10-Year Long-Term Outcomes of Left Main Revascularization
The MAIN-COMPARE Registry and Key Sub-studies

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ESC Guidelines 2018
Elective PCI for LM Stenosis

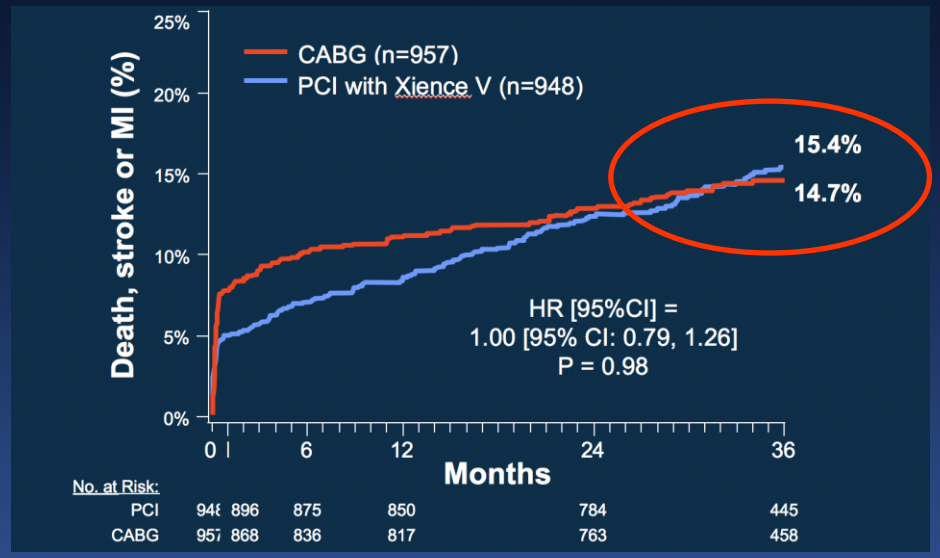
Remaining Issue :
We Are Demanding Very Long-Term (ie,10-Year) Results of PCI and CABG for LM disease

Reference; SYNTAX Study, PRECOMBAT study, MAINCOMPARE registry study and Meta-Analysis. *Patrick, SW et al, NEJM. 2009 March 5;360(10), Park SJ et al, NEJM. 2011 May 5;364(18):1718-27, Levin GN et al. ACC/AHA guidelines. JACC 2011;58:44-122, Capodanno et al, JACC 2011;58:1426-32*

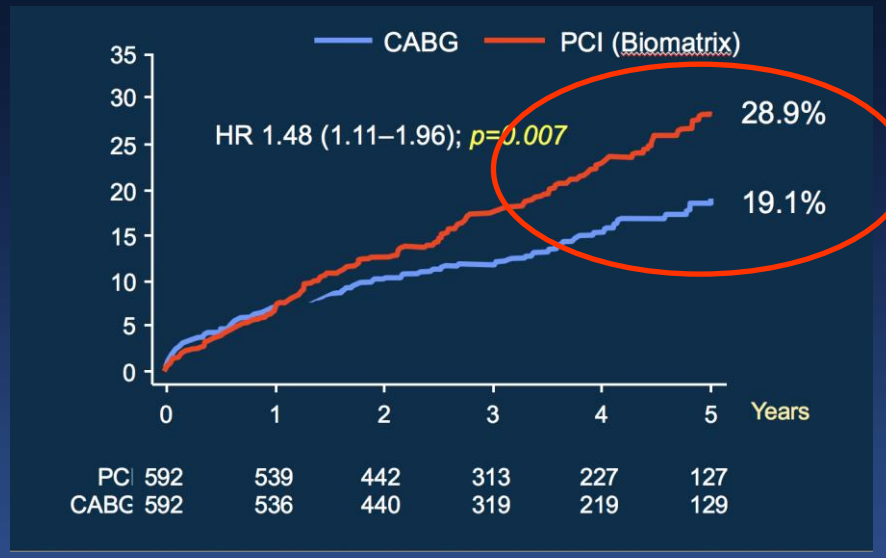
Why We Need Very Long-Term Comparative Outcomes of PCI vs. CABG in LM Disease?

There Is Some Signals...

EXCEL



NOBLE



Longer-term follow-up (beyond 5 years) is necessary to examine additional differences between PCI and CABG over time.

EXCEL

Adjudicated Outcomes at 4 Years (i)

	PCI (n=948)	CABG (n=957)	HR [95%CI]	P-value
Death, stroke or MI (1˚ endpoint)	18.6%	16.7%	1.10 [0.88, 1.36]	0.40
- Death	10.3%	7.4%	1.39 [1.02, 1.89]	0.04
- Definite cardiovascular	4.3%	3.6%	1.17 [0.74, 1.86]	0.50
- Definite non-cardiovascular	5.3%	3.3%	1.61 [1.01, 2.56]	0.04
- Undetermined cause	1.1%	0.7%	1.49 [0.53, 4.19]	0.45
- Stroke	2.6%	3.3%	0.76 [0.44, 1.31]	0.32
- MI	9.5%	8.8%	1.05 [0.77, 1.42]	0.76
- Peri-procedural	3.9%	6.1%	0.65 [0.43, 0.98]	0.04
- Spontaneous	5.7%	3.2%	1.77 [1.12, 2.82]	0.01
- STEMI	1.9%	2.8%	0.65 [0.35, 1.19]	0.16
- Non-STEMI	7.8%	6.3%	1.22 [0.86, 1.72]	0.26

10-Year Report MAIN-COMPARE Registry

Wave 1 (BMS era)

LM disease treated with BMS (n=318) and concurrent CABG (n=448) btw 2000~2003

Wave 2 (DES era)

LM disease treated with DES (n=784) and concurrent CABG (n=690) btw 2003~2006

From January 2000 through June 2006

Total 2240

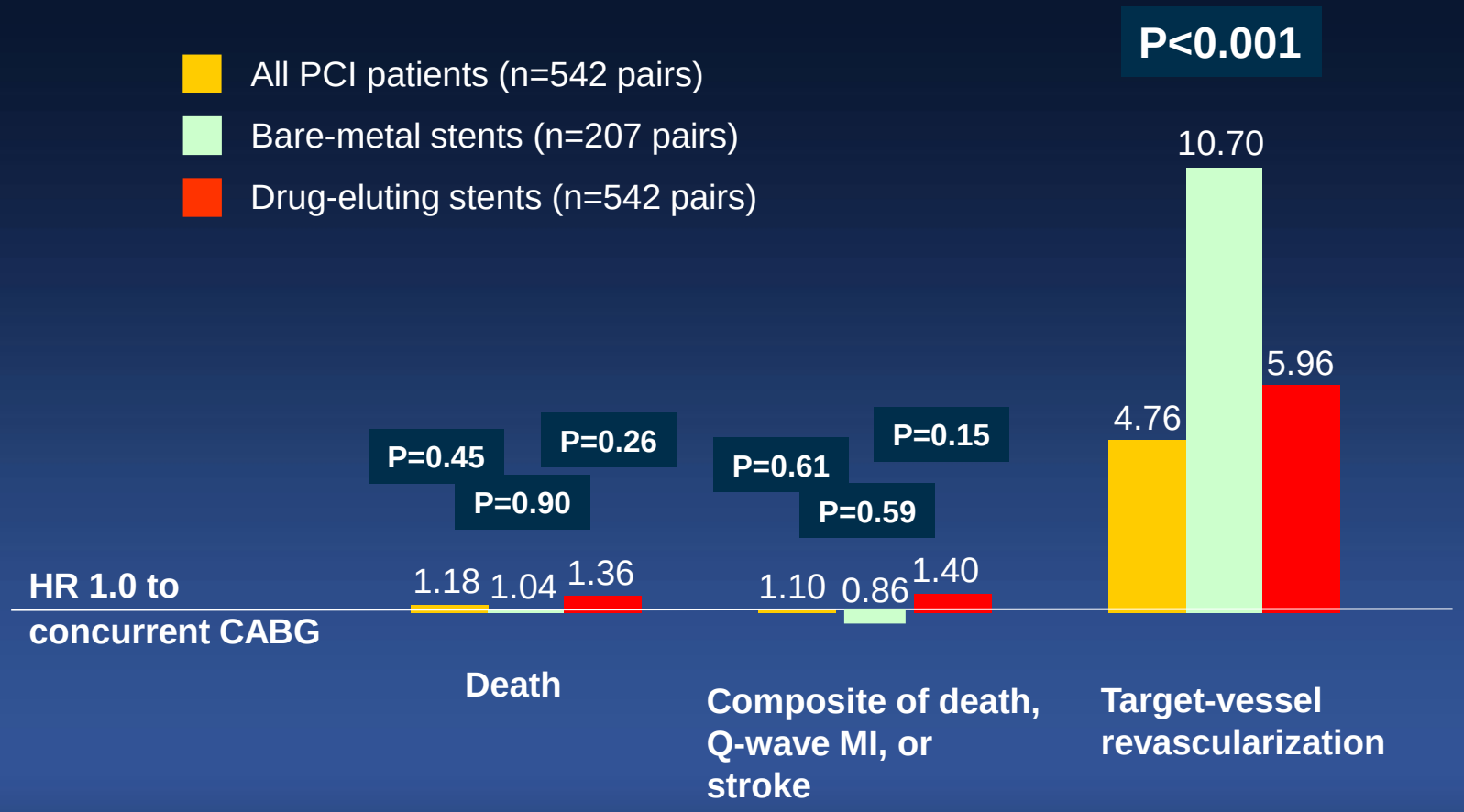
Stent (N=1102)

CABG (N=1138)

Clinical follow-up every 12 months
Death, Composite of Death/MI/Stoke, TVR

MAIN COMPARE Registry, 3-Year

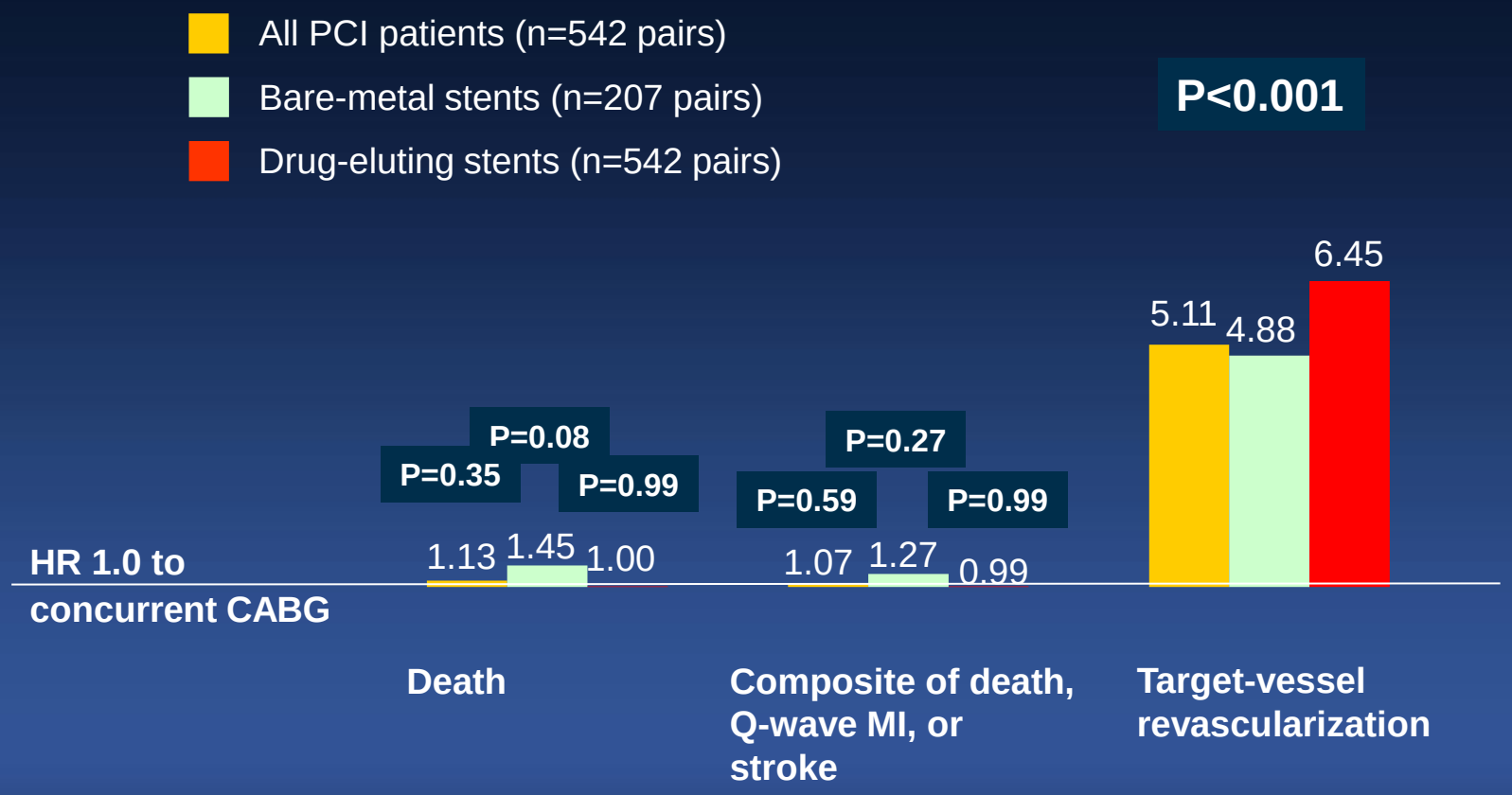
Adjusted HR by Use of PS Matching



Seung KB, Park DW, Park SJ, et al. N Engl J Med 2008;358:1781-92

MAIN COMPARE Registry, 5-Year

Adjusted HR by Use of IPTW Method



Park DW, Park SJ, et al. J Am Coll Cardiol. 2010;56:117-24.

10-Year FU and National DB Linkage

- In this report, the follow-up period was extended through December 31, 2016, to ensure that all patients had the opportunity for at least 10-year follow-up evaluation.
- For validation of complete follow-up data on mortality, information about vital status was obtained from the National Population Registry of the Korea National Statistical Office with the use of a unique personal identification number up to December, 31, 2016.
- The median duration of follow-up among all patients was 12.0 years (IQR, 10.7 to 13.5); the maximum follow-up was 17.6 years.

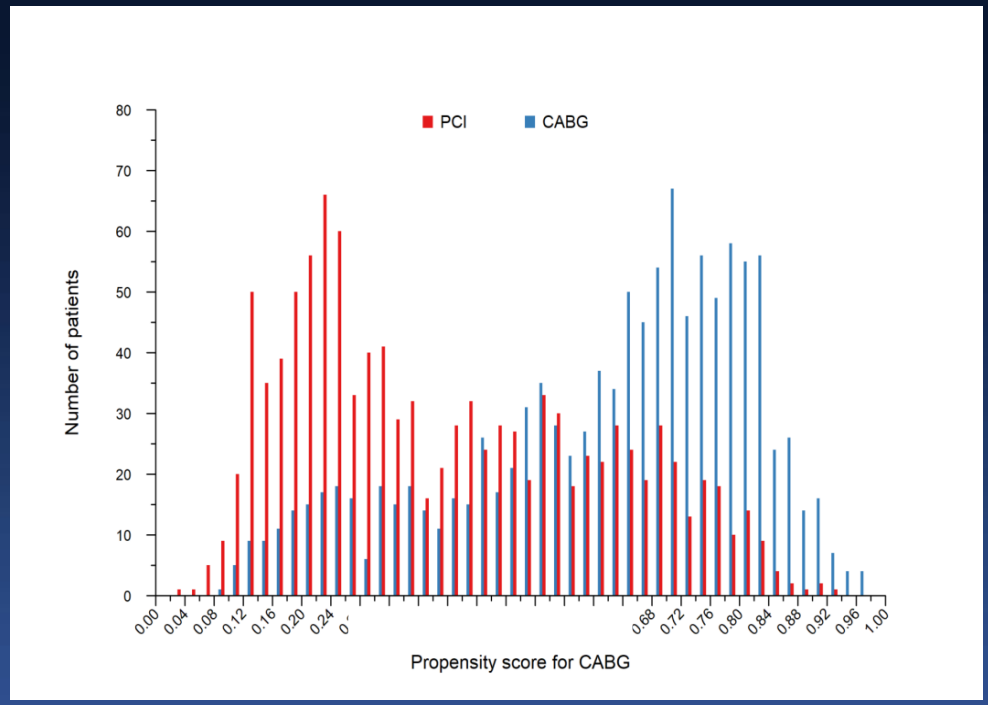
Statistical Analysis for 10-Year Outcomes

- All comparative analyses were performed in the overall cohort, wave 1 (BMS era), and wave 2 (DES era) cohort.
- To adjust baseline characteristics, propensity analyses using (1) the inverse-probability-of-treatment weighting (IPTW) and (2) propensity-score matching were performed.
- To characterize the time-dependent nature of the effects and to compensate for the violation of the proportional-hazard assumption, we performed weighted piecewise Cox regression models with robust standard errors according to a prespecified time point at 5 years.

Baseline Characteristics

	Unadjusted Data		
	PCI (N = 1102)	CABG (N = 1138)	P Value
Age (yr)	61.3±11.7	62.9±9.4	<0.001
Male gender	779 (70.7)	830 (72.9)	0.24
Diabetes mellitus			
Any diabetes	327 (29.7)	395 (34.7)	0.01
Requiring insulin	75 (6.8)	93 (8.2)	0.22
Hypertension	546 (49.5)	562 (49.4)	0.94
Hyperlipidemia	315 (28.6)	371 (32.6)	0.04
Current smoker	282 (25.6)	339 (29.8)	0.03
Previous PCI	200 (18.1)	125 (11.0)	<0.001
Previous MI	89 (8.1)	132 (11.6)	0.005
Previous CHF	27 (2.5)	38 (3.3)	0.21
Chronic lung disease	22 (2.0)	23 (2.0)	0.97
Cerebrovascular disease	78 (7.1)	83 (7.3)	0.84
PVD	16 (1.5)	62 (5.4)	<0.001
Renal failure	30 (2.7)	34 (3.0)	0.71
Ejection fraction (%)	60.6±10.8	57.2±11.9	<0.001

Distribution of Propensity-Score

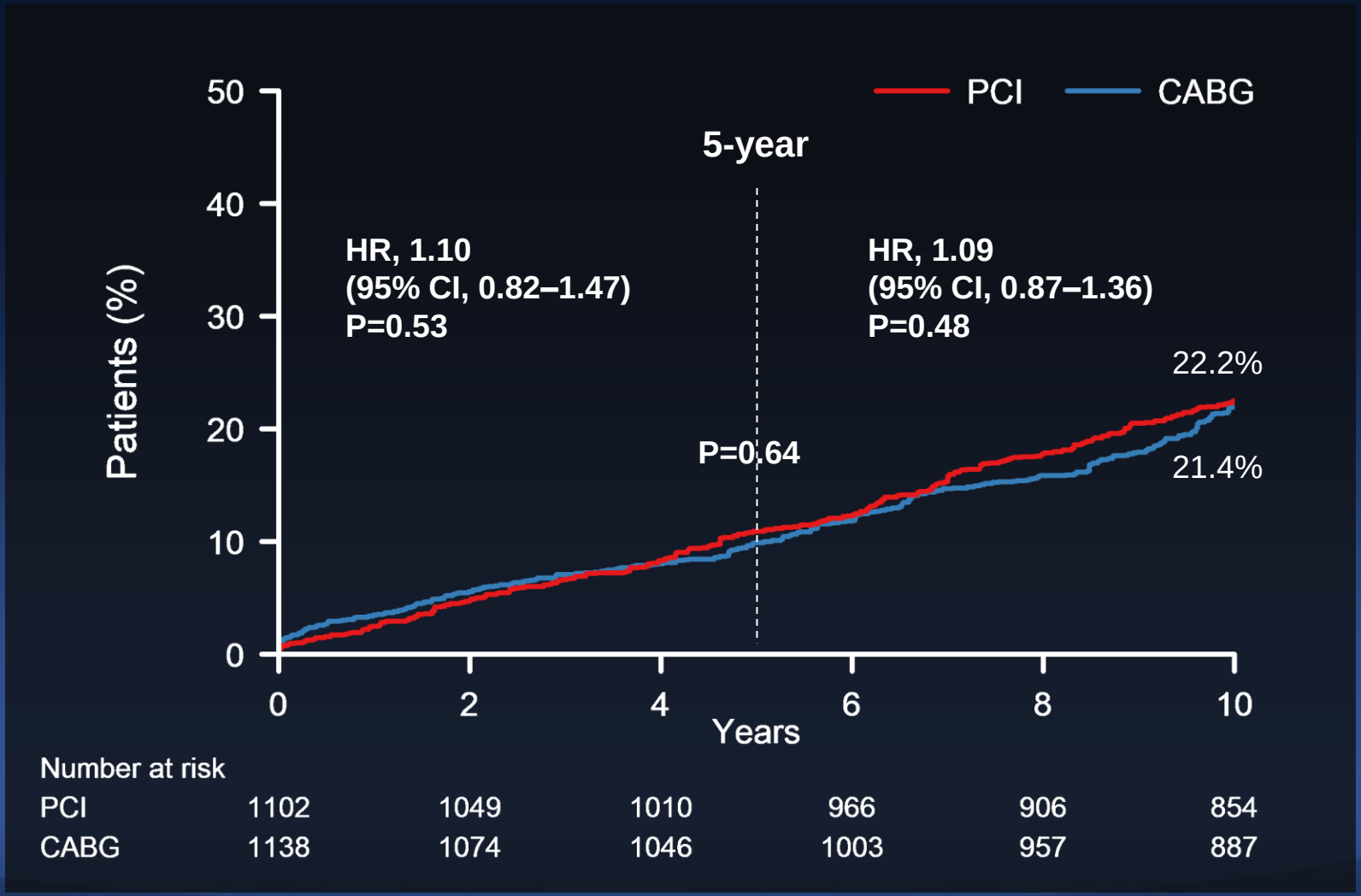


Procedural Characteristics

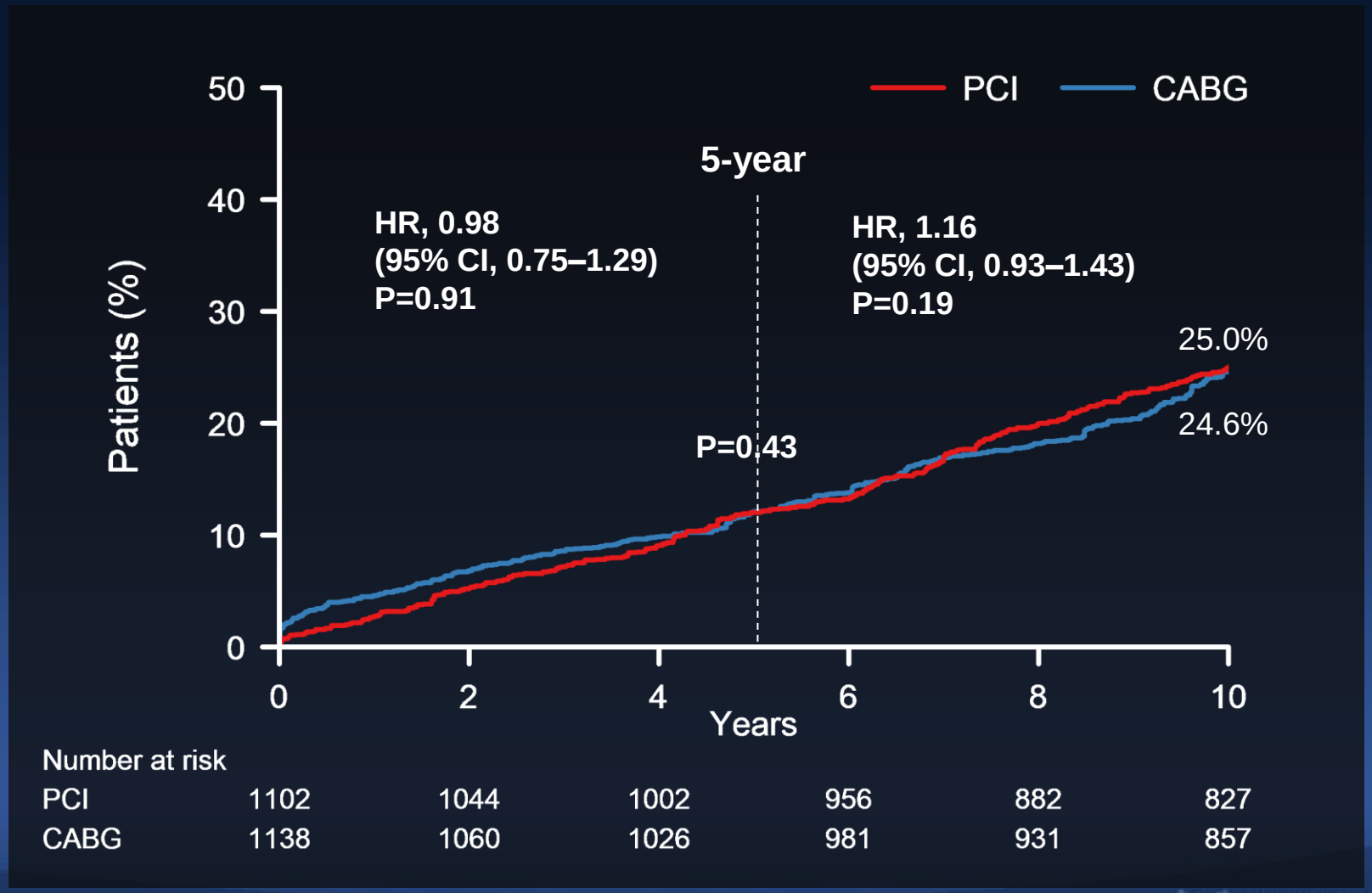
	CABG (n = 1138)	PCI (n = 1102)
CABG Group		
Off-pump surgery (%)	42	-
At least one arterial conduit (%)	98	-
IMA to LAD Graft (%) in patients with arterial conduits	98	-
✓ Grafts / Patients (Mean ± SD)	2.9±1.0	-
PCI Group		
Bare-metal stents(%)	-	29
Drug-eluting stents (%)		71
Sirolimus stents of DES (%)		77
Paclitaxel stents of DES (%)		23
Number of stents at LMCA lesions	-	1.2±0.5
Total length of stents at LMCA (mm)	-	28±21
Average stent diameter at LM site	-	3.5±0.4
✓ Number of stents per patients	-	1.9±1.1

Primary Adjusted Analysis with the Use of IPTW Method

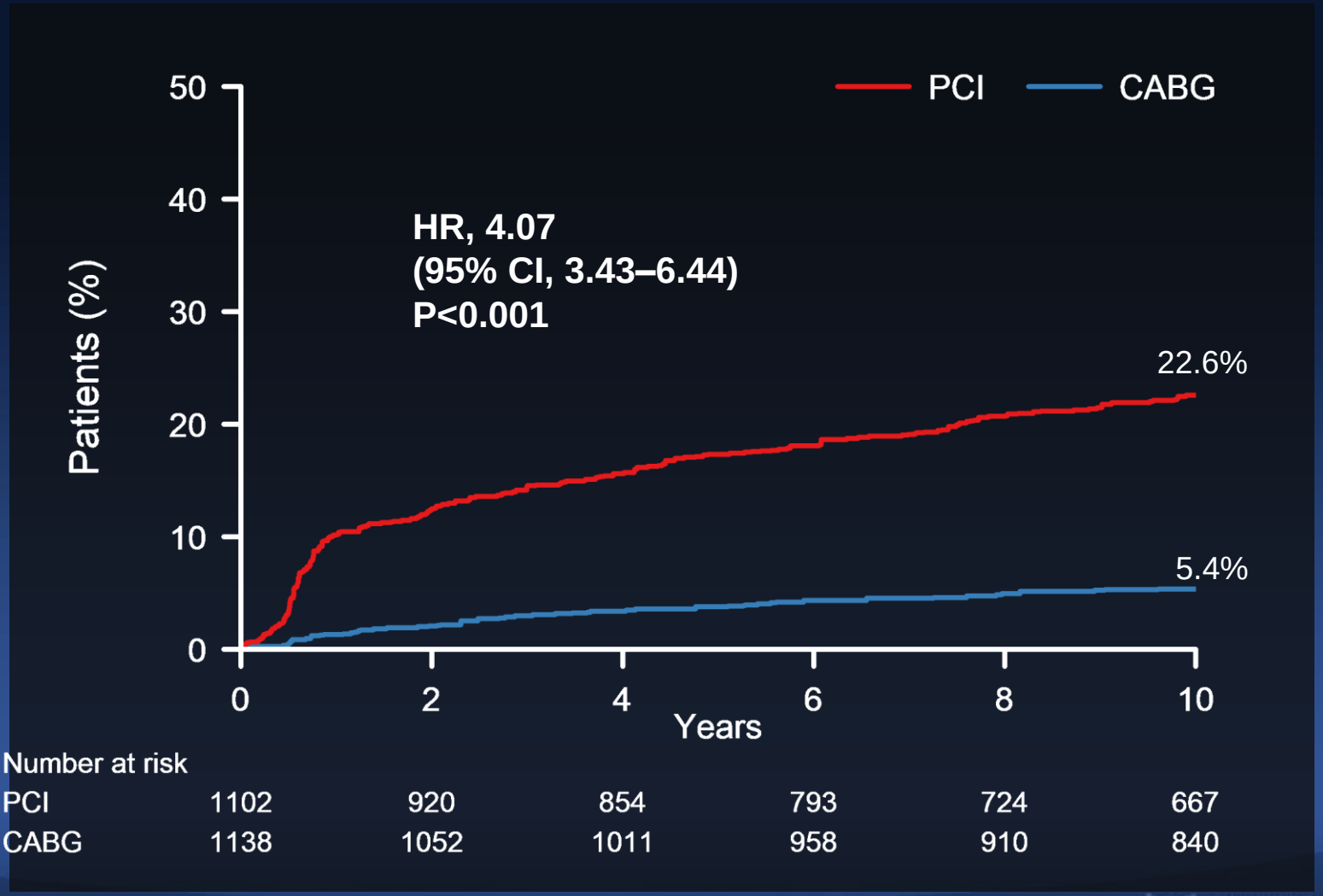
IPTW-Adjusted, Overall Cohort
Death



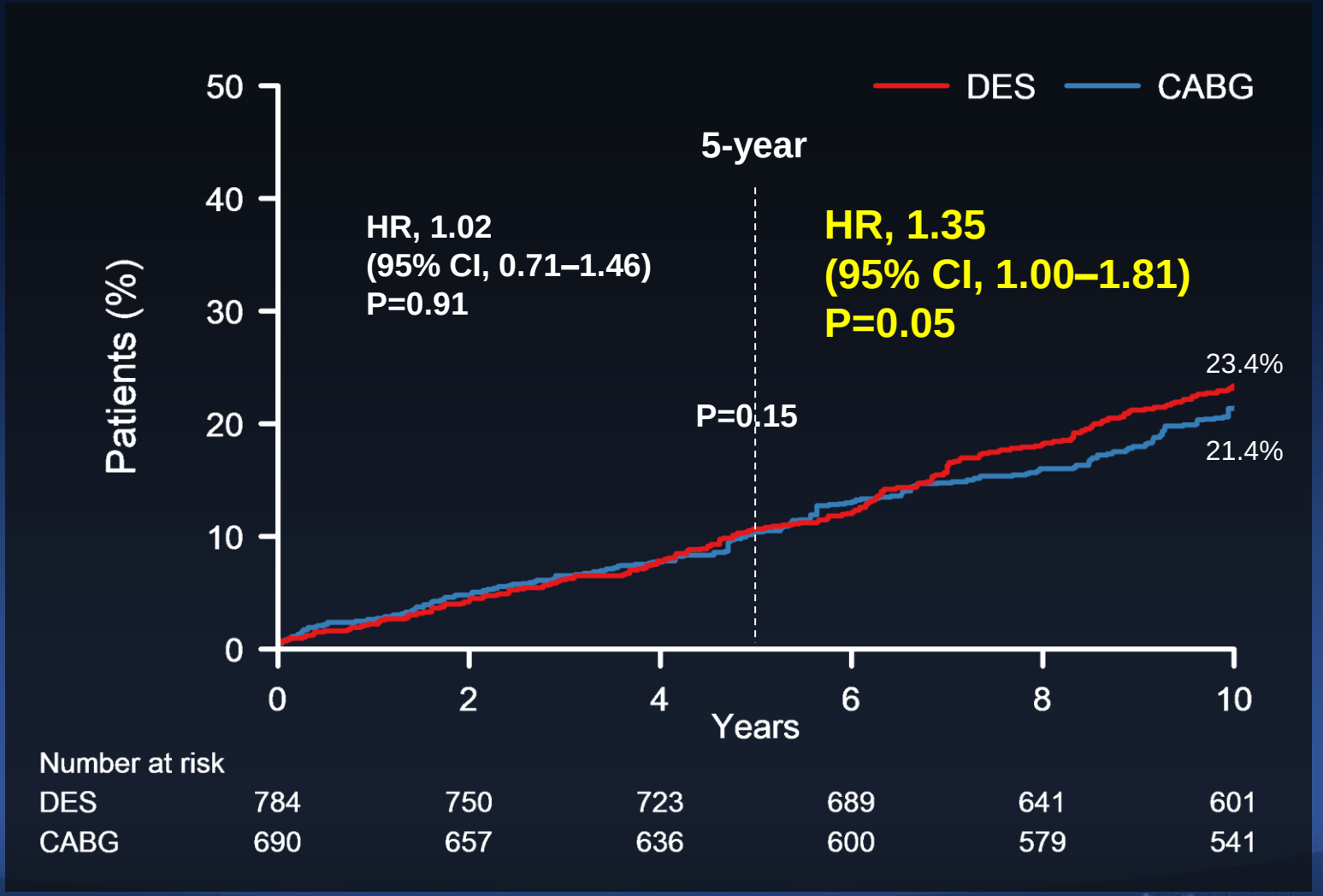
IPTW-Adjusted, Overall Cohort
Death, Q-MI, or Stroke



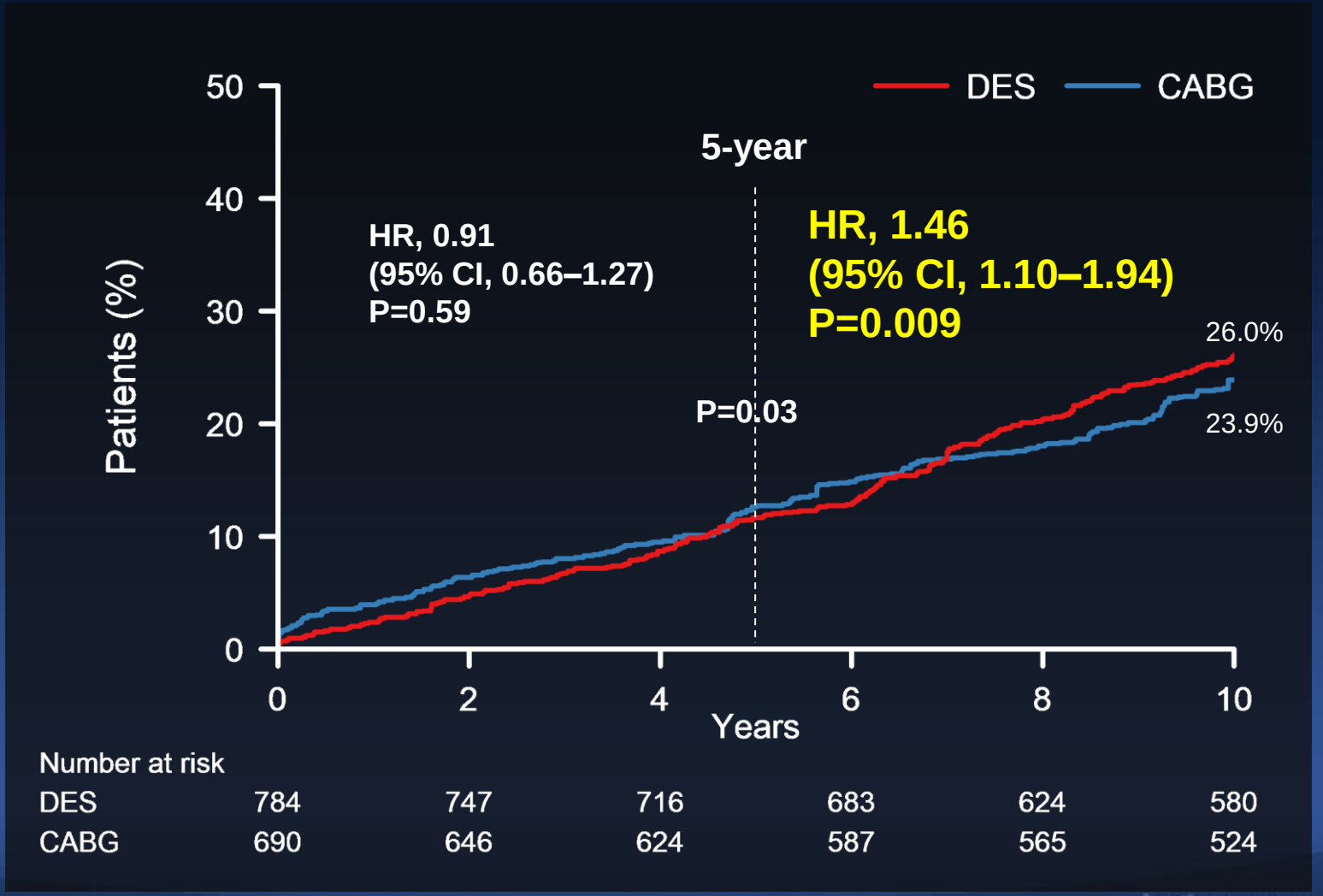
IPTW-Adjusted, Overall Cohort
TVR



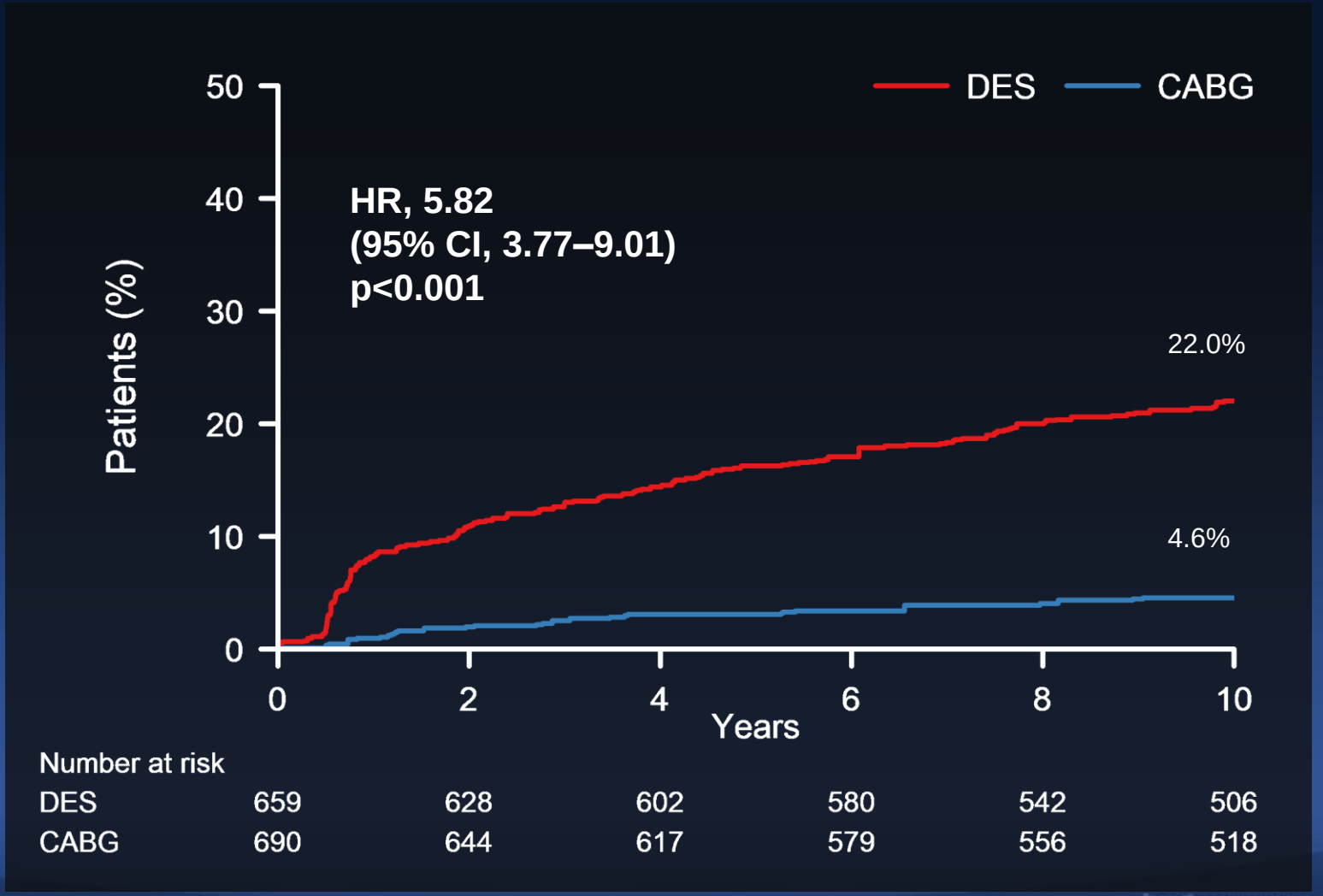
IPTW-Adjusted, Wave 2 (DES vs CABG)
Death



IPTW-Adjusted, Wave 2 (DES vs CABG)
Death, Q-MI, or Stroke



IPTW-Adjusted, Wave 2 (DES vs CABG)
TVR



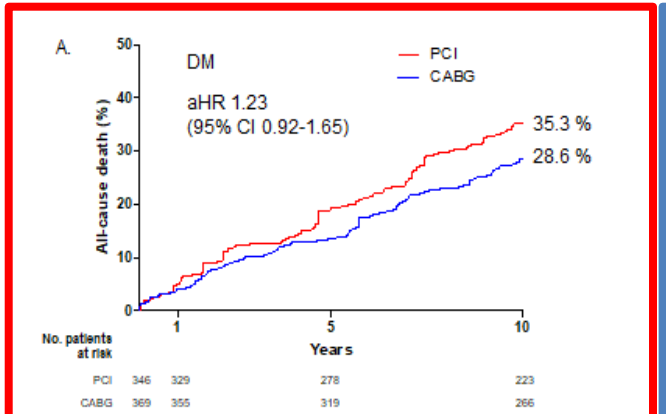
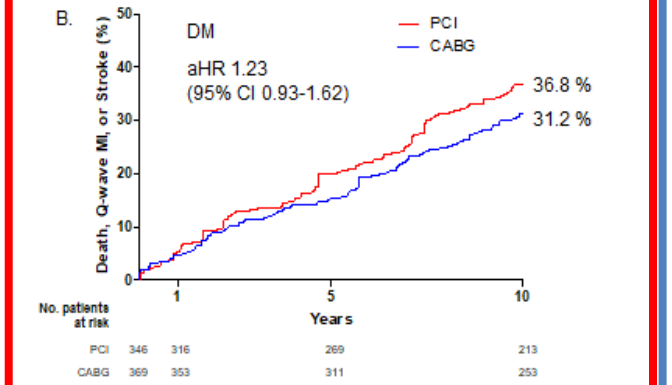
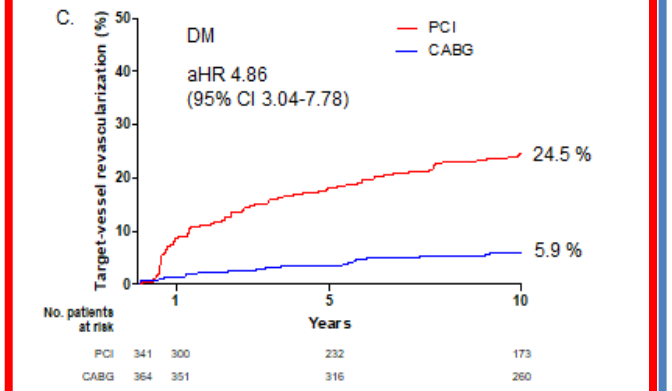
Conclusions

- In this longest FU cohort of patients with LMCA revascularization, there was no difference in the rates of death and serious composite outcome between the PCI and the CABG groups at 10 years.
- However, in the cohort comparing DES and concurrent CABG, DES was significantly associated with higher risks of death and serious composite outcomes compared to CABG after 5 years: the treatment benefit of CABG has diverged over time during continued follow-up.
- The rate of TVR was consistently higher in the PCI group.

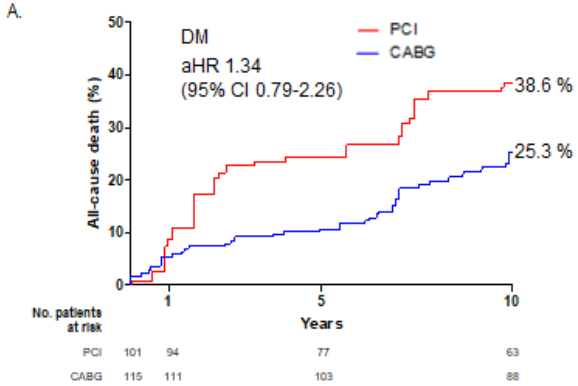
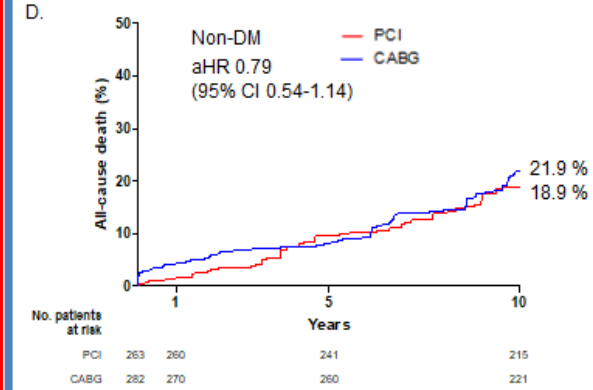
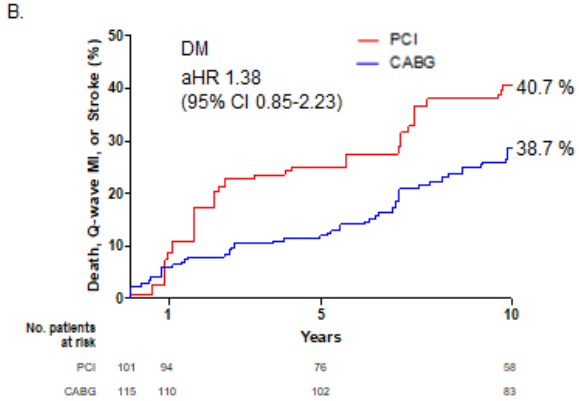
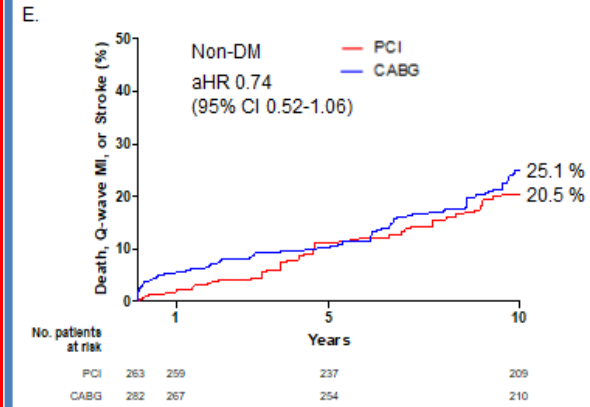
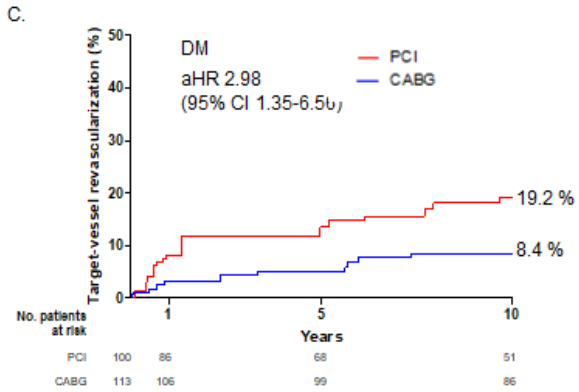
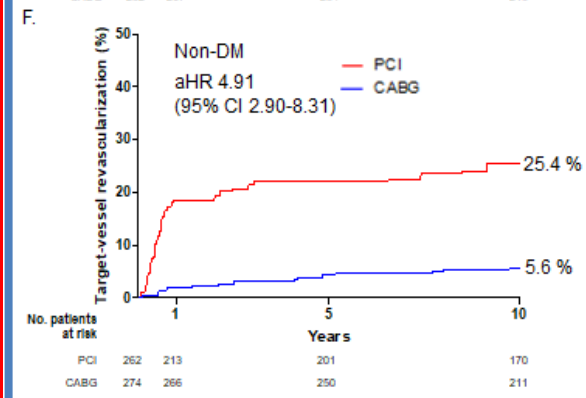
Key Subgroups

- DM vs. NON-DM
- BMS vs. DES
- SES vs. PES
- SA vs. ACS
- SYNTAX Score

Adjusted Curve with IPTW: Overall Cohort

	DM	Non-DM
All Death		P-int=0.41
Death, MI or Stroke		P-int=0.40
TVR		P-int=0.82

Adjusted Curve with IPTW: Cohort of BMS Era

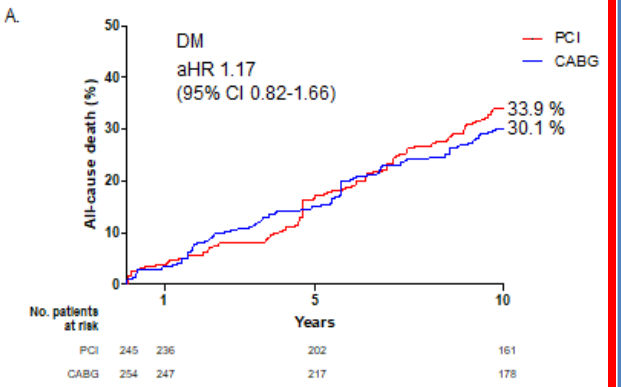
DM		Non-DM
All Death			P-int=0.09
Death, MI or Stroke			P-int=0.04
TVR			P-int=0.23

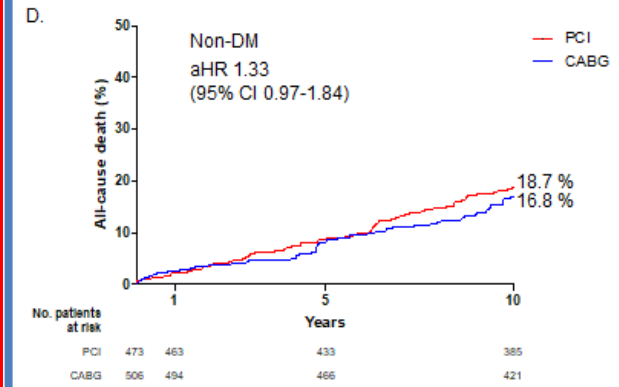
Adjusted Curve with IPTW: Cohort of DES Era

DM

Non-DM

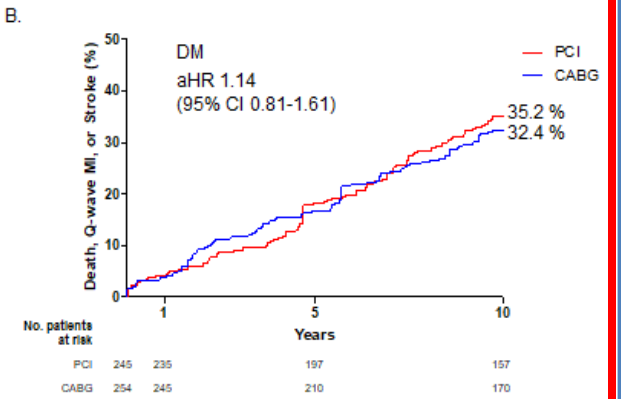
All Death

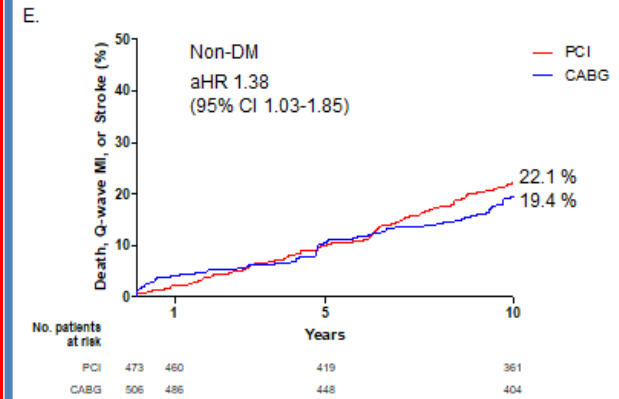




P-int=0.63

Death, MI or Stroke





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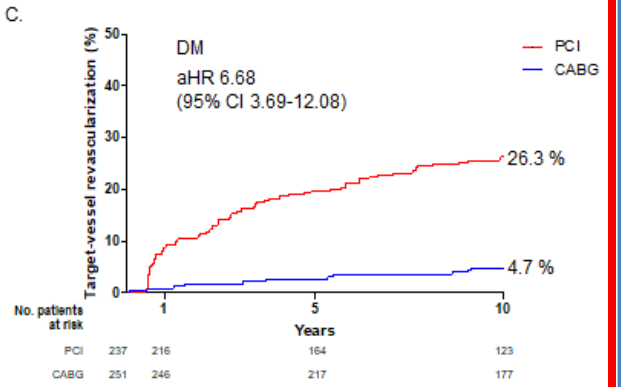
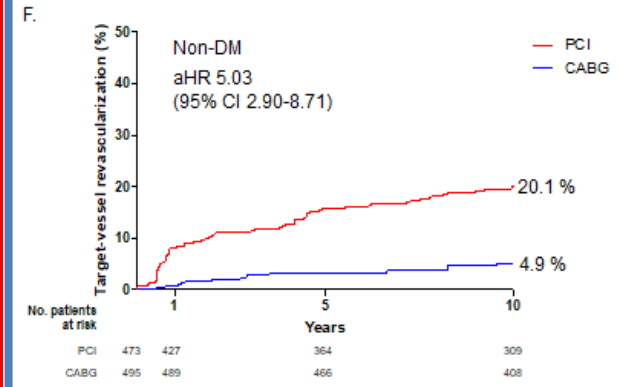
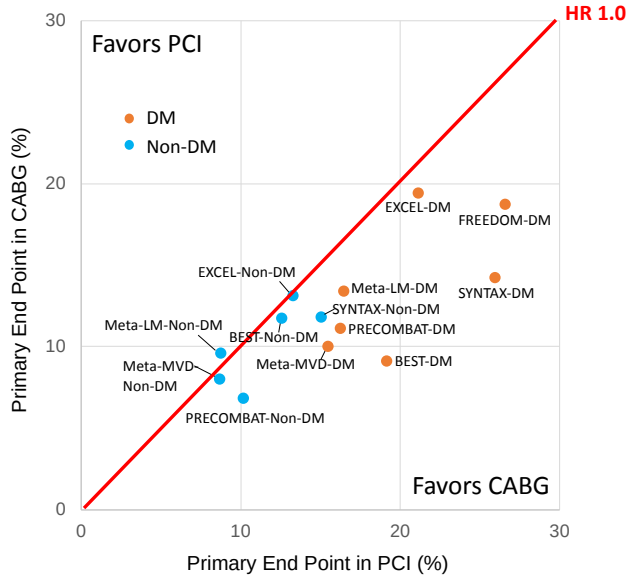
TVR





P-int=0.55

DM: Predictor or Decision-Maker? for Left Main Revascularization



Trial	Primary End-Point	Hazard Ratio		P-Interaction
		DM	Non-DM	
Multivessel CAD				
SYNTAX (N=1800)	Composite of death, MI, stroke, or repeat revascularization	1.83 (1.22–2.73)	1.28 (0.97–1.69)	0.12
FREEDOM (N=1900)	Composite of death, MI, or stroke	<2yr: 1.11 (0.85–1.45) >2yr: 2.06 (1.41–3.02)	NA	NA
BEST (N=880)	Composite of death, MI, or TVR	2.24 (1.25–4.00)	1.07 (0.65–1.76)	0.06
Left Main CAD				
PRECOMBAT (N=600)	Composite of death, MI, stroke, or TVR	1.43 (0.65–3.16)	1.51 (0.76–2.99)	0.92
EXCEL (N=1905)	Composite of death, MI, or stroke	1.04 (0.70–1.55)	0.97 (0.72–1.30)	0.77
NOBLE (N=1184)	Composite of death, MI, stroke or repeat revascularization	15% DM, NA	NA	NA
IPD Meta-Analysis (11RCT) (N=11518)				
Multivessel disease (N=7040)	All-cause death	1.48 (1.19–1.84)	1.08 (0.86–1.36)	0.045
Left main disease (N=4478)	All-cause death	1.34 (0.93–1.91)	0.94 (0.72–1.23)	0.13

Park DW & Park SJ. Editorial to EXCEL DM Subgroup Analysis JACC 2019 April, In-Press

Key Subgroups

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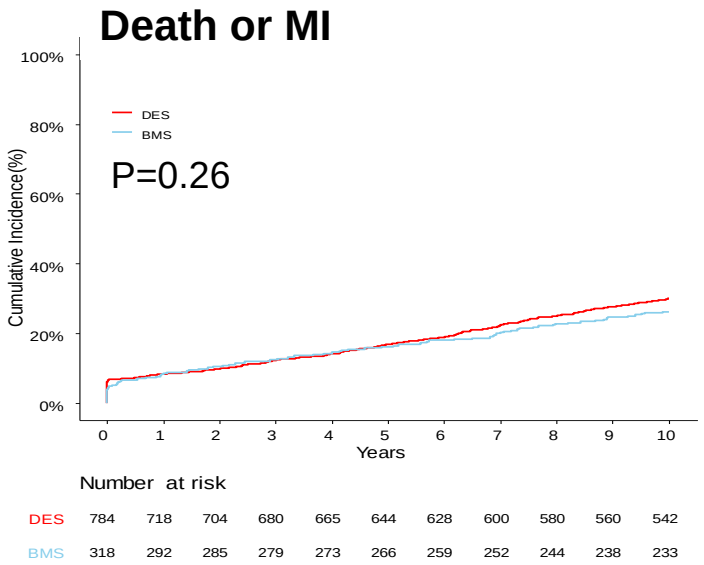
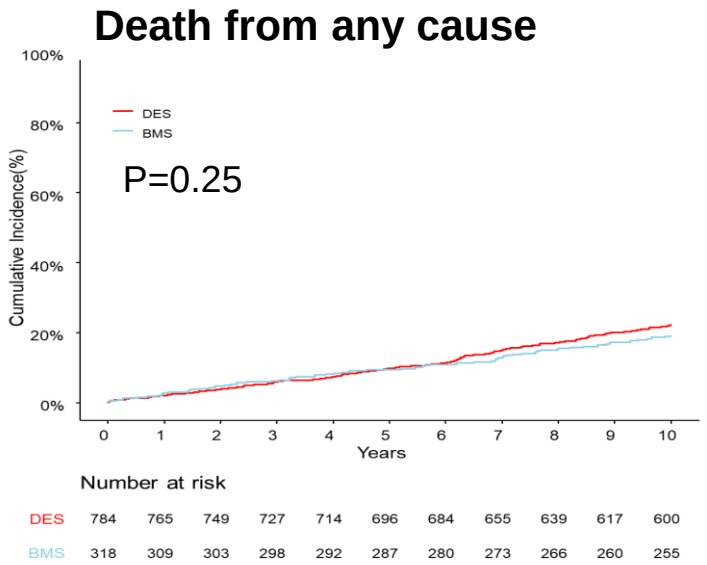
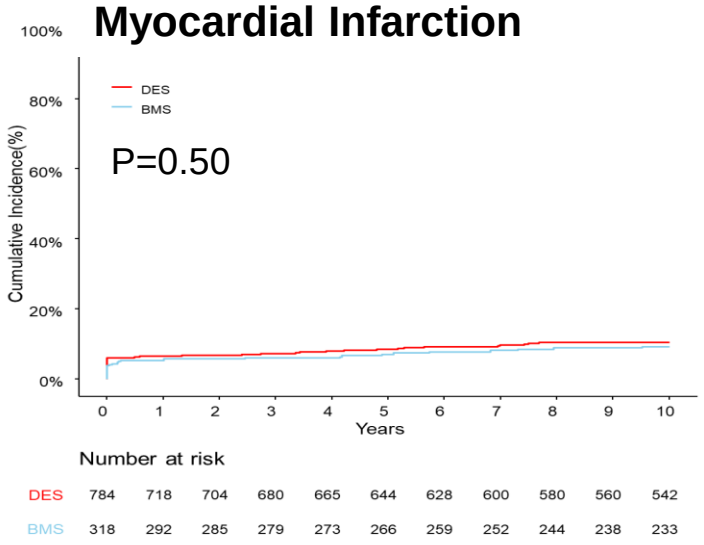
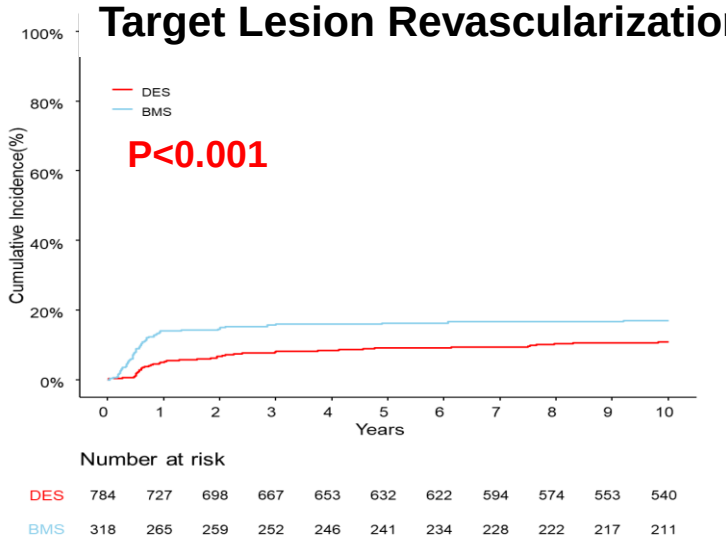
Unadjusted K-M curve: BMS vs. DES

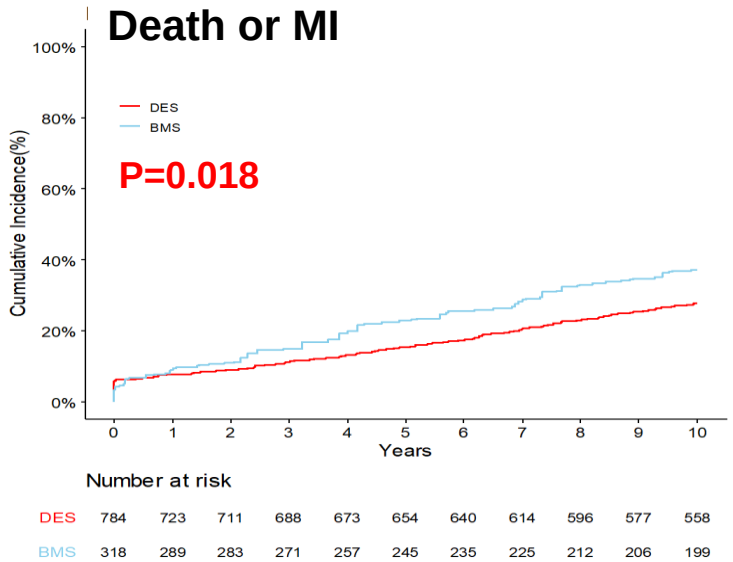


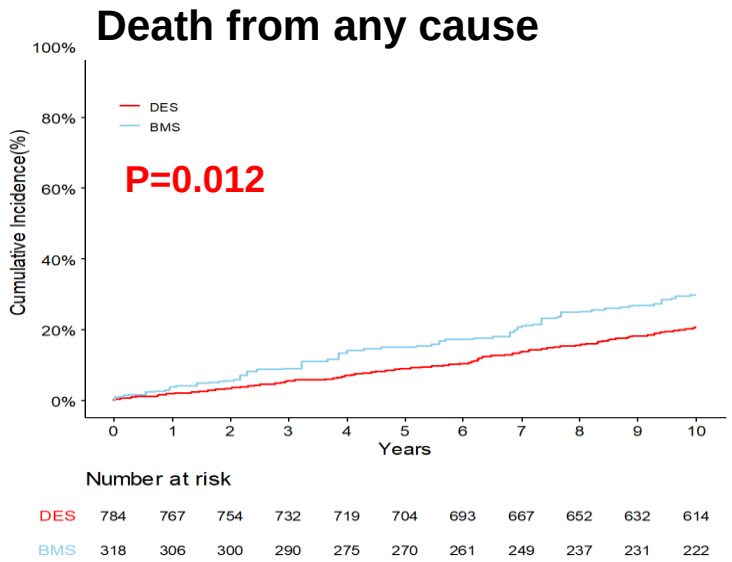


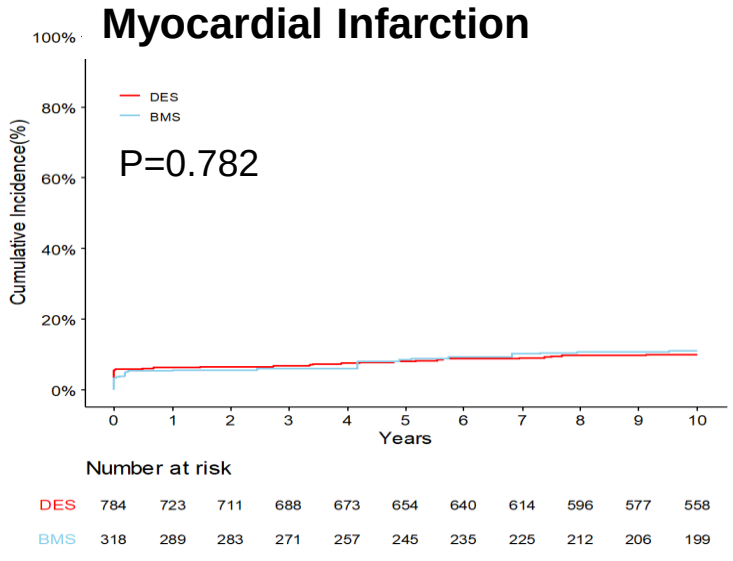


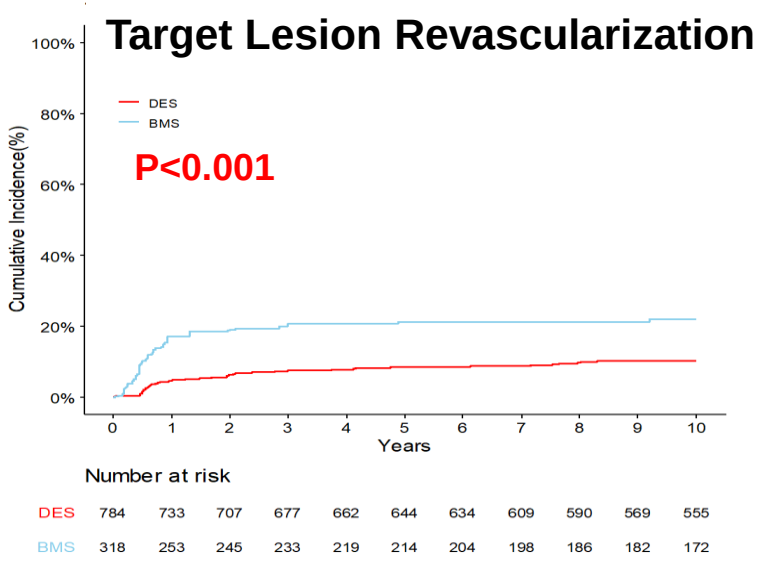


Adjusted Curve with IPTW: BMS vs. DES









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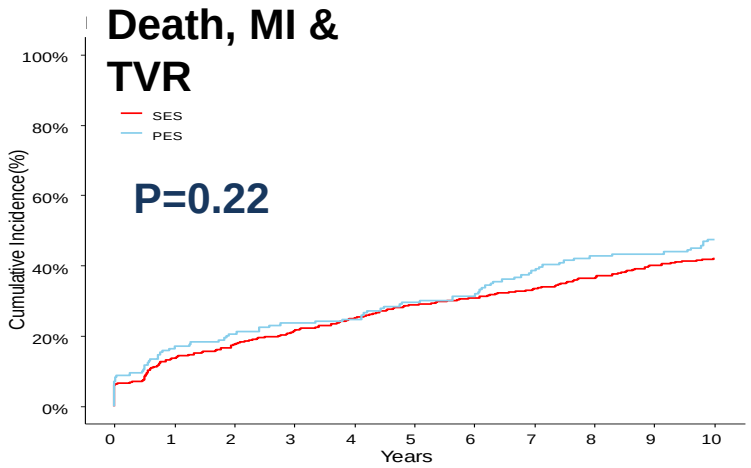
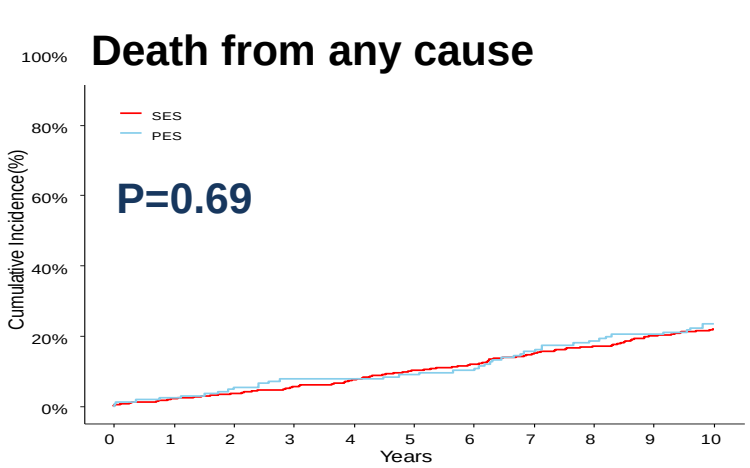
Unadjusted K-M curve: SES vs. PES



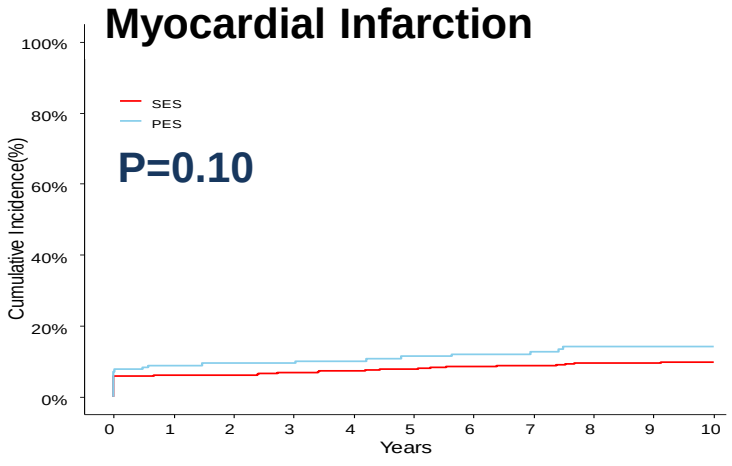
Number at risk

SES	607	524	499	473	450	427	415	399	381	359	348
PES	171	141	134	128	126	118	115	103	96	95	88



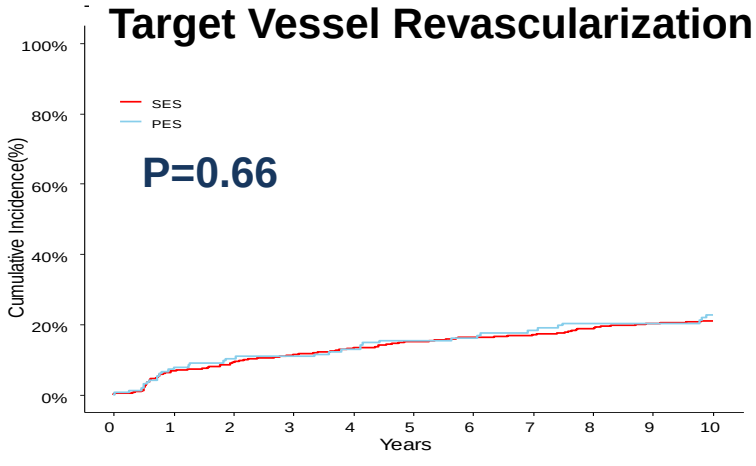
Number at risk

SES	607	595	584	569	556	540	530	510	499	481	469
PES	171	165	160	153	153	151	149	140	135	132	127



Number at risk

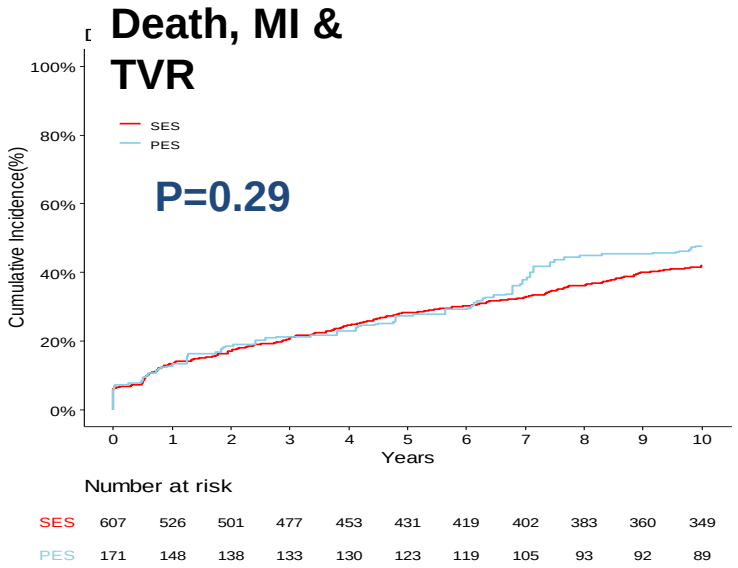
SES	607	562	551	533	519	502	488	469	455	438	425
PES	171	151	148	142	141	137	135	126	120	118	113

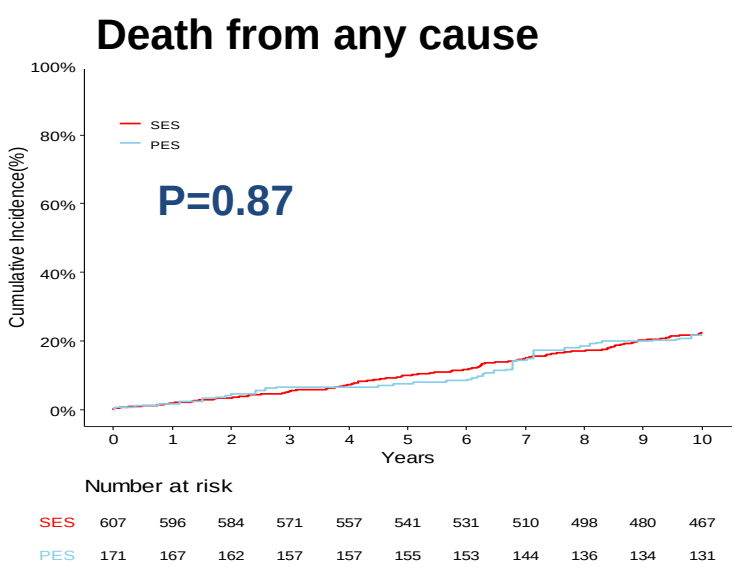


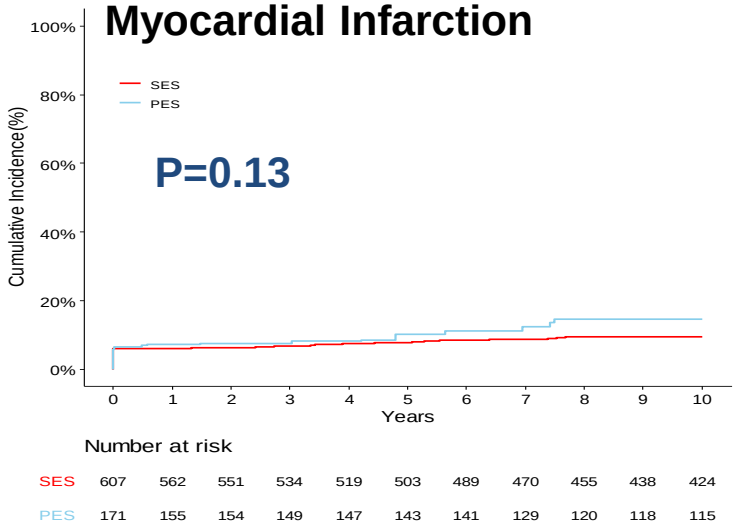
Number at risk

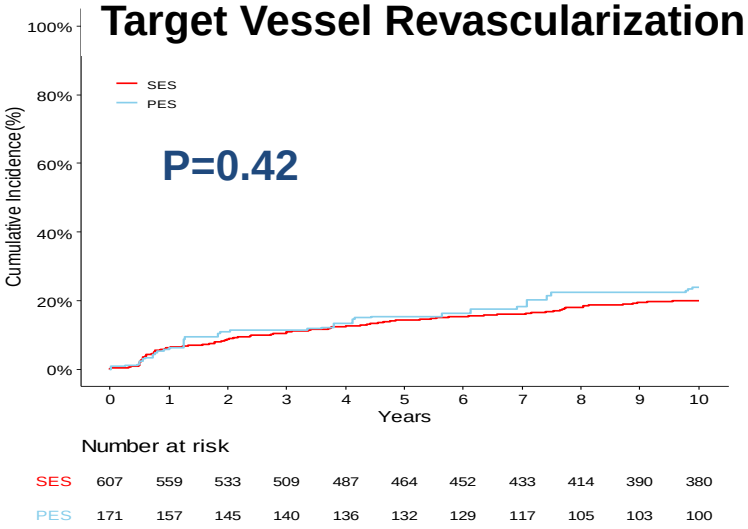
SES	607	556	530	505	483	459	447	429	411	388	378
PES	171	153	144	137	134	128	125	114	107	105	98

Adjusted Curve with IPTW: SES vs. PES









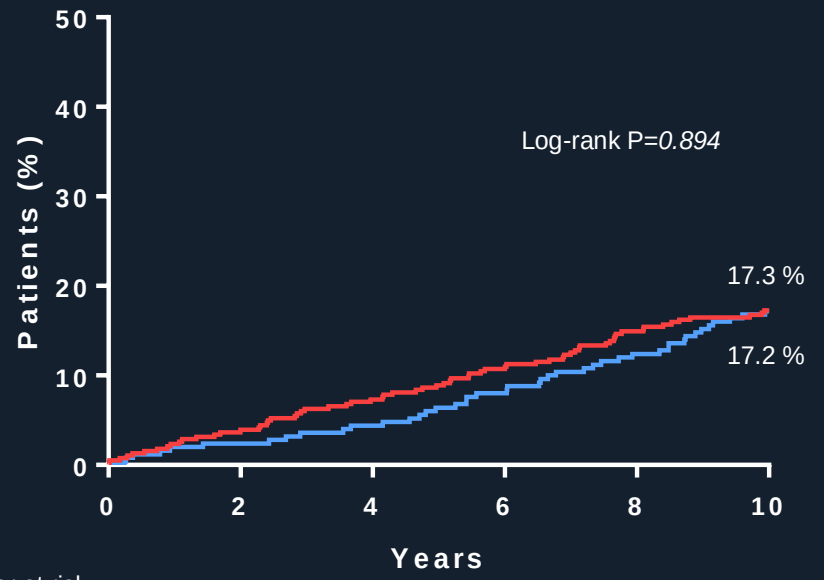
Key Subgroups

- DM vs. NONDM
- BMS vs. DES
- SES vs. PES
- SA vs. ACS
- SYNTAX Score

All-Cause Death

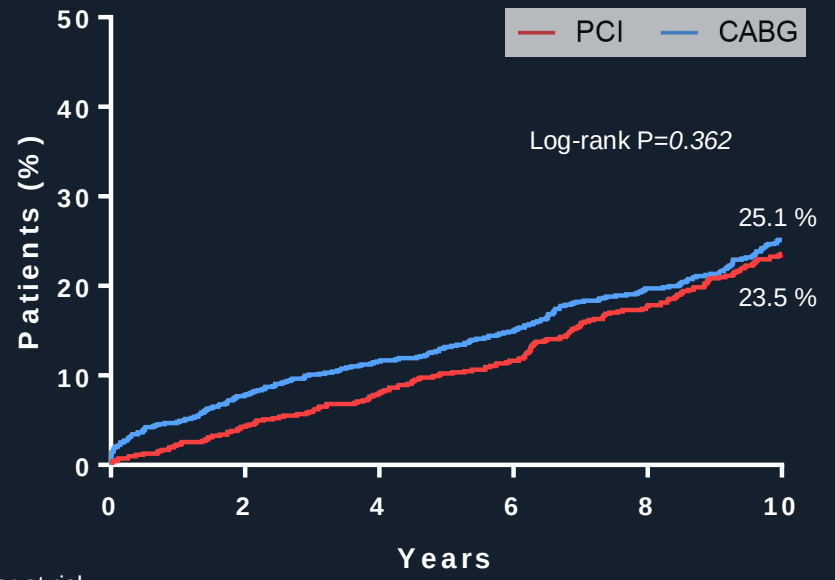
P-for-interaction = 0.62

Non-ACS



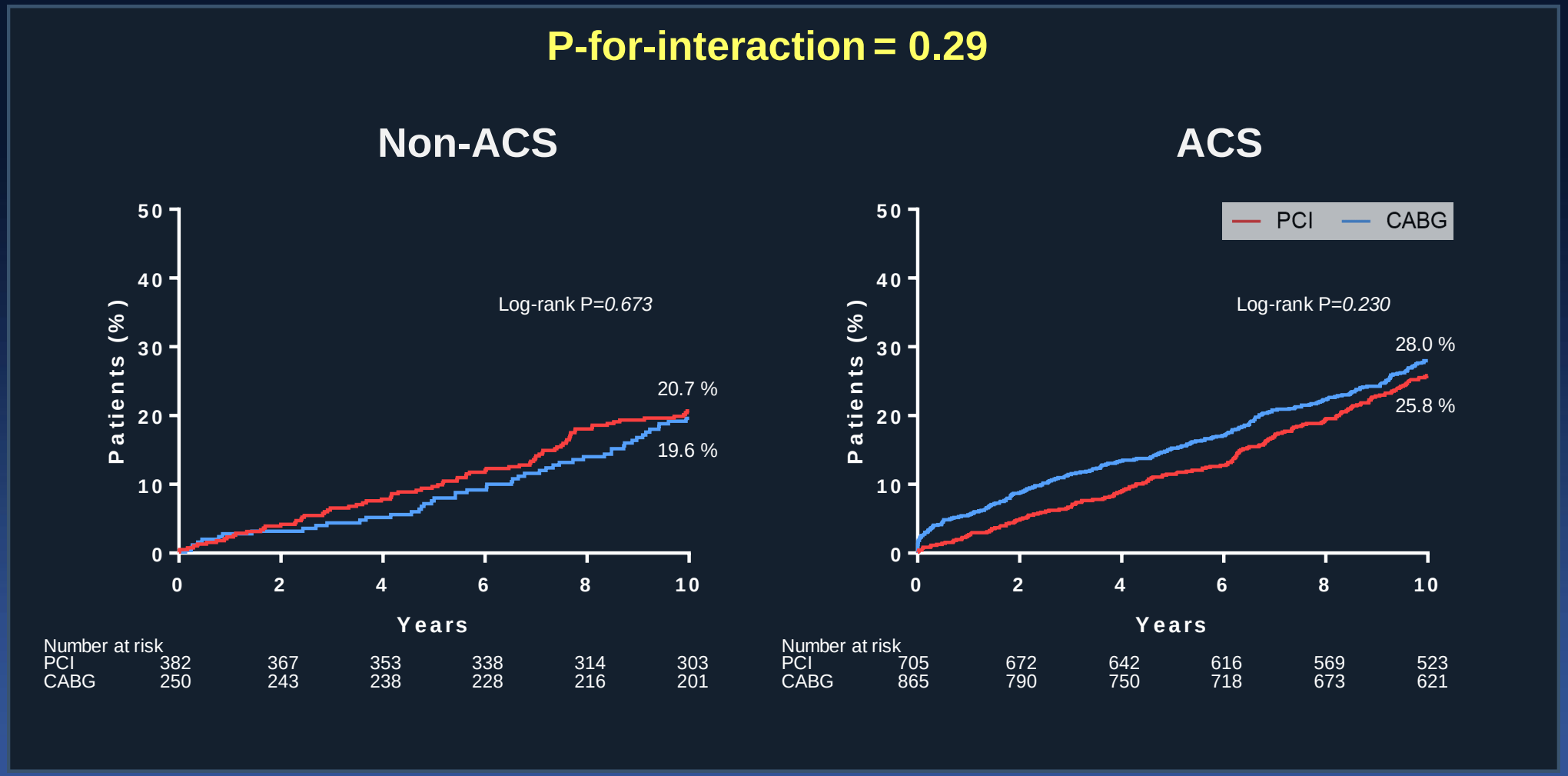
Number at risk						
PCI	386	368	355	342	326	316
CABG	251	245	240	231	220	207

ACS

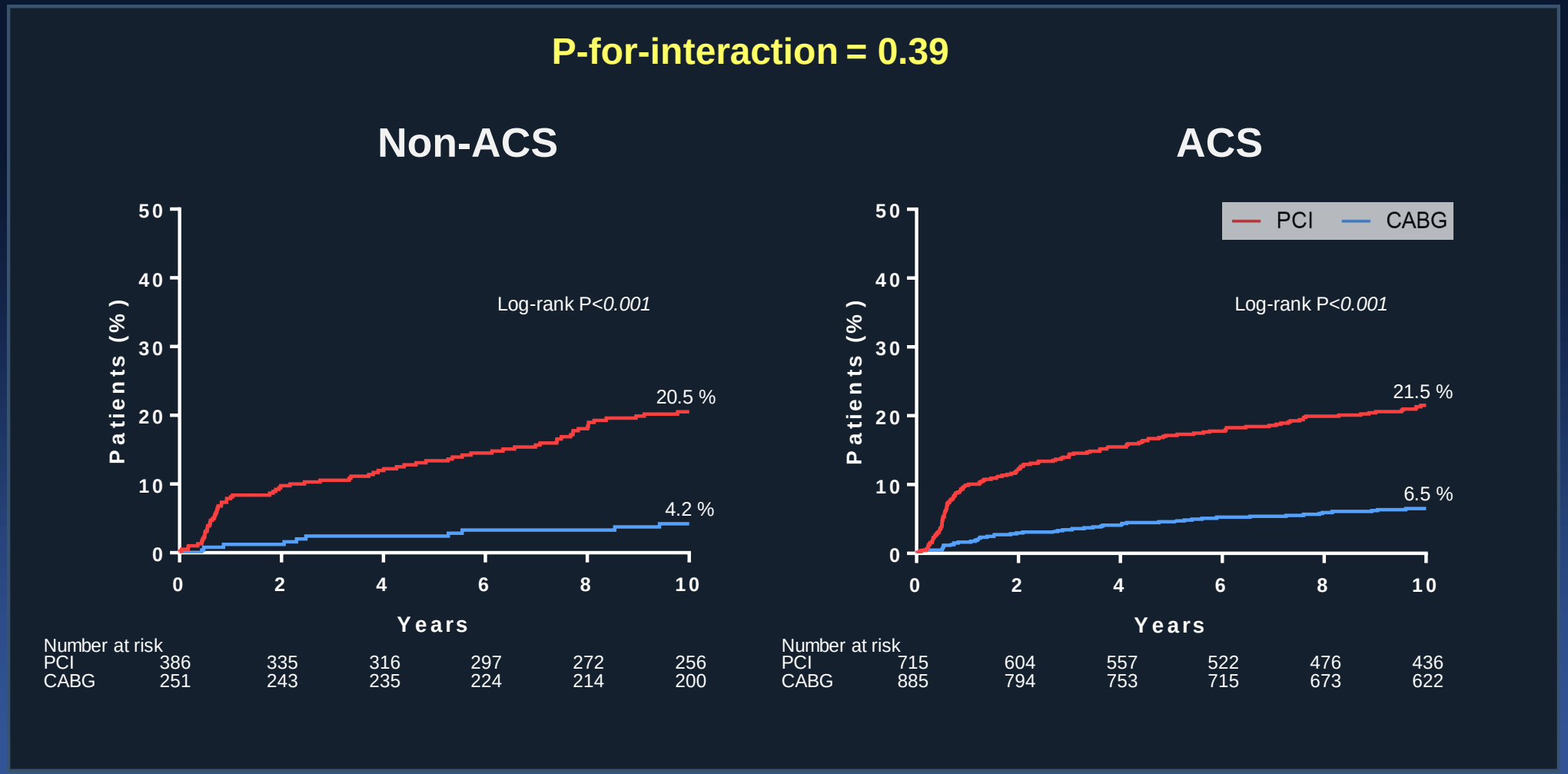


Number at risk						
PCI	715	676	649	624	581	539
CABG	885	804	771	742	700	650

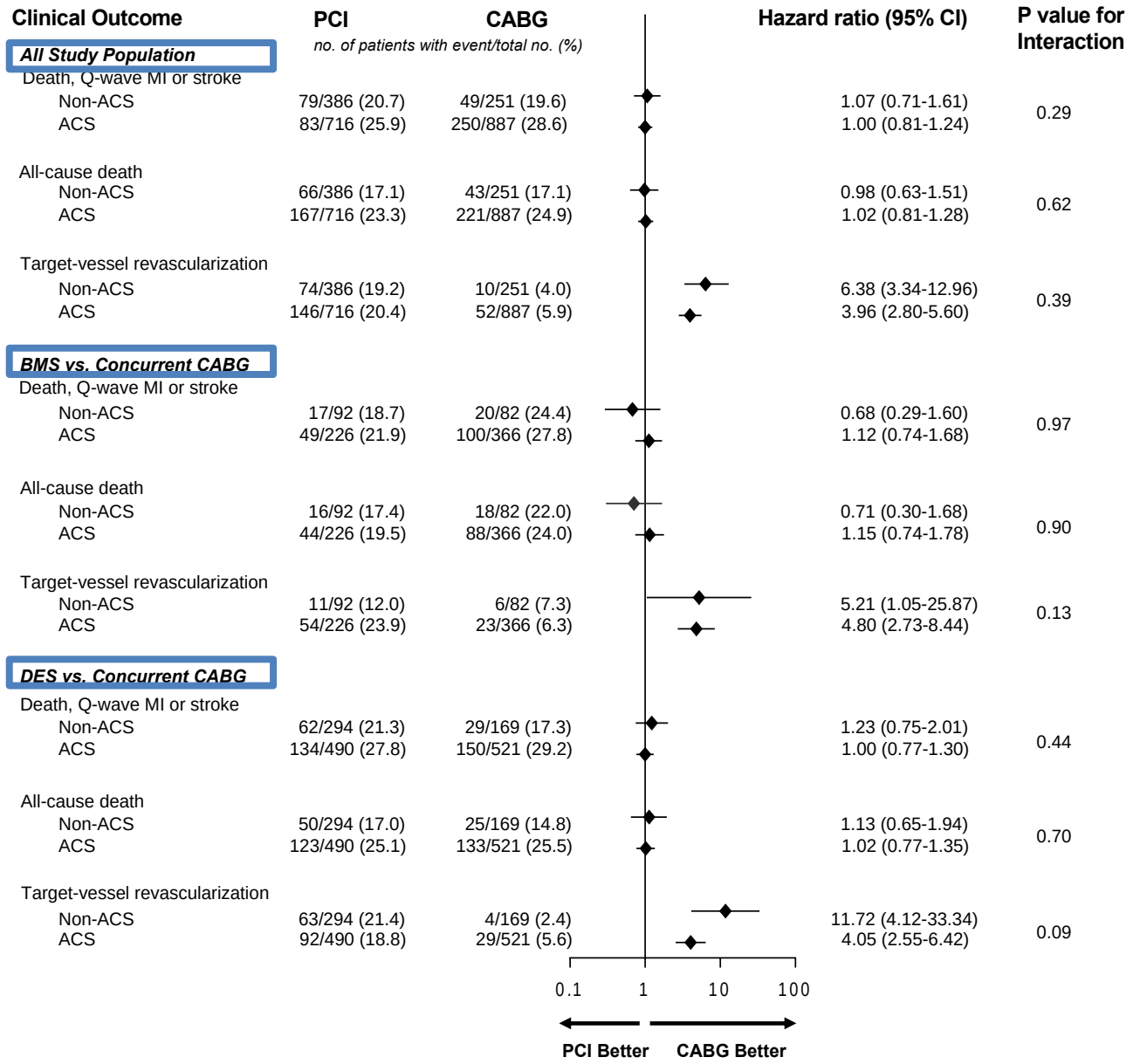
Composite of Death, Q-wave MI, or Stroke



Target-vessel Revascularization



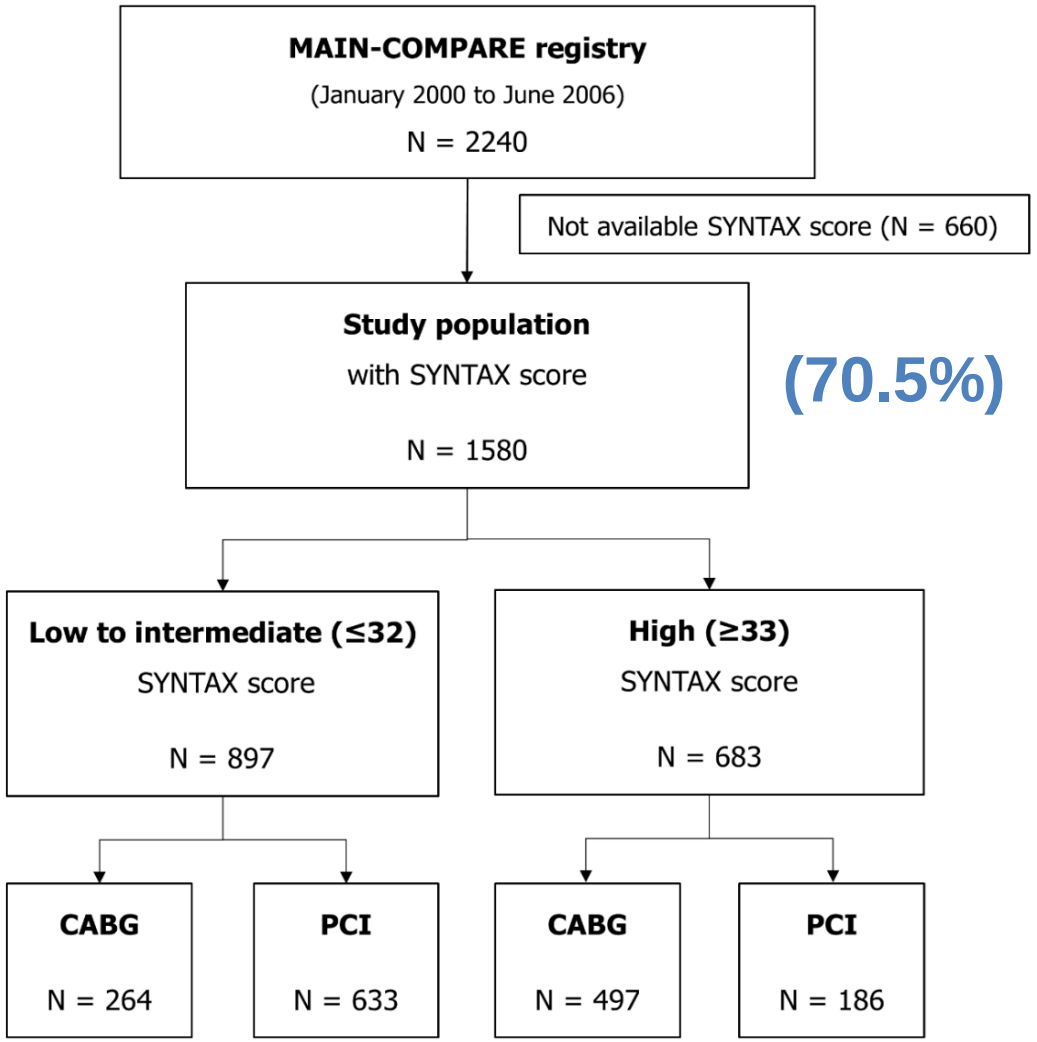
Adjusted Hazard Ratio



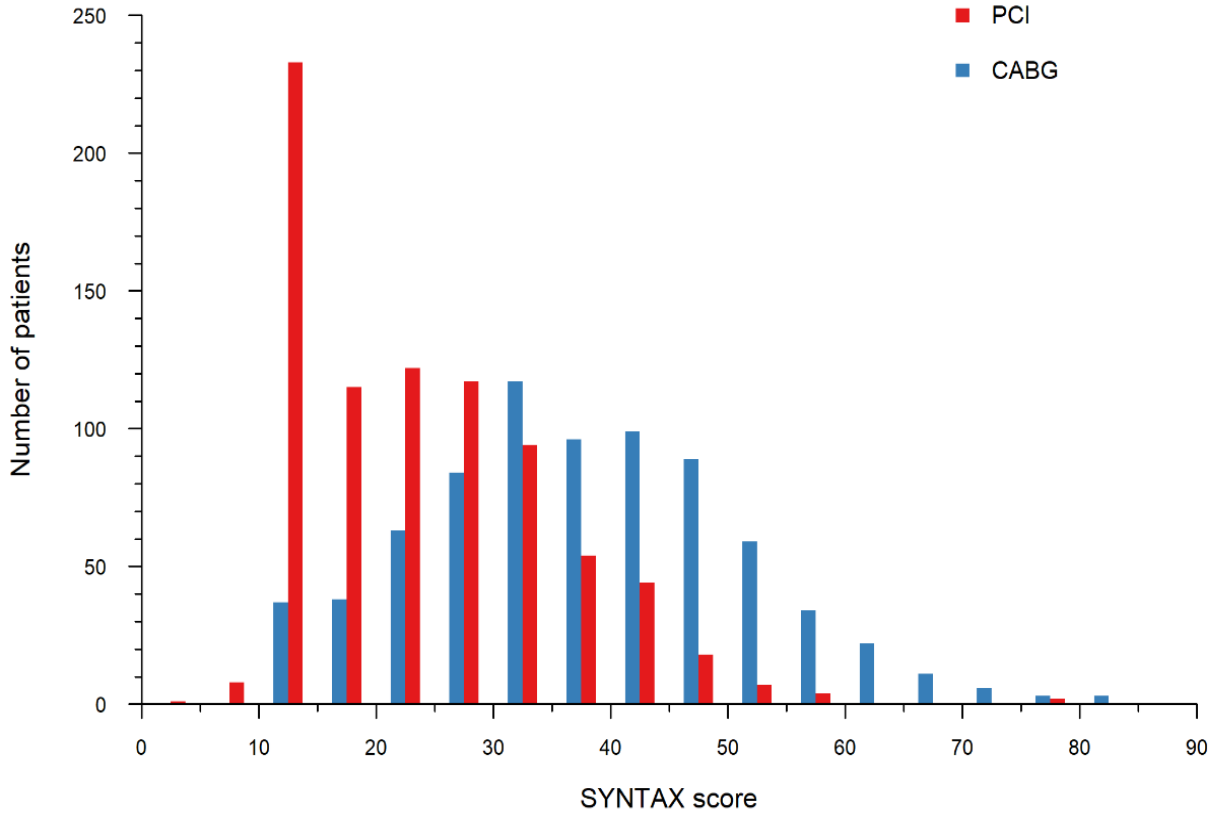
Key Subgroups

- DM vs. NONDM
- BMS vs. DES
- SES vs. PES
- SA vs. ACS
- SYNTAX Score

MAINCOMPARE: Subgroup with available SYNTAX score

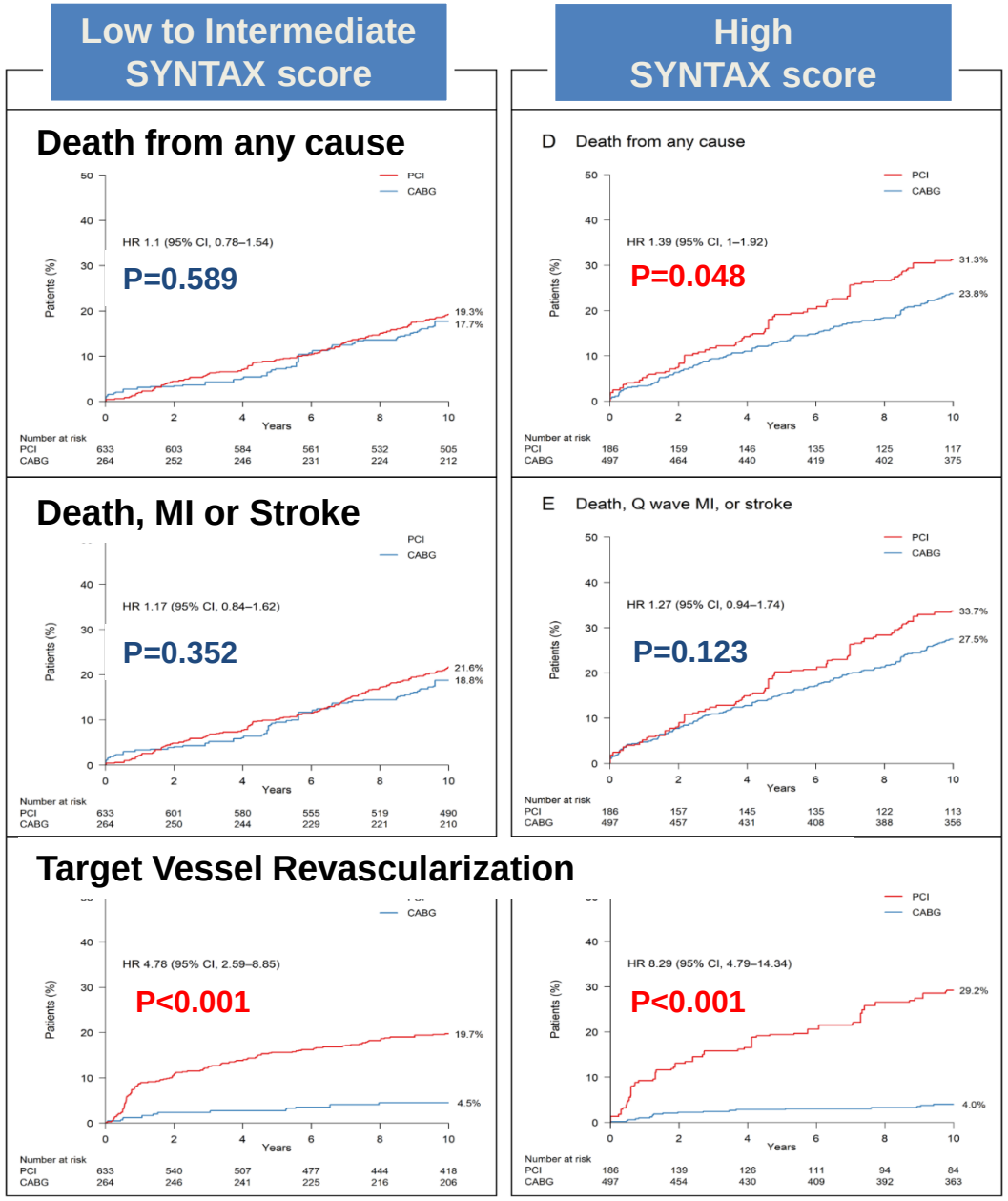


SYNTAX Score Distribution



The median SS:
23.0 (IQR, 14.0–31.2) in PCI arm and
37.5 (IQR 29.0–47.5) in CABG arm

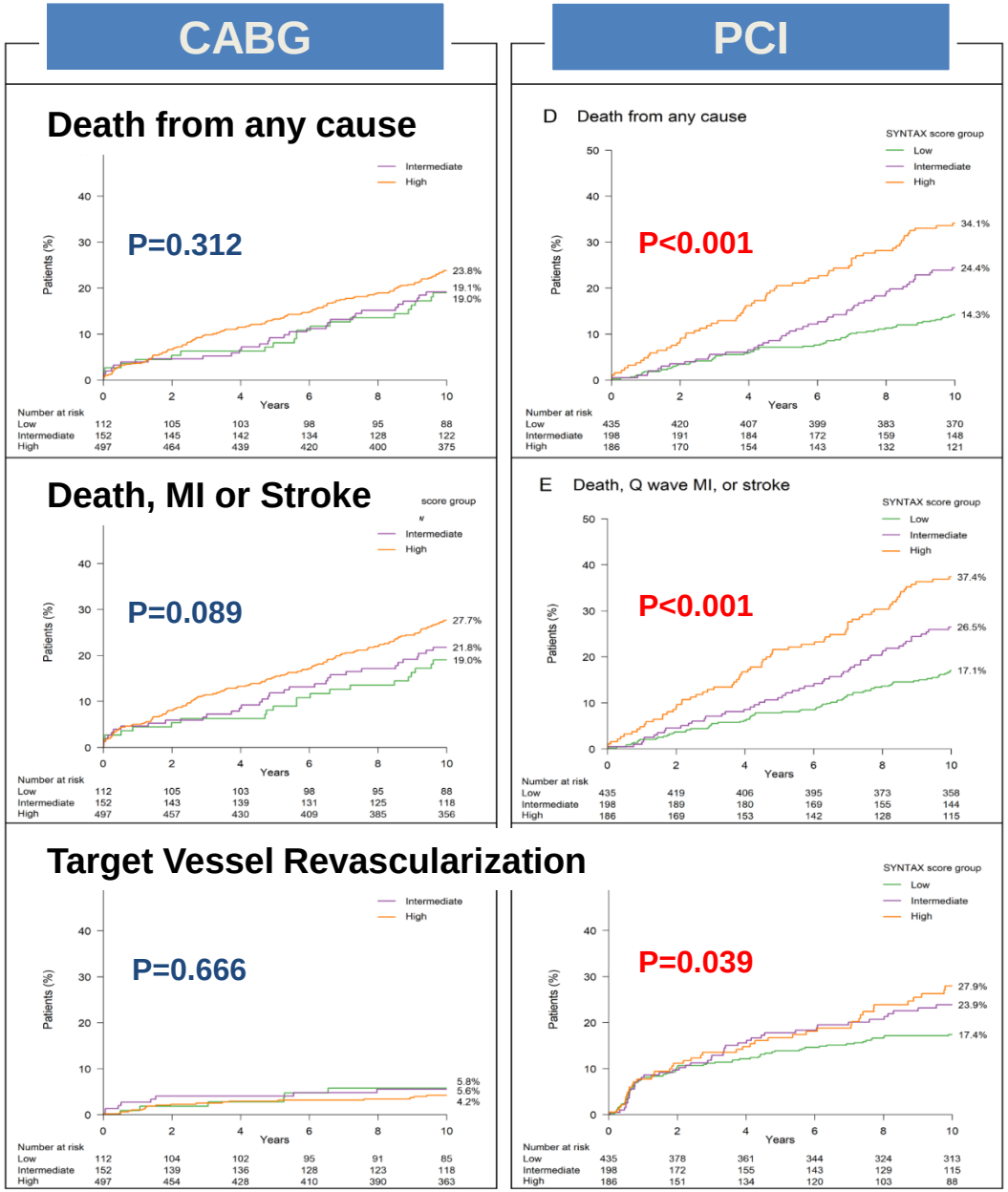
Adjusted Curve with IPTW: PCI vs. CABG



PCI

CABG

10-Year K-M Curves: each CABG and PCI arm



High SYNTAX score

Intermediate

Low

PCI vs. CABG for LM Disease 2019

1. Mortality of PCI with DES is Comparable with CABG
2. Higher Revascularization in PCI
3. 10-Year report of the MAIN-COMPARE registry suggested higher risks of death and serious composite outcomes after DES than after CABG beyond 5 years.
4. Long-term (10 year) comparative outcomes should be confirmed or refuted through extended follow-up of RCTs (EXCEL and NOBLE).

Thank You !

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