

# Acute Coronary Syndromes

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- Professor of Medicine at HMS





# Disclosures

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Amgen; Anthos Therapeutics; AstraZeneca; Boehringer Ingelheim; CCRN; General Medicines; NATF

***Investigational, unlabeled and/or unapproved uses of drugs  
or devices may be discussed in this presentation.***



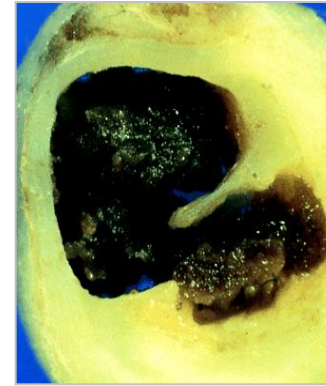
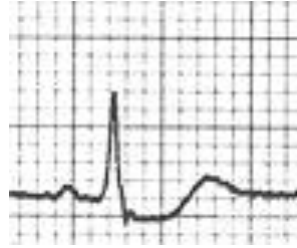
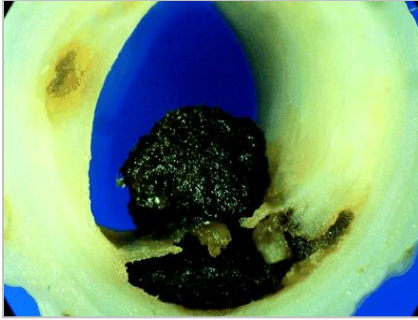


# Objectives

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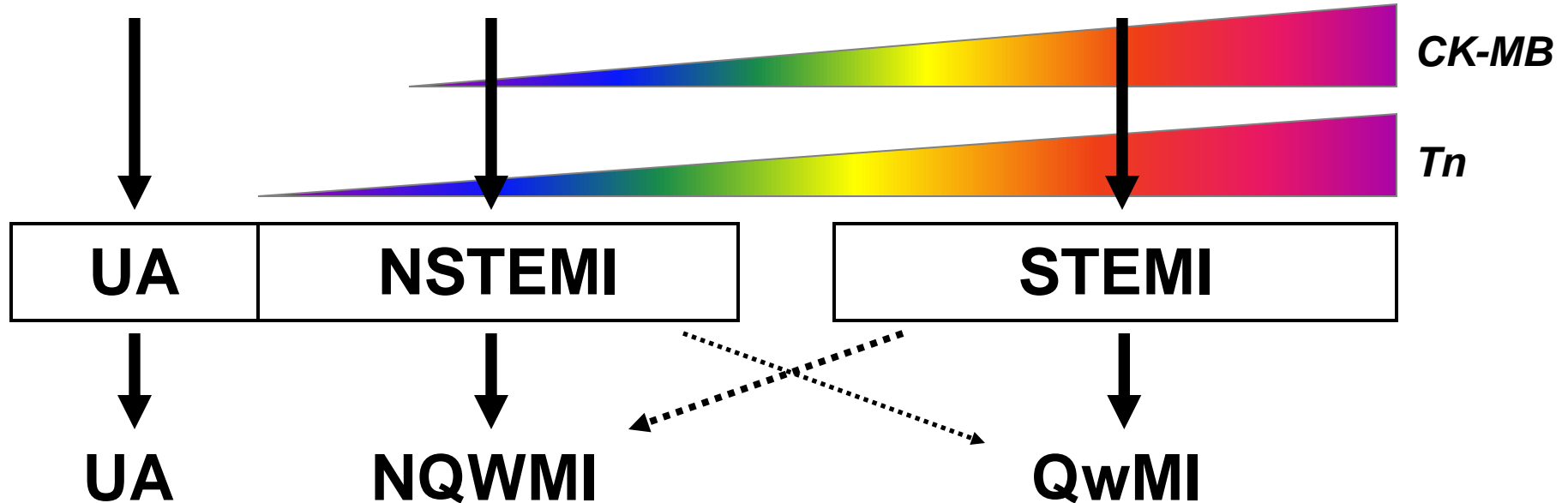
- **Understand how to diagnose ACS**
- **Understand how to treat patients with ACS**

# ACUTE CORONARY SYNDROMES



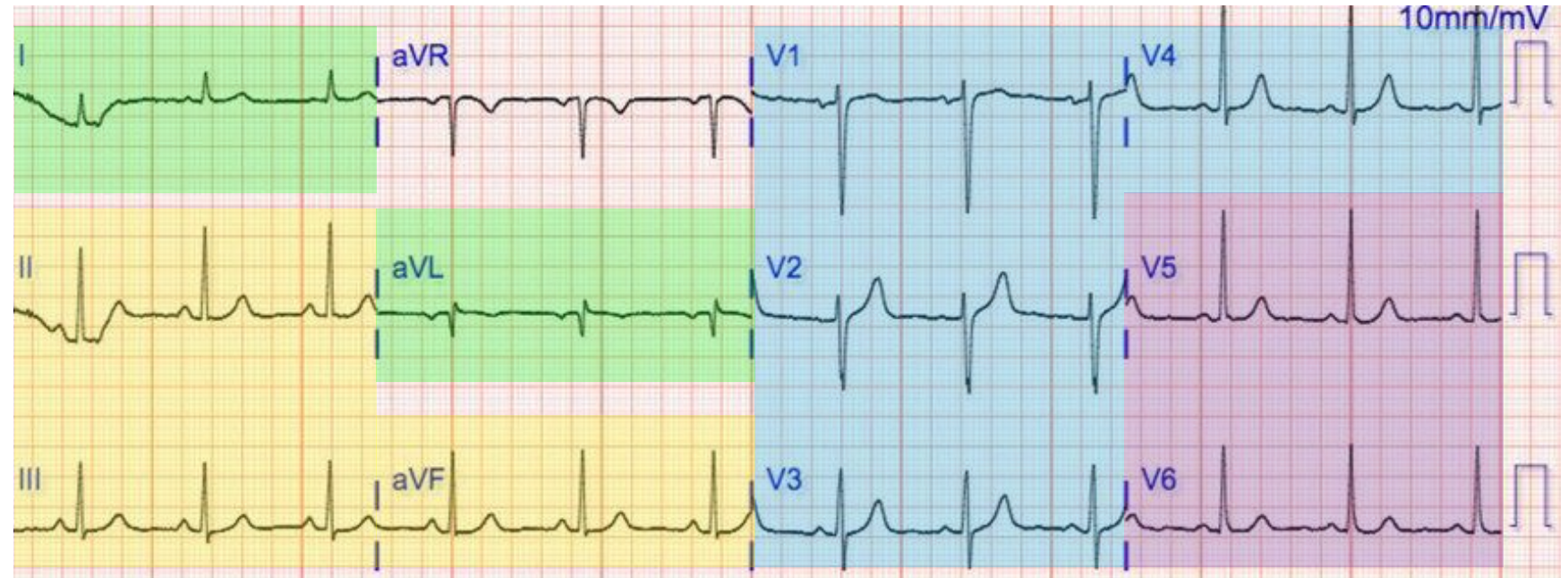
**Non-ST elevation ACS**

**ST elevation ACS**



# ACS: ECG

- **What to look for**
  - STE or LBBB not known to be old
  - ST depression  $\geq 0.5$  mm; TWI  $\geq 2$  mm
  - Coronary distribution





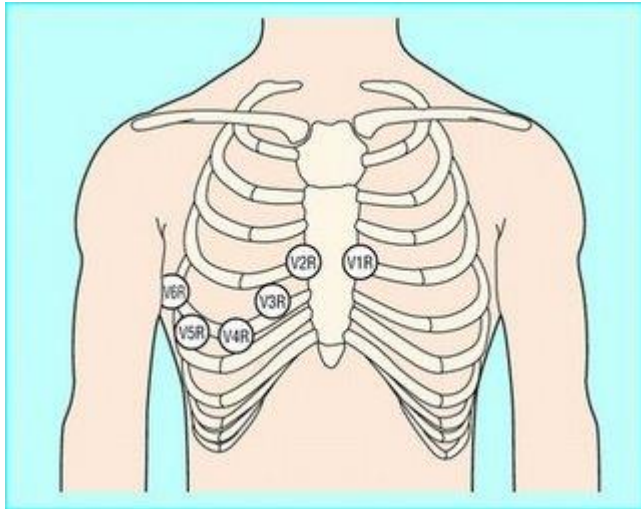
# ACS: ECG

- **What to look for**
  - STE or LBBB not known to be old
  - ST depression  $\geq 0.5$  mm; TWI  $\geq 2$  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 ECGs; obtain serial ECGs
  - R-sided leads if inferior STE; posterior leads if persistent anterior ST depressions or concerning hx and nl ECG



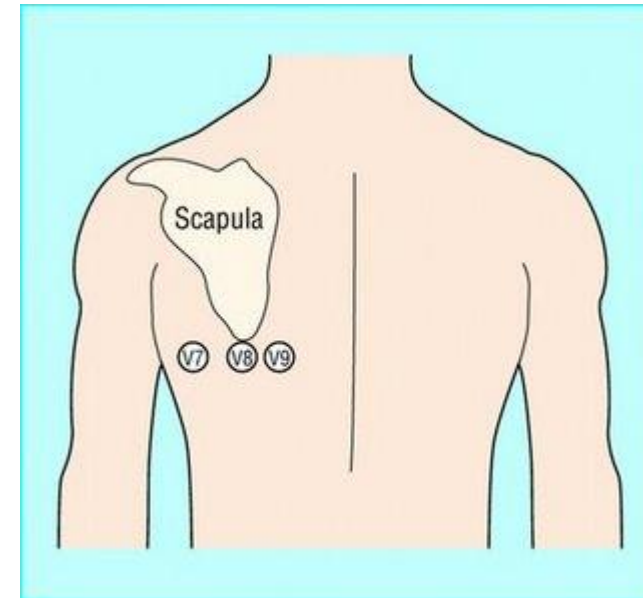
# ECG Special Placement

## 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*





# Ruling In & Ruling Out MI

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## Case #1

**75 yo M p/w chest pain x 15 minutes that started 4 hours ago, now resolved.**

**ECG without abnormalities.**

**Your high-sensitivity troponin testing strategy is:**

- A. Check now; if undetectable, discharge to home
- B. Check now and in 1 hour; if both <99<sup>th</sup> %ile and no change over time, discharge to home
- C. Check now and 3-6 hours after sx onset; if both <99<sup>th</sup> %ile, discharge to home



# Ruling In & Ruling Out MI

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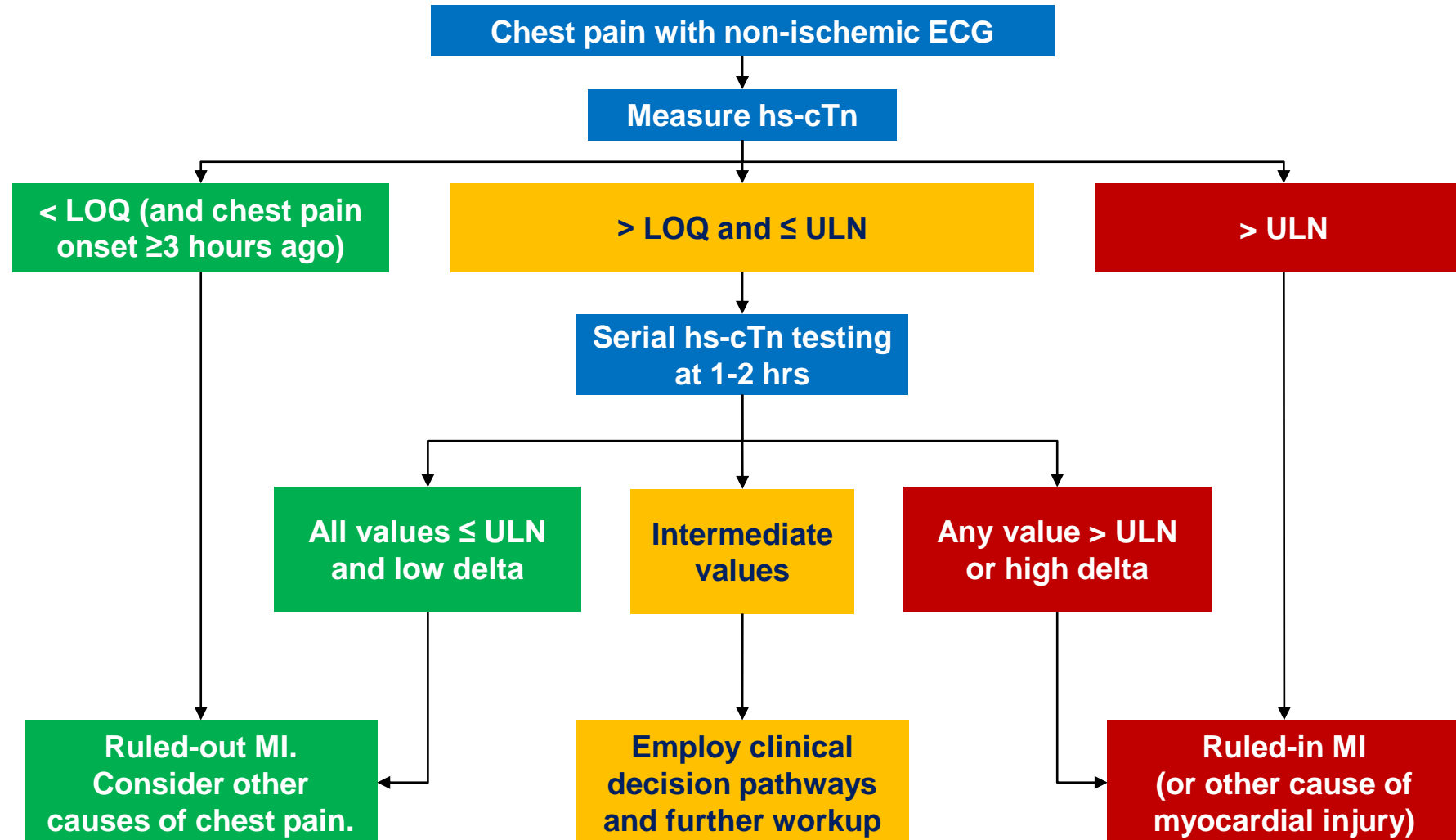
# ACS: Biomarkers

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 x 3
Dawn of modern cardiac markers (1990s)	<b>Troponin</b>	q8 hrs x 3
Recent past	Troponin	<b>3-6 hrs after sx onset</b>
Now	<b>hs-Troponin</b>	<b>1-2 hrs later</b> (depending on time from sx onset to presentation) <b>Examine absolute and <math>\Delta</math></b>



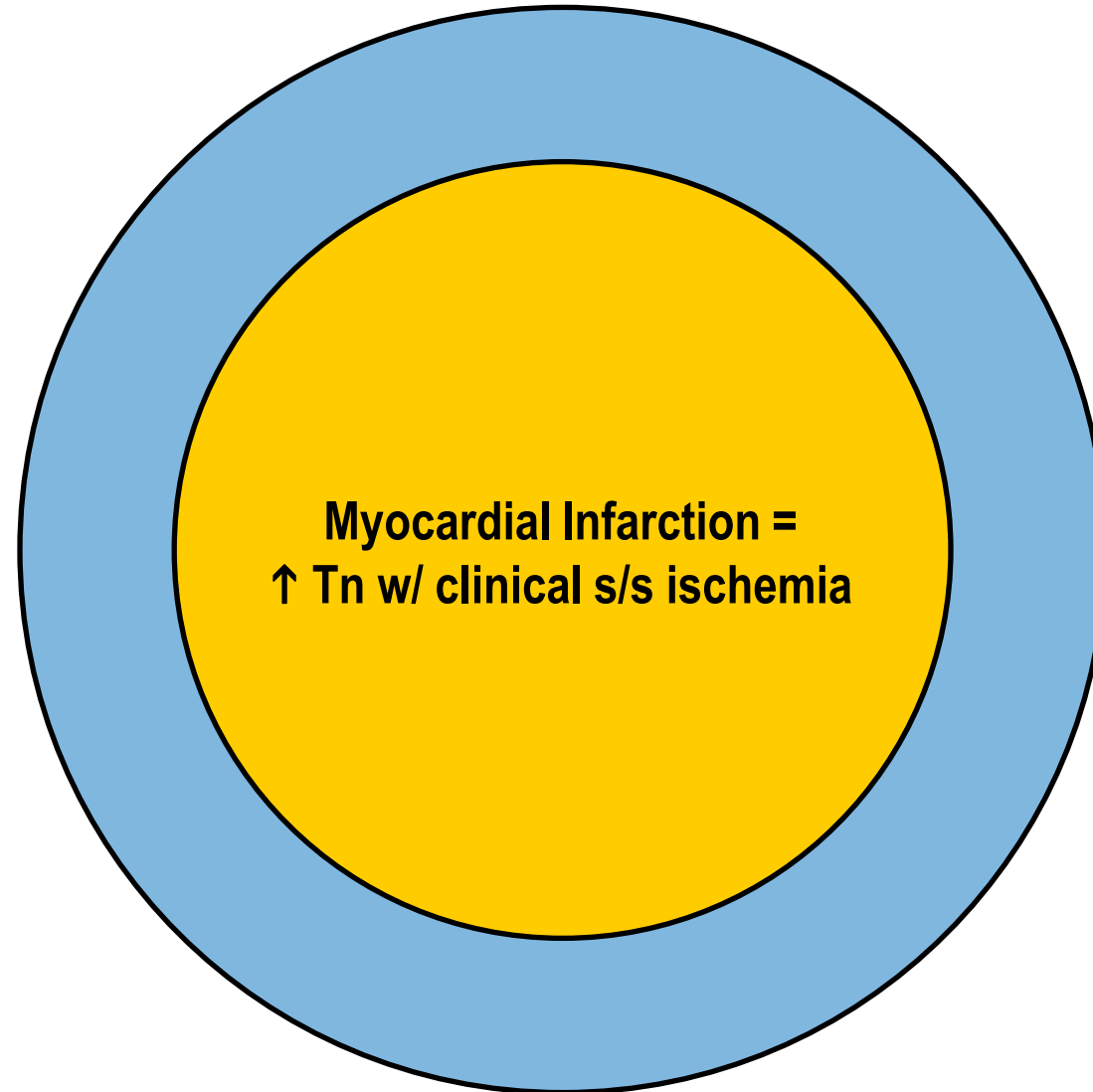


# Troponin Testing Algorithm





# 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

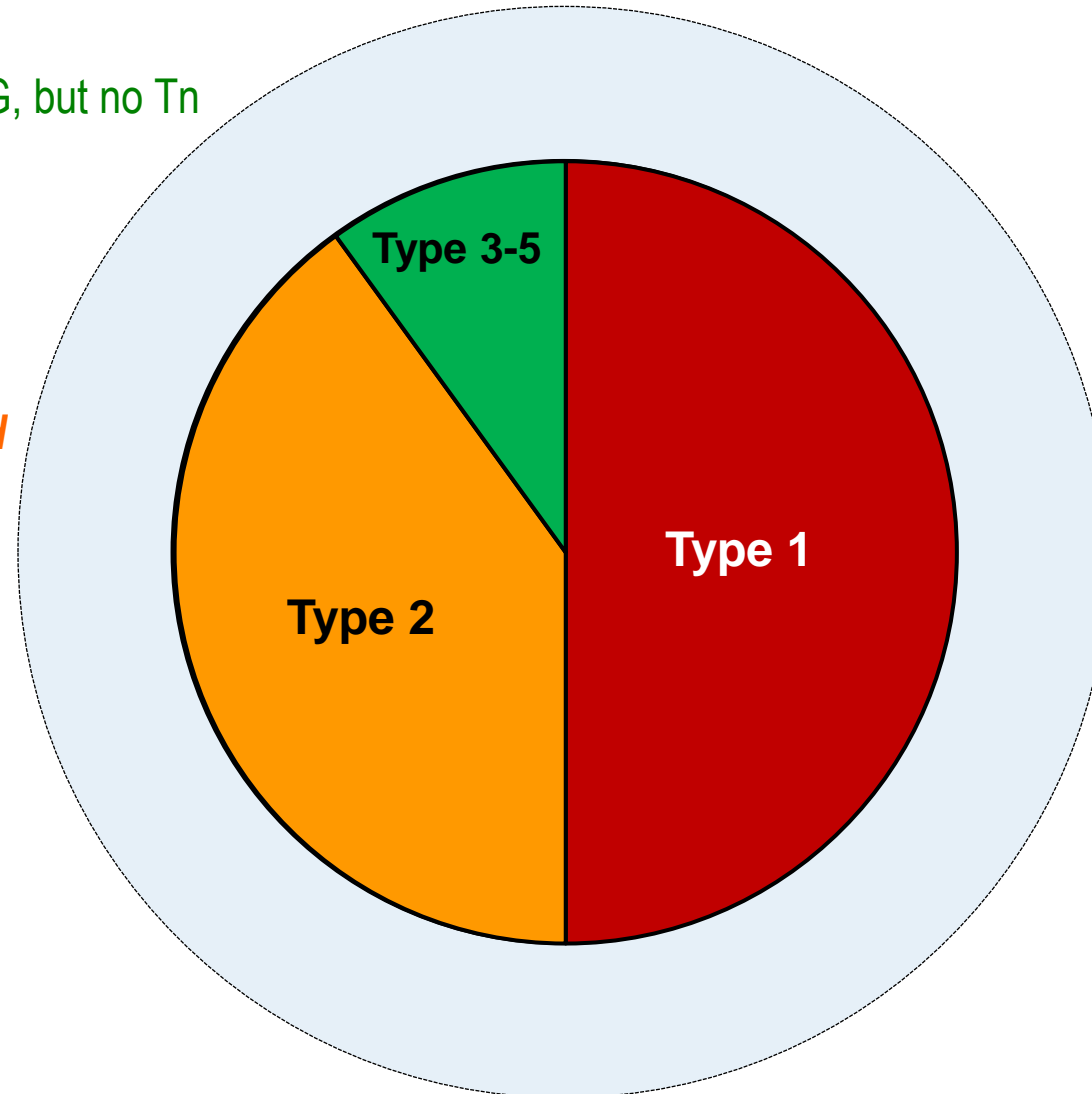
**Type 2 MI = myocardial O<sub>2</sub> supply/demand imbalance *unrelated* to acute atherothrombosis**

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



# Anti-Ischemic Therapy

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- **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  $\beta$ B or  $\beta$ B contra.
- **Morphine**
  - Pain, CHF, agitation; *don't* mask angina
- **Oxygen** (if hypoxemic)





# ST-Elevation MI (STEMI)

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- **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 time from 1<sup>st</sup> med contact to PCI anticipated  $\leq 120$  min)
  - Fibrinolytic (barring contraindications\* and only if within 12 hrs sx onset)

\*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

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## Case #2

**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.**

**What else would you do:**

- A. Low level stress test before discharge
- B. Stent the LAD lesion during this hospitalization or w/in 6 wks
- C. Stent the LAD & LCx lesions now



# Revascularization in STEMI

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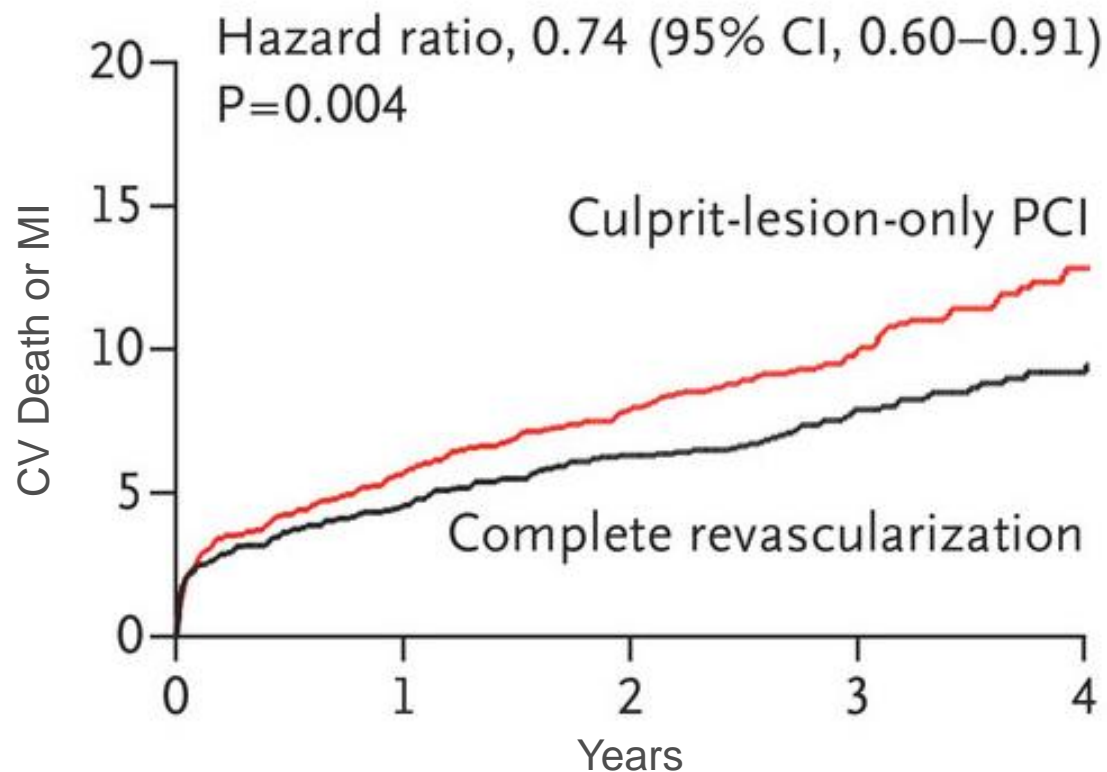
- A. Low level stress test before discharge
- B. Stent the LAD lesion during this hospitalization or w/in 6 wks**
- C. Stent the LAD & LCx lesions now



# Preventive PCI in STEMI

## COMPLETE: 2016 Pts w/ STEMI + MVD

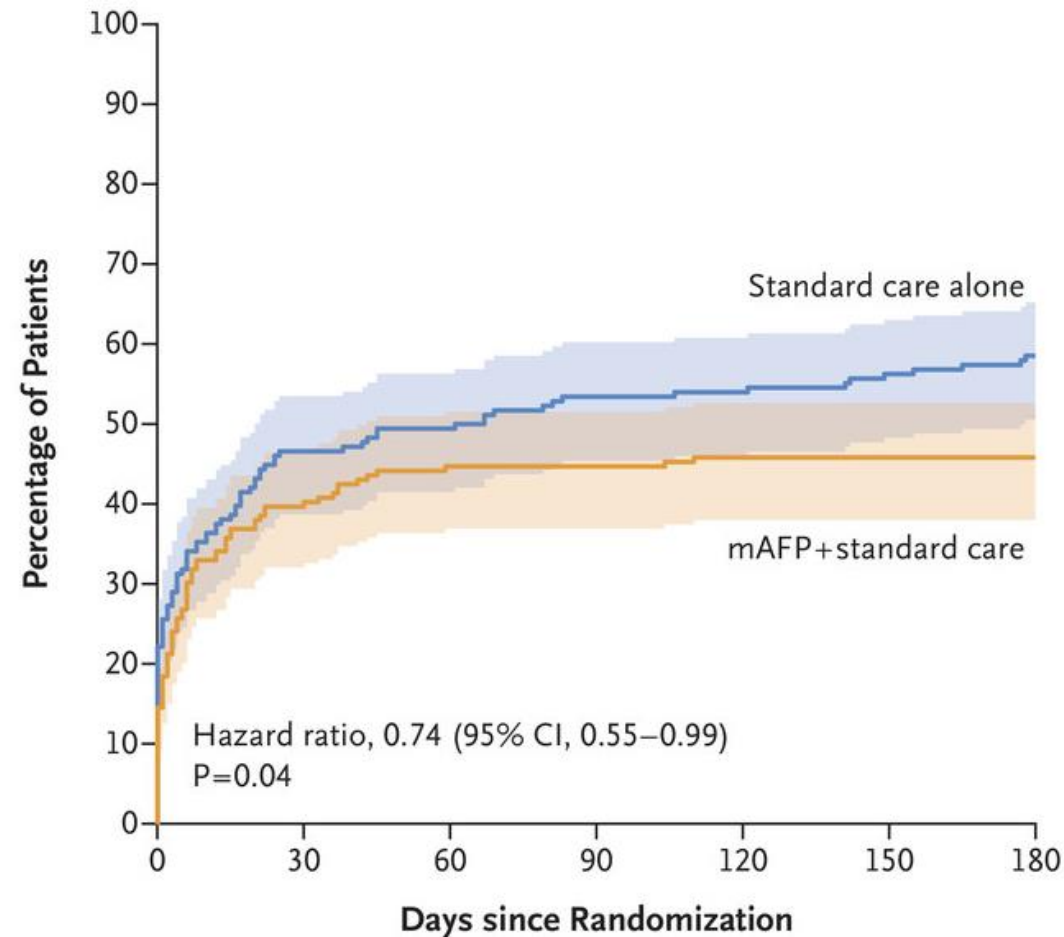
*Revasc of all signif lesions ( $\geq 70\%$  or 50-69% w/  $FFR \leq 0.80$ ) w/in 45 days vs. culprit only*





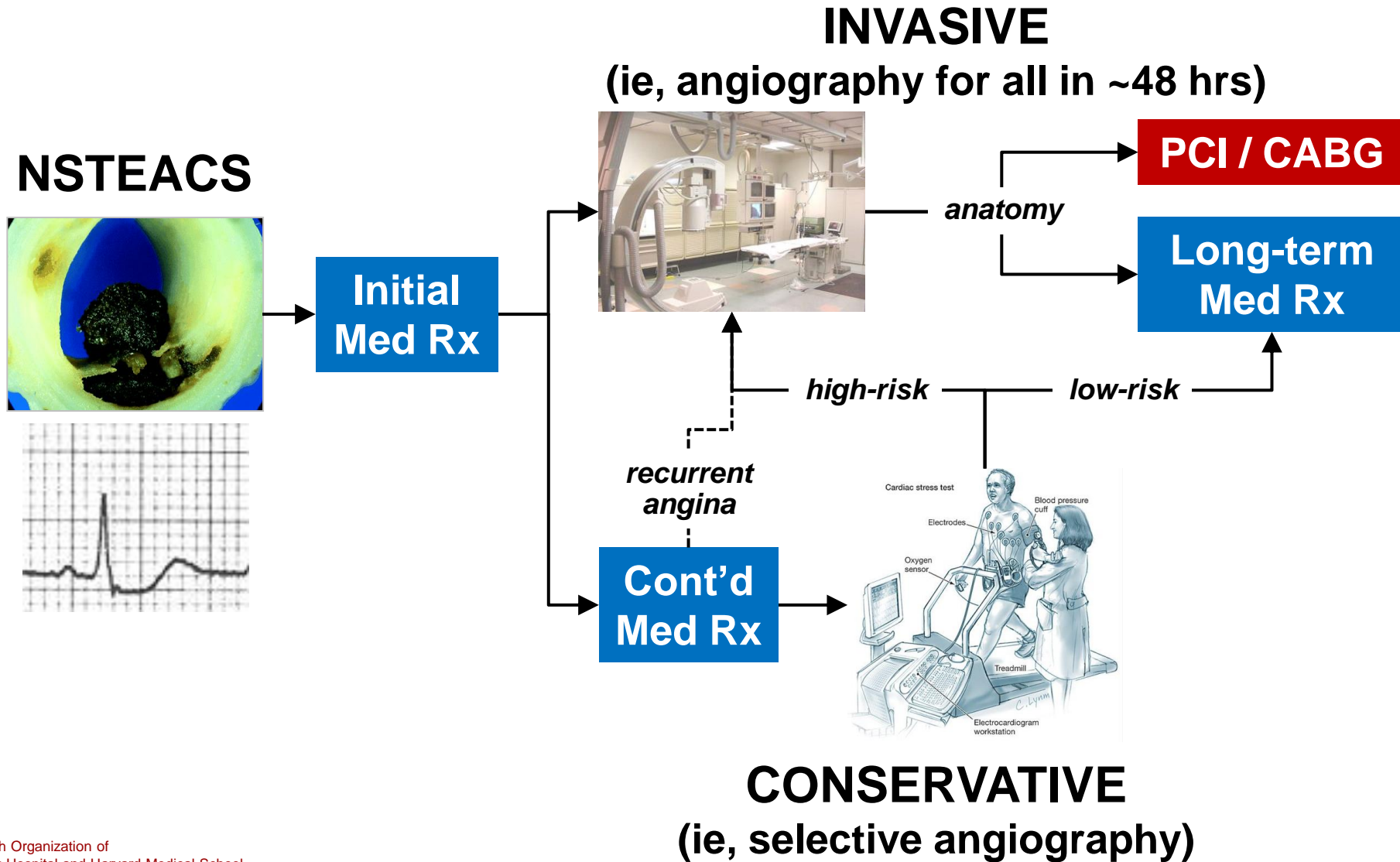
# Cardiogenic Shock in STEMI

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





# Management Strategy in NSTEMIACS





# Which NSTEACS Go to the Cath Lab?

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## Case #3

**72 yo F p/w chest pain that started 3 hours ago.**

**ECG shows inferior ST segment depressions. Troponin elevated.**

**Now chest pain free and ECG normalized.**

- A. Stress test now
- B. Stress test in 48 hours
- C. Cath immediately
- D. Cath within 24 hours
- E. Cath within 72 hours





# Which NSTEACS Go to the Cath Lab?

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## Case #3

72 yo F p/w chest pain that started 3 hours ago.

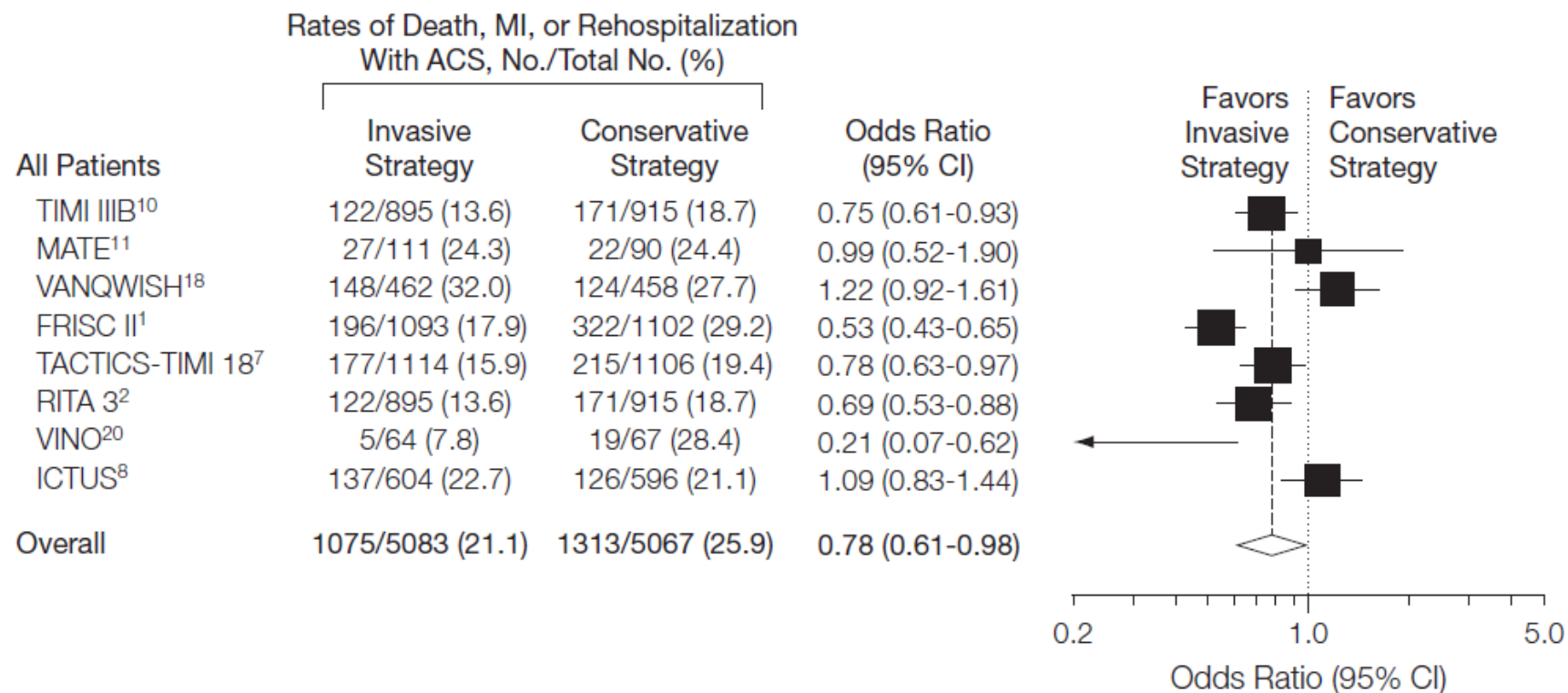
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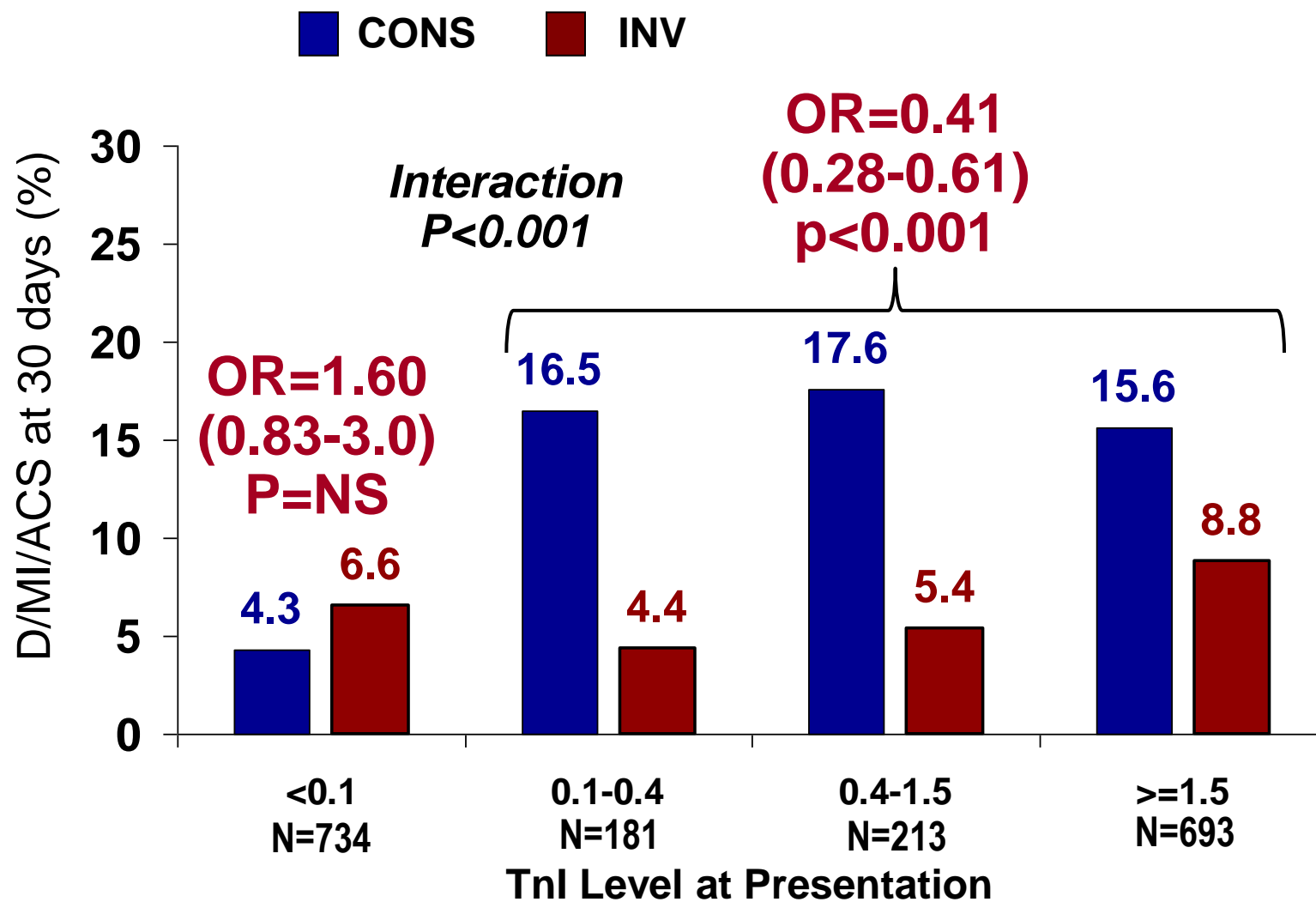
# Benefit of INV vs CONS Strategy



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



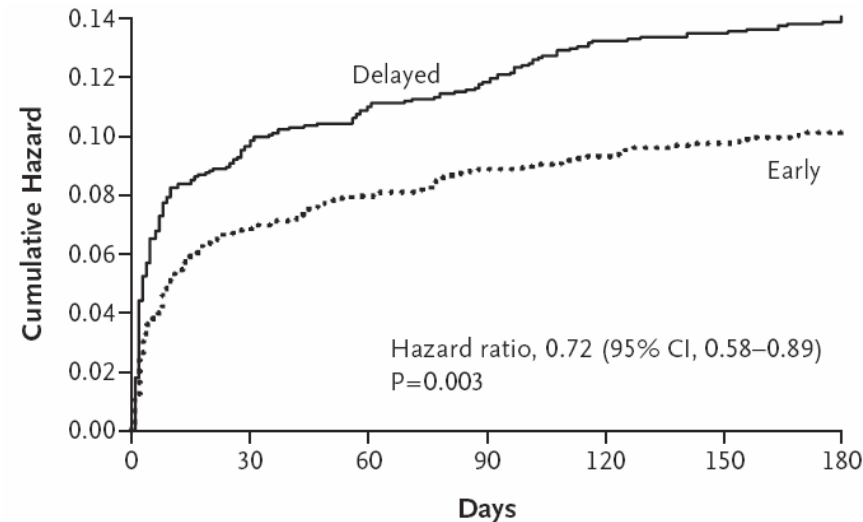
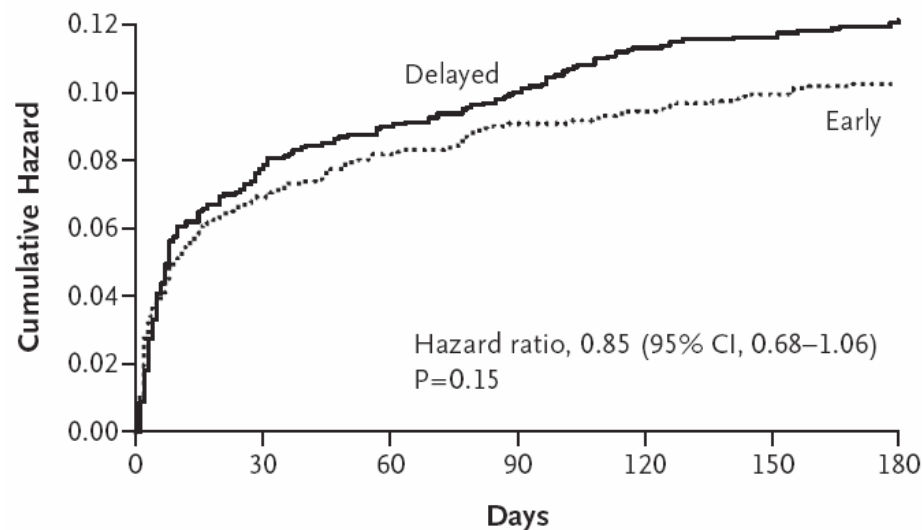
# Troponin Treatment Interaction





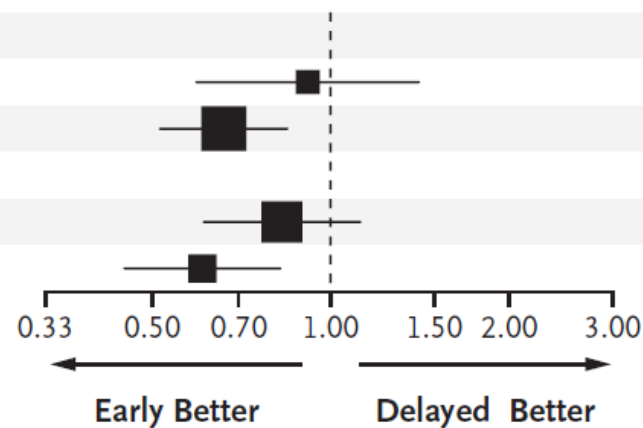
# Timing of Cath in NSTEMACS

**3031 Patients with NSTEMACS: 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)





# 2025 ACC/AHA NSTEACS Guidelines:

## Early Invasive

Unstable Patients	High- or Intermediate-Risk (based on TIMI Risk Score or GRACE Score)		Lower-Risk
Immediate Angio (w/in 2 h)	Early Invasive (w/in 24 h)	Delayed Invasive (w/in 25-72 h)	Routine or Selective Invasive
<ul style="list-style-type: none"><li>• Cardiogenic shock</li><li>• Signs or symptoms of HF or new or worsening MR</li><li>• Refractory angina</li><li>• Hemodynamic or electrical instability</li></ul>	<ul style="list-style-type: none"><li>• GRACE score &gt;140</li><li>• Steeply rising Tn</li><li>• Ongoing ST-segment Δs</li></ul>	<ul style="list-style-type: none"><li>• GRACE score 109-140</li><li>• Stable or downtrending Tn</li><li>• Absence of ongoing ischemic sx</li></ul>	<ul style="list-style-type: none"><li>• TIMI Risk Score 0-1</li><li>• GRACE score &lt;109</li><li>• Tn negative</li><li>• No ECG Δs</li></ul>

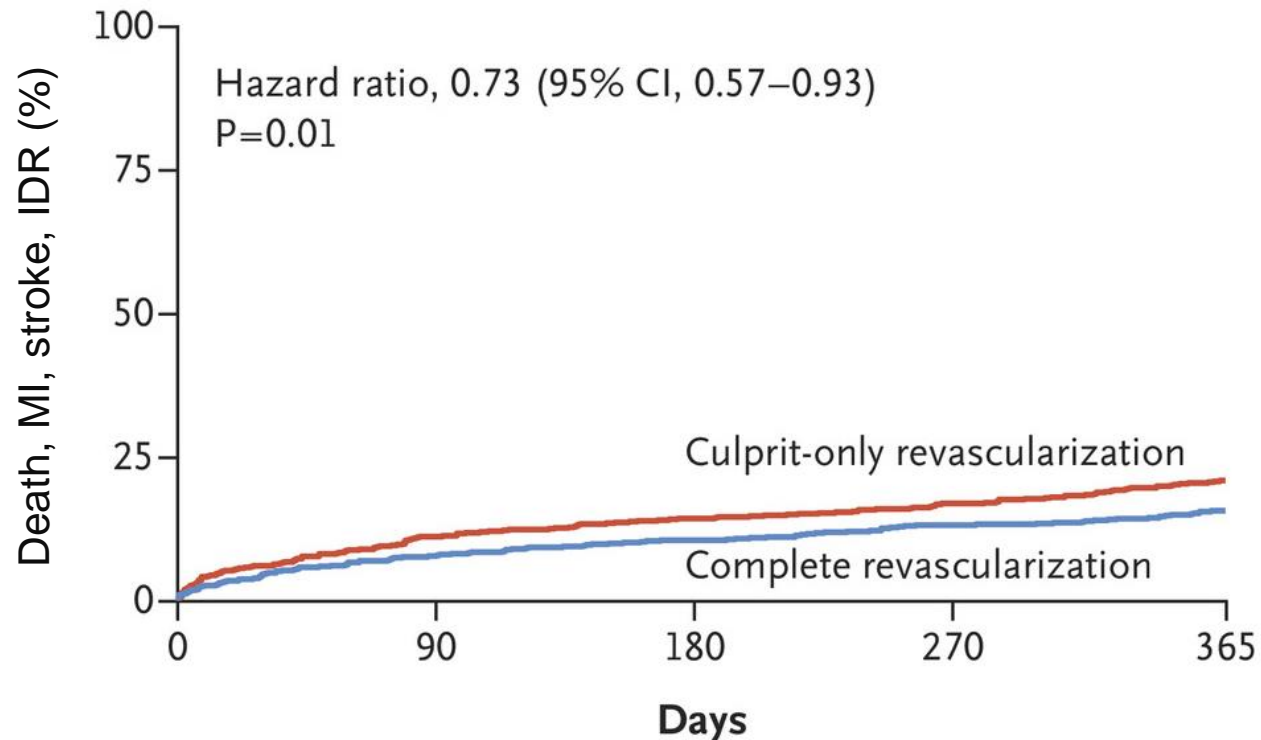




# Complete Revasc in MI

**FIRE: 1445 Older Pts w/ MI (65% NSTEMI) + MVD**

*Physiology-guided complete revasc vs. culprit-only*



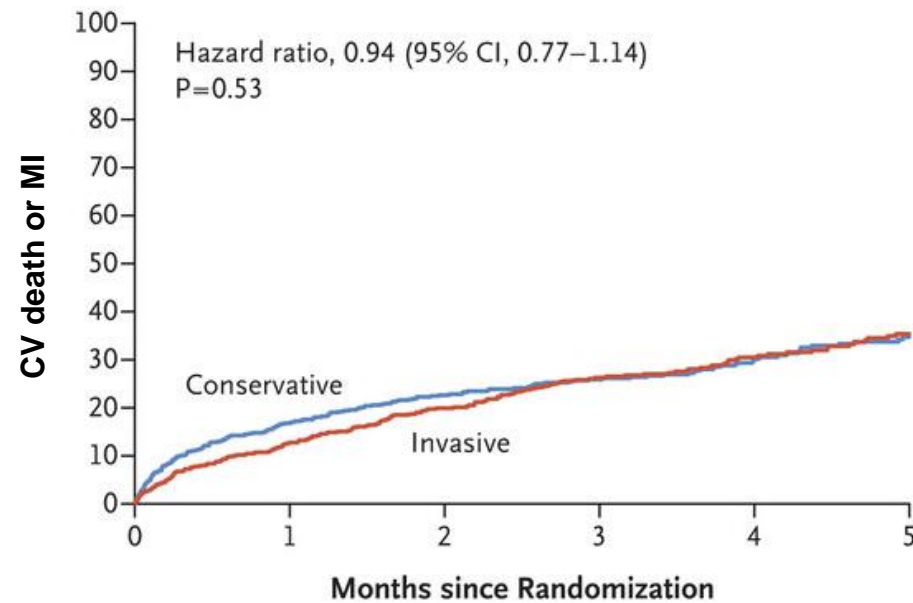
End Point	Complete	Culprit-Only	HR (95% CI)
Primary EP	15.7	21.0	0.73 (0.57-0.93)
Death	9.2	12.8	0.70 (0.51-0.96)
MI	4.4	7.0	0.62 (0.40-0.97)
Stroke	1.7	1.0	1.73 (0.68-4.40)
IDR	4.3	6.8	0.63 (0.40-0.98)

IDR, ischemia-driven revascularization



# INV vs CONS in Elderly

***SENIOR-RITA: INV vs. CONS in 1518 Pts  $\geq 75$  yrs (mean 82 yrs) w/ NSTEMI***





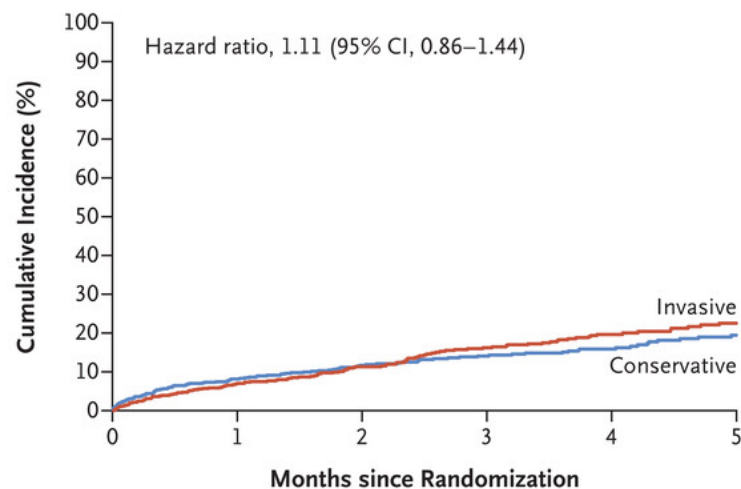


# INV vs CONS in Elderly

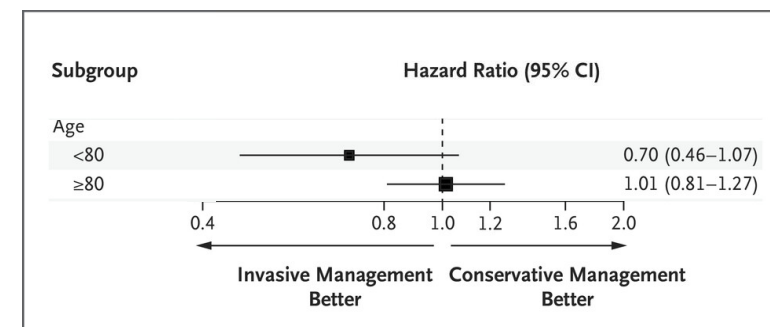
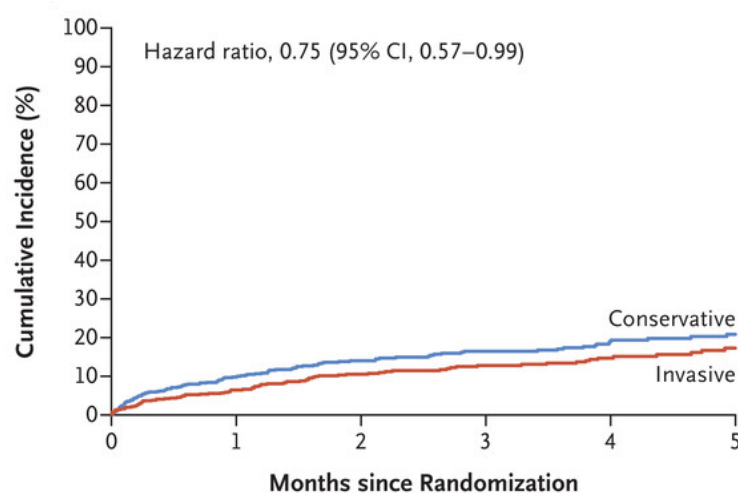
**SENIOR-RITA: INV vs. CONS in 1518 Pts  $\geq 75$  yrs (mean 82 yrs) w/ NSTEMI**

**Revasc in 50% of INV arm (60-75% in other trials)**

## CV Death



## MI



**Procedural complications in <1%**



# Antithrombotic Therapy

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## Case #4

**65 yo M p/w chest pain that started 2 hours ago.**

**ECG shows anterior ST segment depressions. Troponin elevated.**

**He has received aspirin. Plan is for coronary angiography in next 24 hrs.**

**What other antiplatelet therapy should he get?**

- A. Clopidogrel at time of PCI
- B. Prasugrel now
- C. Ticagrelor now or at time of PCI
- D. Cangrelor now
- E. Eptifibatide now



# Antithrombotic Therapy

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# Antiplatelet Therapy Acutely

- ***Start with aspirin***
- ***Almost always add: P2Y<sub>12</sub> inhibitor***
  - Oral agents: **ticagrelor & prasugrel** more potent and preferred over clopidogrel because reduce risk of ischemic events (but more bleeding); prasugrel if anatomy defined and not if prior stroke
  - No clear benefit for starting before PCI, and more bleeding
  - IV agent: cangrelor (fast on & off); can give at time of PCI in P2Y<sub>12</sub>-naïve Pts
- ***Sometimes also add (typically in cath lab): glycoprotein IIb/IIIa inhibitors (eg, abciximab, eptifibatide, tirofiban)***



# 2025 ACC/AHA NSTEACS Guidelines: P2Y<sub>12</sub> Inhibitors

<b>Management strategy</b>	<b>Recommendation</b>	<b>COR</b>	<b>LOE</b>
<b>Invasive</b>	Ticagrelor (180 mg loading dose → 90 mg/bid) or Prasugrel (60 mg loading dose → 10 mg/d)	1	B
	If time to angio anticipated to be >24 hrs, upstream Rx with ticagrelor or clopidogrel may be considered	2b	B
<b>Conservative</b>	Ticagrelor (180 mg loading dose → 90 mg/bid)	1	B
<b>Either</b>	Clopidogrel 300-600 mg load (latter preferred before PCI) → 75 mg/d when ticagrelor or prasugrel are unavailable, cannot be tolerated or are contraindicated	1	B
<b>Either</b>	Prasugrel should not be given if prior stroke or TIA	III: Harm	B



# Anticoagulants in NSTEMACS

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- **INVASIVE STRATEGY**

- **UFH**
- Bivalirudin (to reduce bleeding)
- Enoxaparin (LMWH)
- *Discontinue after uncomplicated PCI*

- **CONSERVATIVE STRATEGY**

- **Enoxaparin** (LMWH) or fondaparinux (*Rx until end of hosp, up to 8 days*)
- UFH (*Rx for 48 hrs*)



# Long-Term Antithrombotic Therapy

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## Case #5

65 yo M p/w NSTEMI.

Drug-eluting stent placed in LAD.

For his long-term anti-platelet regimen, you would recommend:

- A. ASA + P2Y<sub>12</sub> inhibitor for 30 days
- B. ASA + P2Y<sub>12</sub> inhibitor for 1 year
- C. ASA + P2Y<sub>12</sub> inhibitor for >1 year if low bleeding risk
- D. ASA + P2Y<sub>12</sub> inhibitor for 3 months and then P2Y<sub>12</sub> inhib. monoRx





# Long-Term Antithrombotic Therapy

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# Long-Term Antithrombotic Therapy

## What if ...

65 yo M p/w NSTEMI. **History of prior MI and diabetes.**

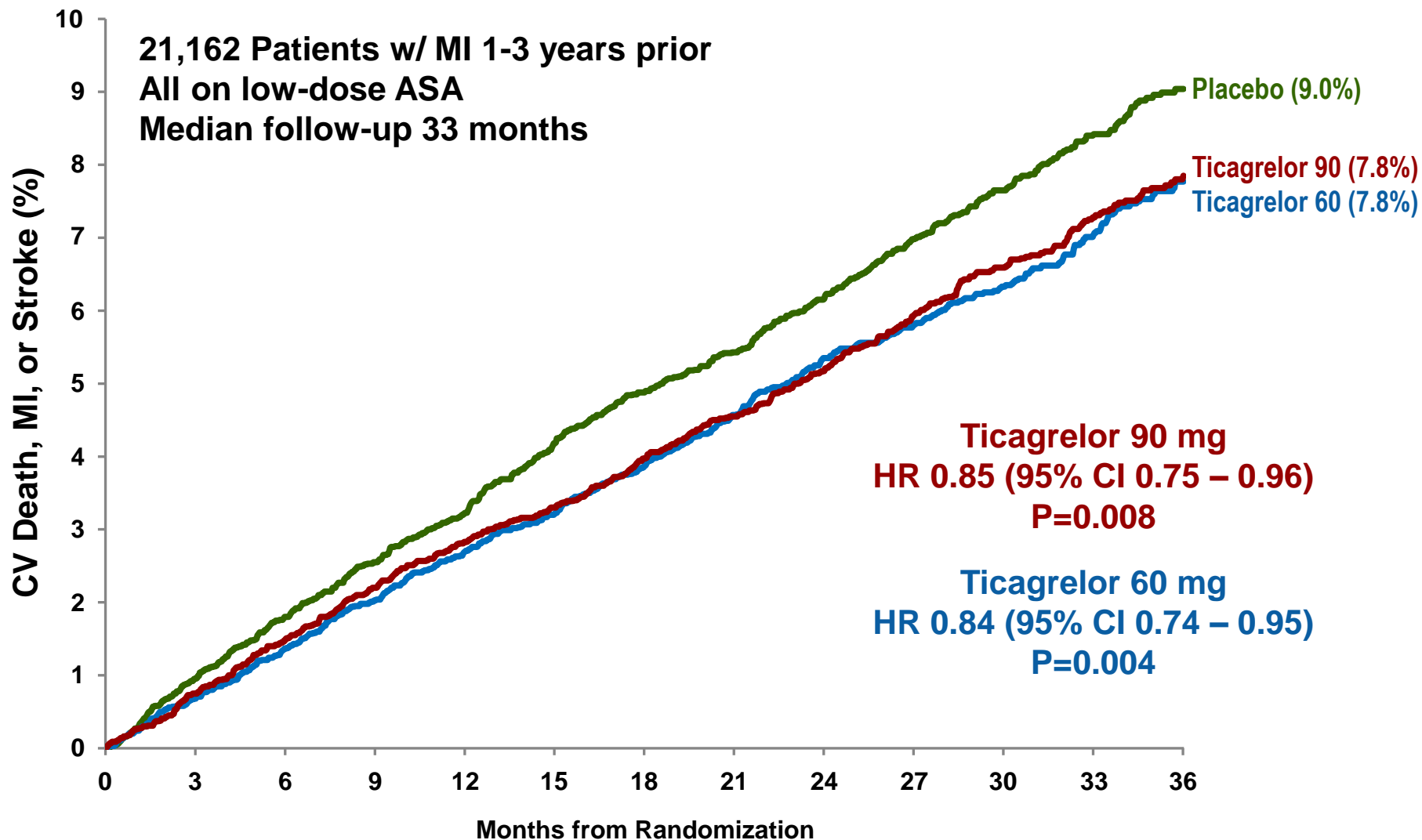
Drug-eluting stent placed in LAD. **Also has non-obstructive disease in LCx & RCA.**

For his long-term anti-platelet regimen, you would recommend:

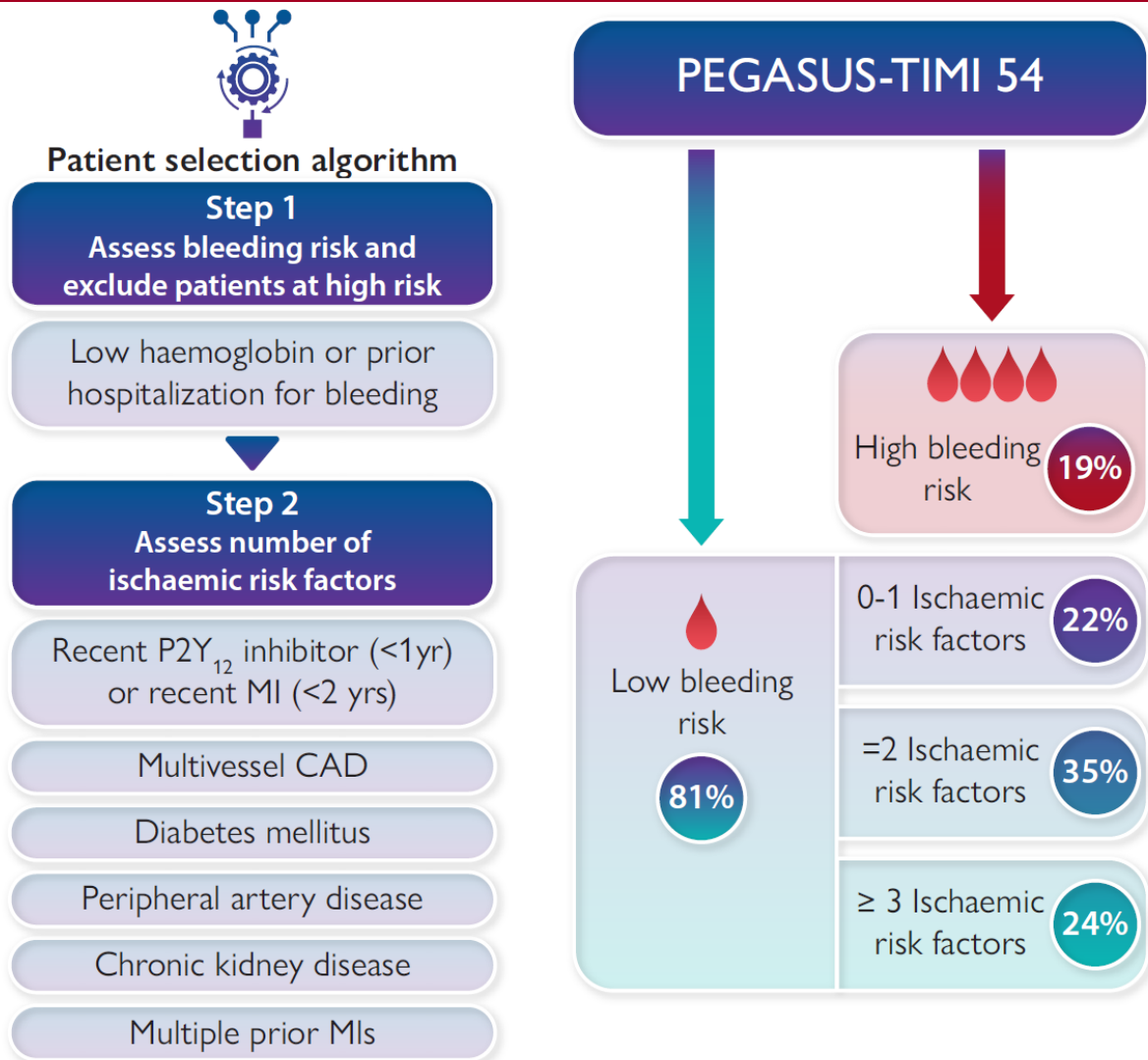
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# Ticagrelor in Patients w/ Prior MI

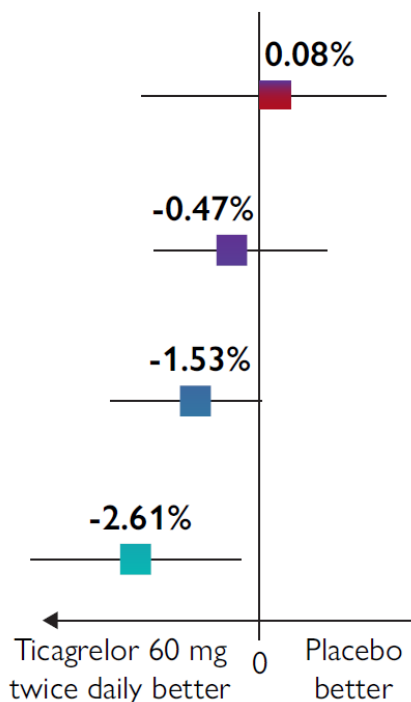


# Risk Stratification



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

(P-trend 0.076)





# Long-Term Antithrombotic Therapy

## What if ...

65 yo M p/w NSTEMI. ~~History of prior MI and diabetes.~~ **History of prior GI bleed.**

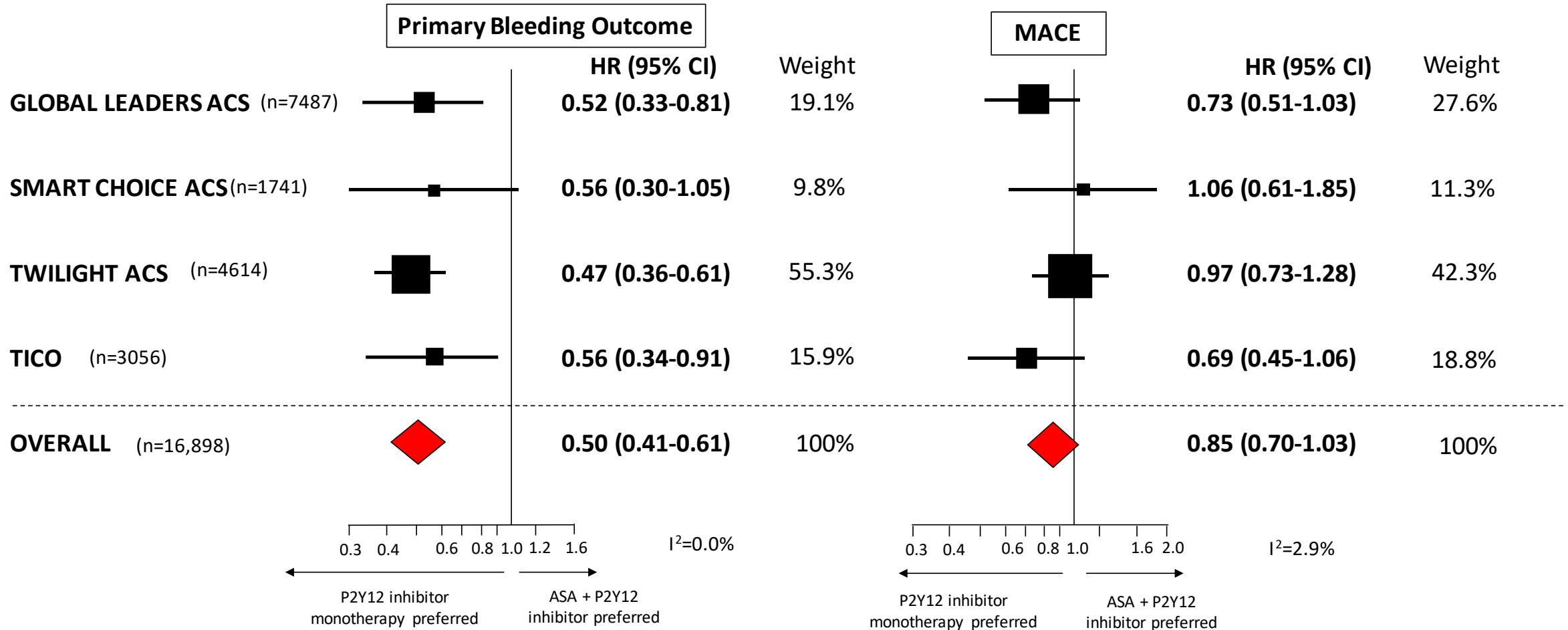
Drug-eluting stent placed in LAD. ~~Also has non-obstructive disease in LCx & RCA.~~

For his long-term anti-platelet regimen, you would recommend:

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- D. ASA + P2Y<sub>12</sub> inhibitor for 3 months and then P2Y<sub>12</sub> inhib. monoRx



# Drop Aspirin after 1-3 Months (ie, P2Y<sub>12</sub> MonoRx)?





# Long-term Antiplatelet Rx

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- Start with DAPT ASA + P2Y<sub>12</sub> inhibitor (ticag or prasugrel preferred)
- For most patients: continue for 12 mos
- In Pts on ASA + ticagrelor, dropping ASA after ≥1 mo ↓ bleeding risk
- If high GIB risk, add PPI
- If very high bleeding risk, consider clopidogrel (✓ *CYP2C19*) over ticag or prasugrel and drop ASA after ≥1 mo
- If low bleeding risk & high ischemic risk (and tolerated DAPT well to date), may consider continuing ASA + P2Y<sub>12</sub> inhibitor beyond 12 mos





# Triple Therapy

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## Case #6

**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 is the best long-term regimen:**

- A. Warfarin (INR 2-3), aspirin and ticagrelor
- B. Full dose DOAC, aspirin, and clopidogrel
- C. Full dose DOAC and clopidogrel
- D. Reduced dose DOAC and clopidogrel





# Triple Therapy

---

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- B. Full dose DOAC, aspirin, and clopidogrel
- C. Full dose DOAC and clopidogrel**
- D. Reduced dose NOAC and clopidogrel



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

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- High rate of bleeding with triple Rx (ASA + P2Y<sub>12</sub> + OAC)
- DOAC preferred over warfarin because less bleeding (no head-to-head, but apixaban w/ best data vs. VKA)
- Would not ↓ DOAC dose b/c may not adequately protect against stroke
- In terms of antiplt, start w/ DAPT: ASA + P2Y<sub>12</sub> inhibitor (clopidogrel)
- Drop ASA at hospital d/c or, if high ischemic risk, after 1 month
- Consider dropping P2Y<sub>12</sub> inhib after 6-12 mos, depending on bleeding risk



# Lipid-Lowering Therapy

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## Case #7

**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?**

- A. Target LDL-C reduction of 50%
- B. Target LDL-C of 70 mg/dL
- C. Add ezetimibe
- D. Add PCSK9 inhibitor
- E. Add ezetimibe and/or PCSK9i to get LDL-C <55 mg/dL



# Lipid-Lowering Therapy

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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.

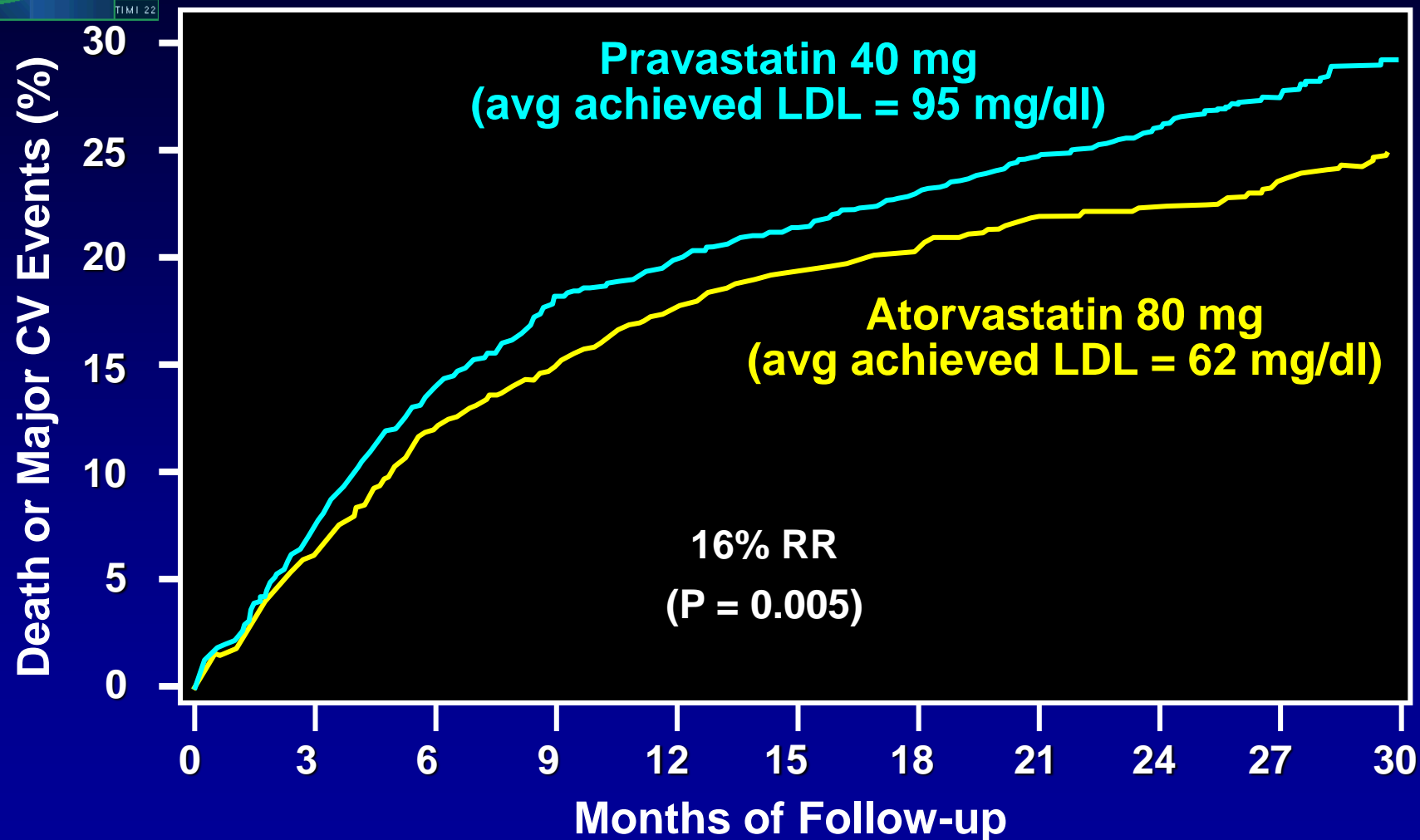
LDL-C on admission (not on any lipid-lowering Rx) was 180 mg/dL. Started on atorva 80 mg. What else would you recommend?

- A. Target LDL-C reduction of 50%
- B. Target LDL-C of 70 mg/dL
- C. Add ezetimibe
- D. Add PCSK9 inhibitor
- E. Add ezetimibe and/or PCSK9i to get LDL-C <55 mg/dL**



# PROVE IT – TIMI 22

4162 patients hospitalized w/in prior 10 d for ACS

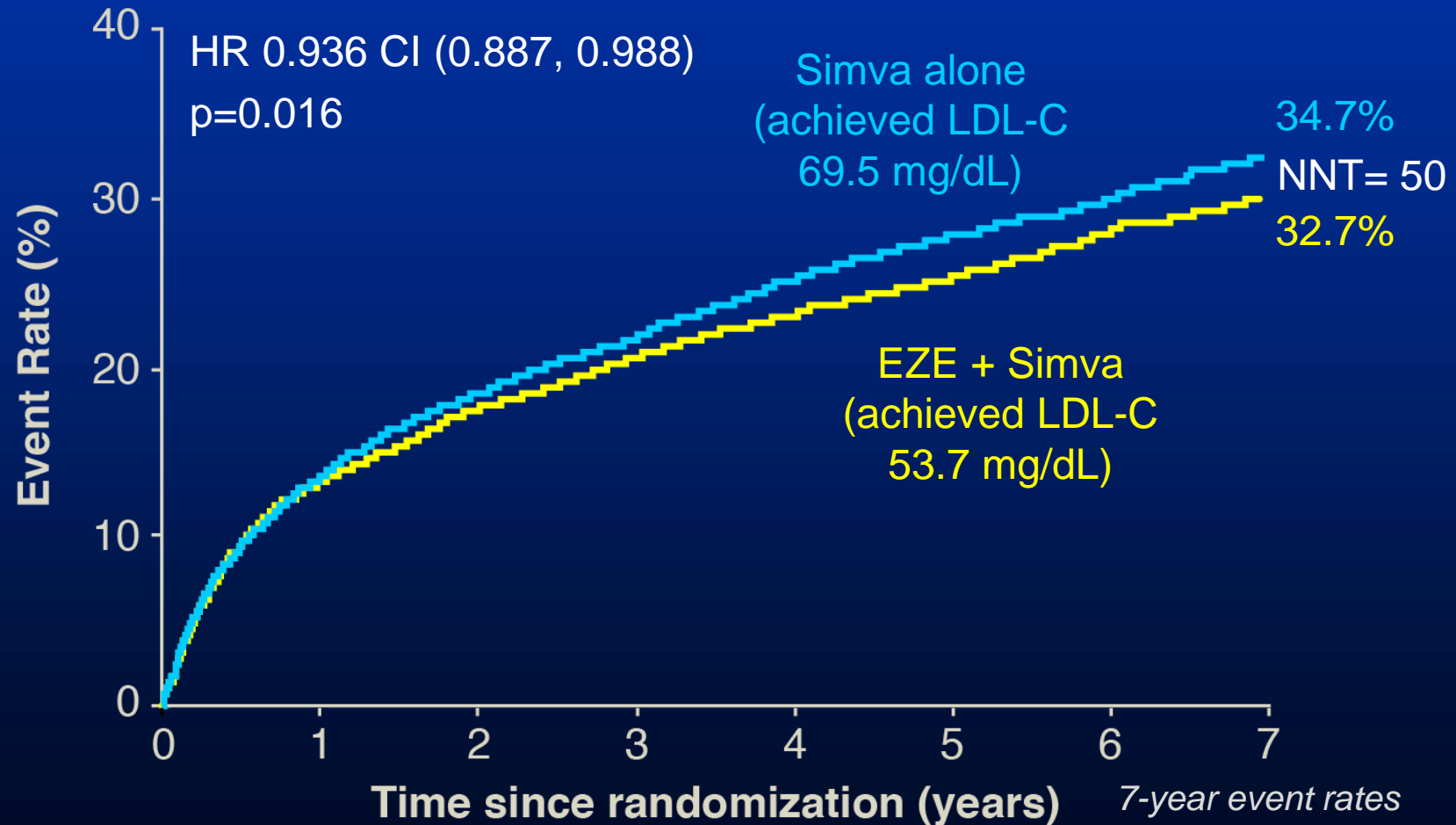


Cannon et al. *NEJM* 2003; 350: 1495

# Primary Endpoint — ITT



*Cardiovascular death, MI, documented unstable angina requiring rehospitalization, coronary revascularization ( $\geq 30$  days), or stroke*

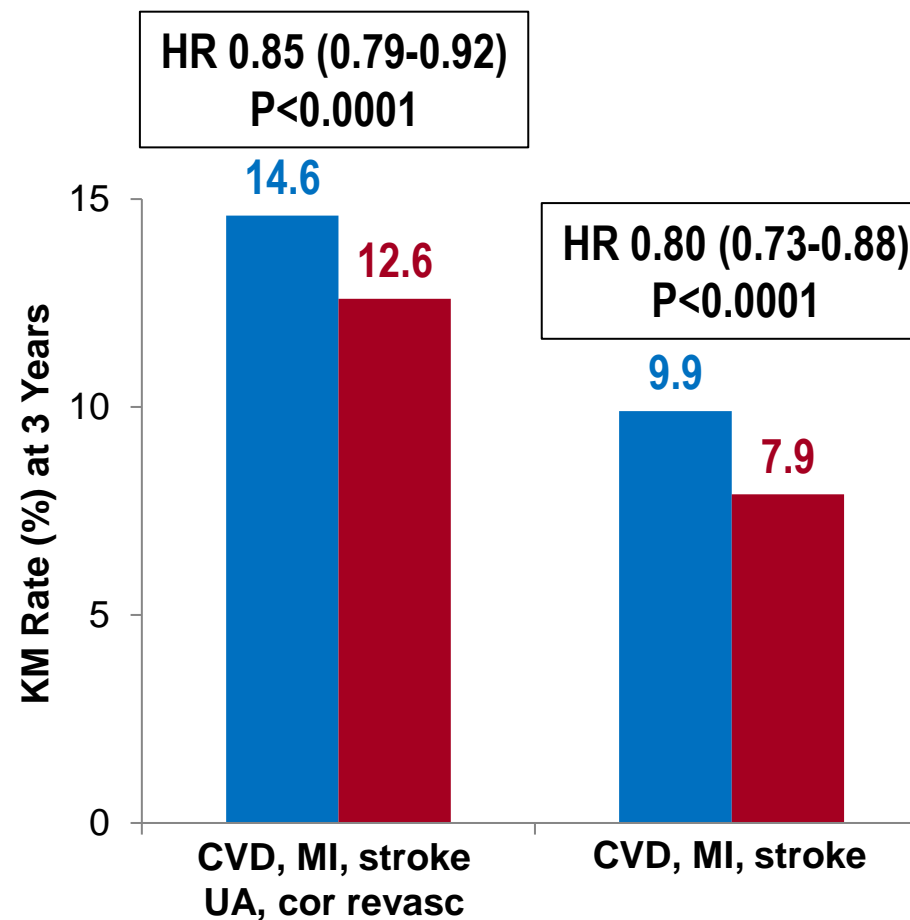
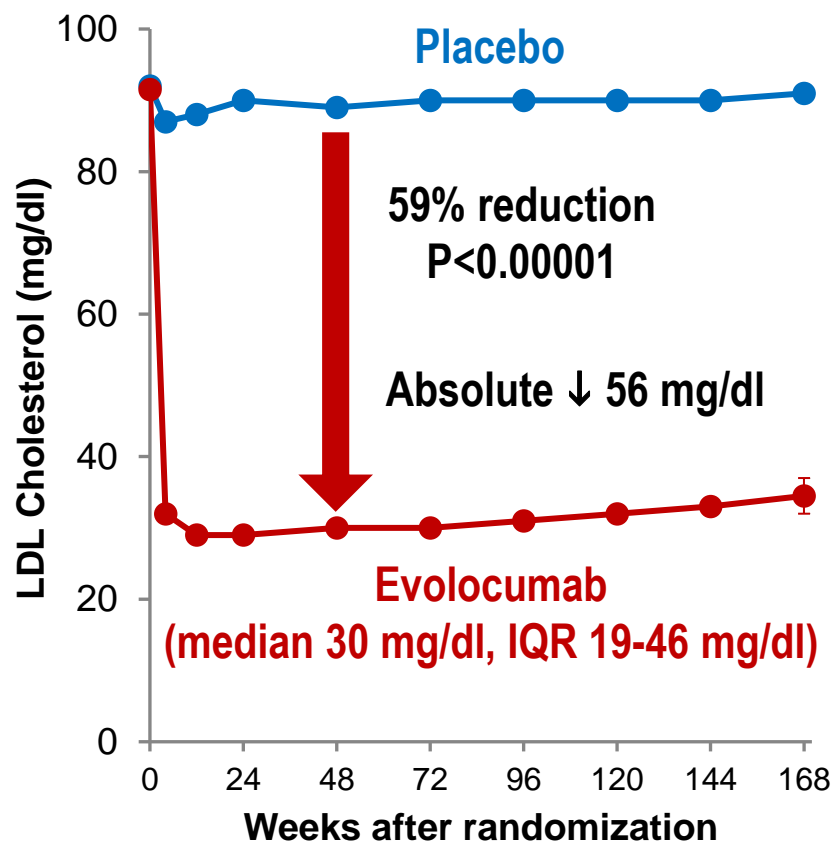




# Summary of Effects of PCSK9i Evolocumab

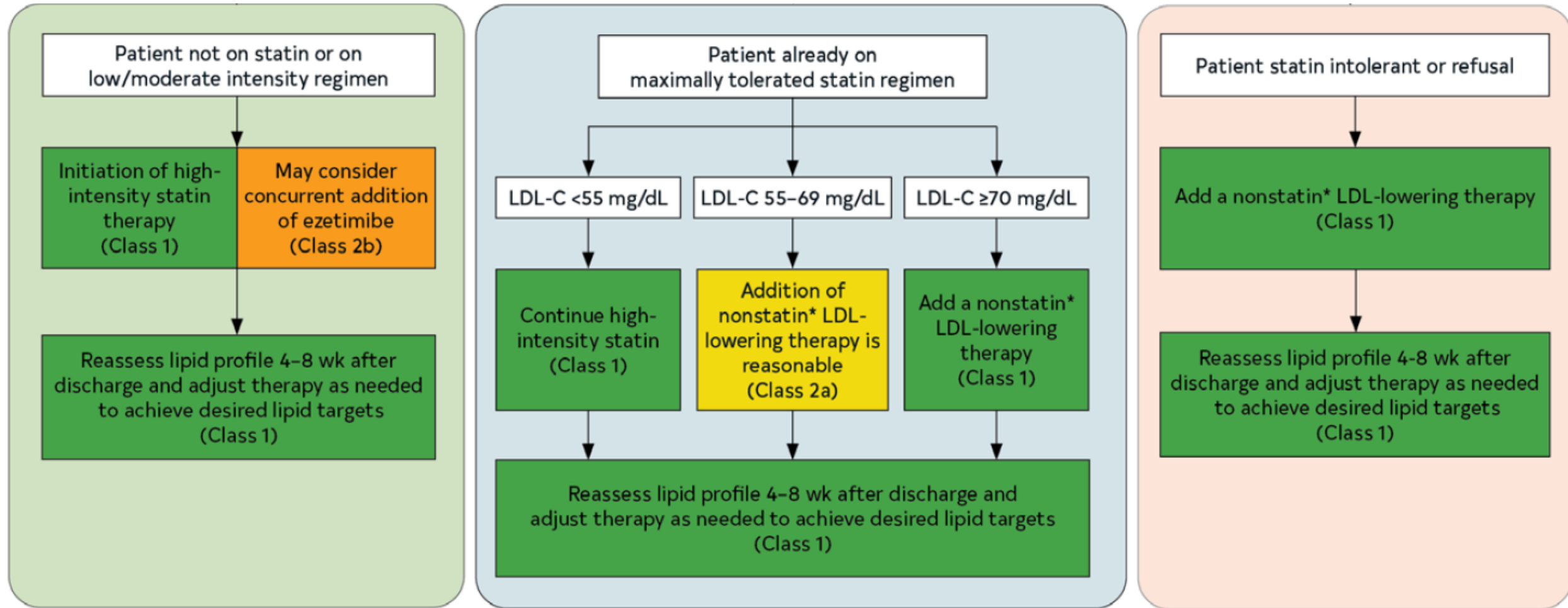


- ↓ LDL-C by 59% down to a median of 30 mg/dl
- ↓ CV outcomes in patients on statin
- Safe and well-tolerated





# Lipid Mgmt

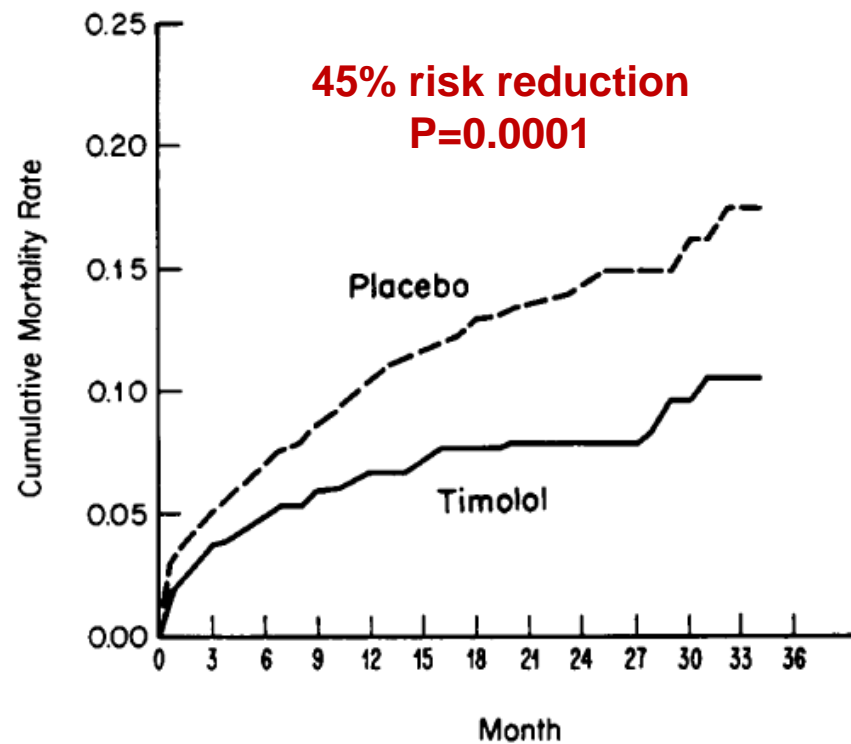






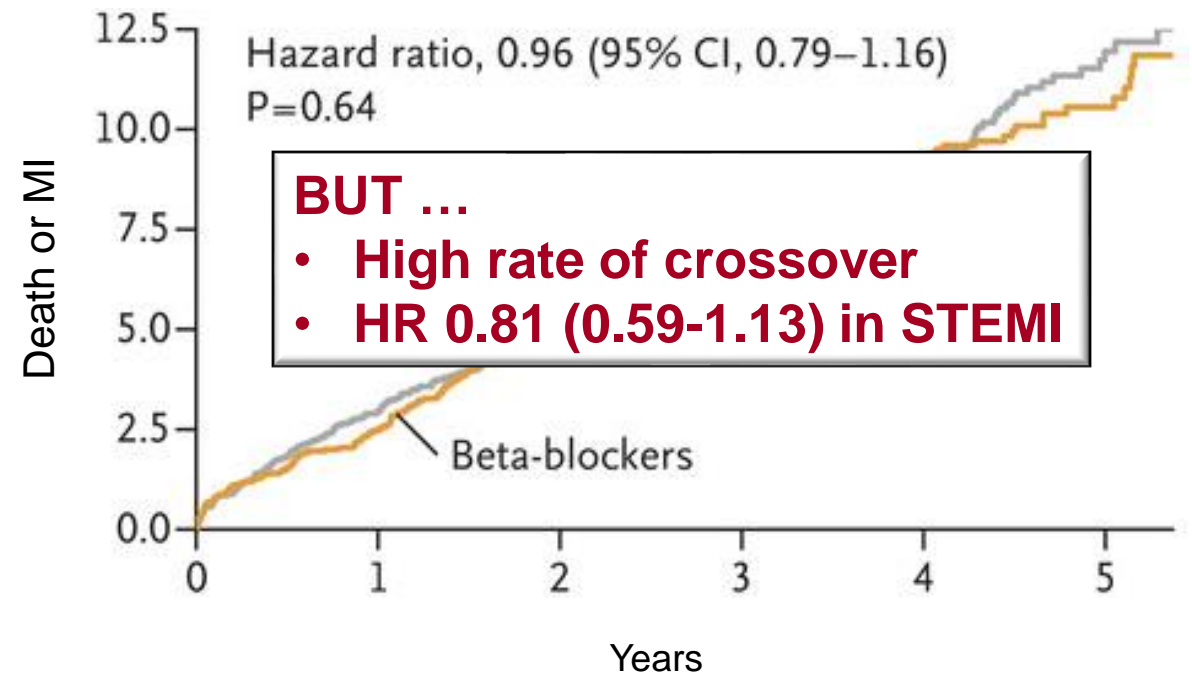
# $\beta$ -blockers

**1884 Patients 1-4 weeks after acute MI**  
**Randomized to  $\beta$ -blocker vs. placebo**



NEJM 1981;304:801

**5020 Patients 1-7 days after acute MI w/ nl LVEF**  
**Randomized to  $\beta$ -blocker vs. placebo**



NEJM 2024;390:1372



# ACEI/ARB, MRA

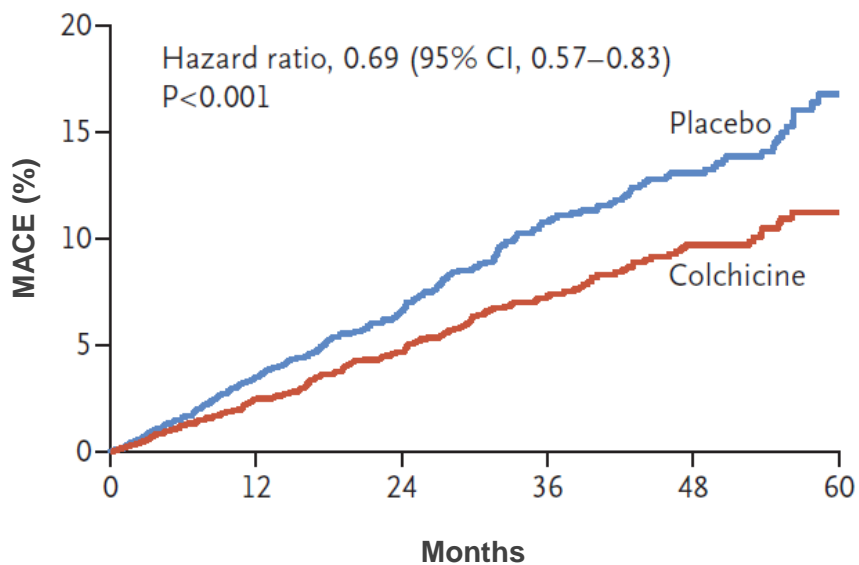
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- **ACEI (or ARB if cannot tolerate ACEI)**
  - LVEF <40%, *or*
  - HTN, diabetes, or stable CKD
- **MRA**
  - If on ACEI/ARB & BB; *and*
  - Cr  $\leq$ 2-2.5, K  $\leq$ 5; *and*
  - LVEF <40% and either clinical s/s of HF or diabetes

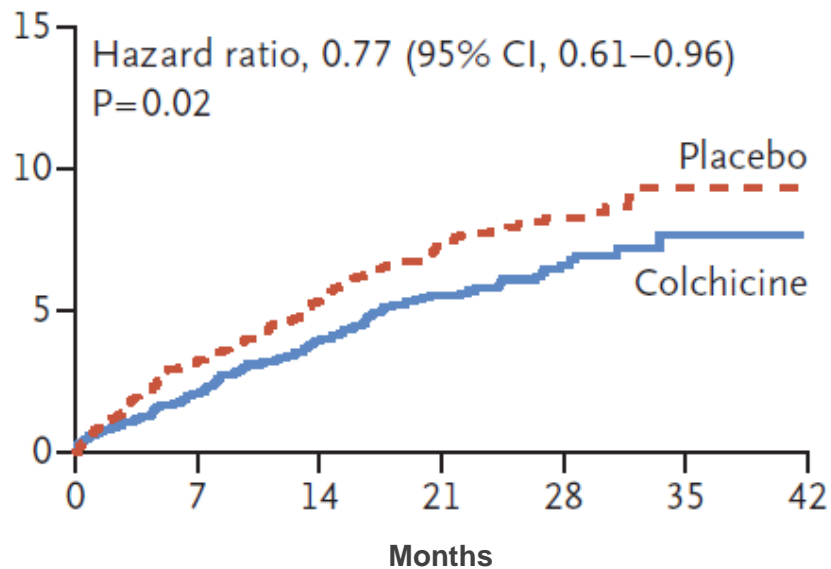


# Treating Inflammation: Colchicine?

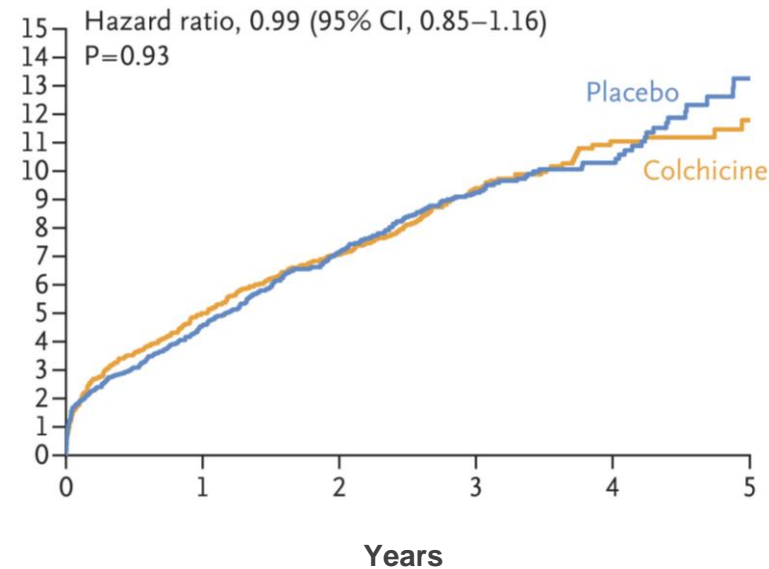
**LoDoCo2**  
5522 Pts w/ CCD



**COLCOT**  
4745 Pts w/in 30d of MI



**CLEAR**  
7062 Pts w/ AMI (>95% STE)





# Take Home Points

- **Diagnose ACS using H&P, 12-lead ECG, troponin**
- **For STEMI: select Primary PCI vs Lytic**
- **For NSTEMI-ACS: select Invasive (eg,  $\oplus$  Tn) vs. Conservative Strategy**
- **Anti-ischemic Rx: beta-blocker, nitrates**
- **Select Antiplatelet Regimen**
  - ASA
  - + P2Y<sub>12</sub> Inhibitor: ticagrelor, prasugrel (or clopidogrel); consider timing
- **Select Anticoagulant: UFH, LMWH, or bivalirudin**
- **Long-term therapy**
  - ASA (maybe drop after 3 mos), P2Y<sub>12</sub> inhibitor (at least 12 mos, if not longer)
  - ?  $\beta$ -blocker (if low LVEF or STEMI)
  - Statin  $\pm$  EZE  $\pm$  PCSK9i
  - ? ACEI, ? MRA





# Key References

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- **Collet et al. EHJ 2021;42:1289**
- **Rao et al. Circ 2025;epub**