CMHC
Cardiometabolic Health Congress

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Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)

A Primer on Acute Coronary Syndromes

Erin Bohula, MD DPhil

Assistant Professor, BWH, HMS

Investigator, TIMI Study Group

BWH BRIGHAM AND WOMEN'S HOSPITAL | Heart & Vascular Center |

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

TIMI Study Group

www.brighamandwomens.org/heart

Disclosures

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  - **Amgen, Novo Nordisk, Servier, Kowa, Medscape, PriMed**

Outline

- Definitions/Pathophysiology
- Epidemiology
- STEMI
  - Diagnosis
  - Risk stratification
  - Revascularization
- NSTE-ACS
  - Diagnosis
  - Risk stratification
  - Revascularization
- Other management (medical therapy)

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ACS: Definitions, Pathophysiology and Epidemiology

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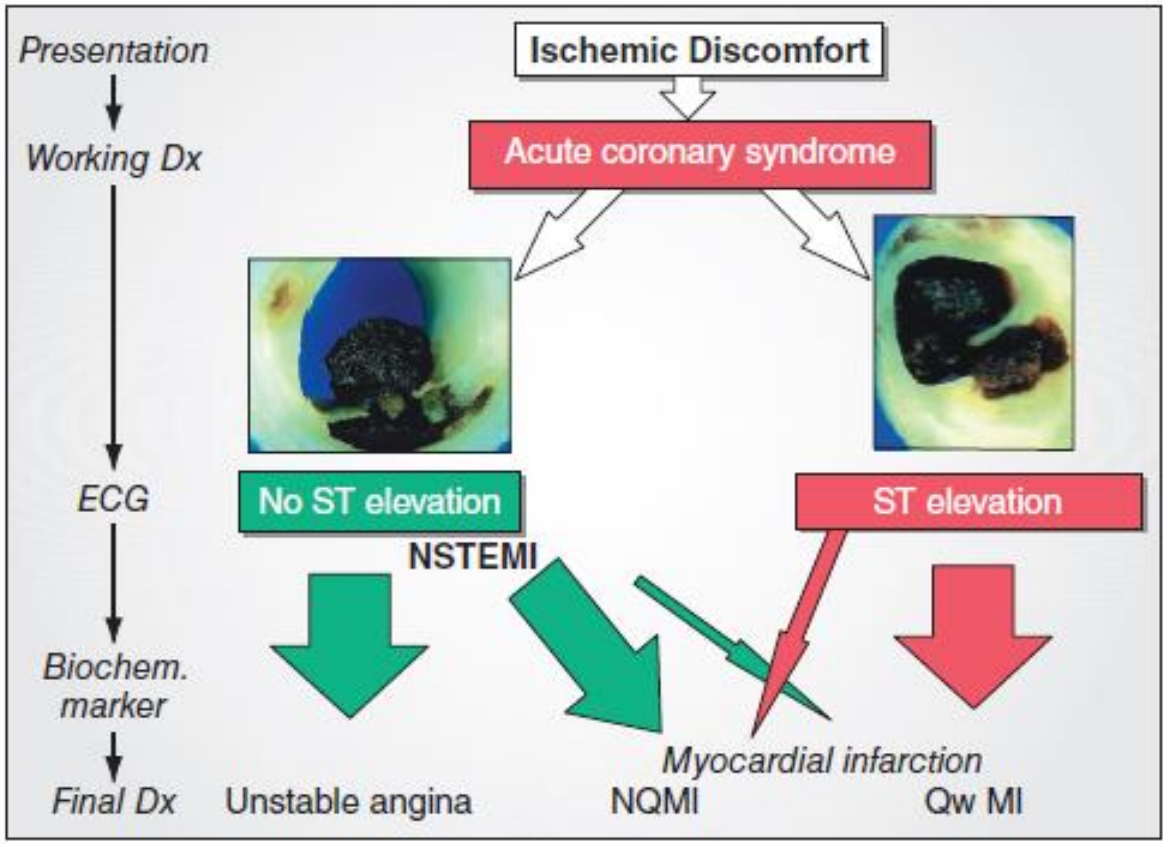
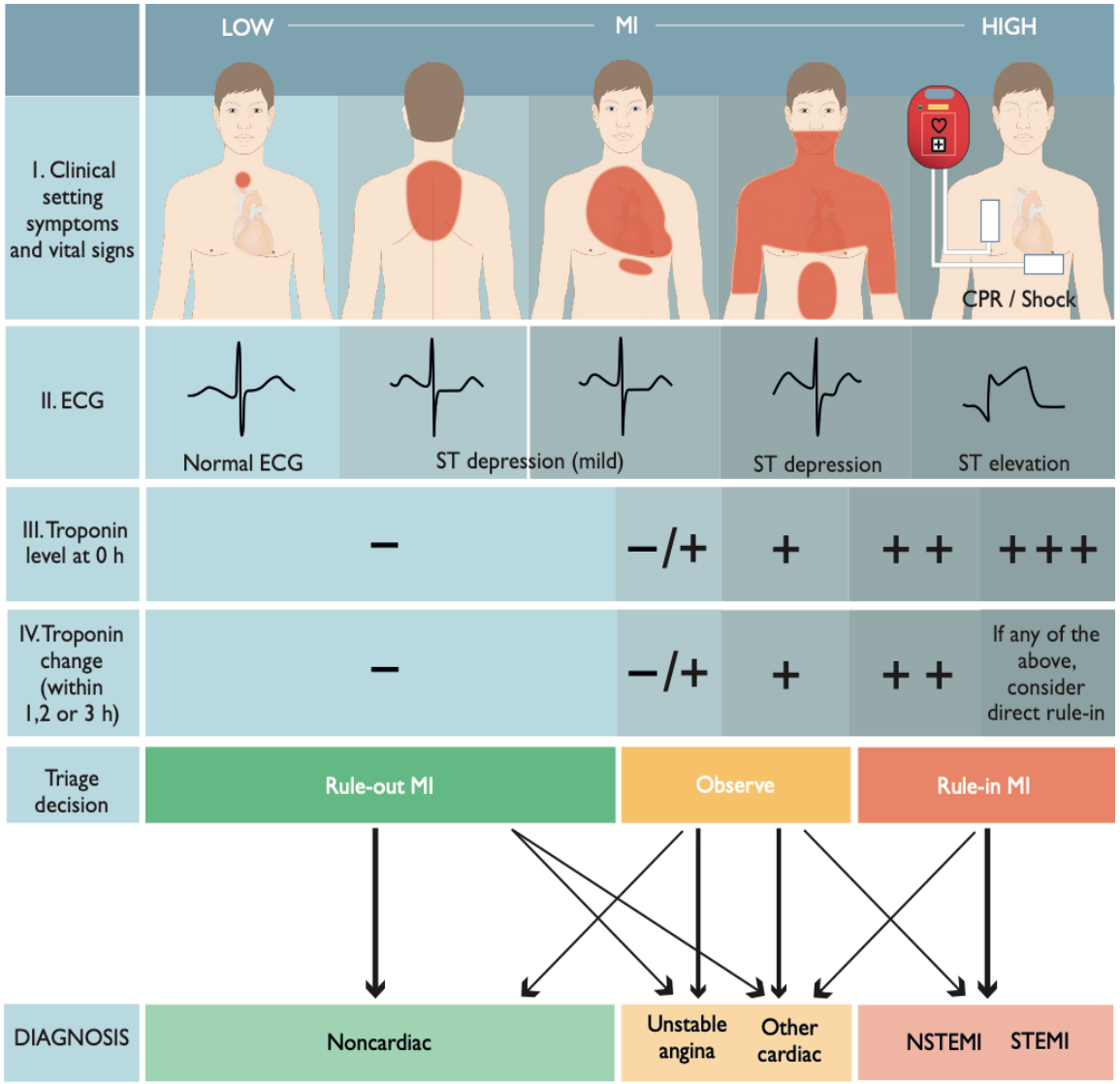
Acute Coronary Syndrome: STEMI, nSTEMI, UA



Davies MJ, Heart 2000;83:361
Hamm CW, Lancet 2001:358:1533



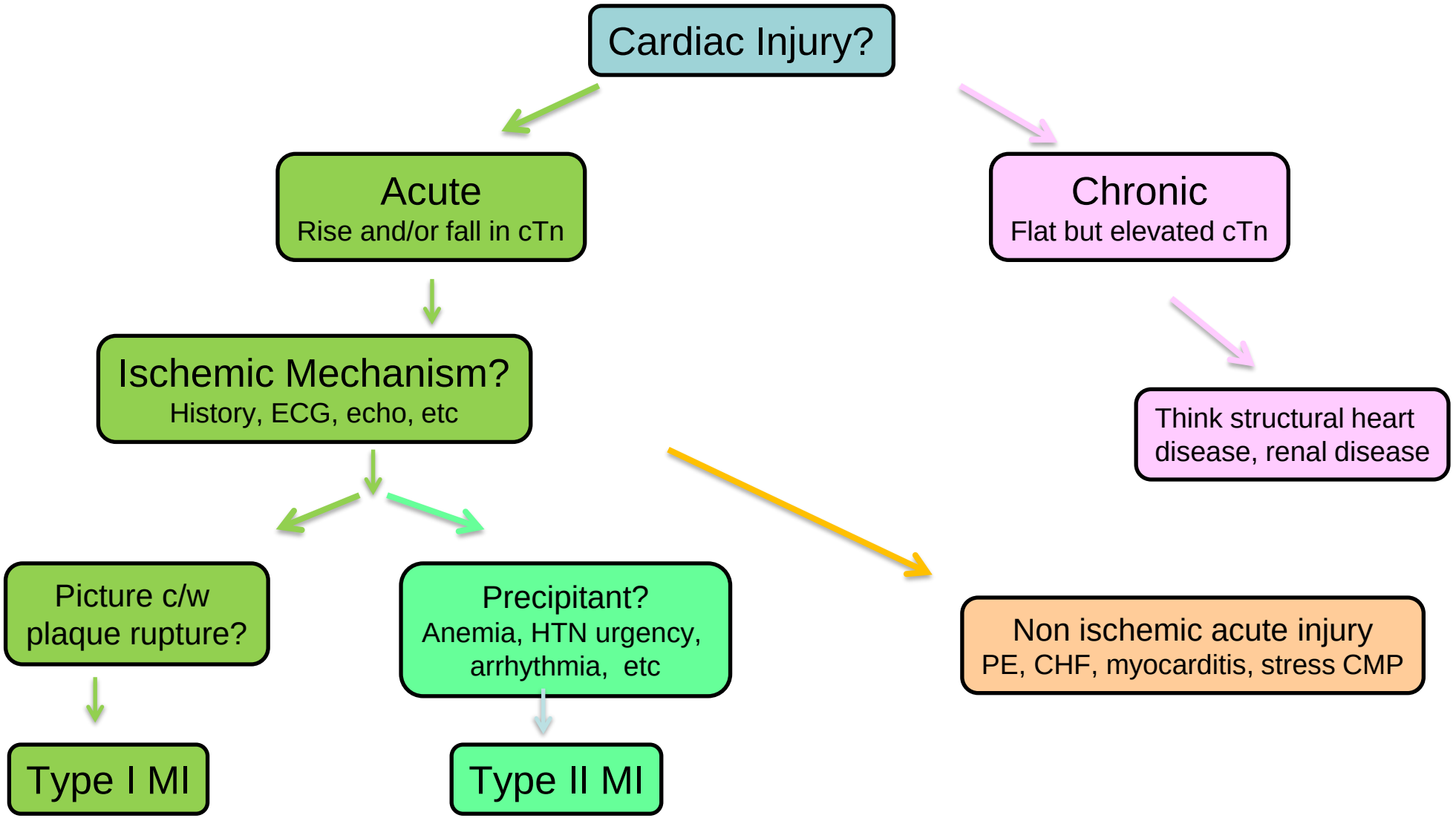
Collet JP et al. "2020 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segement elevation." European Heart Journal Heart 2021; 42.14: 1289-1367

4th Universal Definition of MI

Definition	Criteria
Myocardial **Injury**	Tn >99th %ile (acute if rise and/or fall)
Acute Myocardial **Infarction**	Acute myocardial injury + clinical evidence of acute myocardial ischemia (eg, sx, ECG, imaging)
Type 1	**Atherothrombosis** (plaque rupture or erosion)
Type 2	Imbalance between myocardial O_2 supply & demand **unrelated** to acute atherothrombosis
Type 3	**Cardiac death** w/ sx + ECG Δs before Tn available
Type 4	**PCI-related** (clinical + Tn >5× 99th %ile)
Type 5	**CABG-related** (clinical + Tn >10× 99th %ile)

Thygesen, *Circulation*. 2018.

What is an MI in 2022?



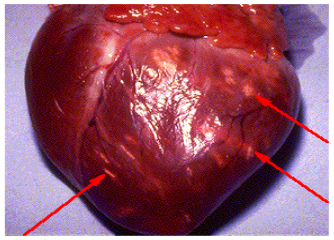
Acute Myocardial Injury vs Type 2 MI

- Acute Myocardial Injury = ↑ Tn w/o clinical signs/symptoms of ischemia
  - Heart failure, myocarditis, CMP, Takotsubo
  - Cardiac ablation, defibrillation, cardiac contusion
  - PE, PHT
  - Stroke, SAH, critical illness

Stress CMP

- Type 2 MI = Ischemic but not due to ACS (plaque rupture)
  - ↓ myocardial perfusion
    - Coronary artery spasm, embolism, dissection/SCAD
    - HoTN, profound sustained bradycardia, severe anemia
  - ↑ myocardial demand
    - Profound sustained tachycardia; HTN

Myocarditis



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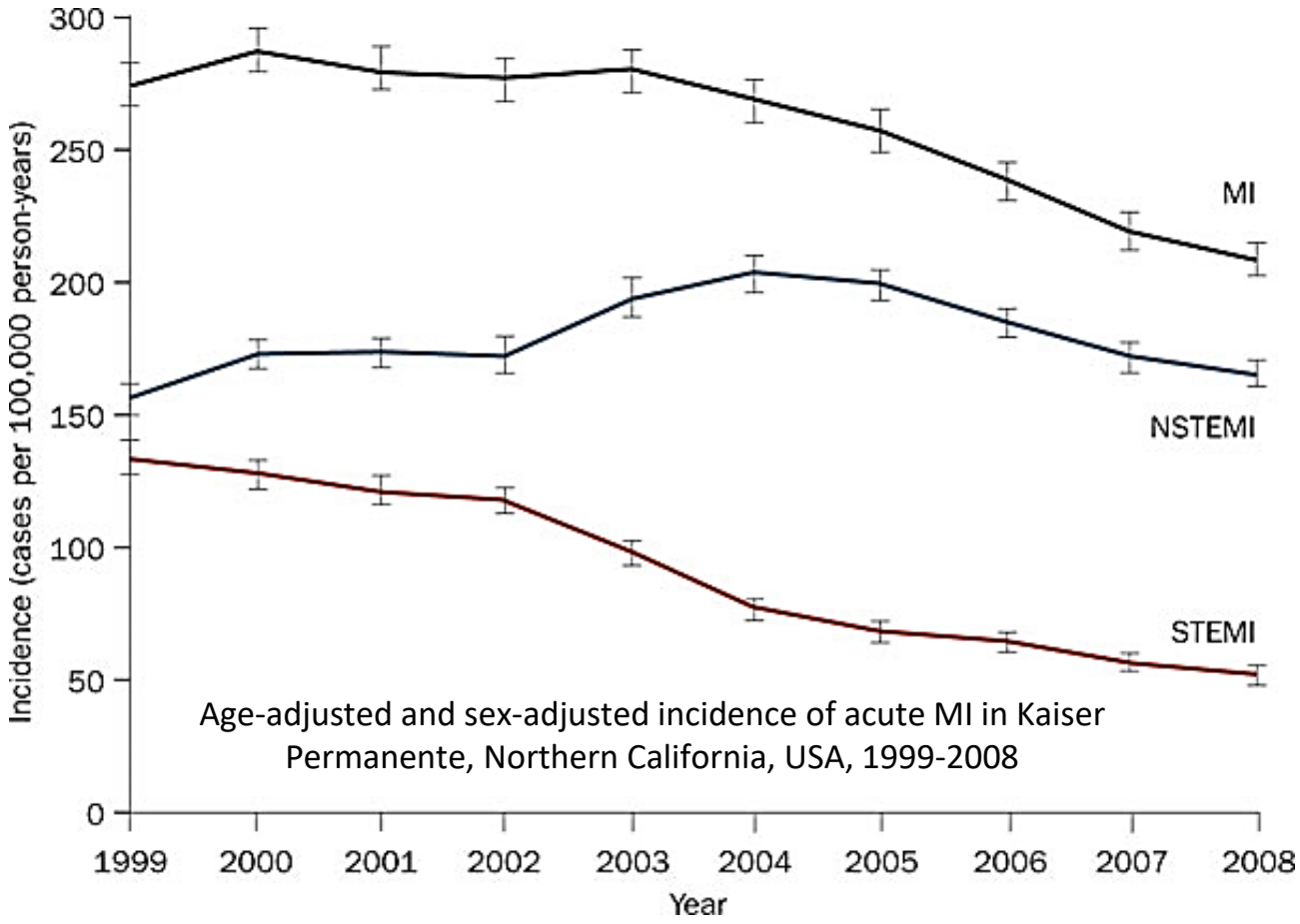
Changing Epidemiology of ACS

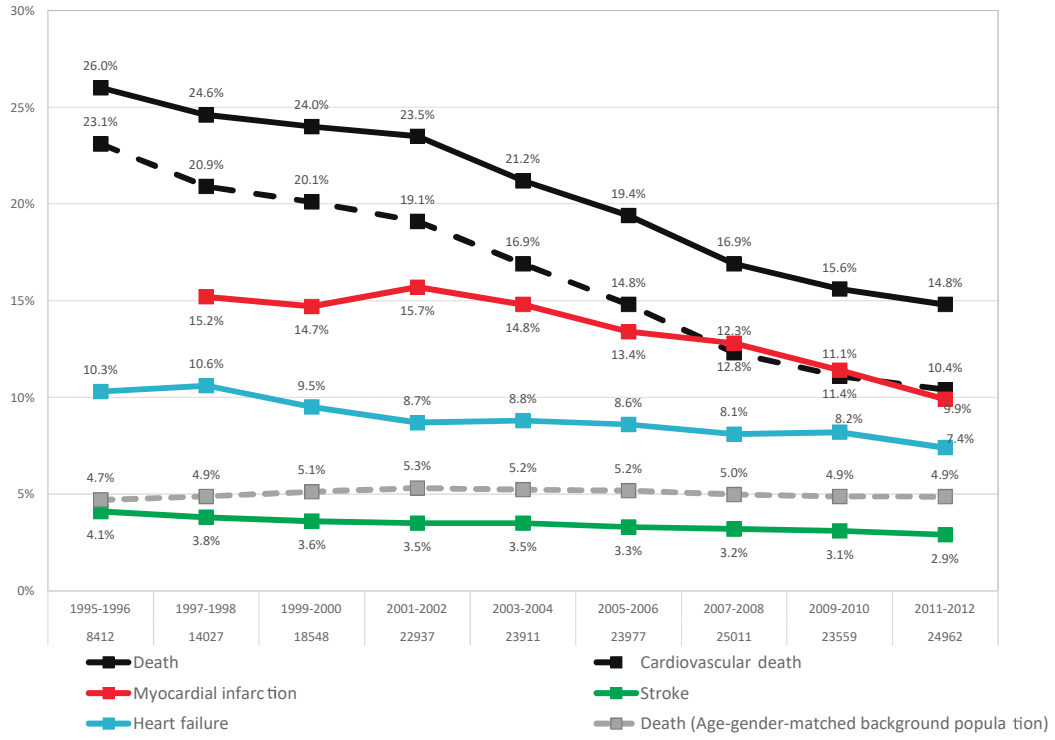


Age-adjusted and sex-adjusted incidence of acute MI in Kaiser Permanente, Northern California, USA, 1999-2008

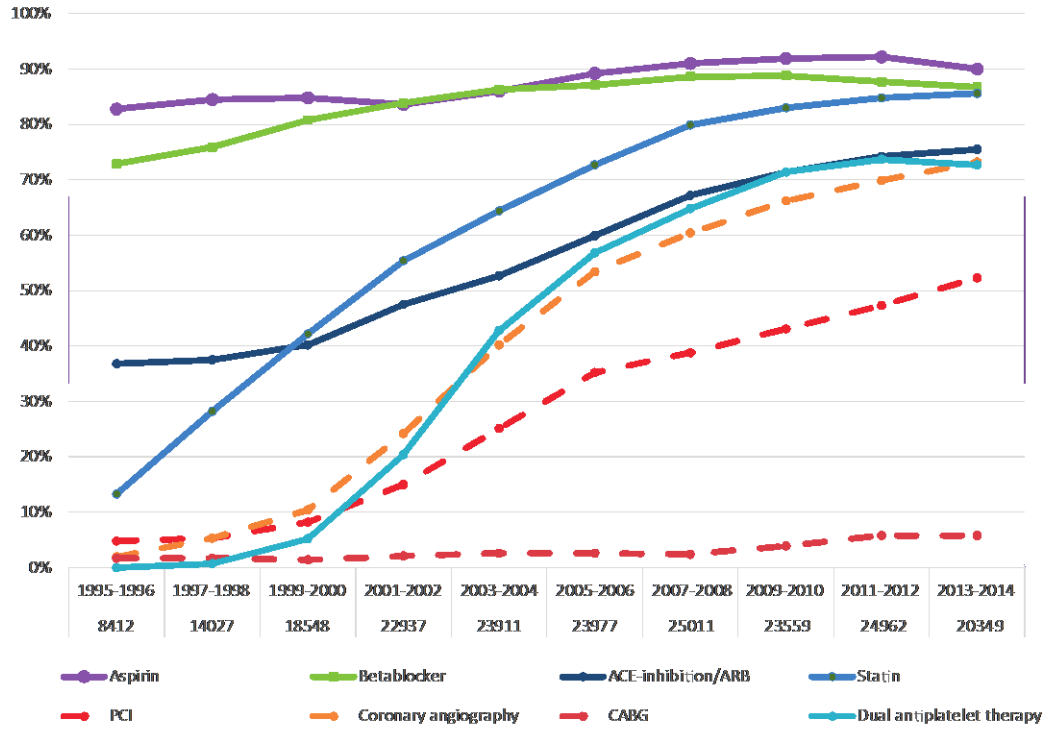
Yeh RW, et al. *N Engl J Med.* 2010.

Outcomes in NSTEMI

Frequency of events in the first year after admission for NSTEMI



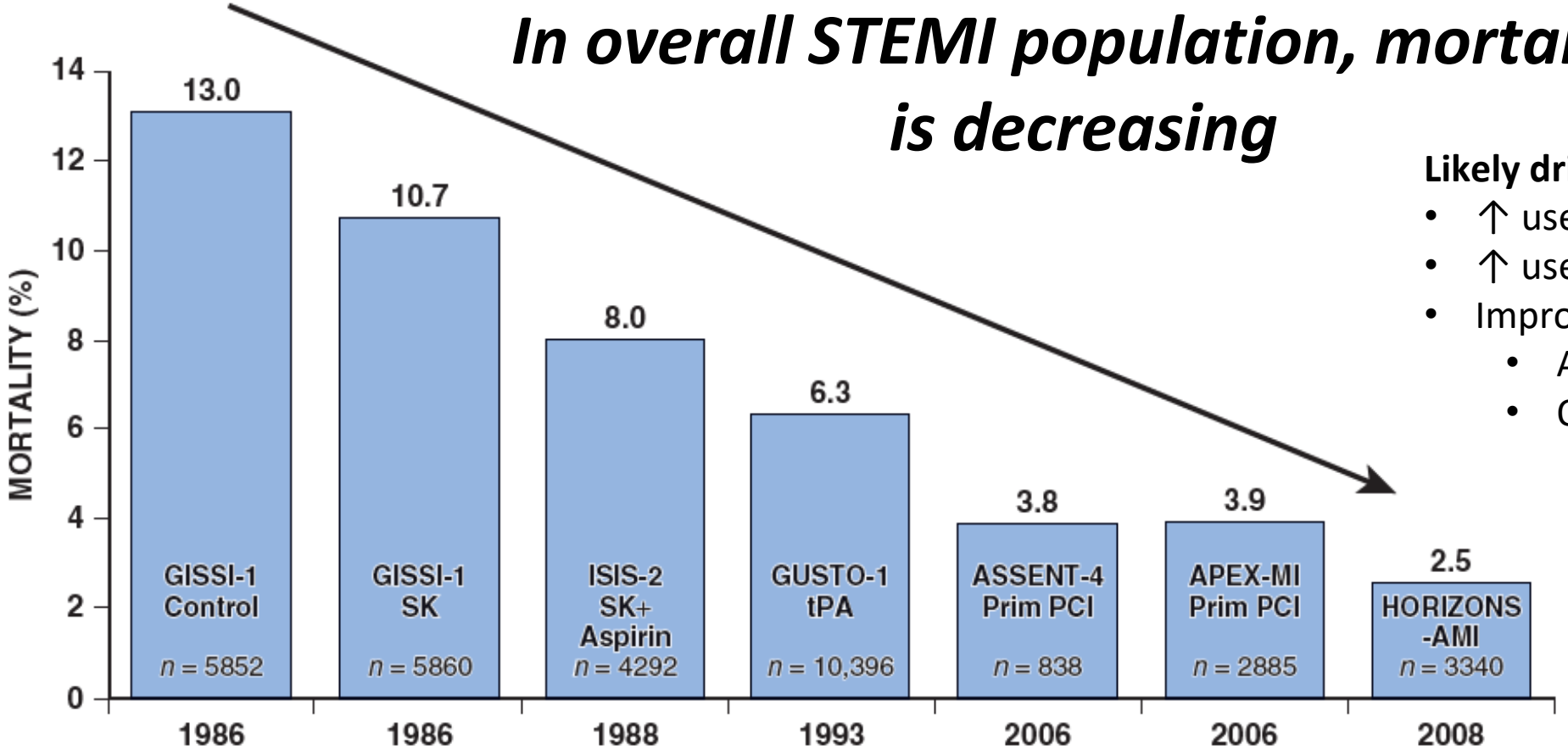
Implementation of in-hospital interventions and discharge medications



European Heart Journal (2018) **39**, 3766–3776

Case Fatality Rate in STEMI

In overall STEMI population, mortality is decreasing



Likely drivers:

- ↑ use of reperfusion
- ↑ use of pPCI
- Improvements in medical therapy
  - Antithrombotics
  - Other secondary prevention

Braunwald's Heart Disease, adapted from EHJ 2014;35:2510-2515.

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STEMI: Diagnosis, Risk Stratification, and Revascularization

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Case

65-year-old woman

- Type I diabetes
- Kidney/pancreas transplant in 1999
- Repeat kidney transplant 2010
- Progressive renal insufficiency
- Hypertension
- HL

Presented to BWH ED with rest chest pain that started 2 hours ago

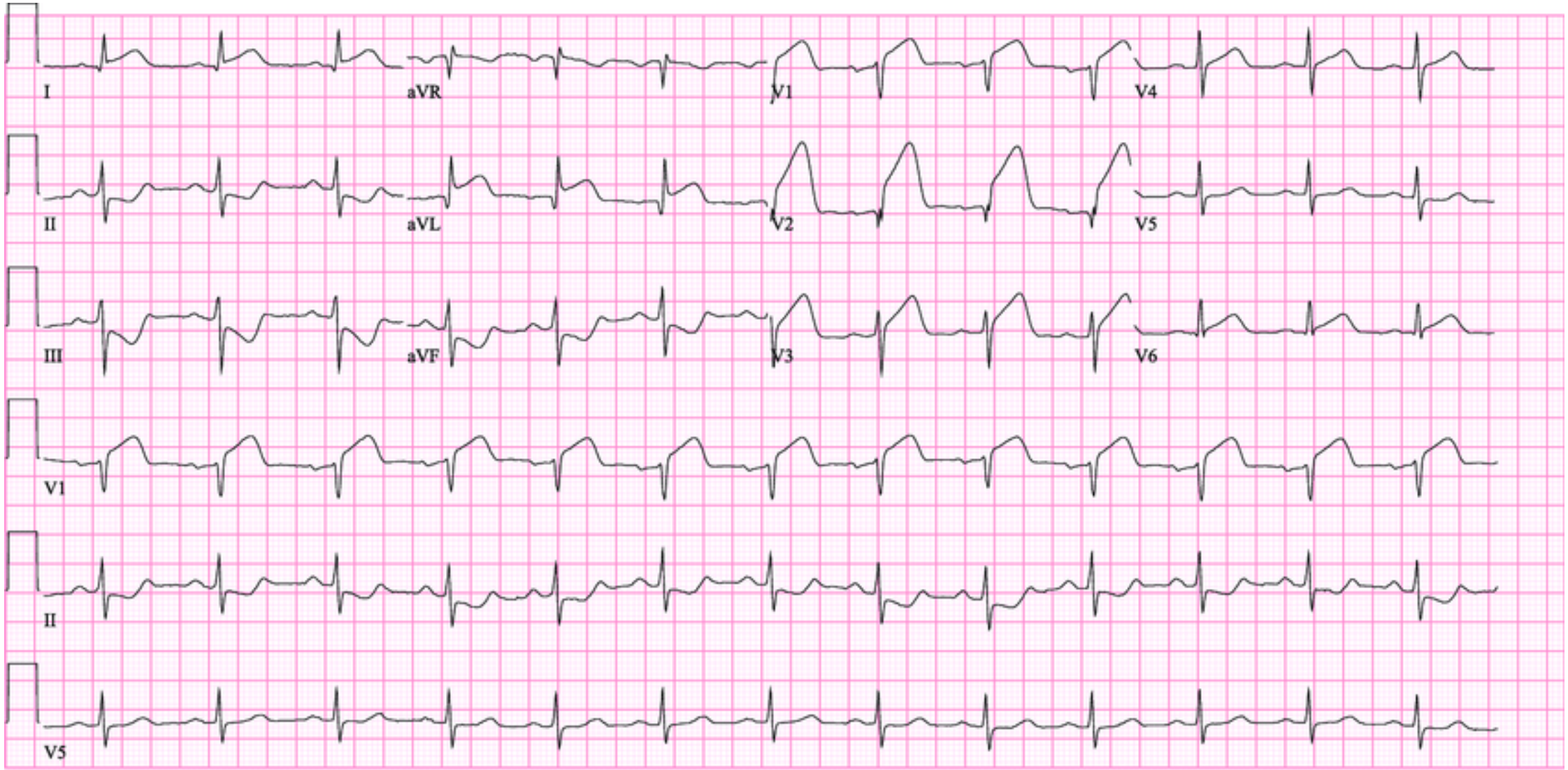
Courtesy of B. Bergmark

Case

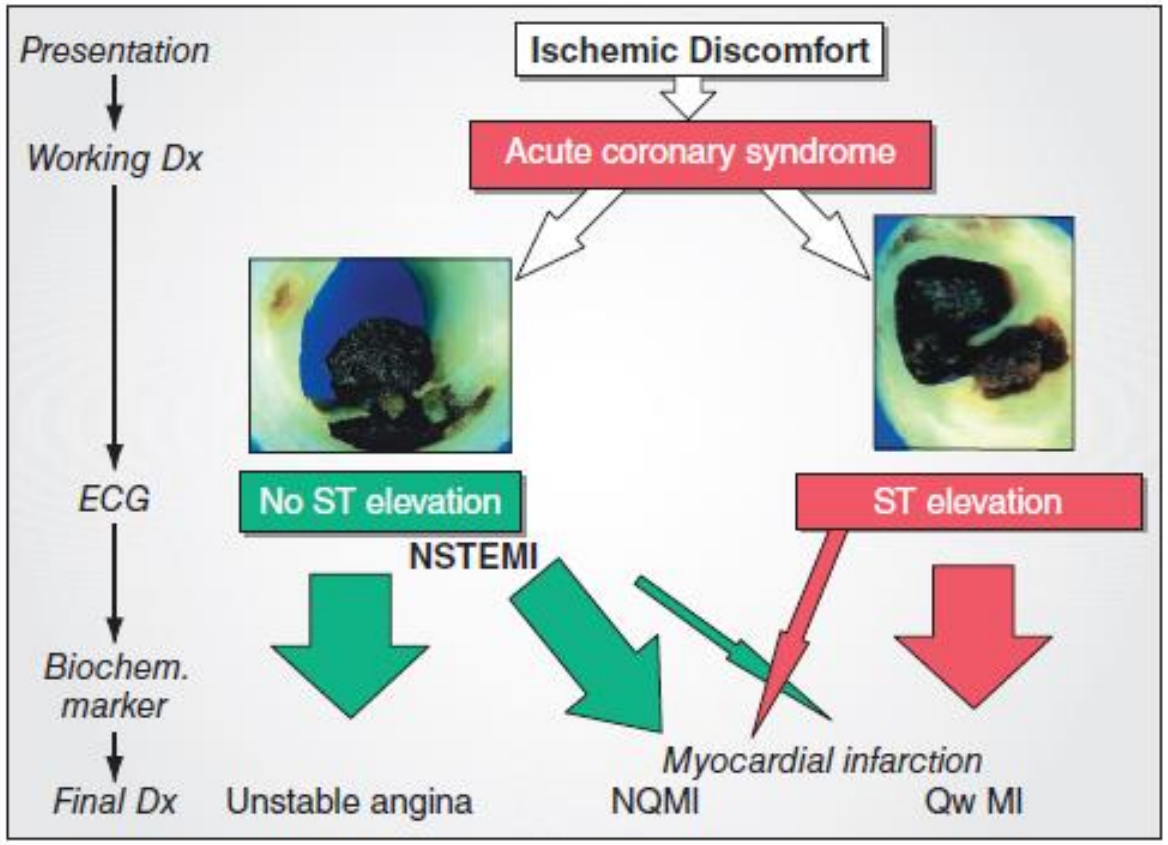
PE: 110BPM **80/50**mmHg **24**RPM **96%4LNC**

Labs:
Cr 2.47 mg/dL (baseline 1.3 mg/dL, eGFR 50)
Hs-TnT 631 ng/L
LDL 150 mg/dL
HbA1c 8%

Courtesy of B. Bergmark


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
V1
II
V5
25mm/s 10mm/mV 40Hz

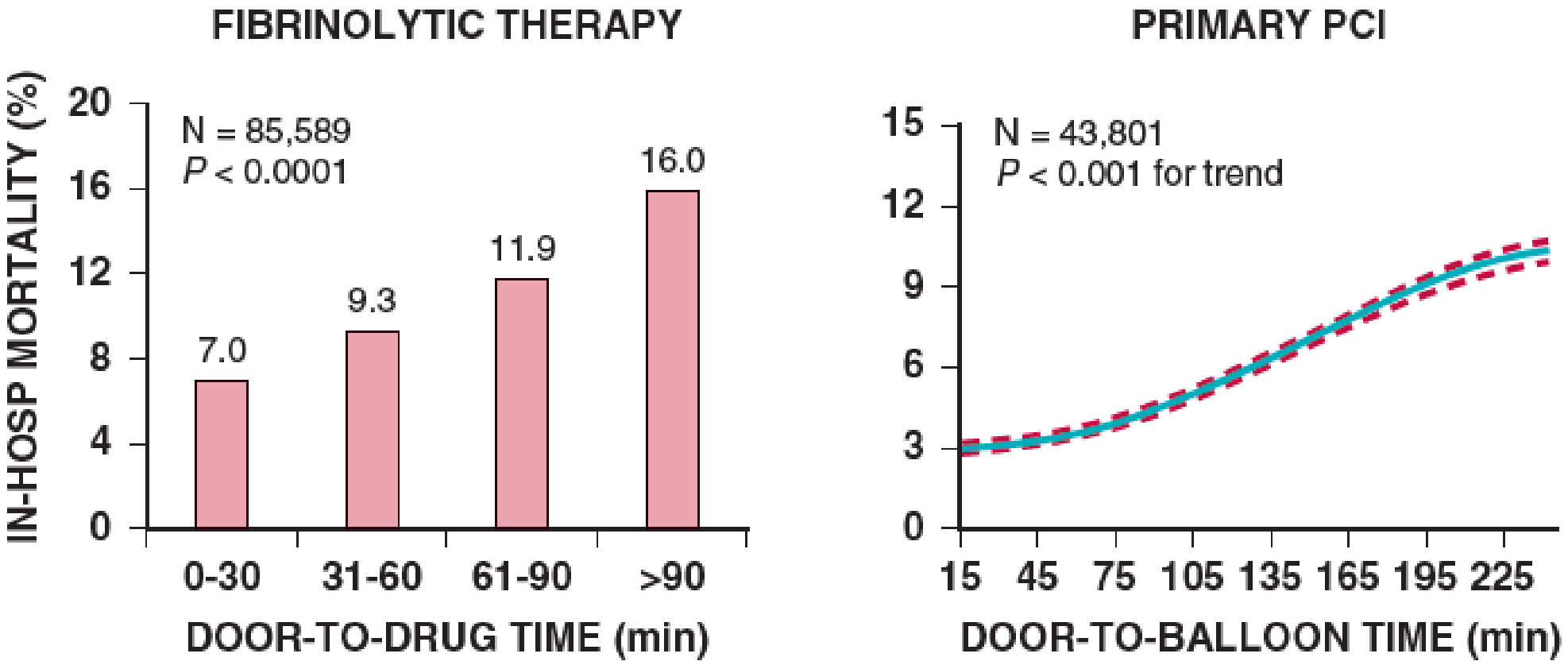
STEMI Pathophysiology: Thrombotic Occlusion



"Time is muscle" → Goal: Rapid diagnosis and Reperfusion

Davies MJ, Heart 2000;83:361; Hamm CW, Lancet 2001:358:1533

Importance of Time to Reperfusion In STEMI



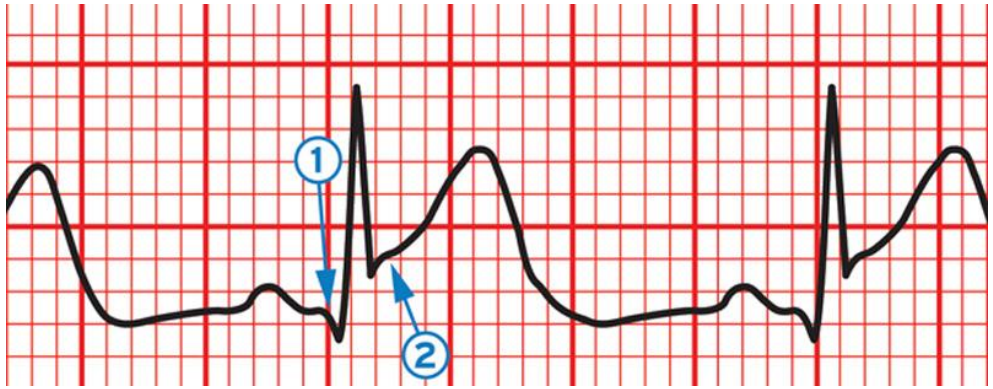
JAMA 2000;283:2941. BMJ 2009;338:1807.

STEMI Diagnosis

- Clinical syndrome of myocardial ischemia
- EKG changes (usually ST elevations)
  - EKG should be done w/in 10 minutes of FMC (even pre-hospital, if possible)

Diagnostic EKG Findings of STEMI

- New STE at J-point in 2 contiguous leads
  - ≥1 mm in most leads
  - Except in V2-V3
    - ≥2 mm in men ≥40yrs
    - ≥2.5 mm in <40 yrs
    - ≥1.5 mm in women

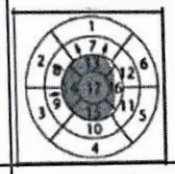
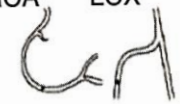


ACC/AHA STEMI Guidelines. JACC. 2013;61(4); Thygesen et al. Circulation 2018;138(20).

STEMI Diagnosis: Important Caveats

- If EKG non-diagnostic but clinical syndrome compelling, recheck EKG every 15-30 minutes
- Artery occlusion (and ST segment changes) may precede detection of myocardial necrosis by hours
  - Dx may be confirmed with evidence of myocardial necrosis, but reperfusion therapy should not be delayed to await biomarkers

EKG Findings & Localization of Territories

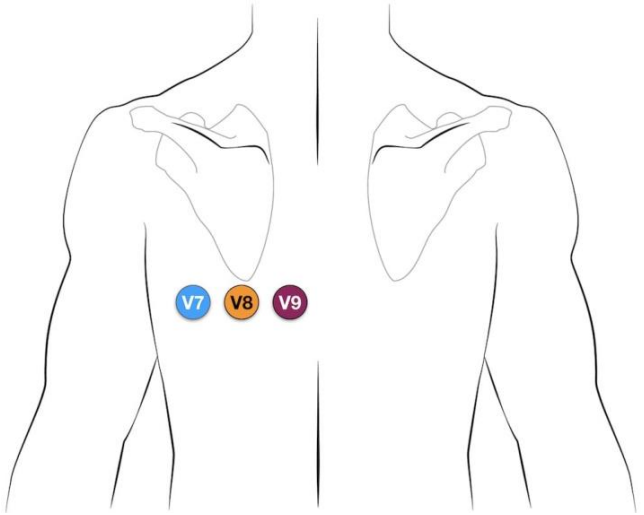
G	Septal	Apical anteroseptal	Extensive anterior	Limited anterior	Lateral	Inferior	Infero-lateral
							
Lesion location	LAD 	LAD 	LAD 	LAD 	LCX 	RCA LCX 	
ECG patterns of ST elevation or Q-waves	V1-2	V1-2 to V4-6	V1-6 occasionally aVL and I	aVl and I, V2-3	I and aVL, V5-6 Reciprocal changes in V1-2	II, III*, aVF	II, III*, aVF, I and aVL, V5-6 Reciprocal changes in V1-2

* STE in III>II suggests RCA vs. LCx

Braunwald's Heart Disease, modified from Circ 2006;114:1755.

EKG Sensitivity for STEMI

- Standard 12-lead EKG not 100% sensitive
  - >95% for LAD
  - >90% for RCA
  - ~60% for LCx -> electrically silent total occlusion
    - Class IIa recommendation for posterior EKG to identify LCx occlusion



Atypical EKG Patterns

Bundle Branch Block

Criteria (Sgarbossa) that can be used to improve the diagnostic accuracy of STEMI in LBBB

- Concordant ST-segment elevation ≥ 1mm in leads with a positive QRS complex
- Concordant ST-segment elevation ≥ 1mm in V_1-V_3
- Discordant ST-segment elevation ≥ 5mm in leads with a negative QRS complex

The presence of RBBB may confound the diagnosis of STEMI

Ventricular Paced Rhythm

During RV pacing, the ECG also shows LBBB and the above rules also apply for the diagnosis of myocardial infarction during pacing; however, they are less specific.

Isolated Posterior Myocardial Infarction

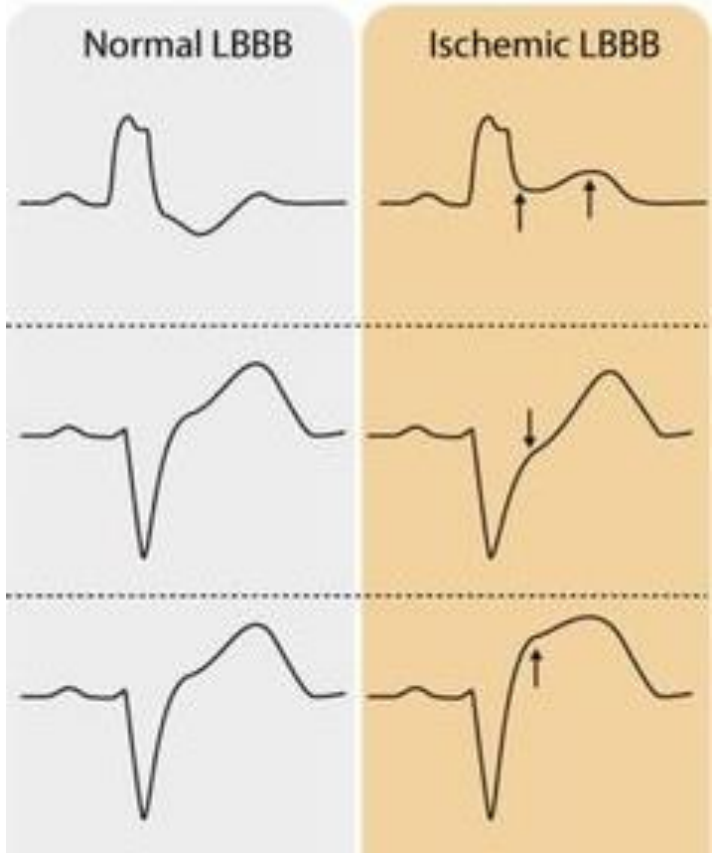
Isolated ST depression ≥ 0.5mm in leads V_1-V_3 and ST-segment elevation (≥ 0.5mm) in posterior chest wall leads V_7-V_9

Ischemia Due to Left Main Coronary Artery Occlusion or Multivessel Disease

ST depression ≥ 1mm in eight or more surface leads, coupled with ST-segment elevation in aVR and/or V_1, suggests left main-, or left main equivalent-coronary obstruction, or severe three vessel ischemia

Sgarbossa's Criteria

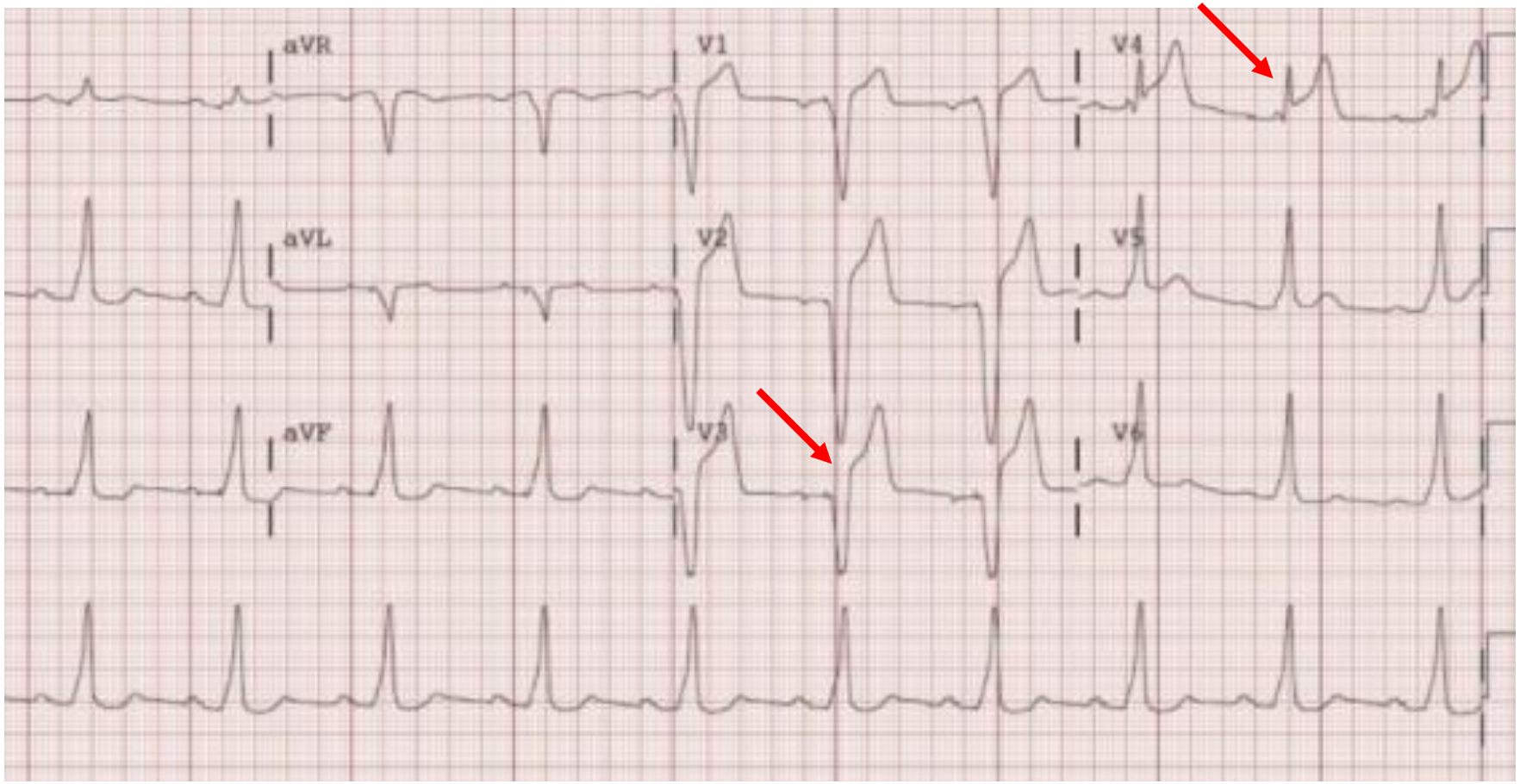
Findings	***Points***
STE>=1mm in positive QRS (V4-6, aVL, I)	***5***
STD>=1mm w/ negative QRS (V1-3)	***3***
STE>=5mm w/ negative QRS (V1-3)	***2***



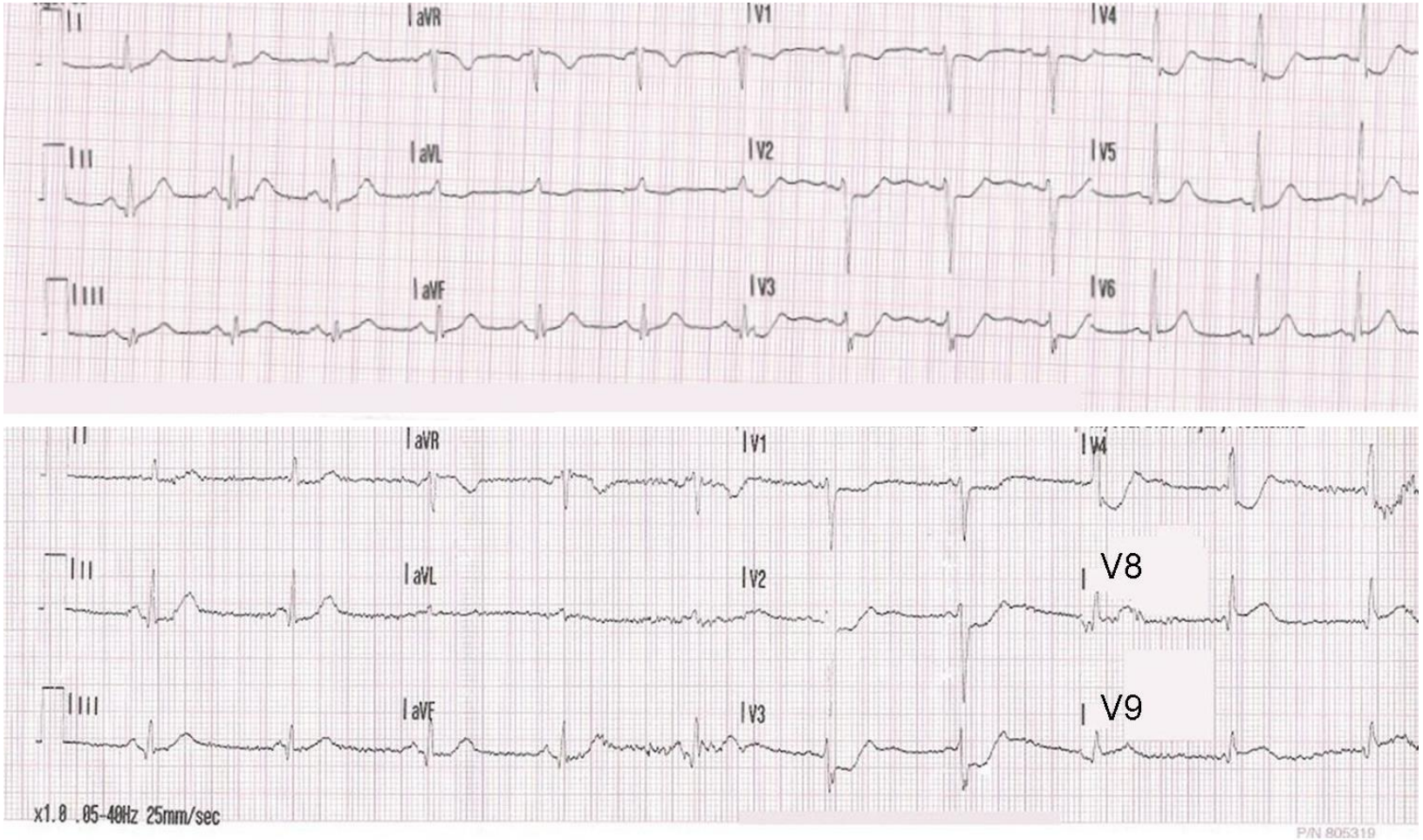
≥3 points = 98% probability of STEMI

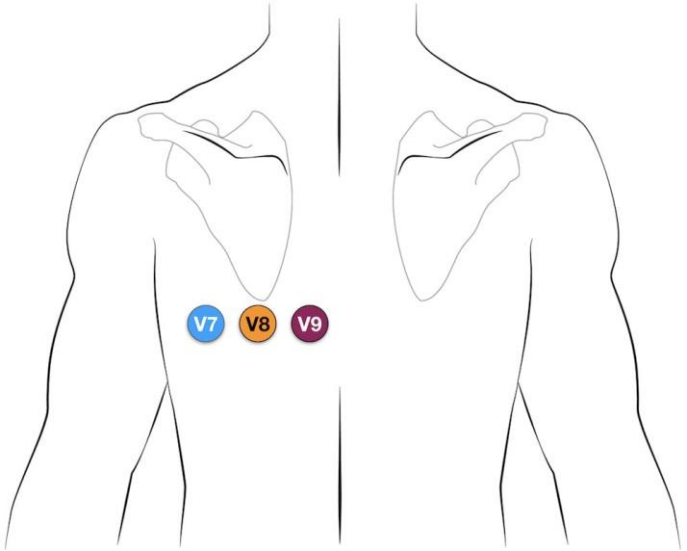
NEJM. 1996. 334(8):481-7

STEMI with LBBB



Isolated Posterior MI





https://www.emsworld.com/article/12088564/acute-isolated-posterior-stemi

CONSIDERATIONS BY MI LOCATIONS

Anterior MI

- Cardiogenic shock –
  - In general, complicates ~5-10% of STEMI
  - Most commonly seen with large anterior MI
- Mechanical complications
  - Free wall rupture
  - LV aneurysm
  - Papillary muscle rupture (anterolateral pap muscle)
  - Apical VSD
- LV thrombus

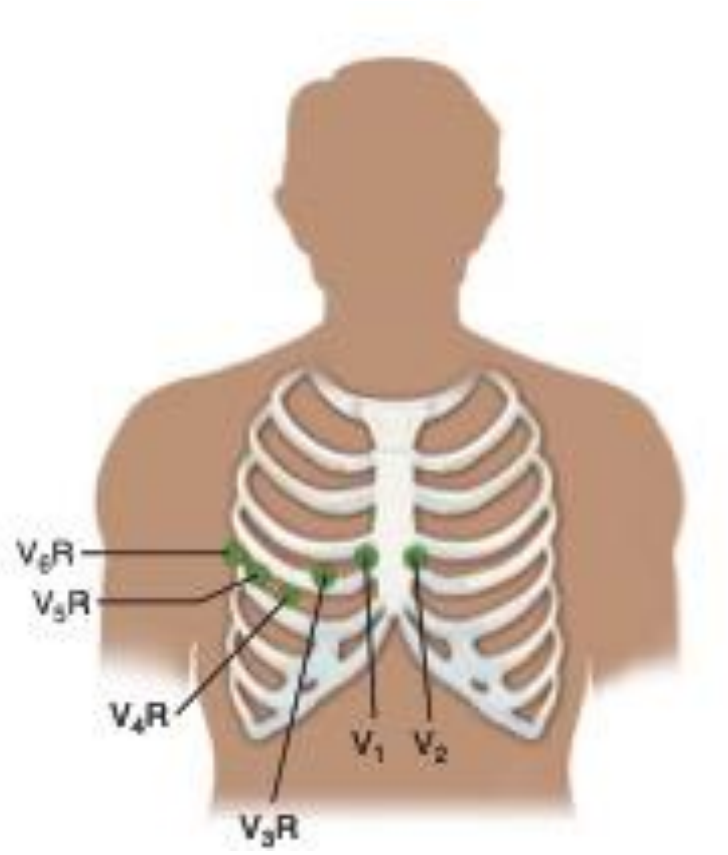
Inferior Infarct

- Rhythm disturbances
  - Sinus bradycardia common (incr vagal tone)
    - Usually self-limited
    - If drives HD instability-> atropine +/- pacing
  - High-degree AVB/CHB (~4%)
- Mechanical complications
  - Inferior-basal VSD (worse prognosis than apical VSD)
  - Papillary muscle rupture (single vascular supply to posteromedial papillary muscle)
- Posterior or RV infarction

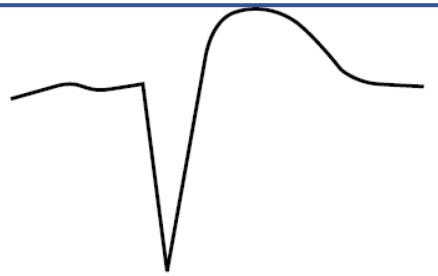
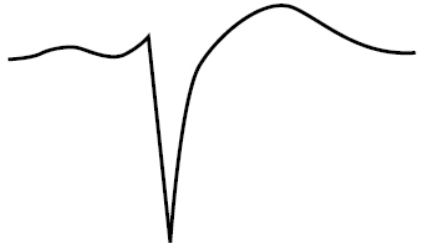
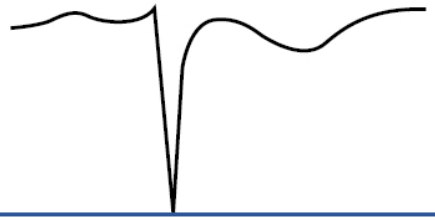
RV Infarction

- Occurs in ~1/3 of inferior LV infarctions
- Classic clinical triad of hypotension, clear lungs, elevated JVP
- Various possible findings:
  - Elevations of right-sided pressures (CVP, RV end diastolic pressures)
  - Kussmaul sign – Increased CVP/JVP w/ inspiration (non-compliant RV)
  - +/- signs of low output on right
    - Low RVSP
    - Low RV pulse pressure
    - Low pulmonary artery pulsatility index (PASP-PADP/RA) (eg < 1)
    - Low cardiac output with nl/low PCWP

Right-Sided EKG



V_4R

Proximal occlusion of right coronary artery		ST-segment elevation ≥1mm and positive T wave
Distal occlusion of right coronary artery		No ST-segment elevation and positive T wave
Occlusion of circumflex coronary artery		ST-segment depression ≥1mm and negative T wave

Management of RV Infarction

- Maintain RV preload
  - Avoid nitrates & diuretics
- Lower RV afterload
- Inotropic +/- mechanical support
- Reperfusion
- Restore AV synchrony

Focused History & Exam

- Presence, nature and duration of ischemic symptoms
- Screen for important contributors (eg, cocaine use) or mimics (eg aortic dissection, PE, pericarditis)
- Evidence of complications (eg, heart failure, mechanical complications)
- Targeted history for possible contraindications to pPCI or fibrinolysis
  - Severe contrast allergy
  - Active or recent bleeding

Initial Laboratory Testing

- Cardiac biomarkers (preferably troponin)
- Serum electrolytes, creatinine, hematocrit, platelet count, coagulation parameters, glucose
- Eventually labs for secondary prevention:
  - Lipid panel, lipoprotein(a)
  - Hemoglobin A1c

Early Markers of Risk

- Anterior (vs inferior)
- High sum total of ST elevation
- Anterior ST depressions in inferior STEMI
  - Posterior extension or LAD ischemia
- ST elevation in V4R in inferior STEMI
  - RV MI
- Advanced heart block (Mobitz type 2 or 3rd degree)
- RBBB in anterior MI
  - Large MI

STEMI Risk Score: TIMI Risk Index

- Age, HR, SBP
- 20-fold gradient of risk for mortality

Risk Index	Risk Group	Risk of Death		
		24 H	In-hosp	30 D
≤12.5	1	0.2	0.6	0.8
>12.5-17.5	2	0.4	1.5	1.9
>17.5-22.5	3	1.0	3.1	3.3
>22.5-30	4	2.4	6.5	7.3
>30	5	6.9	15.8	17.4

1) Calculate Risk Index: $\frac{HR \times (Age/10)^2}{SBP}$

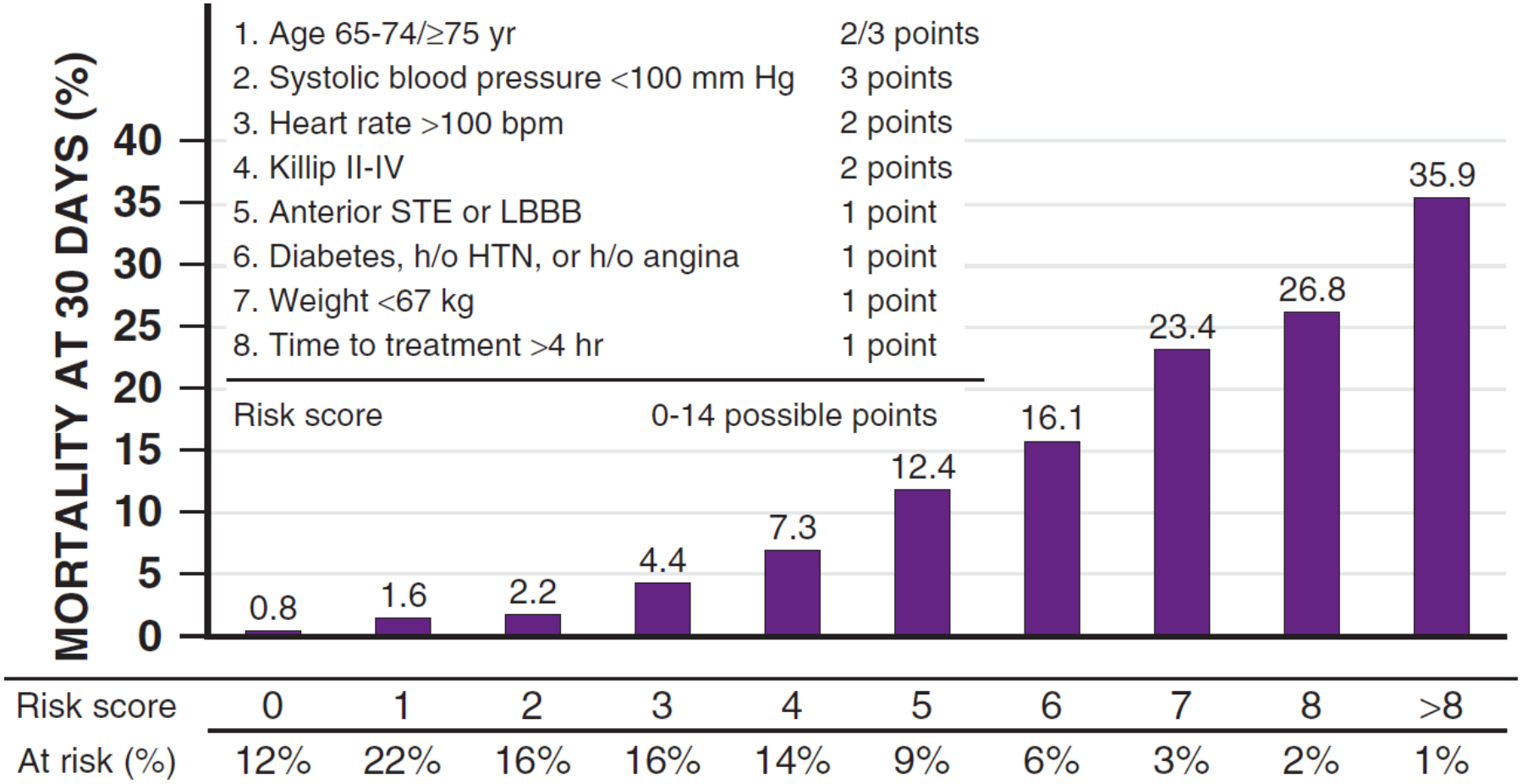
2) Assign Risk Group

3) Mortality Estimate (Data from InTIME II)

HR in bpm; Age in years; SBP in mm Hg

Lancet 2001;358:1571-1575.

STEMI Risk Score: TIMI Risk Score



JAMA 2001;286:1356-1359

ACS Risk Score: GRACE Risk Score

Medical History

	Points
① Age in Years	
≤29	0
30-39	0
40-49	18
50-59	36
60-69	55
70-79	73
80-89	91
≥90	100
② History of Congestive Heart Failure	24
③ History of Myocardial Infarction	12

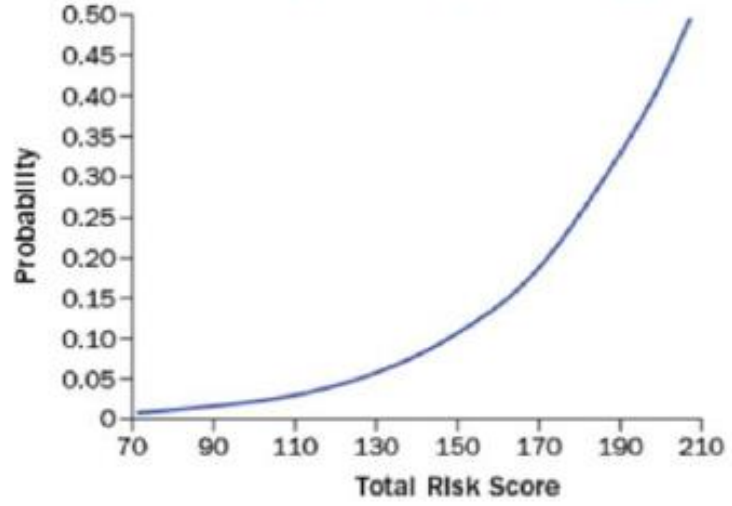
Findings at Initial Hospital Presentation

	Points
④ Resting Heart Rate, beats/min	
≤49.9	0
50-69.9	3
70-89.9	9
90-109.9	14
110-149.9	23
150-199.9	35
≥200	43
⑤ Systolic Blood Pressure, mm Hg	
≤79.9	24
80-99.9	22
100-119.9	18
120-139.9	14
140-159.9	10
160-199.9	4
≥200	0
	1
⑥ ST-Segment Depression	11

Findings During Hospitalization

	Points
⑦ Initial Serum Creatinine, mg/dL	
0-0.39	1
0.4-0.79	3
0.8-1.19	5
1.2-1.59	7
1.6-1.99	9
2-3.99	15
≥4	20
⑧ Elevated Cardiac Enzymes	15
⑨ No In-Hospital Percutaneous Coronary Intervention	14

Predicted All-Cause Mortality From Hospital Discharge to 6 Months



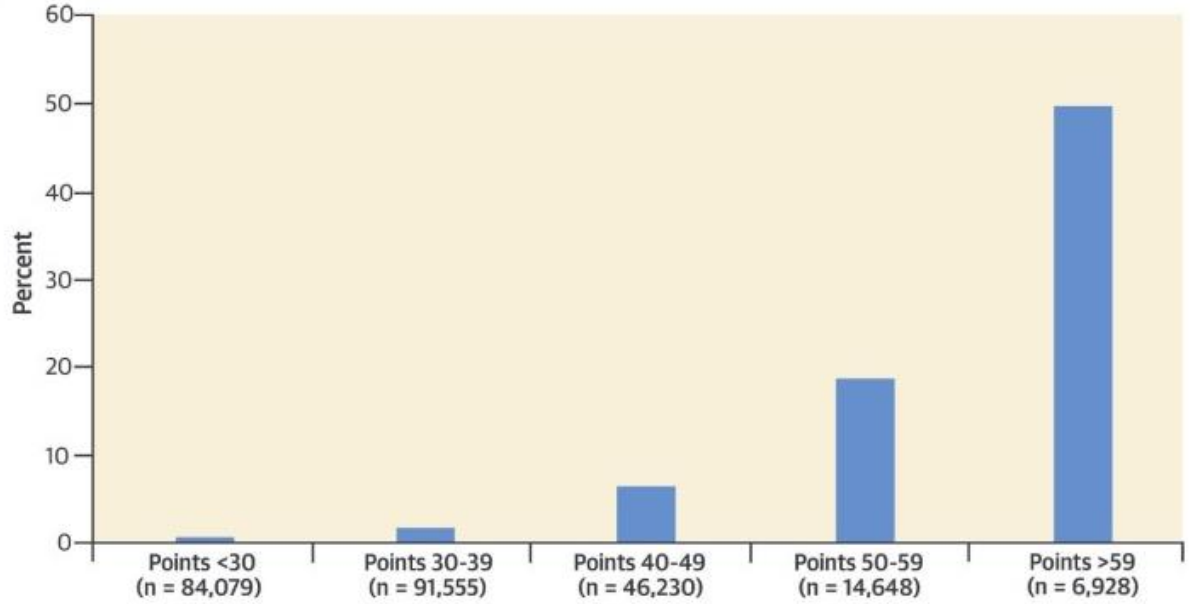
JAMA 2004;291:2727-2733

ACS Risk Score: ACTION GWTG

A. Risk Score Calculator

Age	Pts	SBP	Pts	CrCl	Pts	Cardiac Arrest	Pts	Shock	Pts	Heart Rate	Pts	Heart Failure	Pts	STEMI	Pts	Troponin	Pts
<40	0	>200	0	≥90	0	No	0	No	0	≤40	0	No	0	No	0	<10	0
40-49	3	181-200	3	60-<90	4	Yes	14	Yes	13	41-60	1	Yes	5	Yes	5	10-<20	1
50-59	7	171-180	5							61-70	2					20-<30	2
		161-170	7	45-<60	8					71-80	3					≥30	3
60-69	10	151-160	9							81-100	4						
		131-150	11	30-<45	11					101-110	5						
70-79	13	121-130	13							111-130	7						
				<30 or Dialysis	15					131-150	8						
80-89	17	111-120	15							>150	9						
		91-110	16														
≥90	20	≤90	19														

In-hospital Mortality



JACC 2016;68:626-635.

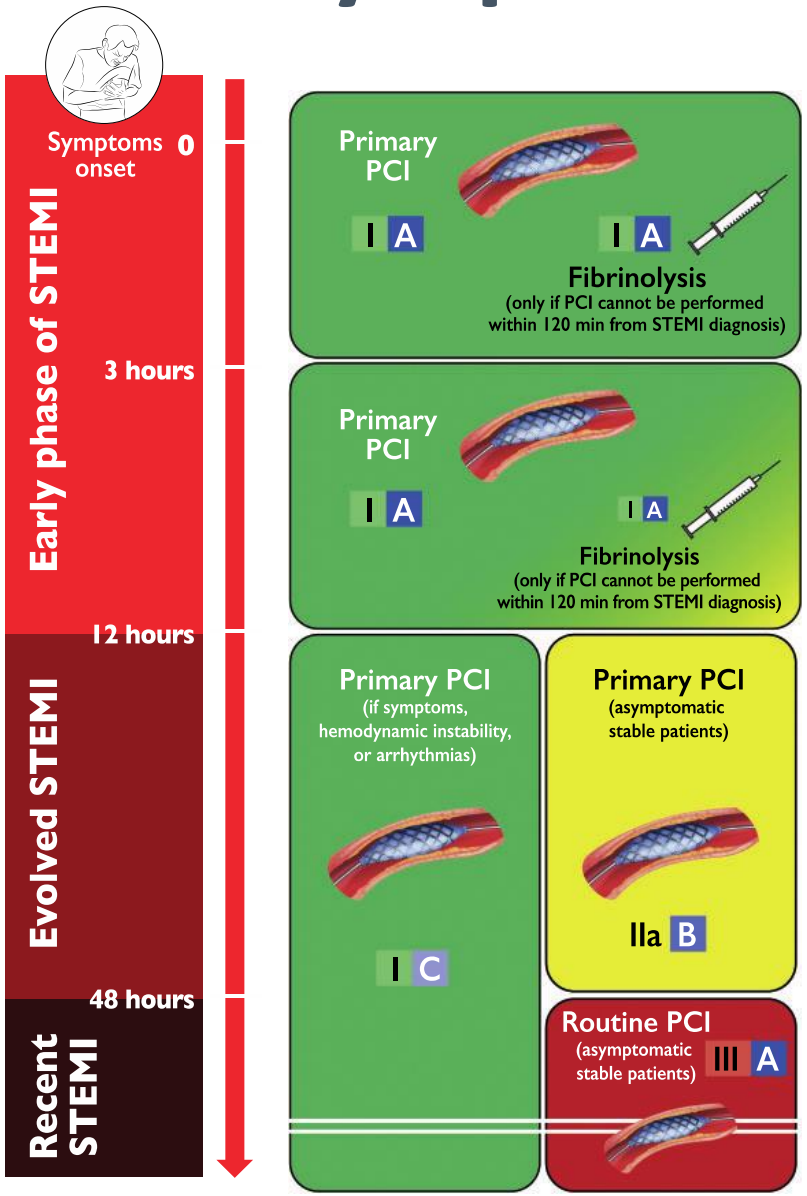
Considerations For Reperfusion

- Time from symptom onset
  - Whether to pursue revascularization
  - How to revascularize (pPCI vs fibrinolysis)
- Time to initiate invasive strategy
  - How to revascularize (pPCI vs fibrinolysis)
- Candidacy for fibrinolysis

Considerations For Reperfusion

- Time from symptom onset
  - Whether to pursue revascularization
  - How to revascularize (pPCI vs fibrinolysis)
- Time to initiate invasive strategy
  - How to revascularize (pPCI vs fibrinolysis)
- Candidacy for fibrinolysis

Time From Symptom Onset



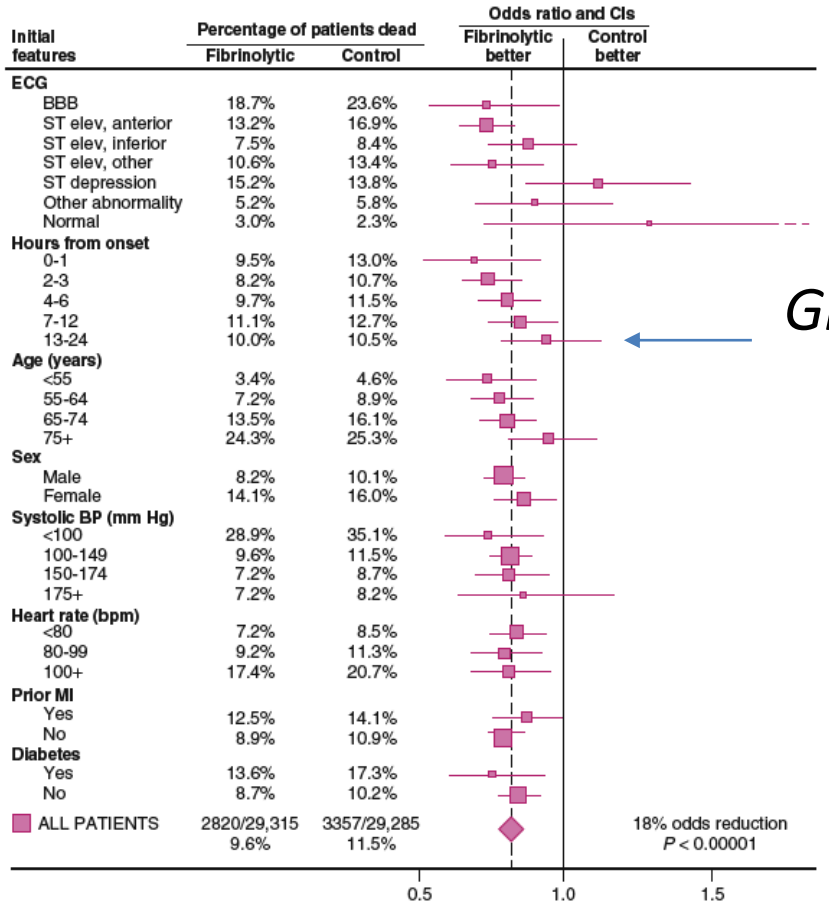
Ibanez et al. ESC 2017 STEMI Guidelines. EHJ 2018(39):119-177

Considerations For Reperfusion

- Time from symptom onset
  - Whether to pursue revascularization
  - How to revascularize (pPCI vs fibrinolysis)
- Time to initiate invasive strategy
  - How to revascularize (pPCI vs fibrinolysis)
- Candidacy for fibrinolysis

Benefit of Fibrinolysis in STEMI

18% reduction in odds of death at 35 days

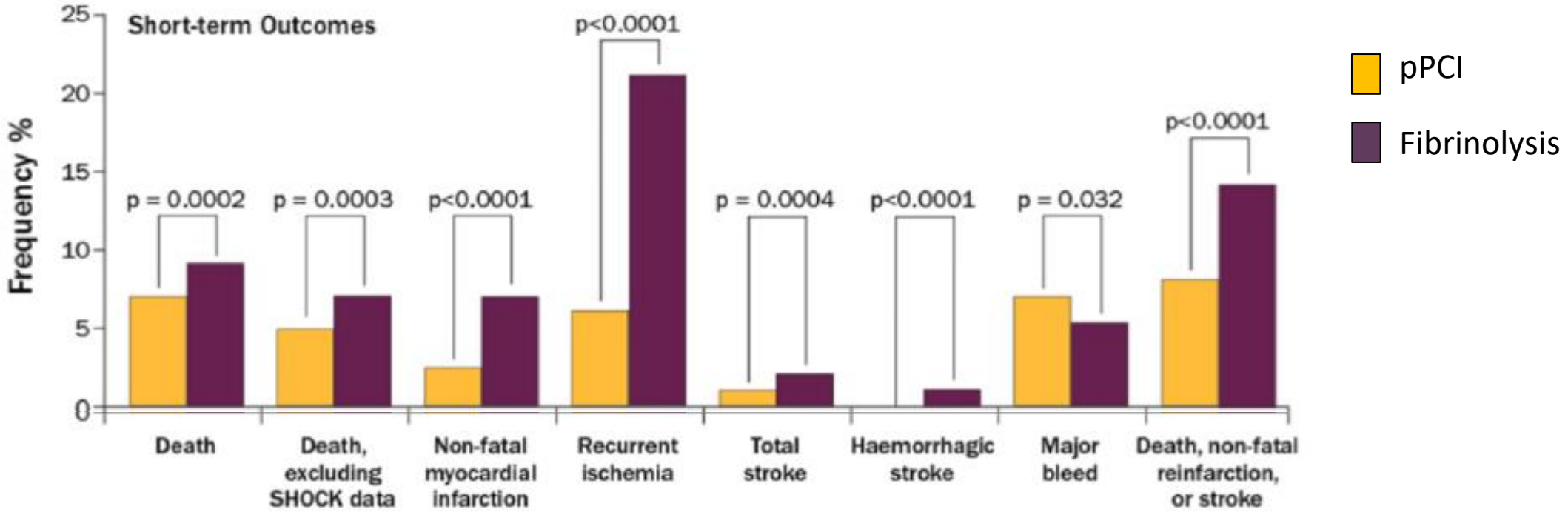


Greater benefit in early period

Lancet 1994;343:311.

Primary PCI vs Fibrinolysis in STEMI

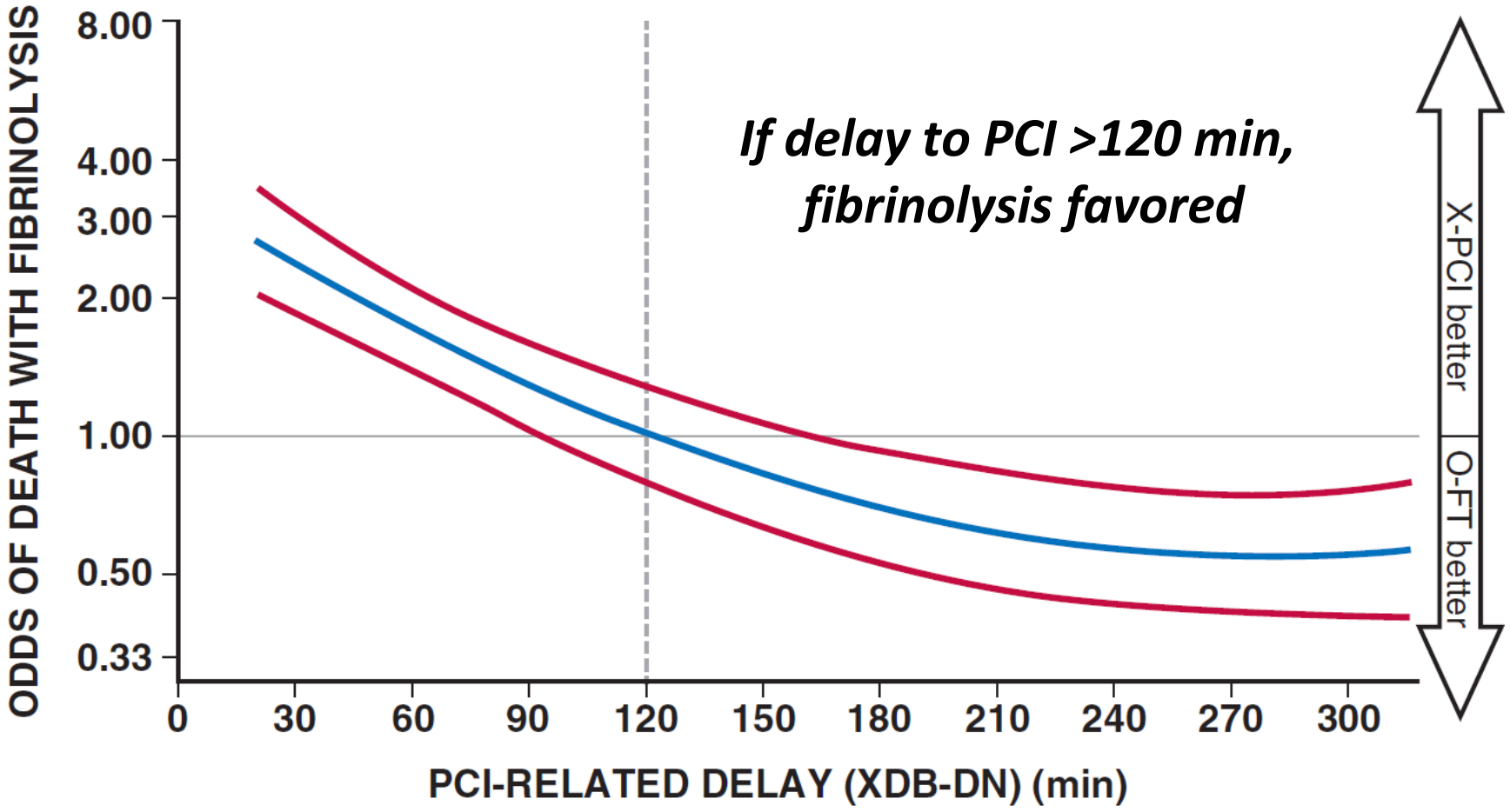
Review of 23 Randomized Trials



Outcomes are generally better with primary PCI

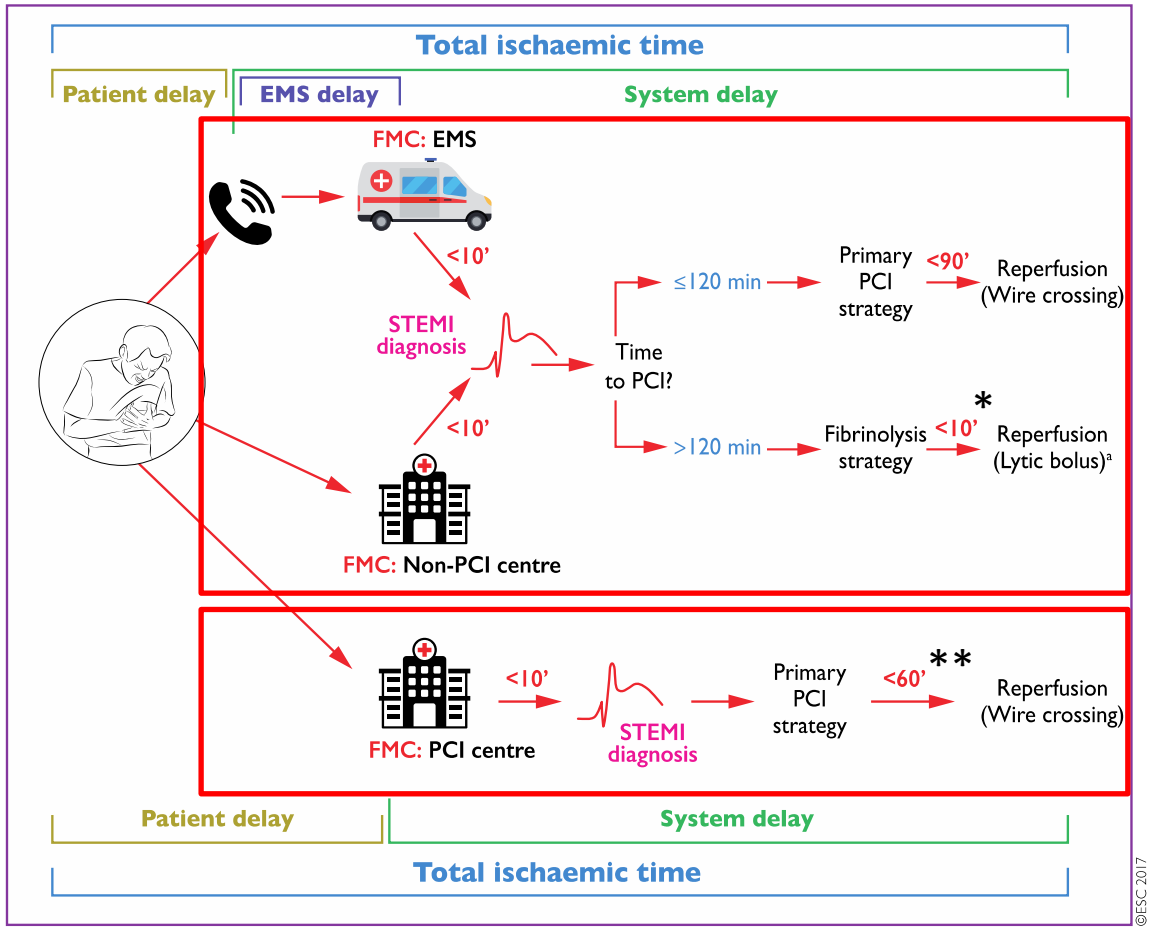
Lancet 2003;361:13-20.

Inflection Point for Delay to pPCI vs Fibrinolysis



Pinto et al. Circulation. 2011;124(23):2512-2521

Triage for Reperfusion



<u>If delay to to pPCI of >120 min, fibrinolysis unless</u>

- Shock or acute severe HF (AHA/ACC Class 1, LOE: B)
- Contraindication to fibrinolytics
- Late presentation (eg., >12 hrs, can consider fibrinolysis for 12-24 hrs if no PCI option)

*ACC/AHA: FMC to bolus < 30 min

**ACC/AHA: FMC to device < 90 min

Ibanez et al. ESC 2017 STEMI Guidelines. EHJ 2018(39):119-177; ACC/AHA STEMI Guidelines. JACC. 2013;61(4).

Contraindications to Fibrinolysis

Absolute	Relative Contraindications
Any prior ICH	History of chronic, severe, poorly controlled HTN
Known structural cerebral vascular lesion	Uncontrolled HTN on presentation (SBP > 180, DBP > 110)
Known intracranial malignant neoplasm	Traumatic or prolonged CPR (>10 min)
Ischemic stroke < 3 months	Major surgery < 3 weeks
Active bleeding	Recent internal bleeding (2-4 weeks)
Significant closed-head or facial trauma < 3 months	Noncompressible vascular access
	Pregnancy
	Active peptic ulcer
	Anticoagulated patients

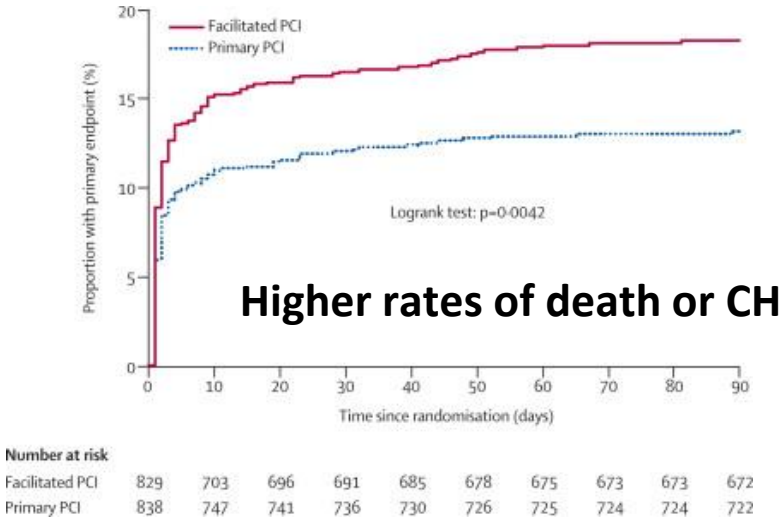
ACC/AHA STEMI Guidelines. JACC. 2013;61(4).

Facilitated PCI

ASSENT-4 (N=1667)

TNK then PCI w/in 1-3 hrs vs PPCI

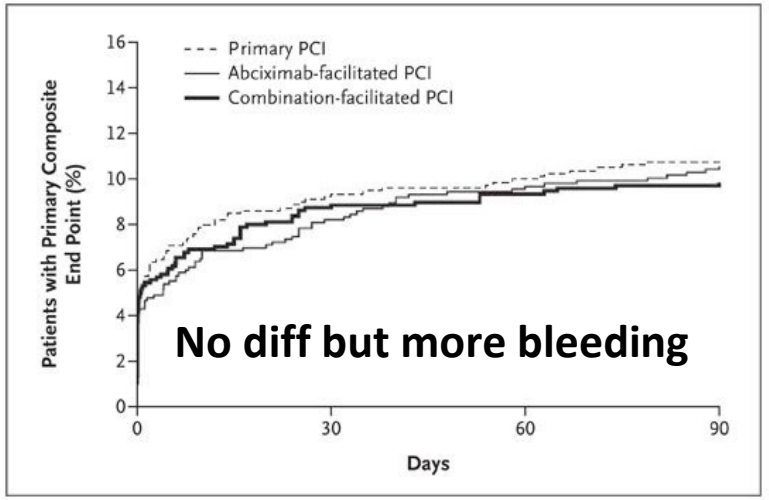
Death or CHF



Higher rates of death or CHF

FINESSE (N=2452)

Death, VF, CS, CHF



No diff but more bleeding

Worse outcomes with facilitated PCI

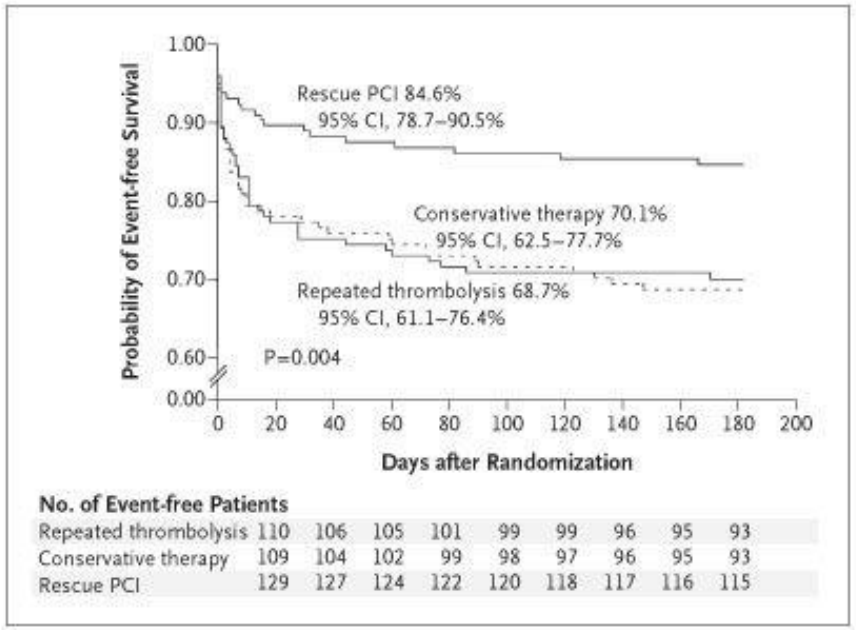
Lancet 2006;367(9510):569. N Engl J Med 2008;358:2205-2217.

Rescue PCI

REACT (N=427)

Pts with <50% STE resolution w/in 90 min lysis

Death, MI, HF, stroke

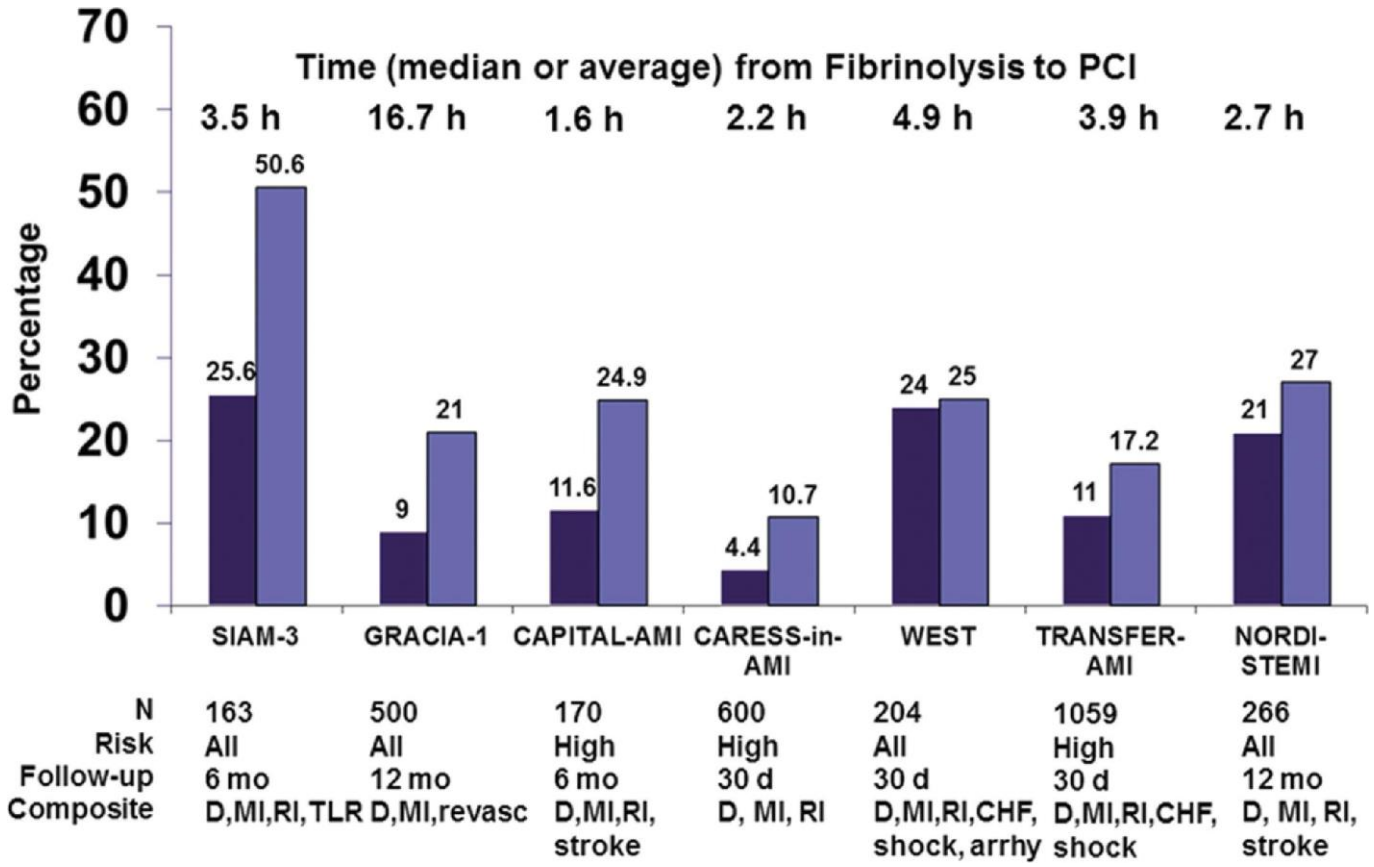


Rescue PCI improves mortality over non-invasive strategies

N Engl J Med 2005; 353:2758-2768

Pharmaco-invasive: Timing of Angiography After Fibrinolysis

- *Routine early angiography*
- *Ischemia-driven or delayed angiography*



Routine early angiography preferred over delayed approach

ACC/AHA STEMI Guidelines. JACC. 2013;61(4).

Indications for Transfer for Angiography After Fibrinolytic Therapy

		COR	LOE
Rescue PCI	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
Pharmaco-Invasive	As part of an invasive strategy in stable* patients with PCI between 3 and 24 h after successful fibrinolysis	IIa	B

Rescue PCI

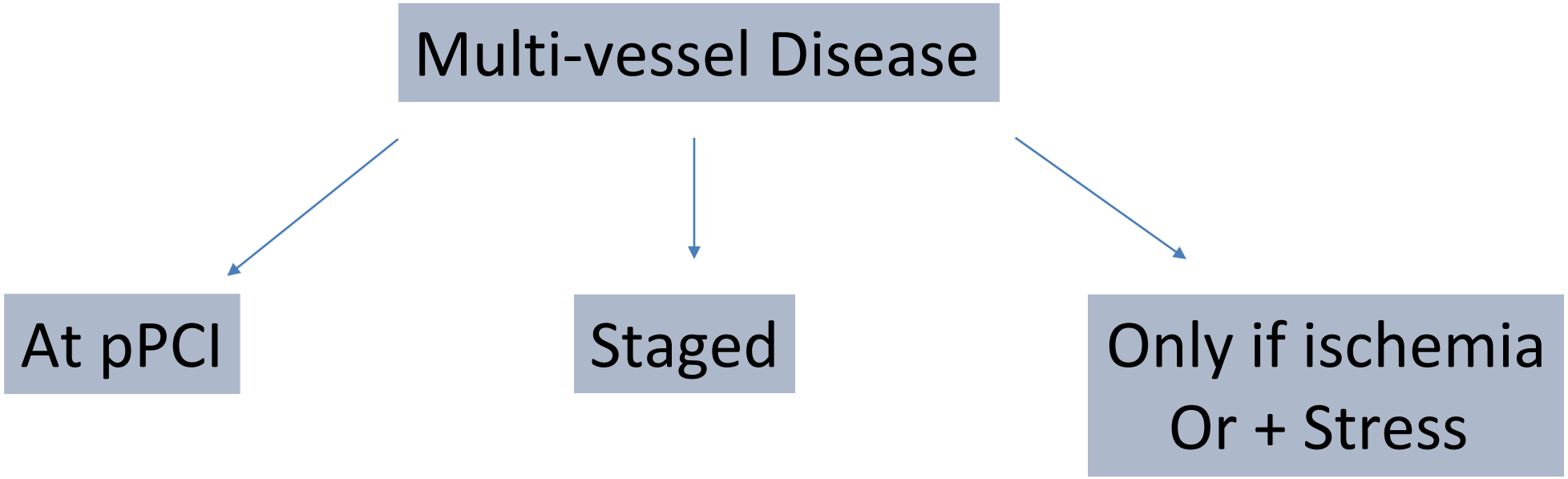
- <50% resolution in 90 min
- Persistent symptoms
- HD or electrical instability

Pharmaco-Invasive for Clinically Stable

- Absence of low output, hypotension, tachycardia, shock, high grade ventricular block or symptomatic SVT, spontaneous recurrent ischemia

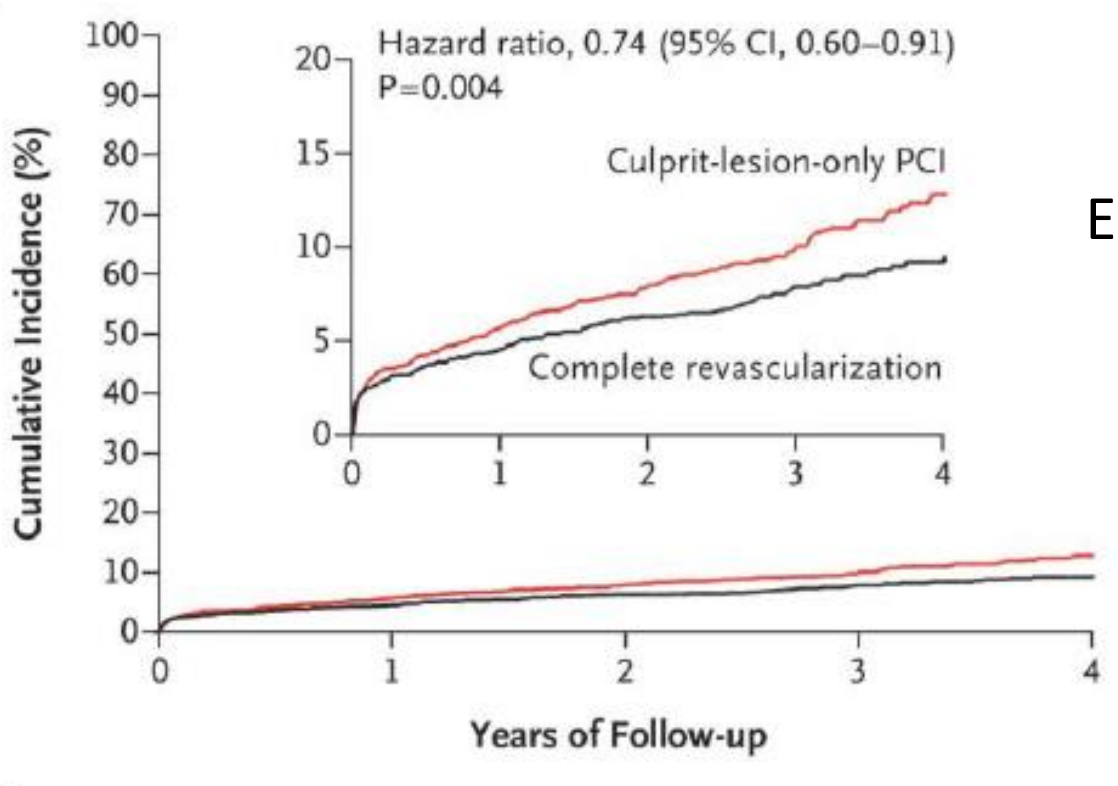
ACC/AHA STEMI Guidelines. JACC. 2013;61(4).

Evaluation of Non-Infarct Related Artery Disease



Non-Culprit PCI in STEMI

COMPLETE (Non-Shock)
(CV death or MI)

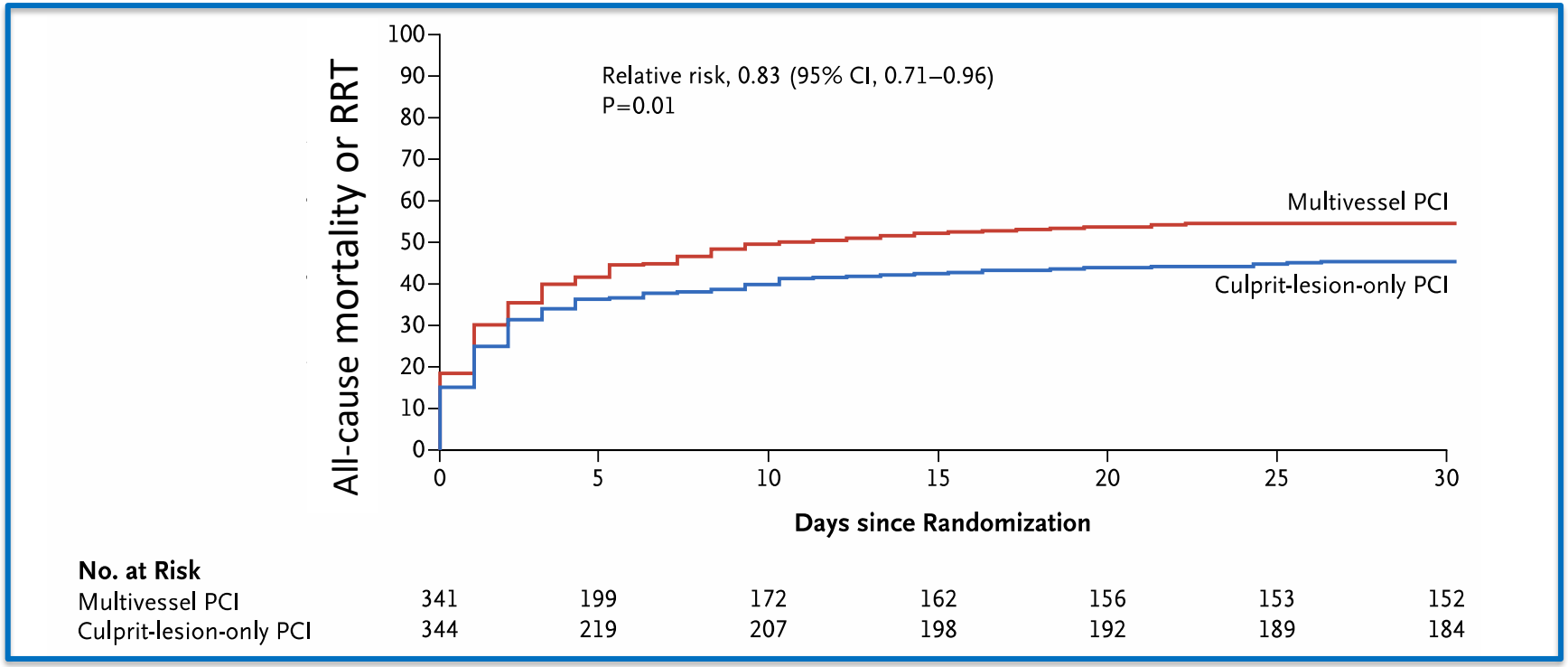


ESC: Class III → IIa (2017)

N Engl J Med 2019; 381:1411-1421

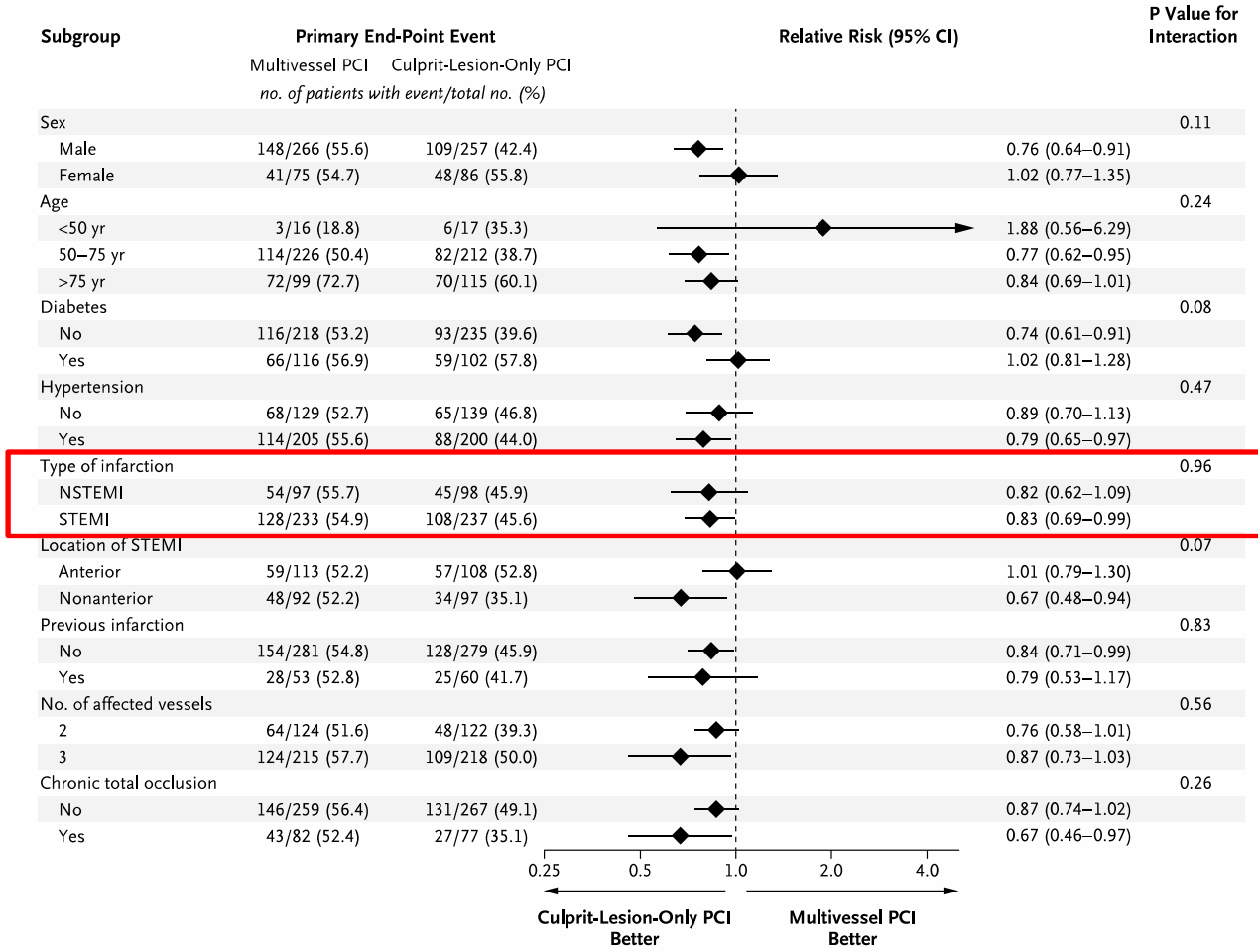
CULPRIT-SHOCK

706 pts with CS due to AMI (61% STEMI/39% NSTEMI) and MVD
Rx: Immediate MV PCI vs Culprit-Only +/- Staged PCI



Thiele H et al. NEJM 2017;377(25).

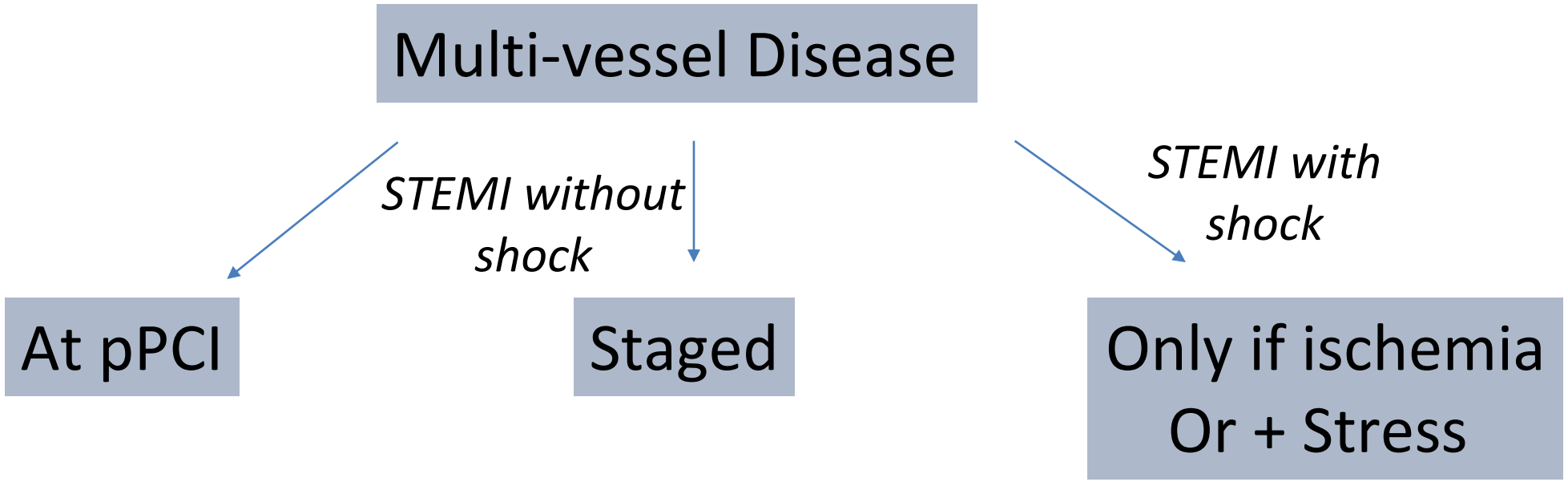
CULPRIT-SHOCK



Subgroup	Primary End-Point Event: Multivessel PCI (no. of patients with event/total no. (%))	Primary End-Point Event: Culprit-Lesion-Only PCI (no. of patients with event/total no. (%))	Relative Risk (95% CI)	P Value for Interaction
Sex				0.11
Male	148/266 (55.6)	109/257 (42.4)	0.76 (0.64–0.91)	
Female	41/75 (54.7)	48/86 (55.8)	1.02 (0.77–1.35)	
Age				0.24
<50 yr	3/16 (18.8)	6/17 (35.3)	1.88 (0.56–6.29)	
50–75 yr	114/226 (50.4)	82/212 (38.7)	0.77 (0.62–0.95)	
>75 yr	72/99 (72.7)	70/115 (60.1)	0.84 (0.69–1.01)	
Diabetes				0.08
No	116/218 (53.2)	93/235 (39.6)	0.74 (0.61–0.91)	
Yes	66/116 (56.9)	59/102 (57.8)	1.02 (0.81–1.28)	
Hypertension				0.47
No	68/129 (52.7)	65/139 (46.8)	0.89 (0.70–1.13)	
Yes	114/205 (55.6)	88/200 (44.0)	0.79 (0.65–0.97)	
Type of infarction				0.96
NSTEMI	54/97 (55.7)	45/98 (45.9)	0.82 (0.62–1.09)	
STEMI	128/233 (54.9)	108/237 (45.6)	0.83 (0.69–0.99)	
Location of STEMI				0.07
Anterior	59/113 (52.2)	57/108 (52.8)	1.01 (0.79–1.30)	
Nonanterior	48/92 (52.2)	34/97 (35.1)	0.67 (0.48–0.94)	
Previous infarction				0.83
No	154/281 (54.8)	128/279 (45.9)	0.84 (0.71–0.99)	
Yes	28/53 (52.8)	25/60 (41.7)	0.79 (0.53–1.17)	
No. of affected vessels				0.56
2	64/124 (51.6)	48/122 (39.3)	0.76 (0.58–1.01)	
3	124/215 (57.7)	109/218 (50.0)	0.87 (0.73–1.03)	
Chronic total occlusion				0.26
No	146/259 (56.4)	131/267 (49.1)	0.87 (0.74–1.02)	
Yes	43/82 (52.4)	27/77 (35.1)	0.67 (0.46–0.97)	

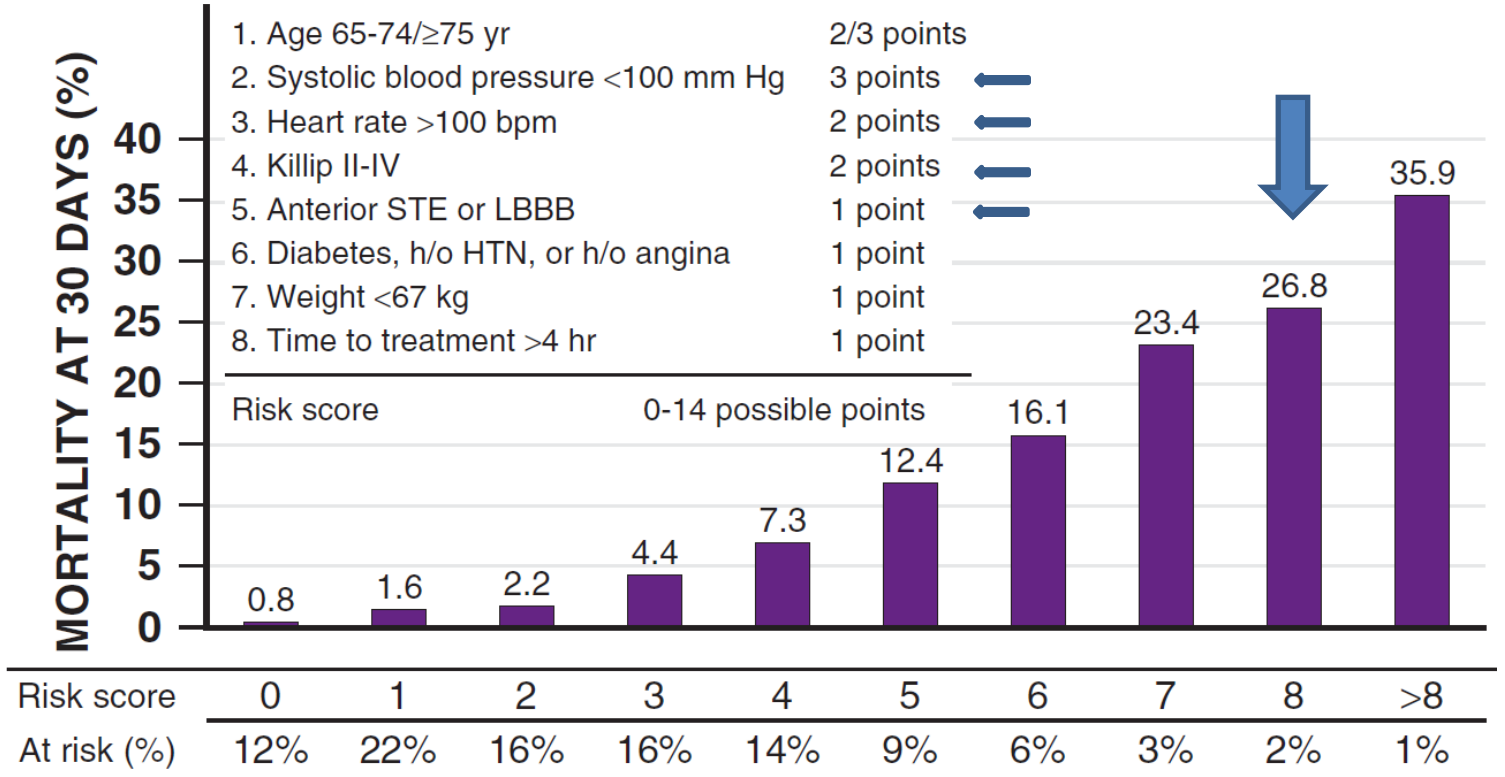
Thiele H et al. NEJM 2017;377(25).

Evaluation of Non-Infarct Related Artery Disease

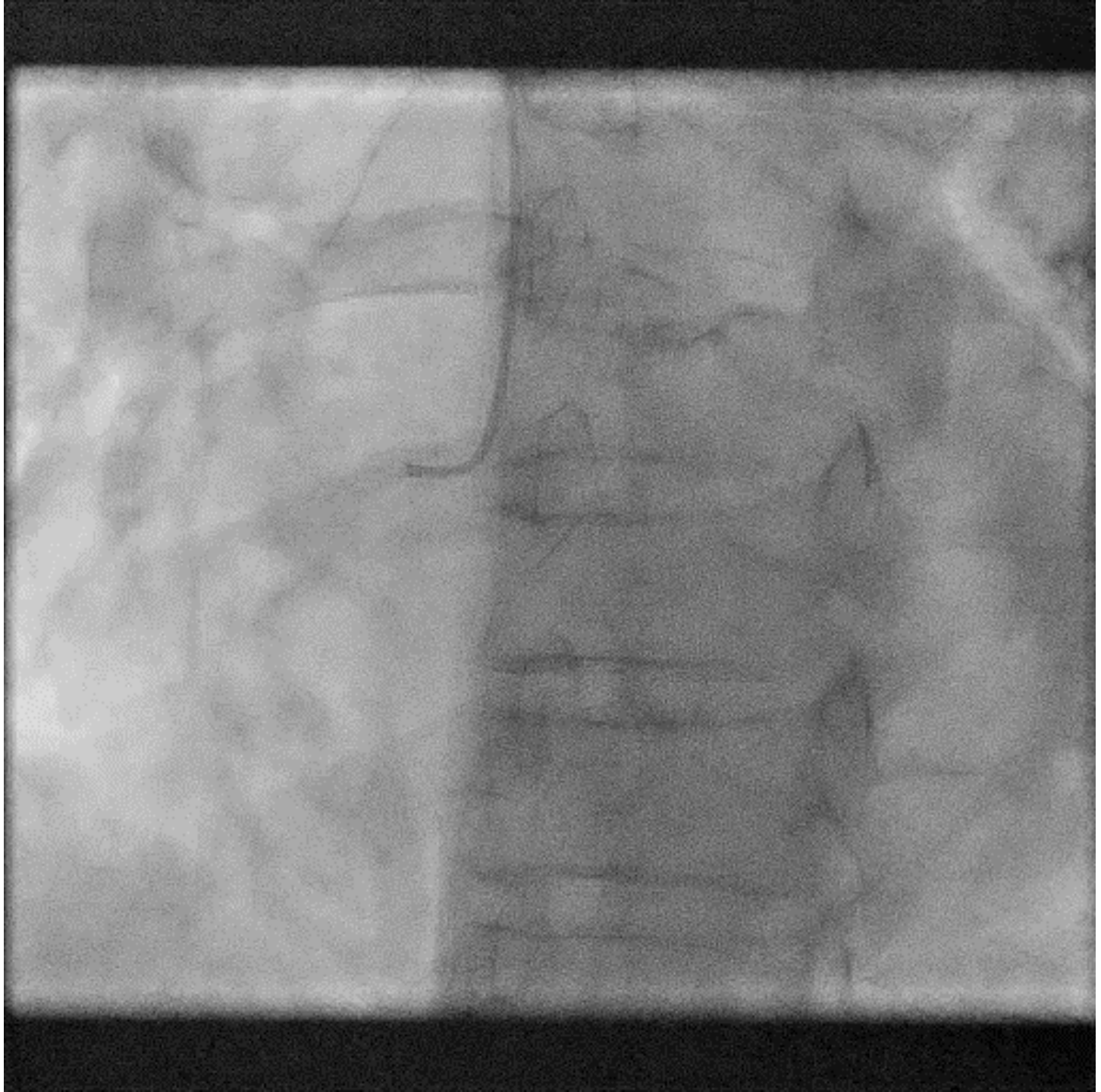


Case

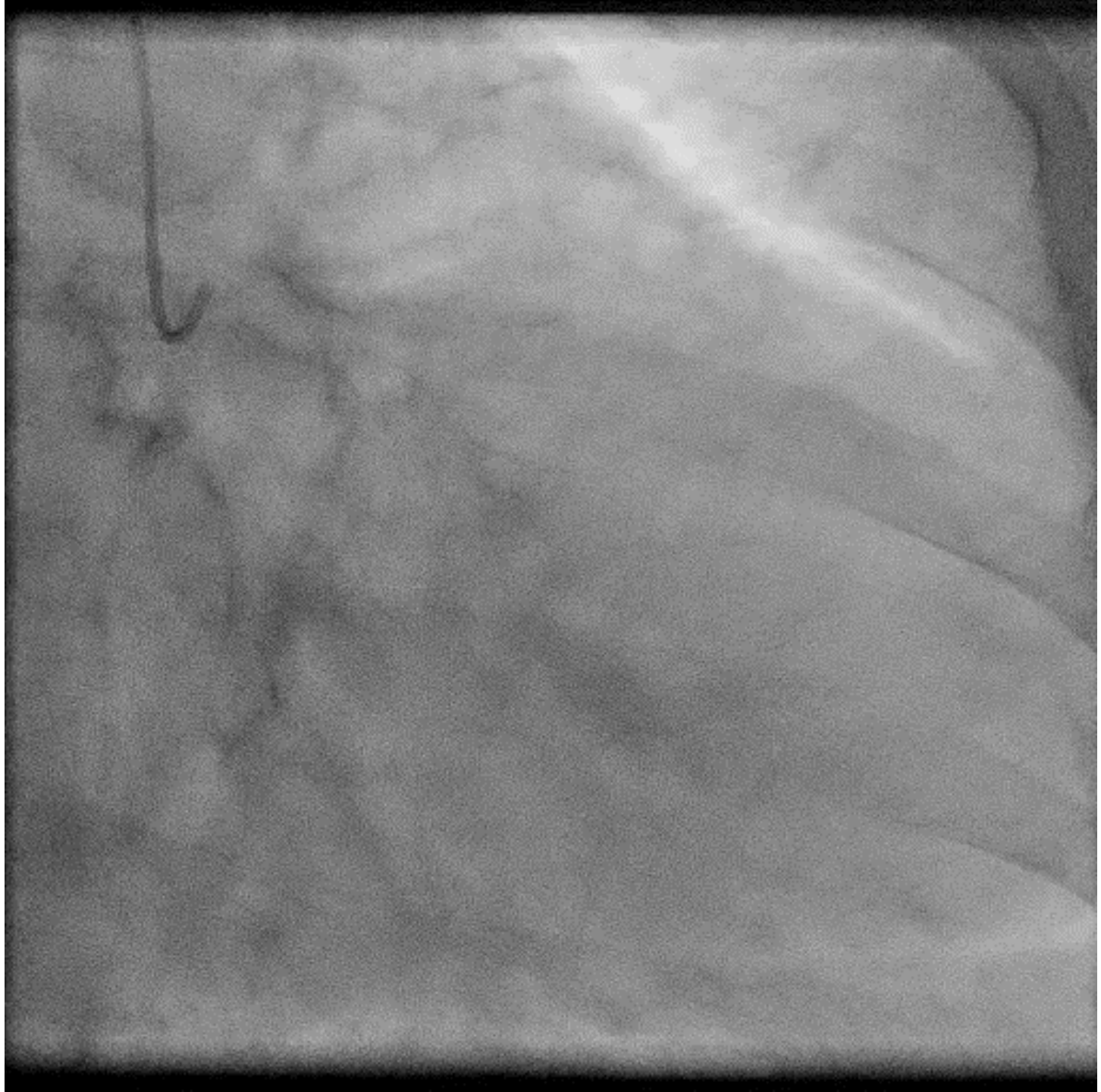
65yo F with DM, renal failure, HTN with CP x 2 hours, STE on EKG & shock



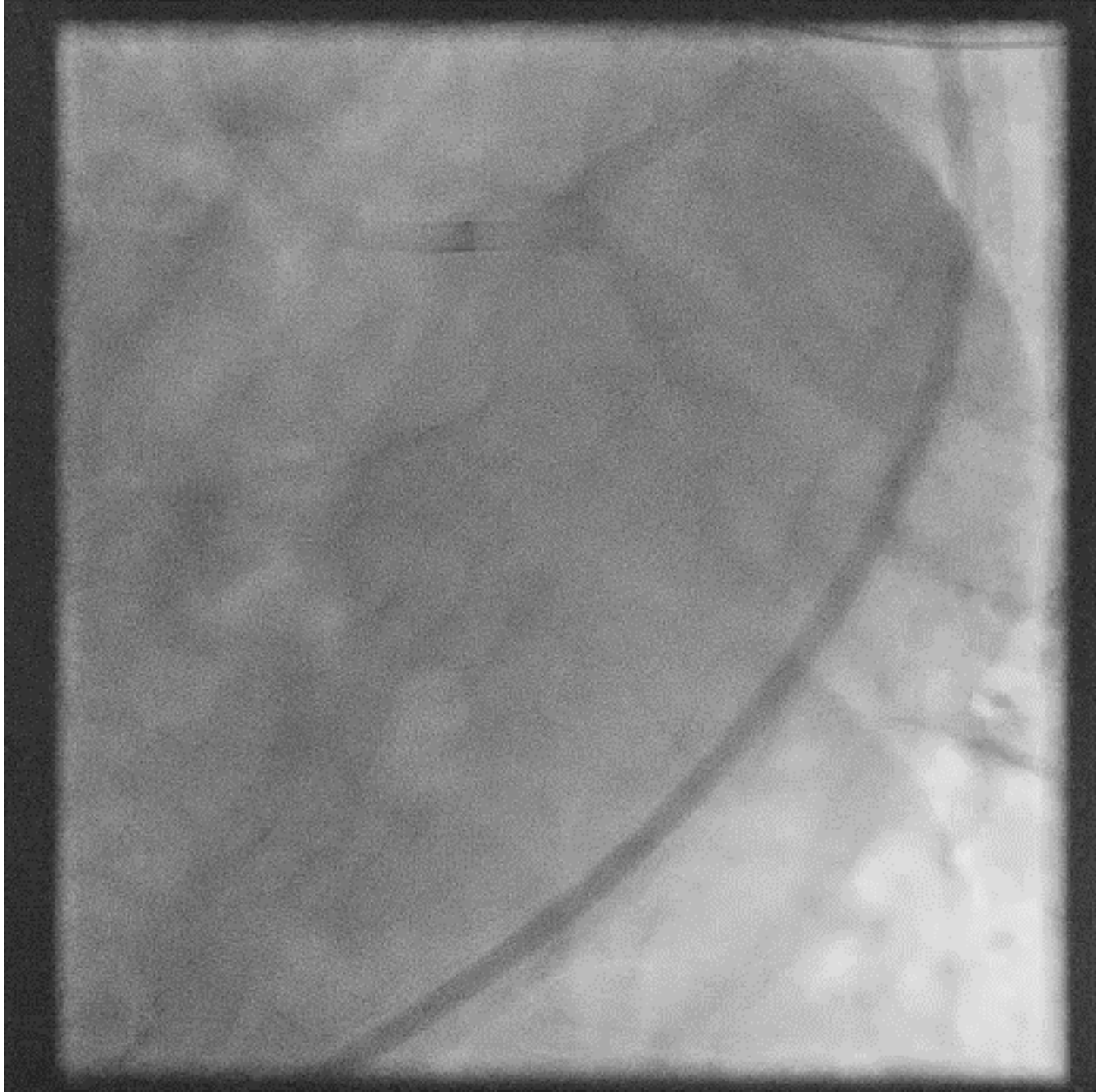
Courtesy of B. Bergmark



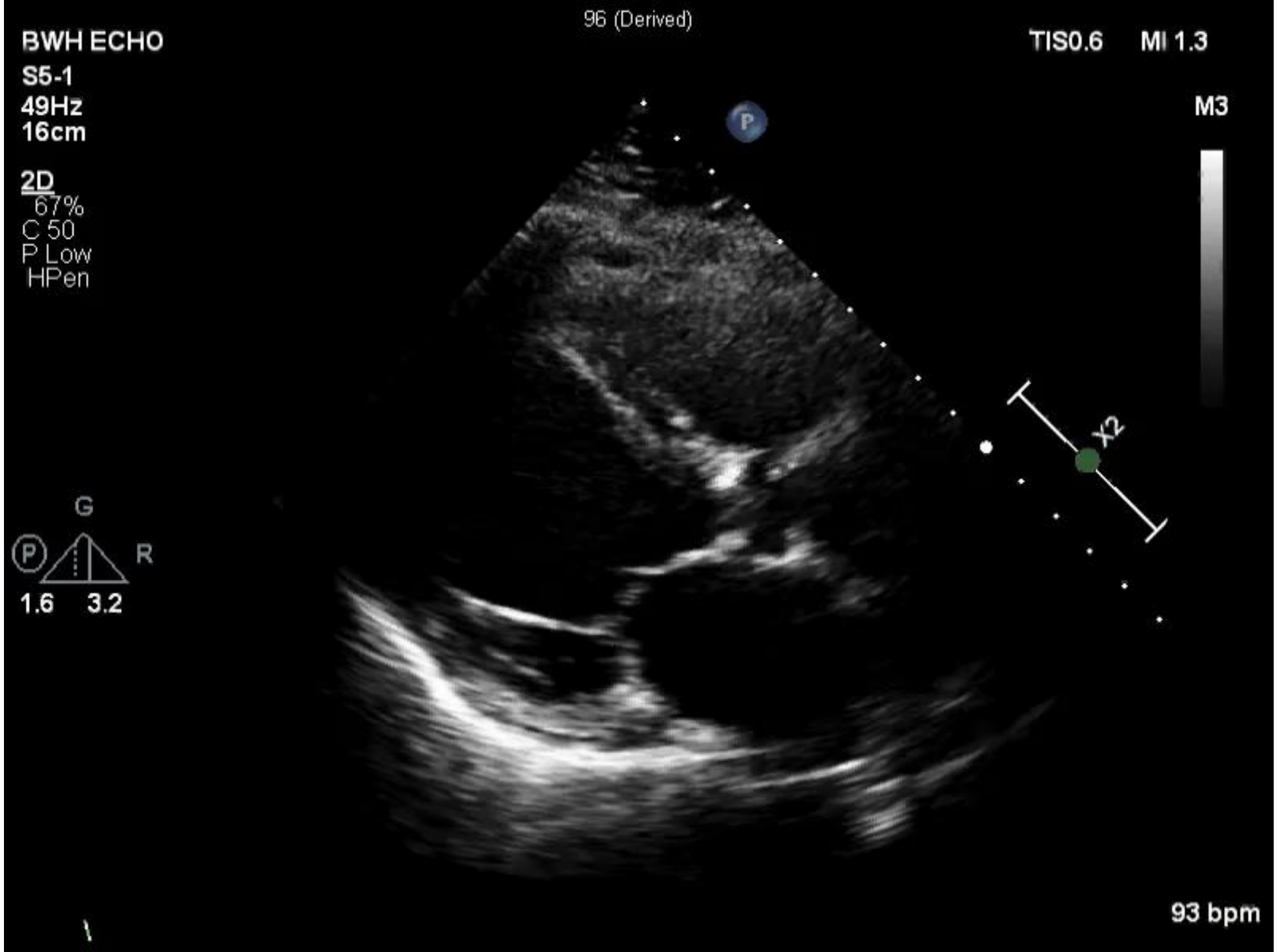
Courtesy of B. Bergmark



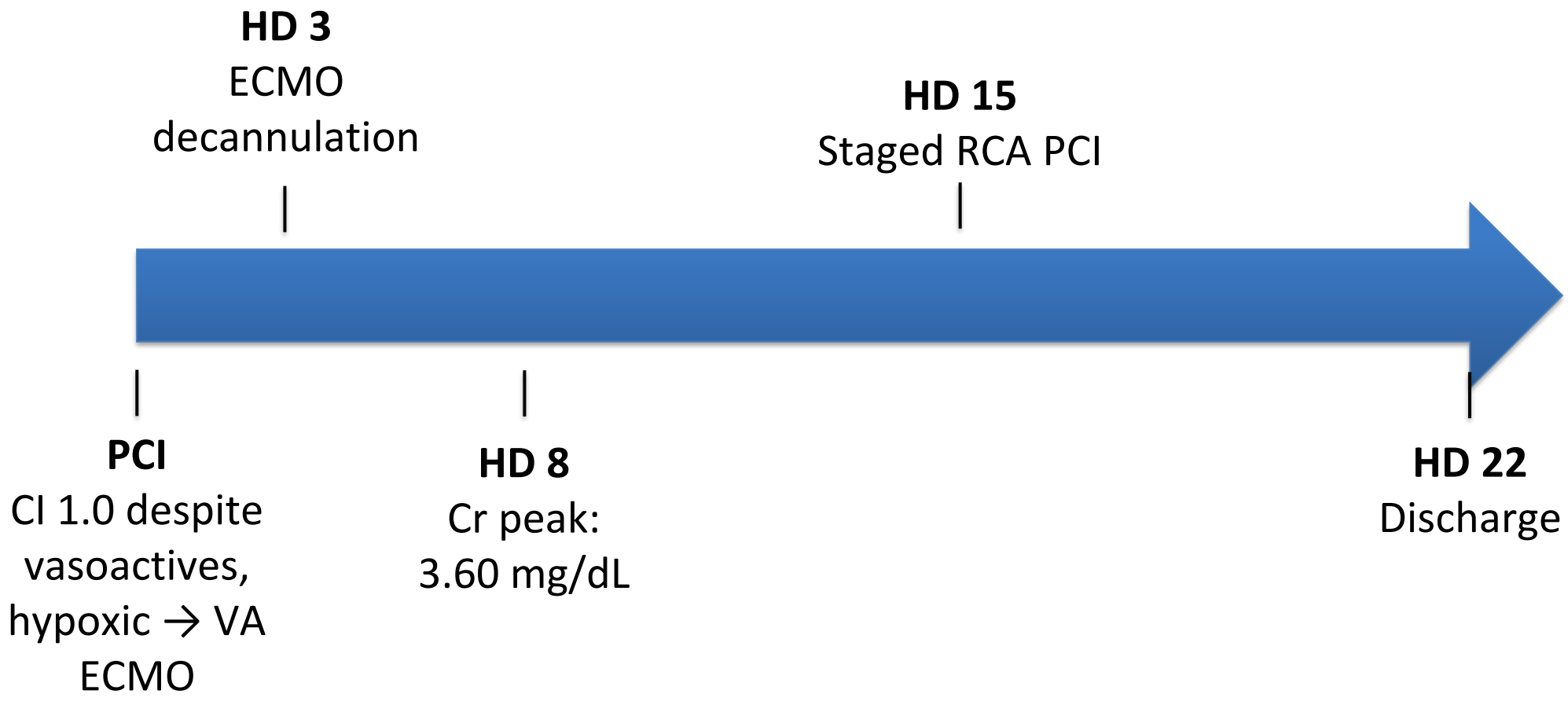
Courtesy of B. Bergmark



Courtesy of B. Bergmark


96 (Derived)
BWH ECHO
S5-1
49Hz
16cm
2D
67%
C 50
P Low
HPen
TIS0.6
MI 1.3
M3
X2
G
P
R
1.6
3.2
93 bpm

Case


HD 3
ECMO
decannulation
HD 15
Staged RCA PCI
PCI
CI 1.0 despite
vasoactives,
hypoxic → VA
ECMO
HD 8
Cr peak:
3.60 mg/dL
HD 22
Discharge

Take Homes

- Rapid diagnosis
- Emergent revascularization
  - Primary PCI preferred (PCI-capable center)
  - Goal < 90 min FMC to device (<60 for ESC guidelines)
  - Focus on culprit lesion on index cath, but can stage revascularization (CULPRIT-SHOCK)
- Acute medical therapy: ASA, heparin, cangrelor/ticagrelor, statin, ezetimibe. No BB/ACEi due to shock.
- Aggressive medical therapy on discharge/follow up (to be discussed later)

CMHC Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)

NSTE-ACS: Diagnosis, Risk Stratification, and Revascularization

Erin Bohula, MD DPhil

Assistant Professor, BWH, HMS

Investigator, TIMI Study Group

BWH BRIGHAM AND WOMEN'S HOSPITAL | Heart & Vascular Center |

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

TIMI Study Group

www.brighamandwomens.org/heart

Outline

- Definitions/Pathophysiology
- Epidemiology
- STEMI
  - Diagnosis
  - Risk stratification
  - Revascularization
- NSTE-ACS
  - Diagnosis
  - Risk stratification
  - Revascularization
- Other management (medical therapy)

Case

65-year-old woman

- Type I diabetes
- Kidney/pancreas transplant in 1999
- Repeat kidney transplant 2010
- Progressive renal insufficiency
- Hypertension
- HL

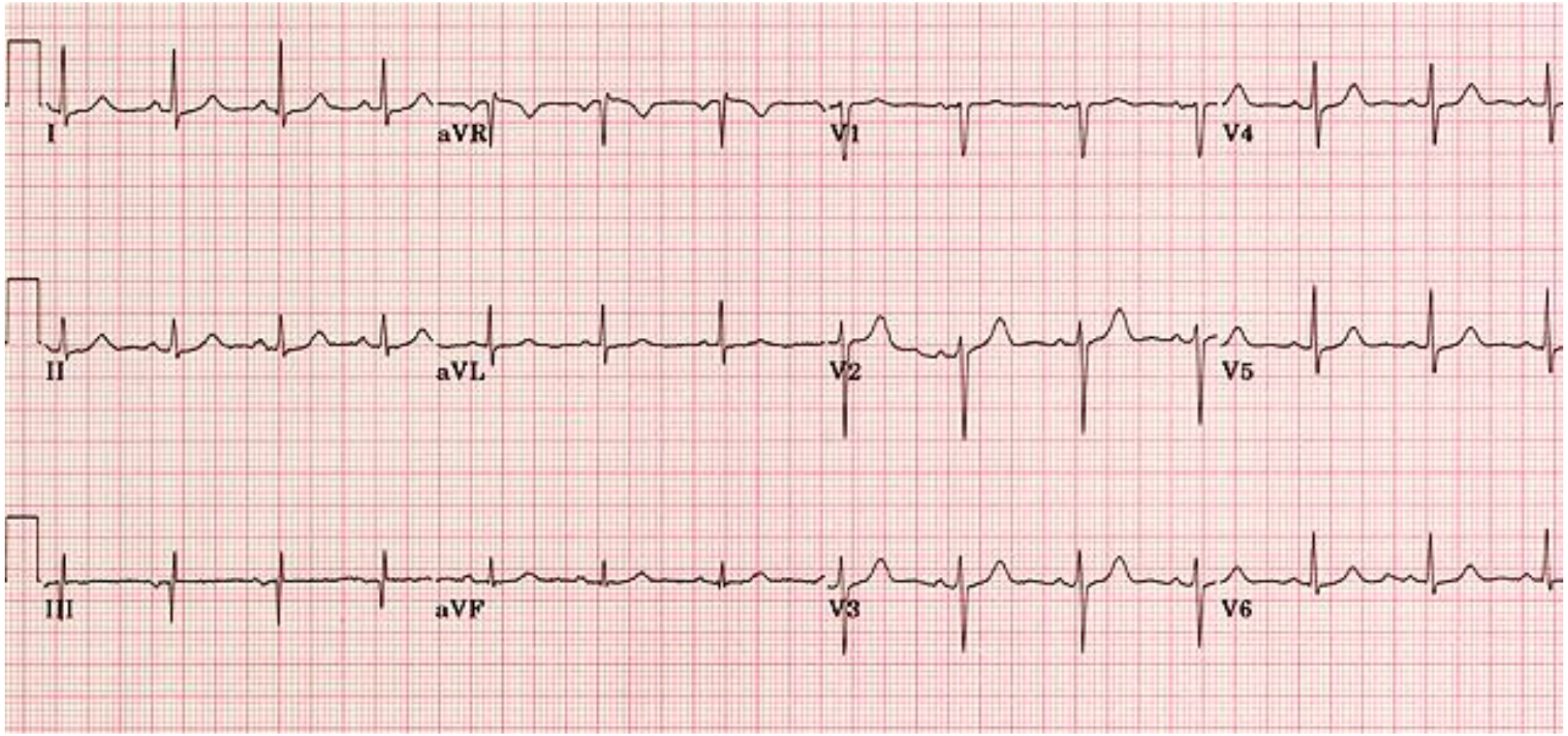
Presented to BWH ED with intermittent rest chest pain that starting 2 hours ago

Case

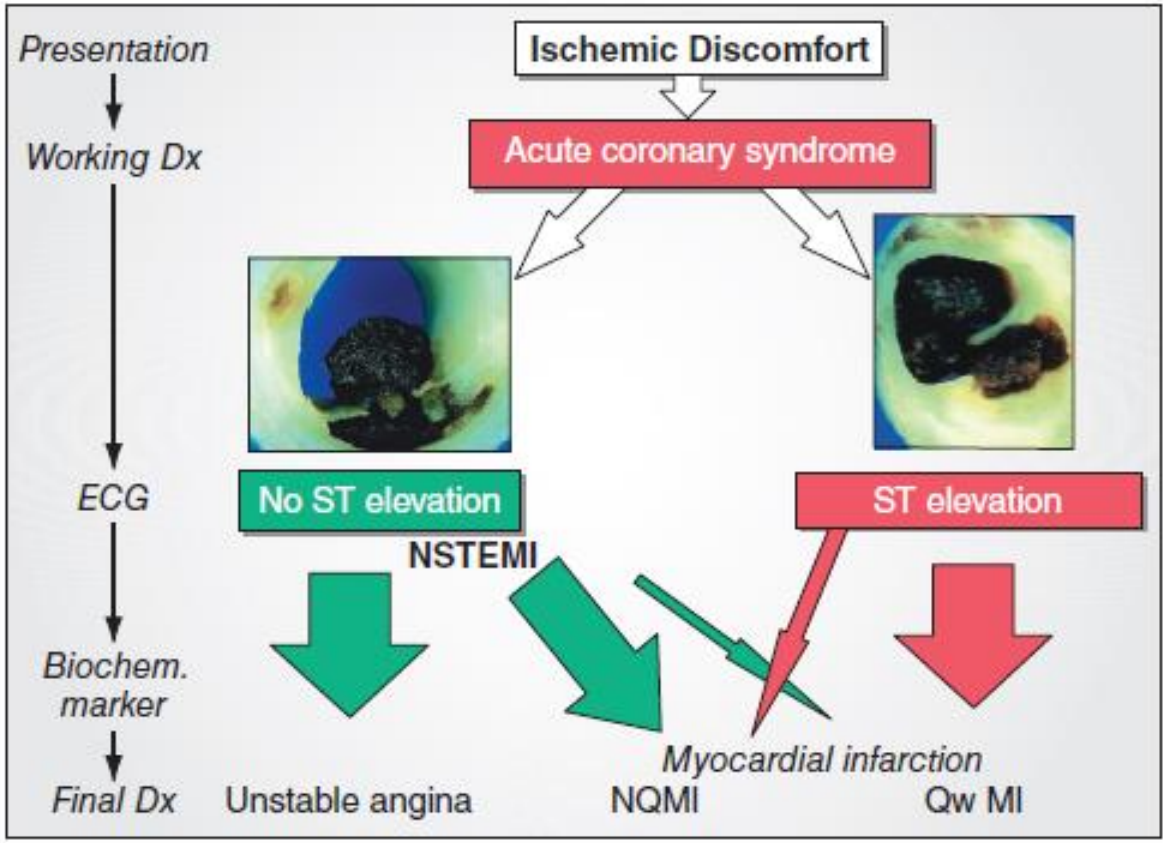
PE: 92BPM **110/80**mmHg **18**RPM **98% RA**

Labs:
Cr 1.6 mg/dL (baseline 1.3 mg/dL, eGFR 50)
Hs-TnT 15 ng/L
LDL 150 mg/dL
HbA1c 8%

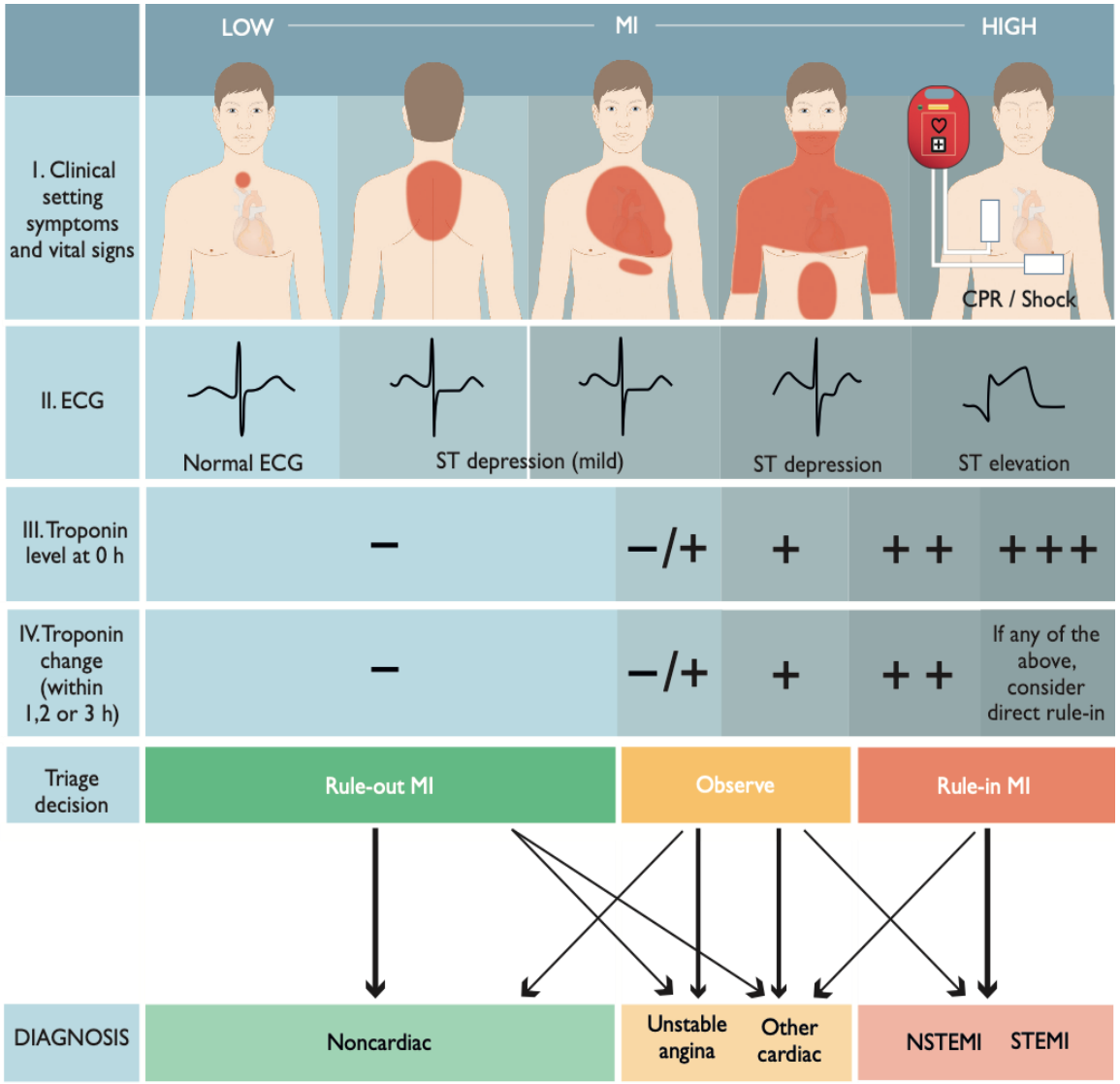
EKG



Acute Coronary Syndrome: STEMI, nSTEMI, UA



Davies MJ, Heart 2000;83:361
Hamm CW, Lancet 2001:358:1533



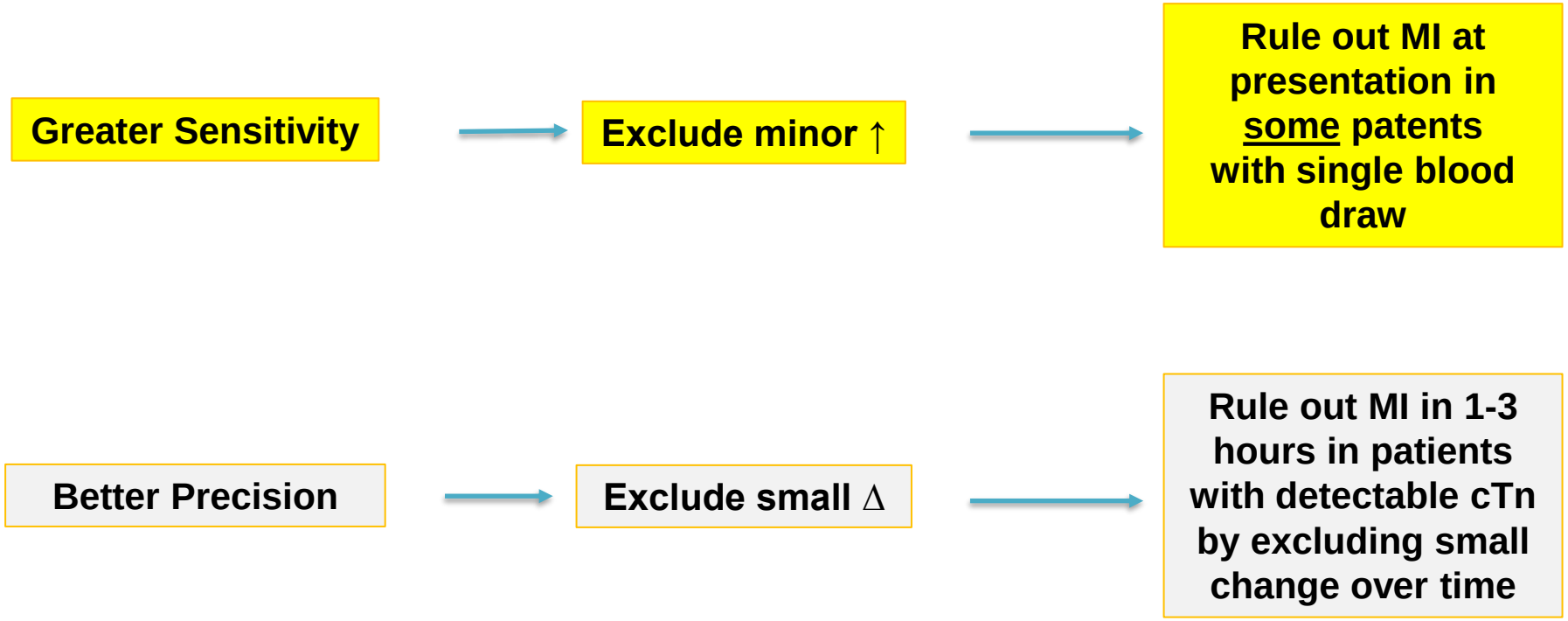
Collet JP et al. "2020 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segement elevation." European Heart Journal Heart 2021; 42.14: 1289-1367

4th Universal Definition of MI

Definition	Criteria
Myocardial **Injury**	Tn >99th %ile (acute if rise and/or fall)
Acute Myocardial **Infarction**	Acute myocardial injury + clinical evidence of acute myocardial ischemia (eg, sx, ECG, imaging)
Type 1	**Atherothrombosis** (plaque rupture or erosion)
Type 2	Imbalance between myocardial O_2 supply & demand **unrelated** to acute atherothrombosis
Type 3	**Cardiac death** w/ sx + ECG Δs before Tn available
Type 4	**PCI-related** (clinical + Tn >5× 99th %ile)
Type 5	**CABG-related** (clinical + Tn >10× 99th %ile)

Thygesen, *Circulation*. 2018.

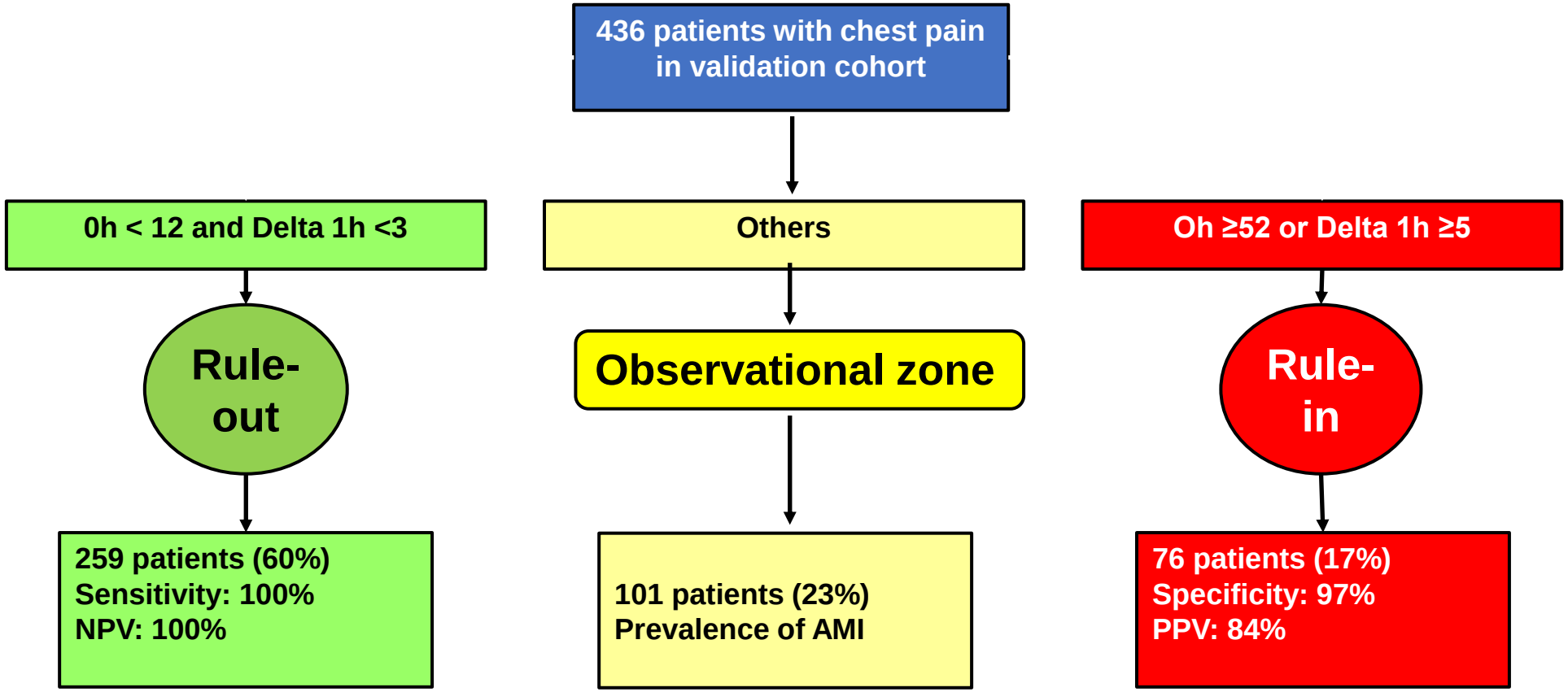
Capitalizing on the Advantages of hs-cTn Assays



Rule out with Single hs-cTnT Measurement

Author, year	hs-cTnT threshold	N	% < LLD	Sensitivity (%)	NPV (%)
Body R. JACC 2011	<3 ng/L	710	28%	100	100

1-hour rule out MI with hs-TnT

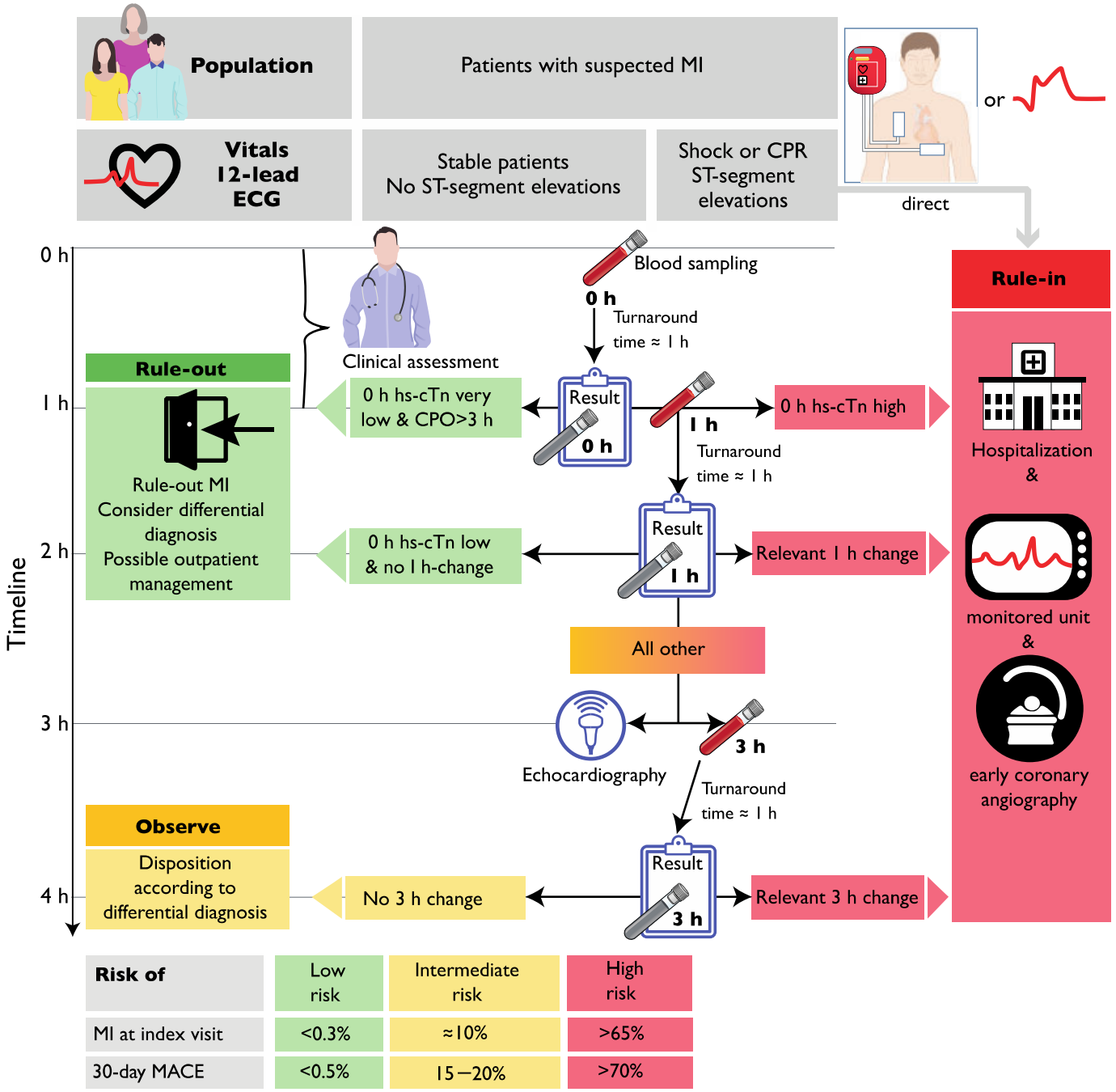


2nd Validation Study			
	813 Patients (63.4%) NPV 99.1%	285 Patient (22.2%) Prevalence of MI (22.5%)	184 Patients (14.4%) PPV 77.2%

Reichlin T. *Arch Int Med* 2012;172:1211-8
Mueller C. *Ann Emerg Med*. 2016 Jul;68(1):76-87

2020 NSTE-ACS GL

European Society of Cardiology



Risk of	Low risk	Intermediate risk	High risk
MI at index visit	<0.3%	≈10%	>65%
30-day MACE	<0.5%	15–20%	>70%

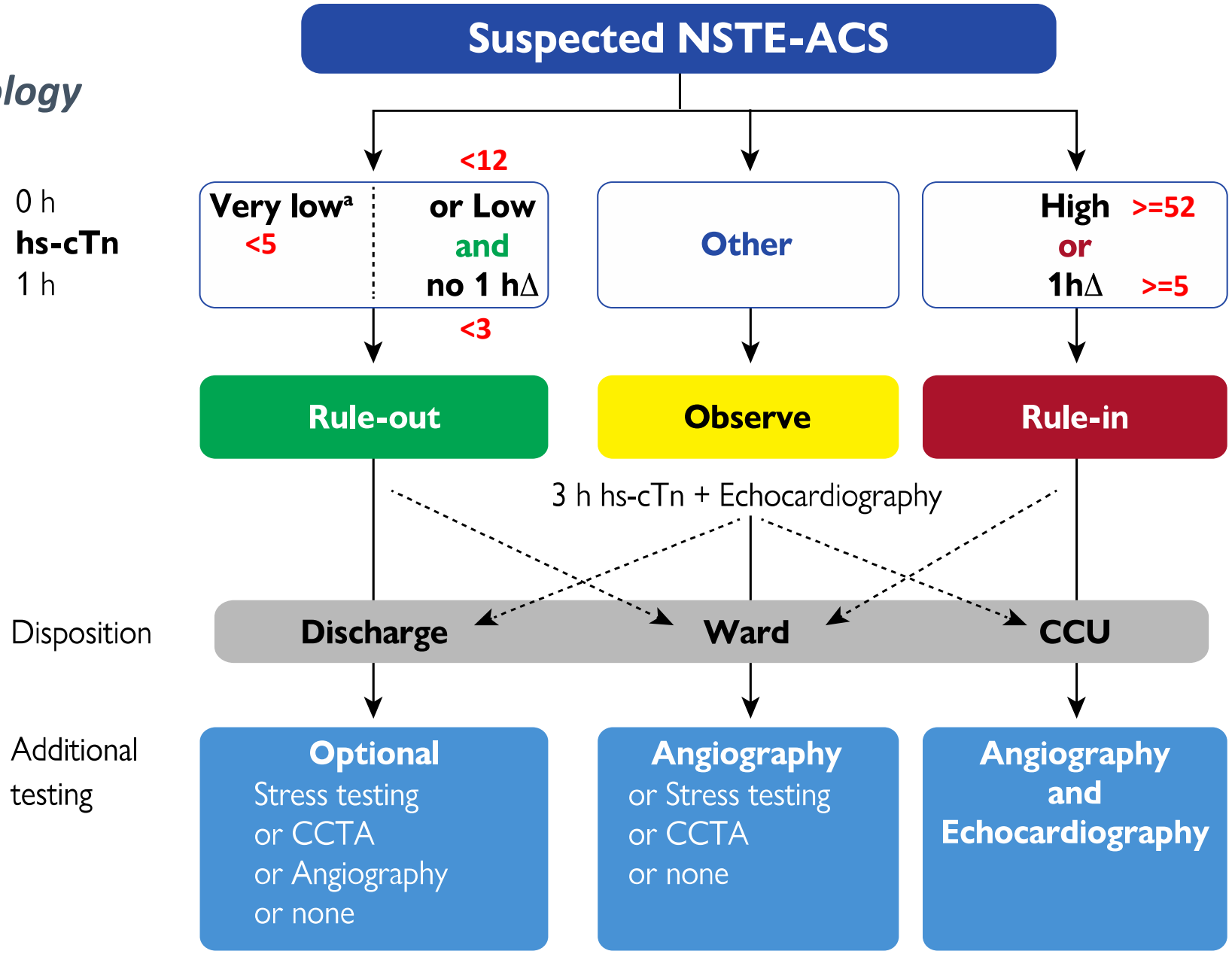
Collet JP et al. European Heart Journal Heart 2021; 42.14: 1289-1367

2020 NSTE-ACS GL

European Society of Cardiology

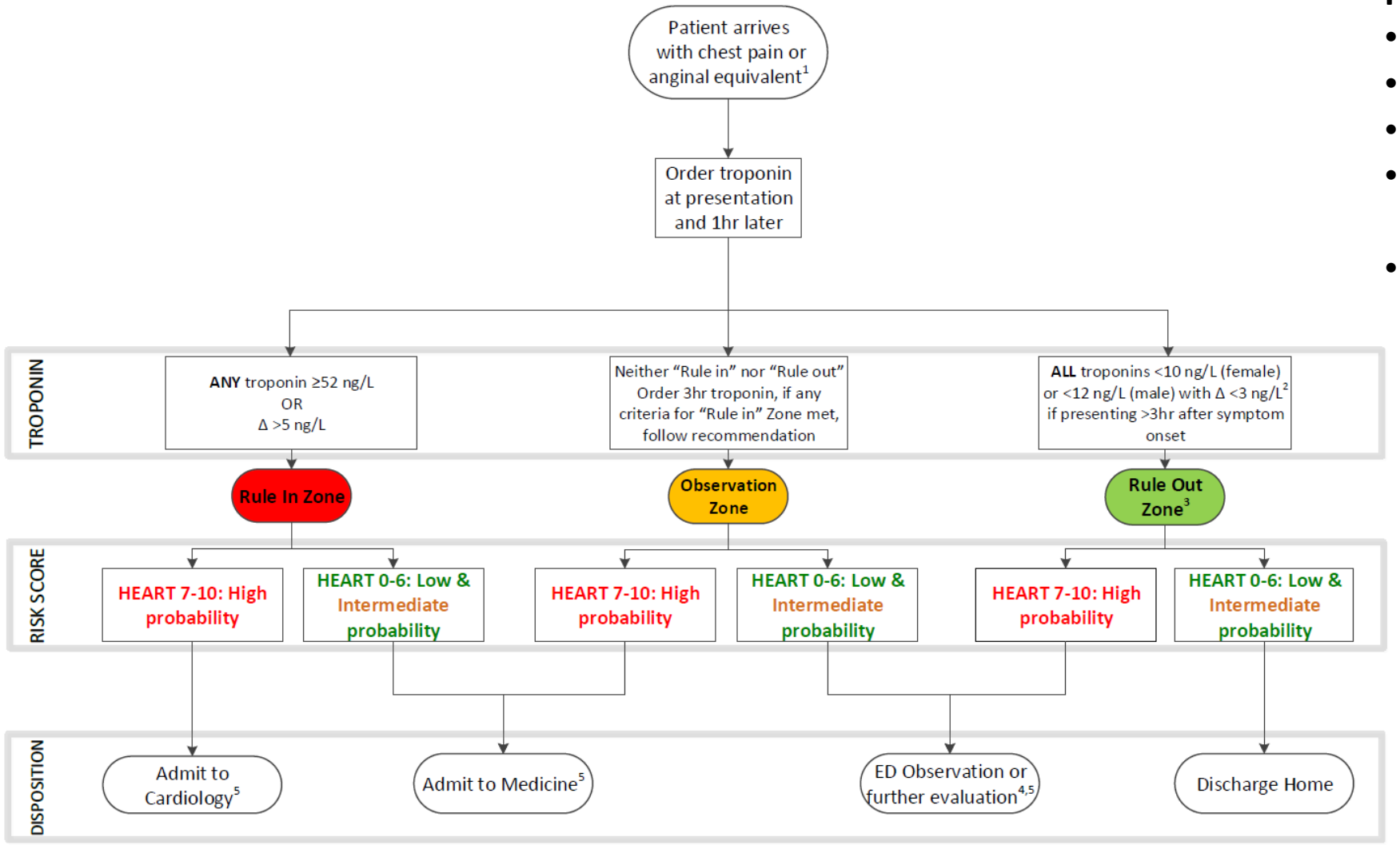
NB: Thresholds vary by hsTn Assay

For hs-cTnT



Collet JP et al. European Heart Journal Heart 2021; 42.14: 1289-1367

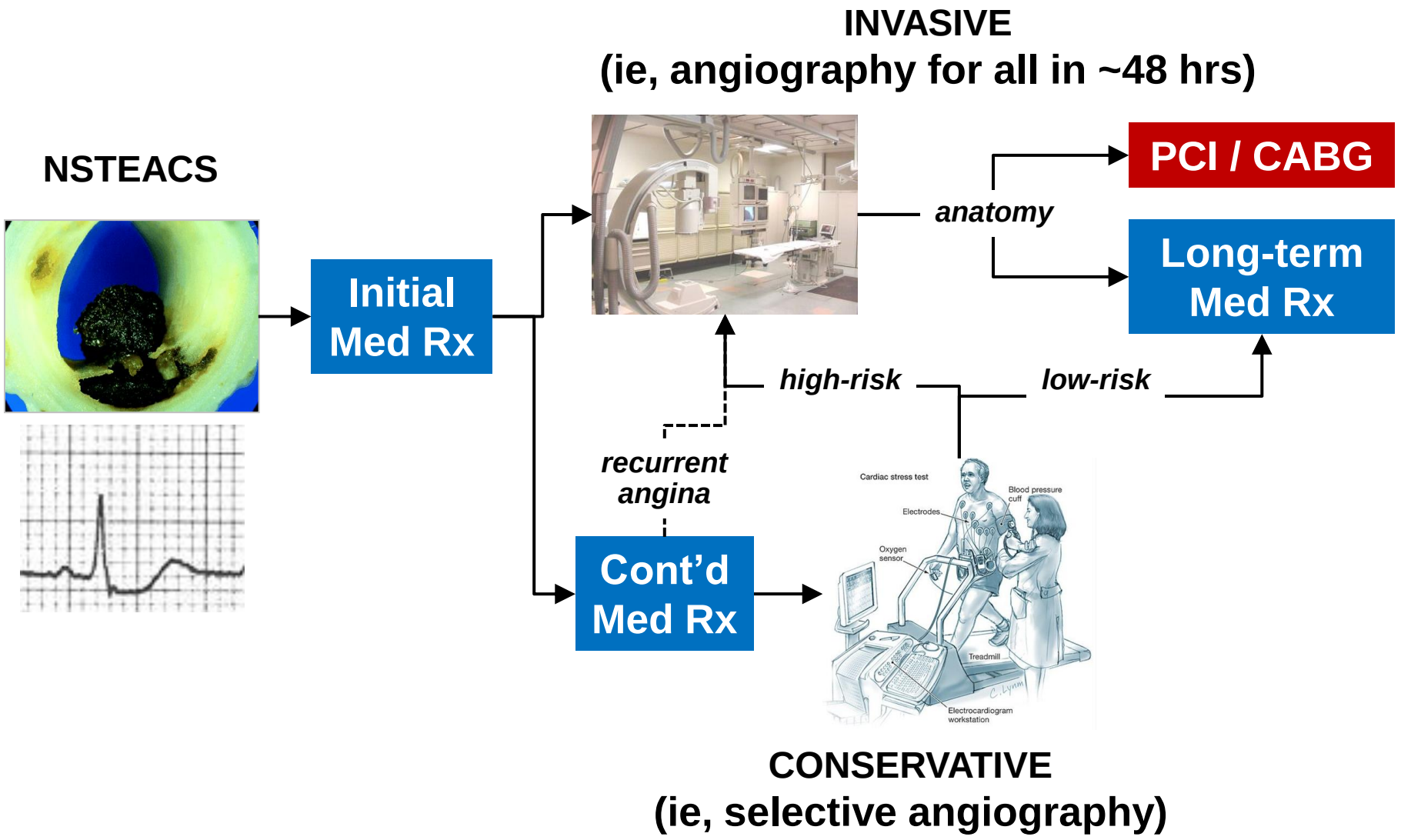
BWH Pathway



HEART Score

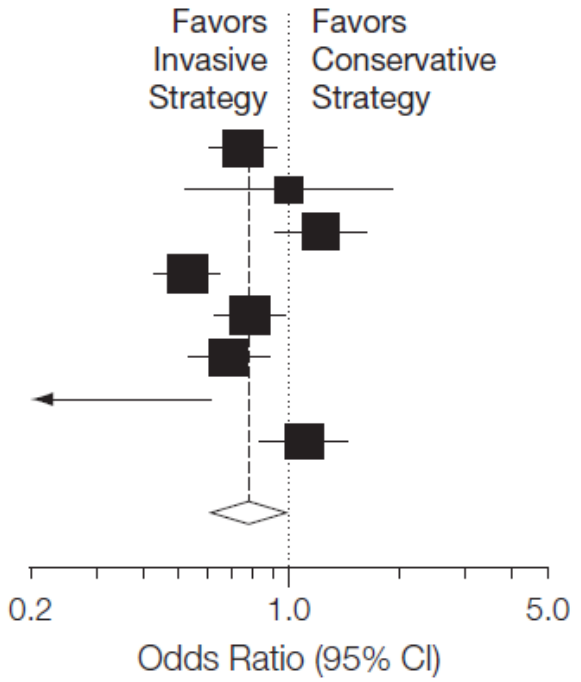
- Clinical history (0-2)
- ECG (0-2)
- Age (0-2)
- Risk factors (HL, HTN, DM smoking, obesity) (0-2)
- *Troponin*

Management Strategy in NSTEACS



Benefit of INV vs CONS Strategy

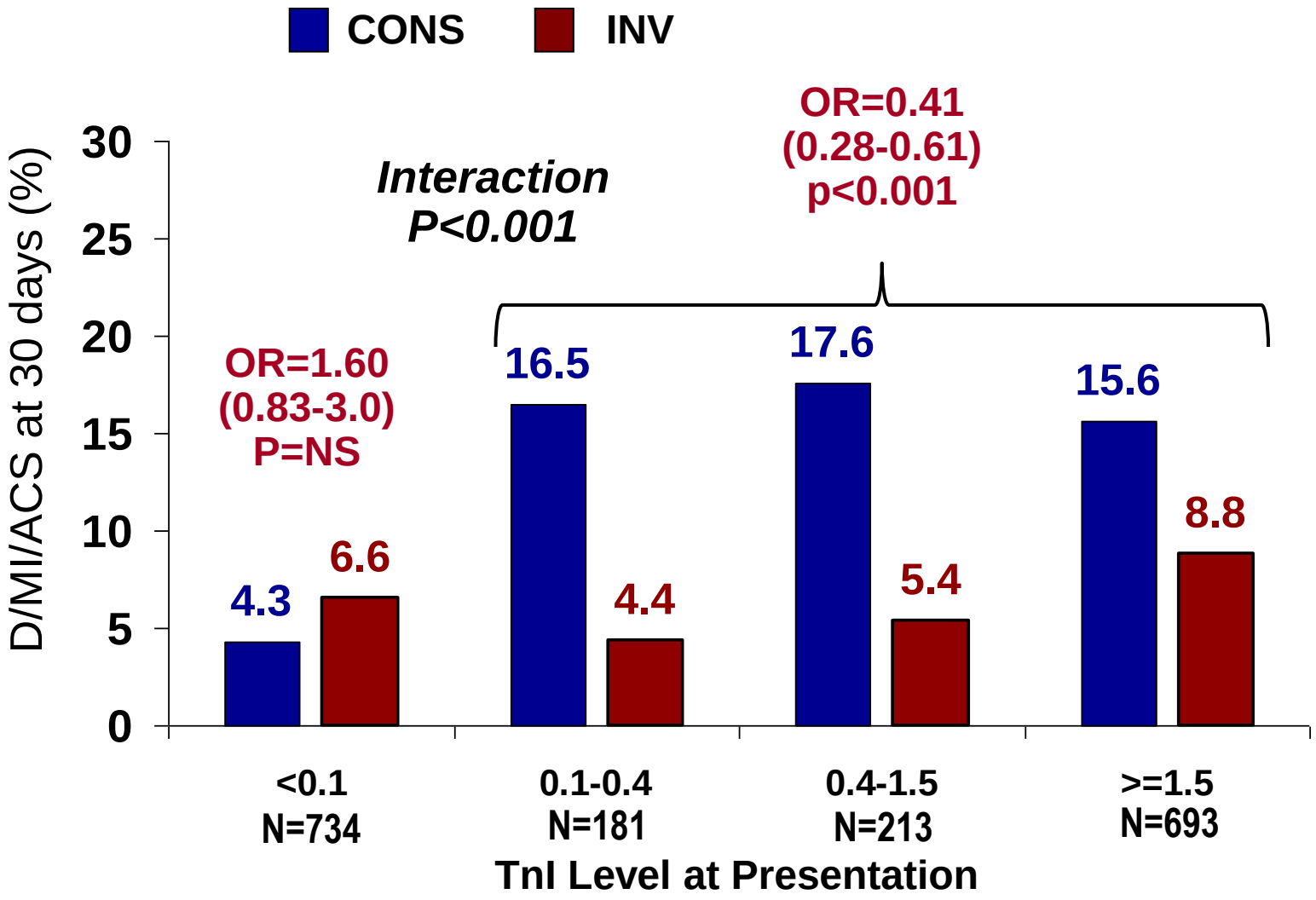
All Patients	Rates of Death, MI, or Rehospitalization With ACS, No./Total No. (%)		Odds Ratio (95% CI)
	Invasive Strategy	Conservative Strategy	
TIMI IIIB[10]	122/895 (13.6)	171/915 (18.7)	0.75 (0.61-0.93)
MATE[11]	27/111 (24.3)	22/90 (24.4)	0.99 (0.52-1.90)
VANQWISH[18]	148/462 (32.0)	124/458 (27.7)	1.22 (0.92-1.61)
FRISC II[1]	196/1093 (17.9)	322/1102 (29.2)	0.53 (0.43-0.65)
TACTICS-TIMI 18[7]	177/1114 (15.9)	215/1106 (19.4)	0.78 (0.63-0.97)
RITA 3[2]	122/895 (13.6)	171/915 (18.7)	0.69 (0.53-0.88)
VINO[20]	5/64 (7.8)	19/67 (28.4)	0.21 (0.07-0.62)
ICTUS[8]	137/604 (22.7)	126/596 (21.1)	1.09 (0.83-1.44)
Overall	1075/5083 (21.1)	1313/5067 (25.9)	0.78 (0.61-0.98)



INV Strategy reduces cardiac complications by ~20%, particularly recurrent ACS

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

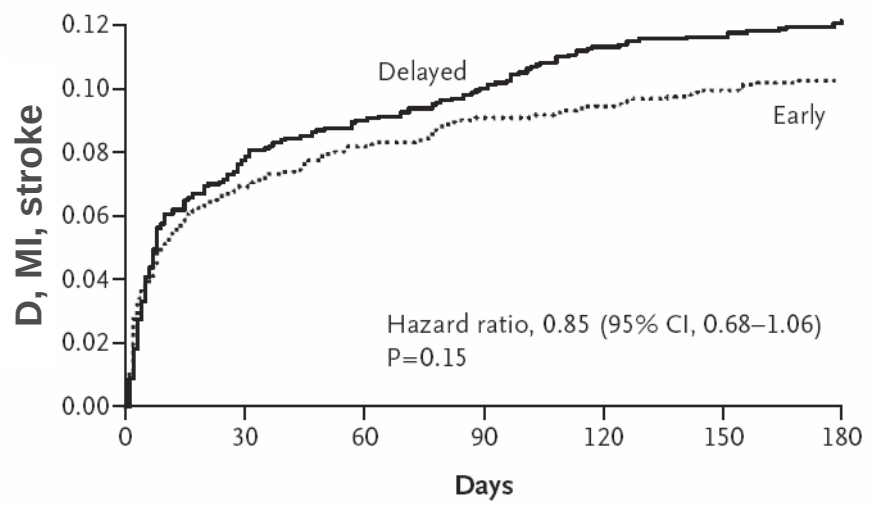
Troponin Treatment Interaction

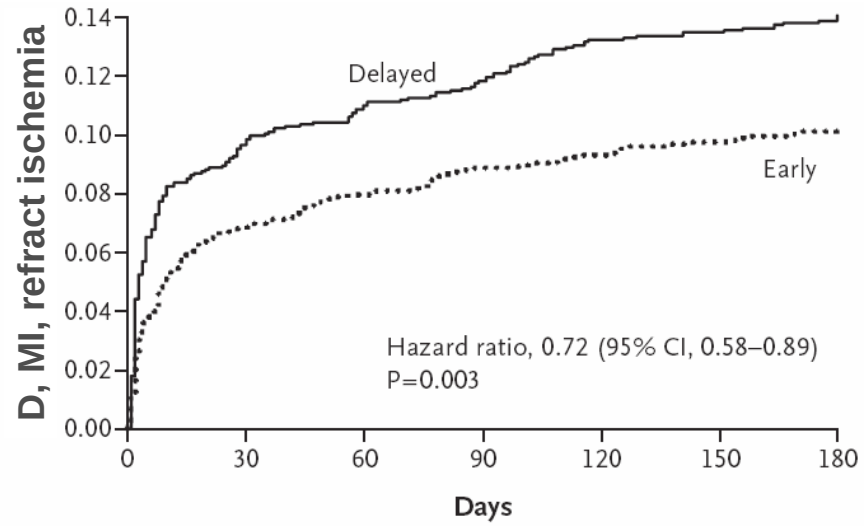


Cannon CP et al. *NEJM* 2001;344:1879

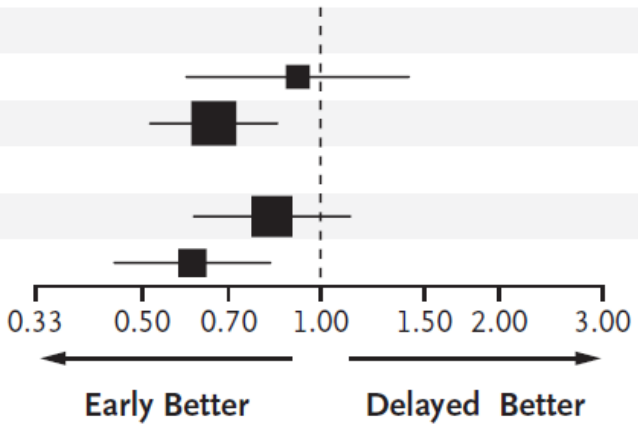
TIMACS

3031 Patients with NSTEACS
Cath w/in 24 h (median 14 h) or >36 h (median 50 h)





Elevated cardiac marker				
No	666	11.8	12.9	0.92 (0.59–1.41)
Yes	2365	8.8	13.0	0.67 (0.52–0.85)
GRACE score				
0–140	2049	7.5	8.8	0.83 (0.61–1.12)
≥141	982	13.7	21.6	0.62 (0.45–0.83)



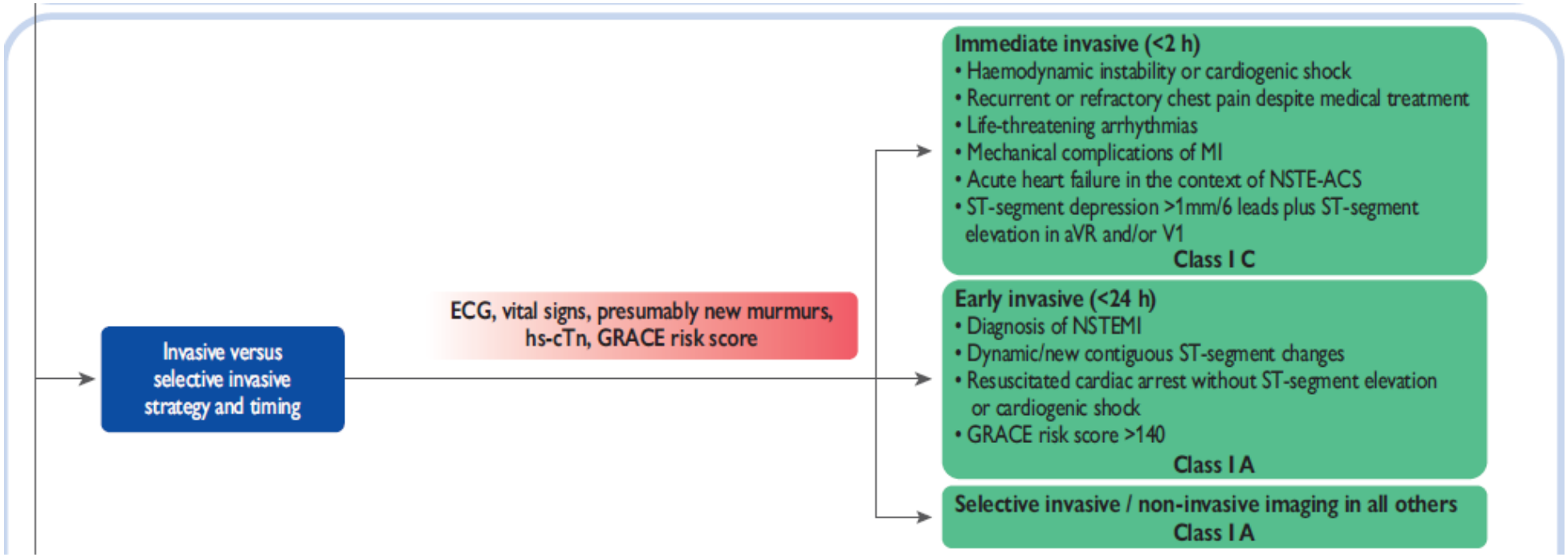
Mehta SR et al. *NEJM* 2009;360:2165-75

2014 ACC/AHA NSTEACS Guidelines: Early Invasive

Immediate (w/in 2 h)	Early Invasive (w/in 24 h)	Delayed Invasive (w/in 25-72 h)	Ischemia-Guided
• Refractory angina • Signs or symptoms of HF or new or worsening MR • Recurrent angina or ischemia at rest or with low-level activity despite intensive med Rx	• GRACE score >140 • Temporal Δ in Tn • New or presumably new ST depression	• TIMI Risk Score ≥2 • GRACE score >109-140 • Diabetes • GFR <60 mL/min/1.73m^2 • EF <0.40 • Early postinfarction angina • PCI w/in 6 mo • Prior CABG	• TIMI Risk Score 0-1 • GRACE score <109 • Low-risk Tn-neg female patient • Patient or clinician preference in absence of high-risk features

Circulation 2014;130:2354-94

2020 ESC NSTEACS Guidelines



Collet JP et al. European Heart Journal Heart 2021; 42.14: 1289-1367

Case

65yo F with DM, renal failure, HTN with intermittent rest CP x 2 hours, ischemic changes on EKG.

On history, reports several weeks of typical exertional chest pain.

Additional Work up:

- 1 hr troponin: 25 mg/dl (delta of 10) -> ruled in for NSTEMI

Plan:

- Started on ASA, heparin, BB, high-dose statin
- Invasive strategy in next 24-48 hours (+NSTEMI, GRACE 111)

Case

65yo F with DM, renal failure, HTN with intermittent rest CP x 2 hours, no ischemic changes on EKG.

Taken urgently to LHC. Single thrombotic RCA lesion -> DES x 1.

Given heparin/cangrelor during LHC -> ticagrelor. Continued on ASA, statin, ezetimibe. Continued on home ACEi, started on MRA.

Echocardiogram with low normal EF (50%)

Additional secondary preventative therapy added on follow up.

Take Homes

- NSTE-ACS diagnosis can be challenging
  - Requires integration of clinical history (? Ischemic symptoms) and documentation of dynamic cardiac injury
  - Rule-in/rule-out algorithms using hs-Tn can assist with diagnosis and triage
- Decision on invasive vs conservative strategy based on risk stratification

CMHC
Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)

Other Management (Medical Therapy)

Erin Bohula, MD DPhil

Assistant Professor, BWH, HMS

Investigator, TIMI Study Group

BWH BRIGHAM AND WOMEN'S HOSPITAL | Heart & Vascular Center |

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

TIMI Study Group

www.brighamandwomens.org/heart

Outline

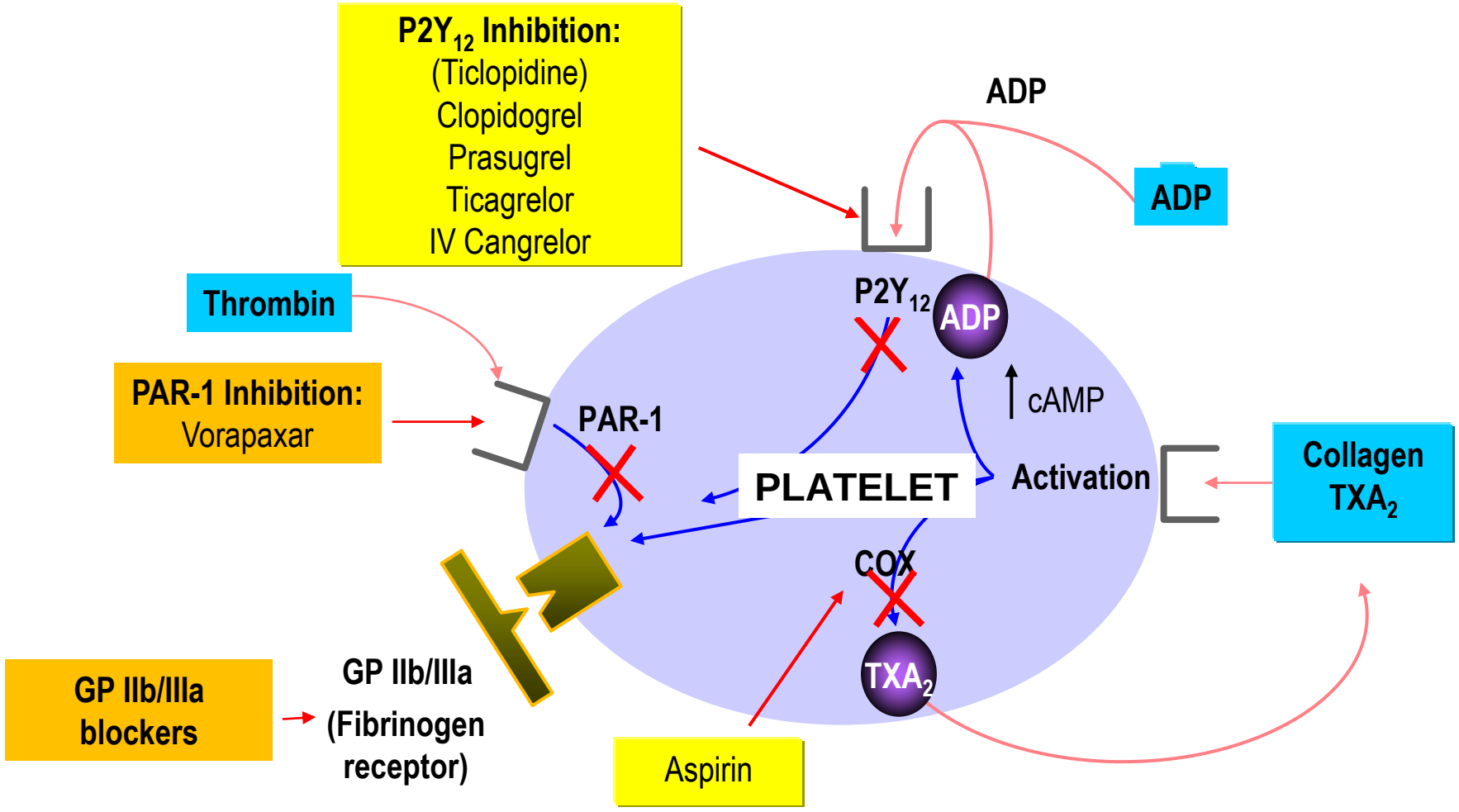
- Definitions/Pathophysiology
- Epidemiology
- STEMI
  - Diagnosis
  - Risk stratification
  - Revascularization
- NSTE-ACS
  - Diagnosis
  - Risk stratification
  - Revascularization
- Other management (medical therapy)

Anticoagulants Acutely

- Unfractionated heparin (UFH)
  - Most commonly used; fast on & fast off; reversible
  - Wt-based dosing; unpredictable PD, requiring ✓ PTT
  - Compared with no anticoagulation: ↓ D/MI by ~33%
- Low-molecular weight heparin (LMWH)
  - More predictable PD; not as reliably reversed
  - Compared with UFH: 9% ↓ D/MI, may ↑ bleeding
  - Consider in *conservatively* managed patients
- Bivalirudin
  - Fast on & fast off
  - Compared with heparin: 9% ↑ MACE, 38% ↑ stent thrombosis, ↓ bleeding (especially if compared with UFH+GP IIb/IIIa inhibitor)
  - Consider in *invasively* managed Pts, espec if at high risk for *bleeding*

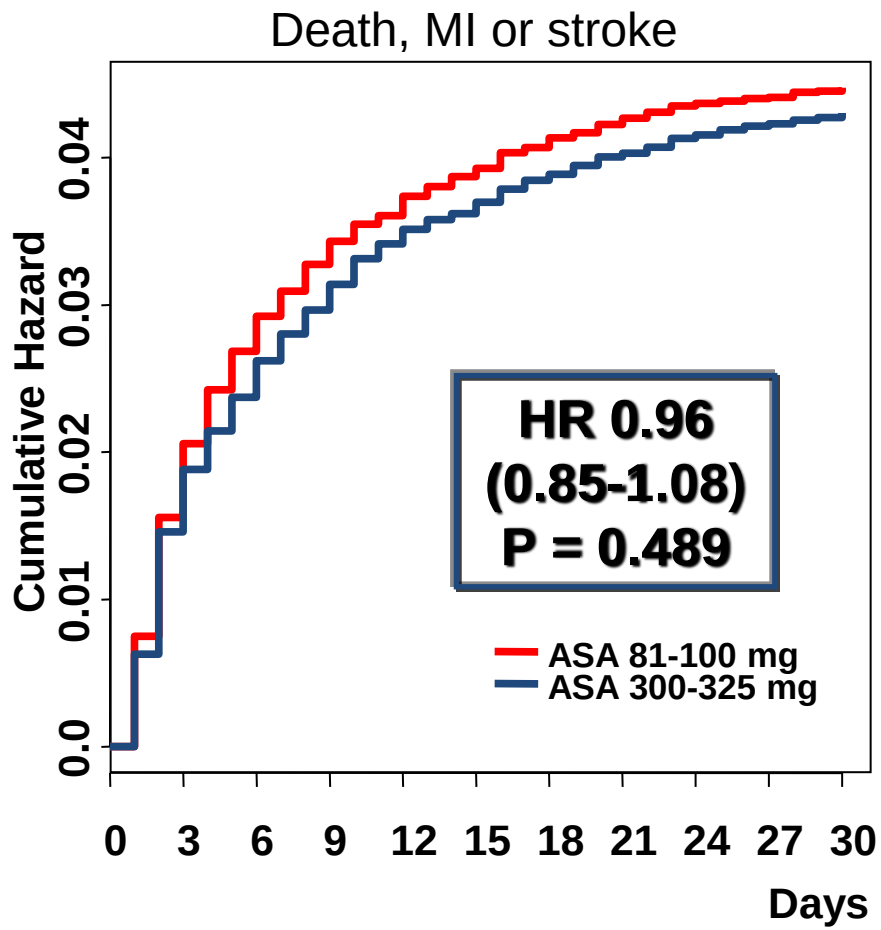
Oler et al. *JAMA* 1996;276:811;
***JAMA* 2004; 292: 45, 55, & 89**
Cavender MA and Sabatine MS.
***Lancet* 2014;384:599-606**

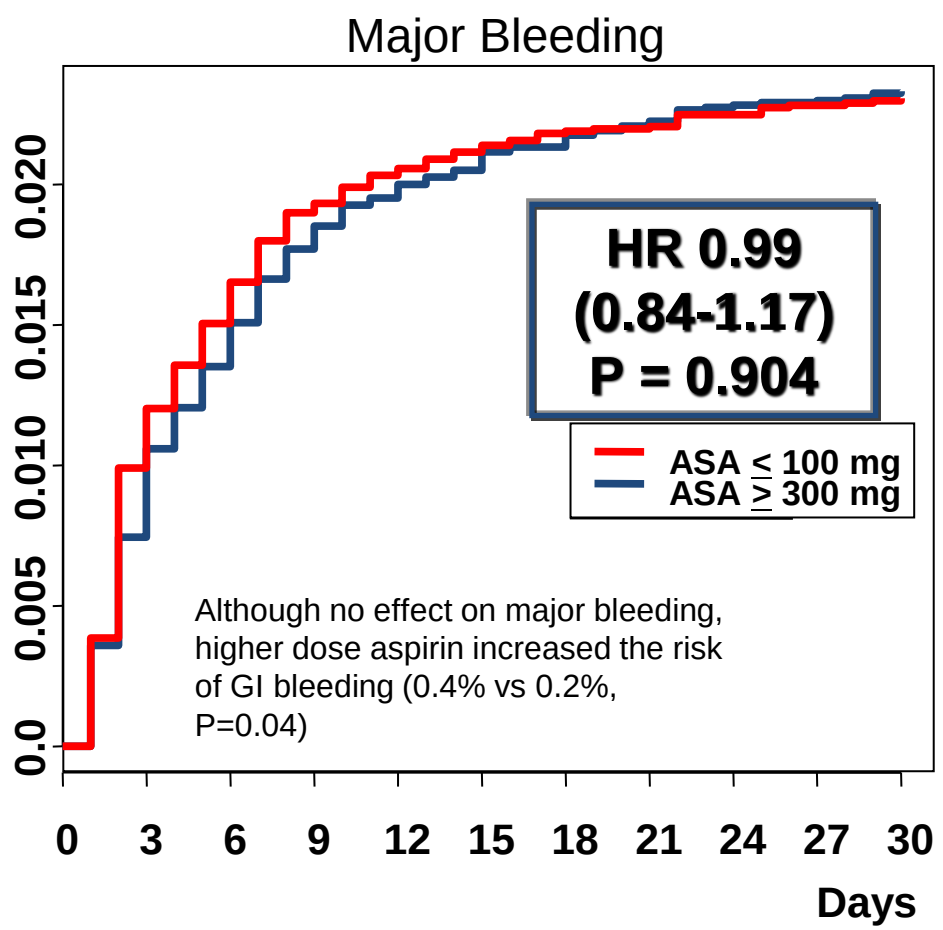
Anti-Platelet Therapies



Adapted from Schafer. *Am J Med*. 1996;101:199-209. Provided by M. O'Donoghue

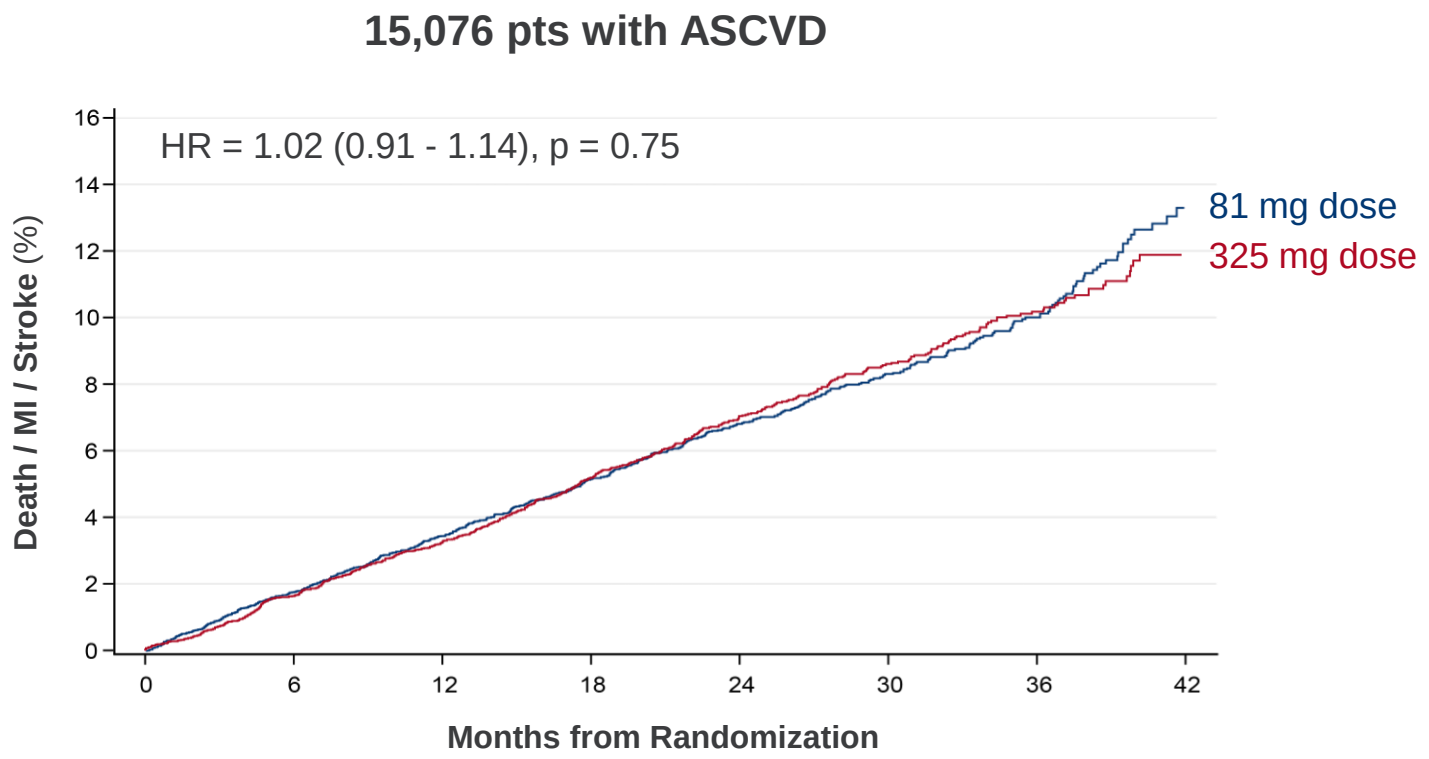
ASA: Is Dosing Still Controversial?





The CURRENT–OASIS 7 Investigators. *N Engl J Med* 2010;363:930-942

ADAPTABLE Trial



	Overall	81 mg	325 mg
Dose switching, % *	24.2%	7.1%	41.6%
Aspirin discontinuation, % **	9.1%	7.0%	11.1%

Jones WS et al. *NEJM* 2021;384:1981-1990

ACC / AHA Guideline Recommendations

Recommendations	COR	LOE
Non–enteric-coated, chewable aspirin (162 mg to 325 mg) should be given to *all* patients with NSTE-ACS without contraindications as soon as possible after presentation, and a maintenance dose of aspirin (81 mg/d to 162 mg/d) should be continued indefinitely.	I	A
In patients with NSTE-ACS who are unable to take aspirin because of hypersensitivity or major gastrointestinal intolerance, a loading dose of clopidogrel followed by a daily maintenance dose should be administered.	I	B

Amsterdam EA et al. *JACC* 2014;64.24: e139-e228

$P2Y_{12}$ Inhibitor Basic Pharmacology

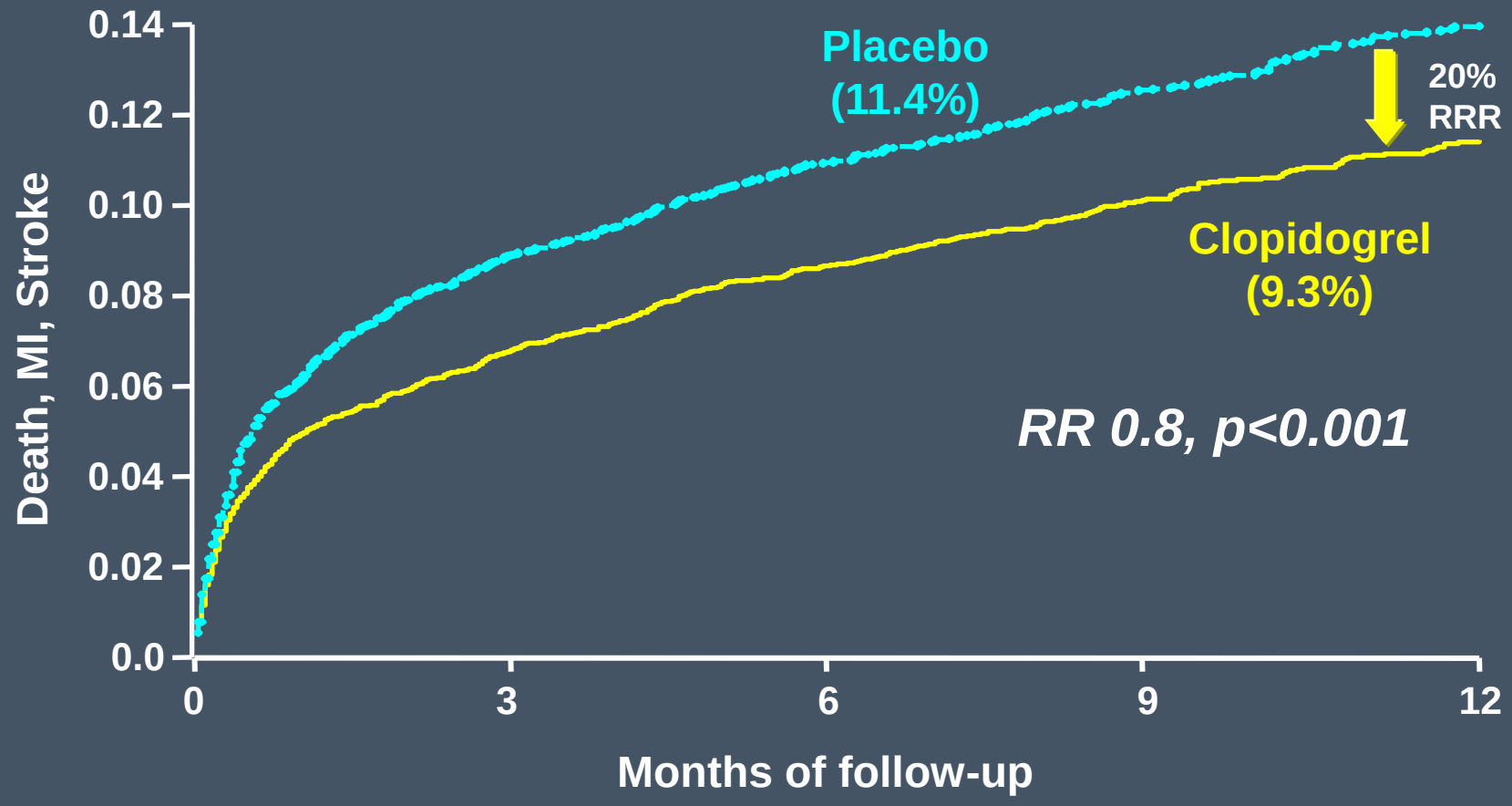
	Clopidogrel	Prasugrel	Ticagrelor
Class	Thienopyridine	Thienopyridine	Triazolopyrimidine
Reversibility	Irreversible	Irreversible	Reversible
Activation	Prodrug, limited by metabolism	Prodrug, not limited by metabolism	Active drug
Onset of Effect*	2-4 hours	30 minutes	30 minutes
Duration of Effect	3-10 days	5-10 days	3-4 days
Withdrawal before major surgery	5 days	7 days	5 days

*50% inhibition of platelet aggregation

Hamm CW, et al. Eur Heart J. 2011.

Clopidogrel in UA/NSTEMI: The CURE Trial

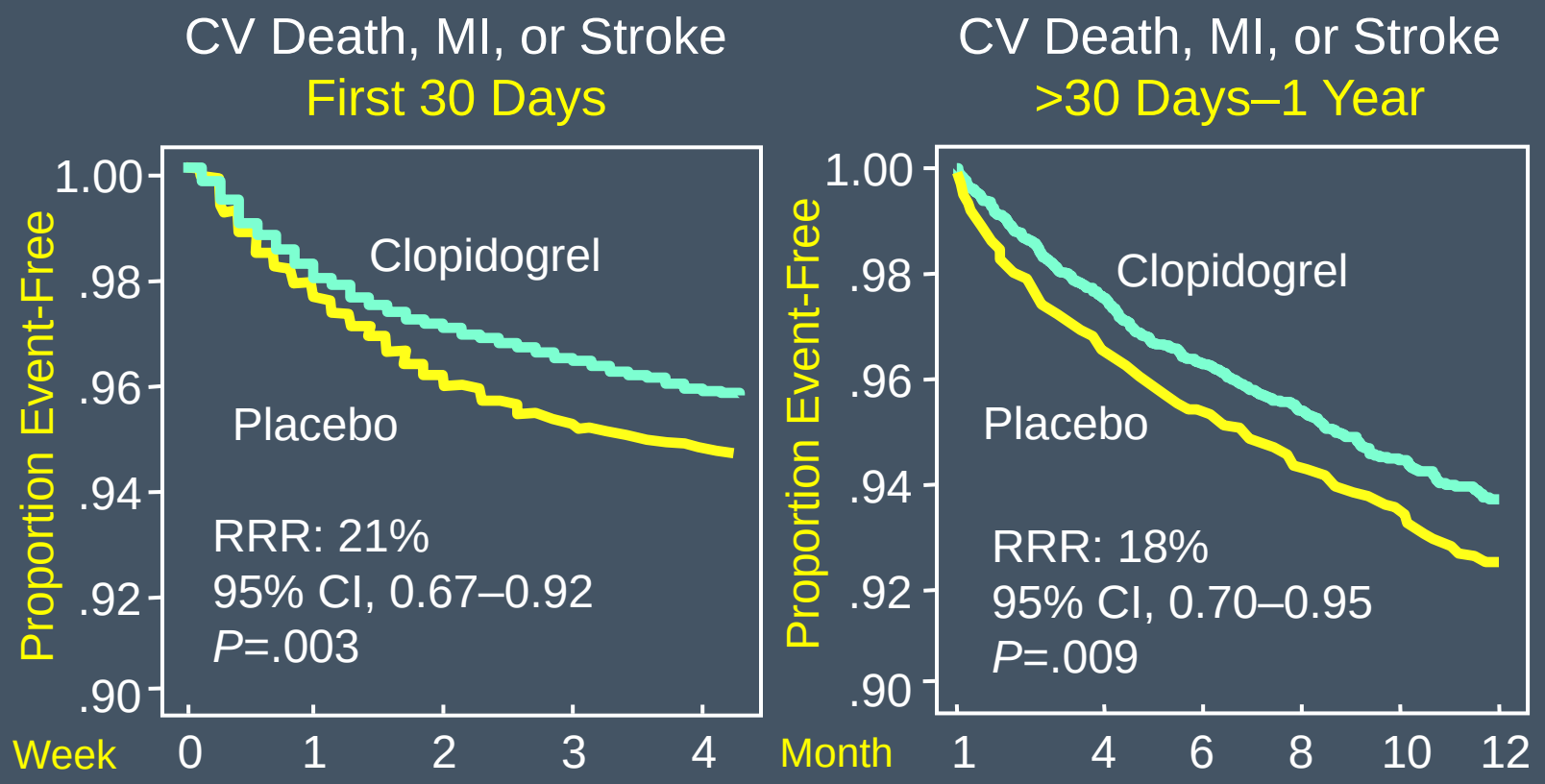
12,563 Pts, early invasive approach *discouraged*



The CURE Investigators. *NEJM* 2001;345:494

CURE: Timing of Benefit

12,562 Patients with NSTEACS (mostly conservatively managed)



Yusuf S, et al. *Circulation*. 2003;107:966-972.

CURE Bleeding Results

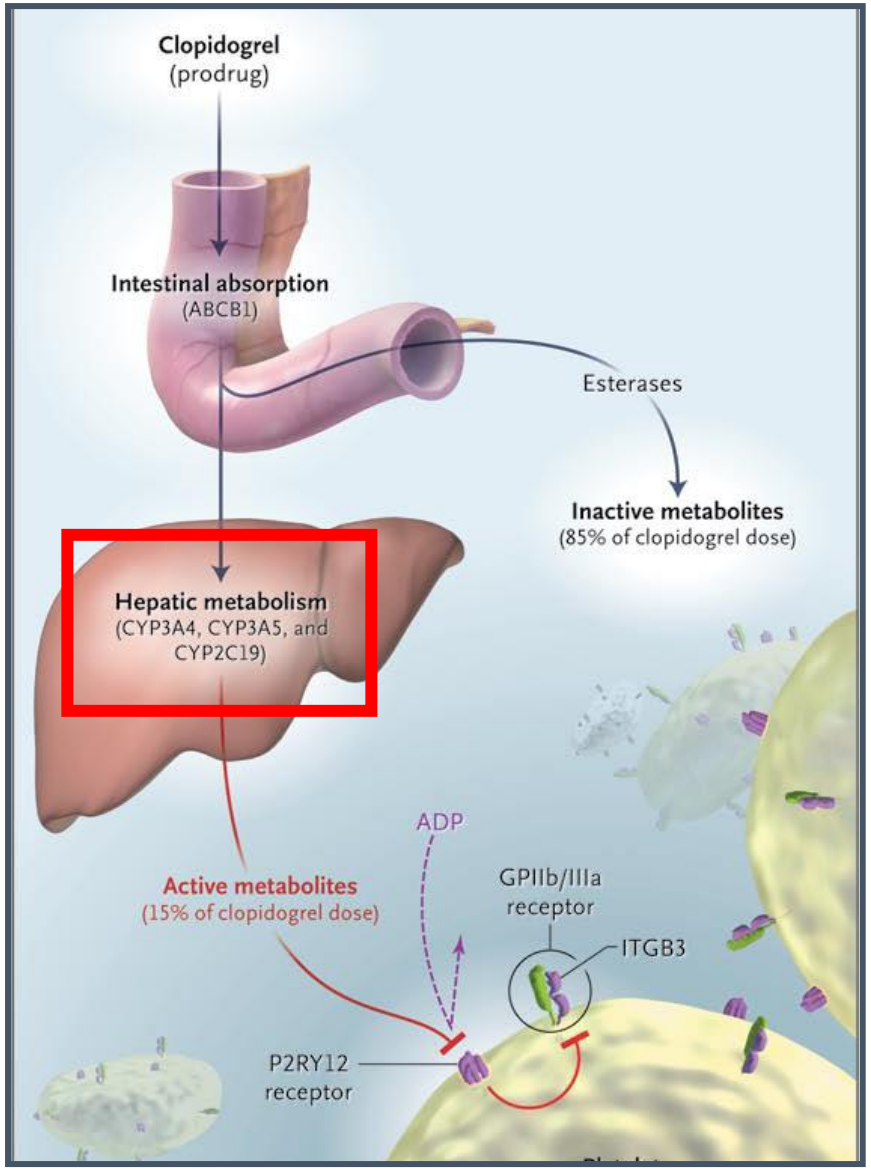
End Point	Placebo + ASA* N = 6303	Clopidogrel + ASA* N = 6259
Major bleeding	2.7%	3.7%**
Life-threatening bleeding	**1.8%**	**2.2%** †
Non-life-threatening bleeding	**0.9%**	**1.5%** ‡
Minor bleeding	2.4%	5.1% §

* In combination with standard therapy

** $P = 0.001$; † P = NS; ‡ $P = 0.002$; § $P < 0.001$.

The CURE Trial Investigators. *N Engl J Med.* 2001;345:494-502.

Clopidogrel pro-drug → Active metabolite



300mg loading dose of clopidogrel requires ~6 hours to reach steady state

Simon T et al. *N Engl J Med* 2009

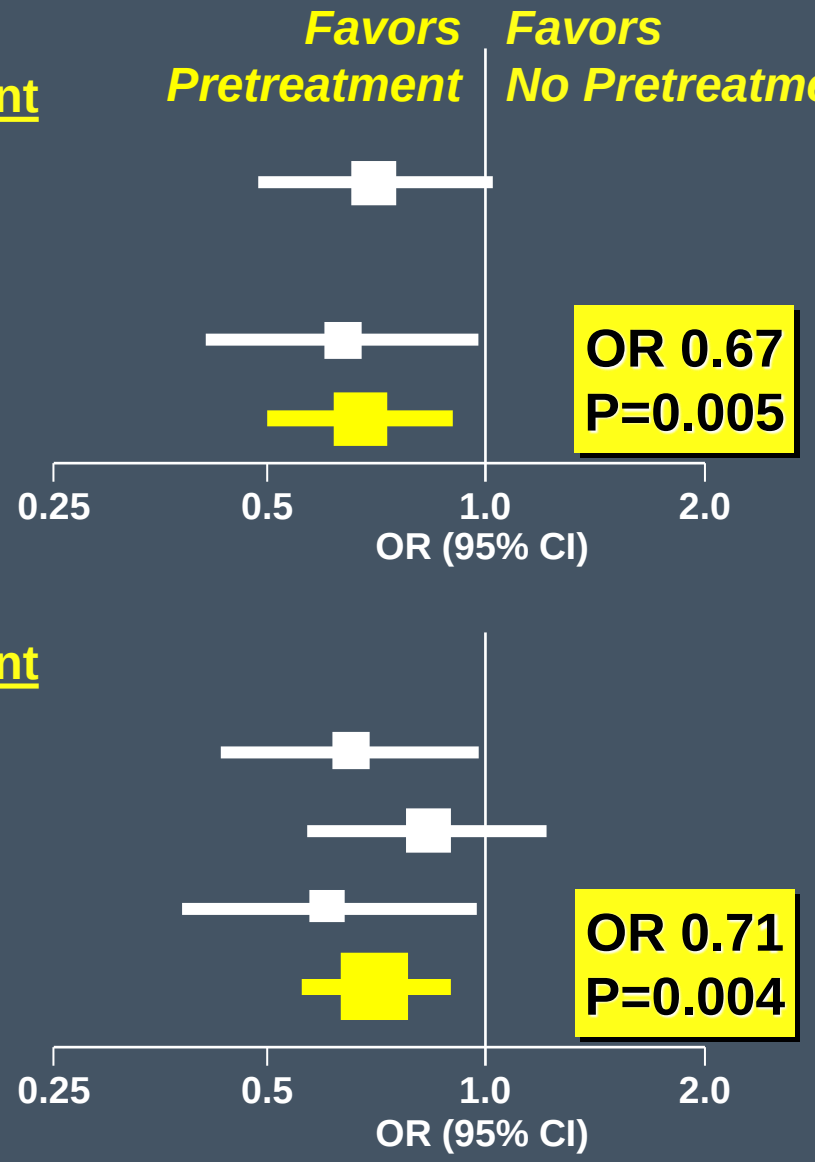
Meta-Analysis of Clopidogrel Pretreatment

MI before PCI (%)

Trial	Clopidogrel Pretreatment	No Pretreatment
PCI-CURE	3.6	5.1
CREDO	n/a	n/a
PCI-CLARITY	4.0	6.1
Overall	3.7	5.5

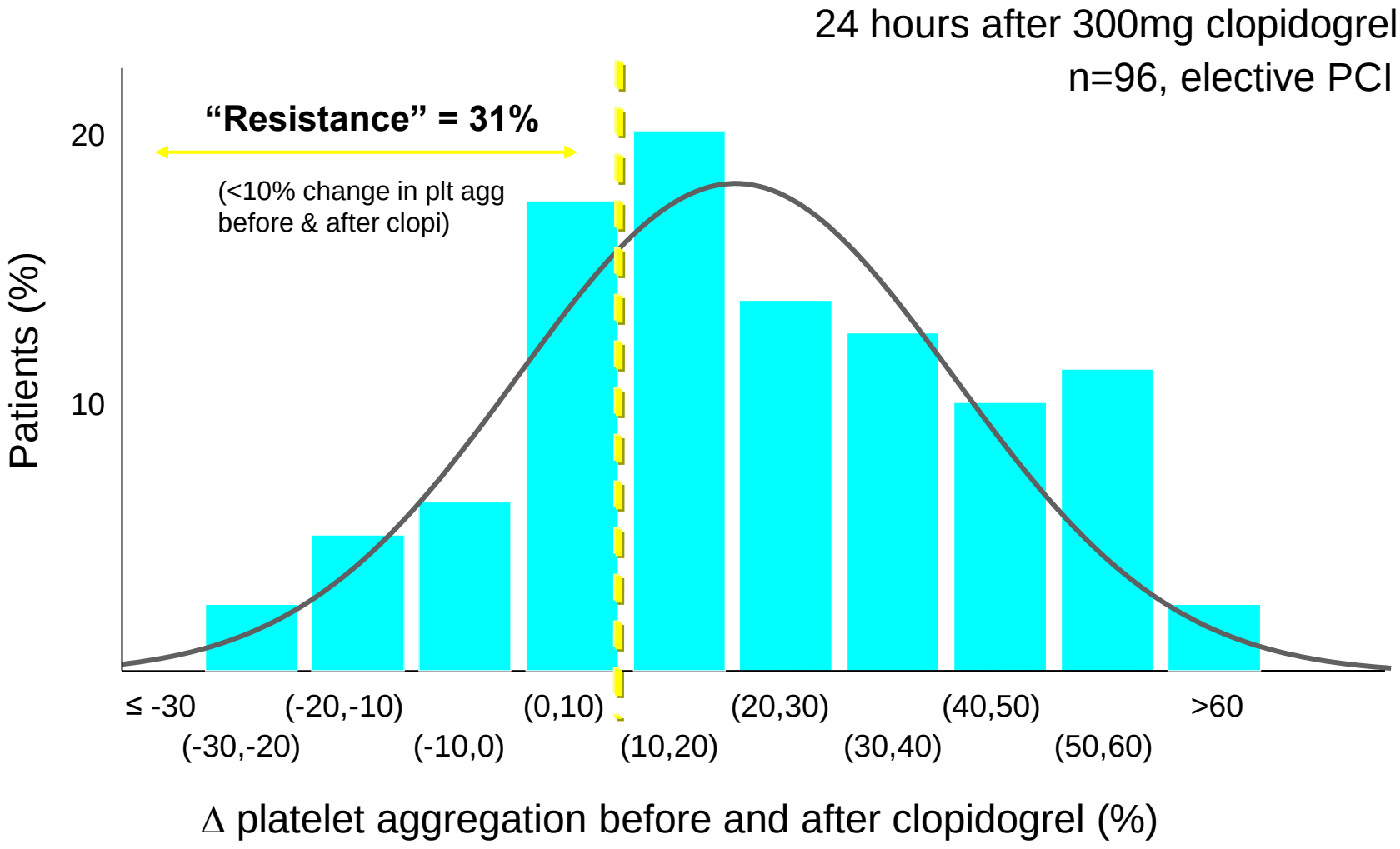
CV Death or MI after PCI (%)

Trial	Clopidogrel Pretreatment	No Pretreatment
PCI-CURE	2.9	4.4
CREDO	6.0	7.1
PCI-CLARITY	3.3	5.4
Overall	3.9	5.5



Sabatine MS et al. *JAMA* 2005; 294: 1224

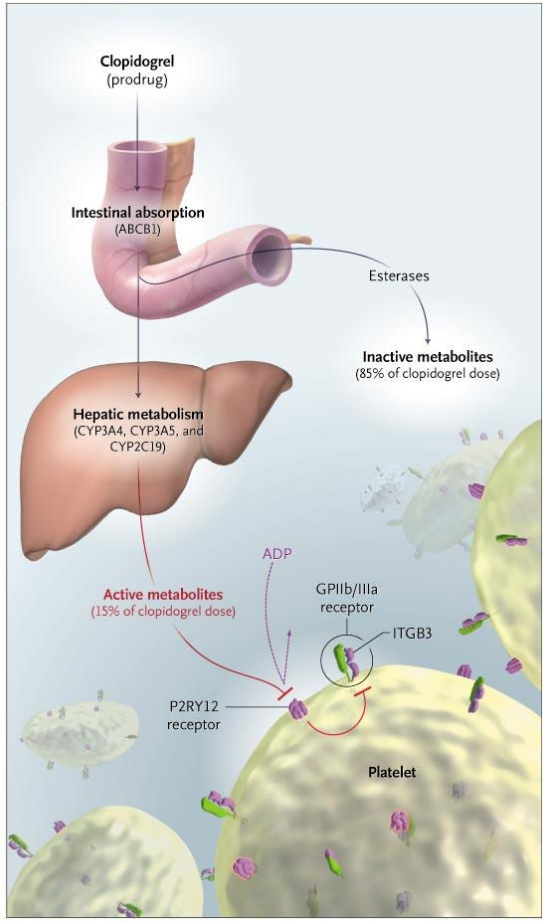
Interpatient Variability to Clopidogrel



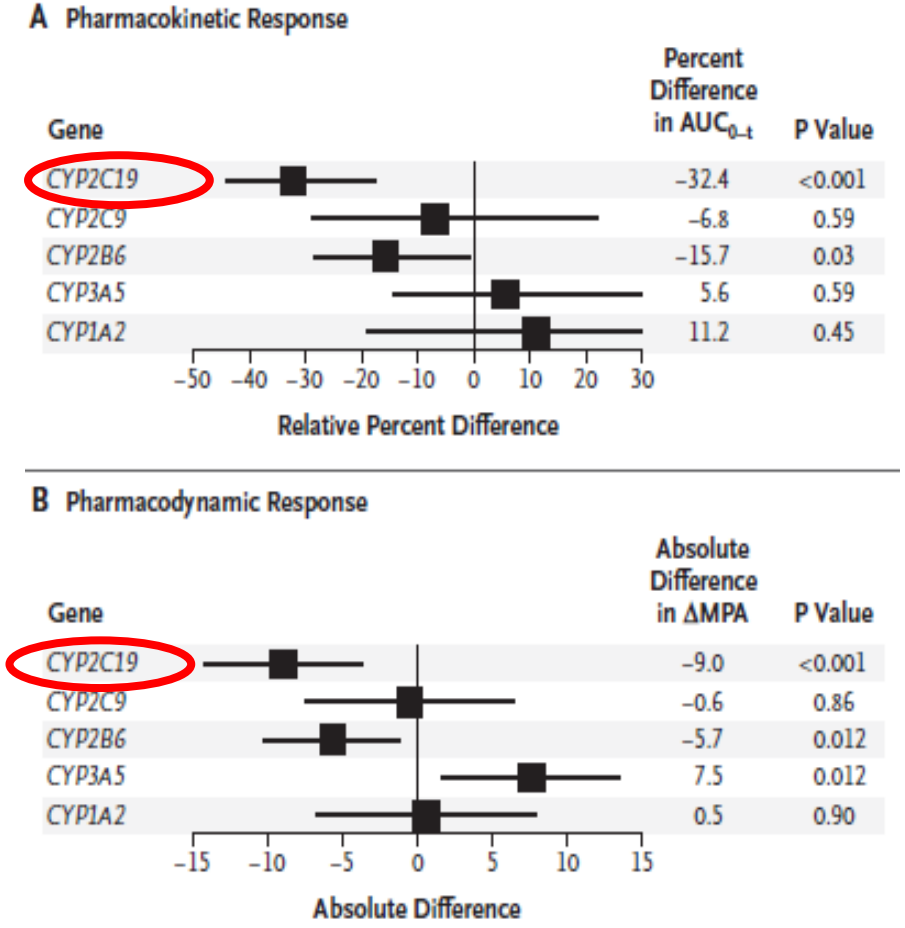
"Resistance" = ≤10% Δ platelet aggregation

Gurbel PA, et al. *Circulation* 2003;107: 2908

CYP2C19 and Metabolism of Clopidogrel



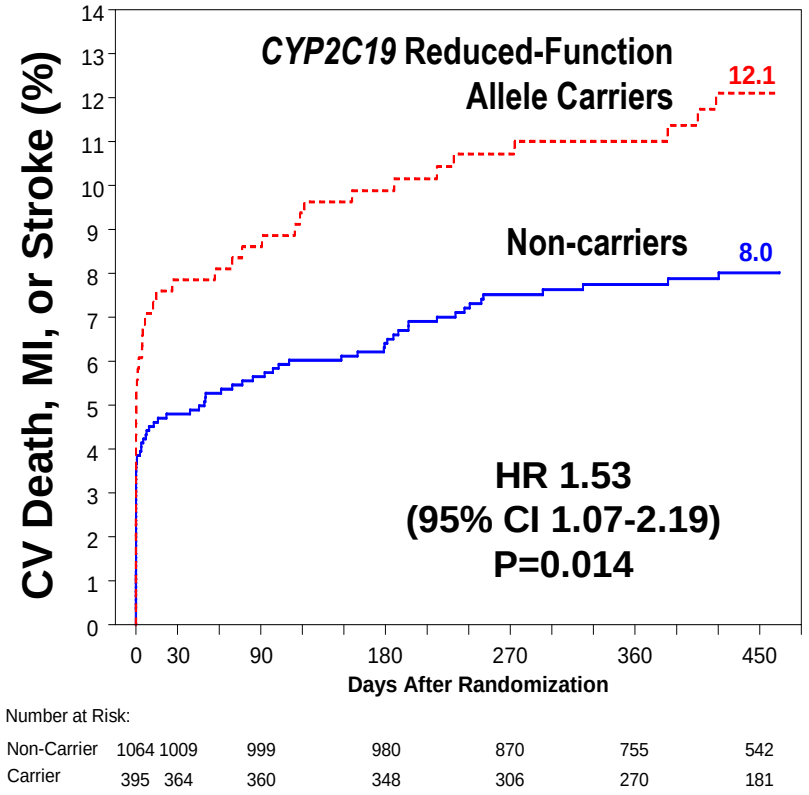
Simon T. et al. *NEJM* 2008.

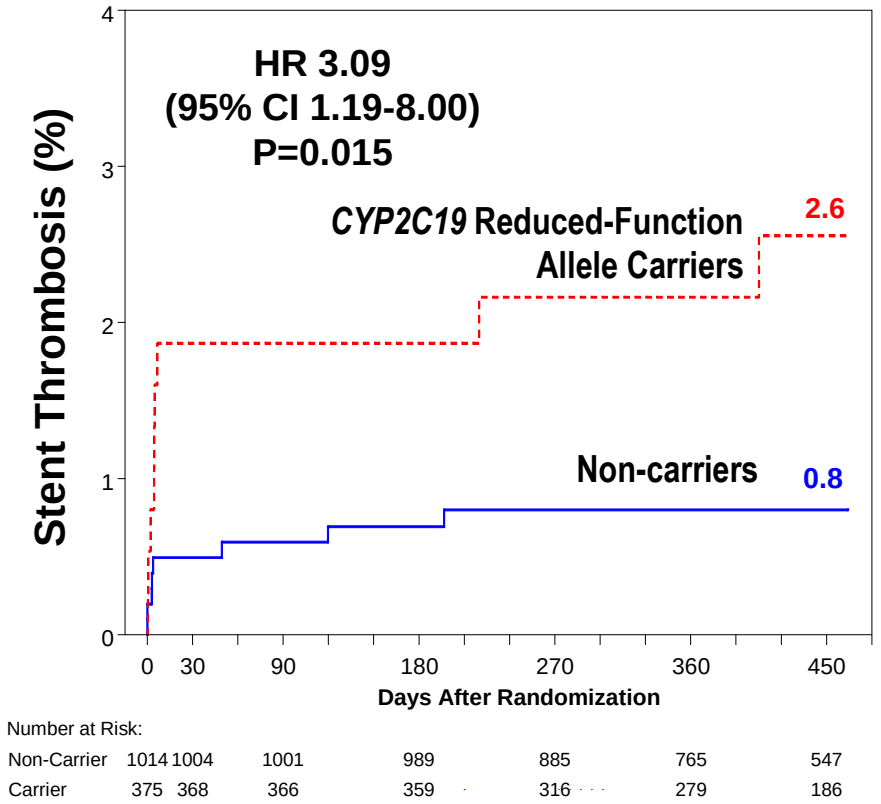


Mega et al. *NEJM* 2008.

CYP2C19 & Clinical Outcomes

1477 Patients w/ ACS and planned PCI Rx'd w/ clopidogrel





Carriers ~30% of the population

Mega JL. *N Engl J Med* 2009;360:354-62.

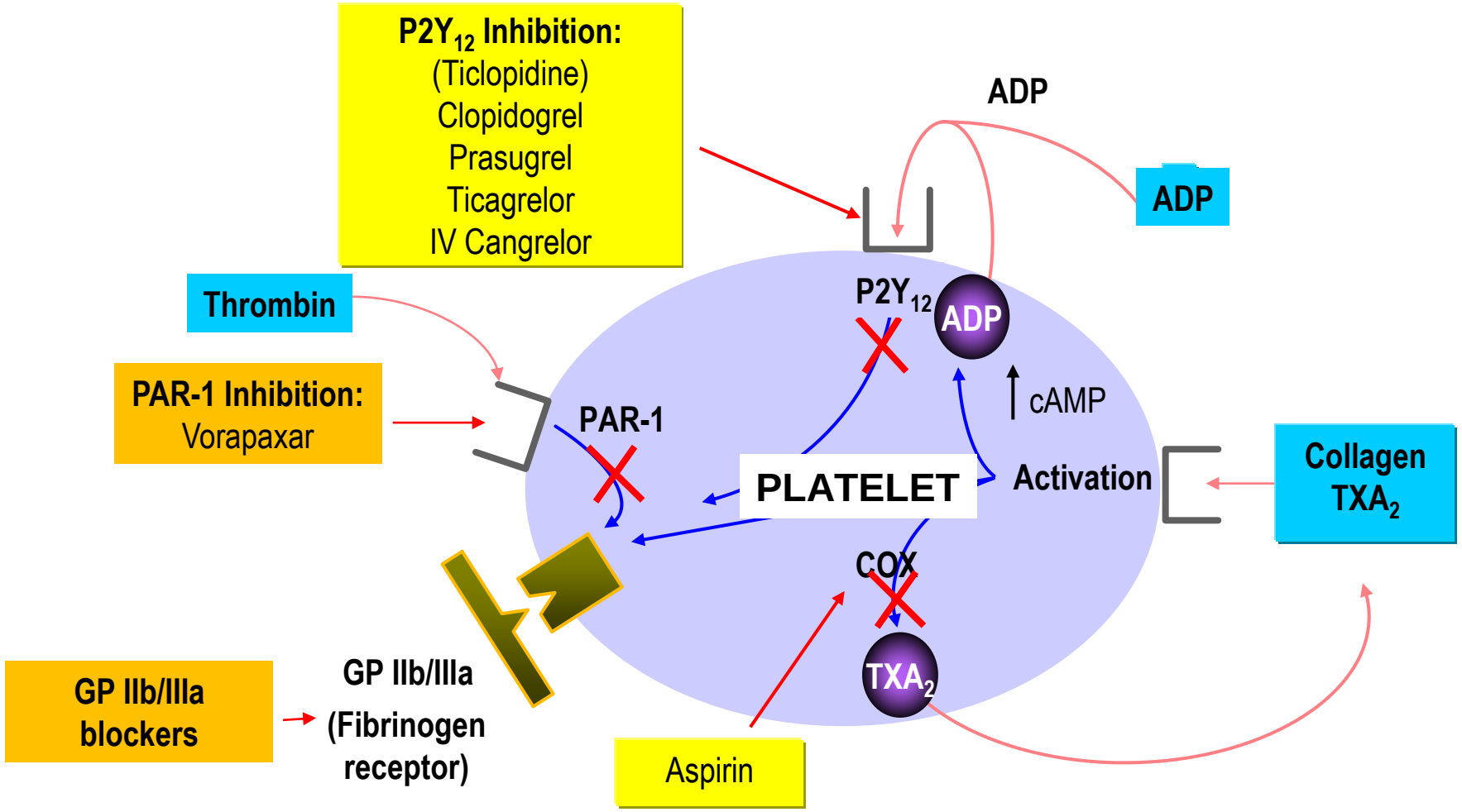
Clopidogrel Boxed Warning

WARNING: DIMINISHED EFFECTIVENESS IN POOR METABOLIZERS

The effectiveness of Plavix is dependent on its activation to an active metabolite by the cytochrome P450 (CYP) system, principally CYP2C19. Plavix at recommended doses forms **less of that metabolite** and has a **smaller effect on platelet function** in patients who are CYP2C19 poor metabolizers. Poor metabolizers with acute coronary syndrome or undergoing percutaneous coronary intervention treated with Plavix at recommended doses exhibit **higher cardiovascular event rates** than do patients with normal CYP2C19 function. Tests are available to identify a patient's CYP2C19 genotype; these tests can be used as an aid in determining therapeutic strategy. **Consider alternative treatment or treatment strategies in patients identified as CYP2C19 poor metabolizers.**

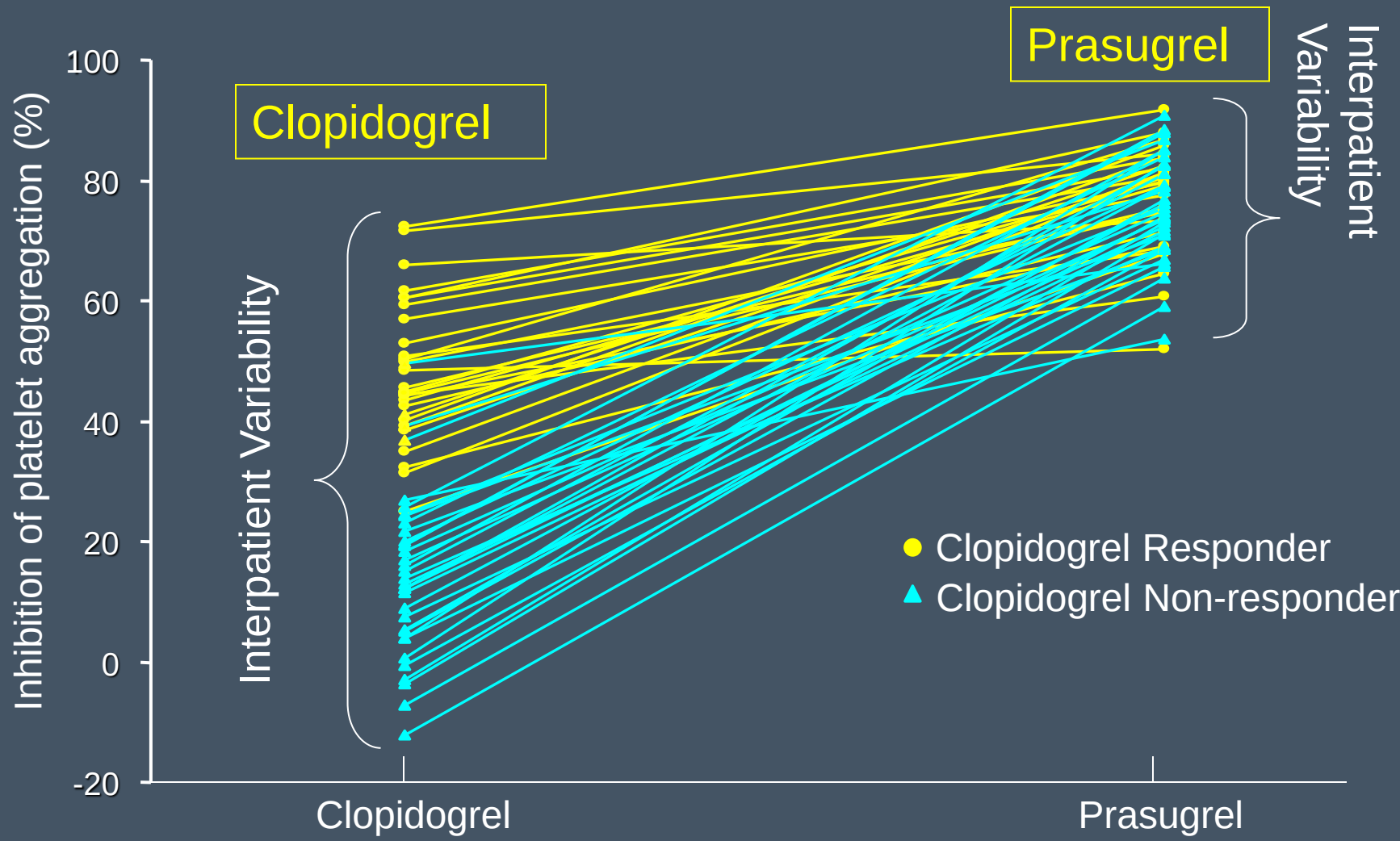
Clopidogrel Label 3/12/2010

Anti-Platelet Therapies



Adapted from Schafer. *Am J Med*. 1996;101:199-209. Provided by M. O'Donoghue

Clopidogrel vs Prasugrel

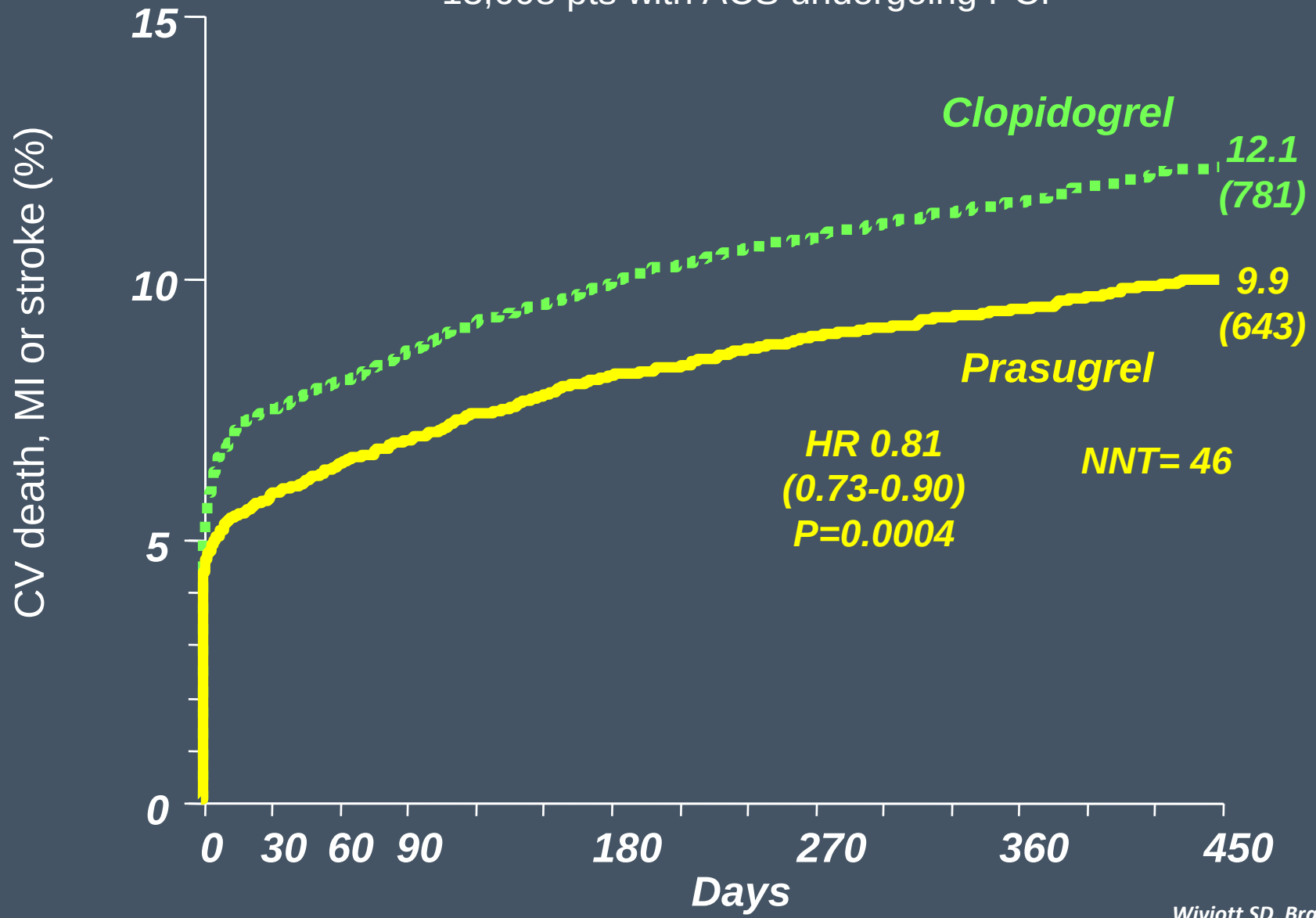


Responder = ≥25% plt inhibition at 4 & 24 h

Brandt et al. *Am Heart J* 2006;153:66.

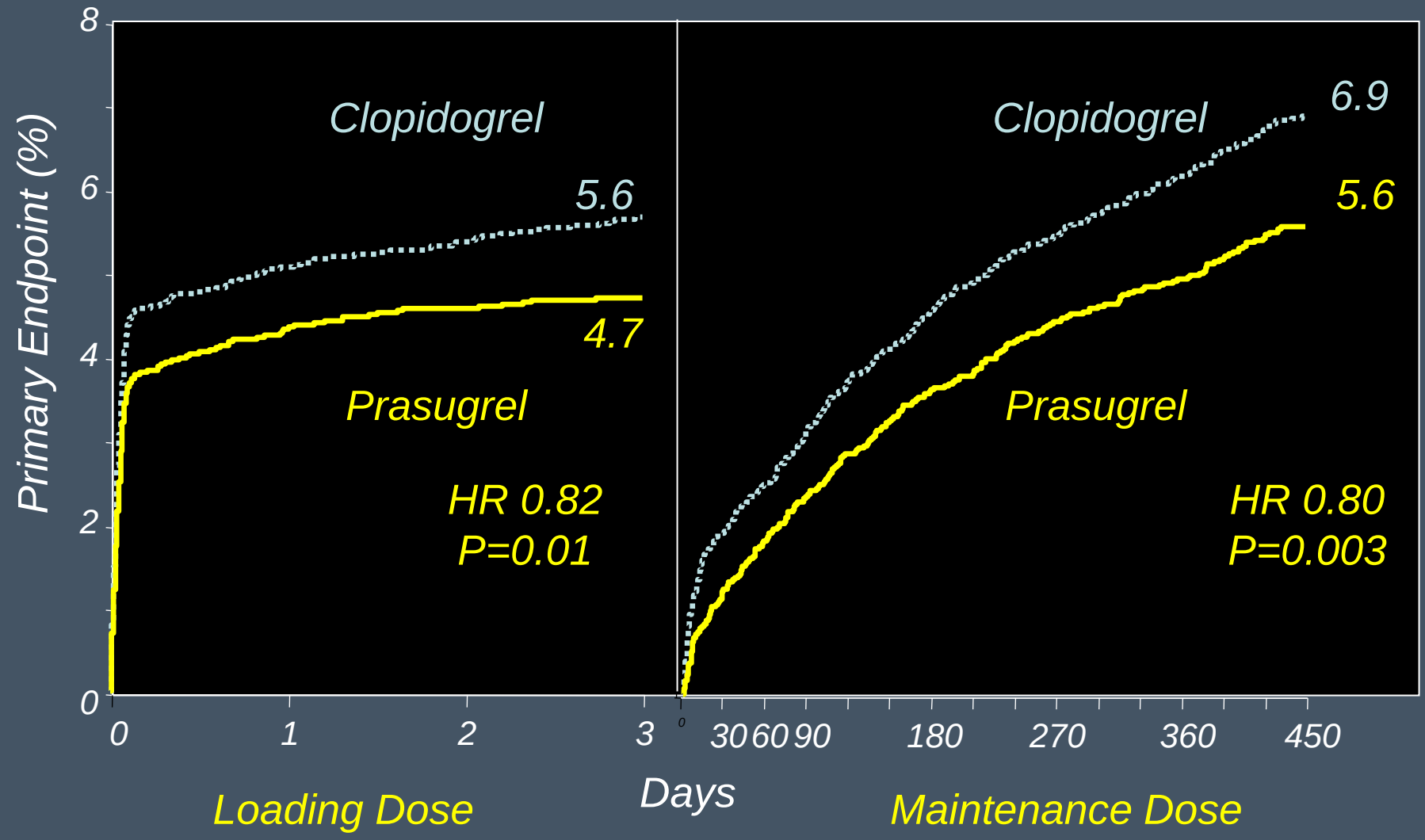
TRITON-TIMI 38 Trial

13,608 pts with ACS undergoing PCI



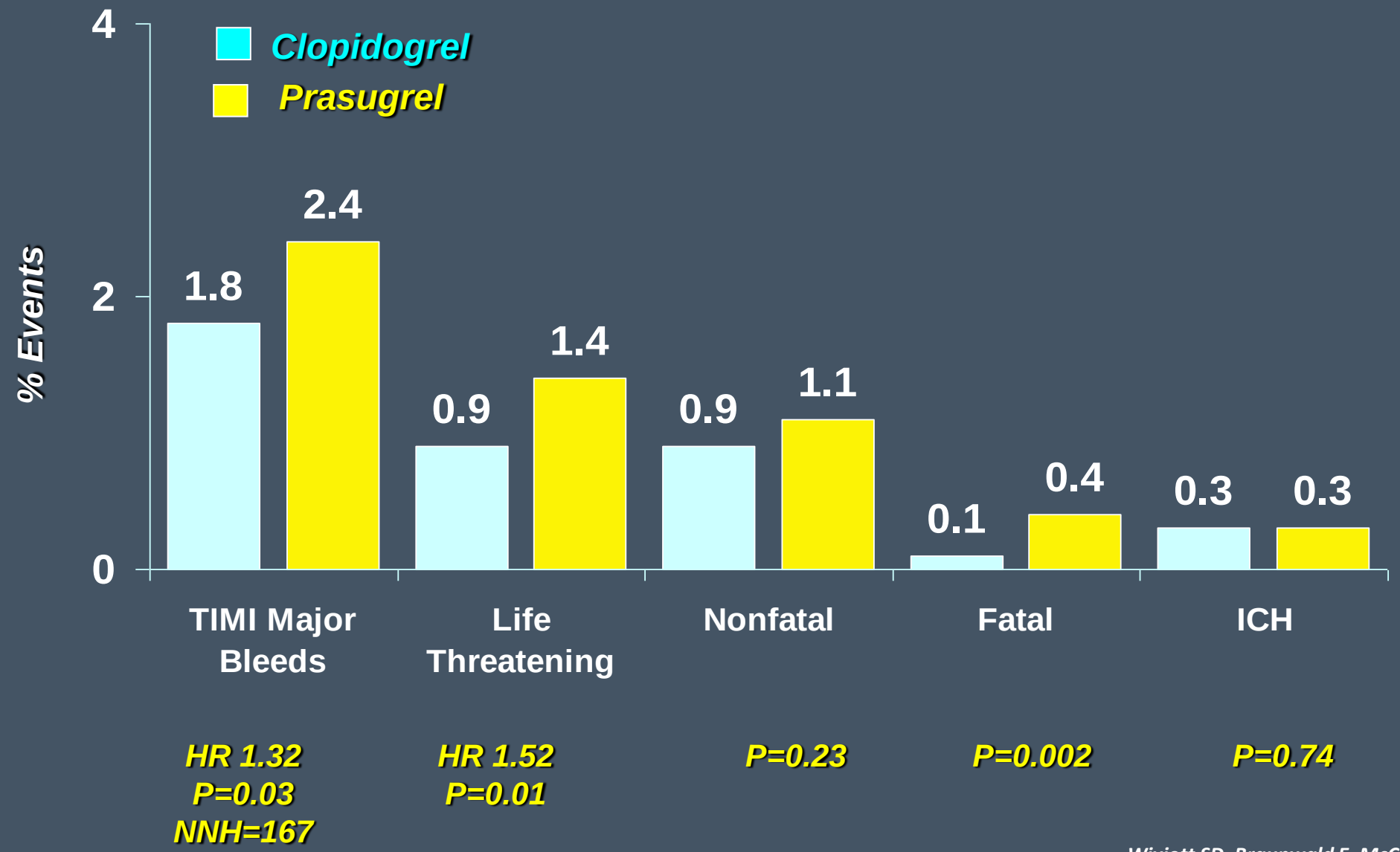
Wiviott SD, Braunwald E, McCabe CH et al NEJM2007

Timing of Benefit
(Landmark Analysis)



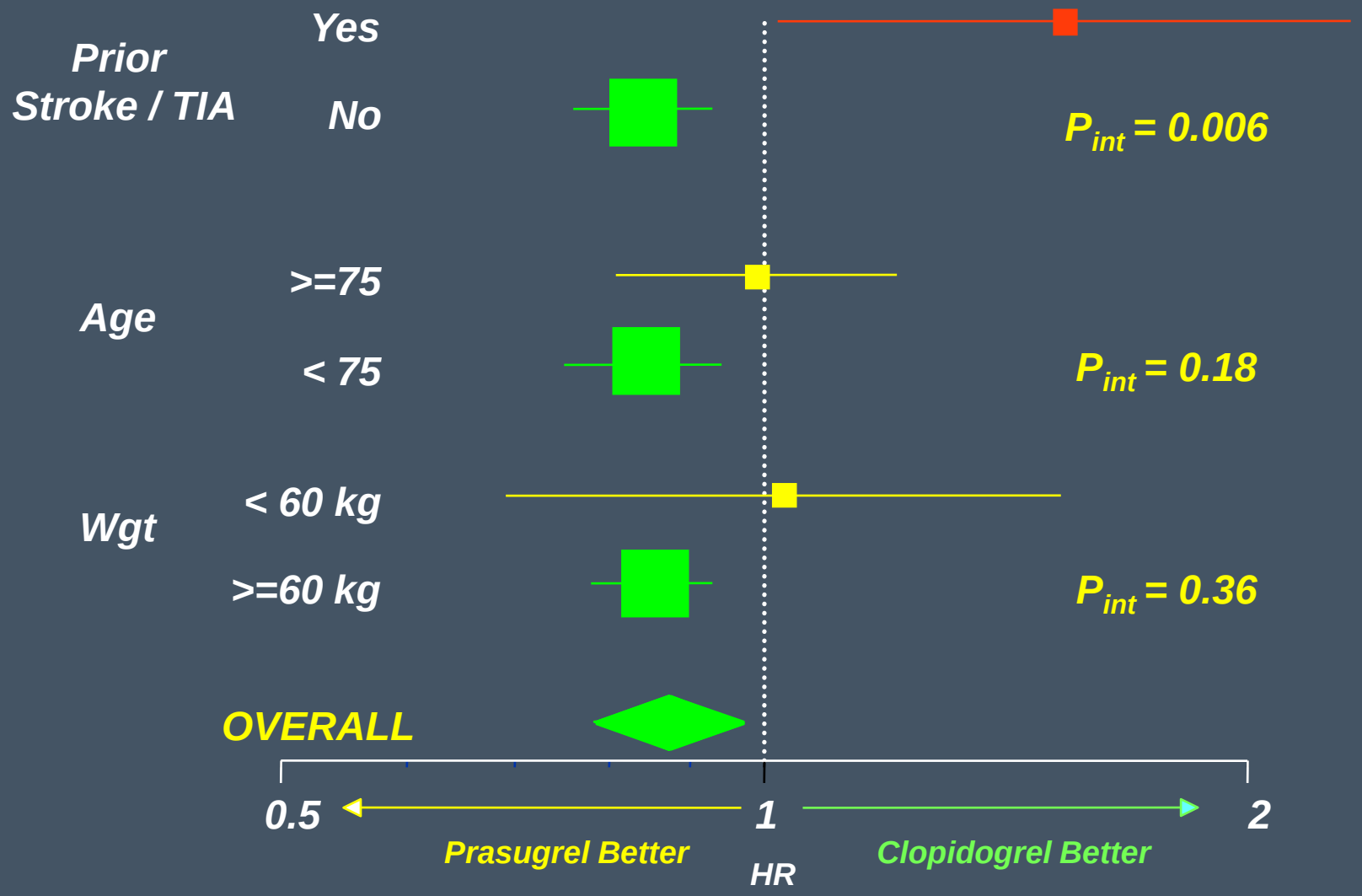
Wiviott SD et al. *NEJM* 2007;357:2001-15

Bleeding with Prasugrel



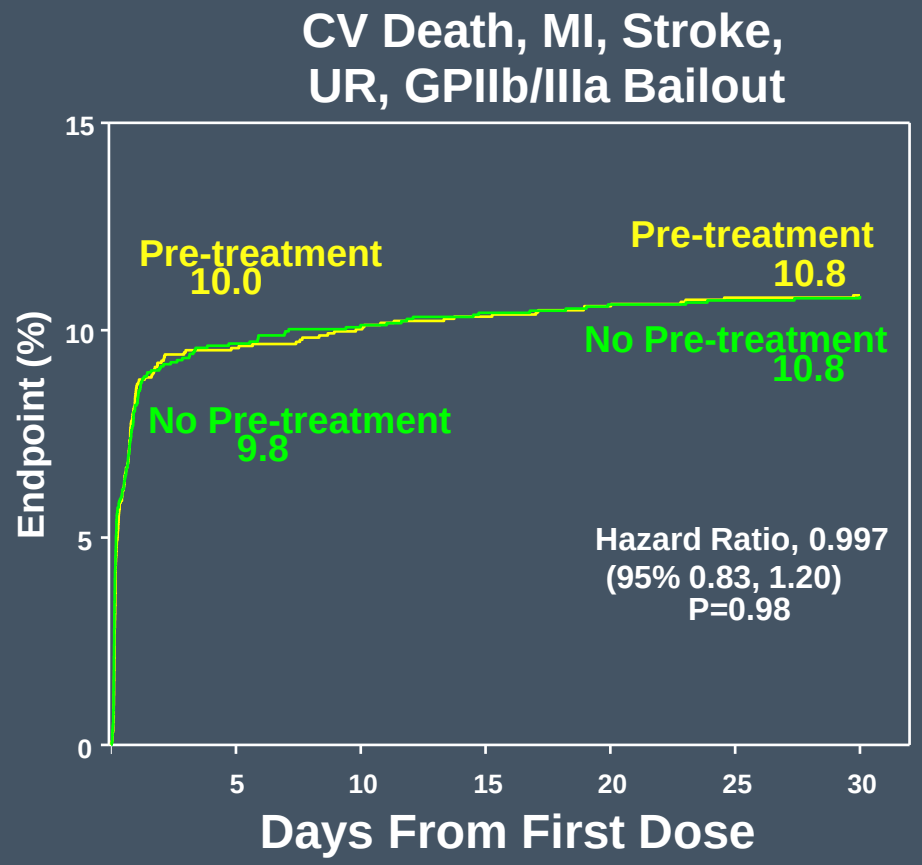
Wiviott SD, Braunwald E, McCabe CH et al NEJM2007

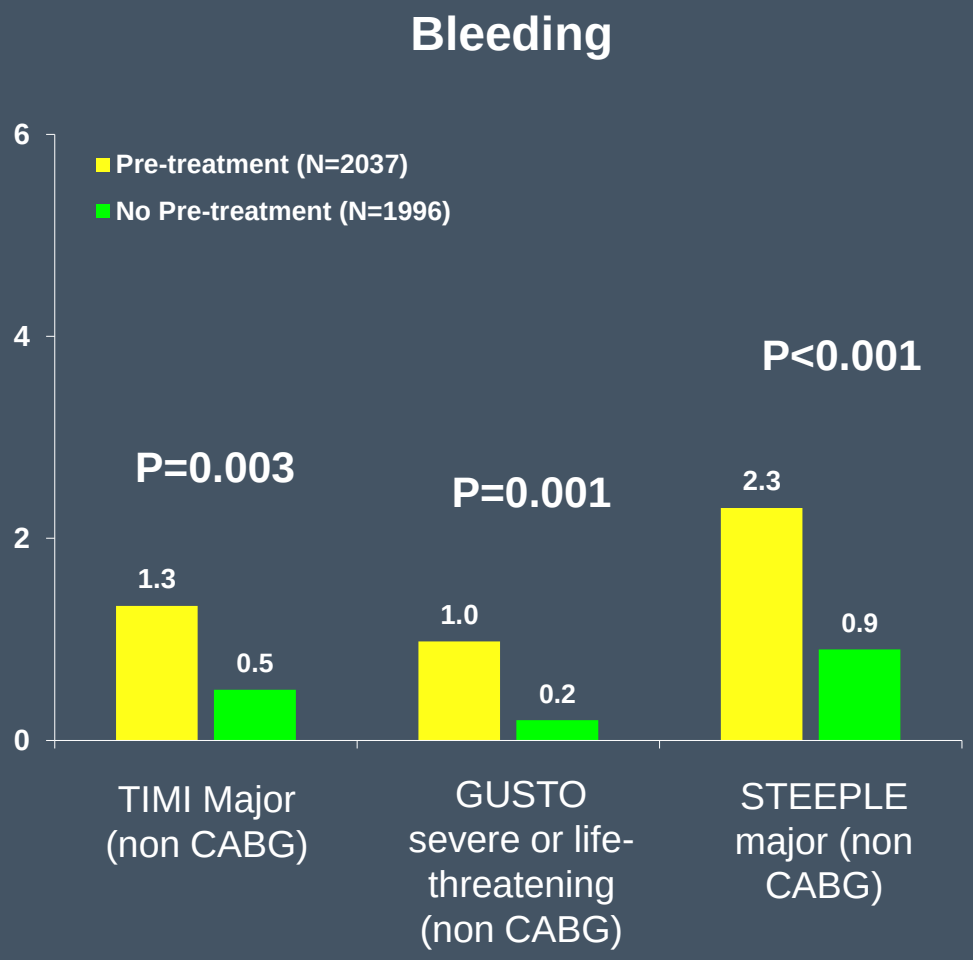
Who shouldn't get prasugrel?



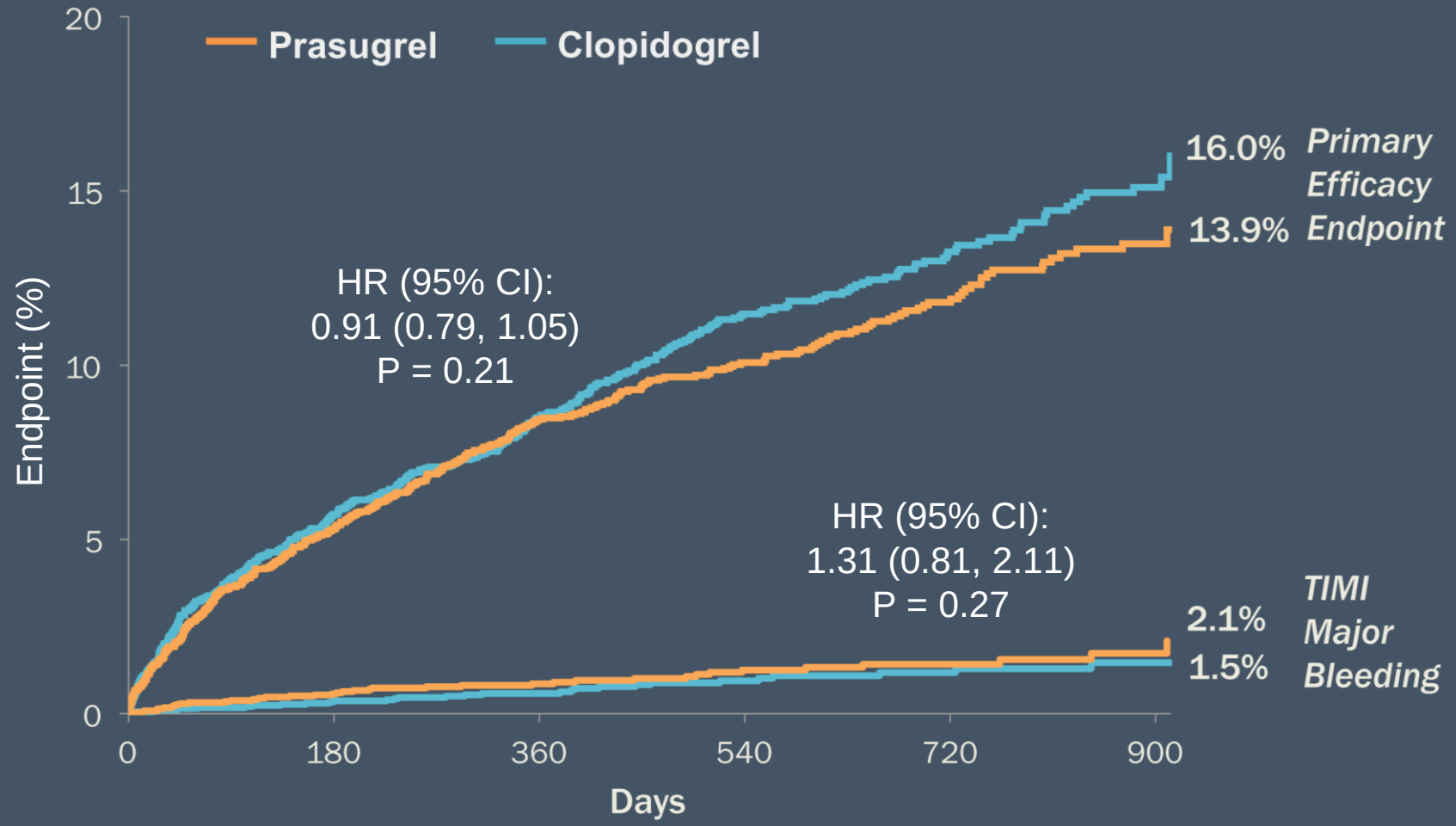
Wiviott SD, Braunwald E, McCabe CH et al NEJM2007

No Benefit to Pre-Treat with Prasugrel Prior to PCI in NSTE-ACS



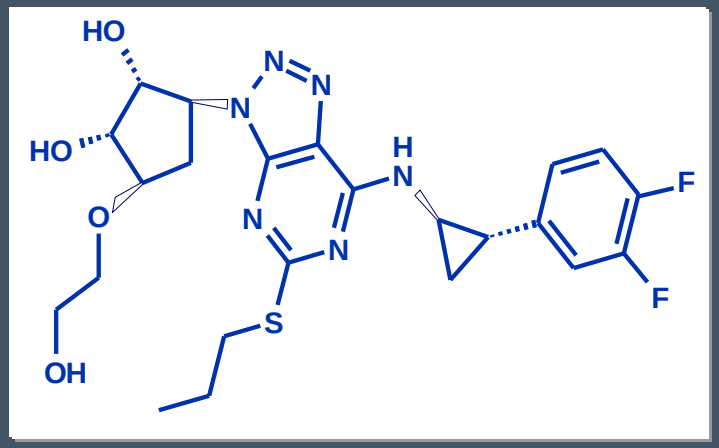


TRILOGY-ACS: No Benefit for Prasugrel in Medically Managed Patients Without PCI



Roe MT et al NEJM 2012

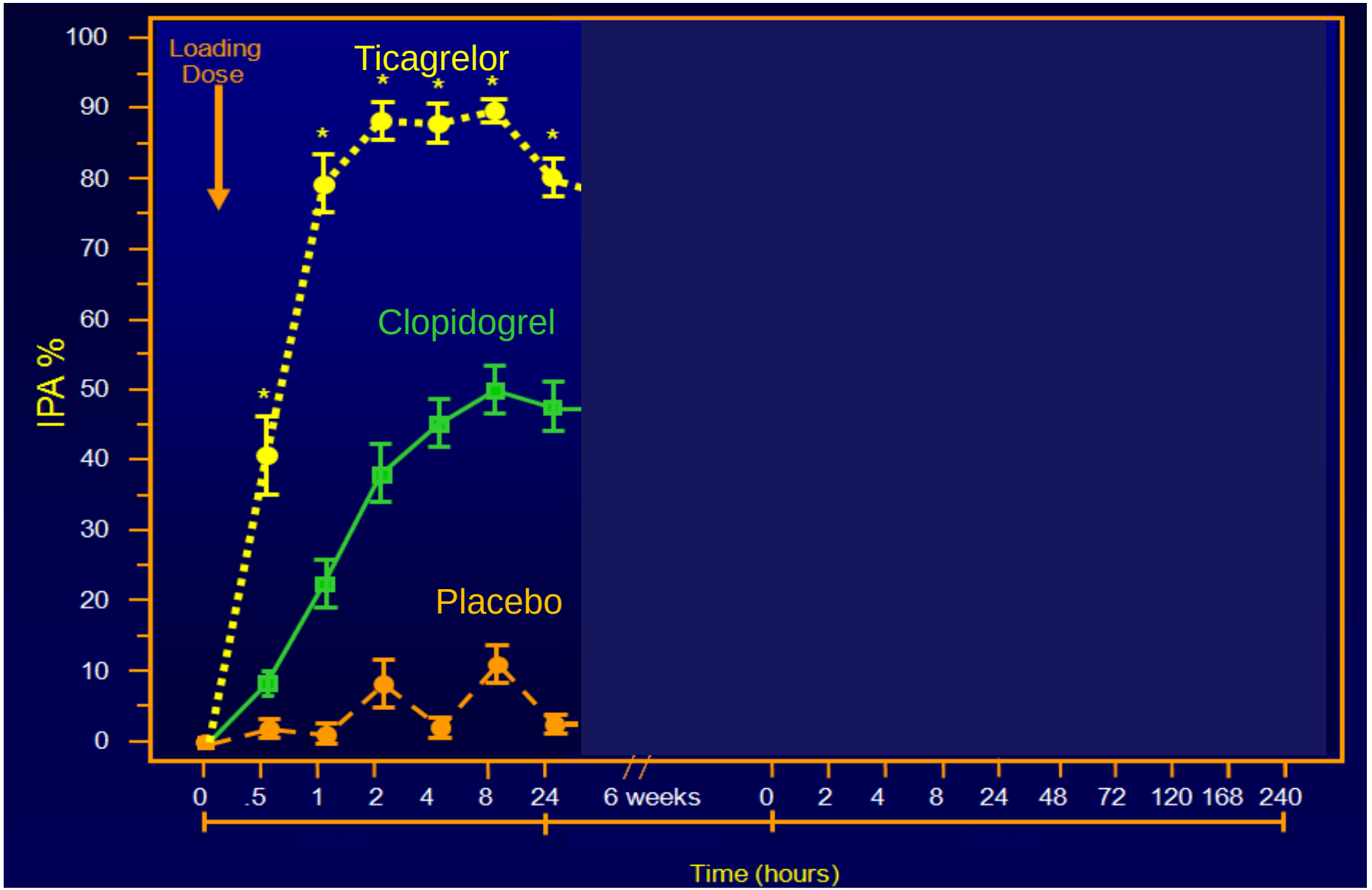
Ticagrelor: an Oral Reversible $P2Y_{12}$ Antagonist



Ticagrelor is a cyclo-pentyl-triazolo-pyrimidine (CPTP) and not a thienopyridine

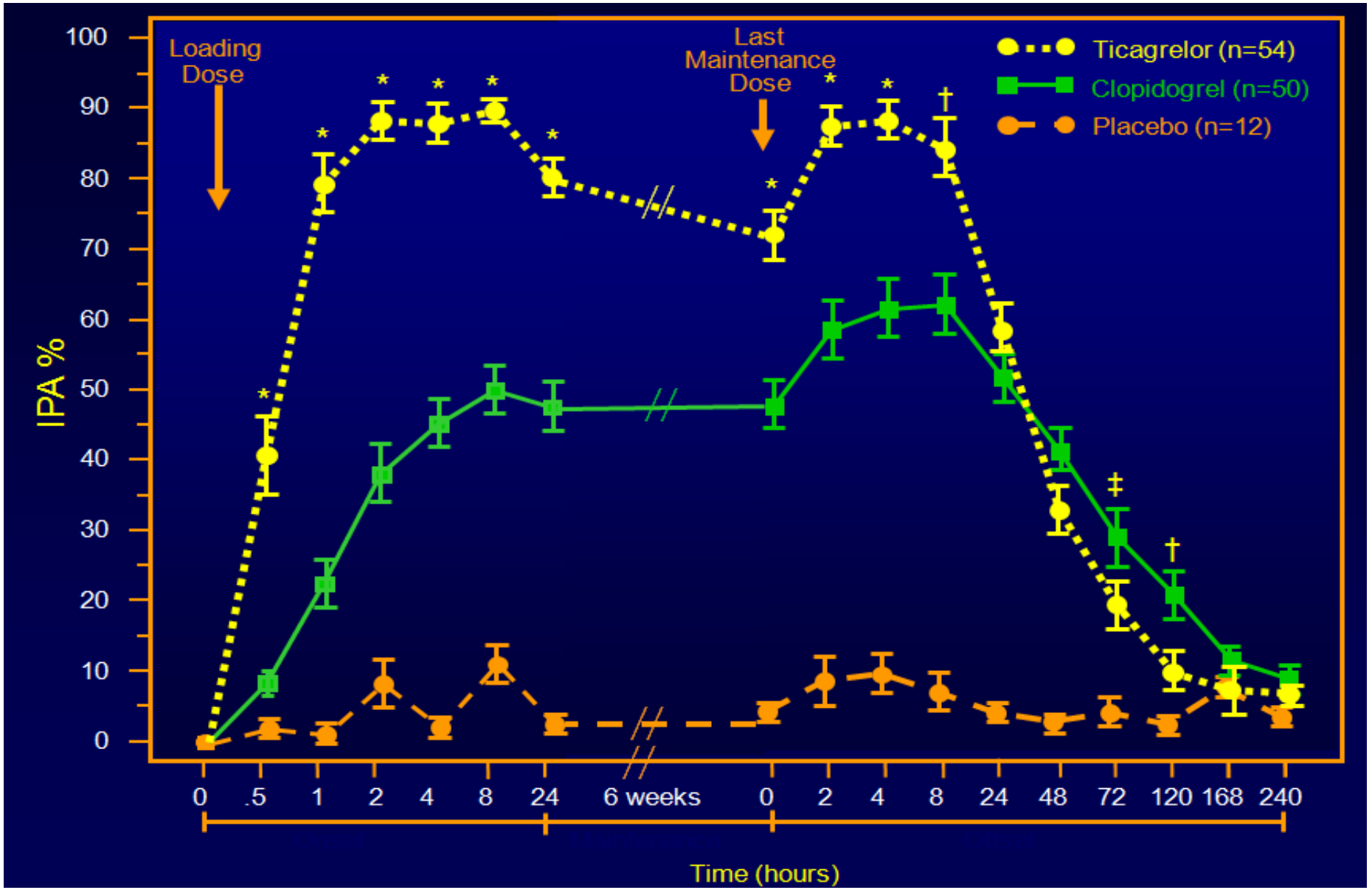
- Direct acting
  - Not a prodrug; does not require metabolic activation
  - Rapid onset of inhibitory effect on the $P2Y_{12}$ receptor
  - Greater inhibition of platelet aggregation than clopidogrel
- Reversibly bound
  - Degree of inhibition reflects plasma concentration
  - Faster offset of effect than clopidogrel
  - Functional recovery of all circulating platelets

Ticagrelor Pharmacodynamics



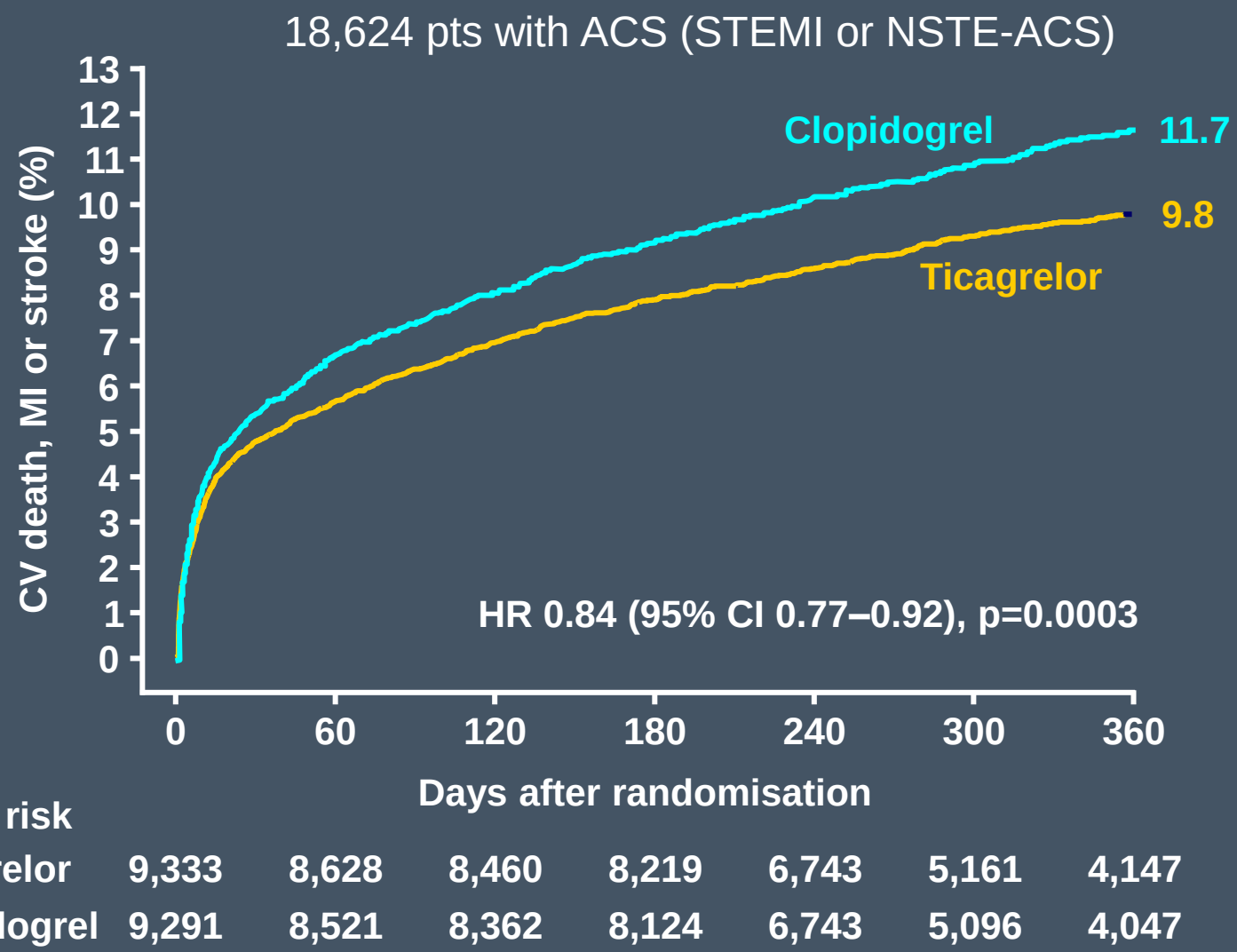
Gurbel PA, et al. Circulation 2009;120;2577-2585

Ticagrelor Pharmacodynamics



Gurbel PA, et al. Circulation 2009;120;2577-2585

PLATO Trial Results

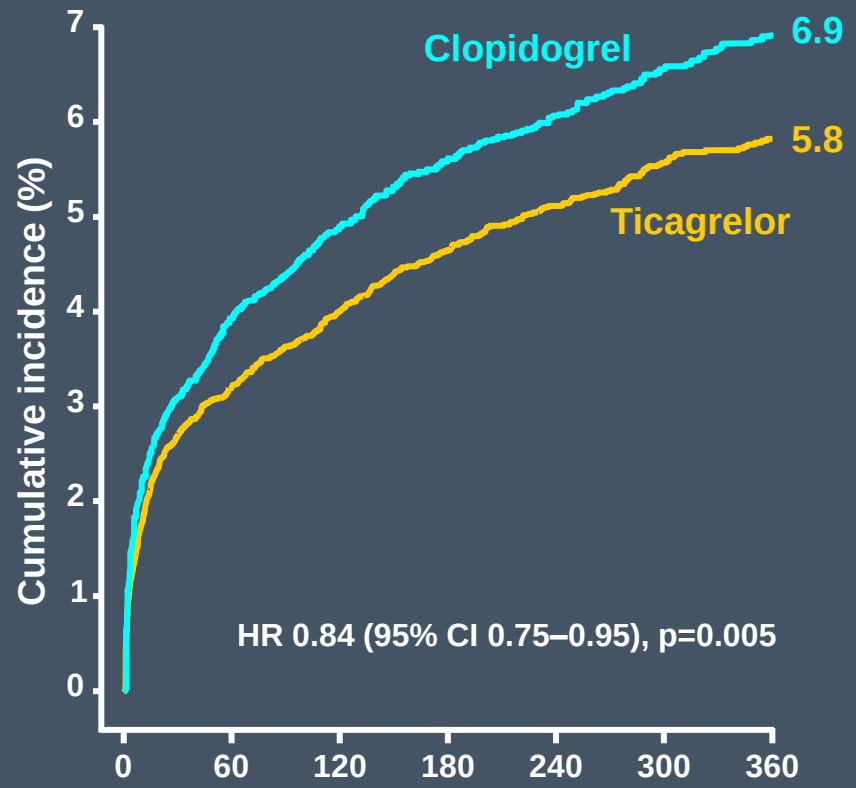


No. at risk							
Ticagrelor	9,333	8,628	8,460	8,219	6,743	5,161	4,147
Clopidogrel	9,291	8,521	8,362	8,124	6,743	5,096	4,047

Wallentin L, et al. *N Engl J Med.* 2009;361:1045-1057

Mortality Benefit with Ticagrelor

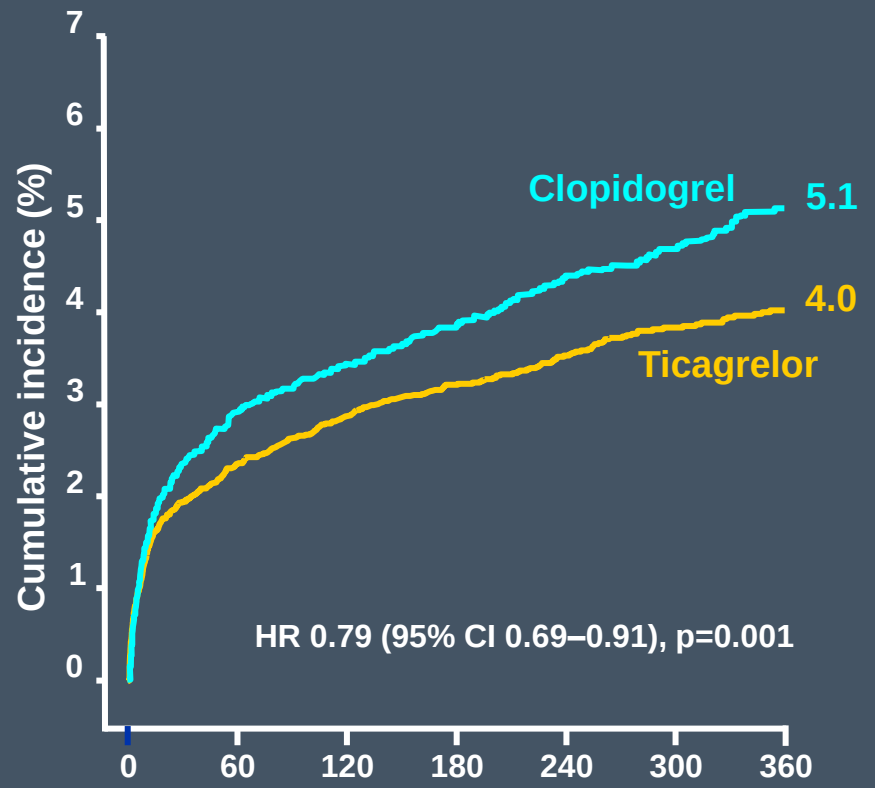
Myocardial infarction



No. at risk

Ticagrelor	9,333	8,678	8,520	8,279	6,796	5,210	4,191
Clopidogrel	9,291	8,560	8,405	8,177	6,703	5,136	4,109

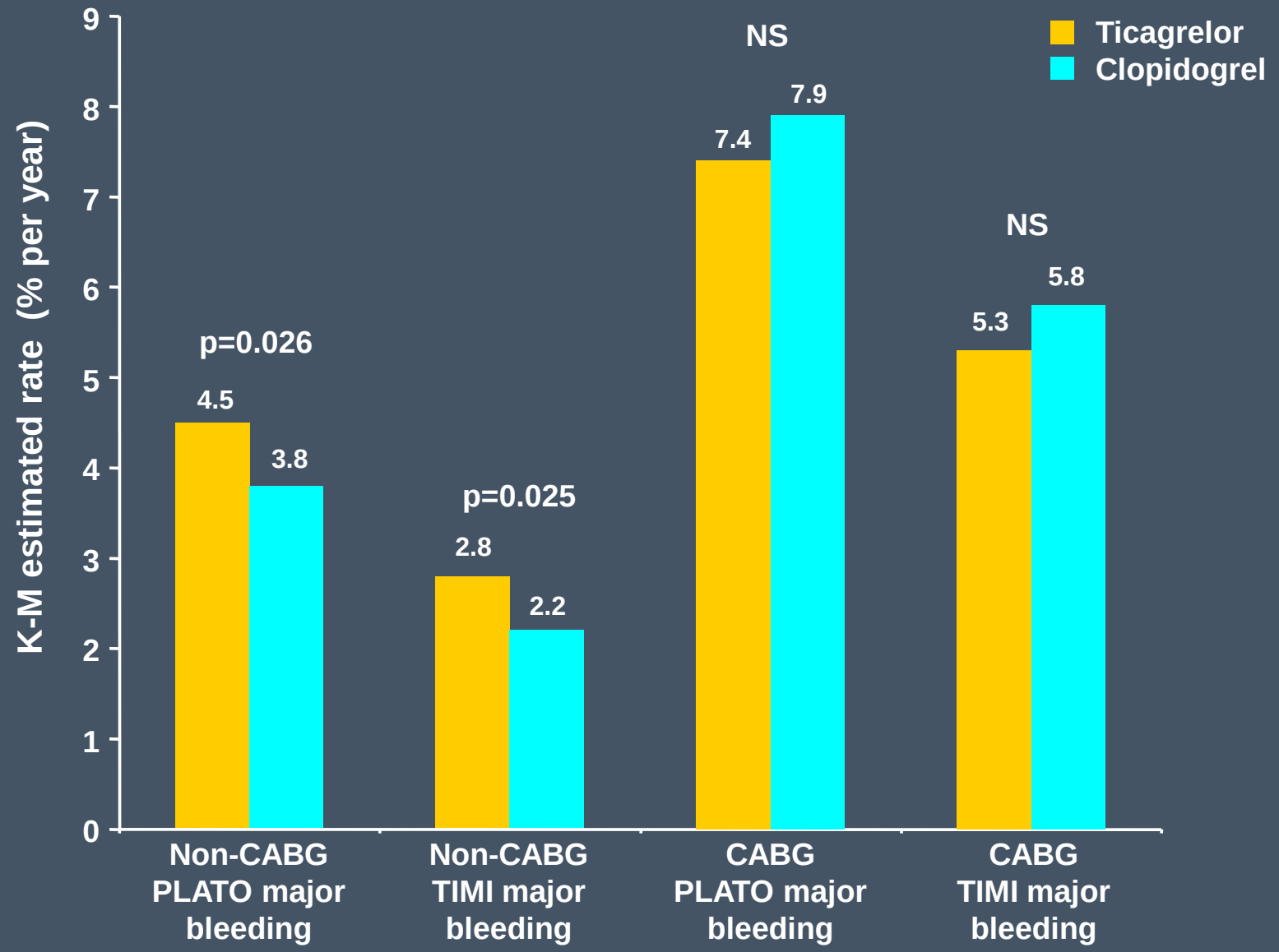
Cardiovascular death



	9,333	8,294	8,822	8,626	7119	5,482	4,419
	9,291	8,865	8,780	8,589	7079	5,441	4,364

Wallentin et al., *NEJM* 2009

Non-CABG and CABG-related major bleeding



Wallentin L, et al. *N Engl J Med.* 2009;361:1045-1057.

Ticagrelor Side Effects

Holter Monitoring at First Week	Ticagrelor (n=1451)	Clopidogrel (n=1415)	*P*-value
Ventricular pauses ≥3 seconds, %	5.8	3.6	0.01
Ventricular pauses ≥5 seconds, %	2.0	1.2	0.10

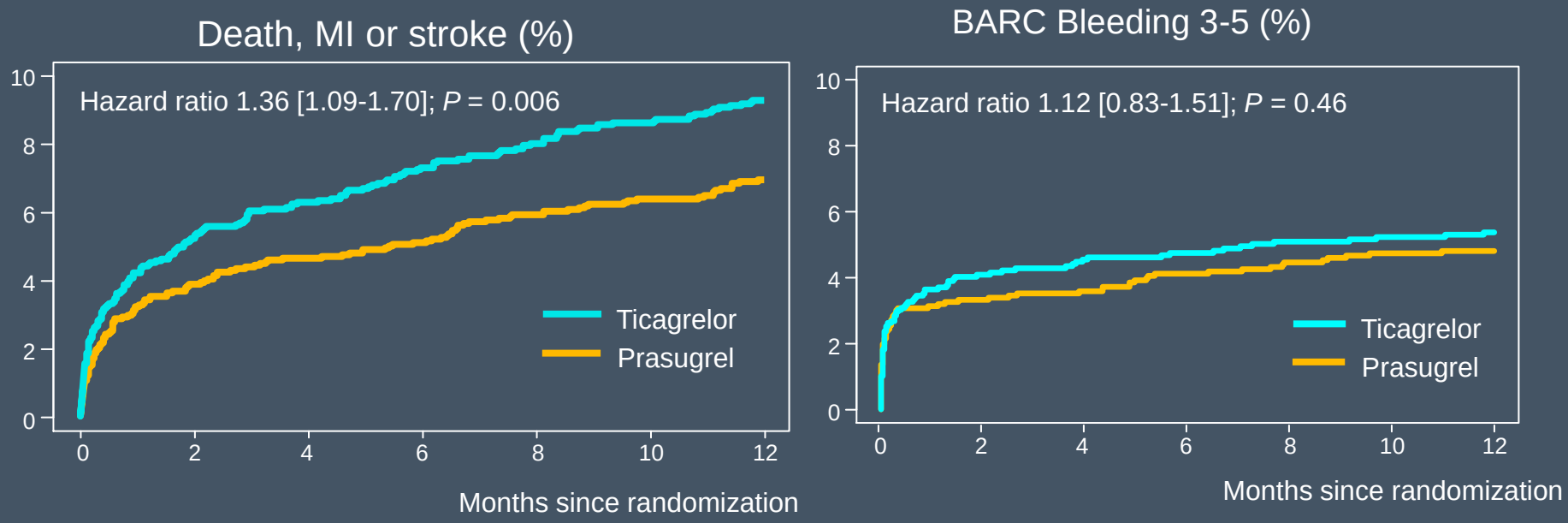
All Patients	Ticagrelor (n=9235)	Clopidogrel (n=9186)	*P*-value
Dyspnea, %	13.8	7.8	<0.001

Wallentin L, et al. *N Engl J Med.* 2009;361:1045-1057.

Prasugrel vs Ticagrelor: Do We Believe the Head-to-Head data?

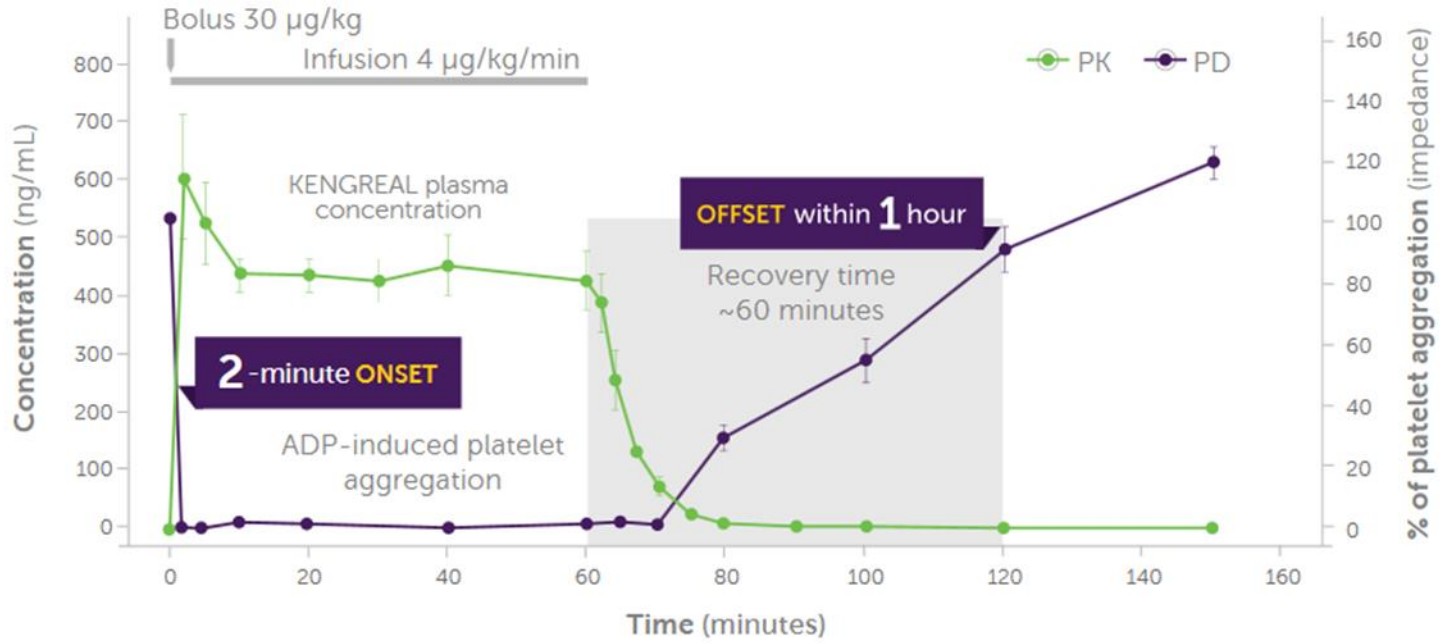
ISAR REACT 5

4018 patients with ACS undergoing planned angiography (open-label)



Schüpke et al., *NEJM* 2019

Cangrelor: Intravenous P2Y12 Inhibitor



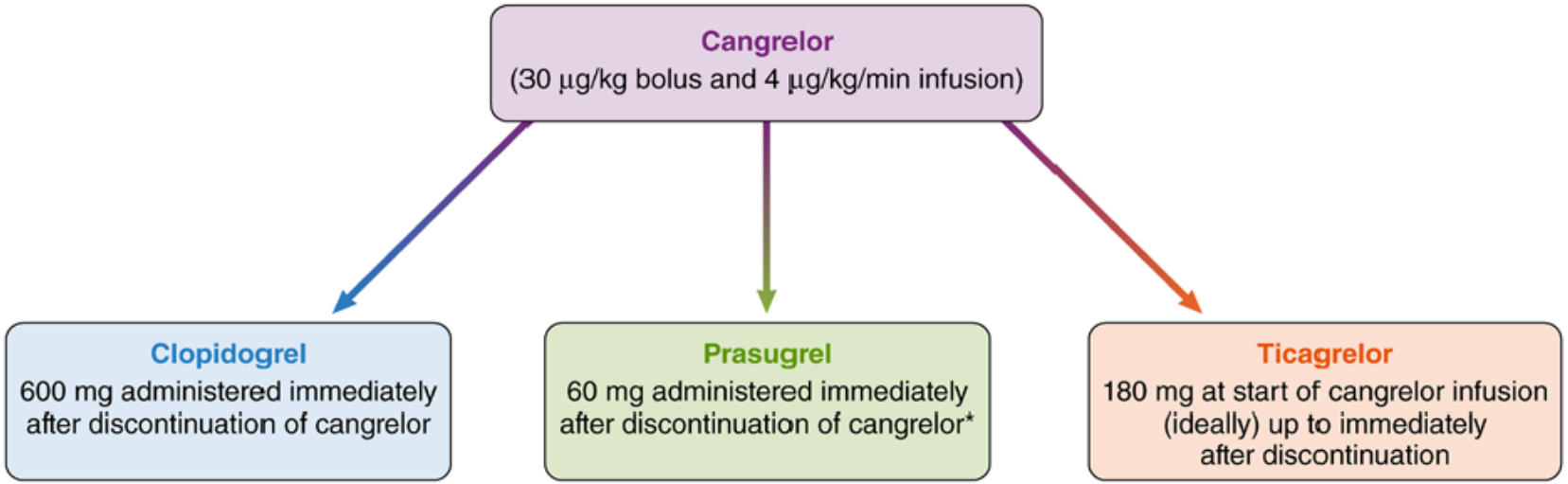
CHAMPION PHOENIX: N = 10,900 patients with stable angina or ACS

Cangrelor (2-4 hrs, then clopidogrel) vs. clopidogrel. Start at time of PCI

	Cangrelor	Clopidogrel	OR (95% CI)	P-value
Death, MI, Ischemic-Driven Revasc, Stent Thrombosis	4.7%	5.9%	0.78 (0.66,0.93)	0.005
Any Blood Transfusion	0.5%	0.3%	1.56 (0.83,2.93)	0.16

NEJM 2013;368:1303

Switching from Cangrelor to Oral P2Y12 inhibitor



2014 ACC/AHA NSTEACS Guidelines: P2Y12 Inhibitors

Recommendation	COR	LOE
Clopidogrel 300-600 mg load (latter preferred before PCI) → 75 mg/d	I	B
Prasugrel 60 mg loading dose → 10 mg/d (PCI only)	I	B
Ticagrelor 180 mg loading dose → 90 mg/bid (initial Rx or PCI)	I	B
Reasonable to use ticagrelor in preference to clopidogrel (initial Rx or PCI)	IIa	B
Reasonable to use prasugrel in preference to clopidogrel (PCI only)	IIa	B
Prasugrel should not be given if prior stroke or TIA	III: Harm	B

Circulation 2014;130:2354-94

ESC 2020 NSTE-ACS Guidelines Update

Prasugrel should be considered in preference to ticagrelor for NSTE-ACS patients who proceed to PCI.

It is not recommended to administer routine pre-treatment with a $P2Y_{12}$ receptor inhibitor to patients in whom the coronary anatomy is not known and early invasive management is planned.

In patients with NSTE-ACS who cannot undergo an early invasive strategy, pre-treatment with a $P2Y_{12}$ receptor inhibitor may be considered depending on bleeding risk.

Collet JP et al. *European Heart Journal* 2021; 42.14: 1289-1367

Antiplatelet Drugs in NSTE-ACS

	NSTEACS	
	INVASIVE	CONS
Aspirin	✓	✓
$P2Y_{12}$ Inhibitor	**Ticagrelor (before or at PCI)** **Prasugrel (at time of PCI)** **Clopidogrel (before or 600mg at PCI)** **IV Cangrelor ? (typically then give oral P2Y12i at end of case)**	**Ticagrelor** **(or Clopidogrel)**
GP IIb/IIIa Inhib.	**?** **(at time of PCI)**	✘ **(unless recurrent ischemia)**

Circulation **2014;130:2354-94**

CMHC Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)

Post-Discharge Antiplatelet Therapy: How Long and How Strong?

Erin Bohula, MD DPhil

Assistant Professor, BWH, HMS

Investigator, TIMI Study Group

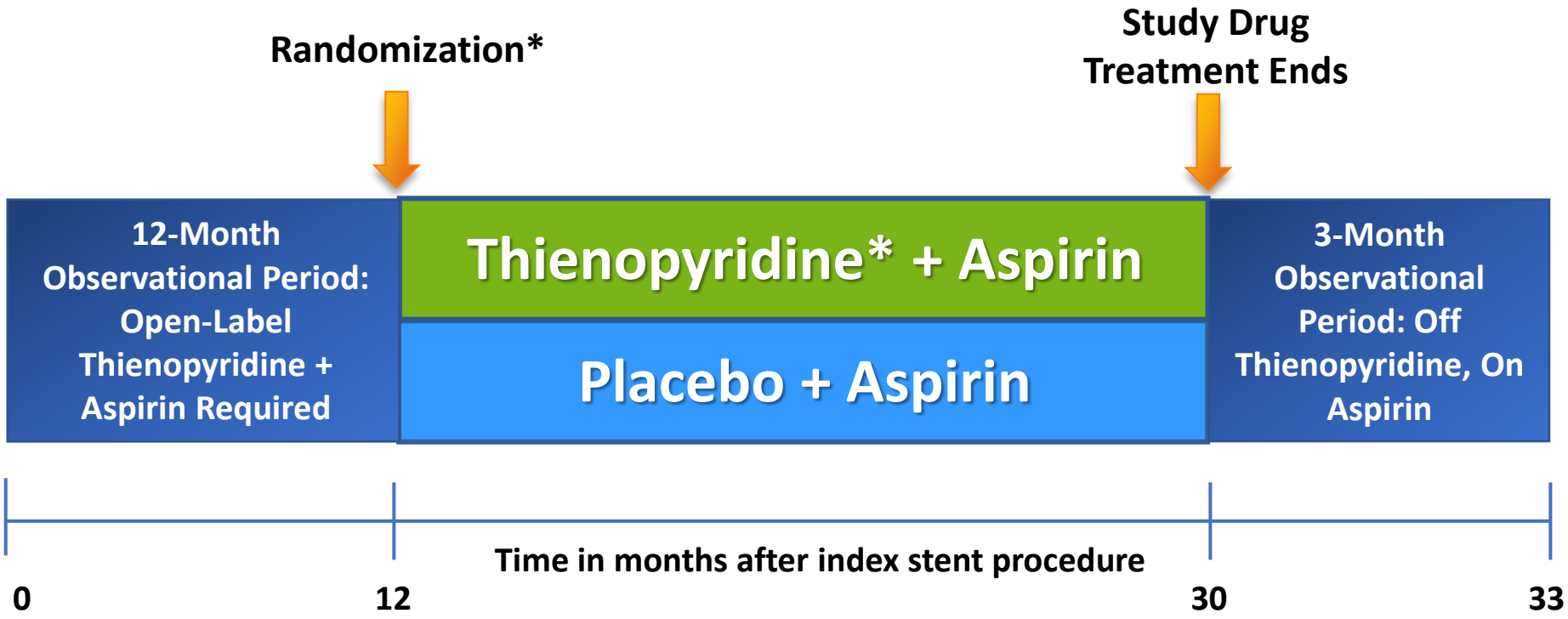
BWH BRIGHAM AND WOMEN'S HOSPITAL | Heart & Vascular Center |

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

TIMI Study Group

www.brighamandwomens.org/heart

Dual Antiplatelet Therapy (DAPT) Study: Design



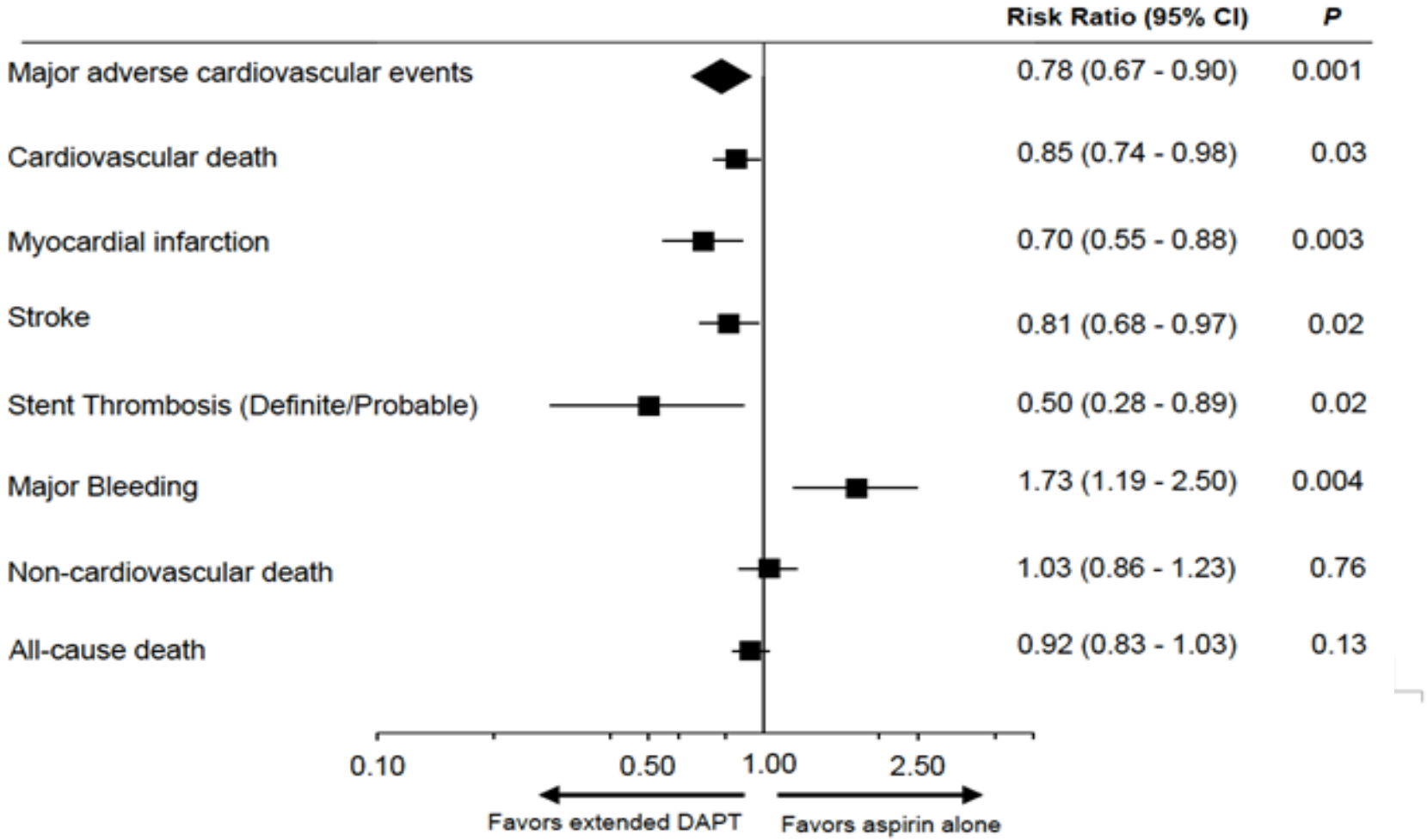
Enrolled: Subjects treated with FDA-approved DES or BMS. Subjects on oral anticoagulant therapy or with life expectancy < 3 years excluded.

Randomized: Free from MI, stroke, repeat revascularization, and moderate or severe bleeding, and adherent with thienopyridine (80% to 120% of doses taken and no interruption > 14 days).

*Clopidogrel or prasugrel

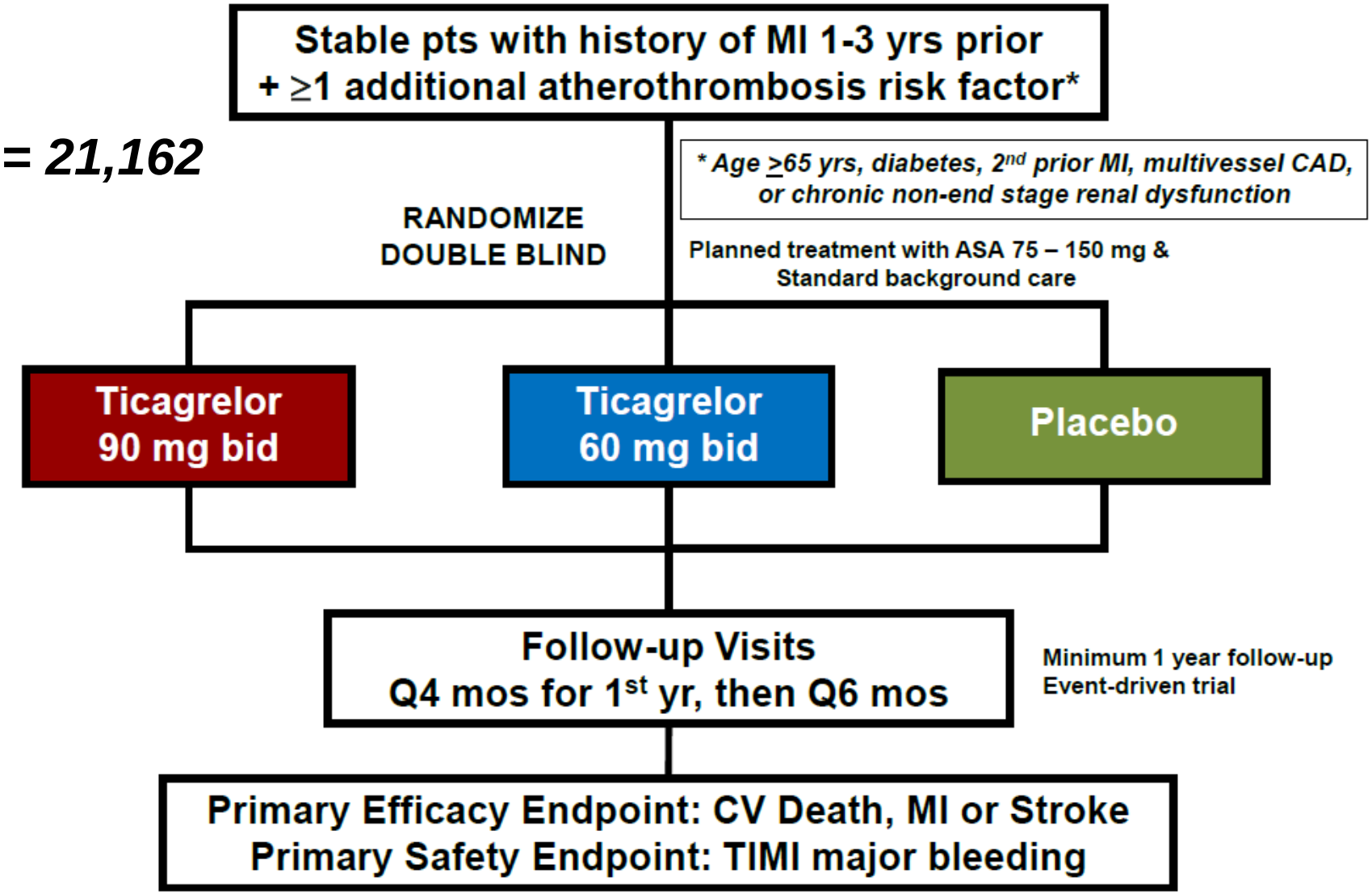
Treatment Effect in ACS Patients

DAPT STUDY



Mauri L *NEJM* 2014;371:2155-66

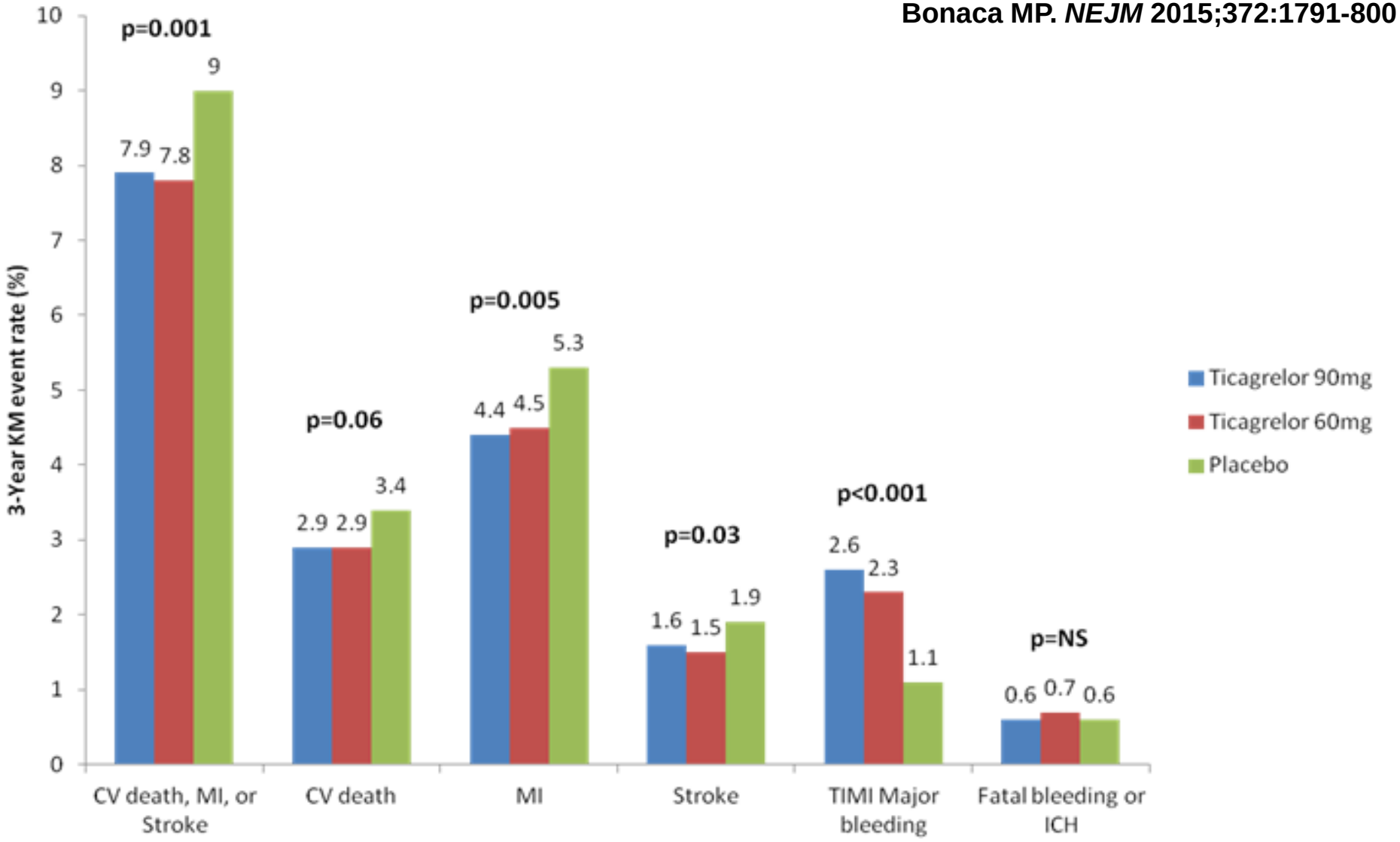
Trial Design



Bonaca MP et al. *Am Heart J* 2014;167:437-44

Key Efficacy And Safety Outcomes

Bonaca MP. *NEJM* 2015;372:1791-800



CV death, MI, or stroke: Ticagrelor 90mg, HR 0.85 (0.75-0.96); Ticagrelor 60mg, HR 0.84 (0.74-0.95)
TIMI major bleeding: Ticagrelor 90mg, HR 2.69 (1.96-3.70); Ticagrelor 60mg, HR 2.32 (1.68-3.21)

PEGASUS TIMI 54

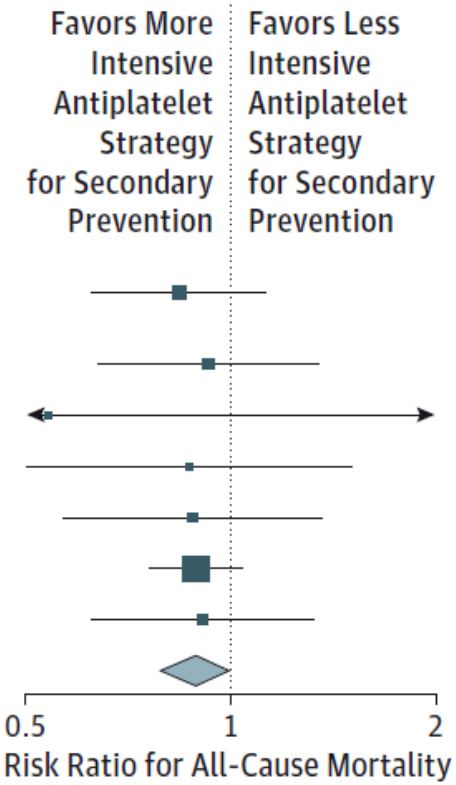
Summary

- Adding ticagrelor to low-dose aspirin in stable patients with a history of MI reduced the risk of CV death, MI or stroke
- The benefit of ticagrelor was consistent
  - For both fatal & non-fatal components of primary endpoint
  - Over the duration of treatment
  - Among major clinical subgroups
- Ticagrelor increased the risk of TIMI major bleeding, but not fatal bleeding or ICH
- The two doses of ticagrelor had similar overall efficacy, but bleeding and other side effects tended to be less frequent with 60 mg bid dose

Bonaca MP, *NEJM* 2015;372:1791-800

Prolonged Intensive Antiplatelet Therapy & Mortality in 2° Prevention

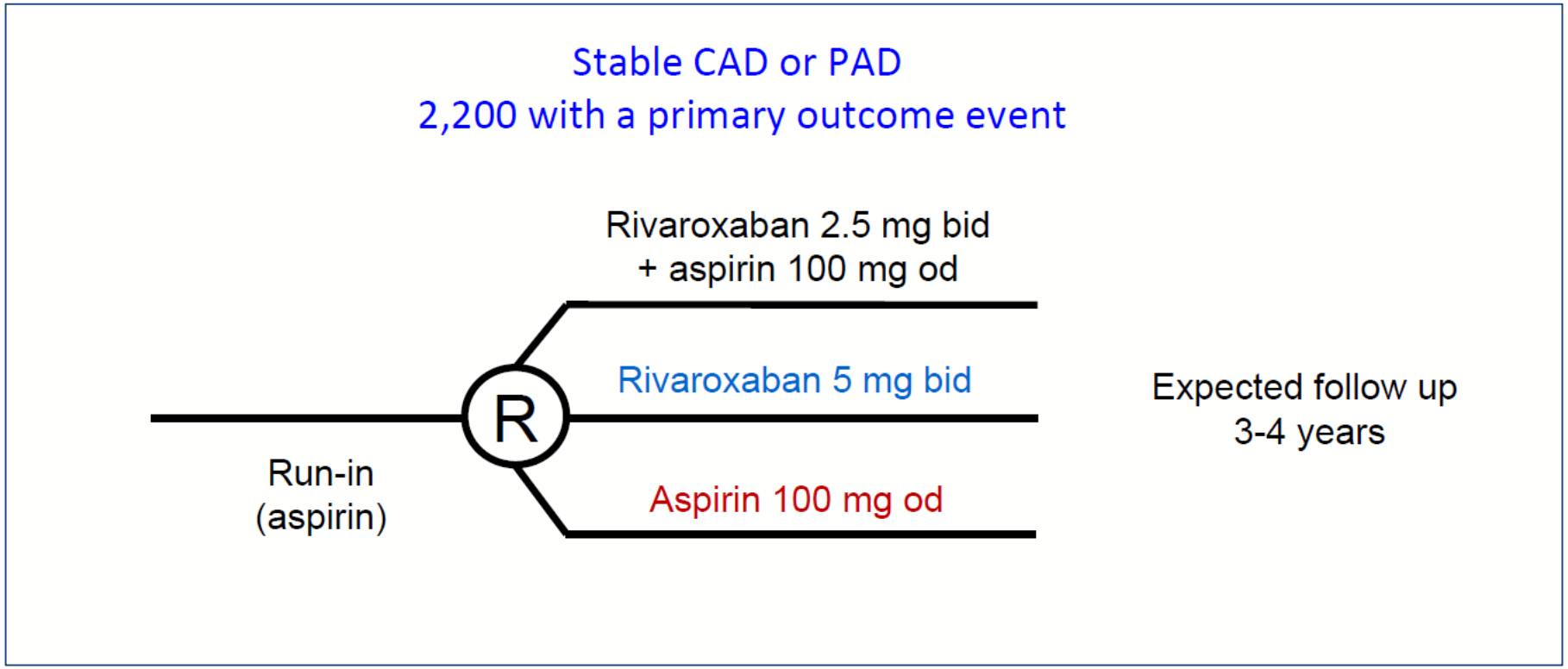
Trial	More Intensive No./Total No.	Less Intensive No./Total No.	Hazard Ratio (95% CI)
CHARISMA (prior myocardial infarction cohort)	82/1903	99/1943	0.84 (0.63-1.13)
PRODIGY	52/732	56/733	0.93 (0.64-1.35)
ARCTIC	1/156	2/167	0.54 (0.05-5.87)
DAPT MI	24/1805	27/1771	0.87 (0.50-1.50)
DES-LATE	37/1512	43/1551	0.88 (0.57-1.37)
PEGASUS-TIMI 54 (60 mg twice daily)	289/7045	326/7067	0.89 (0.76-1.04)
TRA2P-TIMI 50 MI (no stroke/TIA)	238/8458	259/8439	0.91 (0.62-1.33)
Total	723/21611	812/21671	0.89 (0.79-0.99)
			P = .04



11% reduction in all-cause mortality
16.5% reduction in CV mortality
No difference in non-CV mortality

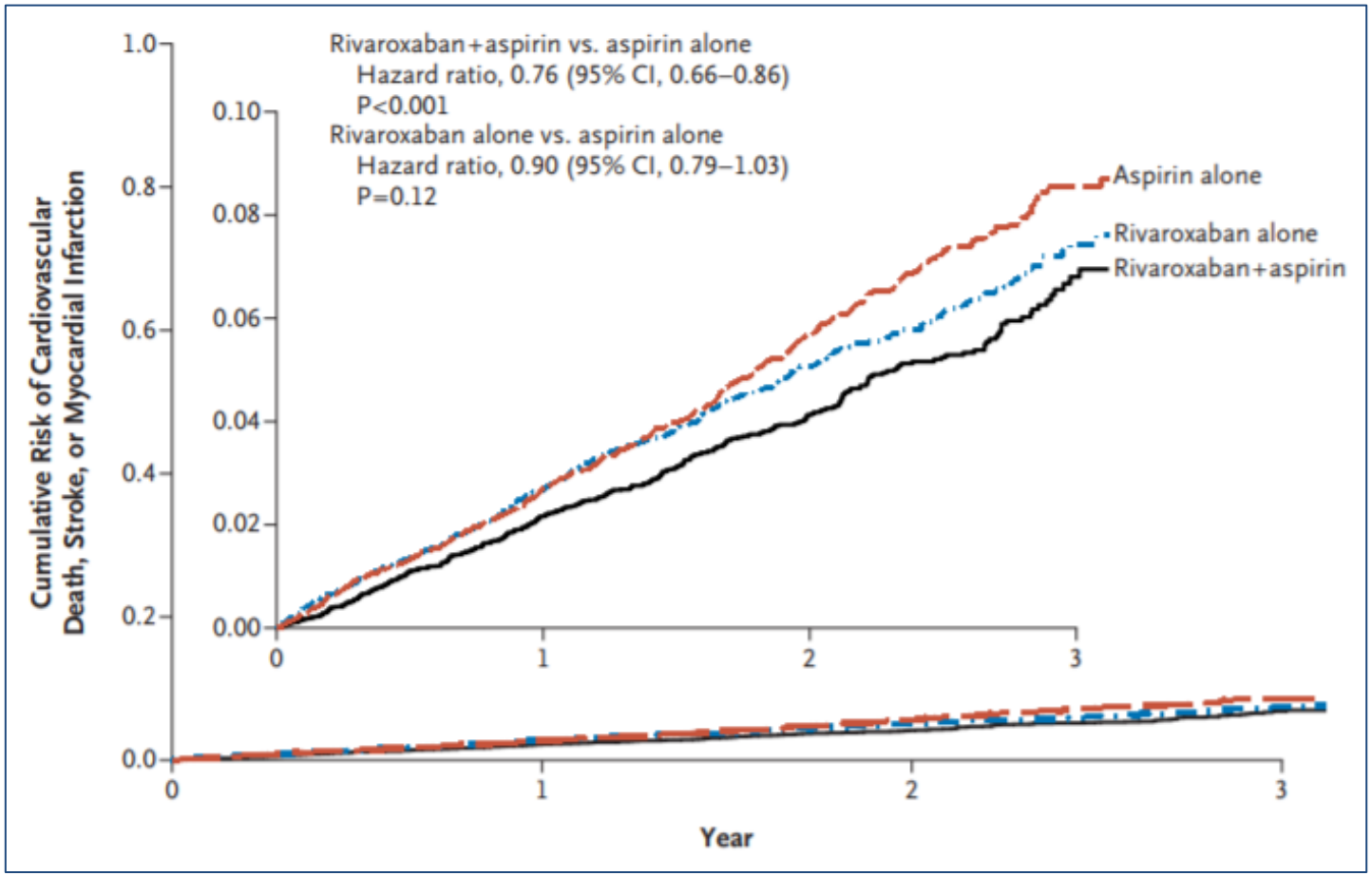
JAMA Cardiology 2016;1:627-8

COMPASS design



Eikelboom JW et al.
N Engl J Med 2017;377:1319

COMPASS Trial: Primary Efficacy Outcome



Eikelboom JW et al.
N Engl J Med 2017;377:1319

COMPASS: Conclusions

Rivaroxaban 2.5 mg bid plus aspirin 100 mg od:

- Reduces CV death, stroke, MI
- Increases major bleeding without a significant increase in fatal, intracranial or critical organ bleeding
- Provides a net clinical benefit

No significant benefit of rivaroxaban alone

Eikelboom JW et al.
N Engl J Med 2017;377:1319

Long-term Antithrombotics – No Afib

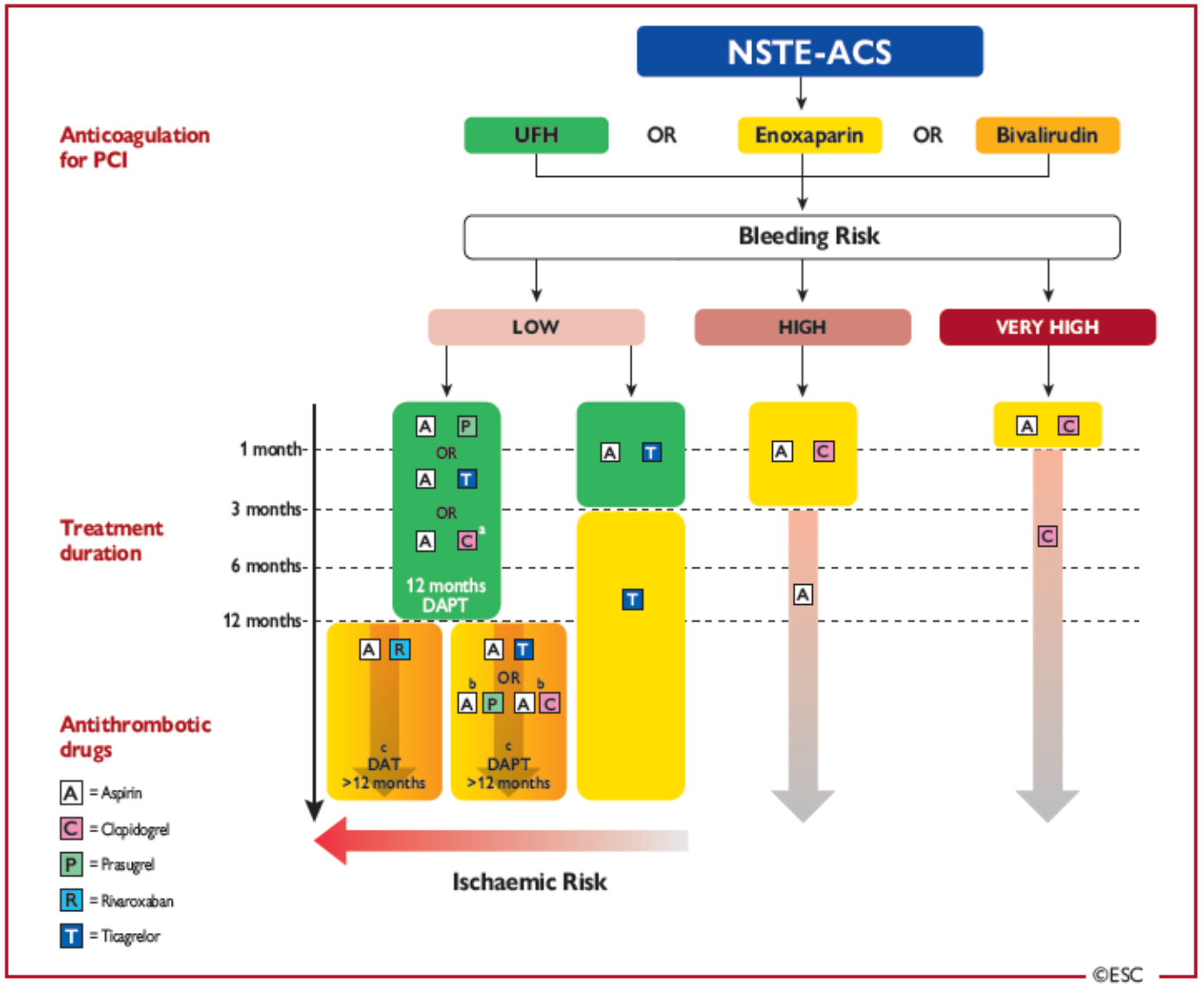


Figure 7 (1)

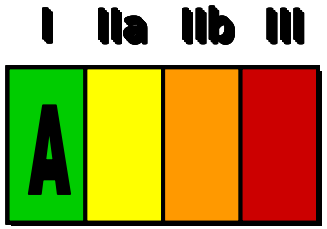
Algorithm for antithrombotic therapy in non-ST-segment elevation acute coronary syndrome patients without atrial fibrillation undergoing percutaneous coronary intervention.

= Class I = Class IIa = Class IIb

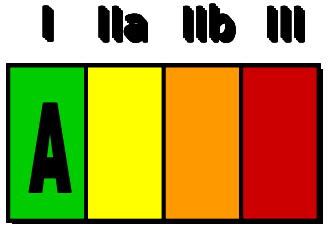
Very HBR is defined as recent bleeding in the past month and/or not deferrable planned surgery.

2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (European Heart Journal 2020 - doi/10.1093/eurheartj/ehaa575)

ACE-I/ARB



An ACE inhibitor should be administered orally within the first 24 h to ACS patients with pulmonary congestion or LV ejection fraction (LVEF) ≤ 40%. Also for pts with STEMI and DM or anterior infarct.



An angiotensin receptor blocker should be administered to ACS patients who are intolerant of ACE inhibitors and have either clinical or radiological signs of HF or LVEF ≤ 40%.

Aldosterone Antagonists

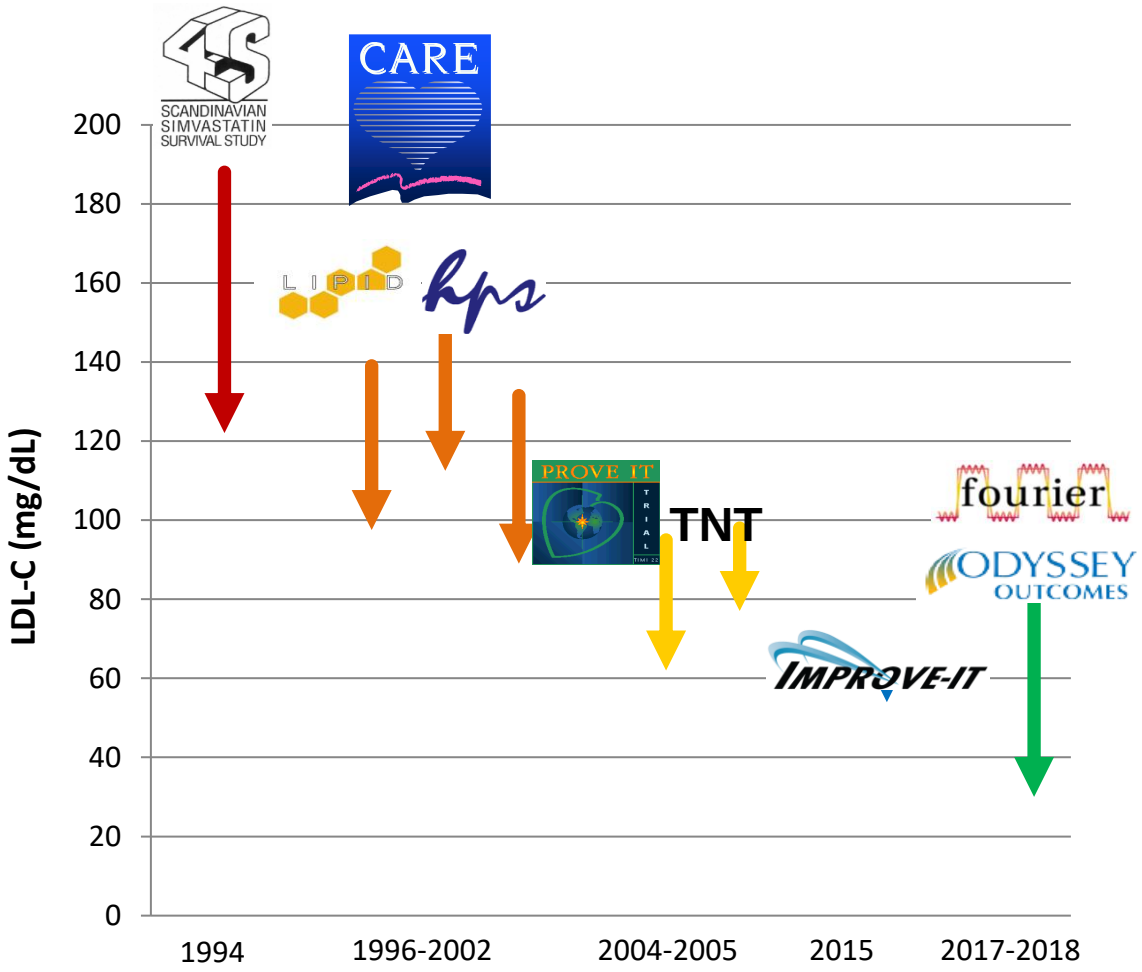
Long-term aldosterone antagonist if:

- **No significant renal dysfunction (eGFR> 30 ml/min) or hyperkalemia (K ≤ 5 mEq/L)**
- **Therapeutic doses of an ACE inhibitor**
- **LVEF ≤ 40%**
- **Either symptomatic HF or diabetes mellitus**

Beta Blockers

Recommendations	Class[a]	Level[b]
Beta-blockers		
Oral treatment with beta-blockers is indicated in patients with heart failure and/or LVEF ≤40% unless contraindicated.[357–361]	I	A
Intravenous beta-blockers should be considered at the time of presentation in patients undergoing primary PCI without contraindications, with no signs of acute heart failure, and with an SBP >120 mmHg.[346–348,350,403]	IIa	A
Routine oral treatment with beta-blockers should be considered during hospital stay and continued thereafter in all patients without contraindications.[344,354–356,404,405]	IIa	B
Intravenous beta-blockers must be avoided in patients with hypotension, acute heart failure or AV block, or severe bradycardia.[344]	III	B

A Quarter of a Century of Treating LDL-C



High is bad

Average is not good

Lower is better

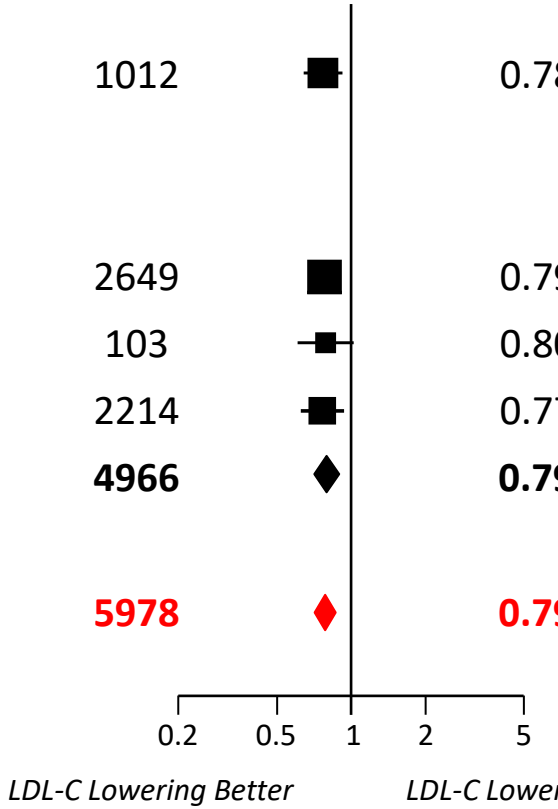
Even lower is even better

Lowest is best

For LDL-C, 1 mmol/L = 38.67 mg/dL.
Courtesy of M. Sabatine and R. Giugliano

Efficacy of LDL-C Lowering Even When Starting LDL-C ≤70 mg/dL (1.8 mmol/L)

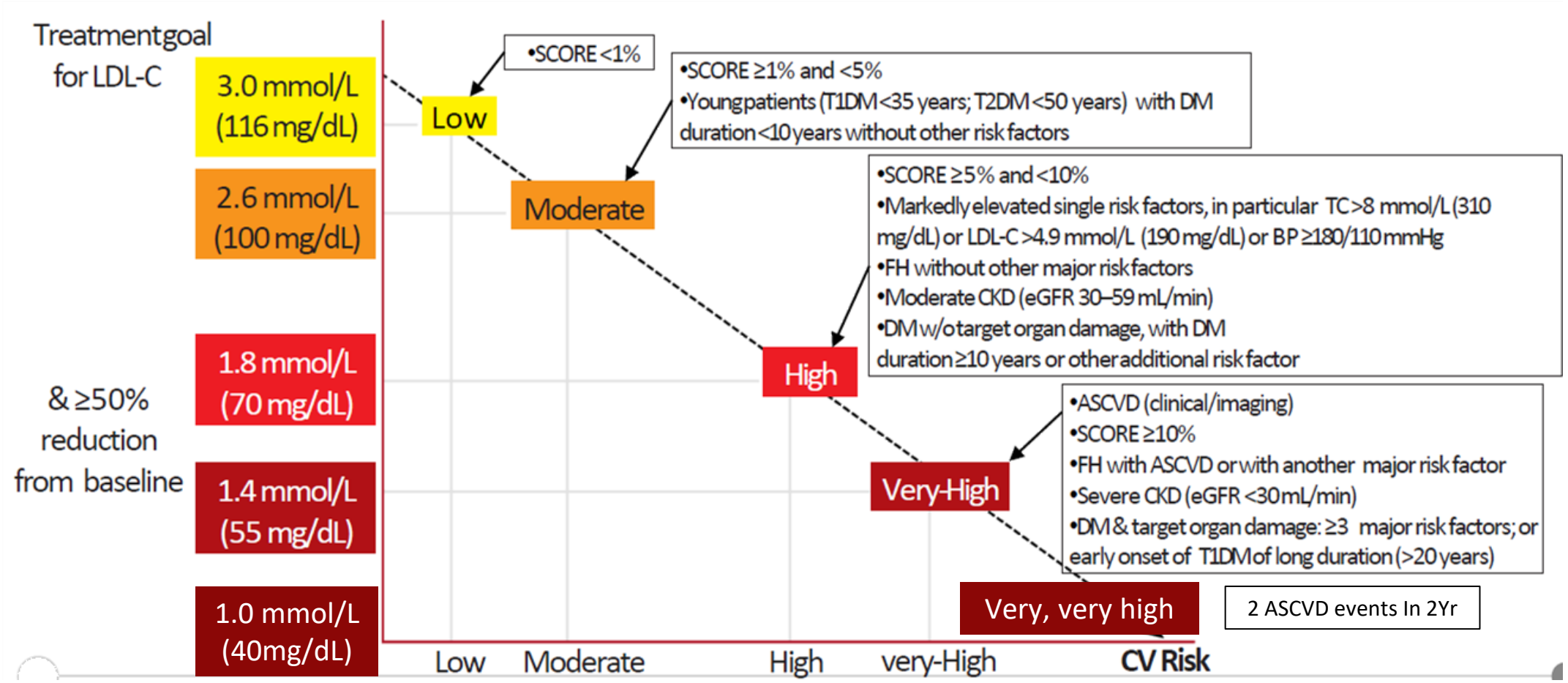
Trial	Starting LDL-C (mg/dL)	Events Expt Arm	Events Ctrl Arm	Major Vascular Events RR (95% CI) per 1 mmol/L ↓ in LDL-C	
Statins					
CTTC <2 mmol/L subgp	66	910	1012	0.78 (0.65–0.94)	
Non-statin LDL-C Lowering					
IMPROVE-IT	70	2455	2649	0.79 (0.67–0.93)	
FOURIER <1.8 mmol/L subgp	66	81	103	0.80 (0.61–1.04)	
REVEAL	63	2068	2214	0.77 (0.63–0.96)	
Summary		**4604**	**4966**	**0.79 (0.70–0.88)**	**P=0.00005**
OVERALL SUMMARY		**5514**	**5978**	**0.79 (0.71–0.87)**	**P=0.000001**



Expt, experimental; subgp, subgroup.
For LDL-C, 1 mmol/L = 38.67 mg/dL.

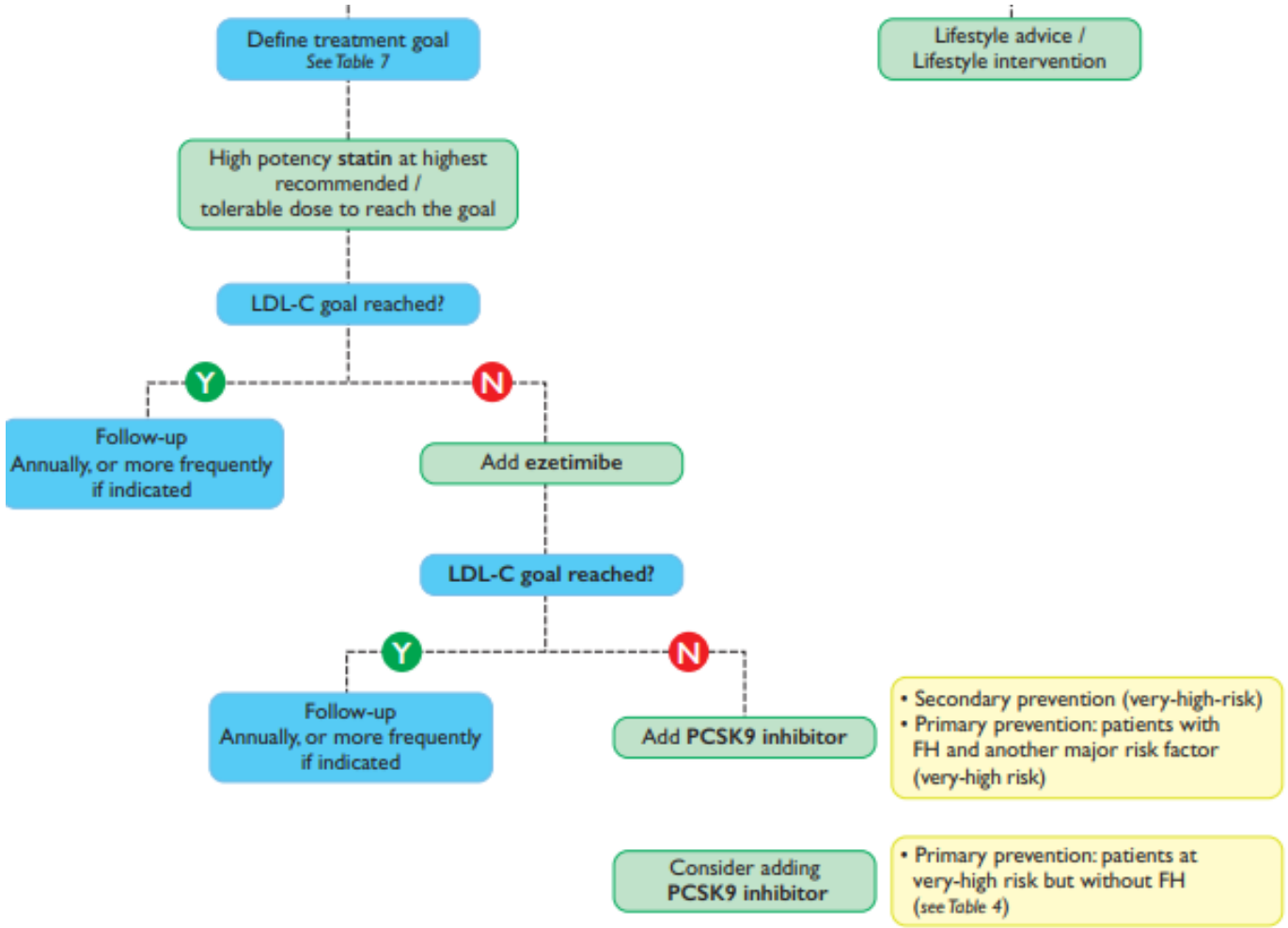
Sabatine MS, et al. JAMA Cardiol 2018;3:823–8.

Cholesterol Guidelines (2019 ESC)



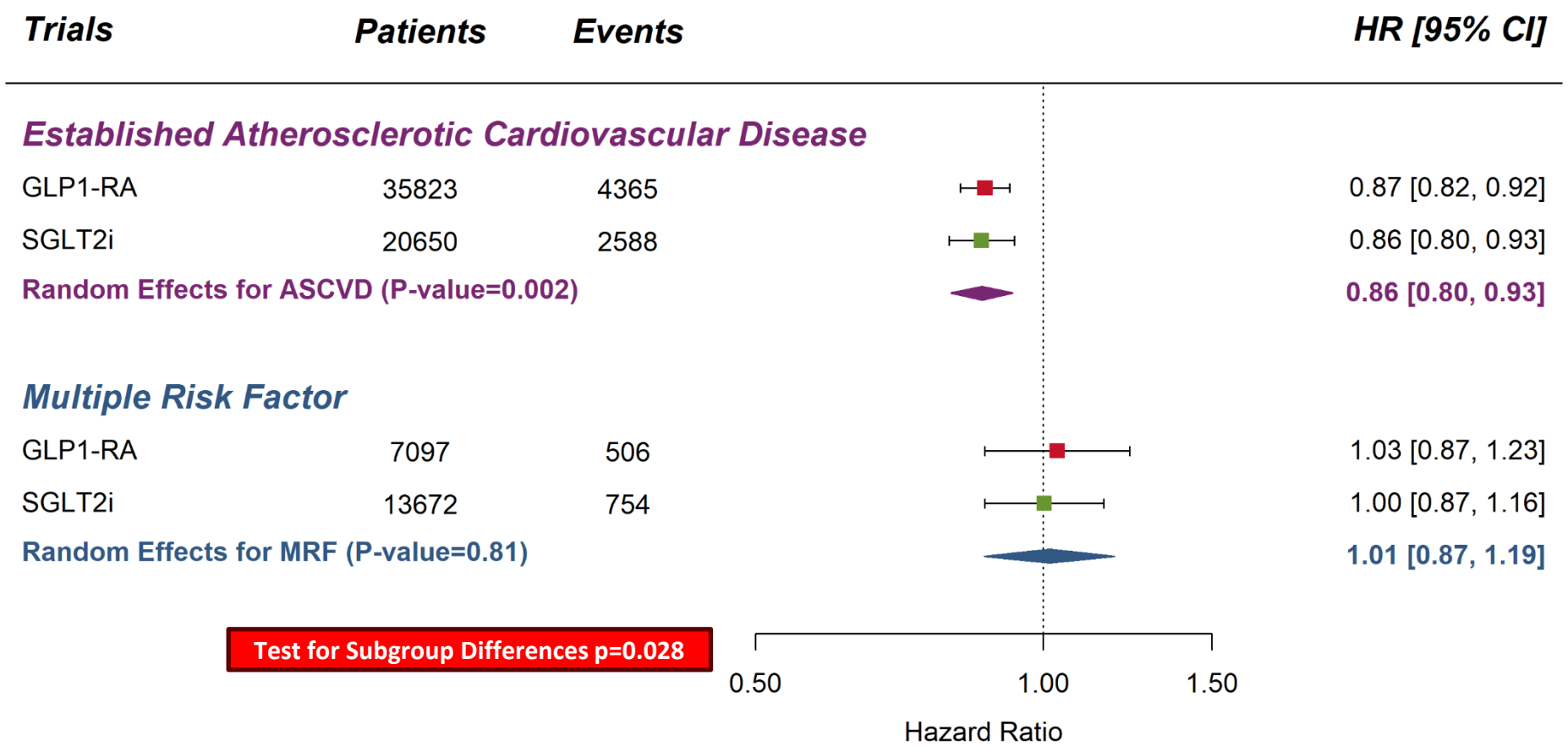
Mach F, et al. *Eur Heart J*. 2020;41:111-188.

Cholesterol Treatment Algorithm (ESC 2019)



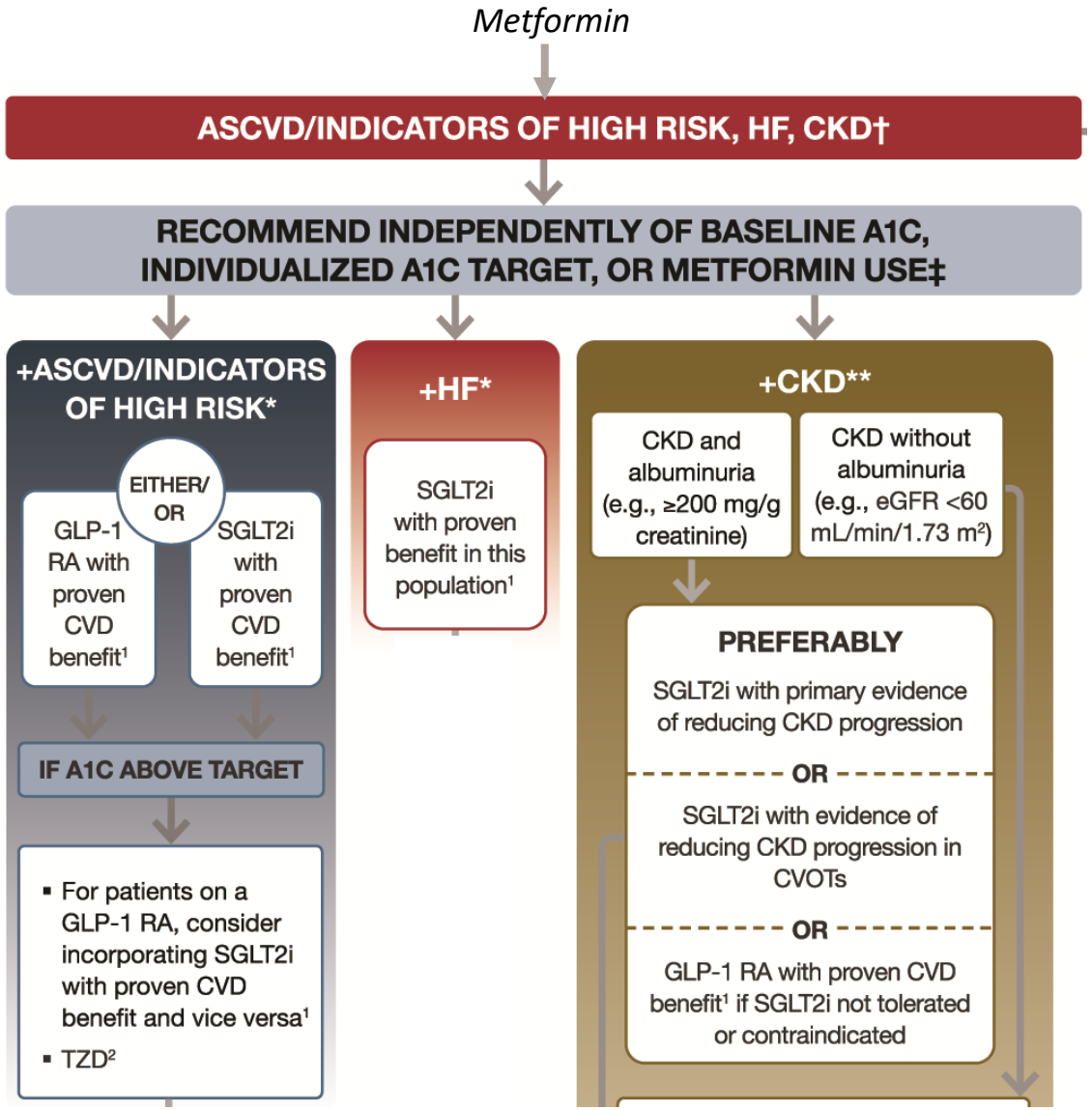
Mach F, et al. *Eur Heart J*. 2020;41:111-188.

SGLT2i & GLP1-RA - MACE



Zelniker TA, Wiviott SD, …, Sabatine MS, Circulation 2019

Management of Diabetes in Pts with ASCVD



Diabetes Care 2022; 45 (Supplement_1): S125-143

Case Conclusion

- 65yo F s/p ACS with PCI, DM, CKD (eGFR 50), HL, HTN, EF 50% without clinical HF
- Goal: Aggressive secondary prevention

European Heart Journal (2021) **42**, 1289–1367
doi:10.1093/eurheartj/ehaa575

- ASA, ticagrelor for at least 12 months
- BB, ACEi, MRA

- Atorva 80, ezetimibe 10 (LDL 65mg/dL)
- Added SGLT2i and GLP-1RA (HbA1c 6.5%)

Summary

- Diagnosis of ACS can be complex
  - ACS does not = + troponin
  - For STEMI, rely on clinical picture + EKG
  - For NSTE-ACS, rely on clinical picture + rule-in/out algorithms
- Once diagnosis is made
  - Risk stratify patients to determine revascularization approach
- Optimize acute and chronic/post-discharge medical therapy to reduce risk for recurrent events