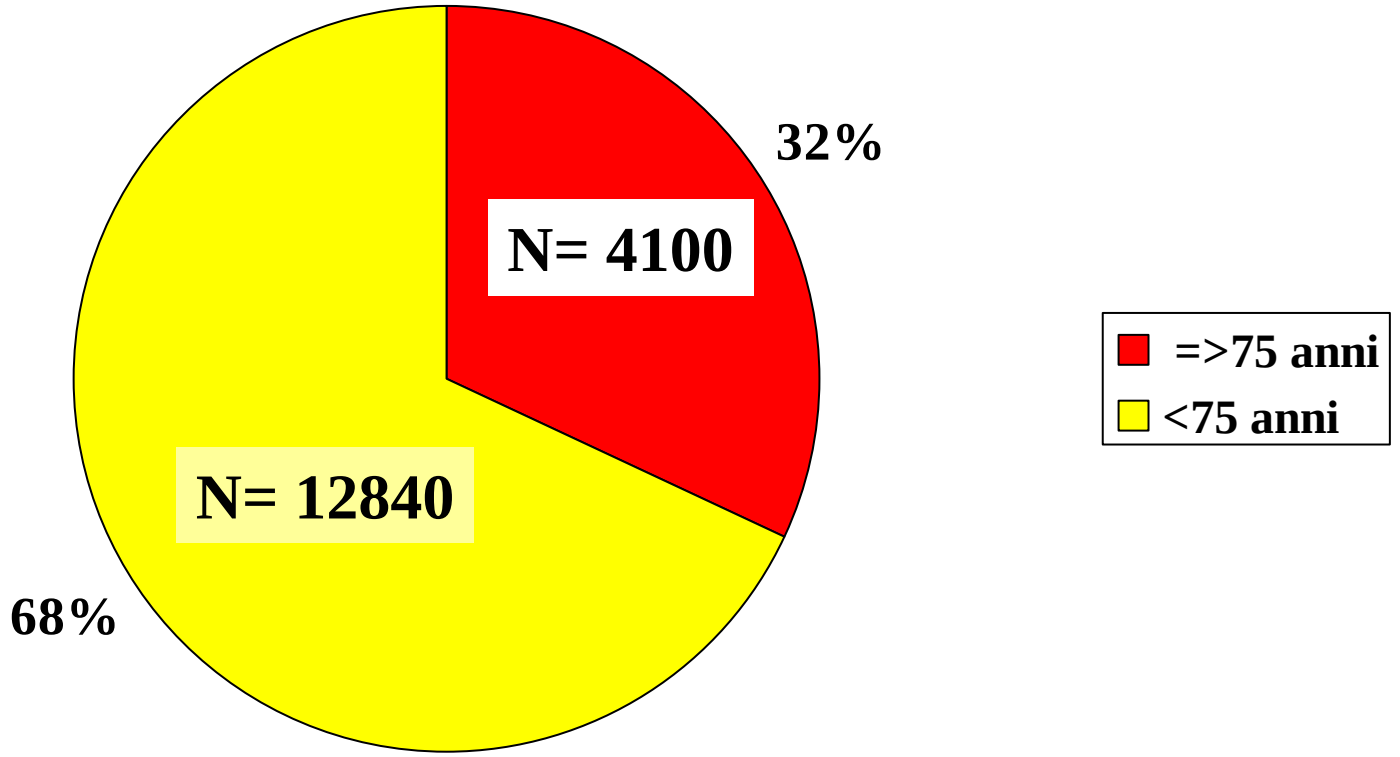
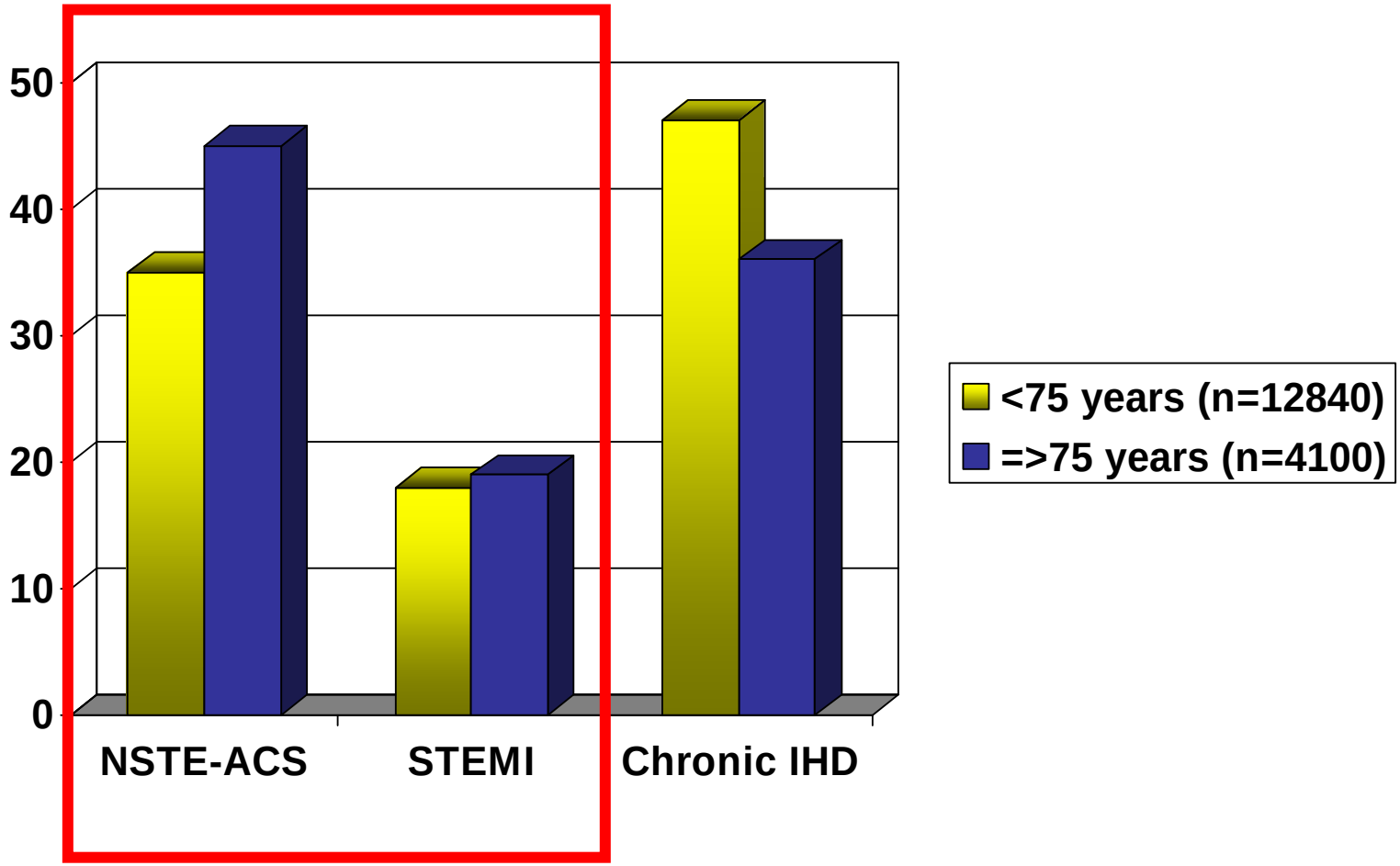
PCI in 16940 patients included in the OSCAR Registry



Indications for PCI in 16940 patients included in the OSCAR Registry

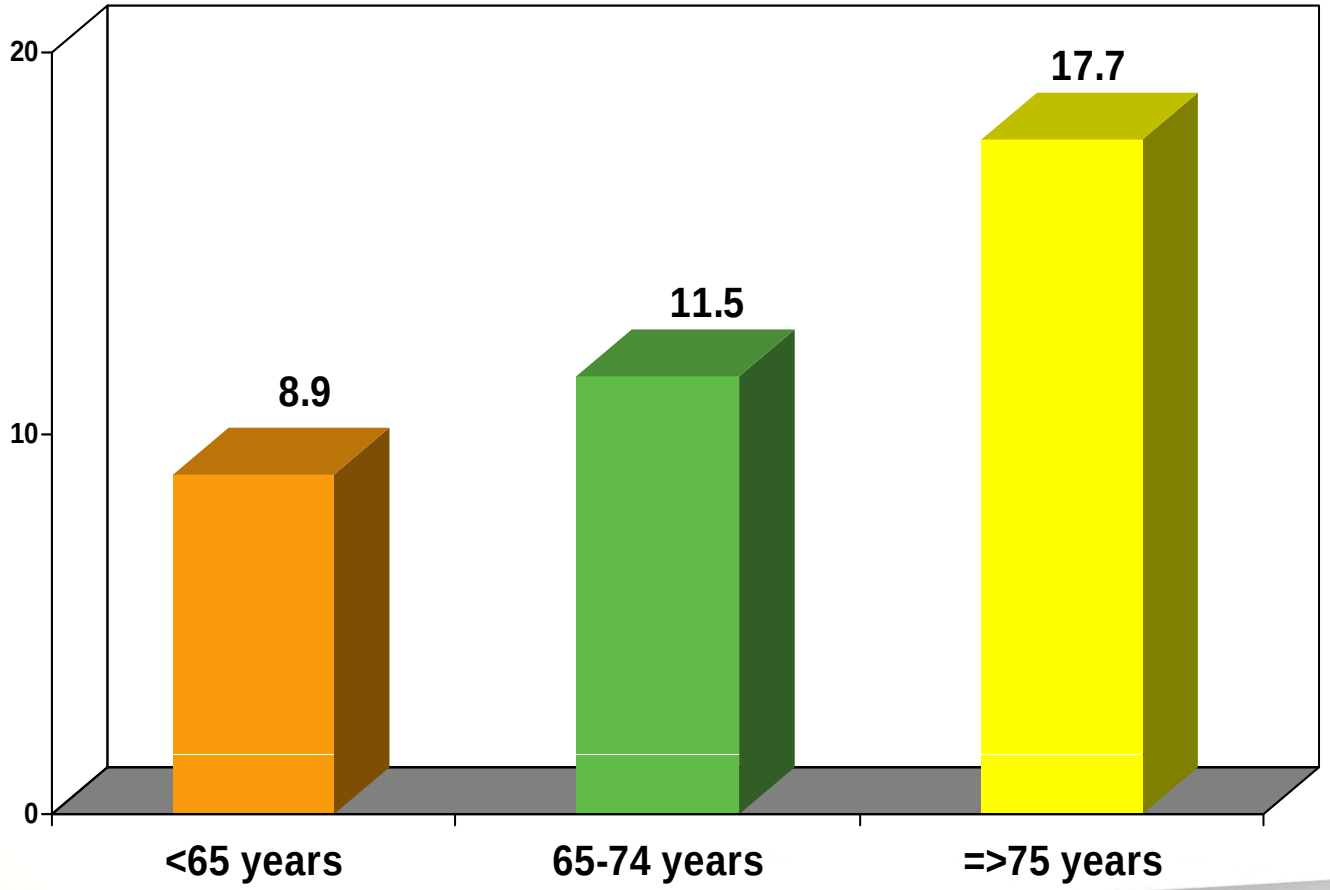


The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 NOVEMBER 15, 2007 VOL. 357 NO. 20

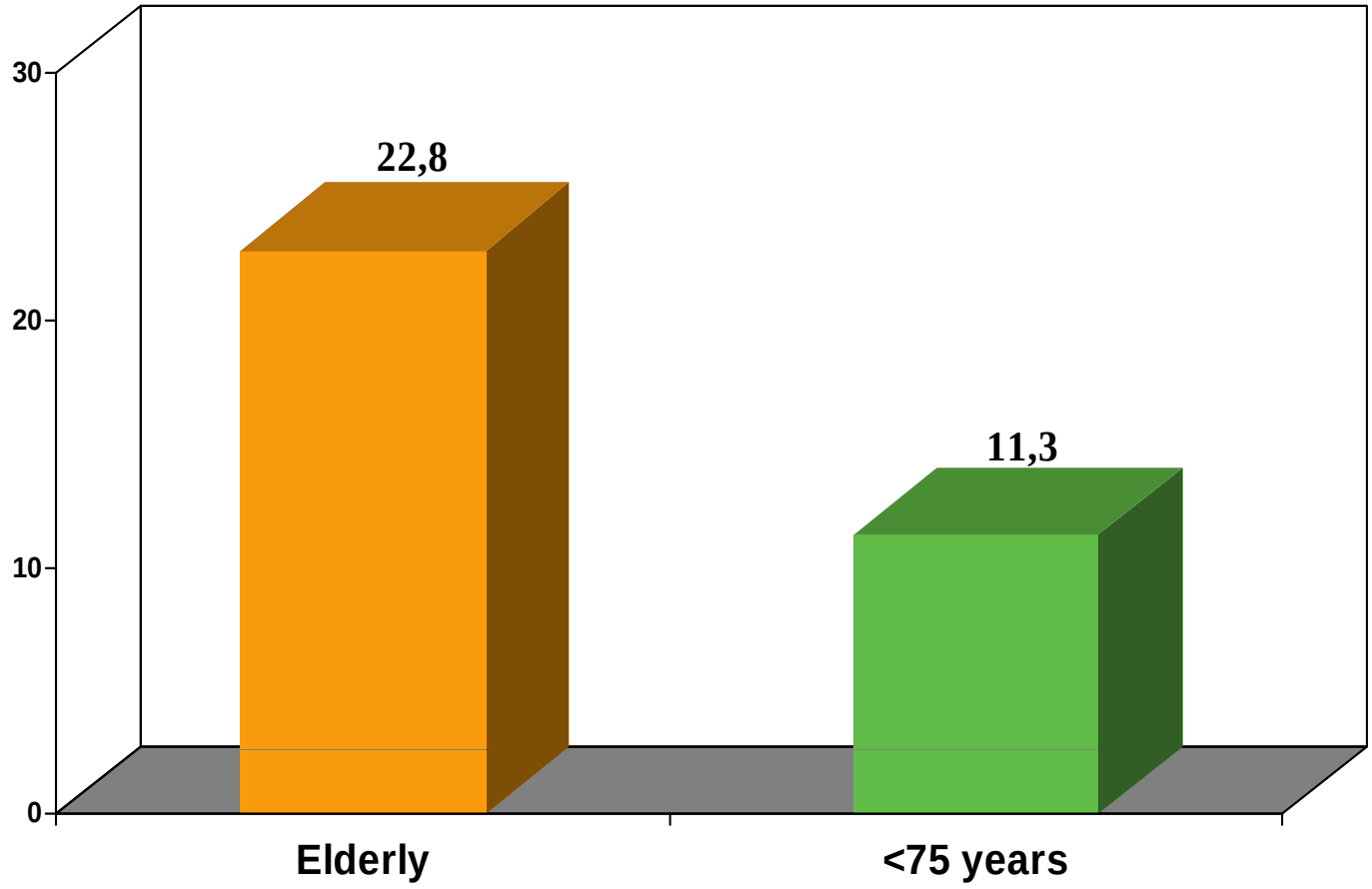
Prasugrel versus Clopidogrel in Patients with Acute Coronary Syndromes

Stephen D. Wiviott, M.D., Eugene Braunwald, M.D., Carolyn H. McCabe, B.S., Gilles Montalescot, M.D., Ph.D., Witold Ruzyllo, M.D., Shmuel Gottlieb, M.D., Franz-Joseph Neumann, M.D., Diego Ardissino, M.D., Stefano De Servi, M.D., Sabina A. Murphy, M.P.H., Jeffrey Riesmeyer, M.D., Govinda Weerakkody, Ph.D., C. Michael Gibson, M.D., and Elliott M. Antman, M.D., for the TRITON–TIMI 38 Investigators*

Ischemic events rate according to age (median f-up:15 months) in the TRITON trial



Recurrent events in elderly vs younger patients in the TRITON trial



Recommendations for Special Populations

2007 ESC Guidelines for NSTE-ACS

- Elderly patients should be considered for routine early invasive strategy, after careful evaluation of their inherent raised risk of procedure-related complications, especially during CABG (I – B).

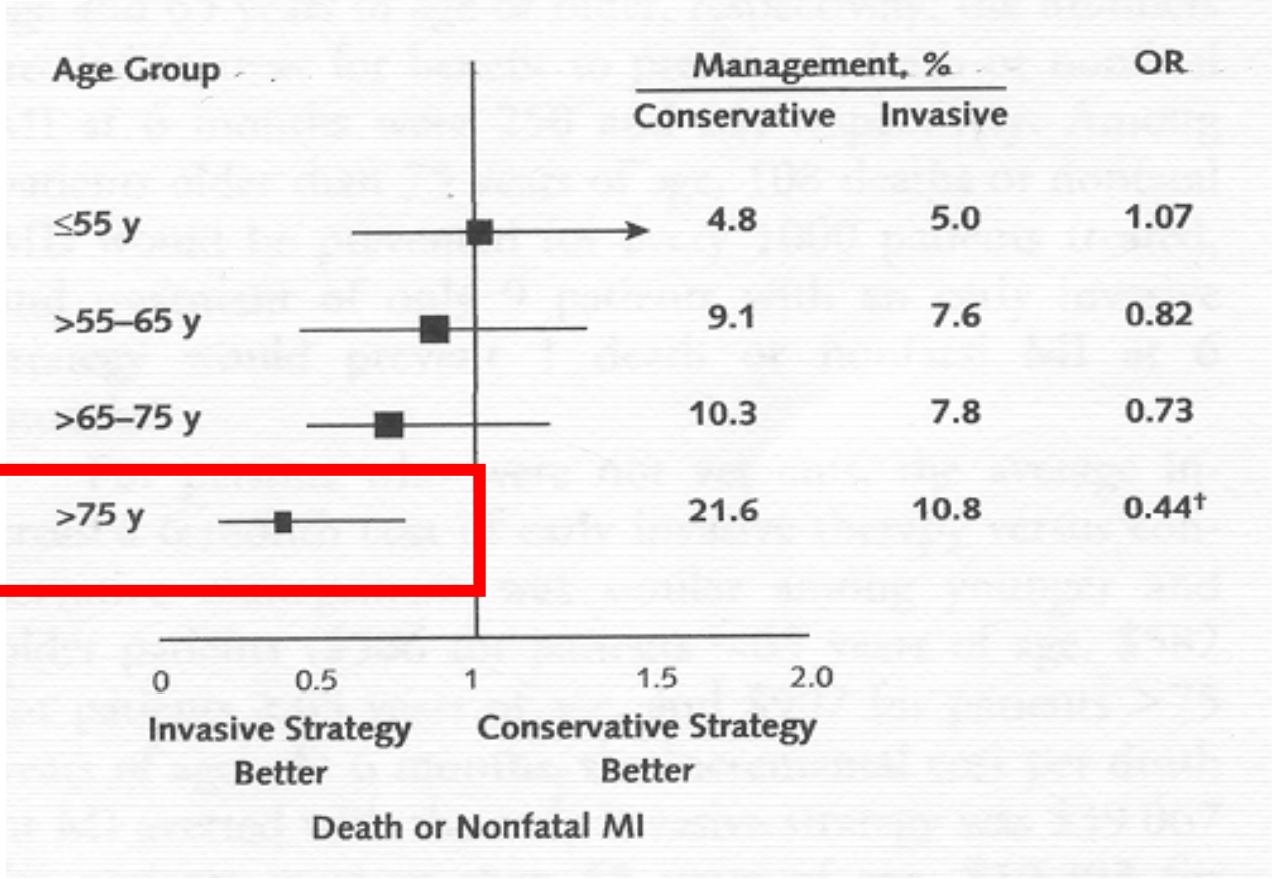
Invasive treatment of elderly ACS patients

- **Evidence (?)**
- Procedural and post-procedural risk
- Bleeding risk

Randomised trials of early invasive treatment in elderly patients with NSTEACS

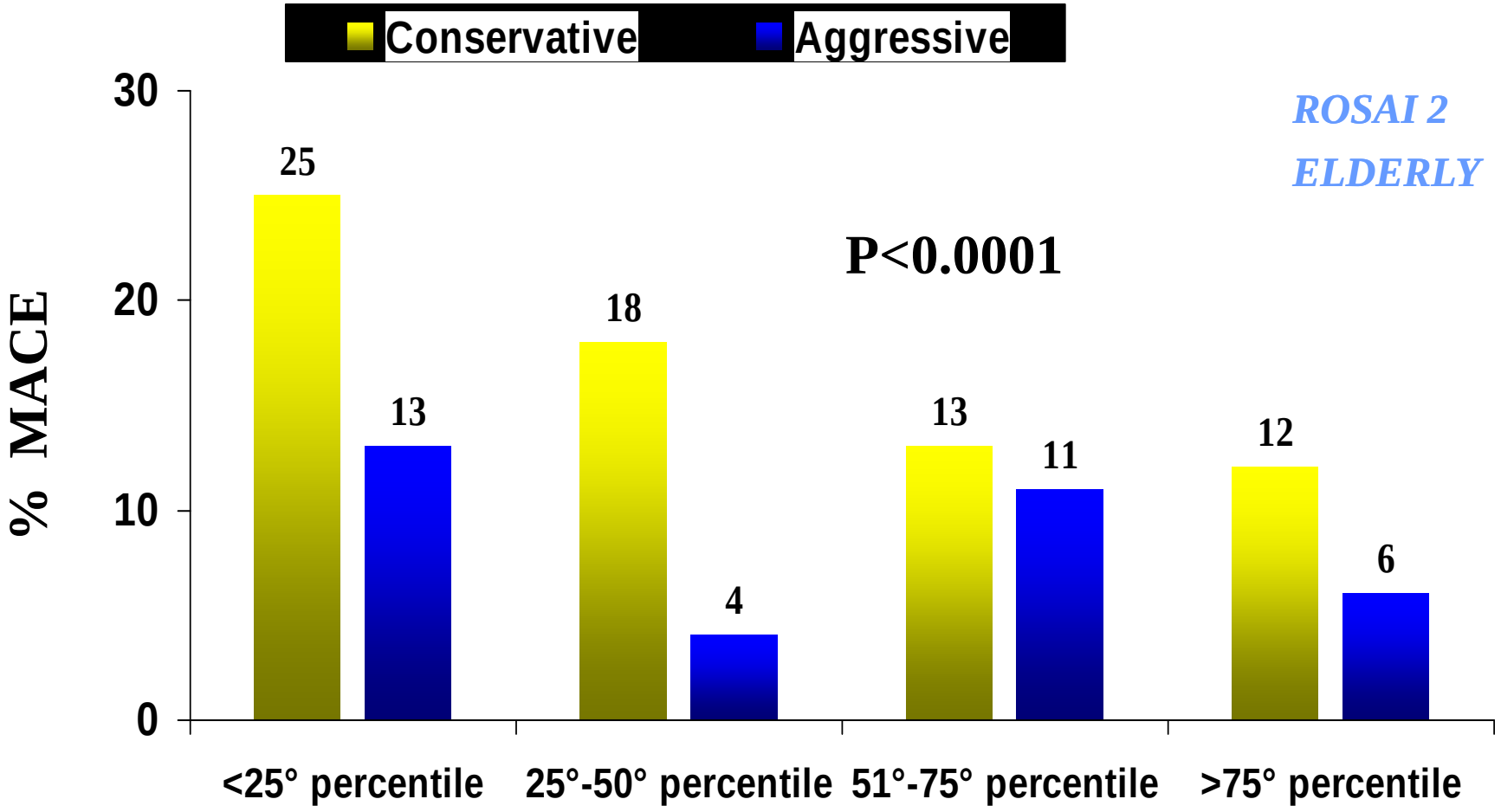
Trial	Average age	% pts ≥75y	Outcome
TIMI IIIB	59	3	Benefit only >65 y
VANQWISH	61	8	No difference
FRISC II	65	Excluded	Benefit only >65 y
RITA 3	63	No age classes reported	Not reported by age
TACTICS	62	12.5	39% RR >65 56% RR >75
ICTUS	61	Not reported	Trend towards > benefit >65y

Elderly patients with NSTE-ACS: early invasive management on outcome at 6 months in the TACTICS-TIMI 18 trial



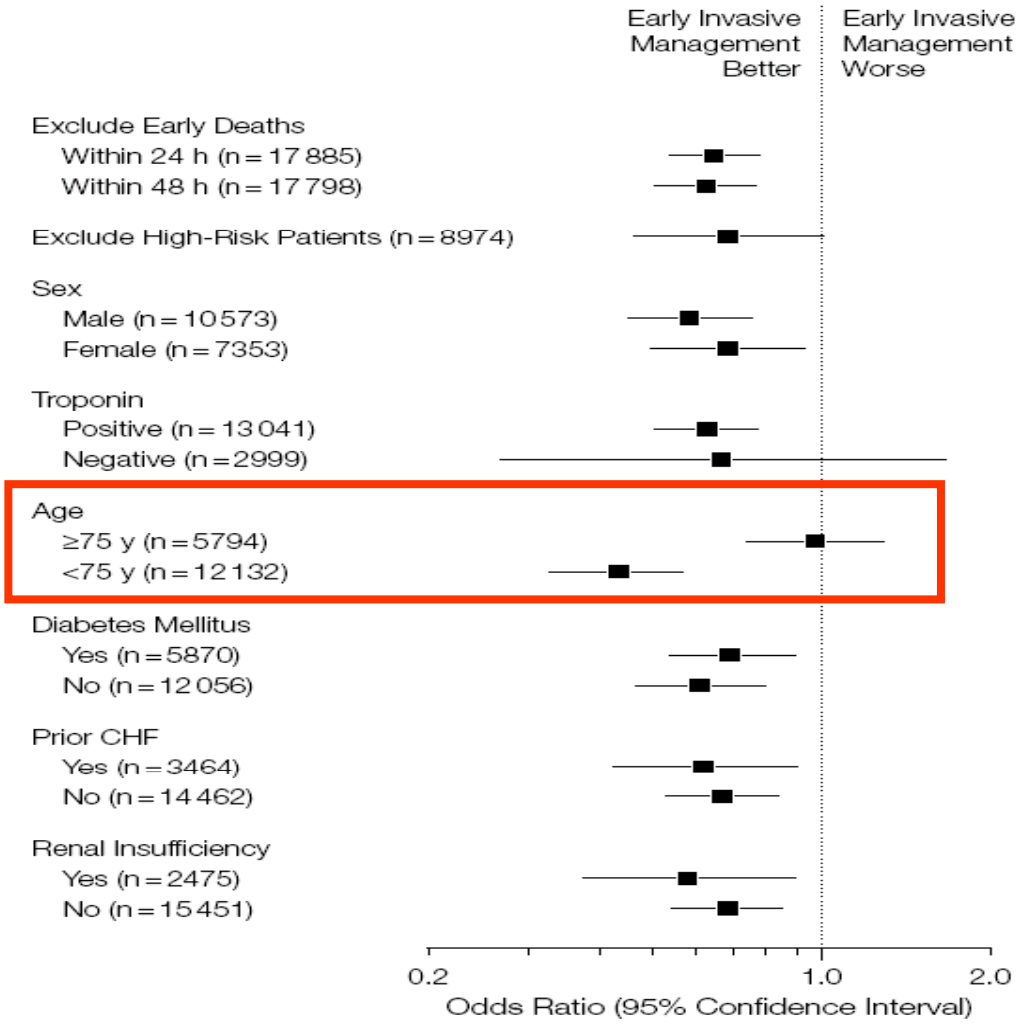
RG Bach et al Ann Intern Med 2004;141:186-195

Major events rate according to propensity score strata



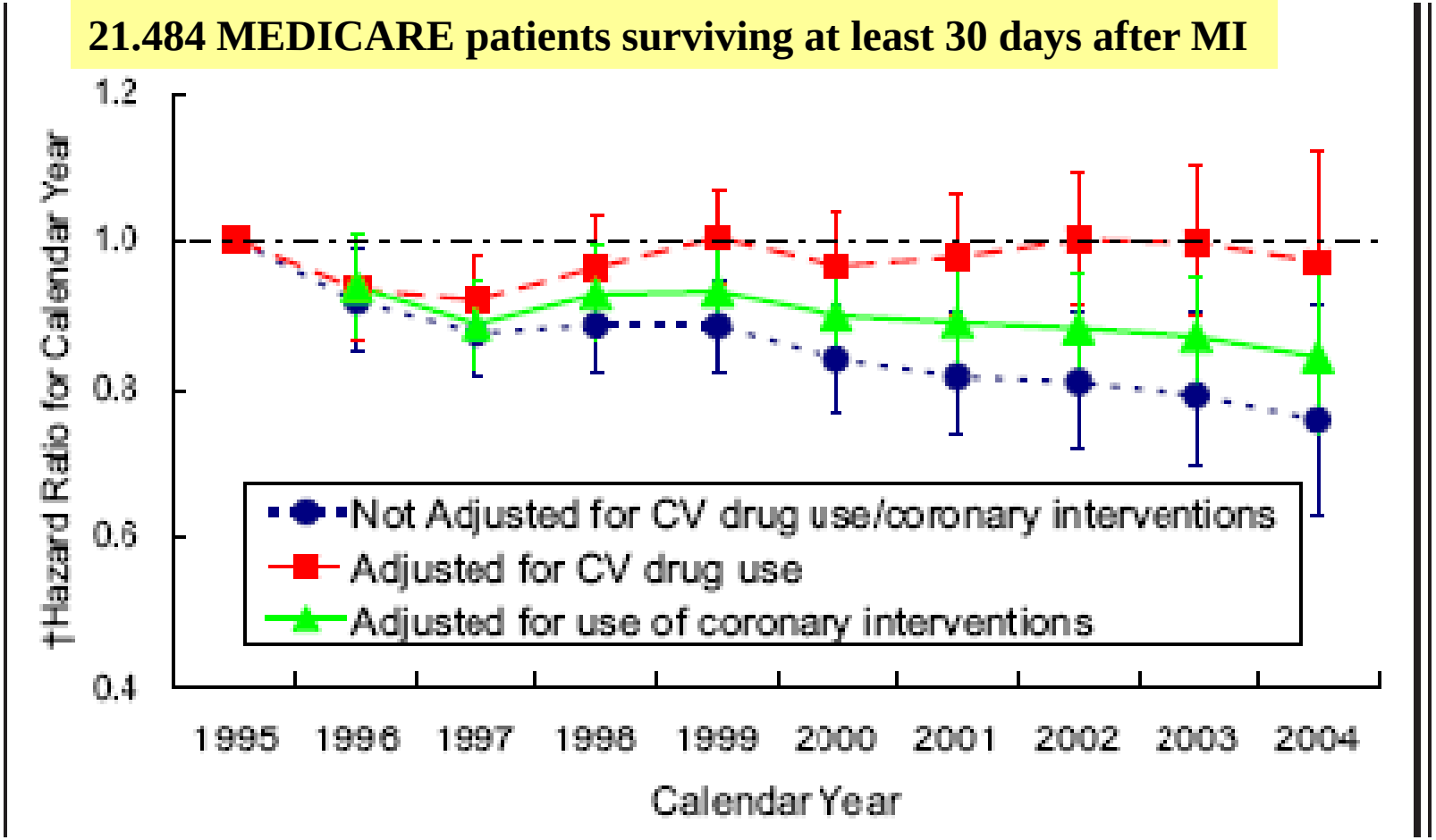
De Servi S et al, Am Heart J 2004

Sensitivity and Subgroup Analyses for Adjusted In-Hospital Mortality by Utilization of an Early Invasive Management Strategy (CRUSADE)



Improvement in long-term mortality in elderly patients with MI and increased use of CV medications after discharge

21.484 MEDICARE patients surviving at least 30 days after MI



"The observed improvement in long-term mortality in elderly patients with MI may be mainly due to increased use of cardiovascular medications after discharge."

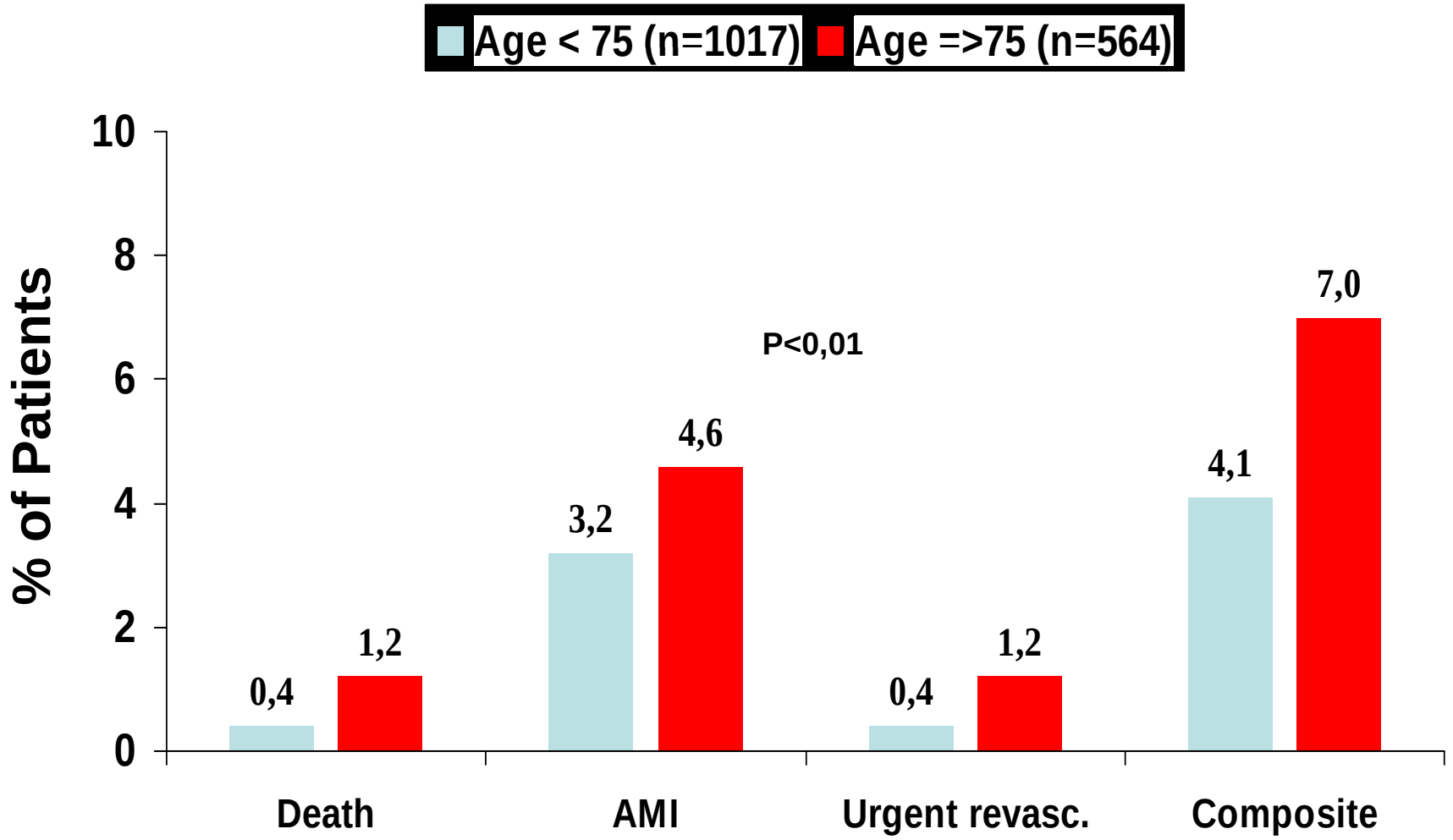
Setoguchi S. JACC 2008;51:1247-54

Invasive treatment of elderly ACS patients

- Evidence (?)
- **Procedural and post-procedural risk**
- Bleeding risk

Complications after PCI in ROSAI-2 registry

S.De Servi et al, AHJ 2004



PCI in the elderly : Increased Procedural Risk

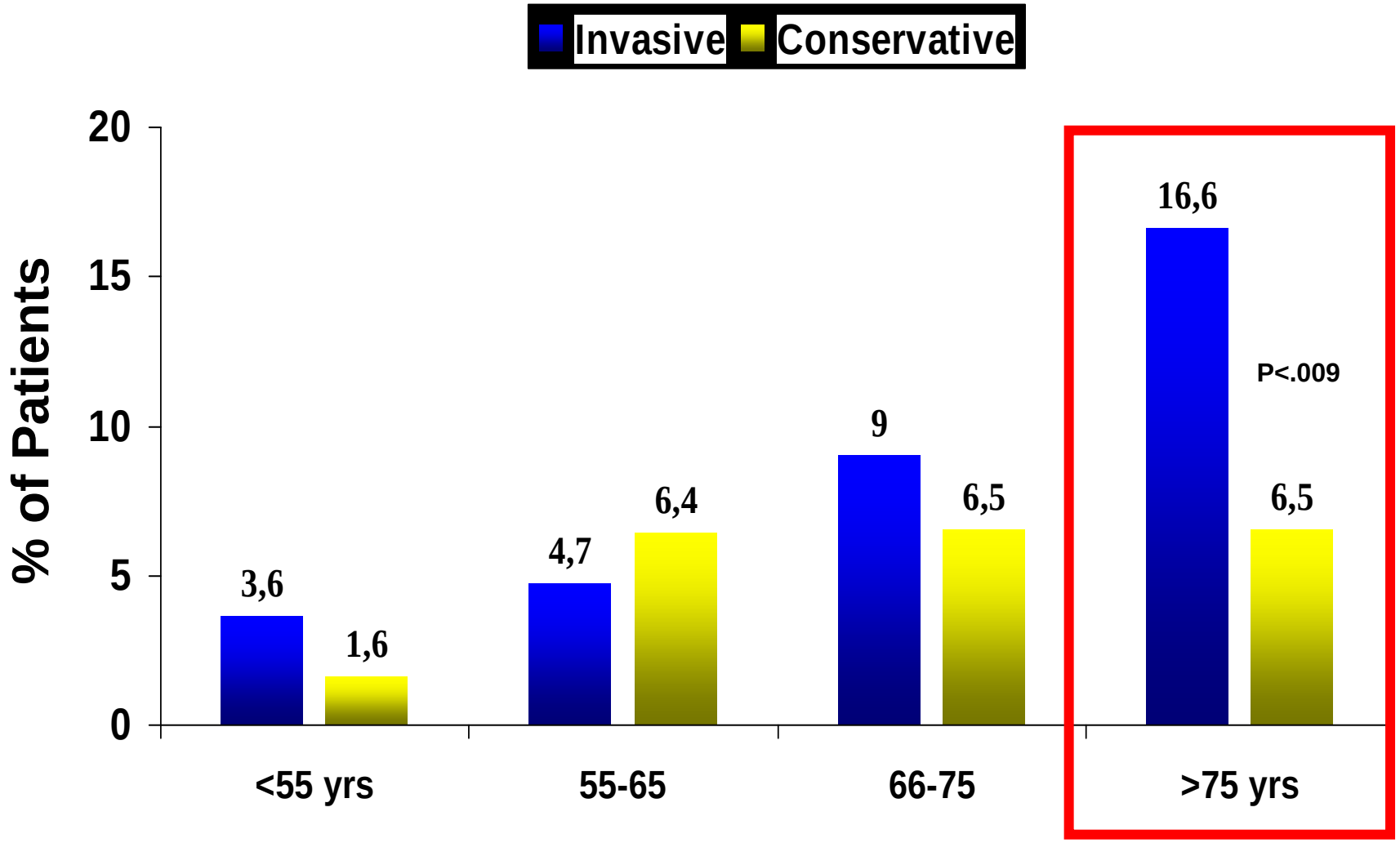
- **Associated morbid conditions (chronic renal failure, anemia, CHF , PVD ….)**
- **Complex anatomy (calcific tortuous lesions , diffuse and severe coronary disease …)**
- **Incomplete revascularization**
- **Increased risk of acute and subacute stent thrombosis**

Invasive treatment of elderly ACS patients

- Evidence (?)
- Procedural and post-procedural risk
- **Bleeding risk**

Bleeding complications associated with early invasive vs conservative strategy in TACTICS-TIMI 18

Bach RG et al, Ann Intern Med 2004;141:186



Advanced Age, Antithrombotic Strategy, and Bleeding in Non–ST-Segment Elevation Acute Coronary Syndromes

Results From the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) Trial

Renato D. Lopes, MD, PhD,* Karen P. Alexander, MD,* Steven V. Manoukian, MD,† Michel E. Bertrand, MD,‡ Frederick Feit, MD,§ Harvey D. White, MD,‖ Charles V. Pollack, Jr, MD, MA,¶ James Hoekstra, MD,# Bernard J. Gersh, MB, ChB, DPhil,** Gregg W. Stone, MD,†† E. Magnus Ohman, MD*

Durham and Winston-Salem, North Carolina; Nashville, Tennessee; Lille, France; New York, New York; Auckland, New Zealand; Philadelphia, Pennsylvania; and Rochester, Minnesota

(J Am Coll Cardiol 2009;53:1021–30)

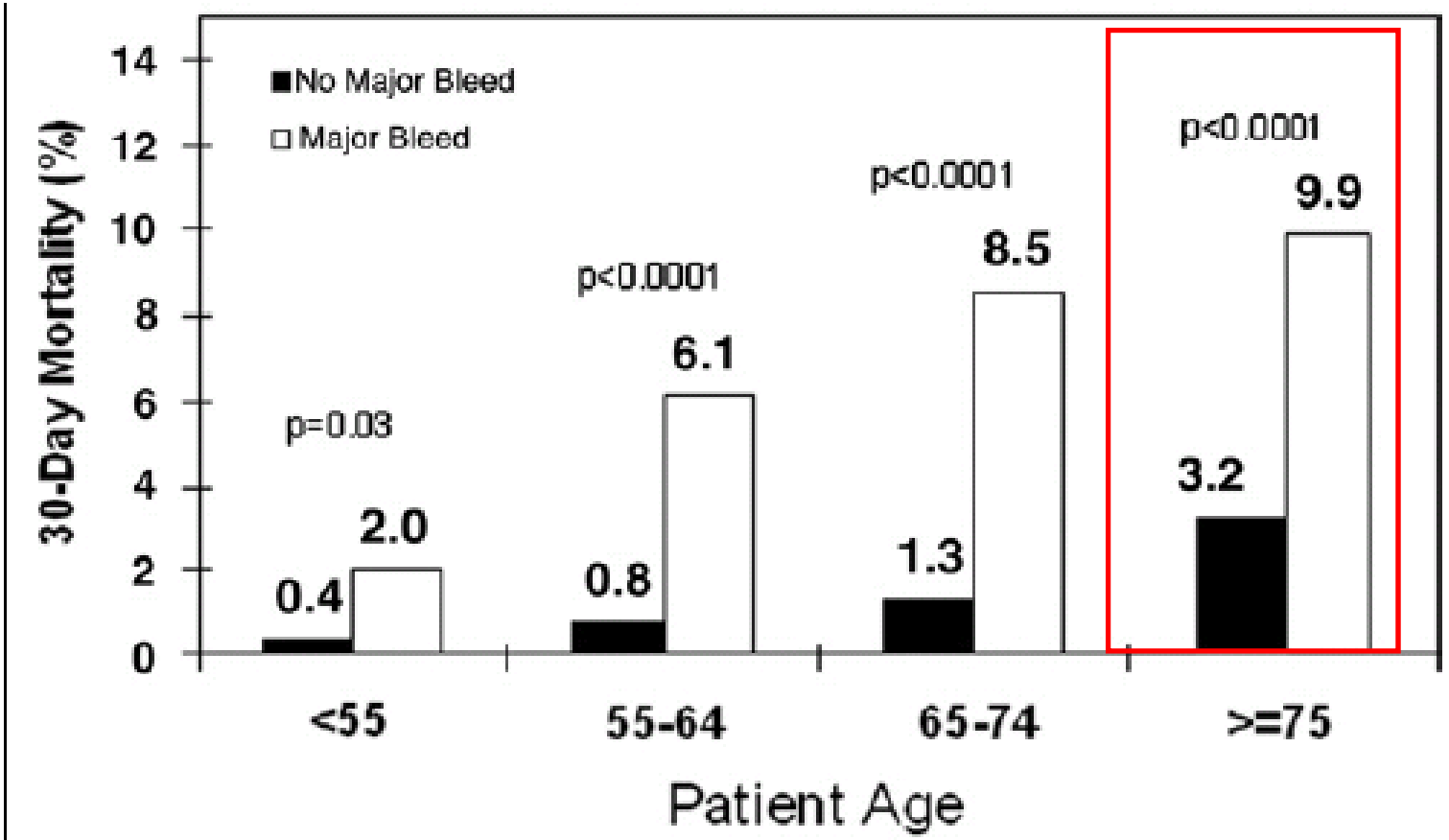


Figure 3 Mortality Rates Among Patients With and Without ACUITY Non-CABG Major Bleeding

Advanced Age, Antithrombotic Strategy, and Bleeding in Non–ST-Segment Elevation Acute Coronary Syndromes

Results From the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) Trial

Renato D. Lopes, MD, PHD,* Karen P. Alexander, MD,* Steven V. Manoukian, MD,† Michel E. Bertrand, MD,‡ Frederick Feit, MD,§ Harvey D. White, MD,‖ Charles V. Pollack, JR, MD, MA,¶ James Hoekstra, MD,# Bernard J. Gersh, MB, CHB, DPHIL,** Gregg W. Stone, MD,†† E. Magnus Ohman, MD*

Durham and Winston-Salem, North Carolina; Nashville, Tennessee; Lille, France; New York, New York; Auckland, New Zealand; Philadelphia, Pennsylvania; and Rochester, Minnesota

(J Am Coll Cardiol 2009;53:1021–30)

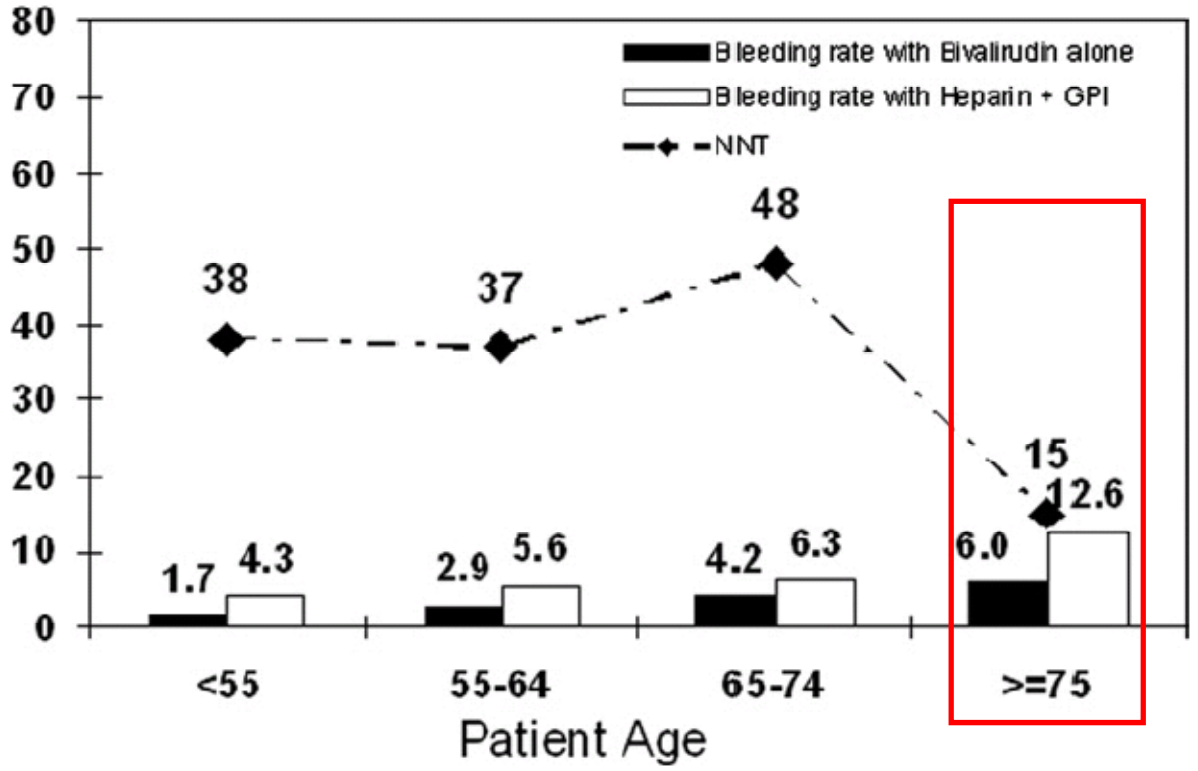


Figure 2 NNT With Bivalirudin Alone Versus Heparin Plus GP IIb/IIIa Inhibitors to Avoid 1 Non-CABG Major Bleeding Event Among Patients Without Excess Dose

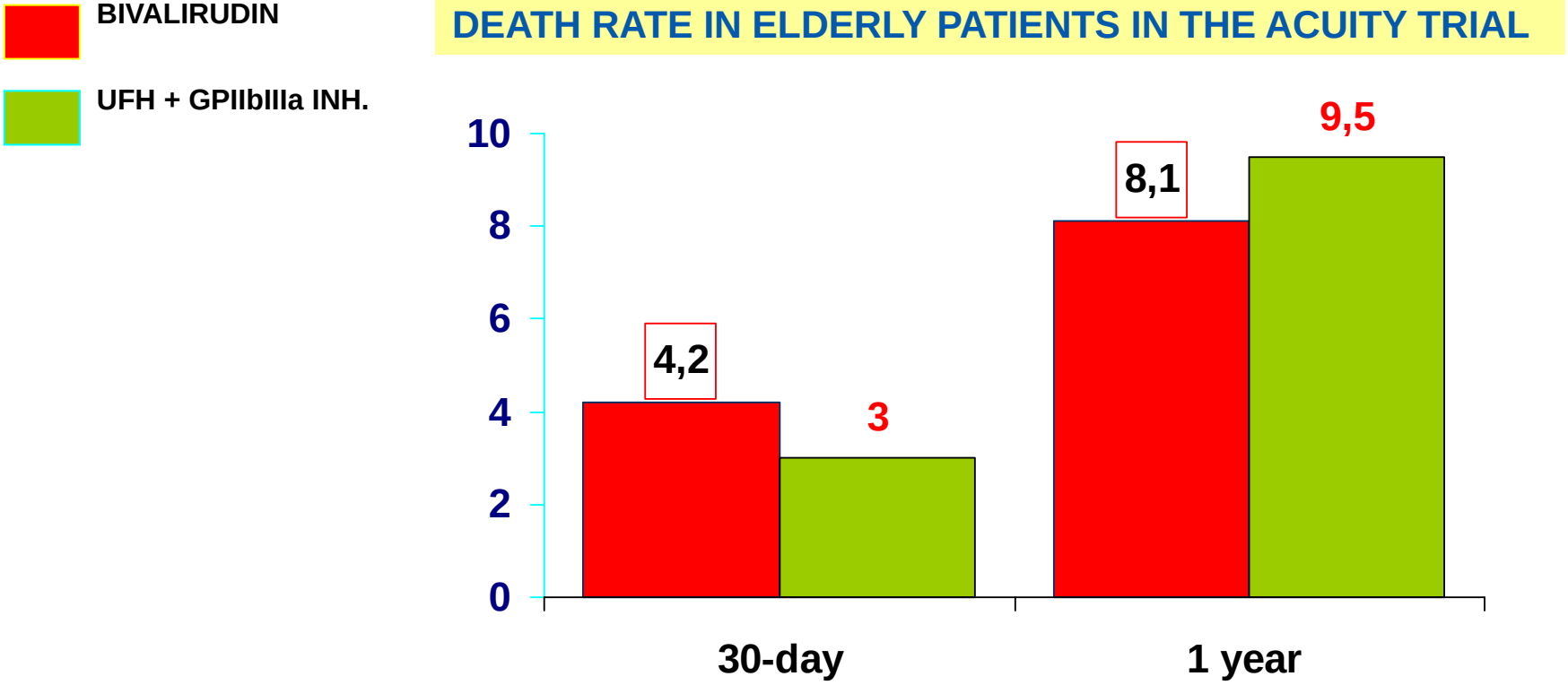
Advanced Age, Antithrombotic Strategy, and Bleeding in Non–ST-Segment Elevation Acute Coronary Syndromes

Results From the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) Trial

Renato D. Lopes, MD, PHD,* Karen P. Alexander, MD,* Steven V. Manoukian, MD,†
Michel E. Bertrand, MD,‡ Frederick Feit, MD,§ Harvey D. White, MD,‖
Charles V. Pollack, JR, MD, MA,¶ James Hoekstra, MD,# Bernard J. Gersh, MB, CHB, DPHIL,**
Gregg W. Stone, MD,†† E. Magnus Ohman, MD*

Durham and Winston-Salem, North Carolina; Nashville, Tennessee; Lille, France; New York, New York; Auckland, New Zealand; Philadelphia, Pennsylvania; and Rochester, Minnesota

DEATH RATE IN ELDERLY PATIENTS IN THE ACUITY TRIAL



AHA Scientific Statement

Acute Coronary Care in the Elderly, Part I

Non–ST-Segment–Elevation Acute Coronary Syndromes

A Scientific Statement for Healthcare Professionals From the American Heart Association Council on Clinical Cardiology

In Collaboration With the Society of Geriatric Cardiology

Karen P. Alexander, MD; L. Kristin Newby, MD, MHS, FAHA; Christopher P. Cannon, MD, FAHA; Paul W. Armstrong, MD, FAHA; W. Brian Gibler, MD; Michael W. Rich, MD, FAHA; Frans Van de Werf, MD, PhD; Harvey D. White, MB, DSc, FAHA; W. Douglas Weaver, MD, FAHA; Mary D. Naylor, PhD, FAHA; Joel M. Gore, MD, FAHA; Harlan M. Krumholz, MD, FAHA; E. Magnus Ohman, MD, Chair

Clinical trial evidence is limited with regard to the efficacy and hazards of pharmacological and invasive management of NSTE ACS in the elderly.

Elderly-specific trials may be needed in certain therapeutic areas to increase certainty about treatment effects and to further our understanding of age-related variability.

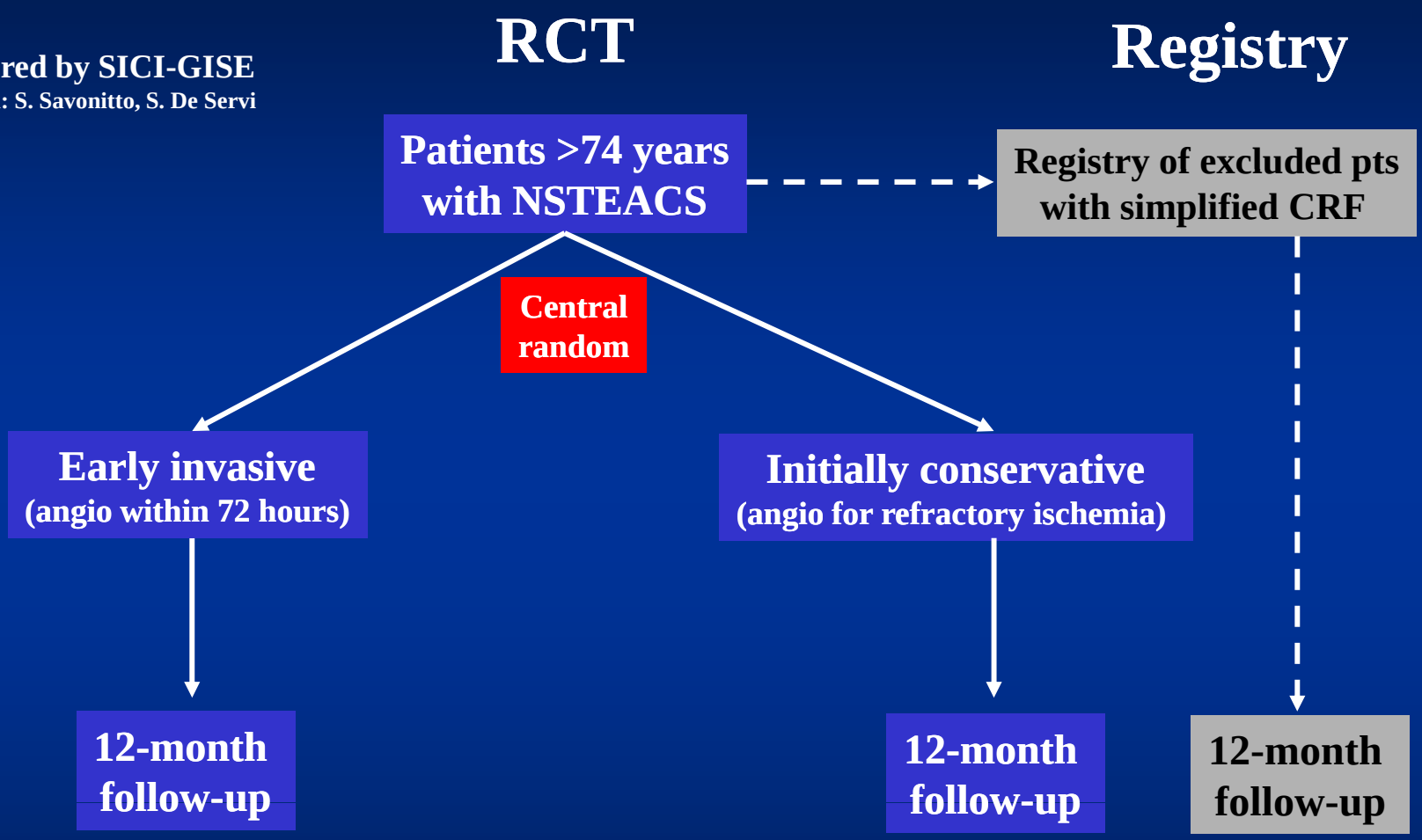
Circulation. 2007;115:2549-2569

The Italian **Elderly** – ACS Study

HOME

Sponsored by SICI-GISE

Chairmen: S. Savonitto, S. De Servi



Primary endpoint

the composite of all-cause mortality, myocardial (re)MI, disabling stroke and re-hospitalization for cardiovascular causes or severe bleeding within 12 months

ClinicalTrials.gov ID: NCT00510185

website: http://elderly.altavianet.it

Patients

Inclusion criteria

- Be >74 year old
- Have had symptoms suggestive of acute myocardial ischemia at rest within 48 h prior to randomization, together with
  - a) ischemic ECG changes and/or
  - b) elevated biochemical markers of myocardial damage.
- Provide written informed consent before randomization.

Patients

Exclusion criteria - I

- Secondary causes of myocardial ischemia
- Ongoing ischemia despite maximally titrated anti-ischemic therapy
- Ongoing signs of heart failure despite treatment
- PCI or surgery within 30 days prior to randomization

Sample size and power calculations: Amendment 1

Calculations are based on the primary-endpoint rates at 12 months in pts >75y adjusted from event rates observed in the retrospective analysis of the TACTICS-TIMI 18 trial, with a primary endpoint rate of 40% in the conservative arm.

In the present study, we aim at detecting superiority of an initially invasive approach with a PE reduction to 25%.

	Two-tailed alpha	Power 1 – β	N per group	N total
ICTUS, STEEPLE ISAR STUDIES	0.05	80	156	312
	0.05	85	175	350
	0.05	90	209	418

The Italian **Elderly** – ACS Study

FIC Federazione Italiana di Cardiologia
Italian Federation of Cardiology

Società Italiana di Cardiologia Invasiva

Chairmen: S. Savonitto, S. De Servi

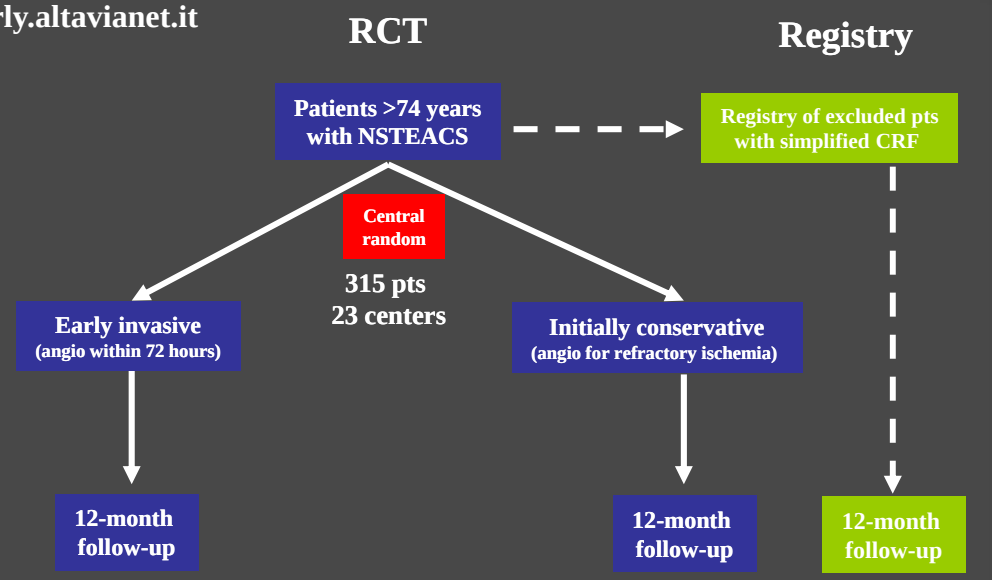
ClinicalTrials.gov ID: **NCT00510185**
website: http://elderly.altavianet.it

Inclusion criteria

- Be >74 year old
- Symptoms suggestive of acute myocardial ischemia at rest within 48 h prior to randomization, together with
  - a) ischemic ECG changes and/or
  - b) elevated CKMB or Tn.
- Written informed consent before randomization.

Main exclusion criteria

- Secondary causes of myocardial ischemia
- Ongoing ischemia despite maximal anti-ischemic rx
- Ongoing signs of heart failure despite treatment
- PCI or surgery within 30 days prior to randomization
- Serum creatinine level >2.5 mg/dL
- History of severe bleeding
- Cerebrovascular accident within the previous month
- Known platelet count of <90,000 cells/mL



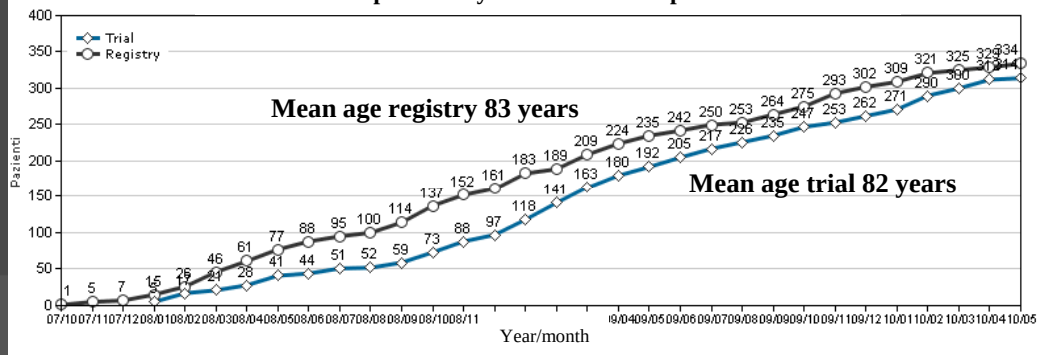
Primary endpoint
the composite of all-cause mortality, myocardial (re)MI, disabling stroke and re-hospitalization for cardiovascular causes or severe bleeding within 12 months

Study design: Savonitto S, J Cardiovasc Med 2008;9:217

Criteria for angiography in the conservative arm

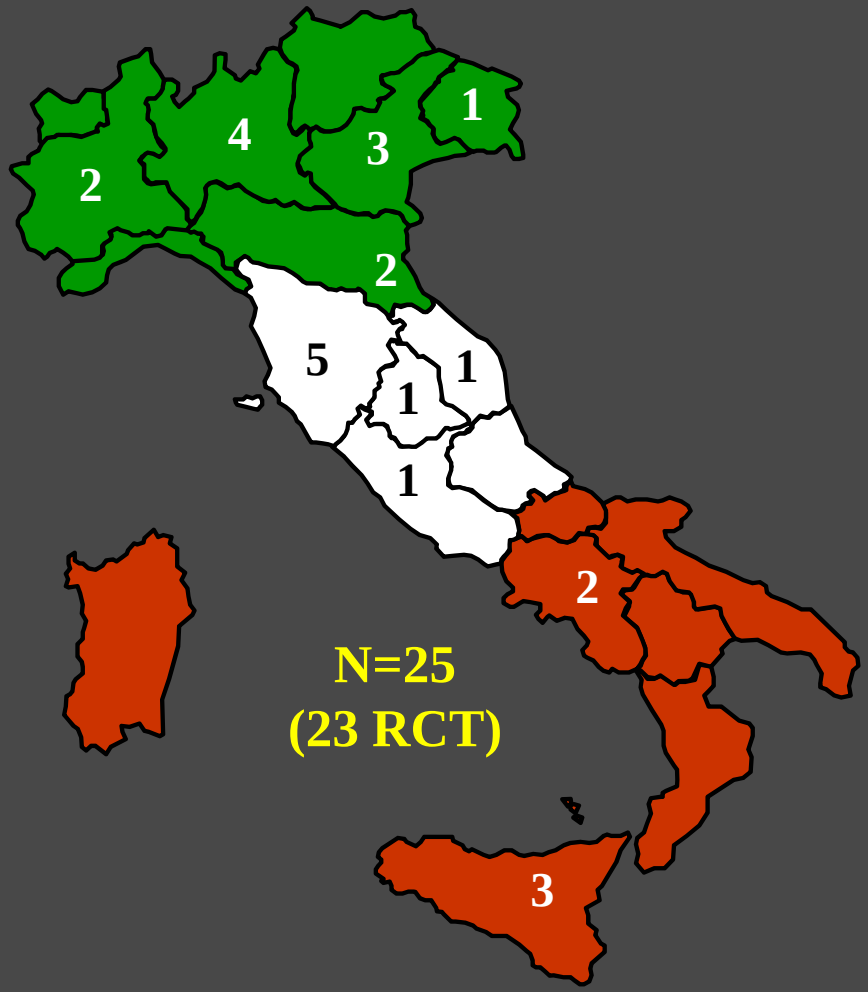
during index admission	after index discharge
• Refractory ischemia: recurrent symptoms and ECG changes >12 hrs after admission despite maximal therapy • Post-admission (re)MI • Heart failure • Malignant ventricular arrhythmia	Recurrent ischemic symptoms (CCS III-IV) despite optimal antianginal therapy, particularly if ischemia shown at provocative testing

Enrolment completed May 2010 – Results expected summer 2011



Centers declaring participation: august 2007

"Active Centers"



Centers

Centers without on-site cathlab
operating in network
with a nearby cathlab able to perform coronary angiography within 48 hours after patient enrolment, or earlier in case of emergency

Centers with on-site cathlab
and a program of
nonsistematic angiography in the study population

Average enrolment / center / month

Years 2008-2010

315 patients / 23 centers / 29 months

= 0.47 patients / center / month

Years 1998-2000

2220 patients / 196 centers / 24 months

= 0.54 patients / center / month

Presentations & Publication

- **GISE MEETING, October 2010, GENOVA: BASELINE DATA**

- **ESC CONGRESS 2011: COMPLETE PRESENTATION 1-YEAR DATA**

Long-Term Outcome of a Routine Versus Selective Invasive Strategy in Patients With Non–ST-Segment Elevation Acute Coronary Syndrome

A Meta-Analysis of Individual Patient Data

Keith A. A. Fox, BSc, MB, ChB,* Tim C. Clayton, BSc, MSc,† Peter Damman, MD,‡ Stuart J. Pocock, BSc, MSc, PhD,† Robbert J. de Winter, MD, PhD,‡ Jan G. P. Tijssen, PhD,‡ Bo Lagerqvist, MD, PhD,§ Lars Wallentin, MD, PhD,§ for the FIR Collaboration

Edinburgh and London, United Kingdom; Amsterdam, the Netherlands; and Uppsala, Sweden

JACC Vol. 55, No. 22, 2010
June 1, 2010:2435–45

						Add to score
Age (years)	<60 0	60-64 +1	65-69 +2	70-74 +3	≥75 +5	
Diabetes	No 0			Yes +4		
Previous MI	No 0			Yes +3		
ST-depression	No 0			Yes +2		
Hypertension	No 0			Yes +1		
BMI	<25 +1		25-<35 0		≥35 +2	
			Total Score			

Figure 6 Nomogram for Integer-Based Risk Score for CV Death or MI at 5 Years

5-years CV death and MI in the pooled analysis of FRISC II-ICTUS-RITA 3

Long-Term Outcome of a Routine Versus Selective Invasive Strategy in Patients With Non–ST-Segment Elevation Acute Coronary Syndrome

A Meta-Analysis of Individual Patient Data

Keith A. A. Fox, BSc, MB, ChB,* Tim C. Clayton, BSc, MSc,† Peter Damman, MD,‡ Stuart J. Pocock, BSc, MSc, PhD,† Robbert J. de Winter, MD, PhD,‡ Jan G. P. Tijssen, PhD,‡ Bo Lagerqvist, MD, PhD,§ Lars Wallentin, MD, PhD,§ for the FIR Collaboration

Edinburgh and London, United Kingdom; Amsterdam, the Netherlands; and Uppsala, Sweden

JACC Vol. 55, No. 22, 2010
June 1, 2010:2435–45

Table 5 Treatment Effect by Integer Risk Category of CV Death or MI

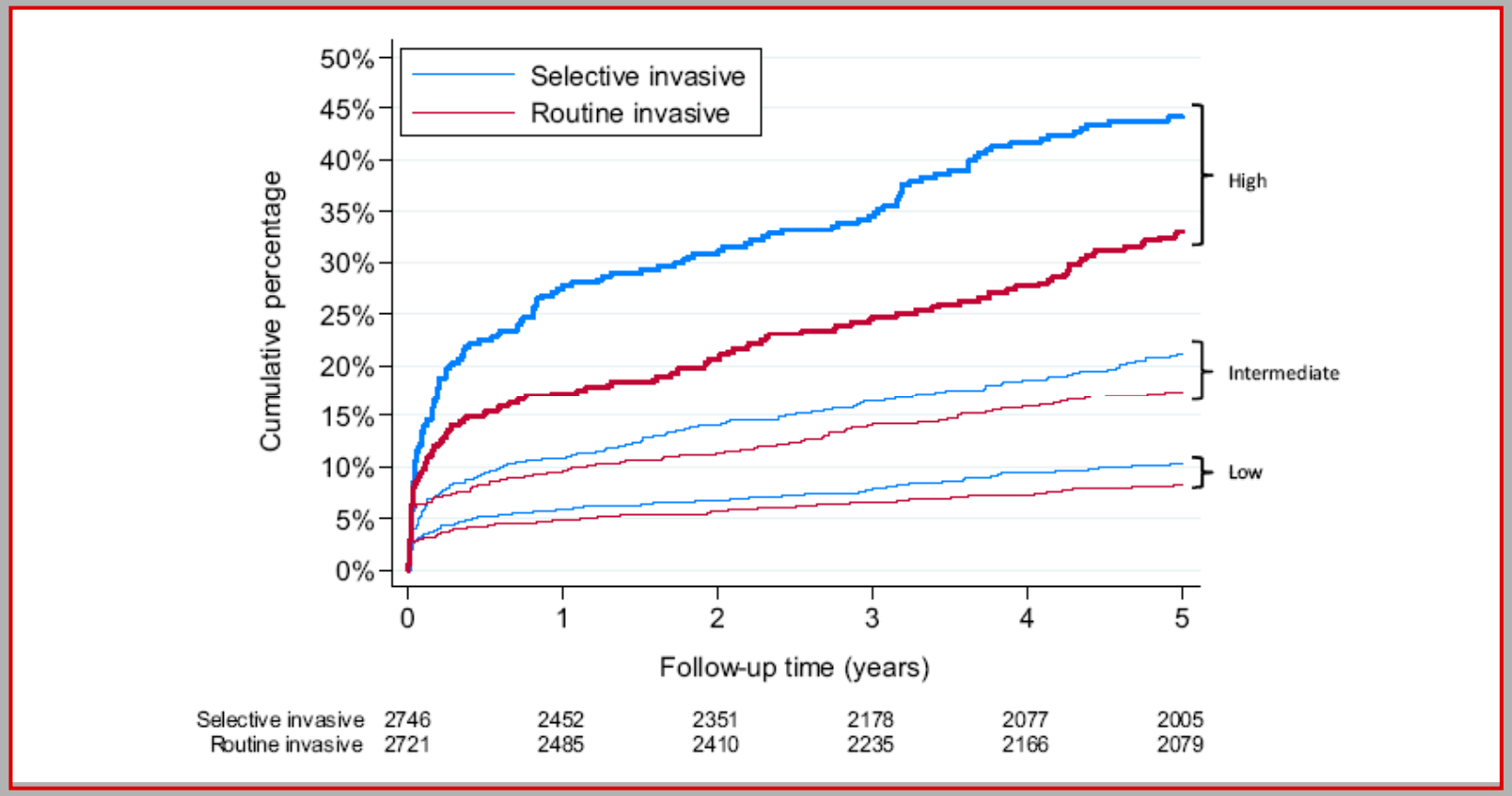
Risk Group*	Risk Score	Treatment Group		HR† (95% CI)	Risk Difference‡ (95% CI)
		SI	RI		
1st (low)	0–4	149/1,503 (10.2%)	114/1,423 (8.2%)	0.80 (0.63 to 1.02)	-2.0% (-4.1% to 0.1%)
2nd (moderate)	5–8	186/912 (21.1%)	155/920 (17.3%)	0.81 (0.66 to 1.01)	-3.8% (-7.4% to -0.1%)
3rd (high)	≥9	140/331 (44.1%)	120/378 (33.0%)	0.68 (0.53 to 0.86)	-11.1% (-18.4% to -3.8%)
Total		475/2,746 (17.9%)	389/2,721 (14.7%)		

Long-Term Outcome of a Routine Versus Selective Invasive Strategy in Patients With Non–ST-Segment Elevation Acute Coronary Syndrome

A Meta-Analysis of Individual Patient Data

Keith A. A. Fox, BSc, MB, ChB,* Tim C. Clayton, BSc, MSc,† Peter Damman, MD,‡
Stuart J. Pocock, BSc, MSc, PhD,† Robbert J. de Winter, MD, PhD,‡ Jan G. P. Tijssen, PhD,‡
Bo Lagerqvist, MD, PhD,§ Lars Wallentin, MD, PhD,§ for the FIR Collaboration
Edinburgh and London, United Kingdom; Amsterdam, the Netherlands; and Uppsala, Sweden

JACC Vol. 55, No. 22, 2010
June 1, 2010:2435–45



Long-Term Outcome of a Routine Versus Selective Invasive Strategy in Patients With Non–ST-Segment Elevation Acute Coronary Syndrome

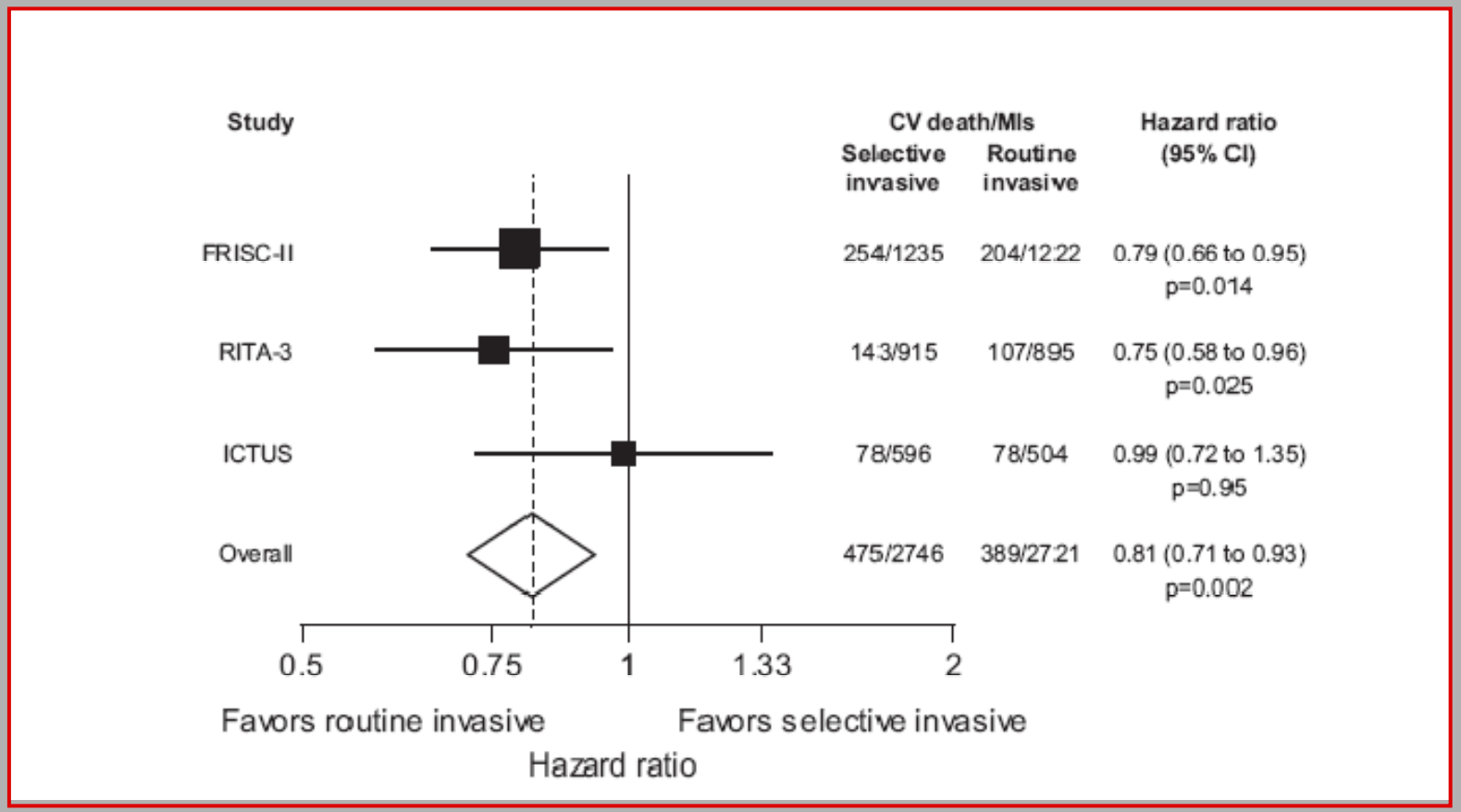
A Meta-Analysis of Individual Patient Data

Keith A. A. Fox, BSc, MB, ChB,* Tim C. Clayton, BSc, MSc,† Peter Damman, MD,‡ Stuart J. Pocock, BSc, MSc, PhD,† Robbert J. de Winter, MD, PhD,‡ Jan G. P. Tijssen, PhD,‡ Bo Lagerqvist, MD, PhD,§ Lars Wallentin, MD, PhD,§ for the FIR Collaboration

Edinburgh and London, United Kingdom; Amsterdam, the Netherlands; and Uppsala, Sweden

JACC Vol. 55, No. 22, 2010
June 1, 2010:2435–45

CV Death and MI – 5 years outcome



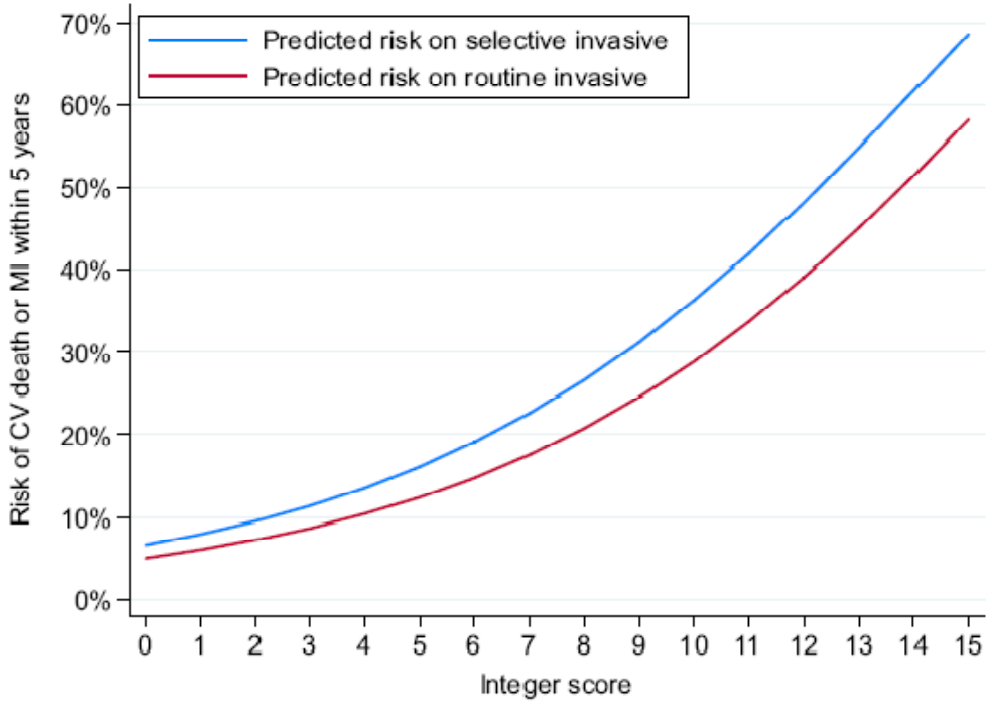
Long-Term Outcome of a Routine Versus Selective Invasive Strategy in Patients With Non–ST-Segment Elevation Acute Coronary Syndrome

A Meta-Analysis of Individual Patient Data

Keith A. A. Fox, BSc, MB, ChB,* Tim C. Clayton, BSc, MSc,† Peter Damman, MD,‡ Stuart J. Pocock, BSc, MSc, PhD,† Robbert J. de Winter, MD, PhD,‡ Jan G. P. Tijssen, PhD,‡ Bo Lagerqvist, MD, PhD,§ Lars Wallentin, MD, PhD,§ for the FIR Collaboration

Edinburgh and London, United Kingdom; Amsterdam, the Netherlands; and Uppsala, Sweden

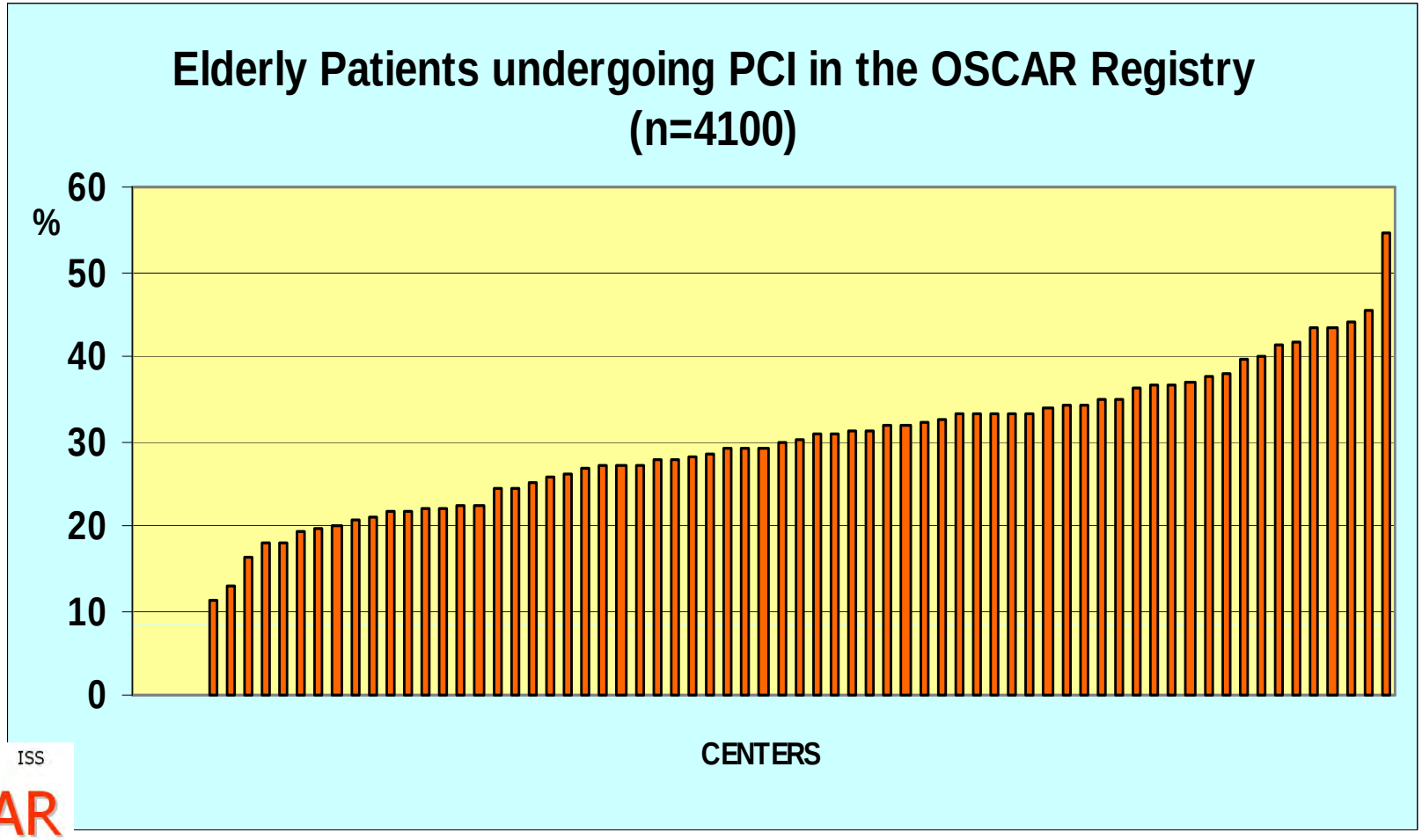
JACC Vol. 55, No. 22, 2010
June 1, 2010:2435–45



Distribution of patients in FIR database

Integer score	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15+	Total
Number of patients	431	525	615	761	594	596	490	415	331	245	174	139	82	31	15	23	5467

DIFFERENT APPROACH TO ELDERLY PATIENTS IN ITALIAN CATH LABS



GISE ISS
OSCAR for Quality

Primary endpoint

The composite of all-cause mortality, myocardial (re)MI, disabling stroke and re-hospitalization for cardiovascular causes or severe bleeding at 12 months

Secondary endpoints

- CV mortality at 1 year
- All-cause mortality and (re)MI at 1 year
- The composite of death, myocardial (re)MI, disabling stroke and re-hospitalization for cardiovascular causes or severe bleeding at 1 year
- Major bleeding within 12 months
- Any stroke within 12 months
- Total n° of days spent in hospital within 12 months after index admission

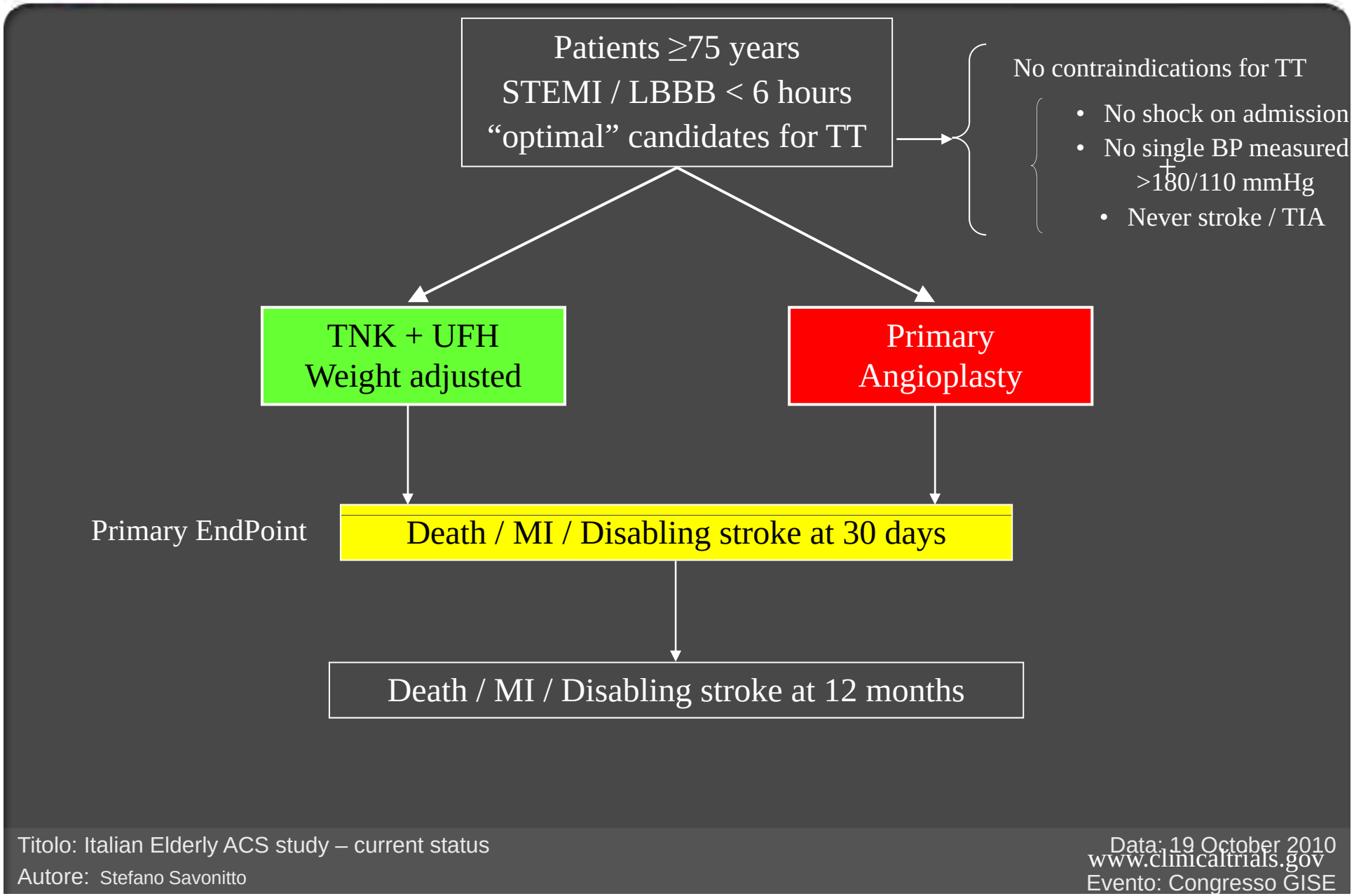
Results: Recruitment

TRIANA

- Study initiated in March 2005
- 23 hospitals participated
- 266 patients were recruited
- Study interrupted in December 2007 for slow recruitment

Study Design

TRIANA



Titolo: Italian Elderly ACS study – current status

Autore: Stefano Savonitto

Data: 19 October 2010

www.clinicaltrials.gov

Evento: Congresso GISE

The Italian **Elderly** – ACS Study

Randomised treatment strategies

Patients >74 years With NSTEACS

Web random

Early invasive
(angio within 72 hours)

Initially conservative
(angio for refractory ischemia)

Angio During index admission

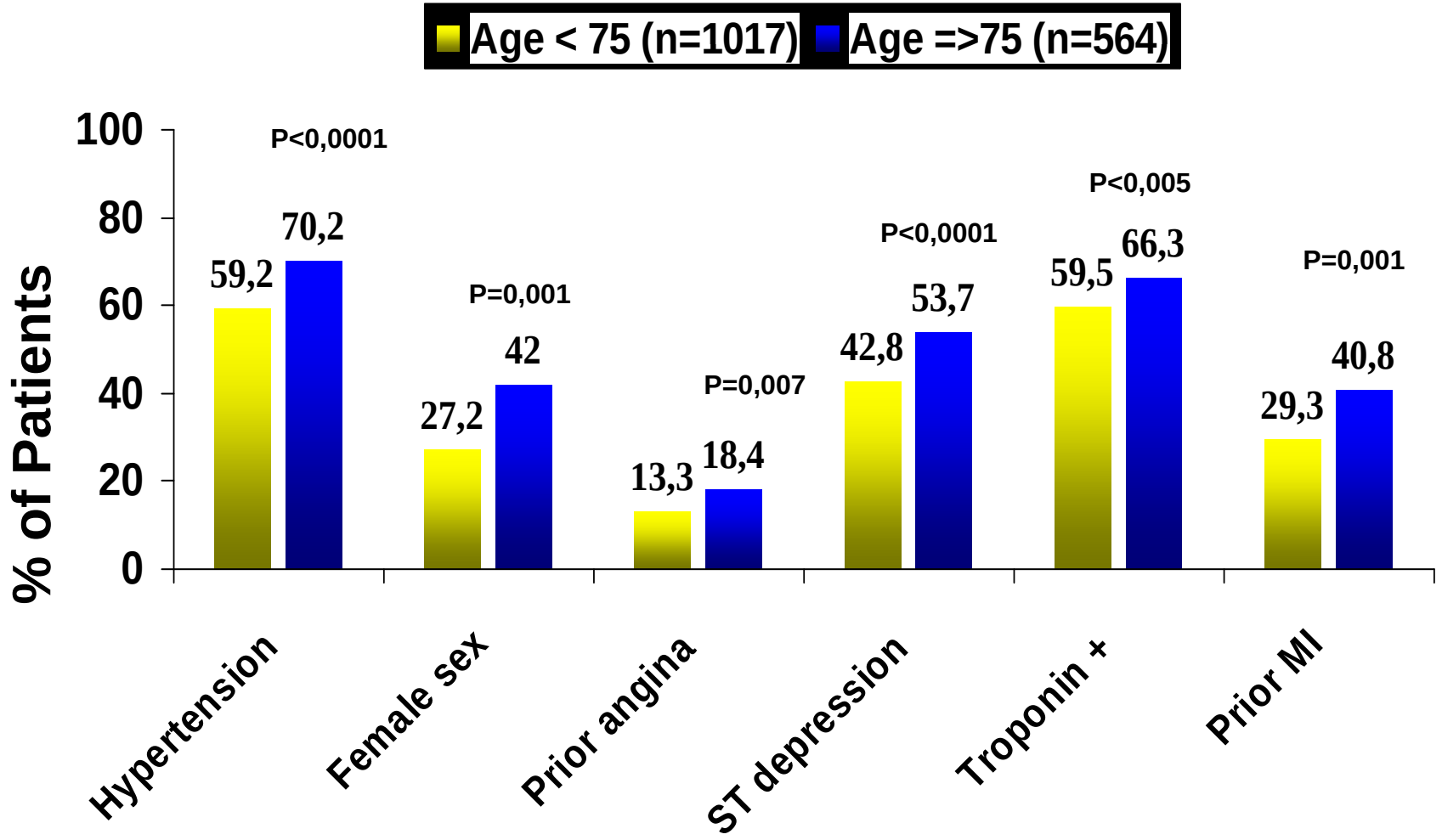
- **Refractory ischemia: recurrent symptoms and ECG changes >12 hrs after admission despite maximal therapy**
- **Post-admission (re)MI**
- **Heart failure**
- **Malignant ventricular arrhythmia**

Angio After index discharge

- **Recurrent ischemic symptoms (CCS III-IV) after index discharge despite optimal antianginal therapy, particularly if ischemia is documented on provocative testing**

Savonitto S, J Cardiovasc Med 2008;9:217

Clinical characteristics of NSTE-ACS patients according to age



Long-Term Outcome of a Routine Versus Selective Invasive Strategy in Patients With Non–ST-Segment Elevation Acute Coronary Syndrome

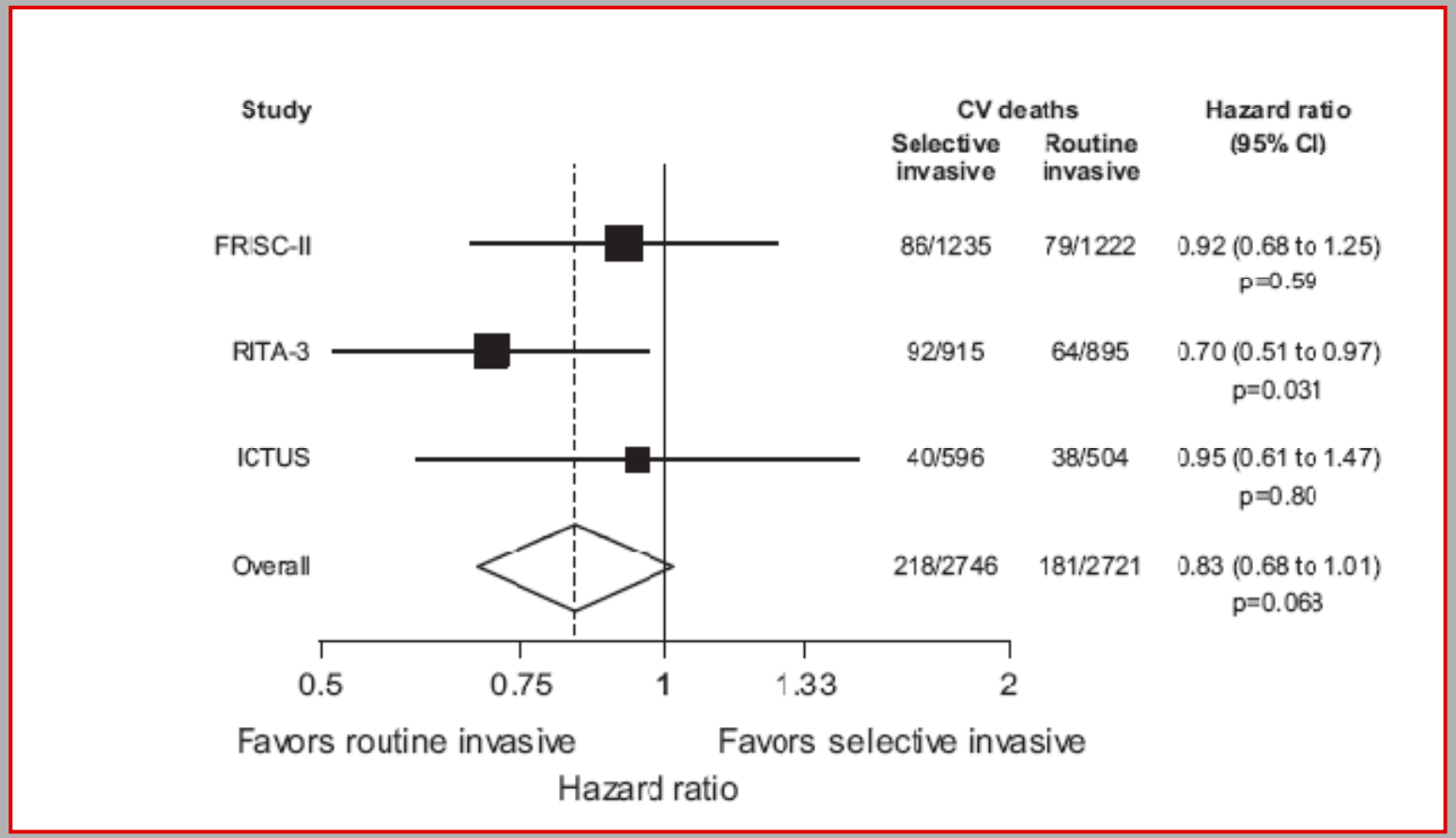
A Meta-Analysis of Individual Patient Data

Keith A. A. Fox, BSc, MB, ChB,* Tim C. Clayton, BSc, MSc,† Peter Damman, MD,‡ Stuart J. Pocock, BSc, MSc, PhD,† Robbert J. de Winter, MD, PhD,‡ Jan G. P. Tijssen, PhD,‡ Bo Lagerqvist, MD, PhD,§ Lars Wallentin, MD, PhD,§ for the FIR Collaboration

Edinburgh and London, United Kingdom; Amsterdam, the Netherlands; and Uppsala, Sweden

JACC Vol. 55, No. 22, 2010
June 1, 2010:2435–45

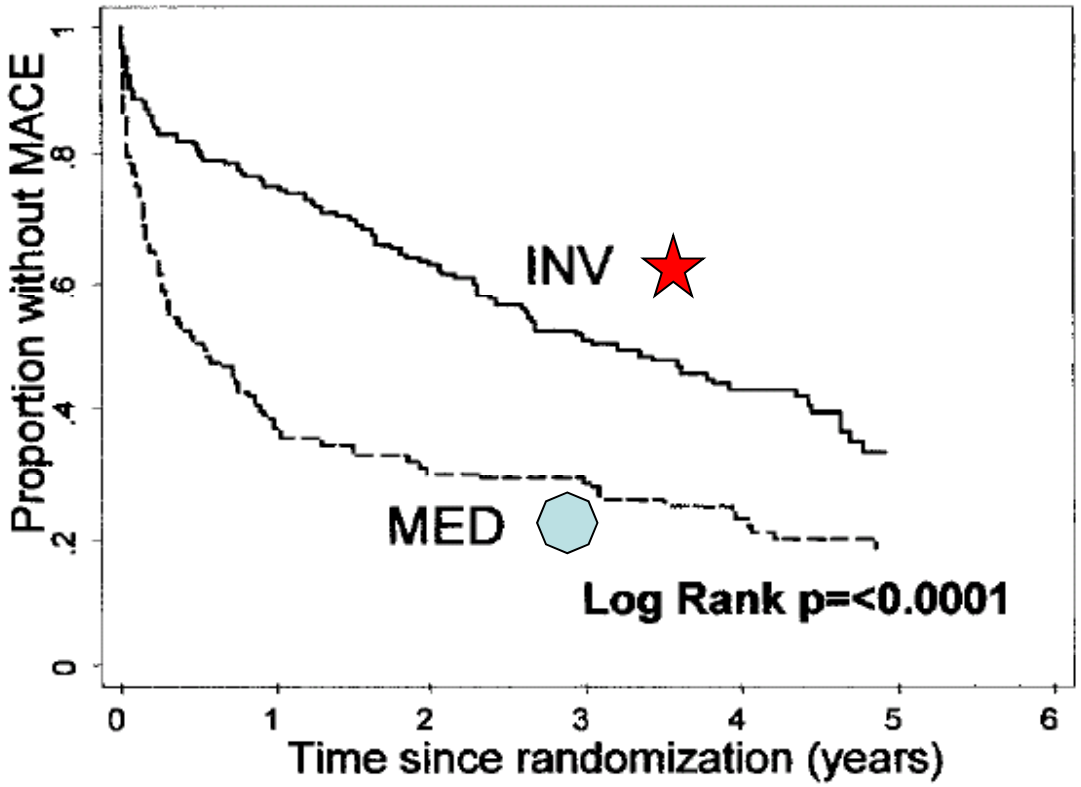
CV Death – 5 years outcome



Long-Term Outcome in Elderly Patients With Chronic Angina Managed Invasively Versus by Optimized Medical Therapy

Four-Year Follow-Up of the Randomized Trial of Invasive Versus Medical Therapy in Elderly Patients (TIME)

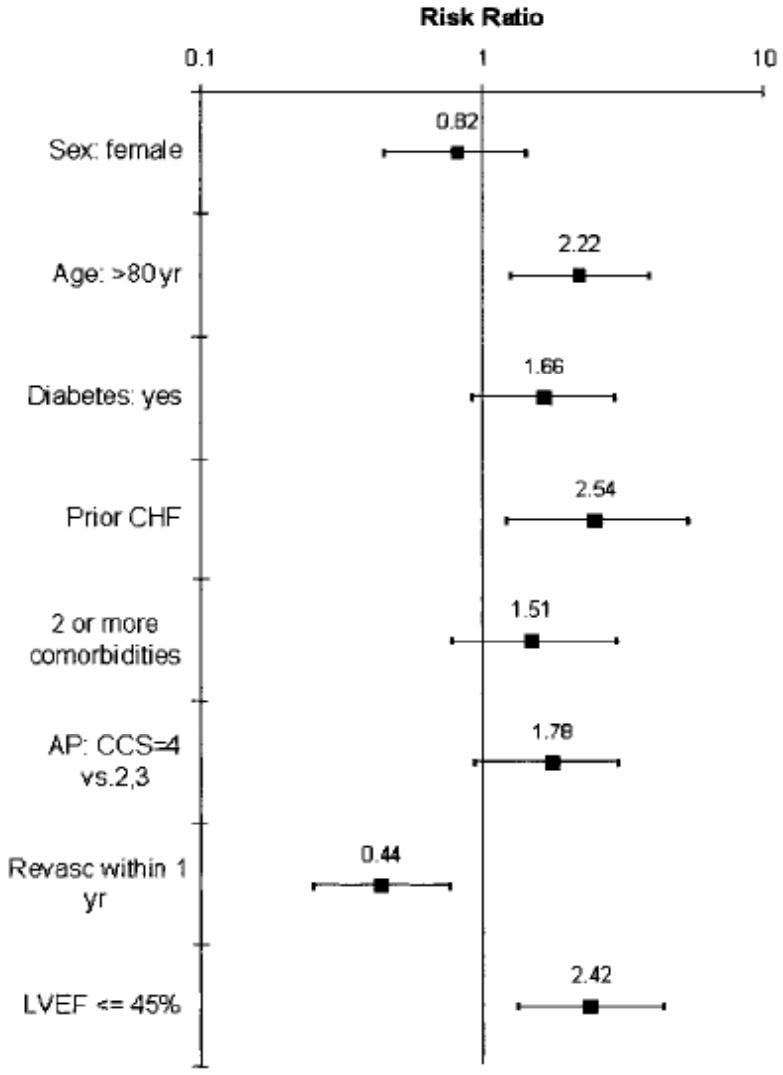
Matthias Pfisterer, MD; for the TIME Investigators*



Long-Term Outcome in Elderly Patients With Chronic Angina Managed Invasively Versus by Optimized Medical Therapy

Four-Year Follow-Up of the Randomized Trial of Invasive Versus Medical Therapy in Elderly Patients (TIME)

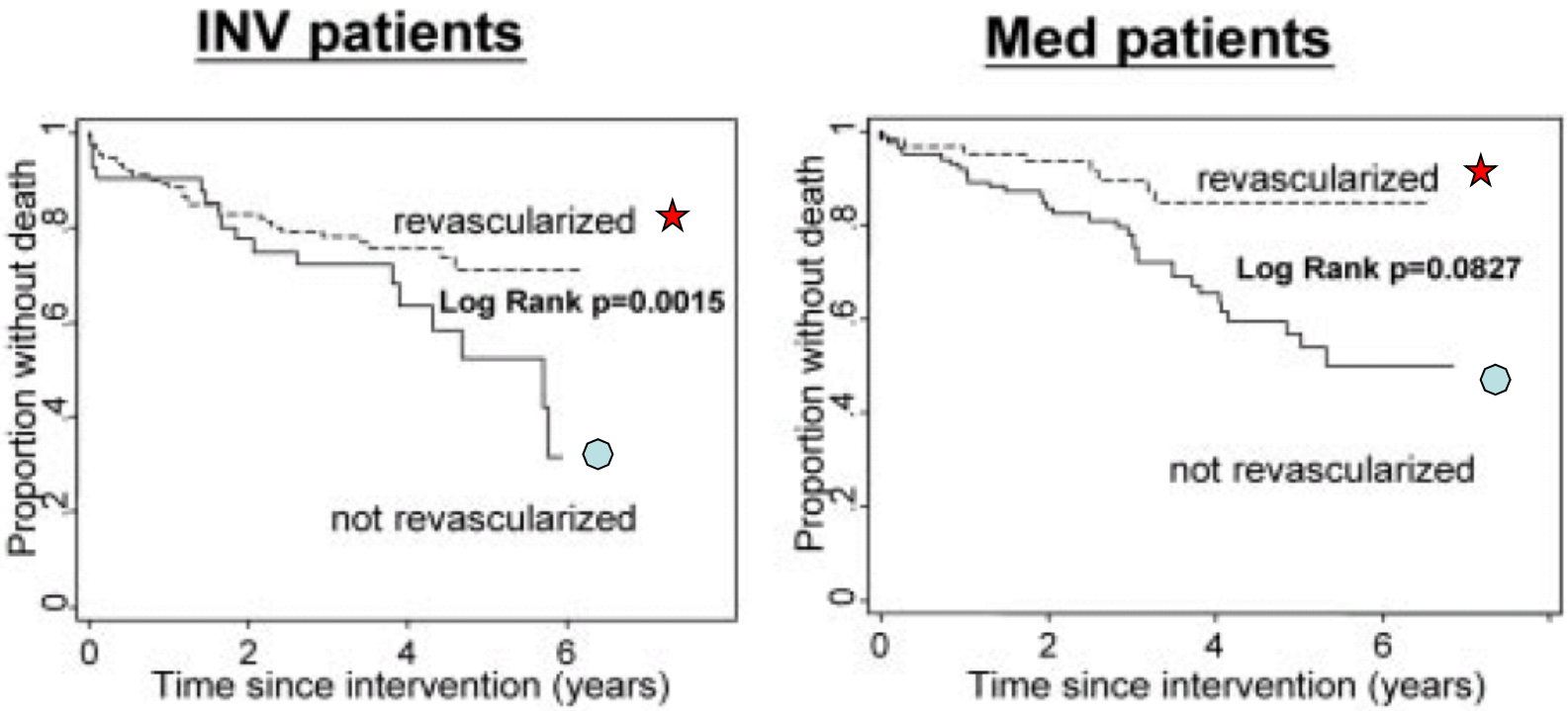
Matthias Pfisterer, MD; for the TIME Investigators*



Long-Term Outcome in Elderly Patients With Chronic Angina Managed Invasively Versus by Optimized Medical Therapy

Four-Year Follow-Up of the Randomized Trial of Invasive Versus Medical Therapy in Elderly Patients (TIME)

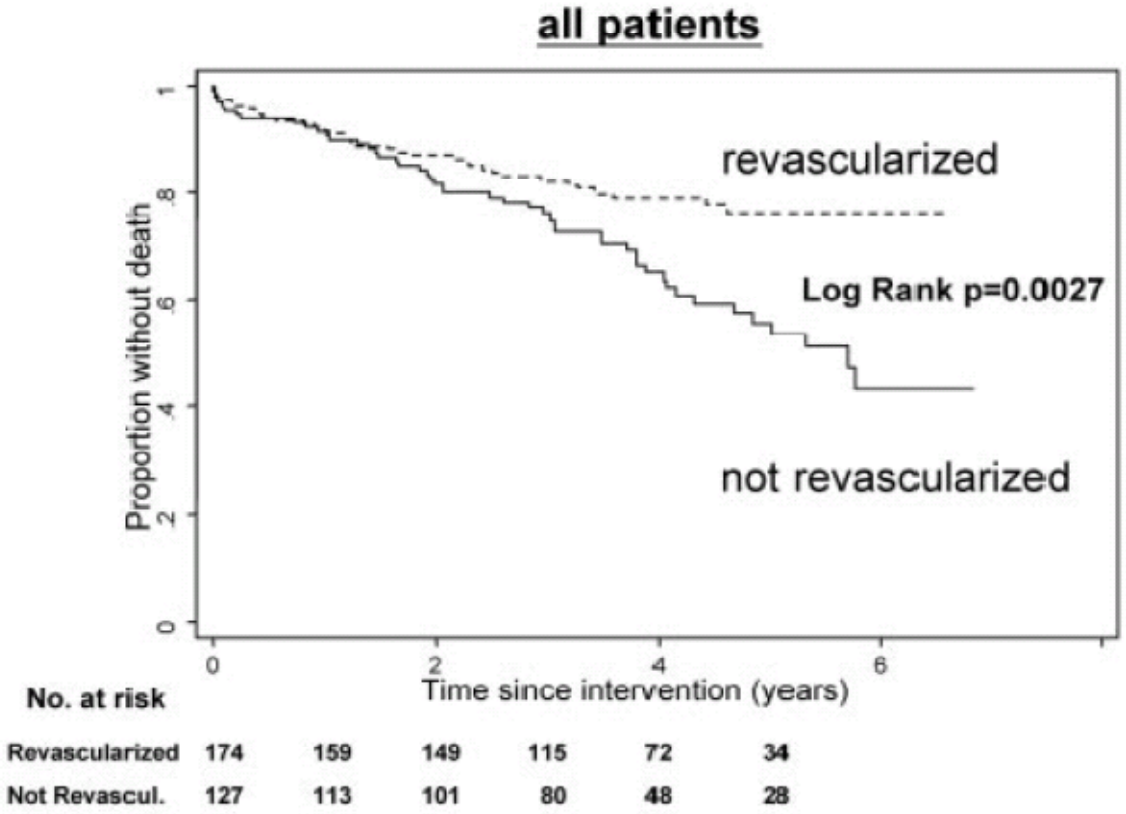
Matthias Pfisterer, MD; for the TIME Investigators*



Long-Term Outcome in Elderly Patients With Chronic Angina Managed Invasively Versus by Optimized Medical Therapy

Four-Year Follow-Up of the Randomized Trial of Invasive Versus Medical Therapy in Elderly Patients (TIME)

Matthias Pfisterer, MD; for the TIME Investigators*



Long-Term Outcome in Elderly Patients With Chronic Angina Managed Invasively Versus by Optimized Medical Therapy

Four-Year Follow-Up of the Randomized Trial of Invasive Versus Medical Therapy in Elderly Patients (TIME)

Matthias Pfisterer, MD; for the TIME Investigators*

Circulation September 7, 2004

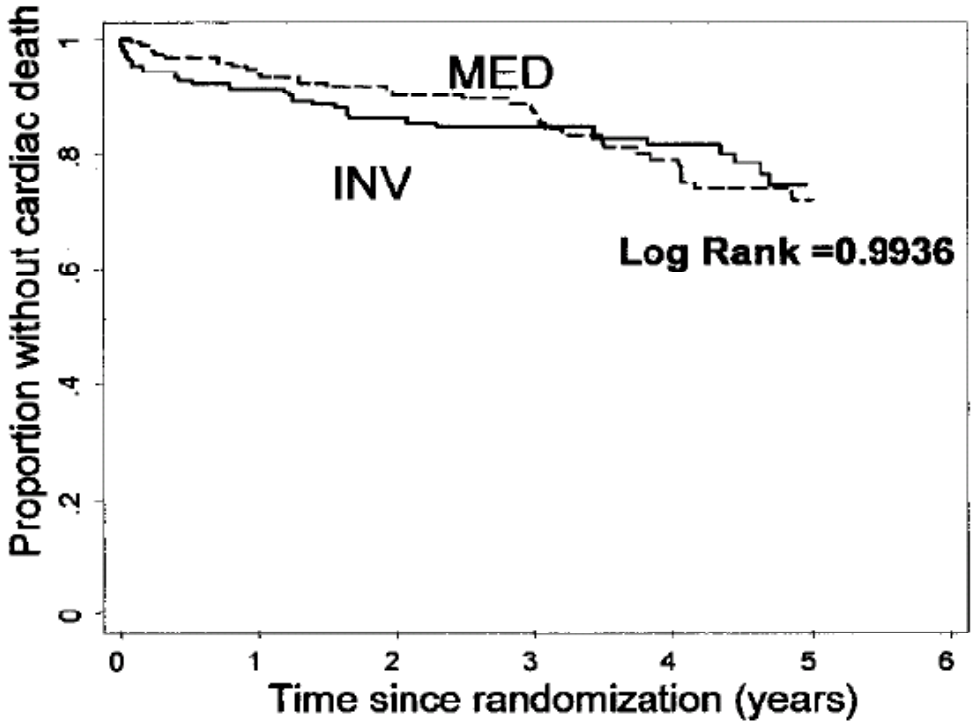


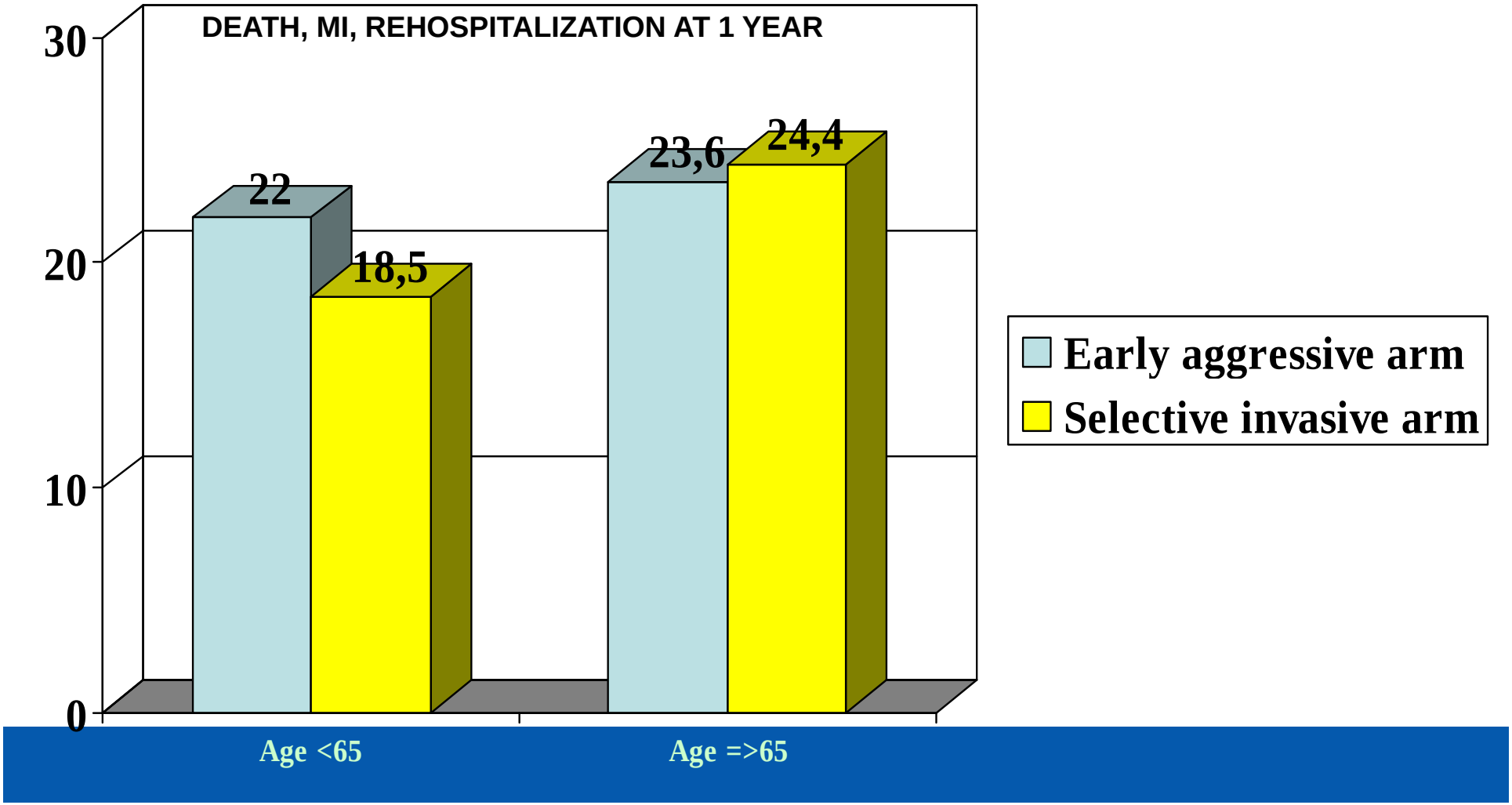
TABLE 2. Major Events During Long-Term Follow-Up (Between Day 365 and Late Follow-Up)

	INV (n=137)	MED (n=139)	*P*	HR	*P*
All death, %	21.2	22.3	0.88	0.68	0.18
Cardiac death, %	13.9	17.3	0.51	0.56	0.10
Patients with nonfatal MI, %	4.4	0.7	0.07	5.24	0.13
Patients with late PCI/CABG, %	2.9	2.9	0.98	1.41	0.67
Patients with cardiac hospitalization, %	20.4	13.0	0.11	2.37	0.01
Patients with major clinical events, %	45.3	37.4	0.22	1.43	0.08

HR indicates hazard ratios adjusted for sex, age, family history of coronary artery disease, peripheral vascular disease, and baseline treatment differences. All other abbreviations are as defined in text.

Primary end point according to age in the ICTUS trial.

De Winter RJ et al, N Engl J Med 2005;353:1095



FIC Federazione Italiana di Cardiologia
Italian Federation of Cardiology

Società Italiana di Cardiologia Invasiva

Early Aggressive vs Initially Conservative Therapy in Elderly Patients with Non-ST-Elevation Acute Coronary Syndrome

The Italian elderly-ACS study
A nationwide trial of the Italian Federation of Cardiology (FIC)
promoted by the Italian Society of Interventional Cardiology SICI-GISE

Steering committee

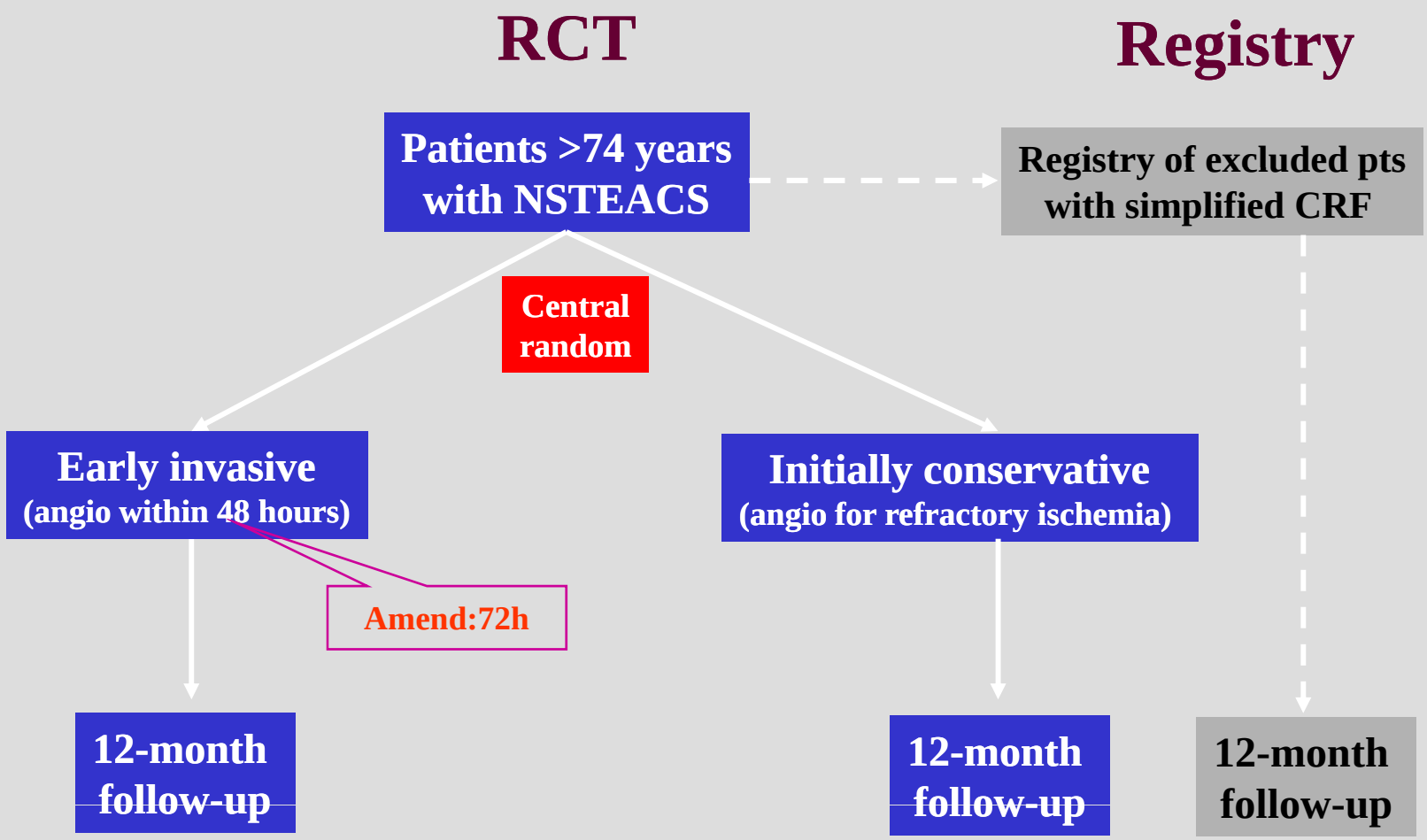
Chairmen: S. Savonitto, S. De Servi

Members: A.S. Petronio, L. Bolognese, C. Greco, C. Cavallini, C. Indolfi, L. Oltrona Visconti, F Piscione

Registry coordinator: G. Steffenino

Event adjudication committee: G. Ambrosio, M. Galvani, A. Marzocchi, I. Santilli

ClinicalTrials.gov ID: **NCT00510185**
website: http://elderly.altavianet.it



Primary endpoint

the composite of all-cause mortality, myocardial (re)MI, disabling stroke and re-hospitalization for cardiovascular causes or severe bleeding within 6 months

Savonitto S, J Cardiovasc Med 2008;9:217

Amend:1year

Randomised treatment strategies

Patients >74 years
With NSTEACS

Web random

Early invasive
(angio within 72 hours)

Angio
During index admission

Initially conservative
(angio for refractory ischemia)

- **Refractory ischemia: recurrent symptoms and ECG changes >12 hrs after admission despite maximal therapy**
- **Post-admission (re)MI**
- **Heart failure**
- **Malignant ventricular arrhythmias**

Patients

Exclusion criteria - 2

- Serum creatinine level >2.5 mg/dL
- Active internal bleeding, history of hemorrhagic diathesis or recent transfusion of RBC, whole blood or platelets
- Cerebrovascular accident within the previous month
- Known platelet count of <90,000 cells/μL
- Ongoing oral anticoagulant treatment or an INR >1.5 at the time of screening
- Gastrointestinal or genitourinary bleeding of clinical significance within 6 weeks prior to randomization

Endpoints

Primary endpoint

The composite of all-cause mortality, myocardial (re)MI, disabling stroke and re-hospitalization for cardiovascular causes or severe bleeding at 6 months

Amended: At 1 year

Secondary endpoints

- CV mortality at 1 year
- All-cause mortality and (re)MI at 1 year
- The composite of death, myocardial (re)MI, disabling stroke and re-hospitalization for cardiovascular causes or severe bleeding at 1 year
- Major bleeding within 12 months
- Any stroke within 12 months
- Total n° of days spent in hospital within 12 months after index admission

Sample size and power calculations: Amendment 1

Calculations are based on the primary-endpoint rates at 12 months in pts >75y adjusted from event rates observed in the retrospective analysis of the TACTICS-TIMI 18 trial, with a primary endpoint rate of 40% in the conservative arm.
In the present study, we aim at detecting superiority of an initially invasive approach with a PE reduction to 25%.

ICTUS, TACTICS ISAR STUDIES

Two-tailed alpha	Power 1 – β	N per group	N total	N per Center (30c)
0.05	80	156	312	10
0.05	85	175	350	12
0.05	90	209	418	14

- **Aspirin, 325 mg p.o on admission, then 75-100 mg throughout follow-up**
- **Clopidogrel, 300 mg on admission, then 75 mg throughout follow-up**
- **GPIIb/IIIa RB: invasive arm (and conservative arm in case of angio)**
  - **either upstream eptifibatide-tirofiban if delay to angio >4 hrs**
  - **or post-angio abciximab, particularly if delay to angio <4hrs**
- **UFH: 2500 i.v. bolus, then start infusion of 7U/kg/hr nomogram-adjusted to a target aPTT of 50-70 seconds up to 30 minutes prior to angiography**
- **Enoxaparin: i.v. bolus of 3000 U, followed by sq administration of 75U/kg (max 6000 U) b.i.d. for 3-5 days. Latest dose ≥8 hrs prior to angio**

No further UFH/enoxa post-angio, except for patients laying in bed (50 U o.d.)

- **Bivalirudin as anticoagulant during PCI, according to REPLACE-2 dosing:**
  - **i.v. bolus 0.75 mg/kg**
  - **1.75 mk/kg/hour infusion during PCI**
- **Fondaparinux, 2.5 mg subq o.d., during the whole hospital stay,particularly in patients treated conservatively**

All other medications as recommended by current practice guidelines

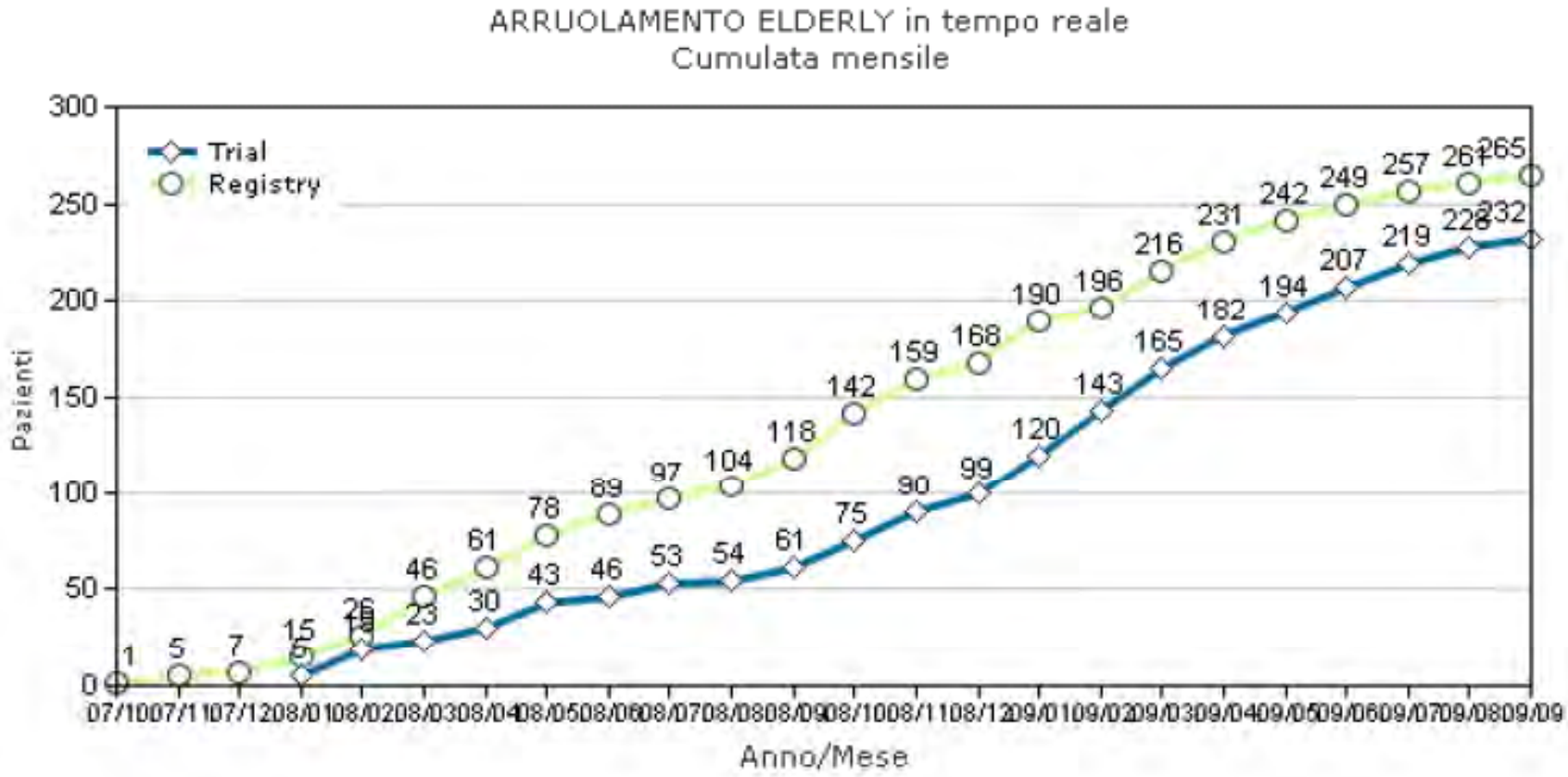
The Italian **Elderly** – ACS Study

Countrywide distribution of the "participating" Centers

"Active Centers": September 2009

- **Arruolamento**: (al 18.09.09) **232**

http://elderly.altavianet.it/)



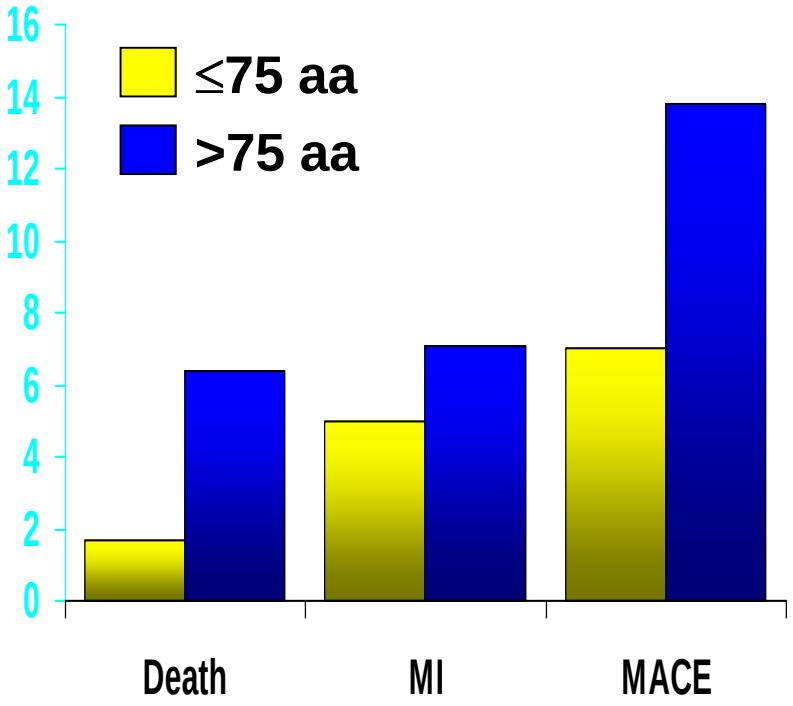
ITALIAN

ELDERLY-ACS STUDY

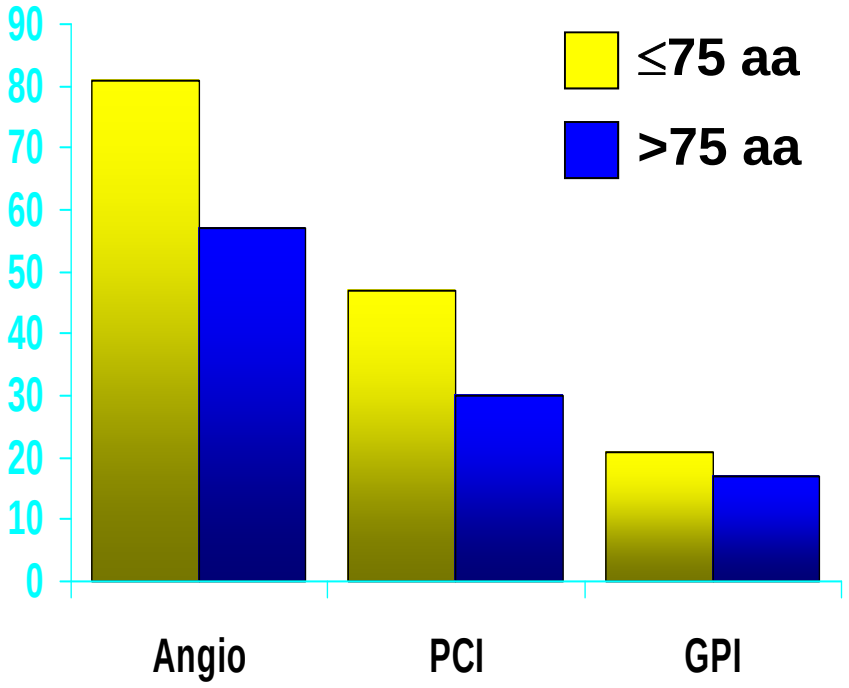
Elderly with NSTEMI

The ROSAI 2-Elderly Study

30-days Outcomes



Treatments



Conservative Strategy: OR 2,31 (1,20-4,48) events at 30 days

De Servi S, et al. Am Heart J 2004; 147: 830-836

AHA Scientific Statement

Acute Coronary Care in the Elderly, Part I

Non–ST-Segment–Elevation Acute Coronary Syndromes

A Scientific Statement for Healthcare Professionals From the American Heart Association Council on Clinical Cardiology

In Collaboration With the Society of Geriatric Cardiology

Karen P. Alexander, MD; L. Kristin Newby, MD, MHS, FAHA; Christopher P. Cannon, MD, FAHA; Paul W. Armstrong, MD, FAHA; W. Brian Gibler, MD; Michael W. Rich, MD, FAHA; Frans Van de Werf, MD, PhD; Harvey D. White, MB, DSc, FAHA; W. Douglas Weaver, MD, FAHA; Mary D. Naylor, PhD, FAHA; Joel M. Gore, MD, FAHA; Harlan M. Krumholz, MD, FAHA; E. Magnus Ohman, MD, Chair

(*Circulation*. 2007;115:2549-2569.)

Recommendations for Special Populations

- Treatment decisions in the elderly should be tailored according to estimated life expectancy, patient wishes and co-morbidities to minimize risk and improve morbidity and mortality outcomes in this frail but high-risk population. (I – C)

- Elderly patients should be considered for routine early invasive strategy, after careful evaluation of their inherent raised risk of procedure-related complications, especially during CABG (I – B).

Recommendations for Special Populations

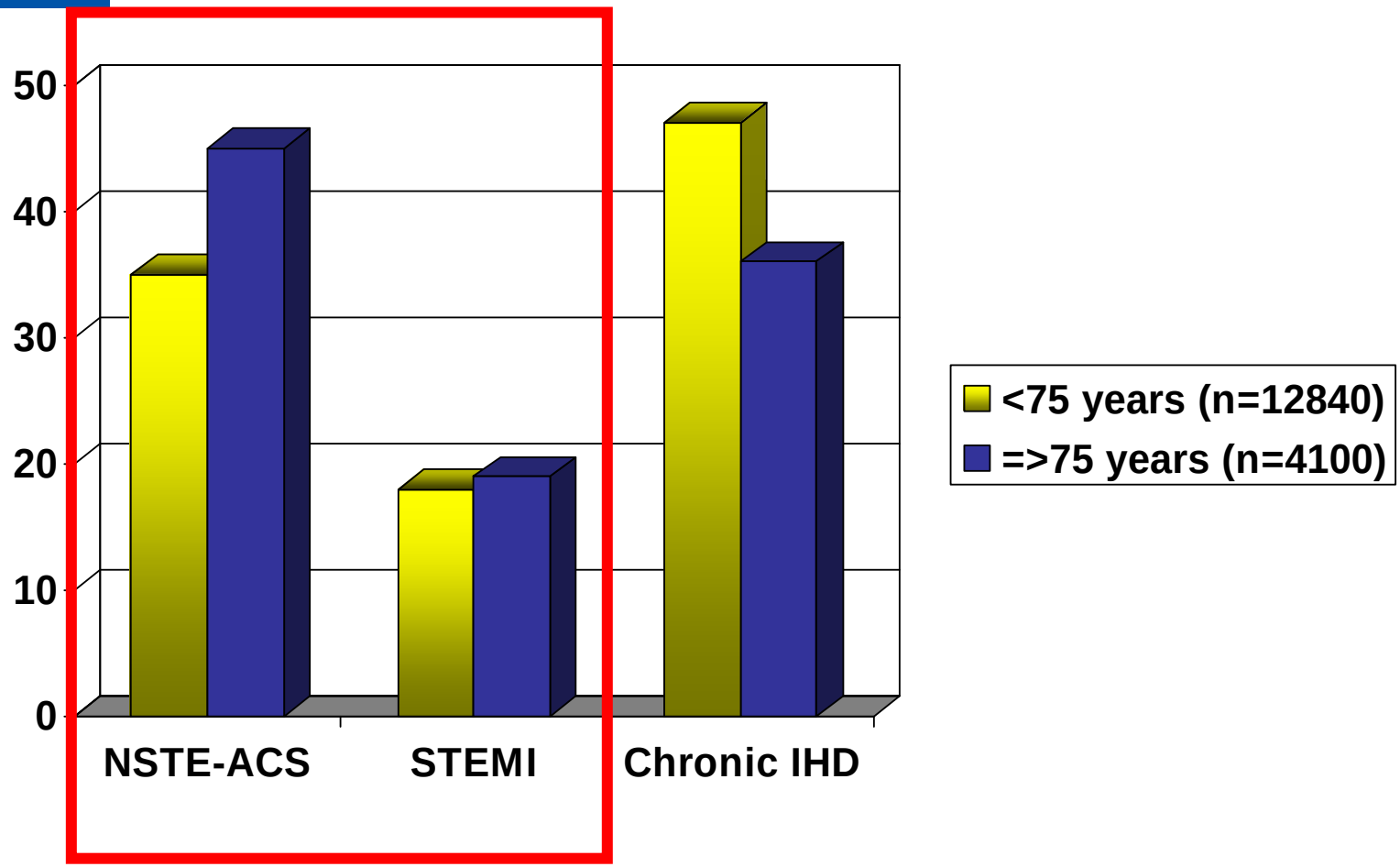
ESC

Patients with CKD with CrCl < 60 ml/min are at high risk of further ischaemic events and therefore should be submitted to invasive evaluation and revascularisation whenever possible (IIa-B).

ACC/AHA

Chronic kidney disease carries a far worse prognosis, but unlike in several other high-risk subsets, the value of aggressive therapeutic interventions is less certain and should be further studied.

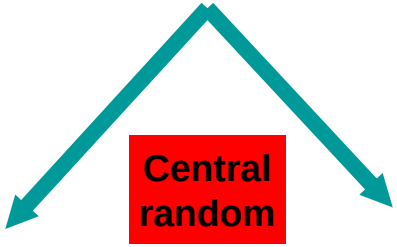
Indications for PCI in 16940 patients included in the OSCAR Registry



The Italian elderly-ACS study

Study design

Patients >74 years with NSTEACS



Early invasive
(angio within 48 hours)

Initially conservative
(angio for refractory ischemia)

all-cause mortality, myocardial (re)MI, disabling stroke and re-hospitalization for cardiovascular causes or severe bleeding

The Italian elderly-ACS study
- Statistical Plan

Sample Size: 700 Pts

50 Recruiting Centers

INVASIVE

Expected Primary EndPoints Rate: 20%

CONSERVATIVE

Expected Primary EndPoints Rate: 30%

95% power to test two-sided type I error of 0.05

Centers without onsite cathlab
operating in network
with a nearby cathlab able to perform coronary angiography within 48 hours after patient enrolment, or earlier in case of emergency

Centers with onsite cathlab
and a program of
nonsistematic angiography in the study population

Exclusion criteria, 3

- Concomitant severe obstructive lung disease, malignancy or neurologic deficit limiting follow-up or adherence to the study protocol
- Participation in any phase of another clinical research study involving the evaluation of an investigational drug or device within 30 days prior to randomization
- Inability to give at least verbal informed consent to the study

Ospedale di Pozzuoli			
INRCA, Ancona			

Totale 29

110 **165**

Centers to become active

Sample size and power calculations

Calculations are based on the primary-endpoint rates at 6 months in pts >75y observed in the retrospective analysis of the TACTICS-TIMI 18 trial, with a primary endpoint rate of 30% at 6 months in the conservative arm. In the present Study, we aim at detecting superiority of an initially invasive approach with a PE reduction to 20%.

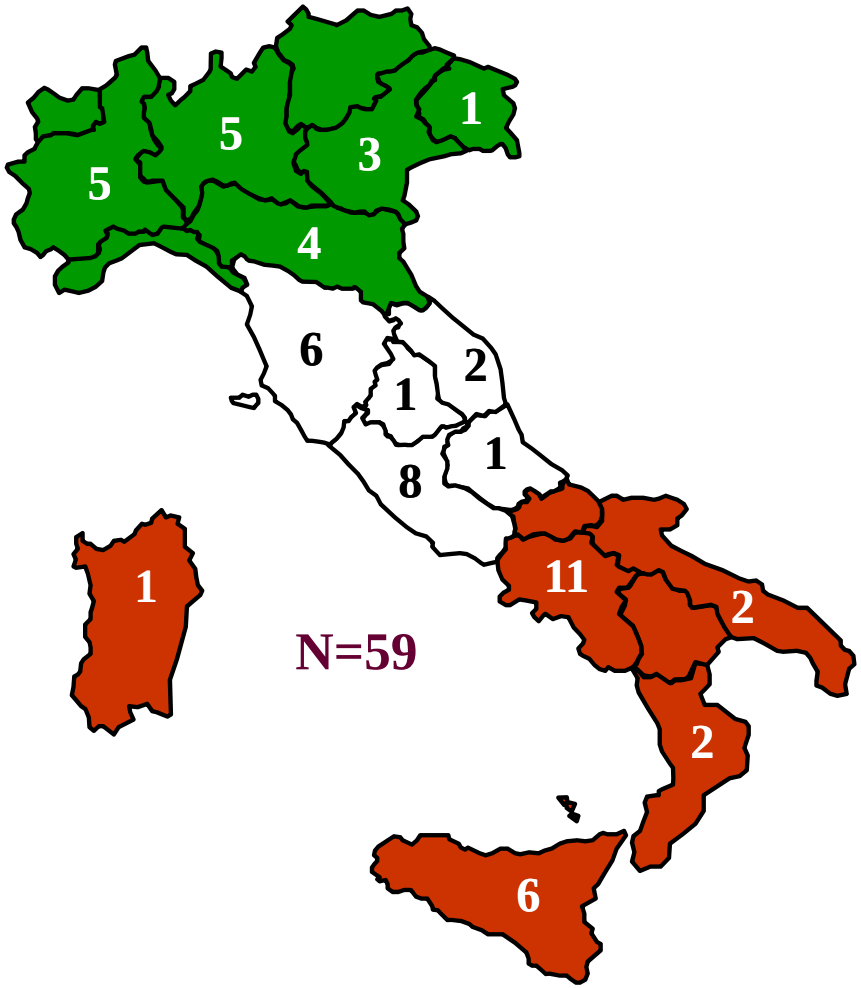
ICTUS, STEEPLE ISAR STUDIES

Two-tailed alpha	Power 1 – β	N per group	N total	N per Center (30c)
0.05	80	252	504	17
0.05	85	289	578	19
0.05	90	338	676	23

The Italian **Elderly** – ACS Study

Countrywide distribution of the "participating" Centers

Centers declaring participation: august 2007



"Active Centers": january 2009

Research trial protocol

Early aggressive vs. initially conservative treatment in elderly patients with non-ST-elevation acute coronary syndrome: The Italian Elderly ACS study

Stefano Savonitto[a], Stefano De Servi[b], Anna Sonia Petronio[c], Leonardo Bolognese[d], Claudio Cavallini[e], Cesare Greco[f], Ciro Indolfi[g], Luigi Oltrona Visconti[h], Federico Piscione[i], Giuseppe Ambrosio[l], Marcello Galvani[m], Antonio Marzocchi[n], Ignazio Santilli[o], Giuseppe Steffenino[p] and Attilio Maseri[q]

Background Elderly patients represent one-third of all admissions for non-ST-elevation acute coronary syndrome (NSTEACS) in the coronary care units. Despite their high-risk characteristics and worse outcomes, compared with younger patients, the elderly receive less aggressive treatments, also due to less clear evidence regarding the most effective treatment strategy.

Purpose The Italian Elderly ACS study includes patients older than 74 years of age with NSTEACS in a multicenter randomized clinical trial, comparing an early aggressive and an initially conservative approach. Patients not enrolled due to specific exclusion criteria or any other reason will be enrolled in a Registry.

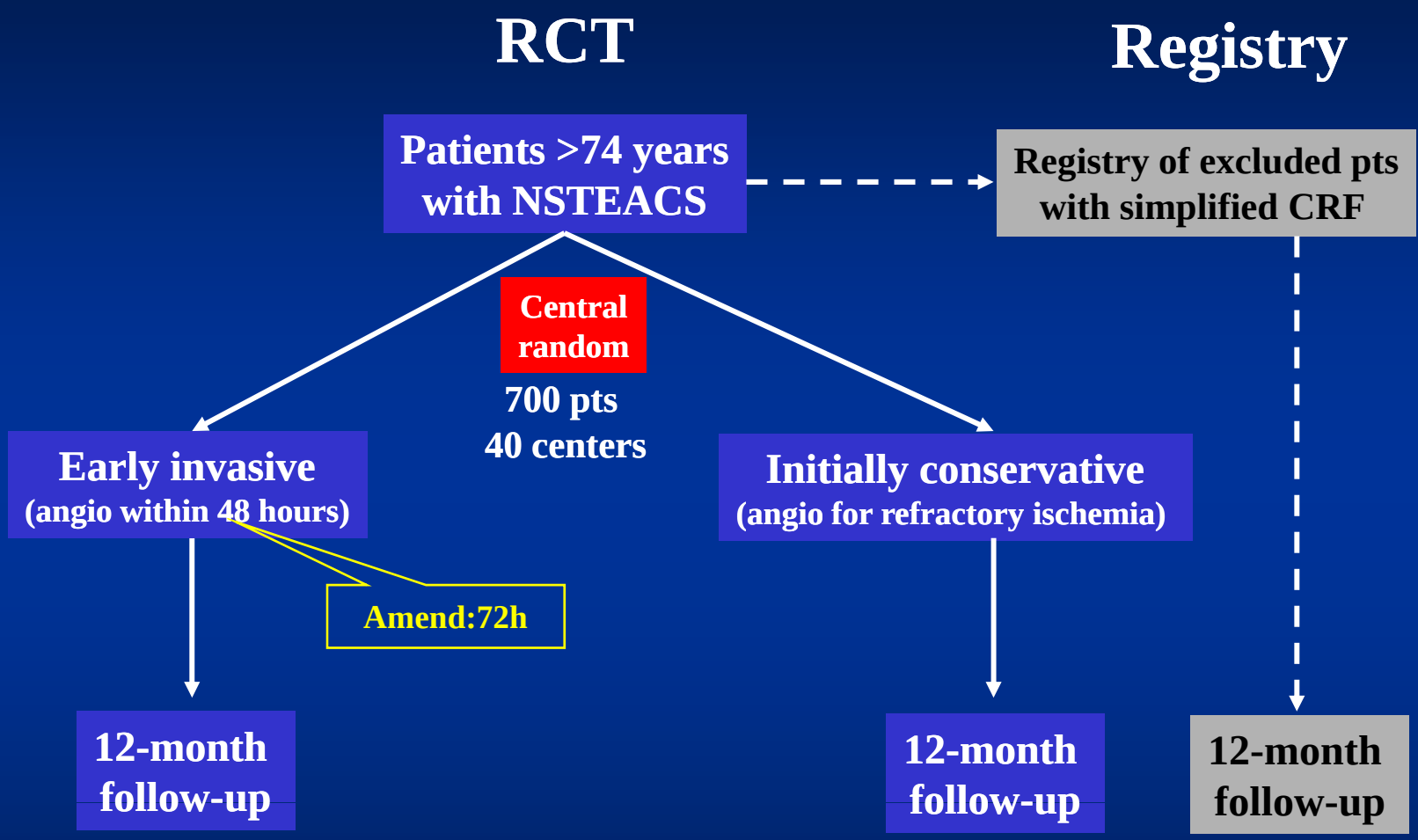
Centers Centers with on-site interventional cathlab and centers without on-site cathlab refering patients to a cathlab within a consolidated percutaneous coronary intervention network.

Primary end point The composite of all-cause mortality, myocardial (re)infarction, disabling stroke, and rehospitalization for cardiovascular diseases or severe bleeding within 6 months.

Sample size Expected primary end point rates of 30% in the conservative arm vs. 20% in the invasive arm. According to these estimates, with two-tailed α of 0.05, power will be 80, 85, or 90% with 252, 289, and 338 patients per group, respectively. The goal is to enroll 700 patients from 50 centers. *J Cardiovasc Med* 9:217–226 © 2008 Italian Federation of Cardiology.

Journal of Cardiovascular Medicine 2008, 9:217–226

Keywords: acute coronary syndrome, elderly, randomized clinical trial, registry



Primary endpoint

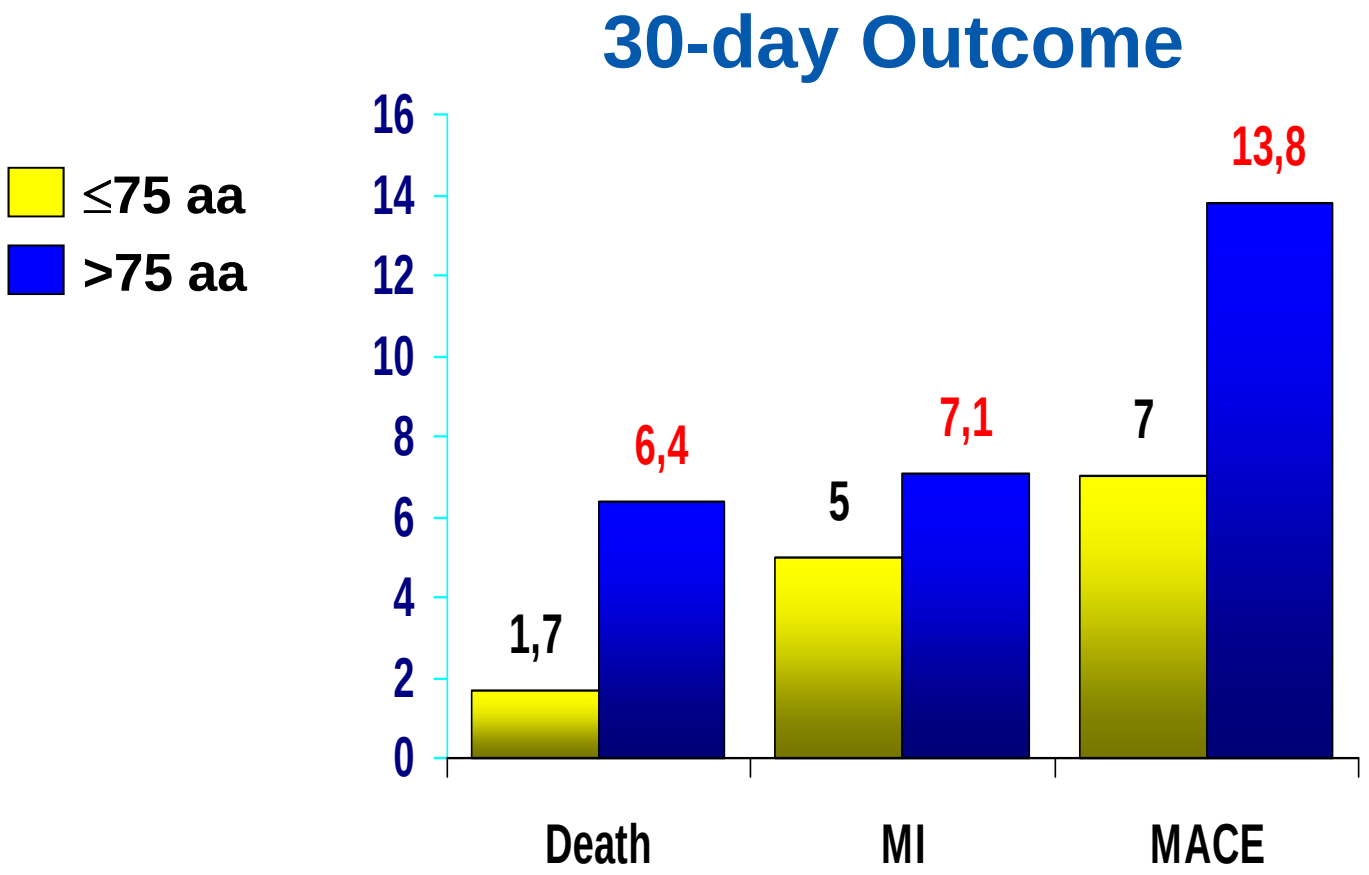
the composite of all-cause mortality, myocardial (re)MI, disabling stroke and re-hospitalization for cardiovascular causes or severe bleeding within 6 months

Savonitto S, J Cardiovasc Med 2008;9:217

Amend:1year

Elderly with NSTE-ACS

The ROSAI 2-Elderly Study



De Servi S, et al. Am Heart J 2004; 147: 830-836