The window for primary PCI

Acute Cardiac Care 2010, Copenhagen

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Potential conflicts of interest:

Speaker's name: Christian Juhl Terkelsen

☐ I have the following potential conflicts of interest to report:

- ☐ Research contracts
- ☐ Consulting
- ☐ Employment in industry
- ☐ Stockholder of a healthcare company
- ☐ Owner of a healthcare company
- ☐ Other(s)

X I do not have any potential conflict of interest

When should we perform primary PCI ?

When can we consider fibrinolysis ?

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ESC/EACTS GUIDELINES

Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Developed with the special contribution of the European Association for Percutaneous Cardiovascular Interventions (EAPCI)‡

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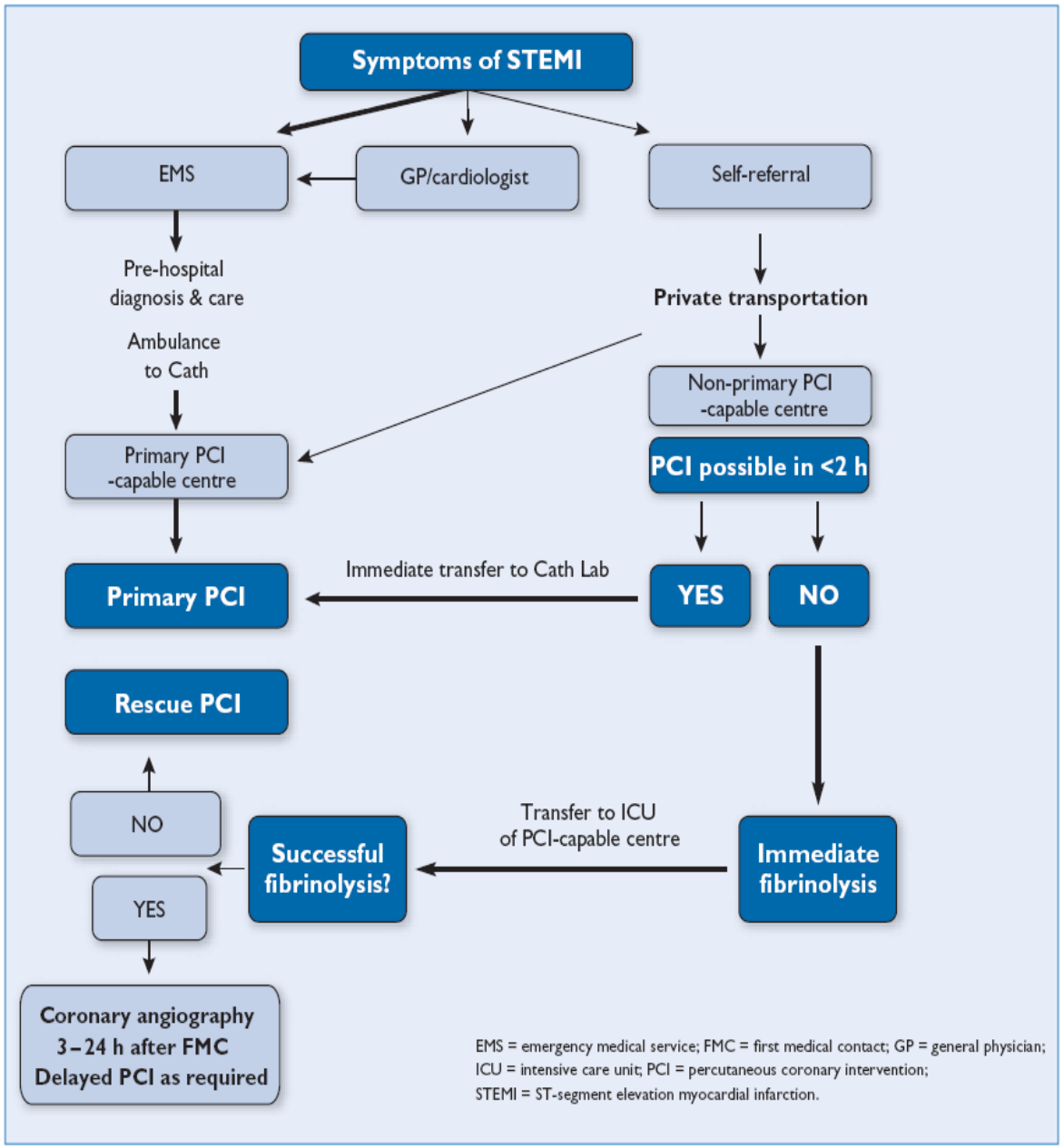

Figure 1 Organization of ST-segment elevation myocardial infarction patient pathway describing pre- and in-hospital management and reperfusion strategies within 12 h of first medical contact.

primary PCI service by a team of high-volume operators. Patients admitted to hospitals without PCI facilities should be transferred to a PCI-capable centre and no fibrinolytics should be administered if the expected time delay between first medical contact (FMC) and balloo 2 h (or >90 min i STEMI and recent non-PCI centre sho be trans-ferred to a PCI-capable centre where angiography and PCI should be performed in a time window of 3–24 h.[77–80]

No data on the association between
First Medical Contact to Balloon
= Total Health Care System Delay
and mortality

System Delay and Mortality Among Patients With STEMI Treated With Primary Percutaneous Coronary Intervention

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Context Timely reperfusion therapy is recommended for patients with ST-segment elevation myocardial infarction (STEMI), and door-to-balloon delay has been proposed as a performance measure in triaging patients for primary percutaneous coronary intervention (PCI). However, focusing on the time from first contact with the health care system to the initiation of reperfusion therapy (system delay) may be more relevant, because it constitutes the total time to reperfusion modifiable by the health care system. No previous studies have focused on the association between system delay and outcome in patients with STEMI treated with primary PCI.

Objective To evaluate the associations between system, treatment, patient, and door-to-balloon delays and mortality in patients with STEMI.

Design, Setting, and Patients Historical follow-up study based on population-based Danish medical registries of patients with STEMI transported by the emergency medical service and treated with primary PCI from January 1, 2002, to December 31, 2008, at 3 high-volume PCI centers in Western Denmark. Patients (N=6209) underwent primary PCI within 12 hours of symptom onset. The median follow-up time was 3.4 (interquartile range, 1.8-5.2) years.

Main Outcome Measures Crude and adjusted hazard ratios of mortality obtained by Cox proportional regression analysis.

Results A system delay of 0 through 60 minutes (n=347) corresponded to a long-term mortality rate of 15.4% (n=43); a delay of 61 through 120 minutes (n=2643) to a rate of 23.3% (n=380); a delay of 121 through 180 minutes (n=2092) to a rate of 28.1% (n=378); and a delay of 181 through 360 minutes (n=1127) to a rate of 30.8% (n=275) ($P<.001$). In multivariable analysis adjusted for other predictors of mortality, system delay was independently associated with mortality (adjusted hazard ratio, 1.10 [95% confidence interval, 1.04-1.16] per 1-hour delay), as was its components, prehospital system delay and door-to-balloon delay.

Conclusion System delay was associated with mortality in patients with STEMI treated with primary PCI.

JAMA. 2010;304(7):763-771 www.jama.com

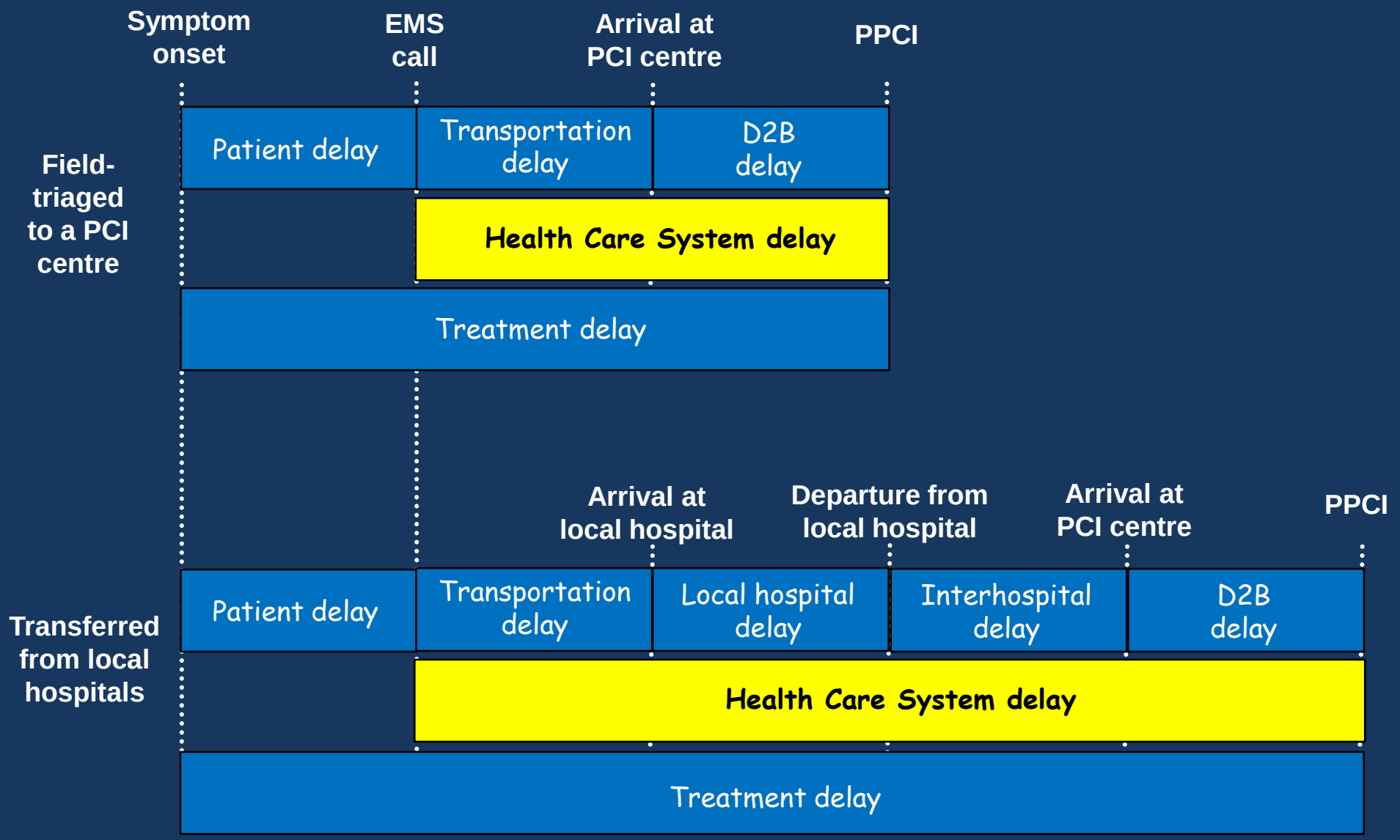
TIMELY REPERFUSION THERAPY with either fibrinolysis or primary percutaneous coronary intervention (PCI) is recommended for patients with ST-segment elevation myocardial infarction (STEMI).[1] However, agreeing on the definition of "timely" is difficult, because the benefit achieved by earlier initiation of reperfusion therapy is controversial. The only unbiased studies that have evaluated the effects of earlier reperfusion therapy on outcome are randomized controlled studies that compared prehospital and in-hospital fibrinolysis. In those studies, prehospital fibrinolysis was associated with earlier initiation (1 hour) of reperfusion therapy, resulting in an ex-

Terkelsen et al, JAMA 2010

Aim:

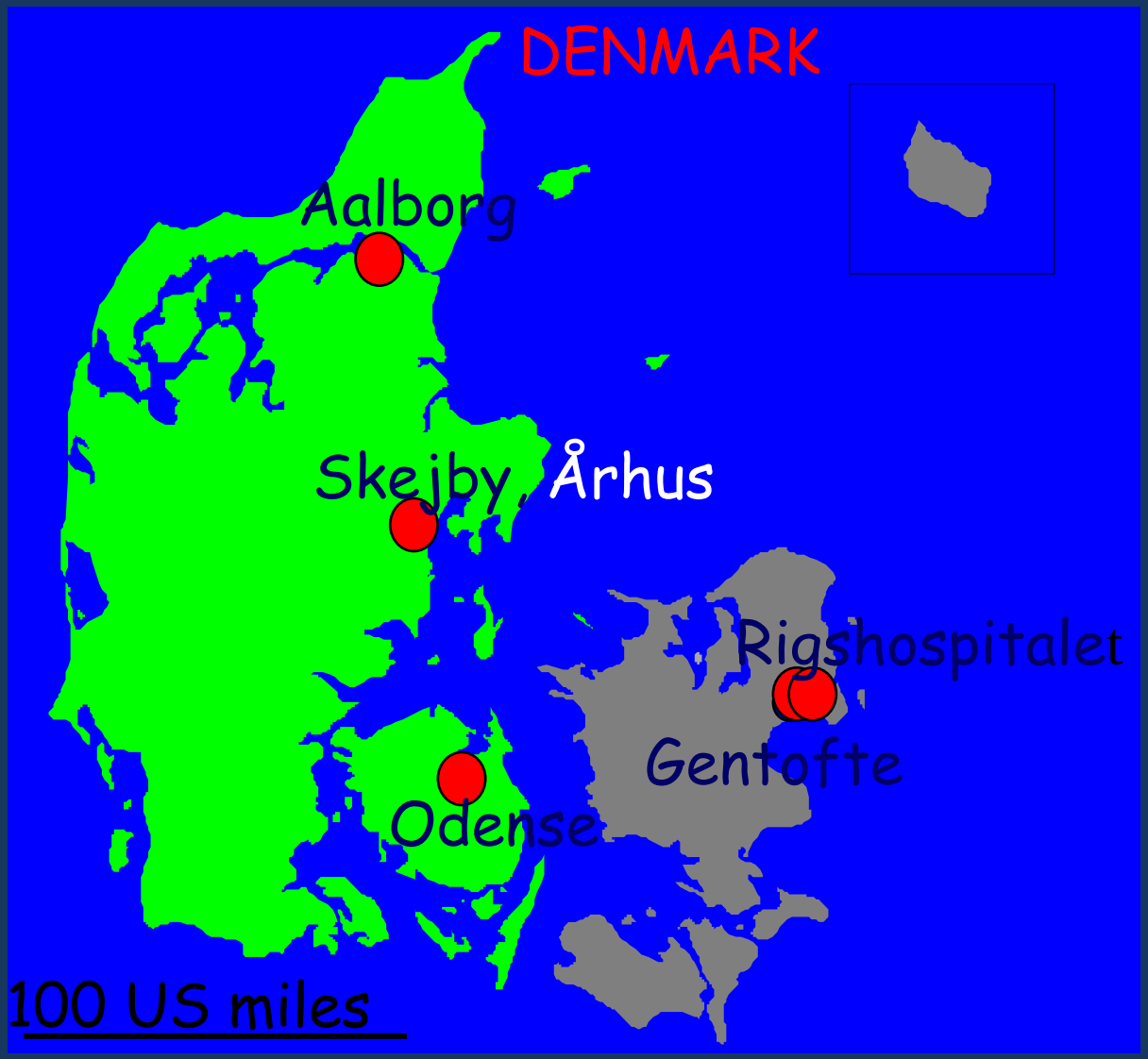
To evaluate the association between
Health Care System delay (=FMC to balloon)
and mortality
in patients with STEMI treated with primary PCI.

Background: Various delays



Setting: Western Denmark, 2002-2008

3 pPCI centers , 24-7, servicing 3.0 mill. inhabitants



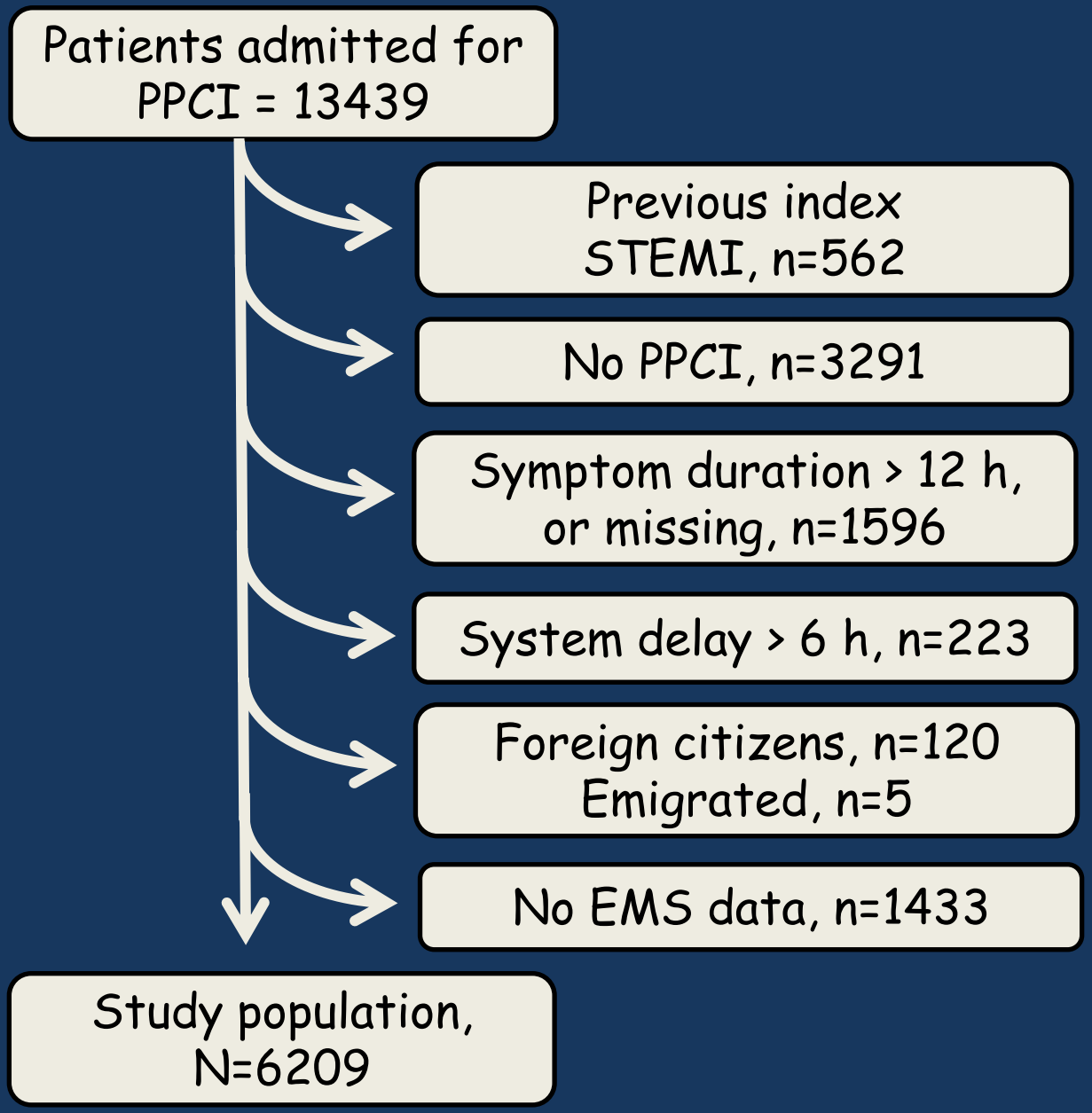
Methods:

1. Western Denmark Heart Registry:
Collects data on all invasive procedures in Western Denmark, including baseline characteristics

2. Emergency Medical Service Database:
Only 6 EMS providers in Denmark, and
one EMS provider covered 85% of the study region

3. The Danish Civil Registration System:
Daily updated vital status for all Danish Citizens, since 1968

Study population:



Univariable Cox regression analysis:

Table 2. Crude Hazard Ratios of Covariates Associated With Long-term Mortality in Univariable Cox Regression Analysis (N = 6209).

Characteristics	Valid Cases	Deaths[a]	HR (95% CI)	Wald Test	*P* Value[b]
Demographics					
Age, per 1-year increase	6209		1.074 (1.069-1.080)	666	<.001
Women	6209	364	1.46 (1.29-1.66)	35	<.001
Comorbid conditions					
Treated hypertension	4574	280	1.45 (1.25-1.69)	25	<.001
Diabetes	4725	146	2.29 (1.91-2.73)	82	<.001
Previous myocardial infarction	4510	122	1.55 (1.28-1.89)	20	<.001
Previous PCI	4506	53	1.19 (0.90-1.58)	1.5	.22
Previous congestive heart failure	5793	102	4.22 (3.43-5.17)	189	<.001
Active or previous smoker	4378	505	0.78 (0.66-0.93)	7.6	.006
Delays and transportation					
Delay, per 1-h increase[c]					
Treatment	6209		1.054 (1.029-1.080)	19	<.001
Patient	5493		1.042 (1.014-1.071)	8.8	.003
System	6209		1.22 (1.15-1.29)	51	<.001
Prehospital system	4652		1.19 (1.11-1.27)	26	<.001
Door-to-balloon	4626		1.13 (1.048-1.22)	10	.002
Transportation distance, per 1-km increase	6209		1.00 (0.999-1.002)	0.45	.50
Clinical characteristics					
Body mass index, per 1-unit increase	3060		0.94 (0.91-0.96)	25	<.001

Univariable Cox regression analysis:

Table 2. Crude Hazard Ratios of Covariates Associated With Long-term Mortality in Univariable Cox Regression Analysis (N = 6209).

Characteristics	Valid Cases	Deaths[a]	HR (95% CI)	Wald Test	*P* Value[b]
Clinical characteristics					
Body mass index, per 1-unit increase	3060		0.94 (0.91-0.96)	25	<.001
Systolic blood pressure, mm Hg	3537	550			
<110	641	170	1 [Reference]	78	<.001
110-129	1111	161	0.49 (0.40-0.61)	42	<.001
130-144	873	101	0.40 (0.31-0.51)	54	<.001
≥145	912	118	0.45 (0.35-0.56)	46	<.001
Diastolic blood pressure, mm Hg	3521	546			
<65	812	191	1 [Reference]	69	<.001
65-74	819	119	0.55 (0.44-0.69)	26	<.001
75-84	1092	157	0.53 (0.43-0.65)	35	<.001
≥85	798	79	0.37 (0.29-0.48)	55	<.001
Killip class	6204	1073			
I	5629	811	1 [Reference]	545	<.001
II	297	97	2.63 (2.13-3.24)	81	<.001
III	140	76	5.09 (4.02-6.44)	184	<.001
IV	138	89	8.65 (6.94-10.8)	370	<.001
Anterior infarct location	5633	467	1.35 (1.19-1.54)	21	<.001
Culprit vessel LM/LAD	6009	520	1.28 (1.14-1.45)	16	<.001
Multivessel disease	5715	640	2.19 (1.92-2.49)	138	<.001

Multivariable Cox regression analyses:

Covariates Remaining Significant in Models[b]	Model 1 HR (95% CI)	Model 1 *P* Value[c]	Model 2 HR (95% CI)	Model 2 *P* Value[c]	Model 3 HR (95% CI)	Model 3 *P* Value[c]
Demographics						
Age, per 1-y increase	1.067 (1.060-1.074)	<.001	1.066 (1.060-1.073)	<.001	1.066 (1.060-1.073)	<.001
Comorbid conditions						
Diabetes	1.97 (1.64-2.37)	<.001	1.94 (1.61-2.33)	<.001	1.95 (1.63-2.35)	<.001
Previous congestive heart failure	1.73 (1.39-2.16)	<.001	1.78 (1.43-2.22)	<.001	1.78 (1.43-2.22)	<.001
Previous or current smoking	1.24 (1.05-1.48)	.01	1.25 (1.05-1.48)	.01	1.26 (1.06-1.50)	.008
Delays, per 1-h increase[d]						
Treatment	1.00 (0.98-1.03)	.54				
Patient			1.00 (0.98-1.03)	.63	1.00 (0.98-1.03)	.64
System			1.10 (1.04-1.16)	.002		
Prehospital system					1.10 (1.02-1.18)	.02
Door-to-balloon					1.14 (1.05-1.24)	.001
Clinical characteristics						
Systolic blood pressure, mm Hg						
<110	1 [Reference]		1 [Reference]		1 [Reference]	
110-129					1-0.89)	.001
130-144					5-0.80)	<.001
≥145					1-0.67)	<.001
Killip class						
I					erence]	
II					1-2.03)	<.001
III	2.47 (1.92-3.18)	<.001	2.55 (1.98-3.28)	<.001	2.51 (1.95-3.23)	<.001
IV	4.73 (3.69-6.06)	<.001	4.71 (3.67-6.05)	<.001	4.57 (3.56-5.87)	<.001
Anterior STEMI or BBBMI	1.30 (1.14-1.48)	<.001	1.29 (1.13-1.47)	<.001	1.29 (1.13-1.47)	<.001
Multivessel disease	1.53 (1.34-1.76)	<.001	1.51 (1.32-1.73)	<.001	1.51 (1.31-1.73)	<.001

The only predictor of outcome that is modifiable in the acute phase is System delay and its componets

Background: Various delays

Treatment delay (and Patient delay) is hampered by:

1. Recall bias:
   When was the acutal symptom onset ?

2. Measurement error:
   Is symptom onset equal to AMI onset ?
   Hours of UAP or spontaneous opening and closure of the culprit vessel ?

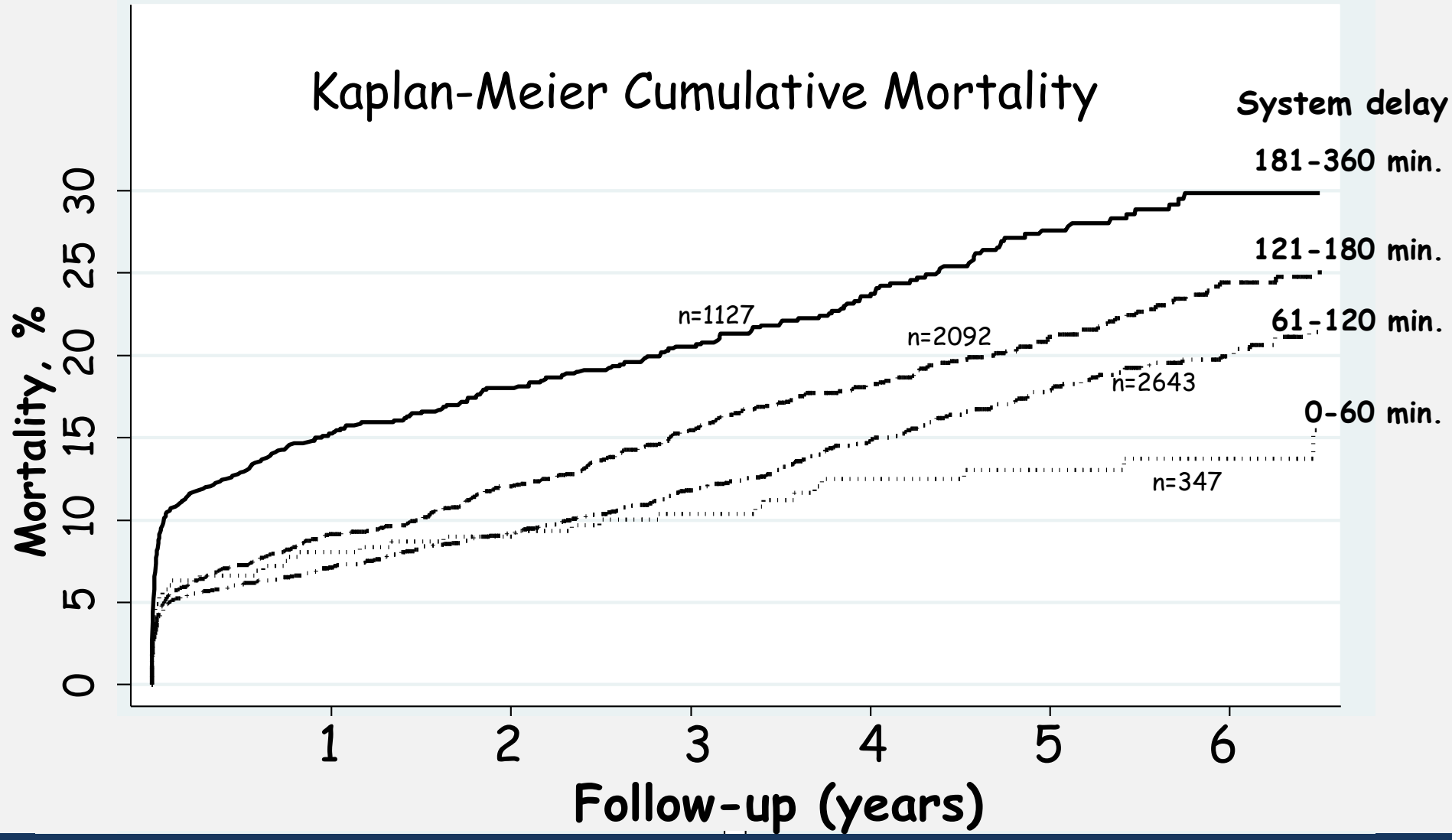
3. Survivor cohort effect:
   Late incomers are survivors of the prehospital phase

Background: Various delays

$$\sigma^2_{\text{treatment delay}} \approx \sigma^2_{\text{patient delay}} + \sigma^2_{\text{system delay}}$$

	Treatment delay	Patient delay	System delay
σ^2	5.8 h	5.1 h	1.0 h
Mean	4.2 h	2.3 h	2.2 h

System delay and mortality



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The overall aim is to keep FMC/EMS call to balloon <2 hours

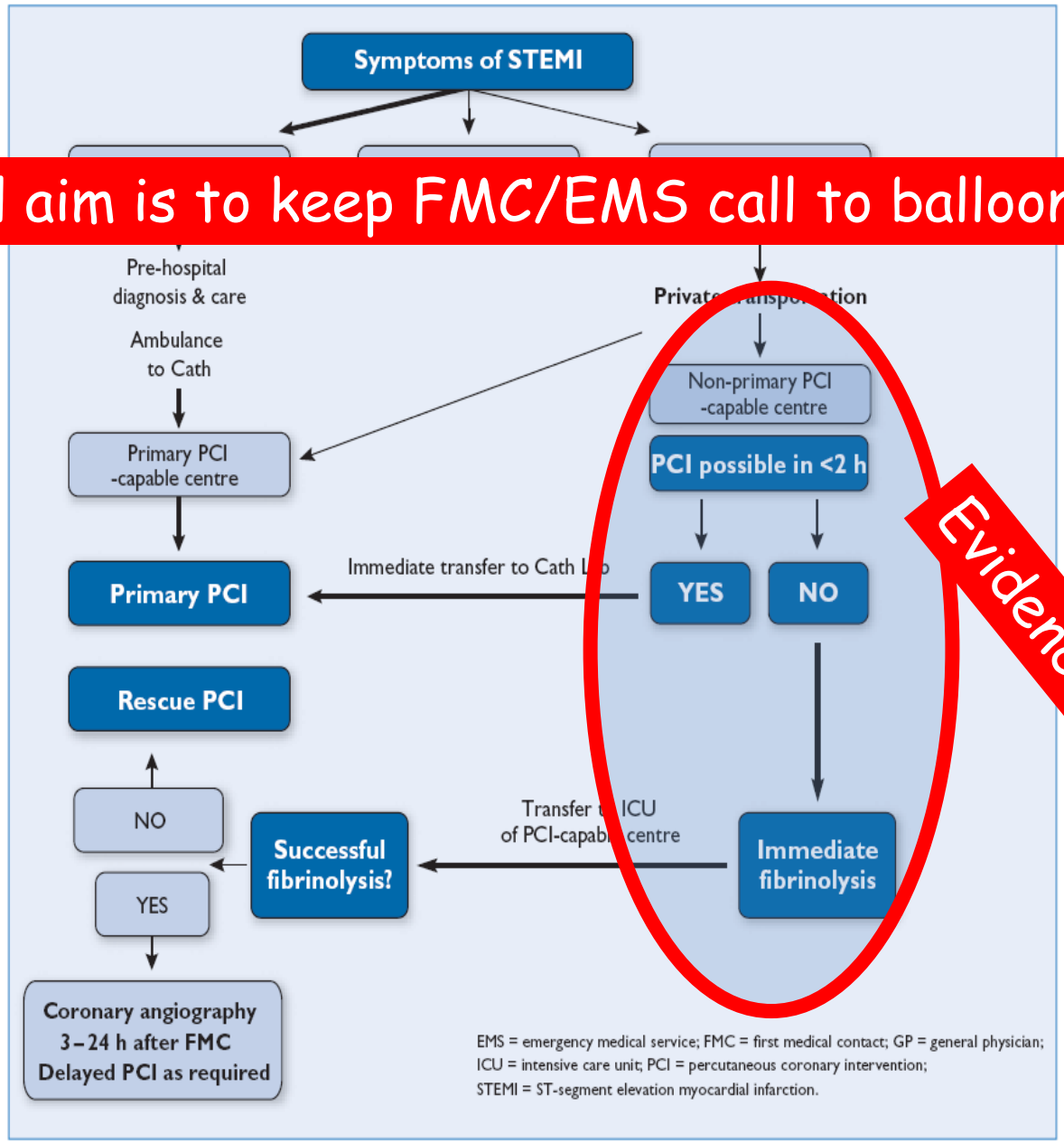

Figure 1 Organization of ST-segment elevation myocardial infarction patient pathway describing pre- and in-hospital management and reperfusion strategies within 12 h of first medical contact.

The window for primary PCI

Fibrinolysis cannot be initiated instantaneously !!!!!

The question is what extra delay is acceptable to perform PPCI instead of fibrinolysis ?

The window for primary PCI

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European Heart Journal
doi:10.1093/eurheartj/ehl810

Clinical research

Does time matter? A pooled analysis of randomized clinical trials comparing primary percutaneous coronary intervention and in-hospital fibrinolysis in acute myocardial infarction patients

Eric Boersma* and The Primary Coronary Angioplasty vs. Thrombolysis (PCAT)-2 Trialists' Collaborative Group

Clinical Epidemiology Unit Thoraxcenter Cardiology, Room Ba563, Erasmus MC, Dr Molewaterplein 40, 3015 GD Rotterdam, The Netherlands

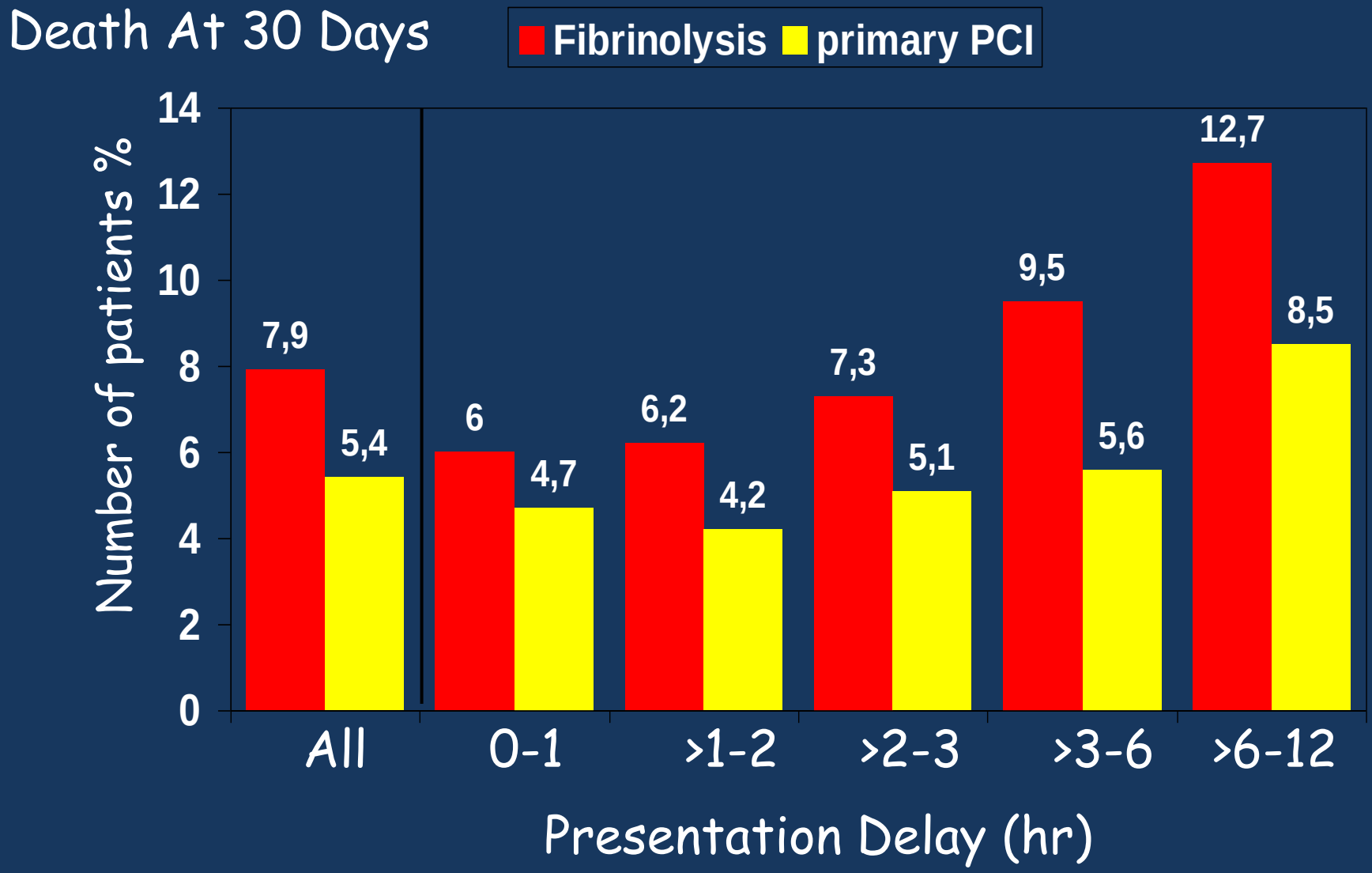
Received 27 October 2005; revised 27 January 2006; accepted 3 February 2006

The window for primary PCI

- **Boersma – AHA 2004**
  - 27 AMI PCI-vs-Lytic trials
  - Asked for individual patient files
  - 2 trials with lost database
  - 1 trial refused – CAPTIM
  - 6903 AMI pts (3452 FL vs. 3451 PP)

Boersma, Eur Heart J 2006.

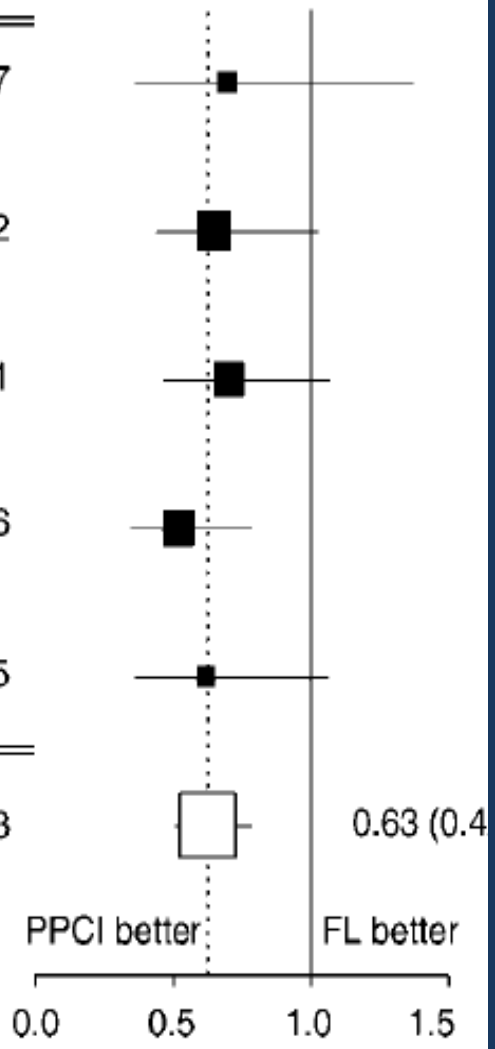
The window for primary PCI



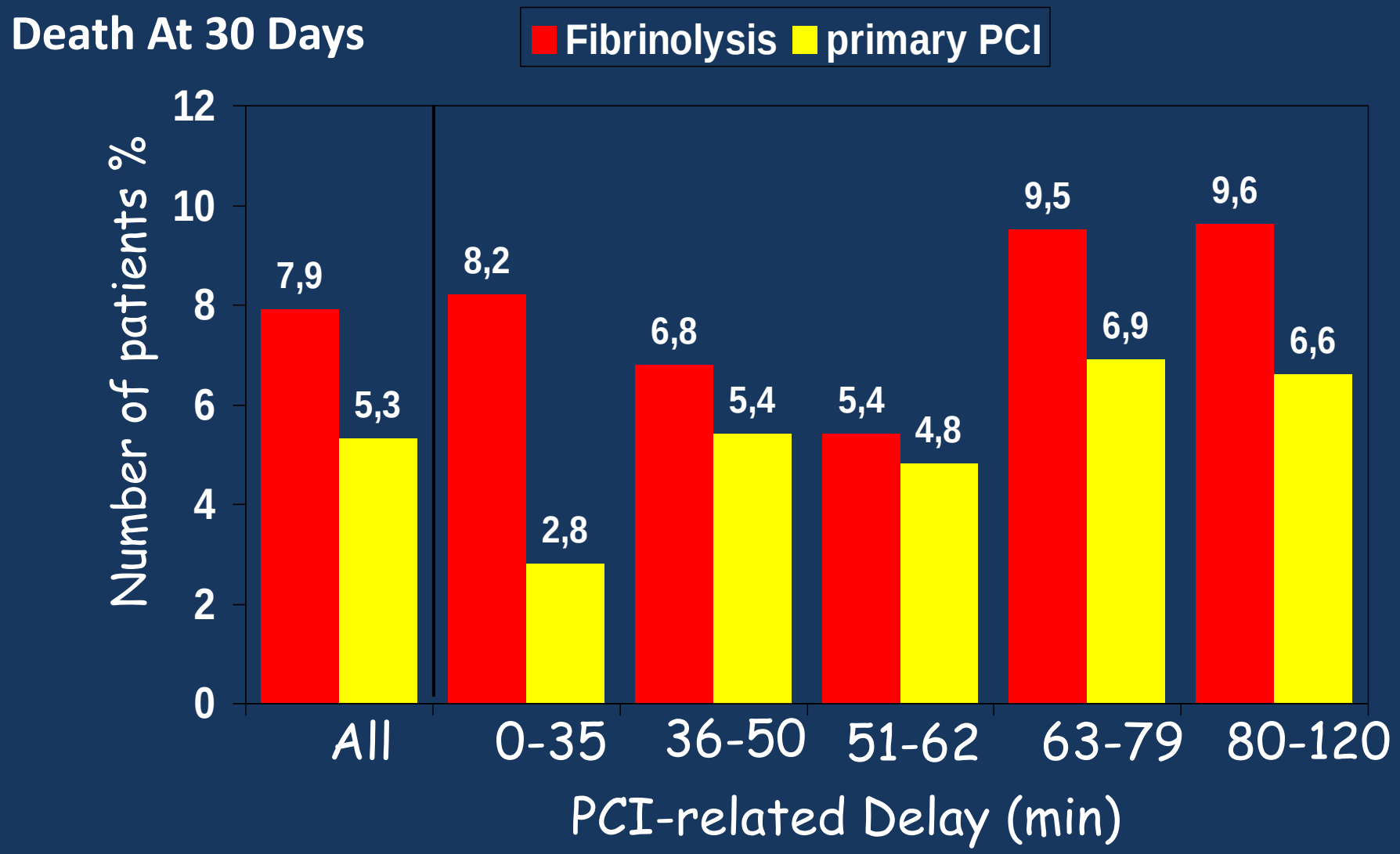
Boersma, Eur Heart J 2006

The window for primary PCI

Presentation delay (h)	Number of patients	30-day death (%)	
		FL	PPCI
0–1	747	6.0	4.7
>1–2	2000	6.2	4.2
>2–3	1712	7.3	5.1
>3–6	1640	9.5	5.6
>6–12	664	12.7	8.5
All patients	6763	7.9	5.3

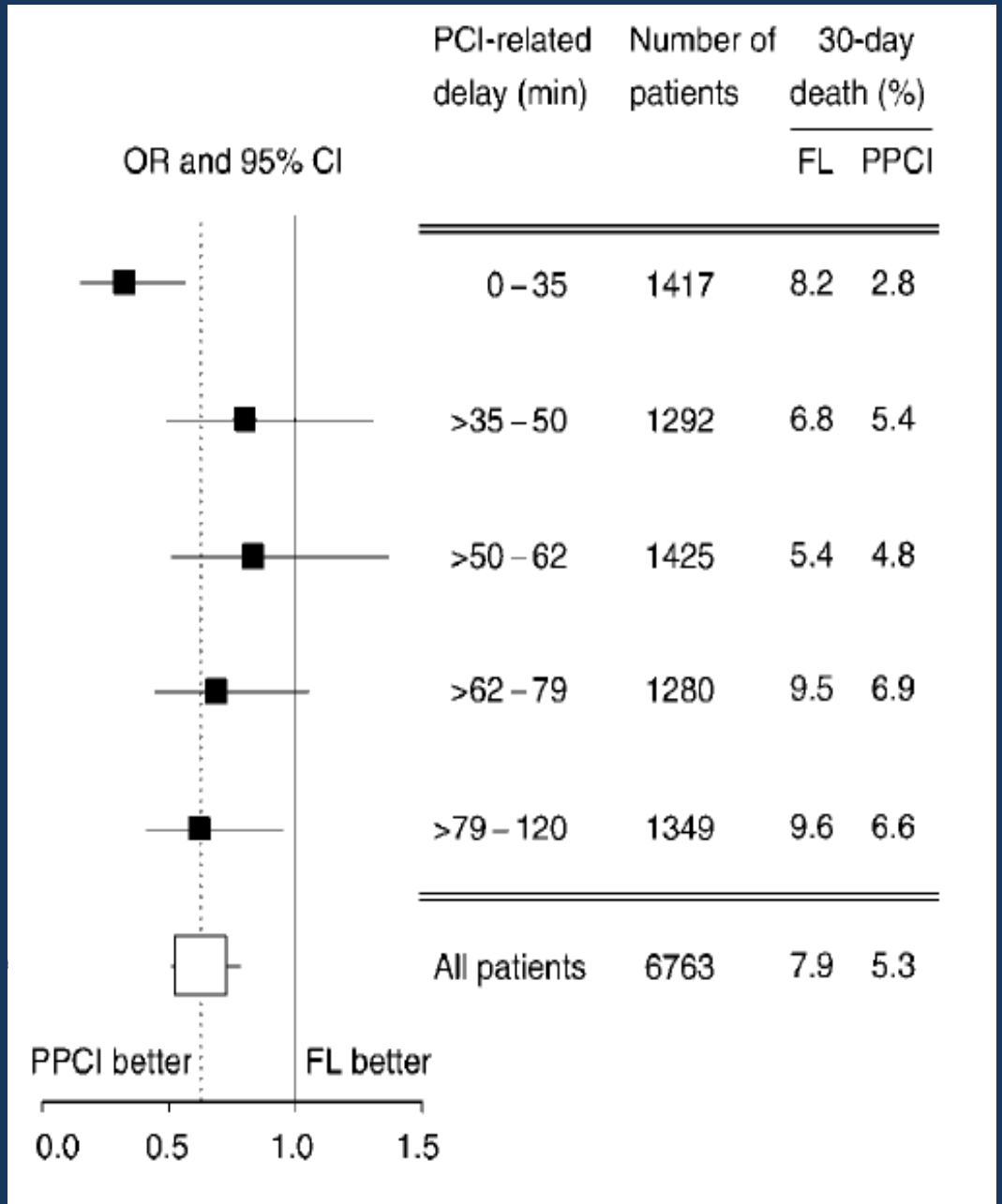


The window for primary PCI



Boersma et al, Eur Heart 2006

The window for primary PCI



The window for primary PCI

Percutaneous Coronary Intervention Versus Fibrinolytic Therapy in Acute Myocardial Infarction: Is Timing (Almost) Everything?

Brahmajee K. Nallamothu, MD, MPH, and Eric R. Bates, MD

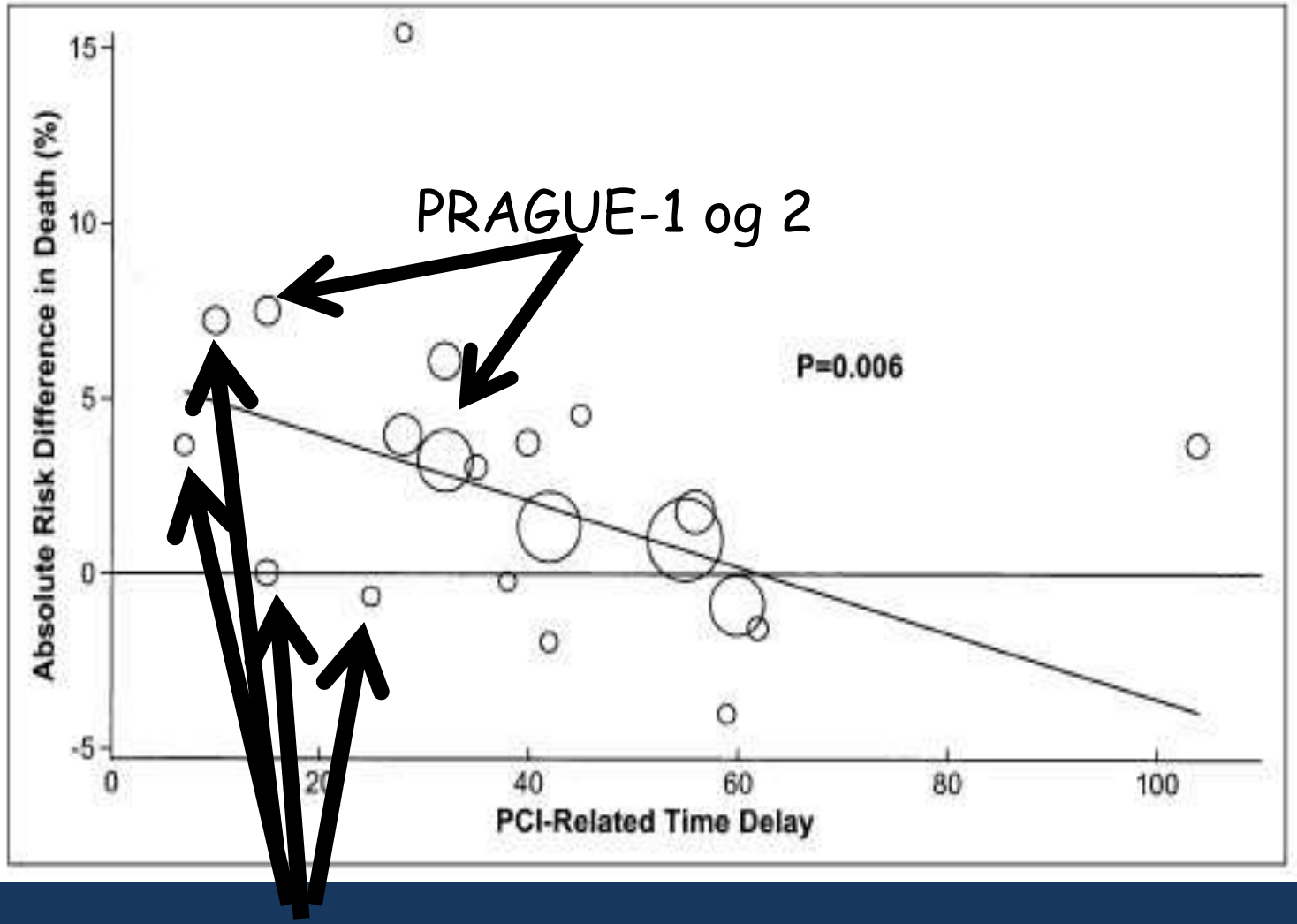
The mortality benefit associated with primary percutaneous coronary intervention in ST-segment elevation myocardial infarction may be lost if door-to-balloon time is delayed by >1 hour as compared with fibrinolytic therapy door-to-needle time. Interventional cardiology laboratories endeavoring to achieve the benefits of primary percutaneous coronary intervention seen in randomized clinical trials should aim to match their short door-to-balloon times.

(Am J Cardiol 2003;92:824–826)

in specific definitions across the studies (i.e., from admission, from randomization, and so forth) became inconsequential. We used variance-weighted linear regression[5] to assess the impact of PCI-related time delay on treatment differences for death in 21 studies and the combined end point of death, reinfarction, or stroke in 13 studies reporting this end point. To assess the influence of outlier reports, we performed multiple sensitivity analyses, individually eliminating studies with results outside of the linear regression 95% confidence intervals. Stata Version 8 (College Station, Texas) was used for all statistical analyses.

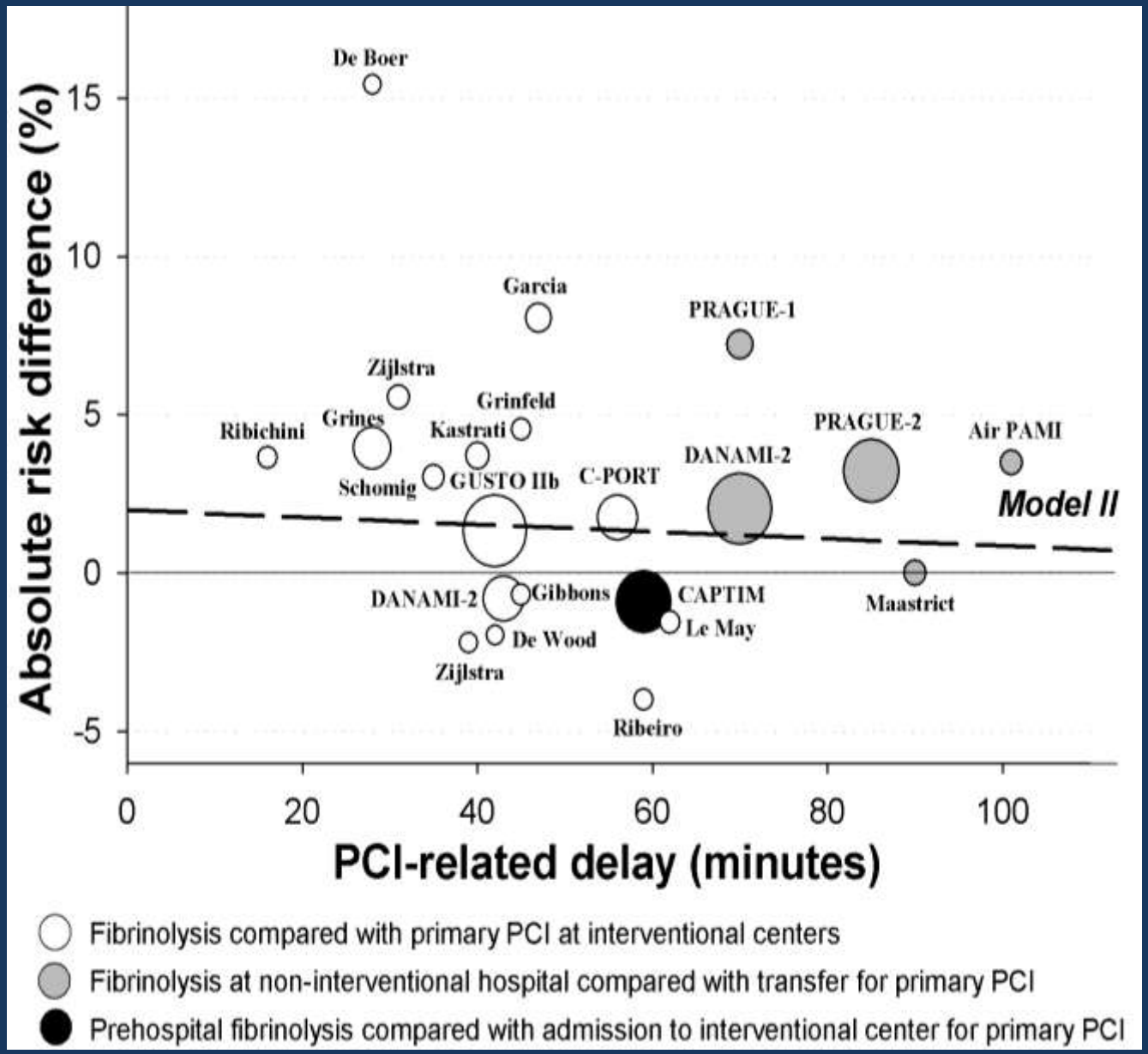
The window for primary PCI

FIGURE 1. Absolute risk reduction in 4- to 6-week mortality rates with primary PCI as a function of PCI-related time delay. *Circle* sizes reflect the sample size of the individual study. Values >0 represent benefit and values <0 represent harm. *Solid line*, weighted meta-regression.



Ribichini, Garcia, Gibbons, Maastrict

The window for primary PCI



Terkelsen CJ et al, Heart 2009

The window for primary PCI

Table 2 Results from variance-weighted linear regression analysis

Model	Trials implemented in the analyses	y-Axis intercept Absolute mortality benefit from PPCI (%)	Slope (95% CI) (%/min)	p Value	x-Axis intercept (95% CI) (min)	p Value
I	All trials	2.72	−0.023 (−0.010 to 0.051)	0.52	119 (−101 to 339)	0.27
II	All trials*	2.16	−0.013 (−0.083 to 0.058)	0.71	171 (−498 to 840)	0.60
III	Fibrin-specific trials	4.40	−0.059 (−0.136 to 0.017)	0.12	74 (39 to 109)	0.001
IV	Fibrin-specific trials*	3.30	−0.039 (−0.115 to 0.037)	0.29	86 (11 to 160)	0.028

Data arranged according to which randomised trials (comparing primary percutaneous coronary intervention (PPCI) with fibrinolysis) were implemented in the analysis and whether DANAMI-2 data were stratified into patients randomised at interventional or non-interventional hospitals (transfer patients).
*DANAMI-2 data split into transfer and non-transfer patients.

The window for primary PCI

Coronary Heart Disease

Hospital Delays in Reperfusion for ST-Elevation Myocardial Infarction

Implications When Selecting a Reperfusion Strategy

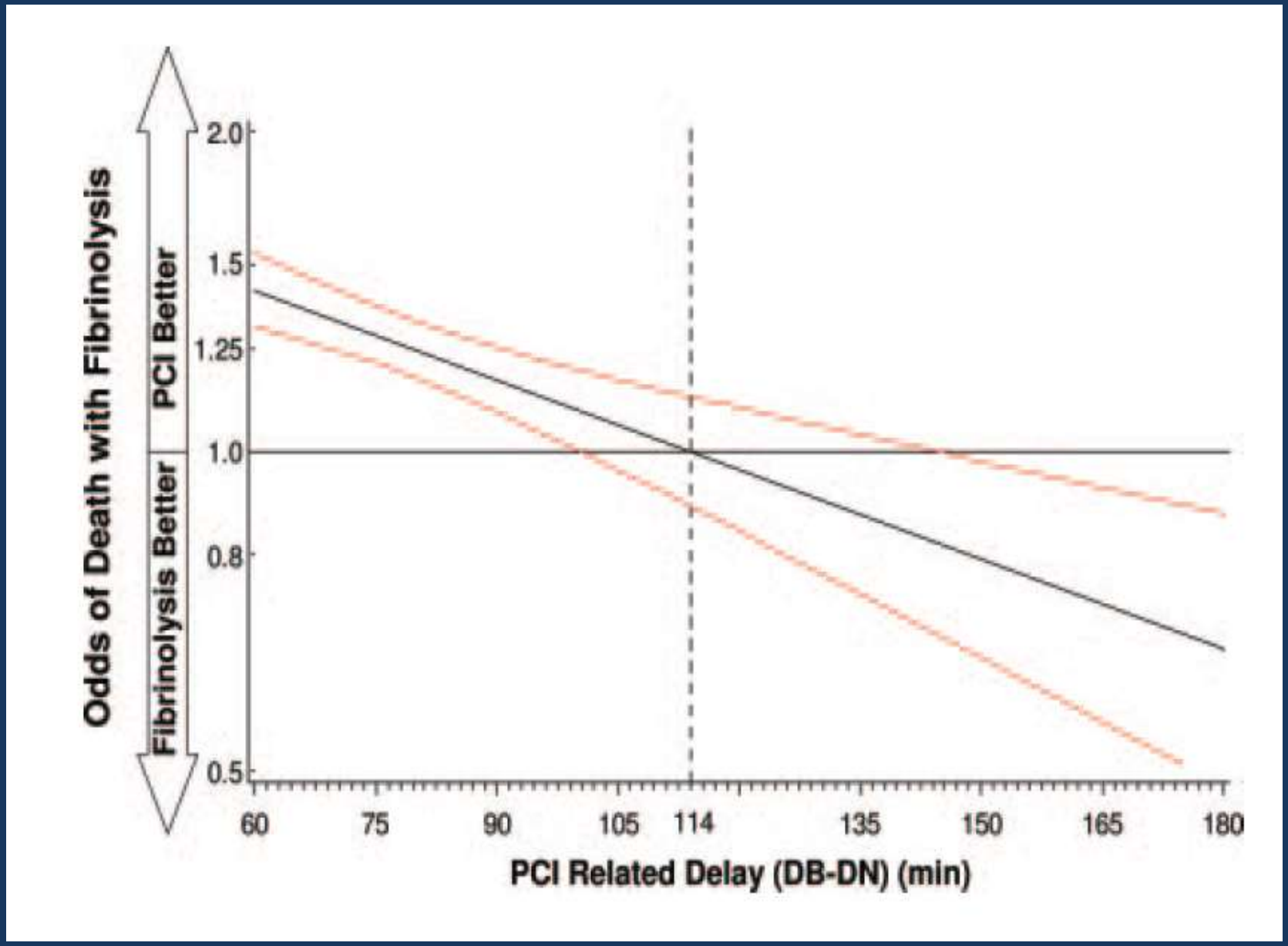
Duane S. Pinto, MD; Ajay J. Kirtane, MD, SM; Brahmajee K. Nallamothu, MD, MPH; Sabina A. Murphy, MPH; David J. Cohen, MD, MSc; Roger J. Laham, MD; Donald E. Cutlip, MD; Eric R. Bates, MD; Paul D. Frederick, MPH, MBA; Dave P. Miller, MS; Joseph P. Carrozza, Jr, MD; Elliott M. Antman, MD; Christopher P. Cannon, MD; C. Michael Gibson, MS, MD

Background—It has been suggested that the survival benefit associated with primary percutaneous coronary intervention (PPCI) in ST-segment elevation myocardial infarction may be attenuated if door-to-balloon (DB) time is delayed by >1 hour beyond door-to-needle (DN) times for fibrinolytic therapy. Whereas DB times are rapid in randomized trials, they are often prolonged in routine practice. We hypothesized that in clinical practice, longer DB-DN times would be associated with higher mortality rates and reduced PPCI survival advantage. We also hypothesized that in addition to PPCI delays, patient risk factors would significantly modulate the relative survival advantage of PPCI over fibrinolysis.

Methods and Results—DB-DN times were calculated by subtracting median DN time from median DB time at a hospital using data from 192 509 patients at 645 National Registry of Myocardial Infarction hospitals. Hierarchical models that adjusted simultaneously for both patient-level risk factors and hospital-level covariates were used to evaluate the relationship between PCI-related delay, patient risk factors, and in-hospital mortality. Longer DB-DN times were associated with increased mortality ($P<0.0001$). The DB-DN time at which mortality rates with PPCI were no better than that of fibrinolysis varied considerably depending on patient age, symptom duration, and infarct location.

Conclusions—As DB-DN times increase, the mortality advantage of PPCI over fibrinolysis declines, and this advantage varies considerably depending on patient characteristics. As indicated in the American College of Cardiology/American Heart Association guidelines, both the hospital-based PPCI-related delay (DB-DN time) and patient characteristics

The window for primary PCI



Pinto et al. Circulation

The window for primary PCI

TABLE 2. Relationship of Prehospital Delay, Age, and Infarct Location to the Loss of PCI-Related Mortality Benefit

	Symptom Duration ≤120 min	Symptom Duration >120 min	Age <65 y	Age ≥65 y	Anterior Infarction	Nonanterior Infarction
Time, min (No. of patients)*	94 (n=125 737)	190 (n=66 772)	71 (n=115 293)	155 (n=77 141)	115 (n=69 331)	112 (n=123 178)
P†	<0.001	0.01	0.001	<0.001	0.001	0.002

*Times represent PCI-related delay (DB-DN time) at which mortality with PCI and fibrinolysis were equal, stratified by symptom duration, age, or location of infarct. To ensure a stable estimate of the mortality difference when primary PCI and fibrinolysis were compared in these subgroups, hospitals were excluded if fewer than 10 STEMI patients were treated with either PCI or fibrinolysis in each category.

†*P* values for the interaction of treatment with fibrinolysis and DB-DN time.

Limitations:

1. An optimal fibrinolytic strategi (92% given fibrin-specific drugs) was compared with an inferior PPCI strategy (21 PPCIs a year per center with D2B of 116 mintues)

2. Based on voluntarily reporting of cases

3. More patients with cardiogenic shock in the PPCI group

Prior congestive heart failure, %	3.4	3.2	3.3	3.7	0.76
Prior PTCA, %	11.1	11.3	10.3	10.7	<0.001
Prior CABG, %	6.0	6.5	6.4	6.7	0.007
Systolic blood pressure (mean±SD), mm Hg	139.0±31.2	138.7±31.0	138.5±31.1	139.6±31.4	0.27
Pulse (mean±SD), bpm	76.7±20.0	77.1±19.9	77.3±19.8	77.7±20.3	<0.001
Hospital characteristics					
DB time (mean of median±SD), min	91±11.7	114±11.1	138±11.1	179±20.8	<0.001
DN time (mean of median±SD), min	41.9±8.6	38.7±8.0	37.2±7.7	37.8±8.8	<0.001
PCI-related delay (DB-DN; mean of median±SD), min	49.1±10.3	75.2±8.1	100.4±8.0	140.7±19.2	<0.001
Proportion transferred in, %	24.1	29.3	33.9	36.1	<0.001
Proportion anterior MI, %	26.2	26.4	27.1	29.6	0.004
PPCI volume per year (n±SD)	23.8±17.9	21.6±14.9	15.7±12.7	10.6±9.4	<0.001
Proportion of STEMI patients treated with PPCI, %	46.2	37.9	27.6	22.1	<0.001
STEMI volume per year (n±SD)	118±74	140±80	140±83	127±82	0.12
TIMI risk score of STEMI patients (mean±SD)	2.5±0.4	2.5±0.3	2.4±0.3	2.6±0.4	0.12

P values are for trend. CABG indicates coronary artery bypass grafting.

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The window for primary PCI

Coronary Heart Disease

Implementation of Guidelines Improves the Standard of Care

The Viennese Registry on Reperfusion Strategies in ST-Elevation Myocardial Infarction (Vienna STEMI Registry)

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Background—The purpose of this study was to determine whether implementation of recent guidelines improves in-hospital mortality from acute ST-elevation myocardial infarction (STEMI) in a metropolitan area.

Methods and Results—We organized a network that consisted of the Viennese Ambulance Systems, which is responsible for diagnosis and triage of patients with acute STEMI, and 5 high-volume interventional cardiology departments to expand the performance of primary percutaneous catheter intervention (PPCI) and to use the fastest available reperfusion strategy in STEMI of short duration (2 to 3 hours from onset of symptoms), either PPCI or thrombolytic therapy (TT; prehospital or in-hospital), respectively. Implementation of guidelines resulted in increased numbers of patients receiving 1 of the 2 reperfusion strategies (from 66% to 86.6%). Accordingly, the proportion of patients not receiving reperfusion therapy dropped from 34% to 13.4%, respectively. PPCI usage increased from 16% to almost 60%, whereas the use of TT decreased from 50.5% to 26.7% in the participating centers. As a consequence, in-hospital mortality decreased from 16% before establishment of the network to 9.5%, including patients not receiving reperfusion therapy. Whereas PPCI and TT demonstrated comparable in-hospital mortality rates when initiated within 2 to 3 hours from onset of symptoms, PPCI was more effective in acute STEMI of >3 but <12 hours' duration.

Conclusions—Implementation of recent guidelines for the treatment of acute STEMI by the organization of a cooperating network within a large metropolitan area was associated with a significant improvement in clinical outcomes. (***Circulation.*** **2006;113:2398-2405.**)

Key Words: myocardial infarction ■ percutaneous coronary intervention ■ thrombolytic therapy ■ guidelines ■ mortality

The window for primary PCI

	Patient delay <2-3 hour	Patient delay >2-3 hour
Expected delay to PPCI > 90 minutes	TT (12% PHT)	PPCI
Expected delay to PPCI < 90 minutes	PPCI	PPCI

If, however, the anticipated delay to PPCI was expected to exceed 90 minutes, patients received TT, either prehospital in the ambulance or in-hospital in the ER. Patients presenting more than 2 to 3 hours after onset of pain and those with uncertain diagnosis, high age, increased bleeding risk, and perceived contraindications against TT were treated with PPCI even if time to balloon dilation was prolonged.

The window for primary PCI

TABLE 2. Delay Times

	Delay Times, min			
	All Patients	PPCI	TT	No Treatment
Onset of pain to hospital arrival	180±156	174±150	132±120	252±222
Onset of pain to reperfusion*		258±168	120±108	
First contact/door to cath lab (arrival)		52±44		
Cath lab to balloon				
First contact/door to balloon (PPCI)				
First contact/door to needle (TT)			17±13	

Cath lab indicates catheterization laboratory. Values are mean±SD.

*Reperfusion means start of infusion of the thrombolytic agent or first balloon dilation.

PCI-related delay 138 minutes !

The window for primary PCI

8.2 % mortality

	Patient delay <3 hour	Patient delay >= 3 hour
Expected delay to PPCI > 90 minutes	TT (12% PHT)	PPCI
Expected delay to PPCI < 90 minutes	PPCI	PPCI

8.1 % mortality

The window for primary PCI

Long-term Outcome of Primary Percutaneous Coronary Intervention vs Prehospital and In-Hospital Thrombolysis for Patients With ST-Elevation Myocardial Infarction

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Context Whether the superior results of percutaneous coronary intervention (PCI) reported in clinical trials in which patients with ST-segment elevation myocardial infarction (STEMI) received reperfusion treatment can be replicated in daily practice has been questioned, especially whether it is superior to prehospital thrombolysis (PHT).

Objective To evaluate the outcome of different reperfusion strategies in consecutive STEMI patients.

Design, Setting, and Patients A prospective observational cohort study of 26 205 consecutive STEMI patients in the Register of Information and Knowledge about Swedish Heart Intensive Care Admissions (RIKS-HIA) who received reperfusion therapy within 15 hours of symptom onset. The registry includes more than 95% of all Swedish patients, of all ages, who were treated in a coronary intensive care unit between 1999 and 2004.

Interventions Seven thousand eighty-four patients underwent primary PCI; 3078, PHT; and 16 043, in-hospital thrombolysis (IHT).

Main Outcome Measures Mortality, reinfarction, and readmissions as reported in the National Health Registries through December 31, 2005.

Results After adjusting for younger age and less comorbidity, primary PCI was associated with lower mortality than IHT at 30 days (344 [4.9%] vs 1834 [11.4%]; hazard ratio [HR], 0.61; 95% confidence interval [CI], 0.53-0.71) and at 1 year (541 [7.6%] vs 2555 [15.9%]; HR, 0.68; 95% CI, 0.60-0.76). Also primary PCI correlated with lower mortality than PHT at 30 days (344 [4.9%] vs 234 [7.6%]; HR, 0.70; 95% CI, 0.58-0.85) and 1 year (541 [7.6%] vs 317 [10.3%]; HR, 0.81; 95% CI, 0.69-0.94). Prehospital thrombolysis predicted a lower mortality than IHT at 30 days (HR, 0.87; 95% CI, 0.76-1.01) and at 1 year (HR, 0.84; CI 0.74-0.95). Beyond 2

SINCE THE LATE 1980S ACUTE REPerfusion with fibrinolytic drugs has been the primary treatment in ST-segment elevation myocardial infarction (STEMI). However, primary percutaneous coronary intervention (PCI) is associated with higher rates of reperfusion and lower risks of reocclusion and reinfarction.[1-3] The initial series of randomized trials comparing primary PCI with in-hospital thrombolytic therapy showed no consistent differences in long-term mortality.[4] However, after additional trials[5,6] several recent meta-analyses[3,7] now provide evidence of improved survival. Still it has been ques-

The window for primary PCI

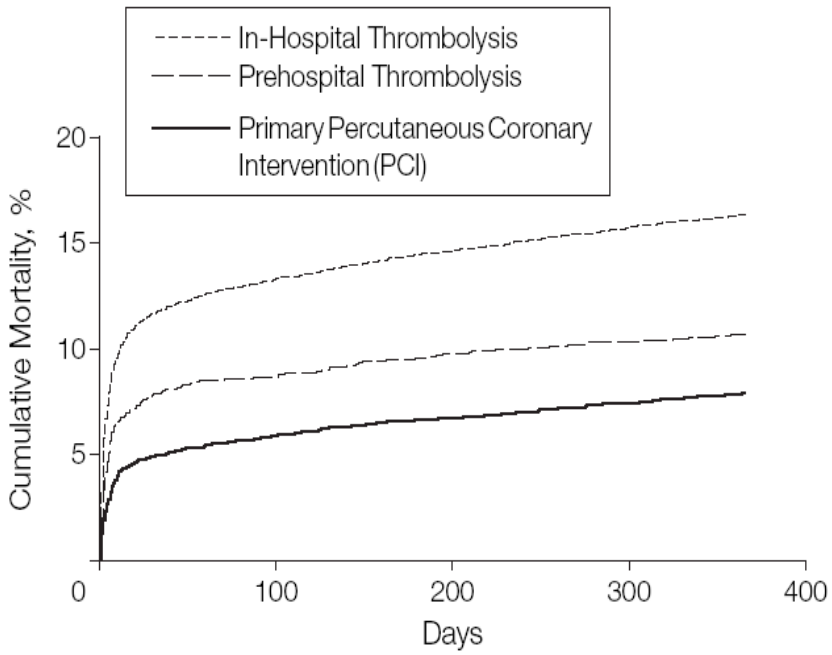
	In-Hospital Thrombolysis (n = 16 043)	Prehospital Thrombolysis (n = 3078)	Primary PCI (n = 7084)
Delay symptom to reperfusion start, median (IQR), h:min			
All	2:47 (1:47-4:37)	2:00 (1:12-3:40)	3:30 (2:15-5:34)

PCI-related delay
90 minutes

Stenestrand U et al, JAMA 2006

The window for primary PCI

Figure 2. Unadjusted Cumulative Mortality During the First Year After the Index Event Admission



No. at Risk				
Thrombolysis				
In-Hospital	14 260	12 322	12 100	11 931
Prehospital	2736	2491	2460	2442
Primary PCI	6030	5661	5607	5555

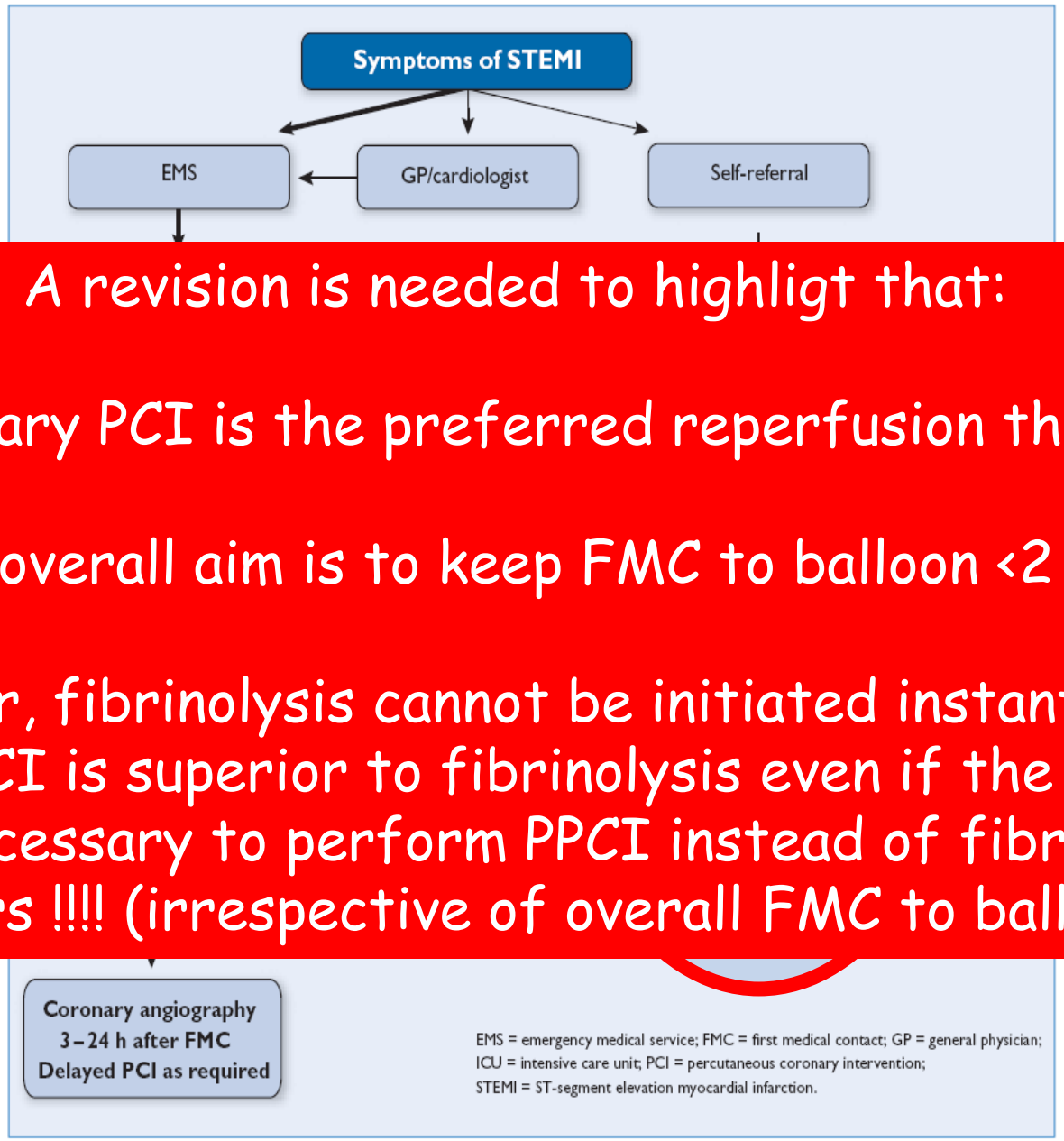
Unadjusted mortality (Kaplan-Meier) first year after index admission for the 26 205 patients with ST-segment elevation myocardial infarction receiving reperfusion therapy between 1999-2004.

Stenestrand U et al, JAMA 2006

The window for primary PCI

bolysis. Therefore, if available, primary PCI today is the treatment of choice for STEMI. Only if delivered within 2 hours of onset of symptoms in areas with more than 4 hours' transportation time to a PCI procedure, PHT might offer a comparable alternative.

Stenestrand U et al, JAMA 2006



A revision is needed to highligt that:

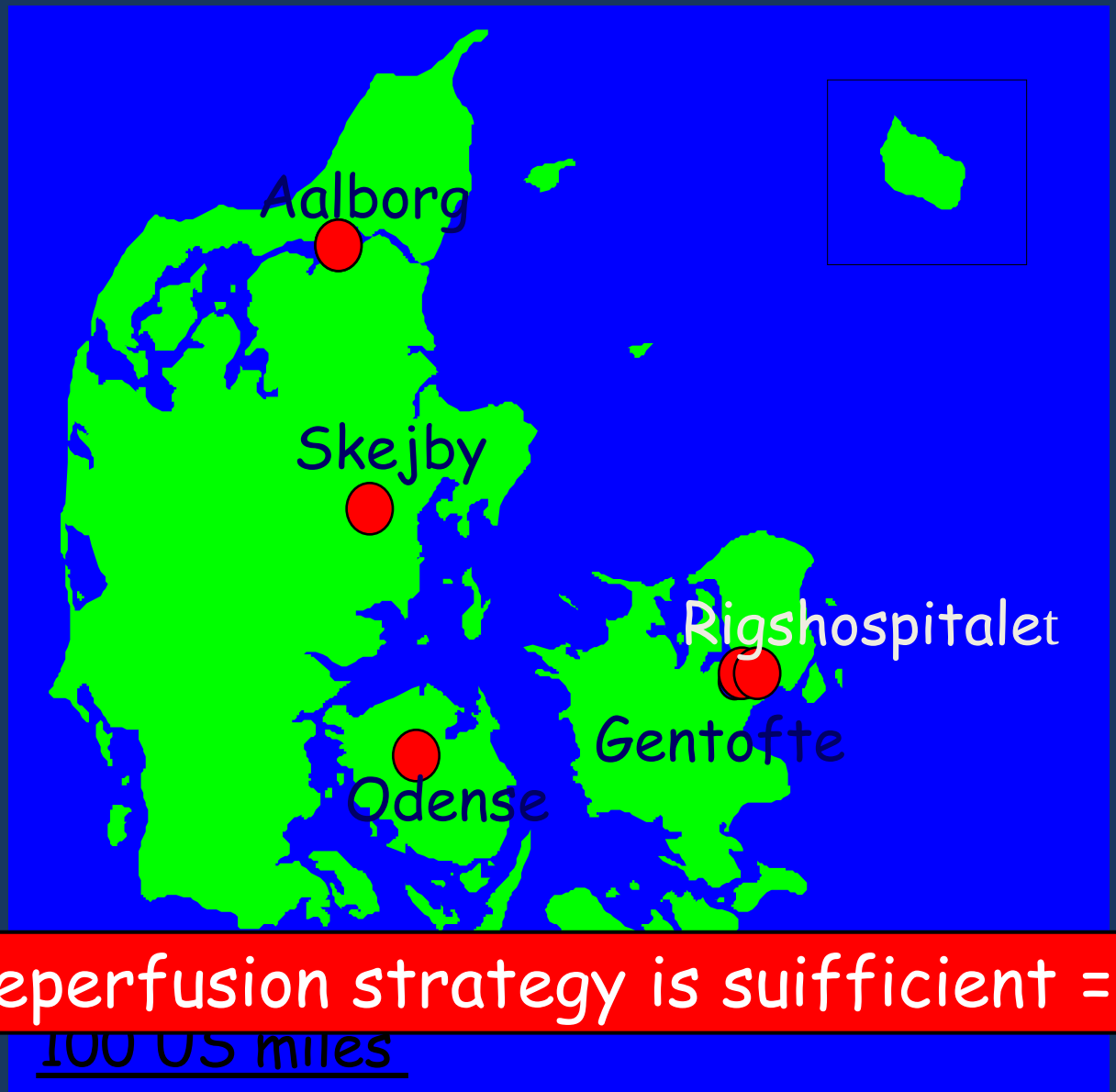
1. Primary PCI is the preferred reperfusion therapy

2. The overall aim is to keep FMC to balloon <2 hours

3. However, fibrinolysis cannot be initiated instantaneously and PPCI is superior to fibrinolysis even if the extra delay necessary to perform PPCI instead of fibrinolysis is 2-3 hours !!!! (irrespective of overall FMC to balloon time)

Figure 1 Organization of ST-segment elevation myocardial infarction patient pathway describing pre- and in-hospital management and reperfusion strategies within 12 h of first medical contact.

DENMARK: 5.4 million inhabitants



One reperfusion strategy is suifficient = PPCI

Thank You

Background: Benefit of earlier fibrinolysis

Mortality and Prehospital Thrombolysis for Acute Myocardial Infarction

A Meta-analysis

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Context Early administration of thrombolysis for acute myocardial infarction (AMI) may improve survival if safely and appropriately delivered. No systematic reviews that have comprehensively examined this topic exist in the literature.

Objective To perform a meta-analysis of randomized controlled trials of prehospital vs in-hospital thrombolysis for AMI measuring in-hospital mortality.

Data Sources The Cochrane search strategy was used to search MEDLINE, EMBASE, and the Science Citation Index (1982-1999); Dissertation Abstracts (1987-1999); and Current Contents (1994-1999) for the terms *thrombolysis*, *thrombolysis therapy*, *pre-*

CARDIOVASCULAR DISEASE RE-

spite these efforts, the time to thrombolysis, or "time to needle," remains high.

One way to address this is to administer thrombolysis before the patient arrives in hospital. The National Heart Attack Alert Program concluded in 1997 that prehospital thrombolysis reduces mortality in a subgroup of patients who require long out-of-hospital transport times (>1 hour) to an emergency department.[3] Accordingly, many North

by 2 other coauthors, blinded to the author, title, journal, introduction, and discussion.

Data Synthesis The results of the 6 randomized trials (n=6434) were pooled and indicated significantly decreased all-cause hospital mortality among patients treated with prehospital thrombolysis compared with in-hospital thrombolysis (odds ratio, 0.83; 95% confidence interval, 0.70-0.98). Results were similar regardless of trial quality or training and experience of the provider. Estimated (SE) time to thrombolysis was 104 (7) minutes for the prehospital group and 162 (16) minutes for the in-hospital thrombolysis group (P=.007).

Conclusions Our meta-analysis suggests that prehospital thrombolysis for AMI significantly decreases the time to thrombolysis and all-cause hospital mortality.

JAMA. 2000;283:2686-2692 www.jama.com

Pre-hospital fibrinolysis was associated with 1 hour earlier reperfusion therapy, and 17-21 extra lives saved per 1000 treated

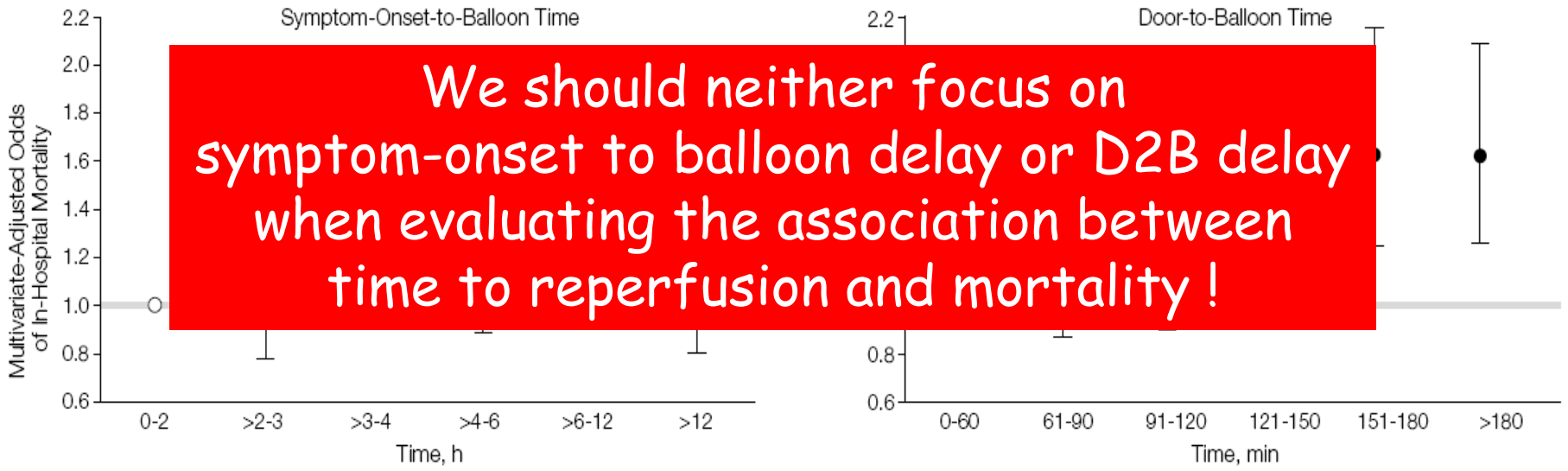
Morrison et al, JAMA 2000
Boersma E et al, Lancet 1996

Background: Benefit of earlier PPCI

Relationship of Symptom-Onset-to-Balloon Time and Door-to-Balloon Time With Mortality in Patients Undergoing Angioplasty for Acute Myocardial Infarction

Cannon et al, JAMA 2000

Background: Benefit of earlier PPCI



No. of Patients	2176	6353	5718	5852	4680	2301
Multivariate OR	1.0	0.99	1.17	1.13	1.19	1.07
95% CI		0.77-1.27	0.91-1.50	0.88-1.45	0.92-1.54	0.80-1.44
P Value		.95	.21	.35	.17	.65

No. of Patients	2230	5734	6616	4461	2627	5412
Multivariate OR	1.0	1.14	1.15	1.41	1.62	1.61
95% CI		0.87-1.48	0.89-1.49	1.08-1.84	1.23-2.14	1.25-2.08
P Value		.35	.29	.01	<.001	<.001

We should neither focus on symptom-onset to balloon delay or D2B delay when evaluating the association between time to reperfusion and mortality !

Conclusion: Monitor D2B time and reduce it to <2 hours !

Cannon CP, JAMA 2000

Background: Various delays

Door-to-balloon delay not ideal because:

1. It only comprise a minor part of the time from FMC to PCI
   D2B delay constitute 30% of FMC to PCI in Denmark

2. Long system delay can be associated with short D2B in transfer patients
   More time to activate the cath. lab. in transfer patients

3. Does not consider the prehospital phase

The window for primary PCI

Impact of Time to Treatment on Mortality After Prehospital Fibrinolysis or Primary Angioplasty

Data From the CAPTIM Randomized Clinical Trial

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Background—CAPTIM was a randomized trial comparing prehospital thrombolysis with transfer to an interventional facility (and, if needed, percutaneous intervention) with primary percutaneous coronary intervention (PCI) in patients with ST-segment–elevation myocardial infarction (STEMI). Because the benefit of thrombolysis is maximal during the first 2 hours after symptom onset, and because prehospital thrombolysis can be implemented earlier than PCI, this analysis studied the relationship between the effect of assigned treatment and the time elapsed from symptom onset.

Methods and Results—Randomization within 2 hours (n=460) or ≥2 hours (n=374) after symptom onset had no impact on the effect of treatment on the 30-day combined primary end point of death, nonfatal reinfarction, and disabling stroke. However, patients randomized <2 hours after symptom onset had a strong trend toward lower 30-day mortality with prehospital thrombolysis compared with those randomized to primary PCI (2.2% versus 5.7%, $P=0.058$), whereas mortality was similar in patients randomized ≥2 hours (5.9% versus 3.7%, $P=0.47$). There was a significant interaction between treatment effect and delay with respect to 30-day mortality (hazard ratio 4.19, 95% CI 1.033 to 17.004, $P=0.045$). Among patients randomized in the first 2 hours, cardiogenic shock was less frequent with lytic therapy than with primary PCI (1.3% versus 5.3%, $P=0.032$), whereas rates were similar in patients randomized later.

Conclusions—Time from symptom onset should be considered when one selects reperfusion therapy in STEMI. Prehospital thrombolysis may be preferable to primary PCI for patients treated within the first 2 hours after symptom onset. **(*Circulation*. 2003;108:2851-2856.)**

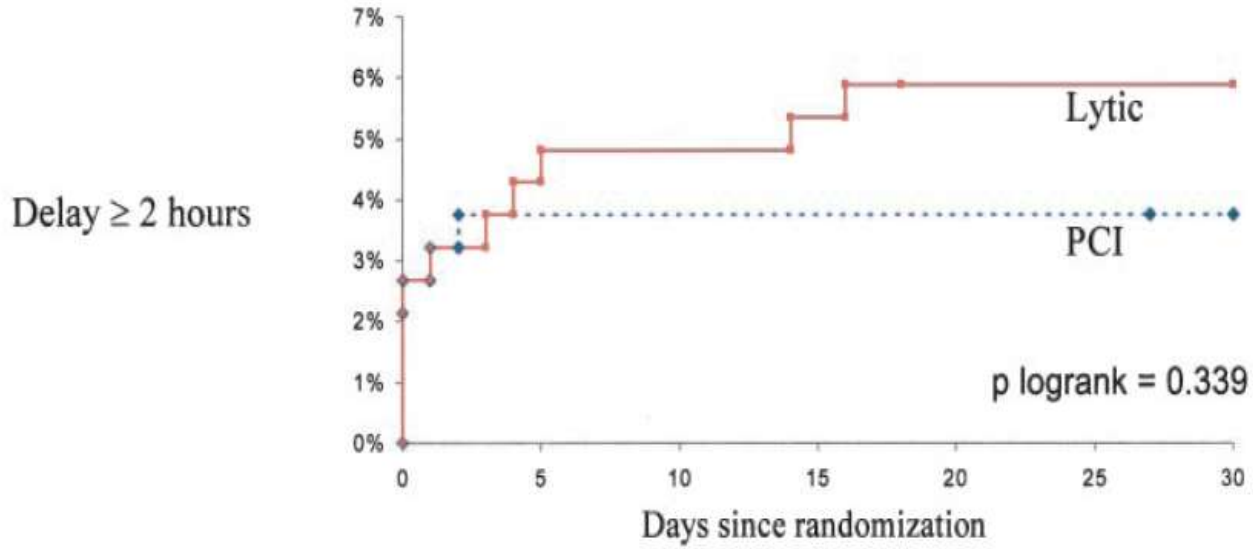
Key Words: angioplasty ■ myocardial infarction ■ reperfusion ■ thrombolysis

The window for primary PCI

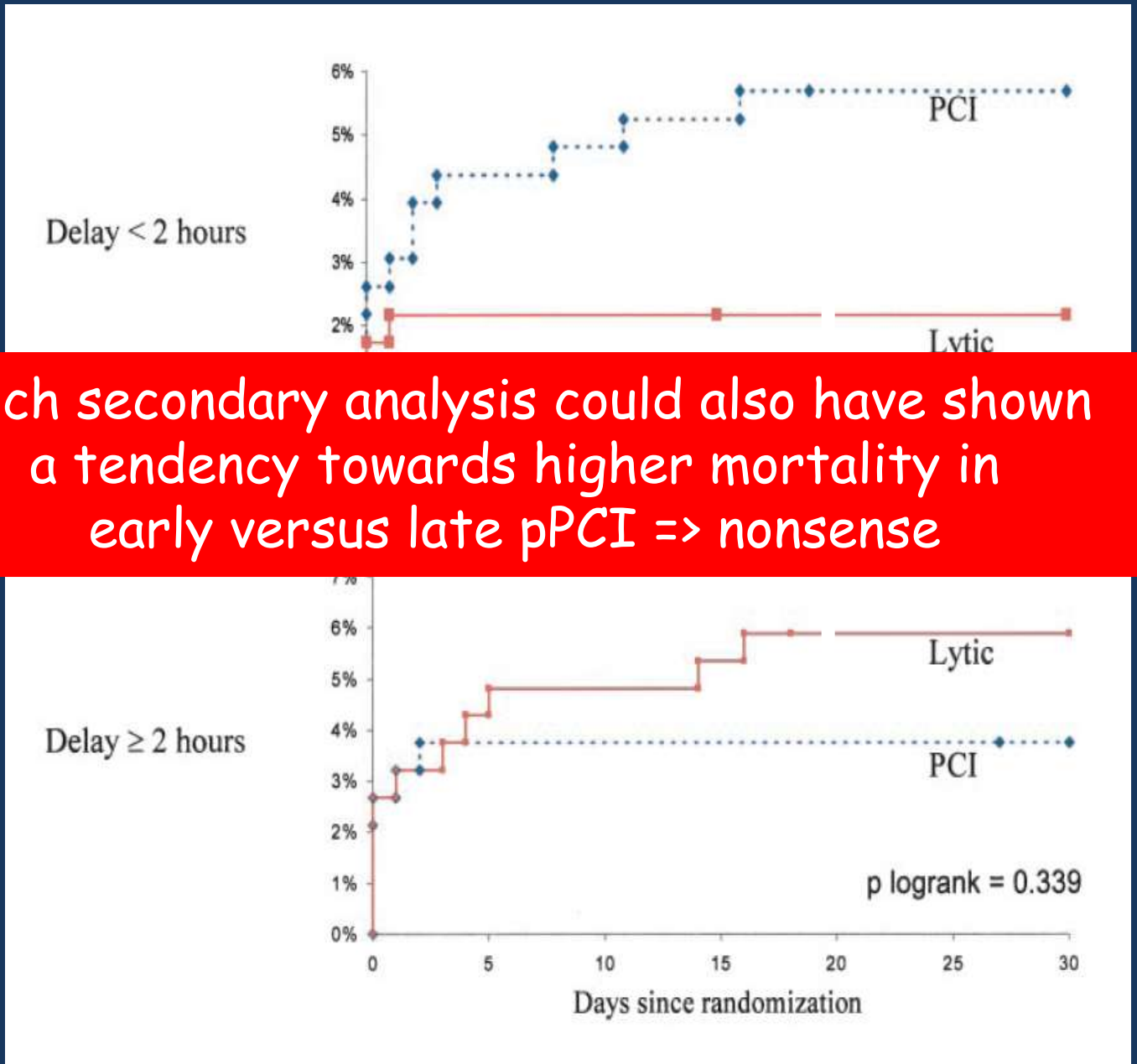
Not prespecified purpose !!!

Main study neutral !!!

Main study terminated before planned
=> power problem !



The window for primary PCI



Such secondary analysis could also have shown a tendency towards higher mortality in early versus late pPCI => nonsense