ΚΛΙΝΙΚΟ ΦΡΟΝΤΙΣΤΗΡΙΟ: Η αντιμετώπιση του διαβητικού στην Καρδιολογική Μ.Ε.Θ.

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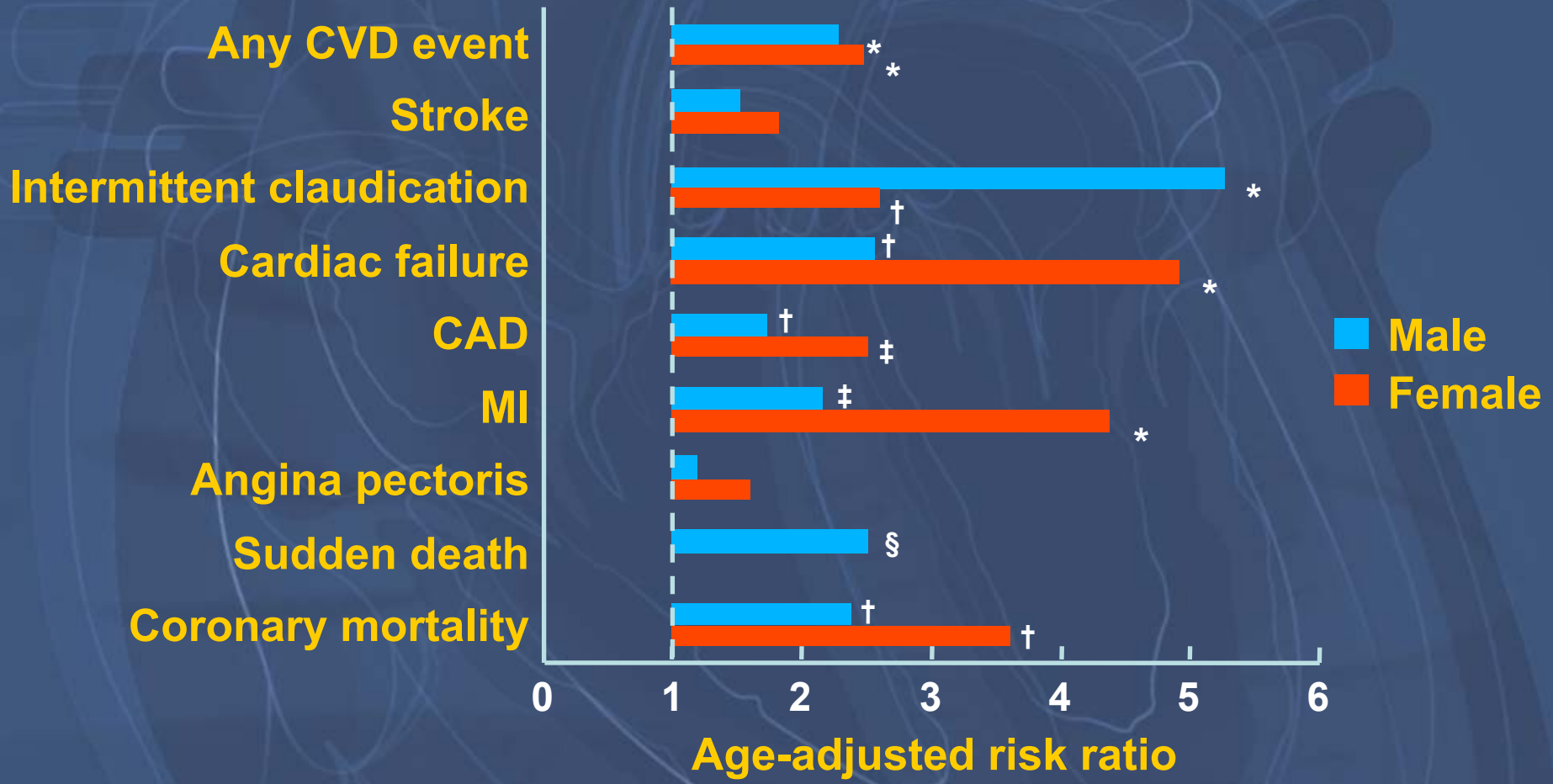
TTE Accreditation Subcommittee

European Association Echocardiography

Relative Risk of CVD in Diabetes: Framingham Heart Study



*P<0.001; †P<0.05; ‡P<0.01; §P<0.1

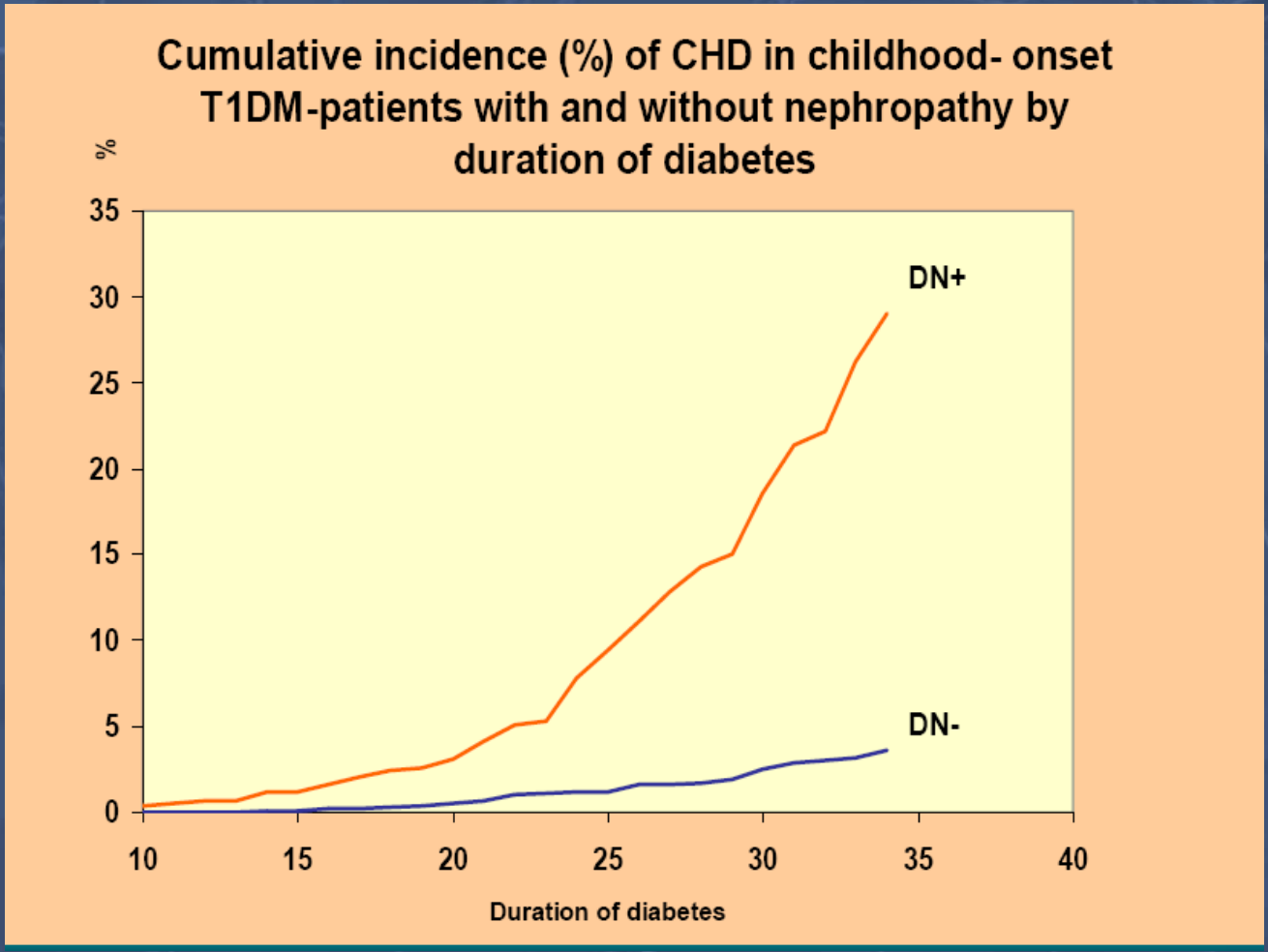
Kannel WB, et al. *Am Heart J* 1990;120:672-676.

Cardiovascular disease:
The major cause of death in diabetics

- Diabetes Type I: **44 % of deaths**
- Diabetes Type II: **52 % of deaths**

WHO Multinational Study of Vascular Disease in Diabetes: Diabetologia 2001;44 (suppl. 2):S14-S21

T1DM: The CHD danger increases dramatically with the onset of nephropathy

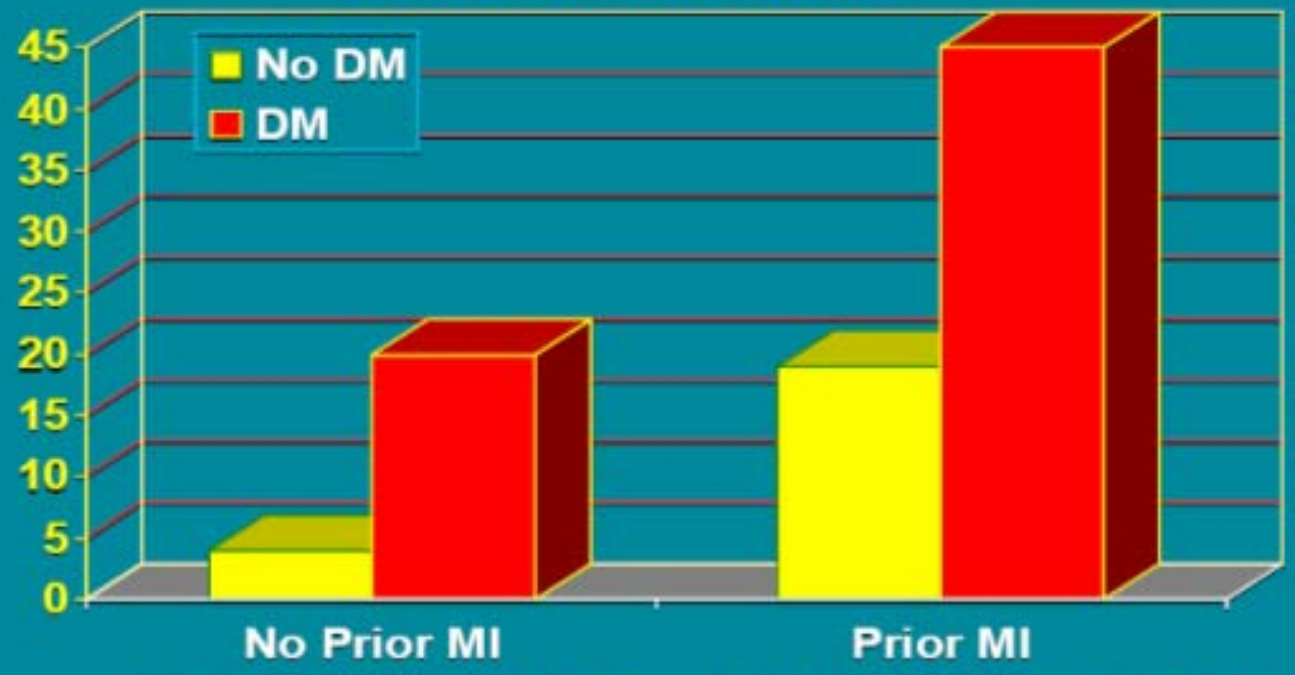


Incidence of myocardial infarction in Type 2 Diabetes

1373 patients without diabetes (DM) and prior myocardial infarction (MI)

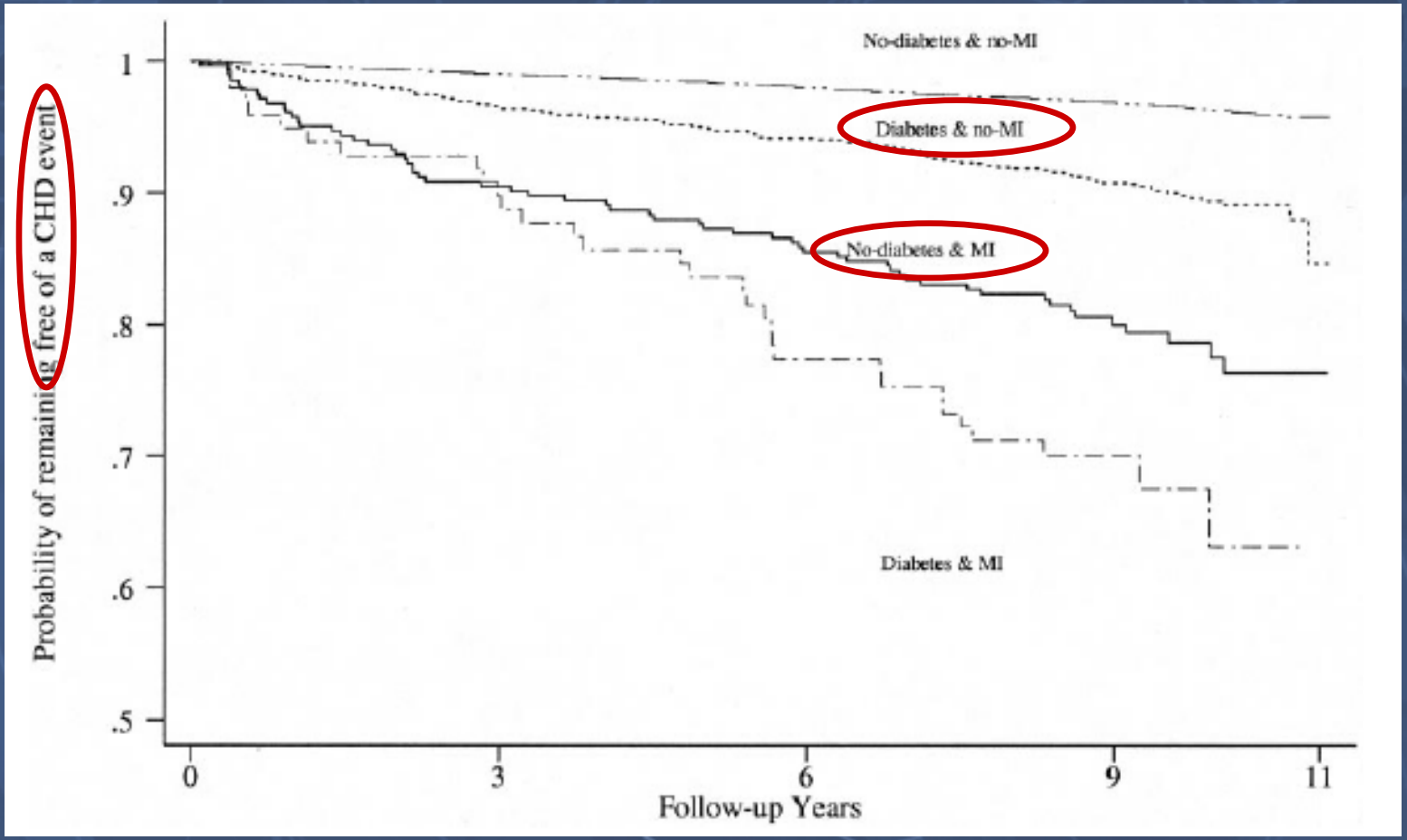
1059 patients with type 2 DM and without prior MI

- Followed for 7 years -



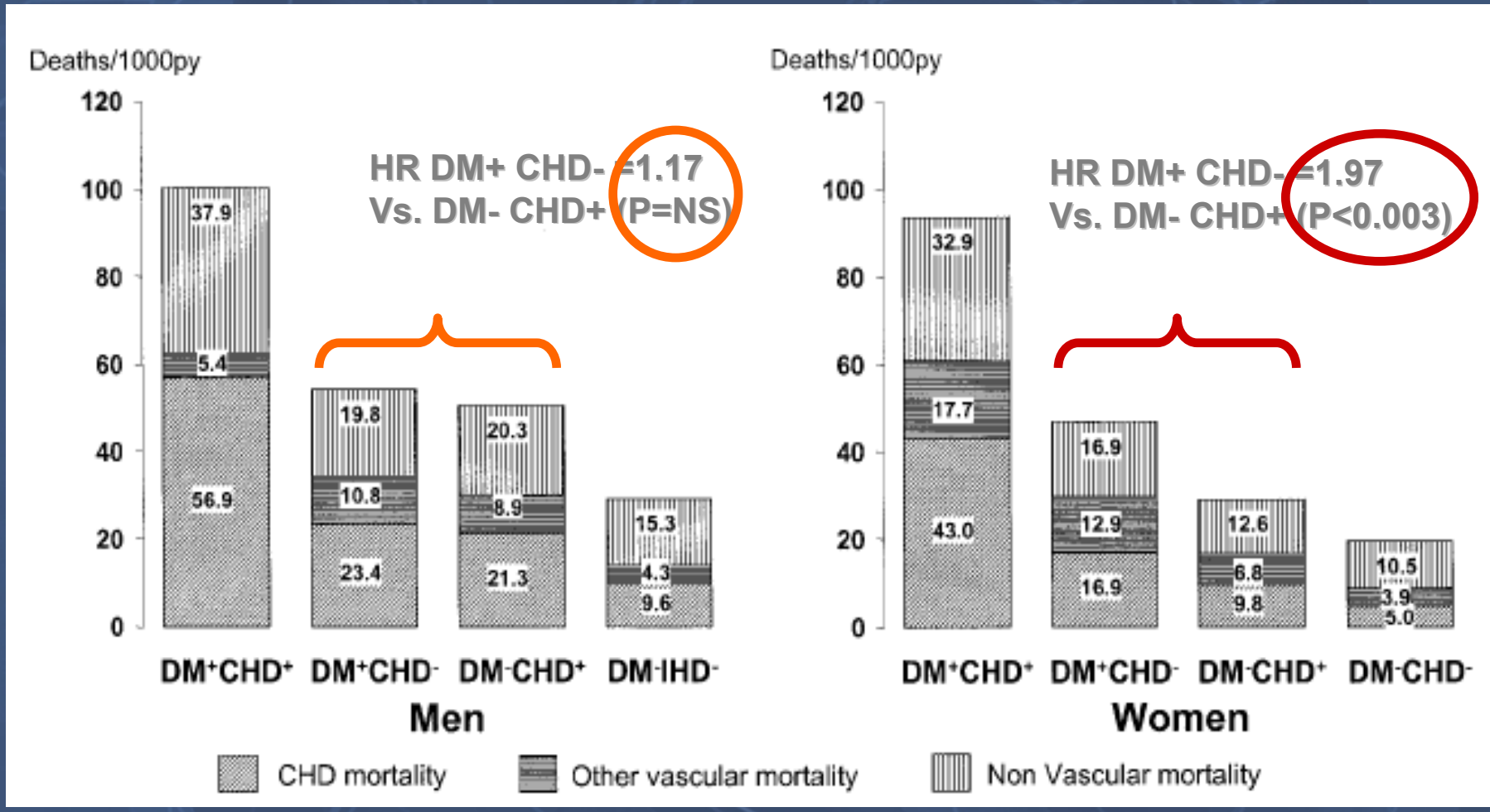
Haffner SM et al. *N Engl J Med.* 1998;339:229.

Risk for CHD event: Diabetes < previous MI



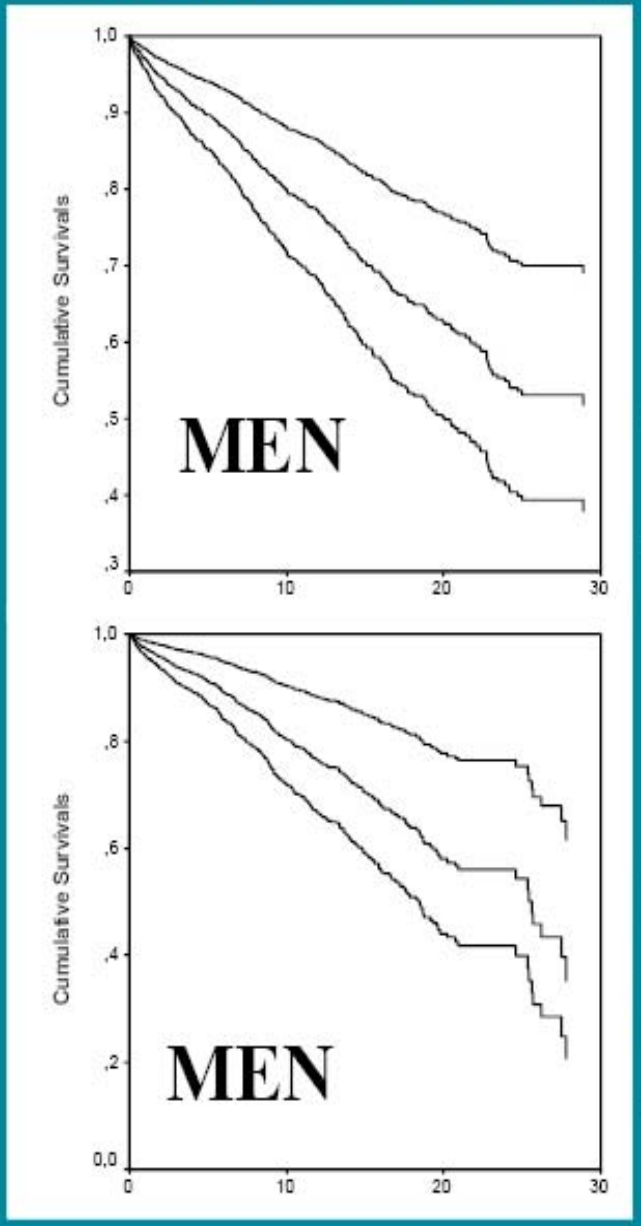
ARIC Study: Circulation 2004; 109:855-860

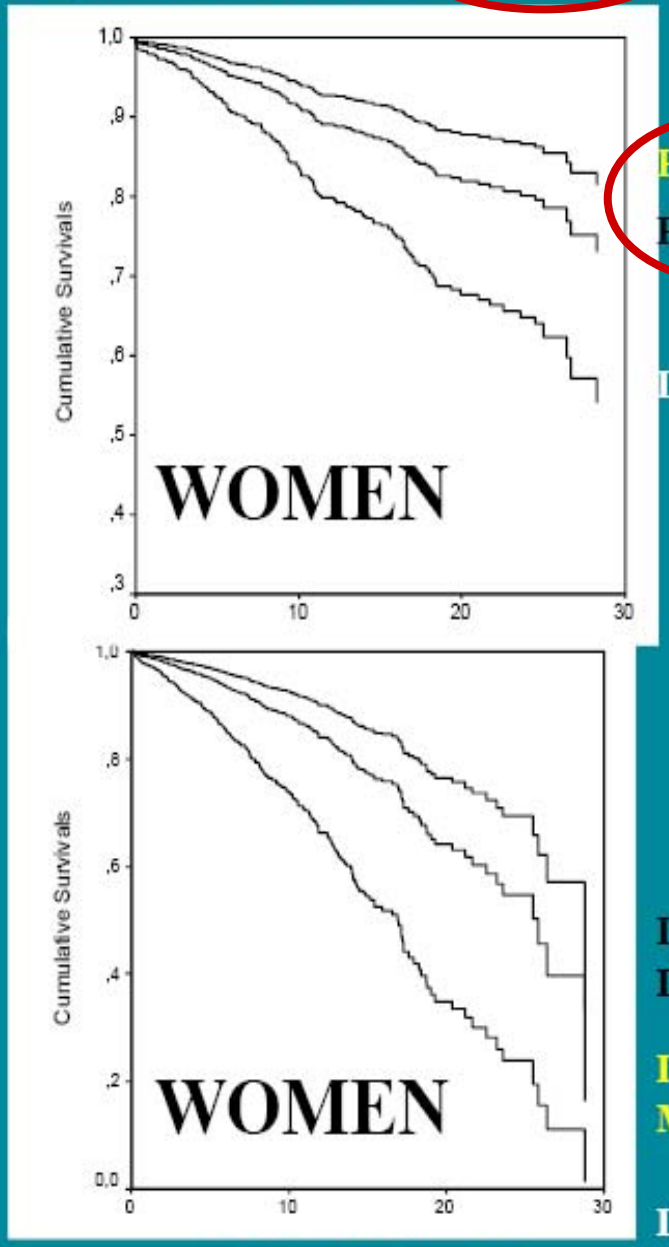
Risk for CHD death: Diabetes > previous MI in women



Whiteley L. et al. Diabetes Care 2005; 28 (7): 1588

CHD mortality by diabetes (DM) and myocardial infarction (MI) at baseline and during the follow-up in men and women



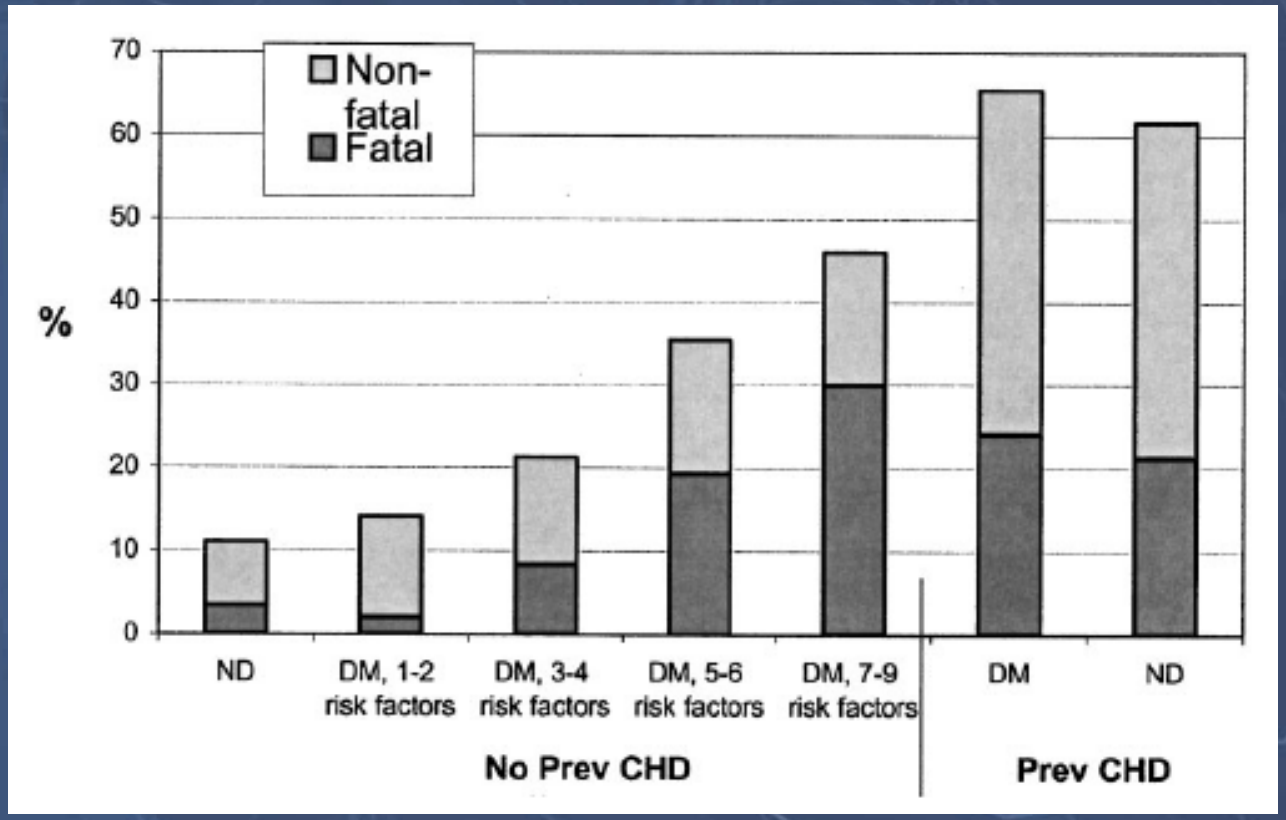


Years of follow-up

Diabetologia 2005;48(5):856-61

Years of follow-up

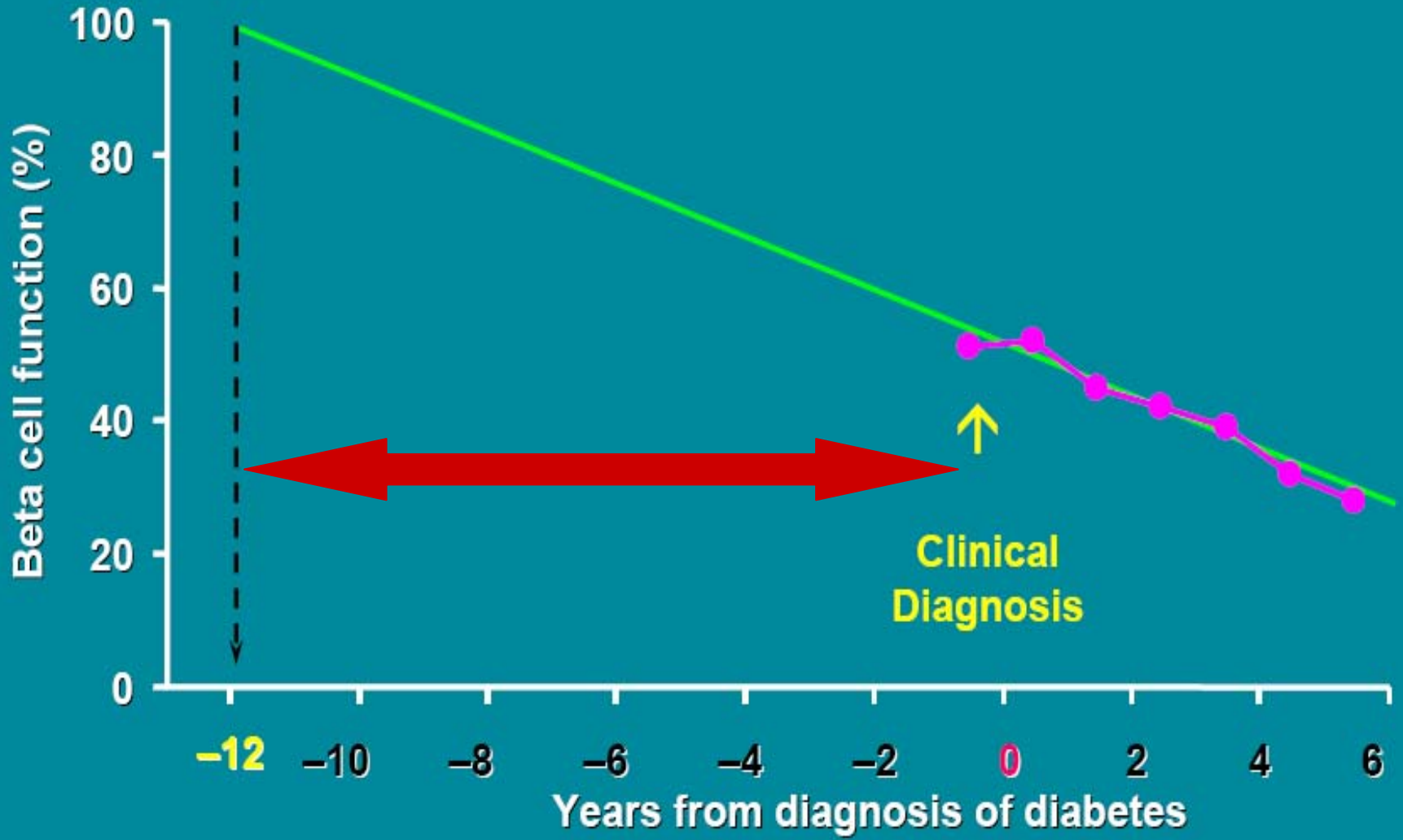
CHD risk equivalence in diabetes depends on concomitant risk factors



- Sex
- LDL>100 mg/dl
- Albuminuria
- HDL<40 mg/dl
- TG>150 mg/dl
- Current smoking
- Fibrinogen>350 mg/dl
- Diabetes> 20 years

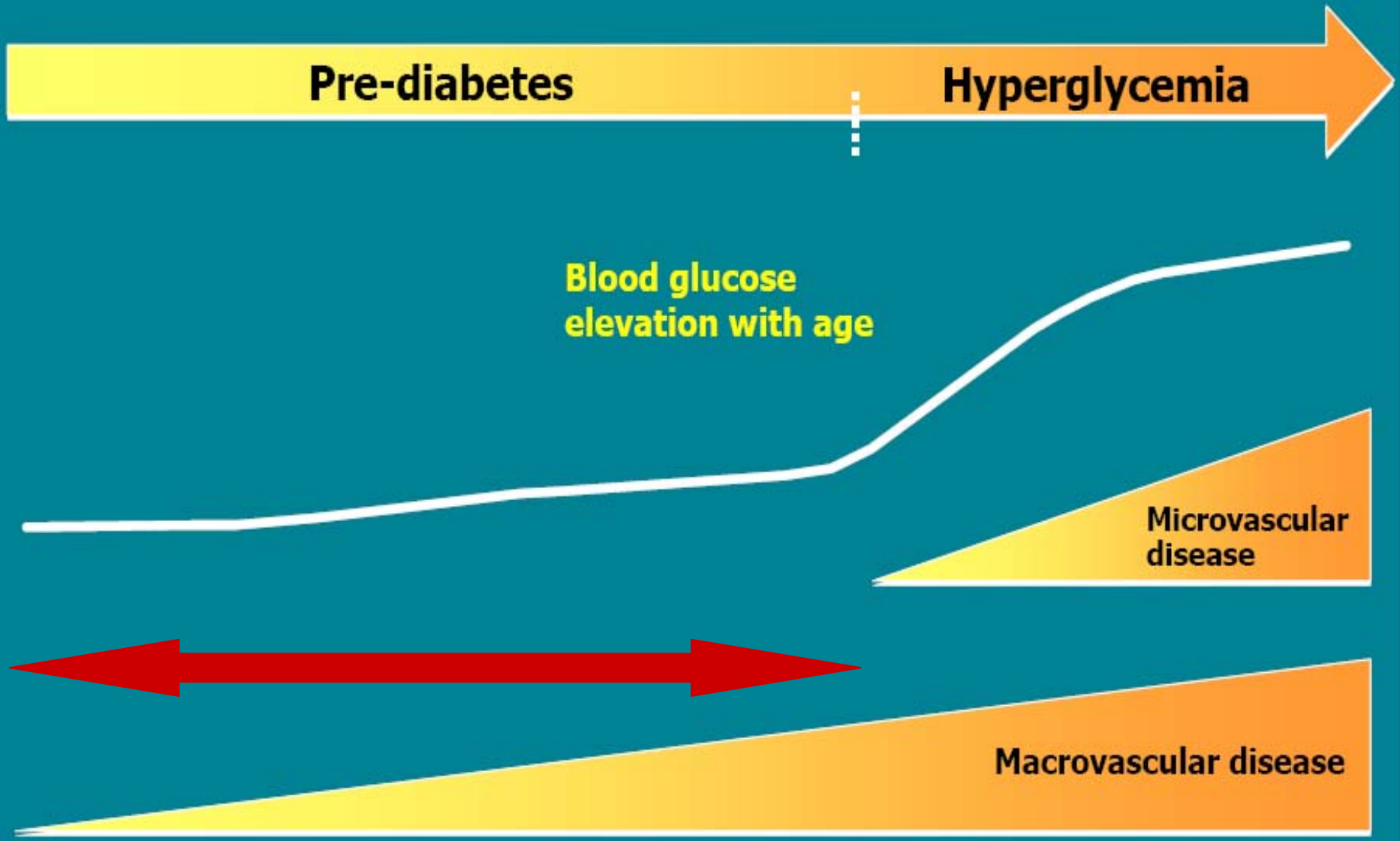
Diabetes Care 2006; 29: 391-397

United Kingdom Prospective Diabetes Study (UKPDS) - deterioration of pancreatic beta cell dysfunction starts long before clinical onset of diabetes

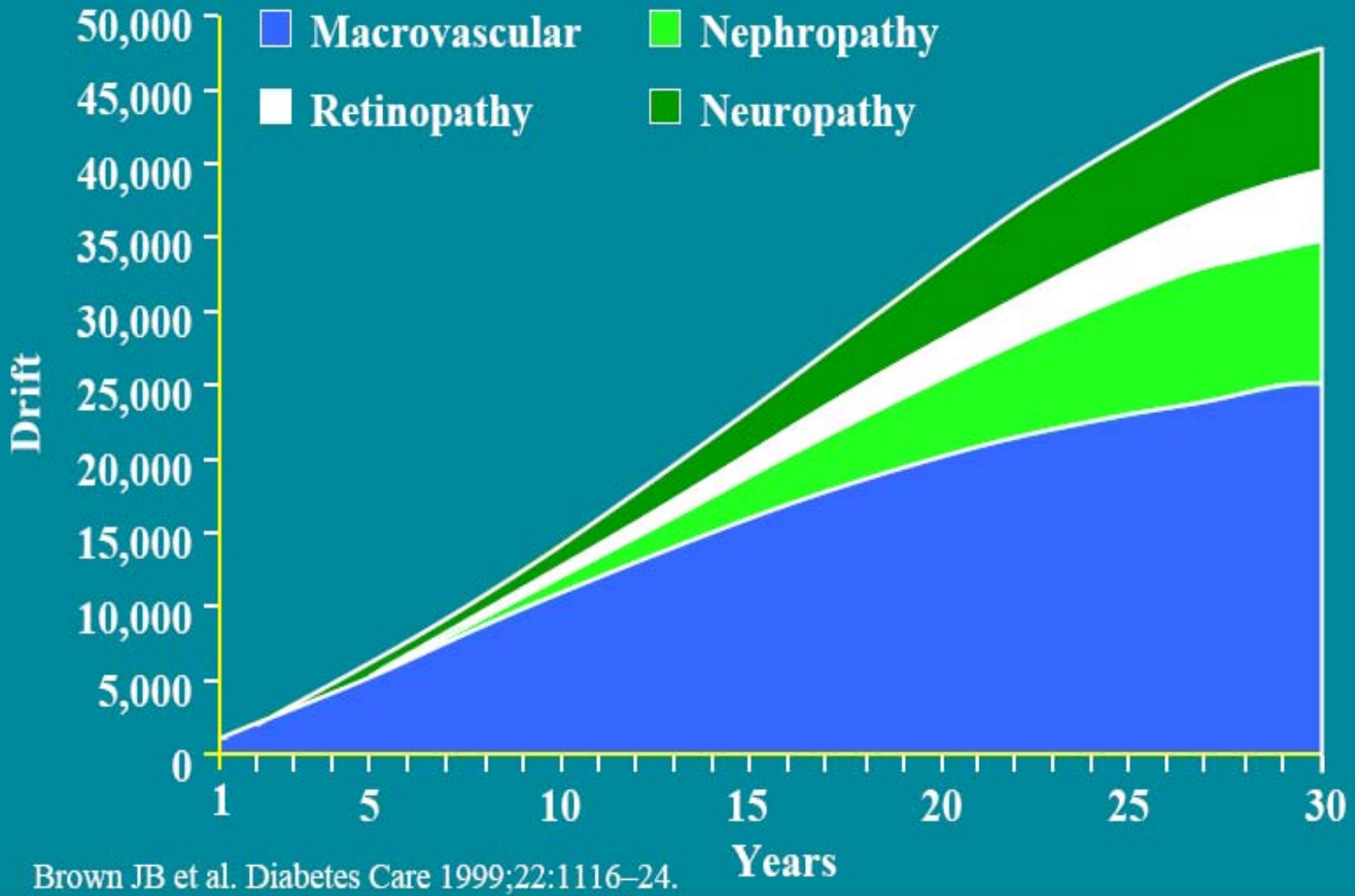


Adapted from UKPDS 16. Diabetes 1995

Development of type 2 diabetes

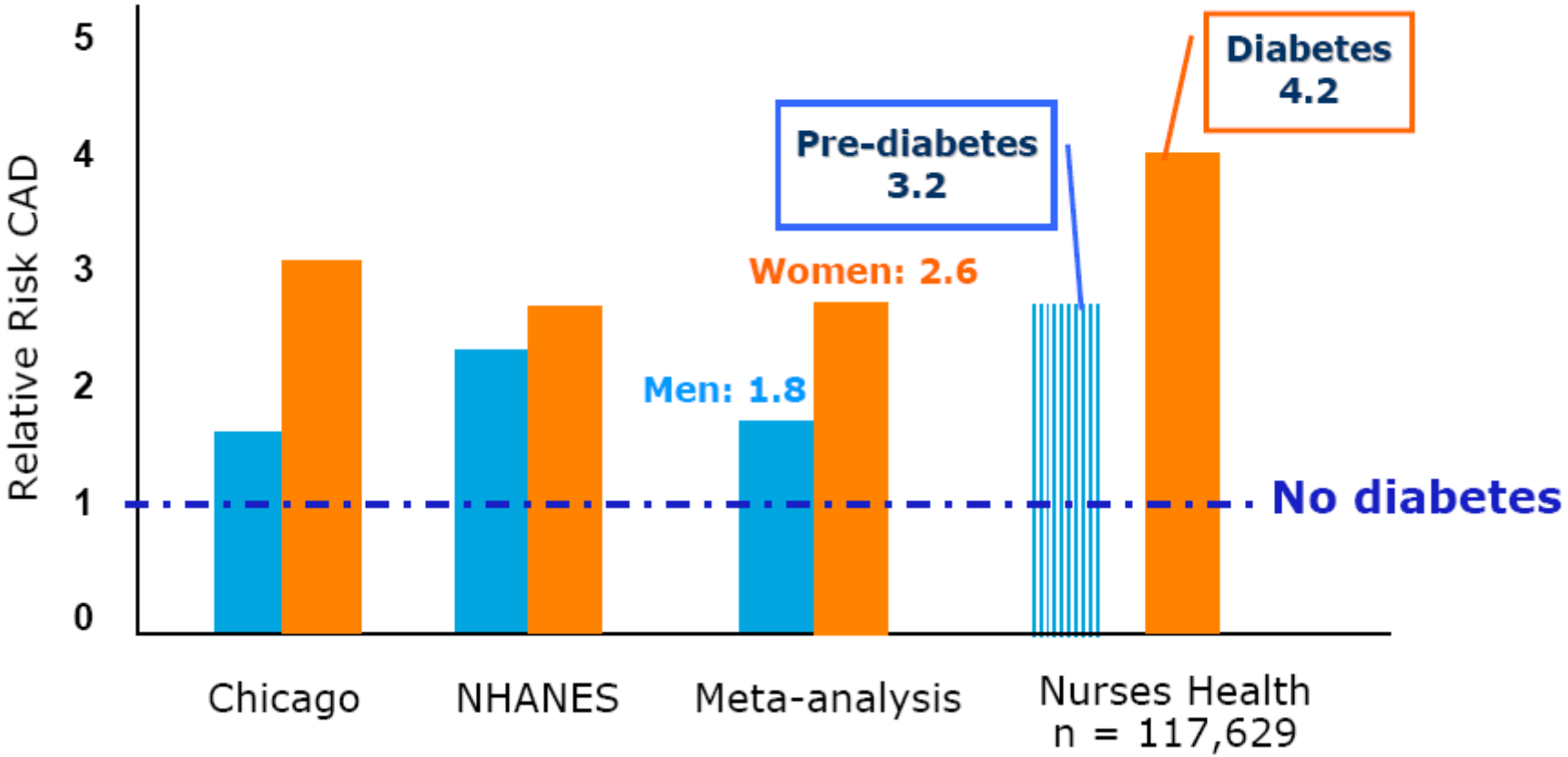


Estimated cumulative cost (average per patient) of managing complications of type 2 diabetes according to type of complication



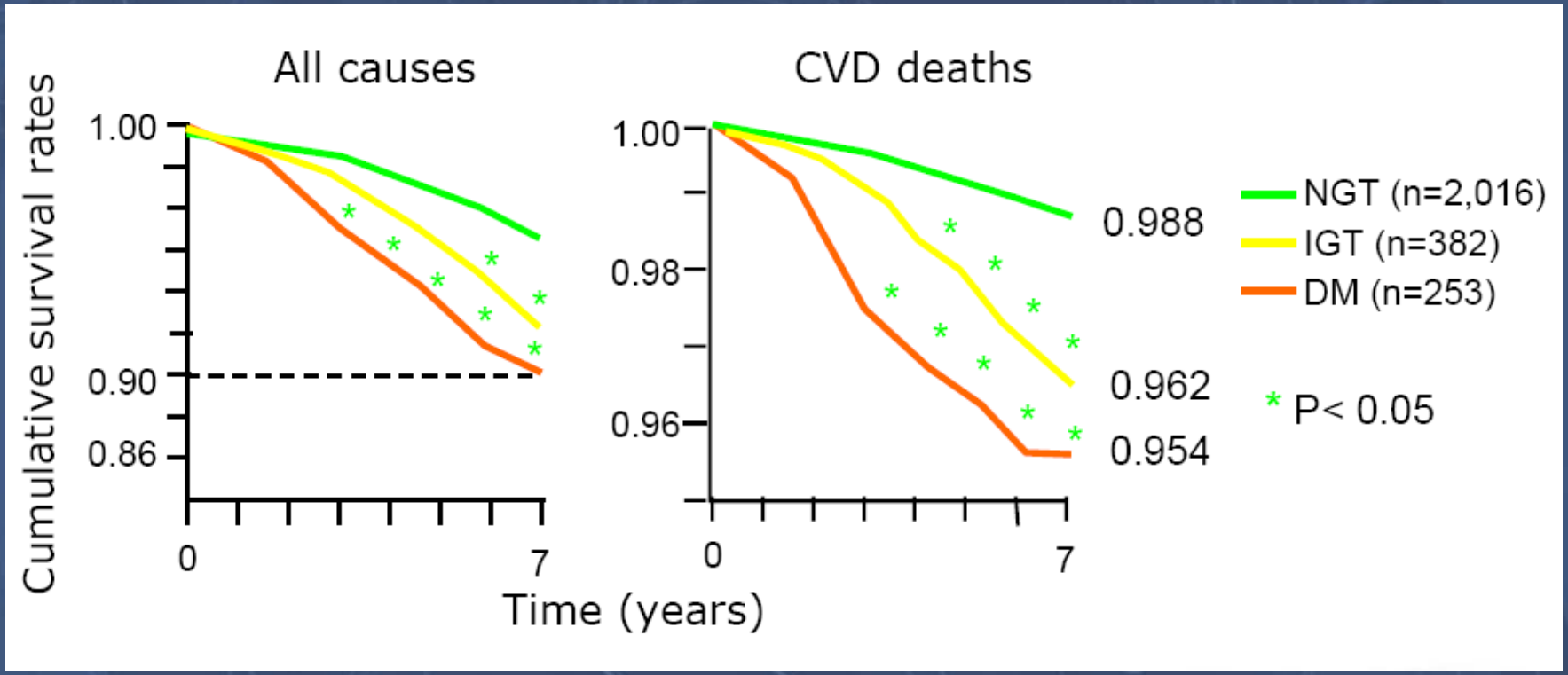
Brown JB et al. Diabetes Care 1999;22:1116–24.

Impact of pre-diabetes & diabetes for cardiovascular disease



Lee WL et al 2002, Hu et al 2002

IGT & DM are risk factors for death from CV diseases

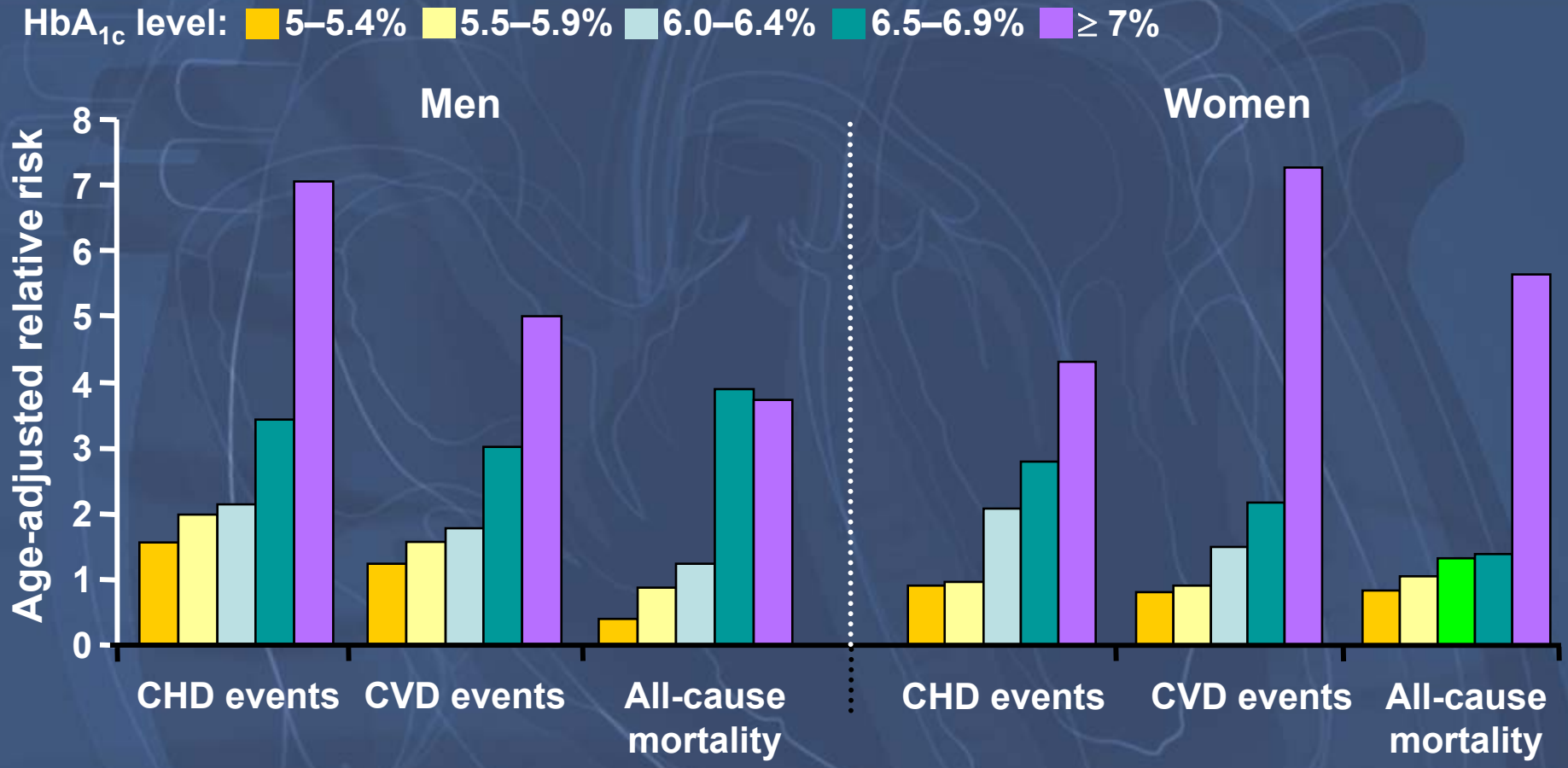


Tominaga m, et al. Diabetes Care 1999;22:920-4

Identifying hyperglycaemia – why measuring FPG is not good enough?

Monnier L. Eur J Clin Invest 2000;30(Suppl 2):3

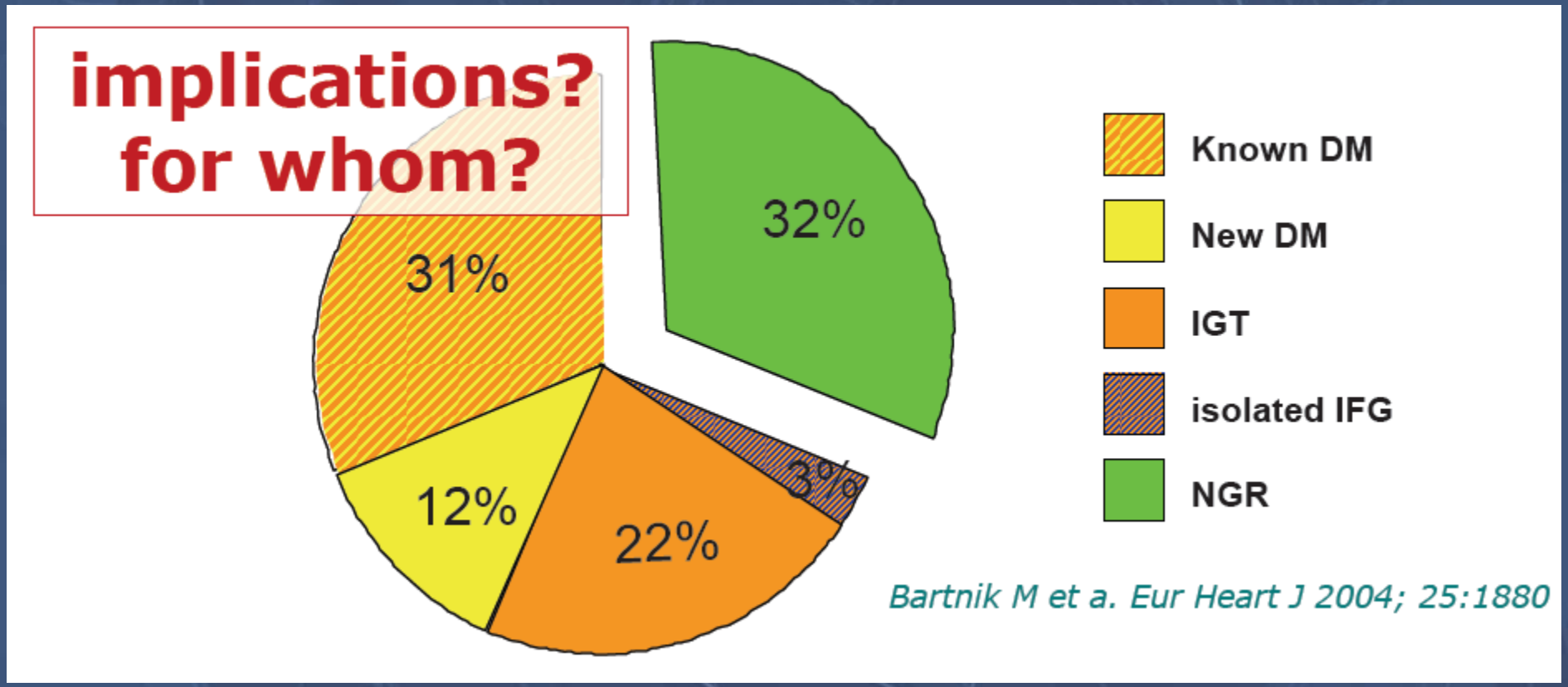
EPIC-Norfolk study: risk of CV events or death associated with HbA_{1c} level



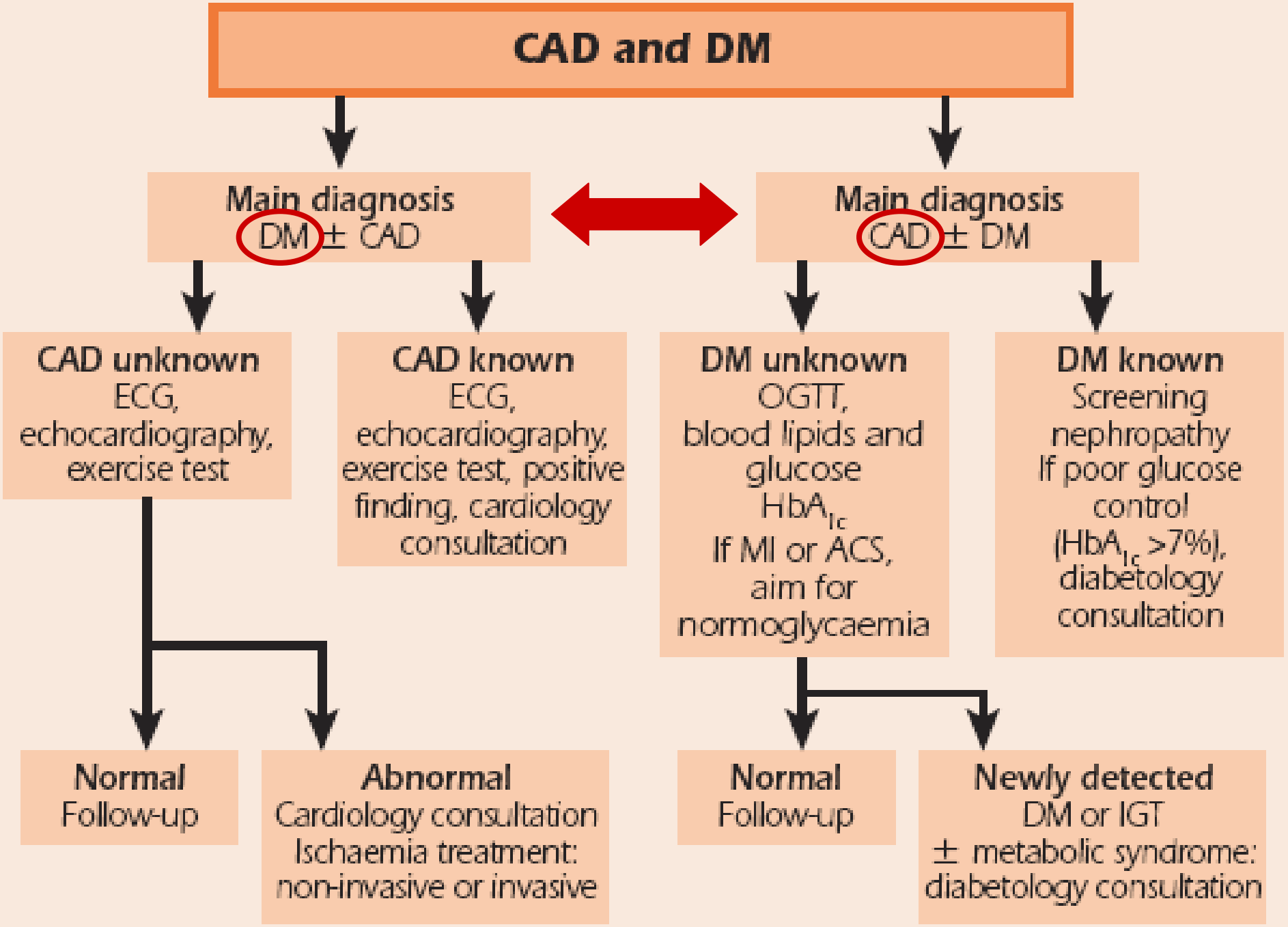
$P < 0.001$ for linear trend across HbA_{1c} categories for all endpoints.

Khaw KT, *et al. Ann Intern Med* 2004; 141:413–420.

The prevalence of hyperglycaemia (DM or IGH) estimated in pts with CAD



Bartnik M et a. Eur Heart J 2004; 25:1880


CAD and DM
Main diagnosis
DM ± CAD
Main diagnosis
CAD ± DM
CAD unknown
ECG, echocardiography, exercise test
CAD known
ECG, echocardiography, exercise test, positive finding, cardiology consultation
DM unknown
OGTT, blood lipids and glucose
HbA1c
If MI or ACS, aim for normoglycaemia
DM known
Screening nephropathy
If poor glucose control (HbA1c >7%), diabetology consultation
Normal
Follow-up
Abnormal
Cardiology consultation
Ischaemia treatment: non-invasive or invasive
Normal
Follow-up
Newly detected
DM or IGT
± metabolic syndrome: diabetology consultation

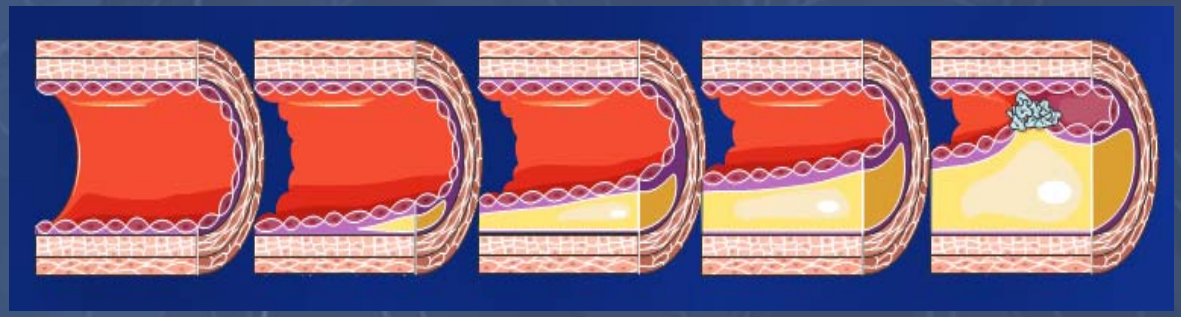
ESC & EASD 2007

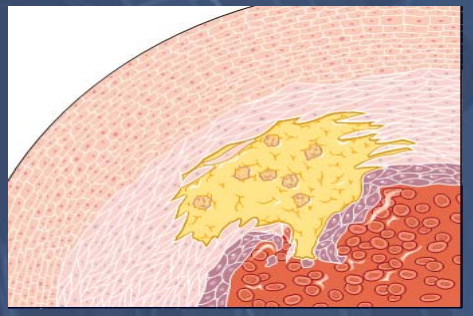
Recommendation	Class	Level
The relationship between hyperglycaemia and CVD should be seen as a continuum. For each 1% increase of HbA_{1c}, there is a defined increased risk for CVD.	I	A
The risk of CVD for people with overt diabetes is increased by two to three times for men and three to five times for women compared with people without diabetes.	I	A
Information on post-prandial (post-load) glucose provides better information about the future risk for CVD than fasting glucose, and elevated post-prandial (post-load) glucose also predicts increased cardiovascular risk in subjects with normal fasting glucose levels.	I	A
Glucometabolic perturbations carry a particularly high risk for cardiovascular morbidity and mortality in women, who in this respect need special attention.	IIa	B

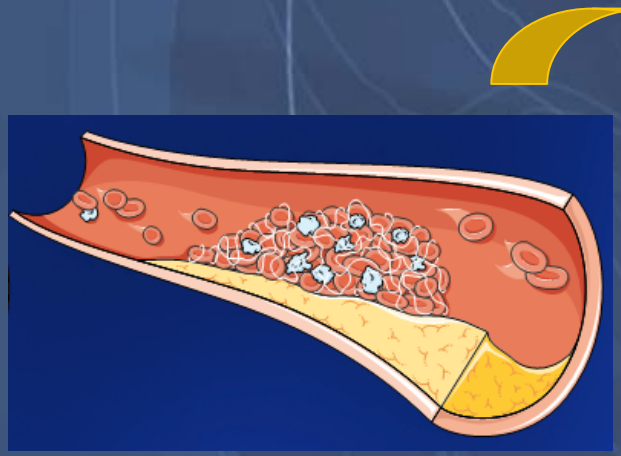
Atherothrombosis:

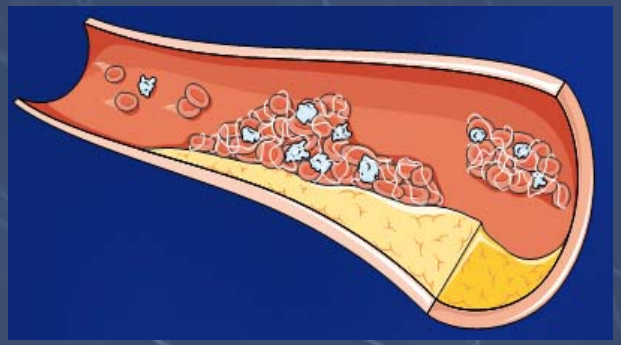
Plaque rapture or erosion, thrombus formation

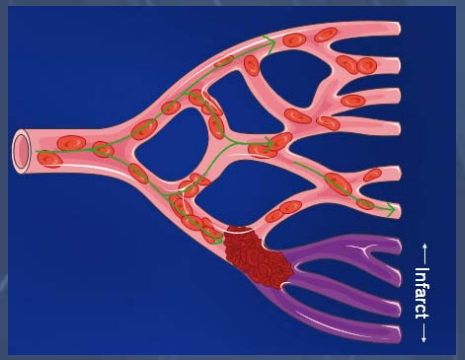
artery occlusion - peripheral emboli





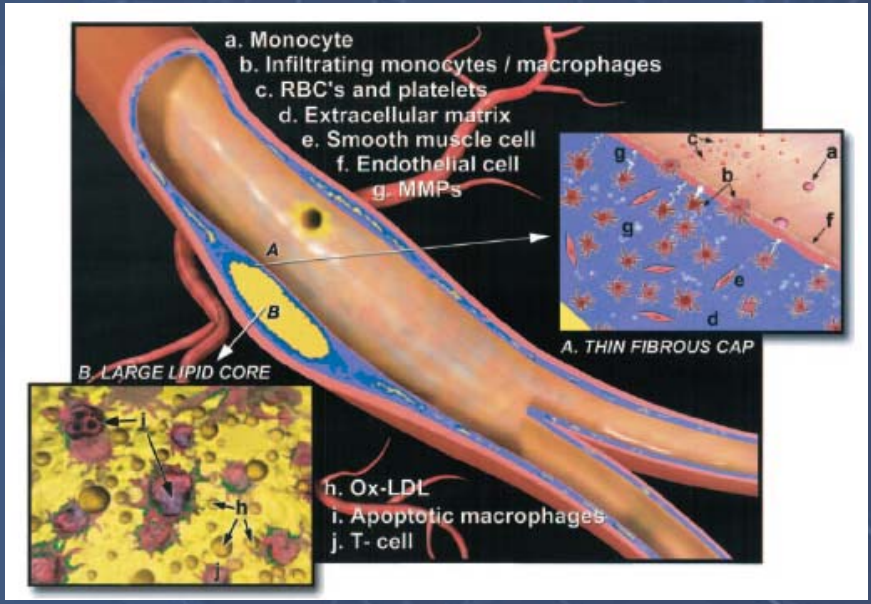






Atherothrombosis

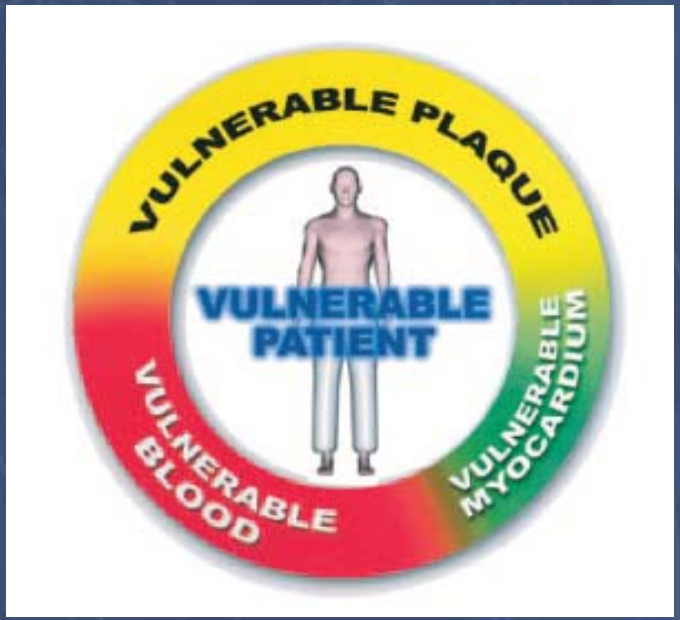
The vulnerable plaque



The vulnerable patient

(diffuse nature of unstable plaques)

Accelerated atherosclerosis

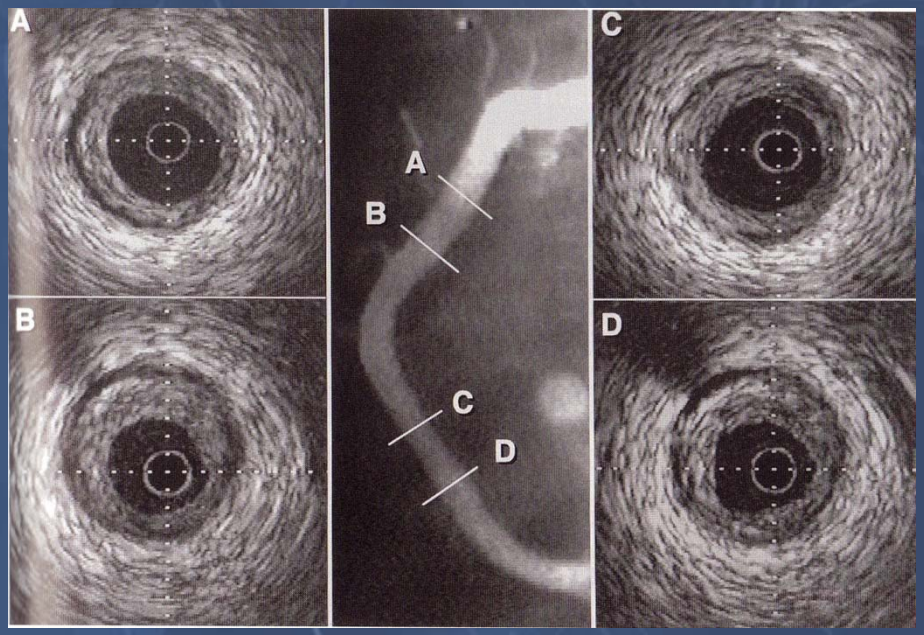


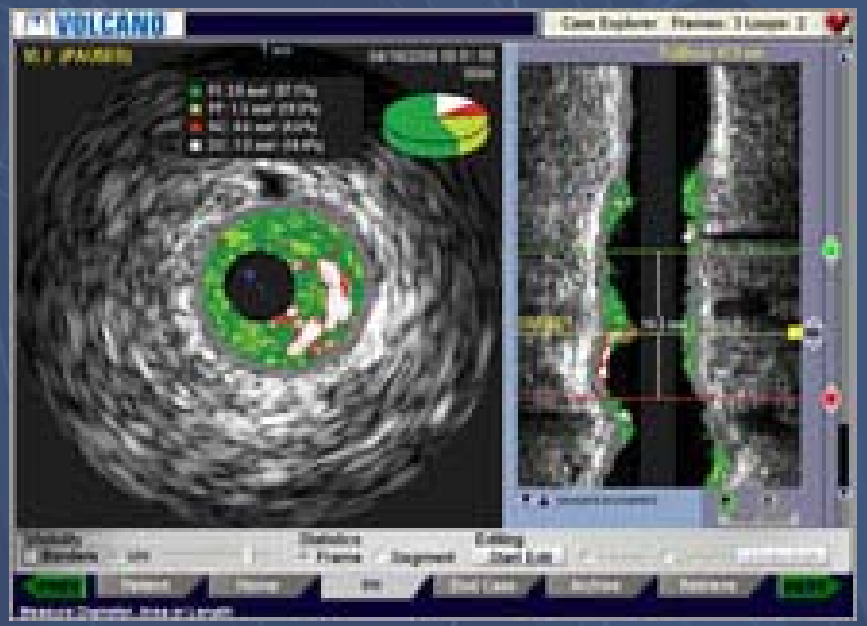
Libby P. Nature 2002

Kaski JC et al. Circulation 1995

Rioufol G, et al. Circulation 2002

Υποκλινική αθηρωμάτωση σε αγγειογραφικά «φυσιολογικές» στεφανιαίες αρτηρίες



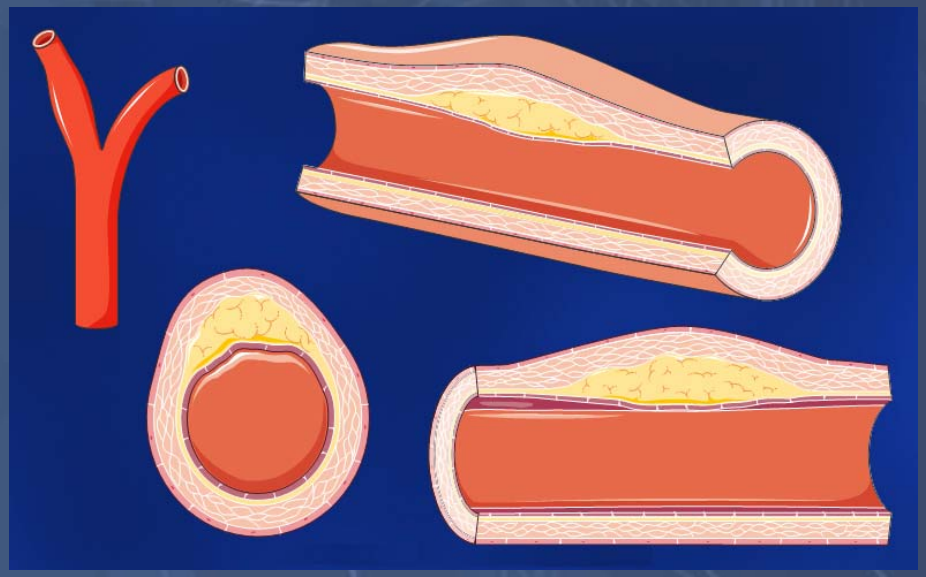


Αθηρωμάτωση: διάχυτη νόσος αρτηριών

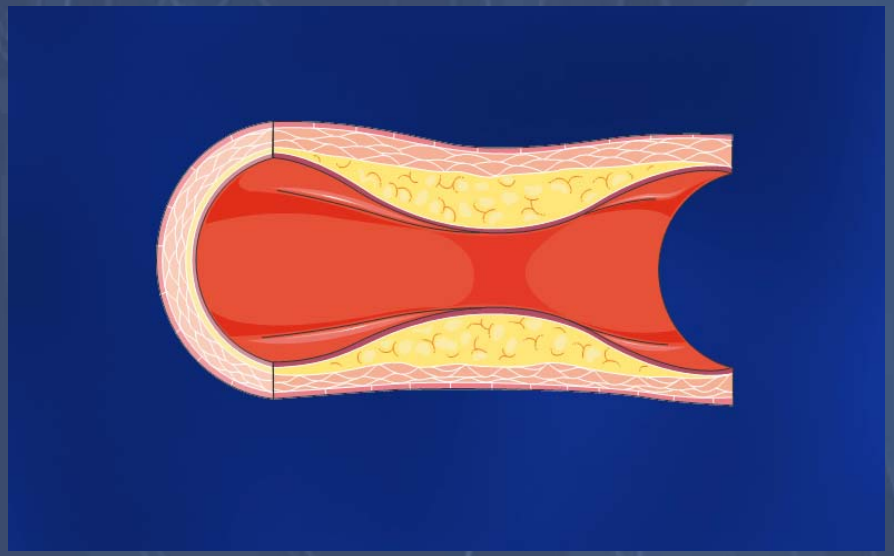
3/4 εμφράγματα: σε μικρή ή μέτρια στένωση

Remodeling of coronary arteries

POSITIVE



NEGATIVE



Effect of diabetes on progression of coronary atherosclerosis and arterial remodeling:

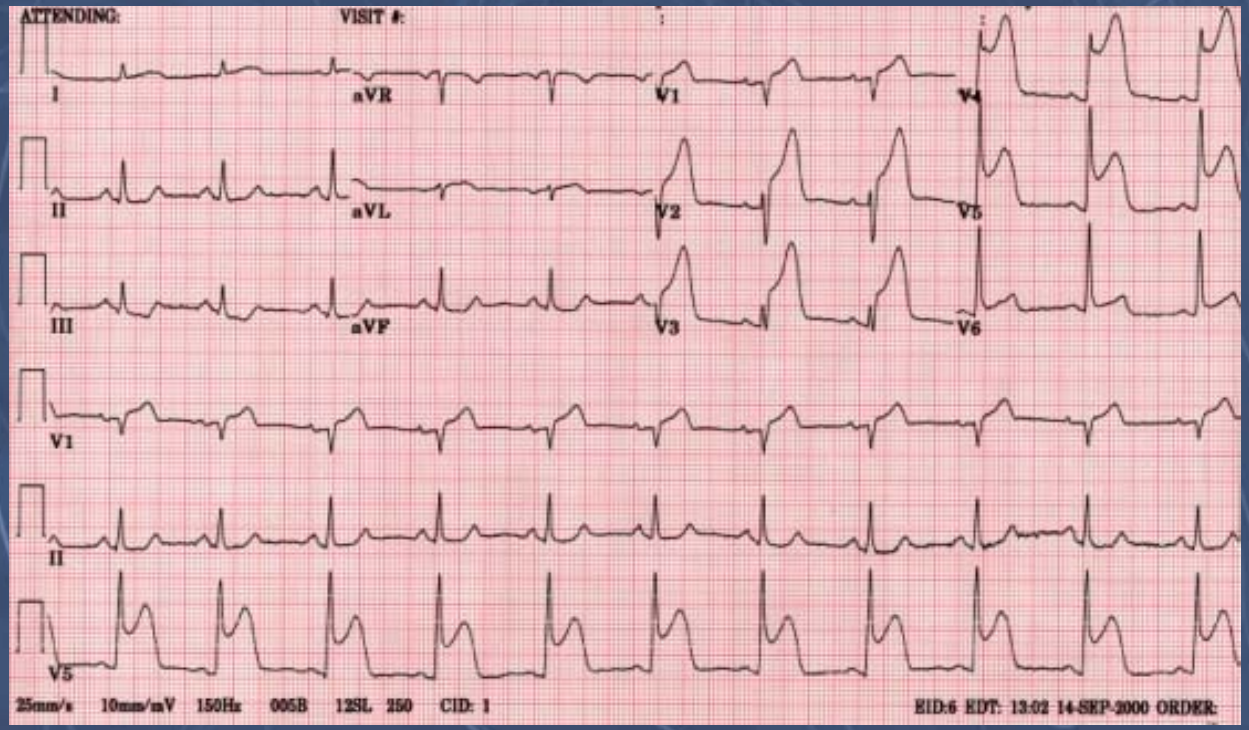
a pooled analysis of 5 intravascular ultrasound trials

Diabetes is accompanied by:

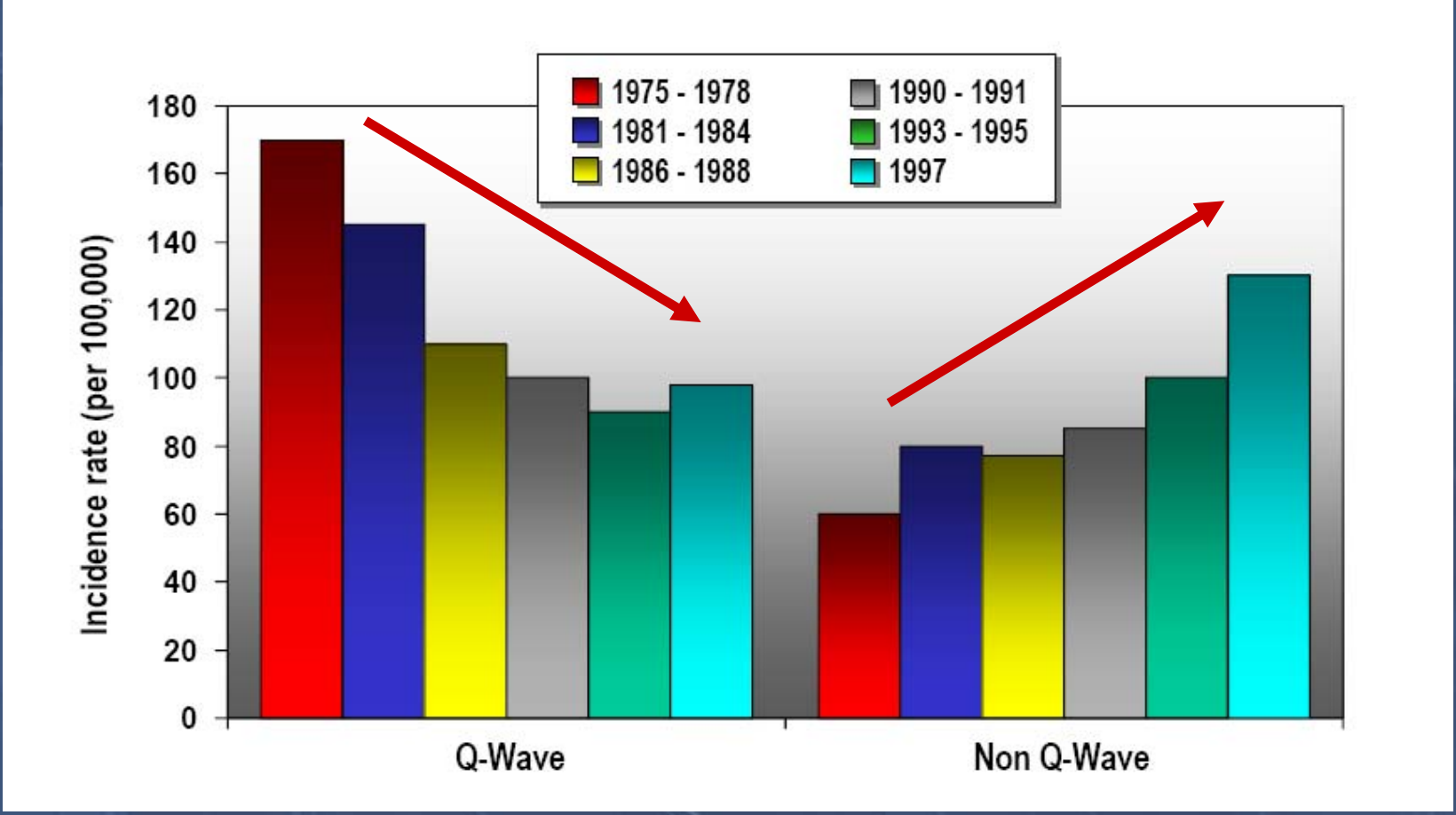
- more extensive atherosclerosis
- inadequate compensatory remodeling

JACC 2008; 52(4): 255-62

Acute Coronary Syndromes



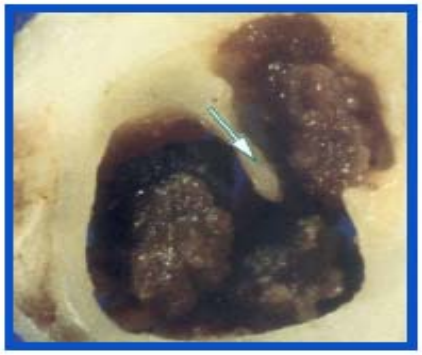
Trends and prognosis in NSTE-ACS



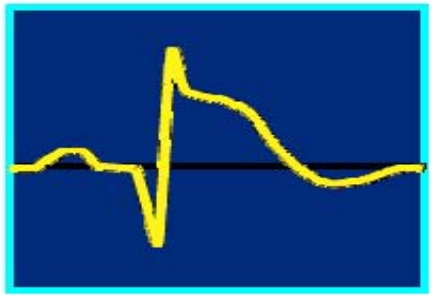
Furman MI et al JACC 2001; 37: 1751-80

ACUTE CORONARY SYNDROMES
STEMI vs NSTEMI

ACS with persistent ST-segment elevation

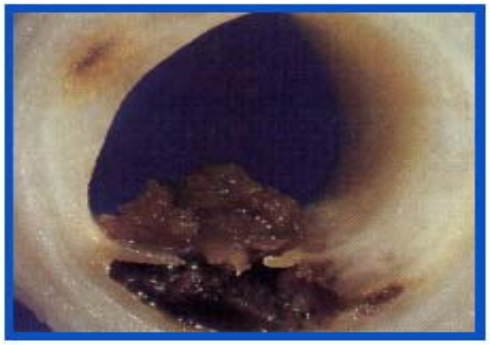


Adapted from Michael Davies

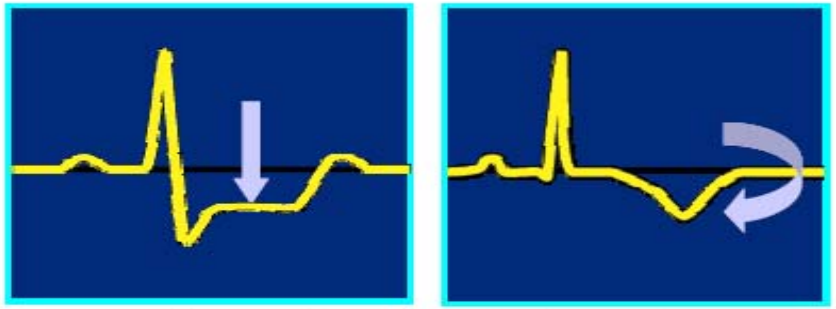


Troponin elevated

ACS without persistent ST-segment elevation



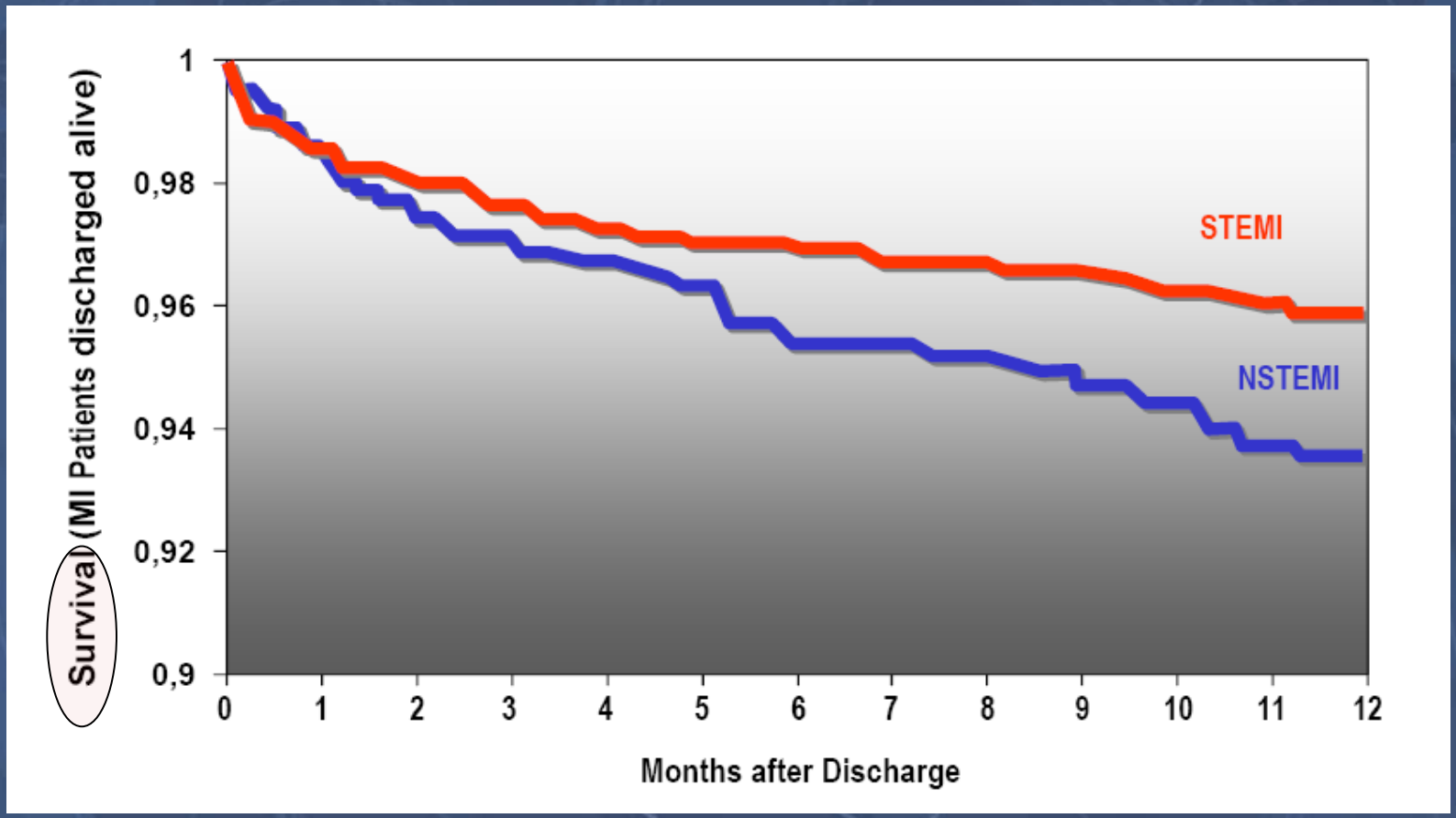
Adapted from Michael Davies



Troponins elevated or not

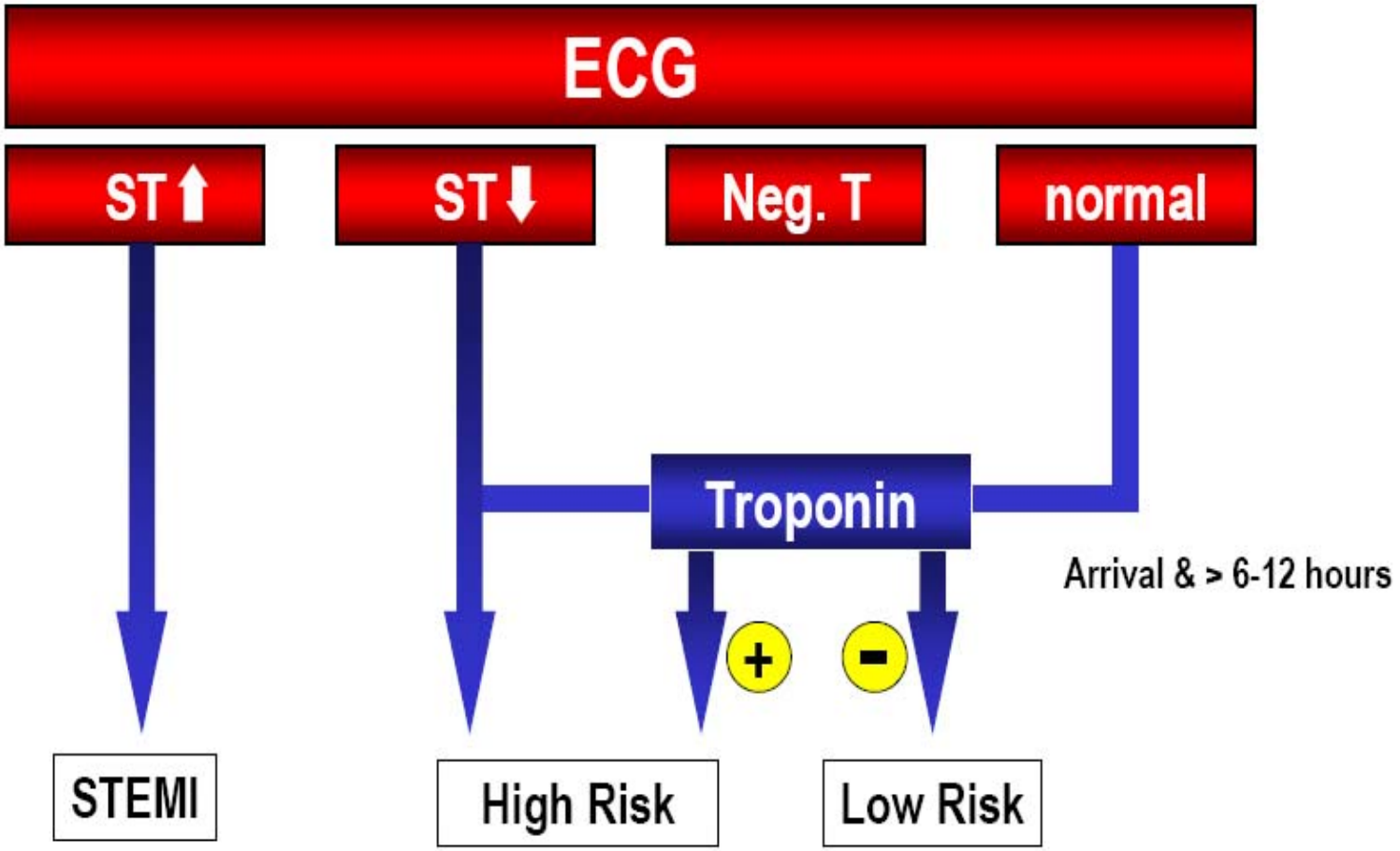
ESC Guidelines for NSTE-ACS EHJ 2007; 28: 1598-1660

STEMI vs NSTEMI
Mortality after discharge

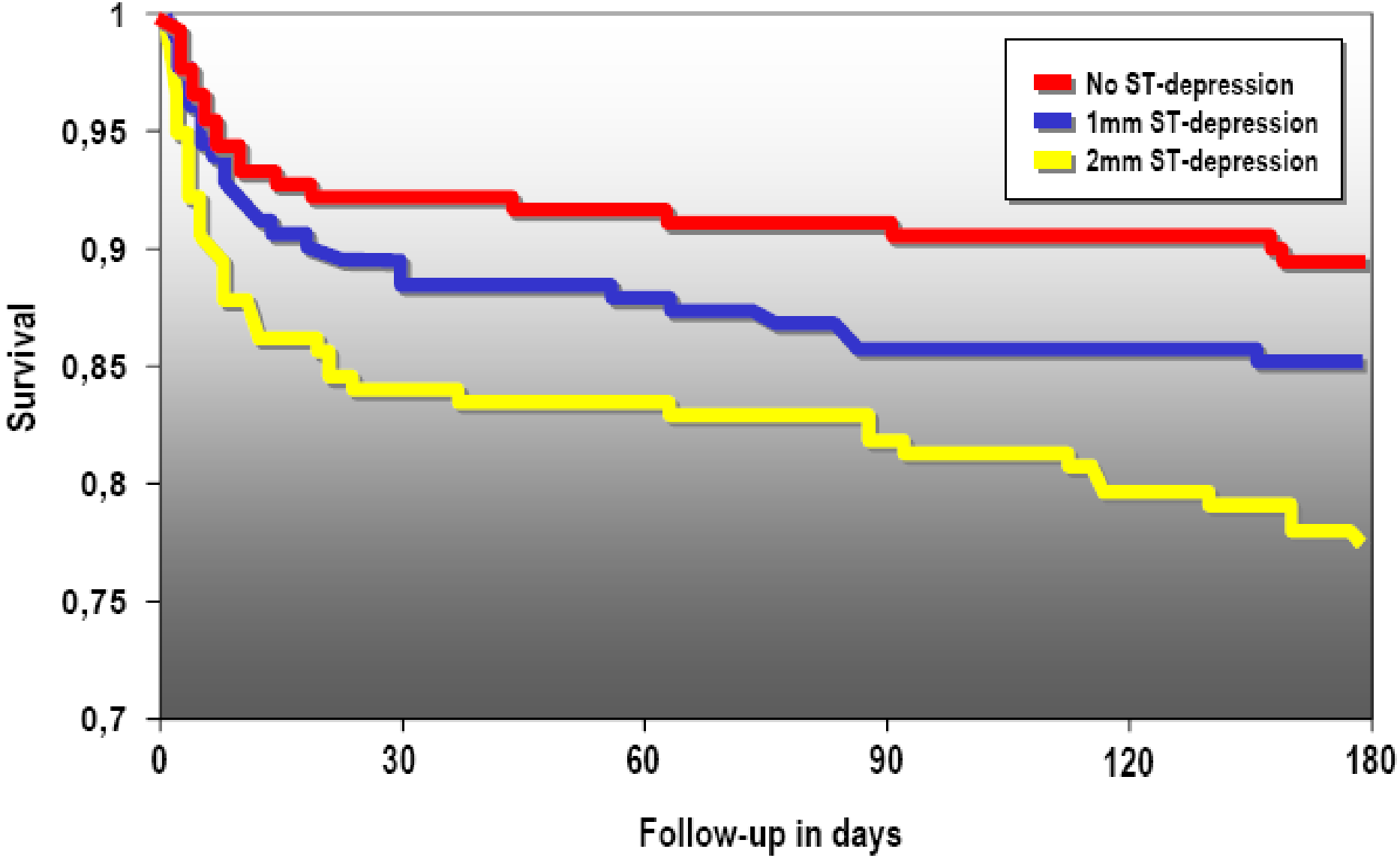


ESC Guidelines for NSTE-ACS EHJ 2007; 28: 1598-1660

ACS
Initial Decision-making Algorithm

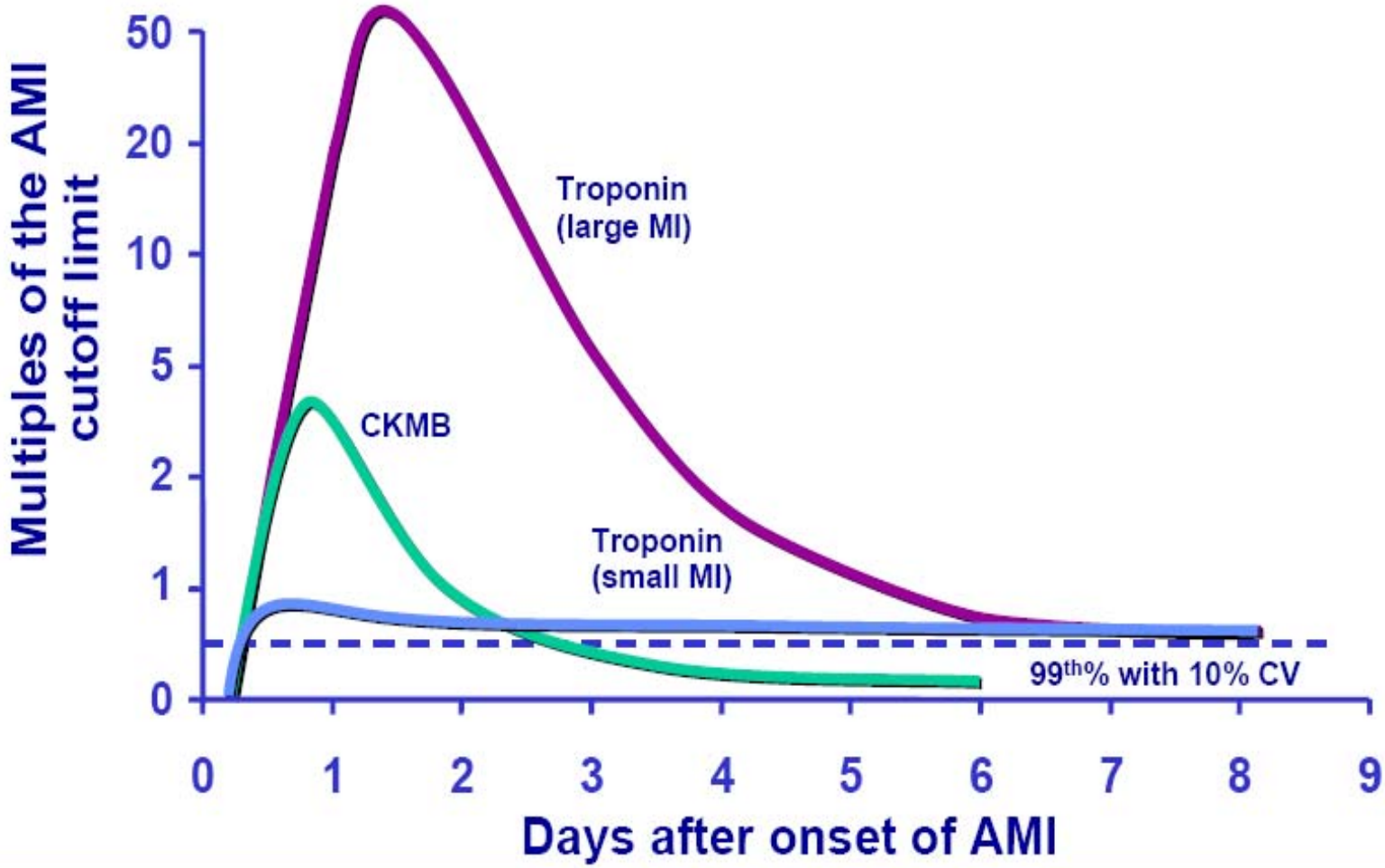


Predictive Value of ST Depression

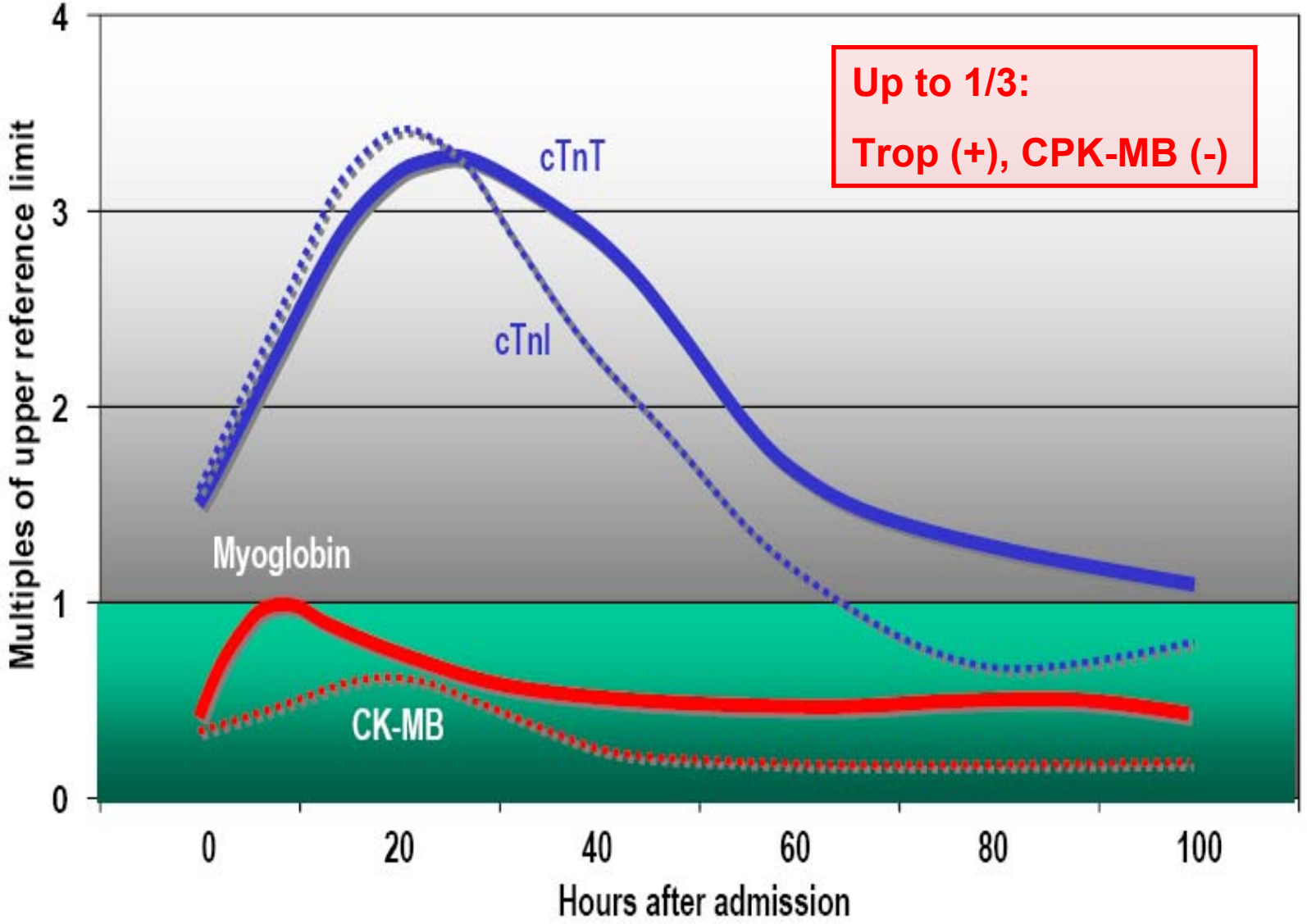


Kaul et al. PARAGON Study. JACC 2003

Appearance of Biomarkers in Blood after Onset of Myocardial Infarction



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



Classification of Myocardial Infarction

Type 1 Spontaneous myocardial infarction related to ischemia due to a primary coronary event such as plaque erosion or rupture, fissuring or dissection

Type 2 Myocardial infarction secondary to ischemia due to imbalance between oxygen demand and supply e.g. coronary spasm, anemia, or hypotension

Type 3 Sudden cardiac death with symptoms of ischemia, accompanied by new ST elevation or LBBB, or verified coronary thrombus by angiography or autopsy, but death occurring before blood samples could be obtained

Type 4a Myocardial infarction associated with PCI

Type 4b Myocardial infarction associated with verified stent thrombosis

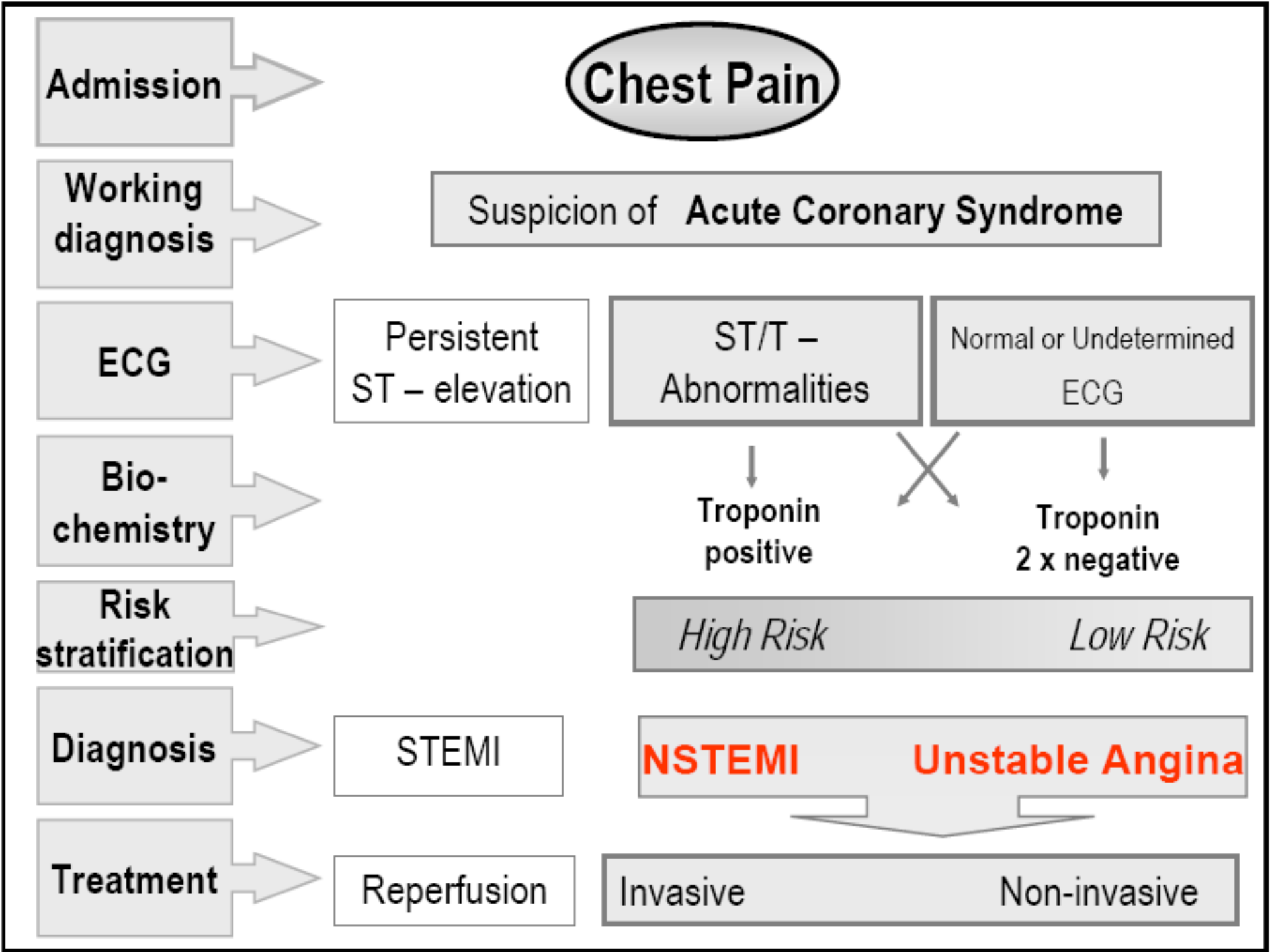
Type 5 Myocardial infarction associated with CABG

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


Admission
Chest Pain
Working diagnosis
Suspicion of Acute Coronary Syndrome
ECG
Persistent ST – elevation
ST/T – Abnormalities
Normal or Undetermined ECG
Bio-chemistry
Troponin positive
Troponin 2 x negative
Risk stratification
High Risk
Low Risk
Diagnosis
STEMI
NSTEMI
Unstable Angina
Treatment
Reperfusion
Invasive
Non-invasive

Diagnosis and risk stratification

STRATEGY

1st step: Initial Evaluation

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

2nd step: Validation & Risk Assessment

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

Non ST elevation ACS

Treatment

3rd step: Invasive Management

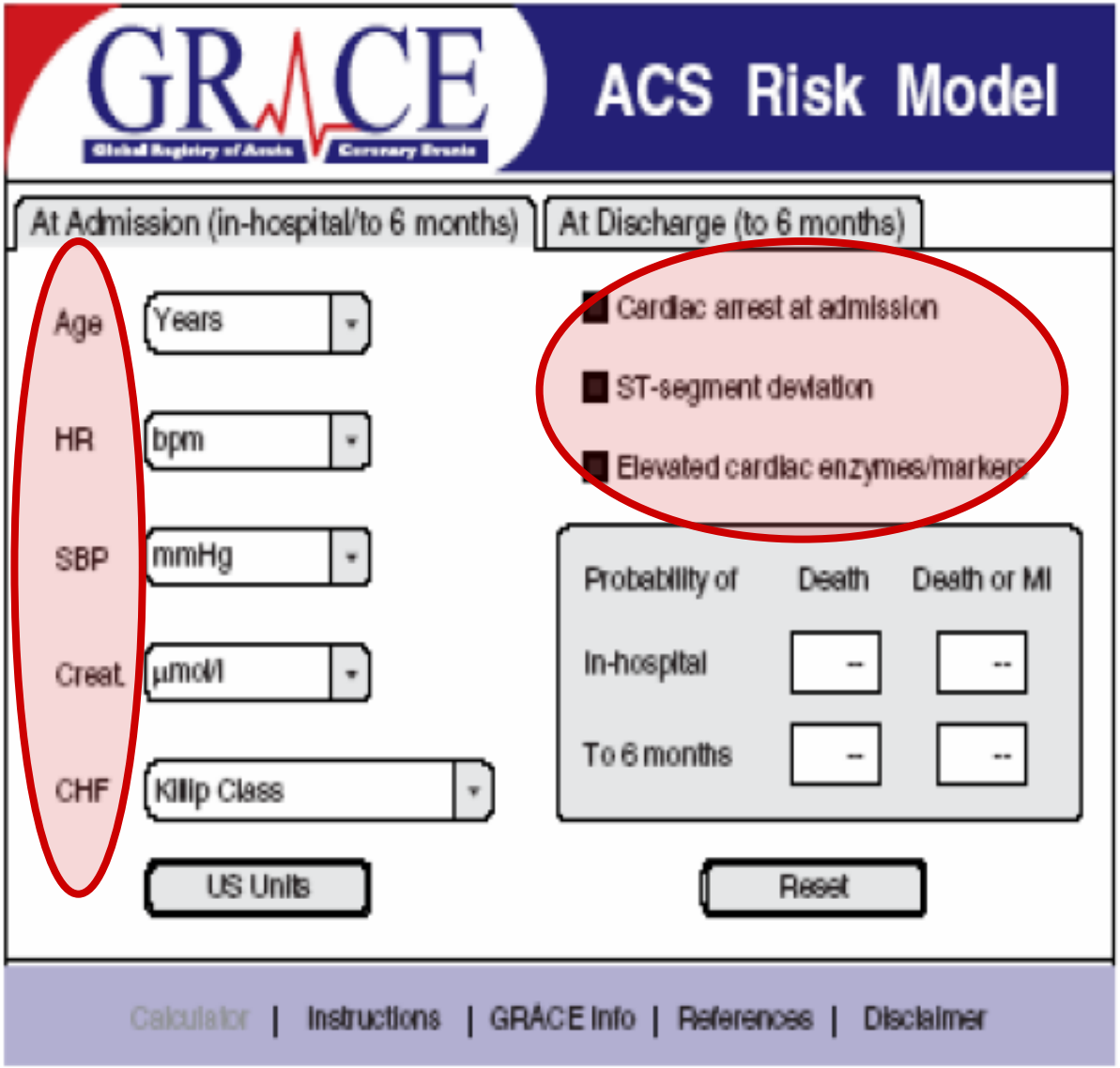
- Emergent
- Early
- No/elective

4th step: Revascularisation

5th step: Long-term management

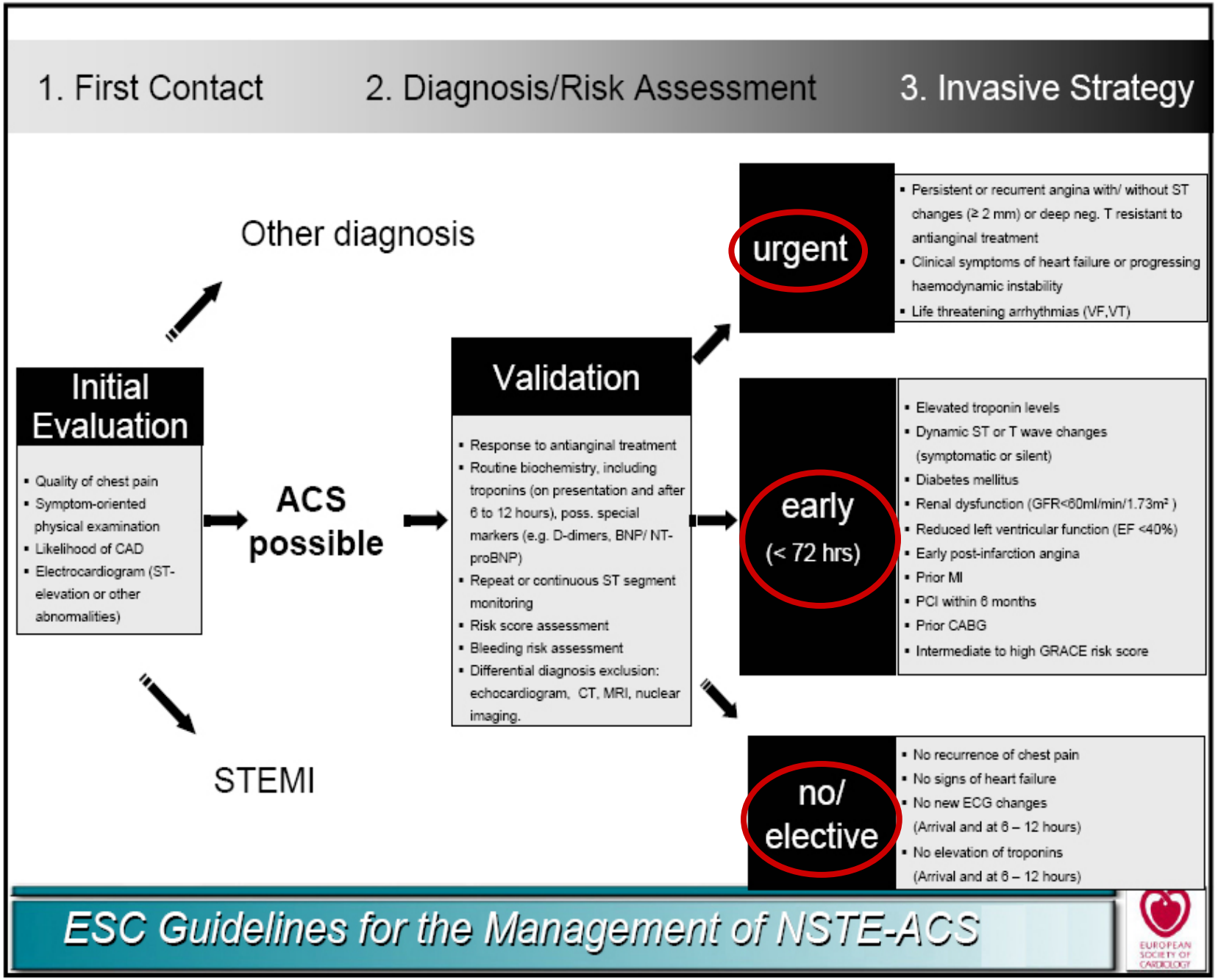
ESC Guidelines for NSTE-ACS EHJ 2007; 28: 1598-1660

GRACE ACS Risk Model



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

Risk category (tertiles)	GRACE Risk Score	In-hospital deaths (%)
Low	<=108	<1
Intermediate	109-140	1-3
High	>140	>3
Risk category (tertiles)	GRACE Risk Score	Post-discharge to 6 months deaths (%)
Low	<=88	<3
Intermediate	89-118	3-8
High	>118	>8


1. First Contact
2. Diagnosis/Risk Assessment
3. Invasive Strategy
Other diagnosis
Initial Evaluation
Quality of chest pain
Symptom-oriented physical examination
Likelihood of CAD
Electrocardiogram (ST-elevation or other abnormalities)
ACS possible
Validation
Response to antianginal treatment
Routine biochemistry, including troponins (on presentation and after 6 to 12 hours), poss. special markers (e.g. D-dimers, BNP/ NT-proBNP)
Repeat or continuous ST segment monitoring
Risk score assessment
Bleeding risk assessment
Differential diagnosis exclusion: echocardiogram, CT, MRI, nuclear imaging.
urgent
Persistent or recurrent angina with/ without ST changes (≥ 2 mm) or deep neg. T resistant to antianginal treatment
Clinical symptoms of heart failure or progressing haemodynamic instability
Life threatening arrhythmias (VF,VT)
early (< 72 hrs)
Elevated troponin levels
Dynamic ST or T wave changes (symptomatic or silent)
Diabetes mellitus
Renal dysfunction (GFR<60ml/min/1.73m²)
Reduced left ventricular function (EF <40%)
Early post-infarction angina
Prior MI
PCI within 6 months
Prior CABG
Intermediate to high GRACE risk score
no/ elective
No recurrence of chest pain
No signs of heart failure
No new ECG changes (Arrival and at 6 – 12 hours)
No elevation of troponins (Arrival and at 6 – 12 hours)
STEMI
ESC Guidelines for the Management of NSTE-ACS
EUROPEAN SOCIETY OF CARDIOLOGY

Risk Stratification

1. **Features of high risk that mandates urgent angiography / revascularization**
   - Refractory angina (e.g. evolving MI without ST abnormalties)
   - Recurrent angina despite intense antianginal treatment associated with ST depression (≥ 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) (≥ 0.5mm)
- Diabetes mellitus
- Reduced renal function (GFR < 60 ml/min/1.73m²)
- Depressed LVEF < 40%
- Early post MI angina
- PCI within 6 months
- Prior CABG
- Intermediate to high risk according to a risk score

Risk Stratification

3 - No features of high risk

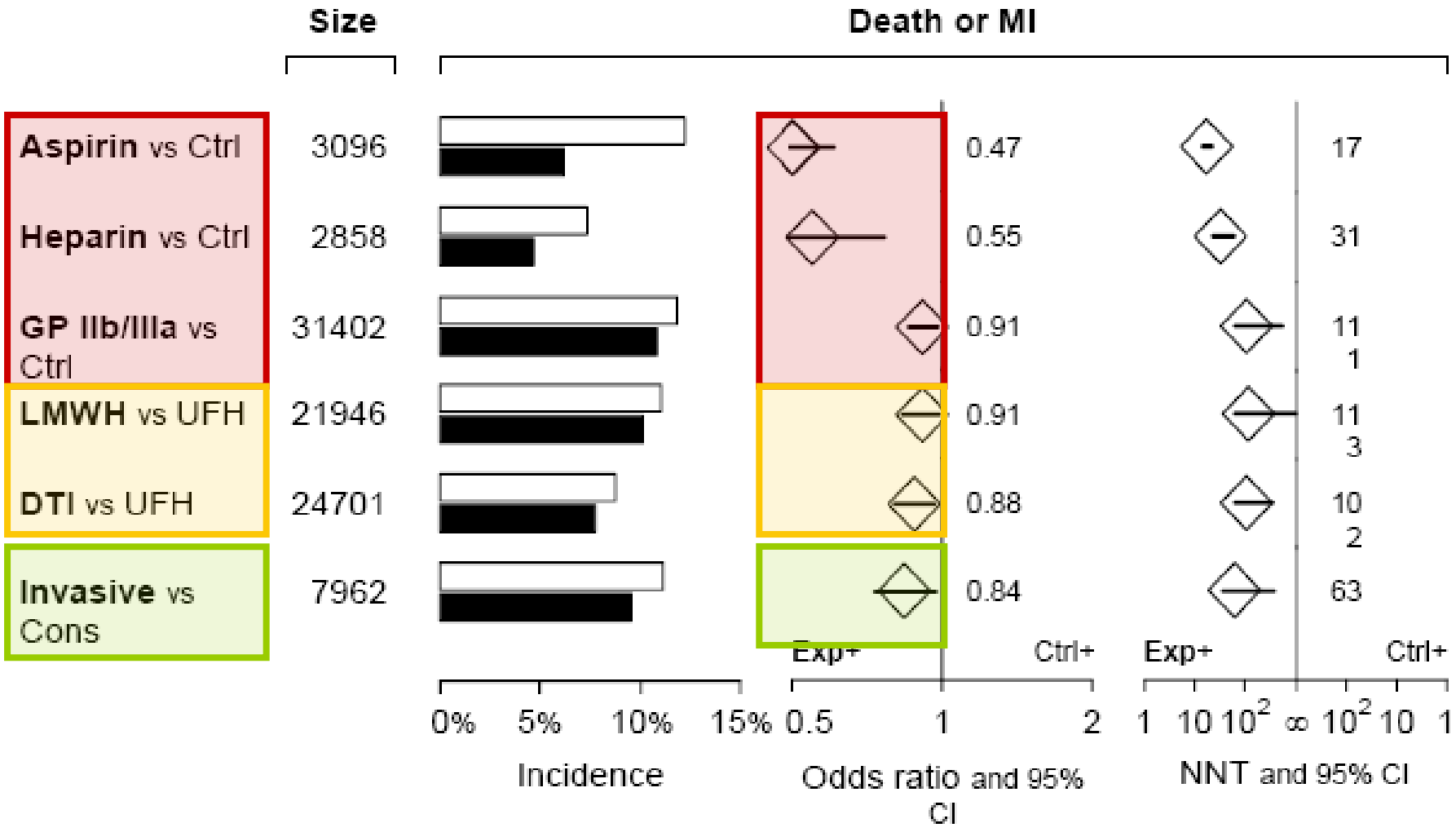
- No recurrence of chest pain
- No signs of heart failure
- No abnormalities in the initial ECG or a second ECG (6 to 12 hours)
- No elevation of troponins (arrival and at 6 – 12 hours)

Therapeutic Options

- Anti-ischaemic agents
- Anti-coagulants
  - UFH or LMWHs
  - Fondaparinux
  - Bivalirudin
- Anti-platelet agents
  - ASA
  - Clopidogrel
  - IIbIIIa Inhibitors
- Revascularisation

Intermediate to high risk:
ST depression
Troponin (+)
Diabetes

NSTE-ACS
Summary of treatment approaches (ESC)



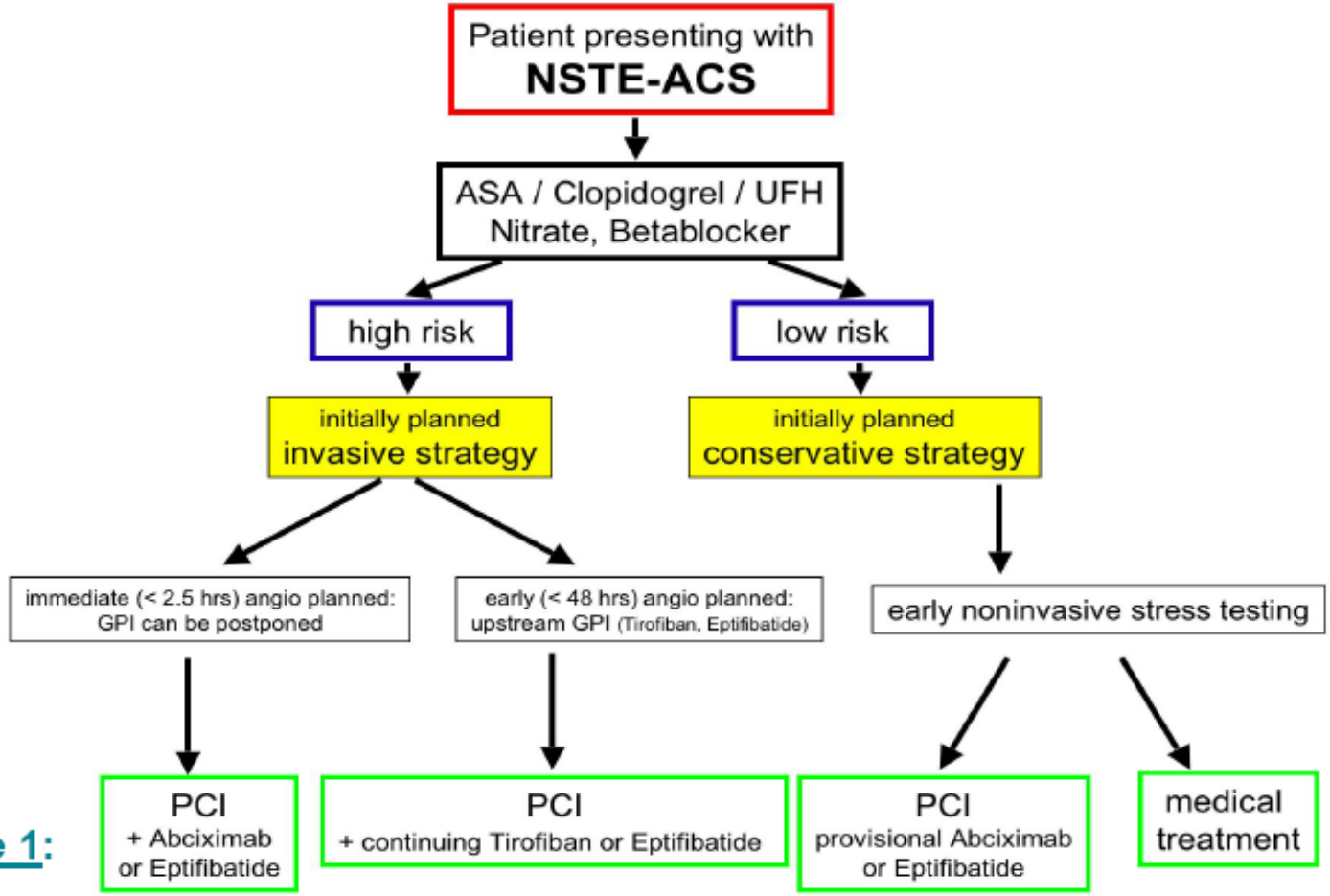
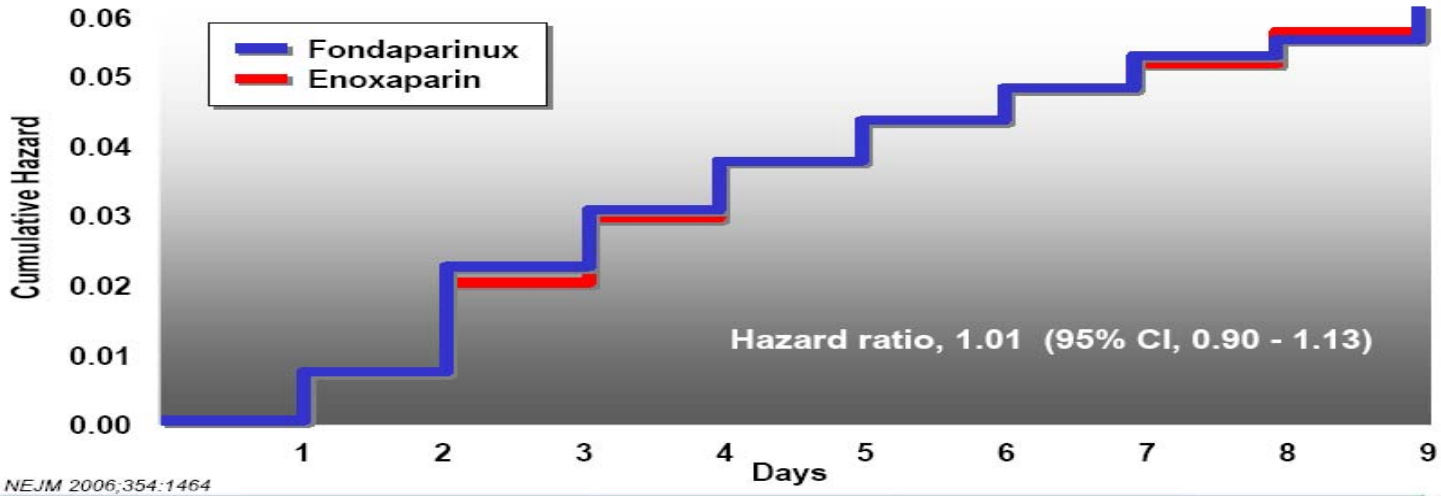


Figure 1:

Flow-chart for planning coronary angiography and PCI, if appropriate, according to risk stratification in patients with NSTE-ACS (unstable angina or NSTEMI). GPI = Glycoprotein IIb/IIIa inhibitor. If for some reason the delay between diagnostic catheterisation and planned PCI is up to 24 hours, abciximab can also be administered. Enoxaparin may be considered as a replacement for UFH in high-risk NSTE-ACS patients, if invasive strategy is not applicable.

OASIS 5 Trial

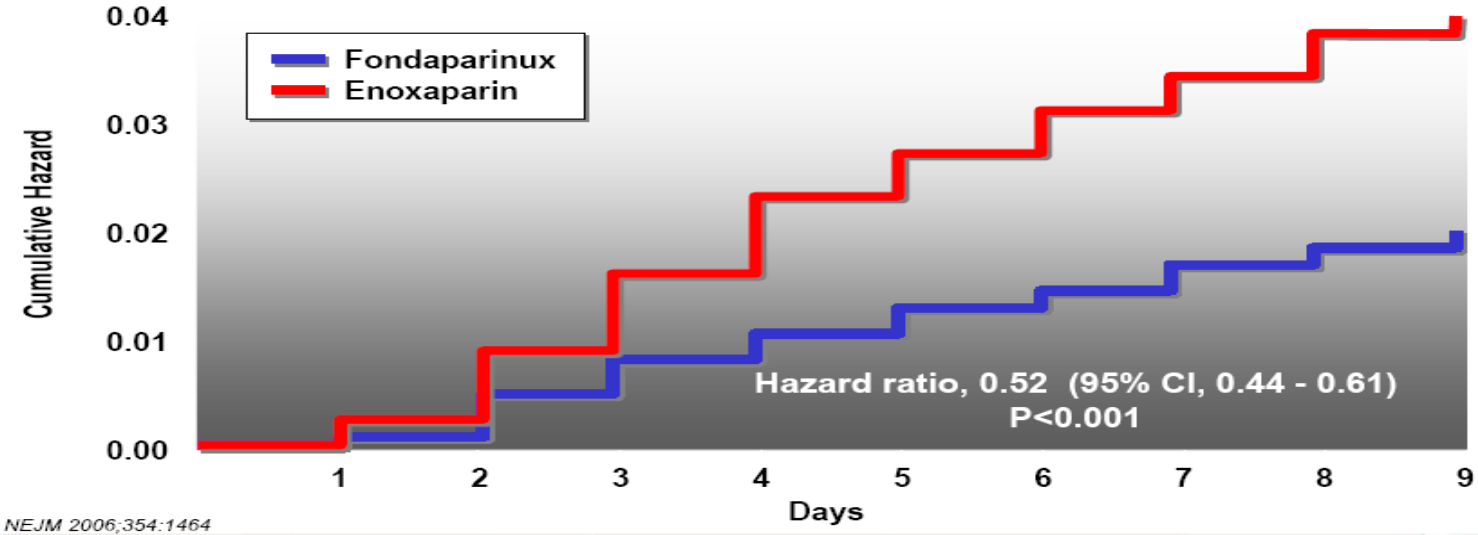
Death, myocardial infarction or refractory ischemia through day 9



NEJM 2006;354:1464

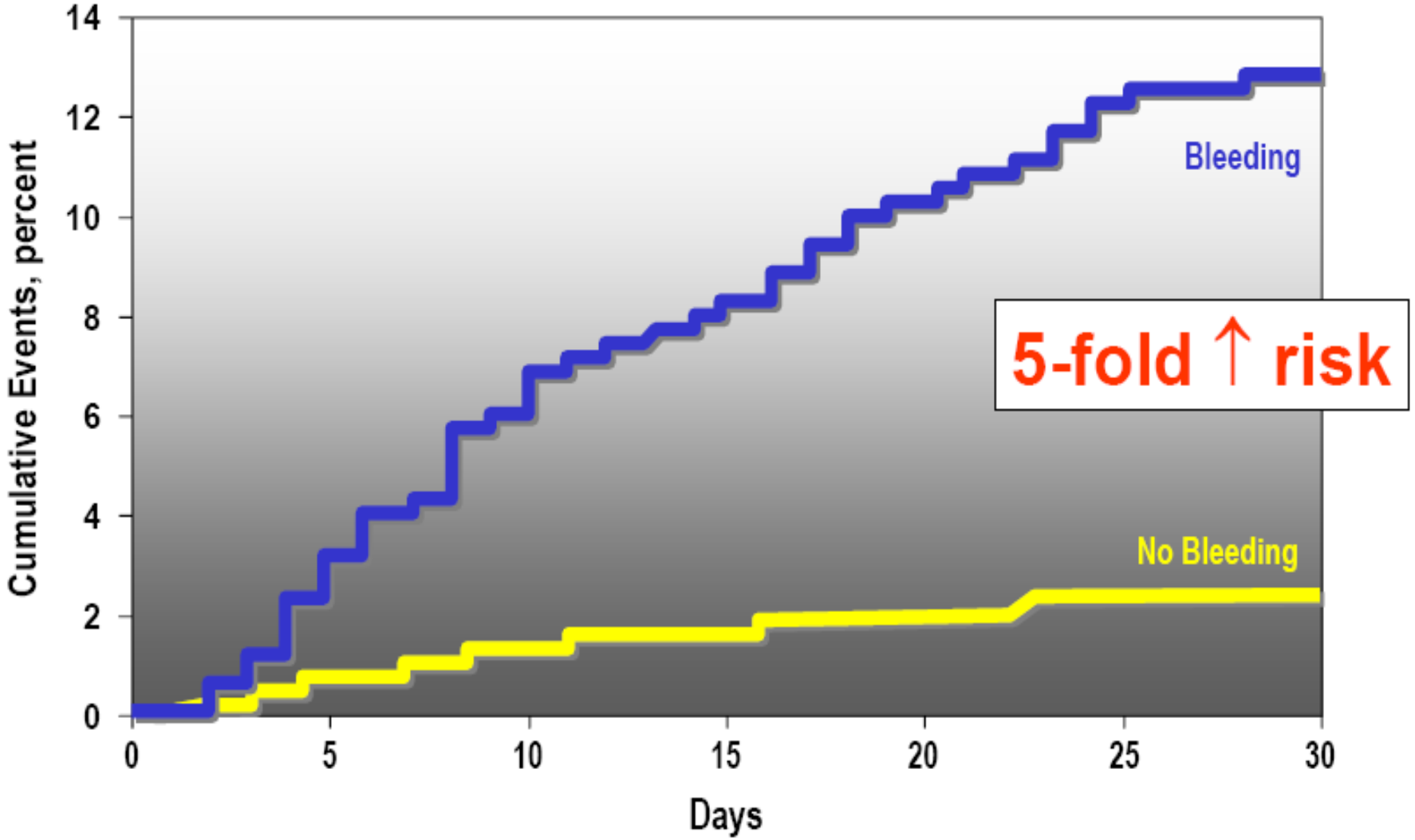
OASIS 5 Trial

Major bleeding through day 9



NEJM 2006;354:1464

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



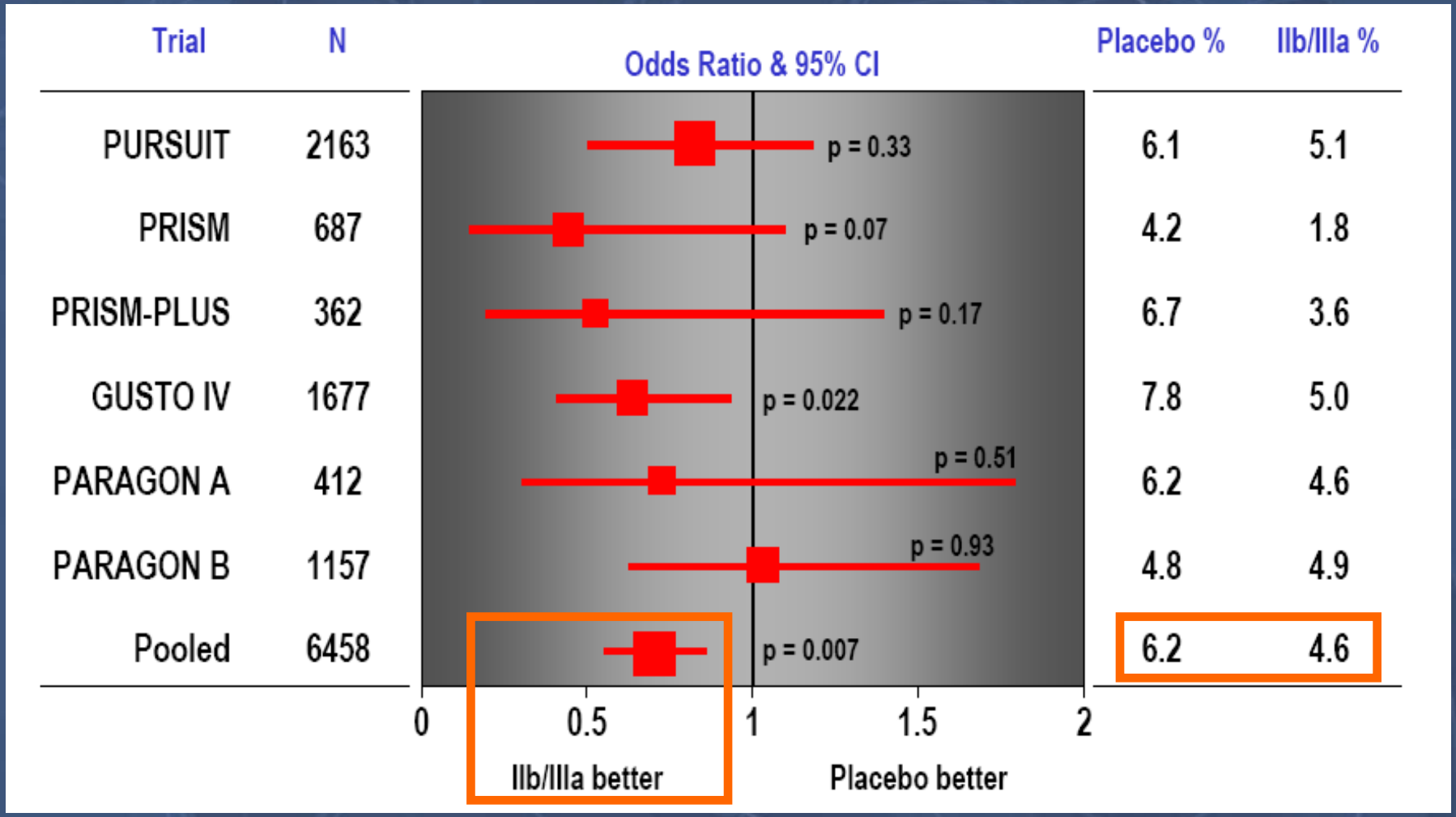
Eikelboom Circulation 2006;114: 774 - 782

Multivariate Model for Major Bleeding in Patients with NSTE-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

IIb/IIIa effect on 30-day mortality among diabetics with NSTE-ACS (6 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 NSTE-ACS in the acute phase (I-C).
- Insulin infusion may be needed to achieve normoglycaemia in selected NSTE-ACS patients with high blood glucose levels at admission (IIa-C)
- Early invasive strategy is recommended for diabetic patients with NSTE-ACS (I – A).
- Diabetic patients with NSTE-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).

ESC Guidelines for the Management of NSTE-ACS (113)

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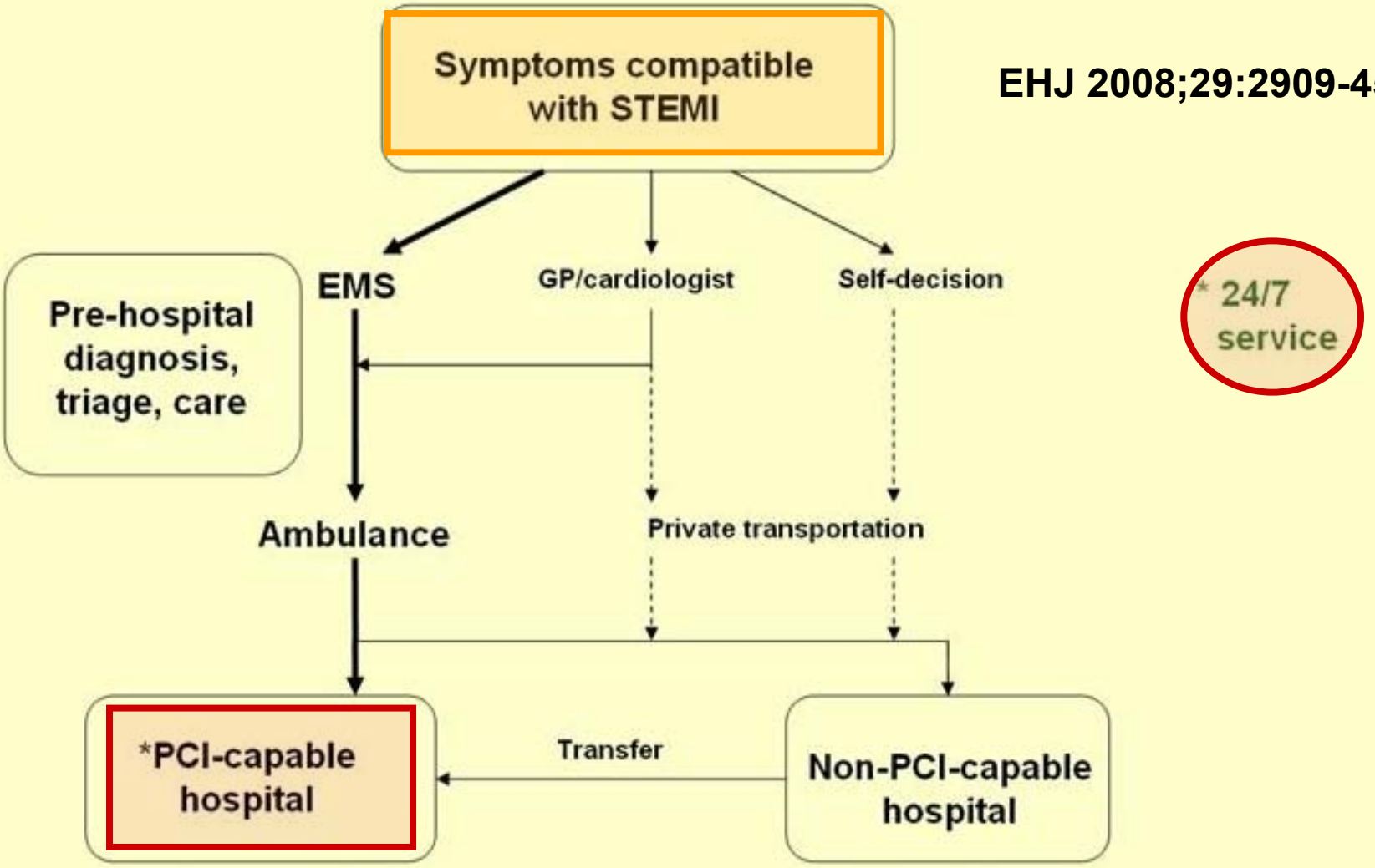
Pre-hospital Management



EHJ 2008;29:2909-45

EMS: Emergency Medical System; STEMI: Acute ST-segment Elevation Myocardial Infarction; GP: General Practitioner; PCI: percutaneous coronary intervention
Thick arrows: preferred patient flow; dotted line: to be avoided

Efficacy of Thrombolysis and Time from Symptom Onset

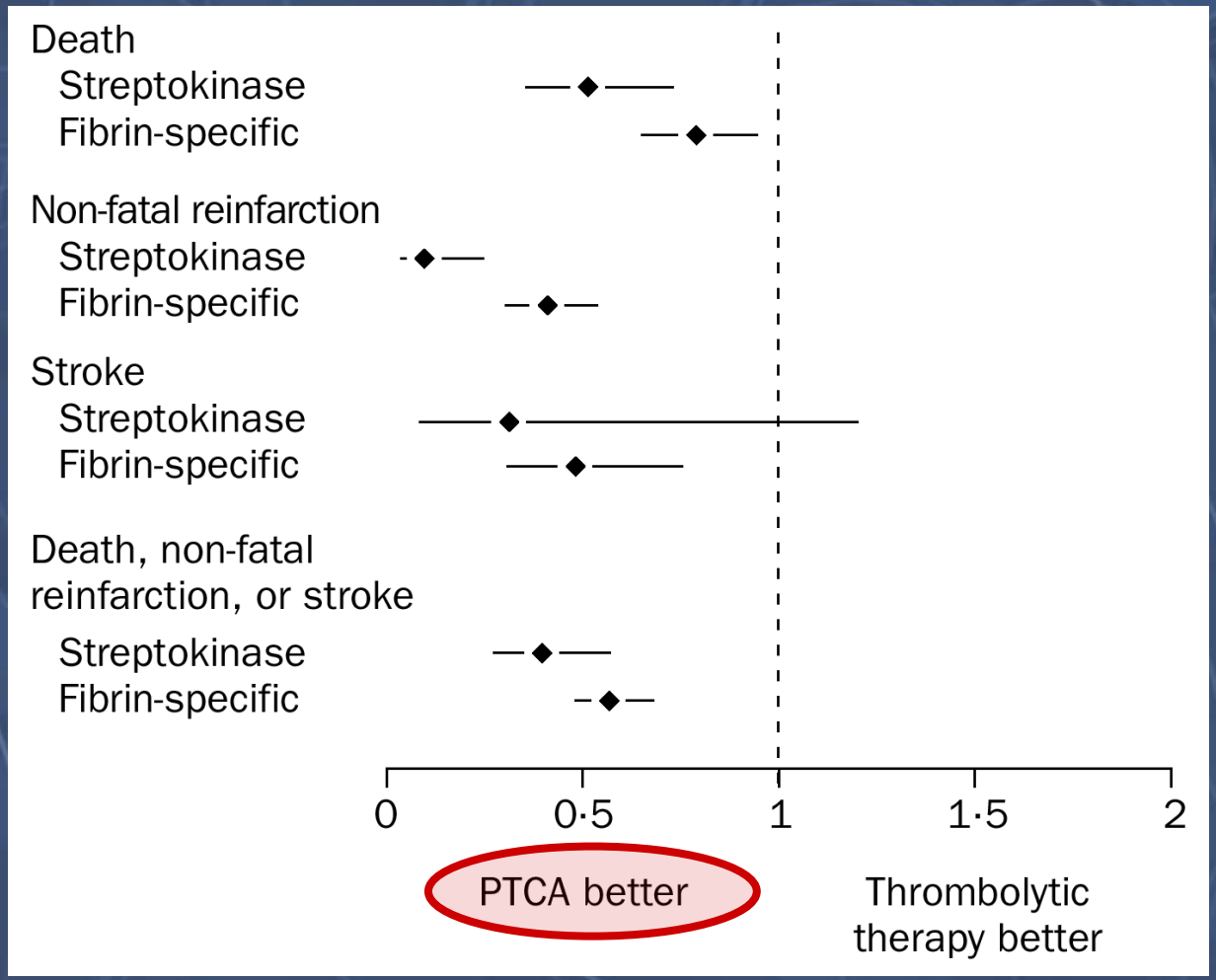
Lives saved per 1000 patients treated

of those with ST ⇑ or LBBB

0-1 hr	**65**
1-2 hr	**37**
2-3 hr	**26**
3-6 hr	**29**

Boersma, Lancet 1996

Short-term Outcomes in Patients Treated with Primary PTCA or Lytics, According to Thrombolytic Agent Used

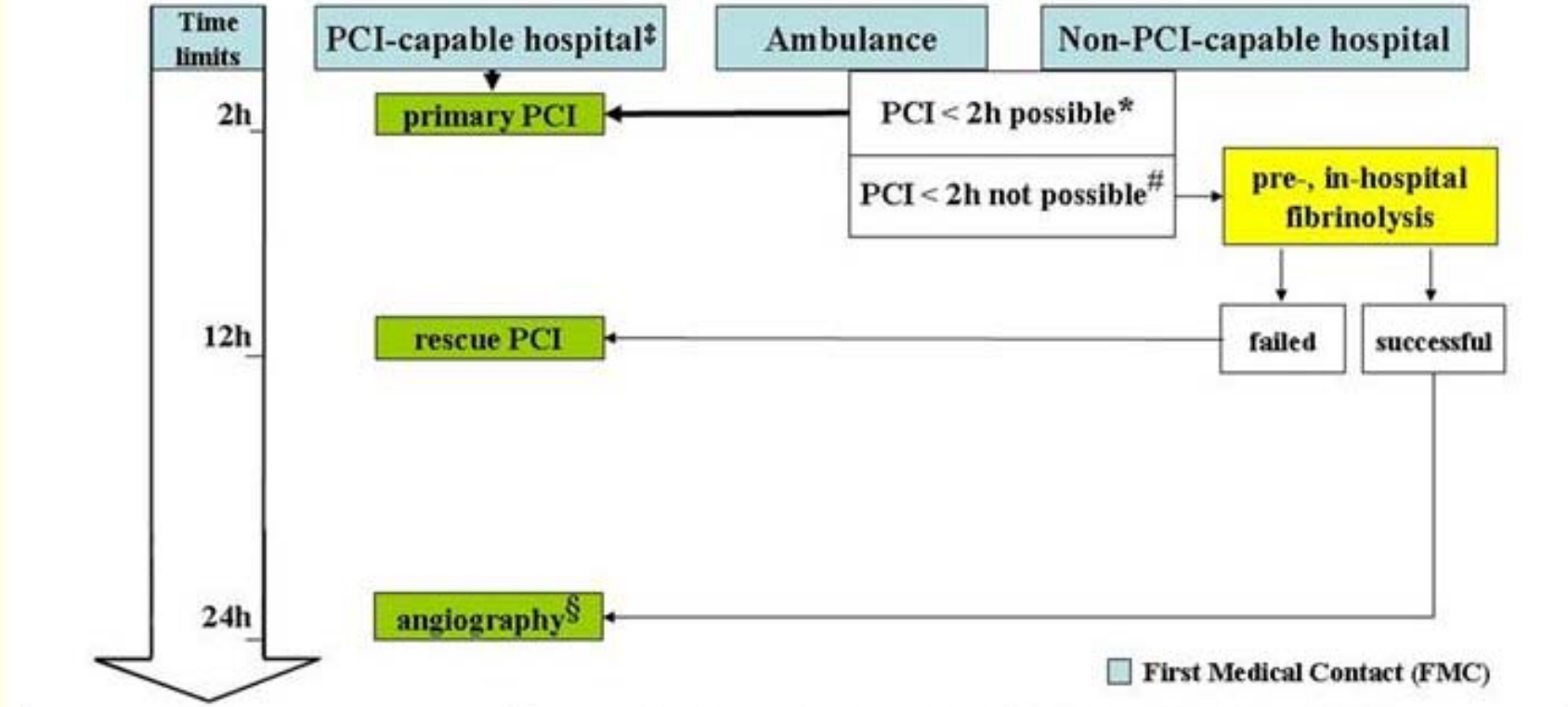


Keeley EC et al. Lancet 2003;361:13-20

Reperfusion Therapy

Recommendations	Class	LOE
▪ Indicated in all pts with chest pain/discomfort of < 12 h and with persistent ST-segment elevation or (presumed) new LBBB	I	A
▪ Should be considered if there is clinical and/or ECG evidence of ongoing ischaemia if symptoms started > 12 h before	IIa	C
▪ Reperfusion (PCI) in stable pts presenting > 12 h to 24 h after symptom onset	IIb	B
▪ PCI of totally occluded infarct artery in stable pts without signs of ischaemia > 24 h after symptom onset	III	B

Reperfusion Strategies



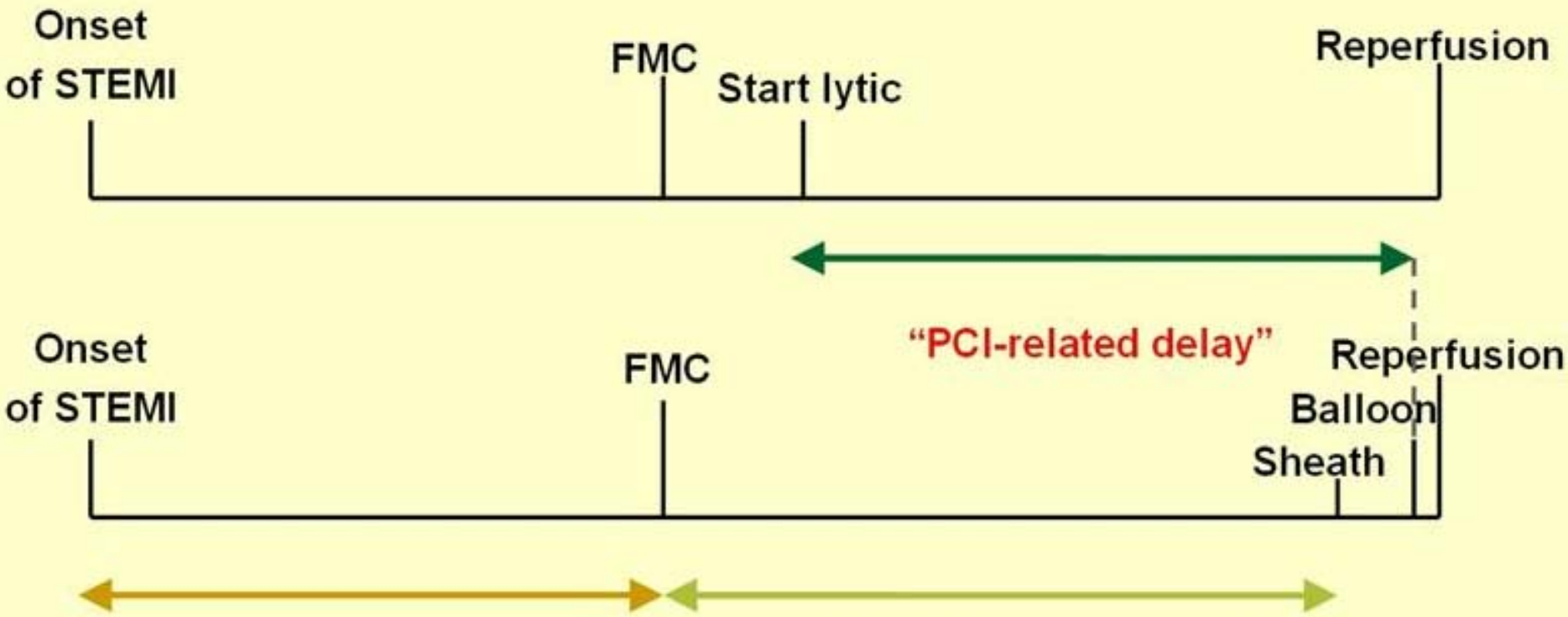
* Time FMC to first balloon inflation must be shorter than 90 min in patients presenting early (< 2 h after symptom onset), with large amount of viable myocardium and low risk of bleeding.

If PCI is not possible < 2 h of FMC, start fibrinolytic therapy as soon as possible.

§ Not earlier than 3 h after start fibrinolysis

‡ 24/7 service

Reperfusion Therapy: Important Time Lines



- Patient-dependent
- (Organization-dependent)
- Organization-dependent

FMC:First Medical Contact

Reperfusion Therapy: Primary PCI

Recommendations	Class	LOE
▪ Preferred reperfusion treatment if performed by an experienced team as soon as possible after FMC	I	A
▪ Time from FMC to balloon should be < 2 h in any case and < 90 min in pts presenting early (< 2 h) with large infarct and low bleeding risk	I	B
▪ Indicated for patients in shock and those with contraindications to fibrinolytic therapy irrespective of time delay	I	B
Rescue PCI ▪ After failed fibrinolysis in patients with large infarcts if performed within 12 h	IIa	A

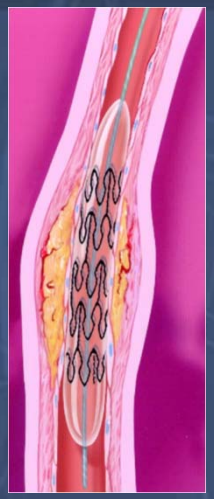
Evolution of PCI for STEMI

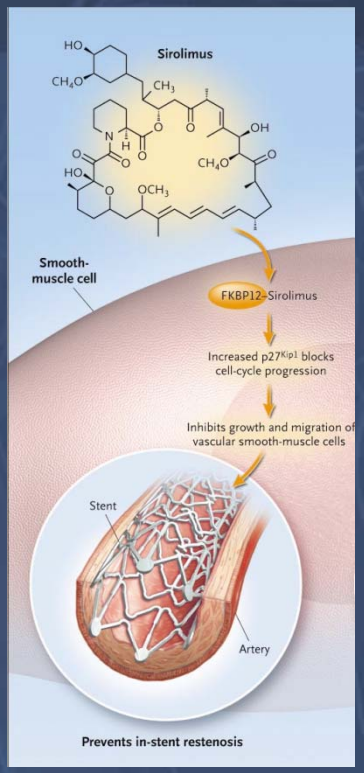
Clopidogrel

ASA

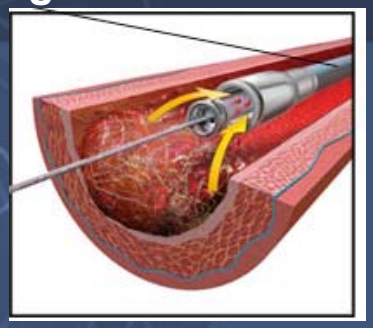
Platelet

GP IIb/IIIa inhibitor

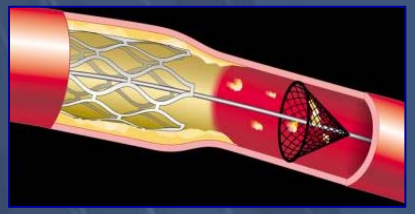




AngioJet



Embolization Protection Device



Balloon

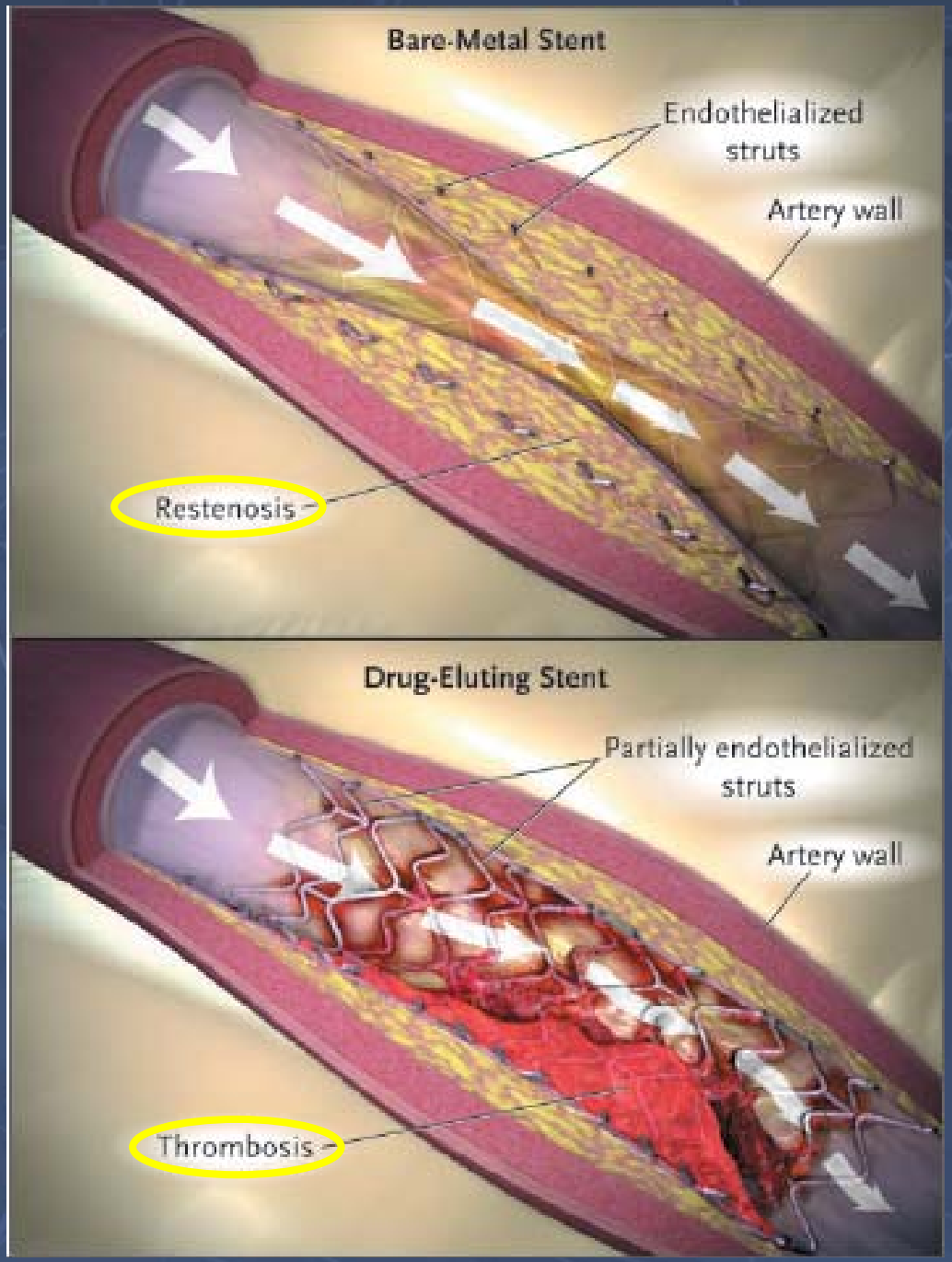
Antiplatelet Rx

Stent

DES

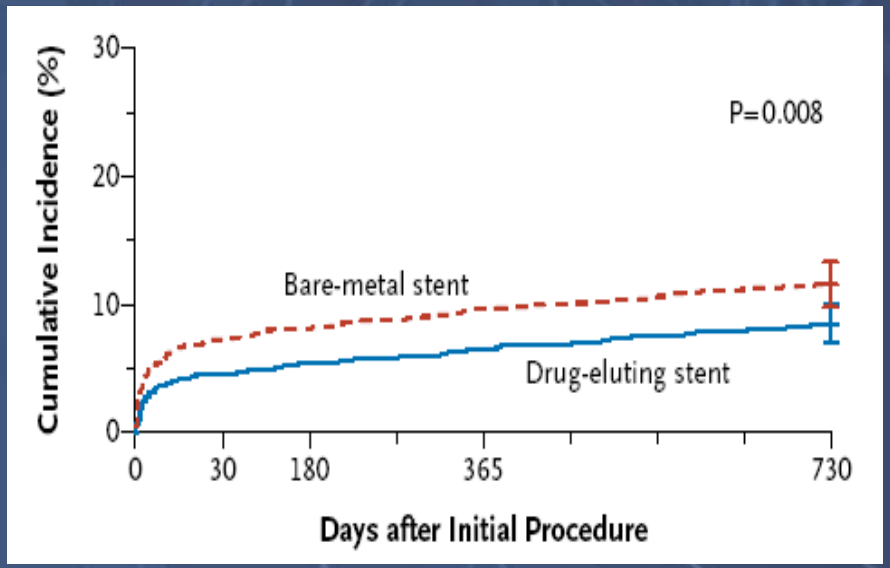
Thrombus Removal and Distal Embolization Protection Devices

Antman. Circulation 2001;103:2310.

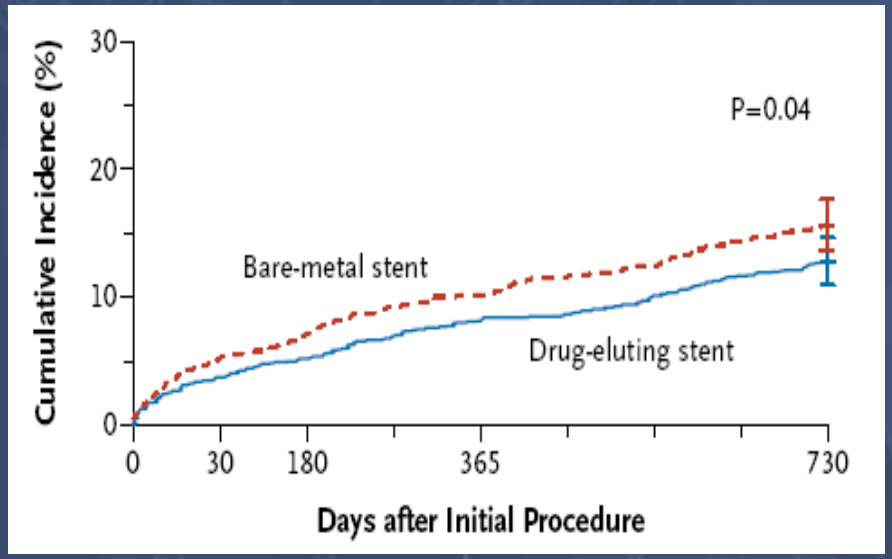

Bare-Metal Stent
Endothelialized struts
Artery wall
Restenosis
Drug-Eluting Stent
Partially endothelialized struts
Artery wall
Thrombosis

Drug-eluting > bare-metal stents for AMI?

STEMI



NSTEMI



N Engl J Med 2008;359:1330-42

Reperfusion Therapy: Fibrinolytic Therapy

Recommendations	Class	LOE
▪ In the absence of contraindications and if primary PCI cannot be performed within the recommended time	I	A
▪ A fibrin-specific agent should be given	I	B
▪ Pre-hospital initiation of fibrinolytic therapy	IIa	B

Fibrinolytic Therapy:
Antithrombotic Co-therapy

Recommendations	Class	LOE
▪ Antiplatelet co-therapy		
▫ if not already on aspirin oral (soluble or chewable/ no enteric-coated) or i.v. dose of aspirin plus	I	B
▫ clopidogrel oral loading dose if age ≤ 75 years	I	B
▫ if age > 75 years start with maintenance dose	IIa	B

Fibrinolytic Therapy:
Antithrombotic Co-therapy

Recommendations	Class	LOE
Antithrombin co-therapy		
with alteplase, reteplase and tenecteplase:		
enoxaparin i.v. bolus followed 15 min later by first s.c. dose, if age > 75 years no i.v. bolus and start with reduced first s.c. dose	I	A
if enoxaparin is not available: a weight-adjusted bolus of i.v. heparin followed by a weight adjusted i.v. infusion with first aPTT control after 3 h	I	A

Angiography after Fibrinolytic Therapy

Recommendations	Class	LOE
Evidence of failed fibrinolysis or uncertainty about success: immediate	IIa	B
Recurrent ischaemia, reocclusion after initial successful fibrinolysis: immediate	I	B
Evidence of successful fibrinolysis: within 3 to 24 h after start of fibrinolytic therapy	IIa	A
In unstable patients who did not receive reperfusion therapy: immediate	I	C
In stable patients who did not receive reperfusion therapy: before discharge	IIb	C

Antithrombotic Treatment without Reperfusion Therapy

Recommendations	Class	LOE
Antiplatelet co-therapy		
▪ if not already on aspirin oral (soluble or chewable /no enteric-coated) or i.v. dose of aspirin	I	A
▪ oral dose of clopidogrel	I	B
Antithrombin co-therapy		
▪ i.v. bolus of fondaparinux followed 24 h later by s.c. dose	I	B
▪ if fondaparinux is not available: enoxaparin i.v. bolus followed 15 min later by first s.c. dose, if age > 75 years no i.v. bolus and start with reduced first s.c. dose or	I	B
▪ i.v. heparin followed by a weight adjusted i.v. infusion with first aPTT control after 3 h	I	B

Routine prophylactic therapies in the acute phase of STEMI

Recommendations	Class[a]	Level[b]
Aspirin: maintenance dose of 75–100 mg	I	A
Clopidogrel: maintenance dose of 75 mg	I	A
Non-selective and selective COX-2 agents	III	C
I.v. β-blocker	IIb	A
Oral β-blocker	I	A
ACE-inhibitor: oral formulation on first day		
for all patients in whom it is not contraindicated	IIa	A
for high-risk patients	I	A
Nitrates	IIb	A
Calcium antagonists	III	B
Magnesium	III	A
Lidocaine	III	B
Glucose–insulin–potassium infusion	III	B

ESC Guidelines for STEMI EHJ 2008;29:2909-45

Long-Term Medical Treatment

Recommendations	Class	LOE
Antiplatelets		
▪ Aspirin for ever (75 to 100 mg daily) in all patients without allergy	I	A
▪ Clopidogrel (75 mg daily) for 12 months in all patients irrespective the acute treatment	IIa	C
▪ Clopidogrel (75 mg daily) in all patients with contraindication to aspirin	I	B

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).

ESC Guidelines for the Management of NSTE-ACS (70)

Response to MI in Patients with and without Diabetes Mellitus

Left ventricular function

Parameter	Diabetics	Non-diabetics	p
EF (%)	61	60	NS
Hyperkinesia non-infarct zone			<0.05
Signs of CHF	22	14	<0.001
Diastolic dysfunction	+++	+/-	

(Woodfield et al: Gusto I angiographic part, J Am Coll Card 1996;28:1661)

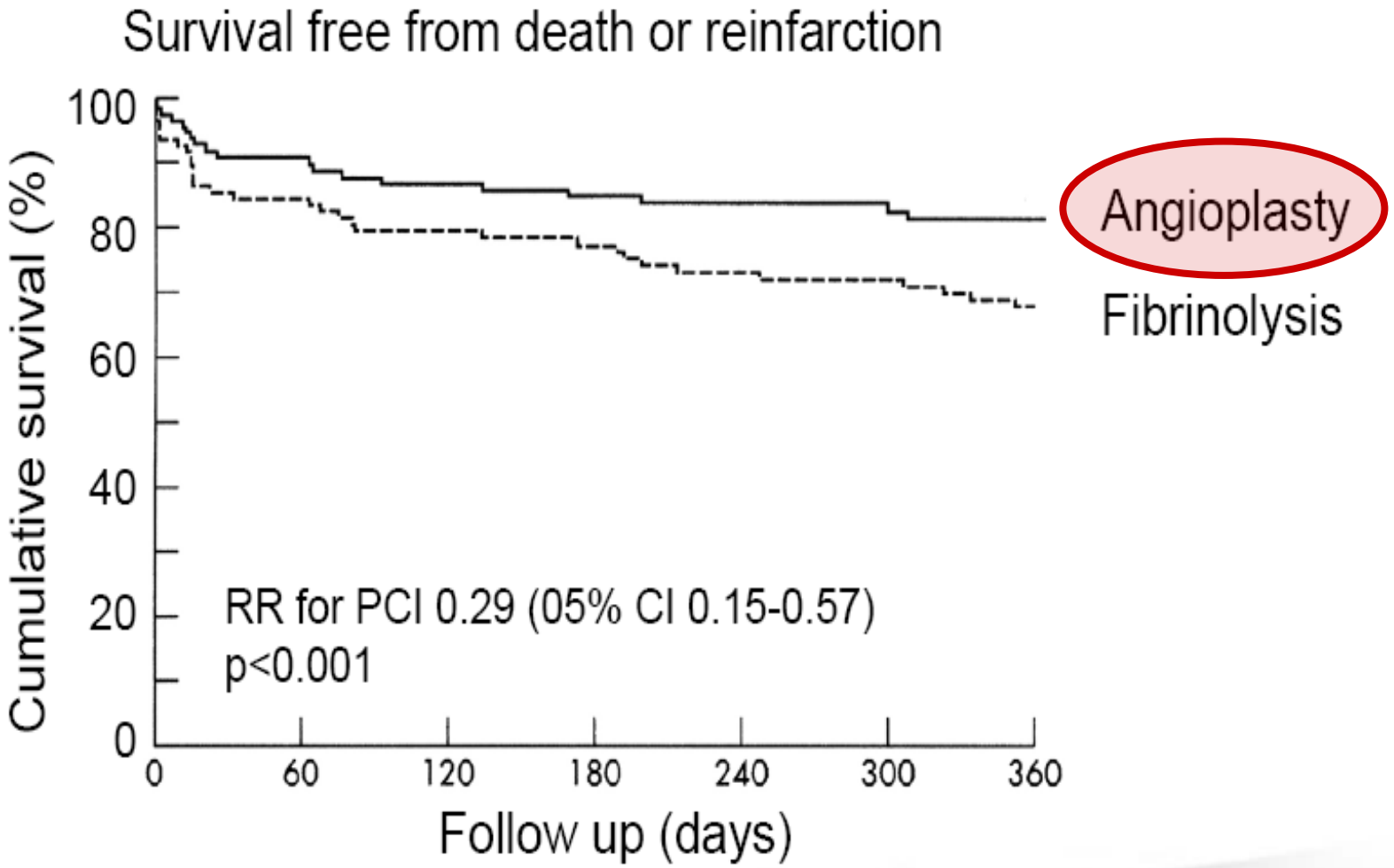
PCI vs. Lytic treatment

Subgroup	*n*	PTCA (%)	Lytic (%)	Relative risk (95% CI)*	NNT
Age (years)					
<60	1178	4.3	8.2		23
60-70	852	6.3	12.8		15
>70	805	13.3	23.6		8
Sex					
Male	2043	5.7	12.2		16
Female	591	11.7	16.4		12
Diabetes					
Yes	367	9.2	19.3		10
No	2151	6.5	11.8		16
Prior MI					
Yes	383	9.7	22.7		8
No	2250	6.6	11.5		17
MI location					
Anterior	1153	8.2	14.5		13
Non-anterior	1469	6.2	12.0		16
Pulse rate					
<65	676	5.3	13.4		14
65-75	513	8.2	9.7		21
76-85	535	6.6	12.9		15
>85	690	8.2	14.8		13
SBP (mmHg)					
<115	595	10.5	17.4		11
115-130	480	5.3	10.3		19
131-150	737	7.8	10.4		19
>150	612	4.5	14.0		14
Risk group					
Low	1186	2.9	7.2		27
Intermediate	758	8.0	12.7		15
High	681	13.1	24.1		8

Grines C, et al. Am Heart Journal 2003;145:47-57

Revascularization in acute coronary syndromes

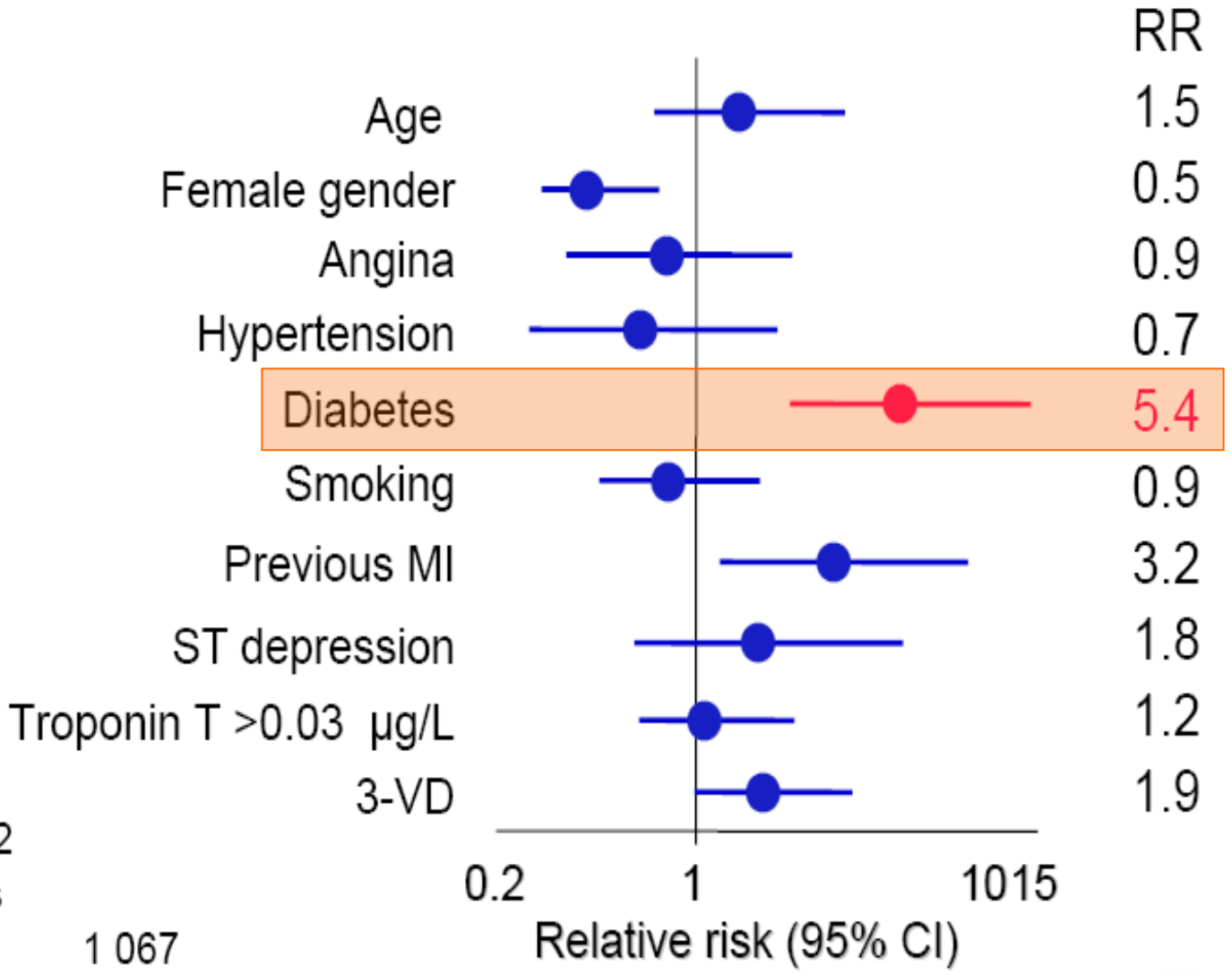
Early PCI vs. thrombolysis in diabetic patients with AMI
Fibrinolysis (n = 99) or Primary PCI (n = 103)



(Hsu et al Heart 2002:88: 268)

Revascularization in acute coronary syndromes

Mortality predictors in invasively managed patients with ACS



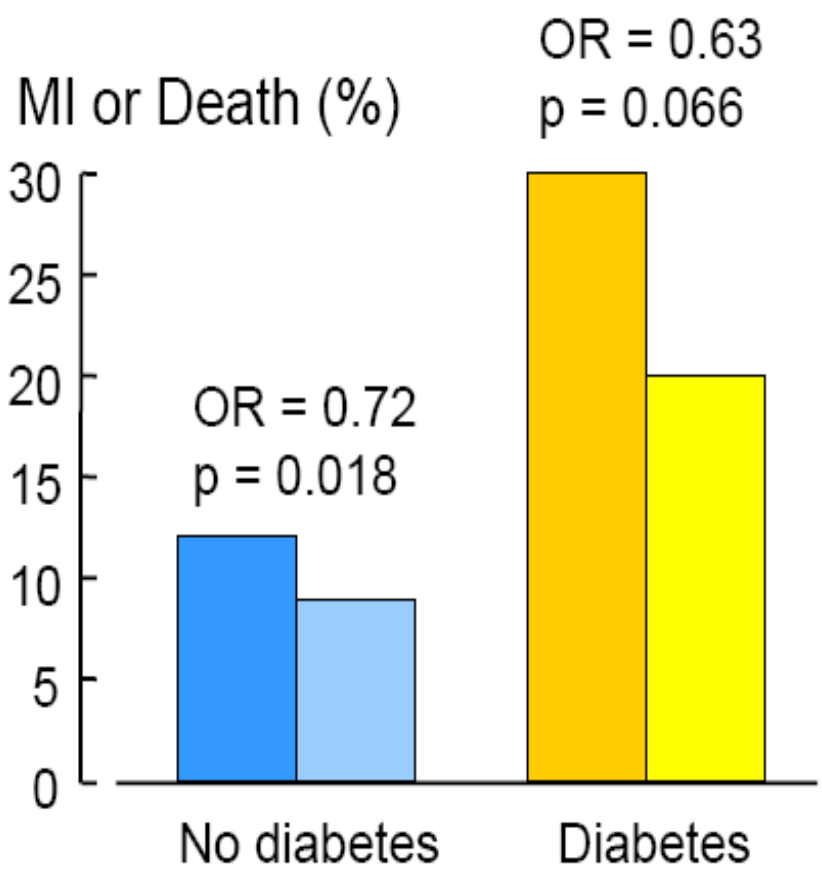
n = 1 222

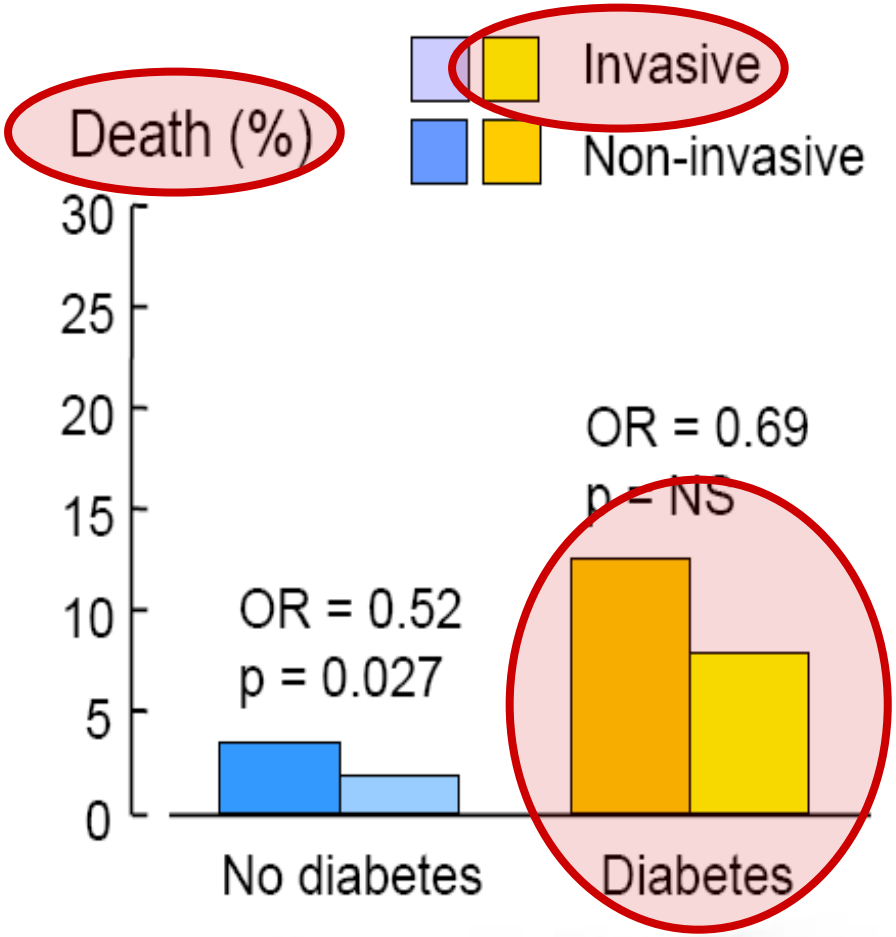
Diabetes	
No	1 067
Yes	155

(Norhammar et al J Am Coll Card 2004; 43; 585)

Revascularization in acute coronary syndromes

Early revascularization in ACS comparing patients with (n=155) and without diabetes (n=1 067)
One year event rate in FRISC II

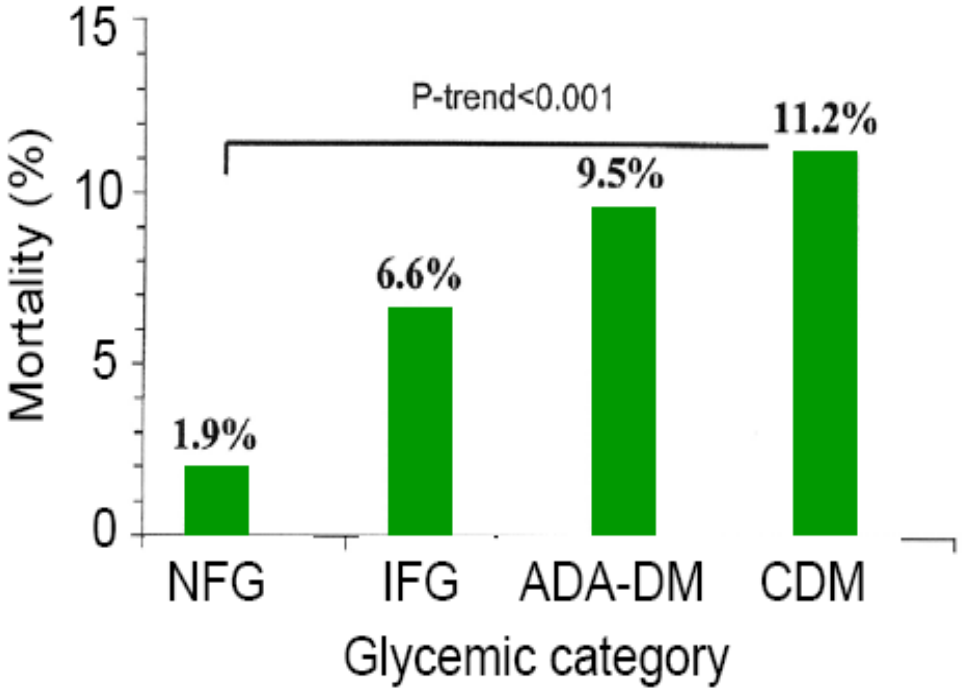


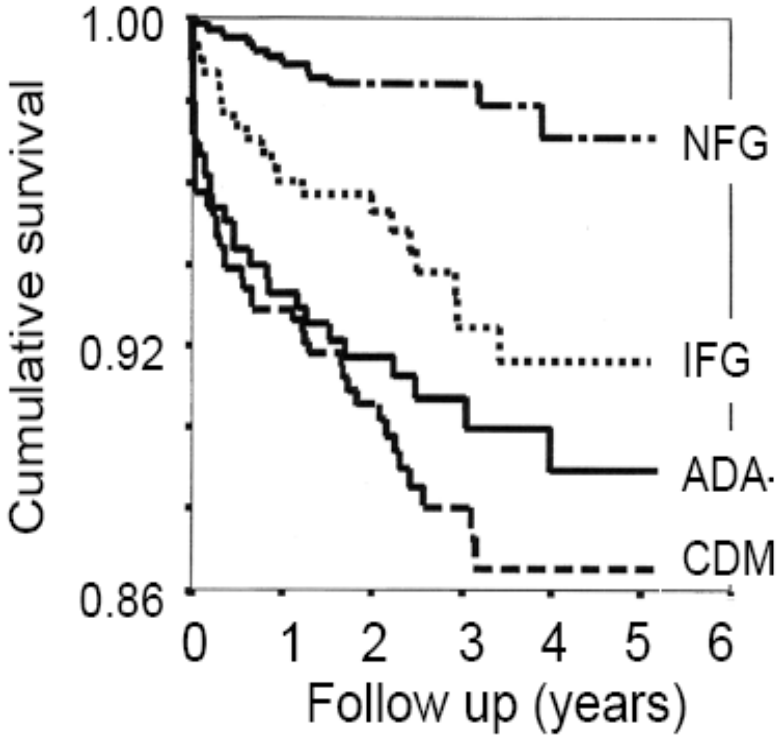


(Norhammar et al J Am Coll Card 2004; 43; 585)

The importance of glucose control

Glycemia and mortality following PCI
(n=1 612)
Glucometabolic classification via fasting glucose





(Muhlestein et al. Am Heart J, 2003:146: 351)

Revascularization in diabetics

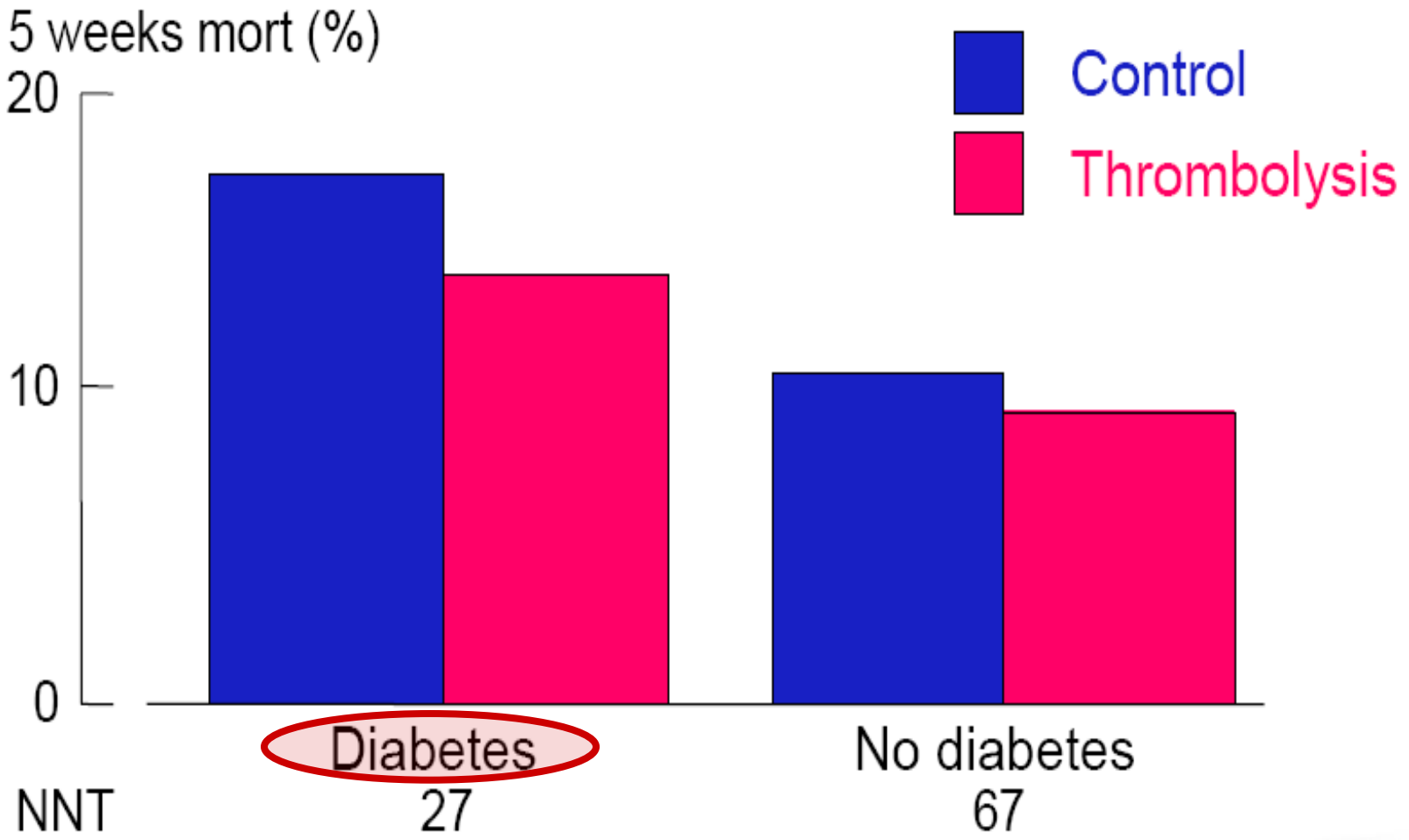
Recommendation	Class	Level
Treatment decisions regarding revascularization in patients with diabetes should favour coronary artery bypass surgery over percutaneous intervention.	IIa	A
Glycoprotein IIb/IIIa inhibitors are indicated in elective PCI in a diabetic patient.	I	B
When PCI with stent implantation is performed in a diabetic patient, drug-eluting stents (DES) should be used.	IIa	B
Mechanical reperfusion by means of primary PCI is the revascularization mode of choice in a diabetic patient with acute MI.	I	A

Guidelines on diabetes, prediabetes and CVD: ESC –EASD. EHJ 2007

Thrombolysis in the diabetic MI patient

From fibrinolytic therapy trialists

n = 43 343 Diabetes ~ 4 300 (10%)



(FTT Collaboration Group Lancet 1994;31)

Σώζονται…

- **15** παραπάνω ζωές σε μη διαβητικούς
- **37** παραπάνω ζωές σε διαβητικούς

Fibrinolytic Therapy Trialists Collaborative Group. Lancet 1994;343:311-322

Thrombolysis in the diabetic patient

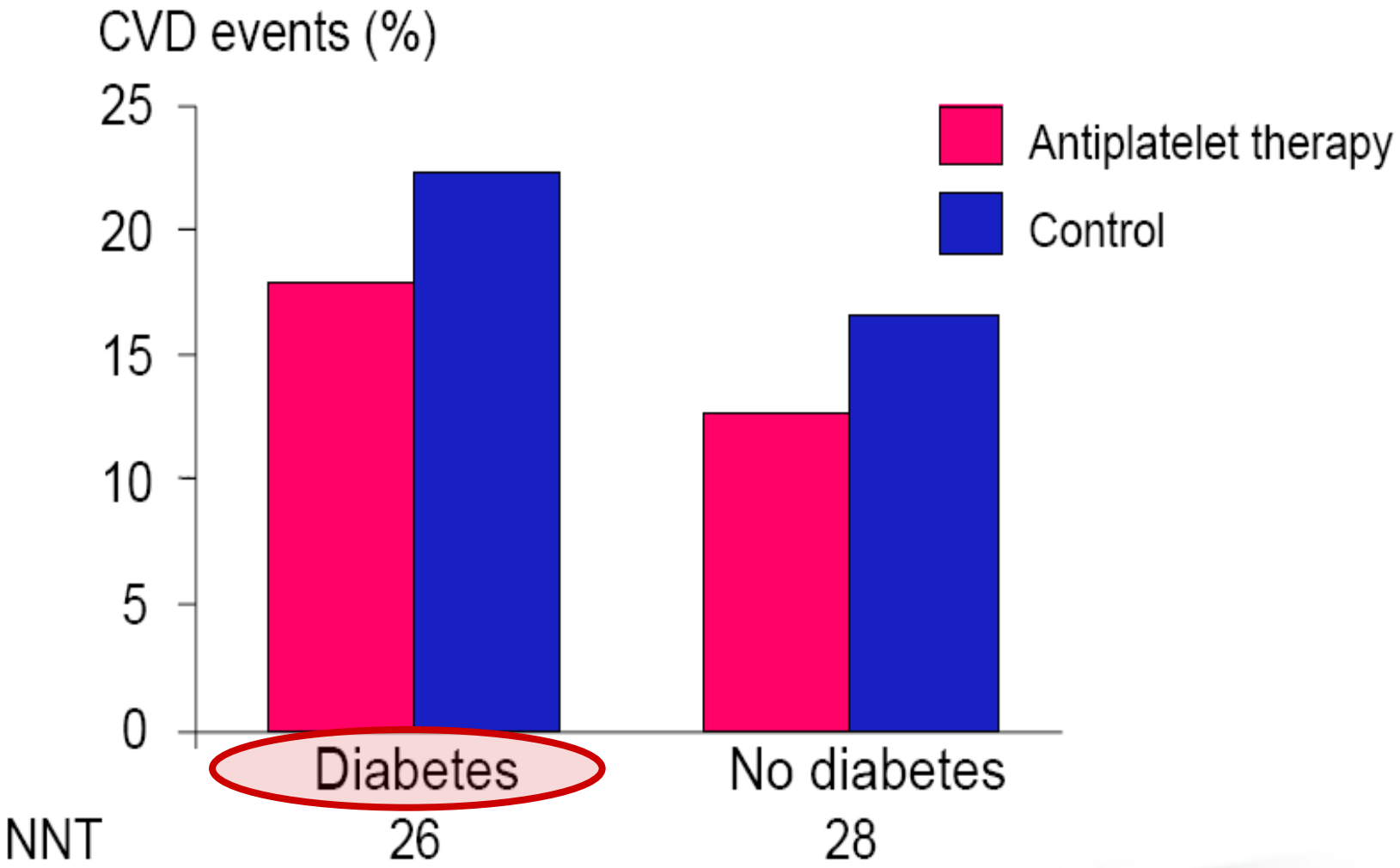
GUSTO I

n = 40 000 Diabetes ~ 6 000 (15%)

Bleeding	Diabetics	Non-diabetics
Extraocular	1	10
Intraocular	0	1

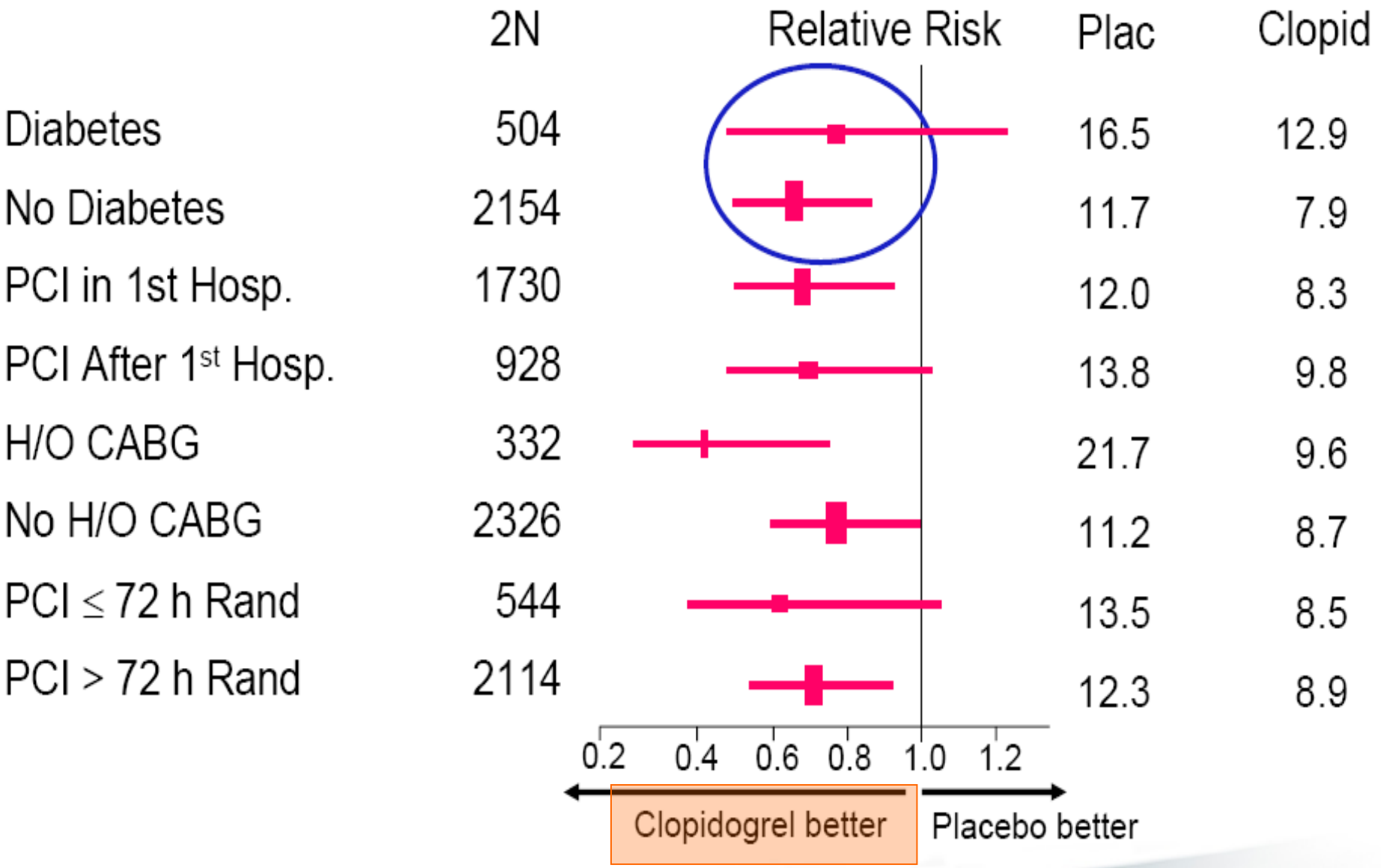
(Mahaffey et al JACC 1997;30:1606)

Effect of anti platelet agents on CVD events in high risk patients: Meta analysis



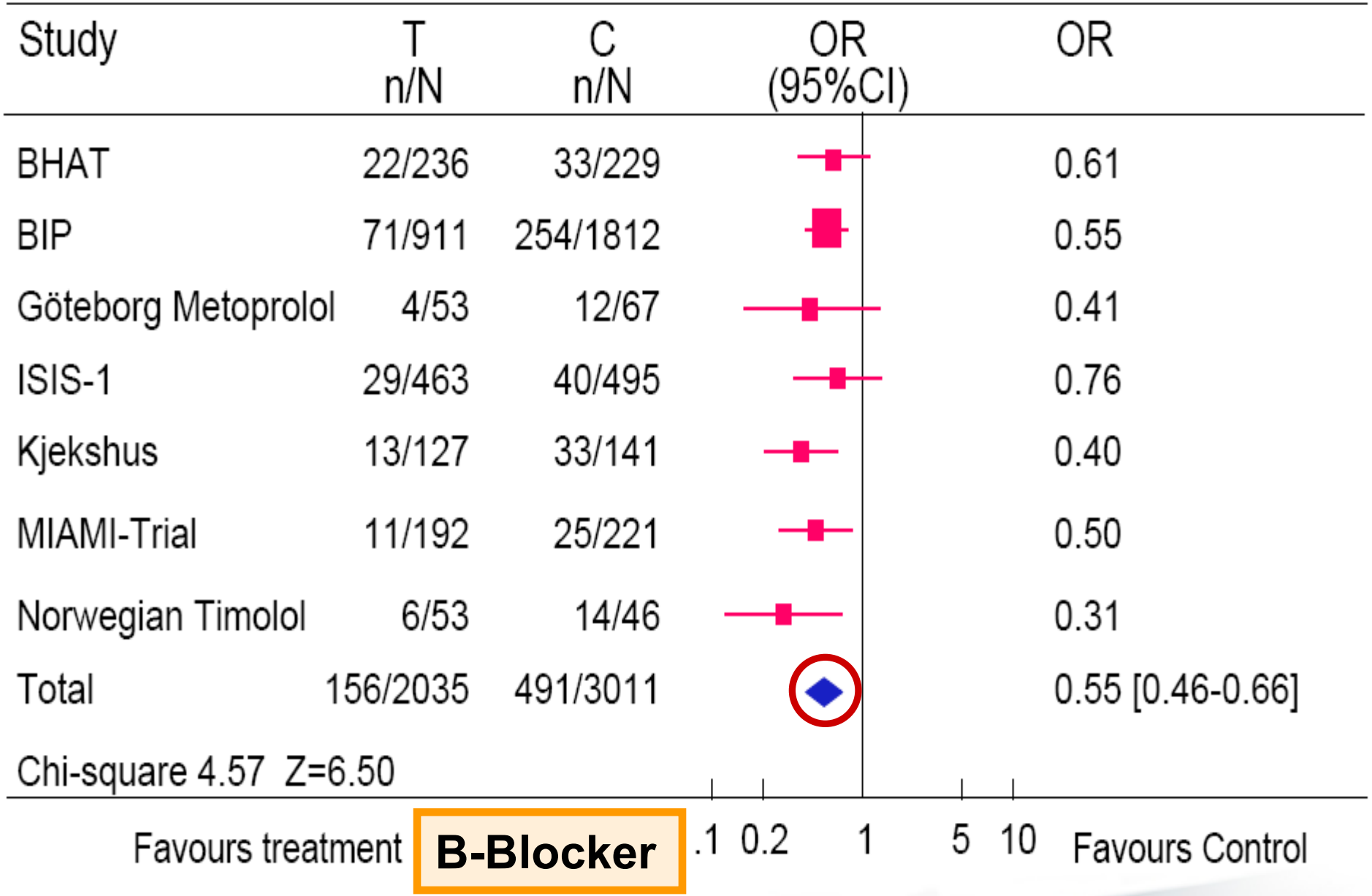
(Antiplatelets Trialists Collaboration BMJ1994;305:81-106)

CV death or MI from randomization to end



(Mehta SR et al. Lancet 2001:358:527-33)

Diabetic patients - All studies

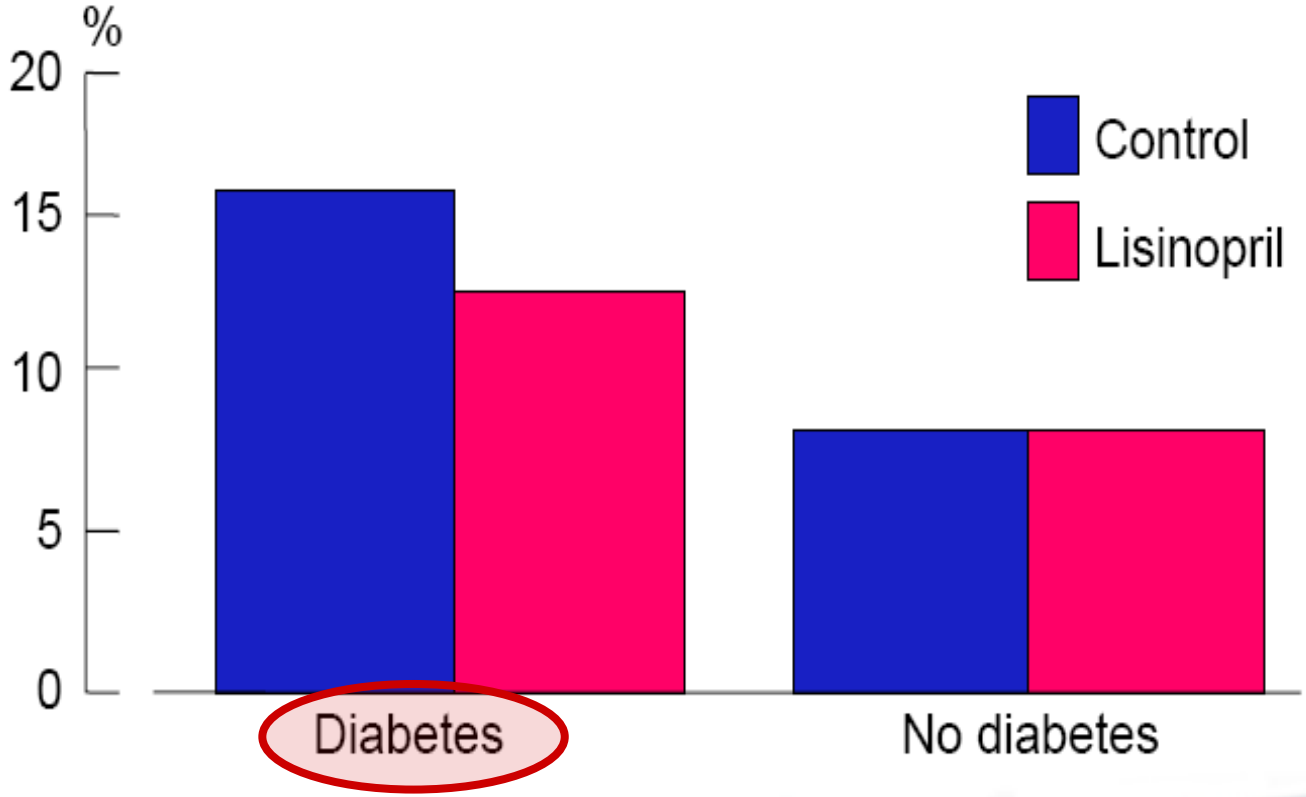


ACE-Inhibitors in diabetic patients with acute myocardial Infarction

GISSI 3

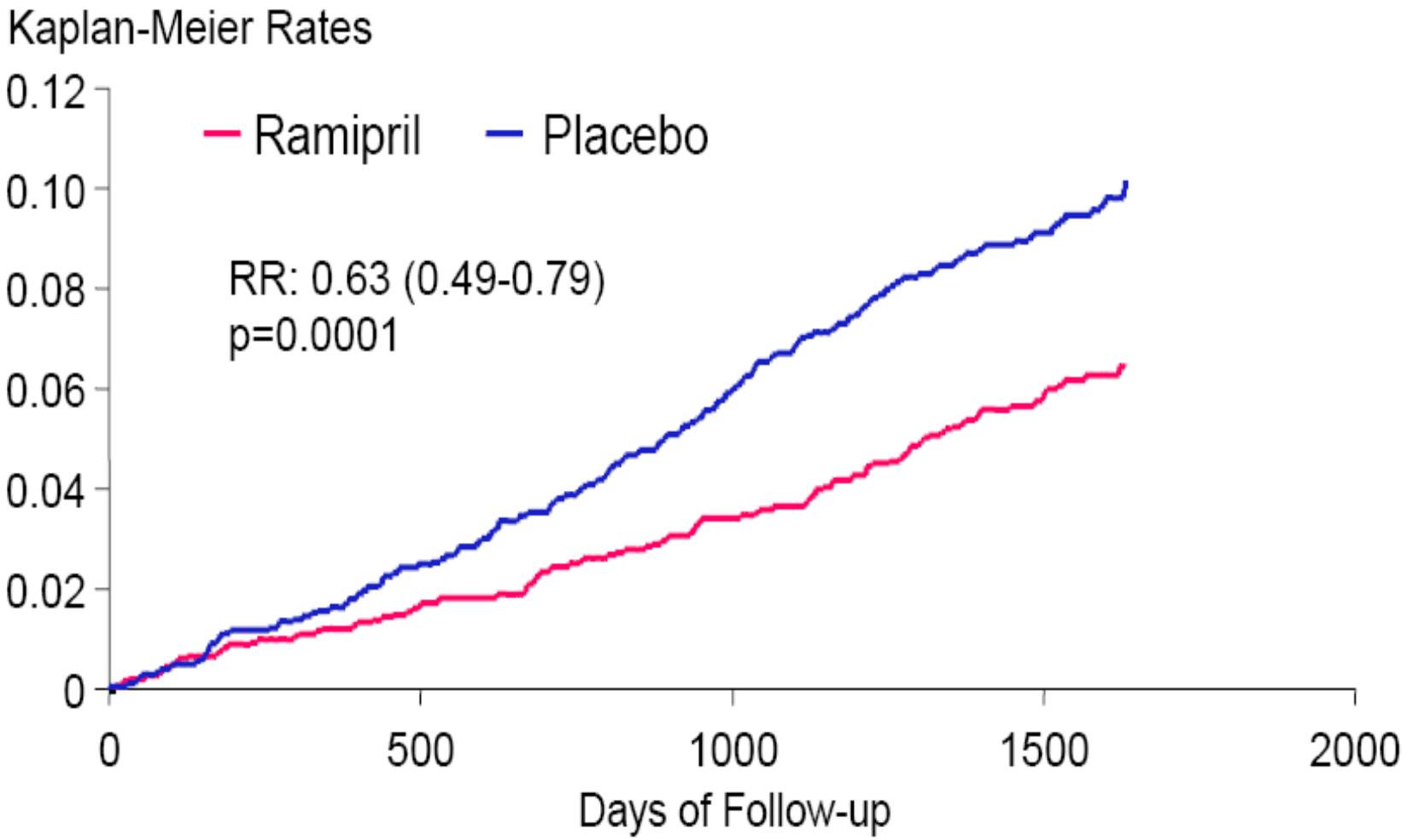
n = 18 000 Diabetes ~ 2 700 (15%)

Six months mortality



(Zuanetti et al Circulation 1997;96:4239)

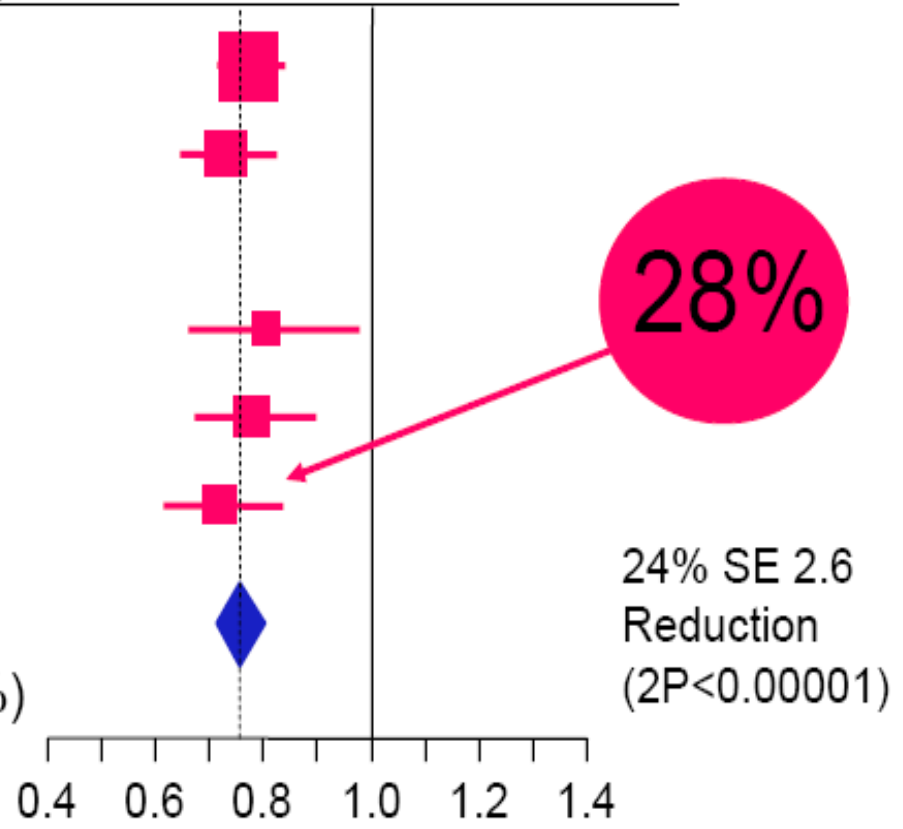
CV Death - Ramipril vs Placebo - DM



(**HOPE Study** investigators Lancet 2000;355:253)

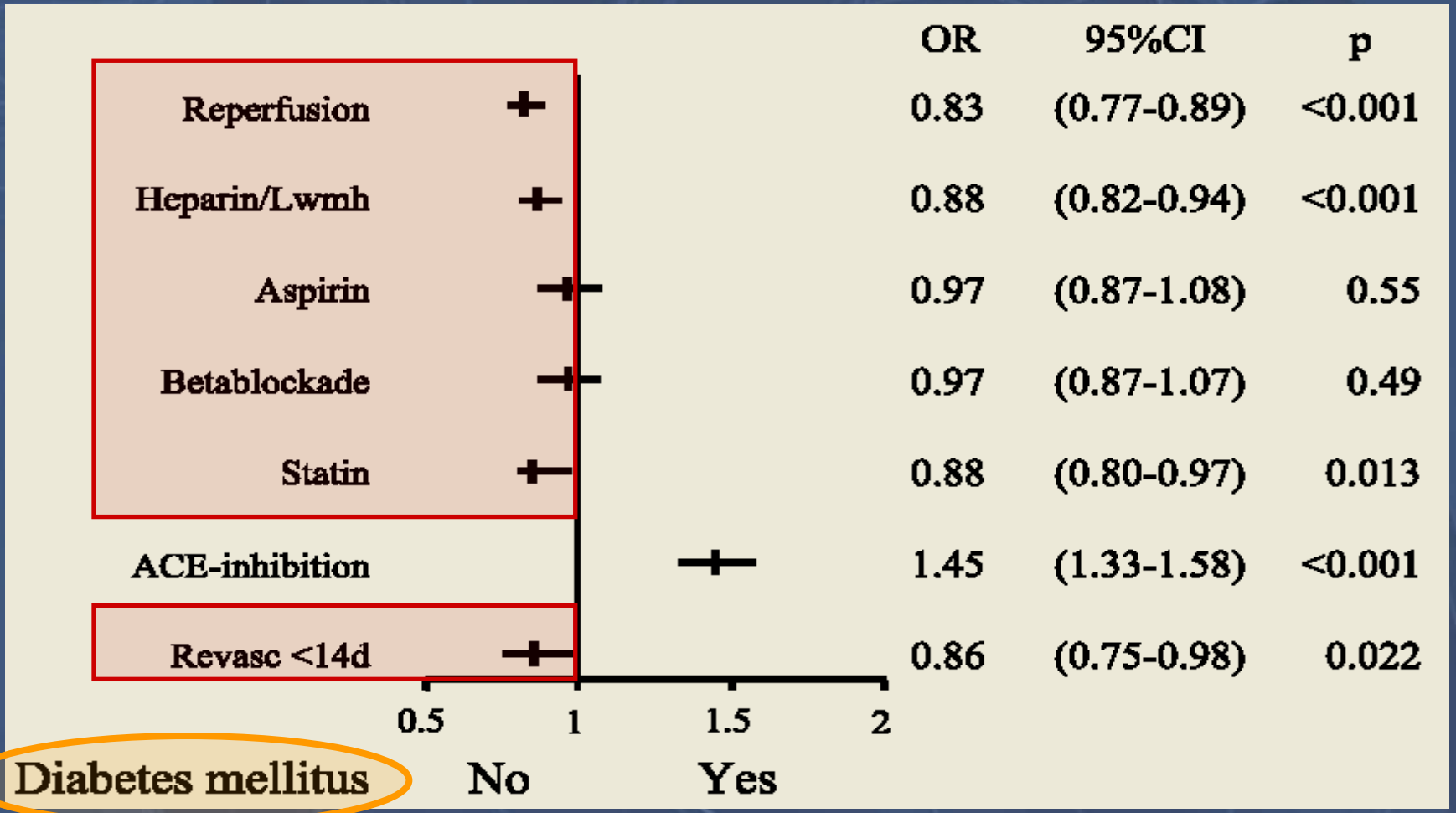
Vascular events by prior disease

Baseline feature	Statin (10269)	Placebo (10267)
Previous MI	1007	1255
Other CHD (not MI)	452	597
No prior CHD		
CVD	182	215
PVD	332	427
Diabetes	279	369
ALL PATIENTS	2042 (19.9%)	2606 (25.4%)



(HPS Collaborative group. Lancet 2003; 361: 2005–16)

ΥΠΟΘΕΡΑΠΕΥΟΜΕΝΟΙ!!!



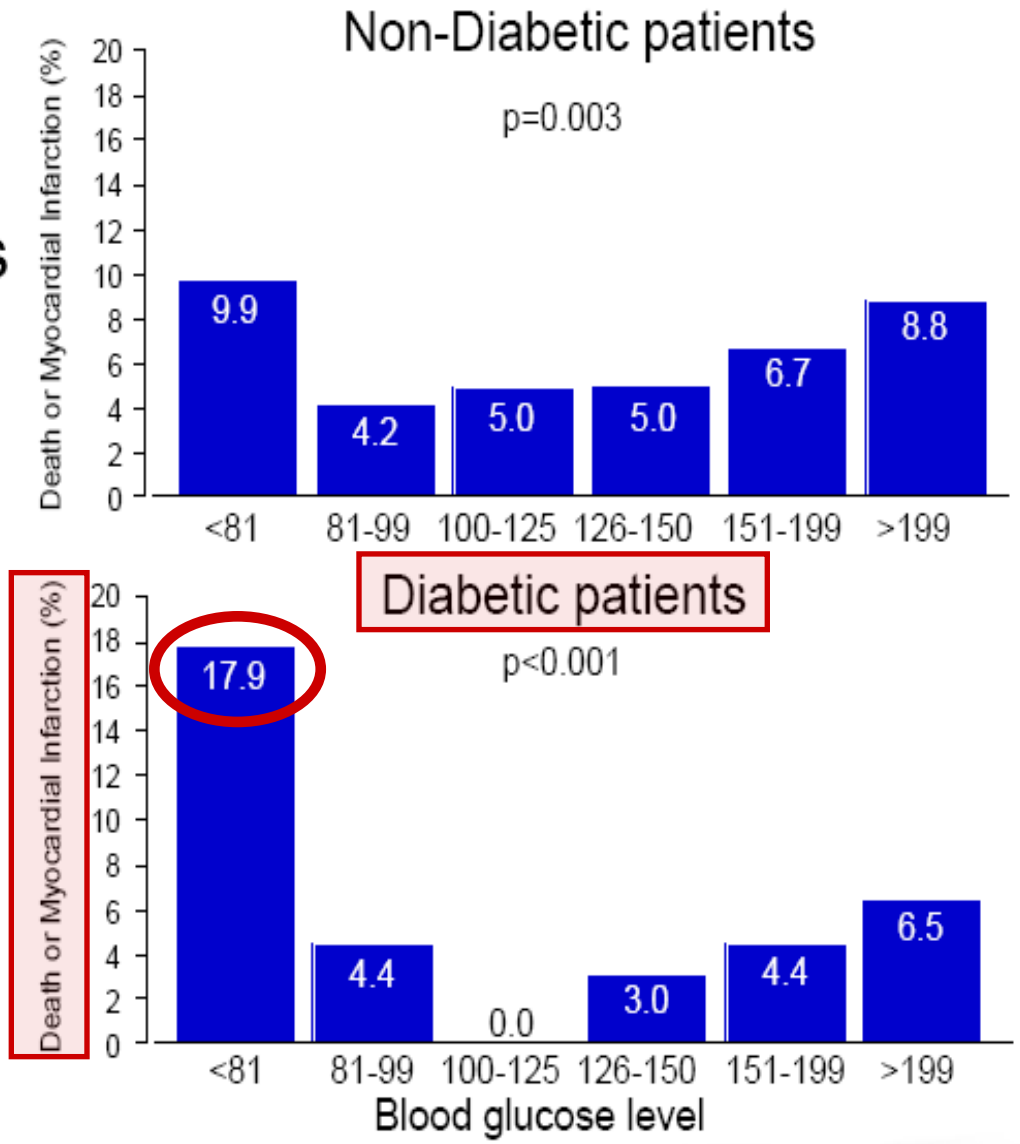
Anna Norhammar et al. Eur Heart J 2003; 24: 838-44

What about hypoglycemia?

U-shaped relation blood glucose and adverse outcome in STEMI patients

Data derived from
- TIMI-10A/B
- LIMIT-AMI
- OPUS-TIMI-16

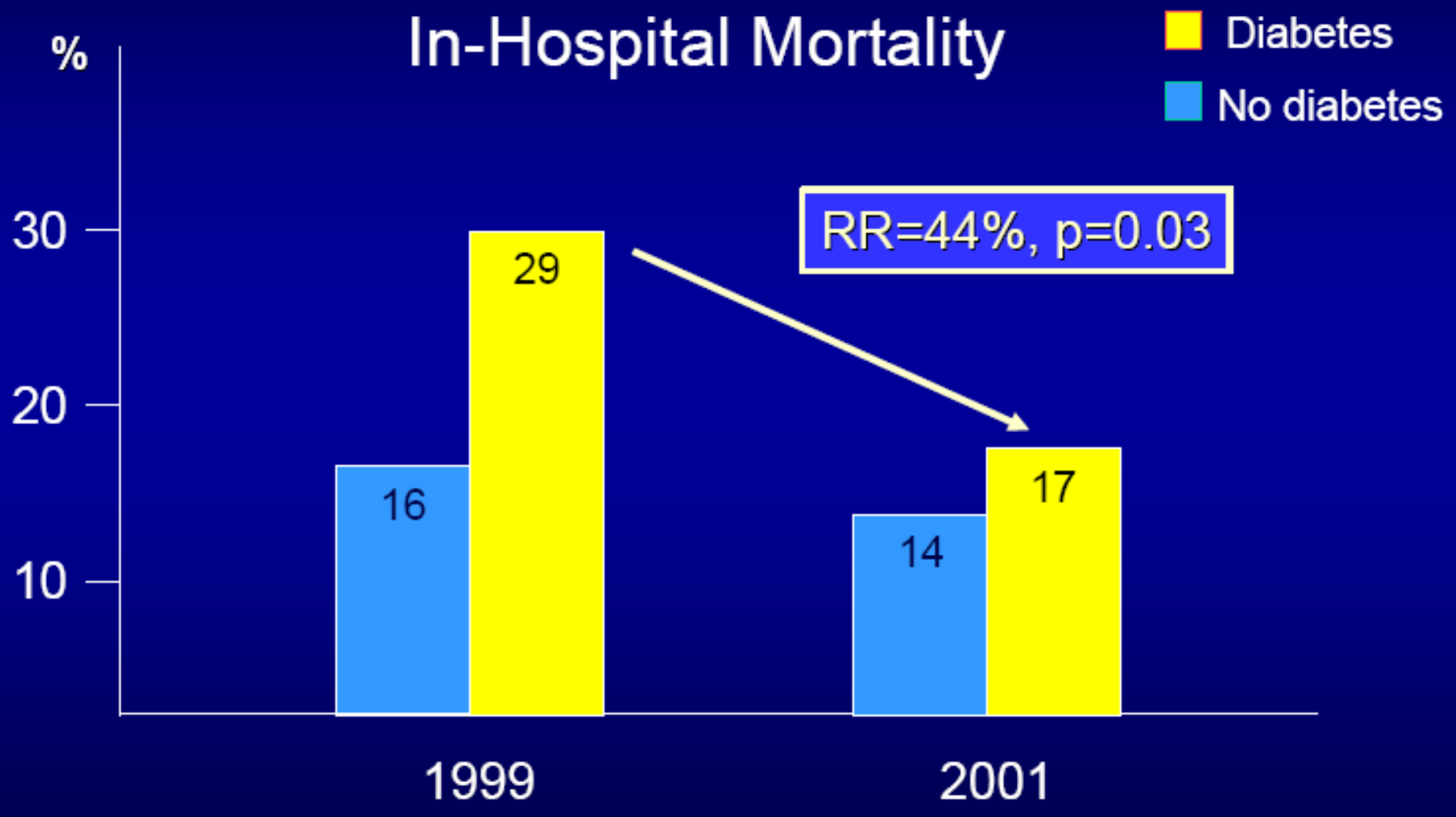
n = 4 224



(Pinto et al J Am Coll Card 2005;46:179)

Recommendation	Class	Level
Early risk stratification should be part of the evaluation of the diabetic patient after ACS.	IIa	C
Treatment targets, as listed in Table 1, should be outlined and applied in each diabetic patient following an ACS.	IIa	C
Patients with acute MI and diabetes should be considered for thrombolytic therapy on the same grounds as their non-diabetic counterparts.	IIa	A
Whenever possible, patients with diabetes and ACS should be offered early angiography and mechanical revascularization.	IIa	B
Beta-blockers reduce morbidity and mortality in patients with diabetes and ACS.	IIa	B
Aspirin should be given for the same indications and in similar dosages to diabetic and non-diabetic patients.	IIa	B
Adenosine diphosphate (ADP) receptor dependent platelet aggregation inhibitor (clopidogrel) may be considered in diabetic patients with ACS in addition to aspirin.	IIa	C
The addition of an ACE-inhibitor to other therapies reduces the risk for cardiovascular events in patients with diabetes and established CVD.	I	A
Diabetic patients with acute MI benefit from tight glucometabolic control. This may be accomplished by different treatment strategies.	IIa	B

Implementation of modern treatment
The Munich registry



(Schnell et al Diabetes Care 2004; 27:453-60)

Classification of HF by structural abnormality (ACC/AHA) or by symptoms relating to functional capacity (NYHA)

ACC/AHA Stages of HF		NYHA Functional Classification	
Stage of heart failure based on structure and damage to heart muscle		**Severity based on symptoms and physical activity**	
Stage A	At high risk for developing HF. No identified structural or functional abnormality; no signs or symptoms.	Class I	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, or dyspnoea.
Stage B	Developed structural heart disease that is strongly associated with the development of HF, but without signs or symptoms.	Class II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnoea.
Stage C	Symptomatic HF associated with underlying structural heart disease.	Class III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity results in fatigue, palpitation, or dyspnoea.
Stage D	Advanced structural heart disease and marked symptoms of HF at rest despite maximal medical therapy.	Class IV	Unable to carry on any physical activity without discomfort. Symptoms at rest. If any physical activity is undertaken, discomfort is increased.

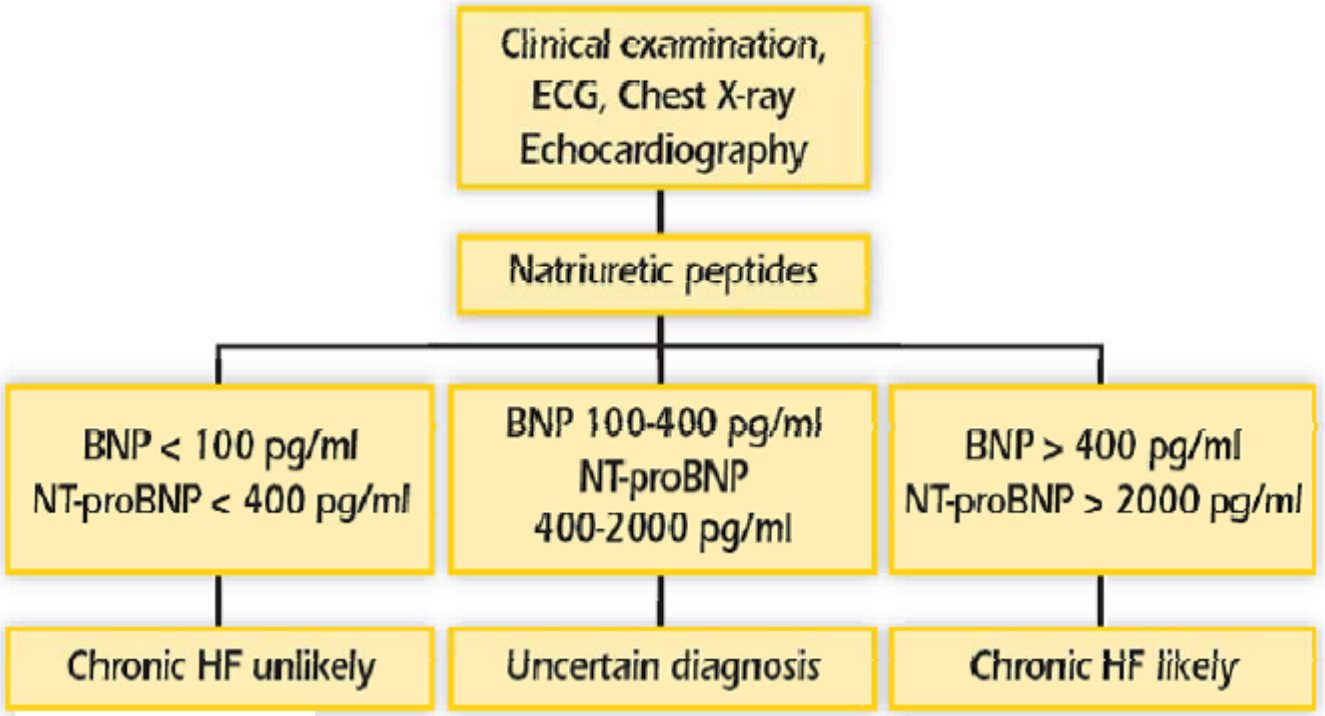
ACC = American College of Cardiology; AHA, American Heart Association.
Hunt SA et al. Circulation. 2005;112:1825-1852.

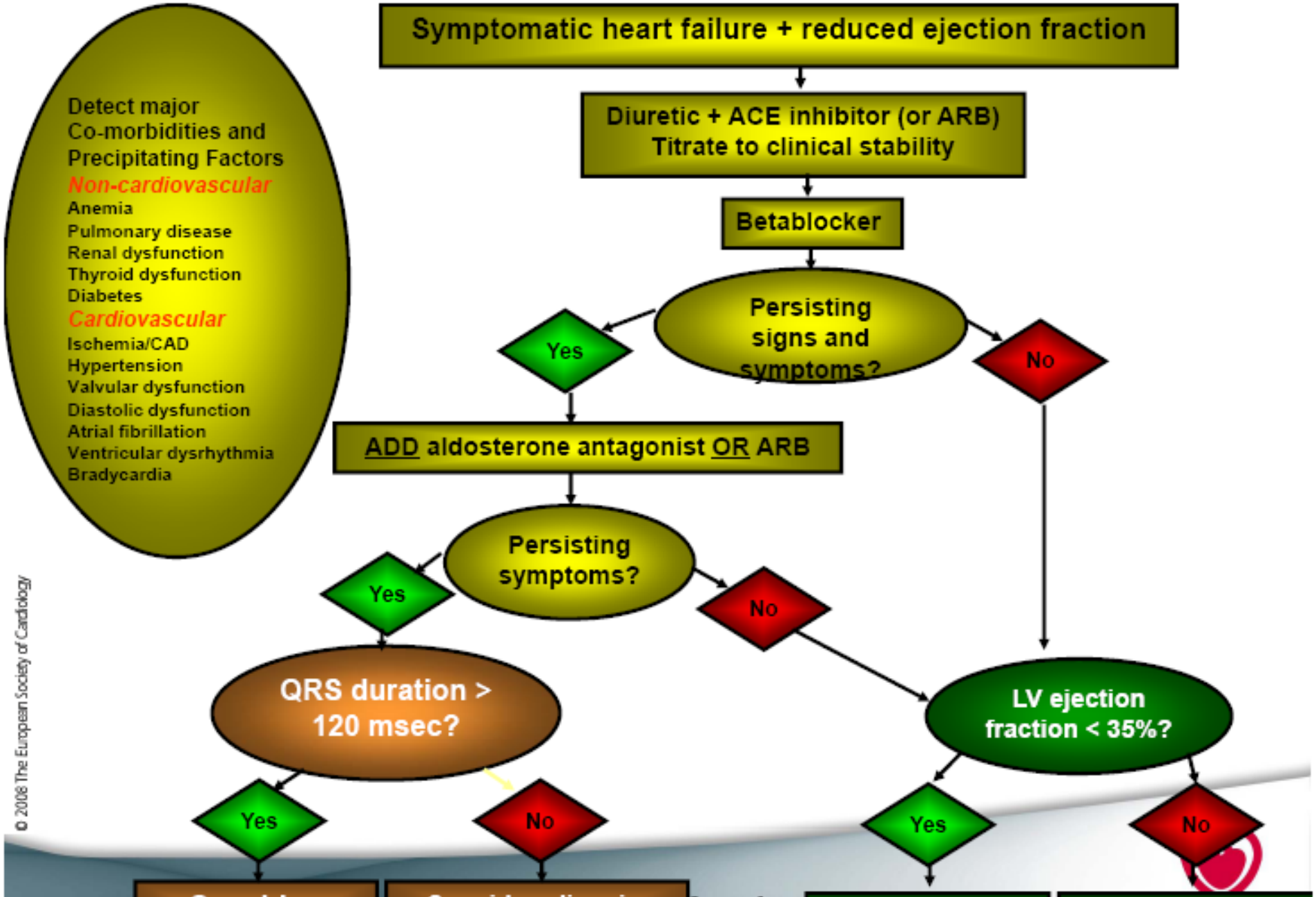
NYHA = New York Heart Association.
The Criteria Committee of the New York Heart Association. Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels. 9th ed. Boston, Mass: Little, Brown & Co; 1994:253-256

ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008

The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM)

Flow-chart for the diagnosis of HF in untreated patients with symptoms suggestive of HF using natriuretic peptides





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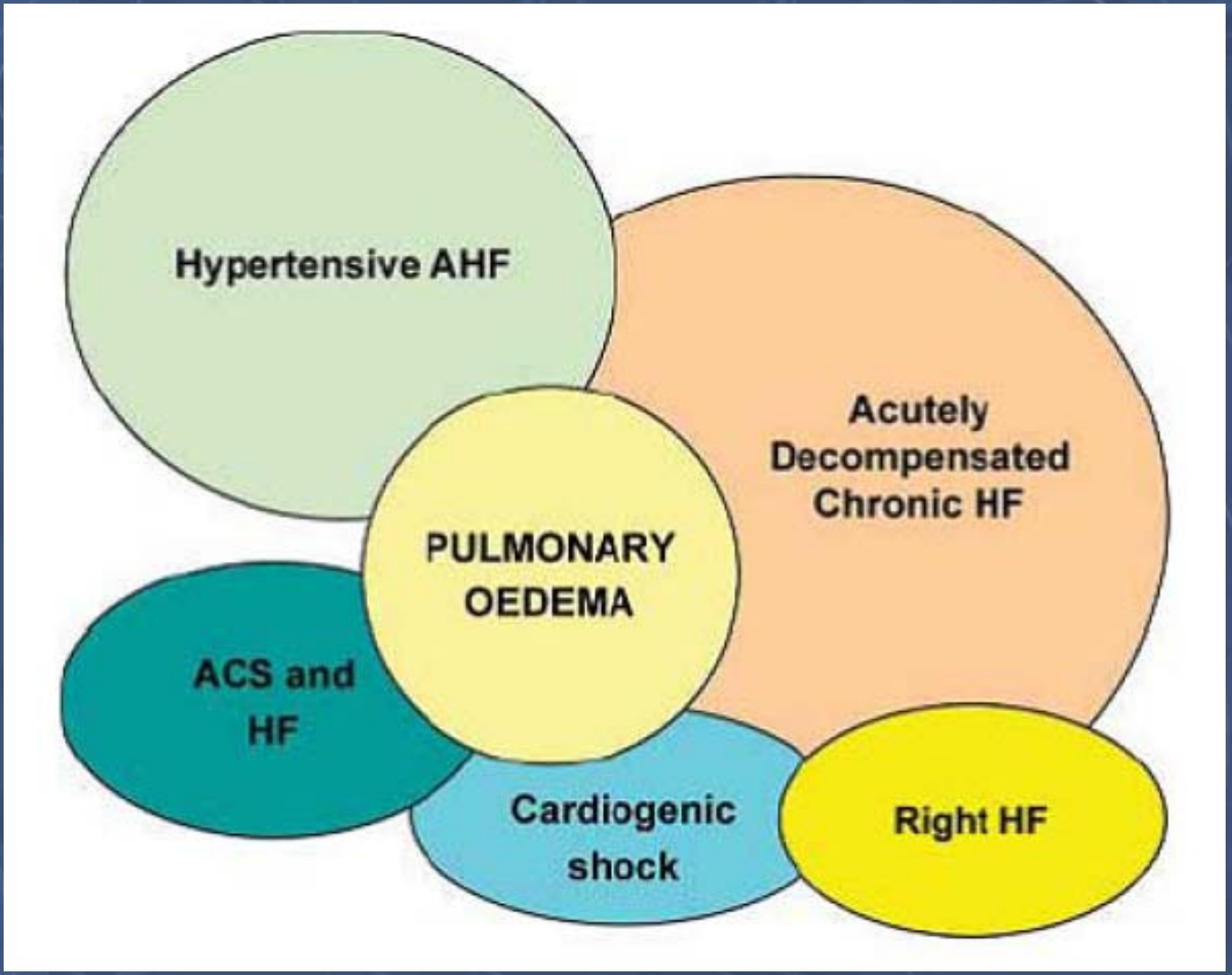
Two classifications of the severity of heart failure in the context of acute myocardial infarction

Killip classification		Forrester classification
Designed to provide a clinical estimate of the severity of circulatory derangement in the treatment of acute myocardial infarction.		Designed to describe clinical and haemodynamic status in acute myocardial infarction.
Stage I	No heart failure. No clinical signs of cardiac decompensation	1. Normal perfusion and pulmonary wedge pressure (PCWP—estimate of left atrial pressure)
Stage II	Heart failure. Diagnostic criteria include rales, S3 gallop, and pulmonary venous hypertension. Pulmonary congestion with wet rales in the lower half of the lung fields.	2. Poor perfusion and low PCWP (hypovolaemic) 3. Near normal perfusion and high PCWP (pulmonary oedema)
Stage III	Severe heart failure. Frank pulmonary oedema with rales throughout the lung fields	4. Poor perfusion and high PCWP (cardiogenic shock)
Stage IV	Cardiogenic shock. Signs include hypotension (SBP <90 mmHg), and evidence of peripheral vasoconstriction such as oliguria, cyanosis and sweating	

Killip T, 3rd, Kimball JT. Treatment of myocardial infarction in a coronary care unit. A two year experience with 250 patients. *Am J Cardiol* 1967;20:457–464.
Forrester JS, Diamond GA, Swan HJ. Correlative classification of clinical and hemodynamic function after acute myocardial infarction. *Am J Cardiol* 1977;39:137–145.

Clinical syndromes of ACUTE HEART FAILURE



ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008

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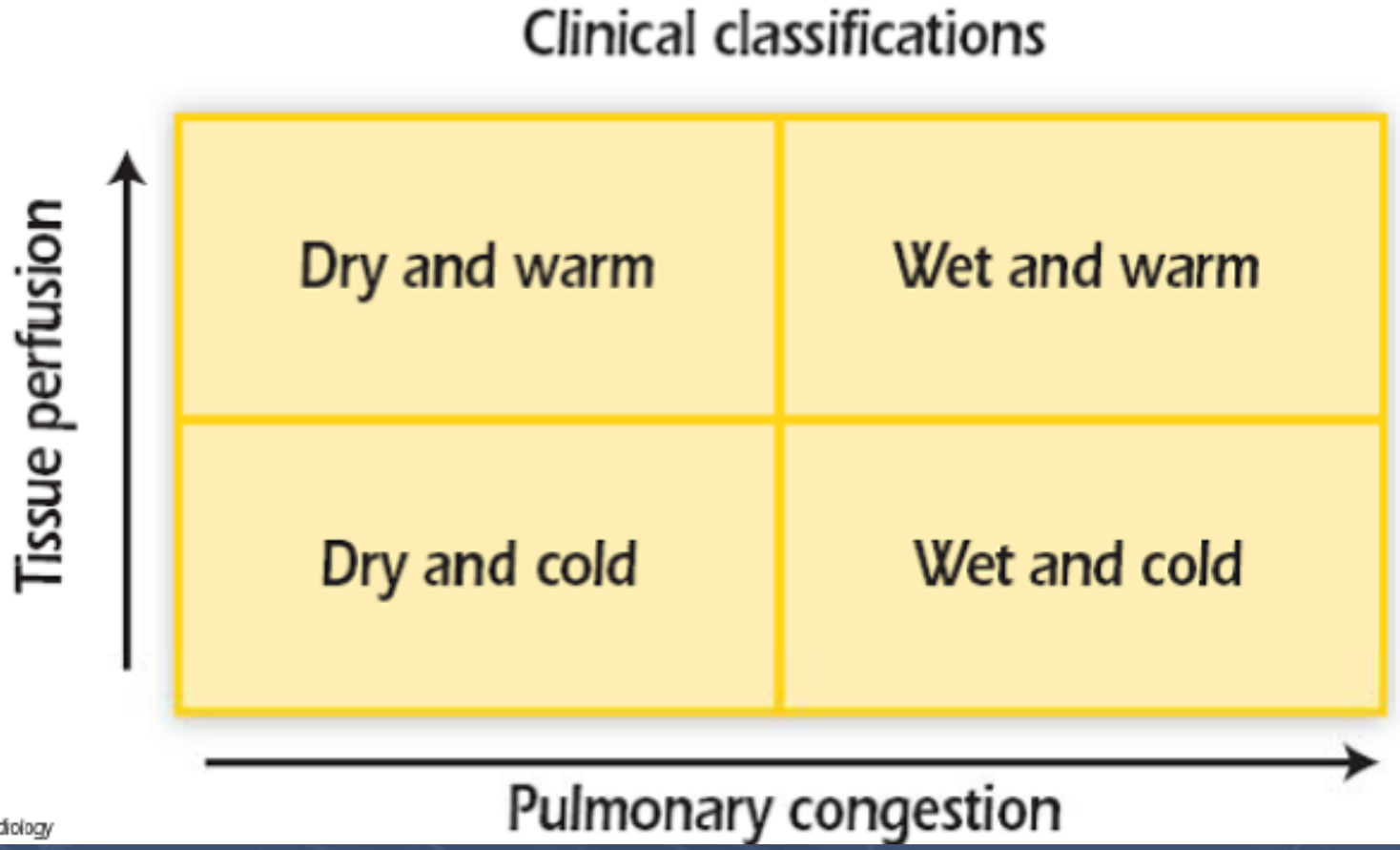
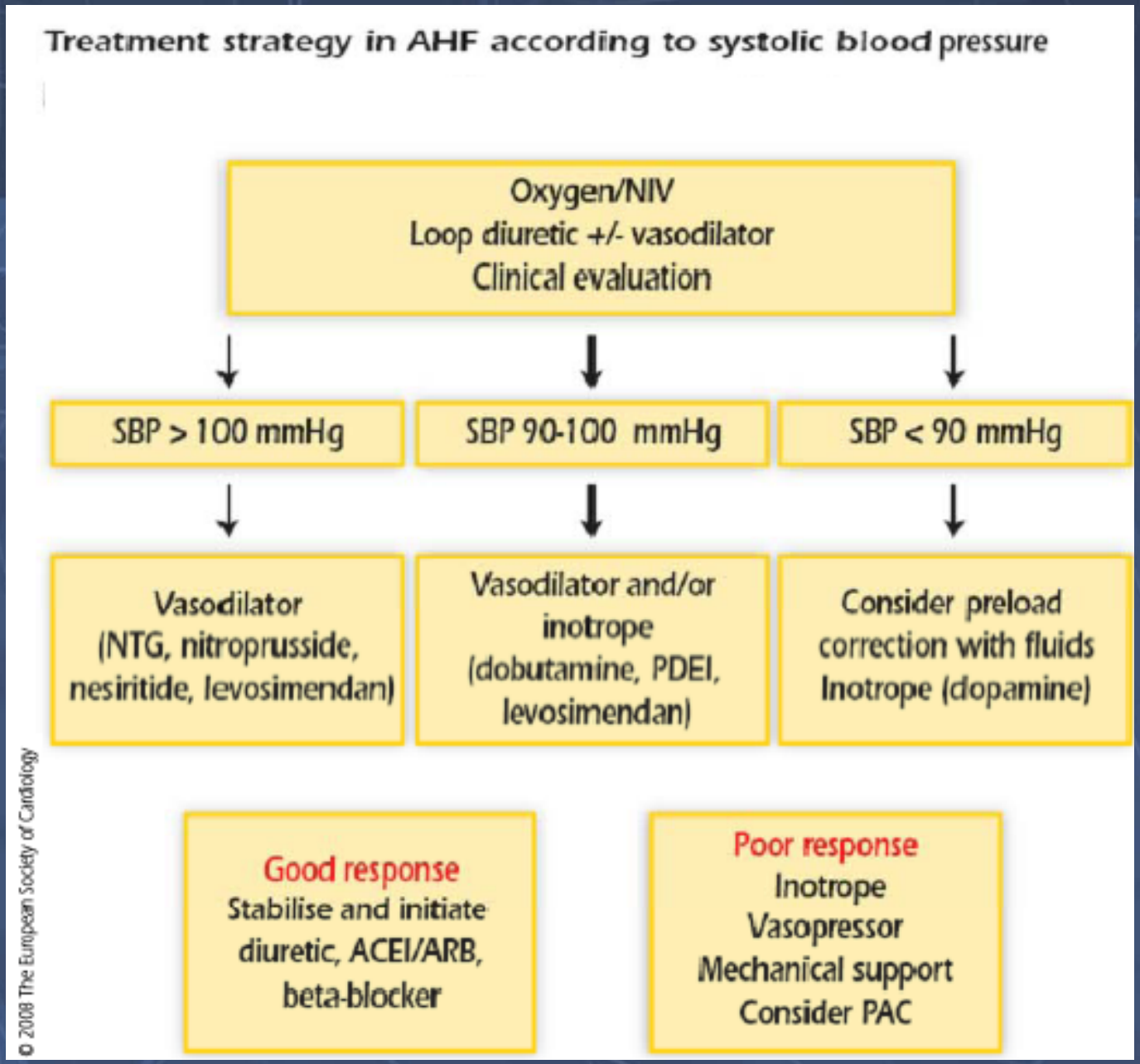
A clinical assessment of patients with AHF



Treatment strategy in AHF according to systolic blood pressure



Στόχος η πρόληψη

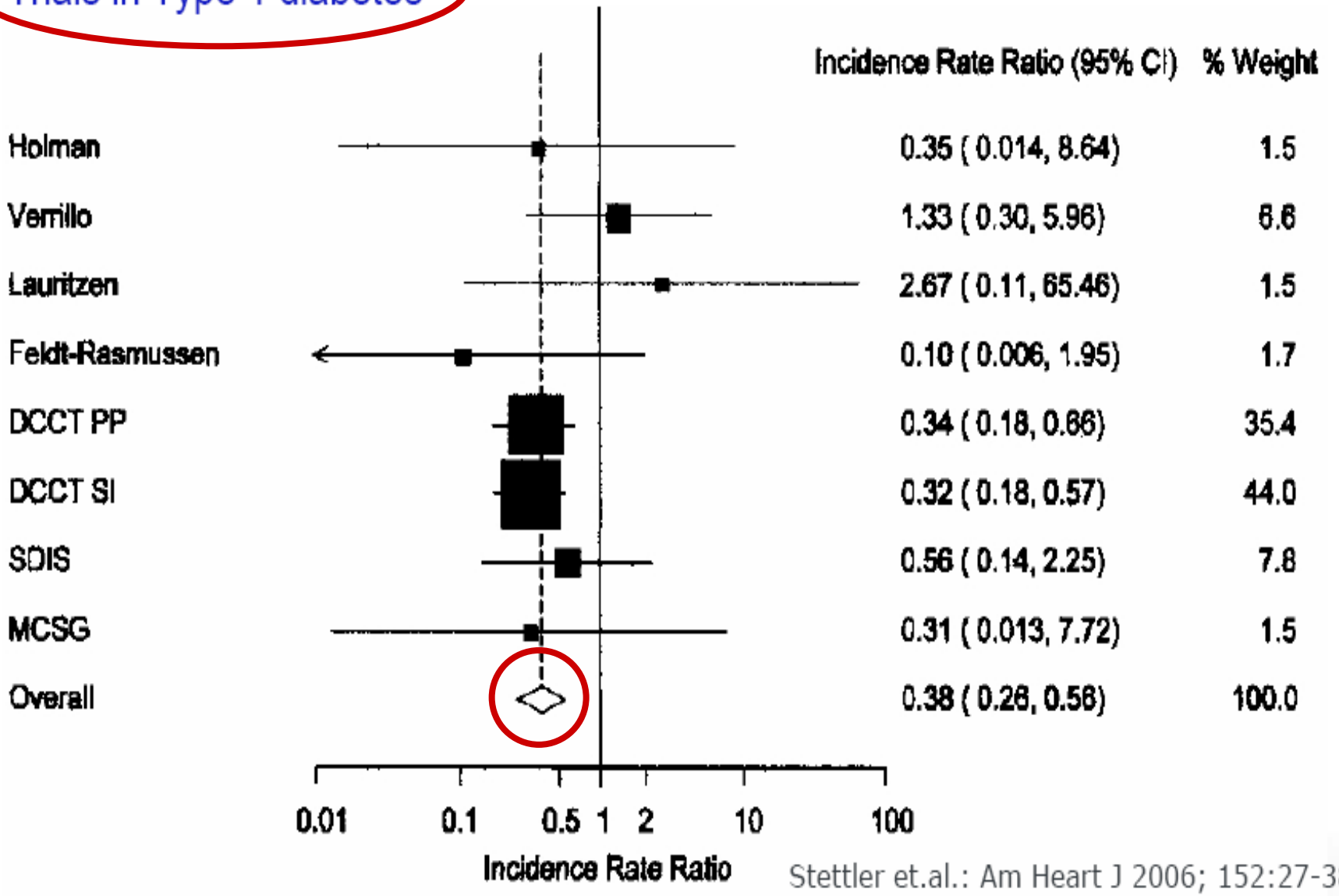
Με πολυπαραγοντική παρέμβαση

Η καλή ρύθμιση μειώνει τις επιπλοκές

	DCCT	Kumamoto	UKPDS
HbA_{1c}	9 → 7%	9 → 7%	8 → 7%
Αμφιβλ/πάθεια	76%	69%	17-21%
Νεφροπάθεια	54%	70%	24-33%
Νευροπάθεια	60%	-	-
Μακροαγγειοπάθεια	41%	-	16%

Glycemic control and macrovascular disease: Meta-analysis of randomized trials

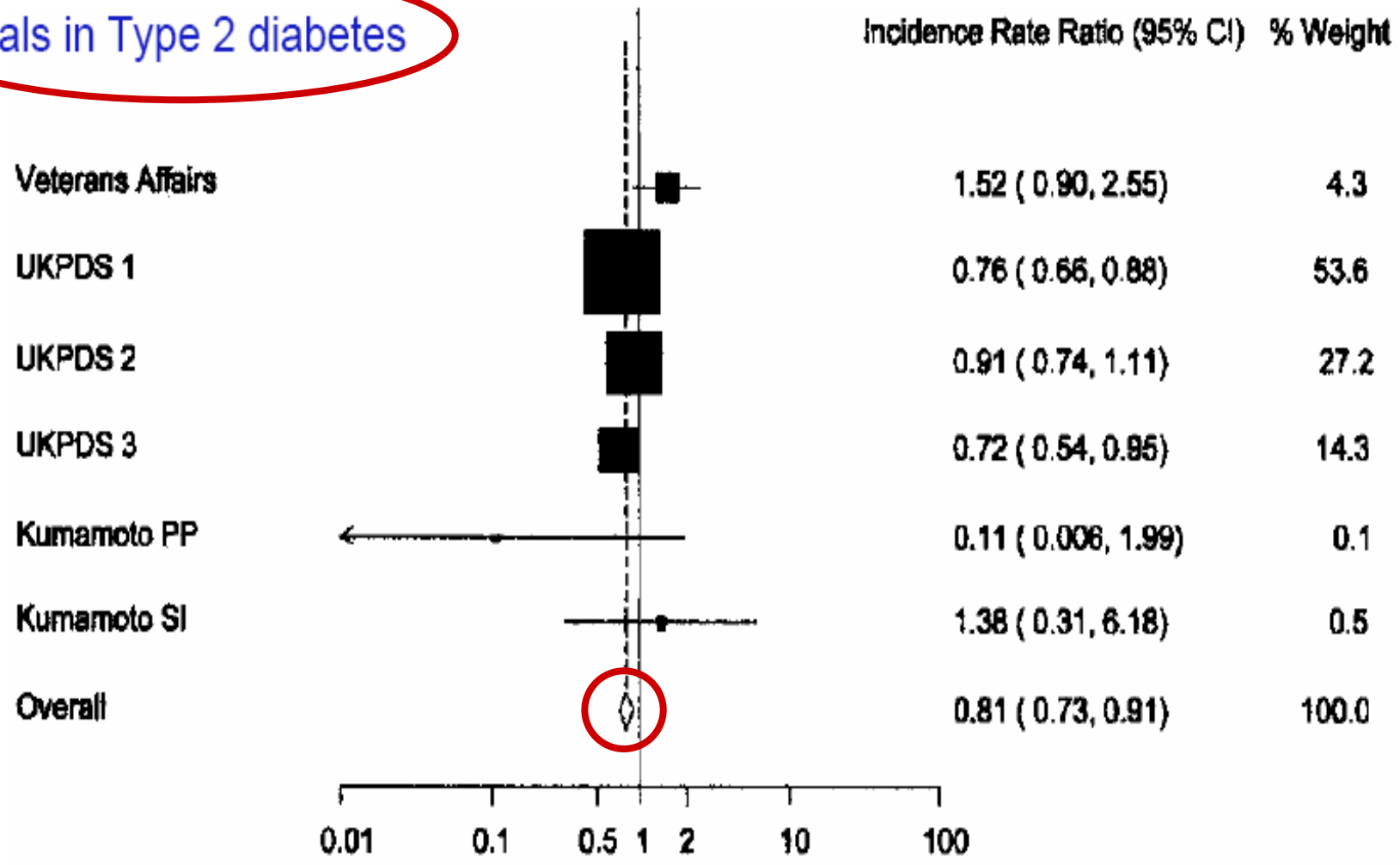
Trials in Type 1 diabetes



Stettler et.al.: Am Heart J 2006; 152:27-38

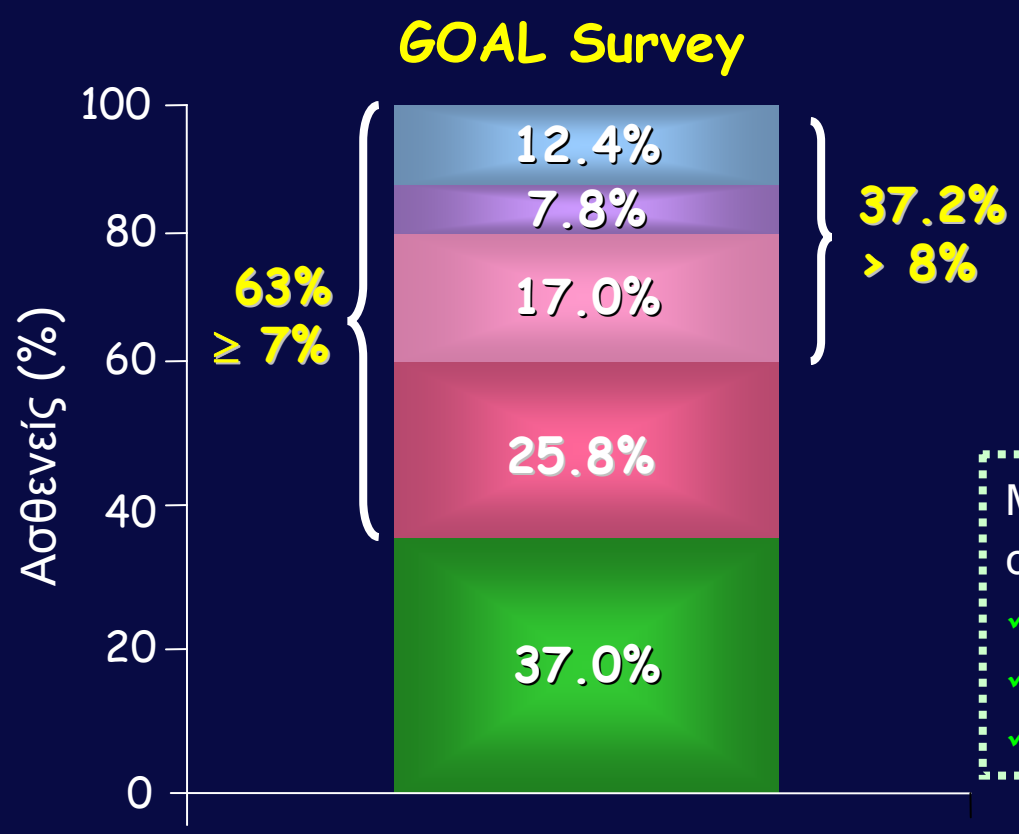
Glycemic control and macrovascular disease: Meta-analysis of randomized trials

Trials in Type 2 diabetes



Stettler et.al.: Am Heart J 2006; 152:27-38

Η πλειοψηφία των ασθενών δεν επιτυγχάνουν το στόχο της ADA για HbA_{1c} <7%



HbA_{1c}
- > 10%
- > 9%
- > 8%
- 7%-8%
- < 7%

Μόνο το 7% των διαβητικών ατόμων στη NHANES 1999-2000, πέτυχαν:
- ✓ HbA_{1C} < 7%
- ✓ Αρτηριακή Πίεση < 130/80 mmHg
- ✓ Ολική Χοληστερόλη < 200 mg/dL

N = 404 διαβητικοί, 20-74 ετών, που συμμετείχαν στη National Health Examination Survey (NHANES), το 1999-2000

Saydah SH et al, JAMA 2004; 291:335-342

EASD
European Association for the Study of Diabetes

New ESC/EASD Guidelines
Treatment targets

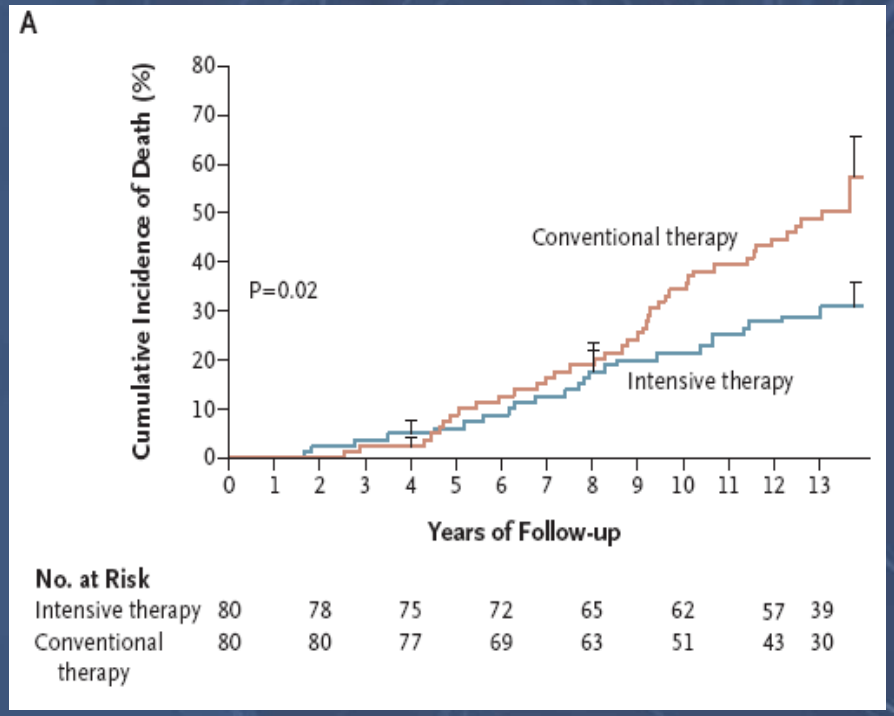
EUROPEAN SOCIETY OF CARDIOLOGY®

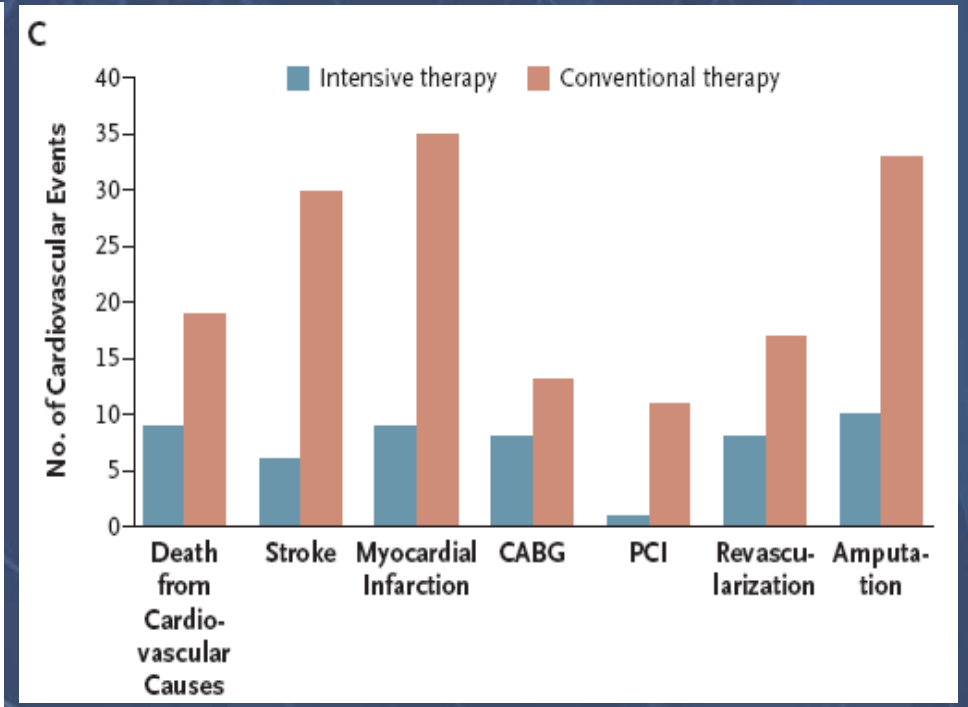
Variable	Target	
Lifestyle modification	Structured education	
Smoking cessation	Obligatory	
BP	<130 / 80 mm Hg	
	Renal dysf <125/75	
HbA1c (DCCT standard)	≤ 6.5%	
Venous plasma glucose	mmol/l	mg/dl
	<6.0	108
Cholesterol	<4.5	175
LDL	<1.8	70
HDL	male >1.0; female >1.2	40; 46
Triglycerides	<1.7	150

Multifactorial intervention in type 2 diabetes: the STENO 2 trial

13.3 years follow up:

intensive therapy → ↓ death & ↓ CV complications

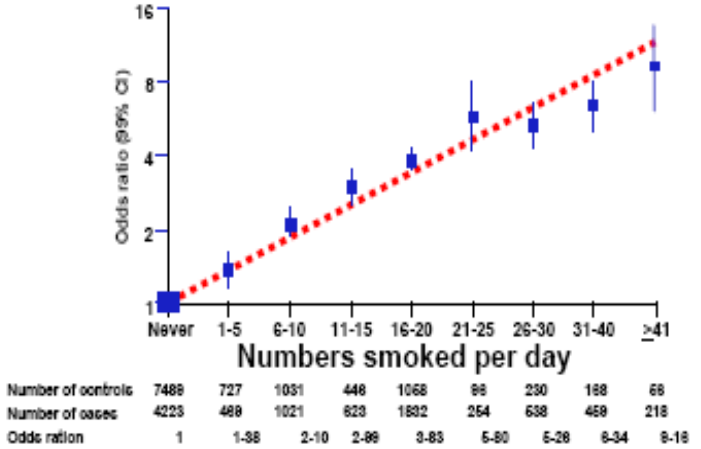


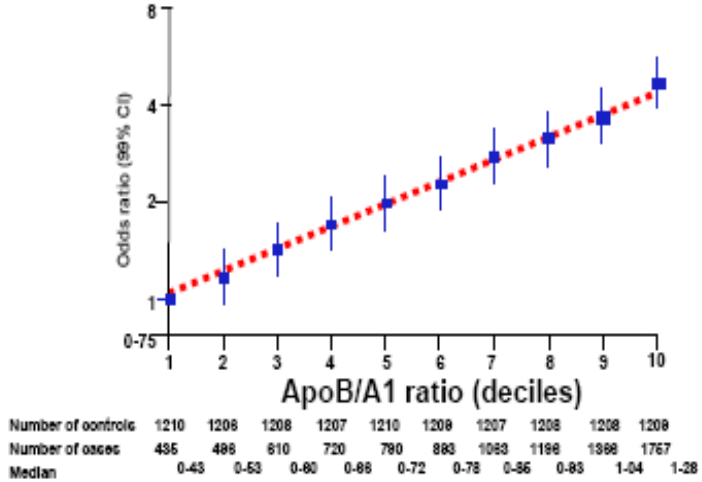


N Engl J Med 2008;358:580-91

INTERHEART Study: Effect of Potentially Modifiable Risk Factors Associated with Myocardial Infarction in 52 Countries

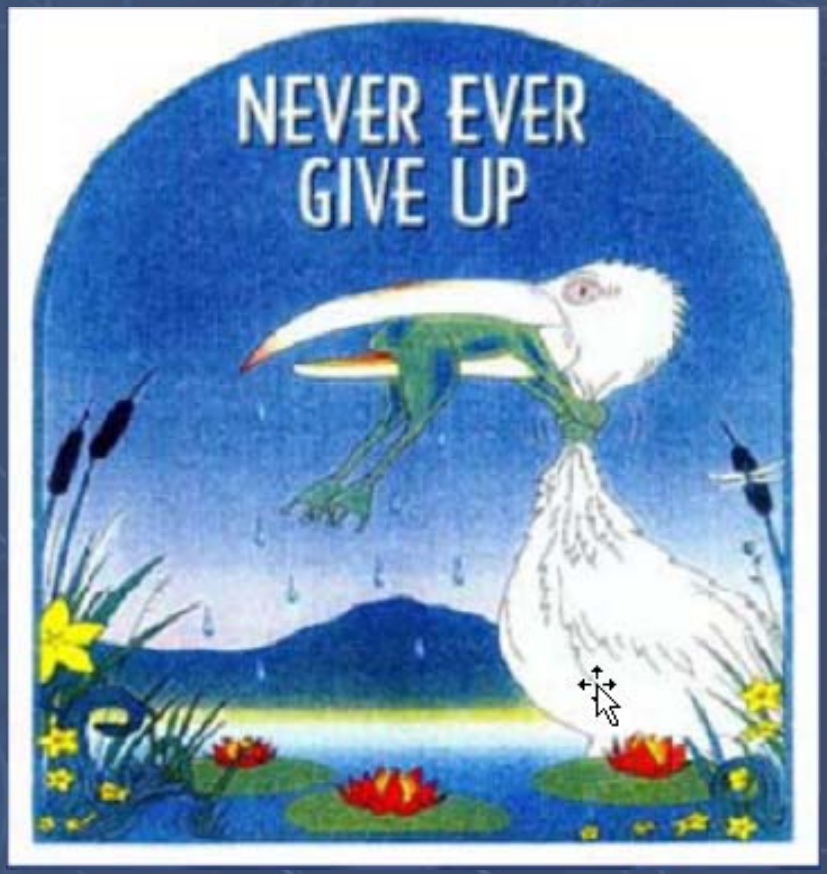
Risk factor	PAR
Smoking	36%
Diabetes	12%
Hypertension	23%
Abdominal obesity	34%
Psychosocial	29%
Veg/fruit daily	13%
Exercise	26%
Alcohol intake	14%
ApoB/ApoA-1ratio (5vs1)	54%
All above combined	90%





(Yusuf et al, on behalf of the INTERHEART Study Investigators Lancet, 2004;364 Pages 937-952)

…ποτέ μην εγκαταλείπετε τη προσπάθεια…



…γιατί όταν φτάσουμε στα άκρα μπορεί ξαφνικά να αλλάξει ο τρόπος που βλέπουμε τα πράγματα…


ΕΥΧΑΡΙΣΤΩ