

Prise en Charge des Syndromes Coronariens Aigus: de L'admission à la Sortie du Patient

**Stratégies à L'admission du Patient:
Place des Inhibiteurs de la Glycoprotéine
IIb/IIIa.**

Dr. Georges Badaoui

The challenge of UAP/NSTEMI

- 3 million ACS events occur annually worldwide
- 30 to 40% of all diagnosed MIs are non–ST-segment elevation
- Up to 15% of patients die or suffer subsequent MI before hospital discharge
- Up to 11% of patients progress to MI or death within 30 days

PHYSIOPATHOLOGY ATHERO-THROMBOSE ?

« L'homme vit avec son
Athérosclérose
mais meurt de son Athéro-
thrombose »

CAILLOT TUEUR

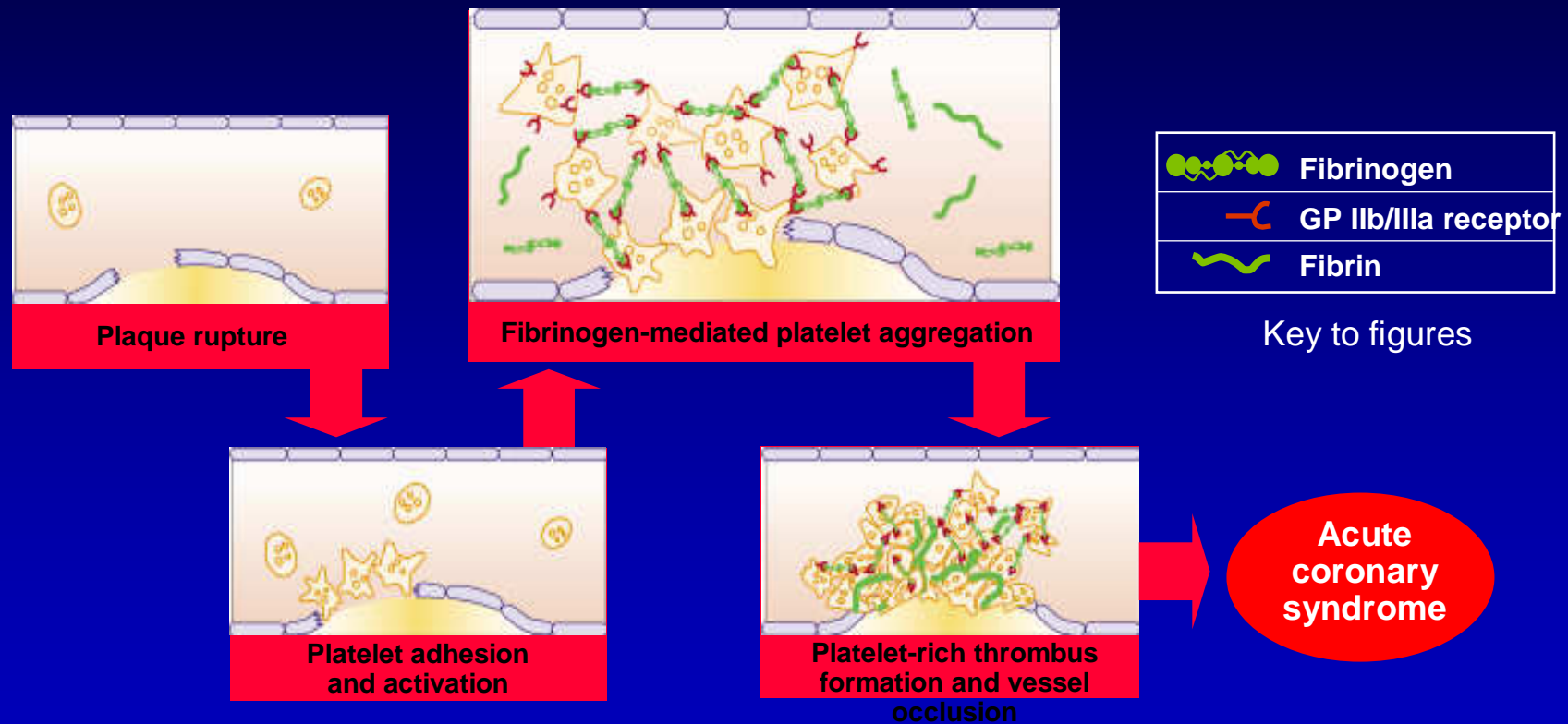


When a killer clot threatens



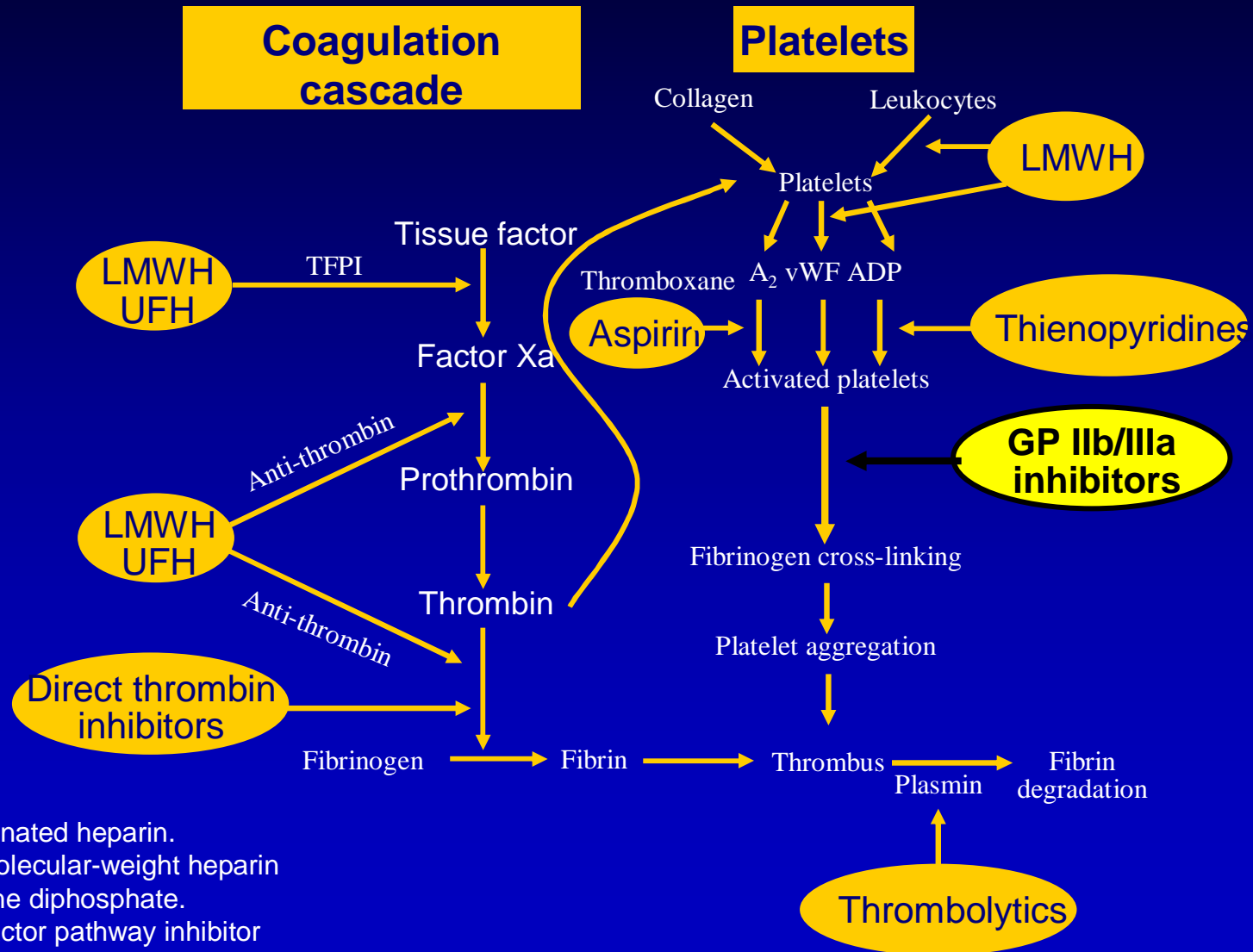
Rupture de la Plaque

Pathophysiology of Acute Coronary Syndromes



Adapted from Fuster V et al *N Engl J Med* 1992;326(4):242-250; Lefkovits J et al *N Engl J Med* 1995;332(23):1553-1559; Collier BS et al *Thromb Haemost* 1995;74(1):302-308.

Rationale for Use: Pharmacologic Intervention in Thrombosis

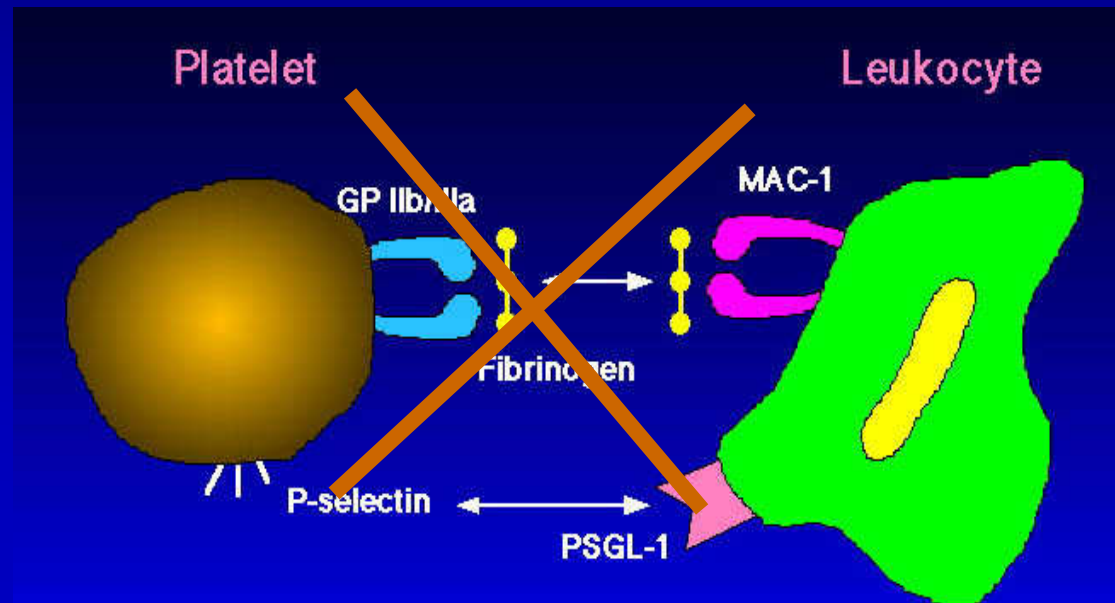


UFH=unfractionated heparin.
 LMWH=low-molecular-weight heparin
 ADP=adenosine diphosphate.
 TFPI=tissue factor pathway inhibitor

Selwyn A. *Am J Cardiol.* 2003;91:3H-11H.

Potential Mechanisms for Plaque Passivation with GP IIb/IIIa Receptor Blockade

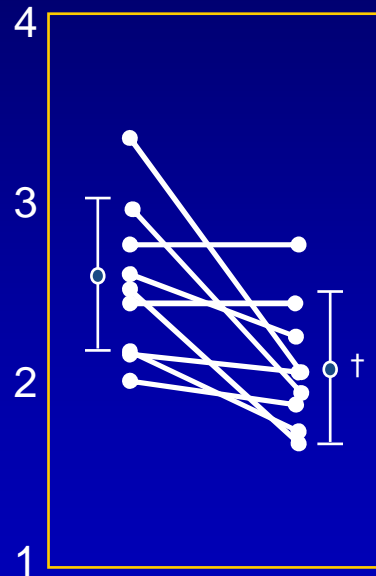
- Profound control of the thrombotic process interrupting the atherothrombotic process.
- Prevention of platelet-leukocyte interaction blocking the connection between thrombosis and inflammation.



Prevention of Platelet-leukocyte Interaction with Tirofiban (30 patients with UA/NSTEMI)

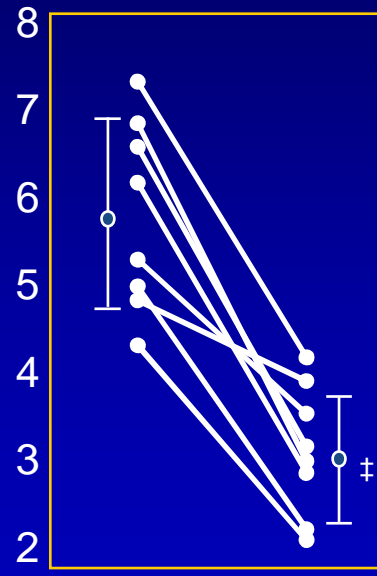
Binding Density of Platelets in Coaggregates

Basal



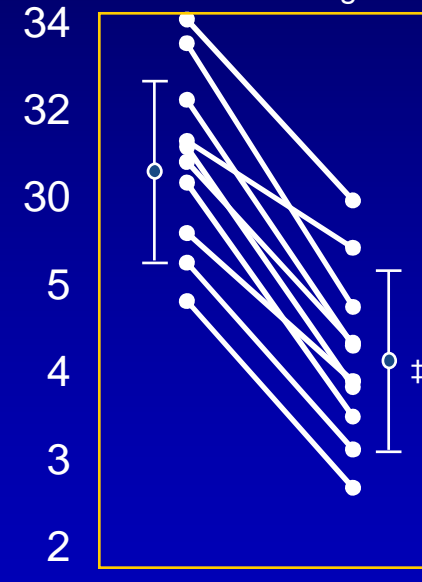
**Before 4 hrs
tirofiban**

ADP (5 μ M)



**Before 4 hrs
tirofiban**

TRAP (5 μ M) thrombin receptor
agonist peptide



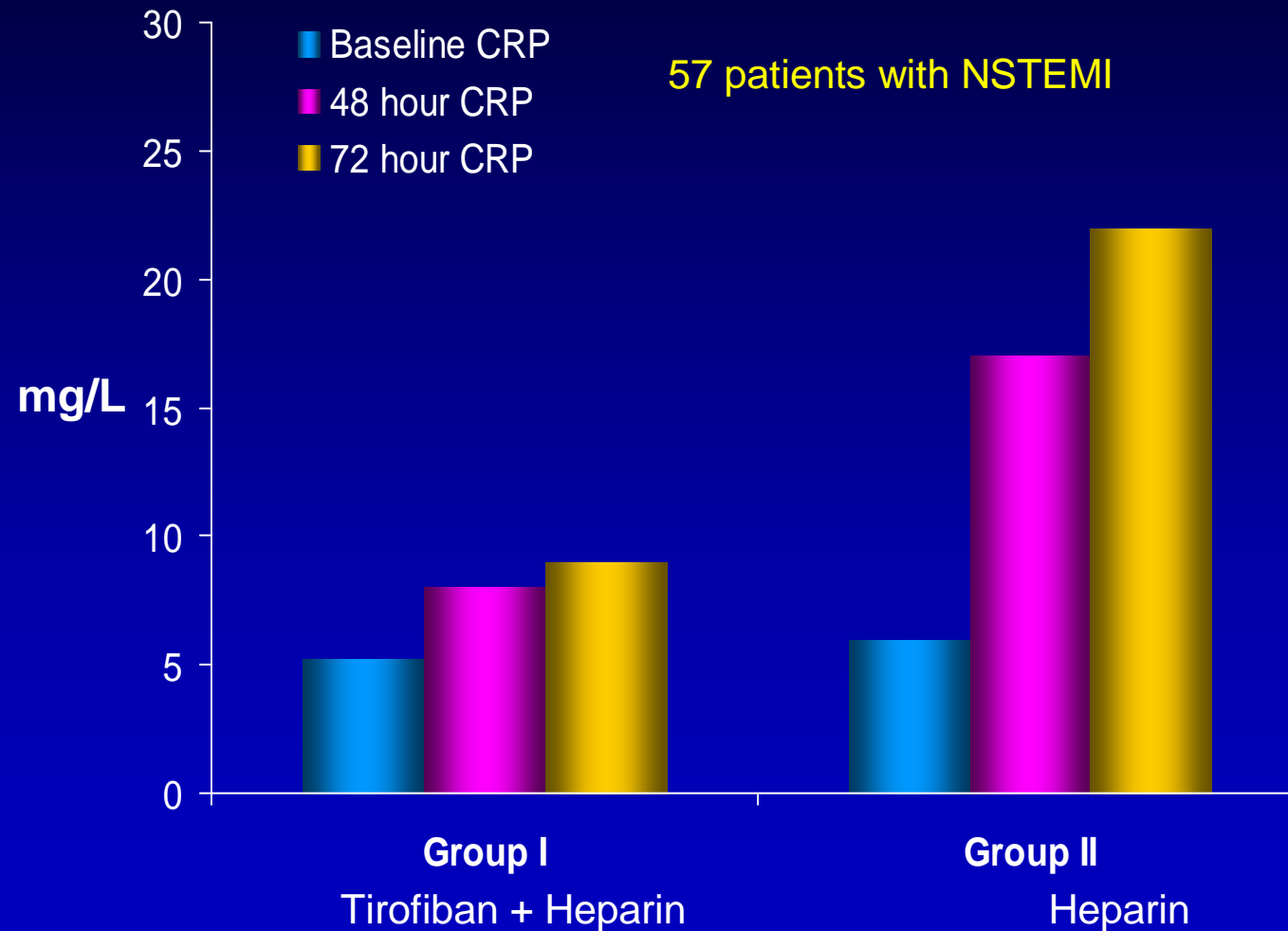
**Before 4 hrs
tirofiban**

† P<0.05 vs before

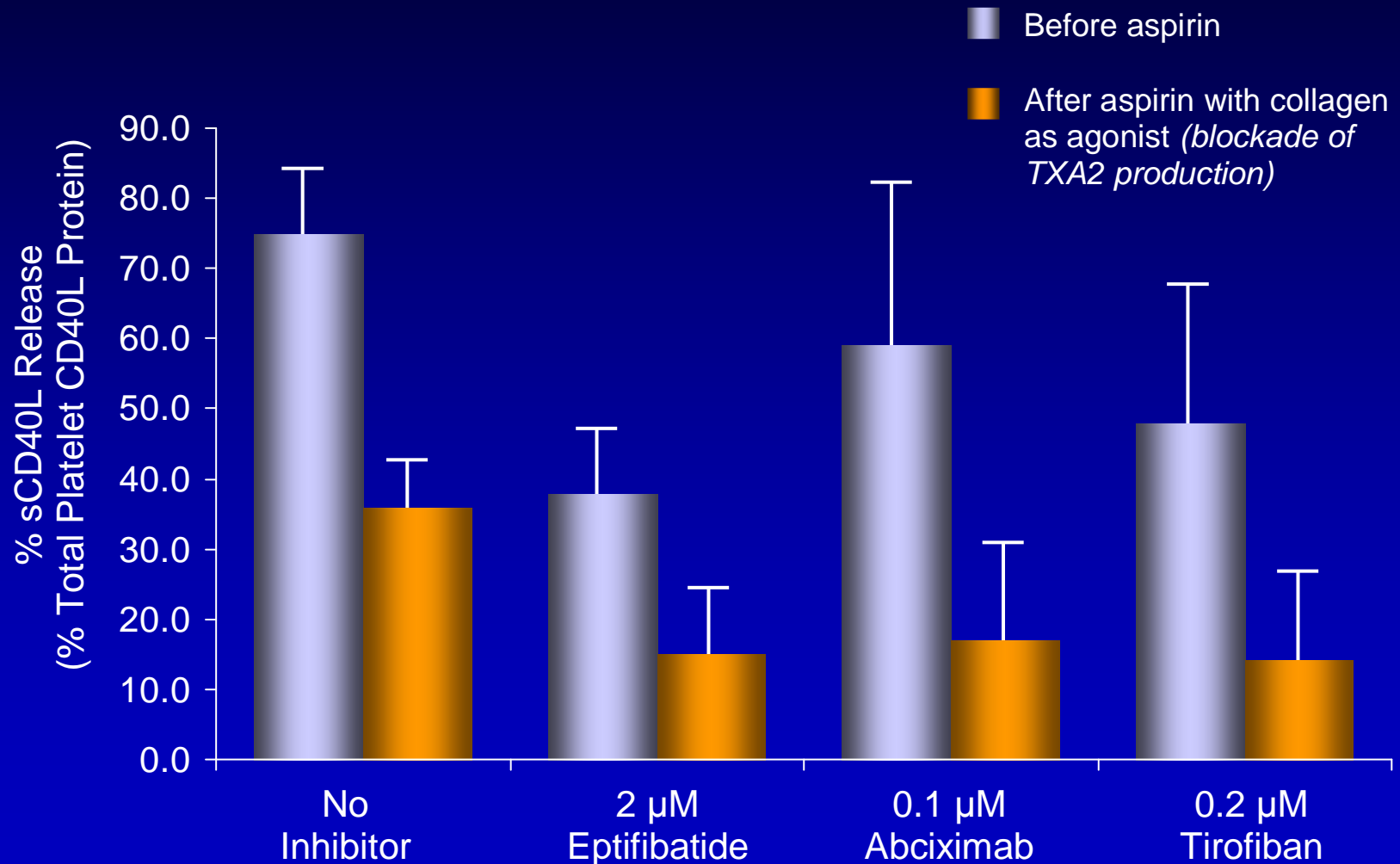
‡ P<0.01 vs before

Xiao Z, et al. *Thromb Haemost.* 1999;81:281-285.

CRP Levels and Tirofiban Therapy

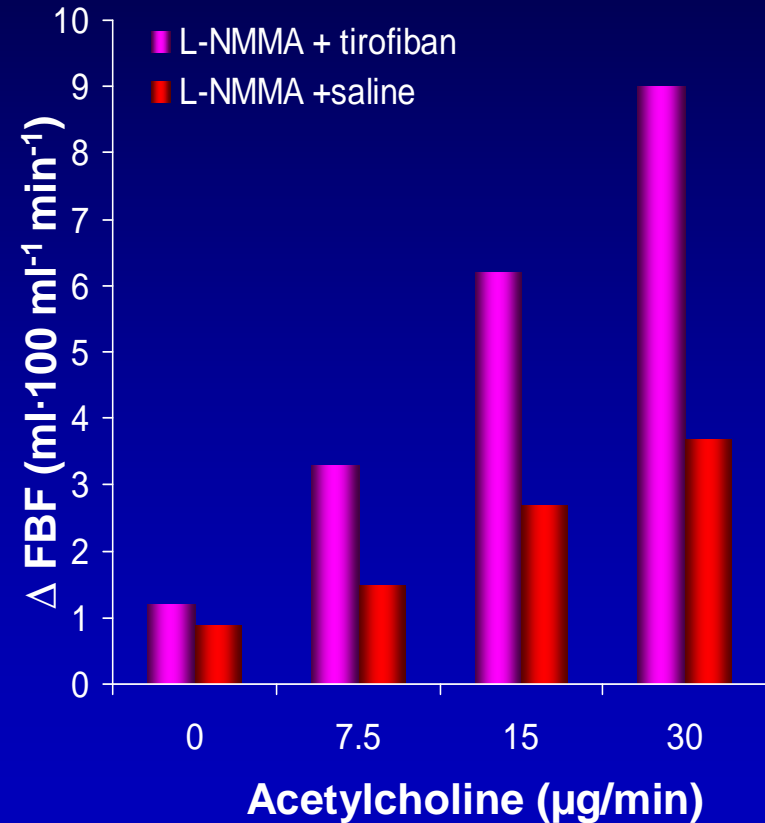
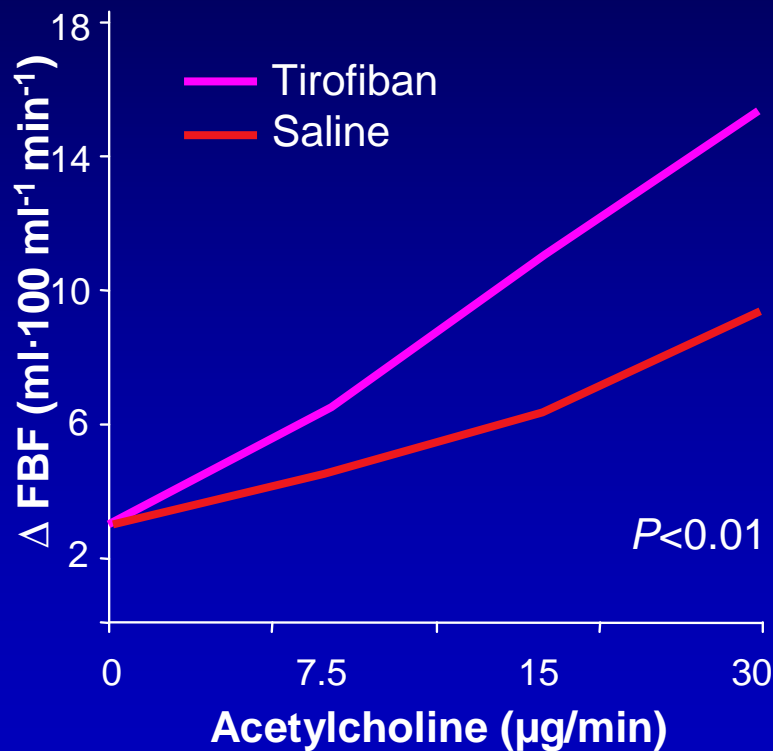


GP IIb/IIIa Antagonists Inhibit Inflammation through Blockade of sCD40L



Nannizzi-Alaimo L, et al. *Circulation*. 2003;107:1123-1128.

GP IIb/IIIa Inhibitors Improve Vascular Nitric Oxide Bioavailability



FBF=forearm blood flow.

L-NMMA=NG-monomethyl-L-arginine.

Heitzer T, et al. *Circulation*. 2003;108:536-541.

Summary

- GP IIb/IIIa inhibitors have effects in factors beyond platelet aggregation
- These effects may potentially contribute to their efficacy

EVIDENCE BASED MEDECINE

META-ANALYSIS for the use of IV GP IIb/IIIa inhibitors in coronary artery disease

*Pooled analysis of 21 trials involving various groups of patients with ischemic heart disease (50 000 pts) The GP IIb/IIIa inhibitor significantly reduced the combined end point of **death, nonfatal MI, or urgent revascularization** at 30 days in :*

- Those undergoing a percutaneous coronary intervention
(relative risk reduction 33 %)
- Those with a non ST segment elevation ACS
(relative risk reduction 11 %)
- Those with an acute ST segment elevation MI treated with angioplasty.
(relative reduction 49 %)

META-ANALYSIS for the use of IV GP IIb/IIIa inhibitors in non-ST elevation ACS

6 randomized trials of 31,400 patients who did not undergo early (<48 hours) revascularization during study drug infusion The following results were observed:

- A significant **17% reduction** in the combined end point (death or MI) at five days.
- The benefit of therapy was limited to:
 - The patients with a positive troponin T or I.

META-ANALYSIS for the use of IV GP IIb/IIIa inhibitors in non-ST elevation ACS in Diabetics

6 randomized trials, 6458 diabetic patients. (PRISM, PRISM-PLUS, PARAGON A, PARAGON B, PURSUIT, and GUSTO IV)

-A significant **26% reduction** in 30-day mortality (6.2 vs 4.6 % p=0,007).

-A significant **70% reduction** in 30-day mortality was also seen in those undergoing a percutaneous coronary intervention n= 1279 pts (4 vs 1.2 %, p=0,002).

META-ANALYSIS for the use of IV GP IIb/IIIa inhibitors in non-ST elevation ACS

CONCLUSION

- Substantial benefit in patients who undergo PCI.
- Modest or Questionable benefit in patients who are not routinely scheduled to undergo PCI
 - unless they are diabetics.
 - unless they are at high risk.
- They are associated with a small but significant increase in major bleeding (2.4 vs 1.4 %) but no increase in intracranial bleeding (0.09 vs 0.06 %).

Cost-effectiveness of the use of IV GP IIb/IIIa inhibitors in non-ST elevation ACS

- In **PURSUIT**, the incremental cost-effectiveness ratio for eptifibatide was \$16,491 per year of life saved;
- In **PURSUIT** Patients who were admitted to a community hospital were less likely to require transfer to a tertiary hospital for an invasive procedure .
- In **PRISM-PLUS**, the cost-saving with tirofiban was largely due to a reduction in the in-hospital costs of treating refractory angina and myocardial infarction.

✓ *These observations suggest that the routine addition of intravenous GP IIb/IIIa inhibitors to the standard care of patients with an ACS is economically justifiable.*

-Cost-effectiveness of platelet glycoprotein IIb/IIIa inhibition with eptifibatide in patients with non-ST-elevation acute coronary syndromes. Mark DB; Topol EJSO - Circulation 2000 Feb 1;101(4):366-71

-Economic assessment of tirofiban in the management of acute coronary syndromes in the hospital setting: an analysis based on the PRISM PLUS trial. Szucs TD; Meyer BJ; Kiowski W. Eur Heart J 1999 Sep;20(17):1253-60

? In Acute Coronary Syndrome
without ST segment elevation \Rightarrow
increasingly aggressive approach?

Routine VS selective invasive strategies in patients with acute coronary syndromes: meta-analysis of randomized trials.

- 7 trials (N = 9212 patients) were eligible.
- Overall, (death or MI) was reduced:
 - (14.4%) in the selective invasive group
 - (12.2%) in invasive group P = 0.001.
- Non significant trend toward fewer deaths (6.0% vs 5.5%; P = 0.33)
- Highest benefit in High-risk patients with elevated cardiac biomarker levels at baseline
- No significant benefit in lower-risk patients with negative baseline marker levels.

Mehta SR, Cannon CP, Fox KA, Wallentin L, Boden WE, Spacek R, Widimsky P, McCullough PA, Hunt D, Braunwald E, Yusuf S.

JAMA. 2005 Jun 15;293(23):2908-17.

FOLLOW UP

- Mean *meta-analysis* F.U. 17 months:
 - 33% reduction in severe angina; $P < .001$
 - 34% reduction in rehospitalization ($P < .001$) with a routine invasive strategy.
- Longest F.U. RITA 3, at 5 years cardiovascular death is reduced by 32%
 $p = 0.026$

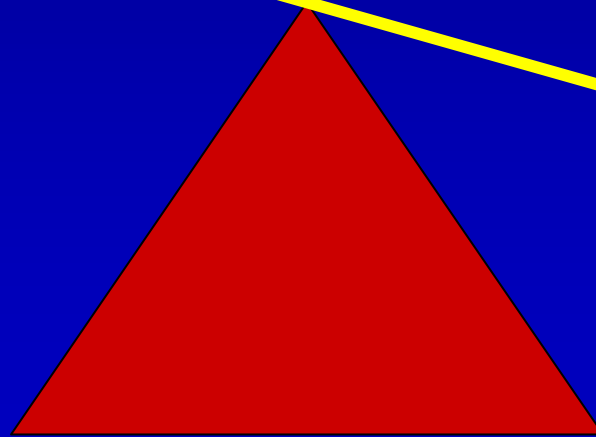
OPTIMAL STRATEGY FOR UA/NSTEMI 2005

VANQWISH

MATE
TIMI III B
ICTUS

ISAR-COOL
VINO
TRUCS
TACTICS-TIMI 18
FRISC II
RITA 3

CONSERVATIVE
N=920



N=2874

INVASIVE
N=7018

IN ACS

Be

Invasive not Conservative
mainly with high risk patients

? Cooling-off or plaque passivation by an extended period of antithrombotic treatment before PCI might reduce the risk associated with the procedure ?

ISAR-COOL

The Intracoronary Stenting with
Antithrombotic Regimen
Cooling-off trial

American Heart Association Scientific Sessions Nov
2002, Neumann FJ.

Patients & methods

N= 410 pts, typical angina.

ST segment depression (65%) and /or Troponin
T elevation $\geq 0,03$ mcg/l (67%)

Patients & methods

Antithrombotic pretrT for 72 to 120 hours
(cooling- off) n= 207

VS

Antithrombotic pretrT for < 6 hours (early
intervention) n=203

Patients & methods

-Antithrombotic pretreatment for both:

Aspirin IV 500mg then 100 mg bid

Clopidogrel 600 mg loading dose then 75mg bid.

Tirofiban (10mcg/ kg bolus then 0,10 mcg/kg/min for 24 hours.

Heparin (60 U/kg, infusion PTT 60-85s)

-Peri-interventional treatment:

Tirofiban (0,15 mcg/kg/min for 24 hours).

Heparin (60 U/kg)

Aspirin 100 mg bid indefinitely

Clopidogrel 75 mg bid for 5 days then 1 a day for 4 weeks

Patients & methods

-Similar major baseline characteristics

-Median time to KT was

2.4 hours in the early intervention group

VS

86 hours in the cooling-off group

Results

Primary endpoint, combined death and non fatal MI within 30 days

	Early Intervention N= 203	Cooling Off N= 207	p
Death & non fatal MIs	12 (5.9%)	24 (11.6%)	0.04
Non fatal MIs	12 (5.9%)	21 (10.1%)	0.012
Death	0	3 (1.5%)	0.23

Results

The entire benefit was gained by shortening the cooling-off phase

	Early Intervention N= 203	Cooling Off N= 207	p
Events Between study entry and KT	1	13	0.002
Events After KT	11	11	0.96

Results

- No cooling-off effect of plaque passivation.
- Bleeding requiring transfusion 3.4% in the cooling-off group VS 1 % in the early intervention group
- No significant differences in non cardiac complications.
- Similar results for subgroups with or without ST depression or positive troponin at inclusion

Conclusion

Extended period of antithrombotic pretreatment is unnecessary in patients with ACS and may even increase the risk to the patients

IN PRACTICE → Straight to the cath lab as soon as possible.

INVASIVE IS BETTER
BUT
IMMEDIATE INVASIVE IS
BEST

RECOMMENDATIONS

ACC/AHA Guidelines :

Recommendations Antiplatelet and Anticoagulation Therapy in Patients with Unstable Angina or a Non-ST-Segment Elevation Myocardial Infarction[†]

Class I

4. A platelet glycoprotein (GP) IIb/IIIa antagonist should be administered, in addition to ASA and heparin, to patients in whom catheterization and PCI are planned. The GP IIb/IIIa antagonist may also be administered just prior to PCI. (Level of evidence : A)

Class IIa

1. Eptifibatid or tirofiban should be administered, in addition to ASA and LMWH or UFH, to patients with continuing ischemia, an elevated troponin or with other high-risk features in whom an invasive management strategy is not planned. (Level of evidence : A)
2. Enoxaparin is preferable to UFH as an anticoagulant in patients with UA/NSTEMI in the absence of renal failure and unless CABG is planned within 24 h. (Level of evidence : A)
3. A platelet GP IIb/IIIa antagonist should be administered to patients already receiving heparin, ASA, and clopidogrel in whom catheterization and PCI are planned. The GP IIb/IIIa antagonist may also be administered just prior to PCI. (Level of evidence : A)

Class IIb

1. Eptifibatid or tirofiban, in addition to ASA and LMWH or UFH, to patients without continuing ischemia who have no other high-risk features and in whom PCI is not planned. (Level of evidence : A)

Class III

1. Intravenous fibrinolytic therapy in patients without acute ST-segment elevation, a true posterior MI, or a presumed new left bundle-branch block (LBBB). (Level of evidence : A)
2. Abciximab administration in patients in whom PCI is not planned. (Level of evidence : A)

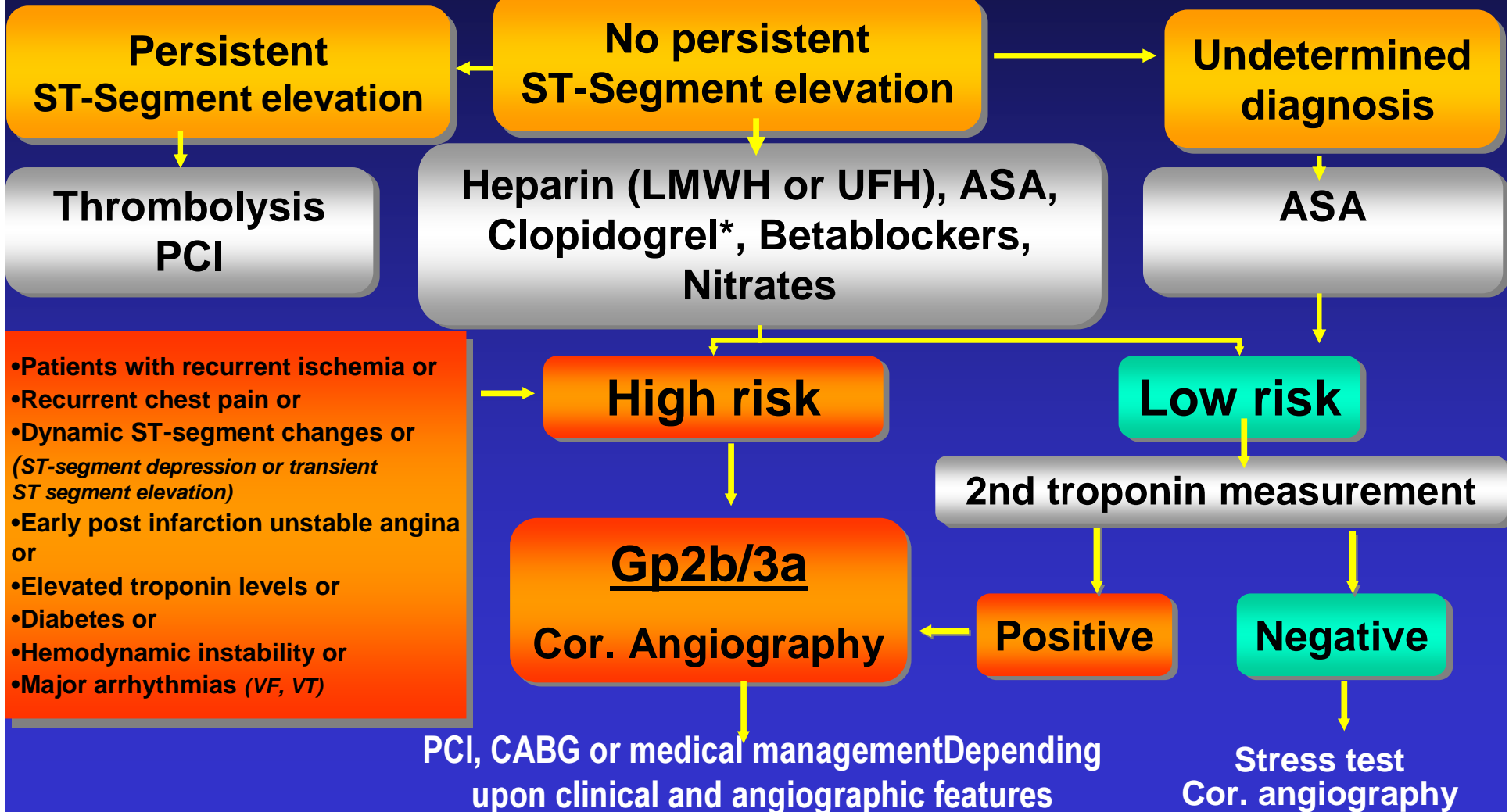
The ACC/AHA guidelines 2002 and the ACCP Consensus Conference 2004 recommended for NSTEMI or UA

- GP IIb/IIIa inhibitor should be given to patients in whom PCI is going to be done or is planned.
- If no PCI, the use of a GP IIb/IIIa inhibitor should be primarily limited to those at high-risk for further cardiac events:
 - Elevated levels of troponin I or T which.
 - Patients with a high TIMI risk score.
 - Patients with continuing ischemia or other high-risk features .
- The GP IIb/IIIa inhibitor infusion should be initiated on presentation and continued for 48 to 72 hours or until PCI .

Clinical suspicion of ACS



Physical examination, (Echocardiogram)
ECG monitoring, Blood samples

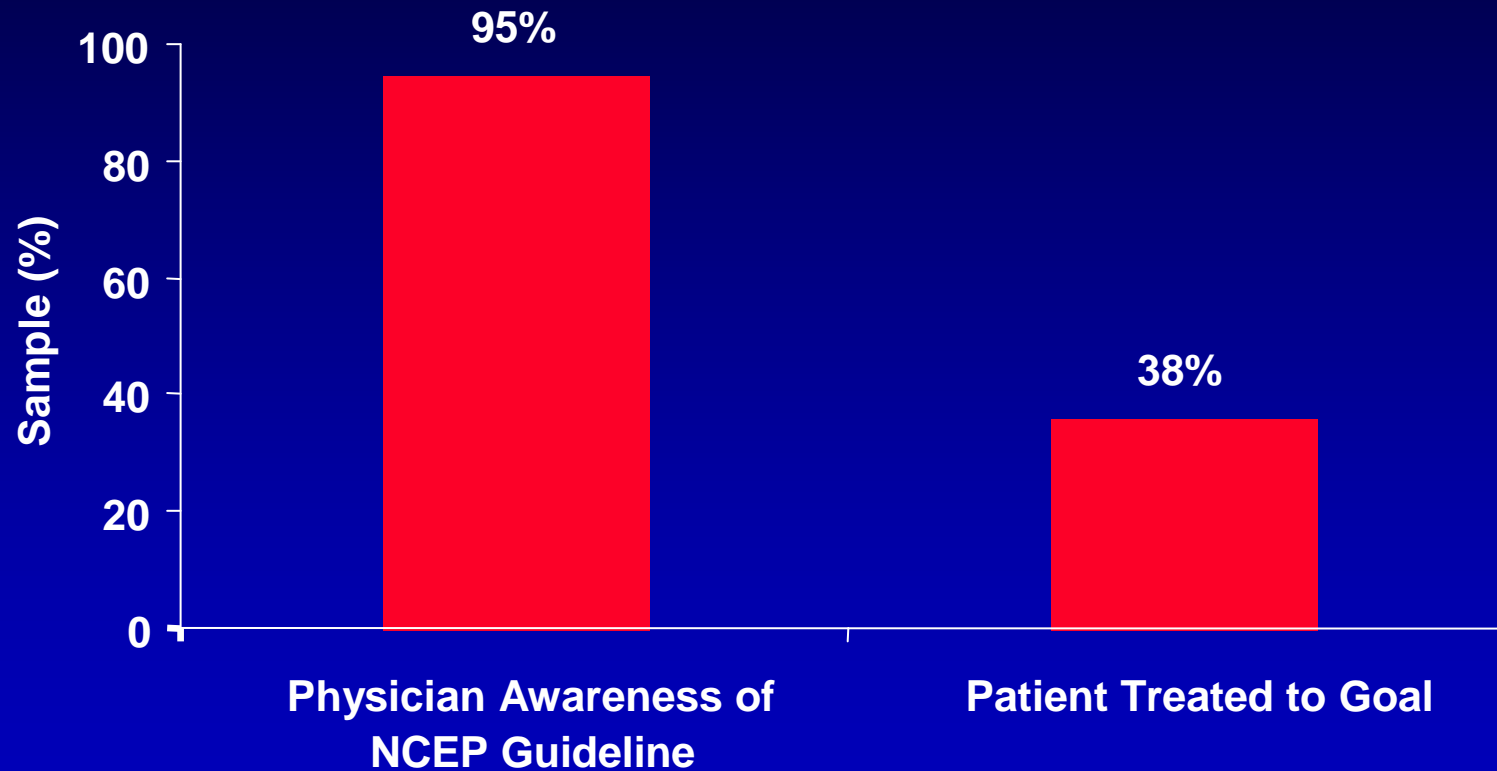


- Patients with recurrent ischemia or
- Recurrent chest pain or
- Dynamic ST-segment changes or (ST-segment depression or transient ST segment elevation)
- Early post infarction unstable angina or
- Elevated troponin levels or
- Diabetes or
- Hemodynamic instability or
- Major arrhythmias (VF, VT)

* omit clopidogel if the patient is likely to go to CABG within 5 days

Implementing the Guidelines?

Awareness Is Not Enough!



NCEP, National Cholesterol Education Program.
Pearson TA, et al. *Arch Intern Med.*
2000;160:459-467.

4888 patients from 5 regions of the United States were studied

Smooth Transition From Acute to Long-term Management



‘Lack of implementation ?’

‘what will impact efficacy?’

“AHA *Get With the Guidelines* program”

The Solution to Bridging
the Treatment Gap:

Get With The
Guidelines

Remember.....

Guidelines that are not
followed are of no value

REAL LIFE ?

Early Use of Glycoprotein IIb/IIIa Inhibitors in Non-ST-Elevation Acute Myocardial Infarction

Observations From the National Registry of Myocardial Infarction IV

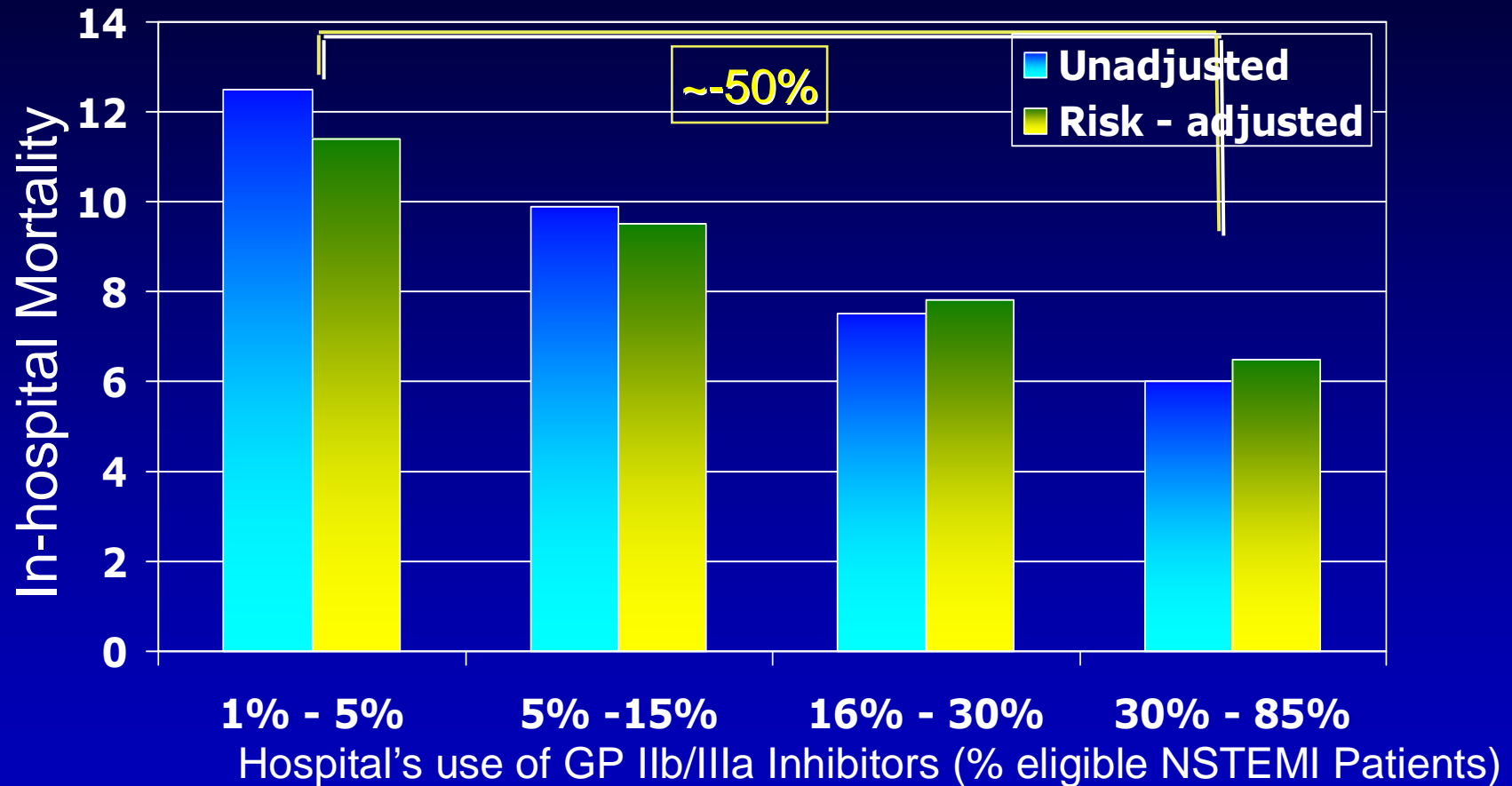
(NRM-4)

60,770 patients with NSTEMI

Eric D. Peterson, MD, MPH,* Charles V. Pollack, JR, MD, MA, Matthew T. Roe, MD,
MHS,*Lori S. Parsons, BS, Katherine A. Littrell, PHD, RN,§ John G. Canto, MD,
MSPH, FACC,||Hal V. Barron, MD,§ for the National
Registry of Myocardial Infarction (NRM) 4 Investigators

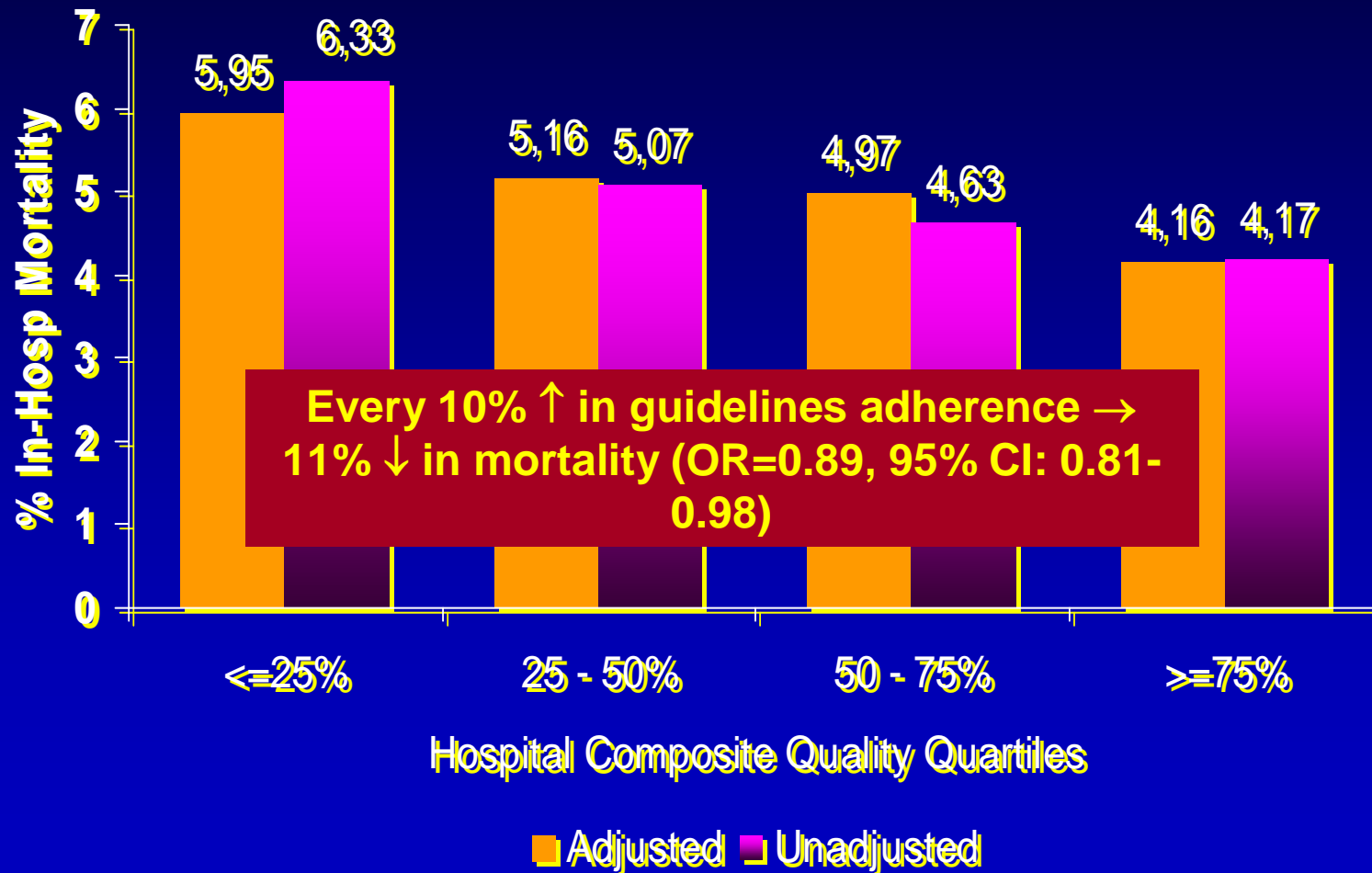
*Durham, North Carolina; Philadelphia, Pennsylvania; Highland Park, Illinois;
South San Francisco, California; and Birmingham, Alabama*

NRMI-4: Results



In-hospital mortality for patients with non-ST-elevation myocardial infarction (NSTEMI), by the proportion of patients at each hospital treated early with a glycoprotein (GP) IIb/IIIa inhibitor.

Link Between Overall Guidelines Adherence and Mortality





Management of Patients with NSTEMI ACS

Latest Insights from CRUSADE

A National Quality Improvement Initiative

Eric D. Peterson, MD, MPH
Duke Clinical Research Institute
Duke University Medical Center
Durham, North Carolina

Goals for CRUSADE

Improve Adherence to ACC/AHA Guidelines
Improve Patient Outcomes

Acute Therapy

- **Aspirin**
 - Clopidogrel
- **Beta Blocker**
- **Heparin (UFH or LMWH)**
- **GP IIb-IIIa Inhibitor**
 - Cath/PCI

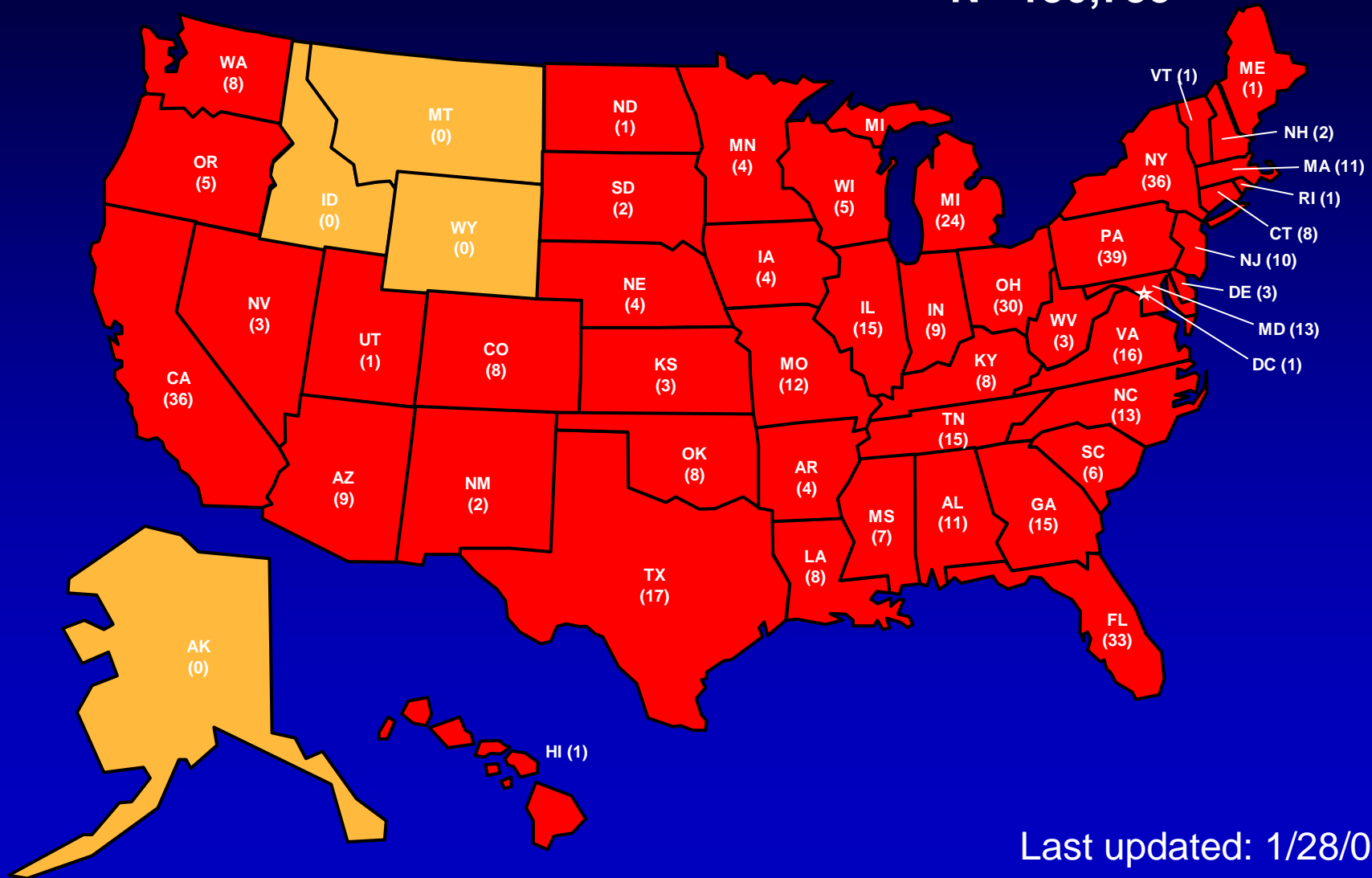
Discharge Therapy

- **Aspirin**
- **Clopidogrel**
- **Beta Blocker**
- **ACE Inhibitor**
- **Statin/Lipid Lowering**
- **Smoking Cessation**
- **Cardiac Rehabilitation**

CRUSADE Site Distribution

Sites Who Have Submitted = 486

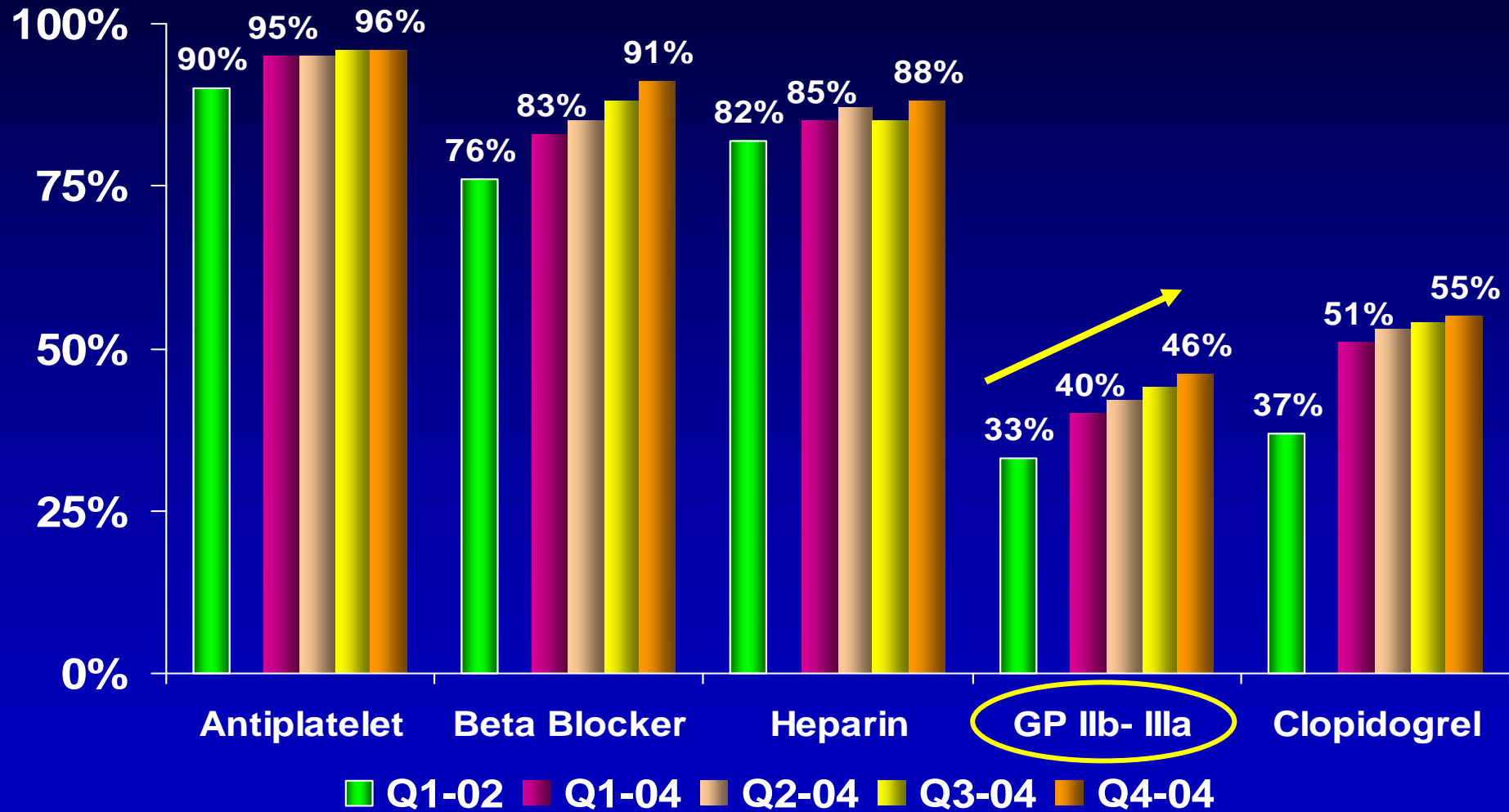
N= 130,735



Last updated: 1/28/05

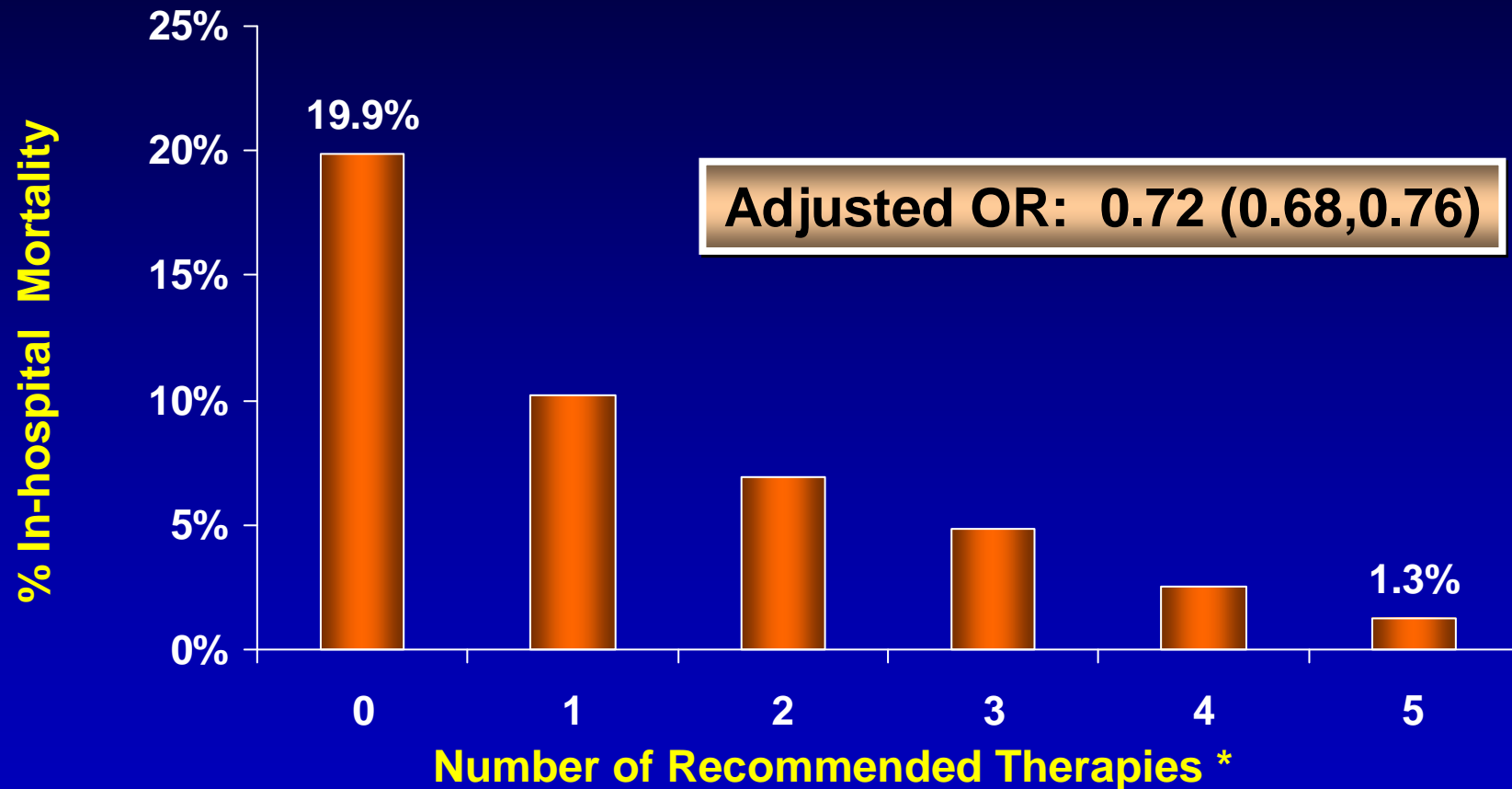
Trends in Acute Therapy Adherence

(Among Patients Without Contraindications)



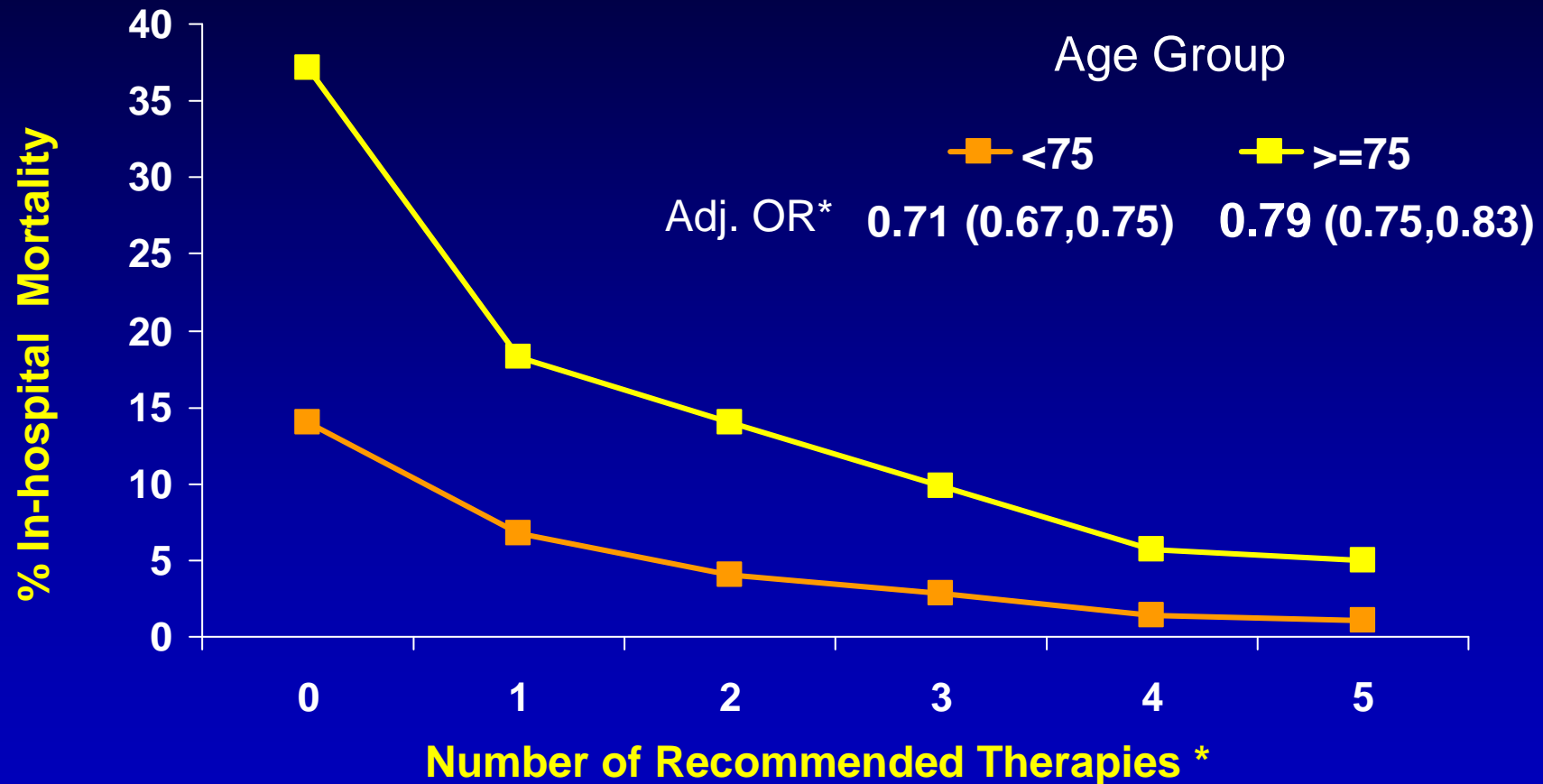
Quarter 1, 2002 through Quarter 4, 2004

Does it Matter? Mortality Rates by # of Acute Guideline Recommended Therapies Received



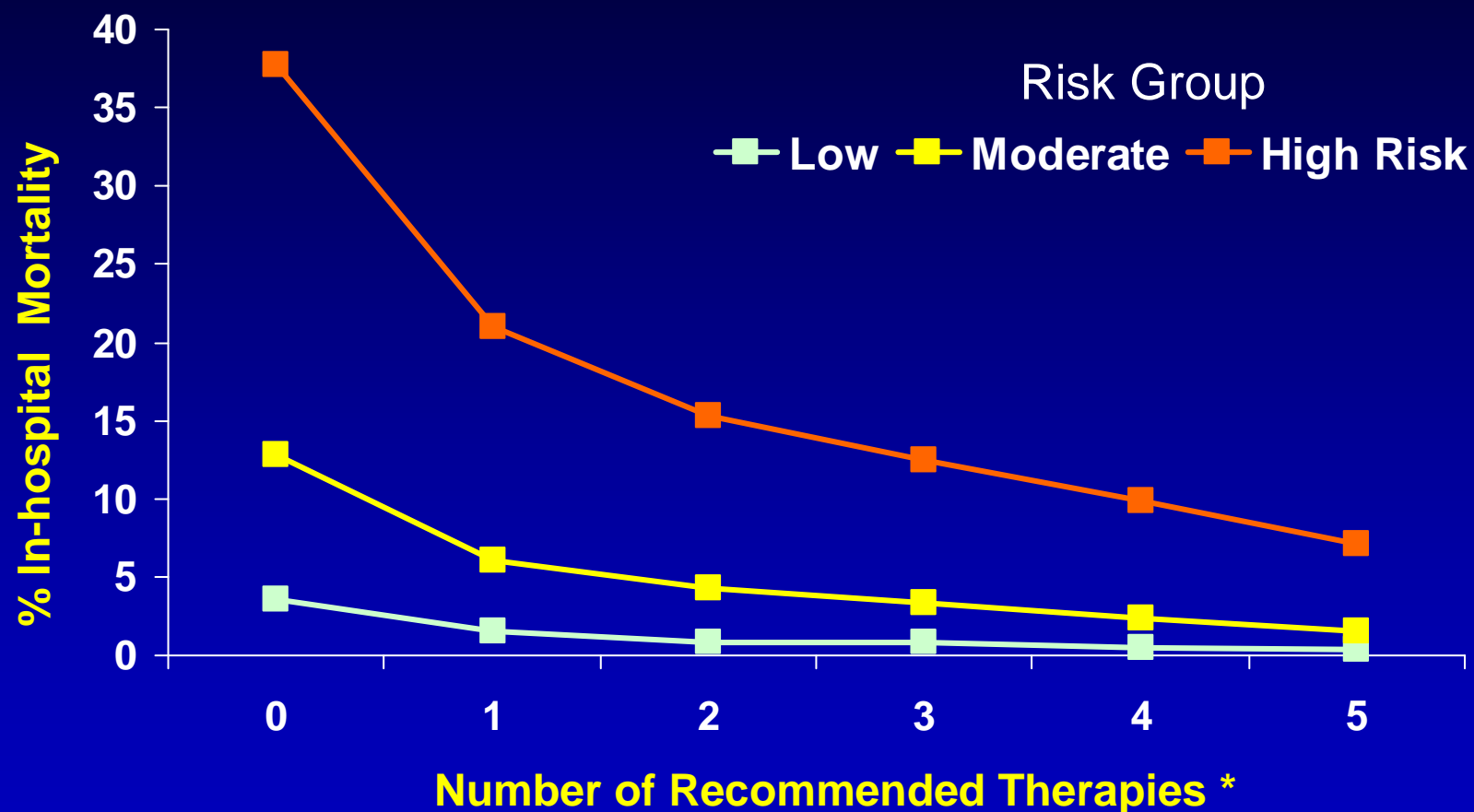
Therapies = Acute Aspirin, Acute Beta-blockers, Acute Heparin, GP IIb/IIIa inhibitors, Cardiac Catheterization <48 hours

Mortality Rates by # of Acute Guideline Recommended Therapies Received by Age Group



Therapies = Acute Aspirin, Acute Beta-blockers, Acute Heparin, GP IIb/IIIa inhibitors, Cardiac Catheterization <48 hours

Mortality Rates by # of Acute Guideline Recommended Therapies Received by Risk Group



Therapies = Acute Aspirin, Acute Beta-blockers, Acute Heparin, GP IIb/IIIa inhibitors, Cardiac Catheterization <48 hours; Based on CRUSADE Risk Score

Latest Results in NSTEMI ACS in US

Conclusions

- ❑ Crusade continues to represent **'real world'** NSTEMI ACS
 - ❑ Older patients
 - ❑ More comorbidity
- ❑ Care for NSTEMI ACS **is improving**:
 - ❑ Continued progress in adherence to ACC/AHA Guidelines for both acute and discharge treatments
 - ❑ More early cath, leading to earlier discharge
- ❑ **Yet opportunities for improvement persist**
 - ❑ **Largest gaps**: acute GP IIb/IIIa, D/C ACE, clopidogrel
 - ❑ "Right dosing" to reduce adverse events
- ❑ **And can lead to even better patient outcomes!**

Survey of Assessment & Management of CoRonary Heart Disease PaTients

- SMART -

*Does Current Practice Mirror
Guidelines Recommendations for
Managing ACS Patients?*

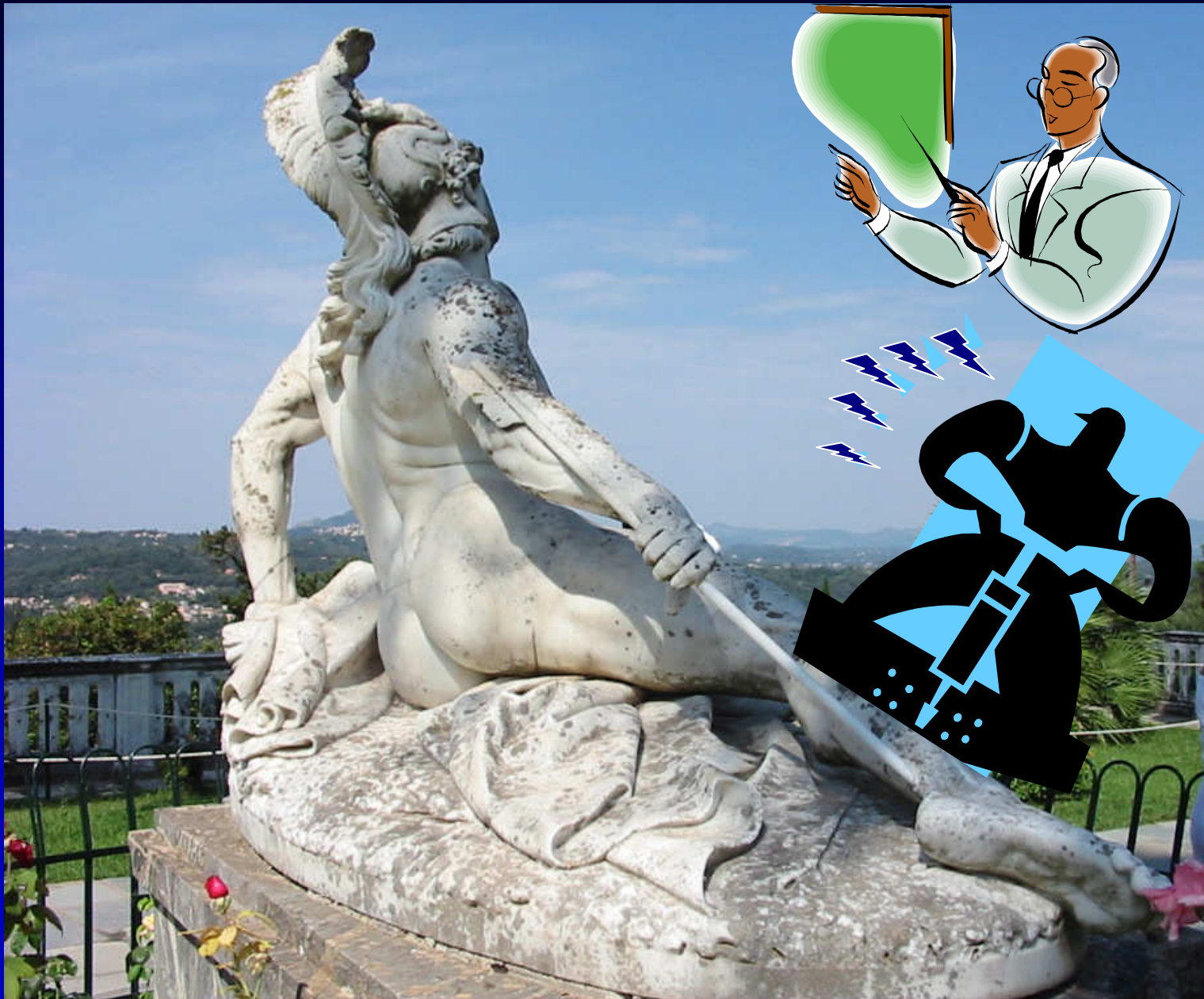
Hotel Dieu de France (HDF) –
Quarterly trends in Therapy adherence

Q2-2003 to Q2-2005

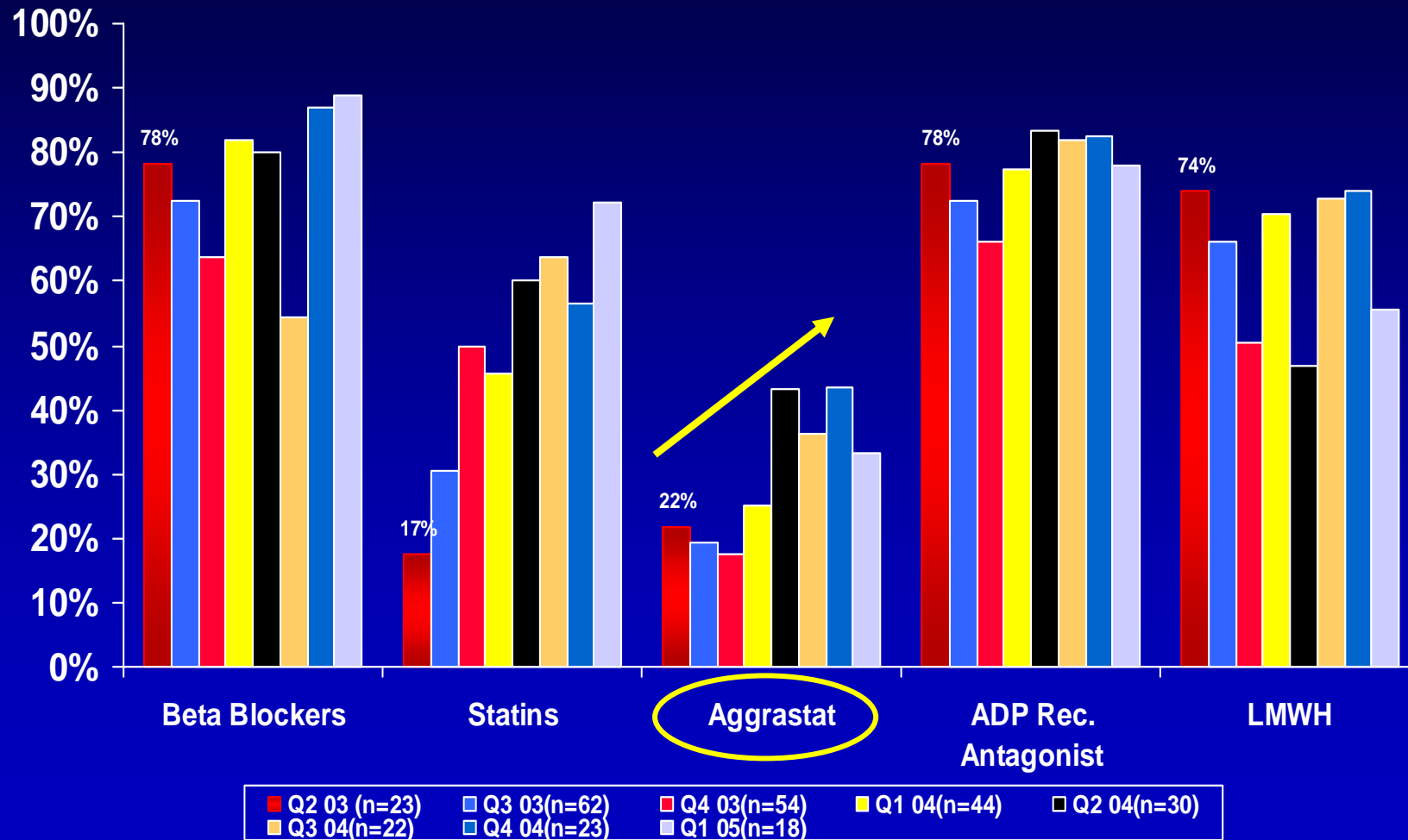
(575 patients)

Lebanon Data 2109 patients enrolled

ACTION

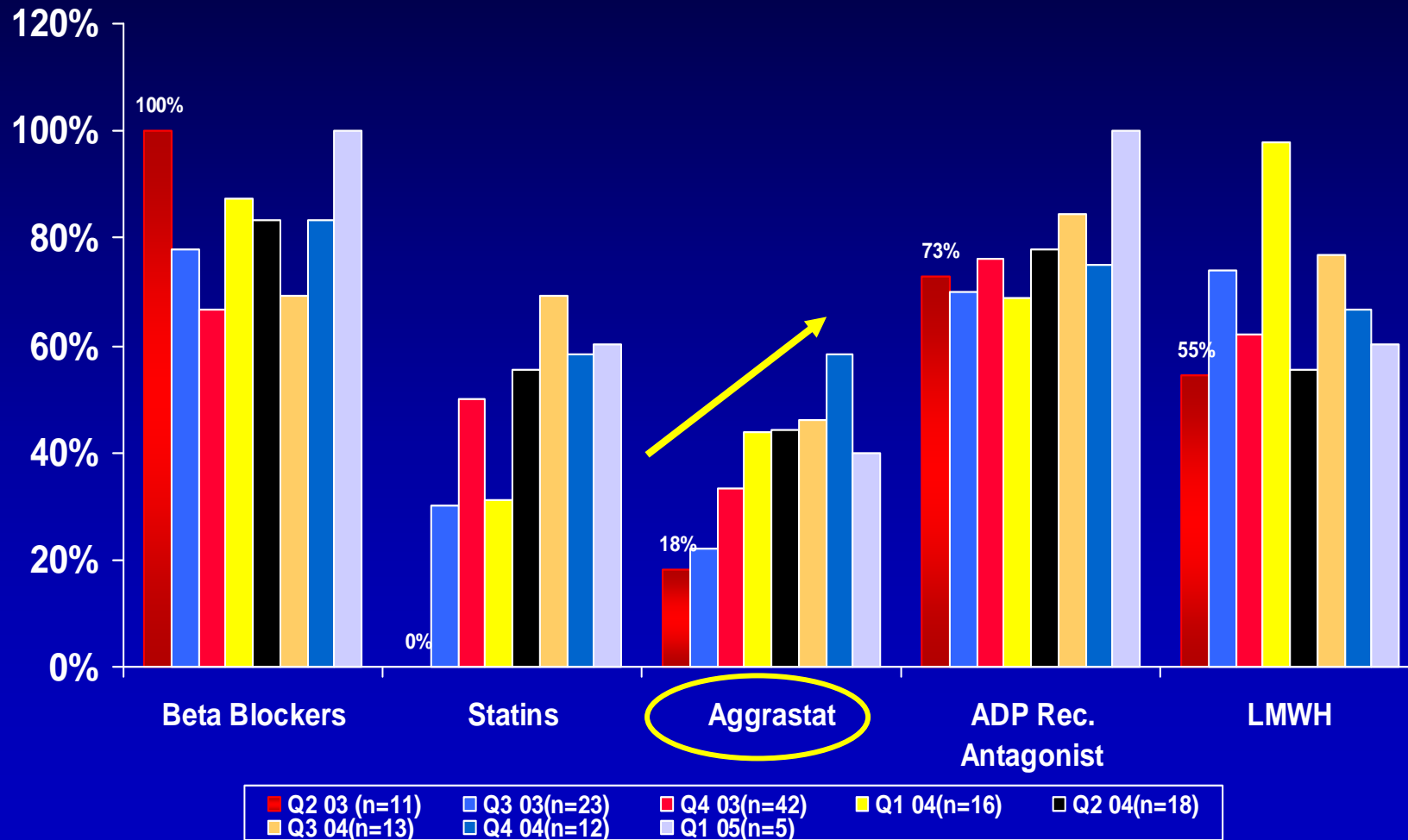


Therapy At Admission vs. Diagnosis (UA / NSTEMI)

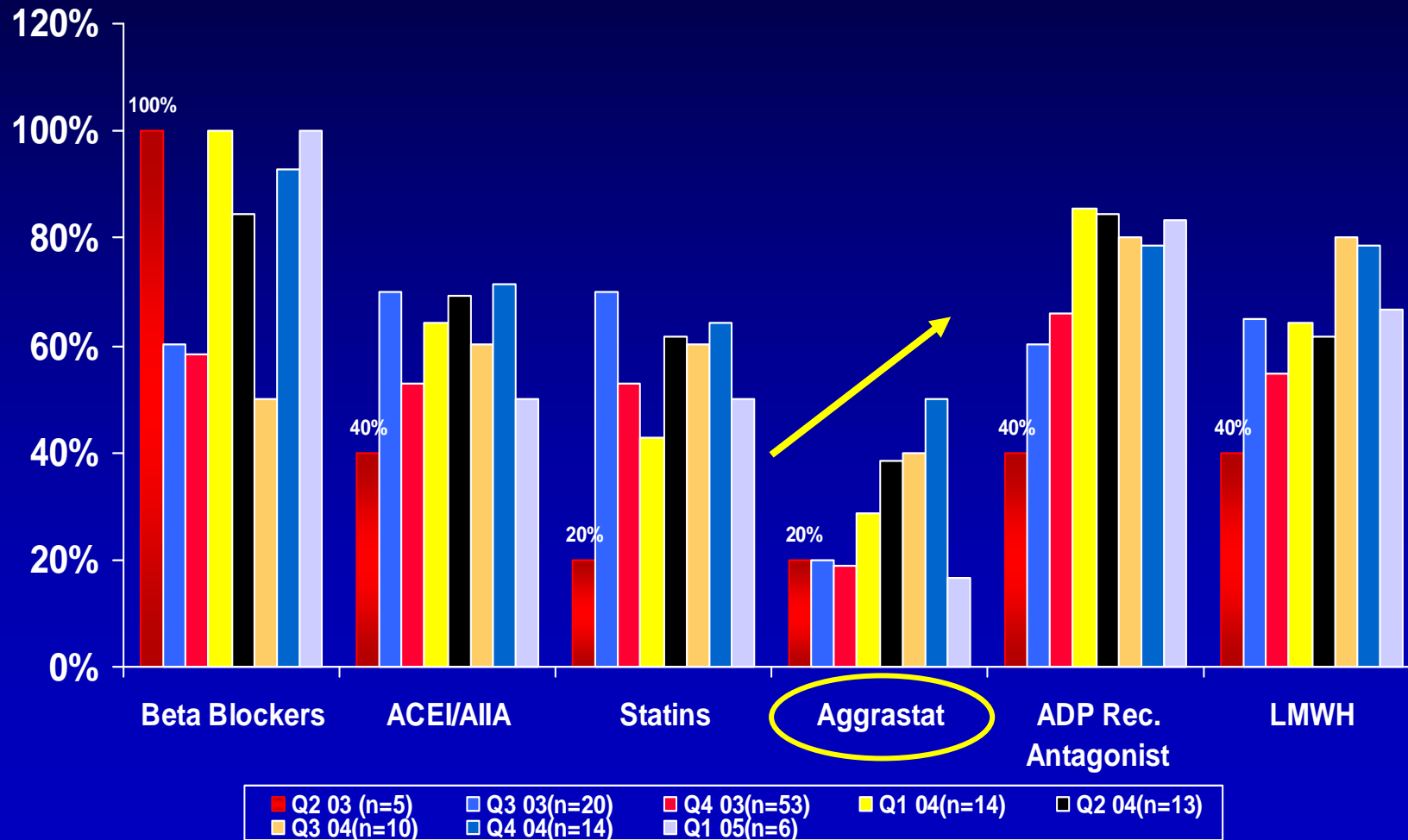


Therapy At Admission vs. Diagnosis

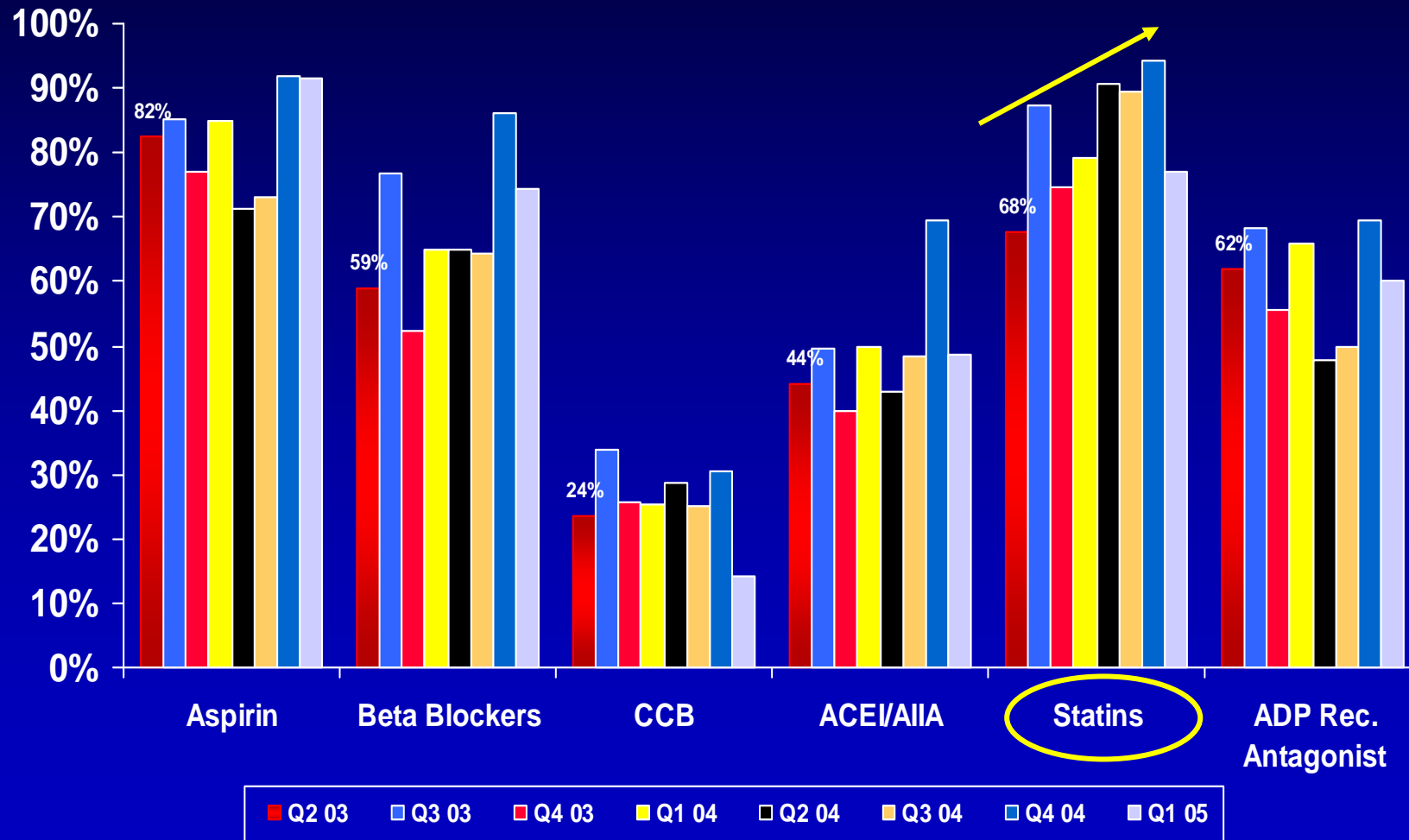
UA/NSTEMI presented with Elevated Troponin



Therapy At Admission vs. Diagnosis UA/NSTEMI with Diabetes



Therapy Prescribed Upon Hospital Discharge



Conclusion

- ✓ Gap between knowledge of guidelines and current practice
- ✓ Intervention programs of this nature could produce a significant positive impact on cardiovascular outcomes if implemented nationally.

What will you do TOMORROW
to improve quality



Collaboration

Working as a team we can
IMPLEMENT the Guidelines to save
more lives.



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
PRESENTATION	
Recent (\leq 24H) severe angina	1
\uparrow cardiac markers	1
ST deviation \geq 0.5 mm	1

RISK SCORE = Total Points (0 - 7)

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 +marker)

Antman et al *JAMA* 2000; 284: 835 - 842

Non ST-Elevation Myocardial Infarction

PATIENT PRESENTS WITH CHEST PAIN OR POTENTIAL CHEST PAIN EQUIVALENT

(Jaw, shoulder, arm, back, or epigastric pain; unexplained dyspnea; syncope; palpitations, etc)

PHYSICIAN'S HISTORY

- Nature of presenting episode and time course
- Cardiac risk factors (previous MI, HTN, lipids, smoking, diabetes, family history) and related past medical (ACSVD, CVA, PVD) and surgical history (PCI/CABG)
- Comorbidities and quick review of systems (to suggest alternative diagnoses such as lung infection or infarction, chest wall or GI pain)

Triage

PHYSICAL EXAMINATION

- Evaluate hemodynamic status and perfusion
- Lung auscultation for rales, ronchi
- Evaluate for possible alternative diagnoses (chest wall pain, pneumonia, PE [evidence of DVT], musculoskeletal, etc)
- Cardiac examination

A flowchart on a dark blue background. At the top, a yellow arrow points down to a red oval. Inside the oval is the text 'Prompt 12- or 15-Lead Electrocardiogram' followed by a horizontal line and a bulleted list. A second yellow arrow points down from the oval to a yellow 3D-style box. Inside the box is text describing ST-segment depression or transient ST-segment elevation not meeting fibrinolytic criteria, with a note in blue text about ECG or clinical evidence of unstable angina. A final yellow arrow points down from the bottom of the box.

Prompt 12- or 15-Lead Electrocardiogram

- 15-lead ECG may detect right ventricular or posterior infarctions early
- Request previous ECG, if available, for comparison

**ST-Segment Depression $>0.5\text{mm}$ OR
Transient ST-Segment Elevation NOT
Meeting Fibrinolytic Criteria
(ECG or Clinical Evidence of Unstable Angina)**

Patient is at High Risk: Initial Management

Assessment and Stabilization

- Intravenous access
- Oxygen and pulse oximetry
- Continuous ECG monitoring
- Send biomarker tests (Troponin I or T +/- CPK and CPK-MB)

Pharmacologic Intervention

- Aspirin 160-325 mg PO (in prehospital setting)
- Nitroglycerin SL/TC/IV for ischemic pain,
Morphine sulfate for immediate relief of pain
- Anticoagulate with enoxaparin (preferred) or UFH
- Consider B-blocker therapy
- Tirofiban infusion whether patient going to cath or not

Catheterization Lab Available In-House or by
Transfer Within 24-36 Hours?

YES

Dominant Strategy: Acute Intervention

- Administer Tirofiban (preferred)
- Expedite transfer to cath lab
- Continue anticoagulation
- Administer clopidogrel (300mg PO then 75 mg PO qd) in catheterization lab if CABG not necessary once coronary anatomy is defined

NO

Alternative Strategy: Medical Management

- Administer clopidogrel (300mg PO then 75 mg PO qd)
- Continue anticoagulation with enoxaparin (preferred) or UFH
- Consider initiating eptifabotide or tirofiban infusion
- Cardiology admission
- Consider transfer for elective catheterization
- Transfer for catheterization if other high risk featured (see below) manifest or if patient deteriorates

High Risk Features

- Persistent ischemic chest pain
- > 20 min chest pain at rest or > 2 episodes of pain in 24 h
- Positive biomarker
- Worsening or persistent ST-segment deviation despite therapy
- Sustain ventricular tachycardia
- Age > 75
- Hemodynamic instability
- Signs of pump failure (rales, new MR murmur, new S3 gallop)

ECG Normal or Nondiagnostic (UA)

PATIENT PRESENTS WITH CHEST PAIN OR POTENTIAL CHEST PAIN EQUIVALENT

(Jaw, shoulder, arm, back, or epigastric pain; unexplained dyspnea; syncope; palpitations, etc)

PHYSICIAN'S HISTORY

- Nature of presenting episode and time course
- Cardiac risk factors (previous MI, HTN, lipids, smoking, diabetes, family history) and related past medical (ACSVD, CVA, PVD) and surgical history (PCI/CABG)
- Comorbidities and quick review of systems (to suggest alternative diagnoses such as lung infection or infarction, chest wall or GI pain)

Triage

PHYSICAL EXAMINATION

- Evaluate hemodynamic status and perfusion
- Lung auscultation for rales, ronchi
- Evaluate for possible alternative diagnoses (chest wall pain, pneumonia, PE [evidence of DVT], musculoskeletal, etc)
- Cardiac examination

**Prompt 12- or 15-Lead
Electrocardiogram**

- 15-lead ECG may detect right ventricular or posterior infarctions early
- Request previous ECG, if available, for comparison

ECG is Nondiagnostic or Normal

Clinical Suspicion of ACS

Initiate On-Going Risk-Oriented Evaluation

- Send biomarker tests (Troponin I or T +/- CPK and CPK-MB)
- Repeat ECG during pain if pain recurs

Markers or ECG Confirm High Risk Status at Any Time During Evaluation

Follow High Risk Initial Management Path

Assessment and Stabilization

- Intravenous Access
- Oxygen and pulse oximetry
- Continuous ECG monitoring
- Send repeat biomarker tests (Troponin I or T +/- CPK and CPK-MB); schedule repeat assay as indicated by time course of ischemic syndromes

Calculate TIMI Risk Score: 1 Point Each for Presence of

- Age > 65 years
- Prior stenosis > 50%
- > 3 CAD risk factors
- ASA in last 7 days
- > 2 anginal events in last 24 hours
- ST deviation
- Elevated biomarkers

TIMI Risk Score = 3-4: INTERMEDIATE RISK INITIAL MANAGEMENT

- Aspirin 160-325mg PO
- Nitroglycerin SL/TC/IV for ischemic pain, morphine sulfate as needed
- Anticoagulate with enoxaparin 1 mg/kg SQ q 12 h
- Consider B-blocker if patient on maintenance B-blocker, if hypertensive, or tachycardic

TIMI Risk Score = 0-2: LOW RISK INITIAL MANAGEMENT

- Aspirin 160-325mg PO
- Nitroglycerin SL/TC/IV for ischemic pain, morphine sulfate as needed
- Anticoagulate with enoxaparin 1 mg/kg SQ q 12 h
- Consider expedited R/O protocol including early provocative testing

Continue Risk-Oriented Evaluation

According to agreements and protocols among departments of emergency medicine, cardiology, radiology, and cath lab

- Lower risk patients may not require an extended observation period
- Serial ECGs, serial troponin, and serial chest X-rays. Consider rest or provocative testing if no high risk features are present.

HIGH RISK Feature Manifests During Risk-Oriented Evaluation

Follow High Risk Initial Management Path

- Persistent ischemic chest pain
- >20 min ischemic chest pain at rest or more than 2 episodes of pain in 24 h
- Positive biomarker
- ST-segment deviation > 0.05mm
- Sustained ventricular tachycardia or hemodynamic instability
- Age > 75
- Positive Objective Ischemia Test or LVEF less than 40%
- Signs of pump failure (rales, new MR murmur, new S3 gallop)

HIGH RISK Feature Not Present During Risk-Oriented Evaluation

Consider Referral for Provocative Testing

If TIMI Risk Score was 3-4:

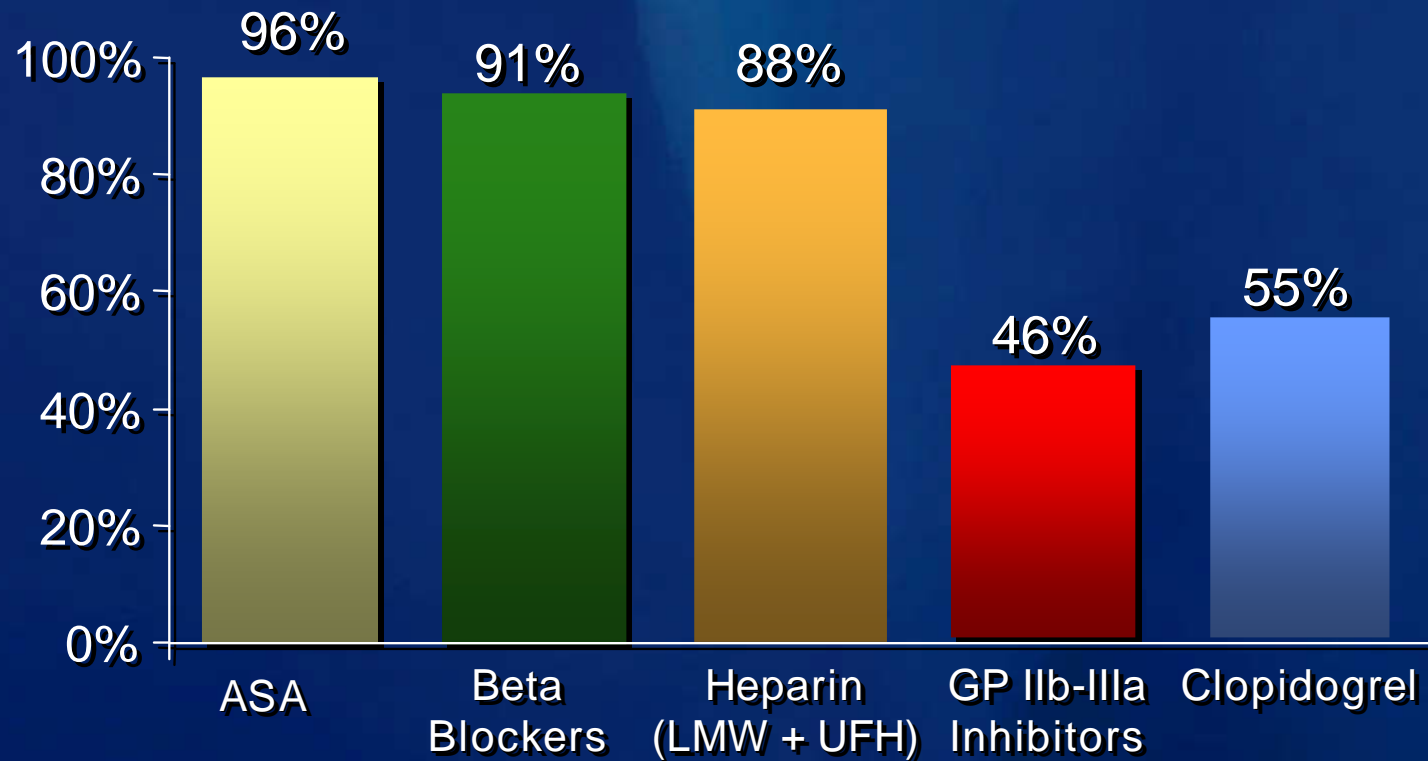
- Cardiology follow-up as outpatient
- Discharge on aspirin 81-162mg PO qd
- Consider discharge on clopidogrel 75 mg PO qd

If TIMI Risk Score was 0-2:

- Primary care physician vs. cardiology as follow-up on outpatient
- Consider discharge on aspirin 81-162 mg PO qd

Acute Medication Use – Q3 2004

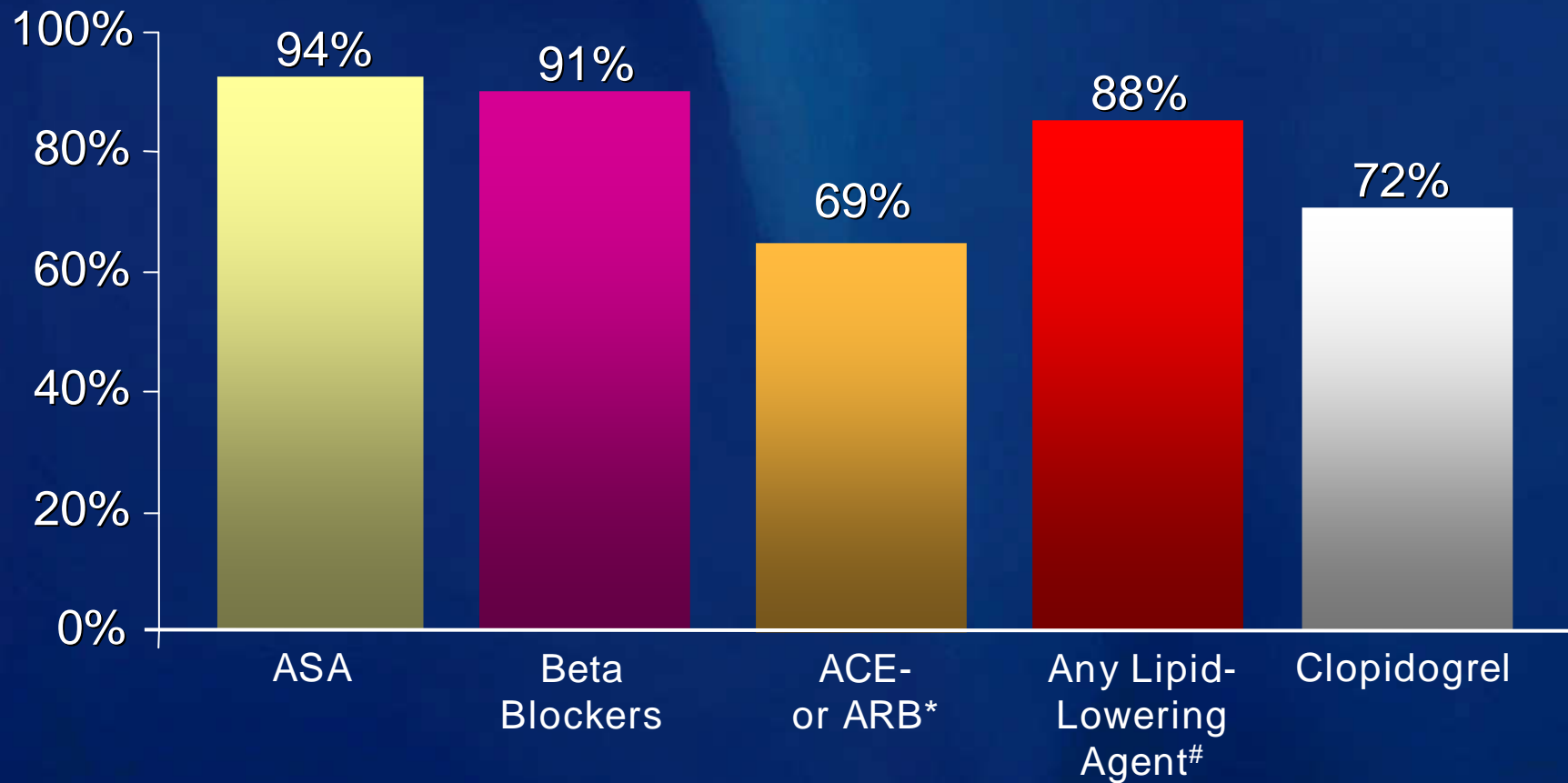
(Within 1st 24 hours in patients without contraindications)



Q4 2004 CRUSADE data

Discharge Medication Use – Q4 2004

(In patients without contraindications)

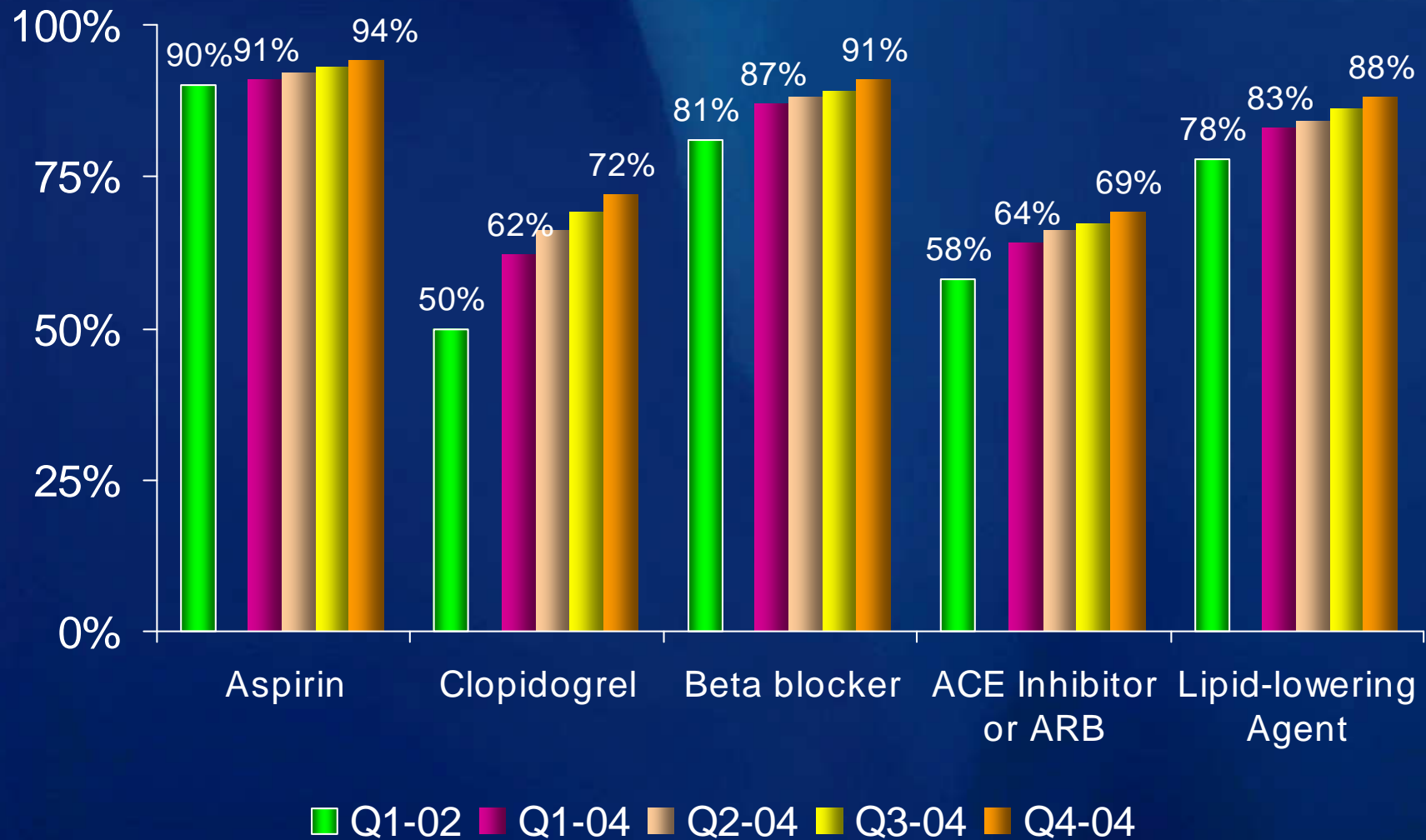


*LVEF < 40%, CHF, DM, HTN

Known hyperlipidemia, ↑ TC, ↑ LDL

Trends in Discharge Therapy

(Among Patients Without Contraindications)



Quarter 1, 2002 through Quarter 4, 2004

ACC/AHA classification

Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective.

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.

Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.

Class IIb: Usefulness/efficacy is less well established by evidence/opinion.

Class III: Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/effective and in some cases may be harmful.

*Data from : Braunwald, E, Antman, E, Beasley, J, et al. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction—summary article. A report of the American College of Cardiology/American Heart Association task force on practice guidelines (Committee on the Management of Patients With Unstable Angina). *J Am Coll Cardiol* 2002; 40:1366; and from Braunwald, E, Antman, EM, Beasley, JW, et al. A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines (Committee on the Management of Patients with Unstable Angina). *J Am Coll Cardiol* 2000; 36:970.