Acute Coronary Syndromes

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Disclosures

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Abbott; Amgen; Anthos Therapeutics; AstraZeneca; Boehringer Ingelheim; Daiichi-Sankyo; Ionis; Merck; Novartis; Pfizer; Saghmos Therapeutics; Verve Therapeutics

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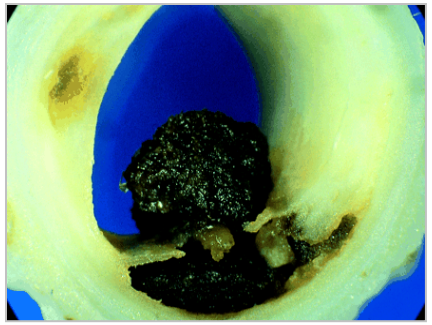
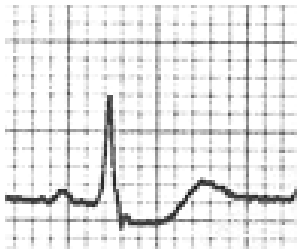
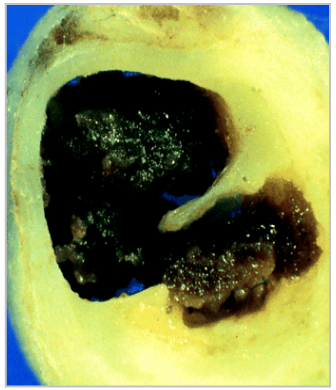
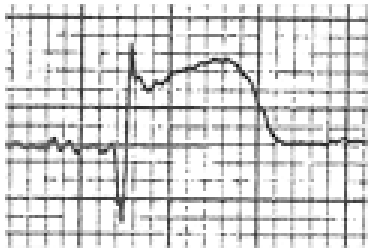
Amgen; AMPEL BioSolutions; Anthos Therapeutics; AstraZeneca; Boehringer Ingelheim; Dr. Reddy's Laboratories

ACUTE CORONARY SYNDROMES









Non-ST elevation ACS

ST elevation ACS

CK-MB

Troponin

UA

NSTEMI

STEMI

UA

NQWMI

QwMI

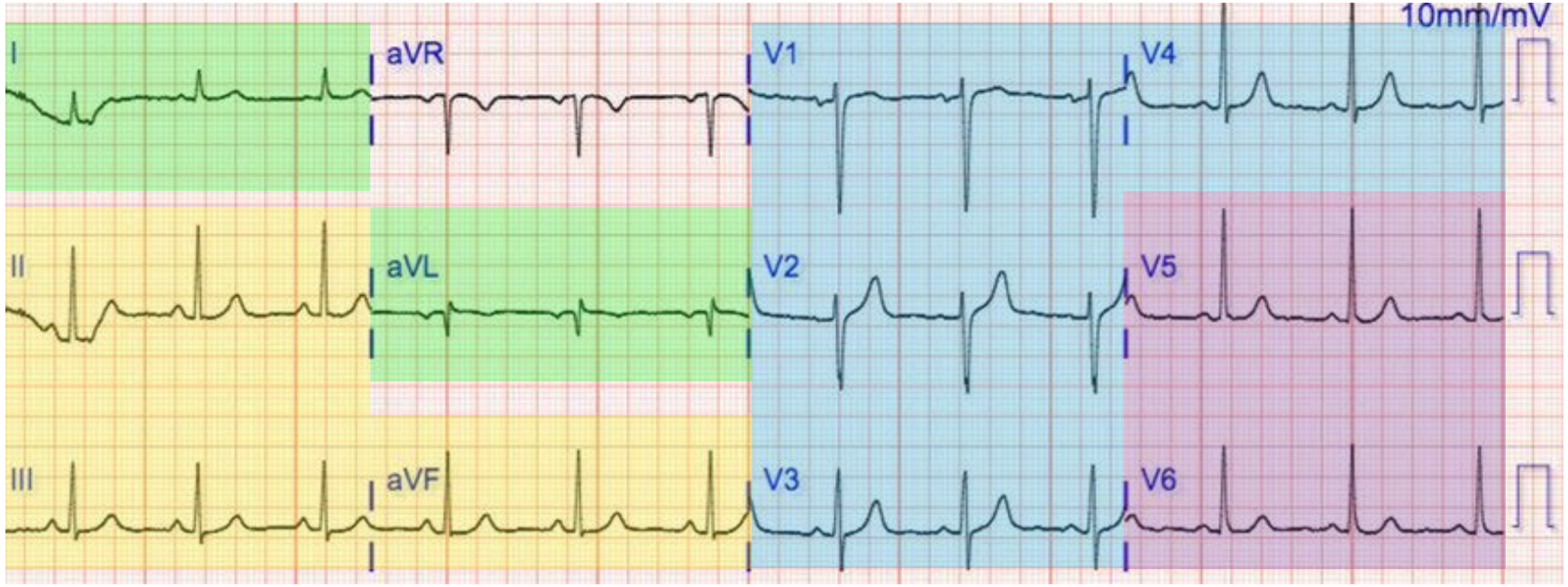
Value of H&P for ACS

Factor	LR (95% CI)
Radiation to right arm or shoulder	4.7 (1.9-12)
Radiation to both arms or shoulders	4.1 (2.5-6.5)
Exertional	2.4 (1.5-3.8)
Radiation to left arm	2.3 (1.7-3.1)
Associated with diaphoresis	2.0 (1.9-2.2)
Associated with nausea or vomiting	1.9 (1.7-2.3)
>Previous angina or ≈ previous MI	1.8 (1.6-2.0)
Described as pressure	1.3 (1.2-1.5)
Pleuritic	0.2 (0.1-0.3)
Positional	0.3 (0.2-0.5)
Sharp	0.3 (0.2-0.5)
Reproducible with palpation	0.3 (0.2-0.4)
Inframammary location	0.8 (0.7-0.9)
Nonexertional	0.8 (0.6-0.9)

***JAMA* 2005;294:2623**

ACS: ECG

- **What to look for**
  - STE or LBBB not known to be old
  - ST depression ≥0.5 mm; TWI >1 mm
  - Coronary distribution

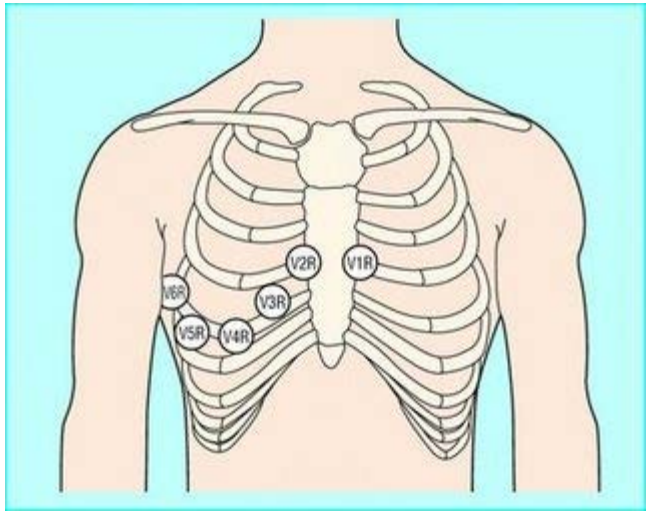


ACS: ECG

- **What to look for**
  - STE or LBBB not known to be old
  - ST depression ≥0.5 mm; TWI >1 mm
  - Coronary distribution
- **What else to look for**
  - Q waves or poor R wave progression (PRWP)
- **How to look for it**
  - 12-lead ECG w/in 10 mins of presentation
  - Compare to prior; obtain serial ECGs (initial ⊕ in <50% ACS Pts)
  - Consider additional leads …

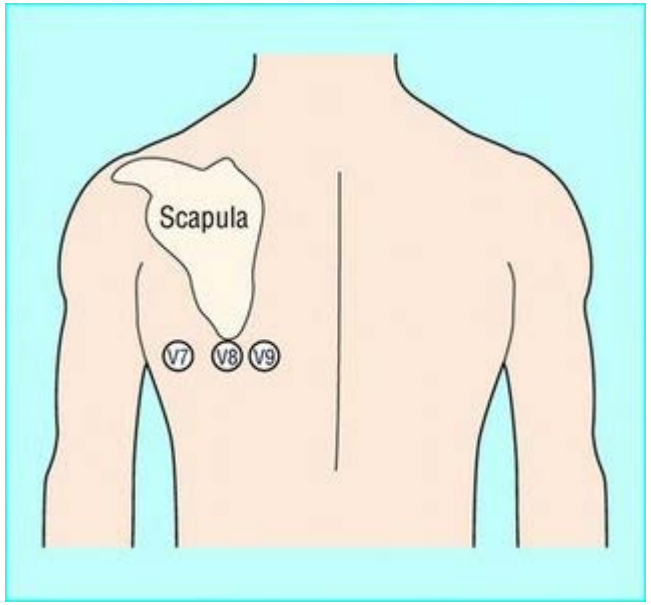
ECG Special Placement

Right-sided leads (V_{4R})



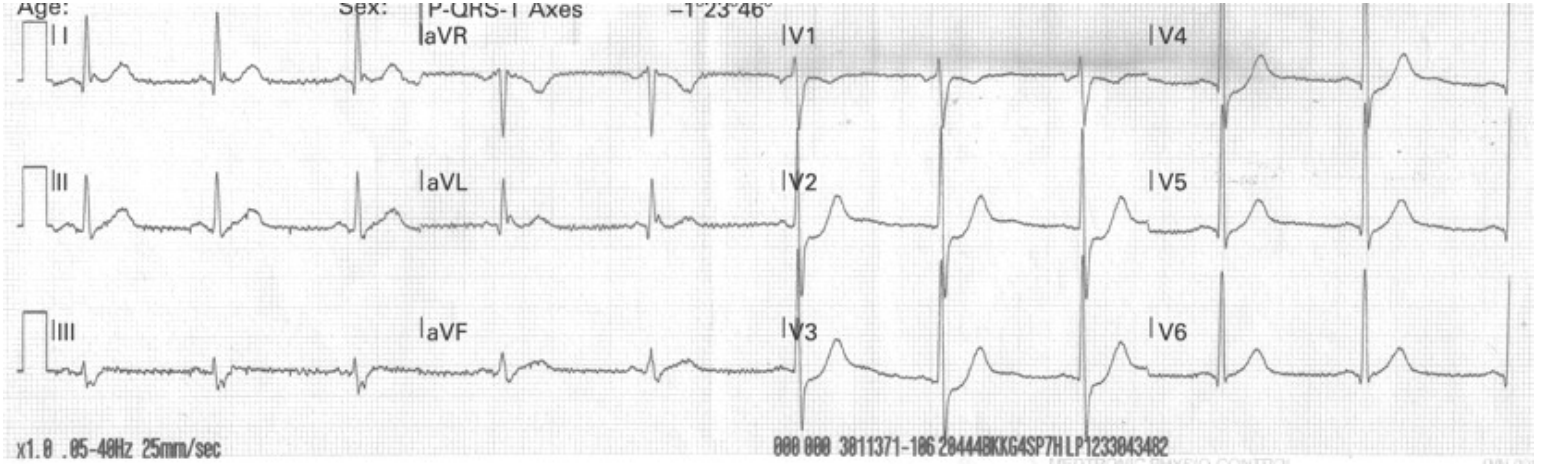
To diagnose RV infarct in setting of inferior STEMI (due to prox RCA occlusion)

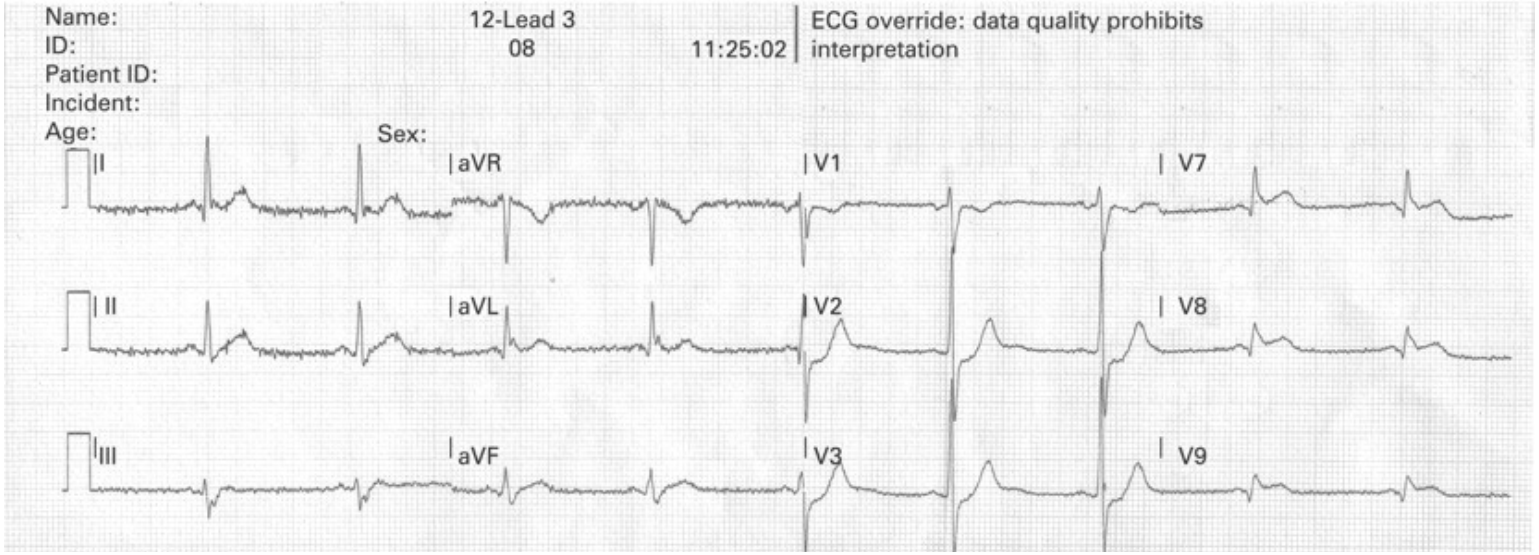
Posterior leads (V_7-V_9)



To diagnose posterior MI (due to LCx occlusion) in setting of concerning sx and either ant. ST depressions or normal ECG

Where is the Lesion?

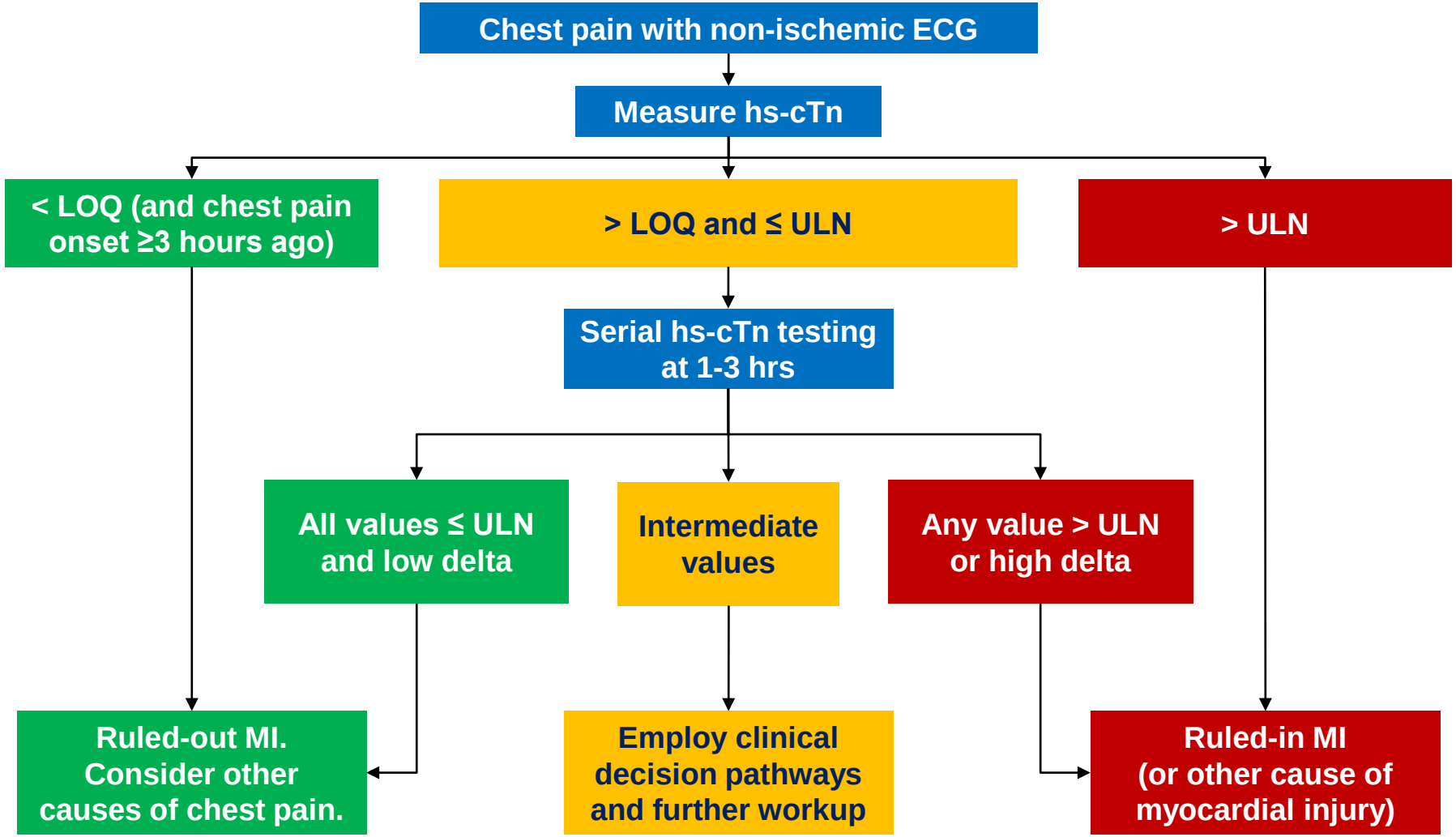




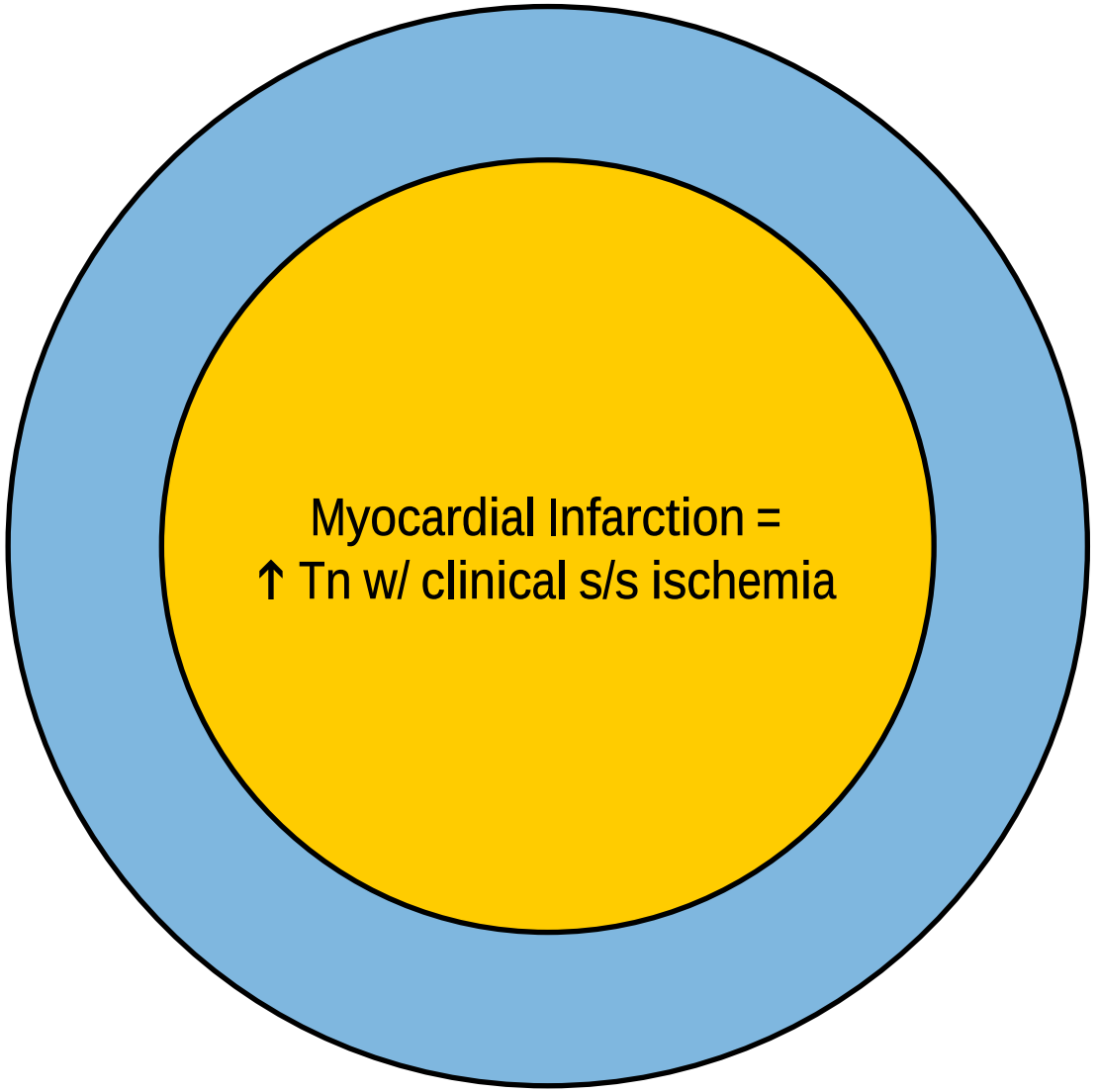
ACS: Biomarkers

Era	Assay	Measure at presentation + …
Ancient History (1950s)	AST & LDH	q12 hrs x 4
Middle Ages (1960s)	CK	q12 hrs x 2
Renaissance (1980s)	CK-MB	q8 hrs × 3
Dawn of modern cardiac markers (1990s)	**Troponin**	q8 hrs × 3
Recent past	Troponin	**3-6 hrs after sx onset**
Now	**hs-Troponin**	**1-3 hrs later** (depending on time from sx onset to presentation) **Examine absolute and Δ**

Troponin Testing Algorithm



Myocardial Injury vs. Infarction



Myocardial Injury (and not MI)

= ↑ Tn w/o clinical s/s ischemia

- Decompensated HF, myocarditis, Takotsubo
- Cardiac ablation, defibrillation, cardiac contusion
- PE, PHT
- Stroke, SAH, critical illness

Type 1 vs. Type 2 MI

Types 3-5 MI:
Cardiac death w/ sx & ECG, but no Tn
PCI-related
CABG-related

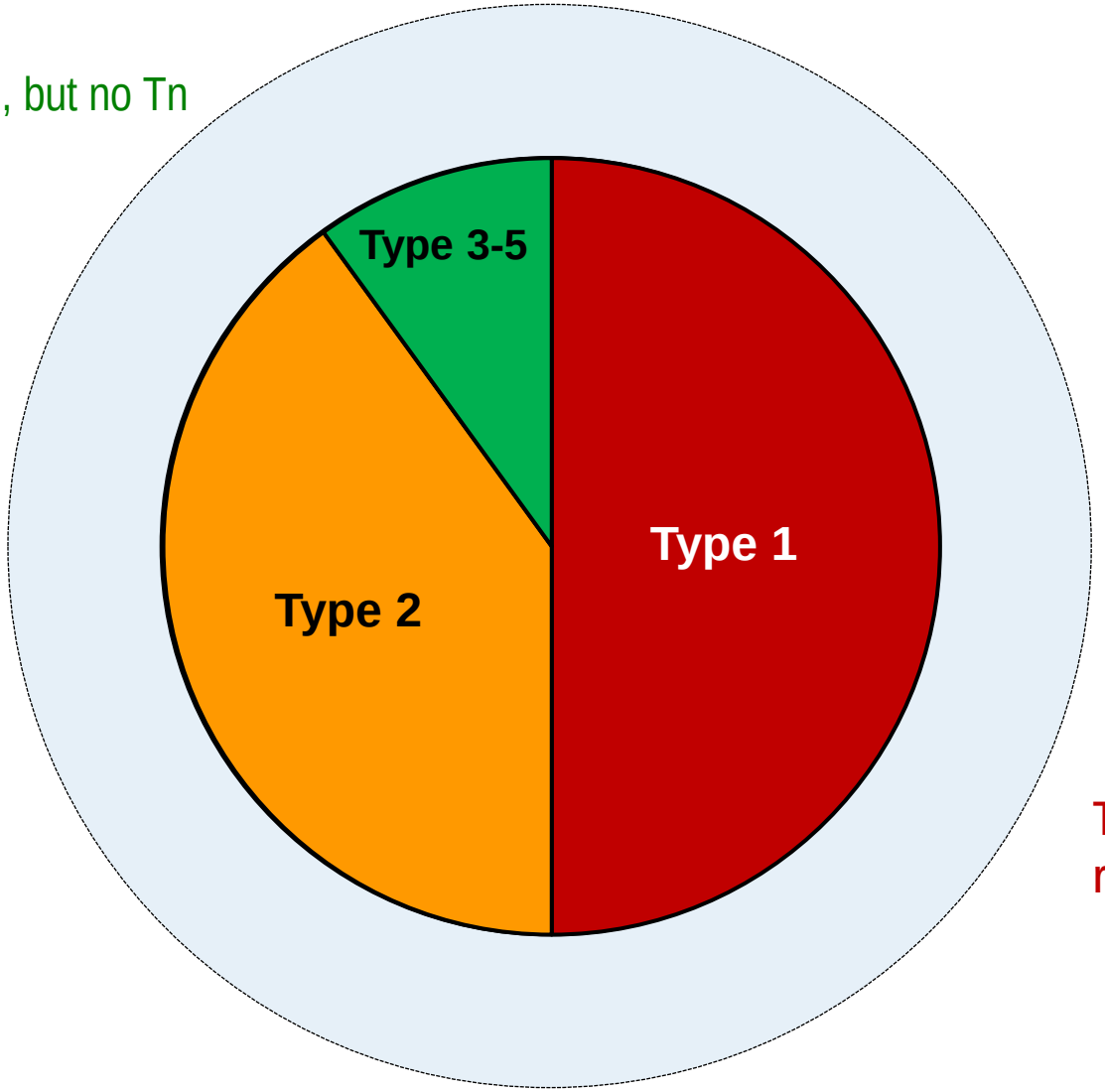
Type 2 MI = myocardial O_2 supply/demand imbalance *unrelated* to acute atherothrombosis

↓ myocardial perfusion

- Coronary artery spasm, embolism, dissection
- HoTN, profound sustained bradycardia, severe anemia

↑ myocardial demand

- Profound sustained tachycardia
- Extreme HTN



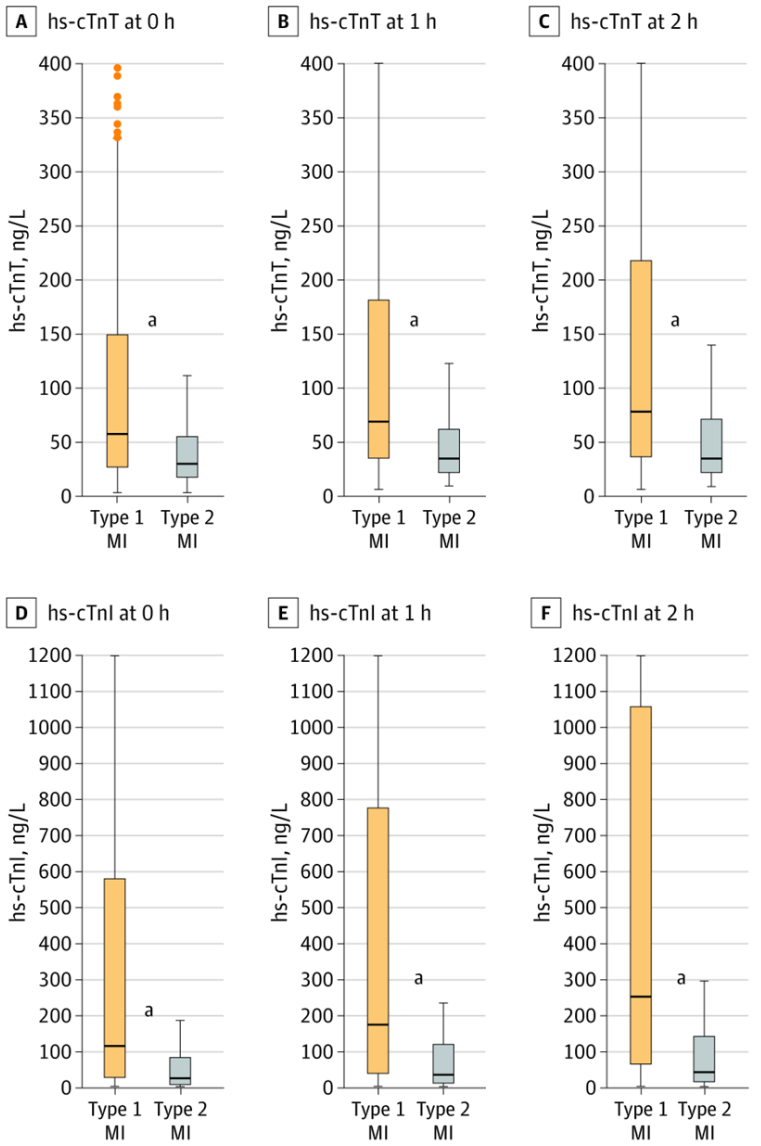
Myocardial Injury (and not MI)
= ↑ Tn w/o clinical s/s ischemia

- Decompensated HF, myocarditis, Takotsubo
- Cardiac ablation, defibrillation, cardiac contusion
- PE, PHT
- Stroke, SAH, critical illness

Type 1 MI = Due to ACS (plaque rupture or erosion)

Type 1 vs. 2 MI

- **Largely a clinical diagnosis …**

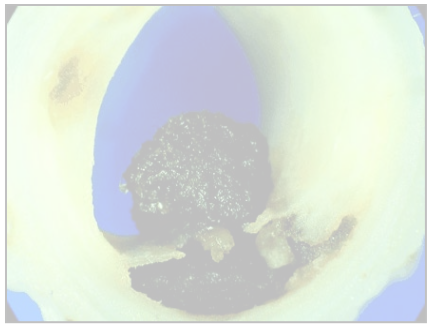


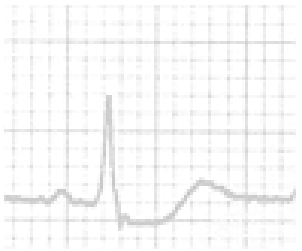
JAMA Cardiol. 2021;6:771-780

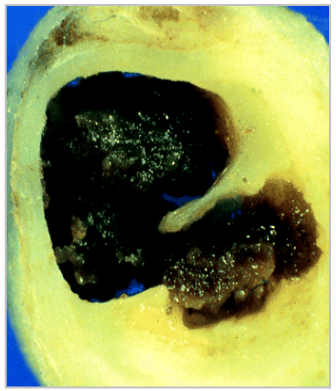
Anti-Ischemic Therapy

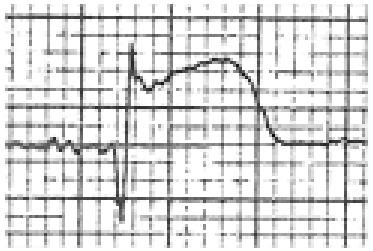
- **Nitrates**
  - Sx relief; no mort benefit (GISSI-3 & ISIS-4)
- **Beta-blockers**
  - ↓ ischemia, ↓ D/MI (in AMI trials)
  - PO (not IV) and only if not in HF or at risk for shock
- **Calcium channel blockers**
  - If ischemia despite max βB or βB contra.
- **Morphine**
  - Pain, CHF, agitation; *don't* mask angina
- **Supplemental oxygen (if hypoxemic)**

ACUTE CORONARY SYNDROMES









Non-ST elevation ACS

ST elevation ACS

CK-MB

Troponin

UA

NSTEMI

STEMI

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NQWMI

QwMI

ST-Elevation MI (STEMI)

- **Consider immediate reperfusion therapy**
- **In whom?**
  - Within 12 hrs of sx onset, or
  - 12-24 hrs after sx onset if clinical or ECG evidence of ongoing ischemia
- **How?**
  - **Primary PCI** (including transfer to PCI-capable hosp if door-in to door-out time will be <30 min & 1st med contact to PCI anticipated <120 min)
  - Fibrinolytic (barring contraindications*)

*Absolute: prior ICH; intracranial neoplasm, aneurysm, or AVM; stroke or head trauma w/in 3 mos; active internal bleeding or diathesis; suspected AoD
*Relative: severe HTN; stroke; prolonged CPR; recent bleed, surgery or trauma; noncompressible vasc puncture; pregnancy; current use of anticoagulants

Revascularization in STEMI

65 yo M p/w STEMI, w/ inferior ST segment elevations.

Brought for immediate coronary angiography and found to have occluded RCA, which is successfully stented and Pt doing well.

Also noted to have 80% mid LAD lesion and a 45% LCx lesion.

Preventive PCI in STEMI

COMPLETE: 2016 Pts w/ STEMI + MVD

Within 3 d of successful PCI of culprit,

randomized to revasc of all signif ***lesions (≥70% or 50-69% w/ FFR ≤0.80) w/in 45 days vs. culprit only***

CV Death or MI

Years

Mehta et al. *NEJM* 2019; 381:1411-1421

STEMI w/ Shock

CULPRIT-SHOCK: 706 Pts w/ AMI & Shock

Immediate PCI of all other lesions >70% (incl CTO) vs. Culprit only, with option for staged PCI

Parameter	Culprit Only	Multivessel PCI	P value
Contrast (ml)	190	250	0.001
Death or RRT (%)	45.9	55.4	0.01
Death	43.3	51.6	
RRT	11.6	16.4	
MI	1.2	0.9	1.0
Bleeding	16.6	22.0	

NEJM 2017;377:2419

Cardiogenic Shock in STEMI

DanGer Shock: 360 (non-comatose) Pts w/ STEMI & Cardiogenic Shock

Table 3. End Points and Adverse Events in the Intention-to-Treat Population.*

Event	Microaxial Flow Pump plus Standard Care (N = 179)	Standard Care Alone (N = 176)	Effect Size (95% CI)†
Primary end point: death from any cause at 180 days — no. (%)	82 (45.8)	103 (58.5)	0.74 (0.55 to 0.99)‡
Secondary end point			
Composite cardiac end point — no. (%)§	94 (52.5)	112 (63.6)	0.72 (0.55 to 0.95)
No. of days alive and out of the hospital (range)¶	82 (0 to 177)	73 (0 to 179)	8 (–8 to 25)
Adverse events			
Composite safety end point — no. (%)‖	43 (24.0)	11 (6.2)	4.74 (2.36 to 9.55)
Moderate or severe bleeding — no. (%)**	39 (21.8)	21 (11.9)	2.06 (1.15 to 3.66)
Limb ischemia — no. (%)	10 (5.6)	2 (1.1)	5.15 (1.11 to 23.84)
Renal-replacement therapy — no. (%)	75 (41.9)	47 (26.7)	1.98 (1.27 to 3.09)
Stroke — no. (%)	7 (3.9)	4 (2.3)	1.75 (0.50 to 6.01)
Cardioversion after ventricular tachycardia or fibrillation — no. (%)	59 (33.0)	52 (29.5)	1.17 (0.75 to 1.83)
Sepsis with positive blood culture†† — no. (%)	21 (11.7)	8 (4.5)	2.79 (1.20 to 6.48)

NEJM 20124;390:1382-93

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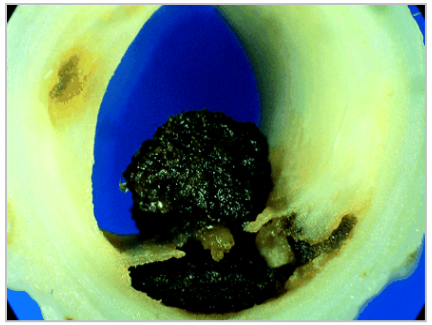

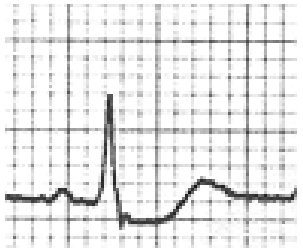

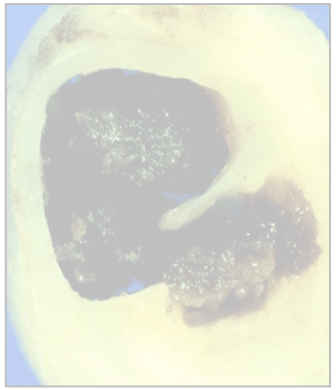

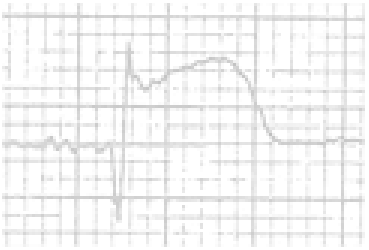

Non-ST elevation ACS

ST elevation ACS

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UA | **NSTEMI**

STEMI

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NQWMI

QwMI

Management of NSTE-ACS

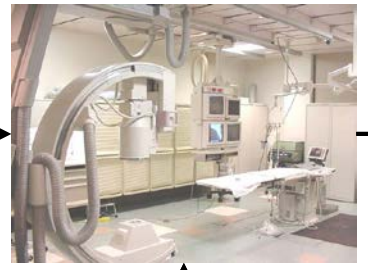
72 yo F p/w chest pain that came on 3 hours ago. Took NTG and chest pain resolved after 20 mins.

ECG shows inferior ST depressions. Tn elevated.

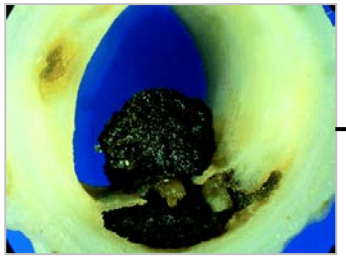
Management Strategy in NSTEACS

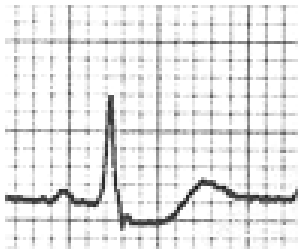
INVASIVE

(ie, angiography for all in ~48 hrs)



NSTEACS





Initial Med Rx

anatomy

PCI / CABG

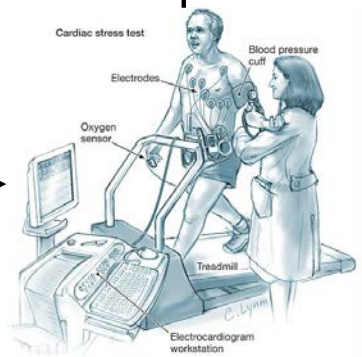
Long-term Med Rx

high-risk

low-risk

recurrent angina

Cont'd Med Rx

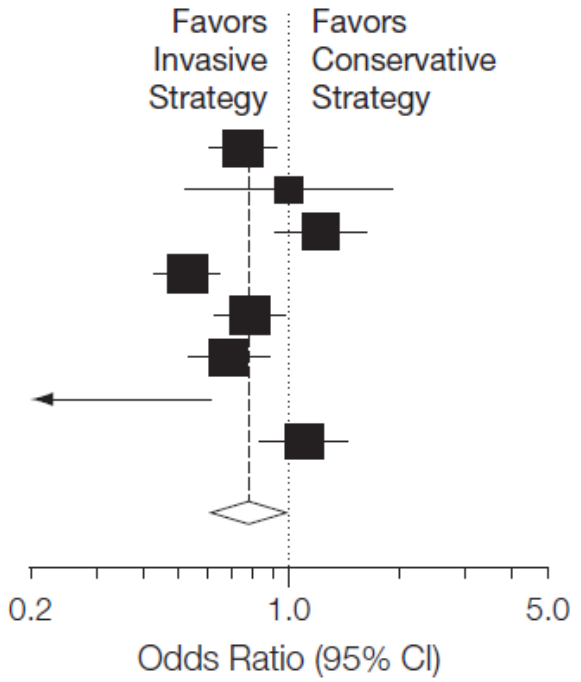


CONSERVATIVE

(ie, selective angiography)

Benefit of INV vs CONS Strategy

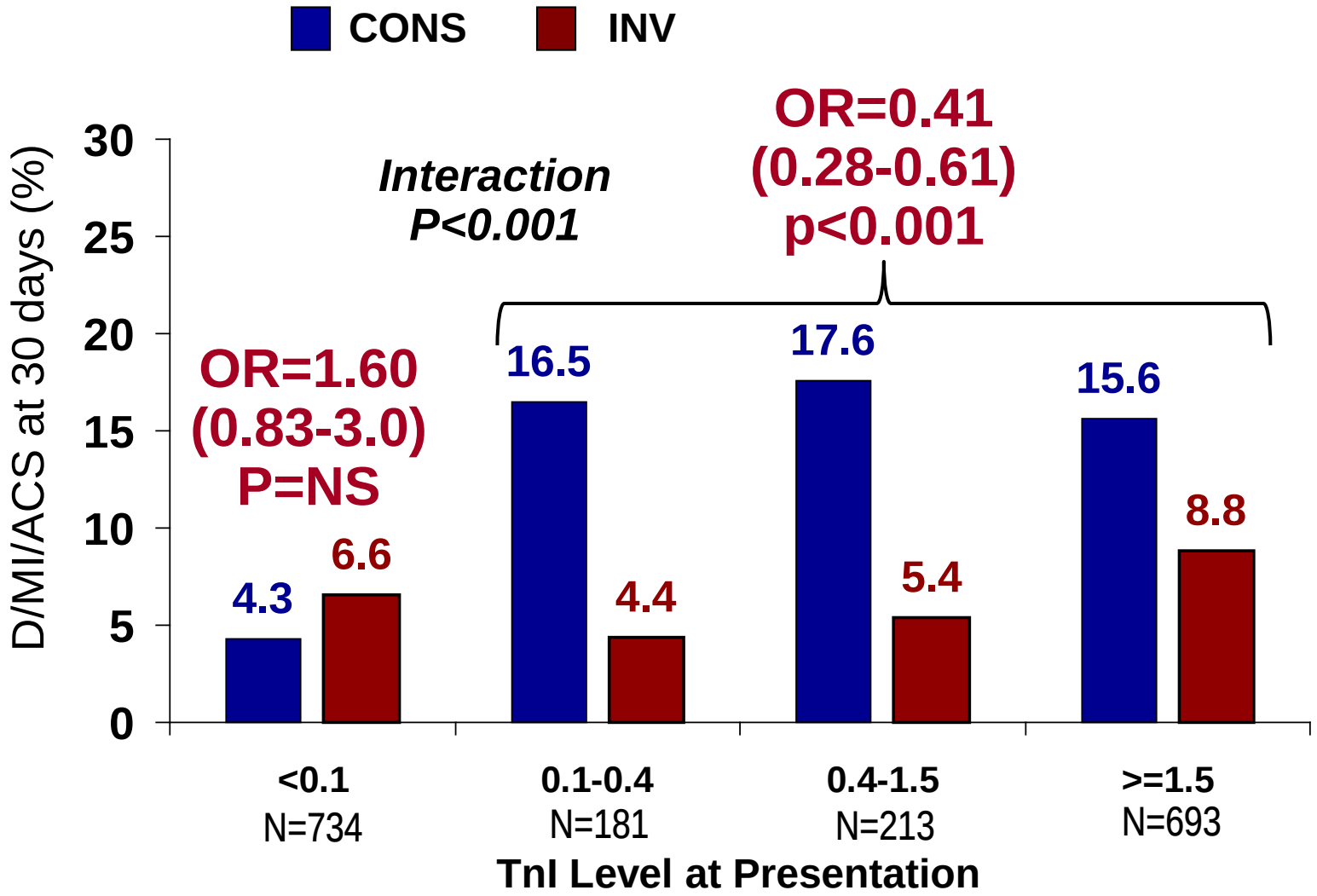
All Patients	Rates of Death, MI, or Rehospitalization With ACS, No./Total No. (%)		Odds Ratio (95% CI)
	Invasive Strategy	Conservative Strategy	
TIMI IIIB[10]	122/895 (13.6)	171/915 (18.7)	0.75 (0.61-0.93)
MATE[11]	27/111 (24.3)	22/90 (24.4)	0.99 (0.52-1.90)
VANQWISH[18]	148/462 (32.0)	124/458 (27.7)	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

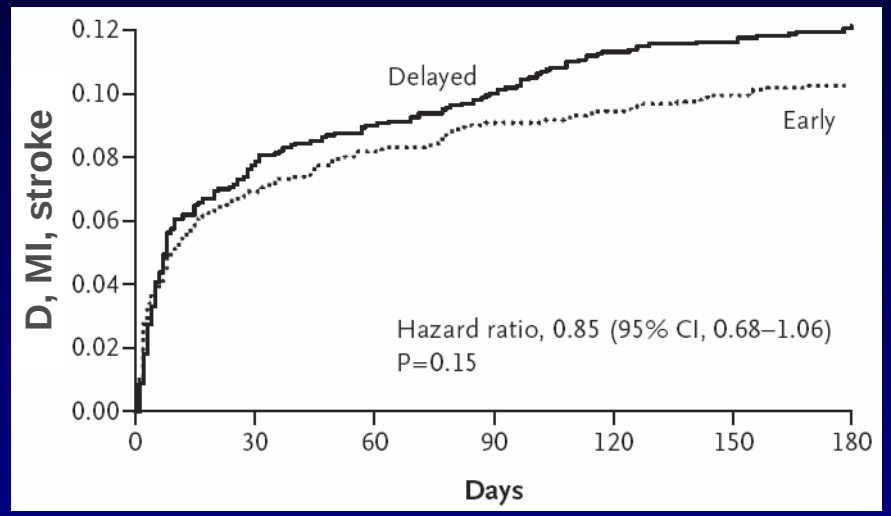
Troponin Treatment Interaction

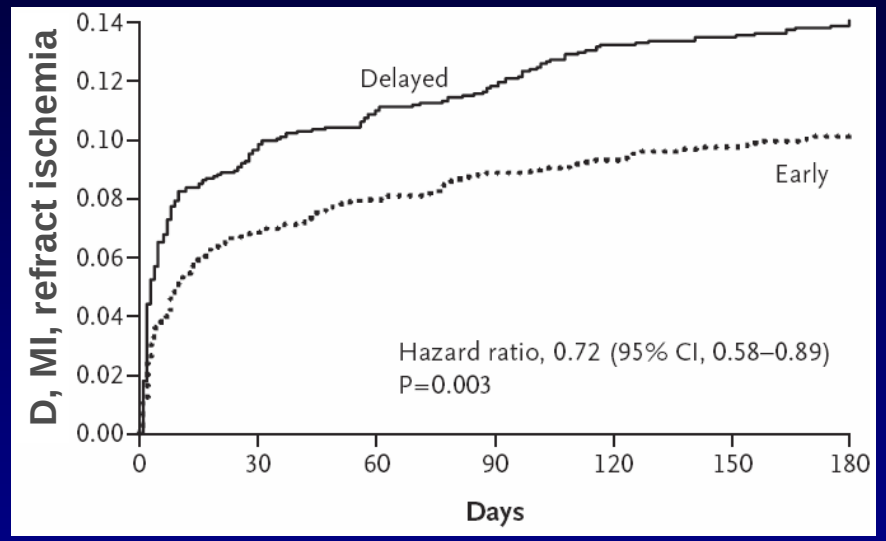


Cannon CP et al. *NEJM* 2001;344:1879

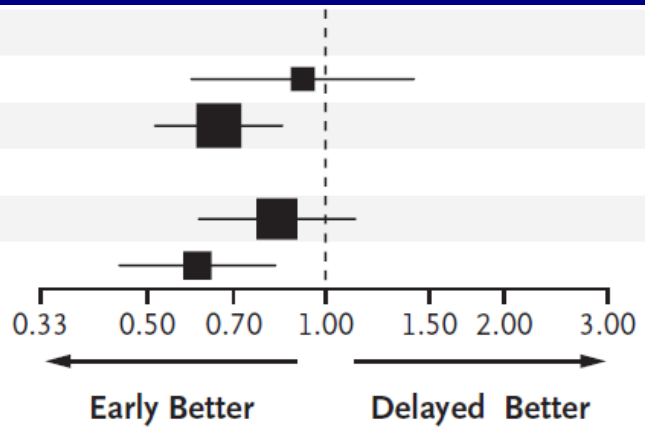
TIMACS

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)



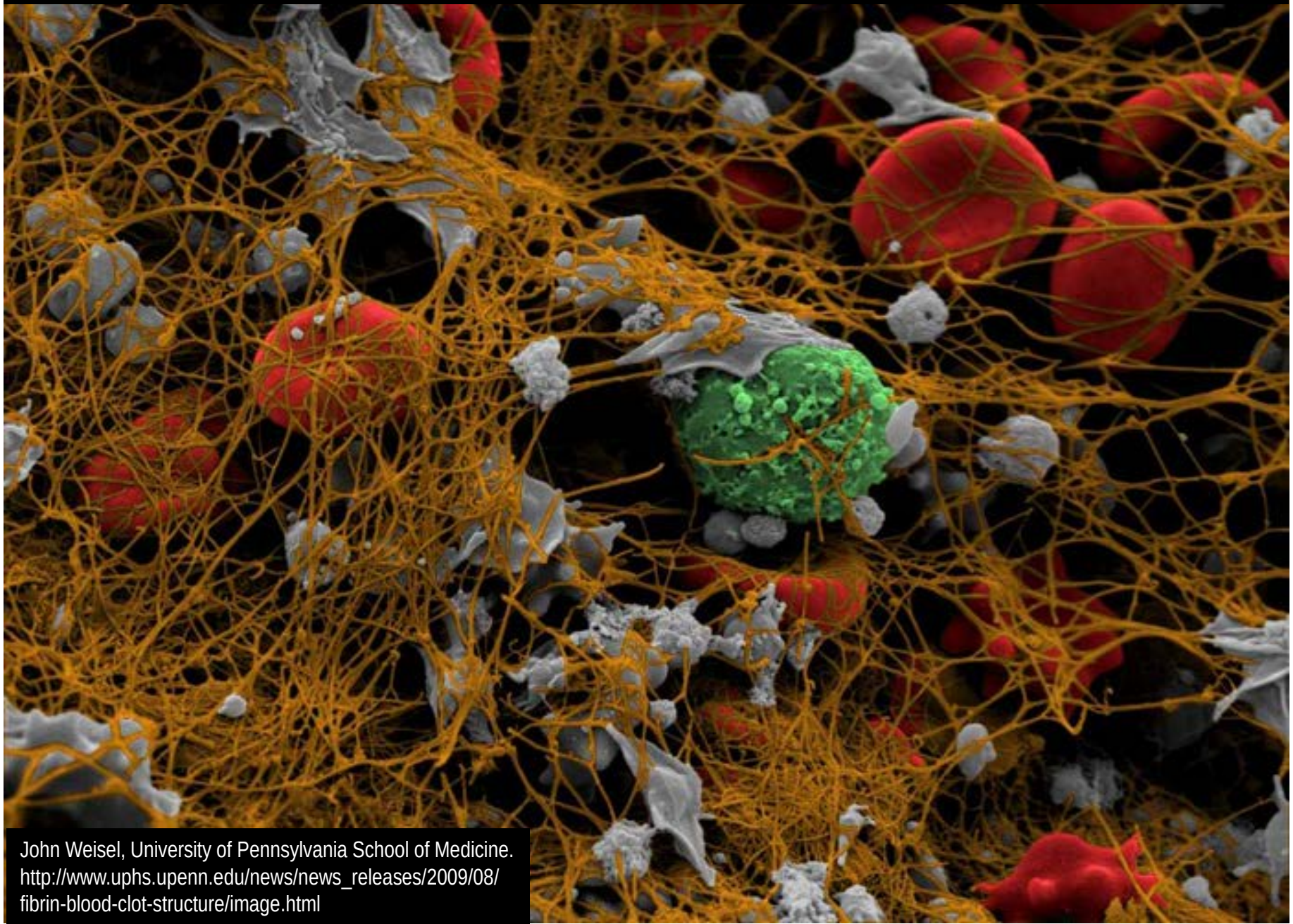
Mehta SR et al. *NEJM* 2009;360:2165-75

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

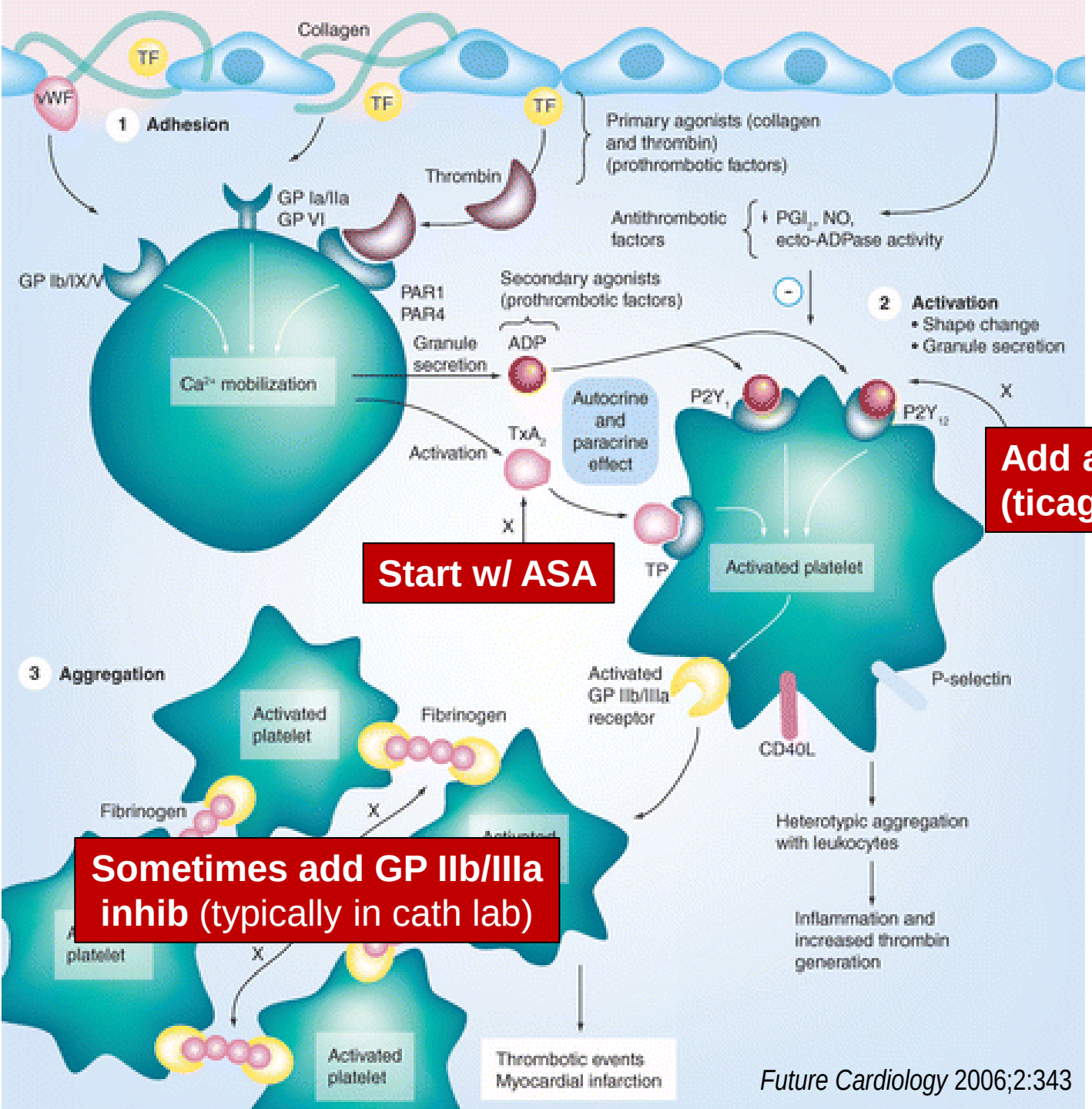
Circulation 2014;130:2354-94

Antithrombotic Therapy



John Weisel, University of Pennsylvania School of Medicine.
http://www.uphs.upenn.edu/news/news_releases/2009/08/fibrin-blood-clot-structure/image.html

Inhibiting Platelets

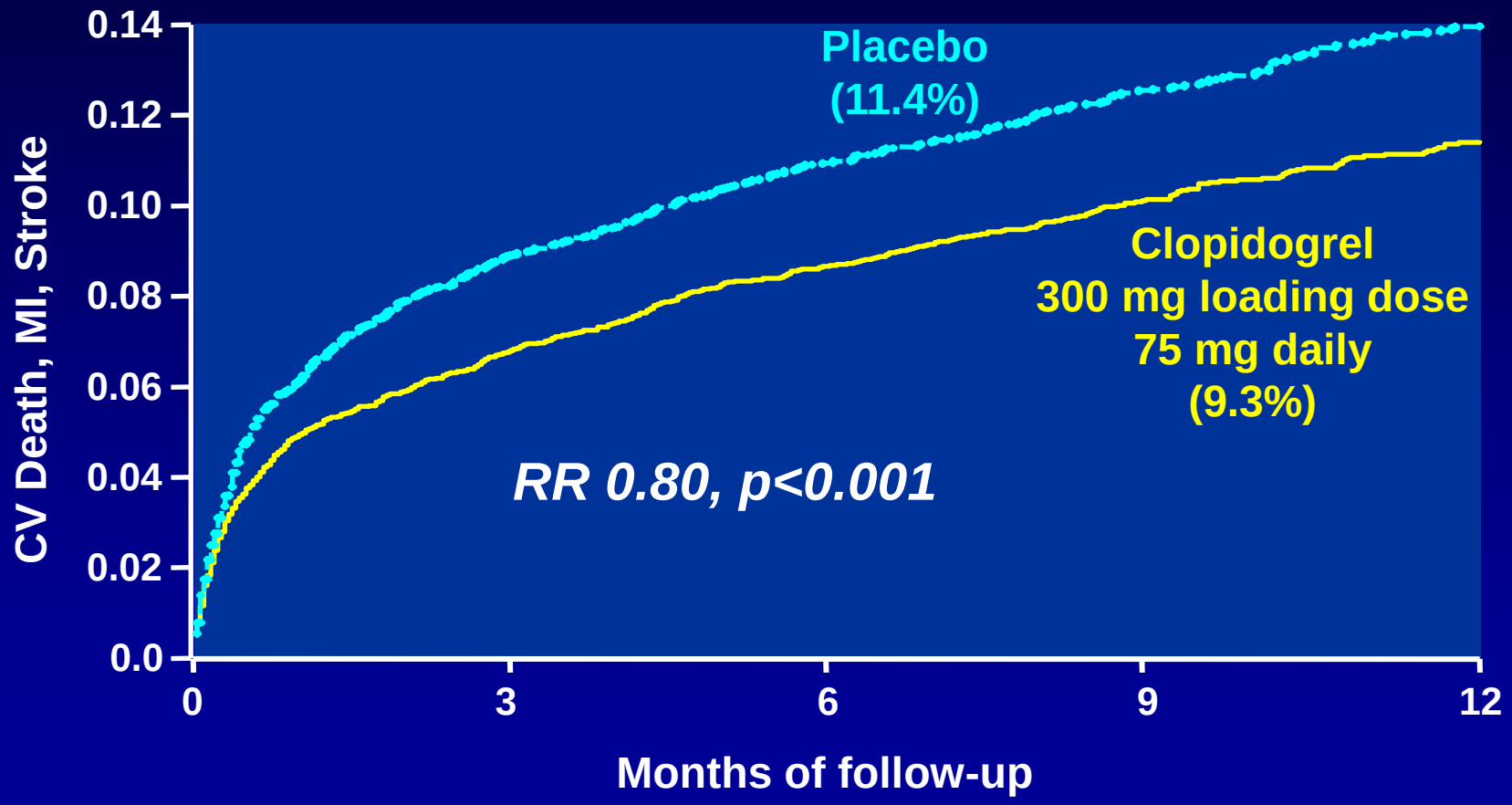


Future Cardiology 2006;2:343

- Oral agents: ticagrelor & prasugrel more potent and preferred over clopidogrel b/c ↓ risk of ischemic events (but ↑ bleeding)
- No clear benefit for starting before PCI, and more bleeding
- IV agent: cangrelor (fast on & off); can give at time of PCI in $P2Y_{12}$-naïve Pts

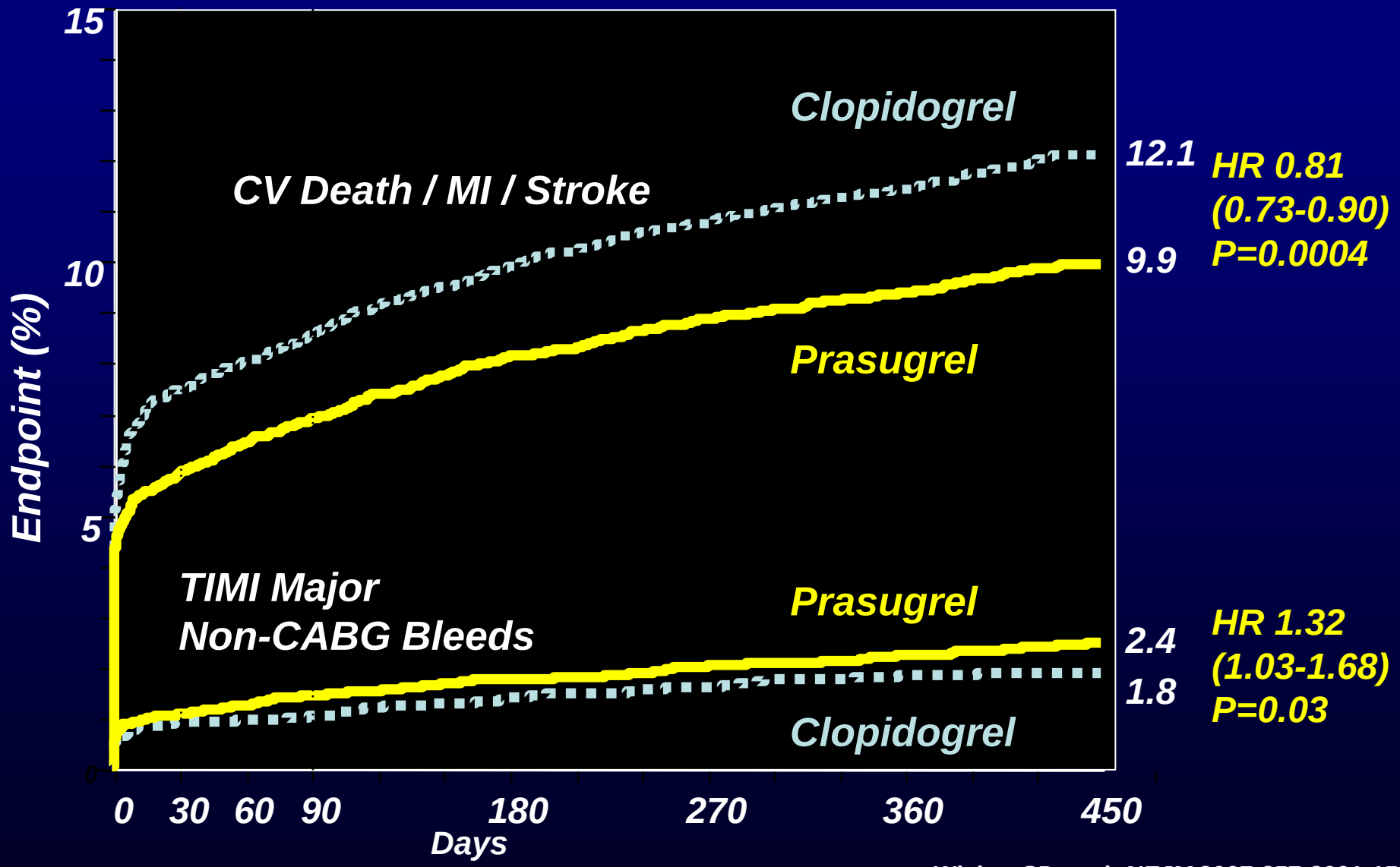
Clopidogrel in NSTE ACS: CURE

12,563 Pts, GP IIb/IIIa & early invasive approach *discouraged*



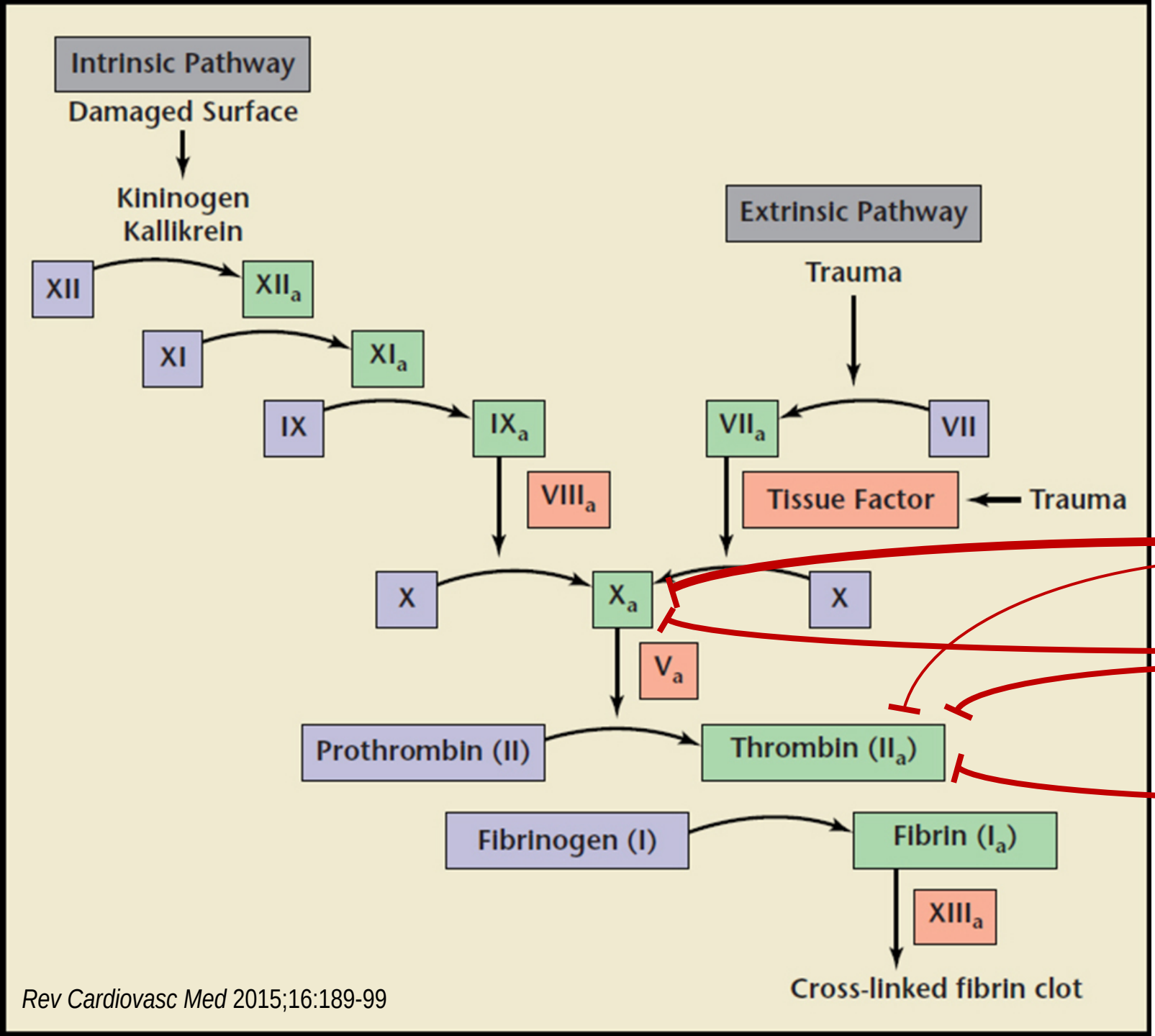
CURE. *NEJM* 2001; 345: 494

13,608 Patients with ACS and Planned PCI Randomized to Prasugrel (60/10) vs. Clopidogrel (300/75)



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

Inhibiting Coagulation Cascade



Rev Cardiovasc Med 2015;16:189-99

ATIII **Low-molecular-wt heparin (LMWH) SC**

ATIII **Unfractionated heparin (UFH) IV**

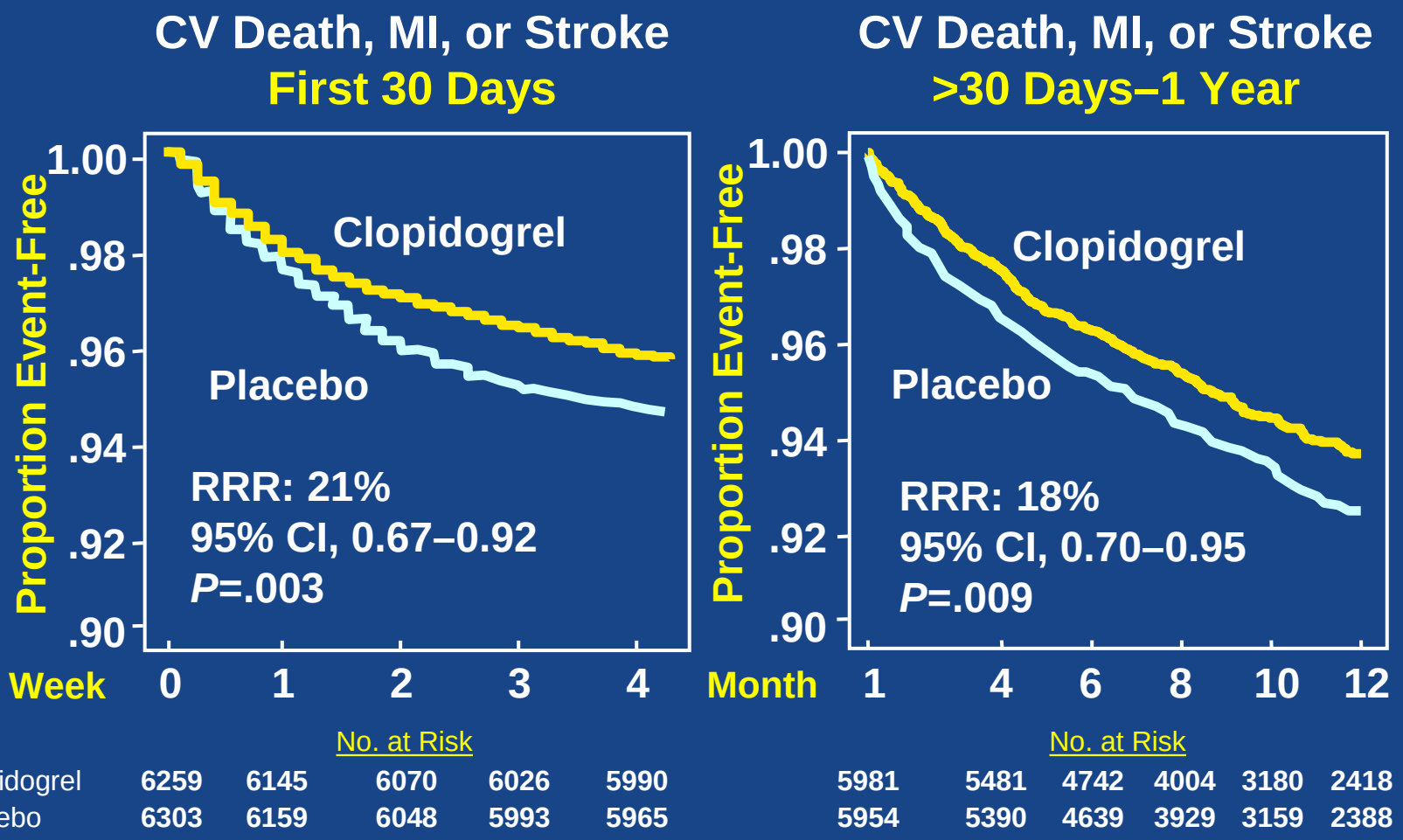
Bivalirudin IV

Pick one!

How long to treat with which antiplatelet medications?

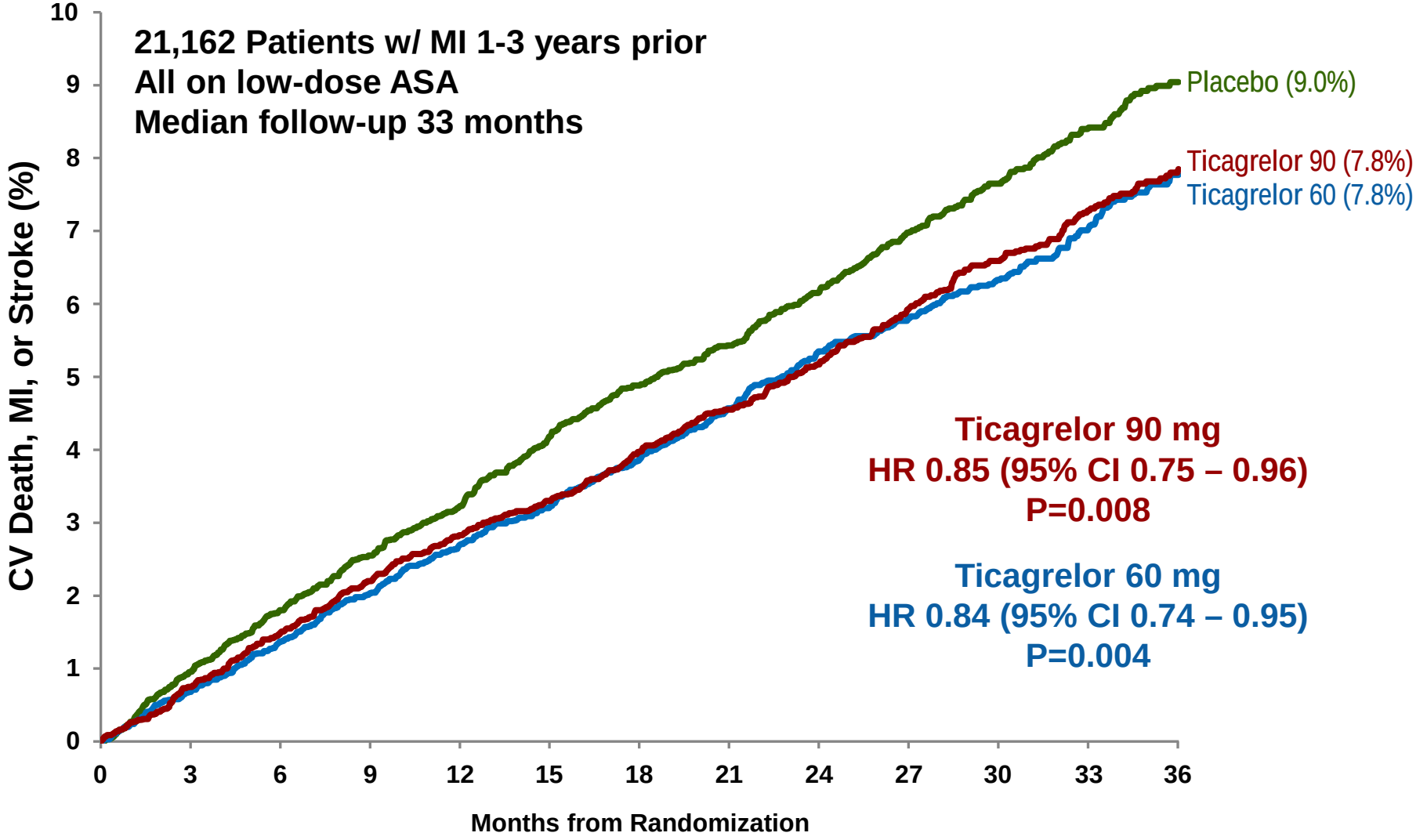
CURE: Long-term benefit of clopidogrel

12,562 Patients with NSTEACS (mostly conservatively managed)



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

Long-Term DAPT: PEGASUS-TIMI 54



Bonaca MP et al. and Sabatine MS. *NEJM* 2015; 372:179

Risk Stratification

Patient selection algorithm

Step 1
Assess bleeding risk and exclude patients at high risk

Low haemoglobin or prior hospitalization for bleeding

Step 2
Assess number of ischaemic risk factors

Recent $P2Y_{12}$ inhibitor (<1yr) or recent MI (<2 yrs)

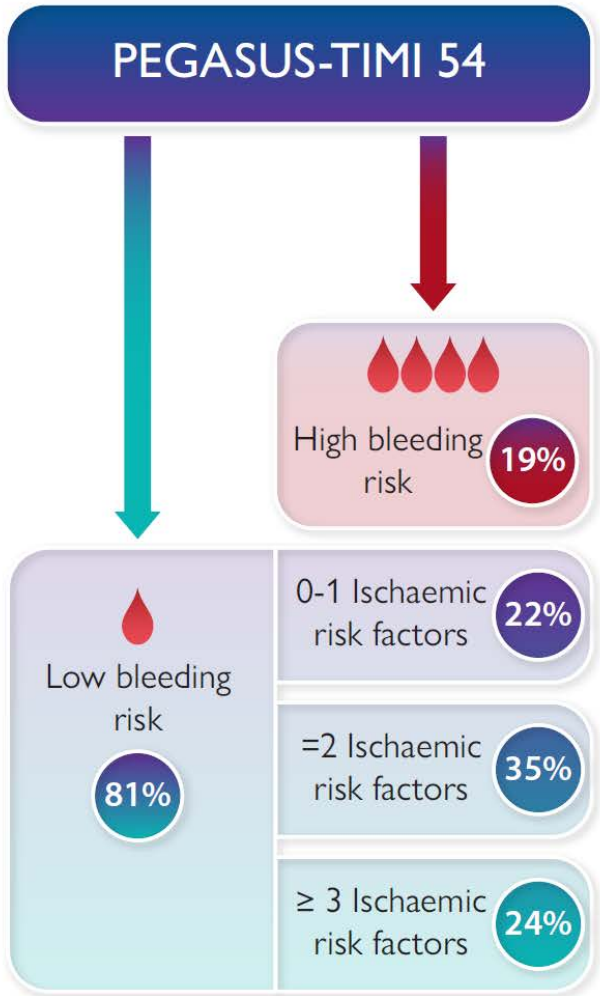
Multivessel CAD

Diabetes mellitus

Peripheral artery disease

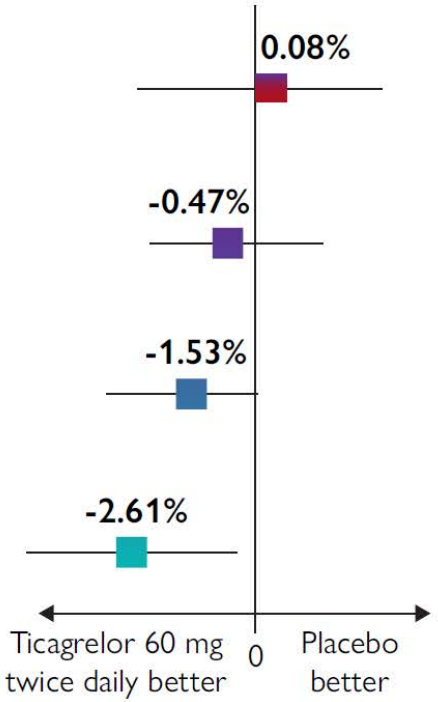
Chronic kidney disease

Multiple prior MIs



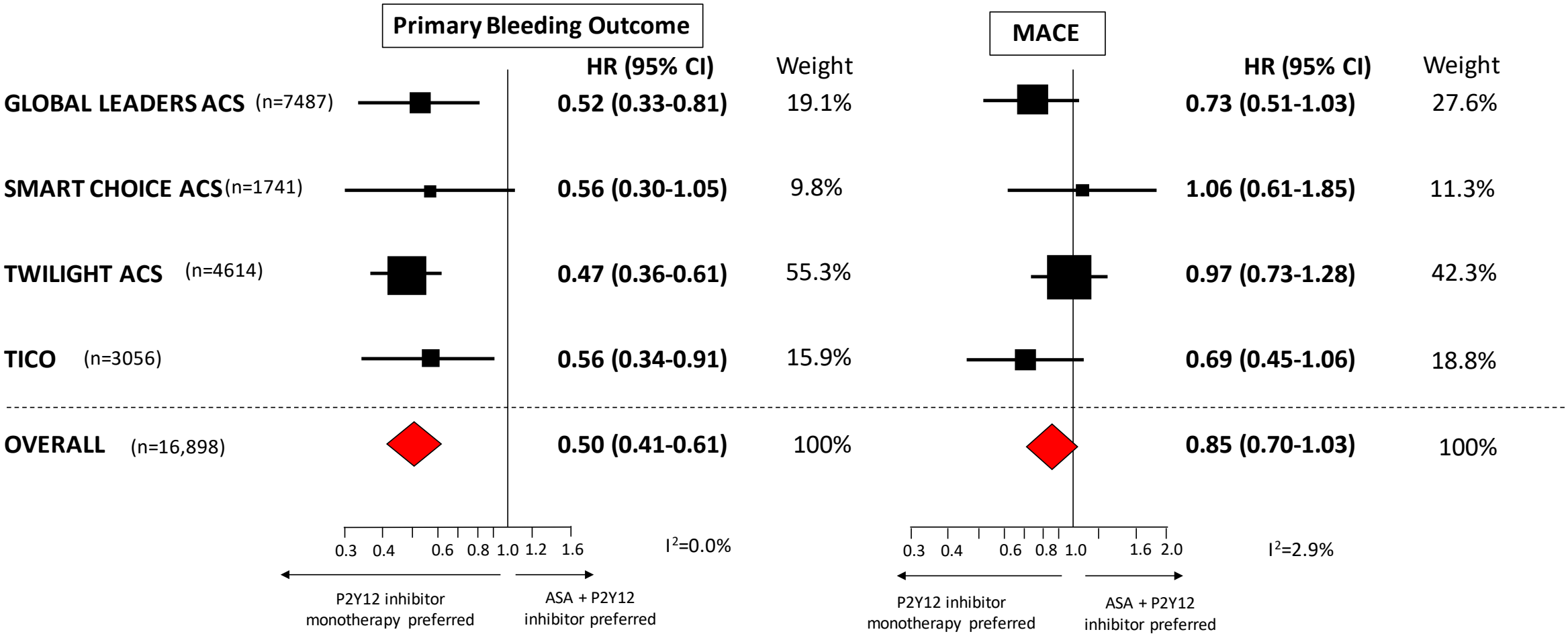
Absolute risk difference in CV death, MI or stroke with Ticagrelor vs Placebo by risk group

(P-trend 0.076)



Bonaca MP et al. and Sabatine MS. *EHJ* 2022;43:5037-44

Drop Aspirin after 1-3 Months (ie, $P2Y_{12}$ MonoRx)?



O'Donoghue ML, Murphy SA, and Sabatine MS. *Circulation* 2020;142:538

Long-term Antiplatelet Rx

- Start with DAPT ASA + $P2Y_{12}$ inhibitor (ticag or prasugrel preferred)
- For most patients: continue for 12 mos
- If high ischemic risk (and low bleeding risk & tolerated DAPT well to date), consider continuing ASA + $P2Y_{12}$ inhibitor beyond 12 mos
- Could consider dropping ASA after 3 mos and just continue $P2Y_{12}$ inhib (ideally ticagrelor)
- If high bleeding risk, would use clopidogrel over ticag or prasugrel and drop ASA after 3 mos

Triple Therapy

72 yo F w/ HTN, DM, prior stroke p/w NSTEMI.

2 drug-eluting stents placed in proximal LAD.

On aspirin and ticagrelor.

Develops AF next day.

What regimen do you discharge her on?

What if the Pt needs OAC (eg, AF)?

- High rate of bleeding with triple Rx (ASA + $P2Y_{12}$ + OAC)
- DOAC preferred over warfarin because less bleeding (no head-to-head, but apixaban w/ best data vs. VKA)
- Would <u>not</u> ↓ DOAC dose b/c may not adequately protect against stroke
- In terms of antiplt, start w/ DAPT: ASA + $P2Y_{12}$ inhibitor (clopidogrel)
- Drop ASA at hospital d/c or, if high ischemic risk, after 1 month
- Consider dropping $P2Y_{12}$ inhib after 6-12 mos, depending on bleeding risk

Lipid-Lowering Therapy

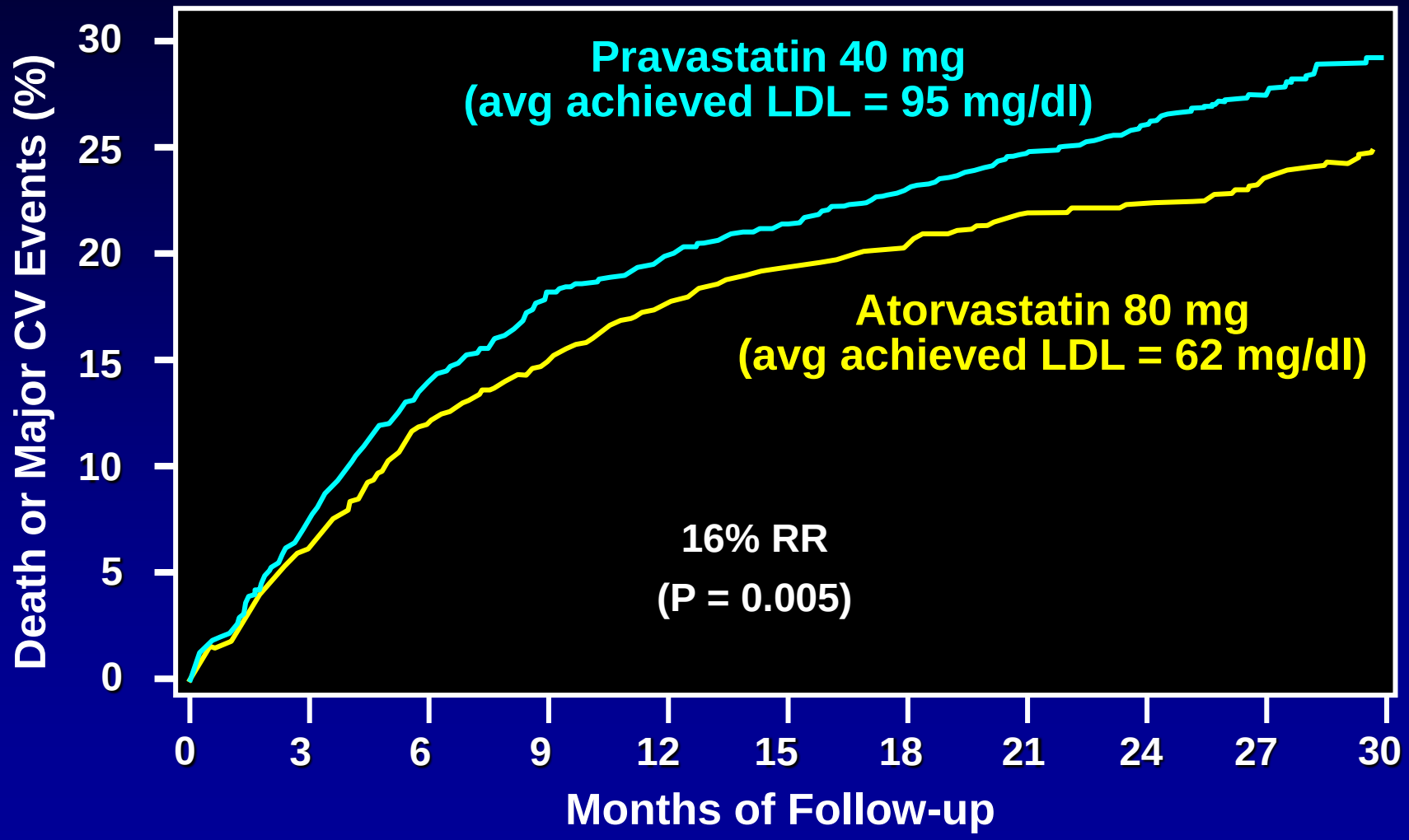
64 yo M w/ h/o NSTEMI 2 years ago now p/w NSTEMI.

Drug-eluting stent placed in LAD. 50% lesions in RCA and LCx.

LDL-C on admission (not on any lipid-lowering Rx) was 180 mg/dL. Started on atorva 80 mg. What else would you recommend?

PROVE IT – TIMI 22

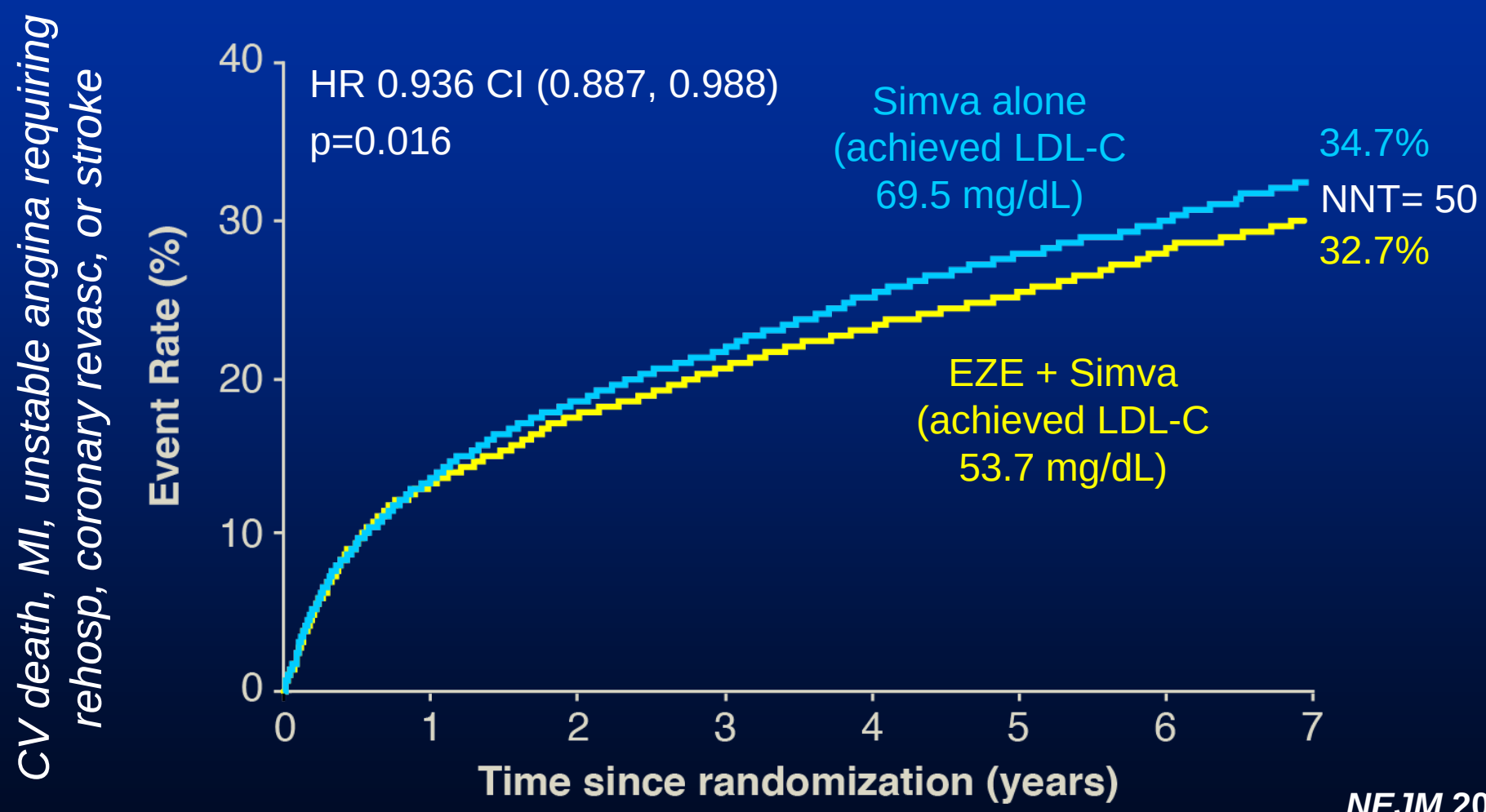
4162 patients hospitalized w/in prior 10 d for ACS



Cannon et al. *NEJM* 2003; 350: 1495

Primary Endpoint — ITT

18,144 Pts w/ ACS w/in 10 d, LDL-C 50-100 mg/dL on a statin (50-125 mg/dl if not on a statin)

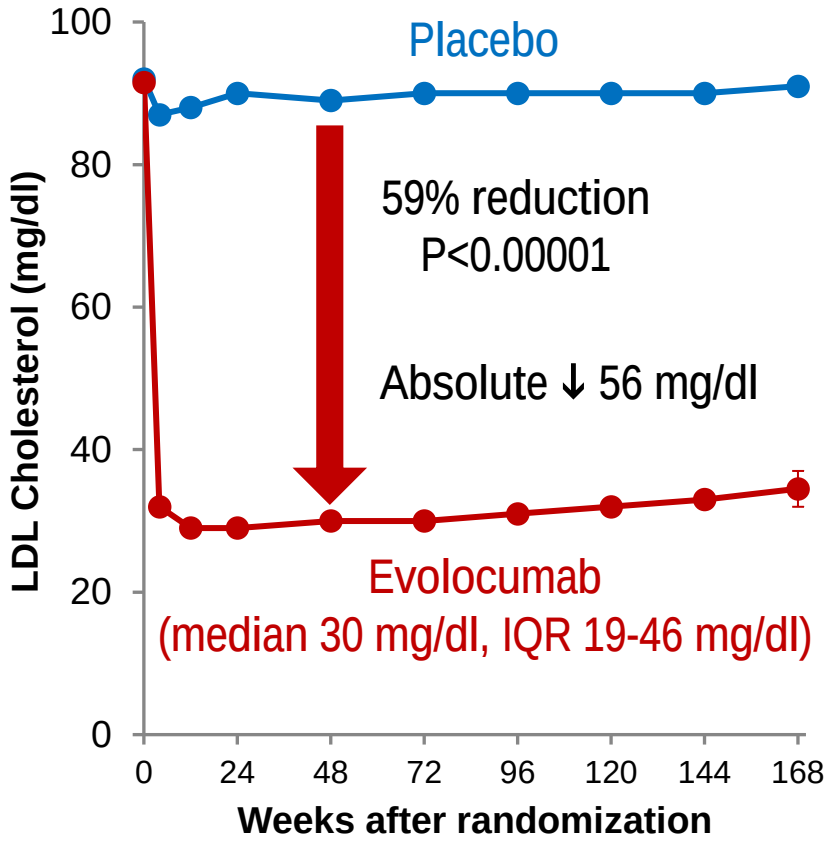


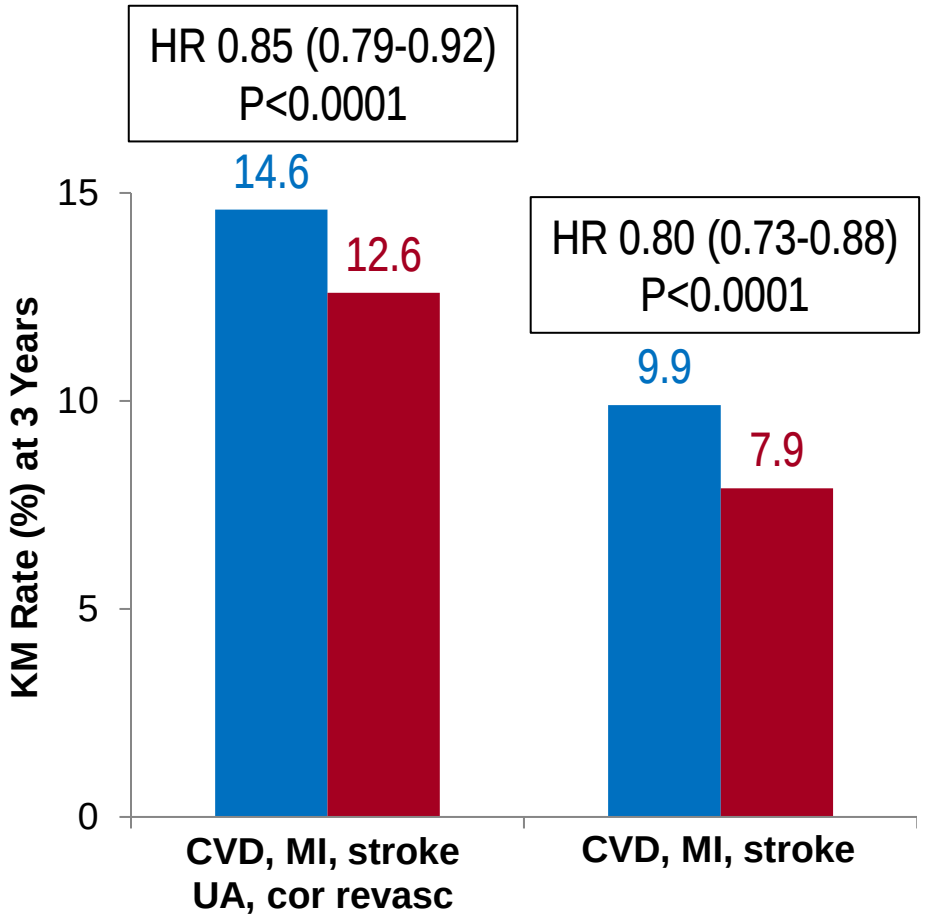
***NEJM* 2015;372:2387-97**

NEJM 2015;372:2387-97

Summary of Effects of PCSK9i Evolocumab

- ↓ LDL-C by 59% down to a median of 30 mg/dl
- ↓ CV outcomes in patients on statin
- Safe and well-tolerated

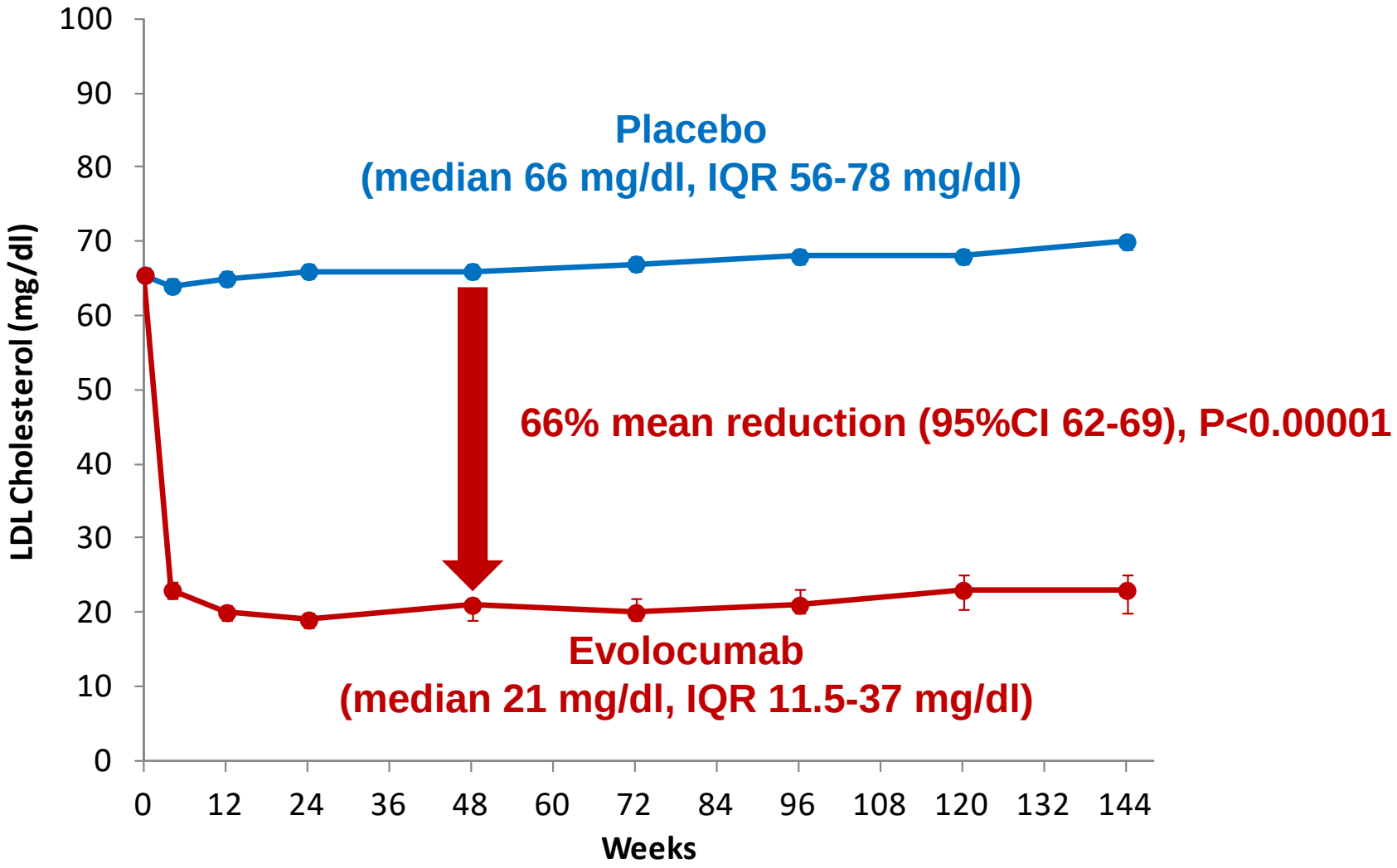




Sabatine MS et al. *NEJM* 2017;376:1713-22

LDL Cholesterol

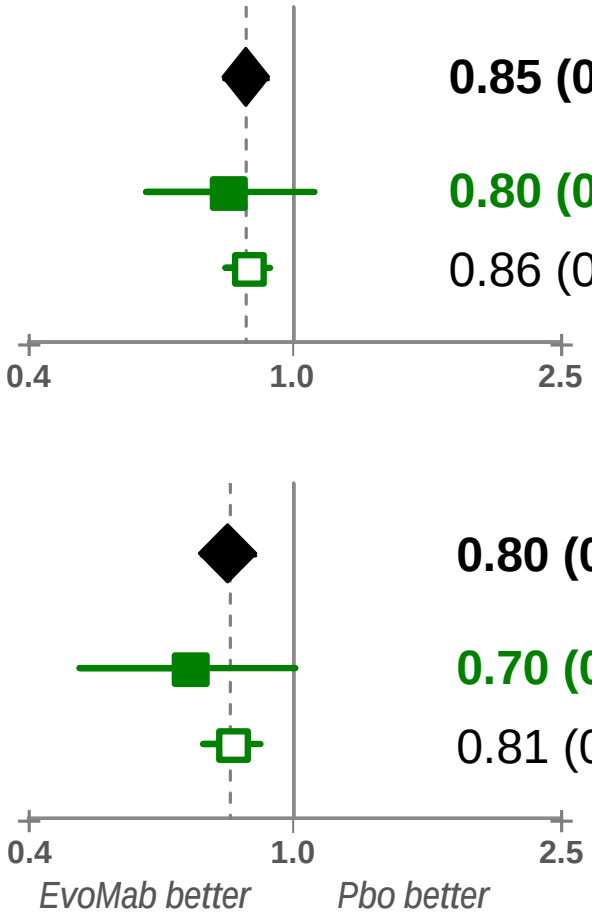
2034 patients w/ baseline LDL-C <70 mg/dL



Giugliano RP et al. and Sabatine MS. *JAMA Cardiol* 2017;2:1385-91

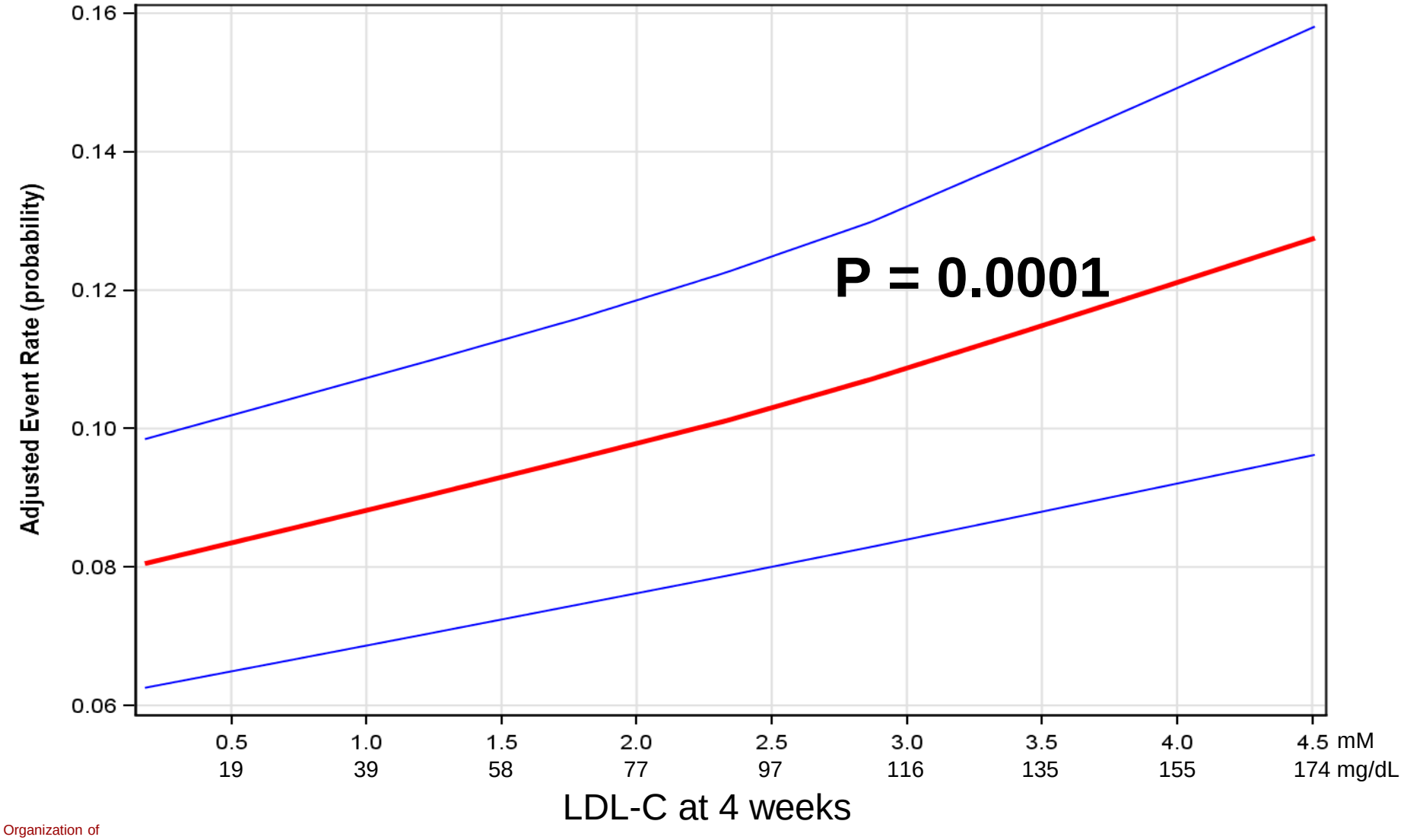
Clinical Outcomes
by Baseline LDL-C

	HR (95% CI)	$P_{interaction}$
CVD, MI, stroke, UA, or cor revasc		
All Patients	**0.85 (0.79-0.92)**	
Baseline LDL-C <70 mg/dL	**0.80 (0.60-1.07)**	0.65
Baseline LDL-C ≥70 mg/dL	0.86 (0.79-0.92)	
CVD, MI, or stroke		
All Patients	**0.80 (0.73-0.88)**	
Baseline LDL-C <70 mg/dL	**0.70 (0.48-1.01)**	0.44
Baseline LDL-C ≥70 mg/dL	0.81 (0.73-0.89)	



Giugliano RP et al. and Sabatine MS. *JAMA Cardiol* 2017;2:1385-91

CV Death, MI, Stroke



Giugliano RP et al. & Sabatine MS. *Lancet* 2017;309:1962-71

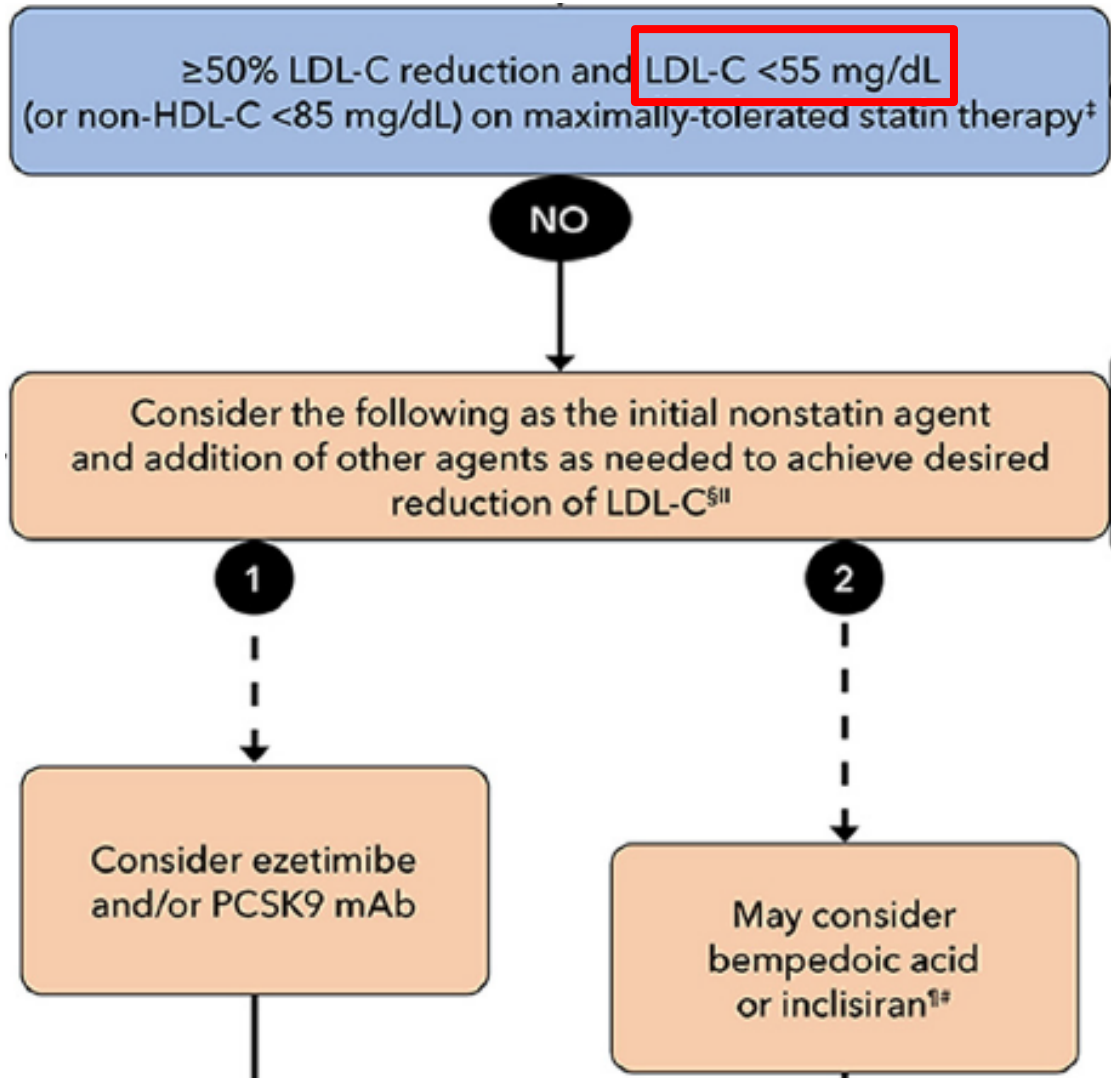
2019 ESC Dyslipidemia Guidelines

Recommendations	Class[a]	Level[b]
In secondary prevention patients at very high risk[c], an LDL-C reduction of at least 50% from baseline[d] and an LDL-C goal of < 1.4 mmol/L (< 55 mg/dL) are recommended.[33-35, 119, 120]	I	A

[c]Prior ACS, stable angina, coronary revascularization, stroke, TIA, PAD

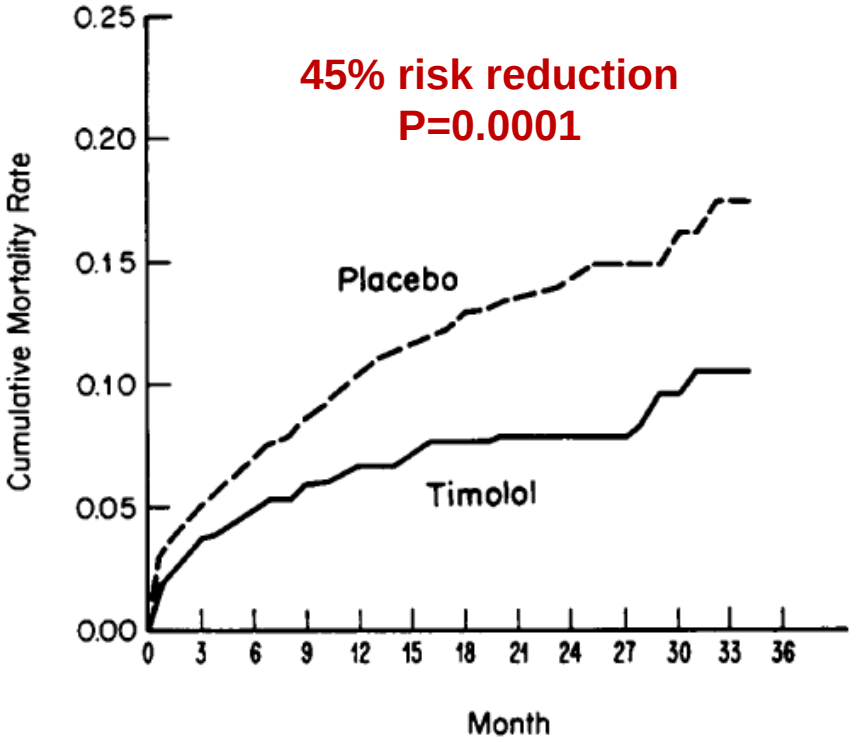
For patients with ASCVD who experience a second vascular event within 2 years (not necessarily of the same type as the first event) while taking maximally tolerated statin-based therapy, an LDL-C goal < 1.0 mmol/L (< 40 mg/dL) may be considered.[119, 120]

2022 ACC Expert Consensus Decision Pathway



β-blockers

1884 Patients 1-4 weeks after acute MI
Randomized to β-blocker vs. placebo



NEJM 1981;304:801

5020 Patients 1-7 days after acute MI w/ nl LVEF
Randomized to β-blocker vs. placebo

Death or MI

BUT …
- **High rate of crossover**
- **HR 0.81 (0.59-1.13) in STEMI**

Years

NEJM 2024;390:1372

ACEI/ARB, MRA

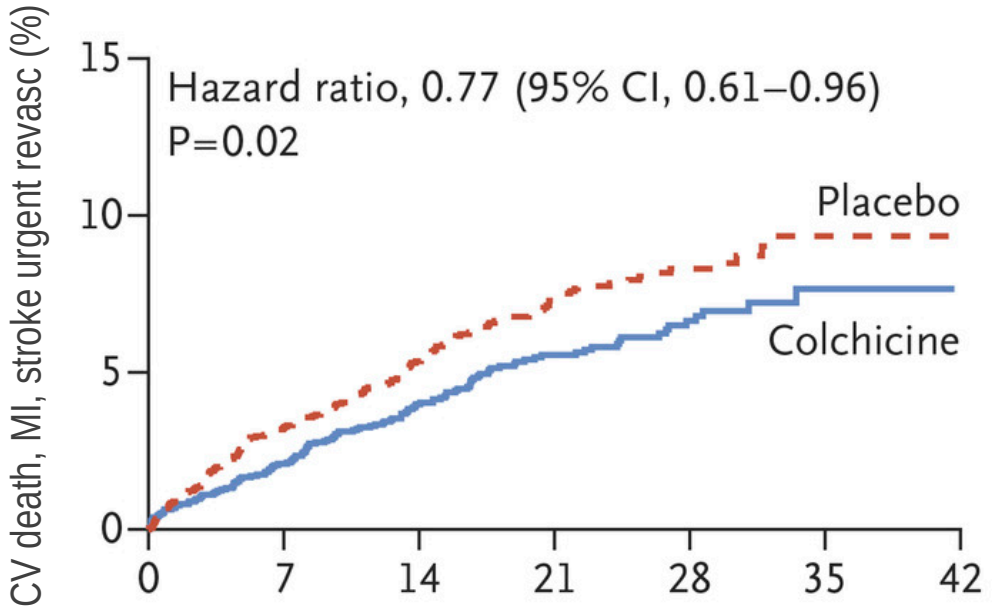
- **ACEI (or ARB if cannot tolerate ACEI)**
  - LVEF <40%, *or*
  - HTN, diabetes, or stable CKD
- **MRA**
  - If on ACEI/ARB & BB; *and*
  - Cr ≤2-2.5, K ≤5; *and*
  - LVEF <40% and either clinical s/s of HF or diabetes

Circulation 2014;130:2354-94

Treating Inflammation?

COLCOT: 4745 Pts within 30d of acute MI

Colchicine 0.5 mg qd vs. placebo



PROS

- **Large relative risk reduction**
- **Benefit of similar magnitude also seen in smaller ACS trial (COPS) trial and in trial of Pts with stable ischemic heart disease (LoDoCo2)**

CONS

- **Rates of non-CV death numerically higher in this trial, COPS, and LoDoCo2 (HR 1.51, 95% CI 0.99-2.31)**

NEJM 2019;381:2497-505

Summary

- **Diagnose ACS using H&P, 12-lead ECG, troponin**
- **STEMI: Primary PCI** (vs Lytic)
- **NSTE ACS: Invasive** (eg, ⊕ Tn) vs. **Conservative Strategy**
- **Anti-ischemic Rx:** beta-blocker, nitrates
- **Select Antiplatelet Regimen**
  - **ASA**
  - + $P2Y_{12}$ Inhibitor: **ticagrelor, prasugrel**, or clopidogrel
- **Select Anticoagulant: UFH**, LMWH, or bivalirudin
- **Long-term therapy**
  - ASA (maybe drop after 1-3 mos) + $P2Y_{12}$ inhibitor (at least 12 mos, if not longer)
  - ? β-blocker (if low LVEF or STEMI), statin + EZE (+ PCSK9i)
  - ? ACEI, ? MRA
  - ? Colchicine

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