



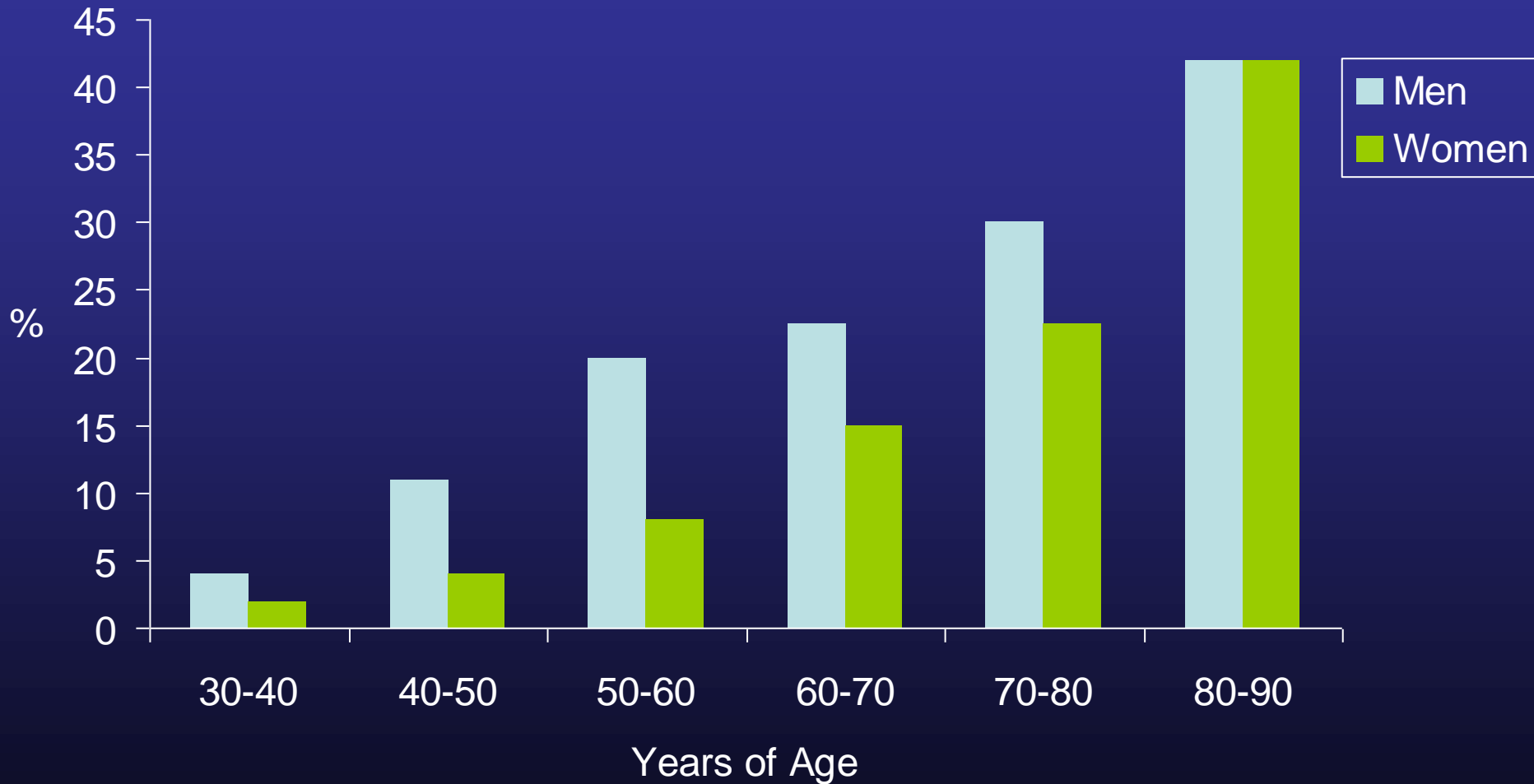
Patrizia Presbitero

CAD and stent in women

XXIV Giornate Cardiologiche Torinesi

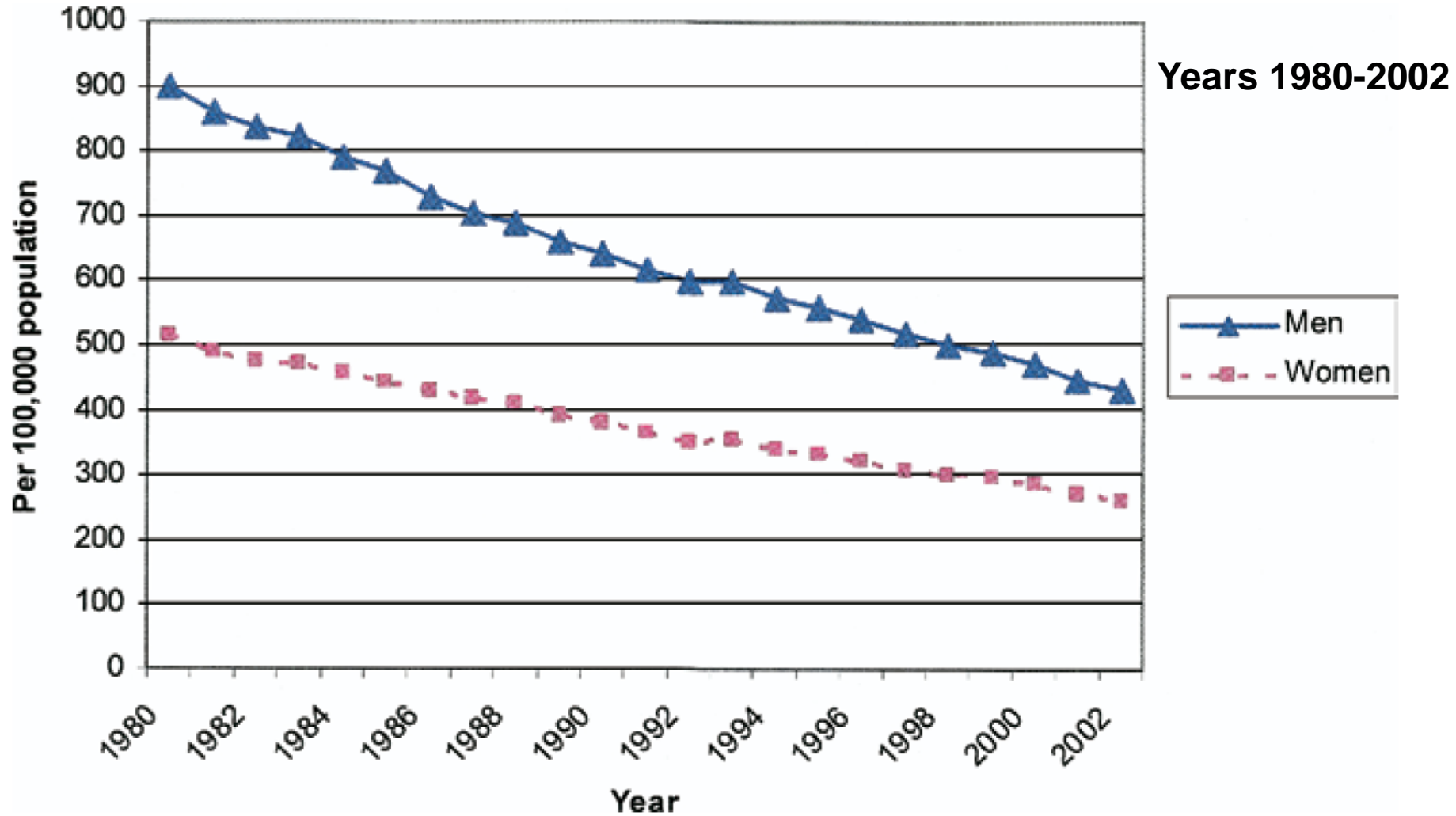
Torino, 20 Ottobre 2011

Incidence of CAD by Decade



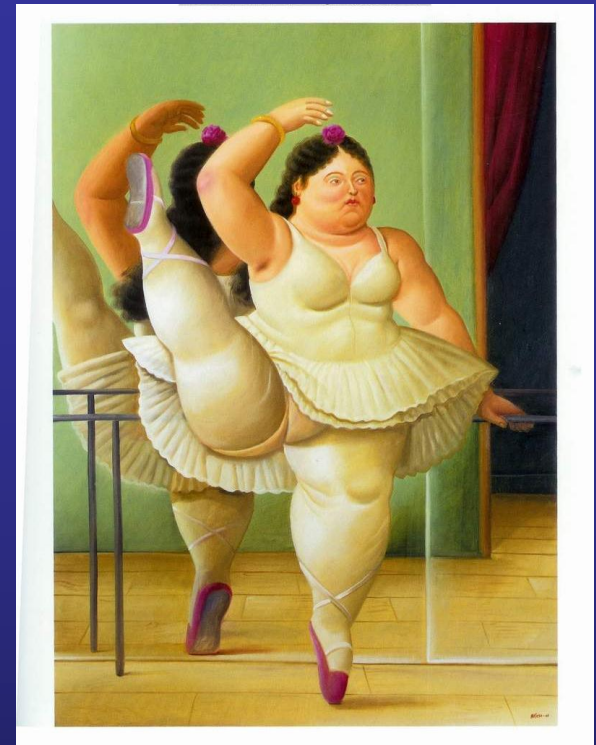
Adapted from Castelli et al. Am J Obstet Gynecol 1988;158:1554.

TEMPORAL TREND IN AGE-ADJUSTED MORTALITY FROM CHD

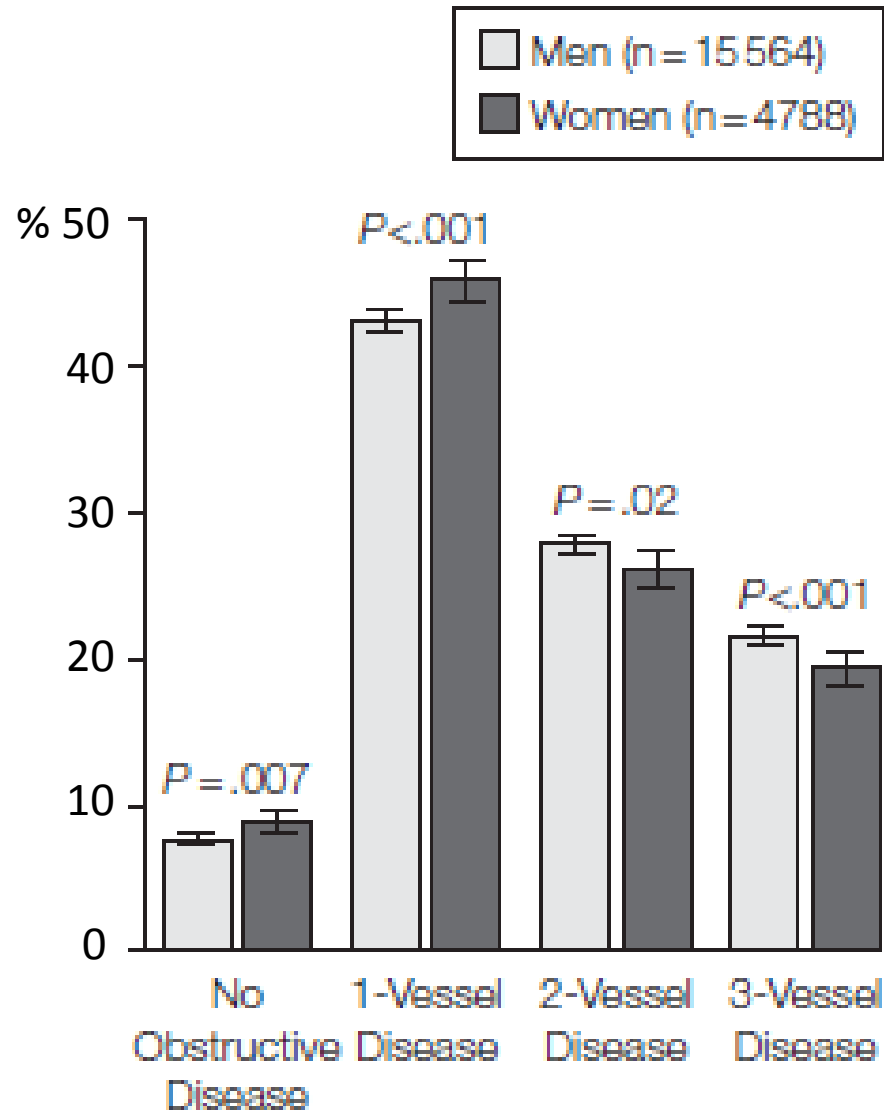


GENDER DIFFERENCES in pts undergoing PCI

- 1. Older age**
- 2. Co-morbidity**
- 3. Presentation more often with unstable angina**
- 4. Less previous infarction and revascularisation**
- 5. Better LV function**
- 6. Small, more calcified and tortuous vessels**



Extent of coronary atherosclerosis



Gender Differences



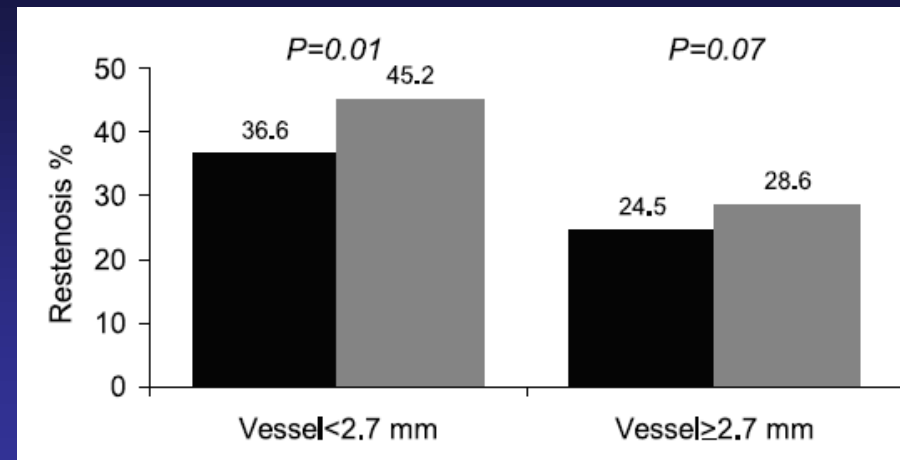
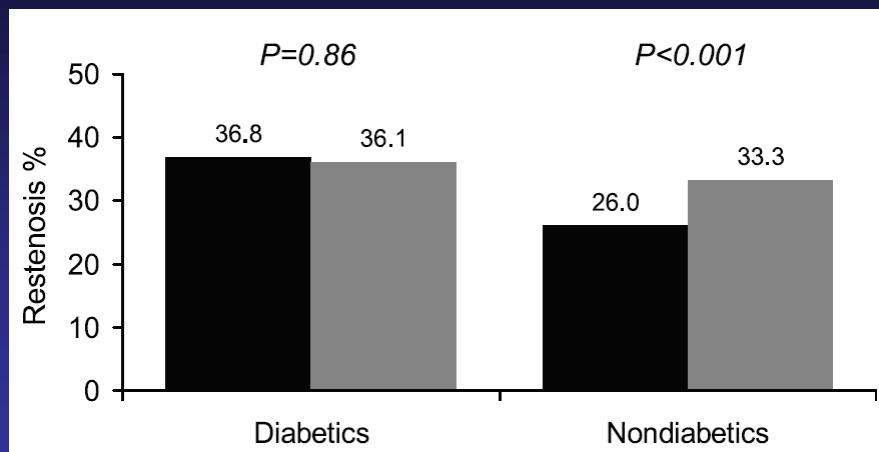
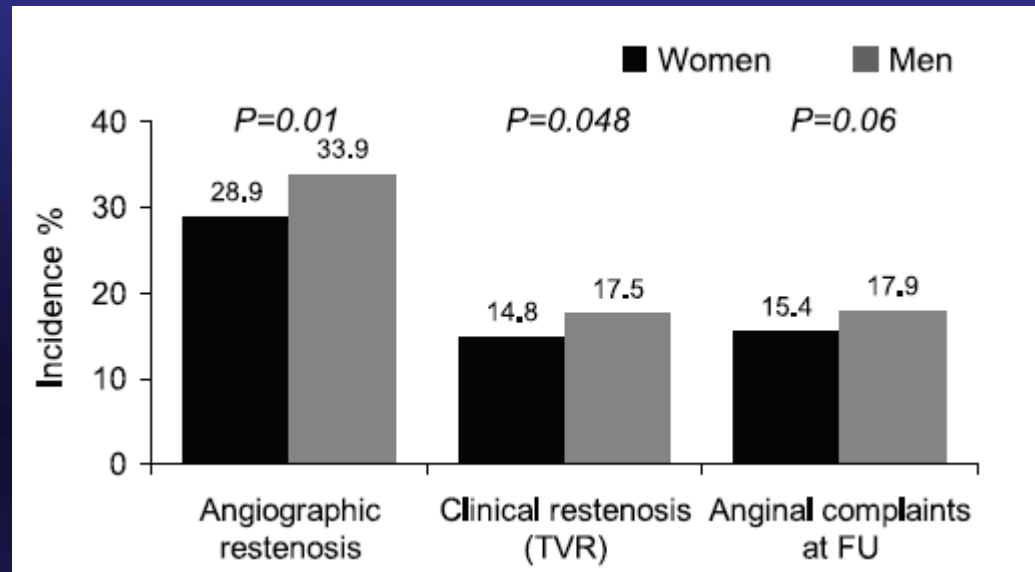
PCI in **women** is associated with a gender-related higher periprocedural hazard, diminished by contemporary widespread coronary stenting

In-Hospital Outcome	Stent Era			Ptrend
	Early (1994–6/95)	Provisional (7/95–1997)	Current (1998–1999)	
Clinical success (%)				
Women	89.03	91.45	93.45	< 0.001
Men	88.25	91.23	94.20	< 0.001
MI (%)				
Women	2.44	1.76	1.71	0.378
Men	2.18	2.09	1.36	0.009
Any CABG (%)				
Women	3.39	2.10	0.94	< 0.001
Men	3.32	1.66	0.83	< 0.001
Emergent CABG				
Women	2.20	1.54	0.60	< 0.001
Men	2.15	1.14	0.55	< 0.001
Nonemergent CABG				
Women	1.08	0.50	0.38	< 0.001
Men	1.04	0.52	0.28	< 0.001
Death (%)				
Women	1.36	1.30	1.04	0.846
Men	1.14	1.27	0.79	0.273

Gender and restenosis after coronary artery stenting

Julinda Mehilli, Adnan Kastrati*, Hildegard Bollwein, Alban Dibra, Helmut Schühlen, Josef Dirschinger, Albert Schömig

Deutsches Herzzentrum and 1. Medizinische Klinik rechts der Isar der Technischen Universität, Munich, Germany



PCI with BMS

N men =3349

N women=1025

Clinical characteristics of pts: BMS vs PES

ICH-PCI-database (1999 - 2005)

BMS

PES

Men
2811

Women
704

p

Men
642

Women
168

p

N°

Age (years±SD)	63.2±10.5	70±9.7	<0.001	63.4±10	68±10.3	<0.001
Diabetes (%)	22.1	28.5	<0.001	29.7	39.9	0.01
Hypertension (%)	59.0	70.3	<0.001	69.8	76.2	0.10
Hyperlipidemia (%)	59.9	63.2	0.11	73.2	65.4	0.05
Smoking (%)	73.4	28.9	<0.001	74.3	34.5	<0.001
Previous MI (%)	46.2	37.5	<0.001	41.7	34.5	0.09
Previous revascul. (%)	31.0	23.1	<0.001	49.7	36.2	0.001
Angina (%)	61.8	70.3	<0.001	51.7	65.5	0.004
Silent Ischemia (%)	11.4	5.1	<0.001	16.5	10.1	0.06
AMI (%)	6.3	8.8	0.01	8.1	8.6	0.83

Long term outcomes of pts, BMS and PES according to gender

ICH-PCI-database (1999 - 2005)

N°	BMS			PES		
	M 2811	W 704	p	M 642	W 168	p
Death (%)	2.9	4.9	0.04	2.1	2.0	1.0
AMI (%)	4.8	4.2	0.78	3.2	3.7	0.79
Angina (%)	31.4	35.0	0.13	22.8	25.5	0.49
Stent thrombosis (%)	0.7	0	0.13	1.2	0	0.18
TLR (%)	20.9	16.7	0.05	11.8	8.3	0.36
All repeat PCI (%)	38.3	28.5	<0.001	28.4	23.5	0.23

The gender paradox

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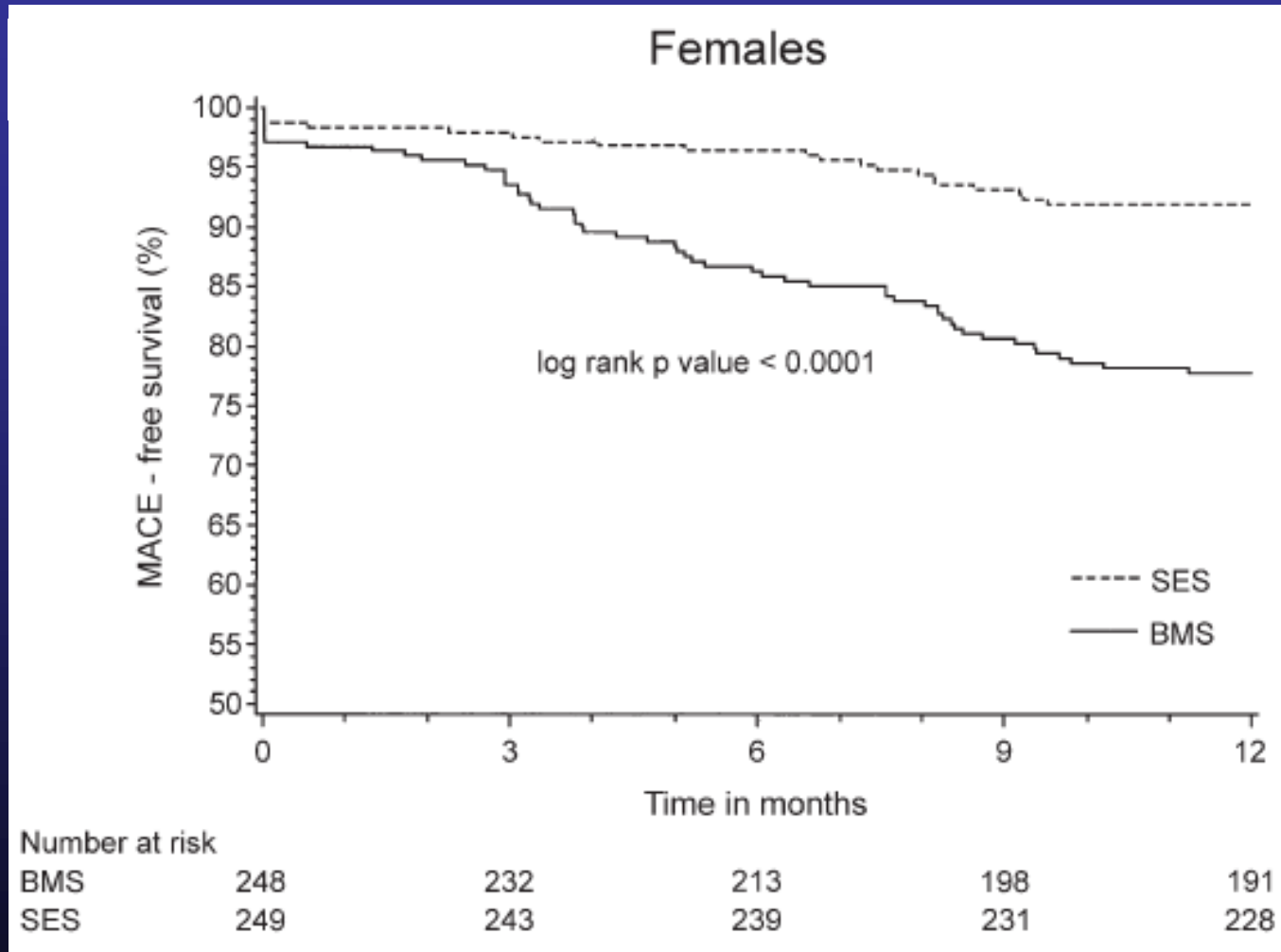
**WORST BASIC CONDITIONS
BETTER LONG TERM RESULTS**

Clinical outcomes after PES implantation

TAXUS IV (1314 pts, 1 year follow up)

	TAXUS Stent			Control Stent			TAXUS vs. Control	
	W	M	p	W	M	p	W p	M p
	187	475		180	472			
MACE	13.5	9.9	0.24	22.7	19.0	0.35	0.02	<0.0001
TV fail	13.0	8.8	0.15	21.6	18.6	0.45	0.03	<0.0001
Death	0.5	1.7	0.25	1.8	1.1	0.53	0.30	0.41
MI	2.7	3.8	0.48	7.9	3.4	0.02	0.03	0.73
TLR	7.6	3.2	0.03	14.9	15.2	0.88	0.02	<0.0001
TVR	10.8	5.7	0.03	17.5	17.0	0.95	0.07	<0.0001
<i>PCI</i>	9.2	4.1	0.02	15.2	13.4	0.69	0.08	<0.0001
<i>CABG</i>	2.2	1.6	0.54	2.2	4.7	0.15	0.95	0.0044
Late ST	0.0	0.8	0.21	0.0	1.1	0.17	—	0.73

Gender-Specific Outcomes After Sirolimus-Eluting Stent Implantation

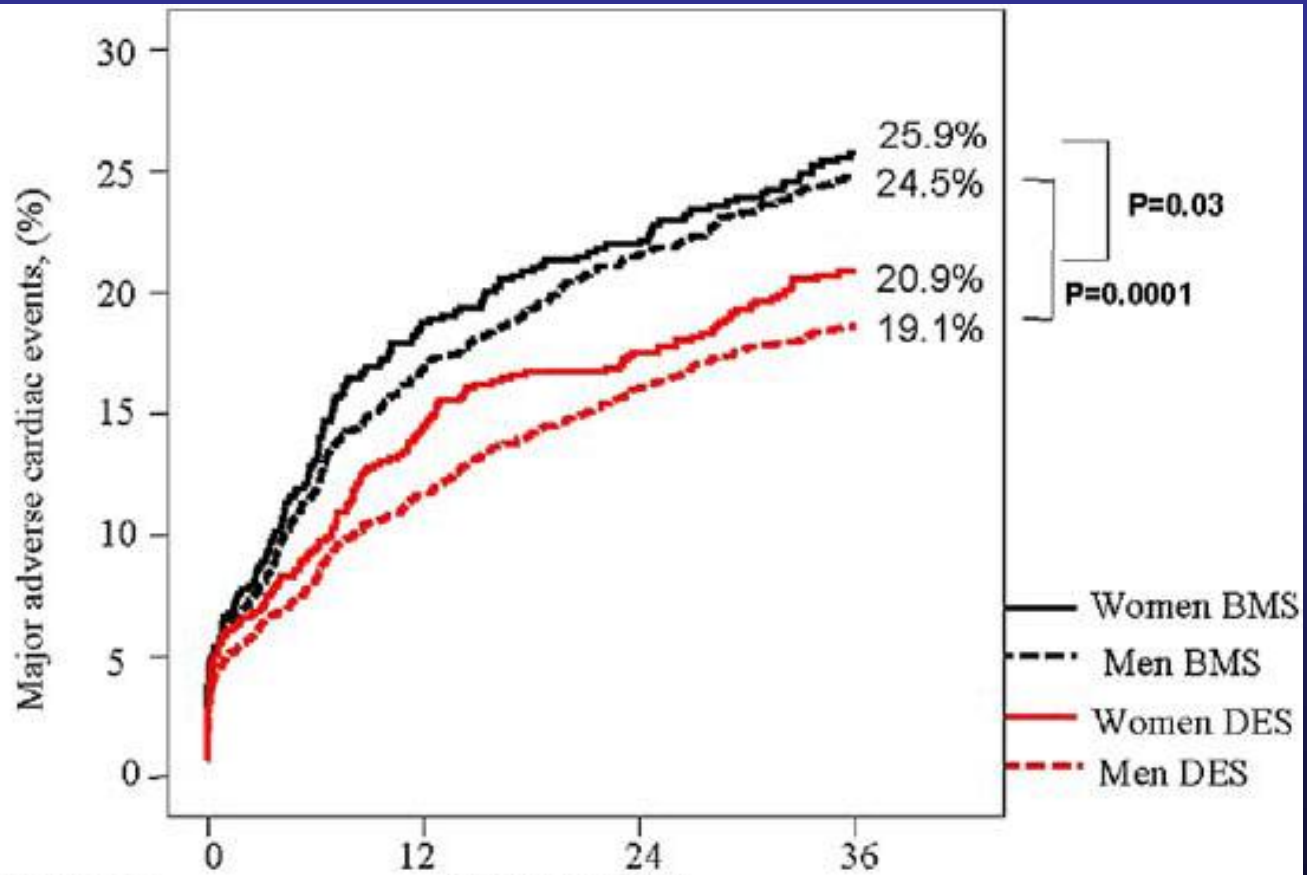


N men =1251

N women=497

Impact of Sex on 3-Year Outcome After Percutaneous Coronary Intervention Using Bare-Metal and Drug-Eluting Stents in Previously Untreated Coronary Artery Disease

Insights From the RESEARCH (Rapamycin-Eluting Stent Evaluated at Rotterdam Cardiology Hospital) and T-SEARCH (Taxus-Stent Evaluated at Rotterdam Cardiology Hospital) Registries



Patient number at risk

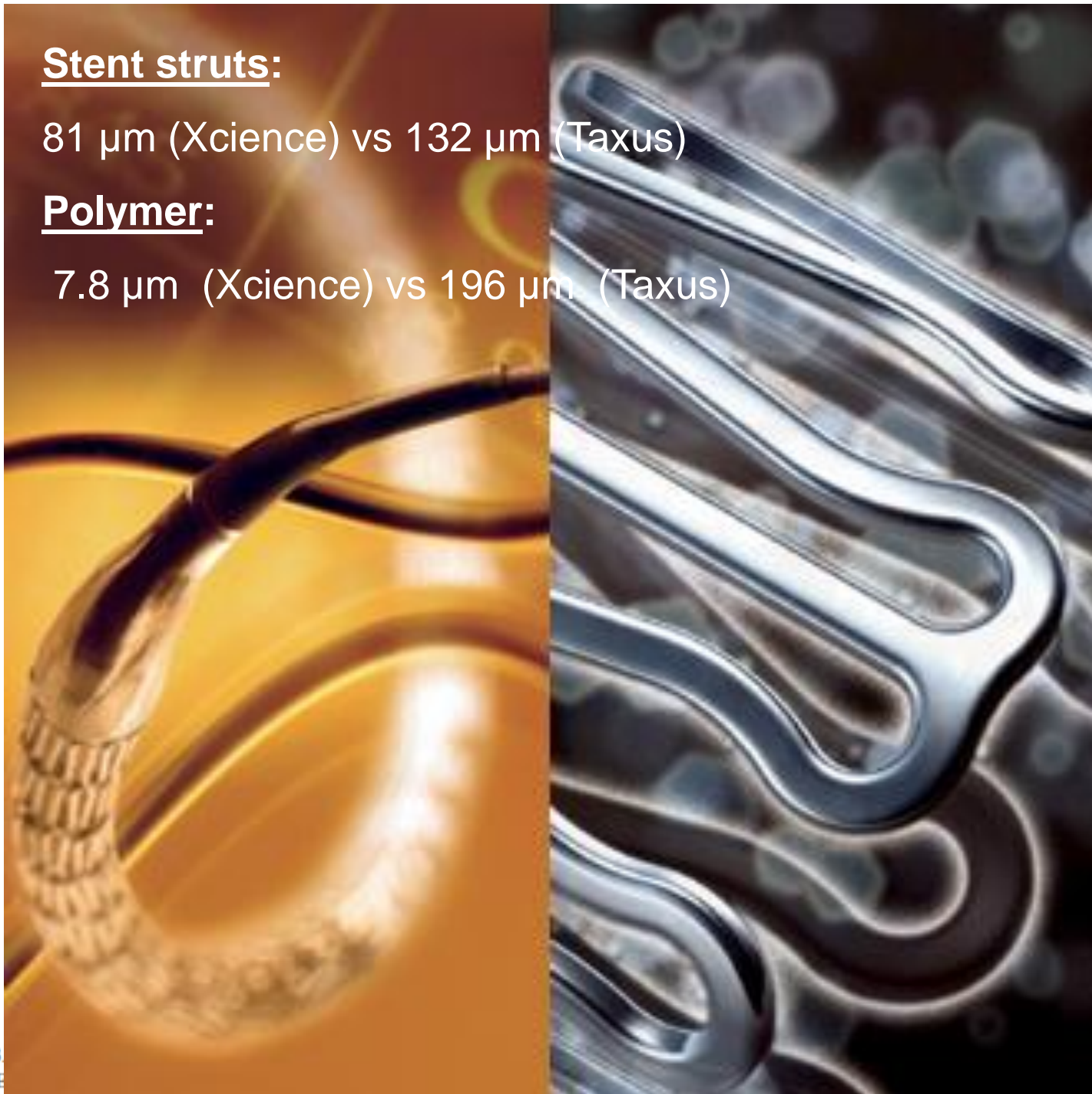
	0	12	24	36
Women BMS	616	501	480	453
Women DES	797	648	615	440
Men BMS	1530	1318	1228	1174
Men DES	2006	1666	1557	1139

Stent struts:

81 μm (Xcience) vs 132 μm (Taxus)

Polymer:

7.8 μm (Xcience) vs 196 μm (Taxus)



SPIRIT WOMEN

Clinical Investigation Title

A Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System in the Treatment of Women with *de novo* Coronary Artery Lesions

Single Arm Study (SAS) 1600 pts

Randomized Control Trial (RCT) 455 pts

2:1 randomization Xcience vs Cypher

Mean Age	69 yrs
Diabetes	34%
Requiring insulin	8%
Lesions class B2/C	72%
Multivessel treatment	32%
Mean n° lesions treated/pt	1.4

SPIRIT WOMEN: SINGLE ARM STUDY (SAS)

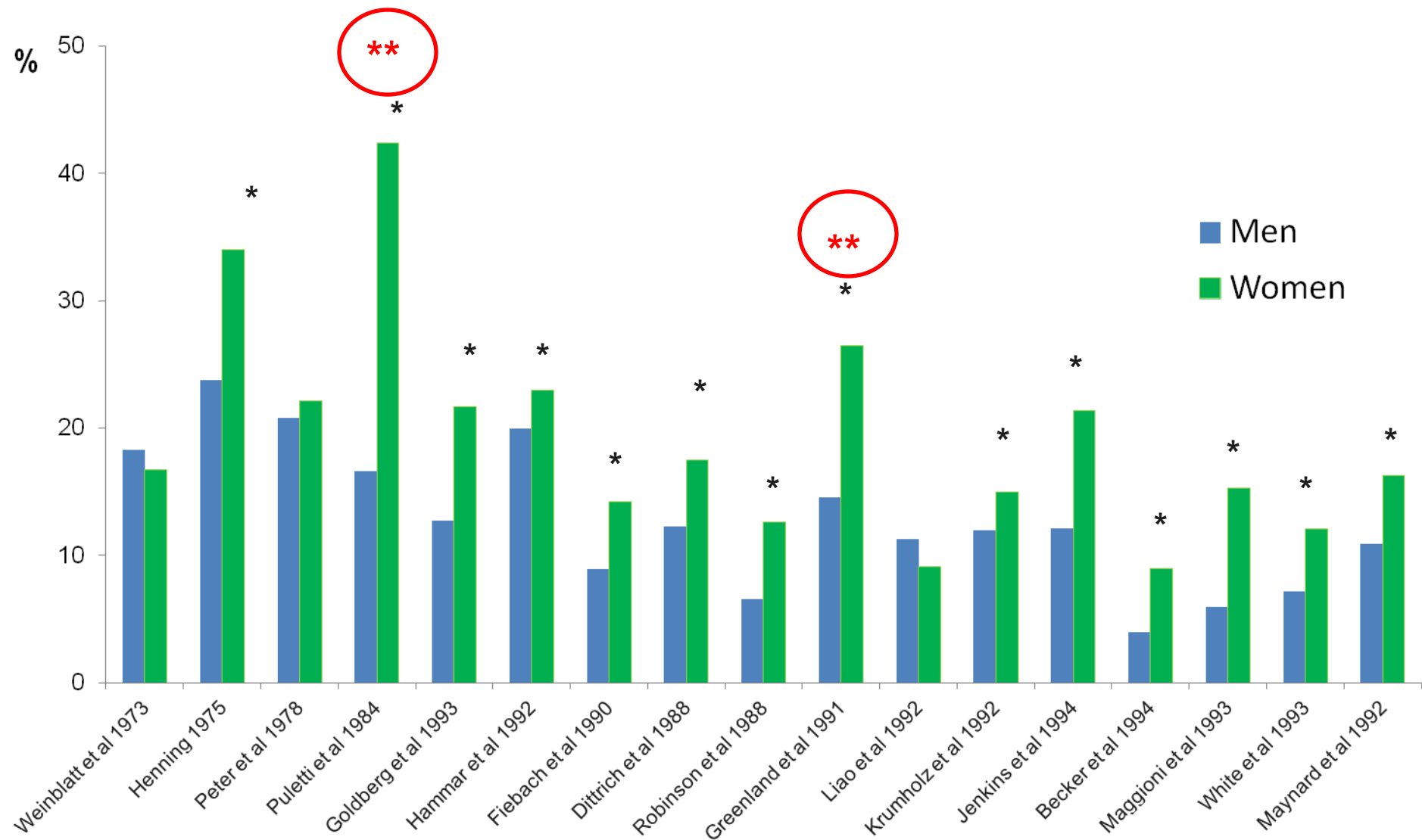
	1 YEAR	2 YEAR
Primary end point (death, MI, TVR)	12.1% (MI 9%)	14.8
TLR	2.3%	3.57%
TVR	3.08%	4.81%
Any revascularization	7%	8.12%
Definite/probable stent thrombosis	0.59%	0.73%

SPIRIT WOMEN: RANDOMIZED CONTROL TRIAL (RCT)

270 days angiographic follow up

	XCIENCE (EES)	CYPHER (SES)
In stent LL (mm)	0.20	0.12
In stent % angiographic binary ristenosis	3.2%	0.7%
1 year stent thrombosis	0.0%	1.39%
Any revascularization	18.7%	19%
TLR	7.8%	7.3%
TVR	9.5%	10.6%
All MACE	28%	30%

Early Mortality (In-Hospital or First Month) After Myocardial Infarction



Vaccarino et al., *Circulation*. 1995;91:1861-1871

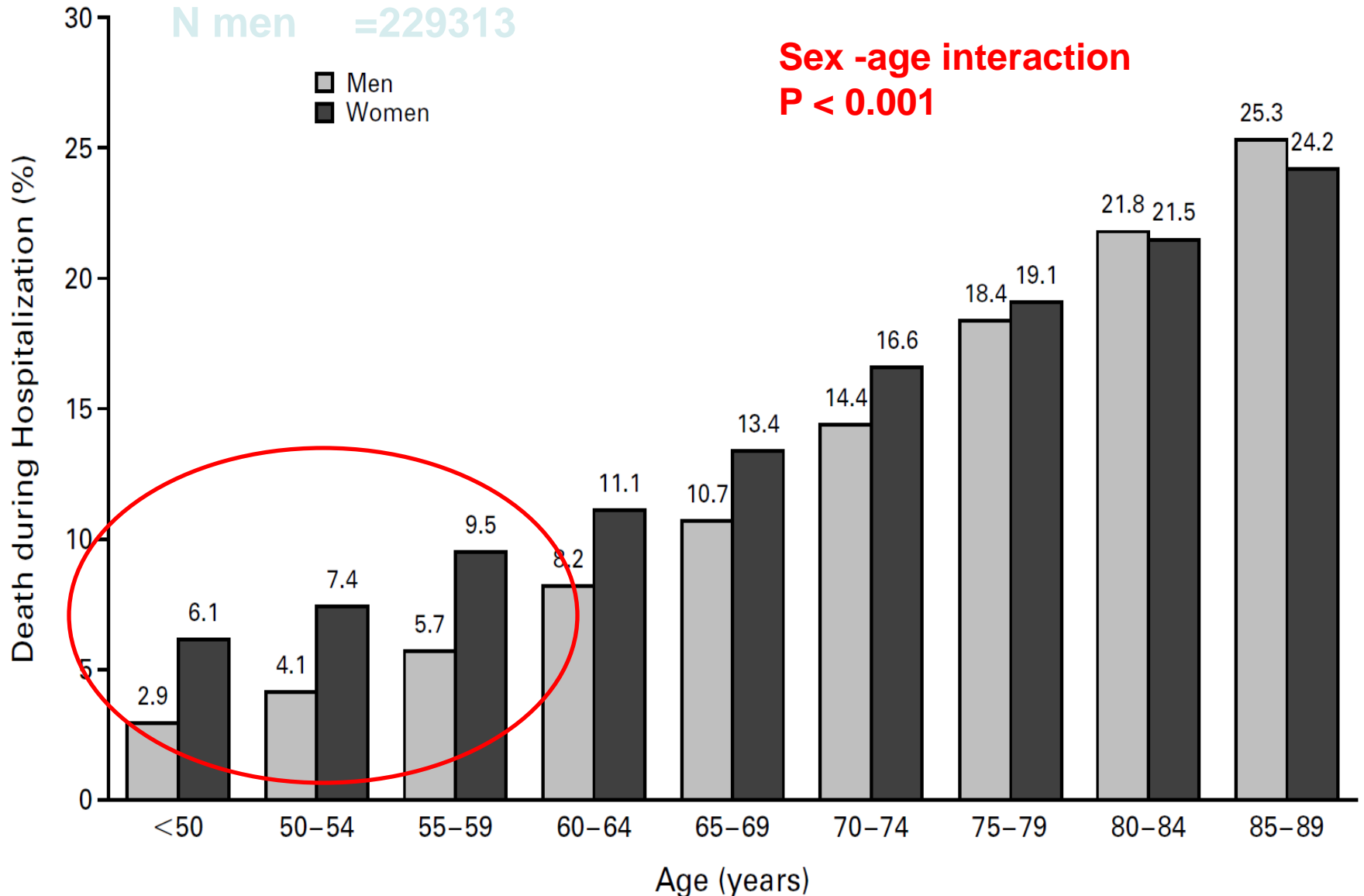
NATIONAL REGISTRY OF MYOCARDIAL INFARCTION 2

N women=155565

N men =229313

Men
Women

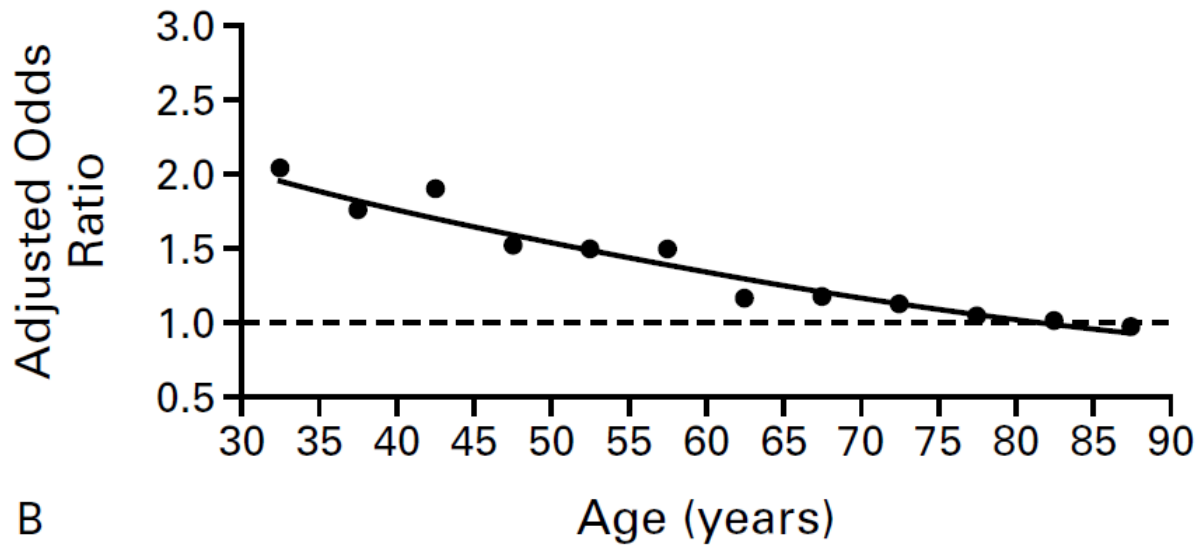
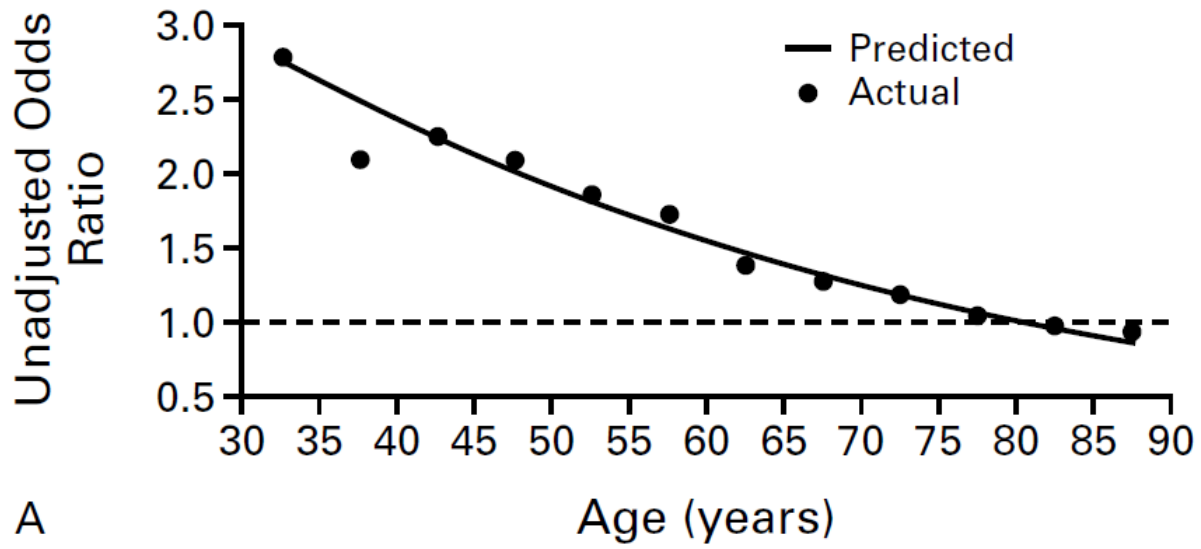
**Sex -age interaction
P < 0.001**



NATIONAL REGISTRY OF MYOCARDIAL INFARCTION 2

Women vs. Men

In-hospital death



Race, medical history, clinical abnormalities, management in the first 24h, time to presentation

TEMPORAL TREND IN SEX-AGE INTERACTION

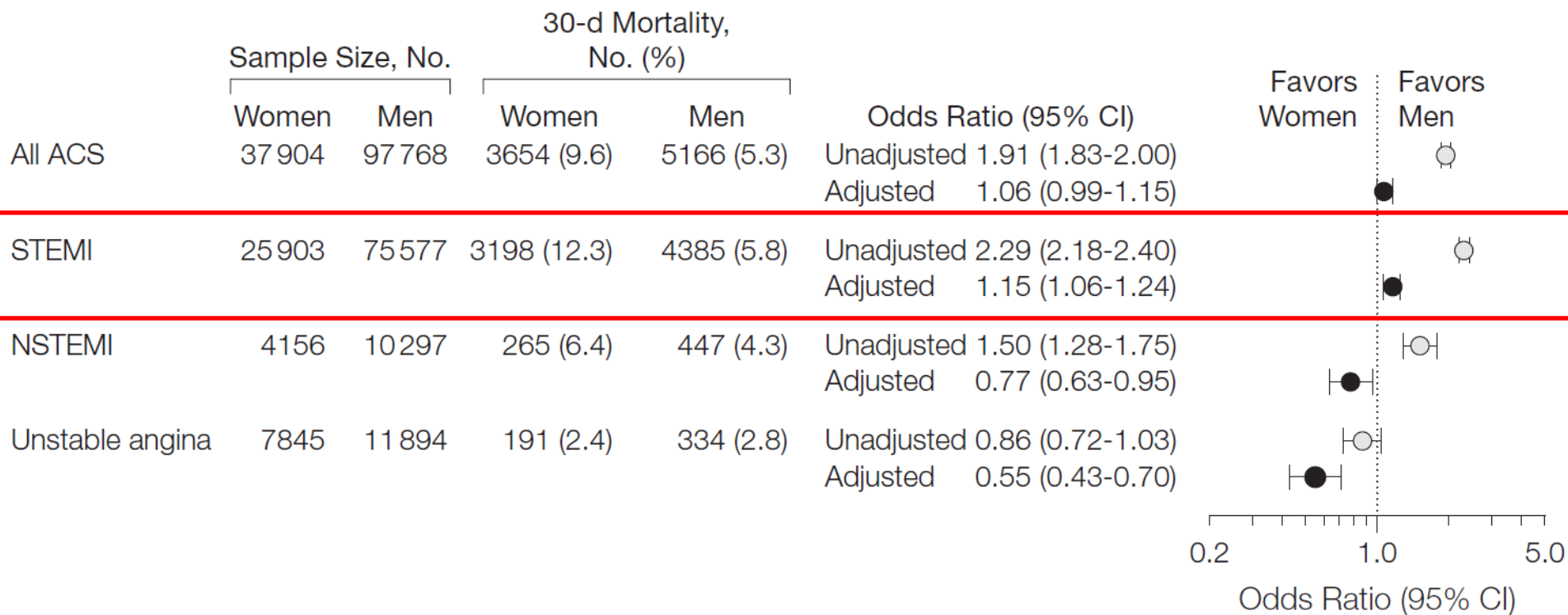
N women=285735

N men =270715

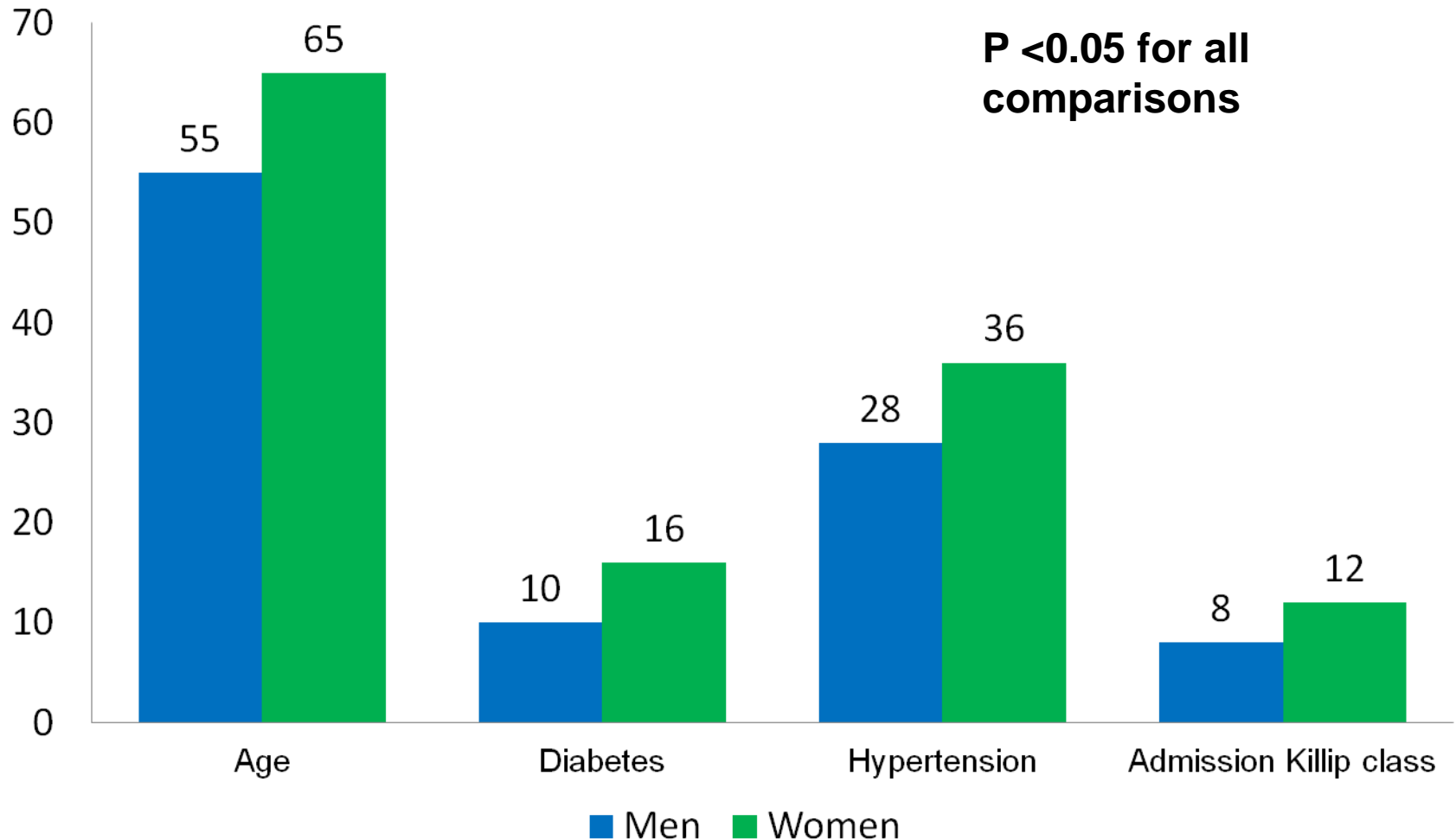
Table 3. Hospital Mortality Rates in Patients Classified According to Sex, Age, and Admission Year

Variable	Hospital Mortality Rate, % ^a						Total Reduction, %	Absolute Rate Reduction	Ratio (1994-1995 vs 2004-2006) ^b
	1994-1995	1996-1997	1998-1999	2000-2001	2002-2003	2004-2006			
Men, y									
<55	2.7	2.6	2.5	2.4	2.2	1.8	33.3	0.9	3.00 ^c
55-64	5.7	5.3	4.7	4.4	4.0	3.3	42.1	2.4	1.71 ^d
65-74	10.5	9.6	9.4	8.8	7.3	5.9	43.8	4.6	1.54 ^e
75-84	18.1	16.1	15.3	14.3	12.6	10.9	39.8	7.2	1.17 ^f
≥85	24.7	23.1	21.6	19.6	18.6	16.0	35.2	8.7	1.24 ^g
Women, y									
<55	5.1	4.9	3.7	3.6	3.3	2.4	52.9	2.7	NA
55-64	8.0	7.9	7.1	6.4	5.6	3.9	51.3	4.1	NA
65-74	13.6	12.3	11.1	9.8	8.5	6.5	52.2	7.1	NA
75-84	19.7	17.7	16.3	14.6	13.1	11.3	42.6	8.4	NA
≥85	25.8	23.5	21.0	19.7	17.9	15.0	41.9	10.8	NA

Pooled analysis 11 RCT, years 1993-2006



Cardiovascular profile

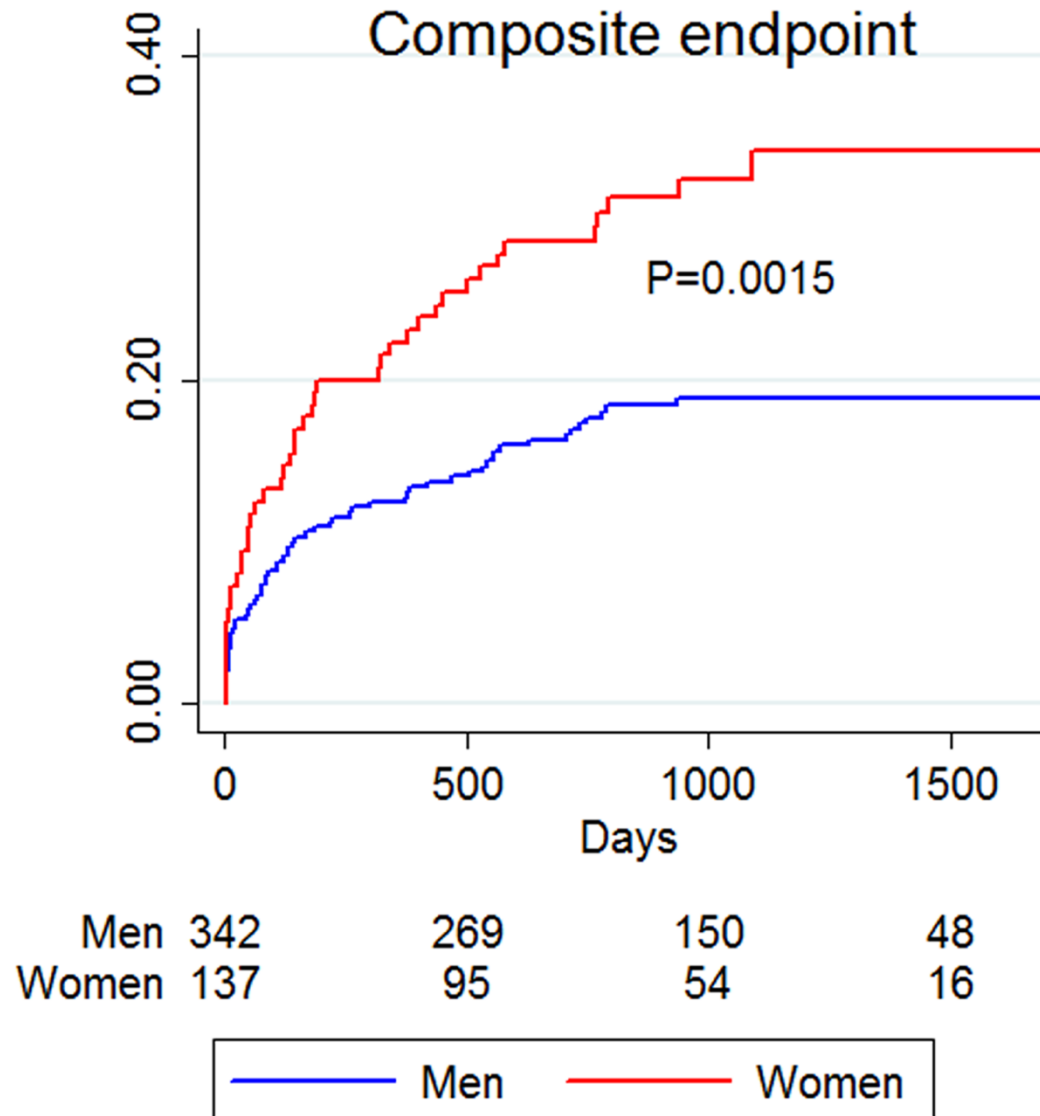


ICH, Years 2004-2008

N men=343

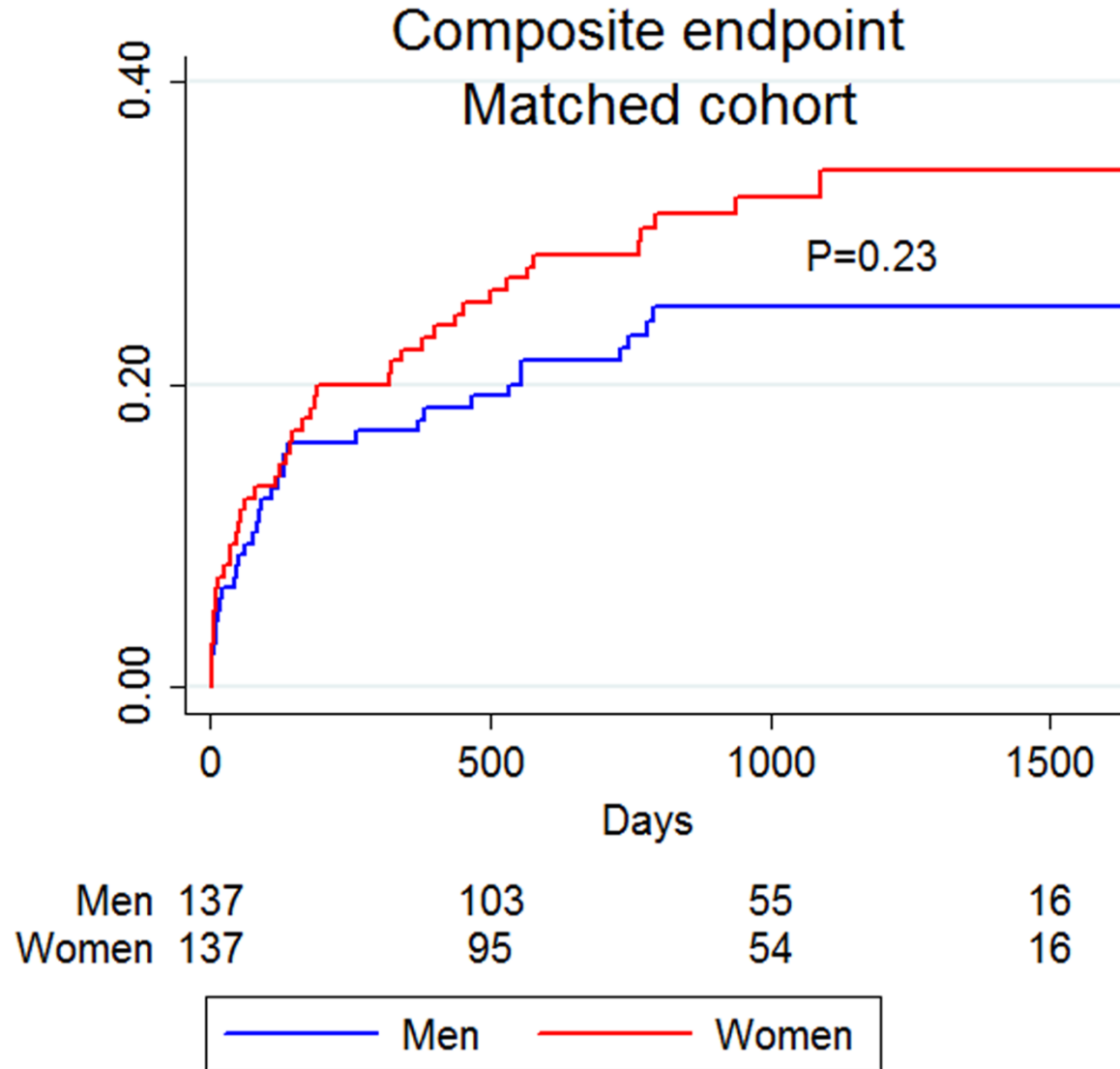
N women=138

**Composite of death,
non fatal MI,
hospitalization
for heart failure**



N men=343
N women=138

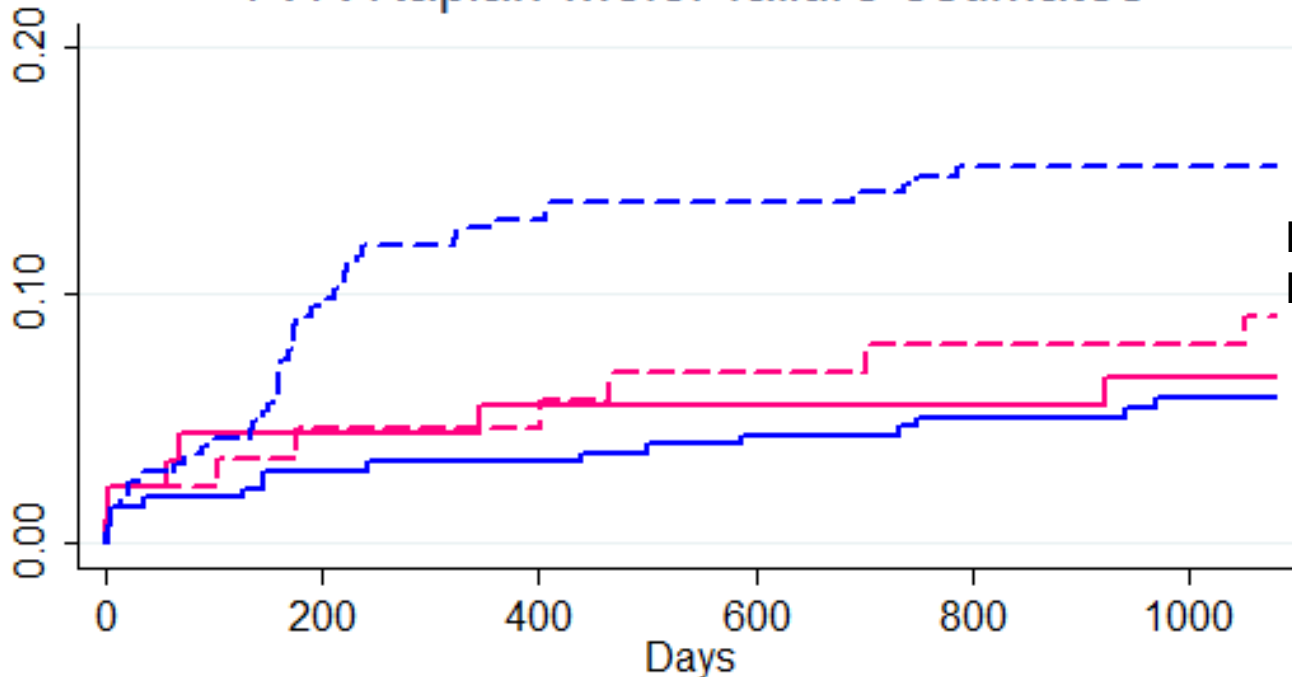
ICH, Years 2004-2008



POST HOC ANALYSIS OF THE MULTISTRATEGY TRIAL

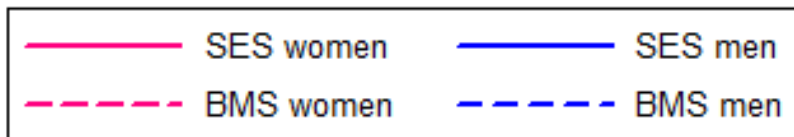
N men =565
N women=179

TVR Kaplan-Meier failure estimates



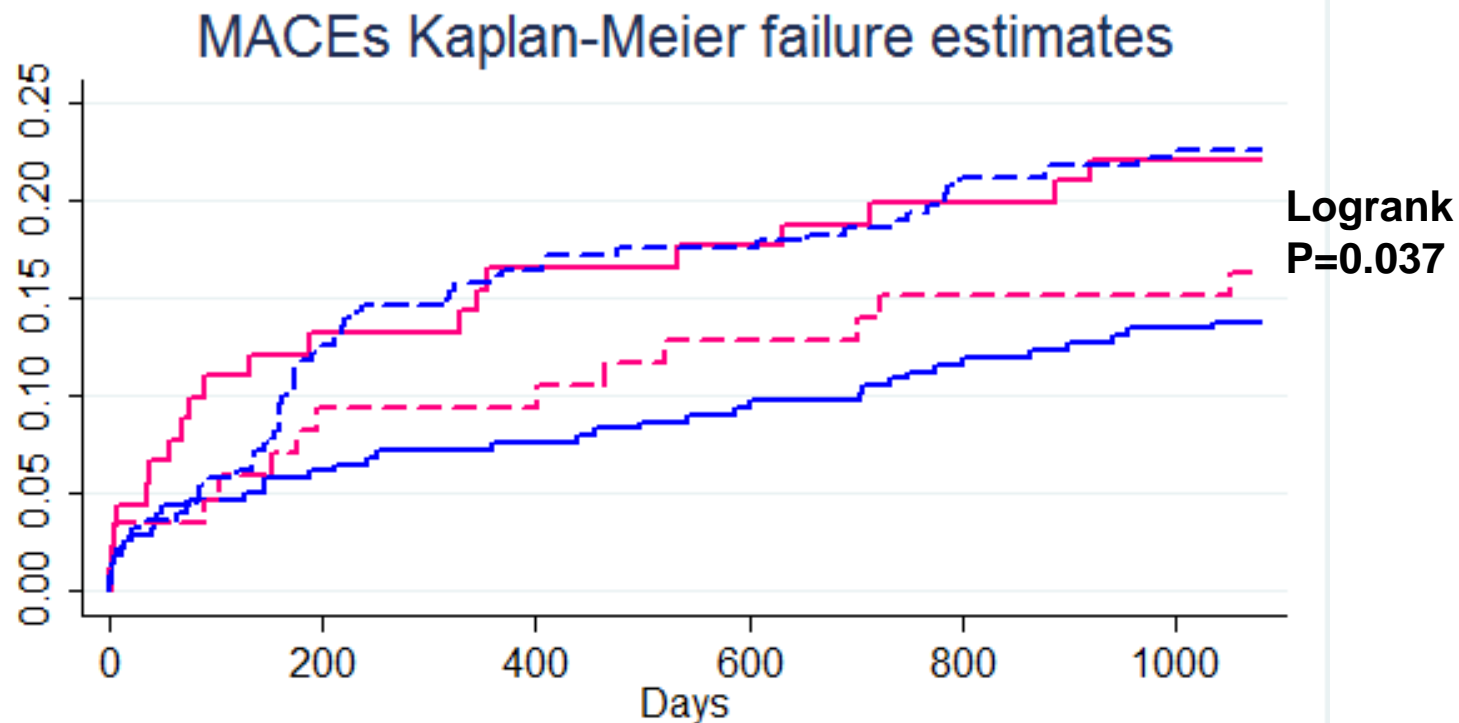
Number at risk

SES women	91	87	85	85	85	84
SES men	280	272	265	262	260	258
BMS women	88	84	84	82	81	81
BMS men	284	256	246	244	240	240



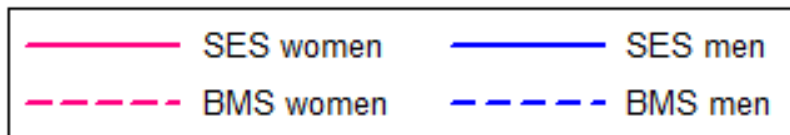
POST HOC ANALYSIS OF THE MULTISTRATEGY TRIAL

N men =565
N women=179



Number at risk

SES women	91	79	75	74	72	70
SES men	280	263	253	248	242	237
BMS women	86	78	78	75	73	73
BMS men	280	245	233	230	220	217



STENT THROMBOSIS ACCORDING TO SEX

	MEN (%)	WOMEN (%)	FUP
<i>Ravel+Sirius:</i>			
SES (Cypher)	0.6	0.4	1 yr
BMS	0.3	1.2	
<i>Research (registry):</i>			
SES+PES (Taxus)	2.6	2	3 yrs
BMS	1.5	1.8	
<i>ENDEAVOR:</i>			
ZES (Endeavor)	0.5	1.3	2 yrs
BMS	1.4	1.4	
<i>SPIRIT III:</i>			
EES (Xcience)	1.1	1.6	3 yrs
PES	2	1	
<i>Multistrategy:</i>			
SES	3.5	5.4	3 yrs
BMS	4.9	3.4	



FACTORS RELATED TO BLEEDING AFTER PCI IN ICH (1997-2010, 7822 pts, 22% women)

	Bleeding	No bleeding	P
Age	68.8±10.9	65.4±11.2	0.014
Creatinine	1.4±1.4	1.2±0.6	0.022
Women	6%	94%	0.01
Men	2.7%	97.3%	
STEMI	7%	93%	0.0001
NSTE-ACS	2%	98%	
GP IIb/IIIa Yes	5%	95%	0.026
No	2.6%	97.4%	

PERIPHERAL VASCULAR COMPLICATIONS ACCORDING TO SEX

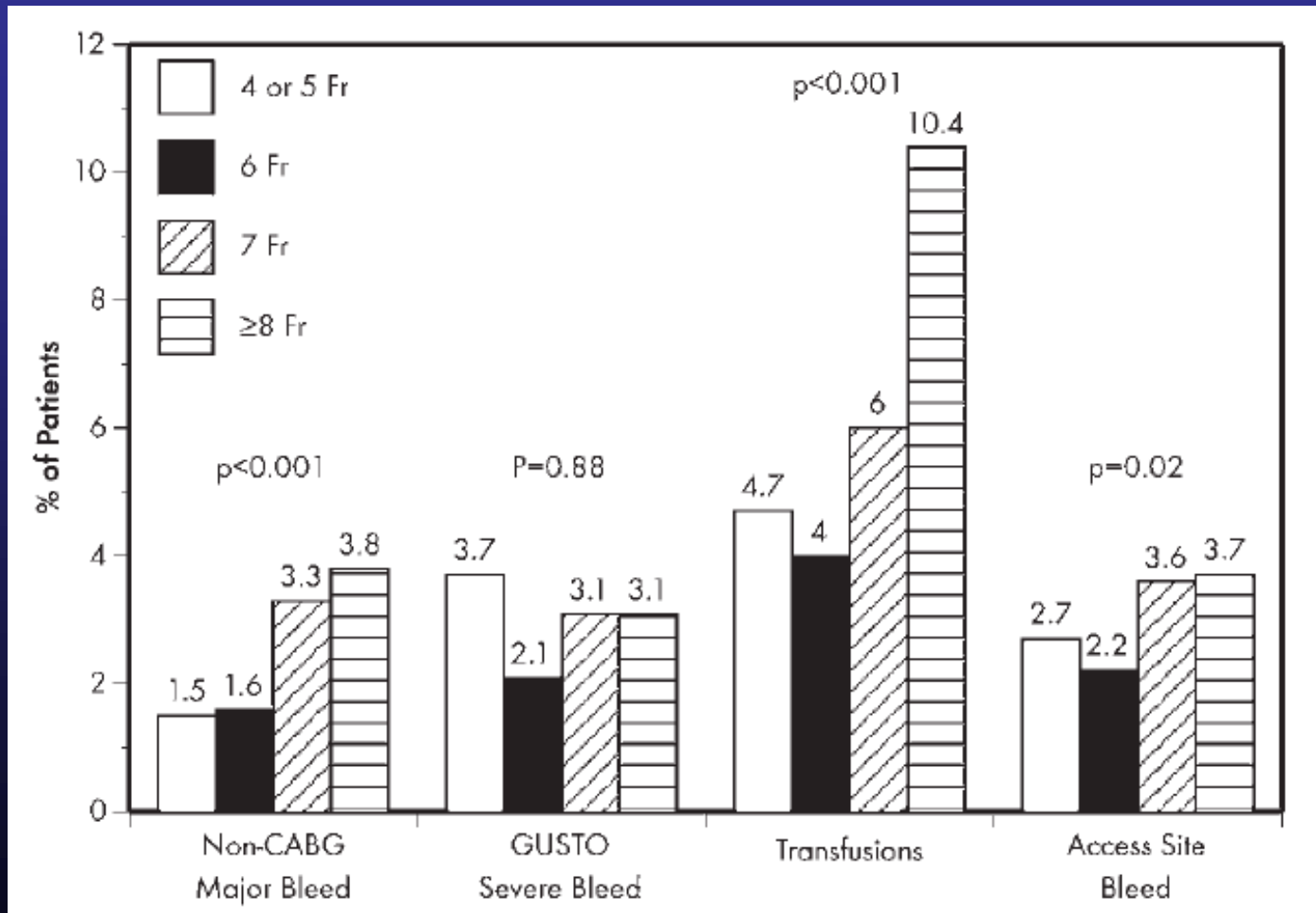
(ICH: 1997-2010, 7822 pts, 22% women)

	Men (%)	Women (%)	p
1997-2003	0.8	2.7	<0.001
2003-2006	1.8	2.8	0.37
2006-2010	0.8	1	ns

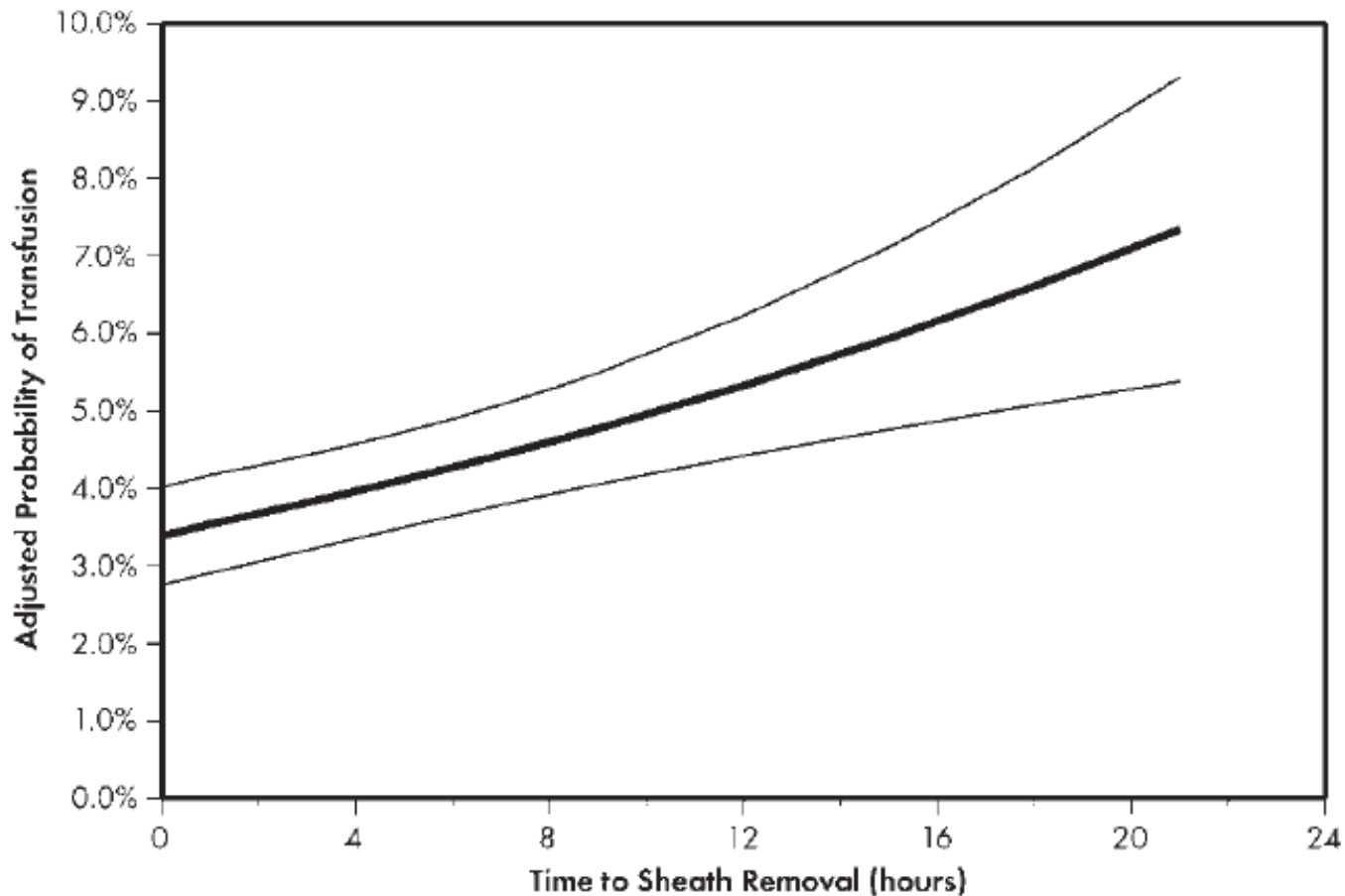
Bleeding Complications in Patients With Acute Coronary Syndrome Undergoing Early Invasive Management Can Be Reduced With Radial Access, Smaller Sheath Sizes, and Timely Sheath Removal

	Femoral (<i>n</i> = 8,922) (%)	Radial (<i>n</i> = 413) (%)
TIMI major bleeding	8.8	5.8
CABG-related major bleeding	6.8	4.6
Non-CABG-related major bleeding	2.0	1.2
GUSTO severe bleeding	2.5	2.7
Transfusions ^b	4.8	0.9
Access site bleeding	19.3	22.5

Bleeding Complications in Patients With Acute Coronary Syndrome Undergoing Early Invasive Management Can Be Reduced With Radial Access, Smaller Sheath Sizes, and Timely Sheath Removal



Bleeding Complications in Patients With Acute Coronary Syndrome Undergoing Early Invasive Management Can Be Reduced With Radial Access, Smaller Sheath Sizes, and Timely Sheath Removal



CONCLUSIONS 1

- **Acute and chronic coronary disease** in women undergoing PCI has nowadays the same procedural success and complication rates as men, despite worst basic conditions
- Long term restenosis after **BMS** implantation is better in women than in men, maybe because of estrogen hormones and receptors that reduce the inflammatory response to vessel injury
- **DES** implantation reduce restenosis rate in both sexes, in different way depending on factors, such as type, quantity and time release of the drug (“-limus” stents seem to be better), the polymer used and stent strut thickness

CONCLUSIONS 2

- **DES** requiring a shorter period of double antiplatelet treatment can reduce the bleeding risk, that is higher in women
- Non-diabetic women undergoing primary PCI seem to benefit from BMS

... WAITING TO HORIZONS-AMI TRAIL GENDER DIFFERENCE RESULTS



Patrizia Presbitero

CAD and stent in women

GRAZIE

XXIV Giornate Cardiologiche Torinesi

Torino, 20 Ottobre 2011

Procedural outcomes of pts, BMS and PES according to gender

ICH-PCI-database (1999 - 2005)

N°	BMS			PES		
	Men	Women	p	Men	Women	p
	2811	704		642	168	
Procedural success (%)	97.9	98.1	0.881	98	100	0.05
Death, (%)	0.7	1.3	0.15	0.5	0	1.0
AMI (%)	0.8	0.7	1.00	0.8	0	0.60
CABG (%)	0.4	0.8	0.11	0.5	0.6	1.0
MACE (%)	1.7	2.8	0.06	1.8	0.6	0.32
Acute vessel thrombosis (%)	0.4	0.3	1.0	0.4	0	1.0
Periph. vasc. complications (%)	0.8	2.7	<0.001	1.8	2.8	0.37

Sex Differences in Neointimal Hyperplasia Following Endeavor Zotarolimus-Eluting Stent Implantation

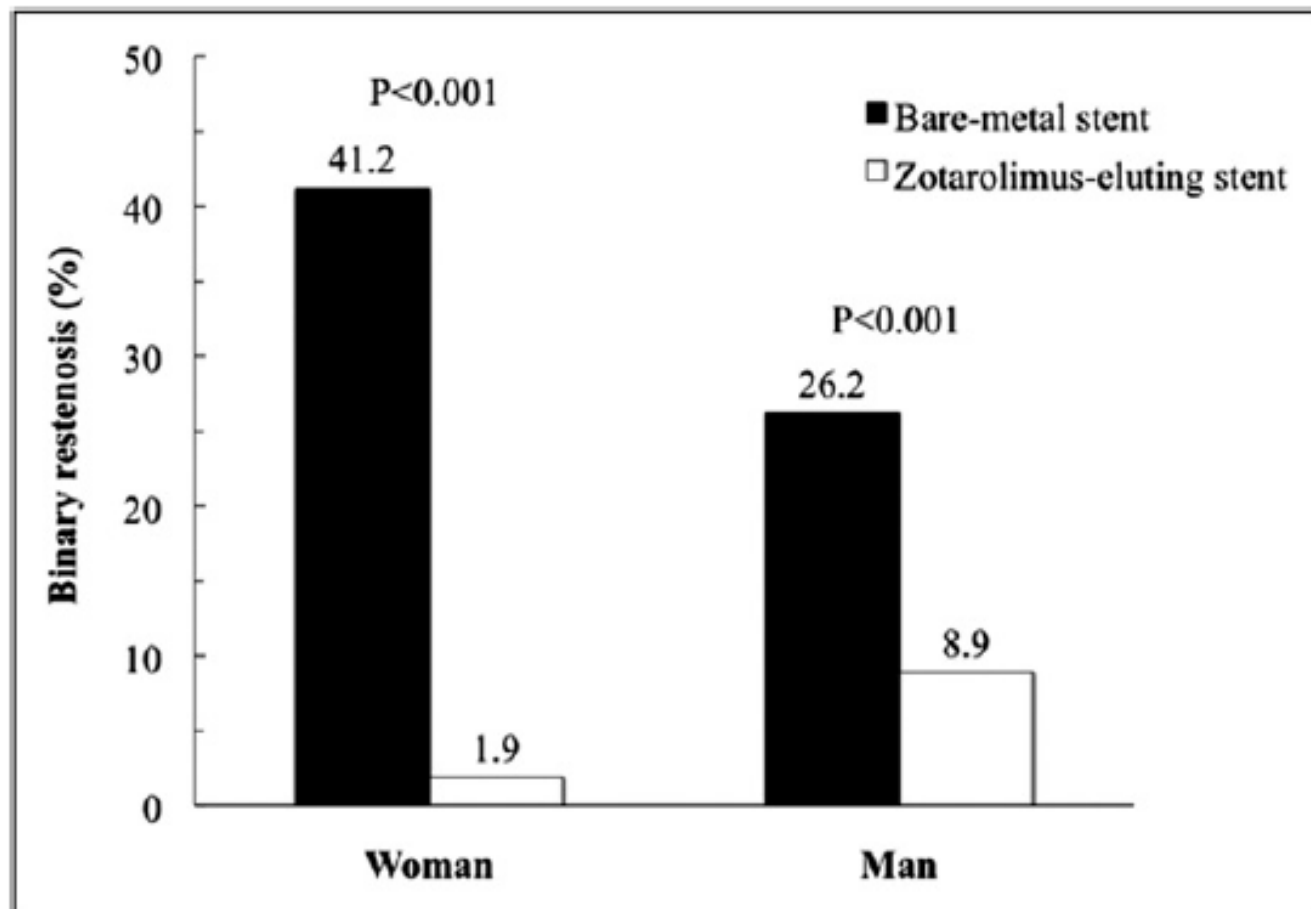
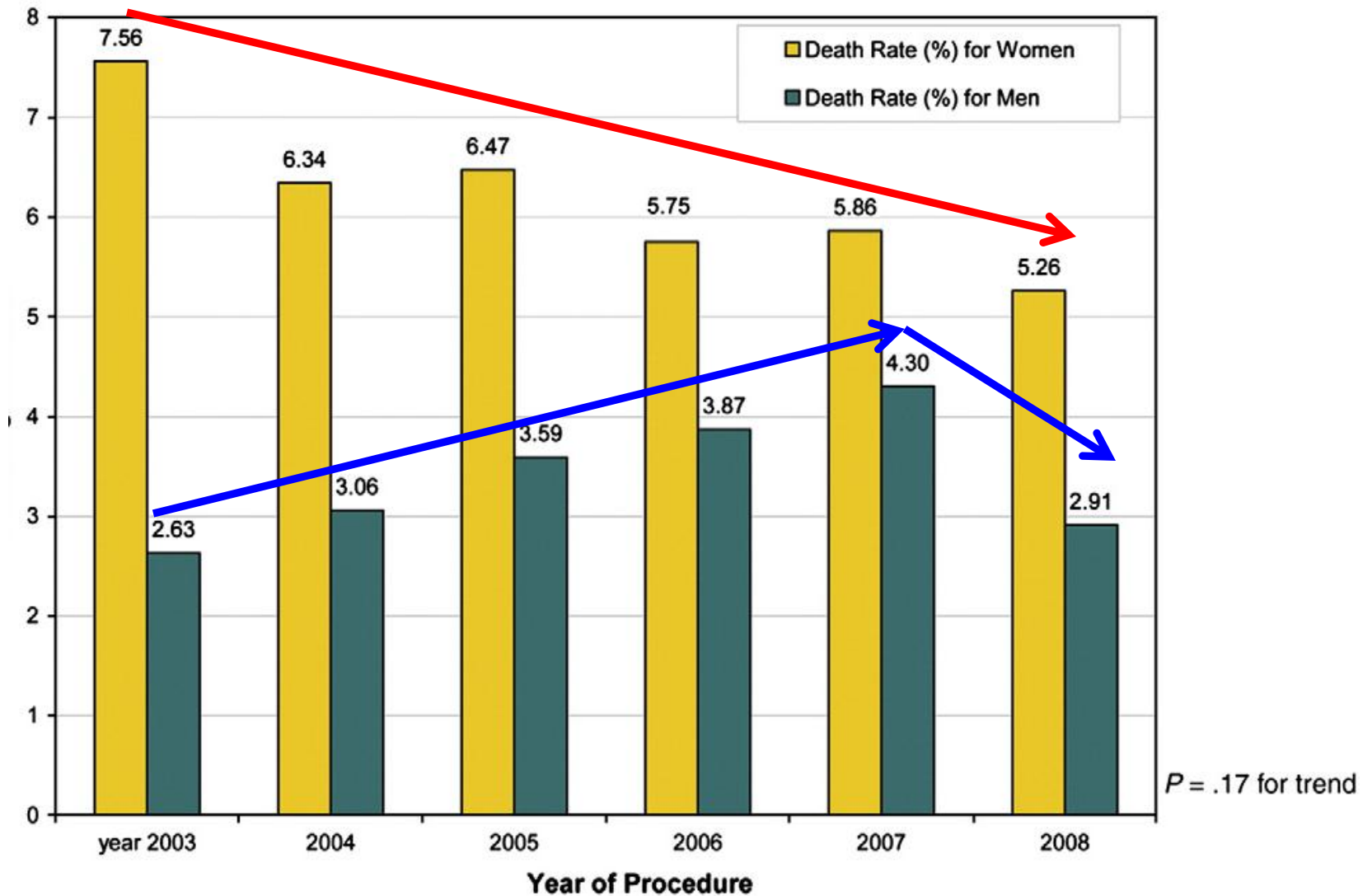


Figure 1. The rate of binary restenosis, defined as $>50\%$ diameter stenosis on angiography at 8-month follow-up, was significantly lower in patients treated with ZES than those with BMS in both genders.

N women = 2384
N men = 6014

BMC2 registry



BMC2 registry

Women vs. men

In-hospital outcomes	All data		
	OR	95% CI	P value
Emergency CABG	1.06	0.70-1.58	.79
All CABG	0.83	0.64-1.08	.17
Gastrointestinal bleeding	1.74	1.36-2.21	<.0001
Contrast nephropathy*	1.75	1.46-2.11	<.0001
Nephropathy requiring dialysis	1.28	0.79-2.06	.31
Postprocedure transfusion	2.84	2.48-3.24	<.0001
Stroke	1.85	1.15-2.97	.01
MI	1.01	0.64-1.60	.96
Death	1.79	1.45-2.22	<.0001
Revascularization (same lesion site)	1.19	0.80-1.78	.38
Vascular complication	2.13	1.75-2.59	<.0001

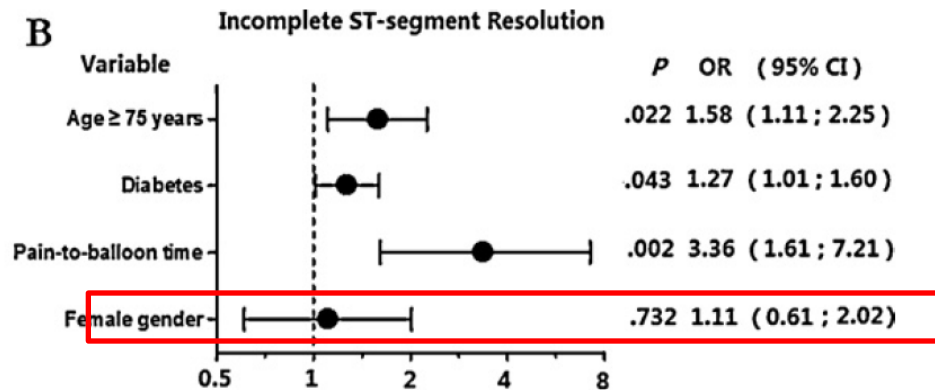
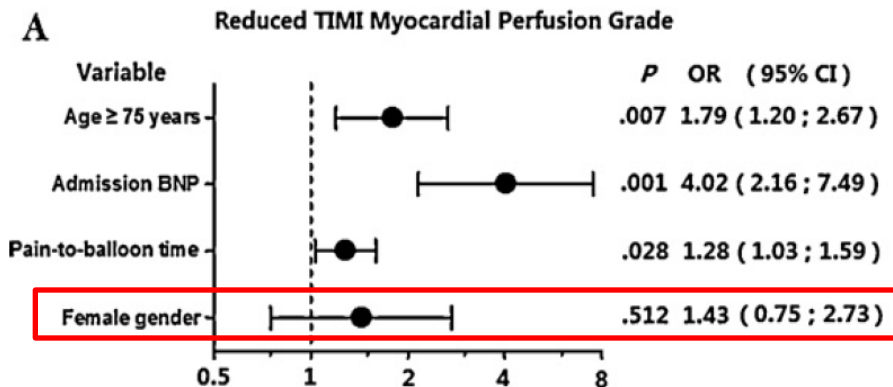
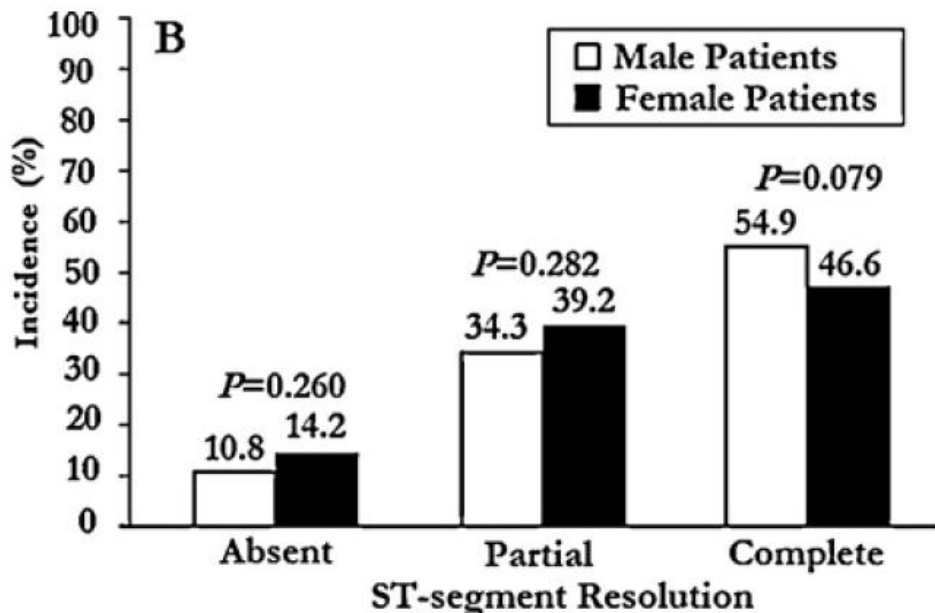
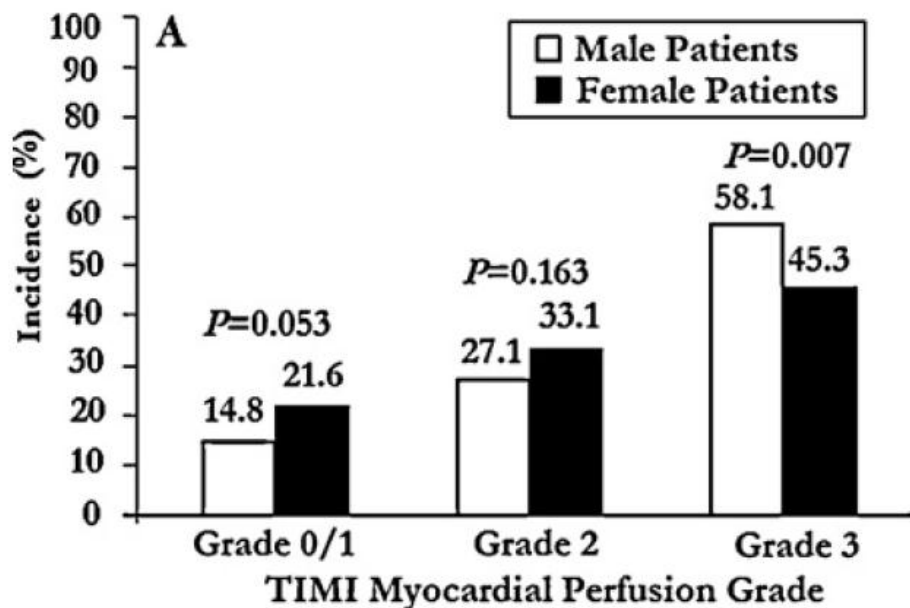
BMC2 registry

Women vs. men

Matched data
(2131 women and 2131 matched men)

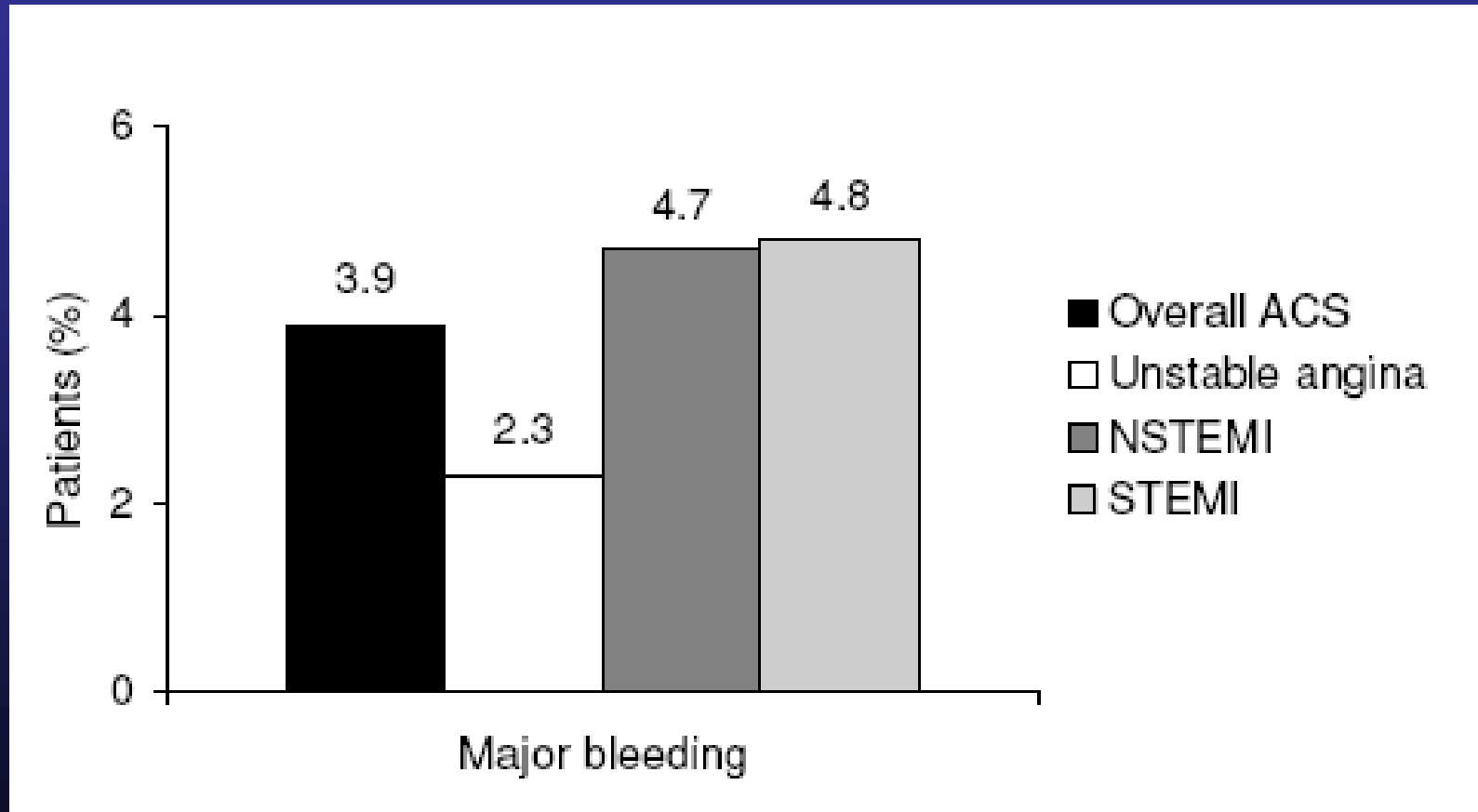
In-hospital outcomes	OR	95% CI	P value
Emergency CABG	1.04	0.60-1.79	.64
All CABG	0.85	0.61-1.19	.35
Gastrointestinal bleeding	1.19	0.87-1.63	.33
Contrast nephropathy*	1.09	0.87-1.37	.44
Nephropathy requiring dialysis	0.85	0.48-1.50	.56
Postprocedure transfusion	1.88	1.57-2.24	<.0001
Stroke	1.37	0.76-2.49	.29
MI	0.87	0.49-1.57	.87
Death	1.30	0.98-1.72	.07
Revascularization (same lesion site)	1.31	0.76-2.26	.33
Vascular complication	1.65	1.26-2.14	.0002

Sex and myocardial reperfusion

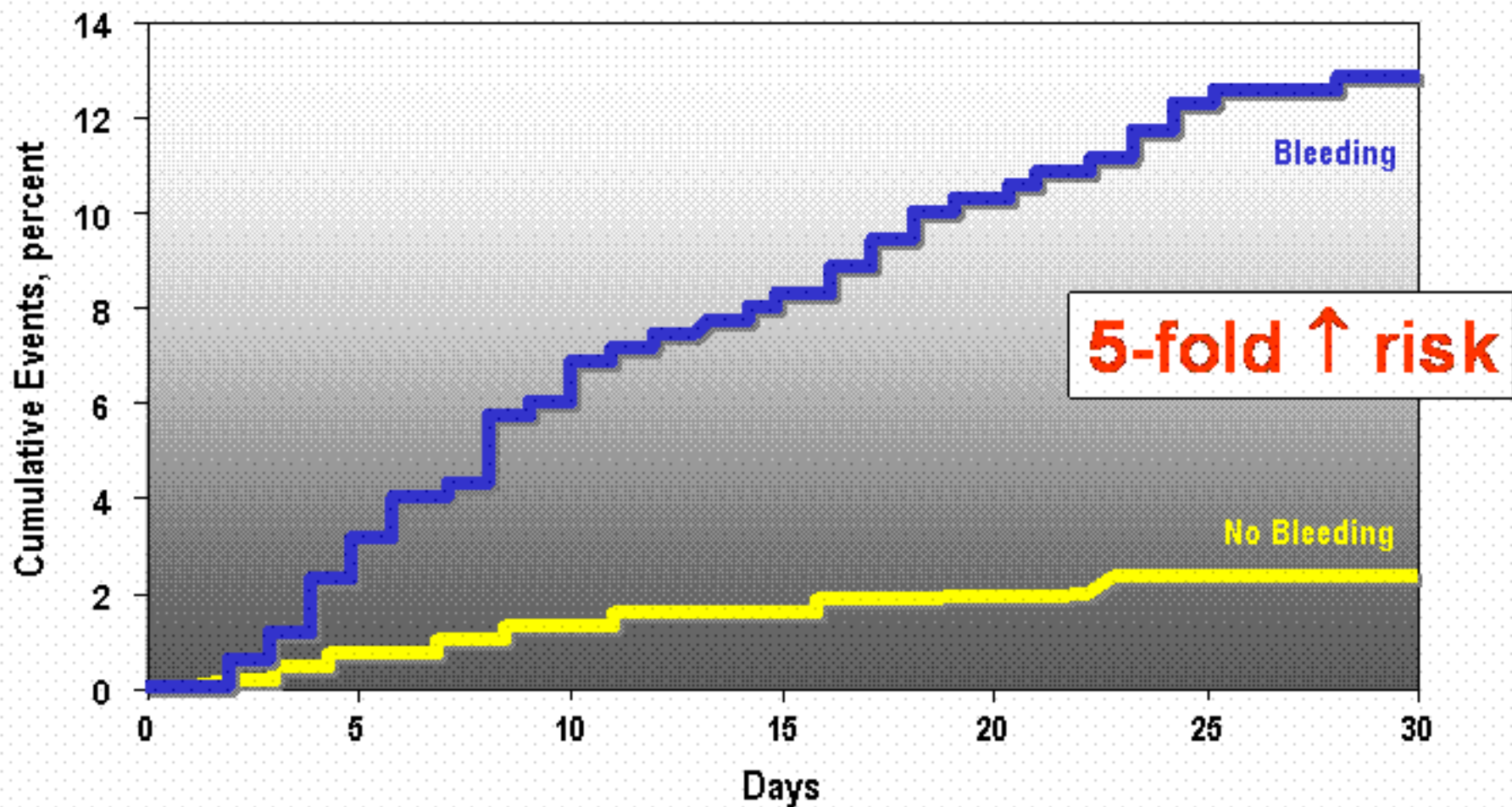


FREQUENCY OF MAJOR BLEEDING

Global Registry of Acute Coronary Events (GRACE)

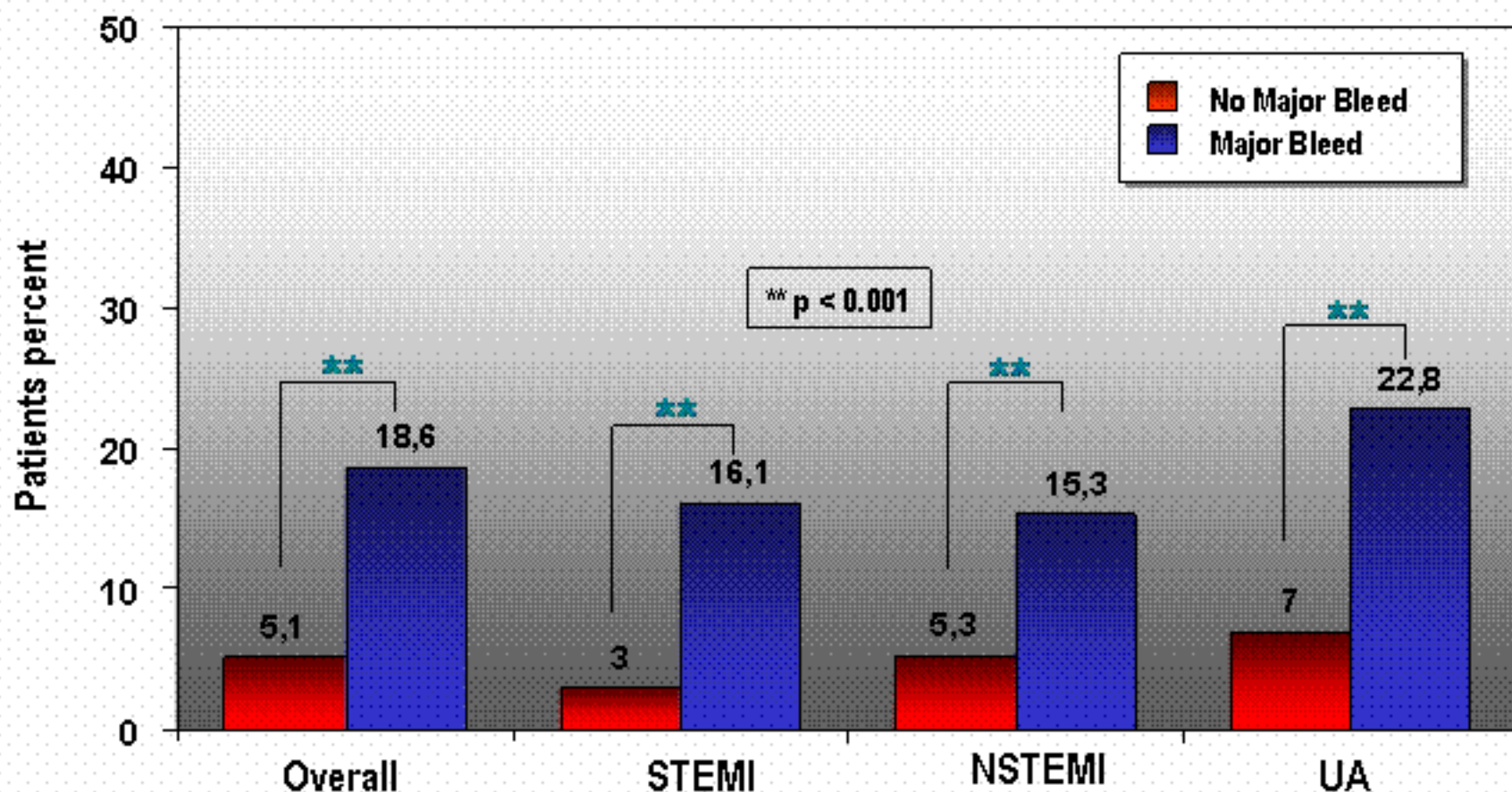


30 Day Death According to Bleeding OASIS Registry, OASIS-2, CURE



Eikelboom *Circulation* 2006; 114: 774 - 782

In-Hospital Death Rates in Patients According to Major Bleeding



Moscucci M et al. *Eur Heart J* 2003; 24: 1815-23.

FACTORS ASSOCIATED WITH MAJOR BLEEDING

- **ADVANCED AGE**
- **FEMALE SEX**
- **HISTORY OF BLEEDING**
- **RENAL INSUFFICIENCY**
- **ANTICOAGULANT MEDICATION**
- **PROCEDURES**

GRACE

Predictors of In-Hospital Bleeding in AMI Within 30 Days

<u>Variable</u>	<u>Total Cohort,† HR (95% CI)</u>
History of prior bleeding	2.70 (1.84–3.96)
Glomerular filtration rate 30 mL/min‡	
Early bleeding (0–2 d)	2.40 (1.76–3.29)
Late bleeding (3–30 d)	1.83 (1.25–2.68)
Pulmonary artery catheter	
Early bleeding (0–1 d)	1.65 (1.18–2.29)
Late bleeding (2–30 d)	2.04 (1.53–2.72)
Percutaneous coronary intervention	1.94 (1.51–2.50)
Treatment with IV vasopressors in first 24 h	1.94 (1.57–2.39)
Female sex	
Early bleeding (0–2 d)	1.36 (1.12–1.65)
Late bleeding (3–30 d)	1.84 (1.44–2.35)
Age per 10-y increase	
Early bleeding (0–2 d)	1.35 (1.25–1.47)
Late bleeding (3–30 d)	1.53 (1.36–1.72)
Fibrinolytic therapy	1.50 (1.16–1.92)
Treatment with GP IIb/IIIa inhibitors in first 24 h	1.48 (1.23–1.77)

WHY WOMEN SHOULD HAVE MORE BLEEDING RISK in PCI?

- OLDER AGE
- LOWER BASELINE HAEMOGLOBIN
- SMALLER VESSEL SIZE
- **MORE PERIPHERAL VASCULAR COMPLICATIONS**
- TENDENCY TO OVER-ANTICOAGULATION BECAUSE OF SMALLER BODY MASS

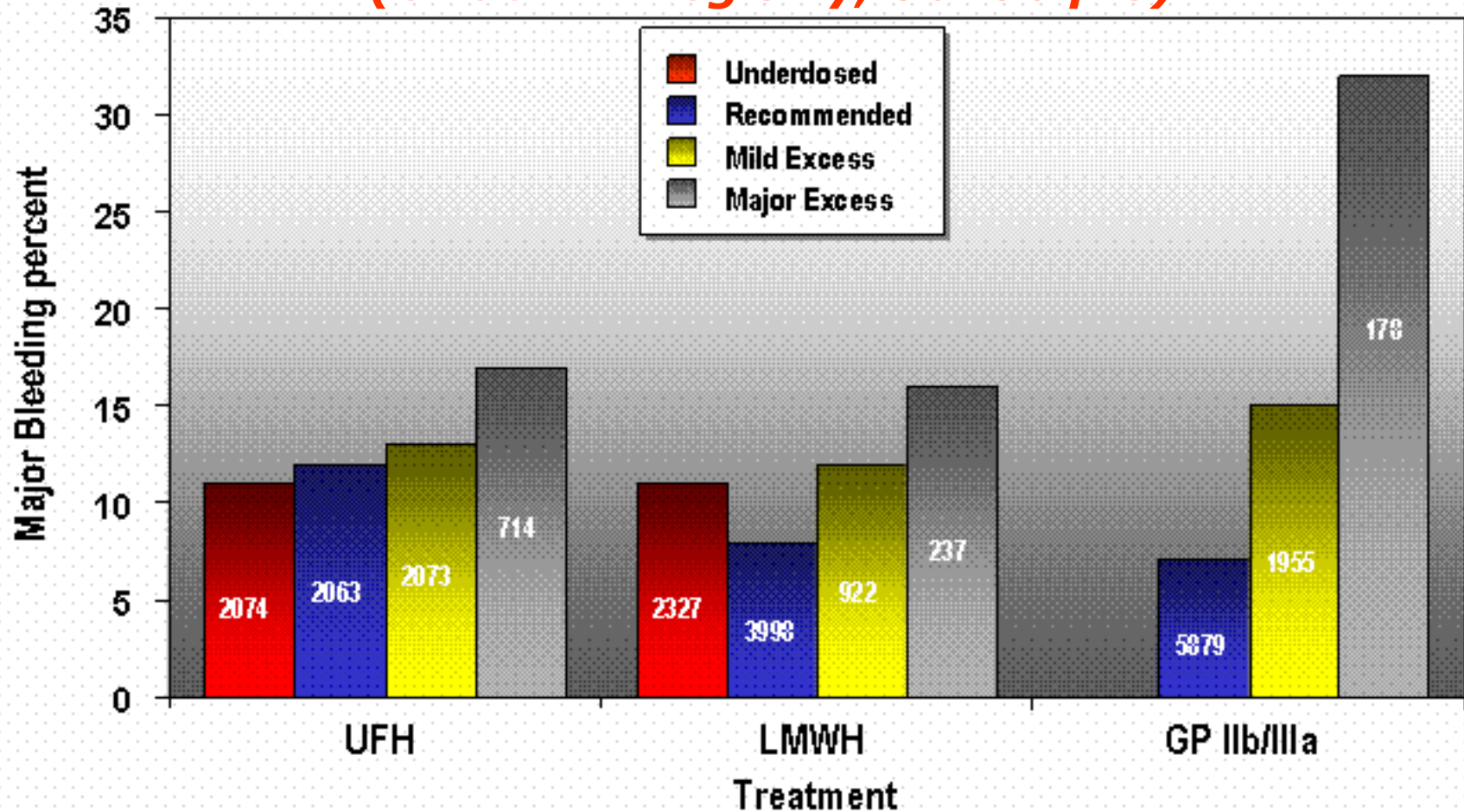
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Dosage of Drugs and Major Bleeding

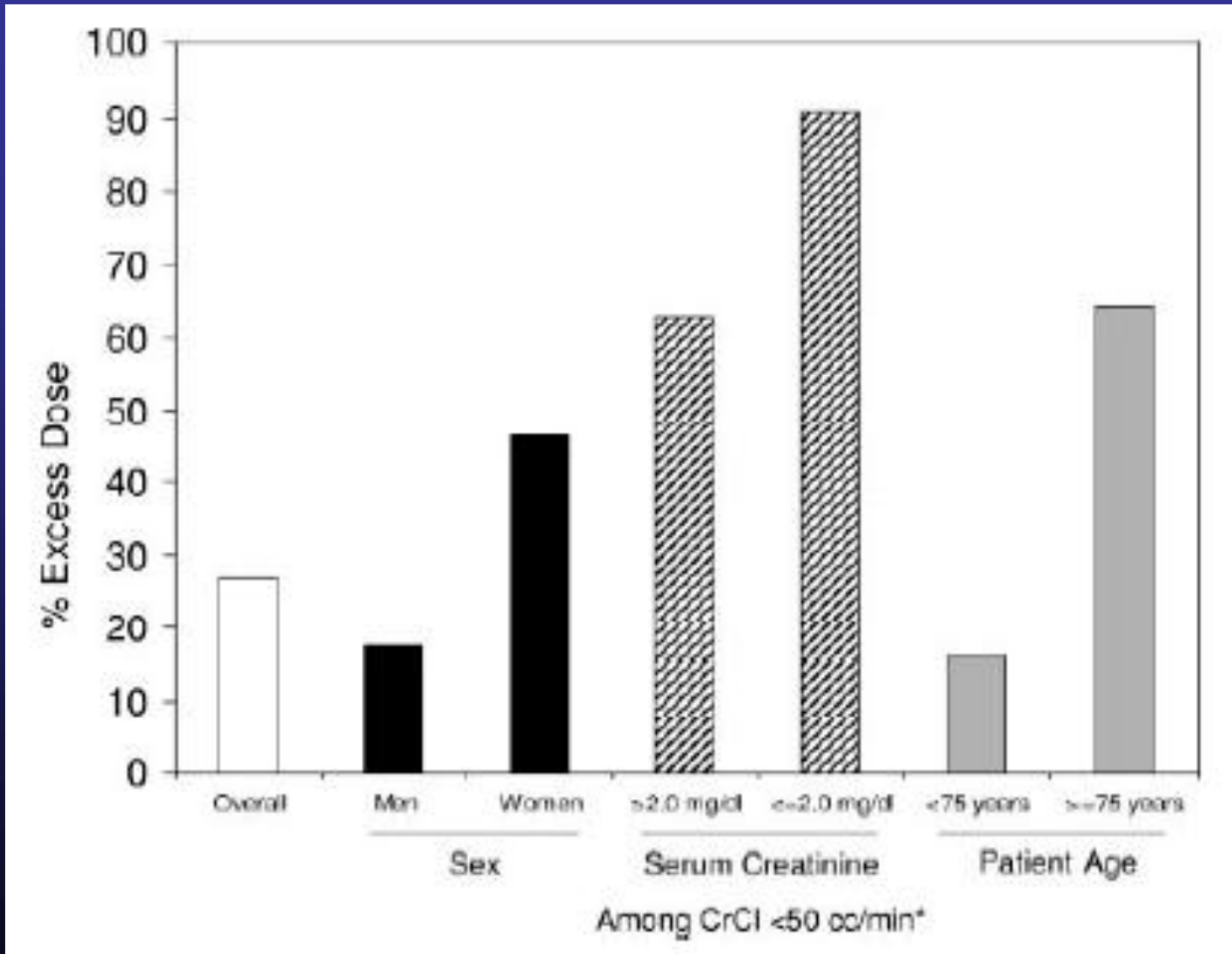
Dose Group

(CRUSADE registry, 30136 pts)

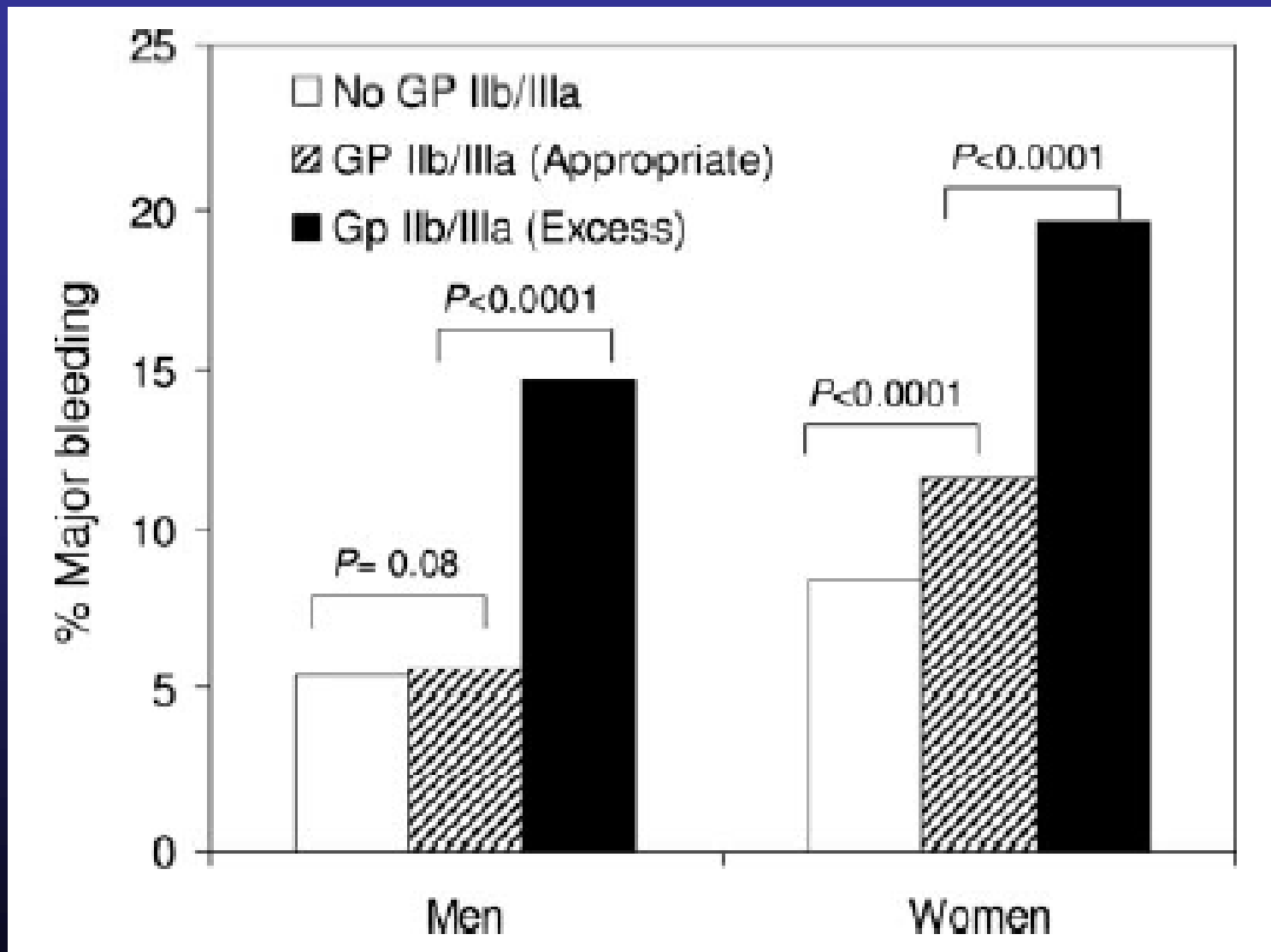


Alexander JAMA 2004; 294:3108

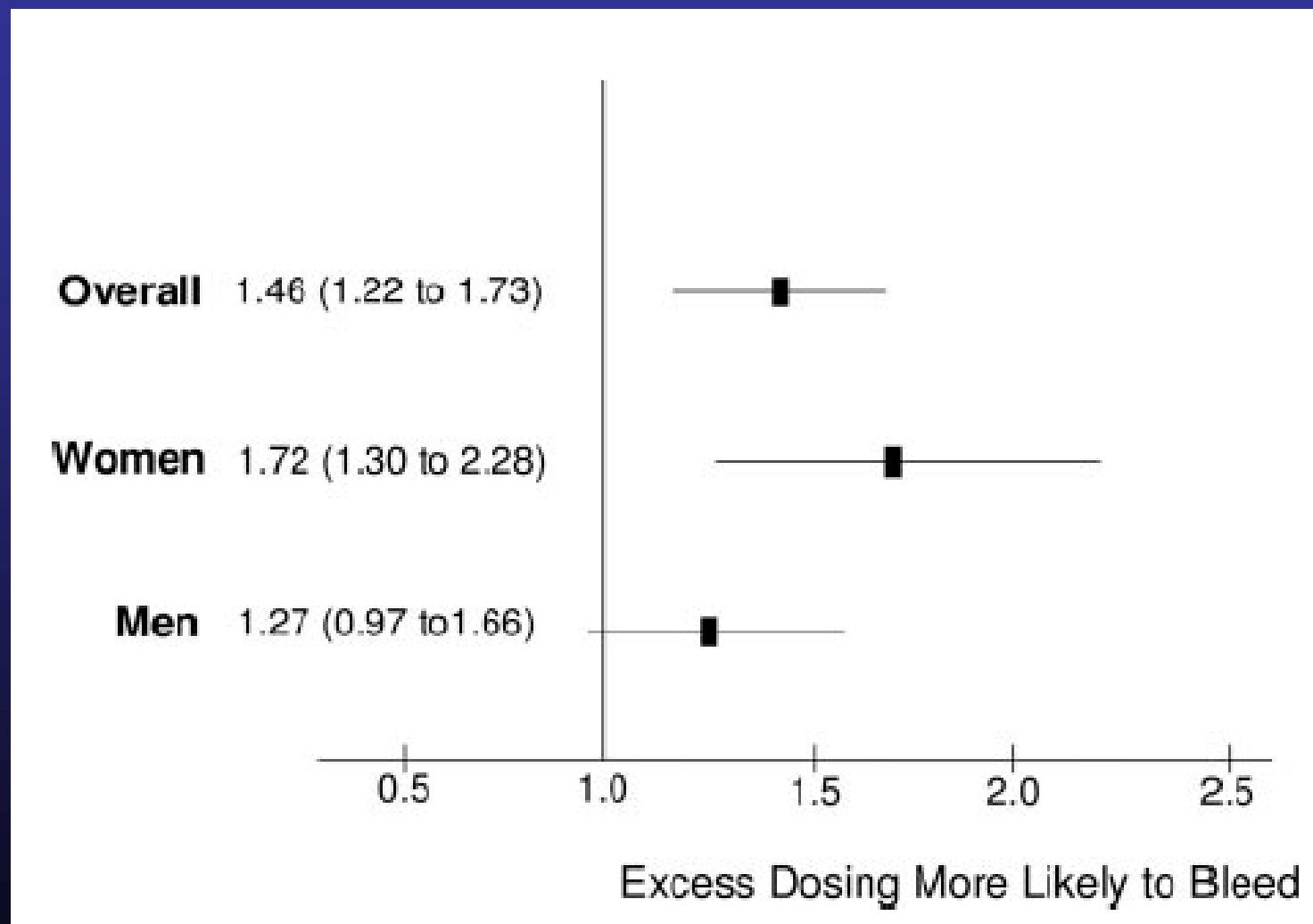
EXCESS DOSING OF GP IIb/IIIa INHIBITORS



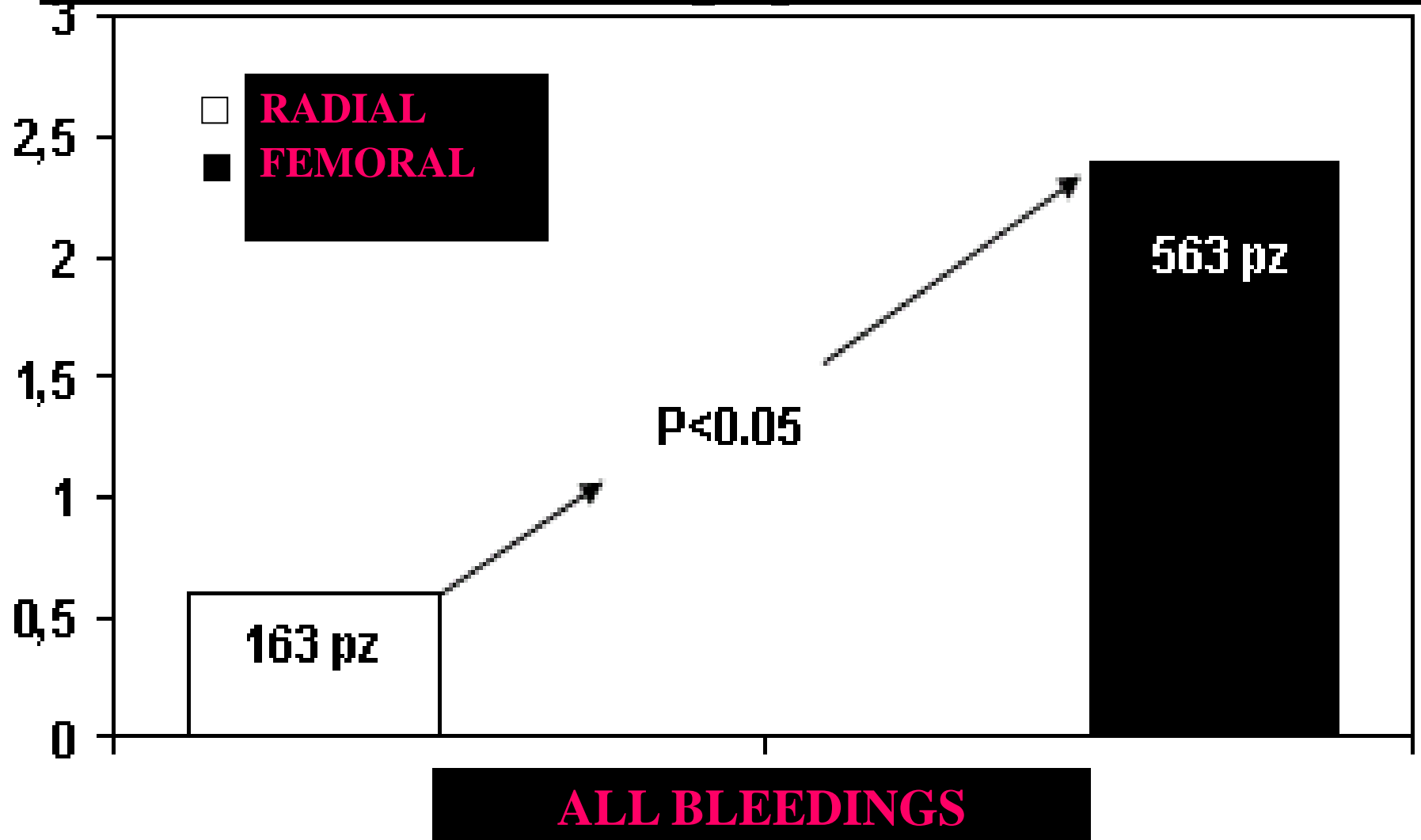
MAJOR BLEEDING BY SEX



RELATIONSHIP BETWEEN EXCESS DOSE OF GP IIb/IIIa INHIBITORS vs NO EXCESS DOSE AND MAJOR BLEEDING

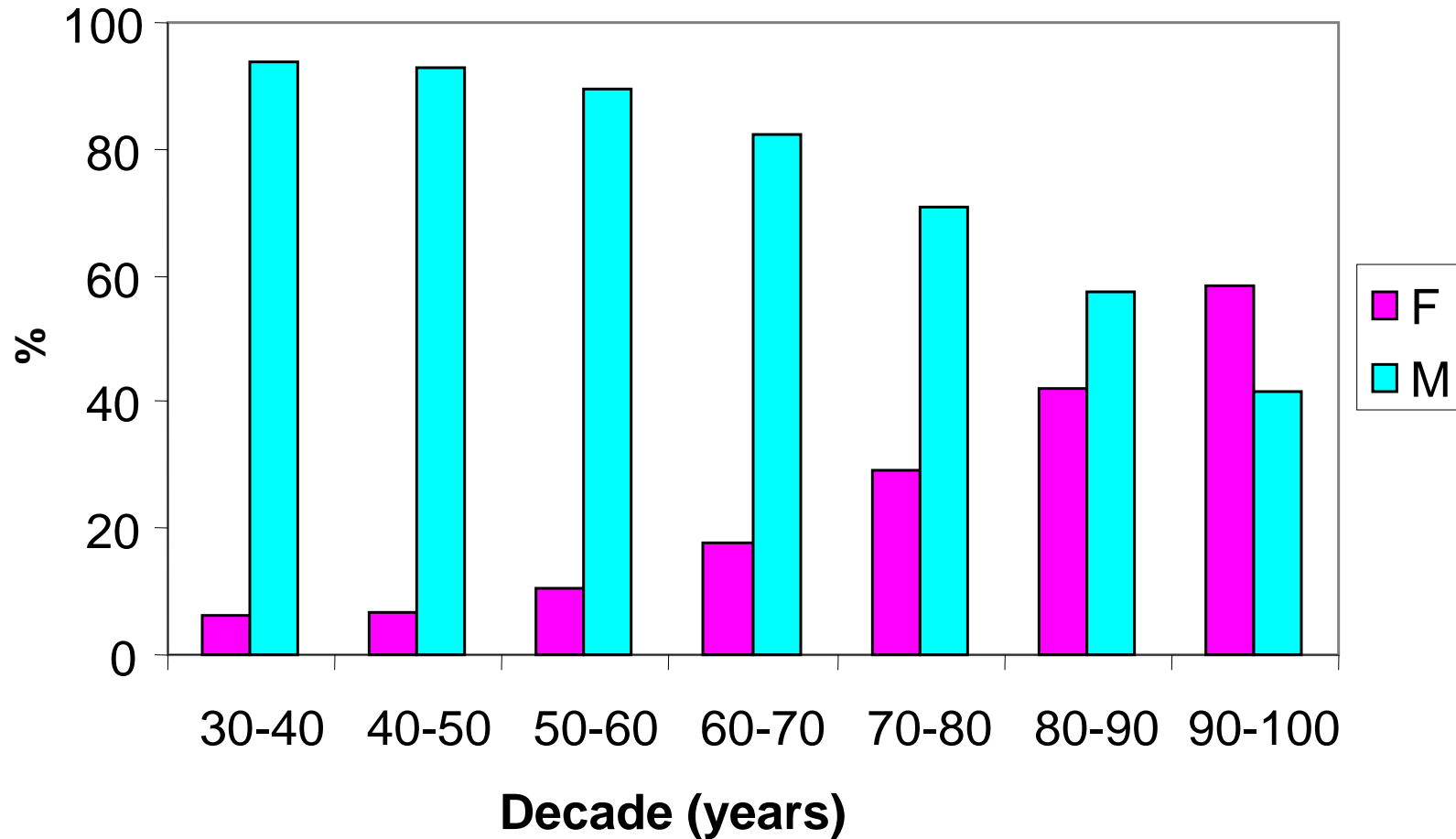


Radial access in pts with STEMI treated with primary PTCA



modified from Valsecchi et al, Ital Heart J 2003

Relative frequency of females and males undergoing PCI in Humanitas data base (1999-2006) (6376 Procedures)



Age- and sex-related utilisation of cardiac procedures and interventions: a multicentric study in Italy

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Edoardo Farinaro^d, Pasquale Gregorio^e, Nicola Nante^f, Pasquale Santè^g, Roberta Siliquini^h,
Gualtiero Ricciardi^{b,i,*} ARPIC Collaborative Group (Giuseppe La Torreⁱ,
Paolo Villari^a, Stefania Boccia^b, Luigi Sirianni^b, Saverio Stranges^d, Paola Simioli^e,
Lucia Garramone^f, Rosario Gregorio^g, Davide Minniti^h)

Abstract

Background: Cardiovascular diseases represent the leading cause of death in Italy and one of the most frequent cause of disability in the elderly. The aim of the study was to investigate the influence of age and sex of patient on the utilisation of cardiac procedure and interventions in Italy. *Methods:* Retrospective analysis of 2805 patients' medical case notes in cardiology, internal medicine and elderly clinics in six Italian Regions during the period 1996–1997, considering coronary catheterisation (CC), percutaneous transluminal coronary angioplasty (PCTA), coronary artery bypass grafting (CABG), thrombolysis (THR) and permanent pacemaker (PPM) implantation. *Results:* Older patients (more than 75 years old) were less likely to undergo CC (OR=0.062). Trends for age and sex did not achieve significance for CABG (OR=0.815 for older patient). Age is a strong predictor of receiving PTCA, with the oldest group of patients being discriminated (OR=0.093 for people older than 75 years), and the same trend was observed for THR (OR=0.264 for patients older than 75 years). For PPM, older patient has a higher likelihood of receiving this type of intervention (OR=3.45 for 65–74 years, and OR=7.77 for patients older than 75 years). As far as gender of patients is concerned, statistically significant differences for all cardiac procedures or interventions considered were not found. *Conclusions:* Clinical management of older patients with cardiac disease in Italy may be different from that of younger patients. One possible explanation would be that these patients are being discriminated against mainly because of their age.

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Advanced age and not female sex is the main factor for not referring patients to coronary catheterisation

Boccia A et al, Int J Cardiology 2005; 101: 179-184

MULTIVARIATE ANALYSIS for factors affecting restenosis

ICH-PCI-database (1999 - 2005)

	BMS		PES	
	M	F	M	F
	2811	704	642	168
VESSEL SIZE	+	+	+	+
LESION LENGHT	+	+	+	-
CTO	+	-	-	-
DIABETES	+	+	-	-

Sex-Specific Outcomes Following Revascularization with Zotarolimus-Eluting Stents: Comparison of Angiographic and Late-Term Clinical Results

-6 ENDEAVOR trials
-2132 pts (608 female)

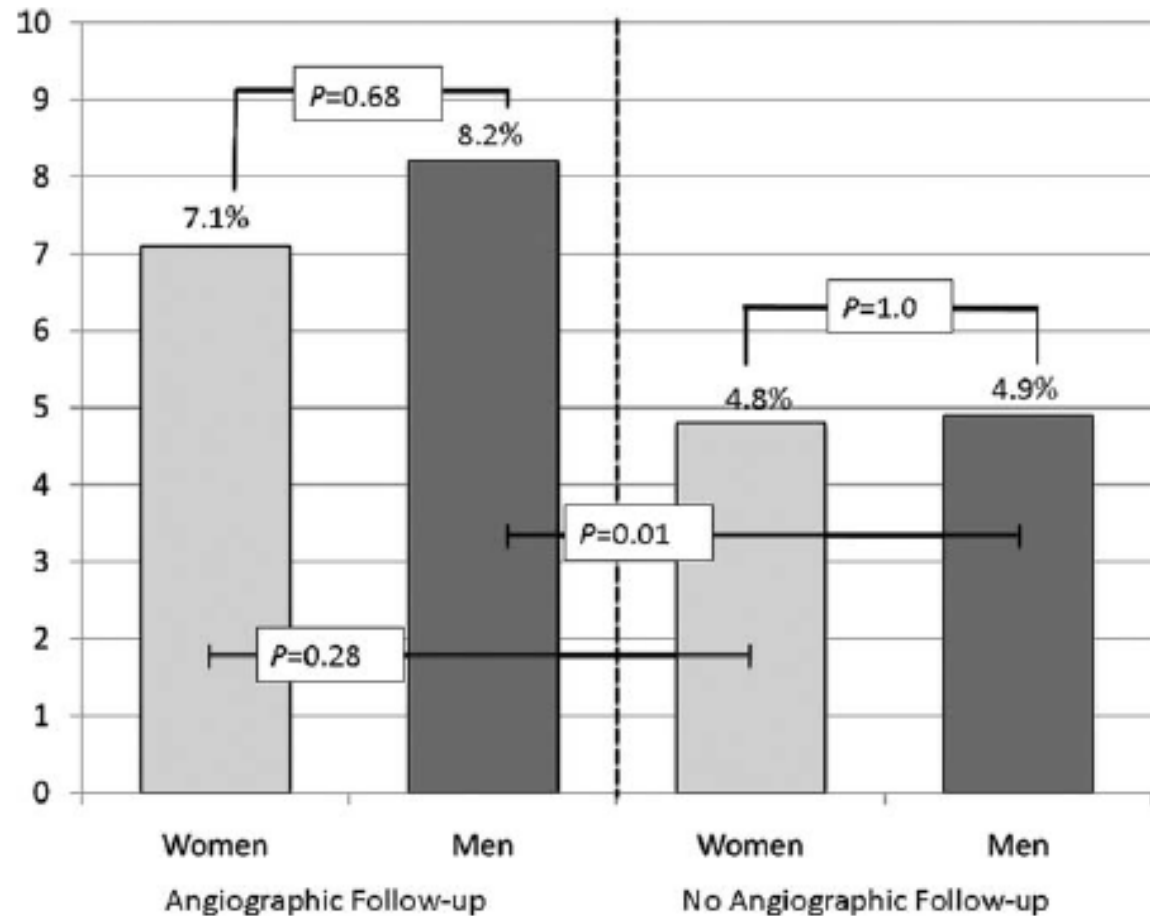
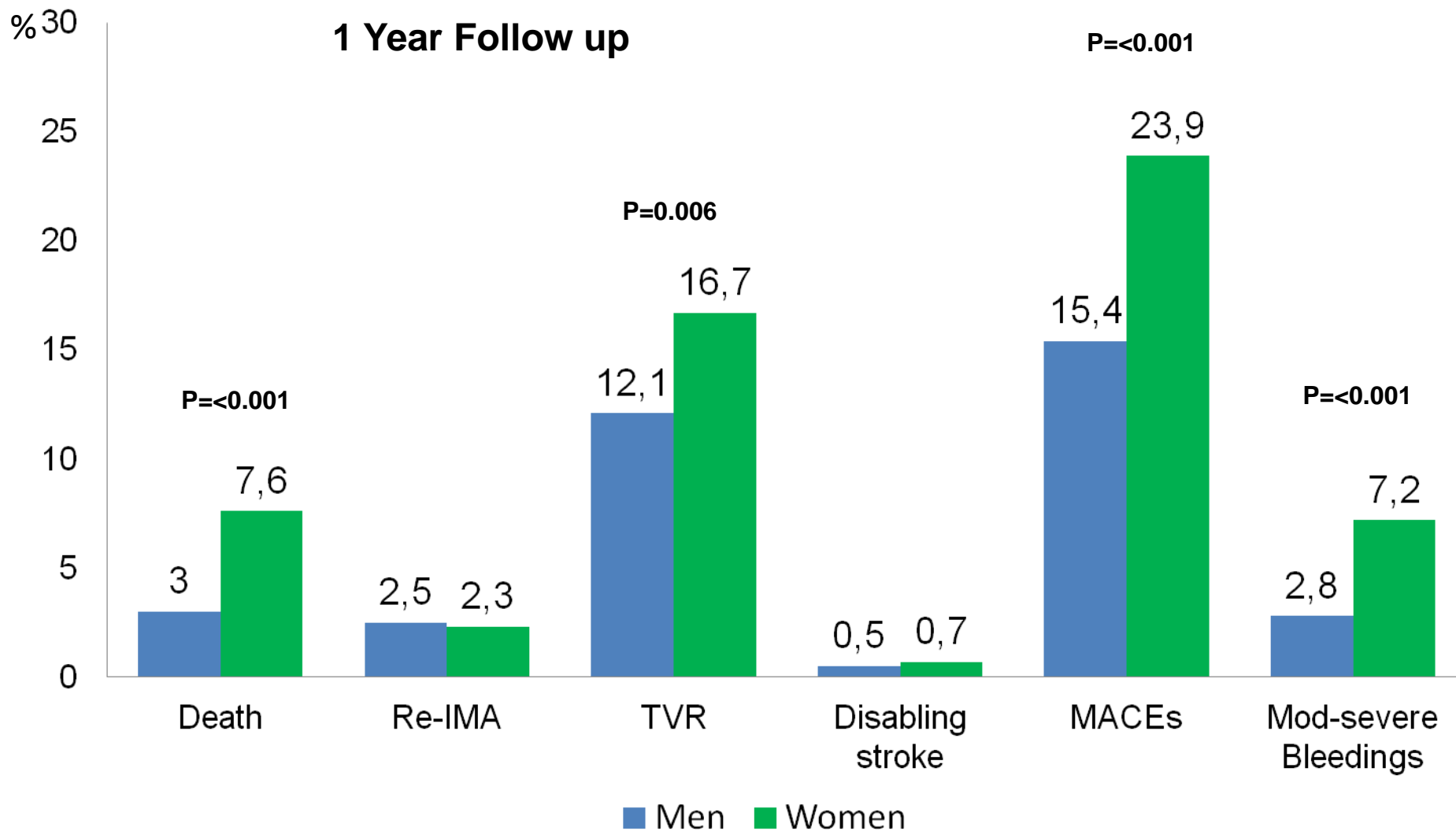


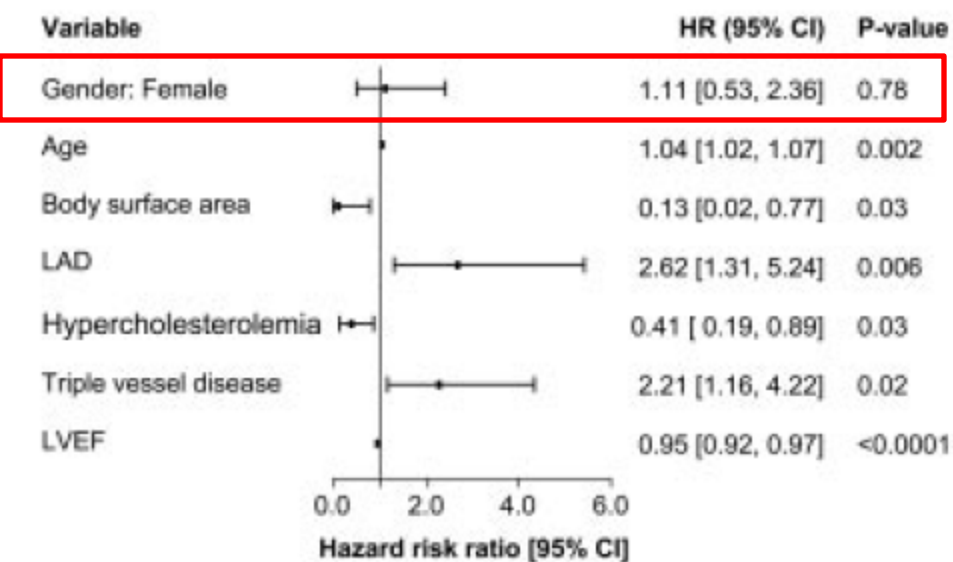
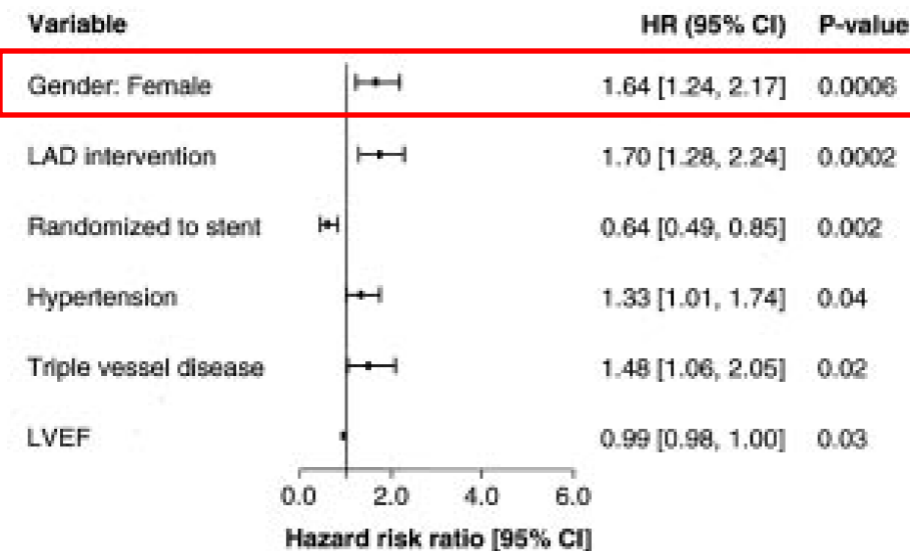
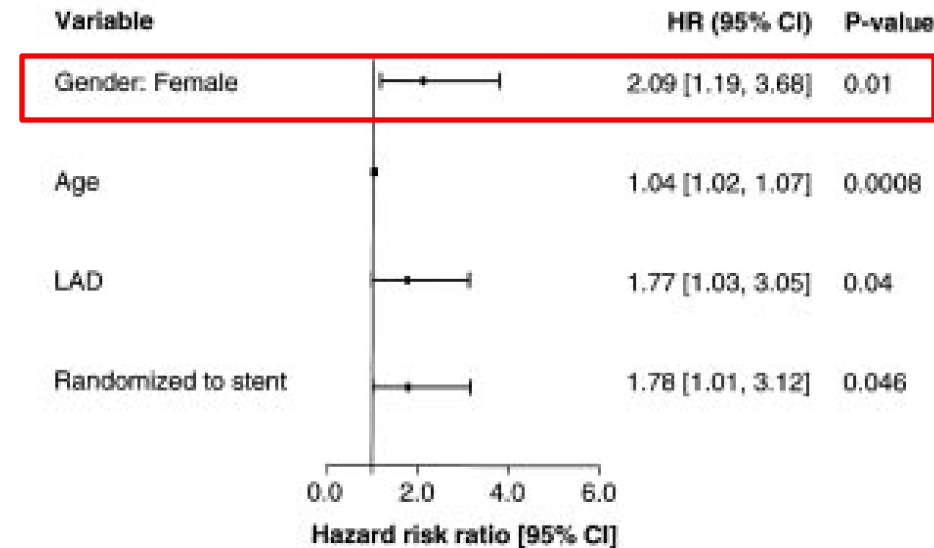
Fig. 1. Rates of clinically driven target lesion revascularization among men and women relative to angiographic follow-up assignment.

CADILLAC STUDY

N women = 562

N men = 1520



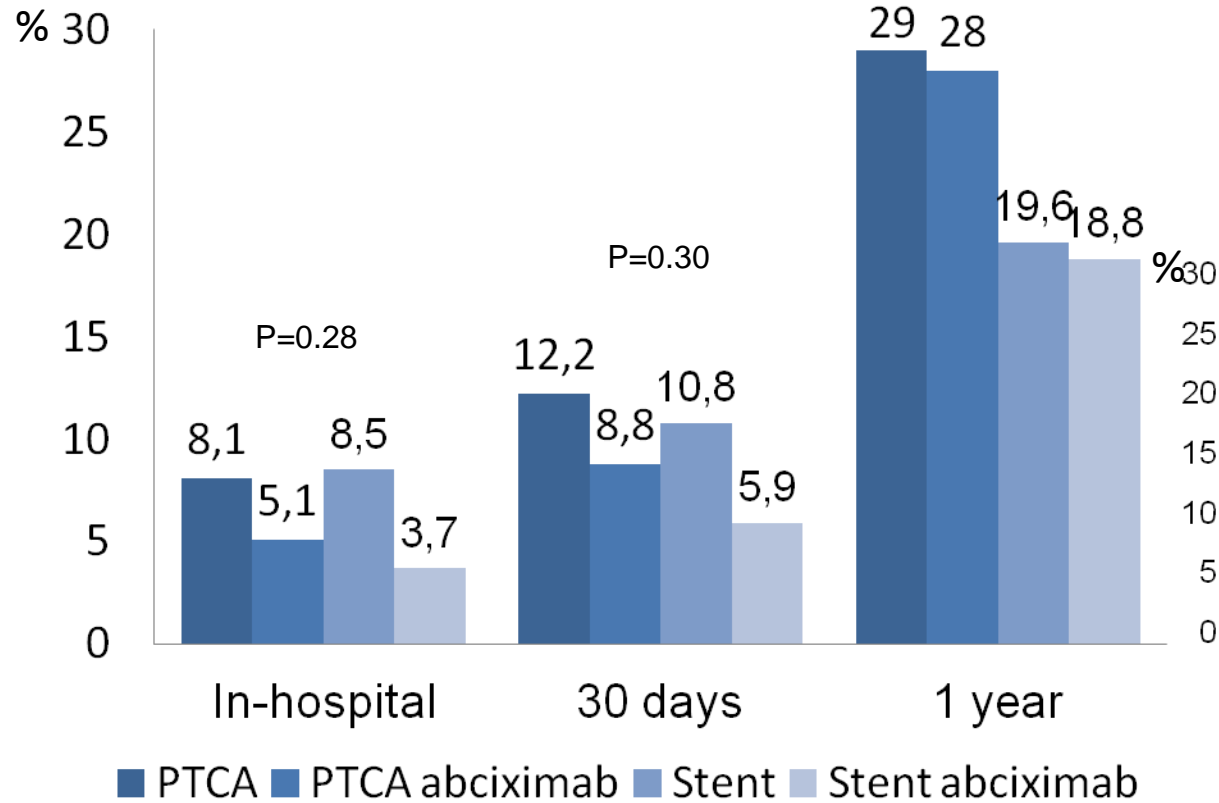
A**Predictors of 1-year Death****C****Predictors of 1-year MACE****E****Predictors of 1-year Moderate/Severe Bleeding**

*Adjusted for BSA

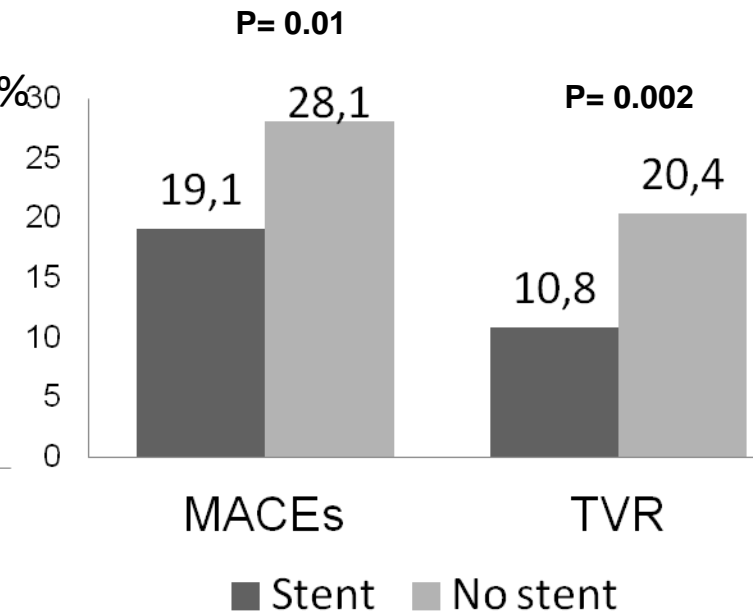
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MACES

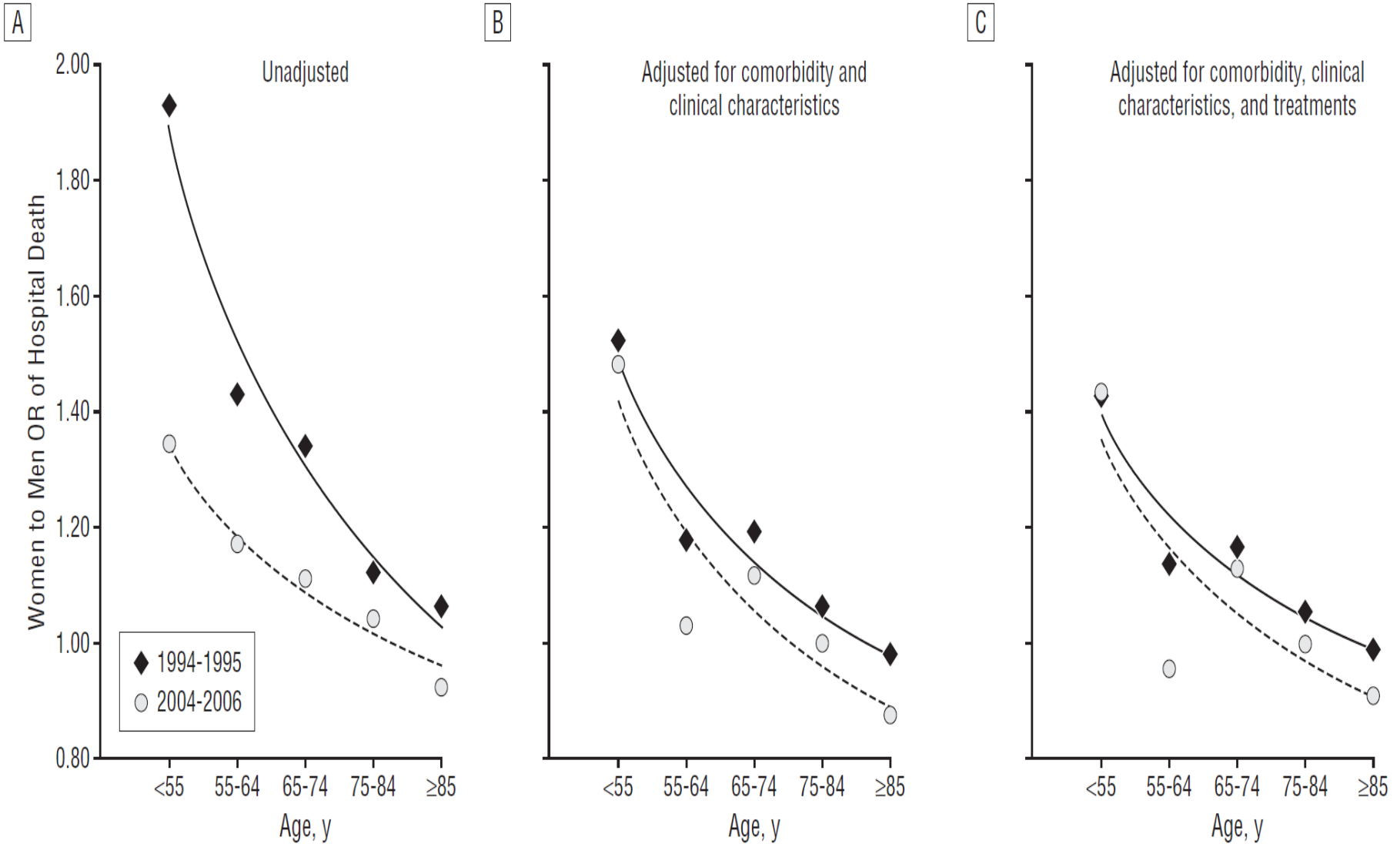


1 Year follow up



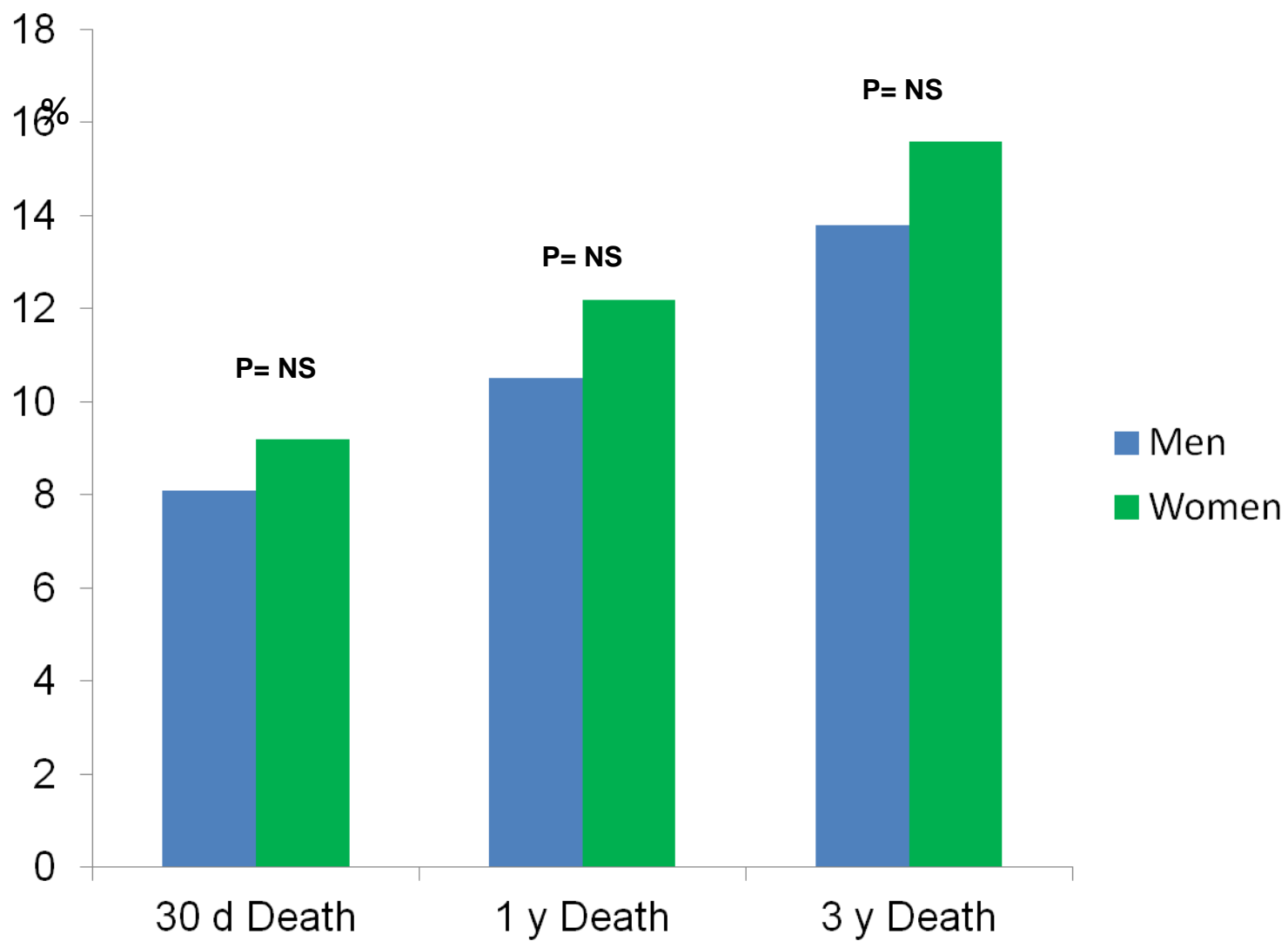
* Multilink BMS

Sex age interaction



N women = 910
N men = 2367

Multicentre registry (1996-2007)



Multicentre registry (1996-2007)

