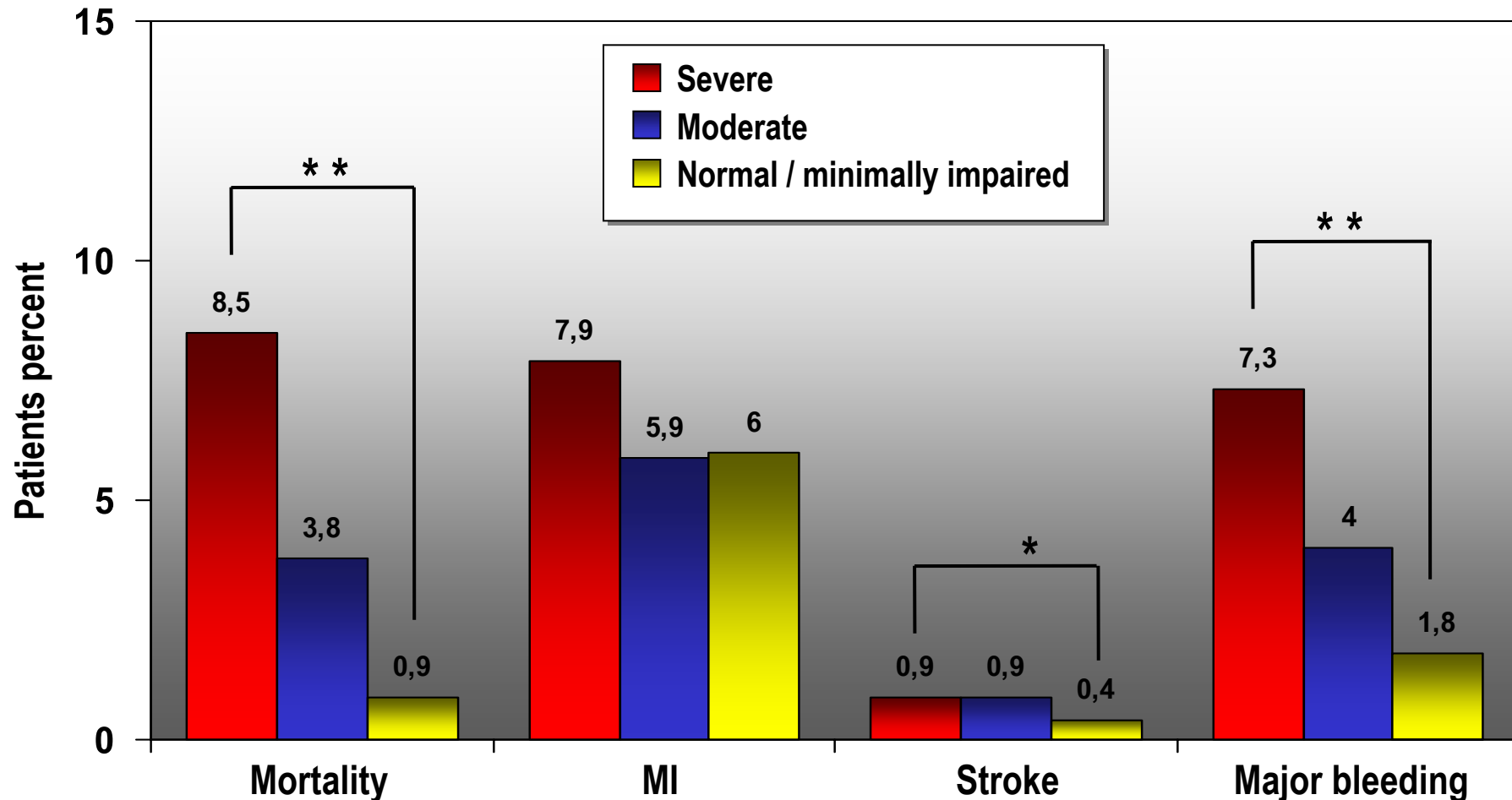
Stage	Description	GFR (mL/min/1.73m <sup>2</sup> )
1	Kidney damage with normal or increased GFR	≥90
2	Kidney damage with mild decrease in GFR	60-89
3	Moderate decrease in GFR	30-59
4	Severe decrease in GFR	15-29
5	Kidney failure	<15 (or dialysis)

# In-hospital Mortality or Bleeding According to the Level of CrCl in Patients Treated with UFH or LMWH



EJH 2005;26:2285

# Outcomes According to Degree of Renal Function Impairment in NSTEMI-ACS Patients in GRACE Registry



Heart 2003;89:1003

ESC Guidelines for the Management of NSTEMI-ACS (119)



# Recommendations for the Use of Drugs in Case of CKD

Drug	Recommendations in case of CKD
Simvastatin*	Low renal elimination. In patients with severe renal failure (CrCl <30ml/min), careful with doses >10mg
Ramipril*	Dose adaptation required if CrCl <30ml/min (initial dose 1.25mg daily). Dose must not exceed 5mg per day.
Losartan*	Recommended for the treatment of hypertension or renal failure in diabetes type 2 with microalbuminuria 50-100mg per day. Regular monitoring of electrolyte balance and serum creatinine is recommended.
Clopidogrel	No information in patients with renal failure
Enoxaparin*	In case of severe renal failure (CrCl<30mL/min), either contraindicated or dose adjustment required, according to country-specific labelling.
Fondaparinux	Contraindicated in severe renal failure (CrCl <30ml/min). However, as much lower risk of bleeding complications were observed in Oasis-5 with fondaparinux as compared with enoxaparin, even in patients with severe renal failure, this drug might be the anticoagulant of choice in this situation.
Bivalirudin	If the CrCl < 30 mL/min, reduction of the infusion rate to 1.0 mg/kg/h should be considered. If a patient is on haemodialysis, the infusion should be reduced to 0.25 mg/kg/h. No reduction in the bolus dose is needed.
Tirofiban	Dose adaptation required in patients with renal failure. 50% of the dose only if CrCl <30ml/min.
Eptifibatide	As 50% of eptifibatide is cleared through the kidney in patients with renal failure, precautions must be taken in patients with impaired renal function (CrCl <50ml/min). The infusion dose should be reduced to 1µg/kg/min in such patients. The dose of the bolus remains unchanged at 180µg/kg. Eptifibatide is contra-indicated in patients with creatinine clearance <30mL/min.
Abciximab	No specific recommendations for the use of abciximab, or for dose adjustment in case of renal failure. Careful evaluation of haemorrhagic risk is needed before using the drug in case of renal failure.
Atenolol	Half dose recommended for patients with CrCl between 15 and 35ml/min (50mg/day). Quarter dose (25mg/day) recommended if CrCl <15ml/min.

# Recommendations for Patients with CKD (1)

- CrCl and/or GFR should be calculated for every patient hospitalised for NSTEMI-ACS (I-B). Elderly people, women and low body weight patients merit special attention as near normal serum creatinine levels may be associated with lower than expected CrCl and GFR levels (I-B).
- Patients with CKD should receive the same first-line treatment as any other patient, in the absence of contra-indications (I-B).
- In patients with CrCl < 30ml/min or GFR <30ml/min/1.73m<sup>2</sup>, a careful approach to the use of anticoagulants is recommended, since dose adjustment is necessary with some, while others are contraindicated. (I-C)

# Recommendations for Patients with CKD (2)

- UFH infusion adjusted according to aPTT is recommended when  $\text{CrCl} < 30\text{ml/min}$  or  $\text{GFR} < 30\text{ml/min}/1.73\text{m}^2$  (I-C).
- GP IIb/IIIa inhibitors can be used in case of renal failure. Dose adaptation is needed with eptifibatide and tirofiban. Careful evaluation of the bleeding risk is recommended for abciximab (I-B).
- Patients with CKD with  $\text{CrCl} < 60\text{ ml/min}$  are at high risk of further ischaemic events and therefore should be submitted to invasive evaluation and revascularisation whenever possible (IIa-B).
- Appropriate measures are advised to reduce the risk of contrast induced nephropathy (I-B).

# Management Strategy

*ESC Guidelines for the Management of NSTEMI-ACS (123)*



# Diagnosis and risk stratification

## 1<sup>st</sup> step: Initial Evaluation

- Quality of chest pain
- Assessment of likelihood of CAD
- ECG (ST elevation or other ECG abnormalities)

**STRATEGY**

## 2<sup>nd</sup> step: Validation & Risk Assessment

- Biochemistry
- Responsiveness to antianginal treatment
- ECG (repeat, continuous monitoring)
- Echocardiography, MRI, CT
- Risk score

# Treatment

## 3<sup>rd</sup> step: Invasive Management

- Emergent
- Early
- No/elective

## 4<sup>th</sup> step: Revascularisation

## 5<sup>th</sup> step: Long-term management

# Risk Stratification

## 1. Features of high risk that mandates urgent angiography / revascularization

- Refractory angina (e.g. evolving MI without ST abnormalities)
- Recurrent angina despite intense antianginal treatment associated with ST depression ( $\geq 2$  mm) or deep negative T waves.
- Clinical symptoms of heart failure or haemodynamic instability (“ shock”)
- Life threatening arrhythmias (ventricular fibrillation or ventricular tachycardia)

# Risk Stratification

## 2 - Features of high risk that mandates early (<72 hours) angiography / revascularization

- Elevated troponin levels
- Dynamic ST or T wave changes (symptomatic or silent) ( $\geq 0.5\text{mm}$ )
- Diabetes mellitus
- Reduced renal function ( $\text{GFR} < 60 \text{ ml/min/1.73m}^2$ )
- Depressed LVEF  $< 40\%$
- Early post MI angina
- PCI within 6 months
- Prior CABG
- Intermediate to high risk according to a risk score

# GRACE ACS Risk Model

The screenshot shows the GRACE ACS Risk Model calculator interface. At the top, the logo for GRACE (Global Registry of Acute Coronary Events) is displayed next to the title 'ACS Risk Model'. Below the title, there are two tabs: 'At Admission (in-hospital/to 6 months)' and 'At Discharge (to 6 months)'. The 'At Admission' tab is active. On the left side, there are input fields for Age (Years), HR (bpm), SBP (mmHg), Creat. (µmol/l), and CHF (Killip Class). A 'US Units' button is located below the CHF field. On the right side, there are three checkboxes: 'Cardiac arrest at admission', 'ST-segment deviation', and 'Elevated cardiac enzymes/markers'. Below these checkboxes is a table showing the probability of death and death or MI for in-hospital and to 6 months. The table has three columns: 'Probability of', 'Death', and 'Death or MI'. The rows are 'In-hospital' and 'To 6 months'. The cells contain dashes. At the bottom right, there is a 'Reset' button. At the very bottom, there is a navigation bar with links for 'Calculator', 'Instructions', 'GRACE Info', 'References', and 'Disclaimer'.

**GRACE** ACS Risk Model  
Global Registry of Acute Coronary Events

At Admission (in-hospital/to 6 months) | At Discharge (to 6 months)

Age:

HR:

SBP:

Creat.:

CHF:

Cardiac arrest at admission  
 ST-segment deviation  
 Elevated cardiac enzymes/markers

Probability of	Death	Death or MI
In-hospital	<input type="text" value="--"/>	<input type="text" value="--"/>
To 6 months	<input type="text" value="--"/>	<input type="text" value="--"/>

Calculator | Instructions | GRACE Info | References | Disclaimer

*ESC Guidelines for the Management of NSTEMI-ACS (127)*

# Risk Stratification

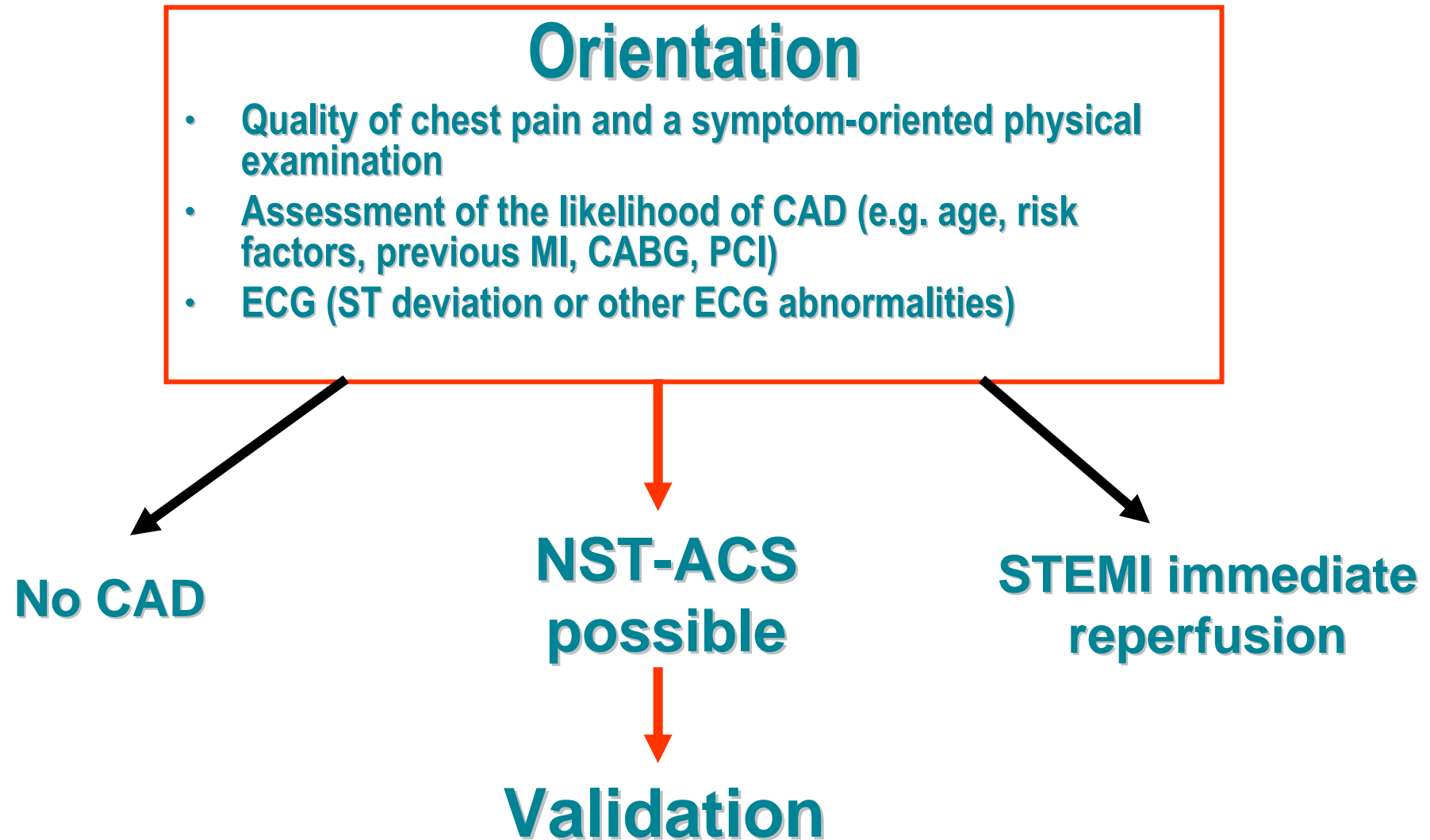
## 3 - No features of high risk

- No recurrence of chest pain
- No signs of heart failure
- No abnormalities in the initial ECG or a second ECG (6 to 12 hours)
- No elevation of troponins (arrival and at 6 – 12 hours)

# Primary therapeutic measures

Oxygen	Insufflation (4 to 8 L/min) if oxygen saturation is < 90%
Nitrates	Sublingually or intravenously (caution if systolic blood pressure < 90mmHg)
Aspirin	Initial dose of 160–325mg non-enteric formulation followed by 75–100 mg/d (intravenous administration is acceptable)
Clopidogrel	Loading dose of 300mg (or 600mg for rapid onset of action) followed by 75 mg daily
Anticoagulation	Choice between different options depends on strategy: <ul style="list-style-type: none"> <li>• UFH intravenous Bolus 60–70 IU/kg (maximum 5000 IU) followed by infusion of 12–15 IU/kg/h (IU/h maximum 1000) titrated to aPTT 1.5–2.5 times control</li> <li>• Fondaparinux 2.5 mg/daily subcutaneously</li> <li>• Enoxaparin 1 mg/kg twice/daily subcutaneously</li> <li>• Dalteparin 120 IU/kg twice/daily subcutaneously</li> <li>• Nadroparin 86 IU/kg twice/daily subcutaneously</li> <li>• Bivalirudin 0.1 mg/kg bolus followed by 0.25 mg/kg/h</li> </ul>
Morphine	3 to 5 mg intravenous or subcutaneous, depending on pain severity
Oral betablocker	Particularly, if tachycardia or hypertension without sign of heart failure
Atropine	0.5 - 1 mg intravenously, if bradycardia or vagal reaction

# Management Strategy



# Management Strategy

## Validation

- Routine clinical chemistry, particularly troponins (on presentation and after 6 to 12 hours) and other markers according to working diagnoses (e.g. D-dimers, BNP, NT-proBNP)
- Repeat, preferably continuous ST segment monitoring (when available)
- Echocardiogram, MRI, CT or nuclear imaging for differential diagnoses (e.g. aortic dissection, pulmonary embolism),
- Responsiveness to antianginal treatment
- Risk score assessment
- Bleeding risk assessment

### Urgent < 120 min

- 1- Refractory angina
- 2- Recurrent angina despite intense antianginal treatment associated with ST depression ( $\geq 2$  mm) or deep negative T waves.
- 3- Clinical symptoms of heart failure or haemodynamic instability
- 4- Life threatening arrhythmias (ventricular fibrillation or ventricular tachycardia)

### Early < 72 hours

- Elevated troponin levels
- Dynamic ST or T wave changes
- Diabetes mellitus
- Reduced renal function (GFR < 60 ml/min/1.73m<sup>2</sup>)
- Depressed LVEF < 40%
- Early post MI angina
- PCI within 6 months
- Prior CABG
- Intermediate to high risk (GRACE risk score)

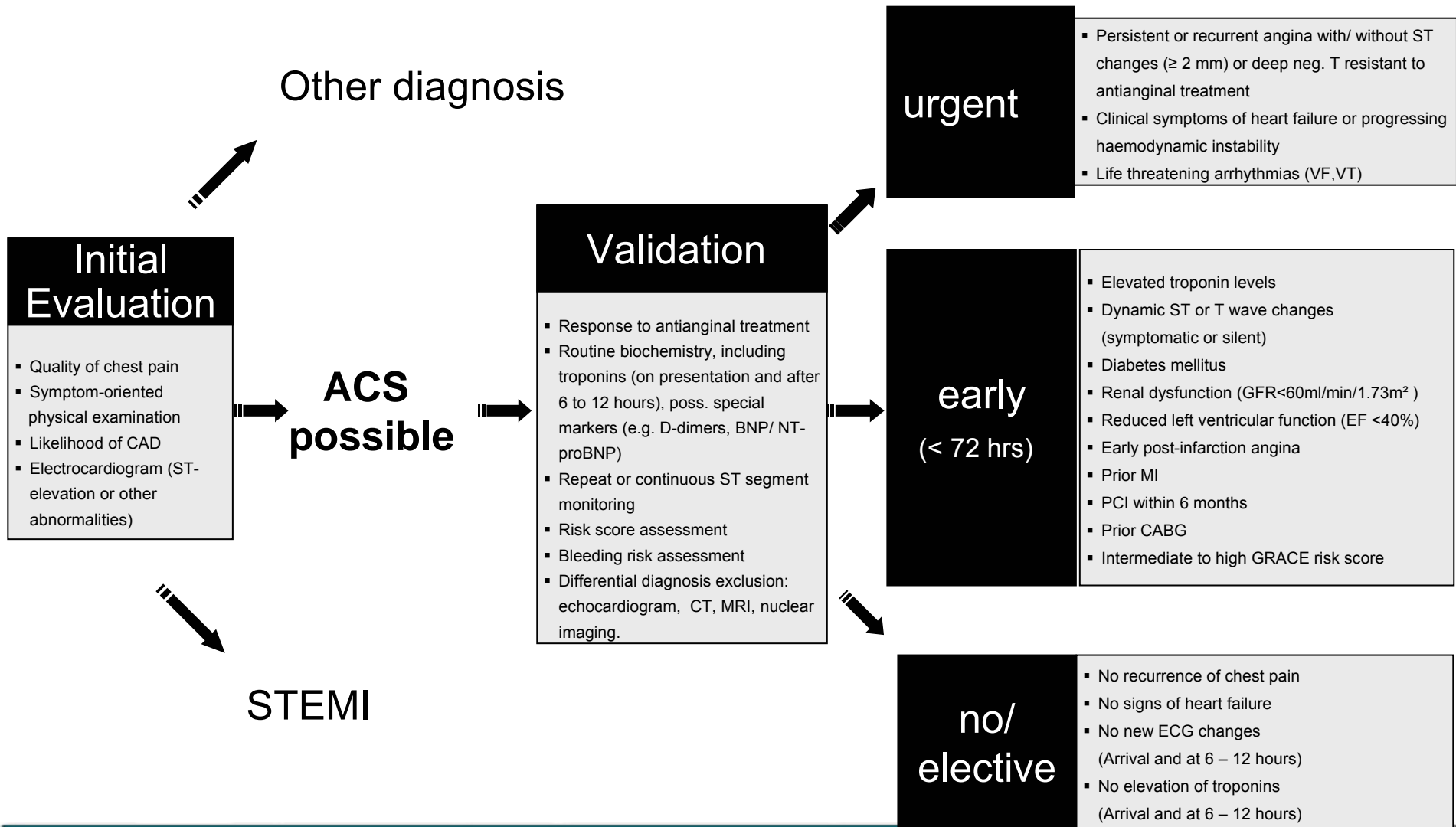
### Elective

- No recurrence of chest pain
- No signs of heart failure
- No abnormalities in the initial ECG or a second ECG (6 to 12 hours)
- No elevation of troponins (arrival and at 6 – 12 hours)

# 1. First Contact

# 2. Diagnosis/Risk Assessment

# 3. Invasive Strategy



# Performance Measures

*ESC Guidelines for the Management of NSTEMI-ACS (133)*



# Recommendations for Performance Measures

- **Development of regional and/or national programmes to systematically measure performance indicators and provide feedback to individual hospitals is strongly encouraged (I-C).**