PCI with Drug-Eluting Stents vs. CABG in Left Main Coronary Artery Disease: An Individual Patient Data Meta-Analysis

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Disclosures

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Background

- Data comparing PCI with DES vs CABG in patients with left main disease stem principally from 4 landmark trials: SYNTAX (LM subgp),[1] PRECOMBAT,[2] NOBLE,[3] and EXCEL[4]
- However, differences in trial composite endpoints and findings have led to persistent uncertainty regarding the optimal revascularization strategy

[1]Morice MC, Serruys PW, Kappetein AP, et al. *Circulation* 2014;129:2388-94. [2]Ahn JM, Roh JH, Kim YH, et al. *JACC* 2015;65:2198-206.
[3]Holm NR, Mäkikallio T, Lindsay M, et al. *Lancet* 2020;395:191-99. [4]Stone GW, Kappetein AP, Sabik JF, et al. *NEJM* 2019;381:1820-30.

Approach

- A collaboration was formed between
  - Independent Investigators: M. Sabatine, B. Bergmark, S. Murphy, P. O'Gara, P. Smith, E. Braunwald
  - Principal Investigators of the four trials: P. Serruys, A. Kappetein, S. Park, D. Park, E. Christiansen, N. Holm, P. Nielsen, G. Stone, J. Sabik

- The Independent Investigators
  - Created the statistical analysis plan
  - Performed all analyses
  - Drafted the manuscript, had complete control over the content, and vouch for the integrity of the analyses and the findings

Methods

- A one-stage meta-analytic approach was used on a combined dataset of individual patient data supplied by each trial
- Primary endpoint: all-cause mortality through 5 years
- 5 Secondary endpoints: cardiovascular death; spontaneous MI; procedural MI; stroke; repeat coronary revascularization
- Landmark analyses; supplemental analyses using 10-year mortality data (available in SYNTAX & PRECOMBAT); subgroup analyses
- Bayesian analyses to help quantify the probability and magnitude of any difference in mortality

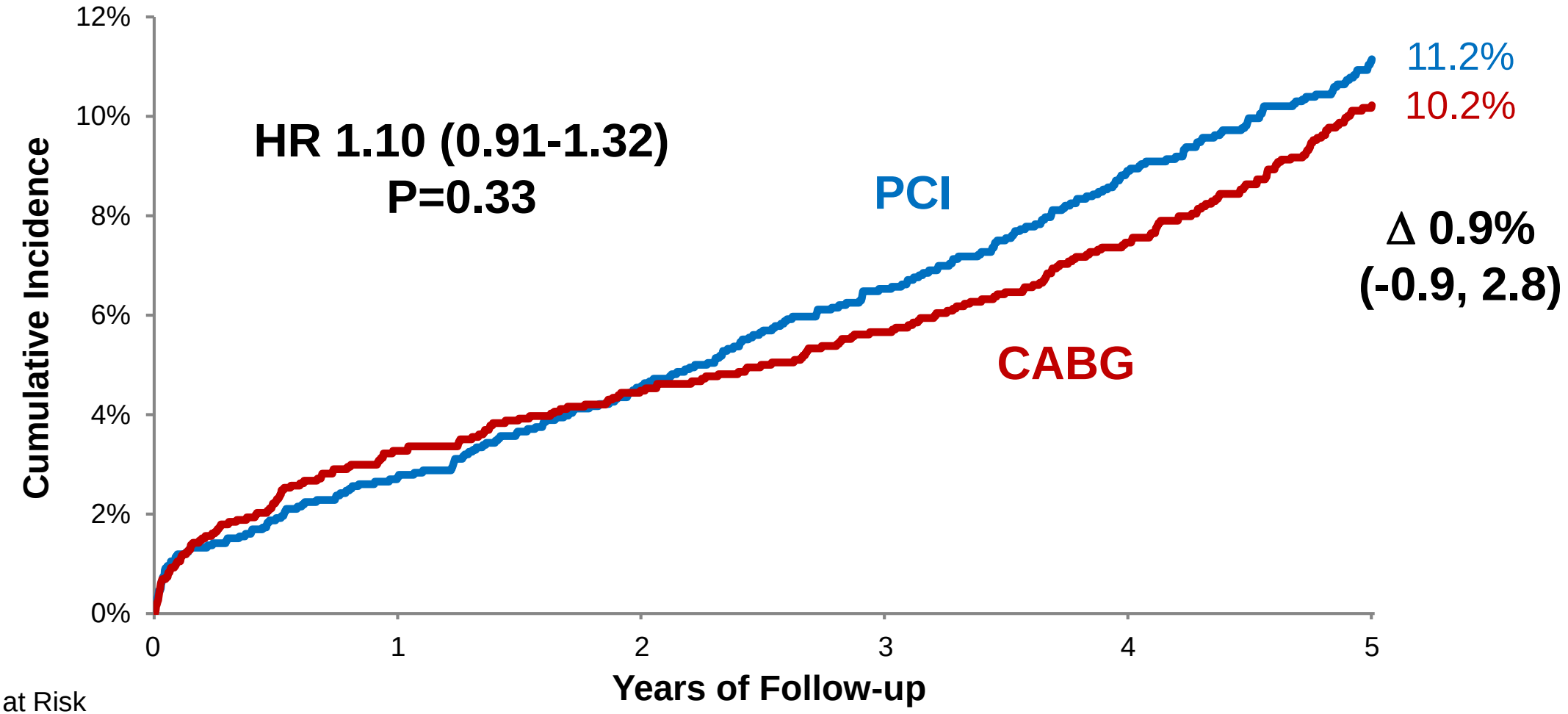
Baseline & Procedural Characteristics

All 4394 patients judged by a Heart Team to be equally suitable candidates for either PCI or CABG

Characteristic	PCI (N=2197)	CABG (N=2197)
Age, years	66 (59-73)	66 (59-72)
Male	77	77
Diabetes	26	25
LVEF <50%	12	12
SYNTAX score	25 (19-31)	24 (18-31)
Left main only	16	16
Left main + multivessel (≥2V) disease	52	53
# stents / conduits	2 (1-3)	2 (2-3)
IVUS use	68	
LIMA		96
All arterial		23

Data presented as median (IQR) or %

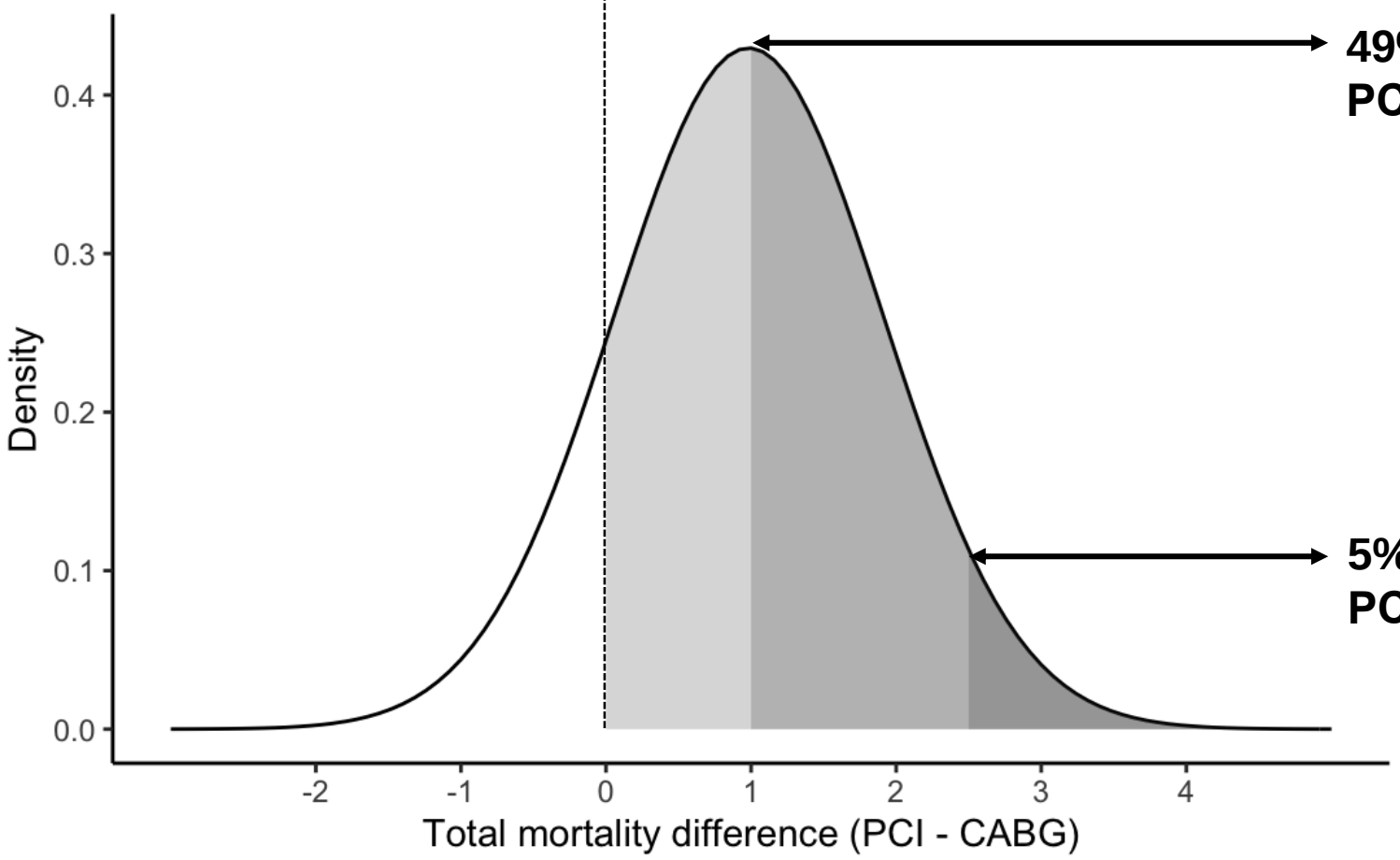
Mortality



Number at Risk

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

Bayesian Analysis of Mortality



86% probability that mortality greater with PCI vs. CABG

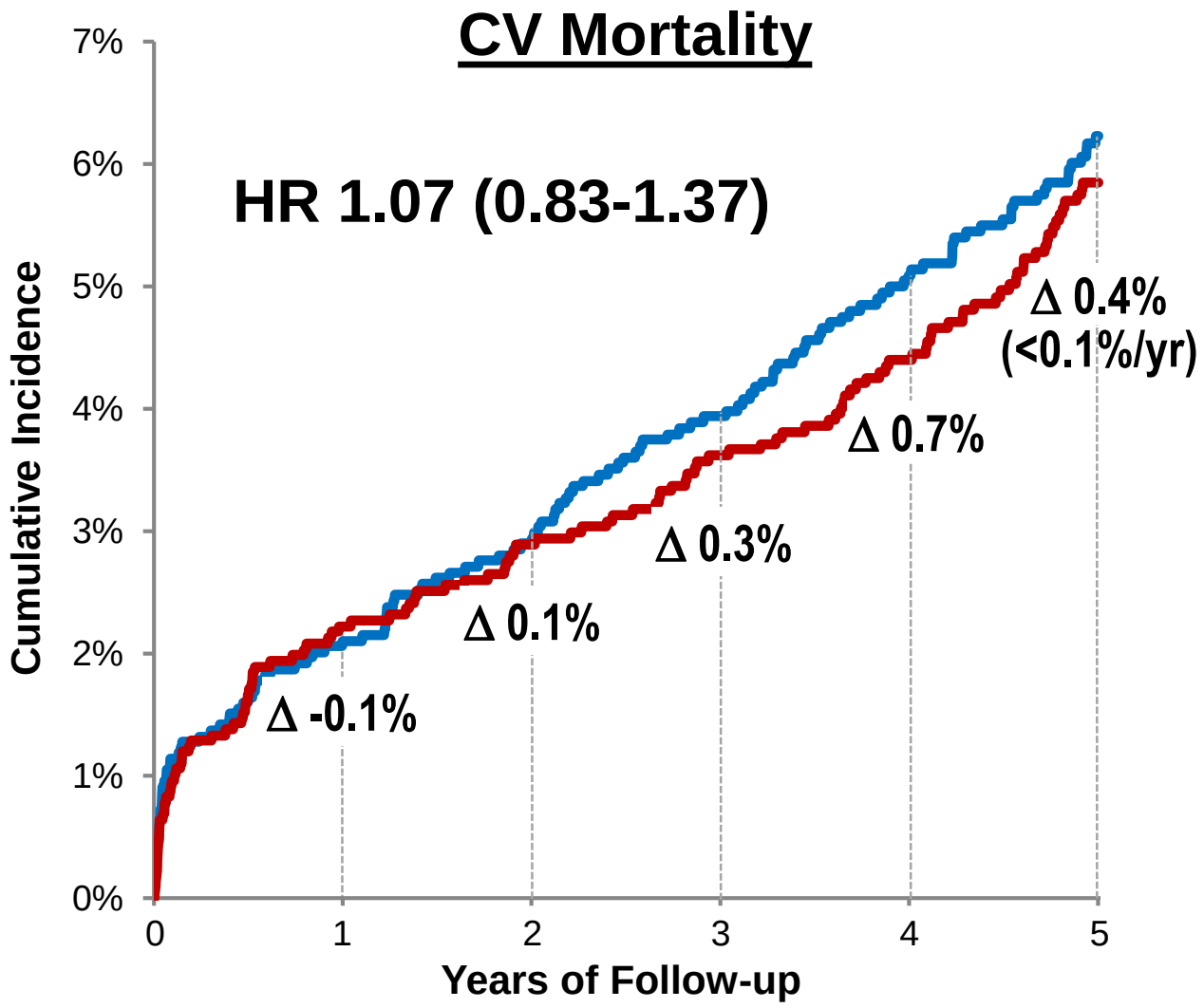
49% probability that mortality Δ between PCI & CABG ≥1% over 5 yrs (≥0.2%/yr)

Absolute risk difference more likely than not <0.2%/yr

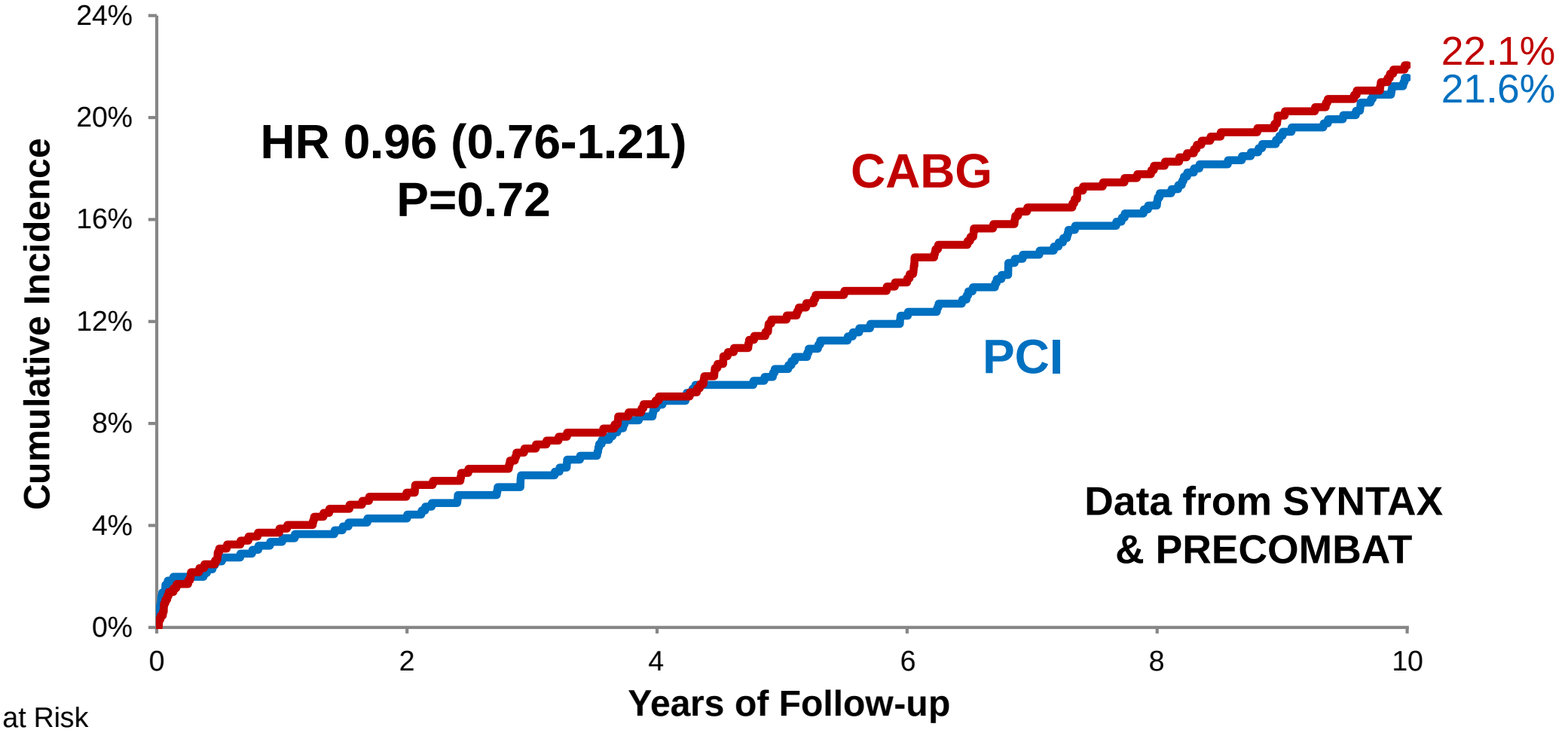
5% probability that mortality Δ between PCI & CABG ≥2.5% over 5 yrs (≥0.5%/yr)

CV & Non-CV Mortality

Type of Death	5-Year KM Rates		
	PCI	CABG	Δ
CV	6.2	5.9	0.4 (-1.1, 1.8)
Non-CV	5.2	4.5	0.7 (-0.6, 2.0)



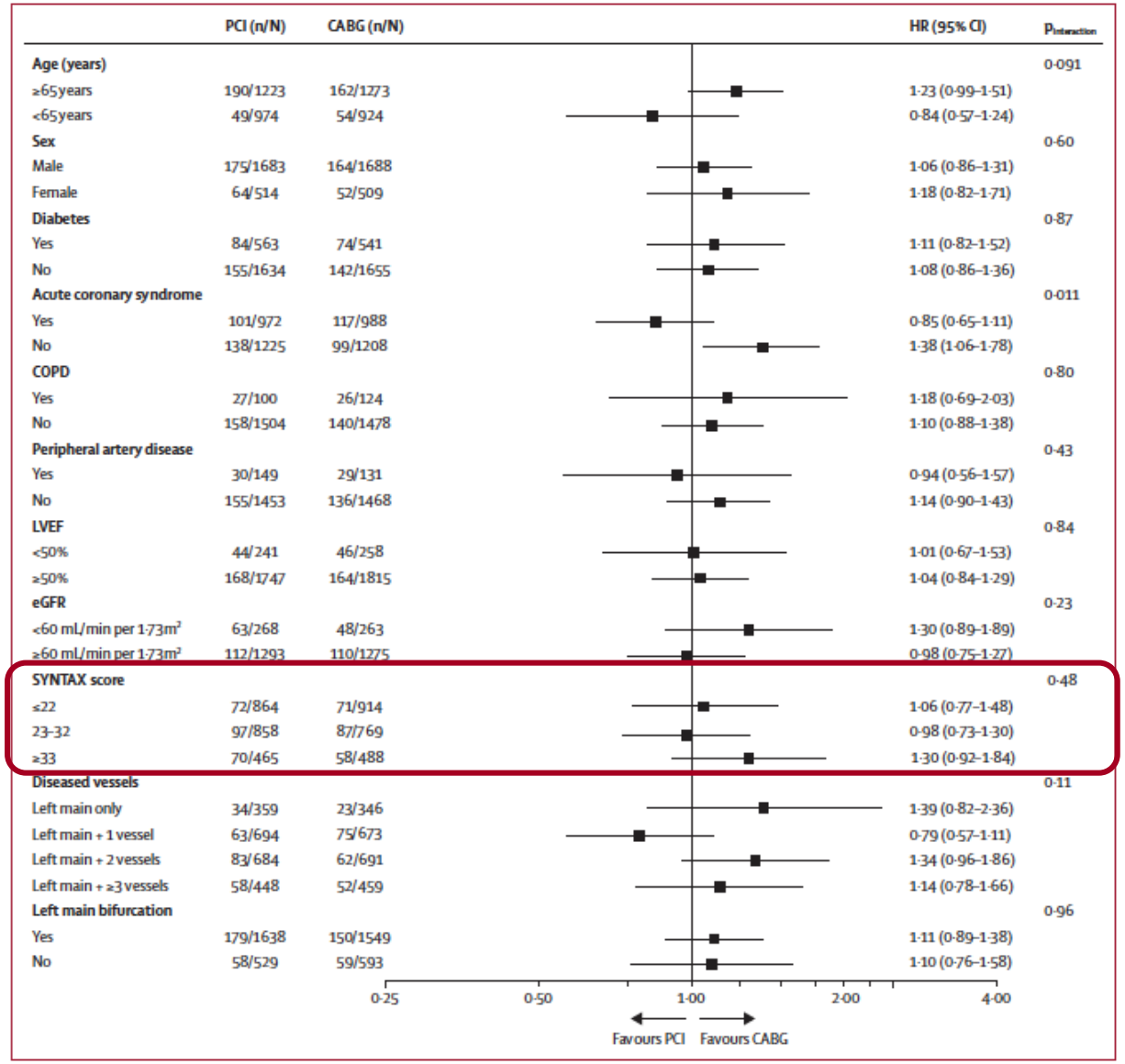
Two Trials with 10-Year Mortality Data



Number at Risk

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

Mortality Analysis Subgroups



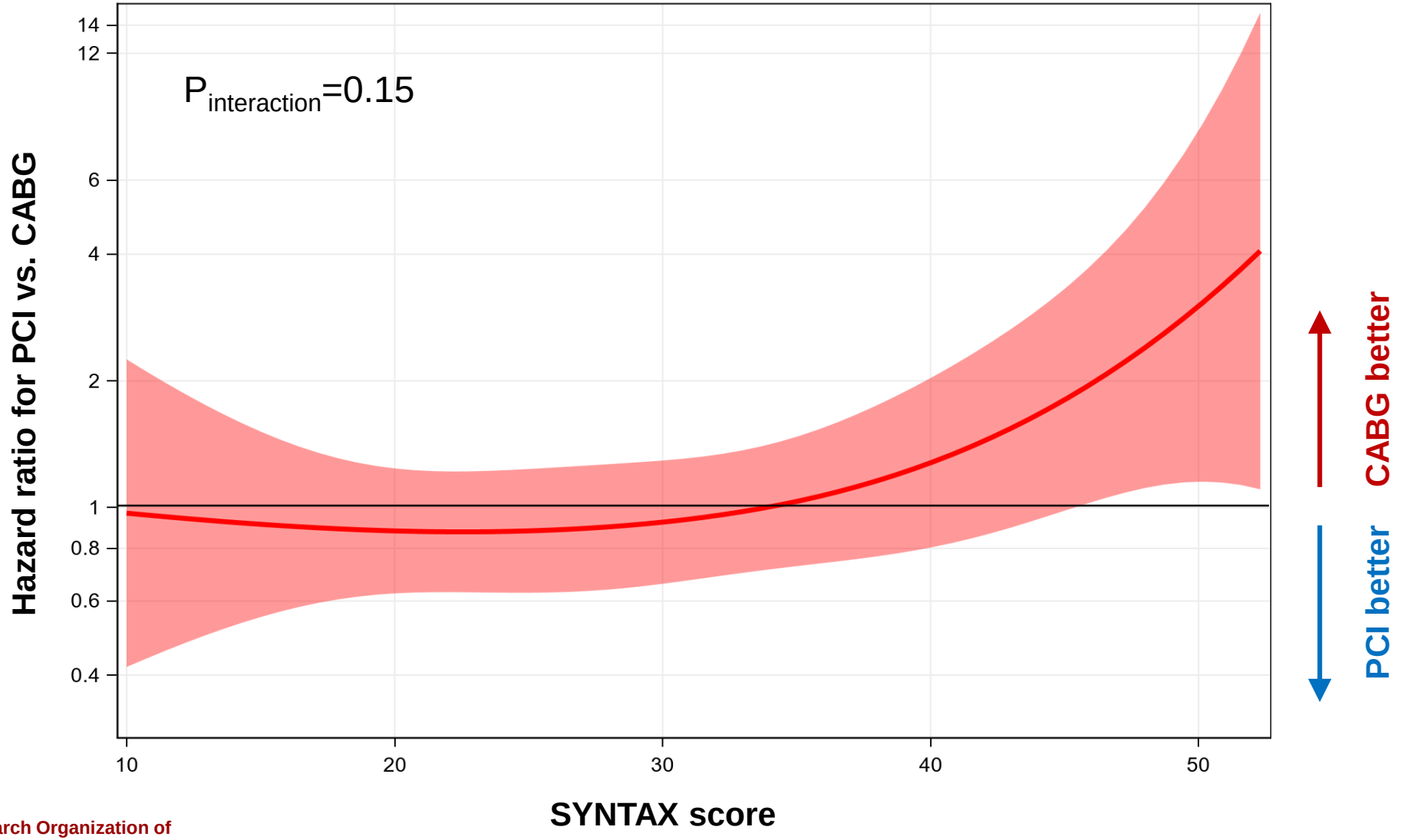
	PCI (n/N)	CABG (n/N)	HR (95% CI)	$p_{interaction}$
Age (years)				0·091
≥65 years	190/1223	162/1273	1·23 (0·99–1·51)	
<65 years	49/974	54/924	0·84 (0·57–1·24)	
Sex				0·60
Male	175/1683	164/1688	1·06 (0·86–1·31)	
Female	64/514	52/509	1·18 (0·82–1·71)	
Diabetes				0·87
Yes	84/563	74/541	1·11 (0·82–1·52)	
No	155/1634	142/1655	1·08 (0·86–1·36)	
Acute coronary syndrome				0·011
Yes	101/972	117/988	0·85 (0·65–1·11)	
No	138/1225	99/1208	1·38 (1·06–1·78)	
COPD				0·80
Yes	27/100	26/124	1·18 (0·69–2·03)	
No	158/1504	140/1478	1·10 (0·88–1·38)	
Peripheral artery disease				0·43
Yes	30/149	29/131	0·94 (0·56–1·57)	
No	155/1453	136/1468	1·14 (0·90–1·43)	
LVEF				0·84
<50%	44/241	46/258	1·01 (0·67–1·53)	
≥50%	168/1747	164/1815	1·04 (0·84–1·29)	
eGFR				0·23
<60 mL/min per 1·73m²	63/268	48/263	1·30 (0·89–1·89)	
≥60 mL/min per 1·73m²	112/1293	110/1275	0·98 (0·75–1·27)	
SYNTAX score				0·48
≤22	72/864	71/914	1·06 (0·77–1·48)	
23–32	97/858	87/769	0·98 (0·73–1·30)	
≥33	70/465	58/488	1·30 (0·92–1·84)	
Diseased vessels				0·11
Left main only	34/359	23/346	1·39 (0·82–2·36)	
Left main + 1 vessel	63/694	75/673	0·79 (0·57–1·11)	
Left main + 2 vessels	83/684	62/691	1·34 (0·96–1·86)	
Left main + ≥3 vessels	58/448	52/459	1·14 (0·78–1·66)	
Left main bifurcation				0·96
Yes	179/1638	150/1549	1·11 (0·89–1·38)	
No	58/529	59/593	1·10 (0·76–1·58)	

0·25 0·50 1·00 2·00 4·00

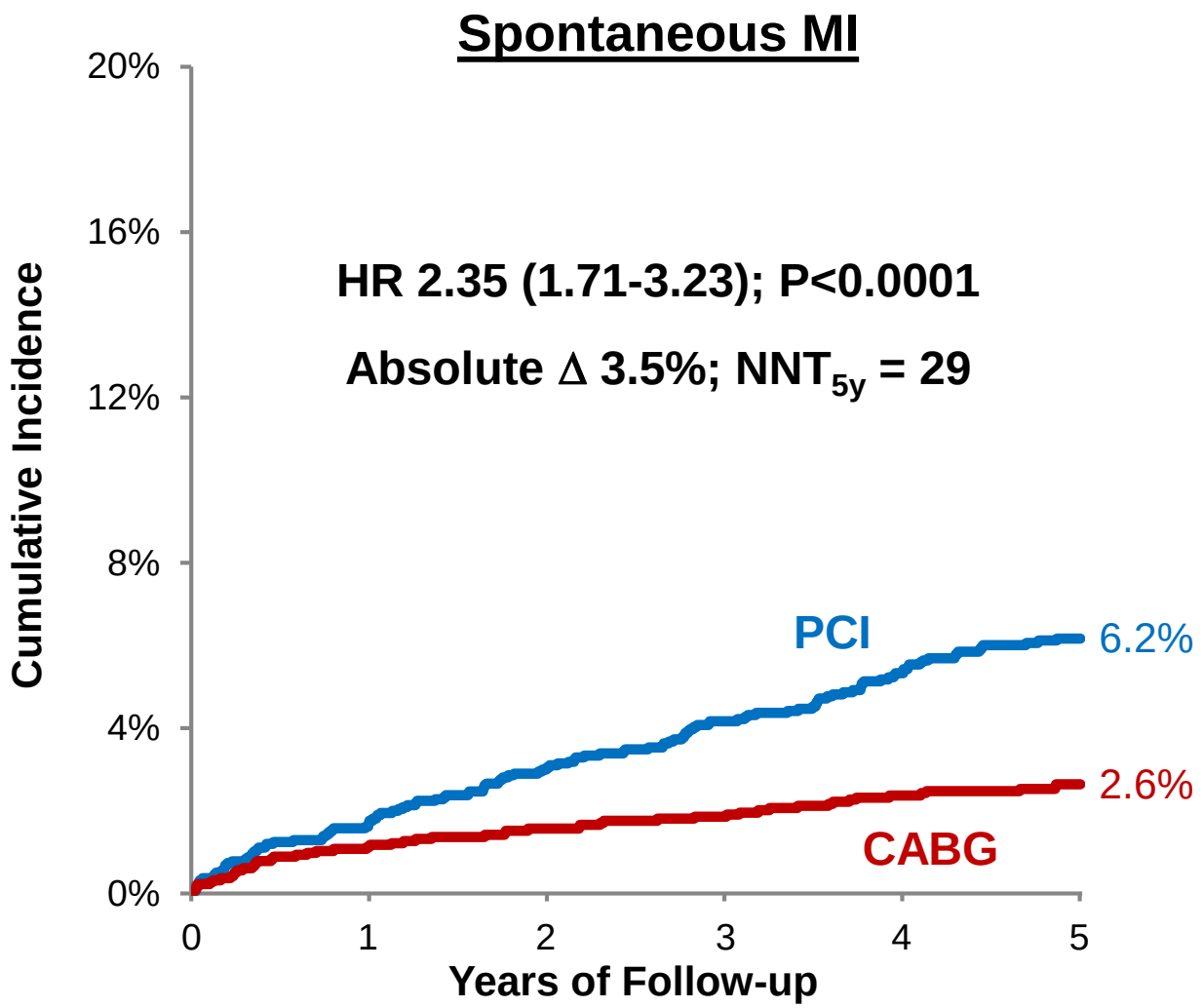
Favours PCI Favours CABG

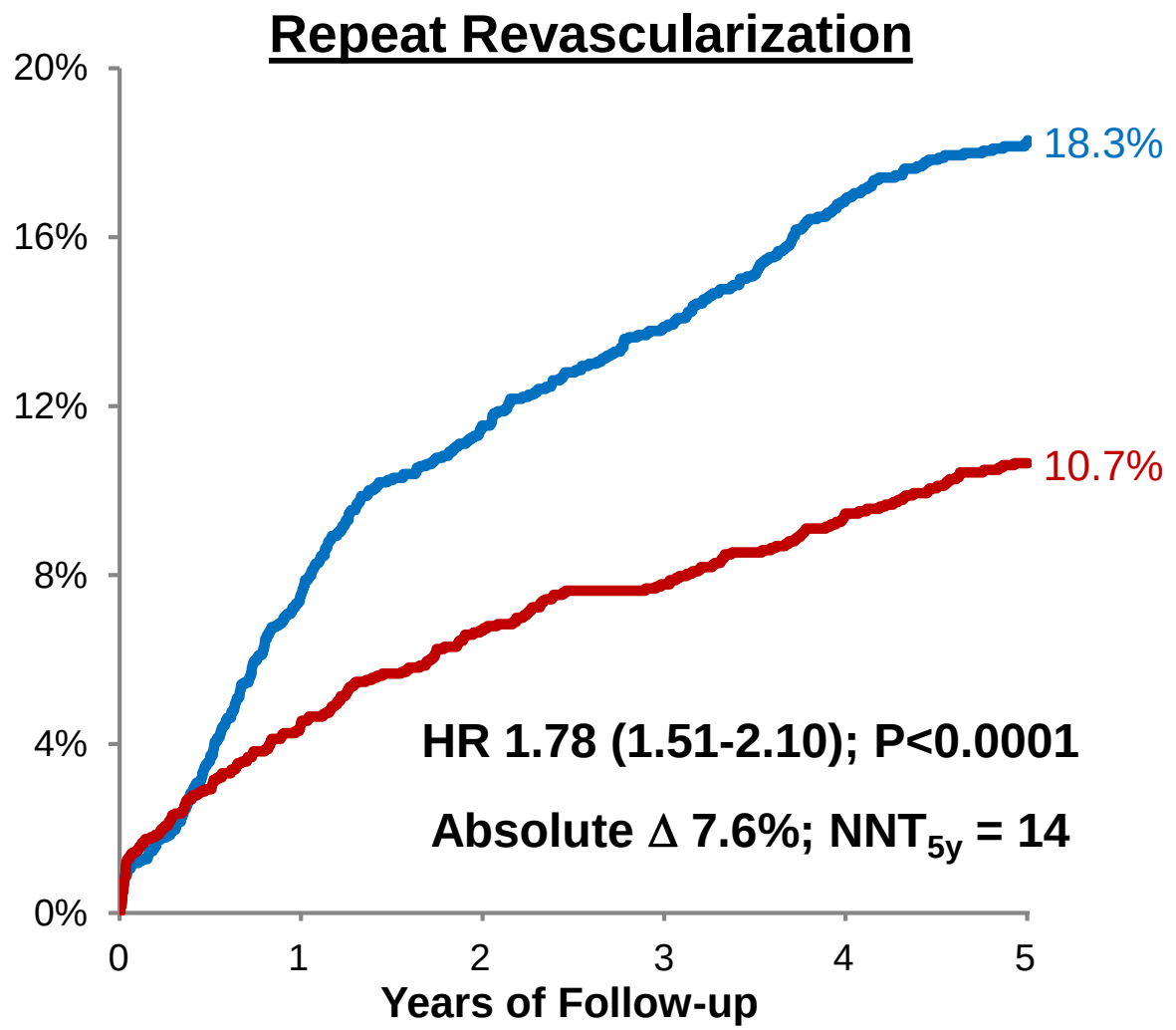
Sabatine MS, Bergmark BA, et al. Lancet. 2021.

CV Mortality and SYNTAX Score

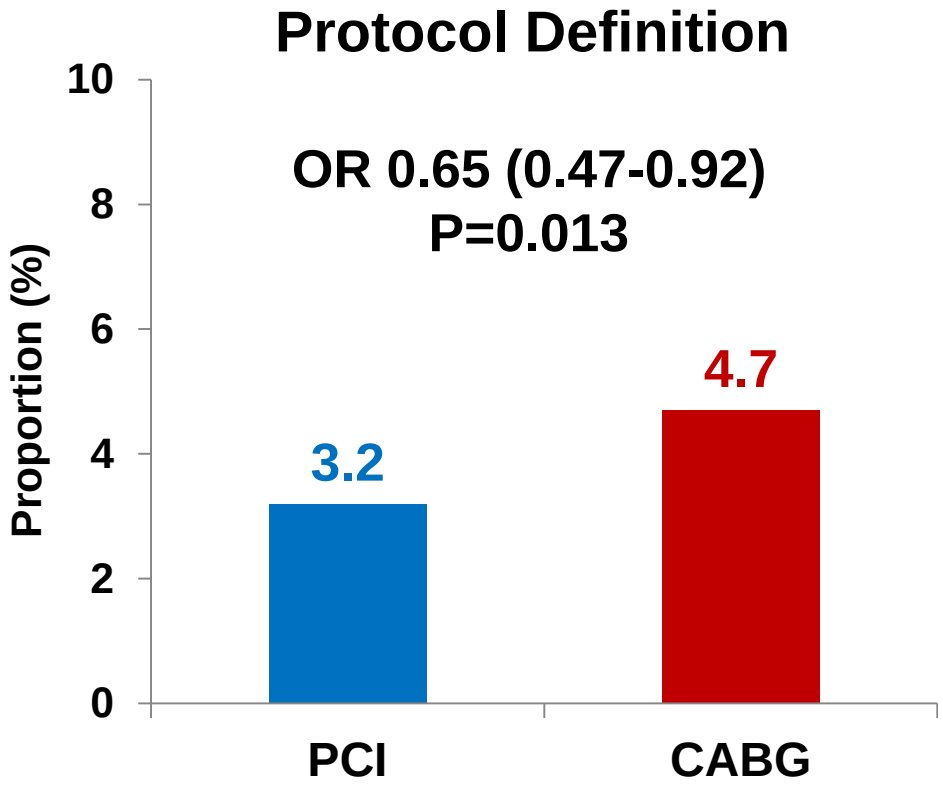


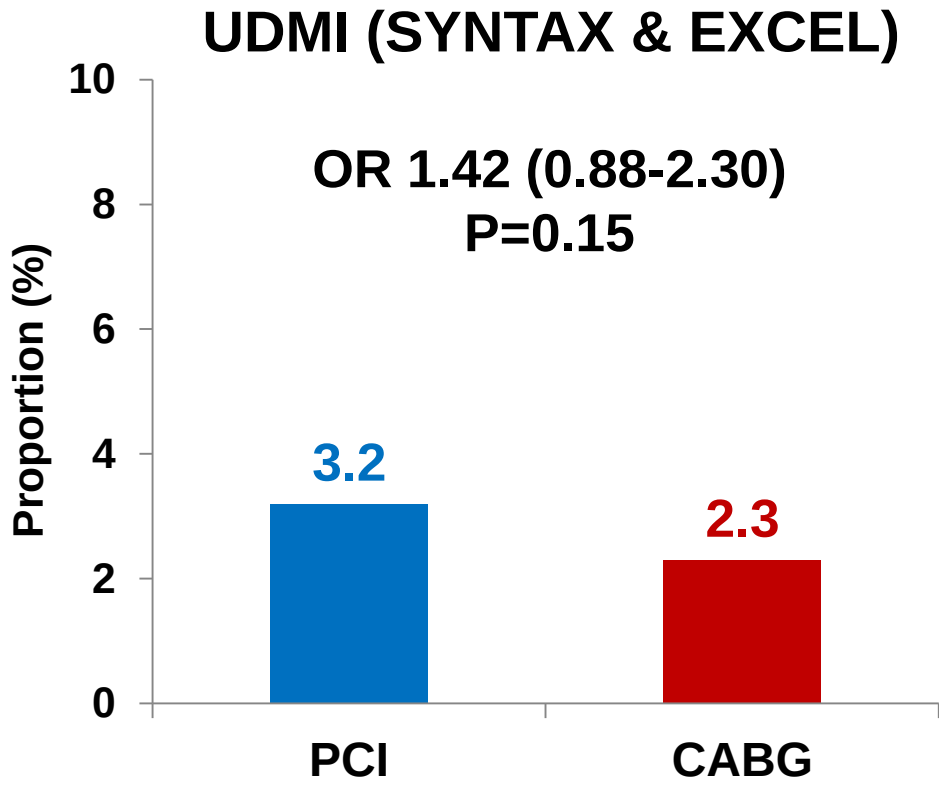
MI & Repeat Revascularization





Procedural MI



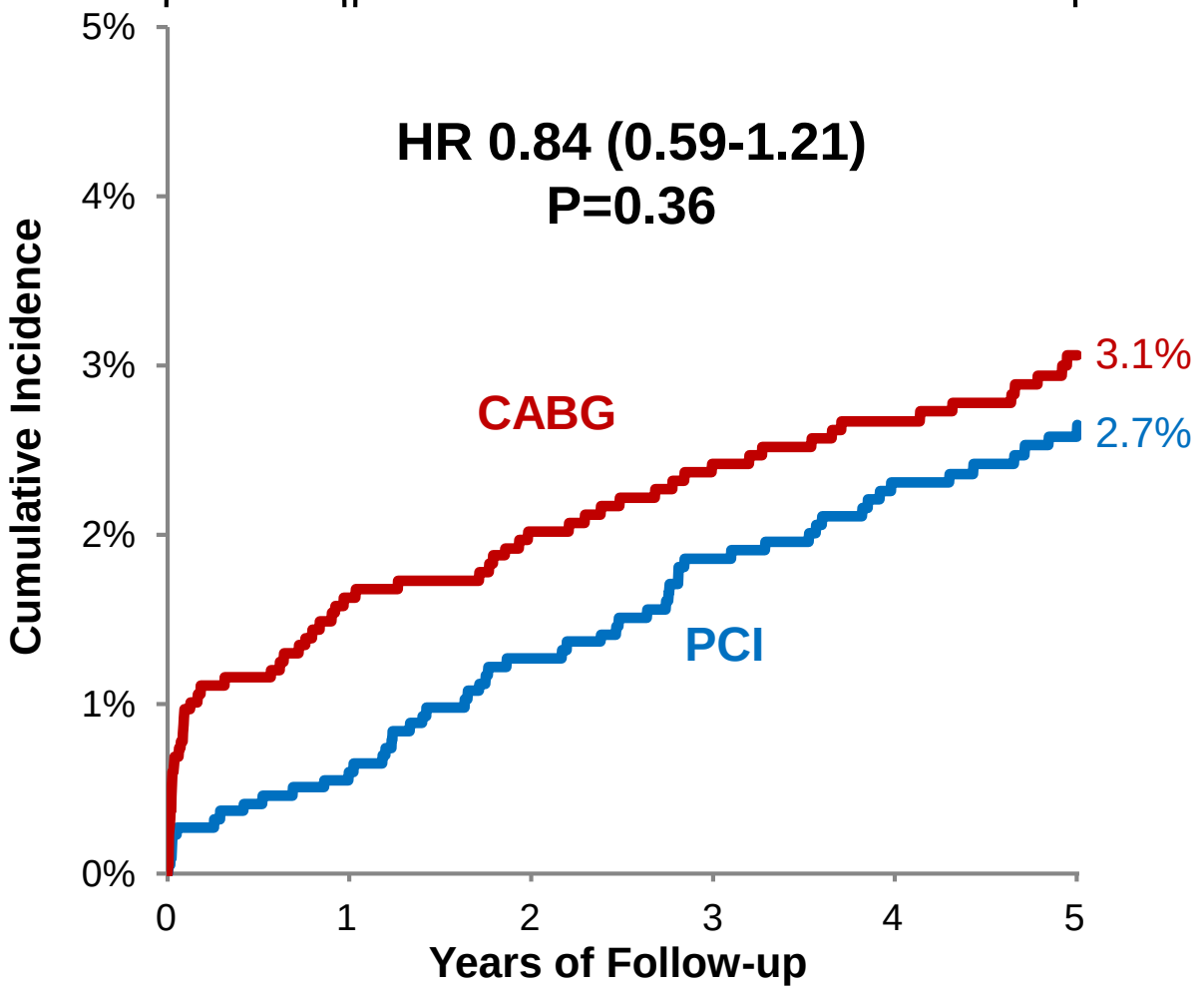


- CK-MB >5× + new Qw [or angio or imaging in some trials]
- [CK-MB >10× in some trials]

- PCI: cTn >5× + ST Δs, Qw, angio, or imaging [or sx]
- CABG: cTn >10× + Qw, angio, or imaging

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)

Summary

Comparing PCI w/ DES vs. CABG in Pts w/ LM CAD, median SYNTAX score of 25, and deemed equally suitable candidates for either revascularization approach:

No statistically significant difference in survival at 5 yrs (and 10 yrs)
Bayesian approach suggested Δ favoring CABG probably exists (more likely than not <0.2%/y)
Possible CV mortality benefit of CABG appeared confined to Pts w/ high SYNTAX scores

PCI

↓ early stroke

CABG

↓ spontaneous MI
↓ repeat revascularization

Differences in risk of procedural MI depended on the definition used

Where do we go from here?

- **These findings apply to a subset of patients with LM disease**
- **A large trial with latest surgical/PCI techniques would be nice, but:**
  - Difficult to achieve adequate power for mortality difference
  - Tension between long-term follow-up and state-of-the-art revasc
- **Perhaps refining the mortality difference point estimate is not the major issue**
  - How do we balance patient values and preferences with the small number of ‘hard’ outcomes for which we have data?

Integrating these findings into patient-centered decision-making is the central challenge moving forward

Thank you

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