Primary PCI
State of the Art

A/Prof Michael Nguyen
Fremantle Hospital/Fiona Stanley Hospital
Perth Australia
JCR Meeting Busan 2014

Content

- Evidence of Primary PCI vs Thrombolysis
  - When, Why, How
  - Transfer PCI
  - Facilitated PCI
  - Pharmacoinvasive approach
- To Aspirate or not to Aspirate
- Adjunctive anticoagulation
- Culprit only vs Preventative PCI
- My Overview

Case: Mr Complex

- 78 yo man presents with severe central chest pain to regional hospital (60 minutes from PCI capable hospital).
- Pain started 60 minute ago
- ECG – 4 mm of inferior ST elevation
- PHX
  - NIDDM
  - Smoker
  - Due to have prostatic surgery for prostate cancer

What next?

- Transfer PPCI?
- Thrombolysis and wait?
- Thrombolysis and transfer for rescue PCI if needed?
- Thrombolysis and invasive strategy irrespective of ST segment resolution?

Reperfusion Therapy

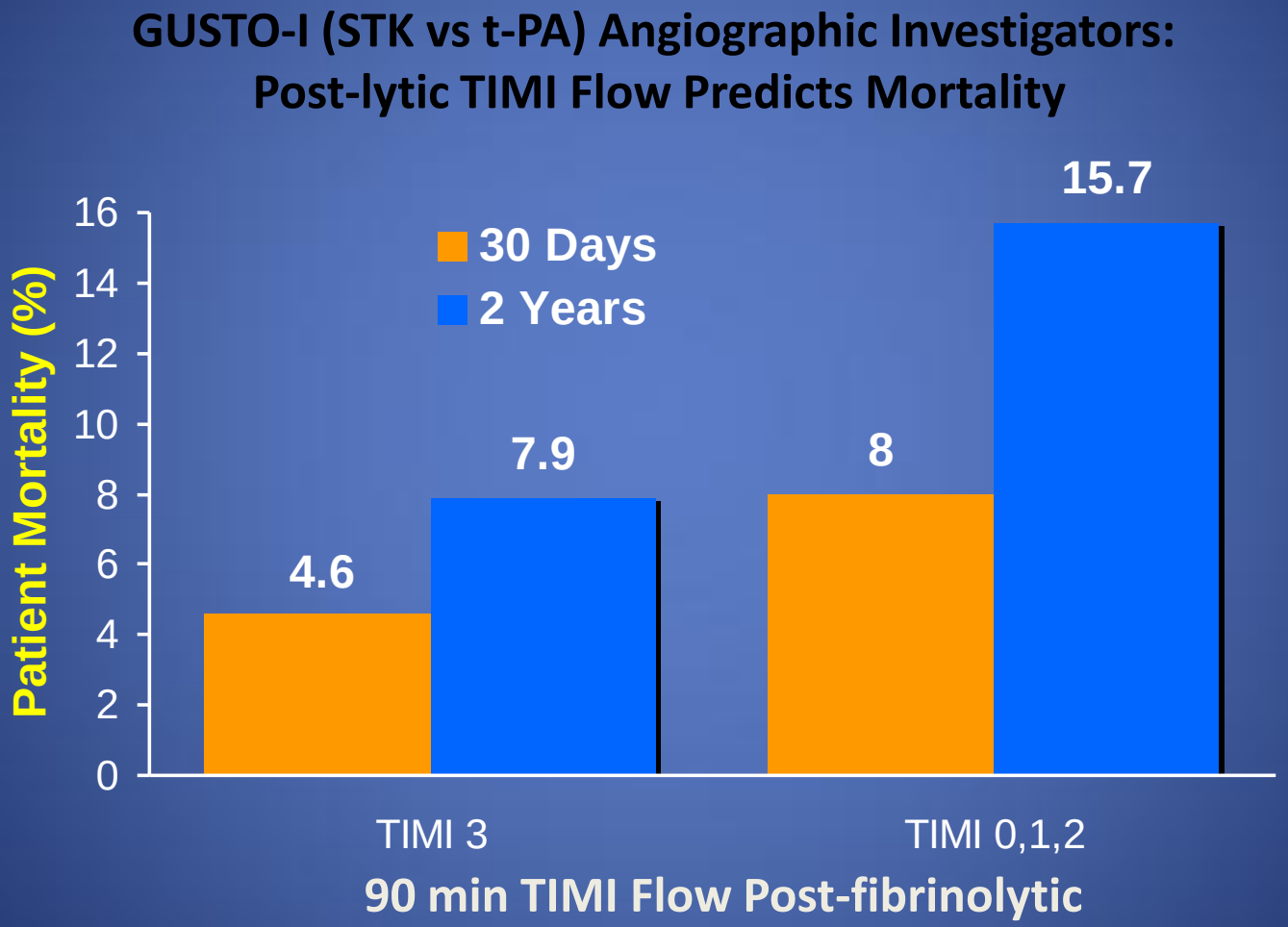
Class I Recommendation

All STEMI patients should undergo rapid evaluation for reperfusion therapy and have a reperfusion strategy implemented promptly after contact with the medical system. (Level of Evidence: A)

Medical system goal is to facilitate rapid recognition and treatment of patients with STEMI such that door-to-needle (or medical contact–to-needle) time for initiation of fibrinolytic therapy can be achieved ***within 30 minutes or that door-to-balloon (or medical contact–to-balloon) time for PCI can be kept within 90 minutes.***

Antman EM, et al. Available at: http://www.acc.org/clinical/guidelines/stemi/index.pdf. Accessed November 1, 2005.

Goal of Fibrinolytic Therapy Alone: Open Arteries and Reduce Mortality



Ross AM, et al. *Circulation*. 1998;97:1549-1556.

Pharmacologic Reperfusion

Available Resources

Class I Recommendations

STEMI patients presenting to a facility without the capability for expert, prompt intervention with primary PCI within 90 minutes of first medical contact **should undergo fibrinolysis** unless contraindicated *(Level of Evidence: A)*

Antman EM, et al. *J Am Coll Cardiol*. Available at: http://www.acc.org/clinical/guidelines/stemi/index.pdf. Accessed November 1, 2005.

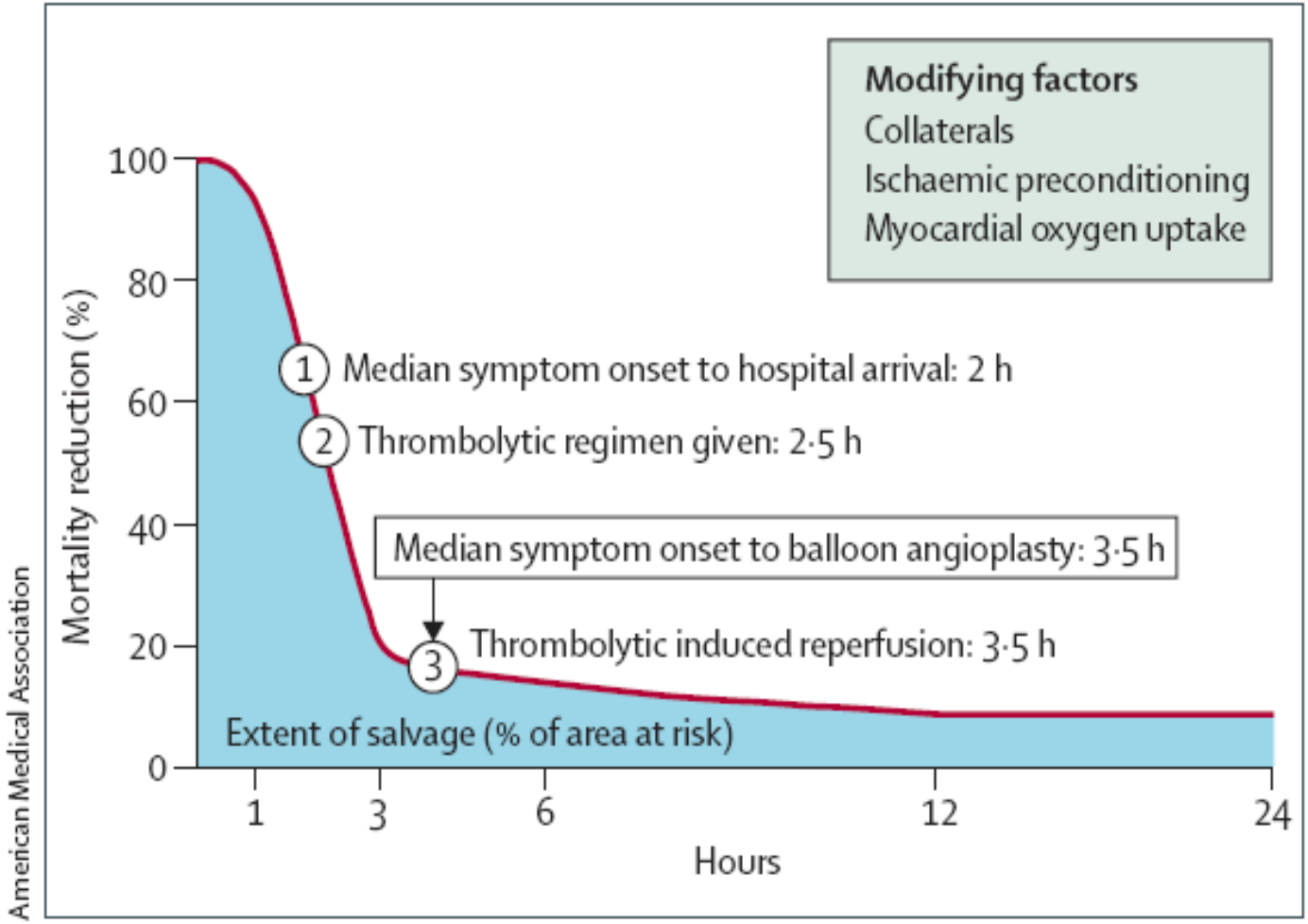
ACC/AHA STEMI Guidelines: Primary Percutaneous Coronary Intervention

Class I Recommendations

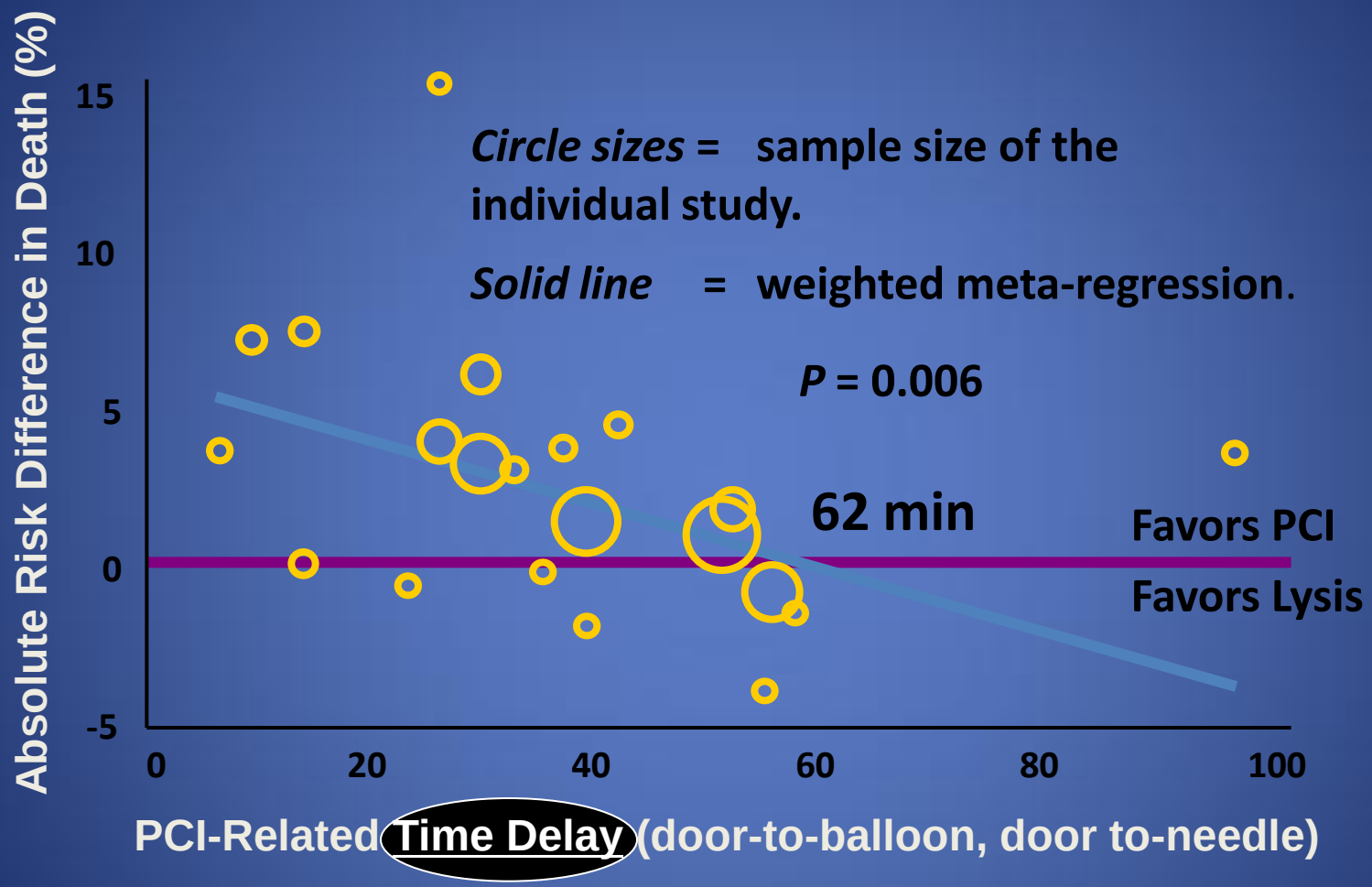
- **Level of Evidence: B**
  - Primary PCI should be performed as quickly as possible (goal of medical contact-to-balloon or door-to-balloon time < 90 minutes).
  - If the symptom duration is within 3 hours and the expected door-to-balloon time minus the expected door-to-needle time is:
    - < 60 mins - primary PCI preferred
    - > 60 mins - fibrinolytic therapy preferred
  - If symptom duration is greater than 3 hours, primary PCI is generally preferred.

Antman EM, et al. *J Am Coll Cardiol*. Available at: http://www.acc.org/clinical/guidelines/stemi/index.pdf

Time Dependency?



Mortality With 1° PCI Vs Time



For every 10 min delay to PCI:
1% reduction in mortality difference vs lytics

Nallamothu BK, Bates ER. *Am J Cardiol*. 2003:92:824

PCI vs Faciliated PCI: Meta-analysis

- 17 STEMI trials
- Received either
  - Primary PCI (N=2267)
  - Facilitated PCI (N=2237)
- Short term outcomes (< 42 days)
  - Death, CVA, non-fatal re-MI
  - Urgent TVR, re-bleed

Keely EC, Boura JA, Grines CL. Lancet, 2006

Facilitated PCI Meta-analysis

	f-PCI (%)	PCI (%)	OR (95% CI)
Initial TIMI 3	37	15	3.18 (2.22, 4.45)
Final TIMI 3	89	88	1.19 (0.88, 1.64)
Death	5	3	1.38 (1.01, 1.87)
Urgent TVR	4	1	2.39 (1.23, 4.66)
ICH	0.7	0.1	P=0.0014

Keely EC, Boura JA, Grines CL. Lancet, 2006

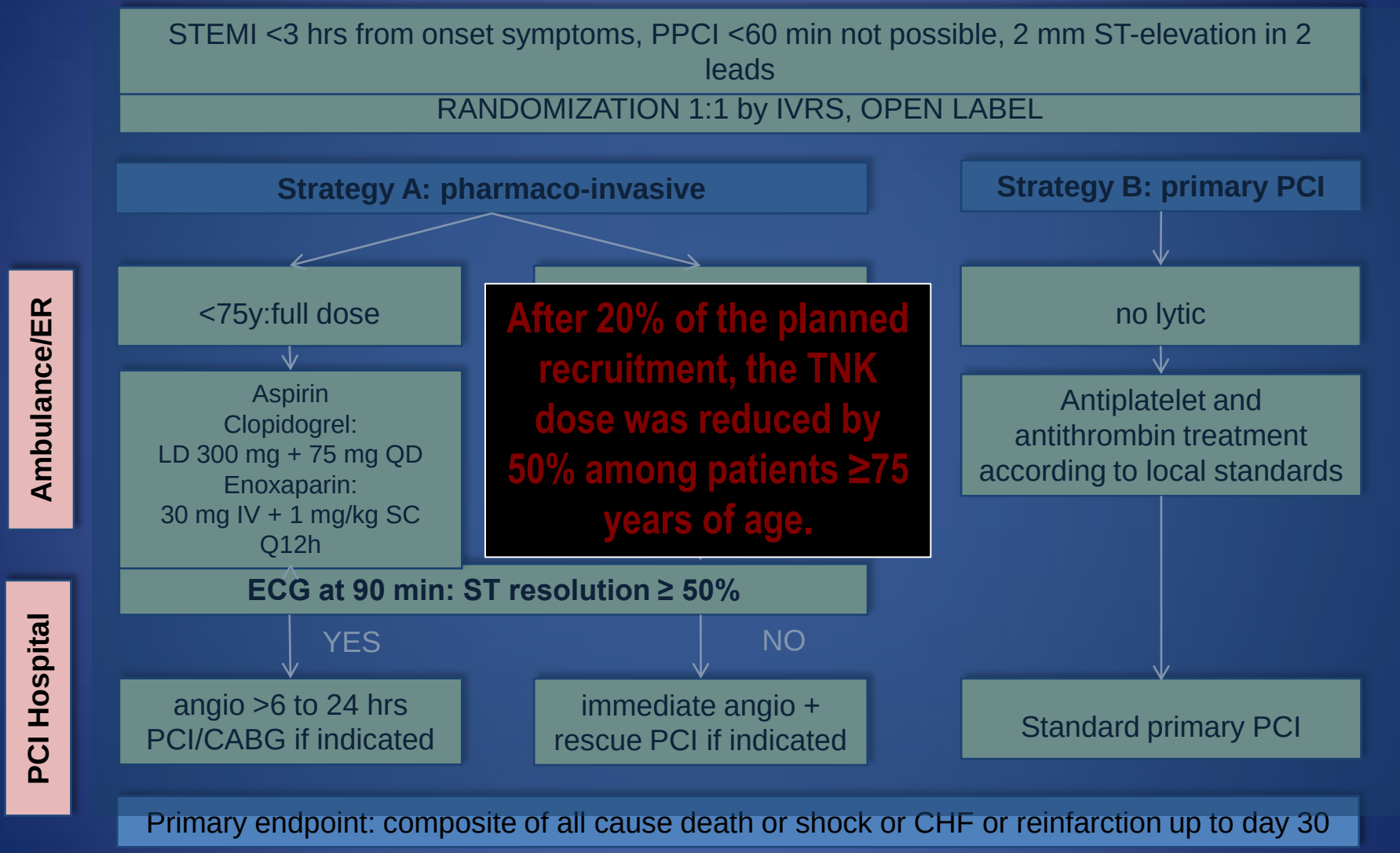
Facilitated PCI Meta-analysis

- Conclusions

  "Facilitated PCI offers no benefit over primary PCI and should not be used outside of the context of randomized clinical trials"

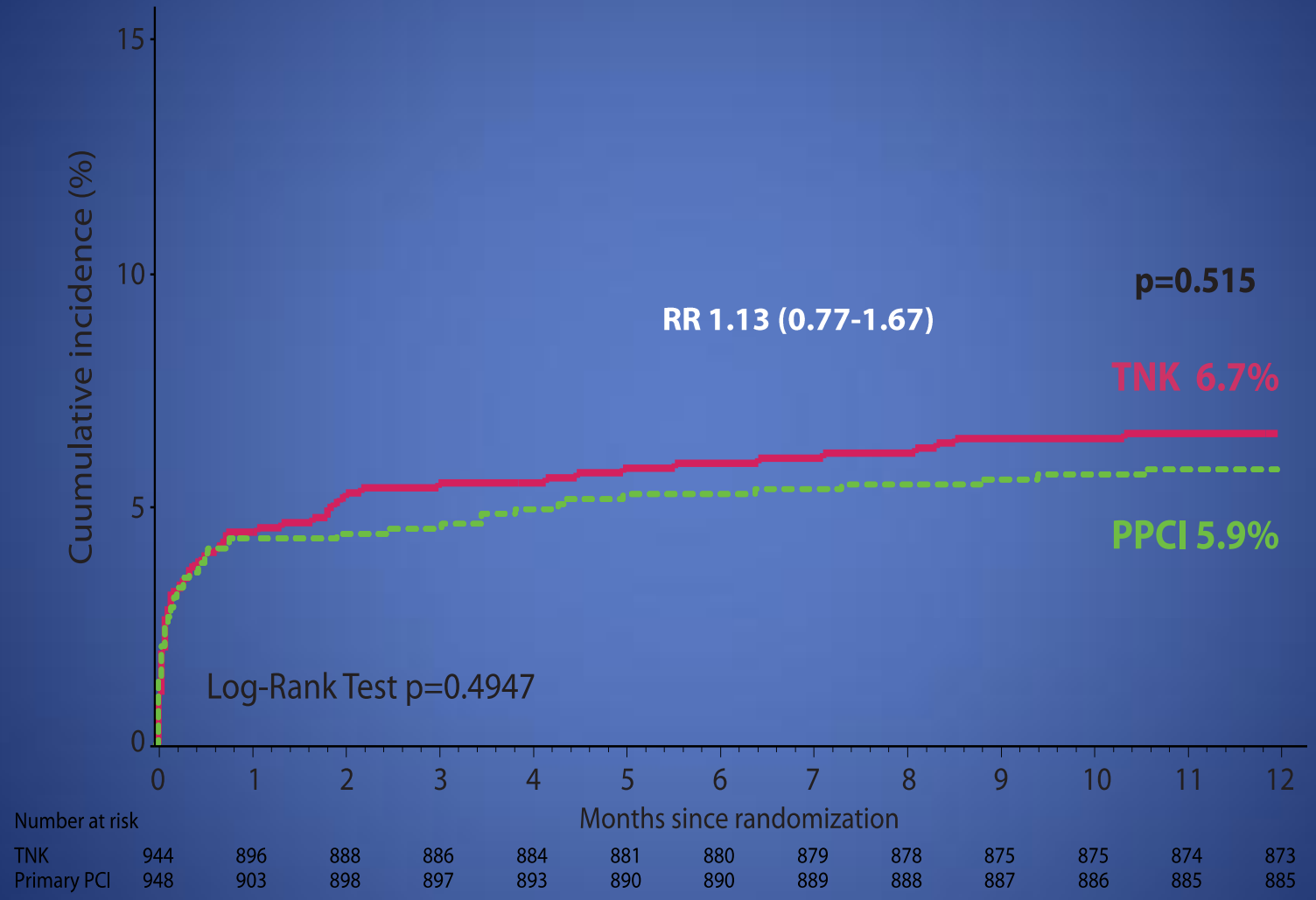
  Furthermore, facilitated interventions with thrombolytic based regimens should be avoided.

STREAM design – Pharmaco-invasive approach

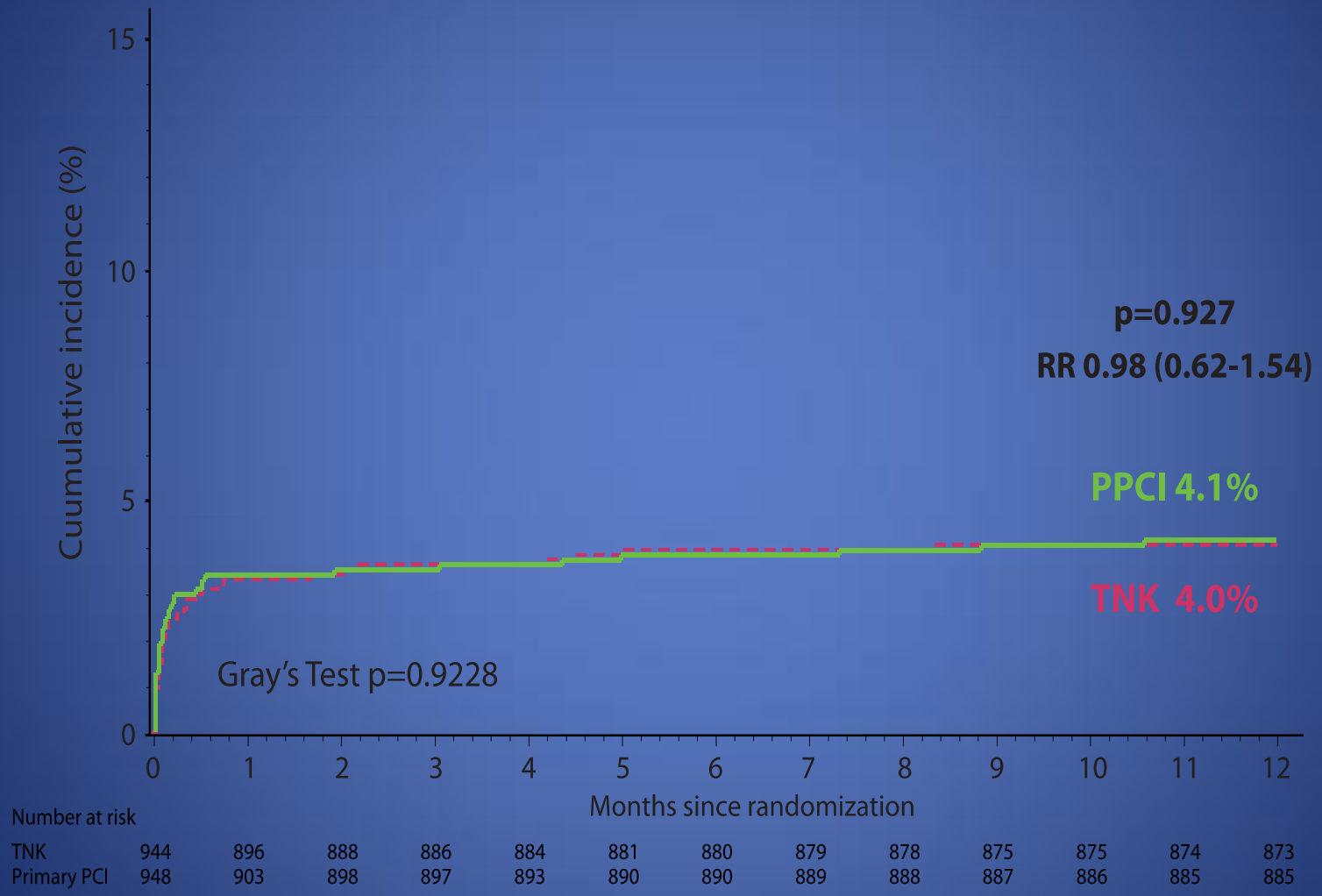


Armstrong et al NEJM 2013;368(15):1379-87

All-cause mortality

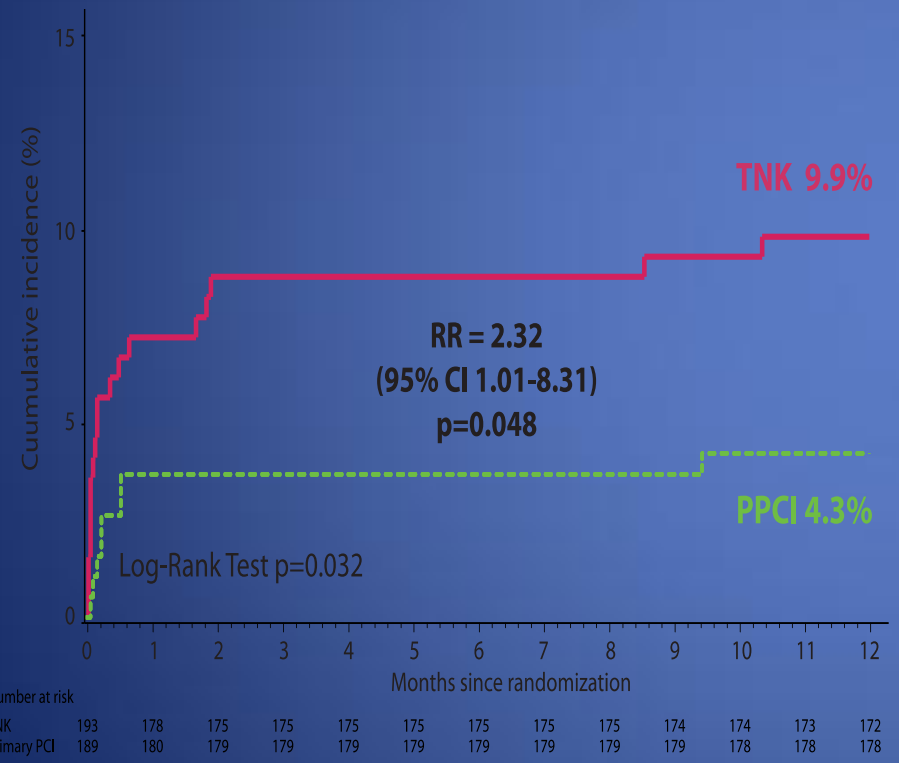


Cardiac mortality



All-cause mortality before & after amendment

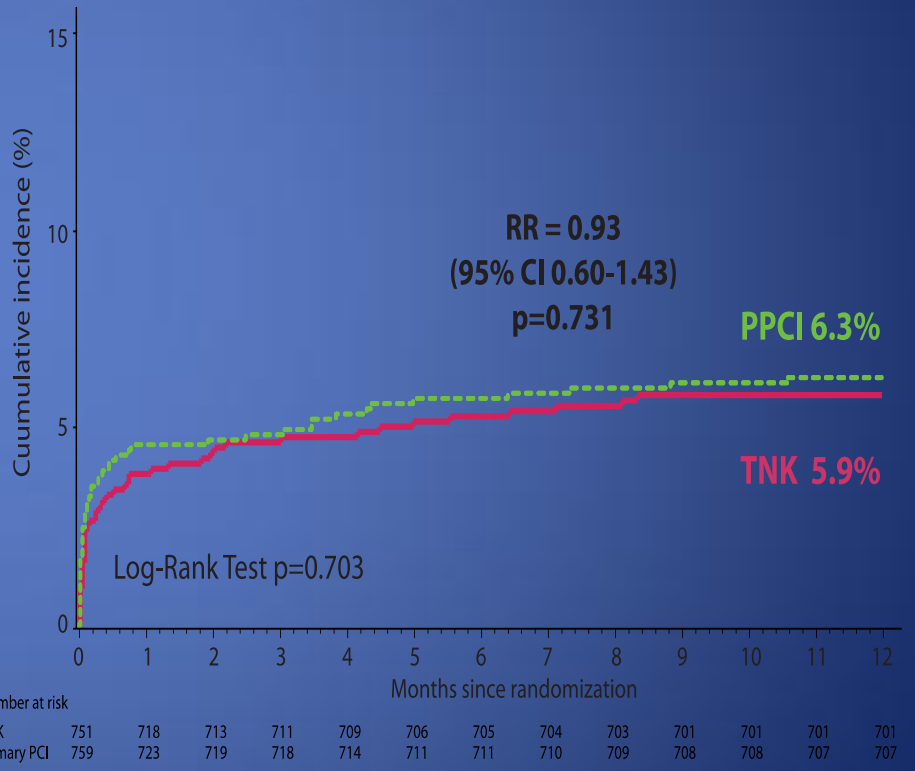
Patients randomized before Am. (n=382)



Number at risk

TNK	193	178	175	175	175	175	175	175	175	174	174	173	172
Primary PCI	189	180	179	179	179	179	179	179	179	179	178	178	178

Patients randomized after Am. (n=1,510)



Number at risk

TNK	751	718	713	711	709	706	705	704	703	701	701	701	701
Primary PCI	759	723	719	718	714	711	711	710	709	708	708	707	707

Mr Complex

- Thrombolysis given at Regional hospital and patient transferred to your hospital.
- On arrival patient still has 2/10 pain and 2mm Inferior ST elevation

- What next?

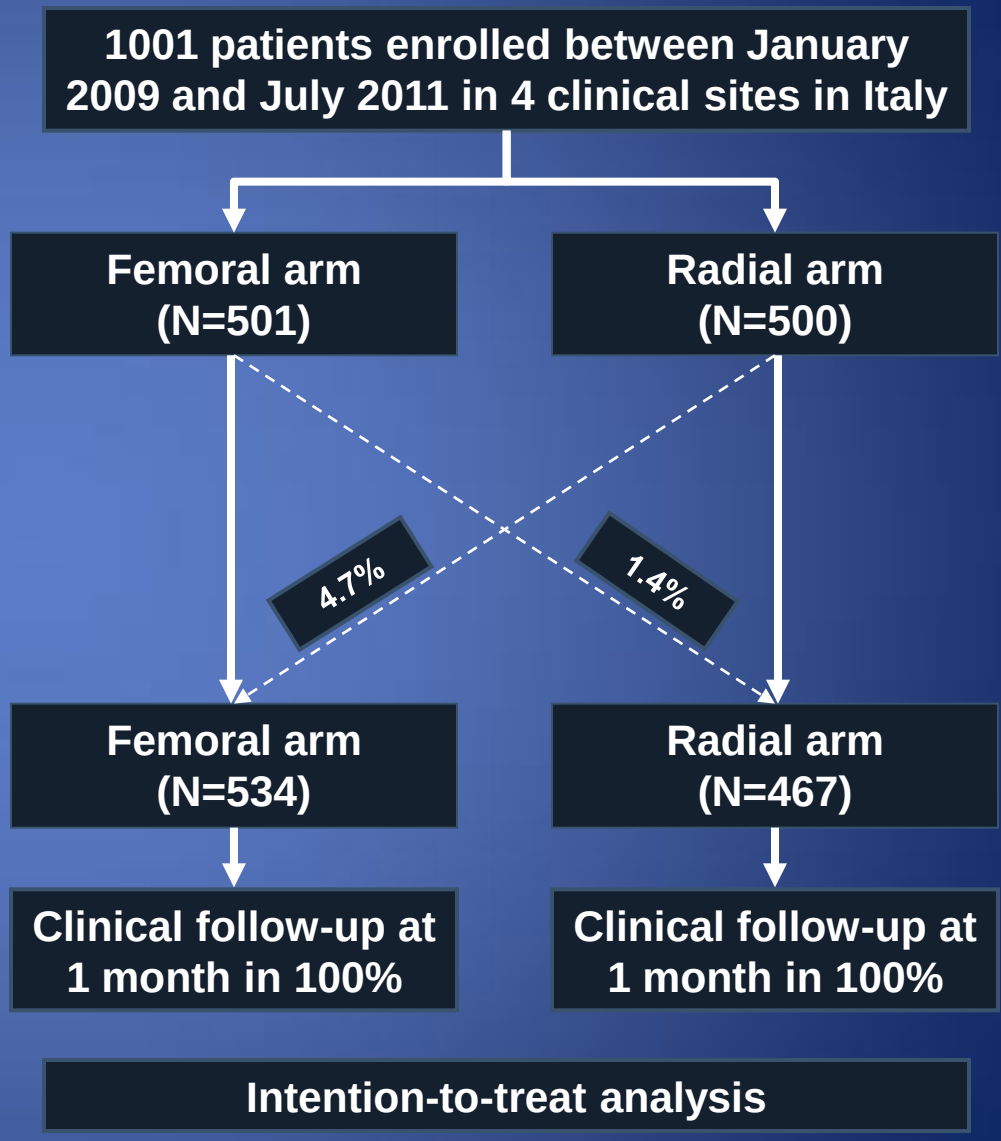
Radial vs Femoral

RIFLE STEACS - flow chart

Design

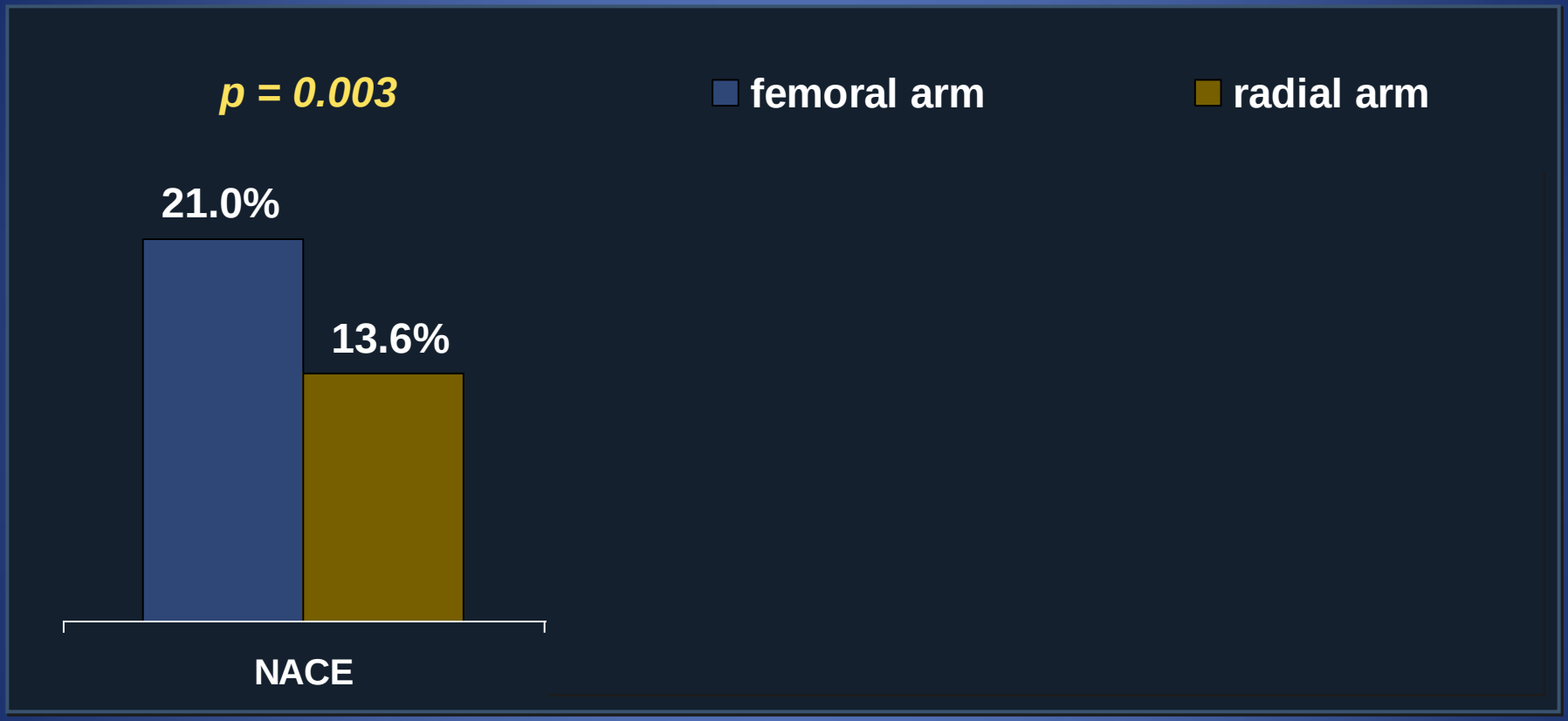
- **DESIGN:**
  Prospective, randomized (1:1), parallel group, multi-center trial.
- **INCLUSION CRITERIA:**
  all ST Elevation Myocardial infarction (STEMI) eligible for primary percutaneous coronary intervention.
- **ESCLUSION CRITERIA:**
  contraindication to any of both percutaneous arterial access.

  international normalized ratio (INR) > 2.0.



RIFLE STEACS – results

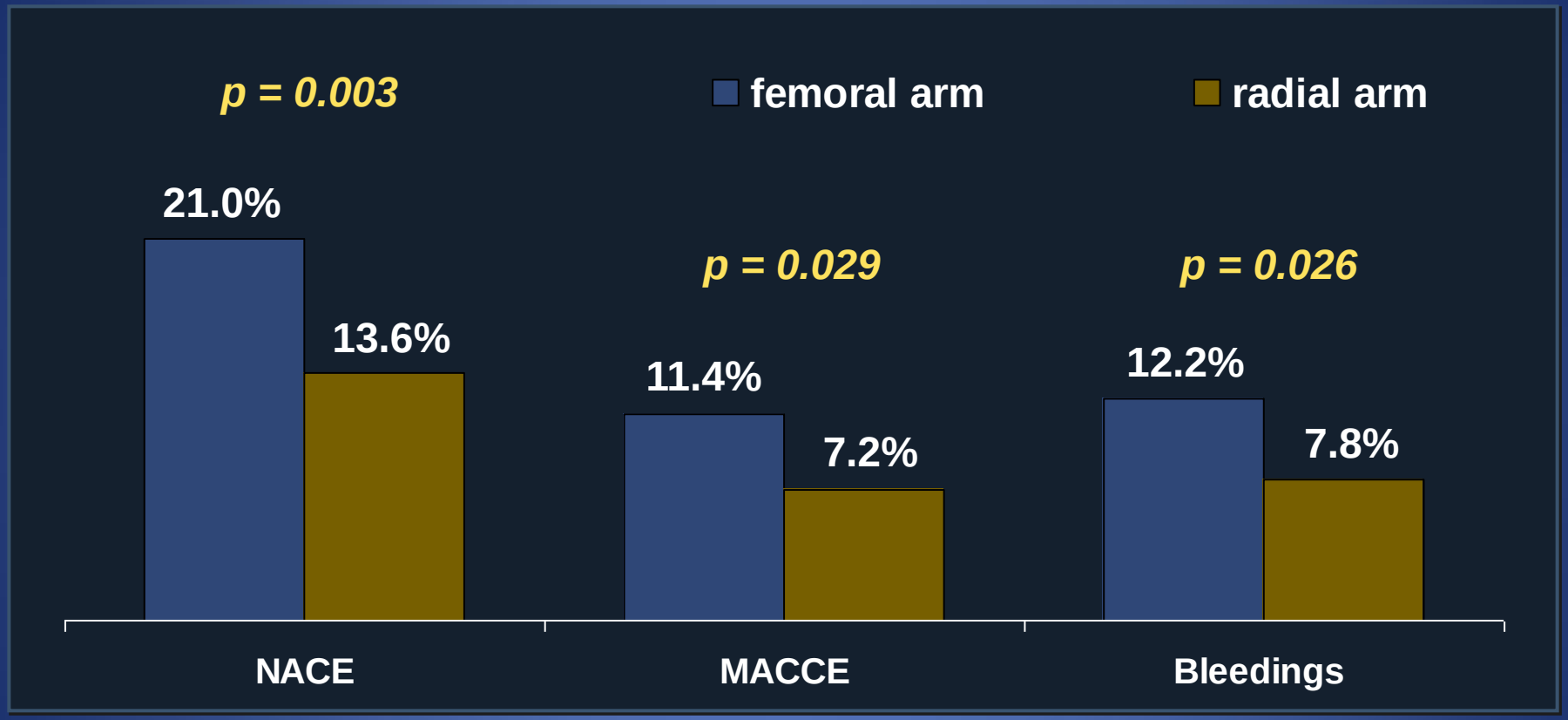
30-day NACE rate



- Net Adverse Clinical Event (*NACE*) = MACCE + bleeding

RIFLE STEACS – results

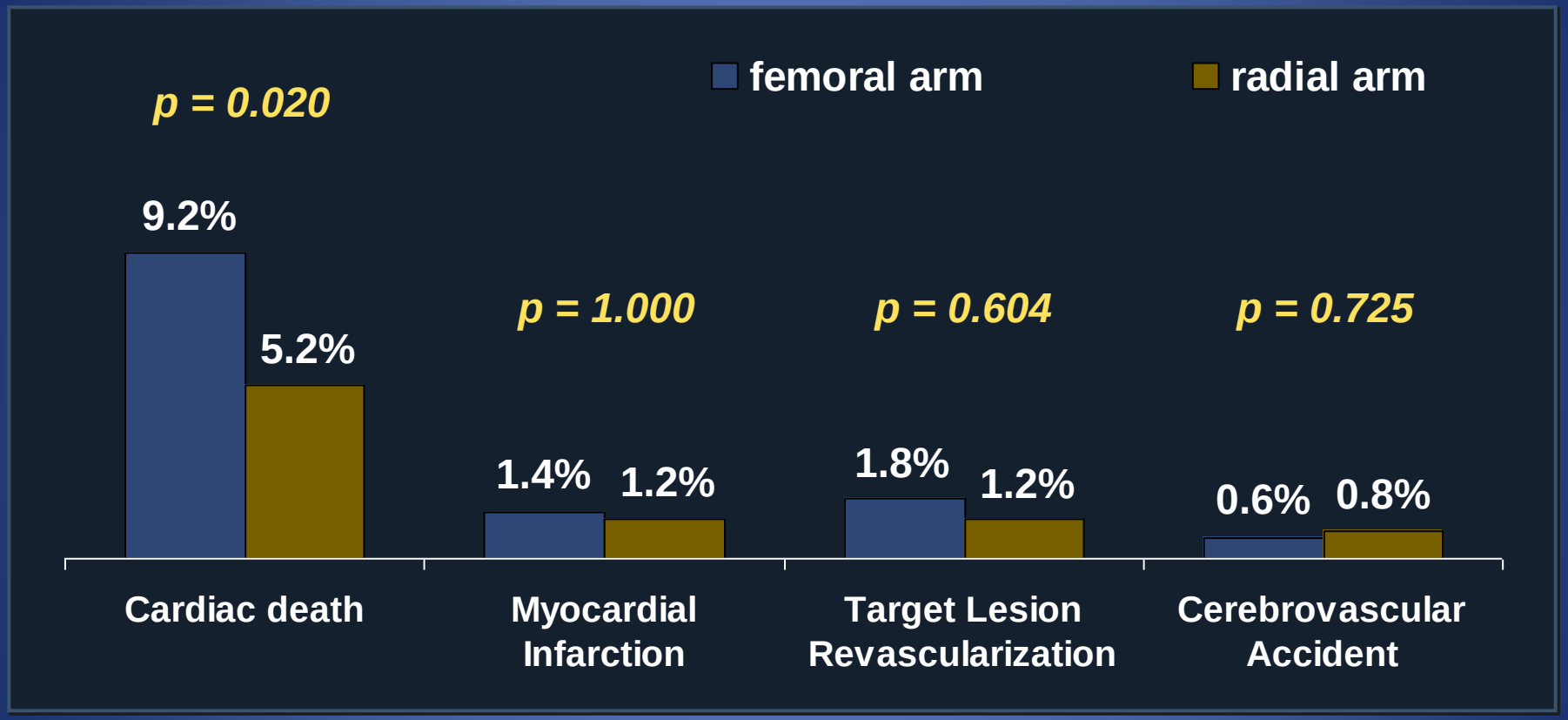
30-day NACE rate



- Net Adverse Clinical Event (*NACE*) = MACCE + bleeding
- Major Adverse Cardiac and Cerebrovascular event (*MACCE*) = composite of cardiac death, myocardial infarction, target lesion revascularization, stroke

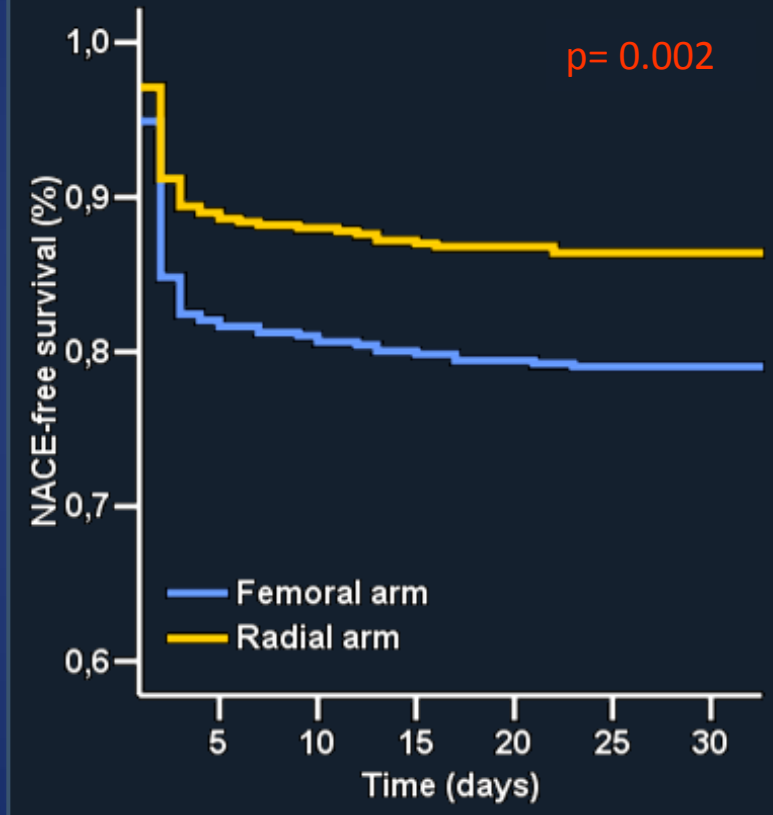
RIFLE STEACS – results

30-day MACCE rate



RIFLE STEACS – results

30-day NACE predictors



	OR	CI 95%	p value
Female gender	1.5	(1.1-2.3)	0.037
CKD	2.1	(1.4-3.1)	0.001
Radial access	0.6	(0.4-0.9)	0.012
Killip class	1.8	(1.5-2.2)	0.001
LAD culprit	1.7	(1.2-2.6)	0.006
TIMI 0 basal	1.4	(1.0-2.1)	0.073
LVEF <50%	1.6	(1.1-2.5)	0.025
TIMI 0-1 final	2.4	(1.1-5.1)	0.024

STEMI-RADIAL

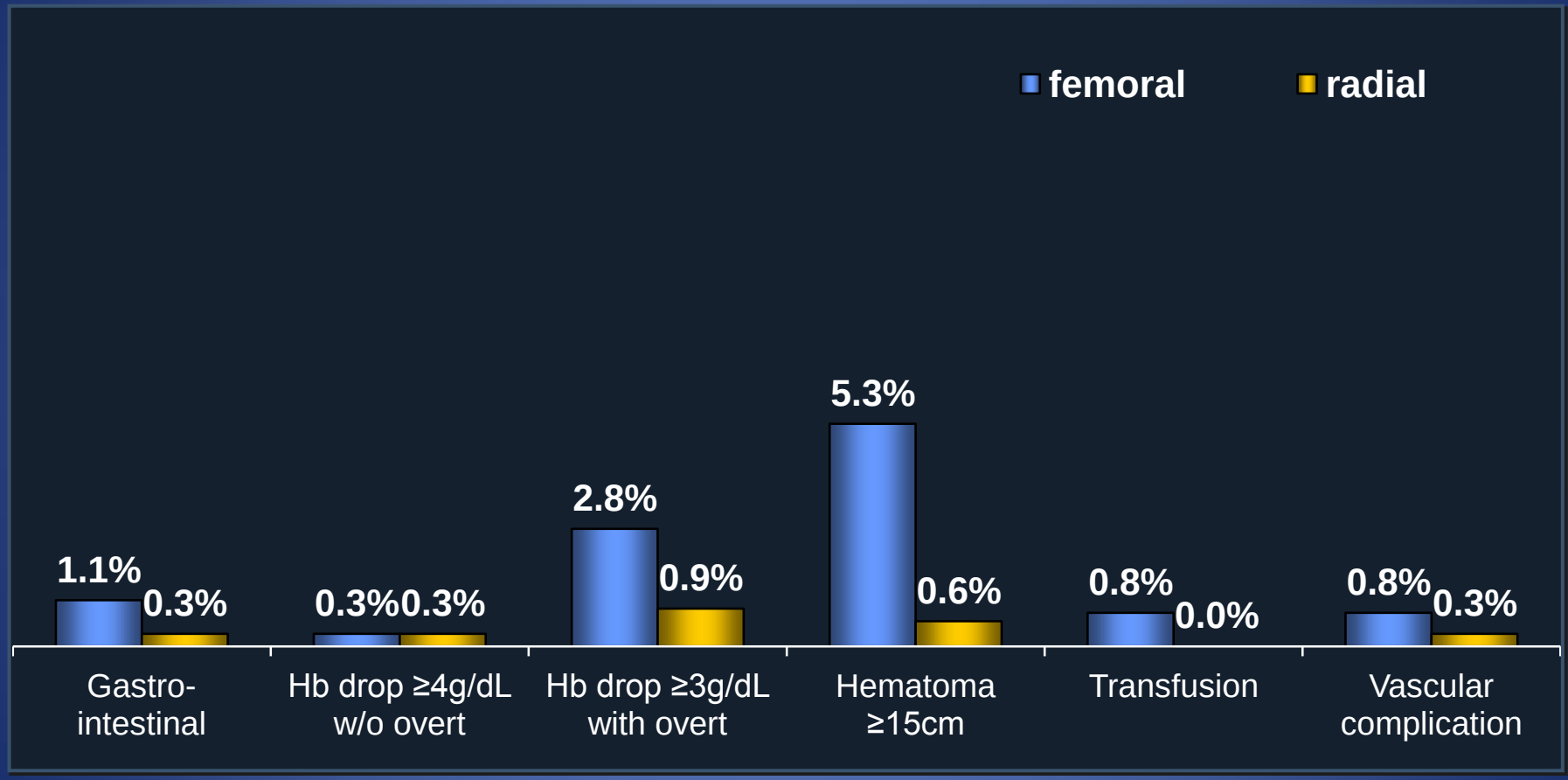
A Prospective Randomized Trial of Radial vs. Femoral Access in Patients with ST-Segment Elevation Myocardial Infarction

STEMI-RADIAL - objectives

To compare radial *vs* femoral approach in primary PCI for patients with STEMI < 12 hours in very high volume radial centers (> 80% primary PCI)

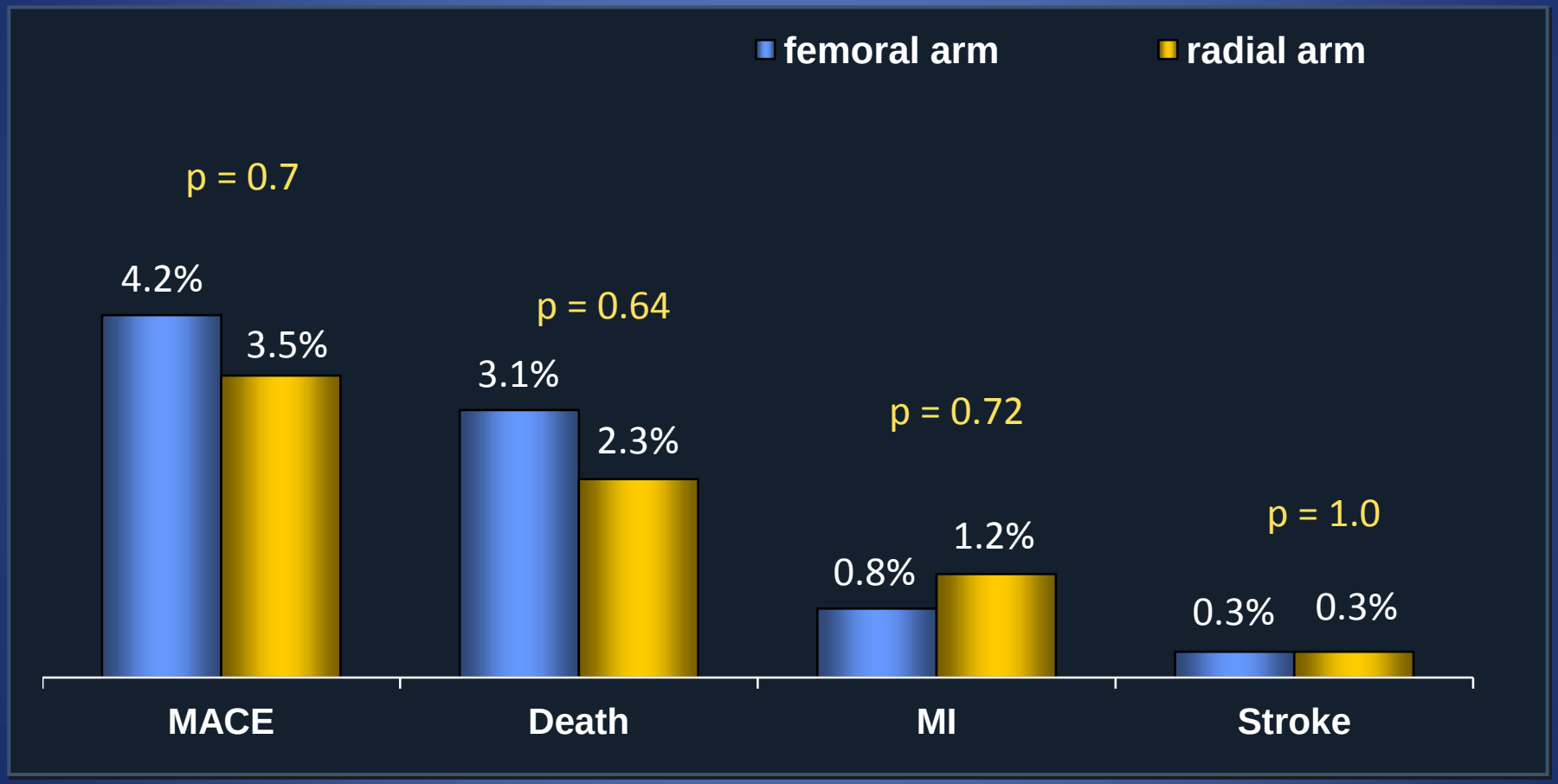
STEMI RADIAL - results

30-day bleeding and access site compl.



STEMI RADIAL - results

30-day MACE



MACE = composite of death, myocardial infarction and stroke

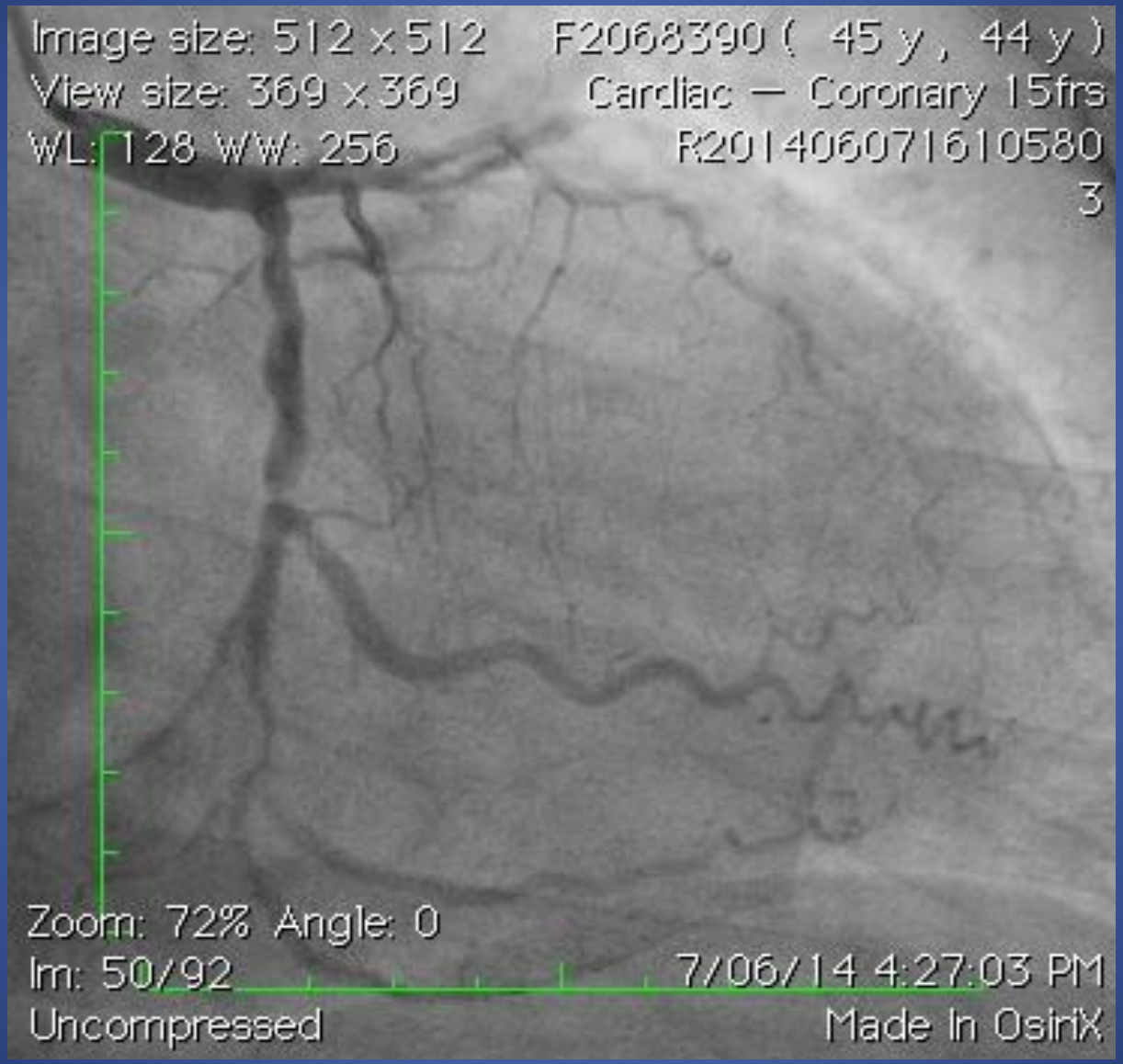


Image size: 512 x 512
View size: 369 x 369
WL: 128 WW: 256
F2068390 (45 y , 44 y)
Cardiac — Coronary 15frs
R20140607161058033
Zoom: 72% Angle: 0
Im: 50/92
Uncompressed
7/06/14 4:27:03 PM
Made In OsiriX

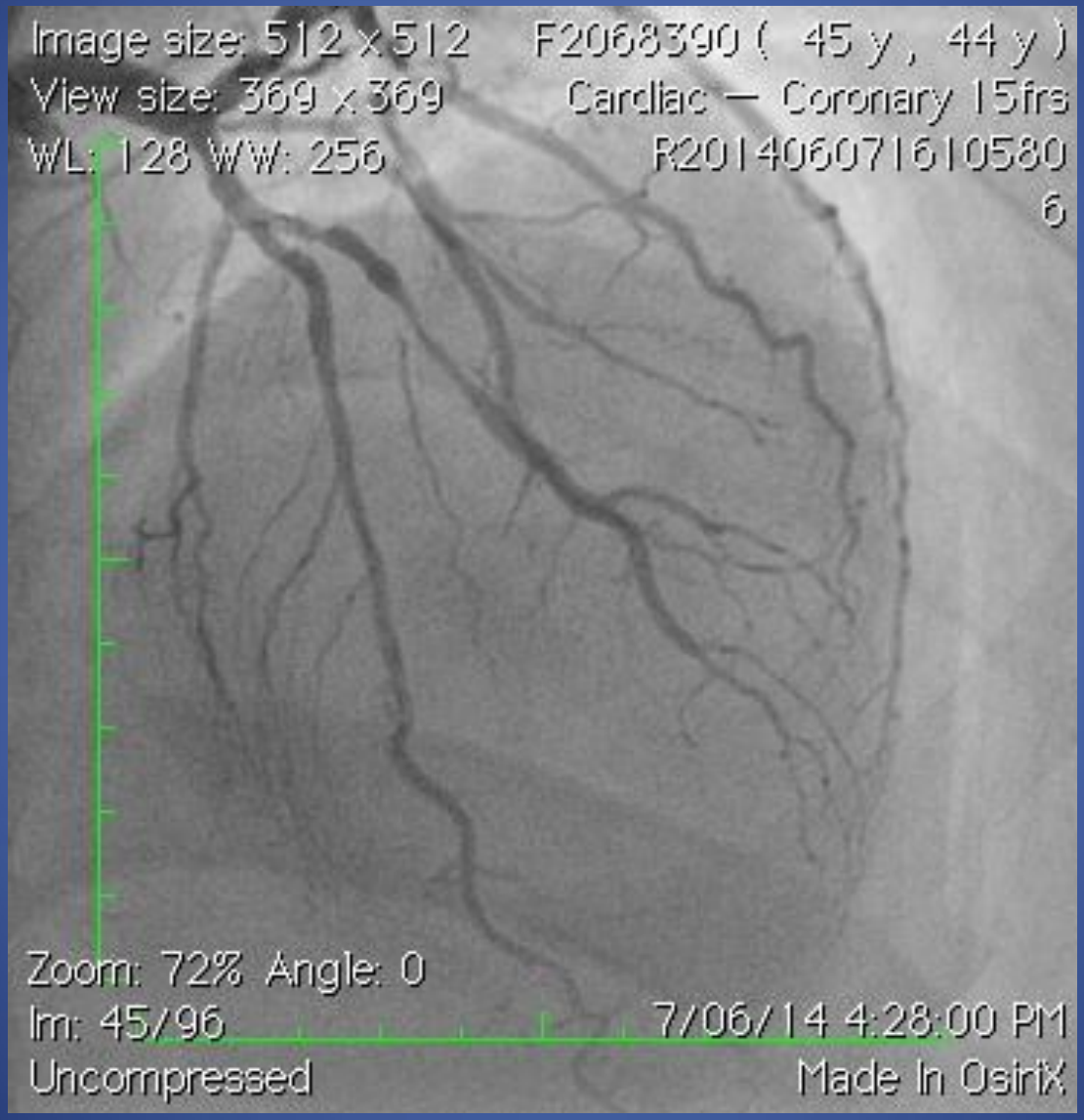


Image size: 512 x 512
View size: 369 x 369
WL: 128 WW: 256
F2068390 (45 y , 44 y)
Cardiac — Coronary 15frs
R20140607161058006
Zoom: 72% Angle: 0
Im: 45/96
Uncompressed
7/06/14 4:28:00 PM
Made In OsiriX

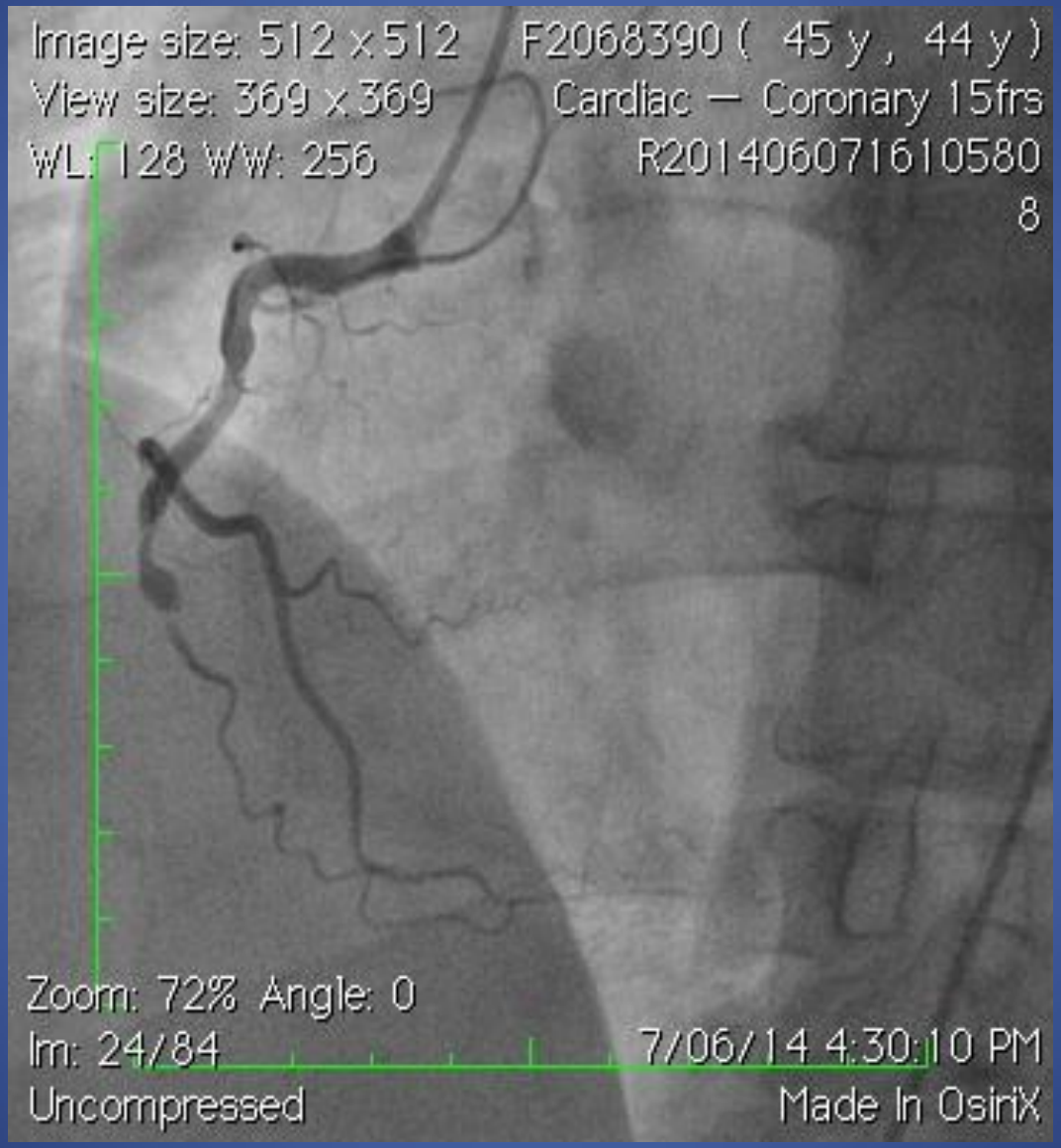


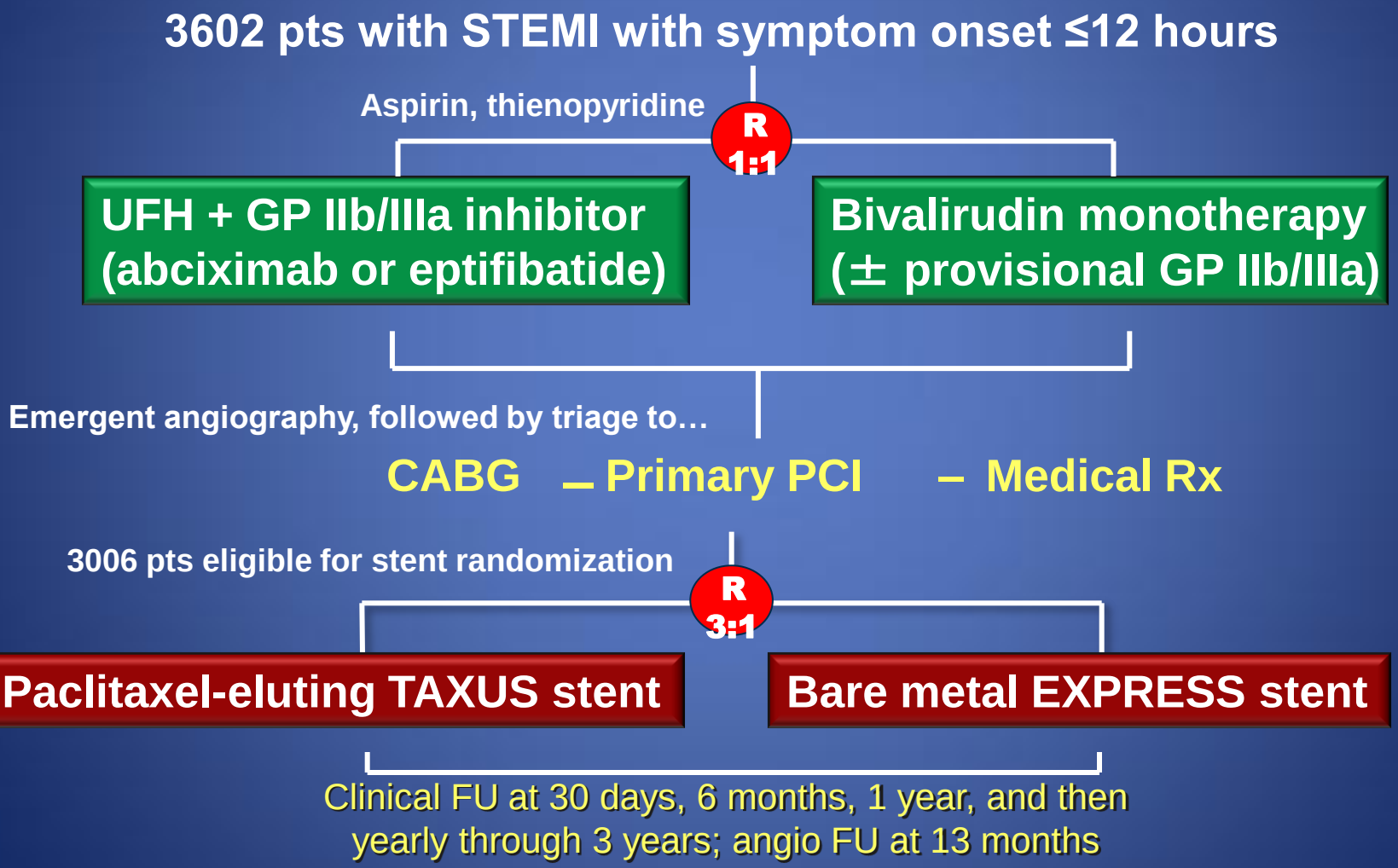
Image size: 512 x 512
View size: 369 x 369
WL: 128 WW: 256
F2068390 (45 y , 44 y)
Cardiac — Coronary 15frs
R20140607161058 0 8
Zoom: 72% Angle: 0
Im: 24/84
Uncompressed
7/06/14 4:30:10 PM
Made In OsiriX

Anticoagulation?

- Heparin alone?
- Heparin and Glycoprotein 2b3a?
- Bivalirudin?

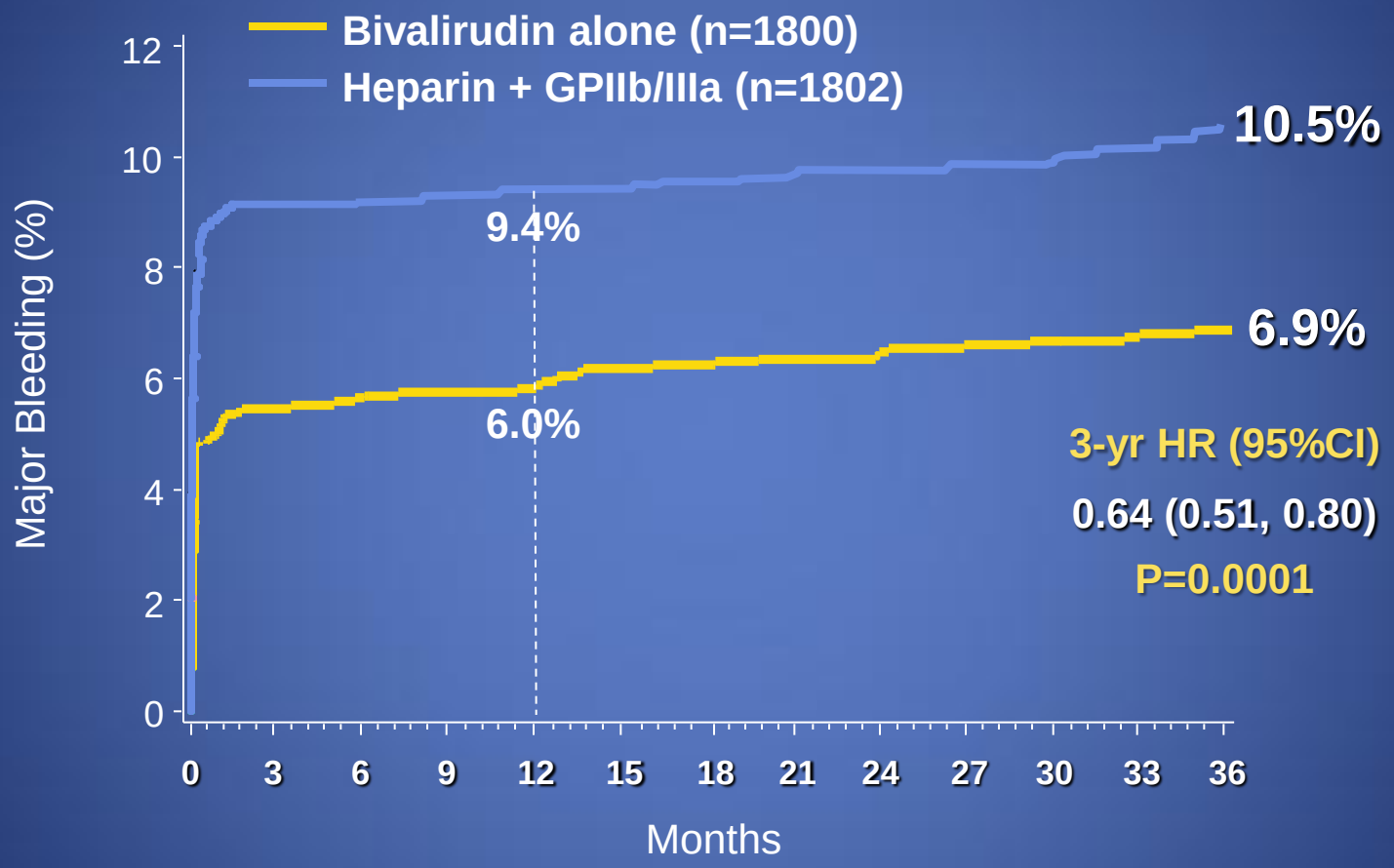
HORIZONS-AMI

Harmonizing Outcomes with Revascularization and Stents in AMI



Stone, GW N Engl J Med 2008;358:2218-30.

3-Year Major Bleeding (non-CABG)*

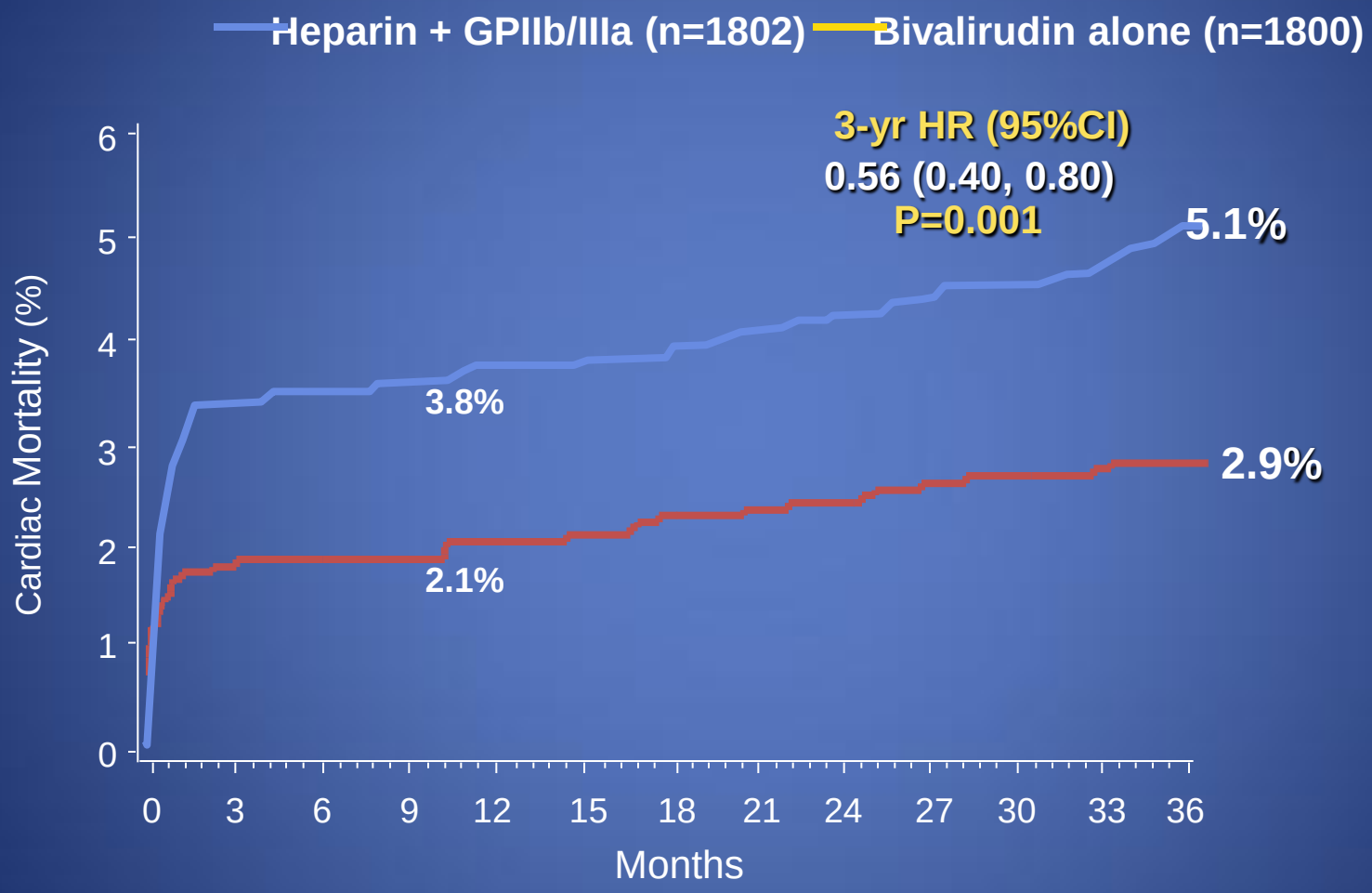


* Intracranial, intraocular, retroperitoneal, access site bleed requiring intervention/surgery, hematoma ≥5 cm, hgb ↓ ≥3g/dL with or ≥4g/dL w/o overt source; reoperation for bleeding; or blood product transfusion

Stone, GW Lancet 2011 Published online June 13. **DOI:10.1016/S0140-6736(11)60764-2**

Time in Months

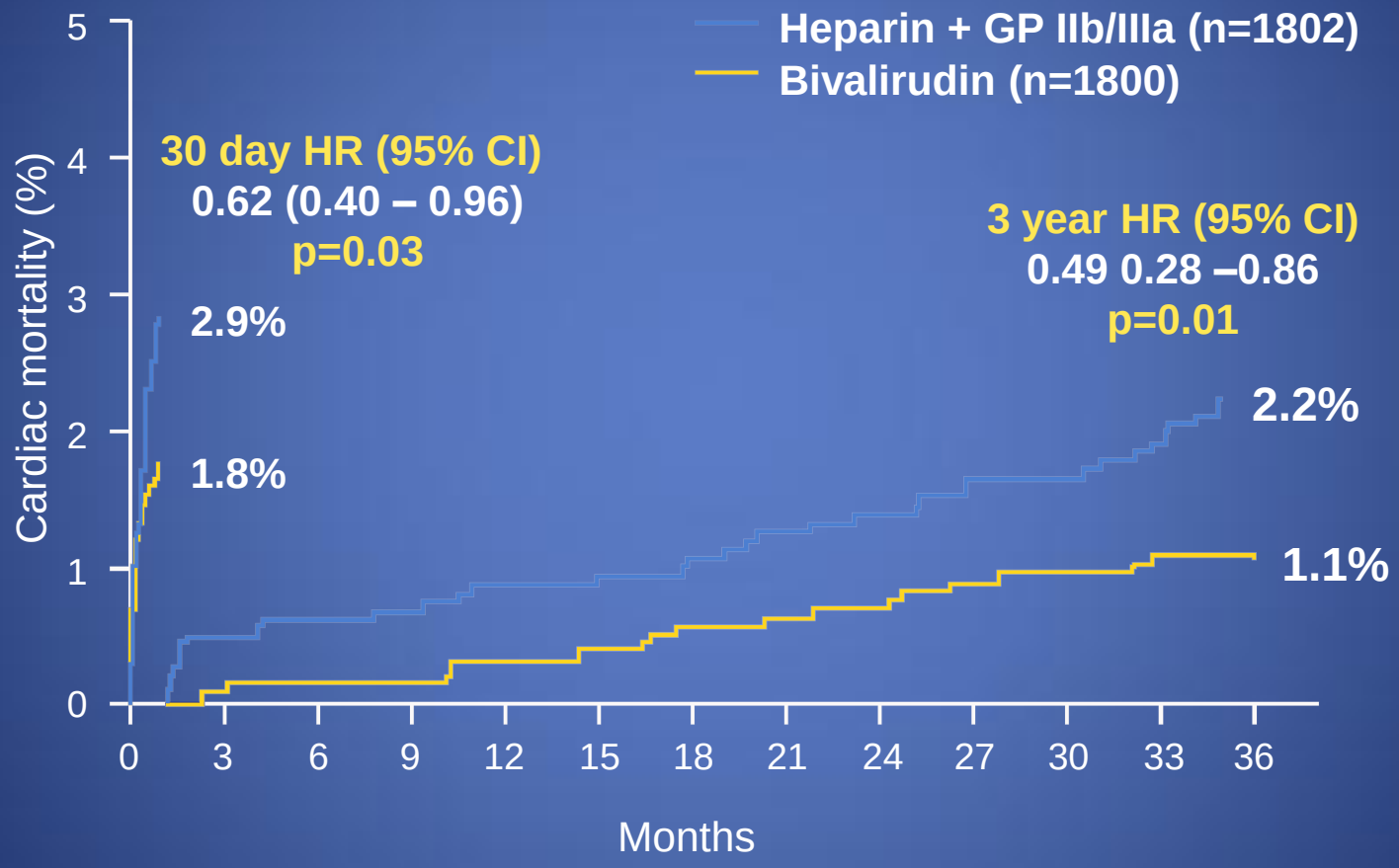
3-Year Cardiac Mortality



Stone, GW Lancet 2011 Published online June 13. **DOI:10.1016/S0140-6736(11)60764-2**

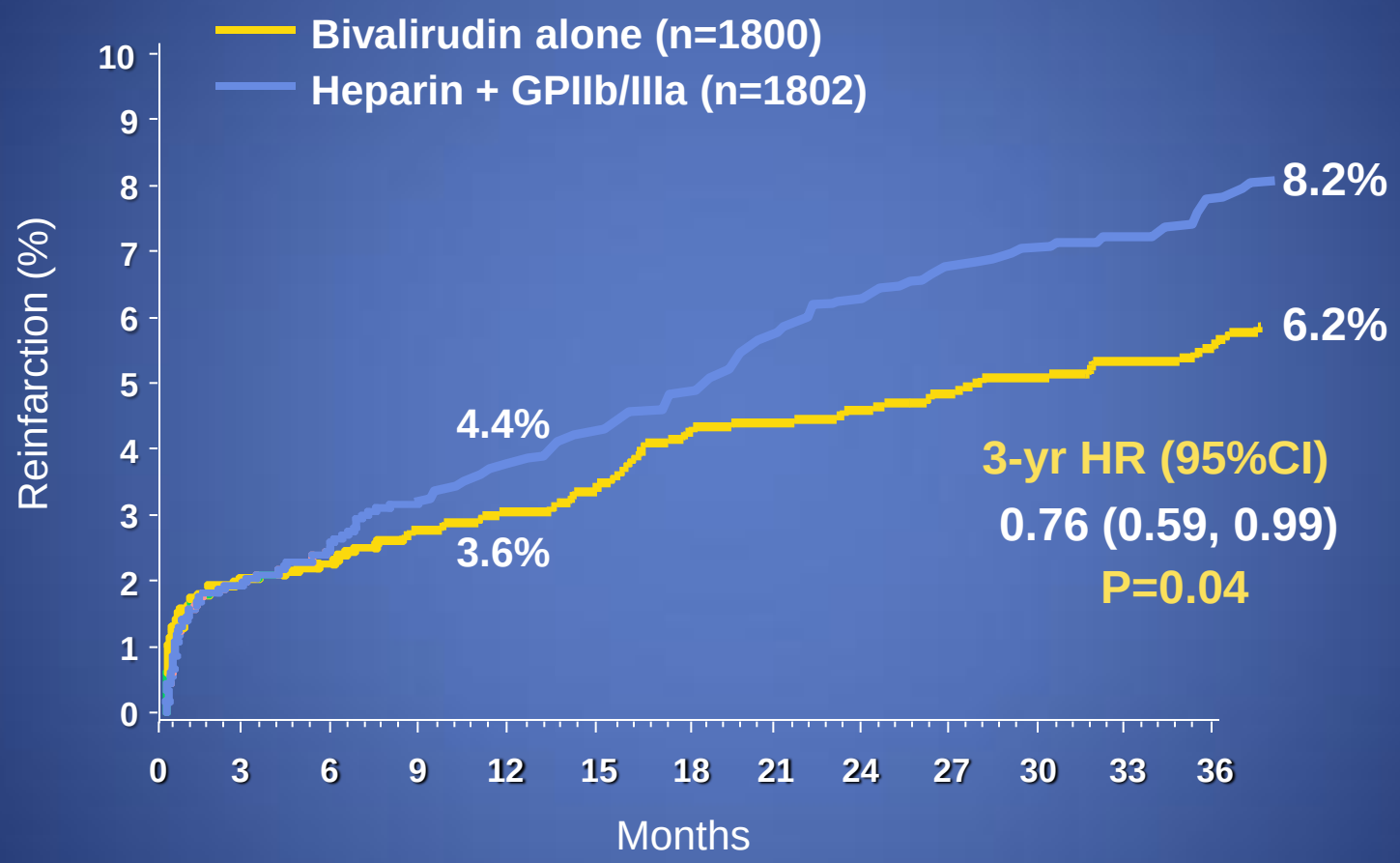
3-Year Cardiac Mortality

Landmark analysis



Stone, GW Lancet 2011 Published online June 13. **DOI:10.1016/S0140-6736(11)60764-2**

3-Year Reinfarction

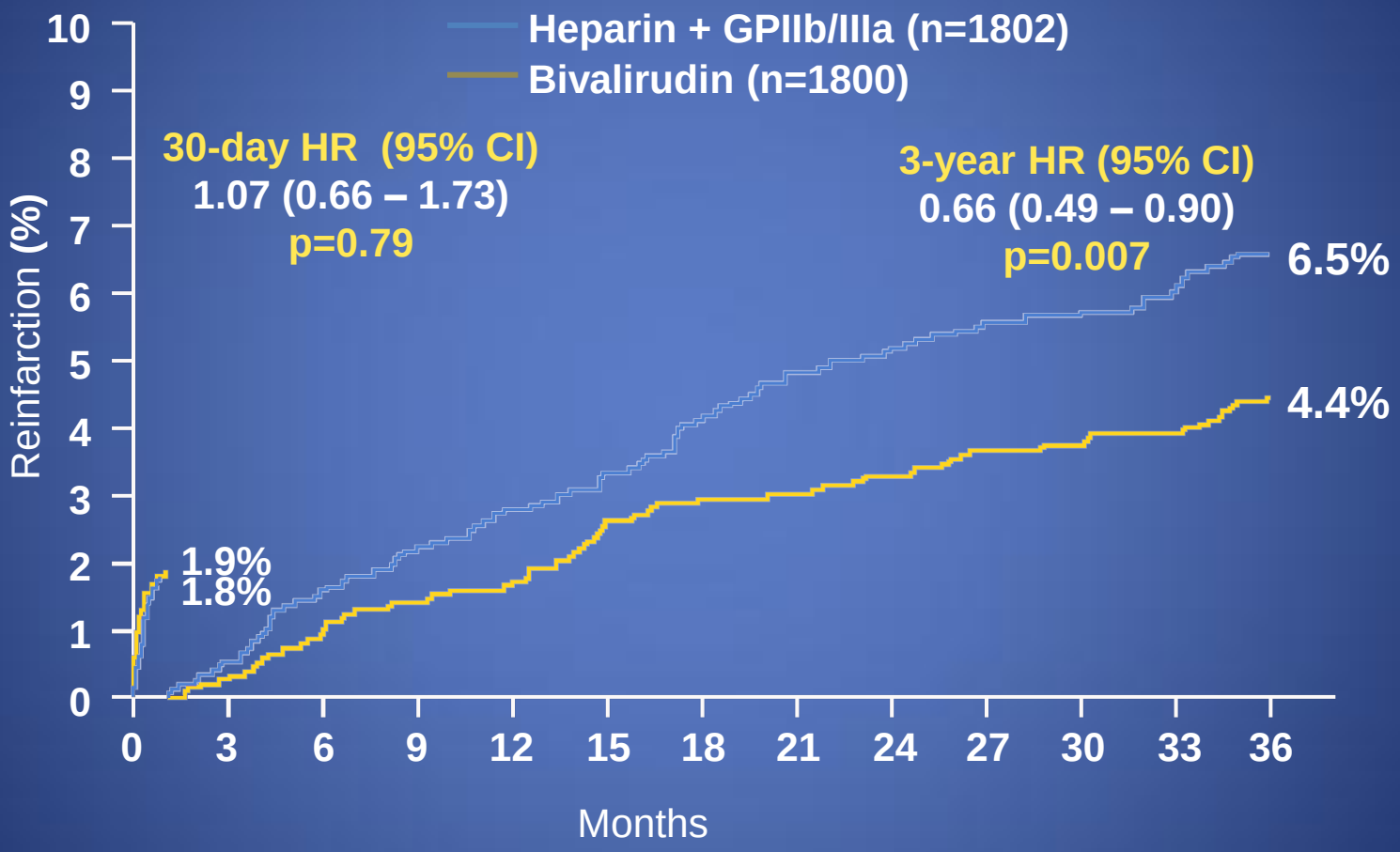


Stone, GW Lancet 2011 Published online June 13. **DOI:10.1016/S0140-6736(11)60764-2**

3-Year Reinfarction

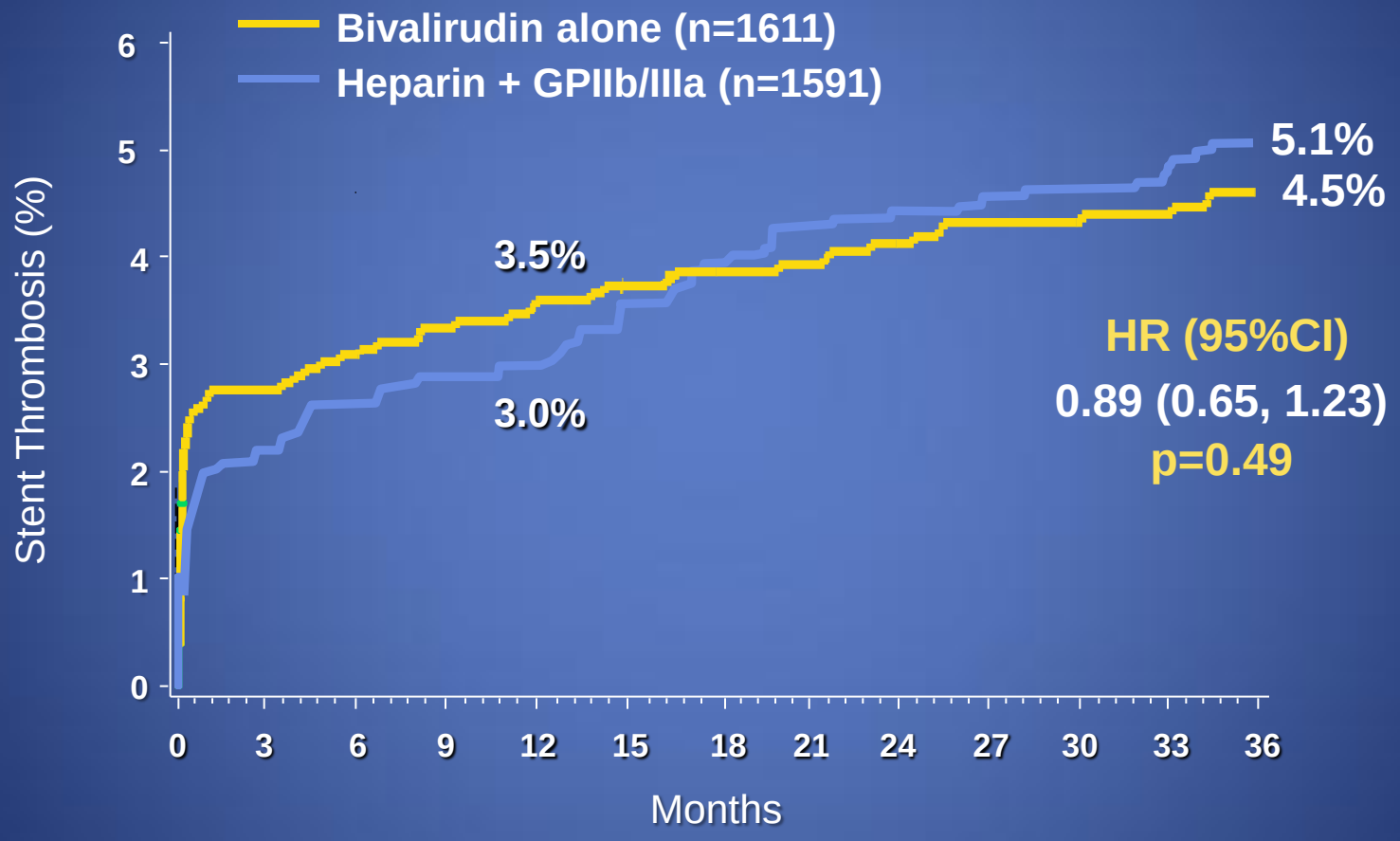
HORIZONS AMI

Landmark analysis



Stone, GW Lancet 2011 Published online June 13. **DOI:10.1016/S0140-6736(11)60764-2**

3-Year Stent Thrombosis (ARC Definite/Probable)



ARC= Academic Research Consortium

Stone, GW Lancet 2011 Published online June 13. **DOI:10.1016/S0140-6736(11)60764-2**

HEAT PPCI

***H**ow **E**ffective are*
A**ntithrombotic **T**herapies in **PPCI

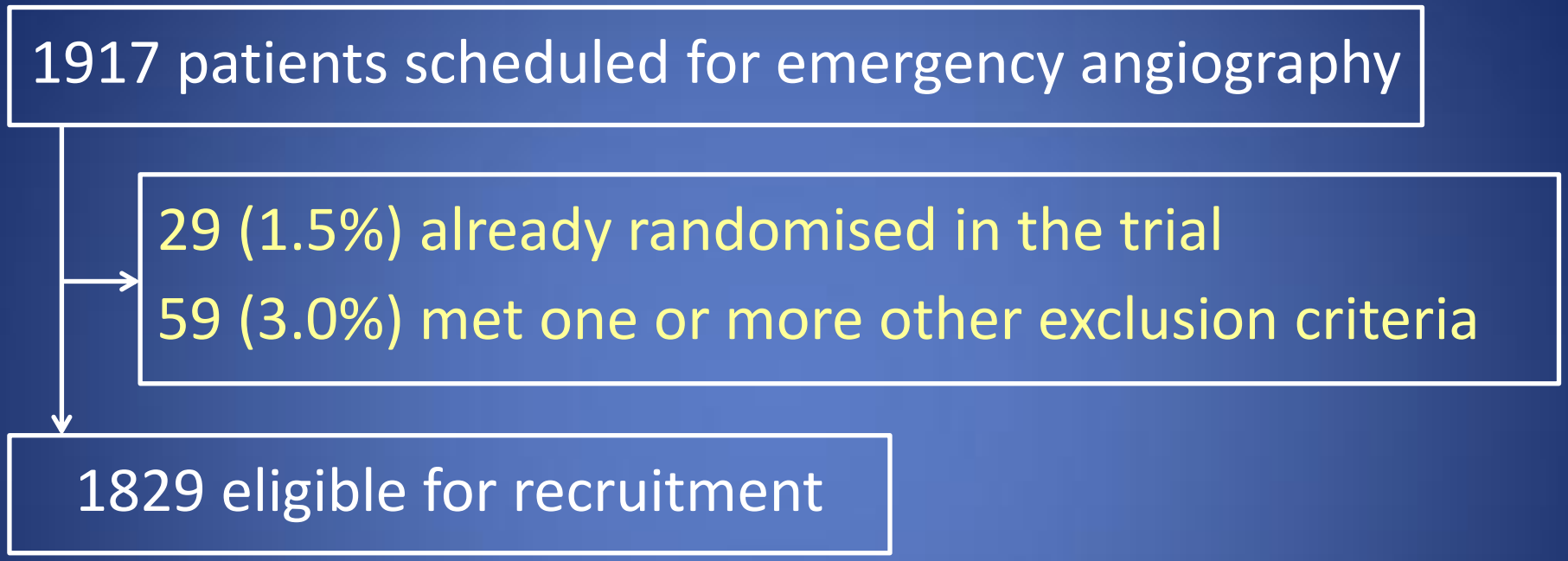
Heparin versus Bivalirudin in PPCI

Dr Adeel Shahzad
Dr Rod Stables (PI)
Liverpool Heart and Chest Hospital
Liverpool, UK

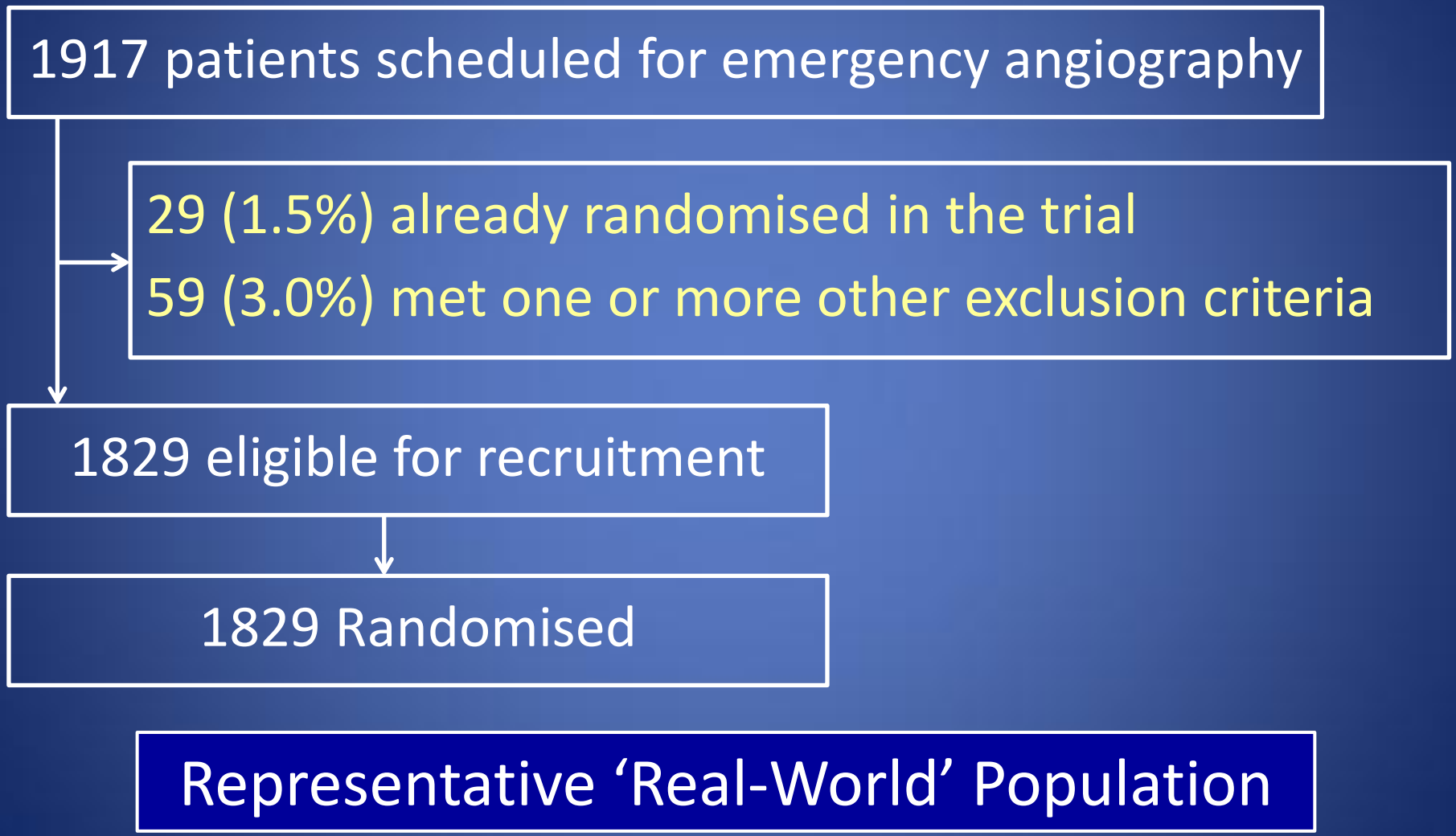
Study Description

- Single centre RCT
- Trial recruitment: Feb 2012 - Nov 2013 22 months
- Bivalirudin v Unfractionated Heparin
- STEMI patients
  - Randomised at presentation
  - Acute phase management with Primary PCI
- Philosophy for clinical teams:
  - Assess *'Every Patient - Every Time'*

Results - Population



Results - Population



Procedural Information

Characteristic	Bivalirudin (%)	Heparin (%)
P2Y12 use - Any	99.6	99.5
- Clopidogrel	11.8	10.0
- Prasugrel	27.3	27.6
- Ticagrelor	61.2	62.7
GPI use	13.5	15.5
Radial arterial access	80.3	82.0
PCI performed	83.0	81.6

Study Medication

- Dual oral anti-platelet therapy pre-procedure
- Heparin: 70 units/kg body weight pre-procedure
- Bivalirudin: Bolus 0.75 mg/kg

  Infusion 1.75 mg/kg/hr - procedure duration

- GPI - Abciximab
  - Selective ('bailout') use in both groups
  - ESC guideline indications

Primary Efficacy Outcome

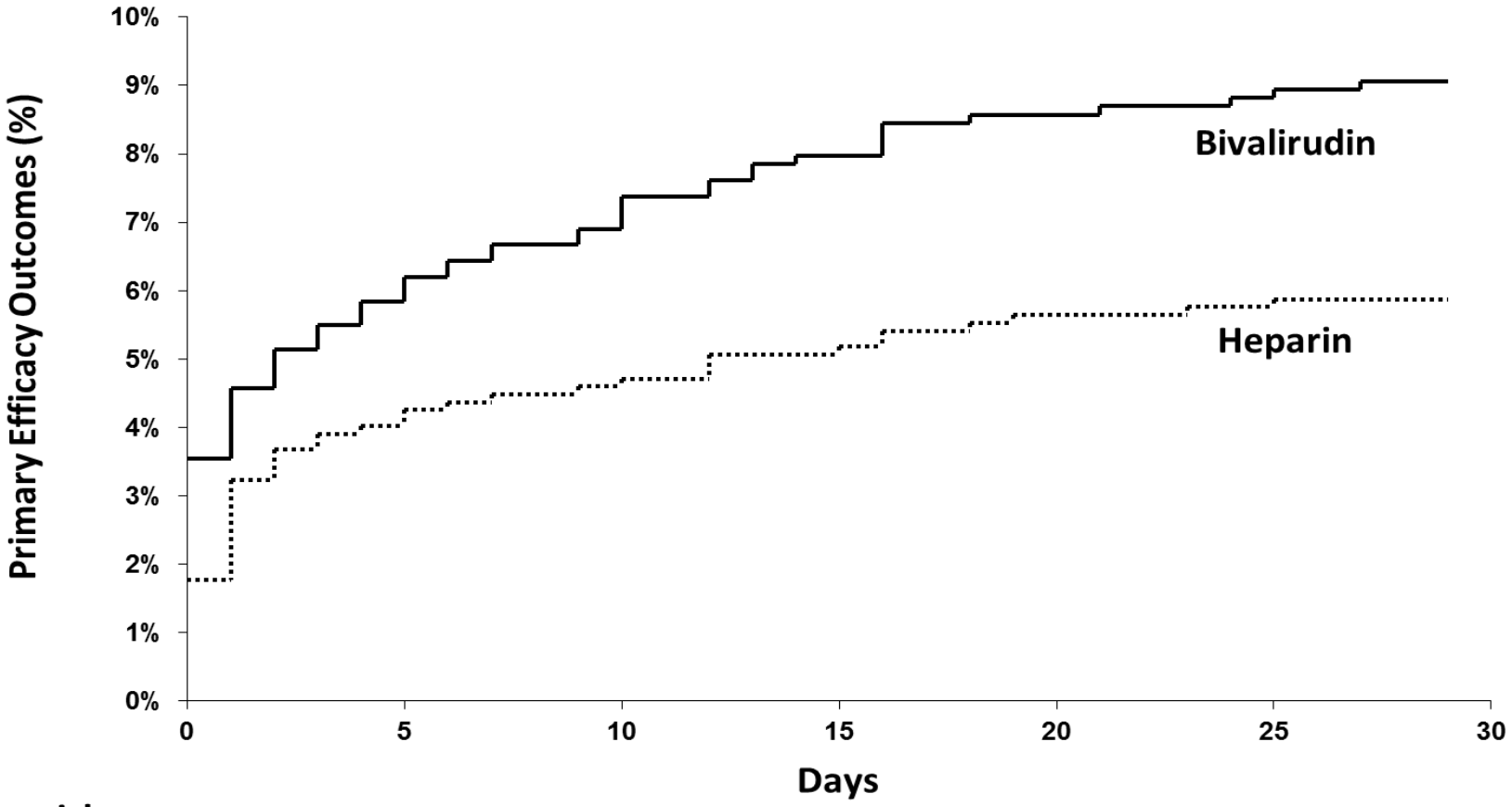
Primary Efficacy Outcome

	Bivalirudin			Heparin	
	n	%		%	n
MACE	79	8.7 %	v	5.7 %	52

Absolute risk increase = 3.0% (95% CI 0.6, 5.4)

Relative risk = 1.52 (95% CI 1.1 – 2.1) P=0.01

Timing of First MACE Event



No. at risk						
Heparin	907	871	866	862	857	856
Bivalirudin	905	853	844	835	830	828

Event curve shows first event experienced

MACE Outcome - All Events

	Bivalirudin			Heparin	
	n	%		%	n
Death	46	5.1 %	v	4.3 %	39
CVA	15	1.6%	v	1.2%	11
Reinfarction	24	2.7%	v	0.9%	8
TLR	24	2.7%	v	0.7%	6
Any MACE	79	8.7 %	v	5.7 %	52

MACE Outcome - All Events

	Bivalirudin			Heparin	
	n	%		%	n
Death	46	5.1 %	v	4.3 %	39
CVA	15	1.6%	v	1.2%	11
Reinfarction	24	2.7%	v	0.9%	8
TLR	24	2.7%	v	0.7%	6
Any MACE	79	8.7 %	v	5.7 %	52

Stent Thrombosis

ARC definite or probable stent thrombosis events

	Bivalirudin			Heparin	
	n	%		%	n
All Events	24	3.4 %	v	0.9 %	6
Relative risk = 3.91 (95% CI 1.6 - 9.5) P=0.001					

Primary Safety Outcomes

Major Bleed BARC grade 3-5

	Bivalirudin			Heparin	
	n	%		%	n
Major Bleed	32	3.5 %	v	3.1 %	28
Relative risk = 1.15 (95% CI 0.7 - 1.9) P=0.59					

Mr Complex

- Heparin alone with plan for GPIIb/IIIa bailout
- Thrombectomy?

Bivalirudin versus Heparin and Heparin plus Tirofiban in Patients with AMI Undergoing PCI

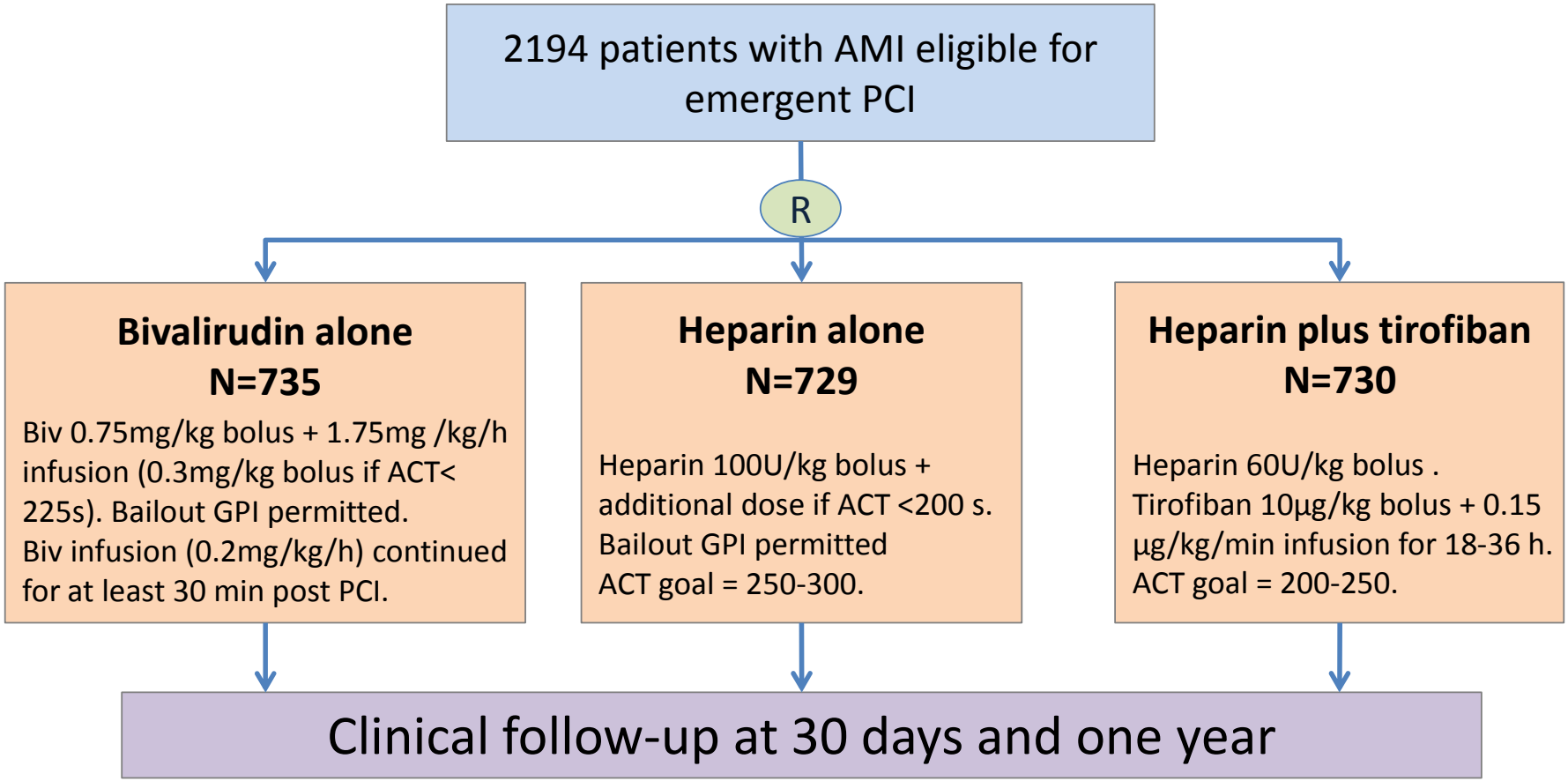
Thirty-Day and One-Year Outcomes of the BRIGHT Trial

Yaling Han, MD, FACC

On behalf of the BRIGHT investigators

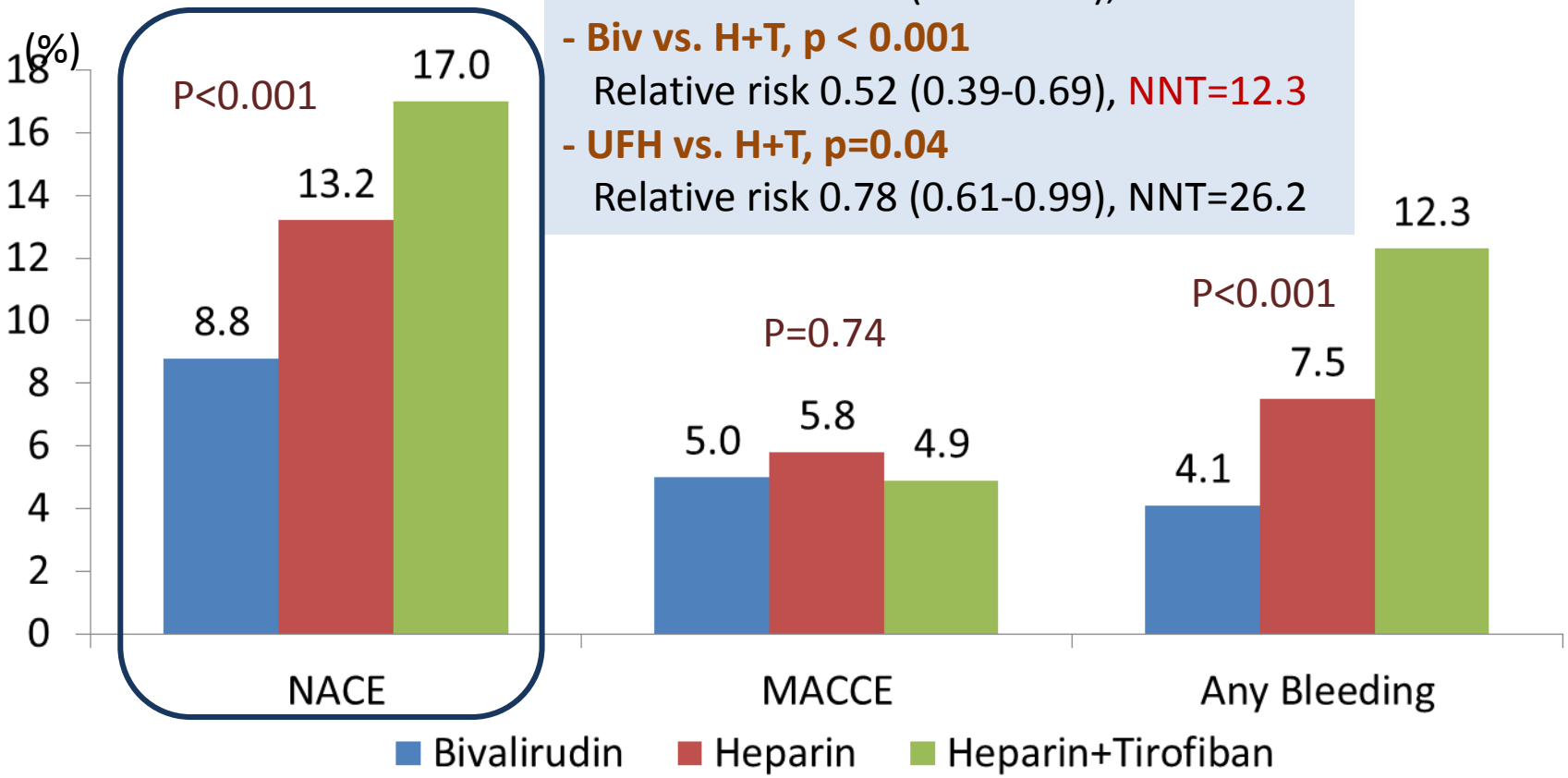
Trial Design

(clinicaltrials.gov number: NCT01696110)



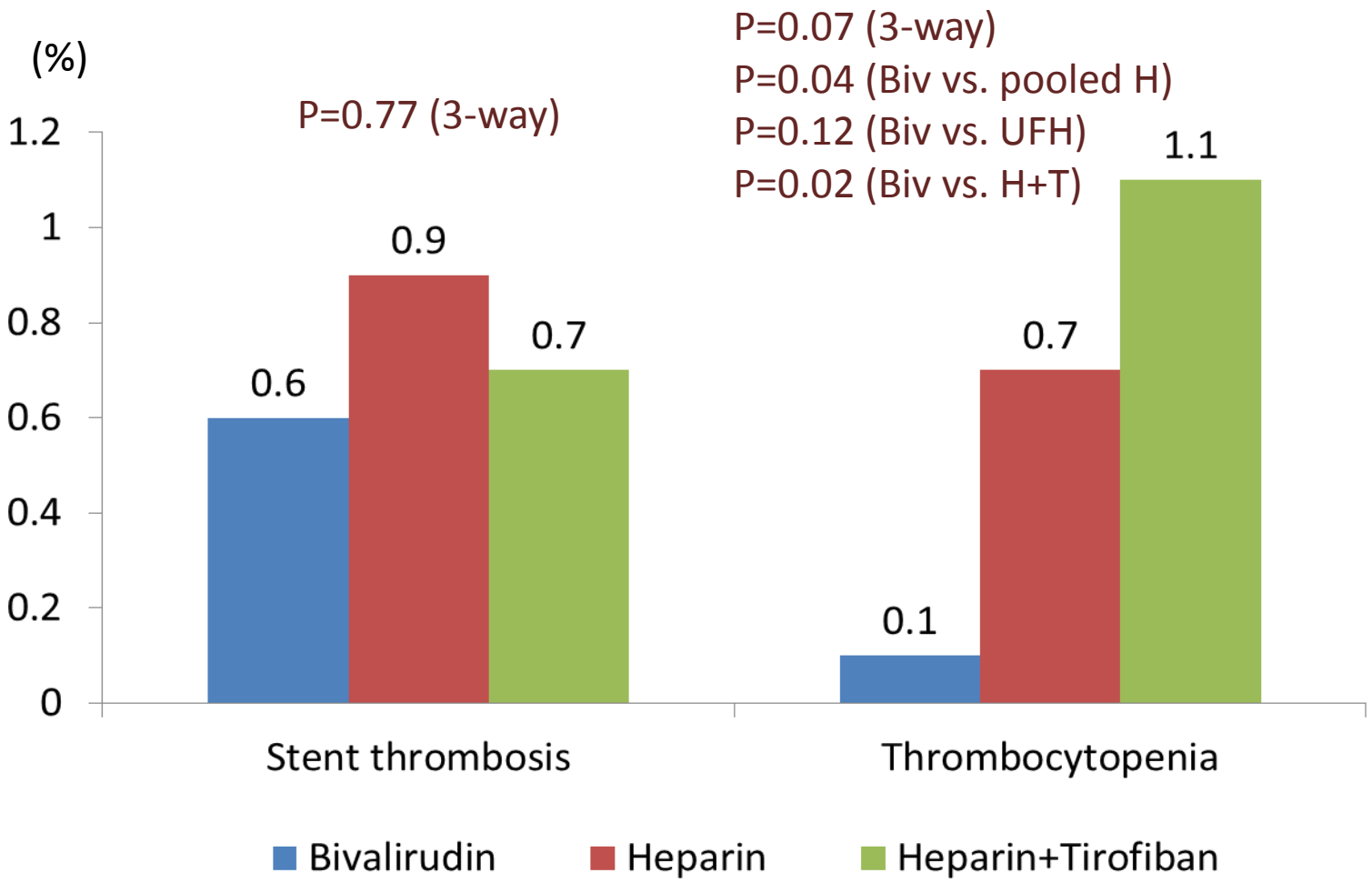
Primary and Principal Secondary Endpoint Events at 30 Days

- **Biv vs. UFH, p=0.009**
  Relative risk 0.67 (0.50-0.90), NNT=23.1
- **Biv vs. H+T, p < 0.001**
  Relative risk 0.52 (0.39-0.69), NNT=12.3
- **UFH vs. H+T, p=0.04**
  Relative risk 0.78 (0.61-0.99), NNT=26.2



Biv=bivalirudin; UFH=Heparin; H+T=heparin + tirofiban

Safety Endpoints at 30 days



Biv=bivalirudin; UFH=Heparin; H+T=heparin + tirofiban

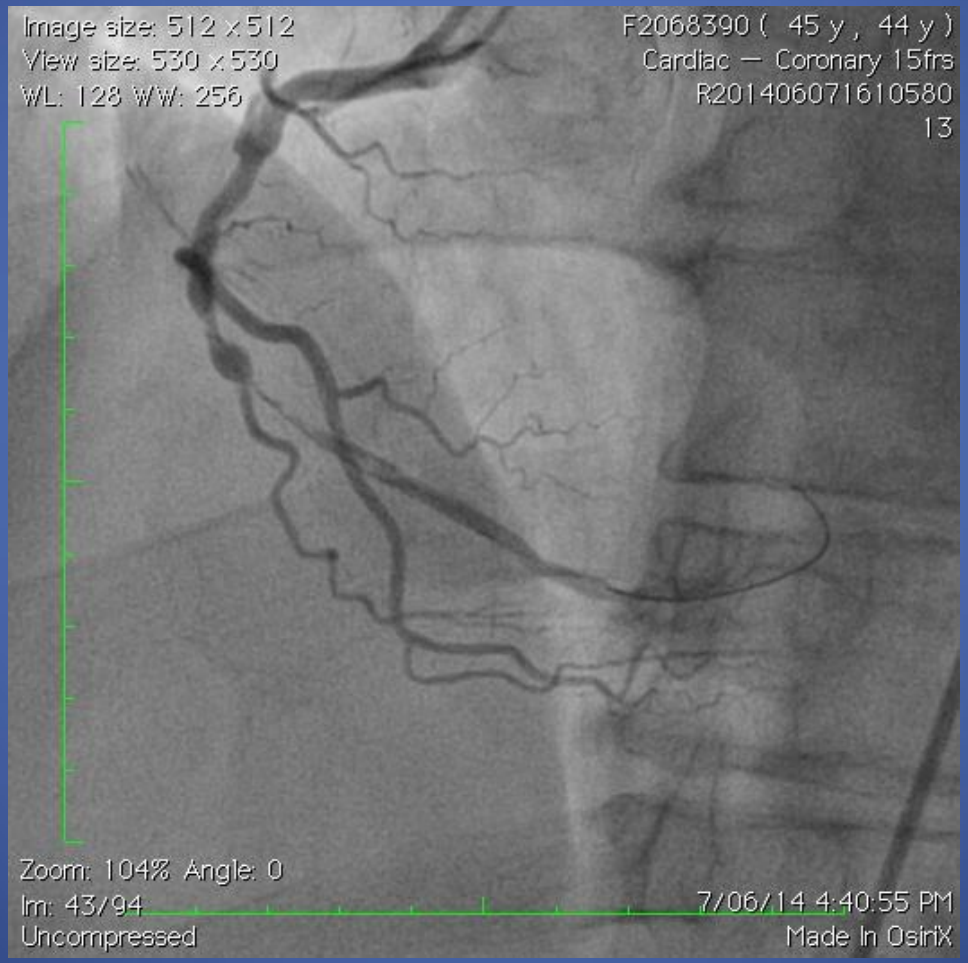
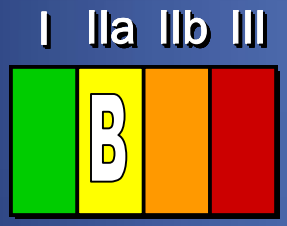


Image size: 512 x 512
View size: 530 x 530
WL: 128 WW: 256
F2068390 (45 y , 44 y)
Cardiac — Coronary 15frs
R201406071610580
13
Zoom: 104% Angle: 0
Im: 43/94
Uncompressed
7/06/14 4:40:55 PM
Made In OsiriX

Thrombus Aspiration During PCI for STEMI

NEW Recommendation

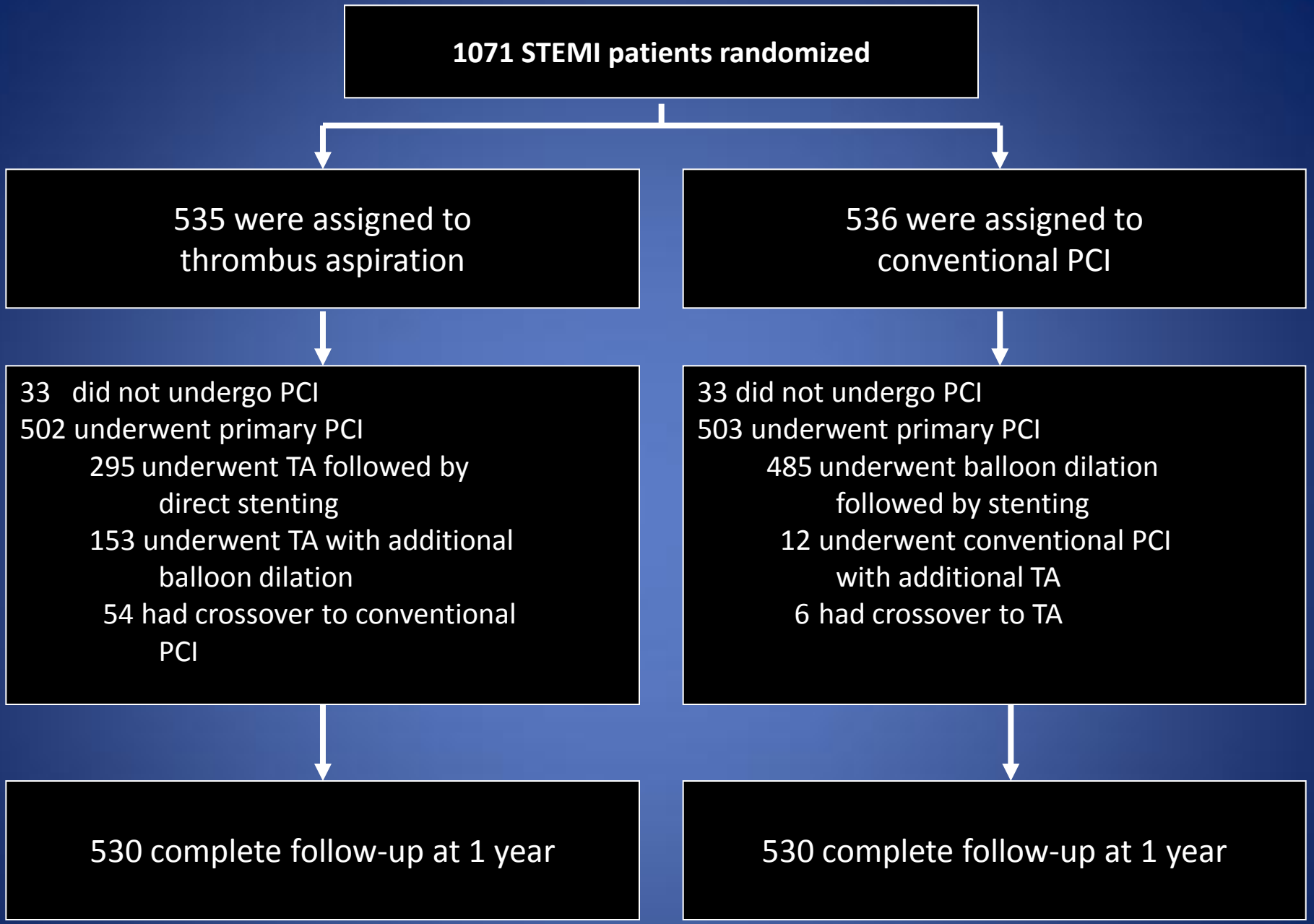


Aspiration thrombectomy is reasonable for patients undergoing primary PCI

Thrombus Aspiration during Percutaneous coronary intervention in Acute myocardial infarction Study (TAPAS)

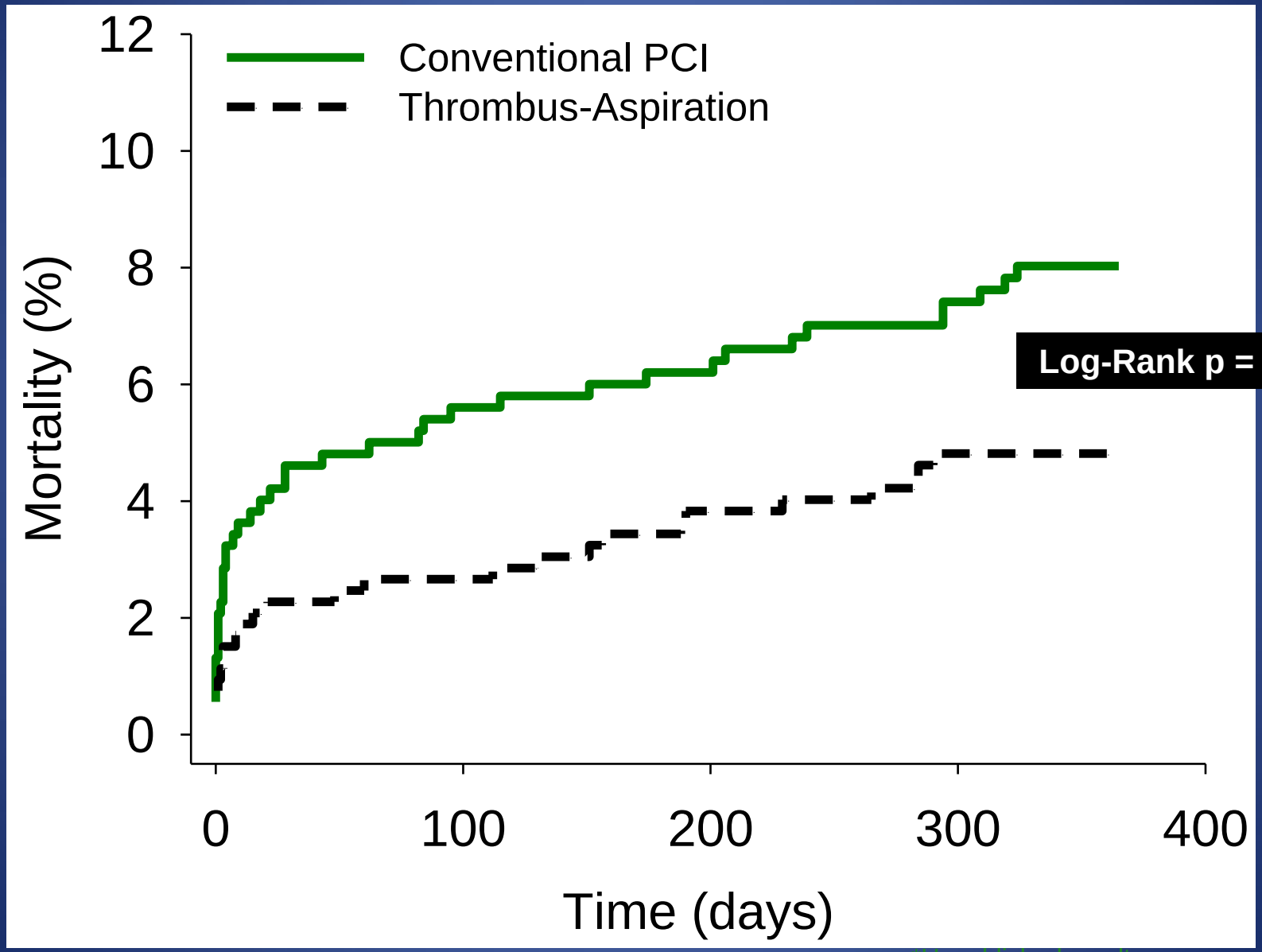
Mortality and reinfarction at 1 year

F. Zijlstra, MD PhD
Thoraxcenter
University Medical Center Groningen,
The Netherlands


1071 STEMI patients randomized
535 were assigned to thrombus aspiration
536 were assigned to conventional PCI
33 did not undergo PCI
502 underwent primary PCI
295 underwent TA followed by direct stenting
153 underwent TA with additional balloon dilation
54 had crossover to conventional PCI
33 did not undergo PCI
503 underwent primary PCI
485 underwent balloon dilation followed by stenting
12 underwent conventional PCI with additional TA
6 had crossover to TA
530 complete follow-up at 1 year
530 complete follow-up at 1 year

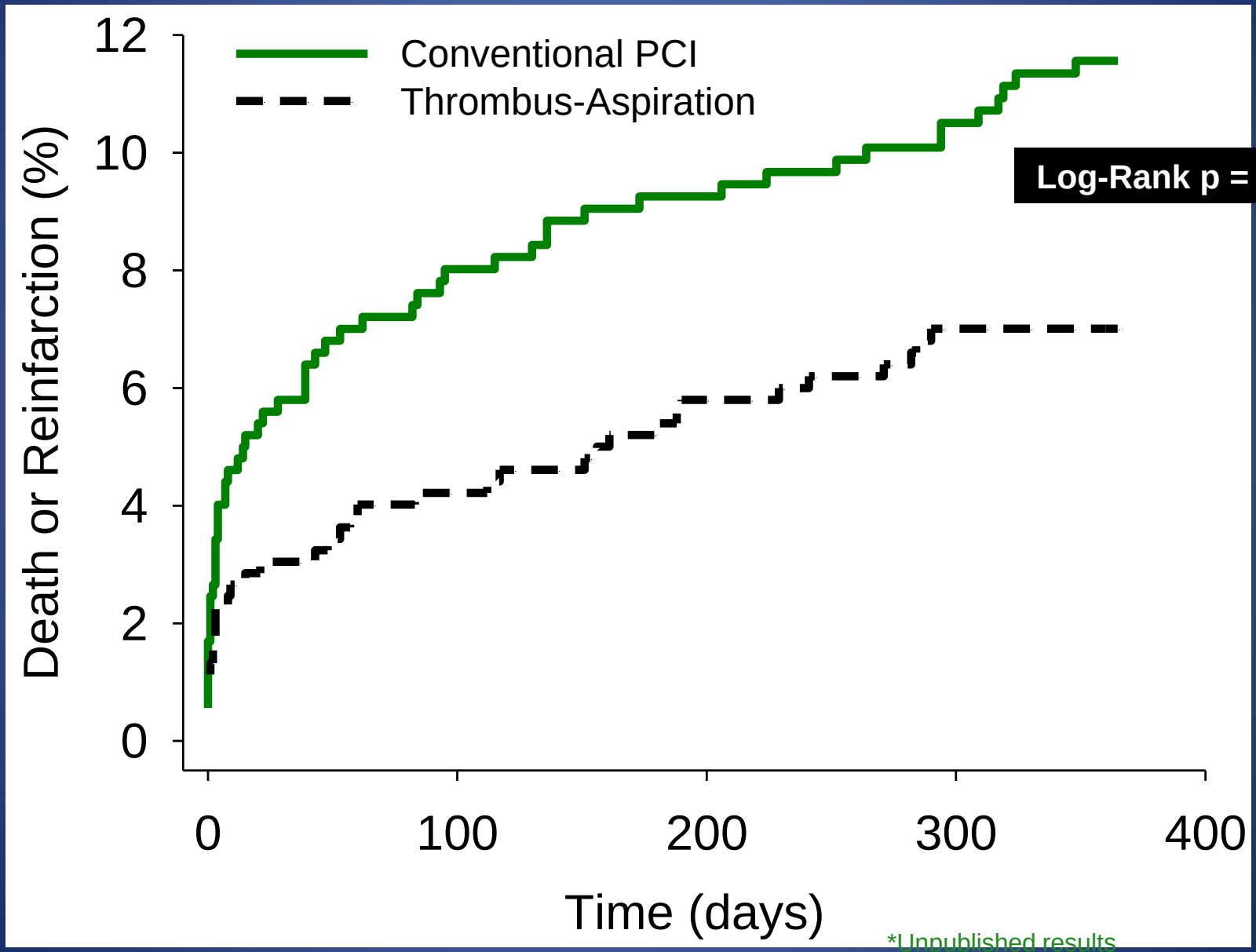
FZ 2008-5

Mortality at 1 year



*Unpublished results

Mortality or non-fatal ReMI at 1 year



*Unpublished results

UCR

Uppsala Clinical
Research Center

SWEDE HEART

Thrombus Aspiration in ST- Elevation myocardial infarction in Scandinavia (TASTE trial)

trial hypothesis

"Aspiration of the blood clot or 'thrombus' that causes a heart attack, before balloon dilatation and stenting, improves survival"

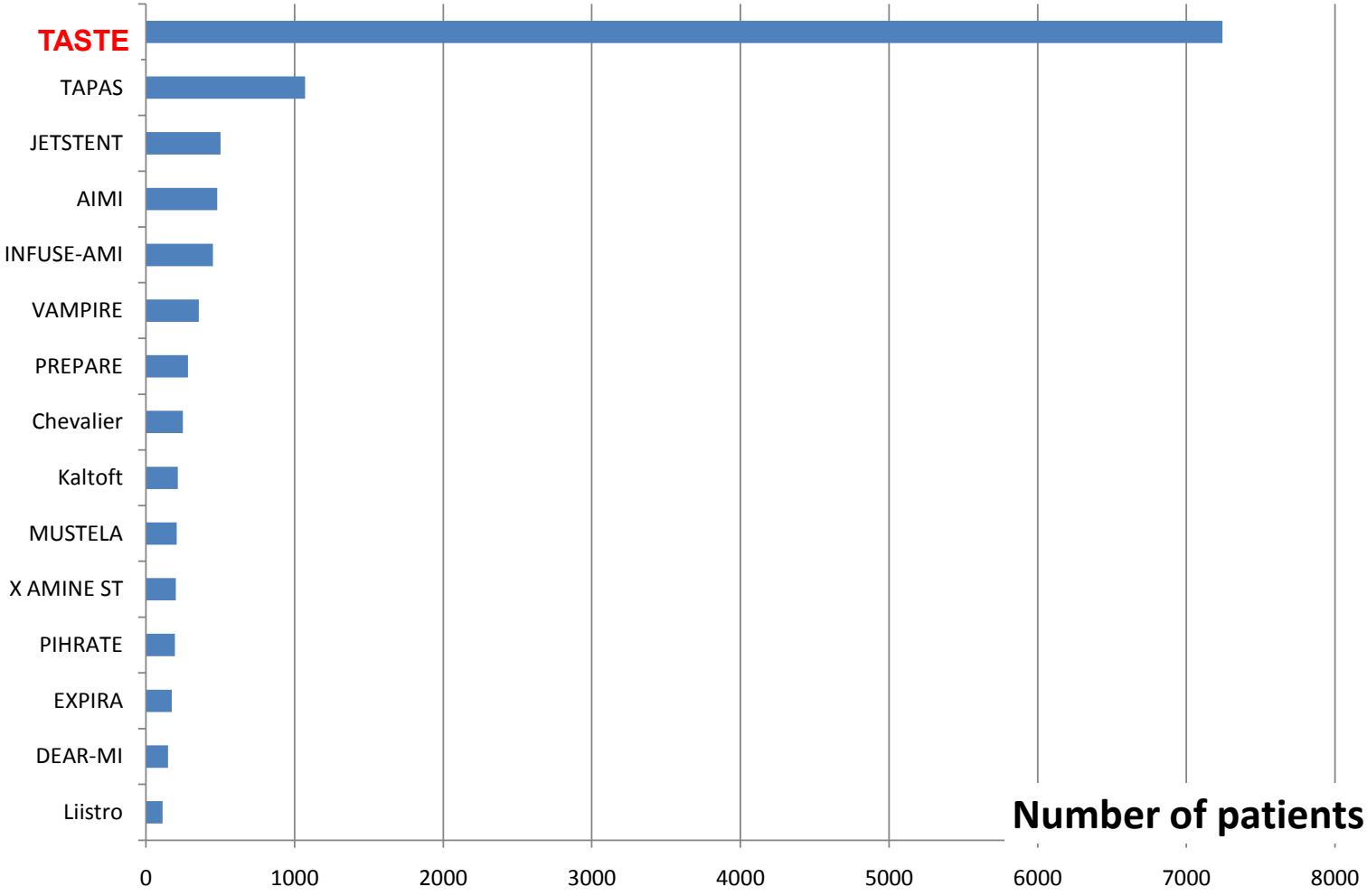
Ole Fröbert, MD, PhD - on behalf of the TASTE investigators

Departement of Cardiology
Örebro University Hospital
Sweden

Methods

- 29 Swedish, 1 Danish and 1 Icelandic hospital
- Multicenter, prospective, randomized, controlled open-label trial enrolling 7244 patients who had a diagnosis of ST-elevation myocardial infarction (STEMI)
- Novel Registry-Based Randomized Clinical Trial concept: national heart registries served as platforms for randomization, case reports and follow-up
  - no patients lost to follow-up
  - powerful tool to capture outcome data with a high degree of fidelity
  - inexpensive
- Half of the patients were assigned to balloon treatment only (known as percutaneous coronary intervention, or PCI) and the other half had their blood clot aspirated before PCI

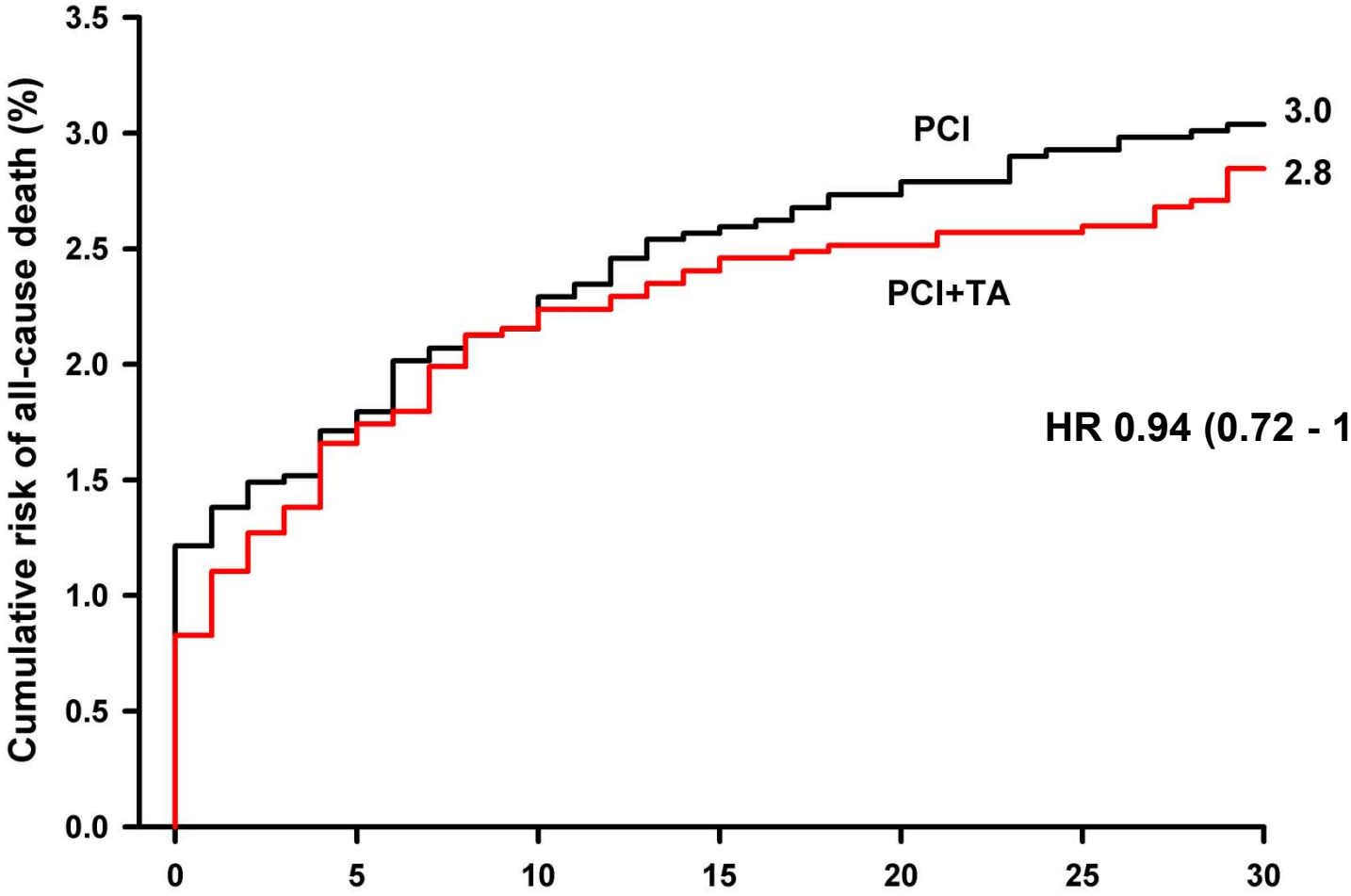
TASTE and previous studies on thrombus aspiration



TASTE

SWEDE HEART

All-cause mortality at 30 days



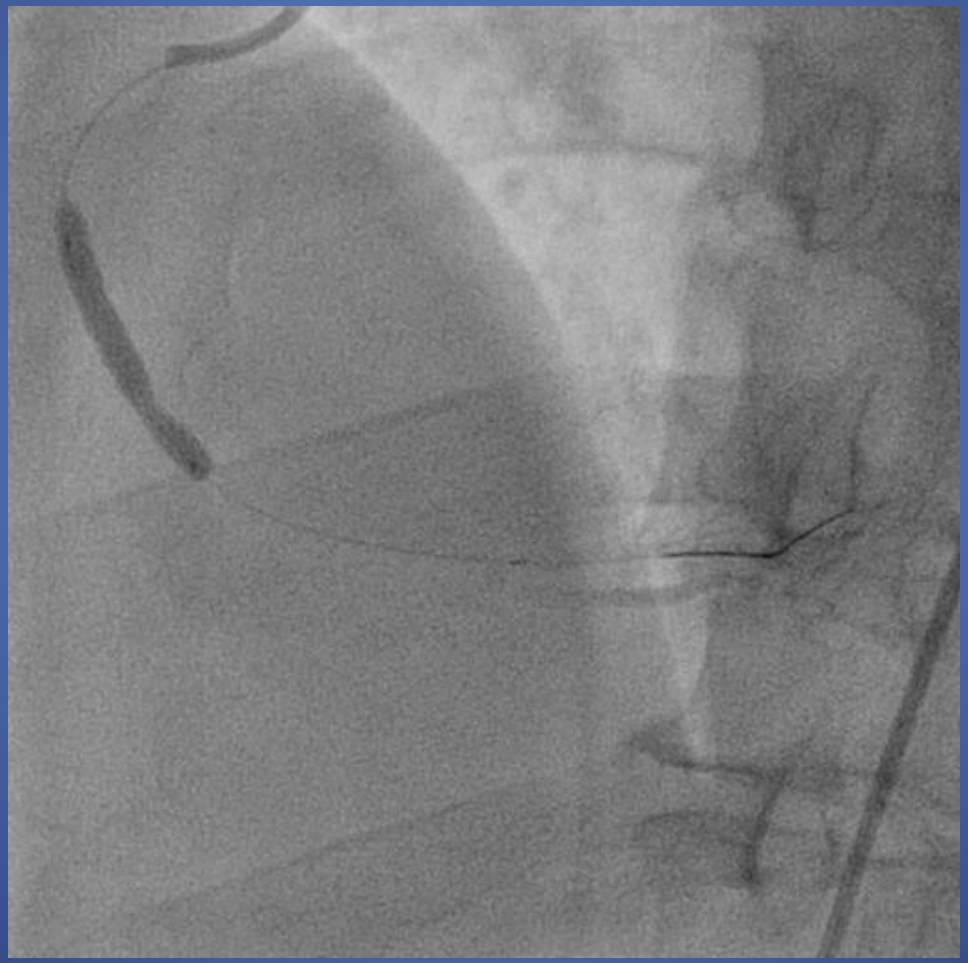
No. at Risk

PCI+TA	3621	3568	3540	3532	3526	3524	3519
PCI	3623	3567	3545	3530	3523	3517	3513

TASTE

Thrombectomy?

- Case by case
- Large thrombus burden
- Complete occlusion of vessel – acts as significant adjunct to PPCI procedure.



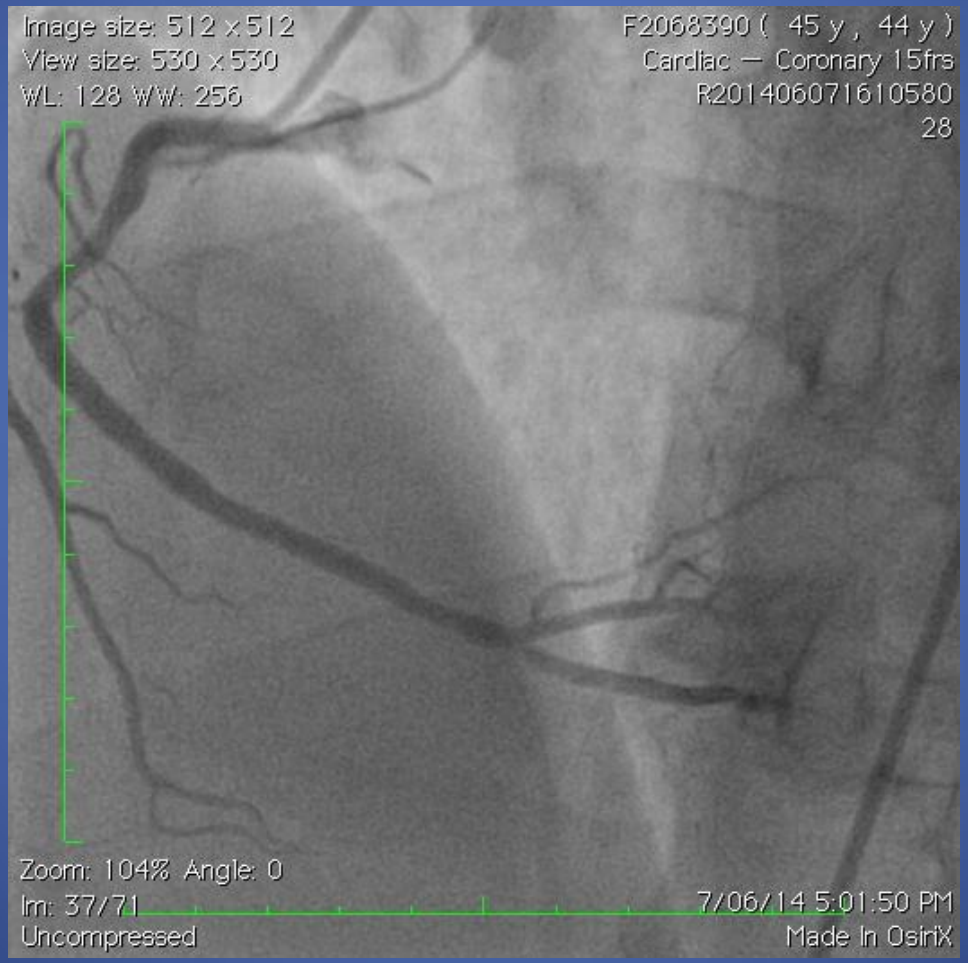
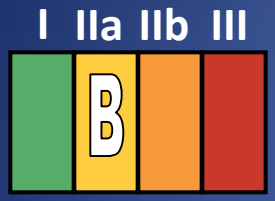


Image size: 512 x 512
View size: 530 x 530
WL: 128 WW: 256
F2068390 (45 y , 44 y)
Cardiac — Coronary 15frs
R201406071610580
28
Zoom: 104% Angle: 0
Im: 37/71
Uncompressed
7/06/14 5:01:50 PM
Made In OsiriX

Mr Complex

- What next?
- PCI to non-culprit lesion during same procedure
- PCI to non-culprit before discharge?
- PCI to non-culprit in 2 weeks?
- PCI only if refractory angina?
- PCI only if objective evidence of ischemia with functional tesing?
- Refer for CABG? (NIDDM, Multi-vessel disease)

Primary PCI in STEMI (ACC 2013 STEMI guidelines)



Primary PCI is reasonable in patients with STEMI if there is clinical and/or ECG evidence of ongoing ischemia between 12 and 24 hours after symptom onset.

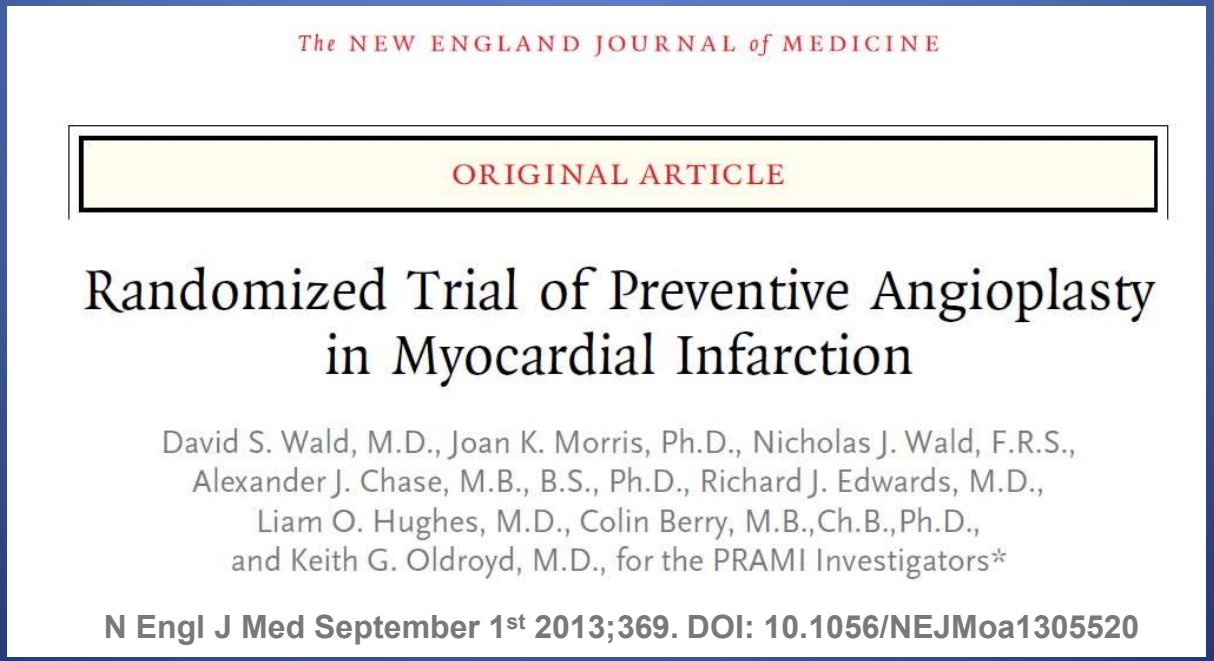
Harm

PCI should not be performed in a noninfarct artery at the time of primary PCI in patients with STEMI who are hemodynamically stable

Preventive Angioplasty in Myocardial Infarction Trial

PRAMI Trial

Randomised multicentre single-blind trial conducted in five UK cardiac centres



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Trial of Preventive Angioplasty in Myocardial Infarction

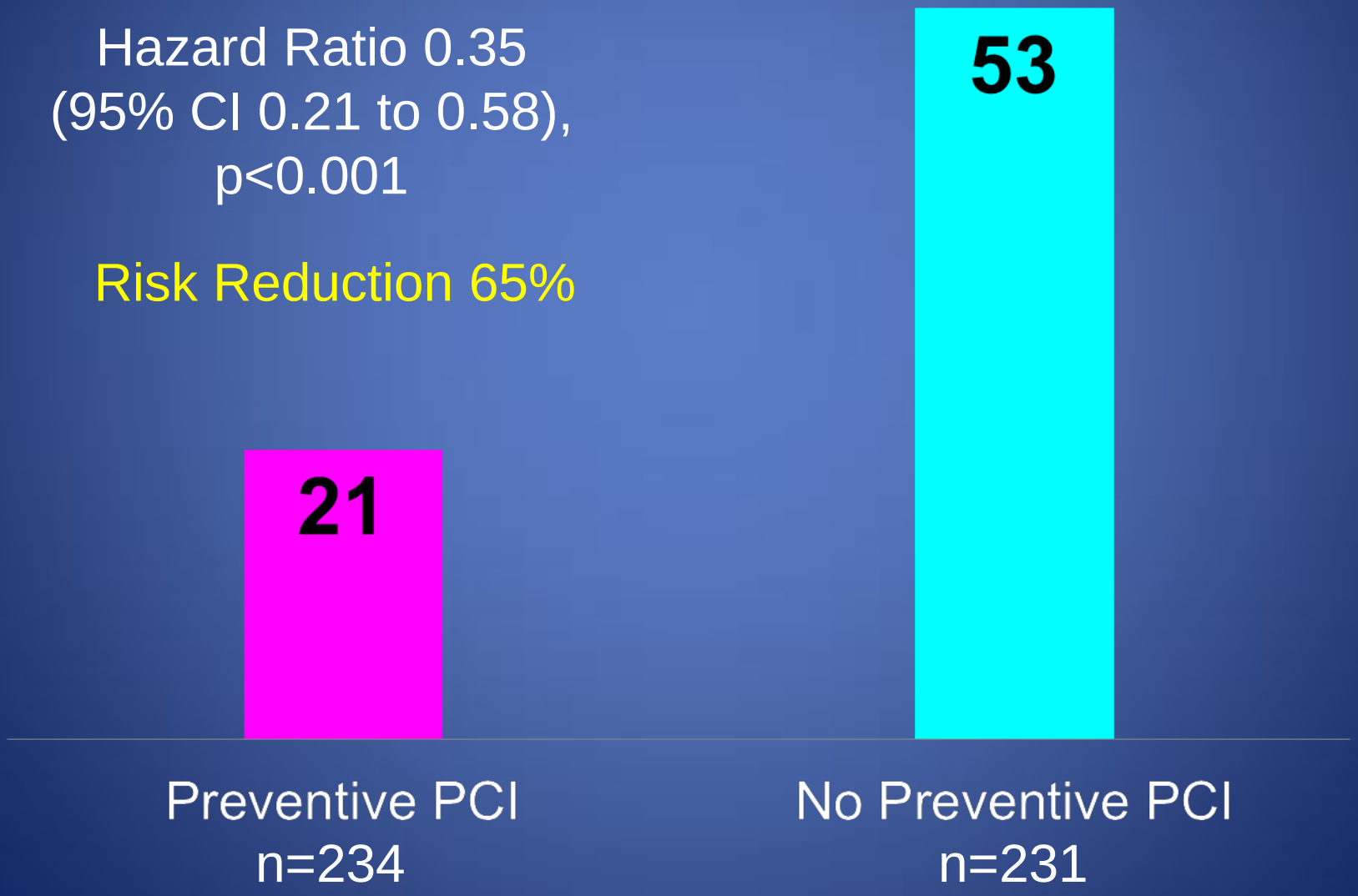
David S. Wald, M.D., Joan K. Morris, Ph.D., Nicholas J. Wald, F.R.S., Alexander J. Chase, M.B., B.S., Ph.D., Richard J. Edwards, M.D., Liam O. Hughes, M.D., Colin Berry, M.B.,Ch.B.,Ph.D., and Keith G. Oldroyd, M.D., for the PRAMI Investigators*

N Engl J Med September 1st 2013;369. DOI: 10.1056/NEJMoa1305520

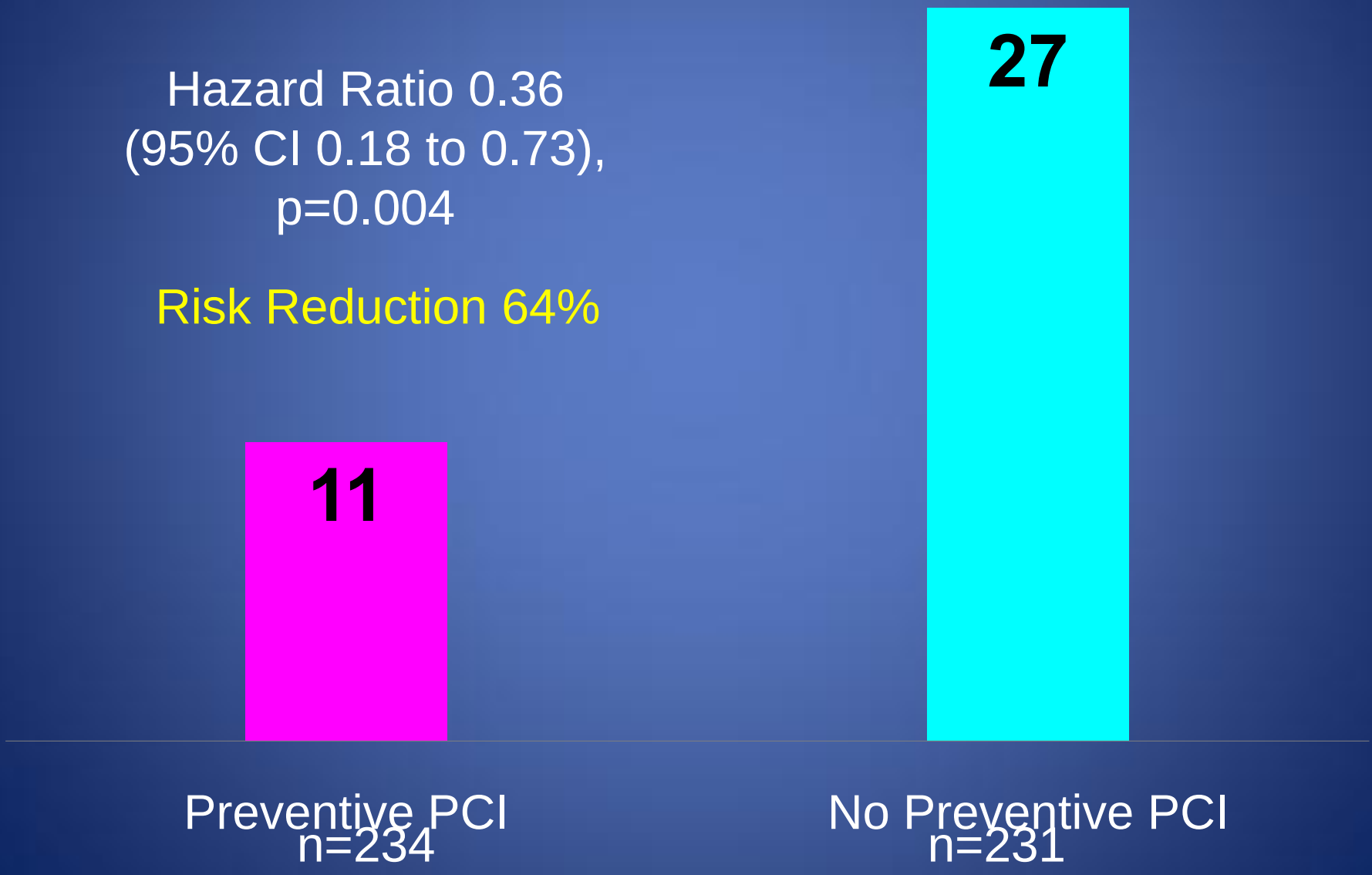
Cardiac Death, Nonfatal MI or Refractory Angina in patients having infarct-artery PCI

Hazard Ratio 0.35
(95% CI 0.21 to 0.58),
p<0.001

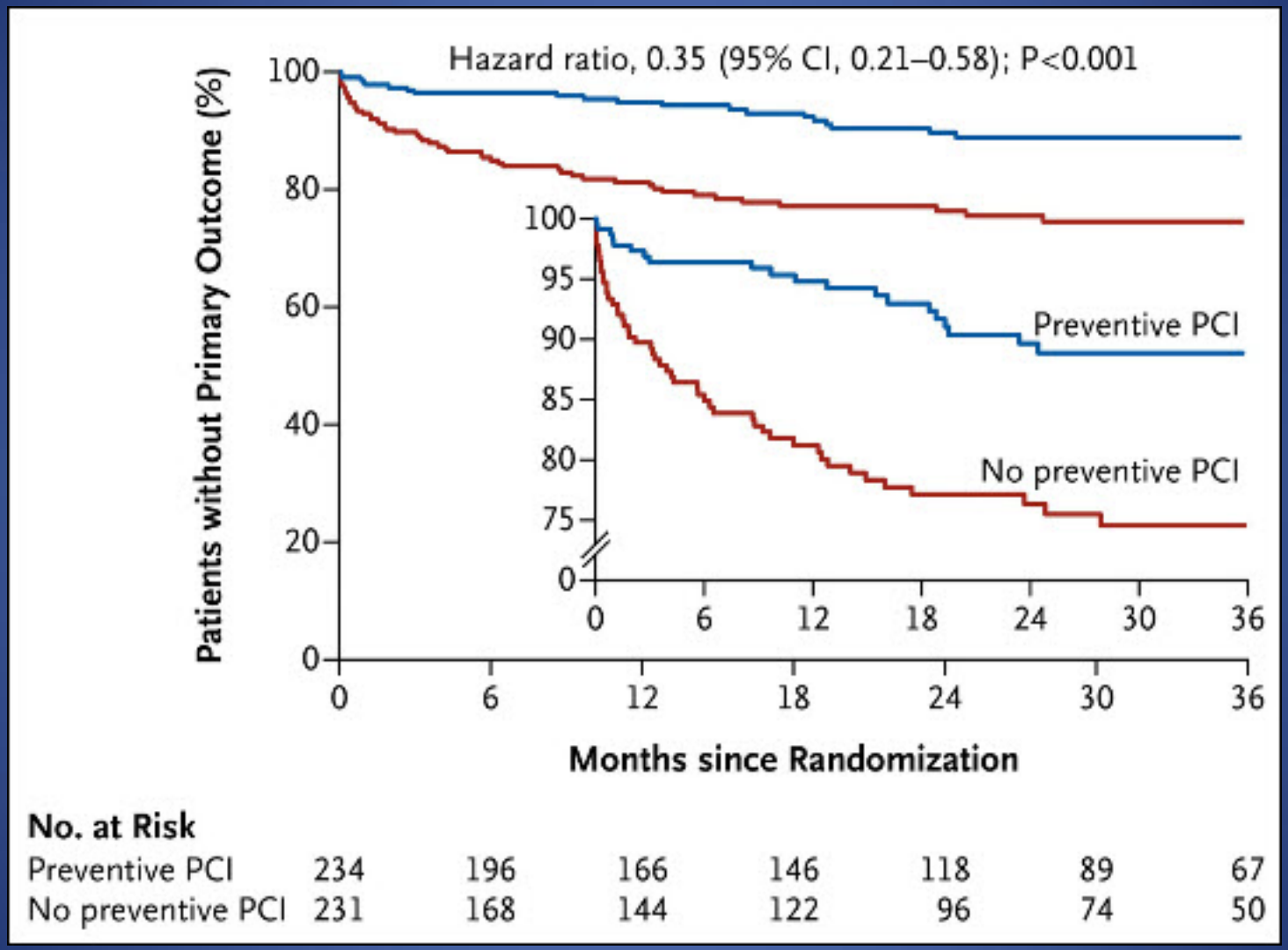
Risk Reduction 65%



Cardiac Death, Nonfatal MI or ~~Refractory Angina~~ in patients having infarct-artery PCI



Prami


Hazard ratio, 0.35 (95% CI, 0.21–0.58); P<0.001
Patients without Primary Outcome (%)
100
80
60
40
20
0
0
6
12
18
24
30
36
Months since Randomization
100
95
90
85
80
75
0
Preventive PCI
No preventive PCI
No. at Risk
Preventive PCI 234 196 166 146 118 89 67
No preventive PCI 231 168 144 122 96 74 50

CVLPRIT trial

Variable	IRA only (N=146)	Complete Revascularisation (N=150)	HR (95% CI)	P value
Time to First Event				
MACE N= (%)	31 (21.2)	15 (10.0)	0.45 (0.24, 0.84)	0.009
Components N=(%)				
All-cause mortality	6 (4.1)	2 (1.3)	0.32 (0.06, 1.60)	0.14
Recurrent MI	4 (2.7)	2 (1.3)	0.48 (0.09, 2.62)	0.39
Heart failure	9 (6.2)	4 (2.7)	0.43 (0.13, 1.39)	0.14
Repeat Revascularisation	12 (8.2)	7 (4.7)	0.55 (0.22, 1.39)	0.2

Content – My Overview

- Evidence of Primary PCI vs Thrombolysis
  - When, Why, How
  - Primary PCI in PCI capable hospital. DTB < 90min
  - Transfer PCI – DTB <120 min from FMC
  - Pharmaco-invasive approach is preferred option if patient presents < 3hrs and Primary or Transfer PCI unable to be achieved.
- To Aspirate or not to Aspirate – Jury is out. Individual cases selection. Reasonable for high thrombotic burden to aid with PCI procedure.

CONTENT – My Overview

- Adjunctive anticoagulation - Heparin with GP Iib/IIIa bailout is reasonable especially with radial access. Data conflicting
- Culprit only vs Preventative PCI – Preventative PCI reasonable option however timing is open – at time of procedure, before discharge, few weeks after discharge, following objective evidence of ischemia all reasonable.