Gender in EXCEL

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Sunday, April 29, 2018, 8:54 AM – 9:02 AM, Room 104, Level 1

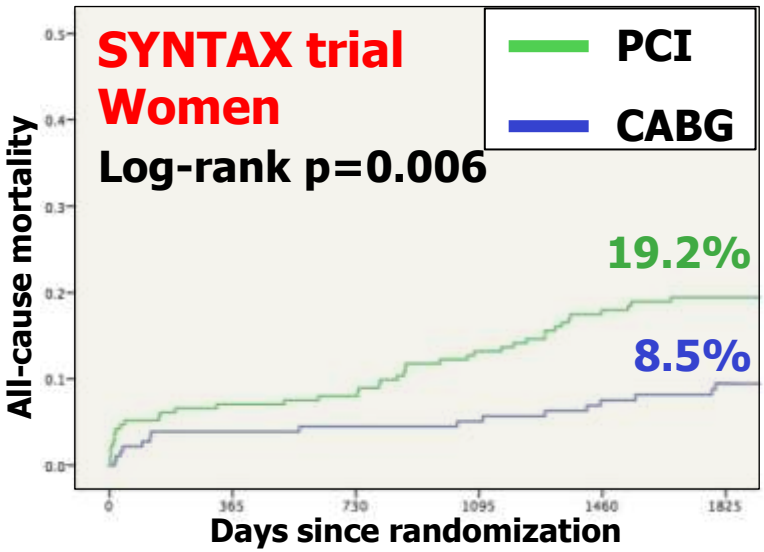
Geographical Difference of the Interaction of Sex With Treatment Strategy in Patients With Multivessel Disease and Left Main Disease

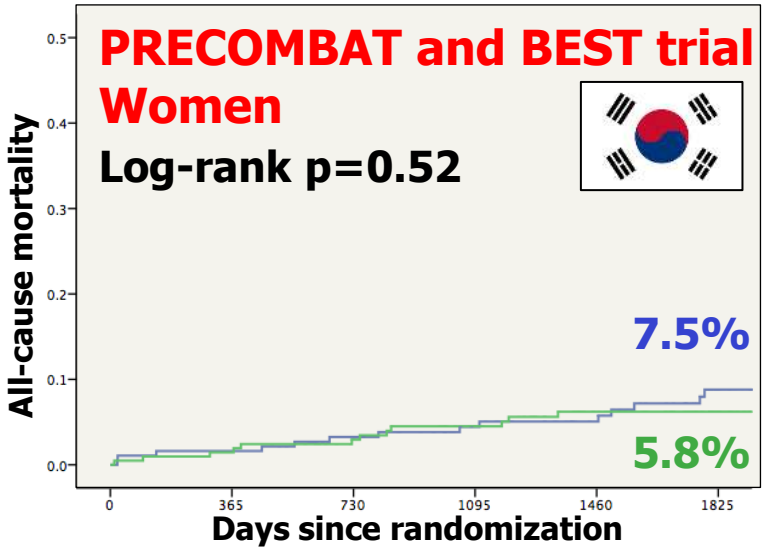
A Meta-Analysis From SYNTAX (Synergy Between PCI With Taxus and Cardiac Surgery), PRECOMBAT (Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients With Left Main Coronary Artery Disease), and BEST (Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients With Multivessel Coronary Artery Disease) Randomized Controlled Trials

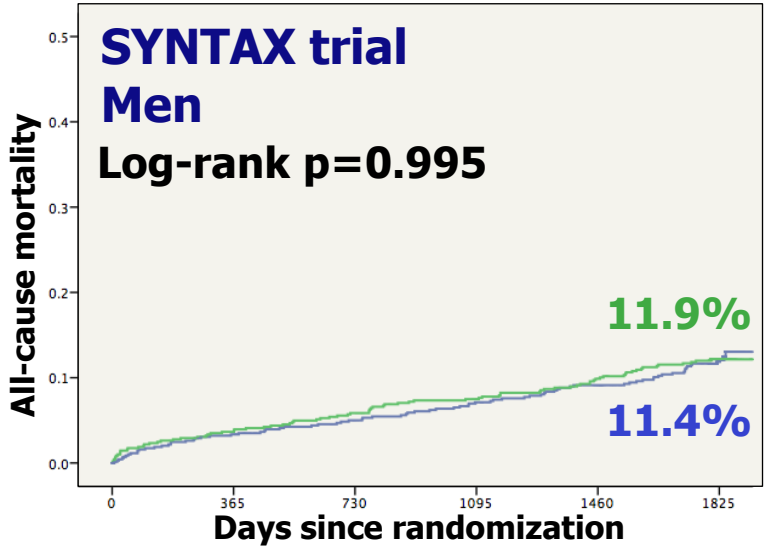
Yohei Sotomi, MD; Yoshinobu Onuma, MD, PhD; Rafael Cavalcante, MD, PhD; Jung-Min Ahn, MD; Cheol Whan Lee, MD; David van Klaveren, MSc; Robbert J. de Winter, MD, PhD; Joanna J. Wykrzykowska, MD, PhD; Vasim Farooq, MD, PhD; Marie-Claude Morice, MD, PhD; Ewout W. Steyerberg, PhD; Seung-Jung Park, MD, PhD; Patrick W. Serruys MD, PhD

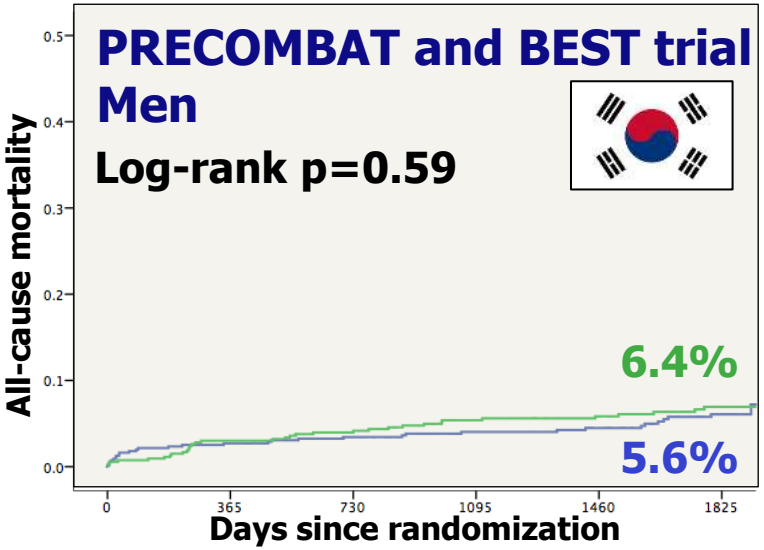
Sotomi Y, et al. Circ Cardiovasc Interv. 2017 May; 10(5)

All-cause 5-year death in women and men by 3trials









Sotomi Y, et al. Circ Cardiovasc Interv. 2017 May; 10(5)

SYNTAX trial – Correlates of 4y Mortality

PCI (n = 903) independent correlates of 4-year mortality ***(variables with a P- value >0.05 italicized)***	**Hazard ratio**	**95% CI**	***P*-value**
No post-procedural anti-platelet therapy[a]	152.16	53.57–432.22	<0.001
Amiodarone therapy on discharge	4.49	1.36–14.83	0.014
Pre-procedural poor LVEF	3.31	1.03–10.64	0.045
History of GI bleeding or peptic ulcer disease	2.93	1.41–6.12	0.004
Peripheral vascular disease	2.13	1.26–3.60	0.005
Age per increase in 10 years	1.62	1.26–2.09	<0.001
Female gender	1.6	1.01–2.56	0.048
Serum creatinine	1.28	0.95–1.72	*0.11*
Diabetes	1.28	0.83–2.00	*0.27*
SYNTAX score per increase in 10 points	1.25	1.06–1.47	0.007

CABG (n = 897) independent correlates of 4-year mortality ***(variables with a P-value >0.05 italicized)***	**Hazard ratio**	**95% CI**	***P*-value**
Lack of discharge aspirin	3.56	2.04–6.21	<0.001
Peripheral vascular disease	2.65	1.49–4.72	0.001
Chronic obstructive pulmonary disease	2.44	1.30–4.60	0.006
History of GI bleeding or peptic ulcer disease	2.14	0.90–5.07	*0.085*
Age per increase in 10 years	1.95	1.41–2.69	<0.001
Pre-procedural poor LVEF	1.86	0.65–5.33	*0.25*
Amiodarone therapy on discharge	1.79	0.95–3.35	*0.07*
Serum creatinine (mg/dL)	1.47	1.17–1.84	0.001
Hypertension	1.28	0.62–2.67	*0.51*
Lack of pre-procedural aspirin	1.18	0.64–2.19	*0.59*

Farooq V, et al. Eur Heart J (2012) 33, 3105–3113

RESULTS

Baseline Characteristics in EXCEL

	Male (n=1464)	Female (n=441)	p value
Age (years)	(+) 65.6 ± 9.4	67.1 ± 10.2 (-)	0.002
Hyperlipidemia	(+) 68.8%	74.1% (-)	0.03
Hypertension	(+) 72.4%	78.7% (-)	0.008
Medically treated Diabetes	(+) 25.2%	30.8% (-)	0.02
Congestive heart failure	(+) 5.5%	10.5% (-)	<0.001
Prior history of anemia	(+) 8.4%	13.9% (-)	<0.001
Mitral regurgitation (mild/moderate)	(+) 27.7%	35.2% (-)	0.004
Creatinine Clearance (ml/min)	(+) 91.6 ± 31.6	82.3 ± 34.0 (-)	<0.001
Never smoked	(-) 33.1%	50.2% (+)	<0.001
Family history of premature CAD	(-) 69.4%	54.6% (+)	<0.001
Prior TIA or CVA	6.4% =	5.9%	0.72
Peripheral Vascular Disease	9.7% =	9.1%	0.72
COPD	7.2% =	9.8%	0.08
Stable angina at presentation	53.1% =	53.0%	0.94
Ejection Fraction (%)	(-) 56.8 ± 9.2	58.1 ± 9.8 (+)	0.002

Anatomic and Procedural Characteristics

	Male (n=1464)		Female (n=441)		p value
SYNTAX score (Corelab)	27.2 ± 9.3		24.2 ± 9.0		<0.001
0-22	(-) 32.6%	<	46.2%	(+)	<0.001
23-32	40.9%	=	37.1%		0.16
≥ 33	(-) 26.5%	>	16.8%	(+)	<0.001
Lesion location					
Ostial lesion	(-) 33.6%	<	46.6	(+)	<0.001
Mid shaft	41.7	=	41		0.80
Distal lesion	(-) 79.3%	>	71.1%	(+)	0.0004
Bifurcation lesion	(-) 35.8%		30.8%	(+)	0.05
IVUS use	(-) 75.1%	<	83.9%	(+)	0.007
Minimal lumen area (mm^2)	4.7 ± 1.1	=	4.6 ± 0.9		0.51
Minimum lumen area ≤ 6.0 mm^2	(+) 17.2%		23.8%	(-)	0.003
FFR use	9.3%		8.1%		0.58
FFR	0.72 ± 0.07		0.71 ± 0.08		0.59
FFR ≤ 0.80	6.3%		6.0%		0.82

Procedural Characteristics

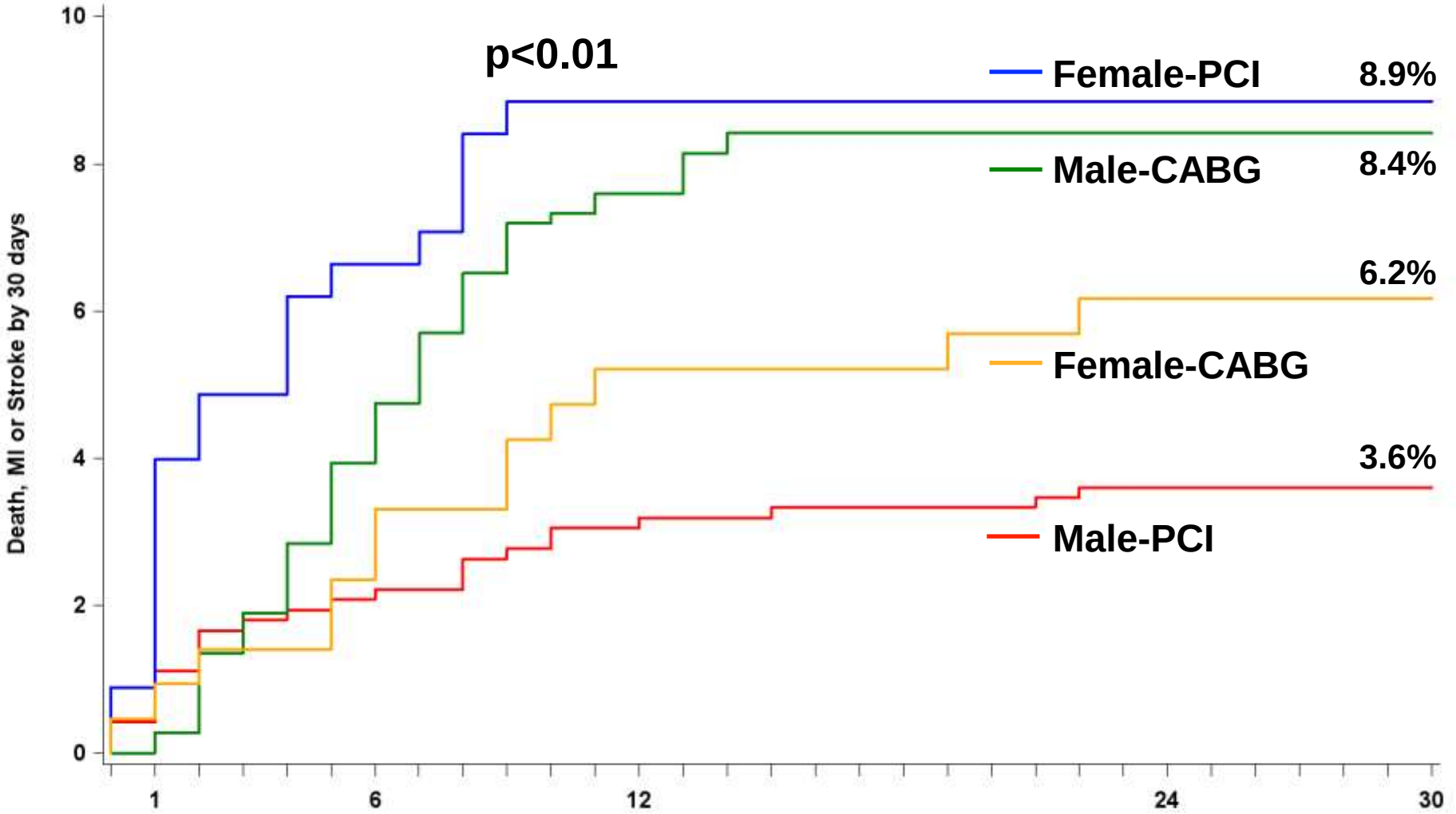
	Male (n=1464)		Female (n=441)	p value
PCI				
Lesions treated by PCI	(-) 1.9 ± 1.1	>	1.8 ± 1.1 (+)	0.01
Stents implanted	2.5 ± 1.5	=	2.3 ± 1.6	0.051
Hemodynamic support during PCI	(+) 4.4%	<	7.9% (-)	0.03
PCI complication	(+) 8.9%	<	14.9% (-)	0.007
Complete revascularization by PCI	(-) 25.4%	<	37.4% (+)	0.001
CABG				
Vessels bypassed	2.3 ± 0.5	=	2.2 ± 0.6	0.07
BITA use	(+) 31.1%	>	20.7% (-)	0.004
Number of total conduits	(+) 2.6 ± 0.8	>	2.4 ± 0.8 (-)	0.002
Number of arterial conduits	(+) 1.4 ± 0.6	>	1.2 ± 0.5 (-)	<0.001
Number of venous conduits	1.2 ± 1.0	=	1.2 ± 0.9	0.66
CABG complication	(+) 8.5%	<	13.2% (-)	0.04

No other significant differences regarding procedural characteristics and technique

Graft occlusion and Stent thrombosis in Men vs. Women

	Male	Female	p value
Graft stenosis or occlusion	2.6%	3.0%	0.67
Stent thrombosis (ARC definite/probable)	0.7%	0.5%	0.62

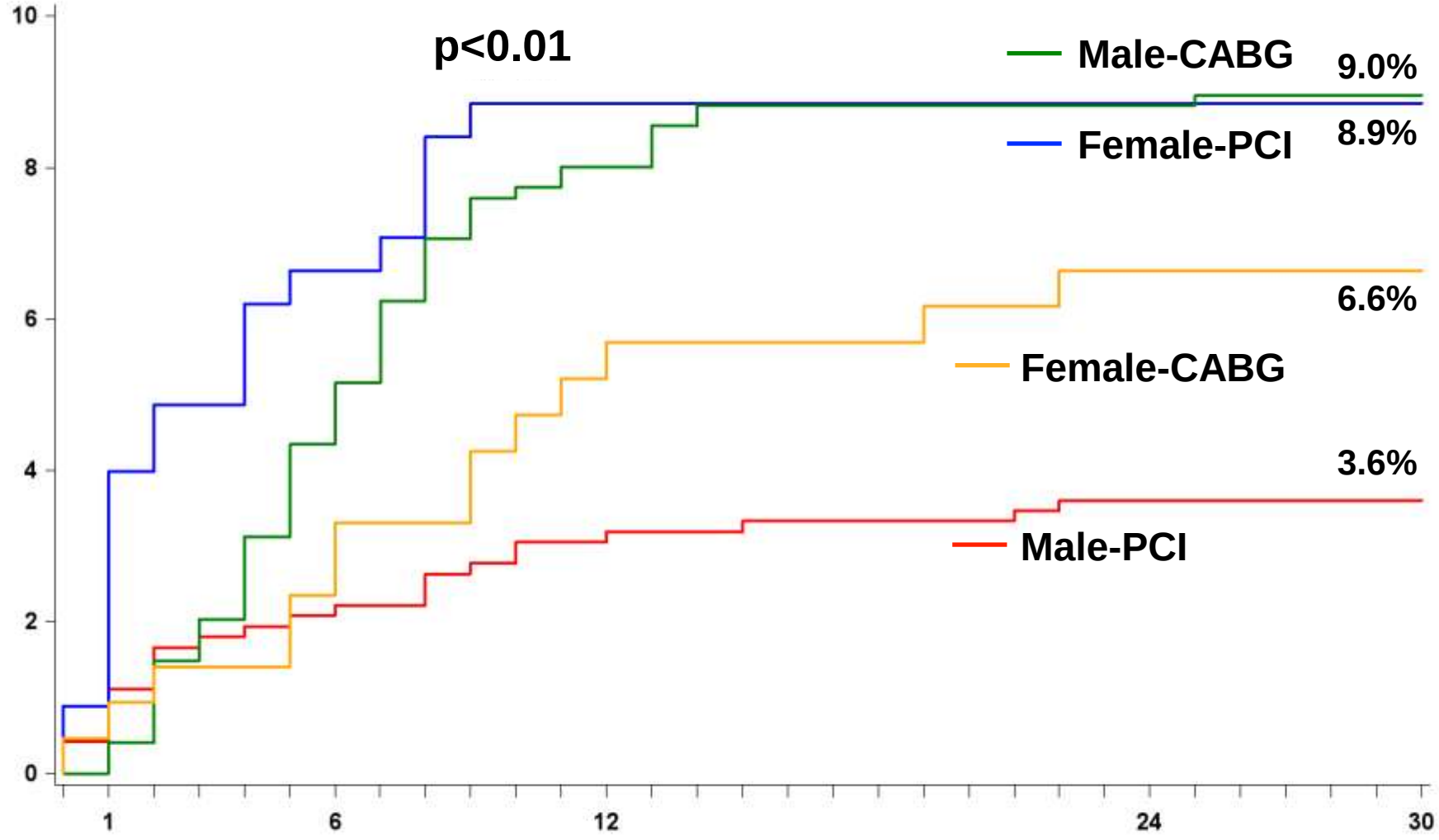
All-cause death, MI or stroke at 30 days



Number at risk:

Male-PCI	722	707	700	696	695	693	693
Female-PCI	226	212	204	204	204	204	204
Male-CABG	742	716	683	674	673	673	673
Female-CABG	215	208	201	199	198	196	195

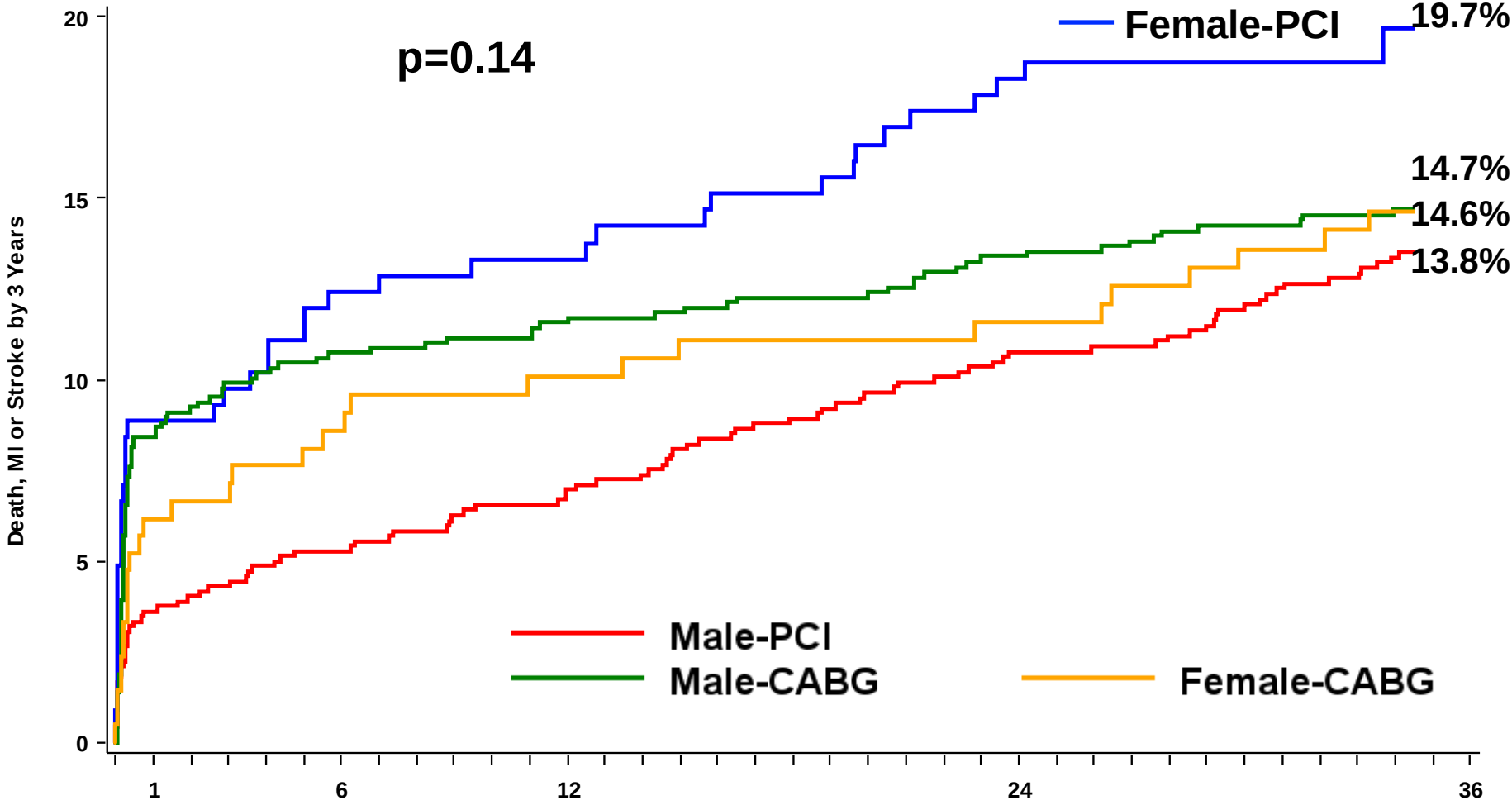
All-cause death, MI, stroke or ischemia-driven revascularization at 30 days



Number at risk:

Male-PCI	722	707	700	696	695	693	693
Female-PCI	226	212	204	204	204	204	204
Male-CABG	742	714	680	671	670	670	669
Female-CABG	215	208	201	198	197	195	194

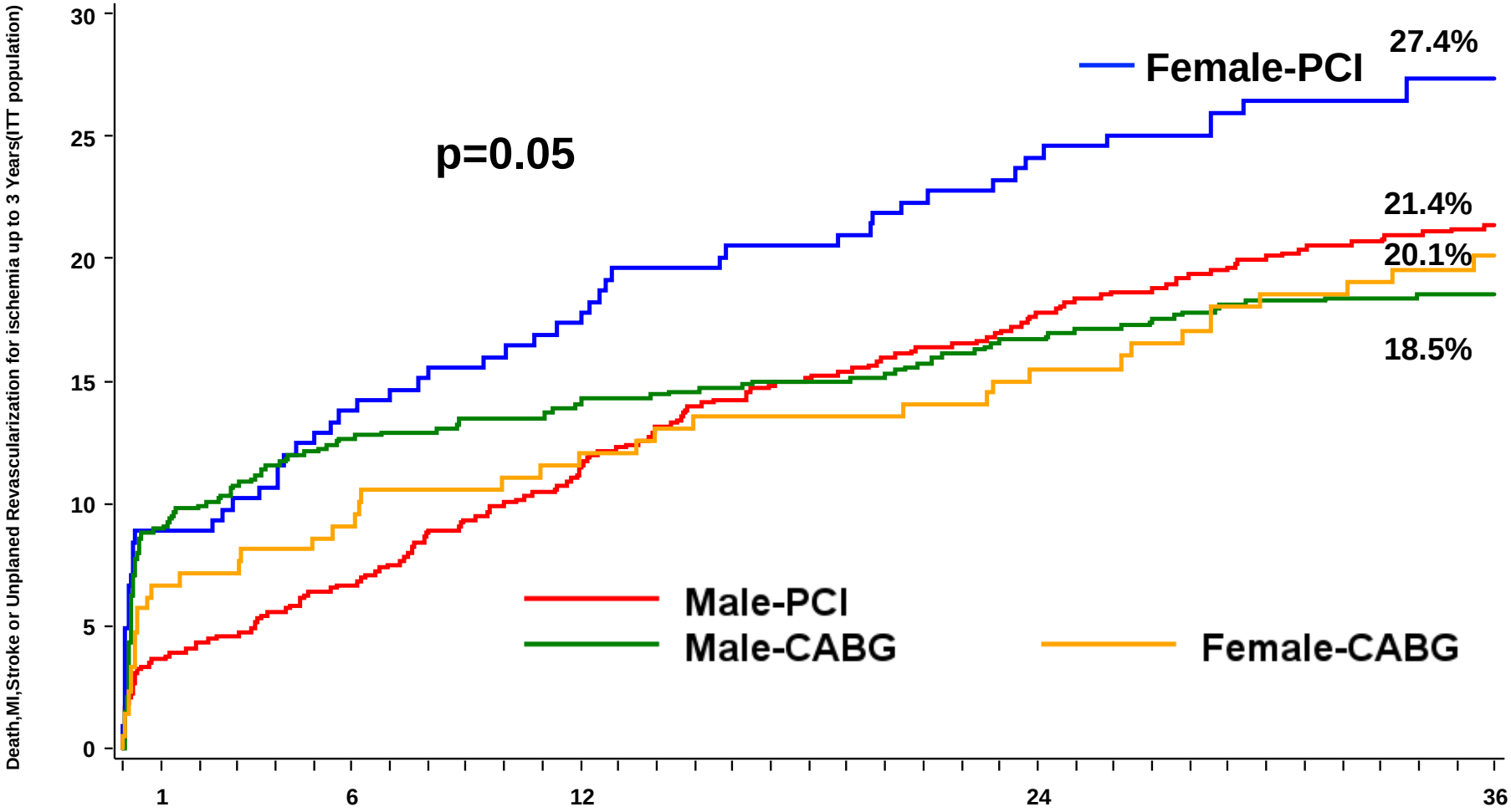
All-cause death, MI or stroke at 3 years



Number at risk:

Male-PCI	722	679	664	628	550
Female-PCI	226	196	193	179	152
Male-CABG	742	651	639	615	546
Female-CABG	215	187	182	178	151

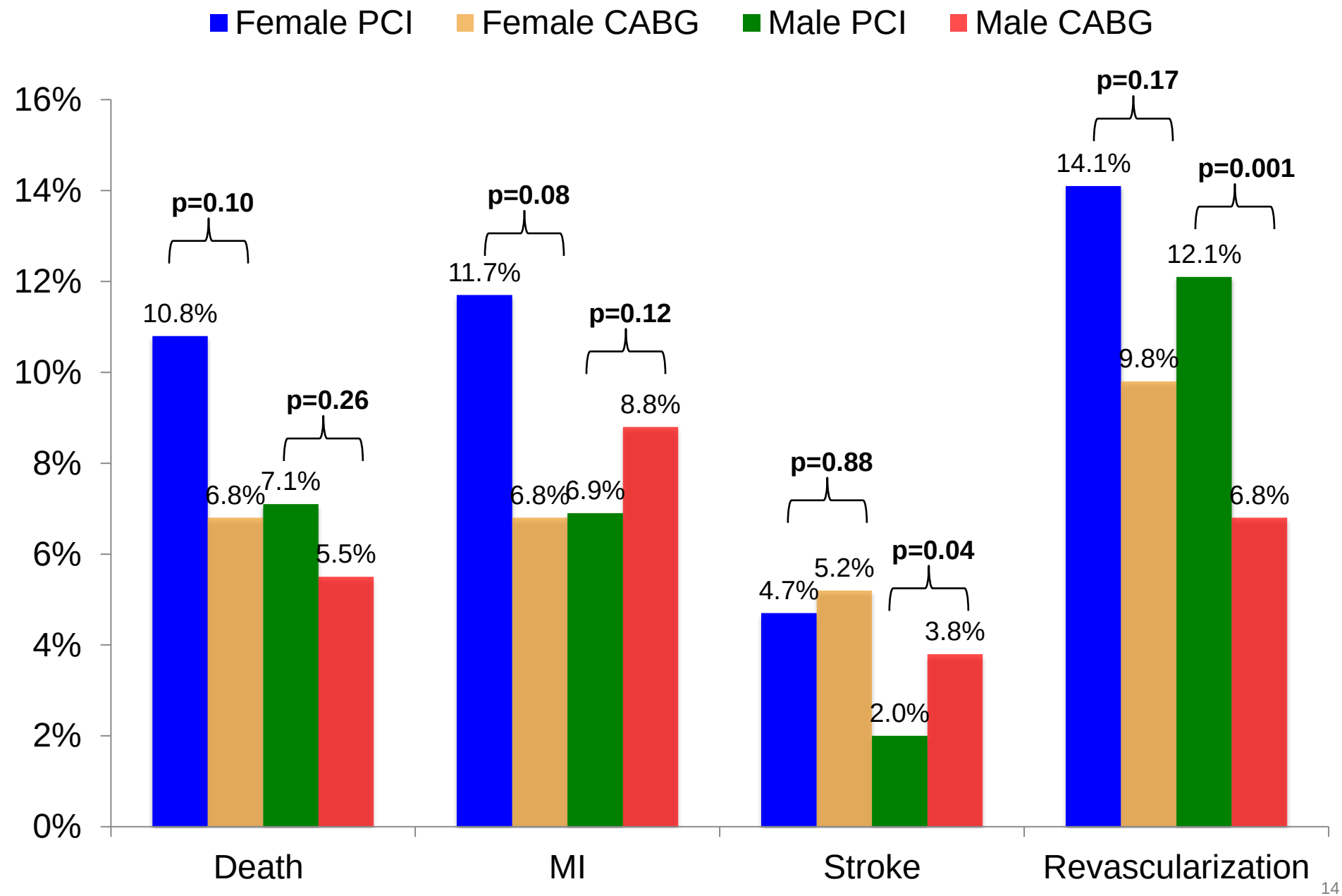
All-cause death, MI, stroke or ischemia-driven revascularization at 3 years



Number at risk:

Male-PCI	722	669	632	579	503
Female-PCI	226	193	184	166	138
Male-CABG	742	637	621	592	522
Female-CABG	215	186	178	170	143

Individual 3-year Outcomes



Death, MI, stroke at *30 days*

Multivariable analysis

PCI arm	HR (95% CI)	p value
Female	2.30 (1.26, 4.21)	*0.007*
CrCl ≤ 60 ml/min	1.20 (0.54, 2.66)	0.66
COPD	1.57 (0.62, 4.00)	0.35
Age (years)	1.01 (0.97, 1.04)	0.77
Diabetes Mellitus	1.05 (0.56, 1.97)	0.87

CABG arm	HR (95% CI)	p value
Female	0.66 (0.35, 1.24)	*0.19*
CrCl ≤ 60 ml/min	1.27 (0.64, 2.49)	0.50
COPD	2.61 (1.42, 4.77)	0.002
Age (years)	0.99 (0.97, 1.02)	0.59
Diabetes Mellitus	1.41 (0.87, 2.29)	0.17

Death, MI, stroke at *3 years*

Multivariable analysis

PCI arm	HR (95% CI)	p value
Female	1.39 (0.96, 2.01)	*0.08*
CrCl ≤ 60 ml/min	1.33 (0.85, 2.07)	0.21
COPD	2.07 (1.27, 3.38)	0.003
Age (years)	1.02 (1.00, 1.04)	0.06
Diabetes Mellitus	1.51 (1.07, 2.13)	0.020

CABG arm	HR (95% CI)	p value
Female	0.83 (0.54, 1.28)	*0.40*
CrCl ≤ 60 ml/min	1.47 (0.92, 2.36)	0.11
COPD	2.49 (1.57, 3.95)	<0.001
Age (years)	1.00 (0.98, 1.02)	0.75
Diabetes Mellitus	1.57 (1.10, 2.24)	0.013

Conclusions (1)

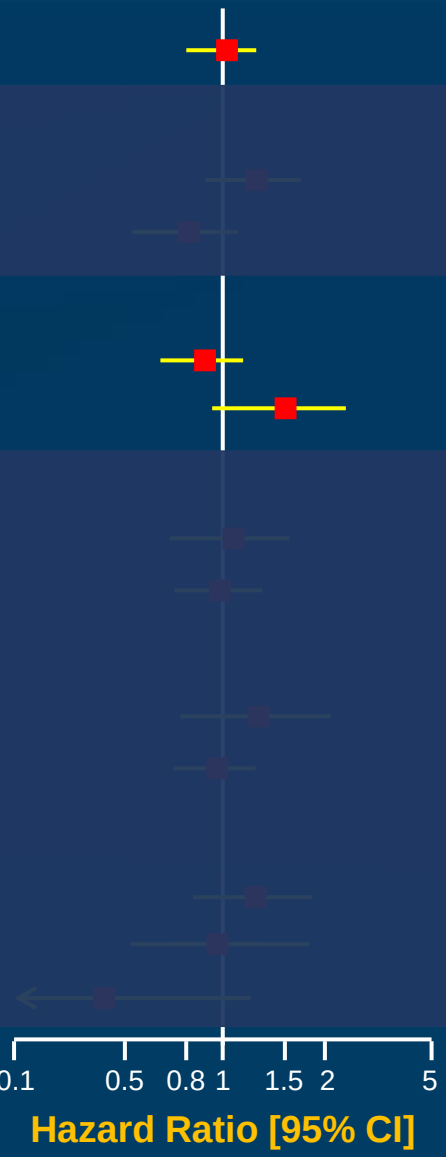
- As compared to men, women were older and showed worse baseline risk profile with:
  - higher prevalence of Hypertension, diabetes, hyperlipidemia, heart failure, mitral regurgitation and anemia
  - Worse renal function
- Women had less anatomic complexity and fewer coronary lesions treated
- IVUS use during PCI was more frequent in women
- No other significant differences in procedural technique were observed

Conclusions (2)

- The rate of the primary endpoint of death, MI or stroke at 3 years was numerically higher in women treated with PCI (19.7%) as compared to women treated with CABG (14.6%) and men treated with either strategy (14.7% CABG, 13.8% PCI) (p=0.10)
- At 30 days, death, MI or stroke occurred more frequently in women treated with PCI and men treated with CABG as compared to men treated with PCI
- An interaction effect between sex and CABG vs. PCI was observed for the primary endpoint, with borderline statistical significance
- This data is consistent with the finding of worse prognosis of women treated with PCI observed in the SYNTAX trial

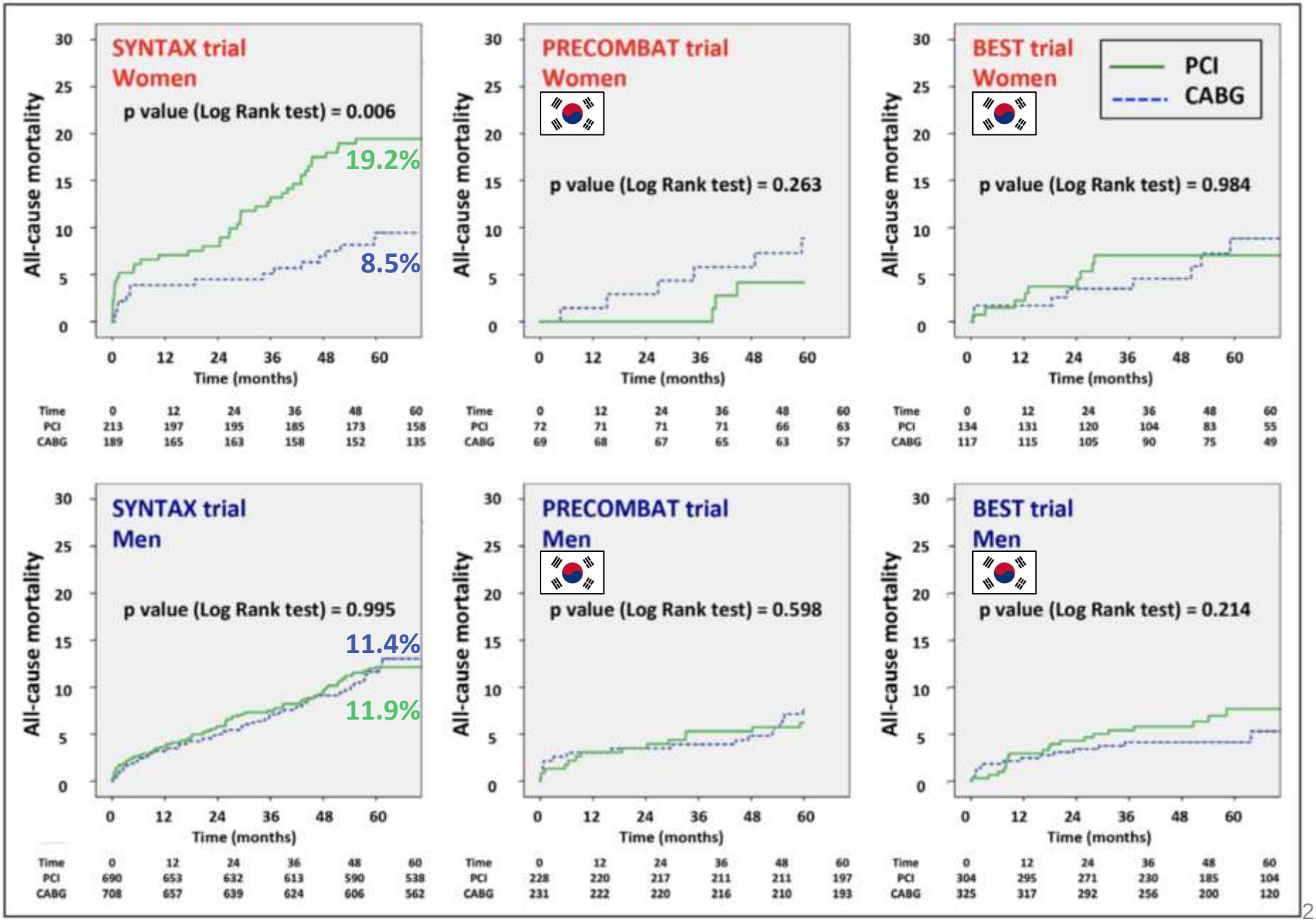
3-Year Death, Stroke or MI

Subgroup	PCI (N=948)	CABG (N=957)	HR [95% CI]	P (Int)
All patients	15.4%	14.7%	1.00 [0.79, 1.26]	
Age (median cutoff)				
- ≥67 years	18.7%	15.0%	1.22 [0.89, 1.69]	0.07
- <67 years	12.2%	14.4%	0.78 [0.55, 1.11]	
Gender				
- Male	14.0%	14.9%	0.87 [0.66, 1.14]	0.056
- Female	19.7%	14.1%	1.48 [0.93, 2.41]	
Diabetes mellitus				
- Yes	21.2%	19.4%	1.04 [0.70, 1.55]	0.77
- No	13.3%	13.1%	0.97 [0.72, 1.30]	
Chronic kidney disease				
- eGFR ≤60 ml/min	24.5%	19.3%	1.24 [0.75, 2.07]	0.36
- eGFR >60 ml/min	13.5%	13.6%	0.95 [0.72, 1.25]	
Geographic location				
- North America	15.5%	12.4%	1.22 [0.82, 1.82]	0.14
- Europe	15.5%	15.6%	0.95 [0.69, 1.29]	
- Other	9.5%	22.2%	0.37 [0.08, 1.20]	



Backup

Cumulative risk of all-cause 5-year death in women and men by 3trials



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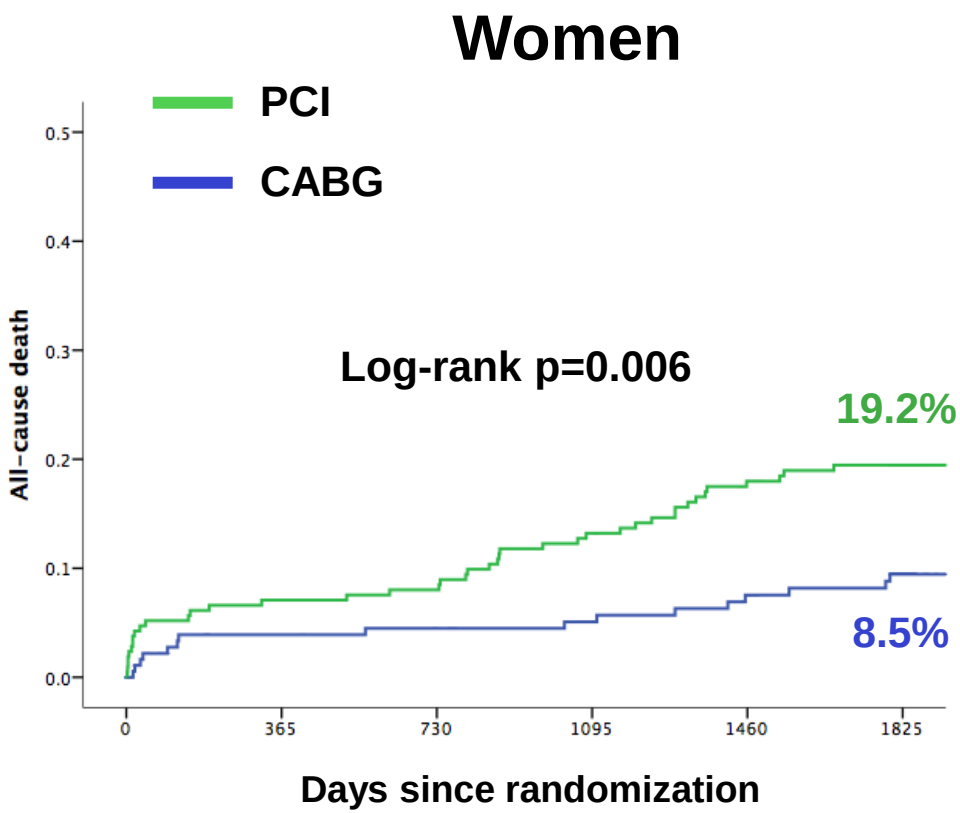
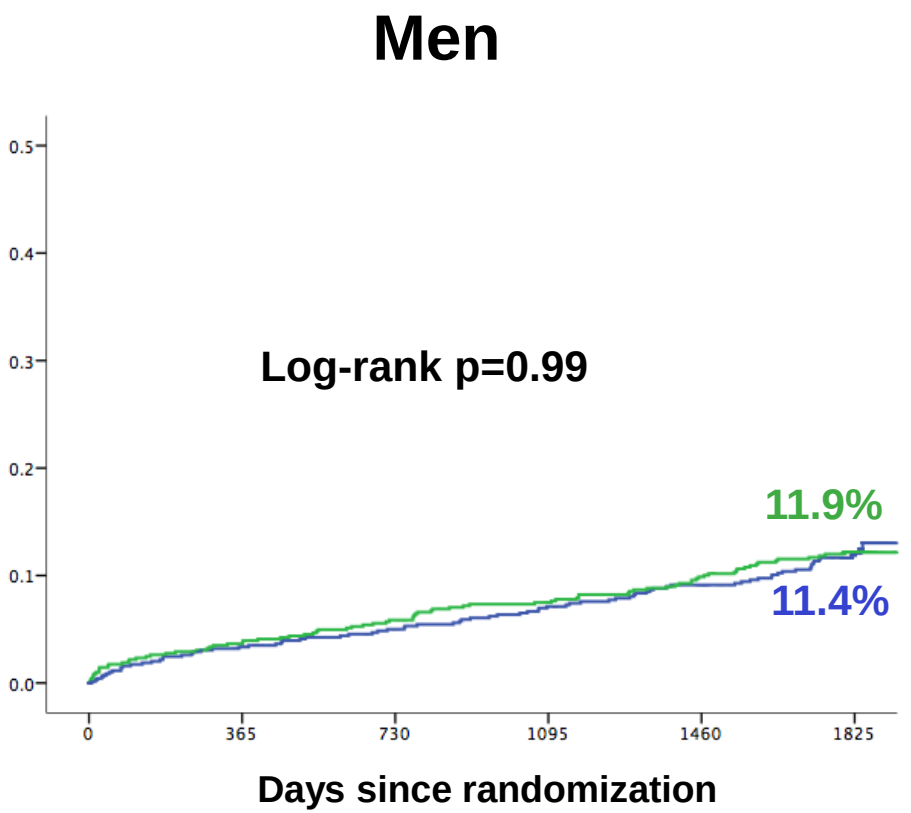
SYNTAX trial (n=1800)
All-cause death at 5 years





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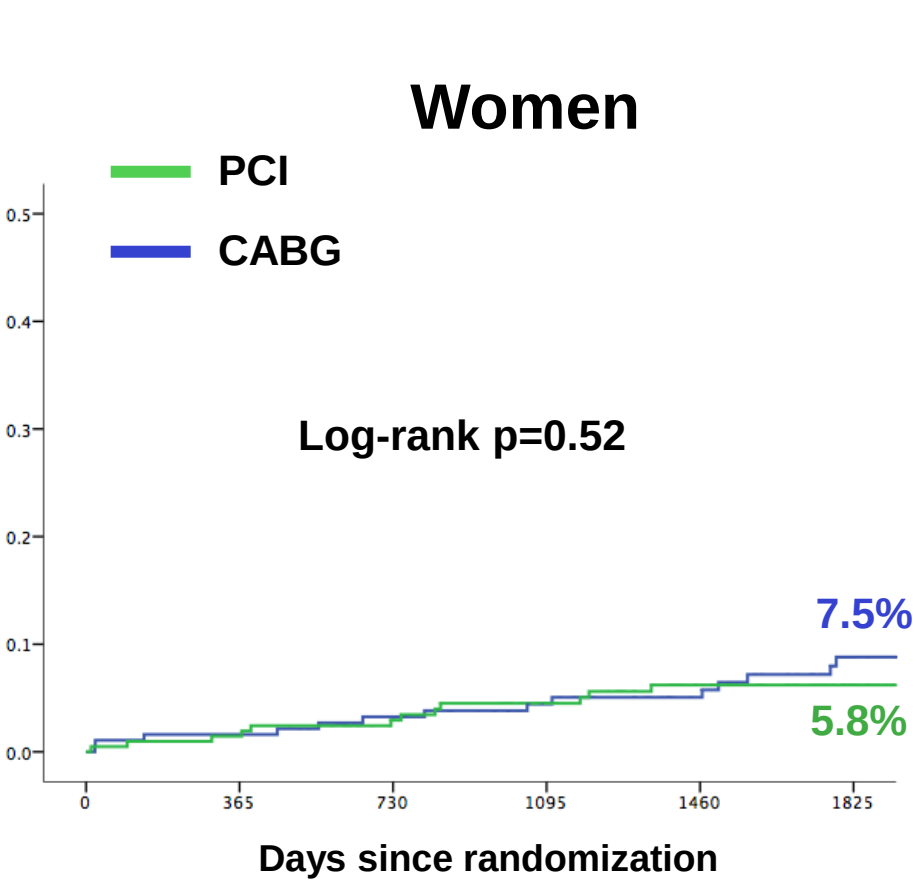
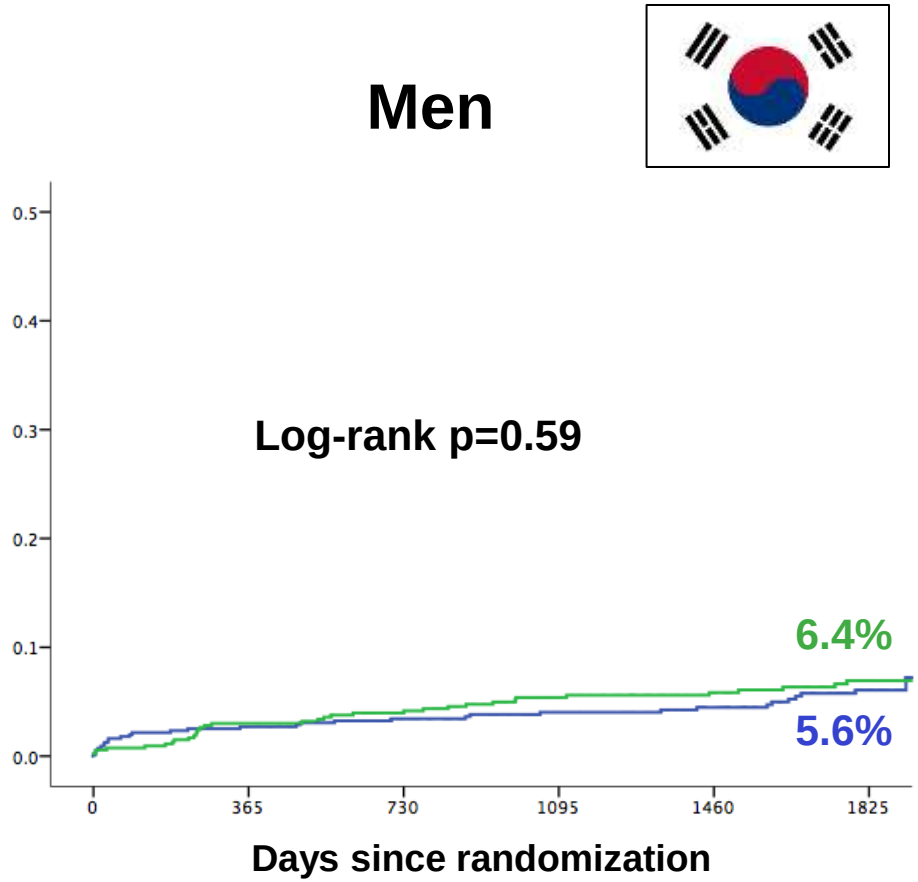
BEST and PRECOMBAT trials (n=1480)
All-cause death at 5 years





Sotomi Y, et al. Circ Cardiovasc Interv. 2017 May; 10(5)

Procedural Characteristics

	Male (n=1464)	Female (n=441)	p value
Lesions treated by PCI	1.9 ± 1.1	1.8 ± 1.1	0.01
Stents implanted	2.5 ± 1.5	2.3 ± 1.6	0.05
Vessels bypassed	2.3 ± 0.5	2.2 ± 0.6	0.07
BITA use	31.1%	20.7%	0.004
Number of total conduits	2.6 ± 0.8	2.4 ± 0.8	0.002
Number of arterial conduits	1.4 ± 0.6	1.2 ± 0.5	<0.001
Number of venous conduits	1.2 ± 1.0	1.2 ± 0.9	0.66

No other significant differences regarding procedural characteristics and technique