Left Main Disease Is Not Surgical Disease Anymore; Data Supported 2015

Seung-Jung Park, MD, PhD

Professor of Medicine, Asan Medical Center,
Heart Institute, University of Ulsan College of Medicine

Survival Benefit of CABG Over Medications in Stable Disease

1. Left Main Disease,
2. 3 Vessel Disease
   with Mild LV dysfunction

Old Story, But Conventional Bible !

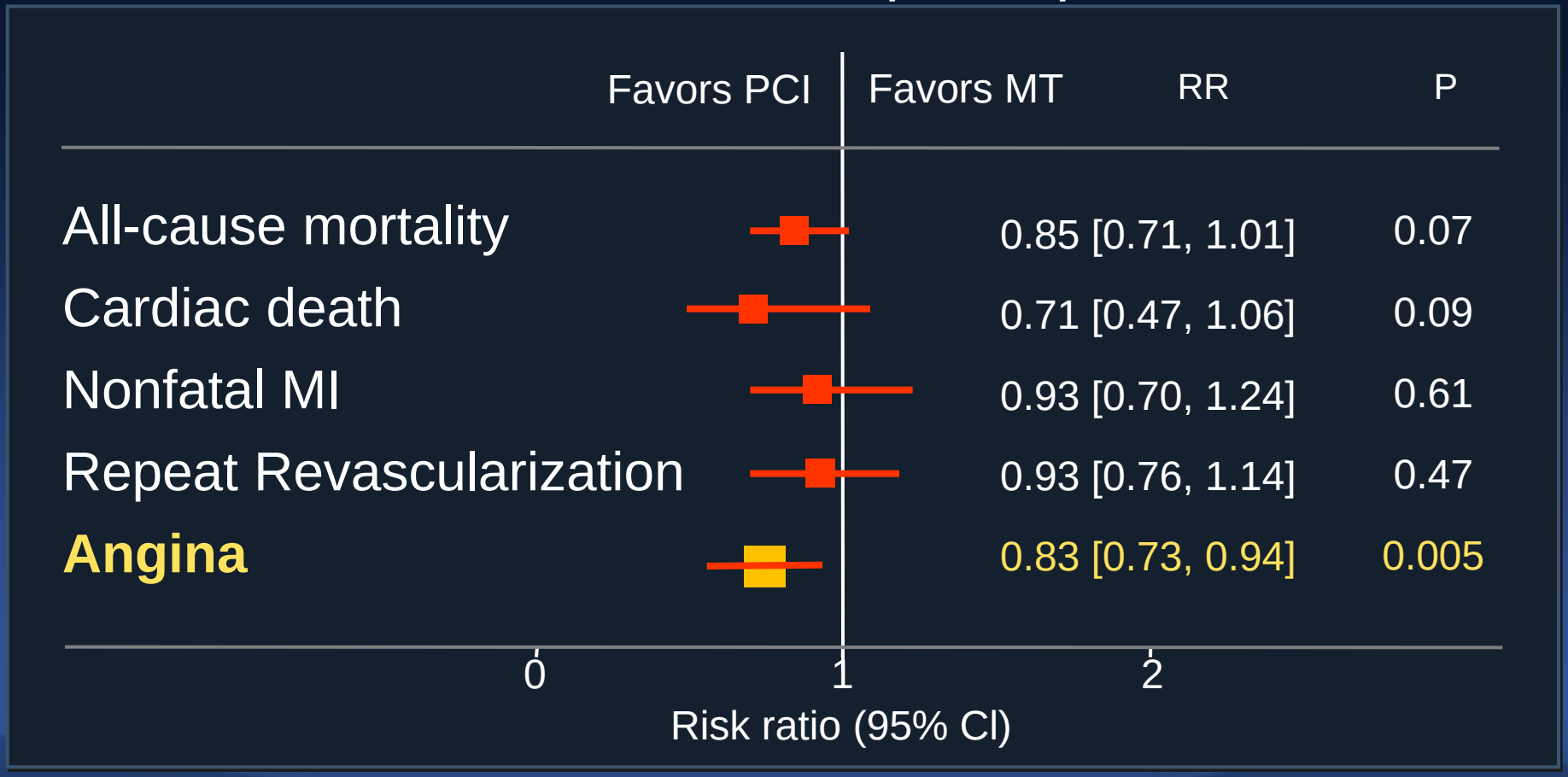
Caracciolo E A et al. Circulation 1995;91:2325-2334
CASS Investigators, Circulation 1983;68:939-950

CardioVascular Research Foundation
UNIVERSITY OF ULSAN COLLEGE MEDICINE
ASAN Medical Center

Survival Benefit of PCI ?

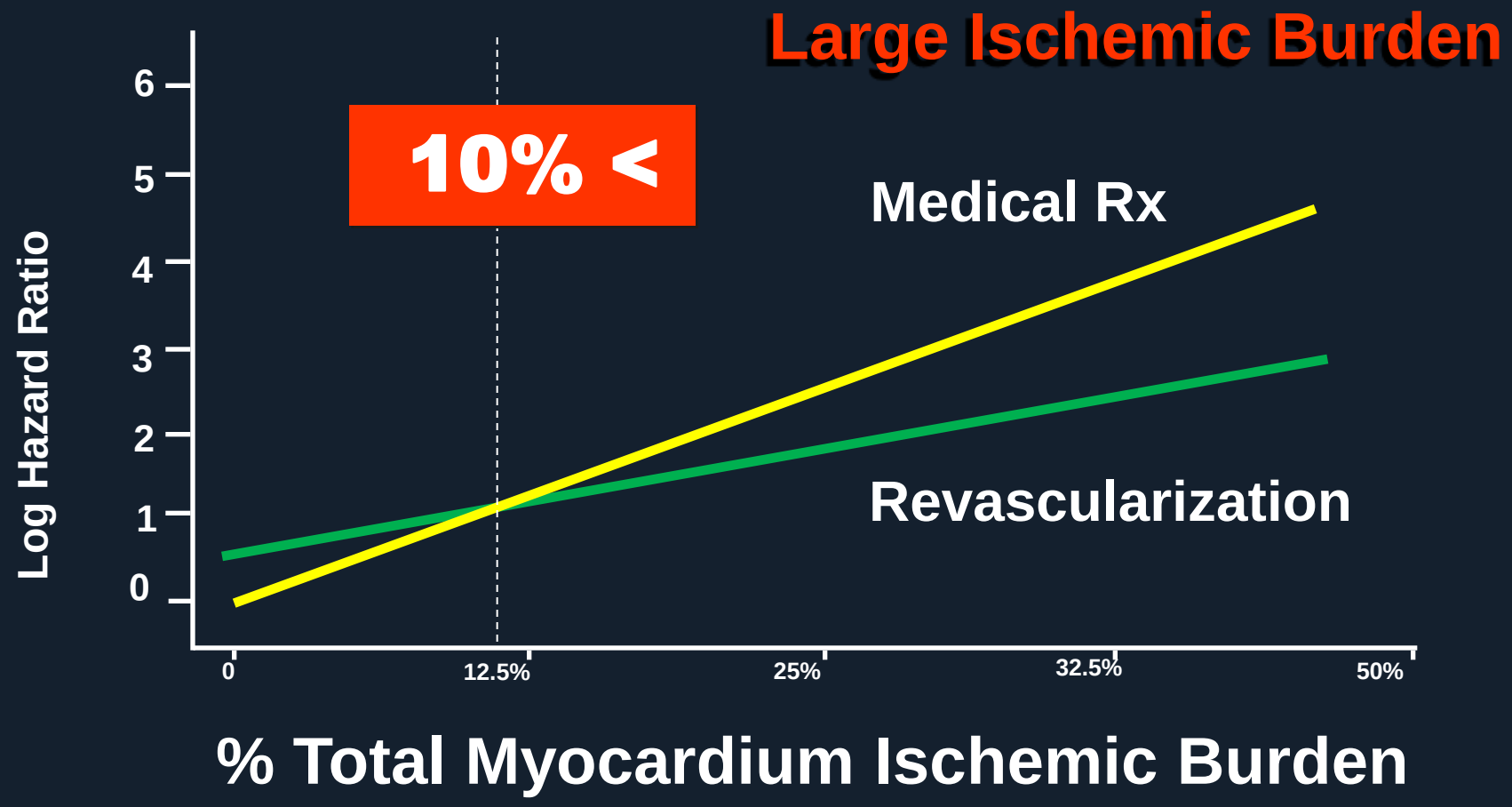
Benefit of PCI
Over Medications in Stable Disease

12 RCTs, 7182 participants



Pursnani et al, Circ CV Intv 2012

Survival Benefit of CABG or PCI Over Medications in Stable Disease

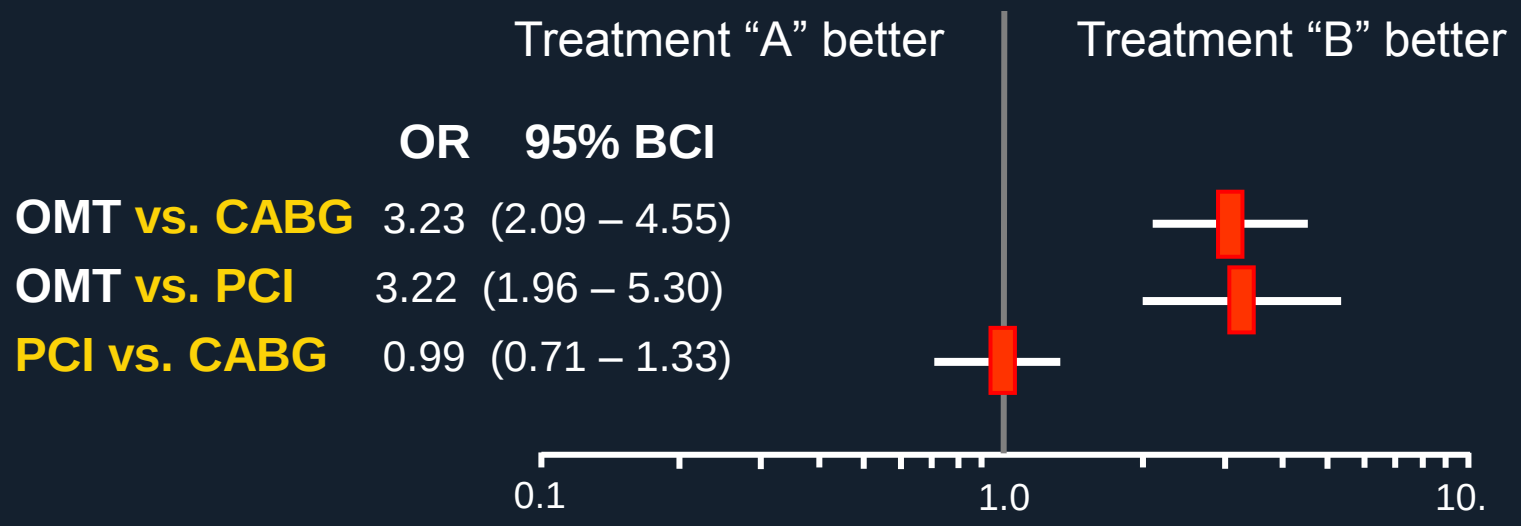


Circulation. 2003;107:2900-2906

Survival Benefit of CABG or PCI Over Medications in Stable Disease

Bayesian Net-work Meta-analysis

1-Year Mortality



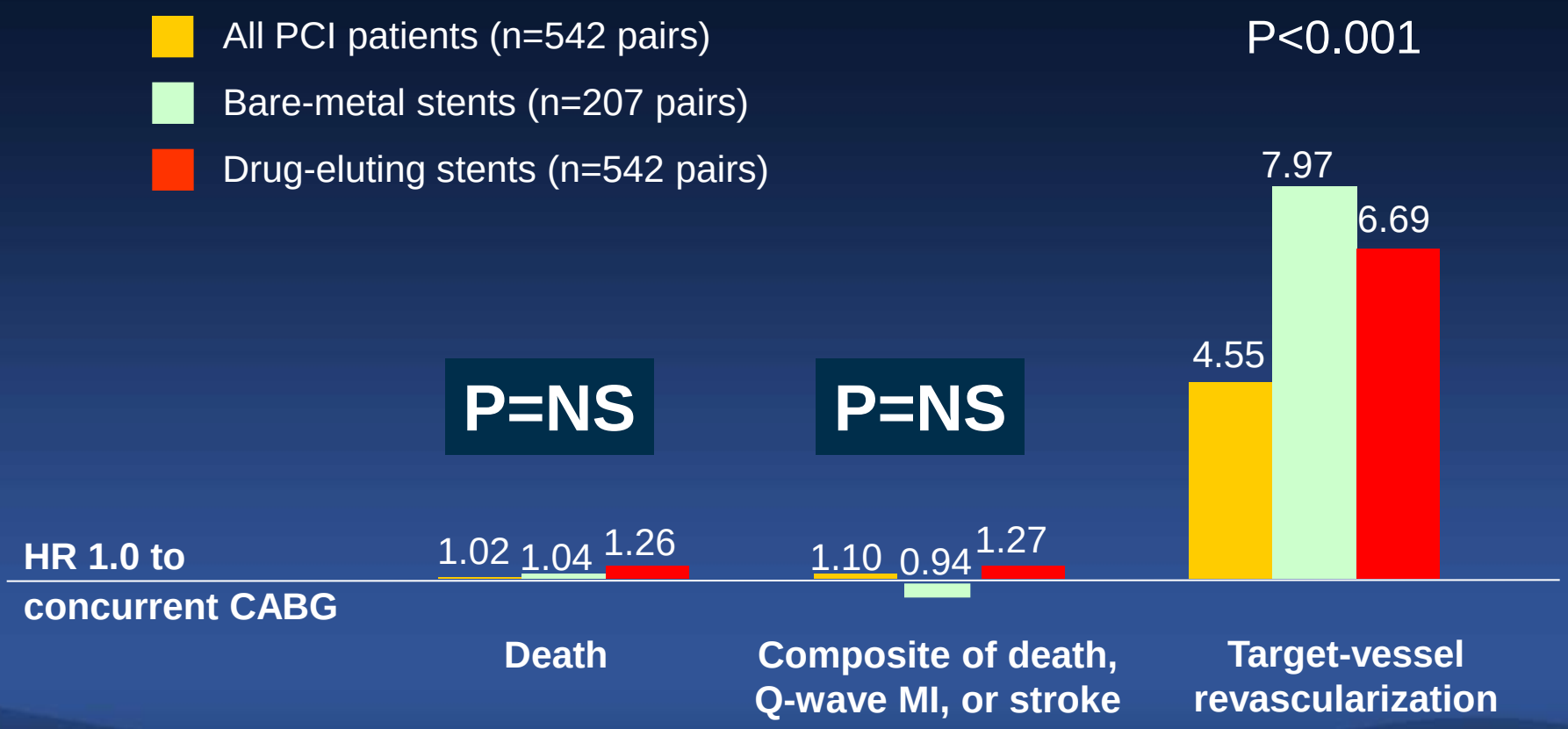
Bittl JA et al. Circulation. 2013;127:2177

PCI vs. CABG

DES vs. CABG
for LM Disease

1. MAIN COMPARE Registry
2. SYNTAX, LM subgroup
3. PRECOMBAT
4. Meta-Analysis of RCTs and Registry
5. Temporal Changes of LM Revascularization

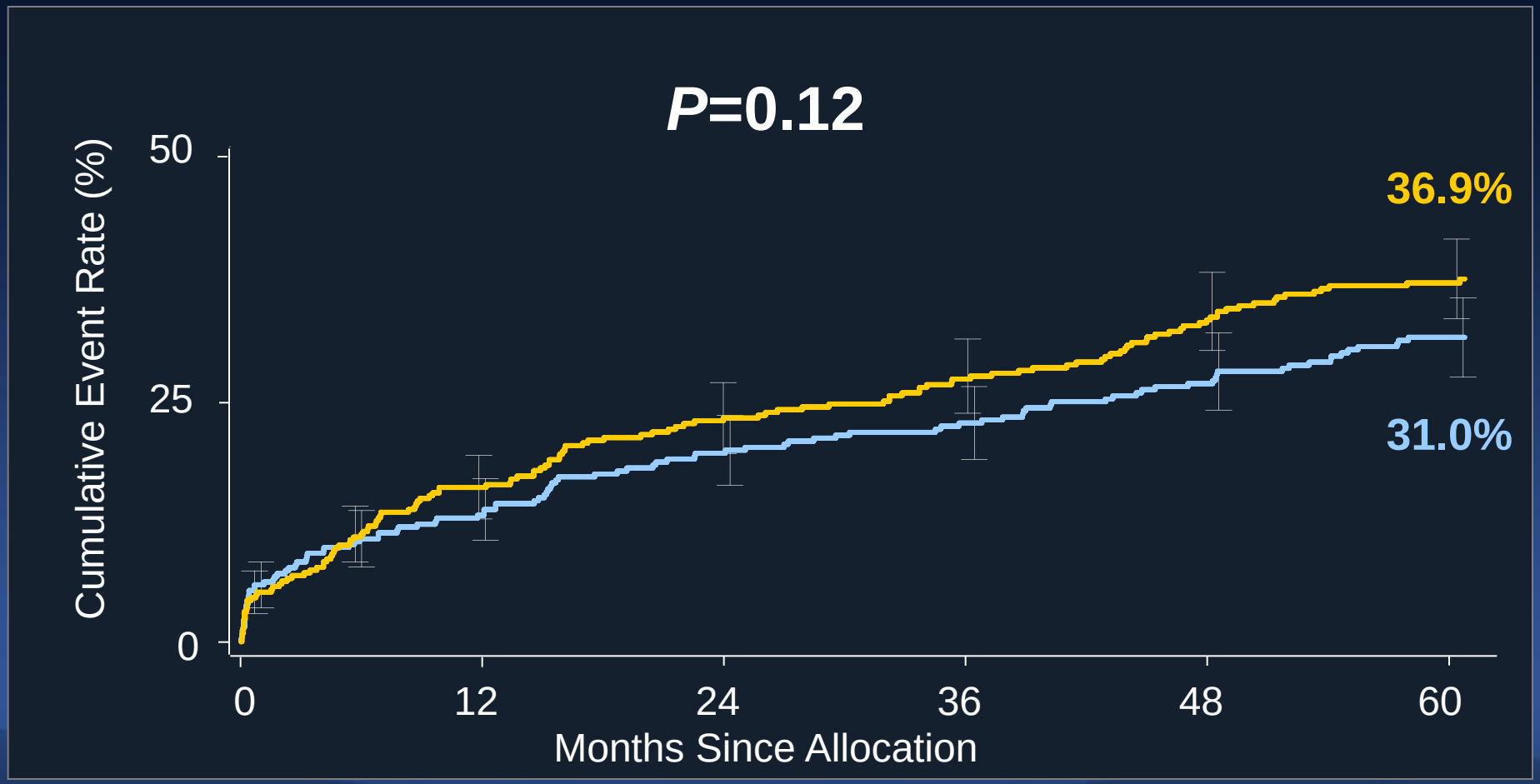
MAIN COMPARE, 5 Year
Death /MI /Stroke



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

CardioVascular Research Foundation
UNIVERSITY OF ULSAN COLLEGE MEDICINE
ASAN Medical Center

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



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

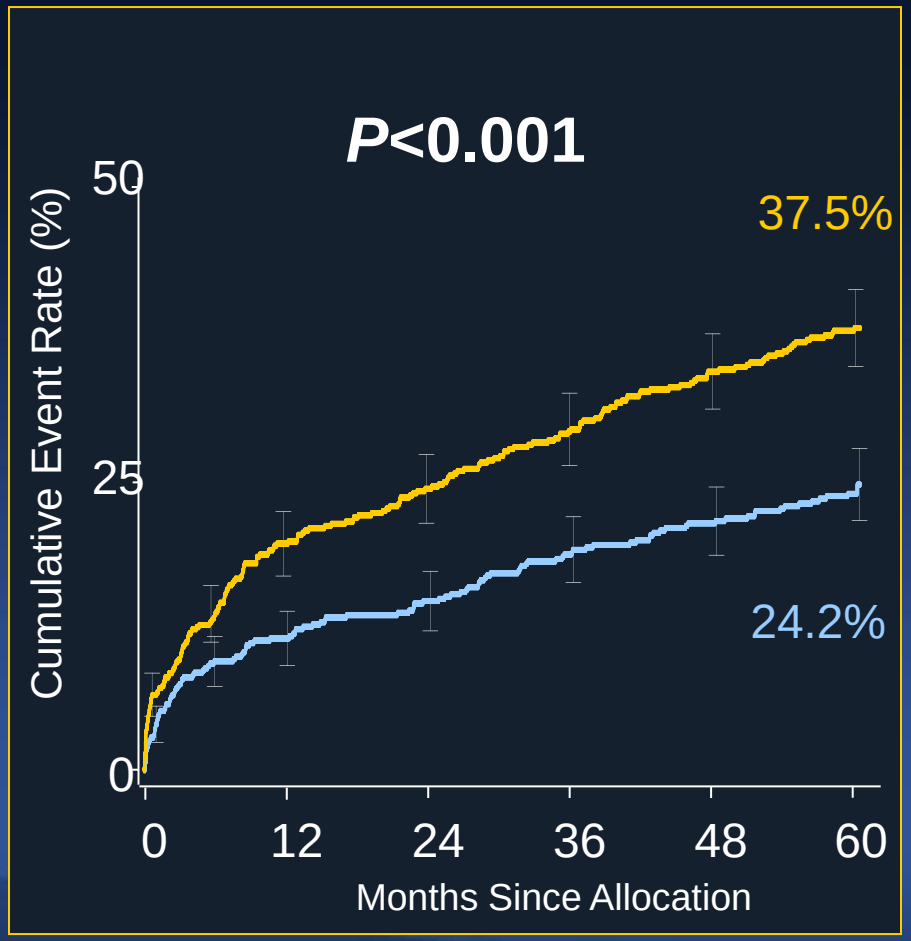
ITT population

CardioVascular Research Foundation
UNIVERSITY OF ULSAN COLLEGE MEDICINE
Medical Center

MACCE to 5 Years, *SYNTAX*

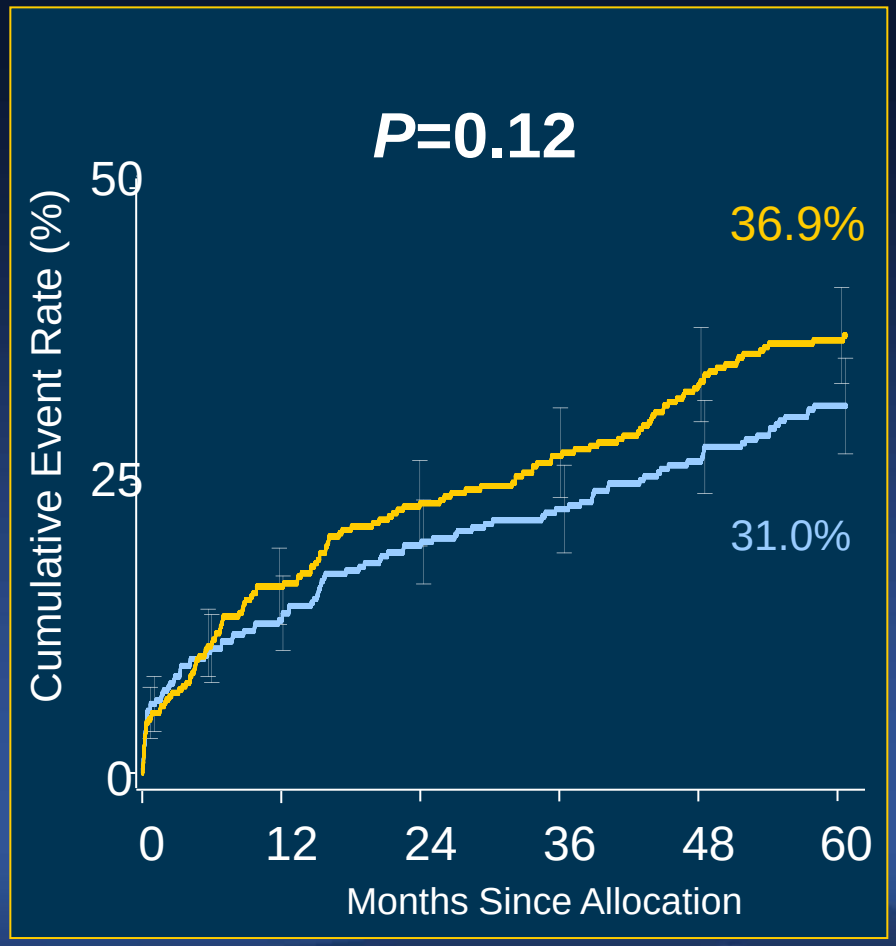
3VD Subset

CABG (N=549) TAXUS (N=546)

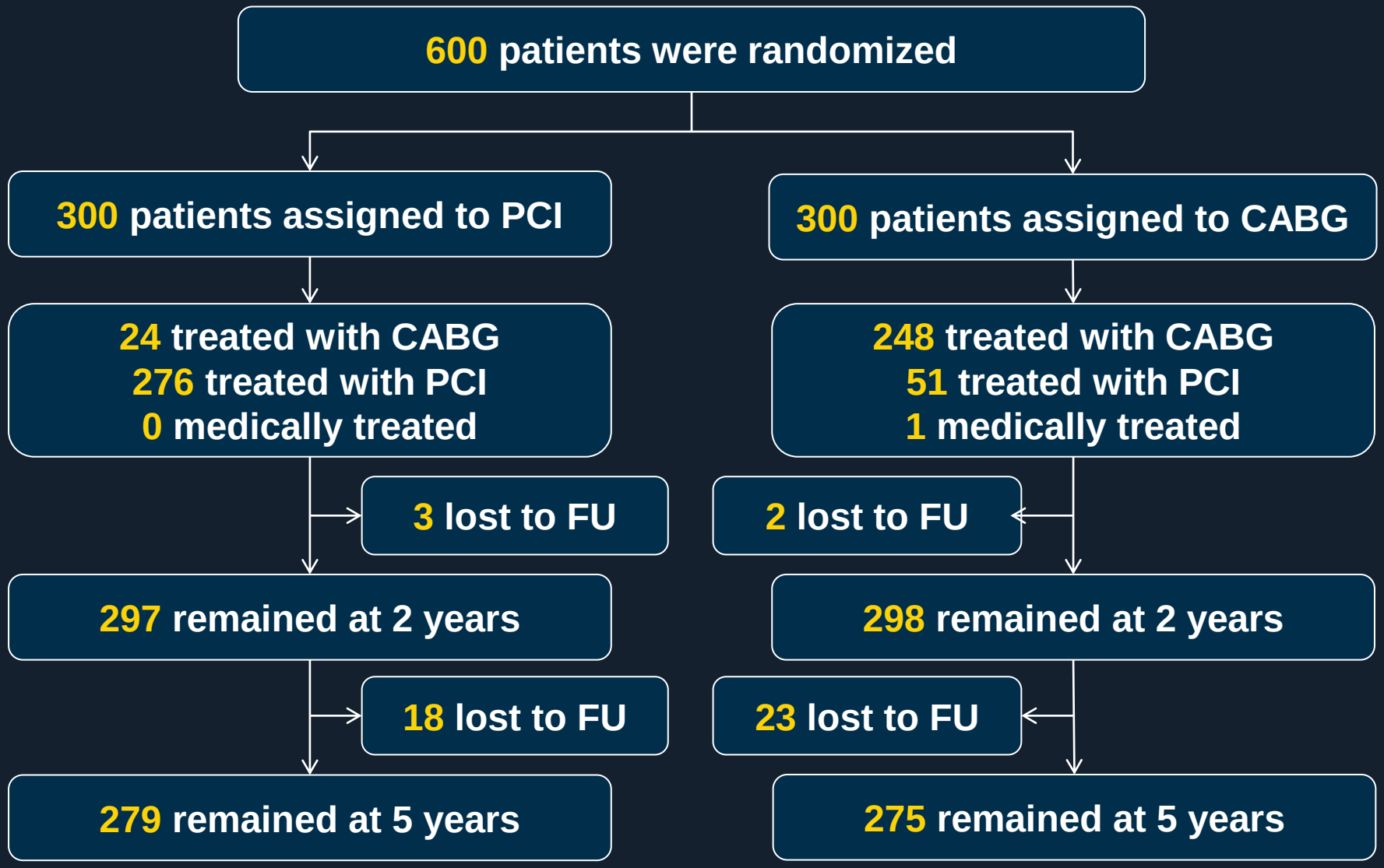


LM Subset

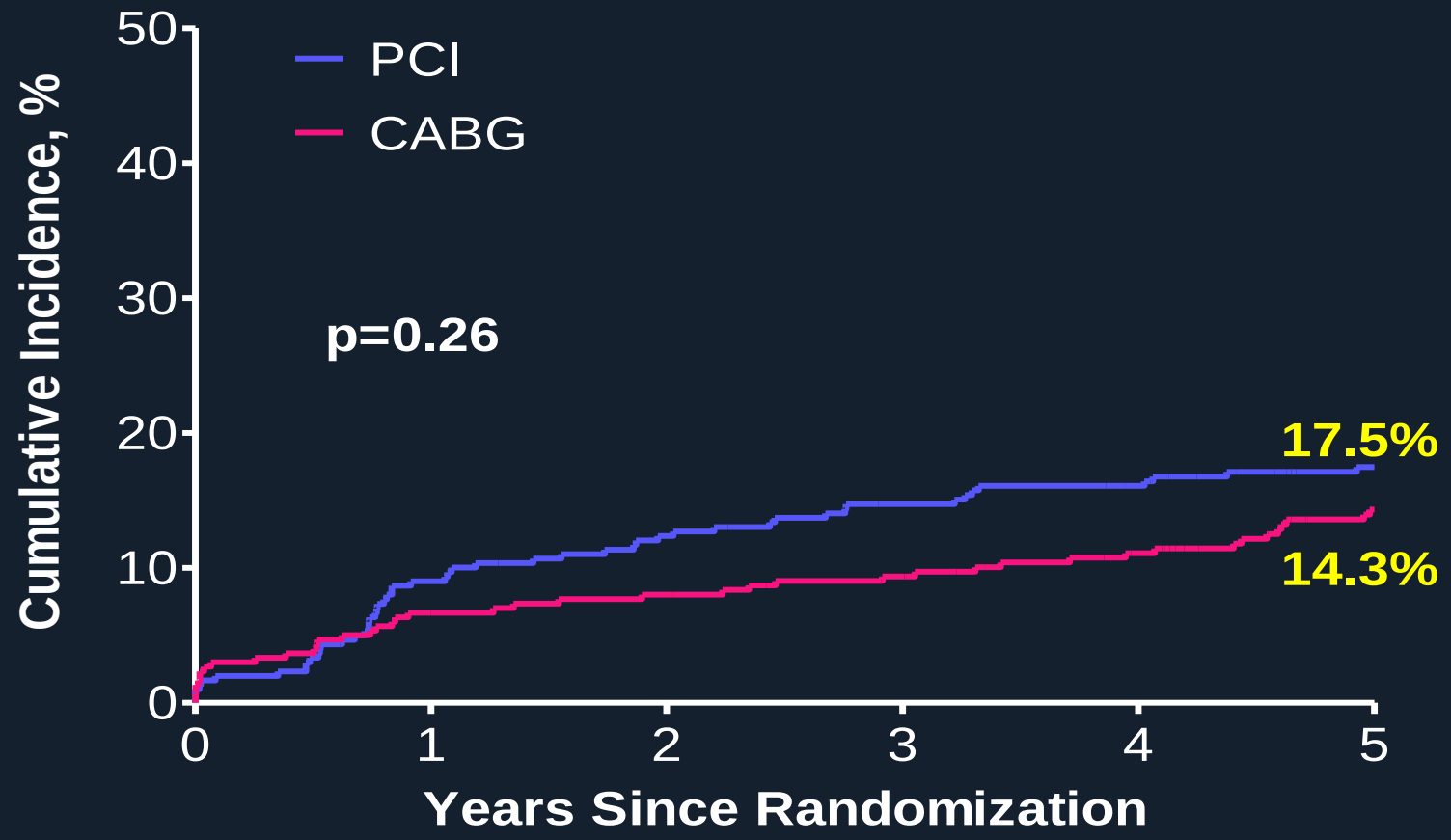
CABG (N=348) TAXUS (N=357)



PRECOMBAT, 5 year



PRECOMBAT, 5 Year
Death. MI, Stoke or iTVR



Patient at risk

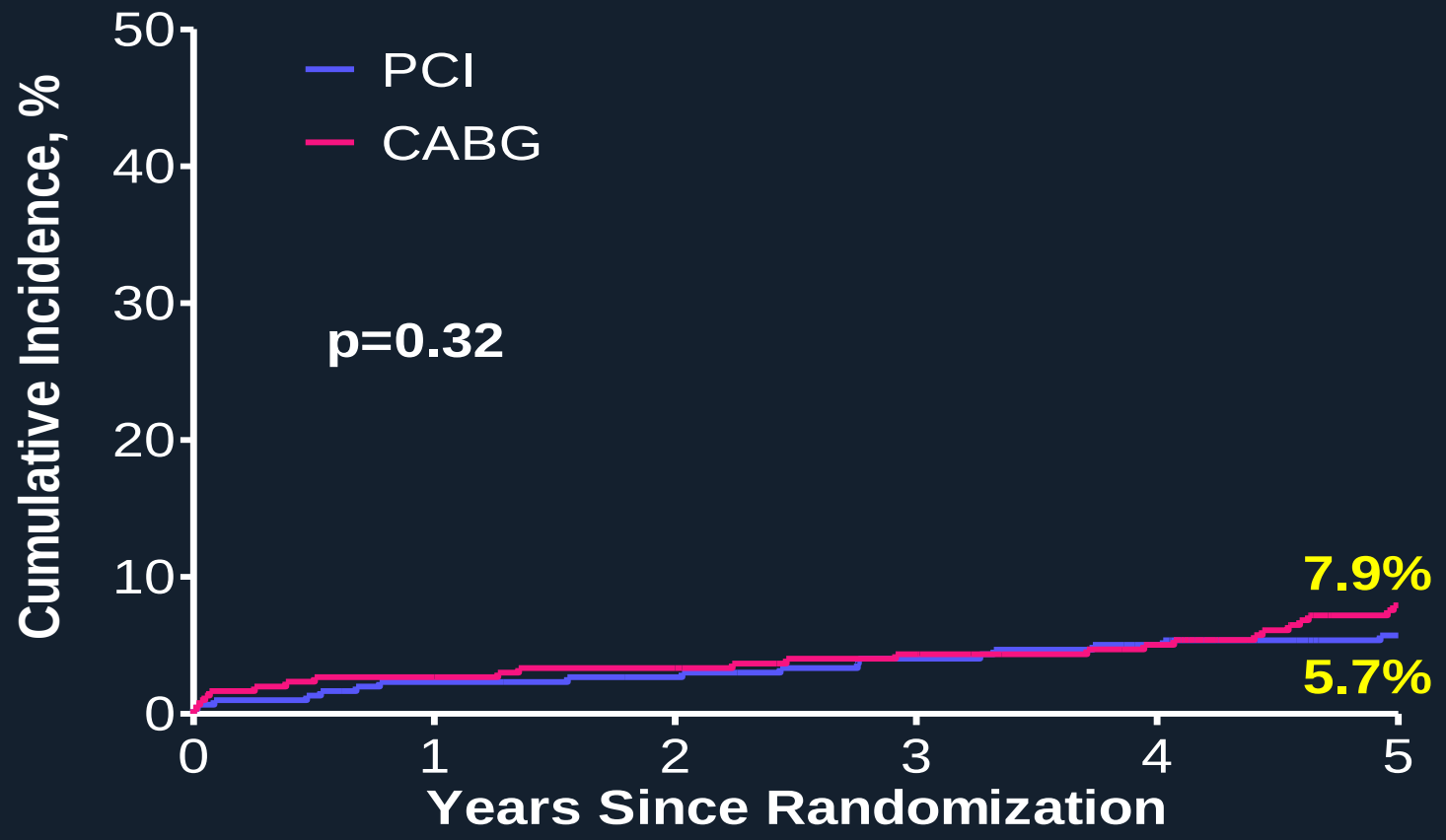
PCI	300	272	261	252	246	231
CABG	300	279	274	267	256	235

CardioVascular Research Foundation

Ahn JM et al, JACC. Published online March 15, 2015

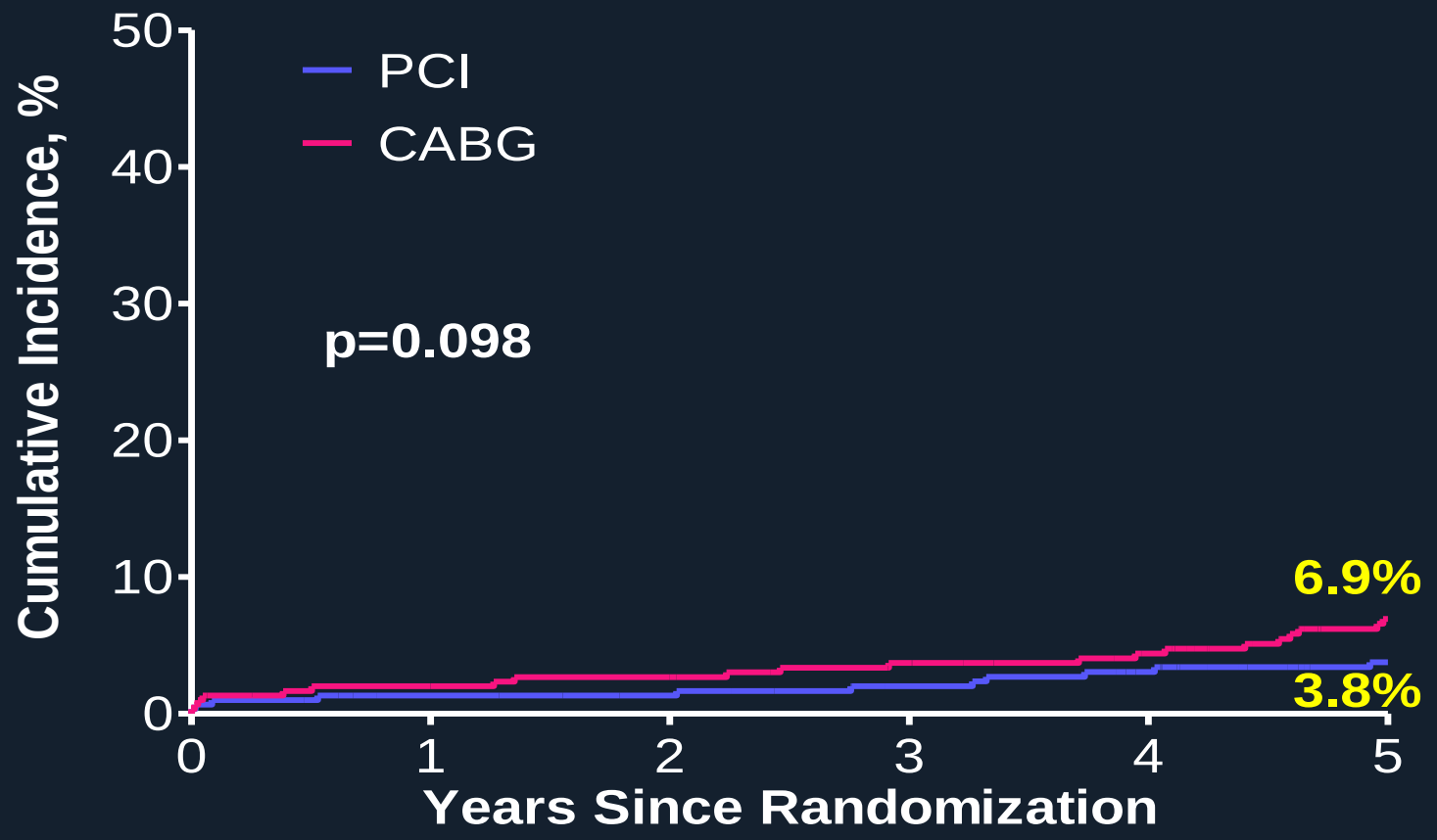
UNIVERSITY OF ULSAN COLLEGE MEDICINE
ASAN Medical Center

Death



Patient at risk						
PCI	300	292	289	283	277	262
CABG	300	291	288	281	273	252

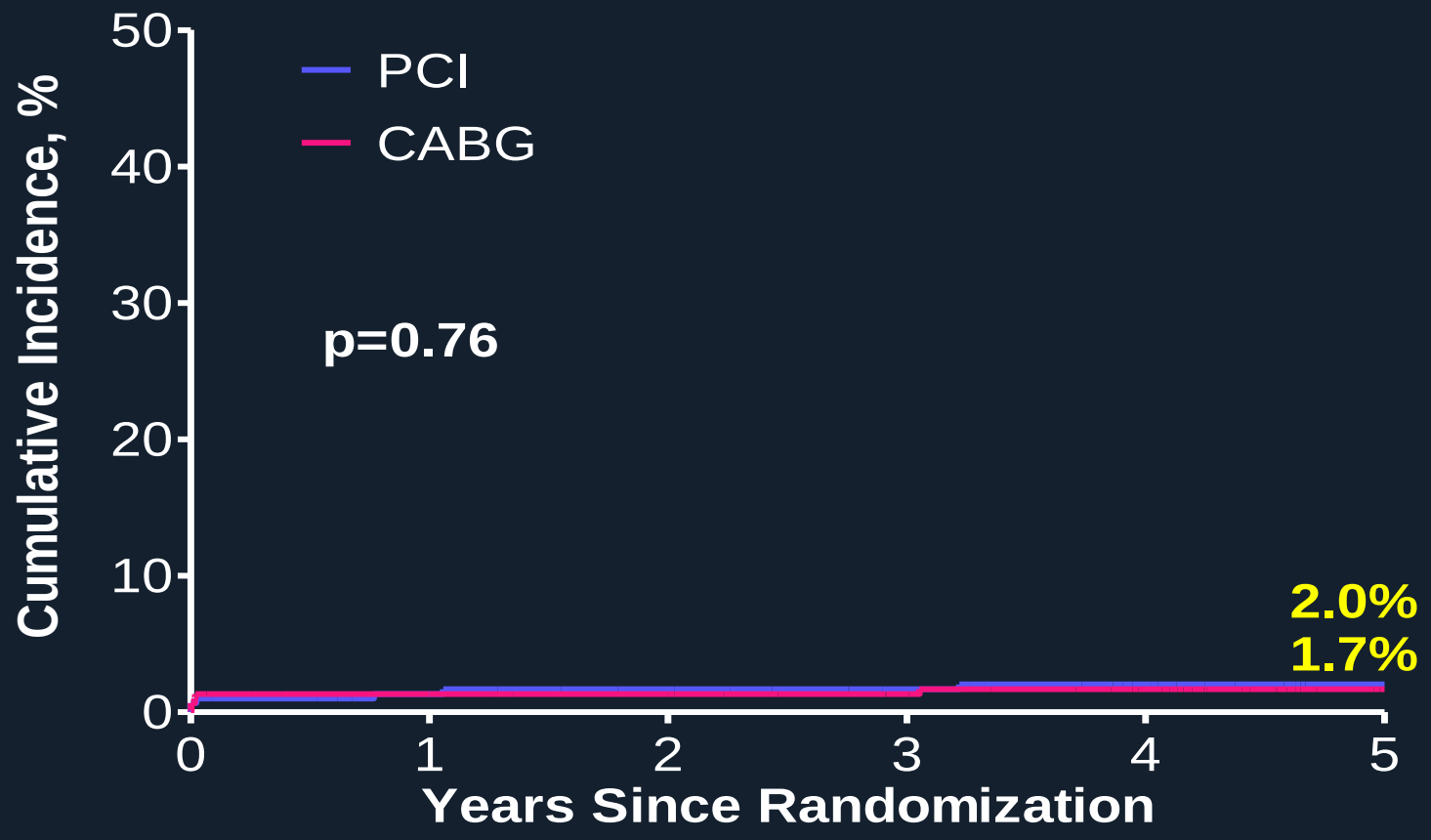
Cardiac Death



Patient at risk

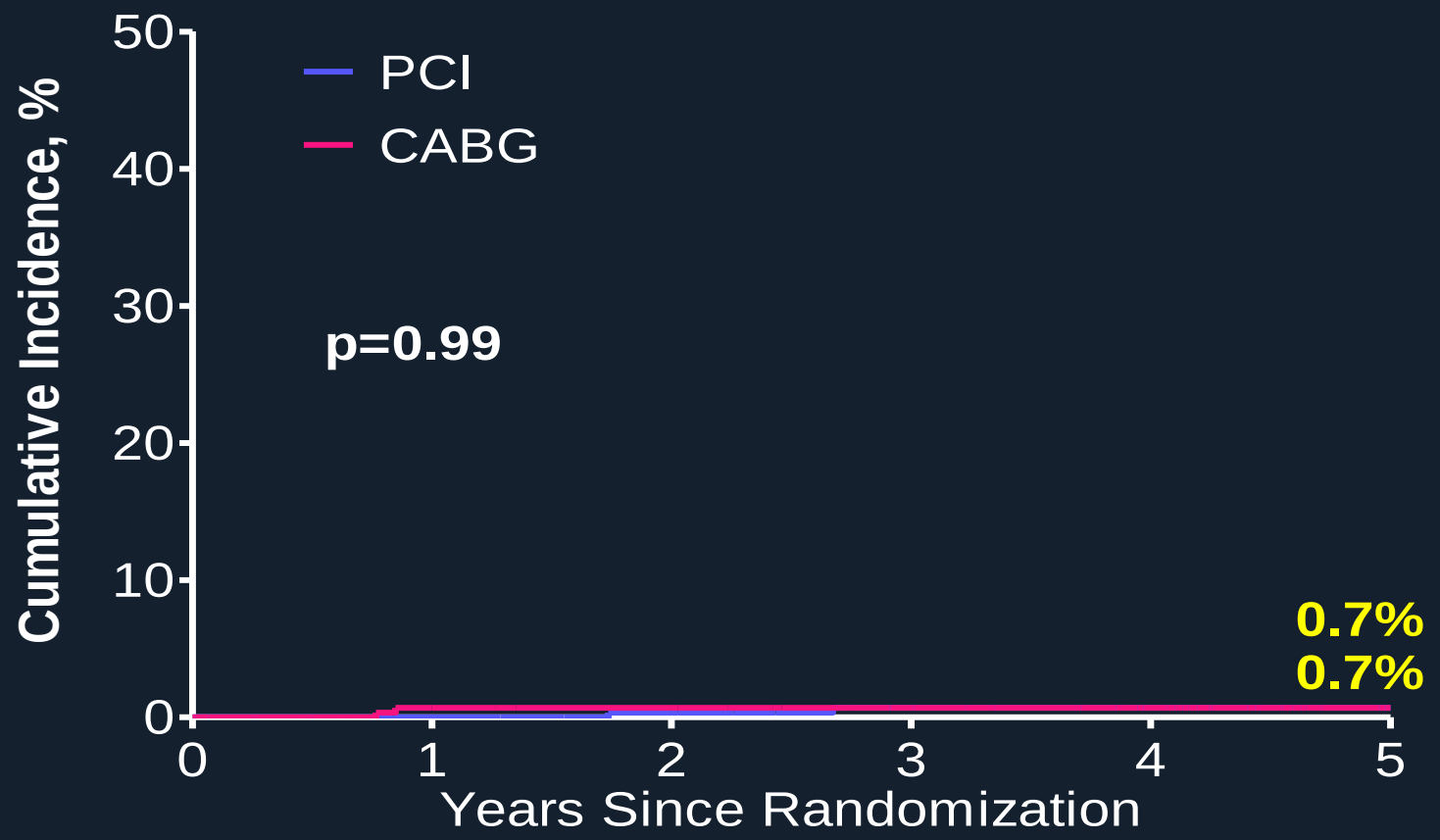
PCI	300	292	289	283	277	262
CABG	300	291	288	281	273	252

Myocardial Infarction



Patient at risk						
PCI	300	288	284	278	271	257
CABG	300	289	286	279	270	249

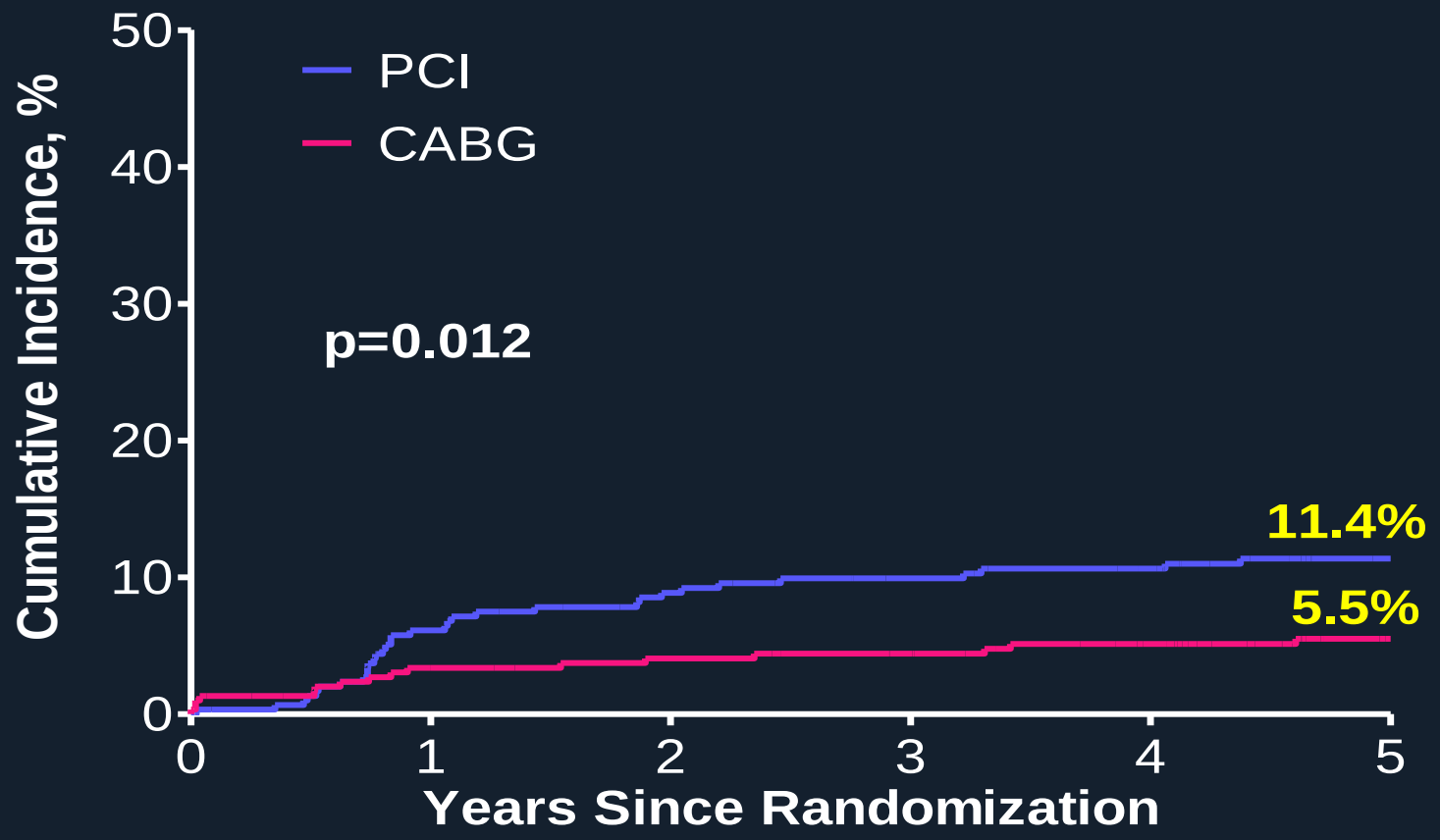
Stroke



Patient at risk

PCI	300	292	289	282	276	261
CABG	300	289	286	279	271	250

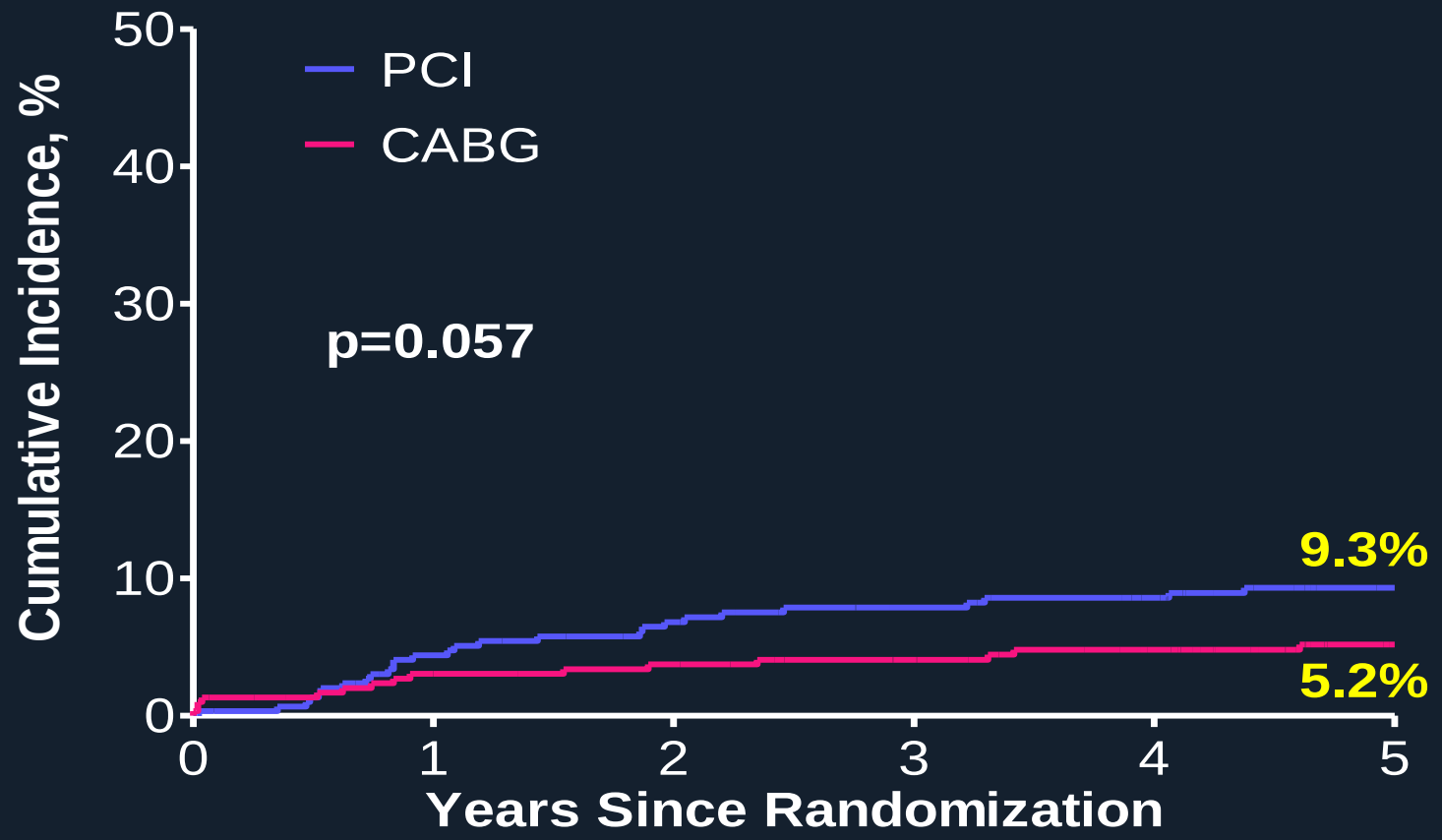
Ischemia-Driven TVR



Patient at risk

PCI	300	274	263	254	248	232
CABG	300	283	278	271	261	240

Clinical-driven TVR



Patient at risk

PCI	300	279	269	260	253	237
CABG	300	284	279	272	262	240

DES vs. CABG
for LM Disease Consensus

1. Stoke is Higher in CABG.
2. TVR is Higher in PCI.
3. Outcomes of PCI with DES is Comparable with CABG.

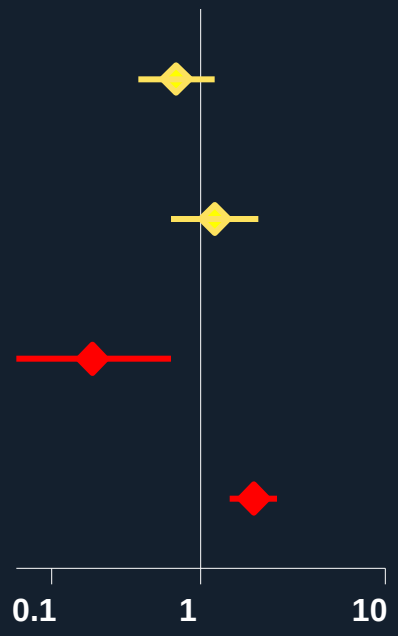
Temporal Changes of MACE

PCI vs. CABG for LM Disease
12 Meta-Analyses, 2009-2014

Author	Journal	Year	RCT	Non-RCT	Pts	FU
Naik et al	JACC Cardiovasc Interv	2009	2	8	3,773	3 yrs
Lee et al	Am J Cardiol	2010	2	6	2,905	1 yr
Capodanno et al	J Am Coll Cardiol	2011	4	0	1,611	1 yr
Ferrante et al	EuroIntervention	2011	4	0	1,611	1 yr
Jiang et al	Am J Cardiol	2012	0	25	7,230	≤3 yrs
Jang et al	Am J Cardiol	2012	3	9	5,079	1 yr
Desch et al	Herz	2013	4	0	1,611	2 yrs
Sa et al	Eur J Cardiothorac Surg	2013	3	13	5,674	1 yr
Alam et al	Circulation J	2013	4	23	11,148	5 yrs
Athappan et al	JACC Cardiovasc Interv	2013	3	21	14,203	5 yrs
Sa et al	Rev Bras Cir Cardiovasc	2013	1	4	2,914	5 yrs
Li et al	TRIALS	2014	4	17	8,413	5 yrs

Meta-analysis (n=1,611) of RCT 2011
Outcomes at 2 Year

	PCI		CABG		Risk Ratio (95% CI)
	Event	Total	Event	Total	
Death	30	804	40	784	0.74 (0.46, 1.19)
MI	28	804	23	784	1.19 (0.69, 2.06)
Stroke	4	804	18	784	0.26 (0.10, 0.69)
TVR	115	804	57	784	1.94 (1.43, 2.61)



Favor PCI **Favor CABG**

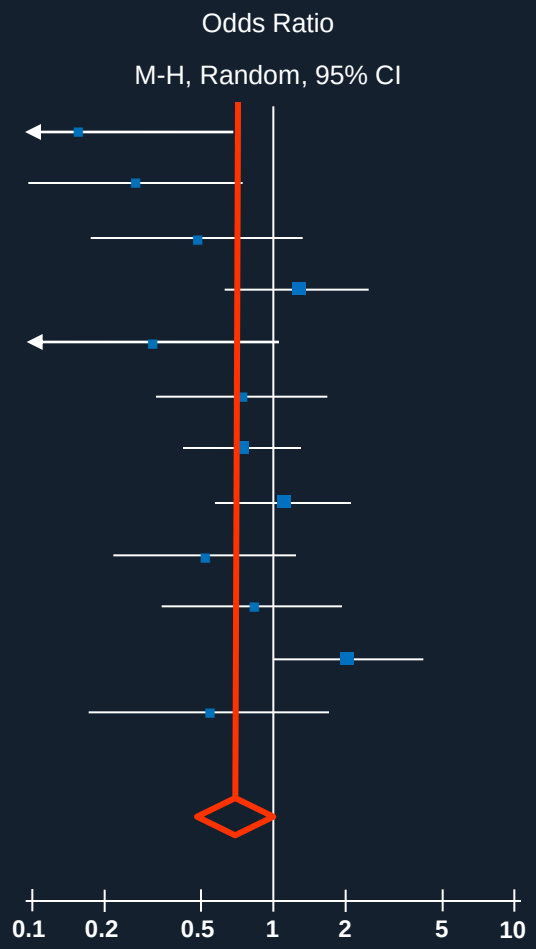
Capodanno D et al. JACC 2011;58:1426-1432, Desch et al. Herz 2013;38:48-56

CardioVascular Research Foundation
UNIVERSITY OF ULSAN
ASAN Medical Center

Meta-analysis (n=5,079), 2012
Death, MI or Stoke at 1 Year

Study or Subgroup	DES Events	DES Total	CABG Events	CABG Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Lee et al.	2	50	26	123	4.3%	0.16 [0.04, 0.68]	2006
Chieffo et al.	5	107	22	142	7.2%	0.27 [0.10, 0.73]	2006
Sanmartin et al.	5	96	25	245	7.3%	0.48 [0.18, 1.30]	2007
MAIN-COMPARE	20	396	16	396	10.4%	1.26 [0.64, 2.48]	2008
Makikallio et al.	3	49	41	238	5.7%	0.31 [0.09, 1.06]	2008
Chenget al.	9	94	27	216	9.1%	0.74 [0.33, 1.64]	2009
SYNTAX left main	25	357	32	348	11.9%	0.74 [0.43, 1.28]	2010
Kang et al.	20	205	23	257	10.9%	1.10 [0.59, 2.06]	2010
Wu et al.	7	131	24	245	8.4%	0.52 [0.22, 1.24]	2010
PRECOMBAT	10	300	12	300	8.5%	0.83 [0.35, 1.95]	2011
CUSTOMIZE	18	222	15	361	10.0%	2.04 [1.00, 4.13]	2011
Boudriot et al.	5	100	9	101	6.2%	0.54 [0.17, 1.67]	2011
Total (95% CI)		**2107**		**2972**	**100.0%**	**0.70 [0.49, 1.00]**	
Total events	129		272				

Heterogeneity: $Tau^2=0.20$; $Chi^2=23.78$, df=11 (p=0.01); $I^2=54\%$



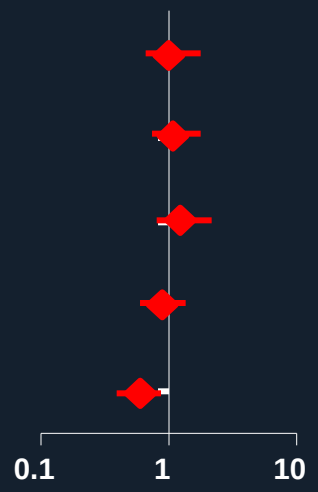
Test for overall effect: Z=1.97 ***(p=0.05)***

Favors DES **Favors CABG**

Jang JS et al. Am J Cardiol 2012;110:1411–1418

Meta-analysis (n=14,203), 2013
Death, MI or Stoke at 5 Year

Time Point	No. of Studies	Sample Size	Statistics: Odds ratio	Lower limit	Upper limit	p-Value
1 Year	9	4515	0.938	0.659	1.337	0.72
2 Year	8	4953	1.011	0.739	1.383	0.95
3 Year	5	3104	1.149	0.608	1.633	0.44
4 Year	4	5329	0.829	0.619	1.110	0.20
5 Year	5	3360	0.641	0.512	0.803	<0.001



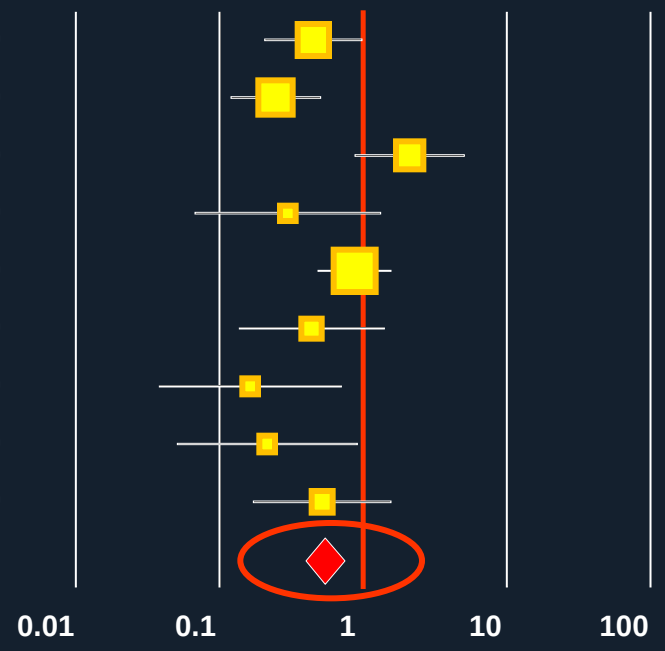
Favor PCI Favor CABG

Athappan et al. JACC: Cardiovascular Interventions 2013;1219-30

CardioVascular Research Foundation
UNIVERSITY OF ULSAN
ASAN Medical Center

Meta-analysis (n=8,413), 2014
Death, MI or Stoke at 5 Year

	PCI		CABG			
Study	Events	Total	Events	Total	Weight	Risk Ratio
Cheng	8	94	37	216	7.6%	0.50 (0.24,1.03)
Chieffo	10	107	42	142	12.3%	0.32 (0.17,0.60)
Kang	13	205	8	257	2.4%	2.04 (0.86,4.82)
Lee	2	50	15	123	3.0%	0.33 (0.08,1.38)
Park	20	176	28	219	8.5%	0.89 (0.52,1.52)
Park SJ	4	300	9	300	3.1%	0.44 (0.17,1.43)
Rittger	2	95	18	155	4.7%	0.18 (0.04,0.76)
Sanmartin	2	96	22	245	4.2%	0.23 (0.06,0.97)
Wu	4	131	14	245	3.3%	0.53 (0.18,1.59)
Total	65	1254	193	1902	49.1%	0.53 (0.40,0.70)



Favors PCI **Favors CABG**

Meta-analysis, 2009-2012

Favor PCI Favor CABG

			Odds Ratio (95% Confidence Interval)				
Author	Year	FU	Death	MI	Stroke	TVR	D/MI/Stroke
Naik et al	2009	1 yr	1.00 (0.70,1.41)	-	-	4.36 (2.60,7.32)	0.84 (0.57,1.22)
		2 yrs	1.27 (0.83,1.94)	-	PCI Better	CABG Better	1.25 (0.81,1.94)
		3 yrs	1.11 (0.66,1.86)	-			1.16 (0.68,1.98)
Lee et al	2010	1 yr	0.71 (0.42,1.23)	-	-	3.23 (1.47,7.14)	0.80 (0.55,1.16)
Capodanno et al	2011	1 yr	0.74 (0.43,1.29)	0.98 (0.54,1.78)	0.15 (0.03,0.67)	2.25 (1.54,3.29)	-
Ferrante et al	2011	1 yr	0.72 (0.42,1.24)	0.97 (0.54,1.74)	0.14 (0.04,0.55)	2.17 (1.48,3.17)	-
Jiang et al	2012	≤2 yrs	0.82 (0.61,1.11)	-	-	3.29 (2.39,4.51)	-
		≤3 yrs	0.88 (0.57,1.37)	-	-	3.60 (2.60,4.99)	-
		>3 yrs	0.72 (0.52,1.00)	-	-	3.49 (2.19,5.56)	-
Jang et al	2012	1 yr	0.68 (0.45,1.02)	-	-	3.52 (2.72,4.56)	0.70 (0.49,1.00)

Meta-analysis, 2013-2014

Favor PCI Favor CABG

			Hazard Ratio (95% Confidence Interval)				
Author	Year	FU	Death	MI	Stroke	TVR	D/MI/Stroke
Desch et al	2013	2 yrs	0.74 (0.46,1.19)	1.19 (0.69, 2.06)	0.26 (0.10,0.69)	1.94 (1.43,2.61)	-
Sa et al	2013	1 yr	0.69 (P=0.051)	-	[illegible]	[illegible]	0.83 (P=0.26)
		5 yrs	0.79 (0.67,1.08)	1.38 (0.71,2.70)	0.27 (0.13,0.55)	3.77 (2.43,5.87)	0.64 (0.51,0.80)
Alam et al	2013	30days	0.47 (0.20,1.10)	1.41 (0.56,3.51)	0.24 (0.10,0.62)	0.74 (0.30,1.85)	0.55 [illegible] (0.[illegible],1.63)
		1 yr	0.71 (0.55,0.92)	1.32 (0.75,2.31)	0.22 (0.10,0.49)	4.20 (3.07,5.75)	0.[illegible] (0.[illegible],0.82)
		~ 5 yrs	0.83 (0.[illegible],0.98)	1.41 (0.94,2.11)	0.33 (0.20,0.55)	3.69 (2.85,4.76)	0.63 (0.49,0.82)
Li et al	2014	<30 day	0.[illegible] (0.30,0.78)	0.97 (0.68,1.38)	0.19 (0.08,0.45)	-	0.53 (0.40,0.70)
		1-5 yrs	0.79 (0.61,0.95)	-	-	3.77 (3.35,4.26)	0.78 (0.71,0.85)

Outcomes of LM PCI Is Getting Better Over Time !

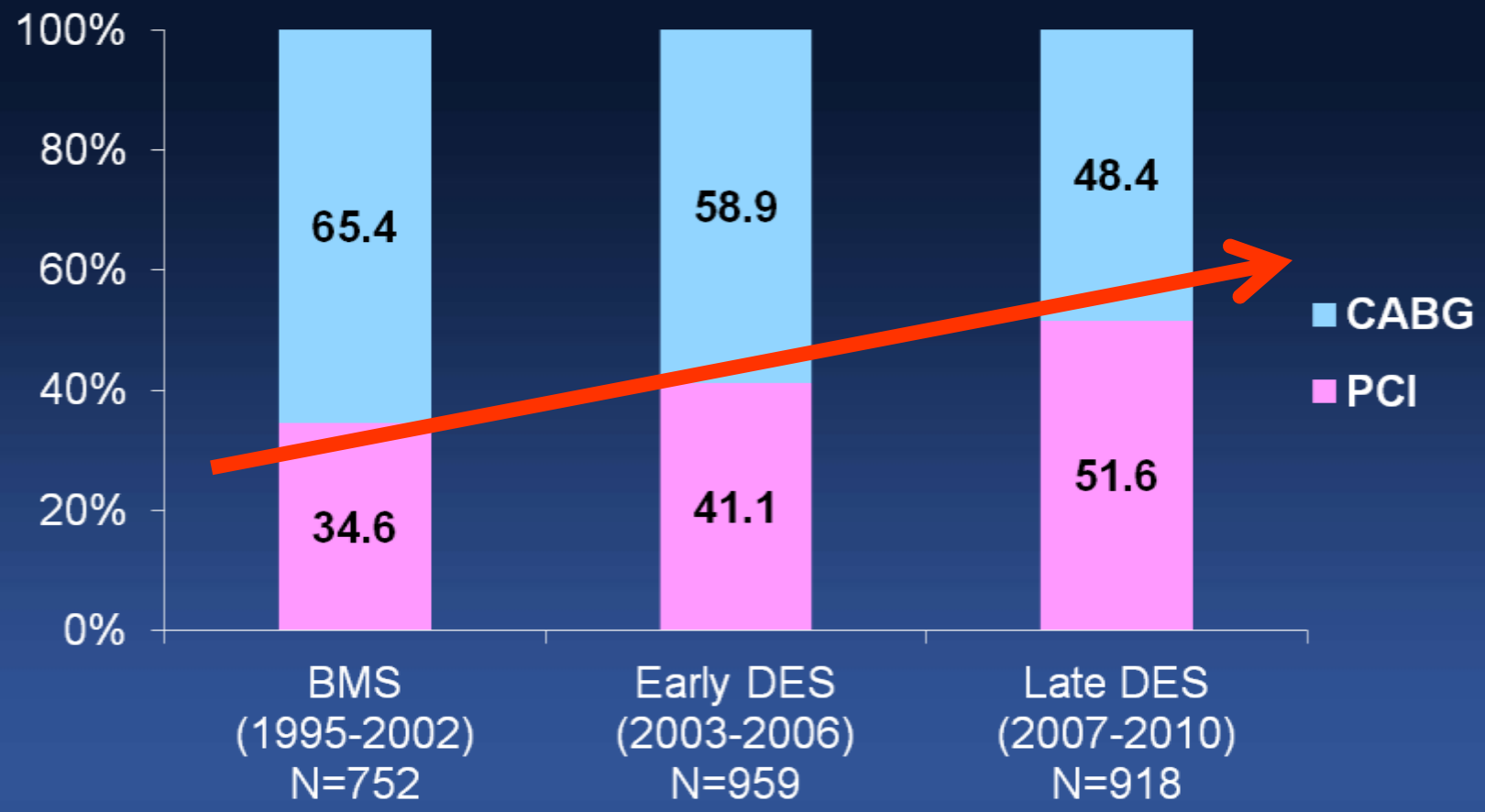
PCI Better

PCI Better

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

Data from ASAN MAIN Registry

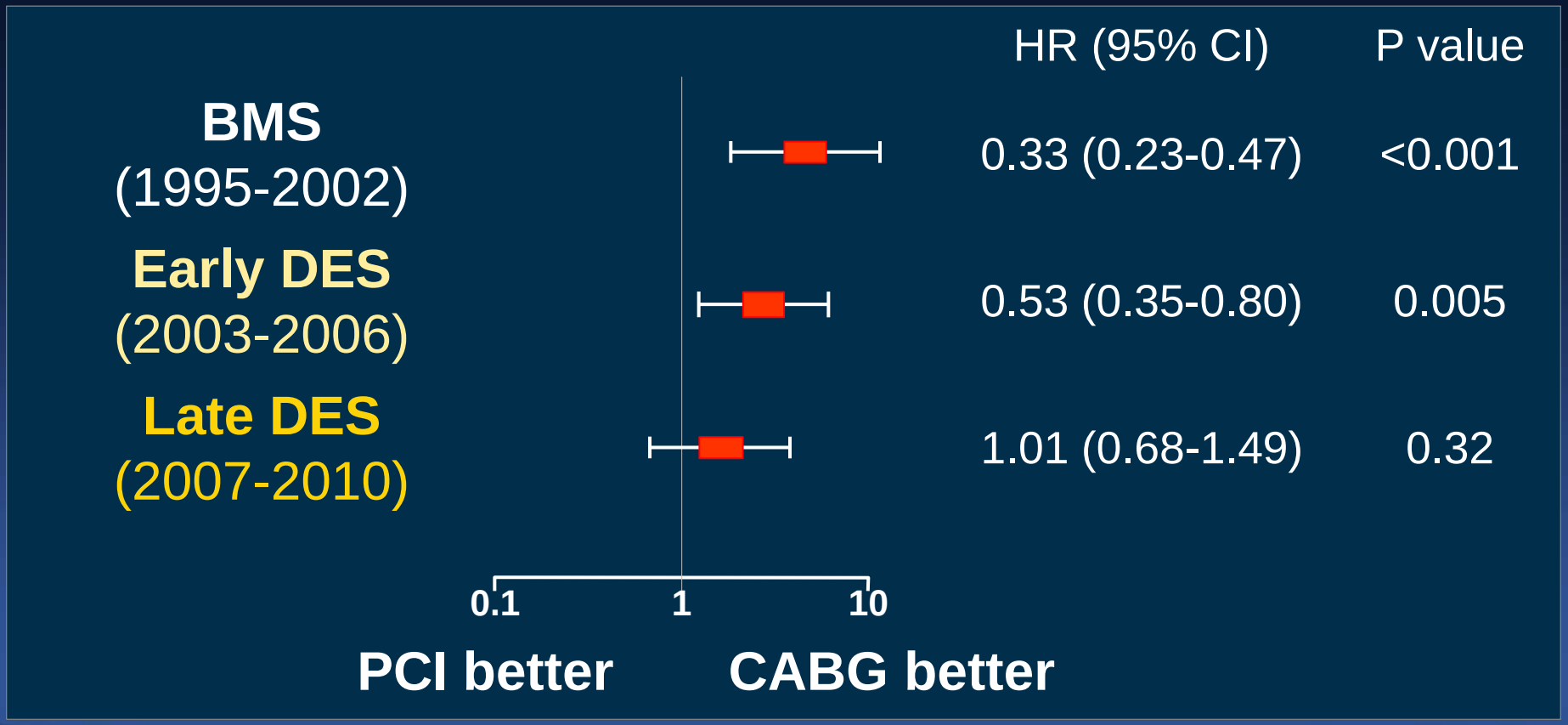
Temporal Trends (n=2,360), 2015
Outcomes of LM Revascularization



Park SJ, et al. Circulation. Cardiovascular Interventions. 2015 Mar;8(3). pii: e001846

Adjusted Hazard Ratios *of MACCE* Between CABG and PCI

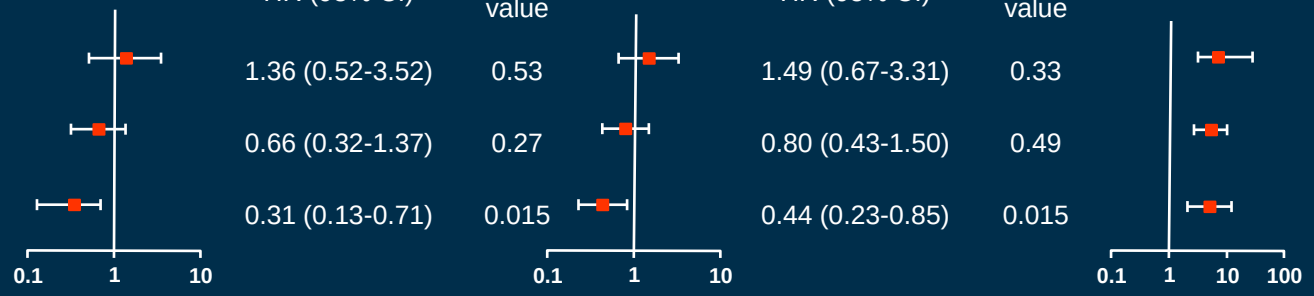
P for Interaction = 0.002



Park SJ, et al. Circulation. Cardiovascular Interventions. 2015 Mar;8(3). pii: e001846

Adjusted Hazard Ratios *of MACCE* Between CABG and PCI

	Death	Death, MI or Stroke	Repeat Revascularization
	P for Interaction = 0.011	*P for Interaction = 0.017*	P for Interaction = 0.20
	HR (95% CI)	HR (95% CI)	HR (95% CI)
BMS	1.36 (0.52-3.52)	1.49 (0.67-3.31)	6.88 (3.21-14.7)
Early DES	0.66 (0.32-1.37)	0.80 (0.43-1.50)	5.26 (2.73-10.1)
Late DES	0.31 (0.13-0.71)	0.44 (0.23-0.85)	5.07 (2.12-12.1)
	P value	P value	P value
BMS	0.53	0.33	<0.001
Early DES	0.27	0.49	<0.001
Late DES	0.015	0.015	<0.001



PCI better | CABG better | PCI better | CABG better | PCI better | CABG better

Park SJ, et al. Circulation. Cardiovascular Interventions. 2015 Mar;8(3). pii: e001846

DES vs. CABG
for LM Disease 2015

1. Stoke is Higher in CABG.
2. TVR is Higher in PCI.
3. Outcomes of PCI with DES is Comparable with CABG, ***Even Better Survival !***

Why,
Outcomes of LM PCI Is Getting Better ?

1. LM disease is Good Target for PCI.
   Proximal and Large Vessel. Easy to Perform Procedure.
2. DES is A Clear Revolution.
3. Better Concept of PCI ; Integrated Use of FFR and IVUS Can Improve the Clinical Outcomes.

EXCEL

4000 pts with left main disease

@ 165 international sites

↓

SYNTAX score ≤32

Consensus agreement by heart team

↓ → **No (N=1500)** ↓ **Enrollment registry**

Yes (N=2500)

R

↙ ↘

PCI (Xience Prime) (N=1250)

CABG (N=1250)

Clinical follow-up: 1 mo, 6 mo, and yearly through 5 years

IRIS - MAIN

To See Current Treatment Modality
(Prospective Cohort, Global Multicenter Registry)

Patients with
Left Main Disease (5,000 pts)

PCI with Any stents	CABG	Medical Treatment

Primary Endpoint: 2-year composite of Death, MI, Stroke, and TVR and annually follow up to 10 years

PI: Seung-Jung Park,MD

ESC Guidelines 2014
Elective PCI for LM Stenosis

LM Disease is
Not Surgical Disease Anymore !

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*