MÉDECINE SORBONNE UNIVERSITÉ

There is still a place for thrombolysis in myocardial infarction - CON.

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COI: Dr Collet has nothing to declare with respect to this presentation (action-coeur.org).

The Goal

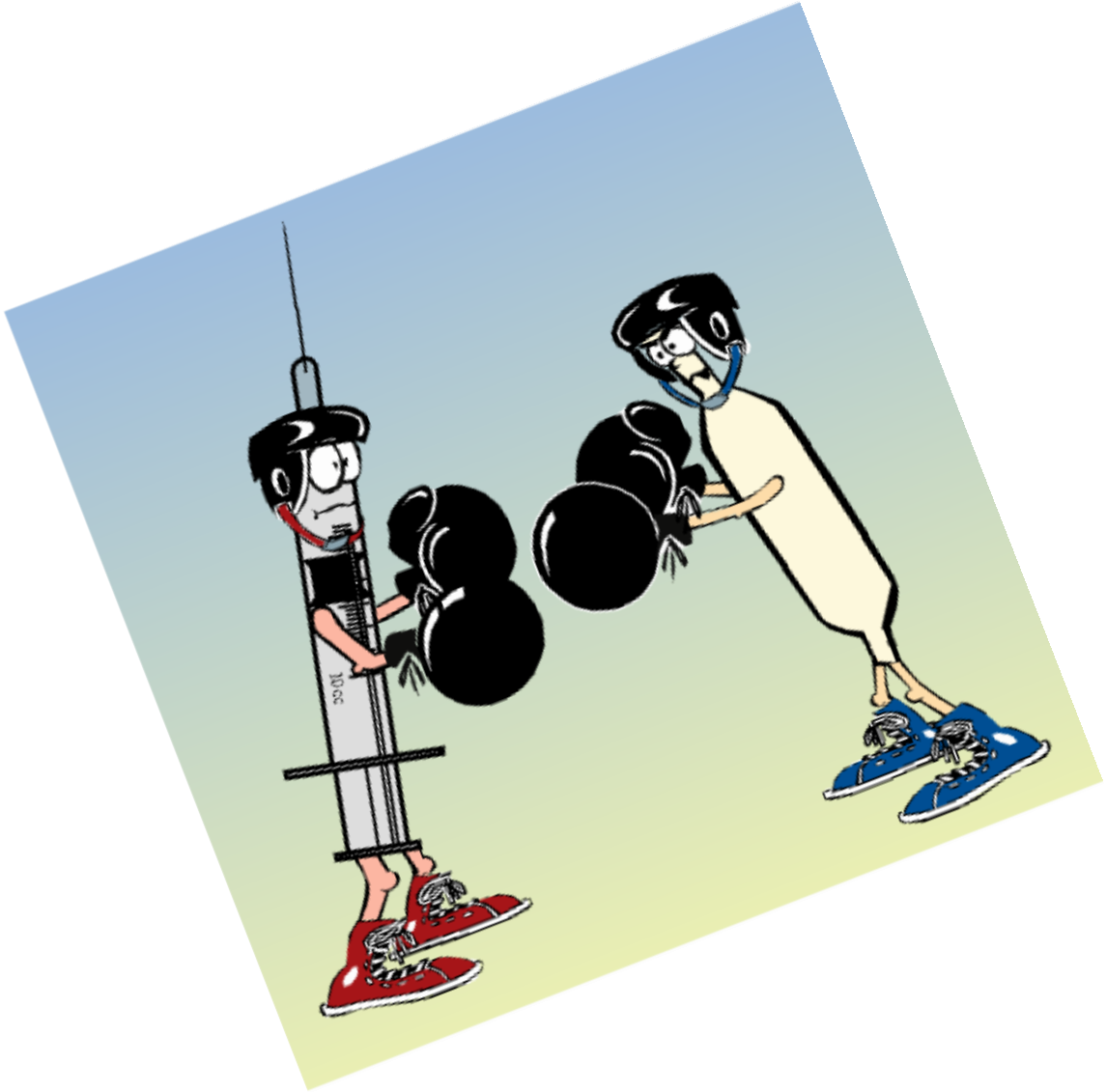
Coronary recanalisation

Myocardial reperfusion

Reduce myocardial necrosis

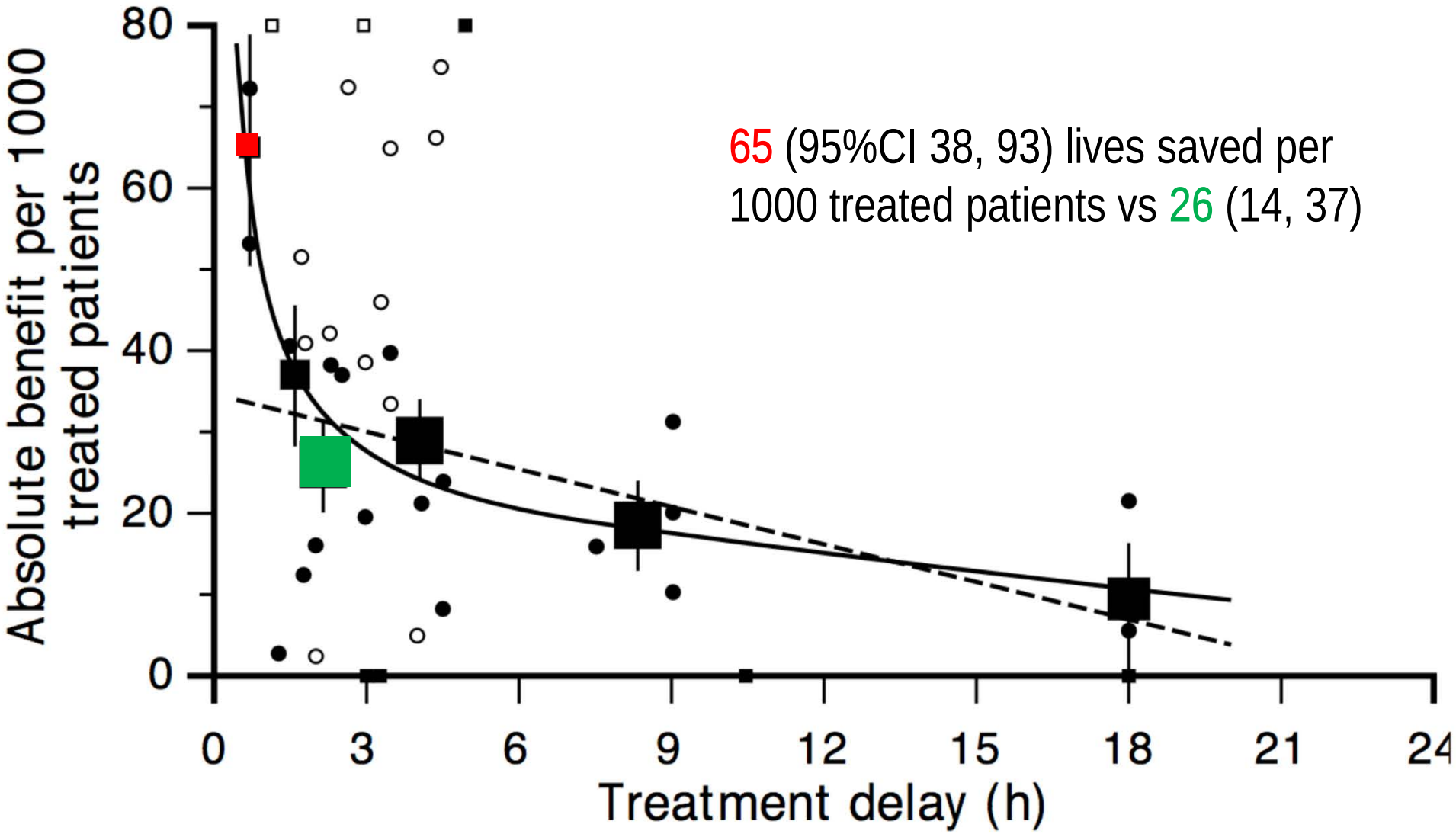
LV function preservation

Mortality reduction


10 cc

The « lytic » era

Mortality reduction by treatment delay
(N=50.246)



65 (95%CI 38, 93) lives saved per 1000 treated patients vs 26 (14, 37)

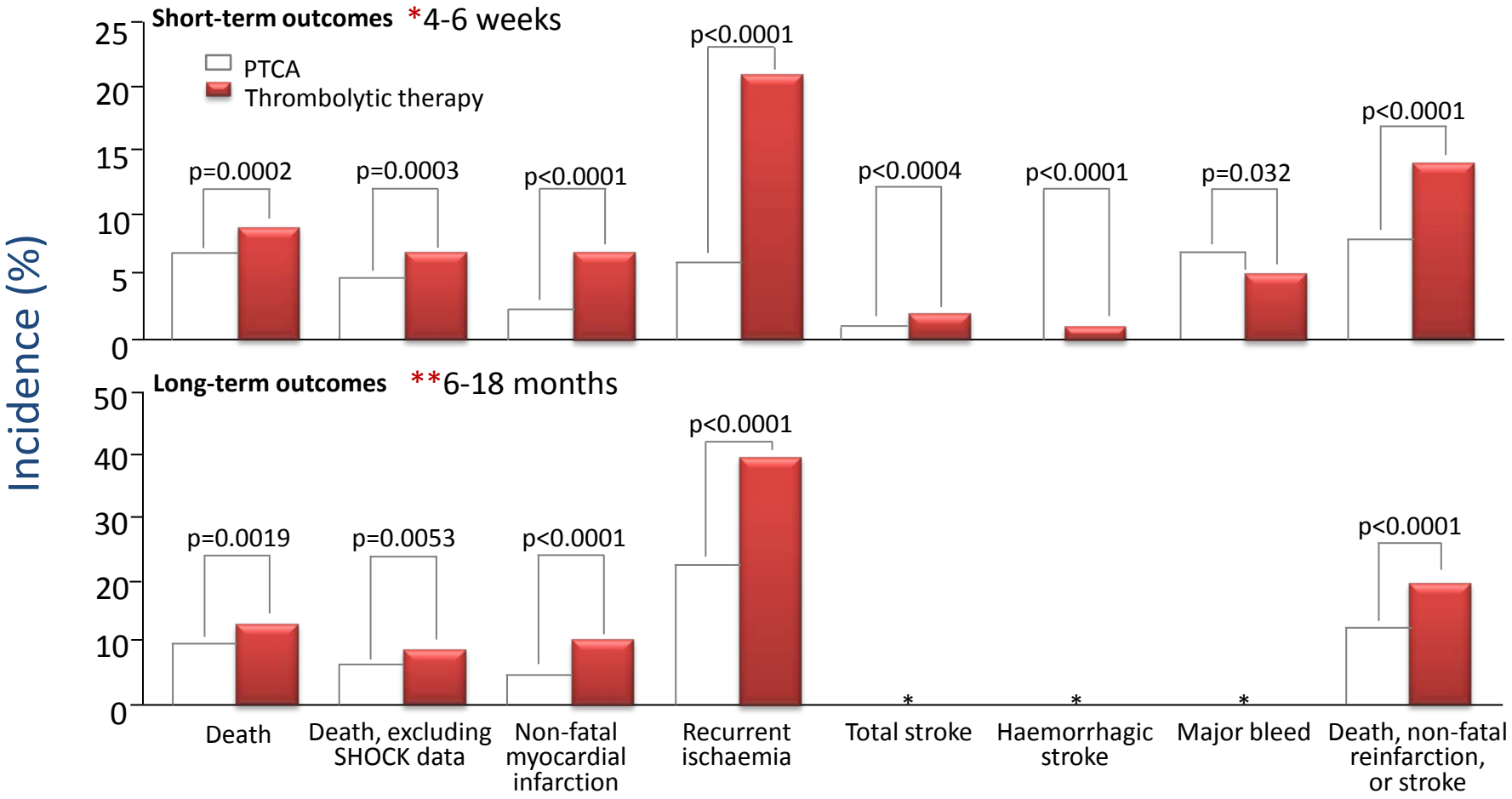
Boersma, *Lancet*, 1996

The « percutaneous » era

Primary PCI is better than fibrinolysis

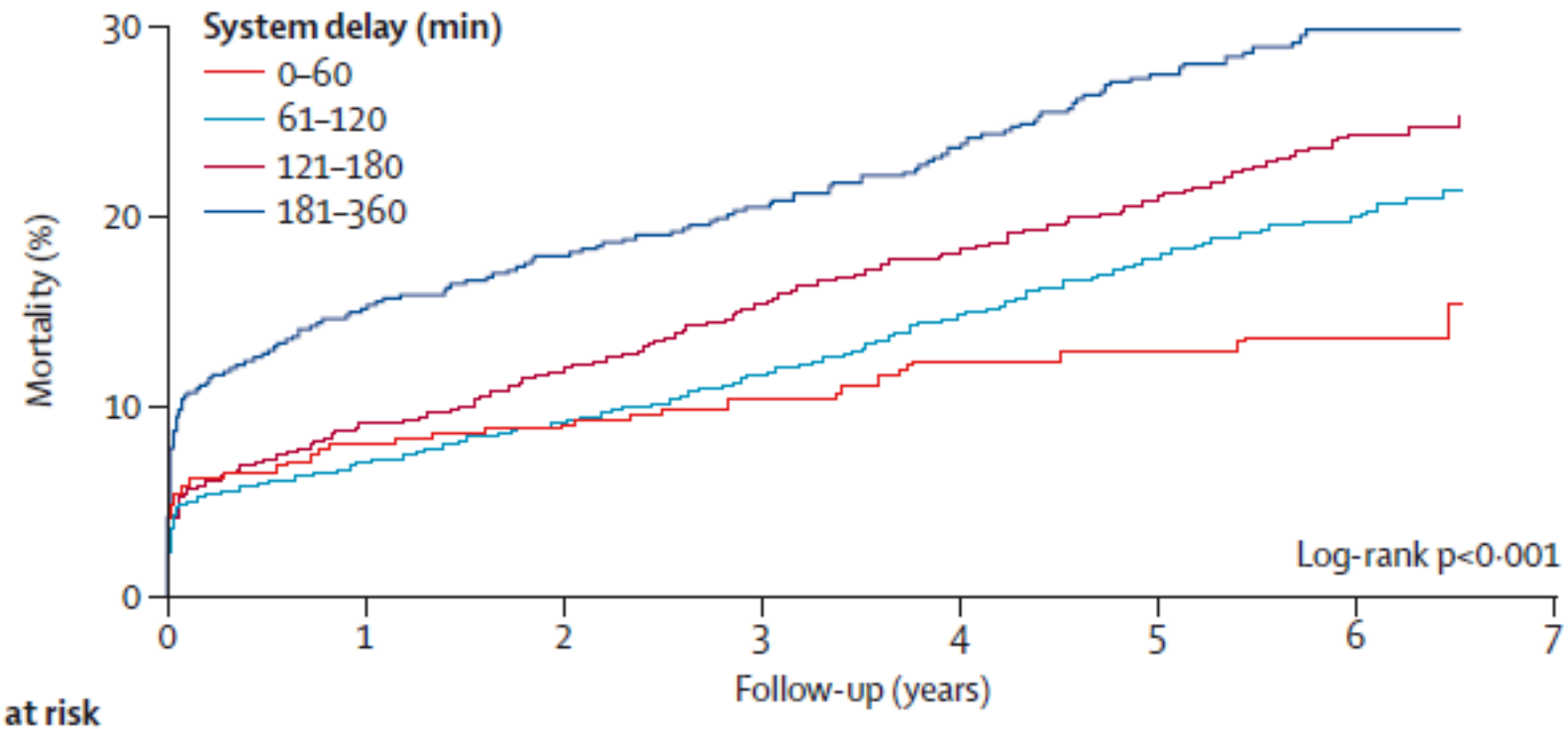
Pooled analysis of 23 randomized clinical trials

- N = 7739 thrombolytic-eligible patients with STEMI
- PPCI (n=3872) or thrombolytic therapy (n=3867)



Keeley EC et al. *Lancet* 2003;361:13-20

Health-care-system delays* and long-term mortality



Number at risk

System delay (min)							
0–60	347	311	278	230	192	138	87
61–120	2643	2339	1906	1420	1006	667	375
121–180	2092	1836	1503	1183	842	533	278
181–360	1127	923	765	647	491	332	172

has the strongest association with long-term mortality among modifiable acute-phase covariates:
HR of 1·22 (p<0·001) per 1 h increase in system delay.

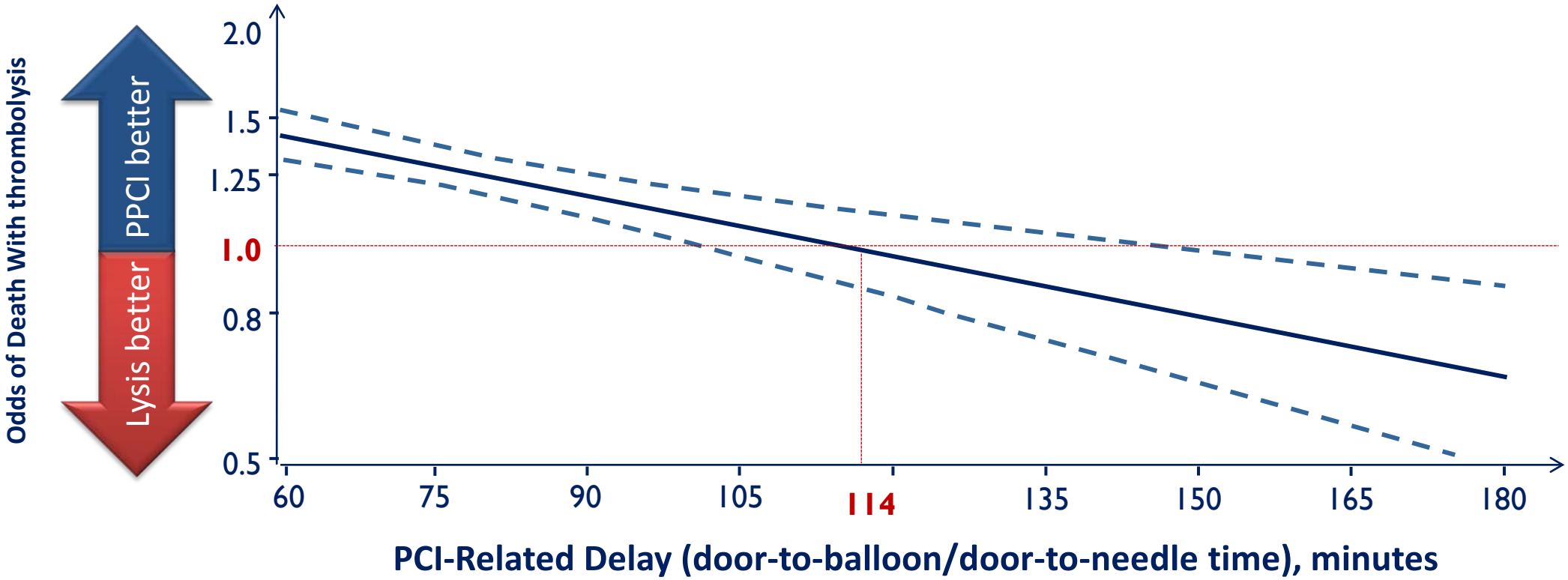
JAMA 2010; **304:** 763–71

*time from first medical contact to **primary percutaneous coronary intervention**

Summary

In observational studies, as D2B– D2N* times increase, the advantage of PPCI over fibrinolysis declines…

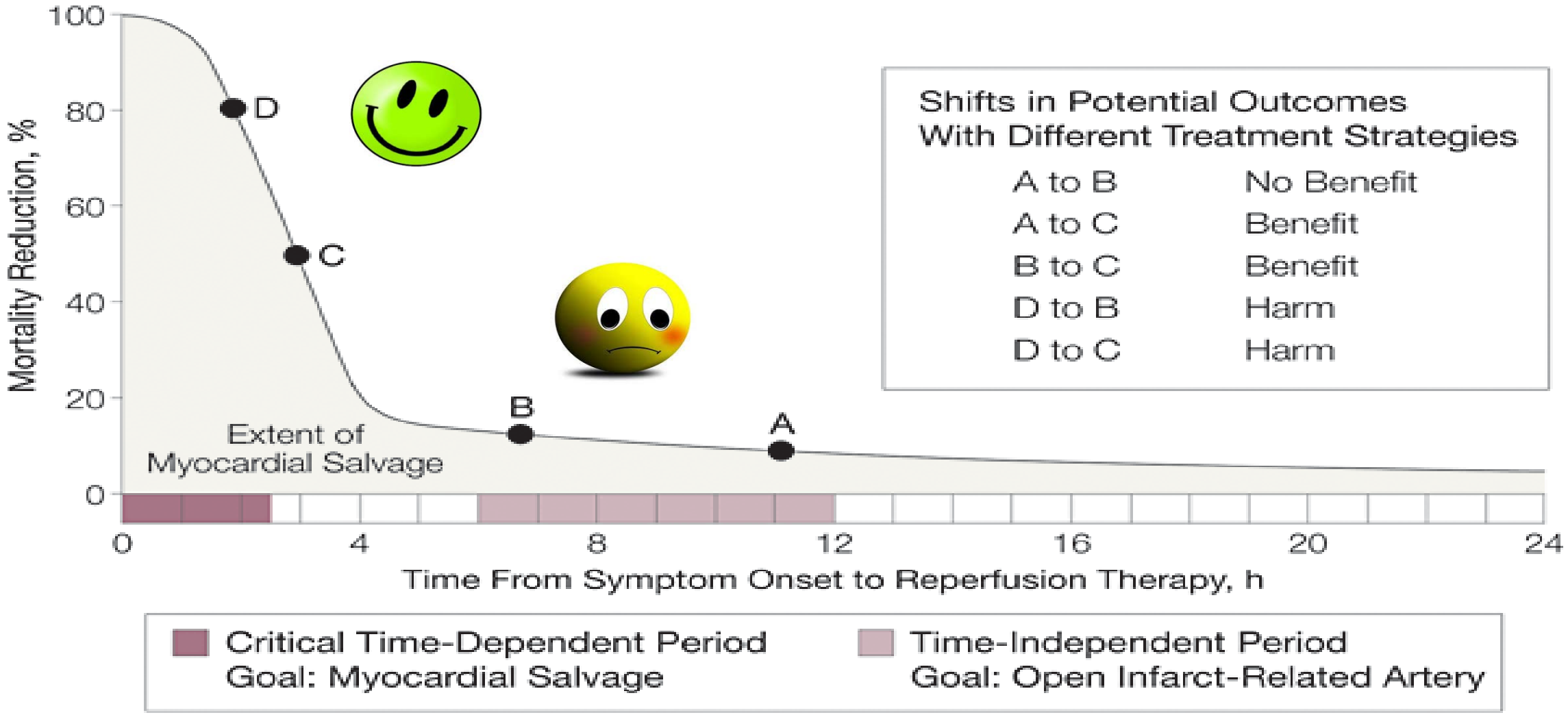
- N =**192,509** patients / **645** hospitals
- Odds of death for **thrombolysis** versus **PPCI** according to time



* D2B door-to-balloon / D2N door-to-needle

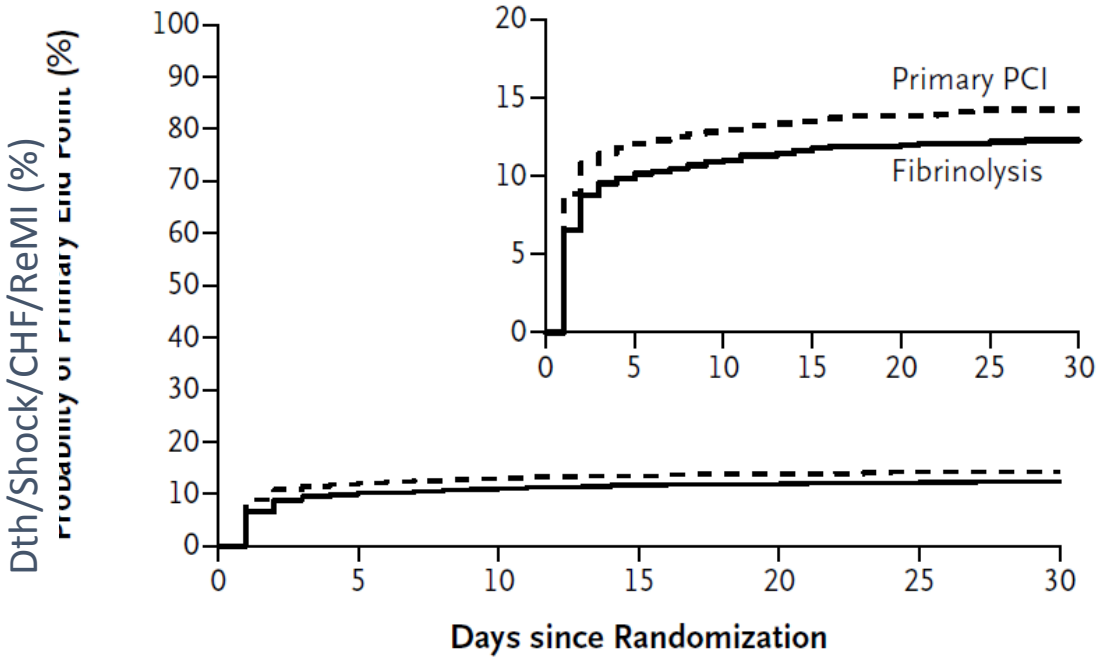
Pinto DS et al. *Circulation* 2006;114:2019-25

The sooner is the better

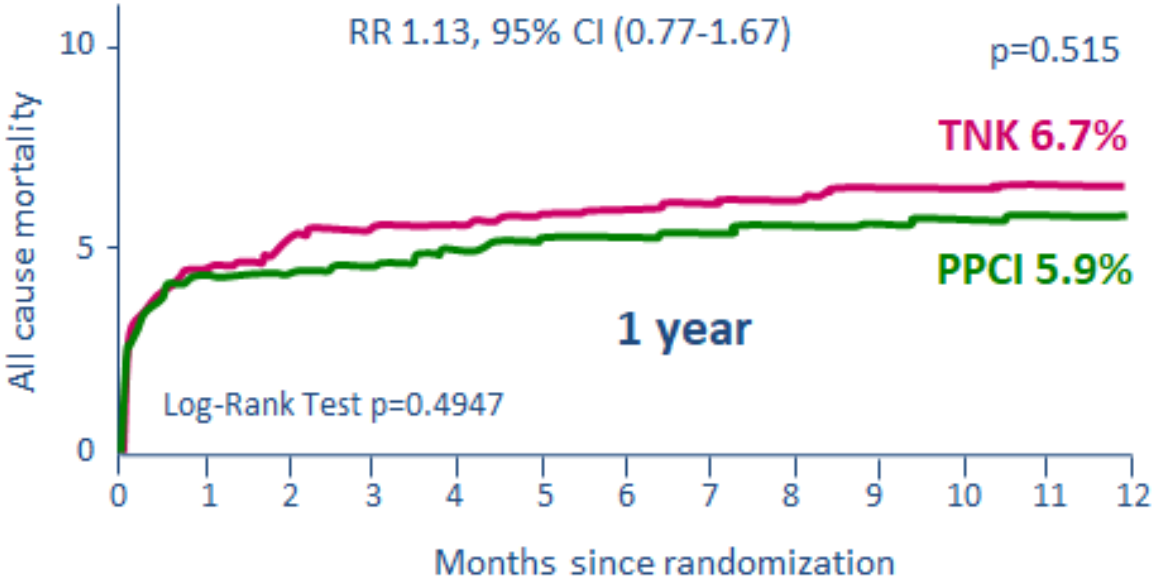


Gersh, B. J. et al. JAMA 2005;293:979-986.

The pharmaco-invasive approach



No. at Risk							
Fibrinolysis	943	848	837	829	827	825	823
Primary PCI	948	836	824	818	815	811	811



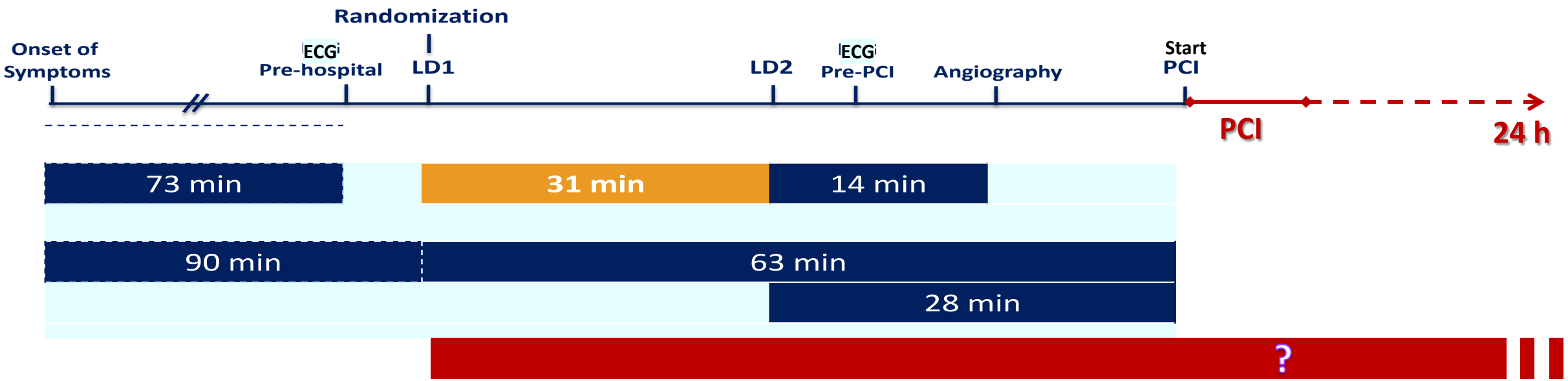
Bleedings	Fibrinolysis (N=944)	PPCI (N=948)	P Value
ICH			
Any	9/939 (1.0)	2/946 (0.2)	0.04
After protocol amendment*	4/747 (0.5)	2/758 (0.3)	0.45
Nonintracranial bleeding			
Major	61/939 (6.5)	45/944 (4.8)	0.11
Minor	205/939 (21.8)	191/944 (20.2)	0.40

* On August 24, 2009, the study protocol was amended to reduce the dose of TNK by 50% in patients 75 years of age or older because of an excess of intracranial hemorrhage in this age group.

Armstrong PW et al. *N Engl J Med* 2013;368(15):1379-87
P Sinnaeve AHA 2013

Whay PCI is better?

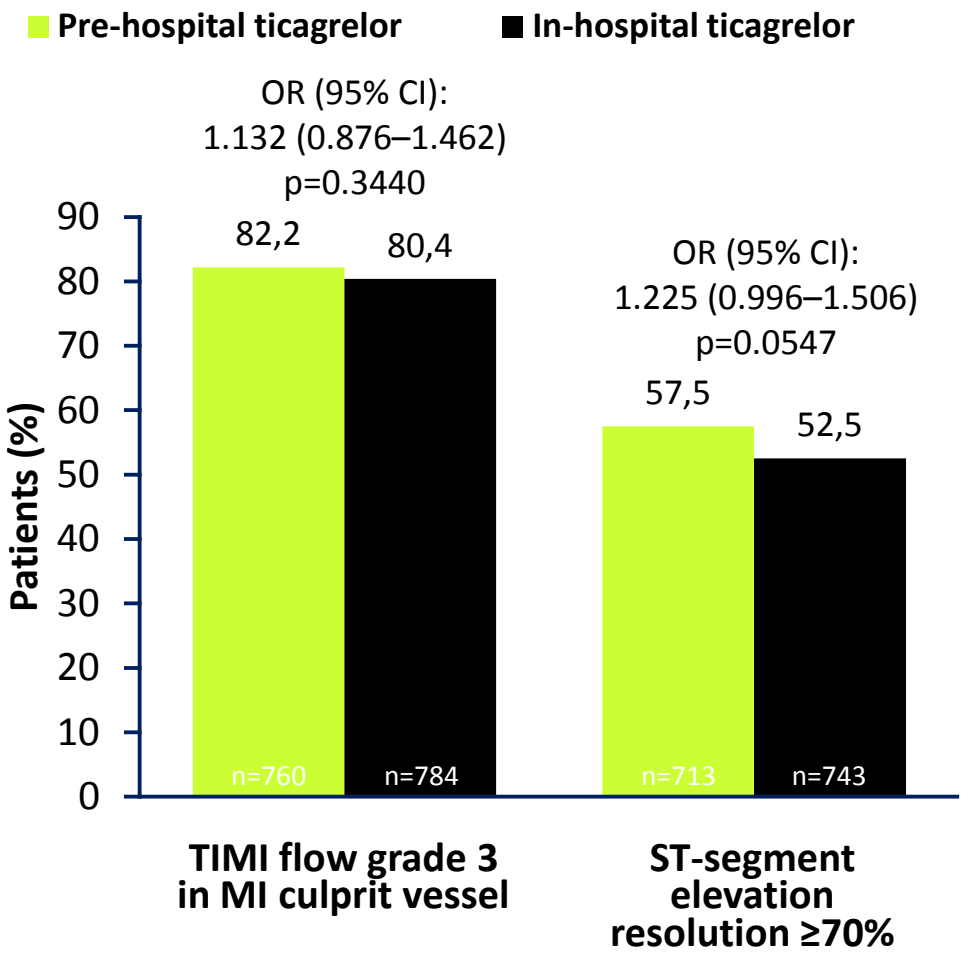
ATLANTIC_24h

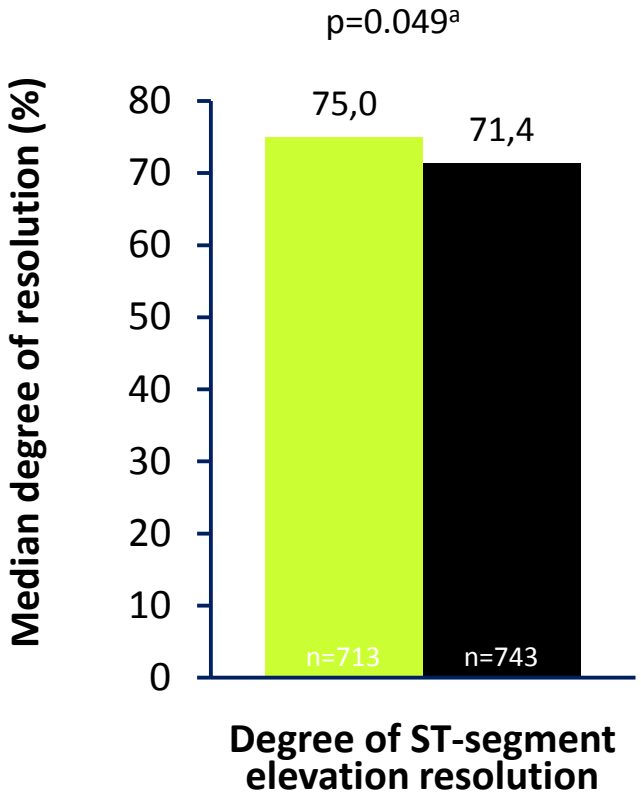


Aim

- The aim of the exploratory ATLANTIC-H24 study was to examine more closely the effects of pre- versus in-hospital ticagrelor on reperfusion, platelet function and clinical endpoints during the first **24 h after primary PCI**. The statistical analysis is exploratory.

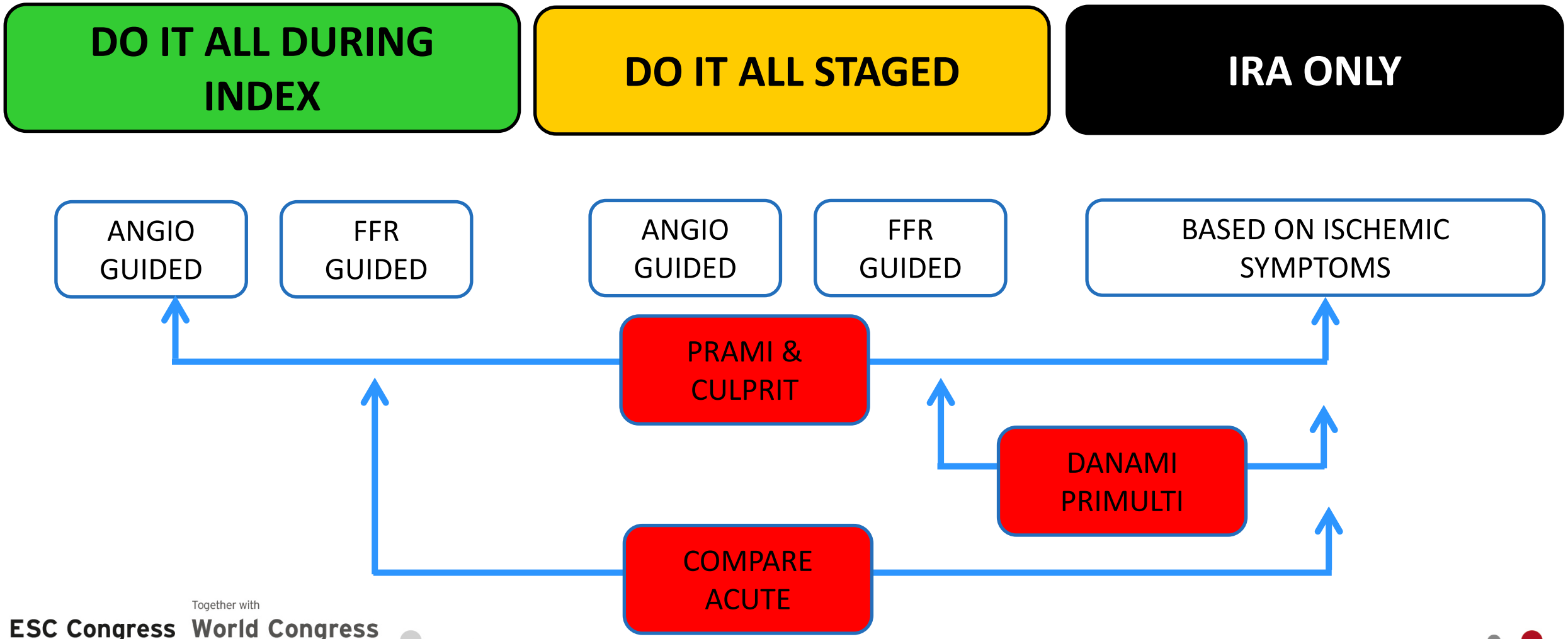
Post-PCI coronary reperfusion



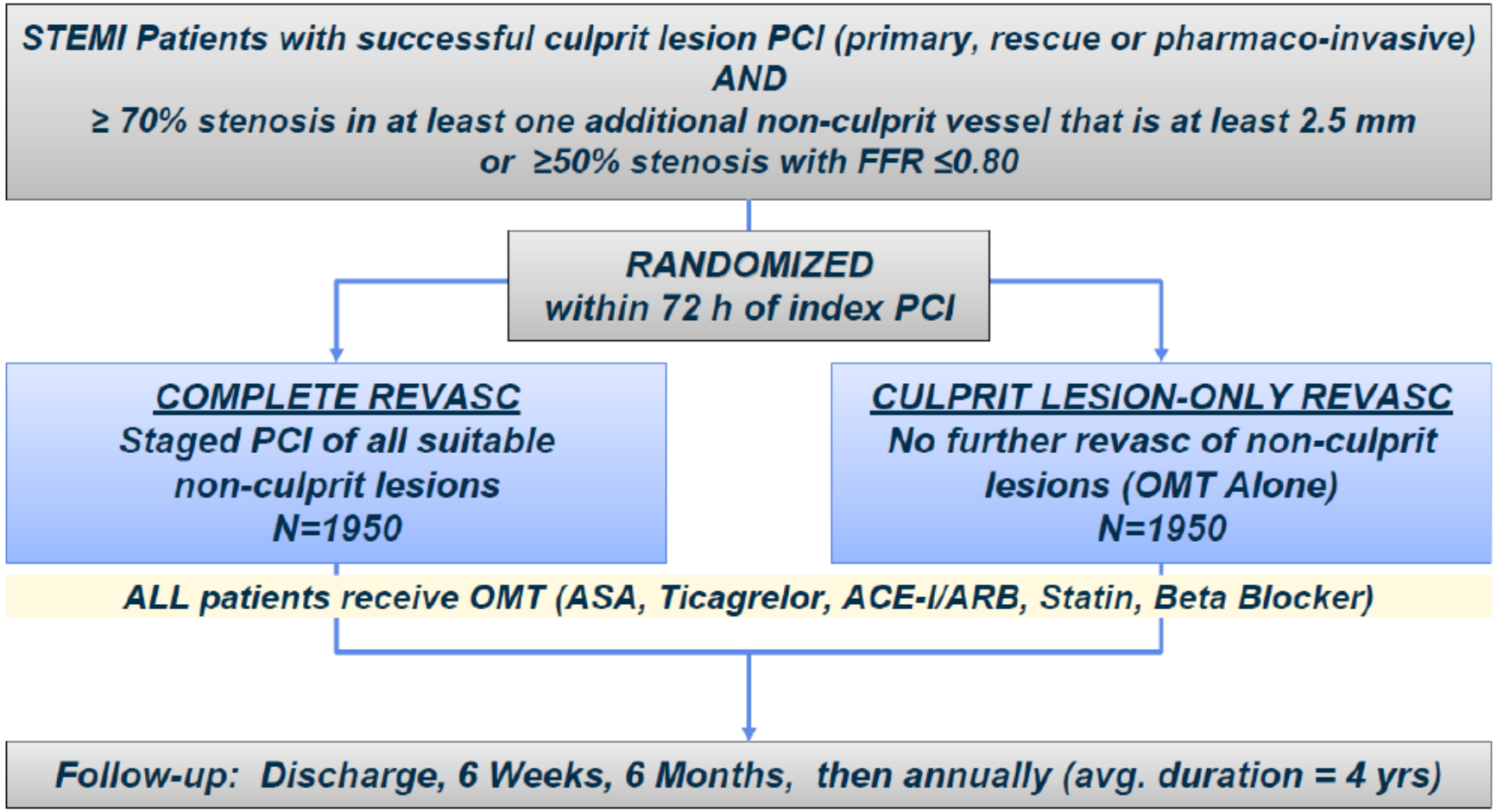


n values are for subjects with PCI performed for the index event and available data on TIMI flow or ST-segment elevation.
[a]Non-parametric Wilcoxon test.

Randomized trials

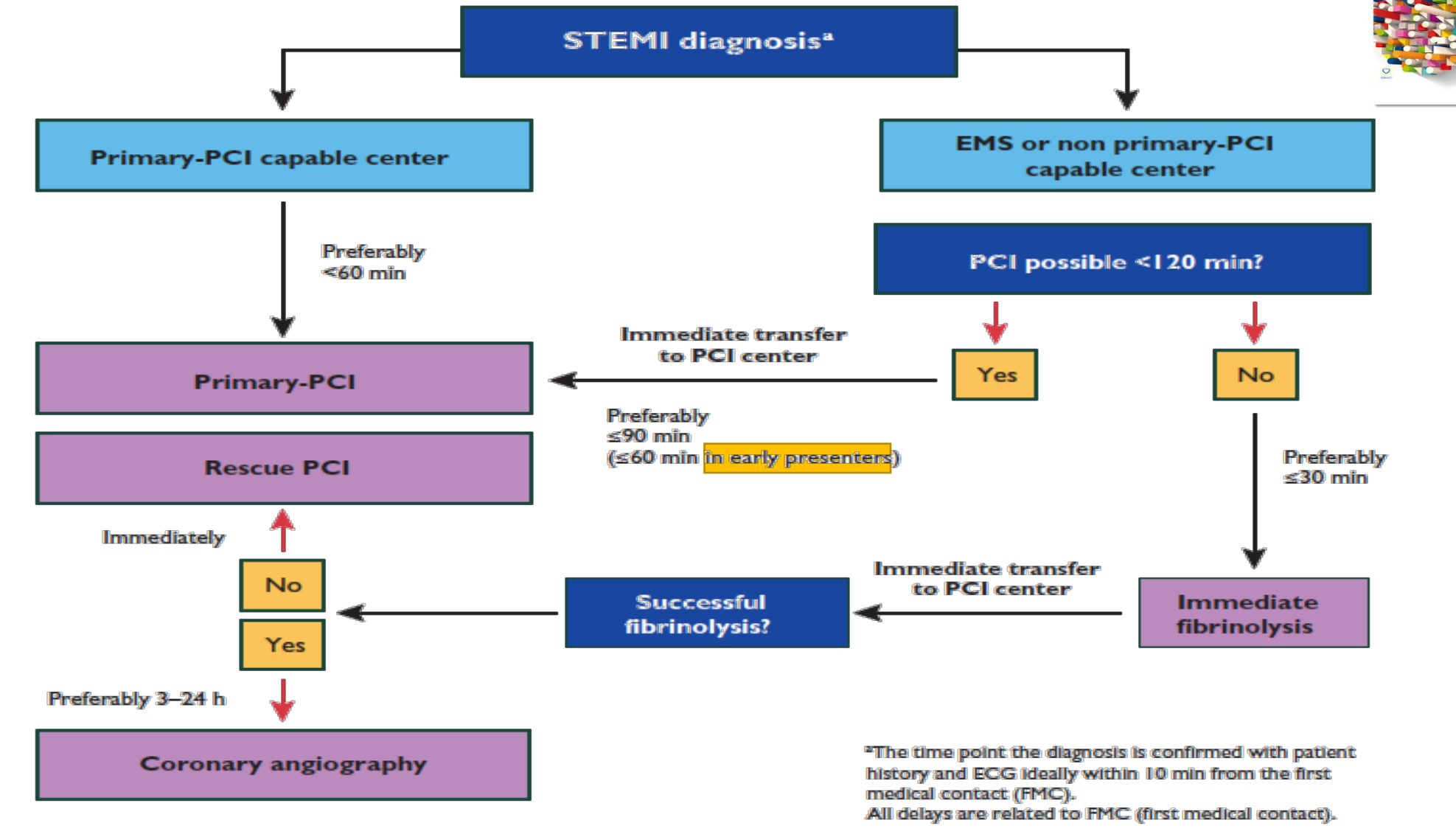


COMPLETE Study Design N=(3900)



Primary Outcome: CV Death / MI
Secondary Outcome: CV Death/MI/Ischemia-driven revascularization

ESC STEMI GUIDELINES 2012-2017



Cath = catheterization laboratory; EMS = emergency medical system; FMC = first medical contact; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

Figure 2 Prehospital and in-hospital management, and reperfusion strategies within 24 h of FMC (adapted from Wijns *et al.*).[4]

Steg, *Eur Heart J*, 2012

What is new in 2017 Guidelines on AMI-STEMI

2017 NEW / REVISED CONCEPTS

MINOCA AND QUALITY INDICATORS:
- New chapters dedicated to these topics.

STRATEGY SELECTION AND TIME DELAYS:
- Clear definition of first medical contact (FMC).
- Definition of "time 0" to choose reperfusion strategy (i.e. the strategy clock starts at the time of "STEMI diagnosis").
- Selection of PCI over fibrinolysis: when anticipated delay from "STEMI diagnosis" to wire crossing is ≤120 min.
- Maximum delay time from "STEMI diagnosis" to bolus of fibrinolysis agent is set in 10 min.
- "Door-to-Balloon" term eliminated from guidelines.

TIME LIMITS FOR ROUTINE OPENING OF AN IRA:
- 0-12h (Class I); 12-48h (Class IIa); >48h (Class III).

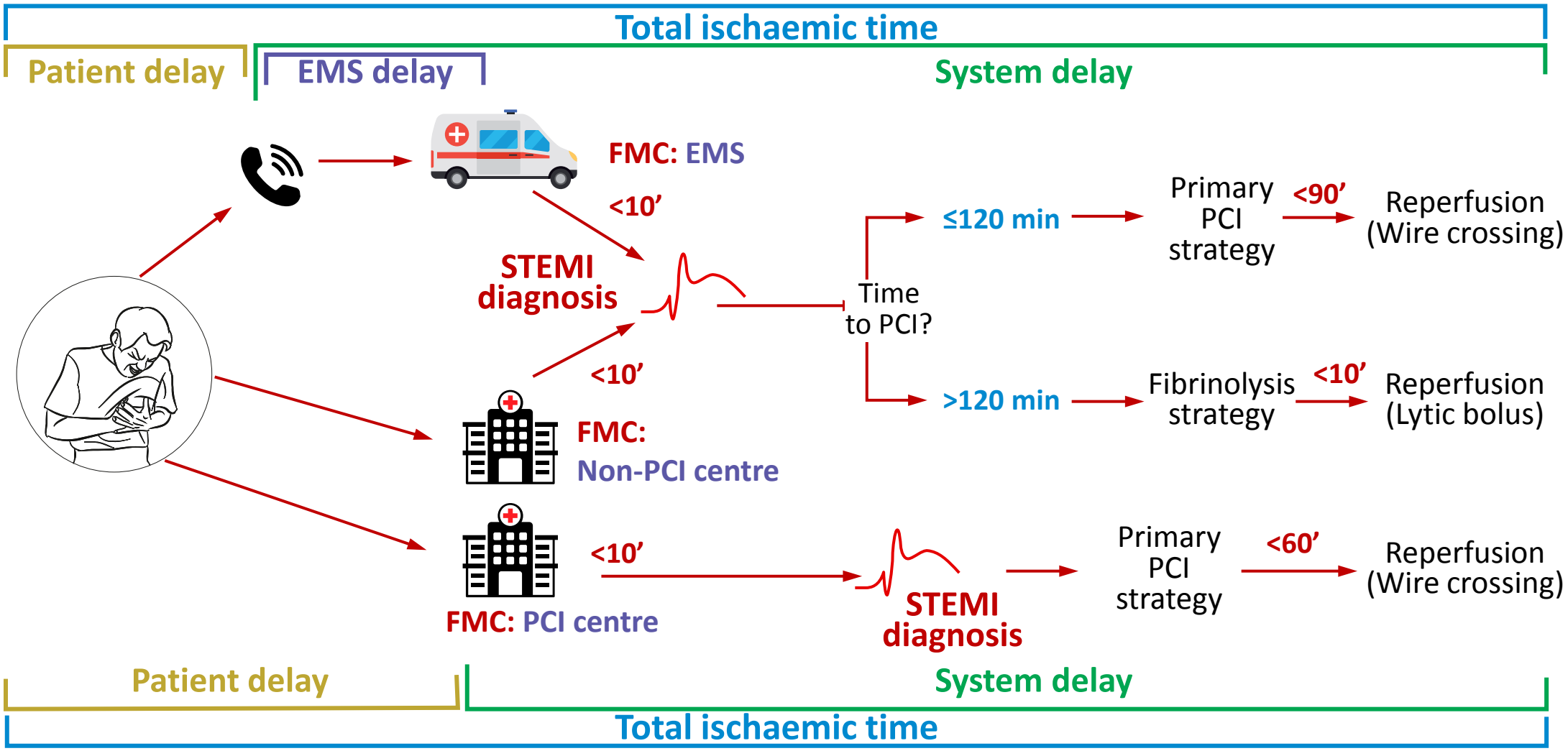
ELECTROCARDIOGRAM AT PRESENTATION:
- Left and right bundle branch block considered equal for recommending urgent angiography if ischaemic symptoms.

TIME TO ANGIOGRAPHY AFTER FIBRINOLYSIS:
- Timeframe is set in 2-24h after successful fibrinolysis.

PATIENTS TAKING ANTICOAGULANTS:
- Acute and chronic management presented.

2017 ESC Guidelines for the Management of AMI-STEMI (European Heart Journal 2017 - doi:10.1093/eurheartj/ehx095)

Modes of patient presentation, components of ischaemic time and flowchart for reperfusion strategy selection



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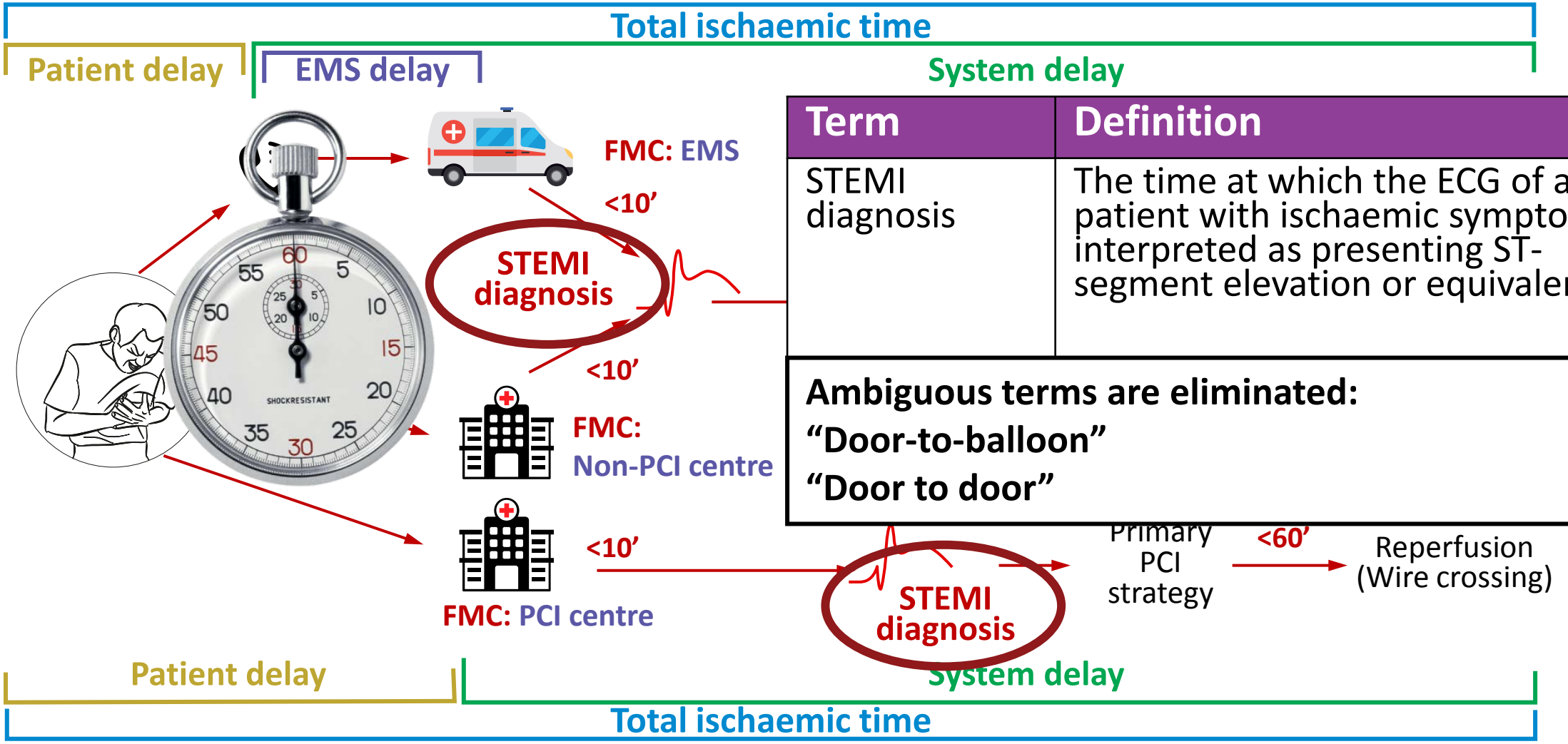


Term	Definition
STEMI diagnosis	The time at which the ECG of a patient with ischaemic symptoms is interpreted as presenting ST-segment elevation or equivalent.

Ambiguous terms are eliminated:
"Door-to-balloon"
"Door to door"

2017 ESC Guidelines for the Management of AMI-STEMI (European Heart Journal 2017 - doi:10.1093/eurheartj/ehx095)

outcomes. This Task Force recognizes the lack of contemporaneous data to set the limit to choose PCI over fibrinolysis. For simplicity, an absolute time from STEMI diagnosis to PCI-mediated reperfusion [i.e. wire crossing of the infarct-related artery (IRA)] rather than a relative PCI-related delay over fibrinolysis has been chosen. This limit is set to 120 min. Given the maximum limit of 10 min from STEMI diagnosis to bolus of fibrinolytics (see below), the 120 min absolute time would correspond to a PCI-related delay in the range of 110–120 min, being in the range of the times identified in old studies and registries as the limit delay to choose PCI.[107,117–120]

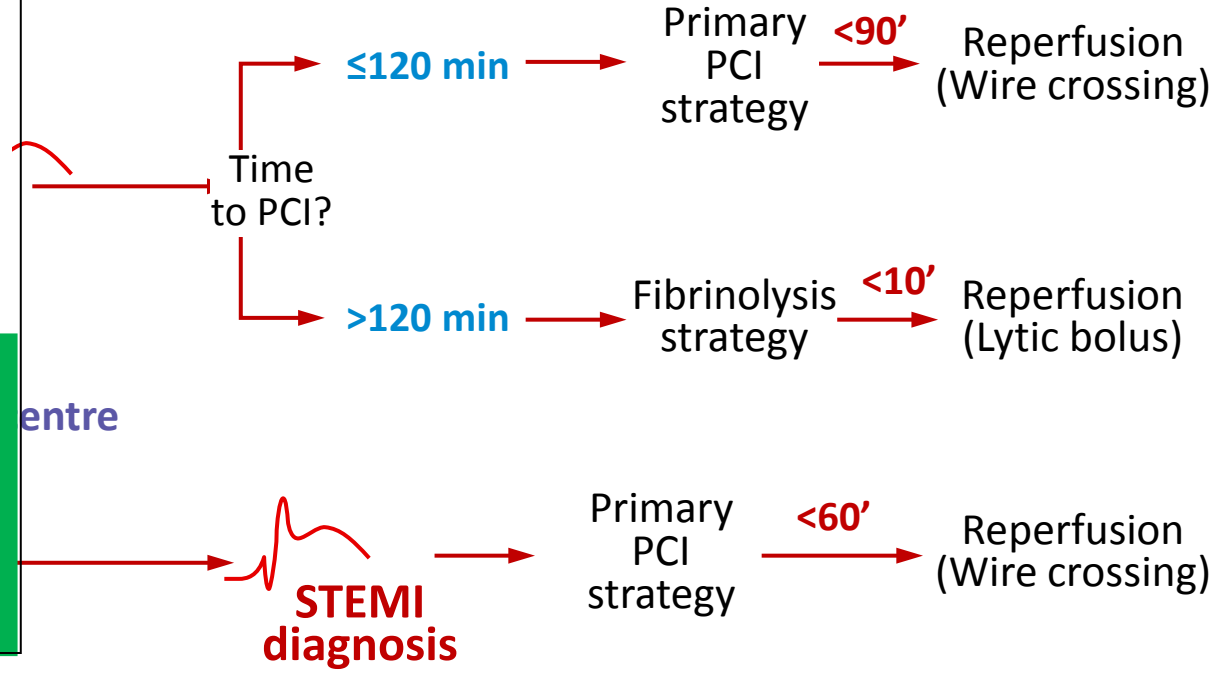
Modes of patient presentation, components of ischaemic time and flowchart for reperfusion strategy selection

Atypical ECG presentations

- Bundle branch block,
- Ventricular pacing,
- Hyper-acute T waves,
- Isolated depression in anterior leads,
- Universal ST depression with aVR elevation

In the presence of symptoms, a primary PCI strategy (urgent angiography and PCI if indicated) should be followed.

Left and right bundle branch block are considered equal for recommending urgent angiography if ischaemic symptoms.



Patient delay

System delay

Total ischaemic time

2017 ESC Guidelines for the Management of AMI-STEMI (European Heart Journal 2017 - doi:10.1093/eurheartj/ehx095)

The MICU prospective

2 MICU = Mobile Intensive Care Unit

- ➔ Patient Diagnosis
- ➔ Prehospital Treatment
- ➔ Direct transfer
- ➔ Impact on clinical trials

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ACTION www.action-coeur.org

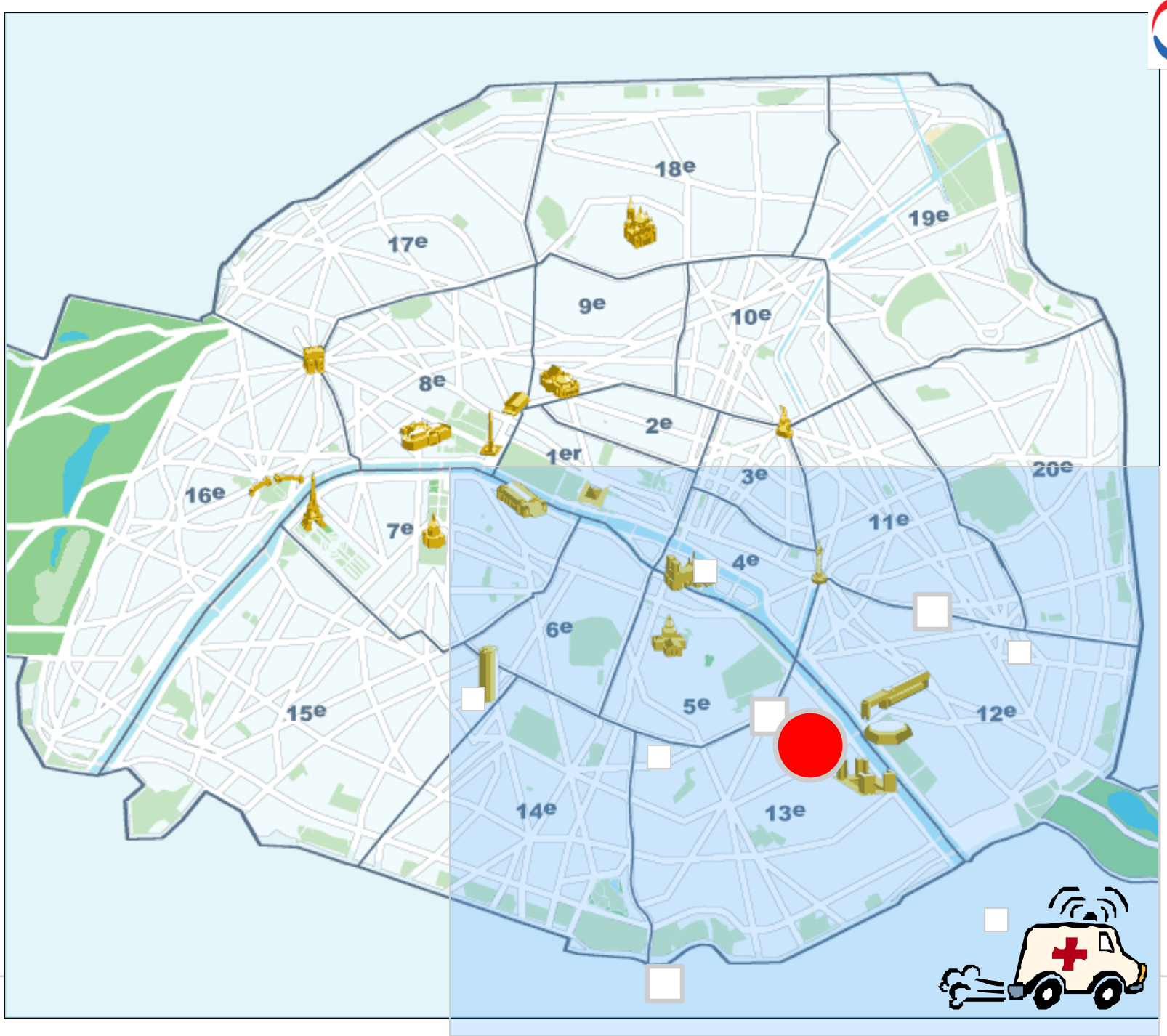
Paris City Public STEMI Network

Pop = 2 168 000

Higher Density in the East Side ++

PCI 24/24H

Emergency Dept



ESC European Society of Cardiology
European Heart Journal (2017) **00**, 1–66
doi:10.1093/eurheartj/ehx393

ESC GUIDELINES

2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC)

Endorsed by cardiac societies

Armenian Cardiologists Association , Austrian Society of Cardiology , Belgian Society of Cardiology , Belorussian Scientific Society of Cardiologists , Association of Cardiologists of Bosnia & Herzegovina , Bulgarian Society of Cardiology , Croatian Cardiac Society , Czech Society of Cardiology , Danish Society of Cardiology , Egyptian Society of Cardiology , Estonian Society of Cardiology , Finnish Cardiac Society , French Society of Cardiology , Georgian Society of Cardiology , German Cardiac Society , Hellenic Society of Cardiology , Hungarian Society of Cardiology , Italian Federation of Cardiology , Association of Cardiologists of Kazakhstan , Latvian Society of Cardiology , Lithuanian Society of Cardiology , Maltese Cardiac Society , Moroccan Society of Cardiology , Norwegian Society of Cardiology , Polish Cardiac Society , Portuguese Society of Cardiology , Romanian Society of Cardiology , Russian Society of Cardiology , San Marino Society of Cardiology , Cardiology Society of Serbia , Slovak Society of Cardiology , Spanish Society of Cardiology , Swedish Society of Cardiology , Swiss Society of Cardiology , Turkish Society of Cardiology

ESC Committee for Practice Guidelines (CPG) and National Cardiac Societies document reviewers: listed in the Appendix.

ESC entities having participated in the development of this document:
Associations: Acute Cardiovascular Care Association (ACCA), European Association of Preventive Cardiology (EAPC), European Association of Cardiovascular Imaging (EACVI), European Association of Percutaneous Cardiovascular Interventions (EAPCI), European Heart Rhythm Association (EHRA), Heart Failure Association (HFA).
Councils: Council on Cardiovascular Nursing and Allied Professions (CCNAP), Council for Cardiology Practice (CCP).
Working Groups: Cardiovascular Pharmacotherapy, Cardiovascular Surgery, Coronary Pathophysiology and Microcirculation, Myocardial and Pericardial Diseases, Thrombosis.

ESC European Society of Cardiology
European Heart Journal (2017) **00**, 1–66
doi:10.1093/eurheartj/ehx393

2017 ESC Guic
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and among the top 3 worldwide. 'I would like to strengthen the role of clinical electrophysiology in the *European Heart Journal* to make the journal even more attractive for physicians subspecialized in electrophysiology', he says.

Cardiac electrophysiology and catheter ablation will be the fastest growing segment in cardiovascular medicine in Europe over the next

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Current research focus
Treatment of acute coronary syndromes and anti-thrombotic treatment in acute myocardial infarction, Hyperemesis and cardiovascular diseas

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Hyperemesis gravidarum and cardiovascular disease

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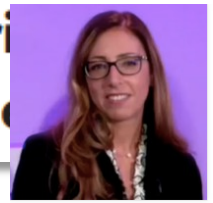

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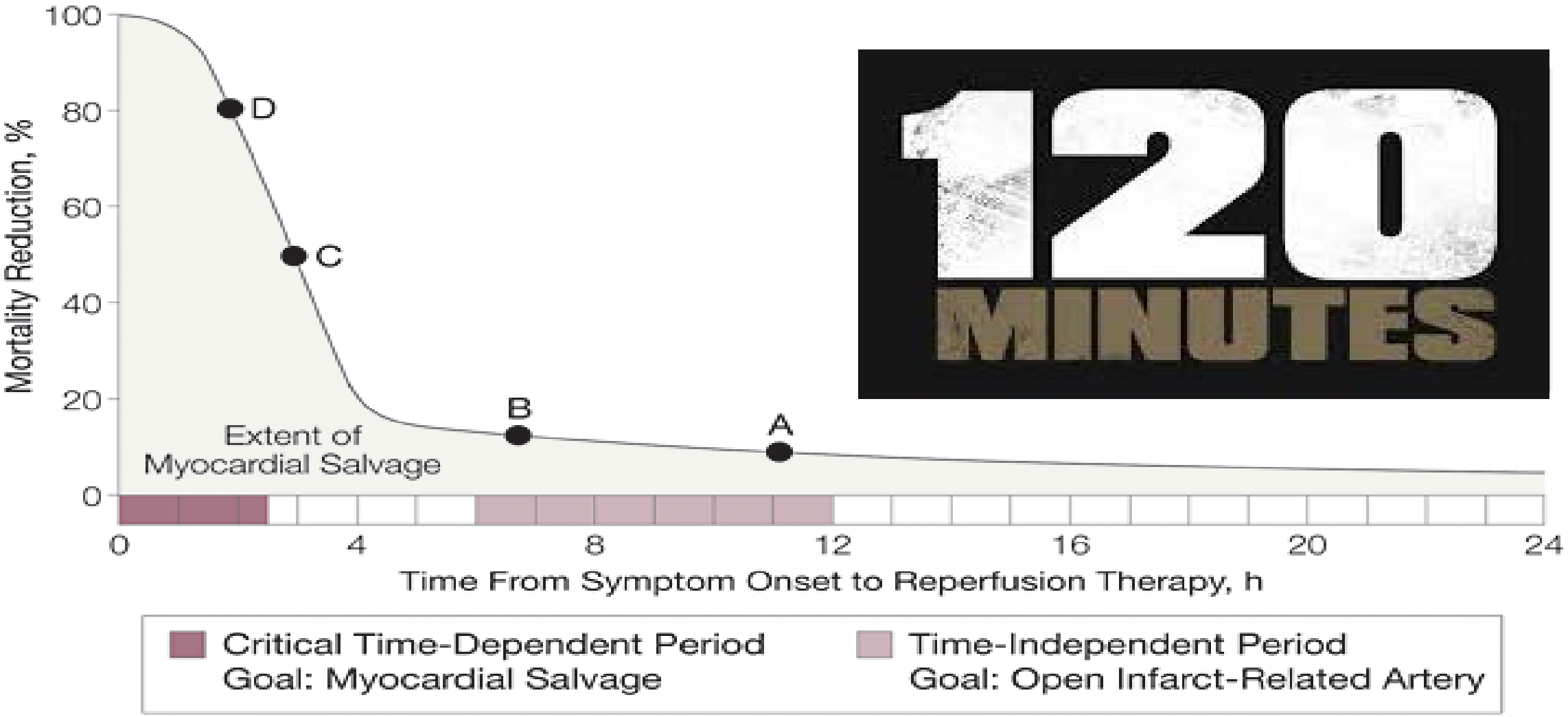
44.58

The golden two-hours time delay



Gersh, B. J. et al. JAMA 2005;293:979-986.

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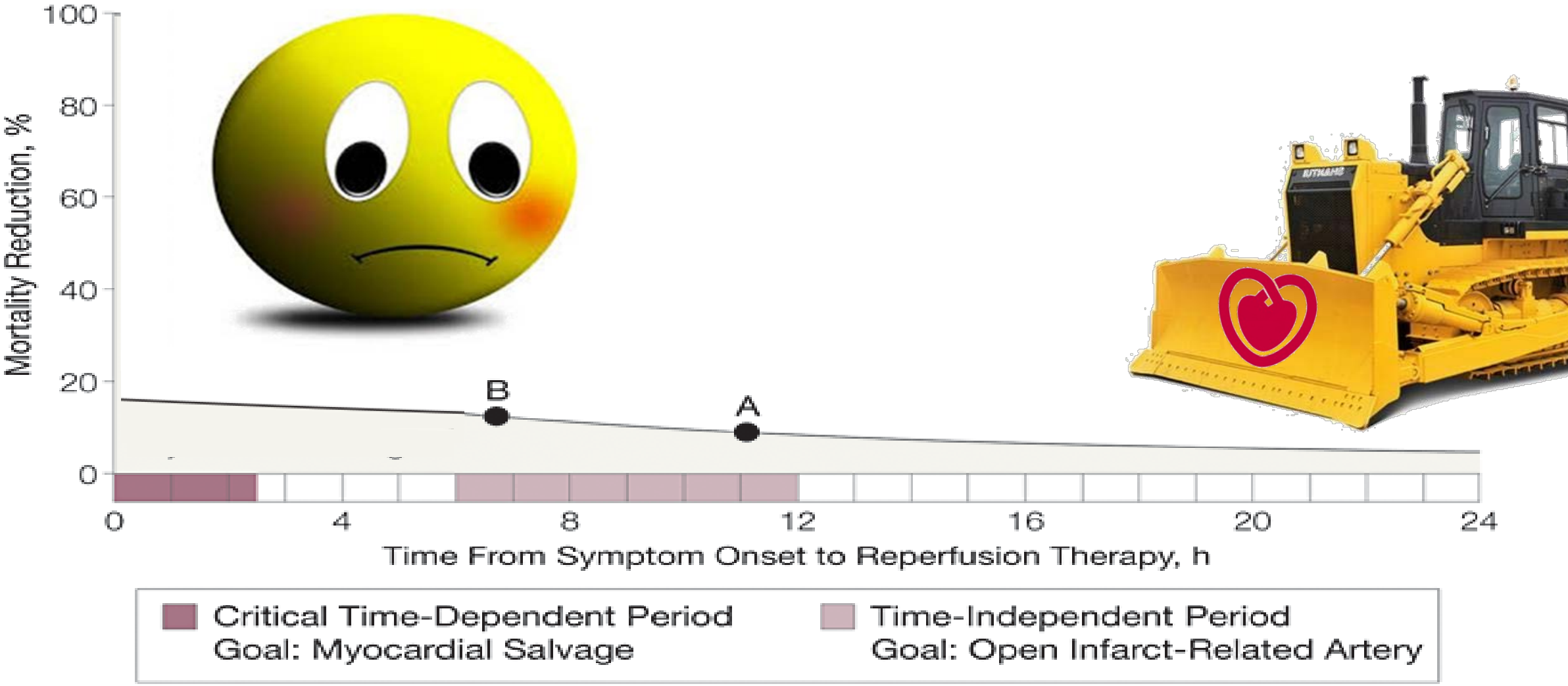

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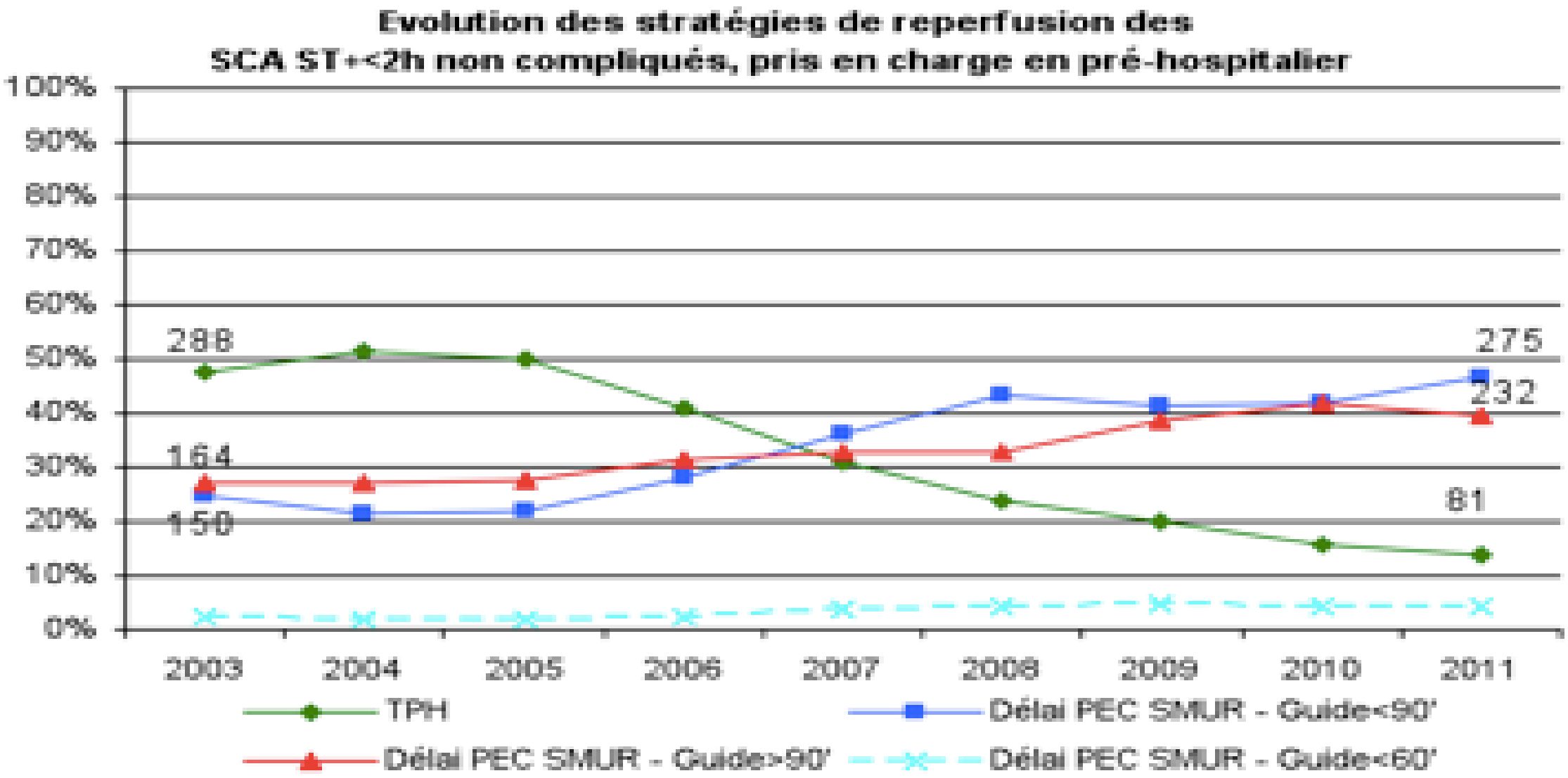
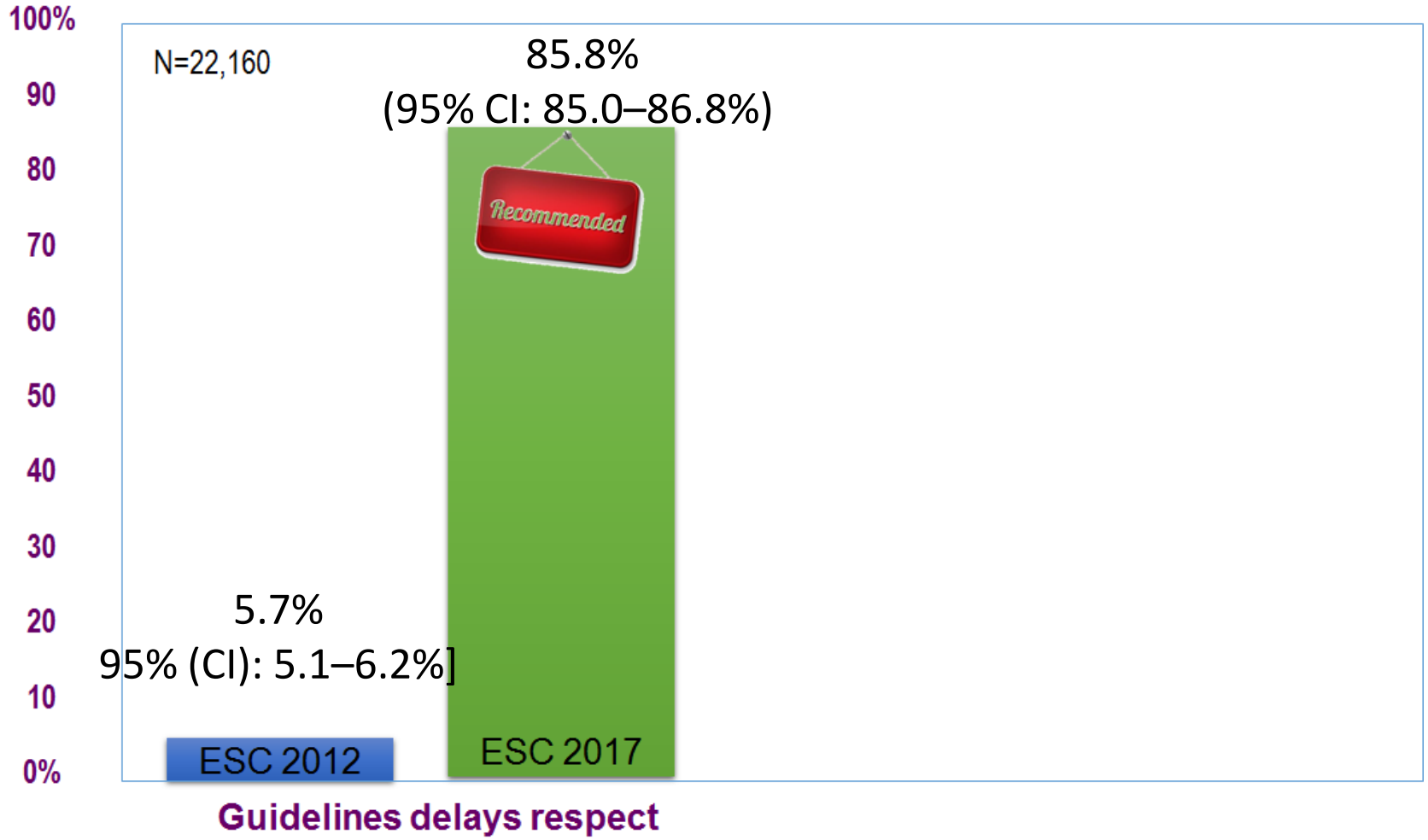
MICU-Arguments

« Early presenters » with pPCI in <60 min



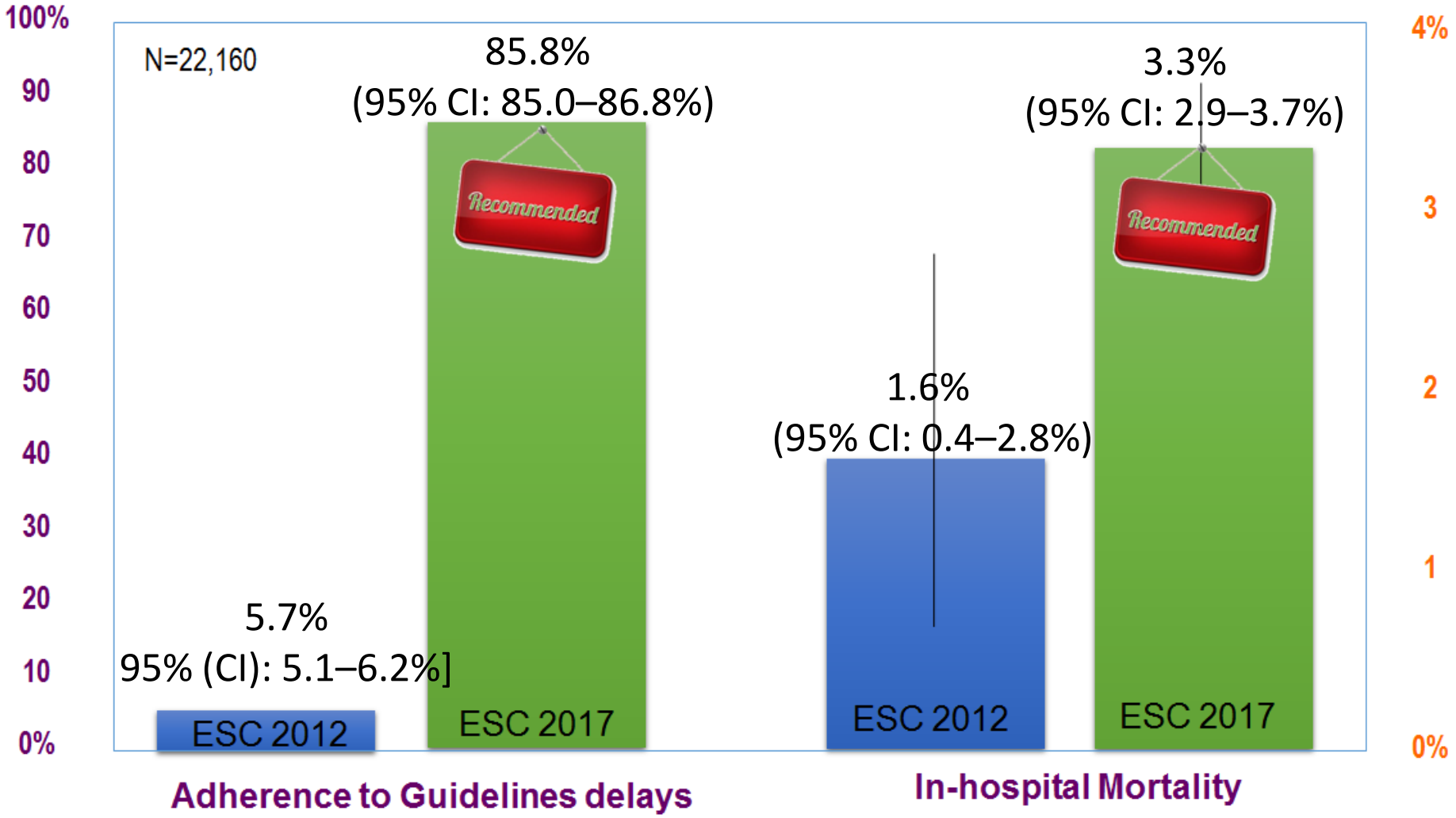
Guidelines Adherence and outcome in STEMI

- N=22,160 (2003-2015) → 61% (13,569) of early presenters (<2 hours from SO-FMC)
- 35% of EP were eligible (n=7684) of whom 2839 had prehospital lytics (<15% of EP)



Lapostolle, *Eur J Emerg Med*, 2019 (in Press)

Guidelines Adherence and outcome in STEMI



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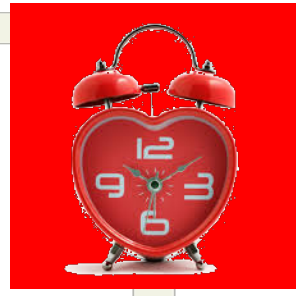
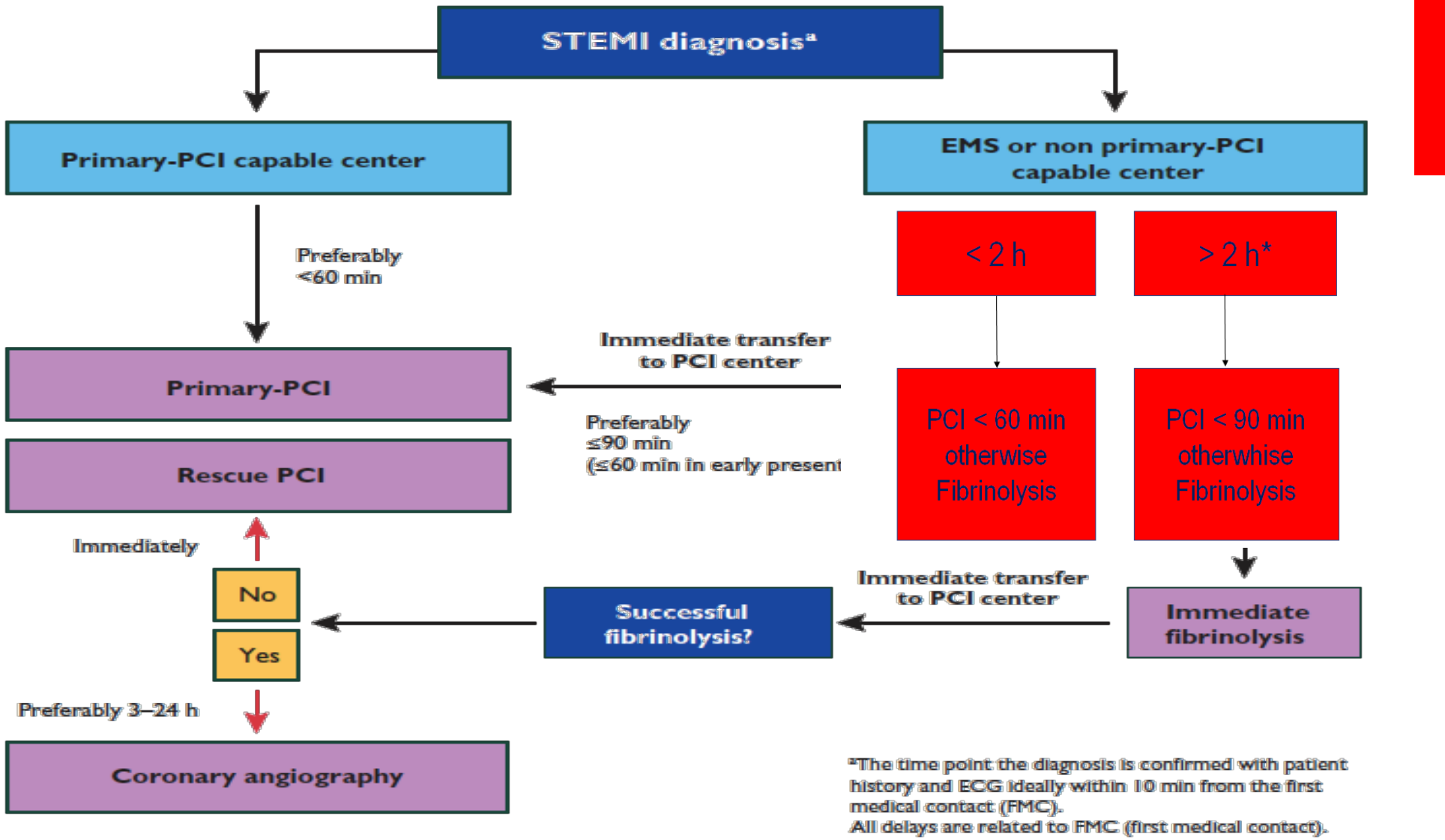




Cath = catheterization laboratory; EMS = emergency medical system; FMC = first medical contact; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

Figure 2 Prehospital and in-hospital management, and reperfusion strategies within 24 h of FMC (adapted from Wijns *et al.*).[4]

Steg, *Eur Heart J*, 2012

* More than 4 hours →discuss

What do I see?

Palmarès 2018 et 2019

INFARCTUS DU MYOCARDE

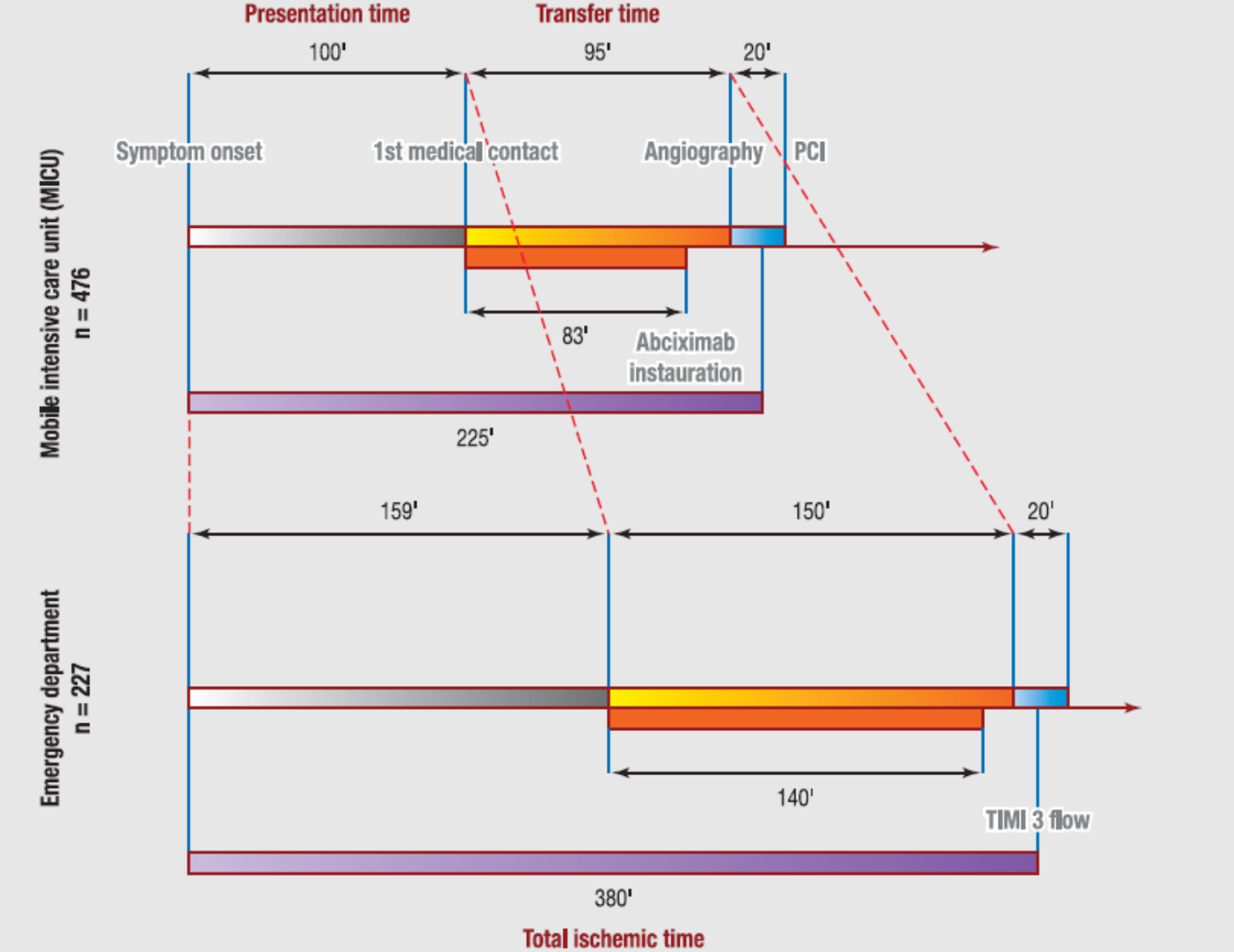
HÔPITAUX	USC	ACTIVITÉ	ANGIOPLASTIES	INDICE DE GRAVITÉ	CHIRURGIE CARDIAQUE	NOTE / 20
1er Hôpital de la Pitié-Salpêtrière, Paris	●	1103	1933	55,5	●	19,47
2e CHU - Hôpital Rangueil, Toulouse (Haute-Garonne)	●	1371	2787	46,8	●	19,45
3e CHU - Hôpital civil, Strasbourg (Bas-Rhin)	●	1208	1721	50,9	●	19,30
4e CHR de Metz-Thionville - Hôp. de Mercy, Ars-Laquenexy (Moselle)	●	1421	2342	44	●	19,18
5e CHU - Hôpital Haut-Lévêque, Pessac (Gironde)	●	1337	1409	51,1	●	19,02
6e CHU, Dijon (Côte-d'Or)	●	1188	16			
7e CHU - Gabriel-Montpied, Clermont-Ferrand (Puy-de-Dôme)	●	932	17			
8e CHU - Hôp. de Brabois, Vandœuvre-lès-Nancy (Meurthe-et-Moselle)	●	1168	14			
9e CHU - Hôp. Arnaud-de-Villeneuve, Montpellier (Hérault)	●	838	18			
10e CHU - Hôpital Nord, Saint-Etienne (Loire)	●	1317	15			
11e CHU, Caen (Calvados)	●	798	15			
12e CHU, Besançon (Doubs)	●	902	15			
13e CHU - Hôp. cardiologique, Lille (Nord)	●	836	13			
14e CHU - Hôpital Dupuytren, Limoges (Haute-Vienne)	●	915	1			
15e CHU, Poitiers (Vienne)	●	821	1			
16e Hôpital Louis-Pradel, Bron (Rhône)	●	1036	1			
17e CHU - Hôp. Trousseau, Tours (Indre-et-Loire)	●	809	1			
18e Hôp. Nord (Croix-Rousse)/CH, Lyon/Villefranche-sur-Saône (Rhône)	●	787	1			
19e CH, Lens (Pas-de-Calais)	●	823	1			
20e CHU - Hôp. Charles-Nicolle, Rouen (Seine-Maritime)	●	913				
21e CH, Avignon (Vaucluse)	●	1149	1			
22e Hôpital européen Georges-Pompidou, Paris	●	661	1			
23e CHU - Hôp. Nord-Laennec, Nantes (Loire-Atlantique)	●	887				
24e CHU, Angers (Maine-et-Loire)	●	777				
25e Hôpital Henri-Mondor, Créteil (Val-de-Marne)	●	764				
26e CHU - Hôpital Pontchaillou,						
27e CHU, Nîmes (Gard)						
28e CH, Annecy (Haute-Savoie)						
29e Hôpital Bichat, Paris						
30e CHR, Orléans (Loiret)						

Infarctus

1

Institut de Cardiologie – Pitié-Salpêtrière

The Pitié-Salpêtrière network experience (2004-2007)

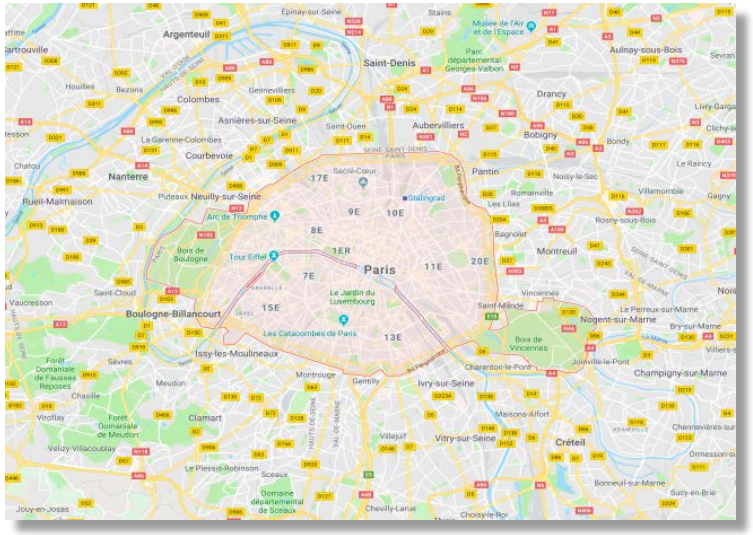


Symptom onset to FMC

- <2h : 51,5%
- <3h : 62,2%
- >4h : 28,4%

EKG- wire

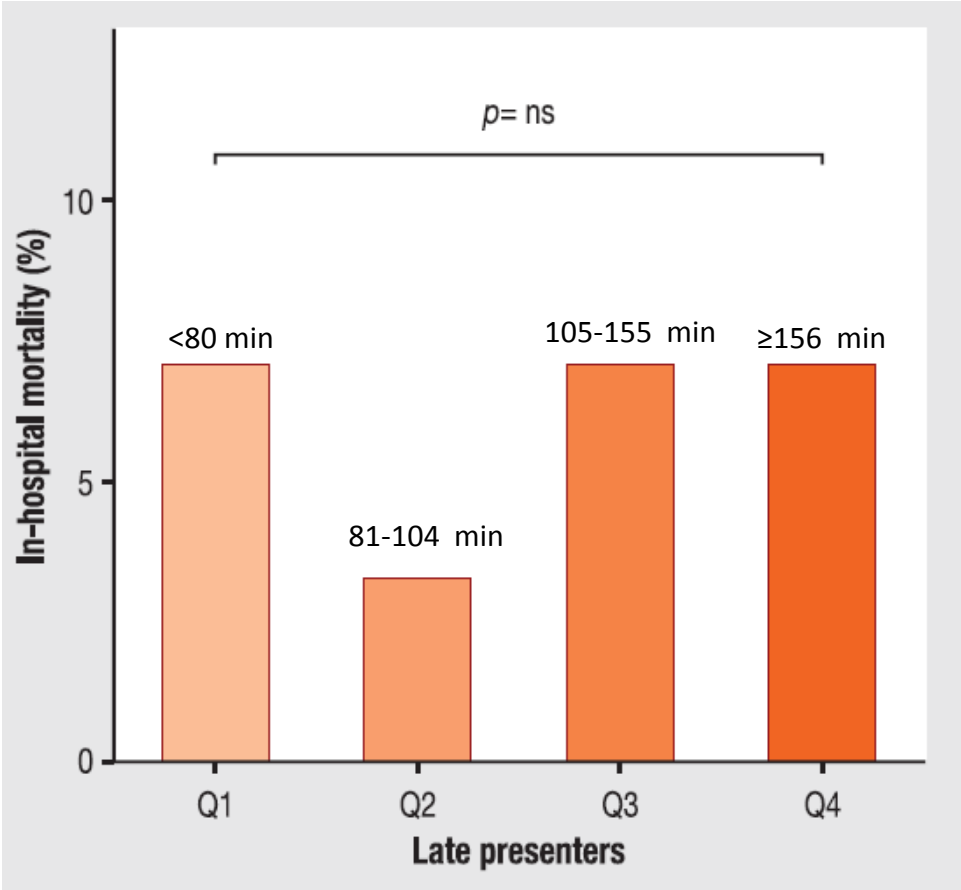
- <90 min : 38,5%
- <120 min: 61,6%

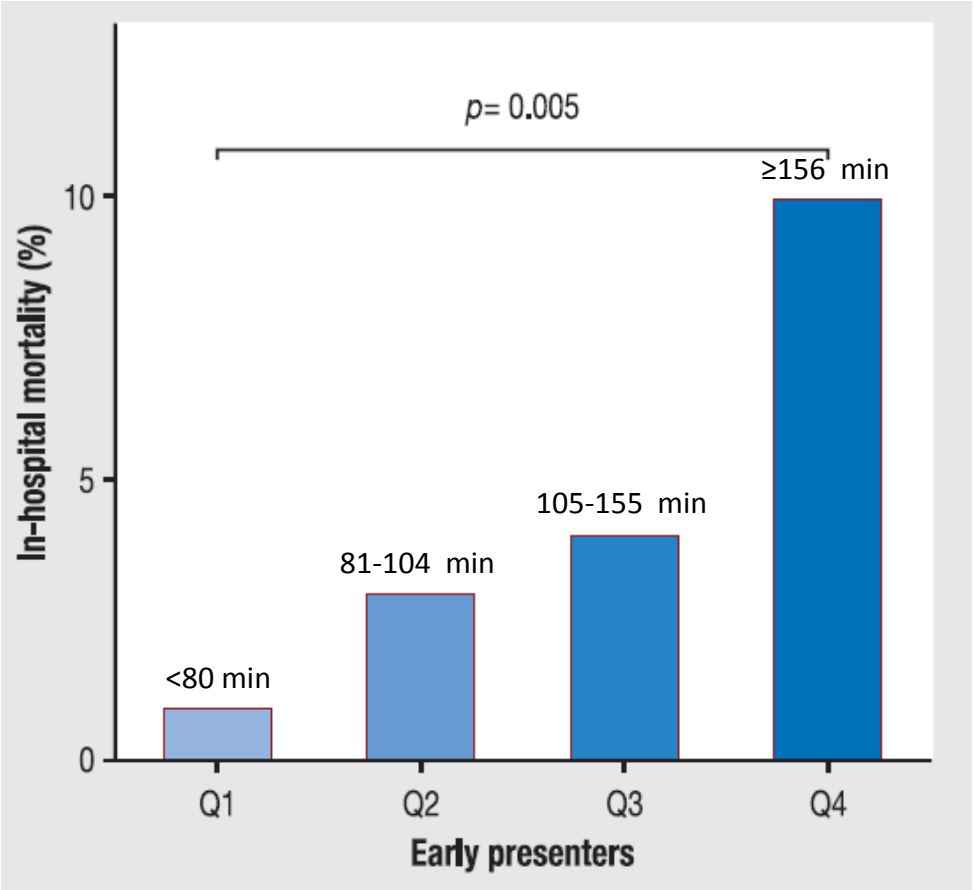


Archives of Cardiovascular Disease (2012) **105**, 639—648

Median PT was 110 minutes (57 min versus 324 min)

Transfer time (SO-angio) and mortality

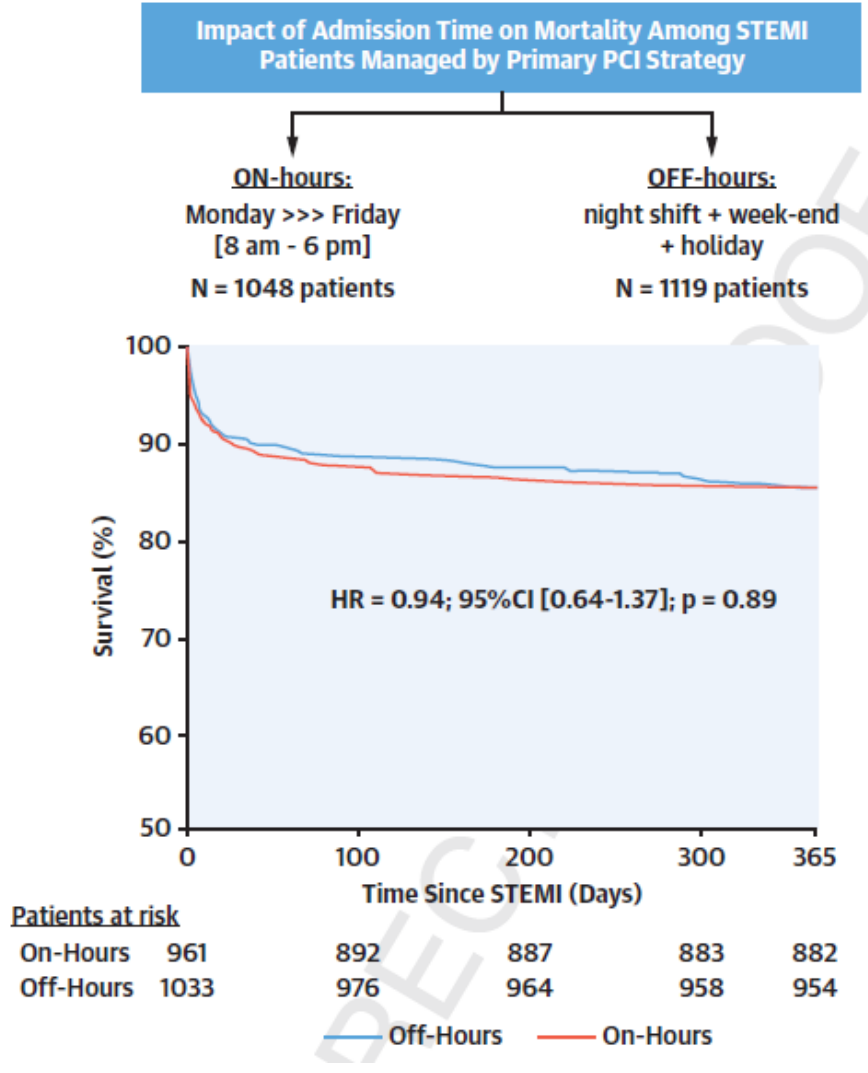


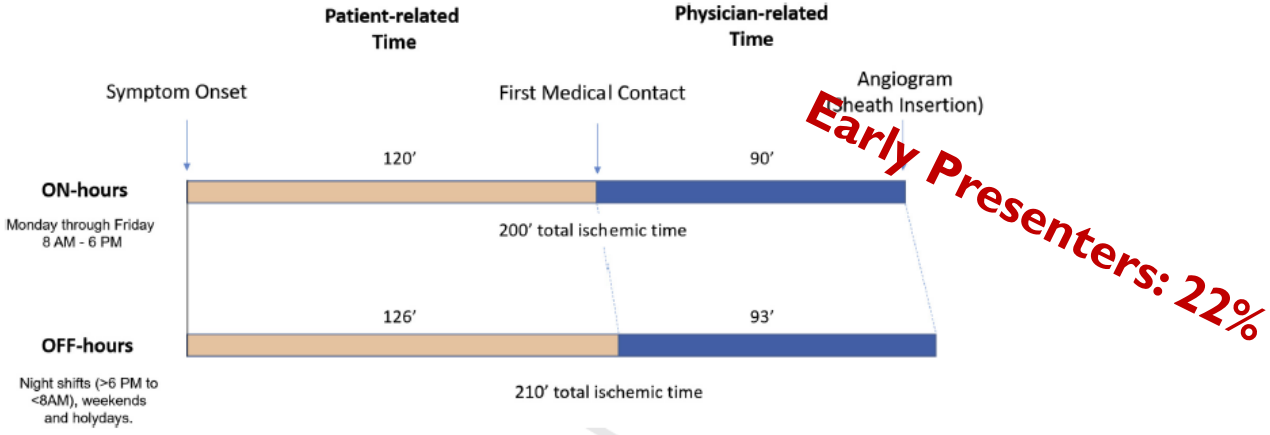


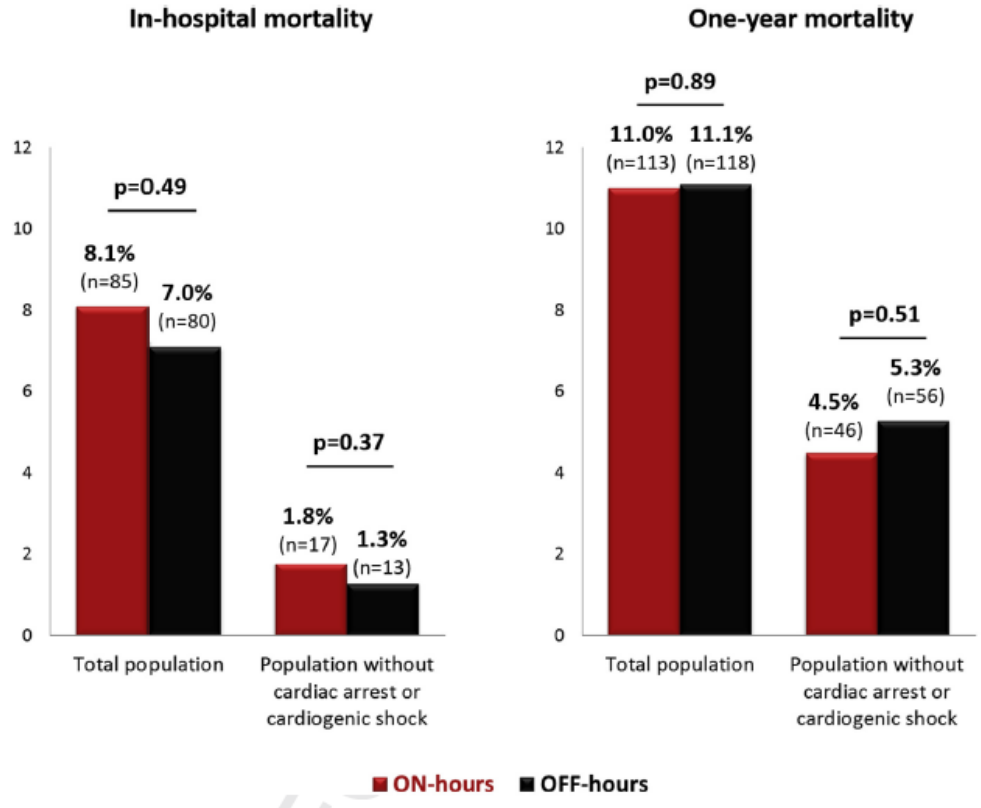
After adjustment for confounding variables such as the severity of patients, the relationship between mortality and transfer time was no longer apparent.

Archives of Cardiovascular Disease (2012) **105**, 639—648

The Pitié-Salpêtrière network experience (2007-2014)







Lattuca, B. et al. J Am Coll Cardiol Intv. 2019

Conclusions

- Better myocardial perfusion
- Time delay for oral drugs to be active
- Pharmaco-invasive is done in less than 10%
- Immediate appraisal of the coronary anatomy
- The best option for shock

Thank you

MÉDECINE SORBONNE UNIVERSITÉ

There is still a place for thrombolysis in myocardial infarction - CON.

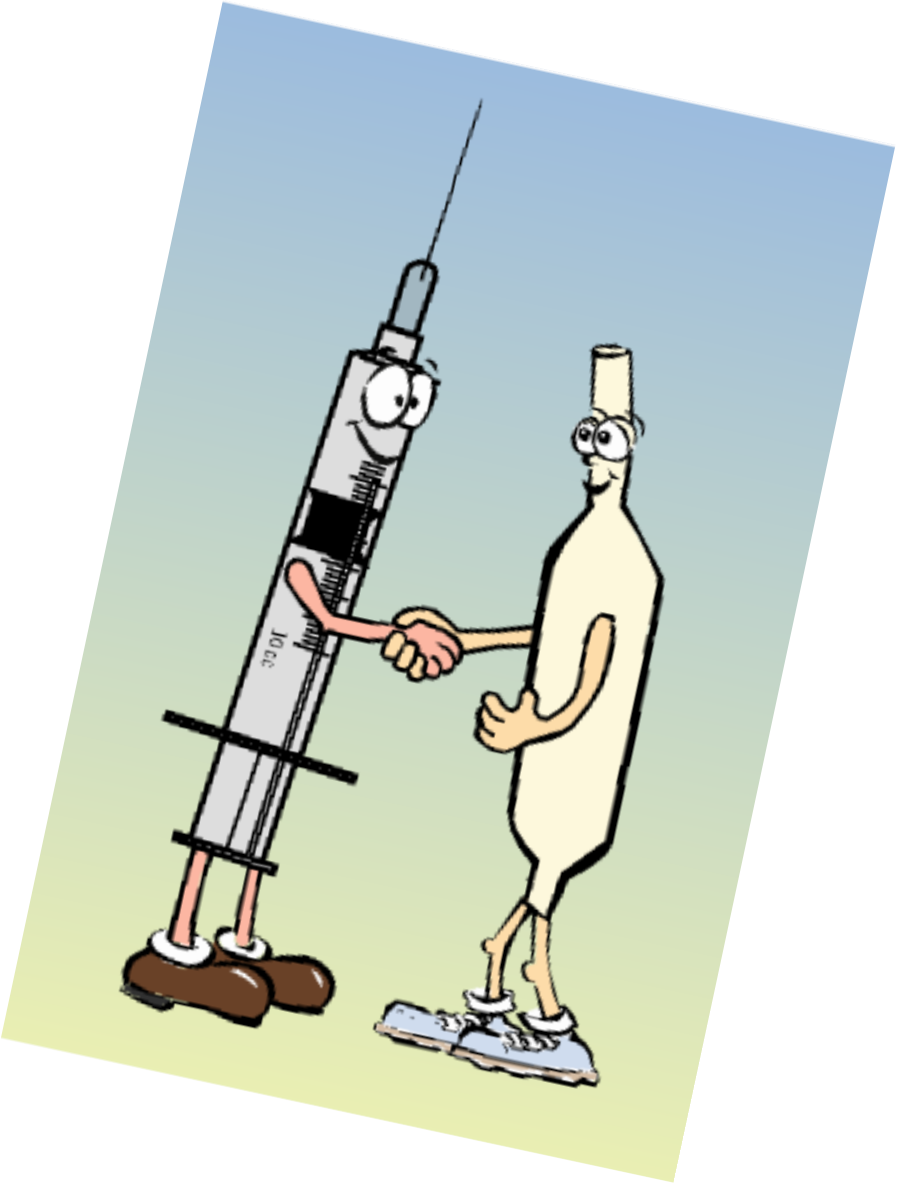
Jean-Philippe COLLET

Sorbonne Université
Action Study Group (action-cœur.org)
Institut de Cardiologie (APHP)
Pitié-Salpêtrière-Paris, France

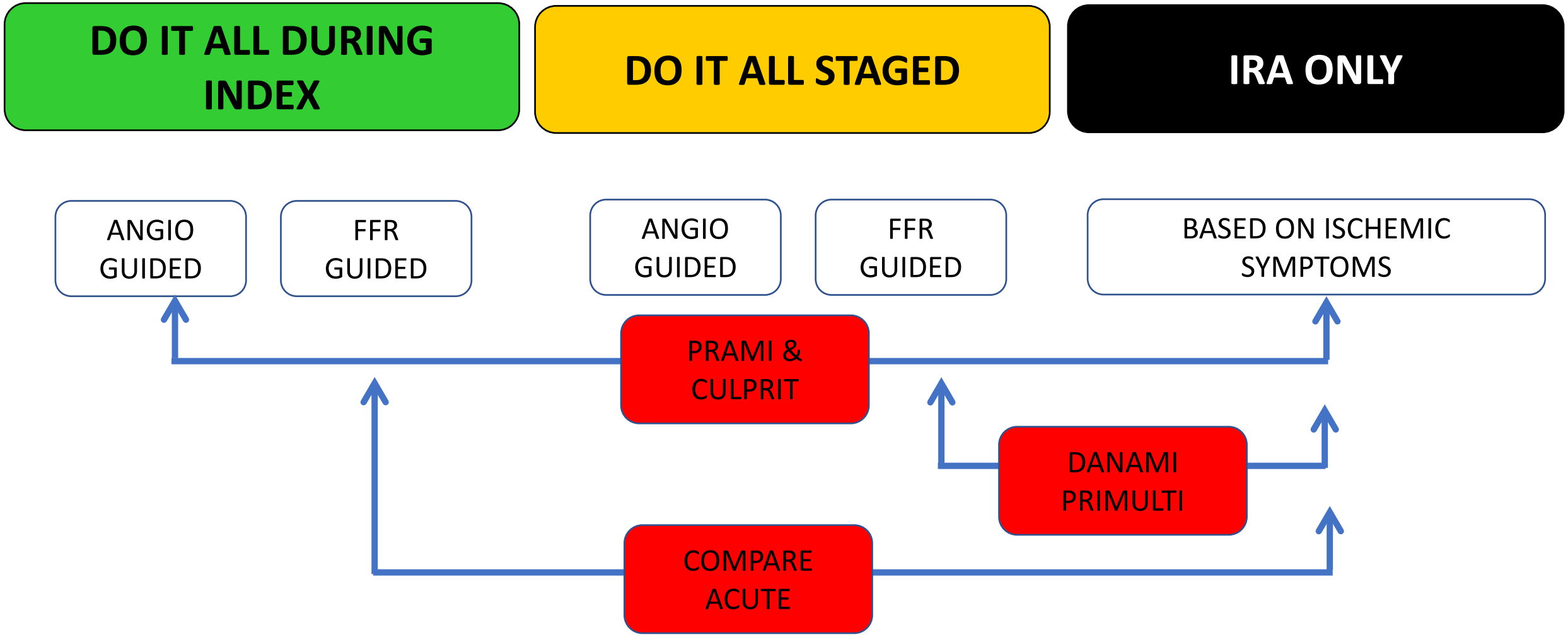
COI: Dr Collet has nothing to declare with respect to this presentation (action-coeur.org).

Action cœur

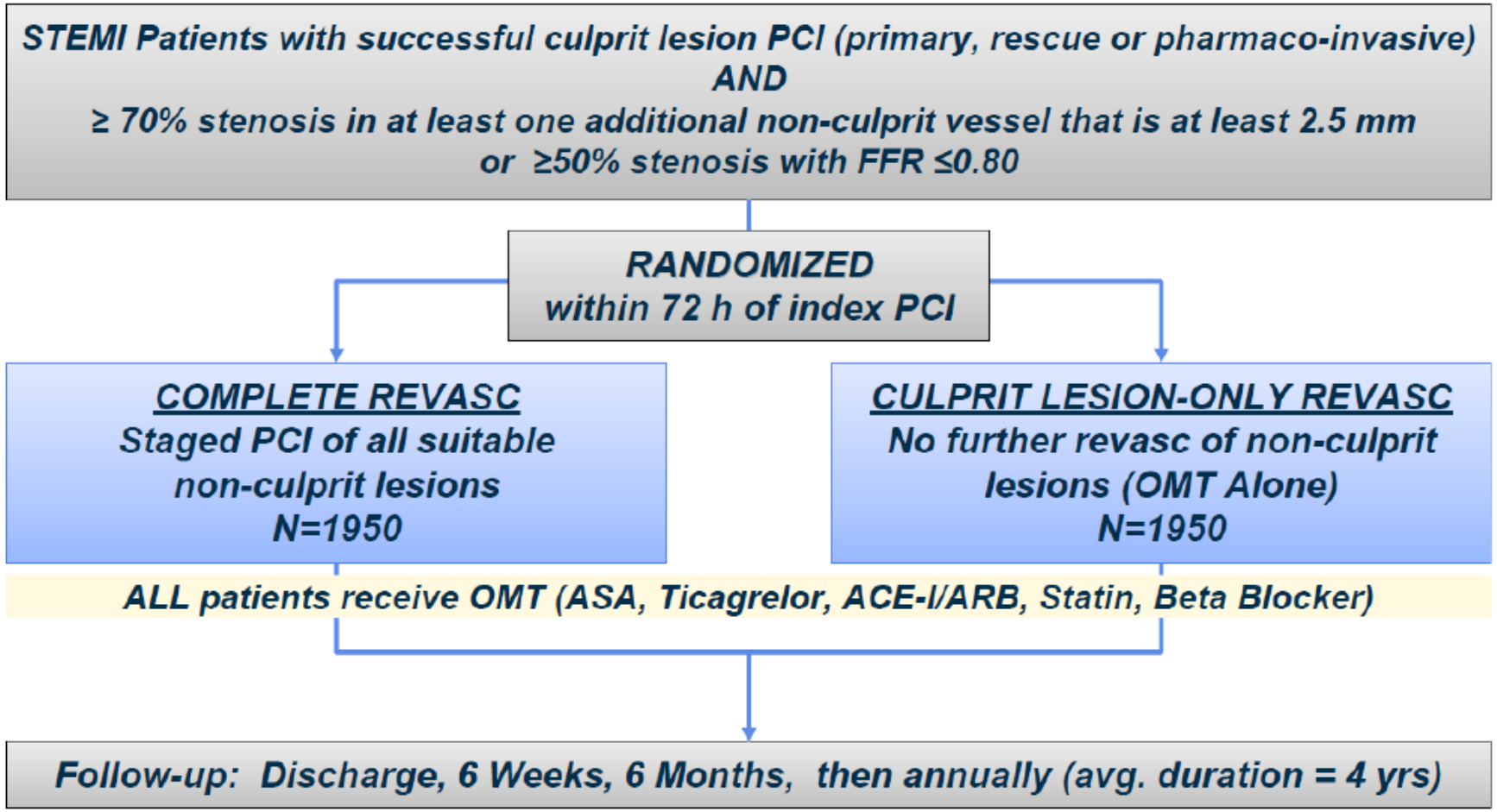
Conclusions



Randomized trials

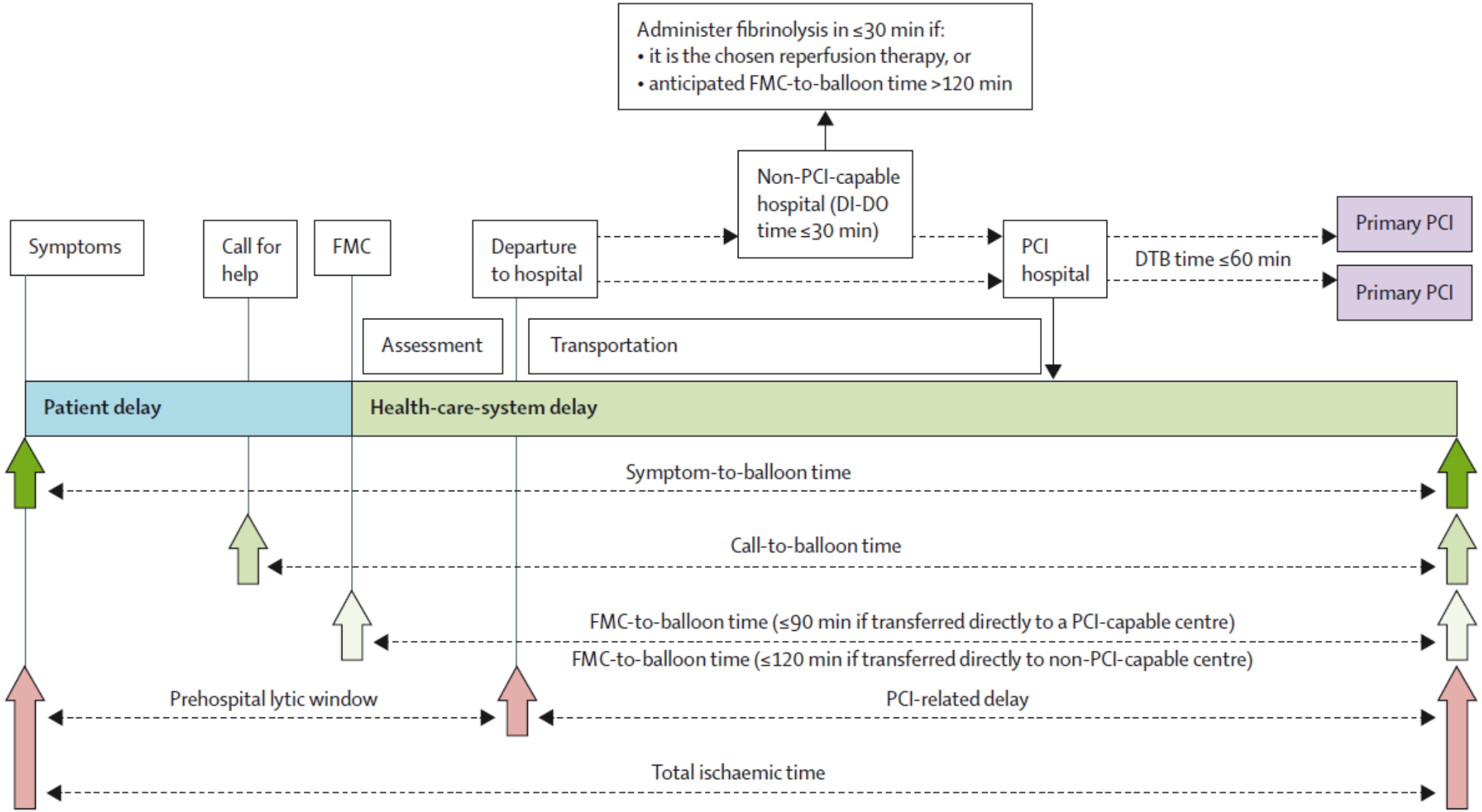


COMPLETE Study Design N=(3900)



Primary Outcome: CV Death / MI
Secondary Outcome: CV Death/MI/Ischemia-driven revascularization

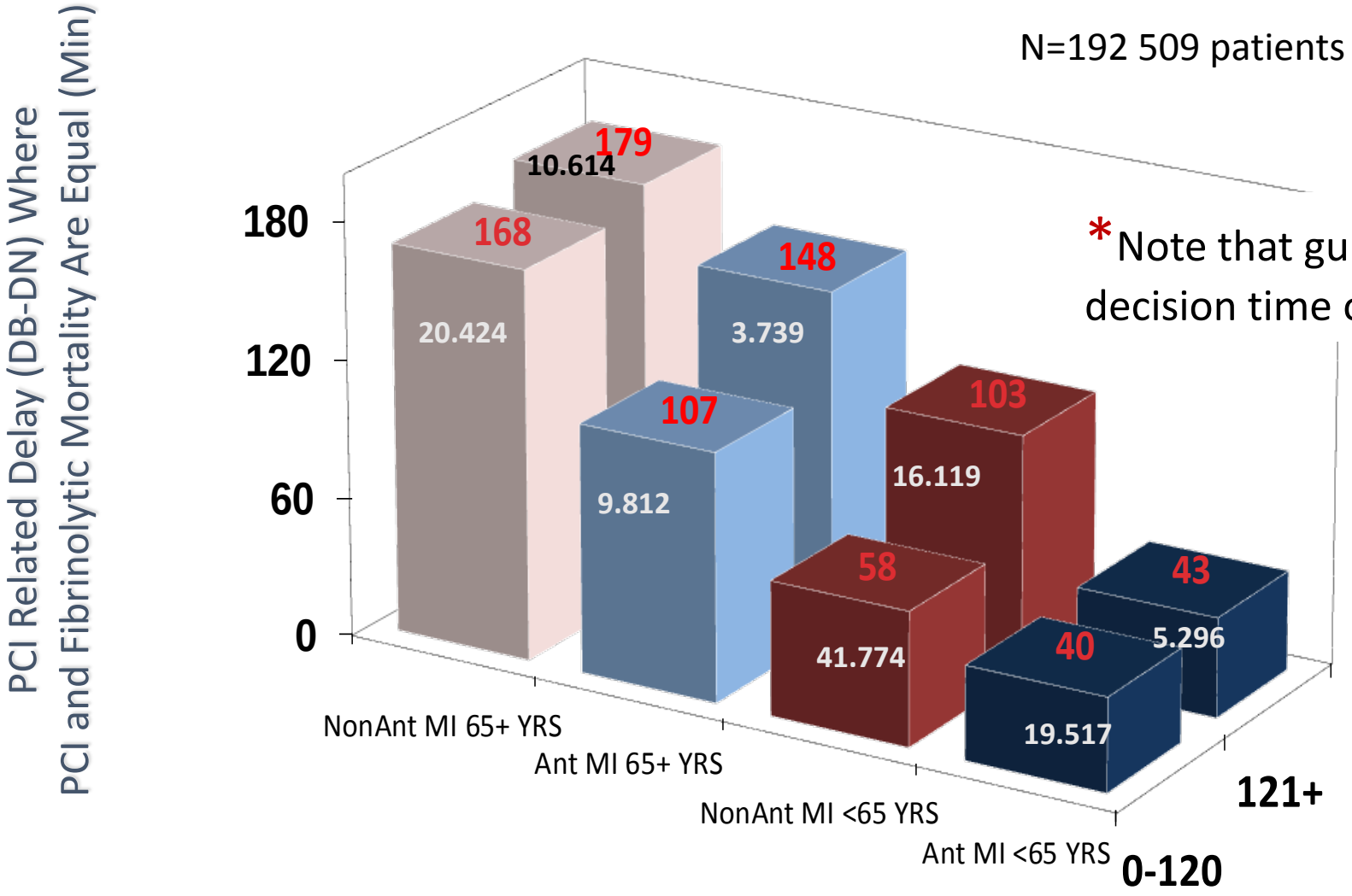
Important timeline metrics in management of STEMI



Lancet 2013; 382: 624–32

One size does not fit all

The acceptable PCI vs thrombolysis related delay depends on patient age, infarct location, and symptom duration



*Note that guidelines recommend a decision time of 120' for all patients

Pinto DS et al. Circulation 2006;114:2019-25