ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

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Disclosures

Honoraria/Consulting/Speakers bureau

Astra Zeneca
Bayer
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Sanofi Aventis

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ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC)

Authors/Task Force Members: Christian W. Hamm (Chairperson) (Germany)*, Jean-Pierre Bassand (Co-Chairperson)*, (France), Stefan Agewall (Norway), Jeroen Bax (The Netherlands), Eric Boersma (The Netherlands), Hector Bueno (Spain), Pio Caso (Italy), Dariusz Dudek (Poland), Stephan Gielen (Germany), Kurt Huber (Austria), Magnus Ohman (USA), Mark C. Petrie (UK), Frank Sonntag (Germany), Miguel Sousa Uva (Portugal), Robert F. Storey (UK), William Wijns (Belgium), Doron Zahger (Israel).

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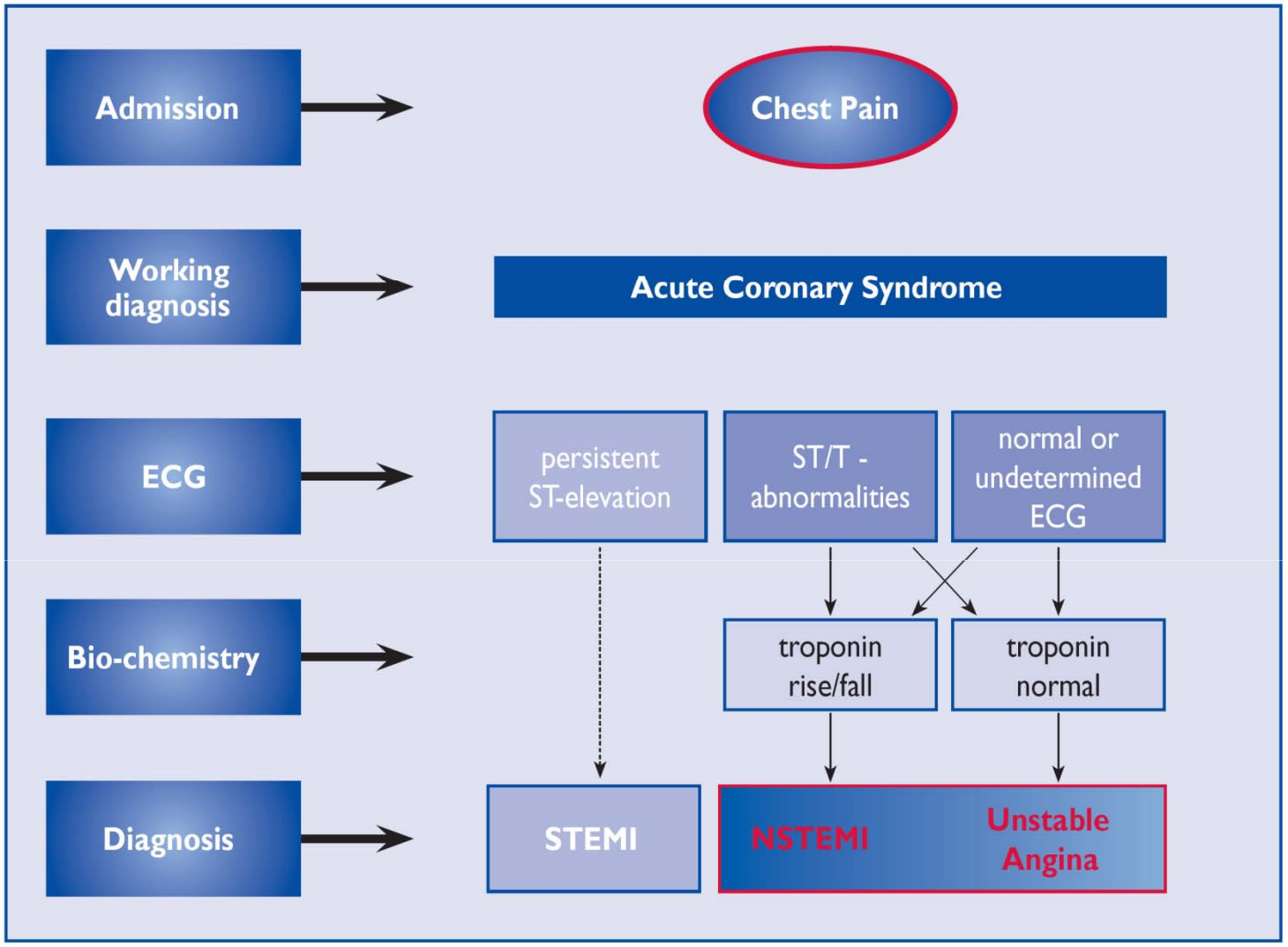

European Heart Journal
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ESC Guidelines

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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What is new?

- **Diagnostic**
  - High-sensitive troponin introduced
  - Echocardiography standard
  - Coronary CT for rule-out in low/intermediate risk patients
- **Risk Stratification**
  - 3-hour fast rule-out protocol
  - Bleeding risk score (CRUSADE)
- **Medical Treatment**
  - Ticagrelor and prasugrel introduced
- **Revascularisation**
  - Timing of revascularisation

Recommendations for diagnosis and risk stratification 1

Recommendations	Class [a]	Level [b]
In patients with a suspected NSTE-ACS, diagnosis and short-term ischaemic/bleeding risk stratification should be based on a combination of clinical history, symptoms, physical findings, ECG (repeated or continuous ST monitoring), and biomarkers.	I	A
ACS patients should be admitted preferably to dedicated chest pain units or coronary care units.	I	C
It is recommended to use established risk scores for prognosis and bleeding (e.g. GRACE, CRUSADE).	I	B
A 12-lead ECG should be obtained within 10 min after first medical contact and immediately read by an experienced physician. This should be repeated in the case of recurrence of symptoms, and after 6–9 and 24 h, and before hospital discharge.	I	B
Additional ECG leads (V_3R, V_4R, V_7–V_9) are recommended when routine leads are inconclusive.	I	C

Mortality in hospital and at 6 months according to the GRACE risk score

Risk category (tertile)	GRACE risk score	In-hospital death (%)
Low	≤108	<1
Intermediate	109–140	1–3
High	>140	>3
Risk category (tertile)	**GRACE risk score**	**Post-discharge to 6-month death (%)**
Low	≤88	<3
Intermediate	89–118	3-8
High	>118	>8

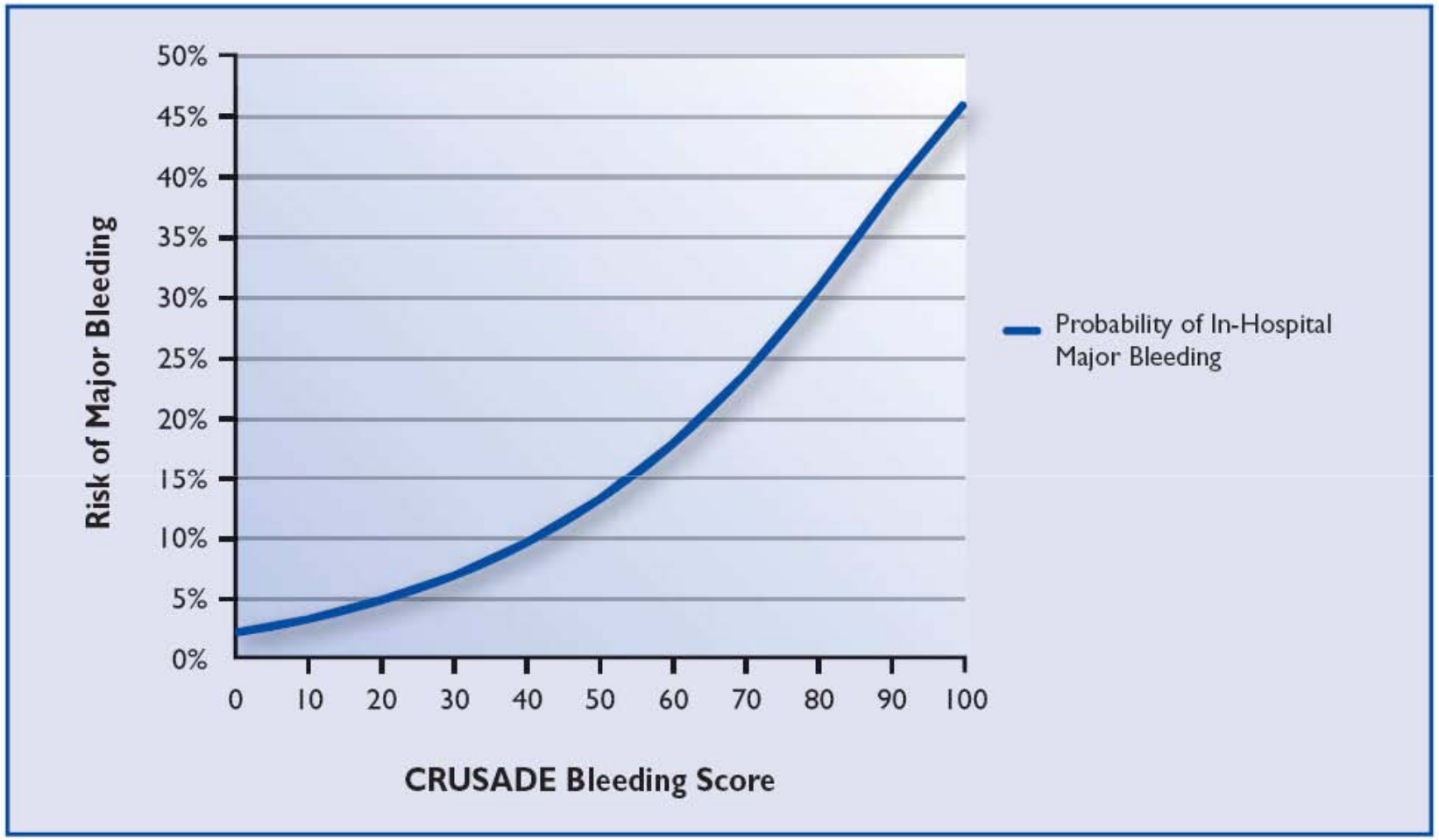
CRUSADE score of in-Hospital major bleeding

Predictor	Score
Baseline haematocrit, %	
<31	9
31–33.9	7
34–36.9	3
37–39.9	2
≥40	0
Creatinine clearance,[a] mL/min	
≤15	39
>15–30	35
>30–60	28
>60–90	17
>90–120	7
>120	0
Heart rate (b.p.m.)	
≤70	0
71–80	1
81–90	3
91–100	6
101–110	8
111–120	10
≥121	11

Predictor	Score
Sex	
Male	0
Female	8
Signs of CHF at presentation	
No	0
Yes	7
Prior vascular disease[b]	
No	0
Yes	6
Diabetes mellitus	
No	0
Yes	6
Systolic blood pressure, mmHg	
≤90	10
91–100	8
101–120	5
121–180	1
181–200	3
≥201	5

www.crusadebleedingscore.org

Risk of major bleeding across the spectrum of CRUSADE bleeding score



Recommendations for diagnosis and risk stratification 2

Recommendations	Class [a]	Level [b]
Blood has to be drawn promptly for troponin (cardiac troponin T or I) measurement. The result should be available within 60 min. The test should be repeated 6–9 h after initial assessment if the first measurement is not conclusive. Repeat testing after 12–24 h is advised if the clinical condition is still suggestive of ACS.	I	A
A rapid rule-out protocol (0 and 3 h) is recommended when highly sensitive troponin tests are available (see *Figure 5*).	I	B
An echocardiogram is recommended for all patients to evaluate regional and global LV function and to rule in or rule out differential diagnoses.	I	C
Coronary angiography is indicated in patients in whom the extent of CAD or the culprit lesion has to be determined (see Section 5.4).	I	C
Coronary CT angiography should be considered as an alternative to invasive angiography to exclude ACS when there is a low to intermediate likelihood of CAD and when troponin and ECG are inconclusive.	IIa	B
In patients without recurrence of pain, normal ECG findings, negative troponins tests, and a low risk score, a non-invasive stress test for inducible ischaemia is recommended before deciding on an invasive strategy.	I	A

Recommendations for diagnosis and risk stratification 1

Recommendations	Class [a]	Level [b]
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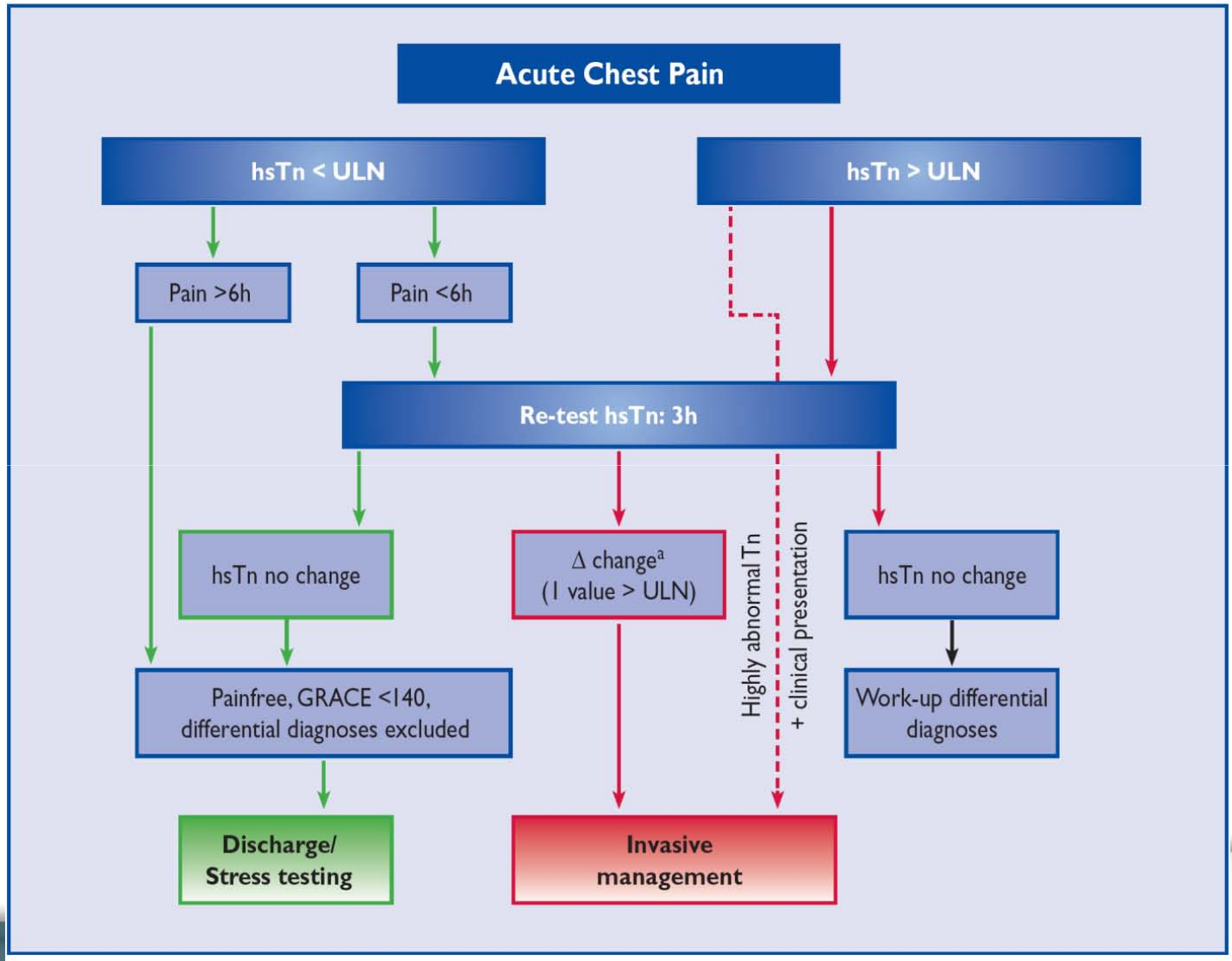
Rapid rule-out of ACS with high-sensitivity troponin.



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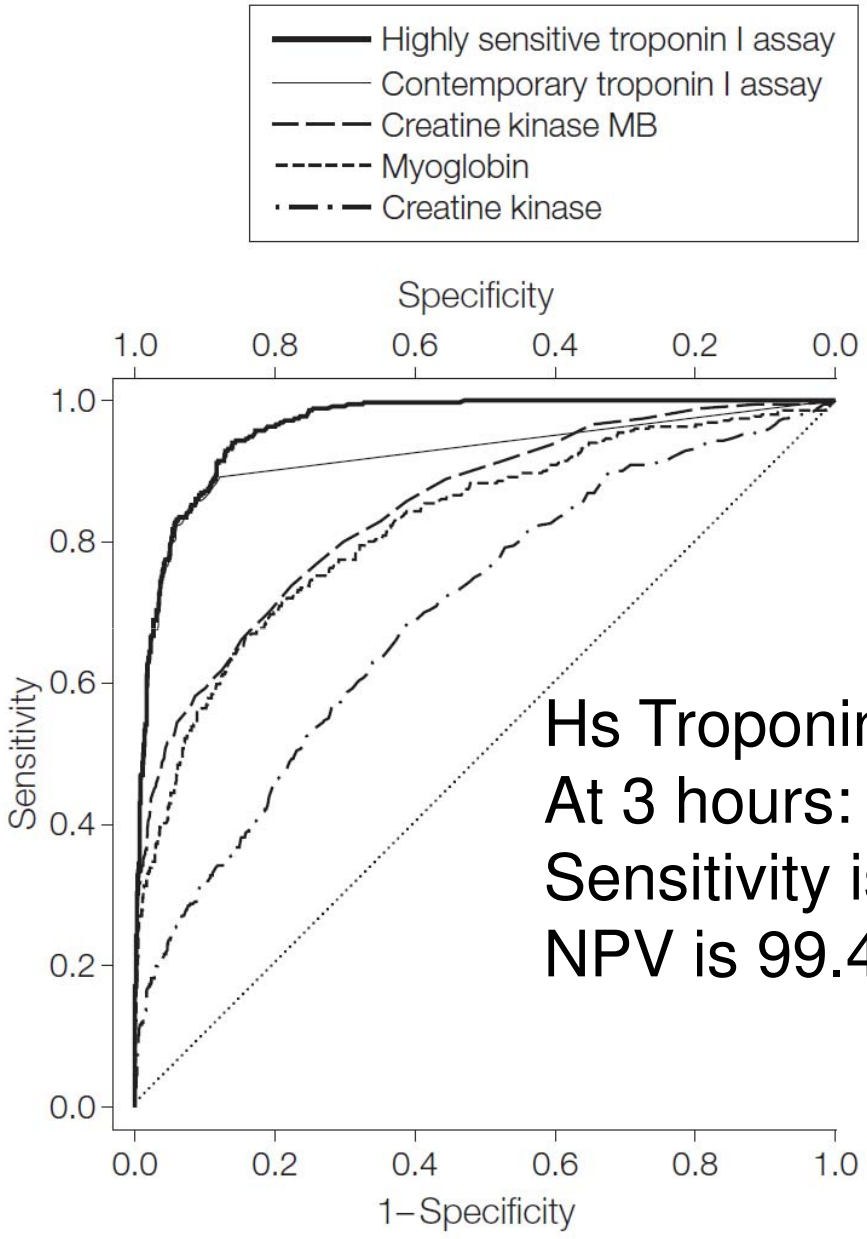
HsTroponin I Assay and Early Diagnosis of MI



Keller T JAMA 2011; 306:2684

Hs Troponin I assay at 99 percentile cut-off
At 3 hours:
Sensitivity is 98.2%
NPV is 99.4%

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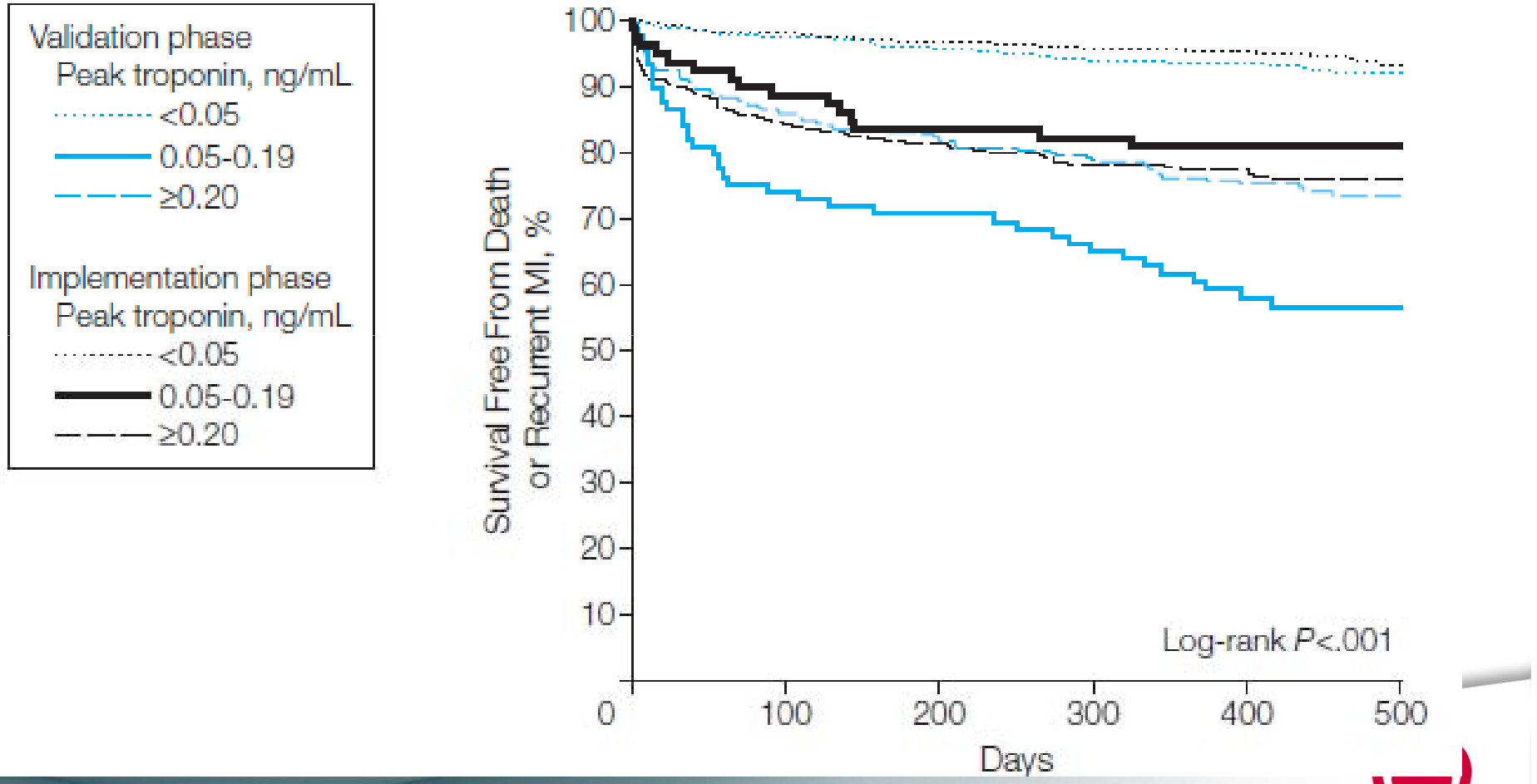
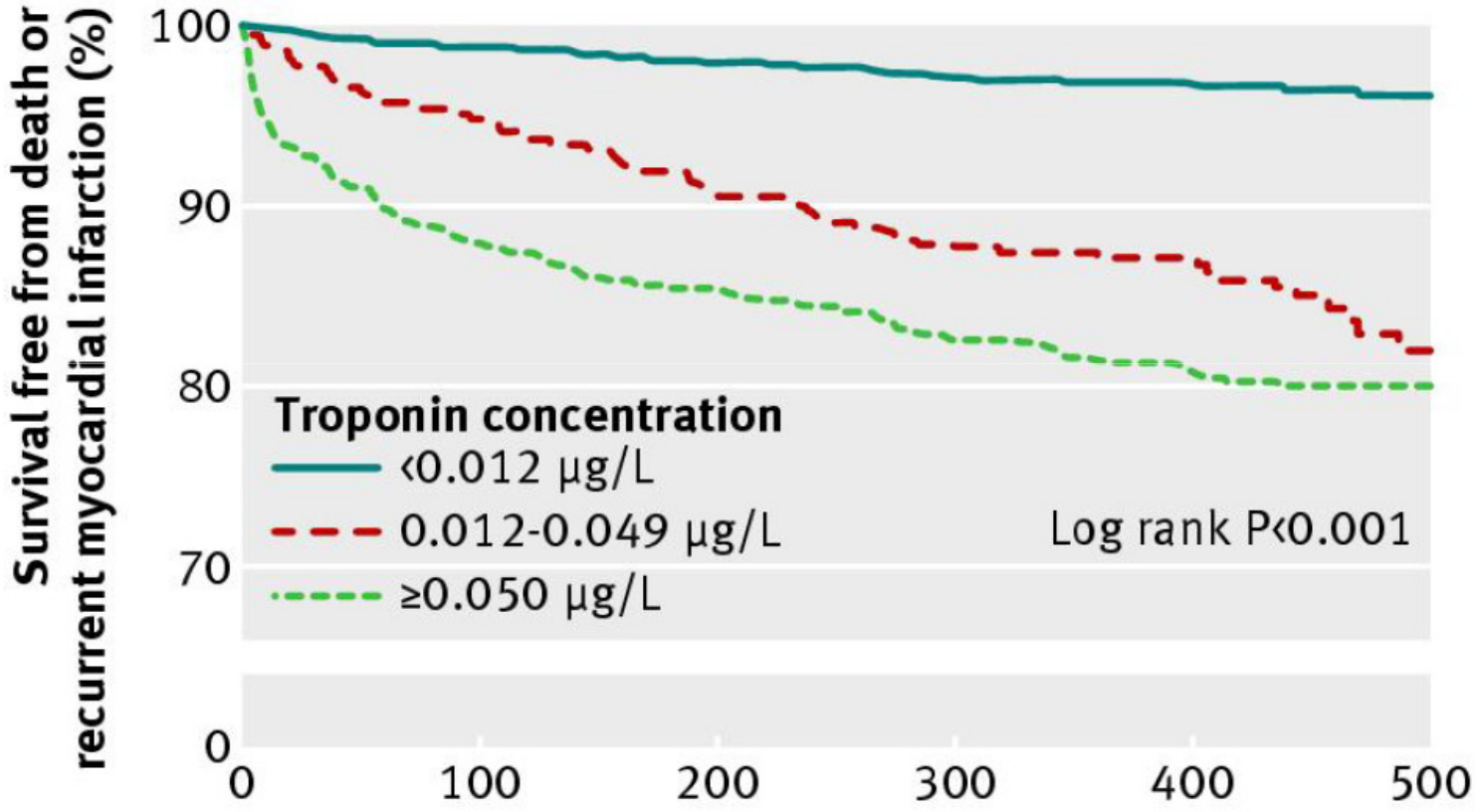
Sensitive Troponin I Assay in ACS



Mills JAMA 2011; 305:1210

Implications of lowering threshold of plasma troponin concentration in diagnosis of myocardial infarction: cohort study



Mills *BMJ 2012;344:e1533 doi: 10.1136/bmj.e1533*

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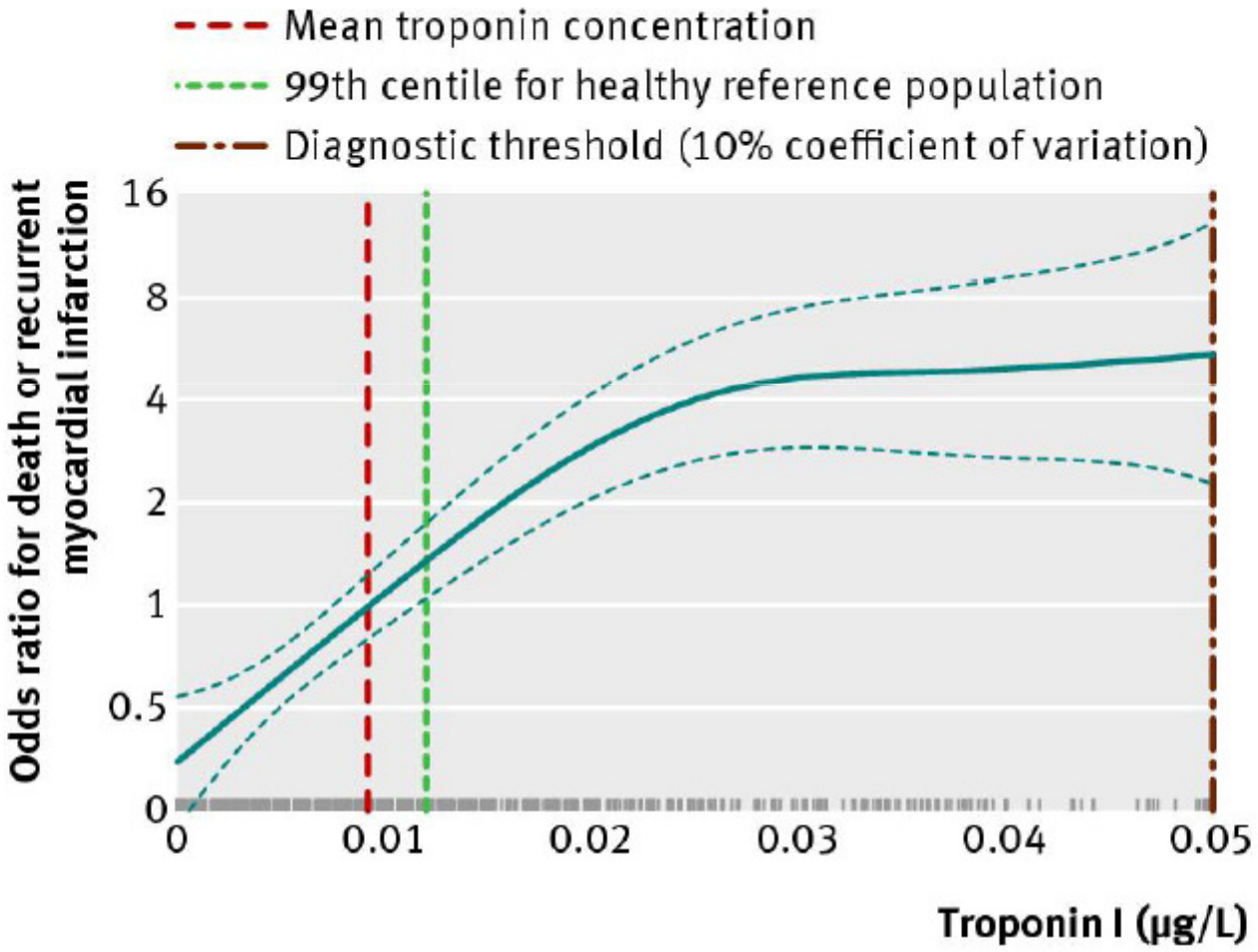

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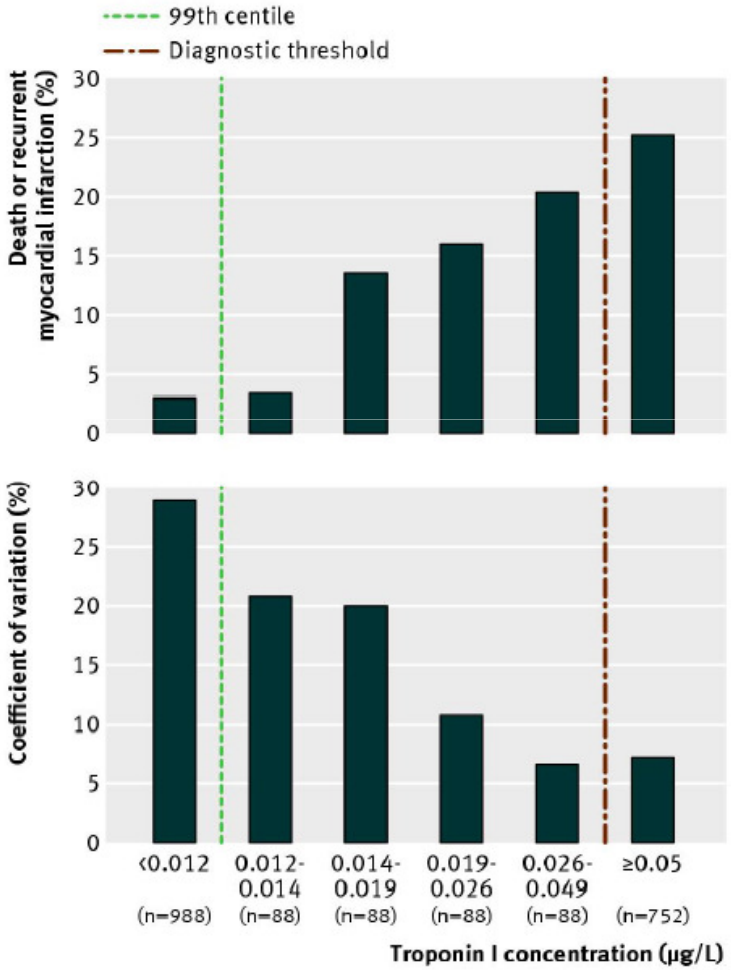

Mills *BMJ 2012;344:e1533 doi: 10.1136/bmj.e1533*

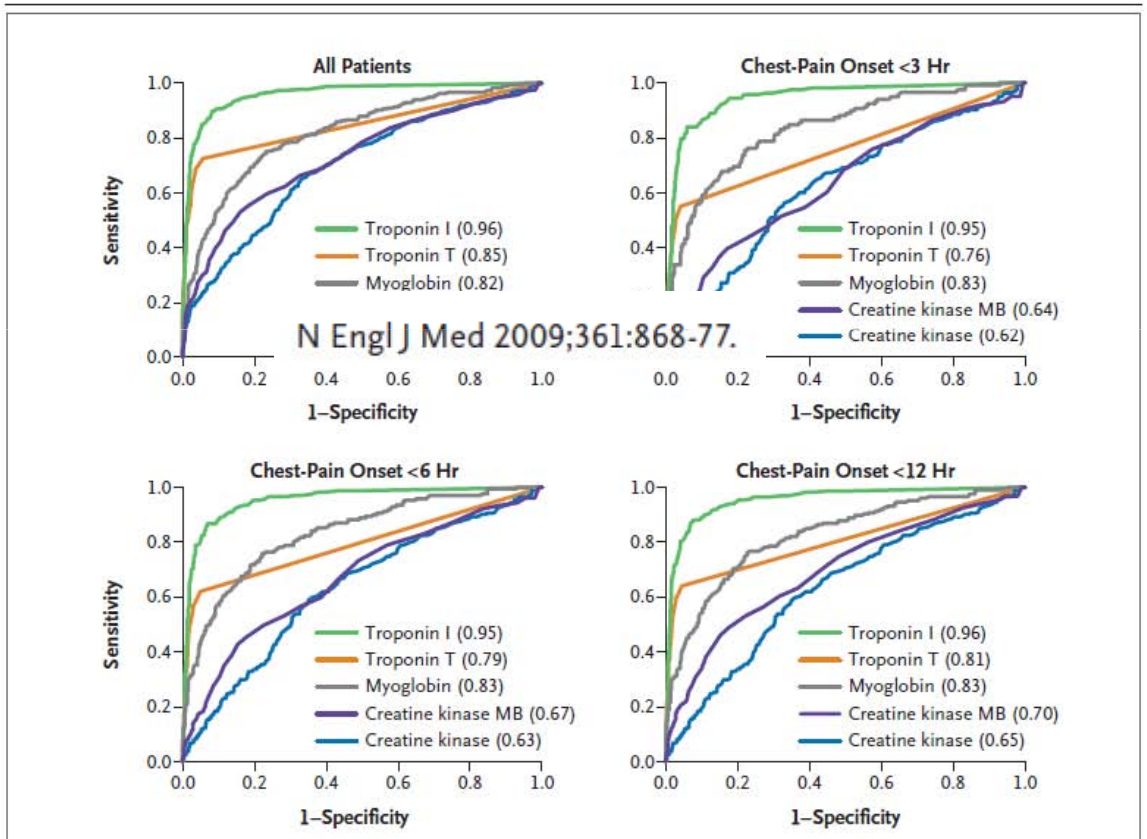

Figure 1. Diagnostic Accuracy of Single Biomarker Testing for Acute Myocardial Infarction.

Keller T N Engl J Med 2009; 361:868

Table 3. Correct Diagnosis of Acute Myocardial Infarction, According to the Time of a Single Sensitive Troponin I Assay.*

Time of Testing	Detection of Myocardial Infarction
	% of patients
On admission	
0 to <6 hr after chest-pain onset	87.7
6 to 12 hr after chest-pain onset	94.5
>12 hr after chest-pain onset	100
After admission	
At 3 hr	100
At 6 hr	100

Keller T N Engl J Med 2009; 361:868

Troponin elevation

Possible non-acute coronary syndrome causes

- **Chronic or acute renal dysfunction**
- Severe congestive **heart failure** – acute and chronic
- **Hypertensive crisis**
- **Tachy- or bradyarrhythmias**
- **Pulmonary embolism**, severe pulmonary hypertension
- Inflammatory diseases, e.g. **myocarditis**
- Acute neurological disease, including **stroke**, or subarachnoid haemorrhage
- Aortic dissection, aortic valve disease or hypertrophic cardiomyopathy
- Cardiac contusion, ablation, pacing, cardioversion, or endomyocardial biopsy
- Hypothyroidism
- Apical ballooning syndrome (Tako-Tsubo cardiomyopathy)
- Infiltrative diseases, e.g. amyloidosis, haemochromatosis, sarcoidosis, sclerodermia
- 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 ACS

Cardiac	Pulmonary	Haematological	Vascular	Gastro-intestinal	Orthopaedic/ infectious
Myocarditis	Pulmonary embolism	Sickle cell crisis	Aortic dissection	Oesophageal spasm	Cervical discopathy
Pericarditis	Pulmonary infarction	Anaemia	Aortic aneurysm	Oesophagitis	Rib fracture
Cardiomyopathy	Pneumonia Pleuritis		Cerebrovascular disease	Peptic ulcer	Muscle injury/ inflammation
Valvular disease	Pneumothorax			Pancreatitis	Costochondritis
Tako-Tsubo cardiomyopathy				Cholecystitis	Herpes zoster
Cardiac trauma					

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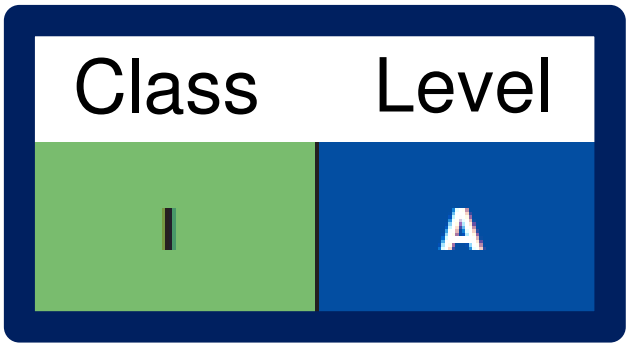
- **Revascularisation**
  - Timing of revascularisation

Aspirin

Aspirin should be given to all patients without contraindications at an initial loading dose of 150–300 mg, and at a maintenance dose of 75–100 mg daily long-term regardless of treatment strategy



$P2Y_{12}$ Inhibitors

	Clopidogrel	Prasugrel	Ticagrelor
Class	Thienopyridine	Thienopyridine	Triazolopyrimidine
Reversibility	Irreversible	Irreversible	Reversible
Activation	Prodrug, limited by metabolization	Prodrug, not limited by metabolization	Active drug
Onset of effect[a]	2–4 h	30 min	30 min
Duration of effect	3–10 days	5–10 days	3–4 days
Withdrawal before major surgery	5 days	7 days	5 days

$P2Y_{12}$ inhibitor recommendations 1

A $P2Y_{12}$ inhibitor should be added to aspirin as soon as possible and maintained over 12 months, unless there are contraindications such as excessive risk of bleeding

Class	Level
I	A

A proton pump inhibitor (preferably not omeprazole) in combination with DAPT is recommended in patients with a history of gastrointestinal haemorrhage or peptic ulcer, and appropriate for patients with multiple other risk factors (H. pylori infection, age ≥65 years, concurrent use of anticoagulants or steroids)

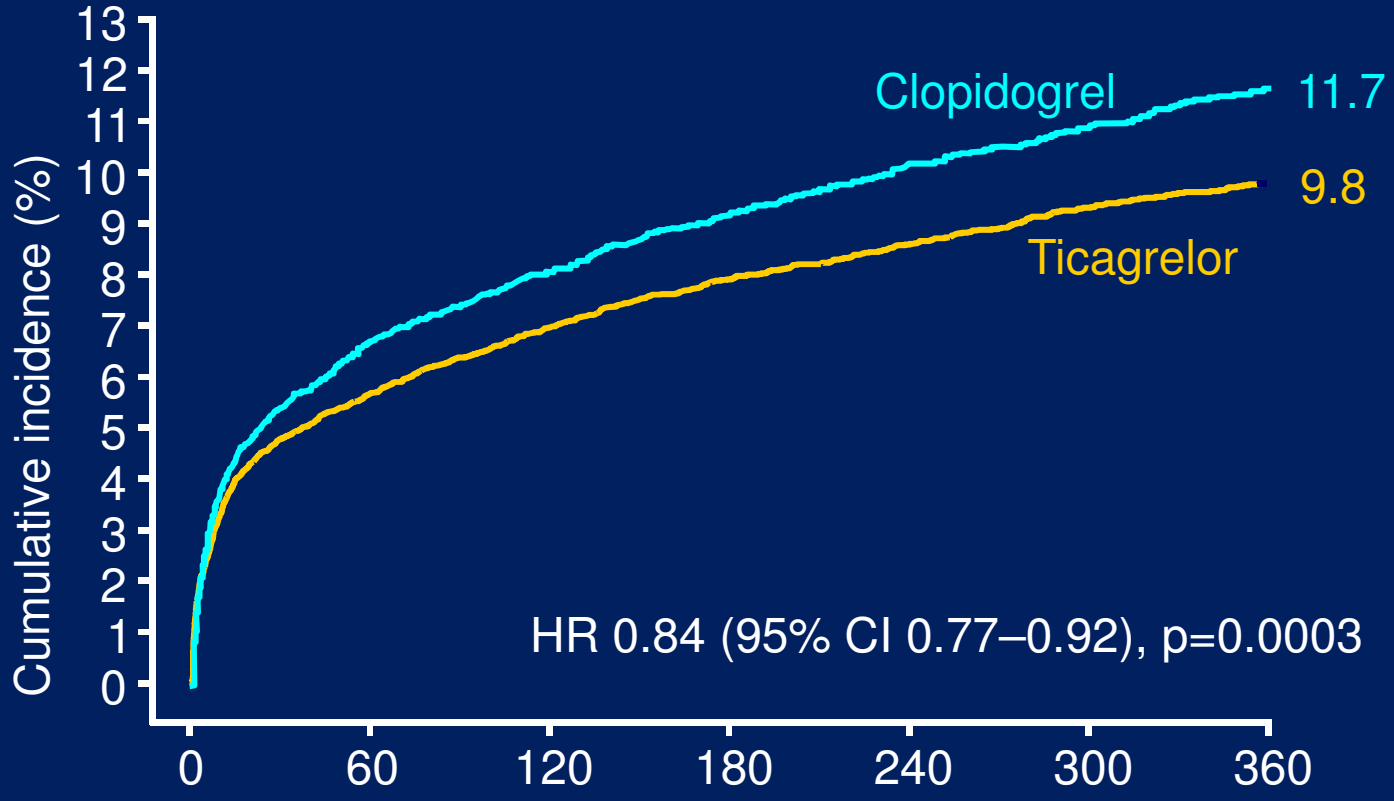
Class	Level
I	A

$P2Y_{12}$ inhibitor recommendations 2

Prolonged or permanent withdrawal of $P2Y_{12}$ inhibitors within 12 months after the index event is discouraged unless clinically indicated

Class	Level
I	C

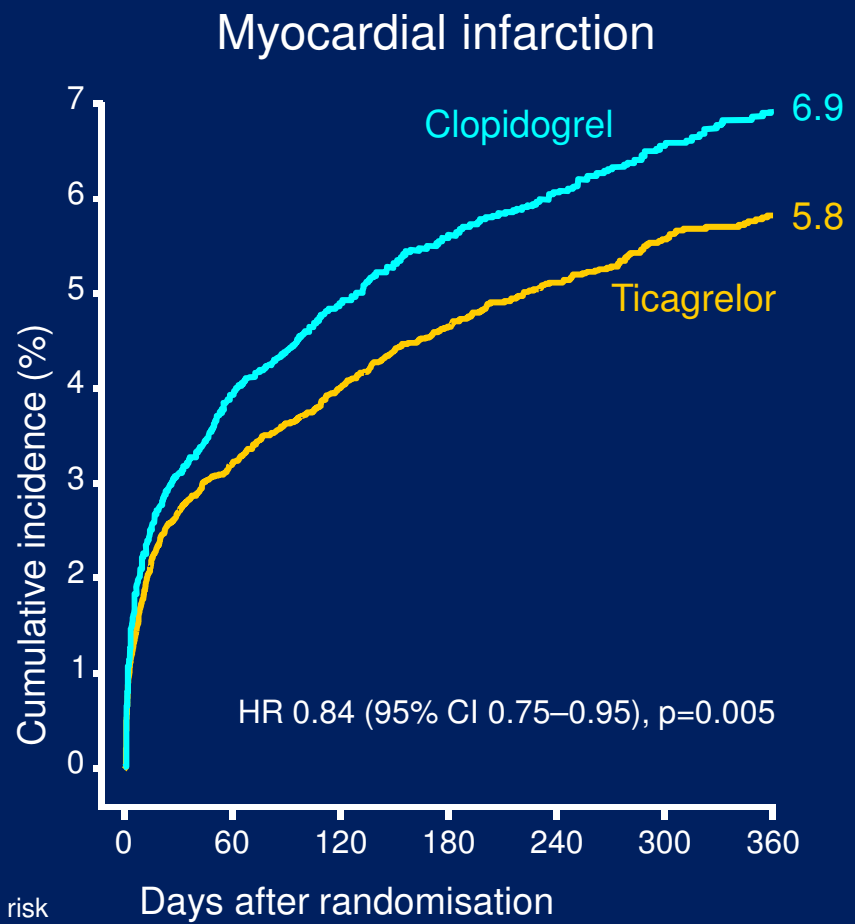
PLATO: time to first primary efficacy event (composite of CV death, MI or stroke)

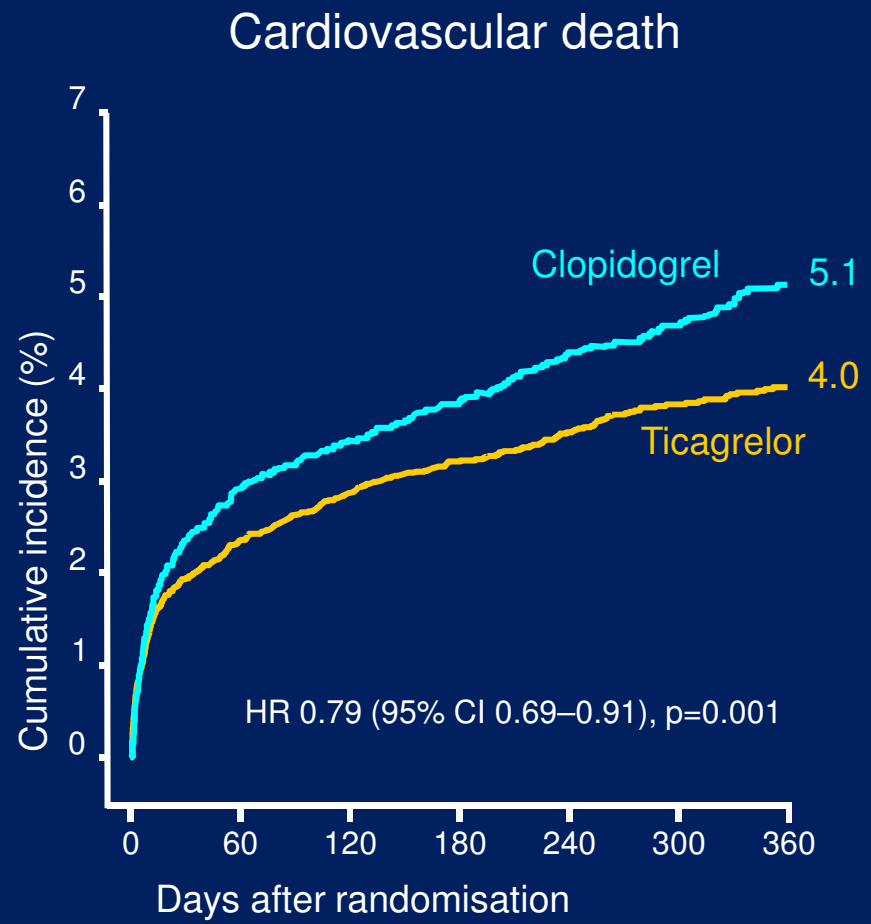


No. at risk							
Ticagrelor	9,333	8,628	8,460	8,219	6,743	5,161	4,147
Clopidogrel	9,291	8,521	8,362	8,124	6,743	5,096	4,047

Curves are Kaplan-Meier rates, HR = hazard ratio; CI = confidence interval

Secondary efficacy endpoints over time





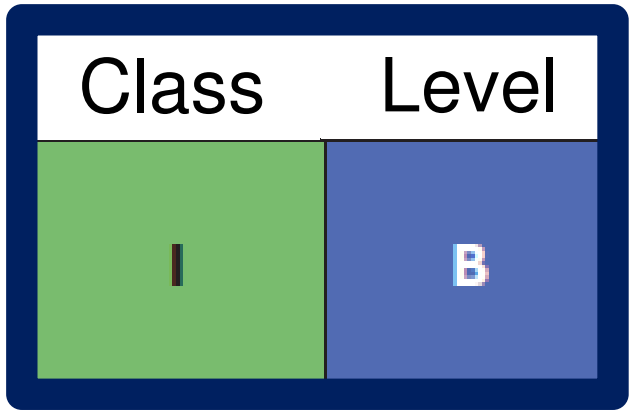
No. at risk

Ticagrelor	9,333	8,678	8,520	8,279	6,796	5,210	4,191
Clopidogrel	9,291	8,560	8,405	8,177	6,703	5,136	4,109

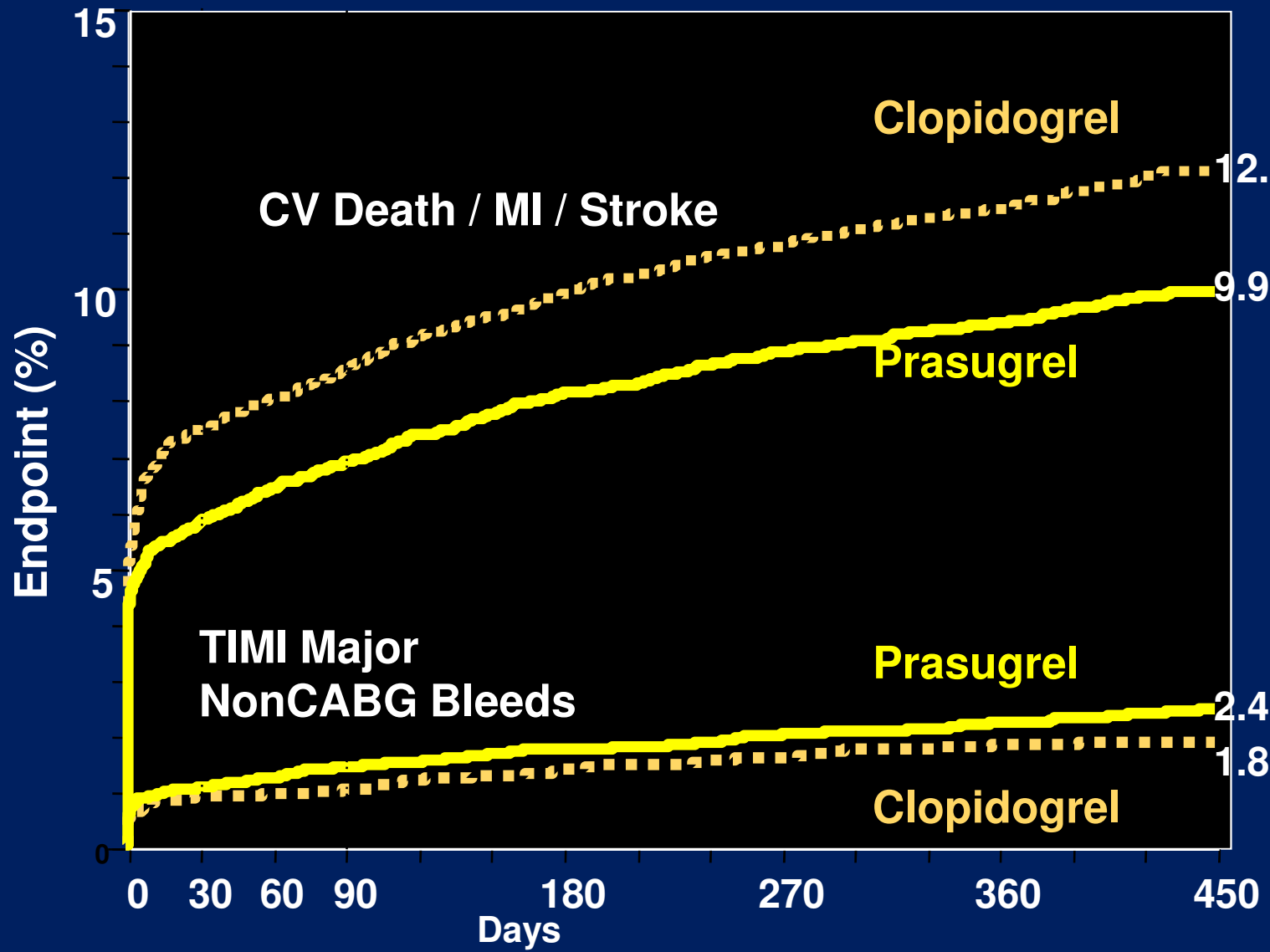
9,333	8,294	8,822	8,626	7119	5,482	4,419
9,291	8,865	8,780	8,589	7079	5,441	4,364

Ticagrelor

Ticagrelor (180-mg loading dose, 90 mg twice daily) is recommended for all patients at moderate-to-high risk of ischaemic events (e.g. elevated troponins), regardless of initial treatment strategy and including those pre-treated with clopidogrel (which should be discontinued when ticagrelor is commenced)



TRITON-TIMI study
Balance of Efficacy and Safety



138 ↓ events

HR 0.81
(0.73-0.90)
P=0.0004

NNT = 46

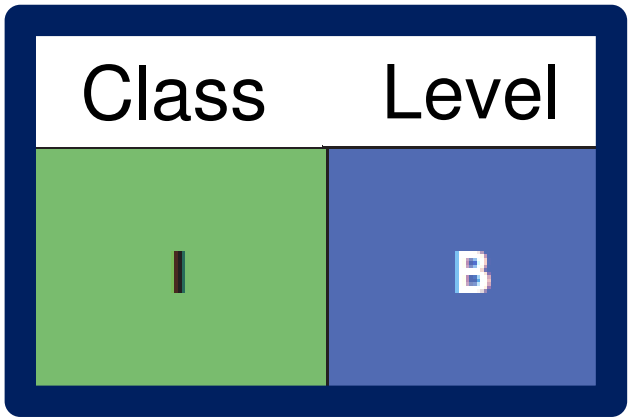
35 ↑ events

HR 1.32
(1.03-1.68)
P=0.03

NNH = 167

Prasugrel

Prasugrel (60-mg loading dose, 10-mg daily dose) is recommended for $P2Y_{12}$-inhibitor-naïve patients (especially diabetics) in whom coronary anatomy is known and who are proceeding to PCI unless there is a high risk of lifethreatening bleeding or other contraindications



Clopidogrel dosing

Clopidogrel (300-mg loading dose, 75-mg daily dose) is recommended for patients who cannot receive ticagrelor or prasugrel

Class	Level
I	A

A 600-mg loading dose of clopidogrel (or a supplementary 300-mg dose at PCI following an initial 300-mg loading dose) is recommended for patients scheduled for an invasive strategy when ticagrelor or prasugrel is not an option

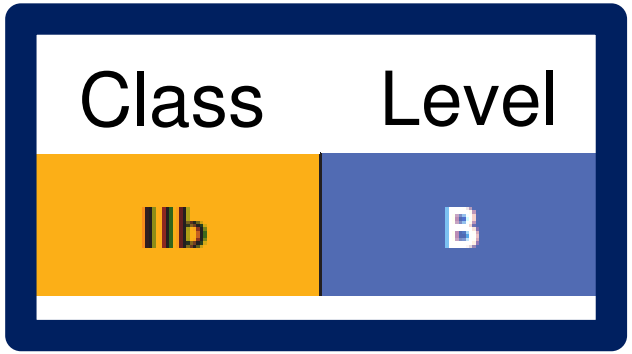
Class	Level
I	B

A higher maintenance dose of clopidogrel 150 mg daily should be considered for the first 7 days in patients managed with PCI and without increased risk of bleeding

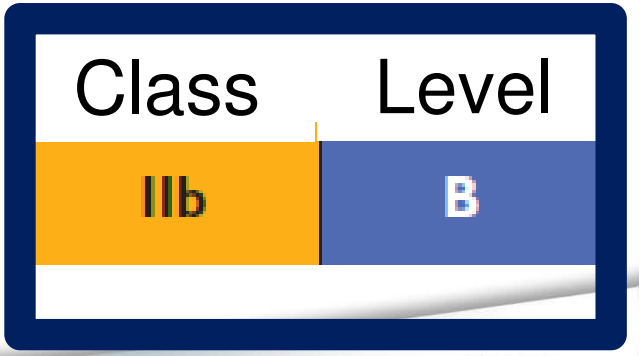
Class	Level
IIa	B

Clopidogrel response variability

Increasing the maintenance dose of clopidogrel based on platelet function testing is not advised as routine, but may be considered in selected cases

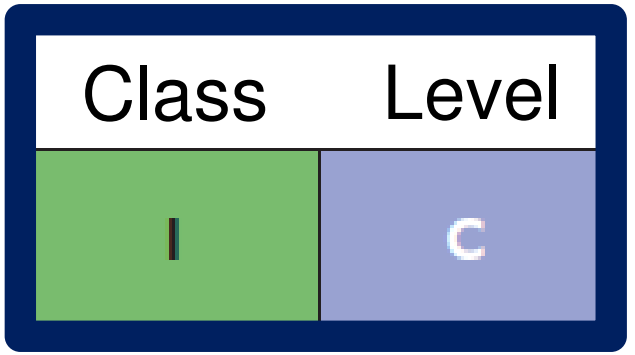


Genotyping and/or platelet function testing may be considered in selected cases when clopidogrel is used

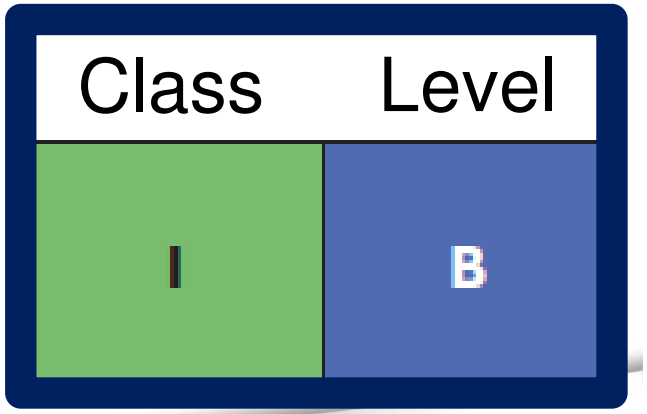


GP IIb/IIIa receptor inhibitor

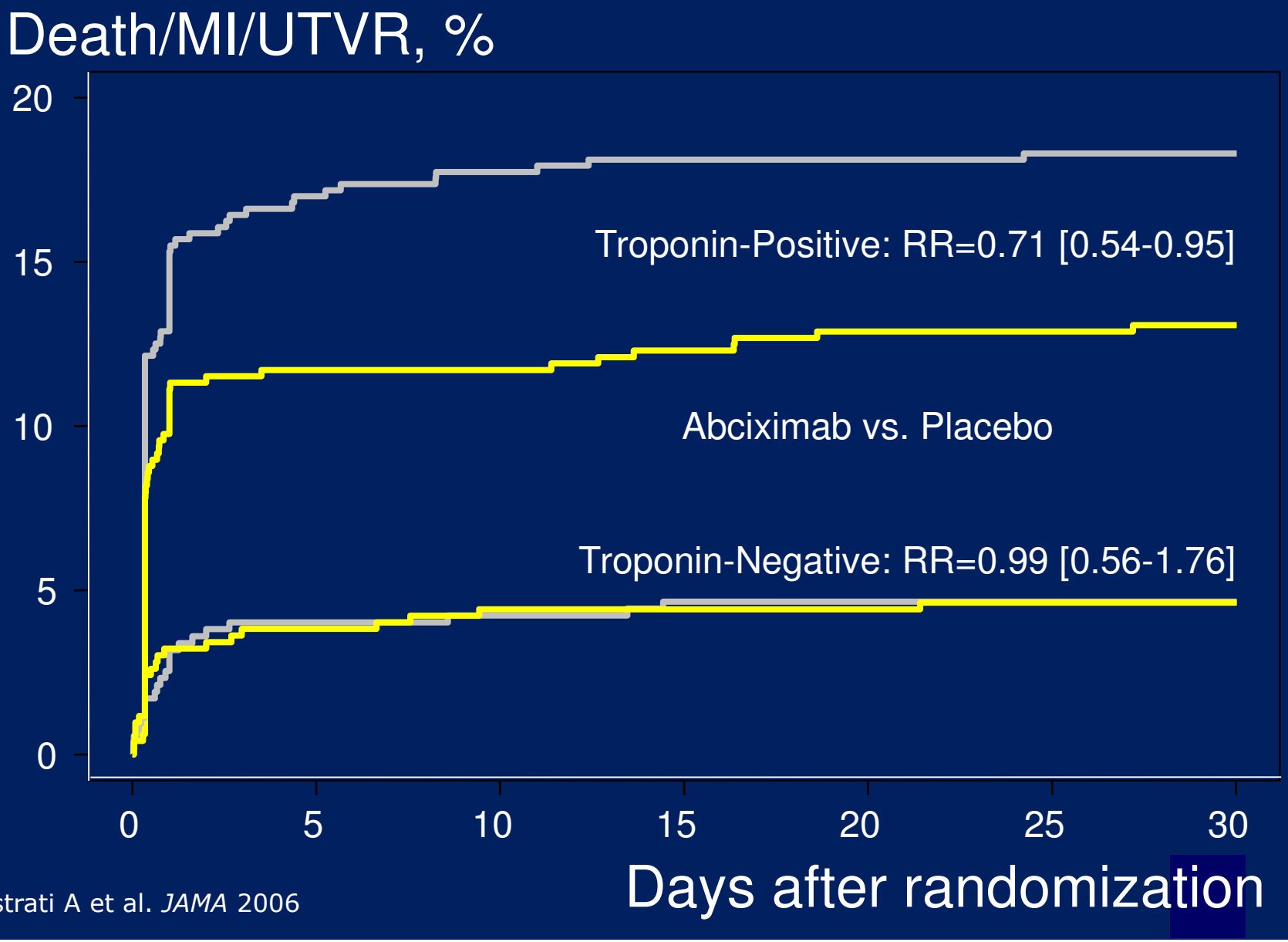
The choice of combination of oral antiplatelet agents, a GP IIb/IIIa receptor inhibitor, and anticoagulants should be made in relation to the risk of ischaemic and bleeding events



Among patients who are already treated with DAPT, the addition of a GP IIb/IIIa receptor inhibitor for high-risk PCI (elevated troponin, visible thrombus) is recommended if the risk of bleeding is low



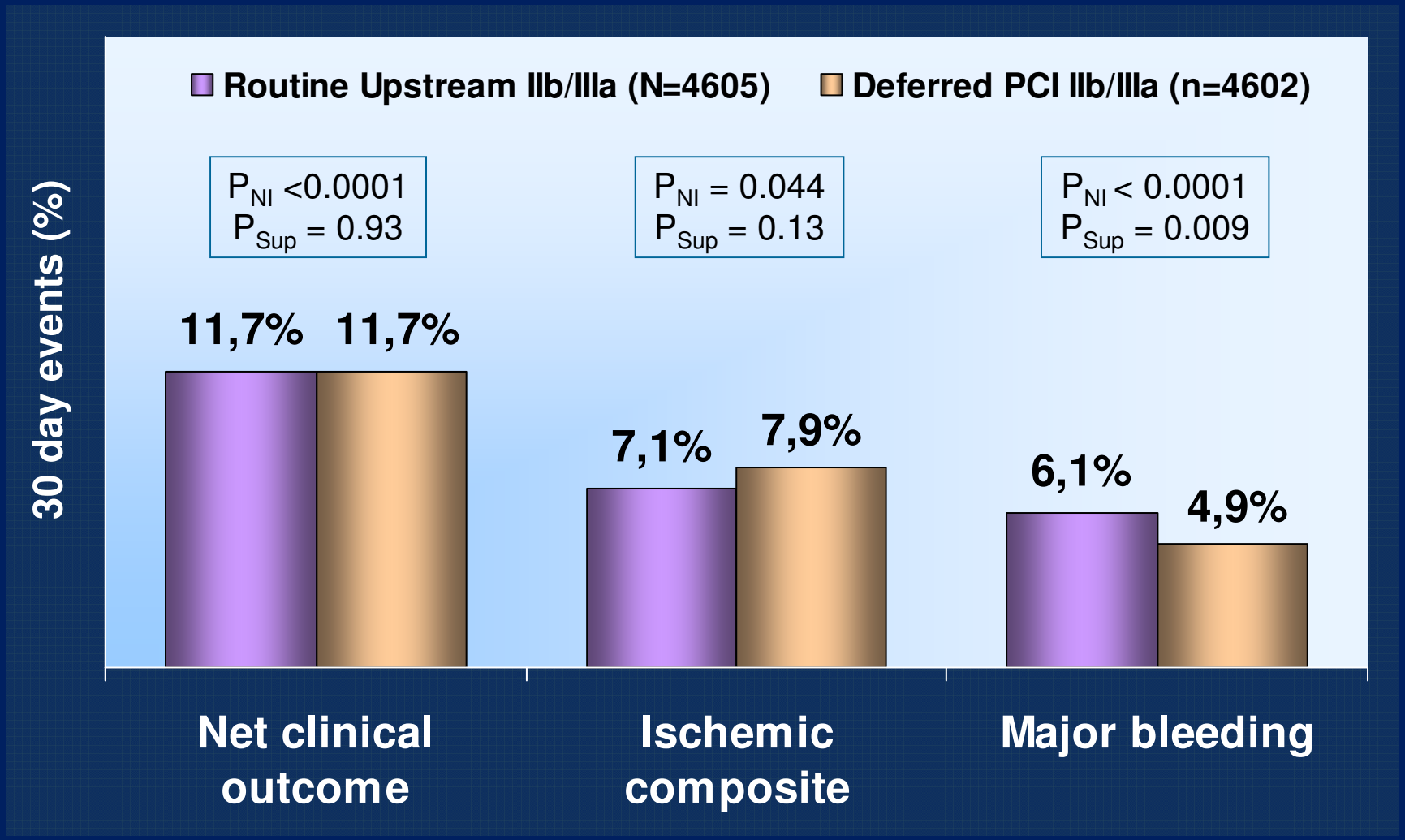
ISAR-REACT 2: Outcomes according to Tn level



Kastrati A et al. *JAMA* 2006

ACUITY Timing

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

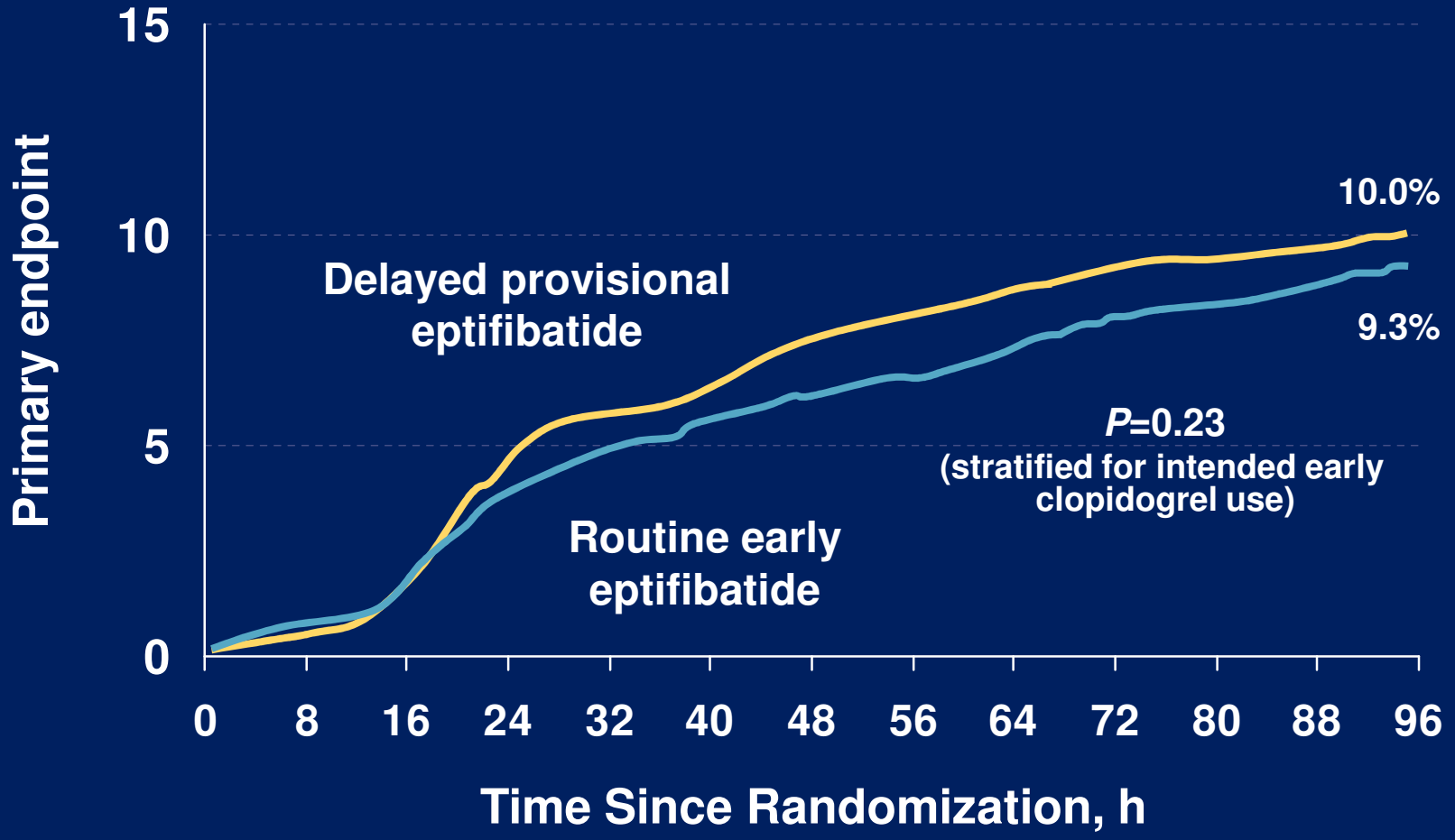


Stone, G. W. et al. JAMA 2007;297:591-602

EARLY ACS

Delayed provisional vs routine early eptifibatide

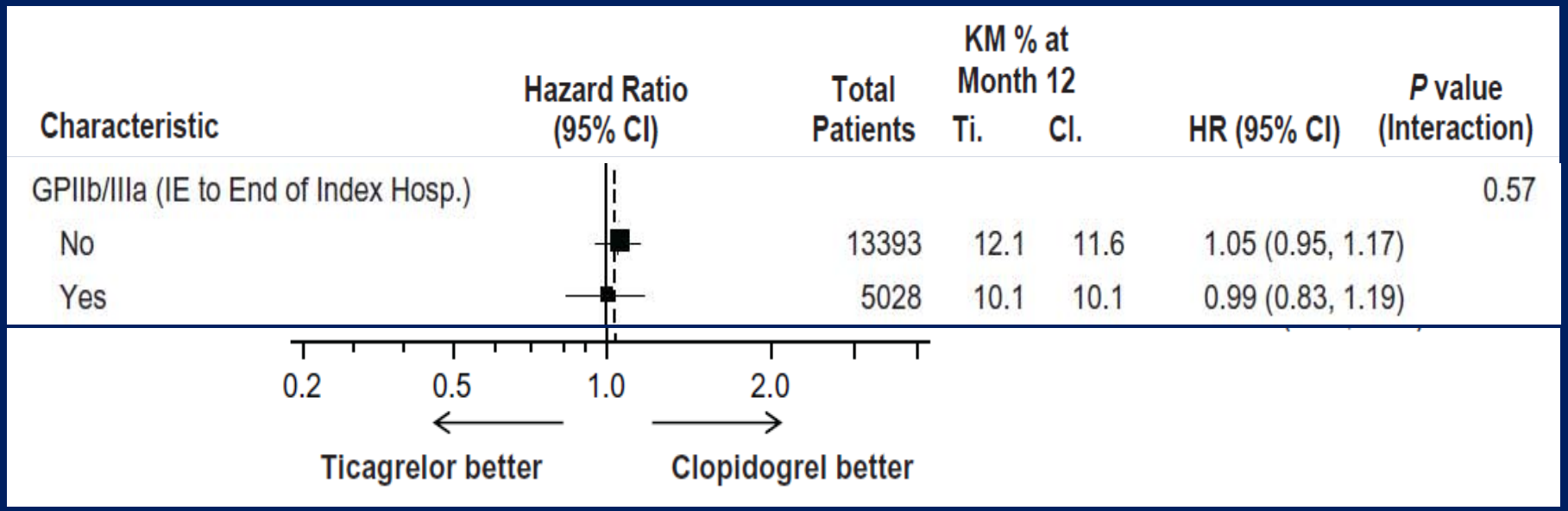
Death, MI, recurrent ischaemia or thrombotic bailout



RIUR = recurrent ischemia requiring urgent revascularization, TBO = thrombotic bailout.

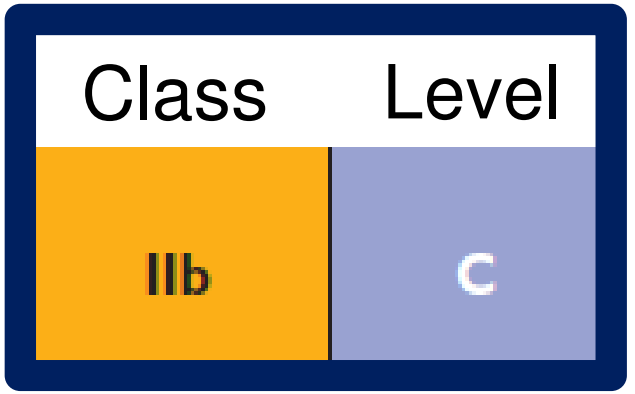
Giugliano RP, et al. *NEJM.* 2009;360:2176-90.

PLATO: major bleeding according to use of GPIIb/IIIa antagonist during hospitalisation

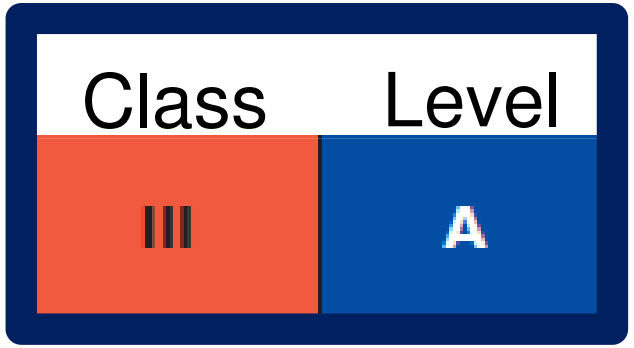


Upstream GP IIb/IIIa receptor inhibitor

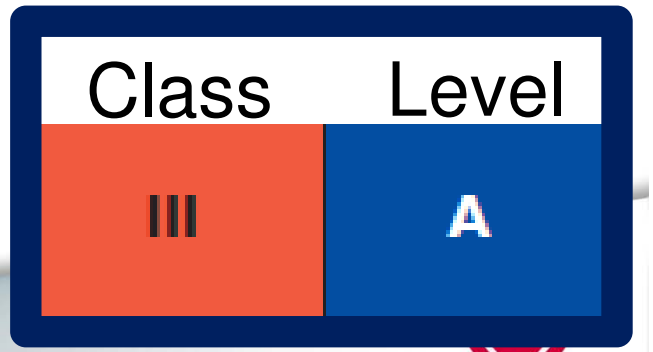
In high-risk patients eptifibatide or tirofiban may be considered prior to early angiography in addition to DAPT, if there is ongoing ischaemia and the risk of bleeding is low



GP IIb/IIIa receptor inhibitors are not recommended routinely before angiography in an invasive treatment strategy

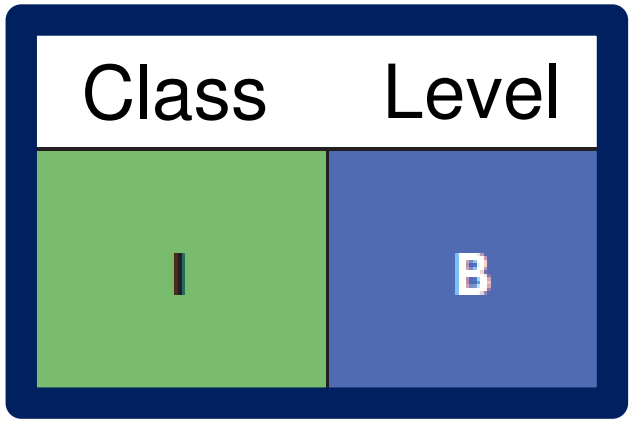


GP IIb/IIIa receptor inhibitors are not recommended for patients on DAPT who are treated conservatively



Bivalirudin vs GPIIb/IIIa antagonists

Bivalirudin plus provisional GP IIb/IIIa receptor inhibitors are recommended as an alternative to UFH plus GPIIb/IIIa receptor inhibitors in patients with an intended urgent or early invasive strategy, particularly in patients with a high risk of bleeding



Anticoagulants

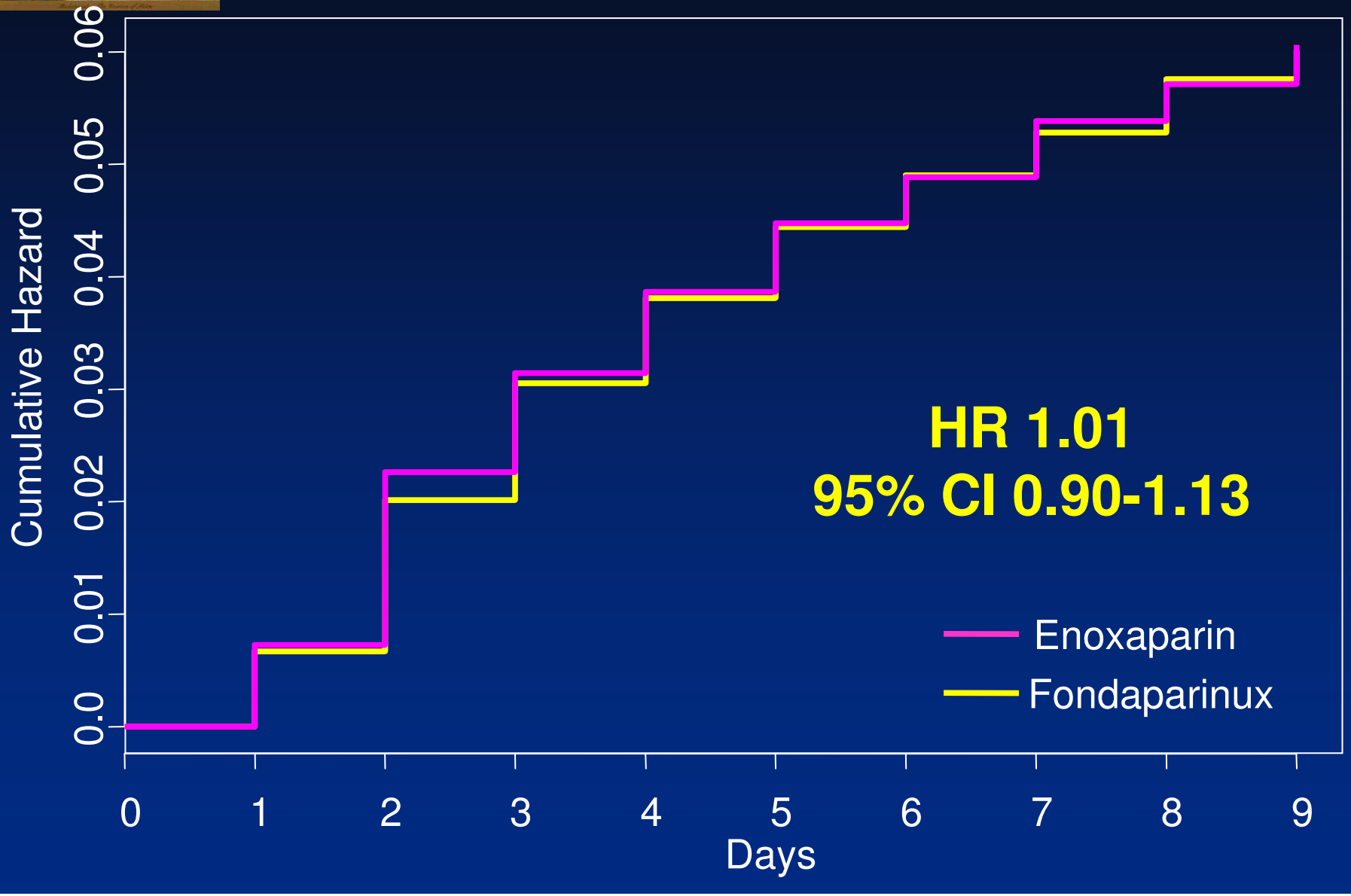
Anticoagulation is recommended for all patients in addition to antiplatelet therapy

Class	Level
I	A

The anticoagulation should be selected according to both ischaemic and bleeding risks, and according to the efficacy–safety profile of the chosen agent

Class	Level
I	C

Death/MI/RI: Day 9



Major Bleeding: 9 Days

Enoxaparin

HR 0.53
95% CI 0.45-0.62
P<<0.00001

Fondaparinux

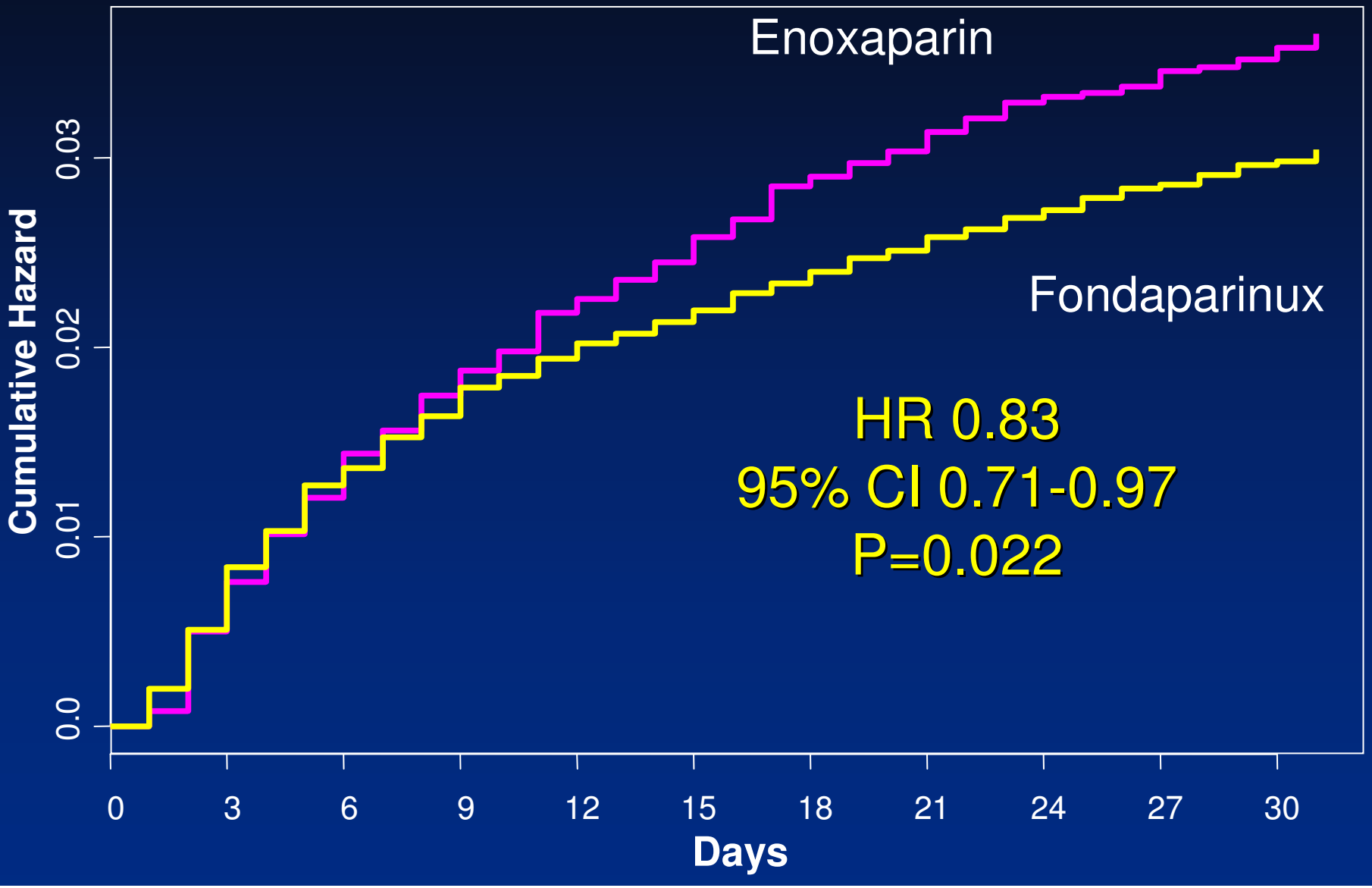
Cumulative Hazard

0.0
0.01
0.02
0.03
0.04

0 1 2 3 4 5 6 7 8 9

Days

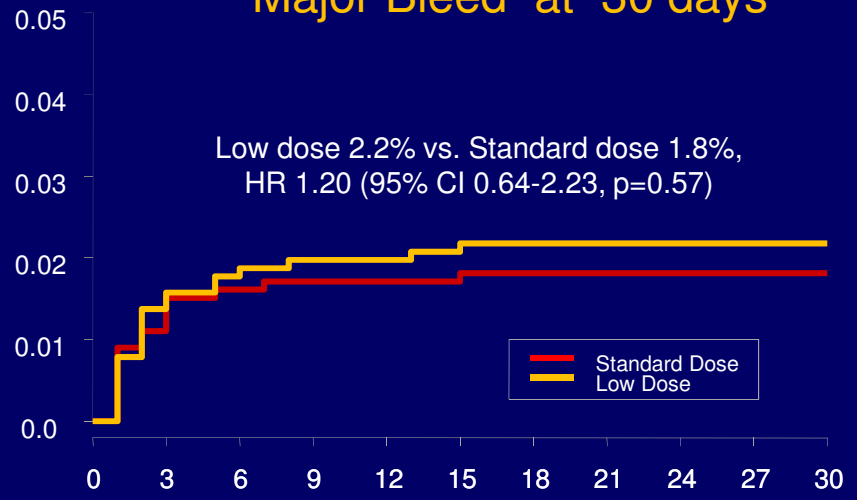
Mortality: Day 30



FUTURA

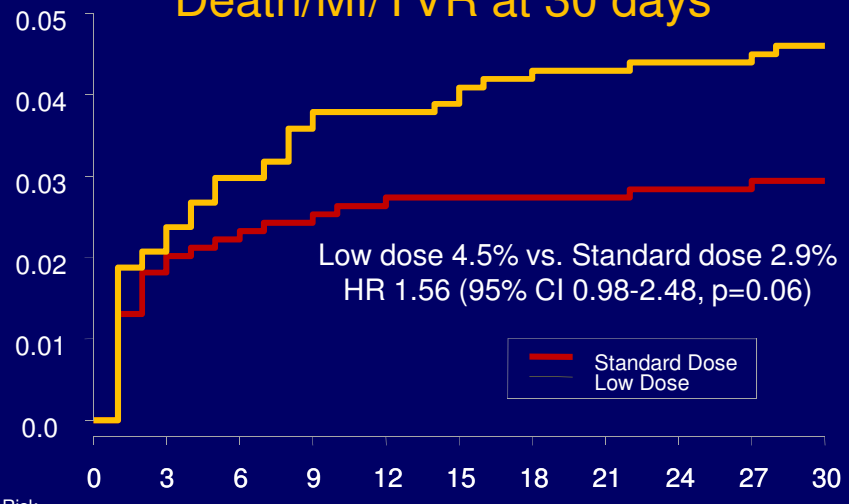
Outcomes to 30 days

Major Bleed at 30 days



No. at Risk						
Standard Dose	1002	986	981	980	980	978
Low Dose	1024	1002	1001	998	997	994

Death/MI/TVR at 30 days

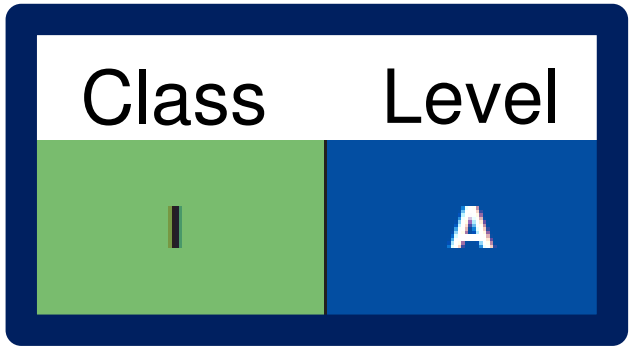


No. at Risk						
Standard Dose	1002	980	975	975	974	971
Low Dose	1024	997	988	982	981	978

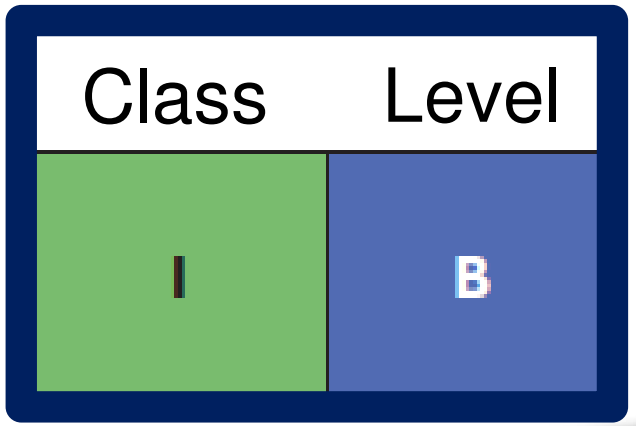
Subgroup analysis showed consistent results for primary outcome and for death/MI/TVR for pre-specified subgroups of: Age, Sex, GP IIb/IIIa, BMI, CrCl, Arterial access site

Fondaparinux

Fondaparinux (2.5 mg subcutaneously daily) is recommended as having the most favourable efficacy–safety profile with respect to anticoagulation

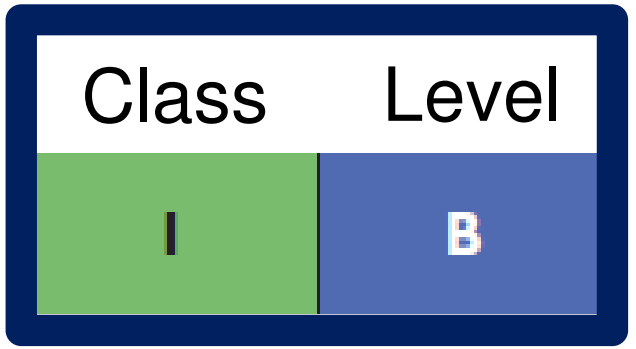


If the initial anticoagulant is fondaparinux, a single bolus of UFH (85 IU/kg adapted to ACT, or 60 IU in the case of concomitant use of GP IIb/IIIa receptor inhibitors) should be added at the time of PCI

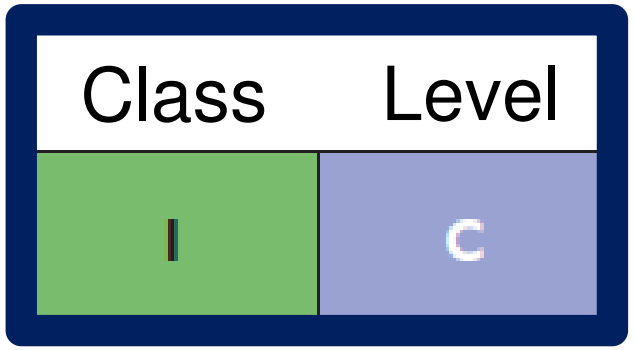


Heparins

Enoxaparin (1 mg/kg twice daily) is recommended when fondaparinux is not available



If fondaparinux or enoxaparin are not available, UFH with a target aPTT of 50–70 s or other LMWHs at the specific recommended doses are Indicated



Use of antithrombotic drugs in chronic kidney disease

Table 10 Recommendations for the use of antithrombotic drugs in CKD

Drug	Recommendations
Clopidogrel	No information in patients with renal dysfunction.
Prasugrel	No dose adjustment necessary, including in patients with end-stage disease.
Ticagrelor	No dose reduction required; no information in dialysis patients.
Enoxaparin	Dose reduction to 1 mg/kg once daily in the case of severe renal failure (CrCl <30 mL/min). Consider monitoring of anti-Xa activity.
Fondaparinux	Contraindicated in severe renal failure (CrCl <20 mL/min). Drug of choice in patients with moderately reduced renal function (CrCl 30–60 mL/min).
Bivalirudin	Patients with moderate renal impairment (30–59 mL/min) should receive an infusion of 1.75 mg/kg/h. If the creatinine clearance is <30 mL/min, reduction of the infusion rate to 1 mg/kg/h should be considered. No reduction in the bolus dose is needed. If a patient is on haemodialysis, the infusion rate should be reduced to 0.25 mg/kg/h.
Abciximab	No specific recommendations for the use of abciximab, or for dose adjustment in the case of renal failure. Careful evaluation of haemorrhagic risk is needed before using the drug in the case of renal failure.
Eptifibatide	The infusion dose should be reduced to 1 μg/kg/min in patients with CrCl <50 mL/min. The dose of the bolus remains unchanged at 180 μg/kg. Eptifibatide is contraindicated in patients with CrCl <30 mL/min.
Tirofiban	Dose adaptation is required in patients with renal failure; 50% of the bolus dose and infusion if CrCl is <30 mL/min.

Recommendations for oral antiplatelet agents 1

Recommendations	Class [a]	Level [b]
Aspirin should be given to all patients without contraindications at an initial loading dose of 150–300 mg, and at a maintenance dose of 75–100 mg daily long-term regardless of treatment strategy.	I	A
A $P2Y_{12}$ inhibitor should be added to aspirin as soon as possible and maintained over 12 months, unless there are contraindications such as excessive risk of bleeding.	I	A
A proton pump inhibitor (preferably not omeprazole) in combination with DAPT is recommended in patients with a history of gastrointestinal haemorrhage or peptic ulcer, and appropriate for patients with multiple other risk factors (*H. elicobacter pylori* infection, age ≥65 years, concurrent use of anticoag… steroids).	I	A
Prolonged or permanent withdrawal of $P2Y_{12}$ inhibitors wi… is discouraged unless clinically indicated.	I	C
Ticagrelor (180-mg loading dose, 90 mg twice daily) is recommended for all patient… to high risk of ischaemic events (e.g. elevated troponins), regardless of initial tr… with clopidogrel (which should be discontinued when ticagrelor is…	I	B
Prasugrel (60-mg loading dose, 10-mg daily dose) is recommende… diabetics) in whom coronary anatomy is known and who are proceeding to P… high risk of life-threatening bleeding or other contraindications.[d]	I	B

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CH9

Recommendations for GP IIb/IIIa receptor inhibitors

Recommendations	Class [a]	Level [b]
The choice of combination of oral antiplatelet agents, a GP IIb/IIIa receptor inhibitor, and anticoagulants should be made in relation to the risk of ischaemic and bleeding events.	I	C
Among patients who are already treated with DAPT, the addition of a GP IIb/IIIa receptor inhibitor for high-risk PCI (elevated troponin, visible thrombus) is recommended if the risk of bleeding is low.	I	B
Eptifibatide or tirofiban added to aspirin should be considered prior to angiography in high-risk patients not preloaded with $P2Y_{12}$ inhibitors.	IIa	C
In high-risk patients eptifibatide or tirofiban may be considered prior to early angiography in addition to DAPT, if there is ongoing ischaemia and the risk of bleeding is low.	IIb	C
GP IIb/IIIa receptor inhibitors are not recommended routinely before angiography in an invasive treatment strategy.	III	A
GP IIb/IIIa receptor inhibitors are not recommended for patients on DAPT who are treated conservatively.	III	A

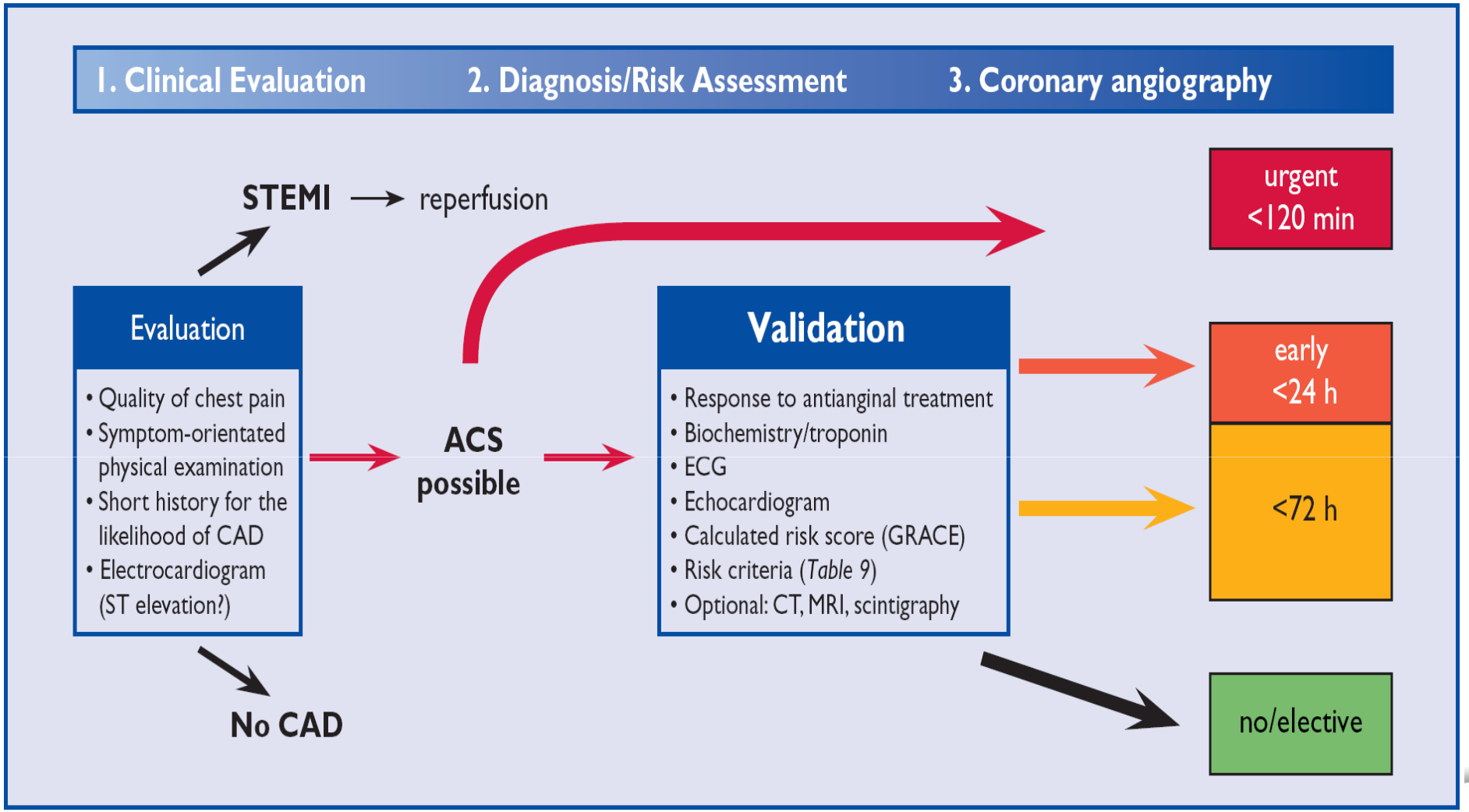
CH9 Tabelle teilen, nebeneinander auf 1 Seite

Prof. Dr. Christian Hamm; 21-8-2011

Recommendations for anticoagulants

Recommendations	Class [a]	Level [b]
Anticoagulation is recommended for all patients in addition to antiplatelet therapy.	I	A
The anticoagulation should be selected according to both ischaemic and bleeding risks, and according to the efficacy–safety profile of the chosen agent.	I	C
Fondaparinux (2.5 mg subcutaneously daily) is recommended as having the most favourable efficacy–safety profile with respect to anticoagulation.	I	A
If the initial anticoagulant is fondaparinux, a single bolus of UFH (85 IU/kg adapted to ACT, or 60 IU in the case of concomitant use of GP IIb/IIIa receptor inhibitors) should be added at the time of PCI.	I	B
Enoxaparin (1 mg/kg twice daily) is recommended when fondaparinux is not available.	I	B
If fondaparinux or enoxaparin are not available, UFH with a target aPTT of 50–70 s or other LMWHs at the specific recommended doses are indicated.	I	C
Bivalirudin plus provisional GP IIb/IIIa receptor inhibitors are recommended as an alternative to UFH plus GP IIb/IIIa receptor inhibitors in patients with an intended urgent or early invasive strategy, particularly in patients with a high risk of bleeding.	I	B
In a purely conservative strategy, anticoagulation should be maintained up to hospital discharge.	I	A
Discontinuation of anticoagulation should be considered after an invasive procedure unless otherwise indicated.	IIa	C
Crossover of heparins (UFH and LMWH) is not recommended.	III	B

Decision-making algorithm in ACS



Recommendations for invasive evaluation and revascularization

Recommendations	Class [a]	Level [b]
An invasive strategy (within 72 h after first presentation) is indicated in patients with: • at least one high-risk criterion (*Table 9*); • recurrent symptoms.	I	A
Urgent coronary angiography (<2 h) is recommended in patients at very high ischaemic risk (refractory angina, with associated heart failure, life-threatening ventricular arrhythmias, or haemodynamic instability).	I	C
An **early** invasive strategy (<24 h) is recommended in patients with a GRACE score >140 or with at least one primary high-risk criterion.	I	A
Non-invasive documentation of inducible ischaemia is recommended in low-risk patients without recurrent symptoms before deciding for invasive evaluation.	I	A

Recommendations	Class [a]	Level [b]
The revascularization strategy (*ad-hoc* culprit lesion PCI/ multivessel PCI/CABG) should be based on the clinical status as well as the disease severity, i.e. distribution and angiographic lesion characteristics (e.g. SYNTAX score), according to the local 'Heart Team' protocol.	I	C
As there are no safety concerns related to the use of DESs in ACS, DESs are indicated based on an individual basis taking into account baseline characteristics, coronary anatomy, and bleeding risk.	I	A
PCI of non-significant lesions is not recommended.	III	C
Routine invasive evaluation of low-risk patients is not recommended.	III	A

Criteria for high risk with indication for invasive management

Primary
• Relevant rise or fall in troponin[a] • Dynamic ST- or T-wave changes (symptomatic or silent)
Secondary
• Diabetes mellitus • Renal insufficiency (eGFR <60 mL/min/1.73 m²) • Reduced LV function (ejection fraction <40%) • Early post infarction angina • Recent PCI • Prior CABG • Intermediate to high GRACE risk score (*Table 5*)

“Management Strategy”

of NSTE - ACS

Management of NSTE - ACS

- Step 1: Initial evaluation
- Step 2: Diagnosis validation and risk assessment
- Step 3: Invasive strategy
- Step 4: Revascularisation modality
- Step 5: Hospital discharge and post-discharge

Initial therapeutic measures

Oxygen	Insufflation (4–8 L/min) if oxygen saturation is <90%
Nitrates	Sublingual or intravenous (caution if systolic blood pressure is <90 mmHg)
Morphine	3–5 mg intravenous or subcutaneously, if severe pain

Checklist of treatments when an ACS diagnosis appears likely

Aspirin	Initial dose of 150–300 mg non-enteric formulation followed by 75–100 mg/day (i.v. administration is acceptable)
$P2Y_{12}$ inhibitor	Loading dose of ticagrelor or clopidogrel[a]
Anticoagulation	Choice between different options depends on strategy: • Fondaparinux 2.5 mg/daily subcutaneously • Enoxaparin 1 mg/kg twice daily subcutaneously • UFH i.v. bolus 60–70 IU/kg (maximum 5000 IU) followed by infusion of 12–15 IU/kg/h (maximum 1000 IU/h) titrated to aPTT 1.5–2.5 × control • Bivalirudin is indicated only in patients with a planned invasive strategy
Oral ß-Blocker	If tachycardic or hypertensive without signs of heart failure

Checklist of antithrombotic treatments prior to PCI

Aspirin	Confirm loading dose prior to PCI.
$P2Y_{12}$ inhibitor	Confirm loading dose of ticagrelor or clopidogrel prior to PCI. If $P2Y_{12}$ naïve, consider prasugrel (if <75 years age, >60 kg, no prior stroke or TIA)
Anticoagulation	• Fondaparinux pre-treated: add UFH for PCI • Enoxaparin pre-treated: add if indicated • UFH pre-treated: titrate to ACT >250 s, or switch to bivalirudin (0.1 mg/kg bolus followed by 0.25 mg/kg/h)
GP IIb/IIIa receptor inhibitor	• Consider tirofiban or eptifibatide in patients with high-risk anatomy or troponin elevation • Abciximab only prior to PCI in high-risk patients.

Measures checked at discharge

Aspirin	Continue life long
$P2Y_{12}$ inhibitor	Continue for 12 months (unless at high risk of bleeding)
β-Blocker	If LV function depressed
ACE inhibitor/ ARB	If LV function depressed Consider for patients devoid of depressed LV function
Aldosterone antagonist/ eplerenone	If depressed LV function (LVEF ≤35%) and either diabetes or heart failure, without significant renal dysfunction
Statin	Titrate to achieve target LDL-C levels <1.8 mmol/L (<70 mg/dL)
Lifestyle	Risk-factor counselling, referral to cardiac rehabilitation / secondary prevention programme

Take Home messages

- **NSTE-ACS is a frequent cause of hospitalization**

  Heterogenous population as regards risk

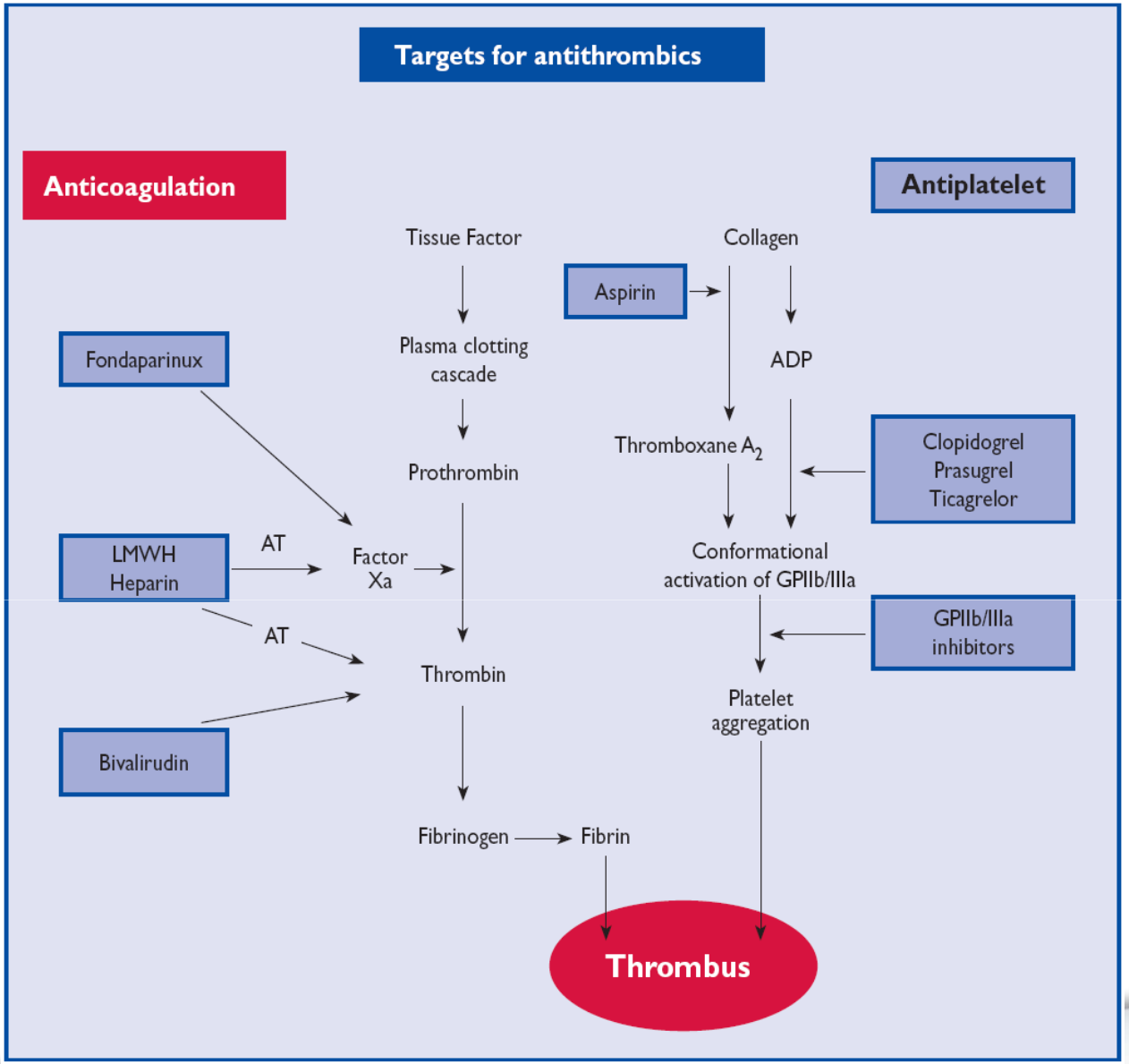
- **Diagnostics**
  - Clinical presentation, ECG, troponin
  - High-sensitive troponin introduced
  - Echocardiography for everybody
  - Coronary CT for rule-out in low/intermediate risk patients
- **Risk Stratification**
  - 3-hour fast rule-out protocol based on hs-troponin
  - Ischaemic risk (GRACE score)
  - Bleeding risk (CRUSADE score)

Take Home messages (continued 1)

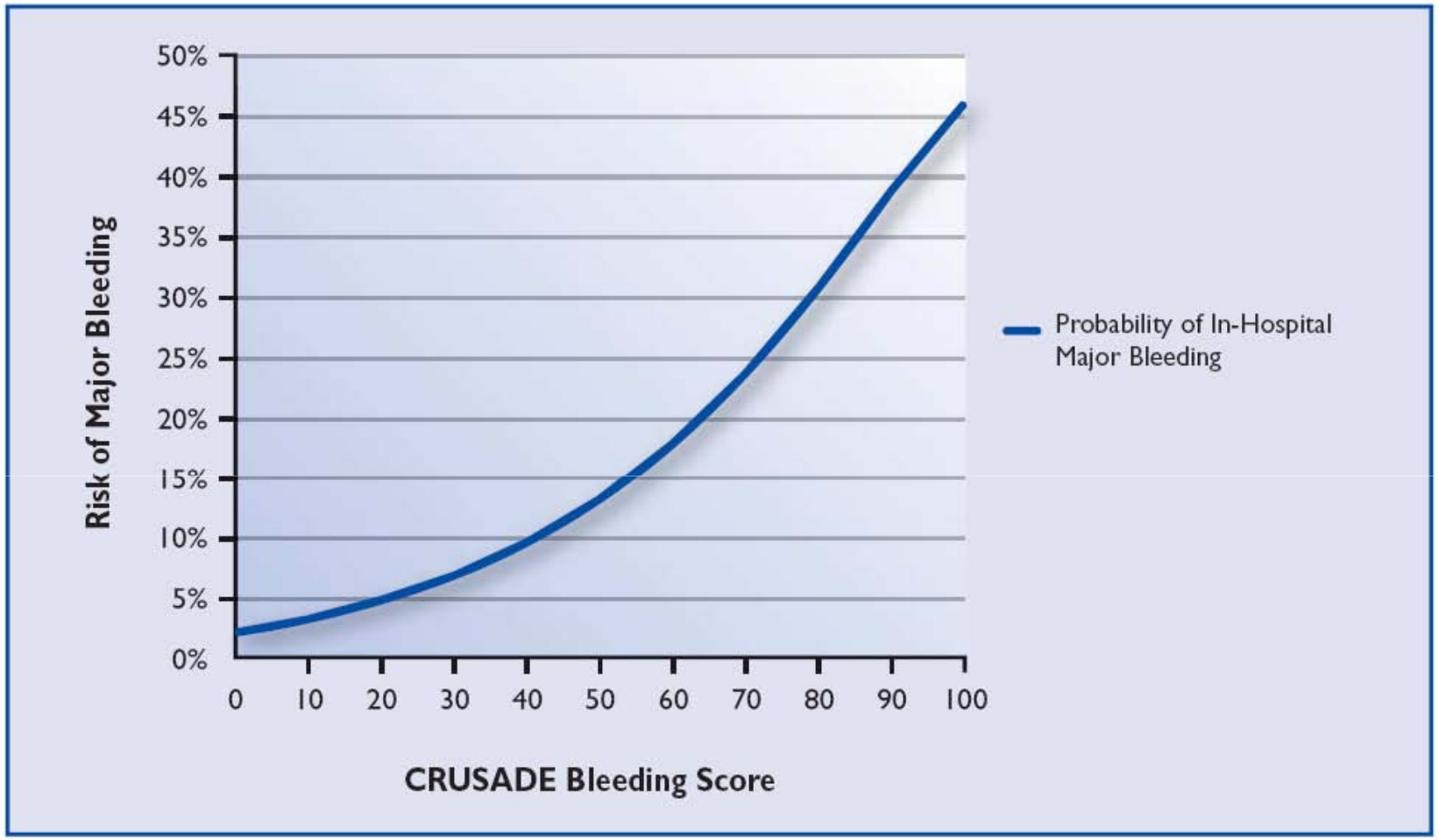
- **First line antithrombotic treatment**
  - Ticagrelor and prasugrel recently introduced
- **Revascularisation**
  - Timing of revascularisation customized according to risk
    - Within 72 hours anyway, but
    - Within 2 hours for very high risk patients (lifethreatening symptoms)
    - Within 24 hours for patients with high risk criteria (GRACE score > 140, troponin release, ST-T changes)
  - Non invasive evaluation for low risk patients

Take Home messages (continued 2)

- **Special populations and situations**
    - Diabetes, elderly, women, CKD, anaemia.....
    - Bleeding complications ...
- **Long term secondary prevention**
    - Secondary prevention programmes
    - Lifestyle
    - Drug therapy



Risk of major bleeding across the spectrum of CRUSADE bleeding score



Ten Take home messages

1 - NSTE-ACS is a frequent cause of hospitalization

2 - Heterogenous population as regards risk

3 - Diagnostic

- Clinical presentation
- ECG
- (High-)sensitive troponin
- Echocardiography standard for all
- Coronary CT for rule-out in low/intermediate risk patients

4 - Risk Stratification

- 3-hour fast rule-out protocol based on hs-troponin
- Ischaemic risk (GRACE score)
- Bleeding risk (CRUSADE score)

Ten Take home messages

5 - Antischaemic Therapy

6 - Antiplatelet treatment

- Aspirin lifelong for all, plus
- Ticagrelor (12 months) or
- Prasugrel (only prior PCI)
- Clopidogrel , if ticagrelor and prasugrel not available
- Glycoprotein IIb/IIIa in high risk patients, but not routinely upstream

7 - Anticoagulation

- Fondaparinux best benefit/ risk profile (add UFH if PCI)
- Enoxaparin, other low molecular weight heparins or unfractionated heparin are less recommended options
- Bivalirudin in high risk bleeding as alternative to GP IIb/IIIa + UFH in patients undergoing PCI

Ten Take home messages

8 - Revascularisation

- Timing of revascularisation customized according to risk
  - Within 72 hours all patients at risk, but
  - Within 2 hours for very high risk patients (lifethreatening symptoms)
  - Within 24 hours for patients with high risk criteria (GRACE score > 140, troponin release, ST-T changes)
- Non invasive evaluation for low risk patients

9 - Special populations and situations

- Special attention to diabetes, elderly, women, CKD, anaemia.
- Adjust medication doses according to renal function

10 - Long term management, secondary prevention

Thank you !