Acute coronary syndromes in 2015

Is complete revascularization in the setting of acute coronary syndrome always needed?

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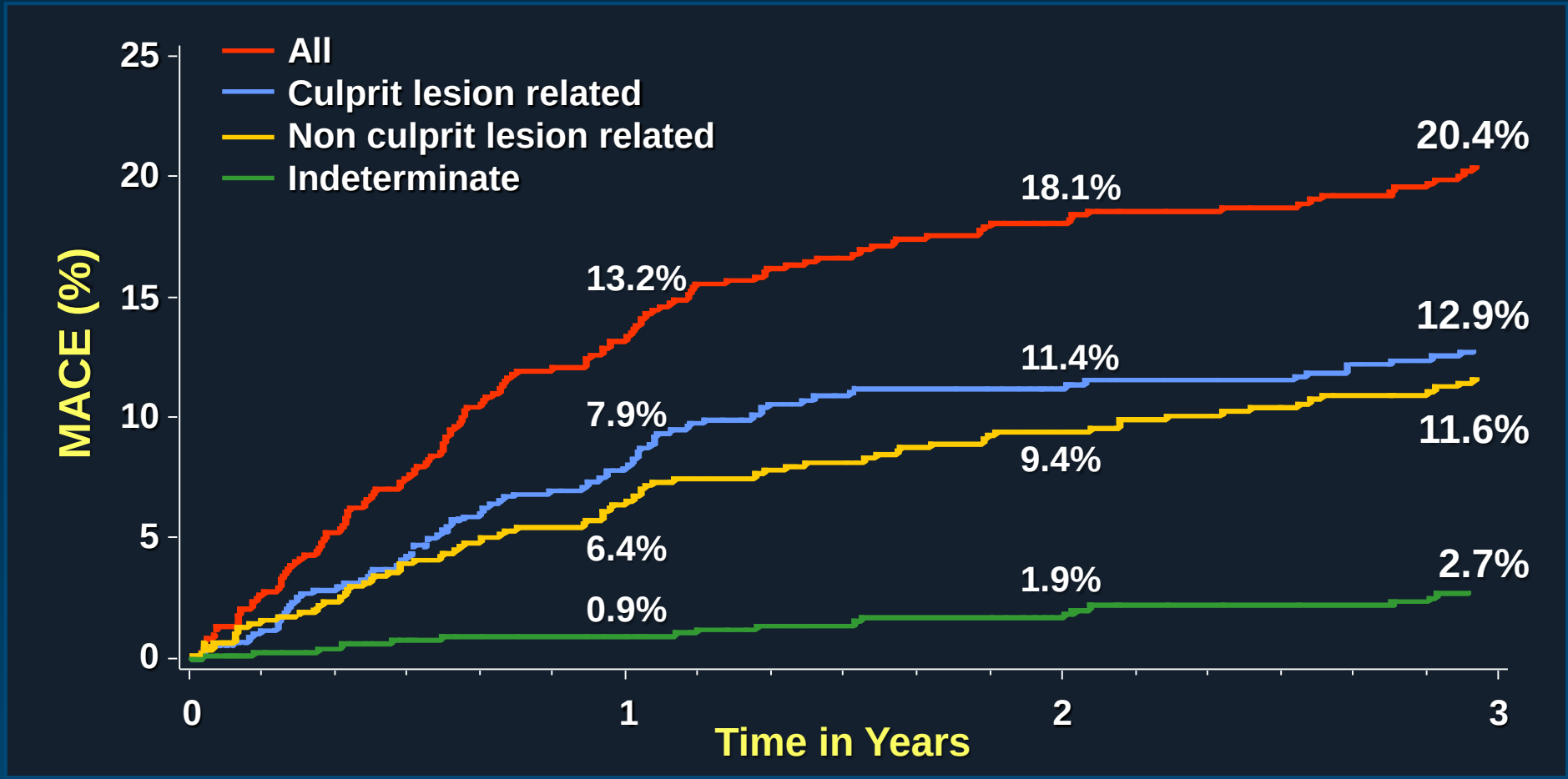
Impact of non-Culprit Lesions in ACS

PROSPECT: A prospective study of 697 ACS patients undergoing three-vessel angiography and gray-scale and radiofrequency intravascular ultrasonographic imaging after PCI



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Stone GW, et al. N Engl J Med. 2011;364:226-35

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Revascularization strategies in ACS

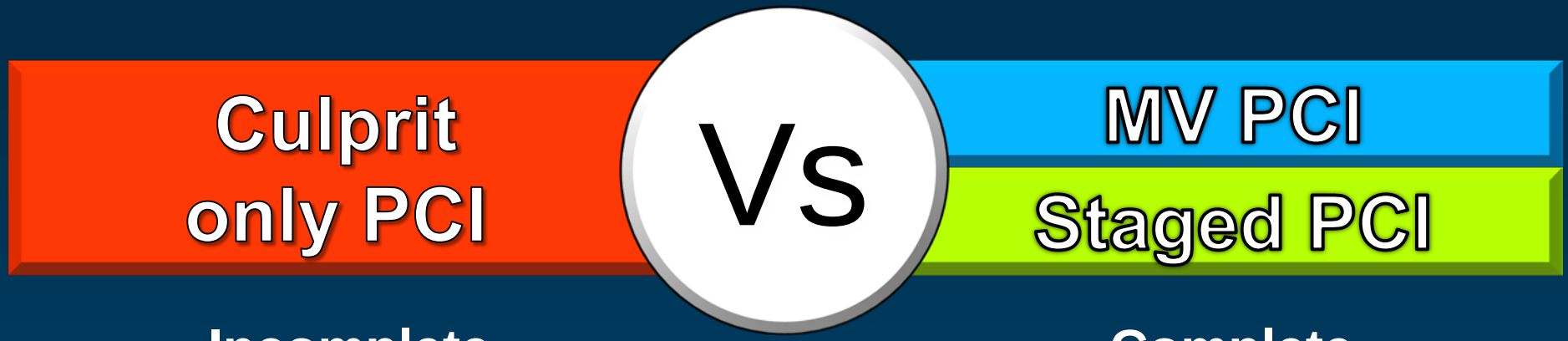
- Culprit only (conservative approach - incomplete rev)
- Staged PCI of non-culprit (intermediate approach - complete rev)
- MV one-time PCI (aggressive approach - complete rev)

	PROs	CONs
Conservative	• No PCI complications on non-culprit lesions, especially in STEMI • PCI of non-culprit lesions supported by evidence of ischemia • Chance to discuss revascularization strategy within the “Heart Team” and with the patient	• Significant ischemic lesions may be left • Patient may need to return to the cathlab in the near future which is also a problem for busy cathlabs with long waiting times
Intermediate	• Complete revascularization may decrease subsequent events • Safer than during the index intervention	• Unnecessary treatment of asymptomatic lesions, in particular if not FFR-guided • Timing of staged PCI uncertain • Need for additional cathlab procedure during the index hospital stay or soon after discharge
Aggressive	• Immediate complete revascularization including treatment of potentially unstable (possible multiple culprit) and residual ischemia • No need for additional PCI– beneficial for patient comfort and for busy cathlab	• PCI complication at non-culprit vessel may lead to additional non-functional myocardium and left ventricular pump failure. • Prothrombotic/inflammatory milieu in acute phase may increase likelihood of stent thrombosis also in non-culprit lesion • Increased contrast volume, radiation exposure

Cuisset T, Noc M. Eurointervention 2014;10-T47-T54

Dealing with Non-IRA after ACS

Question #1. Based on Evidence is the Culprit-only PCI Justified?

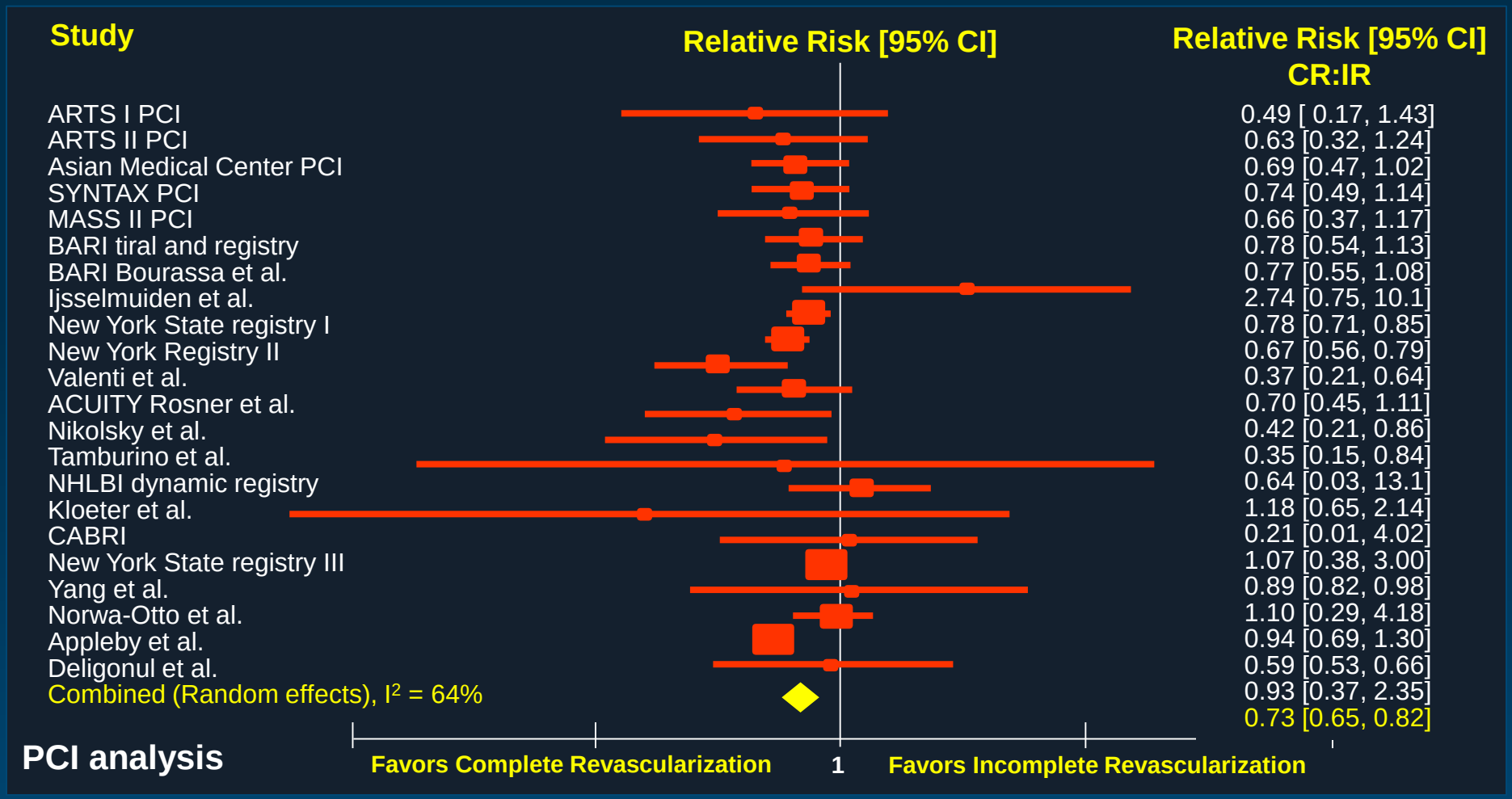


Incomplete Revascularization

Complete Revascularization

Complete Revascularization: 27% Reduction In Mortality

89,883 MVD patients from 35 studies (1 RCT, 5 post-hoc RCTs, 28 OSs, 1 post-hoc OS)



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Garcia S, et al. J Am Coll Cardiol. 2013;62:1421-31

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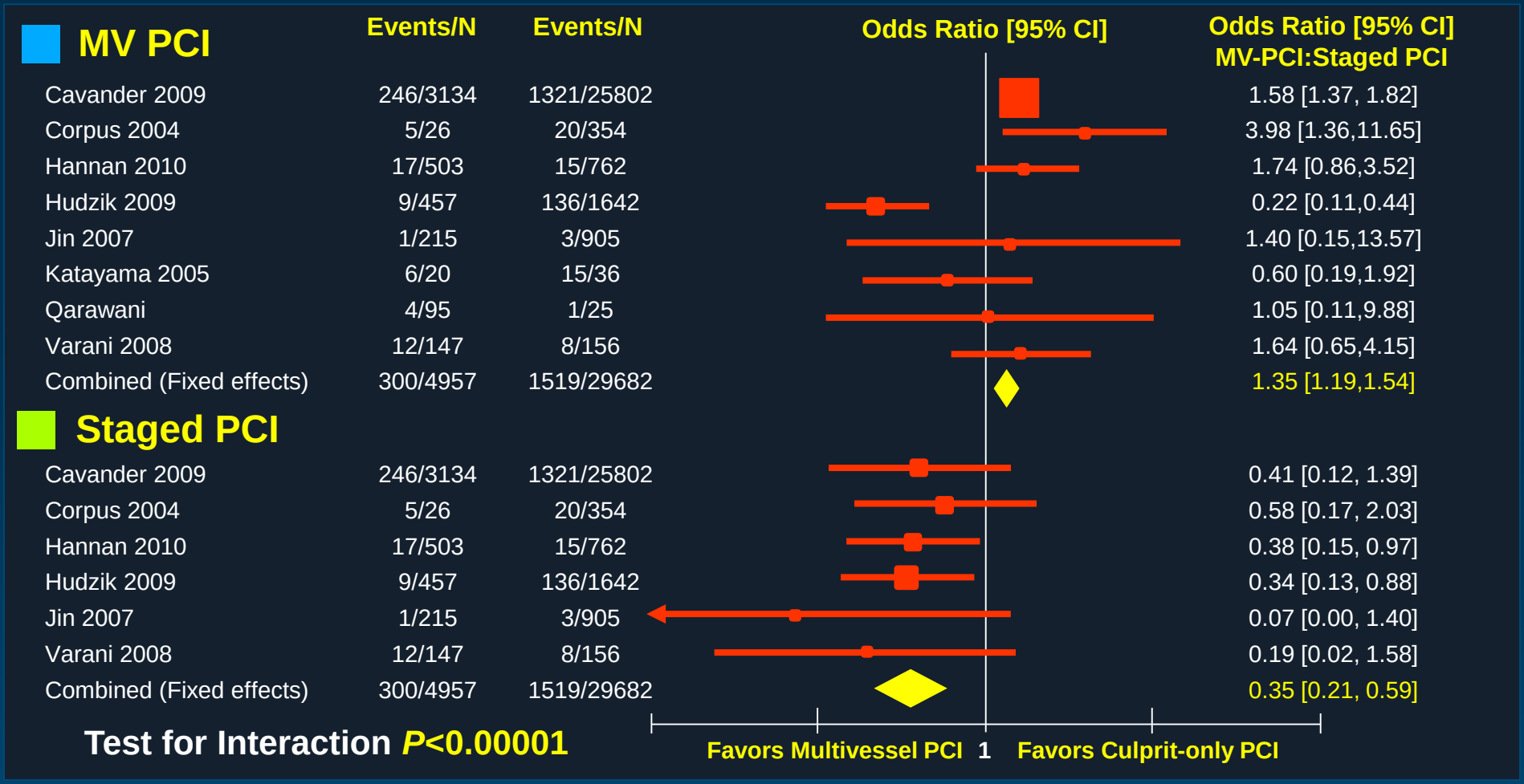
In-Hospital Death By Timing of MV-PCI

7,886 patients undergoing multivessel PCI from 26 studies (3 RCTs, 23 OSs)



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Bainey KR, et al. Am Heart J. 2014;167:1-14

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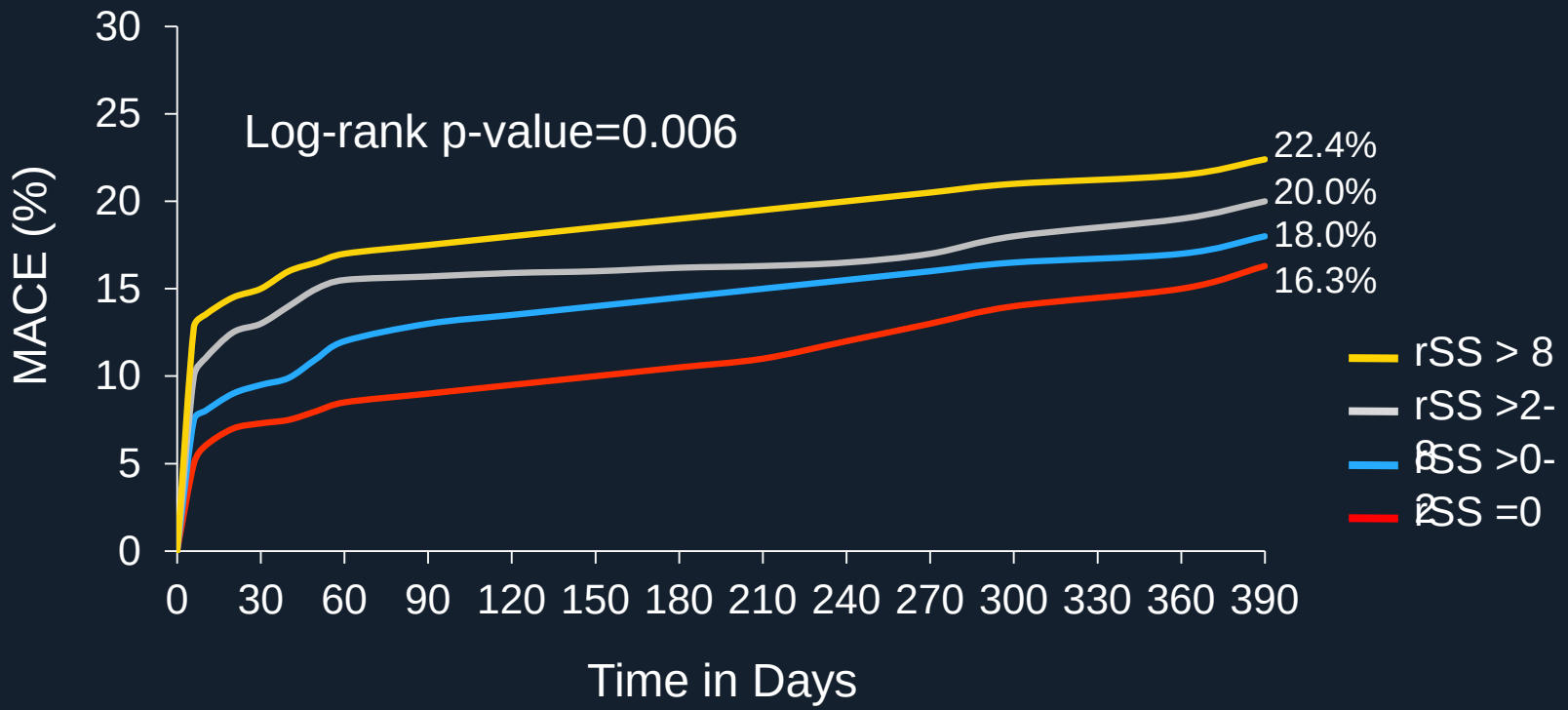
Culprit only vs MV PCI in NSTE-ACS

- **No dedicated randomized trials** addressing the type (complete vs. incomplete) and timing (simultaneous vs. staged) of rev.
- A complete rev should be pursued based on two considerations:
  - several studies showing the benefit of early intervention compared with the conservative approach mandated a complete rev
  - multiple PCI and NSTE-ACS trials have shown a detrimental prognostic effect of incomplete rev
- However, **tailor the need for complete rev** to age, general patient status, comorbidities, anatomy complexity, ventricular function.

Residual SYNTAX score – ACUITY trial

Residual SYNTAX score (rSS) obtained from 2,686 angiograms from patients with moderate- and high-risk acute coronary syndrome (ACS) undergoing PCI.



By multivariable analysis, rSS was an independent predictor of all ischemic outcomes at 1 year (HR: 1.05, 95% CI: 1.02 to 1.09, p = 0.006).

Angio-guided (n=176) vs. FFR-guided (n=174) in NSTEMI: FAMOUS-NSTEMI

- The FFR-guided approach resulted in changes in stenosis classification and patient management in one-fifth of the patients.
- The rate of coronary revascularization was reduced at the index procedure and most of this difference was maintained at 1 year.
- Overall 1-year MACE were similar.
- Material costs during the index procedure increased but overall healthcare costs during the index hospitalization were similar.

Layland J et al. European Heart Journal 2015; 36:100–11

Culprit only vs MV PCI in STEMI

PRAMI - Immediate Multivessel PCI vs Culprit-only PCI

465 patients with STEMI undergoing infarct-related artery PCI
randomized to either preventive PCI or provisional PCI

Outcome (mean FU 23 months)	HR	95% CI	*P* value
CV death, MI or refractory angina	0.35	0.21-0.58	<0.001
CV death or MI	0.36	0.18-0.73	0.004
CV death	0.34	0.11-1.08	0.07
MI	0.32	0.13-0.75	0.009
Refractory angina	0.35	0.18-0.69	0.002
Death from non cardiac causes	1.10	0.38-3.18	0.86
Repeat revascularization	0.30	0.17-0.56	<0.001

PRAMI did not investigate the impact of immediate versus planned staged revascularization of non-IRA (i.e., in-hospital or early after discharge)

Wald DS et al. N Engl J Med. 2013;369:1115-23

CVLPRIT - In-Hospital MV PCI vs Culprit-only PCI

296 patients with STEMI undergoing infarct-related artery PCI
randomized to either in-hospital complete revascularization or provisional PCI

Outcome (12 months)	HR	95% CI	*P* value
MACE	0.45	0.24-0.84	0.009
All-cause mortality	0.32	0.06-1.60	0.14
CV mortality	0.27	0.06-1.32	0.11
Recurrent MI	0.48	0.09-2.62	0.39
Heart failure	0.43	0.13-1.39	0.14
Repeat revascularization	0.55	0.22-1.39	0.20
Major bleed	0.55	0.16-1.87	0.34

CVLPRIT did not investigate the impact of immediate
versus staged revascularization during hospital stay

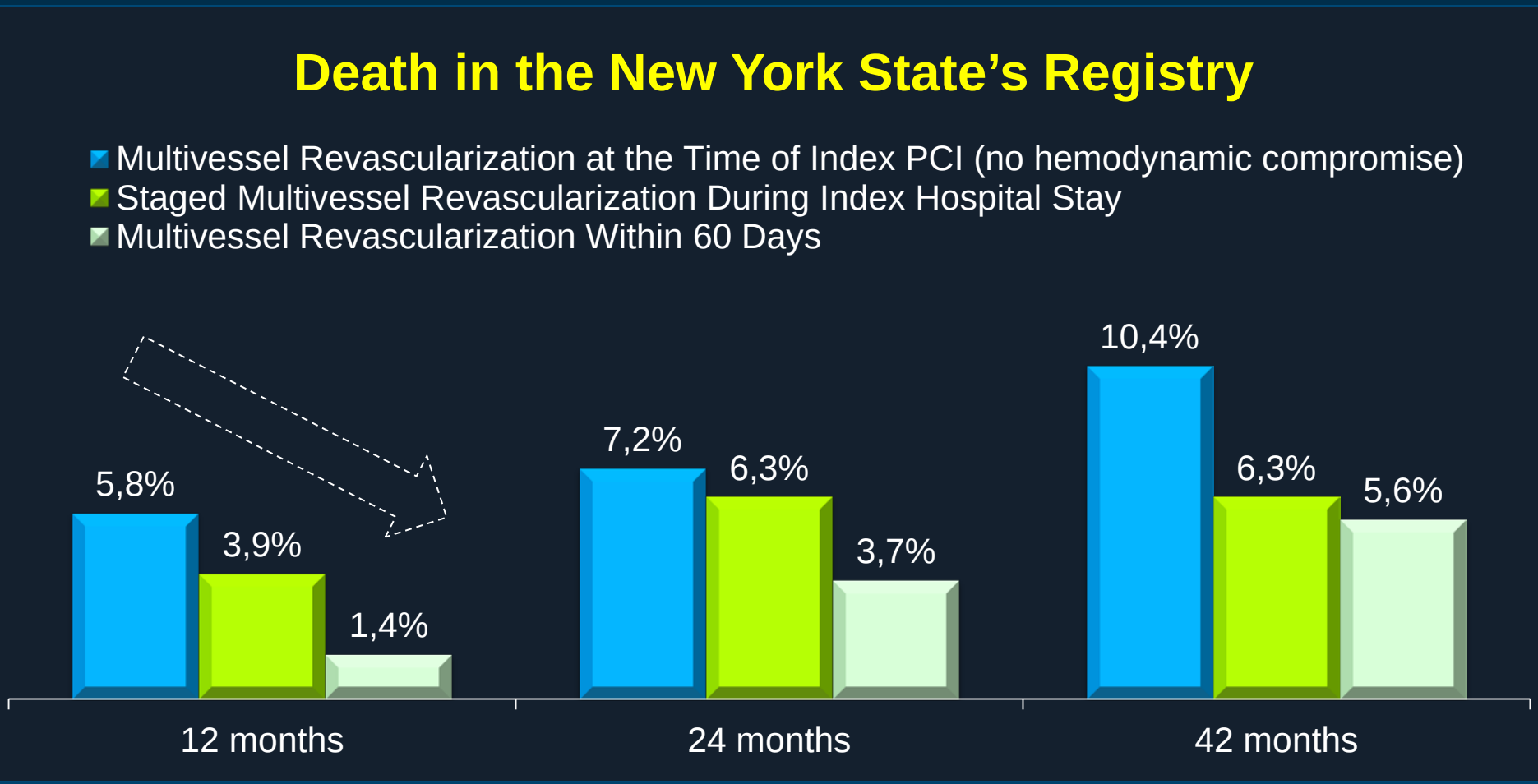
Dealing with Non-IRA after Primary PCI

Question #2. Based on Evidence should we prefer staged non-IRA PCI over immediate MV PCI?

Improved Survival With Longer Delays From Index PCI

Subgroups from 4,024 patients with STEMI and MVD undergoing primary PCI

Death in the New York State's Registry



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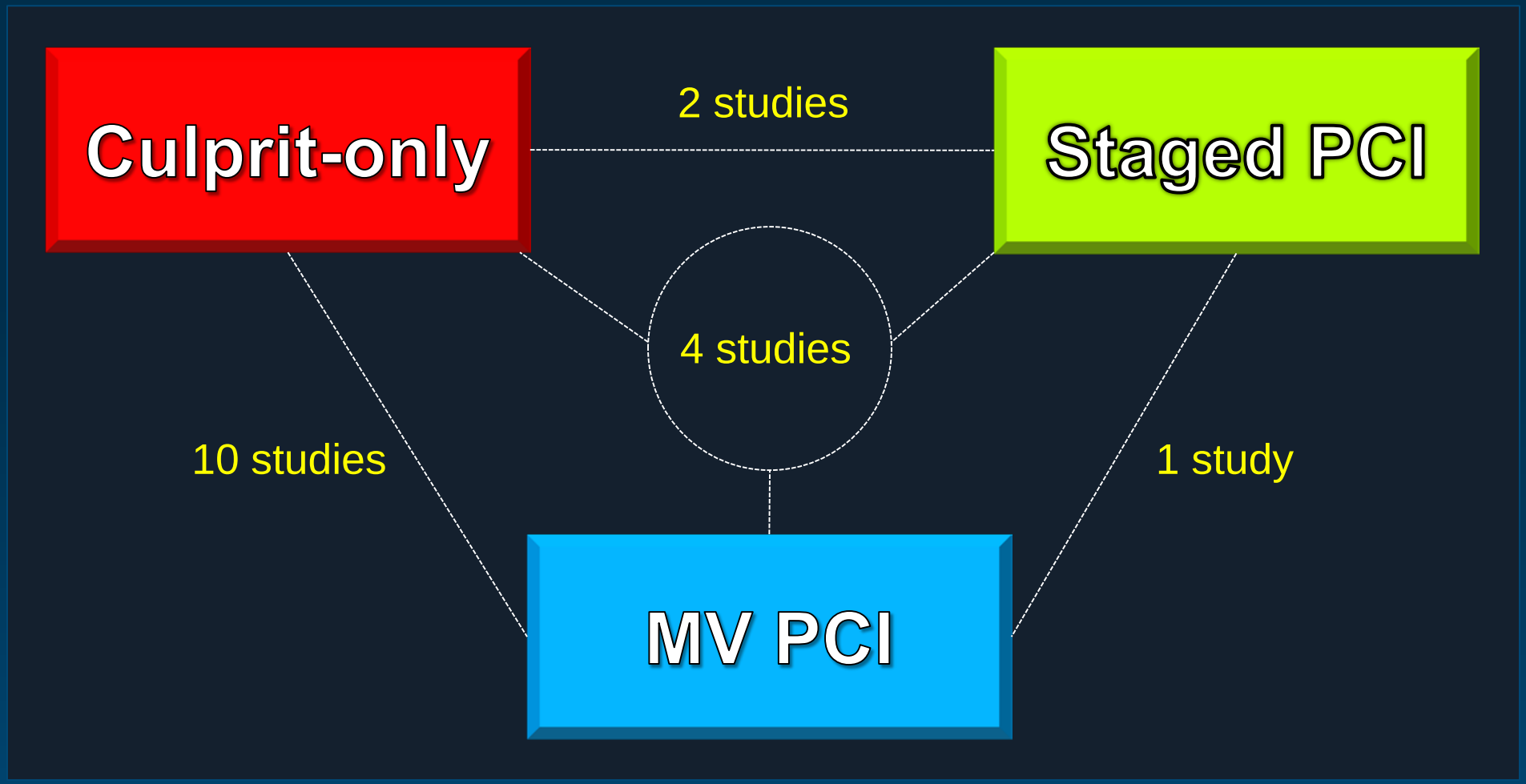
Hannan EL, et al. JACC Cardiovasc Interv. 2010;3:22-31

Culprit-only vs MV vs Staged PCI

Network meta-analyses from 4 prospective and 14 retrospective studies involving 40,280 patients



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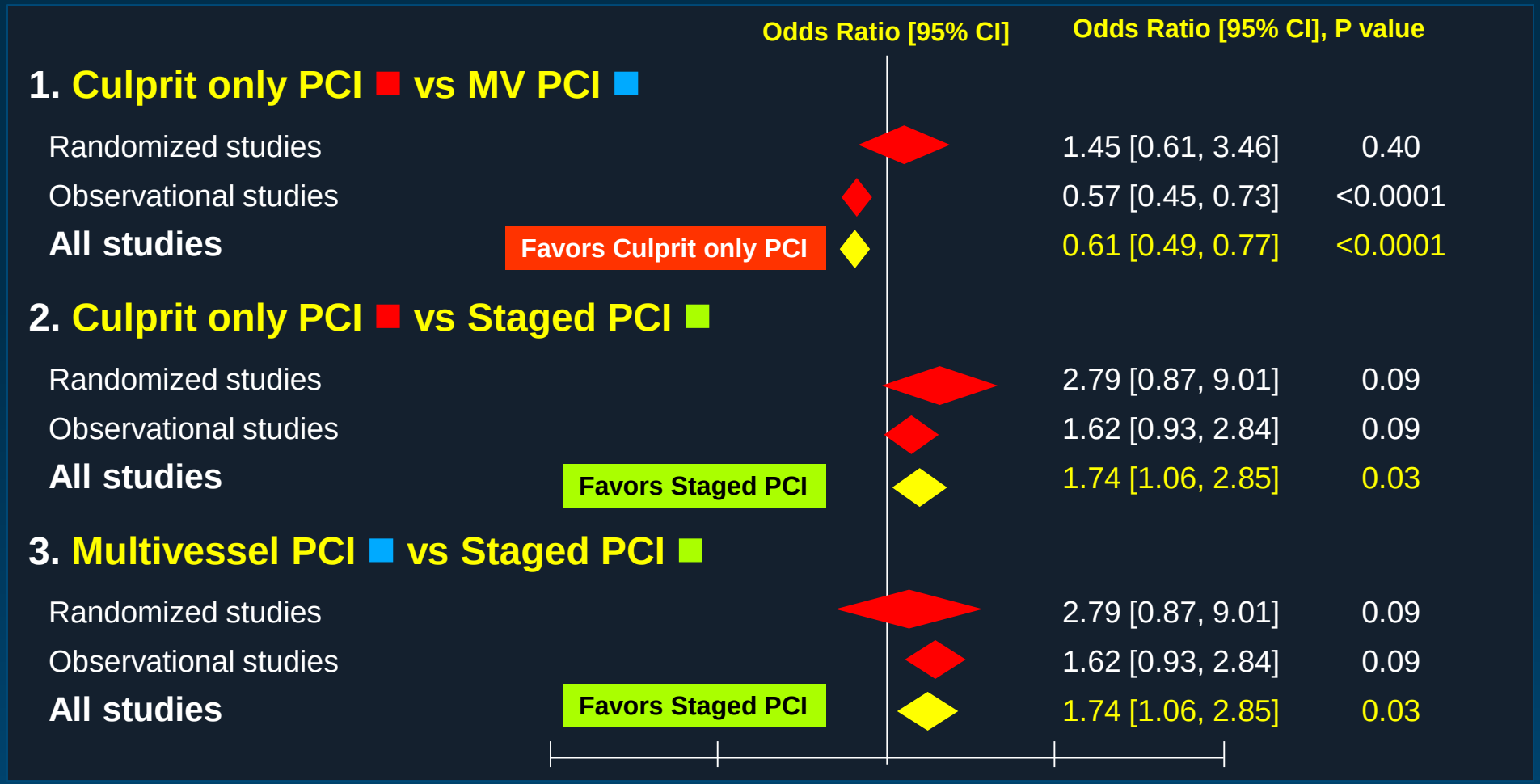
Vlaar PJ, et al. J Am Coll Cardiol. 2011;58:692-703

Long-Term Death by Strategy for non-IRA

Pairwise meta-analyses from 4 prospective and 14 retrospective studies involving 40,280 patients



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Vlaar PJ, et al. J Am Coll Cardiol. 2011;58:692-703

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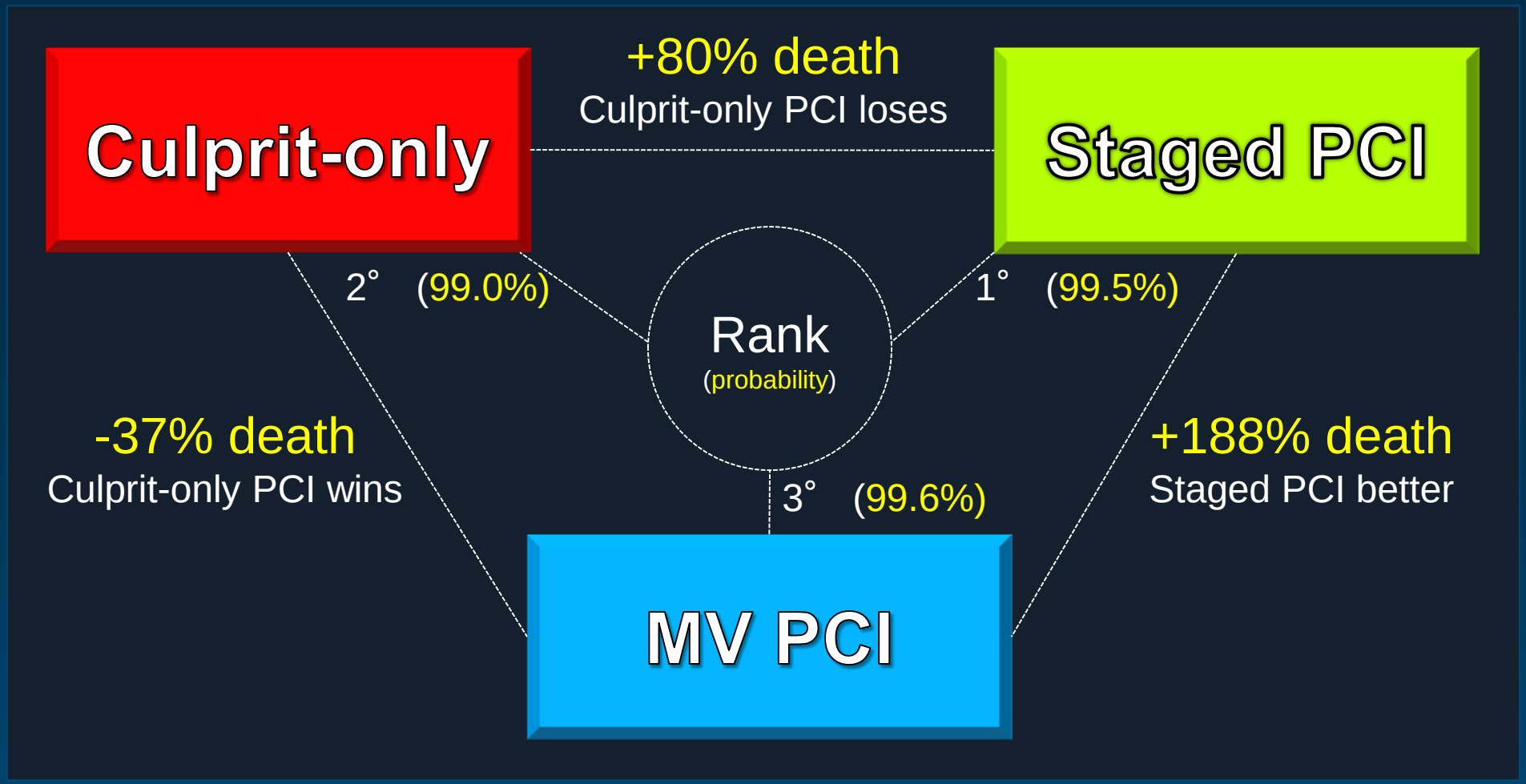
Culprit-only vs MV vs Staged PCI

Network meta-analysis from 4 prospective and 14 retrospective studies involving 40,280 patients



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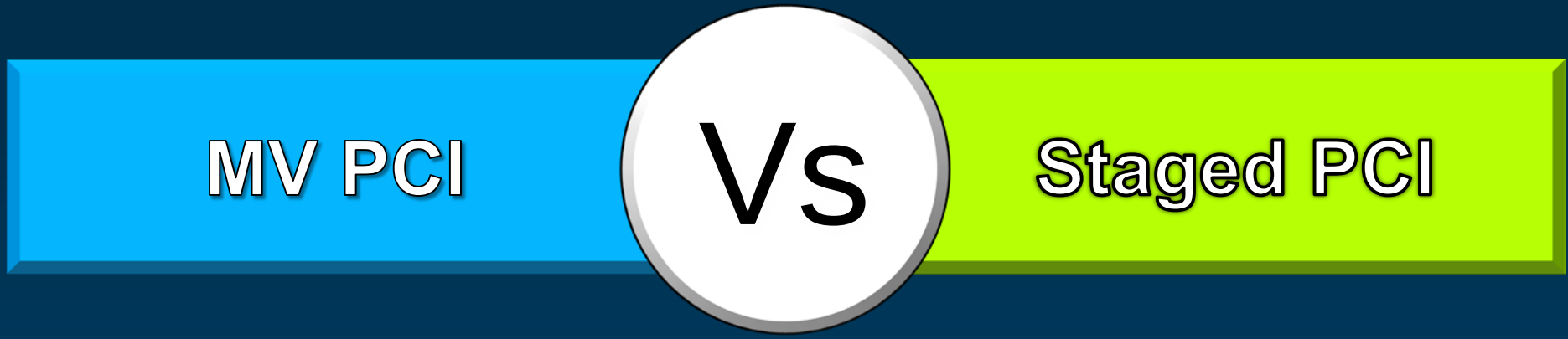
Vlaar PJ, et al. J Am Coll Cardiol. 2011;58:692-703

Dealing with Non-IRA after Primary PCI

Question #2. Based on Evidence before should we prefer staged non-IRA PCI over immediate MV PCI?

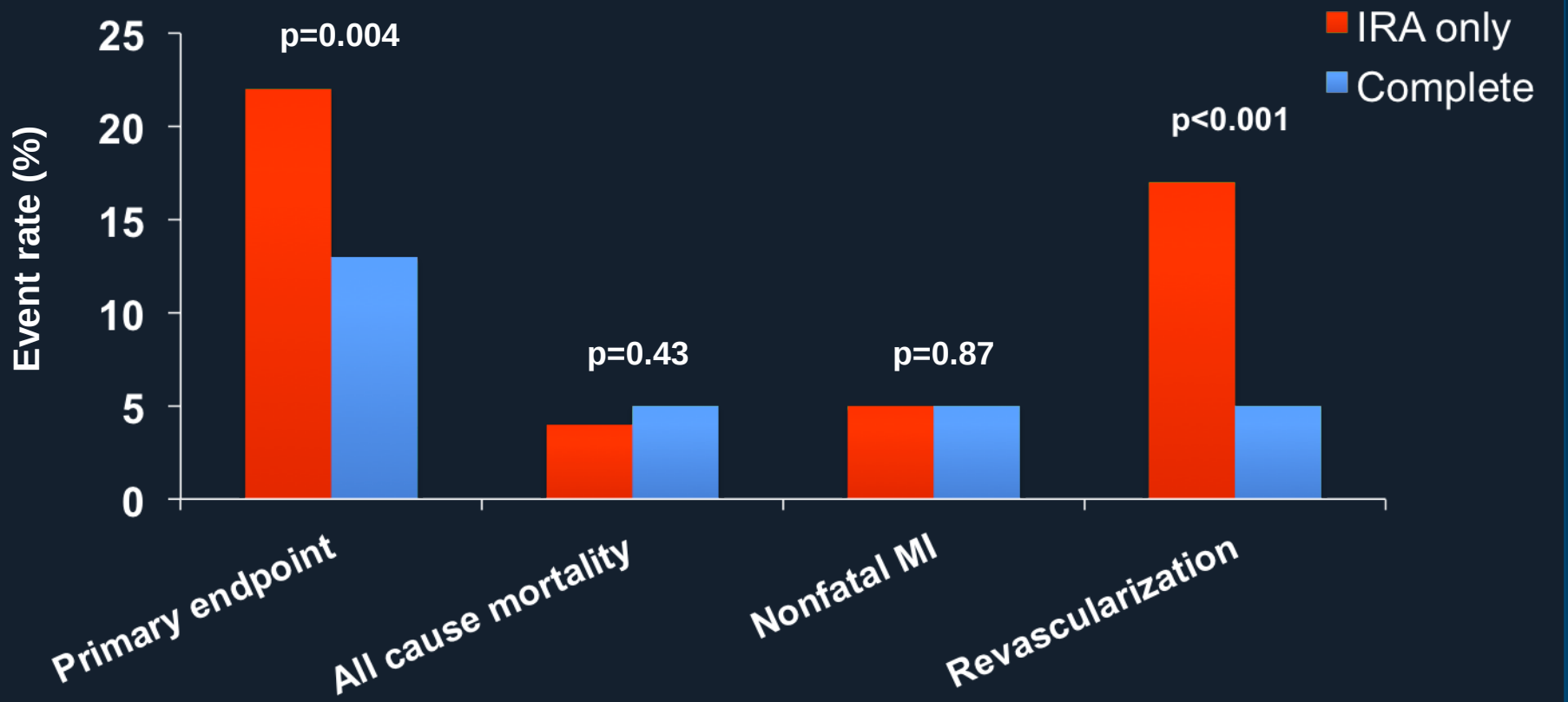


Probably yes. MV PCI increased mortality in a large meta-analysis.

PRAMI and CVLPRIT did not directly address this issue.

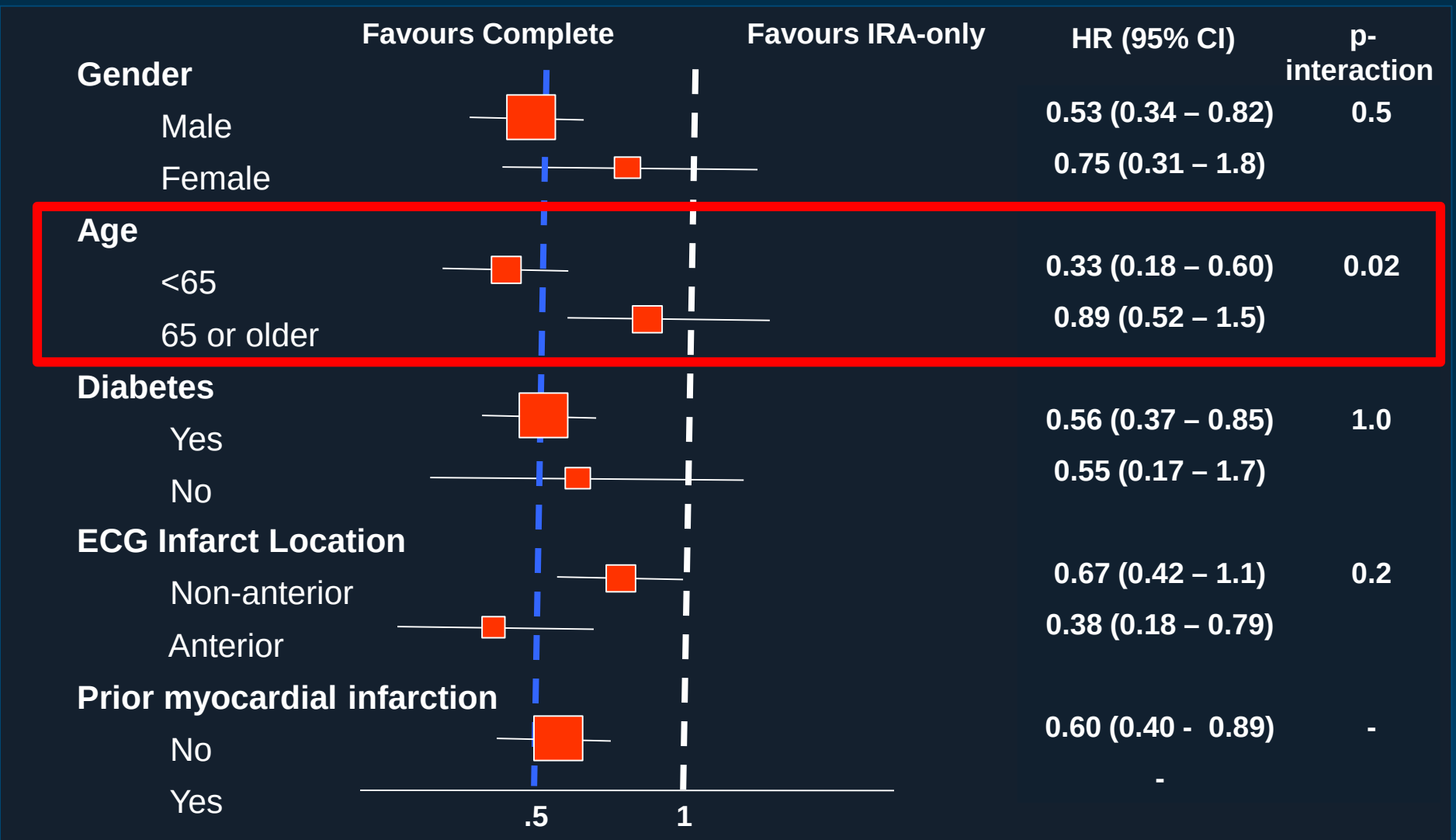
DANAMI3-PRIMULTI Trial

627 patients randomized to FFR-guided revascularization of non-IRA stenoses (n= 314) or IRA-only PCI (n= 313). Complete revascularization performed in a staged procedure within index hospitalization.



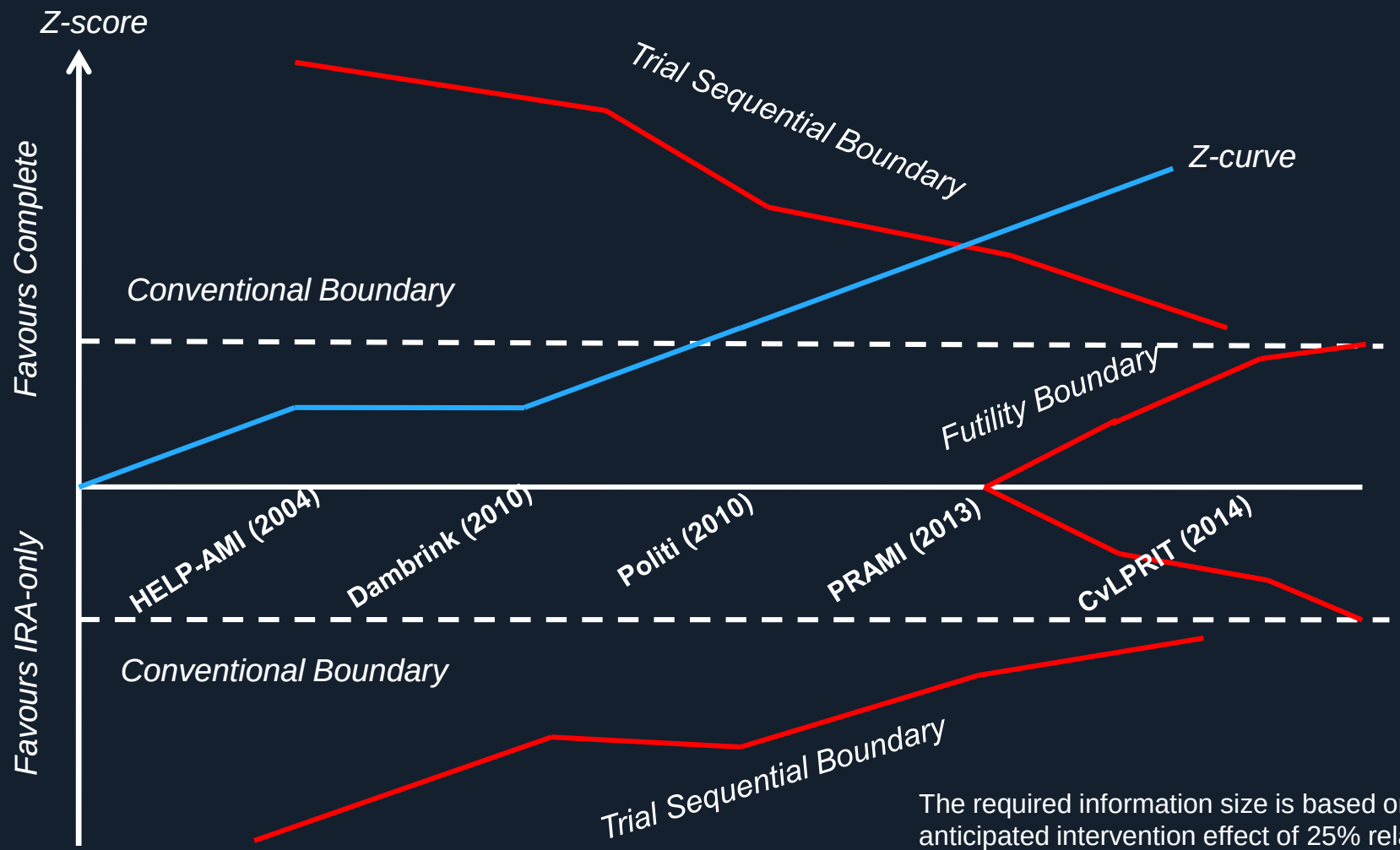
Engstrøm et al. Lancet 2015; 386(9994):665-71

DANAMI3-PRIMULTI Trial – Subgroup analysis



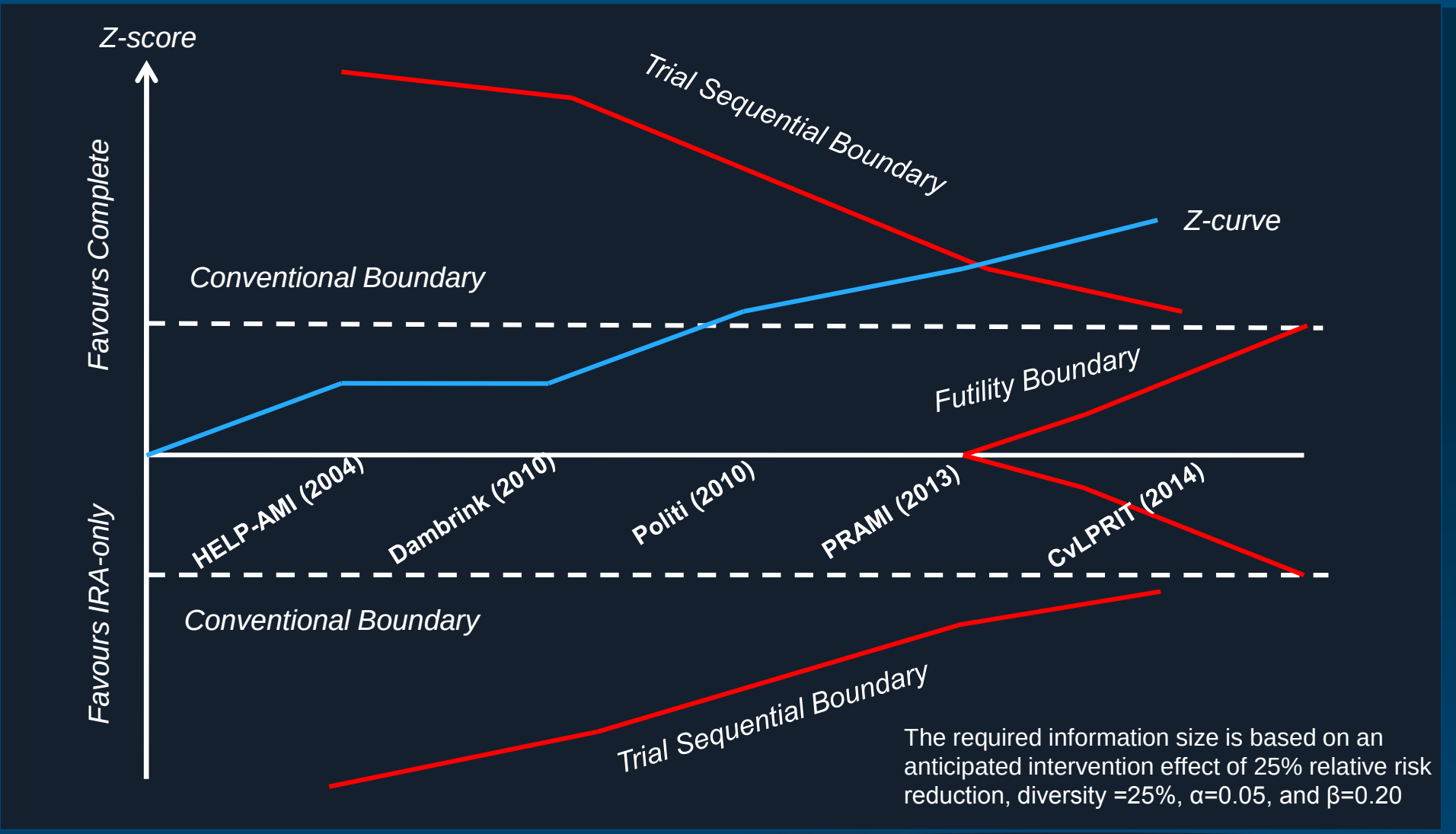
Engstrøm et al. Lancet 2015; 386(9994):665-71

Trial sequential analysis: MACE



The required information size is based on an anticipated intervention effect of 25% relative risk reduction, diversity =25%, α=0.05, and β=0.20

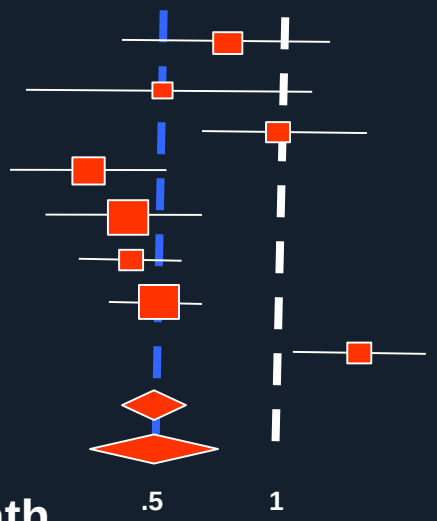
Trial sequential analysis: Repeat revascularization



An updated meta-analysis of available RCTs

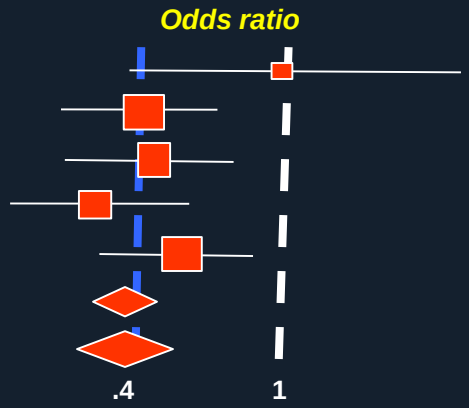
MACE

Study	Events CR	Total CR	Events IRA	Total IRA	OR (95% CI)
Ochala et al.	10	48	12	44	0.70 (0.27; 1.84)
HELP-AMI	11	52	6	17	0.49 (0.15; 1.63)
Dambrink et al.	17	80	9	41	0.96 (0.38; 2.39)
Politi et al.	28	130	42	84	0.27 (0.15; 0.50)
PRAMI	21	234	53	231	0.33 (0.19; 0.57)
CvLPRIT	15	150	31	146	0.41 (0.21;0.80)
DANAMI3-PRIMULTI	40	314	68	313	0.53 (0.34; 0.81)
PRAGUE 13	17	106	15	108	1.18 (0.56; 2.51)
Fixed effect model					*0.48 (0.38; 0.61)*
Random effect model					*0.51 (0.36; 0.72)*



CV Death

Study	Events CR	Total CR	Events IRA	Total IRA	OR (95% CI)
HELP-AMI	1	52	0	17	1.02 (0.04; 26.19)
Politi et al.	6	130	10	84	0.36 (0.13; 1.03)
PRAMI	4	234	10	231	0.38 (0.12; 1.24)
CvLPRIT	2	150	7	146	0.27 (0.05; 1.31)
DANAMI3-PRIMULTI	5	314	9	313	0.55 (0.18; 1.65)
Fixed effect model					*0.41 (0.23; 0.73)*
Random effect model					*0.41 (0.23; 0.73)*



Capranzano et al. Unpublished

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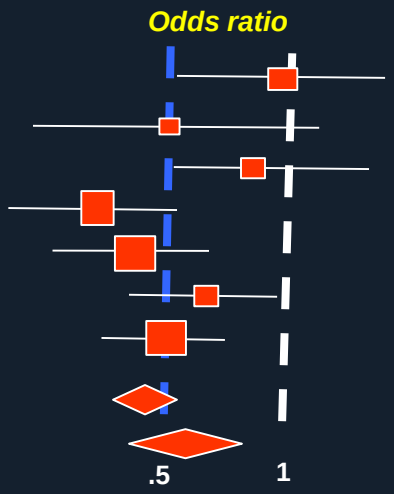
An updated meta-analysis of available RCTs

Revascularization

Study	*Events CR*	*Total CR*	*Events IRA*	*Total IRA*	*OR (95% CI)*
Ochala et al.	11	48	10	*44*	1.01 (0.38; 2.68)
HELP-AMI	9	52	6	17	0.38 (0.11; 1.31)
Dambrink et al.	15	80	9	41	0.82 (0.32; 2.08)
Politi et al.	14	130	28	84	0.24 (0.12; 0.49)
PRAMI	16	234	46	231	0.30 (0.16; 0.54)
CvLPRIT	8	150	16	146	0.46 (0.19; 1.11)
DANAMI3-PRIMULTI	15	314	45	313	0.30 (0.16; 0.55)
Fixed effect model					***0.48 (0.38; 0.61)***
Random effect model					***0.51 (0.36; 0.72)***



Additional analysis:	Pooled ORs	95% CI	p-value
All-cause death	0.75	(0.51 – 1.12)	
Myocardial infarction	0.74	(0.49 – 1.12)	

Statistical analysis: An intention-to-treat meta-analysis was performed in line with recommendations from the Cochrane Collaboration and the PRISMA Statement. Pooled estimates of odd ratios (ORs) with their 95% confidence intervals (CIs) were calculated using the inverse variance weighting method. Random-effects model for OR estimation was obtained with the DerSimonian–Laird method. Random-effects results were then confirmed with a fixed-effect model. All analyses were conducted using the "meta" package implemente in R (vers 3.2.1).

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Safety of complete revascularization

A complete revascularization strategy is associated with:

Increased use of contrast agents
*Weighted mean difference 85.12 ml (95% CI 70.41 – 99.83)**

Longer procedural times
*Weighted mean difference 16.42 min (95% CI 13.22 – 19.63)**

CIN incidence was not different among the two revascularization modalities
*RR=0.65, (*95% CI 0.24–1.74)*

Stent thrombosis had not significant differences between CR and IRA-only PCI groups in PRAMI trial

***Bangalore et al. Circ. Intv. 2015; 8(4): e002142.**

COMPLETE Trial: Study Design

A randomized, comparative effectiveness study of complete versus culprit-only revascularization strategies to treat multi-vessel disease after 1⁰ PCI for STEMI

STEMI with successful PCI for STEMI (primary, rescue or pharmacoinvasive) + ≥ 70% stenosis or ≥ 50% with FFR < 0.80

RANDOMIZED
Within 72 h of index STEMI PCI

COMPLETE REVASC
Staged PCI of all suitable non-culprit lesions (< 45 d)
N=1950

CULPRIT LESION-ONLY REVASC
No further revsac of non-culprit lesions (OMT Alone)
N=1950

ALL patients receive OMT (ASA, Ticagrelor, Statin, Beta Blocker, RF Modification)

Follow-up: Discharge, 30 Days, 6 mos, then Annually (avg. duration = 4 yrs)

Primary Outcome: CV Death / MI
Key Secondary Outcome: CV Death/MI/Ischemia driven revascularization

Randomization stratified for intended timing of PCI: within vs after initial hospitalization

Guidelines and complete revascularization

European Guidelines - STEMI

Recommendations	Class	Lev.
Primary PCI should be limited to the culprit vessel with the exception of cardiogenic shock and persistent ischaemia after PCI of the supposed culprit lesion	IIa	B
Staged revascularization of non-culprit lesions should be considered in STEMI patients with multivessel disease in case of symptoms or ischaemia within days to weeks after primary PCI	IIa	B

Windecker et al. EHJ 2014; **35(37):2541-619**

Closing remarks

1. The benefit of complete rev in ACS was mostly driven by repeat rev, including urgent rev. Possible mortality benefit in meta-analysis?
2. **Staged complete rev** might be probably the optimal option (confirmation data is needed .
3. Several factors may guide the operator to adopt a certain strategy over another for a given patient (i.e., age, clinical state, estimated ischemic burden, risk of the procedure, length of the procedure, contrast load and operator experience). **Decisions based on the individual patient remain the rule.**
4. **Possible role of FFR or other imaging techniques?**