15-Year Temporal Change of Left Main Revascularization : Lessons From ASAN MAIN Registry

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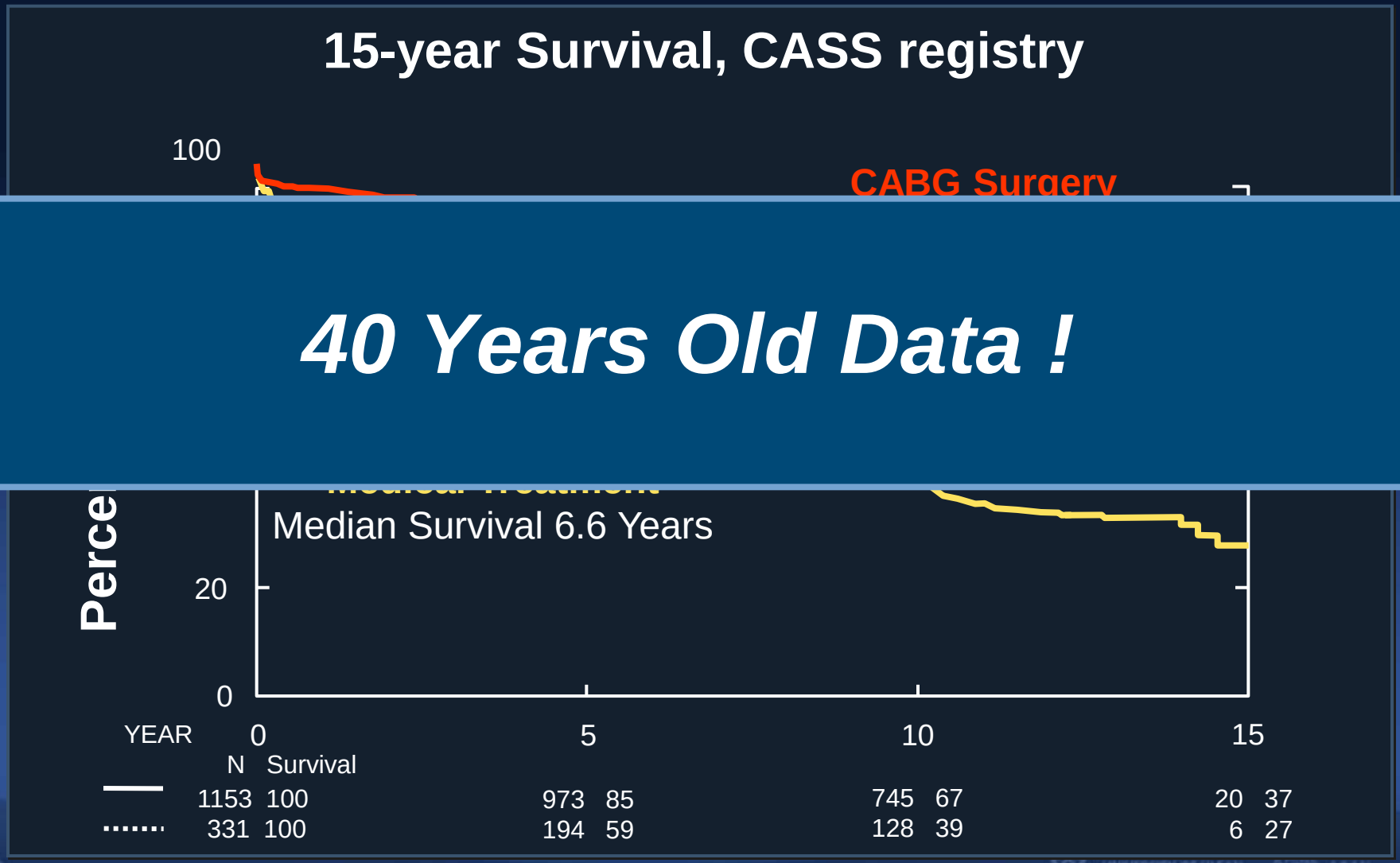
Background
"Surgery is Better" for LM Disease



40 Years Old Data !

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

Background

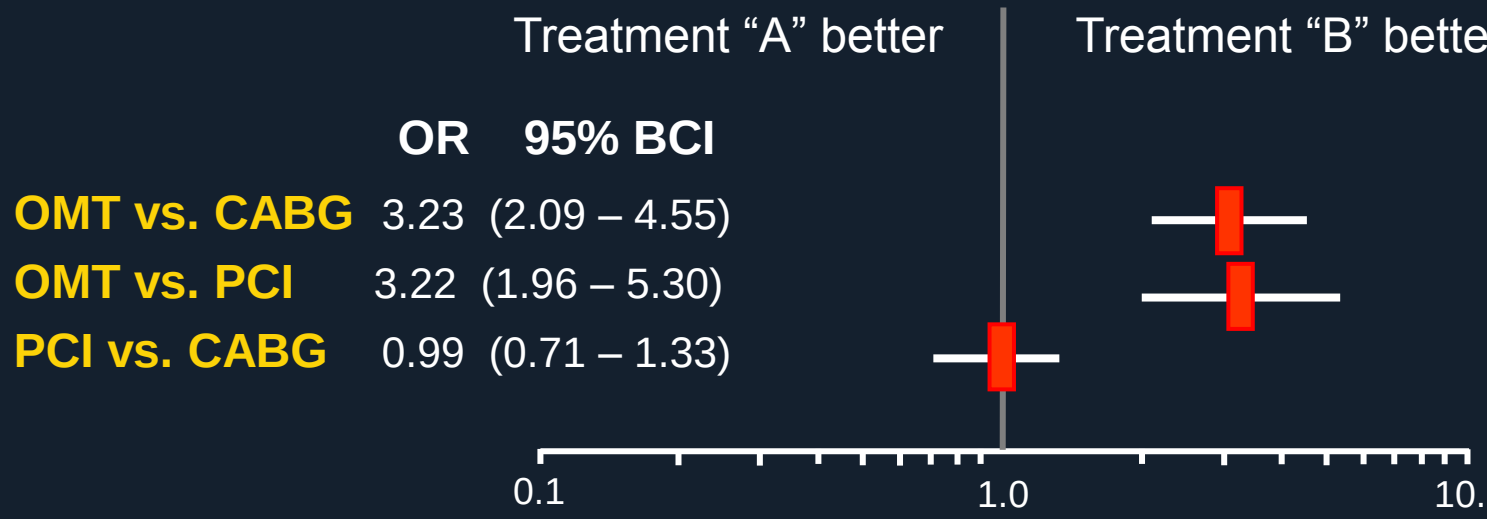
1. *CABG has been considered the standard care for the patients with LM disease.*
2. Since the introduction of PCI, coupled with the accumulation of experience, improved technology and pharmacology has led to this approach being rapidly evolved and broadly adopted in treatment for LM disease.
3. However, temporal changes in revascularization strategies (PCI or CABG) for LM disease are not well documented.

PCI vs CABG
For Left Main Disease

Survival Benefit of PCI or CABG Over Medication

Bayesian Net-work Meta-analysis, PCI vs. CABG vs. Medical Treatment
Posterior Median OR and 95% Bayesian Credible Intervals (BCI)

One-Year Mortality



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

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

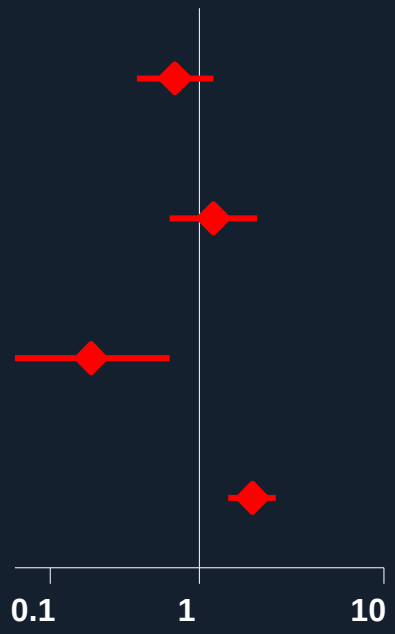
Meta-analysis (n=1,611) of RCT 2011
Outcomes at 1 Year

	PCI (n = 809)	CABG (n = 802)	OR (95% CI)	*P* Value
Primary Endpoint	14.5%	11.8%	1.28 (0.95-1.72)	0.11
Death	3.0%	4.1%	0.74 (0.43-1.29)	0.29
MI	2.8%	2.9%	0.98 (0.54-1.78)	0.95
Stroke	0.1%	1.7%	0.15 (0.03-0.67)	0.013
TVR	11.4%	5.4%	2.25 (1.54-3.29)	< 0.001

Capodanno D et al. JACC 2011;58:1426-1432

Meta-analysis (n=1,611) of RCT 2013
Outcomes at 2 Year

	PCI		CABG		Risk Ratio (95% CI)
	Event	Total	Events	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)



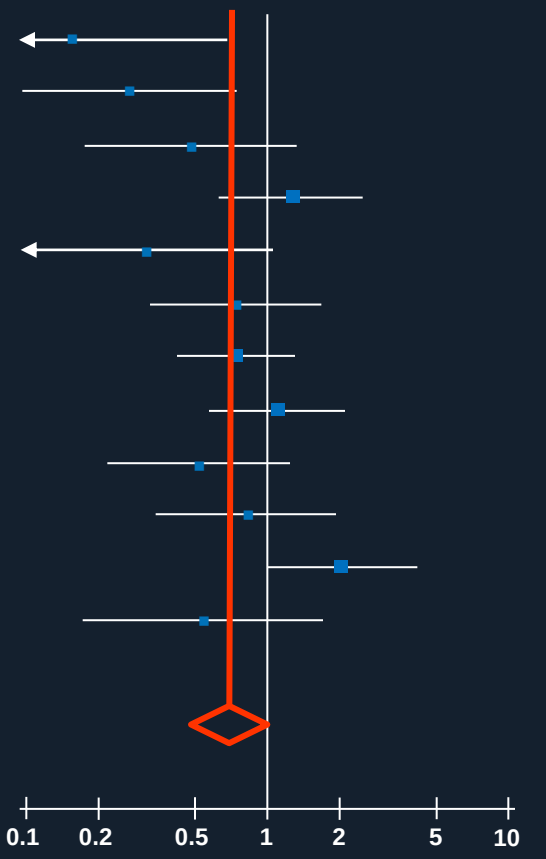
Favor PCI **Favor CABG**

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); $I^2=54\%$

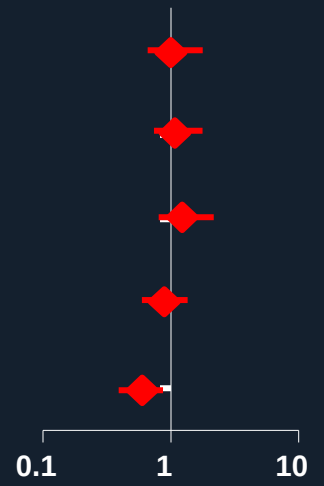
Test for overall effect: Z=1.97 ***(p=0.05)***



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

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

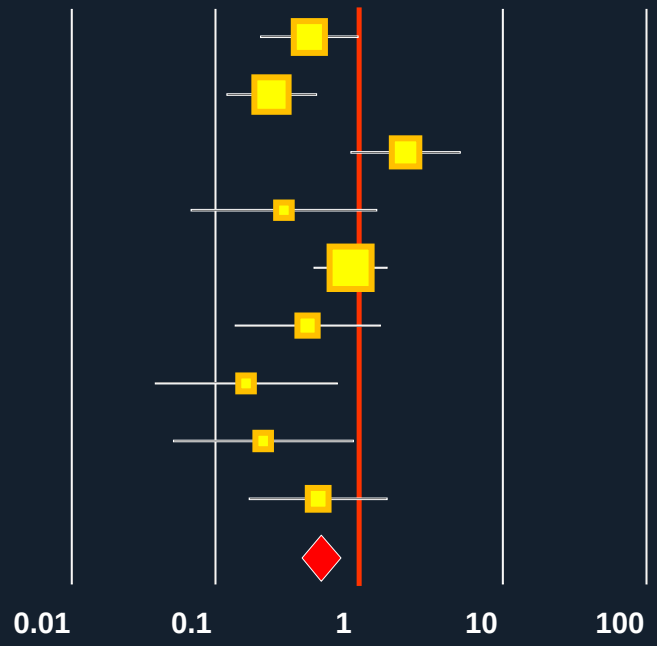
Time Point	No. of Studies	Sample Size	Statistics			
			Odds ratio	Lower limit	Upper limit	p-Value
1 Year	9	4515	0.938	0.659	1.337	0.72
2 Year	8	4953	1.011	0.739	1.383	0.95
3 Year	5	3104	1.149	0.608	1.633	0.44
4 Year	4	5329	0.829	0.619	1.110	0.20
5 Year	5	3360	0.641	0.512	0.803	<0.001



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)	-	-	4.20 (2.21,7.97)	1.25 (0.81,1.94)
		3 yrs	1.11 (0.66,1.86)	-	-	3.30 (0.96,11.3)	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)	-	-	3.60 (P<0.001)	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 (0.18,1.63)
		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)	0.65 (0.52,0.82)
		~ 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)

Outcomes of PCI Is Getting Better Over Time !

Temporal Changes of PCI vs. CABG For LM Disease

Data from ASAN MAIN Registry

Objective

To evaluate temporal trends in revascularization strategies and outcomes in patients who received PCI or CABG for LMCA stenosis.

Study Population (1)

The ASAN MAIN Registry is a single center registry to investigate the outcomes of PCI and CABG for patients with LMCA stenosis.

Between January 1995 and December 2010, a total of 2,630 patients were enrolled.

Study Population (2)

Inclusion Criteria

- All consecutive patients who have significant LMCA stenosis with a visual estimated DS of >50%.
- Revascularization was clinically indicated.

Exclusion Criteria

- Concomitant valvular or aortic surgery
- AMI within 24 hours
- Cardiogenic shock
- life expectancy <12 months.

Study Endpoints

Primary Endpoint

A Composite of MACCE including

- Death
- Myocardial Infarction
- Stroke
- Repeat Revascularization

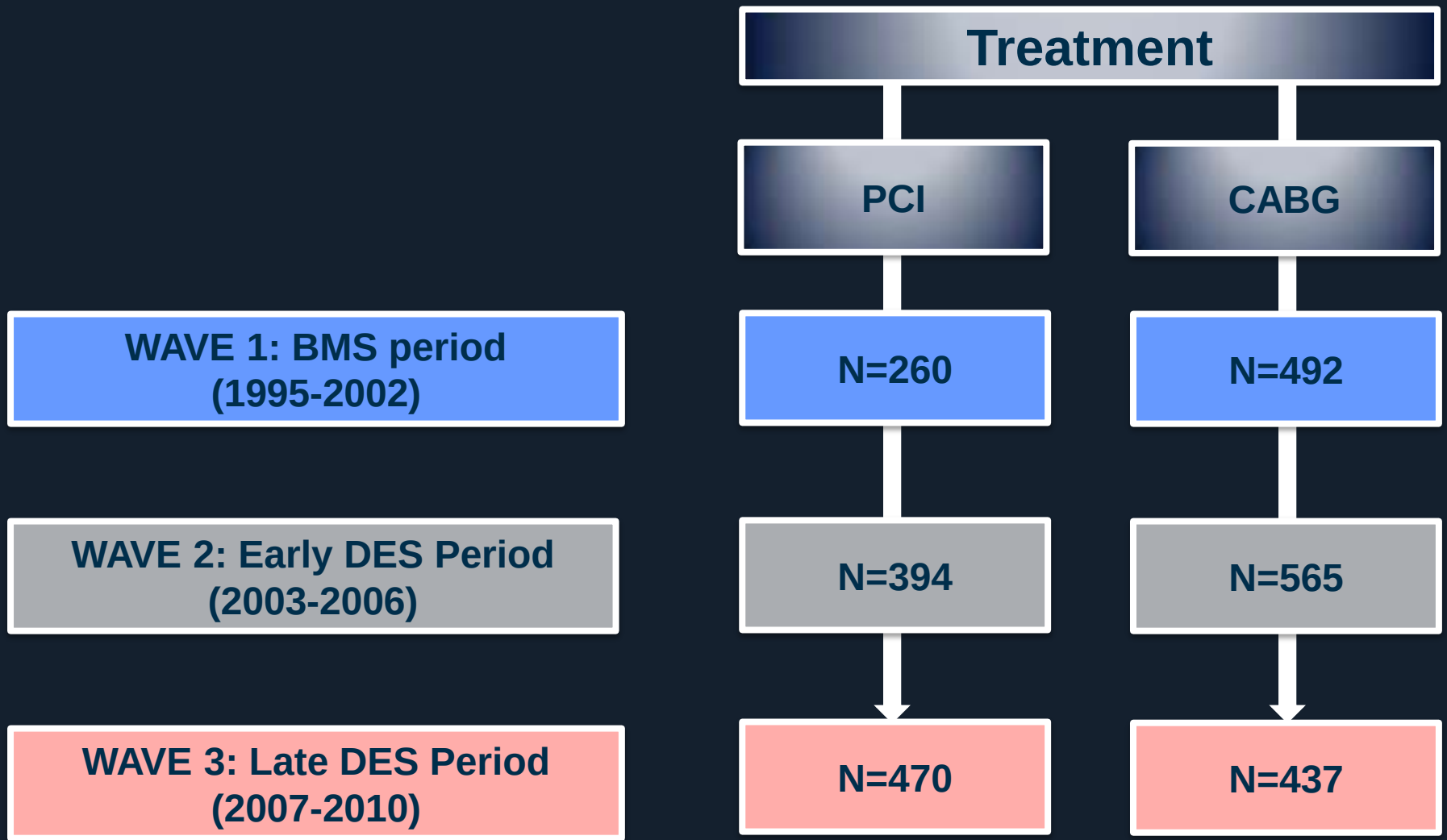
Secondary End Point

- The composite of Death, MI, and stroke
- Any Repeat Revascularization
- Changes in Treatment Strategies

Follow-up

- Clinical, angiographic, procedural, and outcome data were retrospectively recorded in the dedicated PCI database by independent research personnel.
- Patients were clinically followed up at 1, 6, 12, and 24 mons.
- All outcomes of interest were carefully verified and adjudicated by independent clinicians.

Study Periods



Baseline Clinical Characteristics

	PCI			CABG		
	Wave 1 (N=260)	Wave 2 (N=394)	Wave 3 (N=470)	Wave 1 (N=492)	Wave 2 (N=565)	Wave 3 (N=437)
Age	56.7±11.3*	60.9±11.3	63.2±10.5	62.0±9.4*	63.6±8.6	65.1±9.3
Male gender	171 (65.8)*	285 (72.3)	358 (76.2)	380 (77.2)	424 (75.0)	332 (76.0)
BMI, kg/m2	24.5±3.1	24.7±3.4	24.5±2.9	24.5±2.7	24.6±3.0	24.4±2.8
Atrial fibrillation	5 (1.9)	8 (2.0)	11 (2.3)	13 (2.6)	9 (1.6)	9 (2.1)
Hypertension	111 (42.7)*	214 (54.3)	286 (60.9)	260 (52.8)	335 (59.3)	280 (64.1)
Diabetes	58 (22.3)*	125 (31.7)	176 (37.4)	164 (33.3)*	230 (40.7)	179 (41.0)
Smoking	81 (31.2)	104 (26.4)	130 (27.7)	162 (32.9)*	149 (26.4)	115 (26.3)
Hypercholesterolemia	94 (36.2)*	152 (38.6)	265 (56.4)	184 (37.4)*	271 (48.0)	208 (47.6)
Previous MI	38 (14.6)*	34 (8.6)	42 (8.9)	83 (16.9)	93 (16.5)	52 (11.9)

* p<0.05

Baseline Clinical Characteristics

	PCI			CABG		
	Wave 1 (N=260)	Wave 2 (N=394)	Wave 3 (N=470)	Wave 1 (N=492)	Wave 2 (N=565)	Wave 3 (N=437)
Previous PCI	36 (13.8)	74 (18.8)	90 (19.1)	51 (10.4)	84 (14.9)	65 (14.9)
Previous cardiac OP	0	1 (0.3)	6 (1.3)	0	2 (0.4)	0
Previous stroke	8 (3.1)*	27 (6.9)	41 (8.7)	42 (8.5))	46 (8.1)	44 (10.1)
Chronic lung disease	4 (1.5)	12 (3.0)	10 (2.1)	51 (10.4)*	84 (14.9)	65 (14.9)
Chronic renal failure	5 (1.9)	9 (2.3)	12 (2.6)	10 (2.0)*	24 (4.2)	22 (5.0)
Clinical presentation						
Stable angina	77 (29.6)*	178 (45.2)	270 (57.4)	59 (12.0)*	104 (18.4)	196 (44.9)
Unstable angina	156 (60.0)	160 (40.6)	148 (31.5)	401 (81.5)	408 (72.2)	202 (46.2)
NSTEMI	17 (6.5)	25 (6.3)	28 (6.0)	22 (4.5)	37 (6.5)	25 (5.7)
STEMI	4 (3.8)	31 (7.9)	24 (5.1)	10 (2.0)	16 (2.8)	14 (3.2)

* p<0.05

Baseline Angiographic Characteristics

	PCI			CABG		
	Wave 1 (N=260)	Wave 2 (N=394)	Wave 3 (N=470)	Wave 1 (N=492)	Wave 2 (N=565)	Wave 3 (N=437)
Lesion location						
Ostial or shaft	139 (53.5)*	154 (39.1)	155 (33.0)	147 (29.9)	164 (29.0)	111 (25.4)
Bifurcation	121 (46.5)	240 (60.9)	315 (67.0)	345 (70.1)	401 (71.0)	326 (74.6)
Disease extent						
Left main only	102 (39.2)*	63 (16.0)	38 (8.1)	34 (6.9)*	13 (2.3)	11 (2.5)
Left main plus 1VD	75 (28.8)	86 (21.8)	107 (22.8)	51 (10.4)	42 (7.4)	28 (6.4)
Left main plus 2VD	55 (21.2)	113 (28.7)	184 (39.1)	122 (24.8)	100 (17.7)	77 (17.6)
Left main plus 3VD	28 (10.8)	132 (33.5)	141 (30.0)	285 (57.9)	410 (72.6)	321 (73.5)
Ejection fraction, %	62.1±8.2*	60.5±9.0	59.1±8.2	57.9±11.7*	55.2±11.9	56.4±10.8

* p<0.05

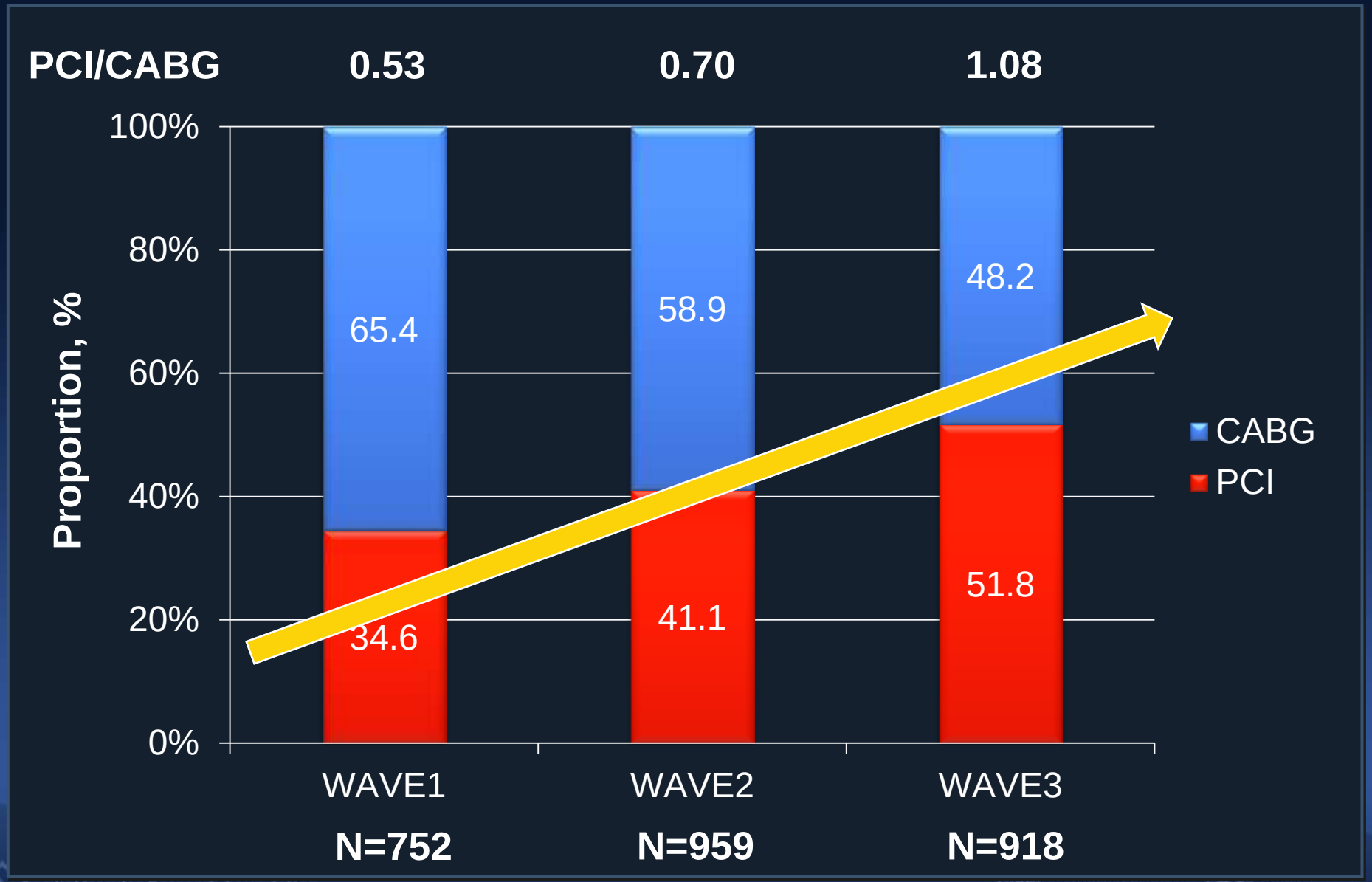
Procedural Characteristics of PCI

	Wave 1 (N=260)	Wave 2 (N=394)	Wave 3 (N=470)	P value
Use of IVUS	207 (79.9)	341 (86.8)	406 (86.6)	0.028
Stent technique				<0.001
Left main stent only	169 (65.0)	110 (28.0)	68 (14.5)	
Simple cross over	54 (20.8)	168 (42.7)	283 (60.3)	
Two-stent technique	37 (14.2)	115 (29.3)	108 (25.1)	
Total stent number in LM	1.3±0.6	1.7±0.9	2.0±1.0	<0.001
Total stent length in LM	16.5±9.5	36.2±25.0	46.3±24.8	<0.001
Total stent number per patient	1.6±0.9	2.4±1.4	2.6±1.4	<0.001
Total stent length per patient	22.5±15.3	54.2±38.7	63.0±36.7	<0.001
Stent type				<0.001
BMS	260 (100)	27 (6.9)	12 (2.6)	
1st DES	0	365 (92.6)	217 (46.1)	
2nd DES	0	2 (0.6)	240 (51.1)	

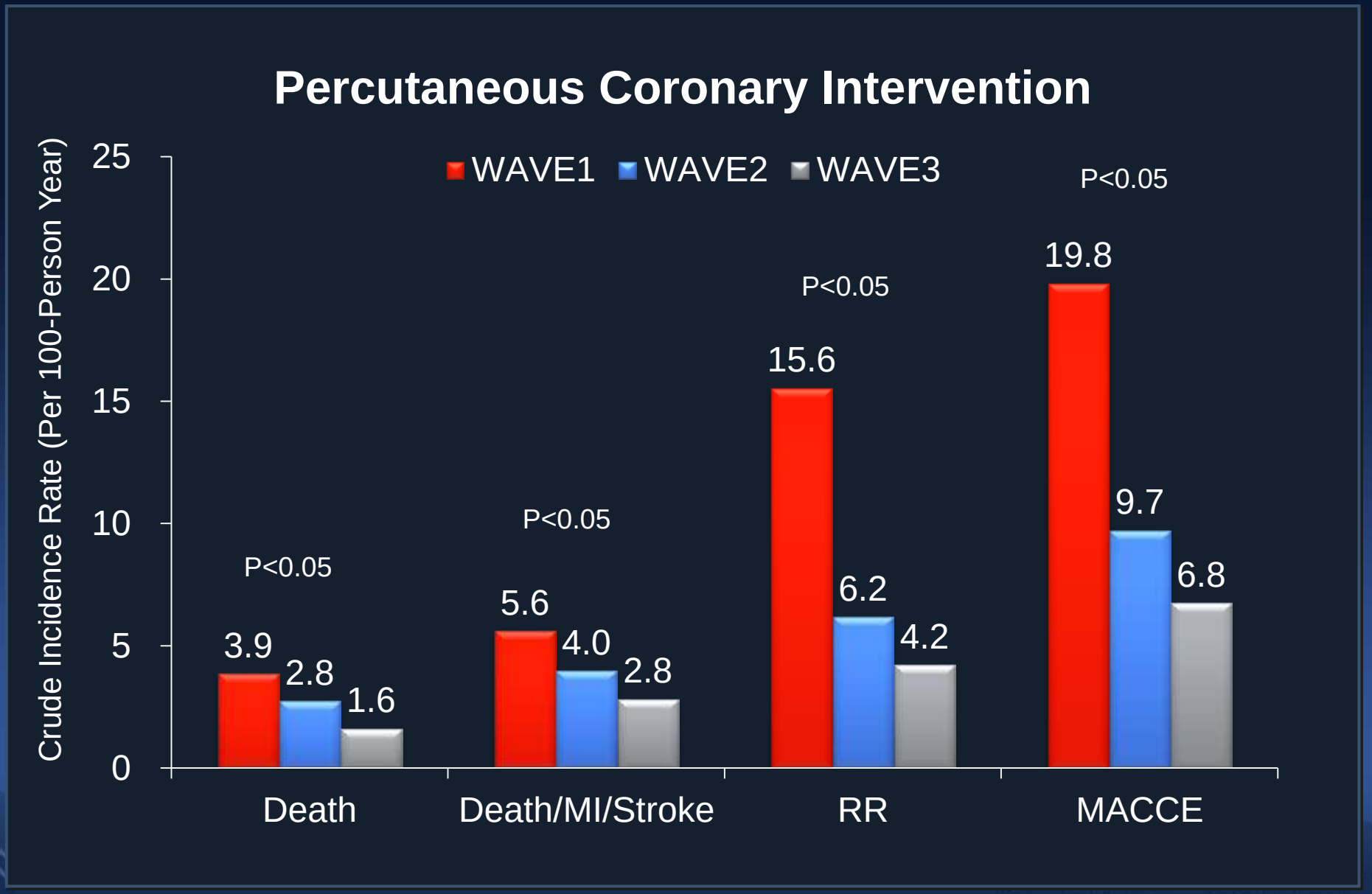
Procedural Characteristics of CABG

	Wave 1 (N=492)	Wave 2 (N=565)	Wave 3 (N=437)	P value
Number of conduit	3.8±1.2	3.2±1.0	2.8±0.9	<0.001
Number of arterial conduit	1.9±1.3	2.4±0.9	1.8±0.8	<0.001
Number of vein conduit	1.9±1.8	0.8±0.7	1.1±1.0	<0.001
Internal thoracic artery	425 (86.4)	542 (95.9)	422 (96.6)	<0.001
Off-pump	73 (14.8)	204 (36.1)	292 (66.8)	<0.001

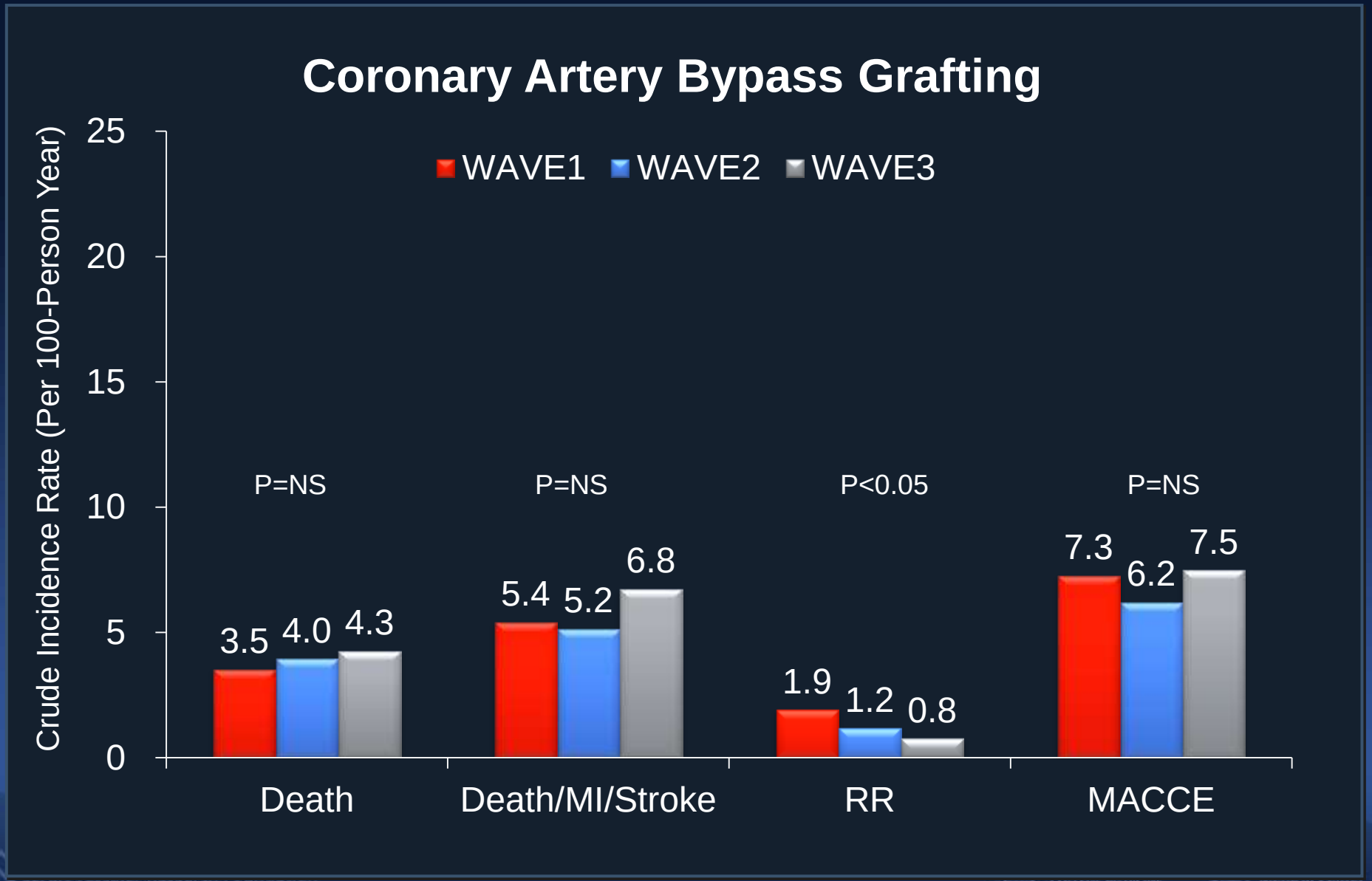
Revascularization Strategy



Crude Incidence Rate (Per 100-Person Year)



Crude Incidence Rate (Per 100-Person Year)



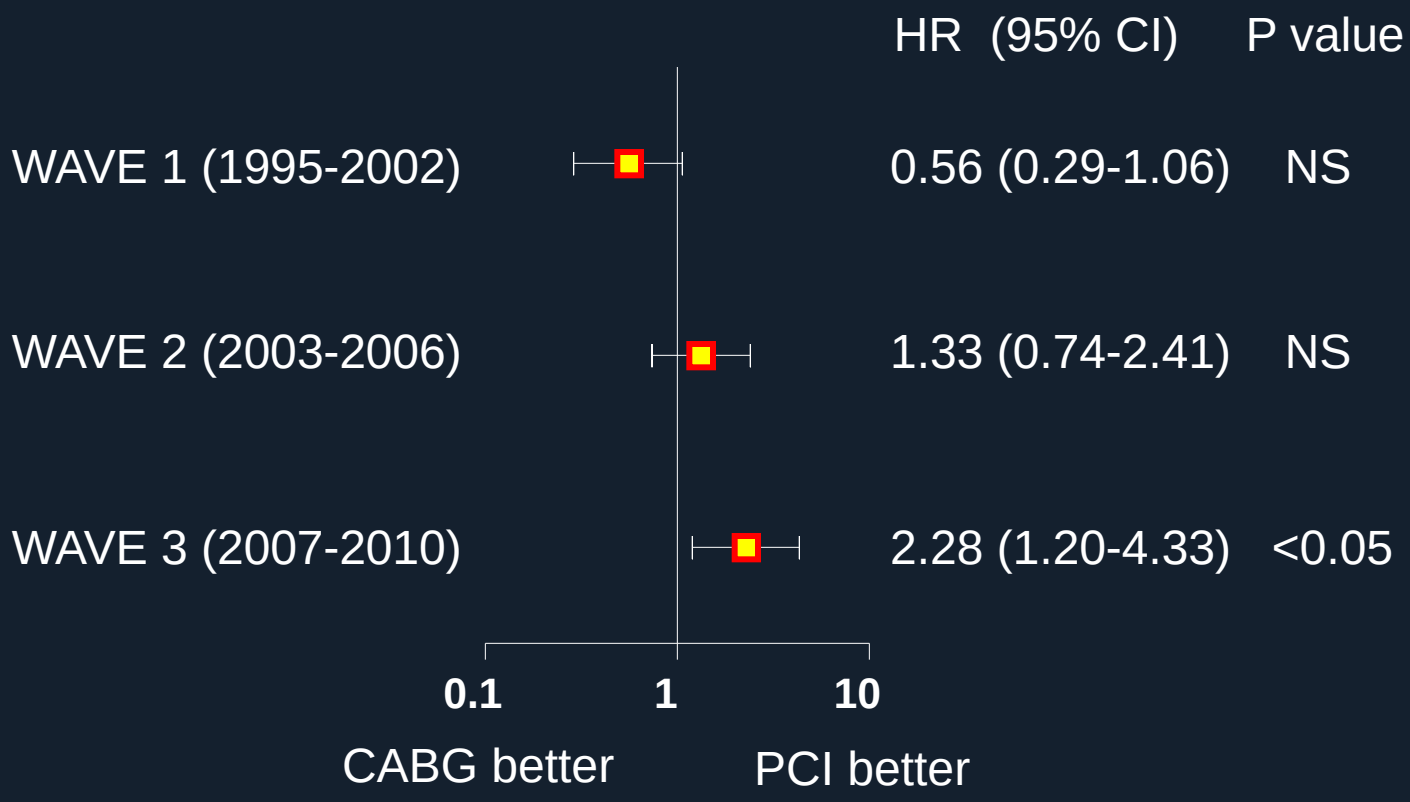
Risk Adjusted Incidence Rate

(Per 100-Person Year)

		Wave 1	Wave 2	Wave 3	Adjusted HR (95% CI)	P for trend
PCI	Death	4.51	2.13	1.62	0.60 (0.41–0.87)	0.008
	Death, MI, or Stroke	6.71	3.61	2.83	0.65 (0.48–0.89)	<0.001
	Repeat Revascularization	14.03	5.99	4.24	0.54 (0.43–0.67)	<0.001
	MACCE	20.18	9.28	6.77	0.57 (0.47–0.70)	<0.001
CABG	Death	4.35	3.77	4.28	0.99 (0.77–1.29)	0.97
	Death, MI, or Stroke	6.09	5.07	6.75	1.06 (0.85–1.31)	0.60
	Repeat Revascularization	2.14	1.24	0.79	0.60 (0.38–0.95)	0.028
	MACCE	7.63	6.03	7.50	0.99 (0.82–1.20)	0.92

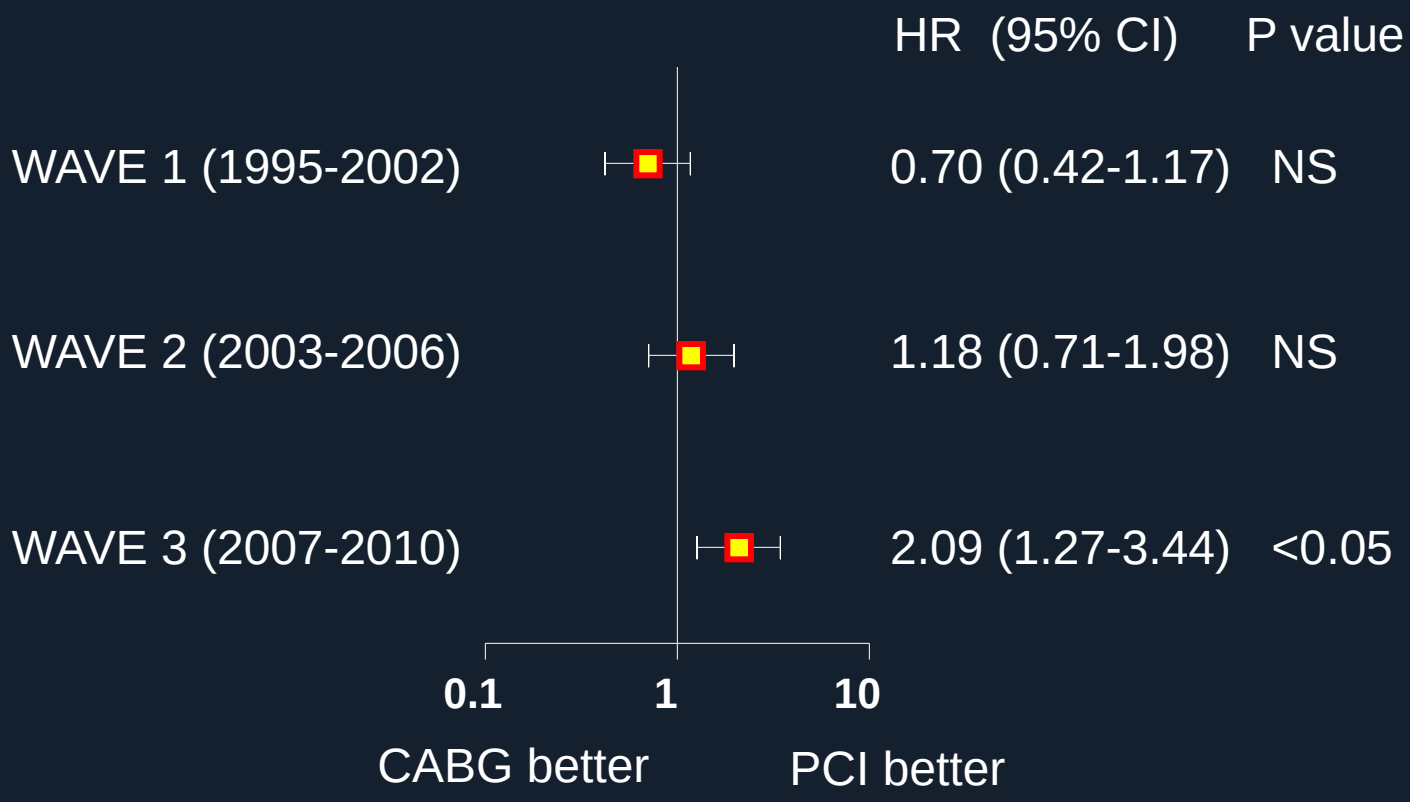
Risk Adjusted Hazard Ratio

Death



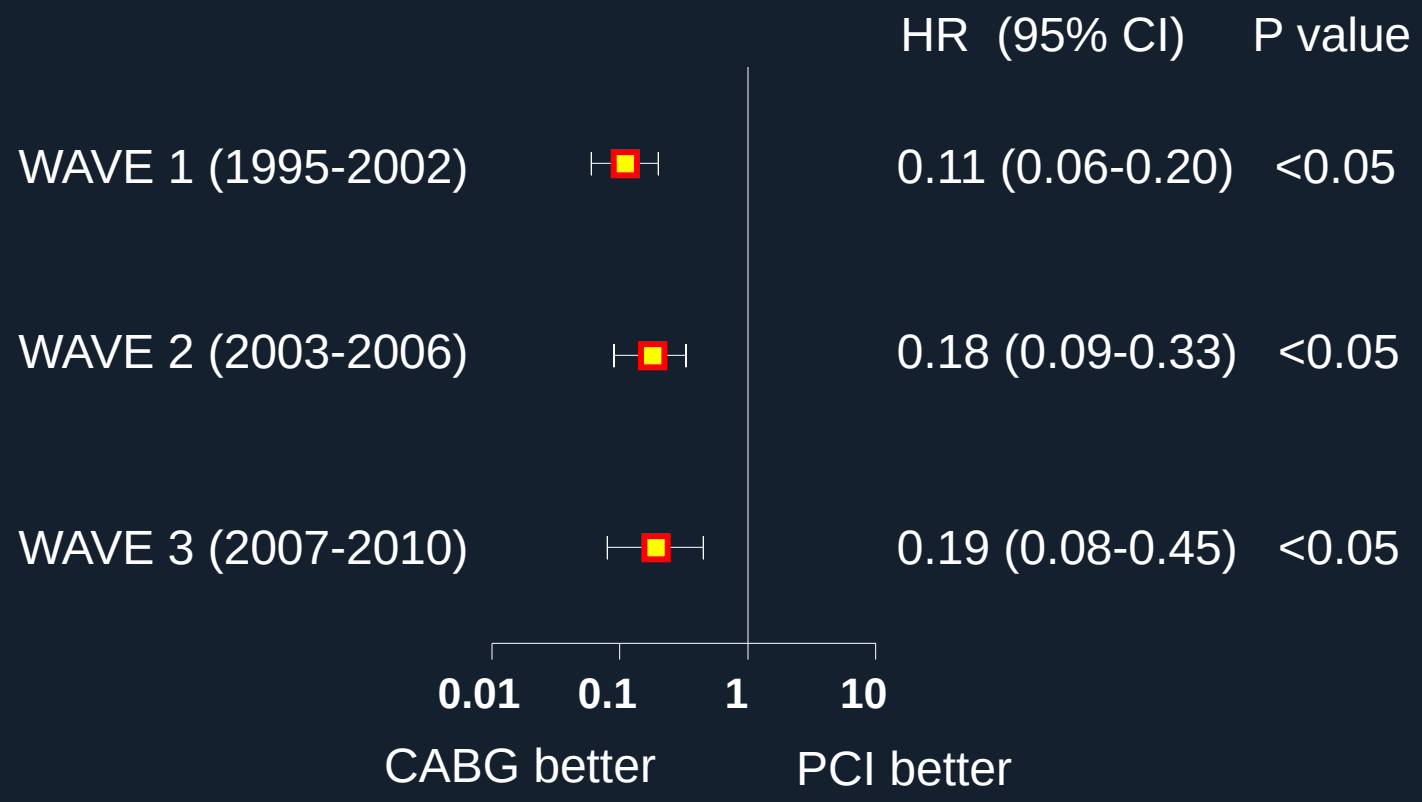
Risk Adjusted Hazard Ratio

Death, MI or Stroke



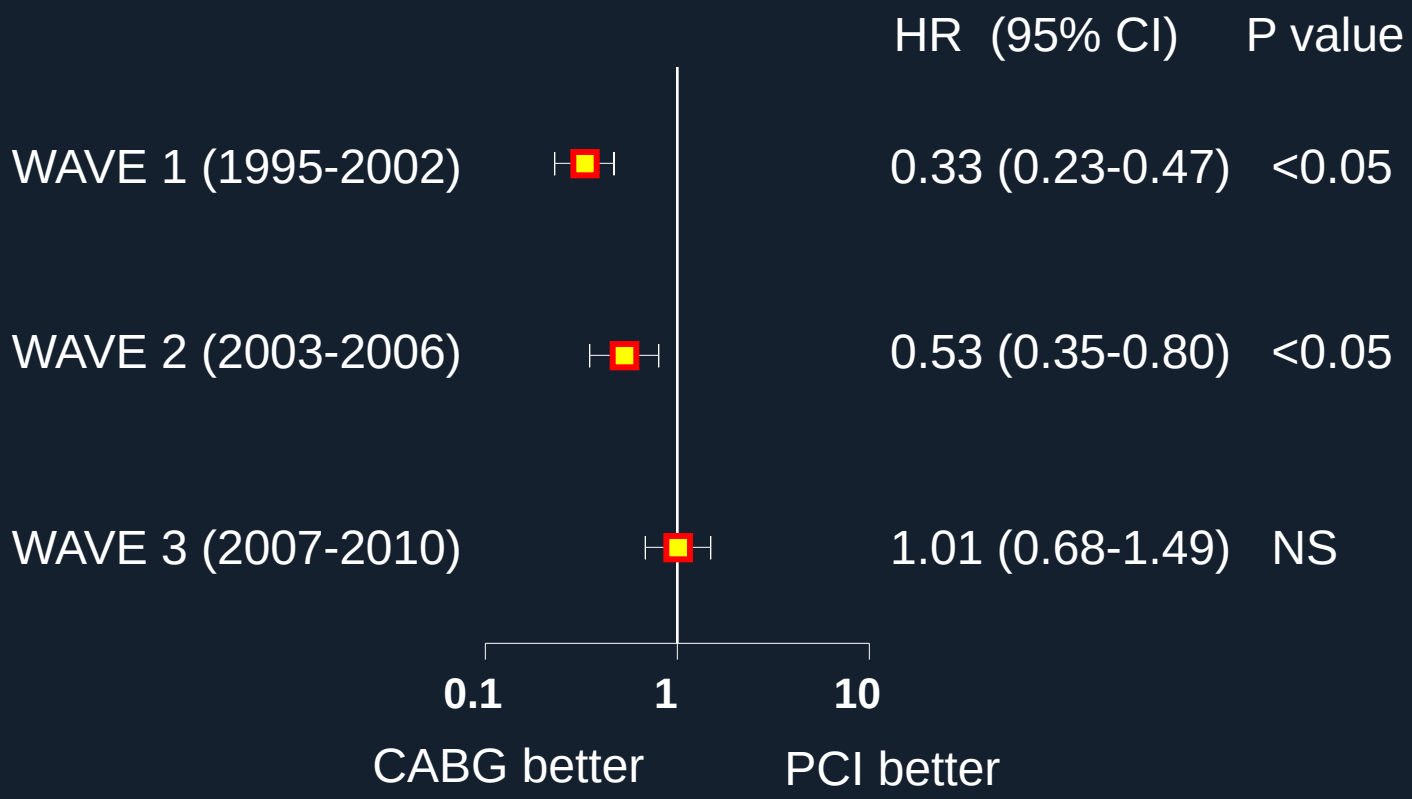
Risk Adjusted Hazard Ratio

Repeat Revascularization



Risk Adjusted Hazard Ratio

MACCE



Why ?

Outcomes of PCI Have Improved !

1. LM Disease is *Totally Different Disease Entity*. Proximally Located Large Vessel. Easy to Approach and Easy to Perform the Procedures.
2. *DES* is *A Clear Revolution.*
3. *Better Concept of PCI with Use of FFR and IVUS*, *the Accumulation of Experience, Improved Technology and Pharmacology* Can Make A Good Clinical Outcomes of PCI.

Conclusion

- This large study demonstrates that *clinical outcomes of patients receiving PCI for ULMCA stenosis have improved* with respect to the safety and efficacy of the procedure during the last 15 years, although patient comorbidities and ULMCA stenosis complexity have worsened over time.
- In addition, *the gap in treatment effect between PCI and CABG has decreased.* As a result, PCI could have been successfully substituted for CABG in a significant portion of revascularizations for ULMCA stenosis.

Thank You !!

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