

Optimising Management in ACS: Insights From New Guidelines

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Spectrum of Acute Coronary Syndrome

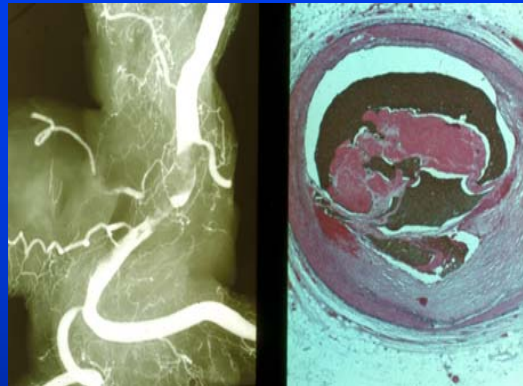
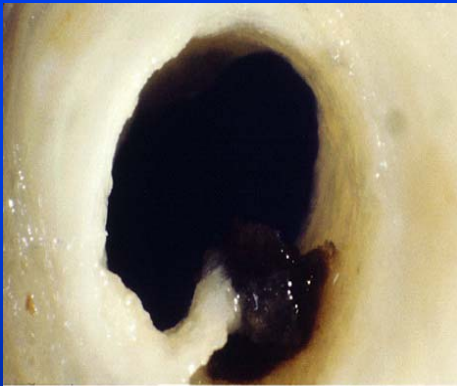
myocardial infarction



unstable
angina

ACS with myocyte
necrosis

ACS with ST \uparrow
myocardial infarction

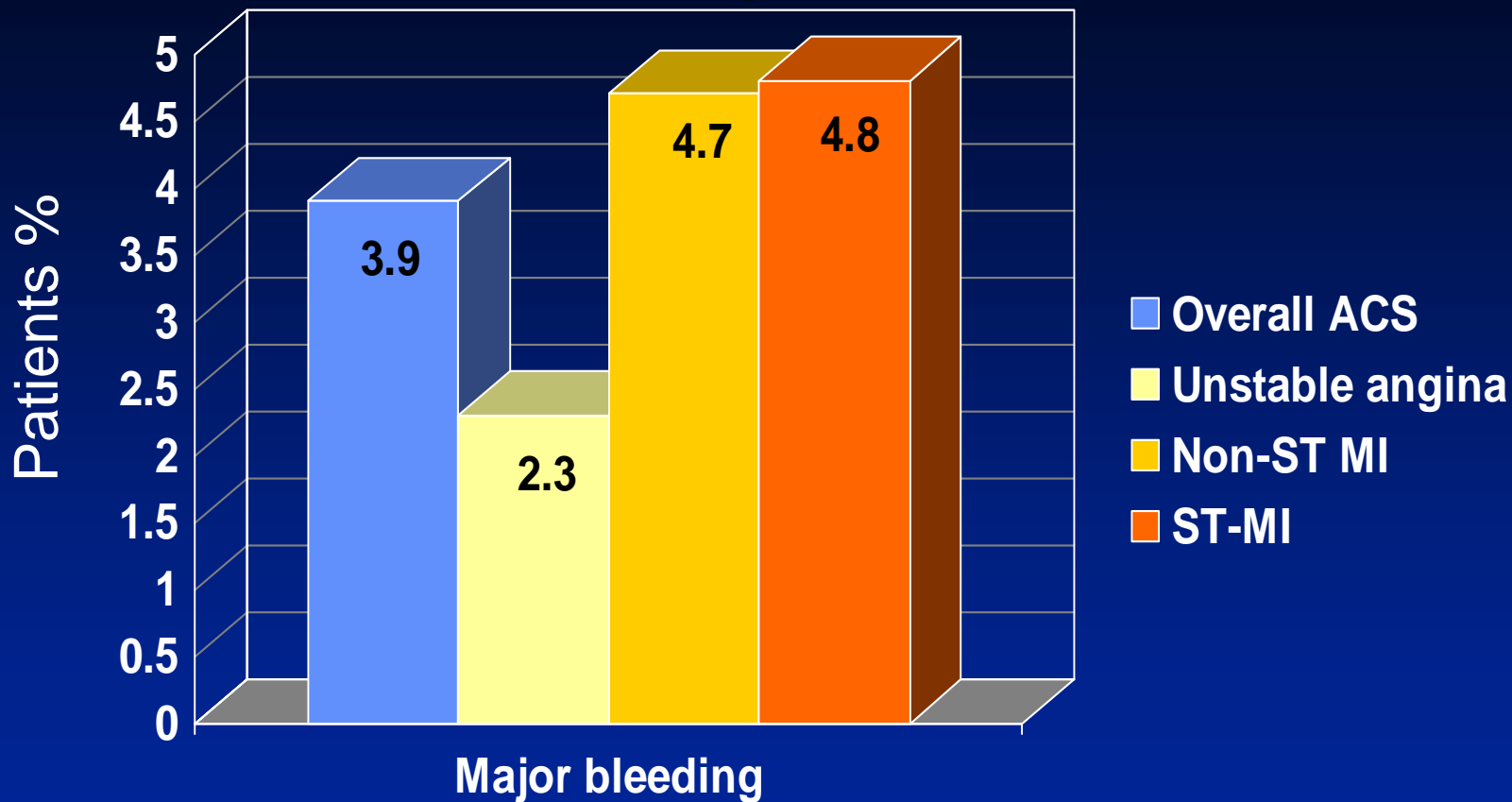


Risk of death: 5-8%

12-15%

Major Bleeding in ACS

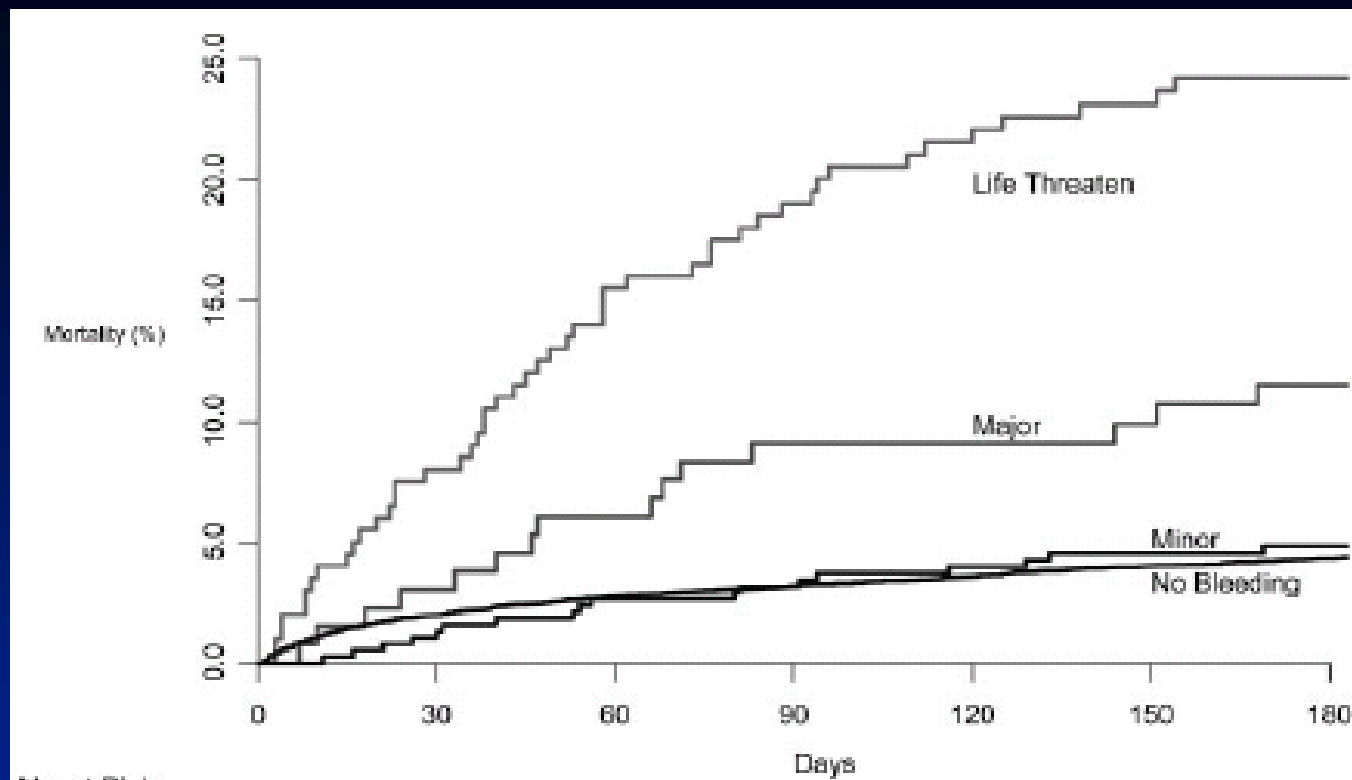
n=24,045 patients



Definition of bleeding:

- Life threatening bleeding requiring a transfusion of 2+ units
- Bleeding resulting in an absolute decrease in hematocrit of $\geq 10\%$
- Bleeding resulting in death

Adverse Impact of Bleeding on Prognosis in ACS



Hazard of bleeding, adjusted for baseline risk:

Death(0-30d)	5.26 (95% CI 3.89–7.11)	p<0.0001
Death(30d-6/12)	1.55 (95% CI 1.01–2.37)	p=0.04
MI (0-30d)	4.51 (95% CI 3.20–6.35)	p<0.0001
Stroke (0-30d)	6.50 (95% CI 3.53–11.98)	p<0.0001

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:

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Italy; Jean-Jacques Blanc, France; Andrzej Budaj, Poland; John Camm, UK;
Veronica Dean, France; Jaap Deckers, The Netherlands; Kenneth Dickstein,**

**NB: the current draft guidelines have been presented
at ESC today (by J-P Bassand), but they are not yet final**

Levels of Evidence

Level of Evidence A	Data derived from at least two randomized clinical trials or meta-analysis.
Level of Evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of Evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

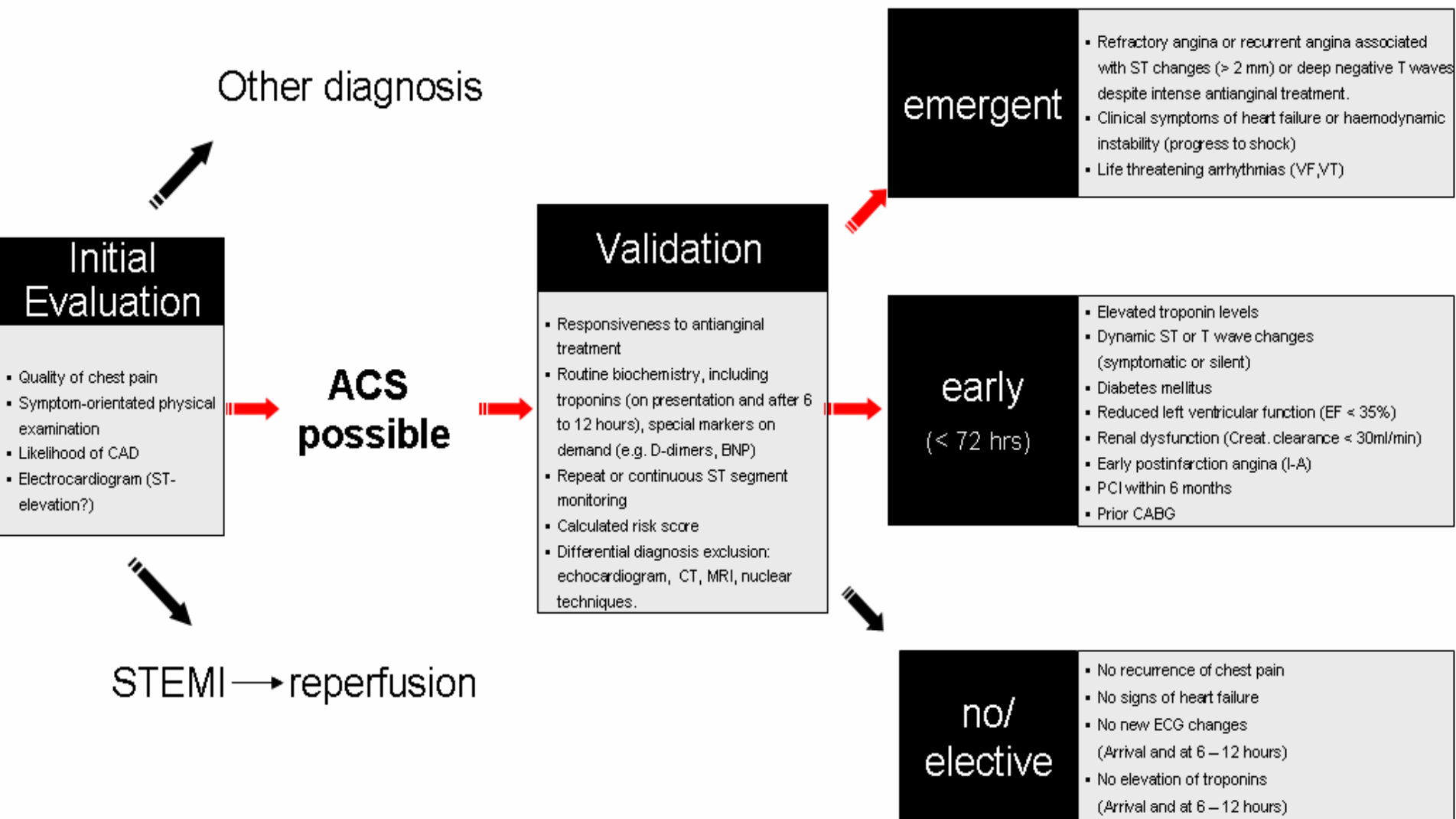
Classes of Recommendations

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

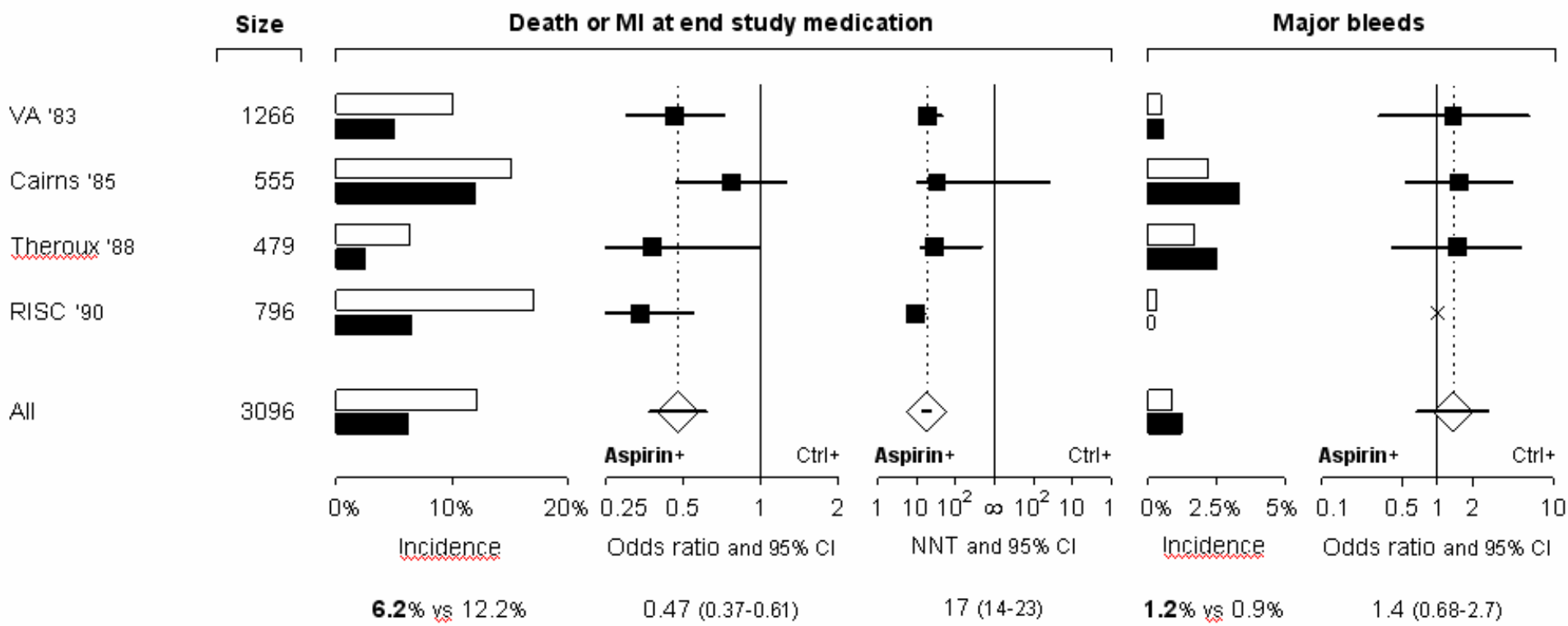
1. First Contact

2. Diagnosis/Risk Assessment

3. Invasive Strategy



Aspirin vs control



Odds ratio for benefit: 0.47 (95% CI 0.37-0.61)
Odds ratio for major bleed 1.4 (95%CI 0.68-2.7)

Recommendations: aspirin

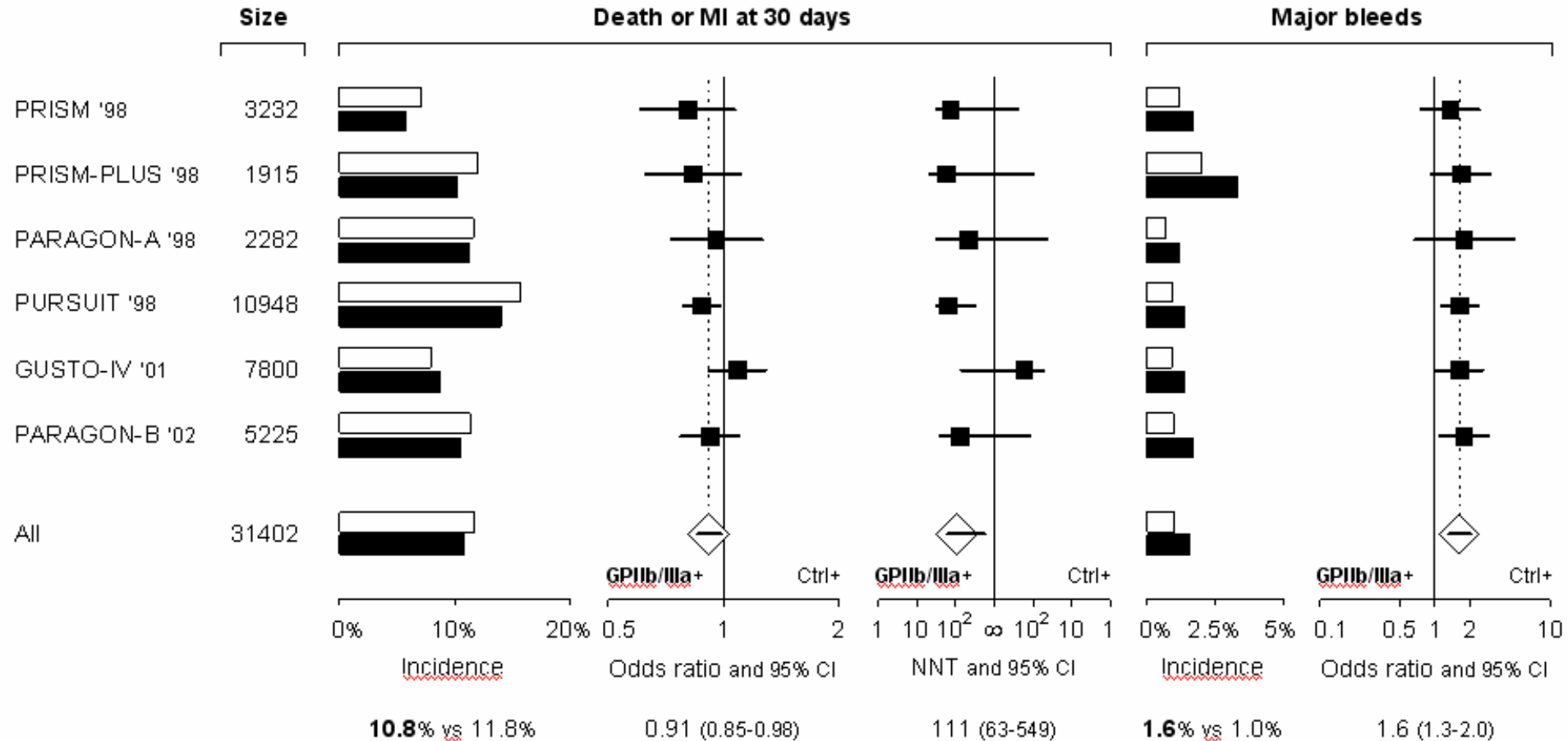
Aspirin recommended for all patients presenting with non-ST elevation ACS, without contraindication (I-A),

initial loading dose of 160 - 325mg (non-enteric) (I-C)

maintenance dose of 75 to 100mg (I-A),

duration lifelong (I-C).

Glycoprotein IIb/IIIa inhibitors versus control in patients not scheduled for PCI



Odds ratio for benefit: 0.91 (95% CI 0.85-0.98)
Odds ratio for major bleed 1.6 (95%CI 1.3-2.0)

Recommendations: glycoprotein IIb/IIIa inhibitors

In high-risk patients, particularly patients with elevated troponin, ST-depression, or diabetes, either eptifibatide or tirofiban for initial early treatment is recommended in addition to other anti-platelet and antithrombin agents. (I-A).

In patients with high-risk features, who received initial treatment with eptifibatide or tirofiban, prior to angiography, these drugs should be maintained during and after PCI. (IIa-B)

In high risk patients not pretreated with GP IIb/IIIa proceeding to immediate PCI, abciximab should be initiated before PCI. (I-A). High dose tirofiban or eptifibatide is less established in this setting. (IIa-C)

Bivalirudin plus IIb/IIIa is similar to UFH/LMWH plus IIb/IIIa.

Bivalirudin (alone) causes less bleeding than UFH/LMWH plus IIb/IIIa.

Long term efficacy of bivalirudin alone, especially in higher risk patients with ACS, is uncertain.

Recommendations: other oral anti-platelet drugs

Clopidogrel recommended for dual antiplatelet therapy (1-A):

immediate 300mg loading dose, then 75mg daily.

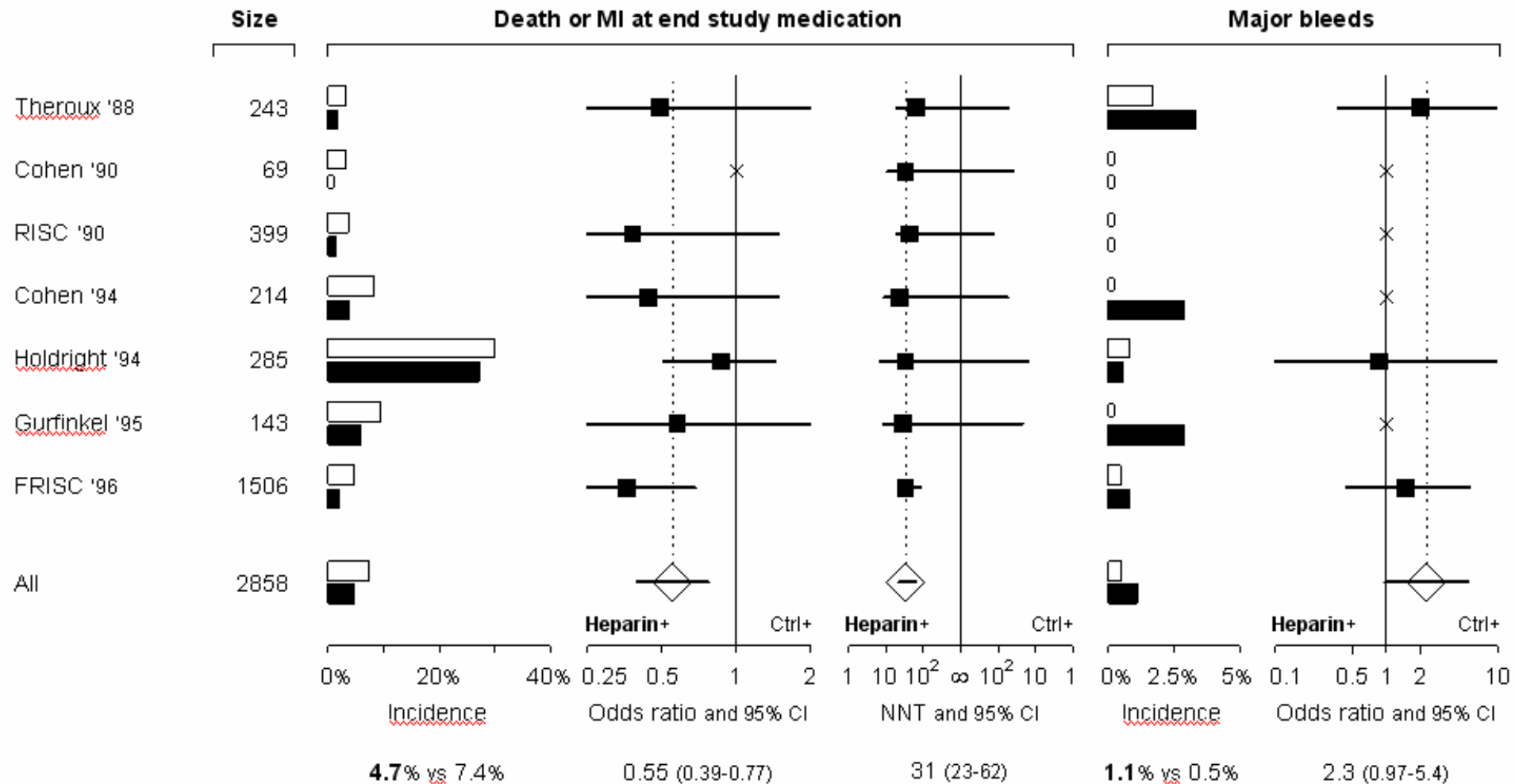
Duration: minimum of 3 months and up to 12 months (1-A).

For aspirin contraindications: clopidogrel lifelong (1-B).

600mg loading dose may be used in patients proceeding to very early angiography/ PCI (IIa-C).

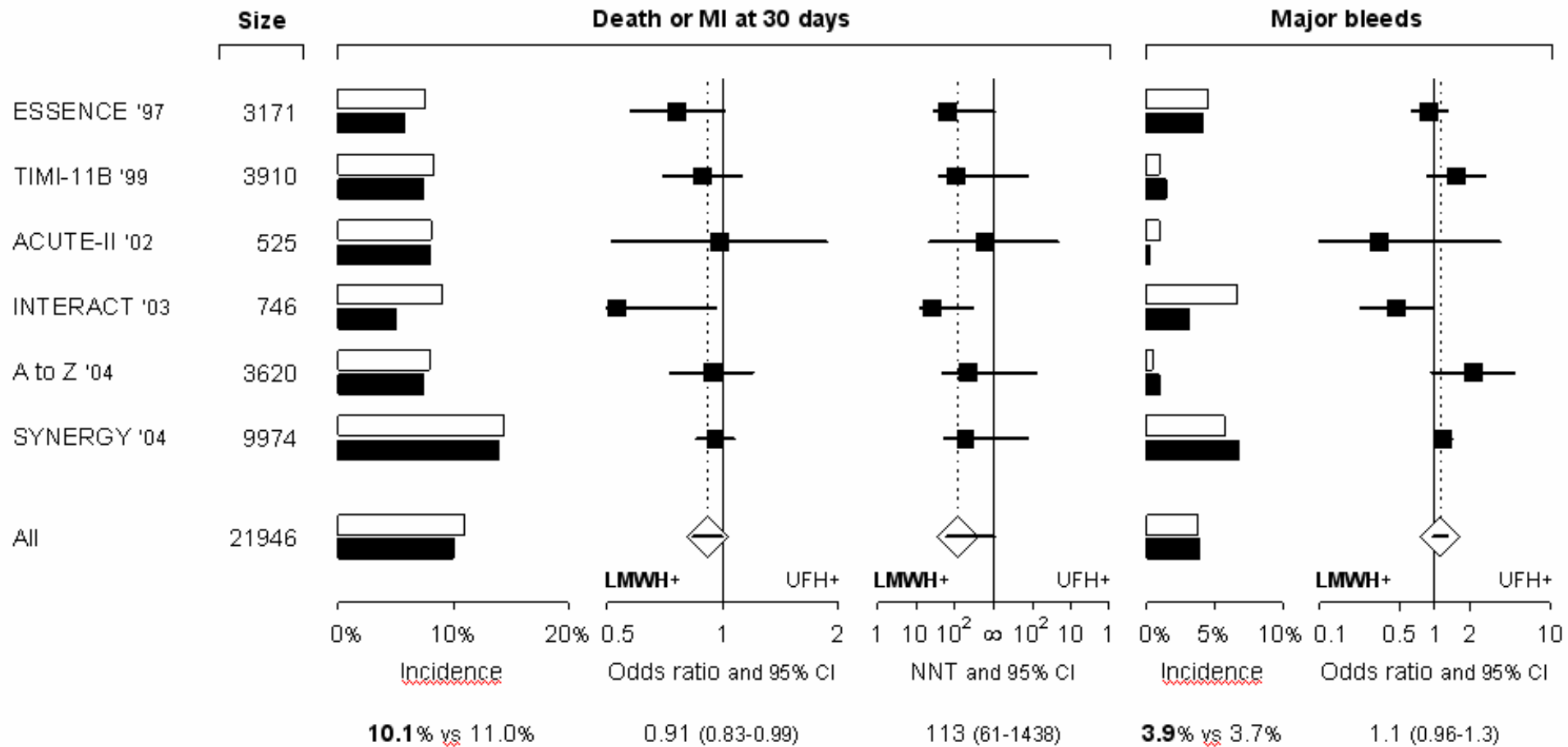
For patients who received a combination of clopidogrel plus aspirin, and who need to undergo CABG surgery, the withdrawal of clopidogrel 5 days before surgery is recommended if clinically feasible (IIa-C).

NSTE-ACS: heparin/LMWH vs control



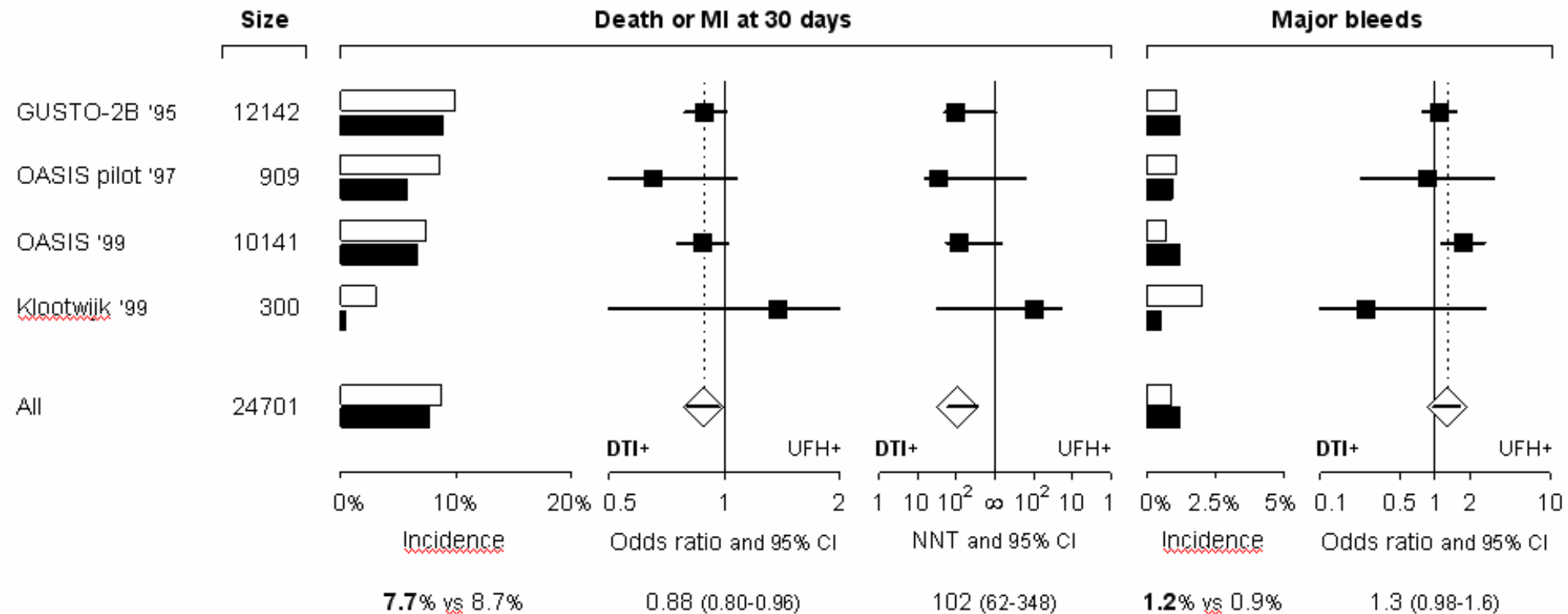
Odds ratio for benefit: 0.55 (95% CI 0.39-0.77)
Odds ratio for major bleed 2.3 (95%CI 0.97-0.54)

LMWH vs UFH



Odds ratio for benefit: 0.91 (95% CI 0.83-0.99)
Odds ratio for major bleed 1.1 (95%CI 0.96-1.3)

Direct thrombin inhibitors vs UFH

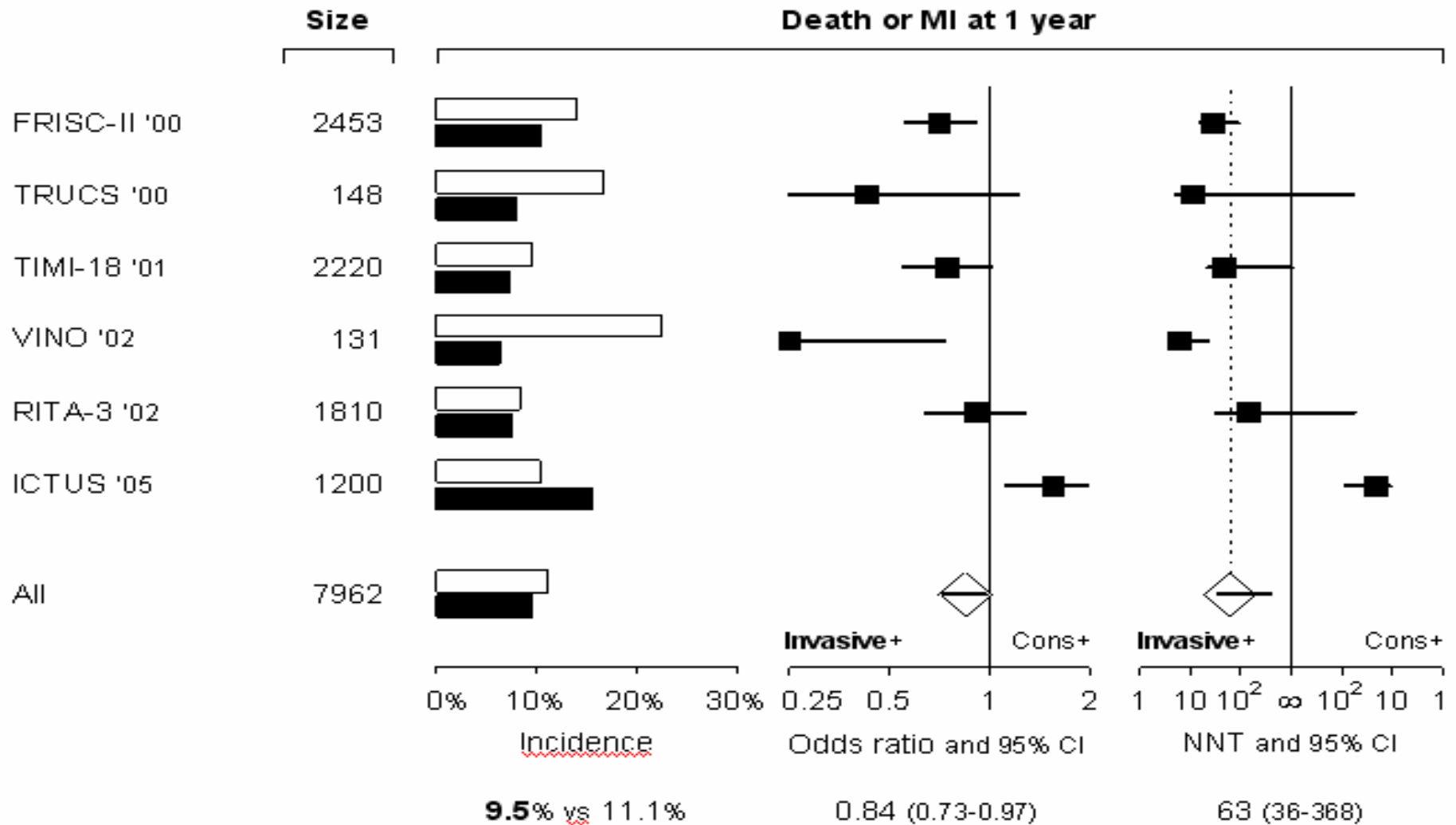


Odds ratio for benefit: 0.88 (95% CI 0.80-0.96)
Odds ratio for major bleed 1.3 (95%CI 0.99-1.6)

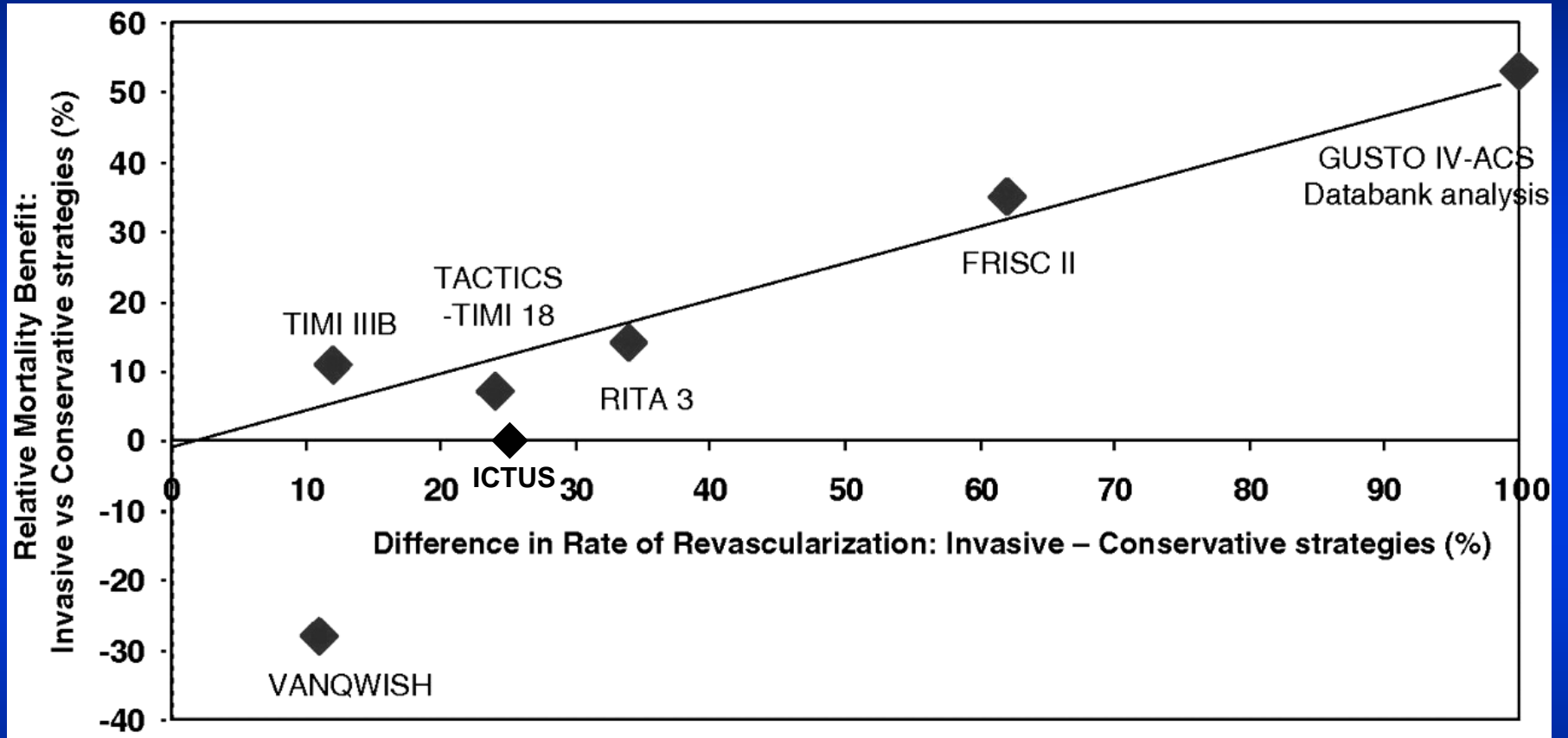
Recommendations: antithrombin treatment

- **Antithrombotic treatment** should be tailored according to the risk of bleeding: (risk increased with higher doses of anti-thrombotics, longer treatment, combinations of antithrombotics, older age, renal dysfunction, low body weight,,female gender, excessive dosage. (I-A)
- **Fondaparinux** recommended as initial anti-thrombotic treatment in NSTEMI-ACS. (esp favourable with increased risk of bleeding e.g older age, renal dysfunction, combination with other antithrombotic medications (I-A).
- **Enoxaparin** may be used as initial anti-thrombotic treatment. (I-A). Risks of bleeding may be reduced with tailored dosing based upon patient characteristics.
- **UFH** may be used as initial treatment for patients with planned urgent invasive procedure (I-A).
- **Bivalirudin** is an alternative to UFH or enoxaparin for patients with an early invasive strategy (I-B).
- **For PCI**, initial anticoagulant treatment should be maintained during the procedure (UFH, enoxaparin or bivalirudin). Additional UFH is necessary with fondaparinux, for PCI (I-C).

Early invasive vs conservative therapy



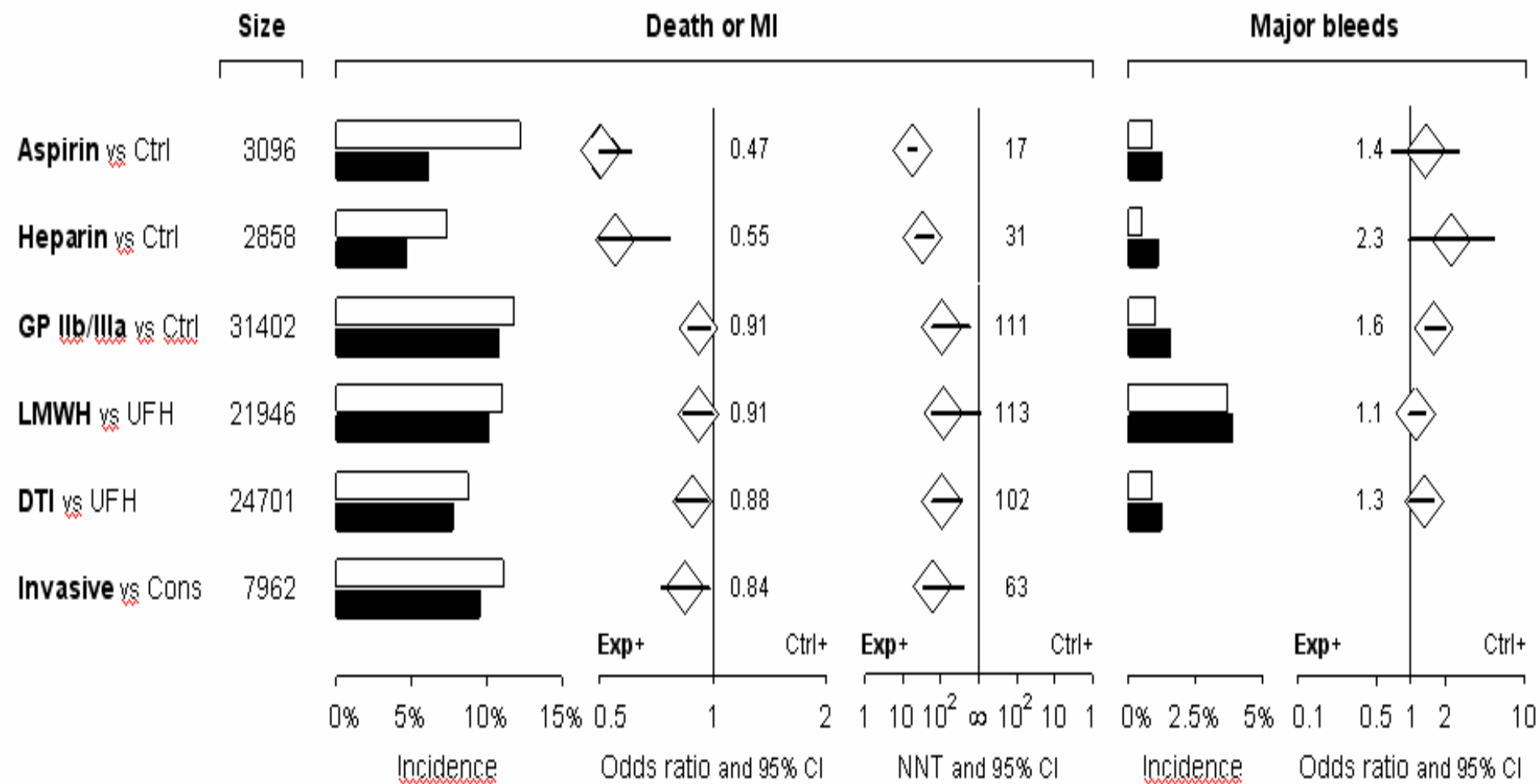
Odds ratio for benefit: 0.84 (95% CI 0.73-0.97)



Recommendations: invasive therapy

- **Emergency coronary angiography** recommended in patients with refractory angina + dynamic ST segment deviation, life threatening arrhythmias or haemodynamic instability (1-C).
- **Early (< 72 hours) coronary angiography** followed by revascularisation in patients with moderate to high-risk features (1-A).
- **Routine invasive evaluation** followed by revascularisation in patients with low-risk features is not recommended (III-A).
- **PCI of lesions without significant stenoses is not recommended** (III-C).
- **Non-invasive assessment of inducible ischaemia** recommended prior to discharge in low-risk patients in whom angiography is not planned (1-C).

Conclusion: risk vs benefit treatment comparisons



A Newton's cradle with five golden spheres is shown against a blue background. The largest sphere on the left is in motion, having just struck or about to strike the others, creating a bright reflection. The background is a gradient of blue, with a horizontal line suggesting a horizon or a reflection on water.

Factor Xa inhibition in acute coronary syndromes:
towards a new paradigm

A Newton's cradle with five brass spheres is shown against a blue background. The spheres are arranged in a diagonal line from the top left to the bottom right. The largest sphere on the left is in motion, having just struck the others, as evidenced by its bright reflection and the slight displacement of the other spheres. The background is a gradient of blue, with a darker blue at the top and a lighter blue at the bottom, suggesting a sky or a calm sea.

Disclaimer

Arixtra is currently not indicated in Acute Coronary Syndromes