Revascularization in Multivessel Disease:

PCI vs. CABG for Non-Diabetic and Diabetic Patients

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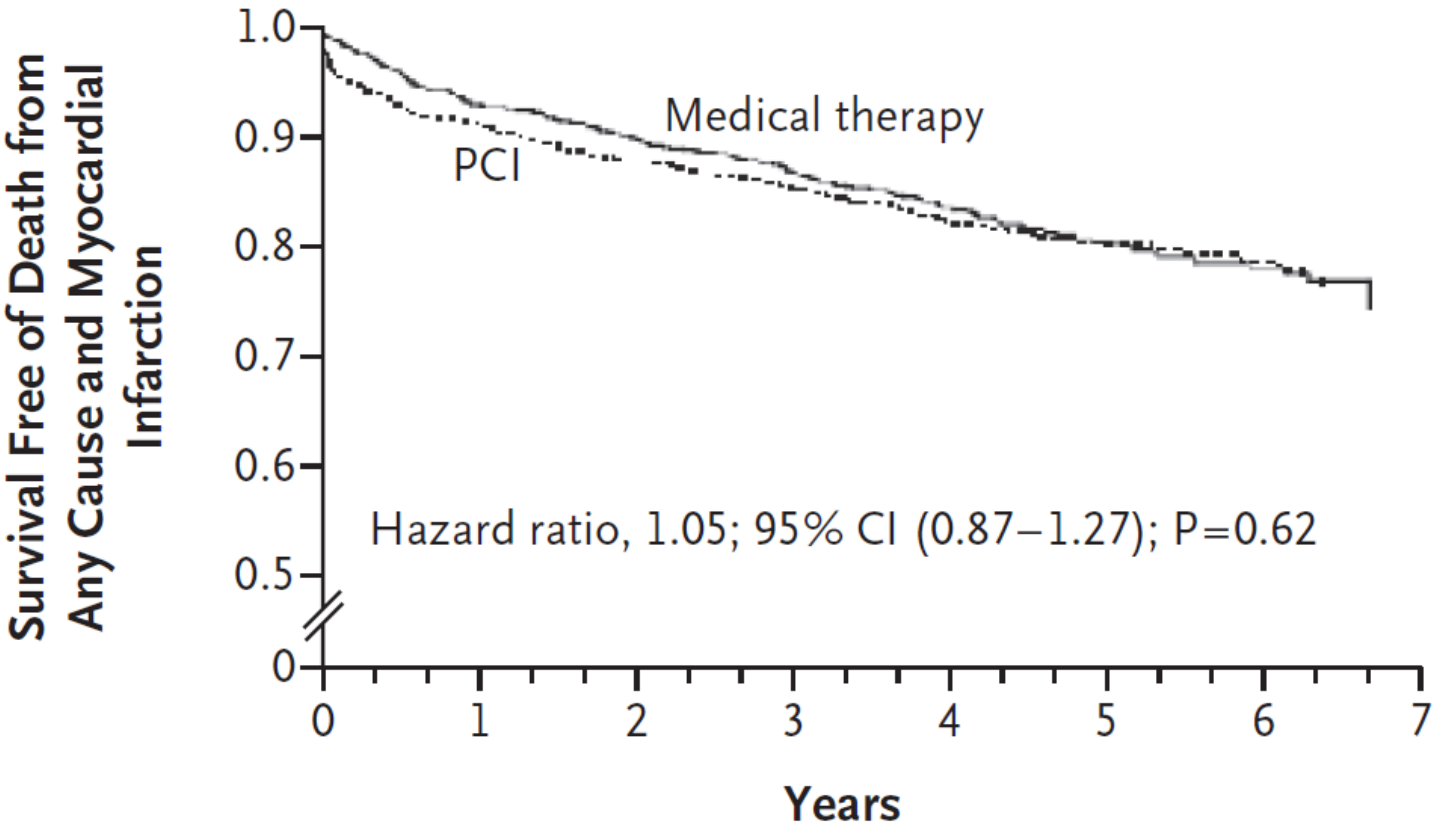
COURAGE

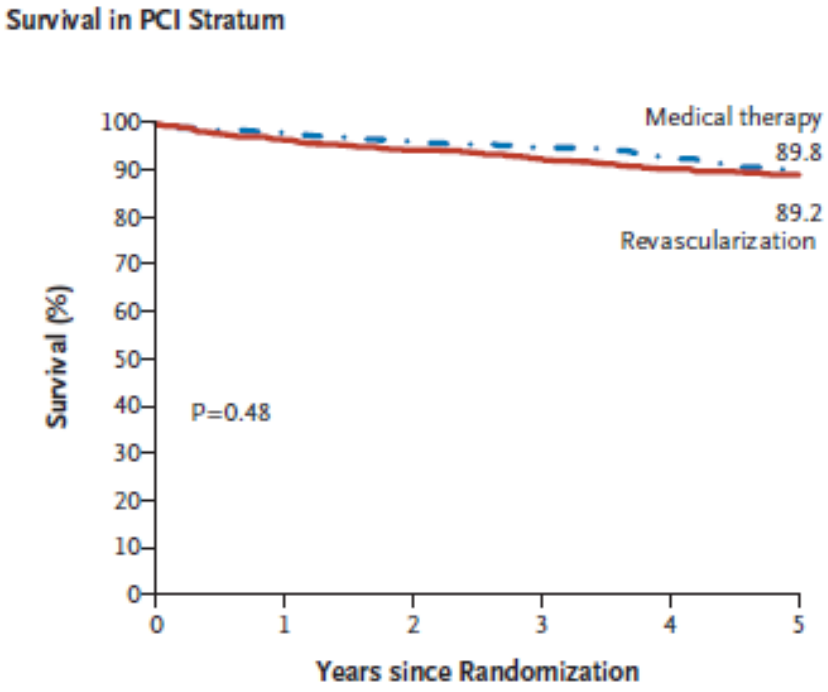
2,287 stable patients with 1,2 or 3 vessel CAD
Randomized to optimal medical therapy or PCI

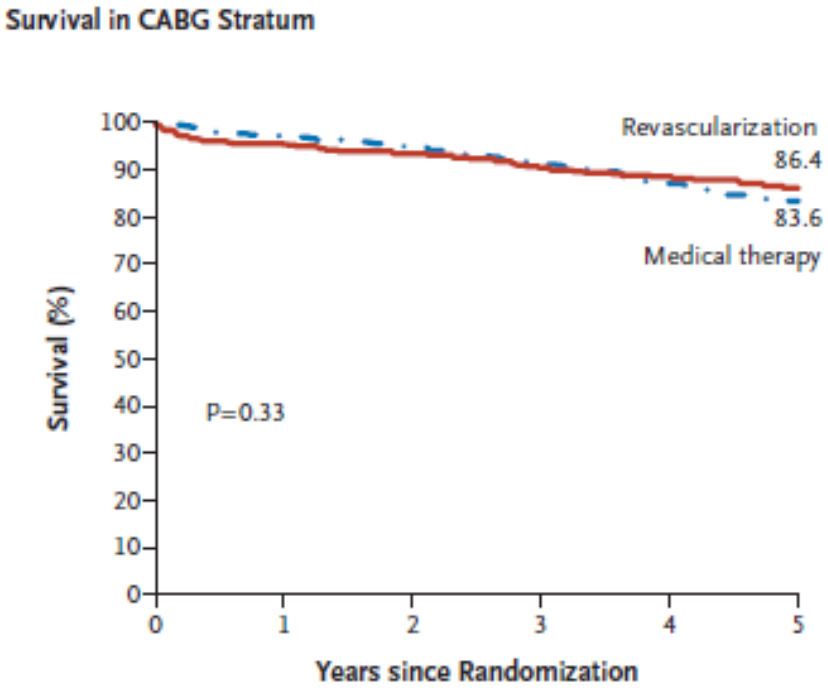


Boden et al., New Engl J Med 2007;356:1503-16.

BARI-2D

2,368 stable CAD patients randomized between CABG vs OMT or PCI vs OMT

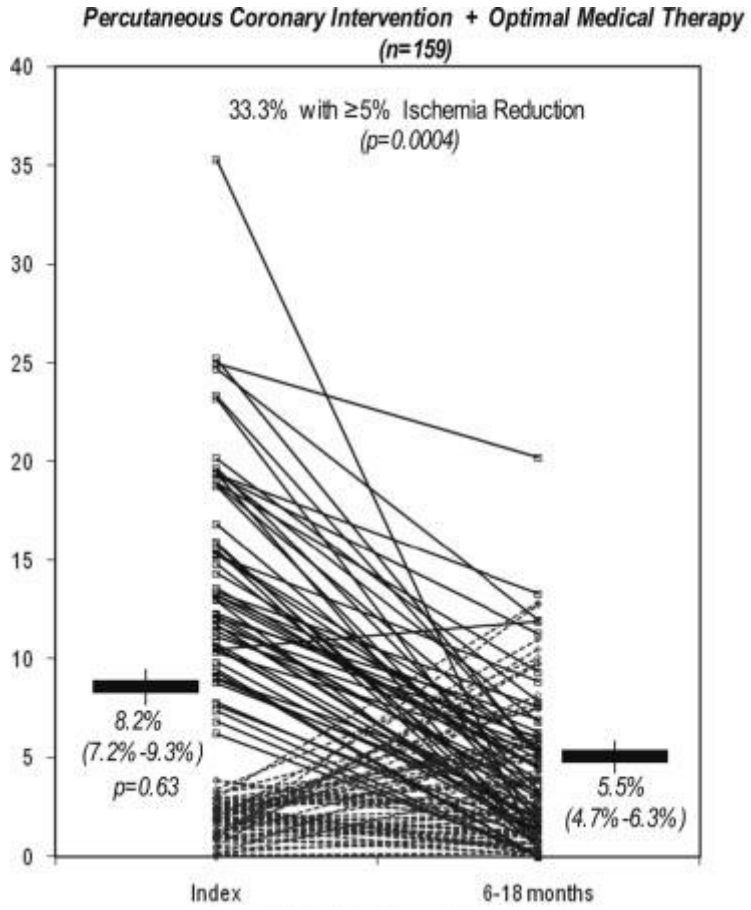




BARI 2D Investigators. N Engl J Med 2009;360:2503-15.

Importance of Ischemia

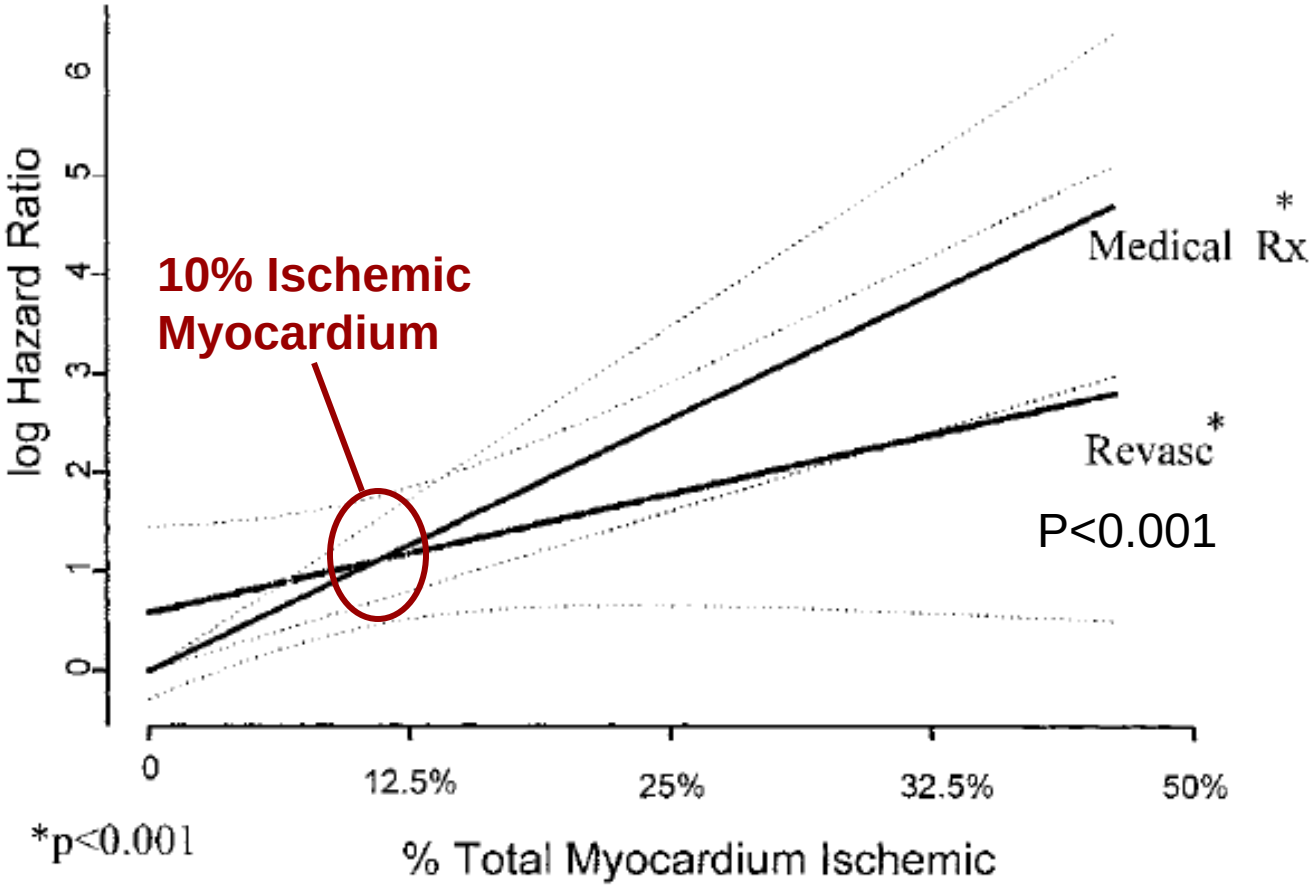
Average of only 8.2% ischemic myocardium in PCI arm of COURAGE
< 1/3 of patients had ≥ 10% ischemic myocardium!



Shaw, et al. Circulation 2008;117:1283-91.

Importance of Ischemia

With greater degrees of ischemia, there is a survival benefit for revascularization



Hachamovitch, et al. Circulation 2003;107:2900-06.

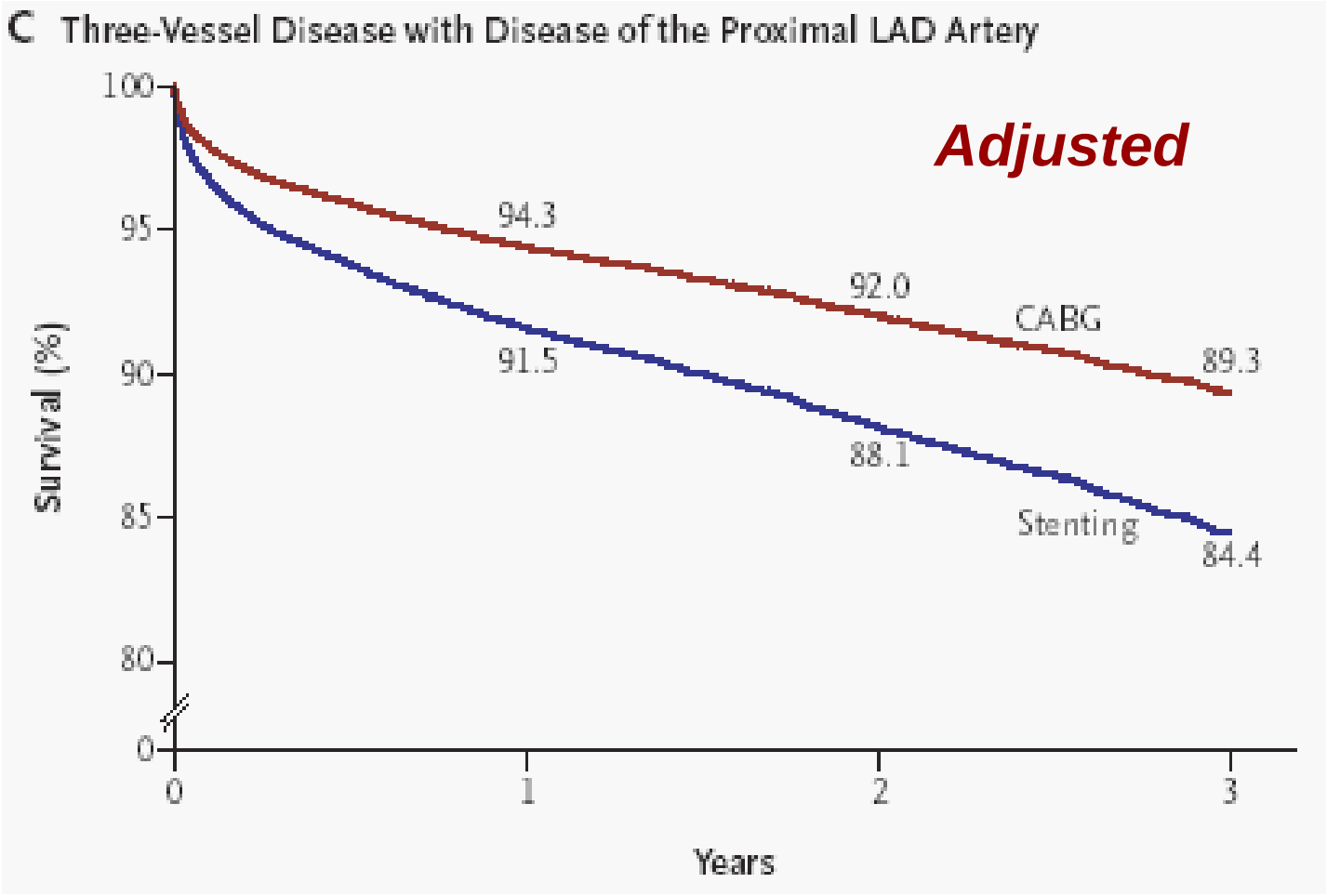
Assuming a large burden of ischemic myocardium…

…what is the role for PCI or CABG?

…and how does diabetes impact the decision?

CABG vs. PCI: *NY Registry*

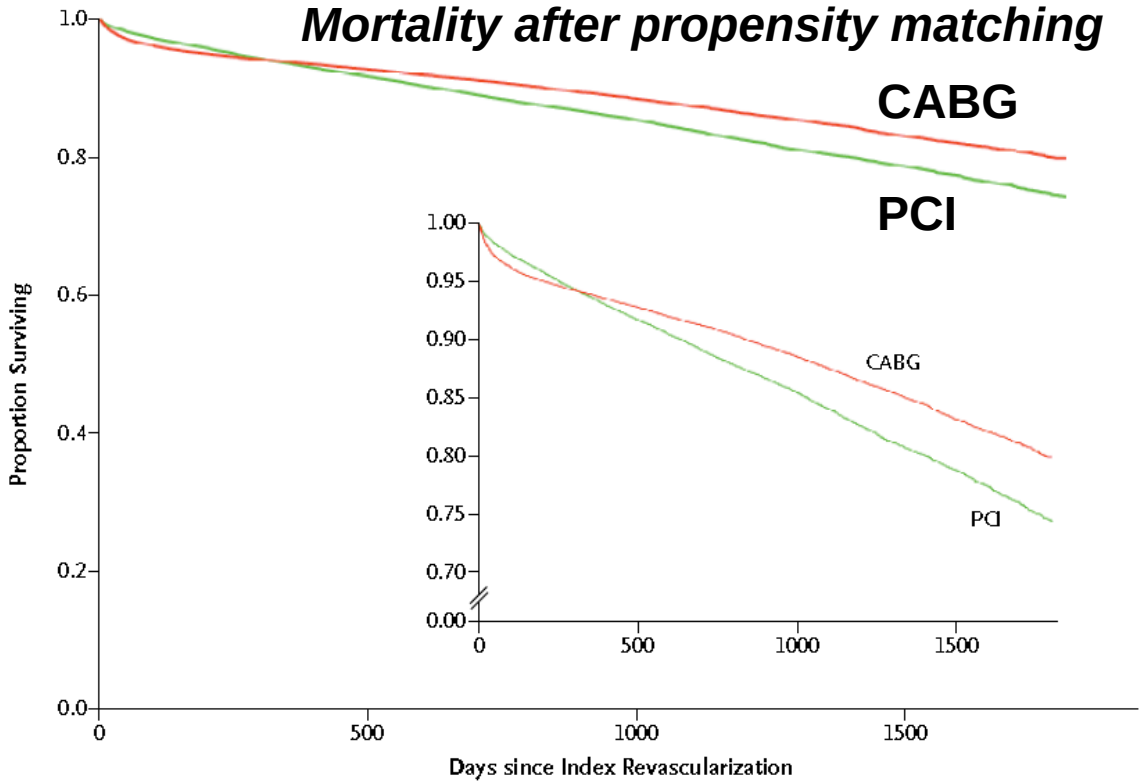
Over 50,000 patients in NY state treated with either PCI or CABG



Hannan et al. New Engl J Med 2005;352:2174-83

CABG vs. PCI: *ASCERT Registry*

~ 189,000 stable patients ≥65 years old treated with either PCI or CABG

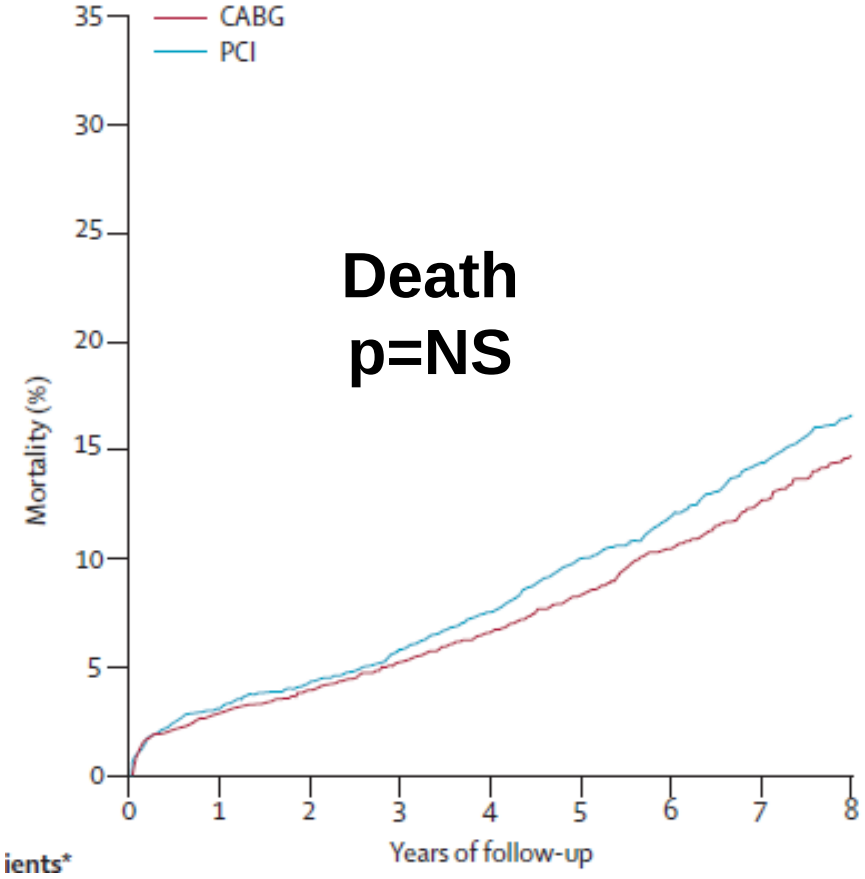


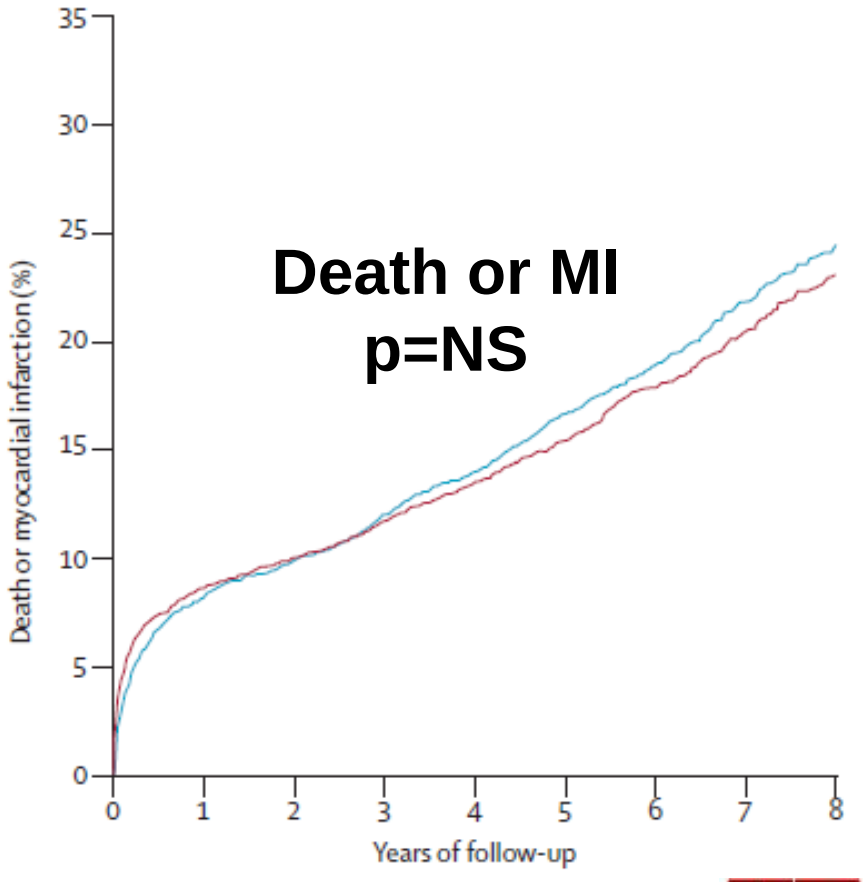
	30-Day	1-Yr	2-Yr	3-Yr	4-Yr
Mortality after CABG, % (95% CI)	2.25 (2.09–2.41)	6.24 (5.97–6.50)	8.98 (8.68–9.29)	12.4 (12.0–12.8)	16.4 (15.9–16.9)
Mortality after PCI, % (95% CI)	1.31 (1.21–1.41)	6.55 (6.35–6.76)	11.3 (11.0–11.6)	15.9 (15.6–16.3)	20.8 (20.4–21.2)
Relative risk with CABG (95% CI)	1.72 (1.52–1.89)	0.95 (0.90–1.00)	0.79 (0.76–0.83)	0.78 (0.75–0.81)	0.79 (0.76–0.82)

Weintraub, et al. New Engl J Med 2012;366:1457-76.

Randomized Trials

Meta-Analysis of 10 randomized CABG vs. PCI trials including >7,000 patients



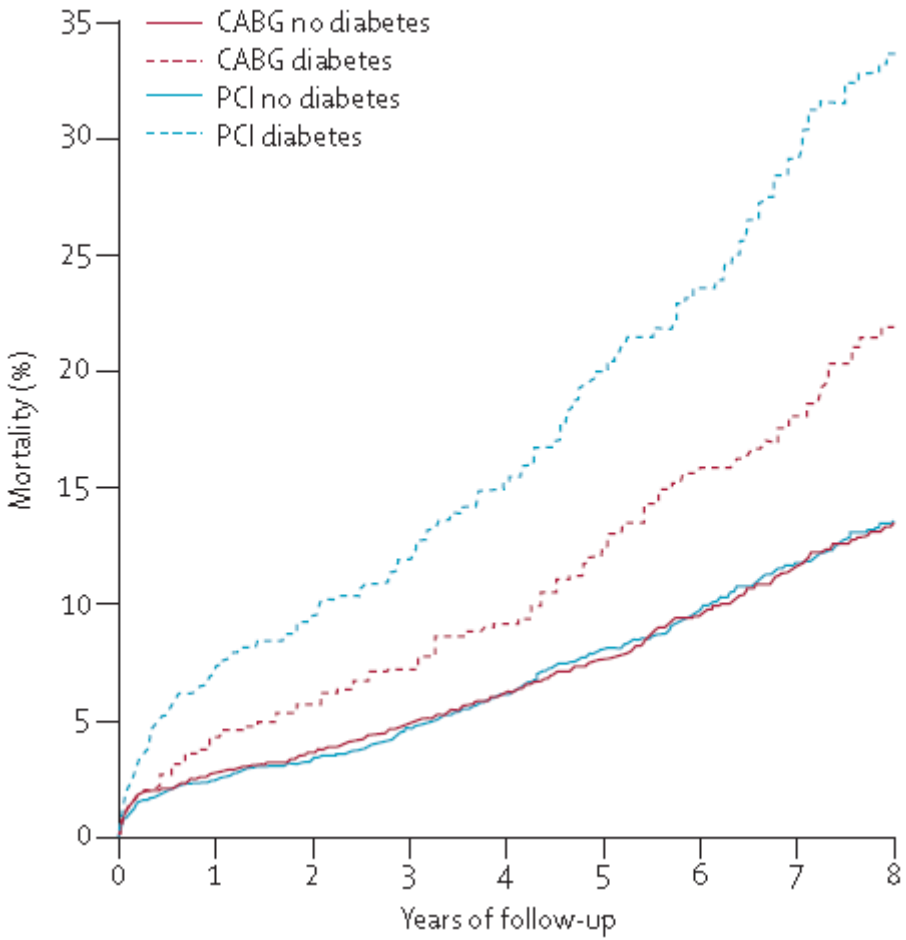


ients*

Hlatky, et al. Lancet 2009;373:1190-97.

Meta-Analysis of CABG vs. PCI Trials

Impact of Diabetes



PCI Diabetes

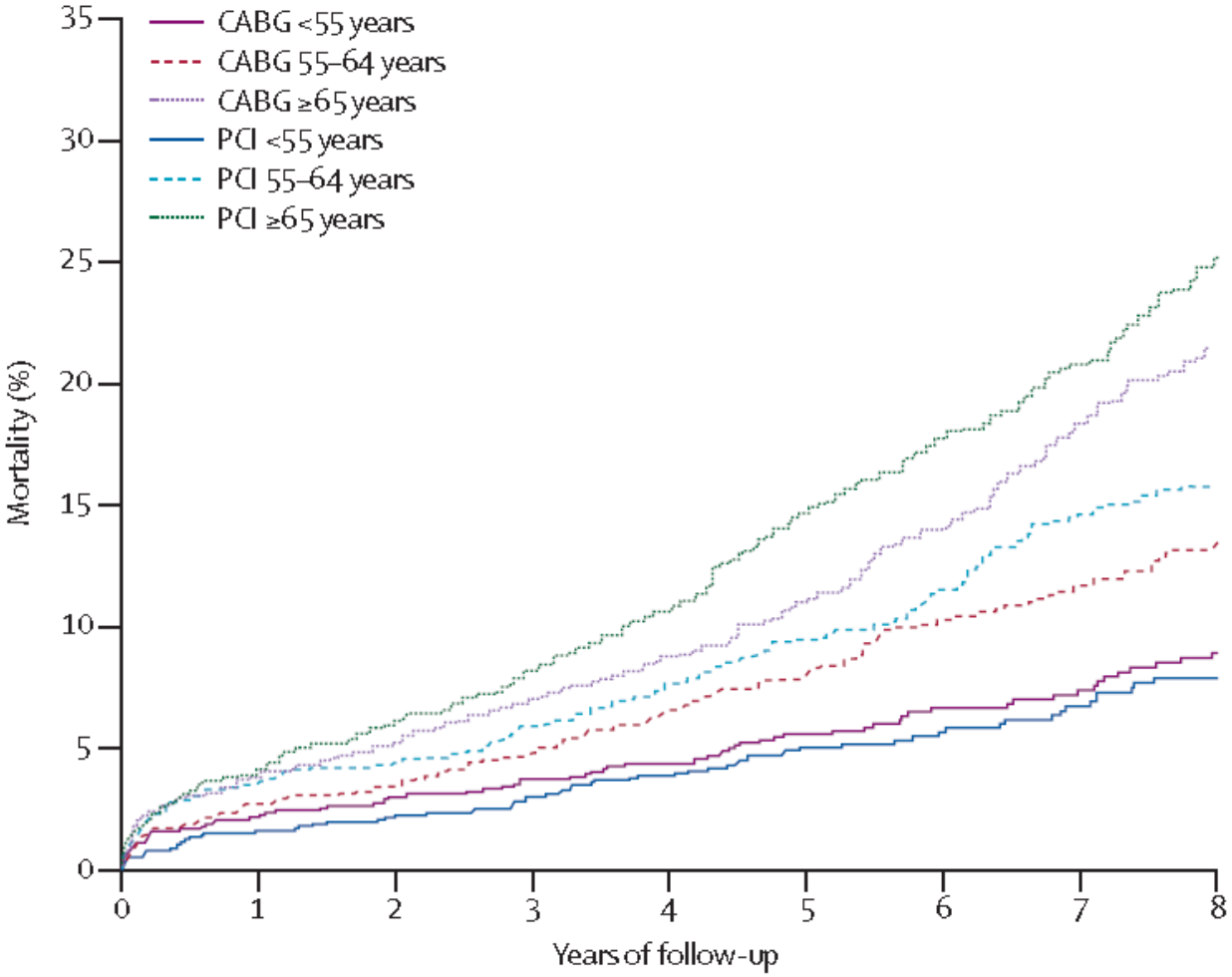
CABG Diabetes

CABG and PCI No Diabetes

Hlatky, et al. Lancet 2009;373:1190-97.

Meta-Analysis of CABG vs. PCI Trials

Impact of Age



PCI ≥65 Years

CABG ≥65 Years

PCI 55-64 Years

CABG 55-64 Years

CABG and PCI <55 Years

Hlatky, et al. Lancet 2009;373:1190-97.

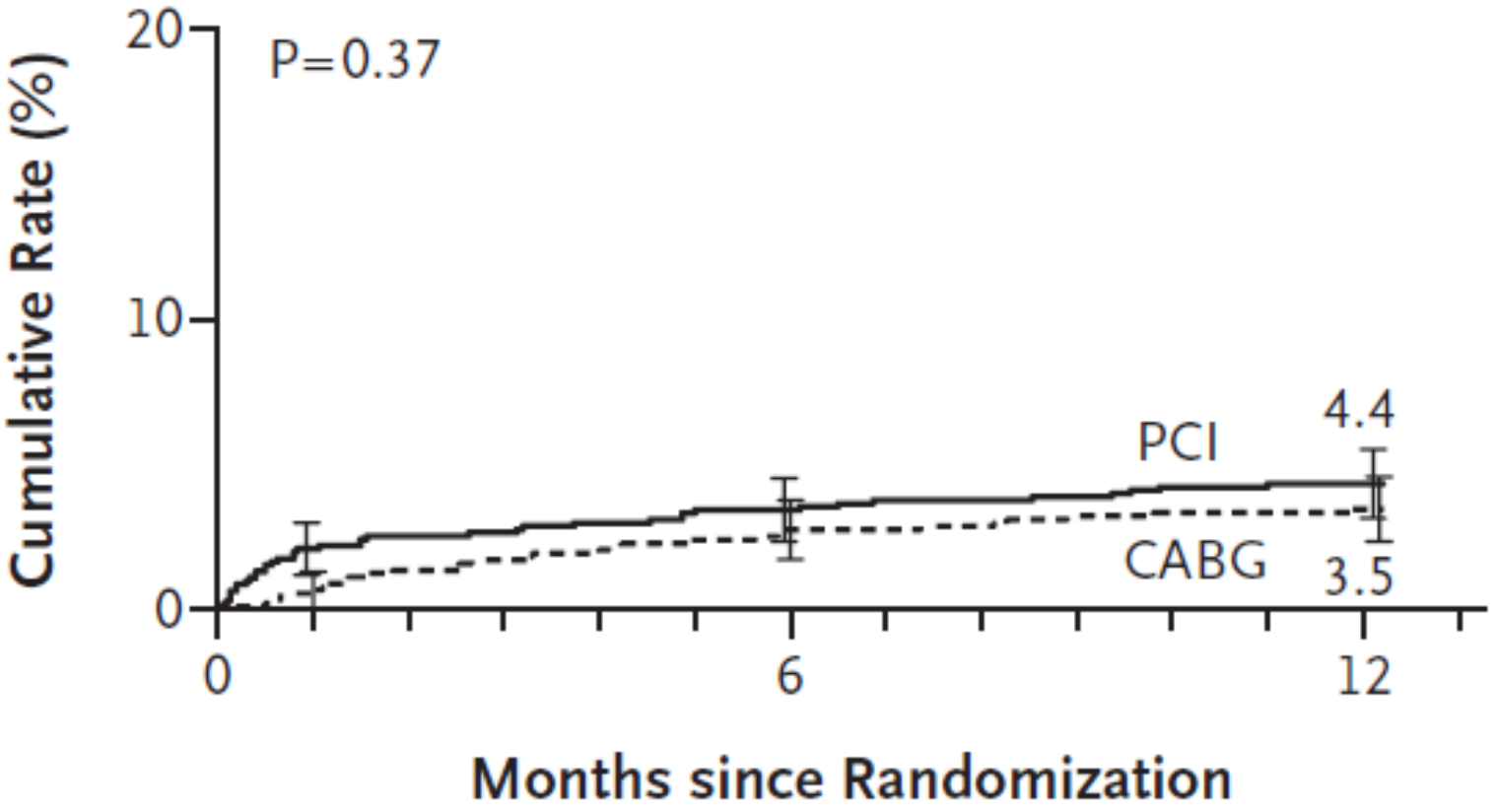
SYNTAX Trial:

- 1800 patients with 3 vessel CAD randomized to PCI with Taxus drug-eluting stents or CABG
  - ~28% diabetic
  - ~33% with LM disease
  - 4.6 stents per patient
  - Average of 86 mm of stent (1/3 with >100 mm)

Serruys, et al. N Engl J Med 2009;360:961-72

SYNTAX

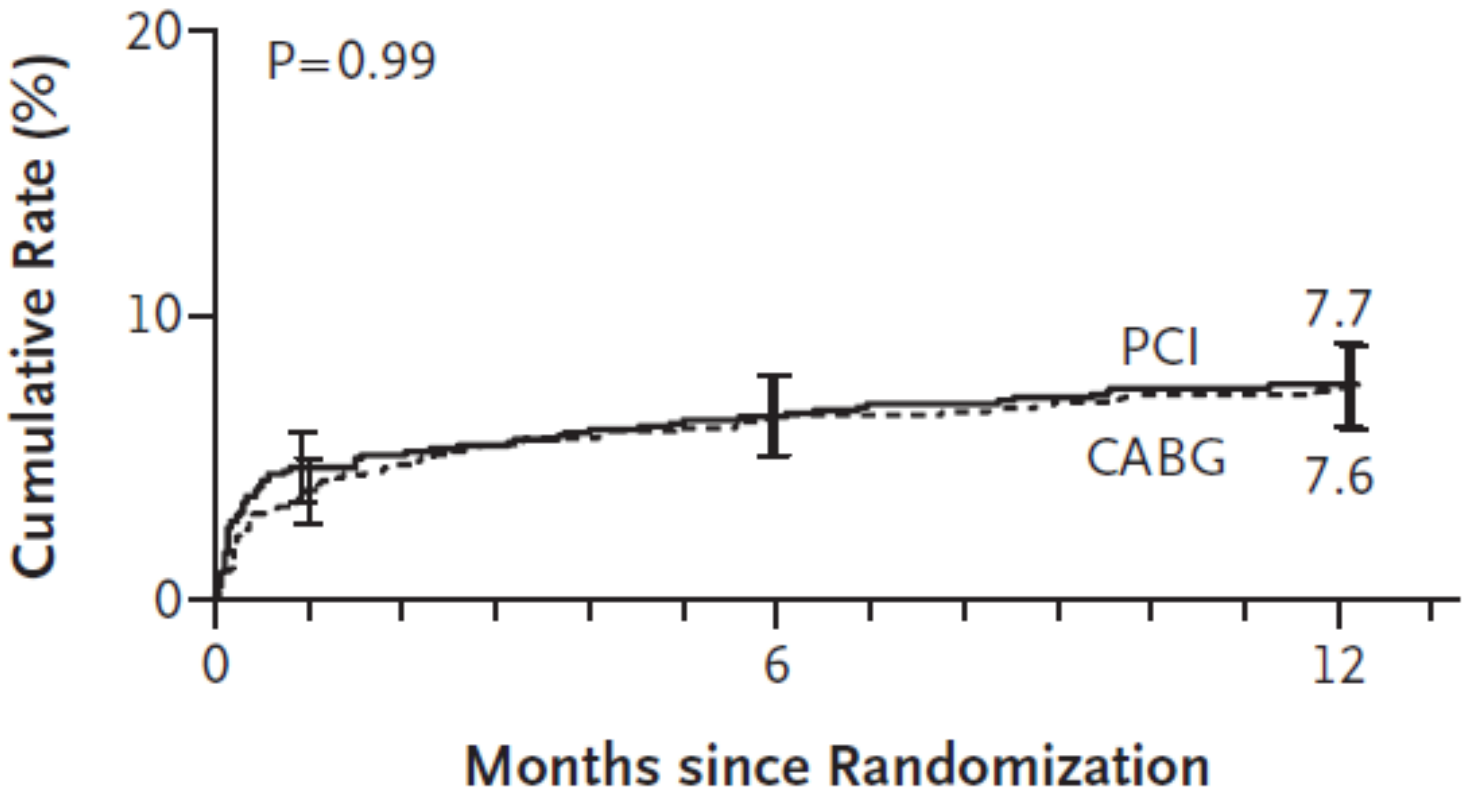
All-Cause Death at 12 Months



Serruys, et al. N Engl J Med 2009;360:961-72

SYNTAX

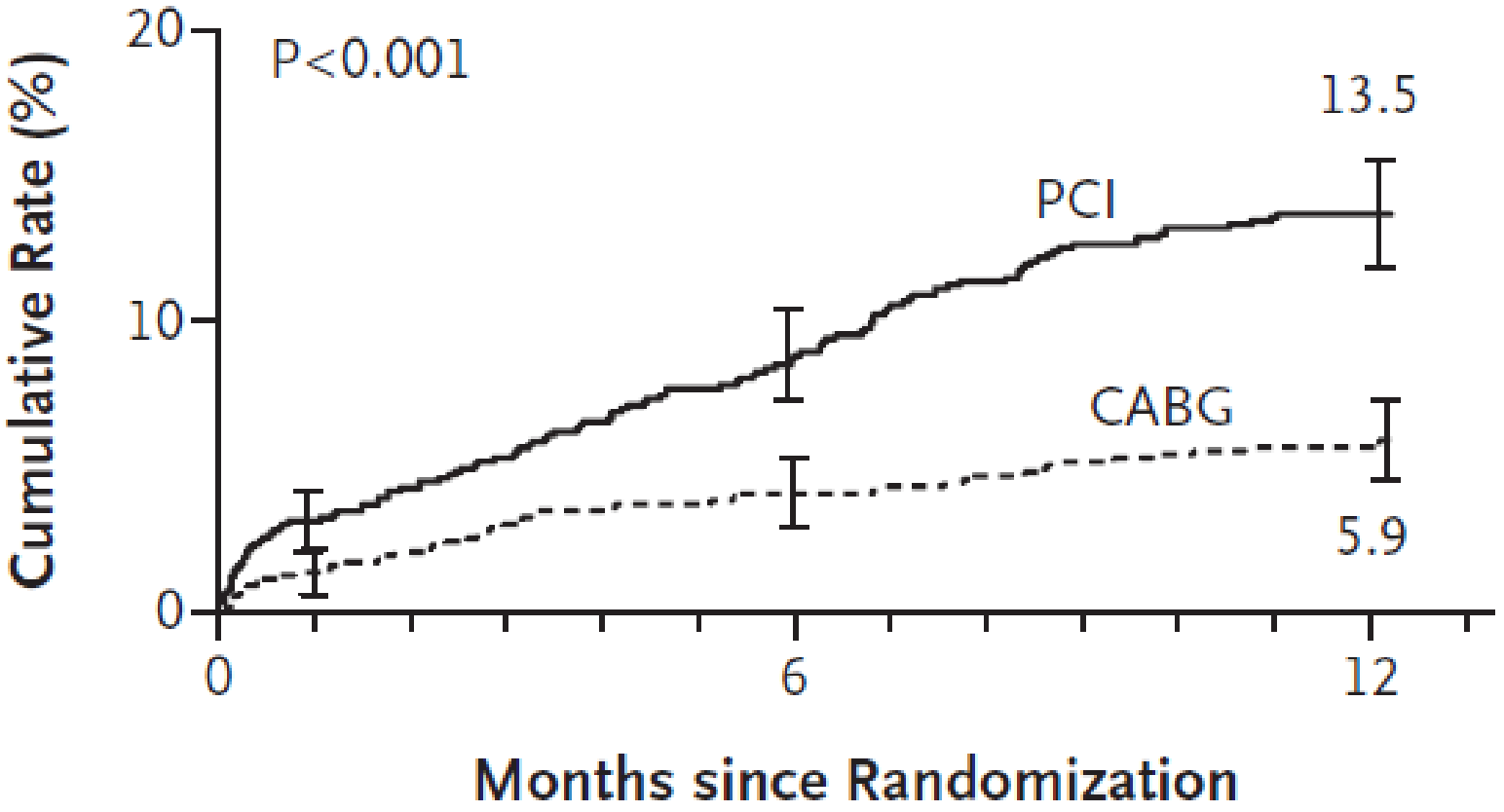
Death from any cause, stroke or MI



Serruys, et al. N Engl J Med 2009;360:961-72

SYNTAX

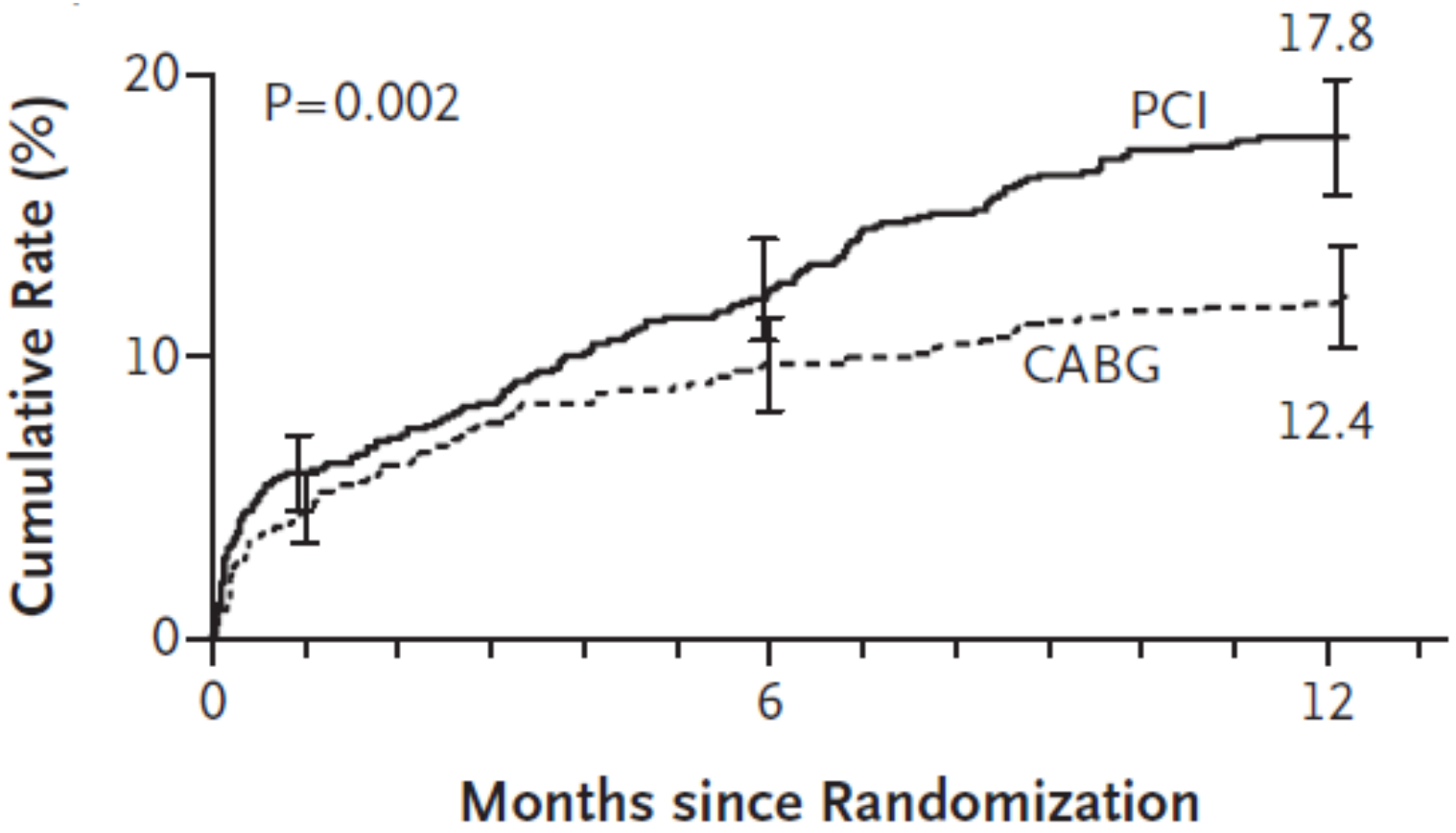
Repeat Revascularization at 12 months



Serruys, et al. N Engl J Med 2009;360:961-72

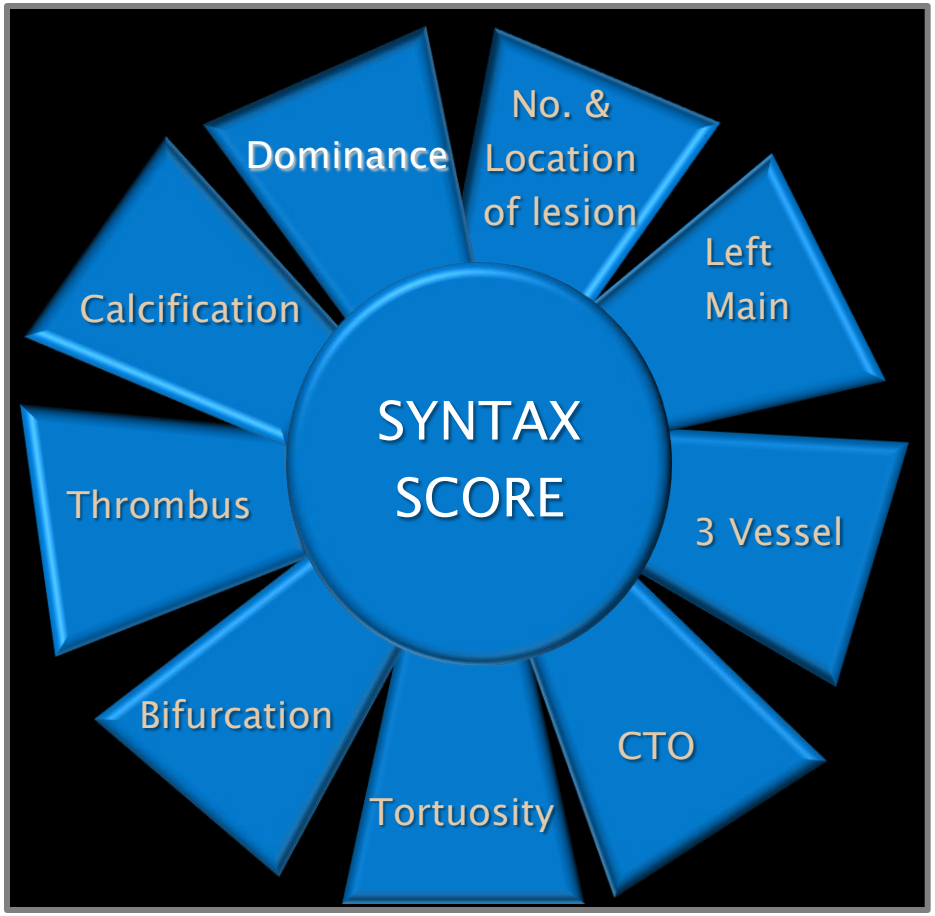
SYNTAX

MACCE at 12 months



Serruys, et al. N Engl J Med 2009;360:961-72

SYNTAX Score

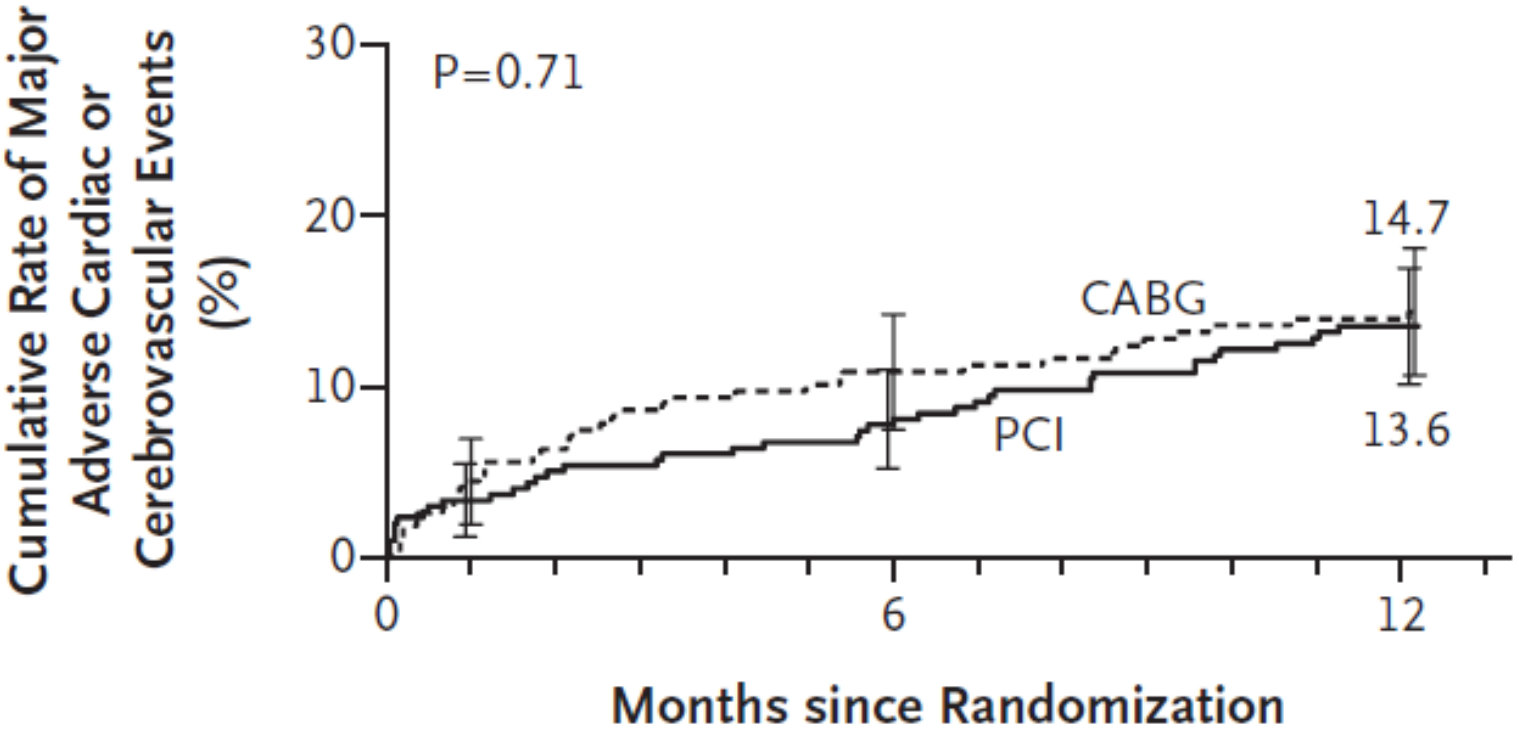


Serruys, et al. N Engl J Med 2009;360:961-72

SYNTAX

Similar outcomes with PCI vs CABG with lower SYNTAX score

Lowest Tertile (SYNTAX score ≤ 22)

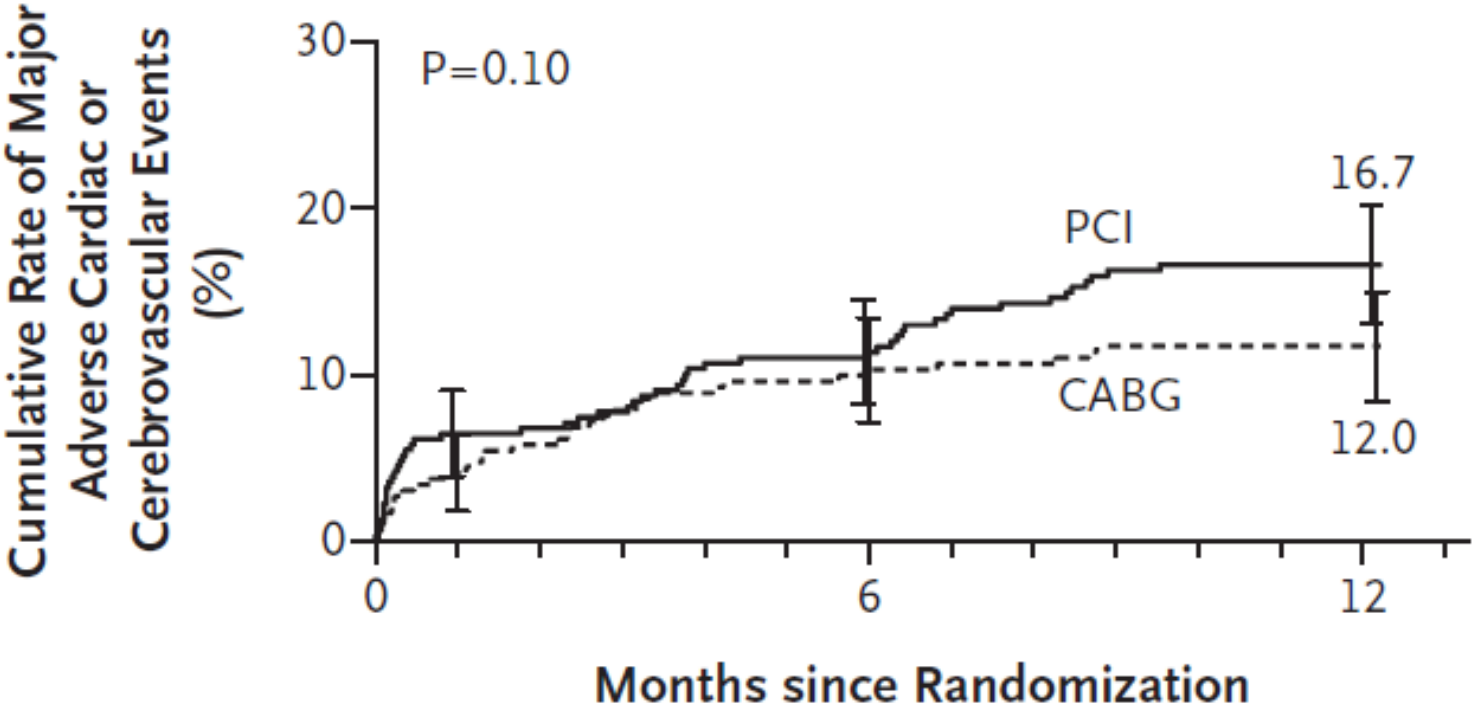


Serruys, et al. N Engl J Med 2009;360:961-72

SYNTAX

Worse outcomes with PCI vs CABG with higher SYNTAX score

Intermediate Tertile (SYNTAX score 23-32)

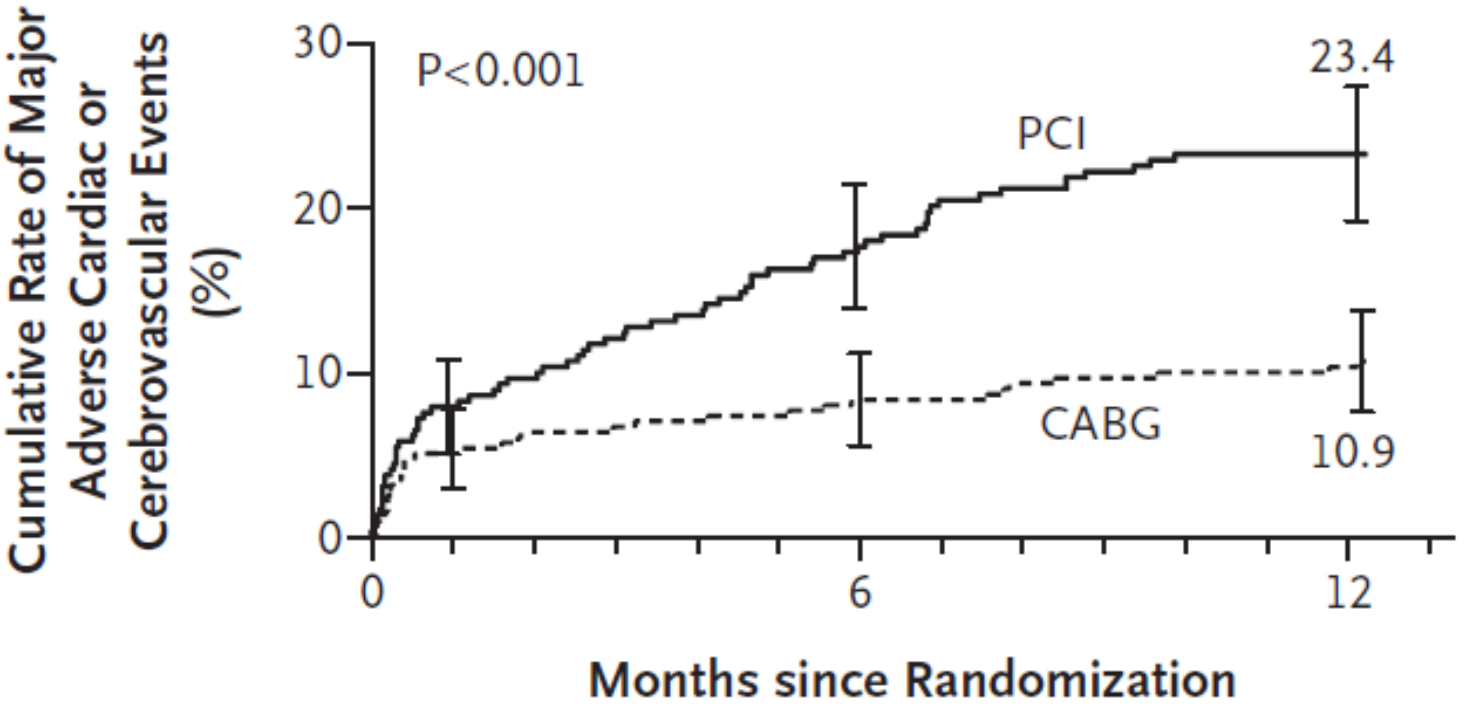


Serruys, et al. N Engl J Med 2009;360:961-72

SYNTAX

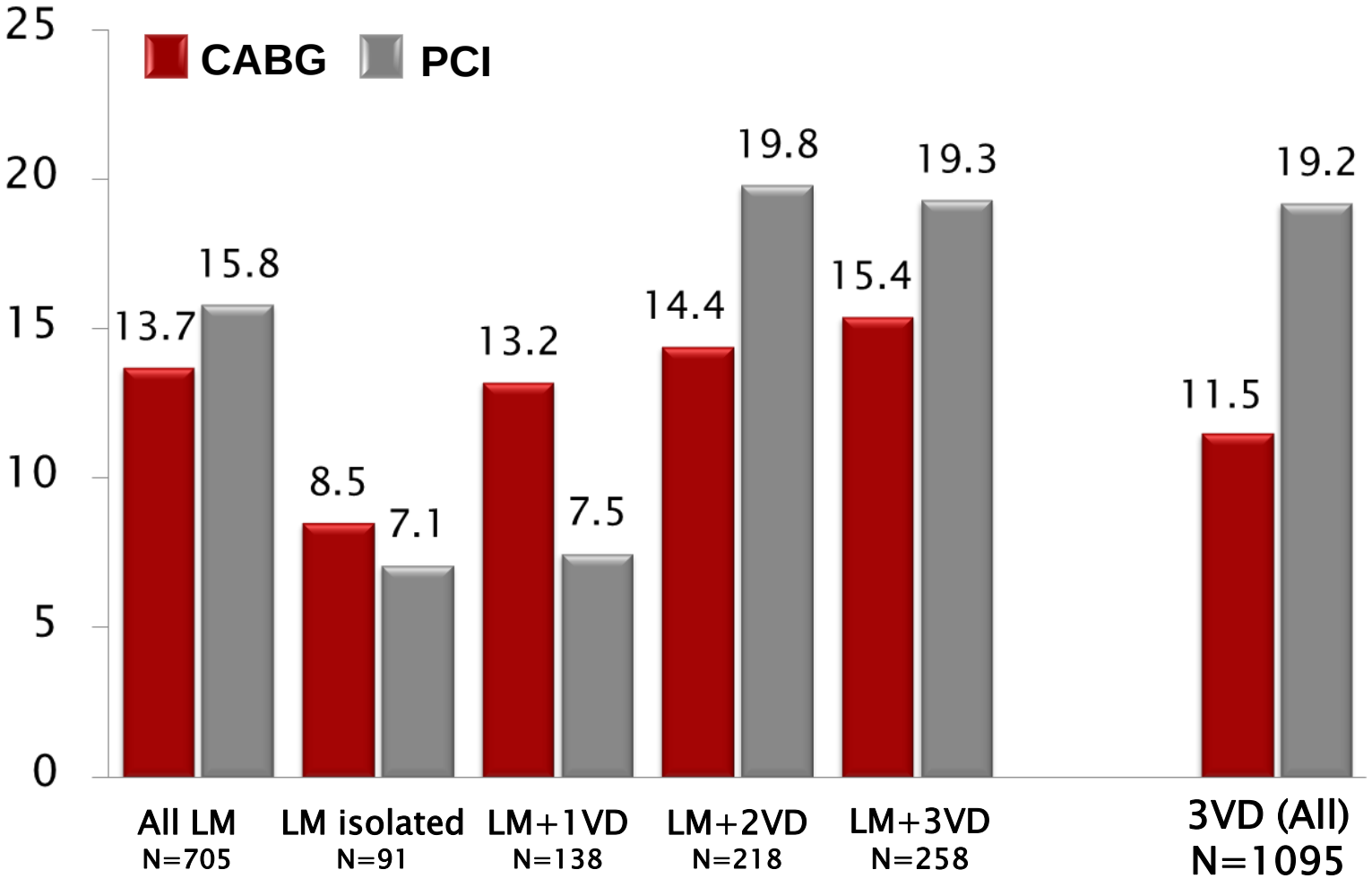
Worse outcomes with PCI vs CABG with higher SYNTAX score

High Tertile (SYNTAX score ≥ 33)



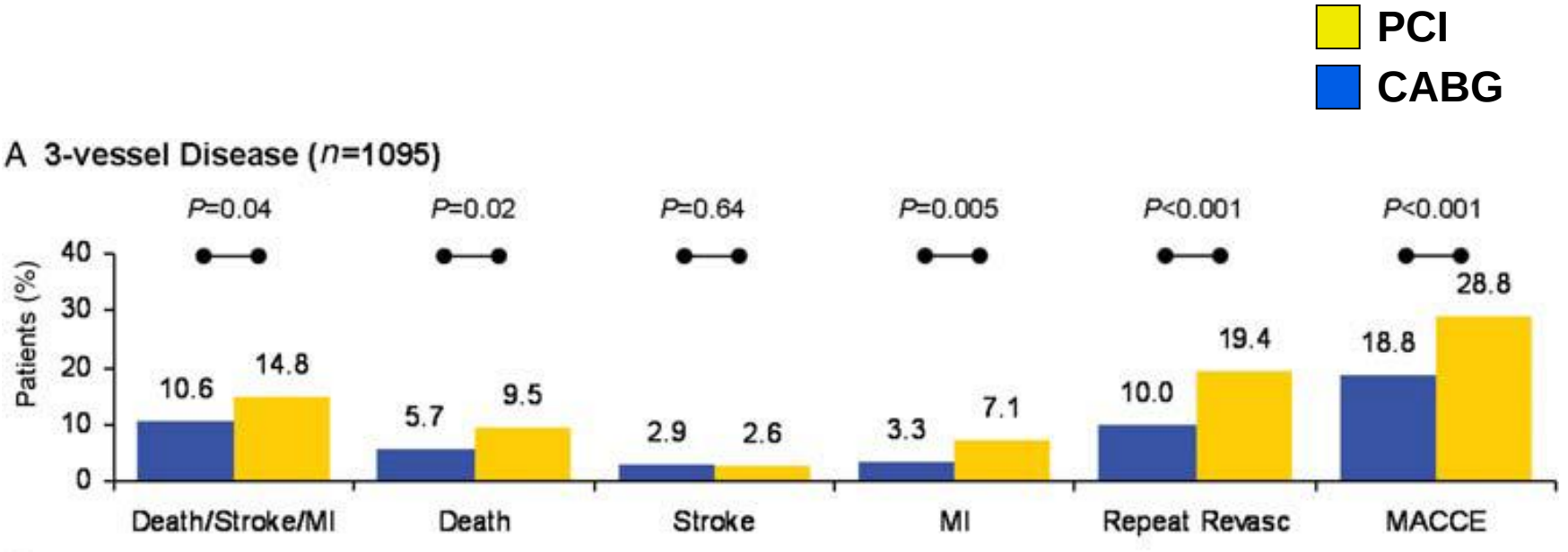
Serruys, et al. N Engl J Med 2009;360:961-72

SYNTAX: *MACCE by Subgroup*



SYNTAX

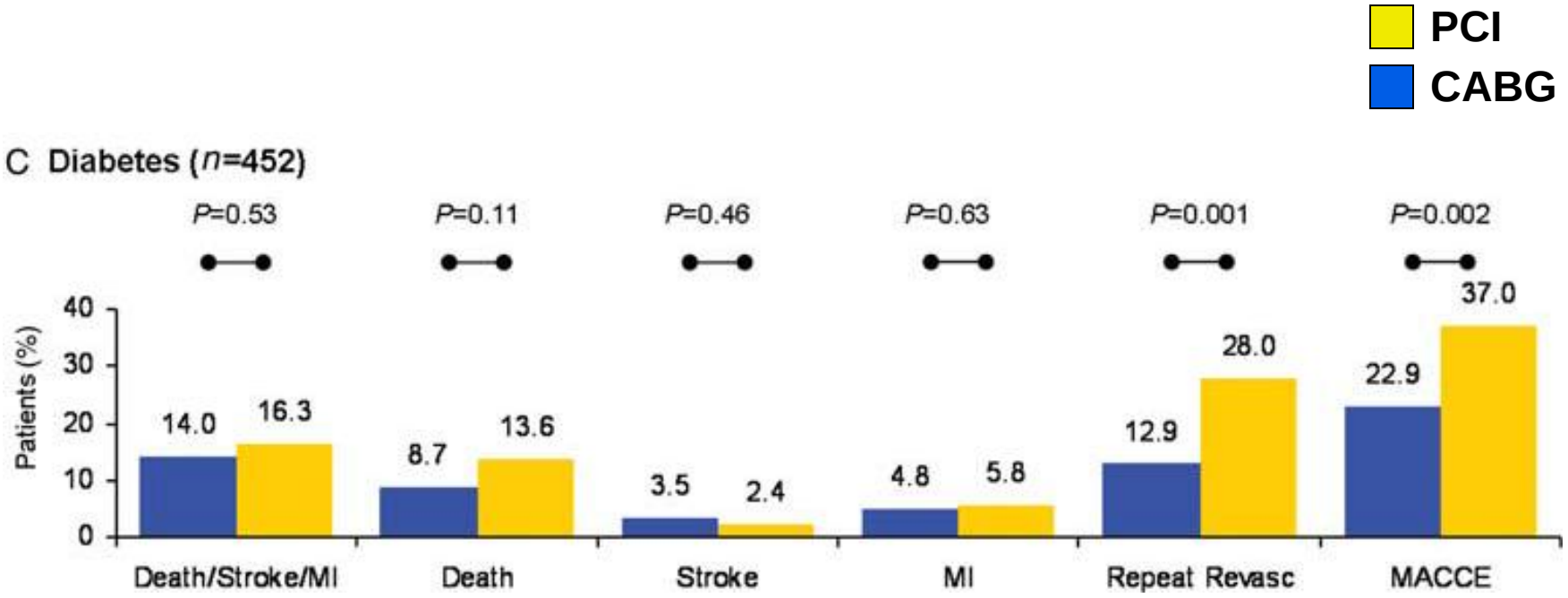
Outcomes at 3 years: 3-Vessel Disease



Kappetein, et al. Eur Heart J 2011;32:2125-34

SYNTAX

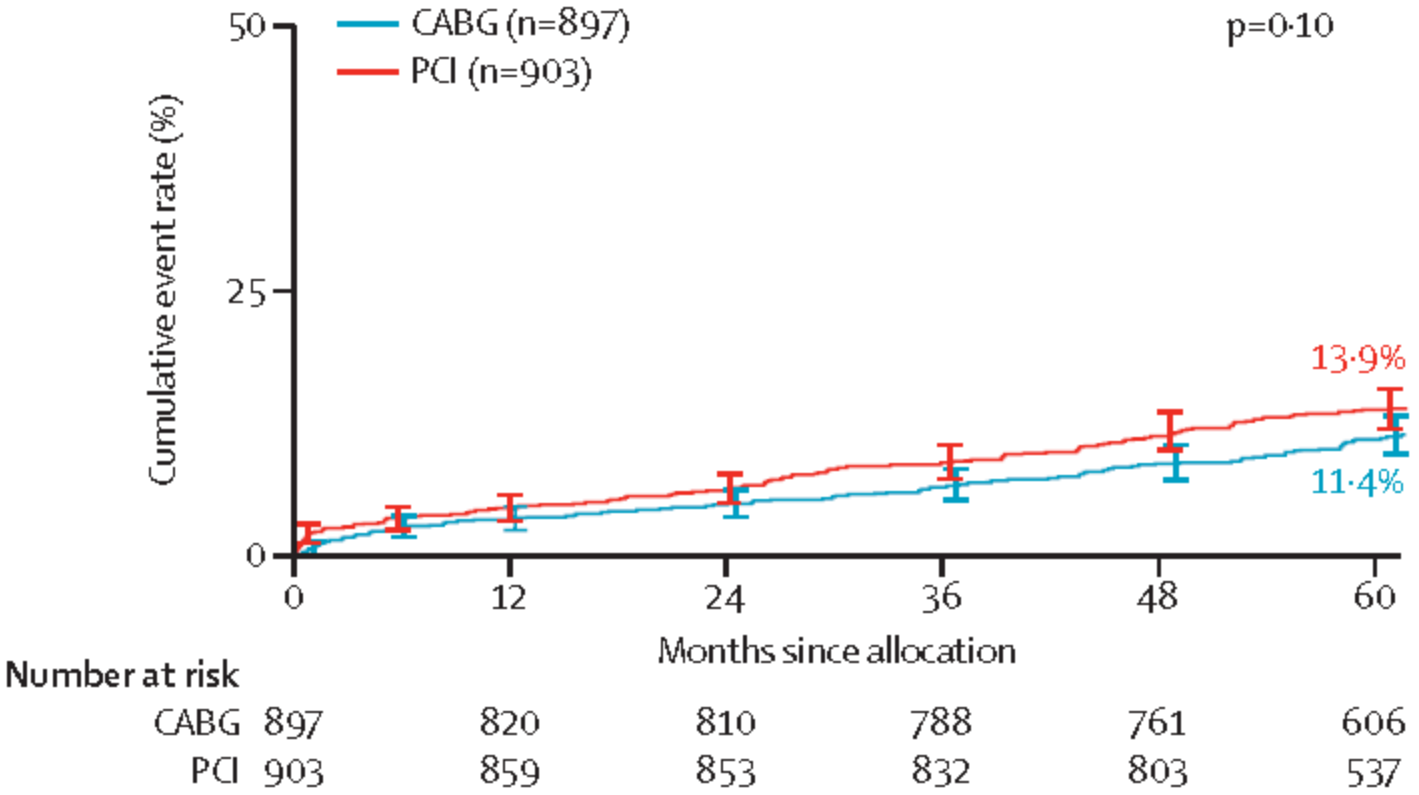
Outcomes at 3 years: Diabetics



Kappetein, et al. Eur Heart J 2011;32:2125-34

SYNTAX

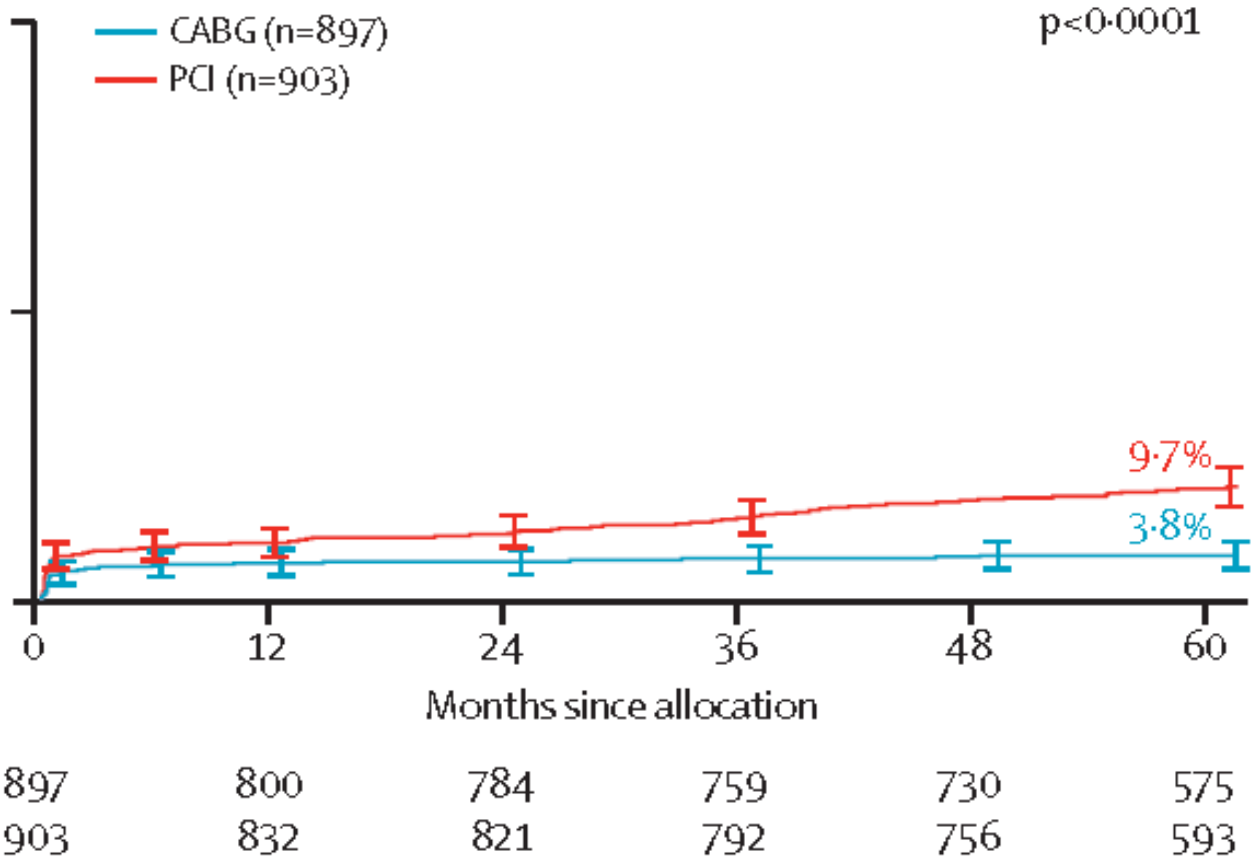
5 Year Outcomes: All Cause Mortality



Mohr, et al. Lancet 2013;381:629-38

SYNTAX

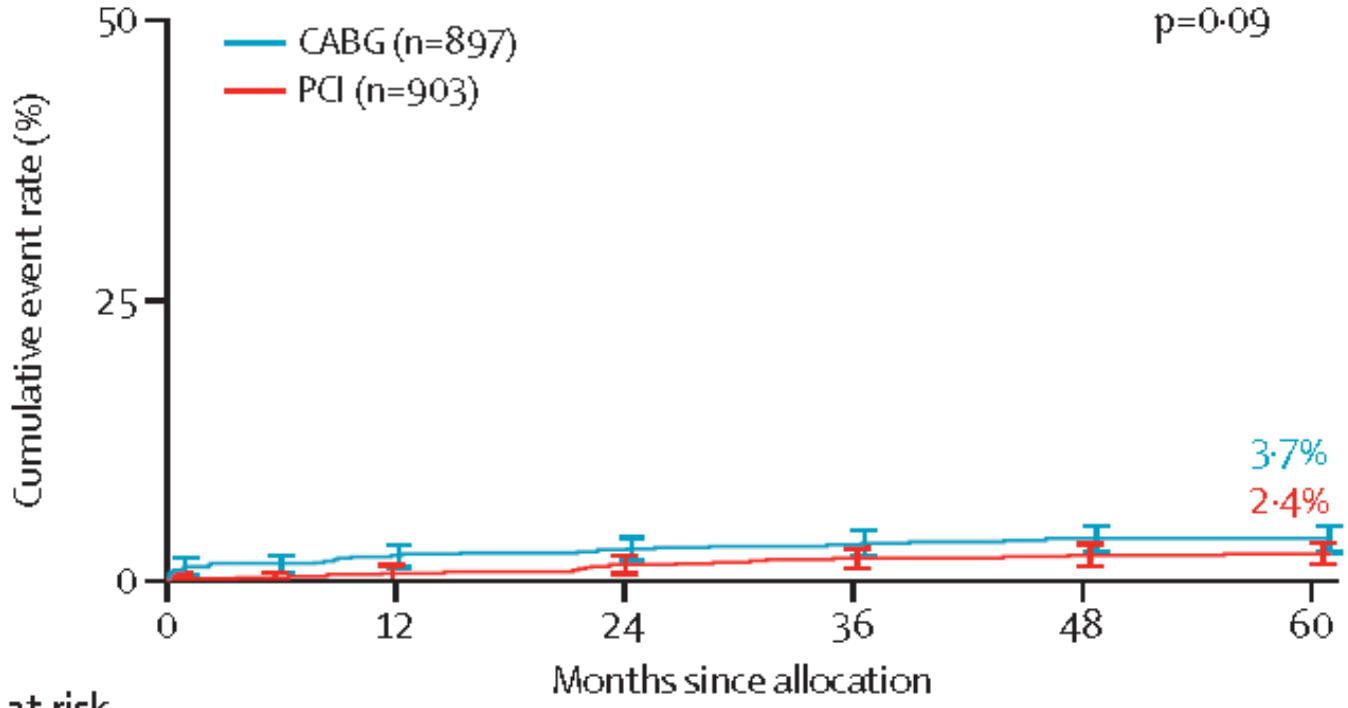
5 Year Outcomes: Myocardial Infarction



Mohr, et al. Lancet 2013;381:629-38

SYNTAX

5 Year Outcomes: Stroke



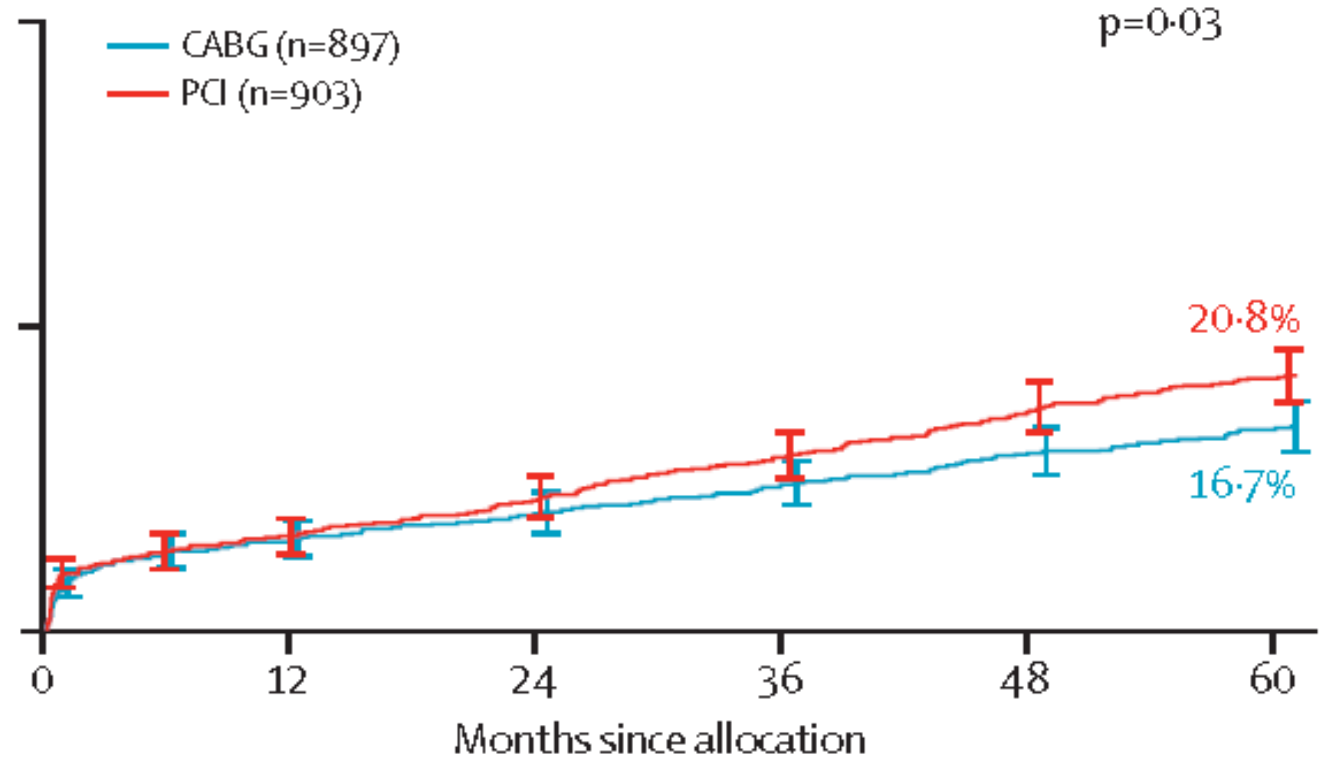
Number at risk

CABG	897	806	790	763	732	579
PCI	903	854	842	815	782	622

Mohr, et al. Lancet 2013;381:629-38

SYNTAX

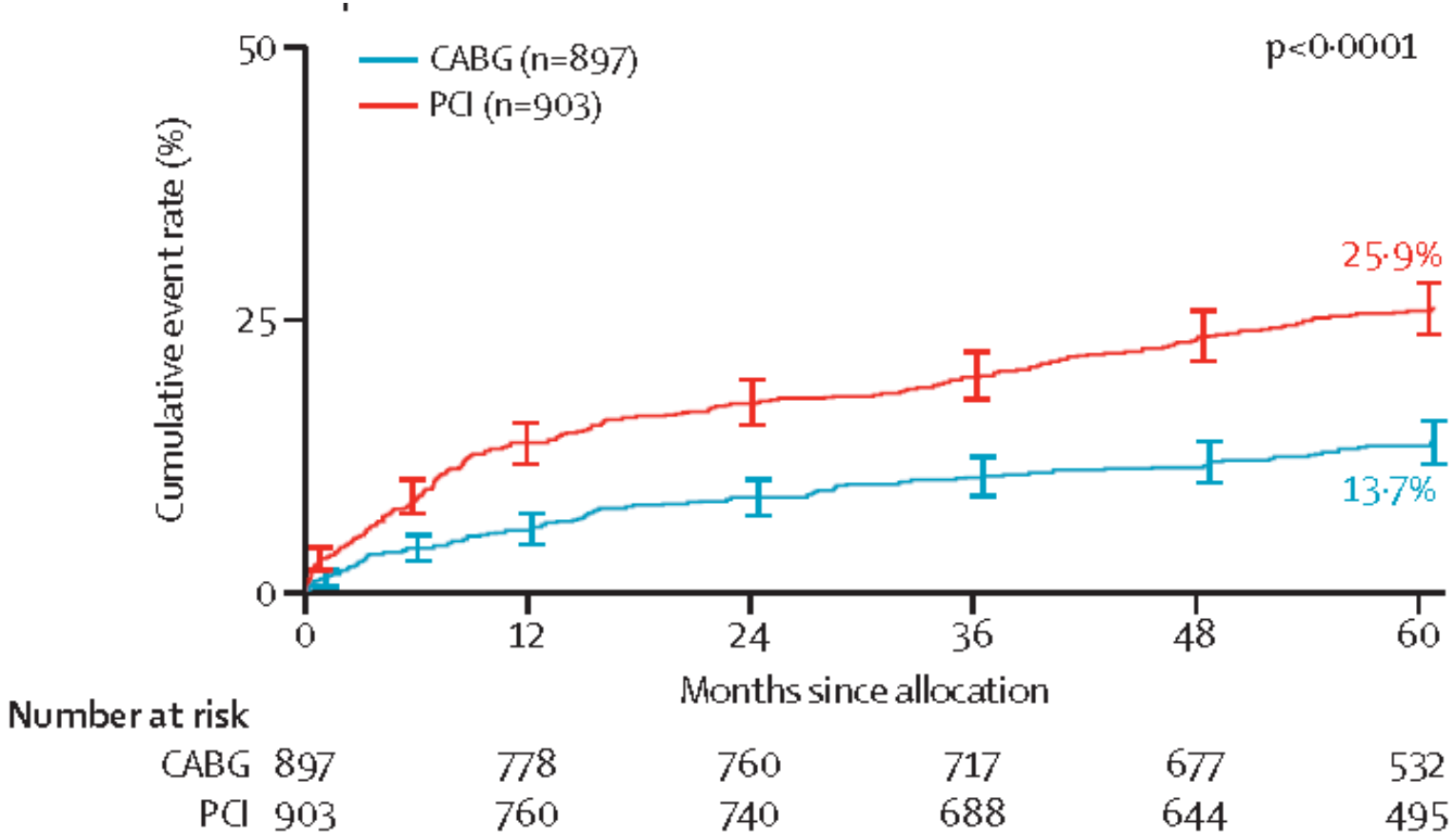
5 Year Outcomes: Death, Stroke, or MI



Mohr, et al. Lancet 2013;381:629-38

SYNTAX

5 Year Outcomes: Revascularization



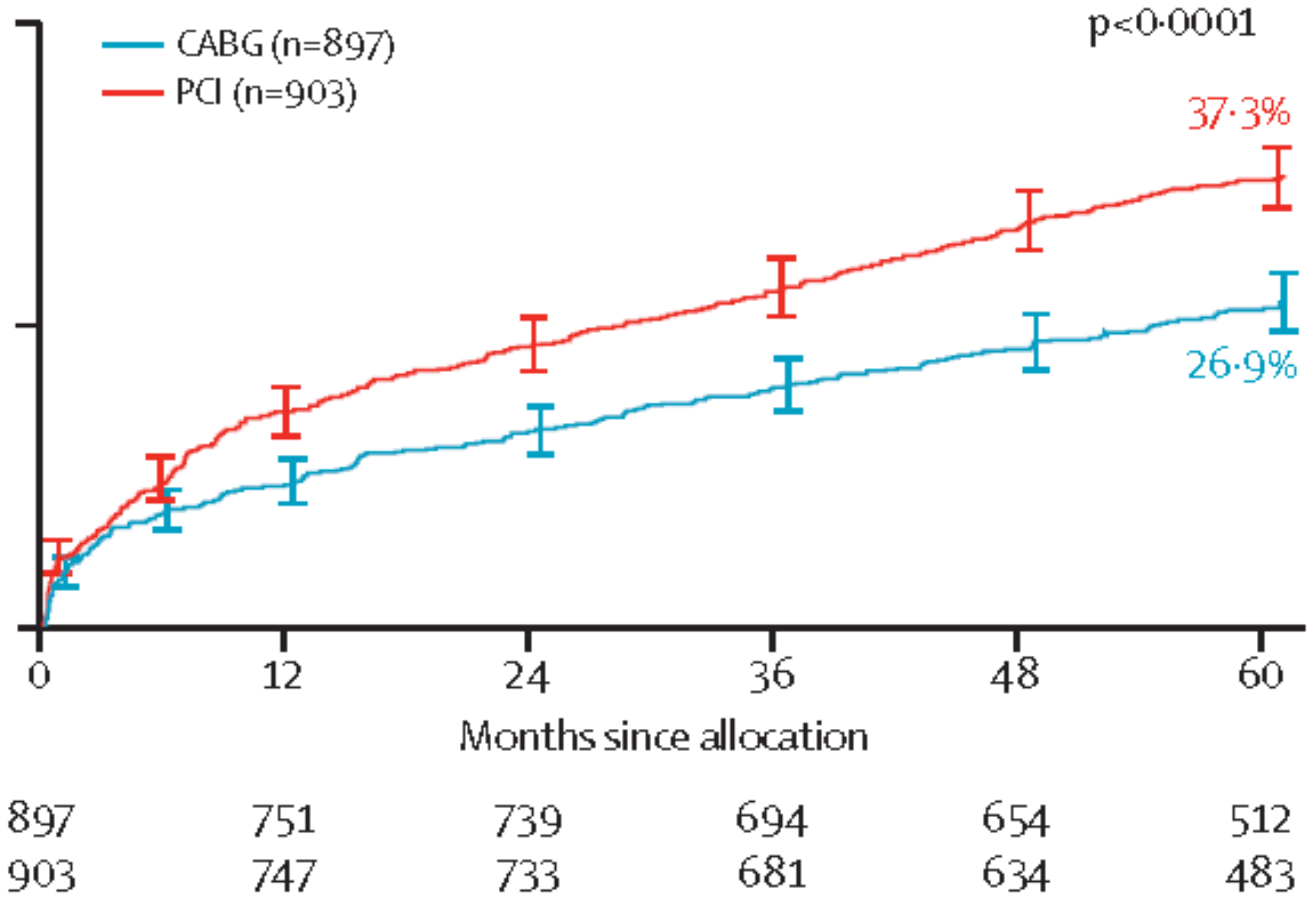
Number at risk

CABG	897	778	760	717	677	532
PCI	903	760	740	688	644	495

Mohr, et al. Lancet 2013;381:629-38

SYNTAX

5 Year Outcomes: MACCE

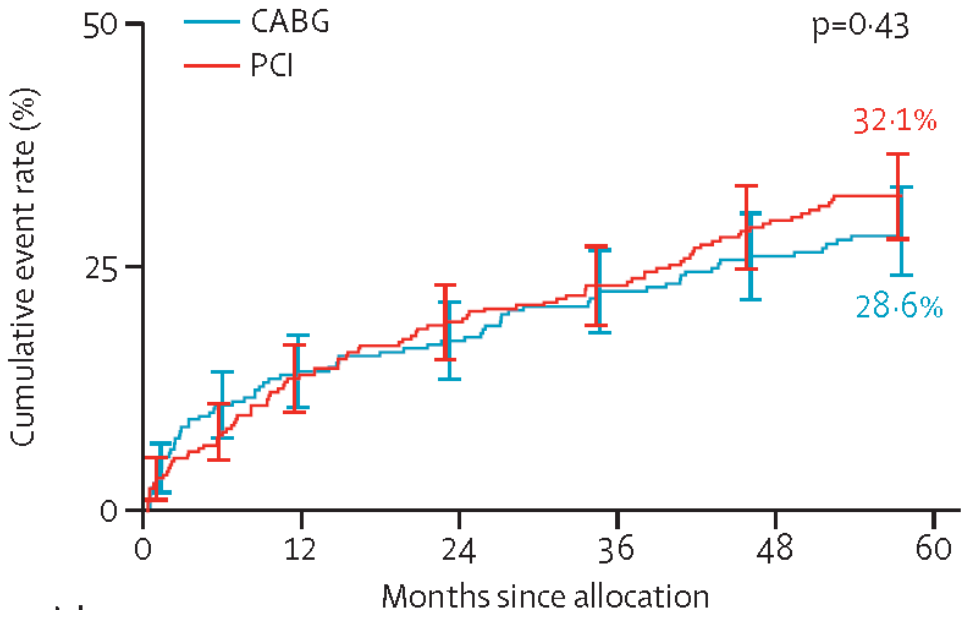


Mohr, et al. Lancet 2013;381:629-38

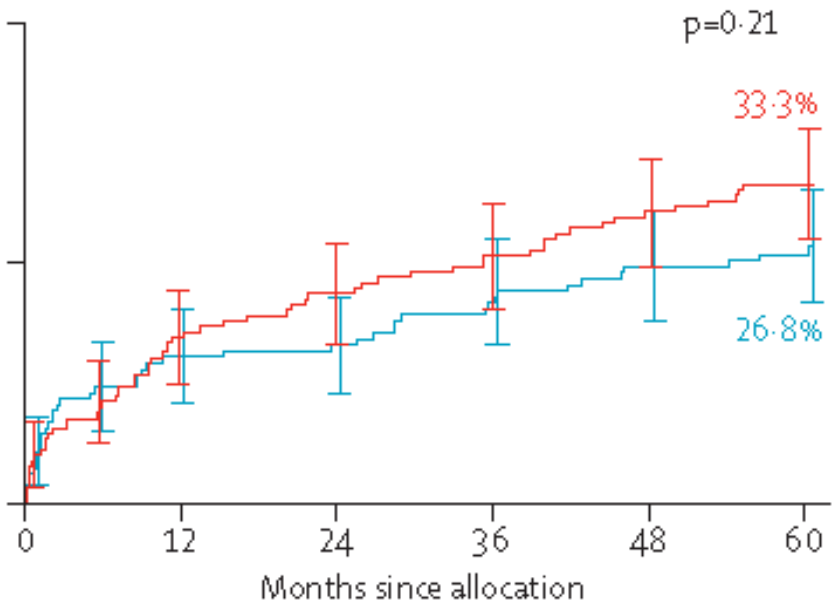
SYNTAX

5 Year Outcomes: Lowest SYNTAX Tertile (0-22)

All Patients



3-Vessel CAD only

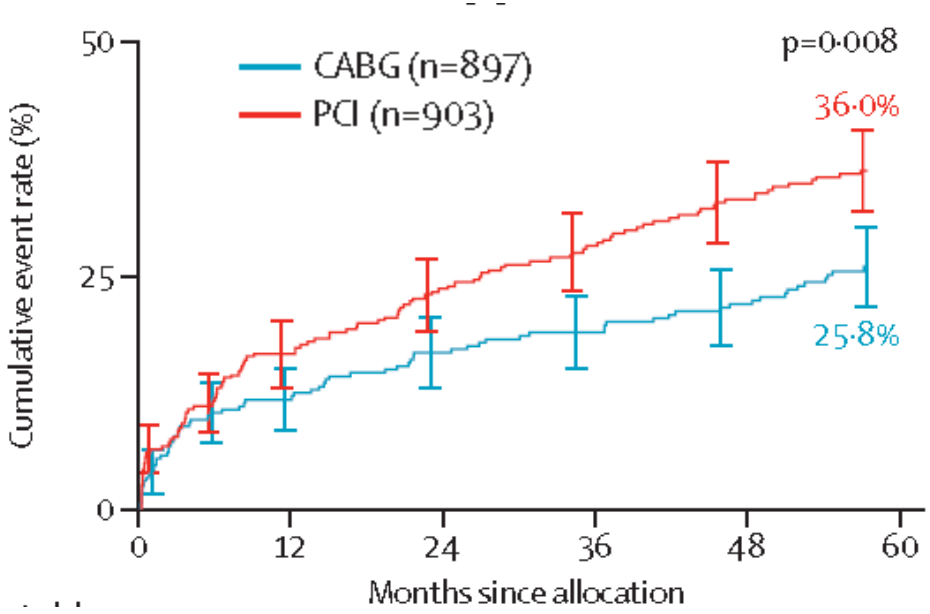


Mohr, et al. Lancet 2013;381:629-38

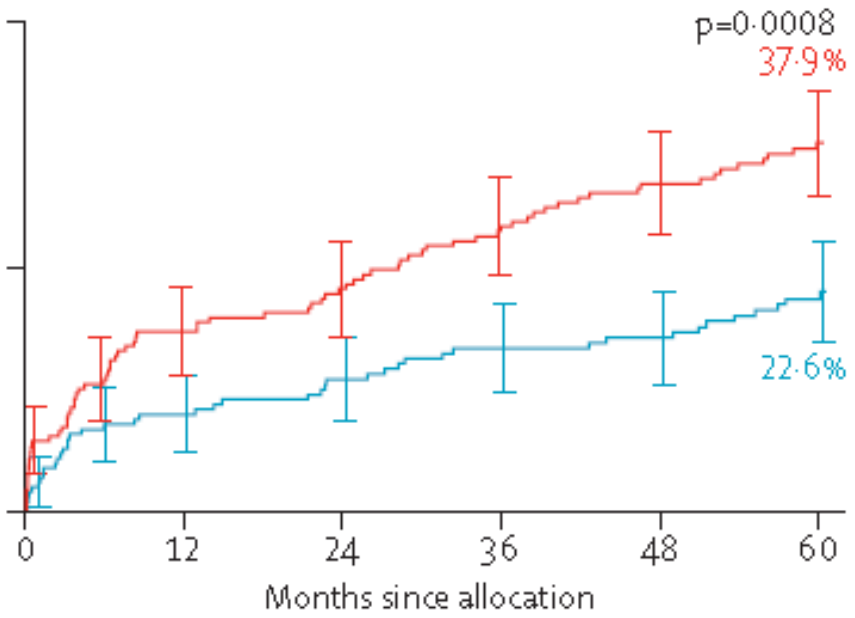
SYNTAX

5 Year Outcomes: Middle SYNTAX Tertile (23-32)

All Patients



3-Vessel CAD only

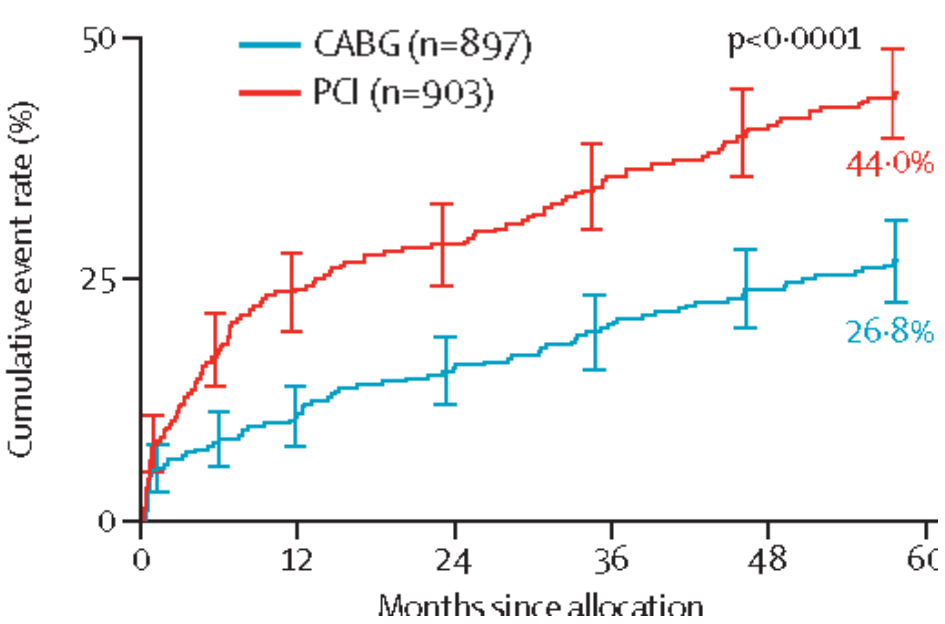


Mohr, et al. Lancet 2013;381:629-38

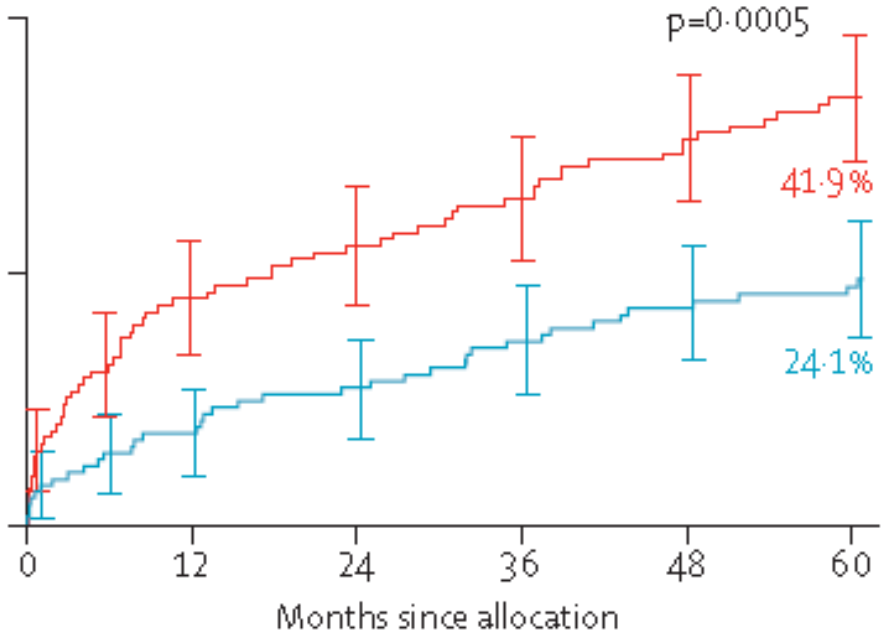
SYNTAX

5 Year Outcomes: Highest SYNTAX Tertile (>32)

All Patients



3-Vessel CAD only



Mohr, et al. Lancet 2013;381:629-38

FREEDOM Trial

- 2005-2010: 1900 diabetics enrolled from 140 international centers
- Mostly first generation drug-eluting stents
- Mean SYNTAX score = 26
- 3.5 lesions stented/patient

Farkouh, et al. N Engl J Med 2012;367:2375-84

FREEDOM Trial

Early Outcomes

Event	30 Days after Procedure			12 Months after Procedure		
	PCI	CABG	P Value	PCI	CABG	P Value
	number (percent)			*number (percent)*		
Major adverse cardiovascular and cerebrovascular events	45 (4.8)	47 (5.2)	0.68	157 (16.8)	106 (11.8)	0.004
Death	8 (0.8)	15 (1.7)	0.12	32 (3.4)	38 (4.2)	0.35
Myocardial infarction	17 (1.8)	15 (1.7)	0.82	54 (5.8)	30 (3.4)	0.02
Stroke	3 (0.3)	16 (1.8)	0.002	8 (0.9)	17 (1.9)	0.06
Repeat revascularization	31 (3.3)	10 (1.1)	0.002	117 (12.6)	42 (4.8)	<0.001

Farkouh, et al. N Engl J Med 2012;367:2375-84

FREEDOM Trial

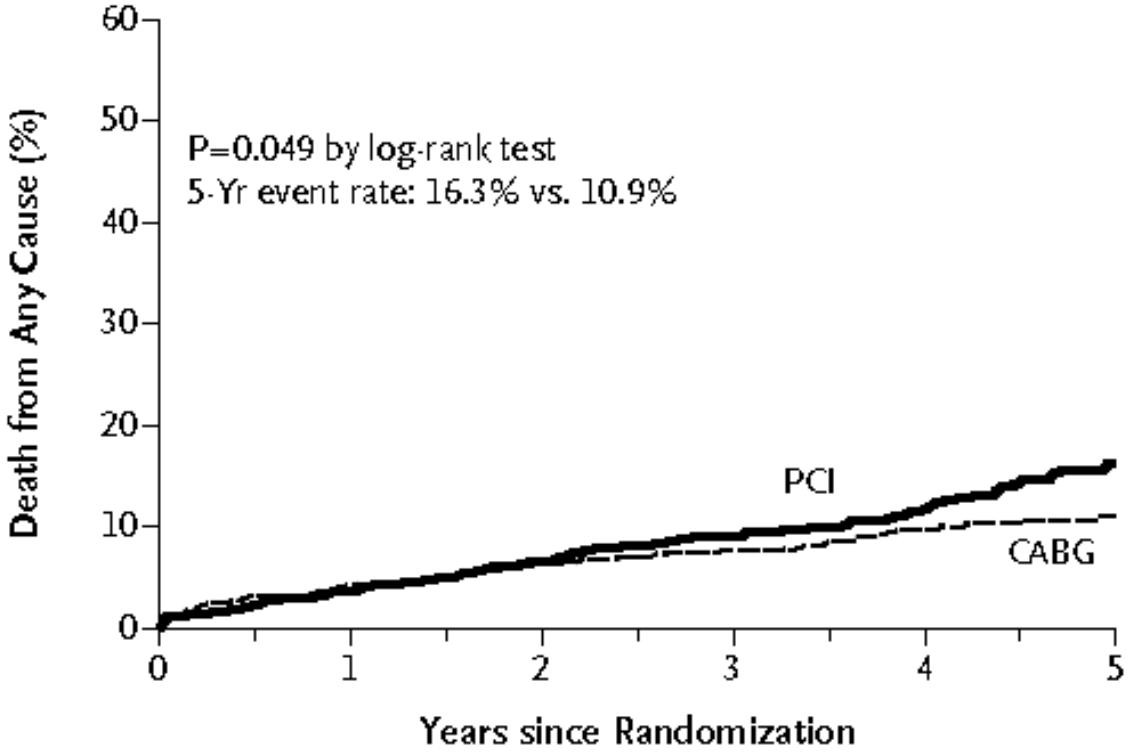
Late Outcomes

Outcome	2 Years after Randomization		5 Years after Randomization		Patients with Event		P Value*
	PCI	CABG	PCI	CABG	PCI	CABG	
	number (percent)				*number*		
Primary composite†	121 (13.0)	108 (11.9)	200 (26.6)	146 (18.7)	205	147	0.005‡
Death from any cause	62 (6.7)	57 (6.3)	114 (16.3)	83 (10.9)	118	86	0.049
Myocardial infarction	62 (6.7)	42 (4.7)	98 (13.9)	48 (6.0)	99	48	<0.001
Stroke	14 (1.5)	24 (2.7)	20 (2.4)	37 (5.2)	22	37	0.03§
Cardiovascular death	9 (0.9)	12 (1.3)	73 (10.9)	52 (6.8)	75	55	0.12

Farkouh, et al. N Engl J Med 2012;367:2375-84

FREEDOM Trial

Mortality



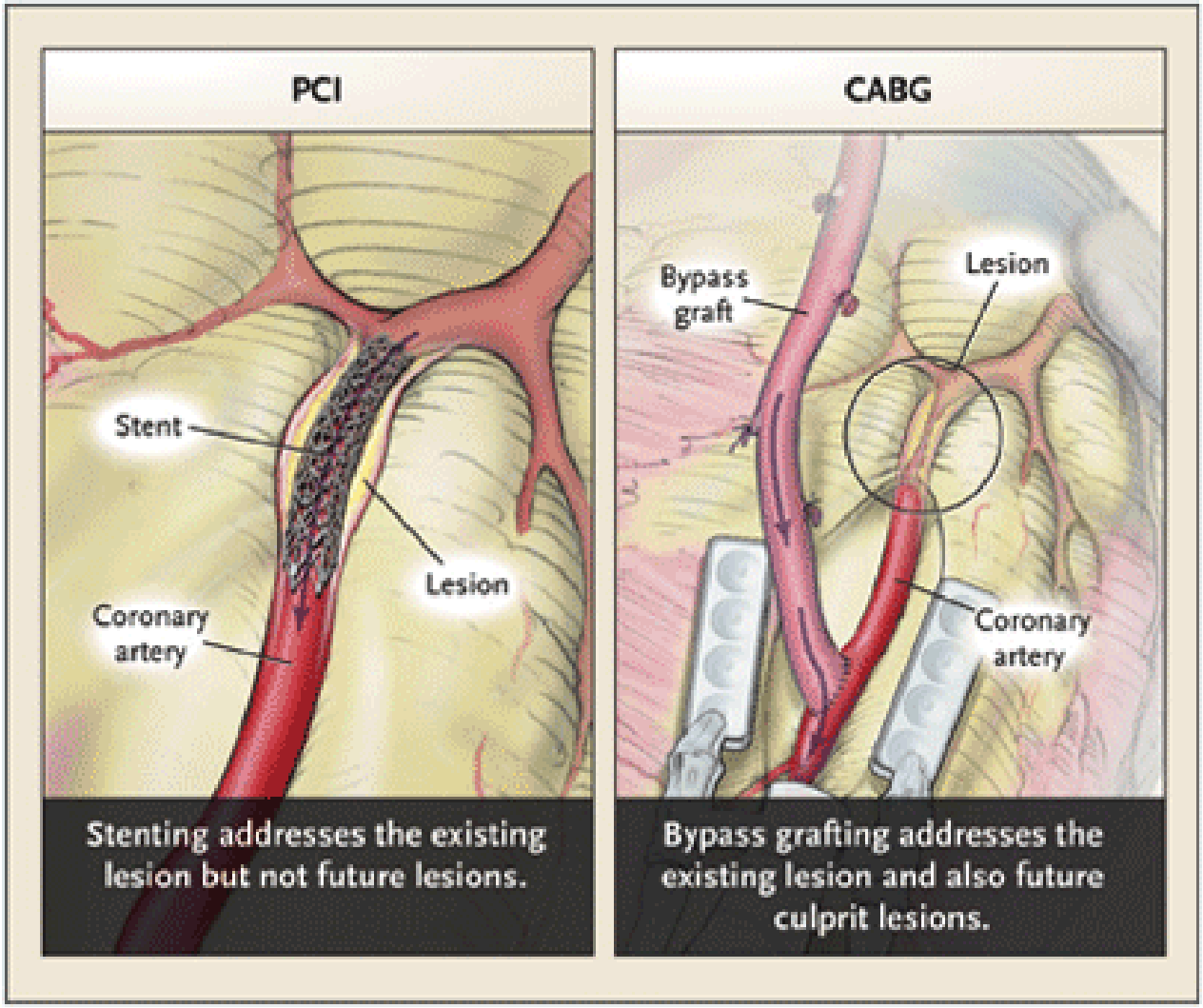
No. at Risk						
PCI	953	897	845	685	466	243
CABG	947	855	806	655	449	238

Farkouh, et al. N Engl J Med 2012;367:2375-84

What have we learned?

- Older patients, patients with more severe CAD, and diabetics fare better with CABG when compared to angiography-guided PCI with first generation drug-eluting stents.

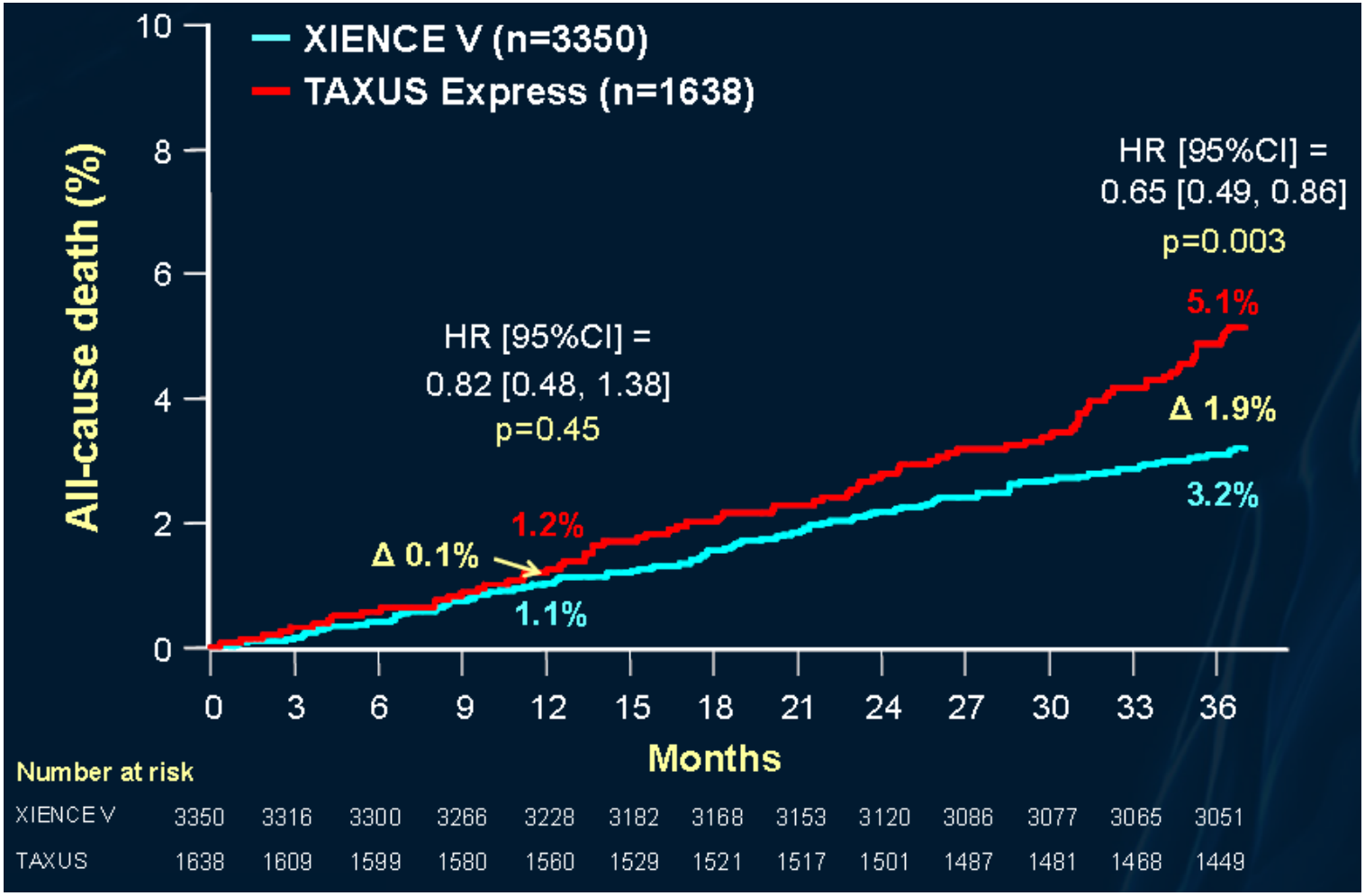
How do we explain this?



Gersh and Frye. New Engl J Med 2005;352:2235

Where do we go from here?

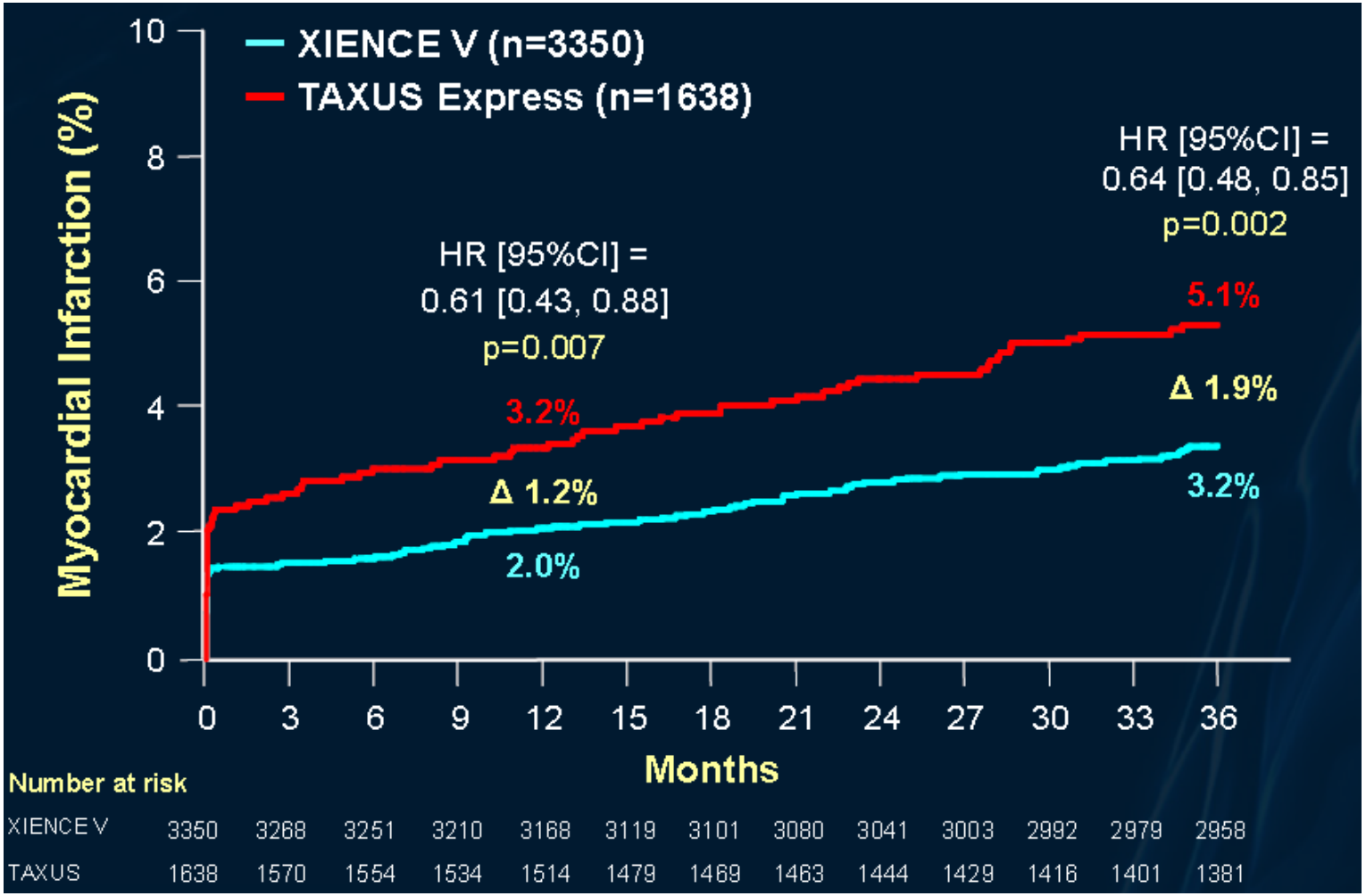
3 Year Mortality Benefit of 2nd Generation DES



Stone GW. TCT 2012

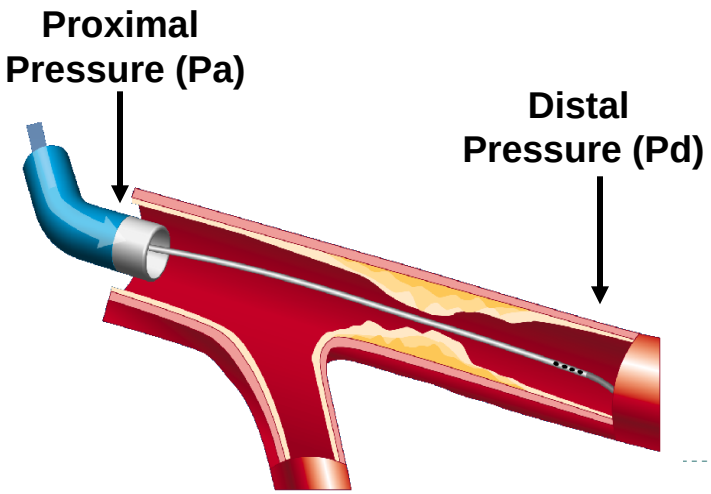
Where do we go from here?

3 Year MI Benefit of 2nd Generation DES



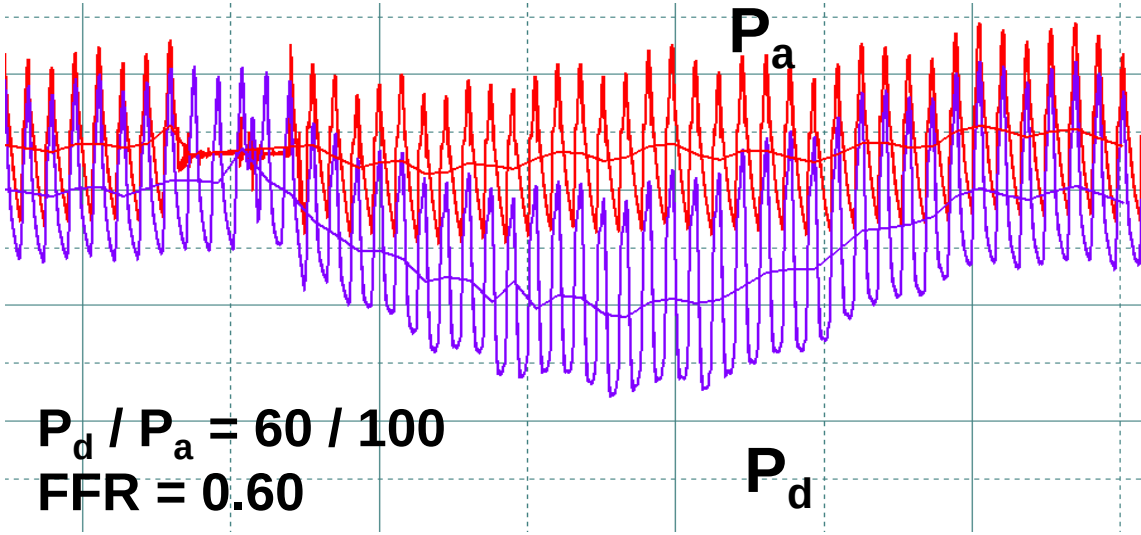
Stone GW. TCT 2012

Where do we go from here?



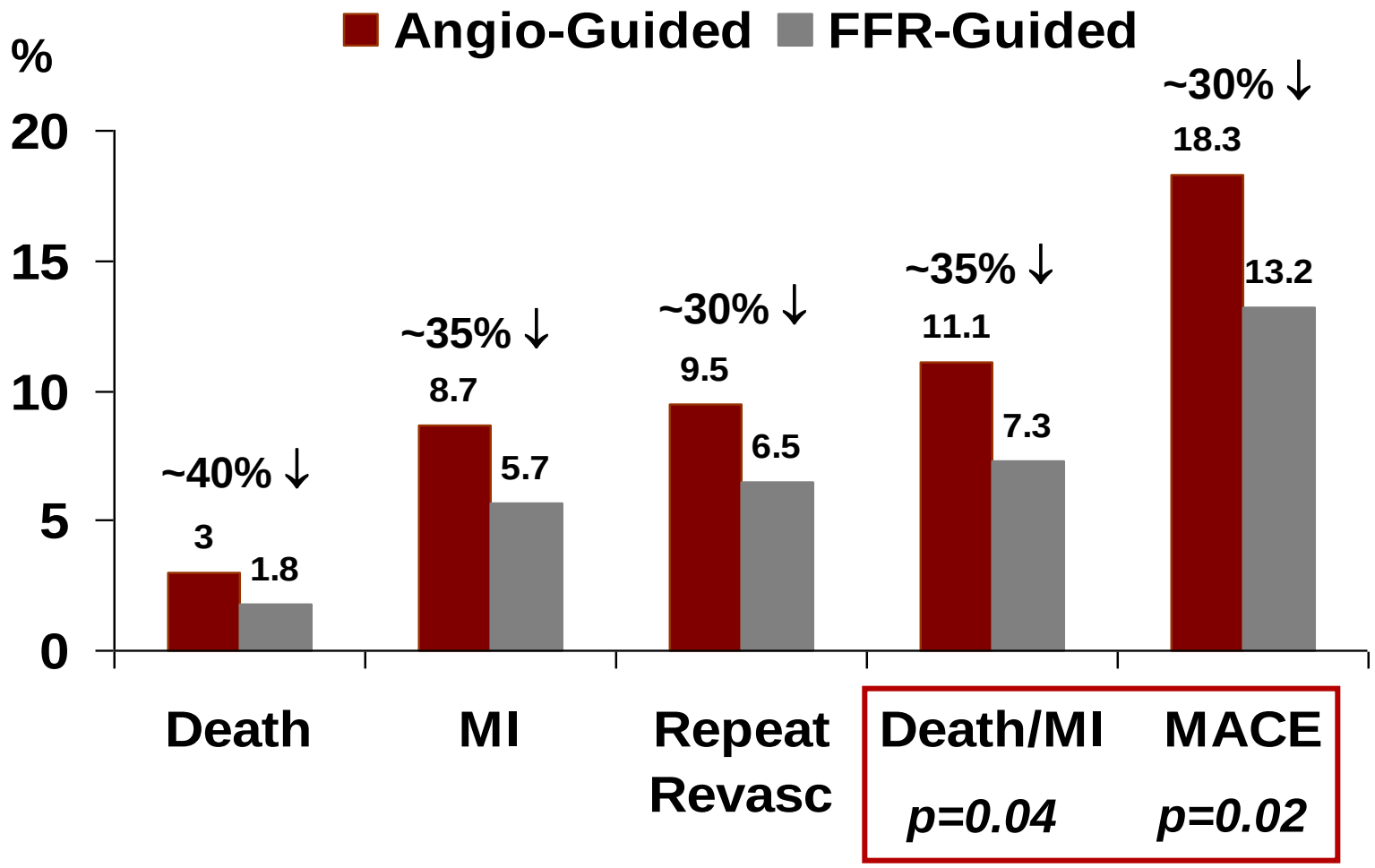
$FFR = P_d / P_a$

during maximal flow



FAME Study: One Year Outcomes

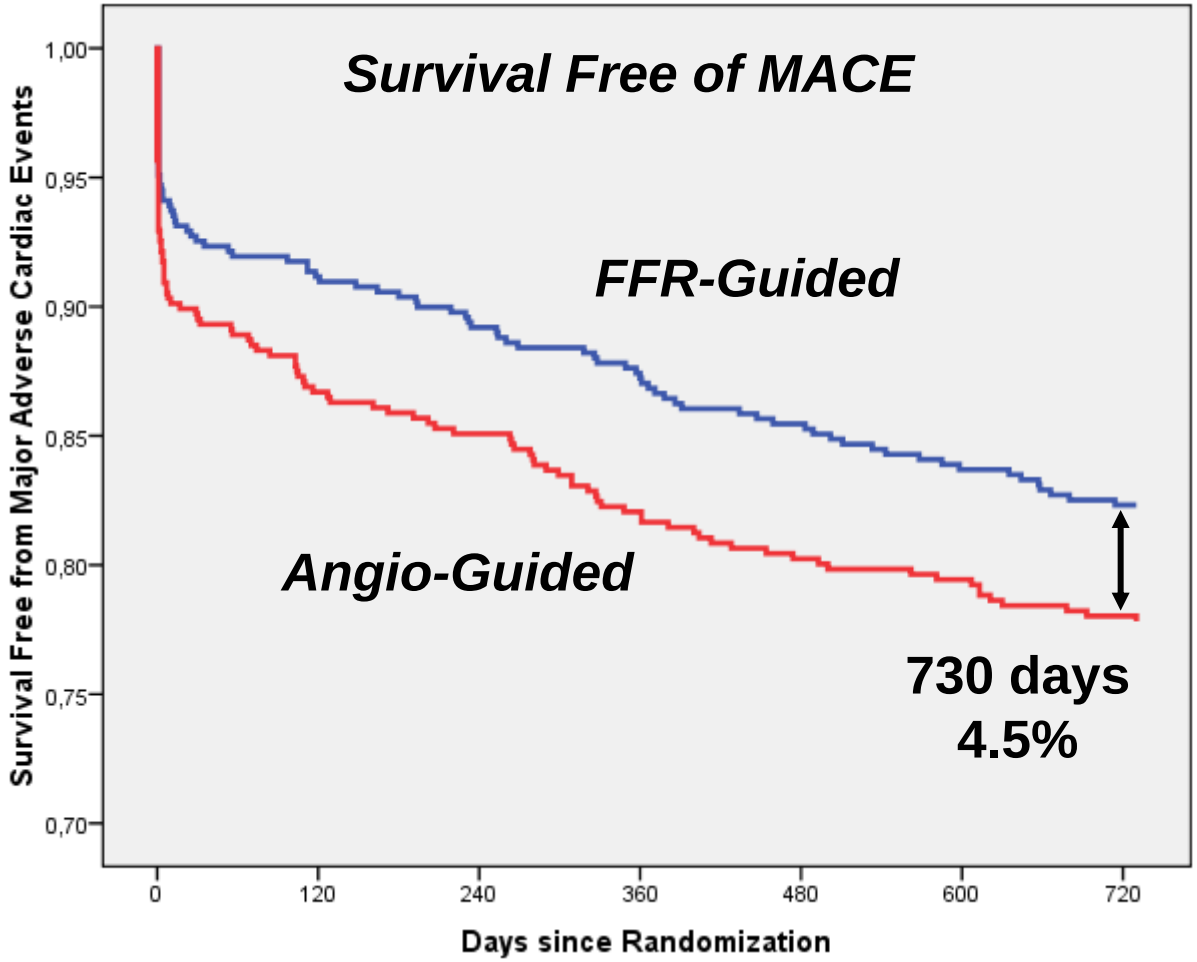
1005 patients with 2-3 vessel CAD randomized to angio or FFR-guided PCI



New Engl J Med 2009;360:213-24.

FAME Study: Two Year Outcomes

Death/MI was significantly reduced from 12.9% to 8.4% (p=0.02)



Pijls, et al. J Am Coll Cardiol 2010;56:177-184

Anatomic vs. Functional CAD

Patients with angiographically 3VD (N=115), proportions per number of diseased vessels after assessment by FFR

Tonino, et al. J Am Coll Cardiol 2010;55:2816-21

Impact of SYNTAX Score on PCI

Recently published Appropriate Use Criteria

	CABG	PCI
Two-vessel CAD with proximal LAD stenosis	A	A
Three-vessel CAD with low CAD burden (i.e., three focal stenosis, low SYNTAX score)	A	A
Three-vessel CAD with intermediate to high CAD burden (i.e., multiple diffuse lesions, presence of CTO, or high SYNTAX score)	A	U
Isolated left main stenosis	A	U
Left main stenosis and additional CAD with low CAD burden (i.e., one to two vessel additional involvement, low SYNTAX score)	A	U
Left main stenosis and additional CAD with intermediate to high CAD burden (i.e., three vessel involvement, presence of CTO, or high SYNTAX score)	A	I

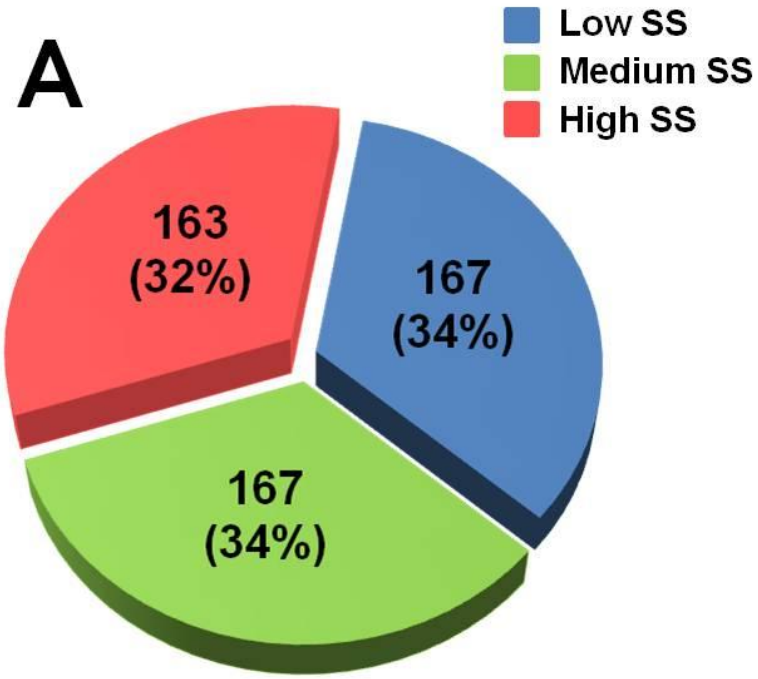
Patel, et al. JACC 2012;59:857-881

Can we enhance the SYNTAX Score?

- By incorporating FFR into the SYNTAX score, termed “Functional SYNTAX Score” (FSS), can we:
  - Convert high/medium risk SYNTAX score patients to a lower risk group?
  - Improve our risk stratification of patients with multivessel CAD undergoing PCI?

Functional SYNTAX Score

Reclassifies > 30% of Cases

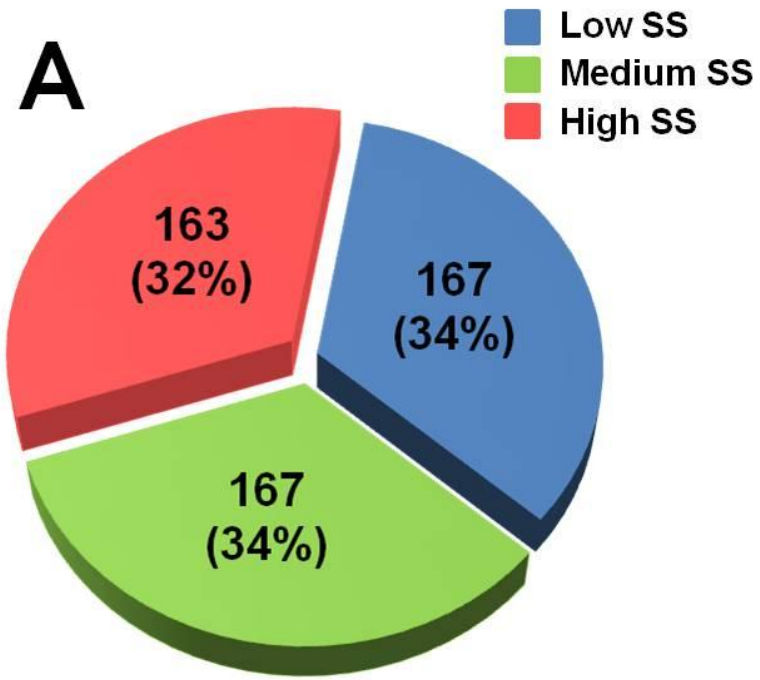


Without FFR

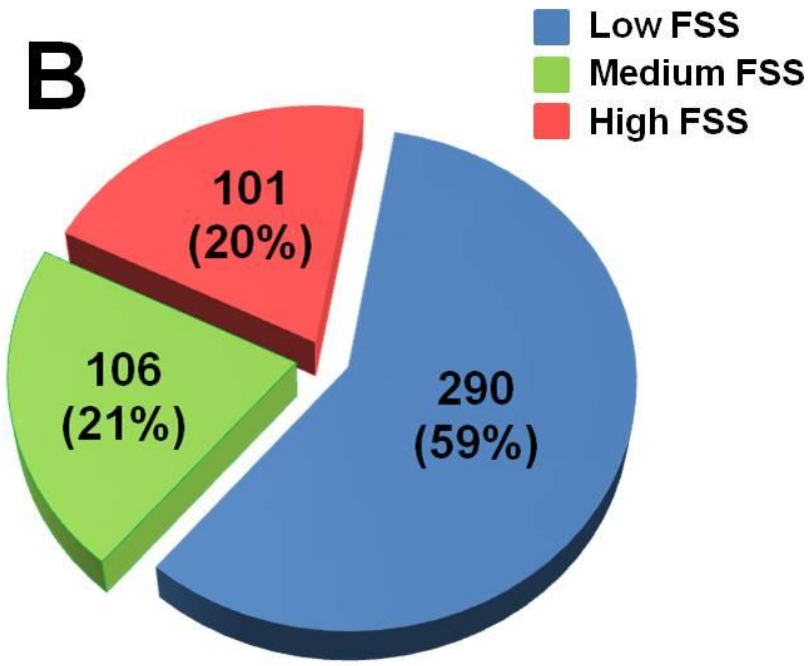
Nam CW, et al. J Am Coll Cardiol 2011;58:1211-8

Functional SYNTAX Score

Reclassifies > 30% of Cases



Without FFR

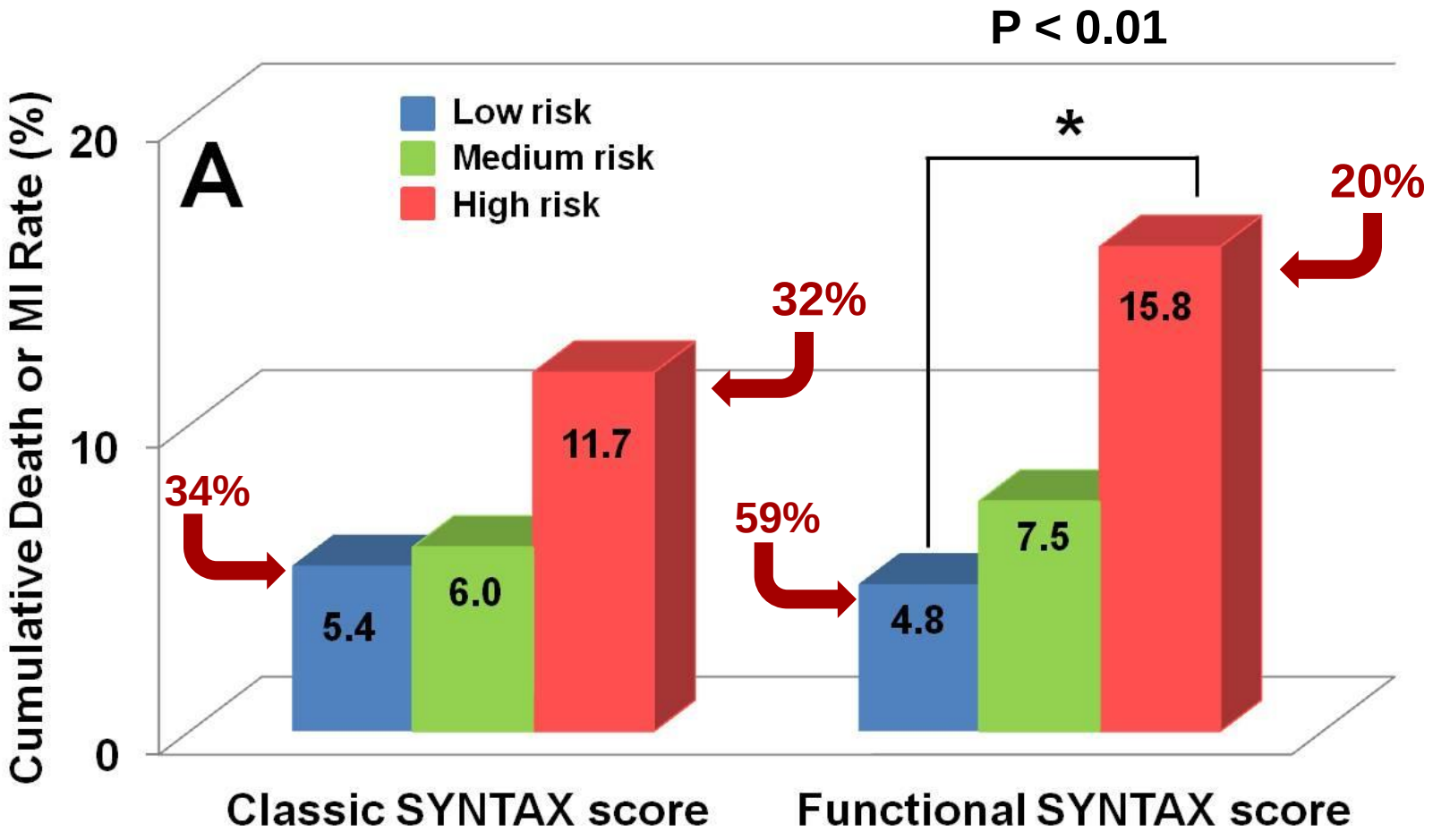


With FFR

Nam CW, et al. J Am Coll Cardiol 2011;58:1211-8

Functional SYNTAX Score

Discriminates Risk for Death/MI



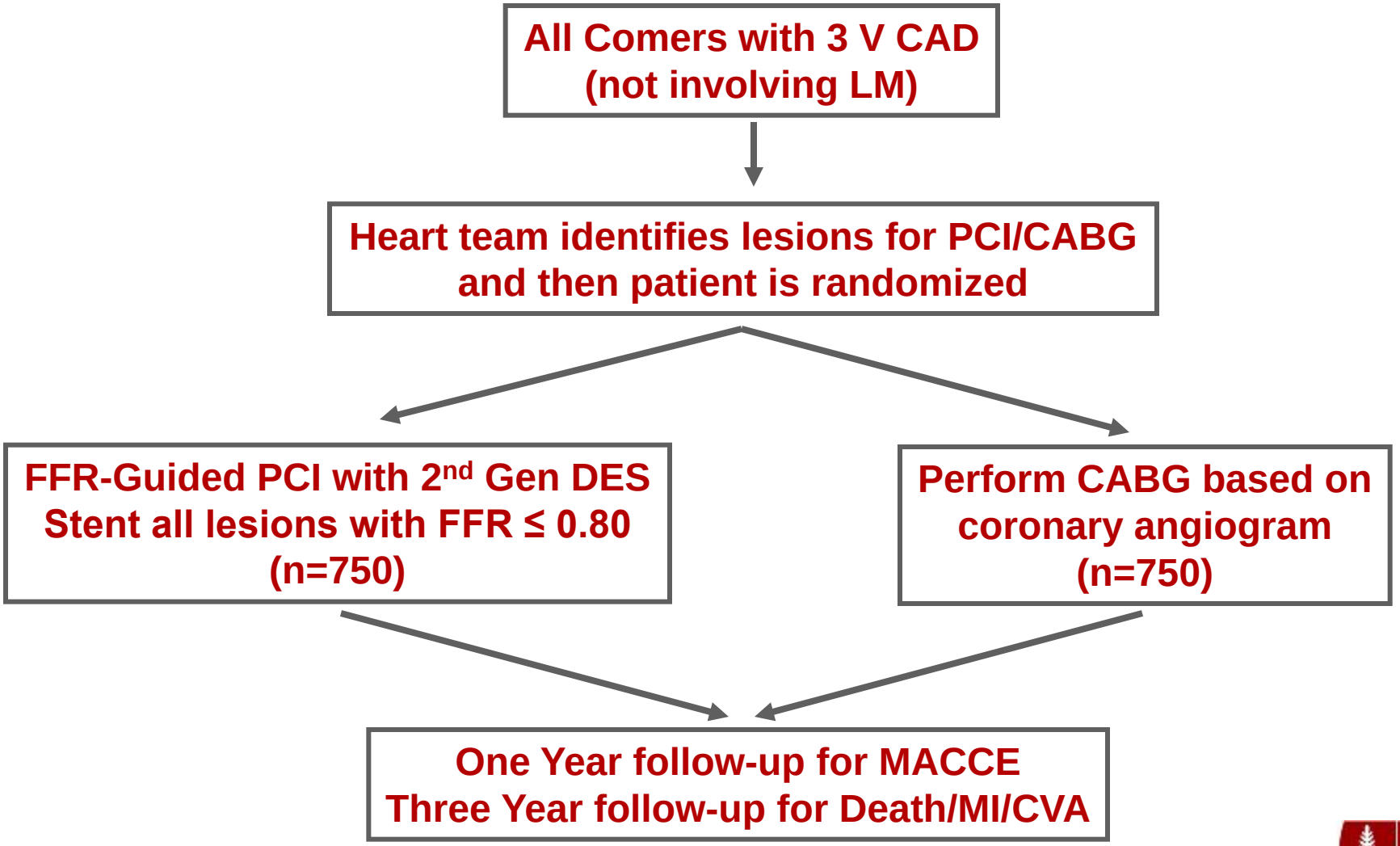
Nam CW, et al. J Am Coll Cardiol 2011;58:1211-8

Where do we go from here?

Can we improve the results of PCI vs. CABG?

- By utilizing current generation DES
- Applying FFR guidance to optimize ischemia reduction and minimize stent complications
- Optimizing medical therapy once ischemia has been relieved to reduce plaque progression

FAME 3 Trial:


All Comers with 3 V CAD
(not involving LM)
Heart team identifies lesions for PCI/CABG
and then patient is randomized
FFR-Guided PCI with 2nd Gen DES
Stent all lesions with FFR ≤ 0.80
(n=750)
Perform CABG based on
coronary angiogram
(n=750)
One Year follow-up for MACCE
Three Year follow-up for Death/MI/CVA