A Collaborative Systemic Review and Meta-Analysis of A Results from 3976 Patients:

BMS vs. DES vs. CABG
Overall Safety and Efficacy Issues of Left Main Intervention

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Background

- Left main coronary artery (LMCA) disease is associated with a poor prognosis when treated medically, and its presence is indicated for coronary artery bypass surgery (CABG).

- Several registries data show promising results of percutaneous coronary intervention (PCI) with stent implantation in terms of safety and feasibility for patients with LMCA disease.

Background

- Despite the favorable outcomes after bare-metal stents (BMS) or drug-eluting stents (DES), subsequent restenosis or possible stent thrombosis limited the widespread use of PCI in LMCA disease.

- Also, previous studies about LMCA intervention were hampered by small numbers of patients, limited duration of follow-up or an retrospective observational study design.

Objective

- Despite the existence of multiple observational studies comparing DES, BMS, or CABG, none of them was individually powered to assess the comparative efficacy of each revascularization strategies in LMCA disease.

- Therefore, by aggregating all available registry data, we performed a collaborative systemic review and meta-analysis to assess the risk-benefit balance of PCI, in itself and in comparison with each PCI intervention (BMS vs. DES) and CABG.

Literature search and study selection

- We searched PUBMED, MEDLINE, EMBASE, and SCOPUS and Websites dedicated to dissemination of results from cardiovascular studies (www.acc.org, www.tctmd.com, www.theheart.org, www.clinicaltrialresults.org) for relevant full reports in any language (from inception to June 2007).

- In addition, we hand searched reference lists and checked relevant reviews and book chapters.

Literature search and study selection

- Two investigators (DWP, SCY) independently assessed reports for eligibility.

- To be included in the analysis, data had to be clinical studies in individuals with symptoms or signs of myocardial ischemia due to LMCA disease, comparing DES with BMS or DES with CABG, or reporting DES or BMS only for unprotected LMCA disease.

- Studies had to have ≥ 30 patients and $\geq$ at least 6 months clinical follow-up duration.

- Duplicate publication, only PCI with balloon PTCA or DCA, only high-risk patients, only protected LMCA, ongoing/unpublished studies, and incomplete data reporting for analysis were excluded.

Pre-Specified End Points

- <u>Study end points</u>
  - Overall mortality
  - Myocardial infarction (MI), including Q-wave or Non-Q-wave MI
  - Target vessel revascularization (TVR)
  - MACE: composite of death, MI, or TVR

** In studies with non-availability of rates of TVR, we used rates of target lesion revascularization as a proxy measure.

** The number of patients experiencing an event and the overall number of patients at risk were recorded separately two time period (<u>within 1 months</u> & <u>within 1 year</u>).

Statistical Analysis

- The rates of mortality, MI, and TVR, as defined in each study, were pooled, and Pearson chi-square values were calculated for each of these individual end points.
- For MACE, there was no double counting of events.
- Generalized linear mixed effect model (GLMM) was used to combine each result of individual treatment modality and overall.
- Pooled estimates of relative risk (RR) were obtained by calculating the weighted average of the logarithm of RR.
- Breslow-Day test was used to address the heterogeneity among the registries.

Results

Identification of eligible studies

232 potentially eligible reports Identified and screened for retrieval

108 reports excluded
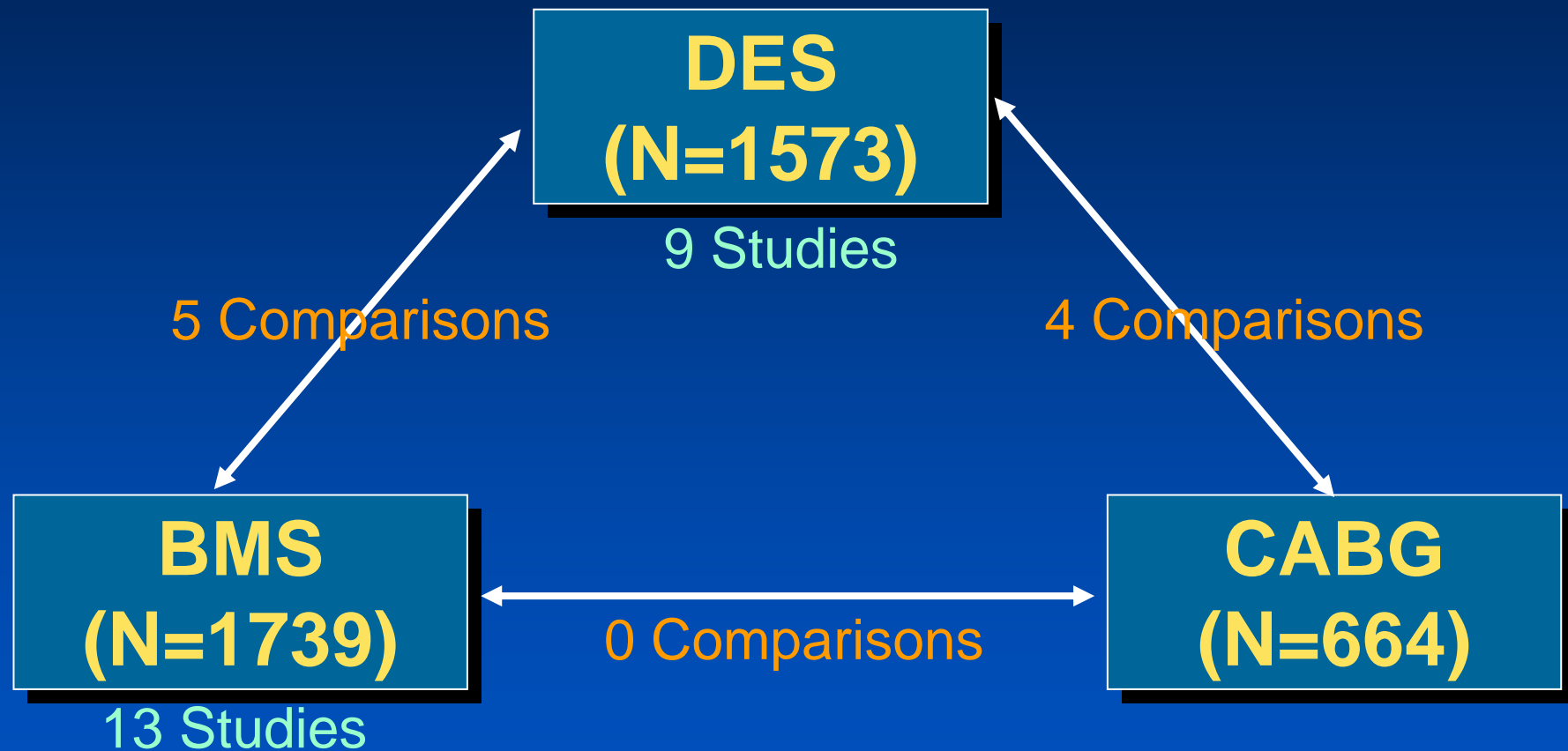: 24 review analyses
56 case-reports
12 mainly balloon angioplasty
16 Incomplete data

124 reports retrieved for detailed evaluation

93 reports excluded
: 51 repetitive data
from same center
9 protected LMCA only
14 high surgical risk only
19 less than 30 patients

31 reports included
: **DES vs. BMS (5 reports)**
DES vs. CABG (4 reports)
DES only (9 reports)
BMS only (13 reports)

Study Framework
(Total 3976 patients)

DES (N=1573)

9 Studies

5 Comparisons

4 Comparisons

BMS (N=1739)

13 Studies

0 Comparisons

CABG (N=664)

5 Comparison Studies: DES vs. BMS

Study	Pt (n)	Gr (n)	In. for PCI	Age (mean)	Male (%)	DM (%)	HTN (%)	ACS (%)	EF (%)	Bifurcation (%)
Park et al (2005)	223	BMS (121)	Stable UA	58	72	21	36	68	62	42
		DES (102)	AMI	60	75	28	47	60	60	71
Cheiffo et al. (2005)	149	BMS (64)	SA UA	66	84	11	56	42	57	58
		DES (85)		63	82	21	59	31	51	81
Valgimili et al. (2005)	216	BMS (86)	SA UA AMI	66	62	22	57	50	42	66
		DES (95)		64	66	31	53	52	41	65
Erglis et al. (2007)	103	BMS (50)	SA UA	63	82	12	50	16	54	68
		DES (53)		61	85	11	58	19	56	81
Ya-ling et al. (2006)	210	BMS (34)	SA UA AMI	64	*	15	*	*	*	32
		DES (176)		62	*	29	*	*	*	72
Total	866	BMS (355)		63	73	18	48	50	54	54
		DES (511)		62	76	26	53	44	52	73

4 Comparison Studies: DES vs. CABG

Study	Pt (n)	Gr (n)	In. for PCI	Age (mean)	Male (%)	DM (%)	HTN (%)	ACS (%)	EF (%)	Bifurcation (%)
Chieffo et al (2006)	209	DES (107)	Stable	64	*	19	59	32	52	81
		CABG (102)	UA AMI	68	*	23	76	22	52	*
Lee et al. (2006)	173	DES (50)	SA	72	50	36	88	66	51	60
		CABG (123)	UA AMI	70	76	31	81	45	52	*
Palmerini et al. (2006)	311	DES (157)	SA	73	70	26	69	66	52	80
		CABG (154)	UA AMI	69	76	25	73	59	55	82
Sanmartin et al. (2007)	341	DES (96)	SA	66	81	19	44	64	51	17
		CABG (245)	UA AMI	66	87	32	60	79	51	*
Total	**1034**	**DES (410)**		**69**	**70**	**24**	**63**	**57**	**52**	**63**
		CABG (624)		**68**	**81**	**30**	**75**	**59**	**52**	***

9 Studies reporting DES results

Study	Center (n)	Pt (n)	In. for PCI	Age (mean)	Male (%)	DM (%)	HTN (%)	ACS (%)	EF (%)	Bifurcation (%)
Khattab et al. (2007)	10	82	SA/UA/AMI	70	73	23	84	50	*	34
Lei et al. (2007)	1	70	SA/UA	63	86	26	64	26	51	100
Morton et al. (2007)	1	30	SA/UA/AMI	63	63	*	*	*	*	100
Cheng et al. (2007)	1	113	SA/UA/NSTEMI	68	77	37	68	84	57	74
Sanmartin et al. (2007)	5	100	SA/UA/AMI	68	78	36	56	63	56	53
Migliorini et al. (2006)	1	101	SA/UA/AMI	70	80	32	88	68	*	87
Price et al. (2006)	1	50	SA/UA/AMI	69	64	26	70	34	*	94
Lee et al. (2005)	5	54	SA/UA/MI	60	67	28	41	65	60	52
De Lezo et al. (2004)	2	52	SA/UA	63	81	35	52	83	57	42
Total	**27**	**652**		**67**	**75**	**31**	**68**	**61**	**54**	**69**

13 Studies reporting BMS results

Study	Pt (n)	In. for PCI	Age (mean)	Male (%)	DM (%)	HTN (%)	ACS (%)	EF (%)	Bifurcation (%)
Run-lin et al.. (2006)	224	SA/UA	60	74	20	11	78	64	32
Peszek et al. (2006)	62	SA/UA	61	73	19	71	50	*	55
Carrie et al. (2005)	57	SA/UA/AMI	70	79	26	58	68	53	100
Marti et al. (2004)	38	UA/AMI	70	87	53	58	100	50	53
ZiaKas et al. (2004)	80	SA/UA/AMI	73	75	38	48	80	52	70
Kelley et al. (2003)	43	SA/UA/AMI	71	77	28	58	*	47	72
Brueren et al. (2003)	71	SA/UA	60	61	7	*	*	*	*
Tan et al. (2001)	279	SA/UA/AMI	66	65	21	46	80	51	58
Black et al. (2001)	92	SA/UA/AMI	74	80	22	45	75	56	7
De Lezo et al. (2001)	155	SA/UA/AMI	63	75	*	*	83	*	54
Silvestri et al. (2000)	140	SA/UA	70	79	14	41	55	61	*
Wong et al. (1999)	55	SA/UA	62	82	24	51	62	55	55
Korowski et al. 1998	88	SA/UA	67	84	28	59	66	42	31
Total	**1384**		**65**	**74**	**22**	**43**	**74**	**55**	**44**

5 Comparison Studies: DES vs. BMS

Mortality (within 1 year)

Park et al.	RR: NA (no event)
Chieffo et al.	RR: 3.98 (1.12-14.13)
Valgimili et al.	RR: 1.19 (0.59-2.39)
Erglis et al.	RR: 1.06 (0.07-16.50)
Ya-ling et al.	RR: 1.73 (0.49-6.05)
Overall	RR: 1.62 (0.76-3.43)

0.1 1 10

BMS Better   **DES Better**
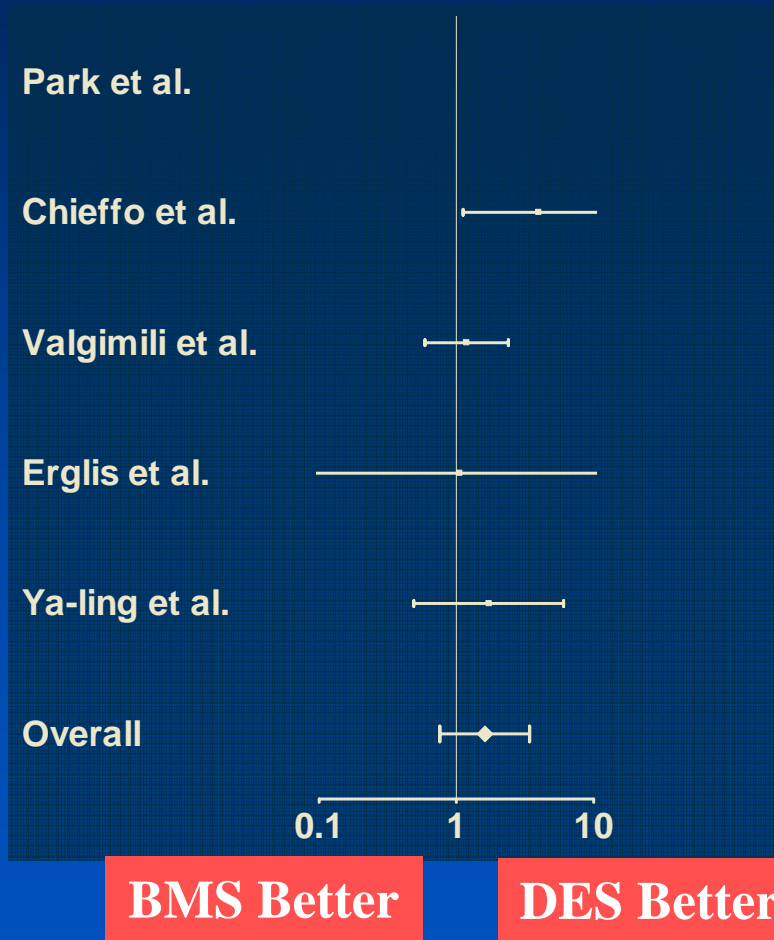
P (Overall Effect) = 0.149
P (Heterogeneity) = 0.484

5 Comparison Studies: DES vs. BMS

MI (within 1 year)

Study		RR
Park et al.		RR: NA (no event)
Chieffo et al.		RR: 1.11 (0.35-3.47)
Valgimili et al.		RR: 2.76 (0.90-8.48)
Erglis et al.		RR: 1.48 (0.50-4.37)
Ya-ling et al.		RR: 2.59 (0.24-27.75)
Overall		RR: 1.11 (0.35-3.47)

Scale: 0.1   1   10
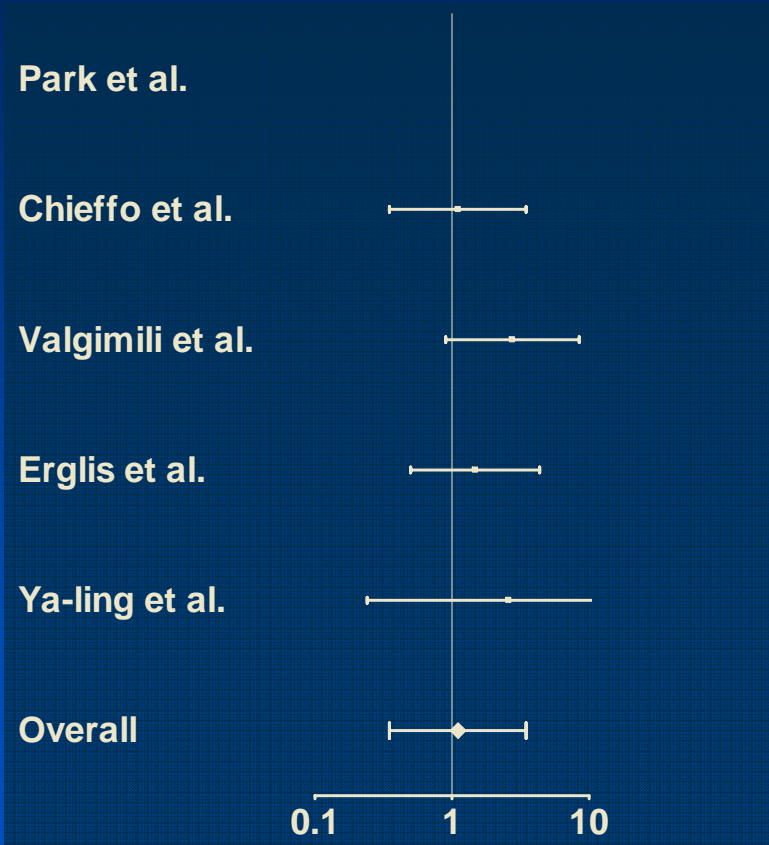
BMS Better   **DES Better**

P (Overall Effect) = 0.151
P (Heterogeneity) = 0.697

5 Comparison Studies: DES vs. BMS

TVR (within 1 year)

Park et al.	RR: 8.85 (2.13-36.85)
Chieffo et al.	RR: 1.58 (0.88-2.82)
Valgimili et al.	RR: 3.68 (1.55-8.74)
Erglis et al.	RR: 8.48 (1.10-65.39)
Ya-ling et al.	RR: 2.88 (1.03-8.05)
Overall	RR: 2.05 (4.63-3.08)

0.1   1   10

BMS Better   **DES Better**
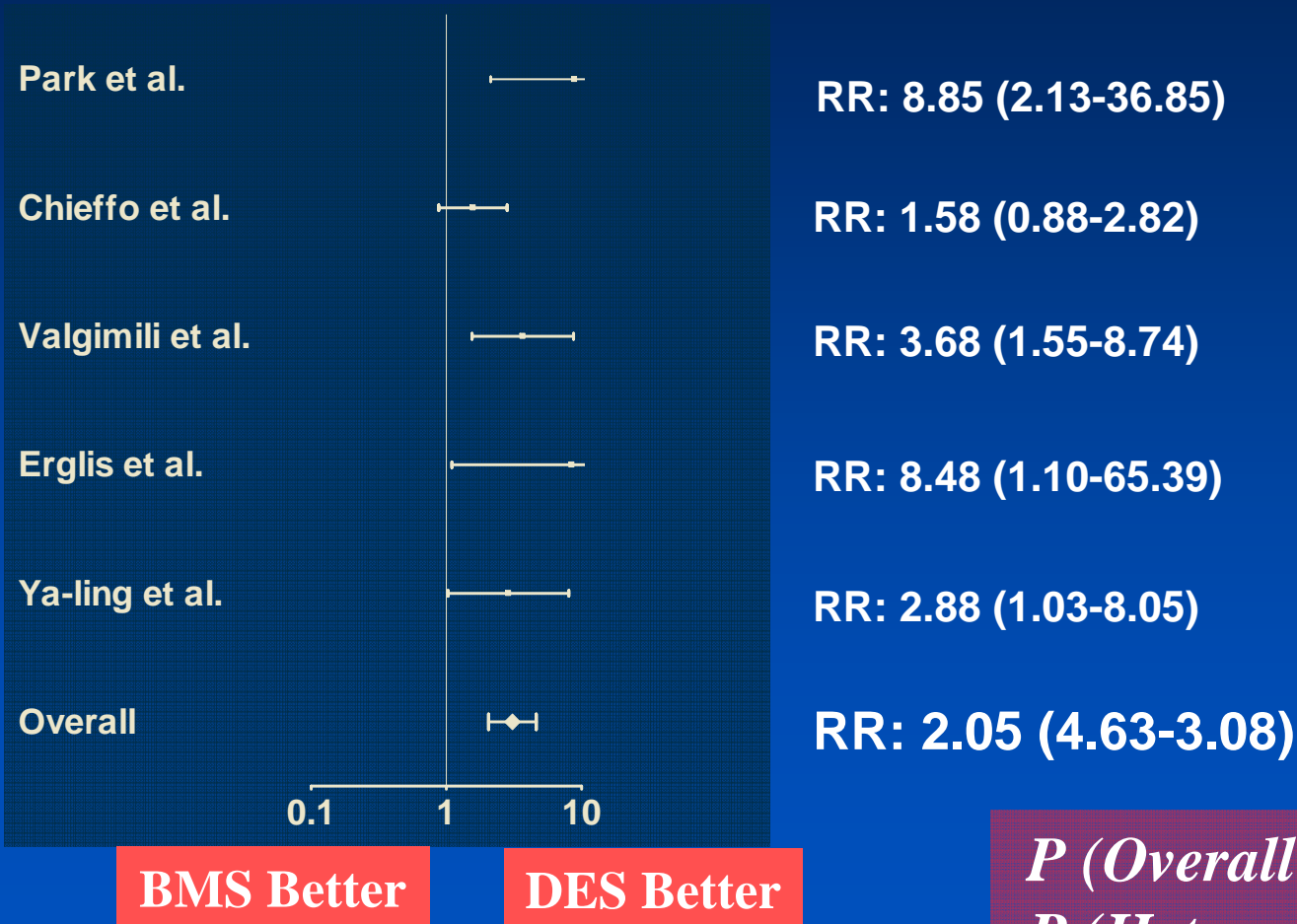
P (Overall Effect) = 0.006
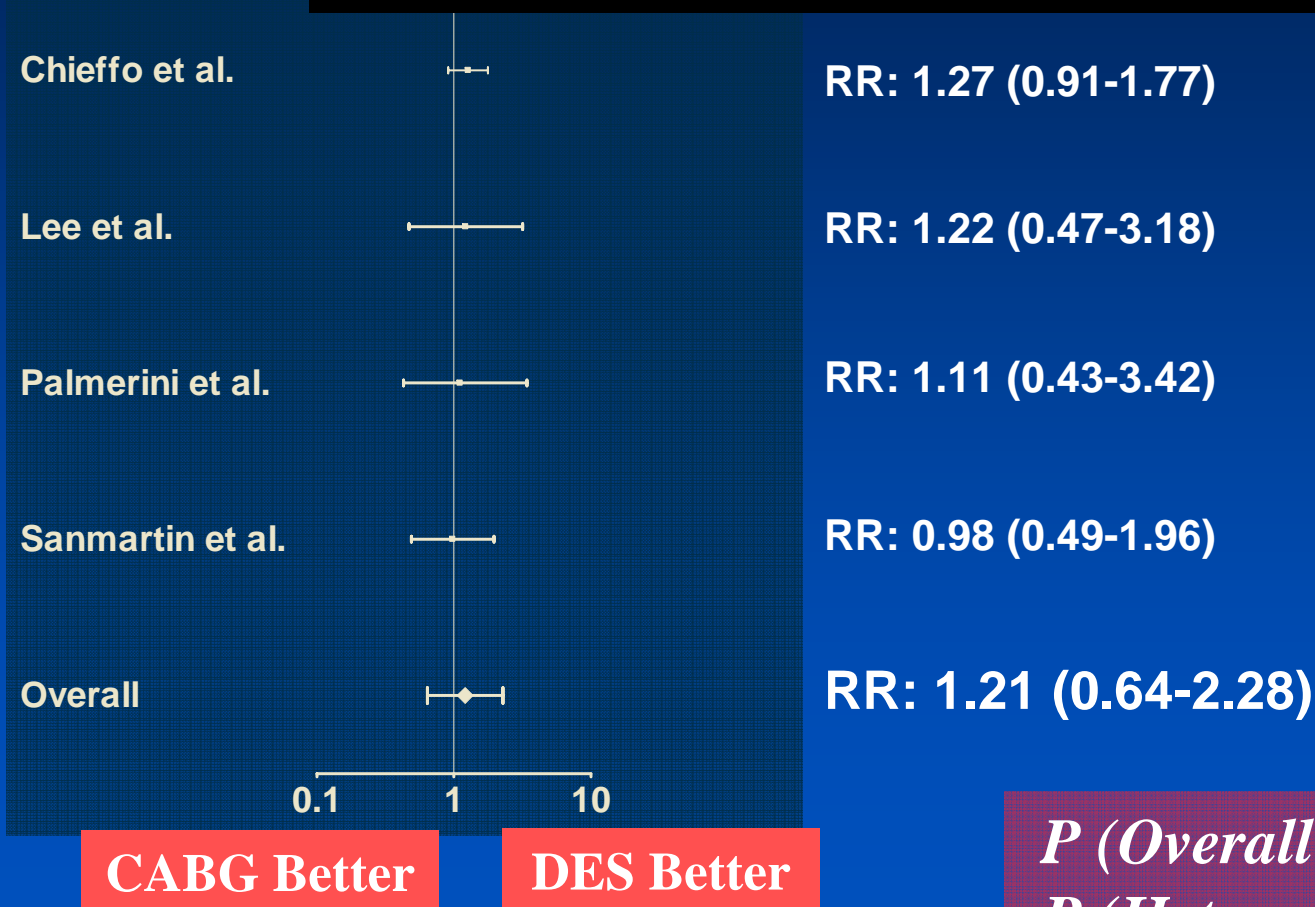*P (Heterogeneity) = 0.157*

5 Comparison Studies: DES vs. BMS

MACE (within 1 year) : Death, MI, or TVR

Park et al.   RR: 8.85 (2.13-36.85)

Chieffo et al.   RR: 1.80 (1.05-3.07)

Valgimili et al.   RR: 1.87 (1.22-2.86)

Erglis et al.   RR: 2.27 (1.01-5.10)

Ya-ling et al.   RR: 2.33 (1.16-4.67)

Overall   RR: 2.19 (1.05-3.07)

0.1   1   10

BMS Better   **DES Better**
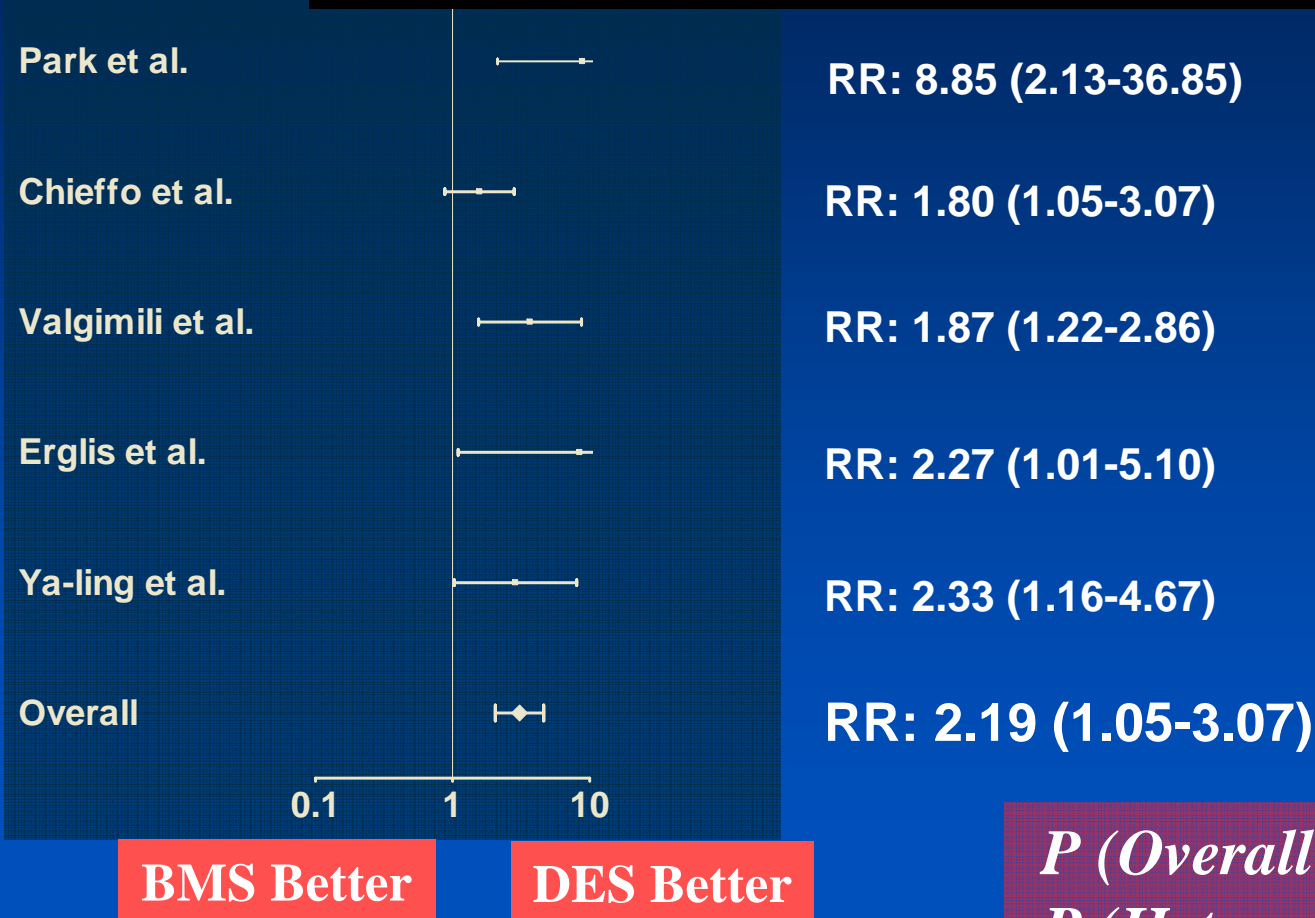
P (Overall Effect) = 0.005
P (Heterogeneity) = 0.414
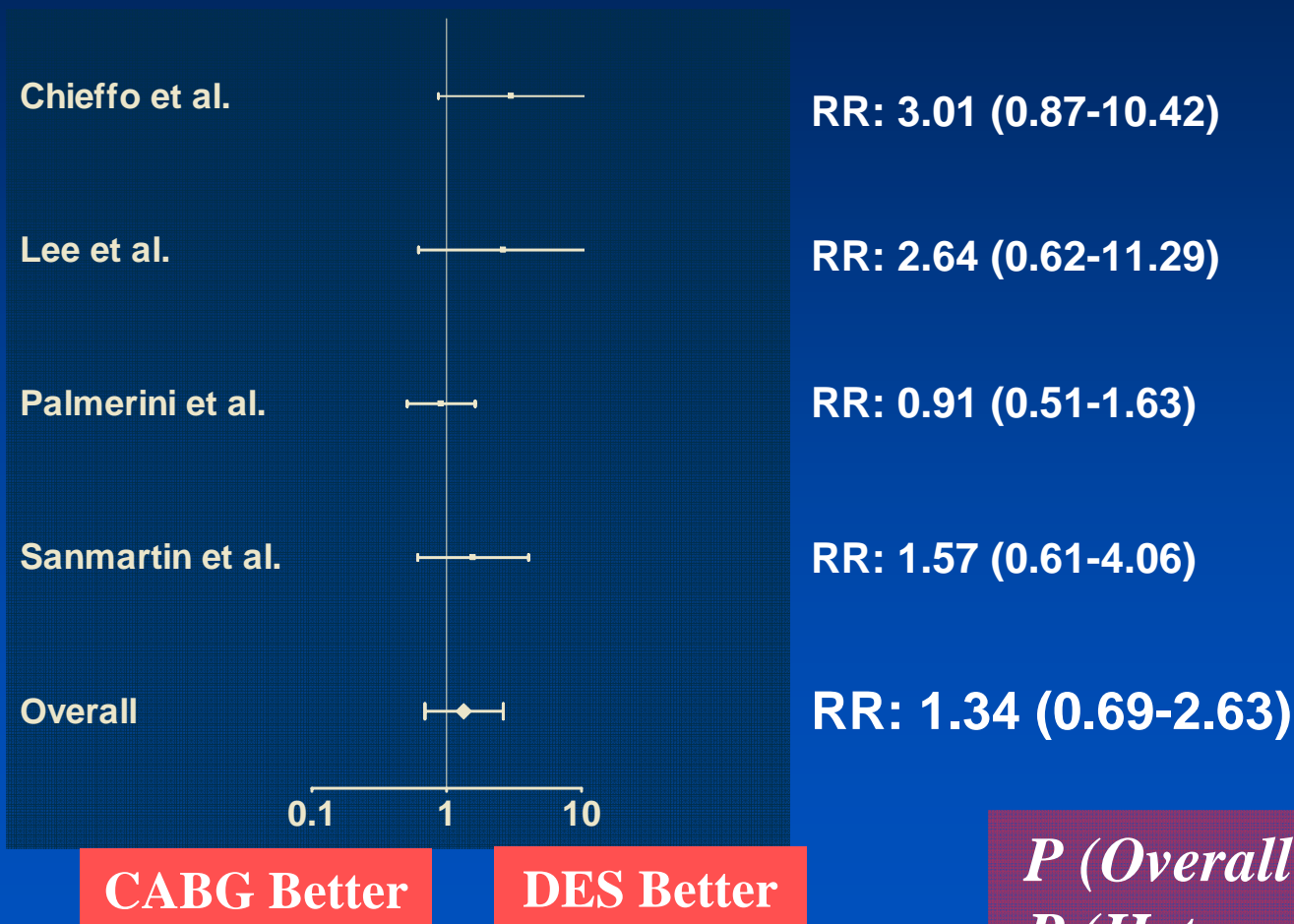
4 Comparison Studies: DES vs. CABG

TVR (within 1 year)

Chieffo et al.	RR: 0.29 (0.13-0.62)
Lee et al.	RR: 0.14 (0.01-1.27)
Palmerini et al.	RR: 0.10 (0.04-0.27)
Sanmartin et al.	RR: 0.16 (0.03-0.79)
Overall	RR: 0.17 (0.07-0.40)

0.1   1   10

CABG Better   DES Better
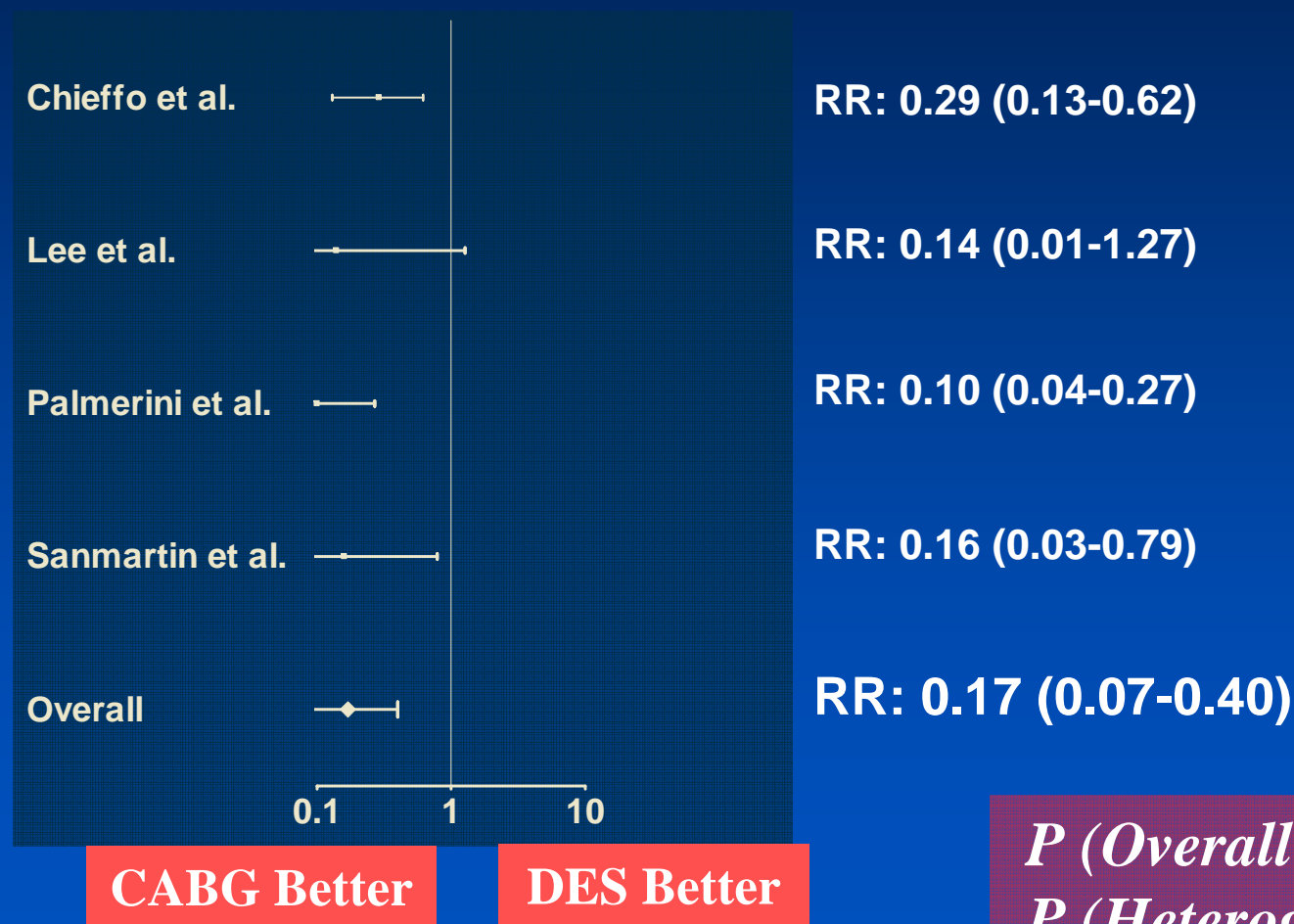
P (Overall Effect) = 0.008
P (Heterogeneity) = 0.409

Early outcomes (overall patients)

1 Month Death

	Estimated incidence (%)	RR with 95% CI	P value for difference
Treatment Group			
DES	2.2 (1.0-4.8)	*	*
BMS	2.1 (0.9-4.6)	*	*
CABG	2.0 (1.7-13.3)	*	*
Comparison			0.168
BMS vs. DES	*	0.94 (0.39-2.25)	0.859
CABG vs. DES	*	2.16 (0.90-5.16)	0.074
CABG vs. BMS	*	2.30 (0.72-7.37)	0.128

Early outcomes (overall patients) 1 Month MI

	Estimated incidence (%)	RR with 95% CI	P value for difference
Treatment Group			
DES	2.1 (1.0-4.4)	*	*
BMS	3.0 (1.3-6.7)	*	*
CABG	4.2 (1.7-10.4)	*	*
Comparison			**0.071**
BMS vs. DES	*	1.41 (0.67-2.99)	**0.301**
CABG vs. DES	*	2.03 (1.08-3.80)	**0.033**
CABG vs. BMS	*	1.43 (0.56-3.70)	**0.388**

Early outcomes (overall patients)
1 Month TVR

	Estimated incidence (%)	RR with 95% CI	P value for difference
Treatment Group			
DES	0.3 (0.1-1.0)	*	*
BMS	0.7 (0.2-2.9)	*	*
CABG	1.1 (0.2-6.3)	*	*
Comparison			0.191
BMS vs. DES	*	2.79 (0.50-15.57)	0.194
CABG vs. DES	*	4.24 (0.63-28.40)	0.112
CABG vs. BMS	*	1.52 (0.17-13.36)	0.655

Early outcomes (overall patients)
1 Month MACE (Death, MI, TVR)

	Estimated incidence (%)	RR with 95% CI	P value for difference
Treatment Group			
DES	4.9 (3.1-7.7)	*	*
BMS	6.5 (3.8-11.2)	*	*
CABG	11.1 (6.1-20.1)	*	*
Comparison			0.012
BMS vs. DES	*	1.34 (0.80-2.23)	0.219
CABG vs. DES	*	2.28 (1.42-3.66)	0.005
CABG vs. BMS	*	1.70 (0.87-3.32)	0.104

Late outcomes (overall patients)
1 Year Death

	Estimated incidence (%)	RR with 95% CI	P value for difference
Treatment Group			
DES	5.2 (3.3-8.1)	*	*
BMS	7.4 (4.8-11.6)	*	*
CABG	7.4 (4.1-13.5)	*	*
Comparison			**0.124**
BMS vs. DES	*	1.45 (0.88-2.38)	**0.121**
CABG vs. DES	*	1.44 (0.89-2.33)	**0.119**
CABG vs. BMS	*	0.99 (0.51-1.91)	**0.978**

Late outcomes (overall patients)
1 Year MI

	Estimated incidence (%)	RR with 95% CI	P value for difference
Treatment Group			
DES	2.7 (1.5-5.0)	*	*
BMS	4.5 (2.4-8.4)	*	*
CABG	4.6 (2.2-9.7)	*	*
Comparison			0.066
BMS vs. DES	*	1.64 (0.88-3.07)	0.104
CABG vs. DES	*	1.67 (0.99-2.84)	0.055
CABG vs. BMS	*	1.02 (0.46-2.26)	0.954

Late outcomes (overall patients)
1 Year TVR

	Estimated incidence (%)	RR with 95% CI	P value for difference
Treatment Group			
DES	8.2 (5.7-11.8)	*	*
BMS	19.7 (14.0-27.9)	*	*
CABG	1.4 (0.7-2.9)	*	*
Comparison			<0.0001
BMS vs. DES	*	2.39 (1.64-3.48)	0.0009
CABG vs. DES	*	0.17 (0.09-0.33)	0.0004
CABG vs. BMS	*	0.07 (0.03-0.15)	<0.0001

Late outcomes (overall patients)
1 Year MACE

	Estimated incidence (%)	RR with 95% CI	P value for difference
Treatment Group			
DES	14.7 (11.0-19.6)	*	*
BMS	29.7 (22.6-39.0)	*	*
CABG	17.7 (11.7-26.9)	*	*
Comparison			**0.0027**
BMS vs. DES	*	2.02 (1.52-2.69)	**0.0009**
CABG vs. DES	*	1.21 (0.86-1.70)	**0.230**
CABG vs. BMS	*	0.60 (0.39-0.92)	**0.026**

DES vs. CABG

Clinical Events (within 1 year)

Death	RR: 1.44 (0.89-2.33)	*P = 0.119*
MI	RR: 1.67 (0.99-2.84)	*P = 0.055*
TVR	RR: 0.17 (0.09-0.33)	*P = 0.0004*
MACE	RR: 1.21 (0.86-1.70)	*P = 0.230*

0.1   1.0   10

CABG Better   **DES Better**

CVRF CardioVascular Research Foundation
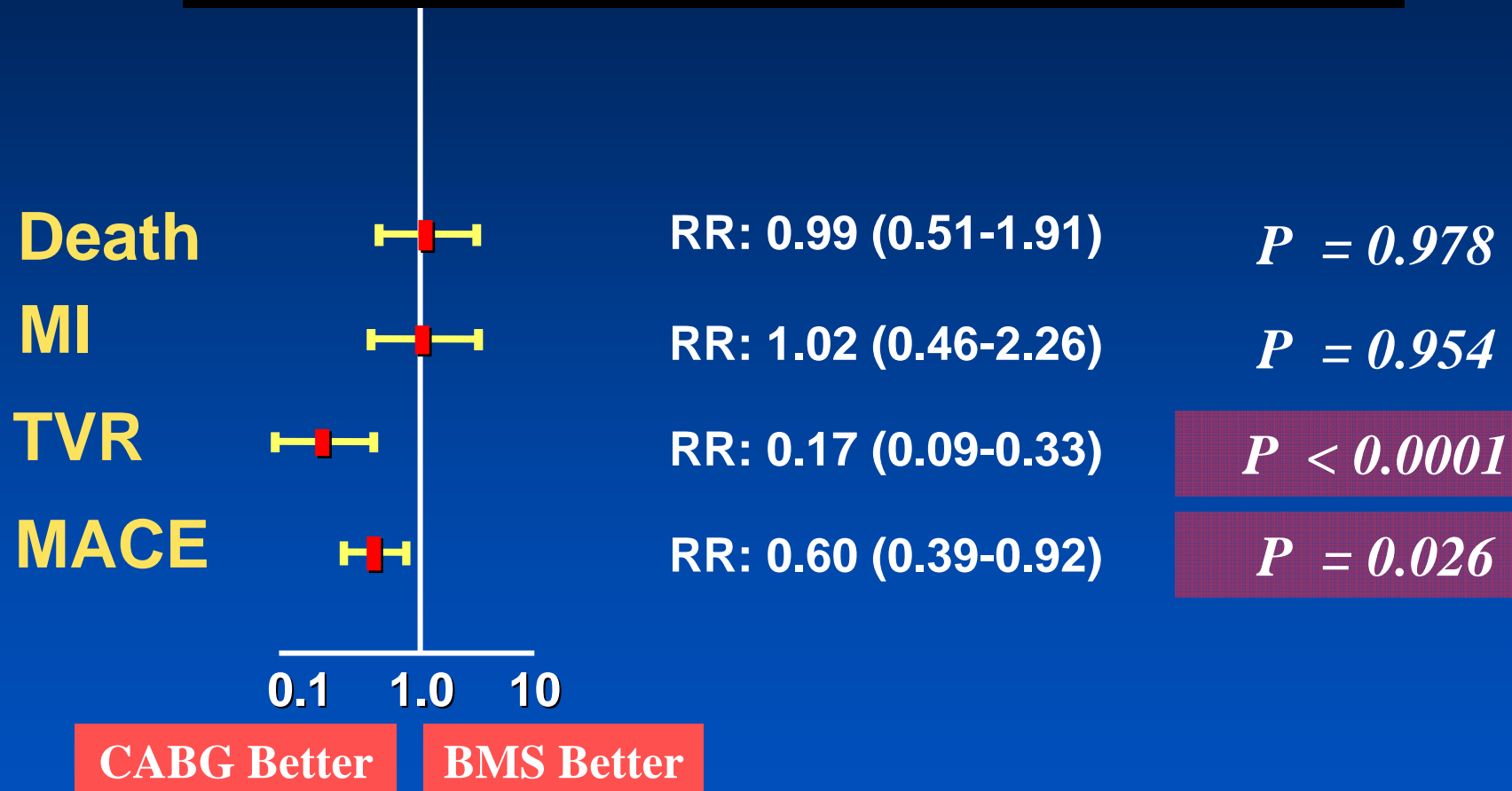
Conclusions

- Percutaneous intervention for LMCA disease with DES or BMS was feasible and safe with comparable early mortality and morbidity to bypass surgery.

- Mortality and MI incidence within 1 year was similar between patients treated with BMS, DES, and CABG.

- Incidence of TVR was significantly lower in CABG patients compared to BMS patients or DES patients.

- BMS patients showed a higher incidence of TVR compared to DES patients.

Conclusions

- The incidence of MACE (composite of death, MI, or TVR) was significantly higher in BMS patients in comparison with DES patients or CABG patients.

- However, DES patients showed the comparable incidence of MACE to bypass surgery.

- The long-term safety and efficacy of DES for unprotected LMCA needs to be ascertained in large, randomized trials.