

# TCTAP 2014

## CABG Is the Best Treatment for Left Main Disease ?

(I have not included RCTs/Registries only reporting 1 year outcomes)

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Professor of Cardiovascular Surgery, University of Oxford



Conflicts of Interest:

- (i) Clinical:** Cardiac Surgeon
- (ii) Commercial:** Consultant to Medtronic, Abbott, AstraZeneca, Novadaq, VGS,
- (iii) One of 25 ESC/EACTS Guidelines Writers** on Myocardial Revascularization
- (iv) Chairman Surgical Committee of EXCEL trial**

STATE-OF-THE-ART PAPER AND COMMENTARY

## Revascularization for Unprotected Left Main Stem Coronary Artery Stenosis

### Stenting or Surgery

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Robert A. Guyton, MD, FACC,¶ Michael J. Mack, MD,# Paul T. Sergeant, MD, PHD,††  
Richard J. Shemin, MD, FACC,\*\* Peter K. Smith, MD, FACC,||  
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*Oxford, United Kingdom; Los Angeles, California; Buffalo, New York; Greenville and Durham,*

○ <90% of LMS are distal/bifurcation (very high risk of restenosis)  
○ <90% have multivessel CAD (CABG already offers survival benefit)

(CABG) is traditionally regarded as the "standard of care" because of its well-documented and durable survival advantage. There is now an increasing trend to use drug-eluting stents for LMS stenosis rather than CABG despite very little high-quality data to inform clinical practice. We herein: 1) evaluate the current evidence in support of the use of percutaneous revascularization for unprotected LMS; 2) assess the underlying justification for randomized controlled trials of stenting versus surgery for unprotected LMS; and 3) examine the optimum approach to informed consent. We conclude that CABG should indeed remain the preferred revascularization treatment in good surgical candidates with unprotected LMS stenosis. (J Am Coll Cardiol 2008;51:885-92) © 2008 by the American College of Cardiology Foundation

## Appropriate use of stents in LMS

**Favorable Long-Term Outcome After Drug-Eluting Stent Implantation in Nonbifurcation Lesions That Involve Unprotected Left Main Coronary Artery**

**A Multicenter Registry [*Circulation*. 2007;116:158-162]**

**Alaide Chieffo, MD; Seung J. Park, MD, PhD; Marco Valgimigli, MD; Young H. Kim, MD, PhD; Joost Daemen, MD; Imad Sheiban, MD; Alessandra Truffa, MD; Matteo Montorfano, MD; Flavio Airoldi, MD; Giuseppe Sangiorgi, MD; Mauro Carlino, MD; Iassen Michev, MD; Cheol W. Lee, MD, PhD; Myeong K. Hong, MD, PhD; Seong W. Park, MD, PhD; Claudio Moretti, MD; Erminio Bonizzoni, PhD; Renata Rogacka, MD; Patrick W. Serruys, MD, PhD; Antonio Colombo, MD**

○ 790 LMS:

- 19% NonBifurcation Lesions
- ostial (52%) or mid shaft (28%) or both (+35% RCA disease)
- 1 hospital death
- 73% repeat angiogram at 6 months with 1 restenosis
- at 2.5 years 3.4% mortality and 5% revascularization

**'Stent thrombosis could not be excluded in the 4 patients (2.7%) who died of unknown causes'**

# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

APRIL 24, 2008

VOL. 358 NO. 17

## 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.

### MAIN-COMPARE Registry of UPLM disease in 1102 stents and 1138 CABG

**Table 3. Hazard Ratios for Clinical Outcomes after Stenting as Compared with after CABG among Propensity-Matched Patients.\***

Outcome	Overall Cohort (N = 542 pairs)		BMS (N = 207 pairs)		DES = 396 pairs)	
	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
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
Composite outcome of death, Q-wave myocardial infarction, 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
Target-vessel revascularization	4.76 (2.80–8.11)	<0.001	10.70 (3.80–29.90)	<0.001	5.96 (2.51–14.10)	<0.001

there was a trend toward higher rates of death and the composite end point in the group that received DES



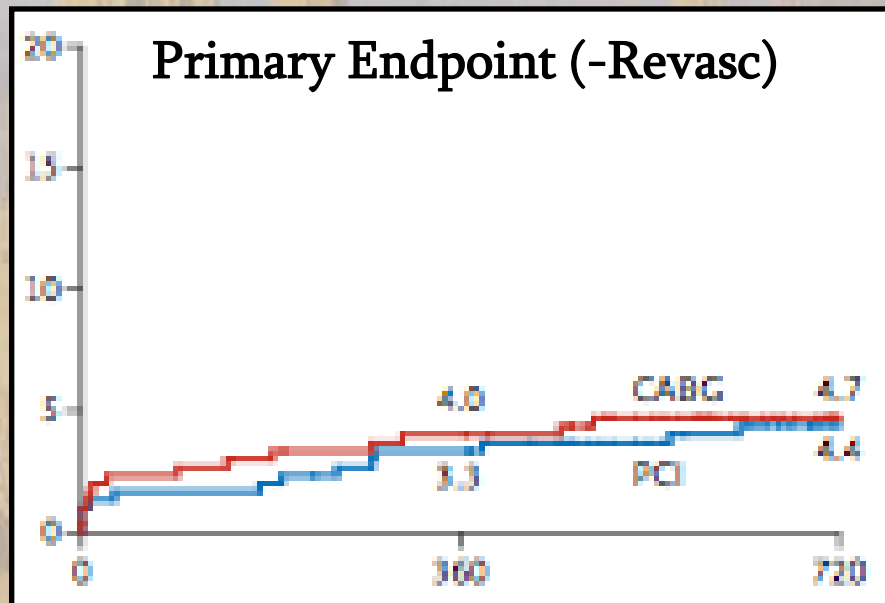
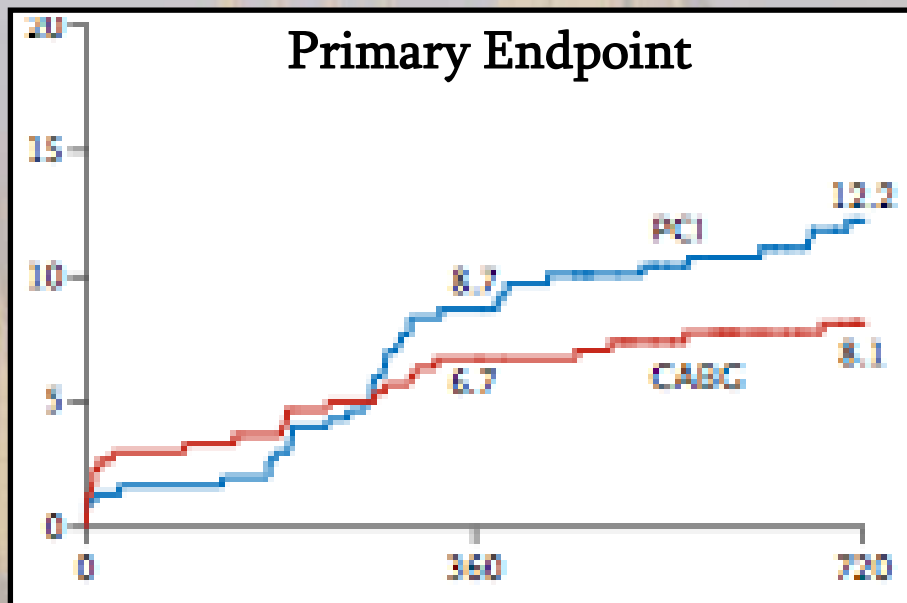
# Randomized Trial of Stents versus Bypass Surgery for Left Main Coronary Artery Disease

NEJM 2011

Seung-Jung Park, M.D., Young-Hak Kim, M.D., Duk-Woo Park, M.D.,

'PRECOMBAT': 600 patient RCT (300 PCI vs 300 CABG)

- Cohort of 1454 LM patients (59% NOT randomized)
- Mean SYNTAX score: 25 (vs 30 in SYNTAX)
- Mean Euroscore: 2.7 (vs 3.8 in SYNTAX)
- Primary endpoint: Death; CVA; MI; Repeat Revasc at 2years



○ Incidence of stroke 0.4% PCI vs 0.7% CABG

○ No increase in mortality or stroke with CABG (vs SYNTAX)

# The NEW ENGLAND JOURNAL of MEDICINE

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MARCH 5, 2009

VOL. 360 NO. 10

## THE SYNTAX TRIAL

### Percutaneous Coronary Intervention versus Coronary-Artery Bypass Grafting for Severe Coronary Artery Disease

Patrick W. Serruys, M.D., Ph.D., Marie-Claude Morice, M.D., A. Pieter Kappetein, M.D., Ph.D., Antonio Colombo, M.D., David R. Holmes, M.D., Michael J. Mack, M.D., Elisabeth Ståhle, M.D., Ted E. Feldman, M.D., Marcel van den Brand, M.D., Eric J. Bass, B.A., Nic Van Dyck, R.N., Katrin Leadley, M.D., Keith D. Dawkins, M.D., and Friedrich W. Mohr, M.D., Ph.D., for the SYNTAX Investigators\*

Landmark trial (most important trial ever of PCI vs CABG)

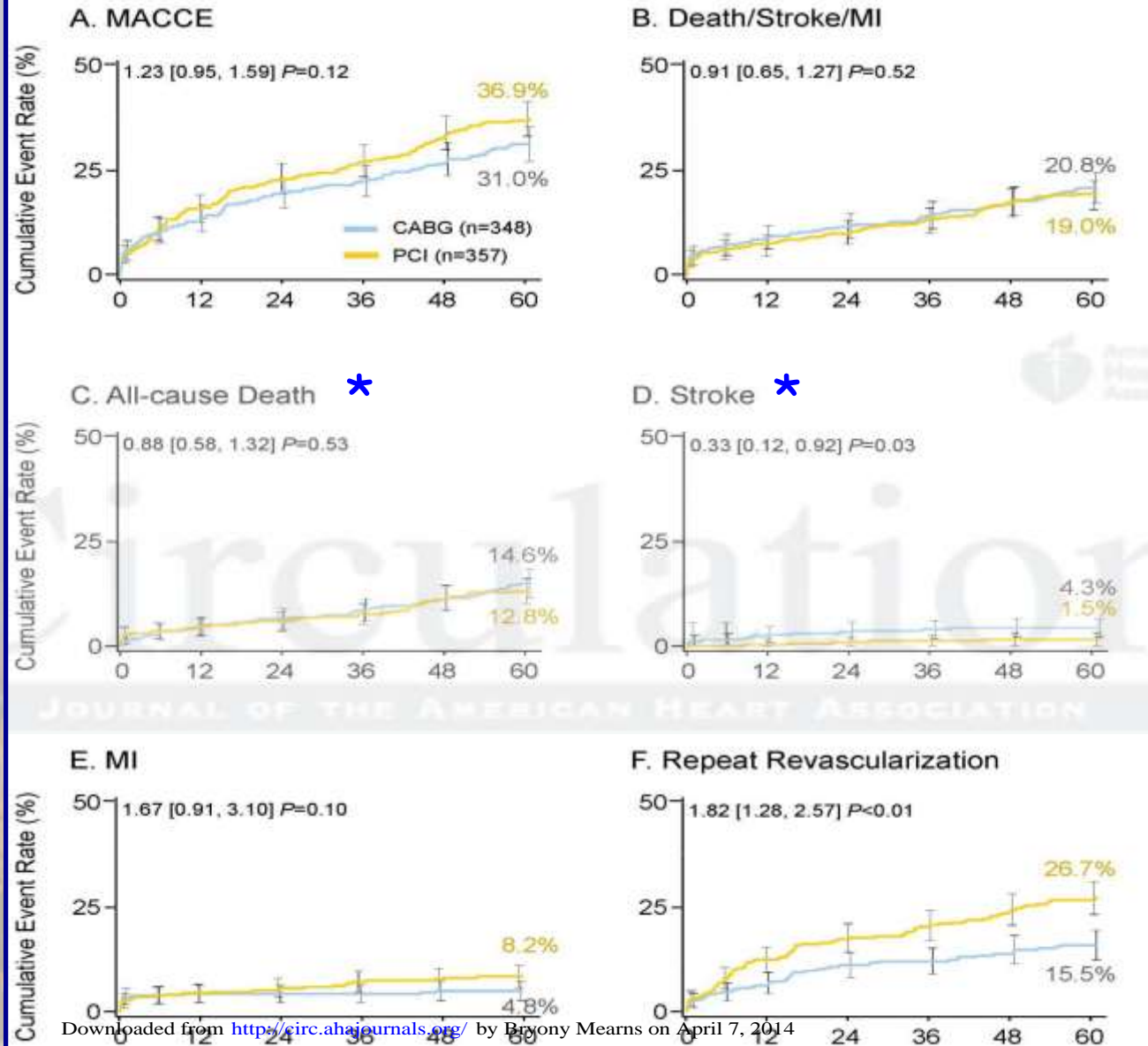
Addressed the two limitations of all previous RCTS

- 'All comer' trial (vs highly select patients in previous RCTs)
- 5 year outcomes death and MACCE [[Lancet Feb 22 2013](#)]
- Parallel Registry (35% of patients straight to CABG !!)

### Five-Year Outcomes in Patients with Left Main Disease Treated with Either Percutaneous Coronary Intervention or Coronary Artery Bypass Grafting in the SYNTAX Trial

Marie-Claude Morice, Patrick W. Serruys, A. Pieter Kappetein, Ted E. Feldman, Elisabeth Ståhle, Antonio Colombo, Michael J. Mack, David R. Holmes, James W. Choi, Witold Ruzyllo, Grzegorz Religa, Jian Huang, Kristine Roy, Keith D. Dawkins and Friedrich Mohr

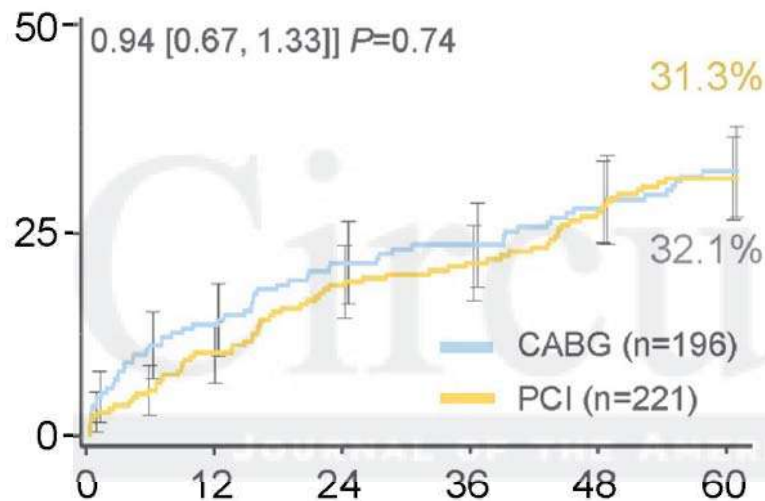
# SYNTAX: 705 Patients LM Disease at 5 years



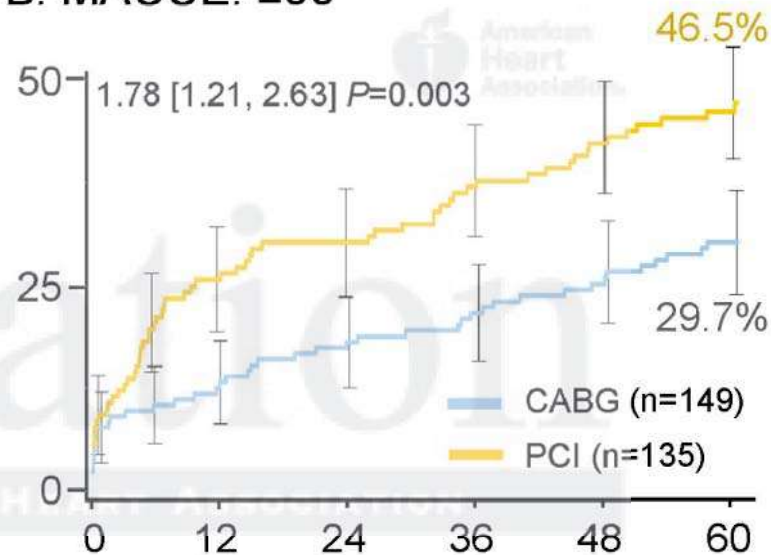
Downloaded from <https://circ.ahajournals.org/> by Bryony Mearns on April 7, 2014

\* = different from SYNTAX 3VD

### A. MACCE: 0-32



### B. MACCE: $\geq 33$



**HYPOTHESIS:** Unlike 3 VD, LM without additional proximal CAD may result in excessive competitive flow for bypass grafts

**NOBLE Trial (planned recruitment of 1200 patients)**

**EXCEL Trial (Abbott Vascular) started Sept 2010**

**only in SYNTAX Score <33**

•3600 patient trial of PCI vs CABG (2600 RCT+1000 Registry)

•1000 registry patients now enrolled

•>1906 RCT patients enrolled to date

•Enrolment stopped for financial costs (march 2014)



## Left Main Coronary Artery Stenosis

### A Meta-Analysis of Drug-Eluting Stents Versus Coronary Artery Bypass Grafting

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**Objectives** The goal of this study was to provide a systematic review comparing the long-term outcomes of percutaneous coronary intervention (PCI) with drug-eluting stents (DES) versus coronary artery bypass graft surgery (CABG) for unprotected left main coronary artery (UPLM) stenosis.

**Background** One-year outcomes from randomized controlled trials, observational studies, and pooled analyses have demonstrated the safety and efficacy of PCI of the UPLM when compared with CABG. However, there remain concerns over the sustainability of PCI with DES at longer follow-up.

**Methods** Studies published between January 2000 and December 2012 of PCI versus CABG for UPLM stenosis were identified using an electronic search and reviewed using meta-analytical techniques.

**Results** Twenty-four studies comprising 14,203 patients were included in the analysis. There was no significant difference for all-cause mortality between PCI or CABG at 1 year (odds ratio [OR]: 0.792, 95% confidence interval [CI]: 0.53 to 1.19), 2 years (OR: 0.920, 95% CI: 0.67 to 1.26), 3 years (OR: 0.94, 95% CI: 0.60 to 1.48), 4 years (OR: 0.84, 95% CI: 0.53 to 1.33), and 5 years (OR: 0.79, 95% CI: 0.57 to 1.08). The need for target vessel revascularization (TVR) was significantly higher in patients undergoing PCI at all time points. The occurrence of stroke, however, was significantly less frequent in patients treated with PCI. The occurrence of nonfatal myocardial infarction showed a statistically significant trend towards a lower incidence in CABG patients at 1 year (OR: 1.62, 95% CI: 1.05 to 2.50), 2 years (OR: 1.60, 95% CI: 1.09 to 2.35), and 3 years (OR: 2.06, 95% CI: 1.36 to 3.1). There was no significant difference in combined major adverse cardiovascular and cerebrovascular events between the 2 groups.

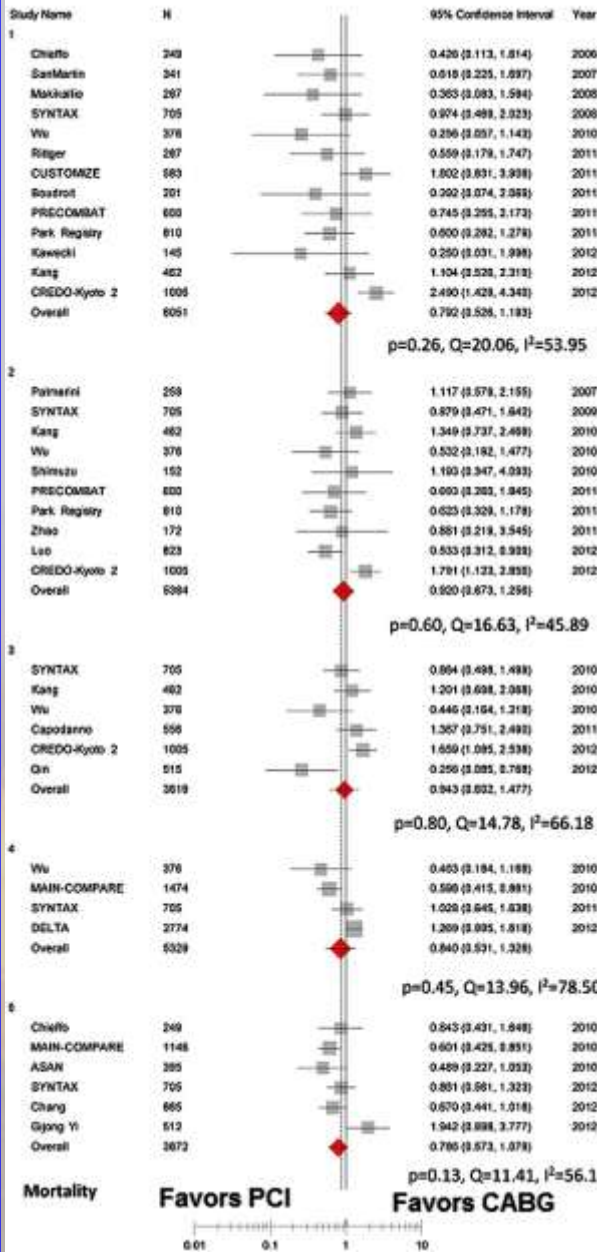
**Conclusions** Our findings suggest that PCI with DES is a safe and durable alternative to CABG for the revascularization of UPLM stenosis in select patients at long-term follow-up. (J Am Coll Cardiol Intv 2013;6:1219–30) © 2013 by the American College of Cardiology Foundation

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24 studies (3 RCTs) with 14203 patients followed up to 5 years

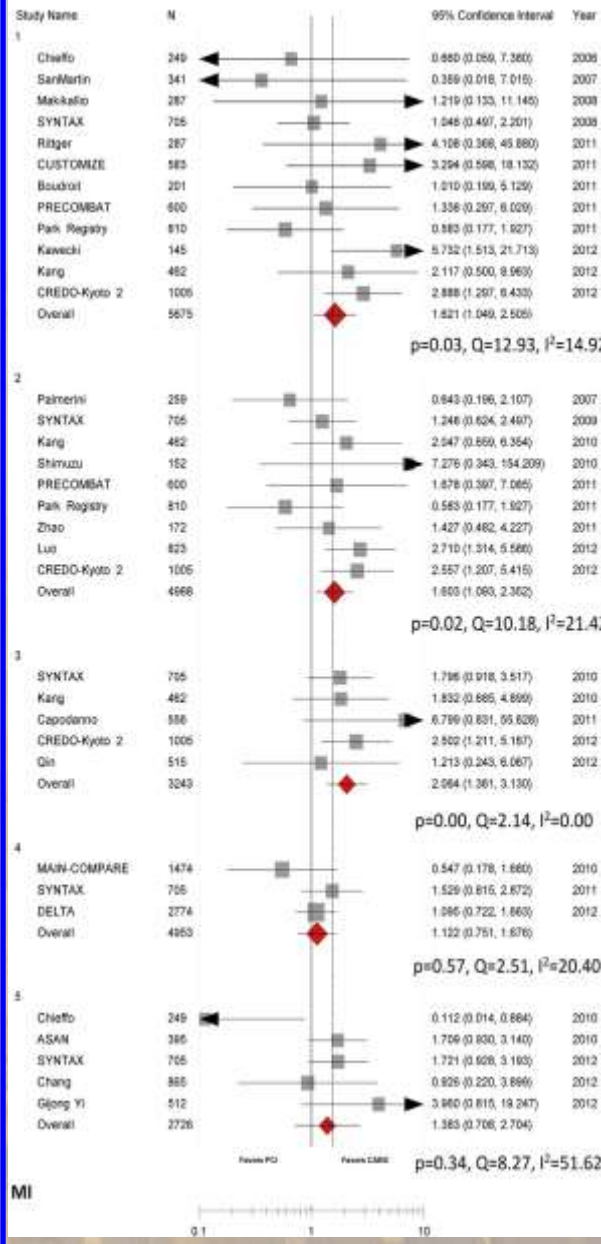
# DEATH:NS over 5 years

PCI with DES vs. CABG for UPLMS



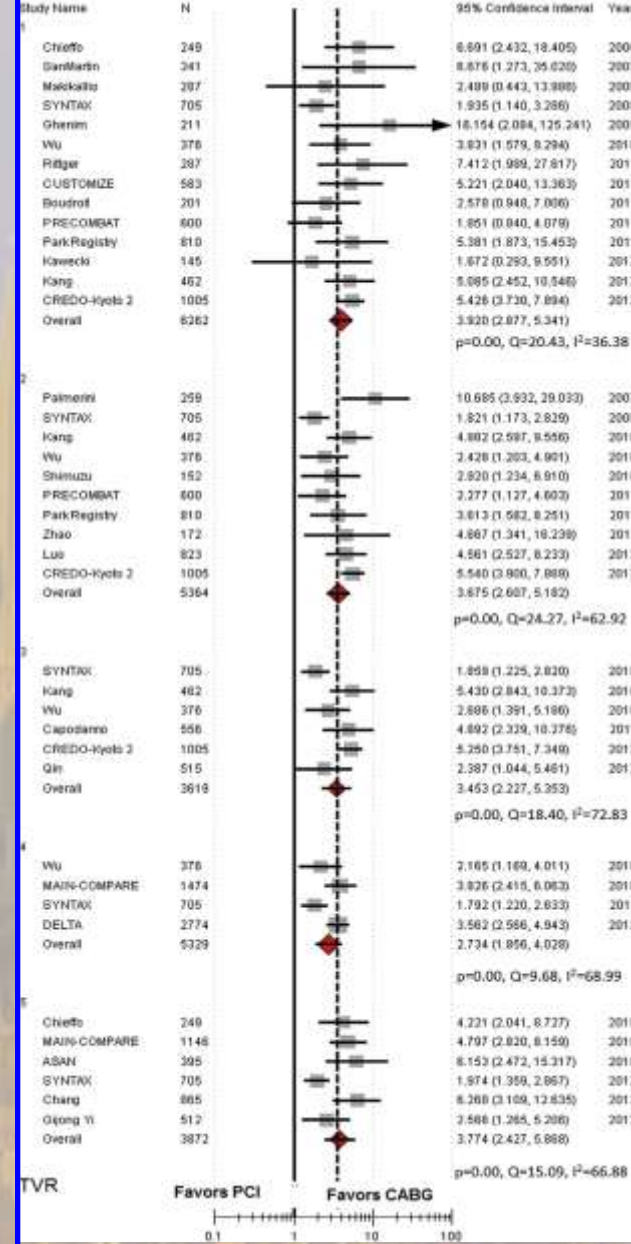
# MI (sig inc PCI 1-3yrs)

PCI with DES vs. CABG for UPLMS



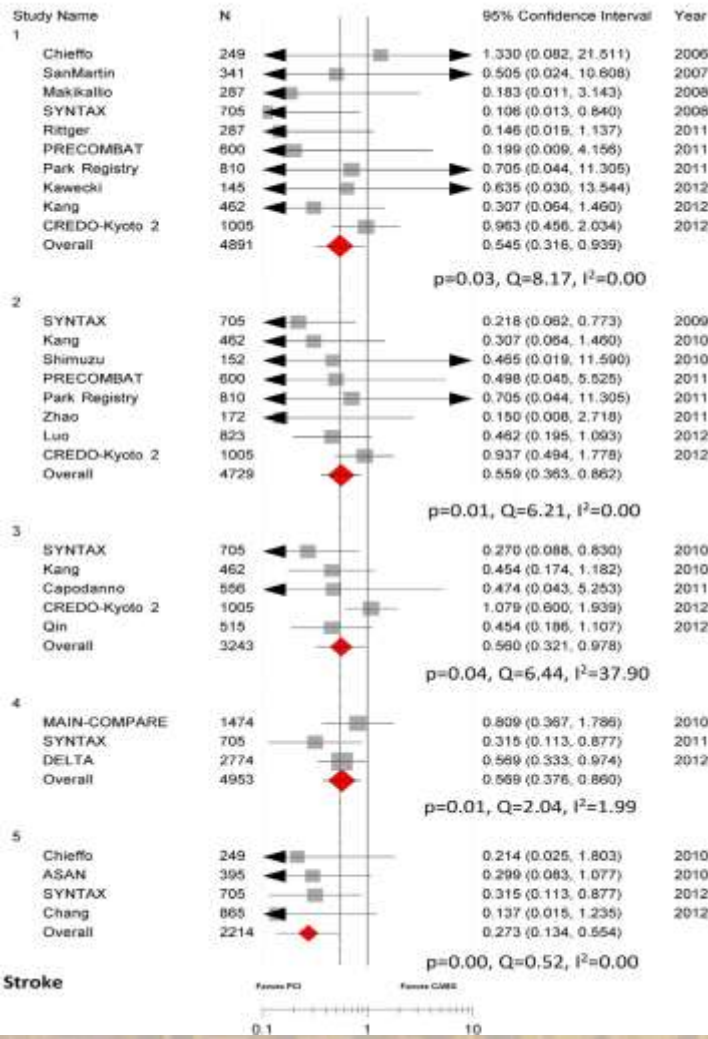
# TVR (sig inc PCI 1-5 yr)

PCI with DES vs. CABG for UPLMS



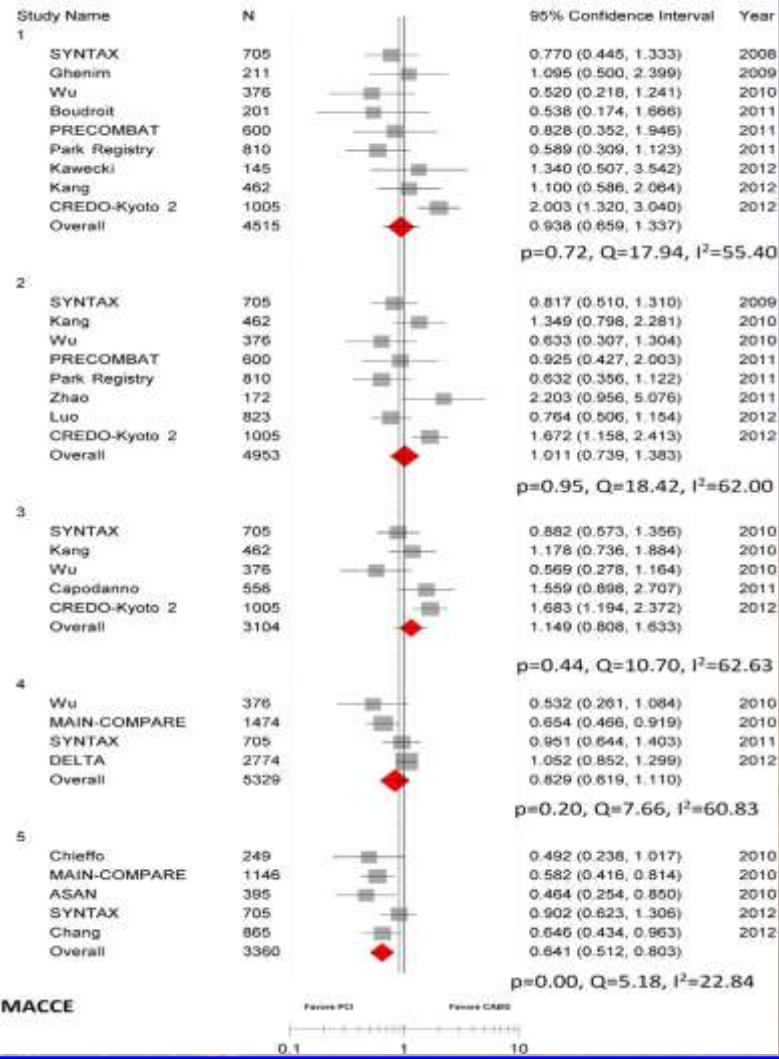
# CVA (sig inc CABG 1-5yr)

## PCI with DES vs. CABG for UPLMS



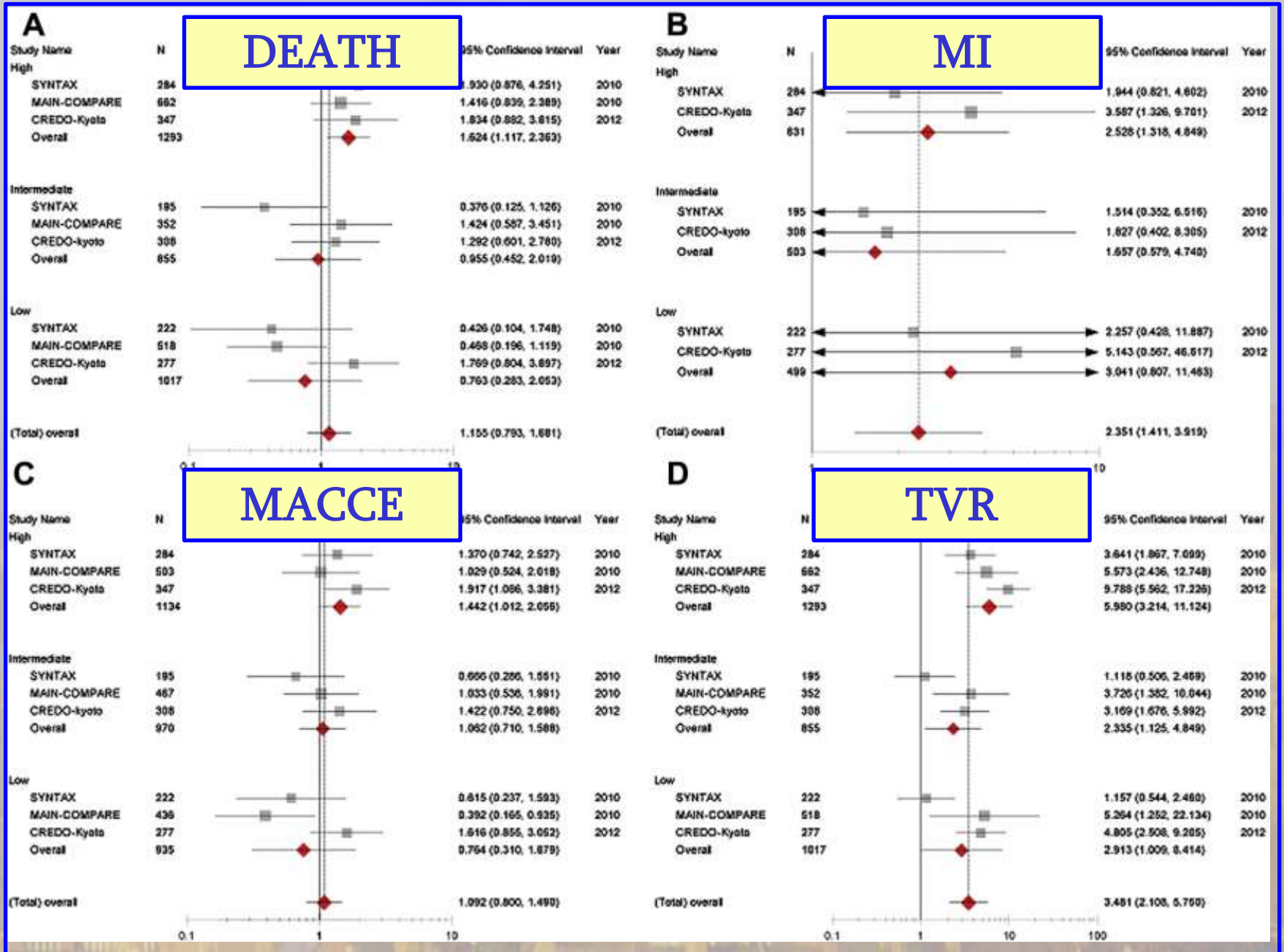
# MACCE (sig inc CABG at 5 yr)

## PCI with DES vs. CABG for UPLMS





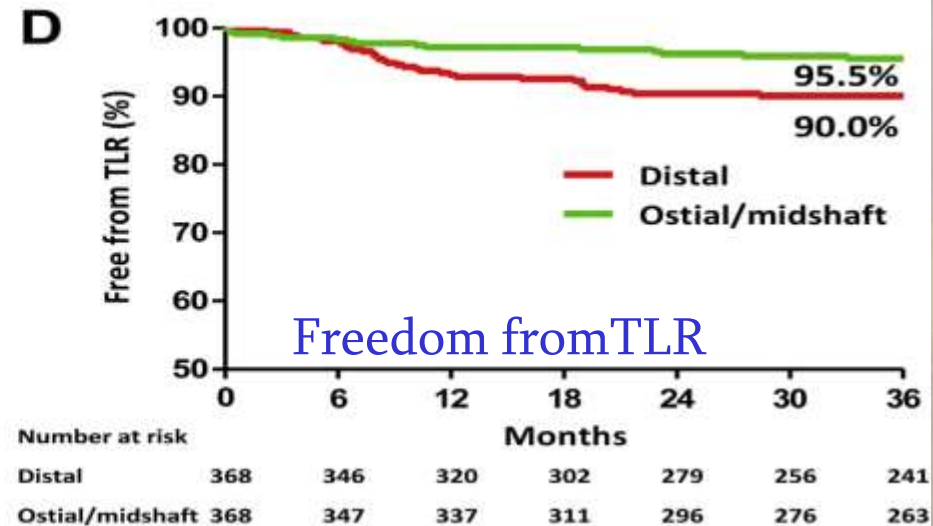
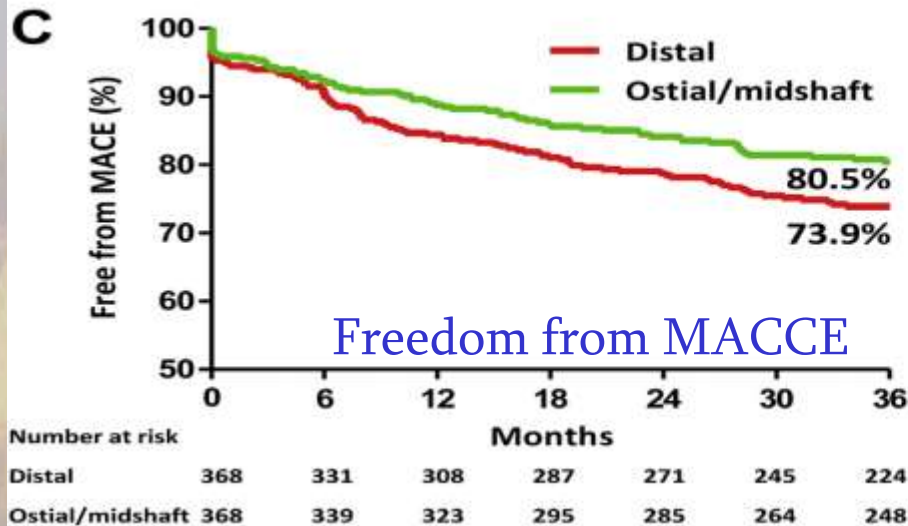
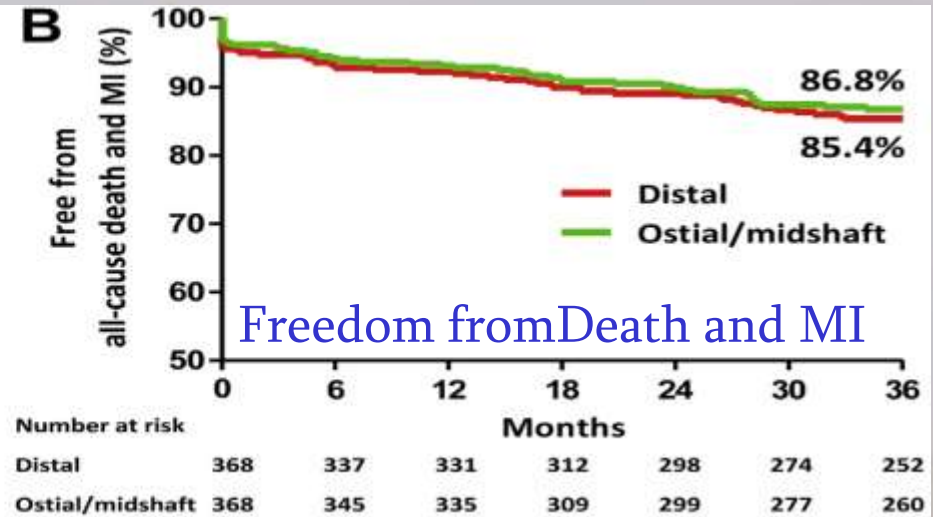
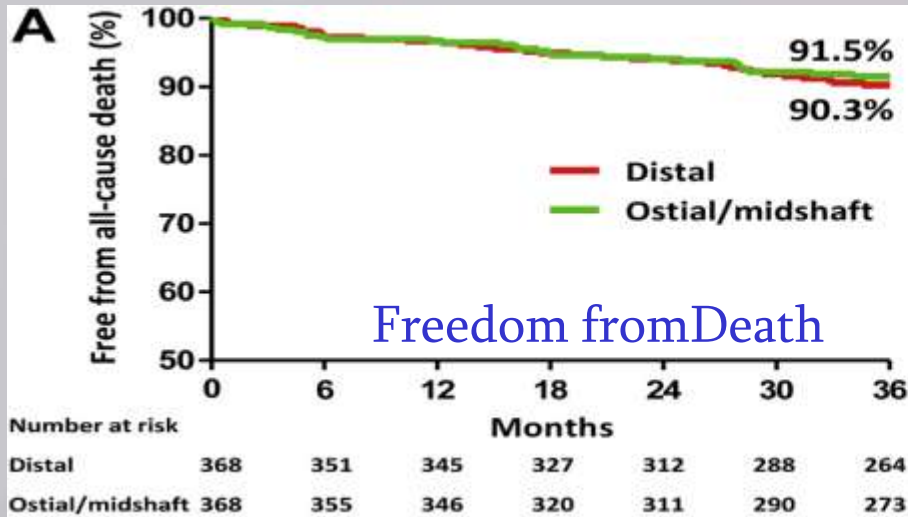
# OUTCOMES ACCORDING TO SYNTAX TERCILES





# DELTA REGISTRY: Ostial/Mid-shaft vs Distal LM [JACC 2013]

736 PPM patients (from total of 1612) at a median of 3.2 years

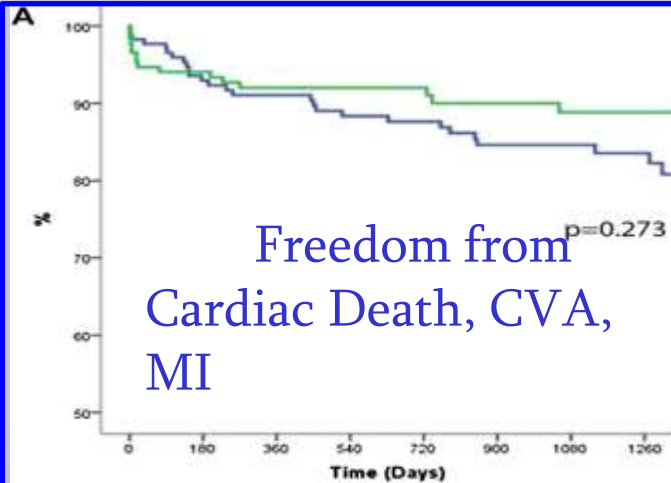


With regard to all-cause death and the composite endpoint of all-cause death and myocardial infarction, propensity-score adjusted analysis suggested a trend toward higher rates of these in the distal ULMCA PCI group, although this was not observed in the propensity-score matched analysis.

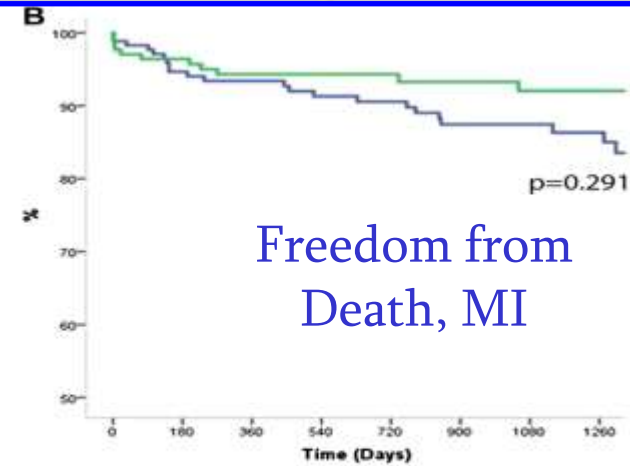
# DELTA REGISTRY: WOMEN [AM J Cardiol 2014]

350 PPM (from total of 817) women at median of 3.2 years

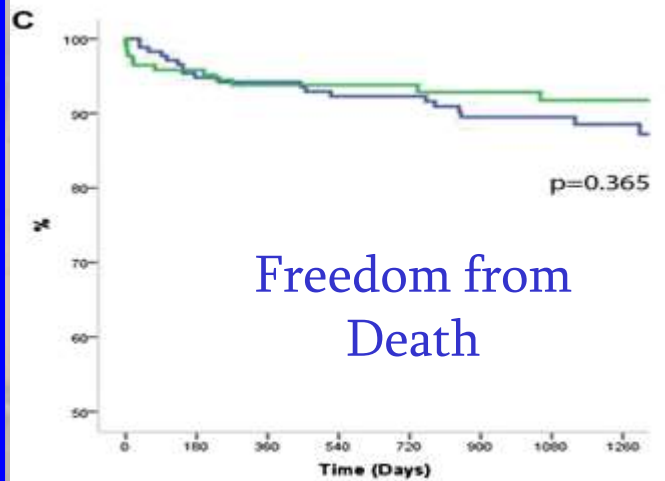
SYNTAX score 26.6 PCI vs 34 CABG



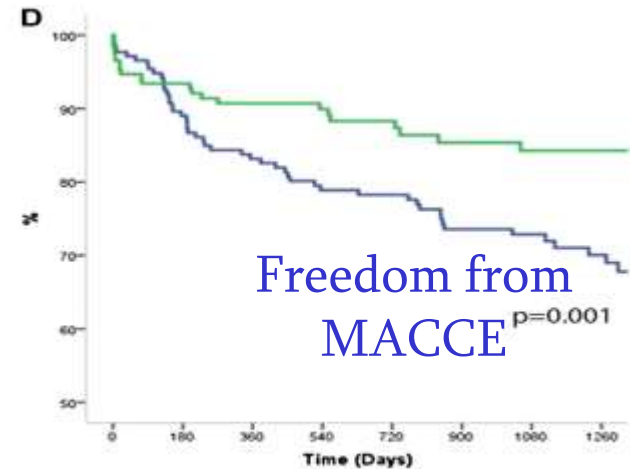
CABG	174	139	130	114	95	80	74	67
PCI	174	153	141	127	12	106	98	68



CABG	174	139	130	114	95	80	74	67
PCI	174	153	141	127	12	106	98	68



CABG	174	143	134	119	102	89	82	73
PCI	174	161	156	144	137	122	114	78



CABG	174	139	130	114	95	80	74	67
PCI	174	153	141	127	12	106	98	68

CABG  
PCI

# Coronary artery bypass graft versus percutaneous coronary intervention with drug-eluting stent implantation for diabetic patients with unprotected left main coronary artery disease: the D-DELTA registry. [Eurointervention 2013]

Meliga E1, De Benedictis M, Chieffo A et al

- 826 patients with DM + ULMCA who received DES (n=520) or CABG (n=306)
- In-hospital
  - ✗ MACCE significantly higher in CABG due to a higher incidence of MI.
- At four-year follow-up CABG resulted in lower risk of :
  - ✓ Death: CABG 87.4% vs PCI 82.5%:  $\Delta$  4.9%, p=0.124
  - ✓ Composite of death, MI and CVA: CABG 85.4% vs PCI 78.9%;  $\Delta$  6.5%; p=0.11
  - ✓ TVR: CABG 95.4% vs PCI 79.4%,  $\Delta$  16%; p<0.001,
  - ✓ MACCE: CABG 81.9% vs PCI 64.7%:  $\Delta$  17.2%; p<0.001).

# Readmission Rate After Coronary Artery Bypass Grafting Versus Percutaneous Coronary Intervention for Unprotected Left Main Coronary Artery Narrowing.

[Am J Cardiol. 2014 Mar 1 \[Epub ahead of print\]](#)

[Roh JH, Kim YH, Ahn JM, Yun SH, Lee JB, Ge J, Le W, Park GM, Lee JY, Park DW, Kang SJ, Lee SW, Lee CW, Park SW, Park SJ.](#)

- unadjusted and adjusted risk of readmissions in 1,352 patients (783 PCI and 569 CABG)
- consecutively enrolled in a multicenter registry of ULMCA stenosis (PRECOMBAT)
- At a median of  $48.7 \pm 16.0$  months of follow-up 26.3% PCI vs 14.8% CABG patients experienced at least 1 readmission after the index procedure during (p <0.001).
- The most frequent causes of readmission were repeat revascularization after PCI (41%) and noncardiac readmissions after CABG (48%).
- PCI was associated with more readmissions than CABG (HR 2.0: 95% CI 1.5 to 2.7, p <0.001), being an independent predictor of readmission (HR 1.8, 95% CI 1.4 to 2.31; p <0.001).
- Except for the first 3 months, when there was no significant difference in readmission rate, a higher rate after PCI was consistently observed over the remainder of the follow-up period.

In conclusion, PCI was associated with a higher risk of readmission than CABG in treating ULMCA. This higher risk was attributable to more frequent revascularization in the PCI group.



## Summary and Conclusions

- ① Traditional view that CABG is the only treatment for LM disease is no longer tenable and there is consistent evidence from RCTs and registries that some LM disease is, at least, as effectively treated by stents as CABG for at least for 4-5 years
- ② Increasing evidence that PCI provides equal if not superior benefit to CABG in patients with lower severity left main (excessive competitive flow for bypass grafts ?)
- ③ CABG results in increased risk of stroke in LM (vs MVD). ?greater burden of aortic disease and a higher incidence of carotid disease
- ④ Some evidence that patients with DM and women may have better outcomes with CABG (certainly the case for 3VD); ?distal LM
- ⑤ CABG: fewer readmissions than PCI mainly because of lower TVR
- ⑥ NOBLE and EXCEL trials are likely to give definitive guidance regarding optimal treatment for LM with SYNTAX scores <32
- ⑦ 40% to 65% of all left main disease have SYNTAX scores >32 and appear to have strong survival advantage with CABG by 3 years and continuing to increase past 5 years
- ⑧ Comparisons of survival outcome of PCI vs CABG should have a minimum follow-up of 5 years

# The 2010 Guidelines...what do they recommend ?

Subset of CAD by anatomy	CABG		PCI		
	ESC/EA CTS	ACC	ESC/EA CTS	ACC	
<b>Heart team for LM or complex CAD</b>	I C	I C	I C	I C	
1 VD: NON proximal LAD	IIb C	III B	I C	III B	
1 VD: proximal LAD	I A	IIa B	IIa B	IIb B	
2 VD: NON proximal LAD	IIb C	IIa B	I C	IIb B	
2 VD: proximal LAD	I A	I B	IIa B	IIb B	
3 VD, simple lesions, full functional revasc achievable with PCI, SYNTAX scores <22	I A	I B	IIa B	IIb B	III B
3 VD, complex lesions, incomplete revasc achievable with PCI, SYNTAX scores >22	I A	I B	III A	IIb B	III B
LM (isolated or 1VD, ostium/shaft)	I A	I B	IIa B	IIa B	
LM (isolated or 1VD, distal bifurcation)	I A	I B	IIb B	IIb B	III B
LM + 2VD or 3VD, SYNTAX scores <33	I A	I B	IIb B	IIb B	III B
LM + 2VD or 3VD, SYNTAX scores >32	I A	I B	III B	IIb B	III B

79%

66%

**Broad agreement between European and North American Guidelines**

# WHY DOES CABG HAVE SUCH A SURVIVAL BENEFIT OVER PCI ?

Anatomically, atheroma is mainly located in the proximal coronary arteries

1. Placing bypass grafts to the **MID CORONARY VESSEL** has **TWO** effects
  - (i) Complexity of '**CULPRIT**' lesion is irrelevant
  - (ii) over the long term offers prophylaxis against **FUTURE** 'culprit' lesionsIn contrast, PCI only treats '**SUITABLE**' localised proximal 'culprit' lesions but has **NO PROPHYLACTIC BENEFIT** against new disease

462  
2

THE NEW ENGLAND JOURNAL OF MEDICINE

Aug. 25, 1988

IMA elutes **NO** into coronary circulation reducing risk of further disease

## DIFFERENCE BETWEEN ENDOTHELIUM-DEPENDENT RELAXATION IN ARTERIAL AND IN VENOUS CORONARY BYPASS GRAFTS

THOMAS F. LÜSCHER, M.D., DENNIS DIEDERICH, M.D., ROBERT SIEBENMANN, M.D., KURT LEHMANN, M.D.,

## Drug-Eluting Stent and Coronary Thrombosis

Biological Mechanisms and Clinical Implications CTRC 2007

impairs re-endothelialization, creates pro-thrombotic environment, impairs endothelial function downstream

3. PCI means incomplete revascularization (*Hannan Circ 2006*)
  - Of 22,000 PCI 69% had incomplete revascularization
  - >2 vessels (+/- CTO) HR for mortality 1.4 (95% CI = 1.1-1.7)

PCI will 'never' match the results of CABG for LM/MVD (POBA;BMS;DES)

# SYNTAX RCT Results (5/5 Years): Left Main: n=705

	PCI	CABG	
nos	357	348	p
Death	12.8	14.6 (+1.8%) *	.53
Cardiac Death	8.6	7.2 (-1.4%)	.46
MI	8.2	4.8 (-3.4%)	.10
CVA	1.5	4.3 (+2.8%) *	.03
D+C+M	19	20.8 (+1.8%)	.57
Revasc	26.7	15.5 (-11.2%)	<0.01

\* = different from SYNTAX 3VD

## EXCEL TRIAL (Abbott Vascular)

- 2600 patient RCT: PCI vs CABG
- **only in SYNTAX Score <33**
- 1000 registry patients now enrolled
- ie 3600 in total
- started Sept 2010
- >1906 RCT patients enrolled to date
- Enrolment stopped for financial costs

Low <23	nos	118	104	
	death	7	11.3	.28
	CVA	1.8	4.1	.28
	MI	6.2	3.1	.32
	D+C+M	13.9	15.2	.71
	Revasc	23	20.3	.65

Intd 23-32	nos	103	92	
	death	8.9	19.3	.04
	CVA	1.0	3.6	.23
	MI	6.0	4.6	.71
	D+C+M	15.7	24.9	.11
	Revasc	22.2	16.6	.40

High >32	nos	135	149	
	death	20.9	14.1	.11
	CVA	1.6	4.9	.13
	MI	11.7	6.1	.40
	D+C+M	26.1	22.1	.33
	Revasc	34.1	11.6	<.001





European Heart Journal  
doi:10.1093/eurheartj/ehq318

**FASTTRACK**  
**ESC HOT LINE**

# Randomized trial to compare bilateral vs single internal mammary coronary artery grafting: 1-year results of the ART Revascularisation Trial (ART)

David P. Taggart<sup>1\*</sup>, Douglas ... , Alastair M. Gray<sup>3</sup>, Belinda Lees<sup>4,5</sup>, Fiona Nugara<sup>4</sup>, Ly-Mee ... Campbell<sup>3</sup> and Marcus Flather<sup>4,5</sup>, on behalf of the ART Investigators

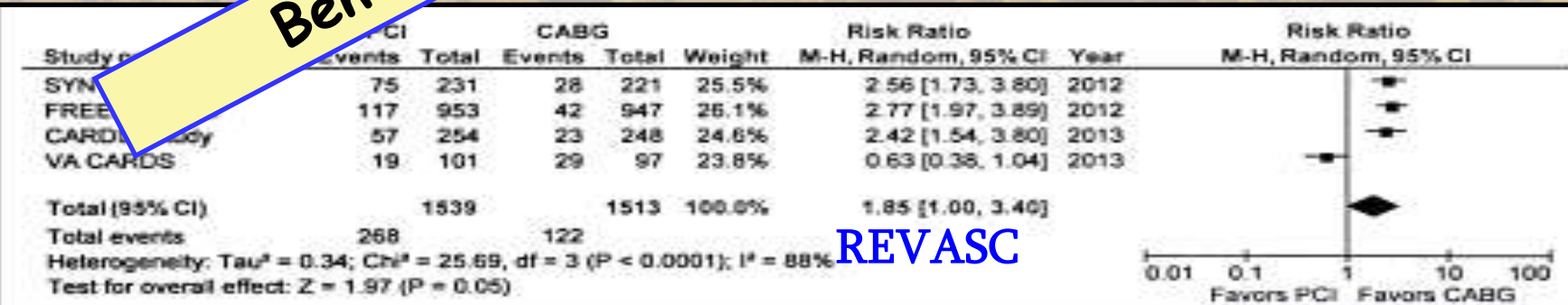
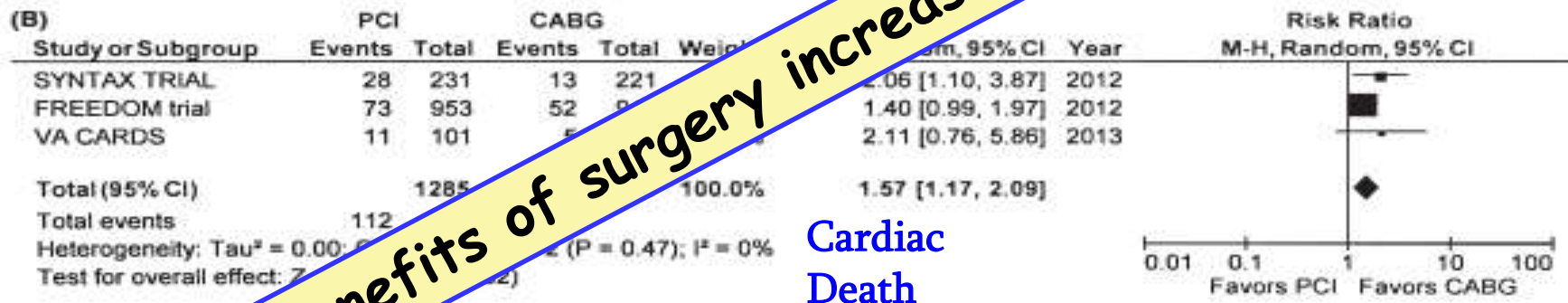
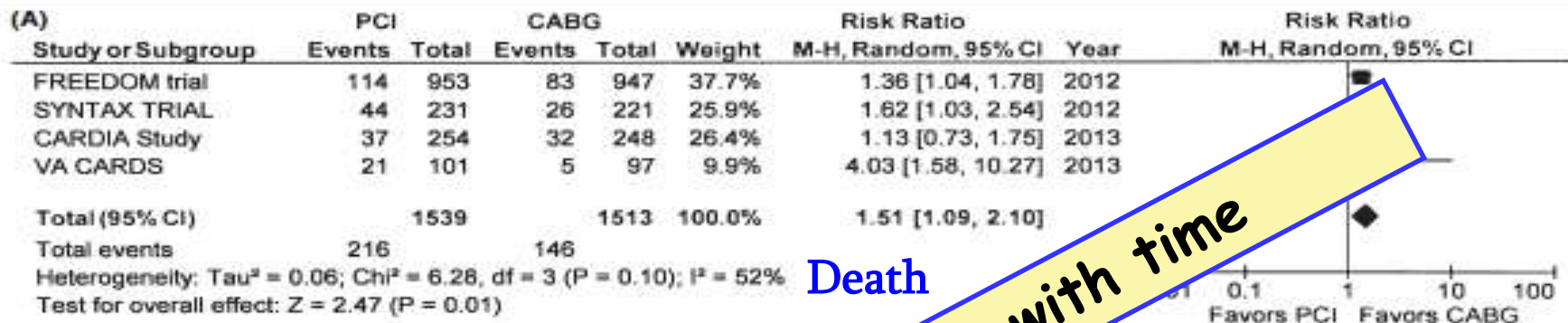
**Only 5% of patients in USA and <10% in Europe receive BIMA**

- 3102 patients randomized to single or bilateral IMA grafts
- Primary outcome is 10 year survival
- 107 surgeons, 28 centres, seven countries
- 30 day mortality 1.2%, 1 yr mortality 2.4%
- 1 year incidence of stroke, MI, repeat revascularization all < 2%
- 5 year outcomes will be reported 2014

# Effectiveness of Percutaneous Coronary Intervention With Drug-Eluting Stents Compared With Bypass Surgery in Diabetics With Multivessel Coronary Disease: Comprehensive Systematic Review and Meta-analysis of Randomized Clinical Data

JAMA 2013

Abdul Hakeem, MD; Nadish Garg, MD; Sabha Bhatti, MD; Naveen Rajpurohit, MD; Zubair Ahmed, MD; Barry F. Uretsky, MD



Benefits of surgery increase with time

## Summary and Conclusions

- ① Consistent evidence that PCI has no clinical benefit over OMT and that DES do not improve clinical outcomes over BMS
- ② 3 VD: 79% of 3 VD (SYNTAX >22) there is a strong survival benefit with CABG by 3-5 years and continuing to increase past 5 years
- ③ Consistent with evidence (from 13 propensity matched registries with > 430,000 patients) of survival benefit of CABG vs PCI
- ④ LM: For 65% of LM (SYNTAX >32) there is a strong survival benefit with CABG by 5 years but for SYNTAX < 32 PCI may be superior to CABG (? Competitive flow)
- ⑤ Comparisons of survival of PCI vs CABG should have > 5 years follow-up
- ⑥ Consistent 'unwarranted' variation in ratios of PCI:CABG between countries and within counties
- ⑦ Strong evidence that ABSENCE of MDTs (using guidelines) means that most elective PCI patients misunderstand its rationale and results in a large number of inappropriate PCI interventions
- ⑧ Guidelines are transparent and protect the patients (against wrong interventions) and doctors and should be mandatory
- ⑨ Professional bodies should persuade statutory bodies/payers that only interventions agreed by an MDT based on guidelines (or documented as to why not) should be reimbursed.



# Evidence Basis for an Intervention (CABG vs PCI)

	RCT The Gold standard	Registries (Propensity Matched)
Strengths	No Bias	>10,000s of Patients Represent real clinical practice (1/20 RCT of CABG vs PCI) Relatively Cheap
Potential Weaknesses	Small numbers of patients Small % of eligible population Atypical patient populations Short duration of follow-up Large numbers of cross-overs (19/20 RCT of CABG vs PCI) EXPENSIVE	Confounding/Bias

Always must consider TWO CRUCIAL factors

- (i) % of eligible population included in trials
- (ii) Length of follow-up