The Timing of Angiography after NSTEMI: Now, or a Little Later or Only if Needed?

Angioplasty Summit 2010

Seoul, Korea

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Presenter Disclosure Information

David R. Holmes, Jr., M.D.

"The Timing of Angiography after NSTEMI:
Now, or a Little Later or Only if Needed?"

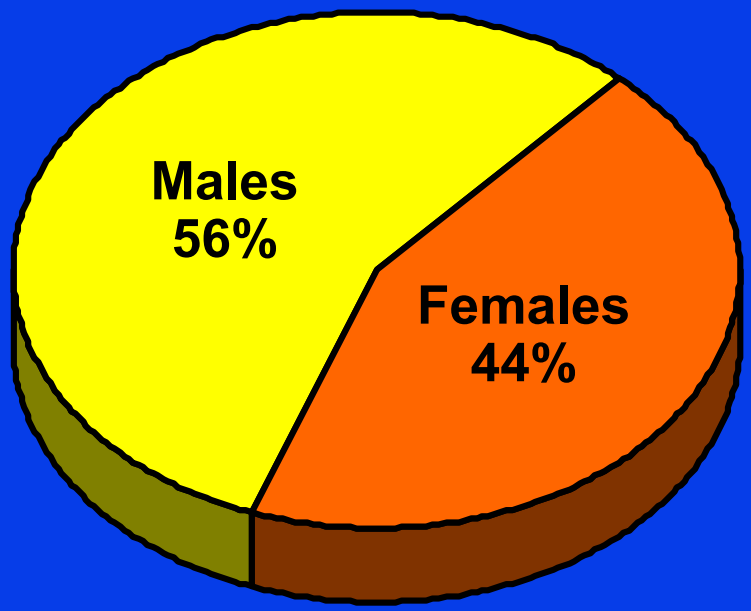
The following relationships exist related to this presentation:

None

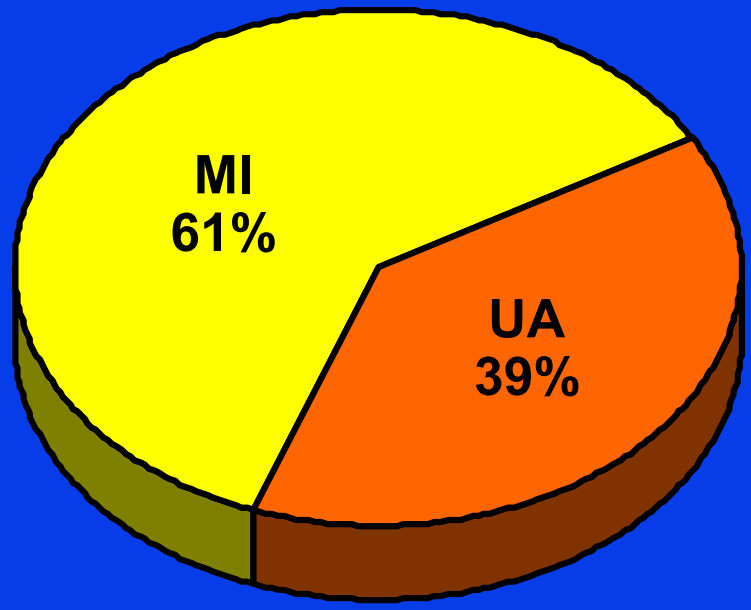

Artery
CLEANERS
1
HOUR

Acute Coronary Syndromes
2006

1,365,000 unique hospitalizations



1,365,000 unique hospitalizations



AHA Stroke/Death Statistics
Circ 2009; 119:e21-181


VERY VERY FINE PRINT

Invasive vs Conservative Strategies
ACS, NSTEMI

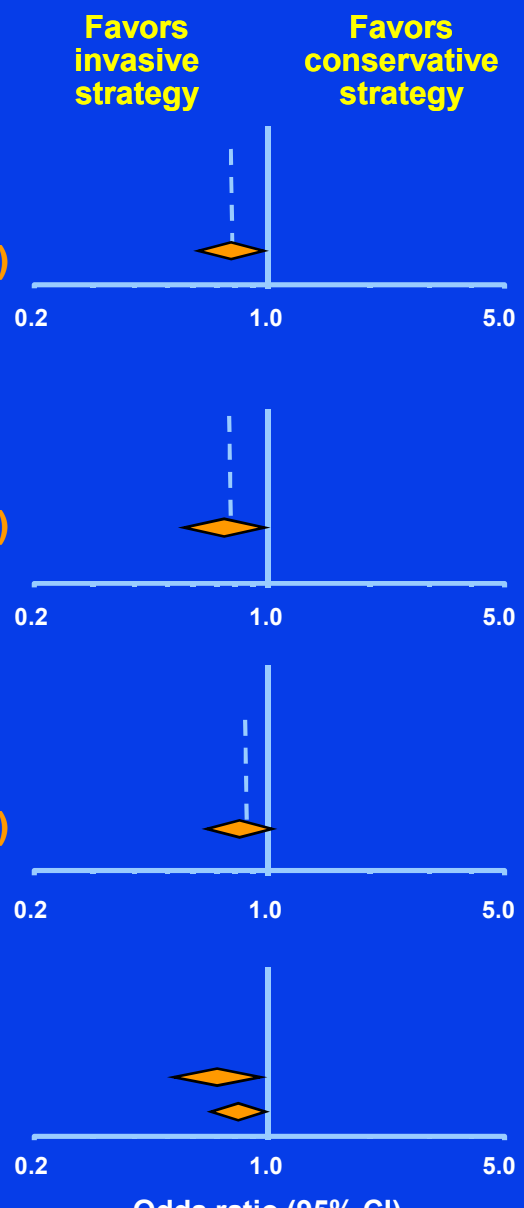
- Meta-analysis of 8 RCT's: 1994-2005
- Evaluate sex specific incidences of death, MI and rehospitalization with ACS at 12 months of follow-up

O'Donoghue M et al, JAMA 300:71-80, 2008

Invasive vs Conservative Treatment Strategy in NSTE ACS

All pt	Invasive strategy No.	%	Conservative strategy No.	%	Odds ratio (95% CI)
Overall	1,075/5,083	21.1	1,313/5,067	25.9	0.78 (0.61-0.98)
	D, MI, Rehosp				
Men					
Overall	751/3,545	21.2	928/3,530	26.3	0.73 (0.55-0.98)
	D, MI, Rehosp				
Women					
Overall	324/1,538	21.1	385/1,537	25.0	0.81 (0.65-1.01)
	D, MI, Rehosp				

Biomarker status	Invasive strategy	Con-servative strategy	Invasive strategy	Con-servative strategy	Odds ratio (95% CI)
Overall					
Present	2,232	2,226	520	669	0.72 (0.54-0.95)
Absent	2,797	2,796	545	633	0.82 (0.69-0.99)



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O'Donoghue M et al: JAMA 300:71, 2008

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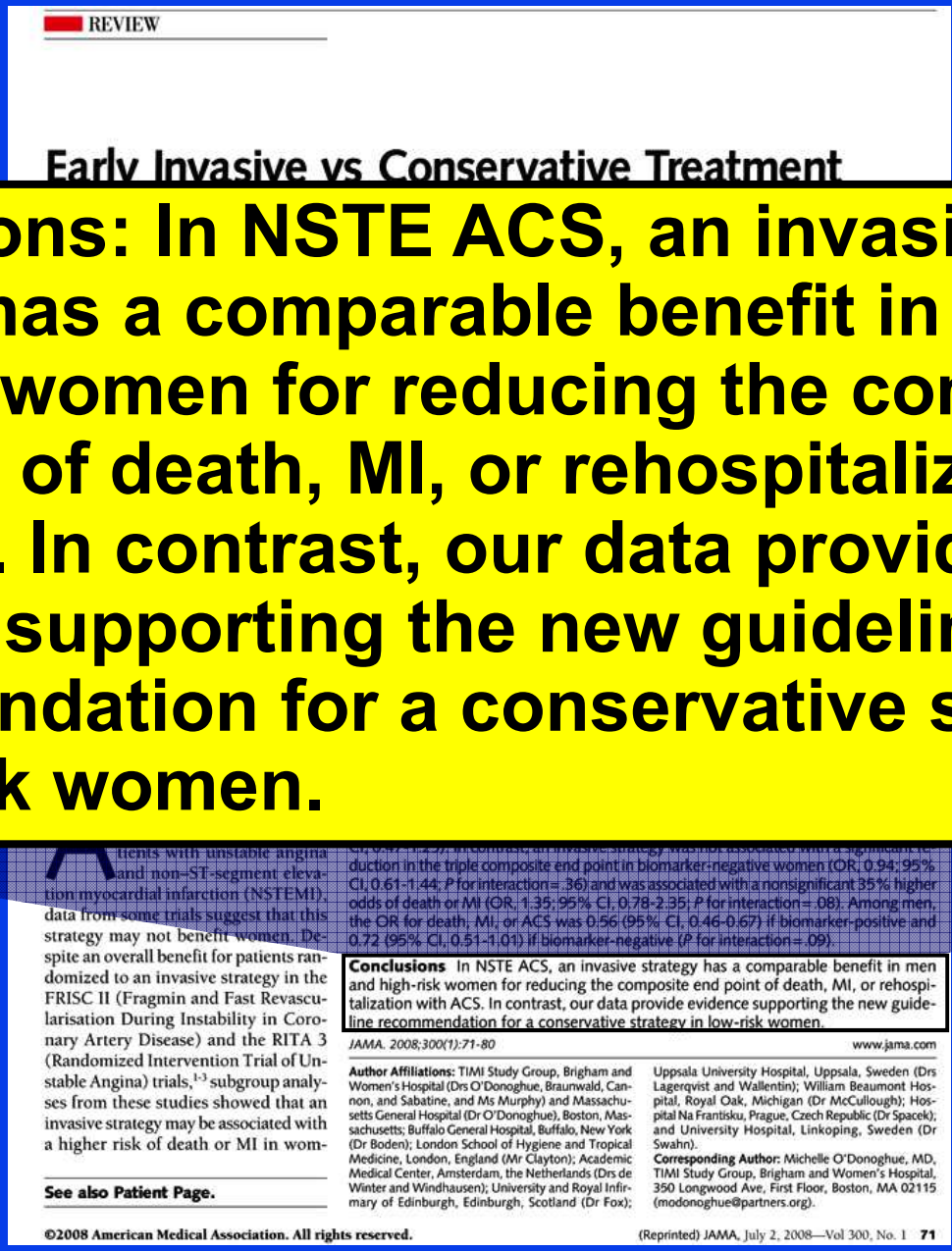

REVIEW

Early Invasive vs Conservative Treatment

Conclusions: In NSTE ACS, an invasive strategy has a comparable benefit in men and high-risk women for reducing the composite end point of death, MI, or rehospitalization with ACS. In contrast, our data provide evidence supporting the new guideline recommendation for a conservative strategy in low-risk women.

tients with unstable angina and non–ST-segment elevation myocardial infarction (NSTEMI), data from some trials suggest that this strategy may not benefit women. Despite an overall benefit for patients randomized to an invasive strategy in the FRISC II (Fragmin and Fast Revascularisation During Instability in Coronary Artery Disease) and the RITA 3 (Randomized Intervention Trial of Unstable Angina) trials,[1-3] subgroup analyses from these studies showed that an invasive strategy may be associated with a higher risk of death or MI in wom-

duction in the triple composite end point in biomarker-negative women (OR, 0.94; 95% CI, 0.61-1.44; *P* for interaction = .36) and was associated with a nonsignificant 35% higher odds of death or MI (OR, 1.35; 95% CI, 0.78-2.35; *P* for interaction = .08). Among men, the OR for death, MI, or ACS was 0.56 (95% CI, 0.46-0.67) if biomarker-positive and 0.72 (95% CI, 0.51-1.01) if biomarker-negative (*P* for interaction = .09).

Conclusions In NSTE ACS, an invasive strategy has a comparable benefit in men and high-risk women for reducing the composite end point of death, MI, or rehospitalization with ACS. In contrast, our data provide evidence supporting the new guideline recommendation for a conservative strategy in low-risk women.

JAMA. 2008;300(1):71-80 www.jama.com

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See also Patient Page.

Invasive vs Conservative Strategies

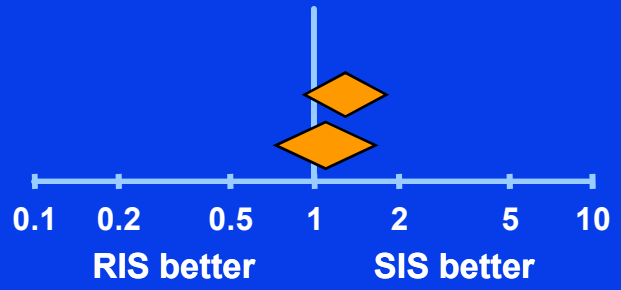
- Systematic review of 10 trials and 10,648 patients with NSTEMI ACS with random assignment to routine invasive or a selective invasive strategy
- Evaluate composite outcome of death or non fatal infarction

Qayyam R et al: Ann Intern Med 148:186, 2008

Qayyam R et al: Ann Intern Med 148:186, 2008

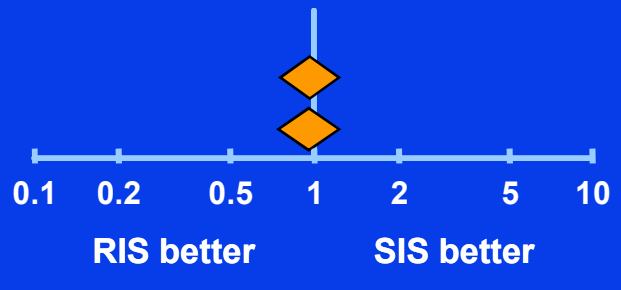
Meta-Analysis, In-hospital death/nonfatal MI

Total	376/5,330	279/5,318	
Relative risk (Q statistic P<0.001; I^2=74.1%)			1.26 (0.91-1.74)
Bayesian relative risk			1.03 (0.65-1.57)



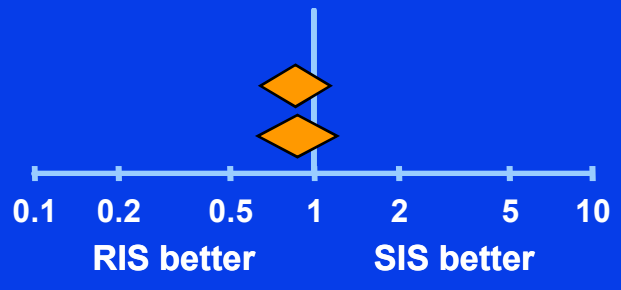
Meta-Analysis, F/U Death

Total	438/5,330	463/5,318	
Relative risk (Q statistic P=0.12; I^2=36.0%)			0.95 (0.80-1.14)
Bayesian relative risk			0.91 (0.72-1.12)



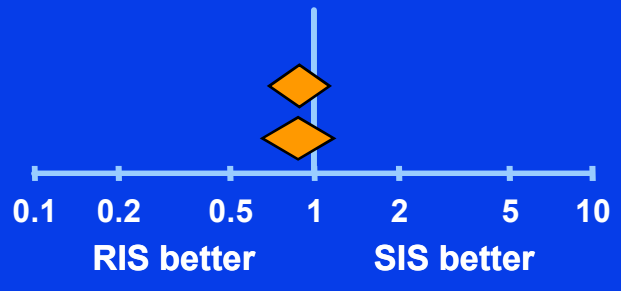
Meta-Analysis, F/U Nonfatal MI

Total	490/5,330	569/5,318	
Relative risk (Q statistic P=0.004; I^2=63.2%)			0.86 (0.68-1.08)
Bayesian relative risk			0.84 (0.64-1.10)



Meta-Analysis, F/U Combined Death or Nonfatal MI

Total	847/5,330	928/5,318	
Relative risk (Q statistic P<0.001; I^2=72.1%)			0.90 (0.74-1.08)
Bayesian relative risk			0.87 (0.67-1.11)



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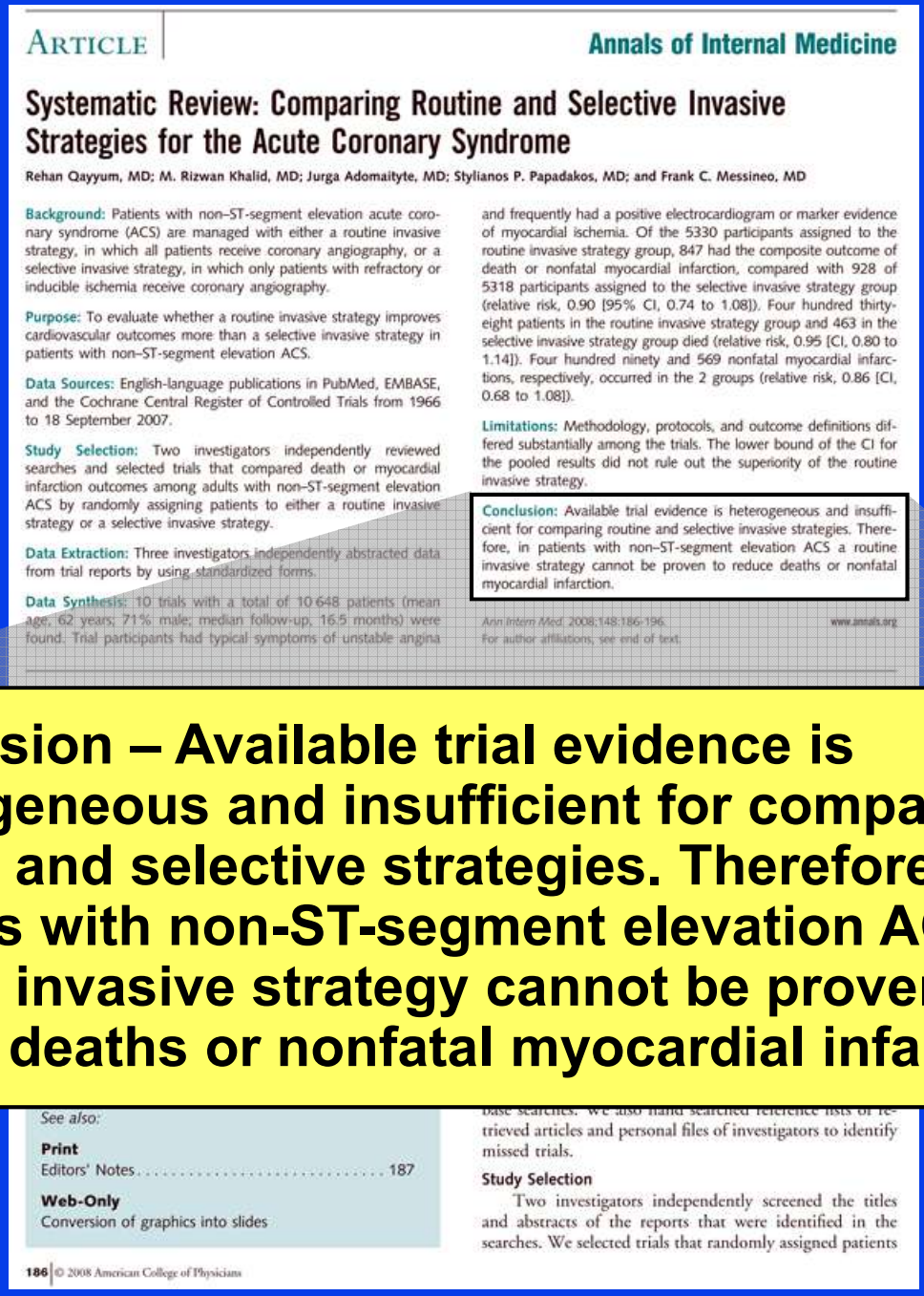

ARTICLE | Annals of Internal Medicine

Systematic Review: Comparing Routine and Selective Invasive Strategies for the Acute Coronary Syndrome

Rehan Qayyum, MD; M. Rizwan Khalid, MD; Jurga Adomaityte, MD; Stylianos P. Papadakos, MD; and Frank C. Messineo, MD

Background: Patients with non–ST-segment elevation acute coronary syndrome (ACS) are managed with either a routine invasive strategy, in which all patients receive coronary angiography, or a selective invasive strategy, in which only patients with refractory or inducible ischemia receive coronary angiography.

Purpose: To evaluate whether a routine invasive strategy improves cardiovascular outcomes more than a selective invasive strategy in patients with non–ST-segment elevation ACS.

Data Sources: English-language publications in PubMed, EMBASE, and the Cochrane Central Register of Controlled Trials from 1966 to 18 September 2007.

Study Selection: Two investigators independently reviewed searches and selected trials that compared death or myocardial infarction outcomes among adults with non–ST-segment elevation ACS by randomly assigning patients to either a routine invasive strategy or a selective invasive strategy.

Data Extraction: Three investigators independently abstracted data from trial reports by using standardized forms.

Data Synthesis: 10 trials with a total of 10 648 patients (mean age, 62 years; 71% male; median follow-up, 16.5 months) were found. Trial participants had typical symptoms of unstable angina and frequently had a positive electrocardiogram or marker evidence of myocardial ischemia. Of the 5330 participants assigned to the routine invasive strategy group, 847 had the composite outcome of death or nonfatal myocardial infarction, compared with 928 of 5318 participants assigned to the selective invasive strategy group (relative risk, 0.90 [95% CI, 0.74 to 1.08]). Four hundred thirty-eight patients in the routine invasive strategy group and 463 in the selective invasive strategy group died (relative risk, 0.95 [CI, 0.80 to 1.14]). Four hundred ninety and 569 nonfatal myocardial infarctions, respectively, occurred in the 2 groups (relative risk, 0.86 [CI, 0.68 to 1.08]).

Limitations: Methodology, protocols, and outcome definitions differed substantially among the trials. The lower bound of the CI for the pooled results did not rule out the superiority of the routine invasive strategy.

Conclusion: Available trial evidence is heterogeneous and insufficient for comparing routine and selective invasive strategies. Therefore, in patients with non–ST-segment elevation ACS a routine invasive strategy cannot be proven to reduce deaths or nonfatal myocardial infarction.

Ann Intern Med. 2008;148:186-196. www.annals.org
For author affiliations, see end of text.

Conclusion – Available trial evidence is heterogeneous and insufficient for comparing routine and selective strategies. Therefore, in patients with non-ST-segment elevation ACS a routine invasive strategy cannot be proven to reduce deaths or nonfatal myocardial infarction.

See also:

Print
Editors' Notes 187

Web-Only
Conversion of graphics into slides

retrieved articles and personal files of investigators to identify missed trials.

Study Selection

Two investigators independently screened the titles and abstracts of the reports that were identified in the searches. We selected trials that randomly assigned patients

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Insight

- Occasional glimpse that life affords us of not just who but what we actually are
- Evaluation of the outcomes of actual treatment received

O'Donnell modified


BOND
ç Alfred Eisenstaedt/Getty

Intended vs Received
ICTUS Trial

- ICTUS
  - Randomized clinical trial of 1200 patients with NSTEMI-ACS
- Randomization to early invasive or selective invasive strategy
- No significant benefit at 4 years with early invasive

Hirsch A et al: EHJ 30:645, 2009

Intended vs Received
ICTUS Trial

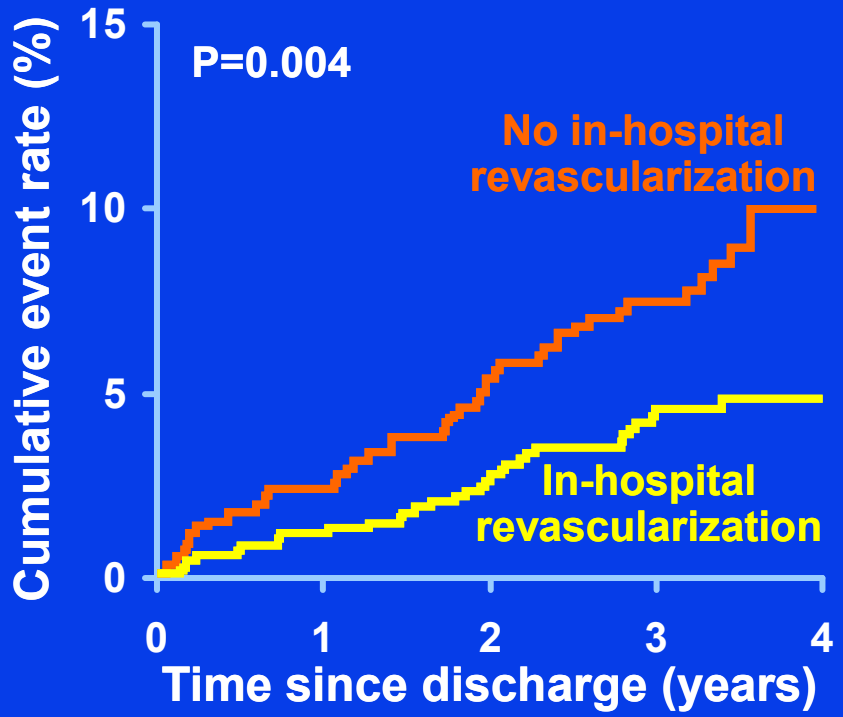
- Question:
  - What is the effect of treatment received on outcome?
- Of 1189 patients, 691 (58%) were treated with revascularization

Hirsch A et al: EHJ 30:645, 2009

Risk of Death

Stratified by Actual In-Hospital Revascularization

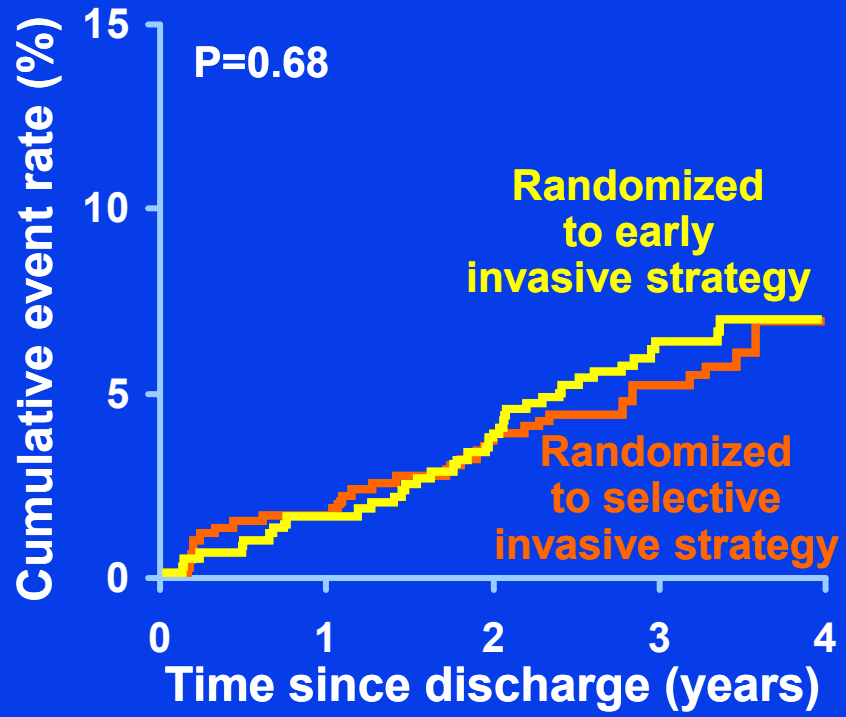
Death



No. at risk					
Revasc	691	683	671	504	127
No revasc	498	485	470	360	96

Stratified by Randomized Treatment Strategy

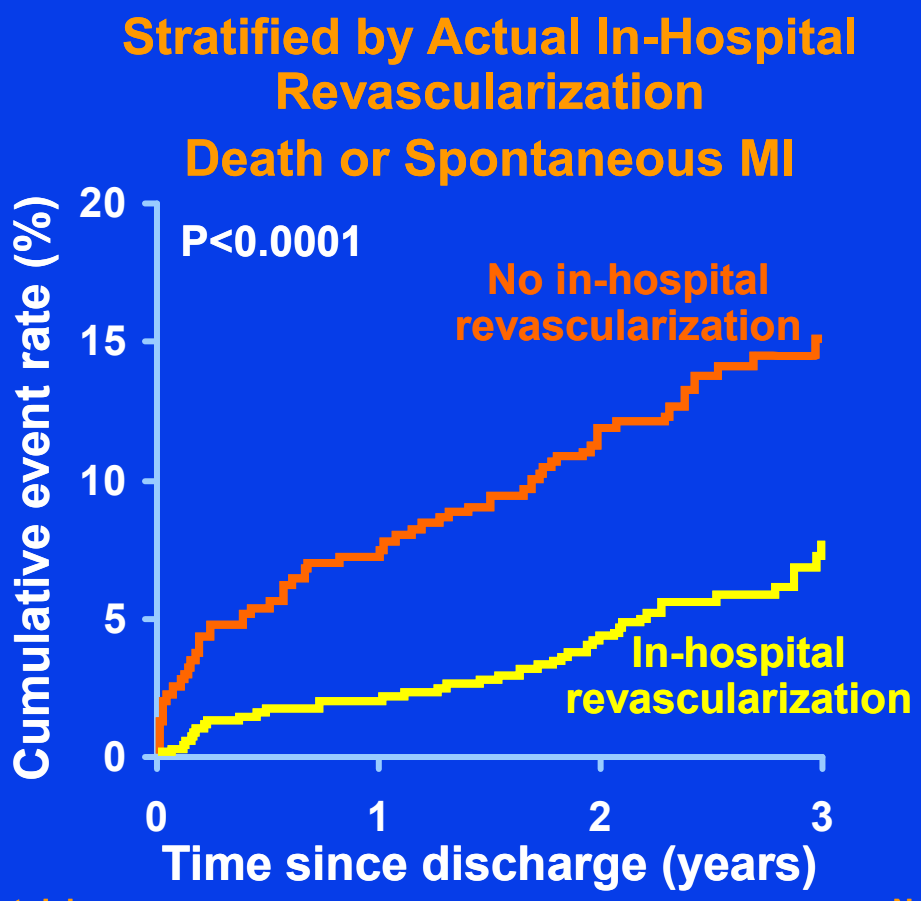
Death



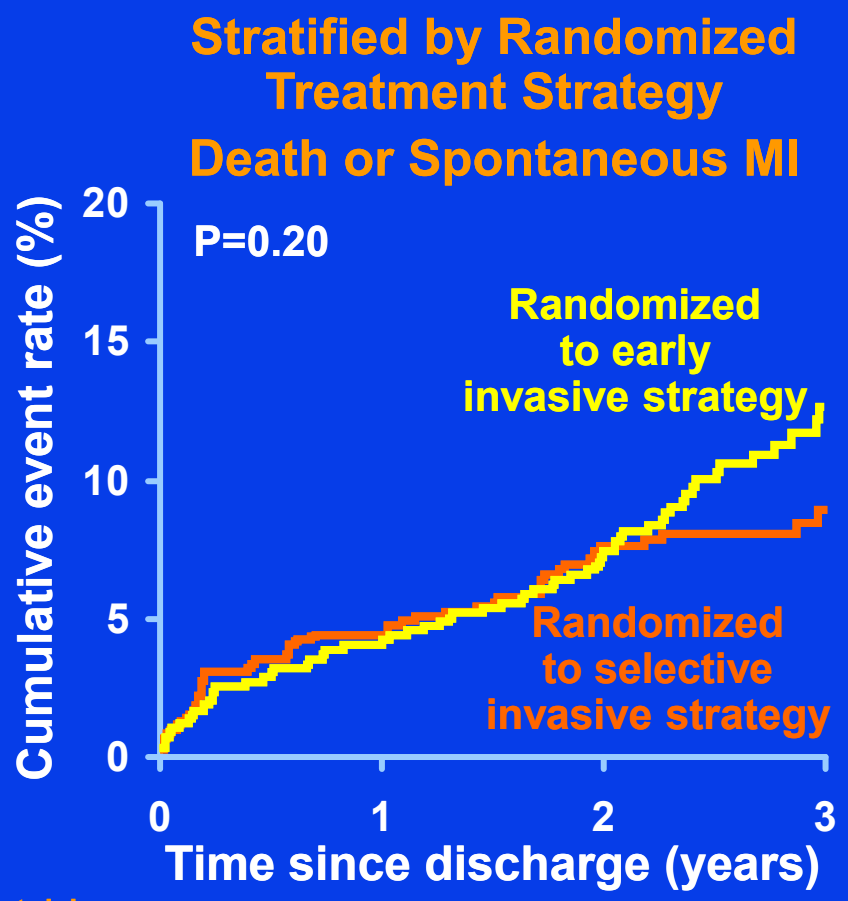
No. at risk					
Early invasive	598	588	574	429	110
Selective invasive	591	580	567	435	113

Hirsch A et al: EHJ 30:645, 2009

Risk of Death or MI

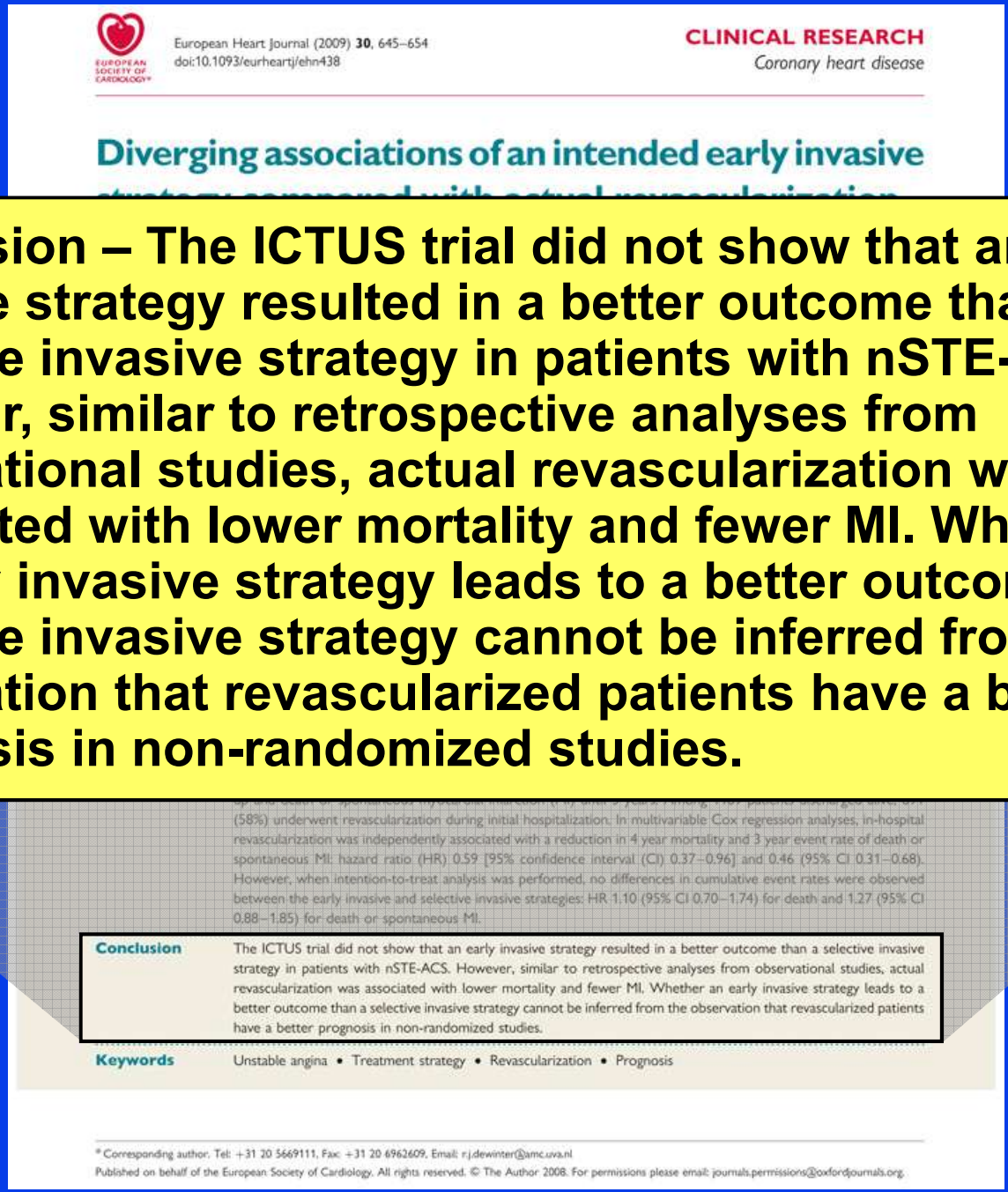


No. at risk				
Revasc	691	677	641	212
No revasc	498	461	424	142



No. at risk				
Early invasive	598	573	538	175
Selective invasive	591	565	527	179

Hirsch A et al: EHJ 30:645, 2009



European Heart Journal (2009) **30**, 645–654
doi:10.1093/eurheartj/ehn438

CLINICAL RESEARCH
Coronary heart disease

Diverging associations of an intended early invasive

Conclusion – The ICTUS trial did not show that an early invasive strategy resulted in a better outcome than a selective invasive strategy in patients with nSTE-ACS. However, similar to retrospective analyses from observational studies, actual revascularization was associated with lower mortality and fewer MI. Whether an early invasive strategy leads to a better outcome than selective invasive strategy cannot be inferred from the observation that revascularized patients have a better prognosis in non-randomized studies.

(58%) underwent revascularization during initial hospitalization. In multivariable Cox regression analyses, in-hospital revascularization was independently associated with a reduction in 4 year mortality and 3 year event rate of death or spontaneous MI: hazard ratio (HR) 0.59 [95% confidence interval (CI) 0.37–0.96] and 0.46 (95% CI 0.31–0.68). However, when intention-to-treat analysis was performed, no differences in cumulative event rates were observed between the early invasive and selective invasive strategies: HR 1.10 (95% CI 0.70–1.74) for death and 1.27 (95% CI 0.88–1.85) for death or spontaneous MI.

Conclusion The ICTUS trial did not show that an early invasive strategy resulted in a better outcome than a selective invasive strategy in patients with nSTE-ACS. However, similar to retrospective analyses from observational studies, actual revascularization was associated with lower mortality and fewer MI. Whether an early invasive strategy leads to a better outcome than a selective invasive strategy cannot be inferred from the observation that revascularized patients have a better prognosis in non-randomized studies.

Keywords Unstable angina • Treatment strategy • Revascularization • Prognosis

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The Right Timing
TIMACS Trial

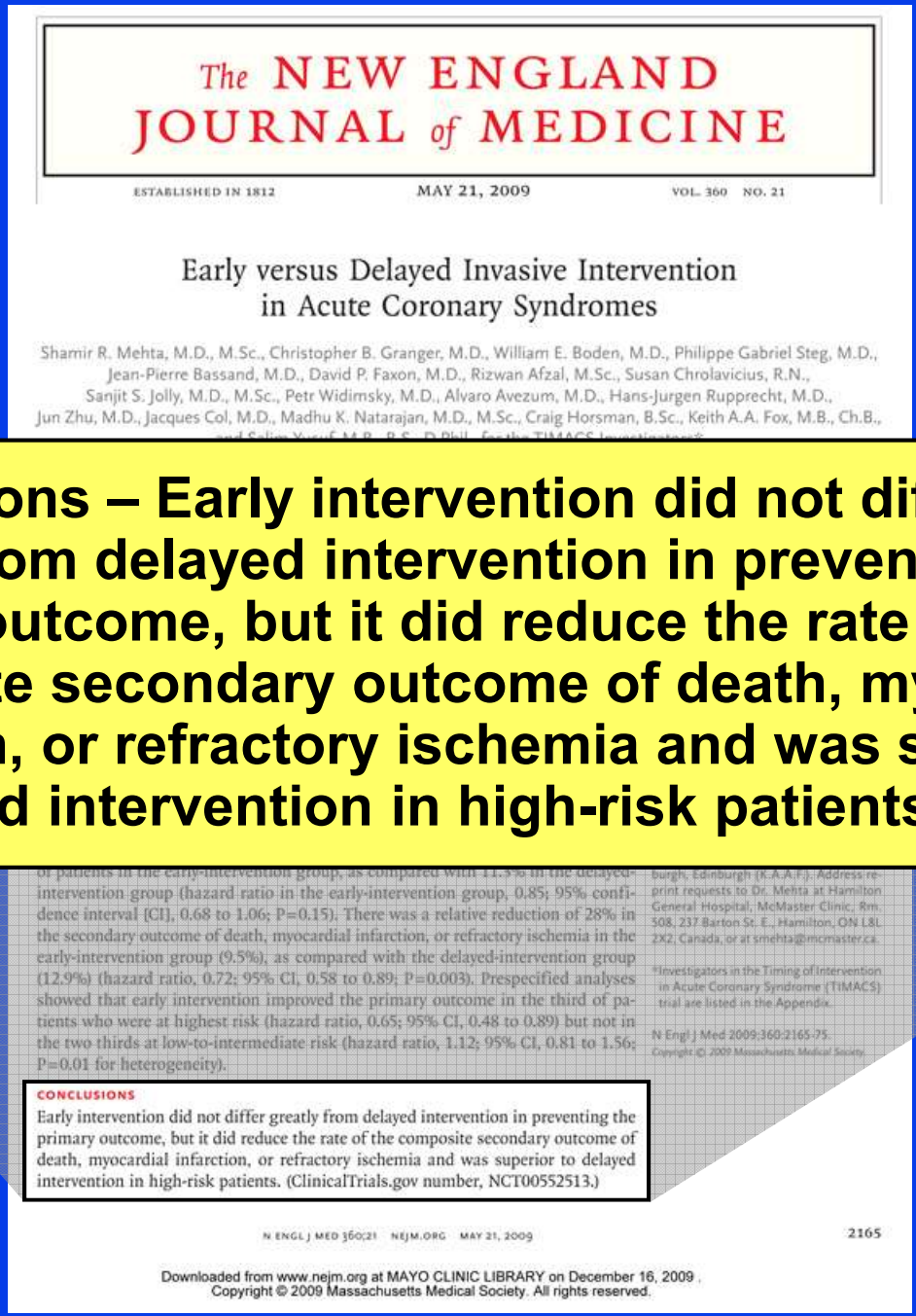
- Multicenter RCT
- 3031 patients with ACS randomized to:
  - Coronary angio/PCI ≤ 24 hours
  - Coronary angio/PCI ≥ 36 hours
- Primary endpoint:
  - Death, MI, stroke at 6 months
- Secondary endpoint:
  - Death, MI, refractory ischemia at 6 months

Mehta SR et al: NEJM 360:2165, 2009

TIMACS TRIAL
What is the Cost of Refractory Ischemia?

- Early intervention reduces refractory ischemia
  - HR 0.30 (95% CI 0.17, 0.54 p<0.001)
    3.3% → 1.0%
- With refractory ischemia
  - Subsequent risk of MI increases >4x
    4.8% → 20.6%

Mehta SR et al: NEJM 360:2165, 2009



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 21, 2009 VOL. 360 NO. 21

Early versus Delayed Invasive Intervention in Acute Coronary Syndromes

Shamir R. Mehta, M.D., M.Sc., Christopher B. Granger, M.D., William E. Boden, M.D., Philippe Gabriel Steg, M.D., Jean-Pierre Bassand, M.D., David P. Faxon, M.D., Rizwan Afzal, M.Sc., Susan Chrolavicius, R.N., Sanjit S. Jolly, M.D., M.Sc., Petr Widimsky, M.D., Alvaro Avezum, M.D., Hans-Jurgen Rupprecht, M.D., Jun Zhu, M.D., Jacques Col, M.D., Madhu K. Natarajan, M.D., M.Sc., Craig Horsman, B.Sc., Keith A.A. Fox, M.B., Ch.B.,

Conclusions – Early intervention did not differ greatly from delayed intervention in preventing the primary outcome, but it did reduce the rate of the composite secondary outcome of death, myocardial infarction, or refractory ischemia and was superior to delayed intervention in high-risk patients.

of patients in the early-intervention group, as compared with 11.9% in the delayed-intervention group (hazard ratio in the early-intervention group, 0.85; 95% confidence interval [CI], 0.68 to 1.06; P=0.15). There was a relative reduction of 28% in the secondary outcome of death, myocardial infarction, or refractory ischemia in the early-intervention group (9.5%), as compared with the delayed-intervention group (12.9%) (hazard ratio, 0.72; 95% CI, 0.58 to 0.89; P=0.003). Prespecified analyses showed that early intervention improved the primary outcome in the third of patients who were at highest risk (hazard ratio, 0.65; 95% CI, 0.48 to 0.89) but not in the two thirds at low-to-intermediate risk (hazard ratio, 1.12; 95% CI, 0.81 to 1.56; P=0.01 for heterogeneity).

CONCLUSIONS

Early intervention did not differ greatly from delayed intervention in preventing the primary outcome, but it did reduce the rate of the composite secondary outcome of death, myocardial infarction, or refractory ischemia and was superior to delayed intervention in high-risk patients. (ClinicalTrials.gov number, NCT00552513.)

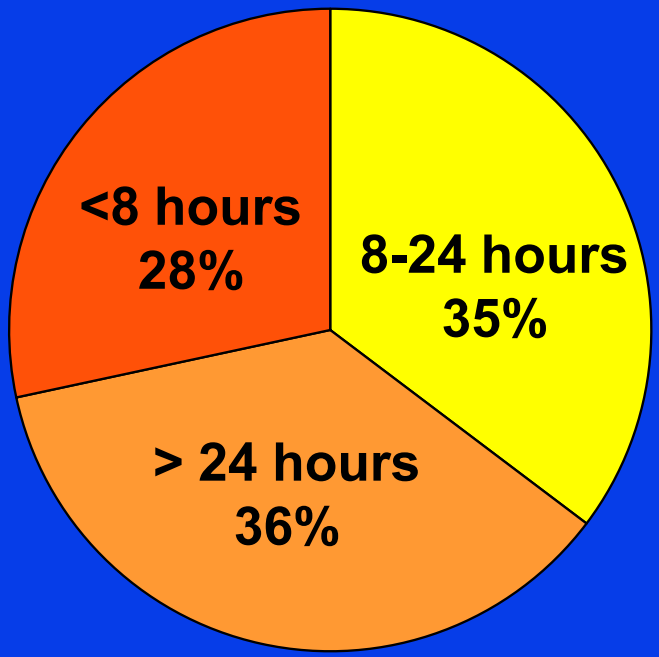
burgh, Edinburgh (K.A.A.F.). Address reprint requests to Dr. Mehta at Hamilton General Hospital, McMaster Clinic, Rm. 308, 237 Barton St. E., Hamilton, ON L8L 2X2, Canada, or at smehta@mcmaster.ca.

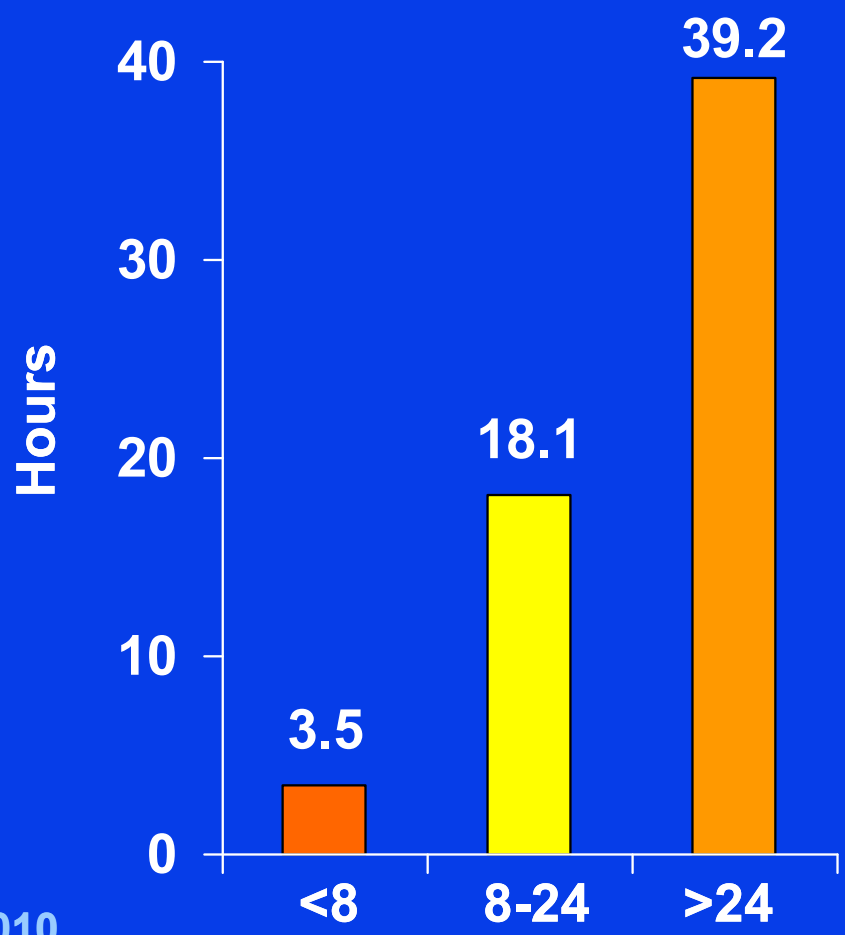
*Investigators in the Timing of Intervention in Acute Coronary Syndrome (TIMACS) trial are listed in the Appendix.

N Engl J Med 2009;360:2165-75.

Acute Coronary Syndromes
Delay to Angioplasty

- ACUITY Trial of NSTEMI patients
- 7,749 patients underwent PCI





Sorajja P et al, J Am Coll Cardiol 55:1416-24, 2010

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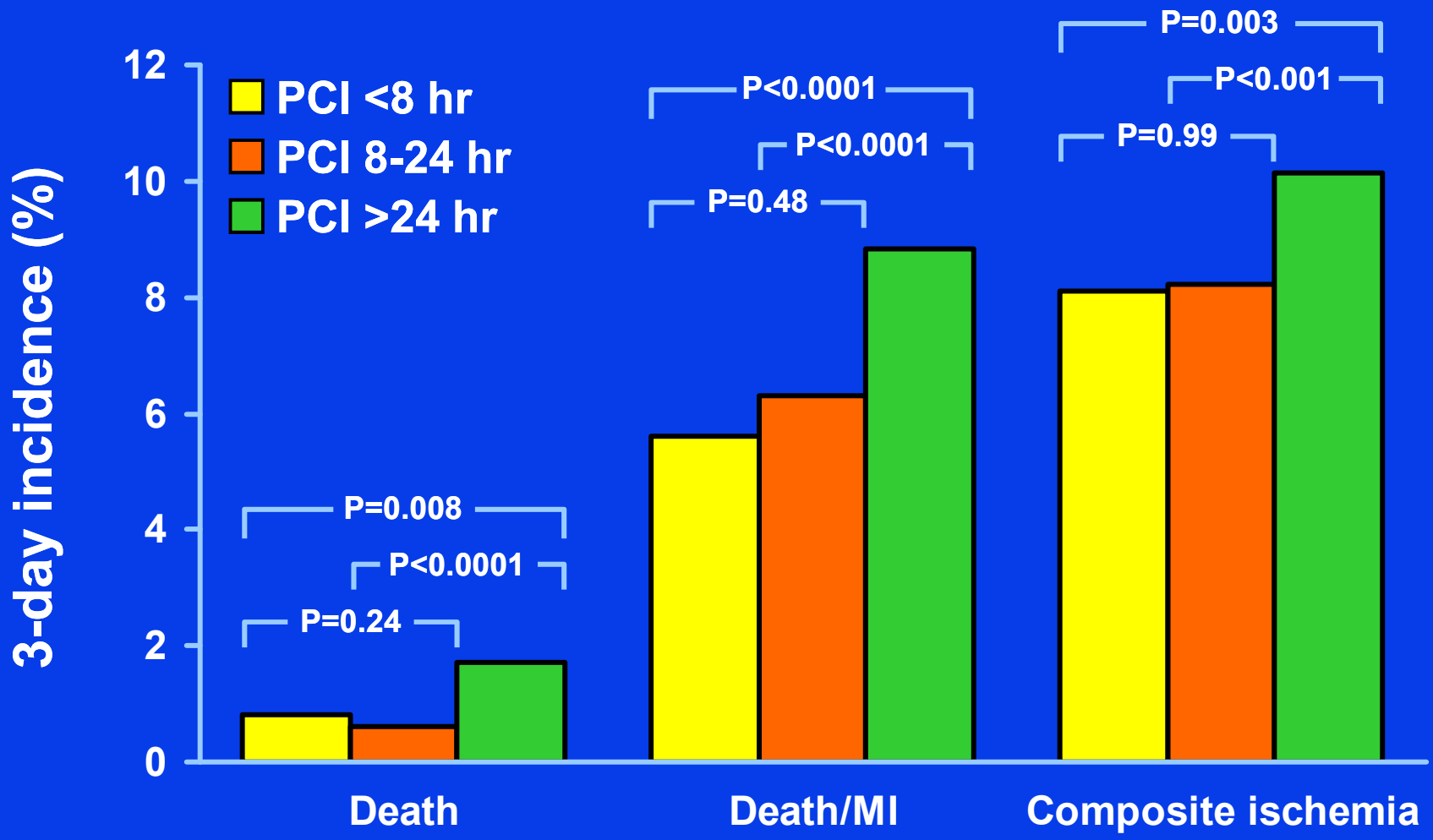
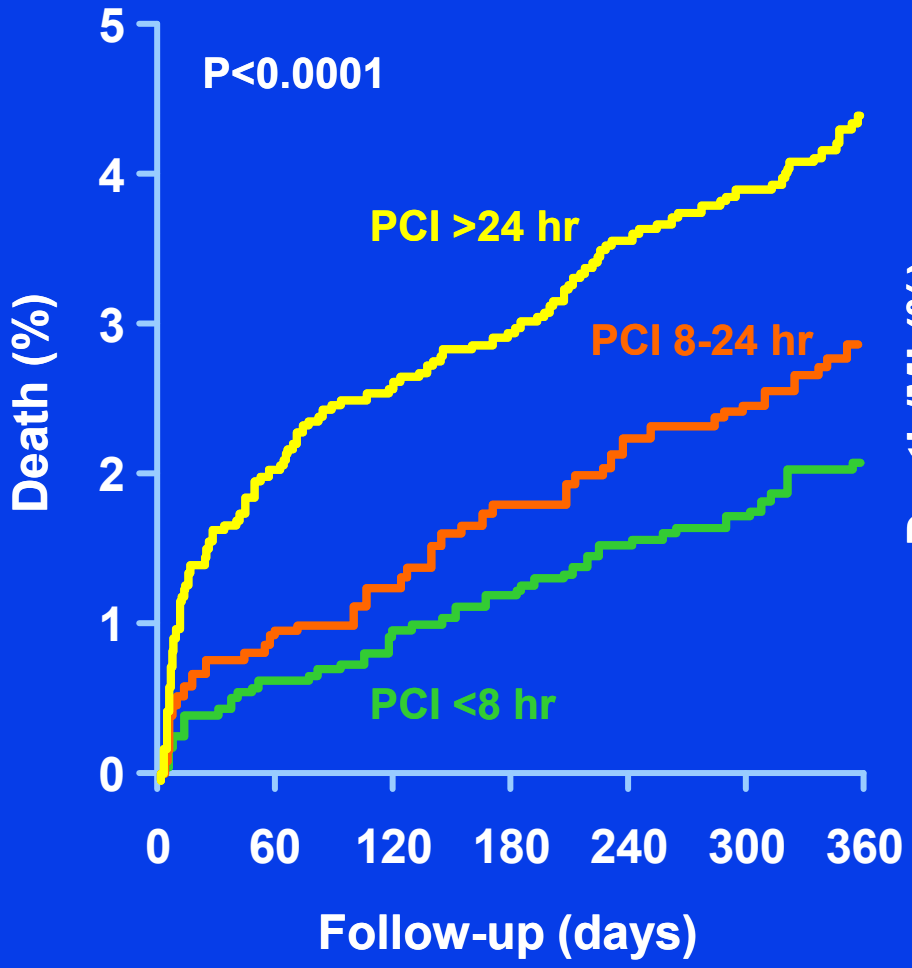
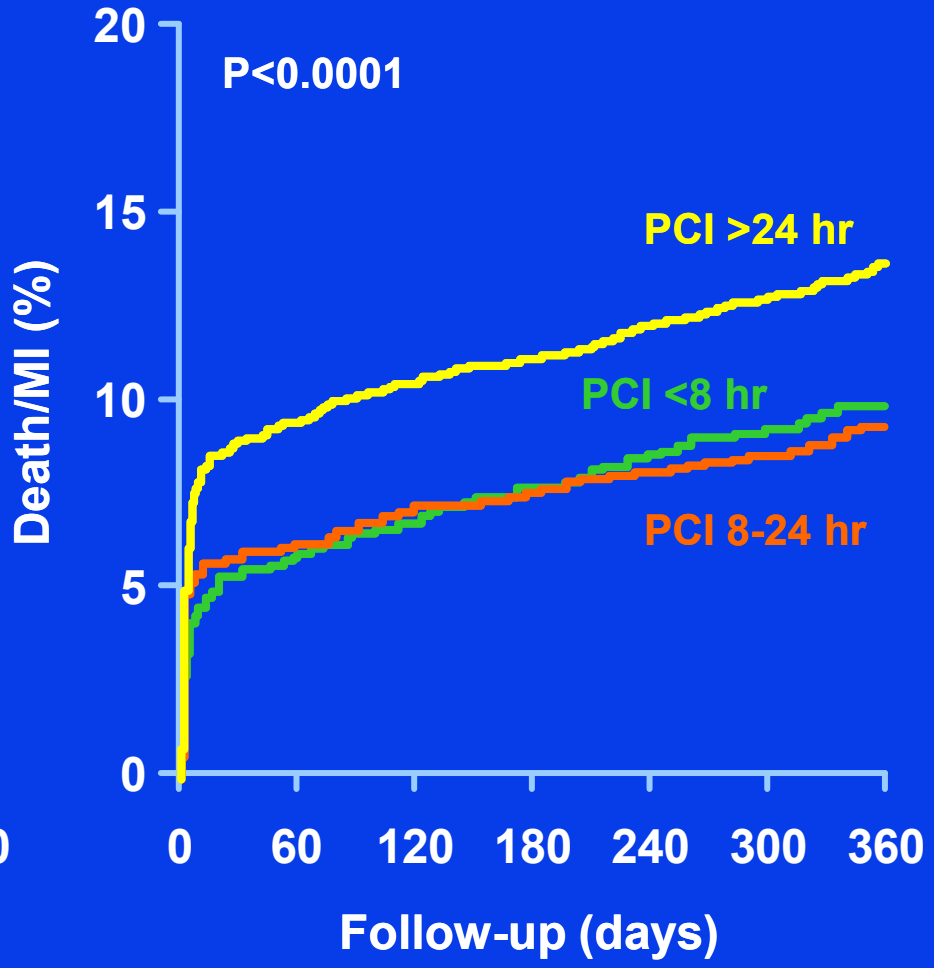
Acute Coronary Syndromes Delay to Angioplasty
Timing of PCI



Sorajja et al: JACC 55:1416, 2010

Acute Coronary Syndromes Delay to Angioplasty

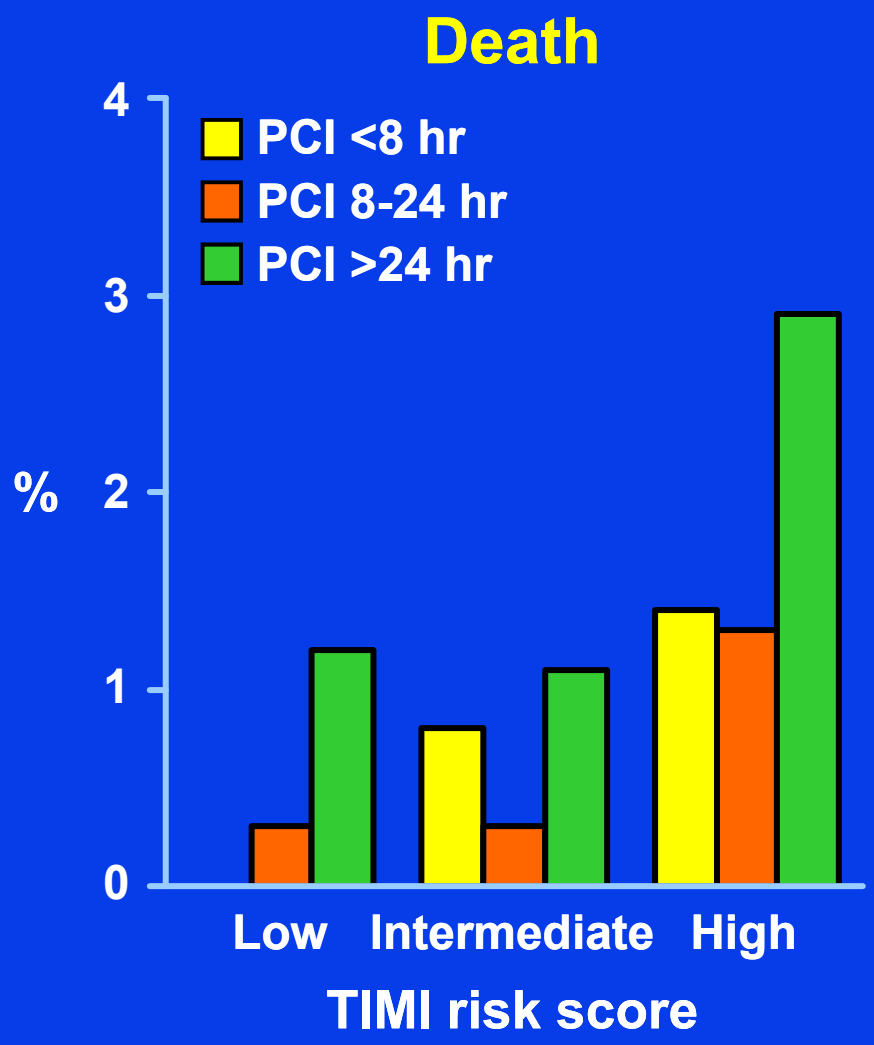


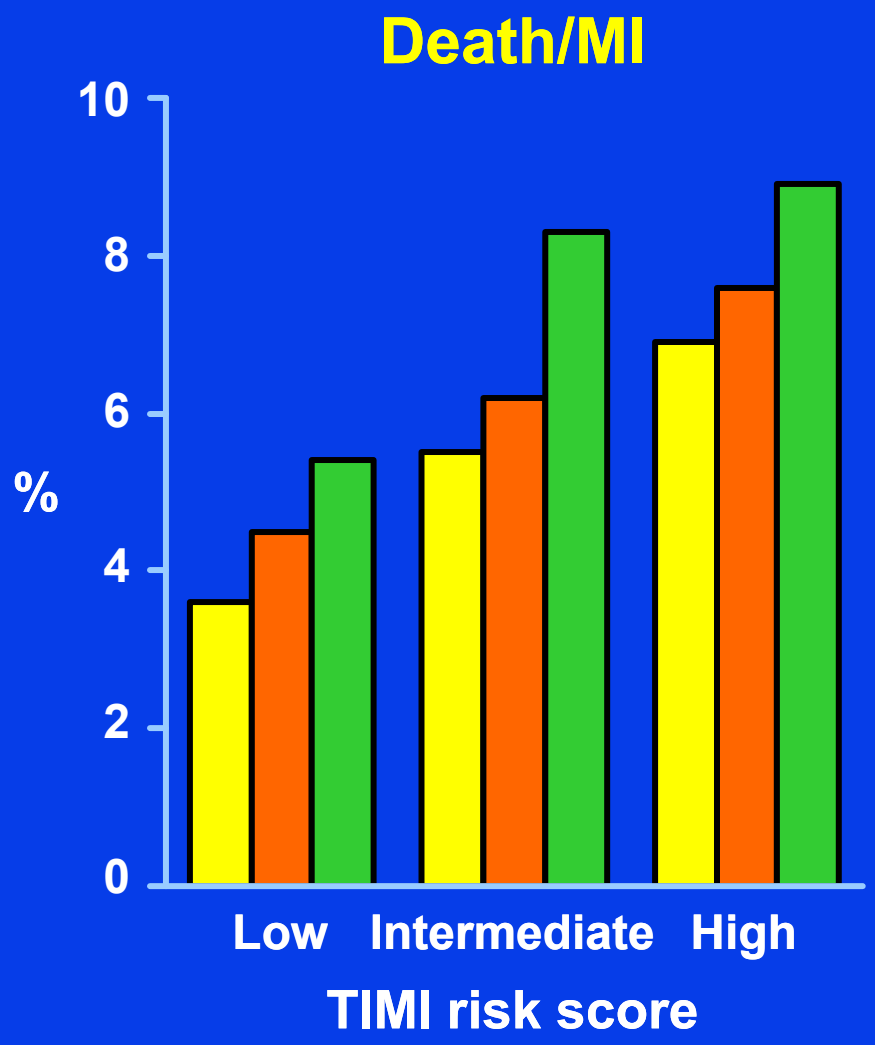


Sorajja et al: JACC 55:1416, 2010

Acute Coronary Syndromes Delay to Angioplasty

30-Day Outcomes by Patient Risk and Timing PCI





Sorajja et al: JACC 55:1416, 2010

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CLINICAL RESEARCH — Invasive and Interventional Cardiology

Impact of Delay to Angioplasty in Patients With Acute Coronary Syndromes Undergoing Invasive Management

In this large-scale study, delaying revascularization with PCI >24 hours in patients with NSTE-ACS was an independent predictor of early and late mortality and adverse ischemic outcomes. These findings suggest that urgent angiography and triage to revascularization should be a priority in NSTE-ACS patients.

non–ST-segment elevation acute coronary syndromes (NSTE-ACS) undergoing an invasive management strategy.

Methods Patients undergoing PCI in the ACUITY (Acute Catheterization and Urgent Intervention Triage strategY) trial were stratified according to timing of PCI after clinical presentation for outcome analysis.

Results Percutaneous coronary intervention was performed in 7,749 patients (median age 63 years; 73% male) with NSTE-ACS at a median of 19.5 h after presentation (<8 h [n = 2,197], 8 to 24 h [n = 2,740], and >24 h [n = 2,812]). Delay to PCI >24 h after clinical presentation was significantly associated with increased 30-day mortality, myocardial infarction (MI), and composite ischemia (death, MI, and unplanned revascularization). By multivariable analysis, delay to PCI of >24 h was a significant independent predictor of 30-day and 1-year mortality. The incremental risk of death attributable to PCI delay >24 h was greatest in those patients presenting with high-risk features.

Conclusions In this large-scale study, delaying revascularization with PCI >24 h in patients with NSTE-ACS was an independent predictor of early and late mortality and adverse ischemic outcomes. These findings suggest that urgent angiography and triage to revascularization should be a priority in NSTE-ACS patients. (J Am Coll Cardiol 2010; 55:1416–24) © 2010 by the American College of Cardiology Foundation

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What Then Could We Say

- In NSTEMI ACS patients, goal should be to get them to the point of care on time
- We should develop systems of care similar to those used for STEMI patients
- Optimize risk stratification
- In higher risk patients aggressive early revascularization improves outcome


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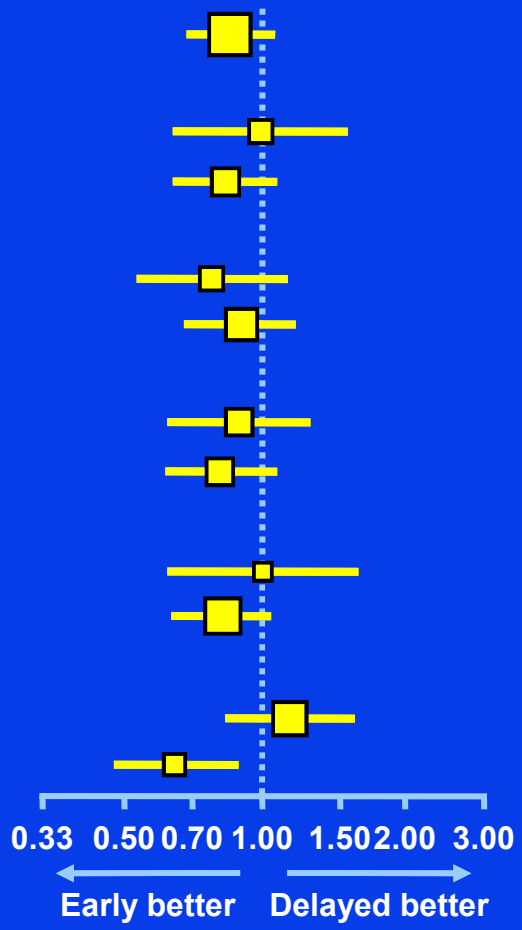
Invasive vs Conservative Strategies
Baseline Characteristics

	Women		Men	
	Invasive n=1571	Conservative n=1581	Invasive n=3641	Conservative n=3619
ST Dep (%)	39.0	38.6	37.6	37.3
T inv (%)	53.9	53.9	43.4	43.3
Bio + (%)	42.9	42.5	55.3	53.7

O'Donoghue M et al, JAMA 300:71-80, 2008

TIMACS Trial
Hazard Ratios

Primary outcome Characteristic	Patients (no.)	Early (%)	Delayed (%)	Hazard ratio for event (95% CI)	P for interaction
Overall	3,031	9.6	11.3	0.85 (0.68-1.06)	
Age					0.46
<65 yr	1,293	6.4	6.4	0.98 (0.64-1.52)	
≥65 yr	1,736	12.2	14.6	0.83 (0.64-1.07)	
Sex					0.53
Female	1,052	9.6	12.3	0.77 (0.53-1.12)	
Male	1,976	9.6	10.7	0.89 (0.68-1.18)	
ST-segment deviation					0.71
No	1,523	7.5	8.2	0.88 (0.62-1.26)	
Yes	1,508	11.6	14.2	0.81 (0.61-1.07)	
Elevated cardiac marker					0.43
No	668	10.4	10.4	1.00 (0.62-1.60)	
Yes	2,363	9.4	11.5	0.81 (0.63-1.04)	
GRACE score					0.01
0-140	2,070	7.6	6.7	1.12 (0.81-1.56)	
≥141	961	13.9	21.0	0.63 (0.48-0.89)	



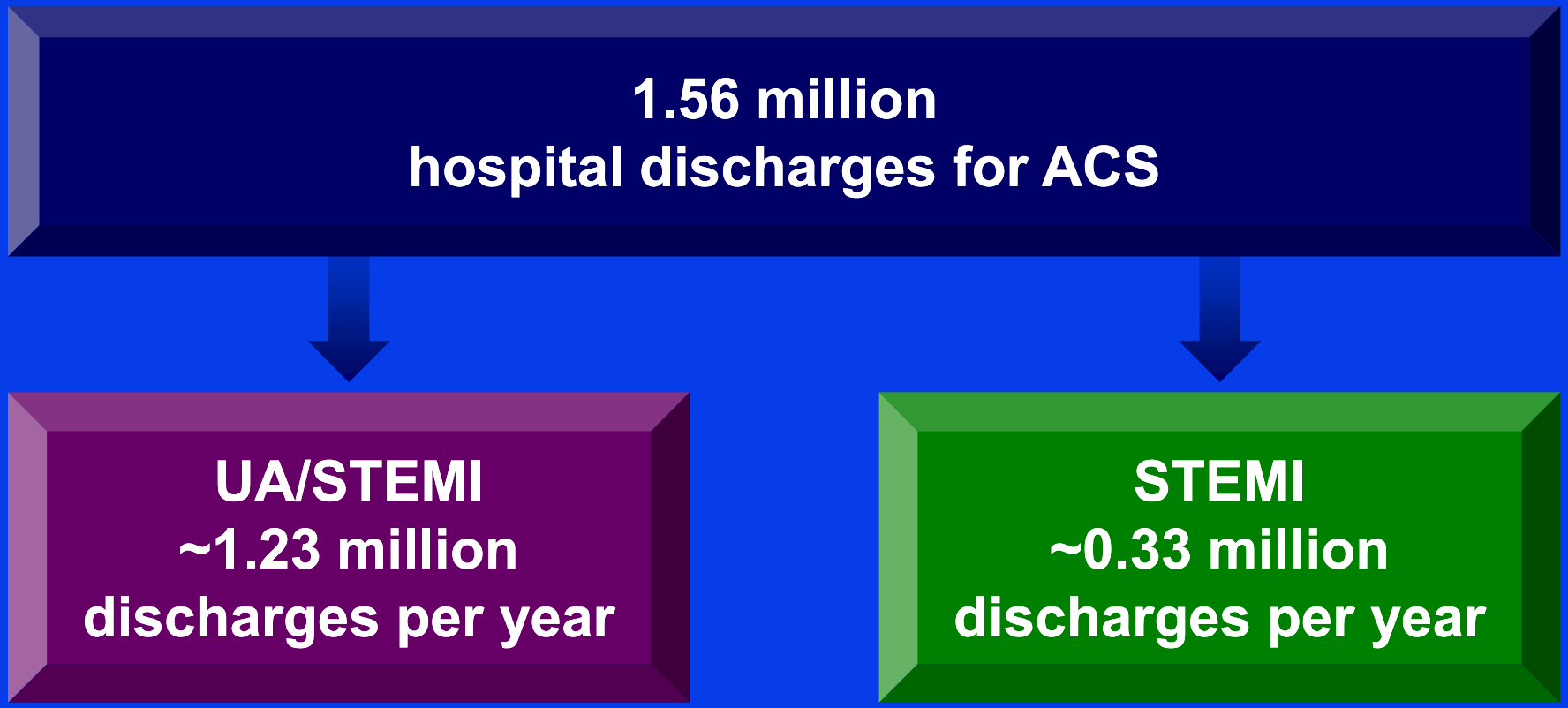
Mehta SR et al: 360:2165, 2009

MAYO CLINIC

Background

- Increasing emphasis on rapid diagnosis, transport and treatment of STEMI (D2B & H2H)
- Question ‘If systems are in place for patients with STEMI, should they be applied for non STEMI?’

Epidemiology of CAD/ACS
UA/NSTEMI vs STEMI



Wiviott S et al: J Am Coll Cardiol 47:1553, 2006

ACC/AHA 2008 Performance Measures for Adults with ST-Elevation and Non-ST Elevation Myocardial Infarction

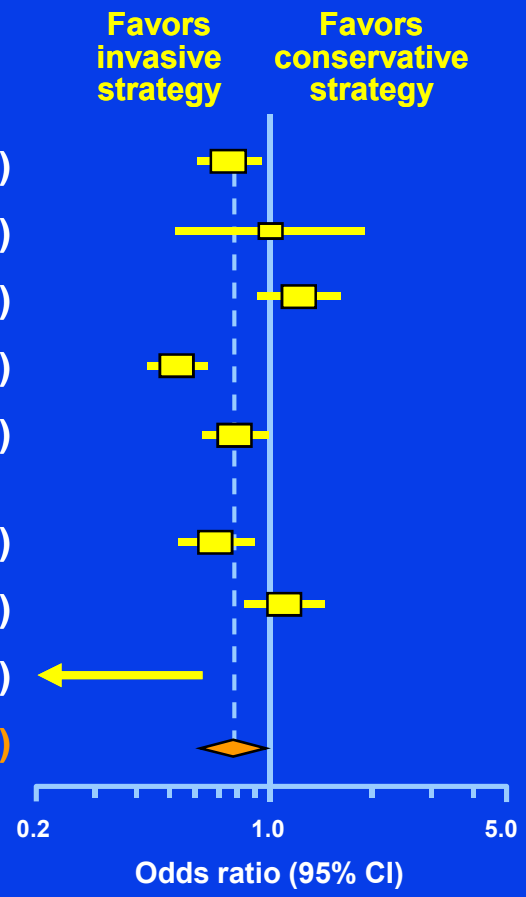
Early Invasive Strategy for High-Risk NSTEMI Patients

The UA/NSTEMI guidelines recommend an early invasive strategy for patients with UA/NSTEMI who have evidence of refractory symptoms and hemodynamic or electric instability (Class I; LOE:B) or an elevated risk for clinical events based on clinical characteristics, including elevated biomarkers or electrocardiographic abnormalities Class I; LOE:A). A conservative selectively invasive strategy also is considered reasonable (Class IIb; LOE:B) for stable patients, including those with elevated biomarkers. The writing committee considered an AMI performance measure to evaluate the use of an early invasive strategy in patients with NSTEMI. However, a measure was not endorsed at this time because of the complexity of the guideline recommendations and the challenges in translating these recommendations into a measure that can be implemented feasibly.

JACC 52:2046-2099, 2008

Invasive vs Conservative Treatment Strategy in NSTE ACS

All pt	Rates of death, MI or rehospitalization with ACS: Invasive strategy No.	Invasive strategy %	Conservative strategy No.	Conservative strategy %	Odds ratio (95% CI)
TIMI IIIB	122/895	13.6	171/915	18.7	0.75 (0.61-0.93)
MATE	27/111	24.3	22/90	24.4	0.99 (0.52-1.90)
VANQWISH	148/462	32.0	124/458	27.7	1.22 (0.92-1.61)
FRISC II	196/1,093	17.9	322/1,102	29.2	0.53 (0.43-0.65)
TACTICS-TIMI 18	177/1,114	15.9	215/1,106	19.4	0.78 (0.63-0.97)
RITA 3	122/895	13.6	171/915	18.7	0.69 (0.53-0.88)
VINO	5/64	7.8	19/67	28.4	0.21 (0.07-0.62)
ICTUS	137/604	22.7	126/596	21.1	1.09 (0.83-1.44)
Overall	1,075/5,083	21.1	1,313/5,067	25.9	0.78 (0.61-0.98)



O'Donoghue M et al: JAMA 300:71, 2008

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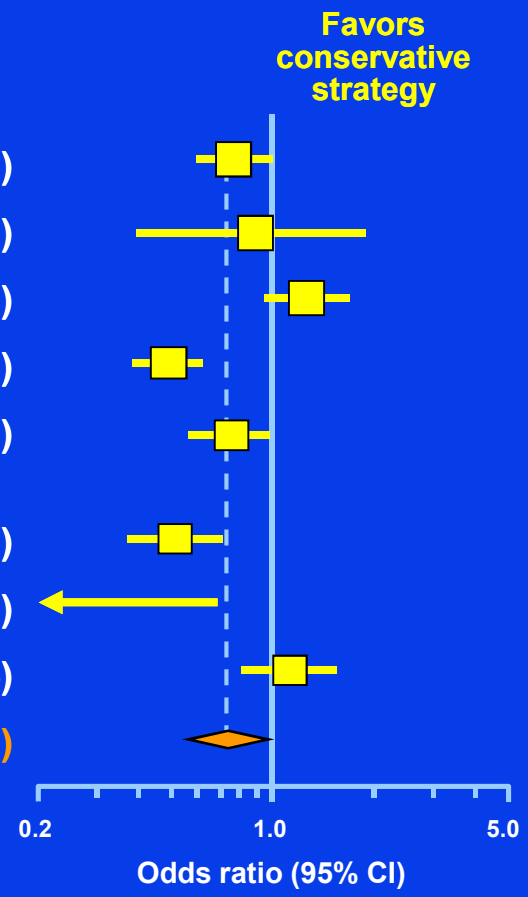
Invasive vs Conservative Treatment Strategy in NSTE ACS

	Rates of death, MI or rehospitalization with ACS				
	Invasive strategy		Conservative strategy		
Men	No.	%	No.	%	Odds ratio (95% CI)
TIMI IIIB	178/491	36.3	206/485	42.5	0.77 (0.60-1.00)
MATE	20/77	26.0	15/52	28.8	0.87 (0.39-1.90)
VANQWISH	146/448	32.6	124/448	27.7	1.26 (0.95-1.68)
FRISC II	131/778	16.8	217/745	29.1	0.49 (0.39-0.63)
TACTICS-TIMI 18	110/719	15.3	144/744	19.4	0.75 (0.57-0.99)
RITA 3	67/545	12.3	125/583	21.4	0.51 (0.37-0.71)
VINO	3/41	7.3	12/39	30.8	0.18 (0.05-0.69)
ICTUS	96/446	21.5	85/434	19.6	1.13 (0.81-1.56)
Overall	751/3,545	21.2	928/3,530	26.3	0.73 (0.55-0.98)



O'Donoghue M et al: JAMA 300:71, 2008

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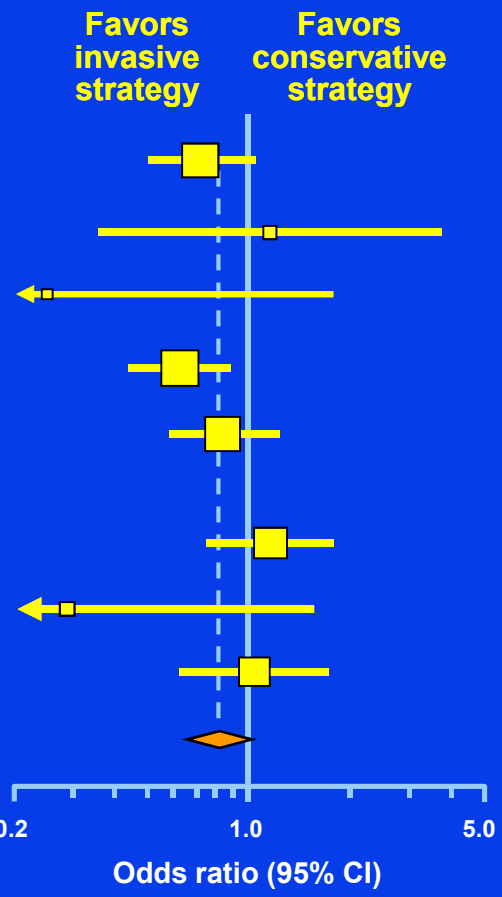
Invasive vs Conservative Treatment Strategy in NSTE ASC

Women	Rates of death, MI or rehospitalization with ACS: Invasive strategy No.	Invasive strategy %	Conservative strategy No.	Conservative strategy %	Odds ratio (95% CI)
TIMI IIIB	85/249	34.1	104/248	41.9	0.72 (0.50-1.03)
MATE	7/34	20.6	7/38	18.4	1.15 (0.36-3.69)
VANQWISH	2/14	14.3	4/10	40.0	0.25 (0.04-1.77)
FRISC II	65/315	20.6	105/357	29.4	0.62 (0.44-0.89)
TACTICS-TIMI 18	67/395	17.0	71/362	19.6	0.84 (0.58-1.21)
RITA 3	55/350	15.7	46/332	13.9	1.16 (0.76-1.77)
VINO	2/23	8.7	7/28	25.0	0.29 (0.05-1.54)
ICTUS	41/158	25.9	41/162	25.3	1.03 (0.63-1.71)
Overall	324/1,538	21.1	385/1,537	25.0	0.81 (0.65-1.01)



O'Donoghue M et al: JAMA 300:71, 2008

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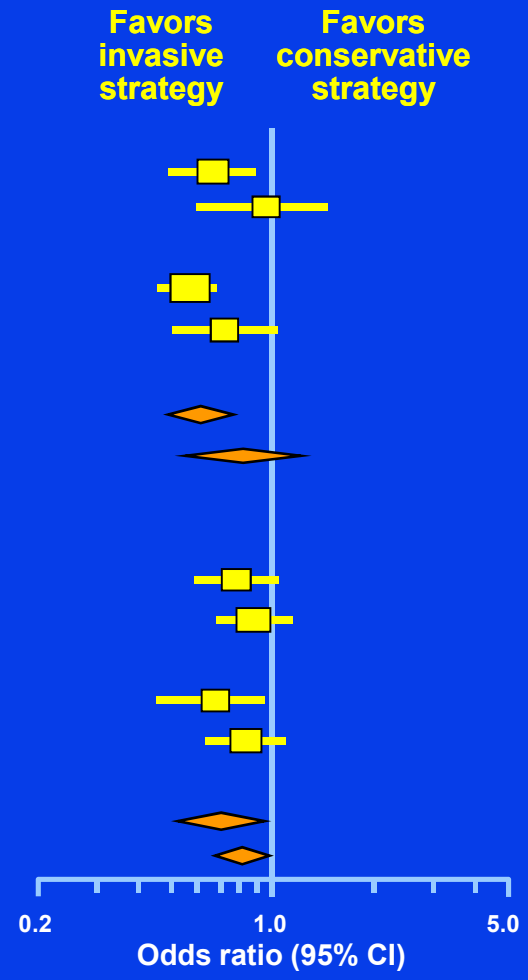
Invasive vs Conservative Treatment Strategy in NSTE ASC

Biomarker status	Individuals (no.)		Death, MI or rehospitalization with ACS events (no.)		Odds ratio (95% CI)
	Invasive strategy	Con-servative strategy	Invasive strategy	Con-servative strategy	
Women					
Positive	550	550	118	156	0.67 (0.50-0.88)
Negative	743	743	152	163	0.94 (0.61-1.44)
Men					
Positive	1,392	1,353	260	382	0.56 (0.46-0.67)
Negative	1,126	1,168	229	300	0.72 (0.51-1.01)
Overall					
Positive	1,942	1,903	378	538	0.59 (0.51-0.69)
Negative	1,869	1,911	381	463	0.79 (0.58-1.06)
ST-segment deviation					
Women					
Present	671	667	160	194	0.77 (0.58-1.02)
Absent	859	864	164	190	0.87 (0.69-1.11)
Men					
Present	1,561	1,559	360	475	0.67 (0.46-0.98)
Absent	1,938	1,932	381	443	0.82 (0.63-1.07)
Overall					
Present	2,232	2,226	520	669	0.72 (0.54-0.95)
Absent	2,797	2,796	545	633	0.82 (0.69-0.99)



O'Donoghue M et al: JAMA 300:71, 2008

Invasive vs Conservative Strategies
ACS, NSTEMI

O'Donoghue M et al, JAMA 300:71-80, 2008

Conclusions: In NSTE ACS, an invasive strategy has a comparable benefit in men and high-risk women for reducing the composite end point of death, MI, or rehospitalization with ACS. In contrast, our data provide evidence supporting the new guideline recommendation for a conservative strategy in low-risk women.

Qayyum R et al: Ann Intern Med 148:186-96, 2008

Conclusions: Available trial evidence is heterogeneous and insufficient for comparing routine and selective invasive strategies. Therefore, in patients with non-ST segment elevation ACS a routine invasive strategy cannot be proven to reduce deaths or nonfatal myocardial infarction.

Invasive vs Conservative Strategies
ACS, NSTEMI

O'Donoghue M et al, JAMA 300:71-80, 2008

Trial	Year
TIMI IIB	1994
MATE	1998
VANQWISH	1998
FRISC II	1999
TACTICS-TIMI 18	2001
VINO	2002
RITA 3	2002
ICTUS	2005

Qayyum R et al: Ann Intern Med 148:186-96, 2008

Trial	Year
FRISC II	2006
ICTUS	2007
MATE	1998
Eisenberg et al	2005
RITA – 3	2005
TACTICS	2001
TIMI IIIB	1995
TRUCS	2000
VANQWISH	1998
VINO	2002

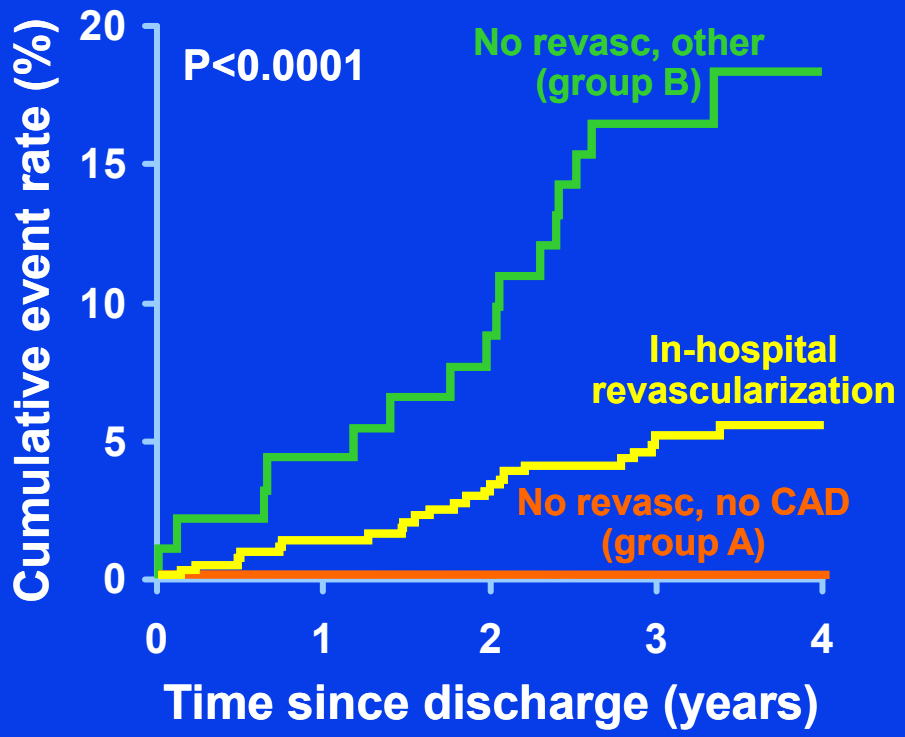
Revascularization Rates

	Early Invasive	Selective Invasive
ICTUS (1 yr)	79%	54%
TIMI IIIB (1 yr)	64%	58%
VANQWISH (23 mo)	44%	33%
FRISC II (6 mo)	77%	37%
TACTICS-TIMI 18	61%	44%
RITA 3 (1 yr)	57%	28%

Hirsch A et al: EHJ 30:645, 2009

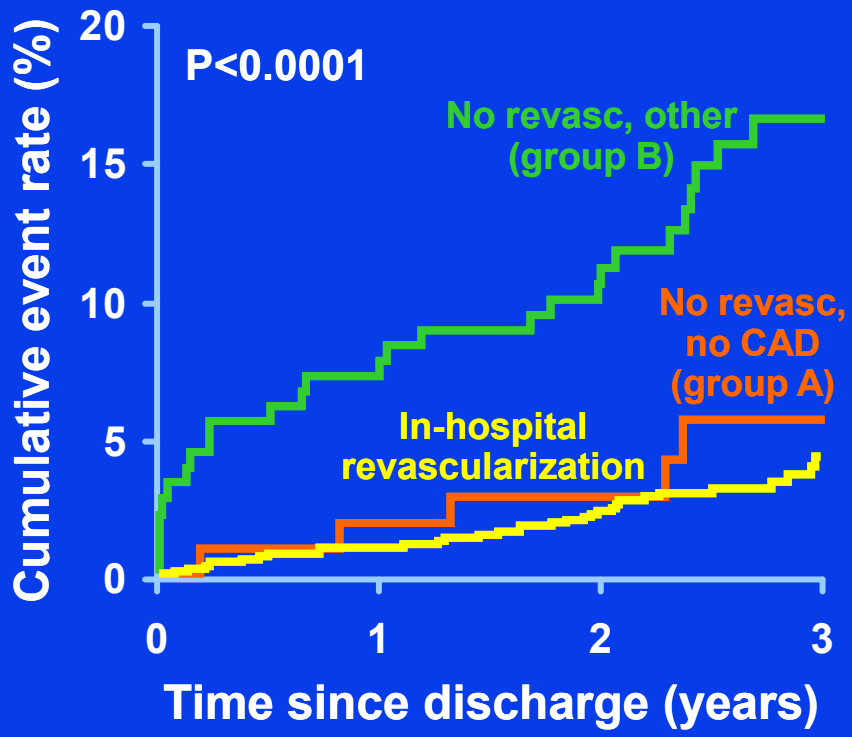
Risk of Death

Death



No. at risk					
Revasc	454	448	438	329	84
No revasc, no CAD	53	53	53	35	8
No revasc, other	91	87	83	65	18

Death or Spontaneous MI



No. at risk				
Revasc	454	445	423	137
No revasc, no CAD	53	51	49	14
No revasc, other	91	77	66	24

Hirsch A et al: EHJ 30:645, 2009

MAYO CLINIC

Primary and Secondary Outcomes
At 30 Days

Variable	Early intervention (n=1,593) %	Delayed intervention (n=1,438) %	Hazard ratio (95% CI)	P
Death, myocardial infarction, or stroke	6.7	7.6	0.88 (0.67-1.15)	0.34
Death, myocardial infarction, or refractory ischemia	6.6	9.3	0.70 (0.54-0.90)	0.006
Death, myocardial infarction, stroke, refractory ischemia, or repeat intervention	12.0	13.0	0.91 (0.75-1.12)	0.37
Death	2.9	3.3	0.86 (0.58-1.29)	0.48
Myocardial infarction	3.6	4.1	0.87 (0.61-1.25)	0.46
Stroke	0.9	0.9	1.04 (0.50-2.19)	0.91
Refractory ischemia	1.0	3.1	0.30 (0.17-0.55)	<0.001
Repeat intervention	5.9	4.2	1.39 (1.01-1.93)	0.05

Mehta SR et al: NEJM 360:2165, 2009

MAYO CLINIC

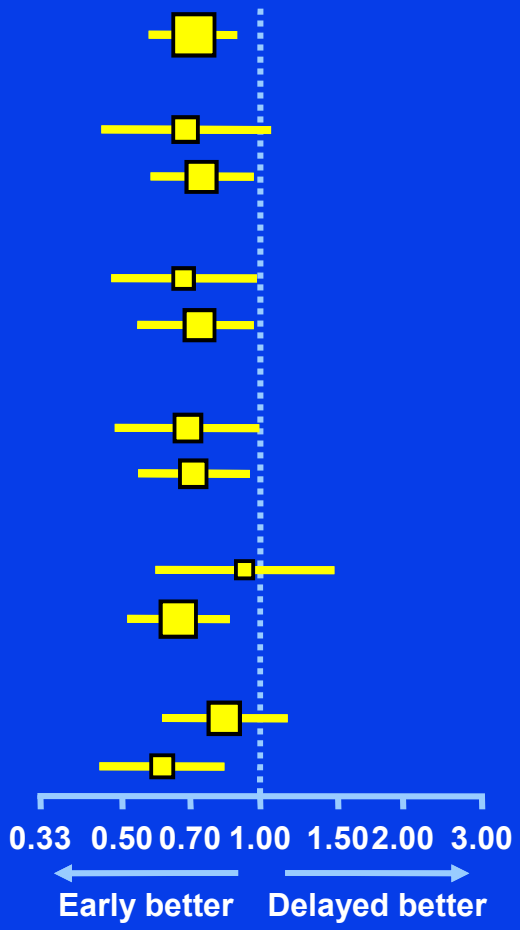
Primary and Secondary Outcomes
At 6 Months

Variable	Early intervention (n=1,593) %	Delayed intervention (n=1,438) %	Hazard ratio (95% CI)	P
Death, myocardial infarction, or stroke	9.6	11.3	0.85 (0.68-1.06)	0.15
Death, myocardial infarction, or refractory ischemia	9.5	12.9	0.72 (0.58-0.89)	0.003
Death, myocardial infarction, stroke, refractory ischemia, or repeat intervention	16.6	19.5	0.84 (0.71-0.99)	0.04
Death	4.8	5.9	0.81 (0.60-1.11)	0.19
Myocardial infarction	4.8	5.7	0.83 (0.61-1.14)	0.25
Stroke	1.3	1.4	0.90 (0.49-1.68)	0.74
Refractory ischemia	1.0	3.3	0.30 (0.17-0.54)	<0.001
Repeat intervention	8.7	8.5	1.04 (0.82-1.34)	0.73

Mehta SR et al: NEJM 360:2165, 2009

TIMACS Trial
Hazard Ratios

Secondary outcome Characteristic	Patients (no.)	Early (%)	Delayed (%)	Hazard ratio for event (95% CI)	P for interaction
Overall	3,031	9.5	12.9	0.72 (0.58-0.89)	
Age					0.86
<65 yr	1,295	6.0	8.3	0.70 (0.46-1.06)	
≥65 yr	1,736	12.3	16.2	0.74 (0.58-0.95)	
Sex					0.69
Female	1,052	9.9	14.3	0.68 (0.48-0.97)	
Male	1,978	9.2	12.2	0.74 (0.56-0.97)	
ST-segment deviation					0.86
No	1,523	7.0	10.0	0.69 (0.49-0.98)	
Yes	1,508	11.9	16.0	0.72 (0.55-0.94)	
Elevated cardiac marker					0.22
No	666	11.8	12.9	0.92 (0.59-1.41)	
Yes	2,365	8.8	13.0	0.67 (0.52-0.85)	
GRACE score					0.15
0-140	2,049	7.5	8.8	0.83 (0.61-1.12)	
≥141	982	13.7	21.6	0.62 (0.45-0.83)	



Mehta SR et al: 360:2165, 2009

MAYO CLINIC

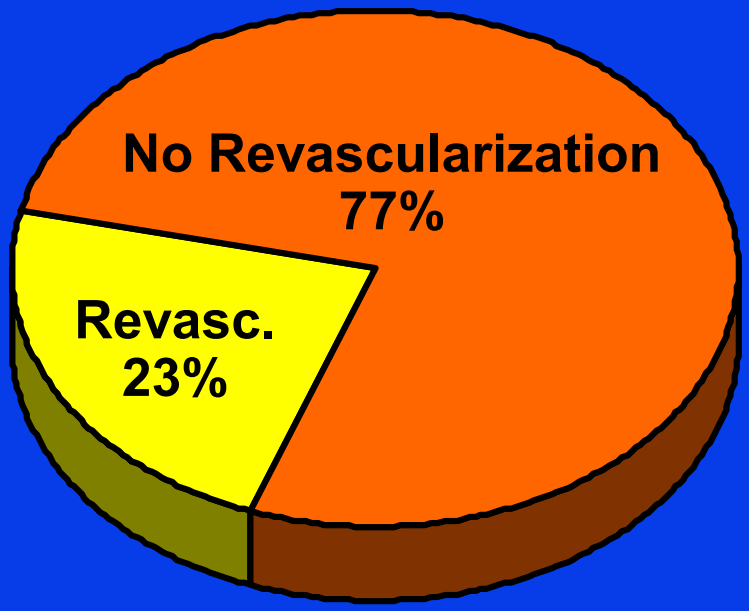
Revascularization and Survival
NSTEMI and CHF

- Global Registry (GRACE)
- 29,844 with NSTEMI between 1999 and 2007
- 4,953 with CHF at presentation (35%)
  K-II or III
- Goal: analyze impact of revascularization on survival

Steg PG et al: Circ 118:1163, 2008

Revascularization and Survival
NSTEMI and CHF

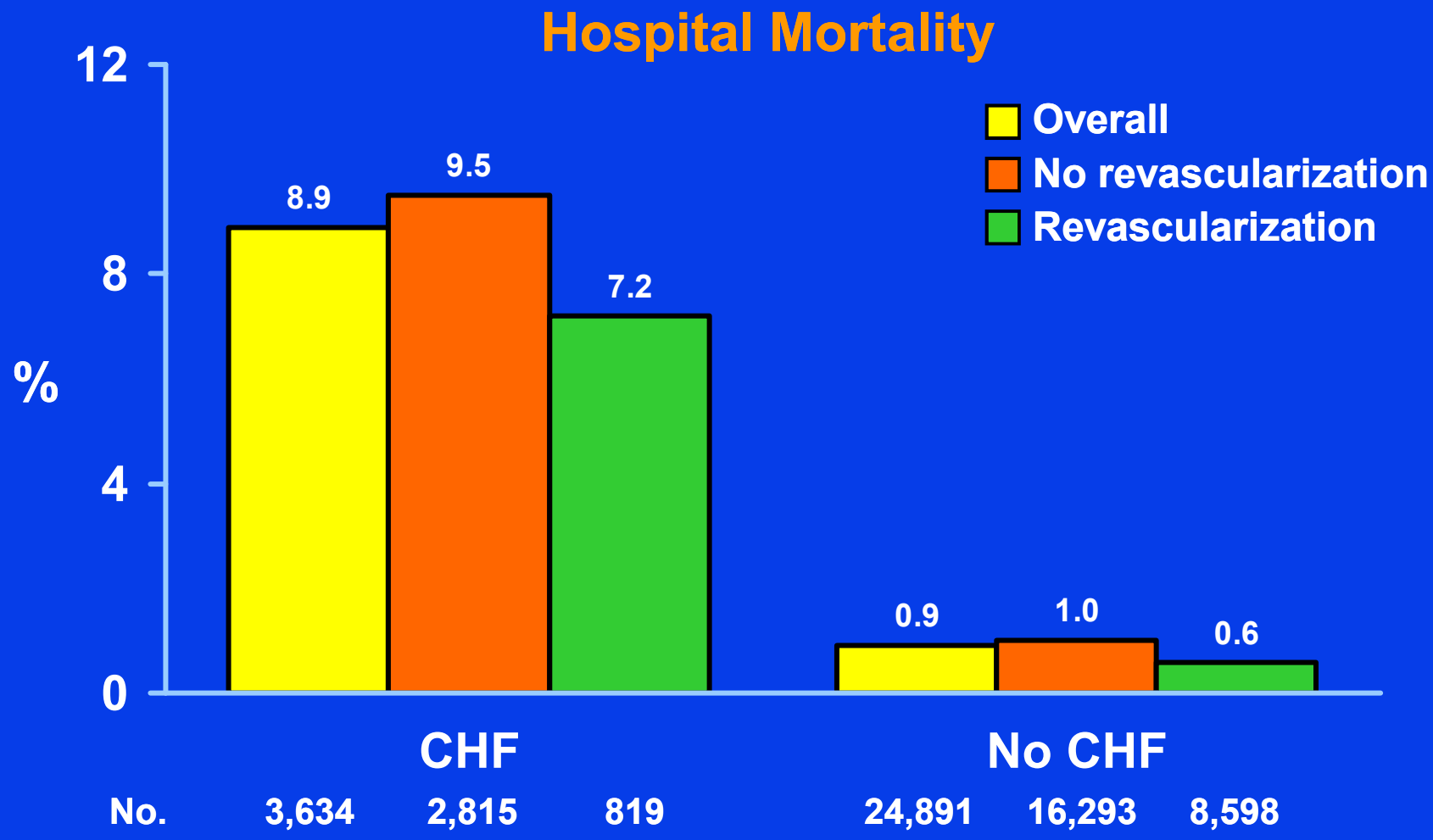
N=3634



	No Revasc	Revasc	P
Male	58%	63%	0.01
Age	75	72	<0.001
EF	40%	50%	<0.001
Hx CHF	34%	24%	<0.001
TIA/CVA	15%	11%	0.01

Steg PG et al: Circ 118:1163, 2008

Revascularization and Survival



Steg PG et al: Circ 118:1163, 2008

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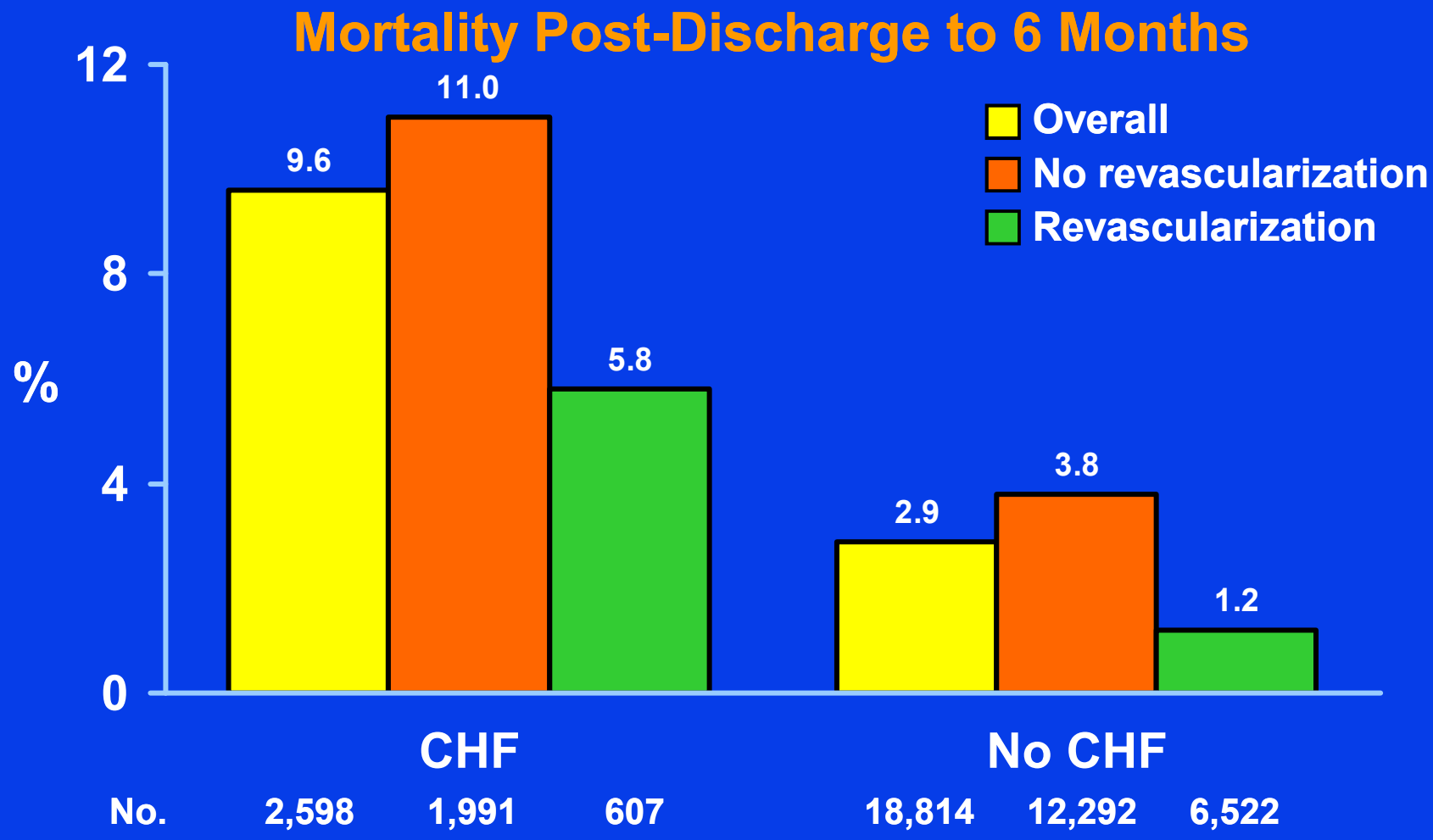
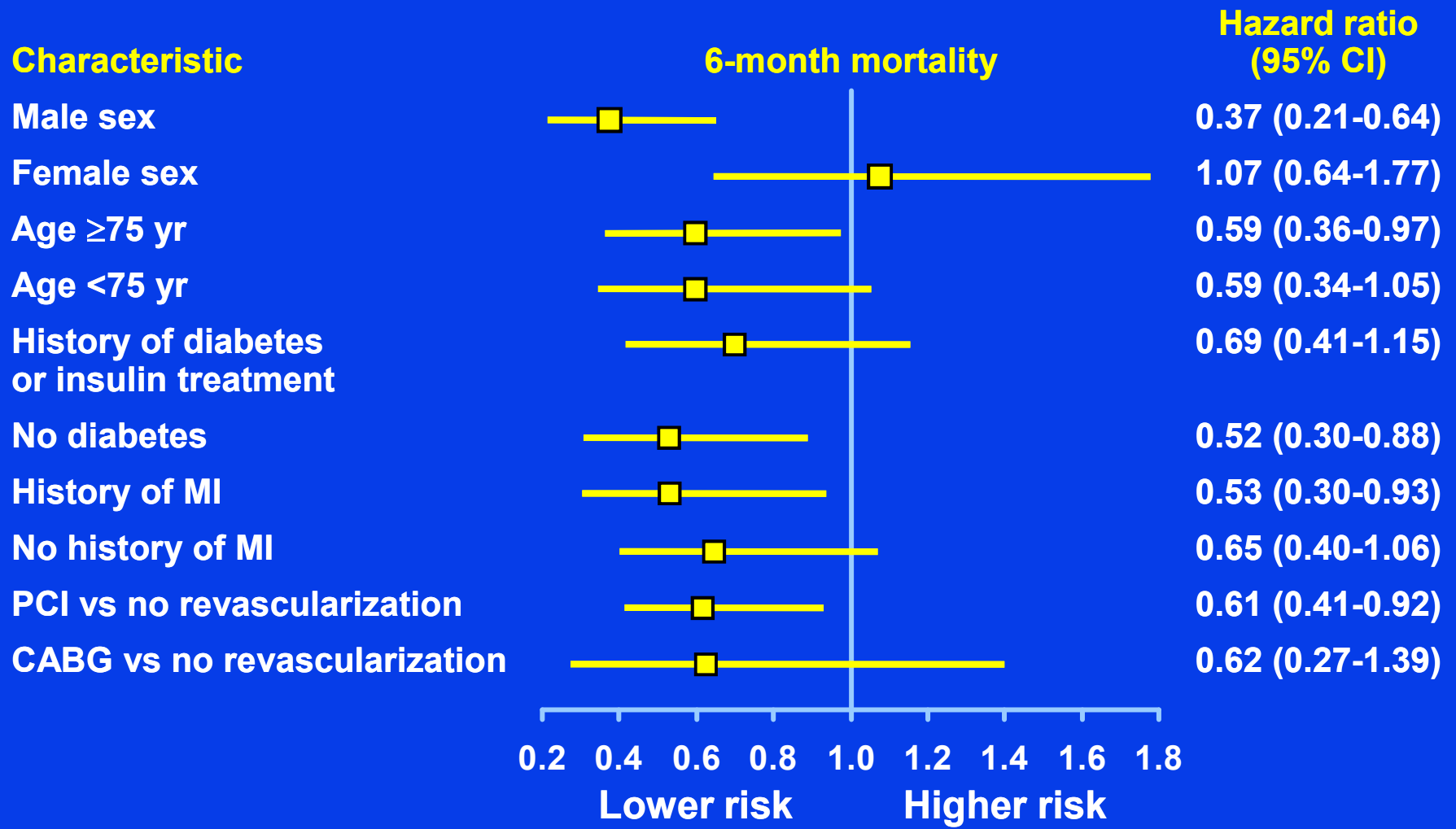
Revascularization and Survival



Steg PG et al: Circ 118:1163, 2008

MAYO CLINIC

Revascularization and Survival
Risk of Death



Steg PG: Circ 118:1163, 2008

MAYO CLINIC

Conclusions – This observational study suggests a low use of in-hospital revascularization in non-ST-elevation acute coronary syndrome patients with CHF. The consistent reduction in postdischarge death in revascularized patients suggests that broader application in this high-risk group may be beneficial.

Impact of In-Hospital Revascularization on Survival in Patients With Non–ST-Elevation Acute Coronary Syndrome

$P=0.005$). When revascularization as a time-varying covariate was taken into account in an adjusted Cox regression, the rate of death was again lower in patients undergoing revascularization (hazard ratio 0.64, 95% confidence interval 0.45 to 0.93, $P=0.02$).

Conclusions—This observational study suggests a low use of in-hospital revascularization in non–ST-elevation acute coronary syndrome patients with CHF. The consistent reduction in postdischarge death in revascularized patients suggests that broader application of revascularization in this high-risk group may be beneficial. (***Circulation*. 2008;118: 1163-1171.)**

Key Words: acute coronary syndromes ■ myocardial infarction ■ heart failure ■ mortality

Congestive heart failure (CHF) is a common complication in patients with an acute coronary syndrome (ACS).[1] In a previous report from the Global Registry of Acute Coronary Events (GRACE) involving nearly 14 000 ACS patients without prior heart failure, one fifth of those with acute myocardial infarction and 10% of those with unstable angina developed heart failure during hospitalization.[2] Patients with an ACS complicated by CHF have a poor prognosis[3]. Patients with unstable angina who present with CHF have 4-fold higher hospital death rates than those without CHF at admission.[4] ACS patients who develop acute de novo heart failure during hospitalization are at even higher risk of death than those with heart failure at admission.[4–6]

Clinical Perspective p 1171

European and American guidelines[7–9] recommend that high-risk non–ST-elevation ACS (NSTE-ACS) patients be candidates for early coronary angiography and revascularization, yet registry data from GRACE have shown that ACS patients with heart failure are less likely than those without to undergo revascularization or receive evidence-based cardiac medications.[4] The goals of the present study are to describe

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The online-only Data Supplement is available with this article at http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.108.789685/DC1.

*A complete list of GRACE investigators is provided in Appendix II in the Data Supplement.

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***Circulation* is available at http://circ.ahajournals.org** **DOI: 10.1161/CIRCULATIONAHA.108.789685**


Okay, now listen up. Noboby gets in here without answering the following question: A train leaves Philadelphia at 1:00 p.m. It's traveling at 65 miles per hour. Another train leaves Denver at 4:00... Say, you need some paper?

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Sub/drp–Job#: YW105/BK – 3039156

Subject: Acute Coronary Syndrome, Sorajja

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