Congratulation !

INTERVENTIONAL CARDIOLOGY 2015

30th Annual International Symposium

Jim, I am getting old too !!

Temporal Changes of PCI vs. CABG for Left Main and Multi-Vessel Disease

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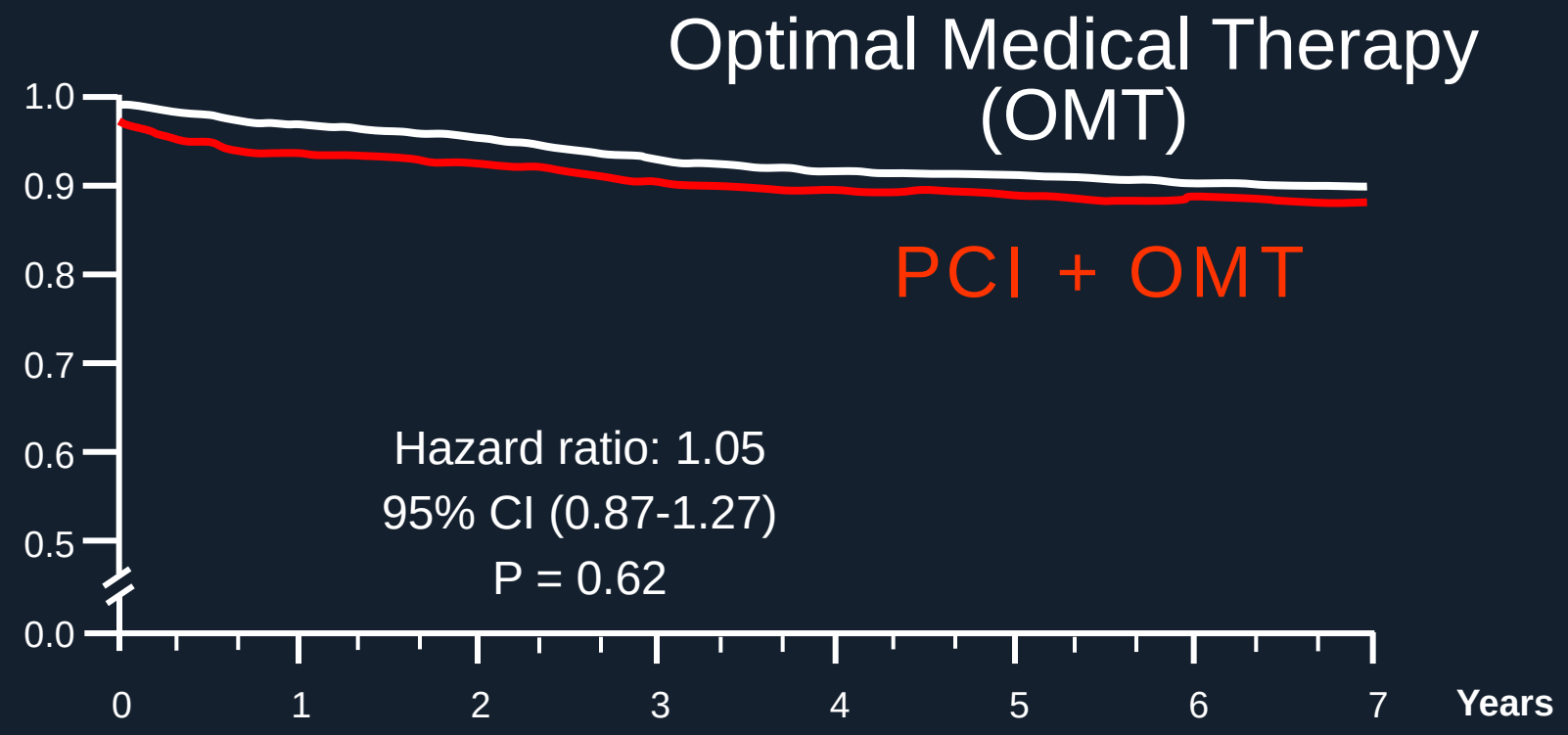
Heart Institute, University of Ulsan College of Medicine

Is
PCI Better ?

Benefit of Stents
Over Medications in Stable Disease

Survival Free From Death and MI

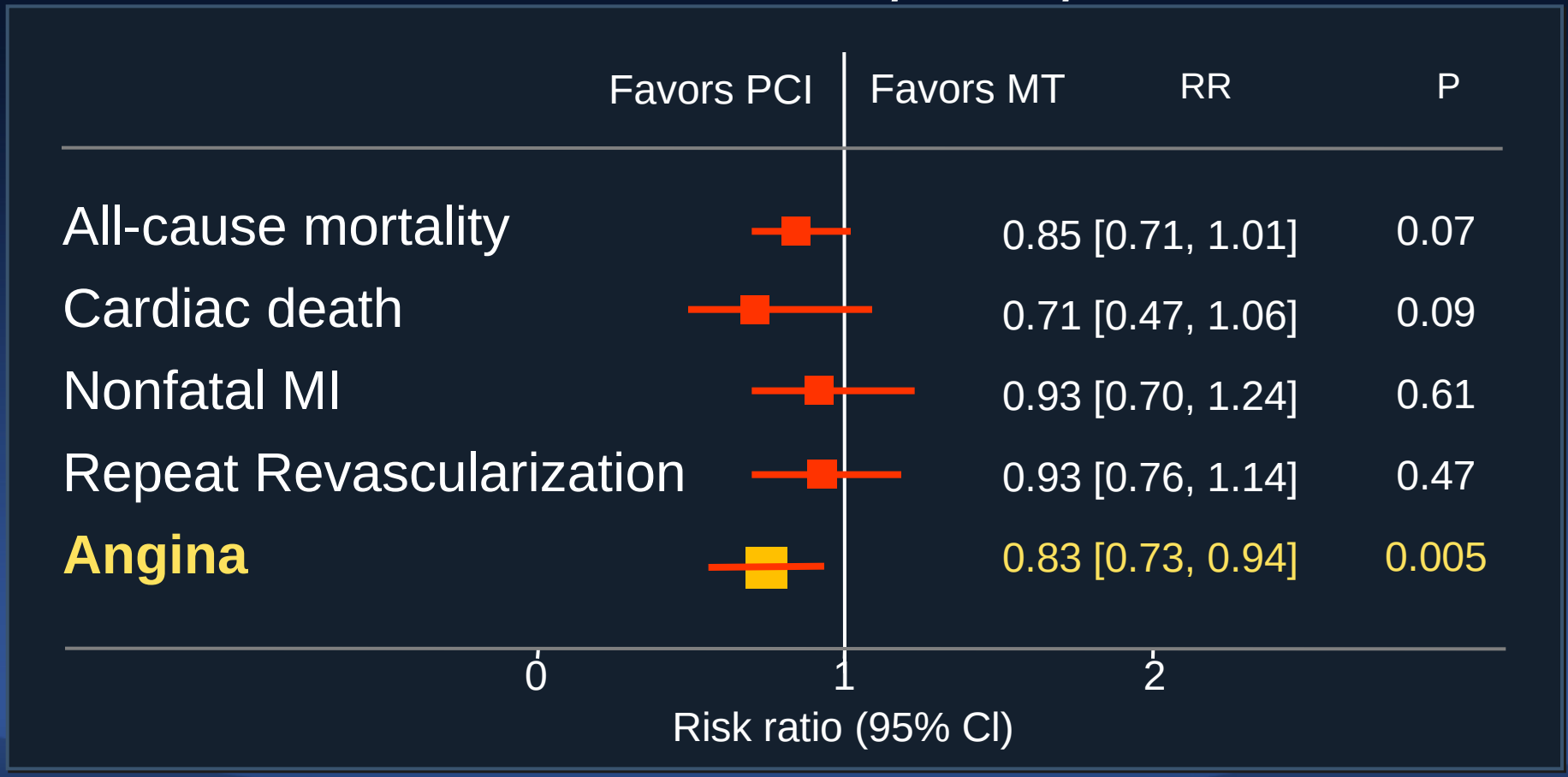
(COURAGE,n=2,287)



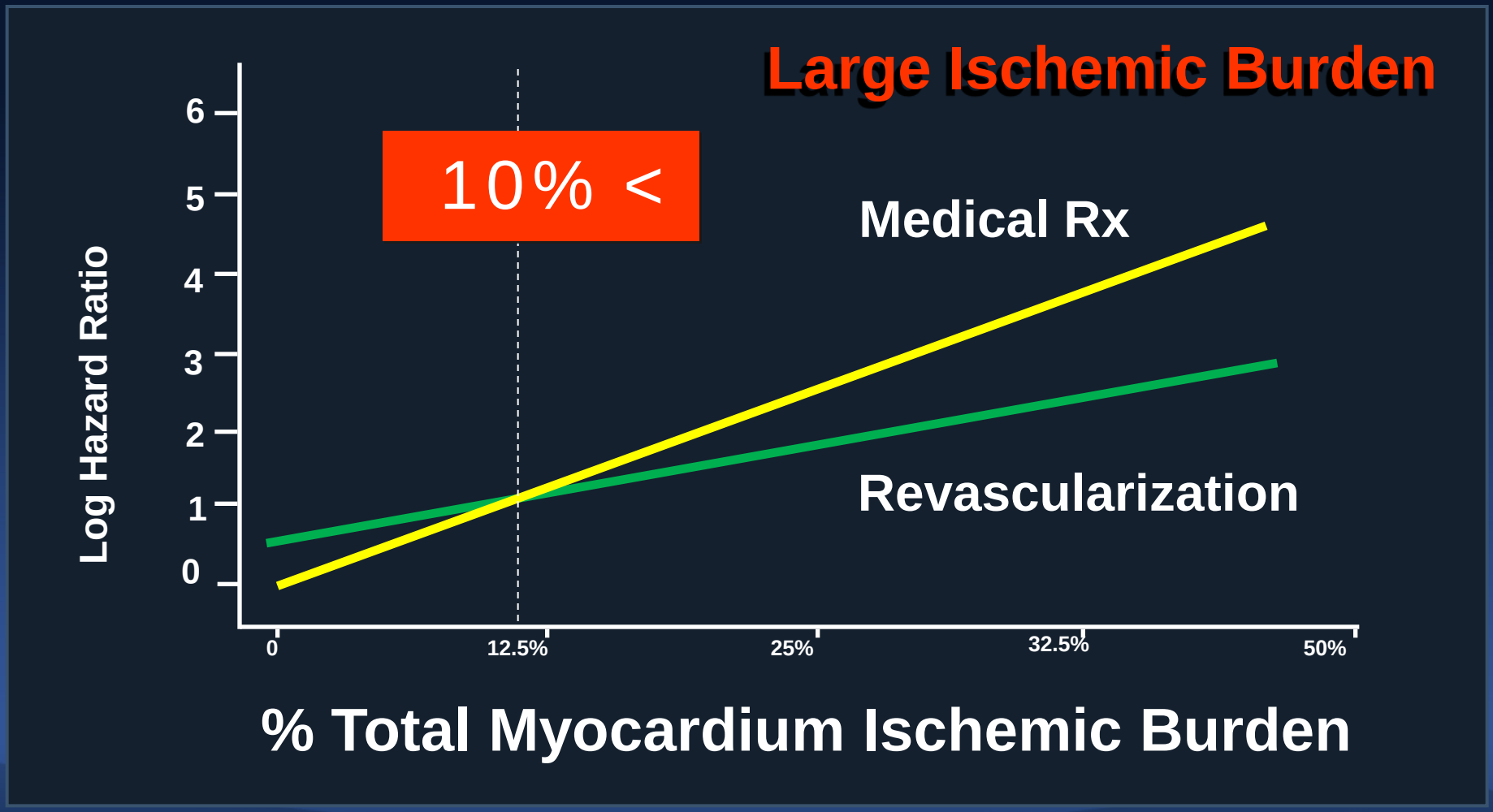
Boden W, N Engl J Med 2007; 356:1503-1516

Benefit of PCI (Stents) Over Medications in Stable Disease

12 RCTs, 7182 participants



Survival Benefit of Revascularization (CABG and/or PCI) Over Medications



Circulation. 2003;107:2900-2906

Survival Benefit of CABG Over Medications in Stable Disease

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

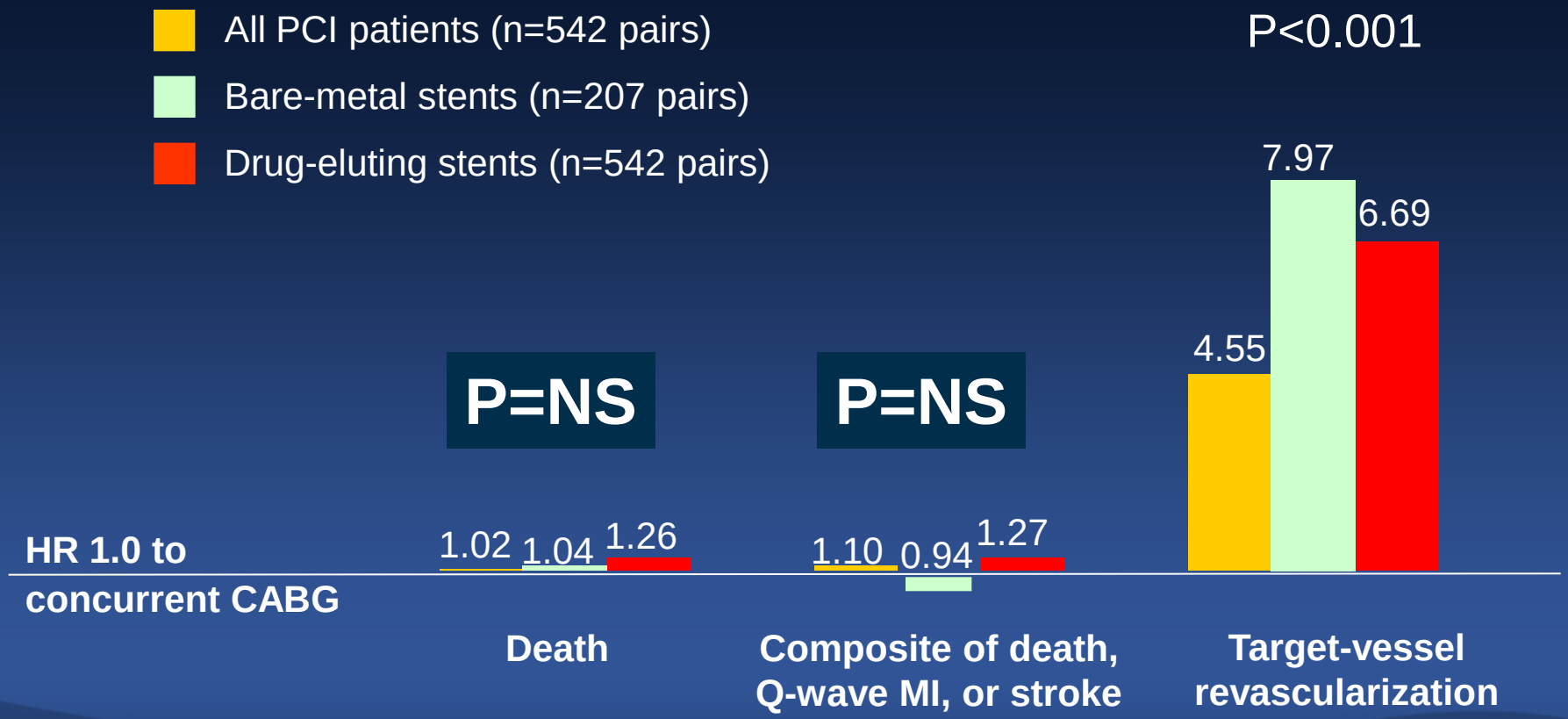
Old Story, But Conventional Bible !

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

DES vs. CABG
for LM Disease

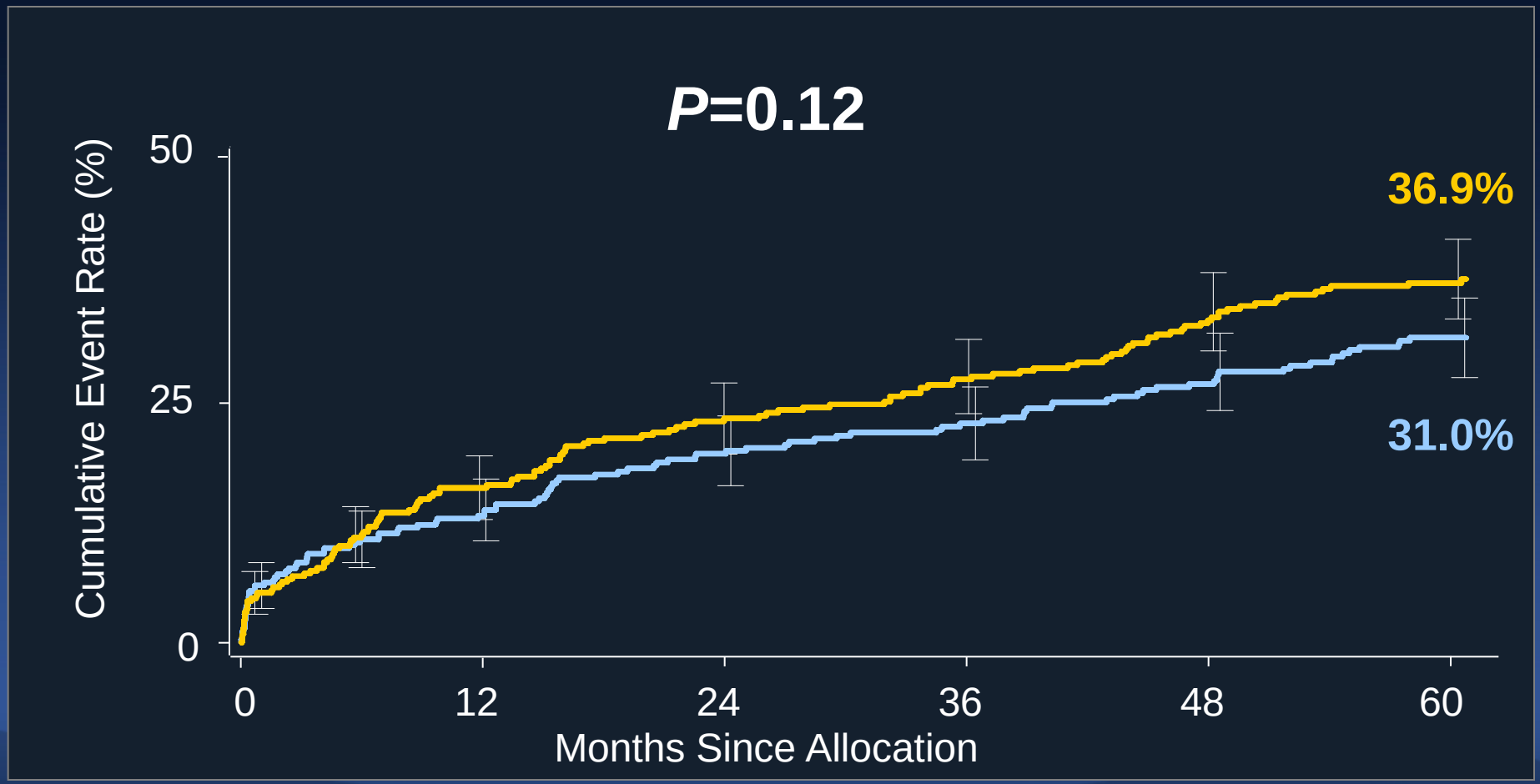
1. MAIN COMPARE Registry
2. SYNTAX, LM subgroup
3. PRECOMBAT
4. Meta-Analysis of RCTs and Registry
5. Temporal Changes of LM Revascularization

MAIN COMPARE, 5 Year
Death /MI /Stroke



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

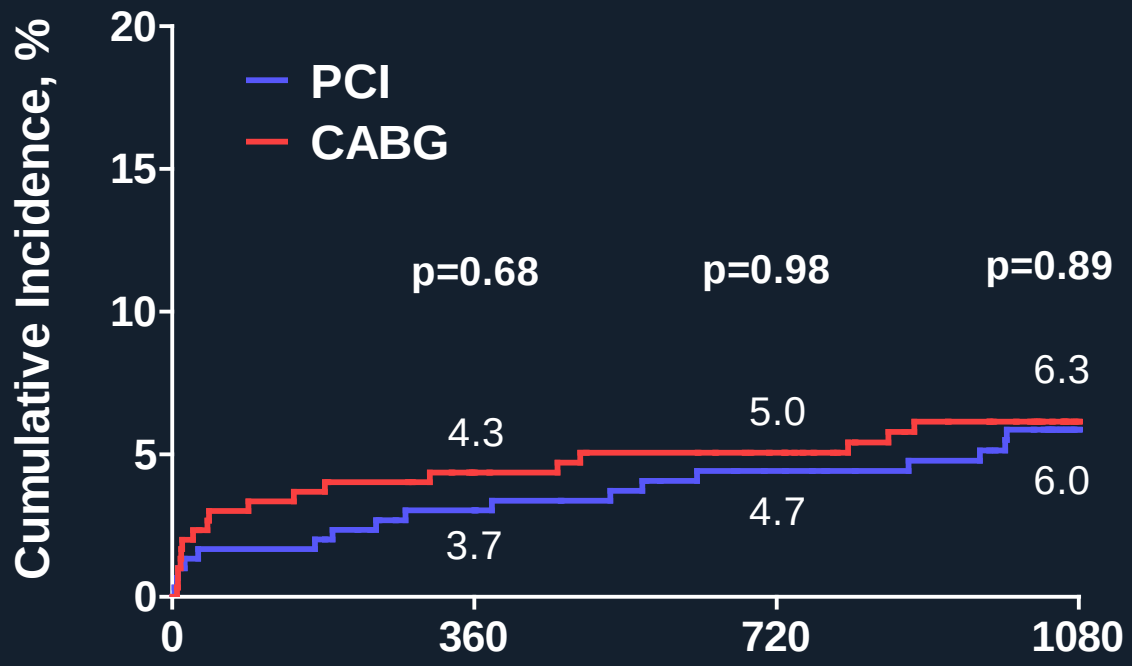
SYNTAX LM Subset, 5 Year
Death /MI /Stroke /Repeat Revascularization



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

ITT population

PRECOMBAT, 3 Year
Death /MI / Stoke

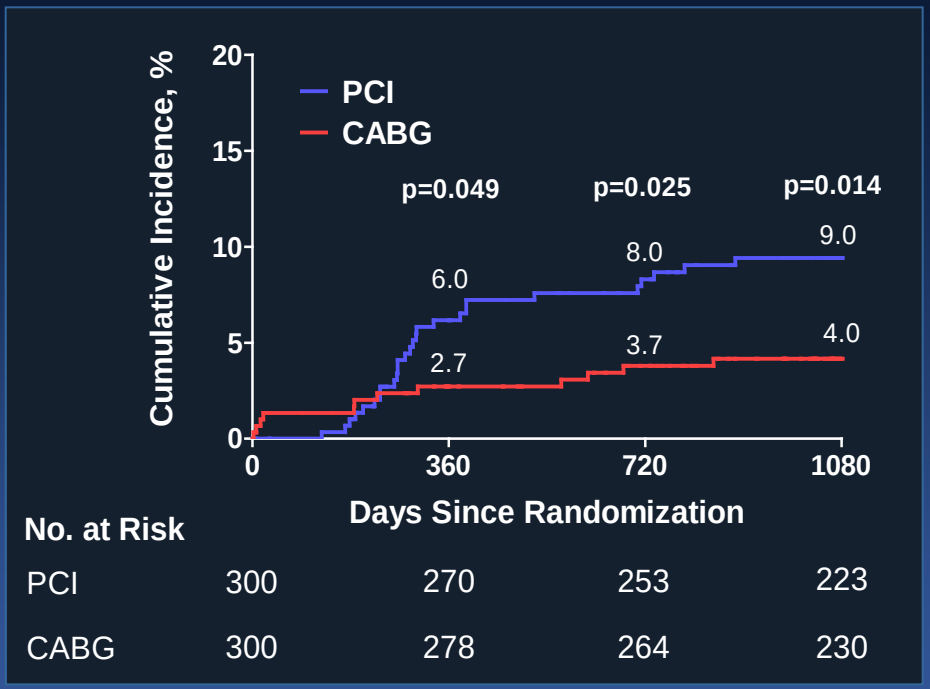


No. at Risk				
PCI	300	284	271	243
CABG	300	279	268	236

Park SJ et al, NEJM. 2011 May 5;364(18):1718-27

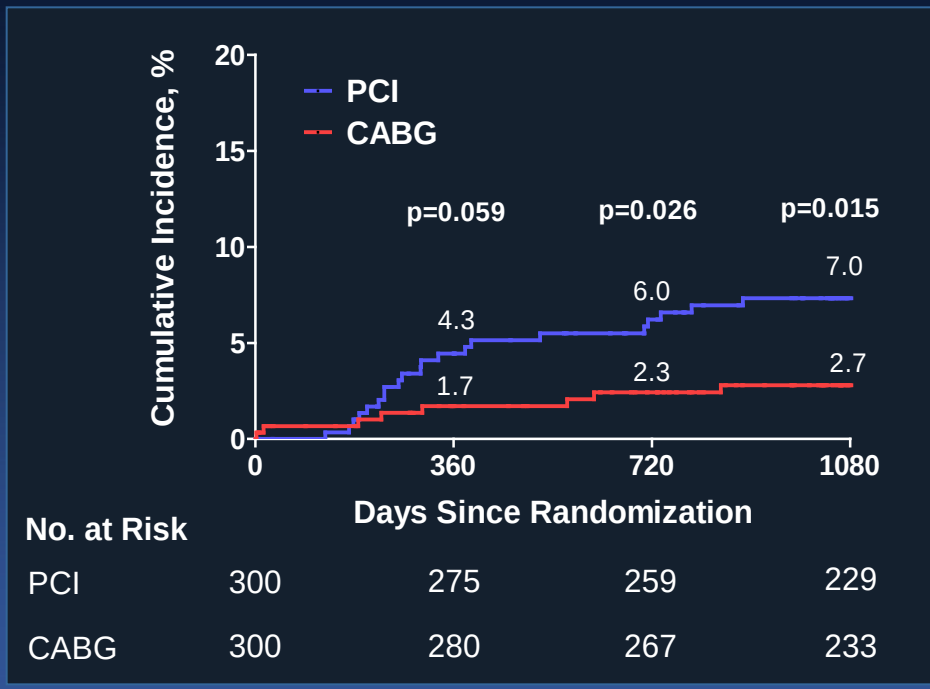
Only Difference is,

Ischemia-Driven TVR



No. at Risk				
PCI	300	270	253	223
CABG	300	278	264	230

Clinical-Driven TVR



No. at Risk				
PCI	300	275	259	229
CABG	300	280	267	233

DES vs. CABG
for LM Disease 2011

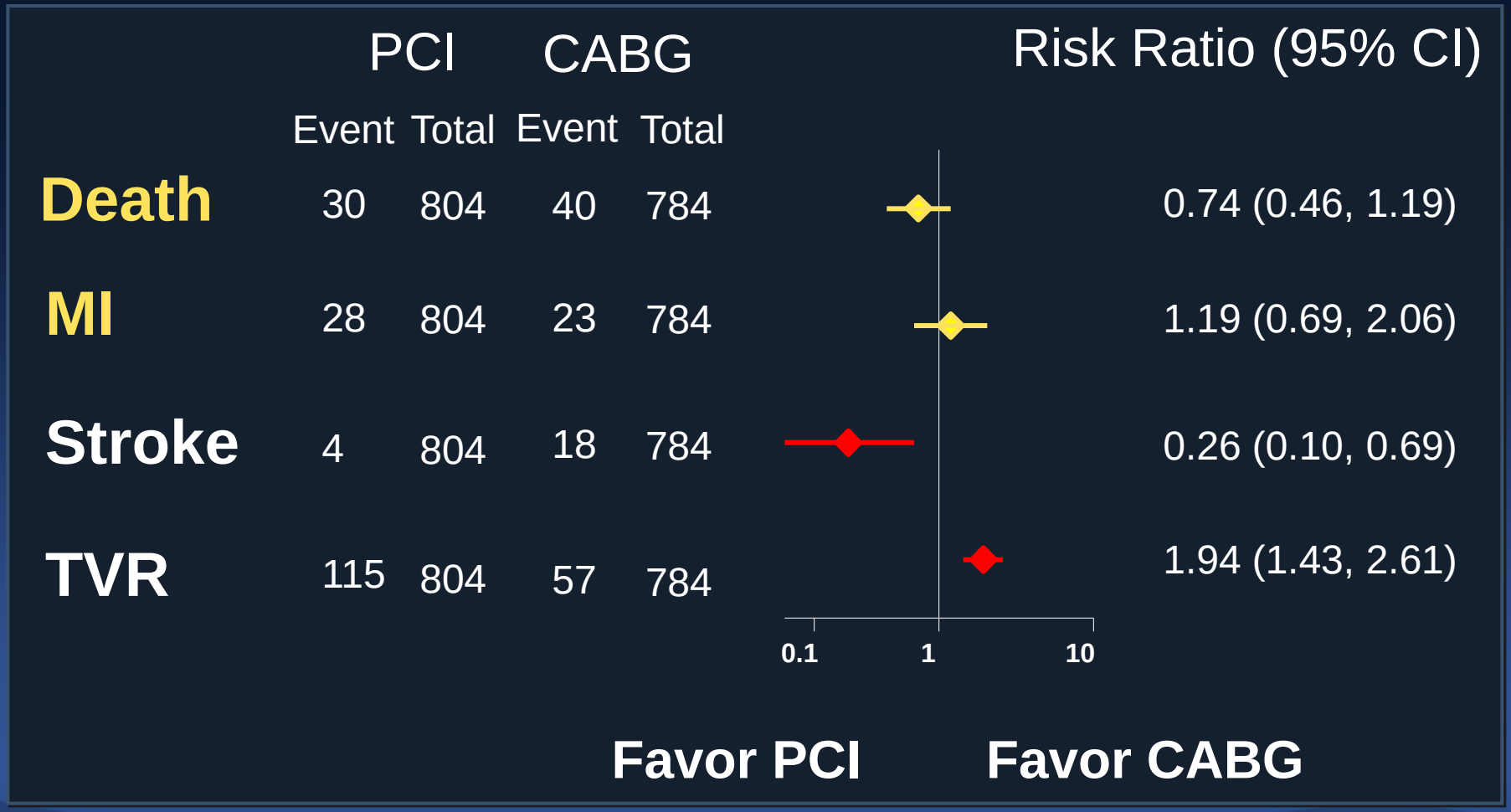
1. Stoke is Higher in CABG.
2. TVR is Higher in PCI.
3. Outcomes of PCI with DES is Comparable with CABG.

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



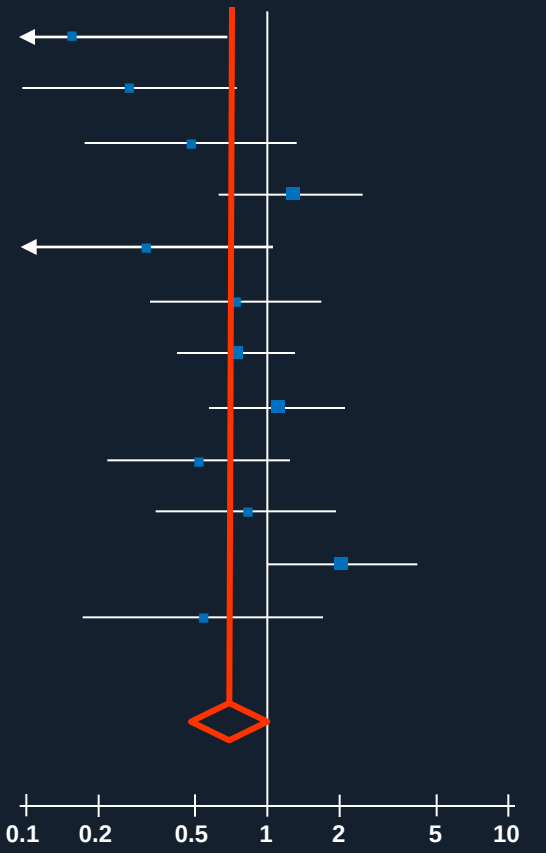
Capodanno D et al. JACC 2011;58:1426-1432, Desch et al. Herz 2013;38:48-56

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

	DES		CABG			Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	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				

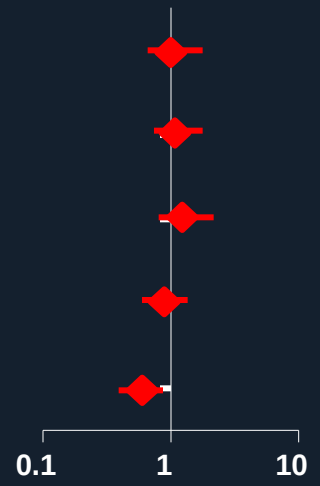
Heterogeneity: $Tau^2=0.20$; $Chi^2=23.78$, df=11 (p=0.01); $I^2=54\%$

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



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

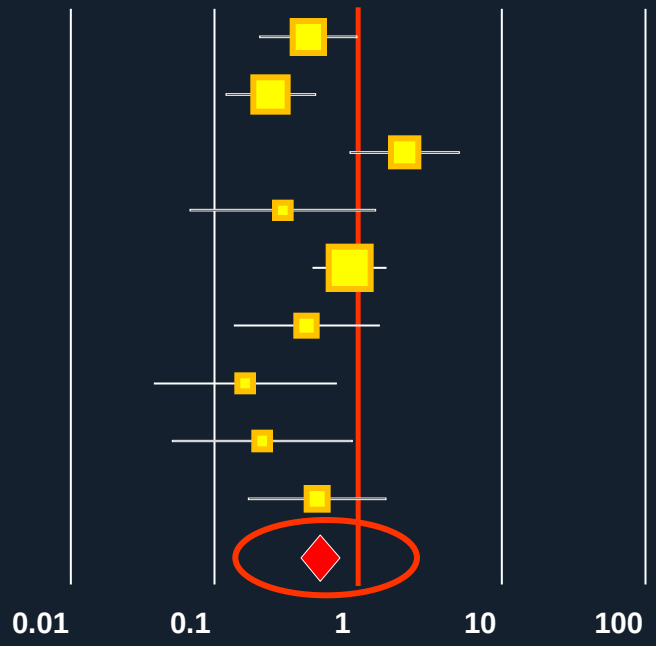


Favor PCI Favor CABG

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

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)



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)	-	PCI	CABG	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 (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 (0.71,0.98)	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	0.49 (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)

PCI Better

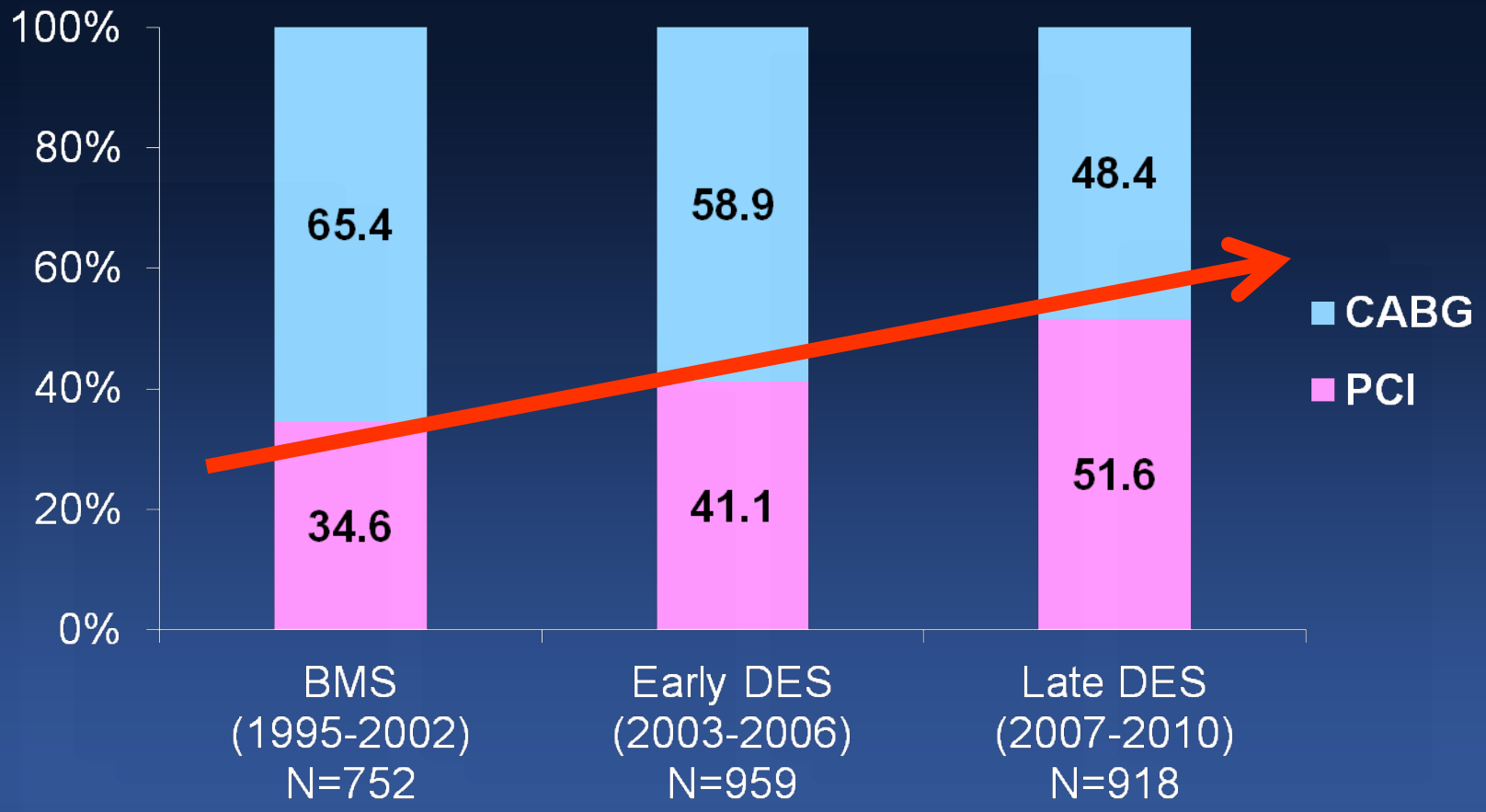
PCI Better

Outcomes of LM PCI Is Getting Better Over Time !

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

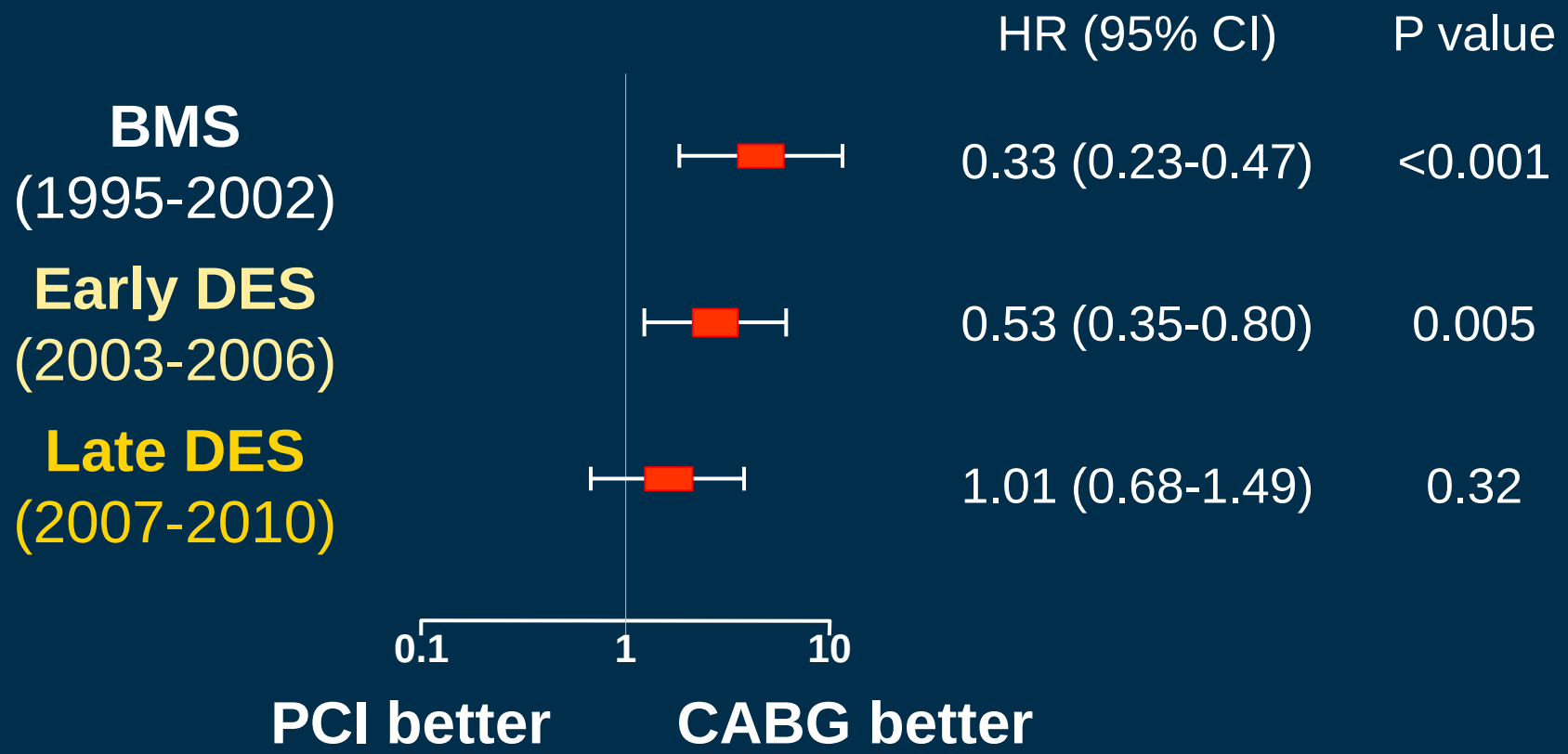
Data from ASAN MAIN Registry

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



Adjusted Hazard Ratios *of MACCE* Between CABG and PCI

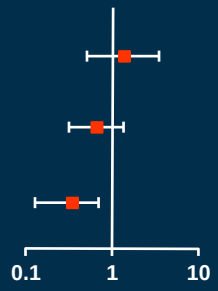
P for Interaction = 0.002



Adjusted Hazard Ratios *of MACCE* Between CABG and PCI

Death

P for Interaction = 0.011

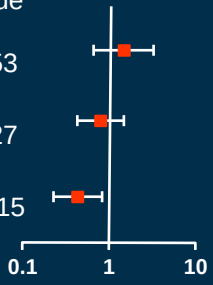


	HR (95% CI)	P value
BMS	1.36 (0.52-3.52)	0.53
Early DES	0.66 (0.32-1.37)	0.27
Late DES	0.31 (0.13-0.71)	0.015

PCI better | CABG better

Death, MI or Stroke

P for Interaction = 0.017

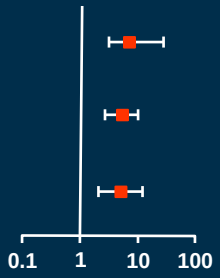


	HR (95% CI)	P value
BMS	1.49 (0.67-3.31)	0.33
Early DES	0.80 (0.43-1.50)	0.49
Late DES	0.44 (0.23-0.85)	0.015

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

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 !***

Could You Explain The Reasons Why, Outcomes of LM PCI Is Getting Better ?

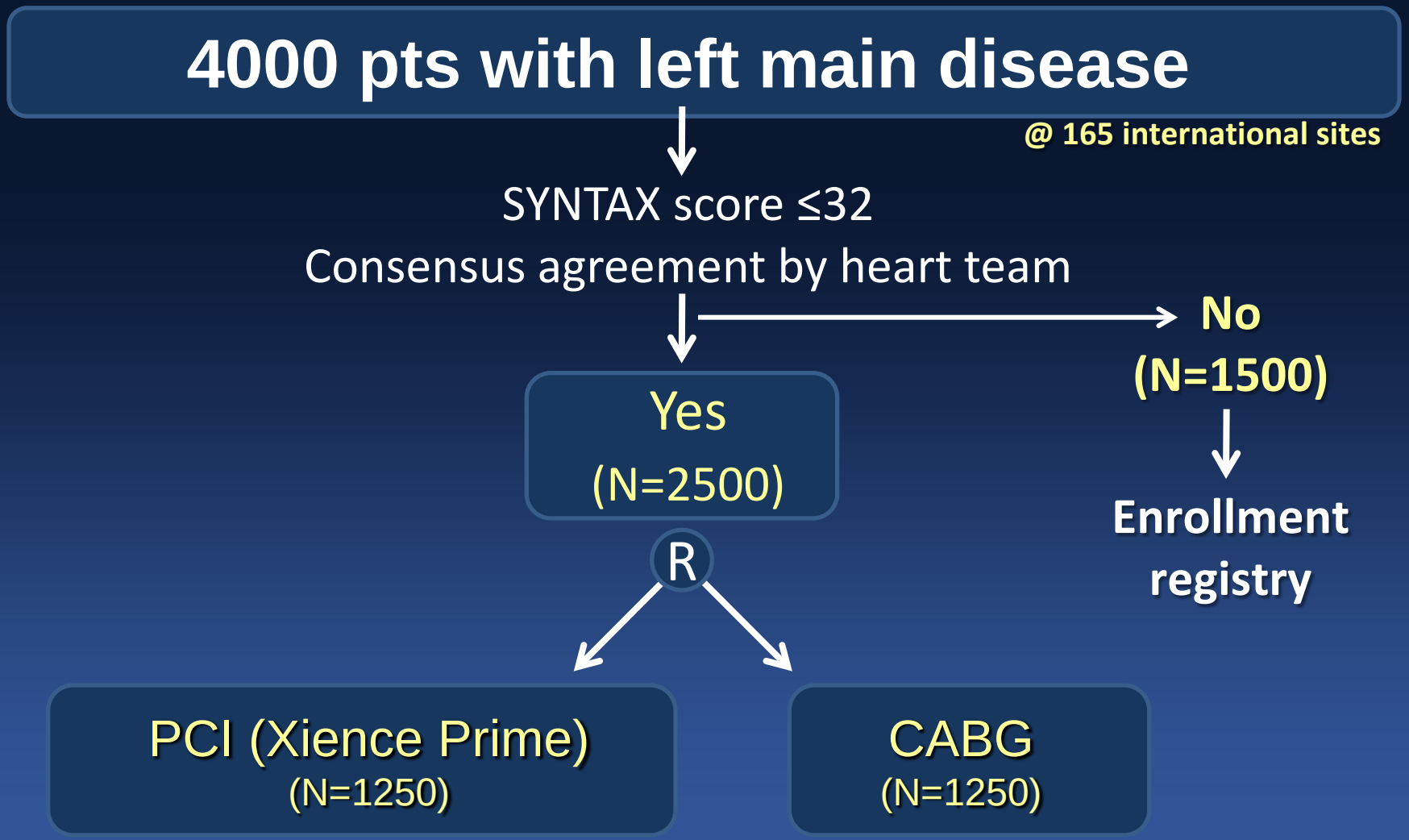
1. LM disease is Good Target for PCI. Proximal and Large Vessel. Easy to Perform Procedure.
2. DES is A Clear Revolution.
3. Better Concept of PCI ; Integrated Use of FFR and IVUS Can Improve the Clinical Outcomes.

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*

EXCEL



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

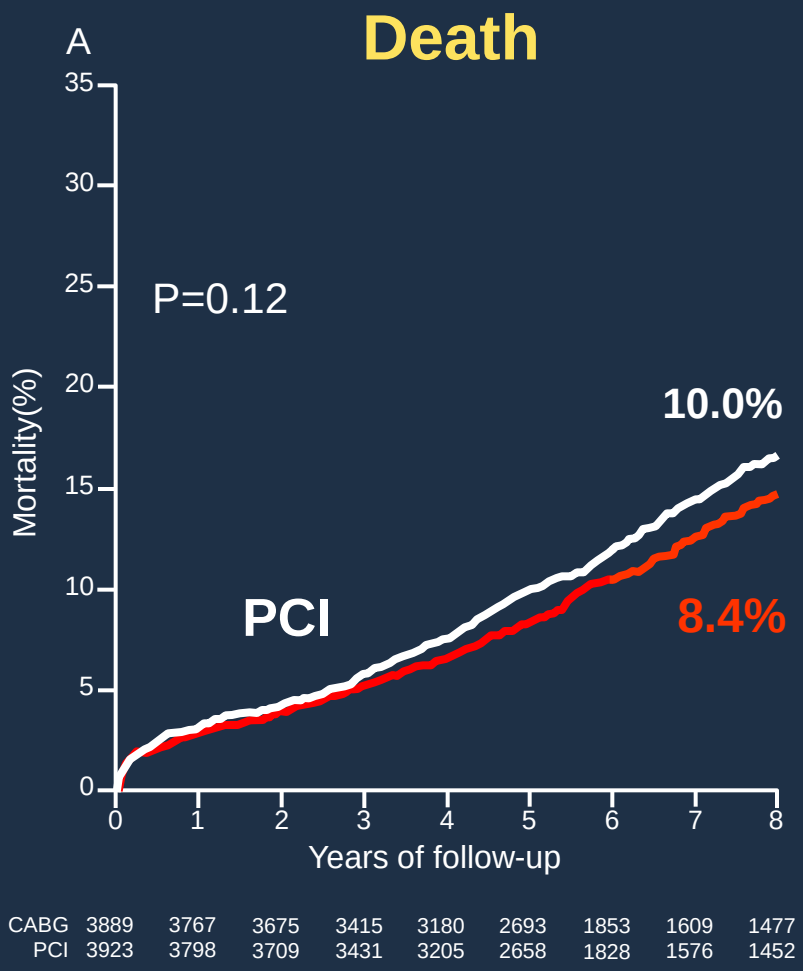
PI: Seung-Jung Park,MD

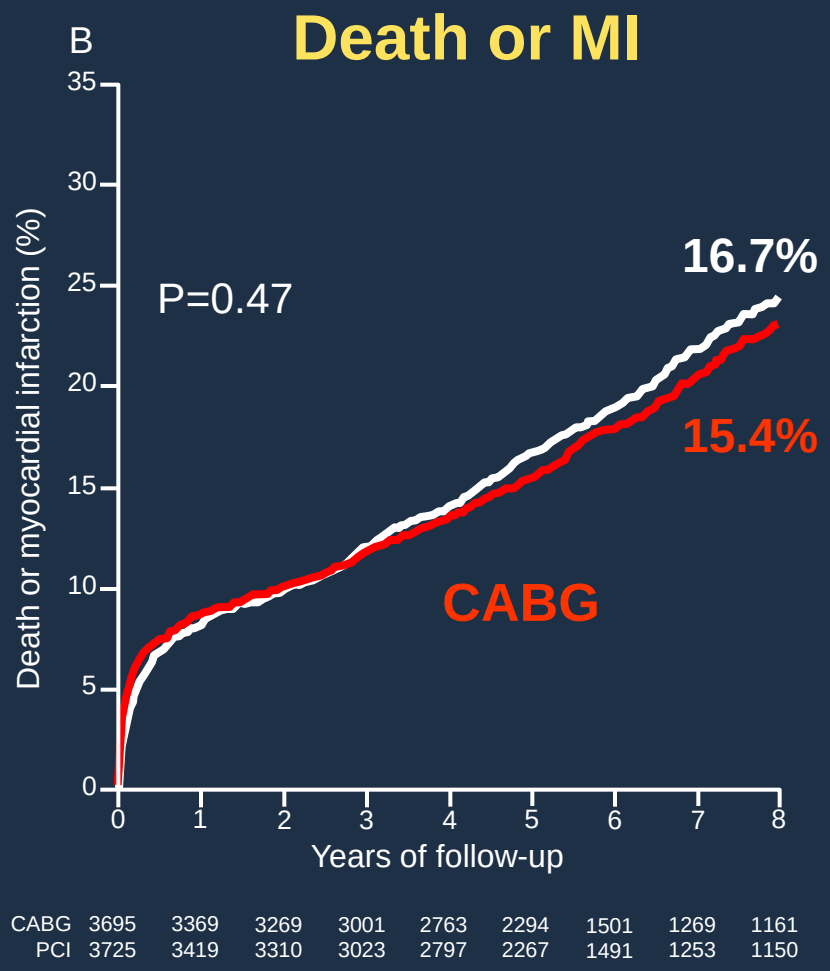
PCI vs. CABG
for Multi-Vessel Disease

1. Meta-Analysis of RCTs
2. BARI 2D
3. FREEDOM
4. SYNTAX

8 Year Survival

Meta-analysis of 10 RCTS, 7,812 Patients Treated with Balloon Angioplasty or BMS vs CABG:

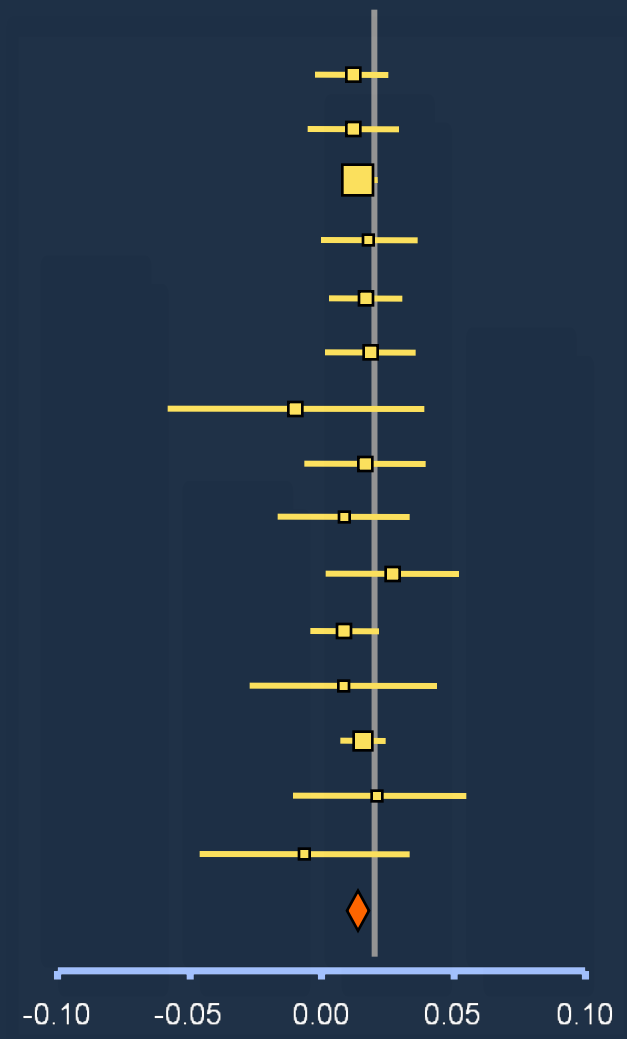




Hlatky MA et al. Lancet 2009;373:1190

More Strokes in CABG

Study, year	Surviving patients/all patients	
	PCI	CABG
ARTS, 2001	590/600	592/605
AWESOME, 2001	220/222	229/232
BARI, 1996	913/915	907/914
EAST, 1994	197/198	191/194
ERACI II,2001	225/225	223/225
GABI, 1994	182/182	175/177
Drenth et al, 2002	50/51	51/51
Diegeler et al, 2002	110/110	109/110
MASS, 1995	72/72	70/70
MASS II, 2004	203/205	197/203
Octostent, 2003	138/138	142/142
Cisowski et al, 2002	50/50	50/50
RITA, 1992	509/510	496/501
Hong et al, 2005	119/119	69/70
SIMA, 2000	62/63	60/60
Overall	3,640/3,660	3,561/3,604

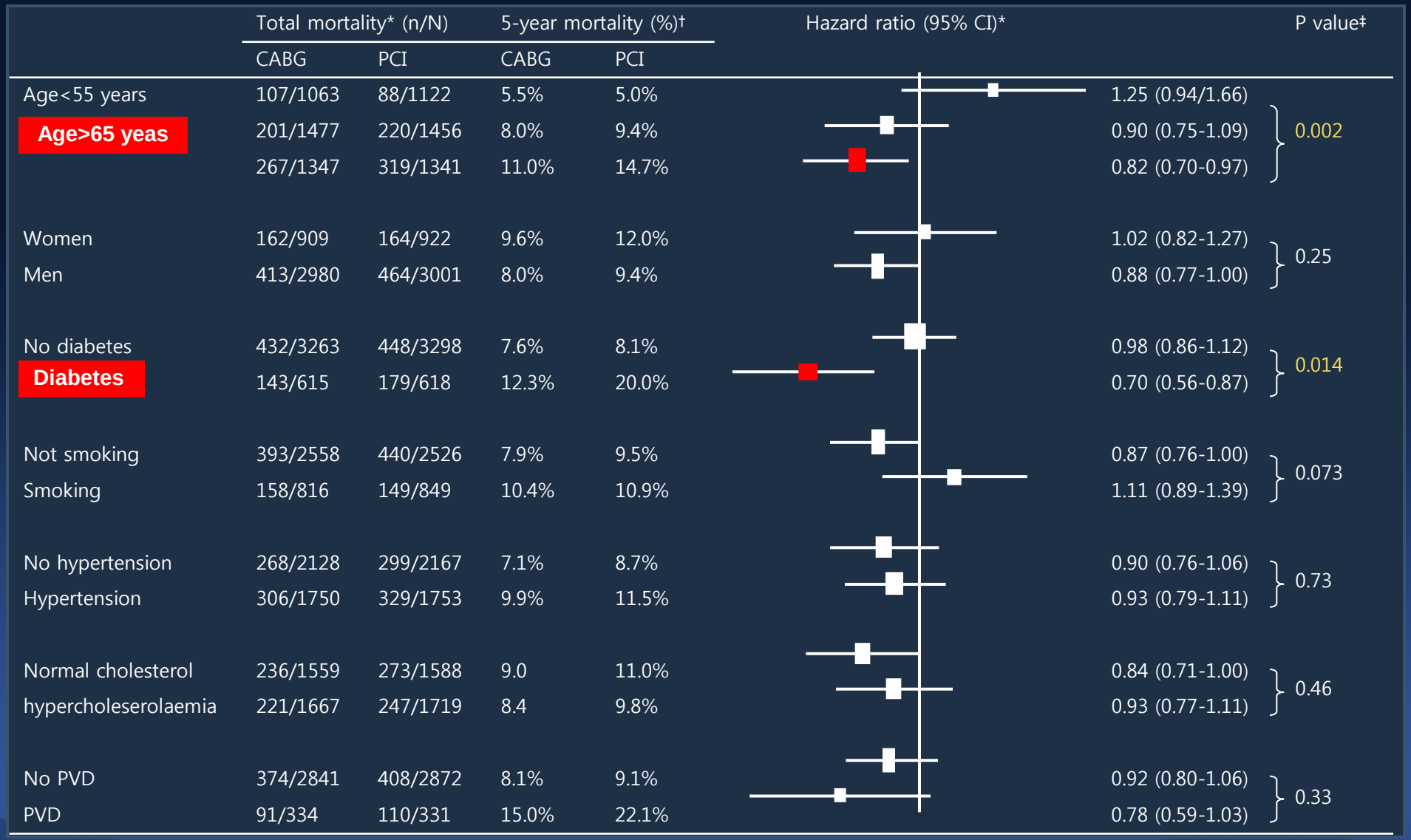


Ann Int Med 147:708, 2007

P=0.002

PCI better **CABG better**

Treatment Effect in Subgroups



	Total mortality* (n/N)		5-year mortality (%)†		Hazard ratio (95% CI)*	P value‡
	CABG	PCI	CABG	PCI		
Age<55 years	107/1063	88/1122	5.5%	5.0%	1.25 (0.94/1.66)	
Age>65 yeas	201/1477	220/1456	8.0%	9.4%	0.90 (0.75-1.09)	0.002
	267/1347	319/1341	11.0%	14.7%	0.82 (0.70-0.97)	
Women	162/909	164/922	9.6%	12.0%	1.02 (0.82-1.27)	
Men	413/2980	464/3001	8.0%	9.4%	0.88 (0.77-1.00)	0.25
No diabetes	432/3263	448/3298	7.6%	8.1%	0.98 (0.86-1.12)	
Diabetes	143/615	179/618	12.3%	20.0%	0.70 (0.56-0.87)	0.014
Not smoking	393/2558	440/2526	7.9%	9.5%	0.87 (0.76-1.00)	
Smoking	158/816	149/849	10.4%	10.9%	1.11 (0.89-1.39)	0.073
No hypertension	268/2128	299/2167	7.1%	8.7%	0.90 (0.76-1.06)	
Hypertension	306/1750	329/1753	9.9%	11.5%	0.93 (0.79-1.11)	0.73
Normal cholesterol	236/1559	273/1588	9.0	11.0%	0.84 (0.71-1.00)	
hypercholeserolaemia	221/1667	247/1719	8.4	9.8%	0.93 (0.77-1.11)	0.46
No PVD	374/2841	408/2872	8.1%	9.1%	0.92 (0.80-1.06)	
PVD	91/334	110/331	15.0%	22.1%	0.78 (0.59-1.03)	0.33

Hlatky MA et al. Lancet 2009;373:1190

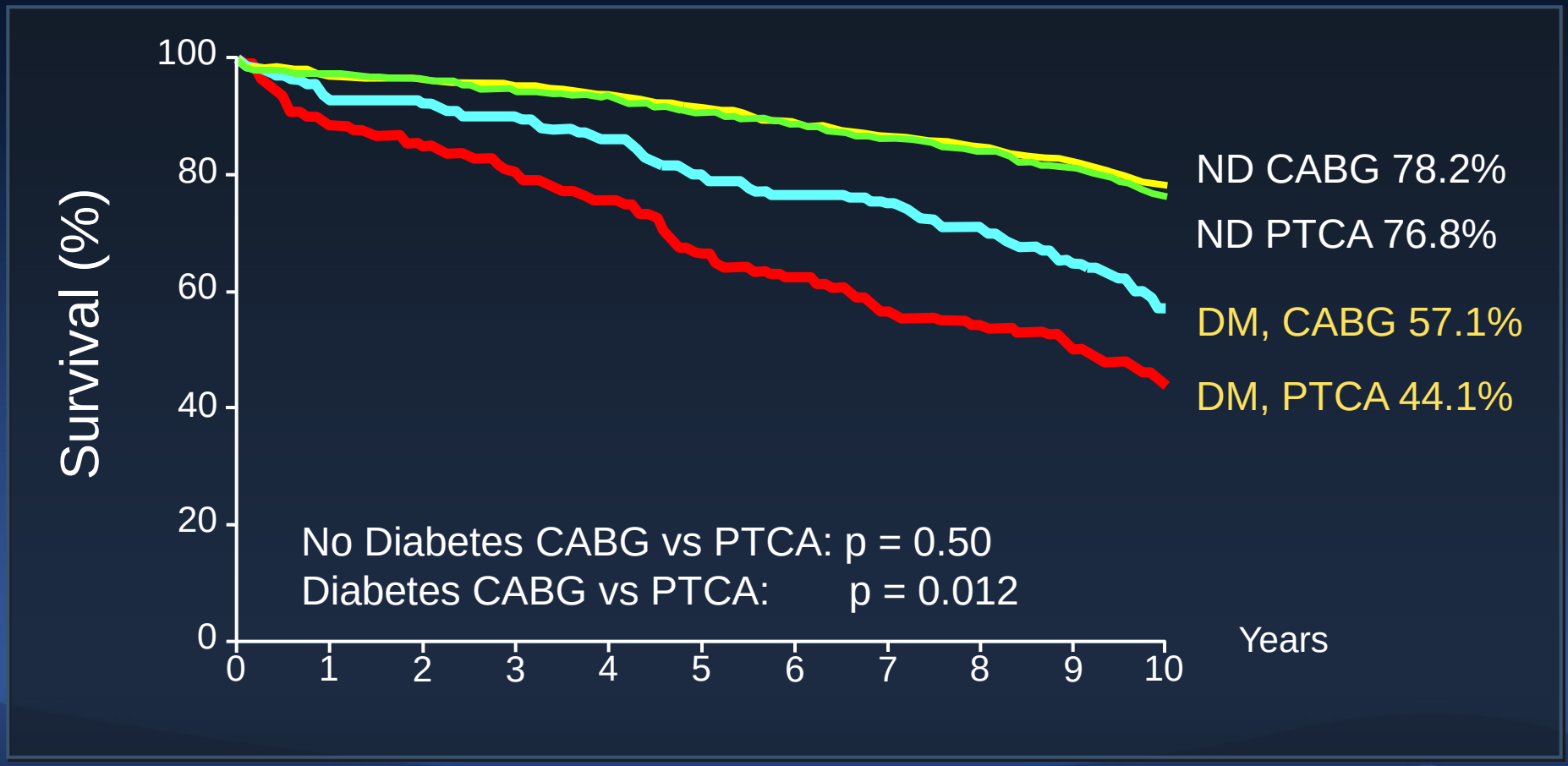
BMS vs. CABG
for Multi-Vessel Disease 2009

1. Outcomes of PCI is Comparable with CABG.
2. Stoke is Higher in CABG.
3. TVR is Higher in PCI.
4. Better Survival with CABG group,
   in Diabetics and Older Age (>65year

Back Ground of Diabetic Concern

BARI, 10-Year Survival

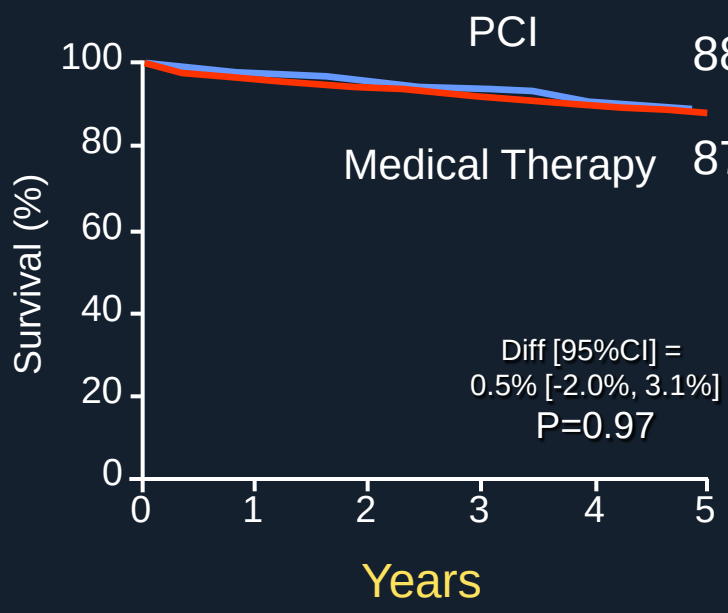
PTCA vs. CABG in Multi-Vessel Disease
From 1988 to 1991 (n=1,829)



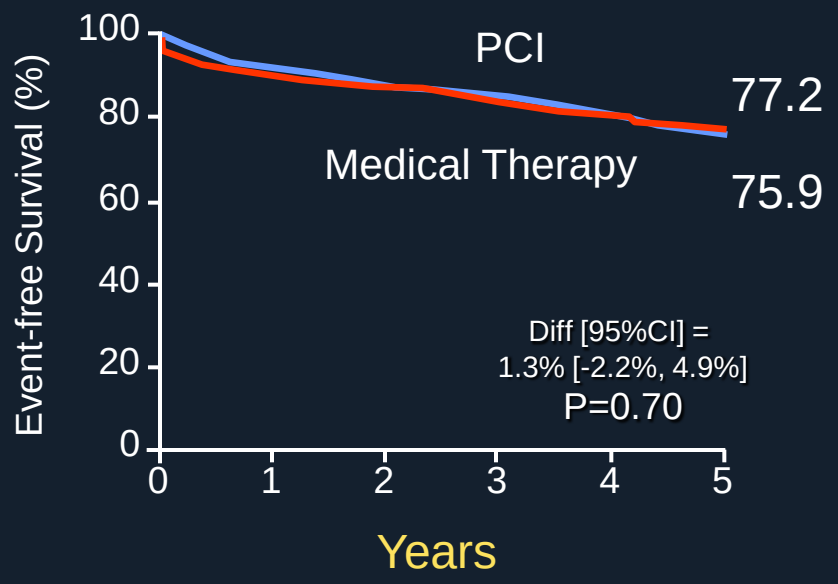
JACC. 2007 Apr 7;49(15):1600-6.

BARI 2D: PCI vs. Medical Treatment
(Lower Risk Diabetic Patients)

Survival



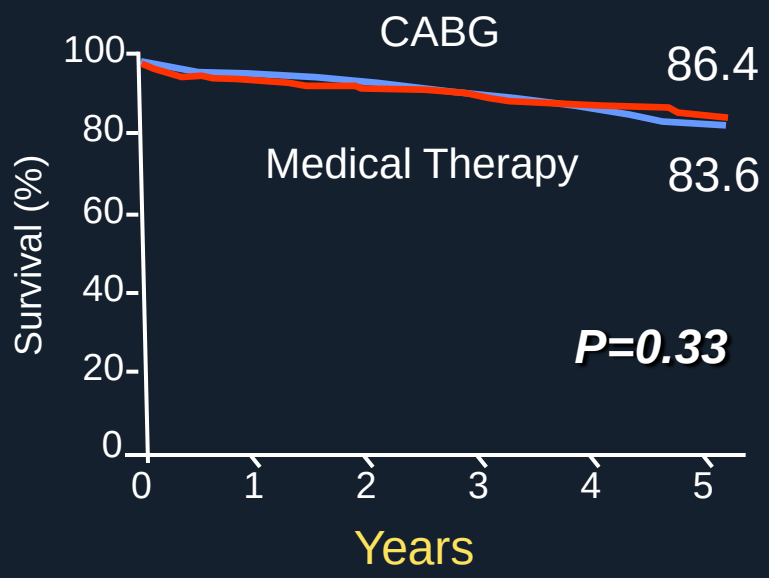
Freedom from MACE (death, MI, or stroke)



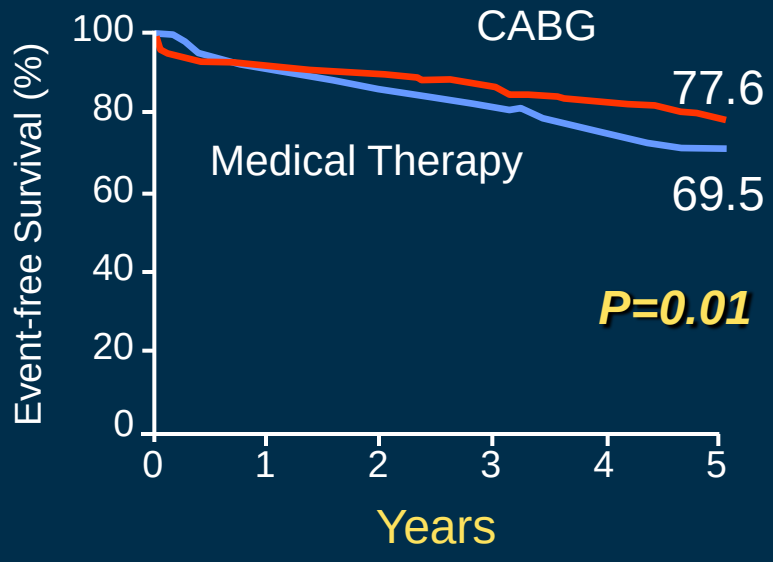
The BARI 2D Study Group. *NEJM* 2009;360:2503-15

BARI 2D: CABG vs. Medical Treatment
(Higher Risk Diabetic Patients)

Survival

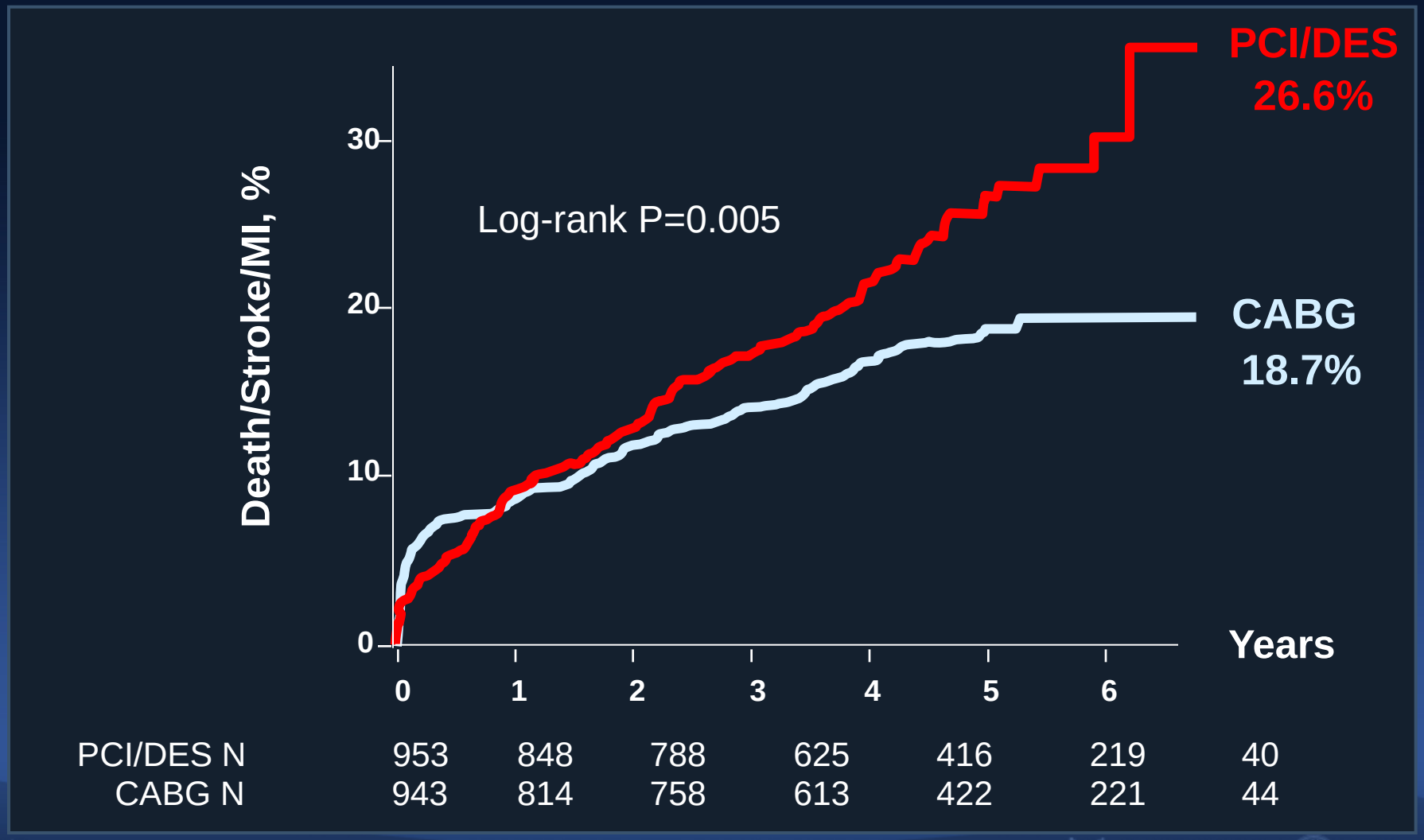


Freedom from MACE (death, MI, or stroke)



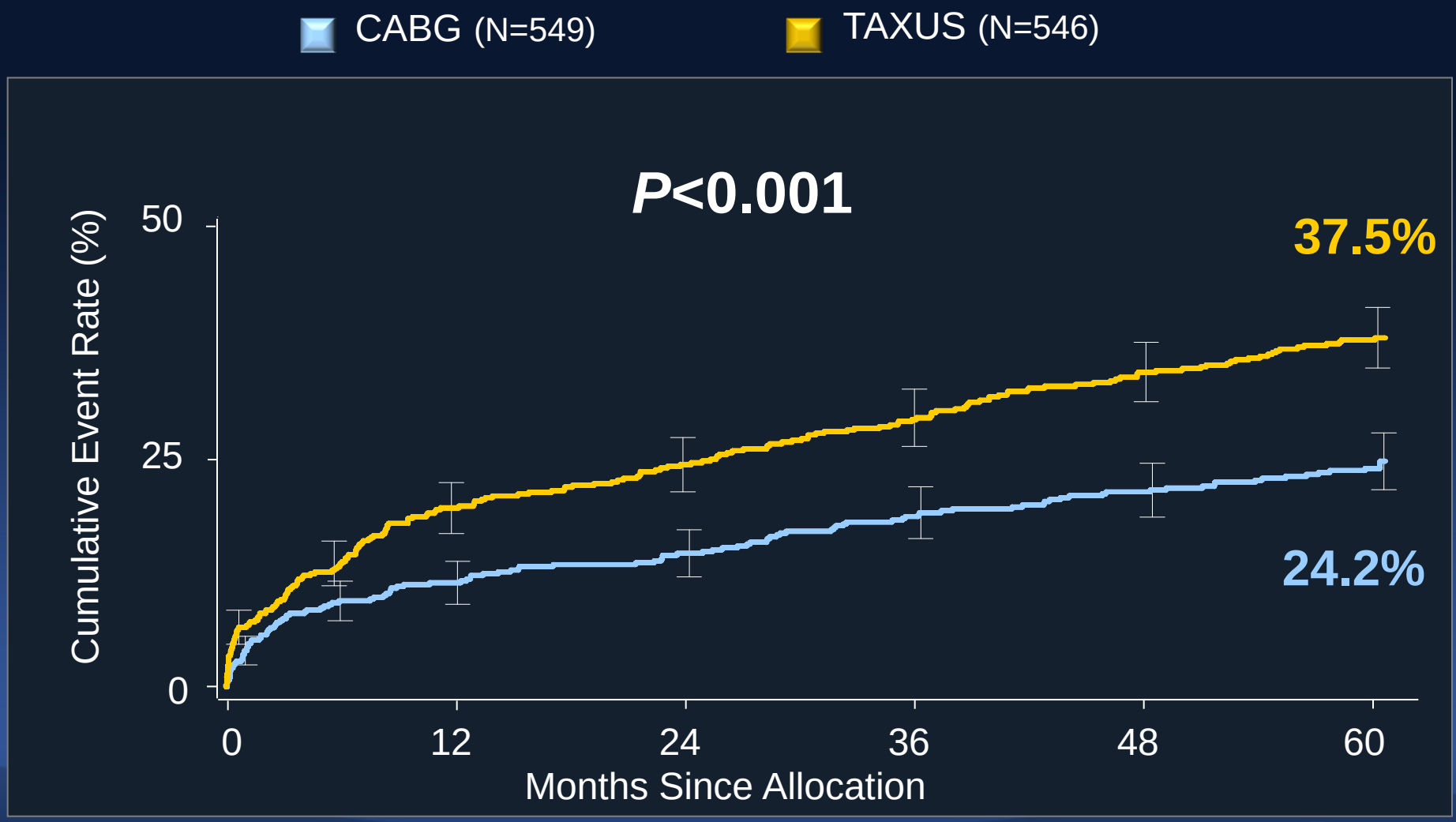
The BARI 2D Study Group. *NEJM* 2009;360:2503-15

FREEDOM *(Diabetics and MVD)*
Death / MI / Stroke at 5 Year



Farkouh et al, *NEJM* 2012 November 4

SYNTAX, *3VD Subset*
MACCE to 5 Year



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

ITT population

DES vs. CABG
for Multi-Vessel Disease 2015

CABG was superior to PCI with DESs in patients with diabetes and advanced CAD (predominantly, 3 VD).

Outcomes of PCI with BMS for MVD 2009 is Comparable with CABG, Outcomes of PCI with DES for MVD 2015 is Bad.

Could You Explain The Reasons Why ?

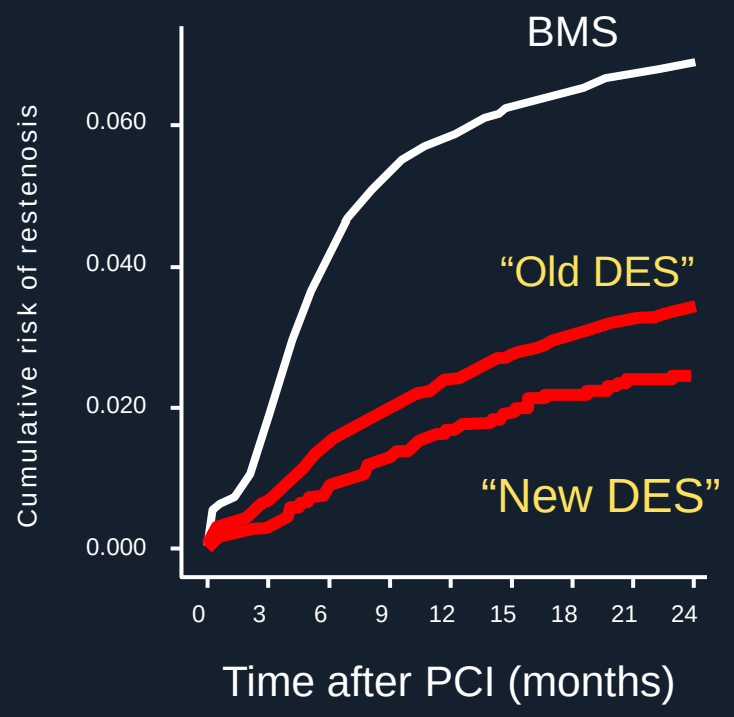
2003~2007, ***Old DES,***

BARI 2D	DES 35%, BMS 56%, Others 9%
FREEDOM	SES 49%, PES 41%, Others 10%
SYNTAX	PES 100%,

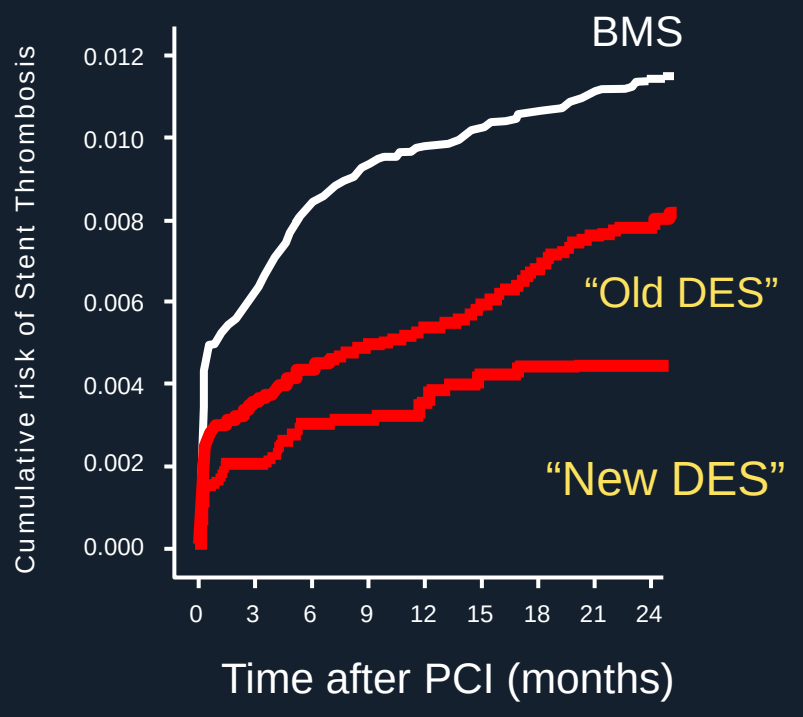
BMS vs. DES

New DES Is Better !

Restenosis



Definite ST



SCAAR Registry (94,384 pts)

Outcomes of PCI with BMS for MVD 2009 is Comparable with CABG, Outcomes of PCI with DES for MVD 2015 is Bad.

We Have Limited Data !

ESC Guidelines 2014
Elective PCI for 3 Vessel Disease

	CABG		PCI	
Recommendation according to extent of CAD	**Class**	**Level**	**Class**	**Level**
3 VD with a SYNTAX score ≤ 22	I	A	I	B
3 VD with a SYNTAX score 23 -32	I	A	III	B
3 VD with a SYNTAX score > 32	I	A	III	B

Reference; SYNTAX Study, *Patrick, SW et al, NEJM. 2009 March 5;360(10),*

SYNTAX *(3VD Subset)*

MACCE to 5 Year

	CABG	TAXUS	P value
MI	[illegible]	[illegible]	[illegible]
Death/CVA/MI	14.0%	22.0%	<0.001
Repeat revascularization	12.6%	25.4%	<0.001
CVA	3.4%	3.04%	0.66

Is the Game Over ?

Message from SYNTAX, 5 Year Outcomes

1. Complete Revascularization of All vessel,
2. Small Vessel (1.5 mm in Diameter) included,
3. Only Angio-Guided (>50%),
4. Too Many TAXUS stent (4.6/pt)

Make a Worst PCI Outcome !

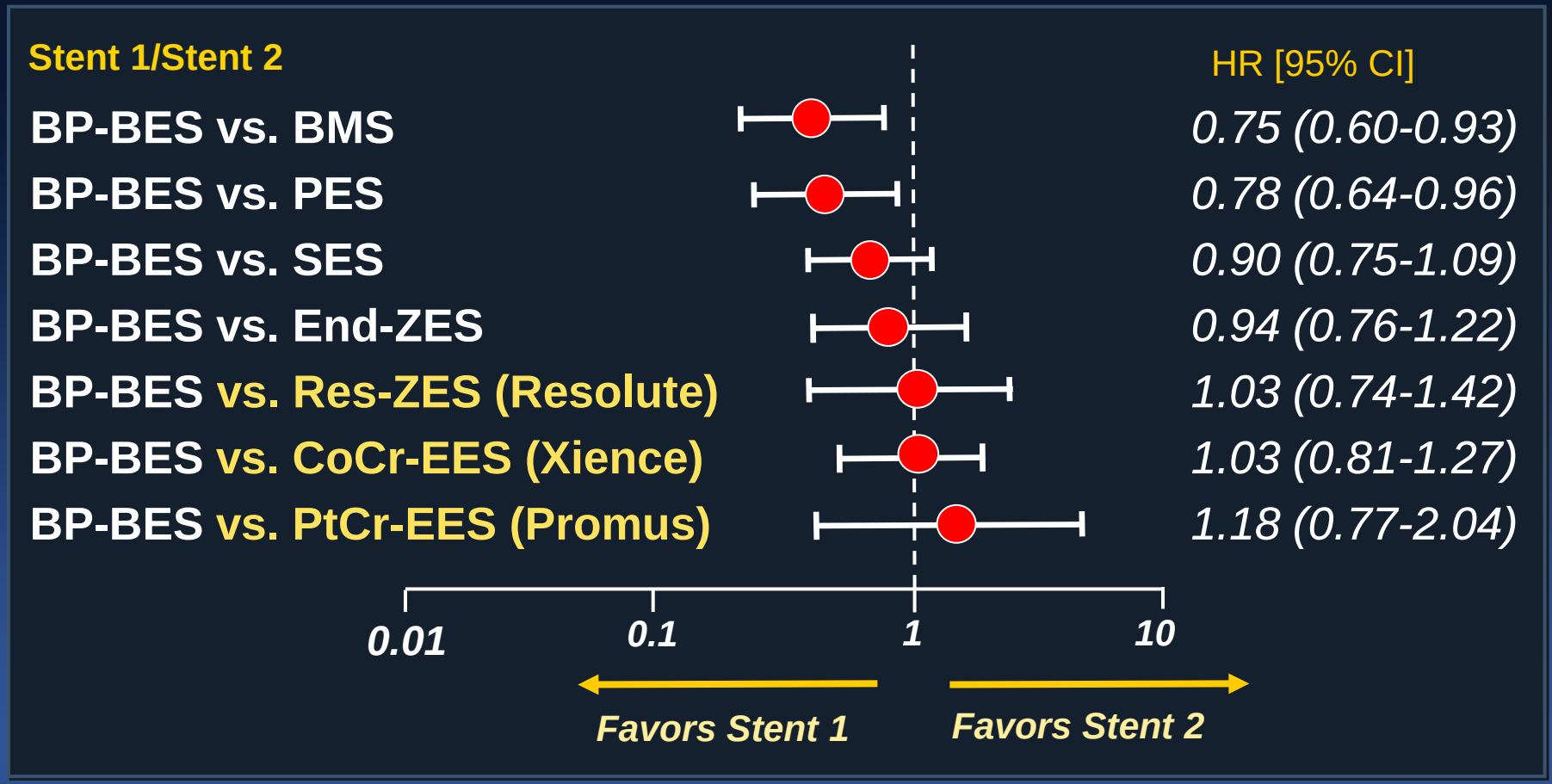
Future Direction,
How to Improve PCI Outcomes 2015 ?

1. **Better DES**
2. **Better Concept**

Cardiac Death and MI

Network Meta-analysis (89 RCTs, 85,490 pts)

New DES Is Better !

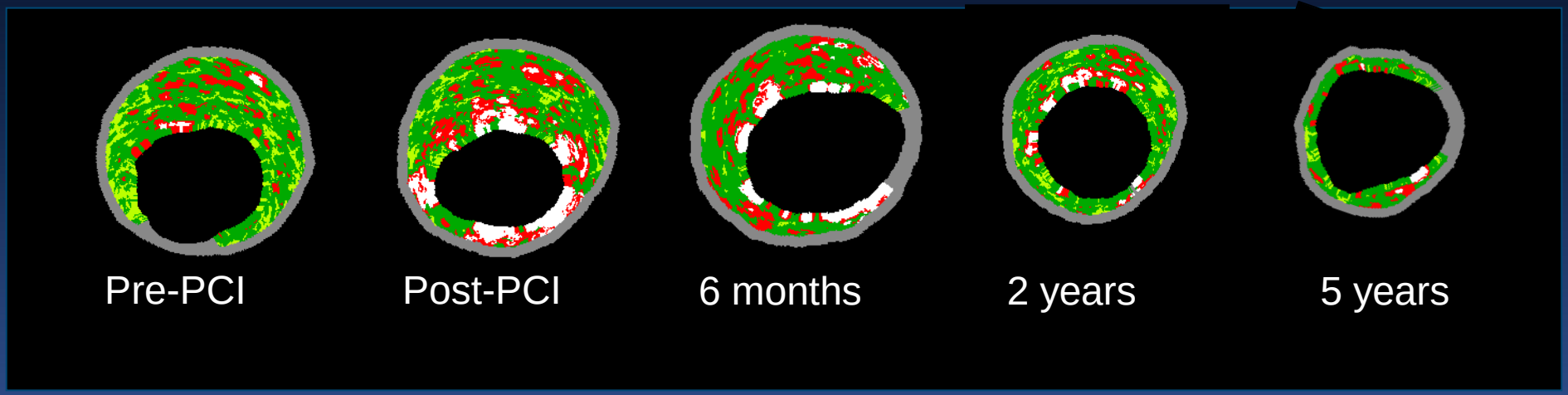


Palmerini et al. J Am Coll Cardiol 2014;63(4):299-307

BVS

Totally Different Concept !

Plaque Stabilization and Lumen Enlargement



BEST Study *(Better DES)*

Patients with
Multi-vessel Disease (Mainly 3VD)

R

PCI with Xience-V

CABG

Primary Endpoint at 2 years:
Death + MI + Repeat R + Stroke

PI : Park Seung-Jung

FUTURE Study *(BVS)*

Patients with
Multi-vessel Disease (Mainly 3VD)

R

PCI with BVS

CABG

Primary Endpoint at 2 years:
Death + MI + Repeat R + Stroke

Impact of FFR on 3 Vessel Disease
(Better Concept)

Functionally,
ant

Totally Different World !
Different Concept !

Tonino et al, JACC 2010;55:2816-2821

Use of FFR *(Better Concept)*

2013, ESC Guidelines

Recommendations	Class	Level
FFR is recommended to identify hemodynamically relevant coronary lesion(s) when evidence of ischemia is not available.	I	A
Revascularization of stenosis with FFR <0.80 is recommended in patients with angina symptoms or a positive stress test.	I	B
Revascularization of an angiographically intermediate stenosis without related ischemia or without FFR <0.80 is not recommended.	III	B

Use of IVUS *(Better Concept)*

Impact of IVUS-Guided

Death/MI, Benefit !
Saves Lives !

Meta					HR (p value)				
Jang et al. JACC interv	2014	3	12	24,869	0.79 (0.001)	0.64 (<0.001)	0.57 (<0.001)	0.59 (0.002)	0.76 (0.01)
Ahn et al. Am J Cardiol	2014	3	14	26,503	0.74 (<0.001)	0.61 (<0.001)	0.57 (<0.001)	0.59 (<0.001)	0.81 (0.046)

Reasonable Incomplete Revascularization *(Better Concept)*

Anatomy	Function	Physiology
Small vessels	Small ischemic area (<10%)	FFR > 0.80
Jailed asymptomatic side branch	Non-viable myocardium	
Not culprit artery	< 5% residual ischemic area,	

FAME3 *(Better Concept)*

Patients with Angiographically 3 Vessel Disease without LM

R

FFR Guided PCI + OMT

CABG

Primary Endpoint at 2 years: Death + MI + Repeat R + Stroke

PI ; William Fearon,MD

PCI vs. CABG in Multi-Vessel Disease, 2015

The Game Is Not Over,

Just Begun !

Thank You !!

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