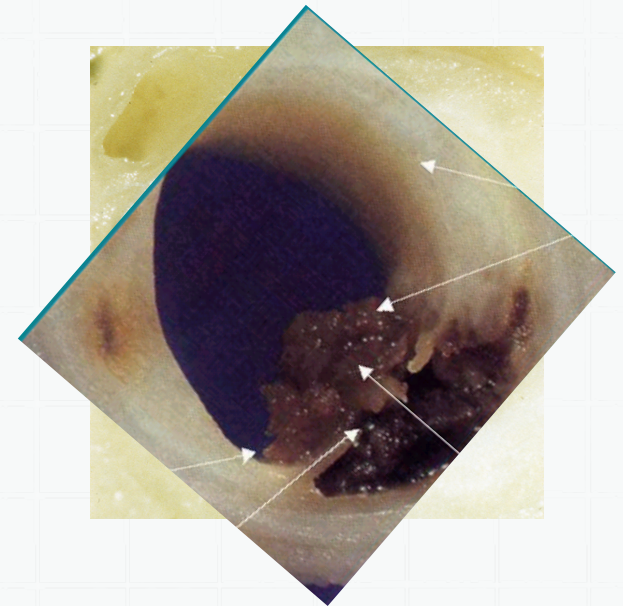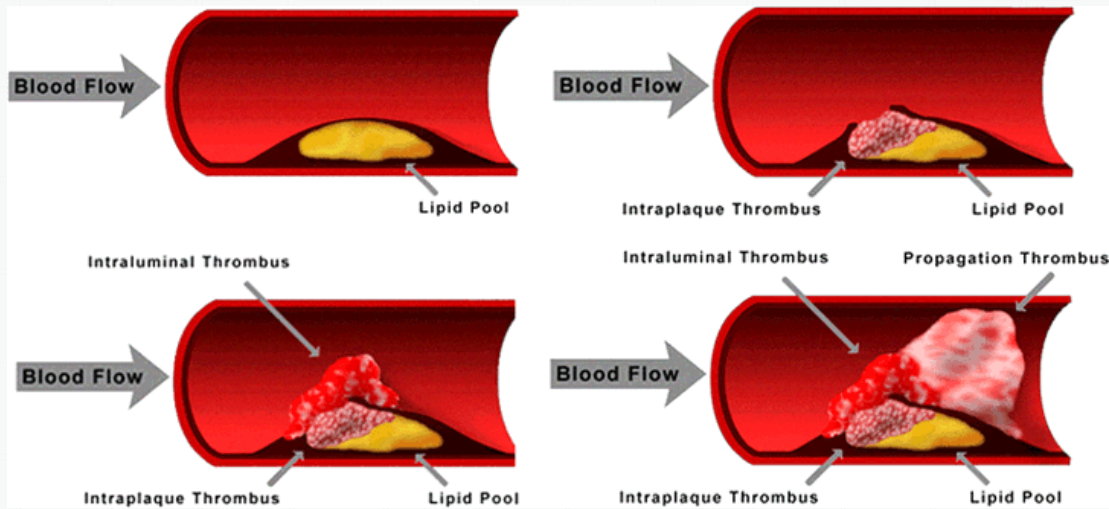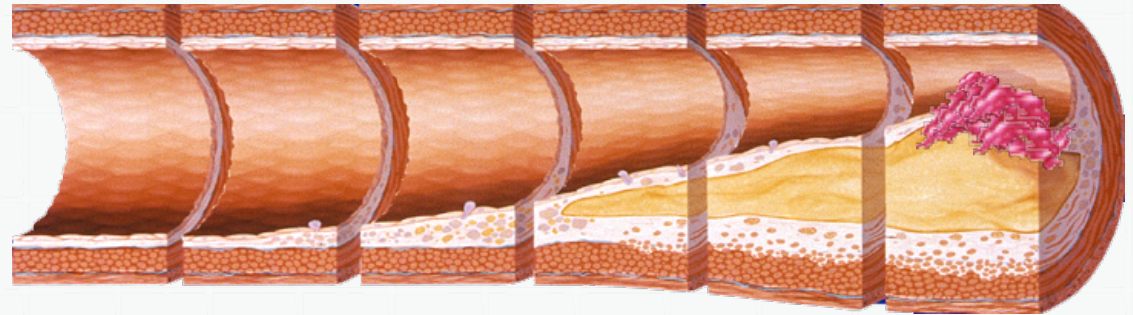# Acute Coronary Syndromes

นายแพทย์อายุส ภมะราภา
รองผู้อำนวยการฝ่ายการแพทย์
หัวหน้าศูนย์หัวใจ
โรงพยาบาลอุตรดิตถ์

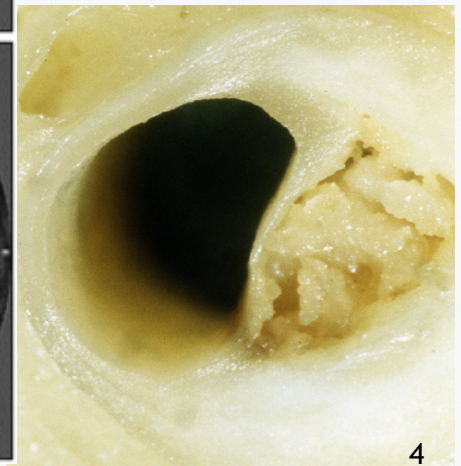Atherosclerosis

Acute Coronary Syndromes

Acute Coronary Syndromes

Cardiovascular disease claims one life every **33** seconds

Every dollar can change a life. Donate today.

The IVUS technique can detect angiographically 'silent' atheroma

Angiogram
No evidence of disease
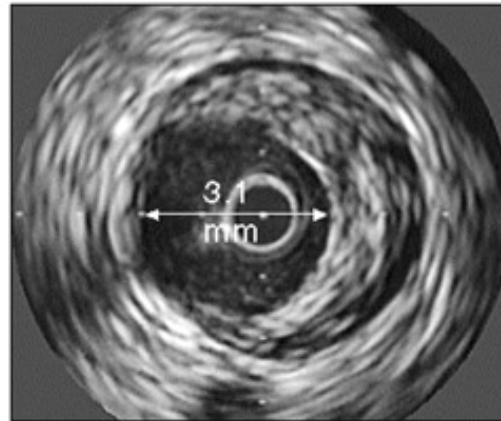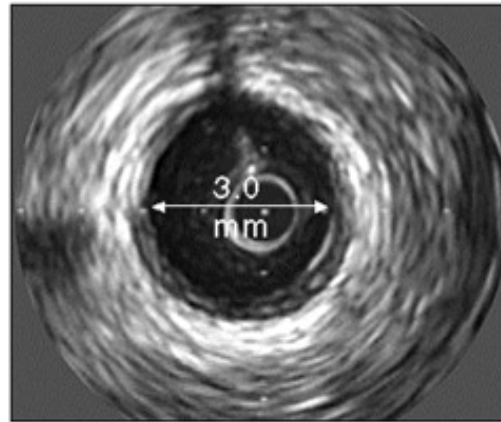
The IVUS technique can detect angiographically 'silent' atheroma

CT   MRT

Endothelial dysfunction

OCT   IVUS

Coronary angiography

Invasive methods

| 20% | 45% | 50% | 70% | 90% |

| Normal | Stary II | Stary III–IV | Stary Va | Stary Vb | Stary Vc |
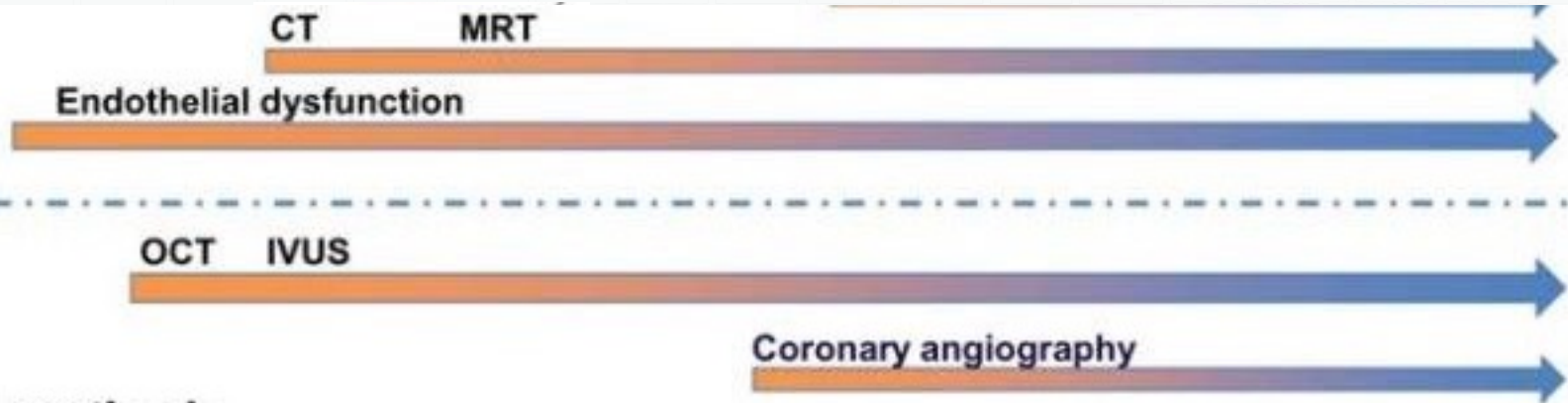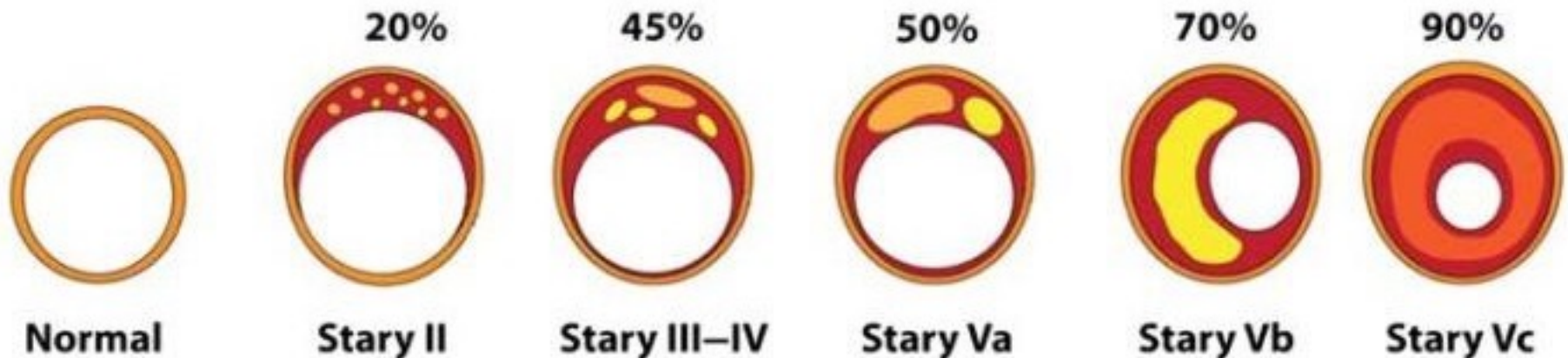
Diagnosis of ACS

- History (angina or angina equivalent)
- Acute ischemic ECG changes
- Typical rise and fall of cardiac biomarkers
  : Cardiac Troponin , CK-MB
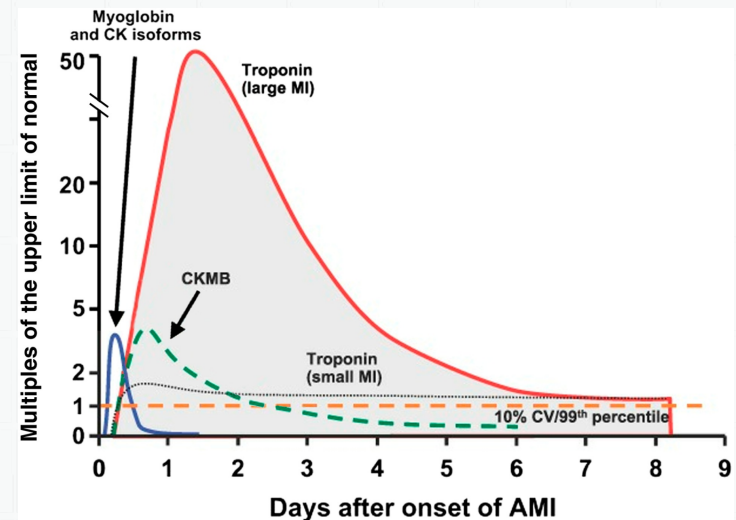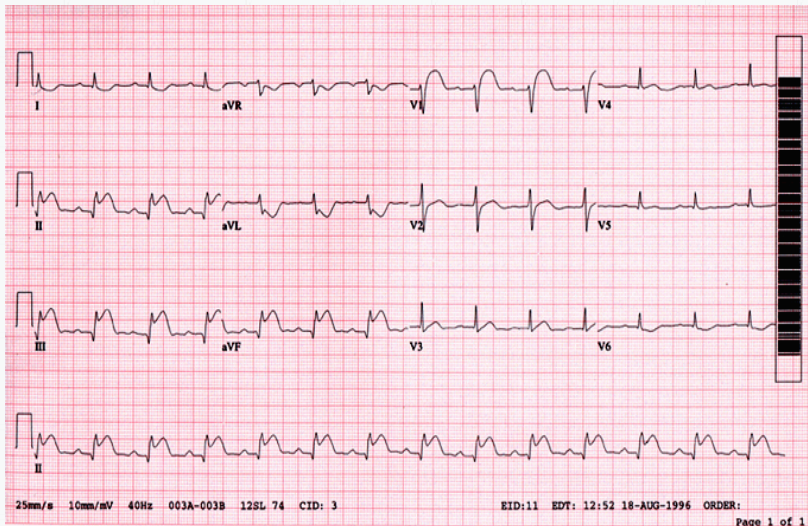
Diagnosis of ACS

- **Presentation: Classic story most often seen in younger (50-65) patients, males**

- **Atypical**
  - **Elderly: tend to present with shortness of breath**
  - **Diabetics: vague symptoms**
  - **Women: complain of feeling fatigued**

- **Those who present atypically tend to present further on in their disease and have worse outcomes**
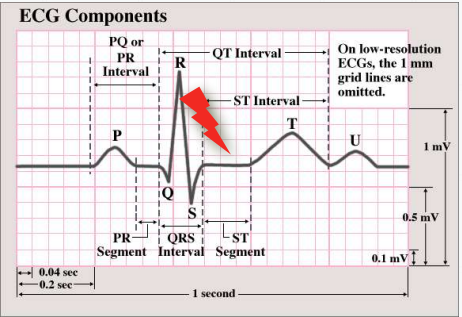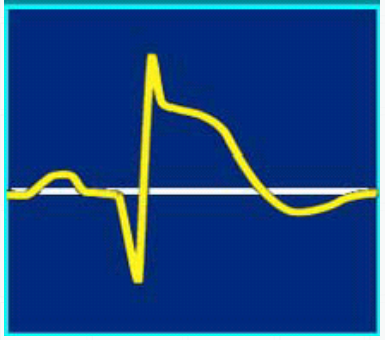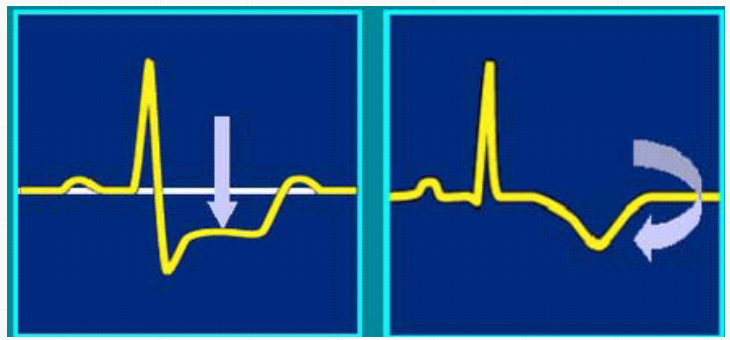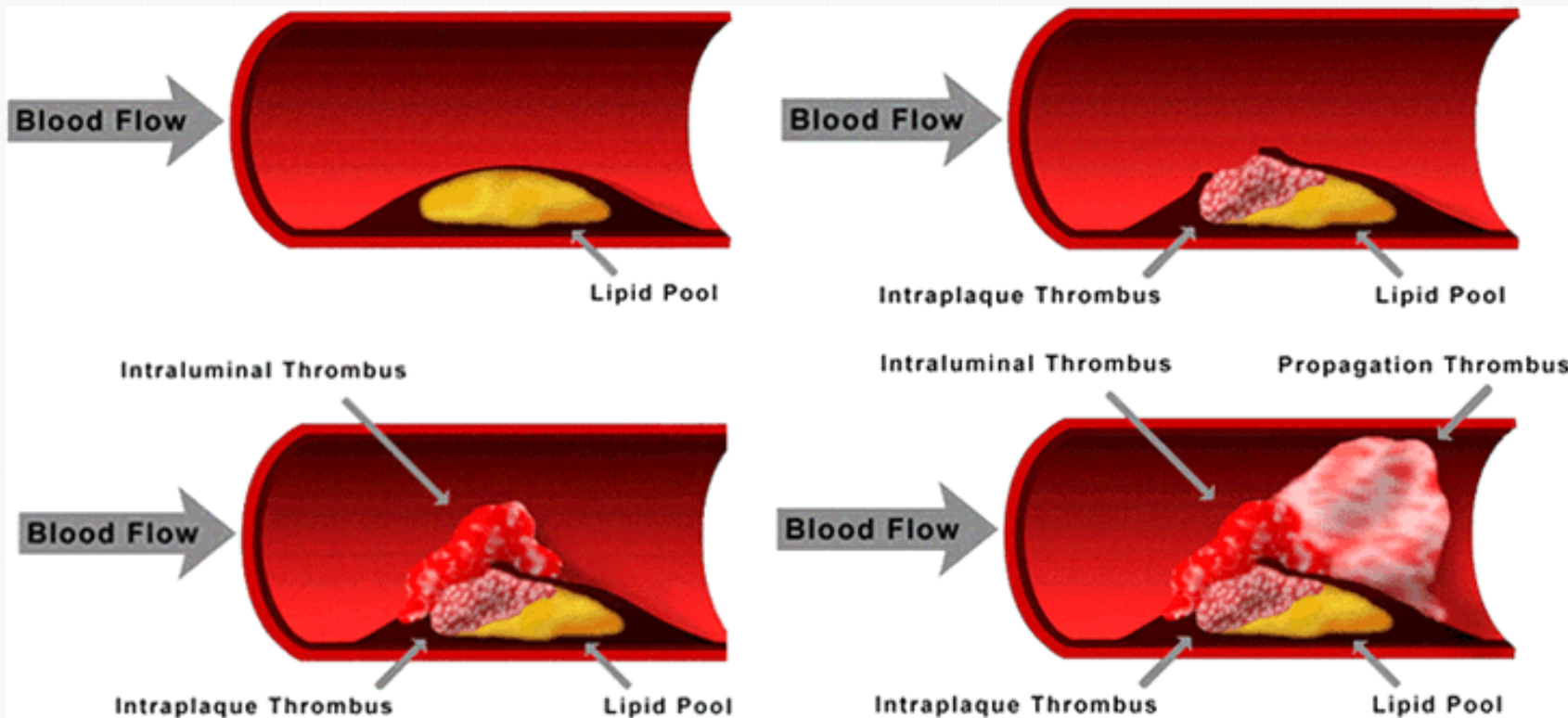
NSTE-ACS   STEMI

MANAGEMENT   STEMI

- Coronary Reperfusion
  fibrinolytic : streptokinase (SK) , rtPA, TNK
  PCI or CABG

MANAGEMENT   STEMI

- Coronary Reperfusion
  fibrinolytic : streptokinase (SK) , rtPA, TNK
  PCI or CABG

Normal Artery — Stenosed Artery — Balloon With Stent Introduced — Lumen Expanded With Balloon — Stent Placed To Keep Lumen Open

Lumen

Muscular layer of arterial wall — Plaque — Wire — Balloon — Balloon inflated. — Stent left behind
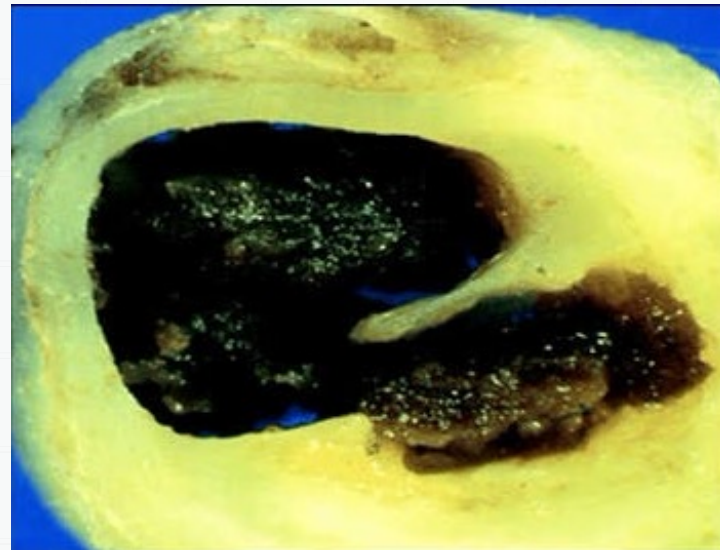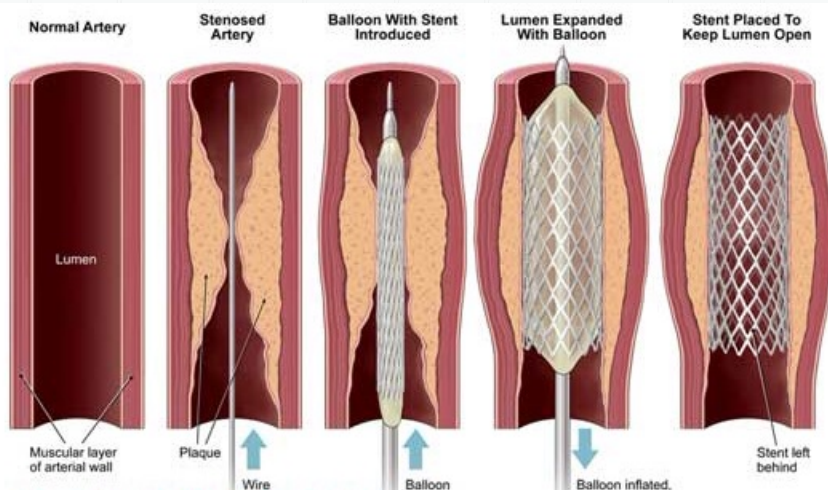
Treatment Delayed is Treatment Denied

STEMI

Symptom Recognition

Call to Medical System

PreHospital
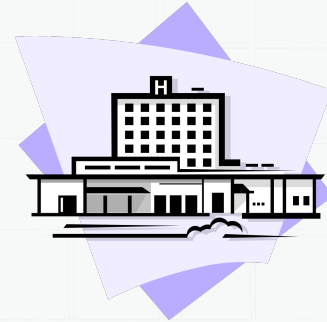
ED

Reperfusion

Increasing Loss of Myocytes

Treatment Delayed is Treatment Denied
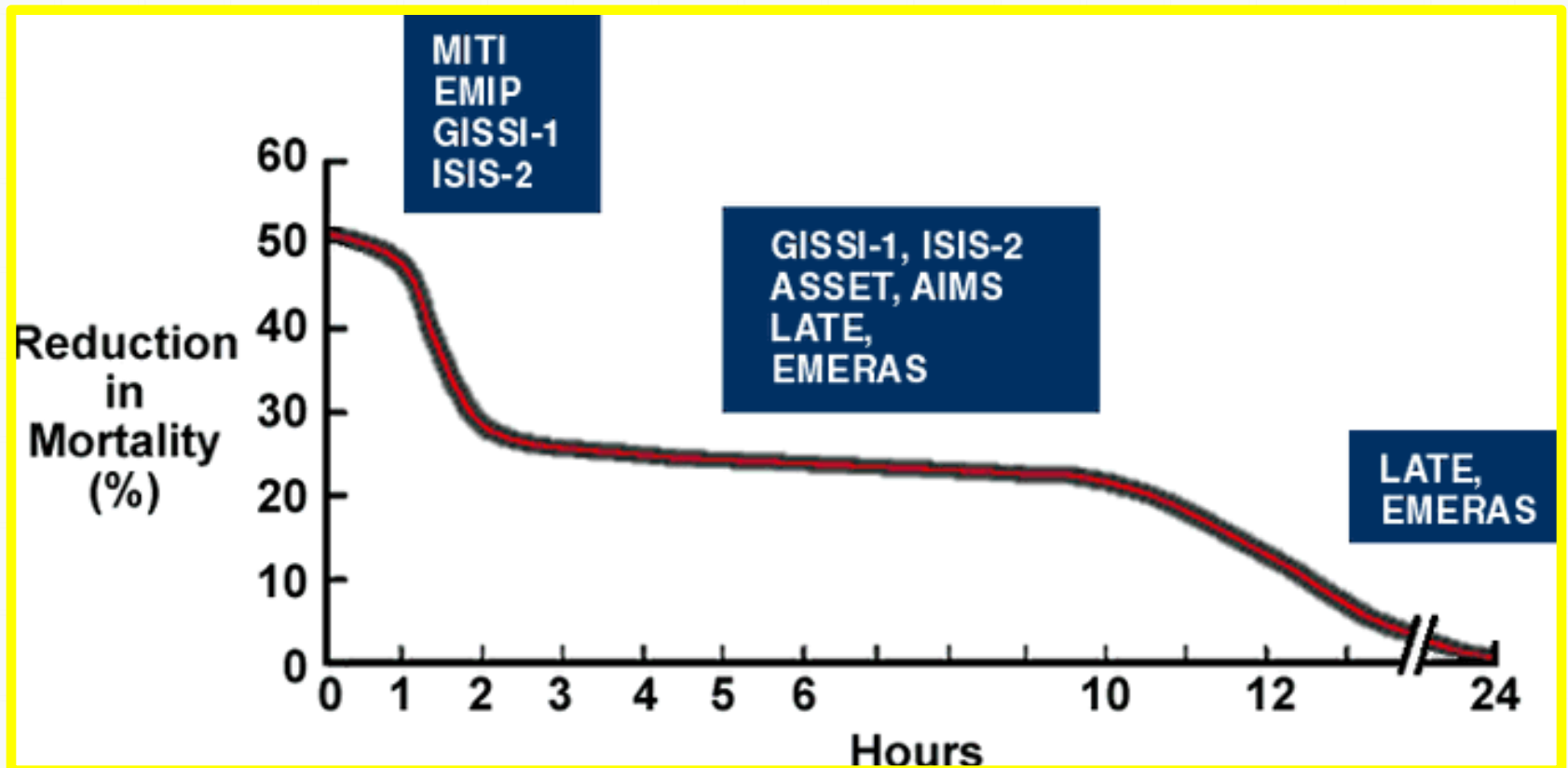
STEMI

Treatment Delayed is Treatment Denied

STEMI

30-minute delay = 8% increase in 1-year mortality
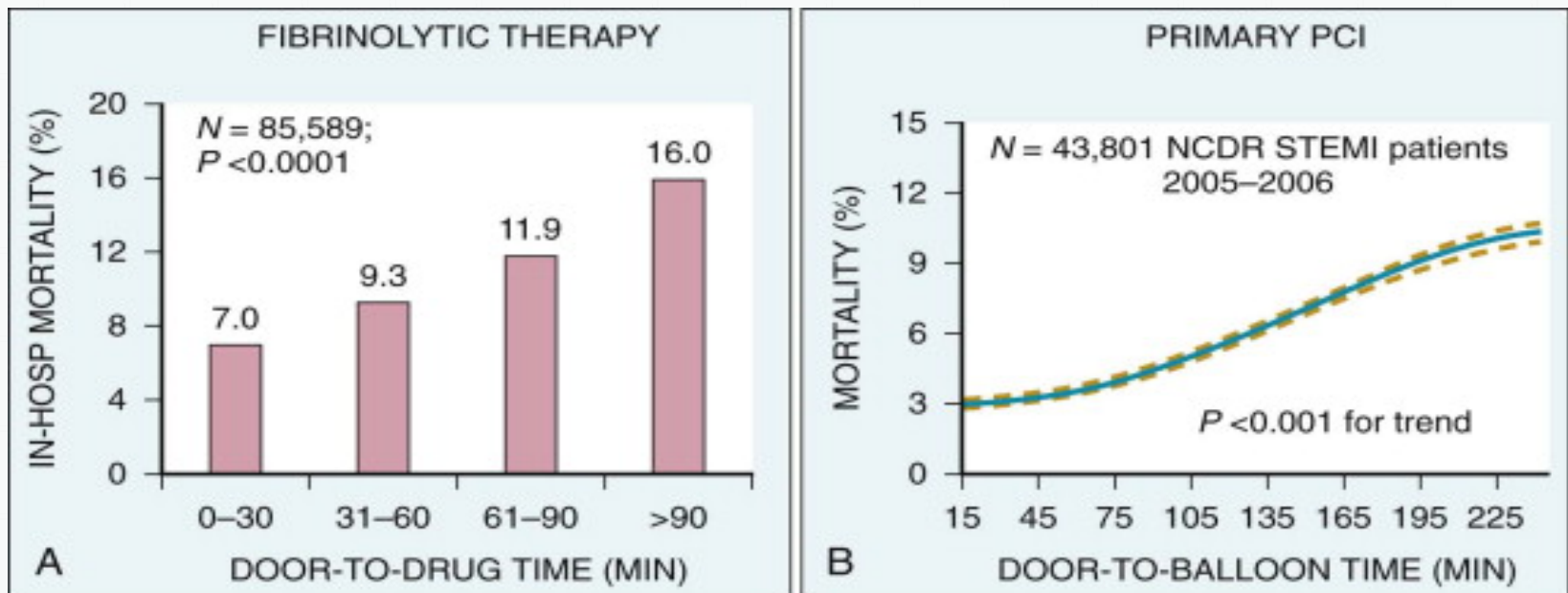
MANAGEMENT

STEMI

- Coronary Reperfusion

  fibrinolytic : streptokinase (SK) , rtPA, TNK

  PCI or CABG

- Adjunctive treatment : ACS
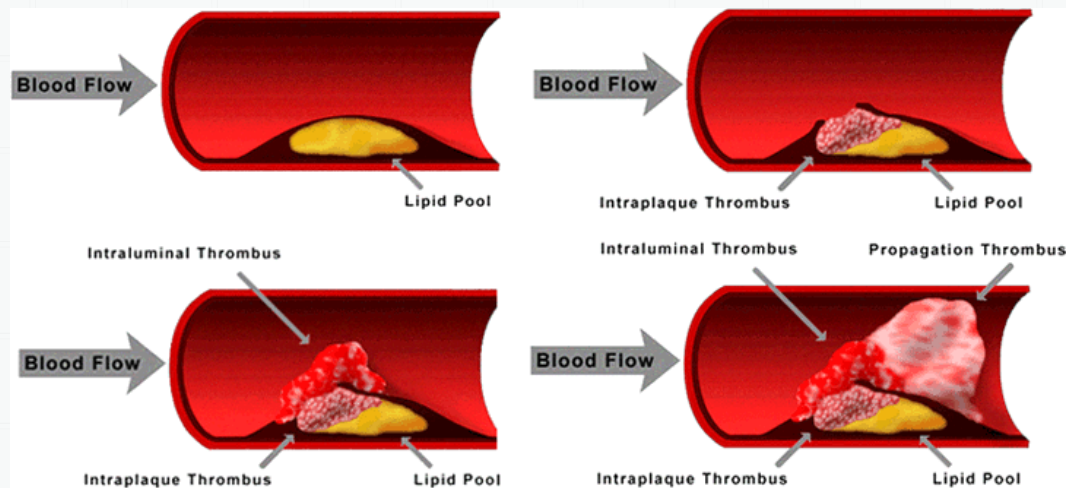
MANAGEMENT
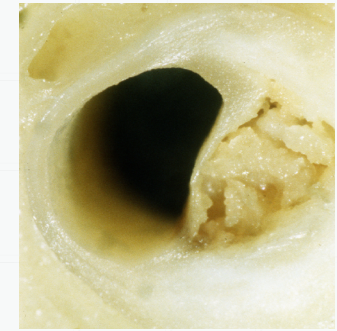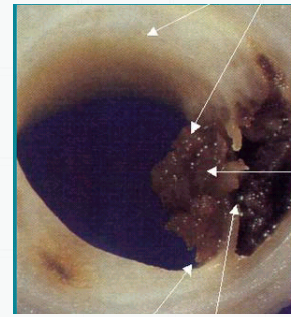
1. Dual Anti-platelets : Aspirin   81 mg/day (160-300 mg:loading)
                        : P2Y12 inhibitors : Clopidogrel 75 mg/day(300mg.)
2. Statin : Simvastatin,Atorvastatin,etc
3. Anti-ischemic : Nitrate, Rest , Oxygen
4. β-Blocker
5. ACEI or ARB especially for patients with CHF, reduced LVEF (EF<0.40) , hypertension, diabetes,or stable CKD
6. Aldosterone antagonist :wIth ACEI +B-blocker for patients : reduced LVEF (EF<0.40)
7. Anticoagulant : heparin (UFH,LMWH),Fondaparinux
8. Supportive
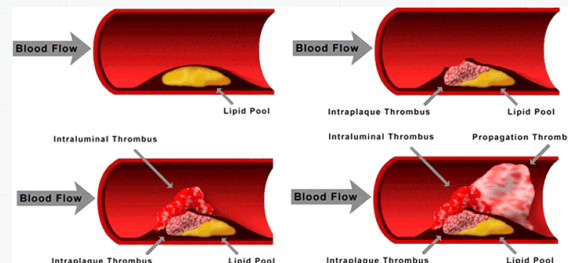
ACS
Post-discharge Mortality Remains High

GRACE Registry

ST depression

ST elevation

Neither

≈ 15% Overall mortality at 1 year

Cumulative Mortality (%)

Days From Admission
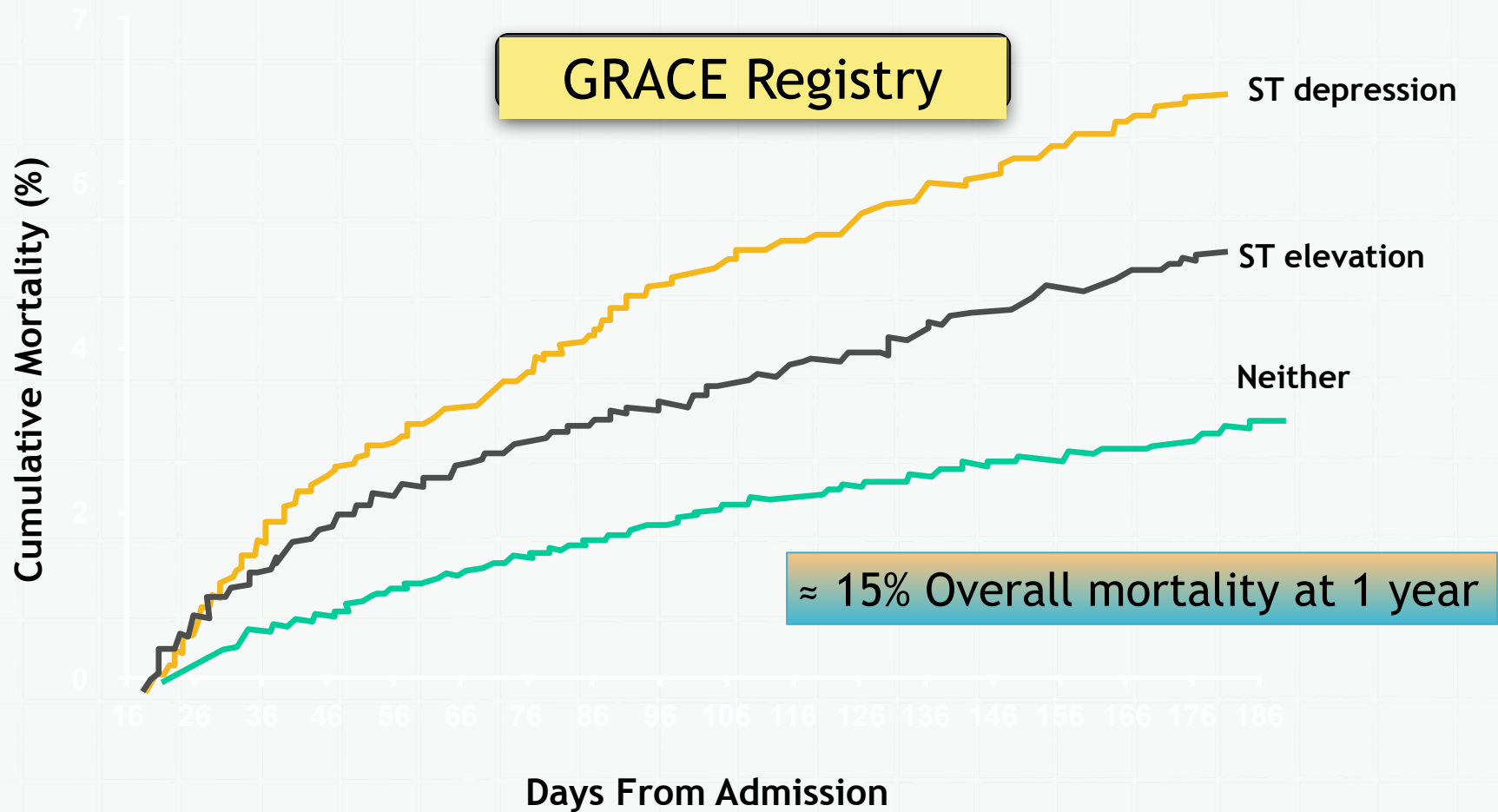
Post-discharge mortality (GRACE registry).

Thai Registry in Acute Coronary Syndrome (TRACS) - An Extension of Thai Acute Coronary Syndrome Registry (TACS) Group: Lower In-Hospital but Still High Mortality at One-Year
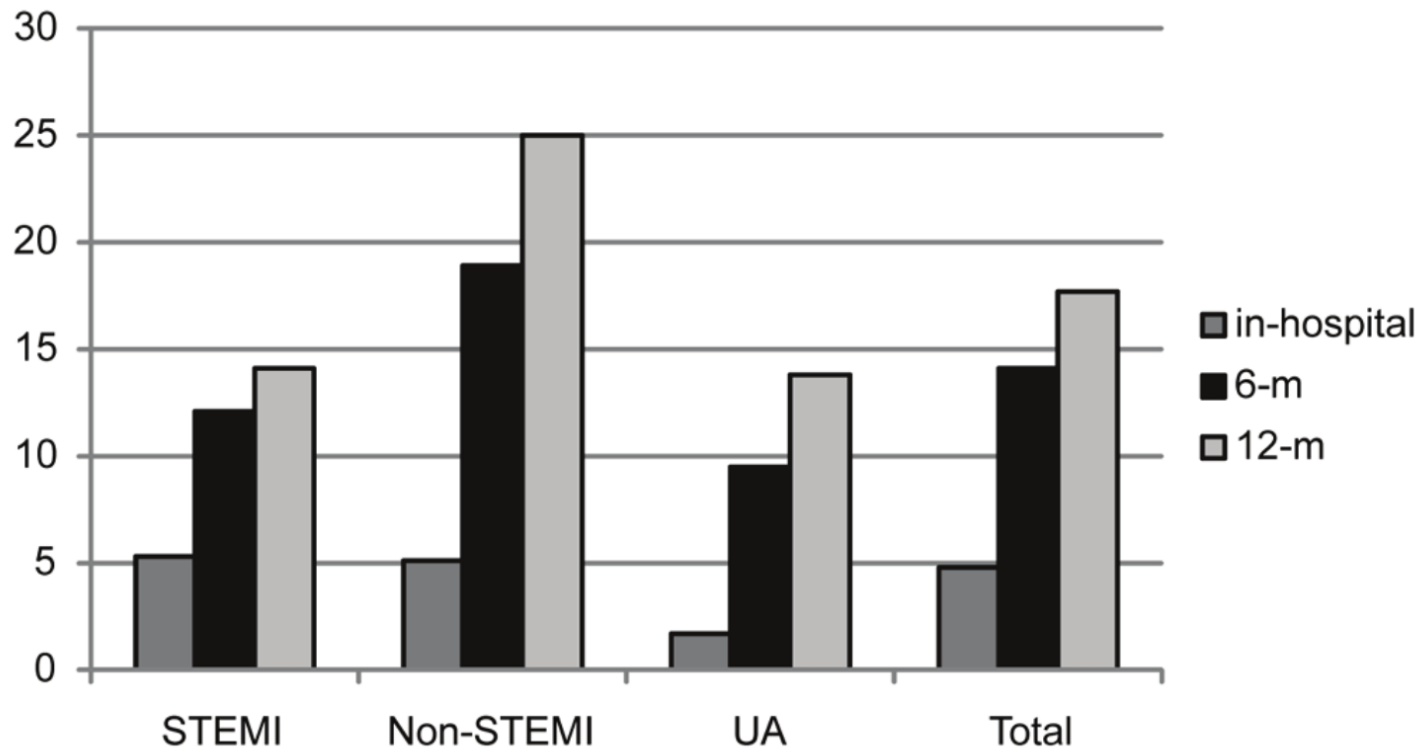
Update Management
Acute Coronary Syndromes

- Invasive strategy : Coronary angiogram:High Risk NSTE-ACS
- Antiplatelets in the management of ACS

  - Clopidogrel (CURRENT/OASIS-7)
  - Prasugrel (TRITON-TIMI 38)
  - Ticagrelor (PLATO)

- Stent : Bioabsorbable polymer
- Bioresorbable Scaffold
- Target LDL

Appropriate Selection of Invasive Strategy or Ischemia-Guided Strategy in Patients With NSTE-ACS

Immediate invasive (within 2 h)	Refractory angina
	Signs or symptoms of HF or new or worsening mitral regurgitation
	Hemodynamic instability
	Recurrent angina or ischemia at rest or with low-level activities despite intensive medical therapy
	Sustained VT or VF
Ischemia-guided strategy	Low-risk score (e.g., TIMI [0 or 1], GRACE [<109])
	Low-risk Tn-negative female patients
	Patient or clinician preference in the absence of high-risk features
Early invasive (within 24 h)	None of the above, but GRACE risk score >140
	Temporal change in Tn (Section 3.4)
	New or presumably new ST depression
Delayed invasive (within 25–72 h)	None of the above but diabetes mellitus
	Renal insufficiency (GFR <60 mL/min/1.73 m²)
	Reduced LV systolic function (EF <0.40)
	Early postinfarction angina
	PCI within 6 mo
	Prior CABG
	GRACE risk score 109–140; TIMI score ≥2

GRACE Risk Score

Mortality in hospital and at 6 months according to the GRACE risk score

Risk category (tertile)	GRACE risk score	In-hospital death (%)
Low	≤ 108	< 1
Intermediate	109-140	1-3
High	> 140	> 3

Risk category (tertile)	GRACE risk score	Post- discharge to 6-month death (%)
Low	≤ 88	< 3
Intermediate	89-118	3-8
High	> 118	> 8

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Appropriate Selection of Invasive Strategy or Ischemia-Guided Strategy in Patients With NSTE-ACS

Immediate invasive (within 2 h)	Refractory angina
	Signs or symptoms of HF or new or worsening mitral regurgitation
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	Early postinfarction angina
	PCI within 6 mo
	Prior CABG
	GRACE risk score 109–140; TIMI score ≥2

TIMI Risk Score* for NSTE-ACS

TIMI Risk Score	All-Cause Mortality, New or Recurrent MI, or Severe Recurrent Ischemia Requiring Urgent Revascularization Through 14 d After Randomization, %
0–1	4.7
2	8.3
3	13.2
4	19.9
5	26.2
6–7	40.9

*The TIMI risk score is determined by the sum of the presence of 7 variables at admission; 1 point is given for each of the following variables: ≥65 y of age; ≥3 risk factors for CAD; prior coronary stenosis ≥50%; ST deviation on ECG; ≥2 anginal events in prior 24 h; use of aspirin in prior 7 d; and elevated cardiac biomarkers.

TIMI Risk Score

TIMI UA Risk Score: 1°EP at 6 mos
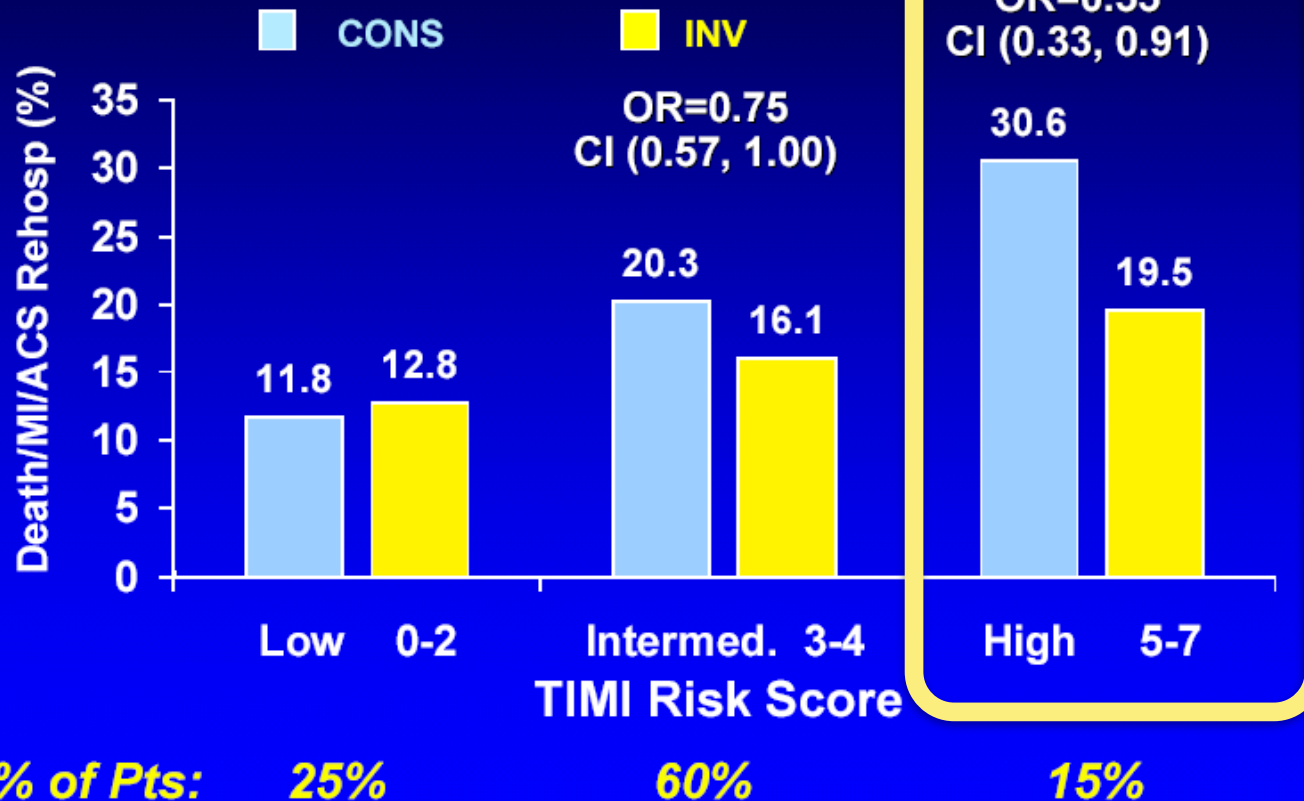
Current ACS Management
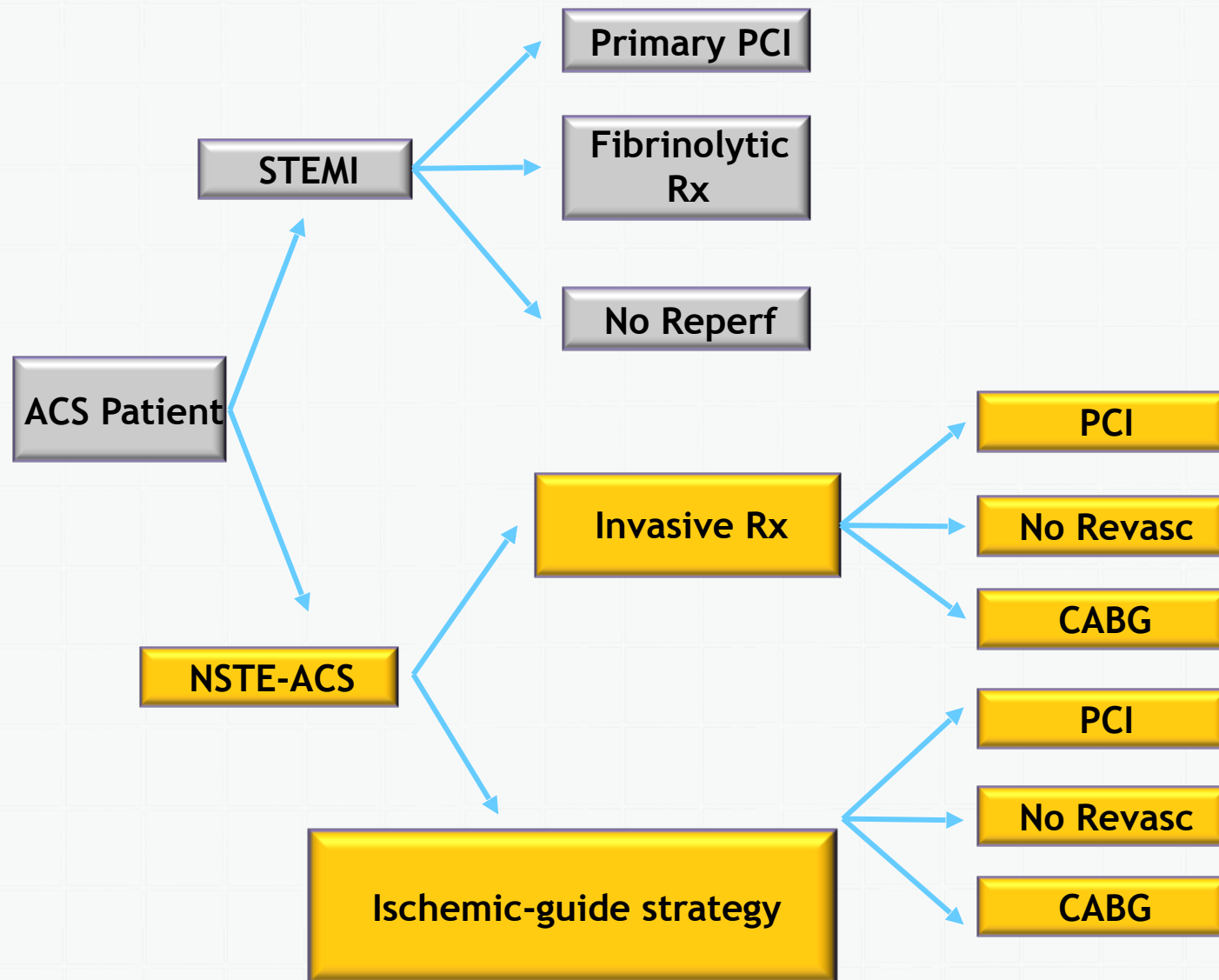
What's New in
Acute Coronary Syndromes?

- **Invasive strategy : Coronary angiogram:High Risk NSTE-ACS**
- **Antiplatelets in the management of ACS**

  - **Clopidogrel (CURRENT/OASIS-7)**
  - **Prasugrel (TRITON-TIMI 38)**
  - **Ticagrelor (PLATO)**

- **Stent : Bioabsorbable polymer**
- **Bioresorbable Scaffold**
- **Target LDL**

Platelet Cascade

Clopidogrel

ADP:P2Y12

Thrombin

EPI

PAF

Collagen

5HT

Platelet

TXA$_2$

ASA

Gp 2b/3a receptor

Platelet Aggregation

Clot
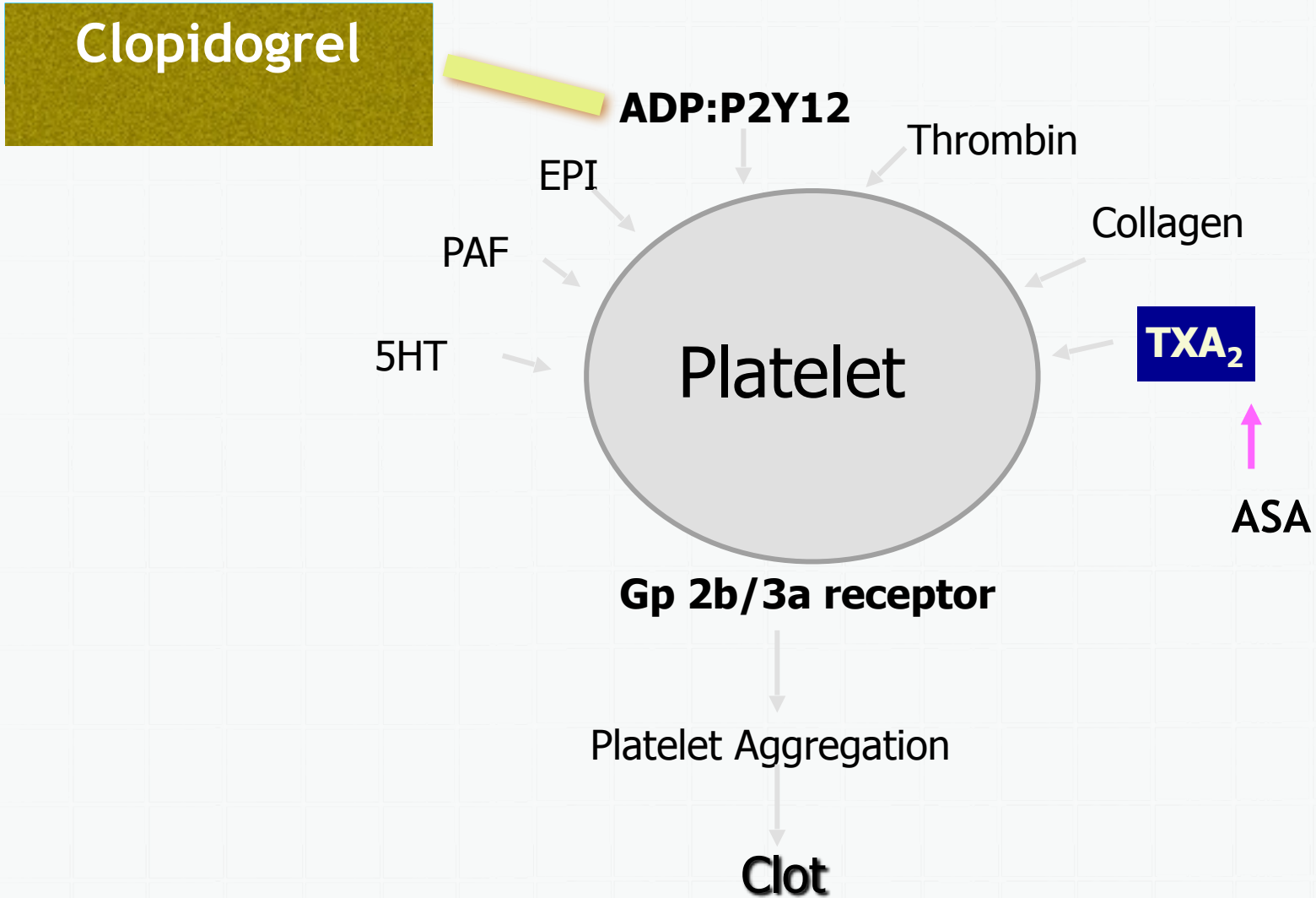
Limitations of Antiplatelet Therapy ASA ,Clopidrogrel

- **Slow Onset**
- **Level of Platelet Inhibition**
- **Variability of Response : 15-40%**
  - **High on-treatment platelet reactivity leads to increased risk of ischemic events**
  - **Medication : CYP 3A4**
  - **Patient factors : CYP 2C19*2: 50-65 % Asia**
  - **Underlying : overweight,DM type II**

Influence of Diabetes Mellitus on Clopidogrel-induced Antiplatelet Effects

Acute phase of treatment

DM

No-DM

P=0.04

38%

6%

56%

8%

14%

78%

24 hrs post 300 mg LD

■ Non-responders (Platelet inhibition <10%)
■ Low responders (Platelet inhibition 10-29%)
■ Responders (Platelet inhibition >30%)
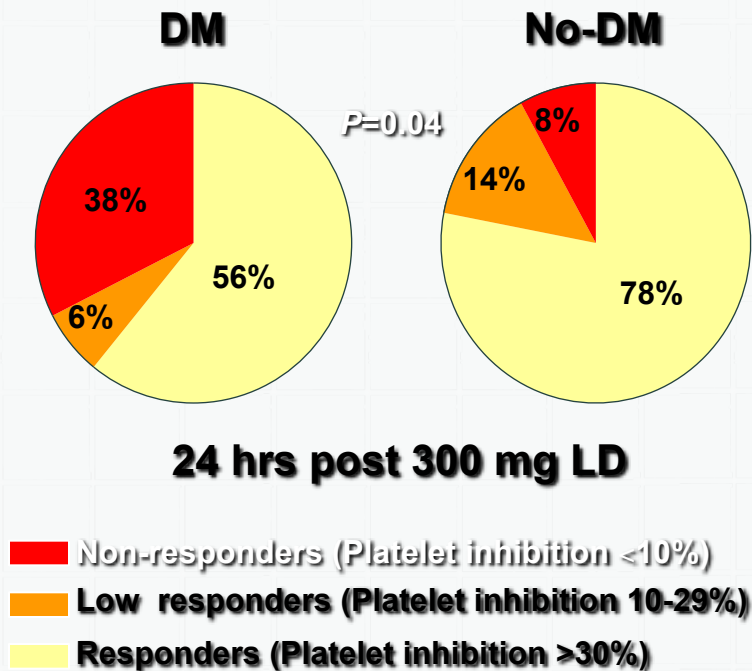
Long-term phase of treatment

P=0.001

P<0.0001

Platelet aggregation (%)

80

60

40

20

0

T2DM   No-DM

ADP 20 μmol/L

T2DM   No-DM

ADP 6 μmol/L

Angiolillo DJ et al. *Diabetes*. 2005;54:2430-5.

Angiolillo DJ et al. *J Am Coll Cardiol* 2006;48:298-304
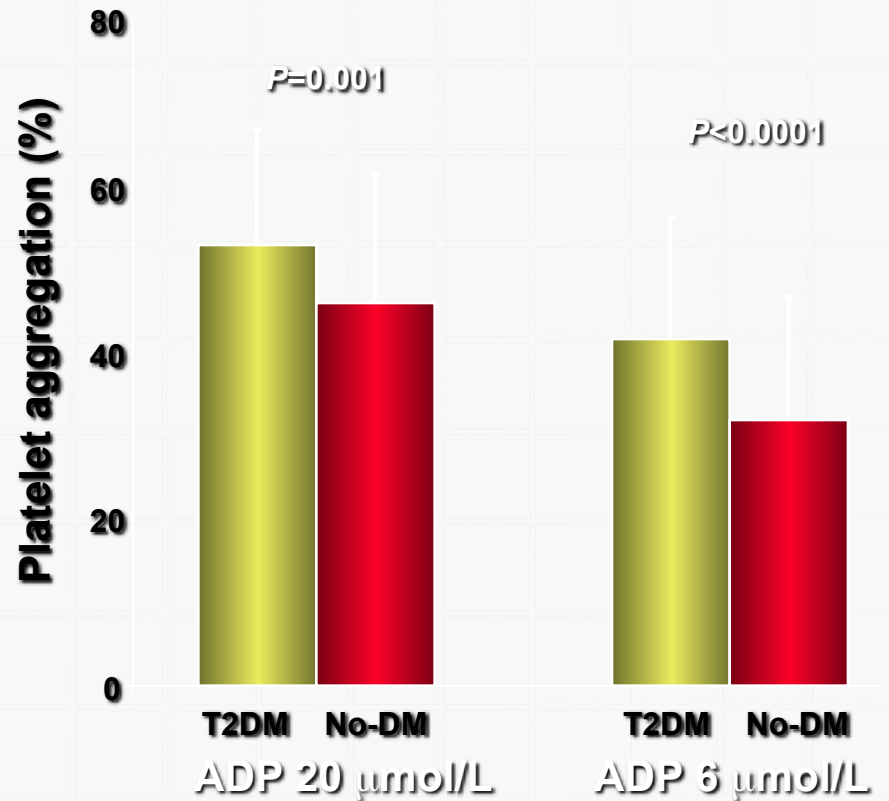
Clopidogrel: Double vs Standard Dose

	Standard	Double	HR	95% CI	P	Intn
CV Death/MI/Stroke						
PCI (2N=17,232)	4.5	3.9	0.85	0.74-0.99	0.036	
No PCI (2N=7855)	4.2	4.9	1.17	0.95-1.44	0.14	0.016
Overall (2N=25,087)	4.4	4.2	0.95	0.84-1.07	0.370	
MI						
PCI (2N=17,232)	2.6	2.0	0.78	0.64-0.95	0.012	
No PCI (2N=7855)	1.4	1.7	1.25	0.87-1.79	0.23	0.025
Overall (2N=25,087)	2.2	1.9	0.86	0.73-1.03	0.097	
CV Death						
PCI (2N=17,232)	1.9	1.9	0.96	0.77-1.19	0.68	
No PCI (2N=7855)	2.8	2.7	0.96	0.74-1.26	0.77	1.0
Overall (2N=25,087)	2.2	2.1	0.96	0.81-1.14	0.628	
Stroke						
PCI (2N=17,232)	0.4	0.4	0.88	0.55-1.41	0.59	
No PCI (2N=7855)	0.8	0.9	1.11	0.68-1.82	0.67	0.50
Overall (2N=25,087)	0.5	0.5	0.99	0.70-1.39	0.950	

CURRENT-OASIS 7 Conclusions

- **High Loading Dose Clopidogrel 600 mg.**
  - ↓ **stent thrombosis and major CV(MI) events in PCI patients**
  - ↑ **CURRENT-defined major bleeds but not TIMI major, ICH or fatal**

- **High Dose ASA > 300 mg.**
  - **No significant difference in efficacy or bleeding**

Platelet Cascade
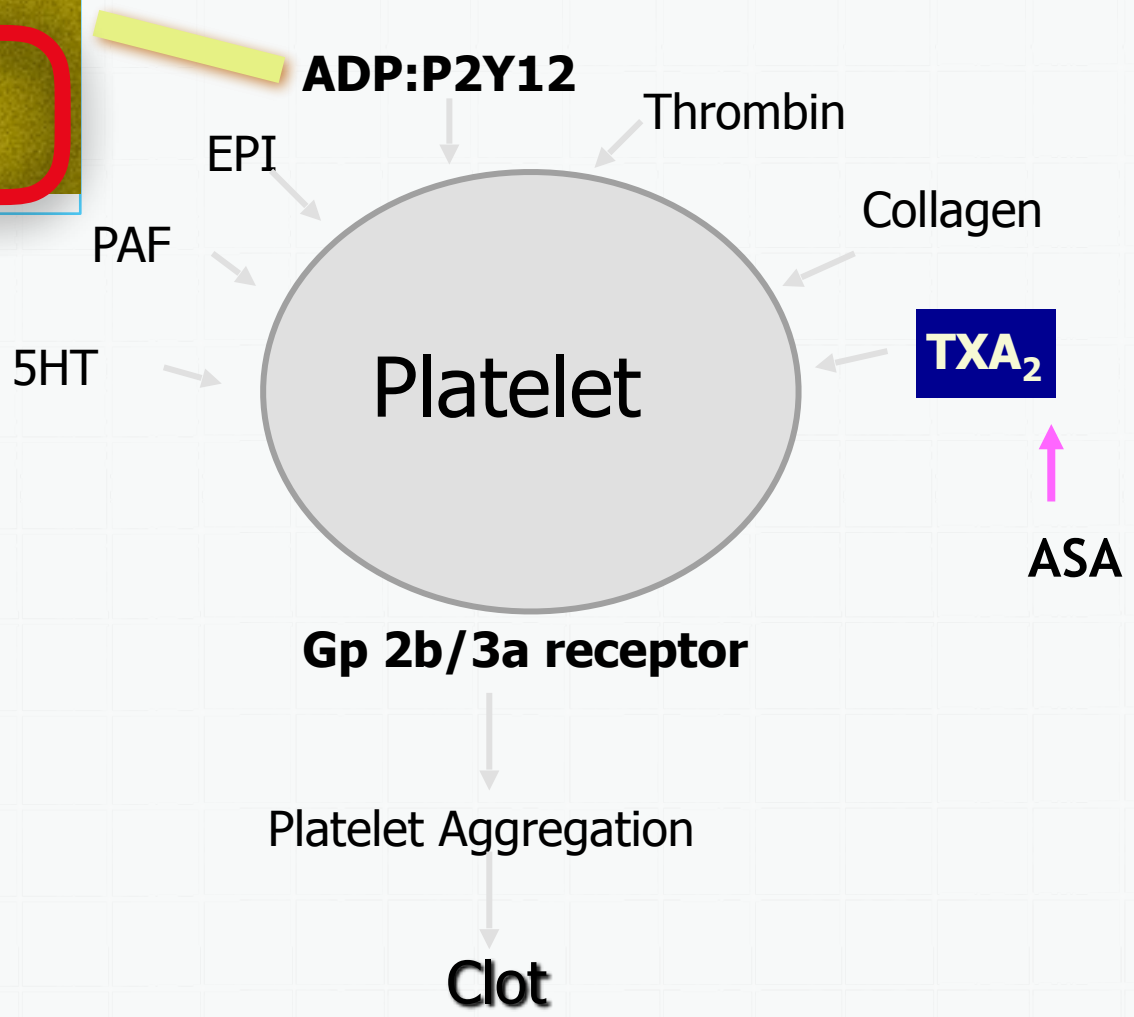
Comparison of Antiplatelet Agents in ACS
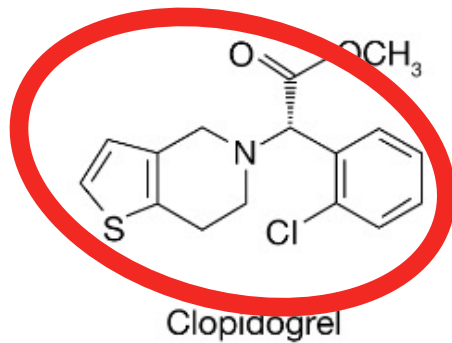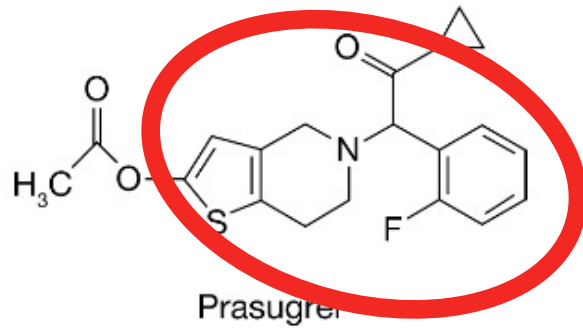
Thienopyridine
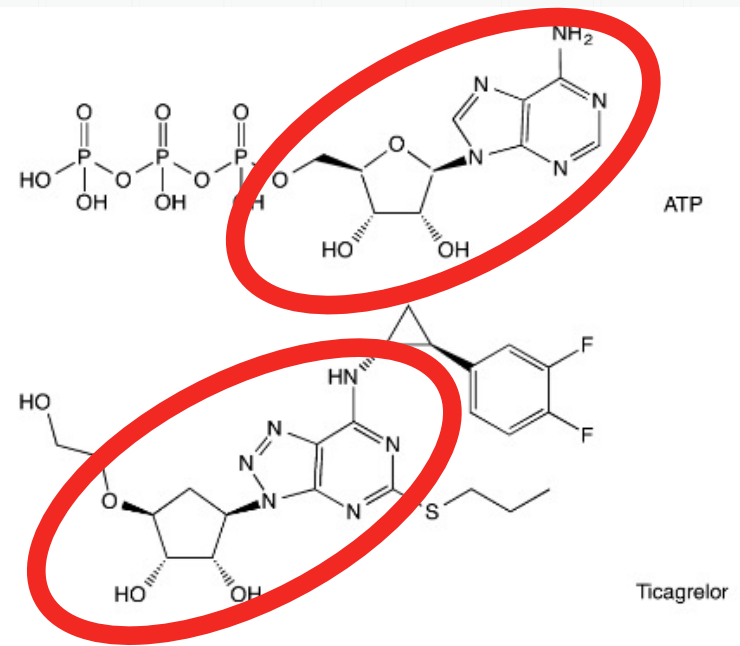
Cyclopentyltriazolo-pyrimidines

Ticagrelor

Prasugrel

Clopidogrel

No in vivo biotransformation

Ticagrelor

Prasugrel

Clopidogrel

Hydrolysis by esterase

CYP-dependent oxidation
CYP3A4/5
CYP2B6
CYP2C19
CYP2C9
CYP2D6

Binding

Platelet

P2Y12

CYP-dependent oxidation
CYP1A2
CYP2B6
CYP2C19

CYP-dependent oxidation
CYP2C19
CYP3A4/5
CYP2B6

● Active compound
● Intermediate metabolite
● Prodrug
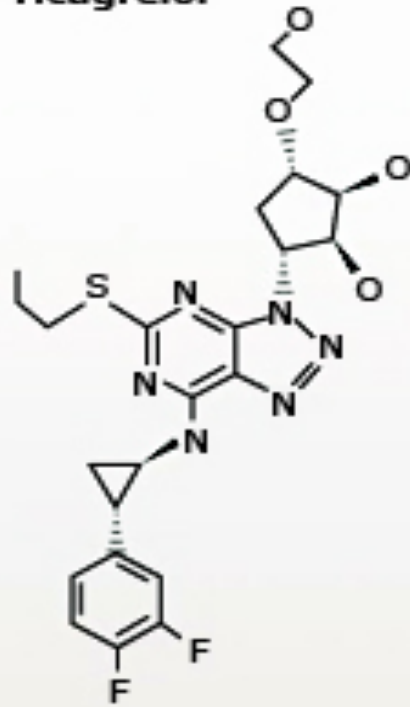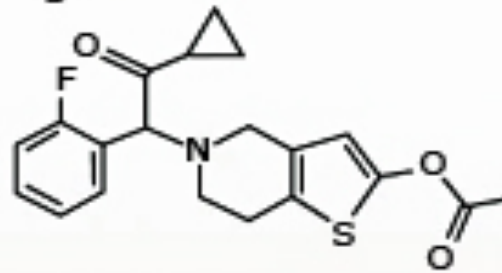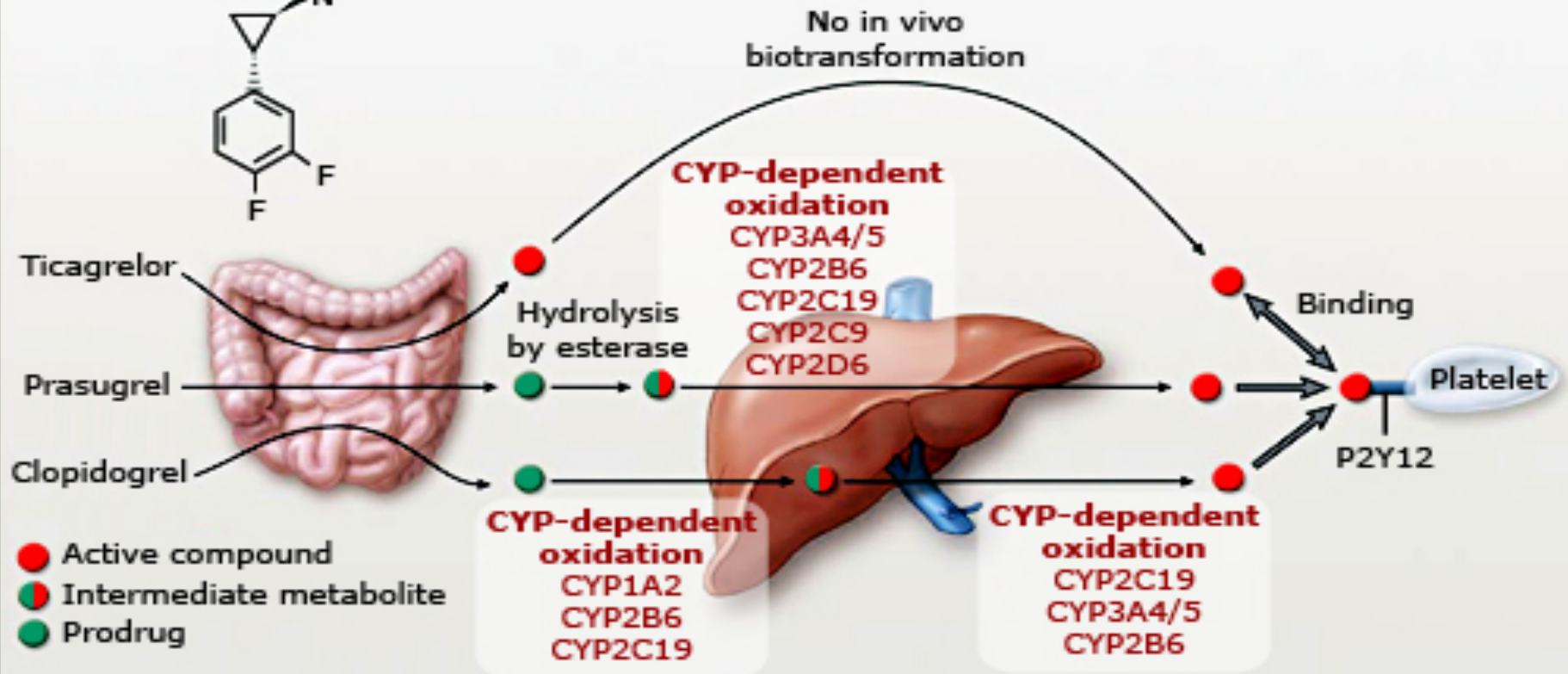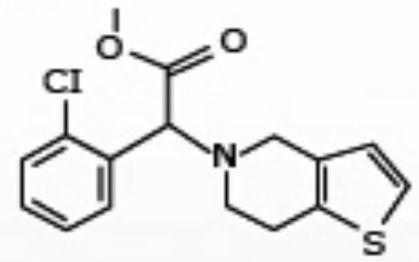
Comparison of Antiplatelet Agents in ACS

	Ticagrelor	Prasugrel	Clopidogrel
Mechanism	Reversible	Irreversible	Irreversible
Inhibitory effect	++	++	+
Onset of loading Dose	30 min	30 min	2-6 hr
Dose : Daily	Twice	Once	Once
Mean IPA at 120 mins %	>80	>80	38-42
Duration	24 – 48 h	5-7 days	5-7 days

TRITON-TIMI 38

Wiviott SD et al. New Engl J Med 2007;357:2001-2015
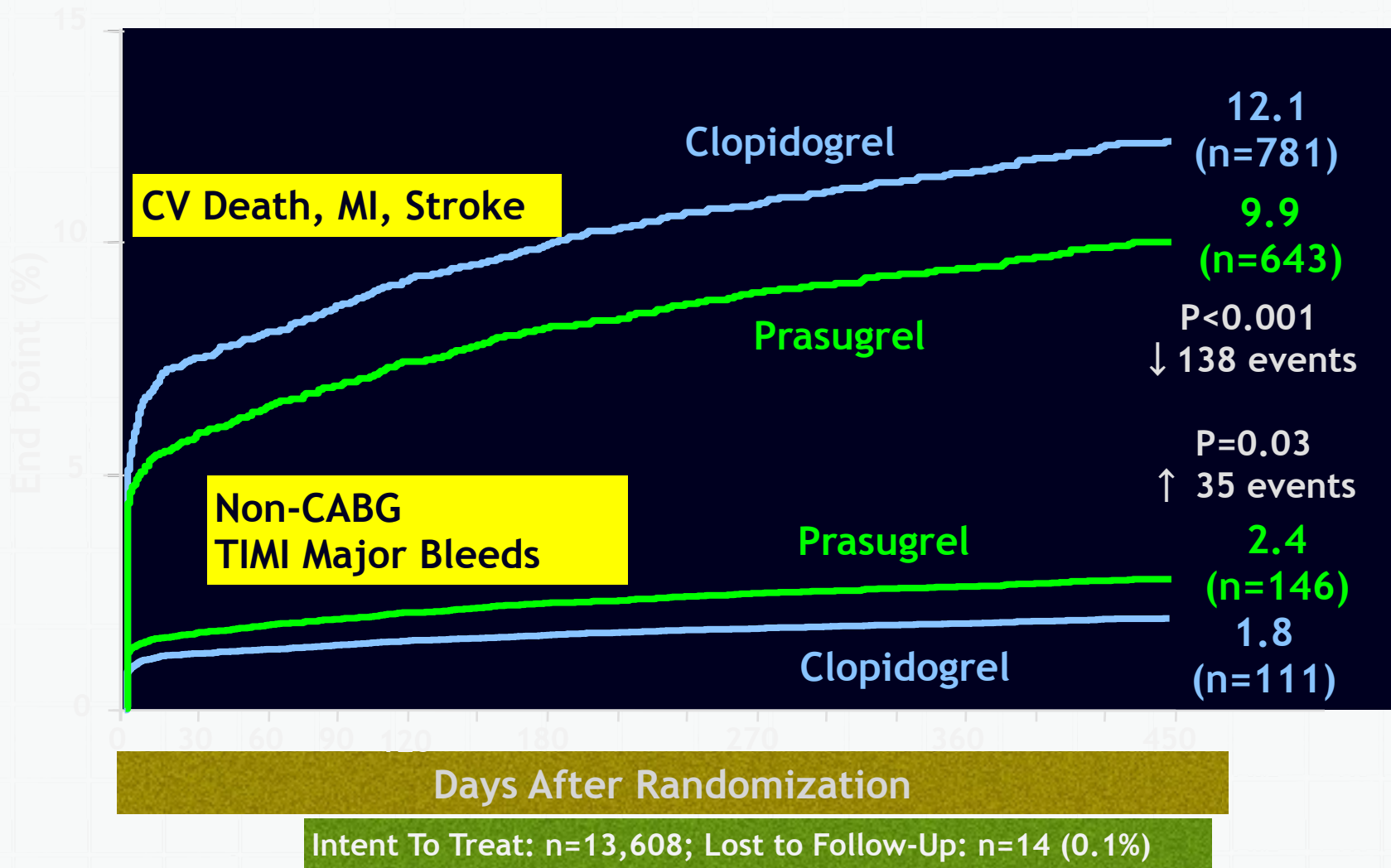
TRITON-TIMI 38: Non-CABG TIMI Major Bleed

History of stroke or TIA

Yes — 0.06
No — 0.08

Any of the following:

**Age ≥75 y,
Body wt. <60 kg,
History stroke/TIA**

Yes — 0.10
No — 0.17

P* value

0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5

HR

Prasugrel Better   Clopidogrel Better
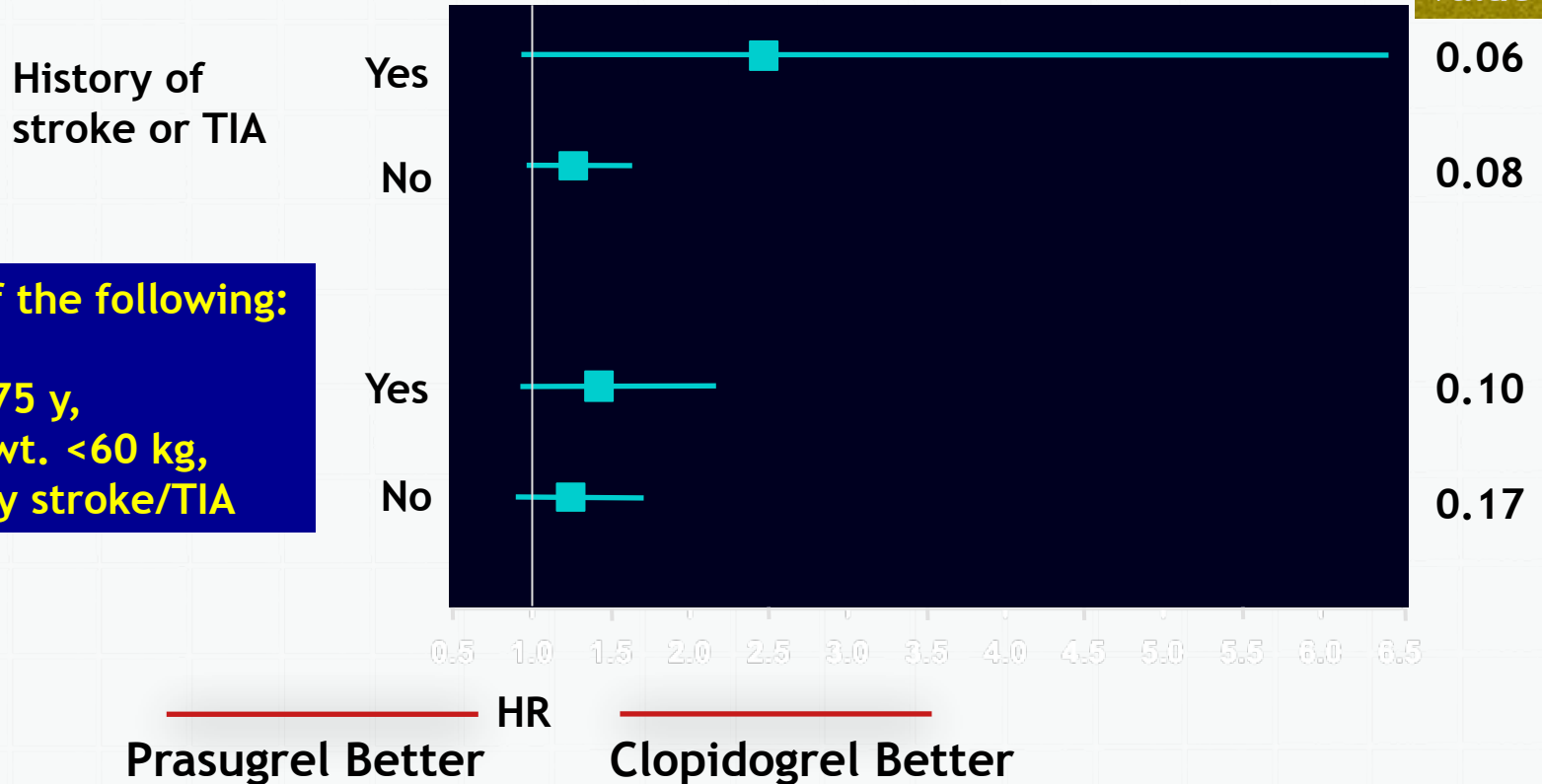
*Tests HR=1.0 within subgroups; **Tests equality HR between subgroups

Wiviott SD et al. New Engl J Med 2007;357:2001-2015

TRITON-TIMI 38: Other TIMI Bleeds

Wiviott SD et al. New Engl J Med 2007;357:2001-2015
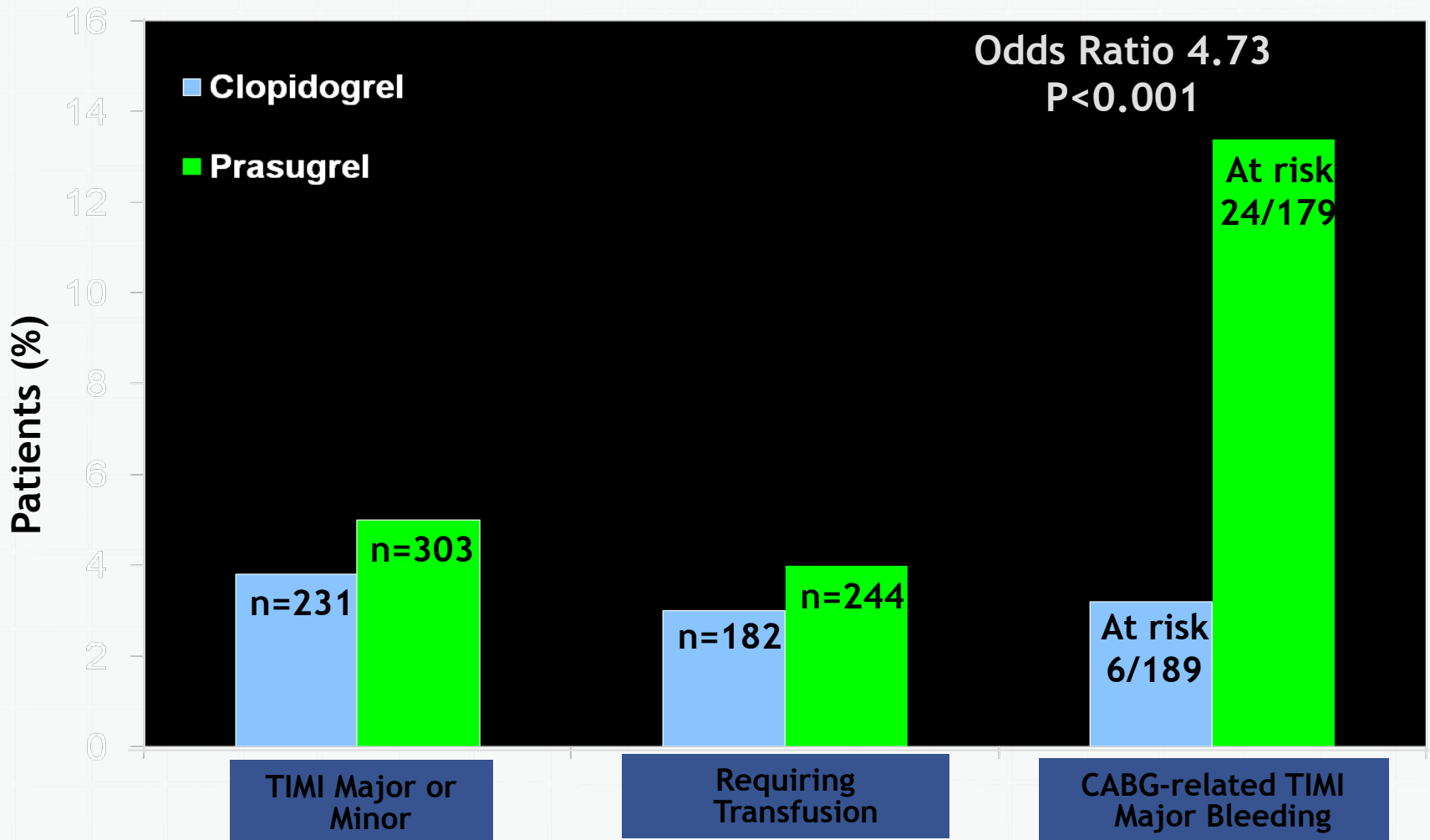
Prasugrel Evidence Medically Manage ACS

Targeted Platelet Inhibition to Clarify the Optimal Strategy to Medically Manage Acute Coronary Syndromes (TRILOGY-ACS)

7243 patients with a medically managed NSTE-ACS randomized to prasugrel (10 mg) or clopidogrel for up to 30 months

CV Death, Nonfatal MI, and Nonfatal Stroke (%)

Primary Efficacy Endpoint

16.0% Clopidogrel

Prasugrel 13.9%

HR=0.91, P=0.21

Clopidogrel 16.0%

Prasugrel 13.9%

No. at risk:						
Prasugrel:	3620	3248	2359	1611	953	389
Clopidogrel:	3623	3244	2390	1596	946	399

Days

Time (Days)
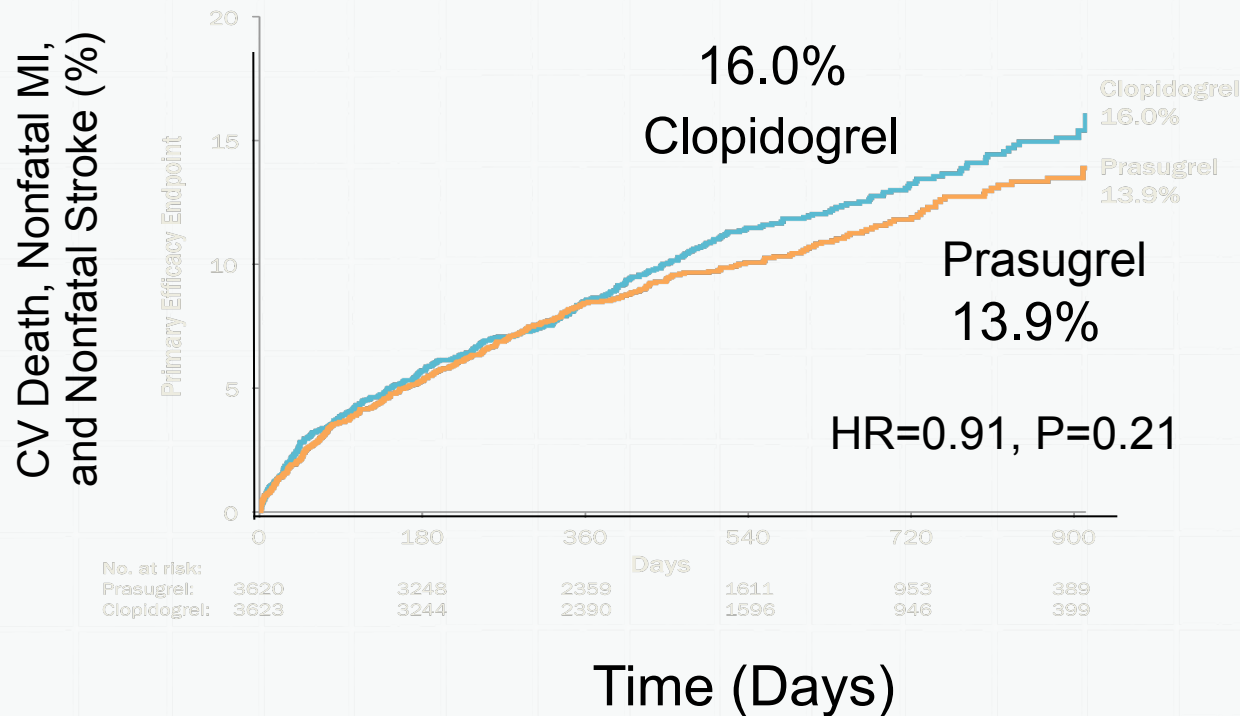
Prasugrel does not provide benefit in medically managed NSTE-ACS

CV=Cardiovascular, MI=Myocardial infarction, NSTE-ACS=Non-ST-segment elevation acute coronary syndrome

Efficacy outcomes of Ticagrelor (NSTE-ACS population)

Primary endpoint (CV death, MI or stroke)

All-cause death

12.3%

10.0%

HR (95% CI) = 0.83 (0.74-0.93) *P*=0.0013

5.8%

4.3%

Clopidogrel

Ticagrelor

HR (95% CI) = 0.76 (0.64-0.90) *P*=0.0020
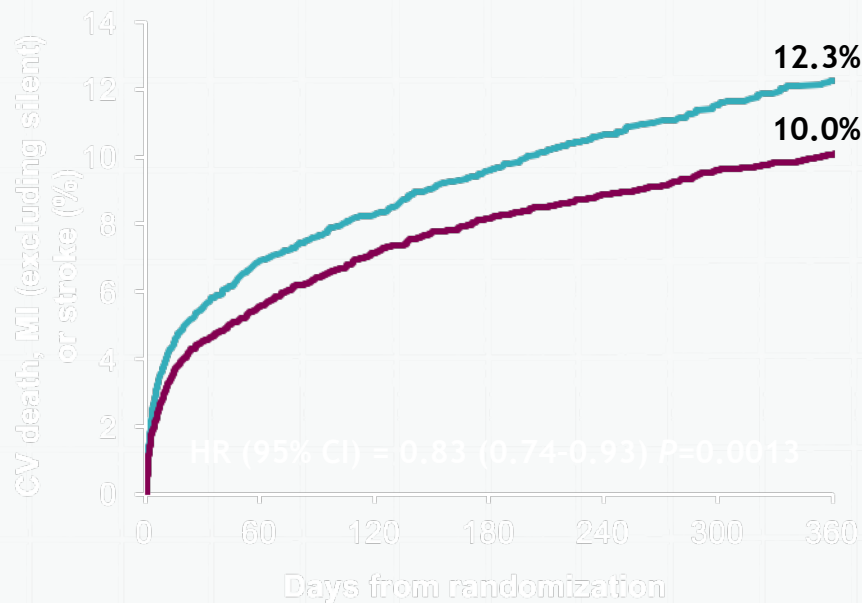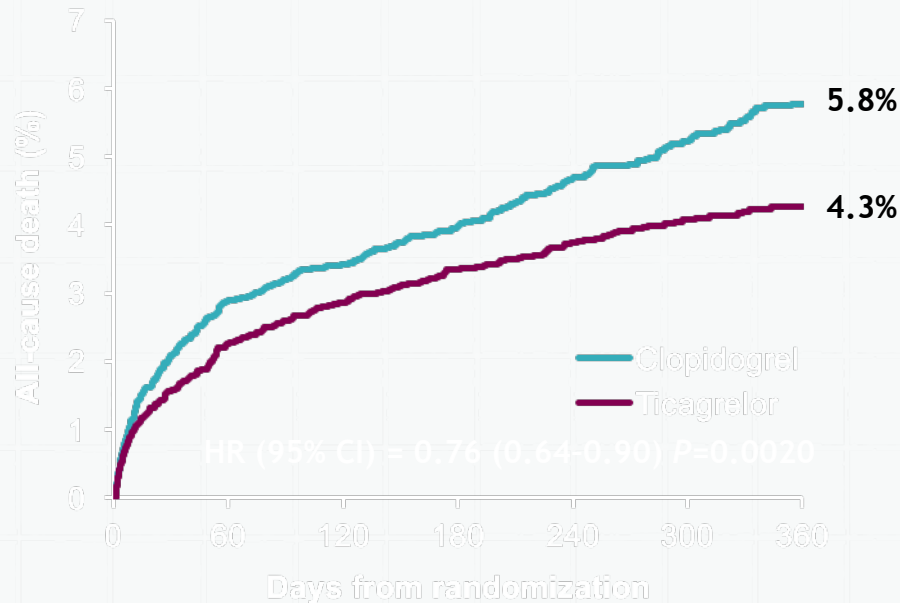
No. at risk							
Clop	5499	5019	4924	4768	3924	2999	2395
Tic	5581	5152	5036	4888	4056	3112	2417

No. at risk							
Clop	5499	5521	5200	5078	4207	3225	2591
Tic	5581	5343	5283	5165	4307	3328	2651

Efficacy outcomes of Ticagrelor (NSTE-ACS population)

Major bleeding

13.4%
12.6%

HR (95% CI) = 1.07 (0.95–1.19) *P*=0.2590

Major bleeding (%)

Days from randomization
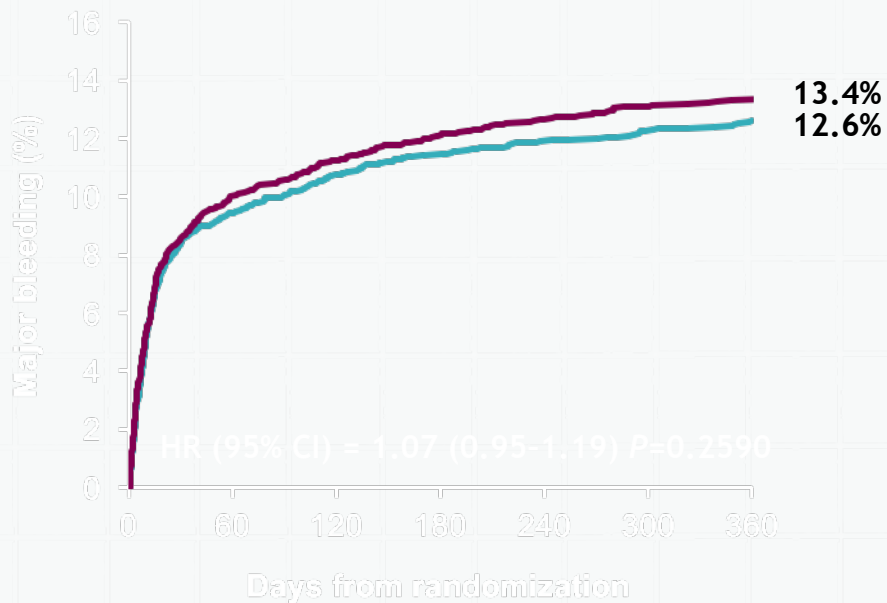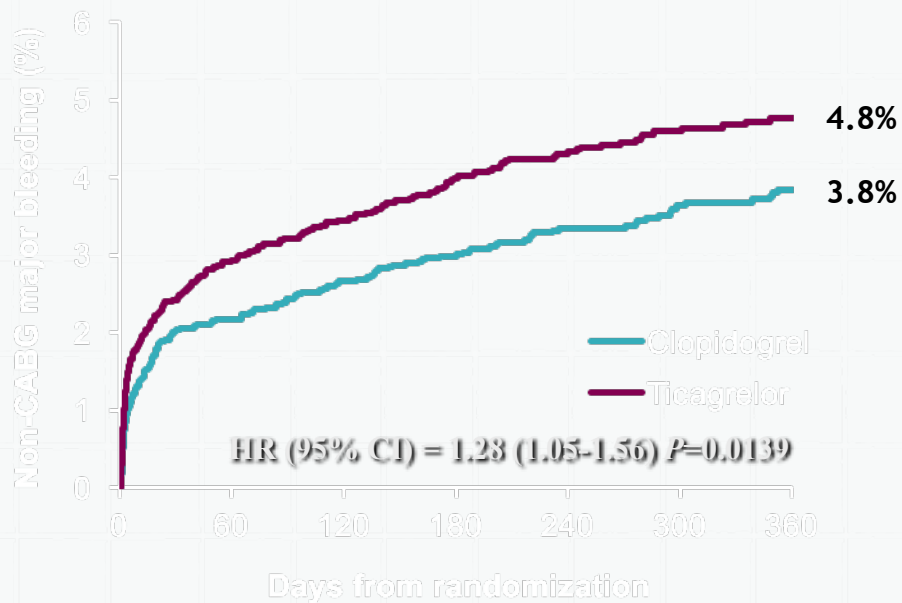
No. at risk

Clop	5434	4211	3956	3811	3006	2212	2000
Tic	5516	4166	3904	3725	2943	2183	1965

Non-CABG major bleeding

4.8%
3.8%

Clopidogrel
Ticagrelor

HR (95% CI) = 1.28 (1.05–1.56) *P*=0.0139

Non-CABG major bleeding (%)

Days from randomization

No. at risk

Clop	5434	4470	4230	4086	3232	2389	2164
Tic	5516	4413	4161	3987	3152	2347	2119

Safety outcomes (total NSTE-ACS population)

NEJM 2009;361:1045-57.

Efficacy outcomes of Ticagrelor (NSTE-ACS population)

Characteristic	N	HR (95% CI)
Overall	5189	0.85 (0.72-1.01)
TIMI >2		
No	603	0.57 (0.22-1.44)
Yes	4345	0.87 (0.73-1.04)
ACS diagnosis		
NSTEMI	2949	**0.81 (0.65-0.99**)
UA	1976	1.04 (0.74-1.46)
Diabetes		
No	3605	0.84 (0.66-1.06)
Yes	1573	0.84 (0.65-1.08)
Smoking		
No	3900	0.84 (0.69-1.02)
Yes	1277	0.89 (0.61-1.28)
Prior MI		
No	3629	**0.77 (0.61-0.97**)
Yes	1549	1.00 (0.77-1.30)
Prion PCI		
No	4391	**0.82 (0.67-0.99**)
Yes	787	1.03 (0.69-1.54)

Scale: 0.25 0.5 1.0 2.0 4.0

Ticagrelor better ← → pidogrel better

Lindholm D et al. Eur Heart J 2014 [doi: 10.1093/eurheartj/ehu160] (Supplementary Appendix)

Efficacy outcomes of Ticagrelor (NSTE-ACS population)

Subgroup

Characteristic	N	HR (95% CI)
Overall	5189	0.85 (0.72–1.01)
Age, years		
<65	2459	1.03 (0.76–1.40)
≥**65**	2730	**0.75 (0.61–0.93**)
Sex		
Male	3190	0.89 (0.72–1.11)
Female	1999	0.78 (0.59–1.05)
Weight, kg		
<**60**	426	**0.54 (0.31–0.95**)
≥60	4745	0.89 (0.74–1.07)
GRACE score		
<100	498	0.93 (0.44–1.98)
100–140	2177	0.96 (0.69–1.33)
>**140**	1976	**0.82 (0.65–1.03**)
Angiography		
No	2733	0.90 (0.72–1.12)
Yes	2423	**0.80 (0.61–1.07)**

0.25 0.5 1.0 2.0 4.0

Ticagrelor better ← | → Clopidogrel better

45

Efficacy outcomes of Ticagrelor (NSTE-ACS population)

Subgroup

CV death/MI/Stroke (In-Hospital Invasive)

- HR 0.76(0.63-0.91): TnT>14 ng/L — 8.5 vs 11.2 ⭐
- HR 0.99(0.53-1.83): TnT<14 ng/L — 12.5 vs 11.5

CV death/MI/Stroke (In-Hospital non-invasive)

- HR 0.81(0.68-0.97): TnT>14 ng/L — 12.4 vs 14.9 ⭐
- HR 1.40(0.66-2.97): TnT<14 ng/L — 3.1 vs 2.4

Cumulative incidence (%)

In-Hospital Invasive

In-Hospital non-invasive
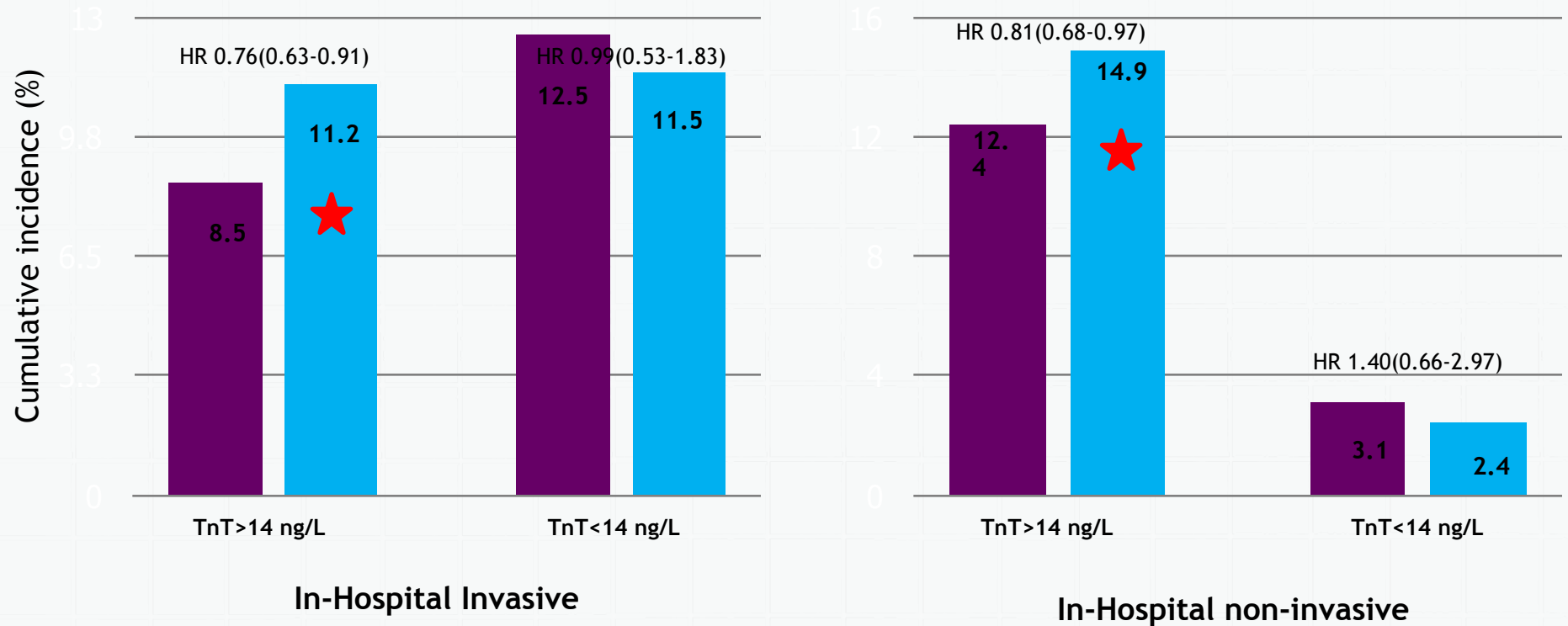
Ticagrelor versus clopidogrel reduced the rate of cardiovascular death, myocardial infarction, and stroke in patients with NSTE-ACS and hs-TnT ≥14.0 ng/L in both invasively and noninvasively managed patients

Wallentin L et al. Circulation. 2014;129:293-303

PLATO: Safety

	Ticagrelor N=9333	Clopidogrel n=9291	p
Dyspnea	13.8%	7.8%	<0.001
Dyspnea requiring discontinuation	0.9%	0.1%	<0.001
Ventricular Pauses			
≥ 3 sec	5.8%	3.6%	0.01
≥ 5 sec	2.0%	1.2%	0.10
Increase in SrCr (%)			
1month	10±22	8±21	<0.001
12 month	11±22	9±22	<0.001
End of Tx	10±22	10±22	0.59

Dose of Antiplatelet Agents in ACS

	Clopidogrel	**Prasugrel**	**Ticagrelor**
Evidence	CURE PCI-CURE	TRITON-TIMI 38	PLATO
Dose	300-600mg X 1 75 mg od (150mg X 7d)	60mg X 1, 10mg od	180mg X 1 90mg bid

High vs Standard Loading Dose Regimens of Ticagrelor and Prasugrel in STEMI patients undergoing PPCI

Results of Prospective, Non-randomized, Pharmacodynamic Studies

Ticagrelor
(360mg, n=45; 180mg, n=38)

Prasugrel
(100mg, n=47; 60mg, n=35)
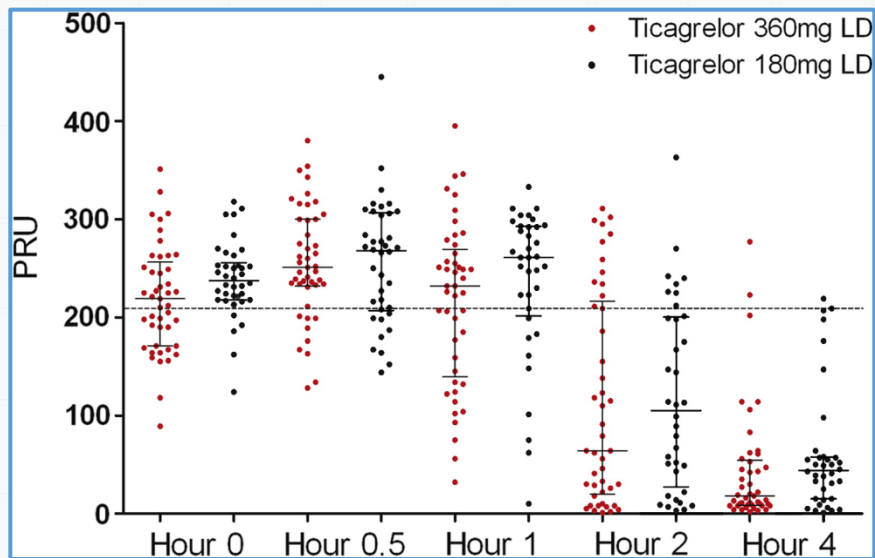
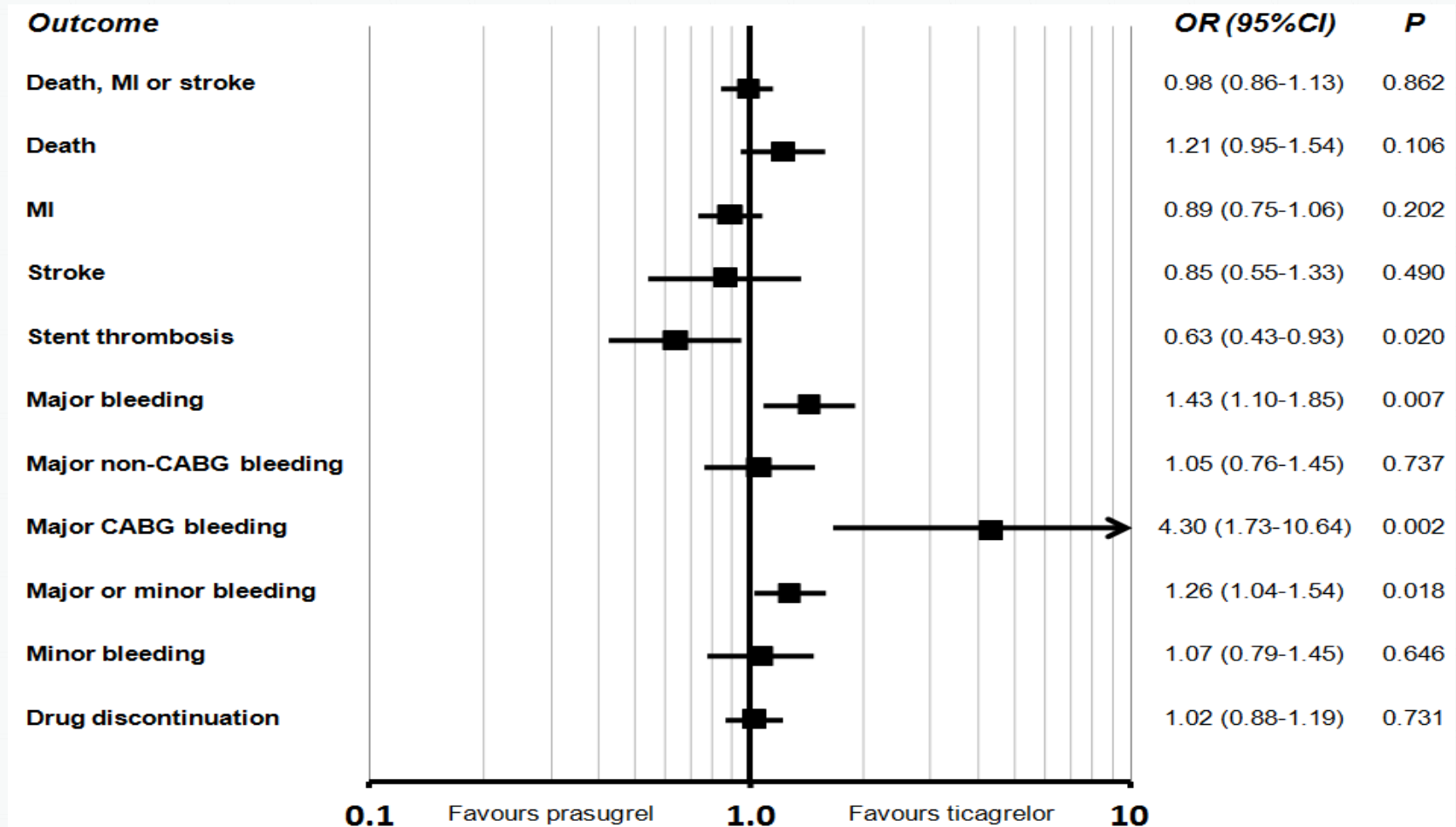

Alexopoulos et al. JACC 2013
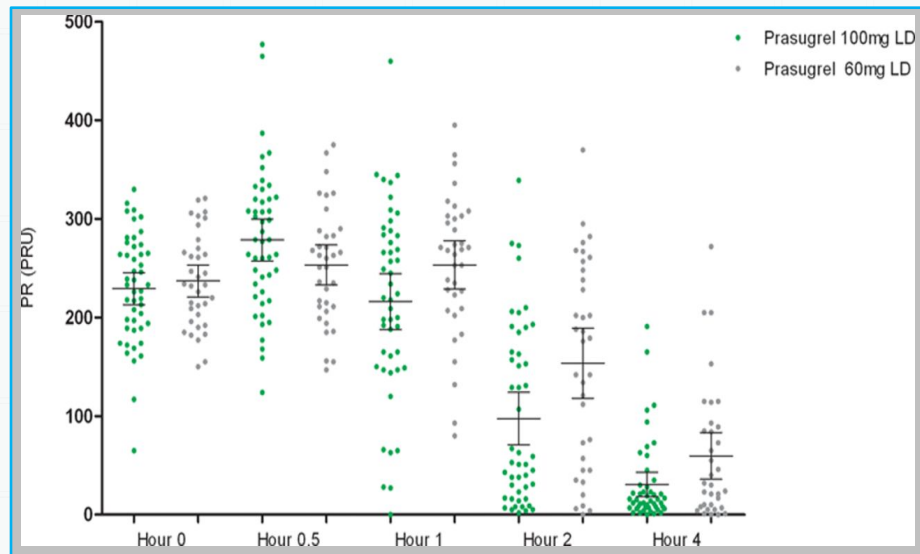
Alexopoulos et al. Circ Cardiovasc Interv. 2014

Is ticagrelor superior to prasugrel for the treatment of acute coronary syndromes? Evidence from a 32,893-patient adjusted indirect comparison meta-analysis

Giuseppe Biondi-Zoccai

**Division of Cardiology, University of Turin, Turin, Italy**

Indirect comparison of prasugrel vs. ticagrelor

| Outcome		OR (95%CI)	P
Death, MI or stroke		0.98 (0.86-1.13)	0.862
Death		1.21 (0.95-1.54)	0.106
MI		0.89 (0.75-1.06)	0.202
Stroke		0.85 (0.55-1.33)	0.490
Stent thrombosis		0.63 (0.43-0.93)	0.020
Major bleeding		1.43 (1.10-1.85)	0.007
Major non-CABG bleeding		1.05 (0.76-1.45)	0.737
Major CABG bleeding		4.30 (1.73-10.64)	0.002
Major or minor bleeding		1.26 (1.04-1.54)	0.018
Minor bleeding		1.07 (0.79-1.45)	0.646
Drug discontinuation		1.02 (0.88-1.19)	0.731

0.1   Favours prasugrel   1.0   Favours ticagrelor   10

Funnel plots comparing prasugrel vs. ticagrelor for the risk of key clinical events. Odds ratios (OR) <1.0 favor prasugrel, whereas odds ratios>1.0 favor ticagrelor.

Comparisons of Ticagrelor and Prasugrel in STEMI patients undergoing PPCI
RAPID Primary PCI Study
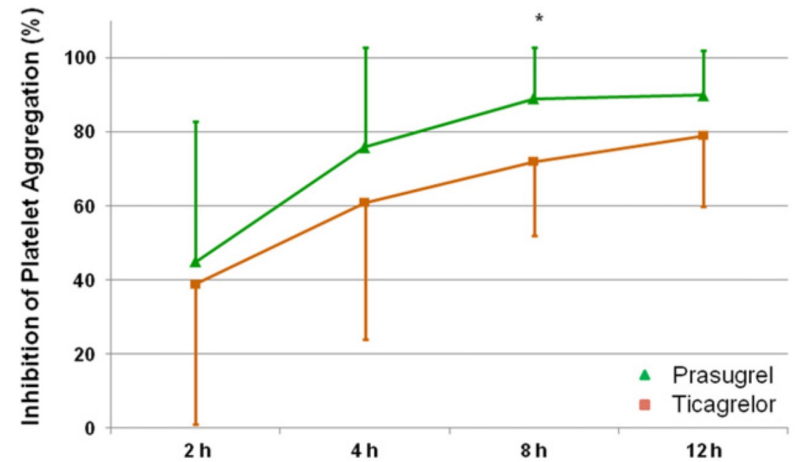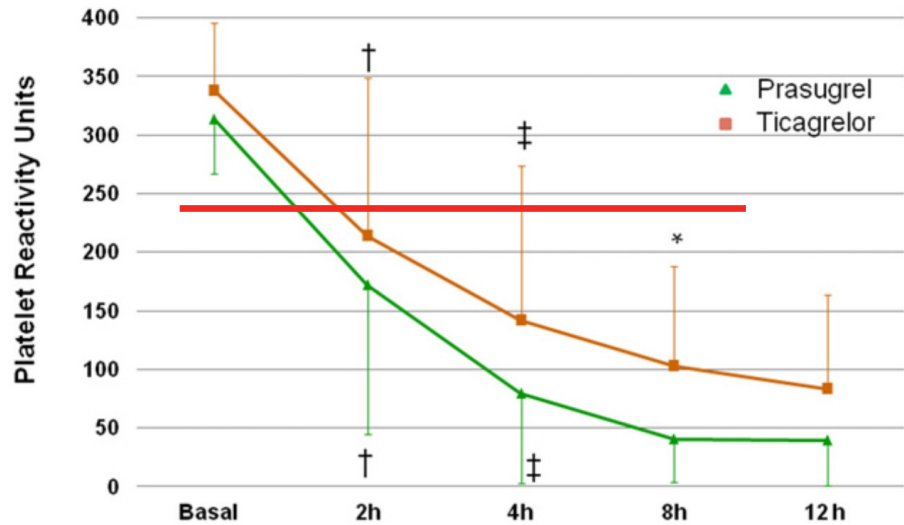
2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease

Developed in Collaboration with American Association for Thoracic Surgery, American Society of Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons

Endorsed by Preventive Cardiovascular Nurses Association and Society for Vascular Surgery

Table Applying Class of Recommendation and Level of Evidence

CLASS (STRENGTH) OF RECOMMENDATION

CLASS I (STRONG) — Benefit >>> Risk

Suggested phrases for writing recommendations:
- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

CLASS IIa (MODERATE) — Benefit >> Risk

Suggested phrases for writing recommendations:
- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

CLASS IIb (WEAK) — Benefit ≥ Risk

Suggested phrases for writing recommendations:
- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well established

COR	Recommendations
I	In patients with STEMI treated with DAPT in conjunction with fibrinolytic therapy, P2Y$_{12}$ inhibitor therapy (clopidogrel) should be continued for a minimum of 14 days (*Level of Evidence: A*) and ideally at least 12 months (*Level of Evidence: C-EO*).
I	In patients treated with DAPT, a daily aspirin dose of 81 mg (range, 75 mg to 100 mg) is recommended.

Duration of DAPT in Patients With ACS Treated With PCI

COR	Recommendations
I	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.
I	In patients treated with DAPT, a daily aspirin dose of 81 mg (range, 75 mg to 100 mg) is recommended.
IIb	In patients with ACS treated with DAPT after DES implantation who develop a high risk of bleeding (e.g., treatment with oral anticoagulant therapy), are at high risk of severe bleeding complication (e.g., major intracranial surgery), or develop significant overt bleeding, discontinuation of $P2Y_{12}$ therapy after 6 months may be reasonable.
III: Harm	Prasugrel should not be administered to patients with a prior history of stroke or TIA.

# Duration of DAPT in Patients With ACS Treated With CABG

COR	Recommendation
I	In patients with ACS being treated with DAPT who undergo CABG, P2Y$_{12}$ inhibitor therapy should be resumed after CABG to complete 12 months of DAPT therapy after ACS.

Duration of DAPT in Patients With ACS Treated With Medical Therapy Alone

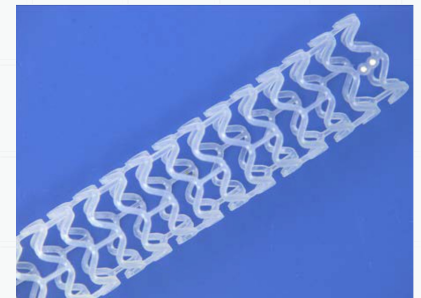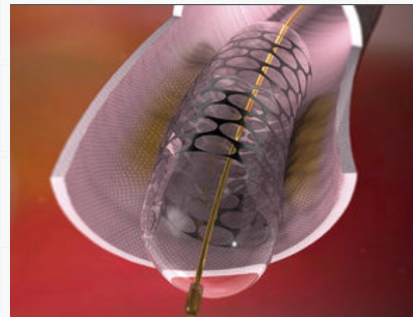| COR	Recommendations
I	In patients with ACS who are managed with medical therapy alone (without revascularization or fibrinolytic therapy) and treated with DAPT, P2Y$_{12}$ inhibitor therapy (clopidogrel or ticagrelor) should be continued for at least 12 months.
I	In patients treated with DAPT, a daily aspirin dose of 81 mg (range, 75 mg to 100 mg) is recommended.

SR indicates systematic review.

Treatment Algorithm for Duration of P2Y$_{12}$ Inhibitor Therapy in Patient With Recent ACS (NSTE-ACS or STEMI)
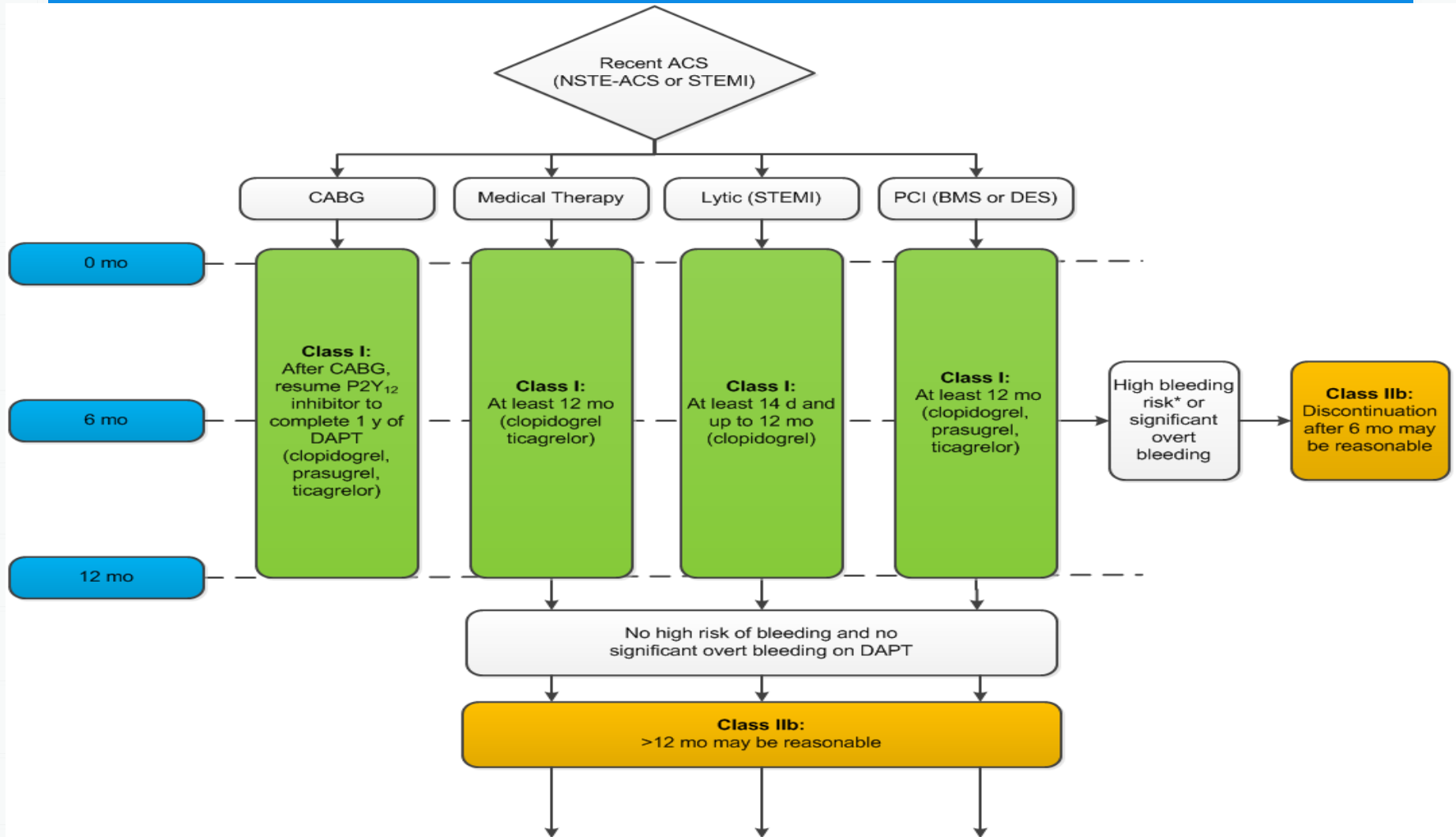
What's New in
Acute Coronary Syndromes?

- **Invasive strategy : Coronary angiogram:High Risk NSTE-ACS**
- **Antiplatelets in the management of ACS**

  - **Clopidogrel (CURRENT/OASIS-7)**
  - **Prasugrel (TRITON-TIMI 38)**
  - **Ticagrelor (PLATO)**

- **Stent : Bioabsorbable polymer**
- **Bioresorbable Scaffold**
- **Target LDL**

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News & Events

FDA News Release

FDA approves first absorbable stent for coronary artery disease

f SHARE   🐦 TWEET   in LINKEDIN   📌 PIN IT   ✉ EMAIL   🖨 PRINT

The U.S. Food and Drug Administration today approved the first fully absorbable stent to treat coronary artery disease. The Absorb GT1 Bioresorbable Vascular Scaffold System (BVS), which releases the drug everolimus to limit the growth of

Release

Español

The U.S. Food and Drug Administration today approved the first fully absorbable stent to treat coronary artery disease. The Absorb GT1 Bioresorbable Vascular Scaffold System (BVS), which releases the drug everolimus to limit the growth of
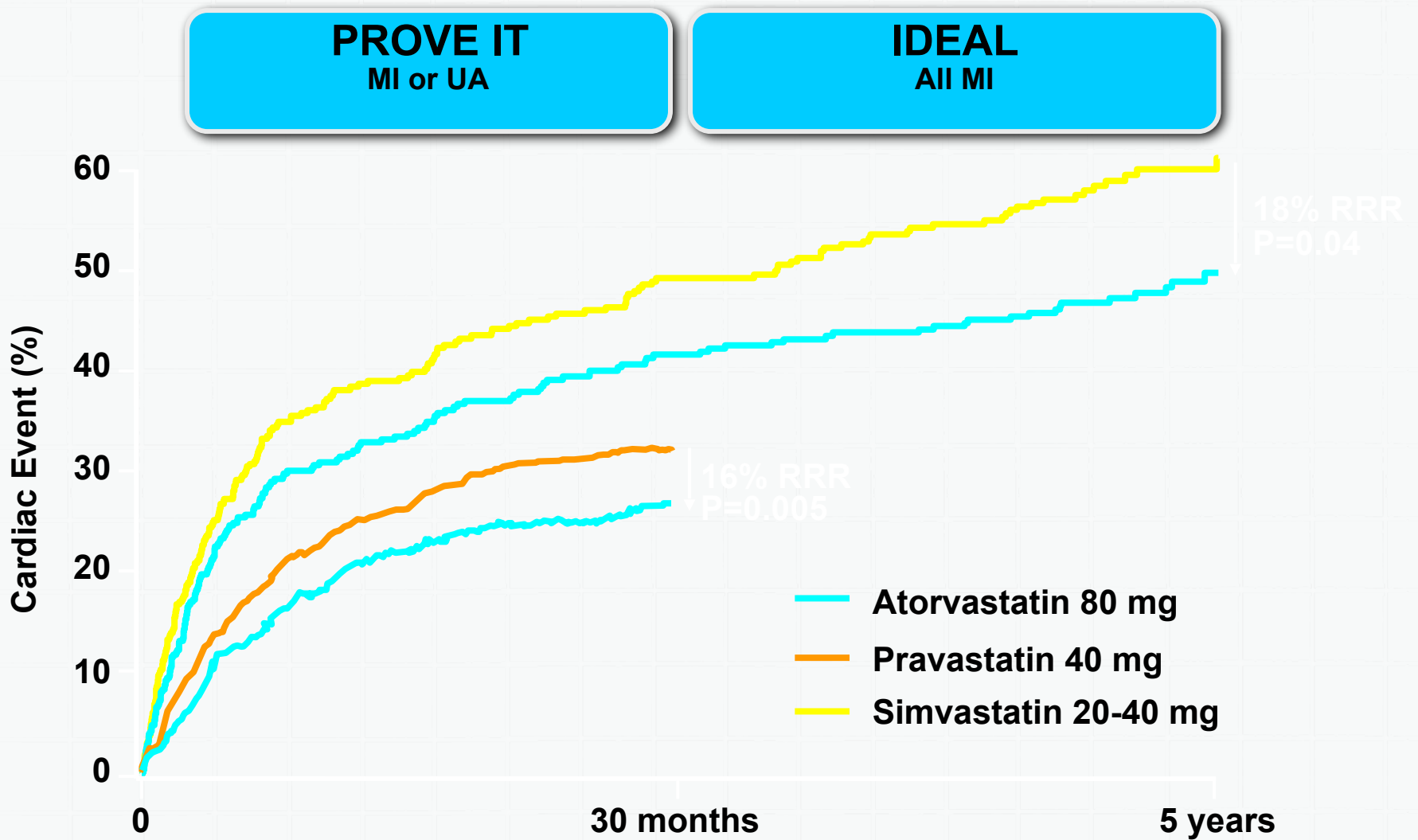
Inquiries

Media

✉ Deborah Kotz
📞 301-796-5349

Related Information

- What is Coronary Heart Disease?
- FDA: Medical Devices
- More on the Absorb GT1 BVS

What's New in
Acute Coronary Syndromes?

- **Invasive strategy : Coronary angiogram:High Risk NSTE-ACS**

- **Antiplatelets in the management of ACS**

  - **Clopidogrel (CURRENT/OASIS-7)**
  - **Prasugrel (TRITON-TIMI 38)**
  - **Ticagrelor (PLATO)**

- **Stent : Bioabsorbable polymer**
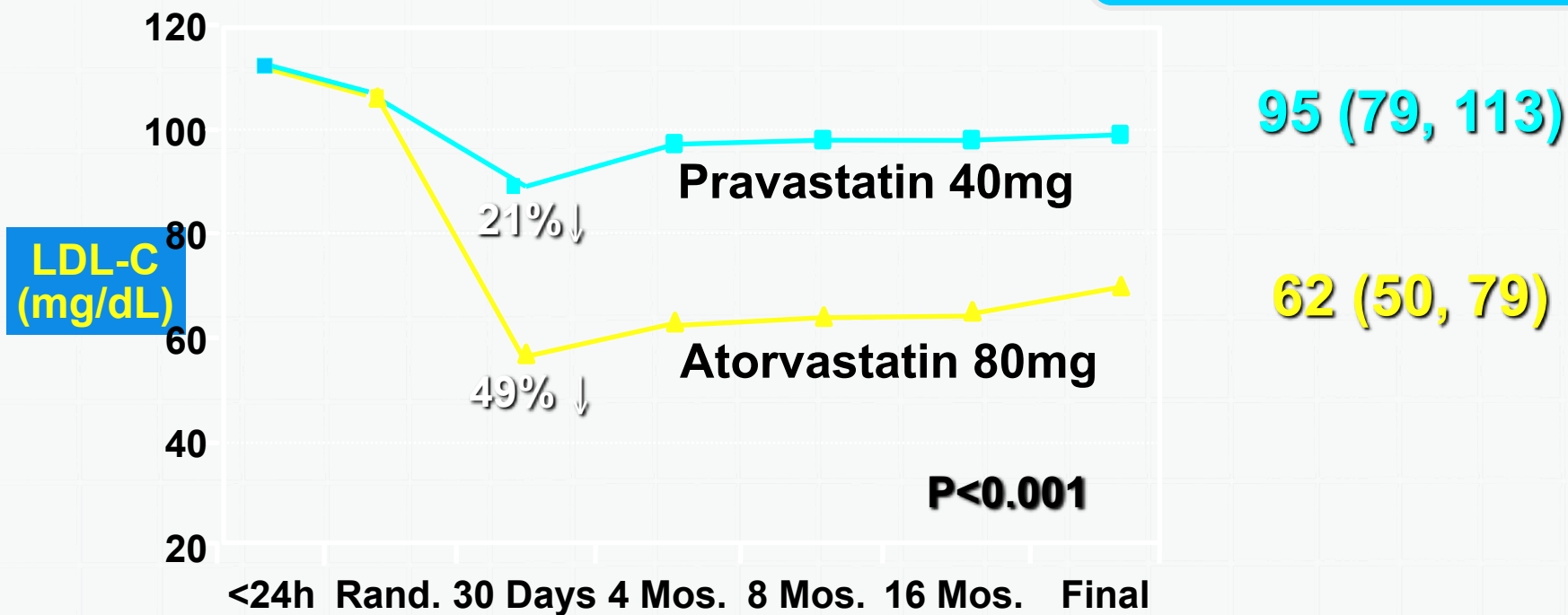- **Bioresorbable Scaffold**
- **Target LDL**

Summary: ACS Patients On Statin Therapy

PROVE IT
MI or UA

IDEAL
All MI

Cardiac Event (%)

60
50
40
30
20
10
0

18% RRR
P=0.04

16% RRR
P=0.005

— Atorvastatin 80 mg
— Pravastatin 40 mg
— Simvastatin 20-40 mg

0   30 months   5 years

Pedersen, Olsson, Cater et al. Presented at World Congress of Cardiology 2006

Median LDL-C

Adapted from Cannon CP et al. NEJM 2004; 350:1495-1504

IMPROVE- IT
ACS

Patients stabilized post ACS ≤ 10 days:
LDL-C 50-125 mg/dL (or 50-100 mg/dL if prior lipid-lowering Rx)

N=18,144

Standard Medical & Interventional Therapy

Simvastatin
40 mg

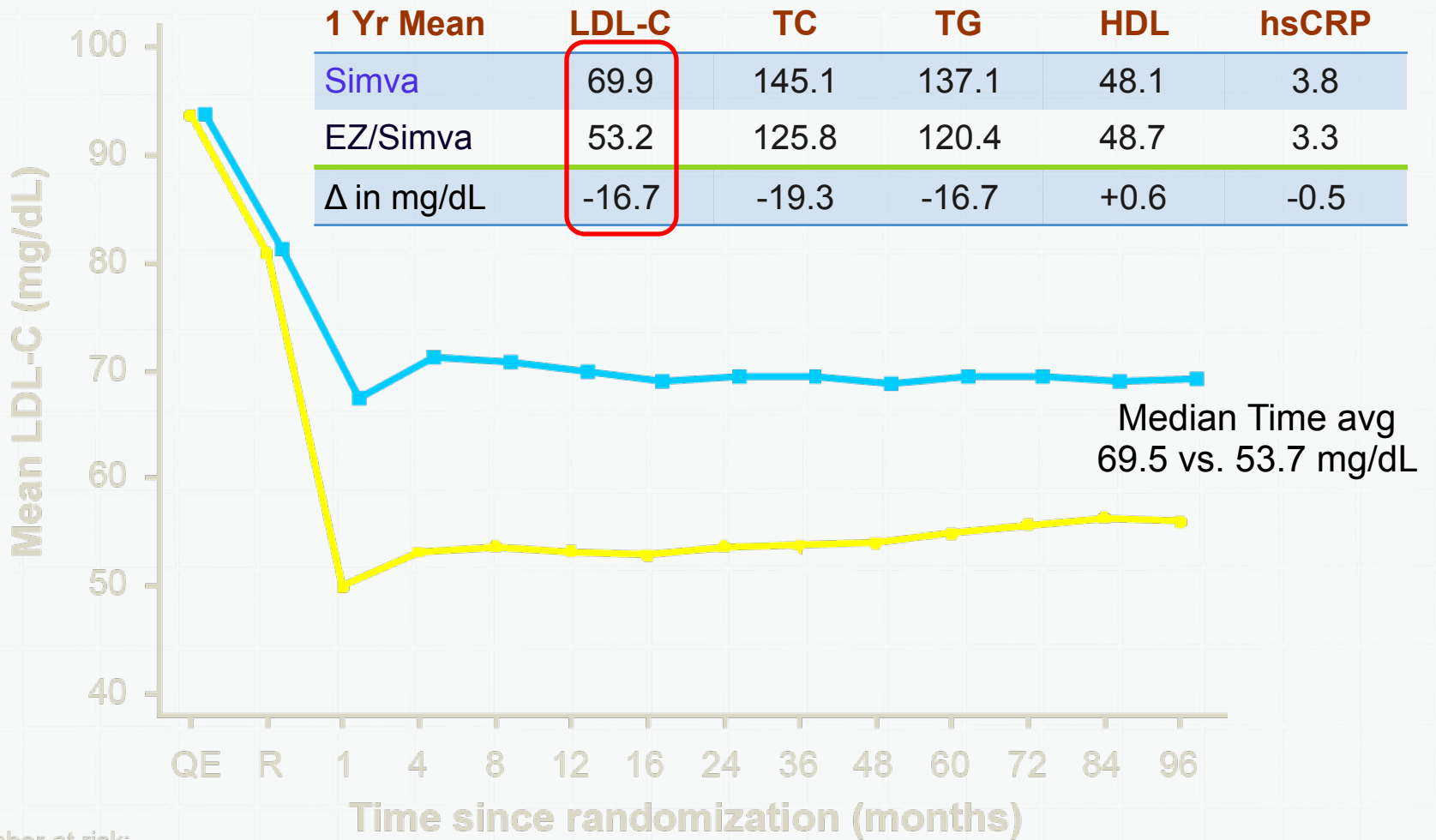*Uptitrated to Simva 80 mg if LDL-C > 79 (halted per FDA label Δ 2011)*

Ezetimibe / Simvastatin
10 / 40 mg

Follow-up Visit Day 30, every 4 months

Duration: Minimum 2 ½-year follow-up **(Final 5314 events)**

Primary Endpoint: CV death, MI, hospital admission for UA, coronary revascularization (≥ 30 days after randomization), or stroke

Cannon CP AHJ 2008;156:826-32;   Califf RM NEJM 2009;361:712-7;   Blazing MA AHJ 2014;168:205-12

LDL-C and Lipid Changes

1 Yr Mean	LDL-C	TC	TG	HDL	hsCRP
Simva	69.9	145.1	137.1	48.1	3.8
EZ/Simva	53.2	125.8	120.4	48.7	3.3
Δ in mg/dL	-16.7	-19.3	-16.7	+0.6	-0.5

Median Time avg
69.5 vs. 53.7 mg/dL

Mean LDL-C (mg/dL)

Time since randomization (months)

QE R 1 4 8 12 16 24 36 48 60 72 84 96

Number at risk:

| EZ/Simva | 8990 | 8889 | 8230 | 7701 | 7264 | 6864 | 6583 | 6256 | 5734 | 5354 | 4508 | 3484 | 2608 | 1078 |
| Simva | 9009 | 8921 | 8306 | 7843 | 7289 | 6939 | 6607 | 6192 | 5684 | 5267 | 4395 | 3387 | 2569 | 1068 |

Primary Endpoint
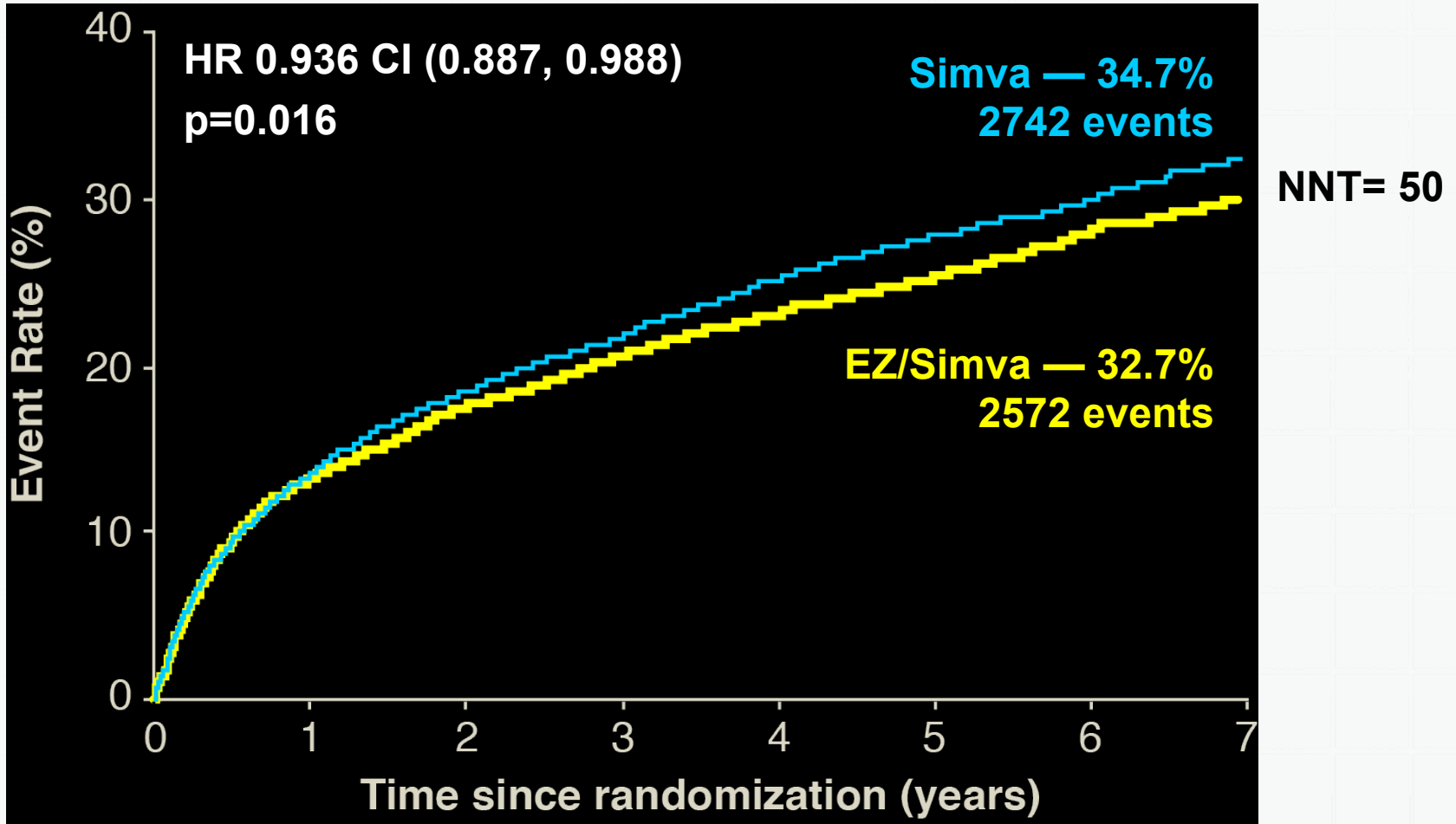
7-year event rates

A
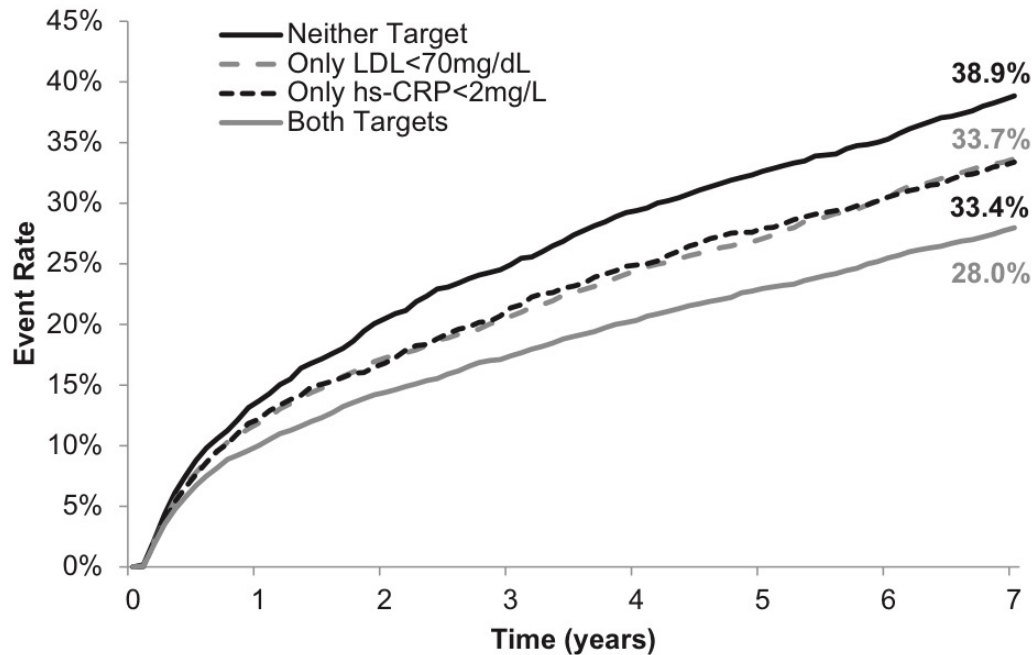
Neither Target	2074	1730	1540	1414	1256	898	704	370
Only LDL<70	5045	4311	3938	3667	3328	2468	1858	1072
Only hs-CRP<2	2065	1753	1619	1500	1386	1041	826	478
Both Targets	5995	5295	4930	4664	4318	3257	2612	1537

B

	Adj HR*	n/N	7yr KM (%)	p-value
Neither Target	Ref	703/2074	38.9	-
Only LDL<70mg/dL	0.83 (0.75, 0.91)	1502/5045	33.7	<0.001
Only hs-CRP<2mg/L	0.89 (0.79, 0.99)	614/2065	33.4	0.041
Both Targets	0.73 (0.66, 0.81)	1508/5995	28.0	<0.001

Adjusted Hazard Ratio* (95% CI) with
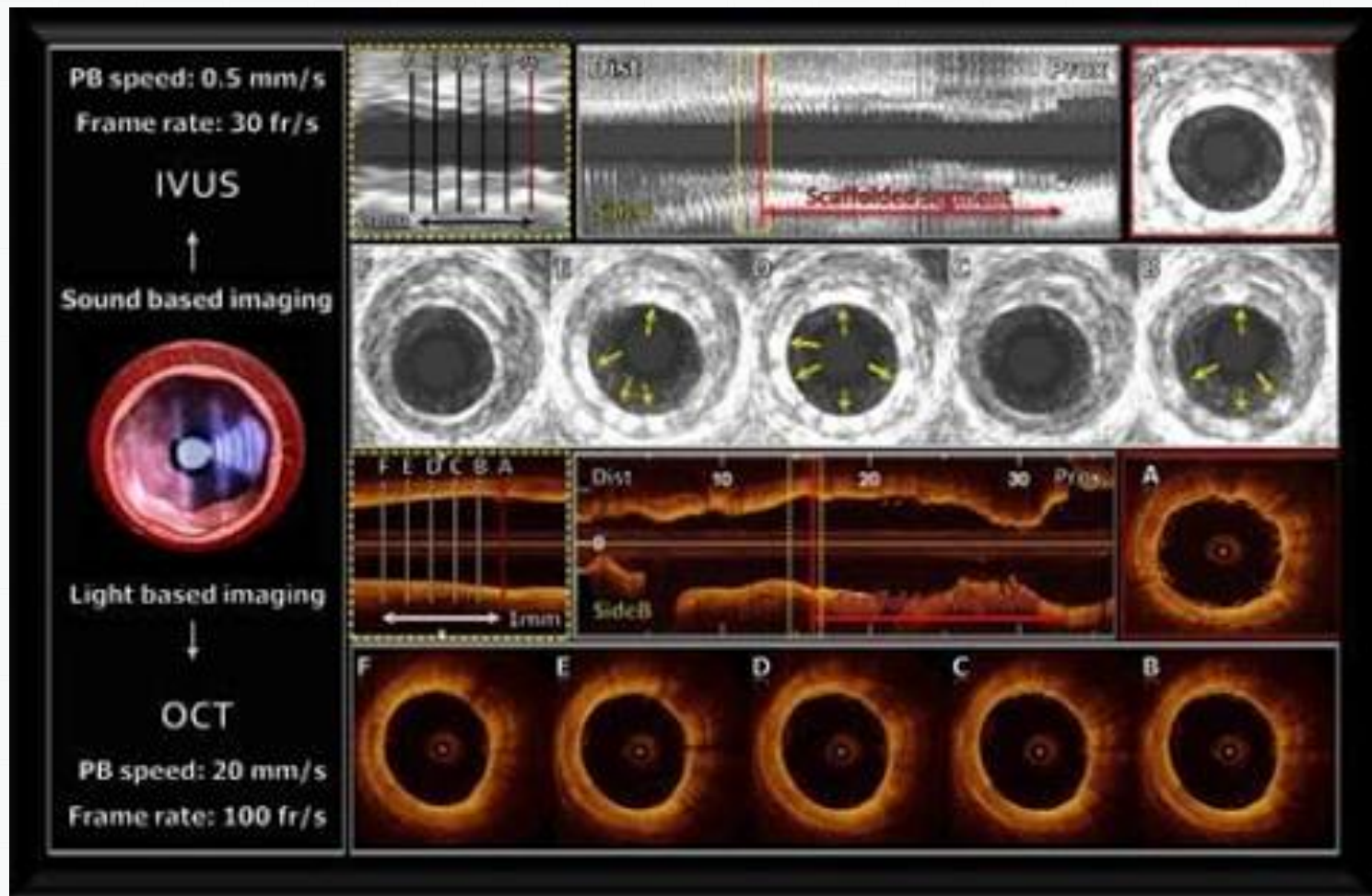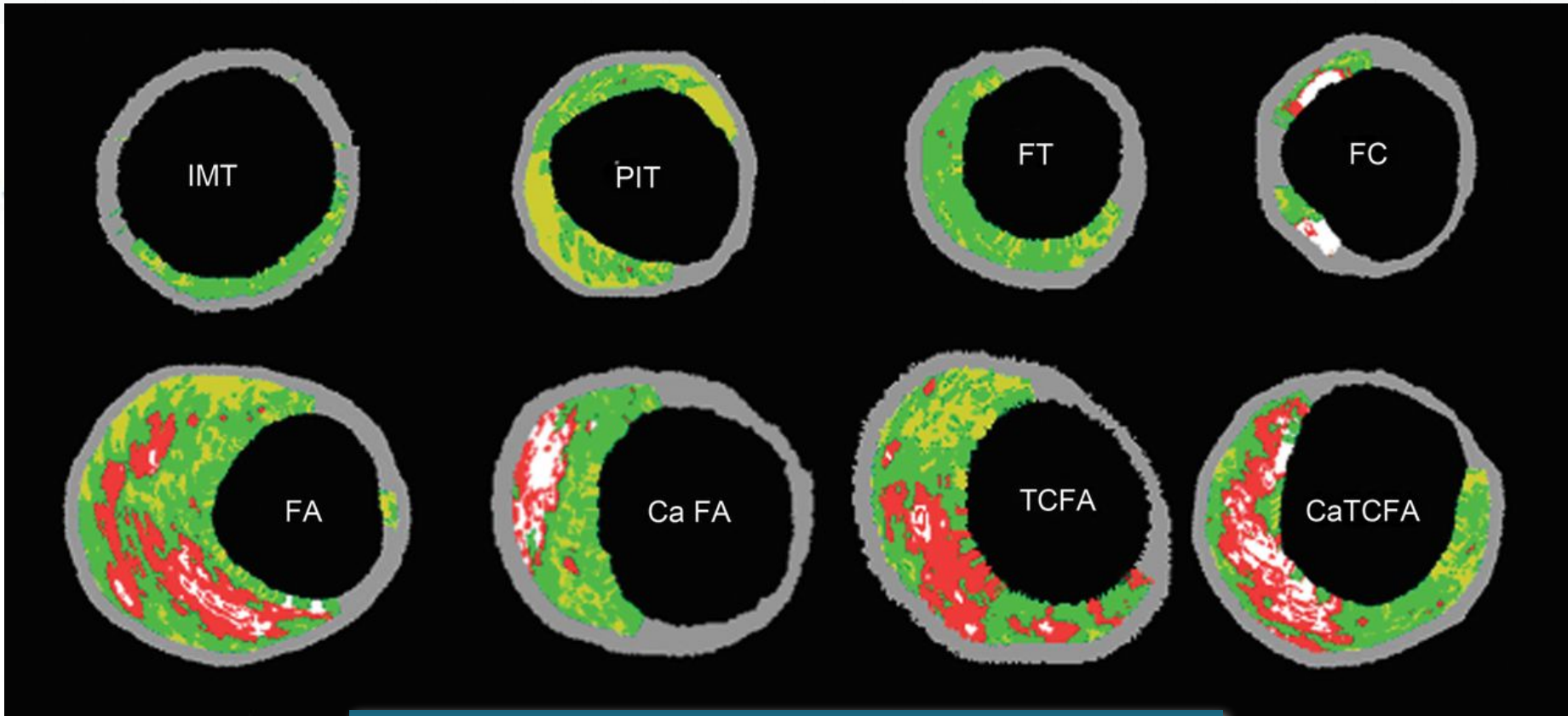LDL≥70 & hs-CRP≥2 as Referent
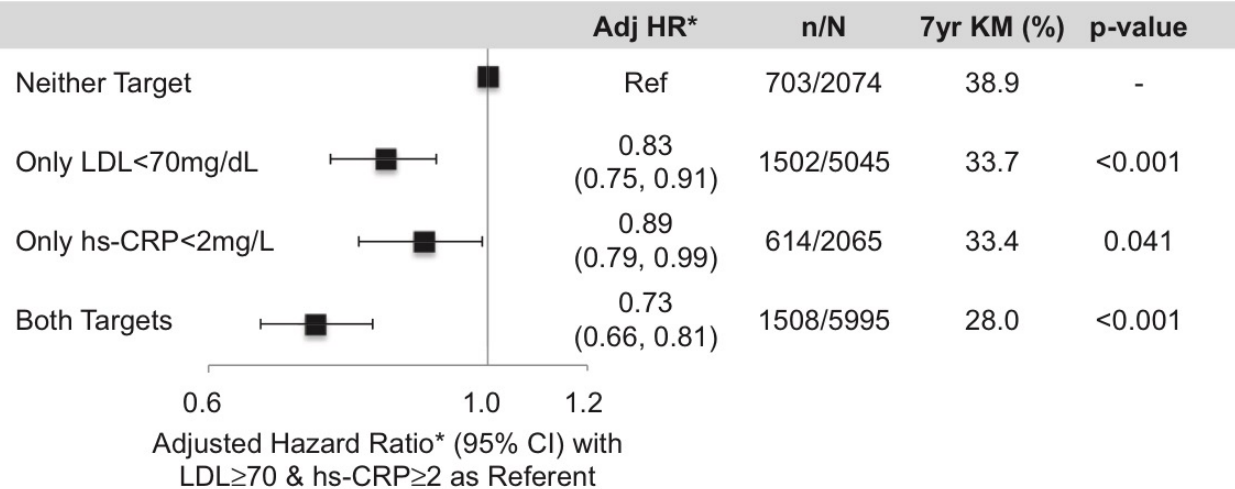
Atherosclerosis: Systemic Disease
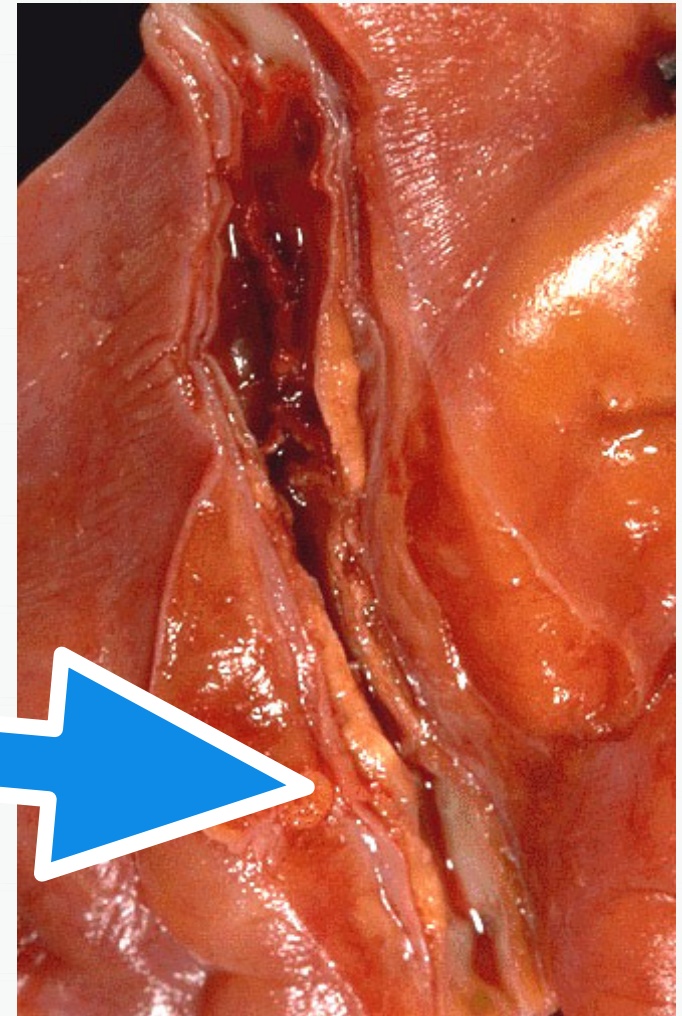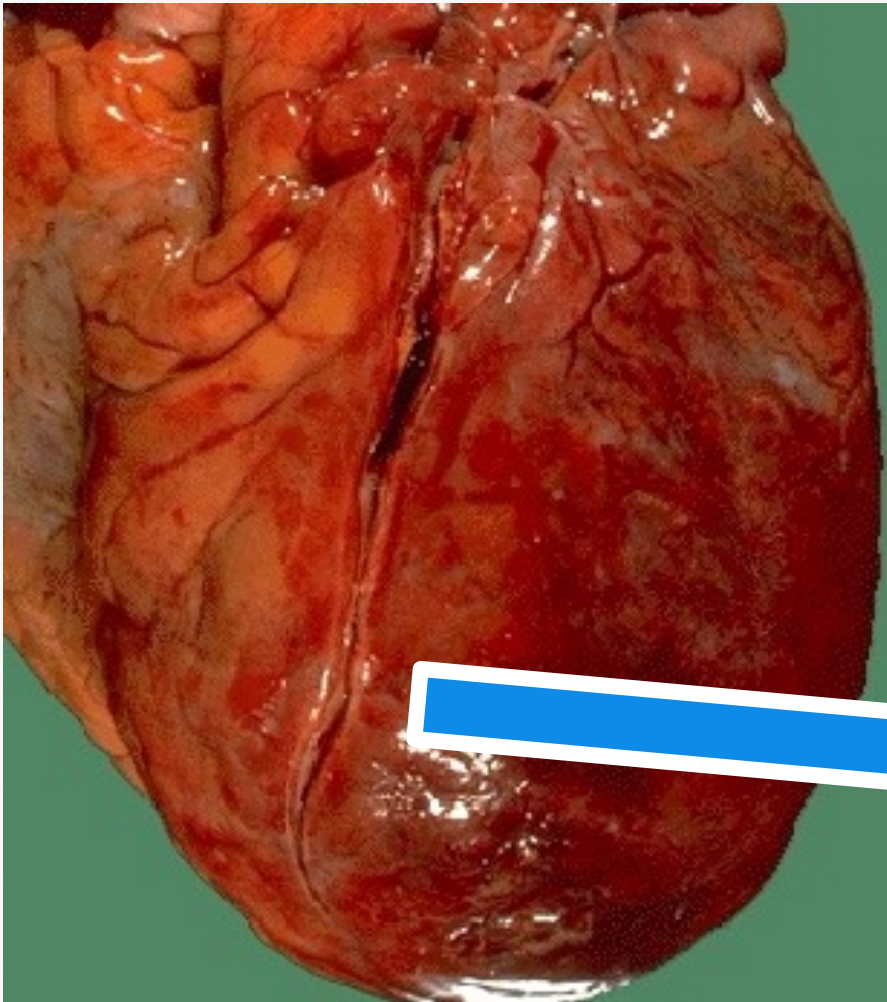
The IVUS technique can detect angiographically 'silent' atheroma

The IVUS technique can detect angiographically 'silent' atheroma

IMT PIT FT FC
FA Ca FA TCFA CaTCFA

Normal   S...   Multiple rupture plaque   y Vb   Stary Vc

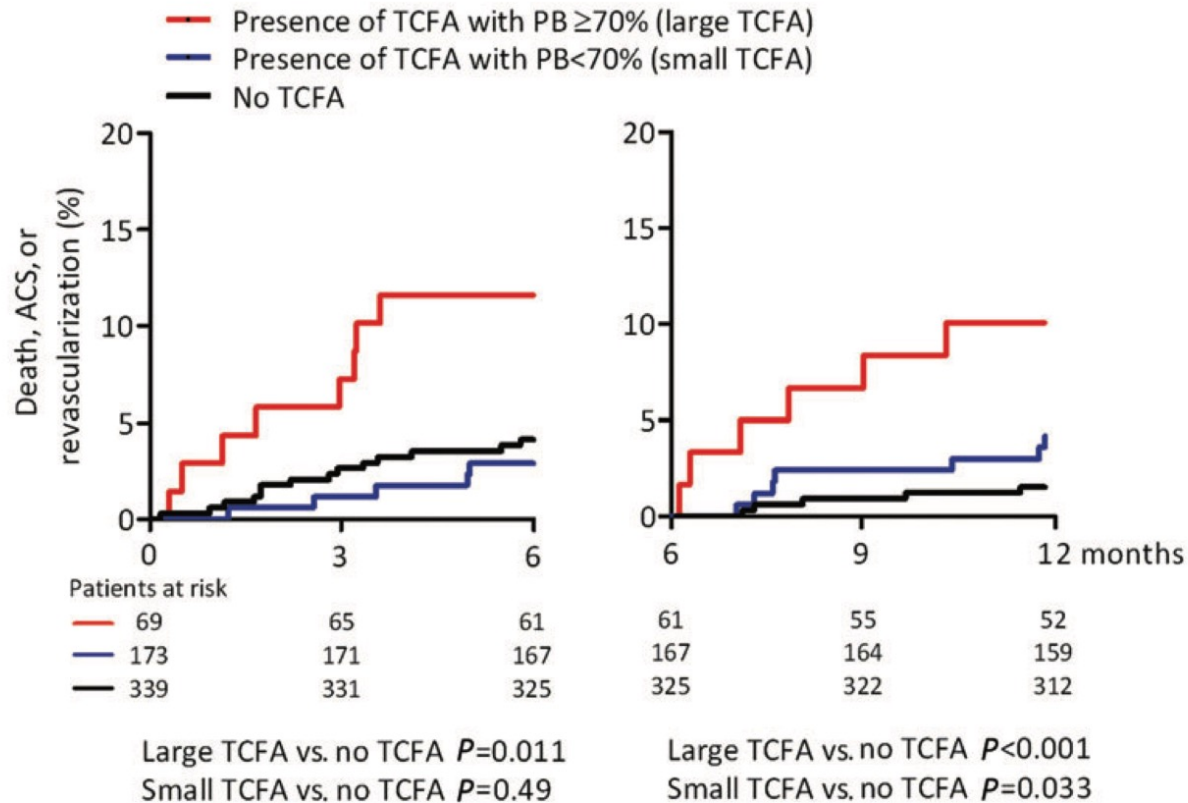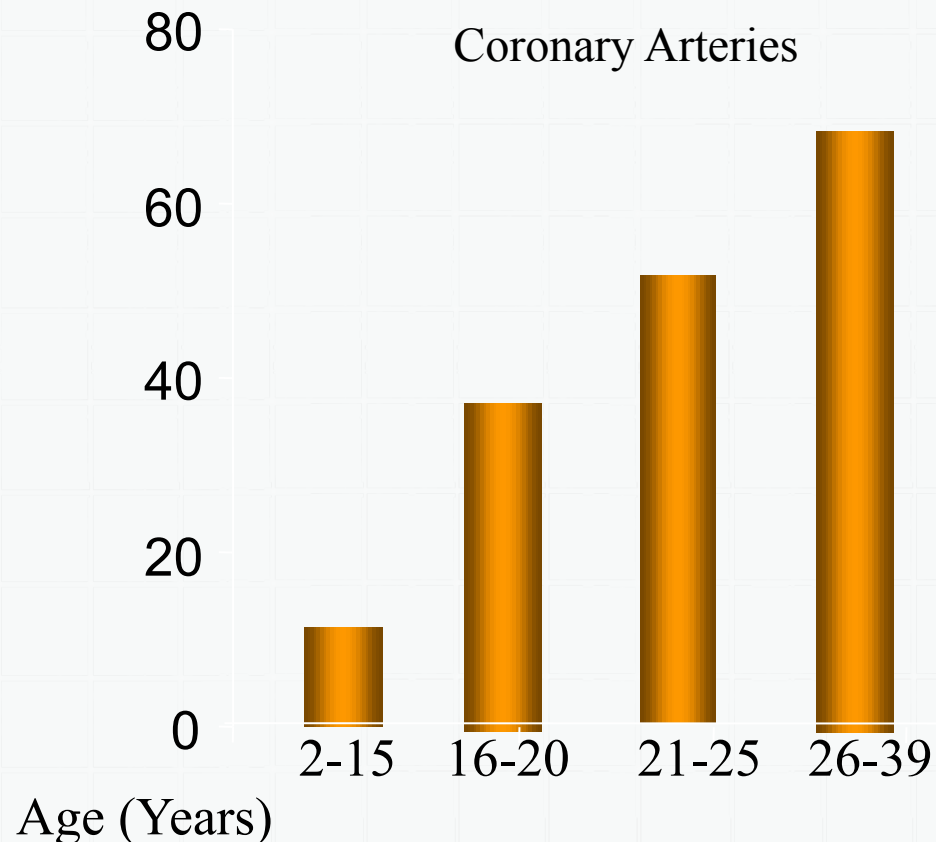# The IVUS technique can detect angiographically 'silent' atheroma

Figure 4 Associations with of short-term and long-term major adverse cardiac events. *P*-values are obtained with the log-rank test. Overall *P*-value 0–6 months is 0.009; overall *P*-value 6–12 months is 0.002. PB, plaque burden; TCFA, thin-cap fibroatheroma.
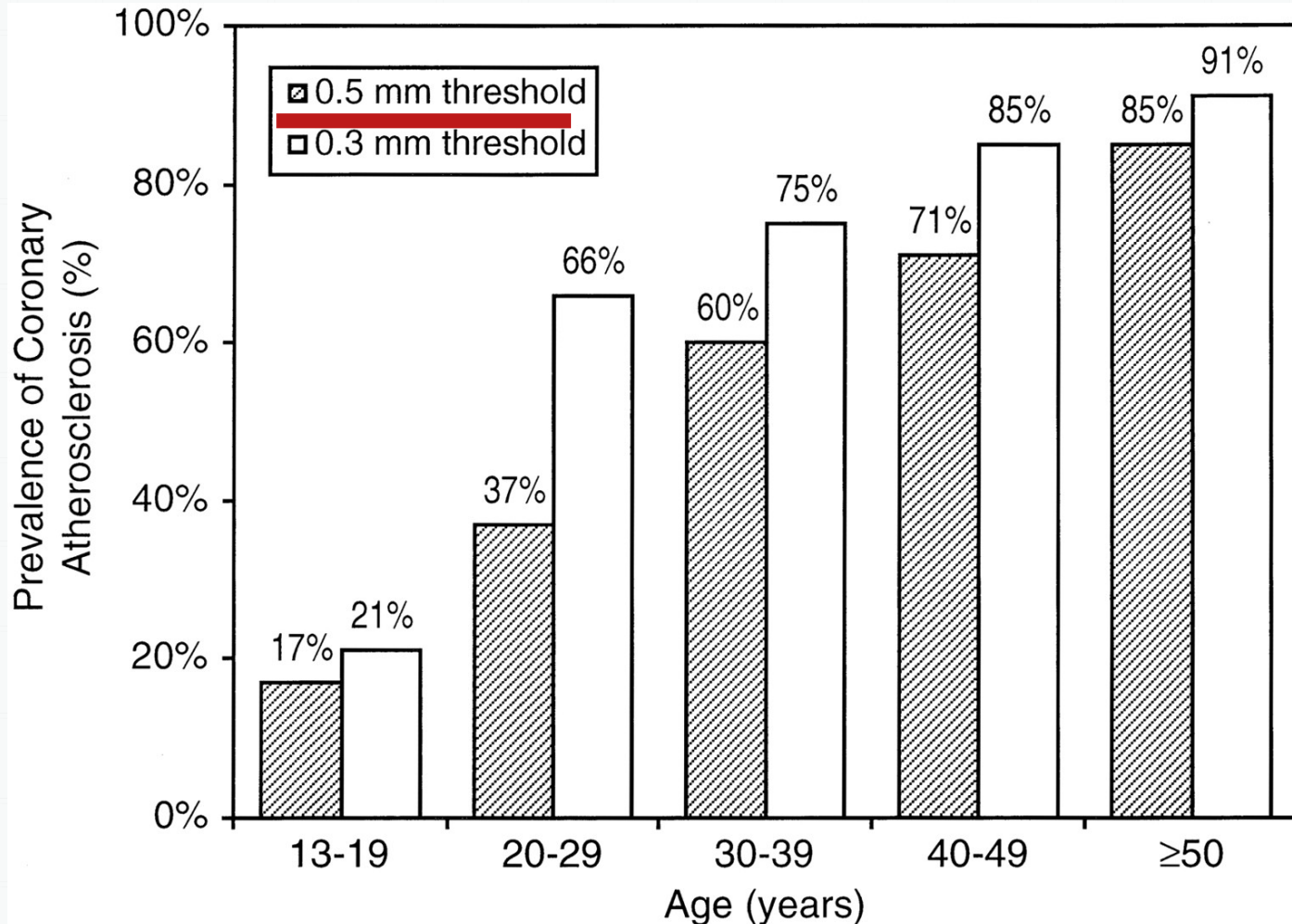
Early Appearance of Atherosclerosis

Prevalence of Fibrous Plaque Lesions

Coronary Arteries

80

60

40

20

0

2-15   16-20   21-25   26-39

Age (Years)

- Bogalusa Heart Study: Fatty streaks at age 3

The IVUS technique can detect angiographically significant 'silent' atheroma
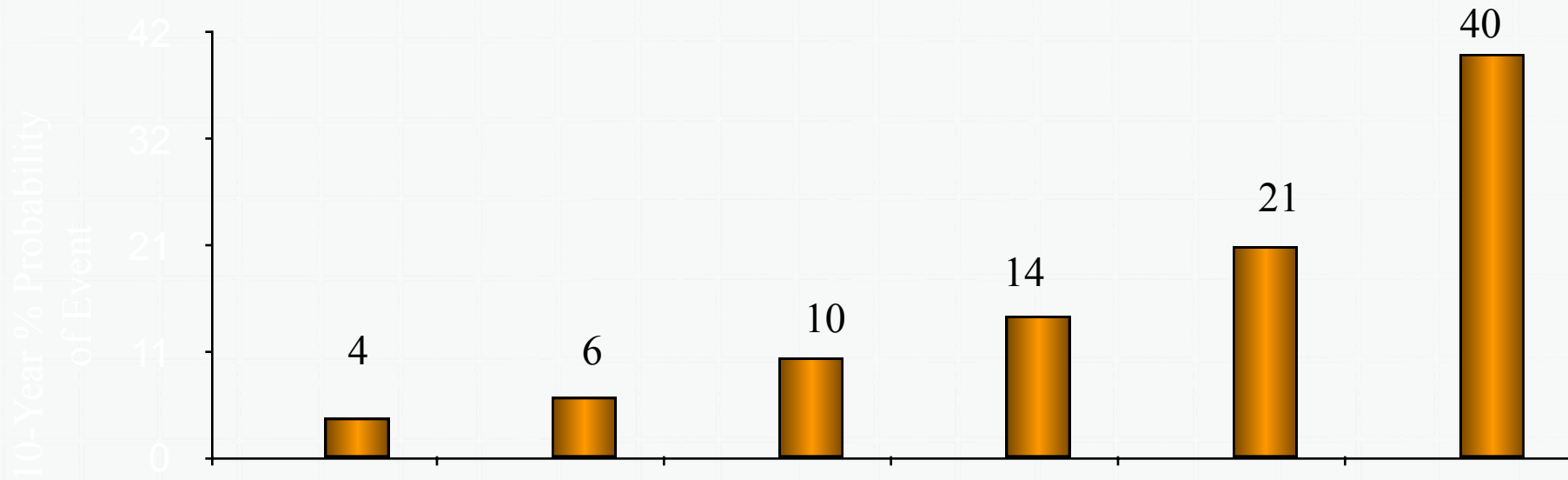
Major Cardiovascular Risk Factors
Atherosclerosis

- **Dyslipidemia : High LDL,Low HDL,High non HDL**
- **Hypertension**
- **Smoking**
- **Obesity (BMI $\geq$ 30) , WC 90,80 cm**
- **Physical inactivity**
- **Diabetes mellitus**
- **Microalbuminuria or GFR < 60ml/min**
- **Advanced age**
  - **Men > 55, women > 65**
- **Family history of premature CV disease**

Effect of Multiple Risk Factors on Probability of CAD: Framingham Study

SBP	+	+	+	+	+	+
Cholesterol.	-	+	+	+	+	+
HDL-C	-	-	+	+	+	+
Diabetes	-	-	-	+	+	+
Cigarettes	-	-	-	-	+	+
ECG-LVH	-	-	-	-	-	+

Established Risk Factors for CHD

Blood cholesterol
10% ↓ = 20%-30% ↓ in CHD

High blood pressure
5-6 mm Hg ↓ = 42% ↓ in Stroke

= 16% ↓ in CHD

Cigarette smoking
Cessation = 50%-70% ↓ in CHD

Body weight
BMI<25 vs BMI>27 = 35%-55% ↓ in CHD

Physical activity
20-minute brisk walk daily = 35%-55% ↓ in CHD

Lifestyle Modifications to Prevent ACS : Risk Factors

- Reduce weight

- Moderate consumption of alcohol

- Reduction of : Sodium ,saturated fat ,cholesterol

- Maintain adequate intake of dietary:
  - potassium
  - calcium
  - magnesium

- Increased aerobic physical activity and exercise

Smoking cessation