

Acute Coronary Syndromes

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***Investigational, unlabeled and/or unapproved uses of drugs
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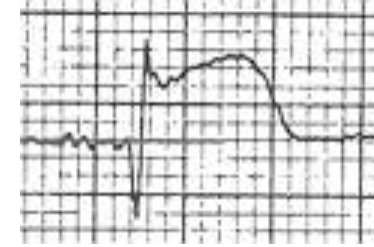
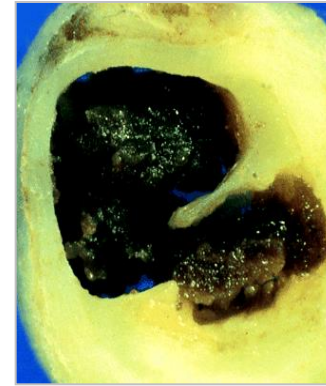
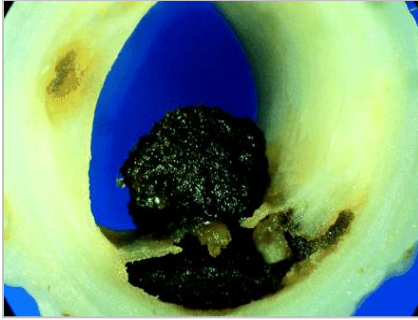




Objectives

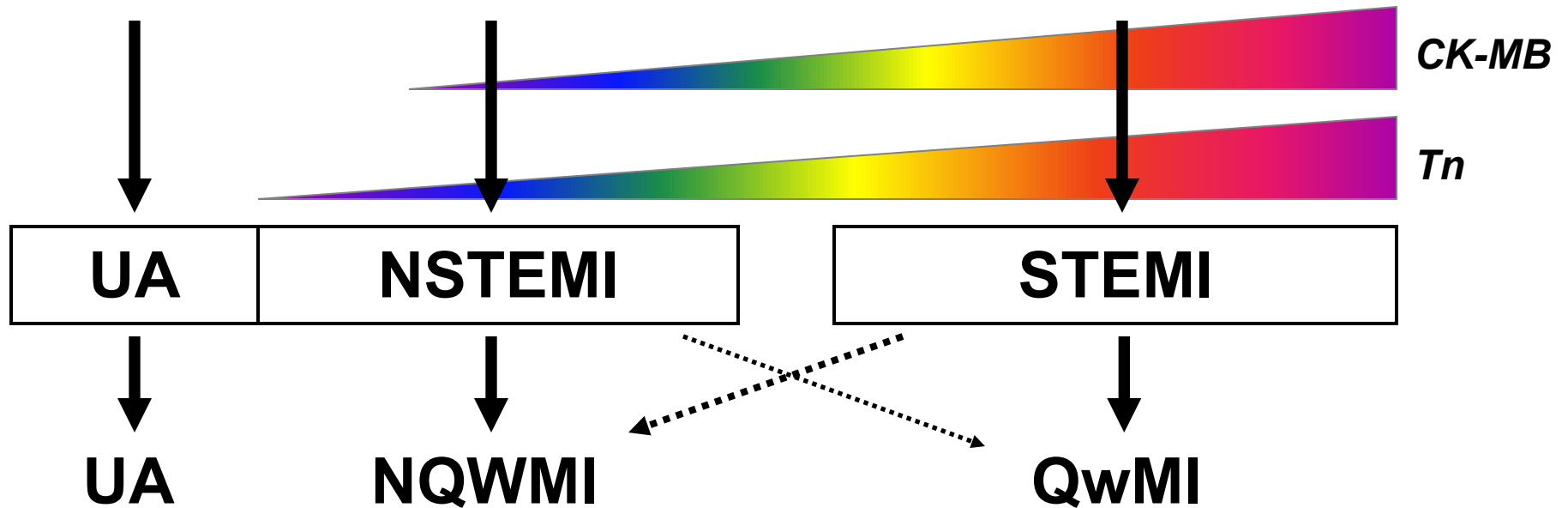
- **Understand how to diagnose ACS**
- **Understand how to treat patients with ACS**

ACUTE CORONARY SYNDROMES



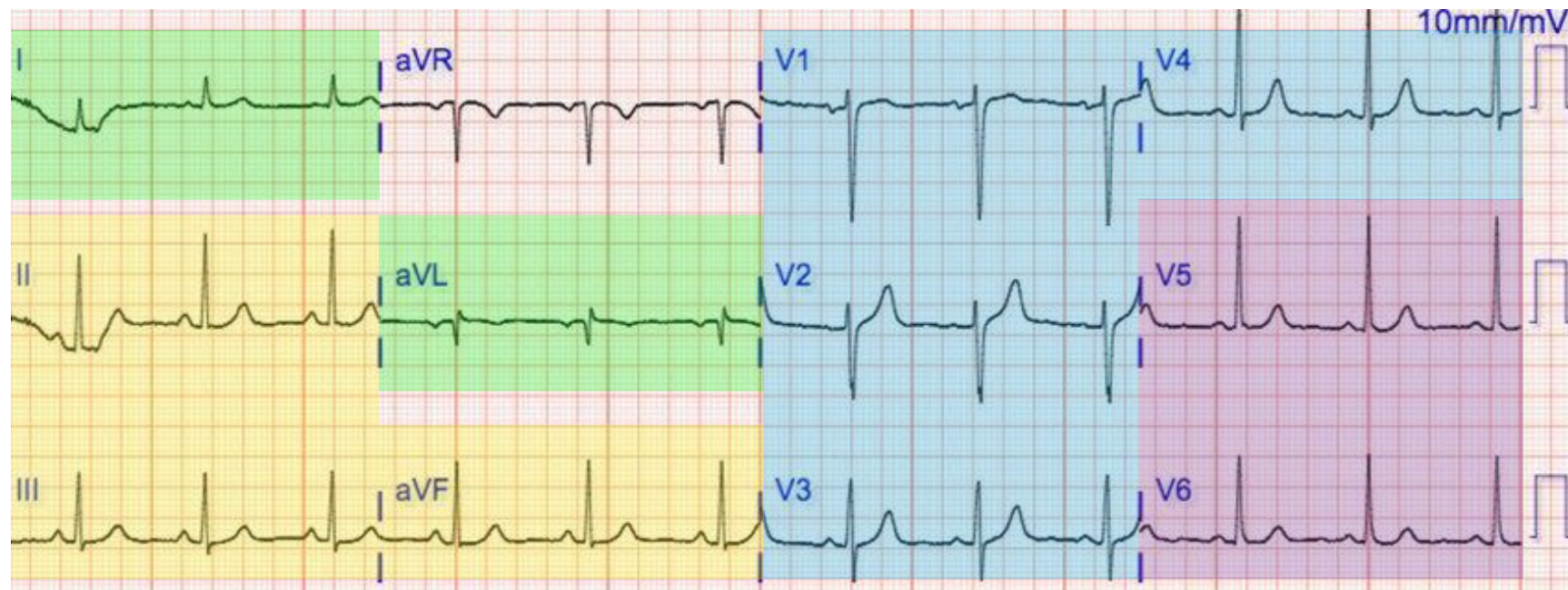
Non-ST elevation ACS

ST elevation ACS



ACS: ECG

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



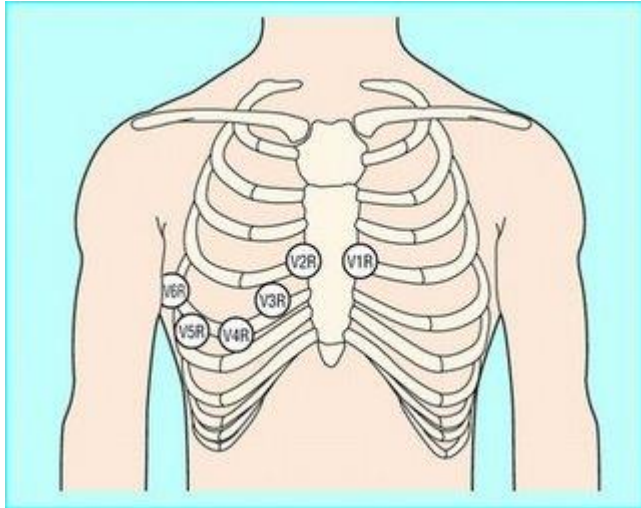


ACS: ECG

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

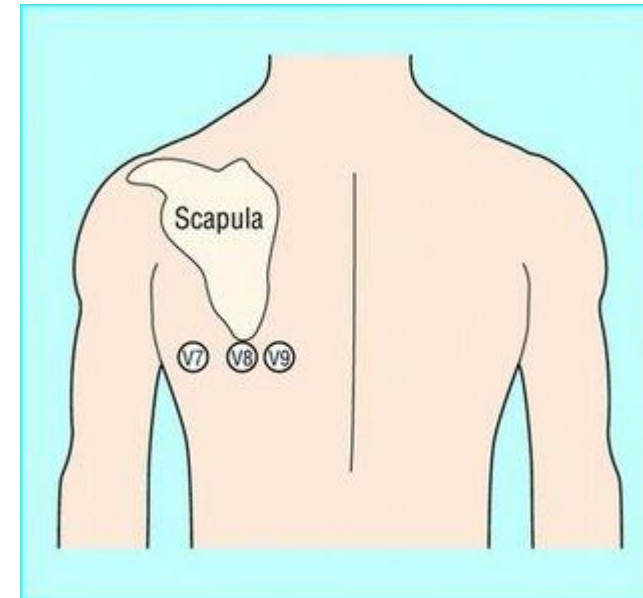
ECG Special Placement

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

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 <99th %ile and no change over time, discharge to home
- C. Check now and 3-6 hours after sx onset; if both <99th %ile, discharge to home



Ruling In & Ruling Out MI

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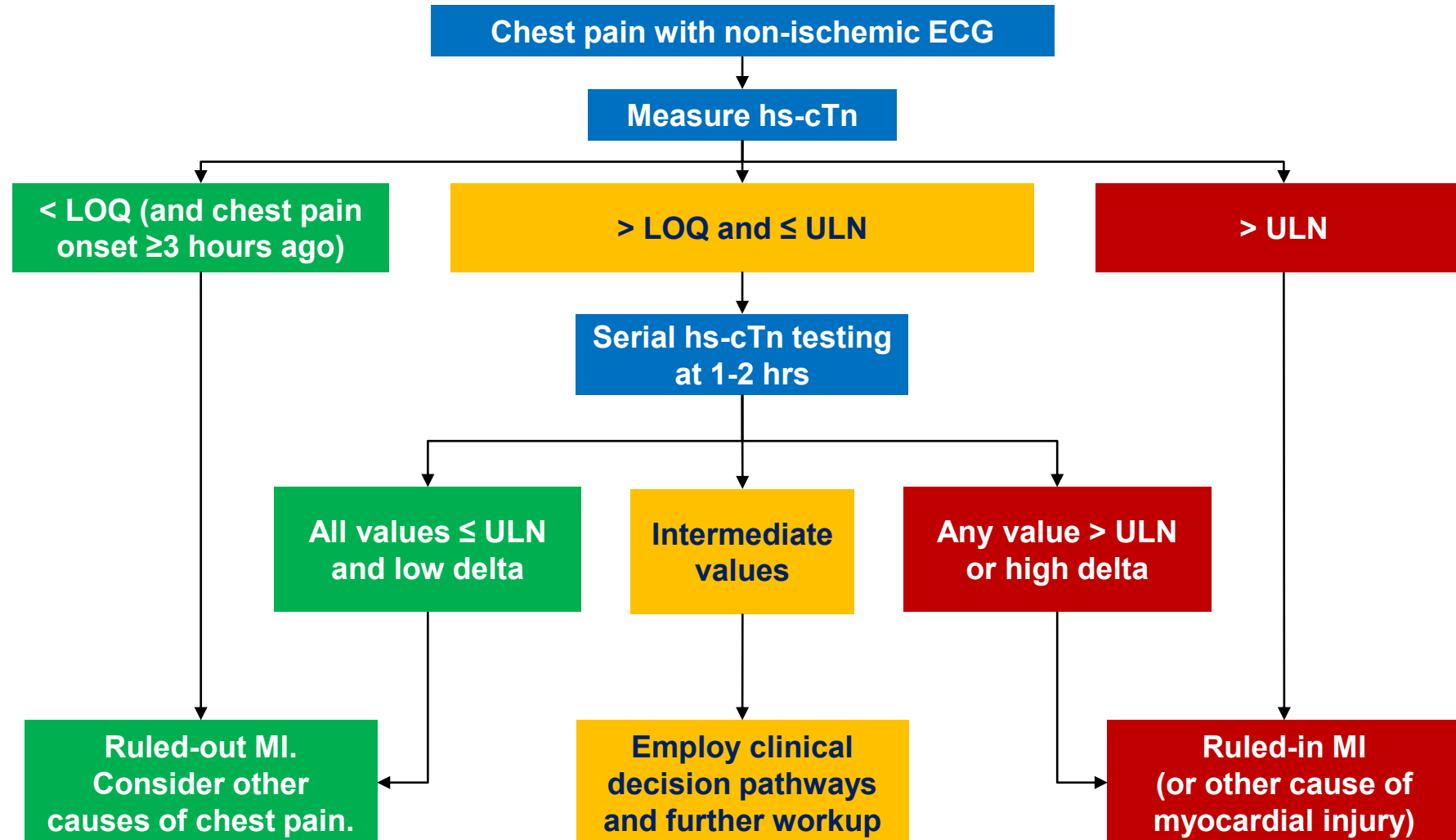
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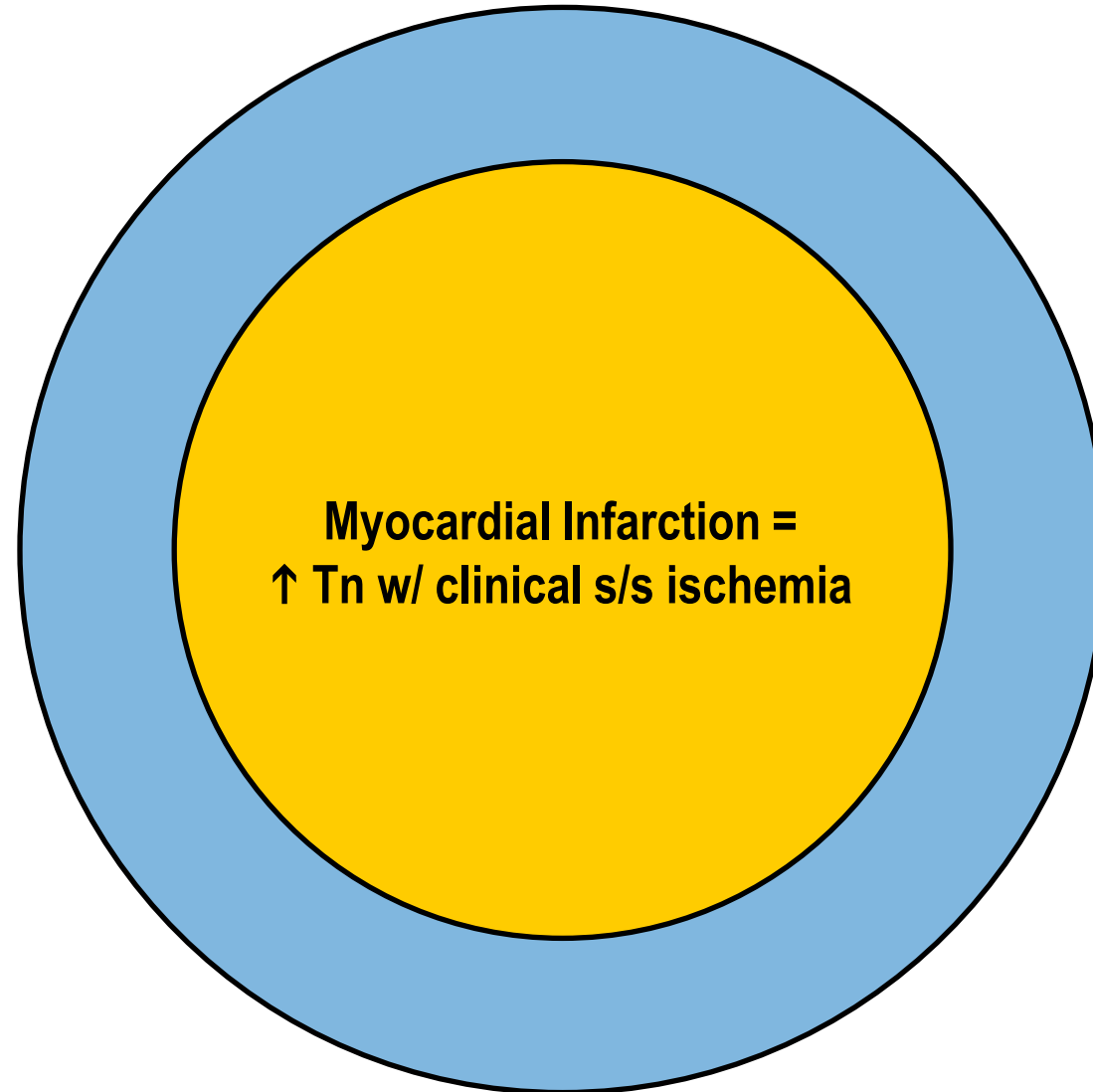


Troponin Testing Algorithm





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

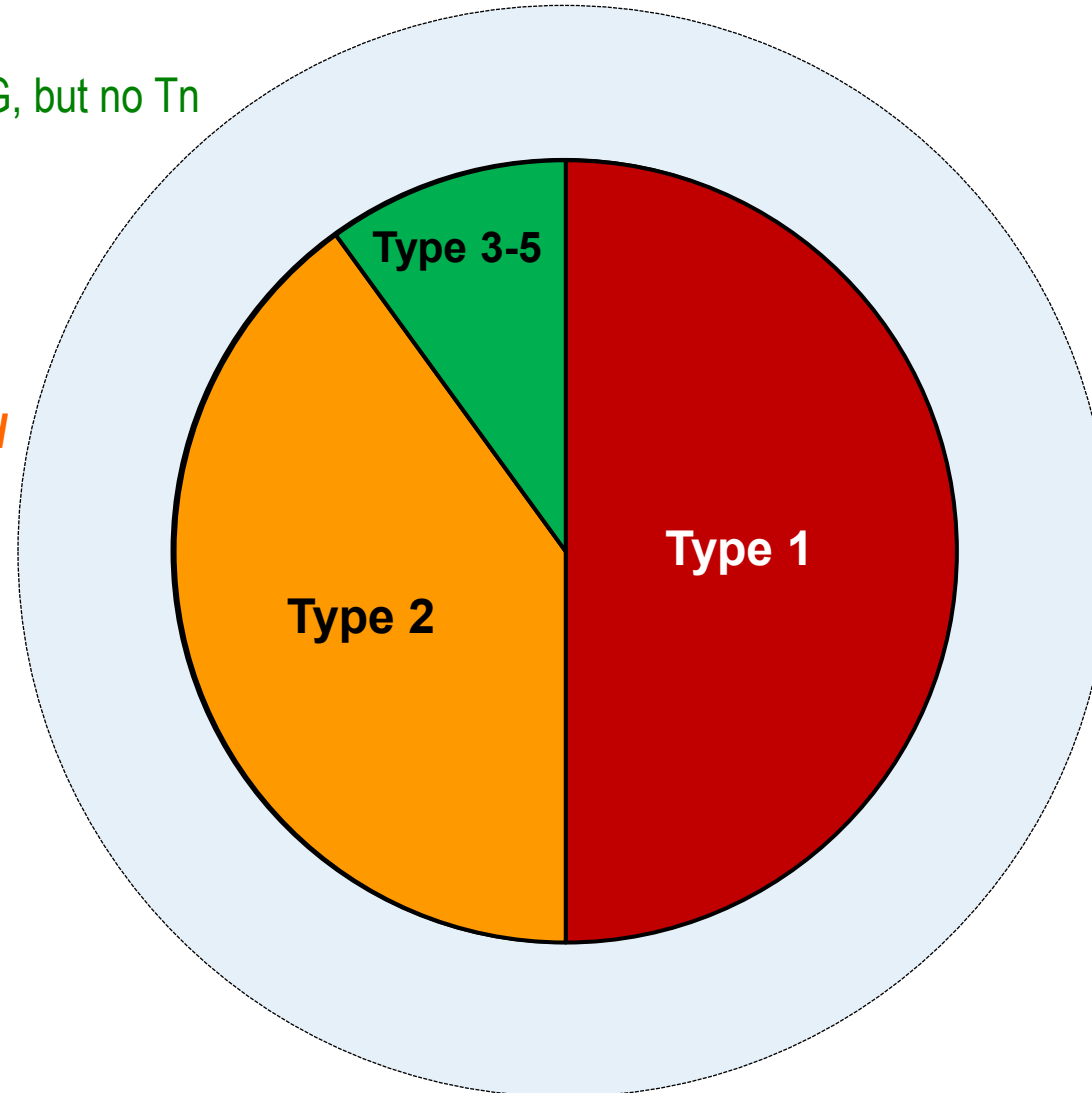
Type 2 MI = myocardial O₂ supply/demand imbalance *unrelated* to acute atherothrombosis

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



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
- **Morphine**
 - Pain, CHF, agitation; *don't* mask angina
- **Oxygen** (if hypoxemic)



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 time from 1st med contact to PCI anticipated ≤ 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

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 later during this hospitalization
- C. Stent the LAD & LCx lesions now



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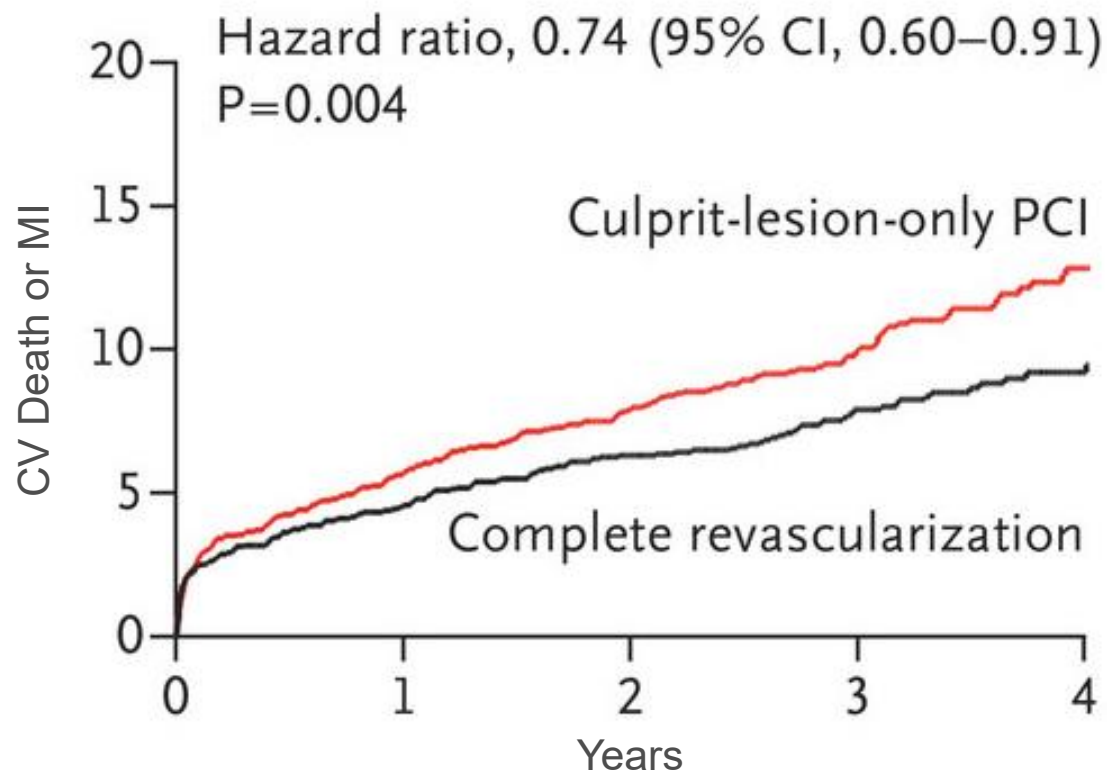
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Preventive PCI in STEMI

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

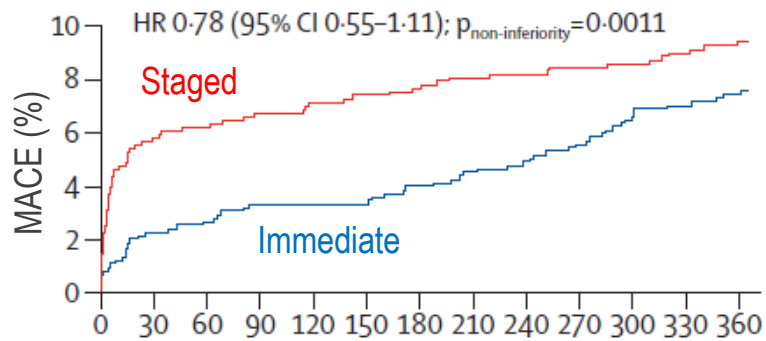




Timing of Complete Revascularization

BIOVASC

1525 STEMI (40%) or NSTEMI
Staged: 15 (4-28) d; 30% in-hosp

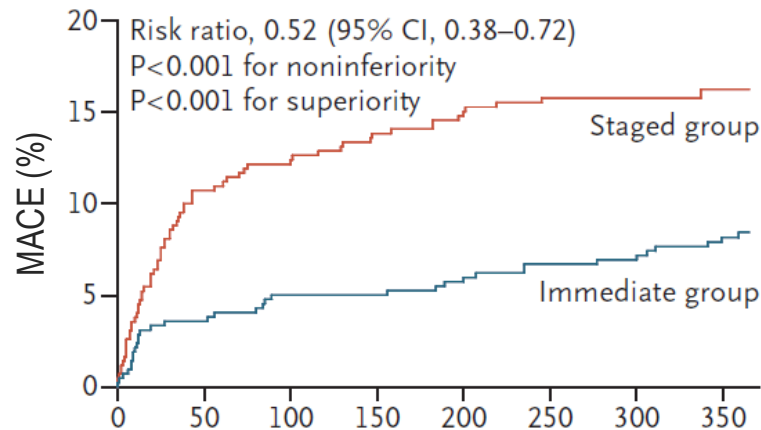


- Mostly driven by ↓ MI & unplanned ischemia-driven revasc
- At 30 days, MI rate 0.7% vs. 2.8%
- MI's in staged arm mostly spontaneous

Lancet 2023;401:1172-82

MULTISTARS

840 STEMI
Staged: 37 (30-43) d

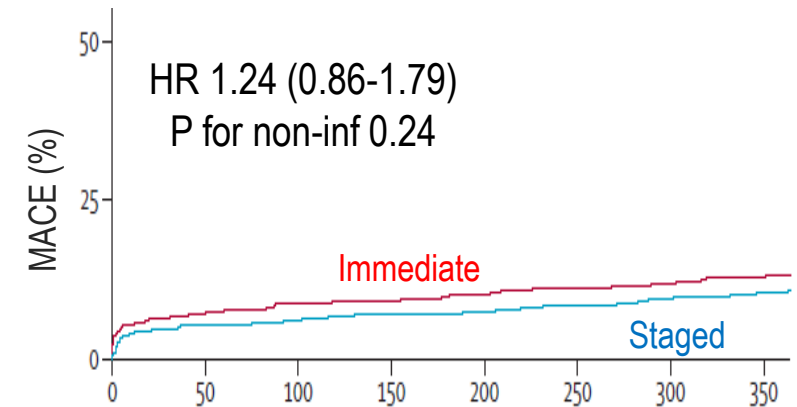


- Low-risk Pts
- Mostly driven by ↓ MI & unplanned ischemia-driven revasc
- Δ in MI's mostly procedural

NEJM 2023;389:1368-79

OPTION-STEMI

994 STEMI
Staged: 3 (2-4) d



- At 30 d, trend towards 2× cardiac death w/ immediate revasc
- Immediate revasc tended to be harmful in those w/ Killip II/III, with nearly 2× rate of cardiogenic shock

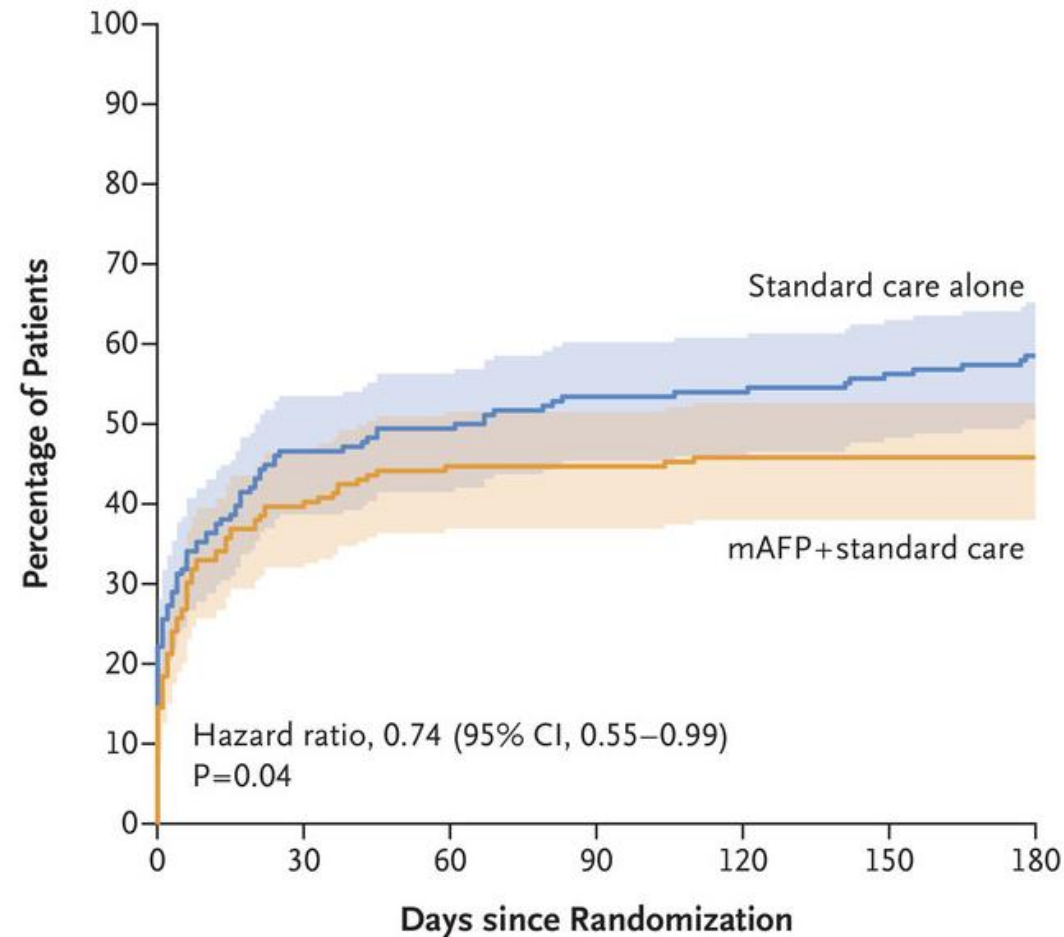
Lancet 2025;406:1032-43





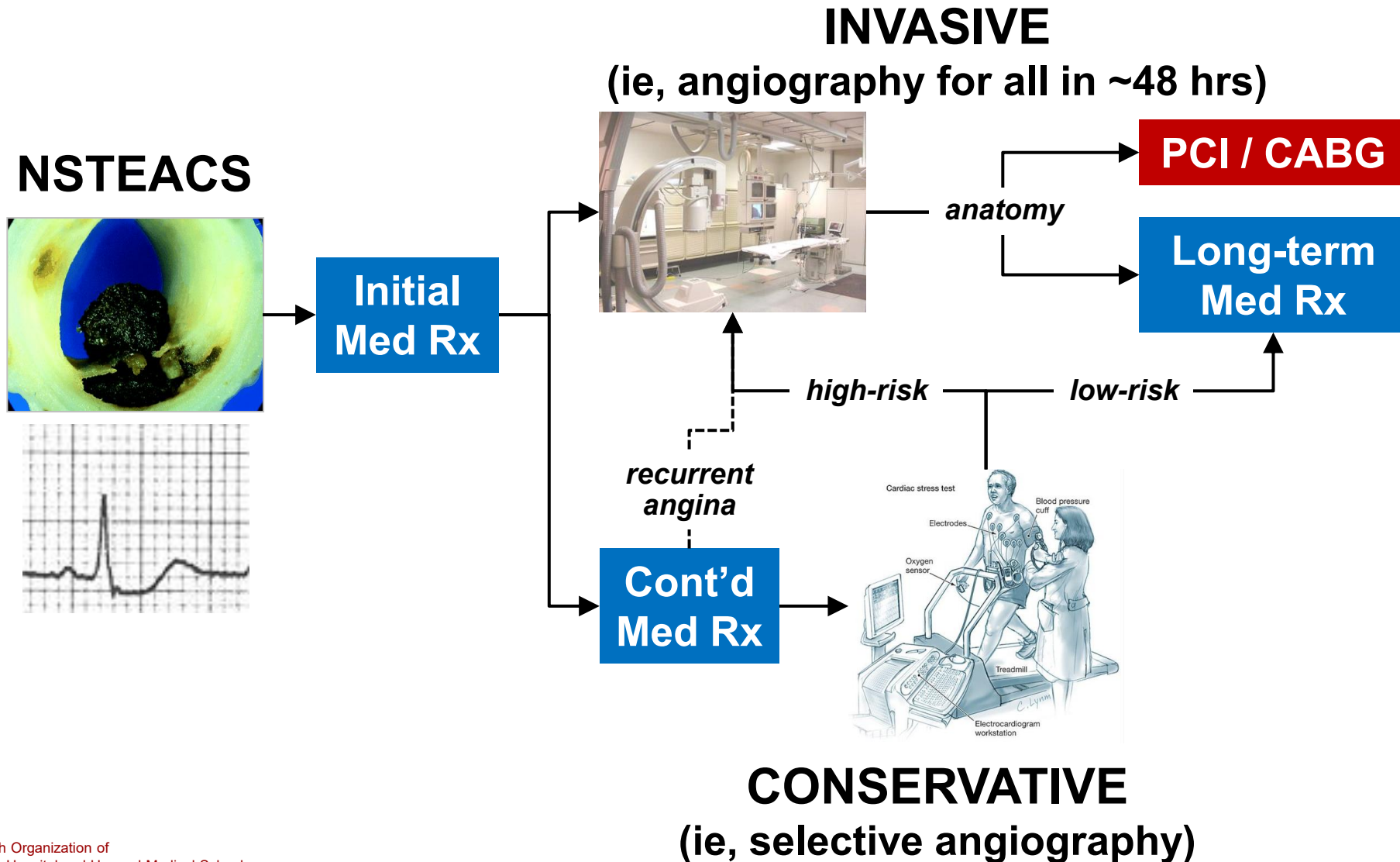
Cardiogenic Shock in STEMI

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





Management Strategy in NSTEMACS





Which NSTEACS Go to the Cath Lab?

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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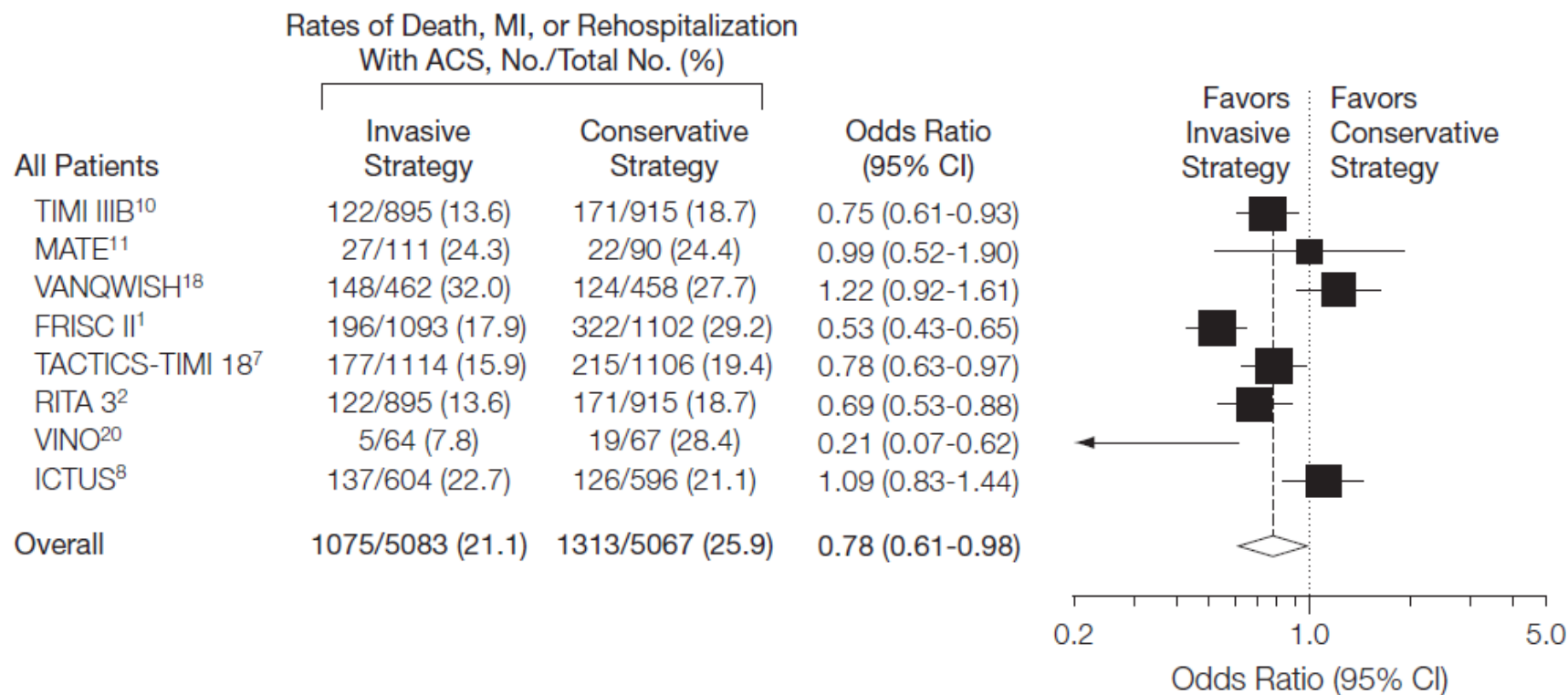
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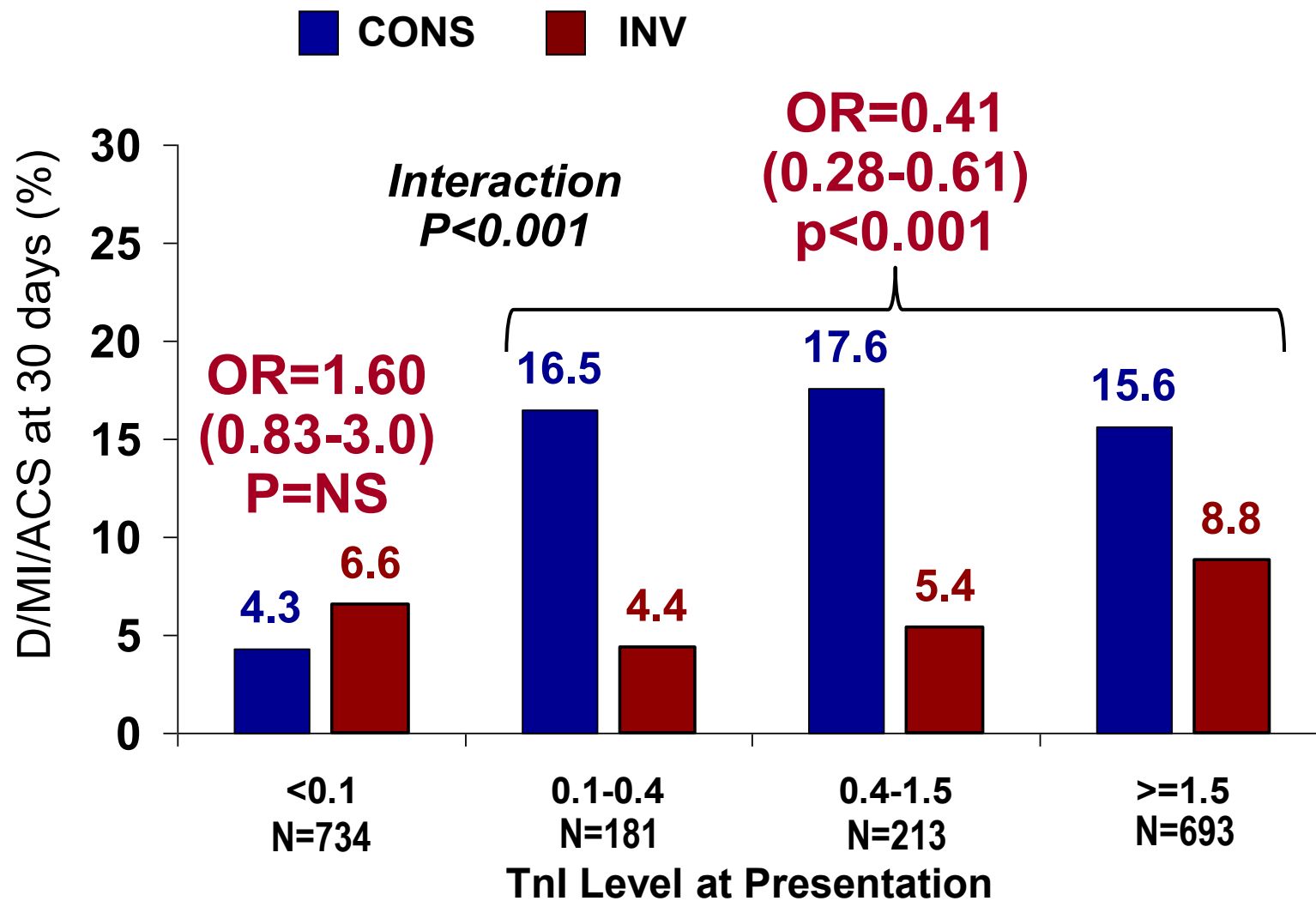
Benefit of INV vs CONS Strategy



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



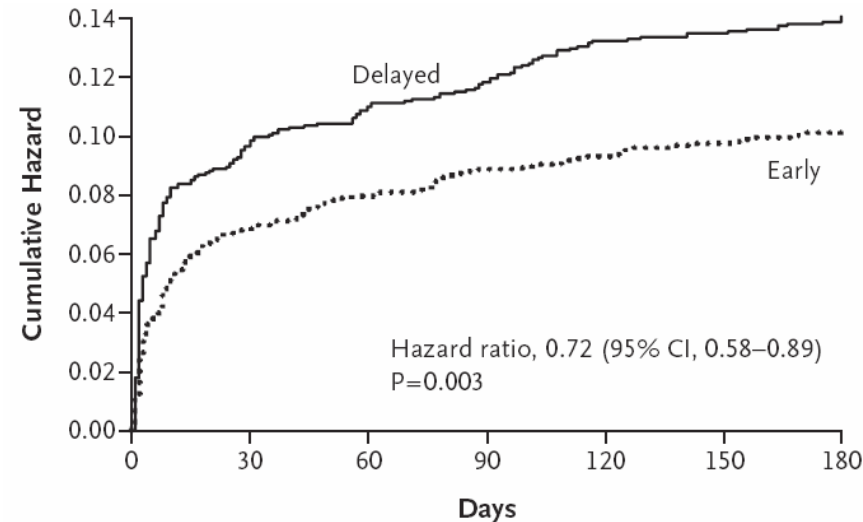
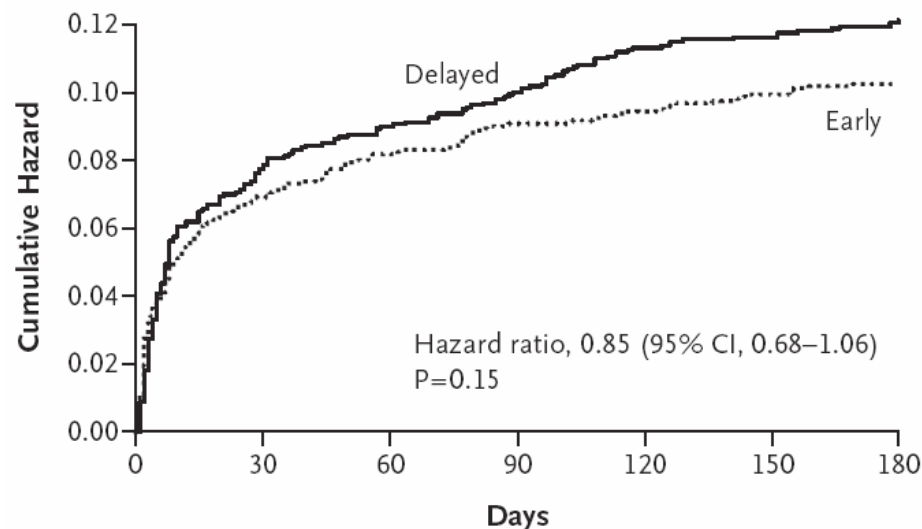
Troponin Treatment Interaction





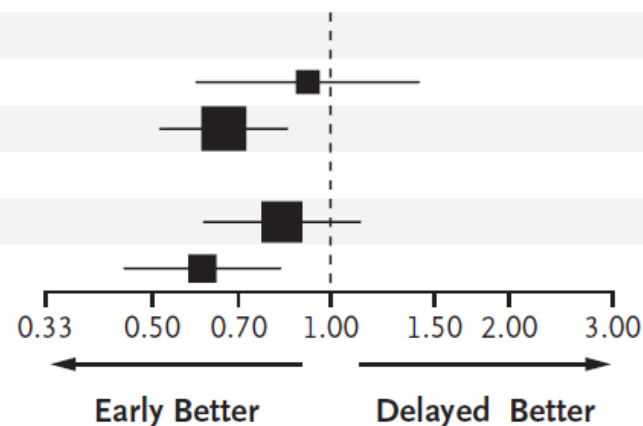
Timing of Cath in NSTEMACS

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

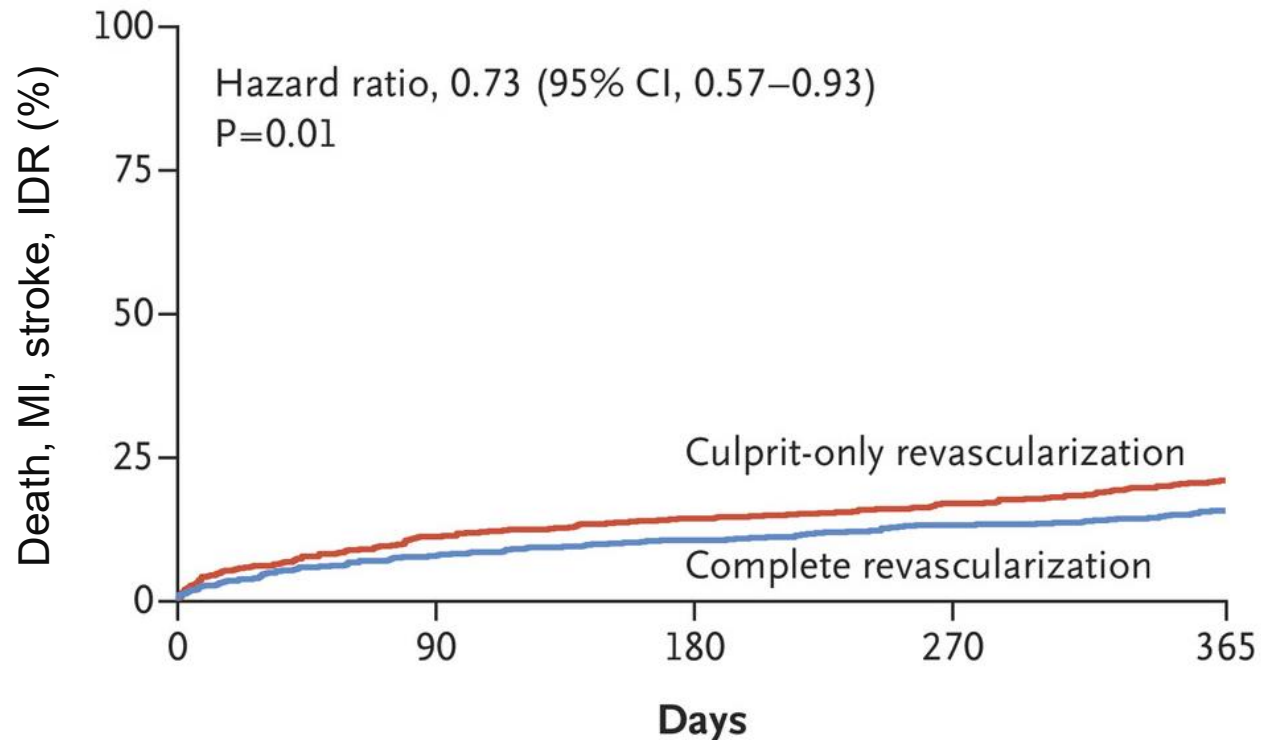
Unstable Patients	High- or Intermediate-Risk (based on TIMI Risk Score or GRACE Score)		Lower-Risk
Immediate Angio (w/in 2 h)	Early Invasive (w/in 24 h)	Delayed Invasive (w/in 25-72 h)	Routine or Selective Invasive
• Cardiogenic shock • Signs or symptoms of HF or new or worsening MR • Refractory angina • Hemodynamic or electrical instability	• GRACE score >140 • Steeply rising Tn • Ongoing ST-segment Δs	• GRACE score 109-140 • Stable or downtrending Tn • Absence of ongoing ischemic sx	• TIMI Risk Score 0-1 • GRACE score <109 • Tn negative • No ECG Δs



Complete Revasc in MI

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

Physiology-guided complete revasc vs. culprit-only



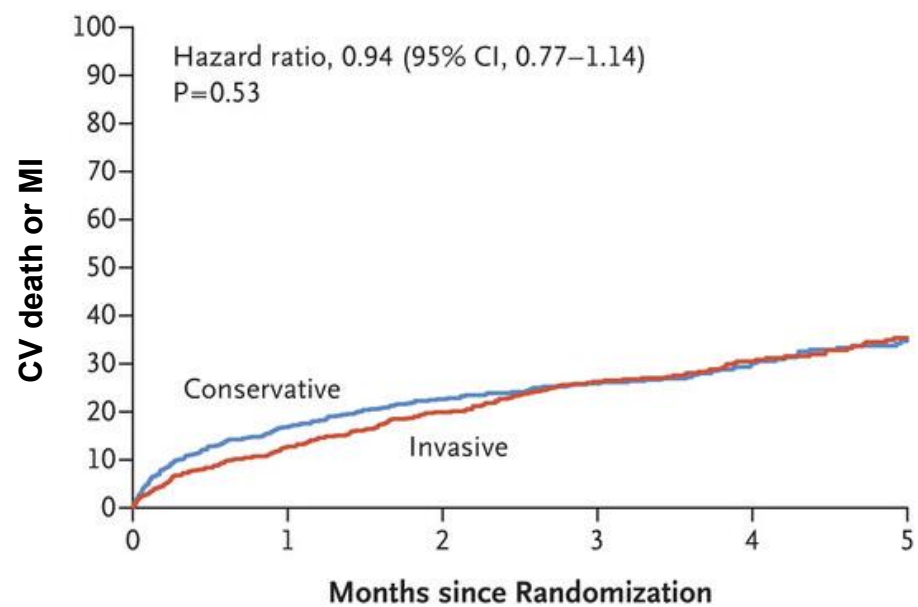
End Point	Complete	Culprit-Only	HR (95% CI)
Primary EP	15.7	21.0	0.73 (0.57-0.93)
Death	9.2	12.8	0.70 (0.51-0.96)
MI	4.4	7.0	0.62 (0.40-0.97)
Stroke	1.7	1.0	1.73 (0.68-4.40)
IDR	4.3	6.8	0.63 (0.40-0.98)

IDR, ischemia-driven revascularization



INV vs CONS in Elderly

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



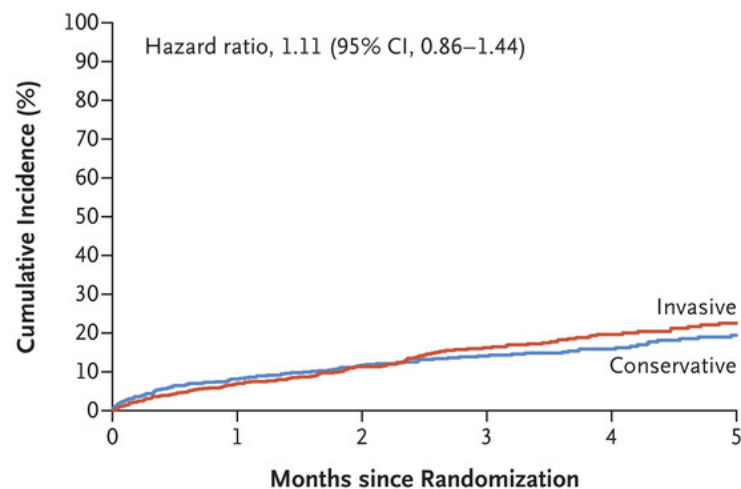


INV vs CONS in Elderly

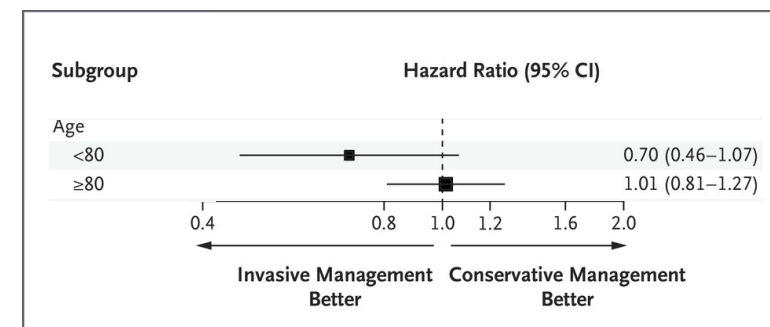
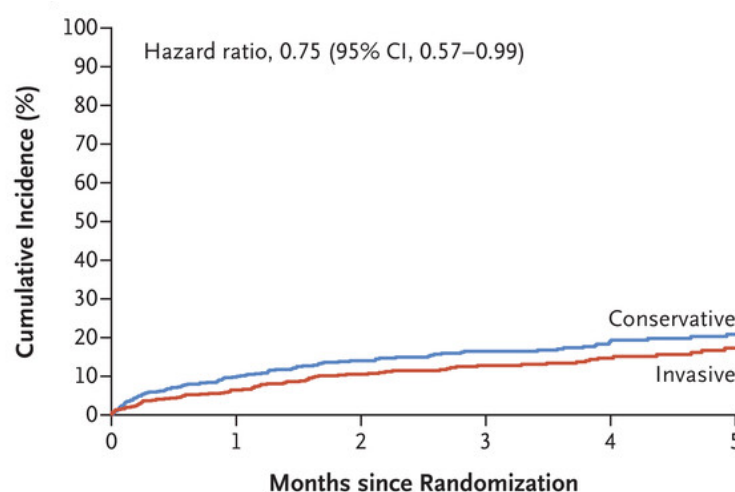
SENIOR-RITA: INV vs. CONS in 1518 Pts ≥ 75 yrs (mean 82 yrs) w/ NSTEMI

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

CV Death



MI



Procedural complications in <1%



Antithrombotic Therapy

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



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Antiplatelet Therapy Acutely

- ***Start with aspirin***
- ***Almost always add: P2Y₁₂ 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 P2Y₁₂-naïve Pts
- ***Sometimes also add (typically in cath lab): glycoprotein IIb/IIIa inhibitors (eg, abciximab, eptifibatide, tirofiban)***





2025 ACC/AHA NSTEACS Guidelines: P2Y₁₂ Inhibitors

Management strategy	Recommendation	COR	LOE
Invasive	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
Conservative	Ticagrelor (180 mg loading dose → 90 mg/bid)	1	B
Either	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
Either	Prasugrel should not be given if prior stroke or TIA	III: Harm	B



Anticoagulants in NSTEMACS

- **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

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 + P2Y₁₂ inhibitor for 30 days
- B. ASA + P2Y₁₂ inhibitor for 1 year
- C. ASA + P2Y₁₂ inhibitor for >1 year if low bleeding risk
- D. ASA + P2Y₁₂ inhibitor for 3 months and then P2Y₁₂ inhib. monoRx



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Long-Term Antithrombotic Therapy

What if ...

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

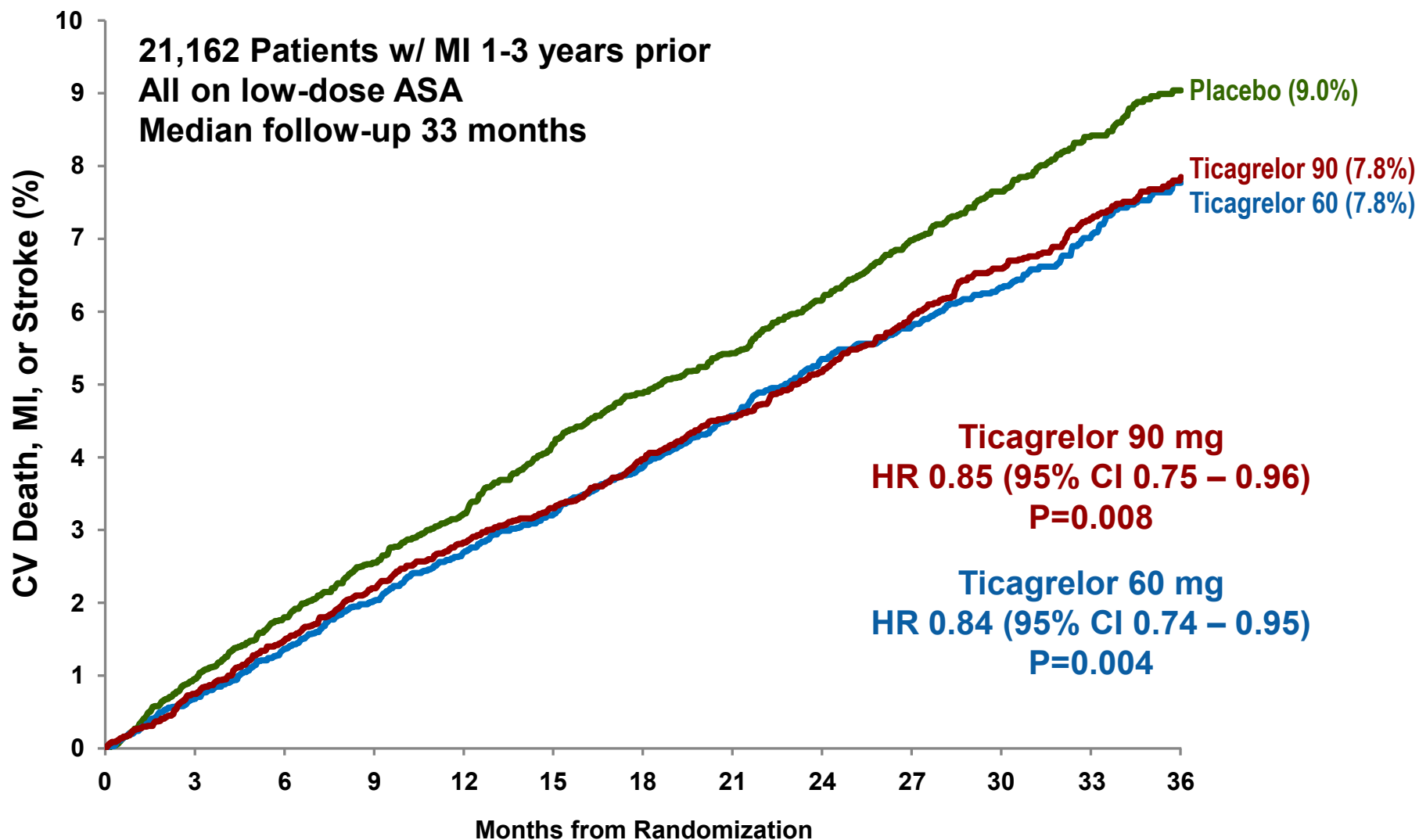
Drug-eluting stent placed in LAD. **Also has non-obstructive disease in LCx & RCA.**

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Ticagrelor in Patients w/ Prior MI





Long-Term Antithrombotic Therapy

What if ...

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

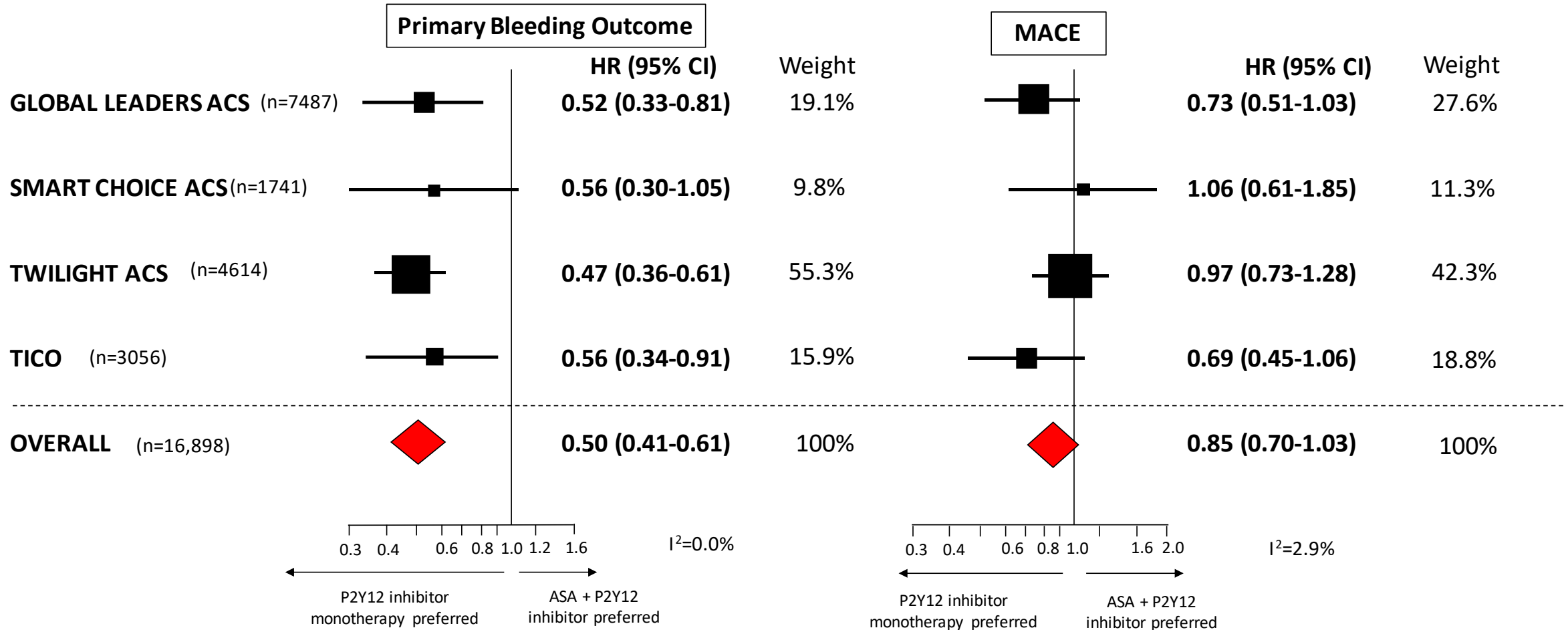
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Drop Aspirin after 1-3 Months (ie, P2Y₁₂ MonoRx)?





Long-term Antiplatelet Rx

- Start with DAPT ASA + P2Y₁₂ inhibitor (ticag or prasugrel preferred)
- Reasonable to plan for 12 mos
- If on potent P2Y₁₂ inhib (ticagrelor or prasugrel), dropping ASA after ≥1 mo ↓ bleeding w/o clear ↑ in MACE
- If very high bleeding risk, consider clopidogrel (✓ *CYP2C19*) over ticag or prasugrel and drop ASA after ≥1 mos
- If high GIB risk, add PPI
- If low bleeding risk & high ischemic risk (and tolerated DAPT well to date), may consider continuing ASA + P2Y₁₂ inhibitor beyond 12 mos



Antiplatelet Rx & Surgery

- **How long to defer surgery after PCI**
 - ≥ 30 days if at all possible
 - 3-6 mos may be considered
 - Ideally 12 mos after ACS
- **Peri-operative**
 - Continue ASA whenever possible
 - Stop ticagrelor 3-5 d, clopidogrel ≥ 5 d, and prasugrel ≥ 7 d before surgery
 - $\pm$ Cangrelor bridge if < 6 mos after stenting
- **Resume P2Y₁₂ inhibitor ASAP post-operatively (typically 24-72 hrs)**



Triple Therapy

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



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



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

- High rate of bleeding with triple Rx (ASA + P2Y₁₂ + 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 + P2Y₁₂ inhibitor (clopidogrel)
- Drop ASA at hospital d/c or, if high ischemic risk, after 1 month
- Consider dropping P2Y₁₂ inhib after 6-12 mos, depending on bleeding risk





Lipid-Lowering Therapy

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



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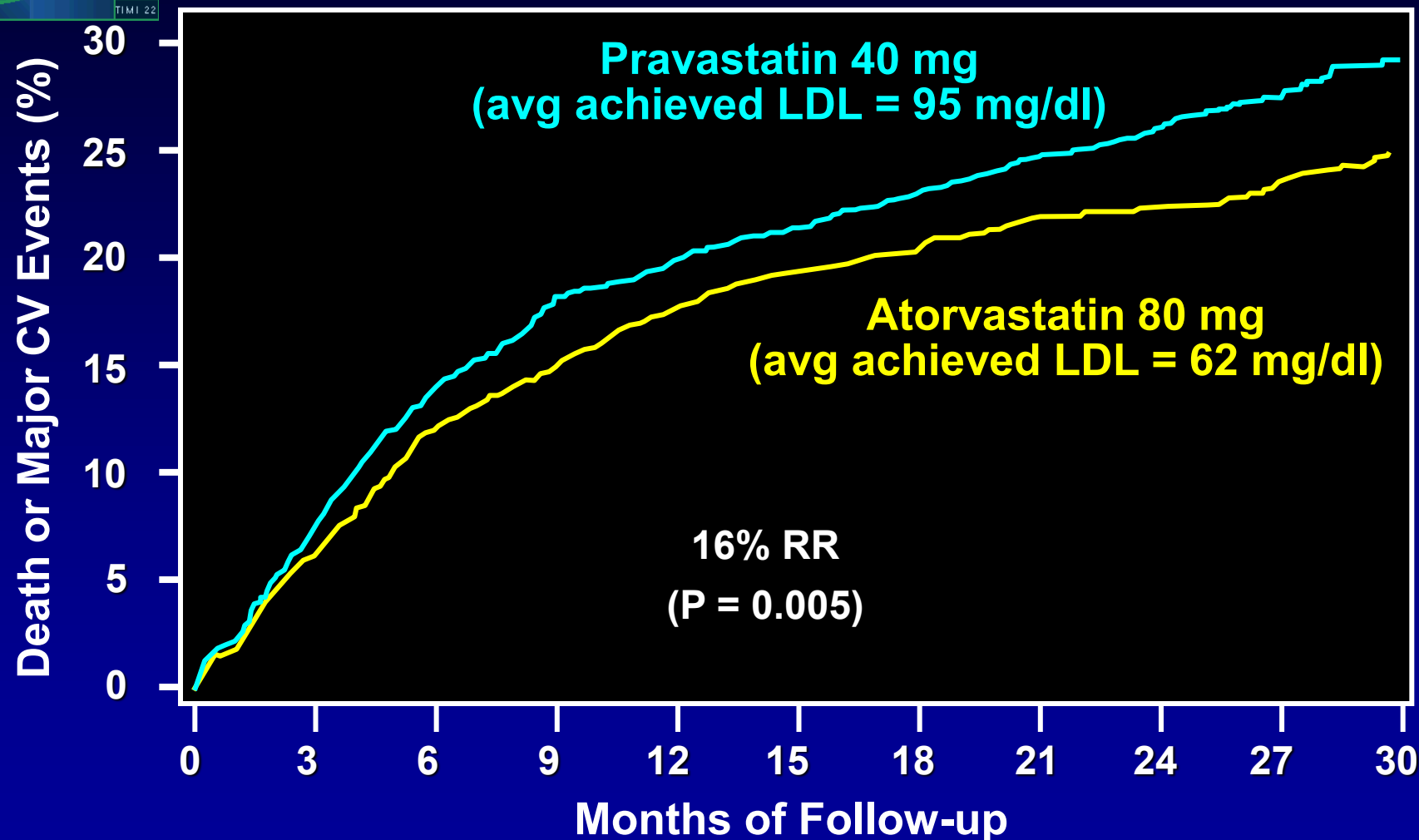
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PROVE IT – TIMI 22

4162 patients hospitalized w/in prior 10 d for ACS

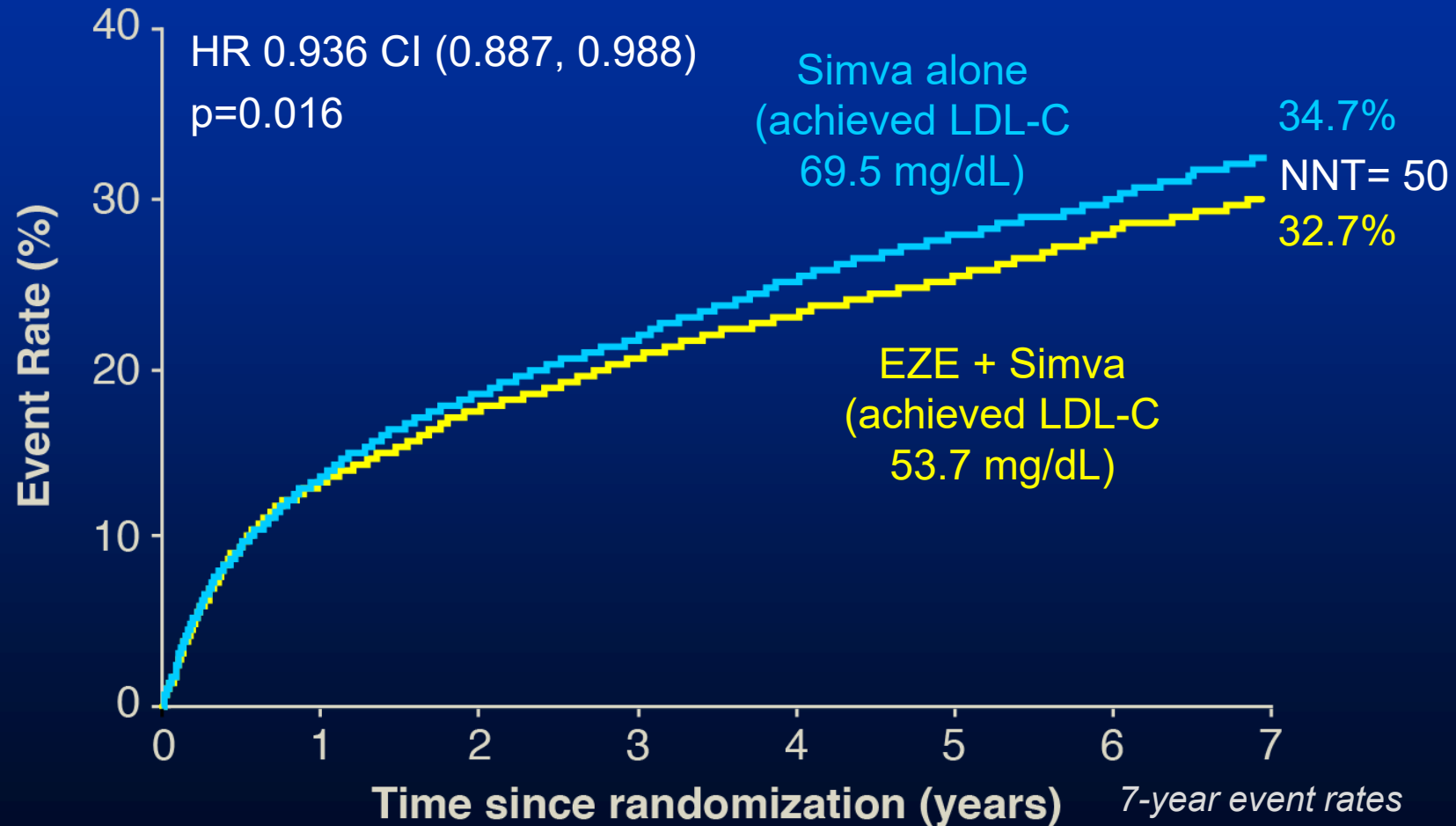


Cannon et al. *NEJM* 2003; 350: 1495

Primary Endpoint — ITT

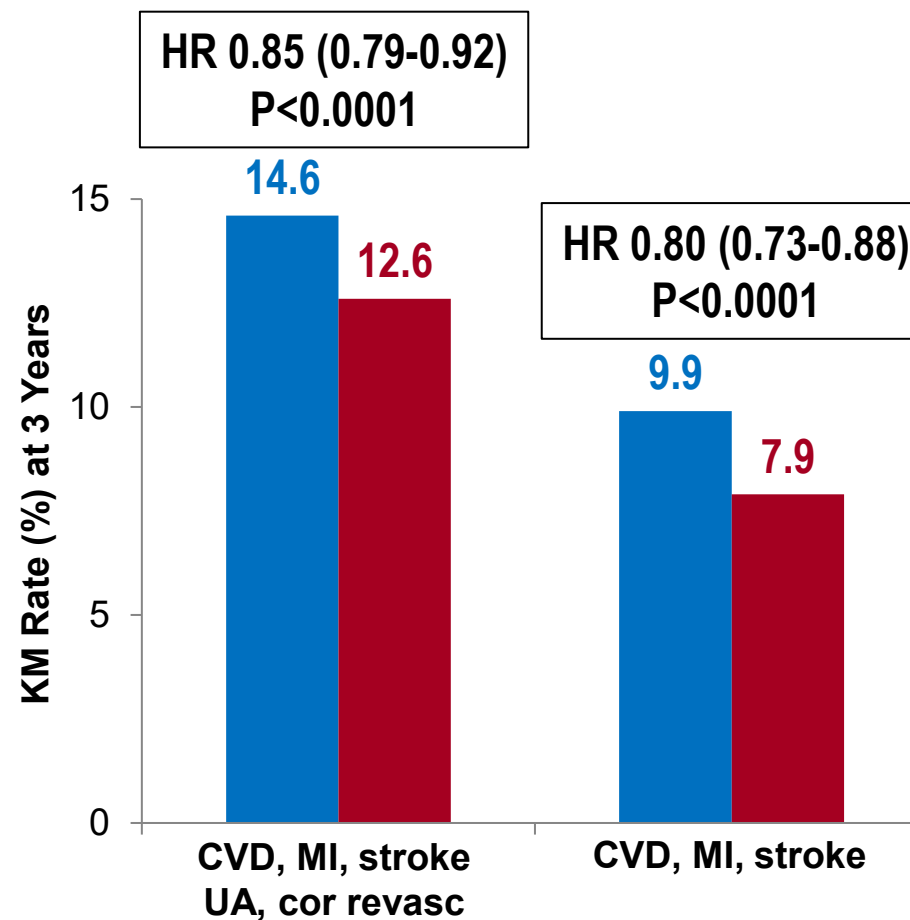
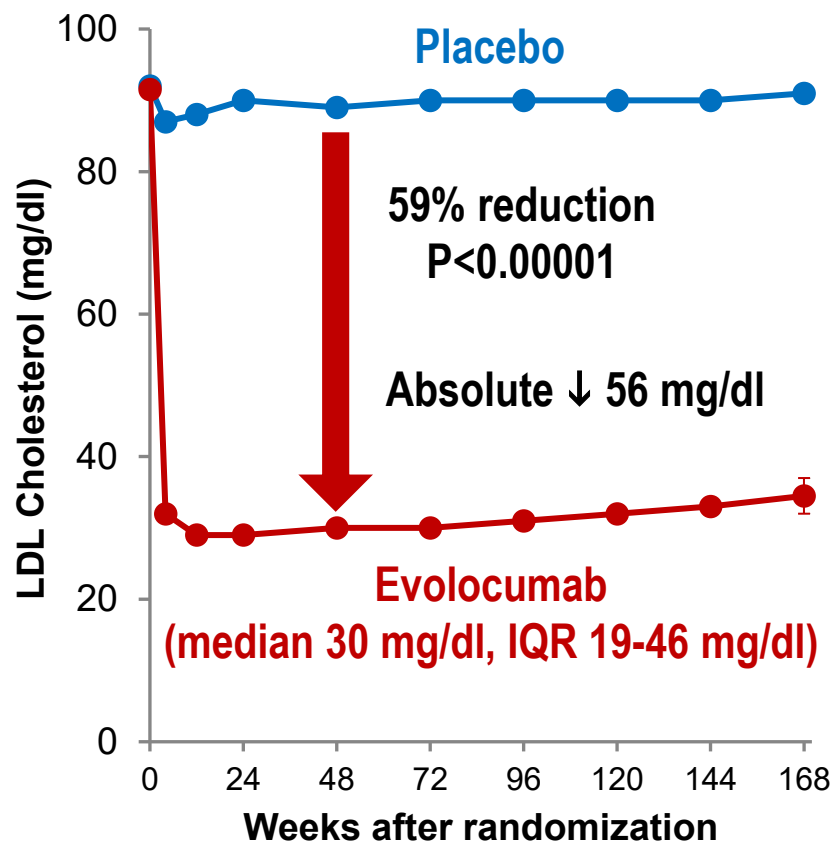


Cardiovascular death, MI, documented unstable angina requiring rehospitalization, coronary revascularization (≥ 30 days), or stroke



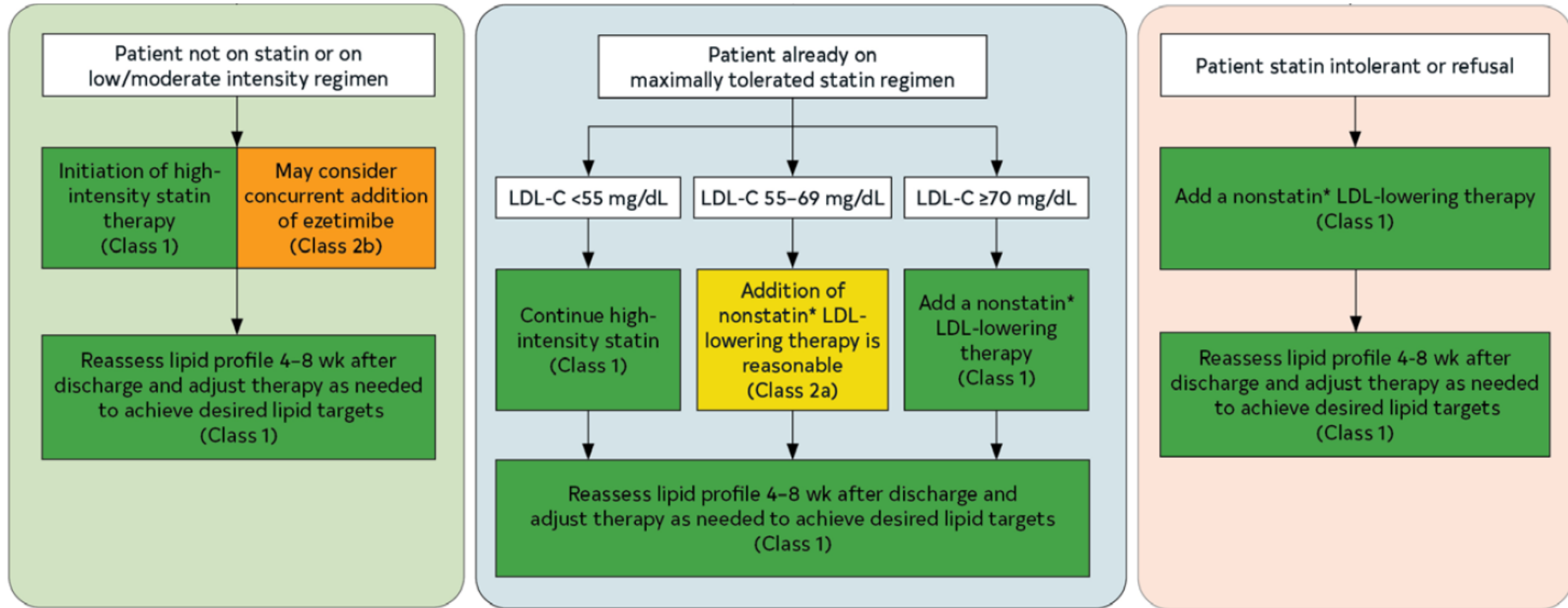
Summary of Effects of PCSK9i Evolocumab

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





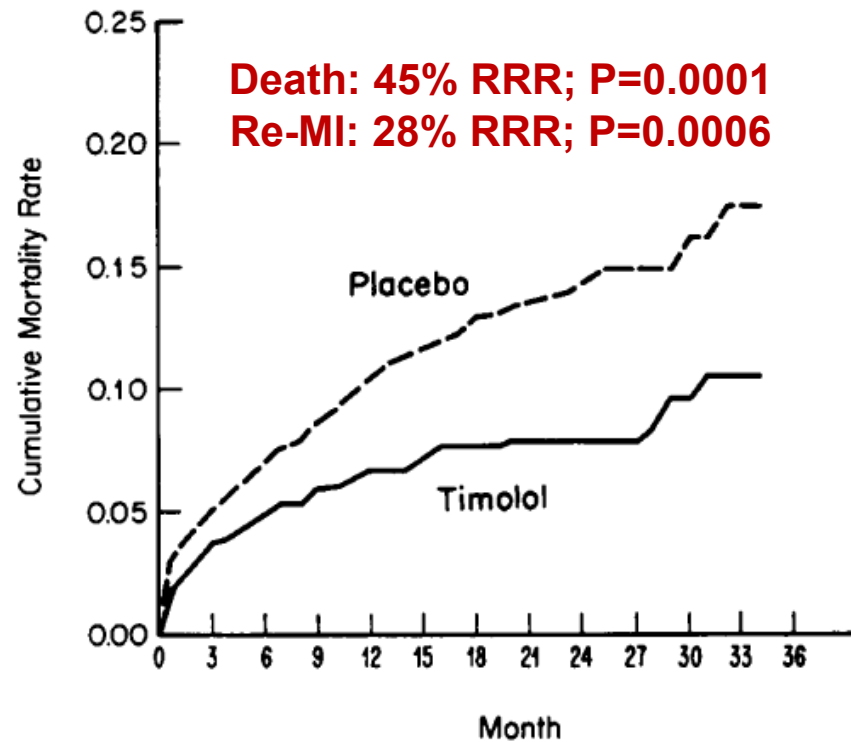
Lipid Mgmt





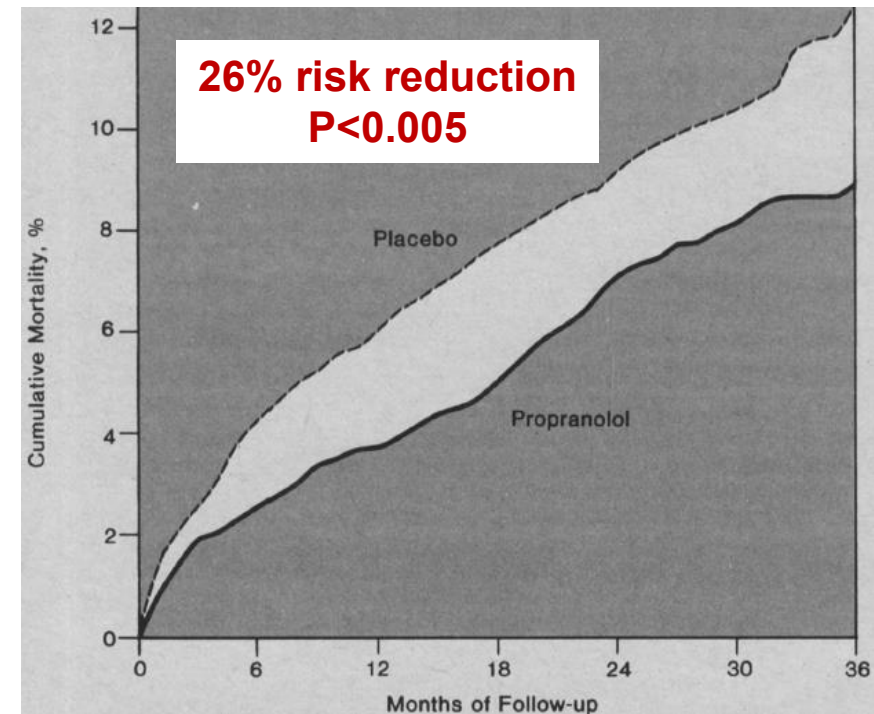
β -blockers: Double-Blind RCTs

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



NEJM 1981;304:801-7

3837 Patients 1-3 weeks after acute MI
Randomized to β -blocker vs. placebo

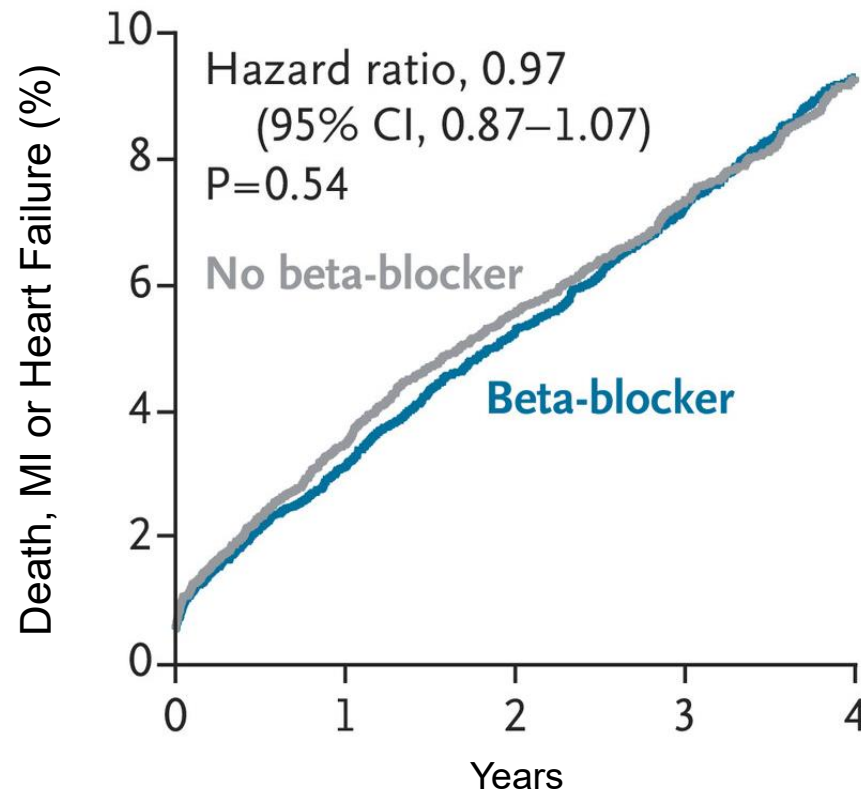


JAMA 1982;247:1707-14



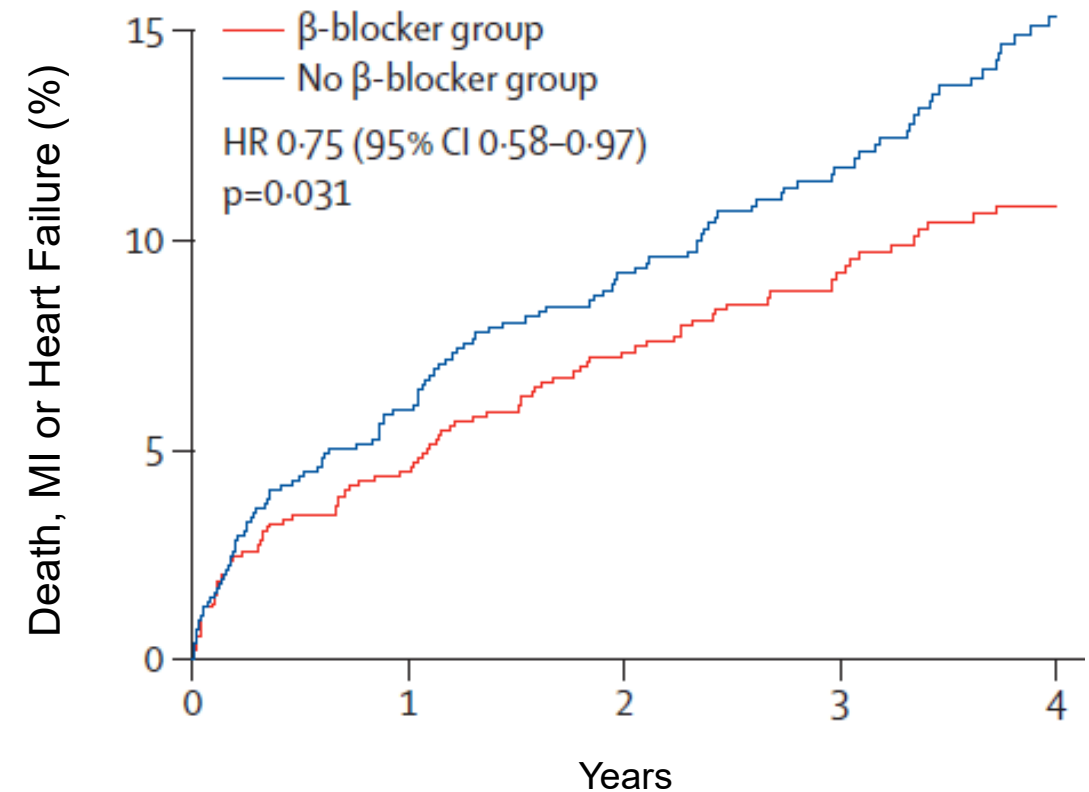
β -blockers: Newer, Unblinded RCTs

Meta-analysis of 5 RCTs, 17,801 Pts w/ EF $\geq$ 50%



NEJM 2026;396:540-50

Meta-analysis of 4 RCTs, 1885 Pts w/ EF 40-49%



Lancet 2025;406:1128-37



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 $\leq$ 2-2.5, K $\leq$ 5; *and*
 - LVEF <40% and either clinical s/s of HF or diabetes



Cardiometabolic Therapies

Definitely not acutely, but to consider before discharge

- **Diabetes**

- GLP-1RA: 16% ↓ in MACE in patients with ASCVD
- SGLT2i: no benefit in AMI per se, but indicated if HF or CKD

- **Overweight or Obese**

- GLP-1RA (at weight-loss doses): 20% ↓ in MACE in patients with prior MI



Take Home Points

- **Diagnose ACS using H&P, 12-lead ECG, troponin**
- **STEMI: Primary PCI** (vs Lytic)
- **NSTE ACS: Invasive** (eg, $\oplus$ Tn) vs. **Conservative Strategy**
- **Anti-ischemic Rx:** beta-blocker, nitrates
- **Select Antiplatelet Regimen: ASA + P2Y₁₂ Inhibitor** (ticagrelor, prasugrel, or clopidogrel)
- **Select Anticoagulant: UFH**, bivalirudin, or LMWH
- **Long-term therapy**
 - ASA (maybe drop after 1-3 mos) + P2Y₁₂ inhibitor (ideally ticag or prasugrel; at least 12 mos)
 - Statin $\pm$ EZE $\pm$ PCSK9i if needed
 - β -blocker (if low LVEF or STEMI)
 - ACEI (if low LVEF, HTN, DM, CKD); MRA (if low LVEF + either HF or DM, and Cr & K okay)
 - Diabetes: cardiorenal protective Rx (GLP-1RA and/or SGLT2i)
 - Overweight or obese: GLP-1RA





Key References

- **Collet et al. EHJ 2021;42:1289**
- **Rao et al. Circ 2025;151:e771**

