Which Patients with Stable CAD Benefit from PCI in the Post-ISCHEMIA Era?

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ISCHEMIA

Relevant Financial Disclosures

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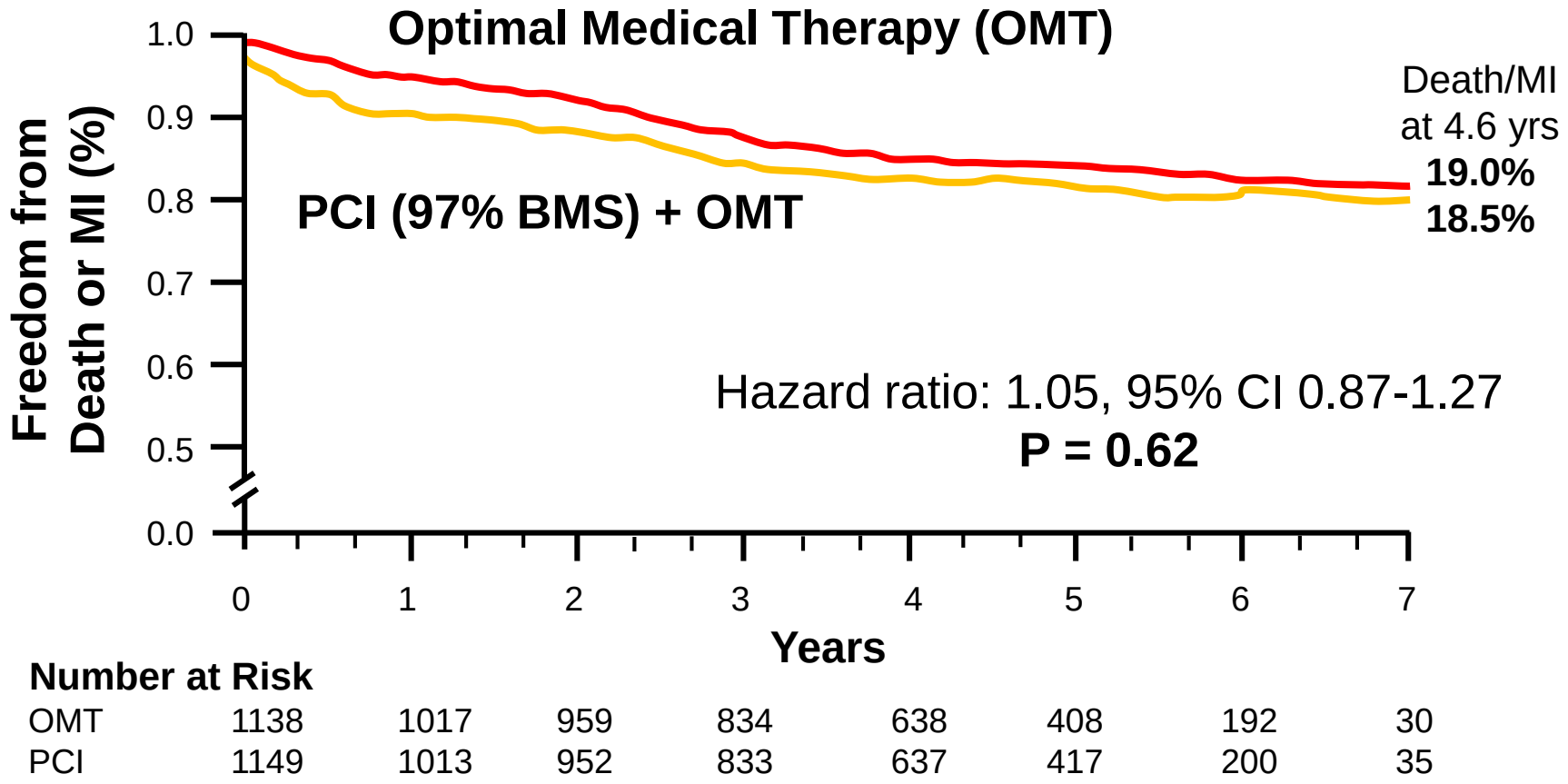
Mount Sinai receives research funding from Abbott

PCI relieves symptoms and improves quality of life,
but does PCI prevent death or MI?

PCI (BMS) in Stable CAD: COURAGE (n=2,287)

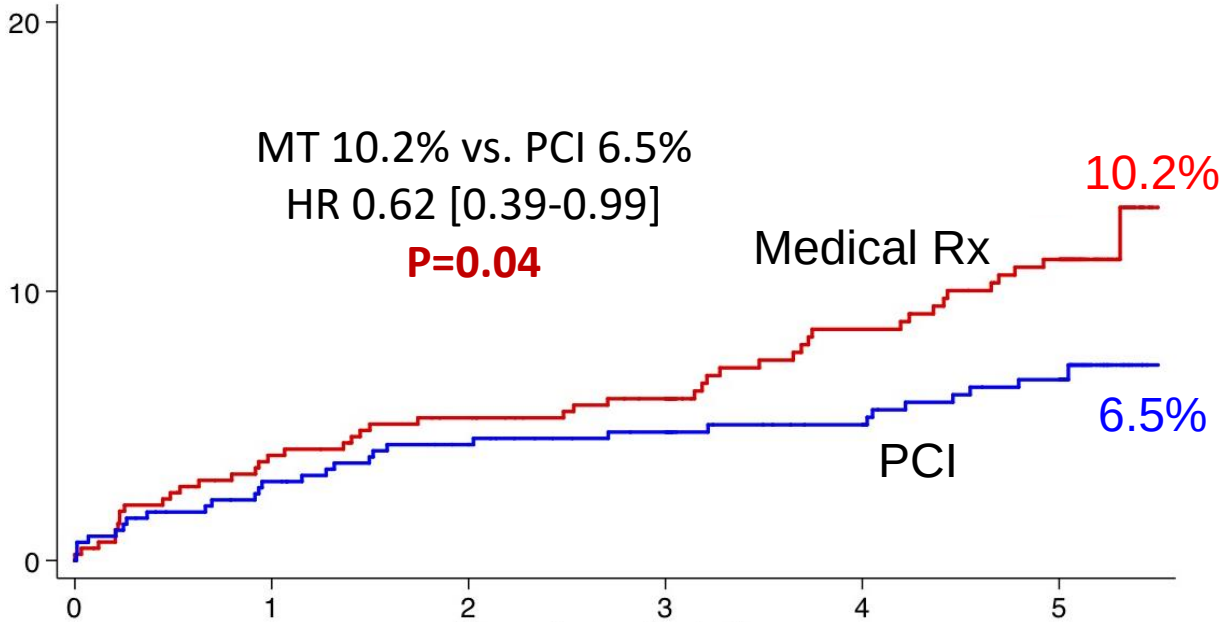


Boden WE et al. NEJM 2007;356:1503-16

FAME 2: 5-year Results

888 pts with stable CAD and 1V, 2V or 3VD w/FFR ≤0.80 randomized to DES vs. MT

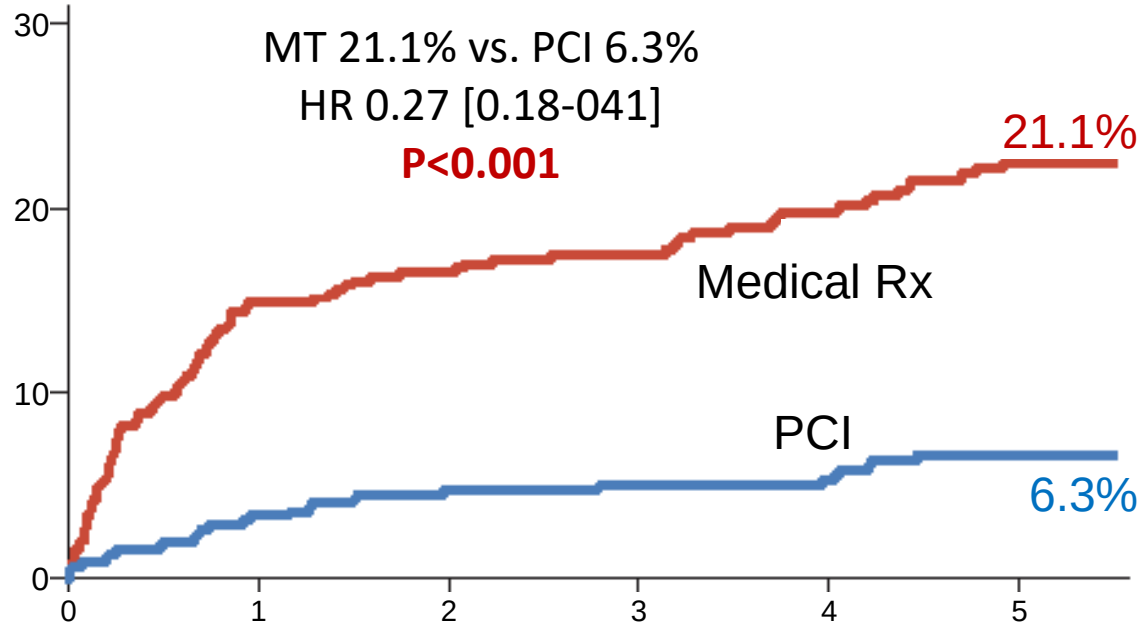
Spontaneous MI



N at risk

MT	441	415	405	394	319	306
PCI	447	428	416	405	345	333

Urgent revascularization

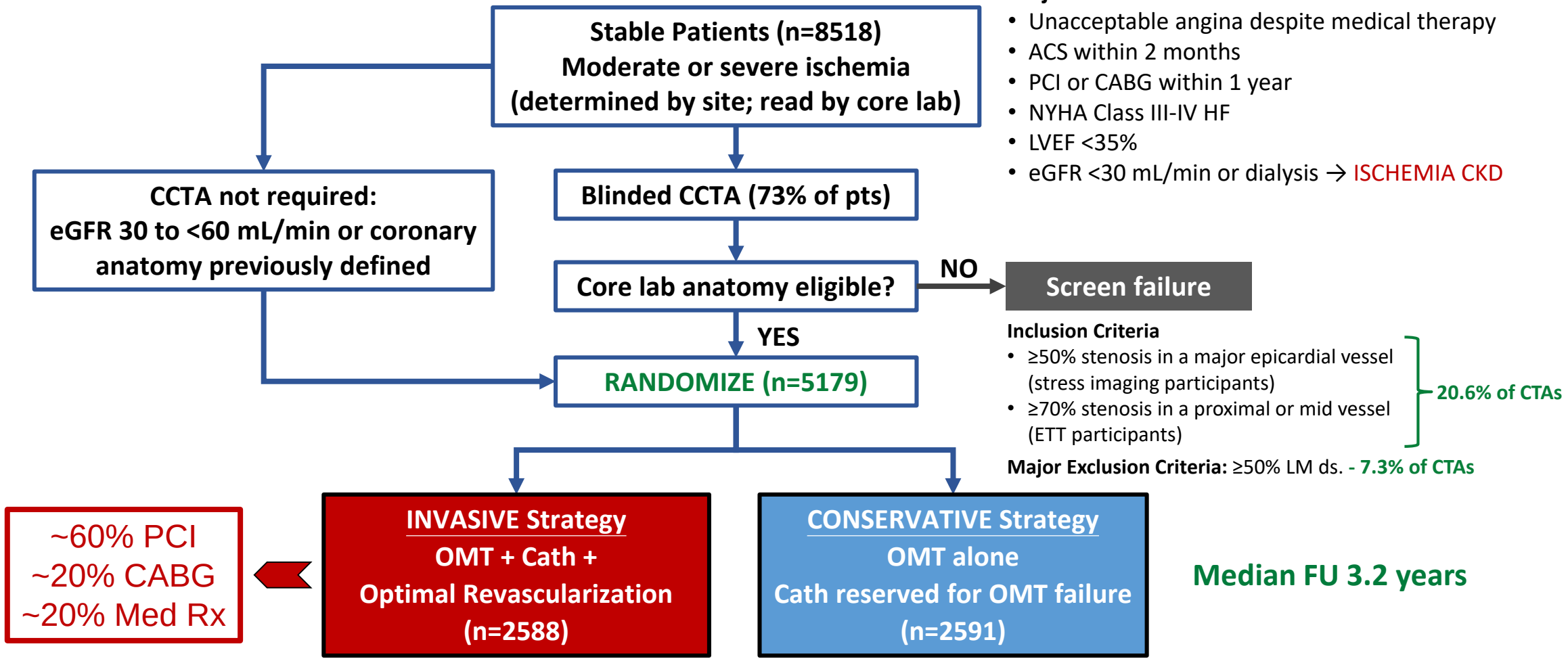


N at risk

MT	441	367	357	345	276	264
PCI	447	424	412	402	344	332

Xaplanteris P et al. NEJM 2018;379:250-9. van Nunen LX et al Lancet. 2015;386:1853-60

ISCHEMIA Trial: Patient Flow (n=5179 randomized)

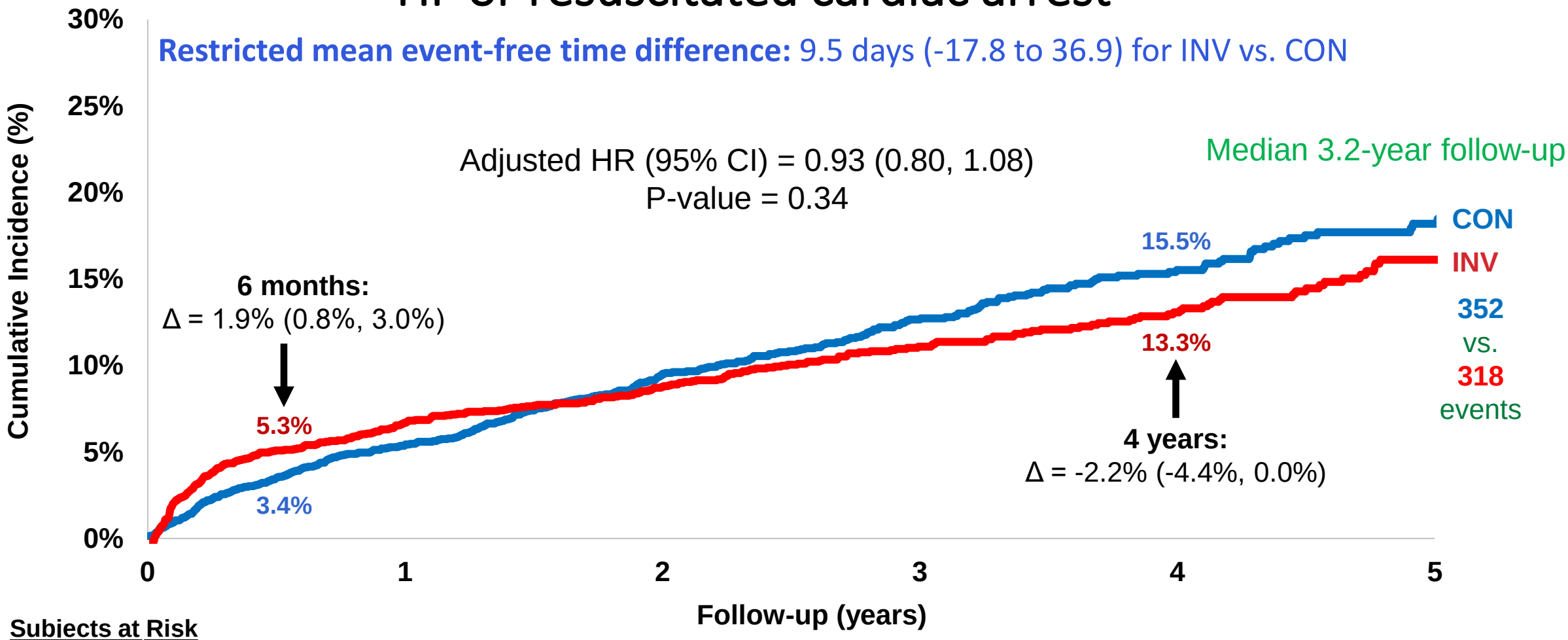


Primary outcome: CV death, MI, hospitalization for resuscitated cardiac arrest, HF or UA

Maron DJ et al. N Engl J Med. 2020;382:1395-1407

ISCHEMIA

ISCHEMIA Primary Outcome: CV Death, MI, hospitalization for UA, HF or resuscitated cardiac arrest



Subjects at Risk

CON	2591	2431	1907	1300	733	293
INV	2588	2364	1908	1291	730	271

Maron DJ et al. N Engl J Med. 2020;382:1395-1407

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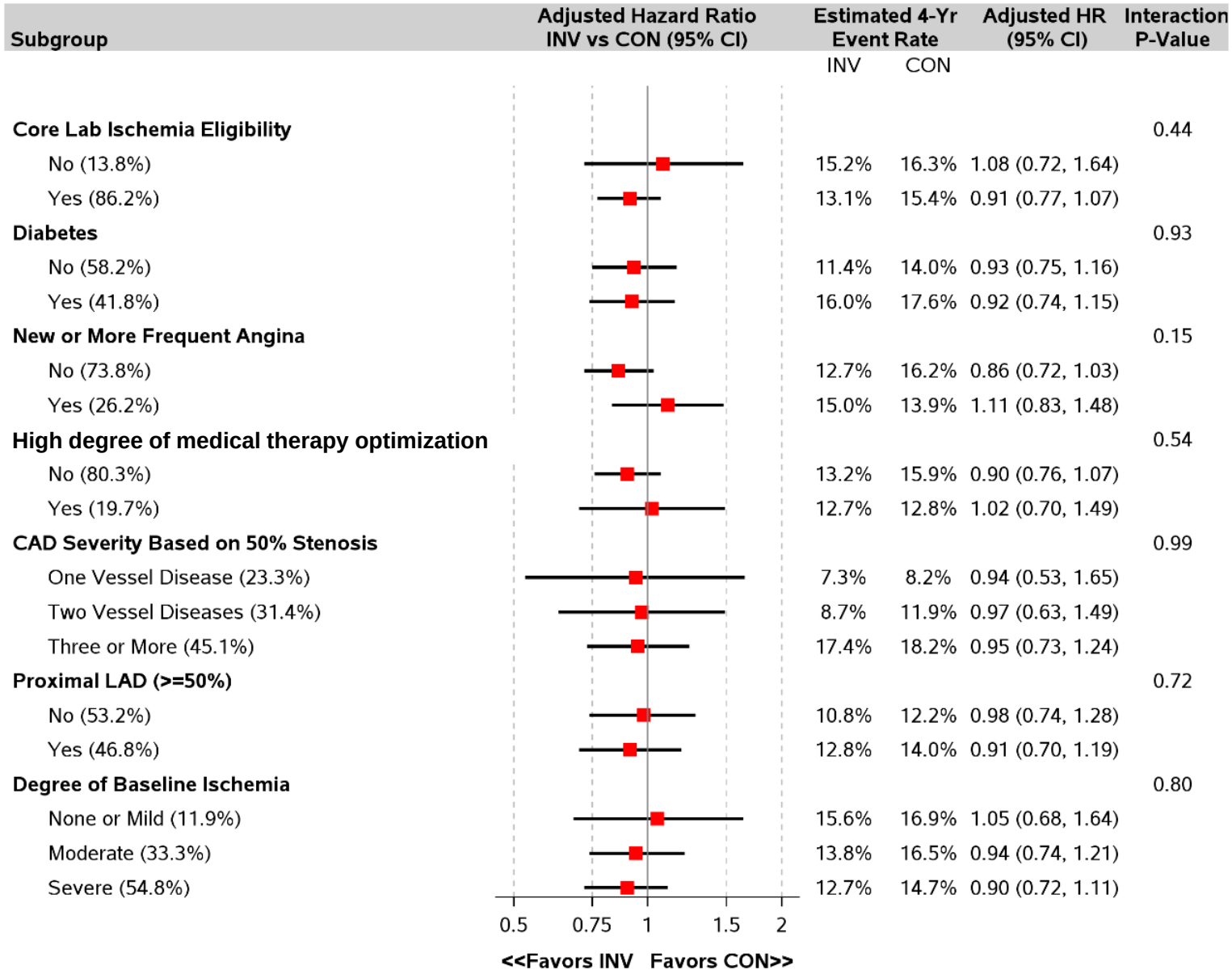
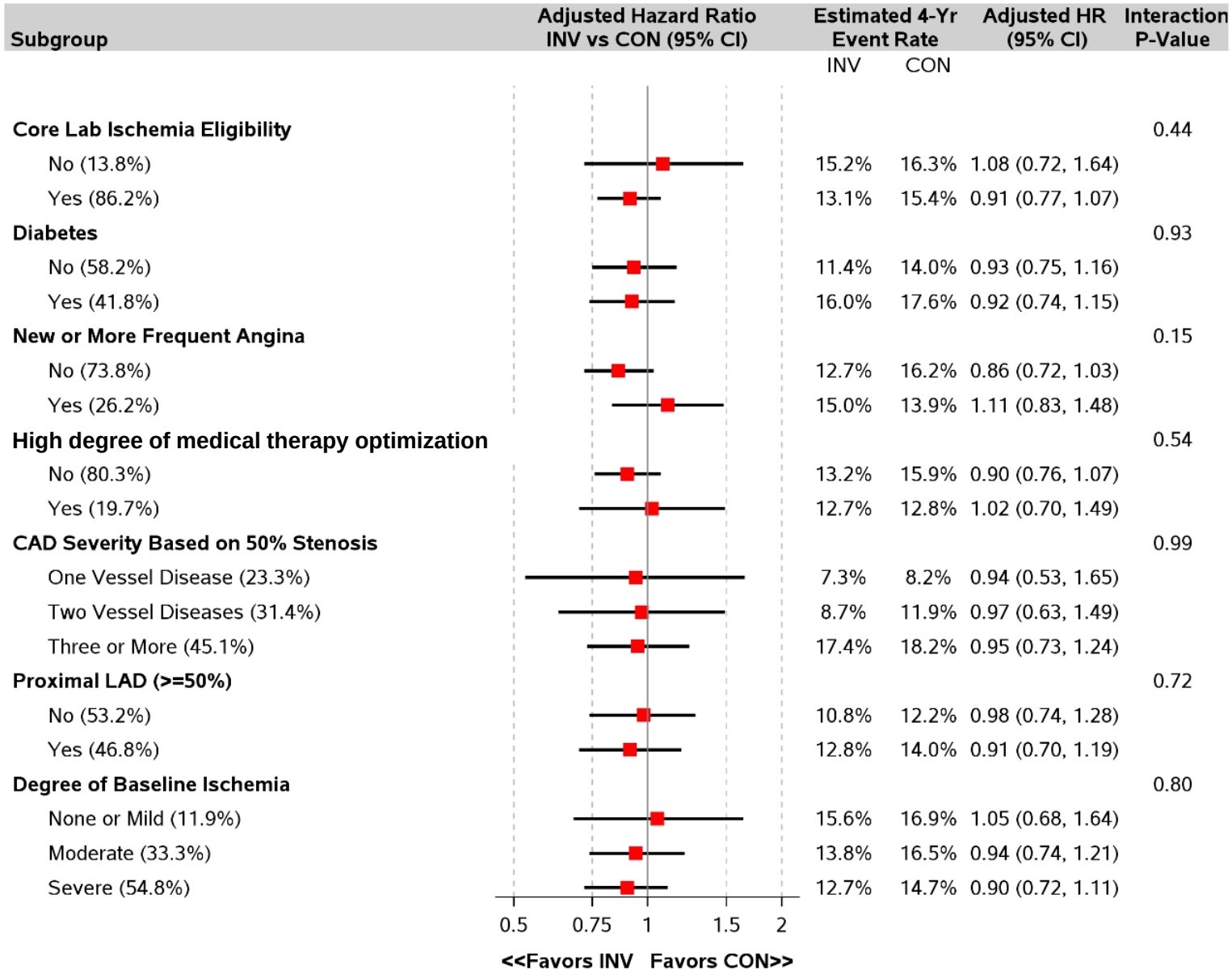
Primary endpoint: Pre-specified Important Subgroups

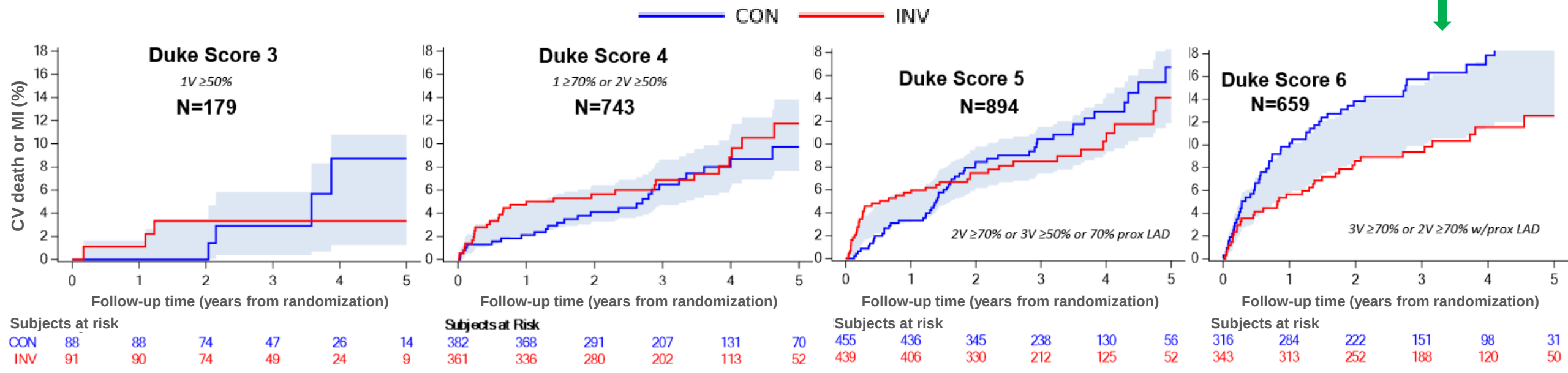


Primary endpoint: Pre-specified Important Subgroups



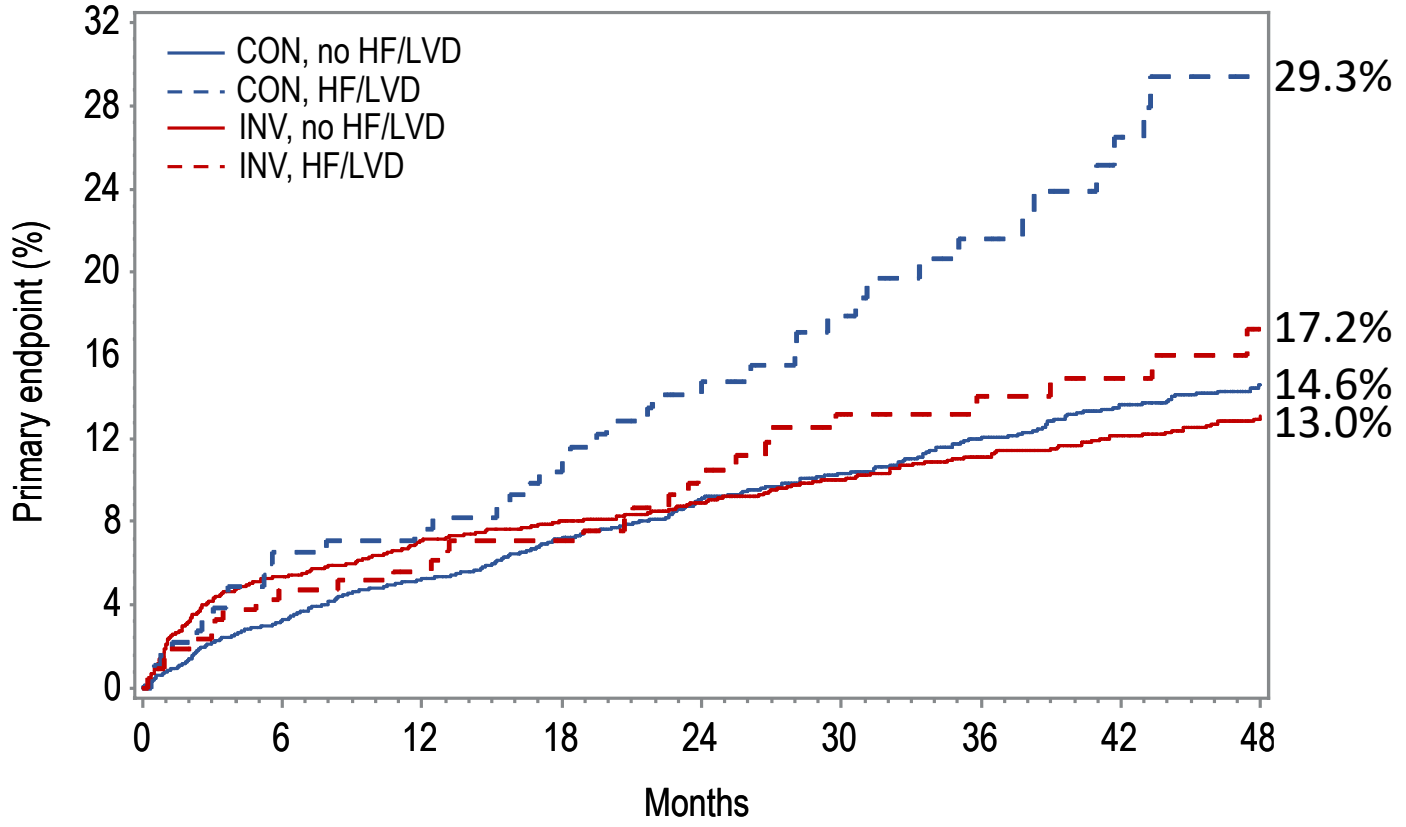
Outcomes According to the Extent of CAD on CTA

	Events, n		4-y event rate, %			
	Invasive strategy	Conservative strategy	Invasive strategy	Conservative strategy	Difference (95% CI), %	Interaction *P* value
Cardiovascular death or myocardial infarction						0.33
1-Vessel CAD ≥50% (N=179)	3	4	3.3 (0.9 to 8.6)	8.7 (2.5 to 19.9)	–5.4 (–14.9 to 4.2)	
1-Vessel CAD ≥70% or 2-vessel ≥50% (N=743)	26	25	8.8 (5.7 to 12.8)	8.7 (5.6 to 12.5)	0.2 (–4.7 to 5.1)	
2-Vessel CAD ≥70% or 3-vessel ≥50% or 70% proximal LAD (N=894)	38	48	10.2 (7.2 to 13.9)	12.8 (9.5 to 16.7)	–2.6 (–7.5 to 2.3)	
3-Vessel CAD ≥70% or 2-vessel ≥70% including proximal LAD (N=659)	34	50	11.6 (8.1 to 15.7)	17.9 (13.4 to 22.8)	–6.3 (–12.4 to –0.2)	



Reynolds HR et al. Circulation. 2021;144:1024-38

398 Patients (7.7%) had LVEF 35% - <45% or Prior HF



LVD or prior HF

Difference [95% CI] =

12.1% [1.6%, 22.6%]

No LVD or prior HF

Difference [95% CI] =

1.6% [-0.7%, 3.8%]

$P_{interaction}$=0.055

Subjects at risk

CON, no HF/LVD	2404	2311	2260	2114	1781	1469	1222	947	690
CON, HF/LVD	184	172	169	156	124	98	77	56	43
INV, no HF/LVD	2372	2218	2164	2040	1764	1455	1189	913	670
INV, HF/LVD	214	203	199	185	143	121	103	84	63

Lopes RD et al. Circulation. 2020;142:1725–35

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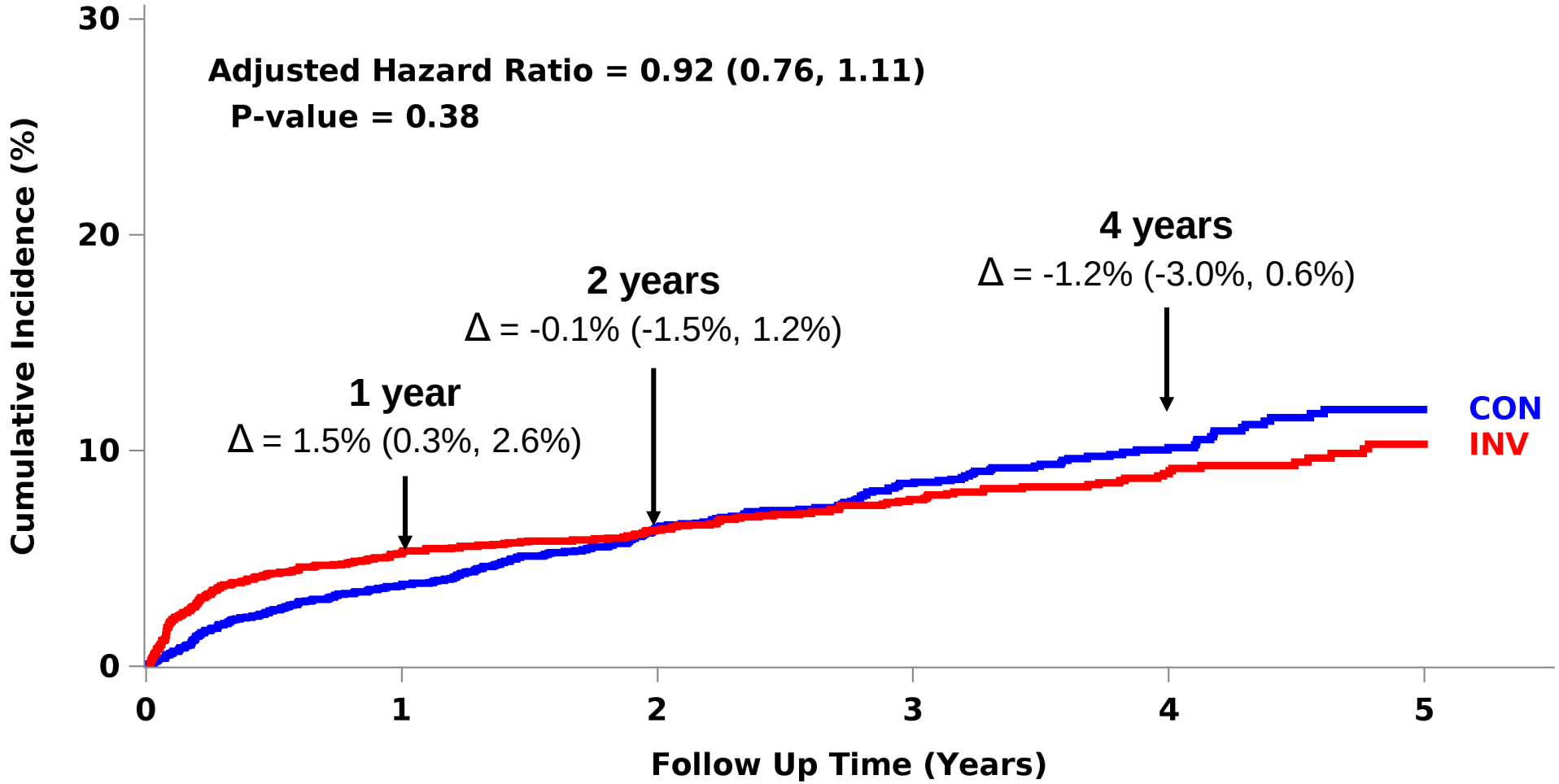
ISCHEMIA: Myocardial Infarction



Subjects at Risk

CON	2591	2452	1931	1321	747	298
INV	2588	2379	1931	1313	742	283

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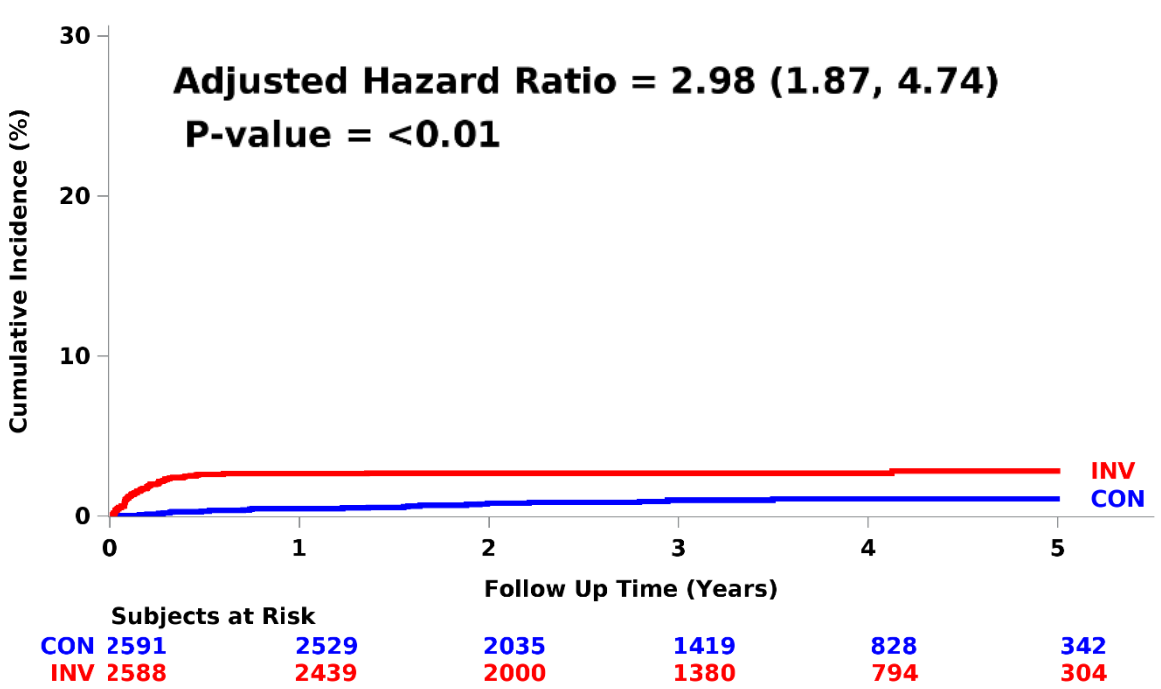
ISCHEMIA: Myocardial Infarction

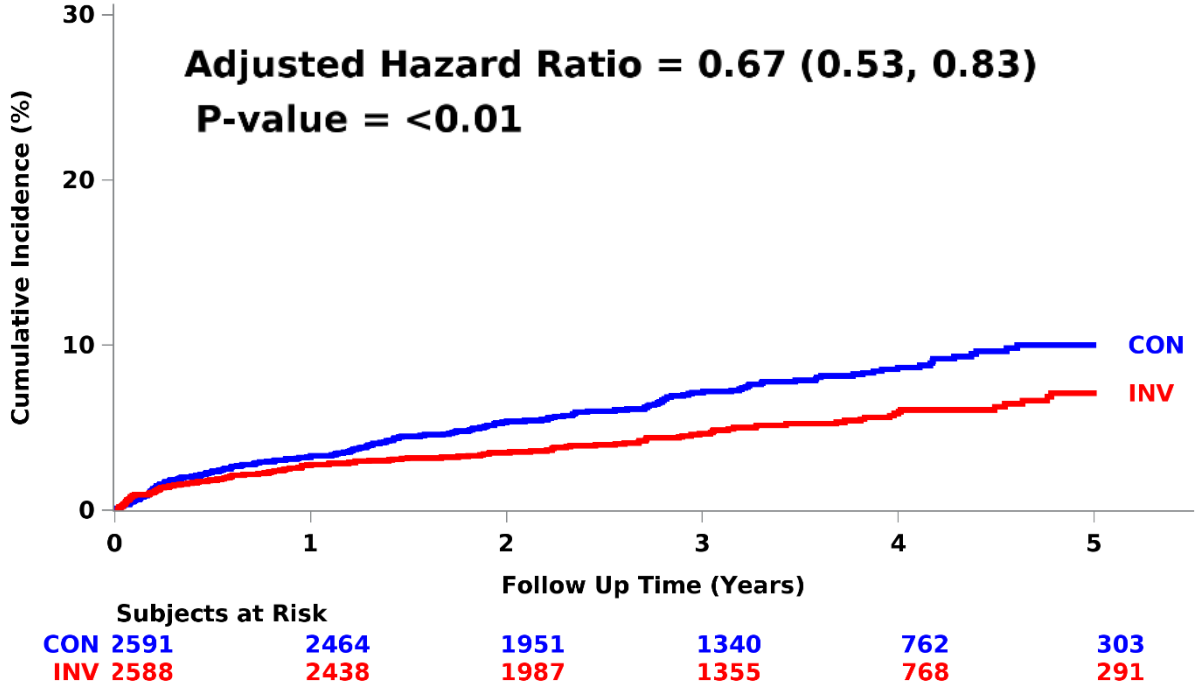
Procedural MI

Types 4a or 5 MI



Non-procedural MI

Types 1, 2, 4b, or 4c MI



Maron DJ et al. N Engl J Med. 2020;382:1395-1407

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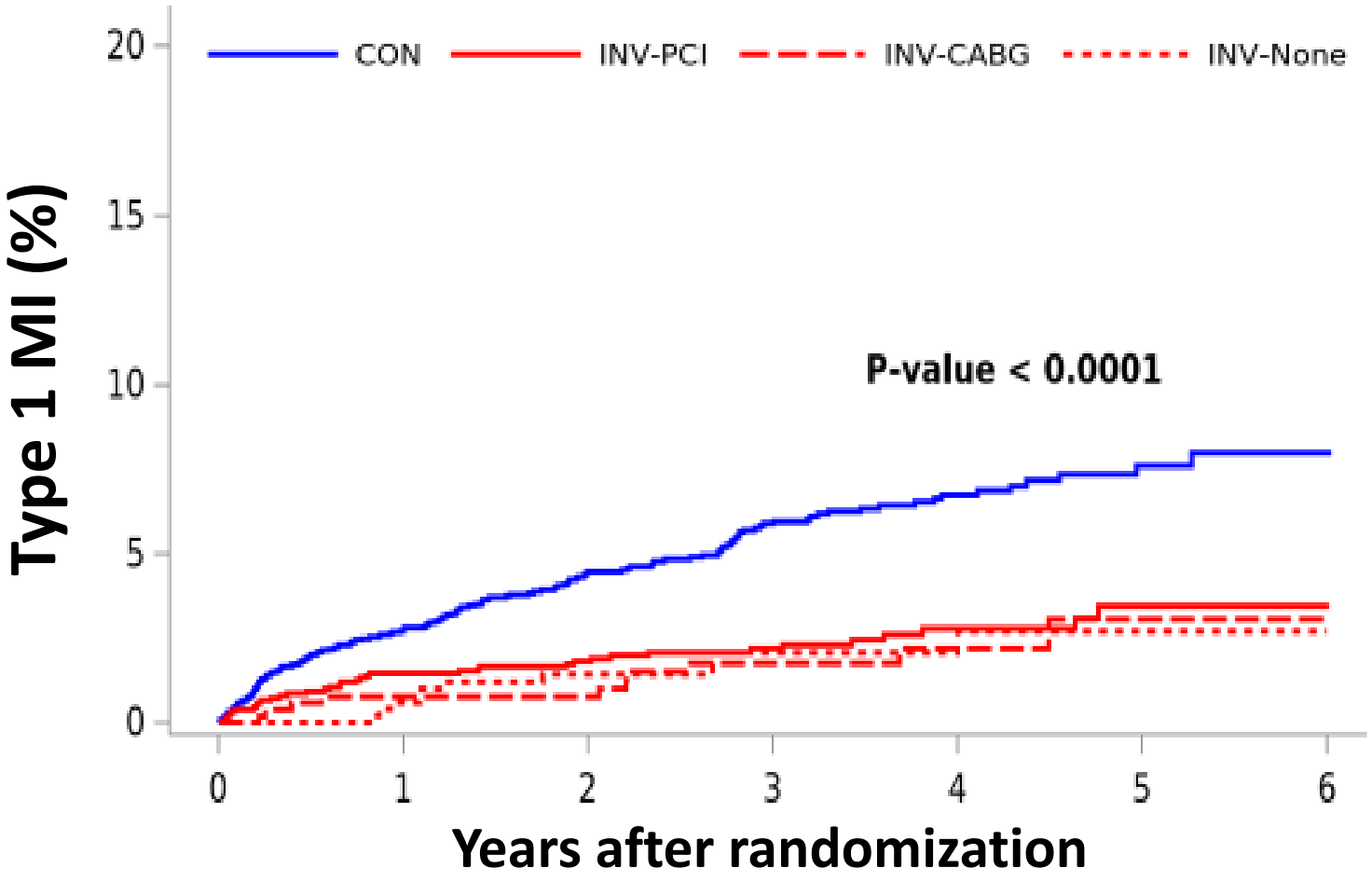
ISCHEMIA: Spontaneous Type 1 MI by Strategy

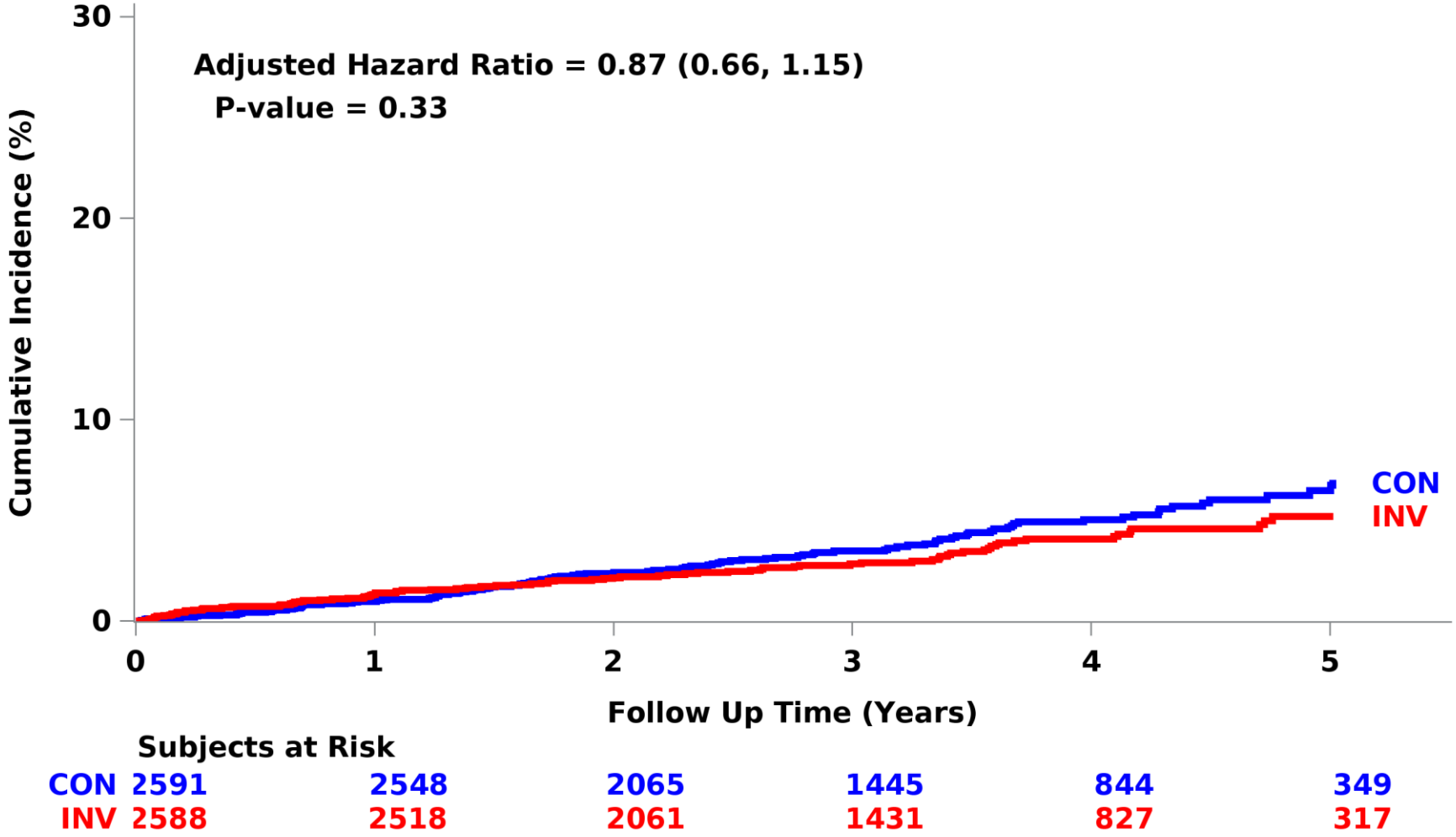


- Spontaneous type 1 MI were significantly reduced with the invasive strategy
- Effect was present after PCI and CABG (and medical Rx)

ISCHEMIA

Chaitman BR et al. Circulation 2021;143:790-804

ISCHEMIA: Cardiovascular Death

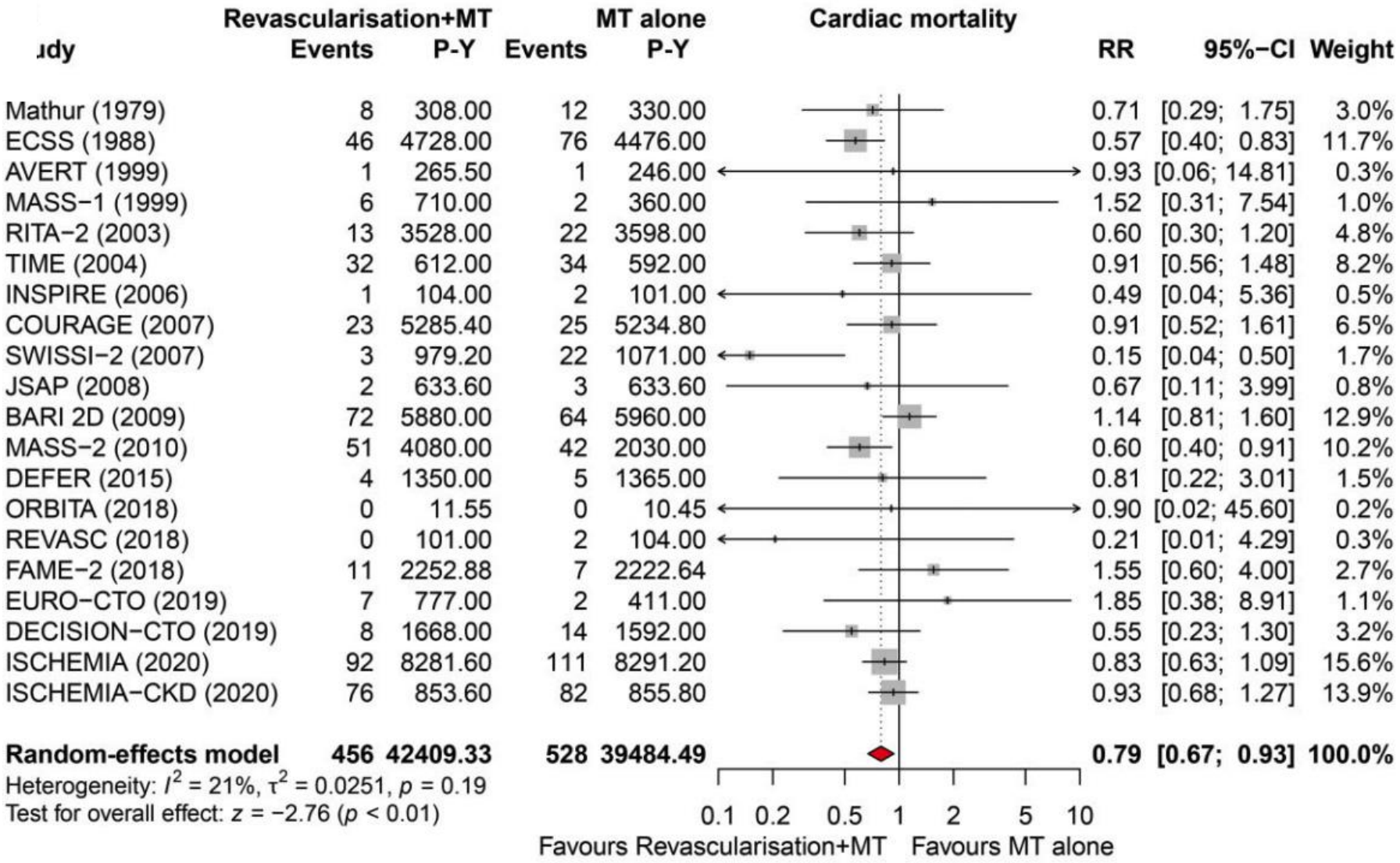


Maron DJ et al. N Engl J Med. 2020;382:1395-1407

ISCHEMIA

Largest Meta-analysis of Elective Revasc in Stable CAD

25 trials, 19,806 pts rand to PCI/CABG vs MT, mean 5.7-year FU



Cardiac death reduced 21%

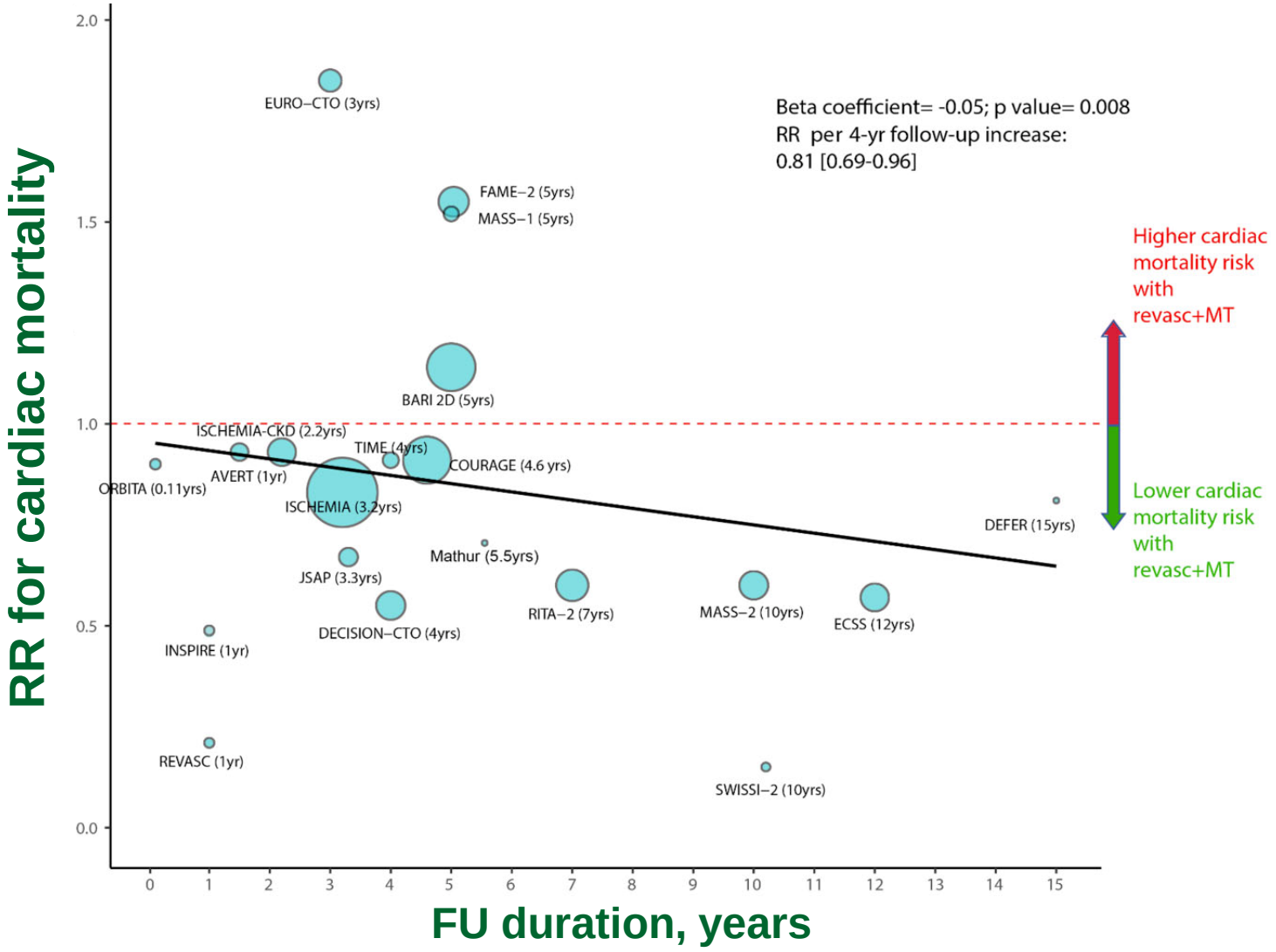
(95% CI 7% - 33%)

I^2=21%

Navarese E et al. *EHJ* 2021;42:4638–51

Largest Meta-analysis of Elective Revasc in Stable CAD

25 trials, 19,806 pts rand to PCI/CABG vs MT, mean 5.7-year FU



The longer the FU duration, the greater the reduction in cardiac death

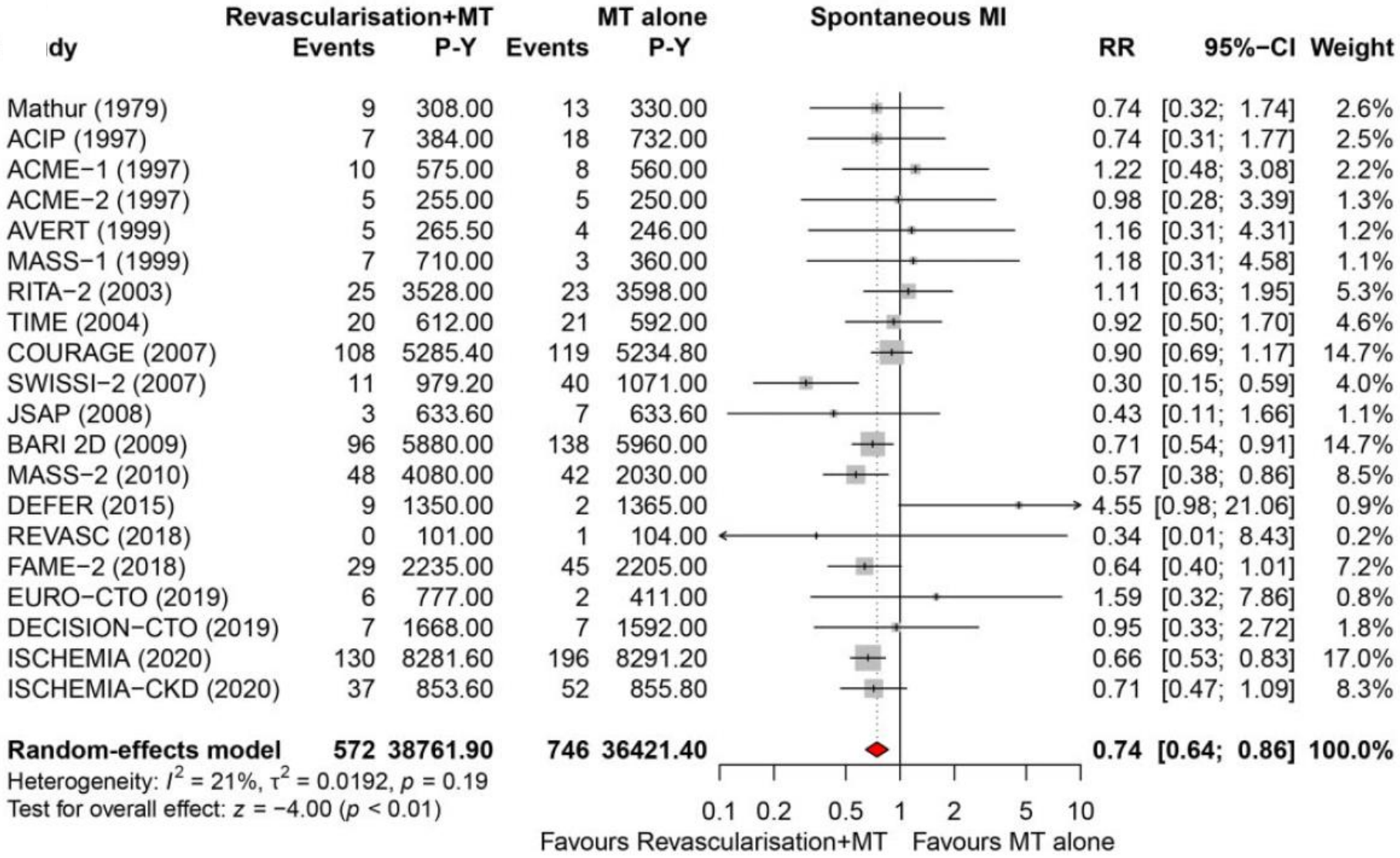
19% RRR/4-yr FU

(95% CI 4%-31%)

Navarese E et al. *EHJ* 2021;42:4638–51

Largest Meta-analysis of Elective Revasc in Stable CAD

25 trials, 19,806 pts rand to PCI/CABG vs MT, mean 5.7-year FU



Spontaneous MI reduced 26%

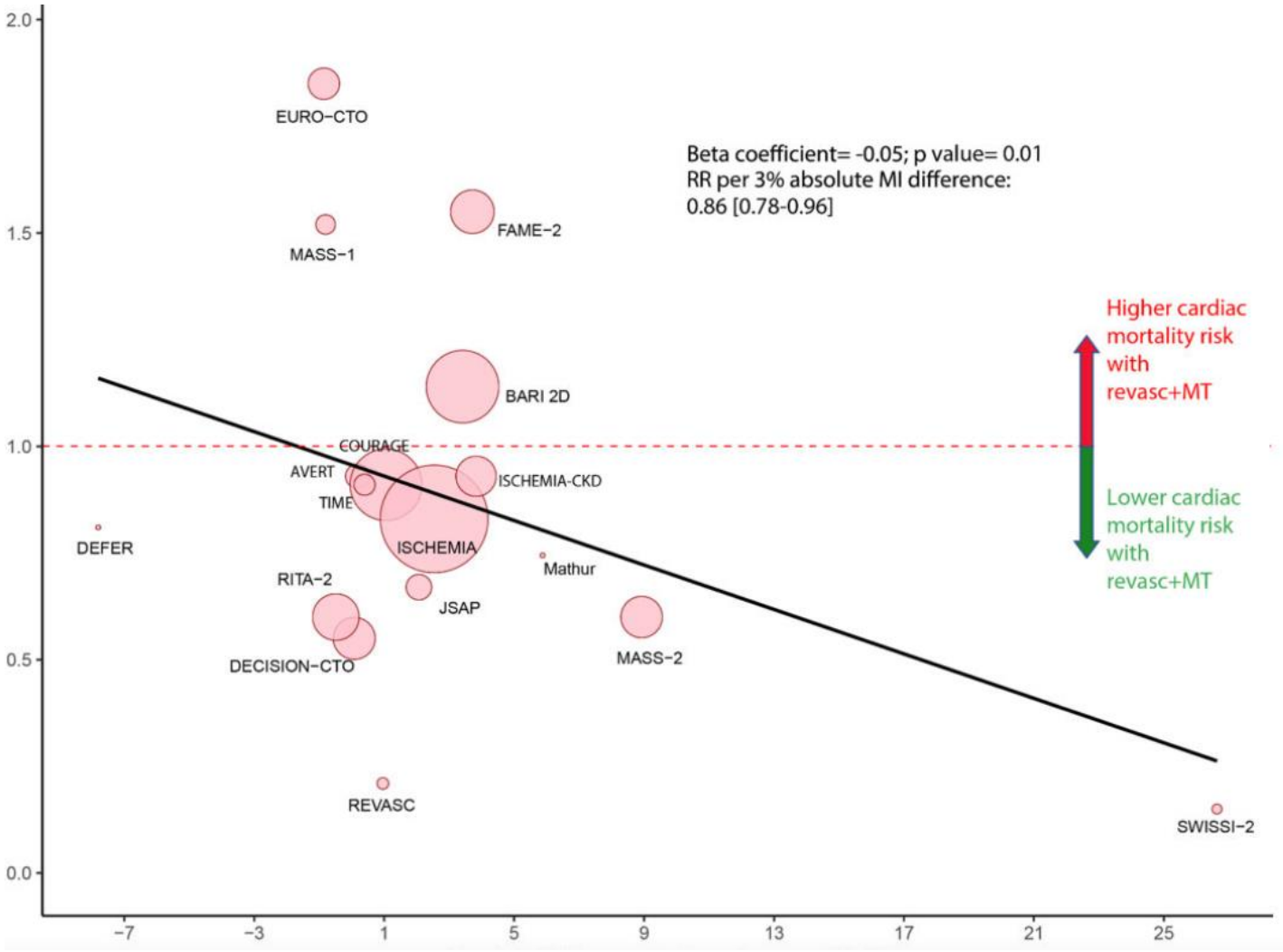
(95% CI 14% - 36%)

I^2=21%

Navarese E et al. *EHJ* 2021;42:4638–51

Largest Meta-analysis of Elective Revasc in Stable CAD

25 trials, 19,806 pts rand to PCI/CABG vs MT, mean 5.7-year FU



Relationship between reductions in spontaneous MI and cardiac death

14% RRR in CD/3% MI↓

(95% CI 4%-22%)

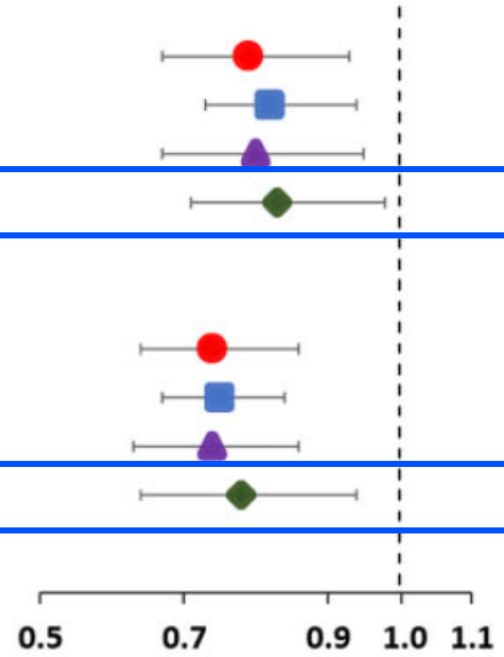
Navarese E et al. *EHJ* 2021;42:4638–51

Largest Meta-analysis of Elective Revasc in Stable CAD

25 trials, 19,806 pts rand to PCI/CABG vs MT, mean 5.7-year FU

Results consistent with PCI vs CABG, and with vs without ACS and CTO

	Revascularization + Med Rx		Med Rx alone				
Cardiac death	**Events**	**P-Y**	**Events**	**P-Y**	**RR [95% CI]**	**P-value**	
All	456	42406.3	528	39487.49	0.79 [0.67;0.93]	<0.01	21% ↓
Without post-ACS	452	41326.1	504	38312.49	0.82 [0.73;0.94]	<0.01	18% ↓
Without CTO	441	39860.3	510	37380.49	0.80 [0.67;0.95]	<0.01	20% ↓
Without CABG	273	26700.3	332	26331.49	0.83 [0.71;0.98]	0.03	17% ↓
Spontaneous MI							
All	572	38610.7	746	36259.4	0.74 [0.64;0.86]	<0.01	26% ↓
Without post-ACS	565	37782.7	708	35350.4	0.75 [0.67;0.84]	<0.01	25% ↓
Without CTO	563	36215.9	738	34314.4	0.74 [0.63;0.86]	<0.01	26% ↓
Without CABG	412	27783.9	550	27741.4	0.78 [0.64;0.94]	0.01	22% ↓

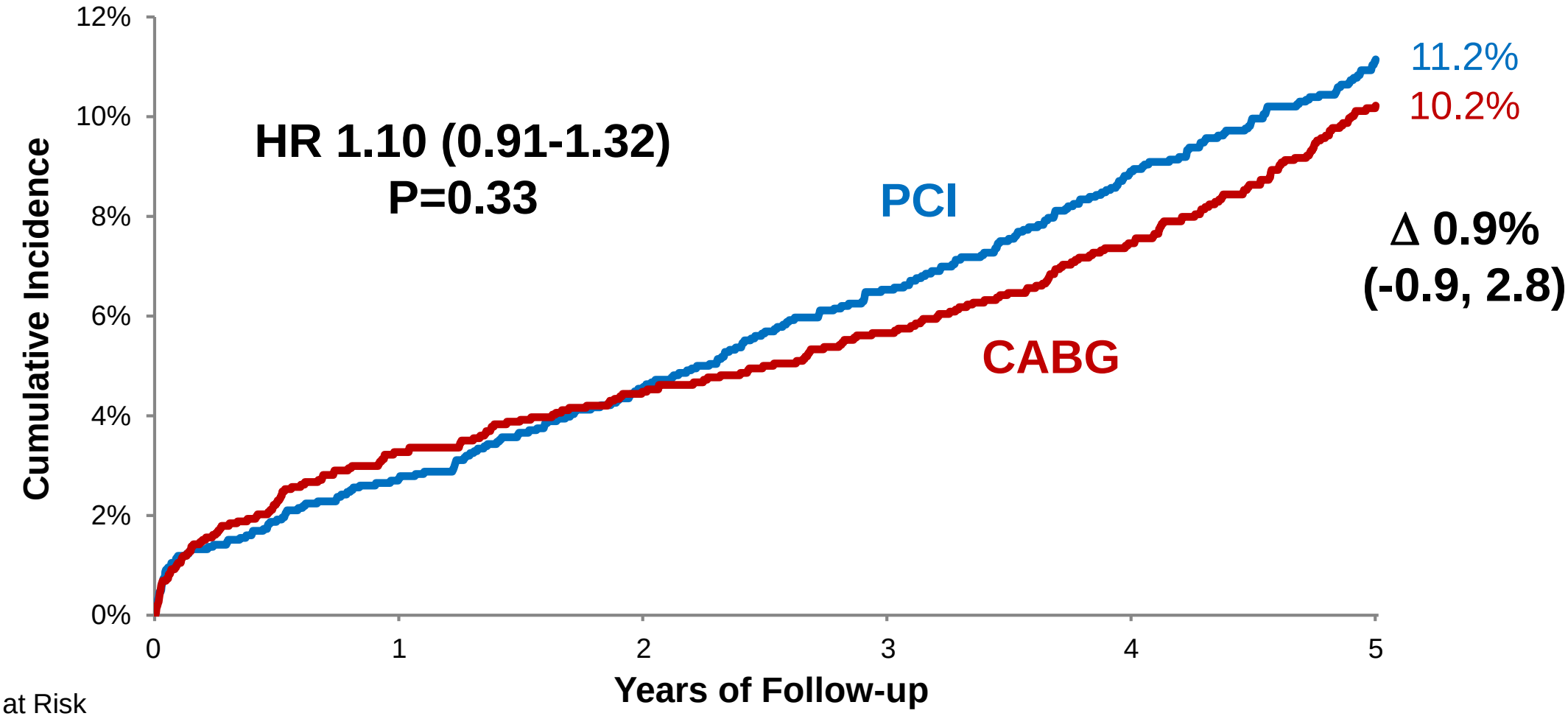


Favors Revasc + Med Rx← →Favors Med Rx alone

Navarese E et al. *EHJ* 2021;42:4638–51

4 Randomized Trials of Left Main PCI with DES vs. CABG (n=4,394)

Primary Endpoint: All-cause Mortality



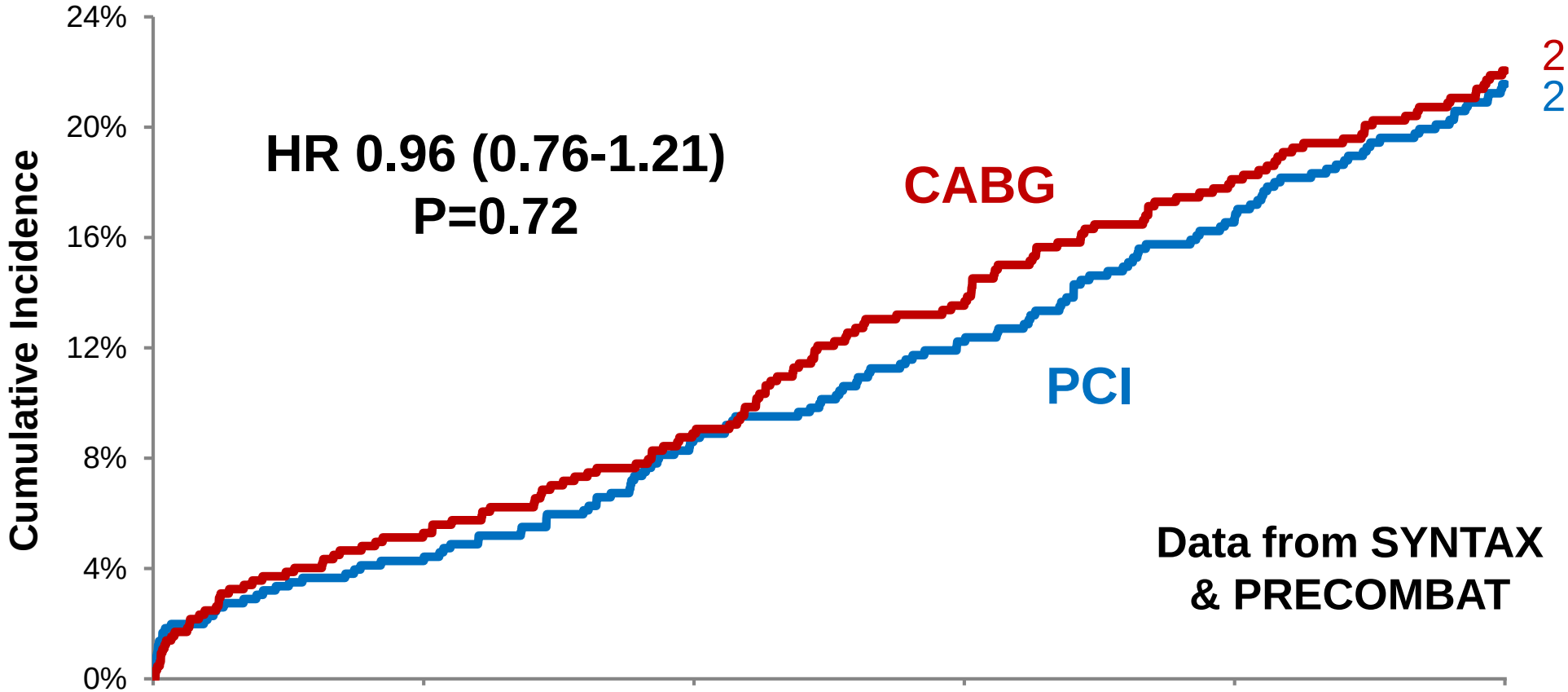
Number at Risk

CABG	2197	2085	2042	2002	1939	1585
PCI	2197	2120	2068	2015	1942	1539

Sabatine MS et al. Lancet 2021;398:2247-57

4 Randomized Trials of Left Main PCI with DES vs. CABG (n=4,394)

Two Trials with 10-Year Mortality Data



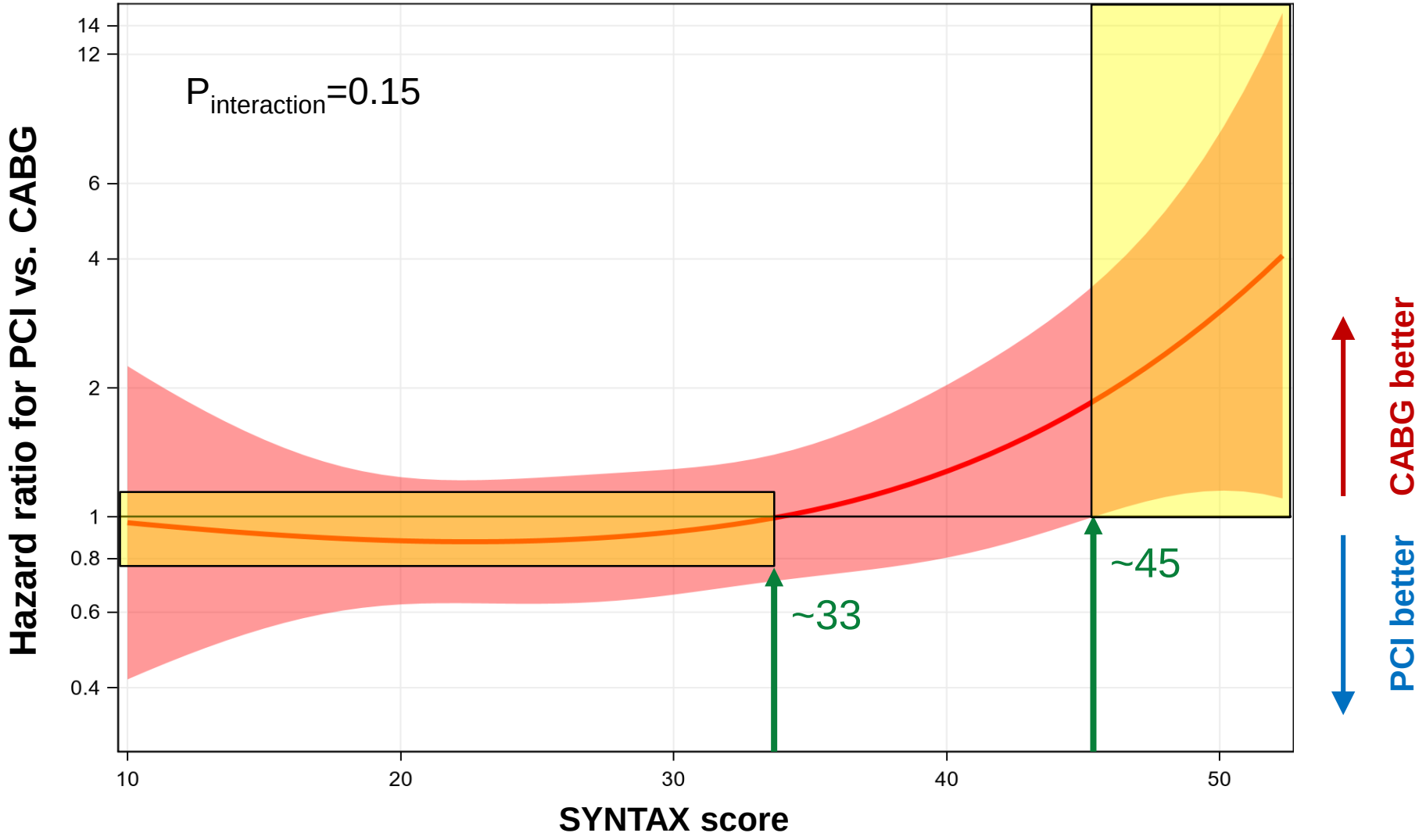
Number at Risk

CABG	648	604	577	531	500	463
PCI	657	623	591	547	519	475

Sabatine MS et al. Lancet 2021;398:2247-57

4 Randomized Trials of Left Main PCI with DES vs. CABG (n=4,394)

CV Mortality and SYNTAX Score: Spline analysis



Sabatine MS et al. Lancet 2021;398:2247-57

4 Randomized Trials of Left Main PCI with DES vs. CABG (n=4,394)

Stroke

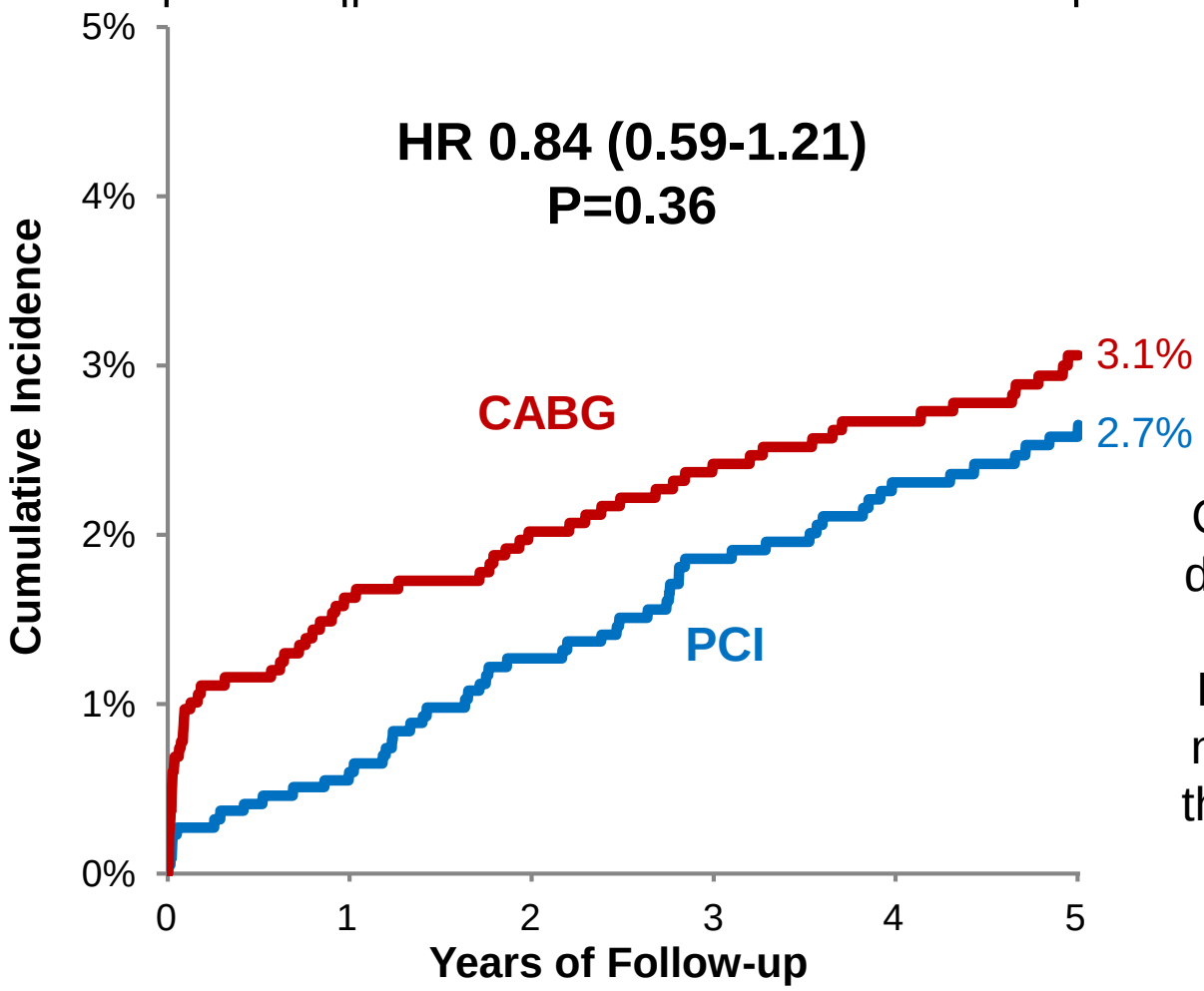
1st Year

13 vs. 35 events

HR 0.37 (0.19-0.69)

P=0.002

Absolute Δ 1.0%



Beyond 1st Year

42 vs. 28 events

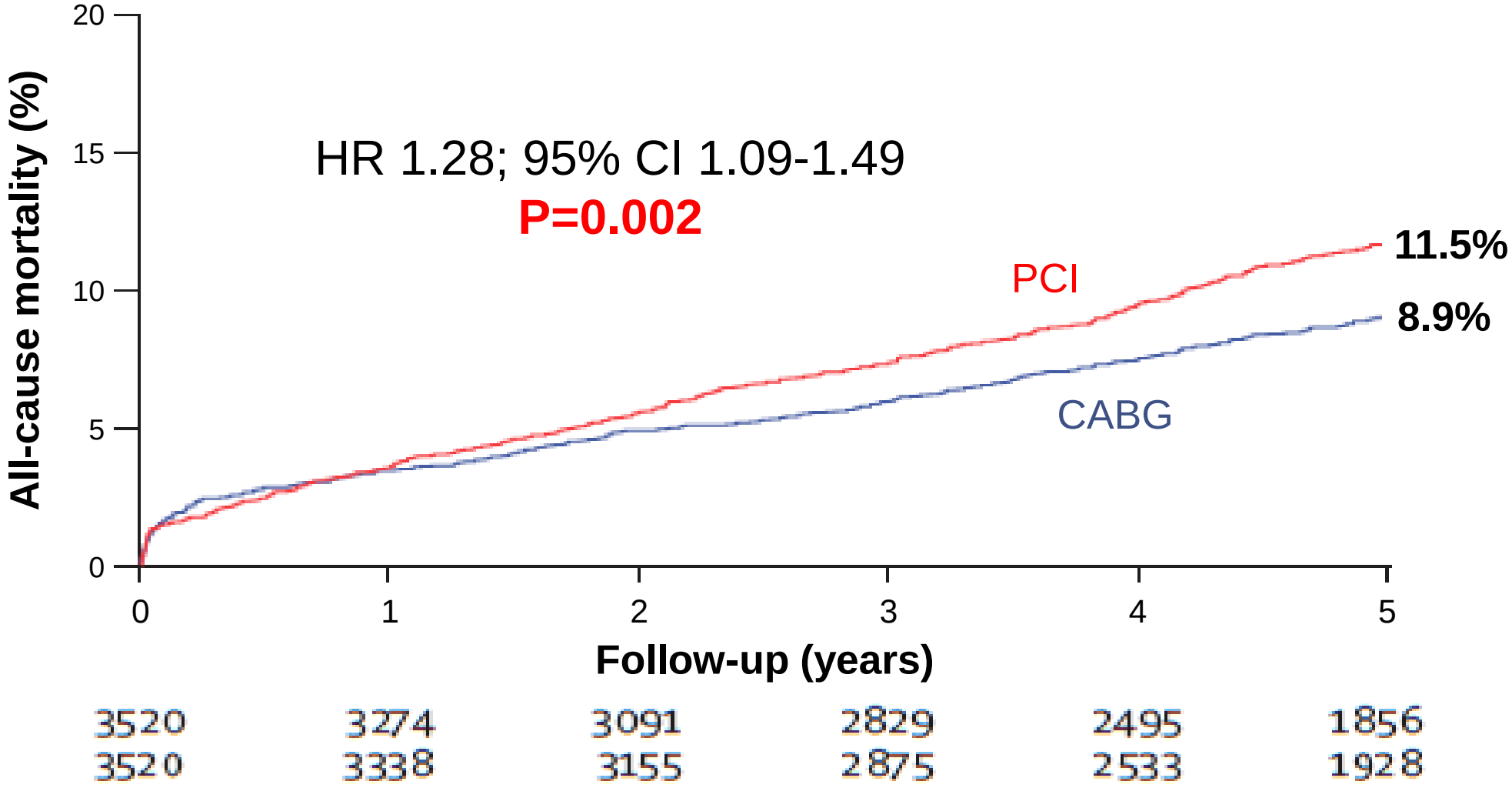
HR 1.49 (0.93-2.41)

Convergence of the curves was driven by a markedly higher rate of late (>1-year) stroke in PCI-treated pts in NOBLE, with no evidence of increased risk in the other 3 trials or any prior trial of PCI vs. CABG.

Sabatine MS et al. Lancet 2021;398:2247-57

PCI vs CABG in Multivessel Disease

Individual-patient-data pooled-analysis, 8 RCTs, 7,040 pts



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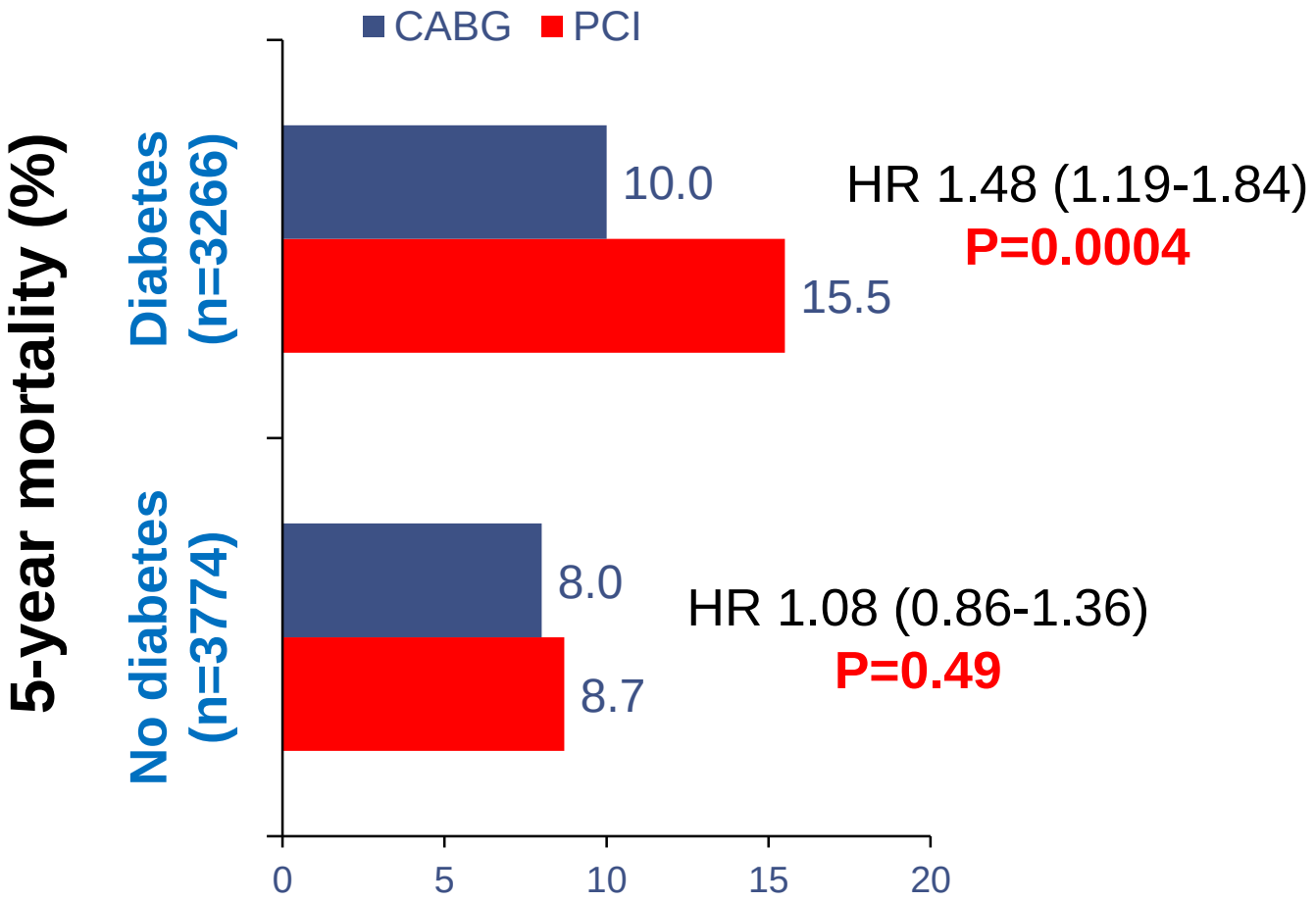
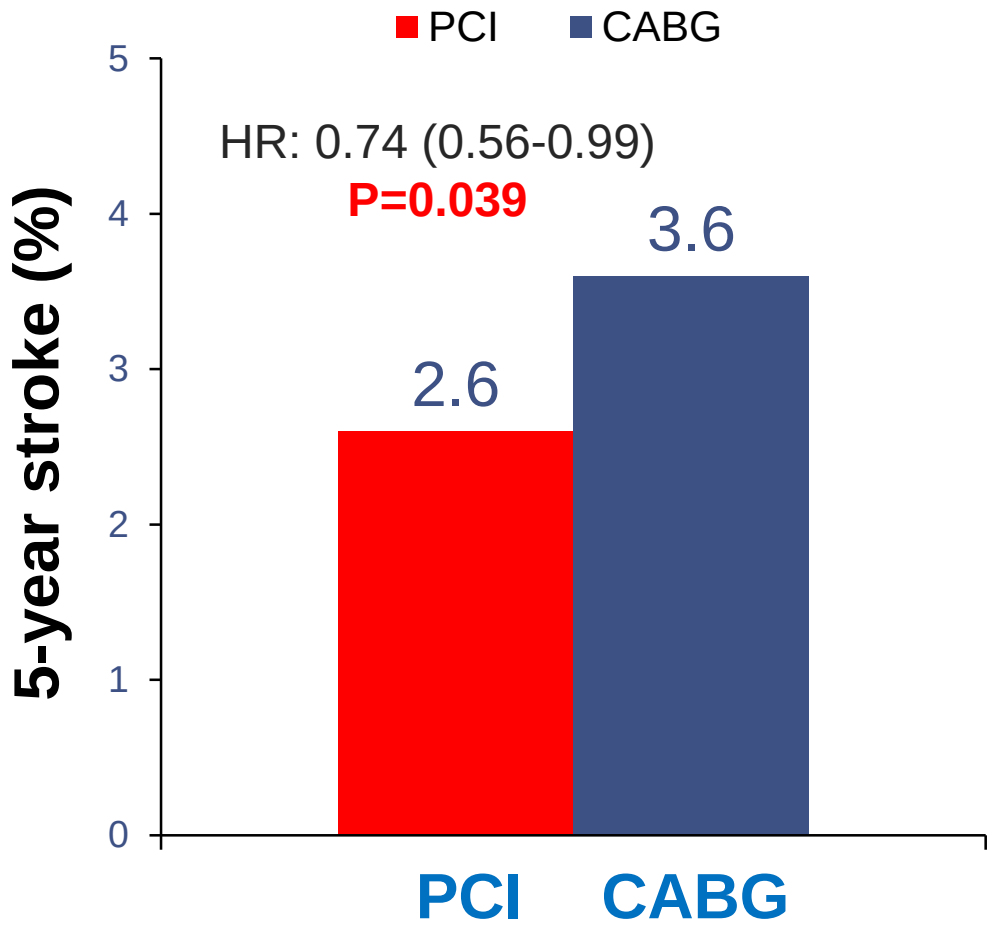
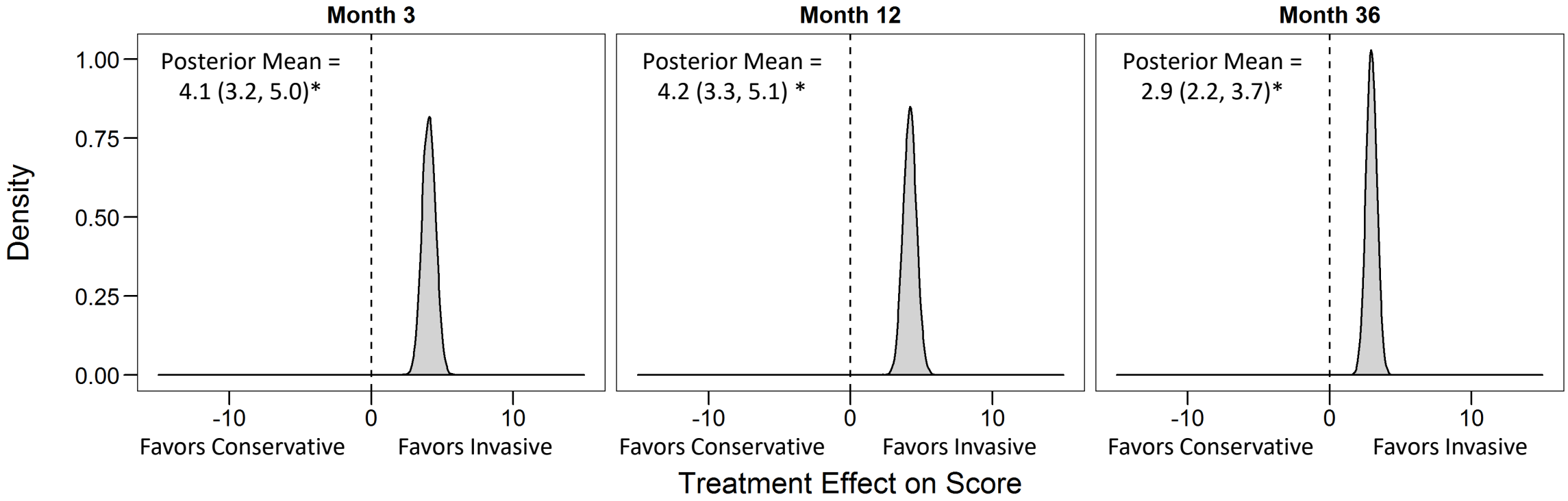




Head SJ et al. Lancet 2018;391:939-48; Head SJ et al. J Am Coll Cardiol 2018;72:386–98

QOL Primary Outcome: Benefit of Invasive Rx on SAQ Summary Score

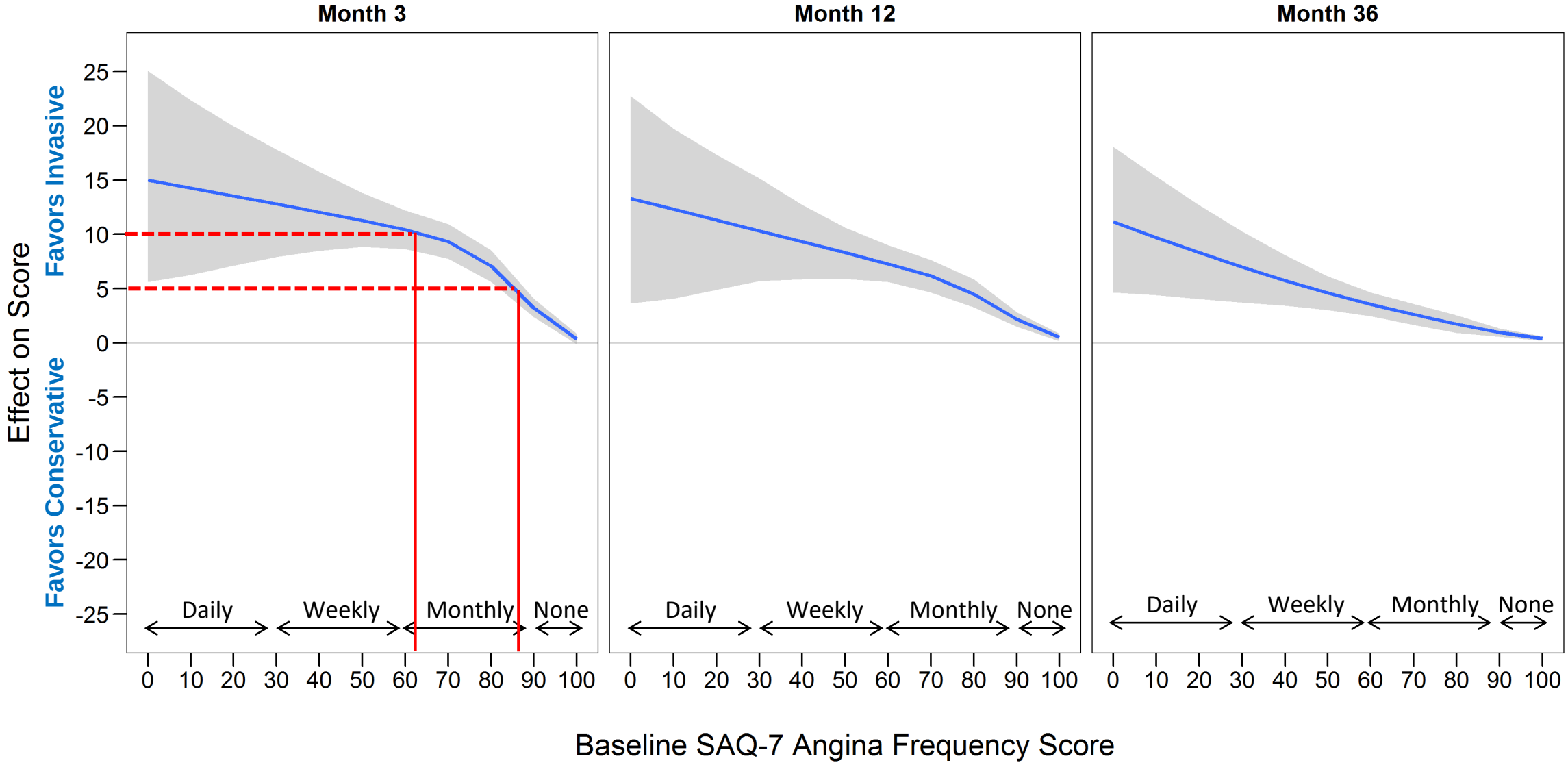
Typical Patient in ISCHEMIA



**95% Highest Posterior Density Interval*

Spertus JA et al. N Engl J Med. 2020;382:1408-1419

Mean SAQ Summary Benefit by Baseline Angina Frequency



Spertus JA et al. N Engl J Med. 2020;382:1408-1419

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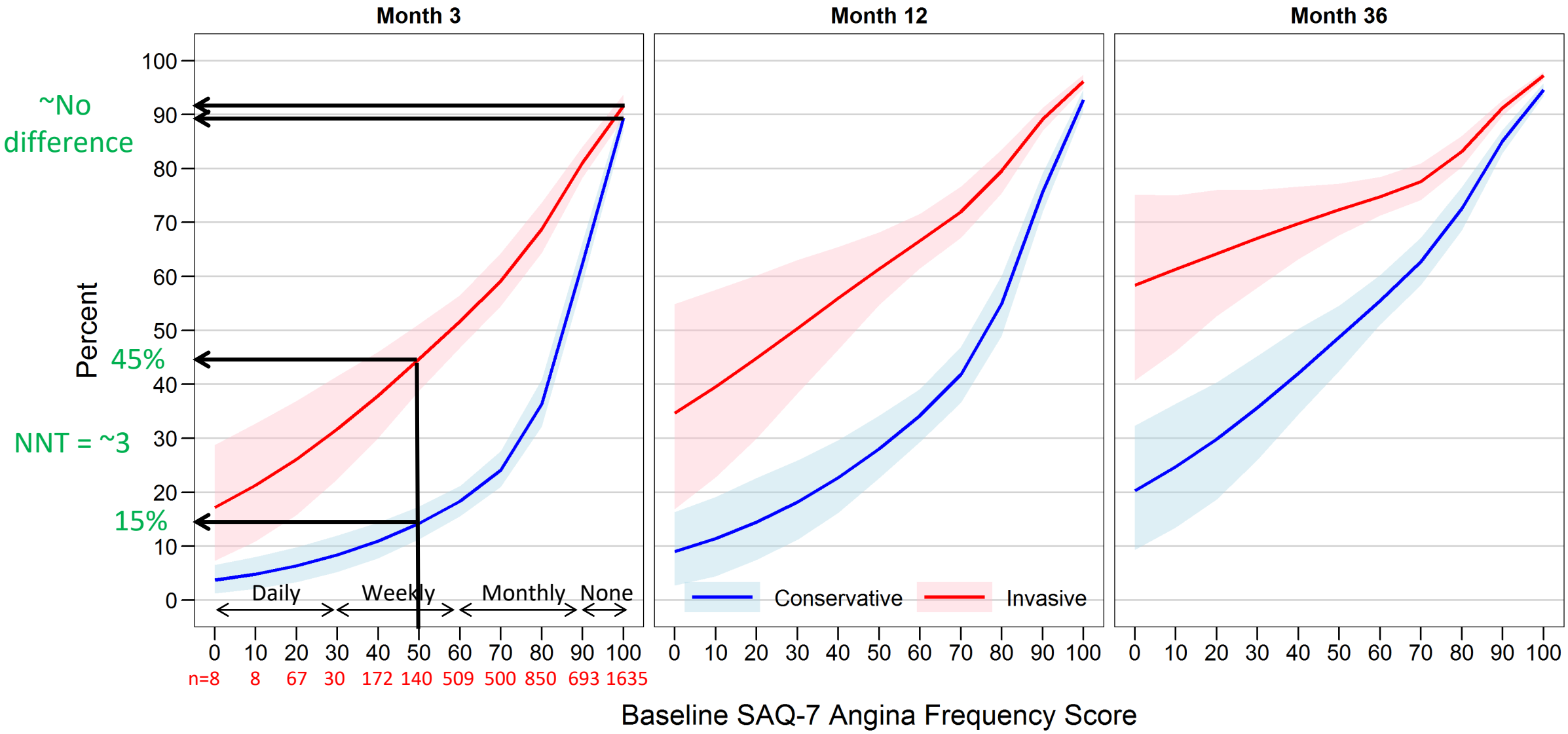
Probability of No Angina by Baseline Angina Frequency



Spertus JA et al. N Engl J Med. 2020;382:1408-1419

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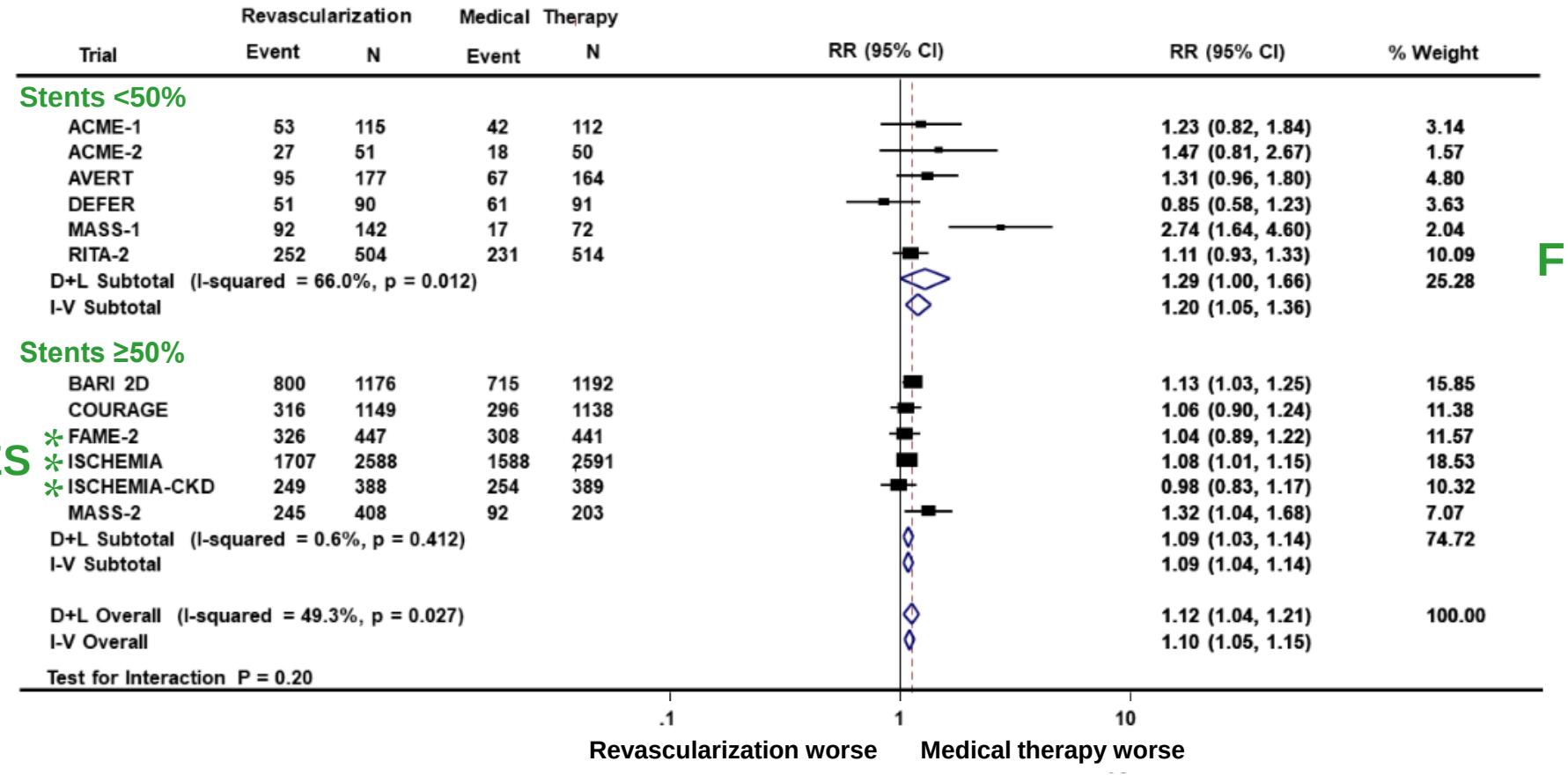
Updated Meta-analysis of Revascularization vs. MT in SIHD

14 RCTs, 14,877 pts, mean weighted 4.5-year FU

Most trials enrolled pts with preserved LVEF, low symptom burden and excluded LM ds.

Revasc arm: Revasc 87.5% (PCI 71.3%, CABG 16.2%). Med arm: Revasc 31.9% during FU.

Freedom from Angina



Freedom from angina
RR (95% CI) =
1.12 (1.04, 1.21)
Favors revasc

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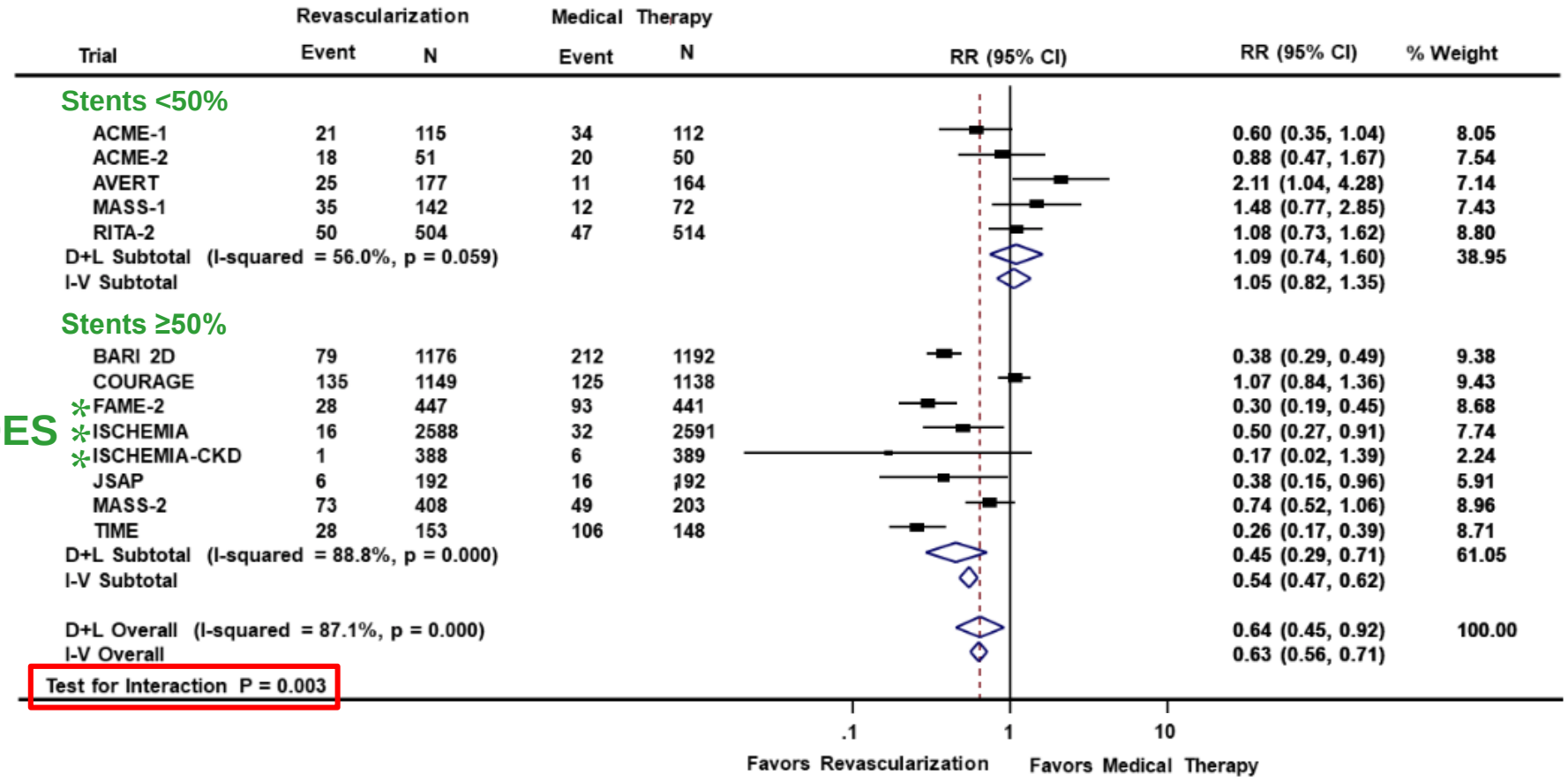
Unstable Angina



Unstable angina

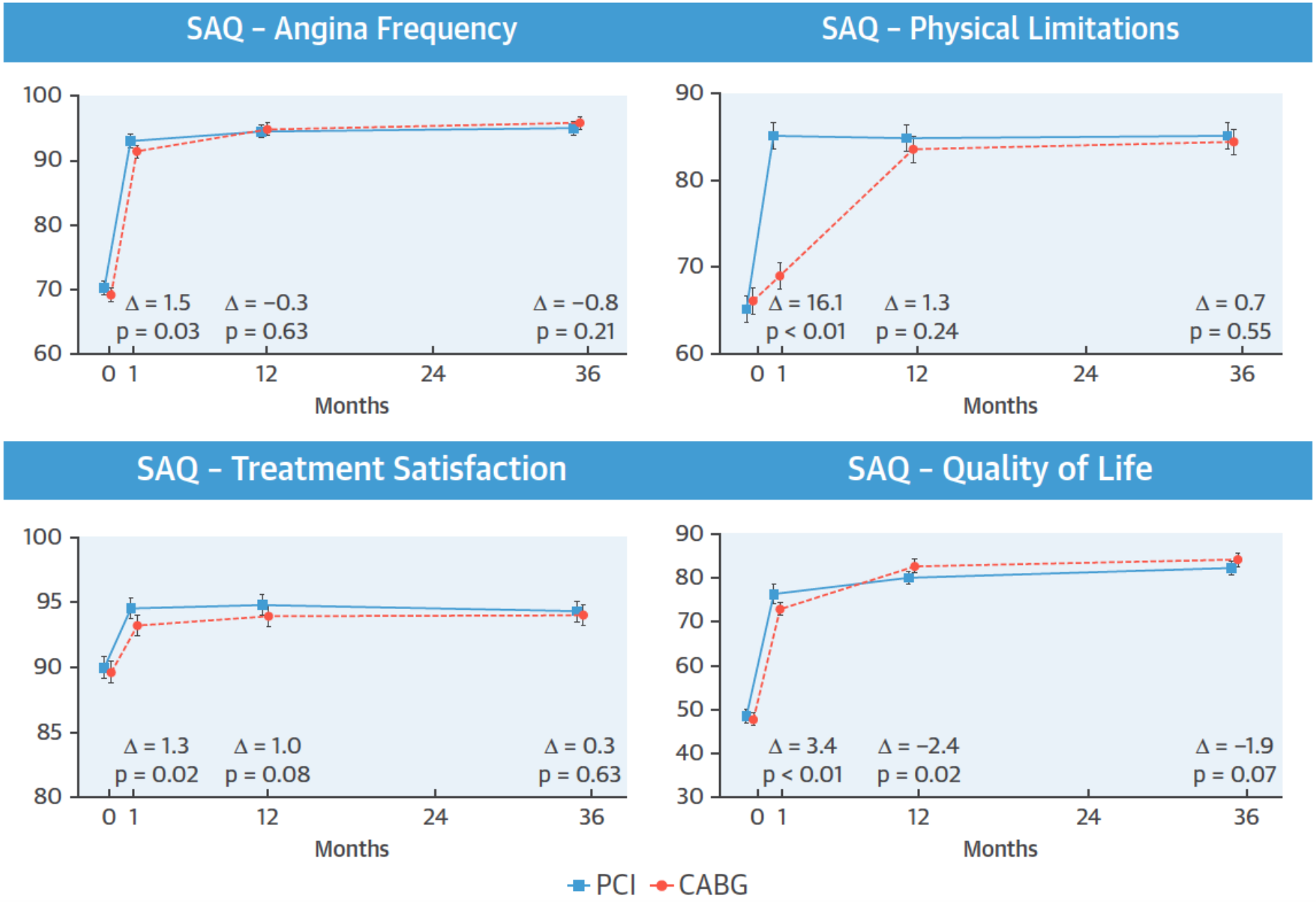
RR (95% CI) = 0.64 (0.45, 0.92)

Favors revasc

EXCEL

1905 pts with Left Main Disease Randomized to PCI with Second Generation Xience DES vs CABG

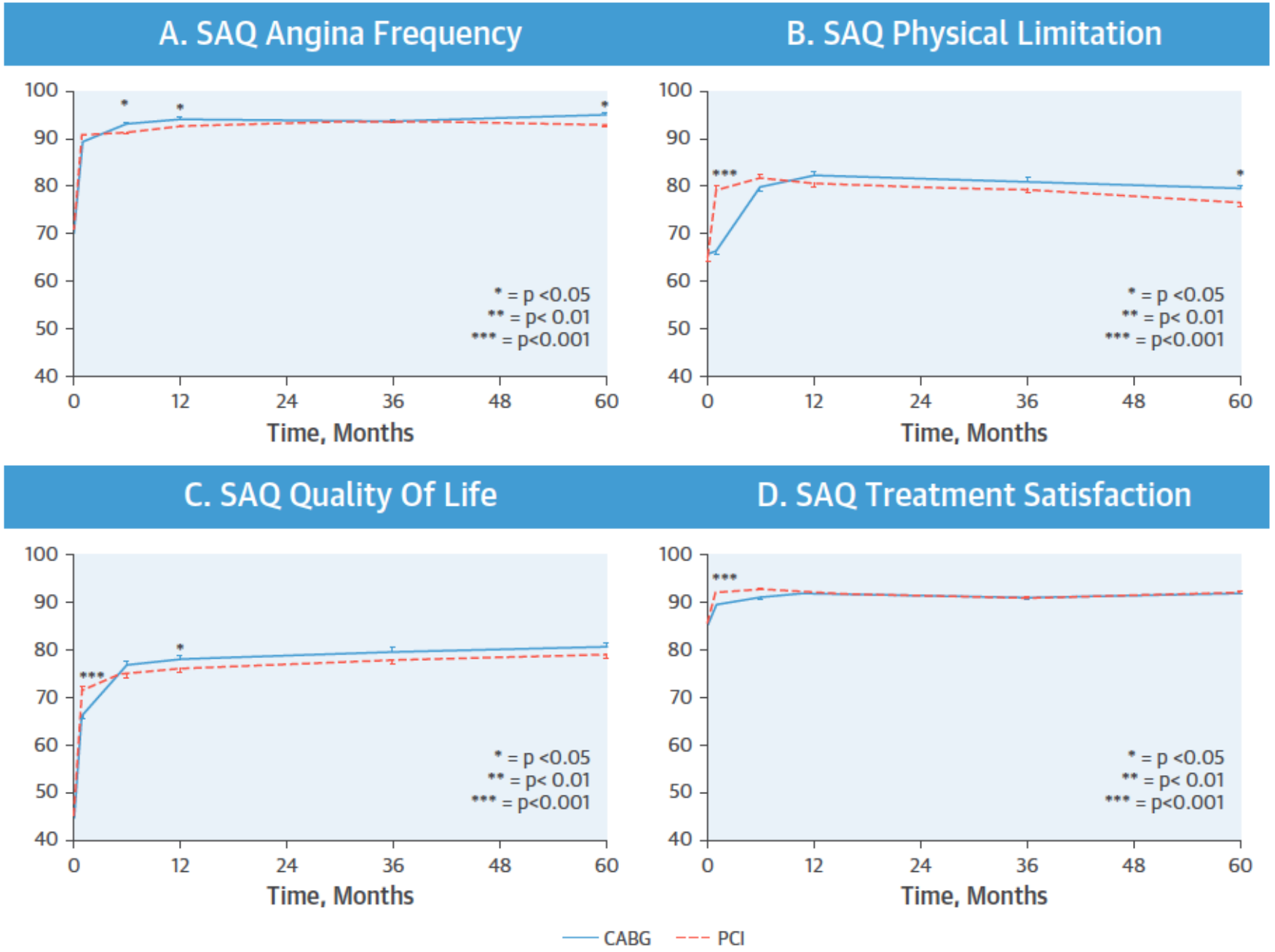
Formal Quality-of-Life Study



SYNTAX

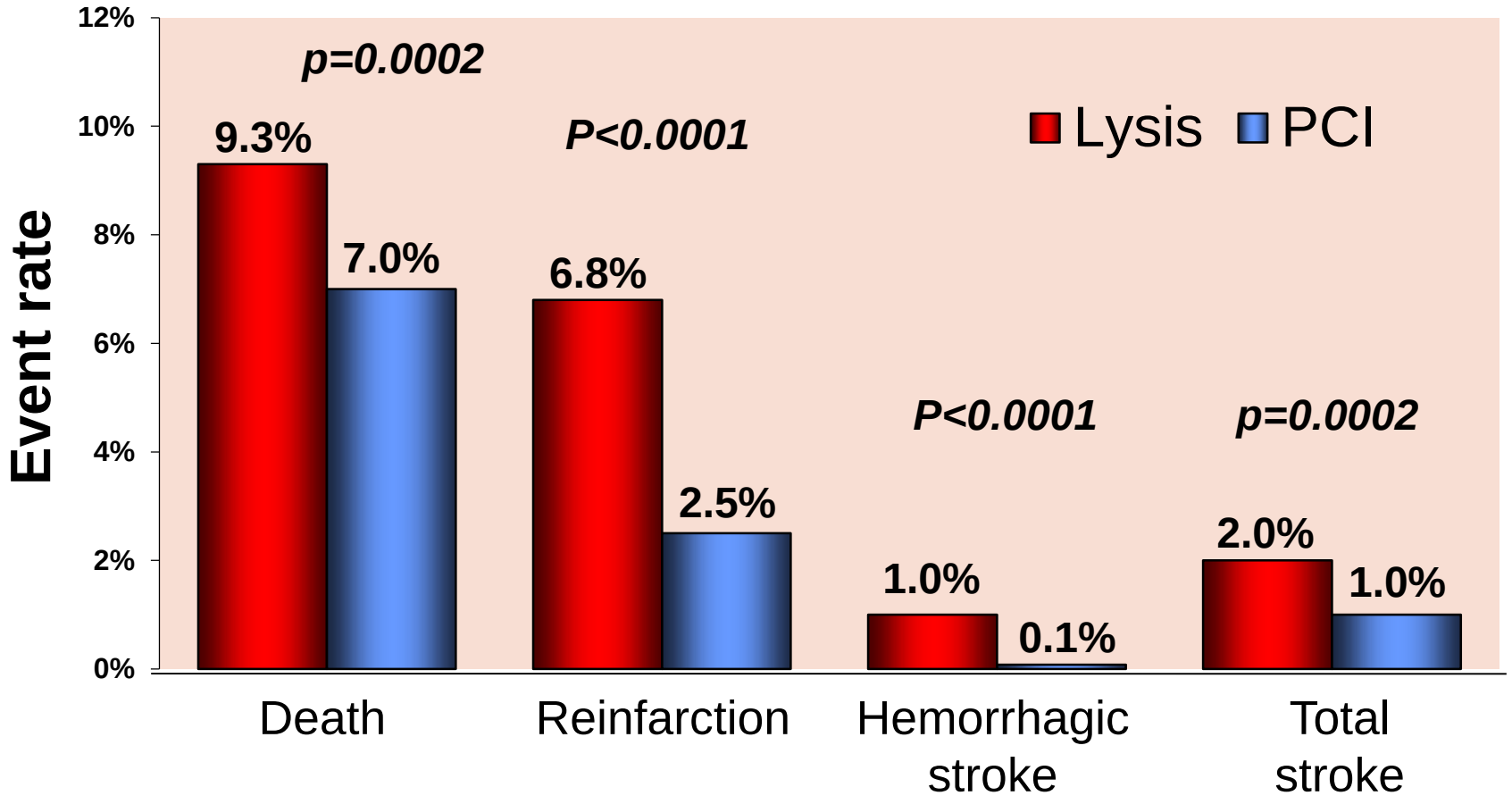
1800 pts with 3VD/LMD Randomized to PCI with First Generation Taxus DES vs CABG

Formal Quality-of-Life Study



STEMI: From PAMI to 23 RCTs of PCI vs. Lysis

N = 7,739

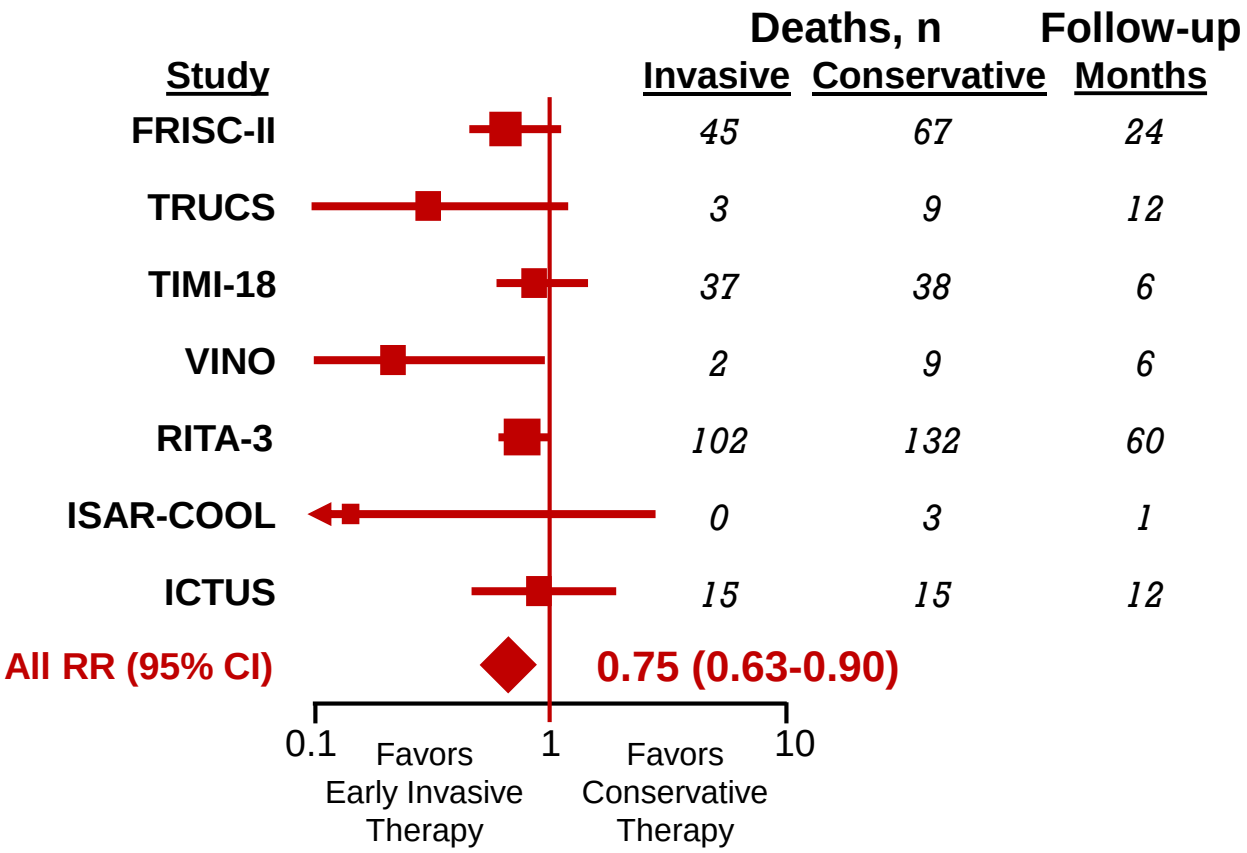


Keeley, Grines. *Lancet* 2003;361:13-20

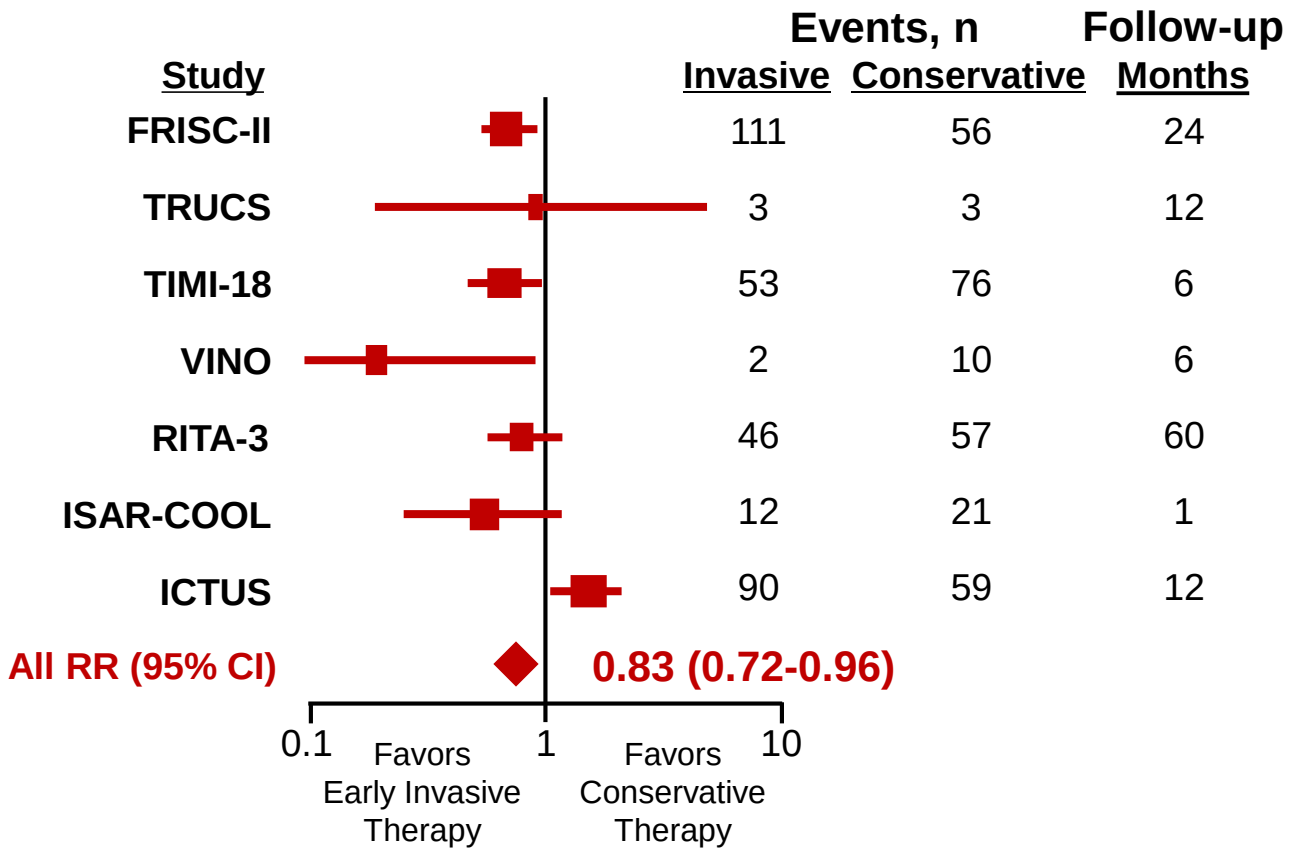
NSTEACS: Early Invasive vs. Conservative Strategies

8,375 pts randomized in 7 trials, mean 2-year FU

Mortality



Myocardial infarction



Bavry AA et al. *JACC* 2006;48:1319-25

Who Are Appropriate Patients for PCI in the Post-ISCHEMIA Era?

- Patients with stable CAD (after a heart team discussion for LM/MVD ds.)
  - Left main disease: For improvement in survival
  - Heart failure and reduced LVEF: For improvement in survival
  - Extensive CAD: For improvement in event-free survival
  - Symptomatic patients: For improvement in symptoms and quality-of-life
- Patients with acute coronary syndromes (NSTEMI and STEMI)
  - For improvement in prognosis: Freedom from death and MI