Left Main Is No Longer Surgical Disease

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Surgery vs. Medical Treatment for Left Main Disease

According to data 40 years ago~

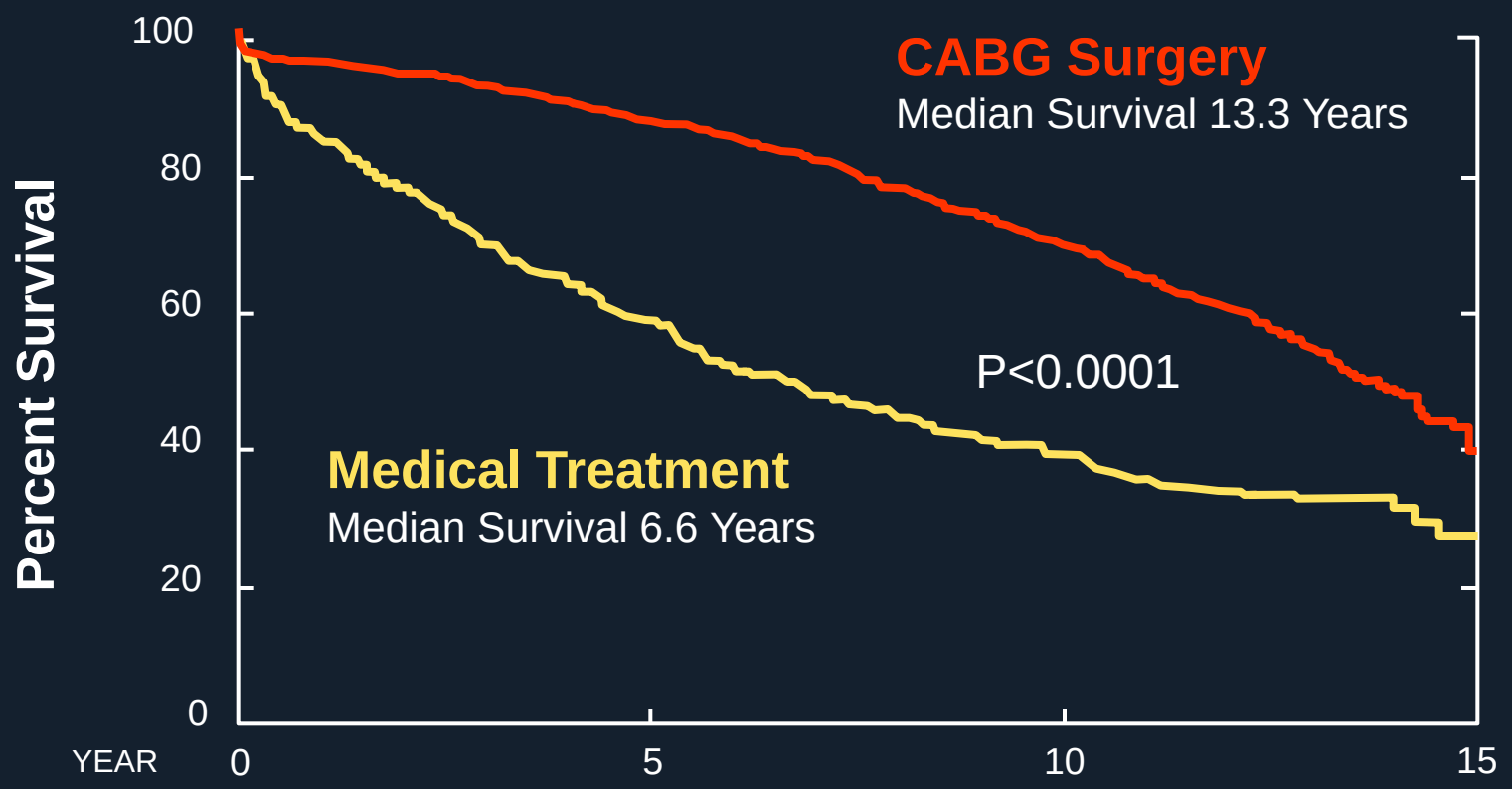
The VA cooperative randomized study of surgery for coronary arterial occlusive disease II.
LM Subgroup from CASS trial.

Abstract ; A subgroup of 113 patients (53 medical, 60 surgery group). 12 of 60 (20%) surgical and 19 of 53 (36%) medical patients ($P < 0.06$) were died at 2 year F/U.

Results ; Survival is better in surgical patients in patients with additional significant disease involving the right coronary artery, with or without left ventricular dysfunction. Angina relief is better in surgical patients

Circulation [1976, 54(6 Suppl):III107-17]

15-year Survival From CASS Registry, Left Main Disease



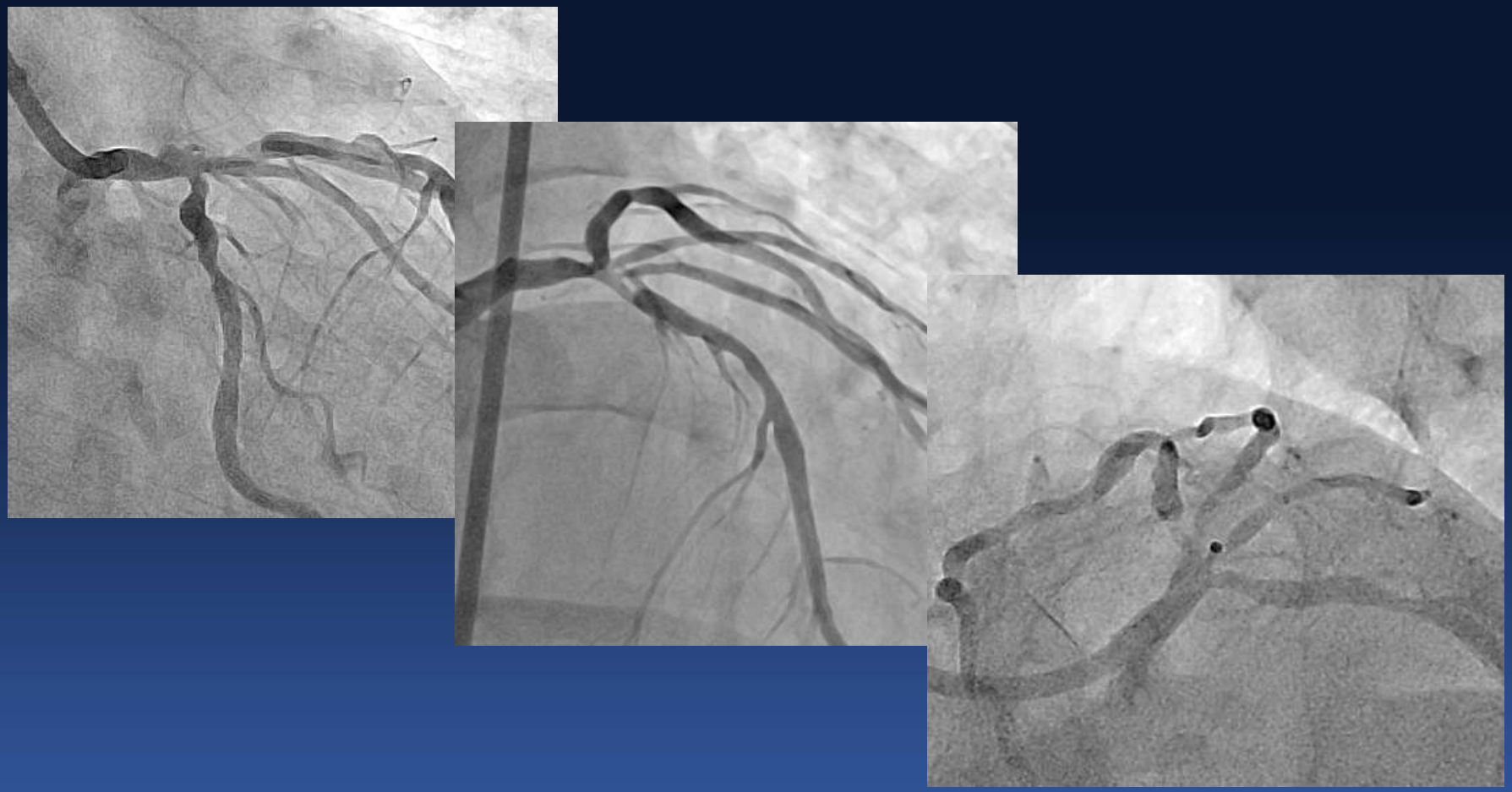
	N	Survival						
———	1153	100	973	85	745	67	20	37
.....	331	100	194	59	128	39	6	27

Caracciolo E A et al. Circulation 1995;91:2325-2334

PCI vs. Surgery
for Left Main Disease

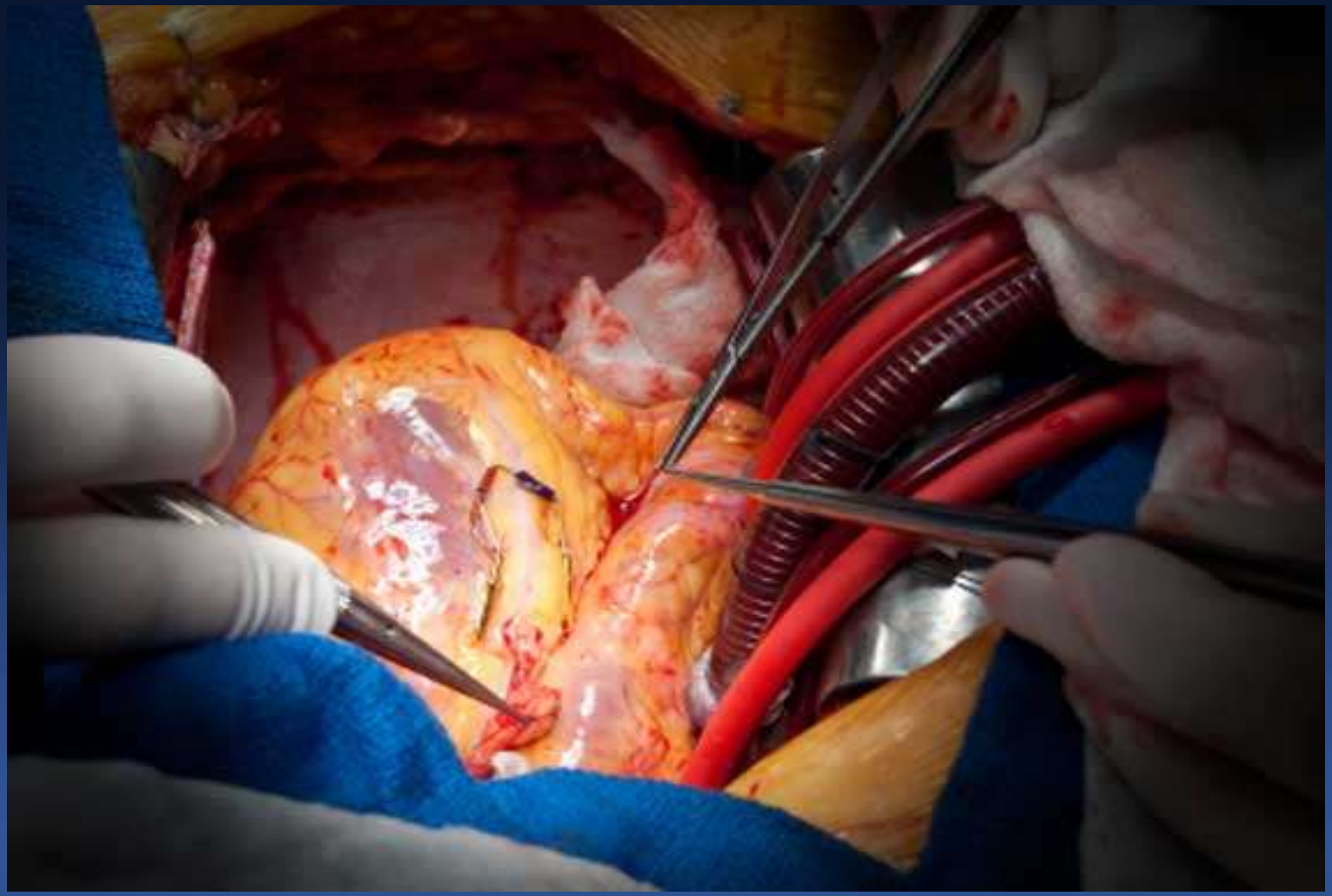
?

52/M, Effort related chest pain

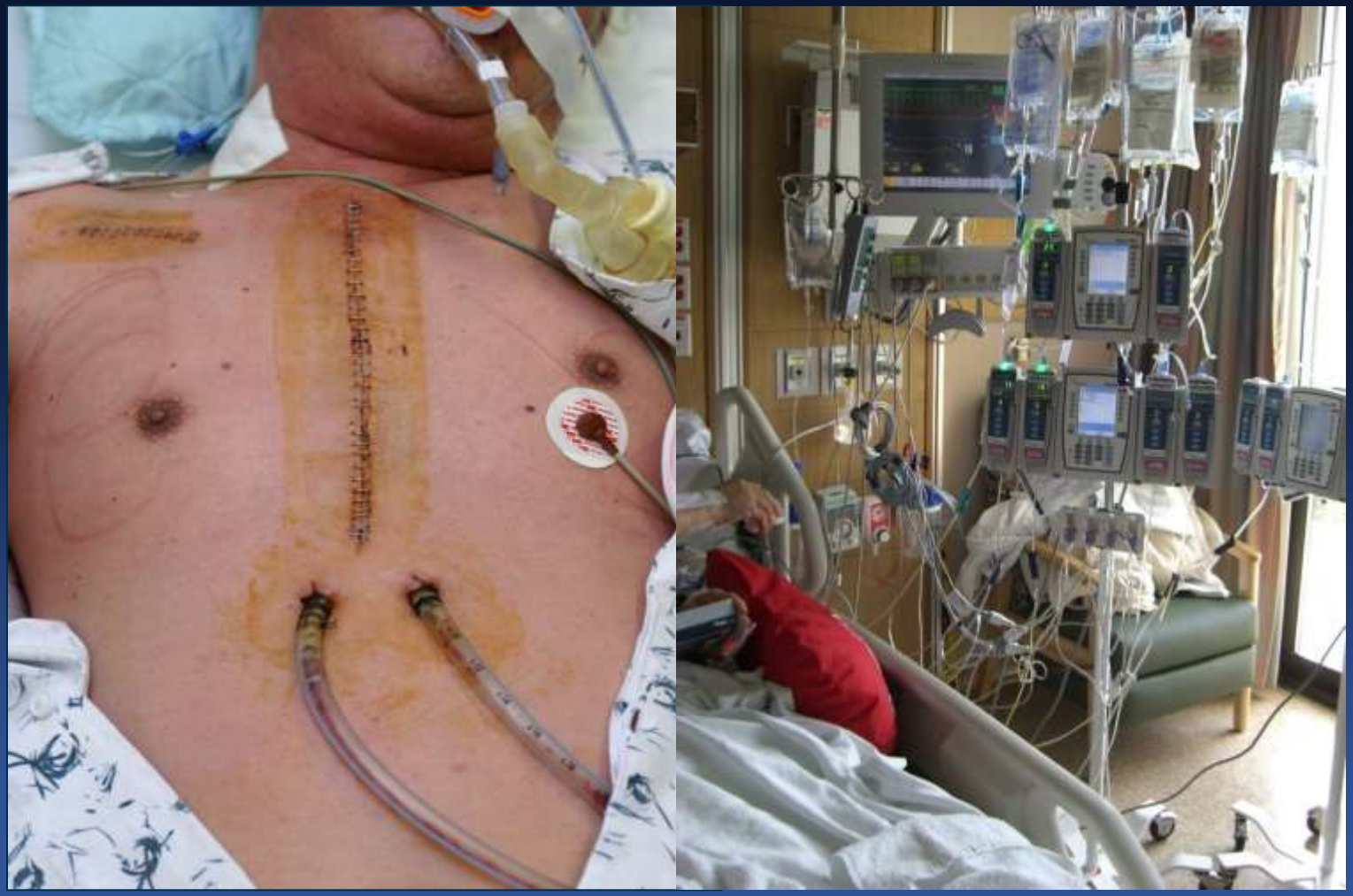


Left Main bifurcation disease

Surgery



Surgery

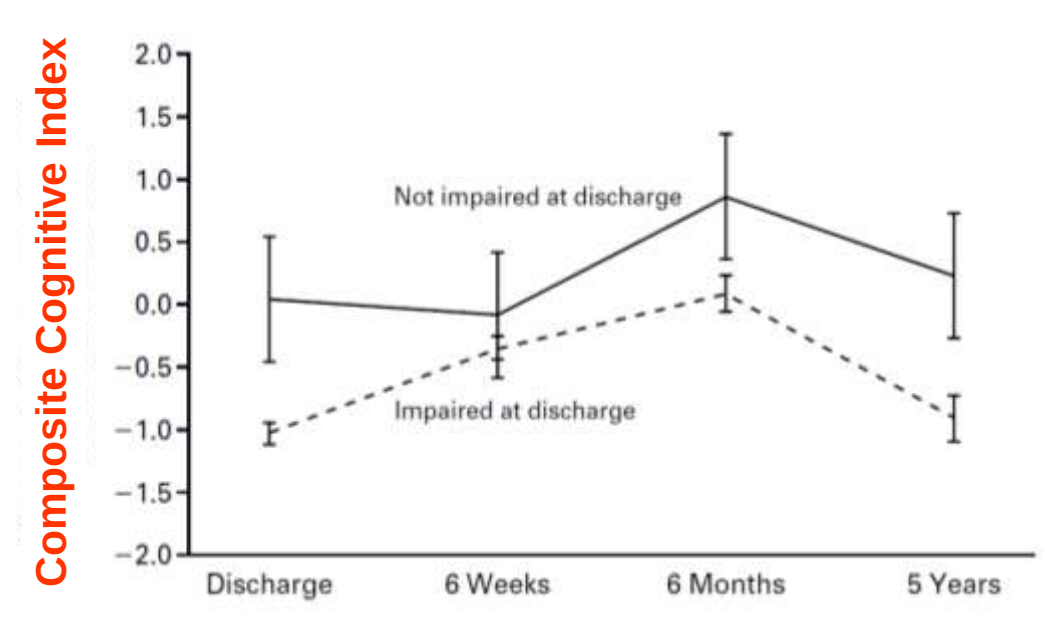


Surgery

Early mortality, morbidity
Need multiple grafts
Post-operative care
Cosmetic problems
Higher incidence of stroke
It takes 4 weeks to recovery

Surgery

>40% of CABG Patients Showed Impaired Cognitive Function at 5 year



It was also associated with early death (HR, 1.2-1.5).

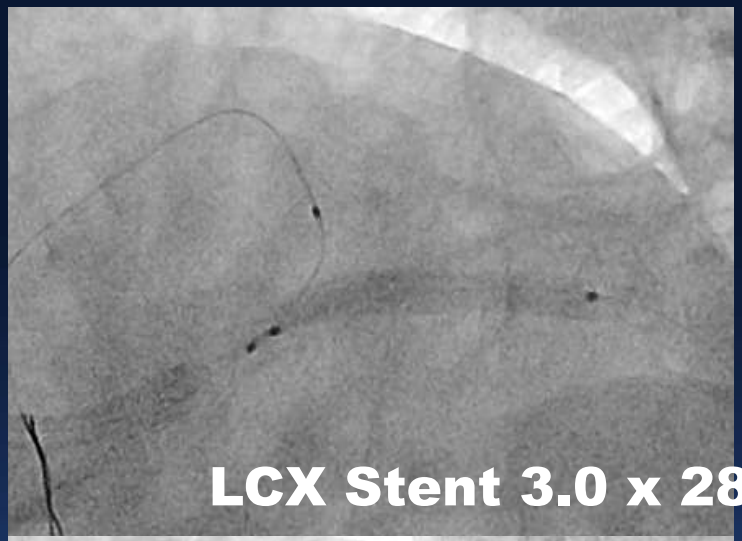
Newman MF et al, New Engl J Med 2001;344:395,
Sachs G, et al. Ann Intern Med. 2011;155:300-308.

Surgery

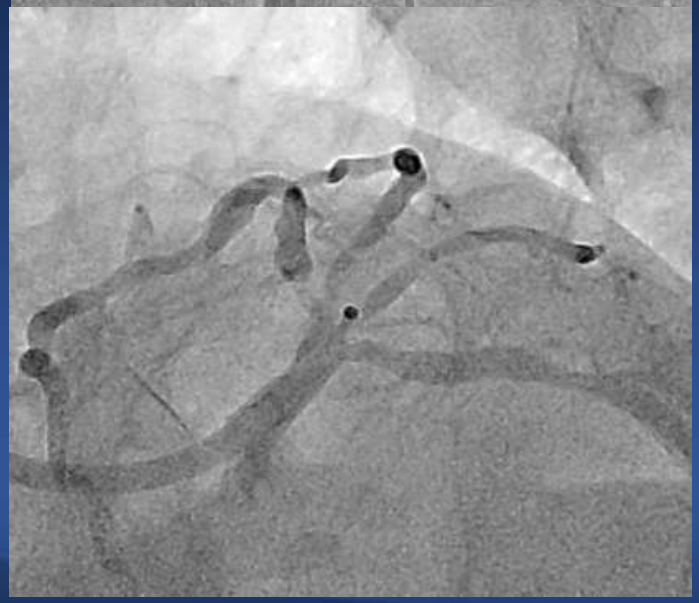
5 years Later…

PCI

PCI

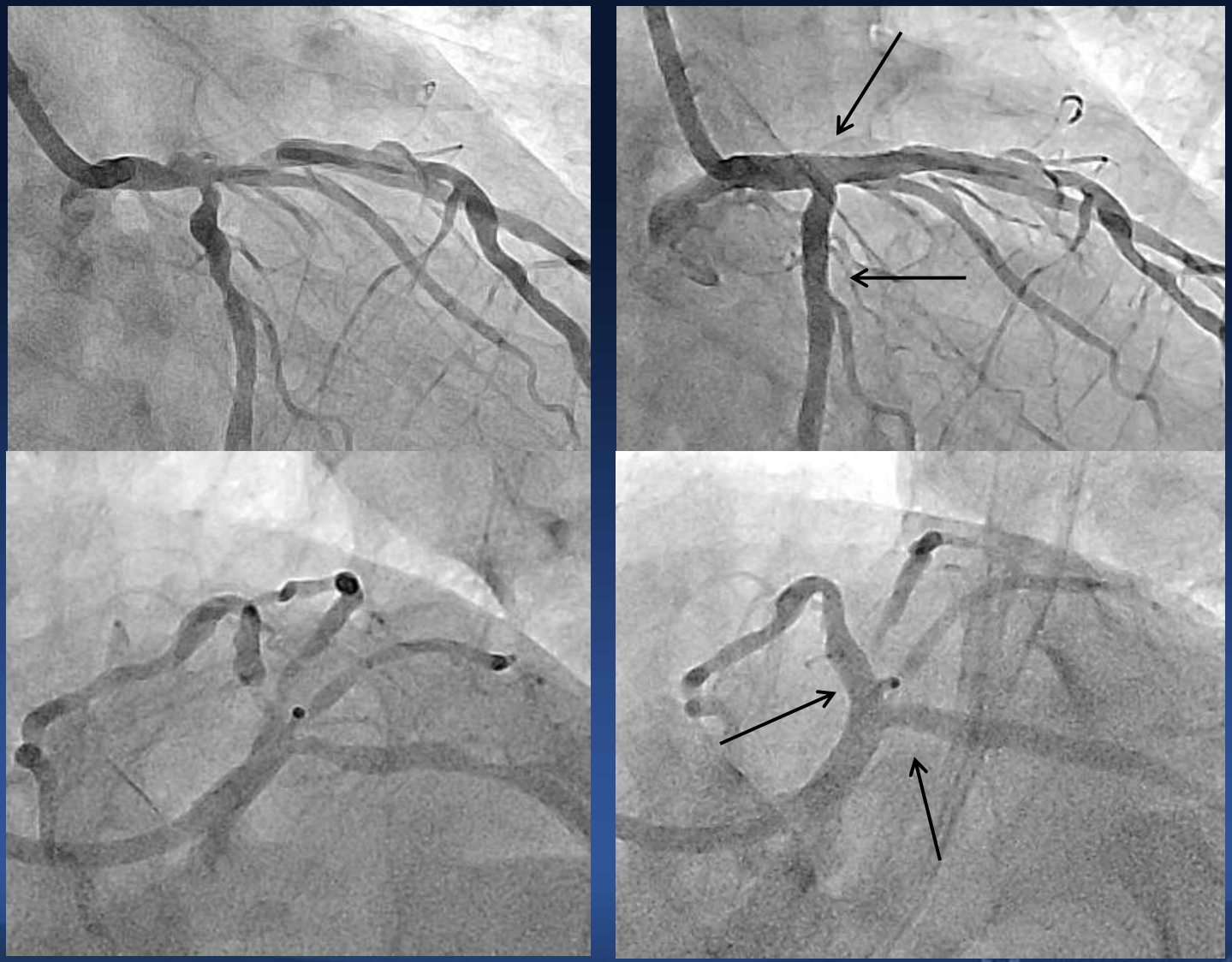


LCX Stent 3.0 x 28 mm



LAD Stent 3.5 x 23 mm
Crush, Kissing

PCI



PCI

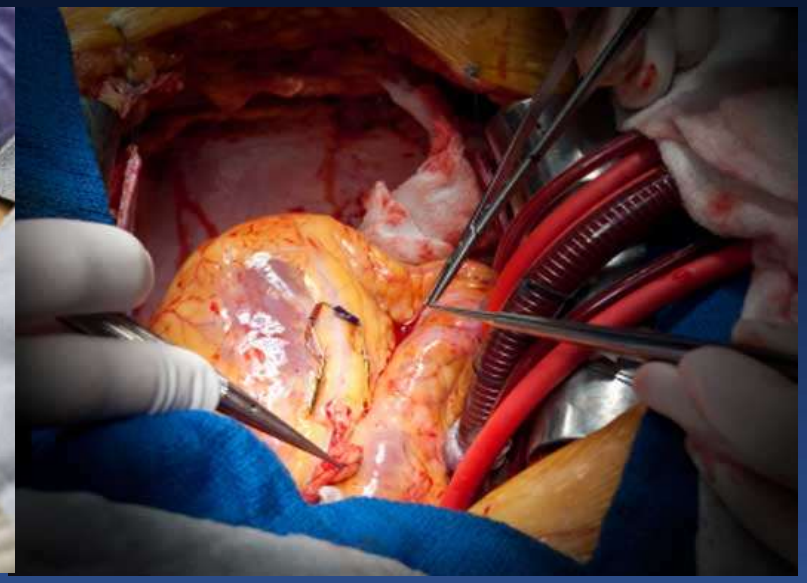
It takes 30 min.

No serious complications

Discharge next day after PCI

TLR < 2%

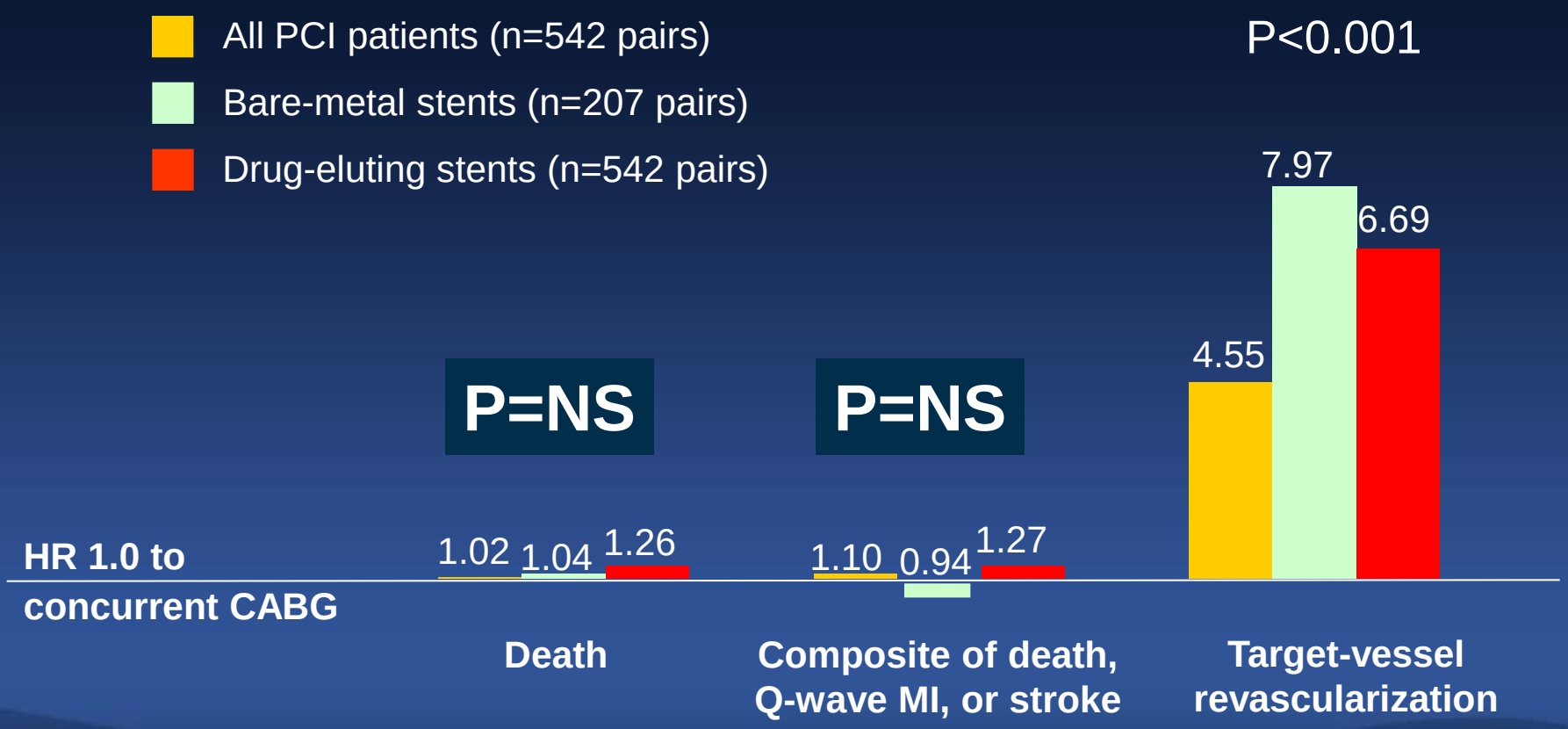
Which One Do You Prefer ?



DES vs. CABG

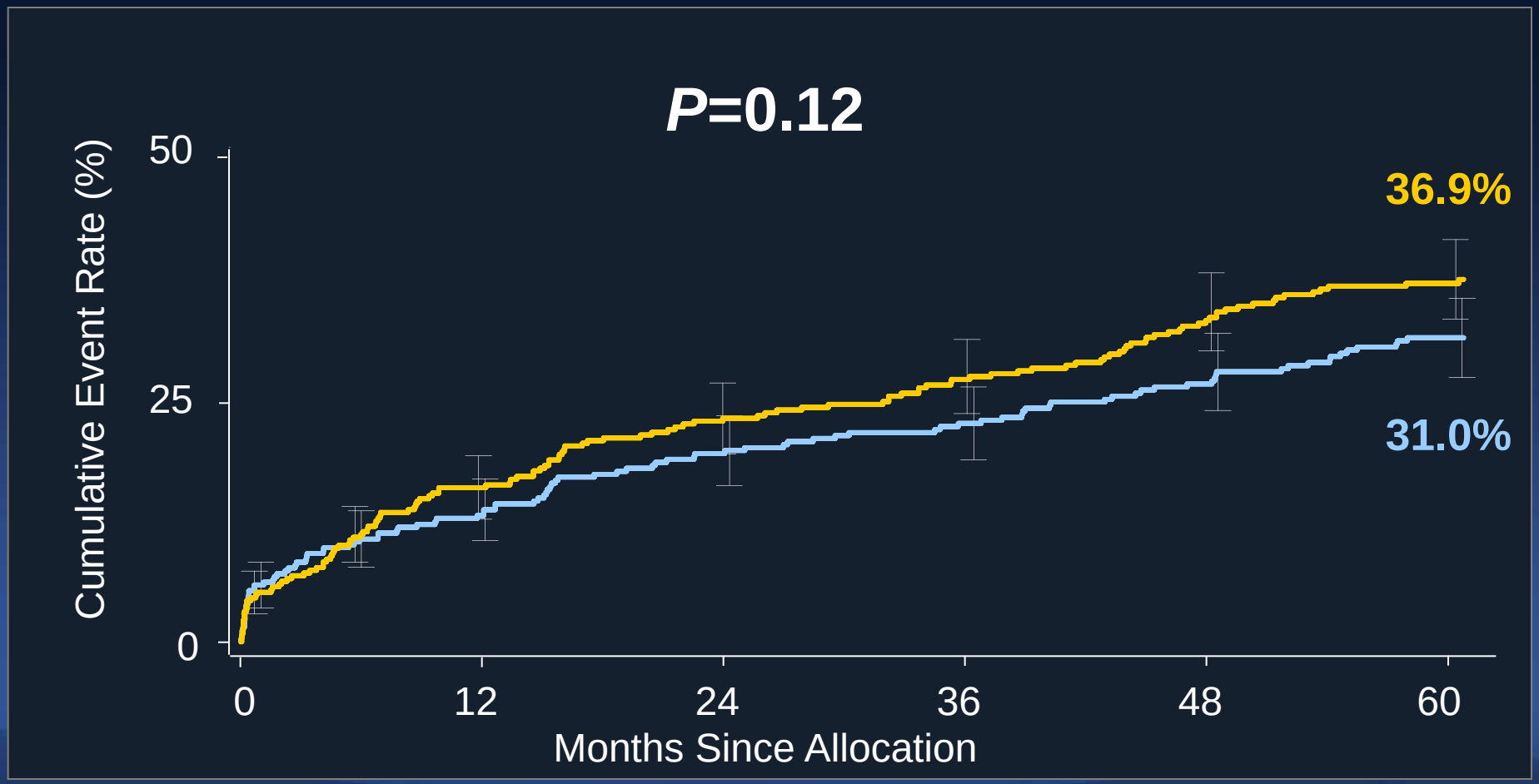
1. MAIN COMPARE Registry
2. SYNTAX, LM subgroup
3. PRECOMBAT
4. Combined Patient Level Meta-Analysis
5. Temporal Changes of LM Revascularization (*AMC Main Registry, IRIS Main Registry)*
6. EXCEL, NOBLE

MAIN COMPARE, 5 Year
Death /MI /Stroke



Park DW, et al. JACC 2010;56:117-24

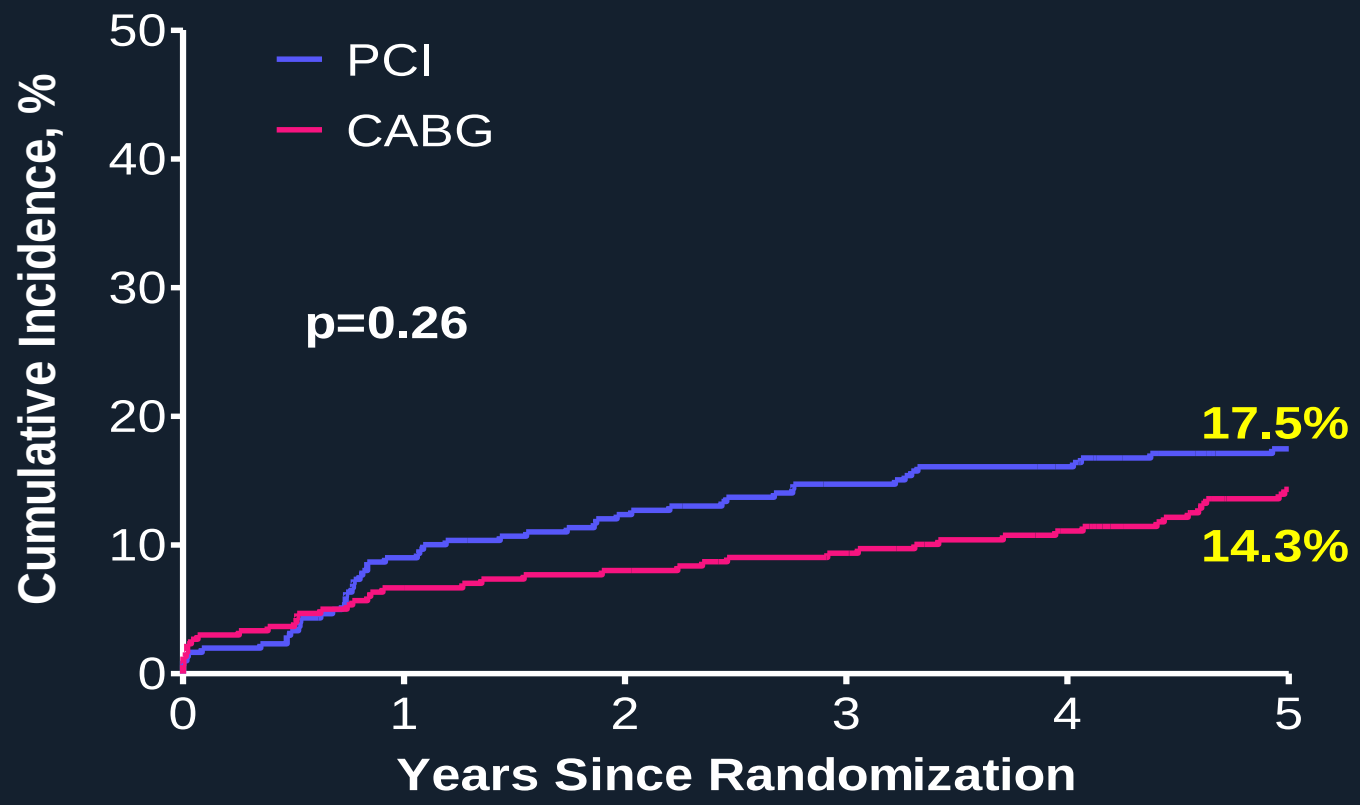
SYNTAX (LM Subset), 5 Year
Death /MI /Stroke /Repeat Revascularization



Cumulative KM Event Rate ± 1.5 SE; log-rank *P* value;*Binary rates

ITT population

PRECOMBAT, 5 Year
Death. MI, Stoke or iTVR



Patient at risk

PCI	300	272	261	252	246	231
CABG	300	279	274	267	256	235

Ahn JM et al, JACC. 2015 Mar 10.

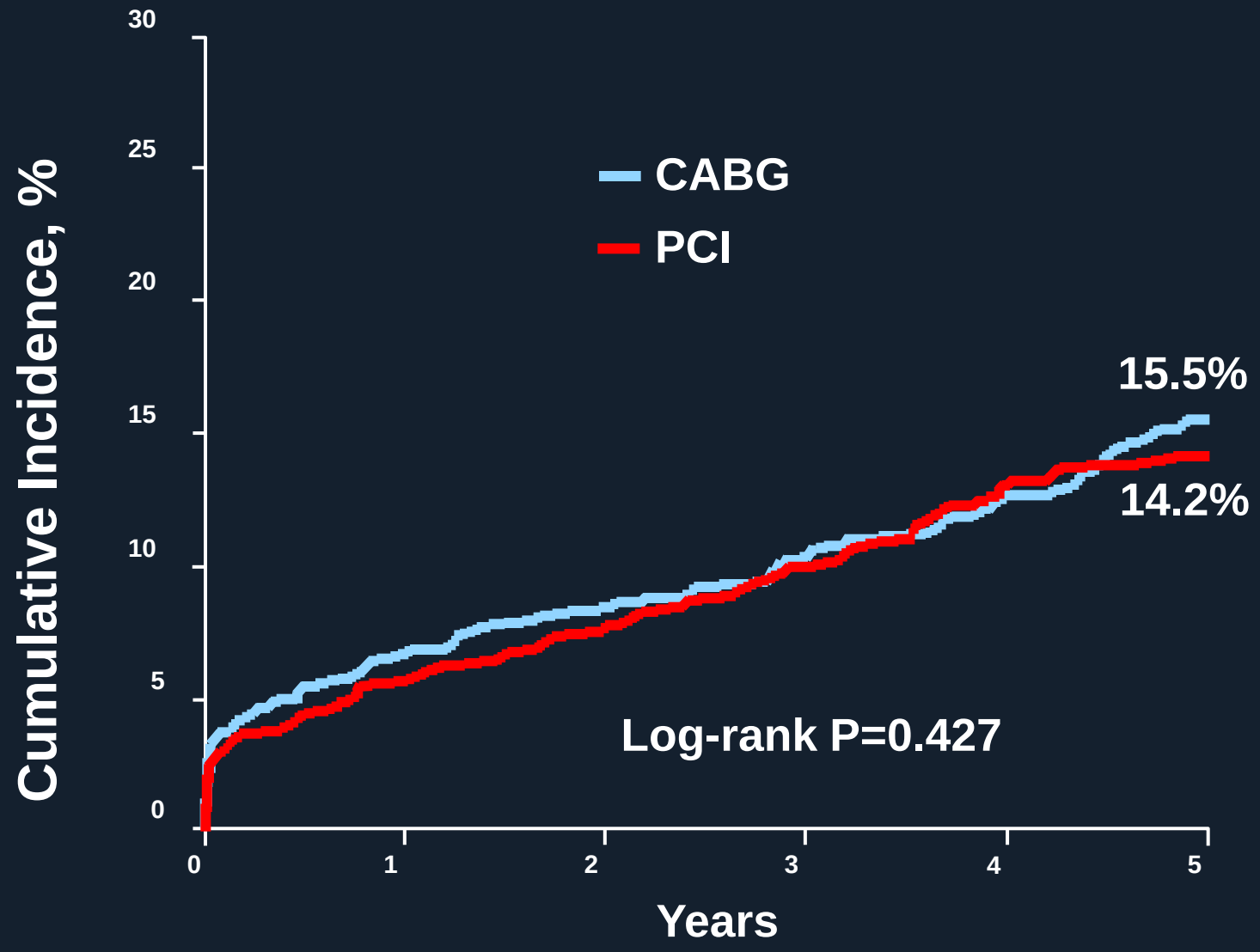
Patient-Level Meta-Analysis (n=3,280)

Database Pooling of
SYNTAX (n=1800, PES),
BEST (n=880, EES), and
PRECOMBAT (n=600, SES) trials.

Lee CW, Park SJ et al, Meta-Analysis from SYNTAX, BEST and PRECOMBAT, 2016

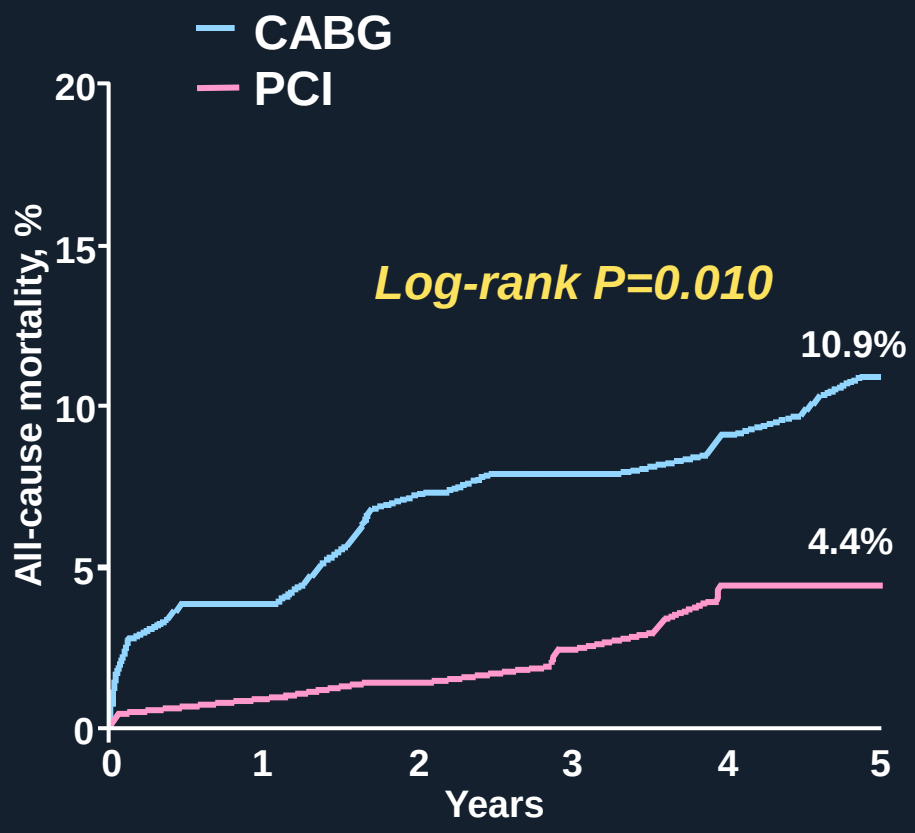
Patient-Level Meta-Analysis (n=3.280)

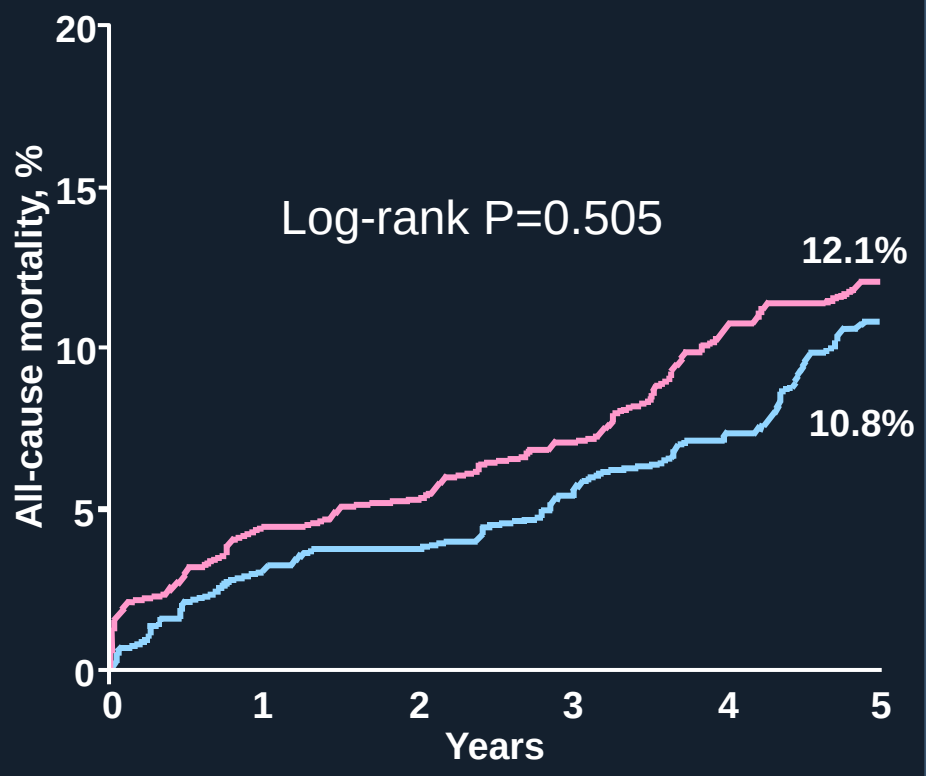
LM Subset / **Death, MI or Stroke**



Patient-Level Meta-Analysis (n=1,293)

LM Subset / All-cause Mortality





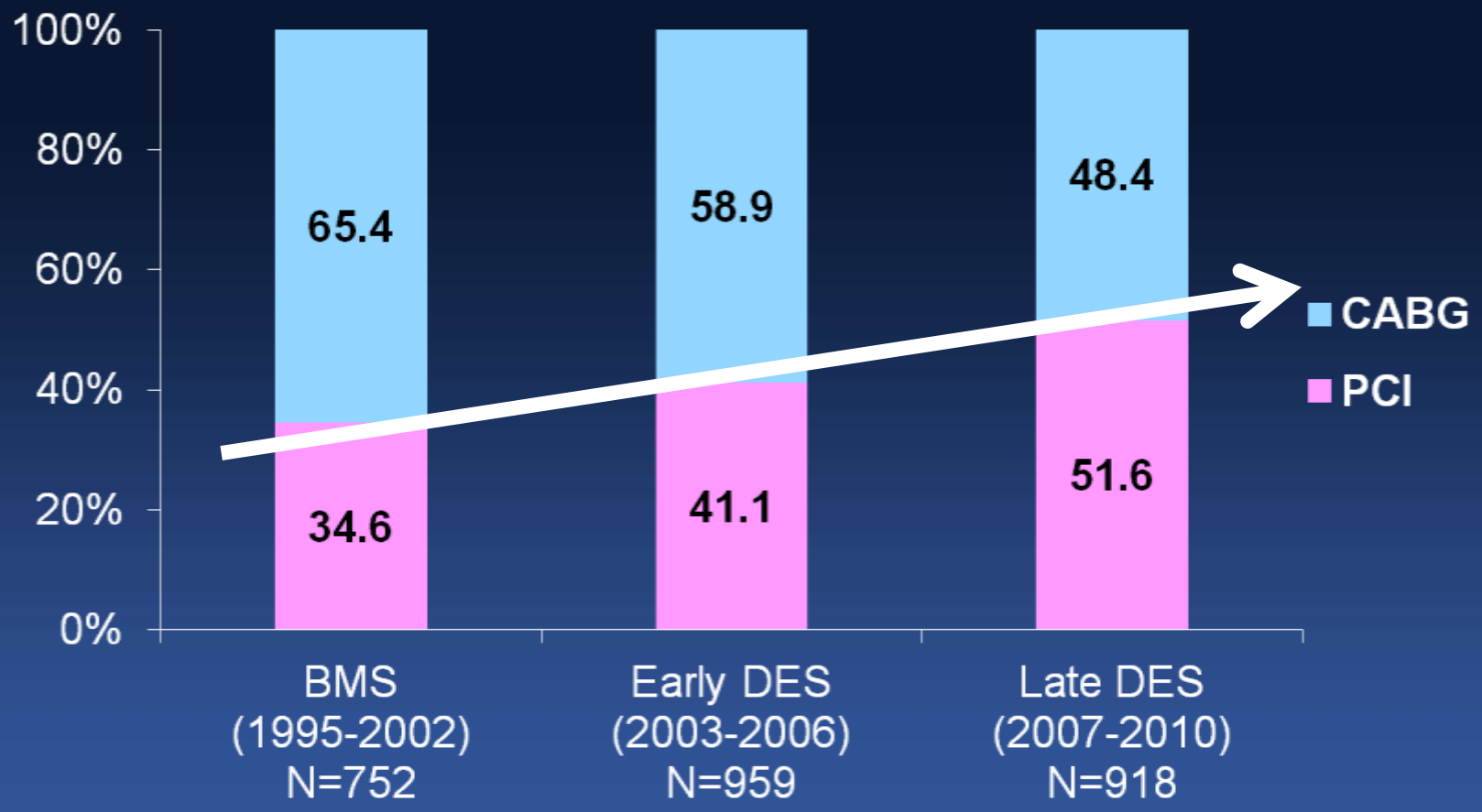
Lee CW, Park SJ et al, Meta-Analysis from SYNTAX, BEST and PRECOMBAT, 2016

20 Years of Temporal Changes In PCI vs. CABG For LM Disease

Data from ASAN and IRIS MAIN Registry

Temporal Trends of LM Revascularization,

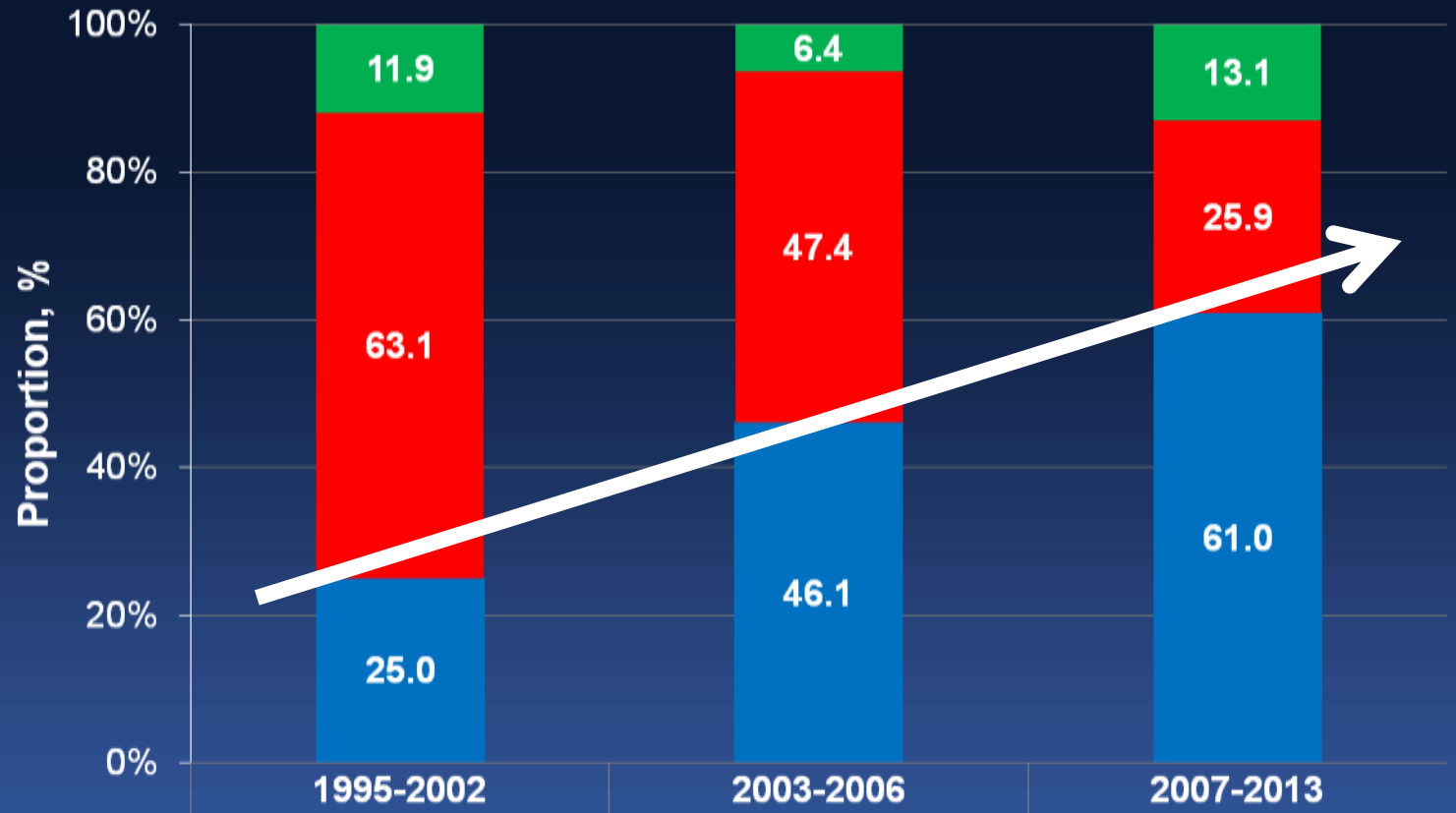
(AMC LM Registry n=2,360), 2015



Park SJ, Ahn JM et al, Circ Cardiovasc Interv. 2015;8:e001846.

Temporal Trends of LM Revascularization,

(IRIS LM Registry n=5,883), 2016



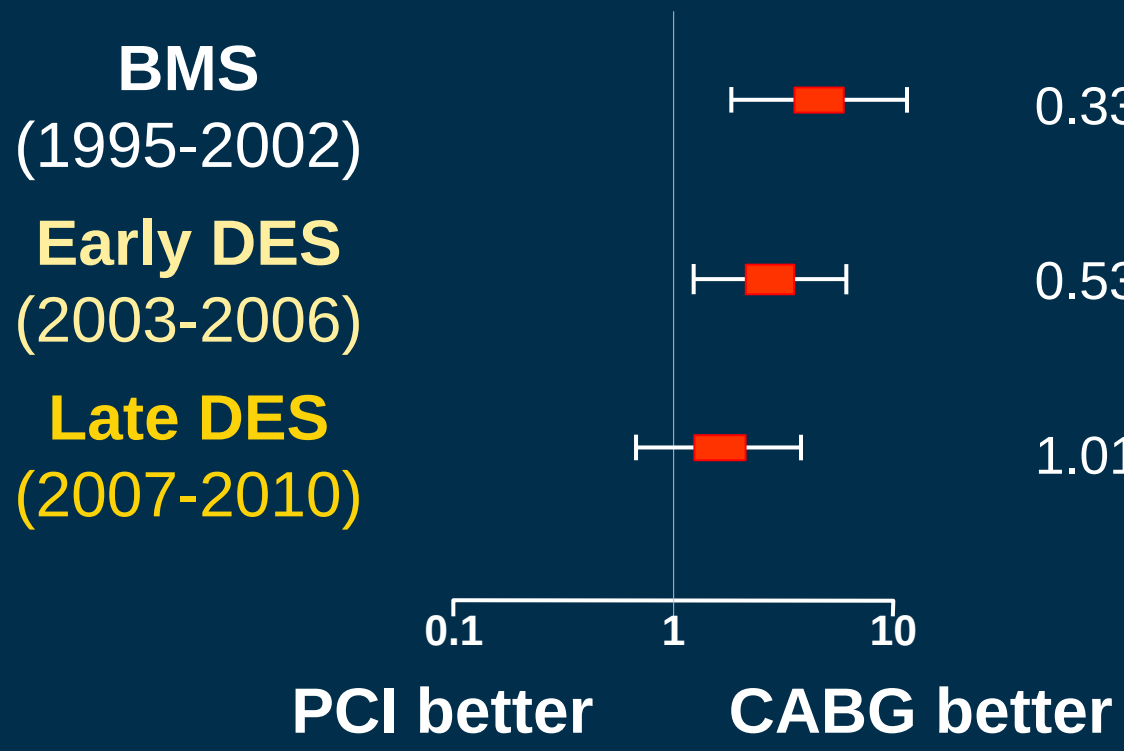
	1995-2002	2003-2006	2007-2013
Medical Tx	129	131	356
CABG	683	964	704
PCI	271	937	1658

PH Lee et al, JACC. 2016 Sep 13;68(11):1233-46.

MACCE

(AMC LM Registry n=2,360)

P for Interaction = 0.002



	HR (95% CI)	P value
BMS (1995-2002)	0.33 (0.23-0.47)	<0.001
Early DES (2003-2006)	0.53 (0.35-0.80)	0.005
Late DES (2007-2010)	1.01 (0.68-1.49)	0.32

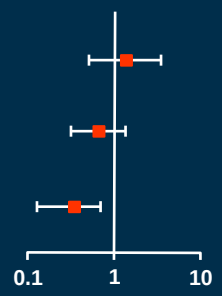
Park SJ, Ahn JM et al, Circ Cardiovasc Interv. 2015;8:e001846.

MACCE

(AMC LM Registry n=2,360)

Death

P for Interaction = 0.011



	HR (95% CI)
BMS	1.36 (0.52-3.52)
Early DES	0.66 (0.32-1.37)
Late DES	0.31 (0.13-0.71)

PCI better | CABG better

Death, MI or Stroke

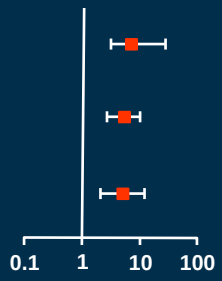
P for Interaction = 0.017

	HR (95% CI)	P value
BMS	1.49 (0.67-3.31)	0.33
Early DES	0.80 (0.43-1.50)	0.49
Late DES	0.44 (0.23-0.85)	0.015

PCI better | CABG better

Repeat Revascularization

P for Interaction = 0.20



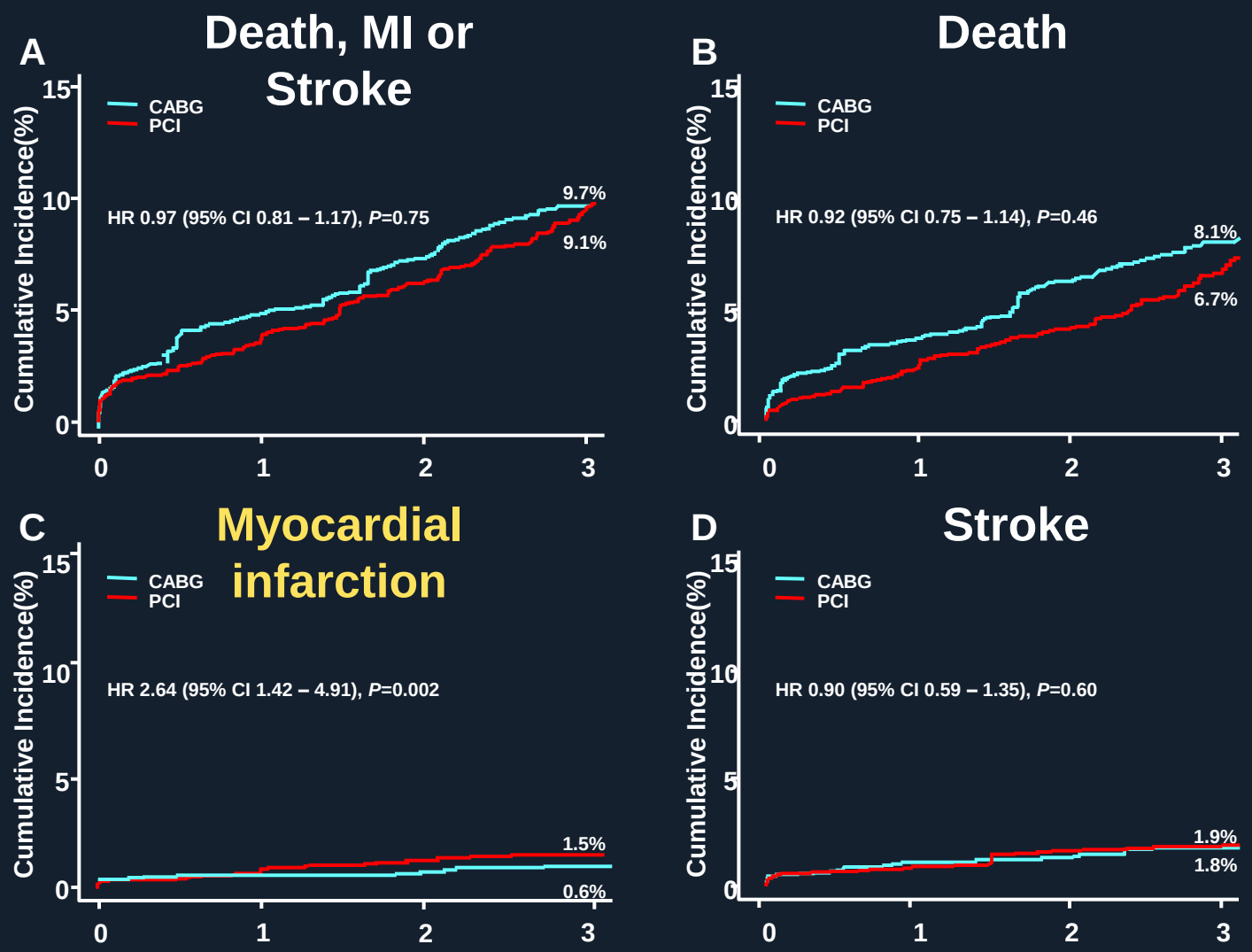
	HR (95% CI)	P value
BMS	6.88 (3.21-14.7)	<0.001
Early DES	5.26 (2.73-10.1)	<0.001
Late DES	5.07 (2.12-12.1)	<0.001

PCI better | CABG better

Park SJ, Ahn JM et al, Circ Cardiovasc Interv. 2015;8:e001846.

Clinical Outcomes at 3 year

(IRIS LM Registry n=5,883)



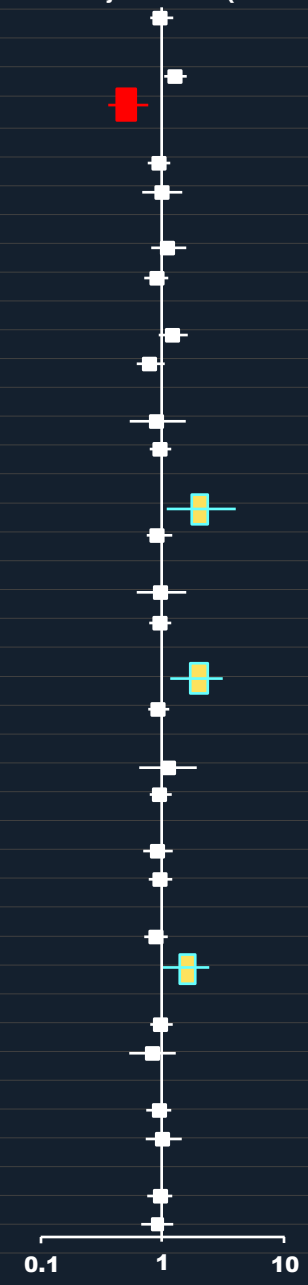
PH Lee et al, JACC. 2016 Sep 13;68(11):1233-46.

Subgroup Analysis

(IRIS LM Registry n=5,883)

PCI better **CABG better**

Subgroup	Adjusted HR (95% CI)	P value	P for interaction
Overall	0.97 (0.81-1.17)	0.75	
			<0.001
Age	1.30 (1.04-1.62)	0.02	
< 65 yr	0.53 (0.37-0.76)	<0.001	
Sex			0.55
Male	0.96 (0.77-1.18)	0.67	
Female	1.02 (0.69-1.50)	0.94	
Body mass index			0.45
≥ 24.6 kg/m2	1.13 (0.82-1.56)	0.45	
< 24.6 kg/m2	0.90 (0.72-1.13)	0.38	
Diabetes			0.03
Yes	1.22 (0.93-1.59)	0.16	
No	0.80 (0.61-1.03)	0.08	
H/O myocardial infarction			0.78
Yes	0.91 (0.53-1.54)	0.71	
No	0.97 (0.80-1.19)	0.79	
H/O heart failure			0.01
Yes	2.05 (1.05-4.02)	0.036	
No	0.93 (0.76-1.13)	0.45	
H/O stroke			0.91
Yes	0.98 (0.61-1.57)	0.93	
No	0.97 (0.79-1.18)	0.74	
Chronic kidney disease			0.003
Yes	1.92 (1.17-3.16)	0.01	
No	0.94 (0.76-1.15)	0.53	
Peripheral vascular disease			0.39
Yes	1.14 (0.66-1.94)	0.64	
No	0.96 (0.79-1.17)	0.67	
Clinical diagnosis			0.59
Stable angina	0.93 (0.69-1.25)	0.62	
NSTE ACS	0.97 (0.76-1.23)	0.79	
Ejection fraction			0.01
≥ 40%	0.91 (0.74-1.12)	0.37	
< 40%	1.55 (0.99-2.43)	0.05	
LMCAD with 2 or 3VD			0.52
Yes	0.99 (0.80-1.22)	0.91	
No	0.84 (0.55-1.30)	0.44	
Bifurcation involvement			0.62
Yes	0.96 (0.77-1.20)	0.70	
No	1.01 (0.72-1.42)	0.96	
RCA involvement			0.74
Yes	0.98 (0.78-1.22)	0.83	
No	0.93 (0.67-1.28)	0.64	

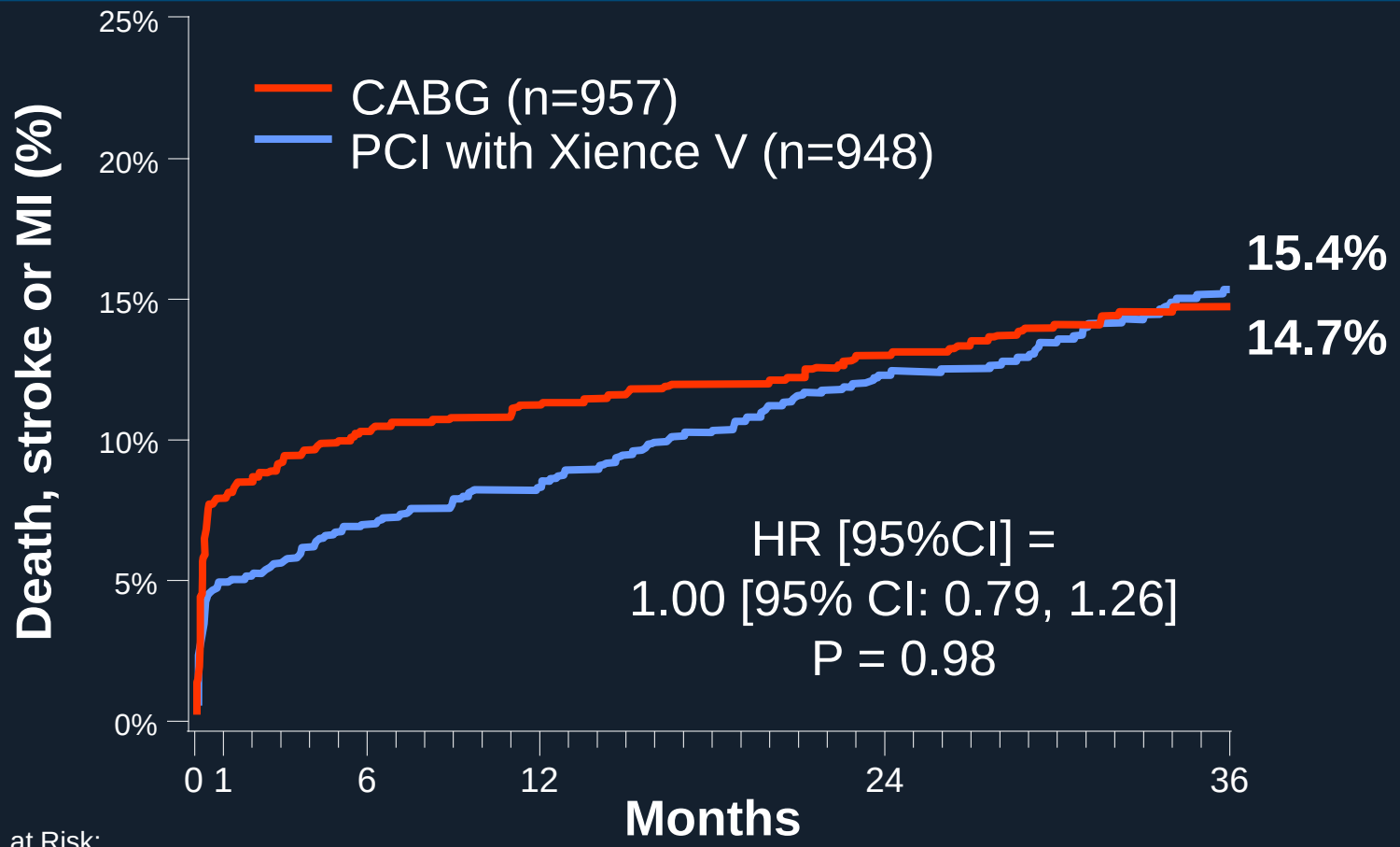


DES vs. CABG
for LM Disease 2017

1. Outcomes of PCI with DES is Comparable with CABG, ***Even Better Survival !***
2. CABG Is Still better In Patients with History of Hear failure, Chronic Kidney Disease and Low EF (<40%).

EXCEL

Primary Endpoint
Death, Stroke or MI at 3 Years



No. at Risk:

PCI	948	896	875	850	784	445
CABG	957	868	836	817	763	458

Adjudicated Outcomes at 30 Days

	PCI (n=948)	CABG (n=957)	HR [95%CI]	P-value
Death, stroke or MI	4.9%	7.9%	0.61 [0.42, 0.88]	0.008
- Death	1.0%	1.1%	0.90 [0.37, 2.22]	0.82
- Stroke	0.6%	1.3%	0.50 [0.19, 1.33]	0.15
- MI	3.9%	6.2%	0.63 [0.42, 0.95]	0.02
- Peri-procedural	3.6%	5.9%	0.61 [0.40, 0.93]	0.02
- Spontaneous	0.3%	0.3%	1.00 [0.20, 4.95]	1.00
- STEMI	0.7%	2.3%	0.32 [0.14, 0.74]	0.005
- Non-STEMI	3.2%	3.9%	0.82 [0.50, 1.32]	0.41
Death, stroke, MI or IDR	4.9%	8.4%	0.57 [0.40, 0.82]	0.002
- Ischemia-driven revasc (IDR)	0.6%	1.4%	0.46 [0.18, 1.21]	0.11
Stent thrombosis, def/prob	0.6%	0.0%	-	0.01
Graft occlusion, symptomatic	0.0%	1.2%	-	<0.001
Definite stent thrombosis or symptomatic graft occlusion	0.3%	1.2%	0.27 [0.08, 0.97]	0.03

Major Adverse Events Within 30 Days

	PCI (n=948)	CABG (n=957)	RR [95%CI]	P-value
Peri-procedural MAE, any	8.1%	23.0%	0.35 [0.28, 0.45]	<0.001
- Death*	0.9%	1.0%	0.91 [0.39, 2.23]	0.83
- Stroke*	0.6%	1.3%	0.50 [0.19, 1.34]	0.16
- Myocardial infarction*	3.9%	6.2%	0.63 [0.42, 0.95]	0.02
- Ischemia-driven revascularization*	0.6%	1.4%	0.47 [0.18, 1.22]	0.11
- TIMI major/minor bleeding	3.7%	8.9%	0.42 [0.28, 0.61]	<0.001
- Transfusion ≥2 units	4.0%	17.0%	0.24 [0.17, 0.33]	<0.001
- Major arrhythmia**	2.1%	16.1%	0.13 [0.08, 0.21]	<0.001
- Surgery/radiologic procedure	1.3%	4.1%	0.31 [0.16, 0.59]	<0.001
- Renal failure†	0.6%	2.5%	0.25 [0.10, 0.61]	<0.001
- Sternal wound dehiscence	0.0%	2.0%	0.03 [0.00, 0.43]	<0.001
- Infection requiring antibiotics	2.5%	13.6%	0.18 [0.12, 0.28]	<0.001
- Prolonged intubation (>48 hours)	0.4%	2.9%	0.14 [0.05, 0.41]	<0.001
- Post-pericardiotomy syndrome	0.0%	0.4%	0.11 [0.01, 2.08]	0.12

*Adjudicated events; others are site-reported. **SVT requiring cardioversion, VT or VF requiring treatment, or bradyarrhythmia requiring temporary or permanent pacemaker.
†Serum creatinine increased by ≥0.5 mg/dL from baseline or need for dialysis.

Adjudicated Outcomes at 3 Years (1)

	PCI (n=948)	CABG (n=957)	HR [95%CI]	P-value
Death, stroke or MI (1˚ endpoint)	15.4%	14.7%	1.00 [0.79, 1.26]	0.98
- Death	8.2%	5.9%	1.34 [0.94, 1.91]	0.11
- Definite cardiovascular	3.7%	3.4%	1.10 [0.67, 1.80]	0.71
- Definite non-cardiovascular	3.9%	2.3%	1.60 [0.91, 2.80]	0.10
- Undetermined cause	0.8%	0.3%	2.00 [0.50, 7.98]	0.32
- Stroke	2.3%	2.9%	0.77 [0.43, 1.37]	0.37
- MI	8.0%	8.3%	0.93 [0.67, 1.28]	0.64
- Peri-procedural	3.8%	6.0%	0.63 [0.42, 0.96]	0.03
- Spontaneous	4.3%	2.7%	1.60 [0.95, 2.70]	0.07
- STEMI	1.3%	2.8%	0.46 [0.23, 0.91]	0.02
- Non-STEMI	7.0%	5.9%	1.15 [0.80, 1.65]	0.46

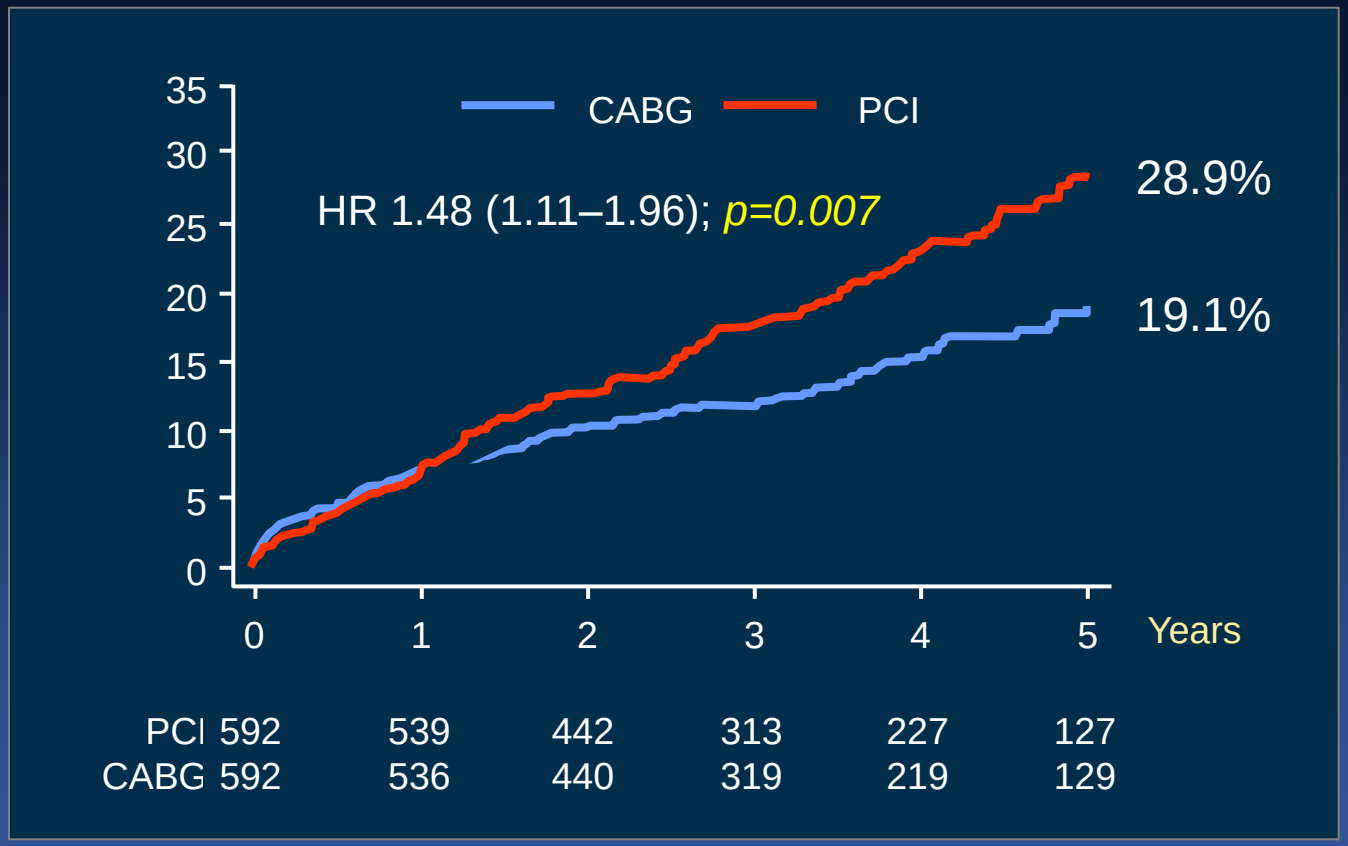
Adjudicated Outcomes at 3 Years (2)

	PCI (n=948)	CABG (n=957)	HR [95%CI]	P-value
Death, stroke, MI or IDR	23.1%	19.1%	1.18 [0.97, 1.45]	0.10
- Ischemia-driven revasc (IDR)	12.6%	7.5%	1.72 [1.27, 2.33]	<0.001
- PCI	10.3%	6.8%	1.57 [1.13, 2.18]	0.006
- CABG	3.5%	0.8%	4.29 [1.88, 9.77]	<0.001
All revascularization	12.9%	7.6%	1.72 [1.27, 2.33]	<0.001
Stent thrombosis, def/prob	1.3%	0.0%	-	<0.001
- Definite	0.7%	0.0%	-	0.01
- Probable	0.7%	0.0%	-	0.01
- Early (0 - 30 days)	0.7%	0.0%	-	0.008
- Late (30 days – 1 year)	0.1%	0.0%	-	0.32
- Very late (1 year - 3 years)	0.5%	0.0%	-	0.05
Graft occlusion, symptomatic	0.0%	5.4%	-	<0.001
Definite stent thrombosis or symptomatic graft occlusion	0.7%	5.4%	0.12 [0.05, 0.28]	<0.001

NOBLE

Primary Endpoint

Death, non-procedural MI, repeat Revascularization and Stroke at 3 Years



Makikallio T et al. Lancet 2016;388:2743–52

5-Year Outcomes

	PCI (n=592)	CABG (n=592)	Hazard Ratio (95% CI)	*p* Value
MACCE	29% (121)	19% (81)	1.48 (1.11-1.96)	0.007
All-cause mortality	12% (36)	9% (33)	1.07 (0.67-1.72)	0.77
- Cardiac death	3% (14)	3% (15)	0.93 (0.45-1.92)	0.84
- Vascular death	1% (2)	<1 (1)	1.96 (0.18-21.66)	0.55
Non-procedural-related MI	7% (29)	2% (10)	2.88 (1.40-5.90)	0.004
Revascularization (total)	16% (71)	10% (47)	1.50 (1.04-2.17)	0.03
- Revasc with PCI	13% (56)	10% (45)	1.23 (0.83-1.83)	0.29
- Revasc with CABG	4% (19)	<1 (2)	9.40 (2.19-40.38)	0.003
- Target lesion revasc	12% (50)	8% (36)	1.38 (0.90-2.12)	0.14
- Target LMCA revasc	10% (41)	9% (33)	1.23 (0.78-1.94)	0.37
- De-novo lesion revasc	6% (24)	3% (11)	2.34 (1.16-4.74)	0.02
Symptomatic graft occlusion or definite stent thrombosis	3% (9)	4% (15)	0.59 (0.26-1.36)	0.22
Possible stent thrombosis	1% (4)	0	–	–
Probable stent thrombosis	<1% (2)	0	–	–
Stroke	5% (16)	2% (7)	2.25 (0.93-5-48)	0.07

EXCEL vs NOBLE

	EXCEL	NOBLE
Number of patients	1905	1201
Number of centers	126	36
Number of countries	17 (US, EU, SA, Asia Pacific, Middle East)	7 (UK, Scandinavia)
SYNTAX score inclusion	≤32	No restriction
Primary endpoint	D, MI or stroke	D, MI, stroke or revasc
- Included peri-procedural MI	Yes	No
Stent	Xience	Biomatrix
- 3-year definite ST rate	0.7%	3%
- Def ST < symptomatic graft occlusion	Yes	No
Stroke: PCI vs CABG	Less with PCI	More with PCI!
Worse PCI prognosis with higher SYNTAX score	Yes	No!

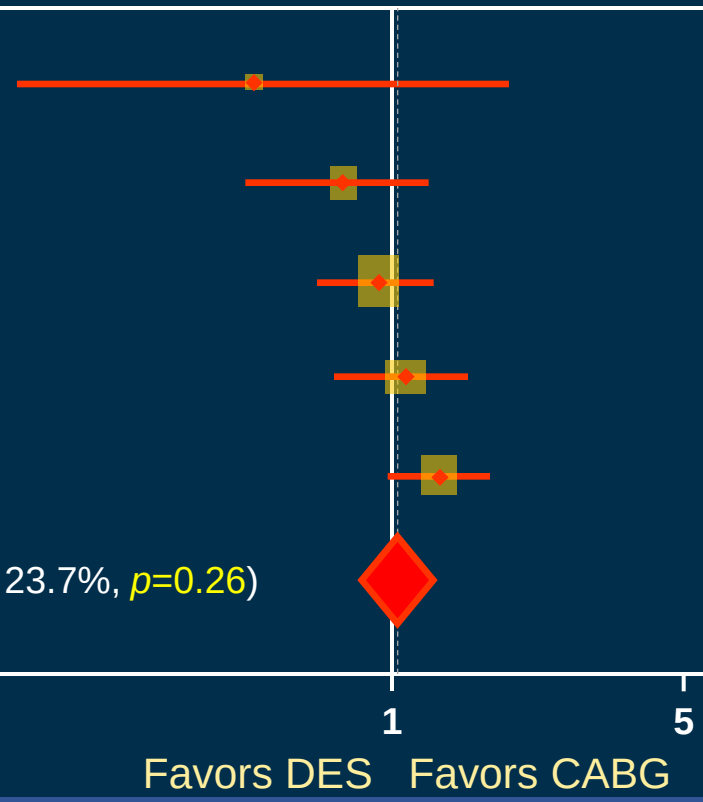
Updated Meta-analysis of LM DES Trials (5 RCTs, 4,594 pts)

EXCEL,
NOBLE,
SYNTAX,
PRECOMBAT,
Boudriot et al

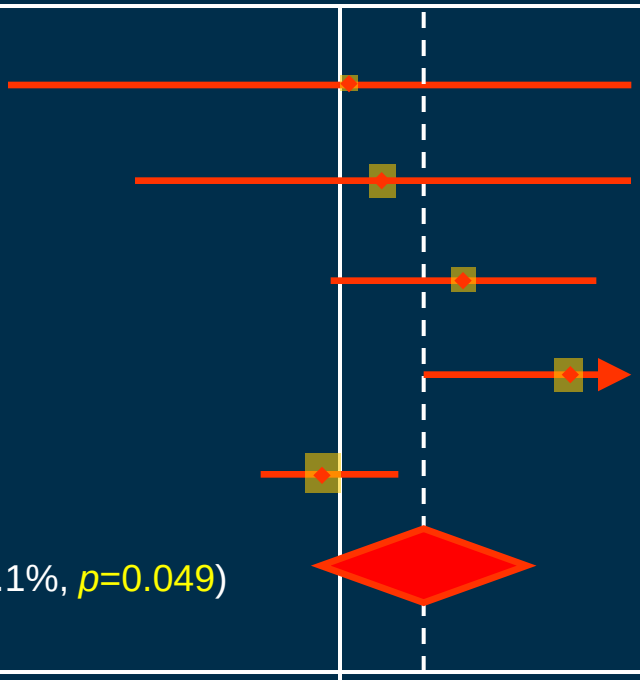
Nerlekar N et al. *Circ Int* 2017:on-line

Death

Trial	OR (95% CI)	Events, DES	Events, CABG	% Weight
Boudriot et al	0.39 (0.07, 2.07)	2/100	5/101	2.60
PRECOMBAT	0.72 (0.38, 1.38)	17/300	23/300	14.59
SYNTAX	0.90 (0.58, 1.39)	45/357	48/348	26.67
NOBLE	1.10 (0.67, 1.78)	36/592	33/592	22.85
EXCEL	1.38 (0.96, 1.99)	71/948	53/957	33.29
Overall (I-squared = 23.7%, *p*=0.26)	1.03 (0.78, 1.35)	171/2297	162/2298	100.00
	P=0.61	7.4%	7.0%	



Myocardial Infarction



Trial	OR (95% CI)	Events, DES	Events, CABG	% Weight
Boudriot et al	1.01 (0.20, 5.13)	3/100	3/101	7.97
PRECOMBAT	1.20 (0.36, 3.99)	6/300	5/300	12.50
SYNTAX	1.77 (0.94, 3.33)	28/357	16/348	24.43
NOBLE	3.00 (1.45, 6.21)	29/592	10/592	21.82
EXCEL	0.94 (0.67, 1.31)	72/948	77/957	33.28
Overall (I-squared = 58.1%, *p*=0.049)	1.46 (0.88, 2.45)	138/2297	111/2298	100.00
	P=0.08	6.0%	4.8%	

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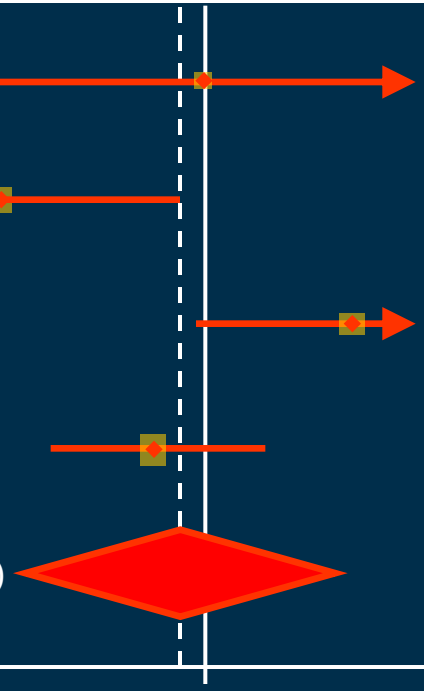
Favors DES Favors CABG

Nerlekar N et al. *Circ Int* 2017:on-line

Stroke



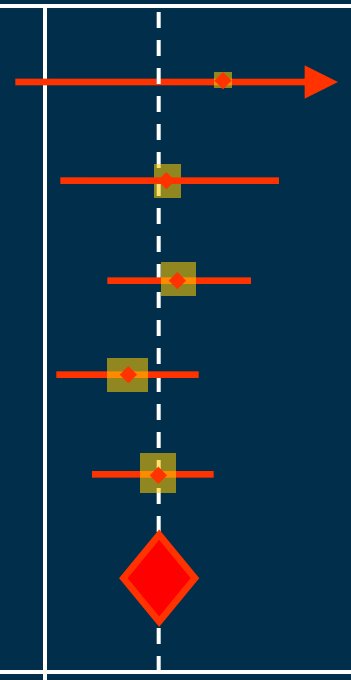
Trial	OR (95% CI)	Events, DES	Events, CABG	% Weight
PRECOMBAT	1.00 (0.14, 7.15)	2/300	2/300	12.06
SYNTAX	0.34 (0.12, 0.95)	5/357	14/348	25.14
NOBLE	2.32 (0.95, 5.68)	16/592	7/592	27.99
EXCEL	0.77 (0.43, 1.39)	20/948	26/957	34.81
Overall (I-squared = 62.5%, *p*=0.046)	0.88 (0.39, 1.97) *P=0.88*	43/2197 2.0%	49/2197 2.2%	100.00

1 5

Favors DES Favors CABG

Repeat Revascularization

Trial	OR (95% CI)	Events, DES	Events, CABG	% Weight
Boudriot et al	2.58 (0.95, 7.01)	14/100	6/101	3.62
PRECOMBAT	1.93 (1.10, 3.37)	38/300	21/300	11.59
SYNTAX	2.06 (1.40, 3.02)	90/357	49/348	24.43
NOBLE	1.58 (1.07, 2.33)	71/592	47/592	24.11
EXCEL	1.82 (1.32, 2.49)	114/948	67/957	36.24
Overall (I-squared = 0.0%, *p*=0.85)	1.85 (1.53, 2.23)	327/2297	67/2298	100.00
	P<0.001	14.2%	8.3%	



DES vs. CABG

- **Mortality :** Similar with PCI and CABG through 5 years
- **MI:** Lower with PCI in the peri-procedural period; higher with PCI during long-term FU, similar through 5 years
- **Stroke:** Still higher in CABG
- **Short-term morbidity:** Substantially less with PCI
- **Revascularization:** Less with CABG

Why, Outcomes of LM PCI *Is Getting Better ?*

1. *LM disease is Good Target for PCI.*
   Proximal and Large Vessel. Easy to Perform Procedure. Plenteous Operator's Experiences May Influence Good Clinical Outcomes with PCI.

2. *Better Concept of PCI ;*
   Integrated Use of FFR and IVUS Can Improve the Clinical Outcomes.

ESC Guidelines 2014
Elective PCI for LM Stenosis

	CABG		PCI	
Recommendation according to extent of CAD	Class	Level	Class	Level
LM disease a SYNTAX score ≤ 22	I	B	I	B
LM disease a SYNTAX score 23 -32	I	B	IIa	B
LM disease a SYNTAX score > 32	I	B	III	B

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*

Does SYNTAX Score (Angiographic Complexity) Really Matter in Current PCI ?

SYNTAX Score Showed
"Poor Discrimination Power"

Original Investigation | August 2014

Prognostic Value of *Site* SYNTAX Score and Rationale for Combining Anatomic and Clinical Factors in Decision Making

Insights From the SYNTAX Trial

Yao-Jun Zhang, PhD*; Javaid Iqbal, MRCP, PhD*; Carlos M. Campos, MD*; David V. Klaveren, MSc‡; Christos V. Bourantas, MD*; Keith D. Dawkins, MD§; Adrian P. Banning, MD‖; Javier Escaned, MD, PhD¶; Ton de Vries, MSc#; Marie-Angèle Morel, BSc#; Vasim Farooq, MD*; Yoshinobu Onuma, MD*; Hector M. Garcia-Garcia, MD, PhD*; Gregg W. Stone, MD**; Ewout W. Steyerberg, PhD‡; Friedrich W. Mohr, MD††; Patrick W. Serruys, MD, PhD*

Conclusions Appropriate training and unbiased assessment are needed when using SS in clinical decision making. sSS and tertiles based on sSS showed poor discrimination among low, intermediate, and high-risk groups. However, combining clinical factors with sSS retained the predictive performance of SS II. (SYNTAX Study: TAXUS Drug-Eluting Stent Versus Coronary Artery Bypass Surgery for the Treatment of Narrowed Arteries; NCT00114972)

Zhang YJ, Patrick SW et al. JACC 2014;64(5):423-432

AMC Practical Guidelines, 2017
Elective PCI for Left Main Disease

LM Disease is
Not Surgical Disease Anymore !