PCI for Unprotected Left Main Coronary Artery Stenosis

Insight from MAIN-COMPARE Study

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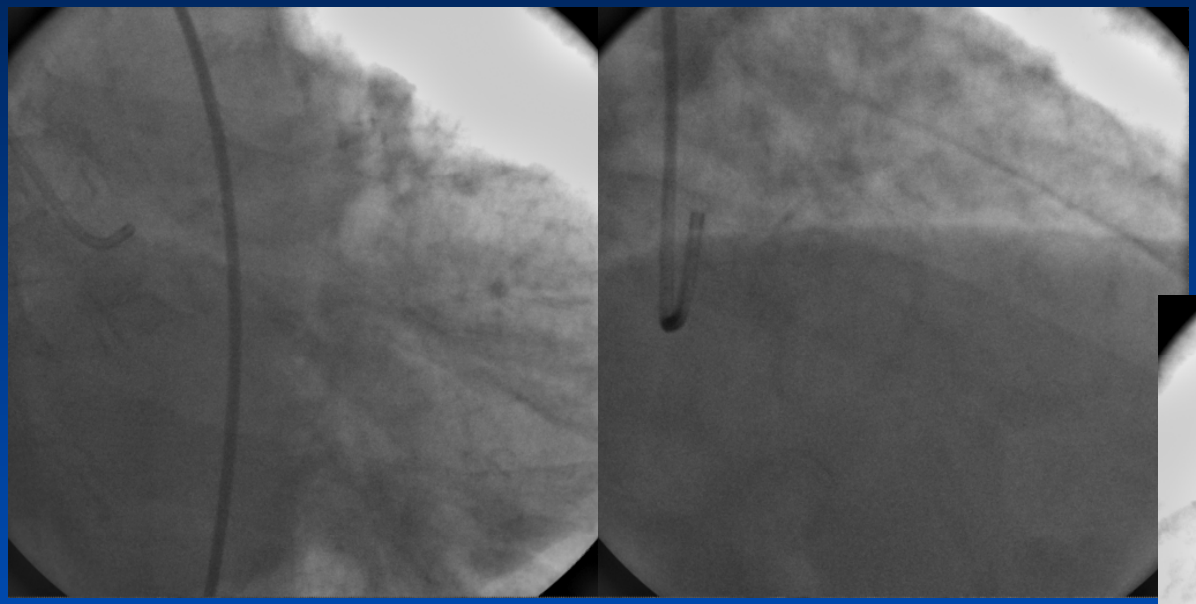
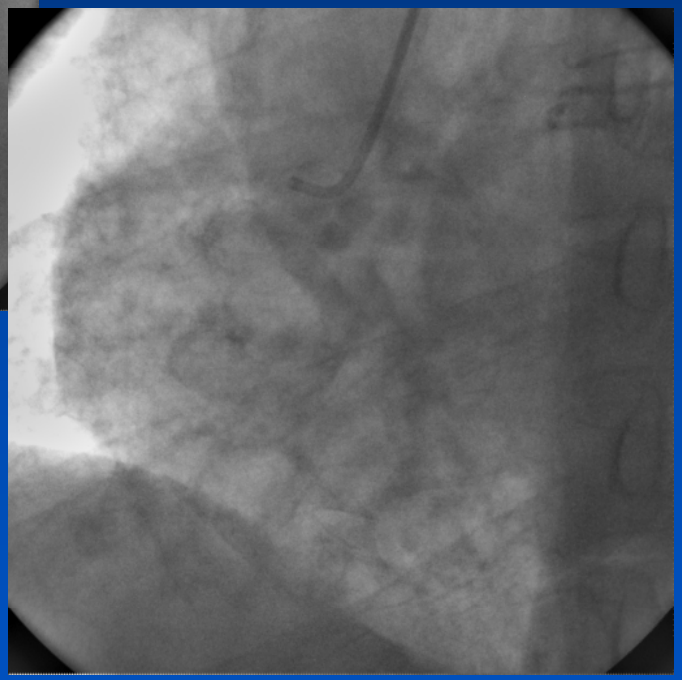
Current Practice for LM Stenosis

What is a real-world ?

What is your plan ?

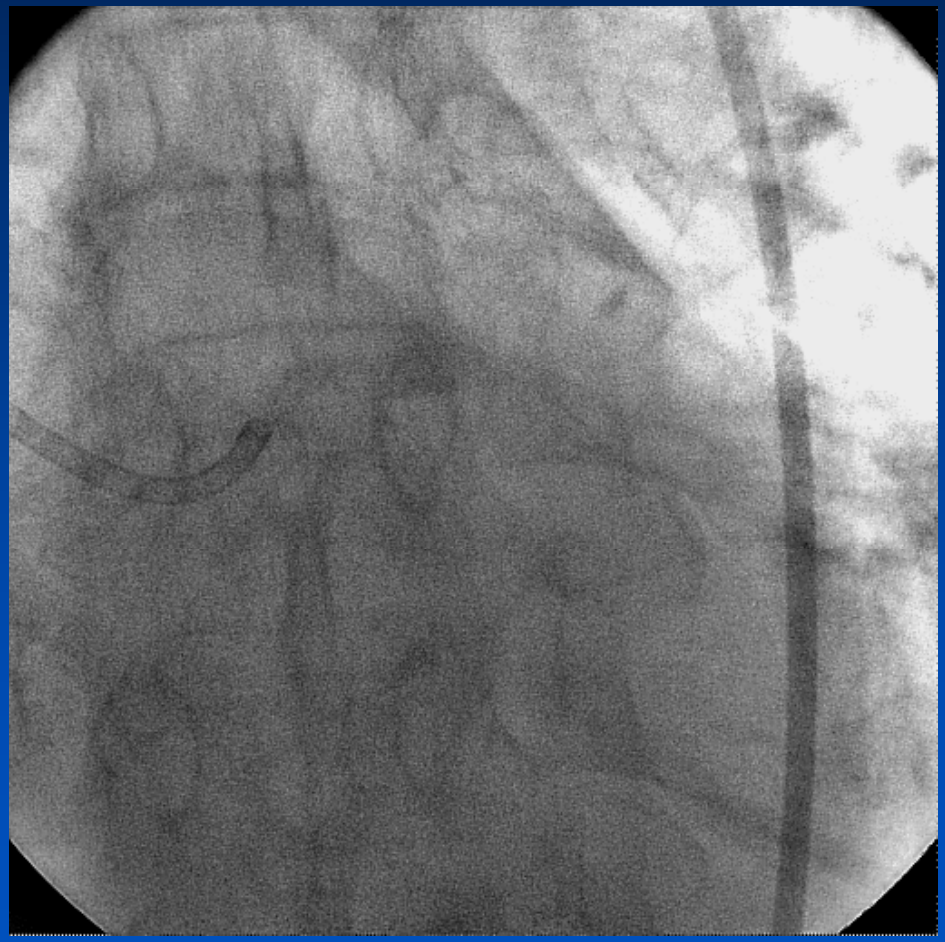
76 Yr Male, Normal EF, LM with 3 Vessel ds





What is your plan ?

58 Yr Male, Normal EF, Isolated LM



What are your considerations ?

- Ejection fraction
- Age
- Right coronary involvement
- Vascular size of LM
- Lesion location at LM
- Extra-LM involvement
- Long-term data compared with CABG
- Economy
- **Stentable or not ?**

LM-PCI has already been popular in Korea !

- Motivation from pioneer
- Excellent educational course of training
- Skilled hands
- Patients' preference
- **Cumulative evidence !**

MAIN-COMPARE Registry

The NEW ENGLAND JOURNAL of MEDICINE

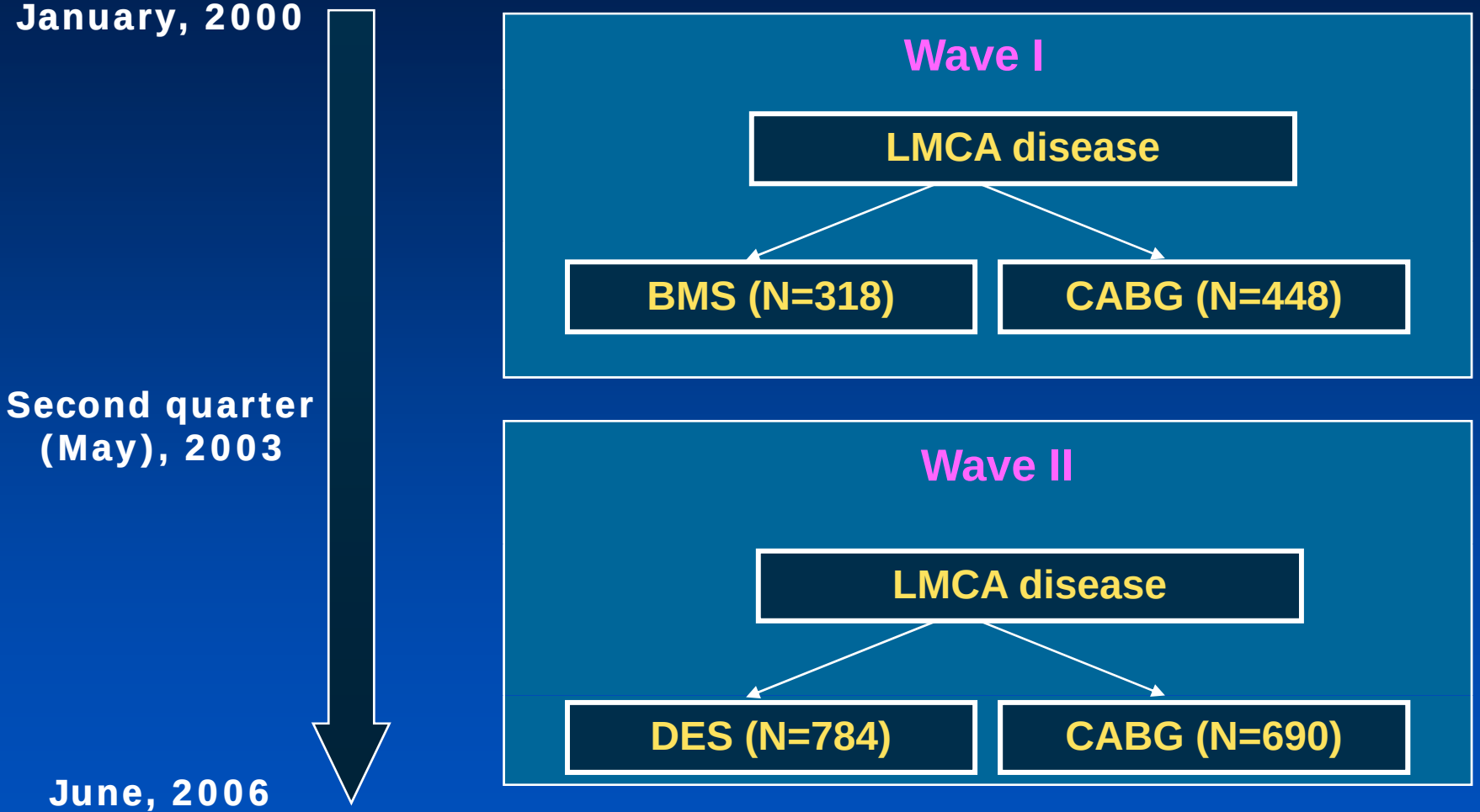
Stents versus Coronary-Artery Bypass Grafting for Left Main Coronary Artery Disease

Ki Bae Seung, M.D., Duk-Woo Park, M.D., Young-Hak Kim, M.D., Seung-Whan Lee, M.D., Cheol Whan Lee, M.D., Myeong-Ki Hong, M.D., Seong-Wook Park, M.D., Sung-Cheol Yun, Ph.D., Hyeon-Cheol Gwon, M.D., Myung-Ho Jeong, M.D., Yangsoo Jang, M.D., Hyo-Soo Kim, M.D., Pum Joon Kim, M.D., In-Whan Seong, M.D., Hun Sik Park, M.D., Taehoon Ahn, M.D., In-Ho Chae, M.D., Seung-Jea Tahk, M.D., Wook-Sung Chung, M.D., and Seung-Jung Park, M.D.

N Engl J Med 2008;358.

MAIN-COMPARE Study

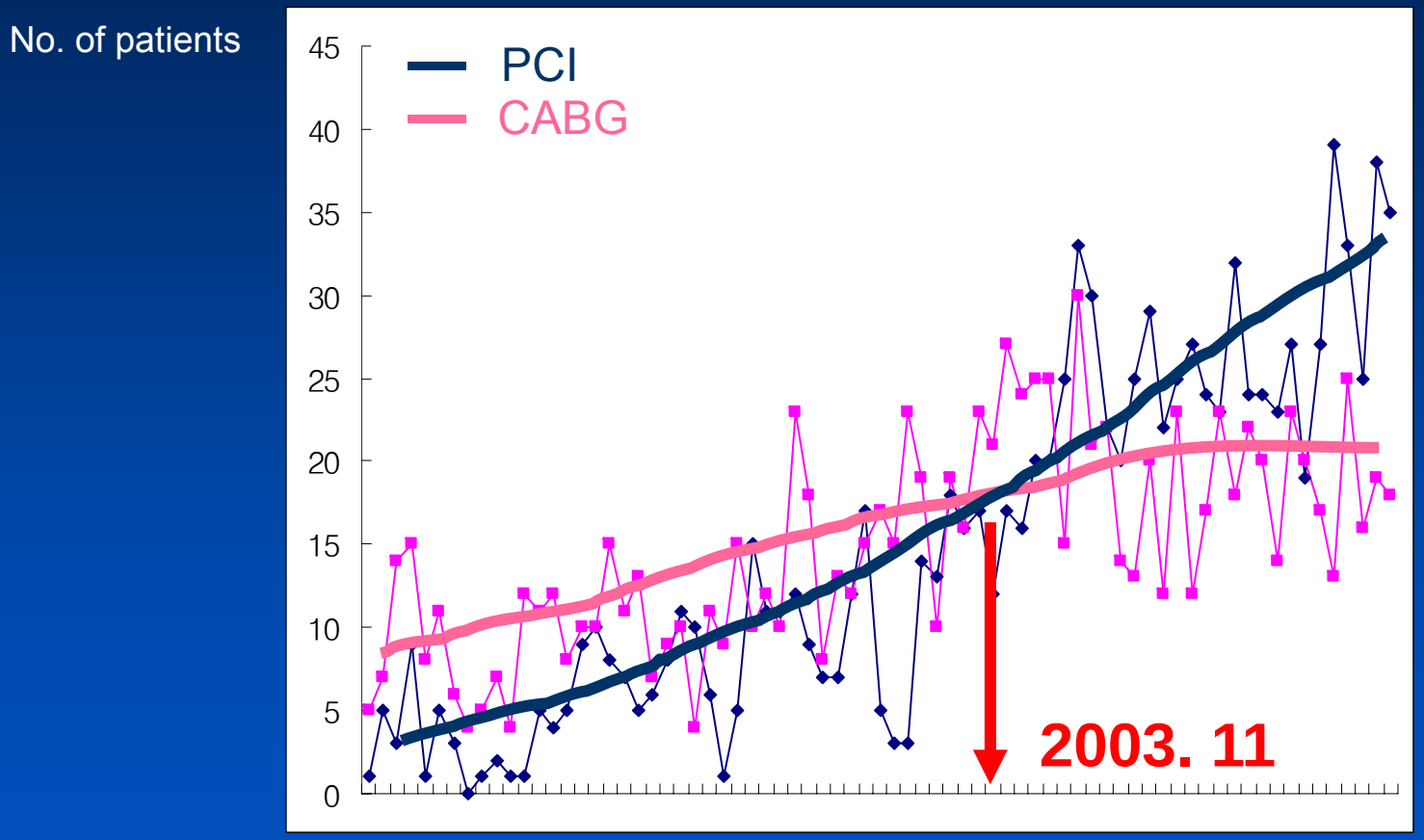
Stenting (BMS or DES) vs. CABG



Total (N=2240) | **PCI (N=1102)** | **CABG(N=1138)**

Prevalence of PCI or CABG in Korea

Unpublished data from MAIN-COMPARE



Current Practice for LM Stenosis

- PCI is now a preferable alternative to bypass surgery for unprotected LM stenosis in Korea.
- With the introduction of DES, PCI for LM stenosis has been a more popular strategy as compared with CABG.
- In many institutions, PCI seems to be the first line therapy for LM stenosis with STENTABLE angiographic morphology.

Safety of
Unprotected LM Stenosis

Adjustment for Confounder in Non-randomized Study

Propensity Score Methodology

- Replace the collection of confounding covariates with one scalar function of these covariates: the propensity score.

Creation of Propensity Score

- Dependent variable : Stent / CABG
- Independent variable : Demographic characteristics, Cardiac or coexisting conditions and Angiographic characteristics

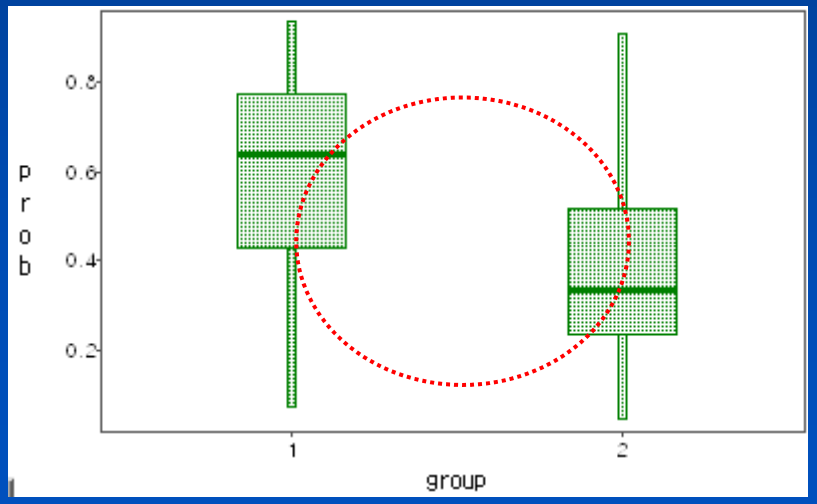
  → logistic regression

```
proc logistic data=yun;
class sex  clin_inx ecgrhyth ext_dis;
model group1=age  sex  dm  dm_insu  htn  hyperlip  smoking  prepci  premi  prechf  cld  cvd  pvd  crf
             mind mlvef  ecgrhyth  clin_inx ext_dis  rca_disresten
             age*sex age*dm  age*dm_insu  age*htn  age*hyperlip  age*smoking  age*prepci  age*premi
             age*prechfage*cld  age*cvd  age*pvd  age*crf  age*mind age*mlvef  age*ecgrhyth  age*clin_inx
             age*ext_dis age*rca_dis  age*resten
             sex*dm sex*dm_insu  htn  sex  *hyperlip sex  *smoking sex  *prepci sex *premi sex  *prechf sex*cld
             sex*cvd sex*pvd  sex*crf sex*mind sex*mlvef  sex*ecgrhyth  sex*clin_inx  sex*ext_dis sex*rca_dis sex*resten
             /selection=s lackfit;
output out=pred p=prob;
run;
```

Creation of Propensity Score

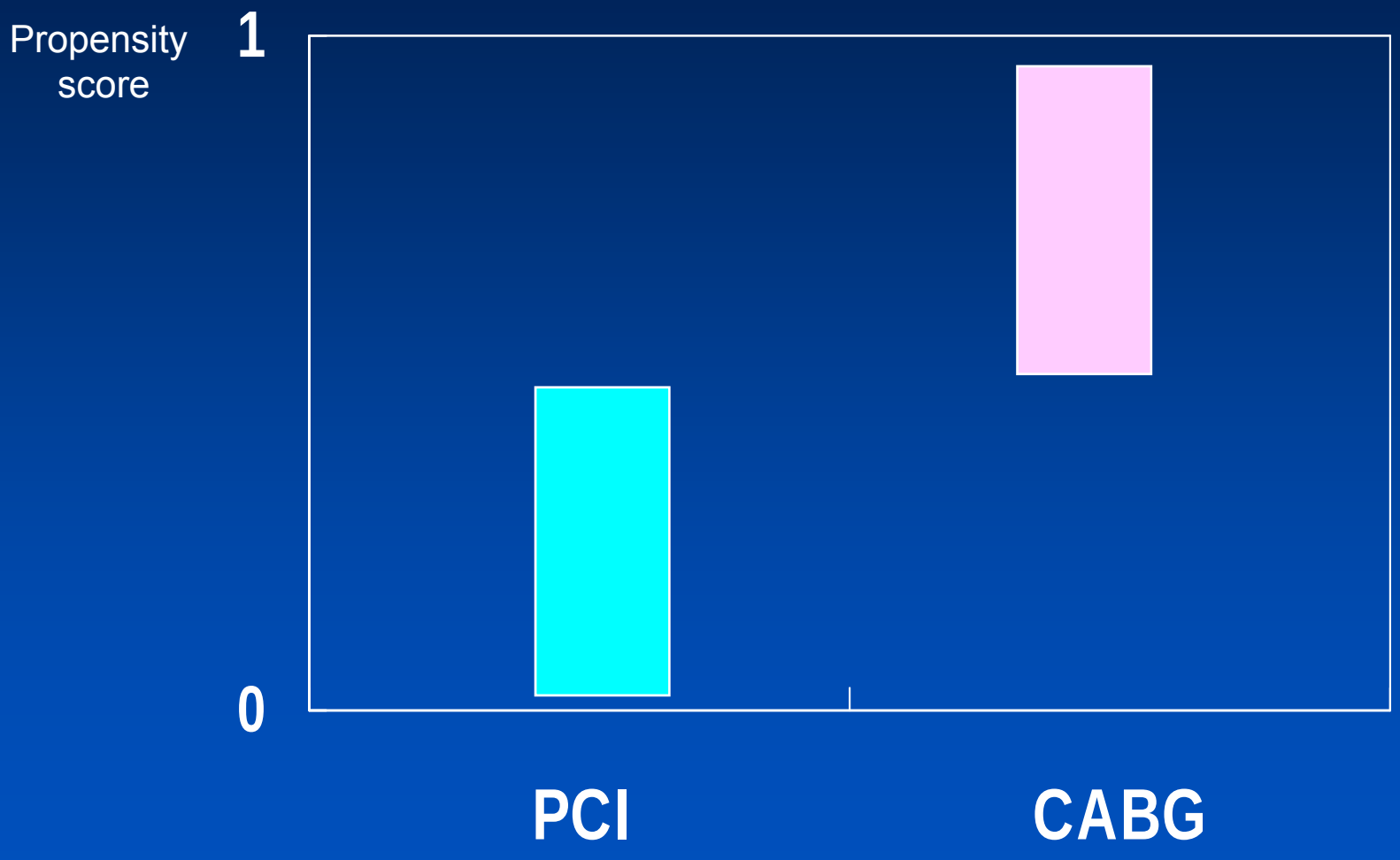
- Dependent variable : Stent / CABG
- Independent variable : Demographic characteristics, Cardiac or coexisting conditions and Angiographic characteristics
  → logistic regression

구간 mitlr	구간 du_dmtlr	구간 dmitvr	구간 du_dmtvr	구간 GROUP1	구간 HTD	구간 PATIENTN	구간 _LEVEL_	구간 prob
1	1579	1	1579	0	1	1	0	0.8785
1	1210	1	1210	0	1	2	0	0.4567
1	1110	1	1110	0	1	3	0	0.8087
1	552	1	552	0	1	4	0	0.7894
1	384	1	384	0	1	5	0	0.7689
1	837	1	837	0	1	6	0	0.6120
1	830	1	830	0	1	7	0	0.6238
1	807	1	807	0	1	8	0	0.7667

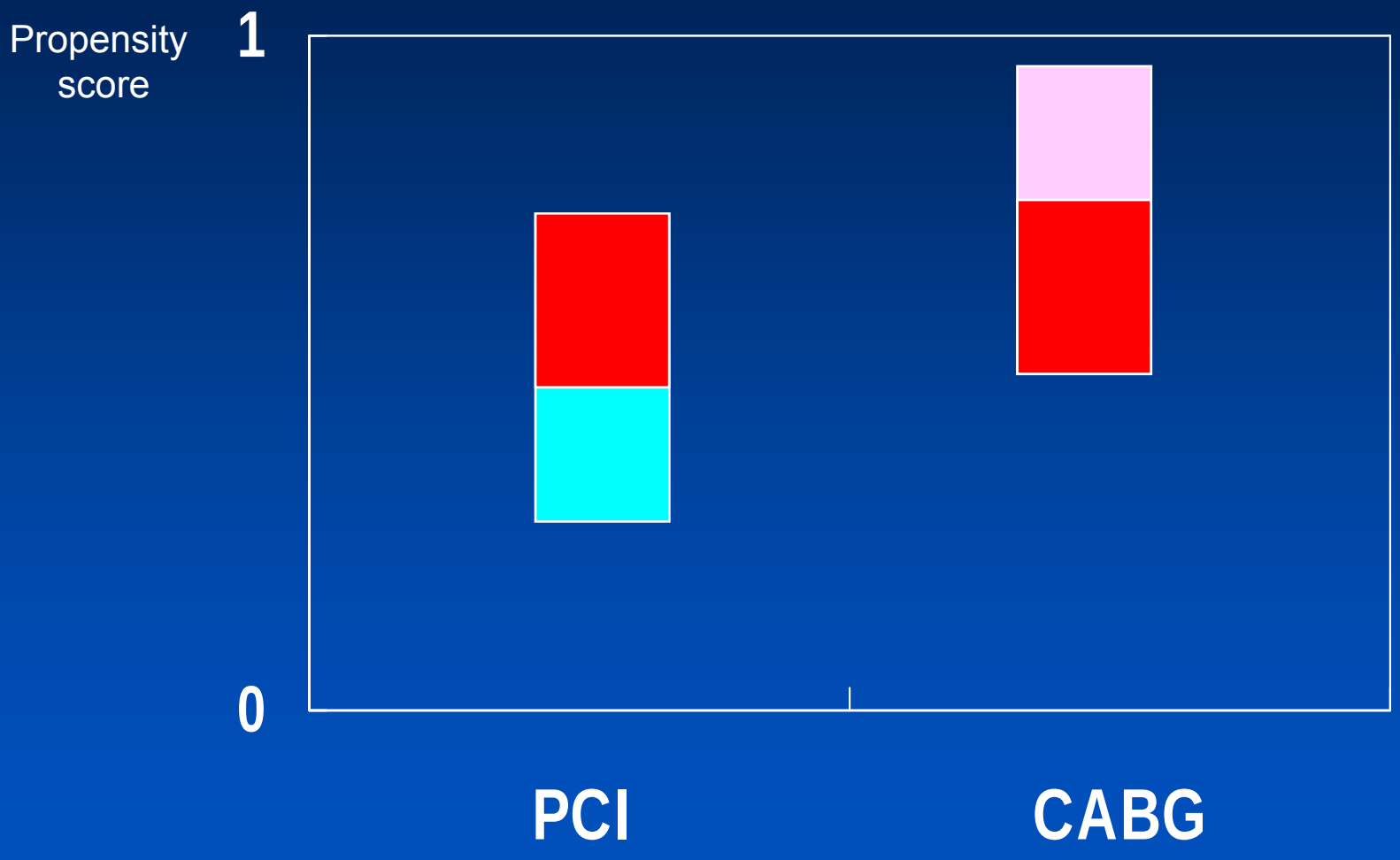


Comparison of Risk Profiles

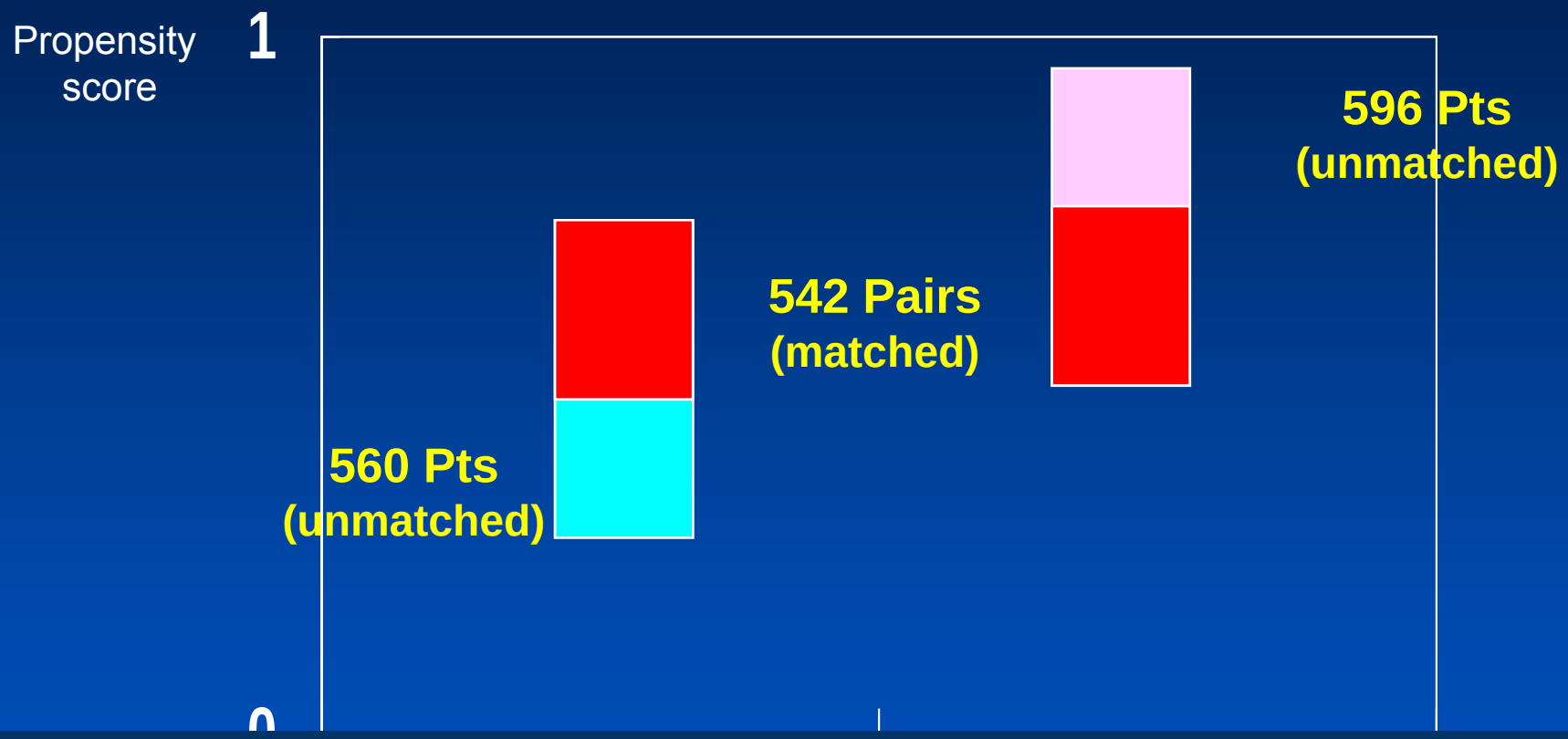
No Overlap : Completely Different Group



Comparison of Risk Profiles
Overlap in Clinical Risks



Propensity-Match in MAIN-COMPARE

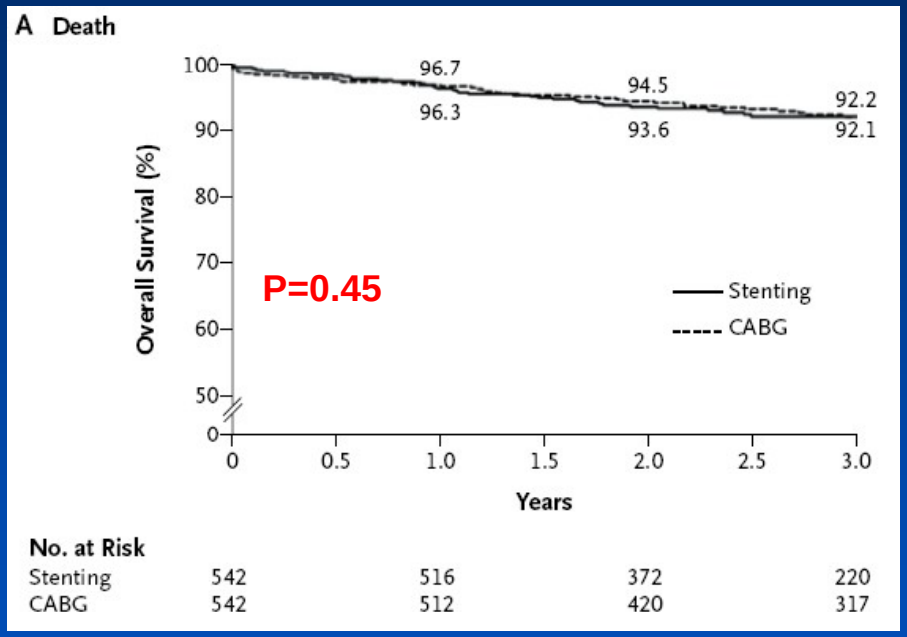


- A half of PCI and CABG patients was at a comparable risk in clinical and angiographic presentations.
- Our patients treated with PCI are not so simple.

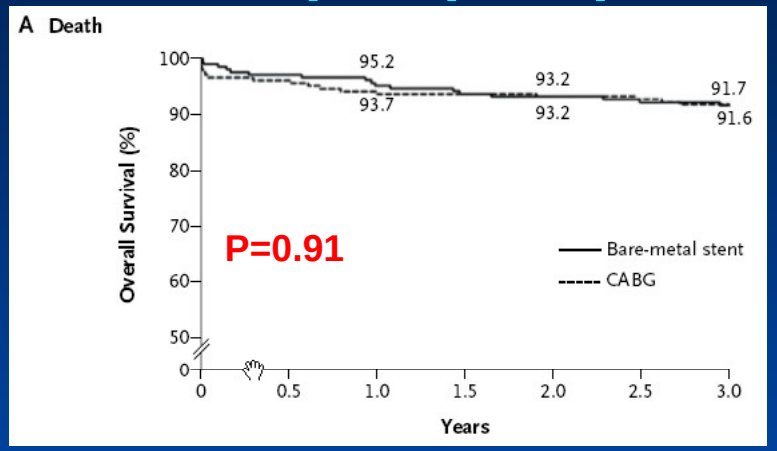
Comparable Incidence of Death

Propensity-Matched Populations

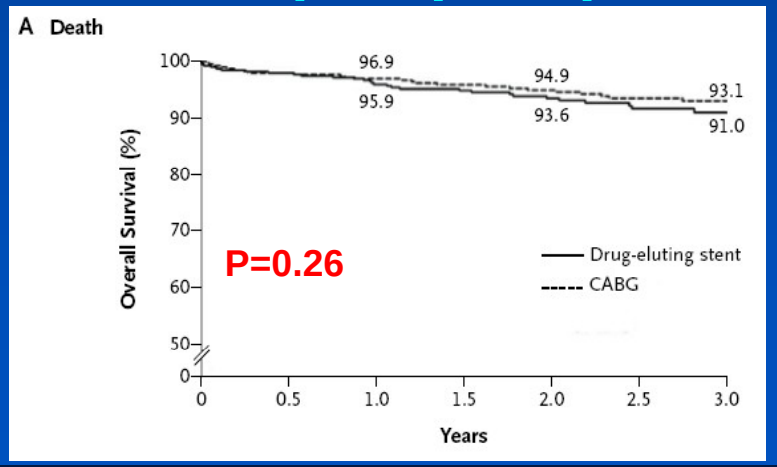
Overall (542 pairs)



BMS (207 pairs)



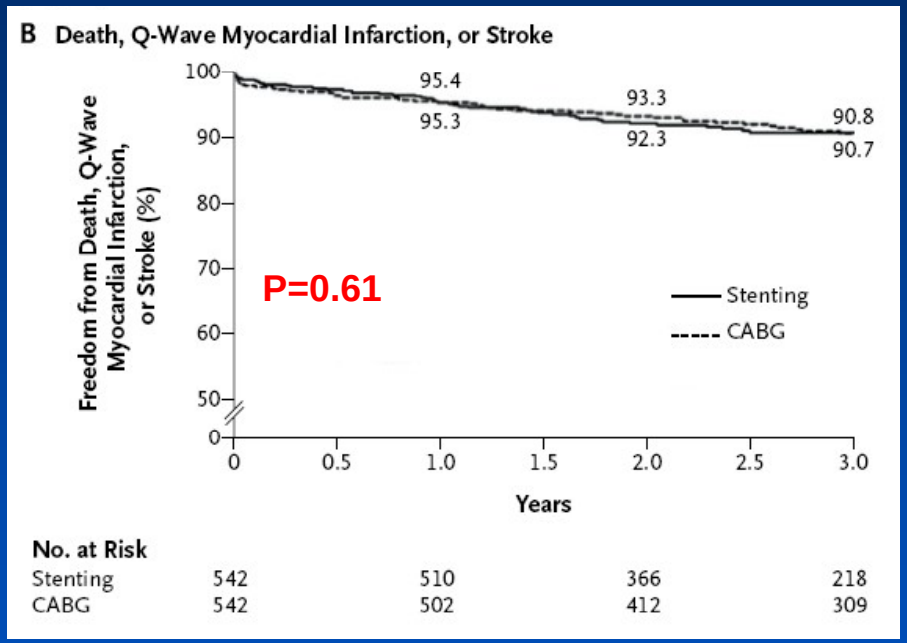
DES (396 pairs)



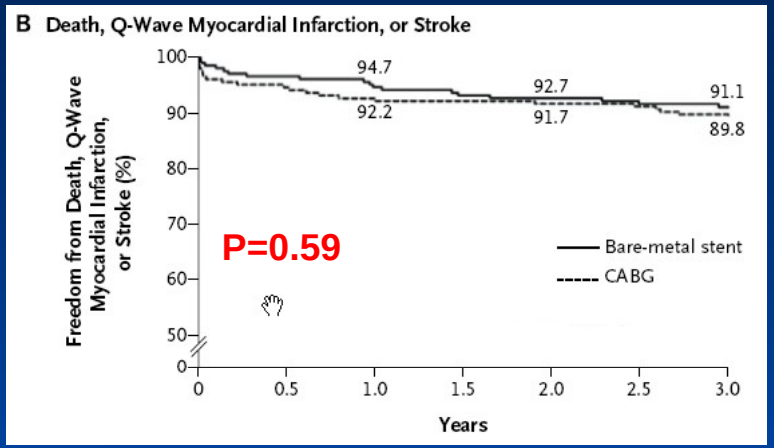
Comparable Incidence of Death/QMI/Stroke

Propensity-Matched Populations

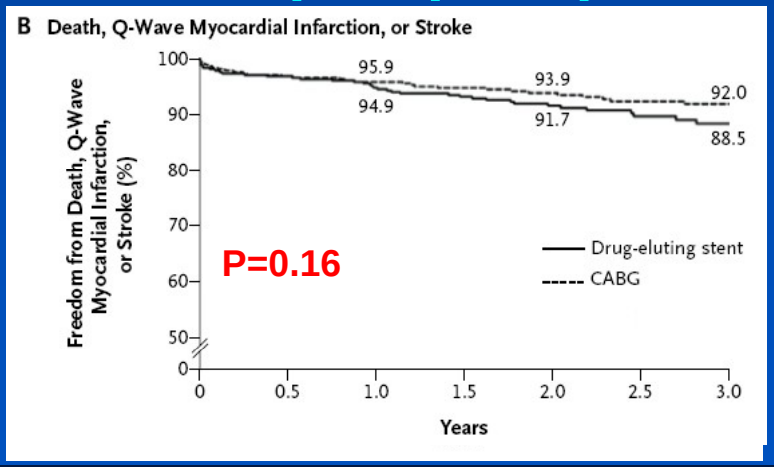
Overall (542 pairs)



BMS (207 pairs)



DES (396 pairs)



Hazard Ratios for Safety Outcomes

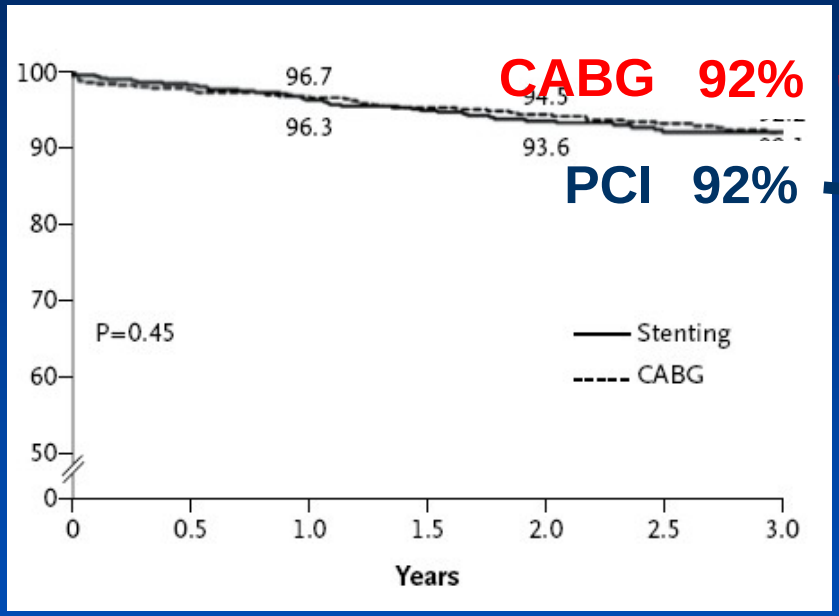
Outcome	Overall (542 pairs)		BMS (207 pairs)		DES (396 pairs)	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Death	1.18 (0.77-1.80)	0.45	1.04 (0.59-1.83)	0.90	1.36 (0.80-2.30)	0.26
Death, Q-MI, or stroke	1.10 (0.75-1.62)	0.61	0.86 (0.50-1.49)	0.59	1.40 (0.88-2.22)	0.15

***HR are for the stenting group, as compared with CABG group**

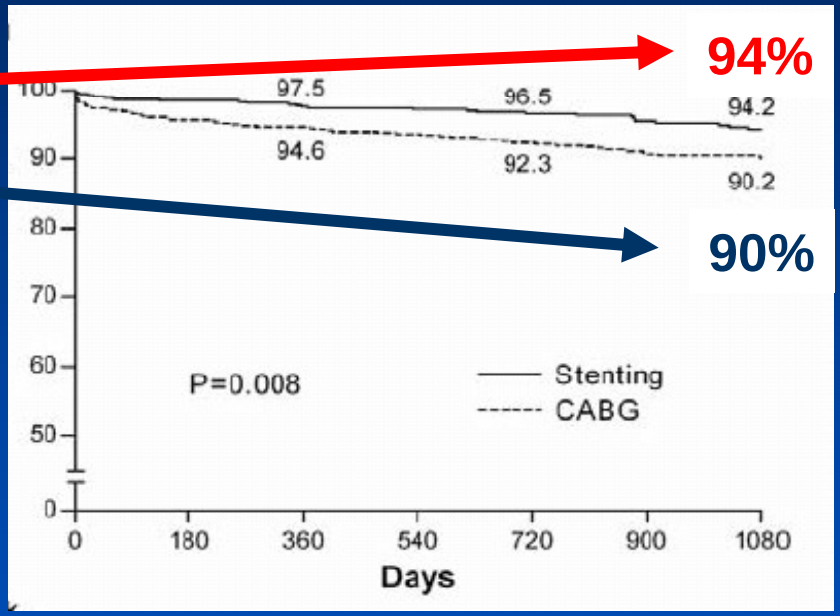
Incidence of Death

Matched and Unmatched Populations

Matched group

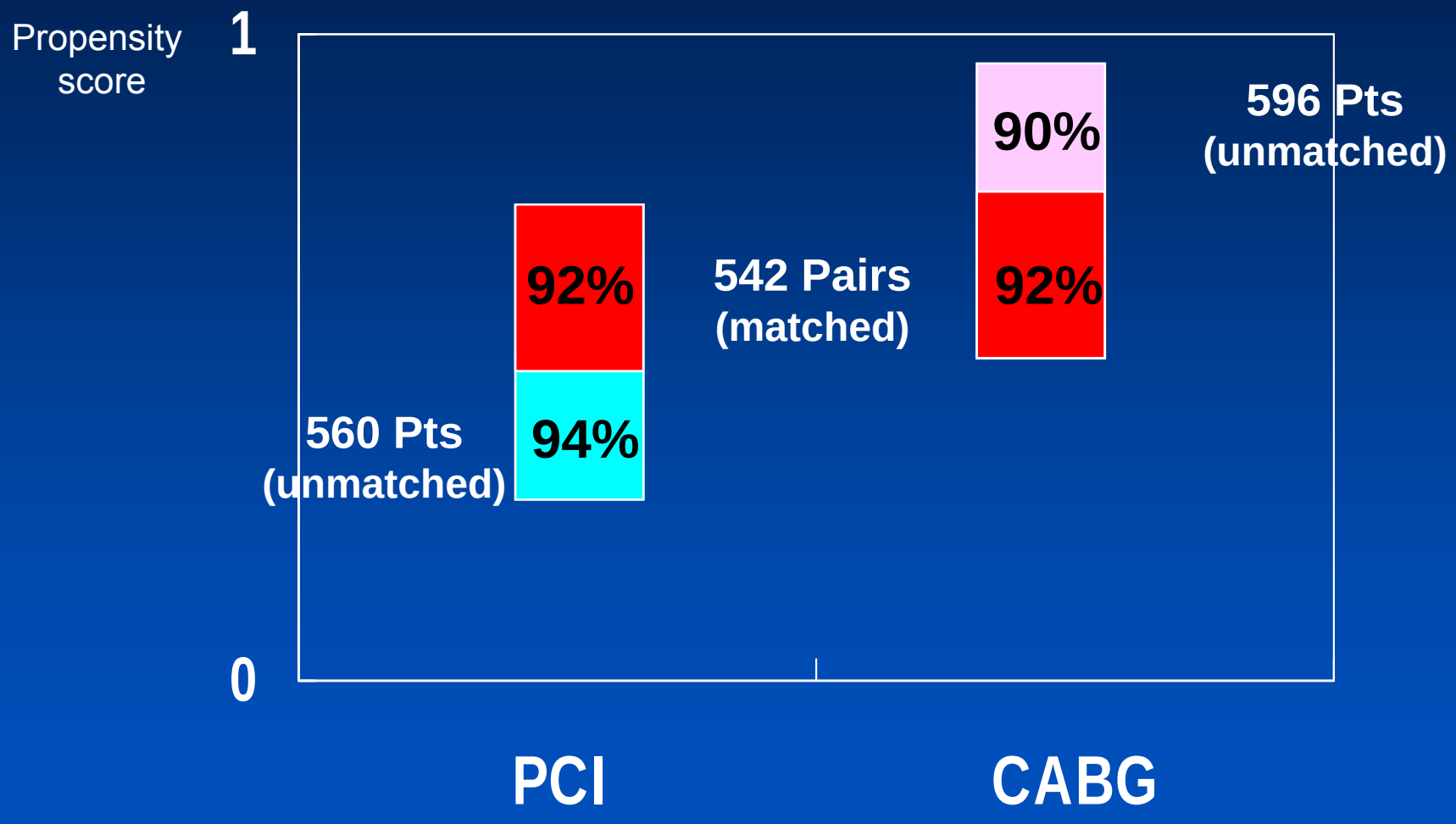


Un-matched group



Incidence of Death

Matched and Unmatched Populations



Safety of PCI for Unprotected LM Stenosis

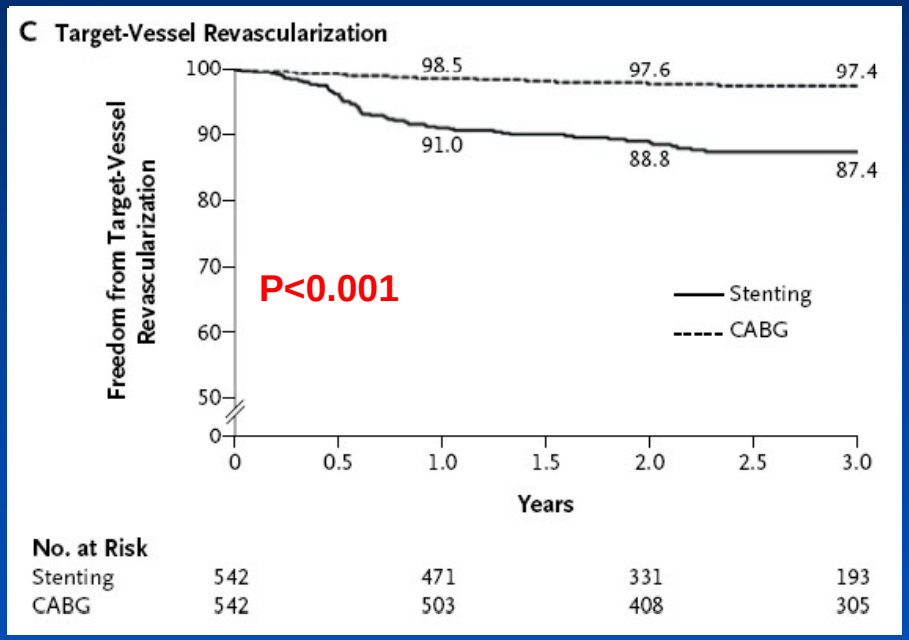
- PCI for unprotected LM stenosis was comparably safe to CABG for patients at a low or moderate clinical risk.
- The risk of mortality was more dependent on the baseline clinical risk of patients than the type of treatment.

Efficacy of Unprotected LM Stenosis

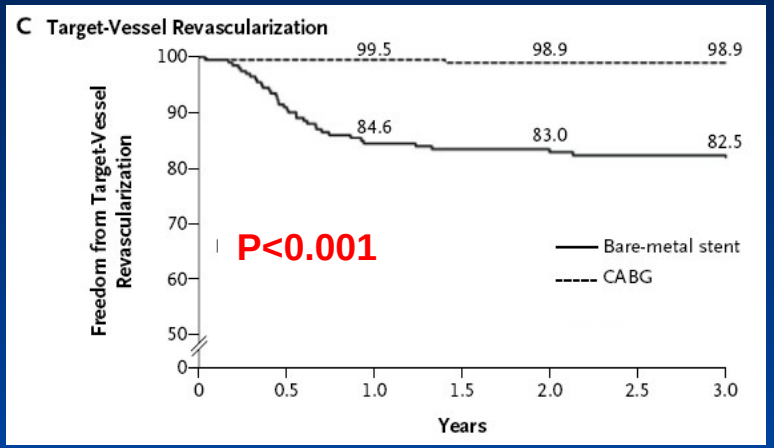
Lower Incidence of TVR By CABG

Propensity-Matched Populations

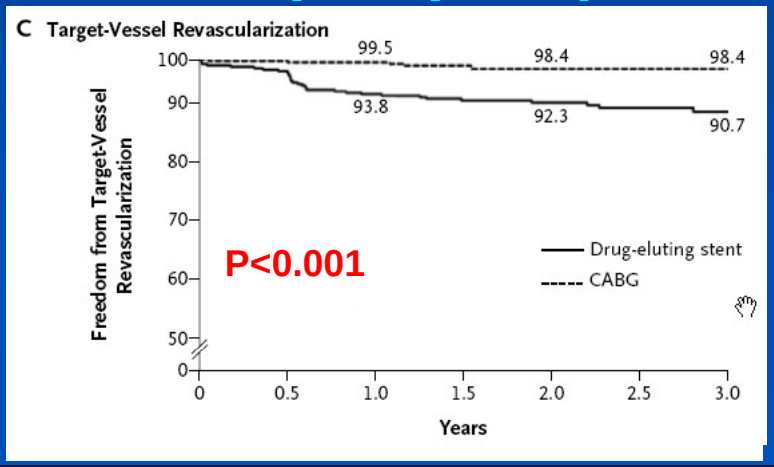
Overall (542 pairs)



BMS (207 pairs)



DES (396 pairs)



PCI had a lower efficacy ?

Outcome	Overall (542 pairs)		BMS (207 pairs)		DES (396 pairs)	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
TVR	4.76 (2.80-8.11)	<0.001	10.70 (3.80-29.90)	<0.001	5.96 (2.51-14.10)	<0.001

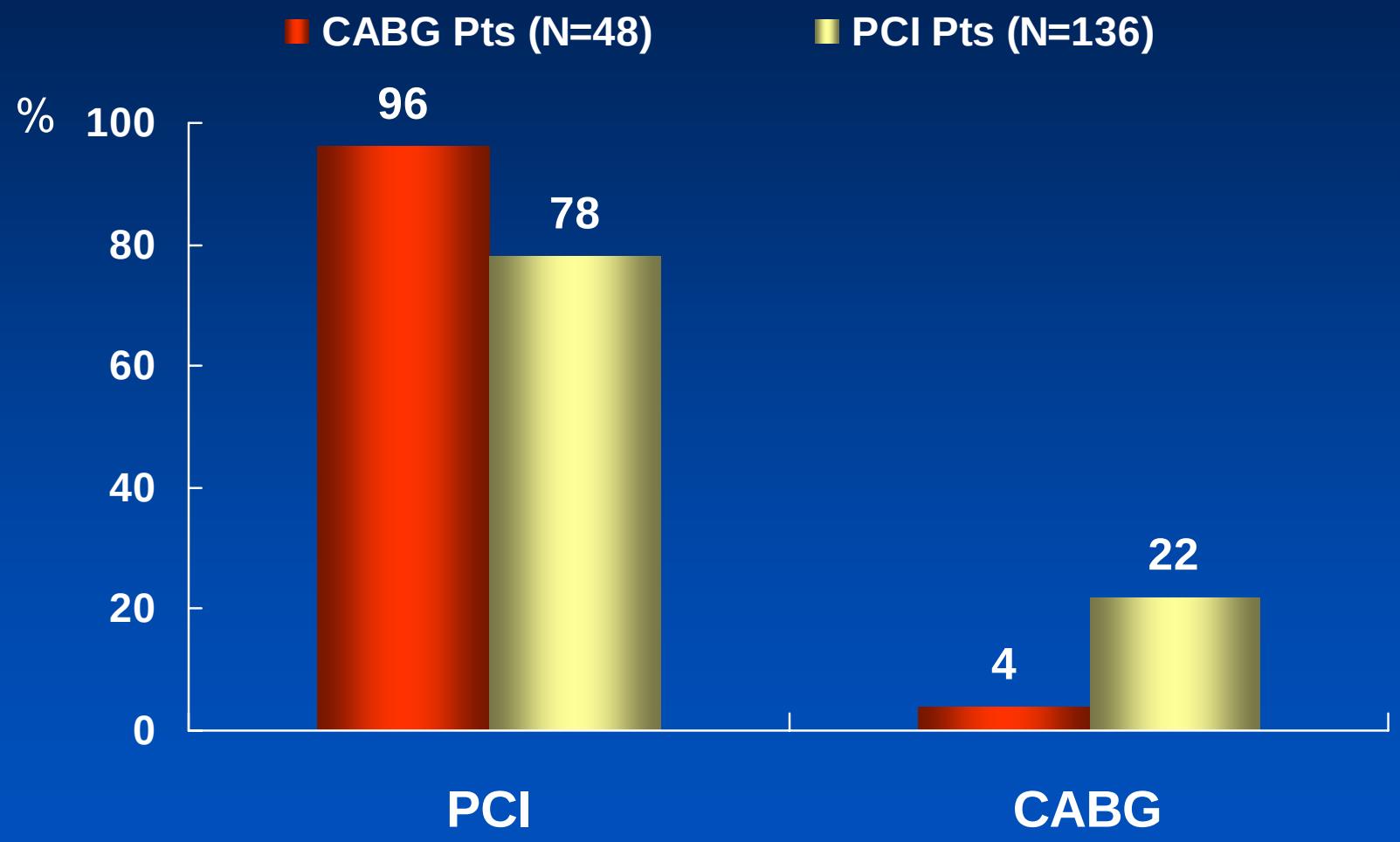
*HR are for the stenting group, as compared with CABG group

Outcomes for Representing Efficacy

For Approval of Drug or Devices by FDA

Class	End points	Safety data requirement	Effect size expected	Minimum strength of evidence needed
A	Mortality or stroke	Minimal	Small	P < 0.05
B	ESRD, MI, CHF	Intermediate	Small	P < 0.01
C1	Hospitalization, procedure	Intermediate to considerable	Moderate	p < 0.01
C2	Symptoms, QOL, Exercise capacity	Considerable	Substantial	P < 0.01 or P < 0.05 in 2 distinct studies
X	Surrogate markers such as blood pressure, lipid	Considerable	Substantial	P < 0.05 in 2 distinct studies

Type of Repeat Revascularization



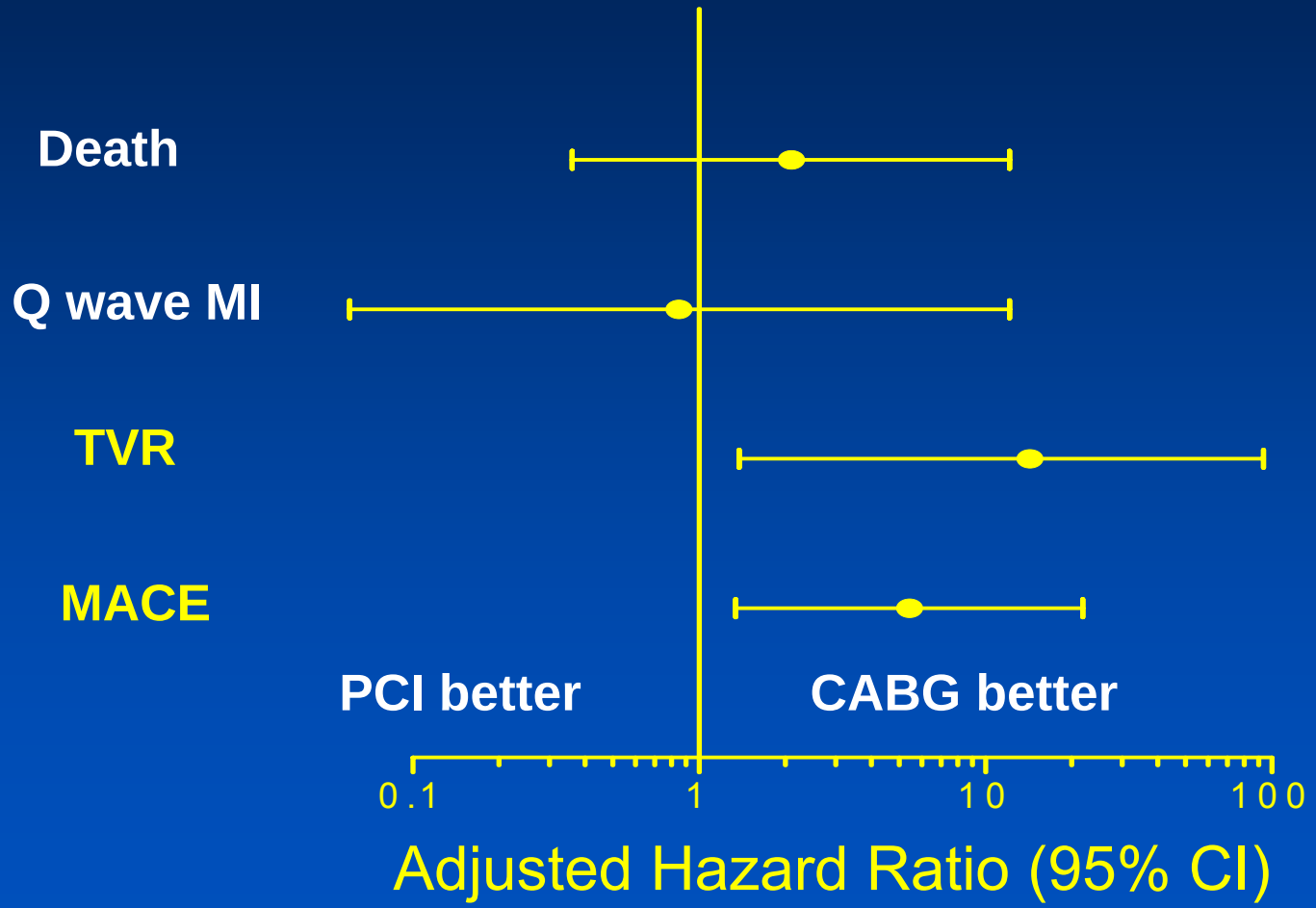
PCI Compared with CABG
In Diabetic Patients

	Crude		Multivariable adjusted	
	Adjusted HR (95% CI)	P	Adjusted HR (95% CI)	P
Death	0.70 (0.38-1.32)	0.27	0.78 (0.38-1.60)	0.50
Q–MI	0.38 (0.04-3.67)	0.39	0.30 (0.02-4.81)	0.39
TVR	9.00 (2.71-29.90)	**<0.001**	13.14 (3.09-55.92)	**<0.001**
CVA	1.29 (0.39-4.22)	0.68	1.72 (0.49-6.02)	0.39
Death/Q-MI/TVR	1.53 (0.95-2.48)	0.08	1.64 (0.96-2.82)	0.07
Death/Q-MI/TVR/CVA	1.41 (0.91-2.20)	0.12	1.95 (1.19-3.22)	**0.01**

PCI Compared with CABG
In Non-bifurcation

Outcome	Crude		Multivariable adjusted	
	HR (95% CI)	P	HR (95% CI)	P
Death	0.97 (0.59-1.59)	0.90	1.001 (0.50-1.99)	0.99
CVA	2.0 (0.61-6.67)	0.25	1.42 (0.37-5.45)	0.61
TVR	3.83 (1.43-10.25)	**0.004**	7.71 (1.78-33.38)	**0.006**
Death, Q-MI, or CVA	0.97 (0.61-1.55)	0.90	1.06 (0.57-1.99)	0.852
Death, Q-MI, CVA, or TVR	1.23 (0.82-1.85)	0.31	1.51 (0.91-2.49)	0.111

PCI Compared with CABG
Isolated LM



DES Compared with BMS

Outcome	Crude		Adjusted for propensity	
	Hazard Ratio (95% CI)	*P*	Hazard Ratio (95% CI)	*P*
Death	0.93 (0.61-1.41)	0.73	0.96 (0.58-1.59)	0.87
MI	1.22 (0.76-1.96)	0.42	0.89 (0.50-1.56)	0.68
TLR	0.39 (0.26-0.60)	**<0.001**	0.33 (0.19-0.55)	**<0.001**
TVR	0.55 (0.38-0.78)	**0.001**	0.37 (0.24-0.57)	**<0.001**
Death/MI	1.04 (0.75-1.44)	0.81	0.87 (0.59-1.28)	0.47
Death/MI/TLR	0.84 (0.64-1.10)	0.20	0.70 (0.51-0.97)	**0.03**
Death/MI/TVR	0.84 (0.66-1.09)	0.19	0.65 (0.48-0.89)	**0.006**

Efficacy of PCI for Unprotected LM Stenosis

- The risk of repeat revascularization is lower with use of CABG than PCI.
- However, repeat revascularization is one of outcomes assessing the efficacy of a certain strategy.
- The majority of restenosis at the LM was treated with PCI.
- The safety and efficacy of PCI was consistently approved in diverse subgroups of patients.

Is it enough to change the guideline ?

Limitations of MAIN-COMPARE

- It is evidenced that PCI is a good alternative to surgery.
- But, it is not sufficient enough to change guideline because…

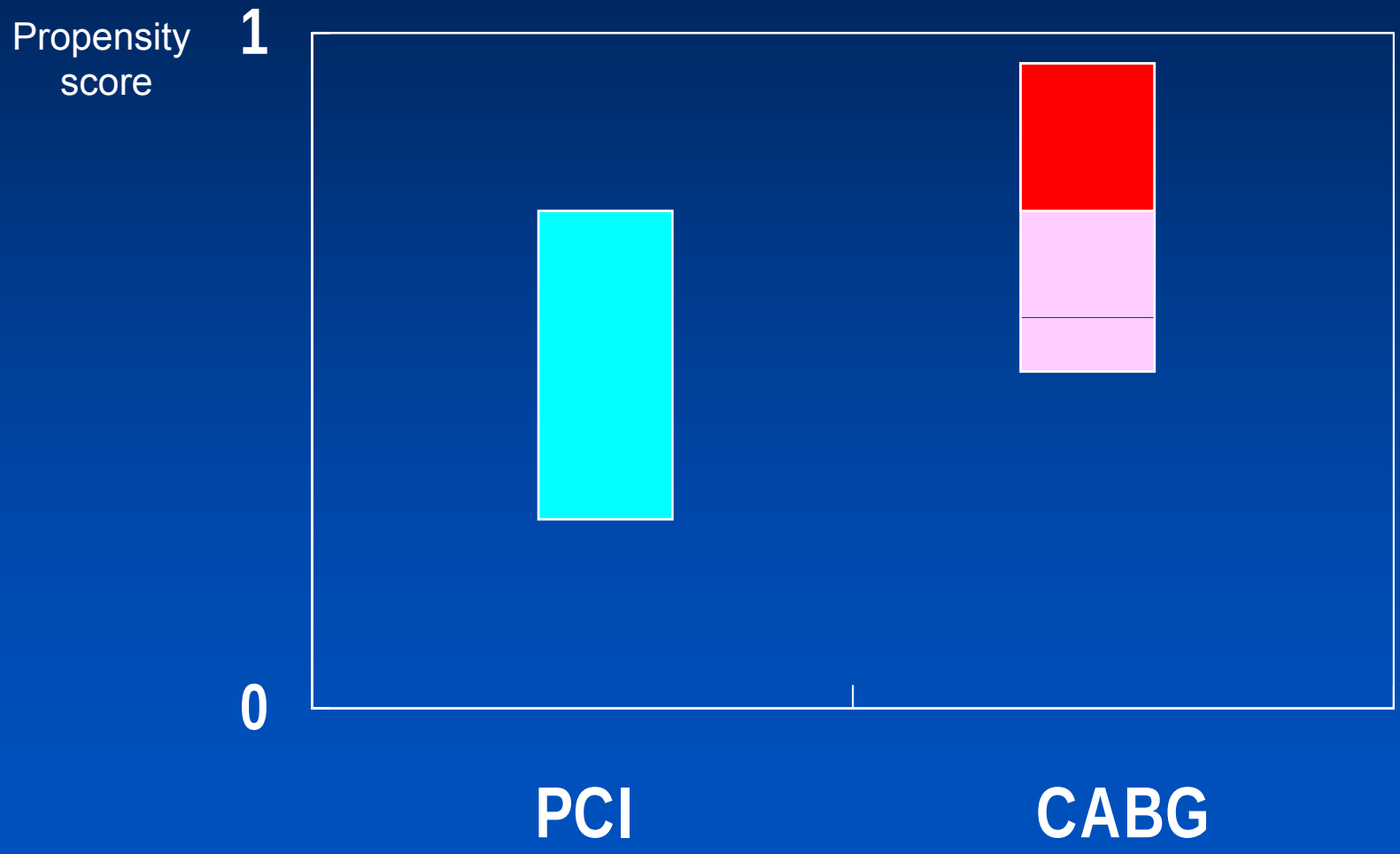
Baseline Characteristics of Propensity-Matched Patients (542 pairs)

Variable	Stents (n=542)	CABG (n=542)
Previous coronary angioplasty	14.8	15.1
Previous myocardial infarction	9.0	10.0
Previous congestive heart failure	2.9	3.0
Chronic obstructive pulmonary disease	2.6	2.2
Cerebrovascular disease	7.4	6.6
Peripheral vascular disease	2.0	2.0
Renal failure	3.7	3.9
Ejection fraction (%)		
Median	61	61
Interquartile range	54-66	55-66

Baseline Characteristics of Propensity-Matched Patients (542 pairs)

Variable	Stents (n=542)	CABG (n=542)
Electrocardiographic findings		
Sinus rhythm	97.6	96.7
Atrial fibrillation	2.4	3.1
Other	0.0	0.2
Clinical indication (%)		
Silent ischemia	2.8	2.7
Chronic stable angina	29.2	28.4
Unstable angina	57.4	57.9
NSTEMI	10.7	11.1

Feasibility of PCI for High-Risk Patients ?

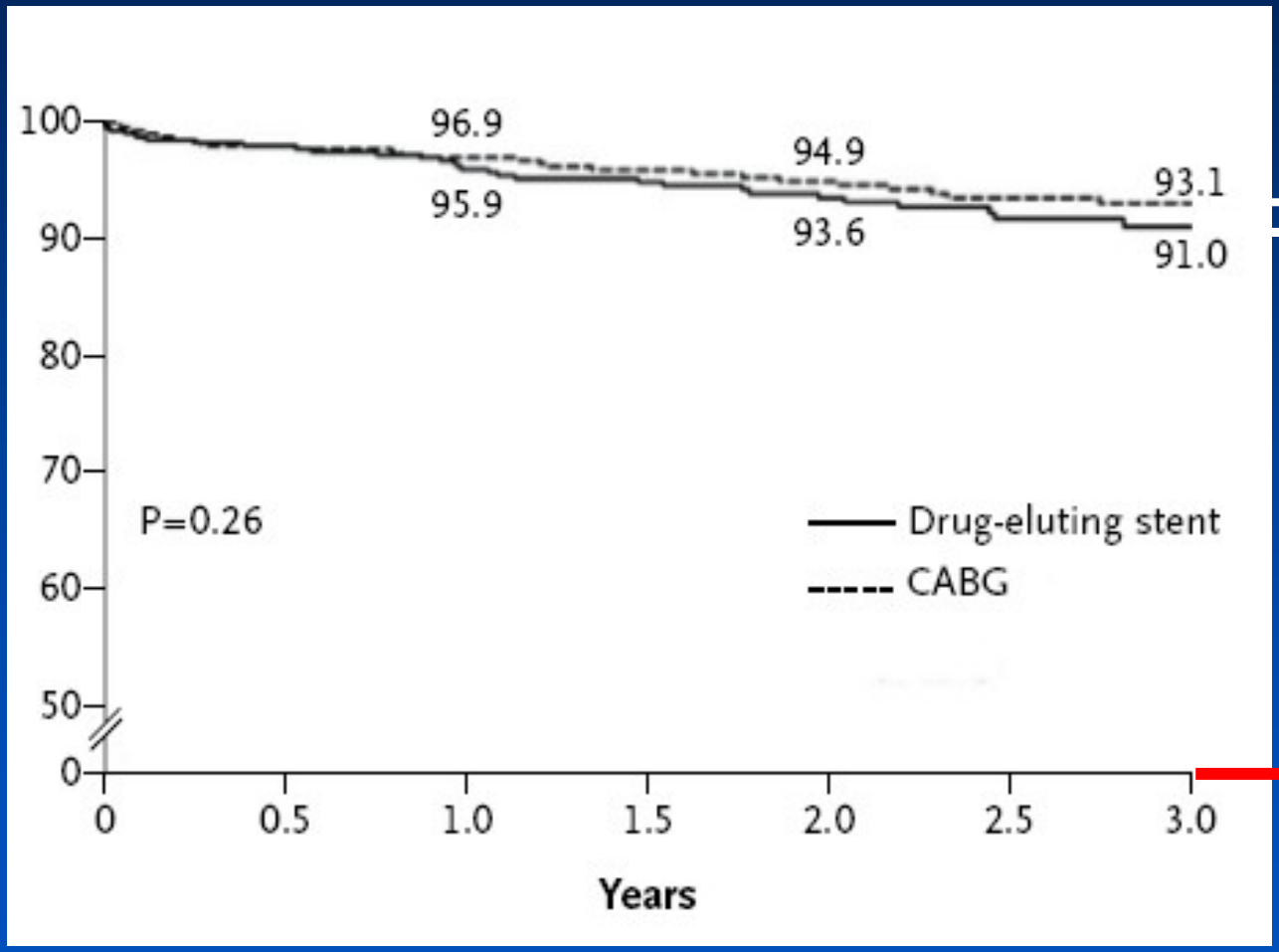


Angiographic Predictors by Detailed Independent Analysis ?

Variable	Stents (n=542)	CABG (n=542)
Angiographic characteristics (%)		
Extent of diseased vessel		
Left main only	11.8	11.1
Left main plus single-vessel disease	17.0	16.2
Left main plus double-vessel disease	31.7	33.9
Left main plus triple-vessel disease	39.5	38.7
Right coronary artery disease	53.7	53.7
Restenotic lesion	1.9	1.8

Incidence of Death

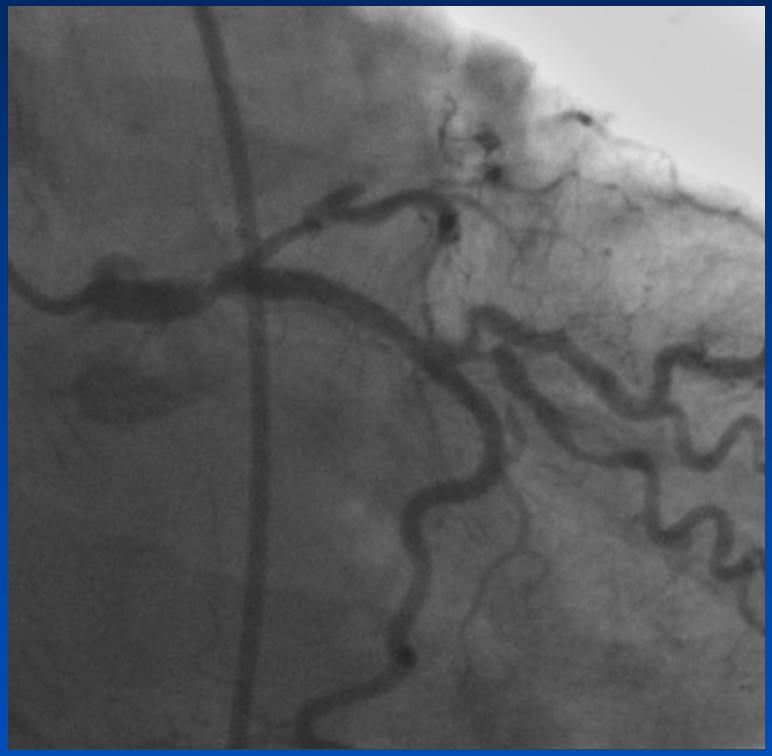
Longer F/U in DES patients is required…



12 Sites in Korea for MAIN-COMPARE
by experienced experts in tertiary hospitals.

- Asan Medical Center, Seoul, Korea
- Kangnam St Mary's Hospital, Seoul, Korea
- Yoido St Mary's Hospital, Seoul, Korea
- Kyungpook National University Hospital, Daegu, Korea
- Gachon University Gil Medical Center, Incheon, Korea
- Seoul National University Hospital, Seoul, Korea
- Seoul National University Bundang Hospital, Seongnam, Korea
- Samsung Medical Center, Seoul, Korea
- Ajou University Hospital, Suwon, Korea
- Yonsei University Medical Center, Seoul, Korea
- Chonnam National Univeristy Hospital, Gwangju, Korea
- Chung-Nam University Hospital, Daejon, Korea

Definitions for LM Study ?



- Where is LM ?
- What is a significant LM stenosis ?
- What is isolated LM disease ?
- What is TLR of LM ?
- What is TVR of LM ?
- How can we measure quantitative angiography at LM ?

Guideline
Level of Evidence from ACC/AHA

- Level A
  - Sufficient evidence from multiple RCT and meta-analysis
- Level B
  - Limited evidence from single RCT or non-randomized trials
- Level C
  - Only expert opinion, case studies

Future Studies to Change the Guideline

- **We need randomized studies performed**
  - Across the countries
  - With a standardized protocol
  - With an adequate calculation of statistical power
  - For very long-term F/U
  - Under the control of experienced organization

What we need to know further…

- Who can be more benefited by PCI ?
- Who can be more benefited by CABG ?
- Who can be comparably treated with either PCI or CABG ?