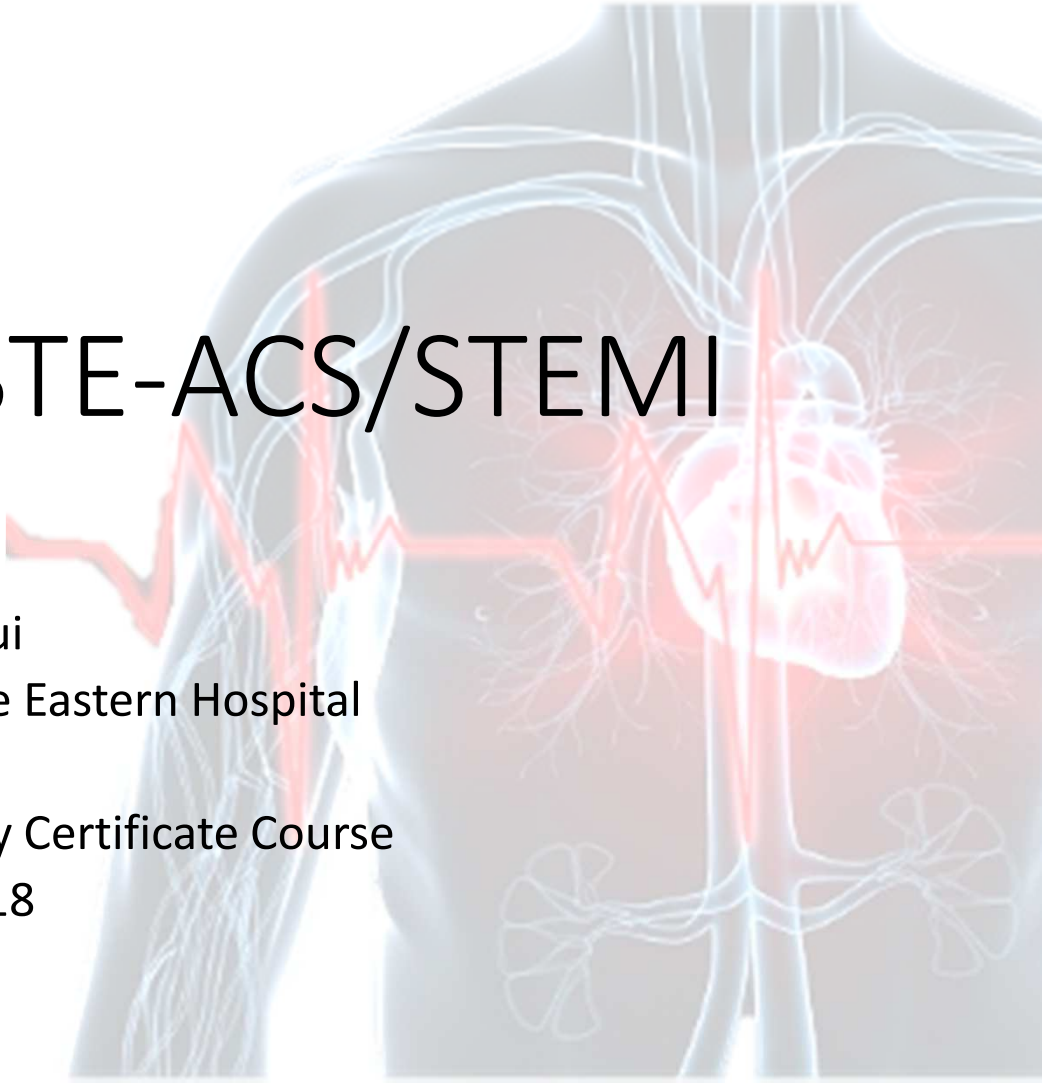
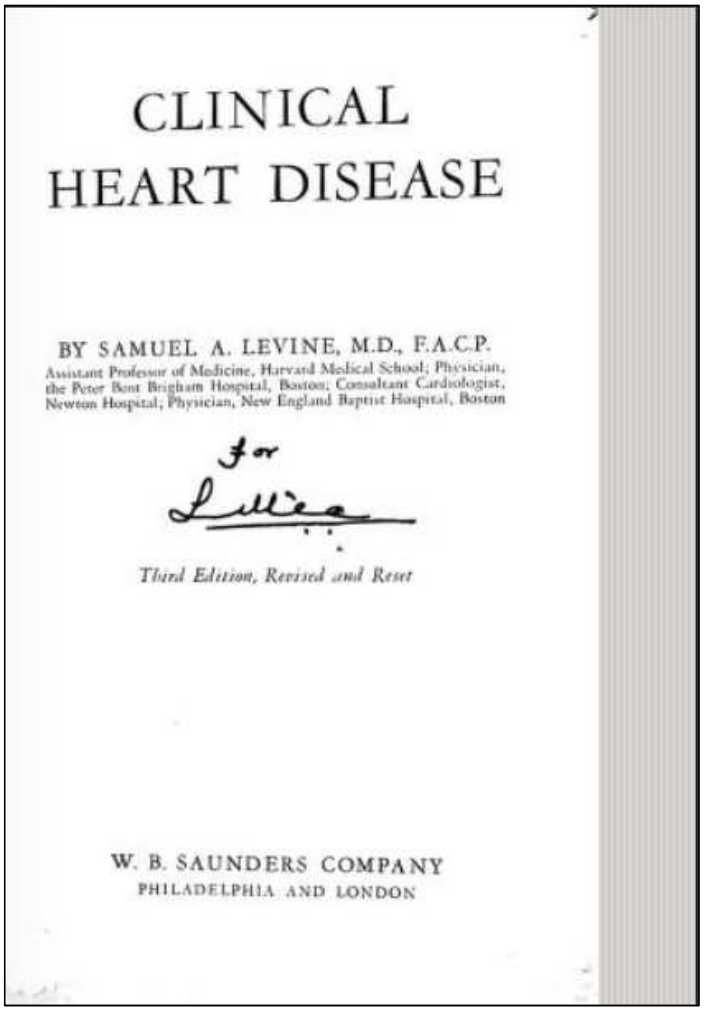
Management of STE-ACS/STEMI



Dr. KL Tsui
Pamela Youde Nethersole Eastern Hospital

Hong Kong Core Cardiology Certificate Course
8 July 2018

Management of AMI: The Past


CLINICAL
HEART DISEASE

BY SAMUEL A. LEVINE, M.D., F.A.C.P.
Assistant Professor of Medicine, Harvard Medical School; Physician, the Peter Bent Brigham Hospital, Boston; Consultant Cardiologist, Newton Hospital; Physician, New England Baptist Hospital, Boston

for
Lilia

Third Edition, Revised and Reset

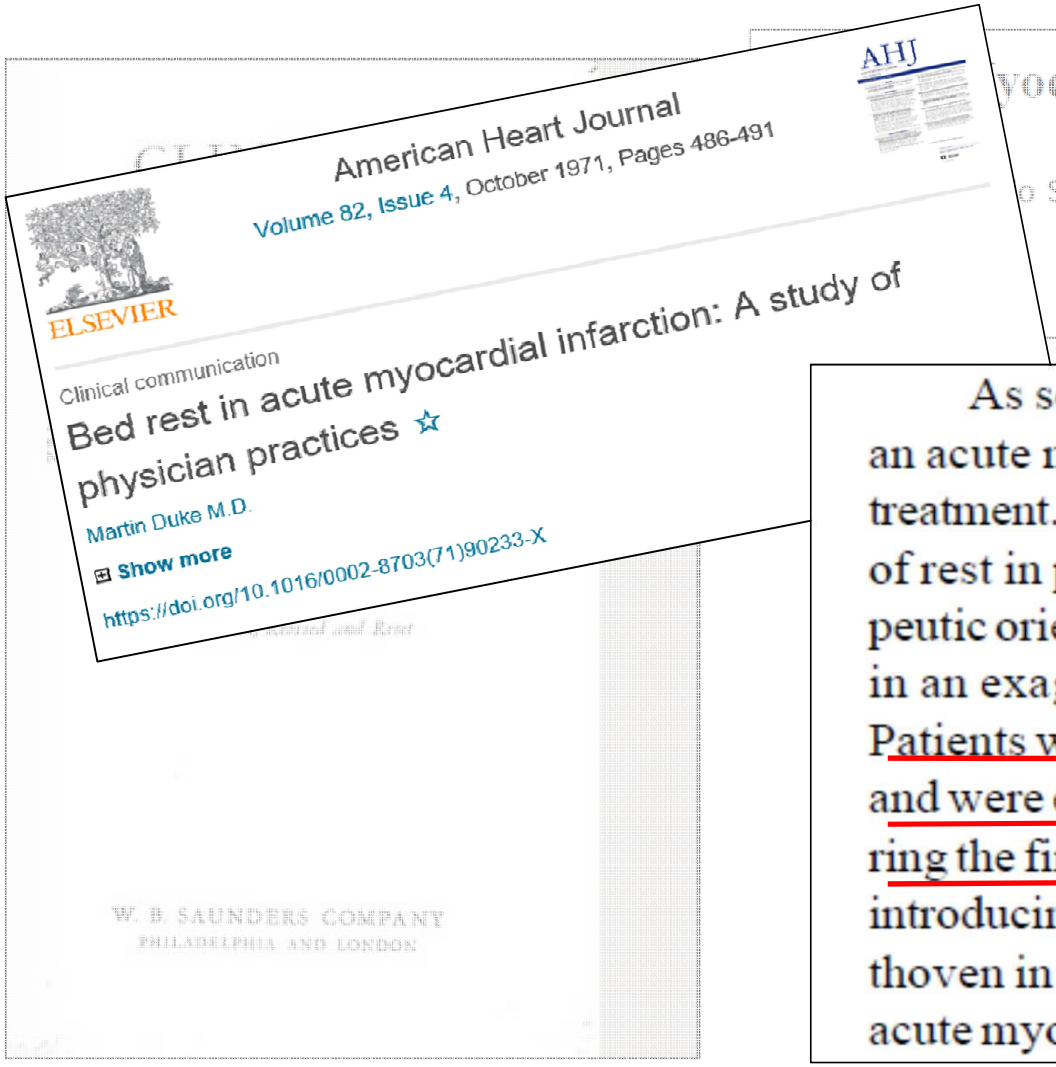
W. B. SAUNDERS COMPANY
PHILADELPHIA AND LONDON

Acute Myocardial Infarction. One Century of History

Rogério Sarmento-Leite, Ana Maria Krepsky, Carlos A. M. Gottschall

Porto Alegre, RS - Brazil

Management of AMI: The Past



As soon as it became evident that one could survive an acute myocardial infarction, attention was drawn to its treatment. In 1912, James Herrick established the importance of rest in postinfarction recovery; rest was the only therapeutic orientation existing at that time, and it was prescribed in an exaggerated way until the beginning of the 1950s. Patients were required to stay bedridden for up to 6 weeks, and were even forbidden to move or to feed themselves during the first week [2]. James Herrick was also responsible for introducing electrocardiography, which was created by Einthoven in 1902, and has been the major diagnostic tool for acute myocardial infarction up until the present time [1].

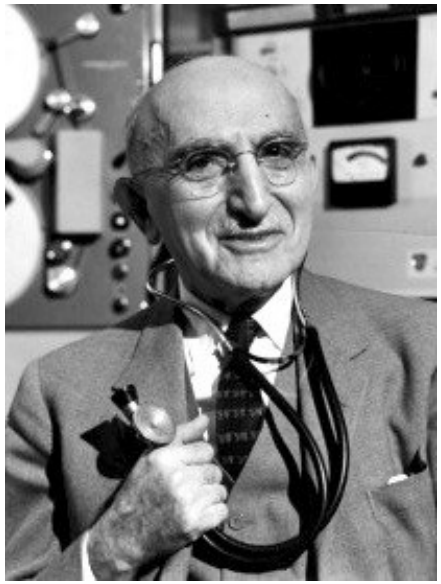
Management of AMI: The Past

THE JOURNAL

of the American Medical Association

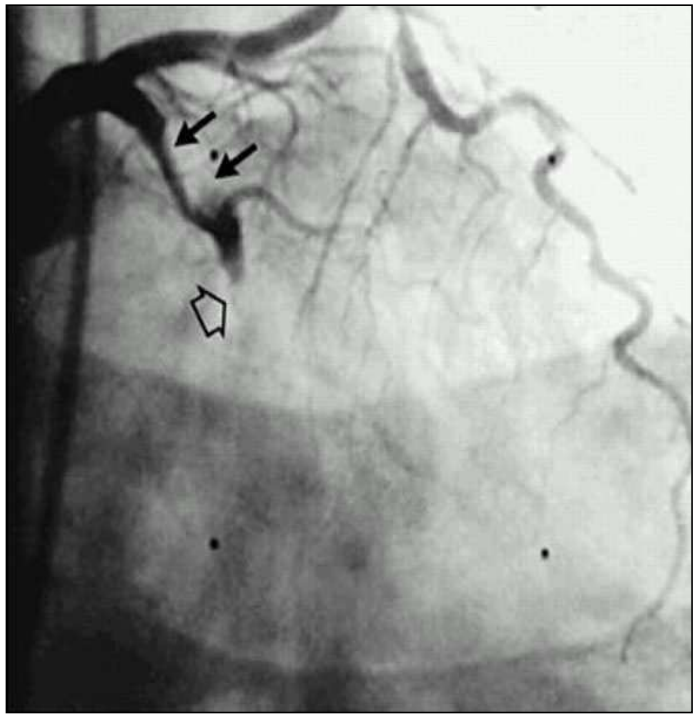
Published Under the Auspices of the Board of Trustees

VOL. 148, NO. 16 CHICAGO, ILLINOIS APRIL 19, 1952



Management of AMI: Target of Reperfusion

AMI: Pathophysiology



Ruptured plaque with occlusive thrombus

Management of AMI: Discovery of Streptokinase

“Chance Favors the Prepared Mind” -- Louis Pasteur

Isaac Newton & the Apply Tree

Management of AMI: Discovery of Streptokinase

"Chance Favors the Prepared Mind" -- Louis Pasteur

Discovery of Streptokinase – 1933

Historical Perspectives

A History of Streptokinase Use in Acute Myocardial Infarction

Nikhil Sikri
Amit Bardia

A serendipitous discovery by William Smith Tillett in 1933, followed by many years of work with his student Sol S... as a thrombolytic agent in t... initial clinical application in c... culous meningitis. In 1958, S... acute myocardial infarction a... Initial trials that used streptok... proach of intracoronary strep... 1979. Subsequently, larger tr... ing from 70% to 90%. The r... randomized multicenter trial... della Streptochinasi nell'Infa... streptokinase as an effective... its use in acute myocardial in... gen activator in developed na... acute myocardial infarction in...

The "Wonder Drug"—Streptokinase

The streptokinase era dates back to 1933, when Dr. William Smith Tillett[19] (Fig. 1) discovered the agent through sheer serendipity. Tillett was Associate Professor of Medicine and Director of the Biological Division at Johns Hopkins University, at that time. The work of Tillett was strikingly distinct from that of his contemporaries, probably because he was such a keen observer. Louis Pasteur's famous saying (now elevated to the status of cliché) applies aptly to Tillett: "Chance favors the prepared mind." He observed that streptococci agglutinated in test tubes that contained human plasma but not in those that contained human serum. While

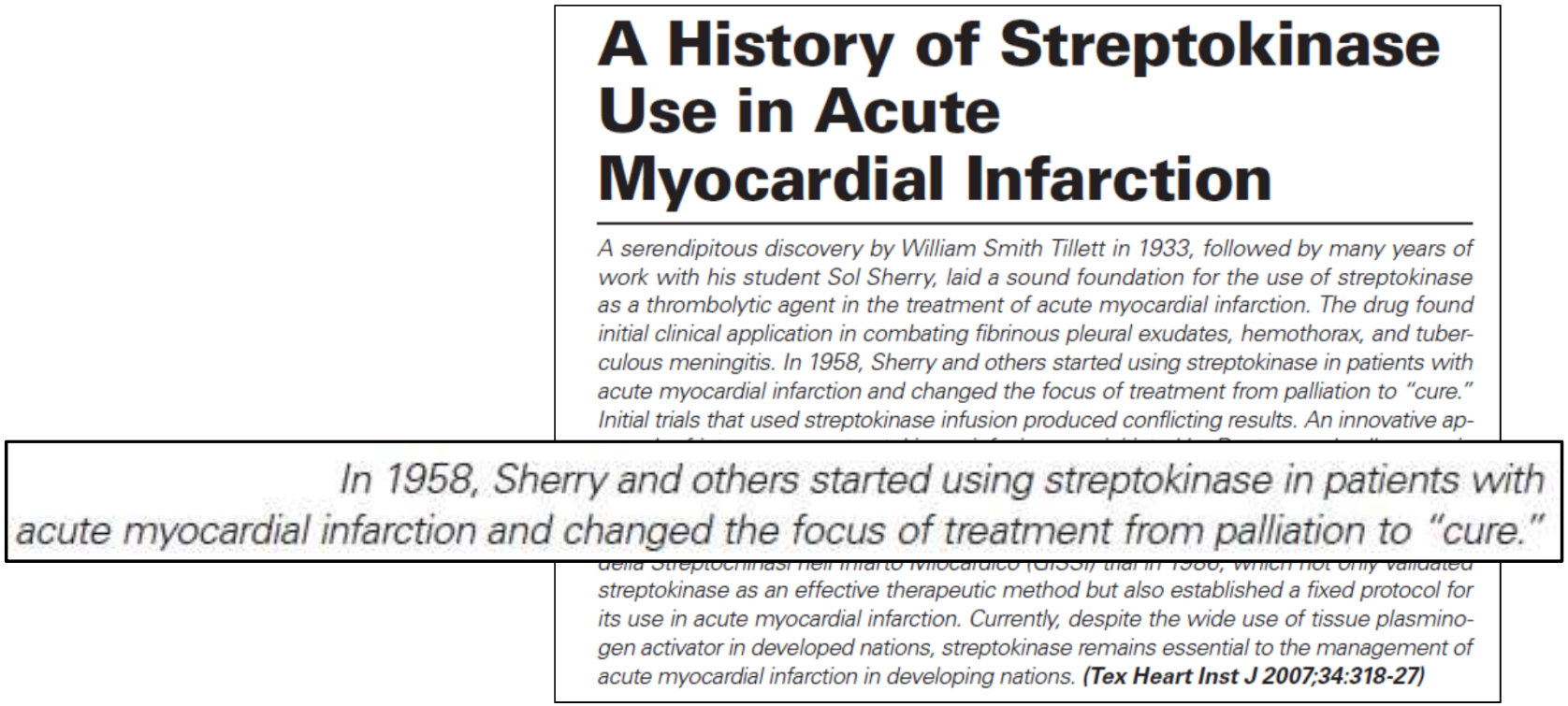
William Smith Tillett

Sol Sherry

(Tex Heart Inst J 2007;34:318-27)

Streptokinase for AMI

- Change the Focus of Treatment from Palliation to “Cure”



A History of Streptokinase Use in Acute Myocardial Infarction

A serendipitous discovery by William Smith Tillett in 1933, followed by many years of work with his student Sol Sherry, laid a sound foundation for the use of streptokinase as a thrombolytic agent in the treatment of acute myocardial infarction. The drug found initial clinical application in combating fibrinous pleural exudates, hemothorax, and tuberculous meningitis. In 1958, Sherry and others started using streptokinase in patients with acute myocardial infarction and changed the focus of treatment from palliation to “cure.” Initial trials that used streptokinase infusion produced conflicting results. An innovative ap-

In 1958, Sherry and others started using streptokinase in patients with acute myocardial infarction and changed the focus of treatment from palliation to “cure.”

streptokinase as an effective therapeutic method but also established a fixed protocol for its use in acute myocardial infarction. Currently, despite the wide use of tissue plasminogen activator in developed nations, streptokinase remains essential to the management of acute myocardial infarction in developing nations. ***(Tex Heart Inst J 2007;34:318-27)***

The American Journal of Cardiology

Volume 6, Issue 2, August 1960, Pages 525-533

Use in Human

Segmental Perfusion of the Coronary Arteries with Fibrinolysin in Man Following a Myocardial Infarction*

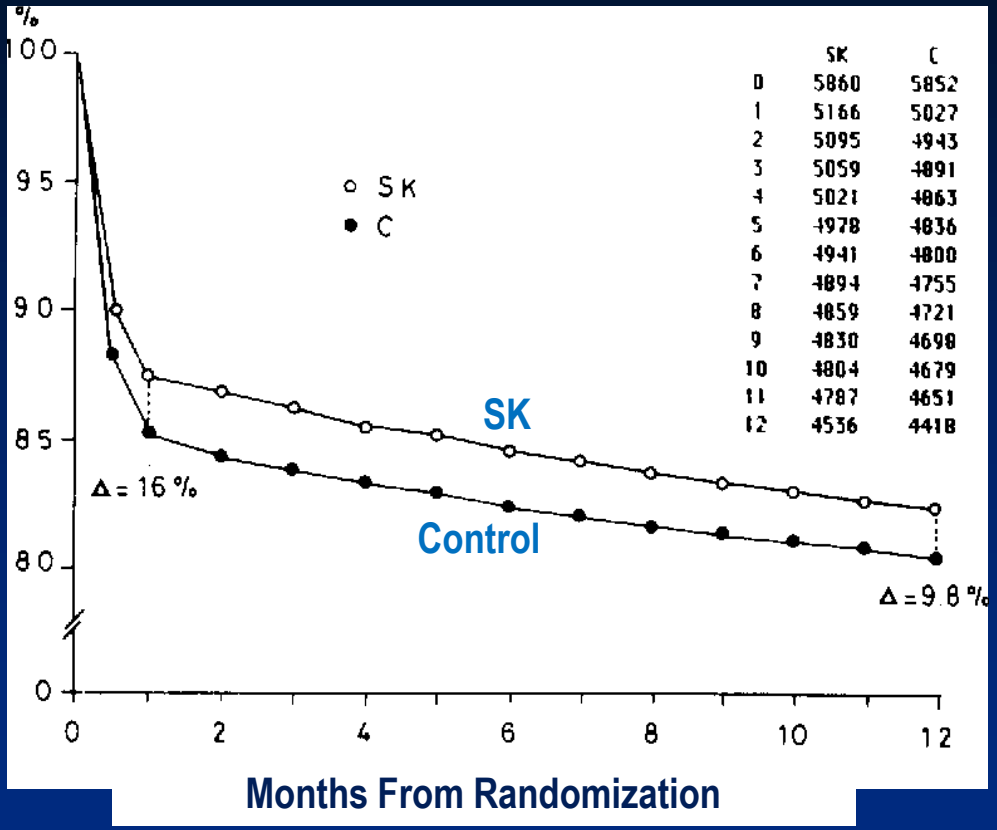
ROBERT J. BOUCEK, M.D. *and* WILLIAM P. MURPHY, JR., M.D., WITH THE TECHNICAL ASSISTANCE OF LEONARD S. SOMMER, M.D. AND IGNATIOS J. VOUDOUKIS, M.D.

Miami, Florida

RECENTLY the possibility of enzymatic digestion of a coronary thrombosis has captured the imagination of investigators. Attempts have been made in the past to supplement the blood supply of an ischemic myocardium by surgically opening the obstructed

tween atherosclerosis and thrombosis. The thrombotic lesions predominated in the proximal portion of the anterior descending branch with an accompanying transmural infarction. In addition, and of the greatest importance to the considerations of this report, a recent thrombus

GISSI-1: Streptokinase for STEMI

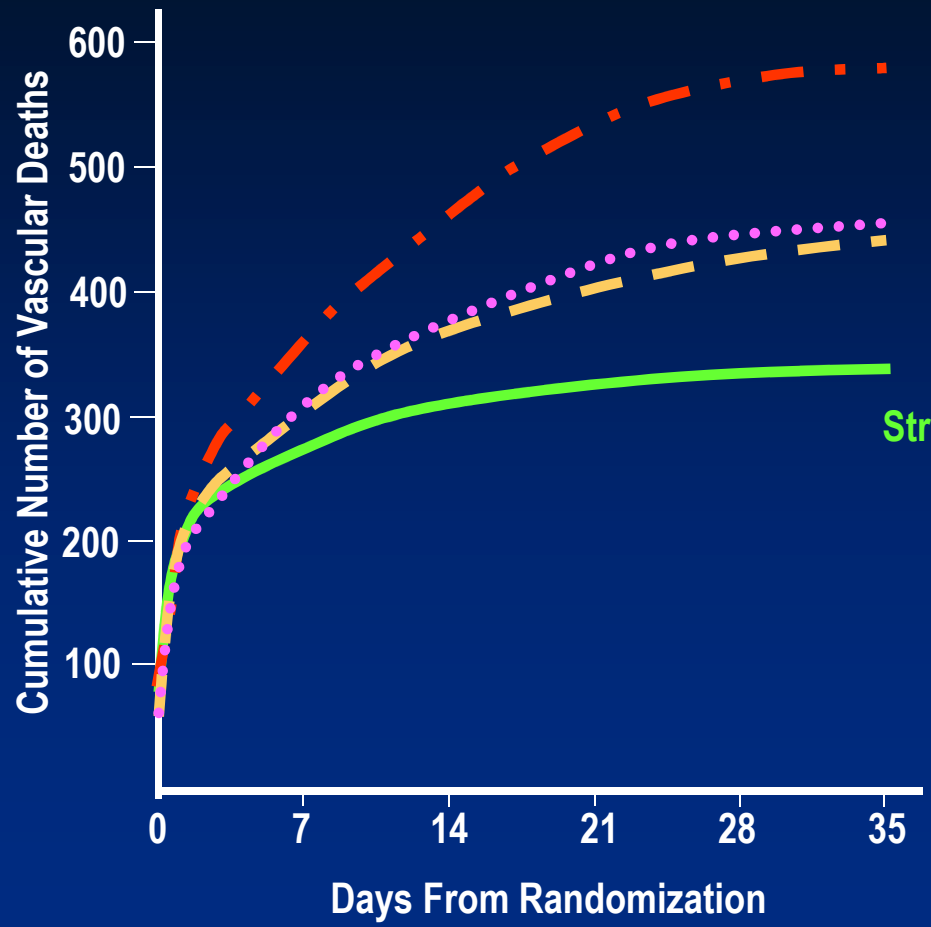


	SK	C
0	5860	5852
1	5166	5027
2	5095	4943
3	5059	4891
4	5021	4863
5	4978	4836
6	4941	4800
7	4894	4755
8	4859	4721
9	4830	4698
10	4804	4679
11	4787	4651
12	4536	4418

Lancet. 1986;1(8478):397.

ISIS-2: Streptokinase & Aspirin for STEMI

CV Death



Placebo alone:
568/4300 (13.2%)

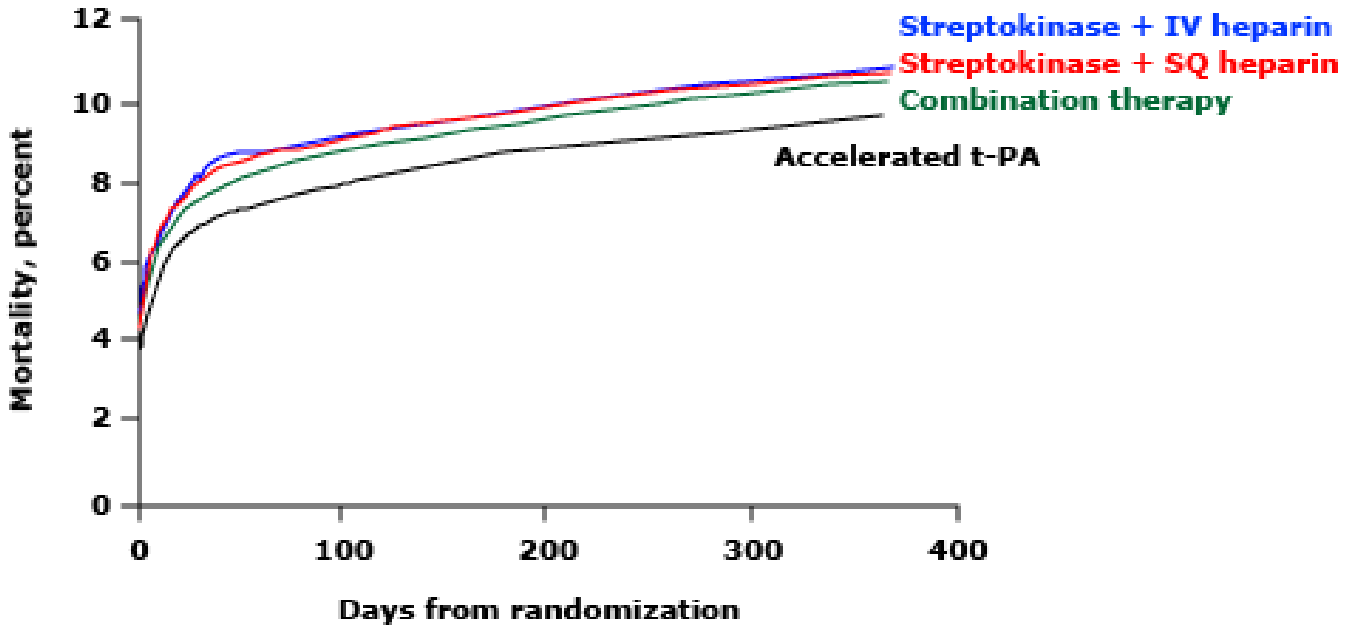
Aspirin alone:
461/4295 (10.7%)

Streptokinase alone:
448/4300 (10.4%)

Streptokinase plus aspirin:
343/4292 (8.0%)

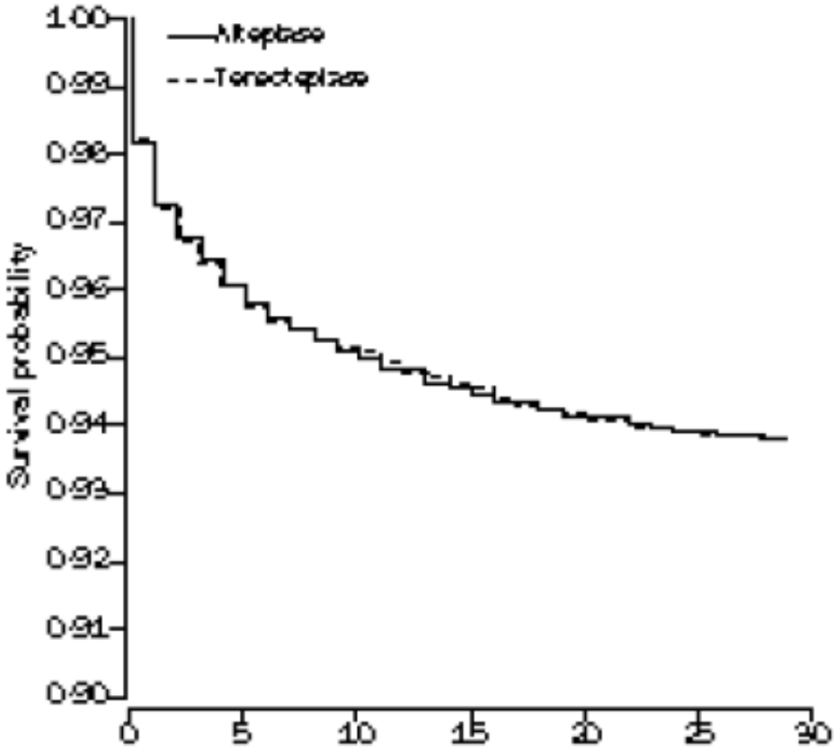
ISIS-2. Lancet 1988;2:349-360.

GUSTO-1: Benefit of accelerated t-PA in acute myocardial infarction



Califf RM, White HD, Van de Werk F, et al for the GUSTO-1 Investigators, Circulation 1996; 94:1233

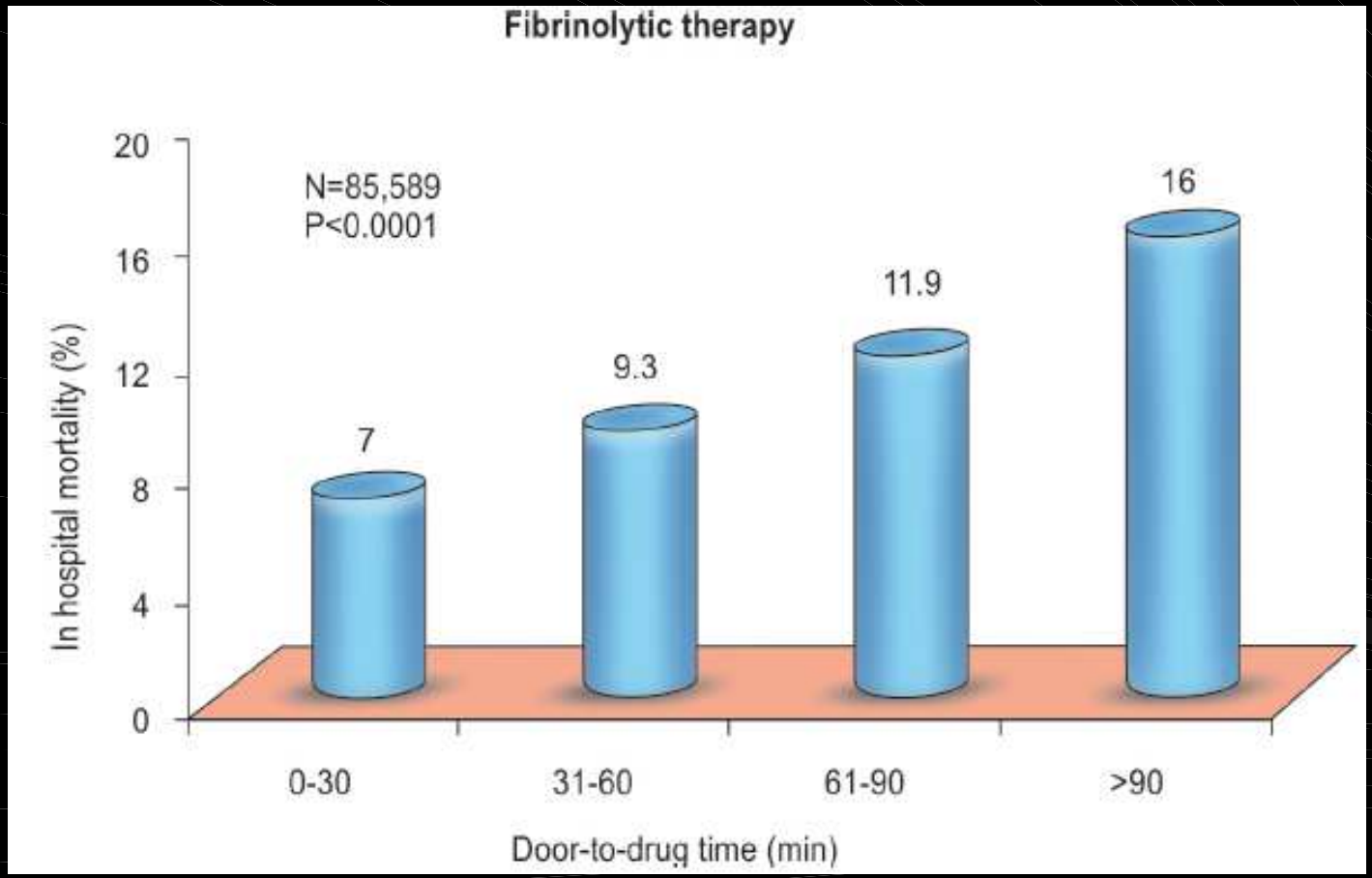
ASSENT II: TNK Vs rTPA



Lancet. 1999;354(9180):716

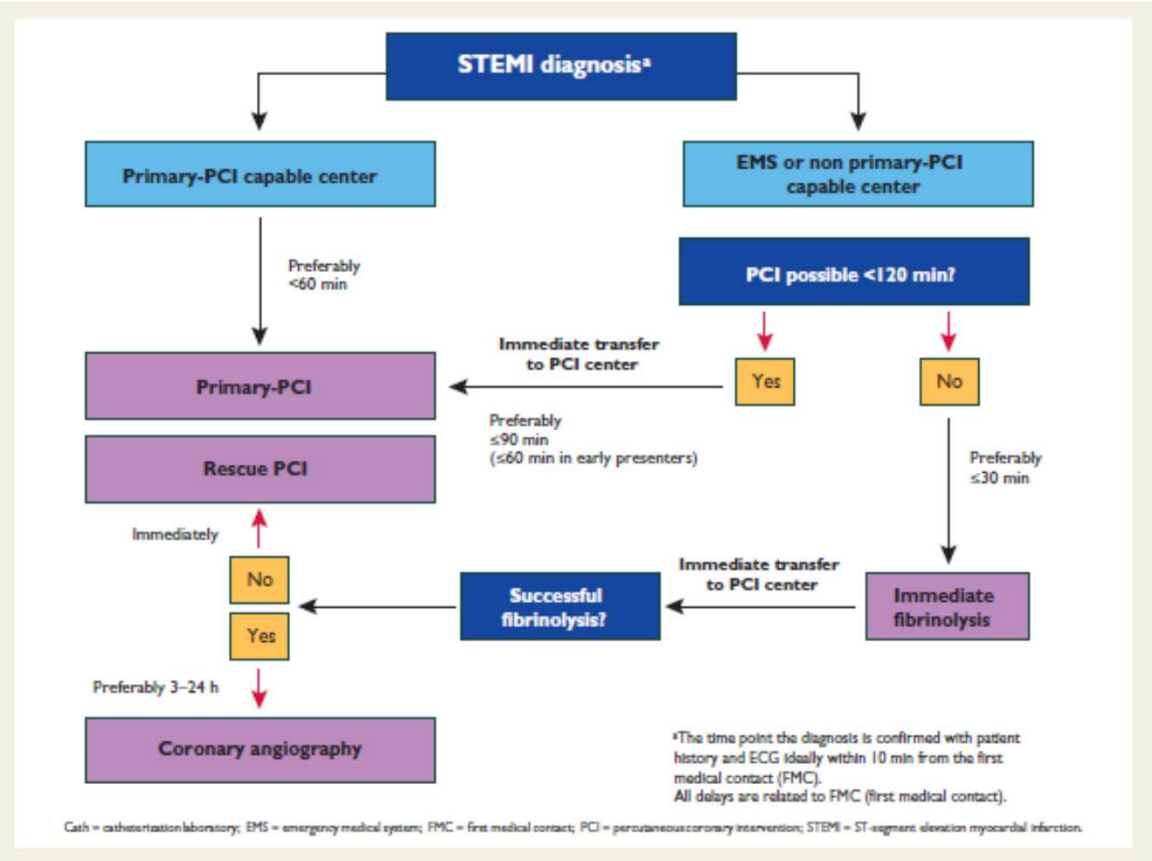
Importance of time to reperfusion in patients undergoing fibrinolysis.

For every 30-minute delay, there is a progressive increase in the in-hospital mortality rate



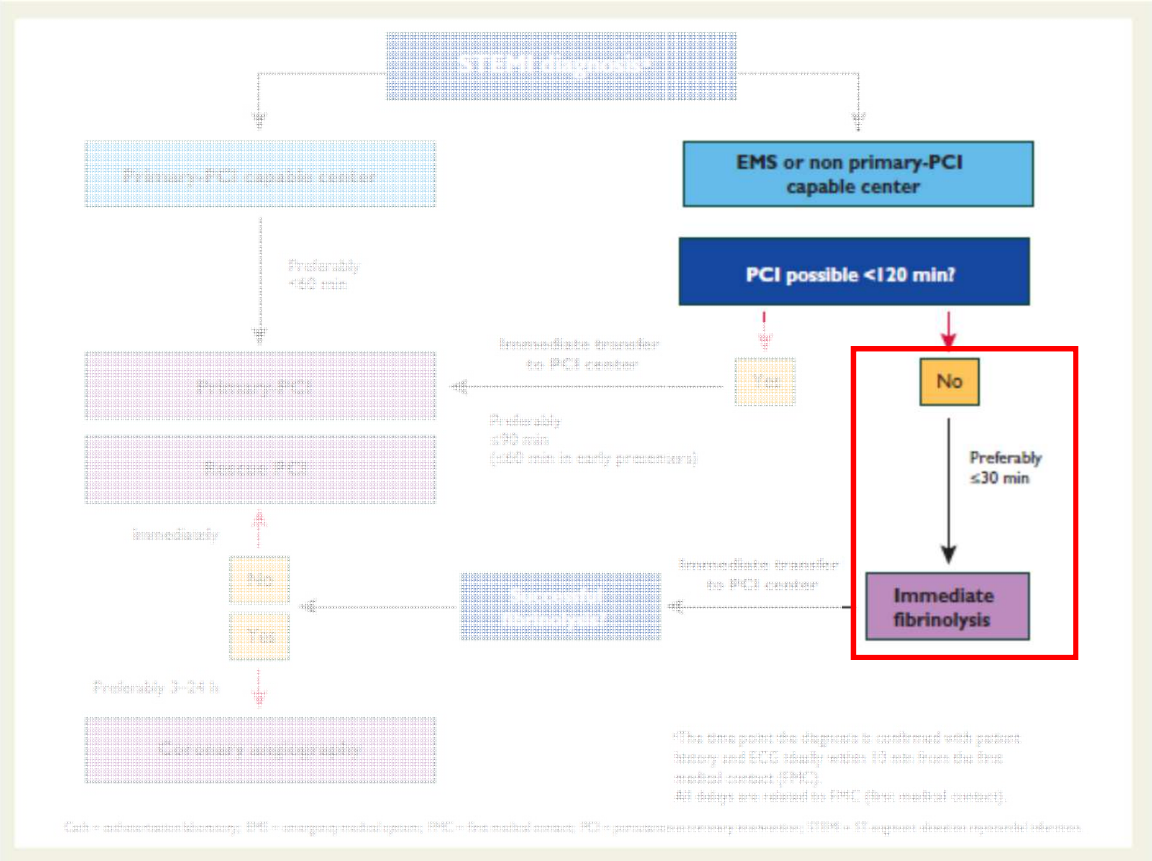
2012

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

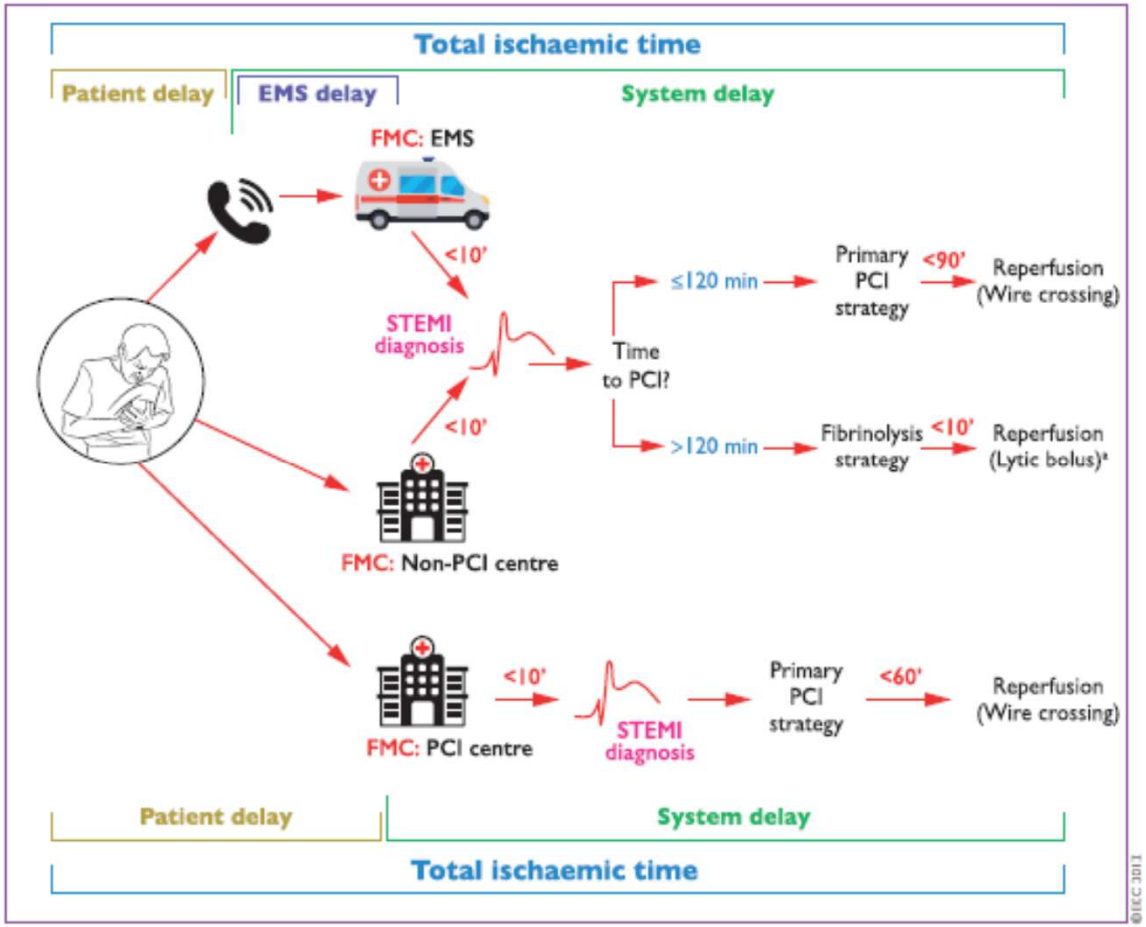


2012

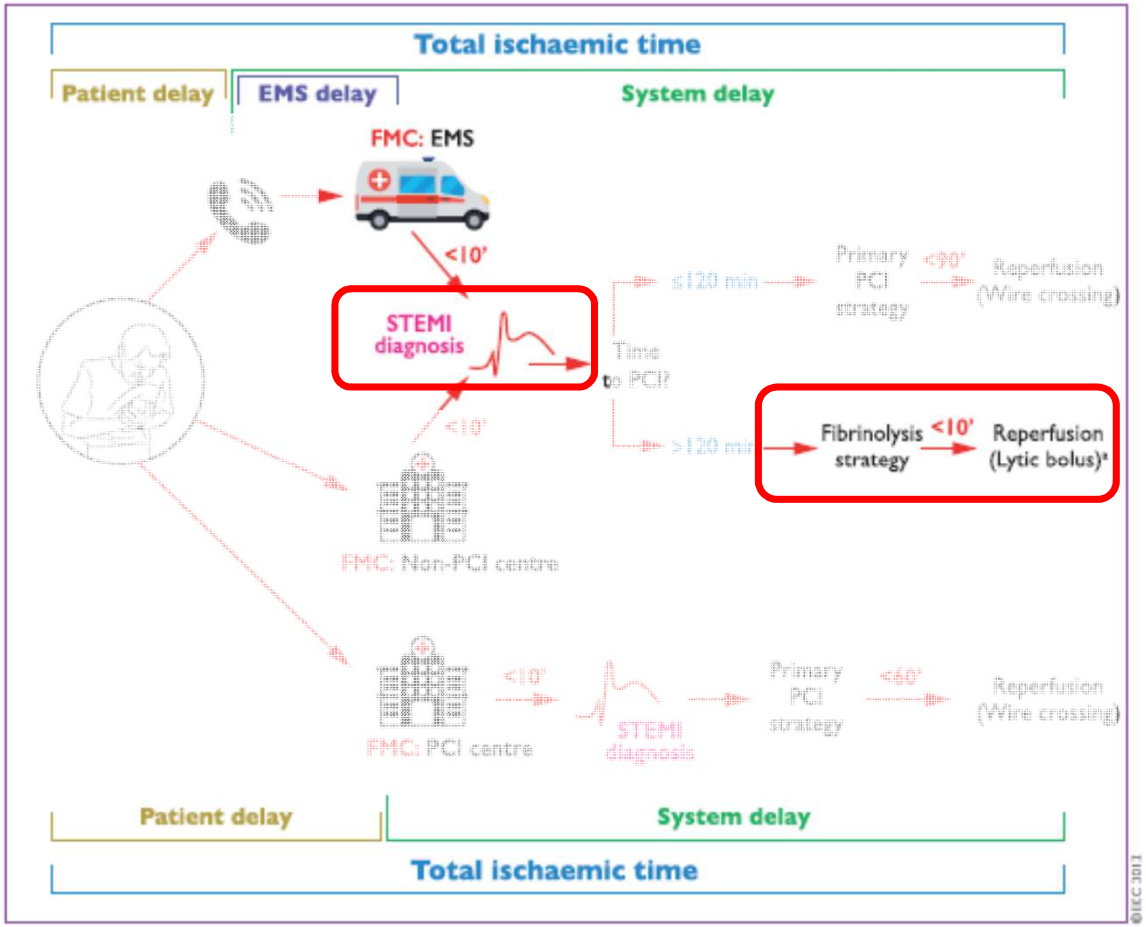
ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation



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



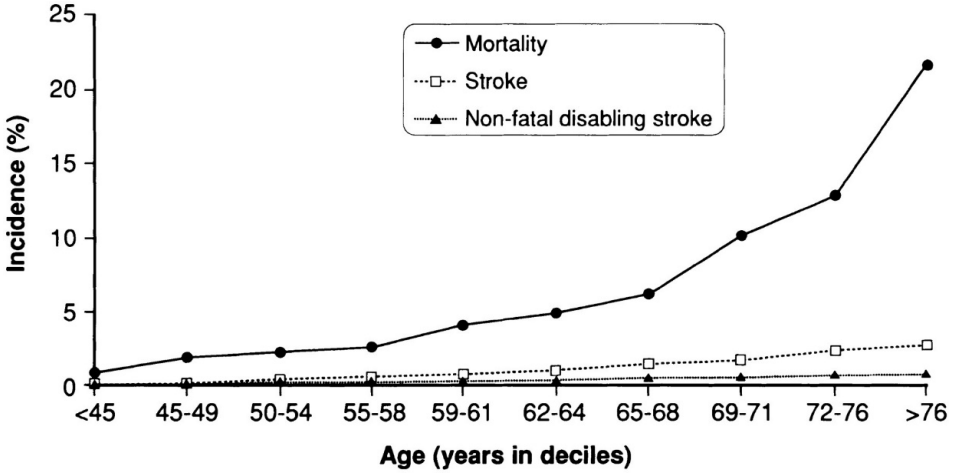
2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

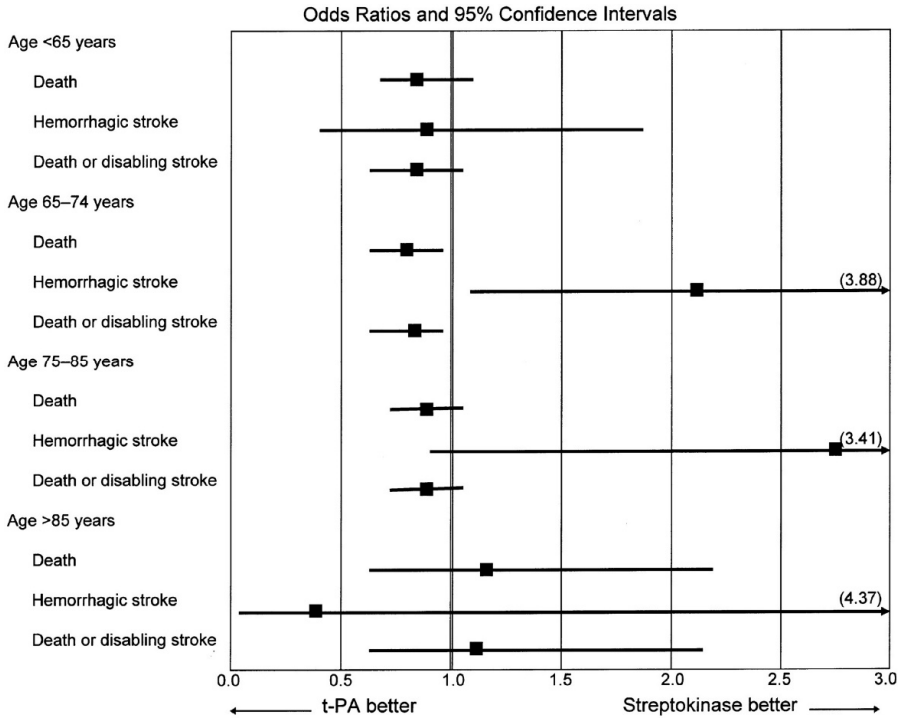


Thrombolytic in Elderly

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

- Under-represented in studies (Exclusion criteria & under-enrollment)
- High bleeding risk & mortality
- Best regimen not defined





GUSTO-1

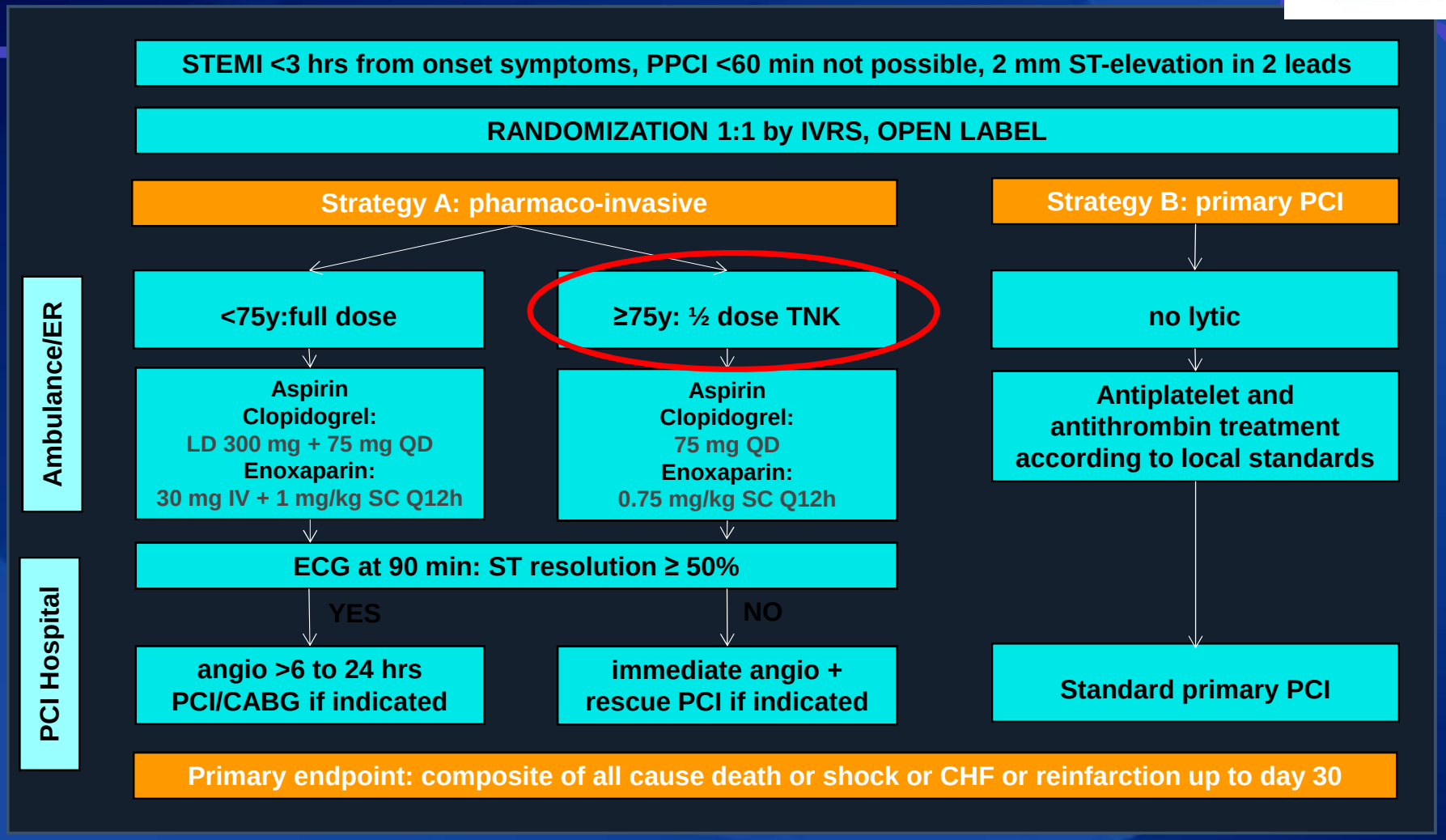
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Fibrinolysis or Primary PCI in ST-Segment Elevation Myocardial Infarction

Paul W. Armstrong, M.D., Anthony H. Gershlick, M.D., Patrick Goldstein, M.D., Robert Wilcox, M.D., Thierry Danays, M.D., Yves Lambert, M.D., Vitaly Sulimov, M.D., Ph.D., Fernando Rosell Ortiz, M.D., Ph.D., Miodrag Ostojic, M.D., Ph.D., Robert C. Welsh, M.D., Antonio C. Carvalho, M.D., Ph.D., John Nanas, M.D., Ph.D., Hans-Richard Arntz, M.D., Ph.D., Sigrun Halvorsen, M.D., Ph.D., Kurt Huber, M.D., Stefan Grajek, M.D., Ph.D., Claudio Fresco, M.D., Erich Bluhmki, M.D., Ph.D., Anne Regelin, Ph.D., Katleen Vandenberghe, Ph.D., Kris Bogaerts, Ph.D., and Frans Van de Werf, M.D., Ph.D., for the STREAM Investigative Team*

STUDY PROTOCOL



SINGLE ENDPOINTS UP TO 30 DAYS

	Pharmaco-invasive (N=944)	PPCI (N=948)	P-value
All cause death	(43/939) 4.6%	(42/946) 4.4%	0.88
Cardiac death	(31/939) 3.3%	(32/946) 3.4%	0.92
Congestive heart failure	(57/939) 6.1%	(72/943) 7.6%	0.18
Cardiogenic shock	(41/939) 4.4%	(56/944) 5.9%	0.13
Reinfarction	(23/938) 2.5%	(21/944) 2.2%	0.74

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

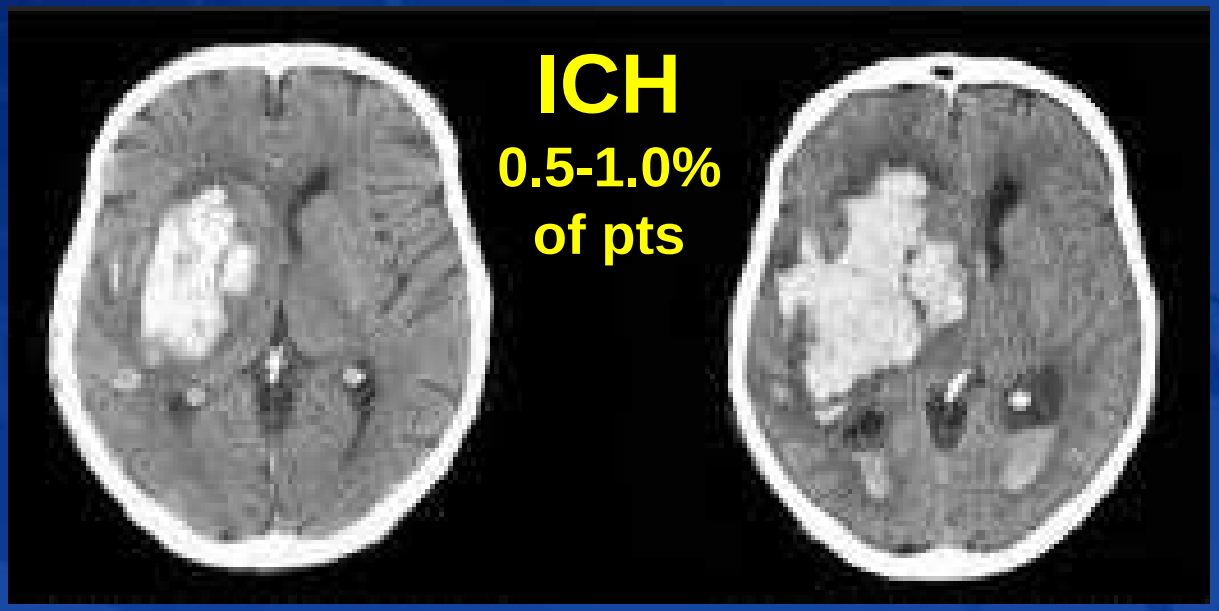
Recommendations	Class[a]	Level[b]
When fibrinolysis is the reperfusion strategy, it is recommended to initiate this treatment as soon as possible after STEMI diagnosis, preferably in the pre-hospital setting.[96,98,123,222]	I	A
A fibrin-specific agent (i.e. tenecteplase, alteplase, or reteplase) is recommended.[223,224]	I	B
A half-dose of tenecteplase should be considered in patients ≥75 years of age.[121]	IIa	B

Fibrinolytic therapy

Did save lives compared to placebo, BUT

- At best, restored TIMI 3 flow in 55% (rt-PA), +
- ↑ Incidence of recurrent ischemia and reinfarction

+



2 hours after t-PA

6 hours after t-PA

Contra-indications to fibrinolytic therapy

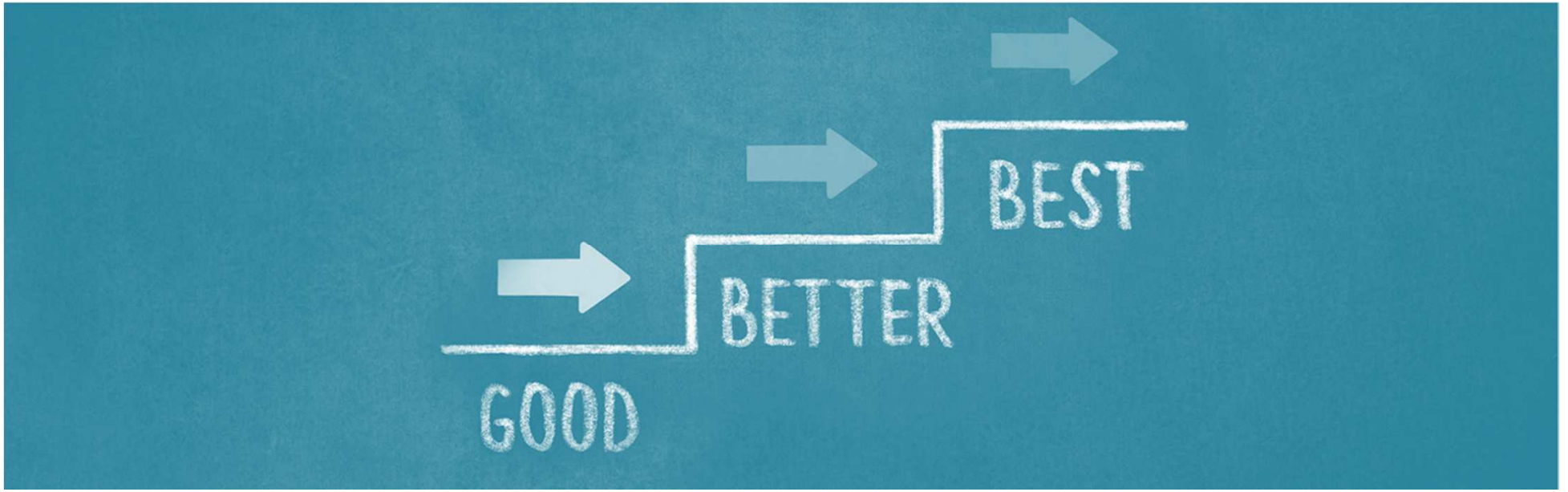
ESC European Society of Cardiology

Absolute
Previous intracranial haemorrhage or stroke of unknown origin at anytime.
Ischaemic stroke in the preceding 6 months.
Central nervous system damage or neoplasms or arteriovenous malformation.
Recent major trauma/surgery/head injury (within the preceding month).
Gastrointestinal bleeding within the past month.
Known bleeding disorder (excluding menses).
Aortic dissection.
Non-compressible punctures in the past 24 hours (e.g. liver biopsy, lumbar puncture).

Contra-indications to fibrinolytic therapy

ESC
European Society of Cardiology

Relative
Transient ischaemic attack in the preceding 6 months.
Oral anticoagulant therapy.
Pregnancy or within 1 week postpartum.
Refractory hypertension (SBP >180 mmHg and/or DBP >110 mmHg).
Advanced liver disease.
Infective endocarditis.
Active peptic ulcer.
Prolonged or traumatic resuscitation.



REPERFUSION: STRIVE FOR BETTER OPTION

ACC Thursday, April 29, 1982

PERCUTANEOUS CORONARY ANGIOPLASTY WITH AND WITHOUT PRIOR STREPTOKINASE INFUSION FOR TREATMENT OF ACUTE MYOCARDIAL INFARCTION, Geoffrey O. Hartzler, M.D., F.A.C.C.; Barry D. Rutherford, M.D., F.A.C.C.; David R. McConahay, M.D., F.A.C.C., Mid-America Heart Institute, St. Luke's Hospital, Kansas City, Missouri.

Coronary angioplasty (PTCA) was successfully performed in 16 pts during acute myocardial infarction (AMI). There were 13 males and 3 females with mean age of 62 yrs (46-74 yrs) catheterized at mean 3.3 hrs (1-10 hrs, mode 2.5 hrs) following onset of continuous chest pain with ST segment elevation in 13 pts, ST depression in 3 pts and new Q-waves in 6 pts. Intracoronary streptokinase (ICSK) opened 6 of 8 total occlusions and removed thrombus in 2 pts with subtotal occlusions (STO) prior to PTCA of residual high-grade atheromatous stenoses. PTCA without ICSK was performed in 2 pts with total occlusions and 6 pts with STO. Twenty segments were dilated including LAD - 8 pts, RCA - 6 pts, Circ - 5 pts, and vein graft - 1 pt. Mean residual stenosis was 28% with reduction of intracoronary pressure gradients from mean 67 mm Hg. to 0-10 mm Hg. One laboratory death occurred following hemodynamically and angiographically successful PTCA in a pt with LV ejection fraction of 7%. A second pt underwent coronary bypass surgery because of additional inaccessible coronary stenoses. The post-procedure course was stable in all pts. Repeat cath in 11 pts at 12 days (5-36 days) showed patency of all dilated segments, improved ejection fraction in 10 pts and improved regional wall motion in 10 pts. At follow-up of 6 mo (1.5-12.5 mo) no AMI have occurred, 13 pts are asymptomatic and 2 pts are functional-Class II. We conclude that urgent PTCA w/without ICSK can relieve pain, stabilize the course and limit myocardial infarction in selected pts with AMI.

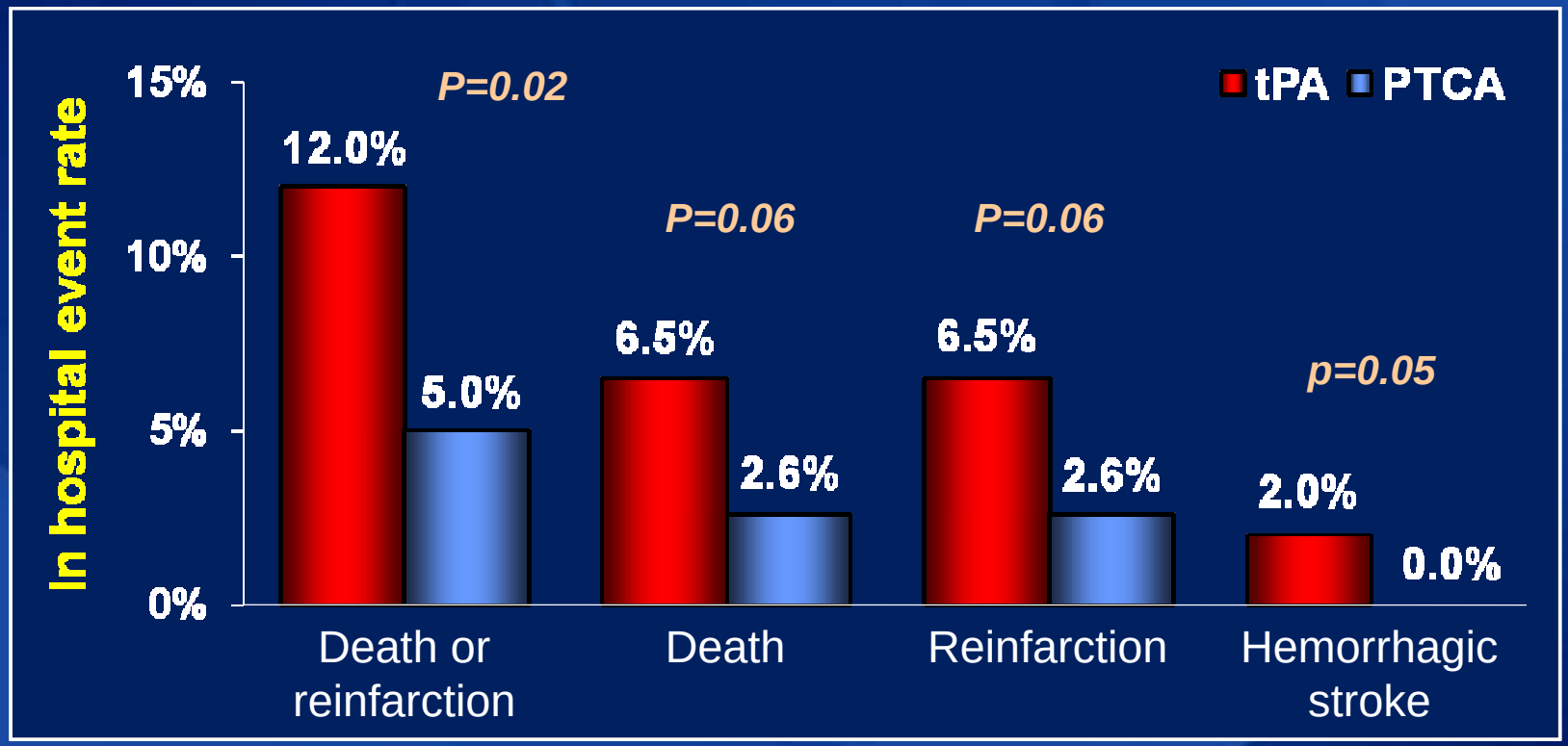
"PTCA without ICSK was performed in 2 pts with total occlusions and 6 pts with subtotal occlusions."

"Repeat cath at 12 days showed patency of all dilated segments…"

"At follow-up of 6 mo no AMIs have occurred, 13 pts are asymptomatic and 2 pts are Class II"

The PAMI (Primary Angioplasty in Myocardial Infarction) Trial

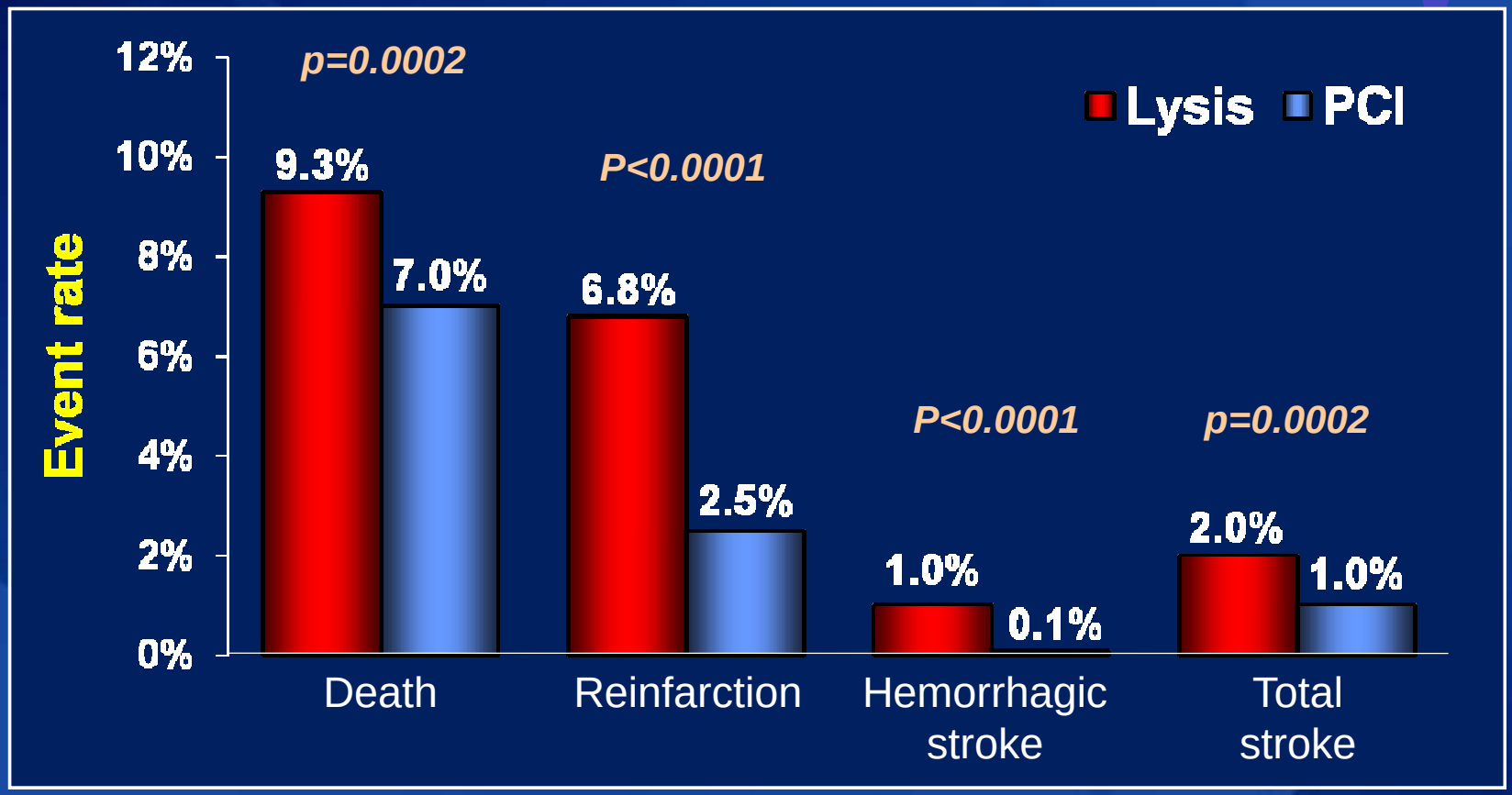
395 pts of any age with AMI <12° duration were prospectively randomized at 12 international centers to primary PTCA vs. a 3° 100 mg t-PA infusion: **93% TIMI-3 flow with PPCI!**



Grines CL et al. NEJM. 1993;328:673-9

From PAMI to 23 RCTs of PCI vs. Lysis

N = 7,739



Keeley, Grines. *Lancet* 2003;361:13-20

Reperfusion therapy

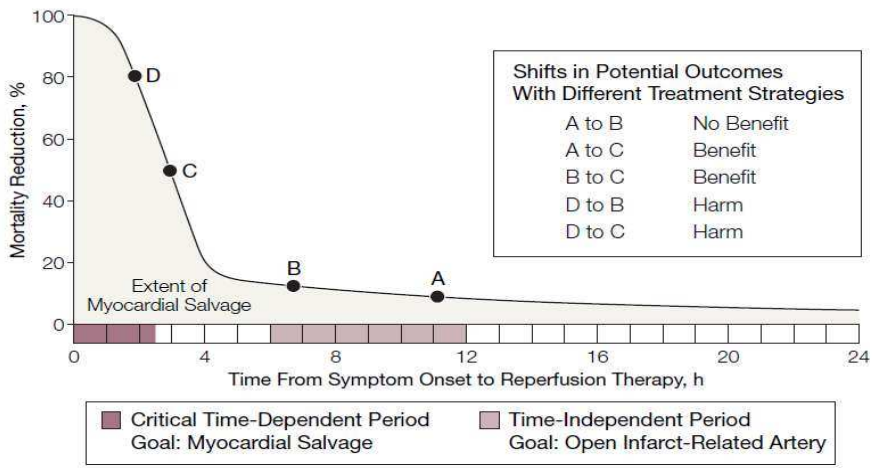
ESC
European Society of Cardiology

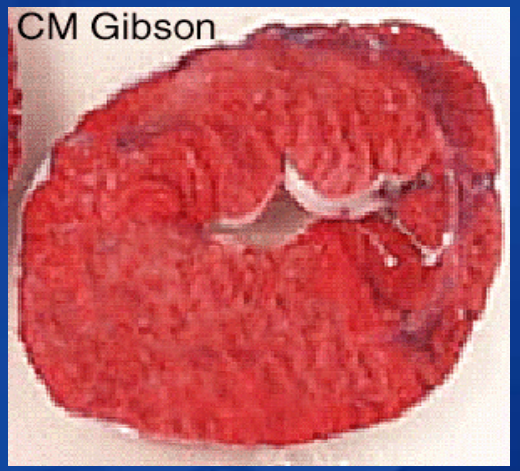
Recommendations	Class	Level
Reperfusion therapy is indicated in all patients with symptoms of ischaemia of ≤12 hours duration and persistent ST-segment elevation.	I	A
A *primary PCI strategy* is recommended over fibrinolysis within indicated time frames.	I	A
If primary PCI cannot be performed timely after STEMI diagnosis, fibrinolytic therapy is recommended within 12 hours of symptom onset in patients without contra-indications.	I	A

Importance of Time In Salvaging Myocardium

Time is Myocardium = Infarct Size is Outcome

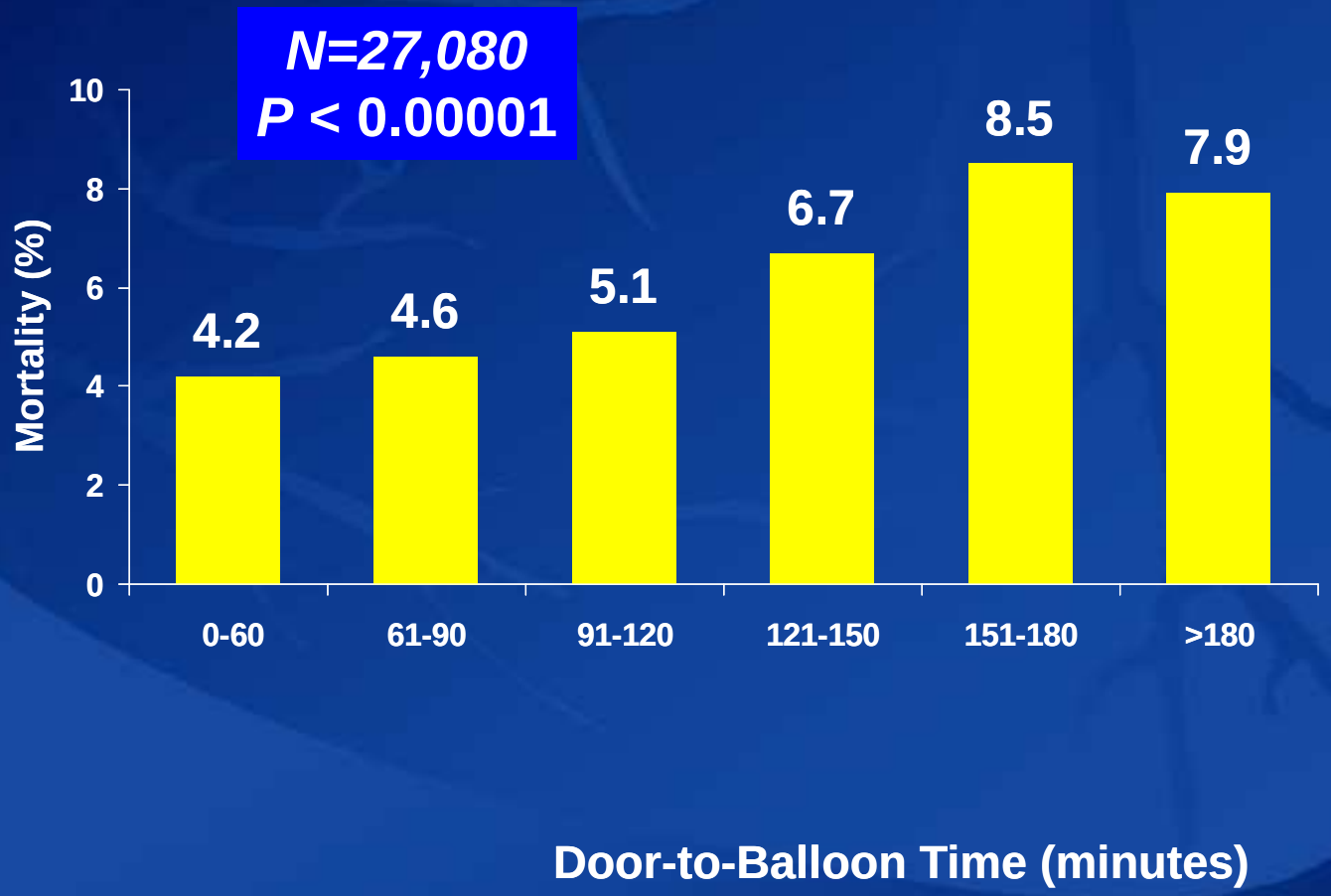
Figure. Hypothetical Construct of the Relationship Among the Duration of Symptoms of Acute MI Before Reperfusion Therapy, Mortality Reduction, and Extent of Myocardial Salvage





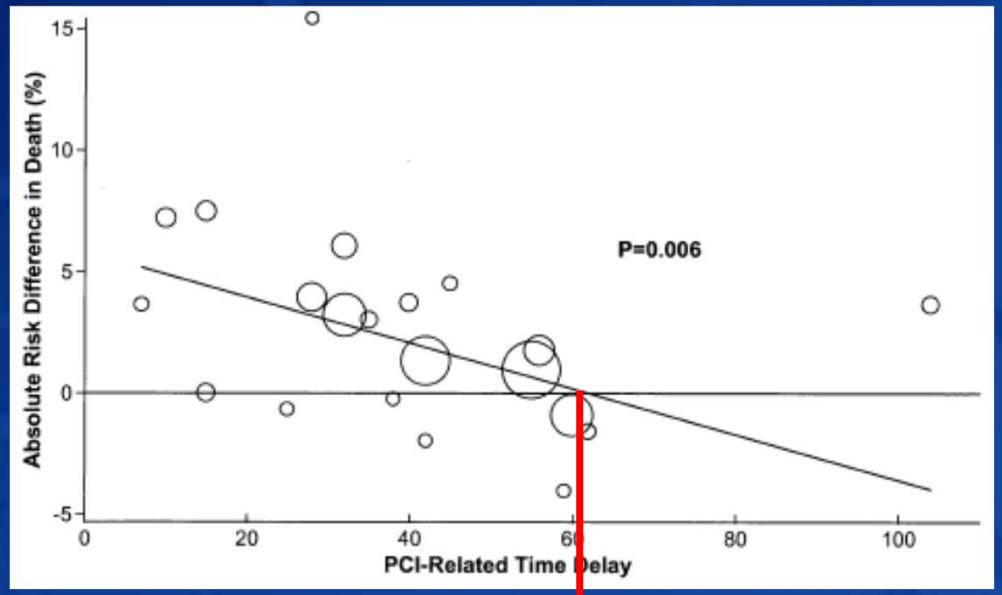
JAMA 2005

NRMI-2: Primary PCI Door-to-Balloon time vs. Mortality



JAMA 2000; 283:2941-7.

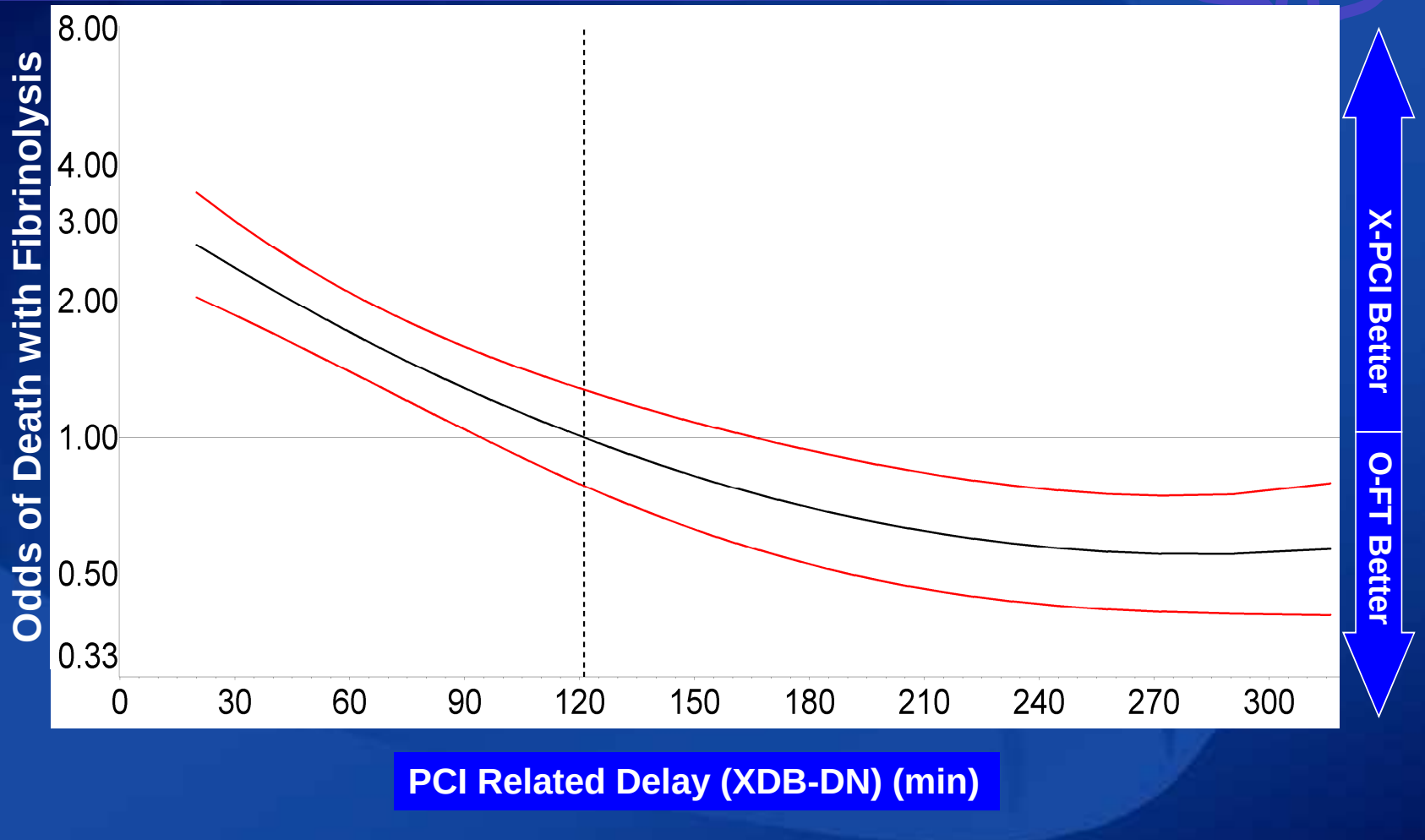
Time issue and reperfusion strategy



If PCI-related time delay >60 min,

the benefit of PCI over thrombolyis vanishes

Loss of PCI Related Mortality Benefit as a Function of Delay



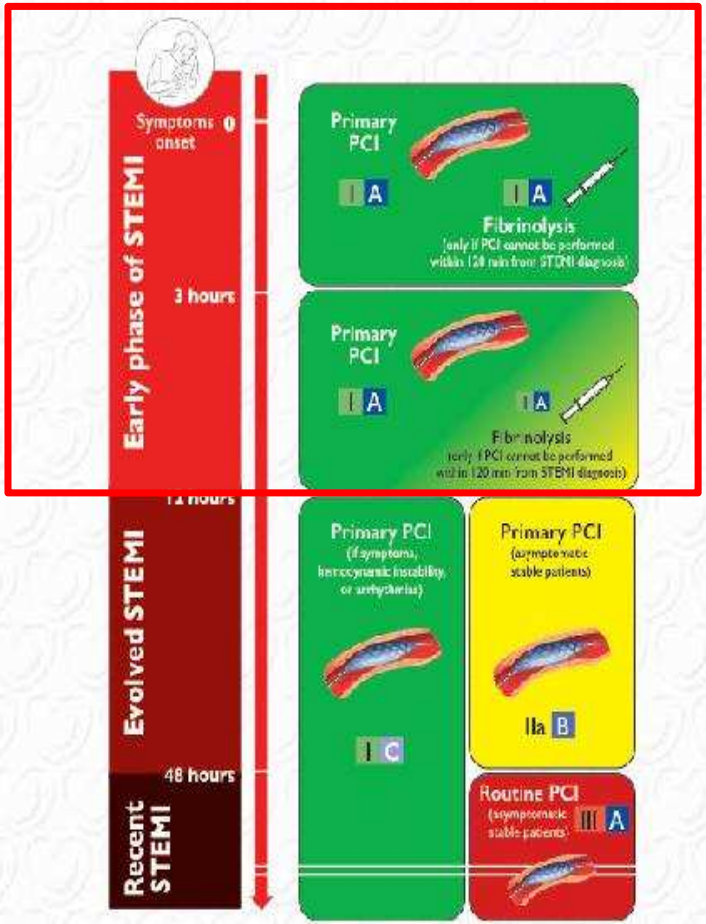
Pinto DS. Circulation 2011

Primary PCI: Time Is the Key

1. Estimated PCI-related delay
   > Decide on primary PCI Vs thrombolytic

2. Once decided, primary PCI as fast as possible

Reperfusion strategies in the infarct-related artery according to time from symptoms onset



ESC European Society of Cardiology

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

Reperfusion strategies in the infarct-related artery according to time from symptoms onset

ESC
European Society of Cardiology

Early phase of STEMI

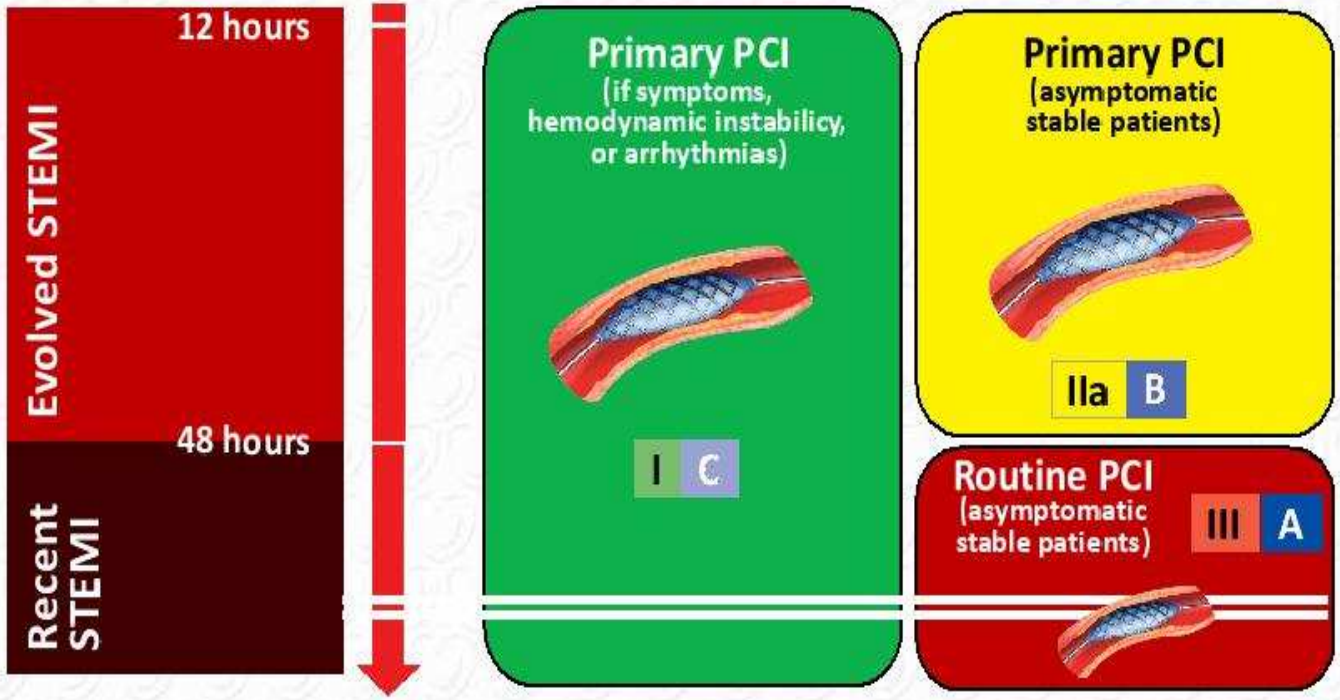
0
Symptoms onset
3 hours
12 hours

Primary PCI
I A
I A
Fibrinolysis
(only if PCI cannot be performed within120 min from STEMI diagnosis)

Primary PCI
I A
I A
Fibrinolysis
(only if PCI cannot be performed within120 min from STEMI diagnosis)

Reperfusion strategies in the infarct-related artery according to time from symptoms onset *(continued)*

ESC
European Society of Cardiology



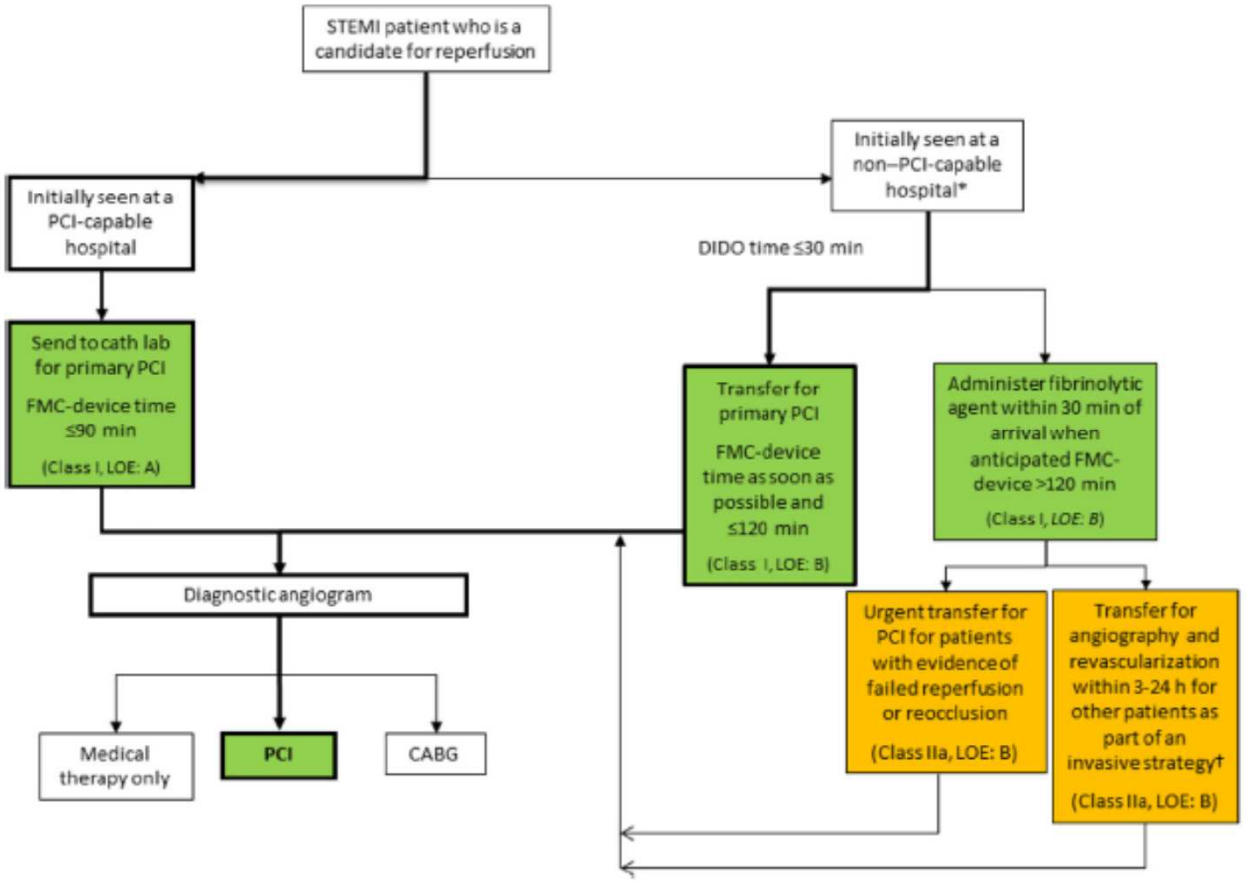
Primary PCI: Time Is the Key

1. Estimated PCI-related delay
   > Decide on primary PCI Vs thrombolytic

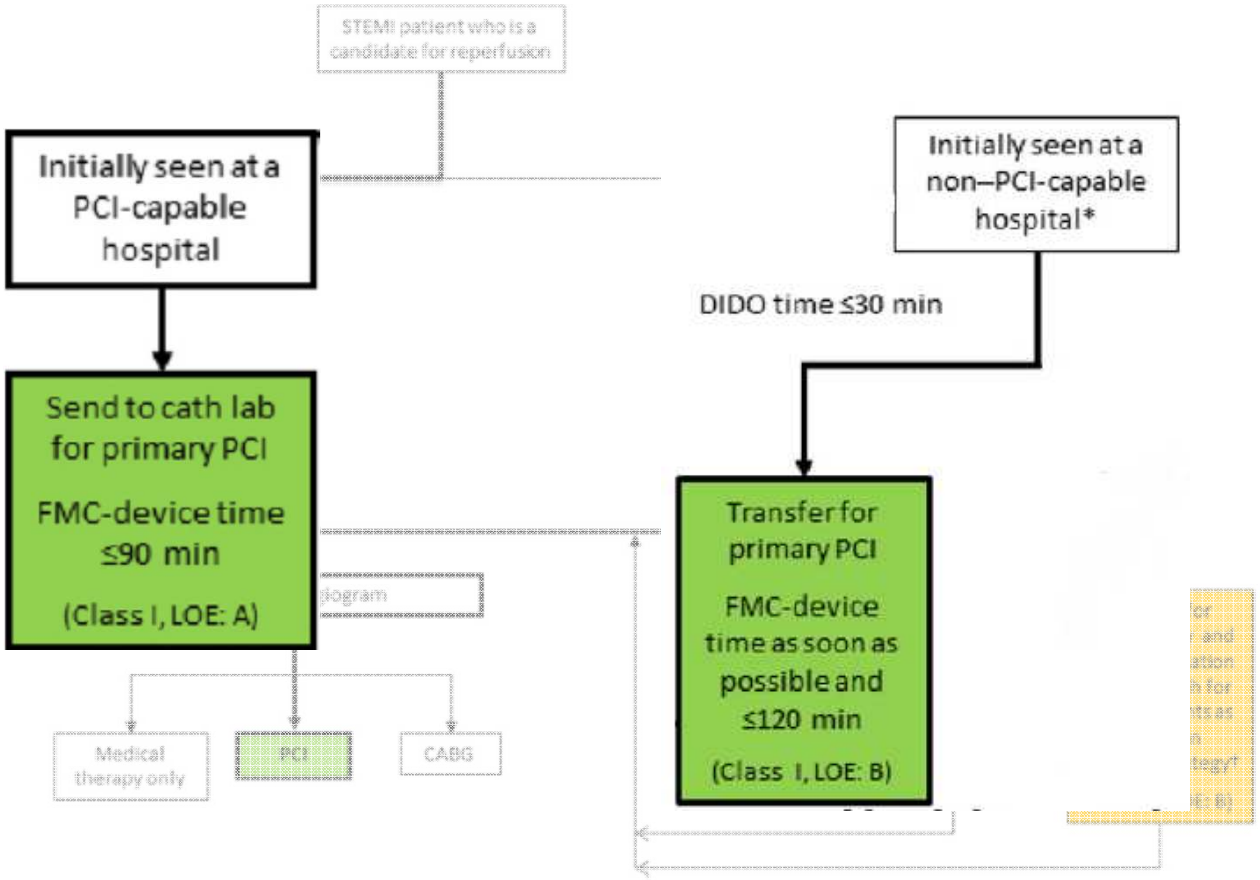
2. Once decided, primary PCI as fast as possible

PERFORMANCE GOALS OF PRIMARY PCI

2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction

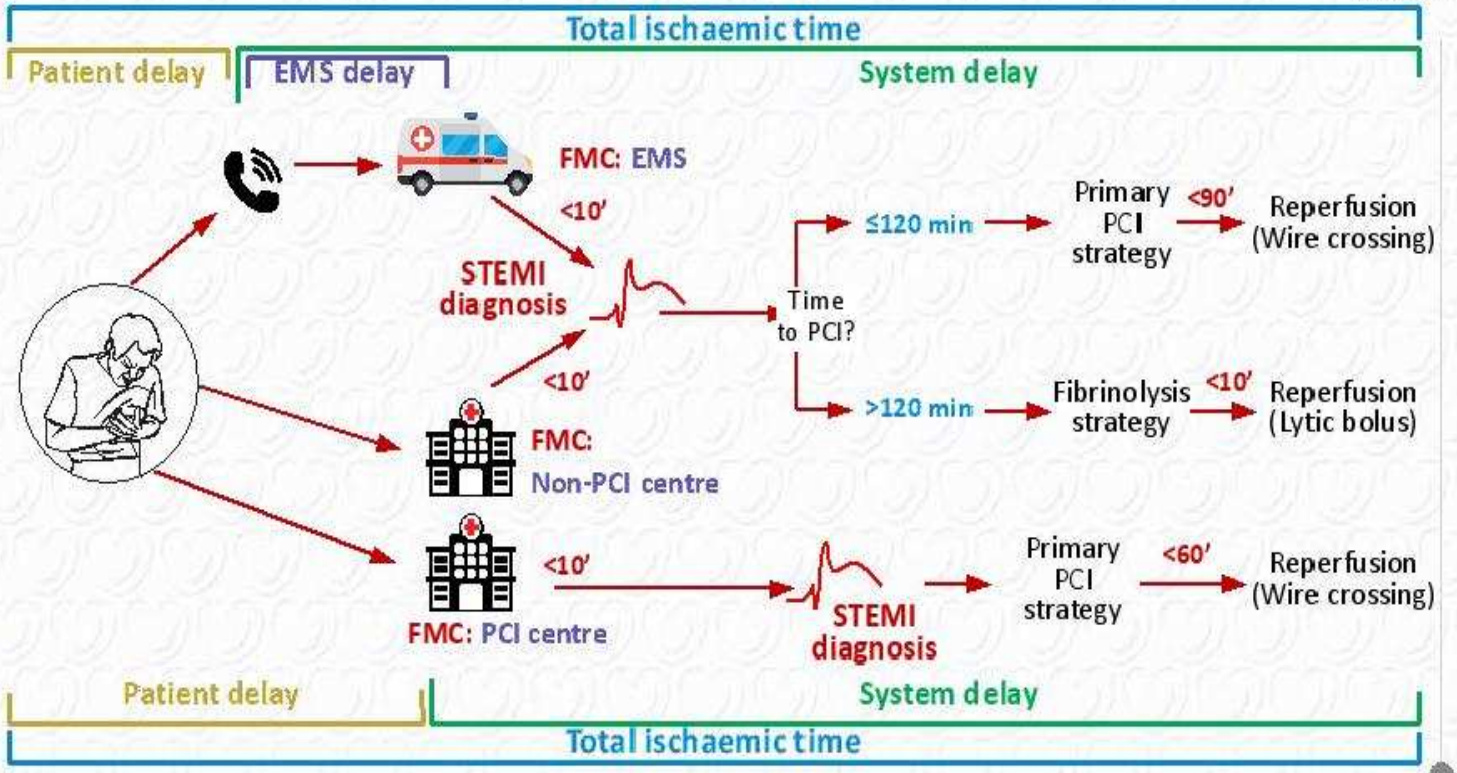


2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction



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

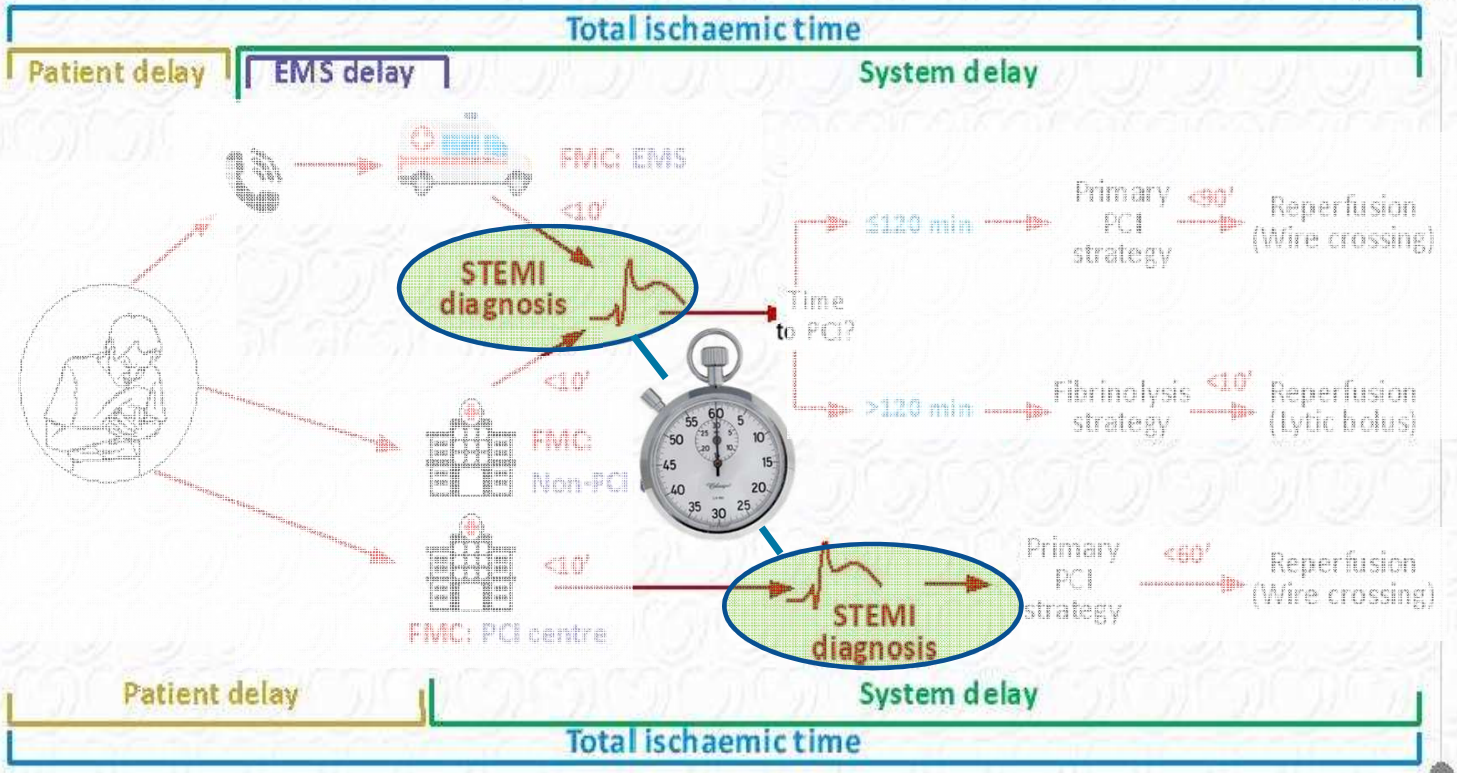
ESC 2017
European Society of Cardiology



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

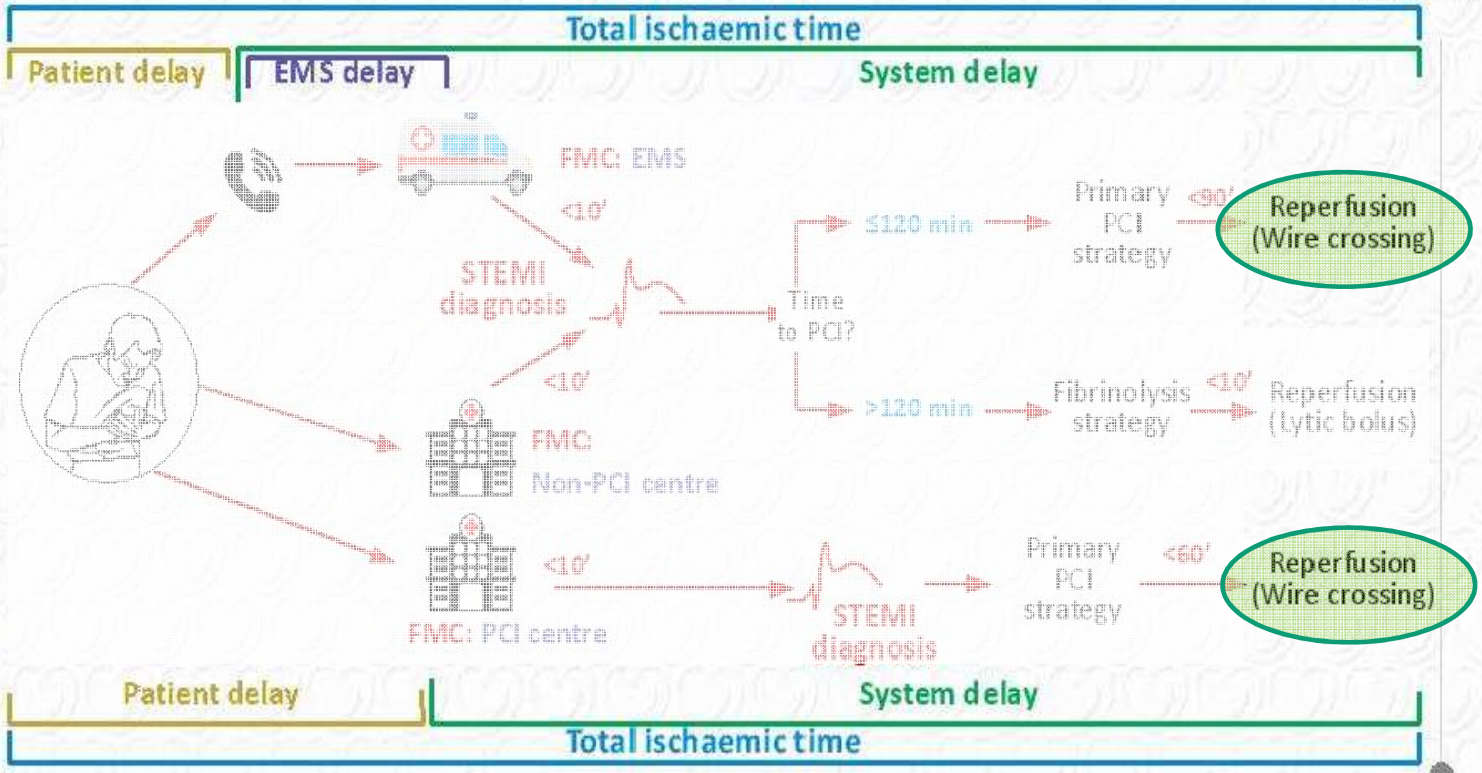
Modes of patient presentation, components of ischaemic time and flowchart for reperfusion strategy selection

ESC 2017
European Society of Cardiology



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

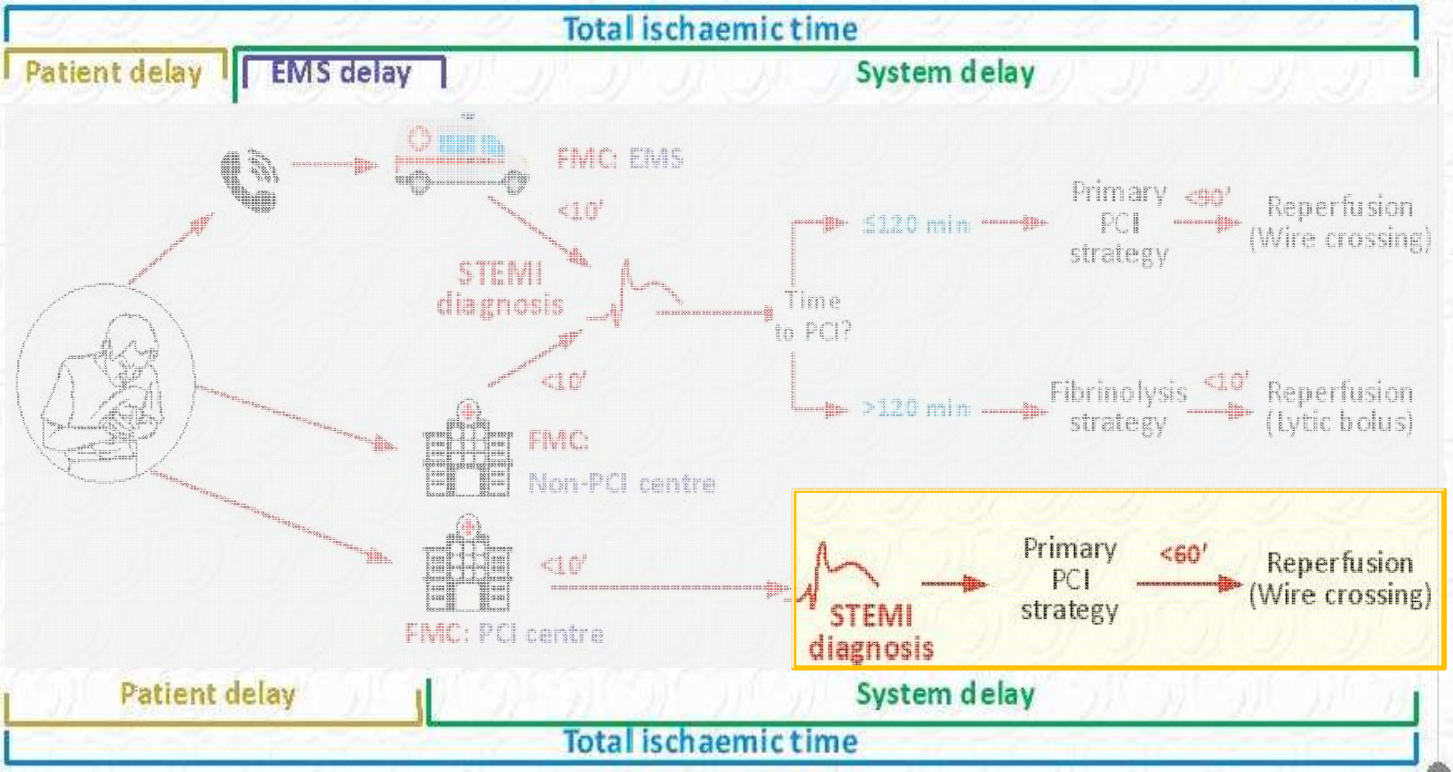
ESC 2017
European Society of Cardiology



www.escardio.org/guidelines 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

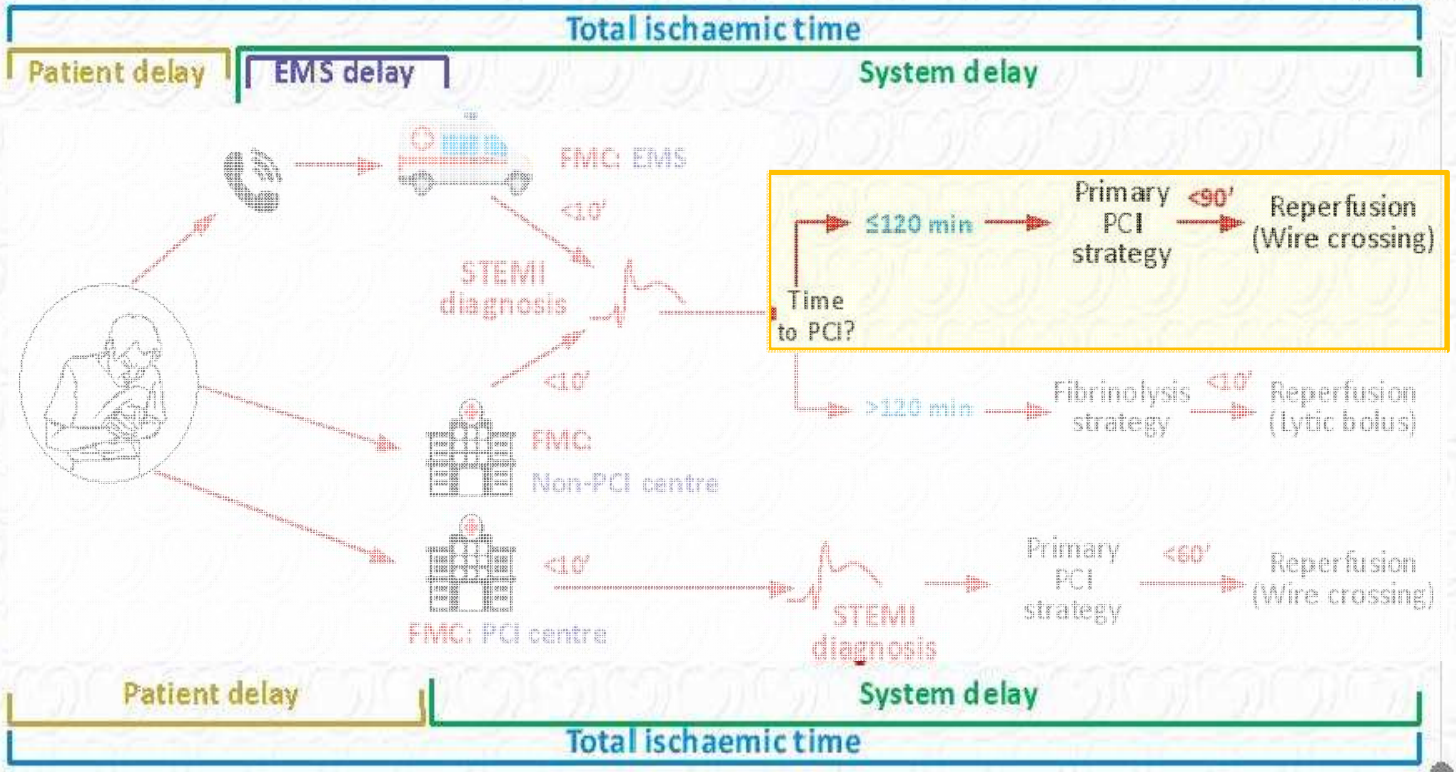
ESC 2017
European Society of Cardiology



www.escardio.org/guidelines 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

ESC 2017
European Society of Cardiology



TARGET BEYOND FMC/DX TO REPERFUSION TIME

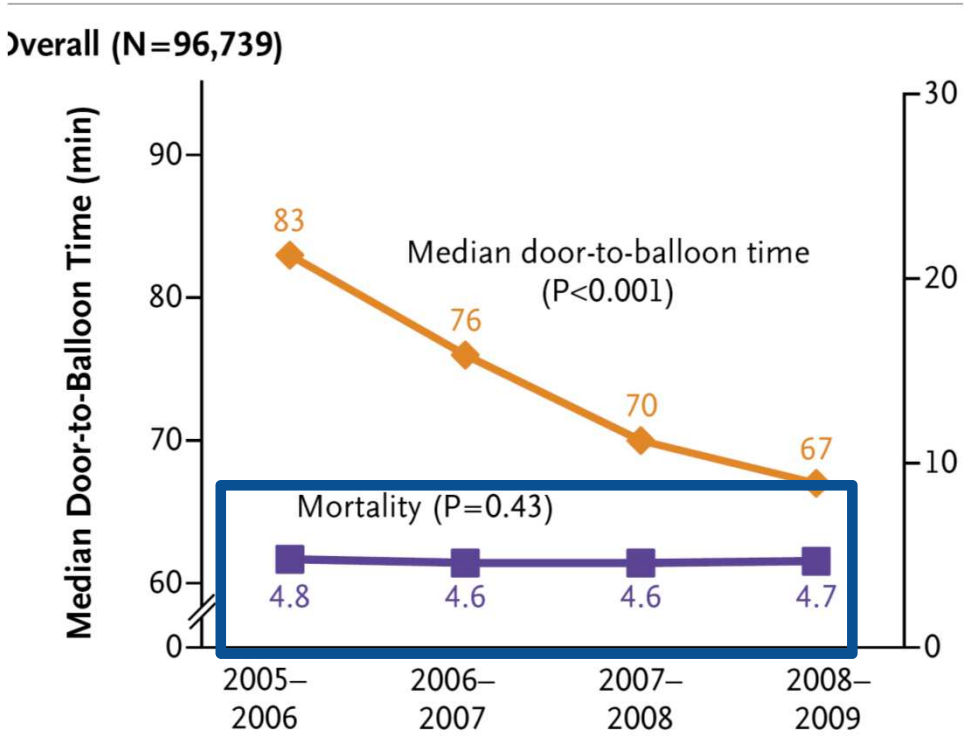
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 5, 2013 VOL. 369 NO. 10

Door-to-Balloon Time and Mortality among Patients Undergoing Primary PCI

Daniel S. Menees, M.D., Eric D. Peterson, M.D., Yongfei Wang, M.S., Jeptha P. Curtis, M.D., John C. Messenger, M.D., John S. Rumsfeld, M.D., Ph.D., and Hitinder S. Gurm, M.B., B.S.

In-hospital mortality unchanged with further reduction in DTBT



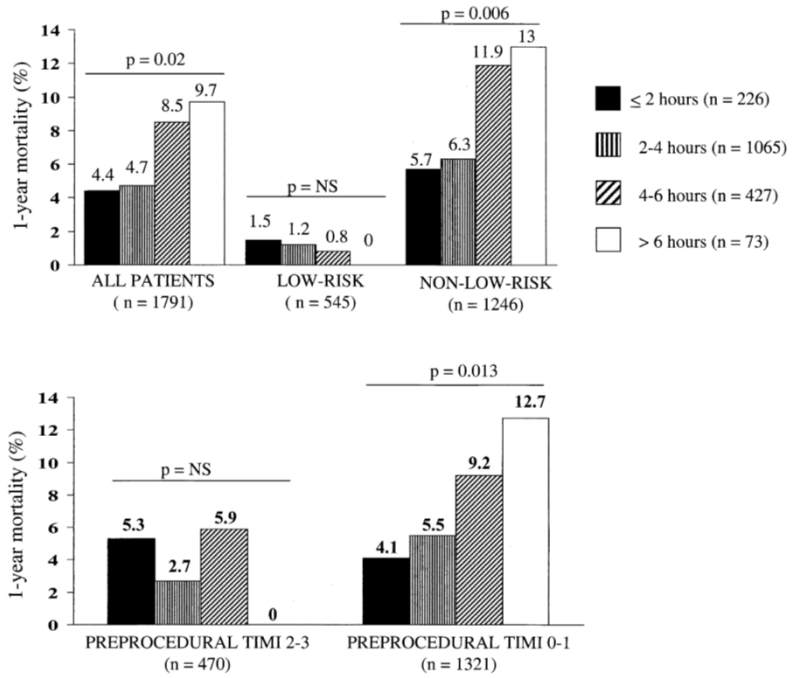
N Engl J Med 2013;369:901-9

Symptom-Onset-to-Balloon Time and Mortality in Patients With Acute Myocardial Infarction Treated by Primary Angioplasty

Giuseppe De Luca, MD, Harry Suryapranata, MD, PHD, Felix Zijlstra, MD, PHD, FACC, Arnoud W. J. van't Hof, MD, PHD, Jan C. A. Hoorntje, MD, PHD, A. T. Marcel Gosselink, MD, PHD, Jan-Henk Dambrink, MD, PHD, Menko-Jan de Boer, MD, PHD, FACC, on behalf of the ZWOLLE Myocardial Infarction Study Group

Zwolle, the Netherlands

JACC Vol. 42, No. 6, 2003
September 17, 2003:991–7

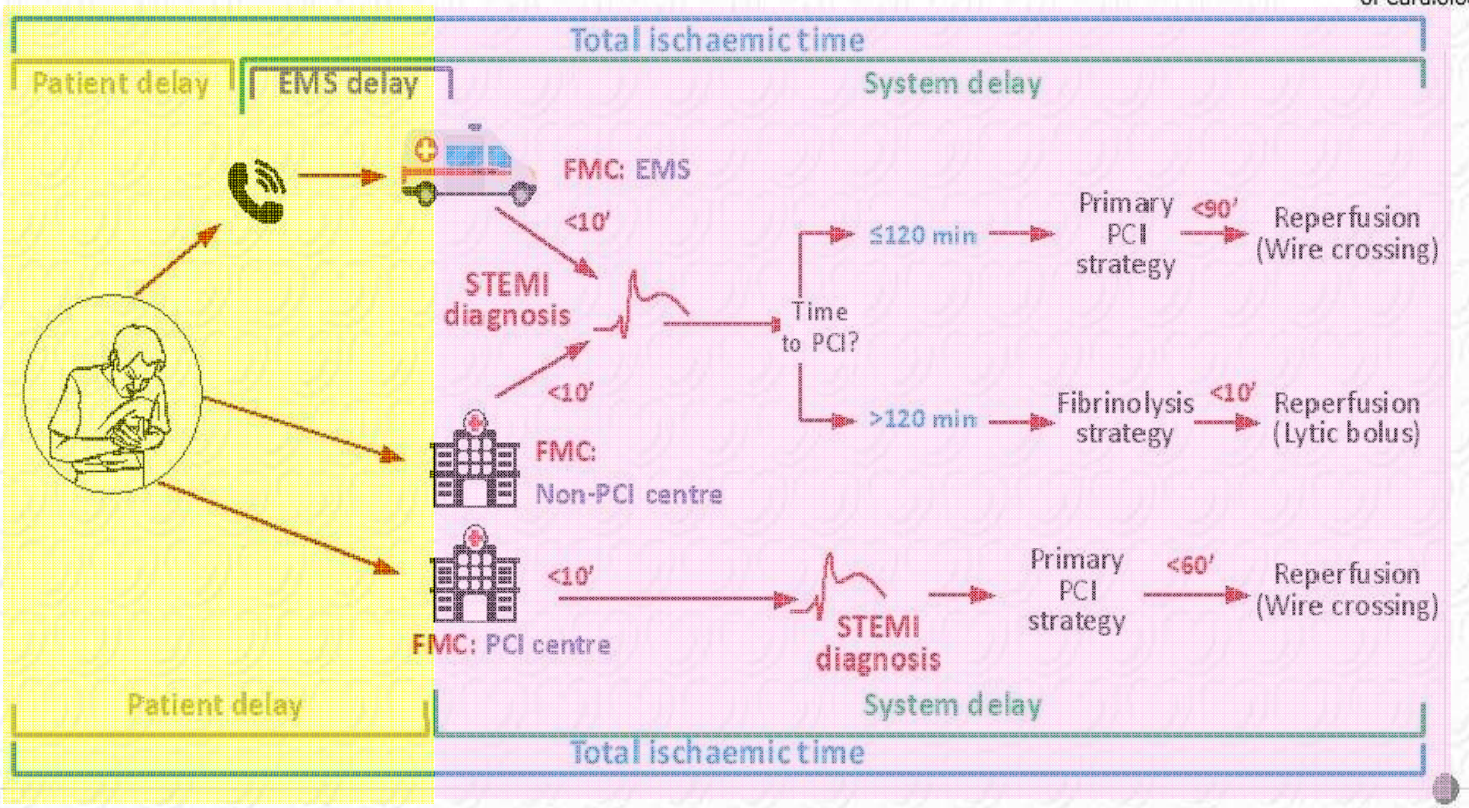


- STB and not DTB was related to mortality for single centers
- Esp if >4 h in the non-low risk group
- Caveat is that DTB<90min

J Am Coll Cardiol 2003;42:991–7

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

ESC 2017
European Society of Cardiology



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

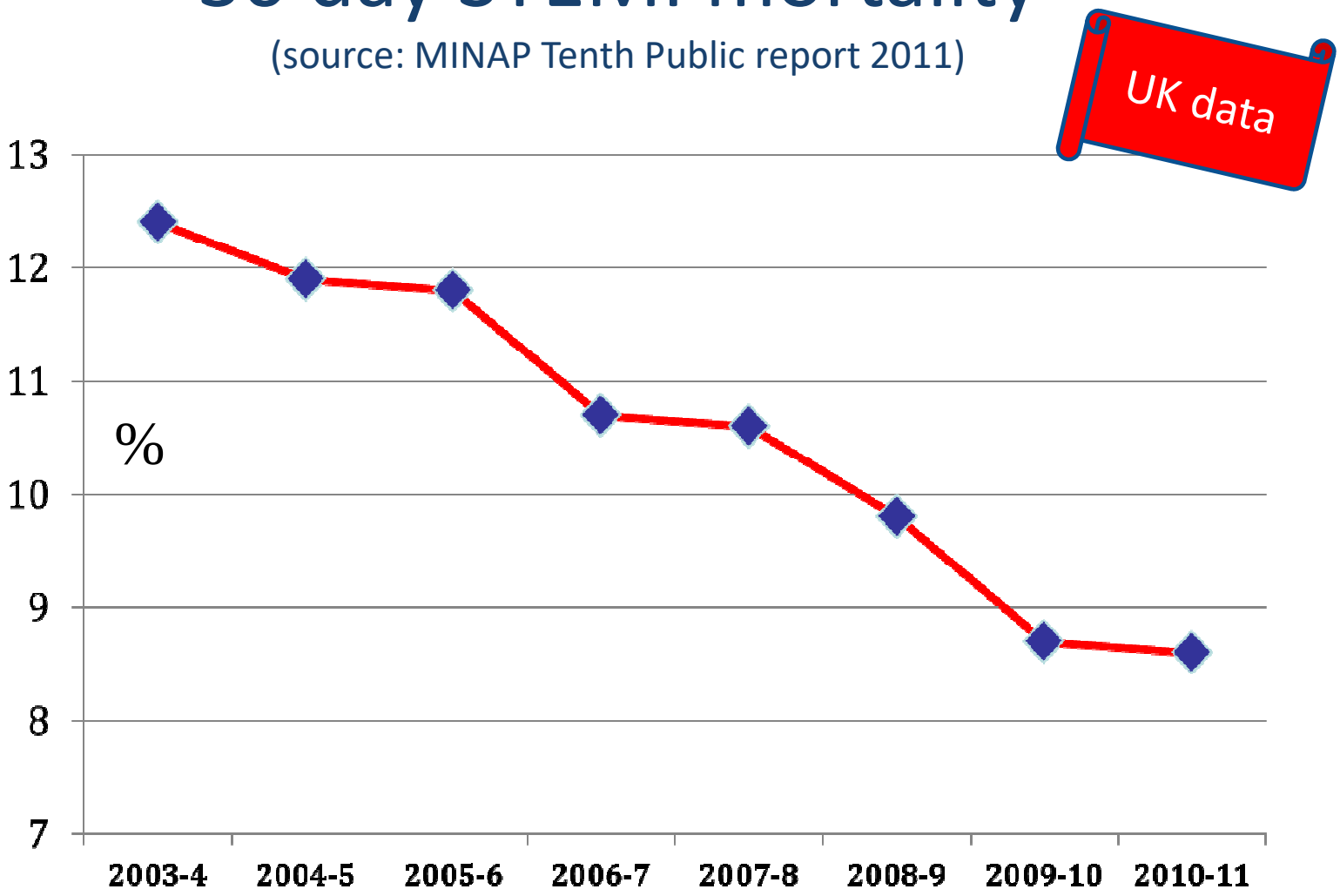
Target: Pushing both DTB & STB times

- **DTB times**: Indicate hospital leadership focus, inter-disciplinary collaboration, constant improvements and audits: <60-90mins
- **STB times**: Indicate public awareness, access to care, pre-hospital ECG and appropriate pre-hospital transfer triage: < 4 hours

WHAT DOES PRIMARY PCI ACHIEVE?

30 day STEMI mortality

(source: MINAP Tenth Public report 2011)



THERE ARE NO "ONE-SIZE-FITS-ALL" SOLUTIONS

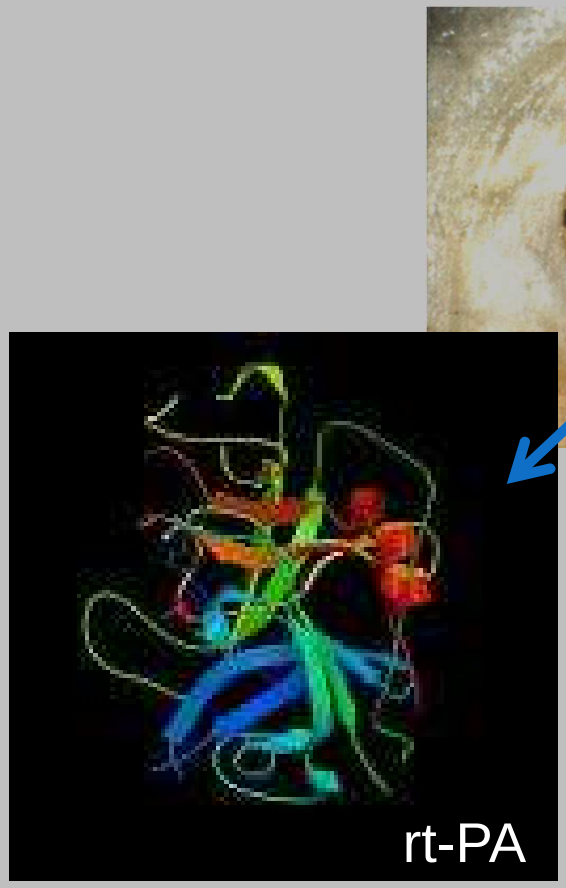
Timely Treatment of STEMI Patients Transferred for Primary PCI Still a Problem

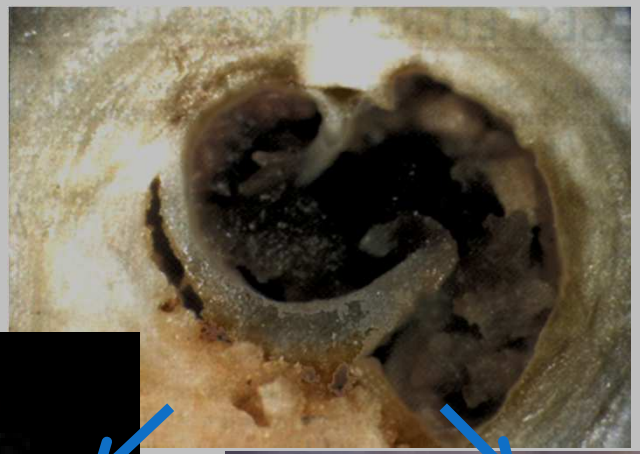
By **Todd Neale** | *June 01, 2015*

Even when the estimated transfer time is less than an hour, 1 in 3 US STEMI patients referred to another center for primary PCI do not meet the recommended first door-to-device goal of 120 minutes or less, according to a study published in the May issue of *Circulation: Cardiovascular Interventions*.

PRIMARY PCI & THROMBOLYTIC: FRIEND OR FOE?

PCI & Thrombolyics: The reperfusion wars?

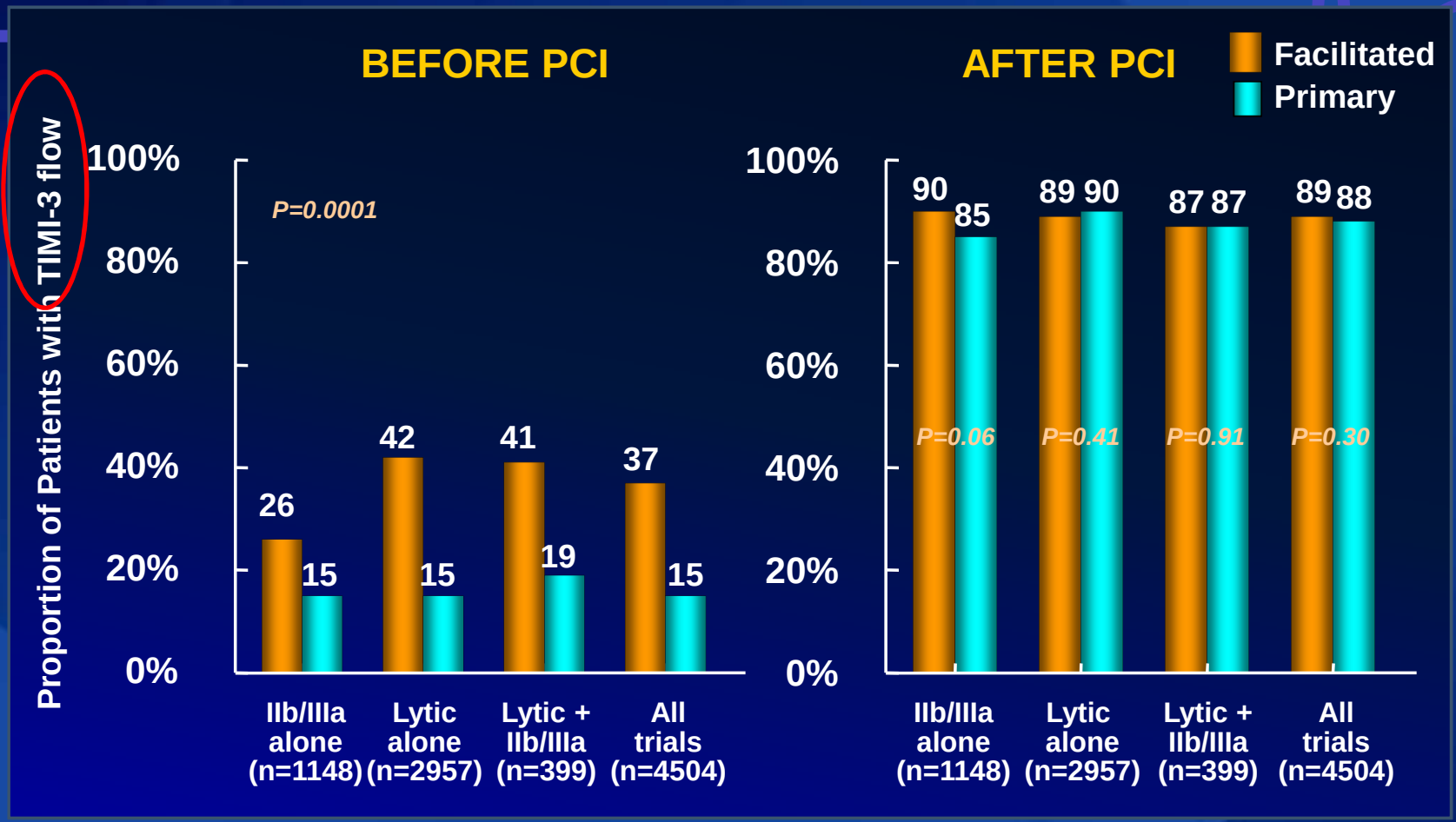




Facilitated PCI

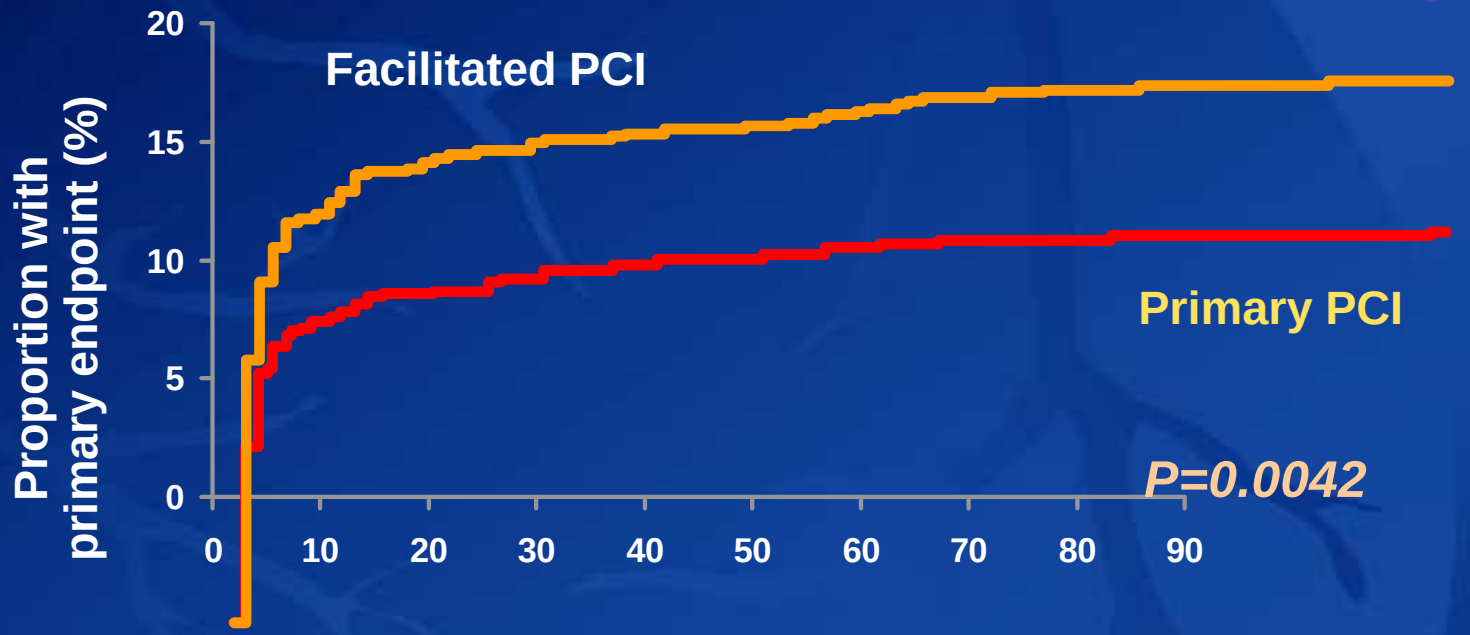
- A strategy to enhance primary PCI by early establishment of infarct vessel patency
- Options include
  - full dose thrombolytics
  - half dose thrombolytics + IIbIIIa inhibitor
  - IIbIIIa inhibitor alone
- Therapy typically administered in the ED or ambulance

Facilitation Enhances Pre-PCI Flow



Keeley, et al, Lancet 2006;367:579-588.

ASSENT 4: Primary Endpoint (Terminated Early)

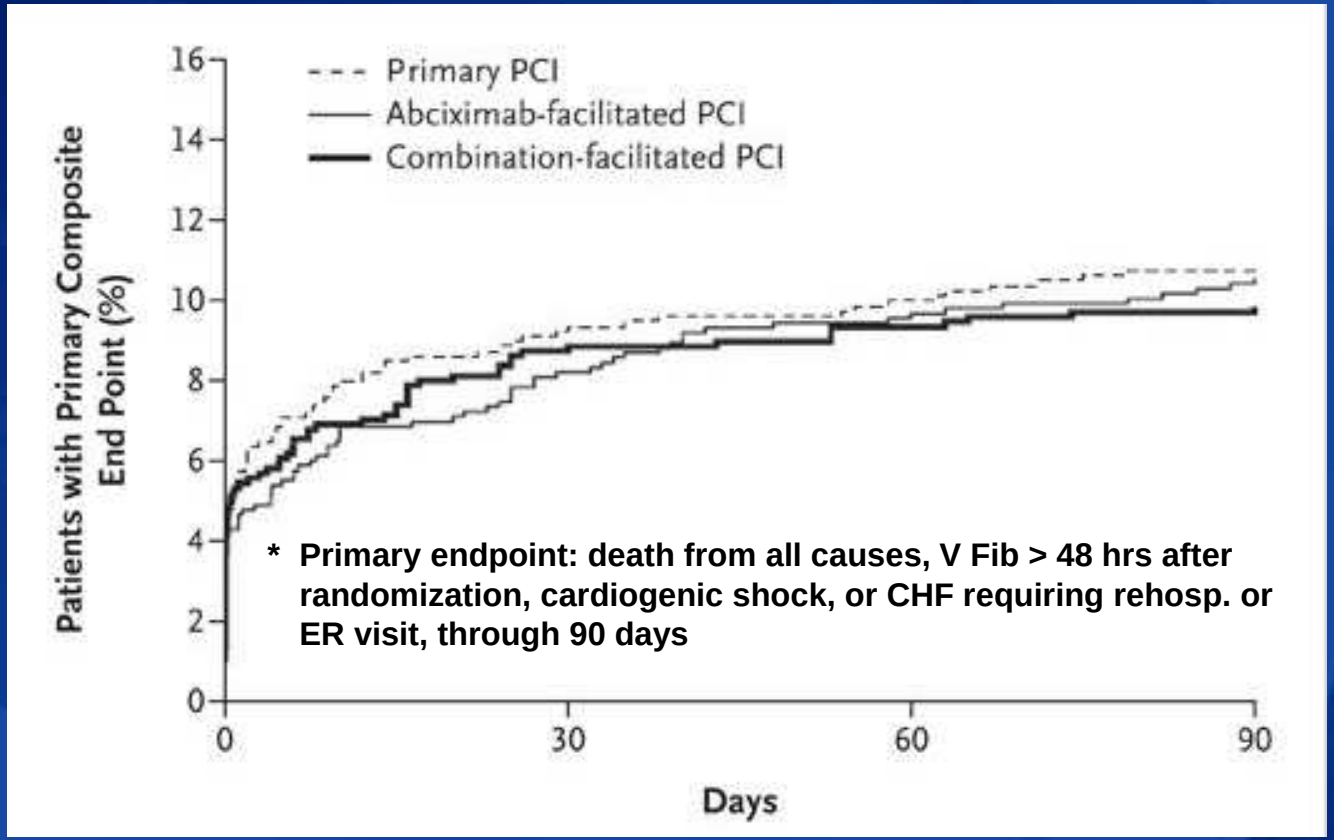


No. at risk									
Facilitated PCI	829	703	696	691	685	678	675	673	673	672
Primary PCI	838	747	741	736	730	726	725	724	724	722

Lancet 367:569, 2006

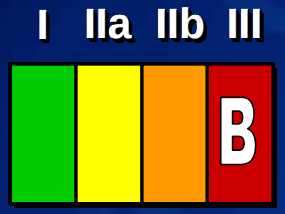
FINESSE:

KM Curves for Pts with Primary Endpoint*

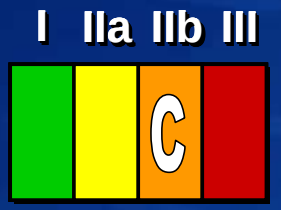


Ellis SG et al. *N Engl J Med* 2008;358:2205-2217

2007 STEMI Update: Facilitated PCI



A planned reperfusion strategy using full-dose fibrinolytic therapy followed by immediate PCI is not recommended and may be harmful



Facilitated PCI using regimens other than full-dose fibrinolytic therapy might be considered as a reperfusion strategy when all of the following are present

a. Patients are at high risk

b. PCI is not immediately available within 90 min

c. Bleeding risk is low (younger age, absence of poorly controlled HTN, normal body weight)

European Heart Journal (2009) **30**, 2817–2828
doi:10.1093/eurheartj/ehp409

Pharmaco-invasive vs. facilitated percutaneous coronary intervention strategies for ST-segment-elevation acute myocardial infarction patients in the new ESC Guidelines

Reviewed by Frans Van de Werf, ESC Guideline Committee chairman

The role of percutaneous coronary interventions (PCIs) in the early hours of an ST-segment-elevation acute myocardial infarction (STEMI) can be divided into primary PCI, PCI combined with pharmacological reperfusion therapy, and 'rescue PCI' after failed pharmacological reperfusion.

Primary PCI can be defined as coronary angioplasty/stenting without prior administration of fibrinolytic agents or GPIIb/IIIa reperfusion (using fibrinolytic agents) with an 'invasive back-up', which means that patients are transported to a PCI hospital for either immediate rescue PCI in case of failed fibrinolysis or non-urgent coronary angiography to determine the need for additional treatment of the culprit lesion (PCI or bypass surgery). This strategy has been shown to be superior to a very conservative approach of in-hospital fibrinolysis with transfer to a PCI centre only in case of

Pharmaco-invasive Strategy Vs Facilitated PCI

Facilitated PCI	Pharmaco-invasive Strategy
Planned urgent PCI	Planned pharmacological reperfusion (thrombolytic)
Pharmacological Rx to bridge the PCI-related time delay - Full dose lytic - Half dose lytic + IIbIIIa - IIbIIIa	PCI as backup - Rescue PCI if failed reperfusion - Non-urgent but *routine* early PCI after successful reperfusion - Transfer to PCI hospital if lytic is given in non-PCI hospital

Rescue PCI

Definition: PCI for failure of fibrinolytics

- Clinical failure assessed at 60-90 minutes after fibrinolytics
  - Persistent chest pain or other active ischemic symptoms
  - Development of complications (e.g. heart failure, shock)
  - EKG with < 50% ST resolution in lead with previous maximal elevations suggests absence of reperfusion
  - Other clues:
    - No “reperfusion arrhythmias” – AIVR
    - No rapid release of biomarkers

Pharmaco-invasive Strategy Vs Facilitated PCI

Facilitated PCI	Pharmaco-invasive Strategy
Planned urgent PCI	Planned pharmacological reperfusion (thrombolytic)
Pharmacological Rx to bridge the PCI-related time delay - Full dose lytic - Half dose lytic + IIbIIIa - IIbIIIa	PCI as backup - Rescue PCI if failed reperfusion - Non-urgent but *routine* early PCI after successful reperfusion - Transfer to PCI hospital if lytic is given in non-PCI hospital

Pharmaco-invasive Strategy Vs ***Standard Primary PCI***

STREAM Trial

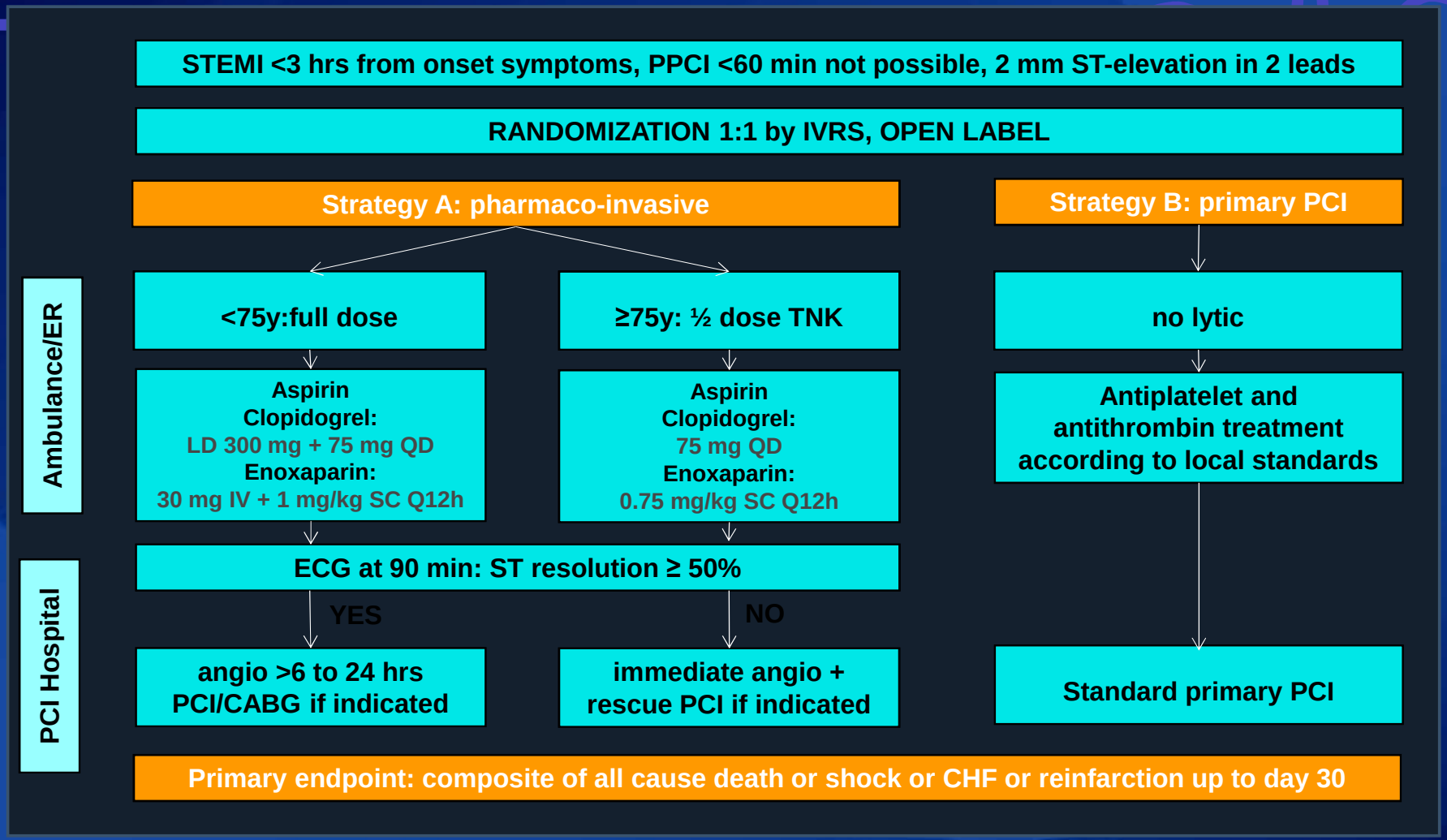
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

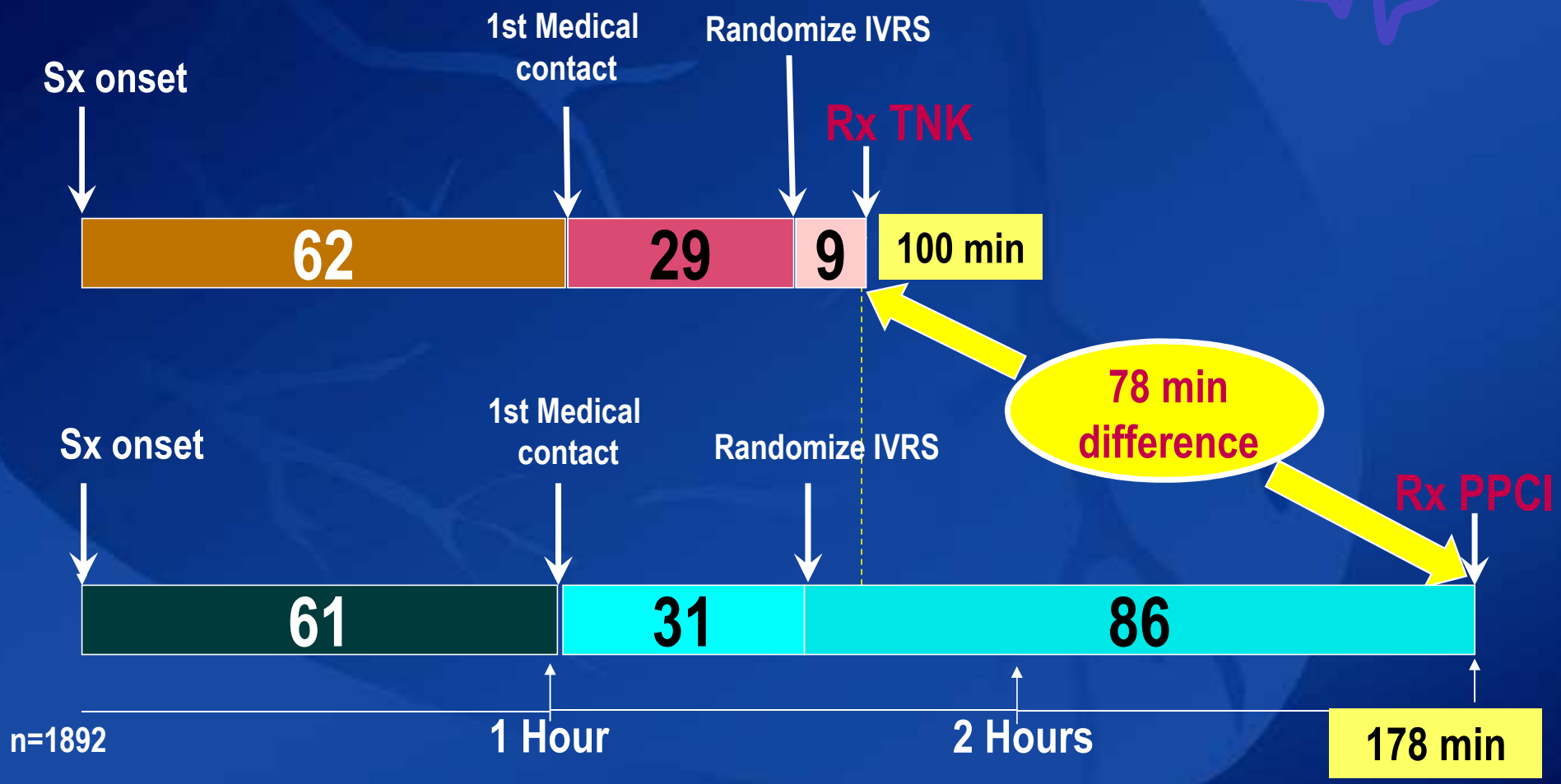
Fibrinolysis or Primary PCI in ST-Segment Elevation Myocardial Infarction

Paul W. Armstrong, M.D., Anthony H. Gershlick, M.D., Patrick Goldstein, M.D., Robert Wilcox, M.D., Thierry Danays, M.D., Yves Lambert, M.D., Vitaly Sulimov, M.D., Ph.D., Fernando Rosell Ortiz, M.D., Ph.D., Miodrag Ostojic, M.D., Ph.D., Robert C. Welsh, M.D., Antonio C. Carvalho, M.D., Ph.D., John Nanas, M.D., Ph.D., Hans-Richard Arntz, M.D., Ph.D., Sigrun Halvorsen, M.D., Ph.D., Kurt Huber, M.D., Stefan Grajek, M.D., Ph.D., Claudio Fresco, M.D., Erich Bluhmki, M.D., Ph.D., Anne Regelin, Ph.D., Katleen Vandenberghe, Ph.D., Kris Bogaerts, Ph.D., and Frans Van de Werf, M.D., Ph.D., for the STREAM Investigative Team*

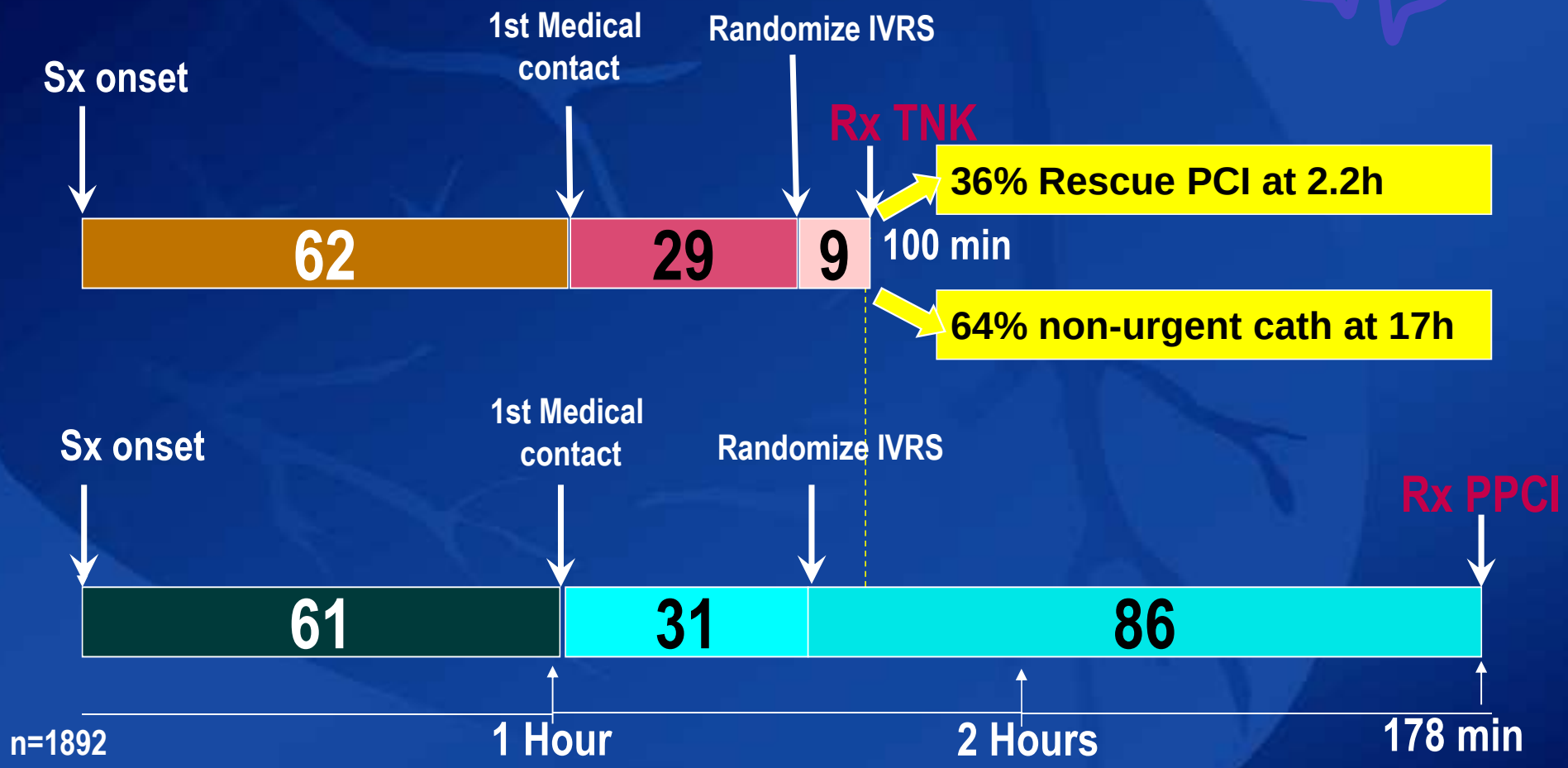
STUDY PROTOCOL



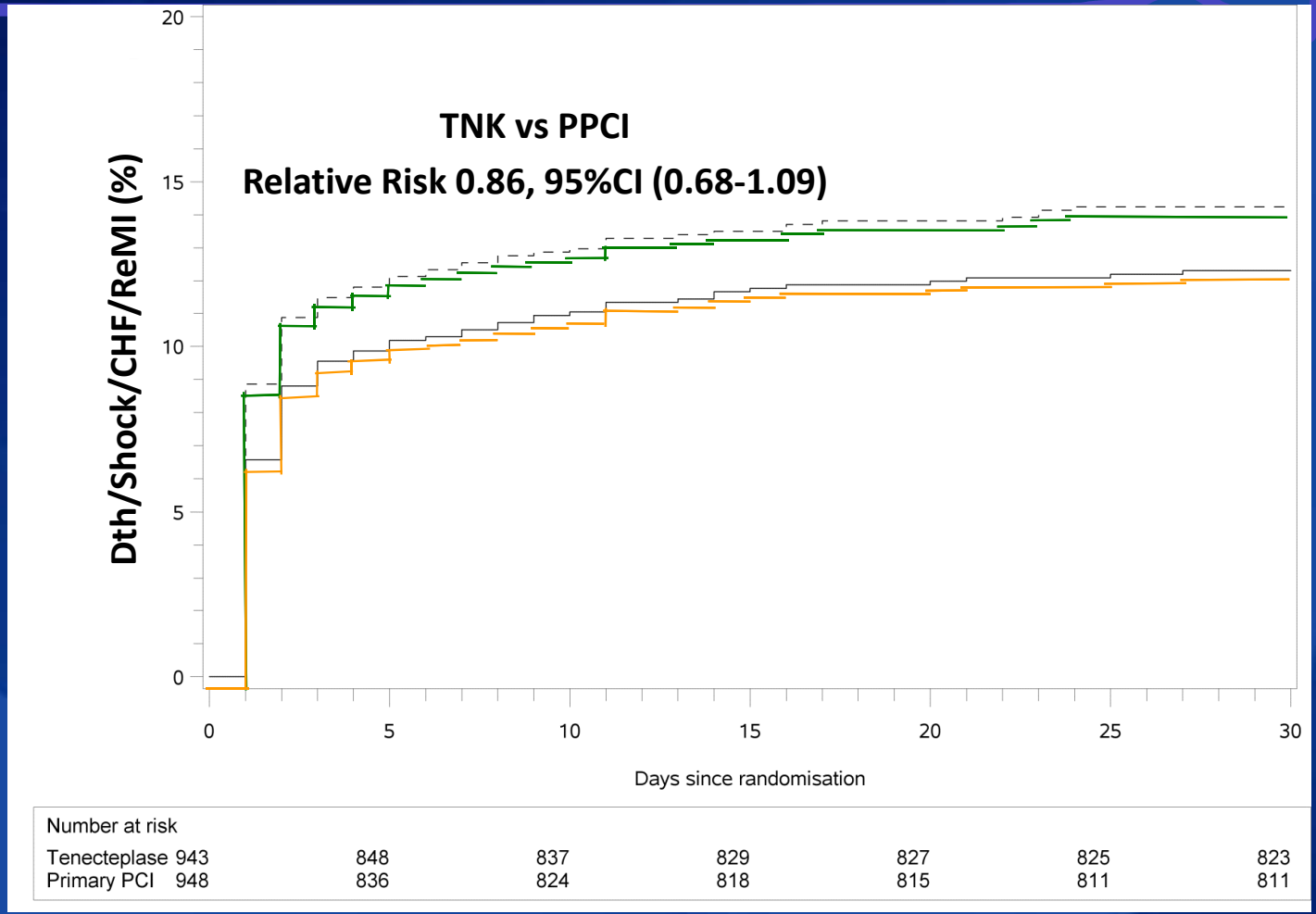
MEDIAN TIMES TO TREATMENT (min)



MEDIAN TIMES TO TREATMENT (min)



PRIMARY ENDPOINT



PPCI 14.3%

TNK 12.4%

p=0.24

SINGLE ENDPOINTS UP TO 30 DAYS

	Pharmaco-invasive (N=944)	PPCI (N=948)	P-value
All cause death	(43/939) 4.6%	(42/946) 4.4%	0.88
Cardiac death	(31/939) 3.3%	(32/946) 3.4%	0.92
Congestive heart failure	(57/939) 6.1%	(72/943) 7.6%	0.18
Cardiogenic shock	(41/939) 4.4%	(56/944) 5.9%	0.13
Reinfarction	(23/938) 2.5%	(21/944) 2.2%	0.74

2013 ACCF/AHA Guideline

Indications for Transfer for Angiography After Fibrinolytic Therapy

	COR	LOE
Immediate transfer for cardiogenic shock or severe acute HF irrespective of time delay from MI onset	I	B
Urgent transfer for failed reperfusion or reocclusion	IIa	B
As part of an invasive strategy in stable* patients with PCI between 3 and 24 h after successful fibrinolysis	IIa	B

*Although individual circumstances will vary, clinical stability is defined by the absence of low output, hypotension, persistent tachycardia, apparent shock, high-grade ventricular or symptomatic supraventricular tachyarrhythmias, and spontaneous recurrent ischemia.

Fibrinolytic therapy *(continued)*

ESC European Society of Cardiology

Recommendations	Class	Level
Anticoagulation co-therapy with fibrinolysis		
Anticoagulation is recommended in patients treated with lytics until revascularization (if performed) or for the duration of hospital stay up to 8 days. The anticoagulant can be:	I	A
• Enoxaparin i.v. followed by s.c. (preferred over UFH).	I	A
• UFH given as a weight-adjusted i.v. bolus followed by infusion.	I	B
• In patients treated with streptokinase: fondaparinux i.v. bolus followed by an s.c. dose 24 hours later.	IIa	B
Transfer after fibrinolysis		
Transfer to a PCI-capable centre following fibrinolysis is indicated in all patients immediately after fibrinolysis.	I	A

Fibrinolytic therapy *(continued)*

ESC European Society of Cardiology

Recommendations	Class	Level
Interventions following fibrinolysis		
Emergency angiography and PCI if indicated is recommended in patients with heart failure/shock.	I	A
Rescue PCI is indicated immediately when fibrinolysis has failed (< 50% ST-segment resolution at 60-90 min) or at any time in the presence of haemodynamic or electrical instability, or worsening ischaemia.	I	A
Angiography and PCI of the IRA, if indicated, is recommended between2 and 24 hours after successful fibrinolysis.	I	A
Emergency angiography and PCI if needed is indicated in the case of recurrent ischaemia or evidence of reocclusion after initial successful fibrinolysis.	I	B

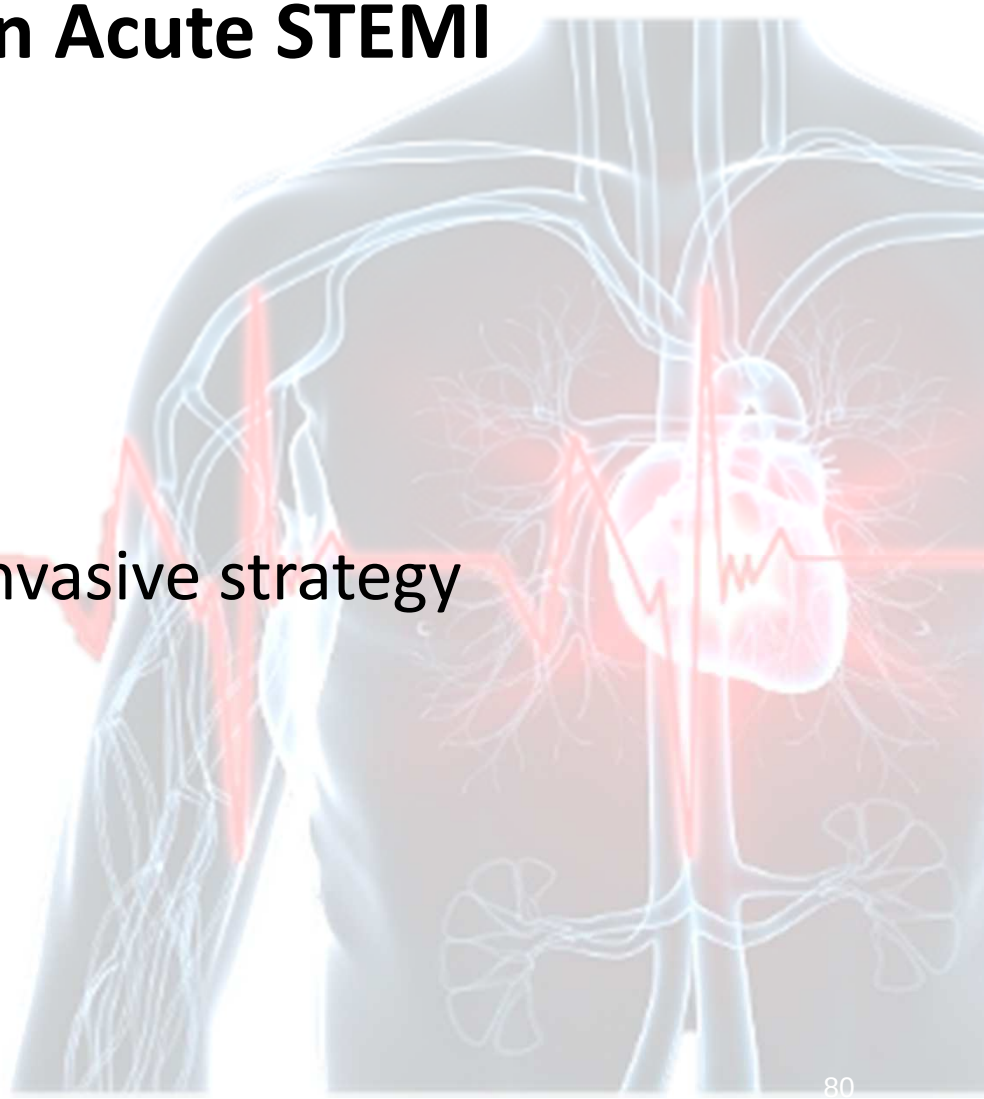
Fibrinolytic therapy *(continued)*

ESC European Society of Cardiology

Recommendations	Class	Level
Interventions following fibrinolysis		
Emergency angiography and PCI if indicated is recommended in patients with heart failure/shock.	I	A
Rescue PCI is indicated immediately when fibrinolysis has failed (< 50% ST-segment resolution at 60-90 min) or at any time in the presence of haemodynamic or electrical instability, or worsening ischaemia.	I	A
Angiography and PCI of the IRA, if indicated, is recommended between2 and 24 hours after successful fibrinolysis.	I	A
Emergency angiography and PCI if needed is indicated in the case of recurrent ischaemia or evidence of reocclusion after initial successful fibrinolysis.	I	B

Reperfusion Strategy in Acute STEMI

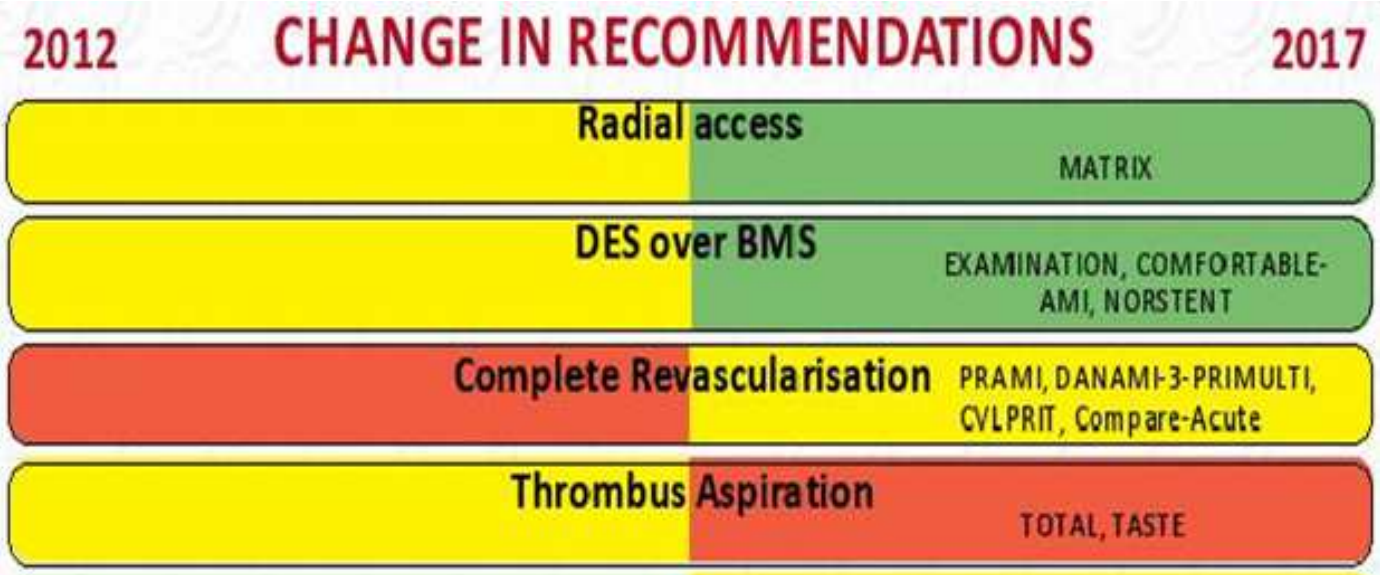
- Primary PCI
- Thrombolysis / Pharmaco-invasive strategy



TECHNICAL ASPECTS OF PPCI

What is new in 2017 Guidelines on AMI-STEMI

ESC
European Society of Cardiology



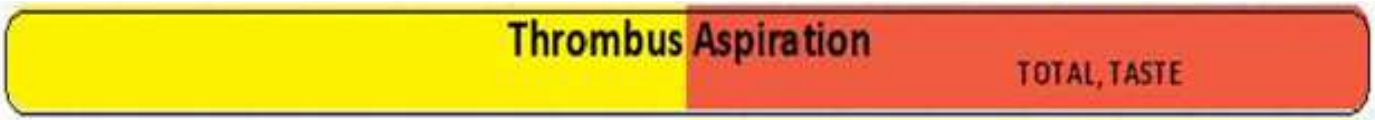
I
IIa
IIb
III

What is new in 2017 Guidelines on AMI-STEMI

ESC
European Society of Cardiology

2012 CHANGE IN RECOMMENDATIONS 2017

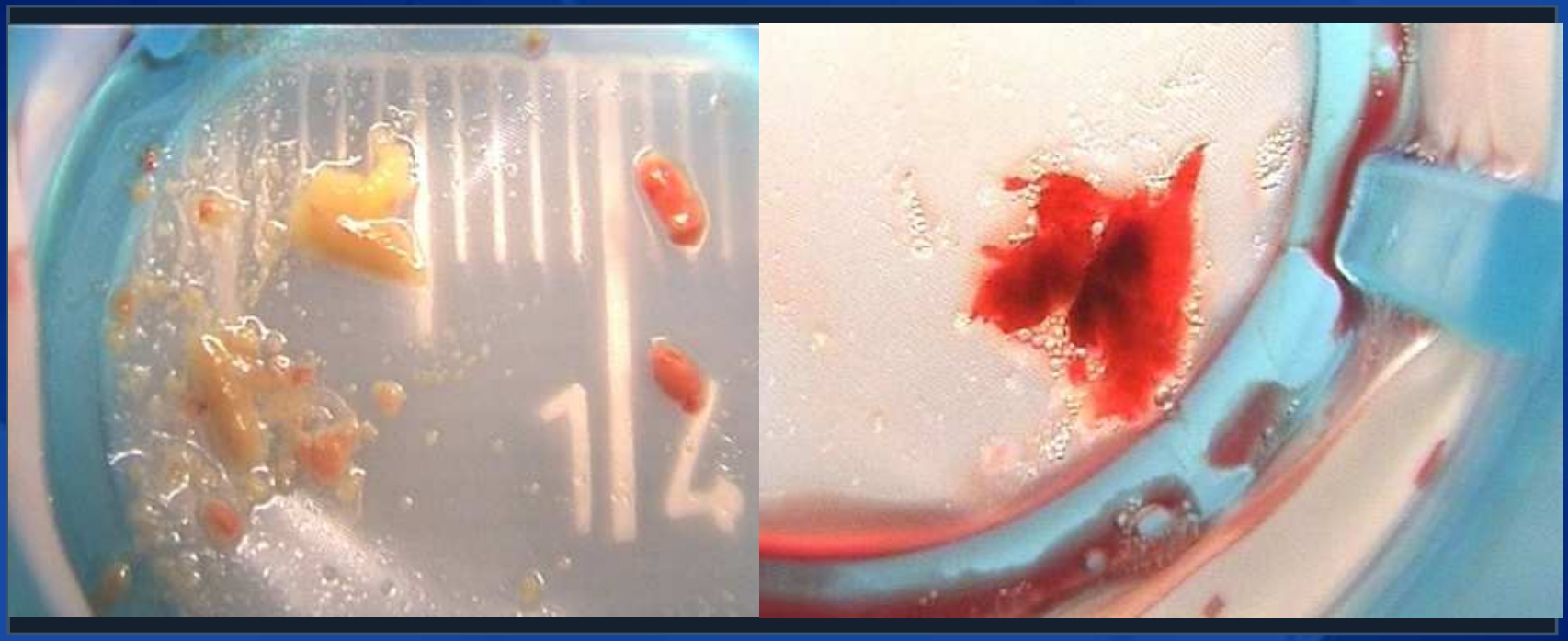
I
IIa
IIb
III



THROMBUS ASPIRATION

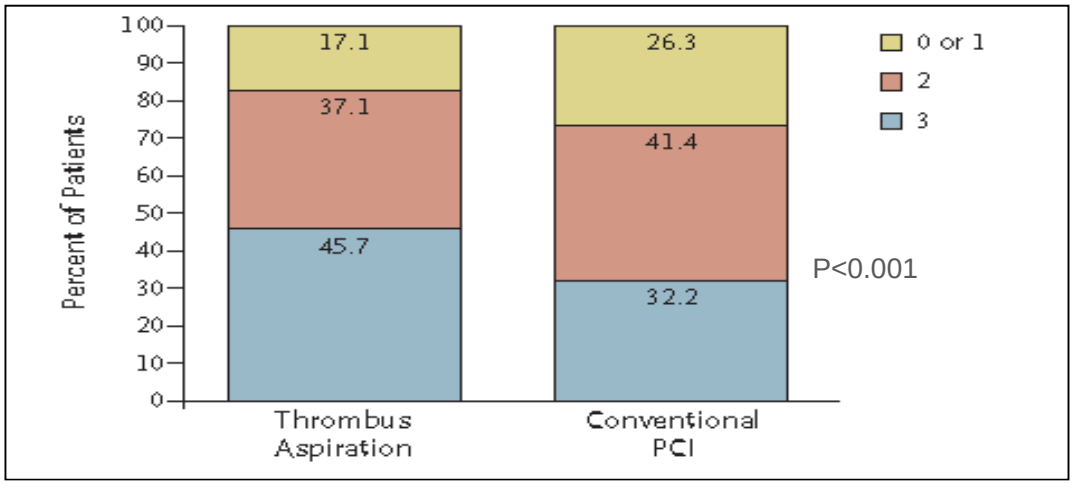
Thrombectomy and Distal Protection in AMI

Macroscopic embolic debris can be retrieved from >75% of cases



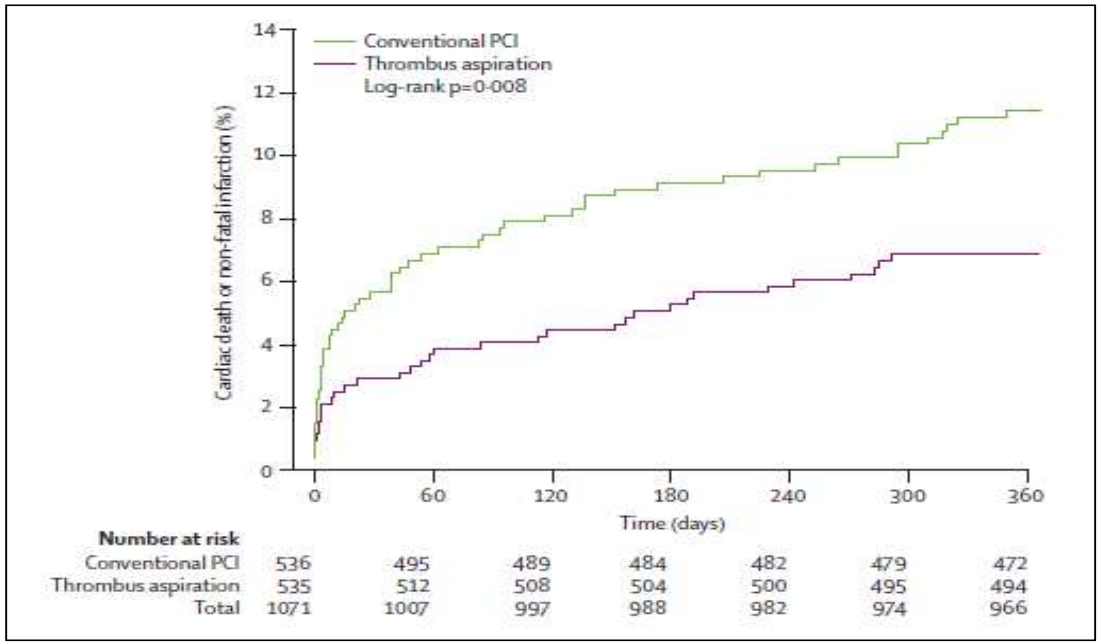
TAPAS

Myocardial Brush Grade



TAPAS: Svilaas T, et al. NEJM 2008;358:557

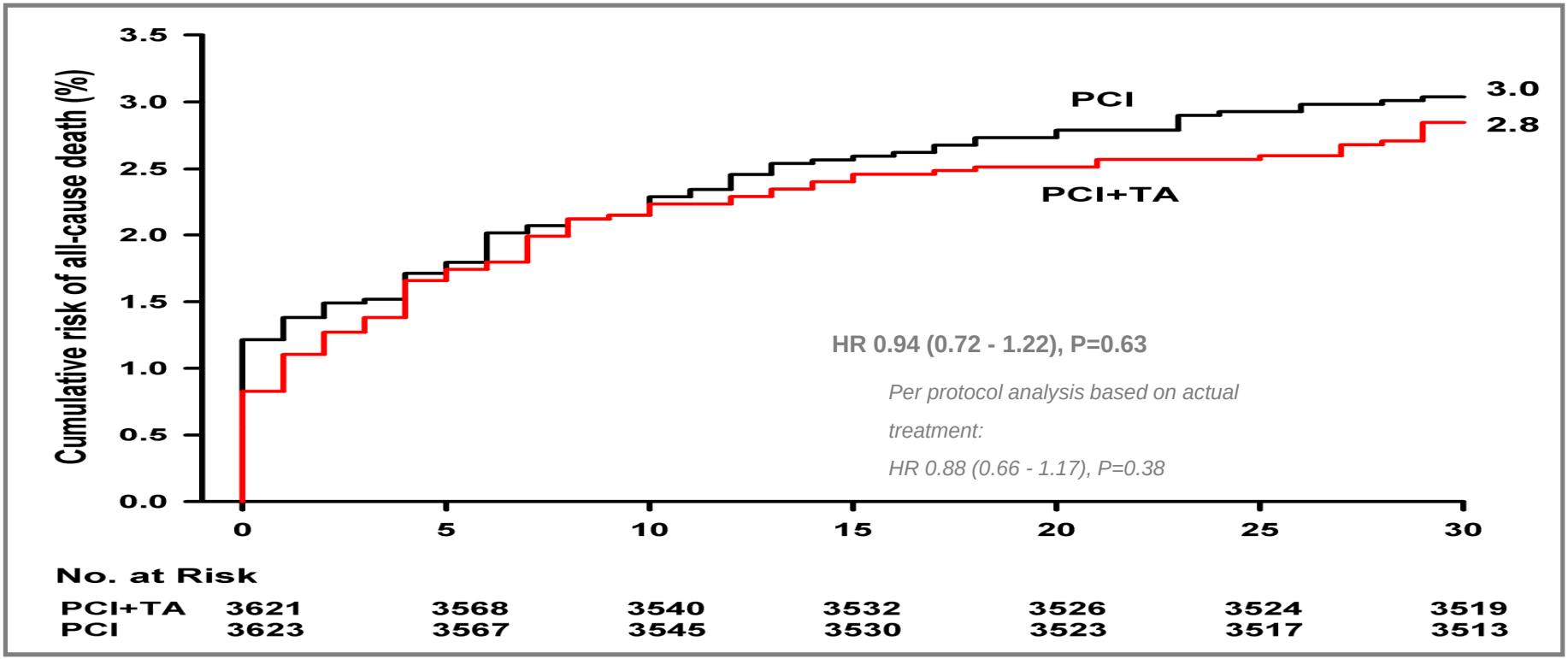
Cardiac death or non-fatal MI



TAPAS: Vlaar PJ, et al. Lancet 2008; 371:1915

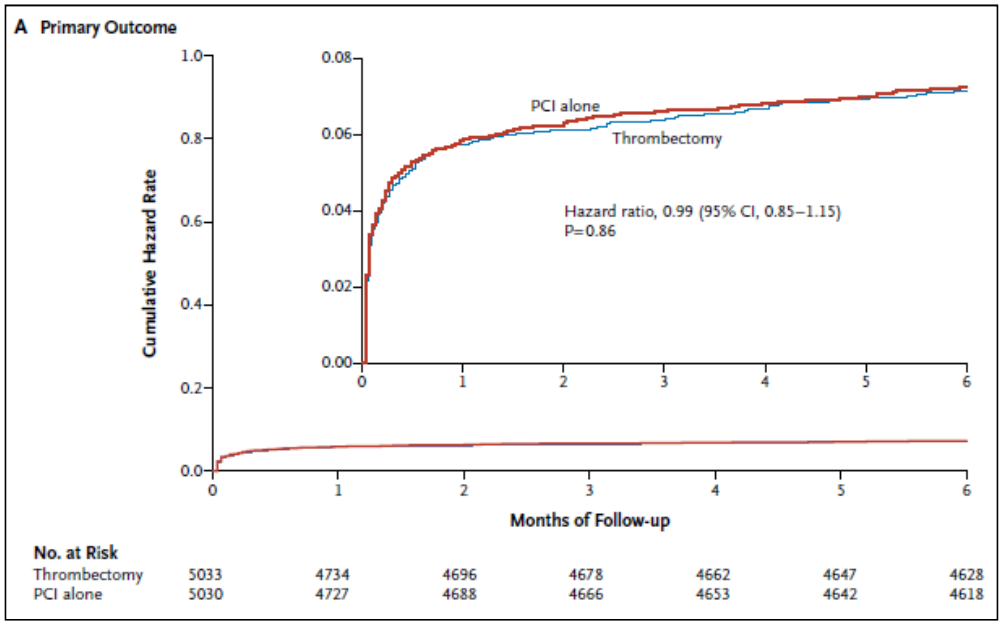
TASTE

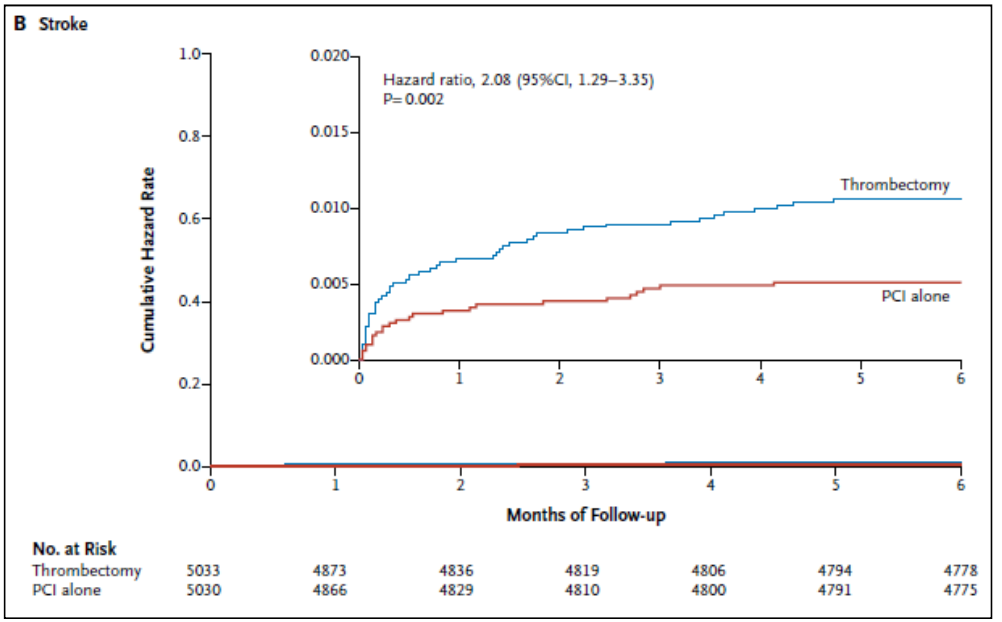
Primary Endpoint 30-Day Death



Froebert et al. NEJM 2013; 369:1587-1597

TOTAL





Jolly SS, et al. NEJM 2015

FOCUSED UPDATE

2015 ACC/AHA/SCAI Focused Update on Primary Percutaneous Coronary Intervention for Patients With ST-Elevation Myocardial Infarction

2011/2013 Recommendation	2015 Focused Update Recommendations	Comments
Class IIa	***Class IIb***	
Manual aspiration thrombectomy is reasonable for patients undergoing primary PCI (29–32). (*Level of Evidence: B*)	The usefulness of selective and bailout aspiration thrombectomy in patients undergoing primary PCI is not well established (33–37). (*Level of Evidence: C-LD*)	Modified recommendation (Class changed from "IIa" to "IIb" for selective and bailout aspiration thrombectomy before PCI).
	Class III: No Benefit *Routine* aspiration thrombectomy before primary PCI is not useful (33–37). (*Level of Evidence: A*)	New recommendation ("Class III: No Benefit" added for *routine* aspiration thrombectomy before PCI).

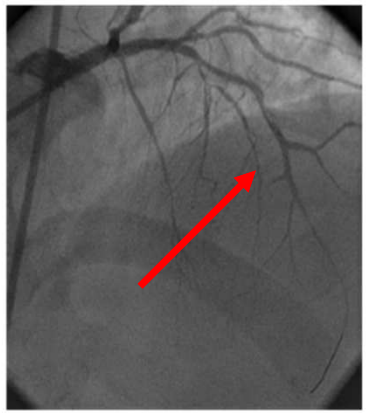
Procedural aspects of the primary percutaneous coronary intervention strategy

ESC European Society of Cardiology

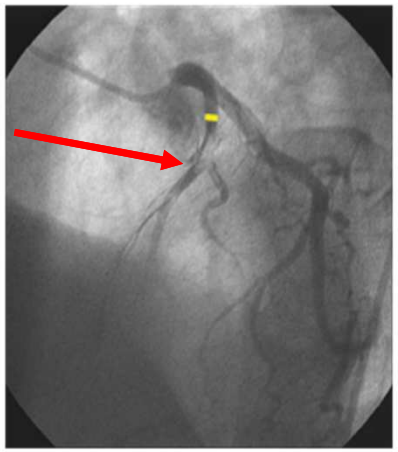
Recommendations	Class	Level
IRA technique (continued)		
Routine use of thrombus aspiration is not recommended.	III	A
Routine use of deferred stenting is not recommended.	III	B
Non-IRA strategy		
In stable patients with multivessel disease before hospital discharge:		
Non-IRA PCI during the index procedure should be considered in patients with cardiogenic shock.	IIa	C
CABG should be considered in patients with ongoing ischaemia and large areas of jeopardized myocardium if PCI of the IRA cannot be performed.	IIa	C

Routine use of thrombus aspiration is not recommended. III A

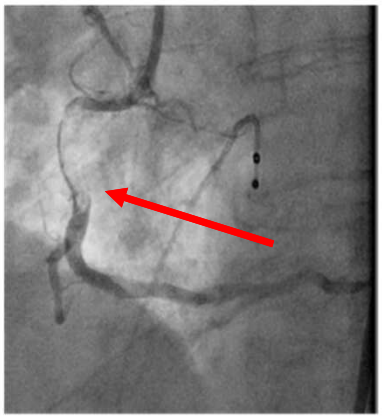
Studies on Thrombus Aspiration
Not Guided by Thrombus Burden



Small thrombus burden



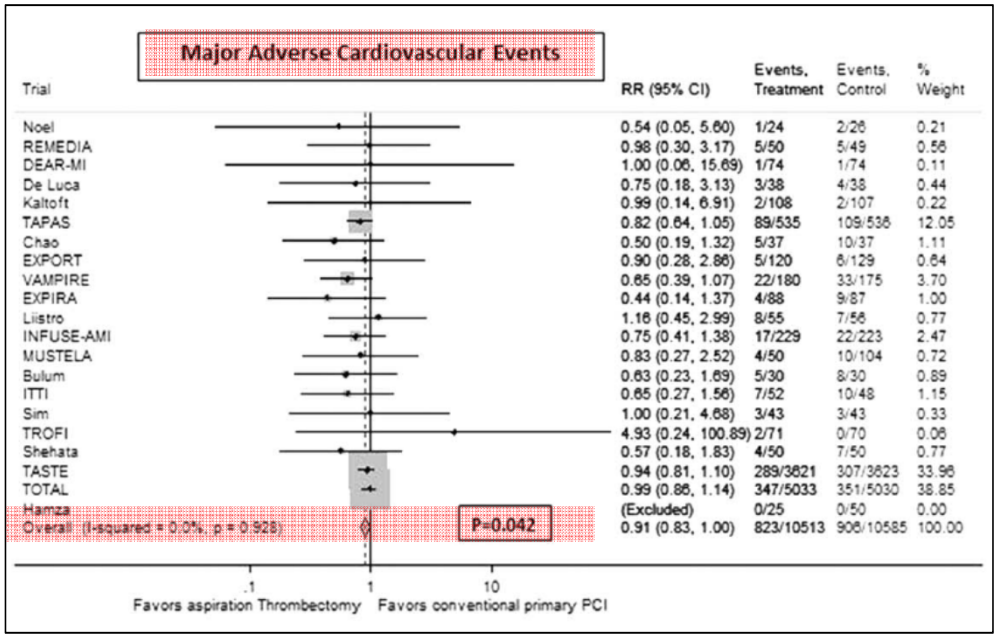
Large thrombus burden

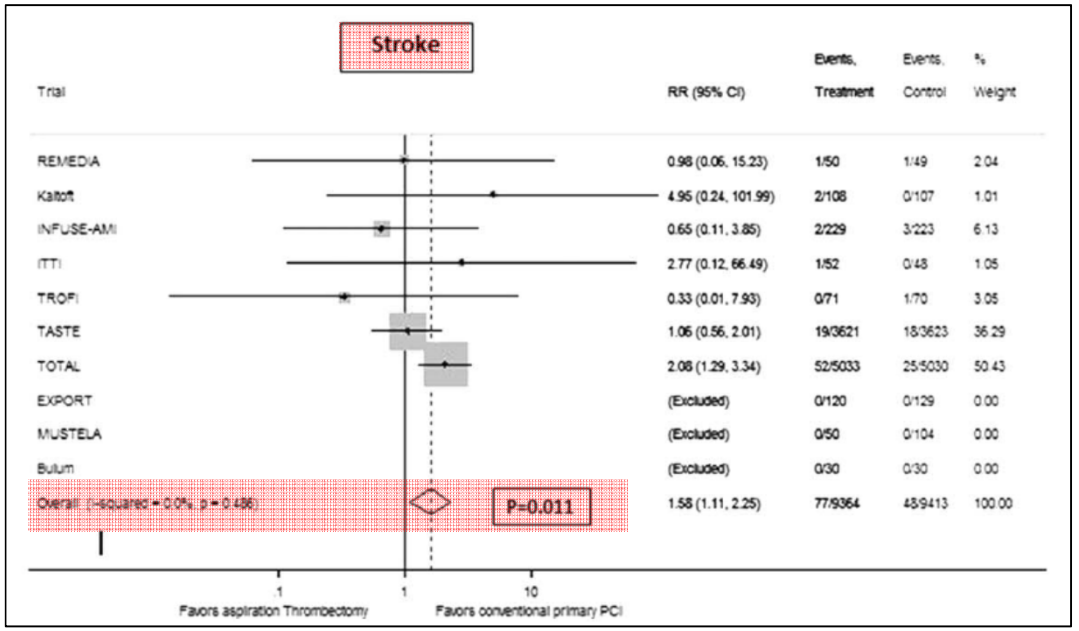


Massive thrombus burden

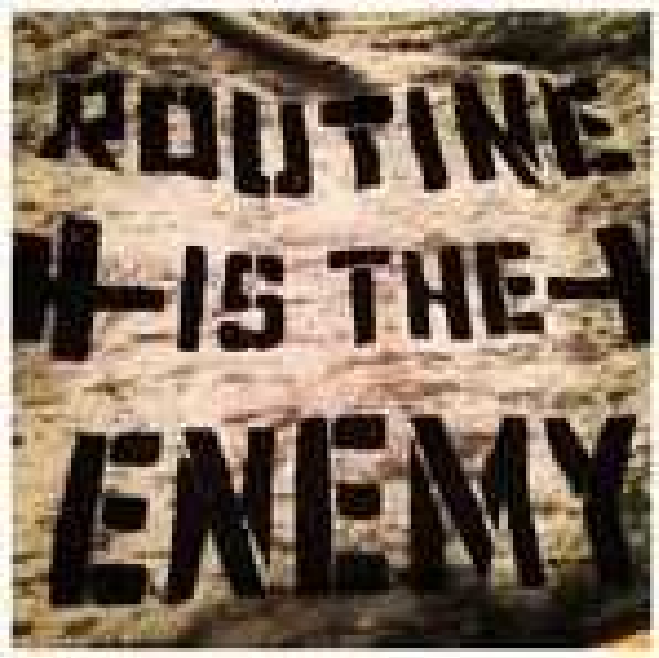
Thrombus Aspiration: Meta-analysis

(Mastoris I, et al. Catheterization & Cardiovascular Interventions. 2016;87:650-60)





Thrombus Aspiration



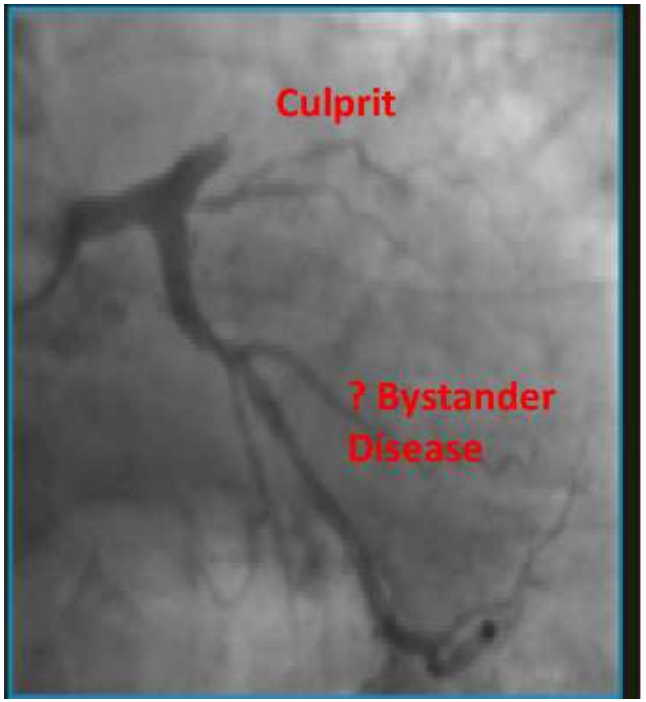
- Not recommended for routine use
- But studies not targeting at large thrombus
- Sensible to be used in large thrombus

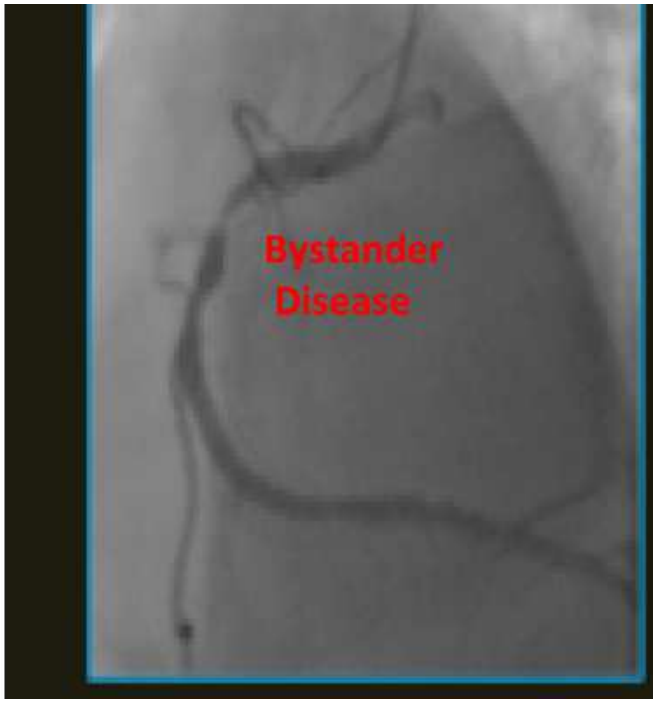
What is new in 2017 Guidelines on AMI-STEMI

ESC
European Society of Cardiology

2012 CHANGE IN RECOMMENDATIONS 2017

I
IIa
IIb
III





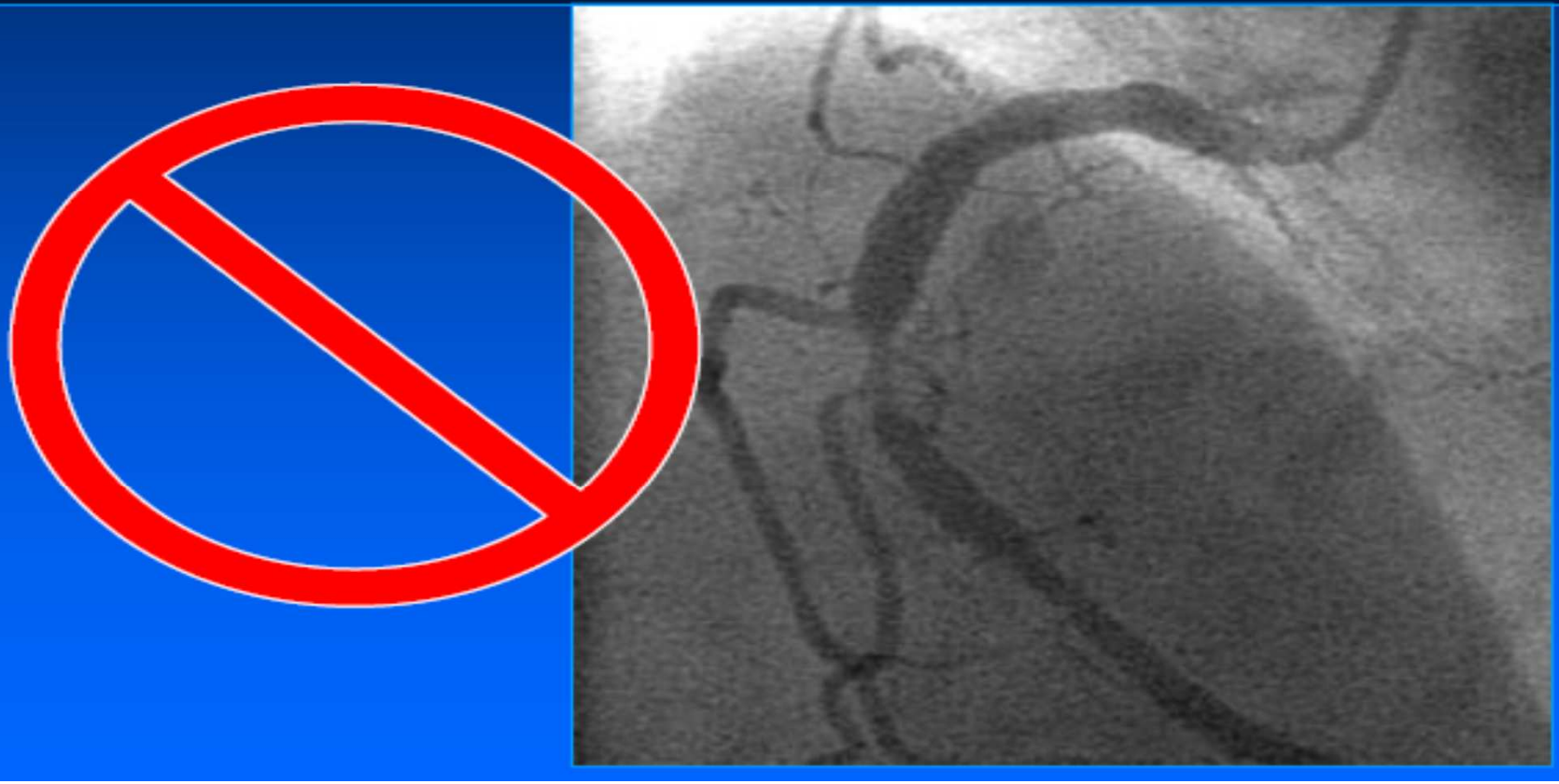
MULTIVESSEL DISEASE

STEMI with Multivessel Disease

- MVD is present in 40% - 50% of patients with STEMI

Ground for Intervening Non-culprit Vessels	Concerns of Intervening Non-culprit Vessels
Higher risk of death, reinfarction,	Increased risk due to enhanced thrombotic and inflammatory state during STEMI
Lack of compensatory hyperkinesis of non-infarct zone	More complex procedure (Time, contrast)
Multi-culprits may be present due to systemic inflammatory state	Non-culprit lesions may be exaggerated during AMI

American Guidelines prior to 2015:
PCI should **not** be performed in a non-infarct artery (Class III)
Current Guidelines Class IIb



STEMI with Multivessel Disease

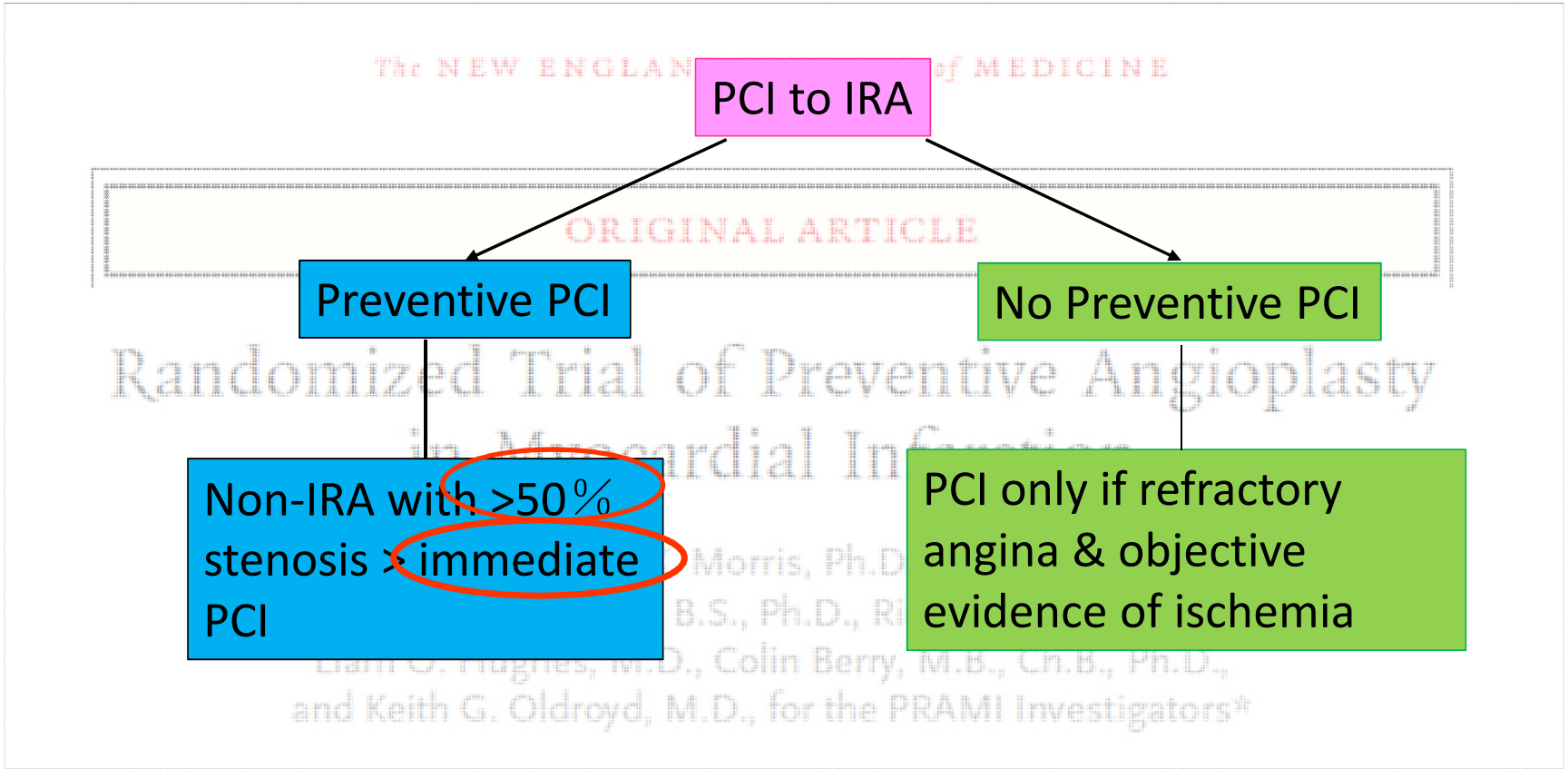
PRAMI

DANAMI3-PRIMULTI

The CvLPRIT Trial

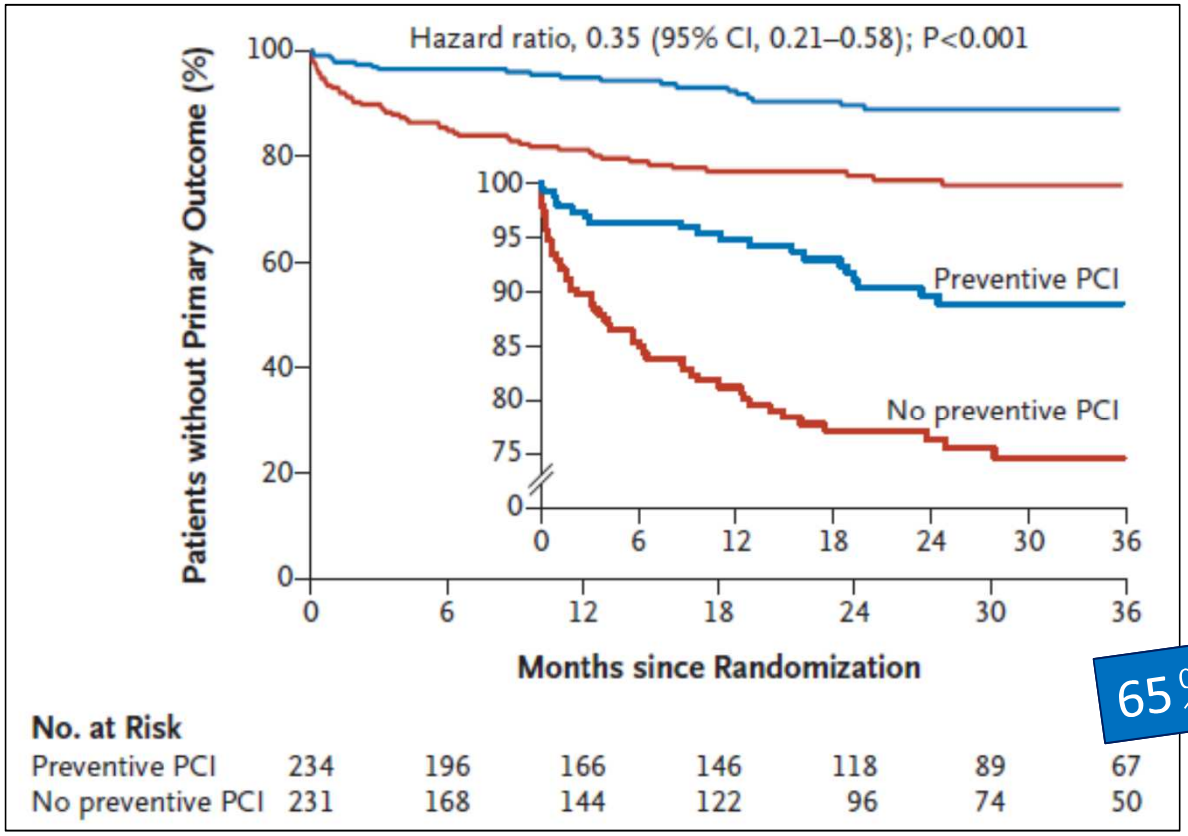
Compare Acute

PRAMI



N Engl J Med 2013;369:1115-23

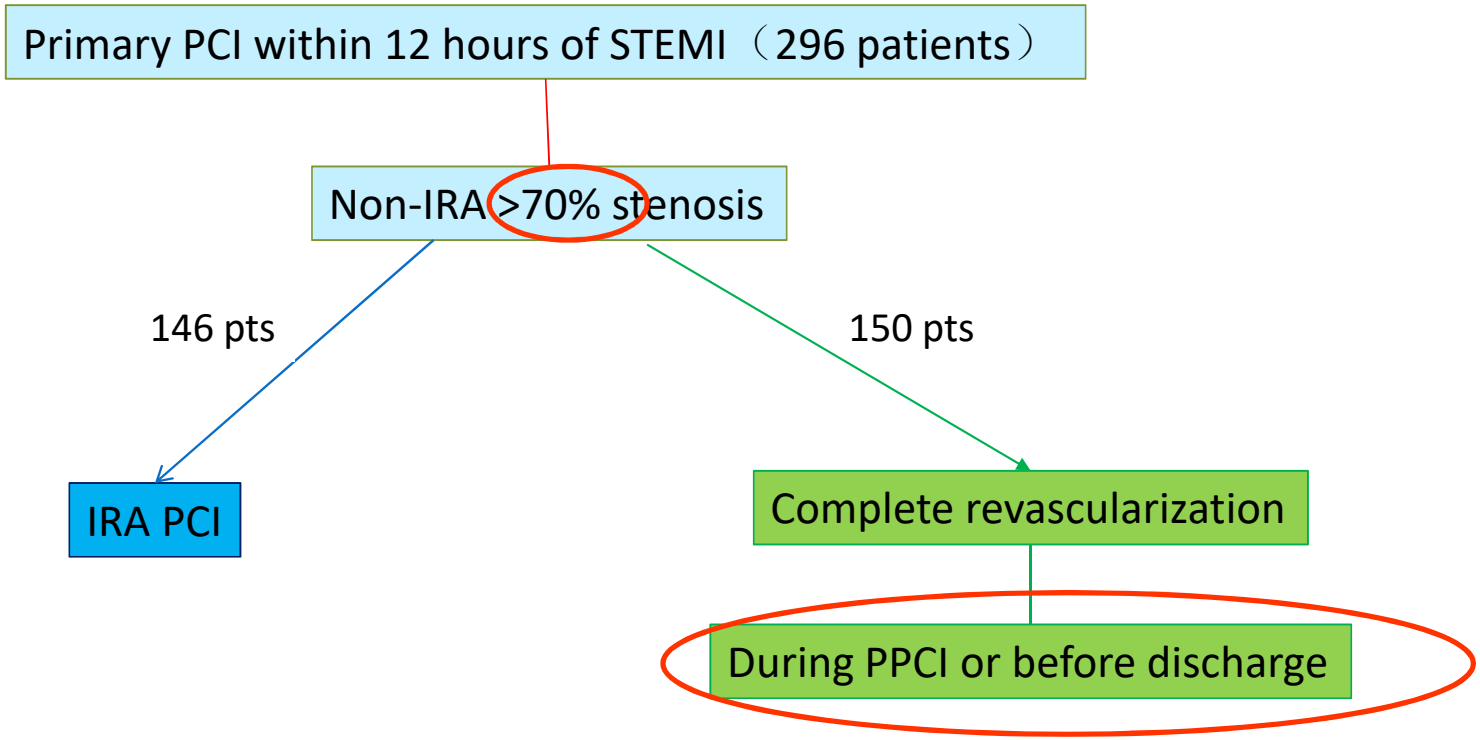
PRAMI



65% reduction in MACE

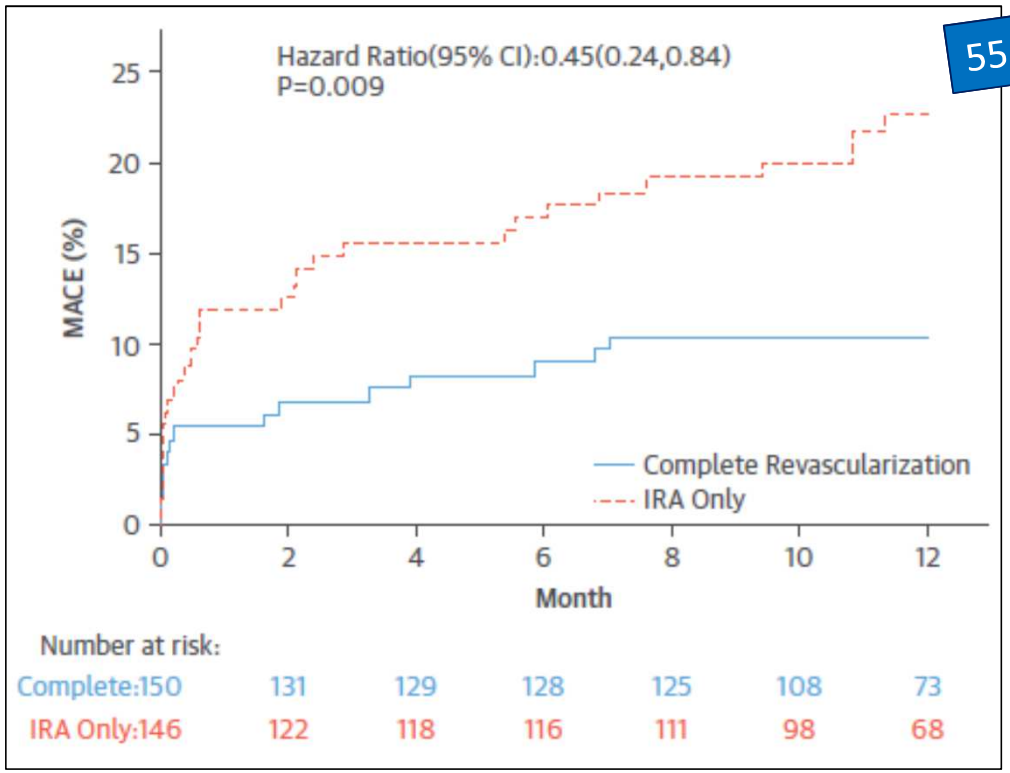
N Engl J Med 2013;369:1115-23

The CvLPRIT Trial



Gershlick AH, et al. J Am Coll Cardiol 2015;65:963–72

The CvLPRIT Trial

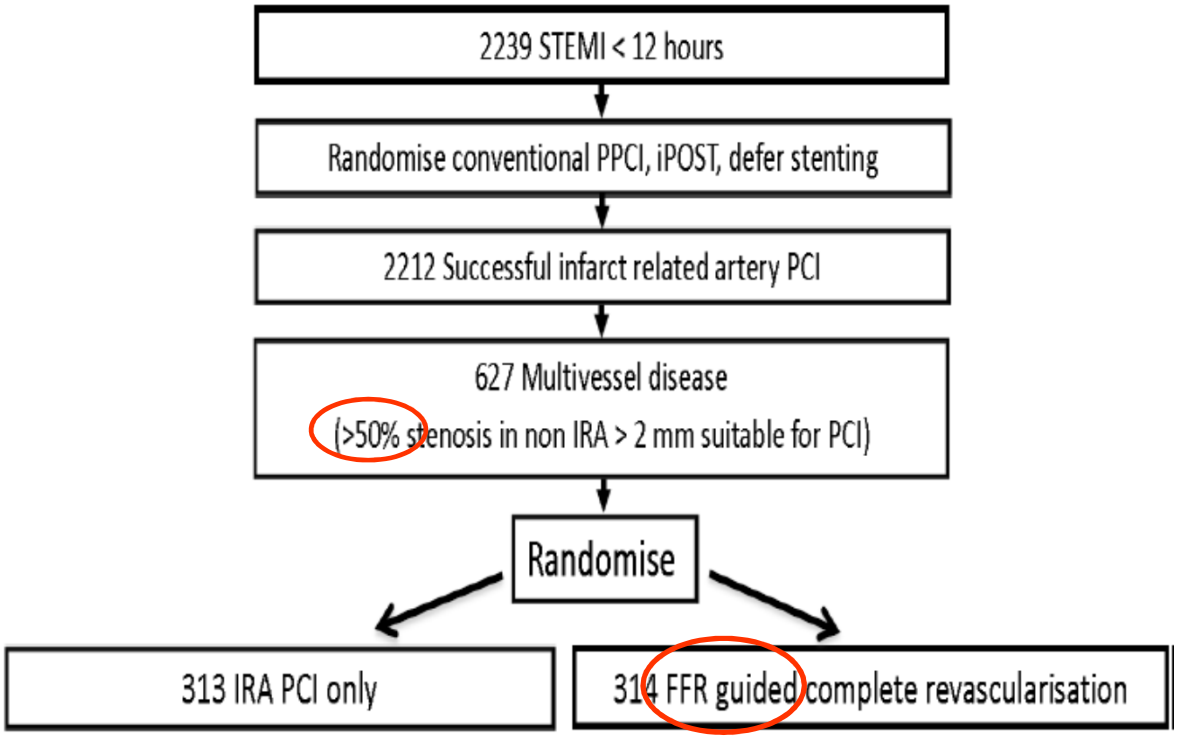


55% reduction in MACE

Event	Complete revascularization N = 150 (%)	IRA PCI N = 146 (%)	HR (95%)	P
Total MACE	15 (10.0)	31 (21.2)	0.45 (0.24, 0.84)	0.009
Mortality	2 (1.3)	6 (4.1)	0.32 (0.06, 1.60)	0.14
Recurrent MI	2 (1.3)	4 (2.7)	0.48 (0.09, 2.62)	0.39
Heart Failure	4 (2.7)	9 (6.2)	0.43 (0.13, 1.39)	0.14
Repeat Revascularization	7 (4.7)	12 (8.2)	0.55 (0.22, 1.39)	0.2

Gershlick AH, et al. J Am Coll Cardiol 2015;65:963–72

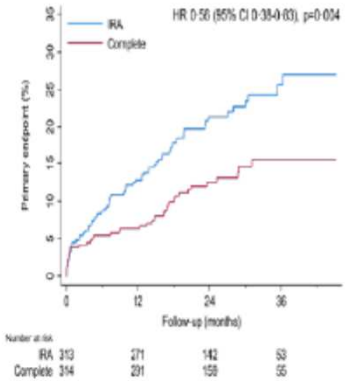
DANAMI3-PRIMULTI



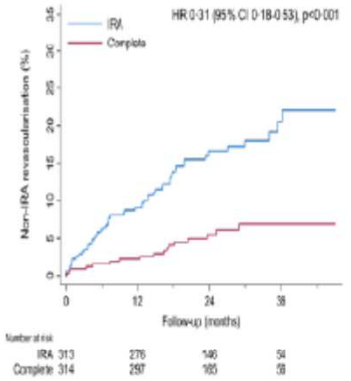
FFR & Complete revascularization performed 2 days after primary PCI
31% had negative FFR

Lancet 2015;386:665-71

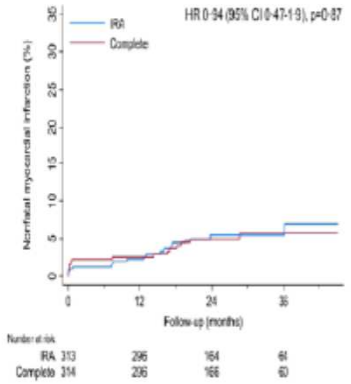
Individual components of primary endpoint



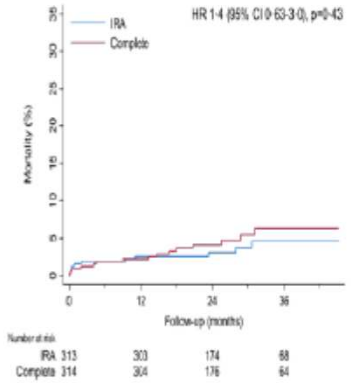
Composite



Revascularisation



Non fatal MI

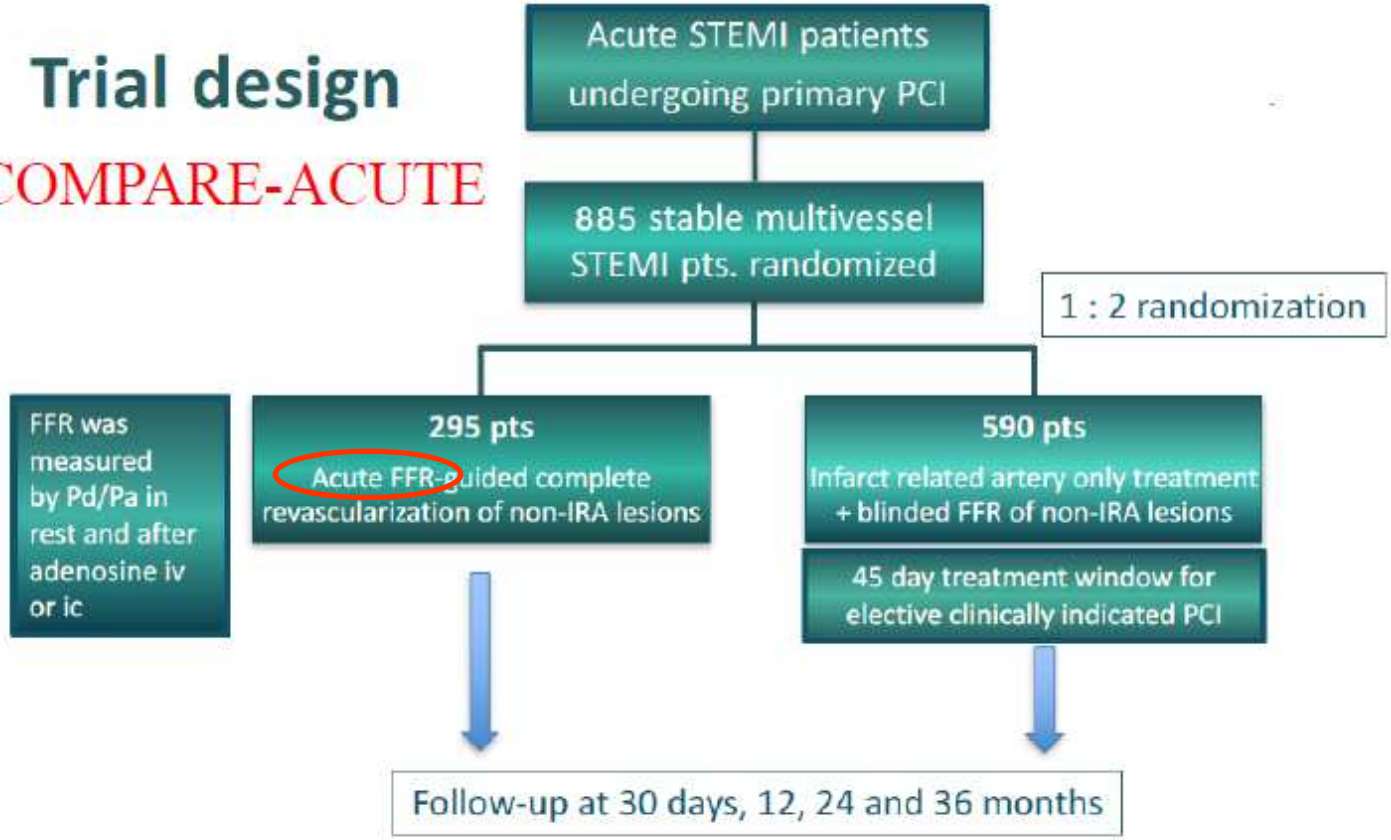


All cause death

Lancet 2015;386:665-71

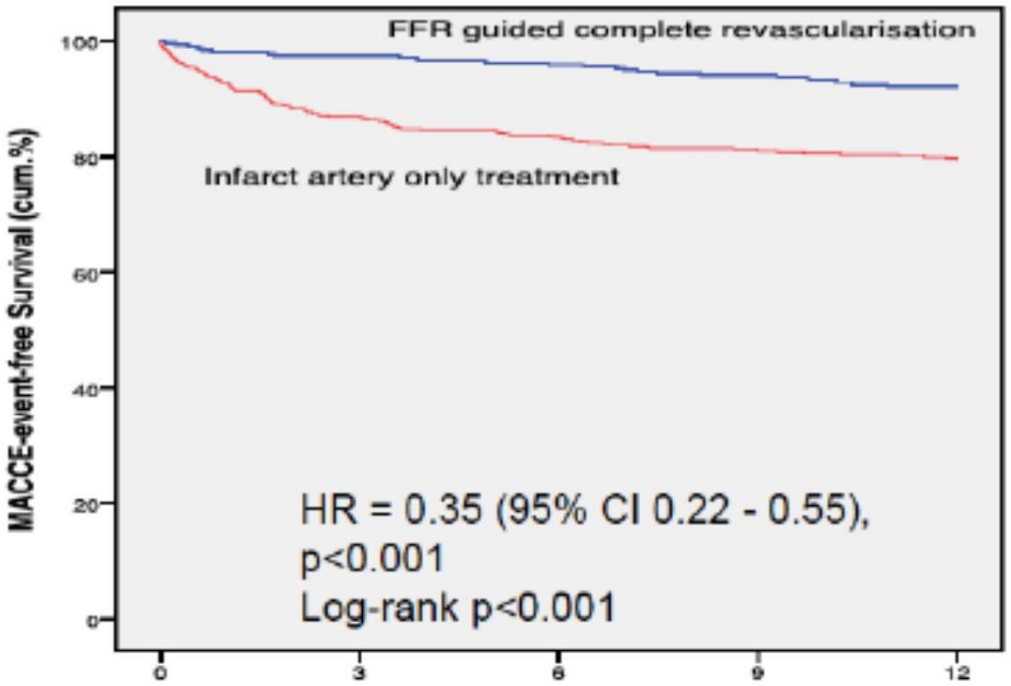
Trial design

COMPARE-ACUTE



N Engl J Med 2017;376:1234-44.

Compare Acute



7.8%

20.5%

No. at risk					
FFR guided complete	295	286	281	264	215
Culprit lesion only	590	512	492	457	371

N Engl J Med 2017;376:1234-44.

Does Timing of Intervening Non-IRA Make a Difference?

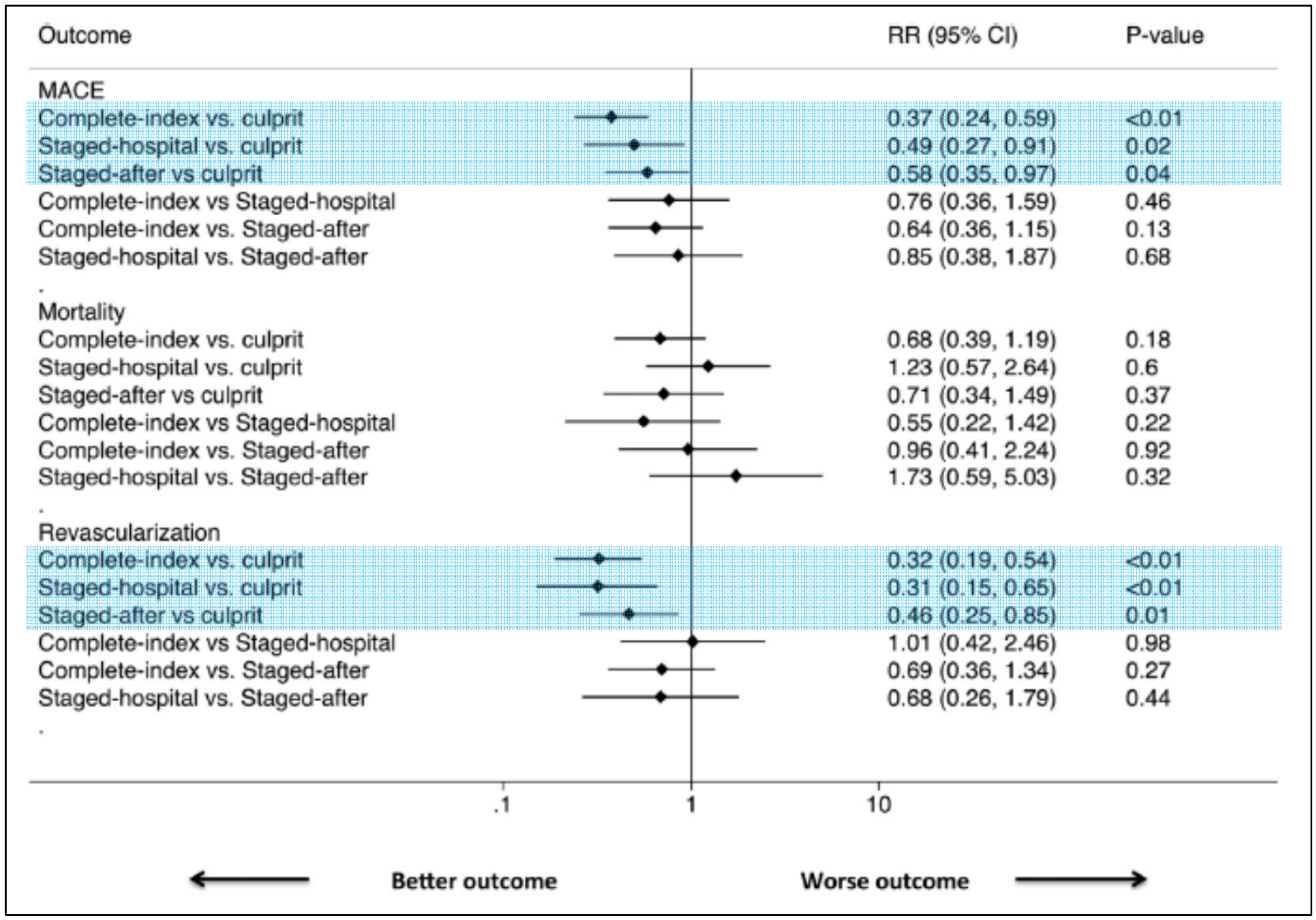
Complete or Culprit-Only Revascularization for Patients With Multivessel Coronary Artery Disease Undergoing Percutaneous Coronary Intervention

A Pairwise and Network Meta-Analysis of Randomized Trials

Islam Y. Elgendy, MD,[a] Ahmed N. Mahmoud, MD,[a] Dharam J. Kumbhani, MD, SM,[b]
Deepak L. Bhatt, MD, MPH,[c] Anthony A. Bavry, MD, MPH[a,d]

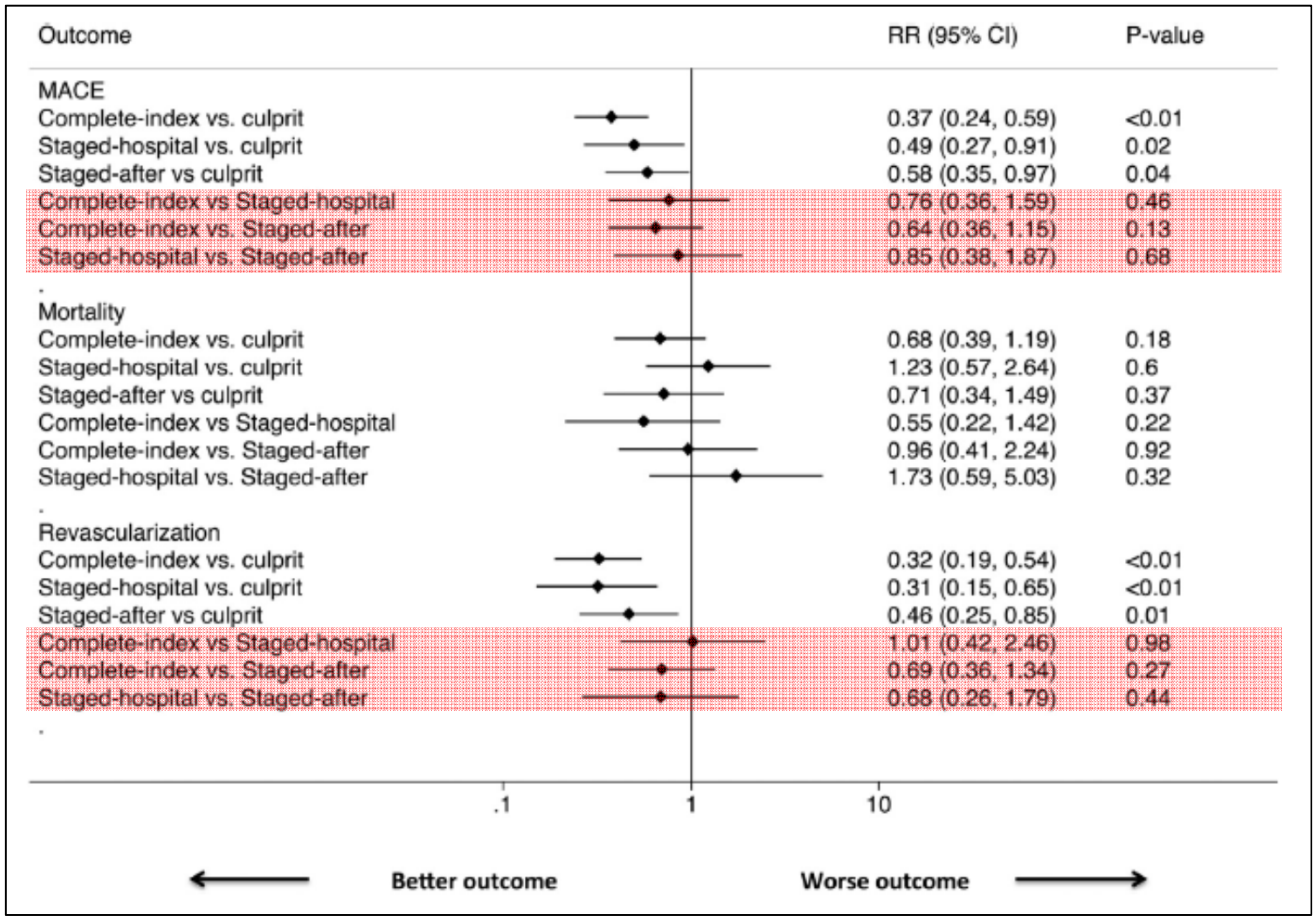
Islam Y. Elgendy et al. JACC interventions 2017;10:315-324

Does Timing of Intervening Non-IRA Make a Difference?



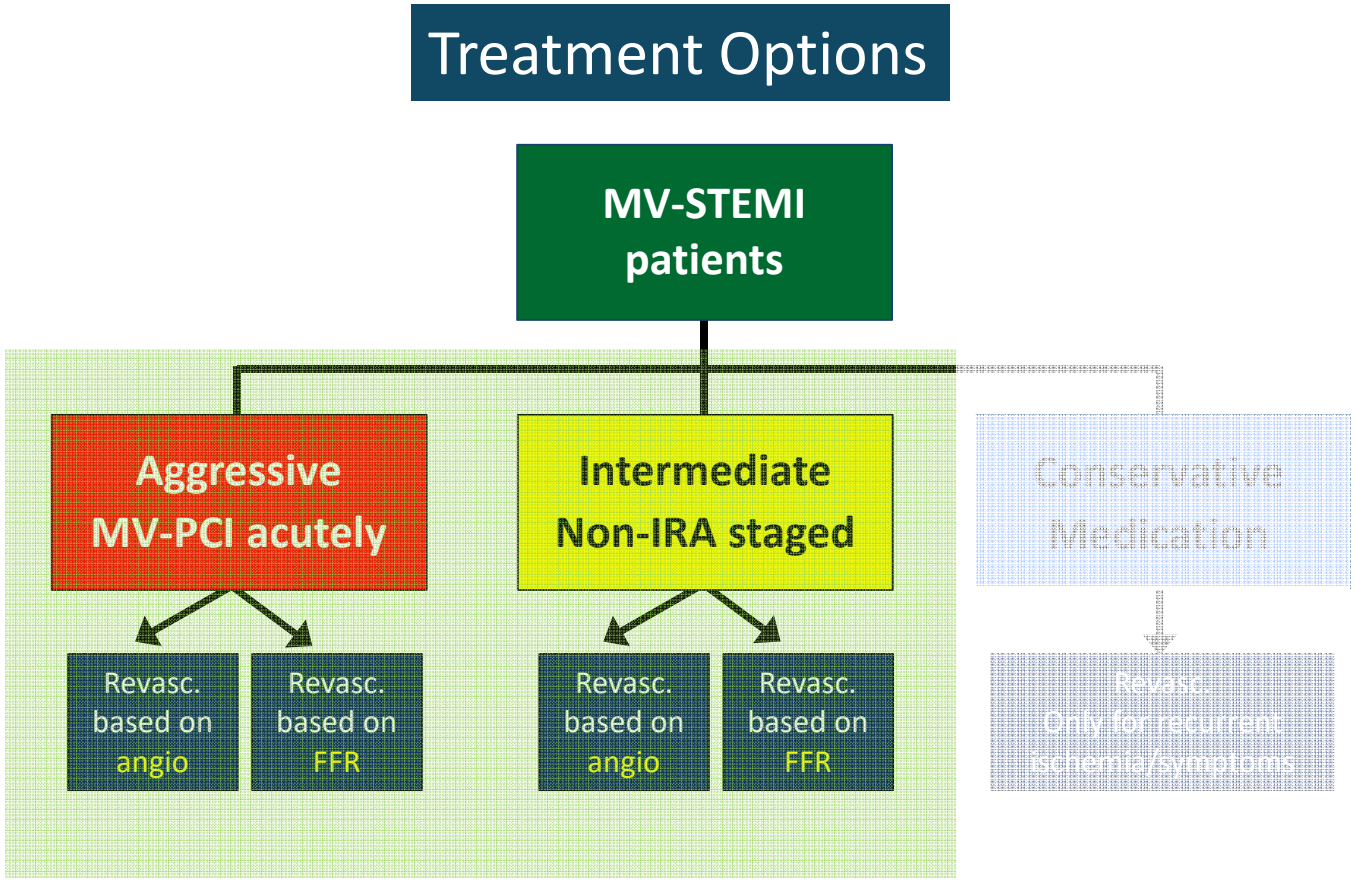
Islam Y. Elgendy et al. JACC interventions 2017;10:315-324

Does Timing of Intervening Non-IRA Make a Difference?



Islam Y. Elgendy et al. JACC interventions 2017;10:315-324

STEMI with Multivessel Disease



Procedural aspects of the primary percutaneous coronary intervention strategy

ESC 2017
European Society of Cardiology

Recommendations	Class	Level
IRA technique *(continued)*		
Routine use of thrombus aspiration is not recommended.	III	A
Non-IRA strategy		
Routine revascularization of non-IRA lesions should be considered in STEMI patients with multivessel disease before hospital discharge.	IIa	A
Non-IRA PCI during the index procedure should be considered in patients with cardiogenic shock.	IIa	C
CABG should be considered in patients with ongoing ischaemia and large areas of jeopardized myocardium if PCI of the IRA cannot be performed.	IIa	C

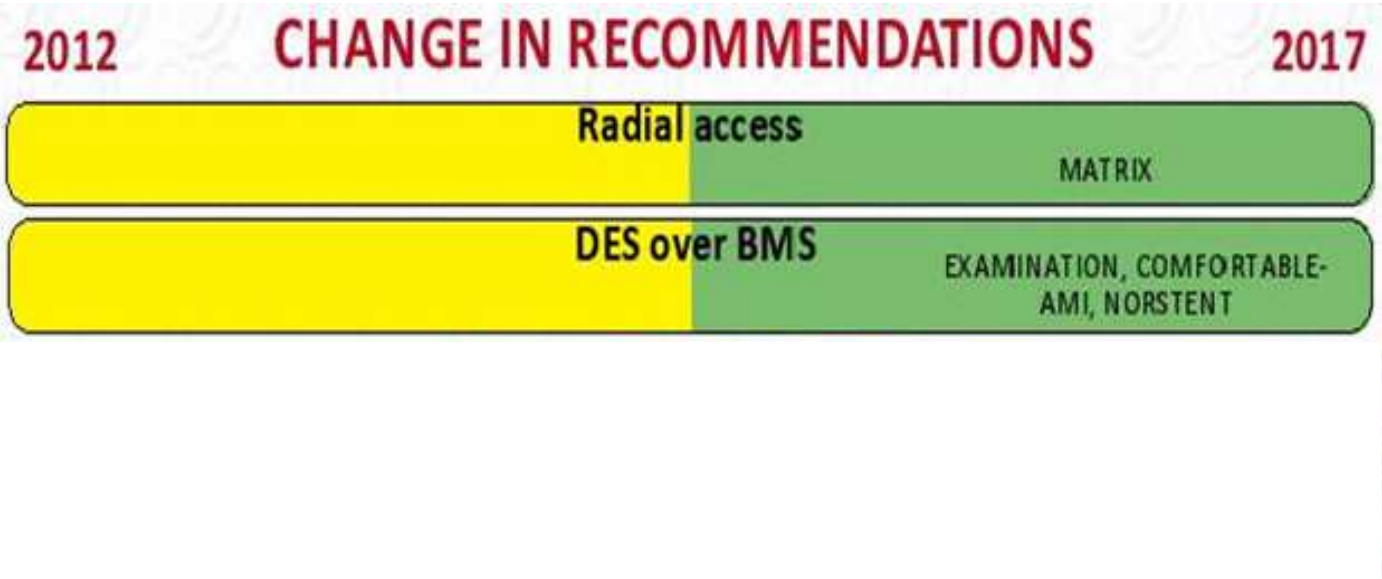
2015 ACC/AHA/SCAI Focused Update on Primary Percutaneous Coronary Intervention for Patients With ST-Elevation Myocardial Infarction: An Update of the 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention and the 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Society for Cardiovascular Angiography and Interventions

2013 Recommendation	2015 Focused Update Recommendation
Class III: Harm PCI should not be performed in a noninfarct artery at the time of primary PCI in patients with STEMI who are hemodynamically stable (11-13). (*Level of Evidence: B*)	**Class IIb** PCI of a noninfarct artery may be considered in selected patients with STEMI and multivessel disease who are hemodynamically stable, either at the time of primary PCI or as a planned staged procedure (11-24). *(Level of Evidence: B-R)*

What is new in 2017 Guidelines on AMI-STEMI

ESC
European Society of Cardiology

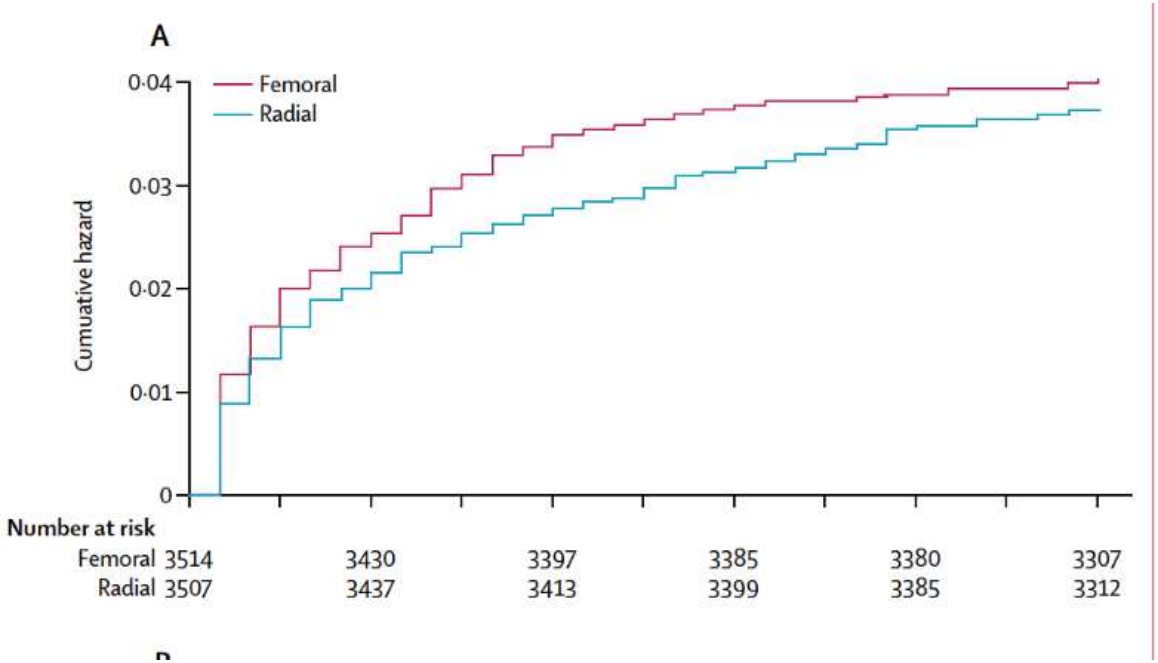


Evidence Based Practice

RADIAL ARTERY ACCESS

Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial

*Sanjit S Jolly, Salim Yusuf, John Cairns, Kari Niemelä, Denis Xavier, Petr Widimsky, Andrzej Budaj, Matti Niemelä, Vicent Valentin, Basil S Lewis, Alvaro Avezum, Philippe Gabriel Steg, Sunil V Rao, Peggy Gao, Rizwan Afzal, Campbell D Joyner, Susan Chrolavicius, Shamir R Mehta, for the RIVAL trial group**

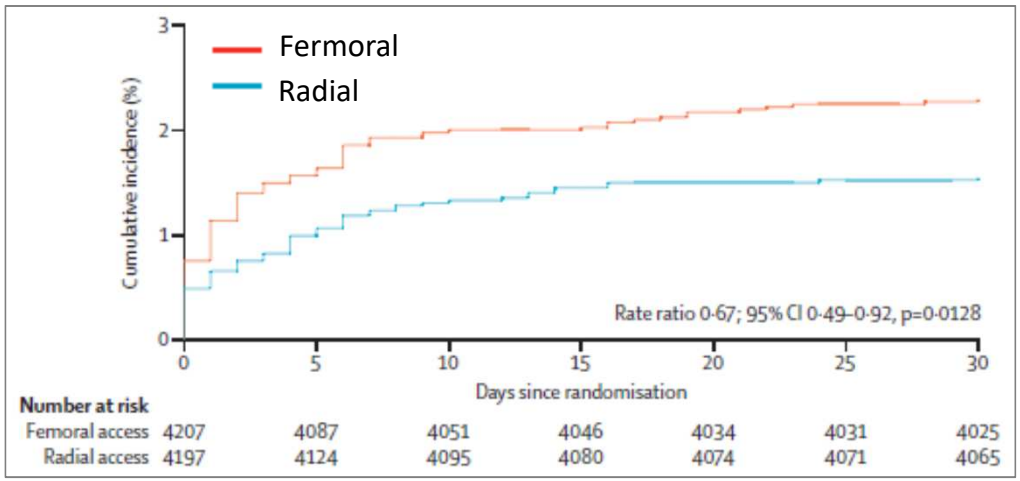


LANCET 2011;3779775):1409-20

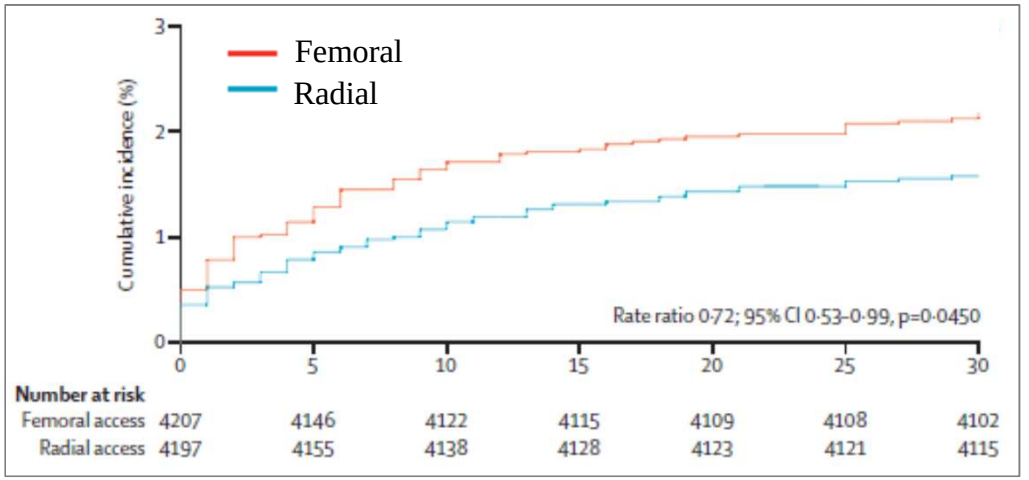
ACS：Radial Vs Femoral “MATRIX” Trial

- **8404 patients**
- **Radial acccess：Reduced 30-day MACE**

Bleeding risk



Mortality



Valgimigli M, et al. LANCET 2015; available on-line 16 March 2015

Evidence Based Practice

DRUG ELUTING STENTS

Stent Thrombosis With Second-Generation Drug-Eluting Stents Compared With Bare-Metal Stents

Network Meta-Analysis of Primary Percutaneous Coronary Intervention Trials in ST-Segment–Elevation Myocardial Infarction

Femi Philip, MD; Shikhar Agarwal, MD; Matthew C. Bunte, MD; Sachin S. Goel, MD; E. Murat Tuzcu, MD; Stephen Ellis, MD; Samir R. Kapadia, MD

Effect of Biolimus-Eluting Stents With Biodegradable Polymer vs Bare-Metal Stents on Cardiovascular Events Among Patients With Acute Myocardial Infarction

The COMFORTABLE AMI Randomized Trial

Lorenz Räber, MD; Henning Kelbæk, MD; Miodrag Ostojic, MD; Andreas Baumbach, MD; Dik Heg, PhD; David Tüller, MD; Clemens von Birgelen, MD, PhD; Marco Roffi, MD; Aris Moschovitis, MD; Ahmed A. Khattab, MD; Peter Wenaweser, MD; Robert Bonvini, MD; Giovanni Pedrazzini, MD; Ran Kornowski, MD; Klaus Weber, MD; Sven Trelle, MD; Thomas F. Lüscher, MD; Masanori Taniwaki, MD; Christian M. Matter, MD; Bernhard Meier, MD; Peter Jüni, MD; Stephan Windecker, MD; for the COMFORTABLE AMI Trial Investigators

Clinical Outcomes With Drug-Eluting and Bare-Metal Stents in Patients With ST-Segment Elevation Myocardial Infarction

Evidence From a Comprehensive Network Meta-Analysis

Tullio Palmerini, MD,* Giuseppe Biondi-Zoccai, MD,† Diego Della Riva, MD,* Andrea Mariani, MD,* Manel Sabaté, MD,‡ Marco Valgimigli, MD,§ Giacomo Frati, MD,† Elvin Kedhi, MD,‖ Pieter C. Smits, MD,‖ Christoph Kaiser, MD,¶ Philippe Genereux, MD,# Soren Galatius, MD,** Ajay J. Kirtane, MD, SM,# Gregg W. Stone, MD#

Bologna, Latina, and Ferrara, Italy; Barcelona, Spain; Rotterdam, the Netherlands; Basel, Switzerland; New York, New York; and Copenhagen, Denmark

Selective use of contemporary drug-eluting stents in primary angioplasty for ST-elevation myocardial infarction: pooled analysis of COMFORTABLE AMI and EXAMINATION

Published on 20 January 2017

Andreas Baumbach[1]*, MD; Dik Heg[2], PhD; Lorenz Räber[3], MD; Miodrag Ostojic[4], MD; Salvatore Brugaletta[5], MD, PhD; Julian W. Strange[1], MD; Thomas W. Johnson[1], MD; Peter Jüni[2], MD; Thomas Engstrøm[6], MD; Patrick W. Serruys[7], MD, PhD; Manel Sabaté[5], MD, PhD; Stephan Windecker[2], MD

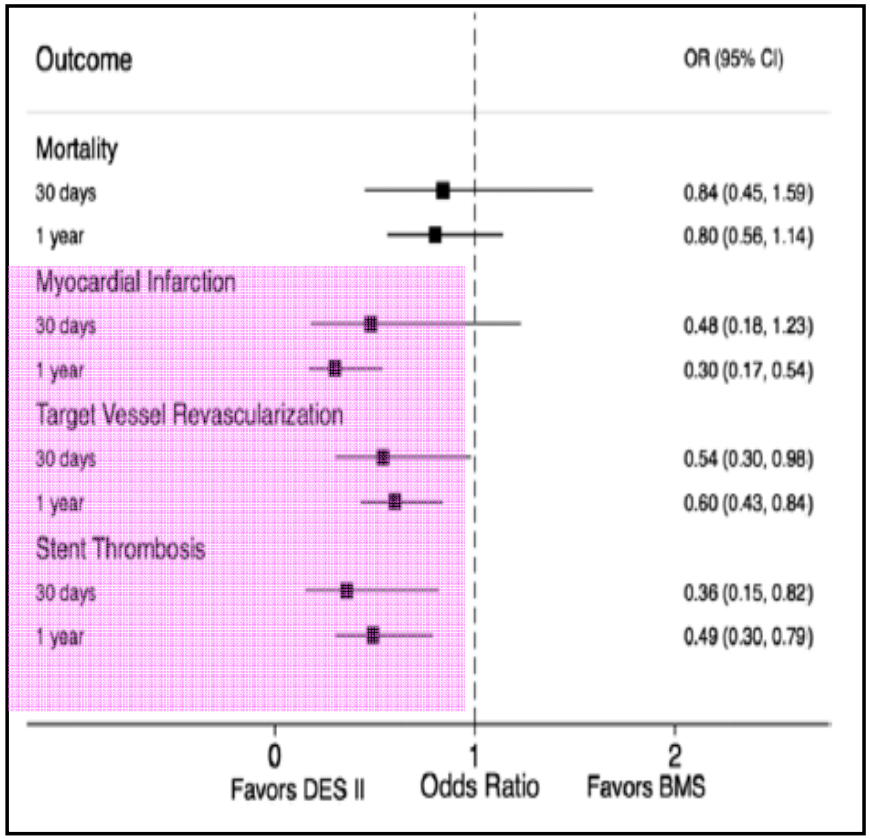
1. Bristol Heart Institute, University Hospitals Bristol NHS Foundation Trust, Bristol, United Kingdom; 2. CTU Bern, Department of Clinical Research, and Institute of Social and Preventive Medicine (ISPM),

KEYWORDS

- drug-eluting stents
- primary angioplasty
- STEMI

2nd Gen DES Vs BMS for PPCI:

Meta-analysis of Randomized Trials

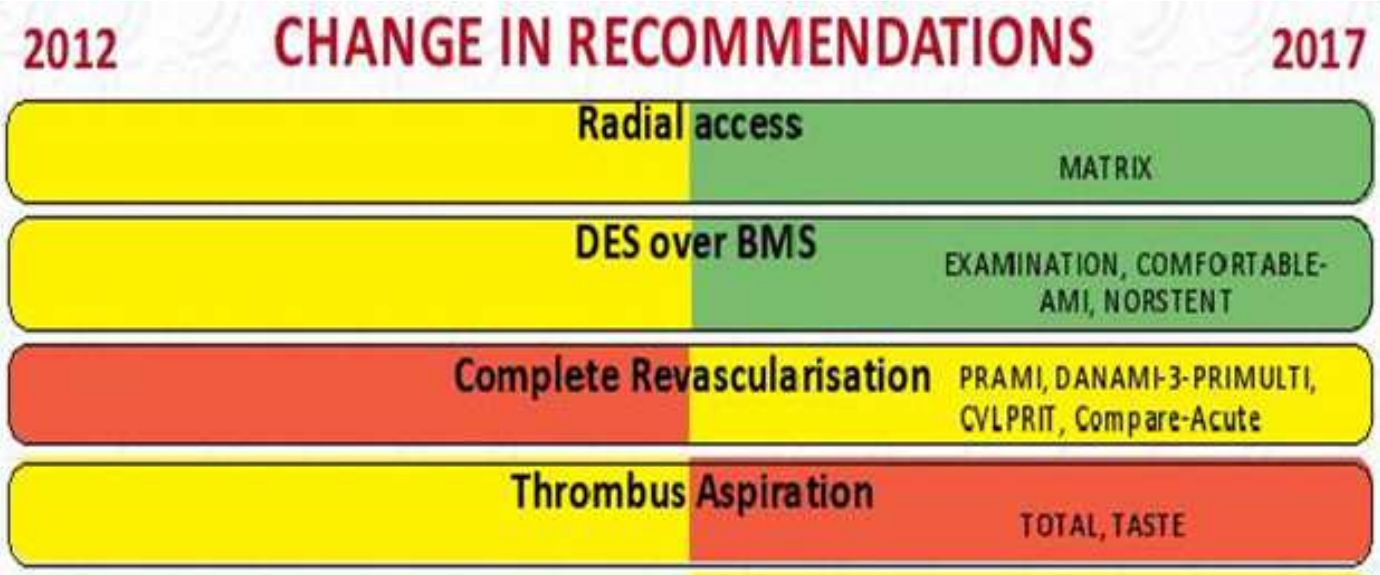


TYPHOON[10]	2003
STRATEGY[23]	2003
PASSION[27]	2003
SESAMI[26]	2003
MISSON[16]	2004
PASEO[25]	2004
Gao et al[15]	2005
SELECTION[24]	2005
MULTISTRATEGY[28]	2005
DEDICATION[22]	2005
GRACIA-3[21]	2005
Diaz de la Llera et al[20]	2005
HAAMU-STENT[19]	2006
DEBATER[18]	2007
HORIZONS-AMI[17]	2007
EXAMINATION[8]	2009
COMFORTABLE-AMI[9]	2010
ZEST-AMI[11]	2006
KROMER[14]	2007
SEZE[13]	2008
XAMI[12]	2008

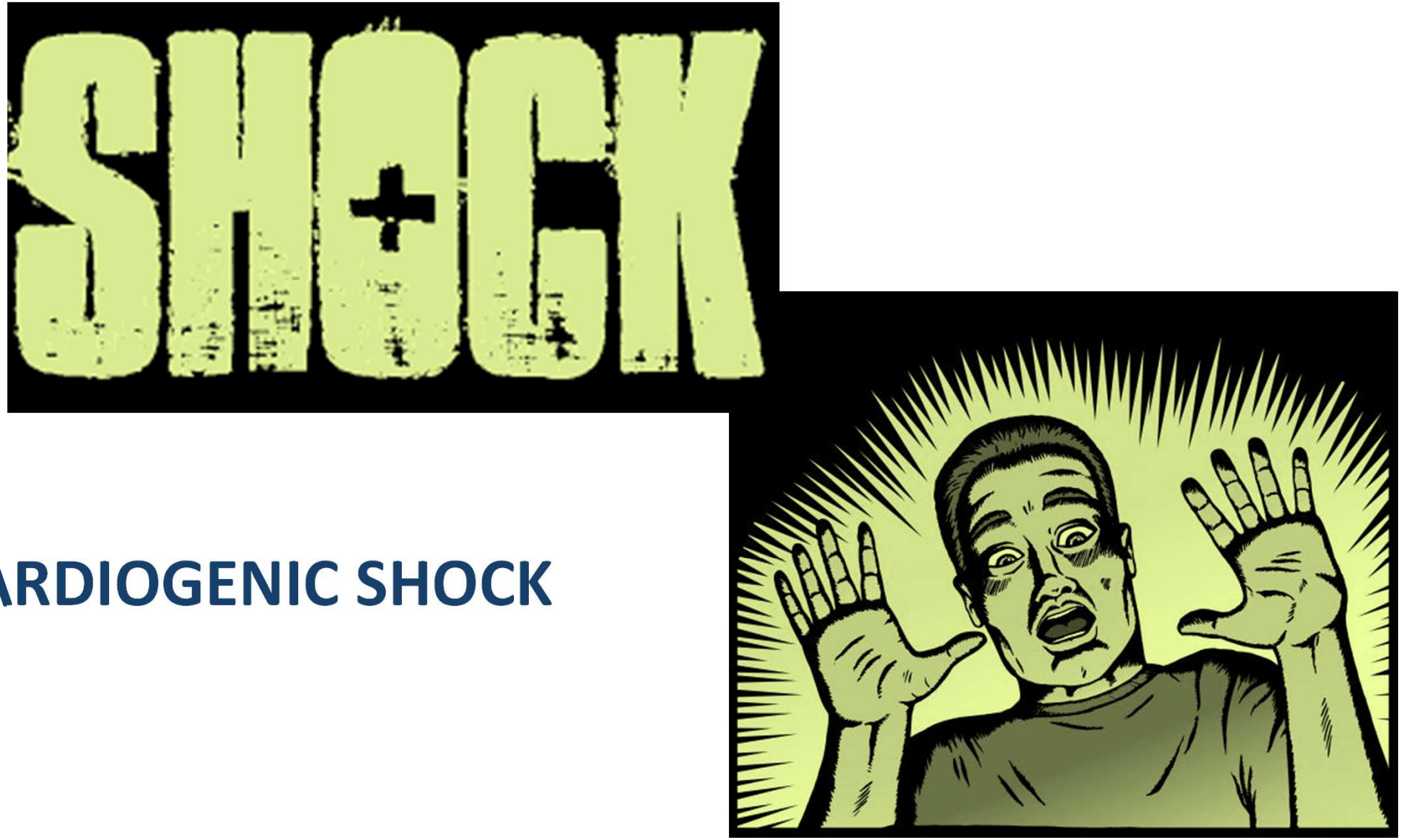
Philip M, et al. Circ Cardiovasc Interv 2014.

What is new in 2017 Guidelines on AMI-STEMI

ESC
European Society of Cardiology



I
IIa
IIb
III



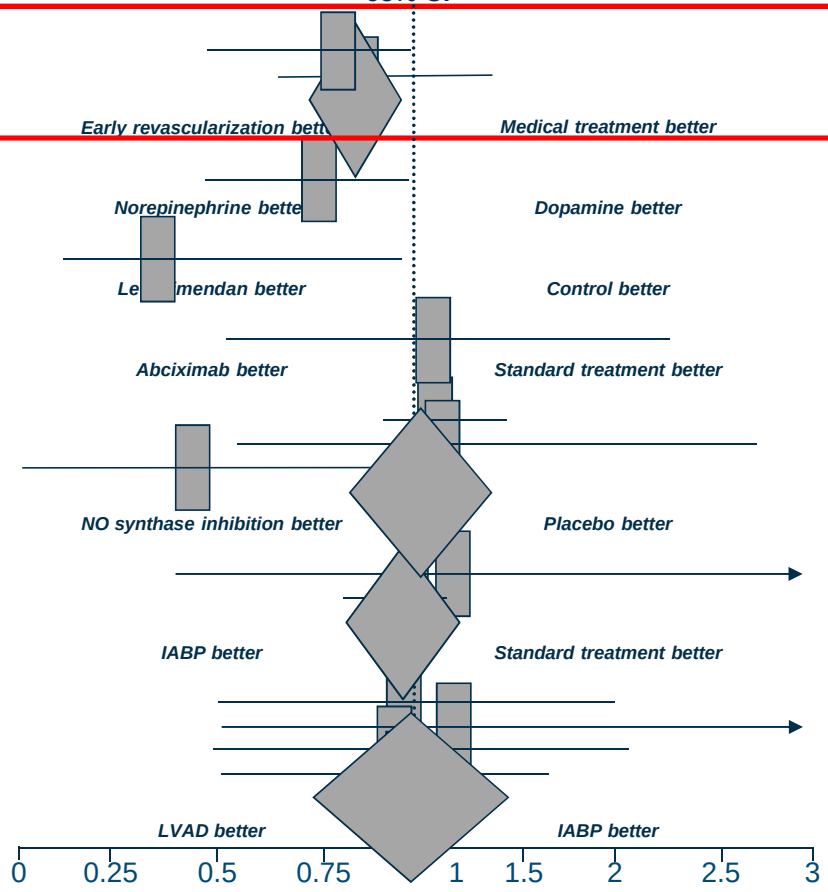
CARDIOGENIC SHOCK

Interventional Strategy

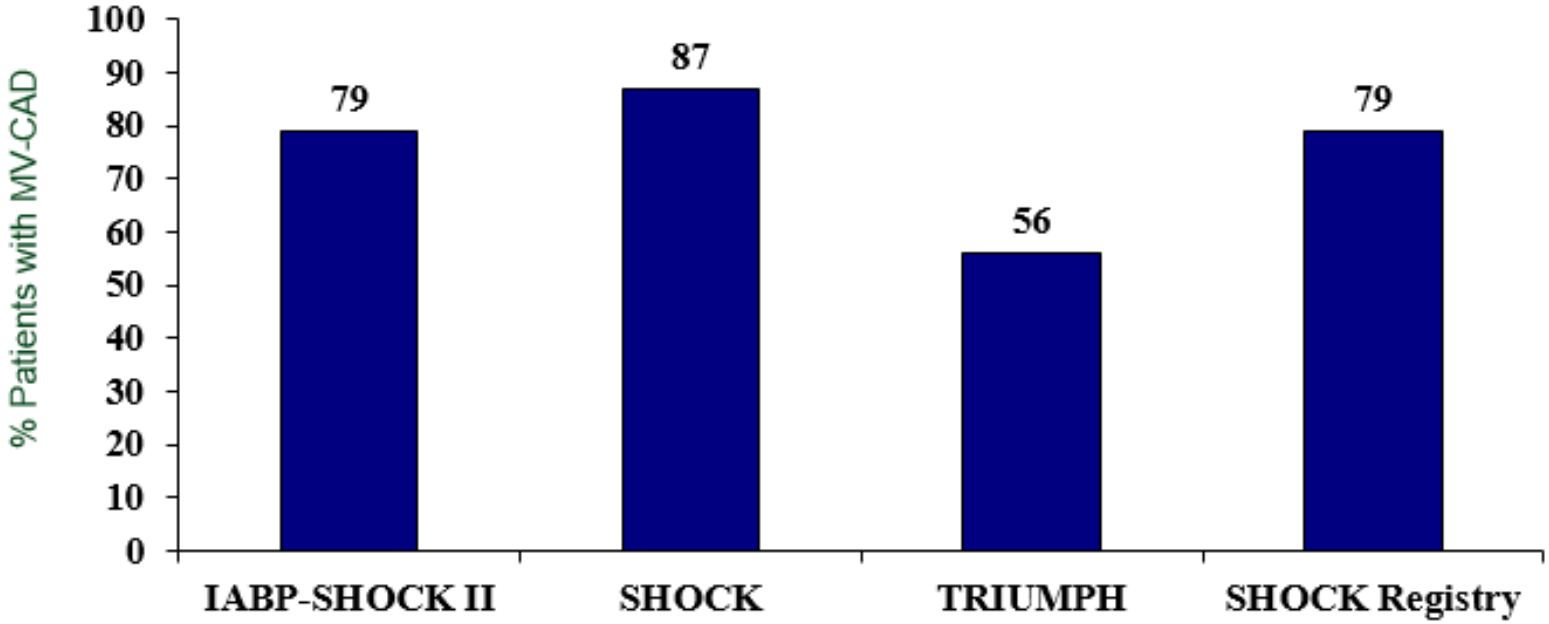
Hemodynamic Support

Randomized Trials Cardiogenic Shock

Trial	Follow-up	n/N	n/N	Relative Risk Mortality 95% CI	Relative Risk 95% CI
Revascularization					
SHOCK	1 year	81/152	100/150		0.72 (0.54;0.95)
SMASH	30 days	22/32	18/23		0.87 (0.66;1.29)
Total		***103/184***	***118/173***		***0.82 (0.69;0.97)***
Vasopressors					
SOAP-2 (CS subgroup)	28 days	64/145	50/135		0.75 (0.55;0.93)
Inotropes					
Unverzagt et al.	30 days	5/16	10/16		0.33 (0.11;0.97)
Glycoprotein IIb/IIIa inhibitors					
PRAGUE-18	In-hospital	15/40	13/40		1.15 (0.59;2.27)
NO synthase inhibitors					
TRIUMPH	30 days	97/201	76/180		1.14 (0.91;1.45)
SHOCK II	30 days	24/59	7/20		1.16 (0.59;2.69)
Cotter et al.	30 days	4/15	10/15		0.40 (0.13;1.05)
Total		***125/275***	***93/215***		***1.05 (0.85;1.29)***
IABP					
IABP-SHOCK I	30 days	7/19	6/21		1.28 (0.45;3.72)
IABP-SHOCK II	30 days	119/300	123/298		0.96 (0.79;1.17)
Total		***126/319***	***129/319***		***0.98 (0.81;1.18)***
LVAD					
Thiele et al.	30 days	9/21	9/20		0.95 (0.48;1.90)
Burkhoff et al.	30 days	9/19	5/14		1.33 (0.57;3.10)
ISAR-SHOCK	30 days	6/13	6/13		1.00 (0.44;2.29)
IMPRESS in Severe Shock	30 days	11/24	12/24		0.92 (0.51;1.66)
Total		***35/77***	***32/71***		***1.01 (0.70;1.44)***



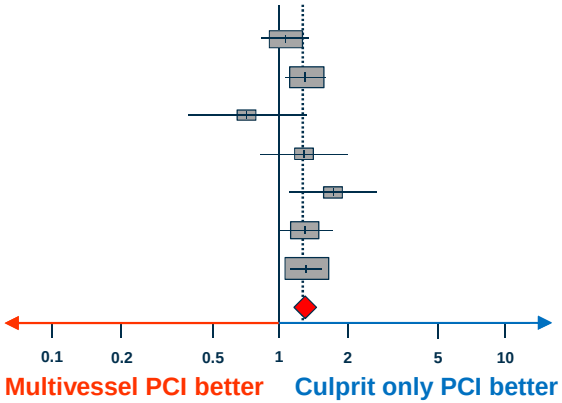
Prevalence multivessel disease in infarct-related shock



Multivessel PCI in Cardiogenic Shock?

Metaanalysis Mortality – Registry-Data

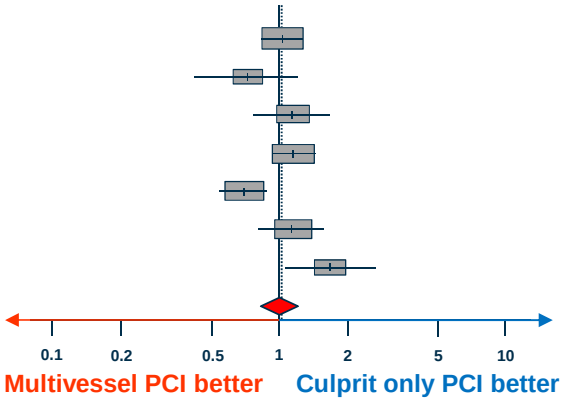
	MV-PCI		C-PCI		Short-term follow-up	RR	95%CI
	Events	Total	Events	Total			
IABP-SHOCK II	75	167	119	284		1.07	[0.86-1.33]
ALKK	81	173	201	562		1.31	[1.08-1.33]
KAMIR	13	124	56	386		0.72	[0.41-1.28]
Yang et al.	19	60	68	278		1.29	[0.85-1.98]
Cavender et al.	20	43	42	156		1.73	[1.14-2.61]
EHS-PCI	40	82	95	254		1.30	[0.99-1.71]
NCDR	158	433	737	2654		1.31	[1.14-1.51]
Overall	**406**	**1082**	**1318**	**4574**		**1.26**	**[1.12-1.41]**



Heterogeneity: τ^2=0.007, I^2=31.0%, p=0.19

Test for overall effect: p=0.001

	MV-PCI		C-PCI		Long-term follow-up	RR	95%CI
	Events	Total	Events	Total			
IABP-SHOCK II	91	167	149	284		1.04	[0.87-1.24]
KAMIR	16	124	69	386		0.72	[0.43-1.19]
Yang et al.	21	60	85	278		1.14	[0.78-1.69]
Cavender et al.	32	43	101	156		1.15	[0.93-1.42]
Mylotte et al.	37	66	82	103		0.70	[0.56-0.89]
van der Schaaf et al.	22	37	66	124		1.12	[0.82-1.53]
SHOCK	7	9	26	57		1.71	[1.09-2.67]
Overall	**226**	**506**	**578**	**1387**		**1.03**	**[0.85-1.25]**



Heterogeneity: τ^2=0.043, I^2=67.8%, p=0.005

Test for overall effect: p=0.77

Multivessel PCI in Cardiogenic Shock
European and American Recommendations 2017

Multivessel coronary artery disease present in up to 80% → higher mortality

Guidelines

ESC

I IIa IIb III

C

ACC/AHA/SCAI

No recommendation

Appropriate Use Criteria

ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS

A (9)

Ibanez et al. ESC STEMI Guidelines 2017. Eur Heart J 2017; epub
Levine et al. J Am Coll Cardiol 2016;67:1235-1250
Patel et al. J Am Coll Cardiol 2017;69:570-591.

The NEW ENGLAND JOURNAL of MEDICINE

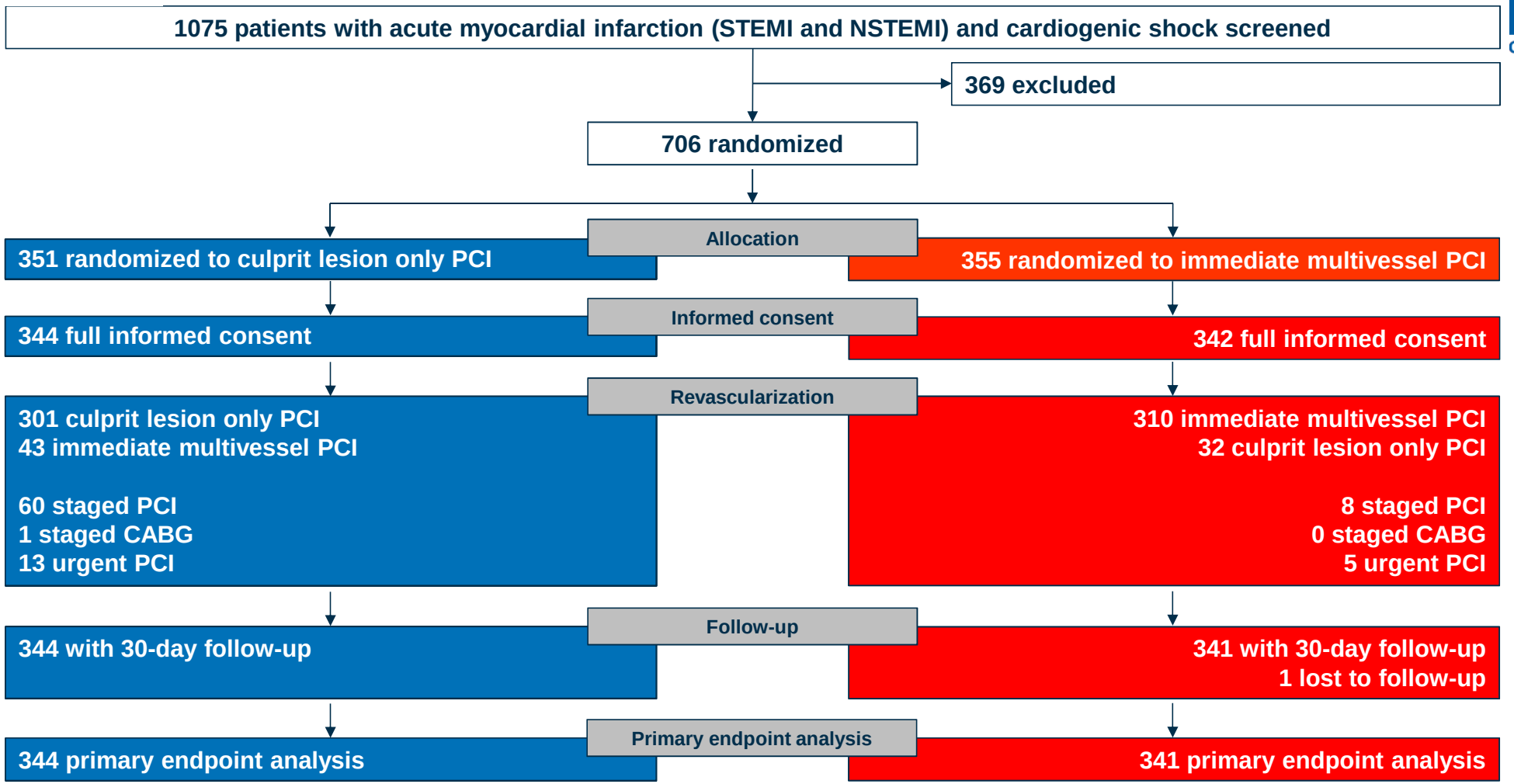
ORIGINAL ARTICLE

PCI Strategies in Patients with Acute Myocardial Infarction and Cardiogenic Shock

H. Thiele, I. Akin, M. Sandri, G. Fuernau, S. de Waha, R. Meyer-Saraei, P. Nordbeck, T. Geisler, U. Landmesser, C. Skurk, A. Fach, H. Lapp, J.J. Piek, M. Noc, T. Goslar, S.B. Felix, L.S. Maier, J. Stepinska, K. Oldroyd, P. Serpytis, G. Montalescot, O. Barthelemy, K. Huber, S. Windecker, S. Savonitto, P. Torremante, C. Vrints, S. Schneider, S. Desch, and U. Zeymer, for the CULPRIT-SHOCK Investigators*

NEJM 2017

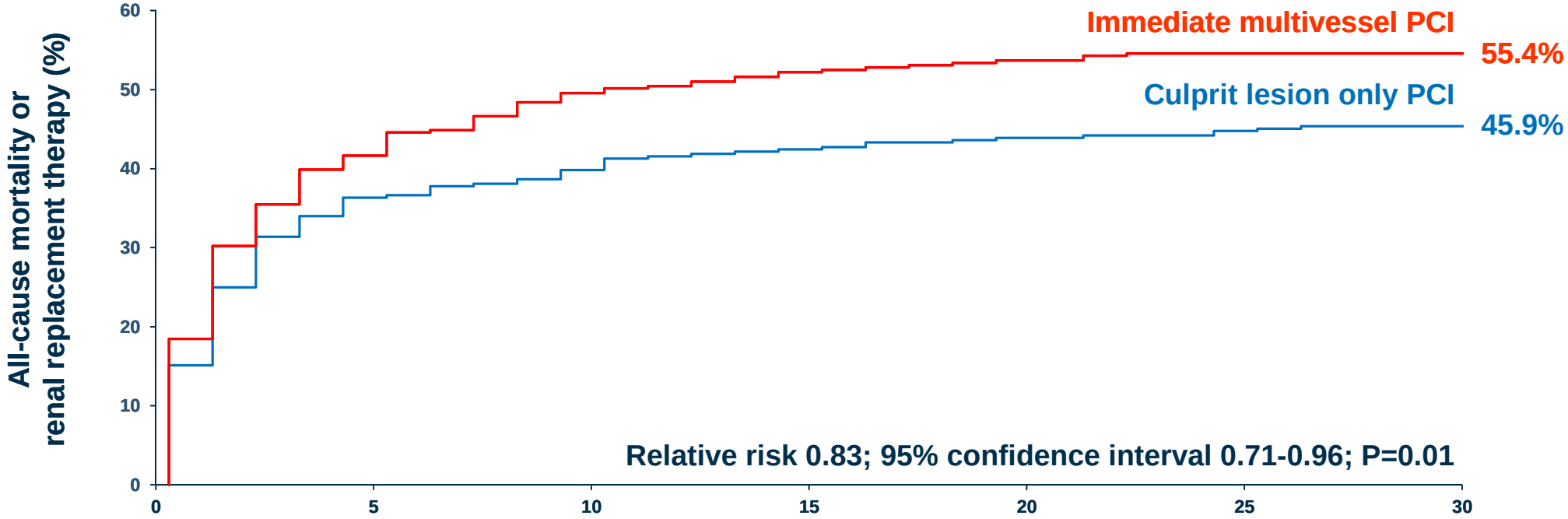
CULPRIT-SHOCK



New Engl J Med 2017;377:2419-2432.

Primary Study Endpoint

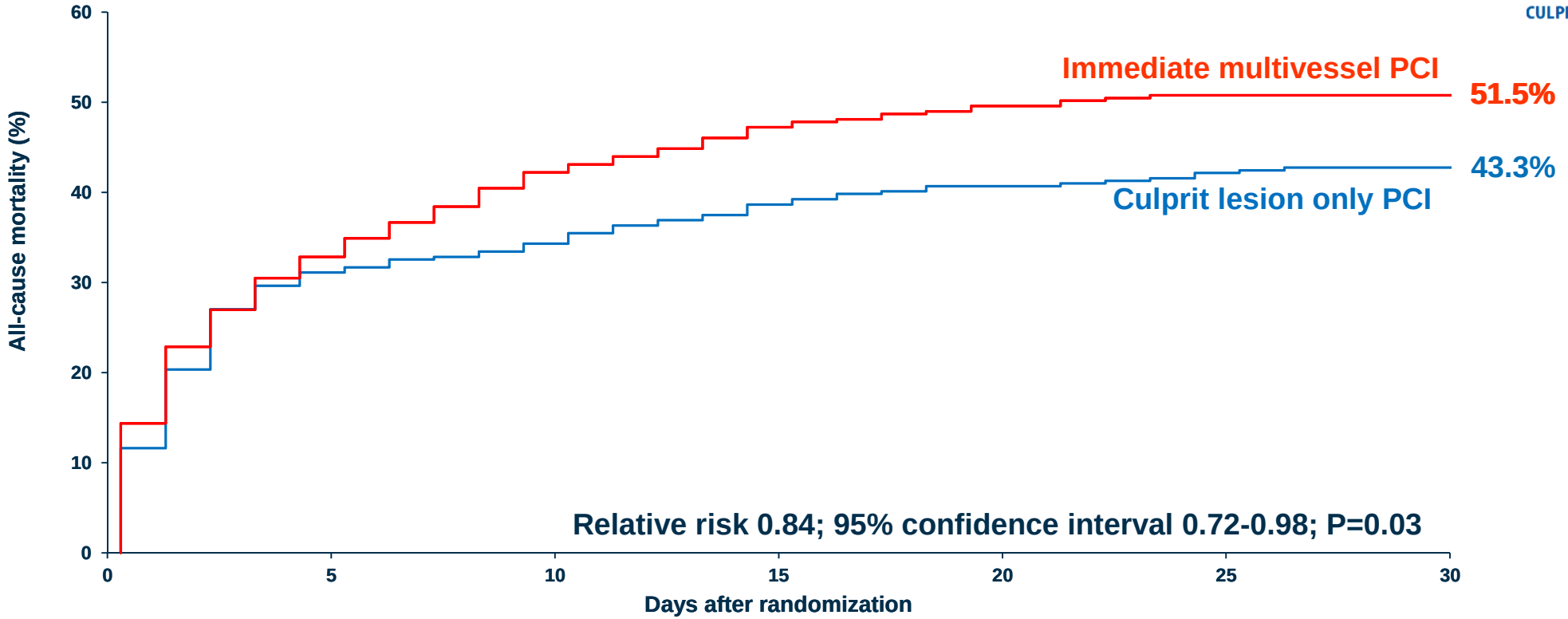
All-Cause Mortality or Renal Replacement Therapy



Number at risk:

Culprit lesion only PCI	344	219	207	198	192	189	184
Immediate multivessel PCI	341	199	172	162	156	153	152

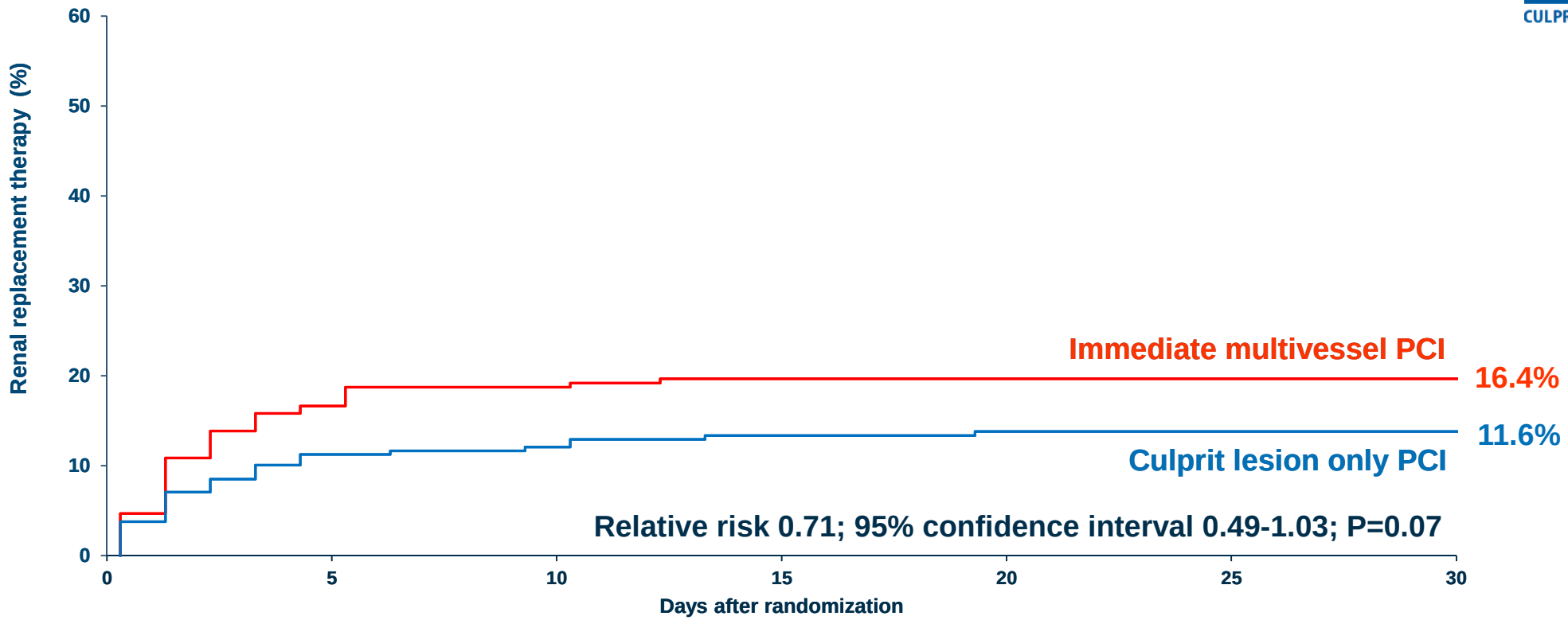
All-Cause Mortality



Number at risk:

Culprit lesion only PCI	344	237	226	211	203	198	193
Immediate multivessel PCI	341	229	197	179	170	166	165

Renal Replacement Therapy



Number at risk:

Culprit lesion only PCI	344	219	207	198	192	189	184
Immediate multivessel PCI	341	199	172	162	156	153	152

Culprit-Shock Questions

- Heterogeneous group of shock patients
- Heterogeneous coronary anatomy & contrast use
- Heterogeneous hemodynamic support

Culprit-Shock Questions

Characteristic	Culprit-Lesion-Only PCI Group (N=344)	Multivessel PCI Group (N=342)
Signs of impaired organ perfusion — no./total no. (%)		
Altered mental status	237/341 (69.5)	224/341 (65.7)
Cold, clammy skin and limbs	233/338 (68.9)	236/335 (70.4)
Oliguria	80/334 (24.0)	93/326 (28.5)
Arterial lactate >2.0 mmol/liter	216/334 (64.7)	224/330 (67.9)
Fibrinolysis <24 hr before randomization — no./total no. (%)	19/341 (5.6)	15/341 (4.4)
Resuscitation before randomization — no./total no. (%)	177/341 (51.9)	189/342 (55.3)
ST-segment elevation myocardial infarction — no./total no. (%)	206/335 (61.5)	209/330 (63.3)
Anterior ST-segment elevation myocardial infarction — no./total no. (%)	108/205 (52.7)	114/206 (55.3)
Left bundle-branch block — no./total no. (%)	52/335 (15.5)	47/331 (14.2)
Systolic blood pressure — mm Hg		
Median	100	100
Interquartile range	83–120	85–130
Diastolic blood pressure — mm Hg		
Median	60	61
Interquartile range	50–80	50–80
Mean blood pressure — mm Hg		
Median	76	76
Interquartile range	63–92	63–93

Culprit-Shock Questions

Characteristic	Culprit-Lesion-Only PCI Group (N=344)	Multivessel PCI Group (N=342)
Signs of impaired organ perfusion — no./total no. (%)		
Altered mental status	237/341 (69.5)	224/341 (65.7)
Cold, clammy skin and limbs	233/338 (68.9)	236/335 (70.4)
Oliguria	80/334 (24.0)	93/326 (28.5)
Arterial lactate >2.0 mmol/liter	216/334 (64.7)	224/330 (67.9)
Fibrinolysis <24 hr before randomization — no./total no. (%)	19/341 (5.6)	15/341 (4.4)
Resuscitation before randomization — no./total no. (%)	177/341 (51.9)	189/342 (55.3)
ST-segment elevation myocardial infarction — no./total no. (%)	206/335 (61.5)	209/330 (63.3)
Anterior ST-segment elevation myocardial infarction — no./total no. (%)	108/205 (52.7)	114/206 (55.3)
Left bundle-branch block — no./total no. (%)	52/335 (15.5)	47/331 (14.2)
Systolic blood pressure — mm Hg		
Median	100	100
Interquartile range	83–120	85–130
Diastolic blood pressure — mm Hg		
Median	60	61
Interquartile range	50–80	50–80
Mean blood pressure — mm Hg		
Median	76	76
Interquartile range	63–92	63–93

Culprit-Shock Questions

No Difference in Cardiac Causes of Death

Cause	Culprit only	Multivessel
Sudden death	11 (7.4%)	12 (6.8%)
Recurrent MI	2 (1.3%)	2 (1.1%)
Refractory Shock	104 (69.8%)	108 (61.4%)

Culprit-Shock Questions

Non-Cardiac Causes of Death

Cause	Culprit only	Multivessel
Brain Injury	11 (7.4%)	25 (14.2%)
Unknown	2 (1.3%)	4 (5.1%)
Other	9 (6%)	12 (6.8%)

Should Cardiac Arrest Patients been Excluded?

Culprit-Shock Questions

Characteristic	Culprit-Lesion-Only PCI Group (N=344)	Multivessel PCI Group (N=342)	
No. of affected vessels — no./total no. (%)			
1	3/343 (0.9)	2/342 (0.6)	
2	122/343 (35.6)	124/342 (36.3)	
3	218/343 (63.6)	216/342 (63.2)	
Vessel related to the infarction — no./total no. (%)			
Left anterior descending artery	132/343 (38.5)	156/342 (45.6)	
Left circumflex artery	76/343 (22.2)	70/342 (20.5)	
Right coronary artery	102/343 (29.7)	89/342 (26.0)	
Left main artery	31/343 (9.0)	22/342 (6.4)	
Bypass graft	2/343 (0.6)	5/342 (1.5)	
≥1 Chronic total occlusion — no./total no. (%)	77/344 (22.4)	82/342 (24.0)	
Total dose of contrast material — ml			<0.001
Median	190	250	
Interquartile range	140–250	200–350	

Culprit-Shock Questions

Characteristic	Culprit-Lesion-Only PCI Group (N=344)	Multivessel PCI Group (N=342)	
Mechanical circulatory support — no./total no. (%)			
Any	99/344 (28.8)	95/342 (27.8)	0.77
Intraaortic balloon pump	25/99 (25.3)	26/95 (27.4)	0.74
Impella 2.5 percutaneous ventricular assist device	16/99 (16.2)	18/95 (18.9)	0.61
Impella CP percutaneous ventricular assist device	30/99 (30.3)	18/95 (18.9)	0.07
TandemHeart percutaneous ventricular assist device	2/99 (2.0)	0/95	0.50
Extracorporeal membrane oxygenation	18/99 (18.2)	27/95 (28.4)	0.09
Other	12/99 (12.1)	8/95 (8.4)	0.40

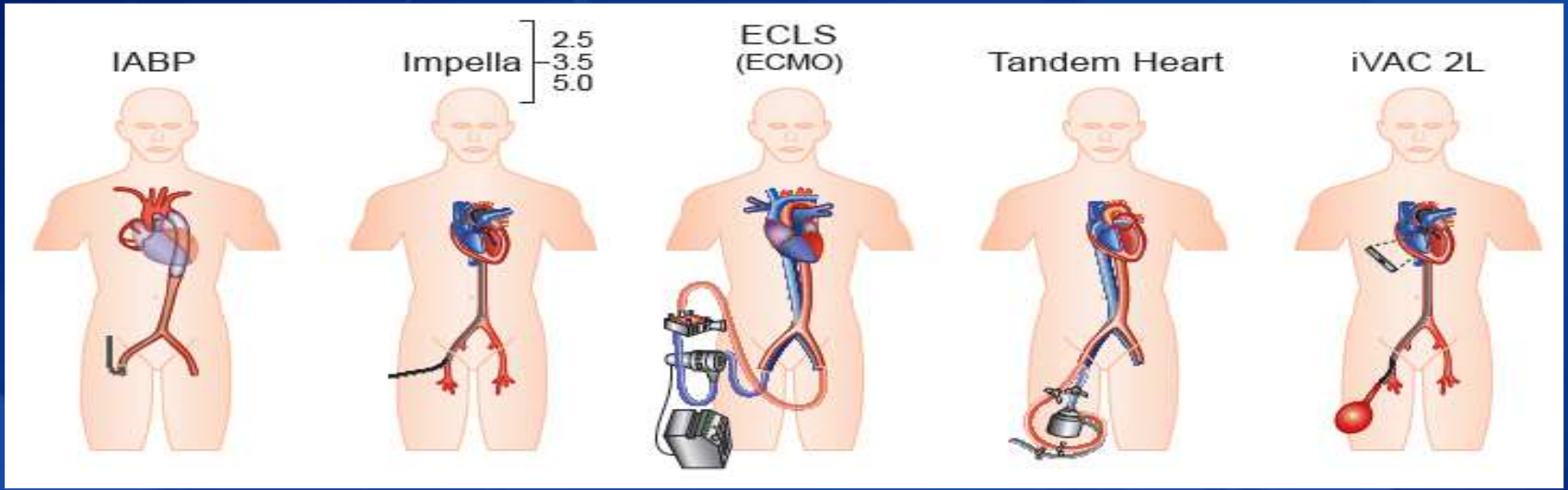
My Take from CULPRIT-SHOCK

- ***ROUTINE*** multivessel PCI not recommended
- Decision based on:
  - Severity of shock
  - Degree of stenoses in non-culprit vessels
  - Expected complexity of intervening non-culprit lesions
  - Neurological status
- Need to consider hemodynamic support

Interventional Strategy

Hemodynamic Support

Mechanical Circulatory Devices in Cardiogenic Shock



Thiele et al. Eur Heart J 2015;36:1223-30

IABP SHOCK II

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

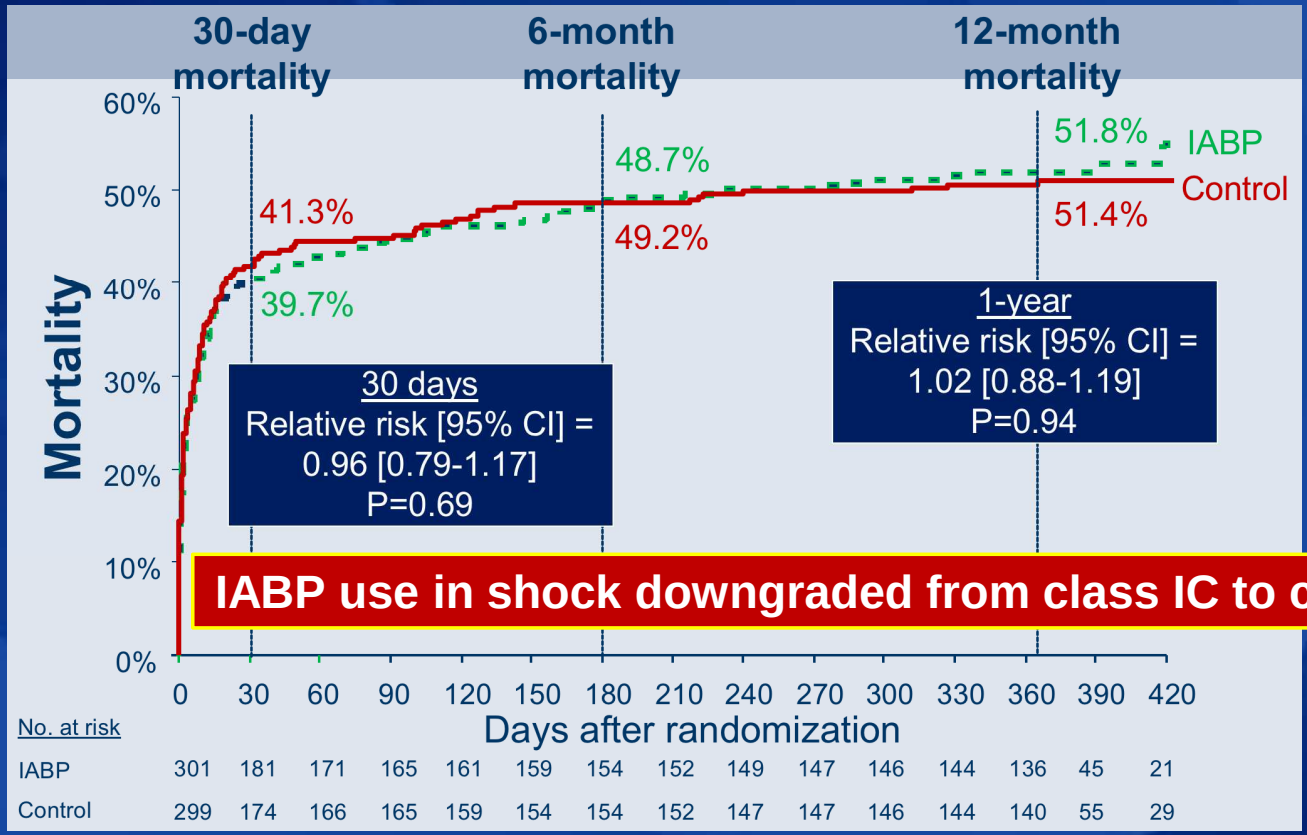
Intraaortic Balloon Support for Myocardial Infarction with Cardiogenic Shock

Holger Thiele, M.D., Uwe Zeymer, M.D., Franz-Josef Neumann, M.D., Miroslaw Ferenc, M.D., Hans-Georg Olbrich, M.D., Jörg Hausleiter, M.D., Gert Richardt, M.D., Marcus Hennersdorf, M.D., Klaus Empen, M.D., Georg Fuernau, M.D., Steffen Desch, M.D., Ingo Eitel, M.D., Rainer Hambrecht, M.D., Jörg Fuhrmann, M.D., Michael Böhm, M.D., Henning Ebelt, M.D., Steffen Schneider, Ph.D., Gerhard Schuler, M.D., and Karl Werdan, M.D., for the IABP-SHOCK II Trial Investigators*

IABP-SHOCK II

600 pts with cardiogenic shock randomized to IABP (median 3 days) vs. no IABP. Median BP 89/55 with 90% on pressors; median LVEF 35%.
Revasc: primary PCI 95.8%, CABG 3.5%; none 3.2%

Primary endpoint: Mortality at 30 days



IABP use in shock downgraded from class IC to class III

Thiele H et al. NEJM 2012;367:1287-96
Thiele H et al. Lancet 2013;382:1638-45

IABP-SHOCK II Trial

Strength:

- biggest randomized shock trial ever performed
- 600 patients included within 32 month
- contemporary CS treatment (>95 % revasc.)
- follow-up: 99.2%

Limitations:

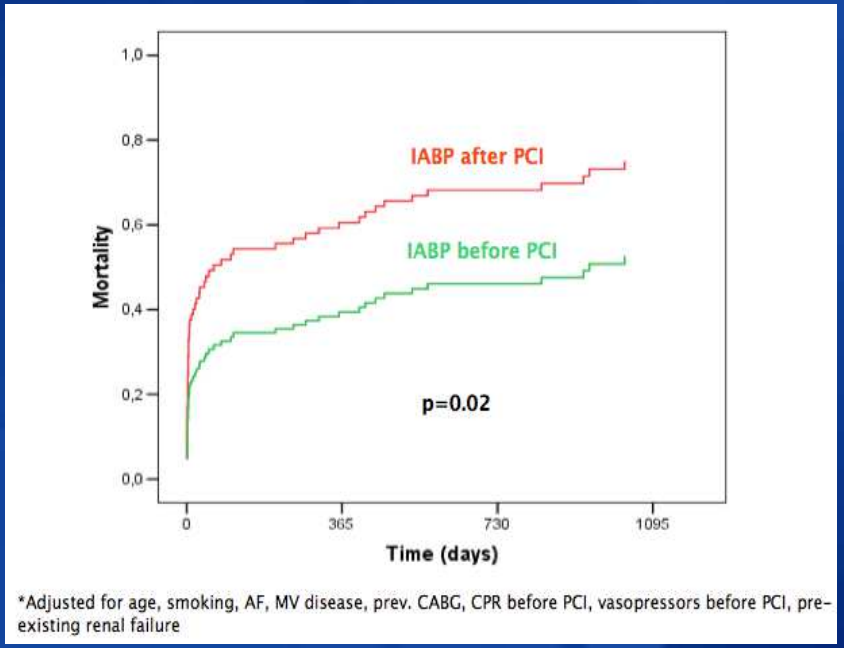
- Still underpowered for the primary endpoint (mortality rate significantly lower than anticipated)
- 10% cross-over to IABP, 4.2% in IABP group did not receive IABP, *with asymmetrical event rates in the 2 crossover groups*
- majority of pts. received IABP post PCI

Impact of IABP-Timing in CS

Design

- **DESIGN:** Single center observational study in 102 patients (Jan. 2005-Dez. 2010).
- **OBJECTIVE:** To evaluate the impact of IABP timing (before or after PCI) in STEMI complicated by cardiogenic shock.
- **ENDPOINTS:** Total mortality, MACCE, renal failure

Total mortality



*Adjusted for age, smoking, AF, MV disease, prev. CABG, CPR before PCI, vasopressors before PCI, pre-existing renal failure

Schwarz et al.

IMPRESS Trial

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 69, NO. 3, 2017

ISSN 0735-1097/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jacc.2016.10.022

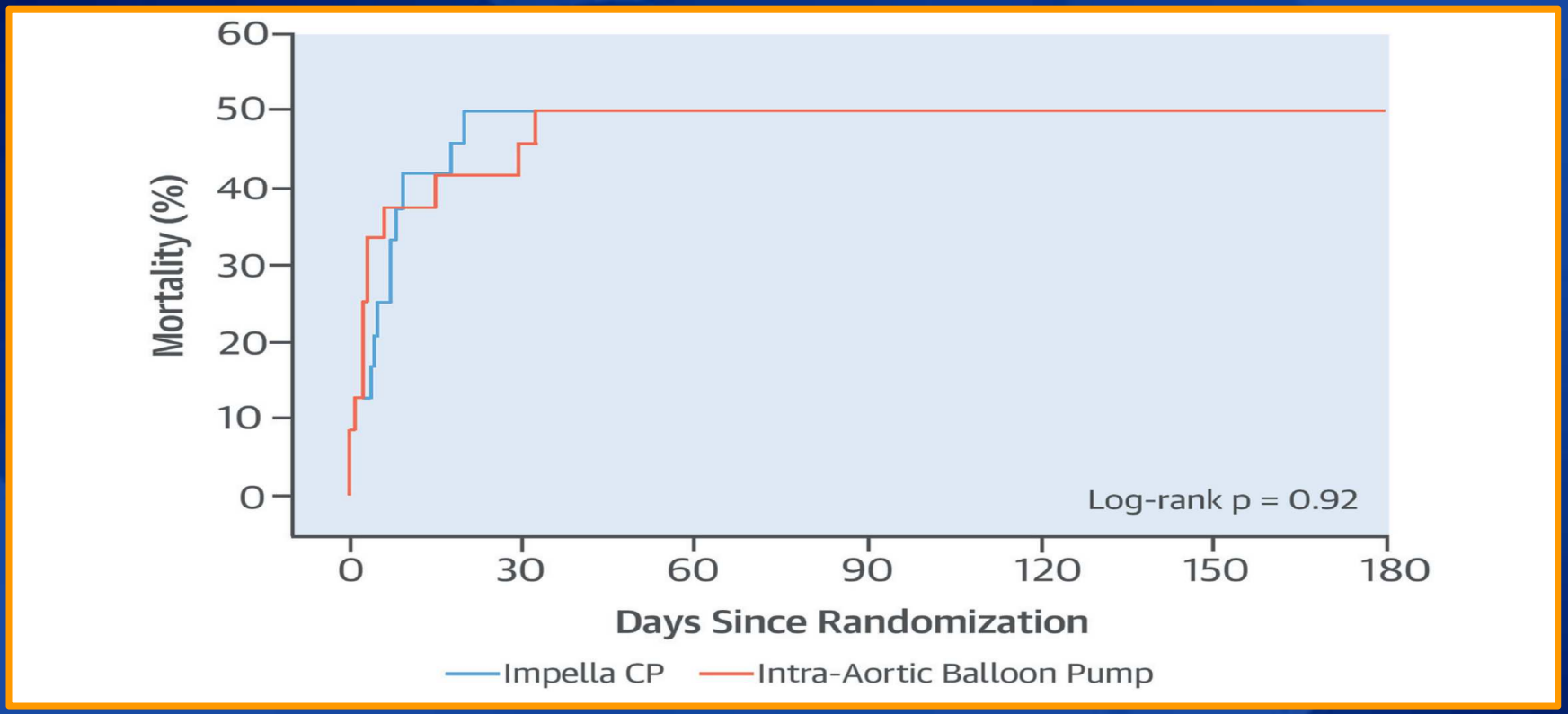
Percutaneous Mechanical Circulatory Support Versus Intra-Aortic Balloon Pump in Cardiogenic Shock After Acute Myocardial Infarction

Dagmar M. Ouweneel, MSc,[a] Erlend Eriksen, MD,[b] Krischan D. Sjauw, MD, PhD,[a] Ivo M. van Dongen, MD,[a] Alexander Hirsch, MD, PhD,[a] Erik J.S. Packer, MD,[b] M. Marije Vis, MD, PhD,[a] Joanna J. Wykrzykowska, MD, PhD,[a] Karel T. Koch, MD, PhD,[a] Jan Baan, MD, PhD,[a] Robbert J. de Winter, MD, PhD,[a] Jan J. Piek, MD, PhD,[a] Wim K. Lagrand, MD, PhD,[c] Bas A.J.M. de Mol, MD, PhD,[a] Jan G.P. Tijssen, PhD,[a] José P.S. Henriques, MD, PhD[a]

IMPRESS-IN-SEVERE-SHOCK

Impella CP versus IABP

Primary endpoint – 30-day mortality



Ouweneel et al. JACC 2017;69;278-287

Intensive Care Medicine
March 2016, Volume 42, Issue 3, pp 370–378 | Cite as

The ENCOURAGE mortality risk score and analysis of long-term outcomes after VA-ECMO for acute myocardial infarction with cardiogenic shock

Authors Authors and affiliations

Grégoire Muller, Erwan Flecher, Guillaume Lebreton, Charles-Edouard Luyt, Jean-Louis Trouillet, Nicolas Bréchot, Matthieu Schmidt, Ciro Mastroianni, Jean Chastre, Pascal Leprince, Amedeo Ansel

Survival

- At discharge: 47%
- At 6-month: 41%
- At 1-year: 38%

Mechanical Support in Cardiogenic Shock

- *ROUTINE* use of IABP not recommended, but studies have limitation, and does not speak against use in selected patients
- Data are lacking to conclude any mechanical support improves clinical outcome
- Target at pairing the right patient with the right device at the right time

Antithrombotic Therapy in STEMI

P2Y12 INHIBITORS

File Edit View Window Help

e123 (1 of 75) 136% Tools Sign

ACC/AHA FOCUSED UPDATE

2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

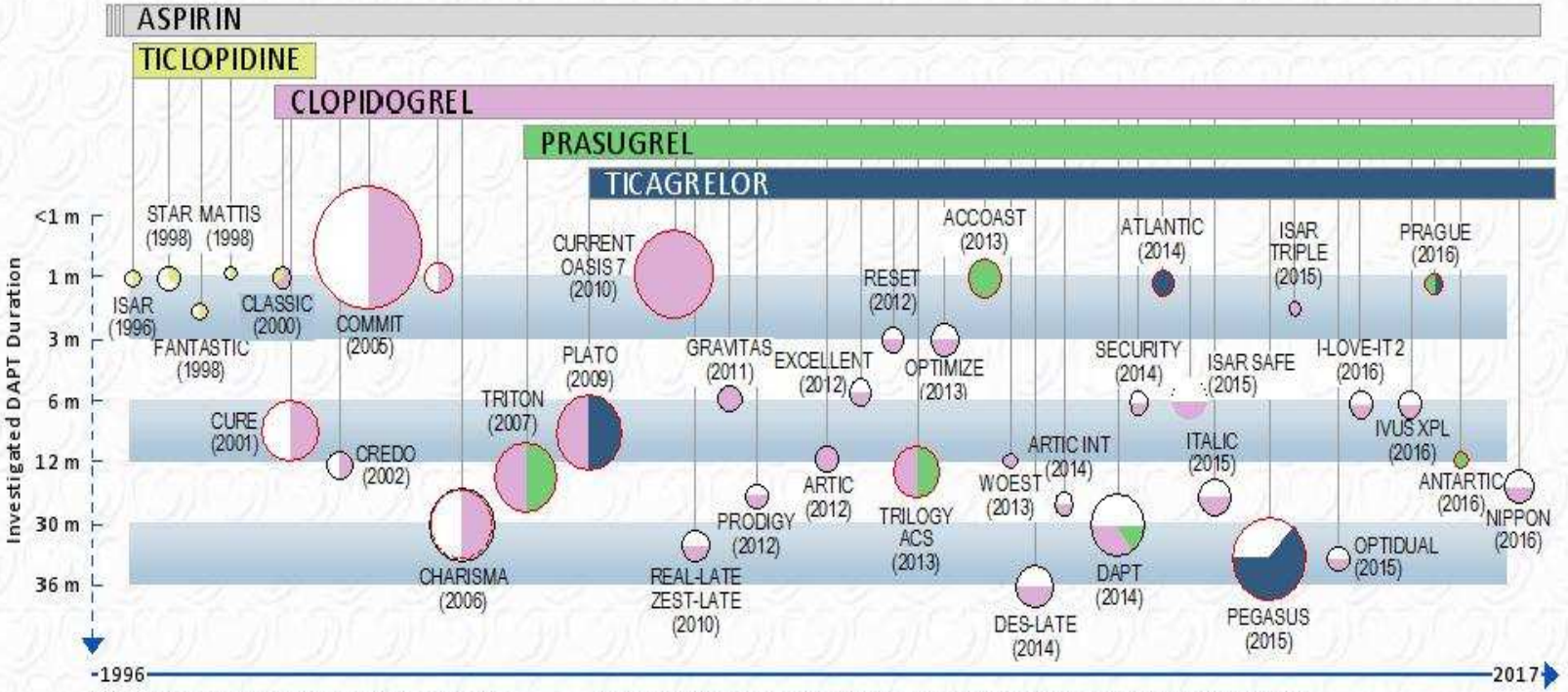
An Update of the 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention, 2011 ACCF/AHA Guideline for Coronary Artery By
Management of Patient
Myocardial Infarction,
Syndromes, and 2014
Undergoing Noncardia

Recommendations for Duration of DAPT in Patients With ACS Treated With PCI

COR	LOE	Recommendations
I	B-R	In patients with ACS (NSTE-ACS or STEMI) treated with DAPT after BMS or DES implantation, $P2Y_{12}$ inhibitor therapy (clopidogrel, prasugrel, or ticagrelor) should be given for at least 12 months.[16,50–55,72,96–98]

History of dual antiplatelet therapy (DAPT) in patients with coronary artery disease

ESC European Society of Cardiology



Size of the circles denotes sample size

2 5 10 20 K pts

Perimeter of the circles denotes type of investigated population

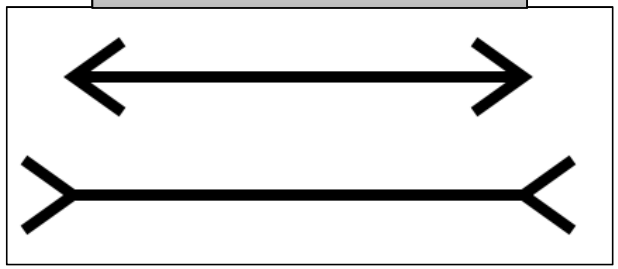
- Mixed clinical presentation at the time of stent implantation
- Acute coronary syndrome at presentation
- DAPT initiated in patients with prior myocardia infarction
- DAPT for primary prevention

www.escardio.org/guidelines 2017 ESC Focused Update on DAPT in Coronary Artery Disease, developed in collaboration with EACTS (European Heart Journal 2017 - doi:10.1093/eurheartj/ehx419)

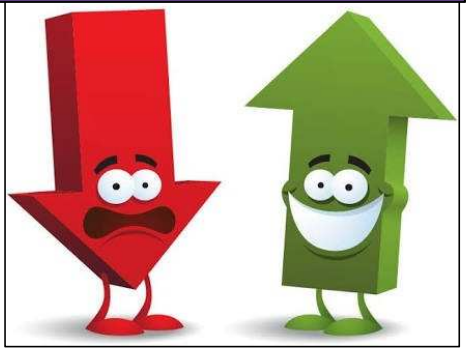
P2Y12 INHIBITORS

Stronger or weaker

Longer or shorter



Go Up or Go Down



Hurry to start?

Too much weight

P2Y12 INHIBITORS

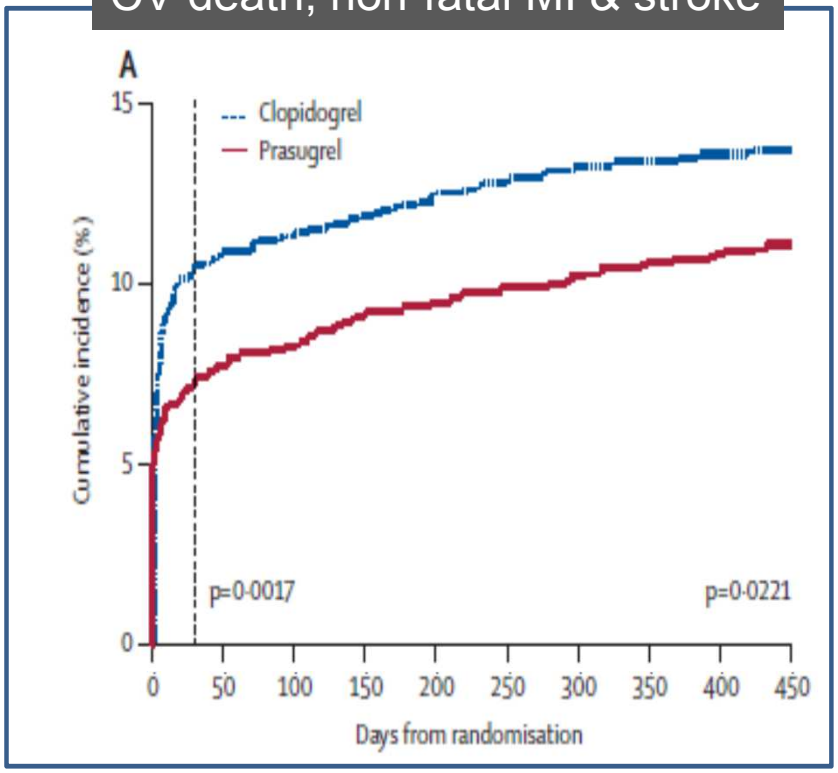
Stronger or weaker

TRITON TIMI 38: STEMI Subgroup

(Montalescot G, et al. Lancet 2009)

Prasugrel Vs Clopidogrel

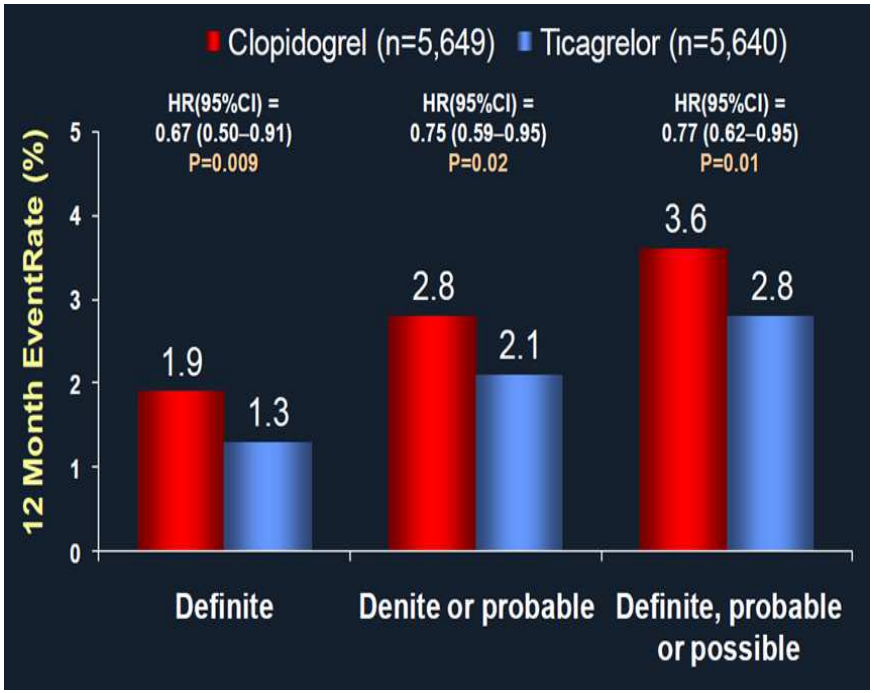
CV death, non-fatal MI & stroke



PLATO:

(Wallentin L, et al. NEJM 2009)

Ticagrelor Vs Clopidogrel

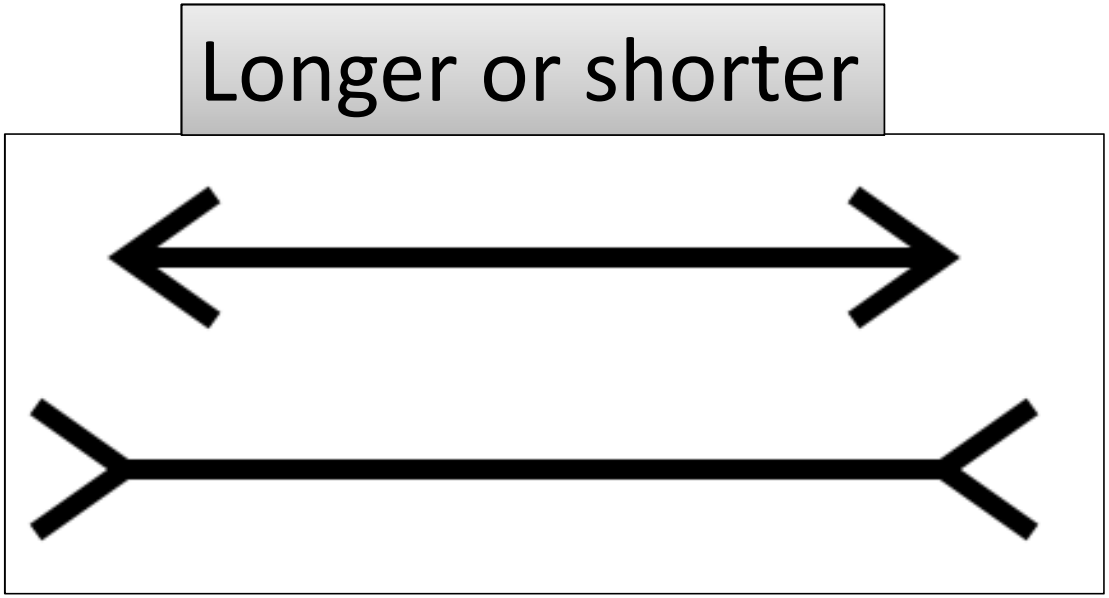


ESC European Society of Cardiology

Maintenance antithrombotic strategy after ST-elevation myocardial infarction

Recommendations	Class[a]	Level[b]
Antiplatelet therapy with low-dose aspirin (75–100 mg) is indicated.[329]	I	A
DAPT in the form of aspirin plus ticagrelor or prasugrel (or clopidogrel if ticagrelor or prasugrel are not available or are contraindicated), is recommended for 12 months after PCI, unless there are contraindications such as excessive risk of bleeding.[186,187]	I	A
PPI in combination with DAPT is recommended in patients at high risk of gastrointestinal bleeding.[c]	I	B
In patients with an indication for oral anticoagulation, oral anticoagulants are indicated in addition to antiplatelet therapy.[5]	I	C
In patients who are at high risk of severe bleeding complications, discontinuation of $P2Y_{12}$ inhibitor therapy after 6 months should be considered.[332,339,340]	IIa	B
In STEMI patients with stent implantation and an indication for oral anticoagulation, triple therapy[d] should be considered for 1–6 months (according to a balance between the estimated risk of recurrent coronary events and bleeding).[5]	IIa	C
DAPT for 12 months in patients who did not undergo PCI should be considered unless there are contraindications such as excessive risk of bleeding.	IIa	C
In patients with LV thrombus, anticoagulation should be administered for up to 6 months guided by repeated imaging.[341–343]	IIa	C
In high ischaemic-risk patients[e] who have tolerated DAPT without a bleeding complication, treatment with DAPT in the form of ticagrelor 60 mg twice a day on top of aspirin for longer than 12 months may be considered for up to 3 years.[333]	IIb	B
In low bleeding-risk patients who receive aspirin and clopidogrel, low-dose rivaroxaban (2.5 mg twice daily) may be considered.[338]	IIb	B
The use of ticagrelor or prasugrel is not recommended as part of triple antithrombotic therapy with aspirin and oral anticoagulation.	III	C

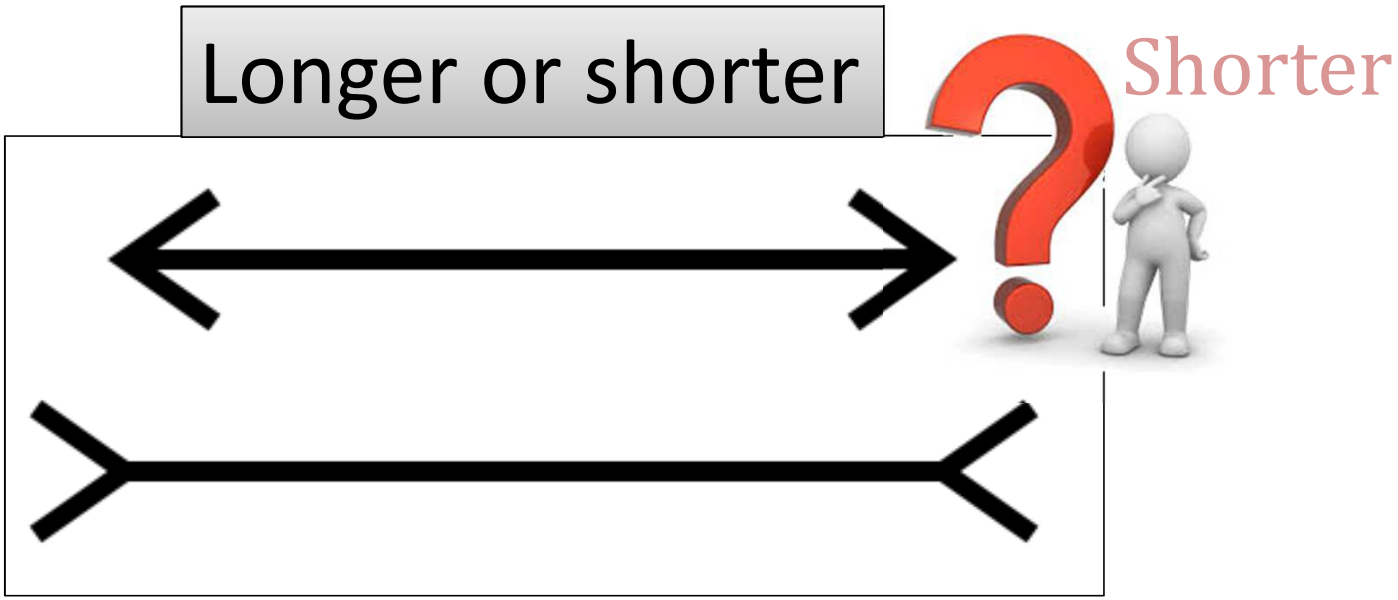
P2Y12 INHIBITORS



Background

- Current guidelines recommended 12 months or longer, but were not based on dedicated randomized controlled trials
- Shorter-term DAPT: Reduce bleeding risk
- Longer-term DAPT: Reduce ischemic risk

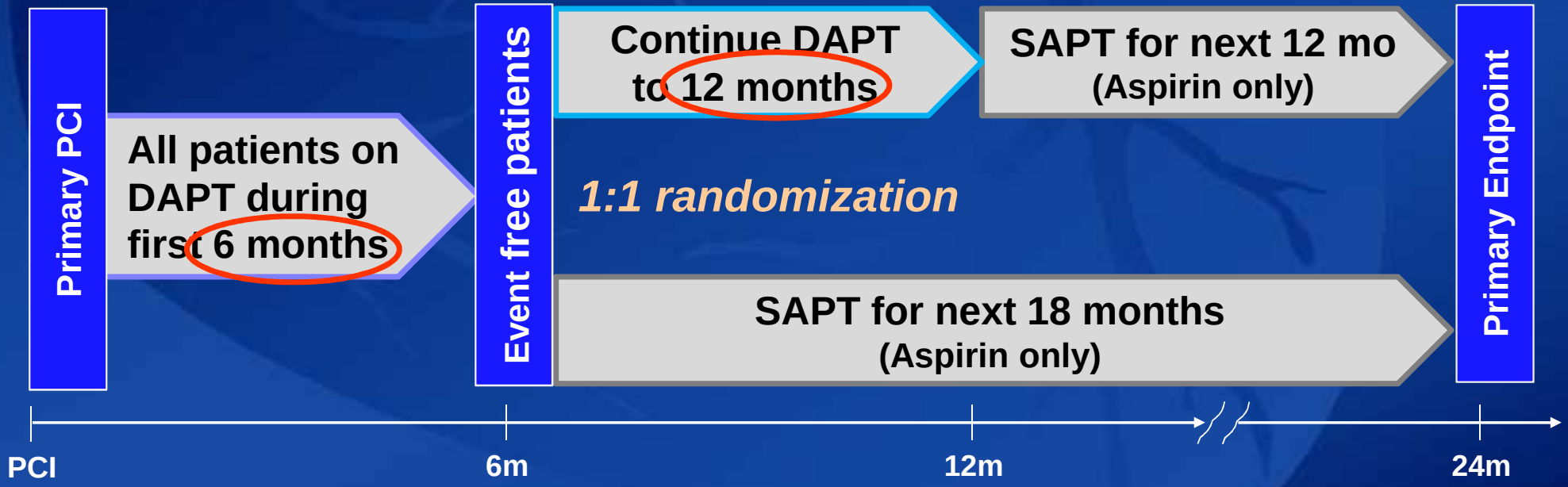
P2Y12 INHIBITORS



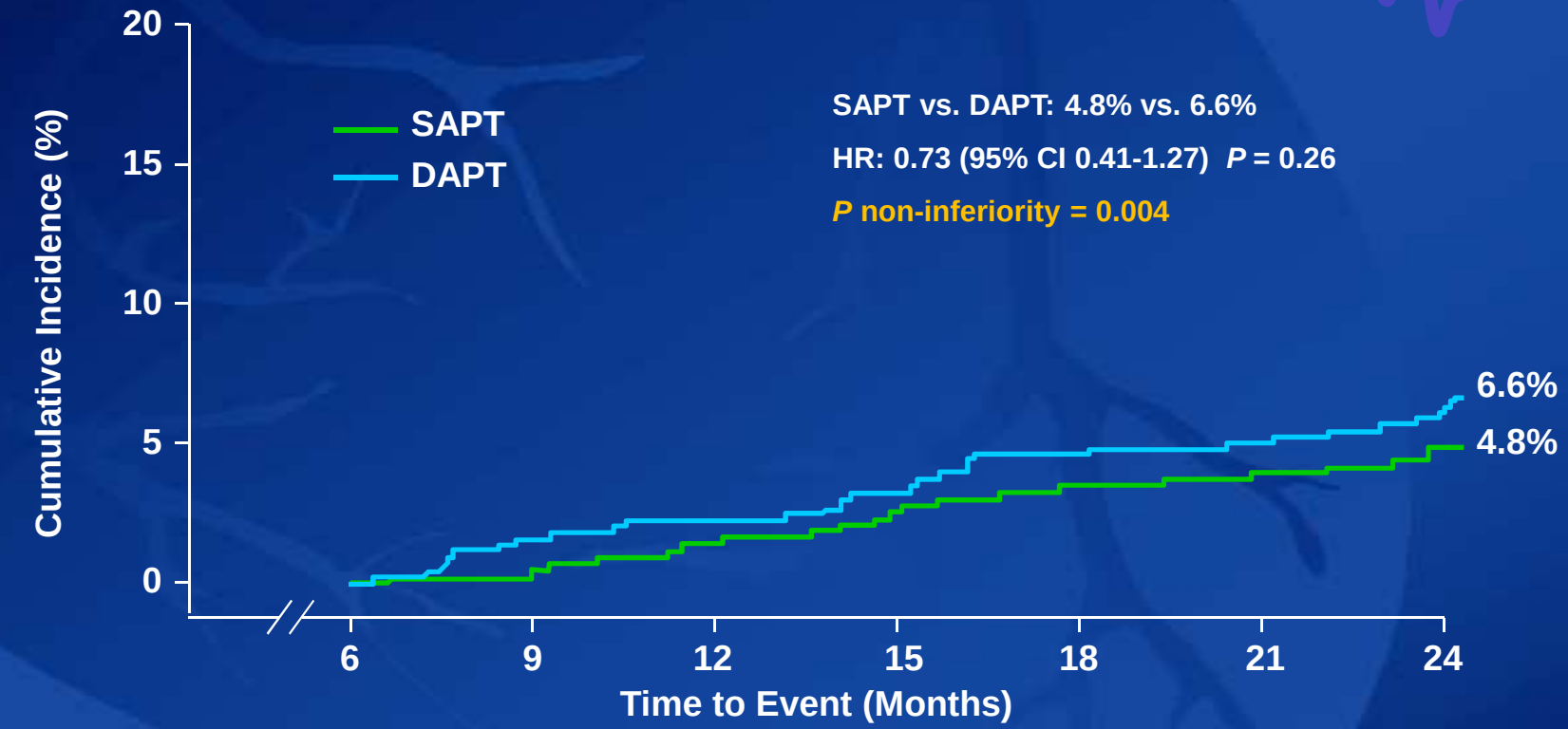
DAPT – STEMI Trial Design

Prospective, International, Randomized, Non-inferiority Trial
STEMI Patients undergoing primary PCI with a second-generation Zotarolimus-eluting stent (Resolute Integrity)

Enrollment took place in 17 centers in The Netherlands, Poland, Switzerland and Norway



Primary Endpoint:
Death, MI, Revascularization, Stroke and Major Bleeding



No. at risk							
SAPT	433	428	424	419	413	411	408
DAPT	437	430	426	421	412	409	403

DIAGRAM • DIAGNOSTIC RESEARCH AND MANAGEMENT

Radboud Universiteit Nijmegen

Radboudumc

REDUCE: A Randomized Trial of 3-Month vs 12-Month DAPT After Implantation of a Bioabsorbable Polymer-Based Metallic DES With a Luminal CD34+ Antibody Coating in Patients With ACS

COMBO™ Dual Therapy Stent

12-Month Clinical Outcomes

Harry Suryapranata, *MD, PhD*

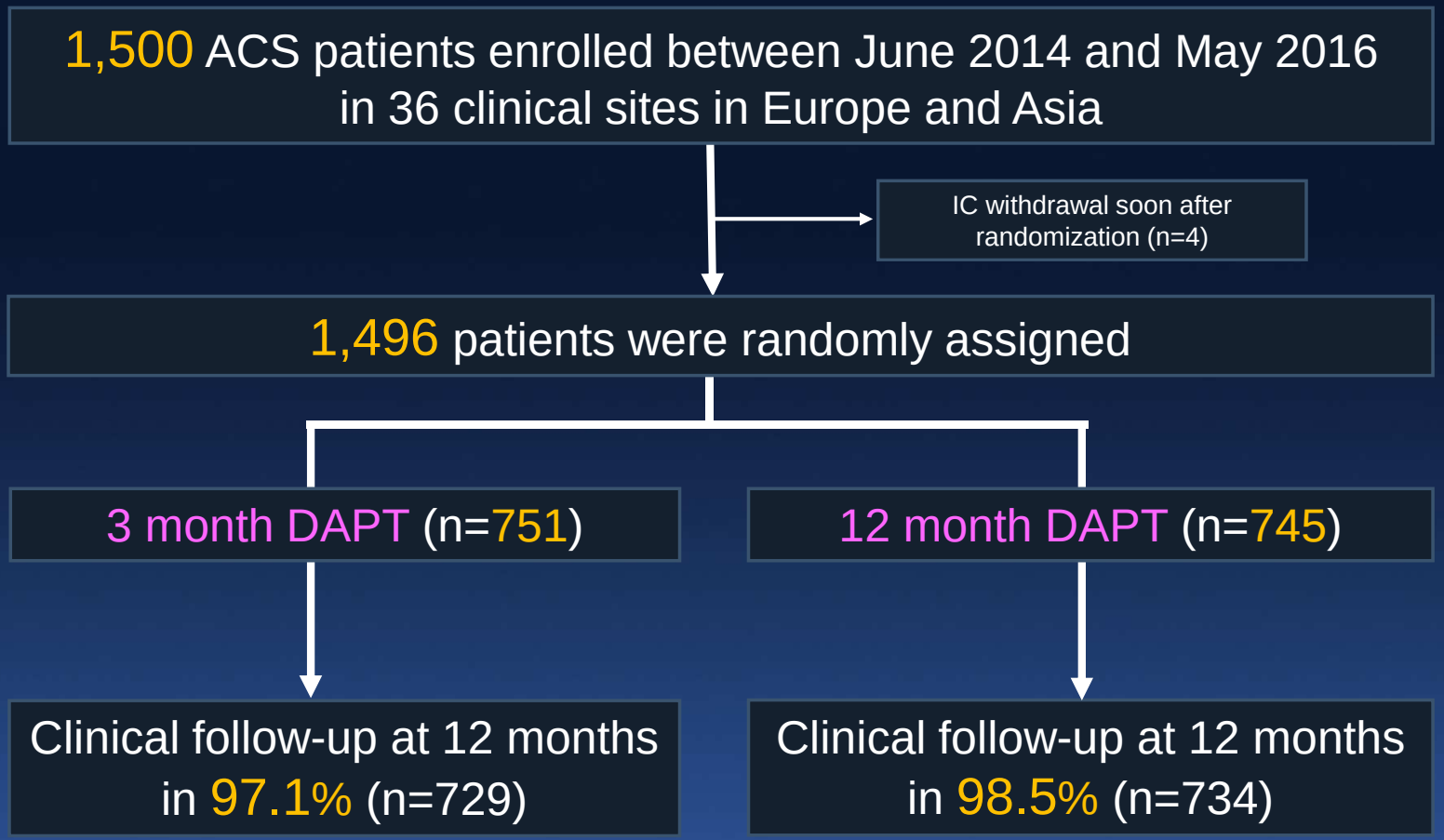
on behalf of the REDUCE trial investigators

tct2017

ClinicalTrials.gov NCT02118870

Cardiovascular Research Foundation

Results: Flow Chart



Results: Baseline

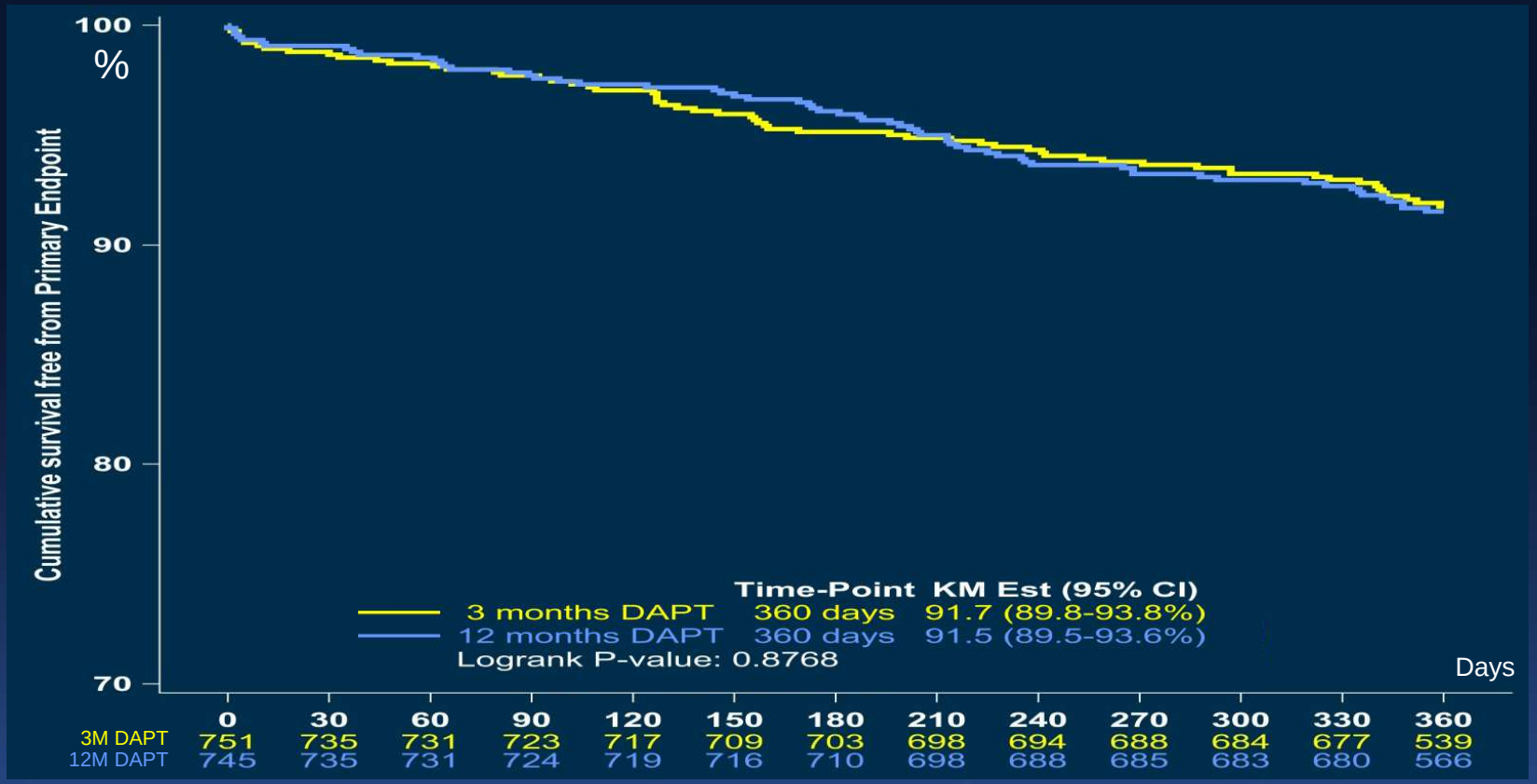
Baseline Characteristics

	3 month DAPT n = 751	12 month DAPT n = 734	P
Age (Mean ± SD)	61.2 ± 11.6	60.5 ± 12.0	NS
Female Gender (%)	17.4	22.7	0.01
STEMI diagnosis	49.3	45.2	NS
Diabetes Mellitus (%)	21.6	19.5	NS
Smoking (%)	42.1	42.7	NS
Hypercholesterolemia (%)	46.3	44.9	NS
Hypertension (%)	50.7	50.7	NS
Family history of CAD (%)	35.0	36.0	NS
Previous ACS (%)	12.5	11.8	NS
Previous PCI (%)	11.7	9.8	NS

Angiographic Characteristics

	3 month DAPT n = 751	12 month DAPT n = 734	P
Radial access (%)	76.1	76.9	NS
Multivessel disease (%)	36.1	33.8	NS
Target vessel (%): - LAD	48.0	44.2	NS
- RCA	31.2	33.0	NS
- RCX	19.5	22.0	NS
Initial TIMI flow 3 (%)	46.6	49.0	NS
Thrombosuction (%)	12.5	13.6	NS
Total stent length (mm, mean ± SD)	25.5 ± 12.8	25.2 ± 12.7	NS
Procedural success (%)	99.3	99.7	NS
PCI additional segments (%)	20.3	21.9	NS

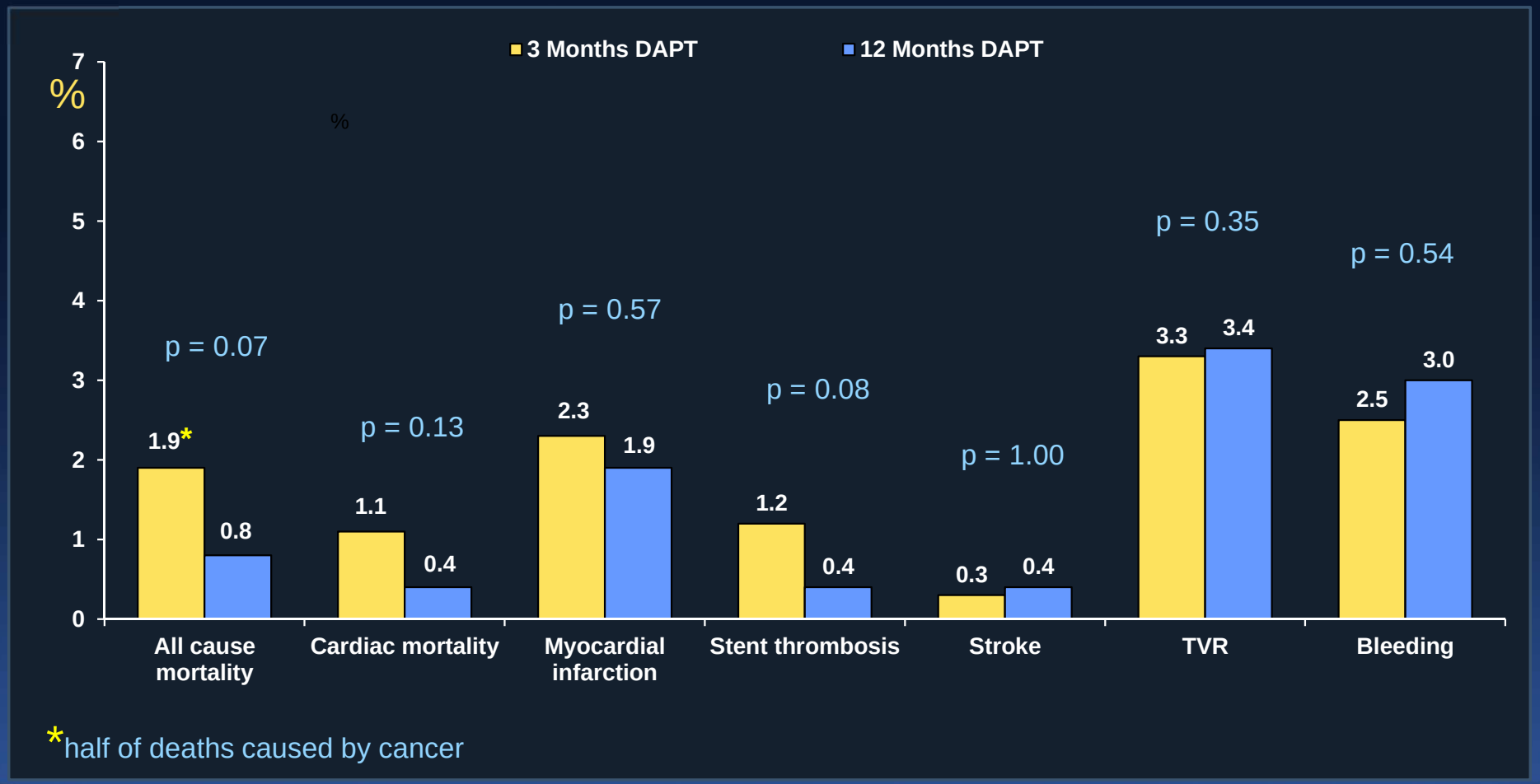
Results: Primary Study Endpoint



Analysis set	3 month DAPT n = 729	12 month DAPT n = 734	Risk difference	Upper bound of 1 sided 97.5% CI	OR (95% CI)	P non-inferiority
Intention to treat	8.2	8.4	-0.002	0.027	0.97 (0.67-1.41)	<0.001

Confirmed by PP and AT analyses, and after adjustment for gender (adjusted OR (95% CI) = 0.95 (0.66–1.38), p=0.81)

Results: Secondary Study Endpoints

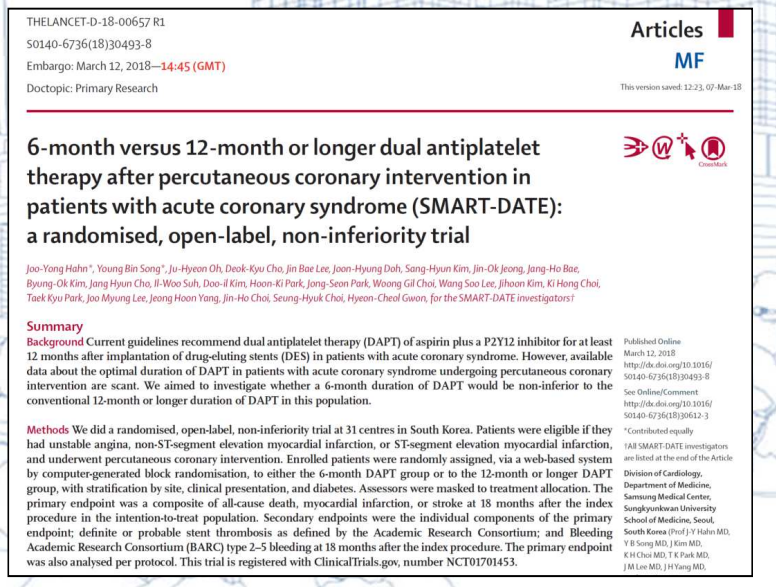


*half of deaths caused by cancer

No difference in any individual secondary endpoint

6-month versus 12-month or longer dual antiplatelet therapy after percutaneous coronary intervention in patients with acute coronary syndrome (SMART-DATE): a randomized, open-label, non-inferiority trial

ACC.18 Late-Breaking Clinical Trials



THELANCET-D-18-00657 R1
S0140-6736(18)30493-8
Embargo: March 12, 2018—14:45 (GMT)
Doctopic: Primary Research

Articles
MF
This version saved: 12:23, 07-Mar-18

6-month versus 12-month or longer dual antiplatelet therapy after percutaneous coronary intervention in patients with acute coronary syndrome (SMART-DATE): a randomised, open-label, non-inferiority trial

Joo-Yong Hahn, Young Bin Song*, Ju-Hyeon Oh, Deok-Kyu Cho, Jin Bae Lee, Joon-Hyung Doh, Sang-Hyun Kim, Jin-Ok Jeong, Jang-Ho Bae, Byung-Ok Kim, Jang Hyun Cho, Il-Woo Suh, Doo-il Kim, Hoon-Ki Park, Jong-Seon Park, Woong Gil Choi, Wang Soo Lee, Jihoon Kim, Ki Hong Choi, Taek Kyu Park, Joo Myung Lee, Jeong Hoon Yang, Jin-Ho Choi, Seung-Hyuk Choi, Hyeon-Cheol Gwon, for the SMART-DATE investigators†*

Summary

Background Current guidelines recommend dual antiplatelet therapy (DAPT) of aspirin plus a P2Y12 inhibitor for at least 12 months after implantation of drug-eluting stents (DES) in patients with acute coronary syndrome. However, available data about the optimal duration of DAPT in patients with acute coronary syndrome undergoing percutaneous coronary intervention are scant. We aimed to investigate whether a 6-month duration of DAPT would be non-inferior to the conventional 12-month or longer duration of DAPT in this population.

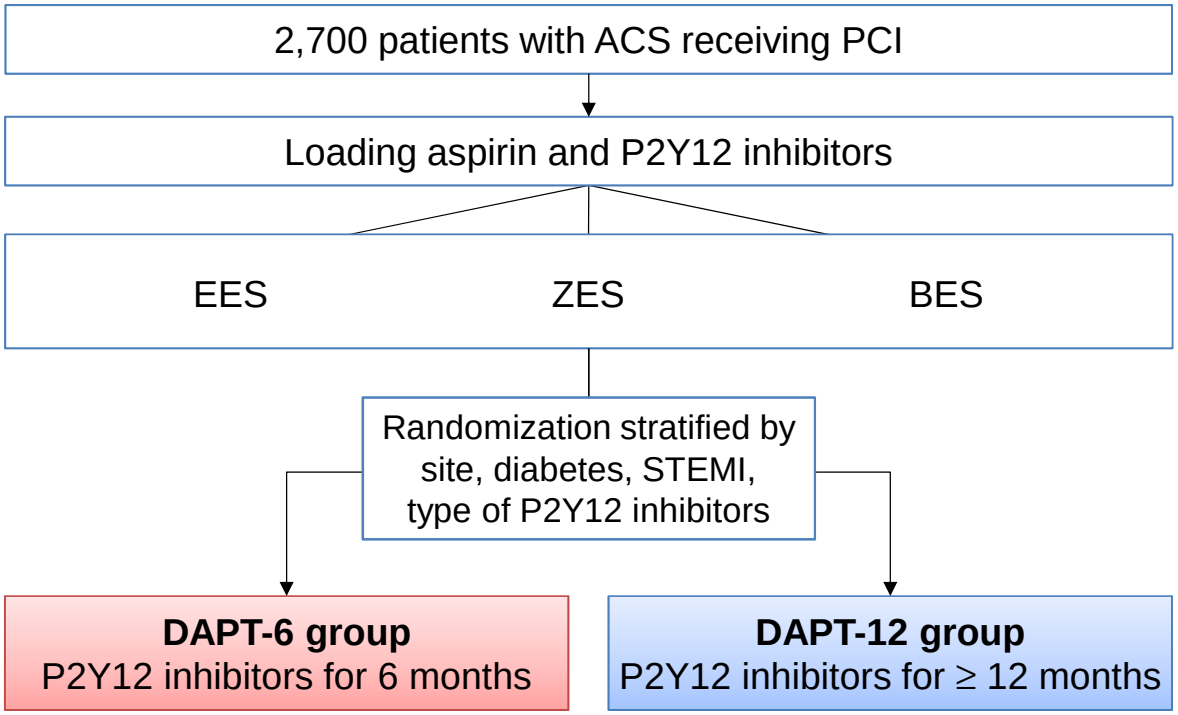
Methods We did a randomised, open-label, non-inferiority trial at 31 centres in South Korea. Patients were eligible if they had unstable angina, non-ST-segment elevation myocardial infarction, or ST-segment elevation myocardial infarction, and underwent percutaneous coronary intervention. Enrolled patients were randomly assigned, via a web-based system by computer-generated block randomisation, to either the 6-month DAPT group or to the 12-month or longer DAPT group, with stratification by site, clinical presentation, and diabetes. Assessors were masked to treatment allocation. The primary endpoint was a composite of all-cause death, myocardial infarction, or stroke at 18 months after the index procedure in the intention-to-treat population. Secondary endpoints were the individual components of the primary endpoint; definite or probable stent thrombosis as defined by the Academic Research Consortium; and Bleeding Academic Research Consortium (BARC) type 2–5 bleeding at 18 months after the index procedure. The primary endpoint was also analysed per protocol. This trial is registered with ClinicalTrials.gov, number NCT01701453.

Published Online
March 12, 2018
http://dx.doi.org/10.1016/S0140-6736(18)30493-8
See Online/Comment
http://dx.doi.org/10.1016/S0140-6736(18)30612-3

*Contributed equally
†All SMART-DATE investigators are listed at the end of the Article
Division of Cardiology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea (Prof J-Y Hahn MD, Y B Song MD, J Kim MD, K H Choi MD, T K Park MD, J M Lee MD, J H Yang MD,

Study design

A prospective, multicenter, randomized, and open-label trial



Primary endpoint: 18-month MACCE
a composite of all-cause mortality, MI, and cerebrovascular events

- PCI=percutaneous coronary intervention
- EES = everolimus eluting stent (Xience Prime)
- ZES = zotarolimus eluting stent (Resolute Integrity)
- BES = biolimus eluting stent (Biomatrix Flex)
- STEMI = ST elevation myocardial infarction
- MI = myocardial infarction

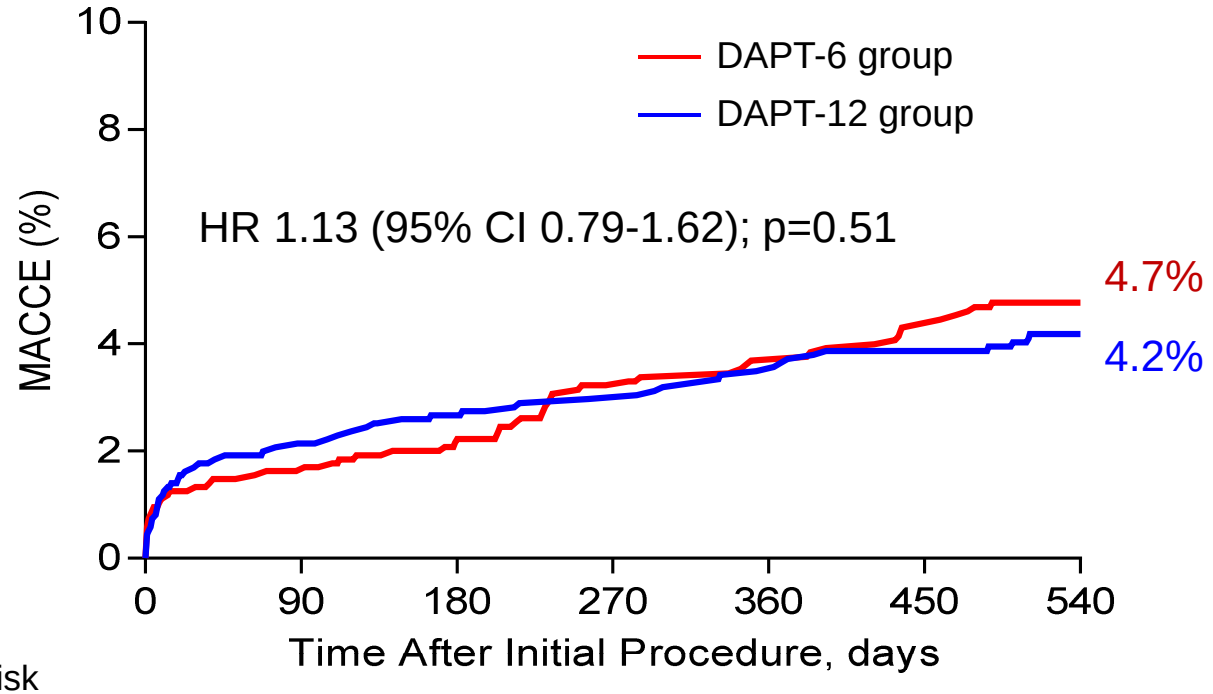
Clinical characteristics

	DAPT-6 group (n=1357)	DAPT-12 group (n=1355)
Age, median (years)	62 [54-71]	63 [53-71]
Male	1016 (74.9%)	1028 (75.9%)
Diabetes mellitus	365/1355 (26.9%)	379/1350 (28.1%)
Hypertension	669/1340 (49.9%)	654/1342 (48.7%)
Dyslipidemia	322/1329 (24.2%)	336/1332 (25.2%)
Current smoking	506/1333 (38.0%)	536/1335 (40.1%)
Previous MI	30/1328 (2.3%)	23/1334 (1.7%)
Previous revascularization	65/1320 (4.9%)	52/1328 (3.9%)
Cerebrovascular disease	52/1330 (3.9%)	58/1332 (4.4%)
Chronic renal failure	13/1327 (1.0%)	6/1328 (0.5%)
Ejection fraction (%)	55.5±11.0	55.4±10.5

	DAPT-6 group (n=1357)	DAPT-12 group (n=1355)
Clinical presentation		
ST-elevation MI	509 (37.5%)	514 (37.9%)
Non-ST-elevation MI	428 (31.5%)	425 (31.4%)
Unstable angina	420 (31.0%)	416 (30.7%)
Discharge medication		
Aspirin	1353 (99.7%)	1354 (99.9%)
P2Y12 receptor inhibitor	1352 (99.6%)	1350 (99.6%)
Clopidogrel	1082 (79.7%)	1109 (81.8%)
Statin	1212 (89.3%)	1238 (91.4%)
ACE inhibitor	529 (39.0%)	557 (41.1%)
ARB	416 (30.7%)	390 (28.8%)
β-blocker	961 (70.8%)	999 (73.7%)

MI = myocardial infarction, ACE = angiotensin converting enzyme, ARB = angiotensin receptor blocker

Primary endpoint (MACCE)



No. at risk							
Long-term	1355	1312	1299	1290	1283	1278	1043
Short-term	1357	1318	1296	1271	1264	1255	1032

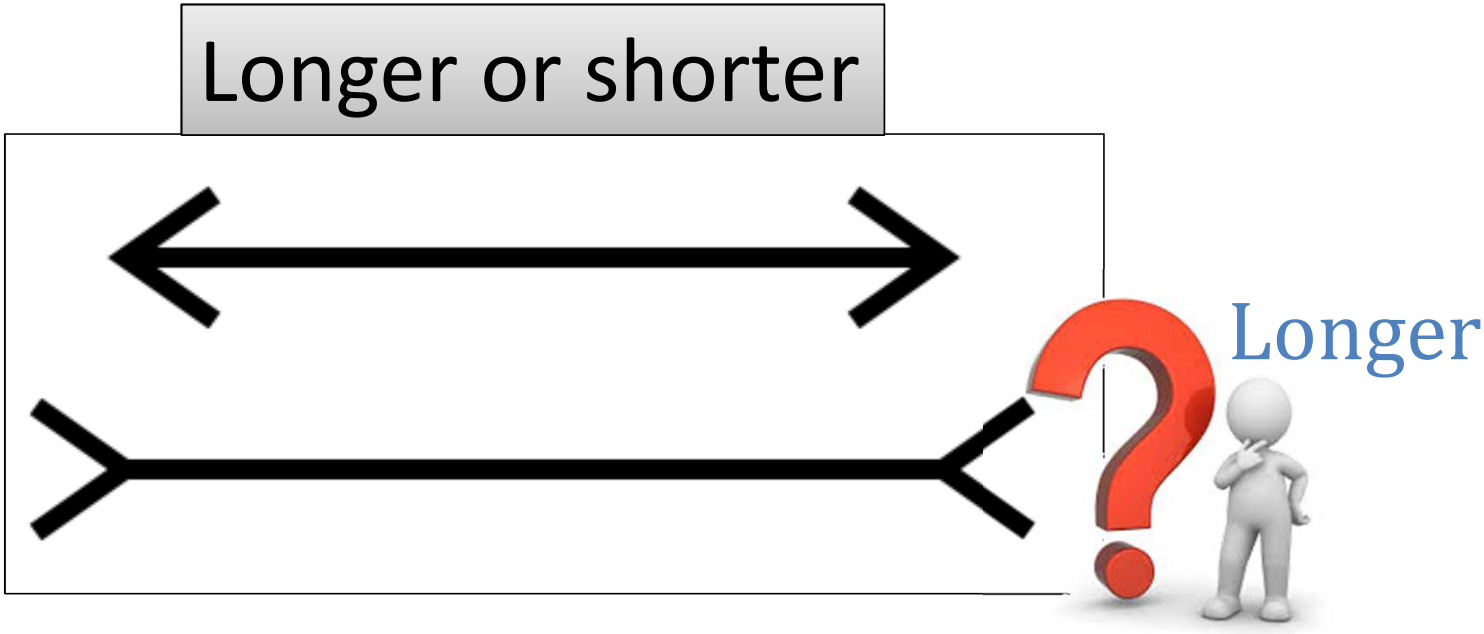
* MACCE = A composite of all-cause mortality, myocardial infarction, and cerebrovascular events

Clinical outcomes at 18 months

Intention-to-treat (ITT)

	DAPT-6 group (n=1357)	DAPT-12 group (n=1355)	**HR (95% CI)**	**p value**
MACCE	63 (4.7%)	56 (4.2%)	1.13 (0.79-1.62)	0.51
Death	35 (2.6%)	39 (2.9%)	0.90 (0.57-1.42)	0.90
Myocardial infarction	24 (1.8%)	10 (0.8%)	2.41 (1.15-5.05)	0.02
Target vessel MI	14 (1.1%)	7 (0.5%)	2.01 (0.81-4.97)	0.13
Non-target vessel MI	10 (0.8%)	3 (0.2%)	3.35 (0.92-12.2)	0.07
Cerebrovascular accident (stroke)	11 (0.8%)	12 (0.9%)	0.·92 (0.41-2.08)	0.84
Cardiac death	18 (1.4%)	24 (1.8%)	0.75 (0.41-1.38)	0.36
Cardiac death or MI	39 (2.9%)	32 (2.4%)	1.22 (0.77-1.95)	0.40
Stent thrombosis	15 (1.1%)	10 (0.7%)	1.50 (0.68-3.35)	0.32
Bleeding BARC type 2-5	35 (2.7%)	51 (3.9%)	0.69 (0.45-1.05)	0.09
Major bleeding (BARC type 3,4,or 5)	6 (0.5%)	10 (0.8%)	0.60 (0.22-1.65)	0.33
Net adverse clinical and cerebral events	96 (7.2%)	99 (7.4%)	0.97 (0.73-1.29)	0.84

P2Y12 INHIBITORS



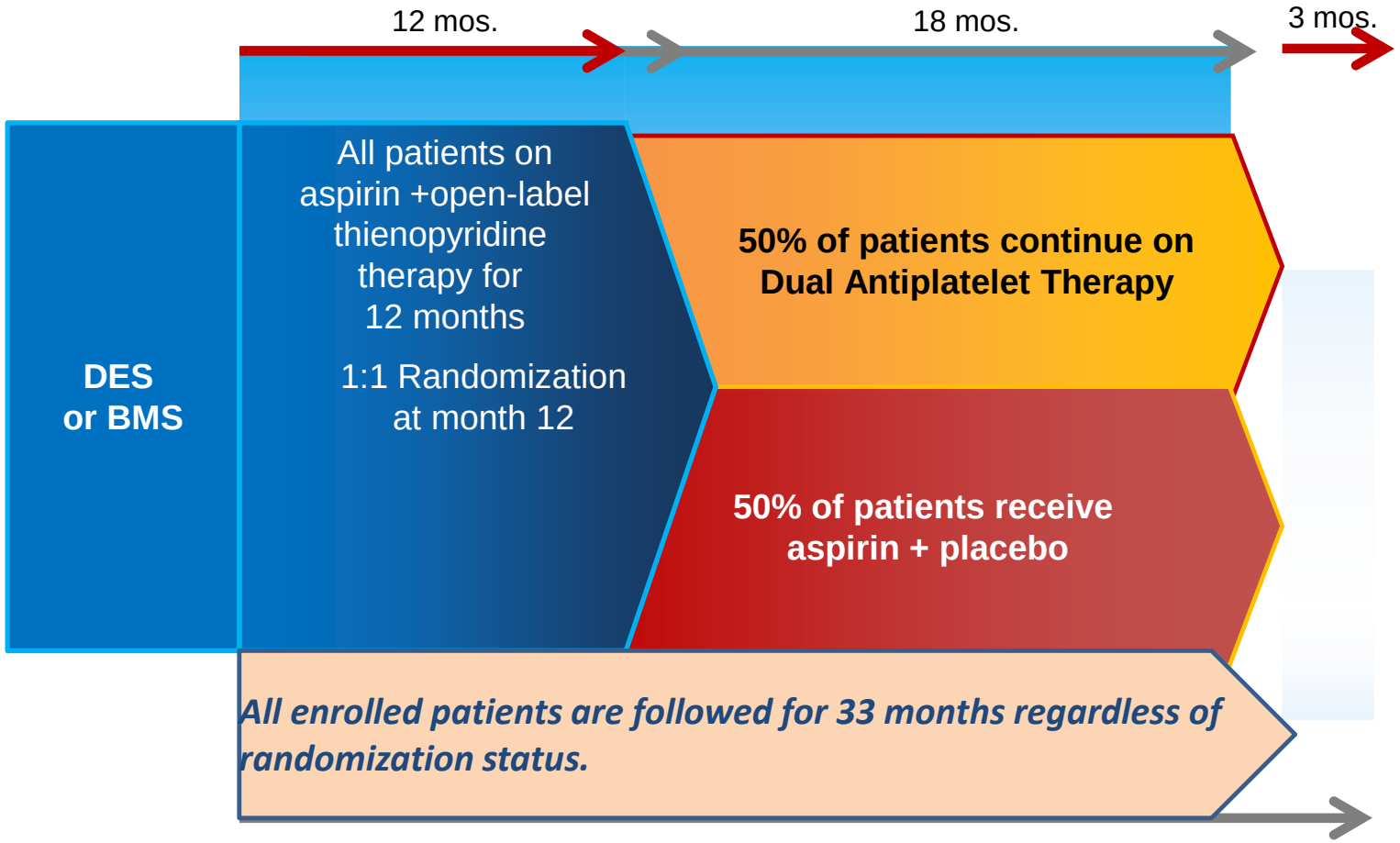
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 4, 2014 VOL. 371 NO. 23

Twelve or 30 Months of Dual Antiplatelet Therapy after Drug-Eluting Stents

Laura Mauri, M.D., Dean J. Kereiakes, M.D., Robert W. Yeh, M.D., Priscilla Driscoll-Shempp, M.B.A., Donald E. Cutlip, M.D., P. Gabriel Steg, M.D., Sharon-Lise T. Normand, Ph.D., Eugene Braunwald, M.D., Stephen D. Wiviott, M.D., David J. Cohen, M.D., David R. Holmes, Jr., M.D., Mitchell W. Krucoff, M.D., James Hermiller, M.D., Harold L. Dauerman, M.D., Daniel I. Simon, M.D., David E. Kandzari, M.D., Kirk N. Garratt, M.D., David P. Lee, M.D., Thomas K. Pow, M.D., Peter Ver Lee, M.D., Michael J. Rinaldi, M.D., and Joseph M. Massaro, Ph.D., for the DAPT Study Investigators*

Design



Total 33 month patient evaluation including additional 3-month follow-up off study drug

174

Characteristic	Continued Thienopyridine (N=5020)	Placebo (N=4941)
Patients		
Indication for PCI — no. (%)		
STEMI	534 (10.6)	511 (10.3)
NSTEMI	776 (15.5)	767 (15.5)
Unstable angina¶	838 (16.7)	825 (16.7)
Stable angina	1882 (37.5)	1870 (37.8)
Other	990 (19.7)	968 (19.6)

175

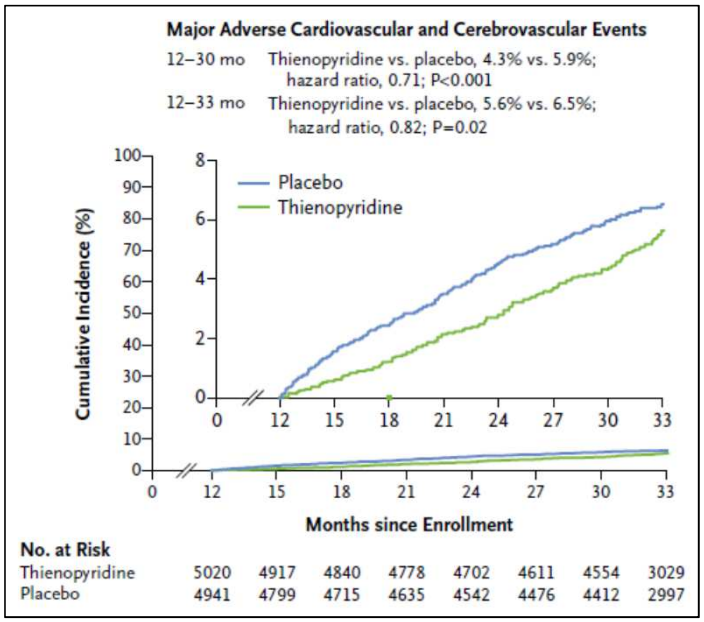


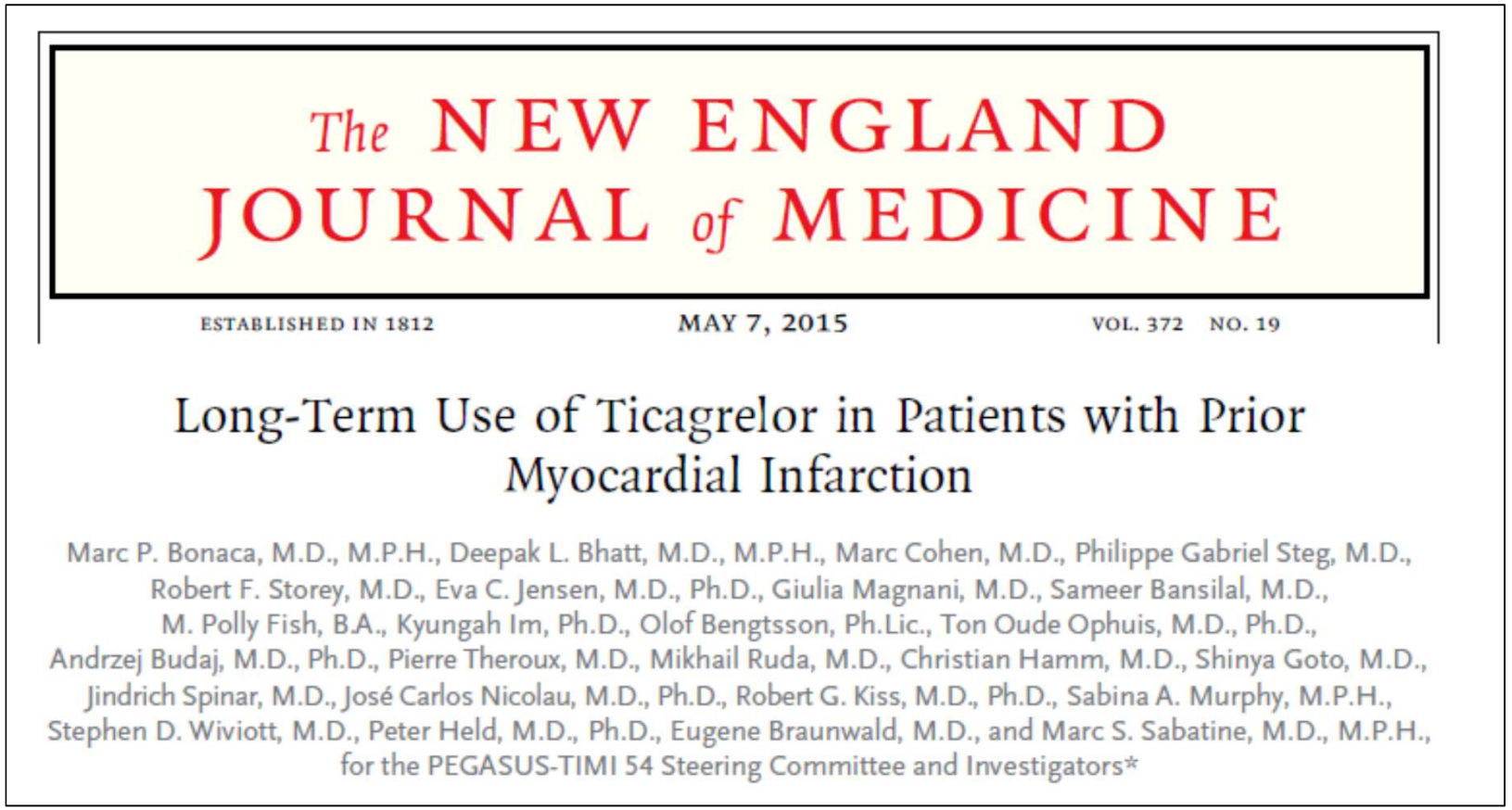
Table 2. Stent Thrombosis and Major Adverse Cardiovascular and Cerebrovascular Events.*

Outcome	Continued Thienopyridine (N=5020)	Placebo (N=4941)	Hazard Ratio, Thienopyridine vs. Placebo (95% CI)†	P Value†
	no. of patients (%)			
Stent thrombosis‡	19 (0.4)	65 (1.4)	0.29 (0.17–0.48)	<0.001
Definite	15 (0.3)	58 (1.2)	0.26 (0.14–0.45)	<0.001
Probable	5 (0.1)	7 (0.1)	0.71 (0.22–2.23)	0.55
Major adverse cardiovascular and cerebrovascular events§	211 (4.3)	285 (5.9)	0.71 (0.59–0.85)	<0.001
Death	98 (2.0)	74 (1.5)	1.36 (1.00–1.85)	0.05
Cardiac	45 (0.9)	47 (1.0)	1.00 (0.66–1.52)	0.98
Vascular	5 (0.1)	5 (0.1)	0.98 (0.28–3.39)	0.98
Noncardiovascular	48 (1.0)	22 (0.5)	2.23 (1.32–3.78)	0.002
Myocardial infarction	99 (2.1)	198 (4.1)	0.47 (0.37–0.61)	<0.001
Stroke	37 (0.8)	43 (0.9)	0.80 (0.51–1.25)	0.32
Ischemic	24 (0.5)	34 (0.7)	0.68 (0.40–1.17)	0.16
Hemorrhagic	13 (0.3)	9 (0.2)	1.20 (0.50–2.91)	0.68
Type uncertain	0	1 (<0.1)	—	0.32

Table 3. Bleeding End Point during Month 12 to Month 30.*

Bleeding Complications	Continued Thienopyridine (N=4710)	Placebo (N=4649)	Difference	Two-Sided P Value for Difference
	no. of patients (%)		*percentage points (95% CI)*	
GUSTO severe or moderate†	119 (2.5)	73 (1.6)	1.0 (0.4 to 1.5)	0.001
Severe	38 (0.8)	26 (0.6)	0.2 (–0.1 to 0.6)	0.15
Moderate	81 (1.7)	48 (1.0)	0.7 (0.2 to 1.2)	0.004
BARC type 2, 3, or 5	263 (5.6)	137 (2.9)	2.6 (1.8 to 3.5)	<0.001
Type 2	145 (3.1)	72 (1.5)	1.5 (0.9 to 2.1)	<0.001
Type 3	122 (2.6)	68 (1.5)	1.1 (0.6 to 1.7)	<0.001
Type 5	7 (0.1)	4 (0.1)	0.1 (–0.1 to 0.2)	0.38

Efficacy of Long-Term Ticagrelor in Patients with Coronary Stents in PEGASUS-TIMI 54



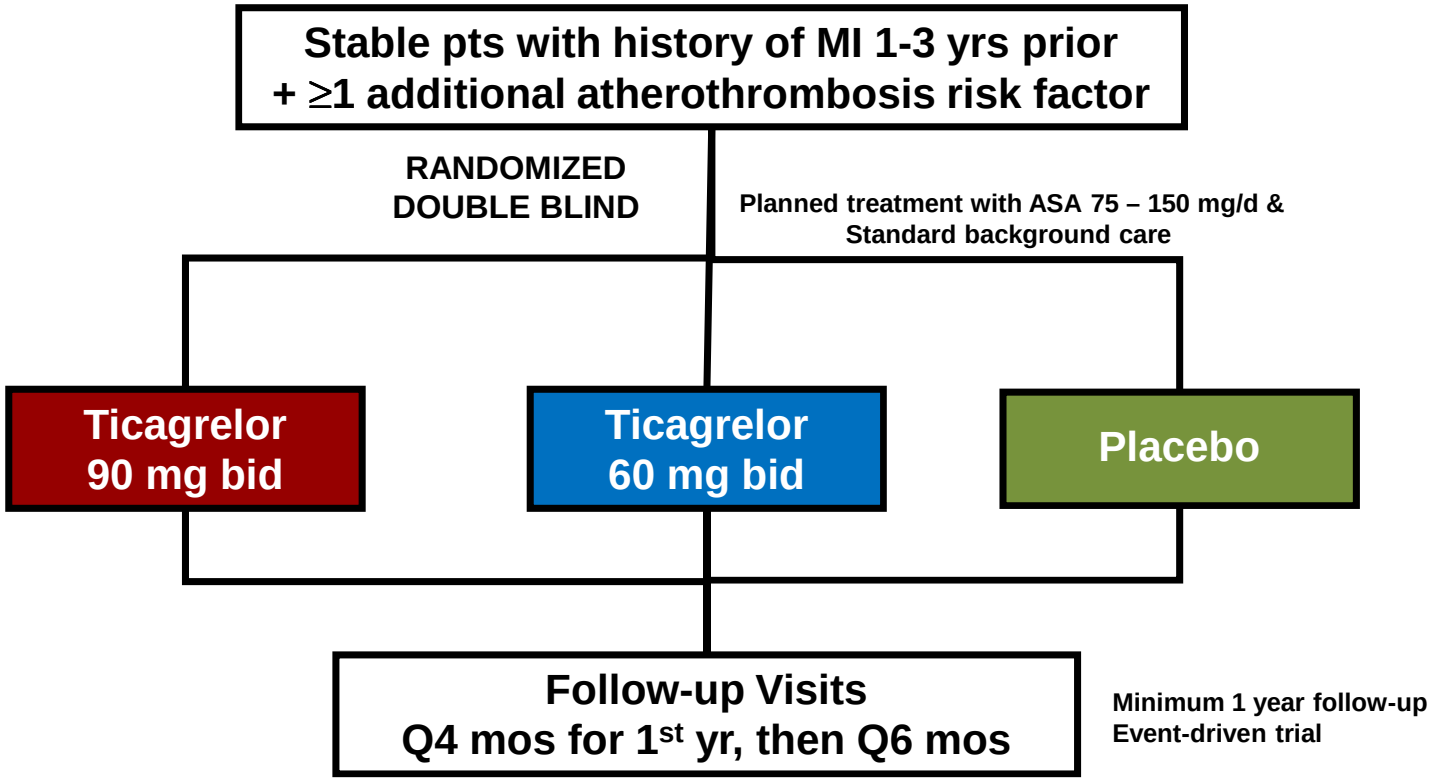
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 7, 2015 VOL. 372 NO. 19

Long-Term Use of Ticagrelor in Patients with Prior Myocardial Infarction

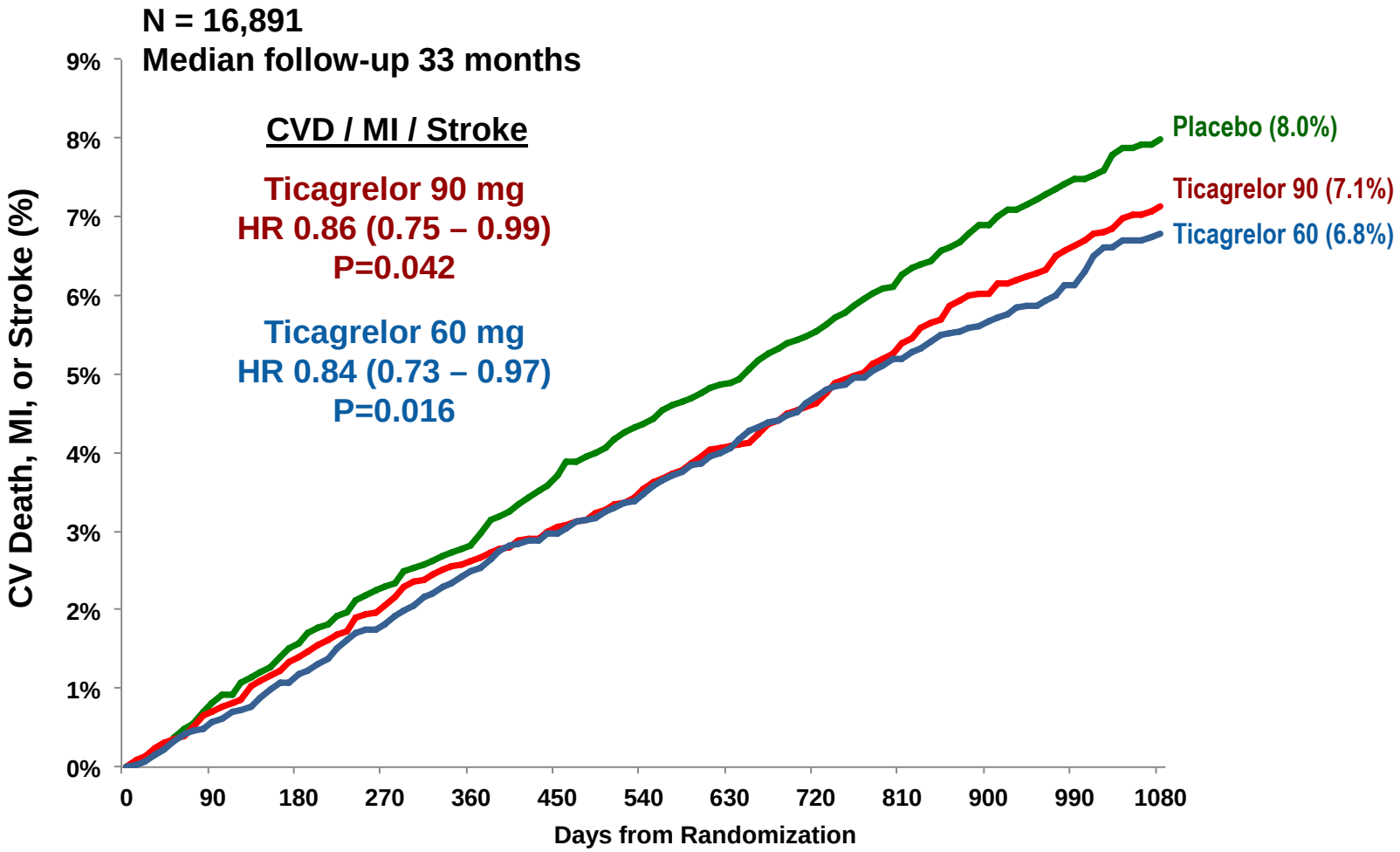
Marc P. Bonaca, M.D., M.P.H., Deepak L. Bhatt, M.D., M.P.H., Marc Cohen, M.D., Philippe Gabriel Steg, M.D., Robert F. Storey, M.D., Eva C. Jensen, M.D., Ph.D., Giulia Magnani, M.D., Sameer Bansilal, M.D., M. Polly Fish, B.A., Kyungah Im, Ph.D., Olof Bengtsson, Ph.Lic., Ton Oude Ophuis, M.D., Ph.D., Andrzej Budaj, M.D., Ph.D., Pierre Theroux, M.D., Mikhail Ruda, M.D., Christian Hamm, M.D., Shinya Goto, M.D., Jindrich Spinar, M.D., José Carlos Nicolau, M.D., Ph.D., Robert G. Kiss, M.D., Ph.D., Sabina A. Murphy, M.P.H., Stephen D. Wiviott, M.D., Peter Held, M.D., Ph.D., Eugene Braunwald, M.D., and Marc S. Sabatine, M.D., M.P.H., for the PEGASUS-TIMI 54 Steering Committee and Investigators*

Background



Bonaca MP et al. NEJM 2015

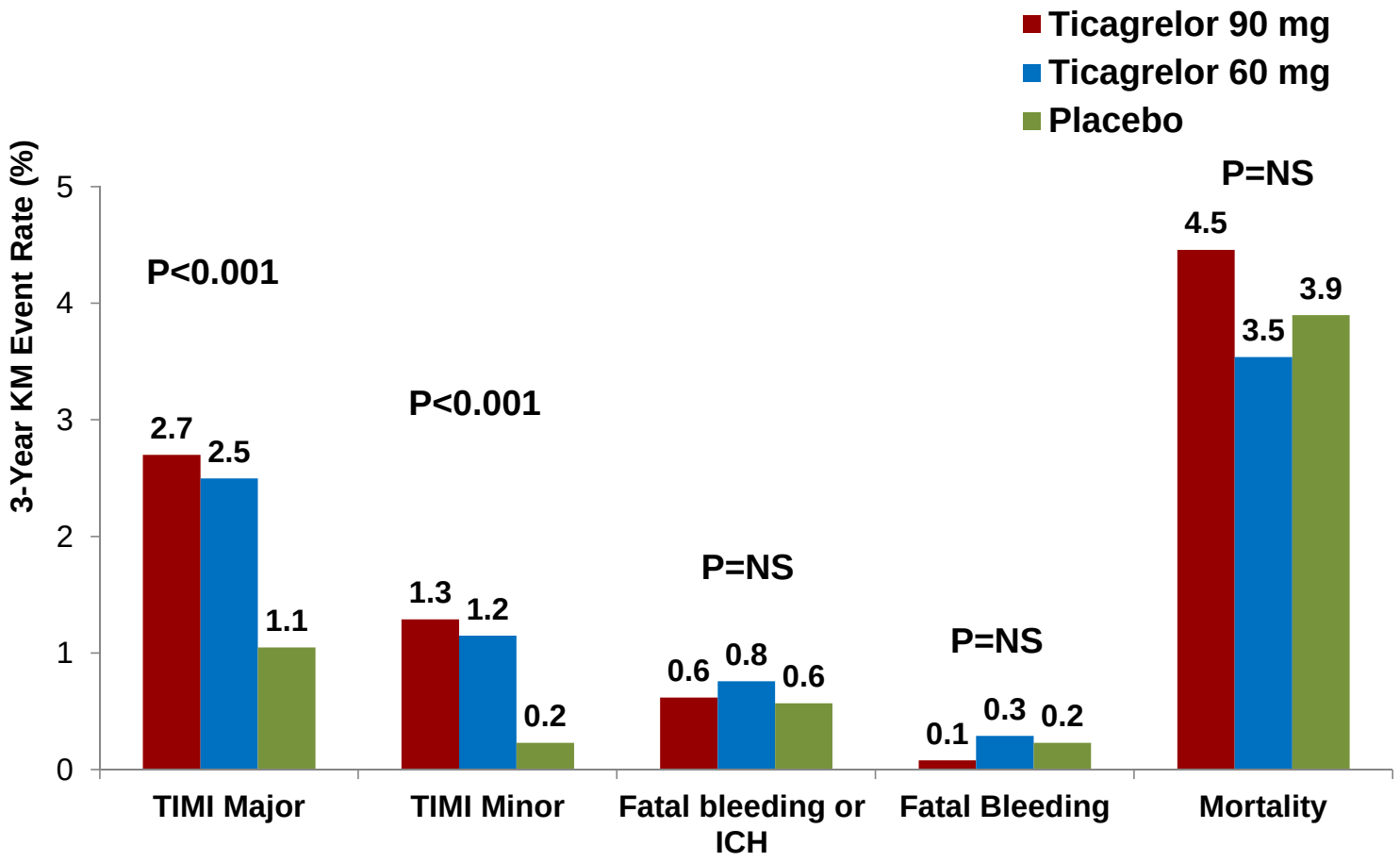
MACE in Patients with Prior PCI/Stent



Safety in Patients with Prior PCI

End Point	Ticagrelor, 90 mg (N=7050)	Ticagrelor, 60 mg (N=7045)	Placebo (N=7067)	Ticagrelor, 90 mg vs. Placebo		Ticagrelor, 60 mg vs. Placebo	
				Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
	number (percent)						
Cardiovascular death, myocardial infarction, or stroke	493 (7.85)	487 (7.77)	578 (9.04)	0.85 (0.75–0.96)	0.008	0.84 (0.74–0.95)	0.004
Death from coronary heart disease, myocardial infarction, or stroke	438 (6.99)	445 (7.09)	535 (8.33)	0.82 (0.72–0.93)	0.002	0.83 (0.73–0.94)	0.003
Cardiovascular death or myocardial infarction	424 (6.79)	422 (6.77)	497 (7.81)	0.85 (0.75–0.97)	0.01	0.85 (0.74–0.96)	0.01
Death from coronary heart disease or myocardial infarction	350 (5.59)	360 (5.75)	429 (6.68)	0.81 (0.71–0.94)	0.004	0.84 (0.73–0.96)	0.01
Cardiovascular death	182 (2.94)	174 (2.86)	210 (3.39)	0.87 (0.71–1.06)	0.15	0.83 (0.68–1.01)	0.07
Death from coronary heart disease	97 (1.53)	106 (1.72)	132 (2.08)	0.73 (0.56–0.95)	0.02	0.80 (0.62–1.04)	0.09
Myocardial infarction	275 (4.40)	285 (4.53)	338 (5.25)	0.81 (0.69–0.95)	0.01	0.84 (0.72–0.98)	0.03
Stroke							
Any	100 (1.61)	91 (1.47)	122 (1.94)	0.82 (0.63–1.07)	0.14	0.75 (0.57–0.98)	0.03
Ischemic	88 (1.41)	78 (1.28)	103 (1.65)	0.85 (0.64–1.14)	0.28	0.76 (0.56–1.02)	0.06
Death from any cause	326 (5.15)	289 (4.69)	326 (5.16)	1.00 (0.86–1.16)	0.99	0.89 (0.76–1.04)	0.14

Safety in Patients with Prior PCI



P2Y12 INHIBITORS

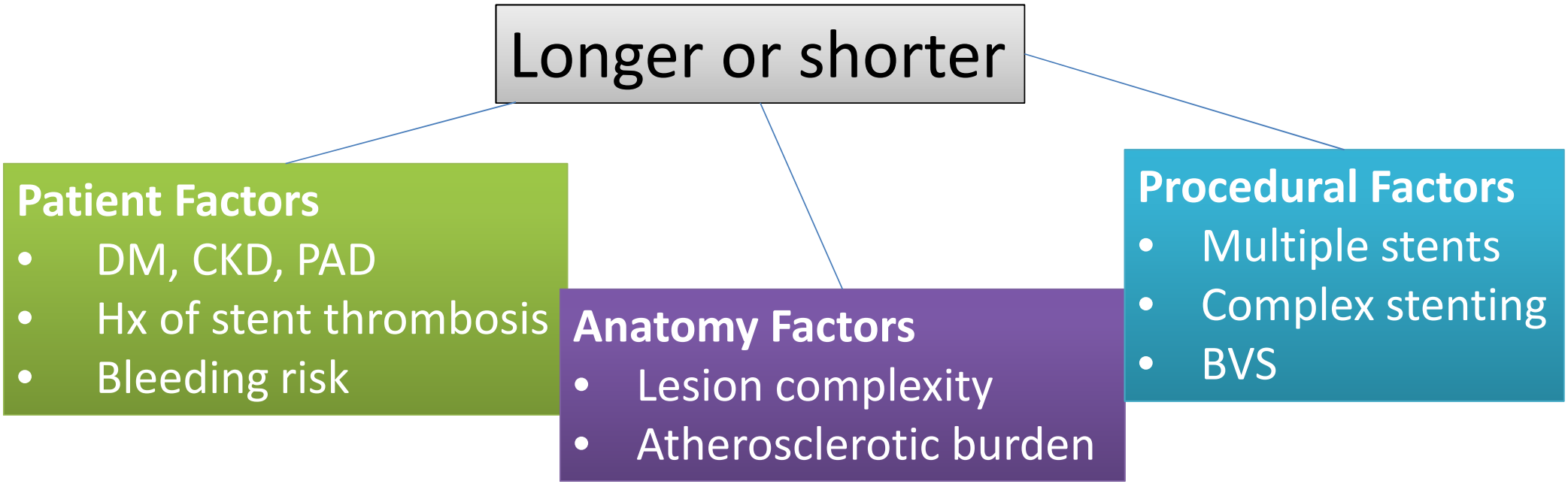
Longer or shorter

P2Y12 INHIBITORS

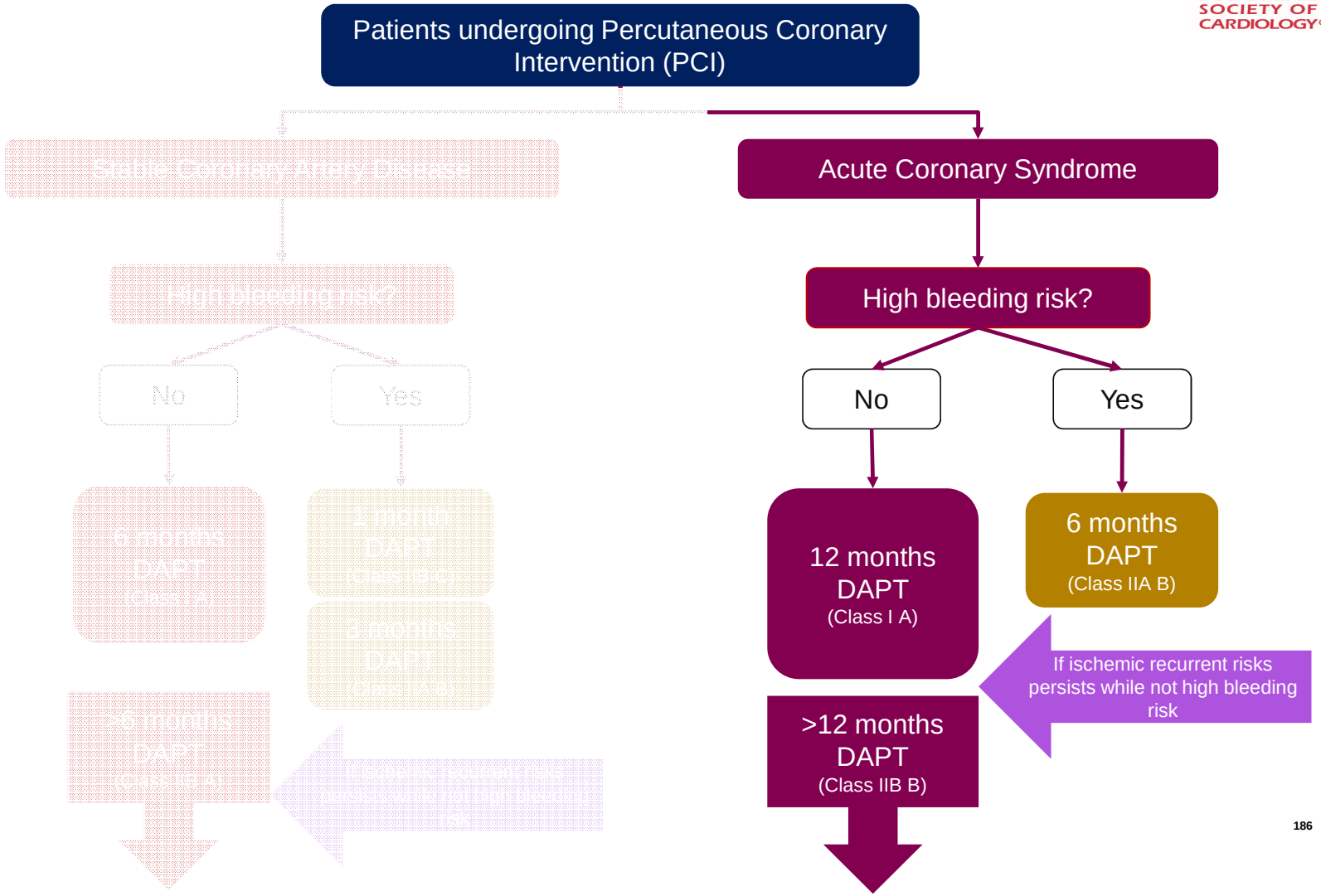
Longer or shorter

Personalized Approach

P2Y12 INHIBITORS



Modified and simplified DAPT duration recommendations adapted from ESC 2017 DAPT guideline



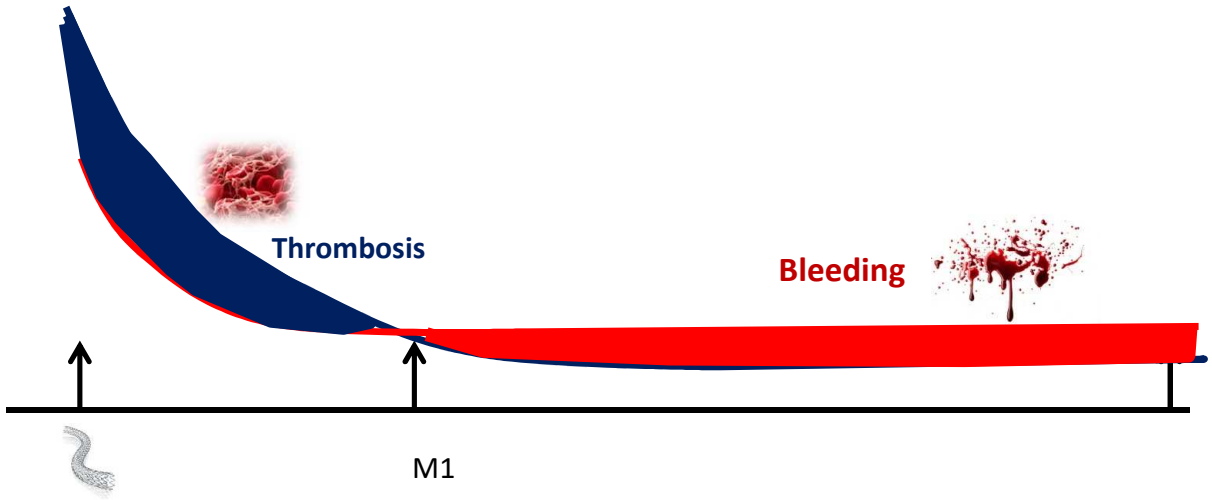
1. 2017 ESC Focused Update on DAPT in Coronary Artery Disease, developed in collaboration with EACTS (European Heart Journal 2017 – doi:10.1093/eurheartj/ehx419)

P2Y12 INHIBITORS

De-Escalating DAPT

Rationale for De-Escalating of DAPT

Ischemic / bleeding risks
Evolution after ACS



Thrombotic risk > Bleeding Risk

Bleeding Risk >Thrombotic risk

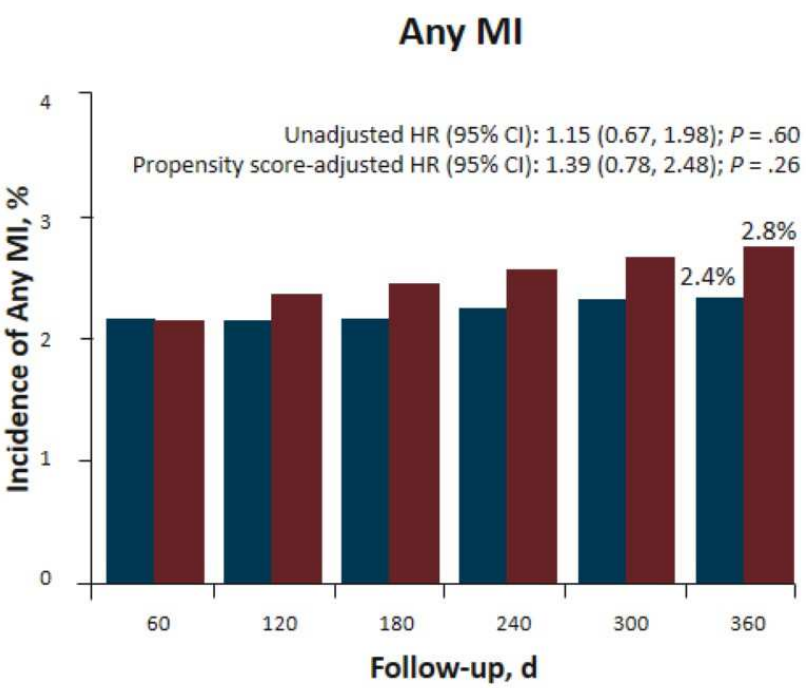
Clopidogrel or ticagrelor in acute coronary syndrome patients treated with newer-generation drug-eluting stents: CHANGE DAPT

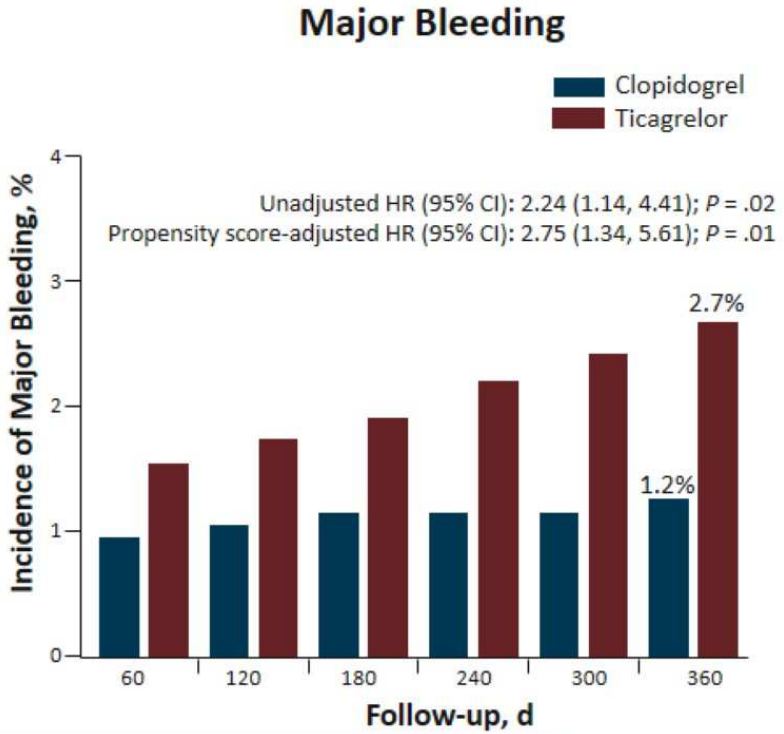
Paolo Zocca[1], MD; Liefke C. van der Heijden[1], MD; Marlies M. Kok[1], MD; Marije M. Löwik[1], PhD; Marc Hartmann[1], MD, PhD; Martin G. Stoel[1], MD, PhD; J. (Hans) W. Louwerenburg[1], MD; Frits H.A.F. de Man[1], MD, PhD; Gerard C.M. Linssen[2], MD, PhD; Iris L. Knottnerus[3], MD, PhD; Carine J.M. Doggen[4], PhD; K. Gert van Houwelingen[1], MD; Clemens von Birgelen[1,4]*, MD, PhD

1. Department of Cardiology, Thoraxcentrum Twente, Medisch Spectrum Twente, Enschede, the Netherlands; 2. Department of Cardiology, Ziekenhuisgroep Twente, Almelo and Hengelo, the Netherlands; 3. Department of Neurology, Medisch Spectrum Twente, Enschede, the Netherlands; 4. Department of Health Technology and Services Research, MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente, Enschede, the Netherlands

This paper also includes supplementary data published online at: http://www.pcronline.com/eurointervention/125th_issue/184

Clopidogrel vs Ticagrelor in Patients With ACS Treated With Newer-Generation DES: CHANGE-DAPT





No ischemic benefit and more bleeding with ticagrelor

Observational data
n = 2062, clopidogrel vs ticagrelor

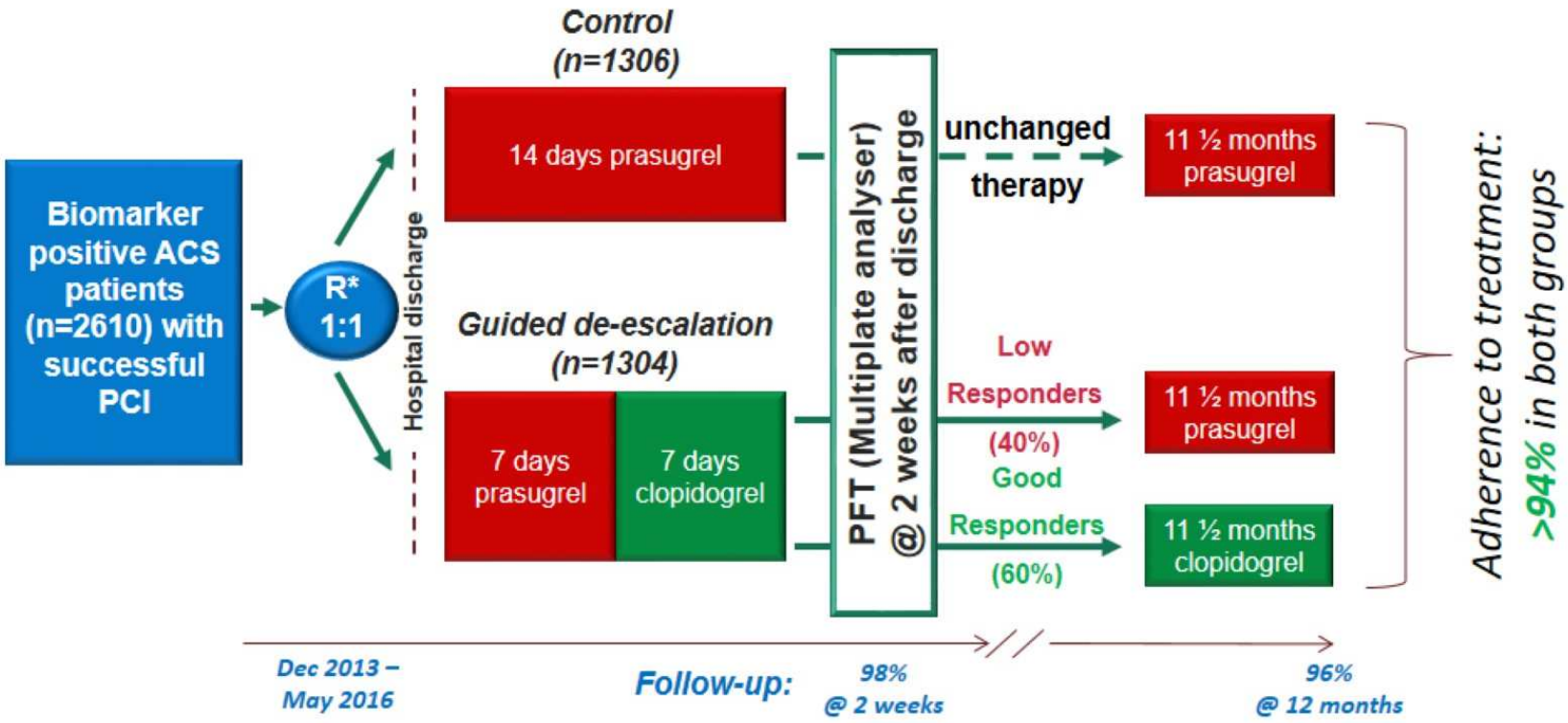
Zocca P, et al. *EuroIntervention*. 2017;13:1168-1176.

Guided de-escalation of antiplatelet treatment in patients with acute coronary syndrome undergoing percutaneous coronary intervention (TROPICAL-ACS): a randomised, open-label, multicentre trial

Dirk Sibbing, Dániel Aradi*, Claudius Jacobshagen, Lisa Gross, Dietmar Trenk, Tobias Geisler, Martin Orban, Martin Hadamitzky, Béla Merkely, Róbert Gábor Kiss, András Komócsi, Csaba A Dézsi, Lesca Holdt, Stephan B Felix, Radoslaw Parma, Mariusz Klopotowski, Robert H G Schwinger, Johannes Rieber, Kurt Huber, Franz-Josef Neumann, Lukasz Koltowski, Julinda Mehilli, Zenon Huczek, Steffen Massberg, on behalf of the TROPICAL-ACS Investigators†*

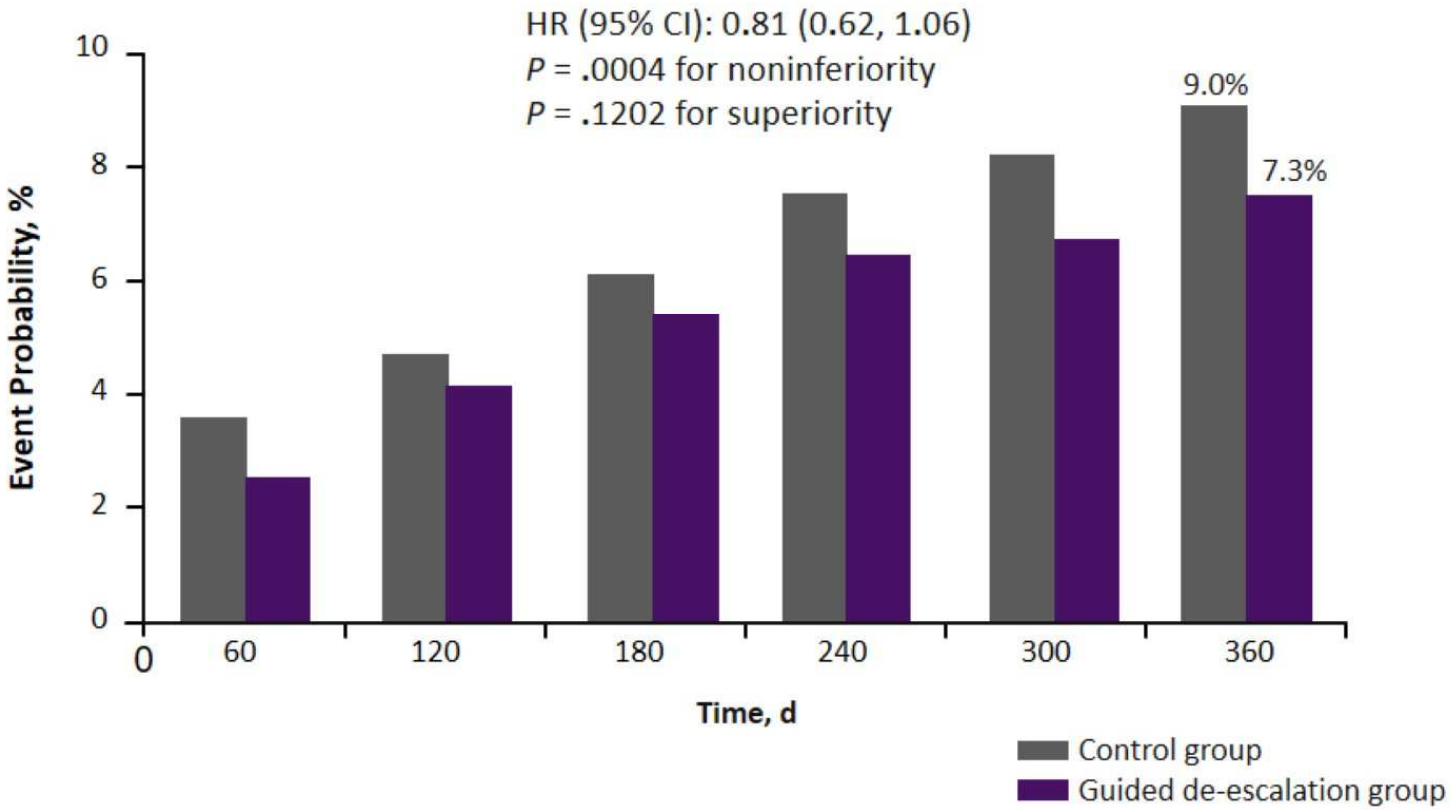
Lancet 2017; 390: 1747–57

Tropical-ACS: Study Design and Groups



Reprinted from Lancet, 390, Sibbing D, et al., Guided de-escalation of antiplatelet treatment in patients with acute coronary syndrome undergoing percutaneous coronary intervention (TROPICAL-ACS): a randomised, open-label, multicentre trial, 1747-1757., Copyright 2017, with permission from Elsevier.

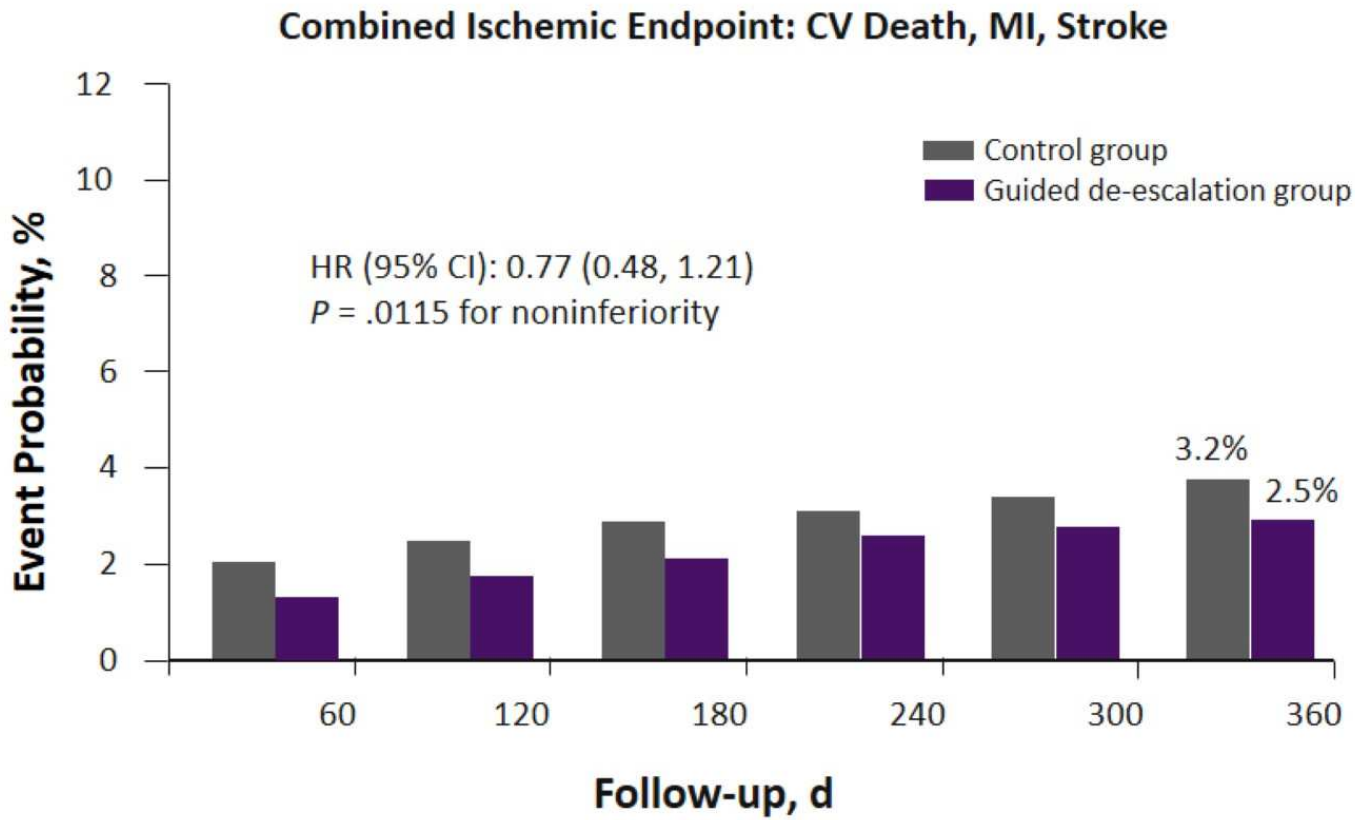
TROPICAL-ACS: Primary Endpoint*



*Composite of CV death, MI, stroke, and BARC grade ≥ 2

Sibbing D, et al. *Lancet.* 2017;390:1747-1757.

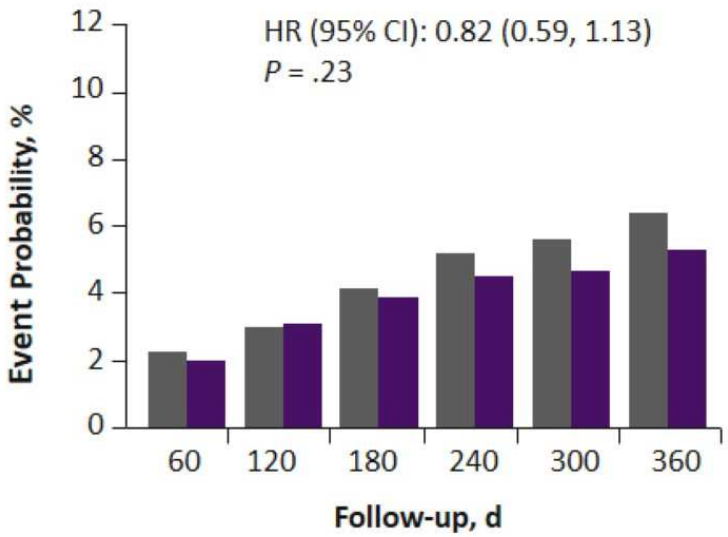
TROPICAL-ACS: Combined Ischemic Endpoint



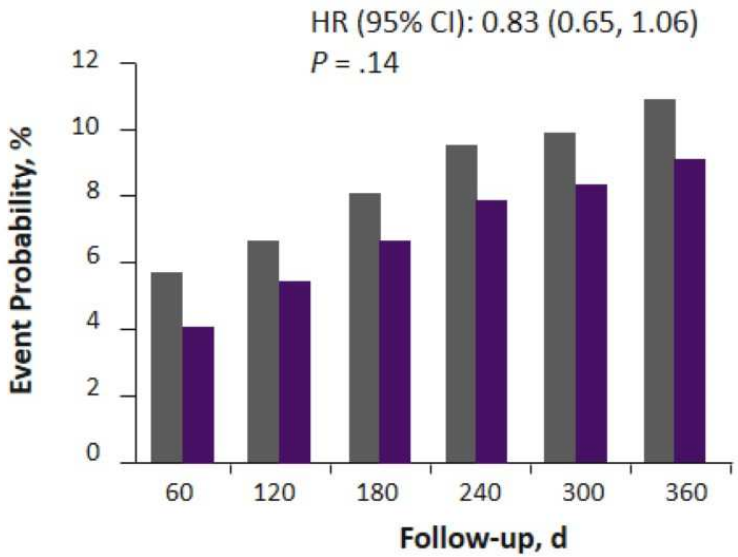
Sibbing D, et al. *Lancet.* 2017;390:1747-1757.

TROPICAL-ACS: Bleeding Events

Key Secondary Endpoint:
BARC ≥2 Bleeding

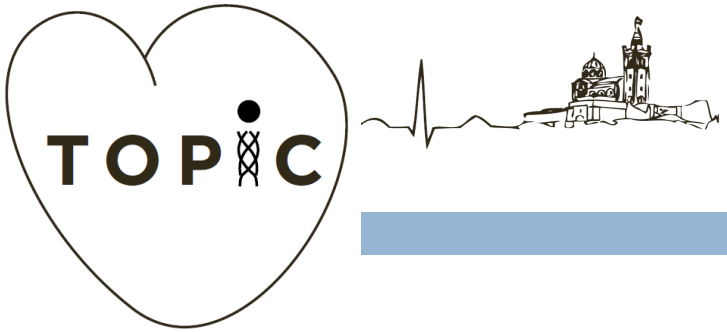


All Bleeding Events:
BARC 1 to 5 Bleeding



Control group
Guided de-escalation group

Sibbing D, et al. *Lancet.* 2017;390:1747-1757.



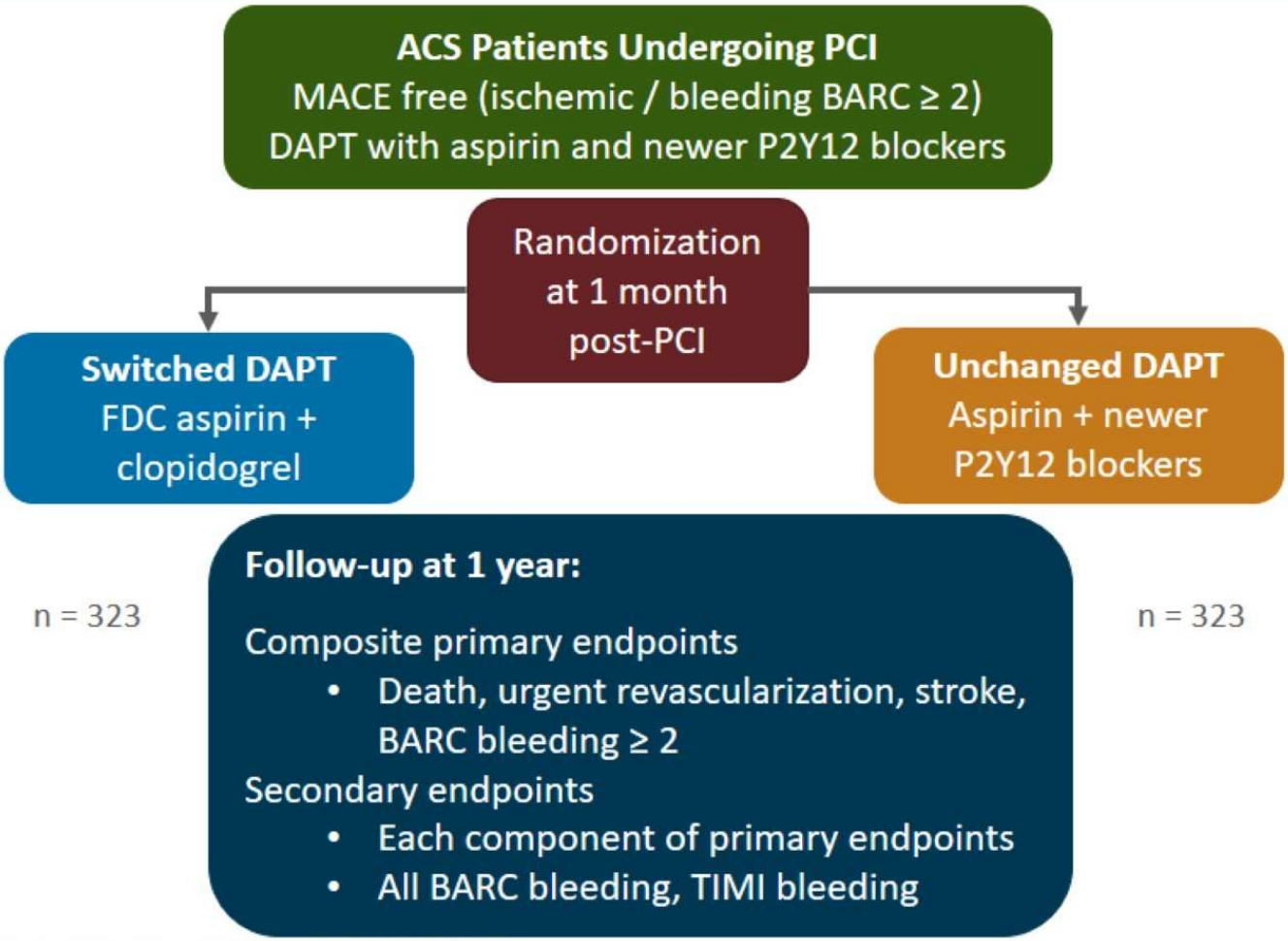
European Heart Journal (2017) **00**, 1–9
doi:10.1093/eurheartj/ehx175

CLINICAL RESEARCH
Acute coronary syndromes

Benefit of switched dual antiplatelet therapy after acute coronary syndrome: the TOPIC (timing of platelet inhibition after acute coronary syndrome) randomized study

Cuisset et al, Eur Heart J 2017
Published online, May 16th

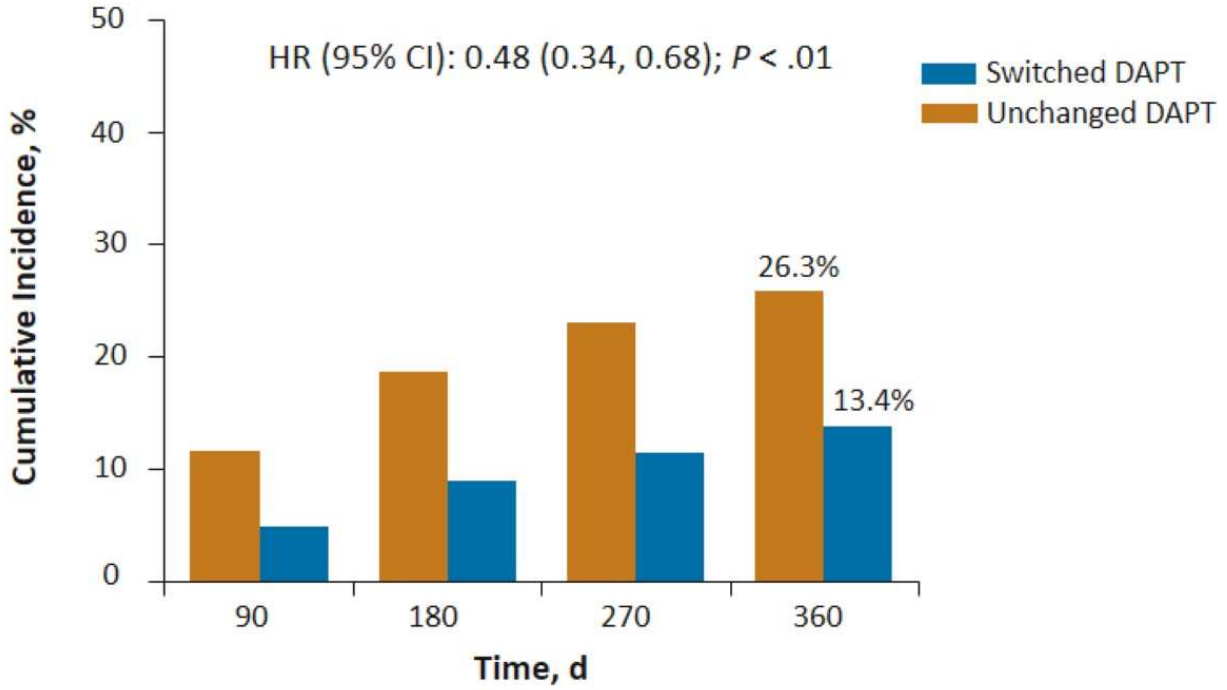
TOPIC: Study Design



Cuisset T, et al. *Eur Heart J*. 2017;38:3070-3078.

TOPIC: Primary Endpoint at 1 Year Post-ACS*

Better Prognosis With Switched DAPT

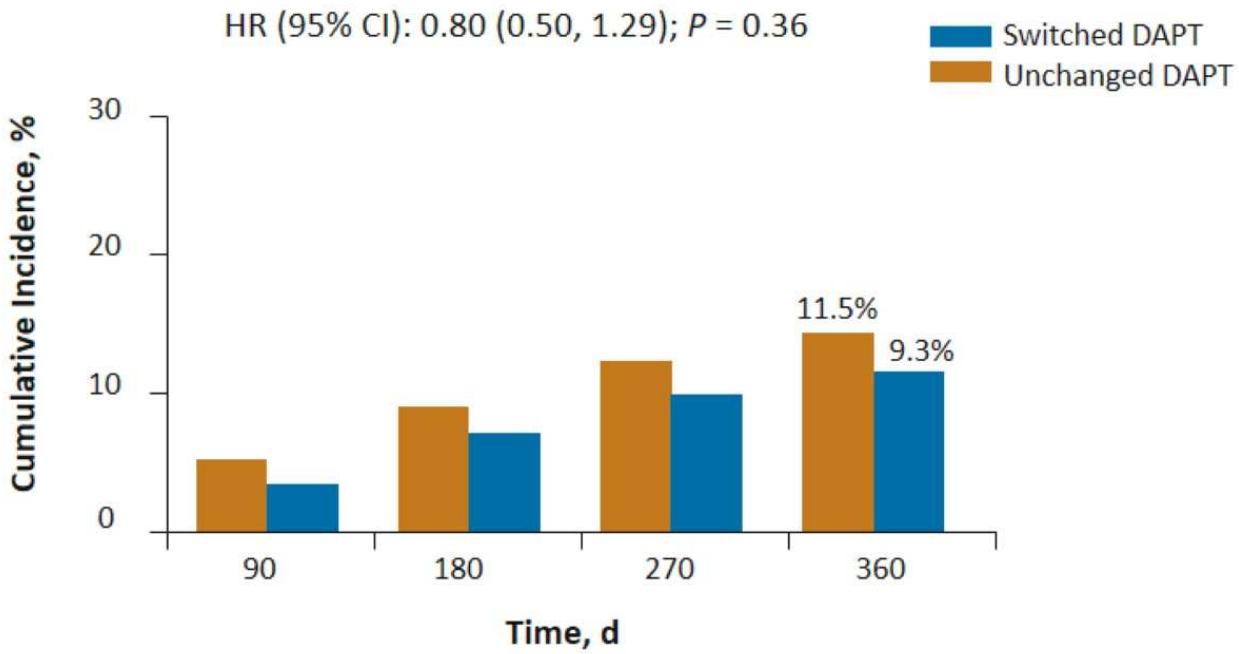


*Composite of CV death, urgent revascularization, stroke, and BARC bleeding ≥ 2

Cuisset T, et al. *Eur Heart J*. 2017;38:3070-3078.

TOPIC: Any Ischemic Endpoint

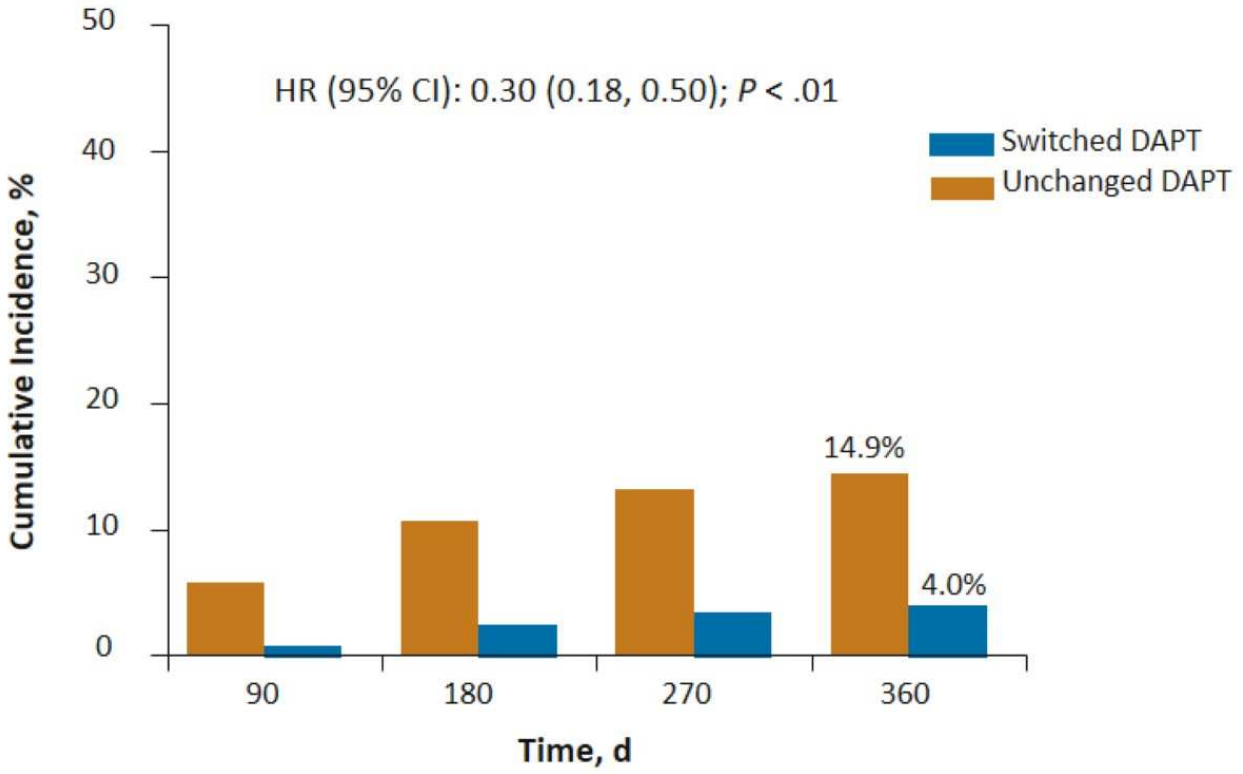
No Difference in Ischemic Event Rate



Cuisset T, et al. *Eur Heart J*. 2017;38:3070-3078.

TOPIC: BARC ≥ 2 Bleeding

Higher Rate of BARC ≥ 2 Bleeding With Unchanged DAPT



Cuisset T, et al. *Eur Heart J*. 2017;38:3070-3078.

P2Y12 INHIBITORS

De-Escalating DAPT

Go Up or Go Down

Personalized Approach

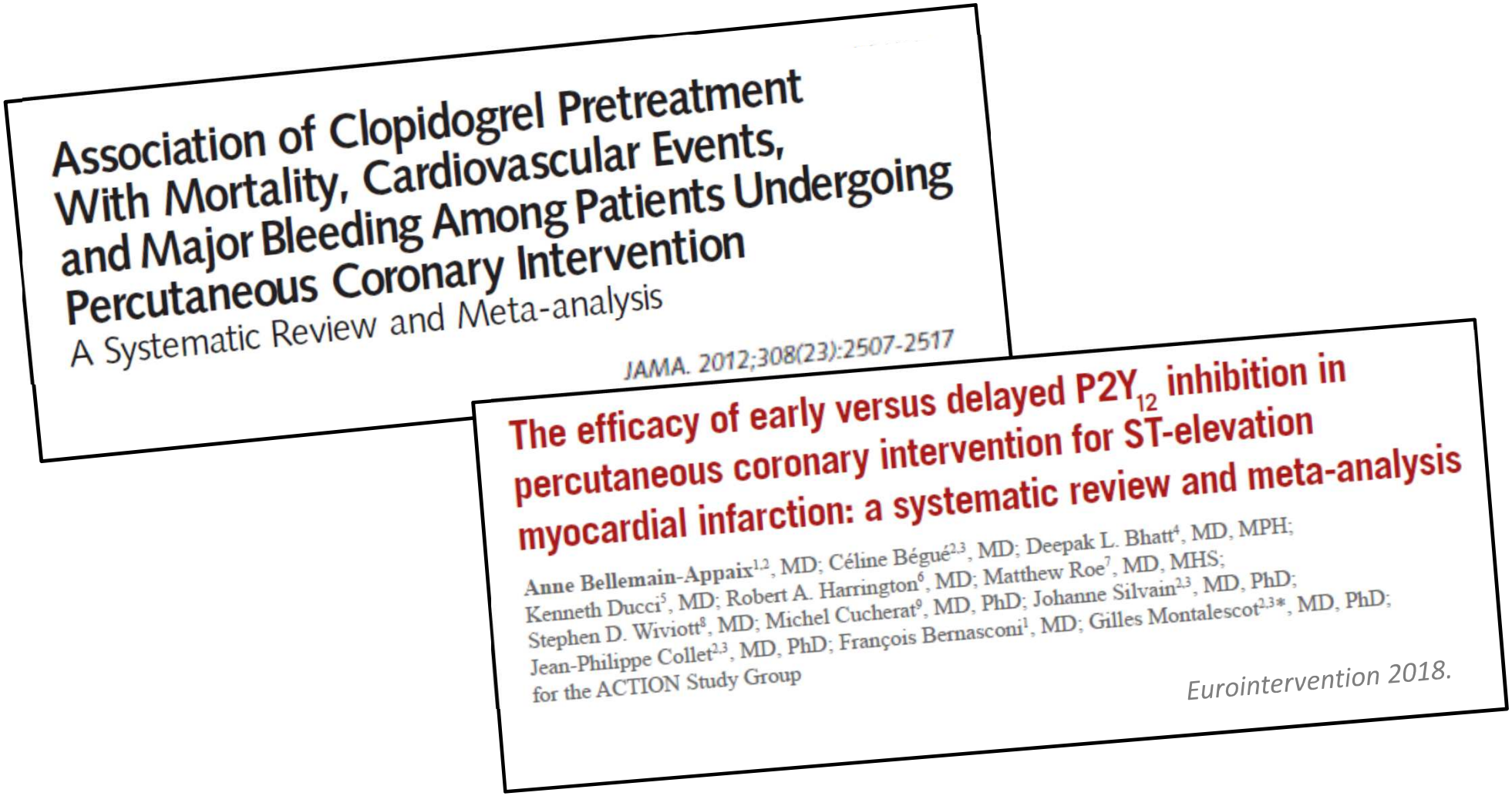
When Should De-Escalation of DAPT Be Considered Following PCI*?

*With latest-generation DES

P2Y12 INHIBITORS

Hurry to start?

Pre-Treatment with P2Y12 Inhibitor before Primary PCI



Association of Clopidogrel Pretreatment With Mortality, Cardiovascular Events, and Major Bleeding Among Patients Undergoing Percutaneous Coronary Intervention

A Systematic Review and Meta-analysis

JAMA. 2012;308(23):2507-2517

The efficacy of early versus delayed P2Y$_{12}$ inhibition in percutaneous coronary intervention for ST-elevation myocardial infarction: a systematic review and meta-analysis

Anne Bellemain-Appaix[1,2], MD; Céline Bégué[2,3], MD; Deepak L. Bhatt[4], MD, MPH; Kenneth Ducci[5], MD; Robert A. Harrington[6], MD; Matthew Roe[7], MD, MHS; Stephen D. Wiviott[8], MD; Michel Cucherat[9], MD, PhD; Johanne Silvain[2,3], MD, PhD; Jean-Philippe Collet[2,3], MD, PhD; François Bernasconi[1], MD; Gilles Montalescot[2,3]*, MD, PhD; for the ACTION Study Group

Eurointervention 2018.

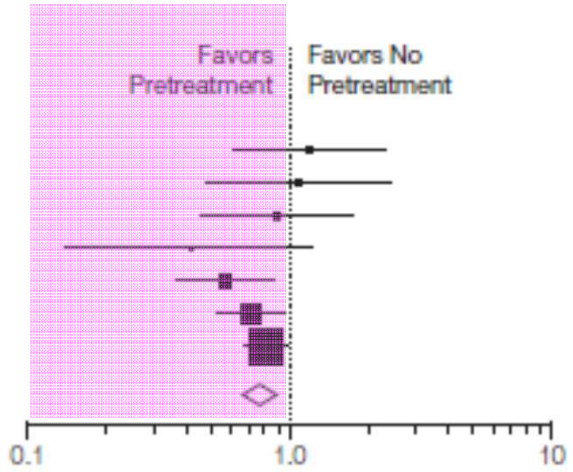
Source	Design	No. of Patients	Pretreatment	No Pretreatment	End Points	Bleeding Definitions[a]	Follow-up
Retrospective trials							
Amin et al,[21] 2011	Cohort	1913	≥600 mg LD <2 h or ≥ 300 mg LD <6 h or 75 mg MD >1 wk	Lower loading doses or no clopidogrel before PCI	Death, MI,	TIMI major or minor	In hospital to
Feldman et al,[25] 2010	Cohort	1041	75 mg MD ≥5 d or 300 mg LD ≥12 h or 600 mg LD ≥2 h	600 mg LD <2 h or just before undergoing the procedure			
Chan et al,[22] 2003	Cohort	4809	300 mg before PCI 56.6%, <2 h; 27.2%, 2-6 h; 16.2%, <6 h (mean 2.1 h)	300 mg LD immediately after PCI			
Prospective trials							
Dörler et al,[23] 2011	Cohort	5955	Dose not specified before hospital or before catheter laboratory LD	Peri-intervention LD			
Fefer et al,[24] 2009	Cohort	383	300-600 mg LD before PCI (in emergency department or on transfer to catheter laboratory	300 mg LD after PCI			
Szük et al,[26] 2007	Cohort	4160	300 mg >6 h and <24 h before PCI	300 mg LD immediately after PCI			

JAMA. 2012;308(23):2507-2517

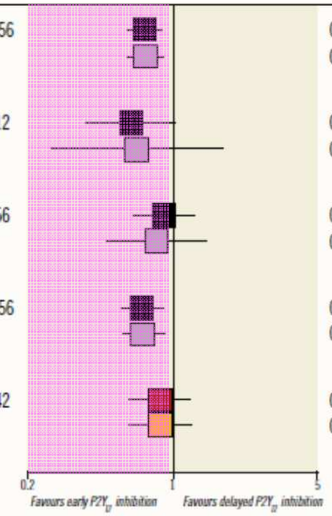
Study	Year	Design	N	Follow-up	Reference LD/chronic	Comparator	GPI	MACE
ATLANTIC [18]	2014	RCDB	1,862	30 days bleeding H48-30d	Ticagrelor in the cathlab	Ticagrelor Pre-hosp (in ambulance)	*Discouraged* Pre-hosp 30.1% In hosp 27.2%	Death, MI, ST, stroke, UVR
Load&Go [17]	2013	RCT not blinded	168	30 days	Clopidogrel 300 mg in cathlab before PCI	Clopidogrel 600-900 mg in ambulance at FMC	*At physician discretion* 84.8% pre-treatment 92.9% no pre-treatment	CV death, MI, stroke, definite ST
PCI CLARITY [3]	2005	RCT Post-random. subgroup	1,863	30 days	Placebo LD and MD Open-label 300 mg LD after CA then 75 mg MD if PCI	300 mg LD pre-PCI (<45 min /start fibrinolysis) (median 3 days) then 75 mg MD	*Left to physician discretion* 33.5%	CV, death, MI, stroke
CIPAMI [19]	2011	PROBE	337	Until 7 days or hospital discharge	600 LD in cath lab post CA	600 mg at FMC	*Left to physician discretion* 47.2% pre-treatment 48.8% no pre-treatment	Death, MI, UTVR
CHAMPION PCI STEMI [15]	2009	Sub-analysis of CHAMPION PCI RCDB	8,877 STEMI 996	30 days	IV placebo + clopidogrel 600 mg 30 min before PCI+placebo at the end of PCI	Placebo po + cangrelor 30 µg/kg bolus 30 min before PCI, 4 µg/kg/min 2 hrs, then clopidogrel 600 mg	*Left to physician discretion* Not allowed <12 hrs before PCI cangrelor 52.3% clopidogrel 50.4%	Death/MI/TVR for ischaemia
CHAMPION PHOENIX [14]	2013	RCDB	11,145 STEMI 1992	48 hrs	IV placebo+clopidogrel 300-600 mg (74%) before or at the end of PCI, +placebo at the end of PCI	Placebo po+cangrelor 30 µg/kg bolus 30 min before PCI, 4 µg/kg/min 2 hrs, then clopidogrel 300-600 mg	*Only in bail-out** cangrelor: 2.3% clopidogrel: 3.5% Not available for STEMI patients	Death/MI/UVR/ stent thrombosis

Eurointervention 2018

Source	Major Coronary Event: No. of Events, Pretreatment	No. of Events, No Pretreatment	No. of Patients, Pretreatment	No. of Patients, No Pretreatment	OR (95% CI)	Relative Weight, %
RCTs						
ARMYDA-5 PRELOAD,[17] 2010	21	18	204	205	1.19 (0.62-2.31)	4.9
Davlouros et al,[16] 2009	15	13	103	96	1.09 (0.49-2.42)	3.4
PRAGUE 8,[18] 2008	17	19	513	515	0.89 (0.46-1.74)	4.8
CIPAMI,[7] 2007	5	12	164	171	0.42 (0.14-1.21)	1.9
CLARITY PCI,[6] 2005	34	58	933	930	0.57 (0.37-0.88)	11.2
CREDO,[3] 2002	89	122	1053	1063	0.71 (0.53-0.95)	24.2
PCI CURE,[5] 2001	240	292	1313	1345	0.81 (0.67-0.98)	49.7
Overall	421	534	4283	4325	0.77 (0.66-0.89)	100
					P<.001	



Global results		"Early" group (n/N)	"Delayed" group (n/N)	Odds ratio, 95% CI	p-value
MACE	Fixed-effect model	219/4,792	296/4,856	0.73 (0.61-0.88)	0.0008
	Random-effects model			0.74 (0.61-0.90)	0.003
	Heterogeneity: I^2=9%, Q=6.61, df=6, p=0.36				
Stent thrombosis	Fixed-effect model	23/3,647	38/3,712	0.63 (0.38-1.06)	0.08
	Random-effects model			0.67 (0.26-1.73)	0.40
	Heterogeneity: I^2=48%, Q=3.88, df=2, p=0.14				
Death	Fixed-effect model	60/4,792	67/4,856	0.91 (0.64-1.29)	0.58
	Random-effects model			0.84 (0.48-1.47)	0.55
	Heterogeneity: I^2=43%, Q=8.81, df=5, p=0.12				
Myocardial infarction	Fixed-effect model	129/4,792	178/4,856	0.71 (0.57-0.90)	0.004
	Random-effects model			0.71 (0.57-0.90)	0.005
	Heterogeneity: I^2=0%, Q=1.44, df=5, p=0.92				
Major bleeding	Fixed-effect model	65/4,784	76/4,842	0.87 (0.62-1.21)	0.41
	Random-effects model			0.88 (0.62-1.23)	0.45
	Heterogeneity: I^2=0%, Q=4.39, df=6, p=0.62				



Euorintervention 2018

The NEW ENGLAND JOURNAL of MEDICINE

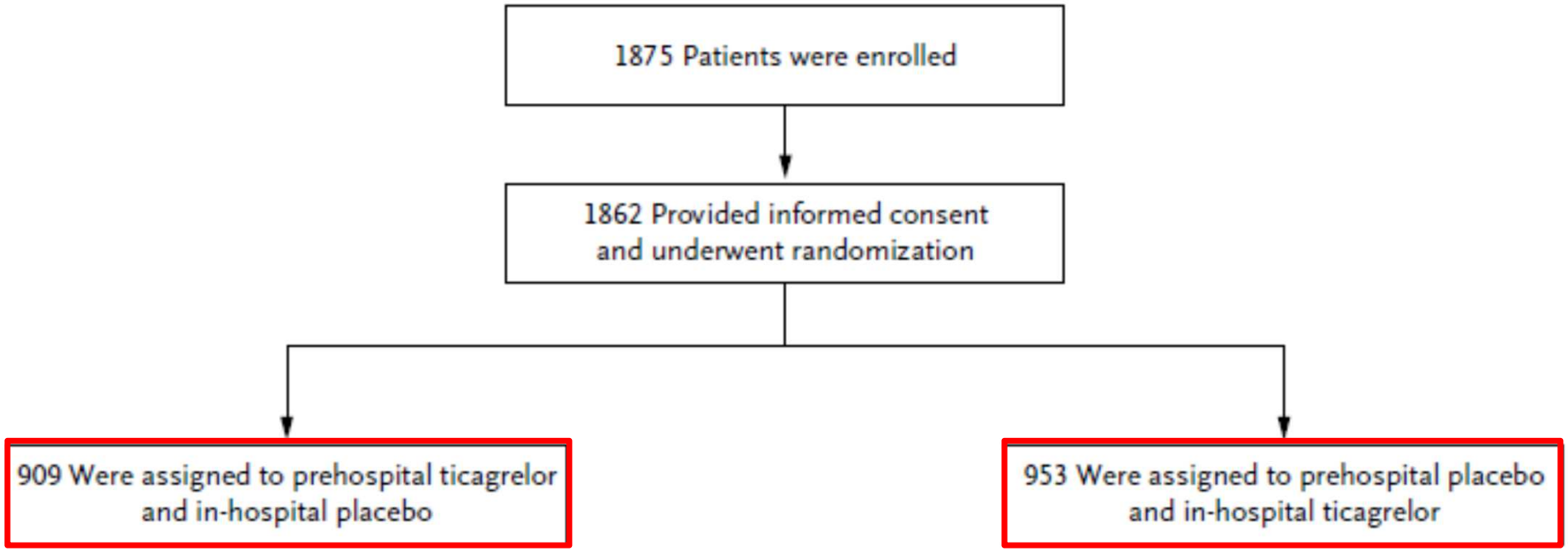
ORIGINAL ARTICLE

Prehospital Ticagrelor in ST-Segment Elevation Myocardial Infarction

Gilles Montalescot, M.D., Ph.D., Arnoud W. van 't Hof, M.D., Ph.D., Frédéric Lapostolle, M.D., Ph.D., Johanne Silvain, M.D., Ph.D., Jens Flensted Lassen, M.D., Ph.D., Leonardo Bolognese, M.D., Warren J. Cantor, M.D., Ángel Cequier, M.D., Ph.D., Mohamed Chettibi, M.D., Ph.D., Shaun G. Goodman, M.D., Christopher J. Hammett, M.B., Ch.B., M.D., Kurt Huber, M.D., Magnus Janzon, M.D., Ph.D., Béla Merkely, M.D., Ph.D., Robert F. Storey, M.D., D.M., Uwe Zeymer, M.D., Olivier Stibbe, M.D., Patrick Ecollan, M.D., Wim M.J.M. Heutz, M.D., Eva Swahn, M.D., Ph.D., Jean-Philippe Collet, M.D., Ph.D., Frank F. Willems, M.D., Ph.D., Caroline Baradat, M.Sc., Muriel Licour, M.Sc., Anne Tsatsaris, M.D., Eric Vicaut, M.D., Ph.D., and Christian W. Hamm, M.D., Ph.D., for the ATLANTIC Investigators*

N Engl J Med 2014;371:1016-27.

ATLANTIC Study



ATLANTIC Study

Table 2. Coprimary Efficacy End Points and Related Secondary End Points in the Modified Intention-to-Treat Population.*

End Point	Prehospital Ticagrelor (N=906)	In-Hospital Ticagrelor (N=952)	Odds Ratio (95% CI)†	P Value†	Difference (95% CI)‡
	no./no. of patients who could be evaluated (%)				
Coprimary end points					
Absence of ST-segment elevation resolution ≥70% before PCI	672/774 (86.8)	722/824 (87.6)	0.93 (0.69 to 1.25)	0.63	−0.008 (−0.041 to 0.025)
Absence of TIMI flow grade 3 in infarct-related artery at initial angiography	681/824 (82.6)	711/856 (83.1)	0.97 (0.75 to 1.25)	0.82	−0.004 (−0.040 to 0.032)
Met one or both coprimary end points					
Both	541/744 (72.7)	571/777 (73.5)	0.96 (0.77 to 1.21)	0.73	−0.008 (−0.052 to 0.037)
One or both	677/719 (94.2)	710/751 (94.5)	0.93 (0.60 to 1.45)	0.75	−0.004 (−0.027 to 0.020)
Secondary end points					
Absence of ST-segment elevation resolution ≥70% after PCI	303/713 (42.5)	353/743 (47.5)	0.82 (0.66 to 1.004)	0.05	−0.050 (−0.101 to 0.001)
Absence of TIMI flow grade 3 in infarct related artery after PCI	135/760 (17.8)	154/784 (19.6)	0.88 (0.68 to 1.14)	0.34	−0.019 (−0.058 to 0.020)
Met one or both secondary end points					
Both	73/763 (9.6)	87/775 (11.2)	0.84 (0.60 to 1.16)	0.29	−0.017 (−0.047 to 0.014)
One or both	339/684 (49.6)	371/703 (52.8)	0.88 (0.71 to 1.09)	0.23	−0.032 (−0.085 to 0.020)

P2Y12 INHIBITORS

After Thrombolytic

Too much weight

P2Y12 INHIBITORS

After Thrombolytic

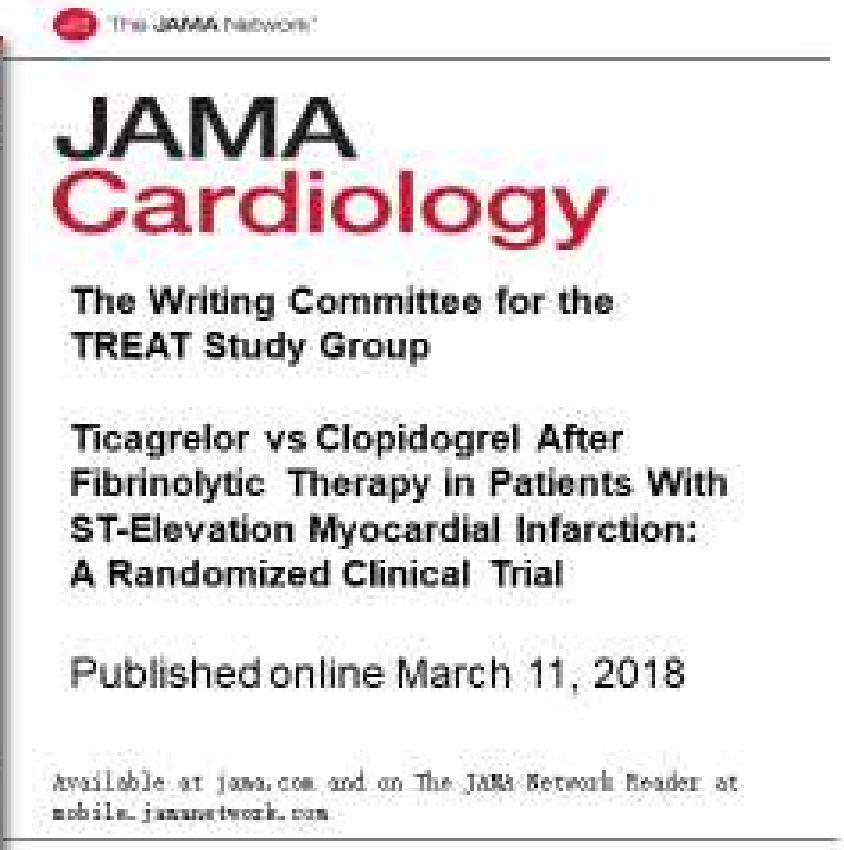
ESC European Society of Cardiology

Clopidogrel is the $P2Y_{12}$ inhibitor of choice as co-adjuvant and after fibrinolysis. Potent $P2Y_{12}$ inhibitors have not been properly tested in patients undergoing fibrinolysis, and safety (i.e. bleeding complications) is not well established. However, in patients who underwent PCI after fibrinolysis, after a safety period (arbitrarily considered 48 h), there are no biological grounds to consider that potent $P2Y_{12}$ inhibitors will add risk and not exert a benefit over clopidogrel as in the primary PCI setting.

The safety of ticagrelor in STEMI patients in the first 24 hours after fibrinolysis remains uncertain.

Treat TRIAL


Ticagrelor vs Clopidogrel After Fibrinolytic Therapy in Patients With ST-Elevation Myocardial Infarction
A Randomized Clinical Trial



Study Design

Male and Female Patients (Age ≥ 18 years and ≤ 75 years) with STEMI with onset in the previous 24h and treated with fibrinolytic therapy (N=3,799)

Ticagrelor
180 mg as early as possible after the index event and not >24 h post event
90 mg twice daily for 12 months

Clopidogrel
300 mg as early as possible after the index event and not >24 h post event
75 mg/day for 12 months

I T T

I T T

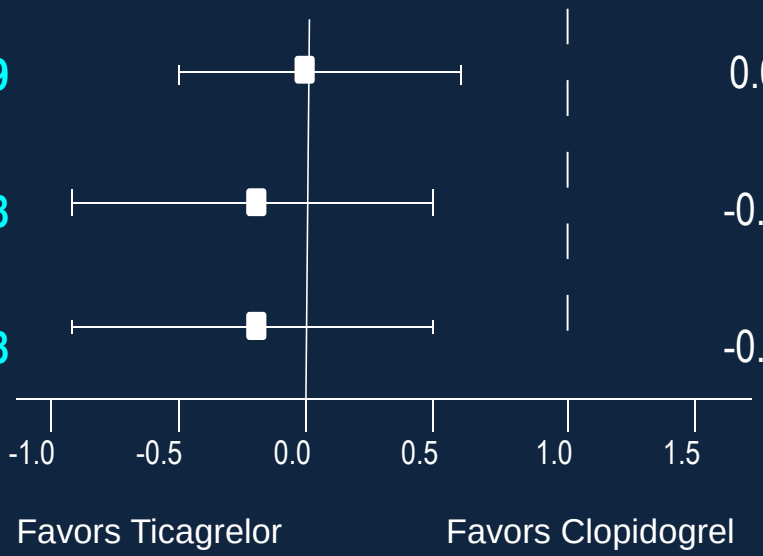
Follow up visits at hospital discharge or 7th day, 30 days, 6 and 12 months

Primary safety outcome: TIMI Major Bleeding
Secondary safety outcomes: Other bleeding events (PLATO trial, BARC, TIMI)
Exploratory efficacy outcomes: CV death, MI, or stroke

CV = cardiovascular ; MI = Myocardial infarction; TIA = transient ischemic attack
TIMI = Thrombolysis in Myocardial Infarction; BARC = Bleeding Academic Research Consortium

Major Bleeding at 30 Days

	Ticagrelor (n=1913)	Clopidogrel (n=1886)	Difference , 95% CI	P noninf.
TIMI Major Bleeding (Primary Endpoint)	0.73	0.69	0.04 [-0.49; 0.58]	<0.001
PLATO Major Bleeding	1.20	1.38	-0.18 [-0.89; 0.54]	0.001
BARC Type 3 - 5 Bleeding	1.20	1.38	-0.18 [-0.89; 0.54]	0.001

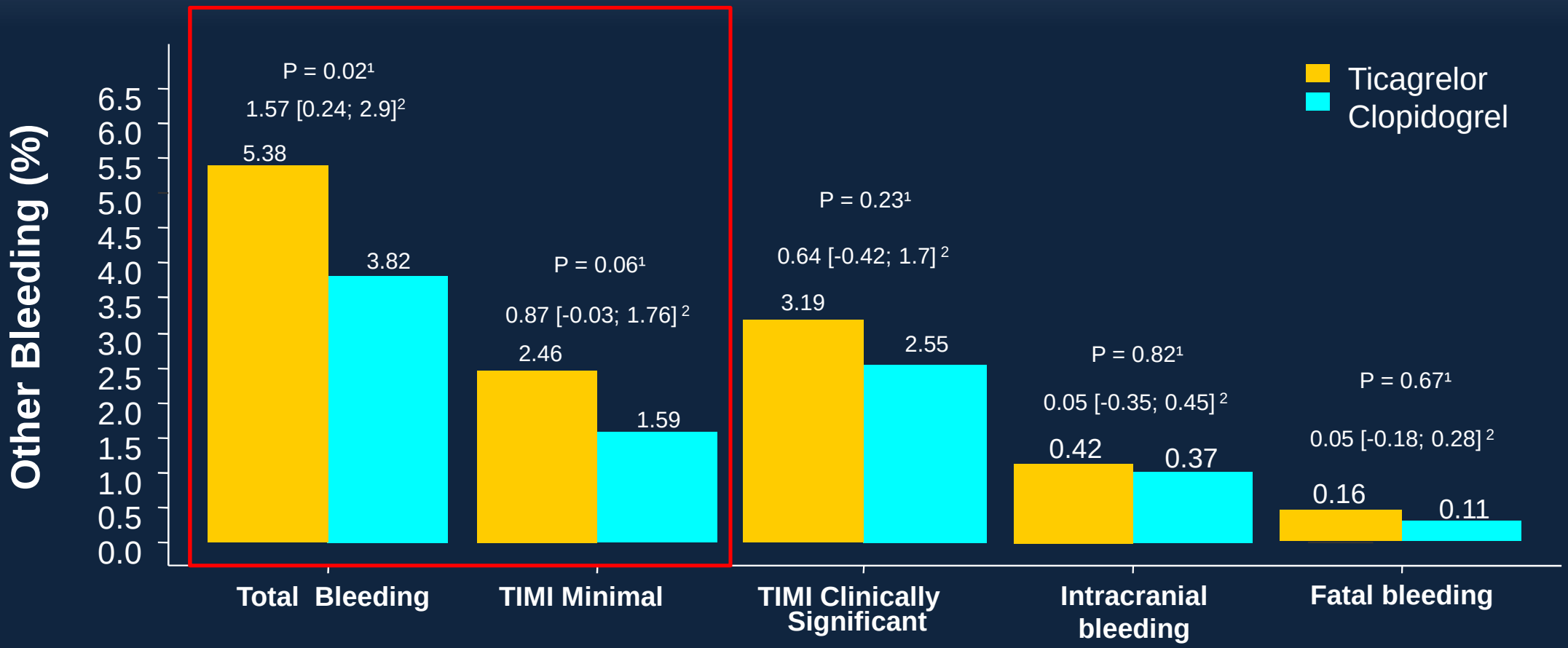


Data presented as no. (%)

* Absolute difference (in percentage) presented as bilateral 95% confidence interval.

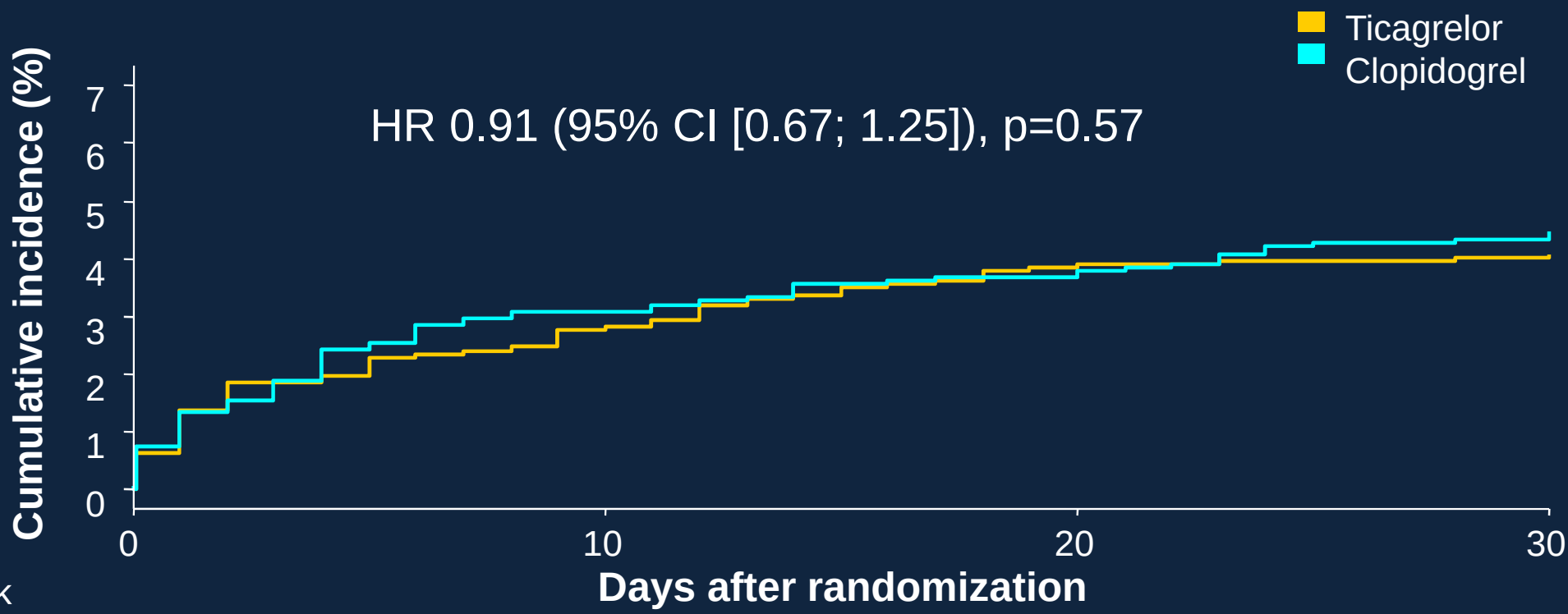
† 1% absolute difference margin non inferiority test. Non-inferiority test was done considering an one sided test.

Other Bleeding Outcomes



Major bleeding refer to adjudicated events analysed.
*Proportion of patients (%)
1 two-sided proportions
2 Absolute difference (%), 95% CI = confidence interval

CV Death, MI, or Stroke



No. at risk				
Ticagrelor	1913	1855	1834	1658
Clopidogrel	1885	1824	1812	1613

K-M = Kaplan-Meier; HR = hazard ratio; CI = confidence interval

Conclusions and Implications

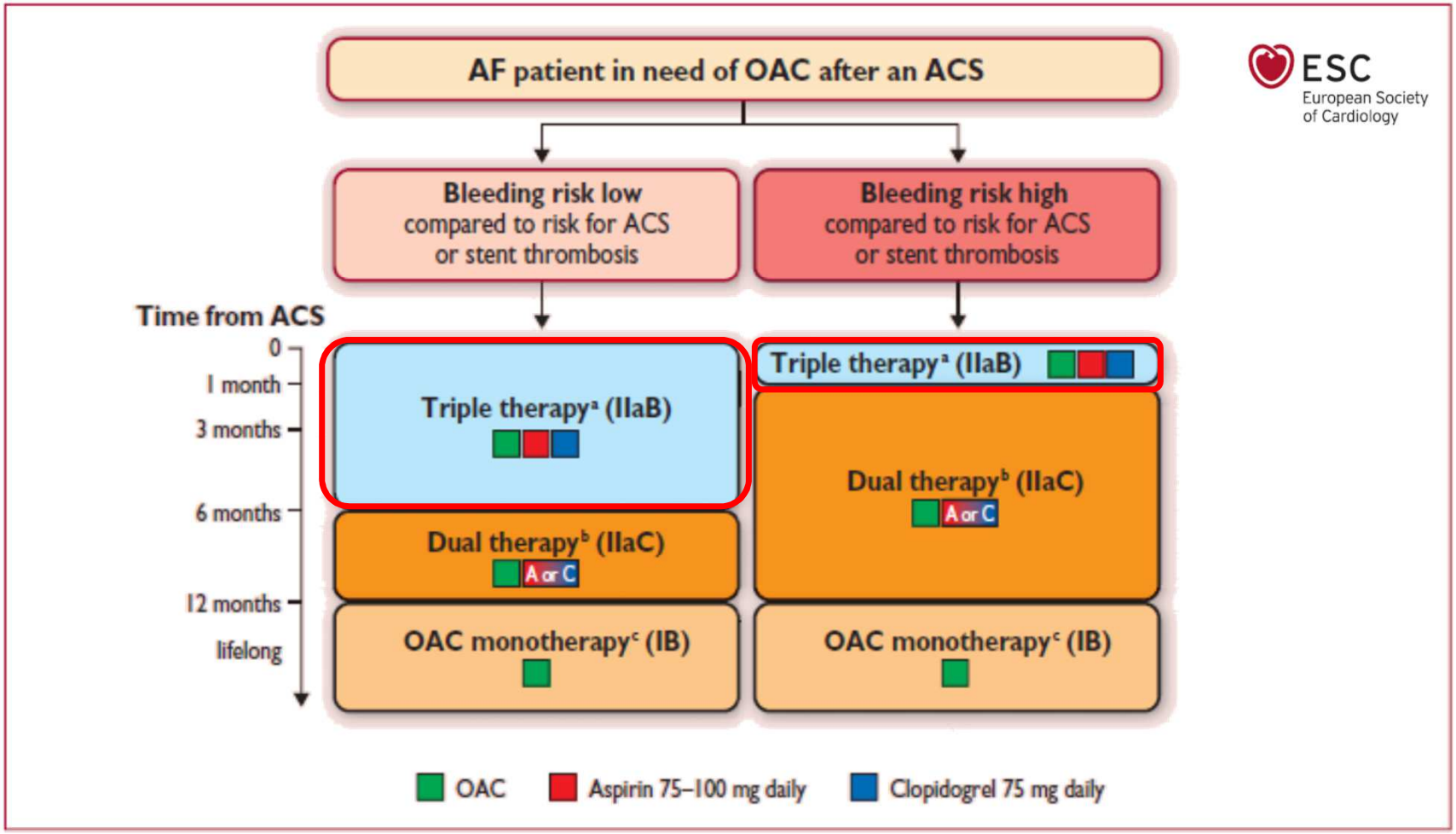
In patients aged ≤ 75 years with STEMI, ticagrelor after fibrinolytic therapy:

- Noninferior to clopidogrel for TIMI major bleeding at 30 days.
- Total bleeding was increased with ticagrelor
- No benefit on efficacy outcomes.

➢ *Clopidogrel remains the standard*

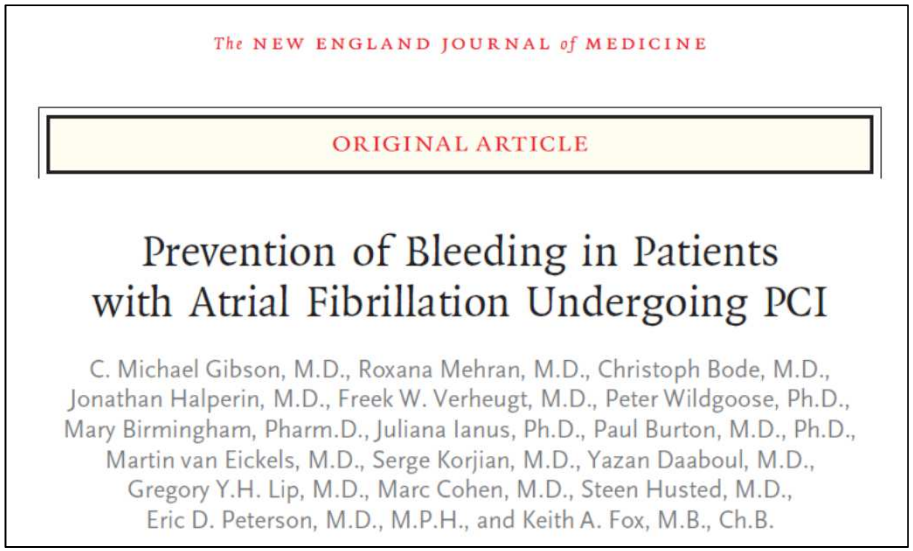
➢ *Ticagrelor can be considered if there is clinical need*

Anticoagulant in Combination with Antiplatelet Therapy



NOAC in Combination with Antiplatelet Therapy

PIONEER AF-PCI



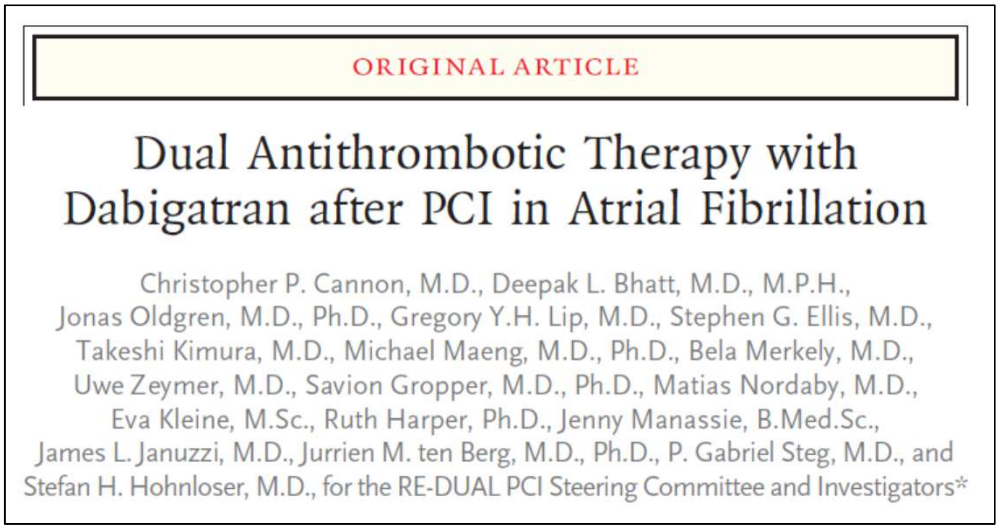
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Prevention of Bleeding in Patients with Atrial Fibrillation Undergoing PCI

C. Michael Gibson, M.D., Roxana Mehran, M.D., Christoph Bode, M.D., Jonathan Halperin, M.D., Freek W. Verheugt, M.D., Peter Wildgoose, Ph.D., Mary Birmingham, Pharm.D., Juliana Ianus, Ph.D., Paul Burton, M.D., Ph.D., Martin van Eickels, M.D., Serge Korjian, M.D., Yazan Daaboul, M.D., Gregory Y.H. Lip, M.D., Marc Cohen, M.D., Steen Husted, M.D., Eric D. Peterson, M.D., M.P.H., and Keith A. Fox, M.B., Ch.B.

RE-DUAL PCI

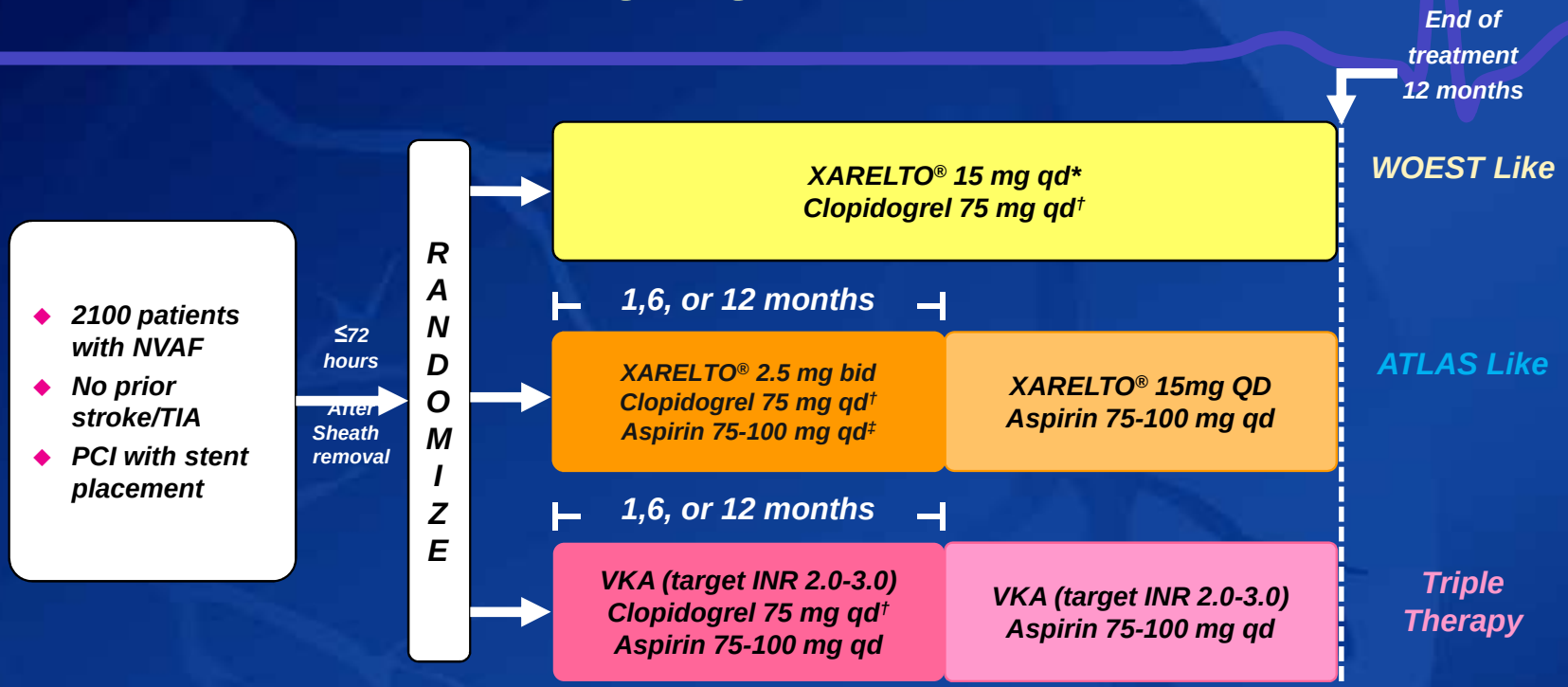


ORIGINAL ARTICLE

Dual Antithrombotic Therapy with Dabigatran after PCI in Atrial Fibrillation

Christopher P. Cannon, M.D., Deepak L. Bhatt, M.D., M.P.H., Jonas Oldgren, M.D., Ph.D., Gregory Y.H. Lip, M.D., Stephen G. Ellis, M.D., Takeshi Kimura, M.D., Michael Maeng, M.D., Ph.D., Bela Merkely, M.D., Uwe Zeymer, M.D., Savion Gropper, M.D., Ph.D., Matias Nordaby, M.D., Eva Kleine, M.Sc., Ruth Harper, Ph.D., Jenny Manassie, B.Med.Sc., James L. Januzzi, M.D., Jurrien M. ten Berg, M.D., Ph.D., P. Gabriel Steg, M.D., and Stefan H. Hohnloser, M.D., for the RE-DUAL PCI Steering Committee and Investigators*

XARELTO® (Rivaroxaban) Use in Patients With AF Undergoing PCI: PIONEER AF-PCI



- Primary endpoint: TIMI major + minor + bleeding requiring medical attention
- Secondary endpoint: CV death, MI, and stroke

**XARELTO® dosed at 10 mg once daily in patients with CrCl of 30 to <50 mL/min.*

†Alternative $P2Y_{12}$ inhibitors: 10 mg once-daily prasugrel or 90 mg twice-daily ticagrelor.

‡Low-dose aspirin (75-100 mg/d).

Data on File. Janssen Pharmaceuticals, Inc.

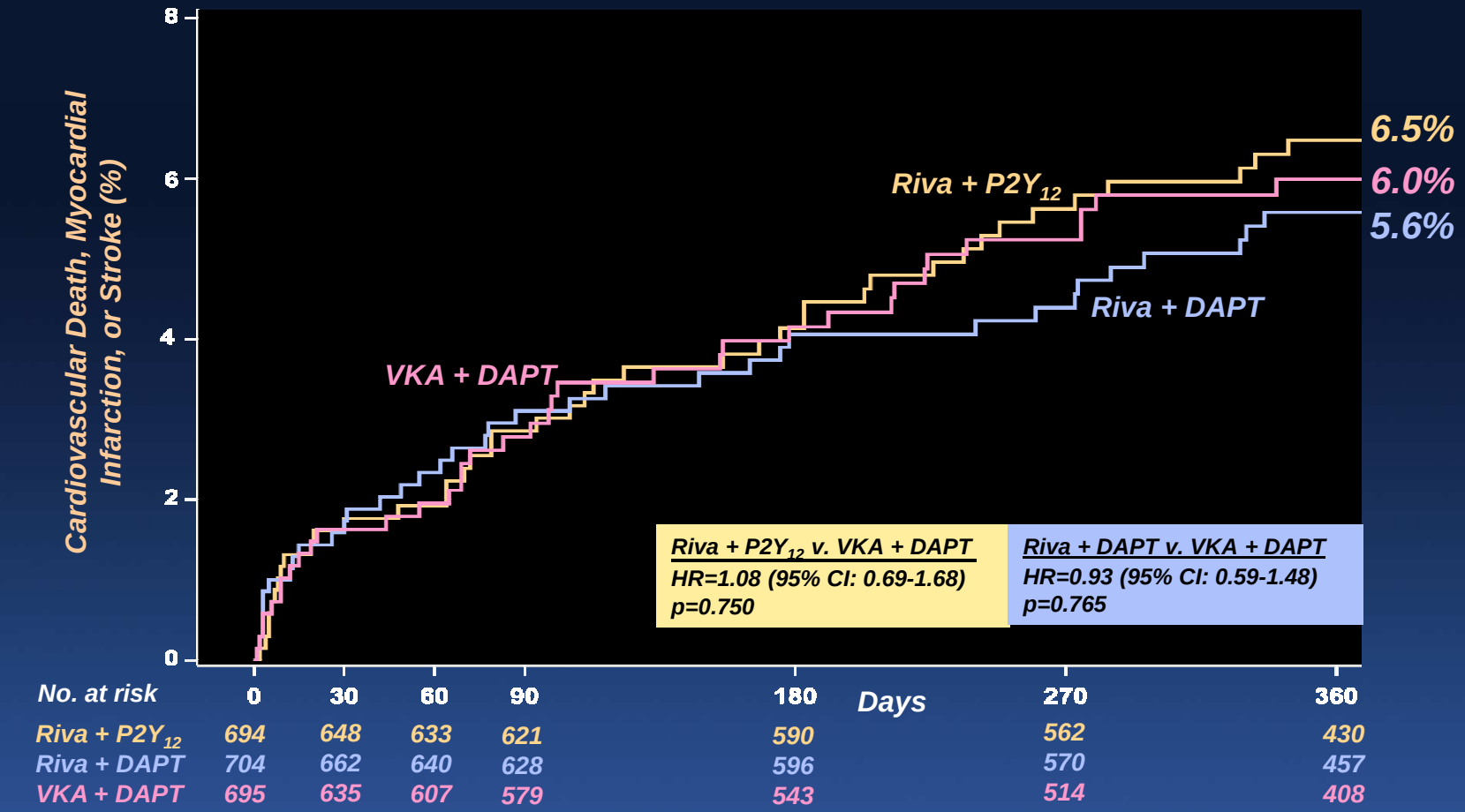
Gibson CM et al N Engl J Med. 2016 Dec 22;375(25):2423-2434

XARELTO® (Rivaroxaban) Use in Patients With AF Undergoing PCI: PIONEER AF-PCI

Type of index event — no./total no. (%)§			
NSTEMI	130/701 (18.5)	129/703 (18.3)	123/691 (17.8)
STEMI	86/701 (12.3)	97/703 (13.8)	74/691 (10.7)
Unstable angina	145/701 (20.7)	148/703 (21.1)	164/691 (23.7)

Gibson CM et al N Engl J Med. 2016 Dec 22;375(25):2423-2434

Kaplan-Meier Estimates of First Occurrence of CV Death, MI or Stroke

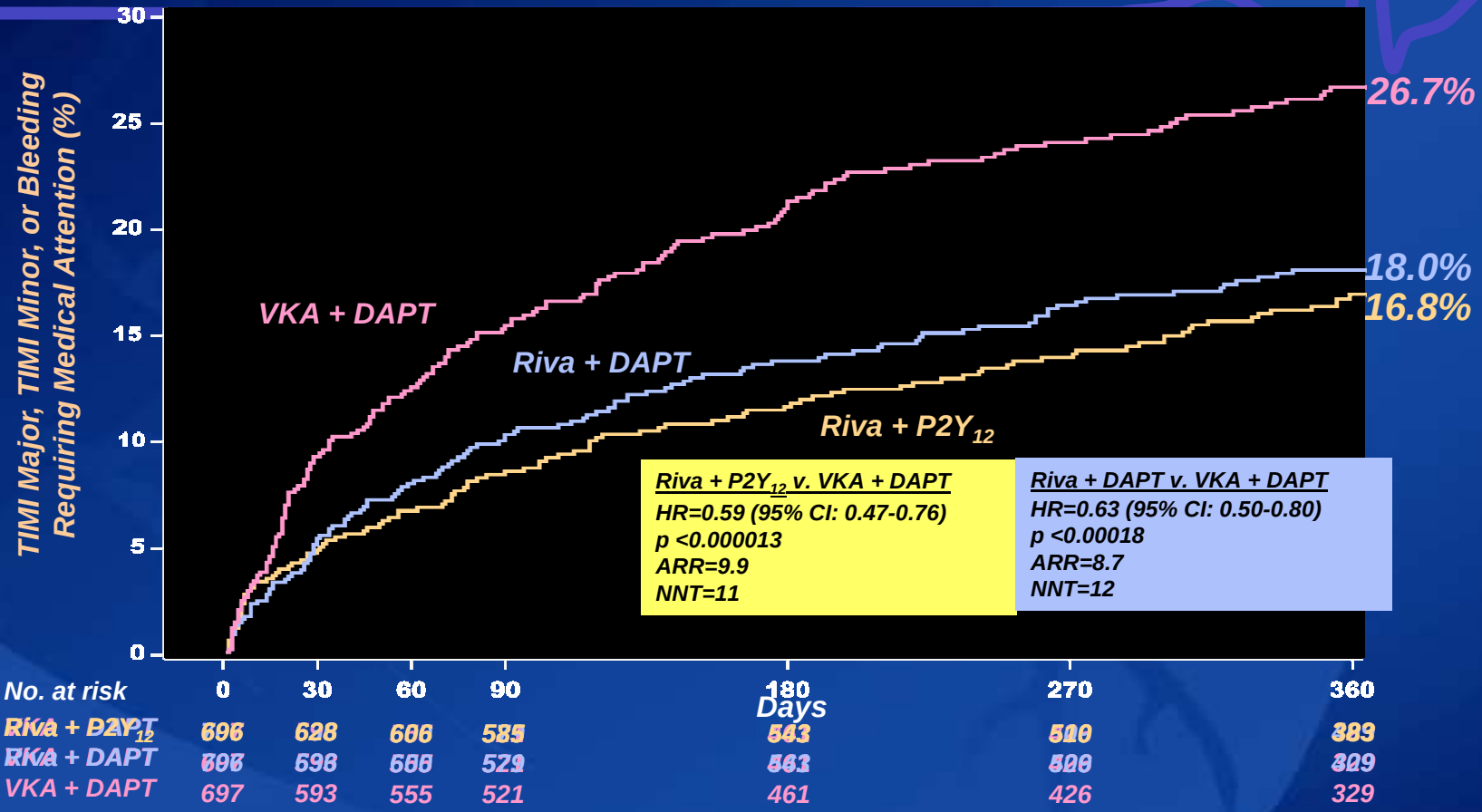


No. at risk	0	30	60	90	180	Days	270	360
Riva + P2Y12	694	648	633	621	590		562	430
Riva + DAPT	704	662	640	628	596		570	457
VKA + DAPT	695	635	607	579	543		514	408

Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug. Composite of adverse CV events is composite of CV death, MI, and stroke. Hazard ratios as compared to VKA group are based on the (stratified, only for the Overall, 2.5 mg BID/15 mg QD comparing VKA) Cox proportional hazards model. Log-Rank P-values as compared to the VKA group are based on the (stratified, only for Overall, 2.5 mg BID/115 mg QD comparing VKA) two-sided log rank test. 6 Subjects were excluded from all efficacy analyses because of violations in Good Clinical Practice guidelines

Gibson CM et al N Engl J Med. 2016 Dec 22;375(25):2423-2434

Kaplan-Meier Estimates of First Occurrence of Clinically Significant Bleeding Events

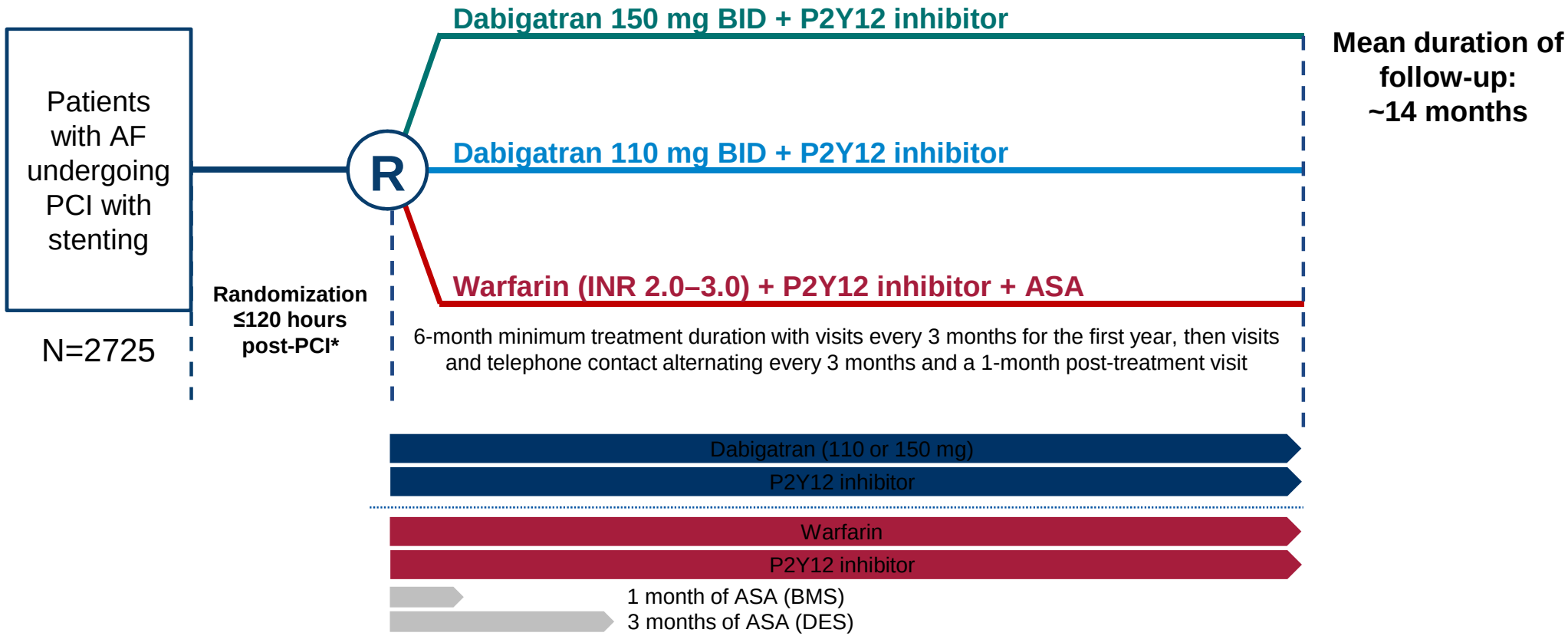


Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug. Clinically significant bleeding is the composite of TIMI major, TIMI minor, and BRMA. Hazard ratios as compared to the VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) Cox proportional hazards model. Log-Rank P-values as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) two-sided log rank test.

Gibson CM et al N Engl J Med. 2016 Dec 22;375(25):2423-2434

Study Design: Multicenter, randomized, open-label trial following a PROBE design

RE-DUAL PCI
Study in NVAF patients undergoing PCI



***Study drug should be administered 6 hours after sheath removal and no later than ≤120 hrs post-PCI (≤72 hrs is preferable).** PROBE, prospective, randomized, open, blinded end-point; R, randomization; BMS, bare metal stent; DES, drug-eluting stent. ClinicalTrials.gov: NCT02164864; Cannon et al. Clin Cardiol 2016

Baseline characteristics

RE-DUAL PCI
Study in NVAF patients undergoing PCI

	Dabigatran 110 mg dual therapy (n=981)	Warfarin triple therapy (n=981)	Dabigatran 150 mg dual therapy (n=763)	Corresponding Warfarin triple therapy (n=764)
Age, years, mean	71.5	71.7	68.6	68.8
≥80 (US, ROW), ≥70 (Japan), %	22.9	22.9	1.0	1.0
<80 (US, ROW), <70 (Japan), %	77.1	77.1	99.0	99.0
Male, %	74.2	76.5	77.6	77.7
Baseline CrCl, mL/min, mean	76.3	75.4	83.7	81.3
Diabetes mellitus, %	36.9	37.8	34.1	39.7
CHA_2DS_2–VASc score (mean)	3.7	3.8	3.3	3.6
Modified HAS-BLED score at baseline (mean)	2.7	2.8	2.6	2.7
ACS indication for PCI, %	51.9	48.4	51.2	48.3
DES only, %	82.0	84.2	81.4	83.5

ROW, rest of world

Additional individual thromboembolic endpoints

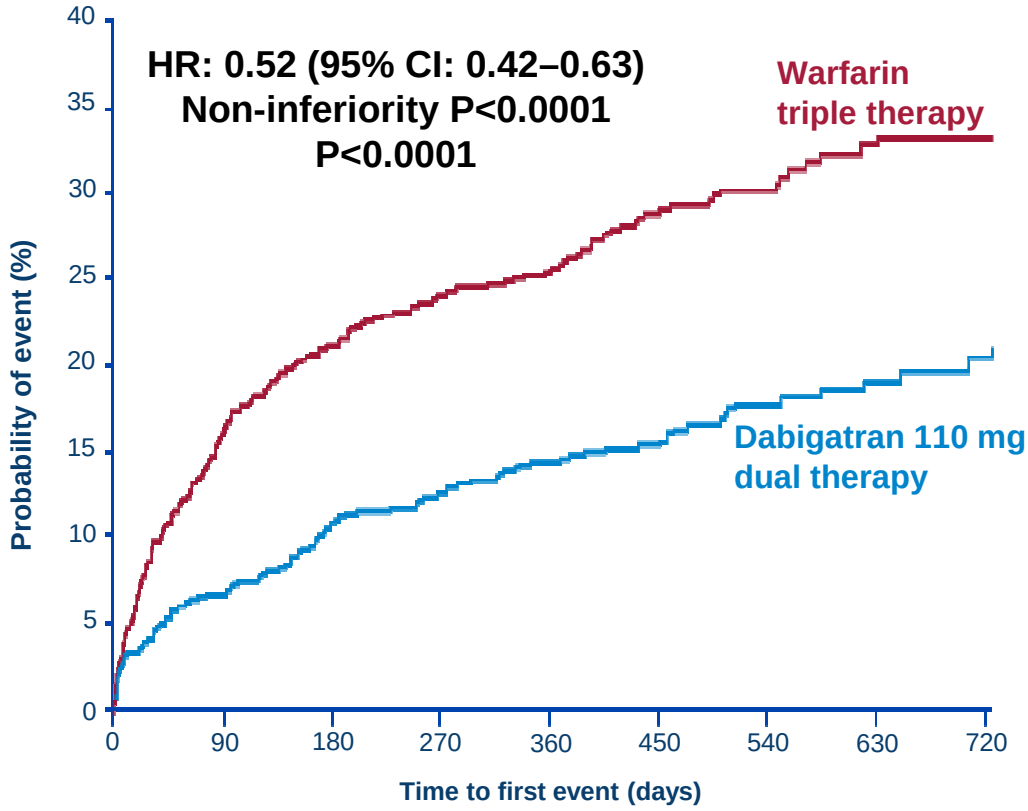
RE-DUAL PCI
Study in NVAF patients undergoing PCI

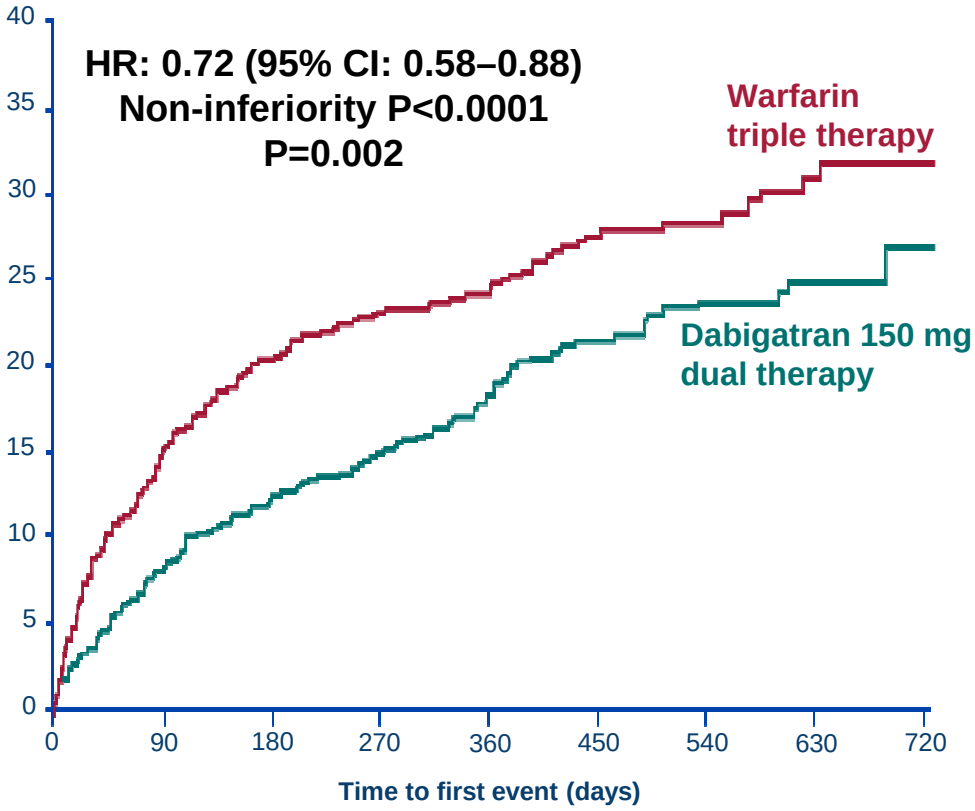
	Dabigatran 110 mg dual therapy (n=981) n (%)	Warfarin triple therapy (n=981) n (%)	D110 DT vs warfarin TT HR (95% CI)	D110 DT vs warfarin TT P value	Dabigatran 150 mg dual therapy (n=763) n (%)	Warfarin triple therapy (n=764) n (%)	D150 DT vs warfarin TT HR (95% CI)	D150 DT vs warfarin TT P value
All-cause death	55 (5.6)	48 (4.9)	1.12 (0.76–1.65)	0.56	30 (3.9)	35 (4.6)	0.83 (0.51–1.34)	0.44
Stroke	17 (1.7)	13 (1.3)	1.30 (0.63–2.67)	0.48	9 (1.2)	8 (1.0)	1.09 (0.42–2.83)	0.85
Unplanned revascularization	76 (7.7)	69 (7.0)	1.09 (0.79–1.51)	0.61	51 (6.7)	52 (6.8)	0.96 (0.65–1.41)	0.83
MI	44 (4.5)	29 (3.0)	1.51 (0.94–2.41)	0.09	26 (3.4)	22 (2.9)	1.16 (0.66–2.04)	0.61
Stent thrombosis	15 (1.5)	8 (0.8)	1.86 (0.79–4.40)	0.15	7 (0.9)	7 (0.9)	0.99 (0.35–2.81)	0.98

Results presented are times to event. Stent thrombosis is time to definite stent thrombosis

Primary Endpoint: Time to first ISTH major or clinically relevant non-major bleeding event

RE-DUAL PCI
Study in NVAF patients undergoing PCI





Full analysis set presented. HRs and Wald CIs from Cox proportional-hazard model. For the dabigatran 110 mg vs warfarin comparison, the model is stratified by age, non-elderly vs elderly (<70 or ≥70 in Japan and <80 or ≥80 years old elsewhere). For the dabigatran 150 mg vs warfarin comparison, an unstratified model is used, elderly patients outside the USA are excluded. Non-inferiority P value is one sided (alpha=0.025). Wald two-sided P value from (stratified) Cox proportional-hazard model (alpha=0.05)

Summary

Reperfusion Therapy

- Achieving primary PCI is the goal
- Thrombolytic as an option if timely primary PCI not feasible

  > Rescue PCI & early routine PCI as pharmaco-invasive strategy
- For lytic, half dose TNK for elderly >75 yrs

Summary

Reperfusion Therapy

- Achieving primary PCI is the goal
- Thrombolytic as an option if timely primary PCI not feasible
  - > Rescue PCI & early routine PCI as pharmacoinvasive strategy
- For lytic, half dose TNK for elderly >75 yrs

PCI Strategy

- **Multivessel disease:**
  - PCI to non-culprit vessel in same setting or as early stage procedure
- **Thromboaspiration:**
  - not routine, to be personalized
- **Cardiogenic shock:**
  - PCI to non-culprit lesion not routine, to be personalized
  - IABP not routine, to be personalized
  - Optimal use of hemodynamic support needs to be defined

Summary

Antithrombotic Therapy

- DAPT with potent P2Y12 inhibitors for 12 months recommended
  - Using less potent P2Y12 inhibitors: Personalized
  - Longer or shorter duration: Personalized
  - De-escalation: Personalized
- Pretreatment before CCL less essential for potent P2Y12 inhibitors
- Triple antithrombotic for 1 to 6 months for those requiring anticoagulants: Personalized

Thank You!