

# Oxfordshire PCT CPD for Primary care

- Advances in the treatment of ACS
  - Dr Rajesh Kharbanda
- Rhythm problems
  - Dr Kim Rajappan
- Valves and their replacements
  - Dr Bernard Prendergast

# Acute Coronary Syndrome

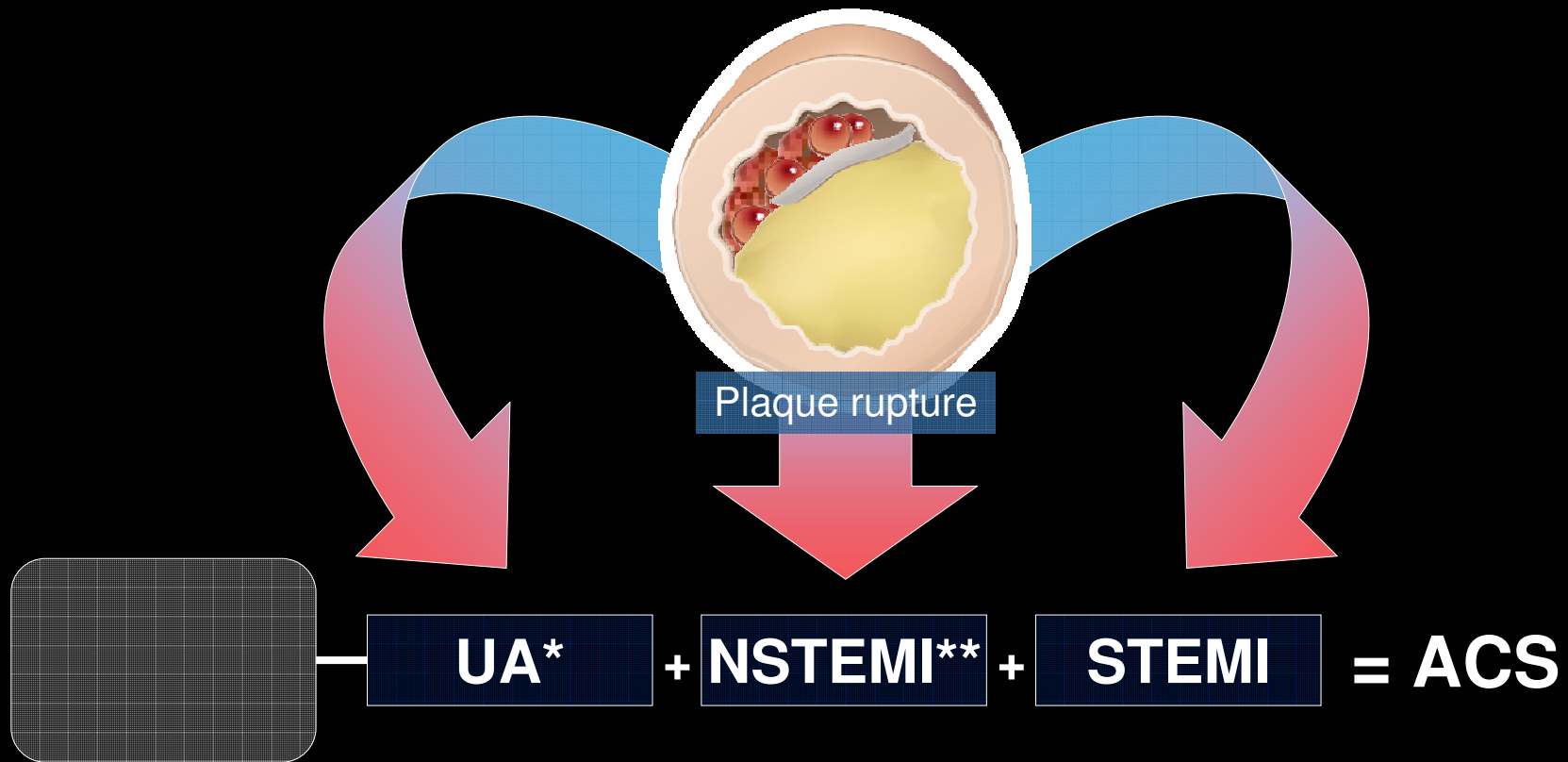
## An update

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# Learning objectives

- Update on current pathophysiology of ACS
- Knowledge of recent guidelines
- Treatment algorithm for ACS
- Knowledge of treatments offered in ACS

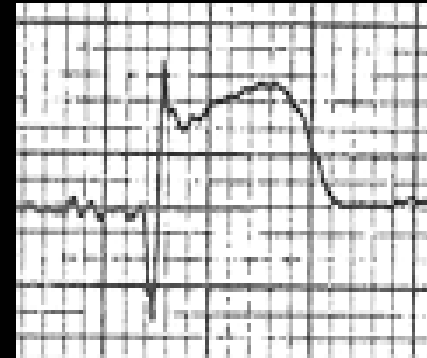
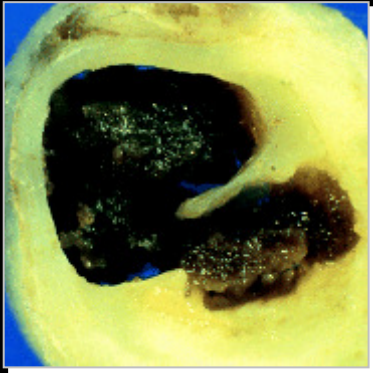
# Atherothrombosis



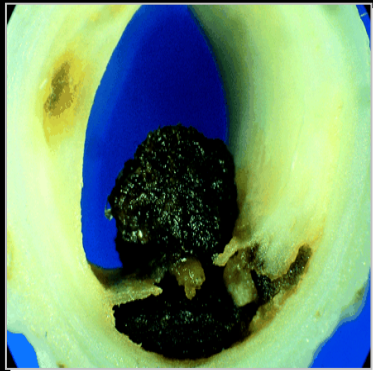
\* Unstable angina

\*\* Non-ST-segment elevation myocardial infarction

# Pathology of STEMI and UA/NSTEMI

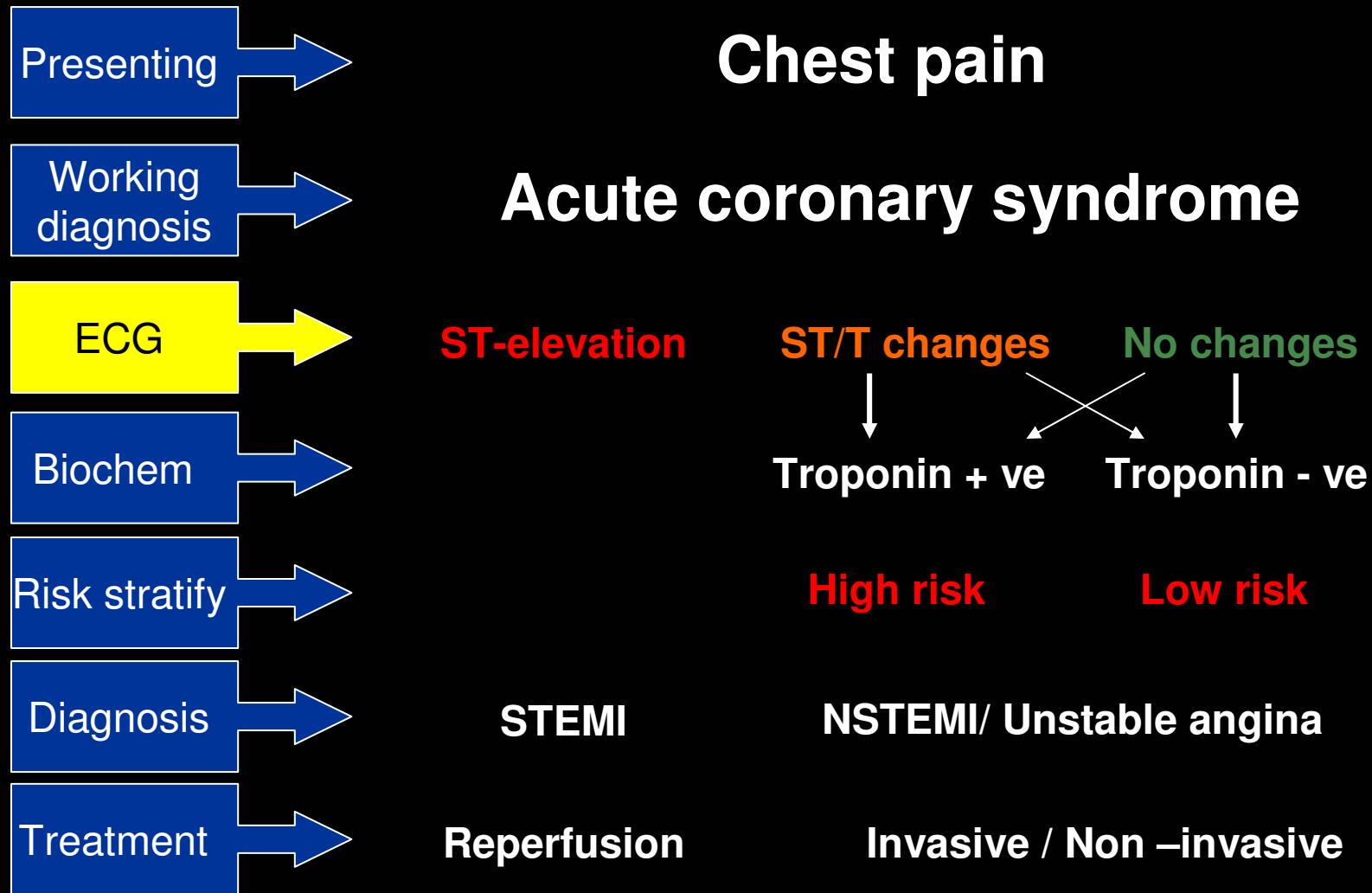


- In general terms ST elevation is a marker of complete coronary occlusion



- Incomplete occlusion is associated with ST depression, variable T wave abnormalities or with a normal ECG

# Acute coronary syndromes



Adapted from: ESC guidelines European Heart J. 2007; 28 : 1598

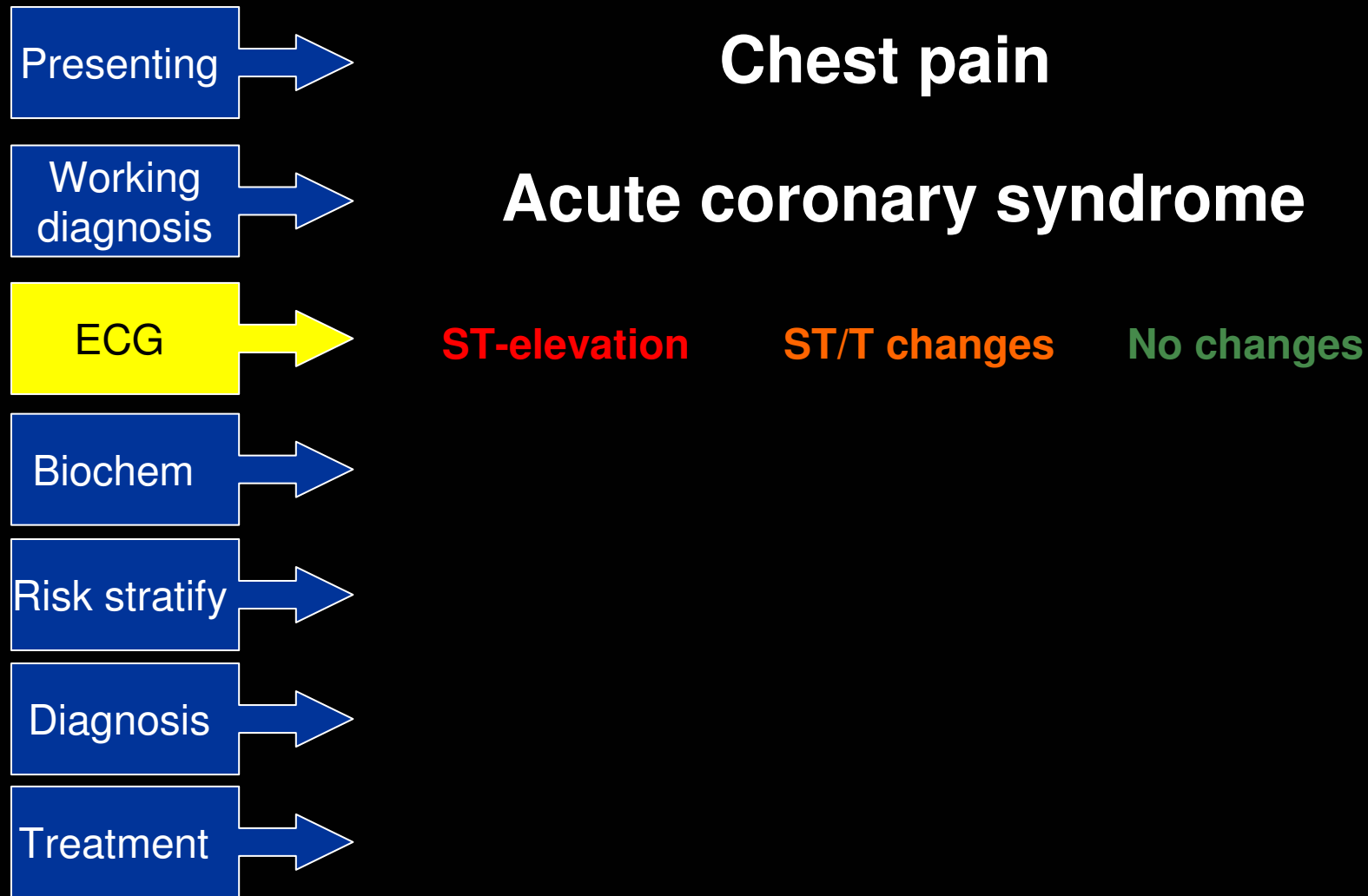
# Chest pain hospital admissions

- Chest pain is the biggest cause of presentation to A&E in the UK:
  - 600,000 patients per year
  - 150,000 have UA/NSTEMI (1 in 4)<sup>1</sup>
  - 60,000 have STEMI (1 in 10)<sup>1</sup>

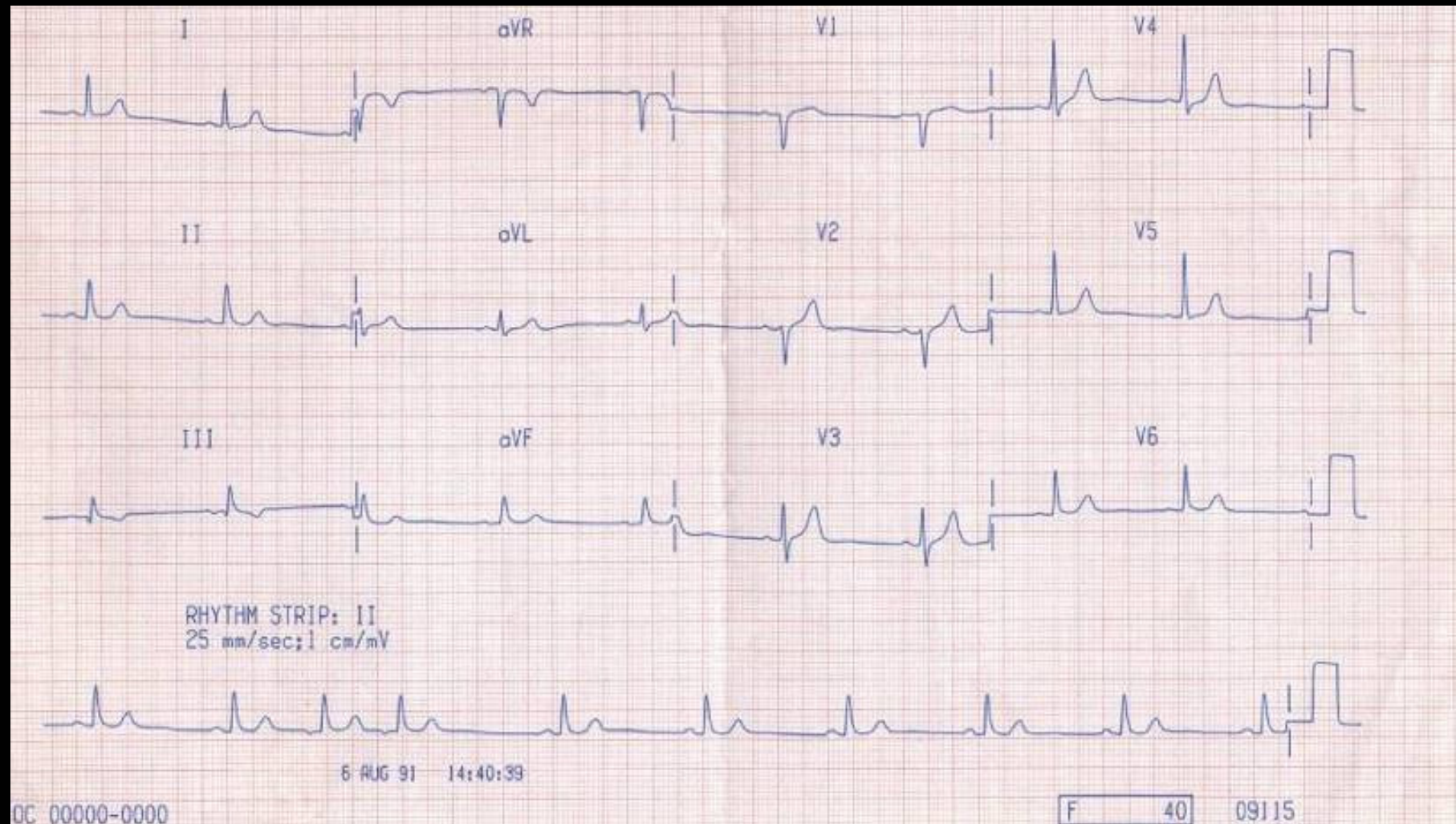
**CHEST PAIN AT REST\* = EMERGENCY ADMISSION**

\*Even if chest pain only lasts a few minutes

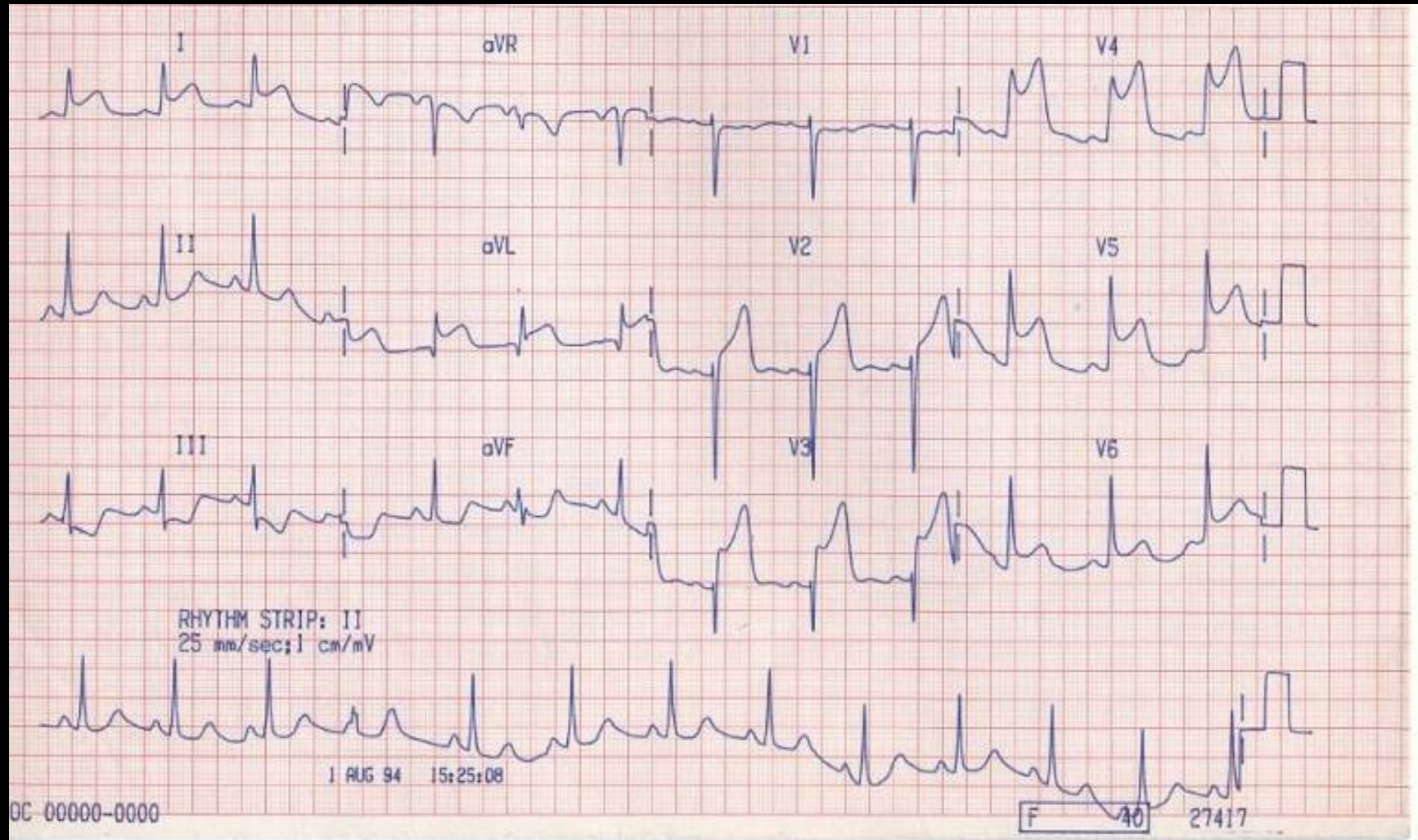
# Acute coronary syndromes



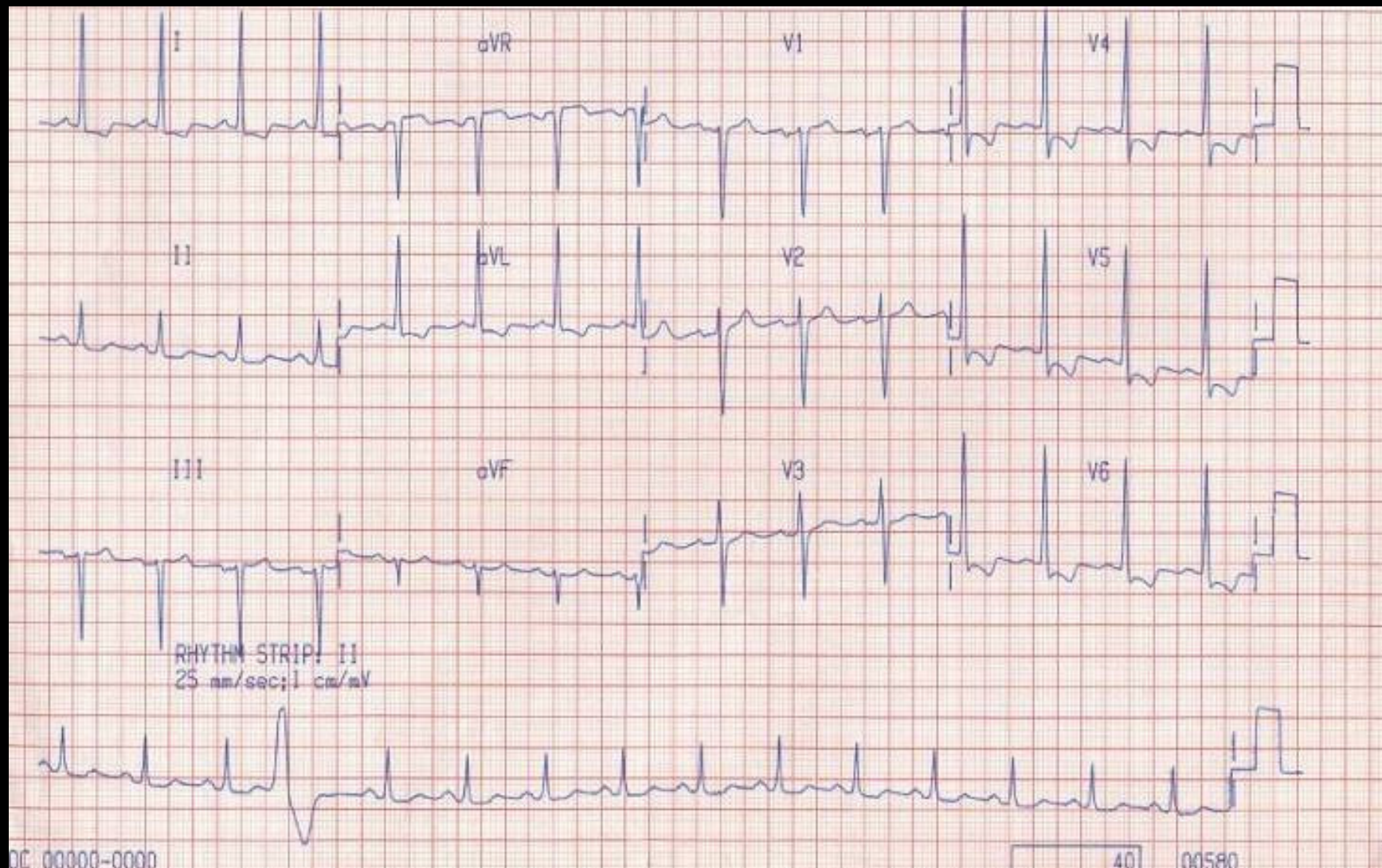
# Normal ECG



# Anterolateral STEMI with reciprocal inferior changes



# Lateral ST segment depression



# Acute coronary syndromes

Presenting →

**Chest pain**

Working diagnosis →

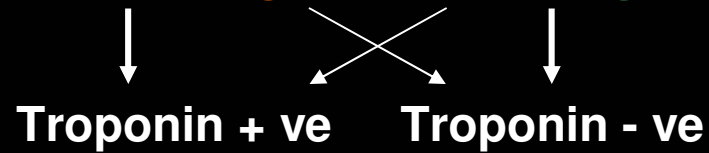
**Acute coronary syndrome**

ECG →

**ST/T changes**

**No changes**

Biochem →

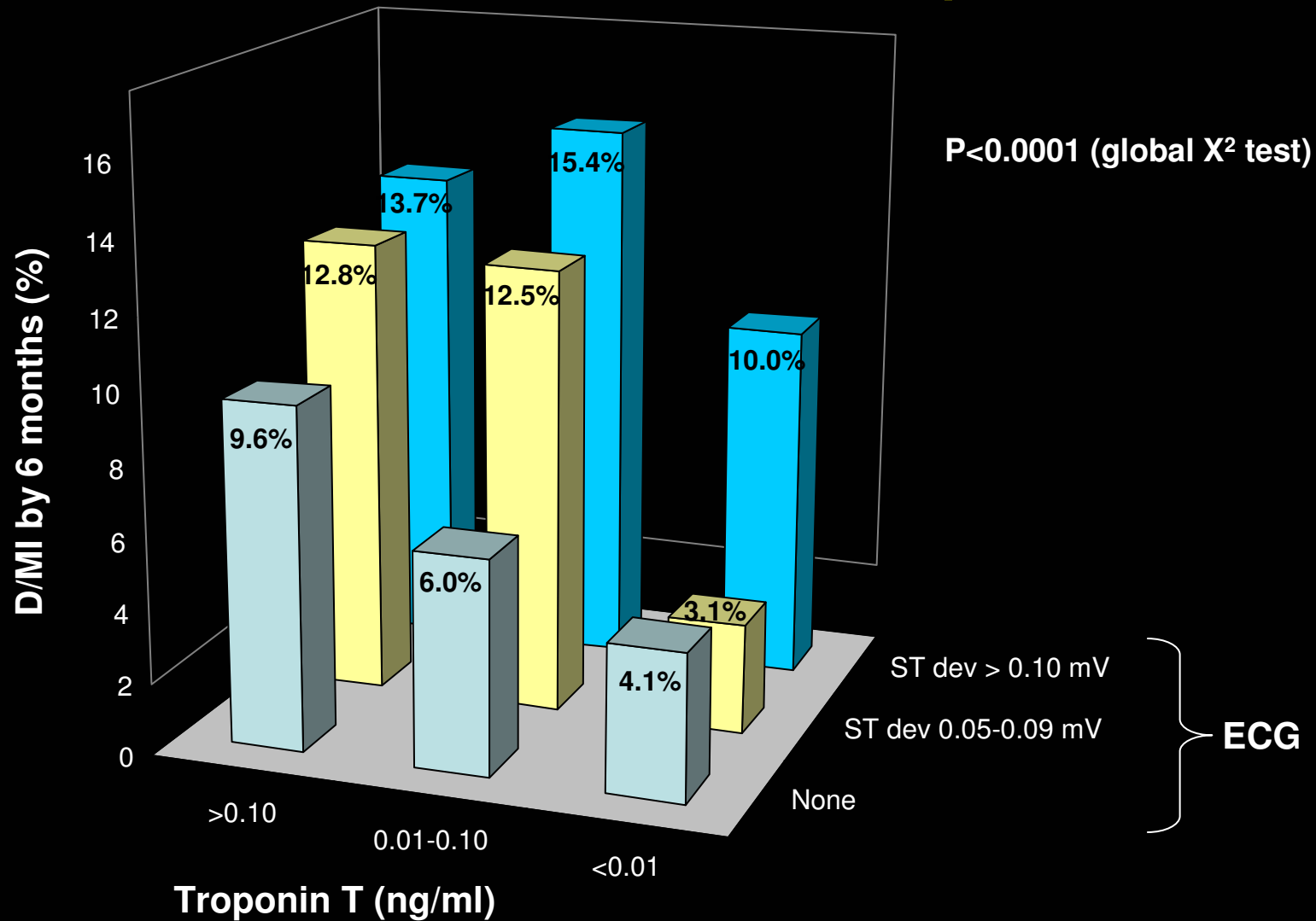


Risk stratify →

Diagnosis →

Treatment →

# Rate of death or MI in relation to ST deviation and troponin



# Risk of what, when?

- What?
  - Death
  - Myocardial infarction
  - Revascularisation
  - Refractory angina
  - Readmission
- When?
  - During admission
  - Within 48 hours
  - Within 14 days
  - Within 6 weeks, 6 months, 1 year.....

# Factors that might determine risk

- Pre-morbid
  - Age
  - Gender
  - Ethnicity
  - History of CAD
  - Co-morbidity
  - Burden of atheroma\*
  - LV function\*
- The event
  - Symptoms
  - Haemodynamic status
  - ECG changes
  - Cardiac enzyme elevation\*
  - Markers of inflammation\*

\*Unavailable on admission

# Factors that might determine risk

- The treatment
  - Type of hospital
  - Facilities available
  - Medical expertise
  - Quality of care\*
- The response to treatment
  - Recurrent pain\*
  - Dynamic ECG changes\*
  - Residual LV function\*
  - Stress testing\*

\*Unavailable on admission

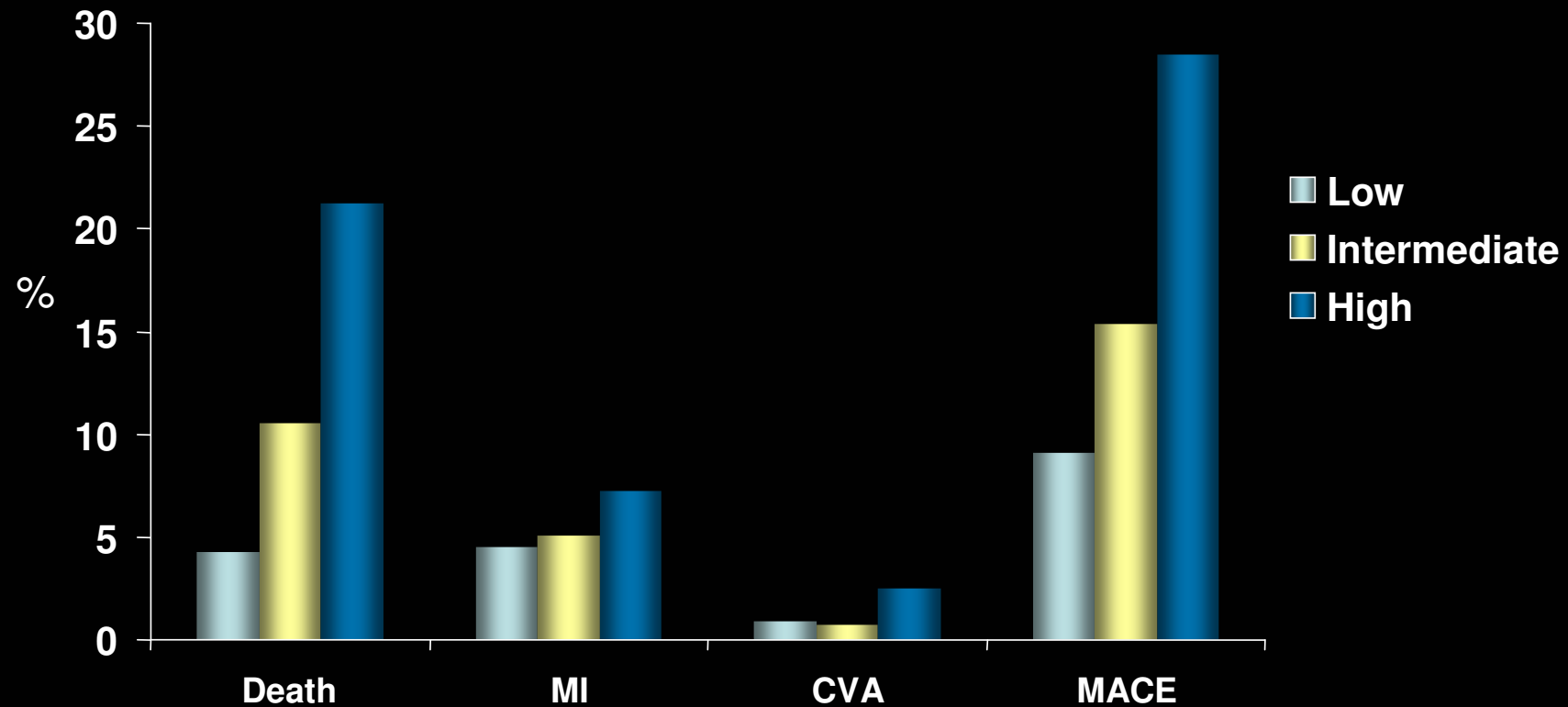
# TIMI risk score for UA/NSTEMI

HISTORICAL	POINTS
Age $\geq 65$	1
$\geq 3$ CAD risk factors (FHx, HTN, $\uparrow$ chol, DM, active smoker)	1
Known CAD (stenosis $\geq 50\%$ )	1
ASA use in past 7 days	1
<b>PRESENTATION</b>	
Recent ( $\leq 24$ H) severe angina	1
$\uparrow$ Cardiac markers	1
ST deviation $\geq 0.5$ mm	1
<b>RISK SCORE = Total Points (0–7)</b>	

RISK OF CARDIAC EVENTS (%) BY 14 DAYS IN TIMI 11B*		
RISK SCORE	DEATH OR MI	DEATH, MI OR URGENT REVASC
0/1	3	5
2	3	8
3	5	13
4	7	20
5	12	26
6/7	19	41

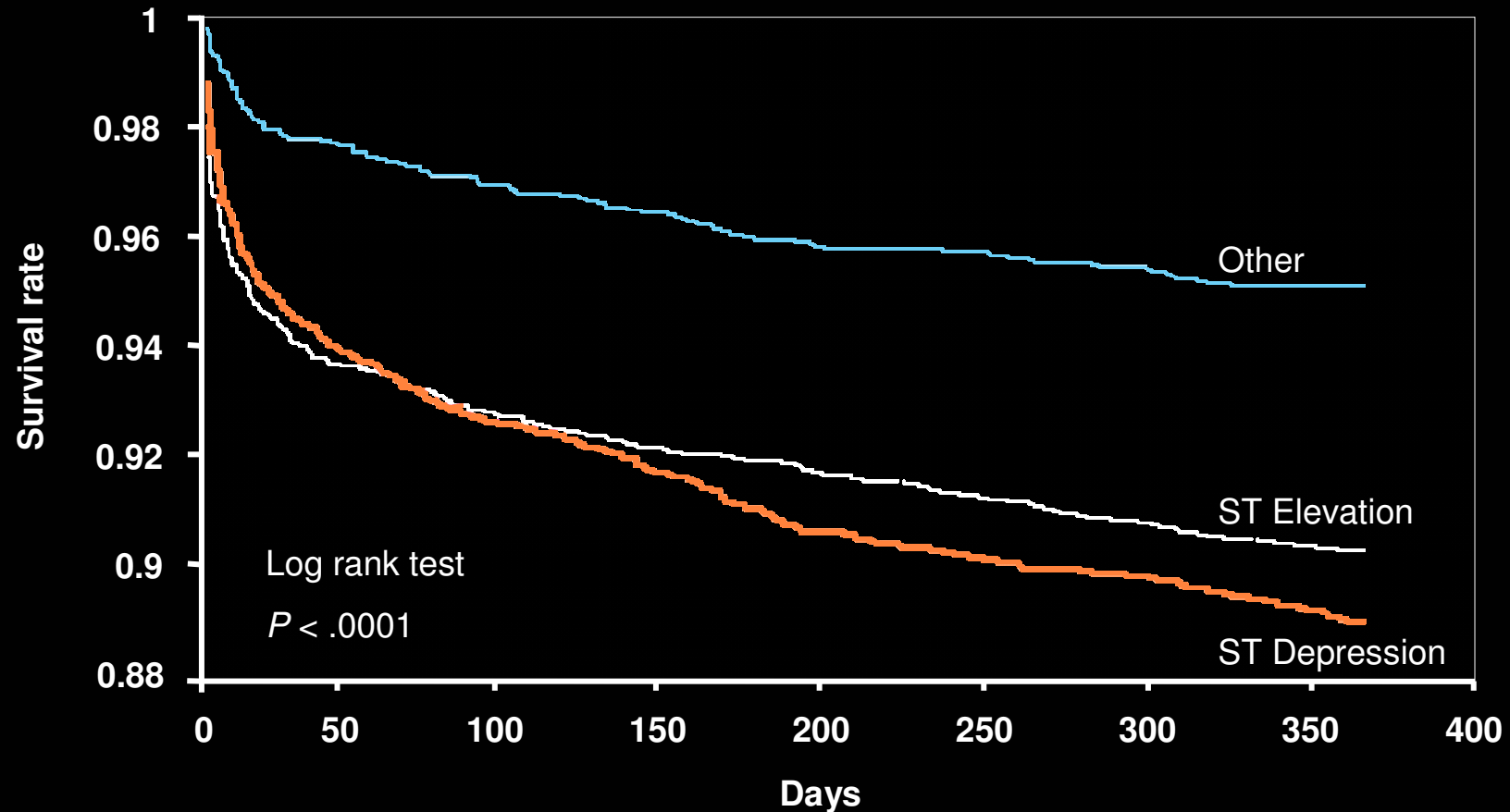
\*Entry criteria: UA or NSTEMI defined as ischemic pain at rest within past 24H, with evidence of CAD (ST segment deviation or positive marker)  
Antman et al. *JAMA* 2000;284:835-842.

# Impact of TIMI score on clinical outcomes



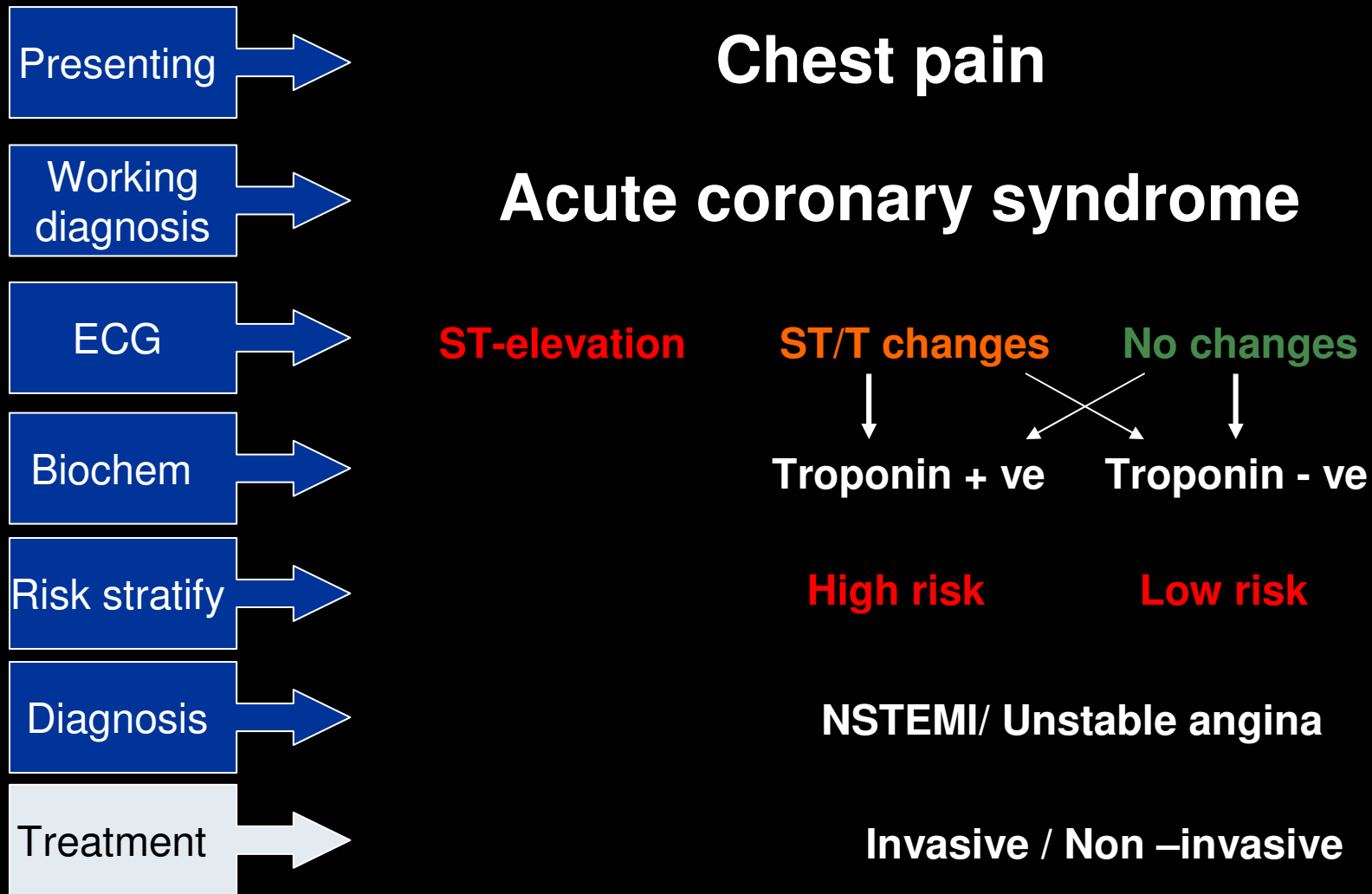
6 month mortality & morbidity in patients with ACS stratified by TIMI risk score  
n=1264

# Mortality in ACS is high – Irrespective of ECG subtype



One-year mortality was higher among ST-depression and ST-elevation subgroups compared to those with other ECG changes on admission

# Acute coronary syndromes



# Drug therapy in ACS management

- Aspirin<sup>1</sup>
- Clopidogrel<sup>1</sup>
- GPIIb/IIIa receptor antagonists<sup>1</sup>
- LMWH<sup>1</sup>
- Beta blockers<sup>1</sup>
- Nitrates (if ongoing pain/LVD)<sup>1</sup>
- Statins<sup>1</sup>
- ACE inhibitors (optional)

# Antiplatelets in ACS

## Aspirin

- Aspirin reduces death/MI in patients with ACS<sup>1</sup>
- Aspirin 300 mg loading dose, followed by 75 mg
- Patients often receive 300 mg aspirin in ambulance/A&E
- ESC guidelines in ACS recommended aspirin in all patients with suspected ACS<sup>2</sup>

1. ATTC. *BMJ* 2002;324:71-86.

2. ESC ACS Task Force. *Eur Heart J* 2007;28:1598-1660

# Antiplatelets in ACS

## Clopidogrel in UA/NSTEMI

- A loading dose (300 mg) should be followed by 75 mg clopidogrel o.d. (in combination with aspirin if not contraindicated)<sup>1,2,3</sup>
- ESC ACS guidelines recommended clopidogrel in the acute and long-term treatment of UA/NSTEMI patients<sup>4</sup>
- NICE guidance recommends clopidogrel, in combination with low-dose aspirin for 12 months, for the management of patients with UA/NSTEMI<sup>5</sup>

1. CURE Trial Investigators. *N Engl J Med* 2001;345:494–502. 2. Chen ZM et al. *Lancet* 2005;366(9497):1607–21.  
3. Sabatine M et al. *New Engl J Med* 2005;352:1179–1189.  
4. ESC ACS Task Force. *Eur Heart J* 2007;28:1598-1660 5. <http://www.nice.org.uk/page.aspx?o=213432>

# Beta blockers in ACS

- Beta blockers decrease myocardial oxygen consumption
- Beta blockers are recommended in ACS in the absence of contraindications (asthma, acute LV dysfunction, impaired atrioventricular conduction)<sup>1</sup>
- Long term outcome data

# Nitrates in ACS

- Major therapeutic benefit is probably related to venodilator effects resulting in decreased myocardial oxygen consumption
- The dose should be titrated upwards until symptoms are relieved or side effects (notably headache or hypotension) occur<sup>1</sup>
- Intravenous nitrates should be given to patients with prolonged or recurrent pain
- Reduces ischaemia

# Statins in ACS

- Effective doses of lipid-lowering therapy should be initiated without delay before hospital discharge<sup>1–3</sup>
- HMG-CoA reductase inhibitors substantially decrease mortality and coronary events in patients with high/intermediate/and even low levels of LDL cholesterol (Heart protection study)<sup>1</sup>
- Statins may provide an immediate benefit in ACS (PURSUIT, PRISM, PRISM-PLUS)<sup>1</sup>

1. ESC ACS Task Force. *Eur Heart J* 2007;28:1598-1660.  
2. Sacks FM. *Eur Heart J* 2004;6 (Supplement A):A32–36.  
3. Ray KK *et al.* *JACC* 2005;46(9):1405–10.

# ACE inhibitors

- There are currently no published placebo controlled trials of ACE inhibitors in ACS
- Support for long-term outpatient use
  - Heart Outcomes Prevention Evaluation (HOPE)<sup>1</sup>
  - European Trial On Reduction of Cardiac Events With Perindopril in Stable Coronary Artery Disease (EUROPA)<sup>2</sup>
  - Treatment with ACE inhibitors resulted in a 20% to 22% relative risk reduction in the combined end point of CV death, MI, and stroke or cardiac arrest ( $P < 0.001$  for all)
- Less evidence for lower risk patients

1. Yusuf et al. *N Engl J Med* 2000;342:145–153.

2. Fox et al. *Lancet* 2003;362:782–788.

# GPIIb/IIIa inhibitors in ACS

- GPIIb/IIIa inhibitors are potent intravenous antiplatelet drugs<sup>1</sup>
- Most likely to be used in high-risk patients
- May be recommended by cardiologist as bridge to cath lab in patients with ongoing pain or dynamic ECG changes
- ESC guidance recommends GPIIb/IIIa inhibitors for UA/NSTEMI patients with comorbid diabetes<sup>2</sup>
- NICE guidance recommends that GPIIb/IIIa inhibitors should be considered early in the management of ACS<sup>3</sup>

1. Williams. *Pharm J* 2002;269:747-49.

2. ESC ACS Task Force. *Eur Heart J* 2007;28:1598-1660.

3. <http://www.nice.org.uk/age.aspx?o=36351>.

# ACS: treatment summary

**Diagnosis**

UA/NSTEMI ACS

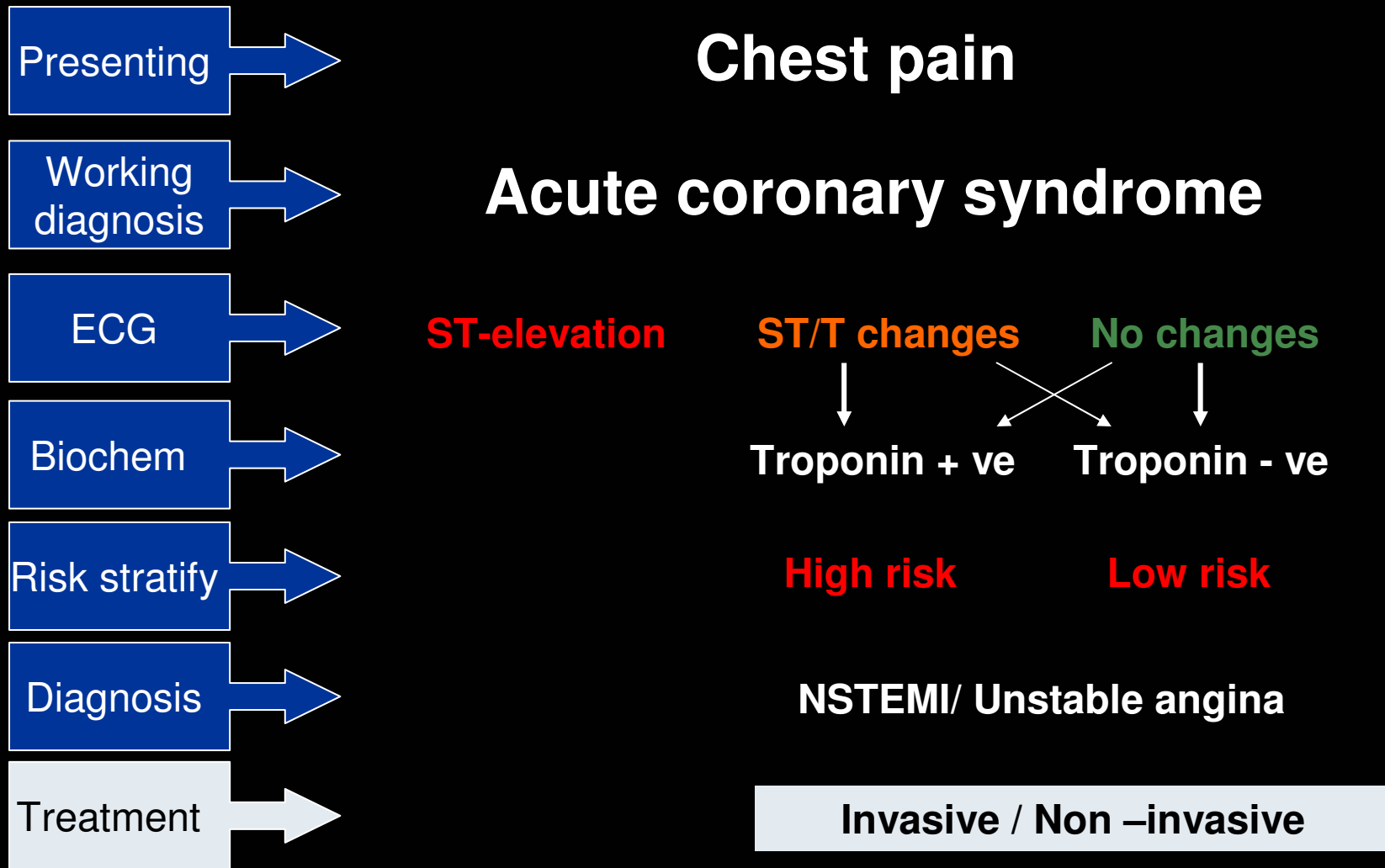
**Treatment**

aspirin, clopidogrel, LMWH, beta blockers, nitrates, GPIIb/IIIa inhibitors

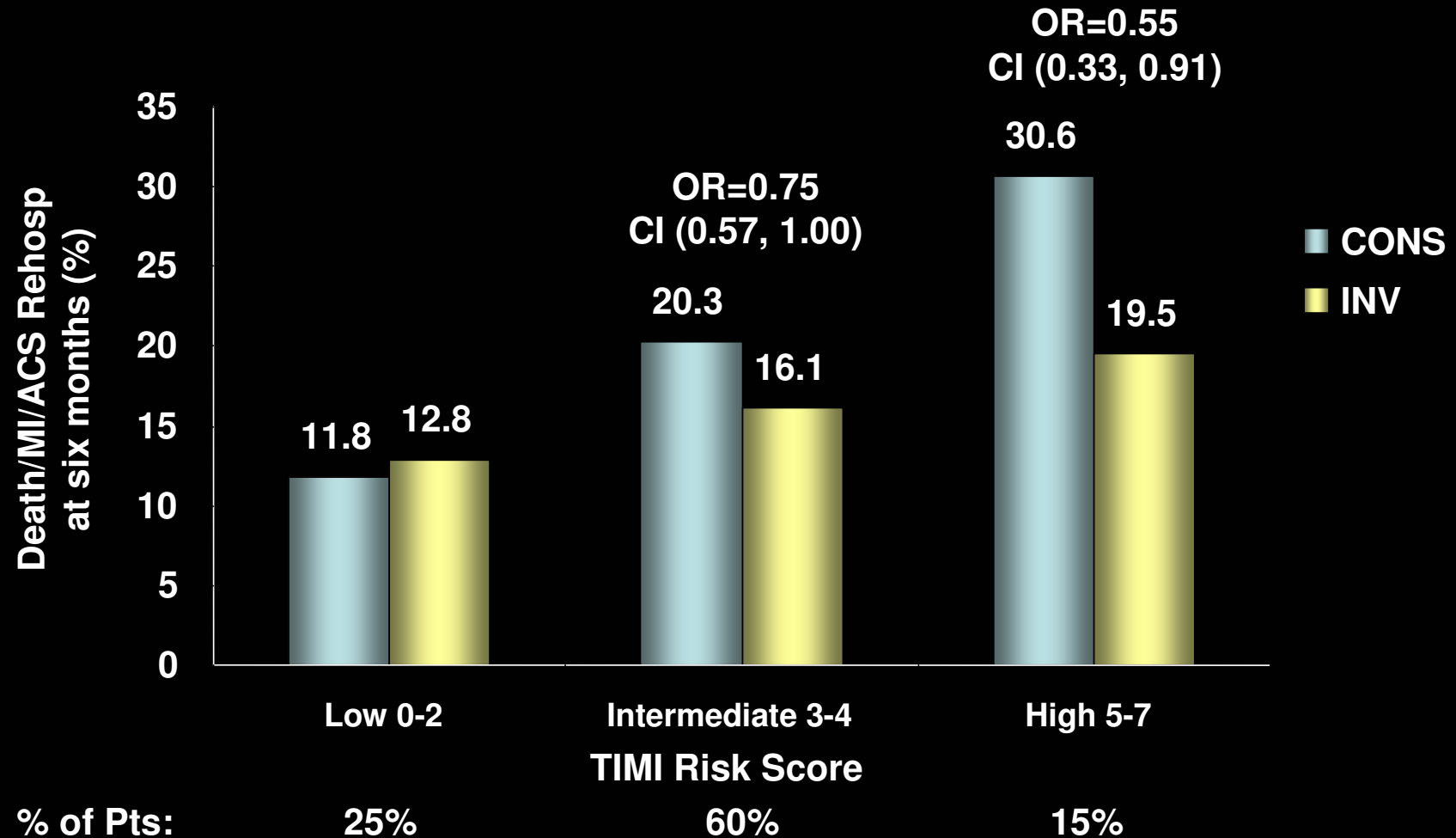
**Secondary prevention**

aspirin, clopidogrel, beta blockers, statin, ACE inhibitors

# Acute coronary syndromes



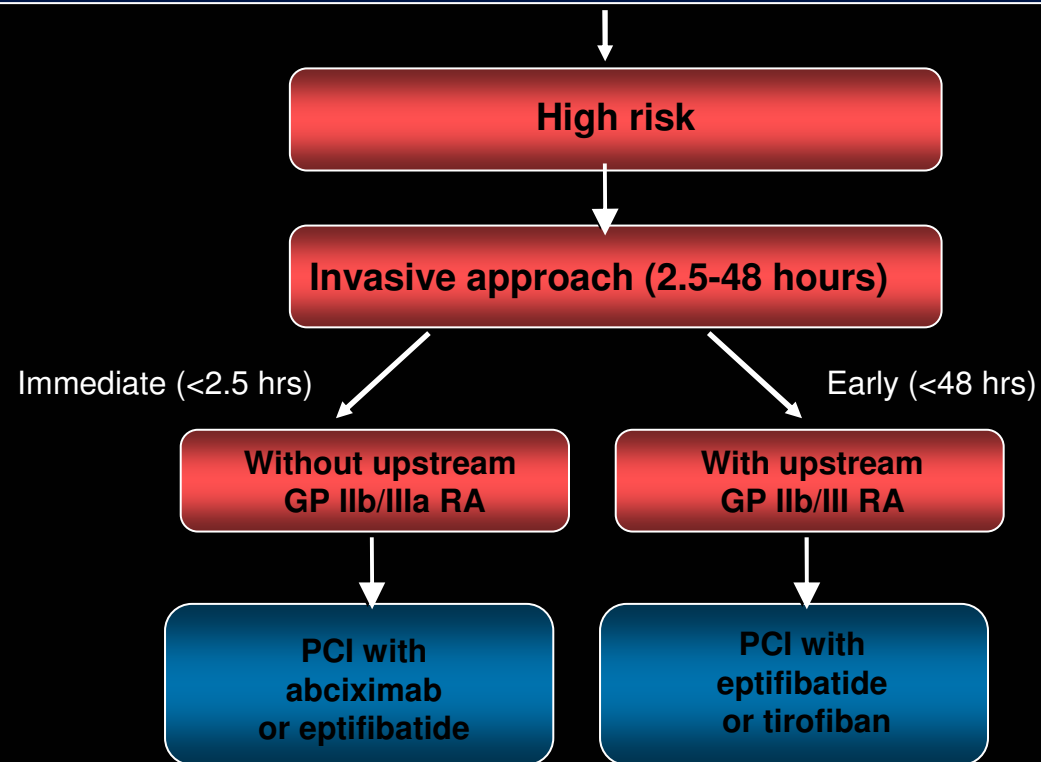
# Outcome by risk score at 6 months



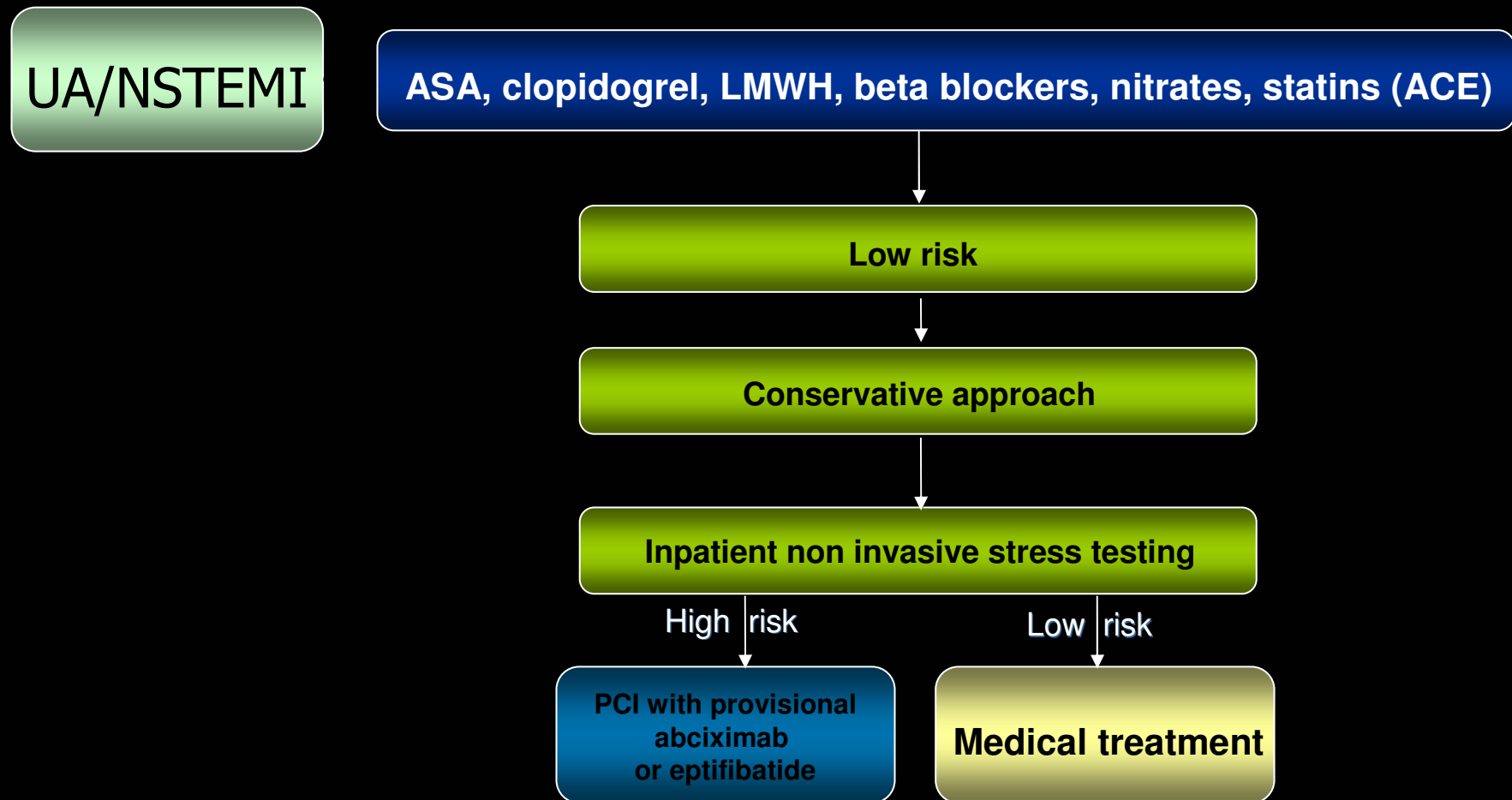
# ESC guidelines for UA/NSTEMI

UA/NSTEMI

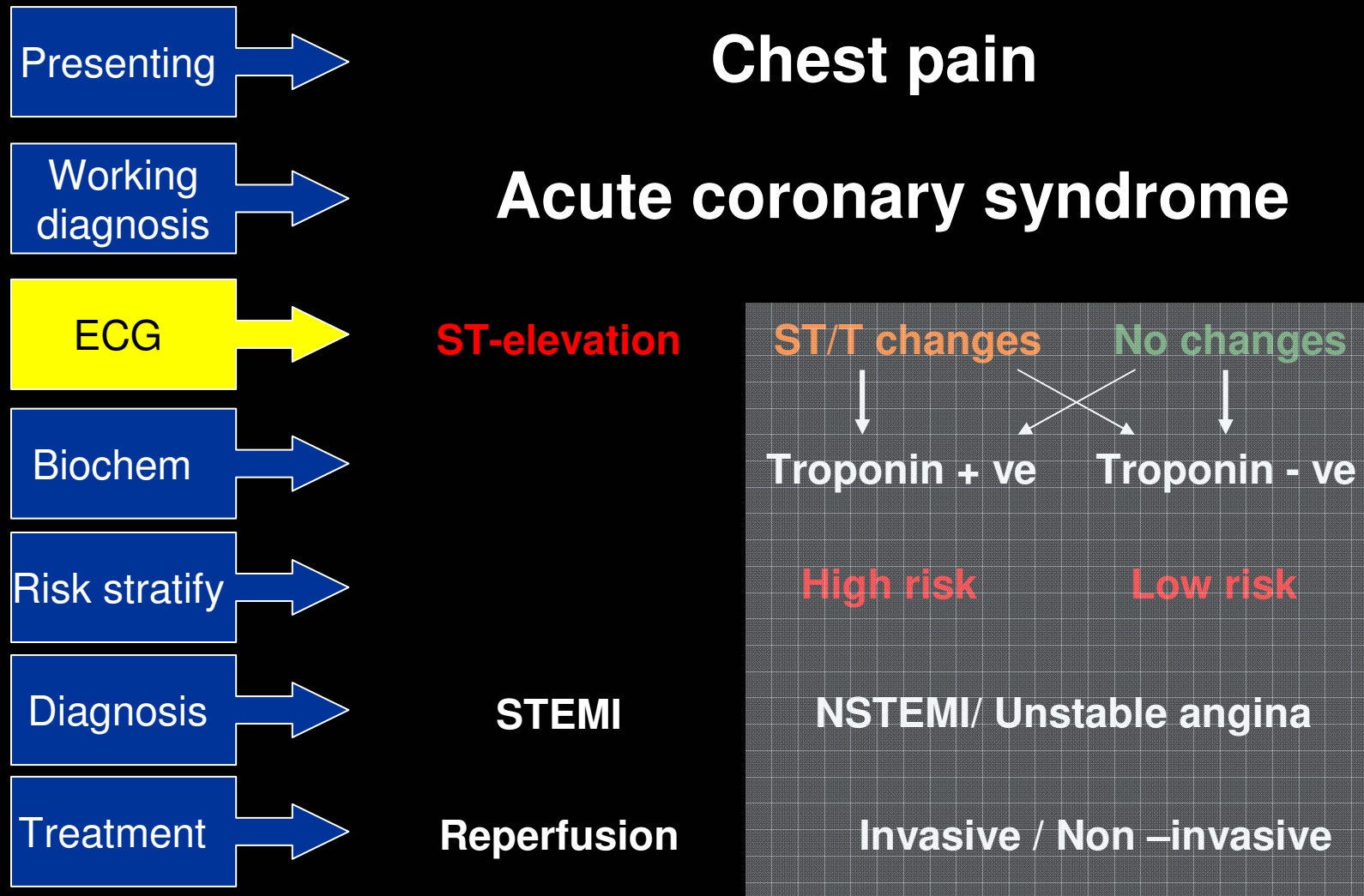
ASA, clopidogrel, LMWH, beta blockers, nitrates, statins (ACE)



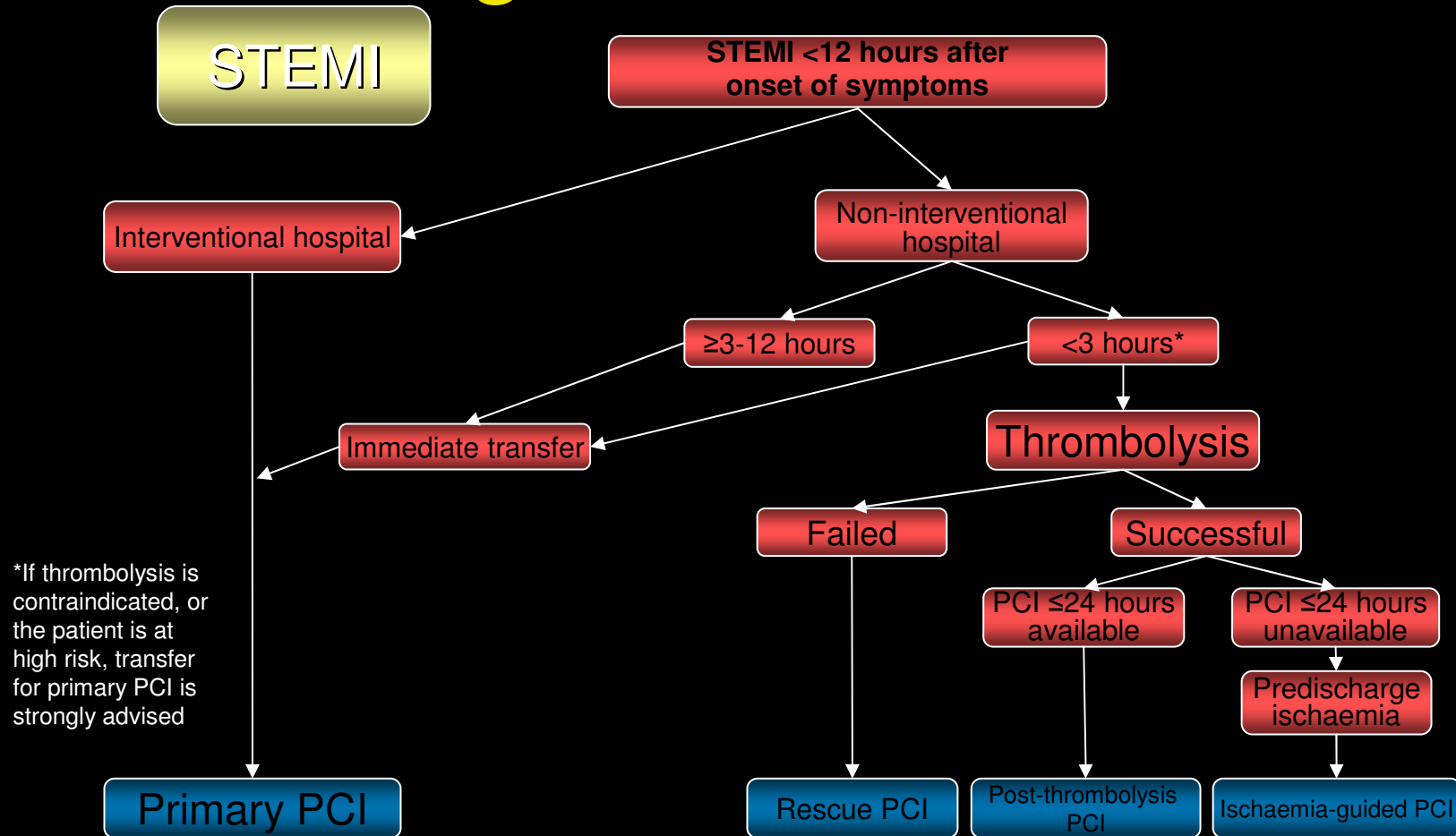
# ESC guidelines for UA/NSTEMI



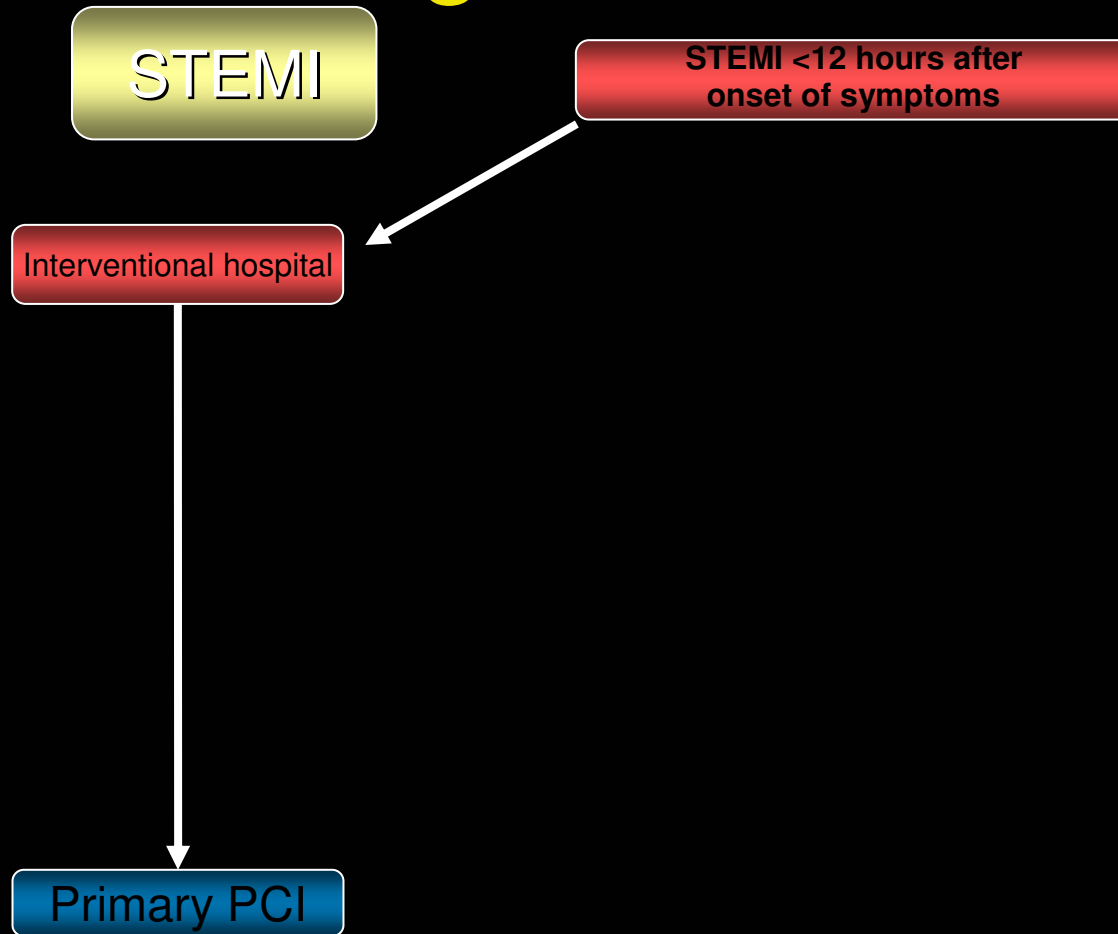
# Acute coronary syndromes



# ESC PCI guidelines for STEMI

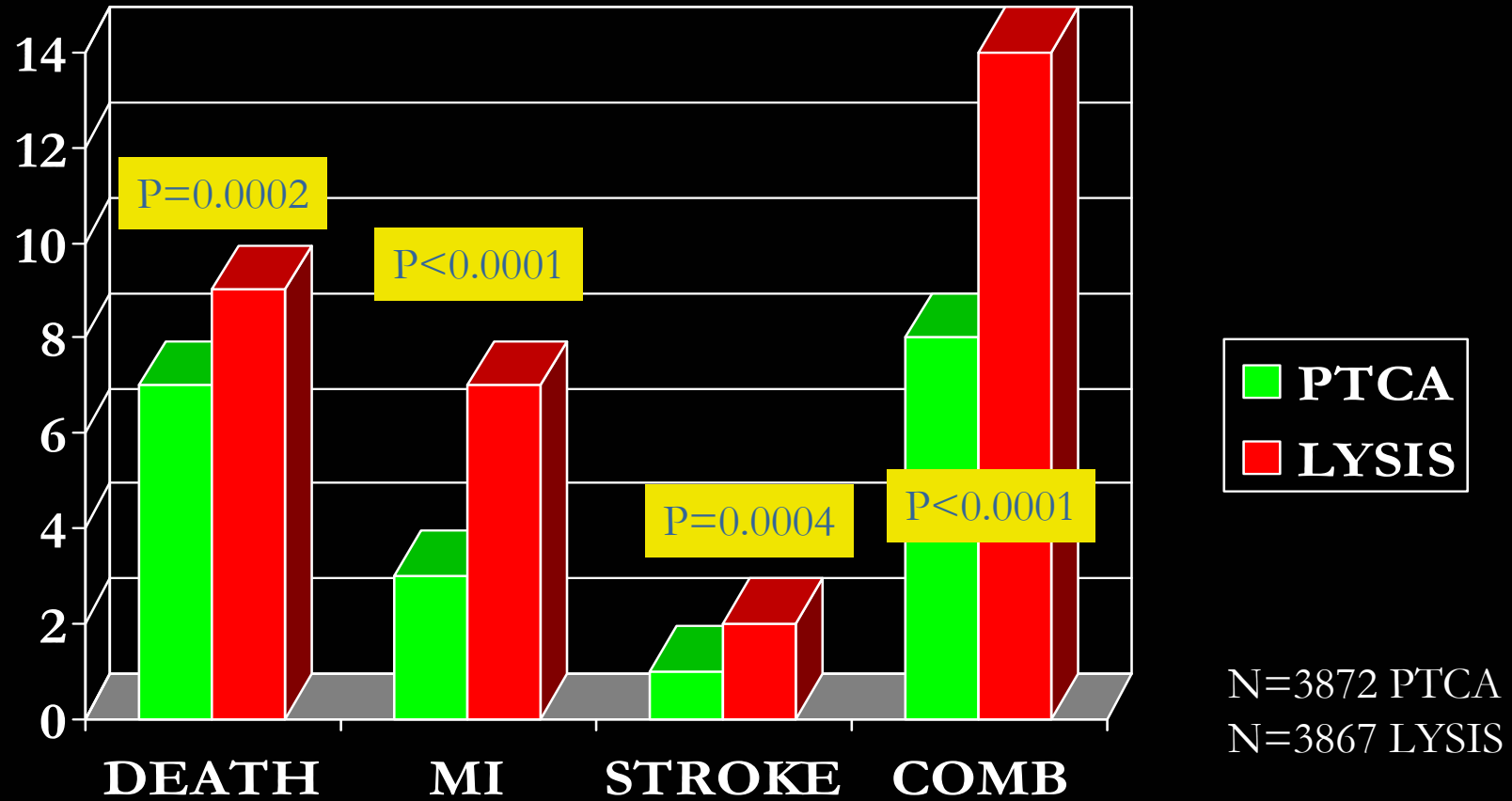


# ESC PCI guidelines for STEMI



*Adapted from Silber S et al. ESC PCI guidelines, Eur Heart J 2005. 26; 804–847*

## PRIMARY PCI V S THROMBOLYSIS: META-ANALYSIS OF 23 RANDOMISED TRIALS

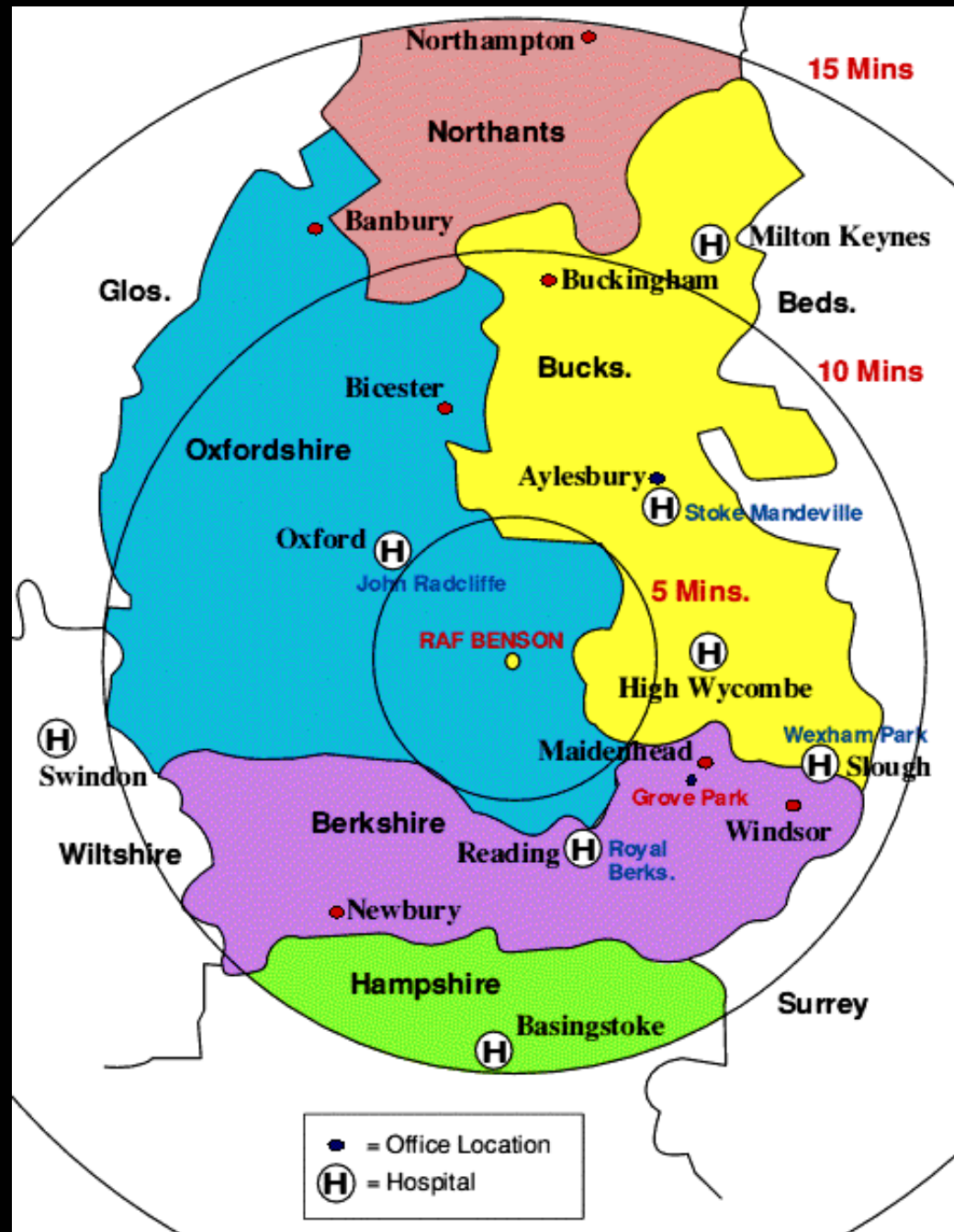


Keeley EC, Boura JA, Grines CL.  
Lancet. 2003 Jan 4;361(9351):13-20.

# Initial medical management – Reperfusion therapy

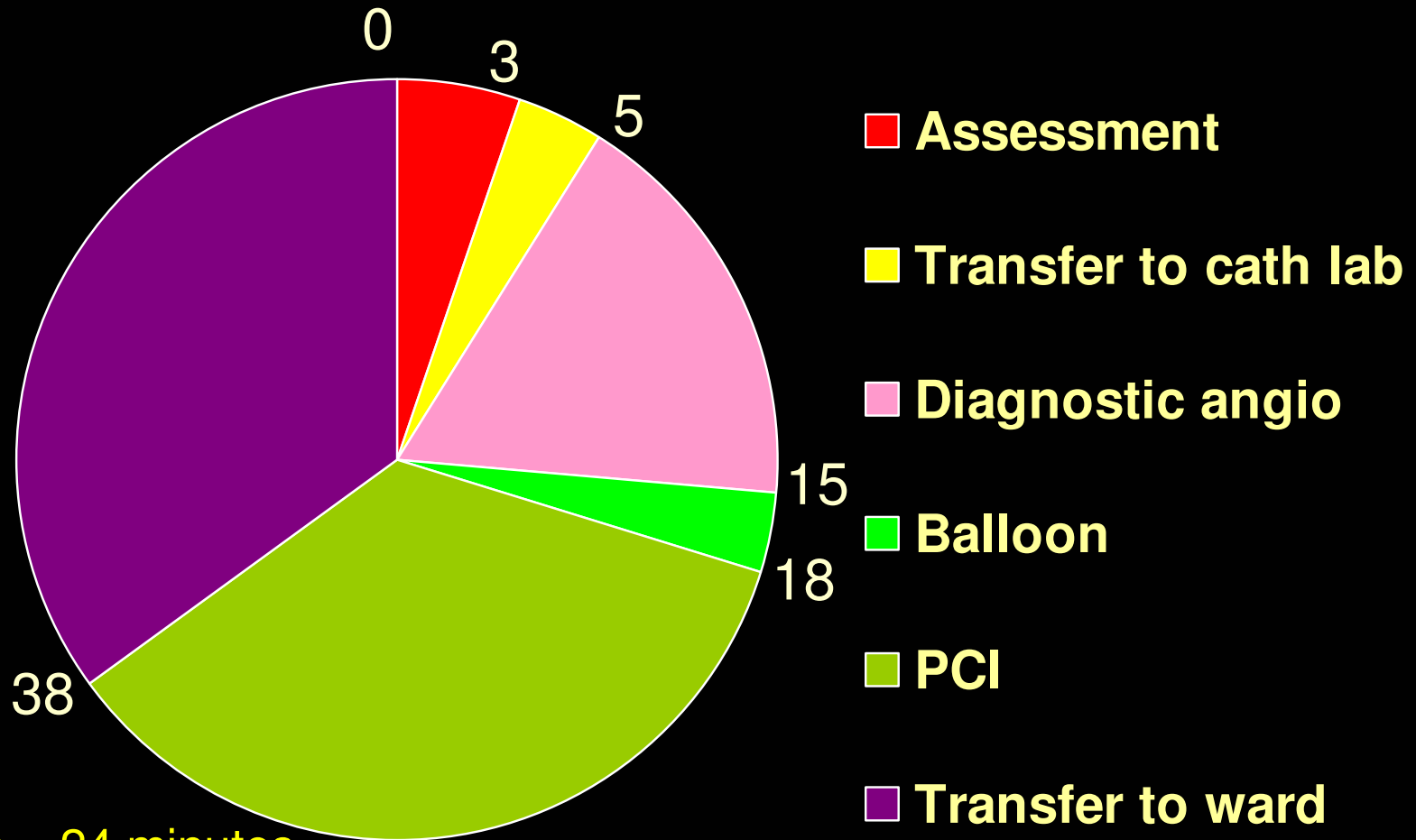
- Choice of reperfusion therapy
  - Fibrinolysis reduces mortality in STEMI, but no benefit to patients who have UA/NSTEMI<sup>1</sup>
  - Primary PCI (primary angioplasty)
    - higher patency and
    - lower rates of recurrent MI than in-hospital fibrinolysis<sup>1</sup>
  - In the UK, of those patients having reperfusion treatment for heart attack, 22% now receive primary PCI - previously would have had fibrinolytic drugs<sup>2</sup>
  - Clinical evidence suggests primary PCI is superior to fibrinolytic therapy<sup>3</sup>

1. Task Force on the management of acute myocardial infarction of the European Society of Cardiology. *Eur Heart J.* 2003;24:28-66
2. Department of Health. Vascular Programme Team. National Infarct Angioplasty Project: Interim report. February 2008
3. Betriu A. *Am J Cardio.* 2005;95:100-101



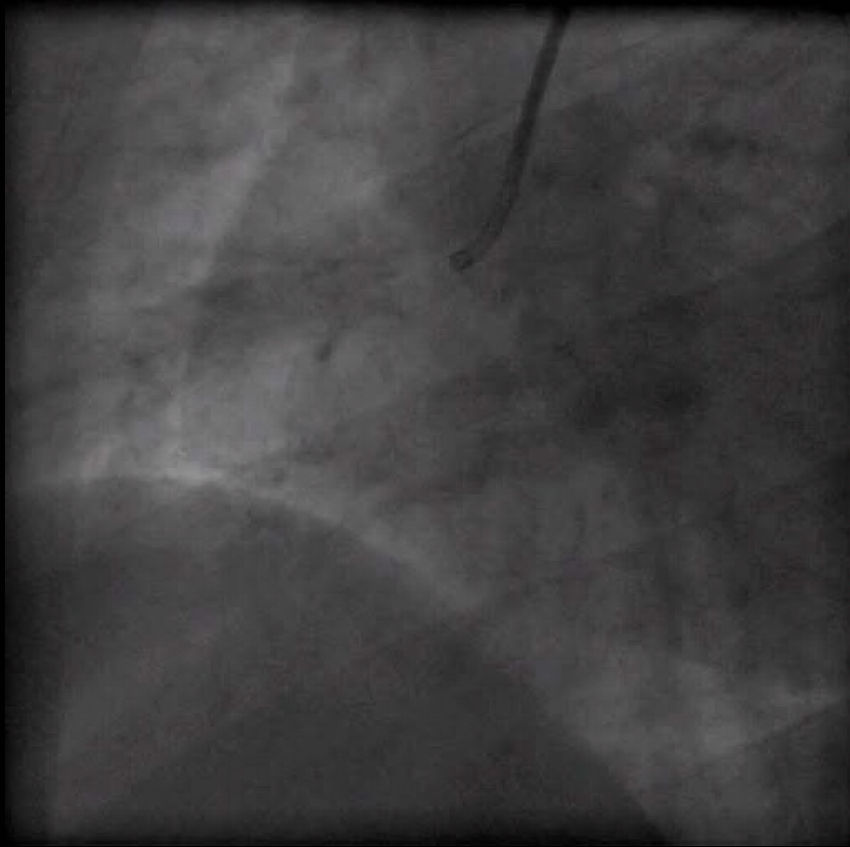


# Door to balloon times

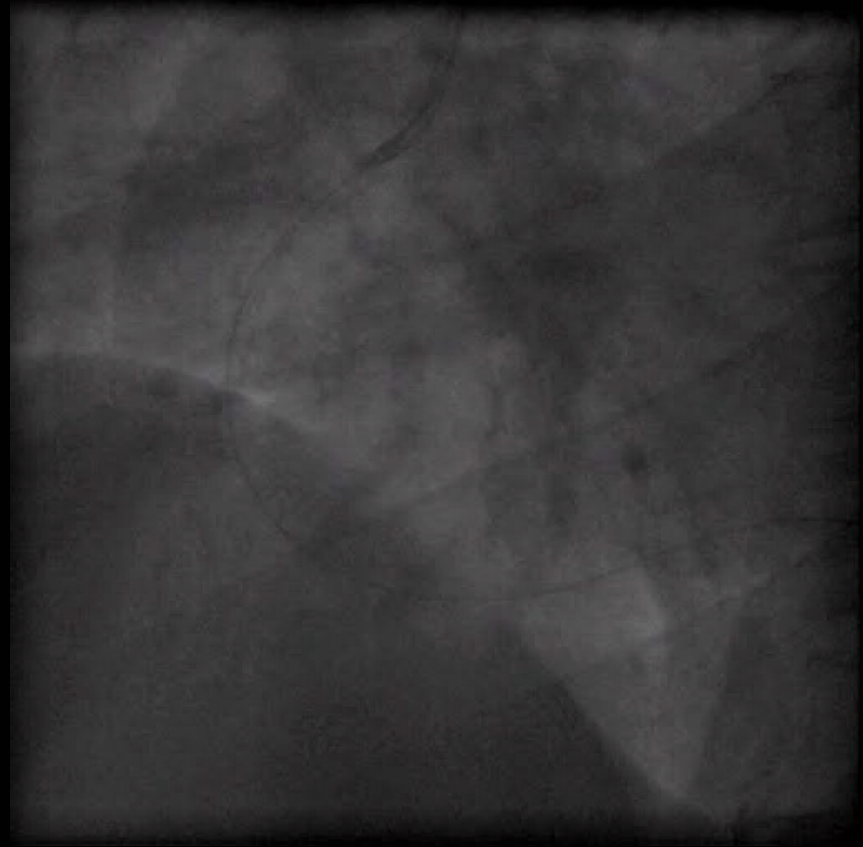


Median = 24 minutes

# Chest pain and inferior STEMI

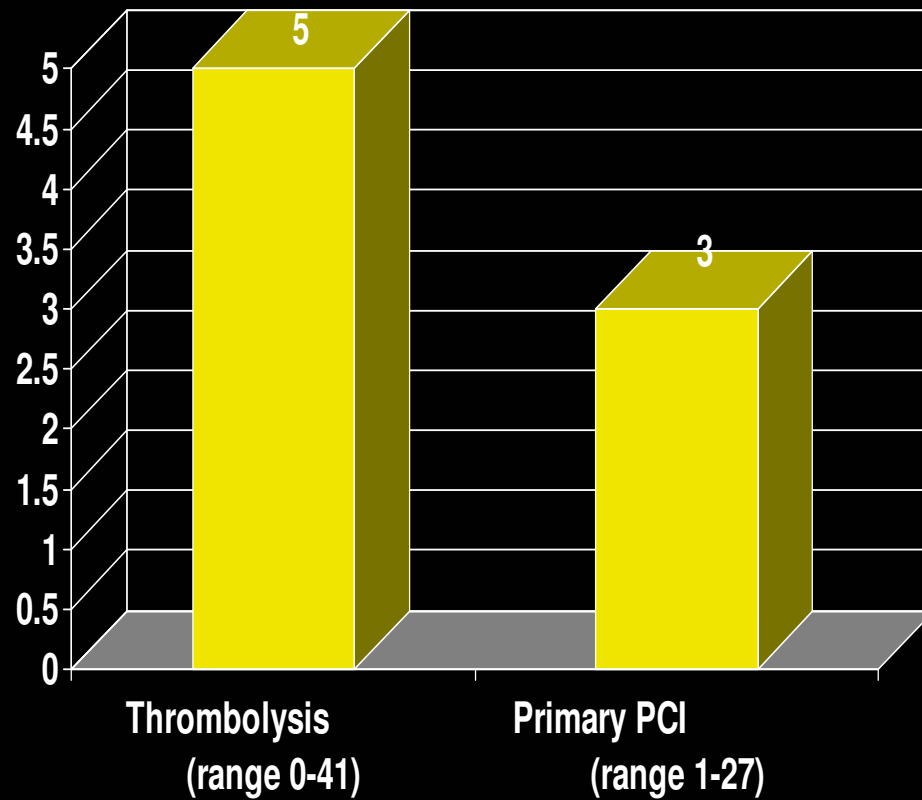


**Before**



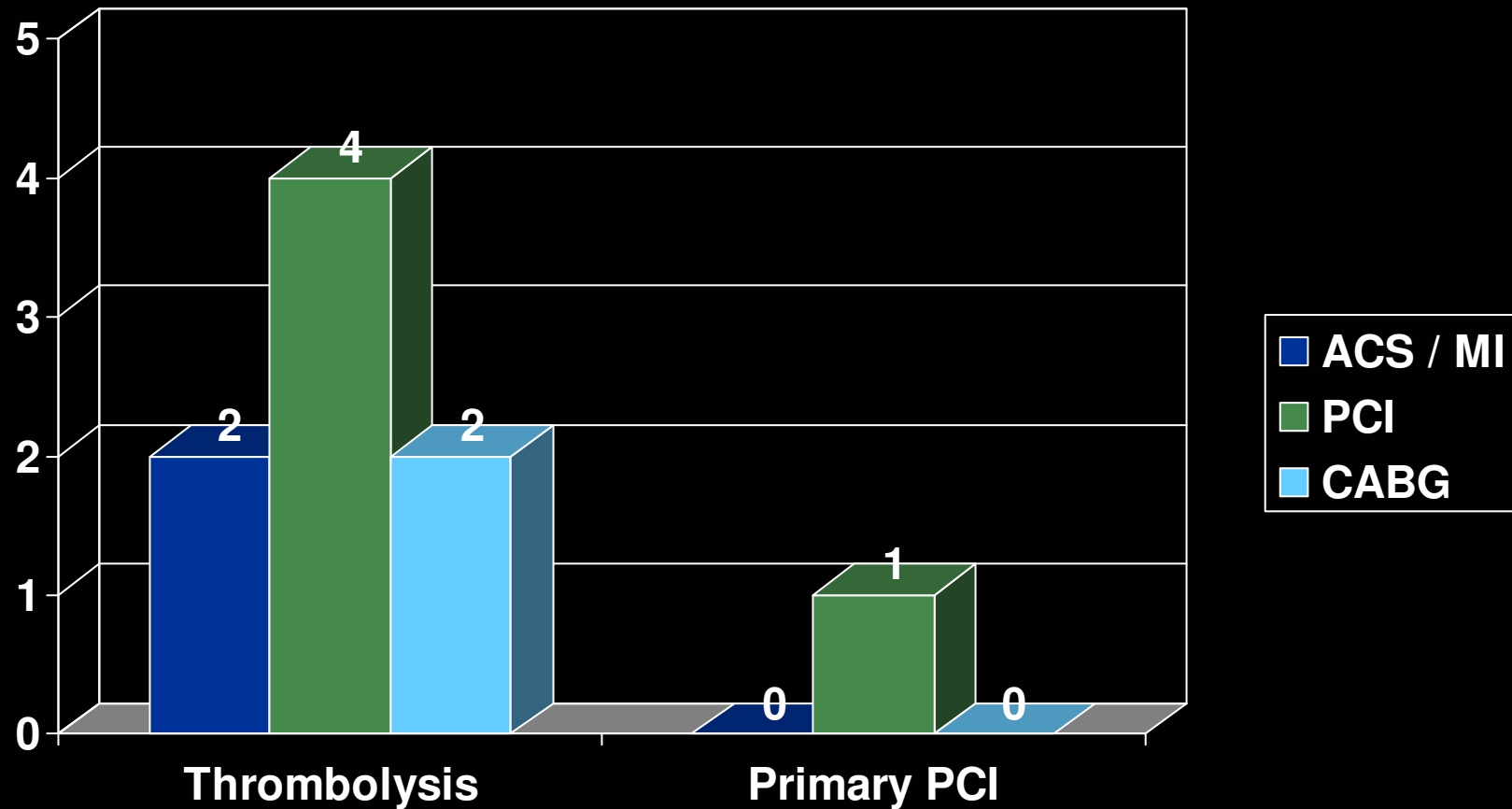
**After**

# Reduced hospital stay – ORH



- Very early discharge
- 48 hours if uncomplicated
- 42% home at 48 hours
- 78% home day 3

# Readmission at 30 Days – ORH



# Continued medical management

- Long term risk factor management:
  - Antithrombic therapy – aspirin, combination antiplatelets<sup>1</sup>
  - Other drugs – ACE inhibitors, ARBs<sup>1</sup>
  - Cholesterol reduction – Statins<sup>1</sup>
  - Blood pressure reduction<sup>1</sup>
  - Non-drug treatment – cardiac rehabilitation (exercise) and smoking cessation

1. Gami A *et al.* Secondary prevention of ischaemic cardiac events. *BMJ Clin Evid.* 2007  
Available at [www.bmj.com](http://www.bmj.com). [Last accessed January 2008]

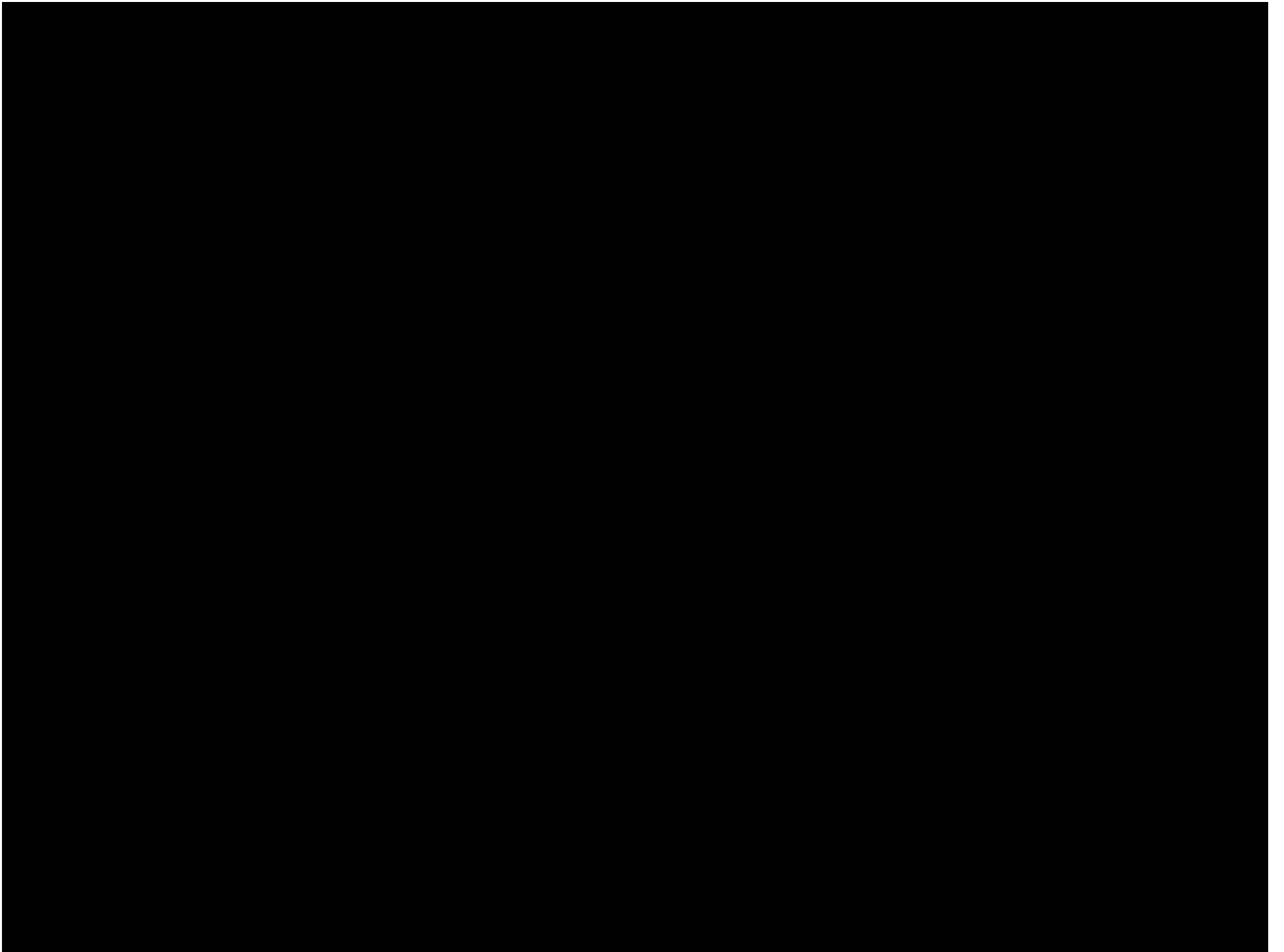
# ACS: Treatment summary

Diagnosis	STEMI	UA/NSTEMI
Early treatment	Morphine, oxygen, nitrates and antiplatelets <sup>1</sup>	Morphine, oxygen, nitrates, and antiplatelets <sup>2</sup>
In-hospital treatment	Aspirin, Clopidogrel, B blocker, statin and ACE +/- reopro, heparin <b><u>PPCI</u></b>	Aspirin, Clopidogrel, B blocker, statin and ACE +/- reopro, heparin <b><u>? PCI</u></b>
Long term Community	Aspirin, clopidogrel, ACE inhibitor, B blocker statins <sup>3,6</sup>	Aspirin, clopidogrel, ACE inhibitor, B blocker statins <sup>3,6</sup>

1. Task Force on the management of acute myocardial infarction of the European Society of Cardiology. *Eur Heart J.* 2003;24:28-66
2. Task Force for the diagnosis and treatment of Non-ST-Segment Elevation Acute Coronary Syndromes of the European Society of Cardiology. *Eur Heart J.* 2007;28:1598-1660
3. NICE clinical guideline 48 available at <http://www.nice.org.uk/guidance/index.jsp?action=byID&o=11008> [Last accessed January 2008]
4. Sabatine MS *et al.* The CLARITY-TIMI 28 Investigators. *NEJM.* 2005;352:1179-1189
5. The CURE Investigators. *NEJM.* 2001;345:494-503
6. The COMMIT Investigators. *Lancet.* 2005;366:1607-1621

# Major changes in ACS

- Updated guidelines – ESC 2007
- Aggressive medical therapy: early
- Aggressive early interventional/  
revascularisation therapy
- Early risk factor modification (hospital)
- Long-term risk factor modification  
(community)



# Antiplatelets in ACS

## Clopidogrel in STEMI<sup>1,2</sup>

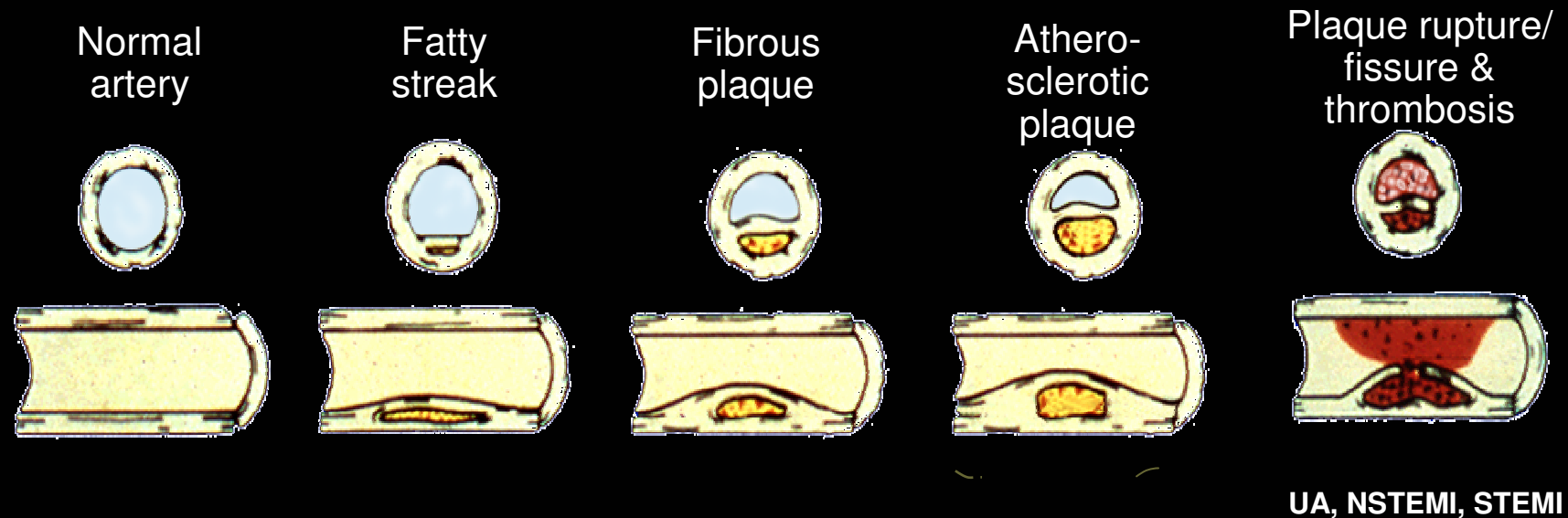
- A loading dose (300 mg) should be followed by 75 mg clopidogrel o.d. (in combination with aspirin if not contraindicated) in patients <75 years<sup>2</sup>
- Loading doses have not been studied in STEMI patients >75 years<sup>1</sup>
- The effects of clopidogrel have only been examined up to 28 days in patients with STEMI<sup>1</sup>

1. Chen ZM et al. Lancet 2005;366(9497):1607–21

2. Sabatine M et al. New Engl J Med 2005;352:1179–1189

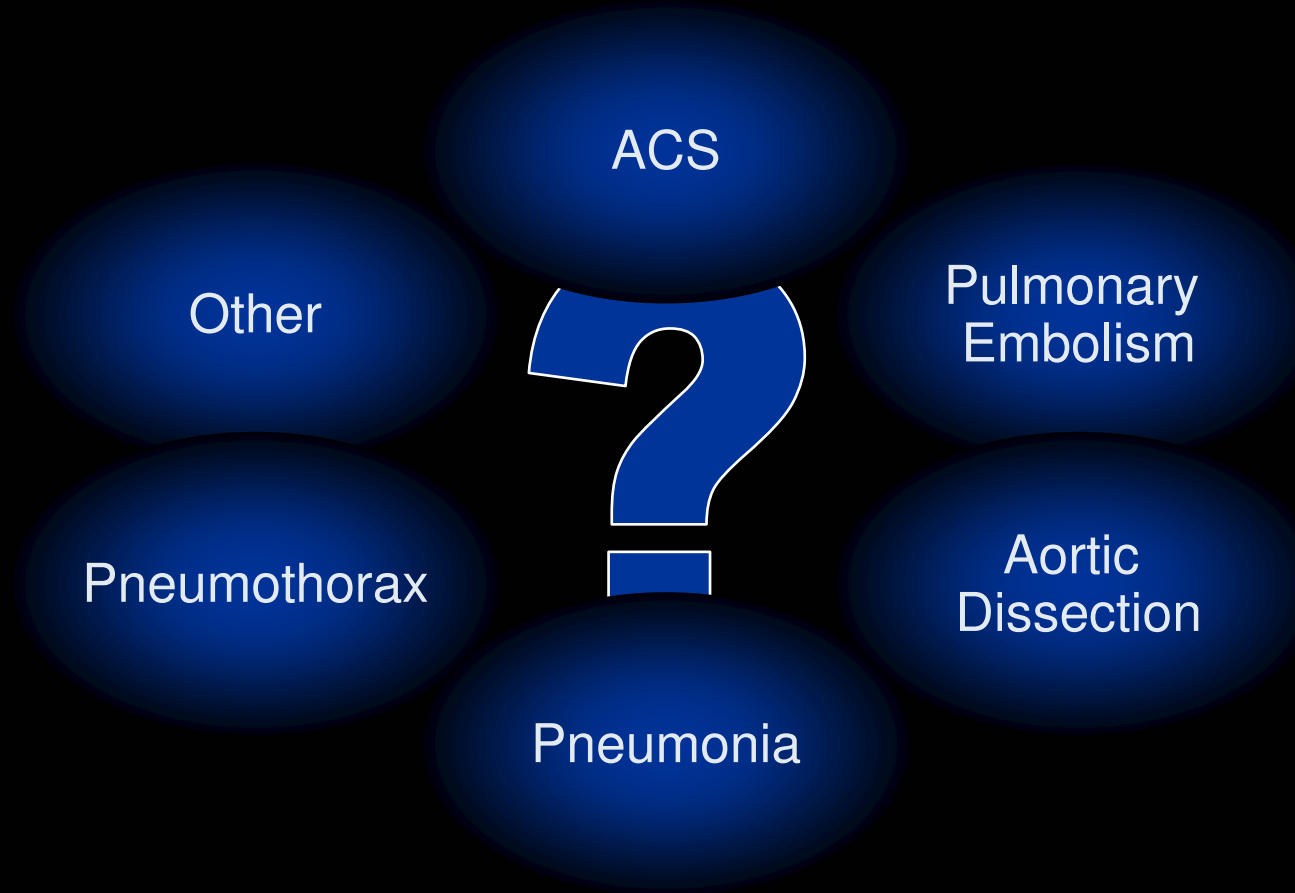
# Pathological Progression to Atherothrombosis

- ACS is characterised by thrombosis on atherosclerotic plaque



- 80% of ACS patients have ruptured plaques located in vessels other than the culprit lesion<sup>1</sup>
  - Risk persists in ACS in both the short and longterm

# Working diagnosis?



Having ruled out non-ACS causes ?