Lecture Fees (Kastrati) from:

Bristol-Myers, Cordis, Glaxo, Lilly, Medtronic, Sanofi-Aventis

Meta-Analyses of Randomized Trials of Sirolimus-Eluting Stents vs. Paclitaxel-Eluting Stents or Bare Metal Stents: An Independent, Individual Patient Data Based Study

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Inclusion Criteria

- Randomized trial, published or presented at meetings assessing sirolimus-eluting stent (SES) vs. paclitaxel-eluting stent (PES) or bare metal stent (BMS)
- ≥1 year clinical follow-up

Objective of the Study

To analyze long-term outcome individual patient data of 2 kinds of randomized trials:

Sirolimus-Eluting Stents vs. Paclitaxel-Eluting Stents

Sirolimus-Eluting Stents vs. Bare Metal Stents

Study End Points

Primary end point:

- All cause mortality

Secondary end points:

- Composite of death or myocardial infarction (MI)
- Composite of death, MI or target lesion revascularization (MACE)

during the entire available follow-up interval

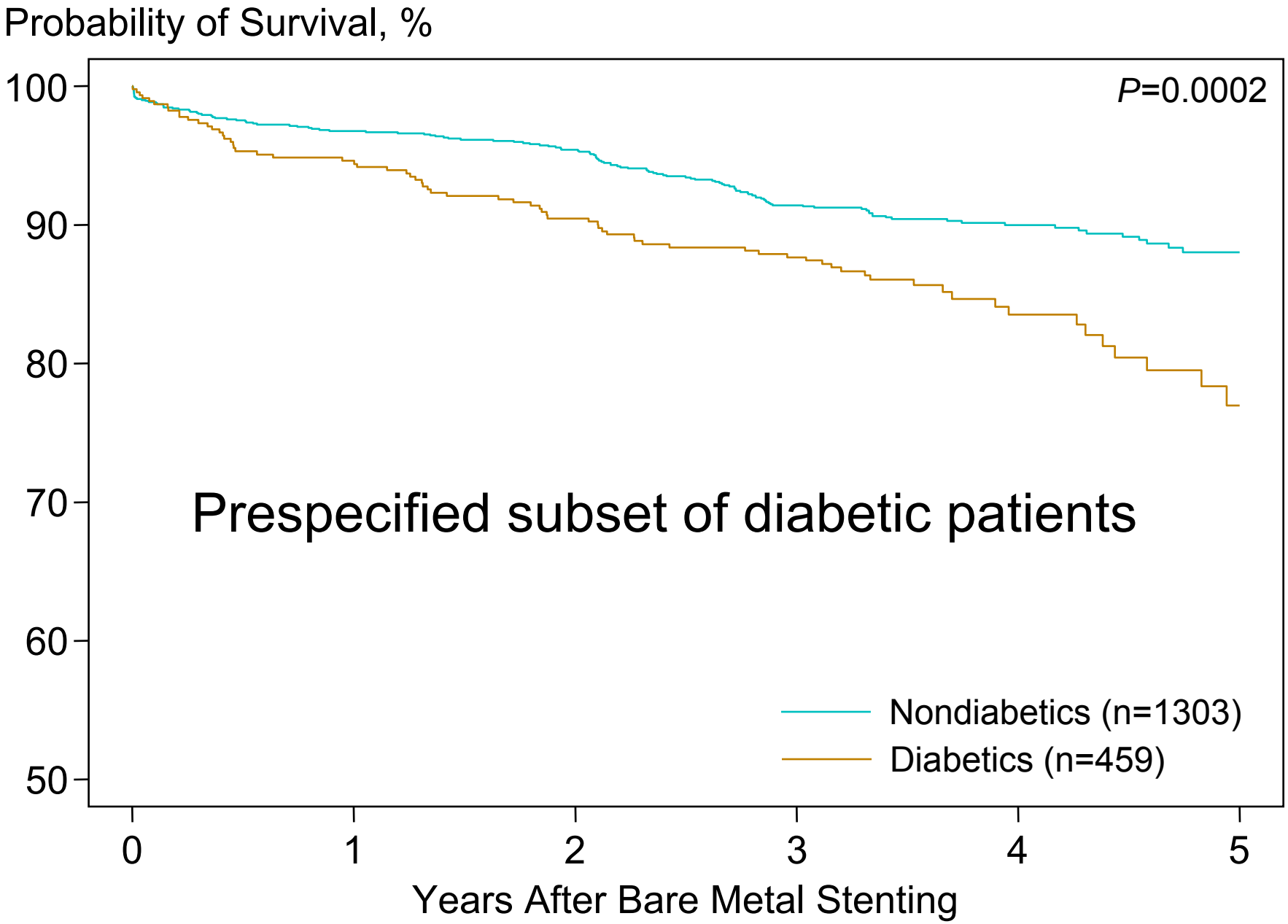
Statistical Methods

Mantel-Cox method for calculating hazard ratios for individual trials.

Fixed and random effect models for calculating overall harzard ratios and check for hetereogeneity.

Kaplan-Meier survival curves for all trials combined.

Diabetes: An Adverse Prognostic Factor in the BMS Era

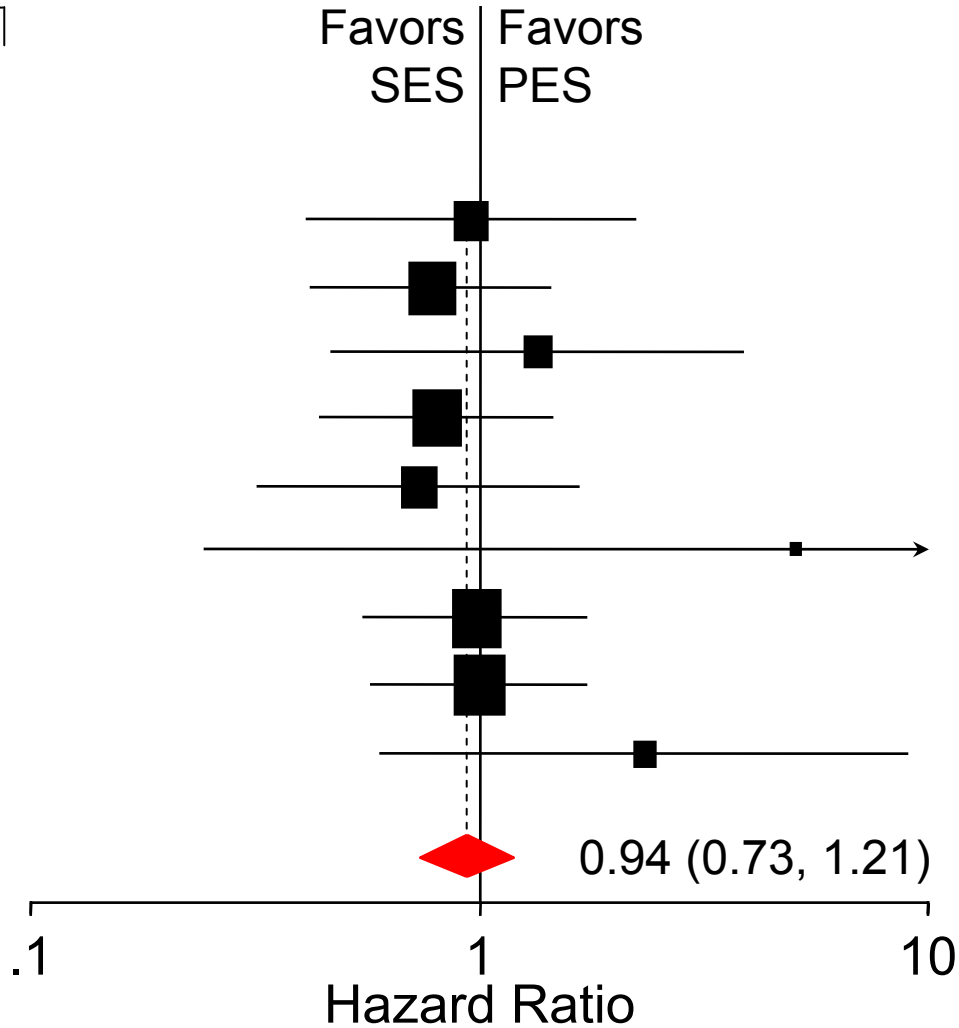


Main Characteristics of the SES vs. PES Trials

Trial	Total No. of patient	Total No. of diabetic patients	Mean Clinical FU in months	Special notes
BASKET	545	93	18.2	
CORPAL	652	202	30.5	
ISAR-DESIRE	200	58	33.9	Bare metal in-stent restenosis
ISAR-DIABETES	250	250	32.1	Diabetic patients
ISAR-SMART 3	360	0	33.9	Small vessels, no diabetics
LONGDES II	500	166	13.0	
REALITY	1353	379	24.1	
SIRTAX	1012	201	24.2	
TAXI	202	69	36.9	
Overall	**5074**	**1418**	**25.1**	

Hazard Ratios for Death
-All Patients-

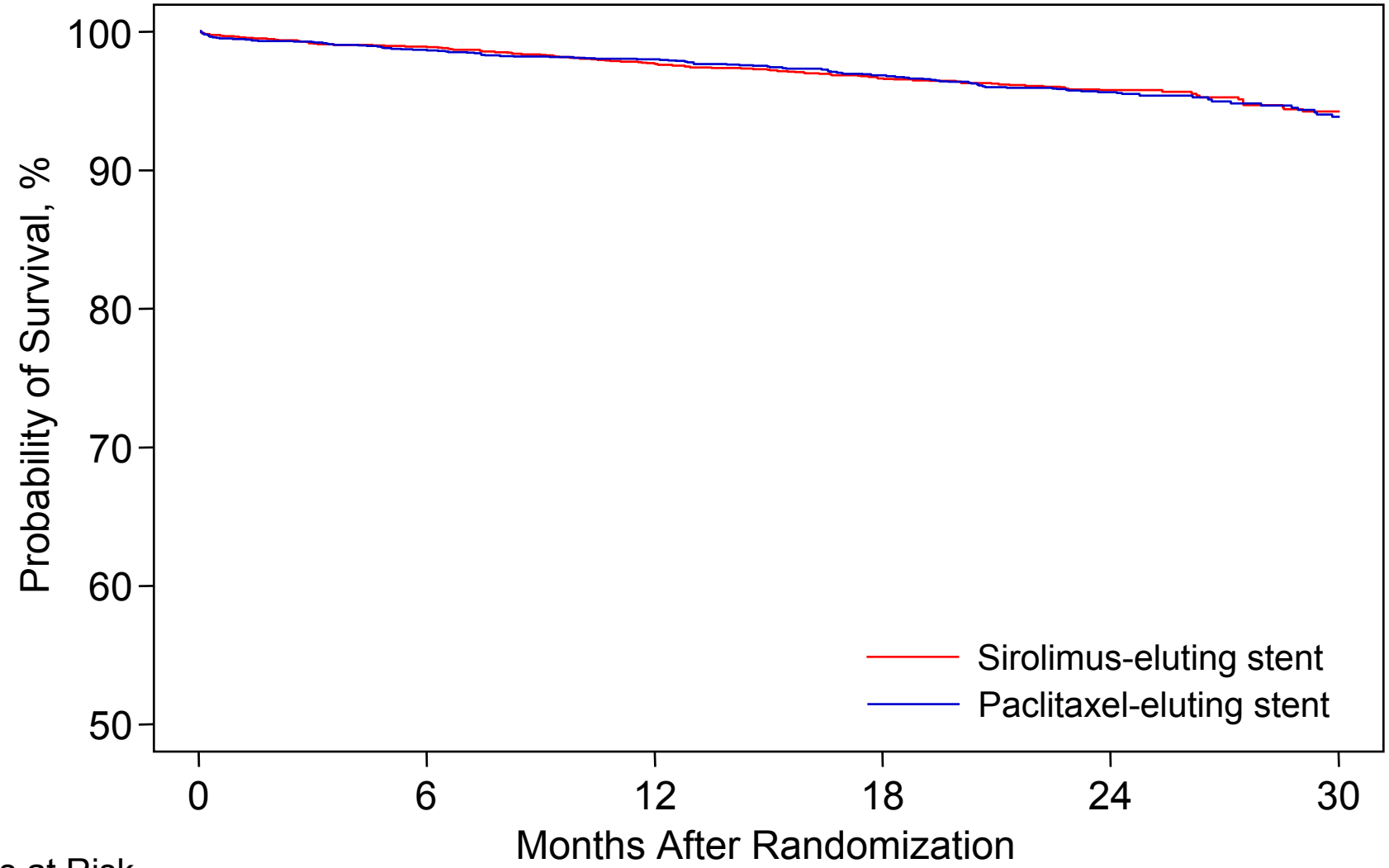
Trial	No. of events / Total No. of patients: SES group	PES group
BASKET	10/264	11/281
CORPAL	18/331	22/321
ISAR-DESIRE	8/100	6/100
ISAR-DIABETES	21/125	22/125
ISAR-SMART 3	10/180	13/180
LONG-DES II	2/250	0/250
REALITY	23/684	23/669
SIRTAX	25/503	25/509
TAXI	7/102	3/100
Overall	124/2539	125/2535



Test for Heterogeneity: *Cochran Q*=4.4 (*d.f.*=8) *P*=.82

Test for Inconsistency: I^2 =0.0%

Kaplan-Meier Curves of Survival
-All Patients-

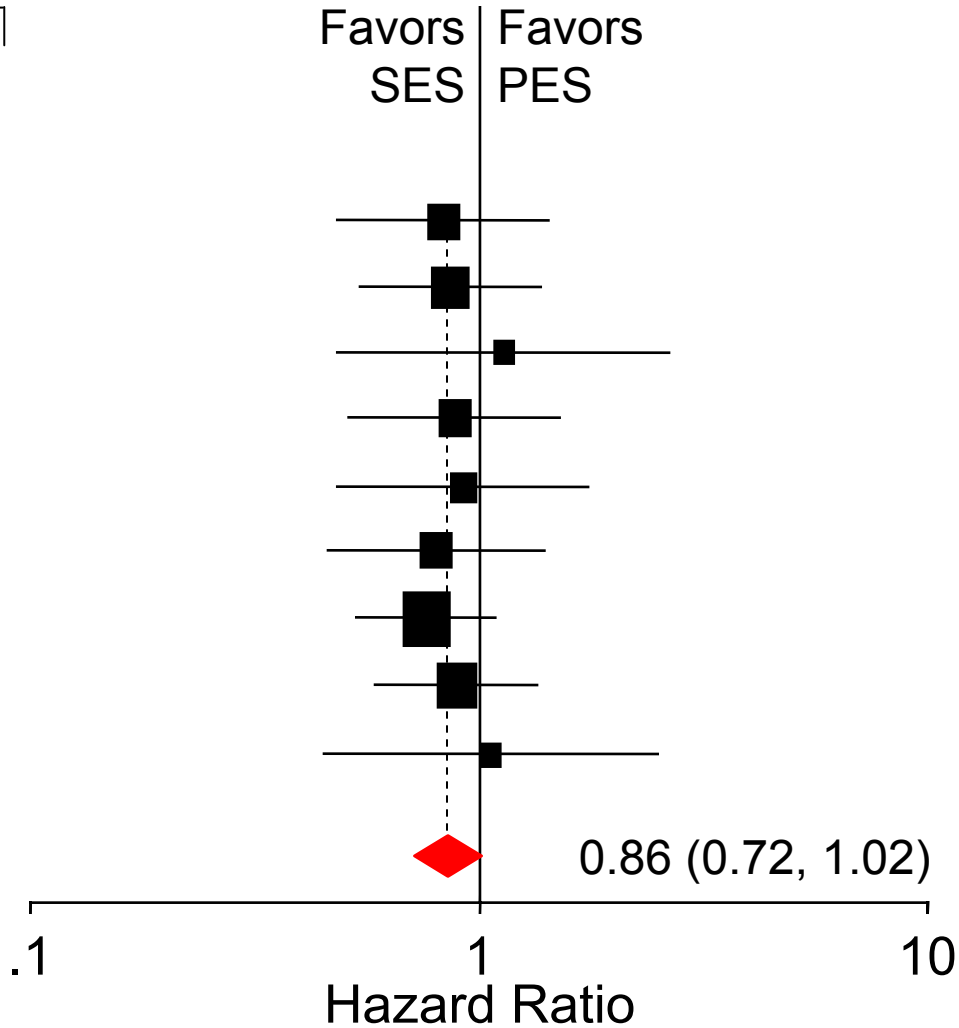


Patients at Risk

SES	2539	2498	2336	2170	1666	608
PES	2535	2475	2338	2152	1631	552

Hazard Ratios for Death or MI
-All Patients-

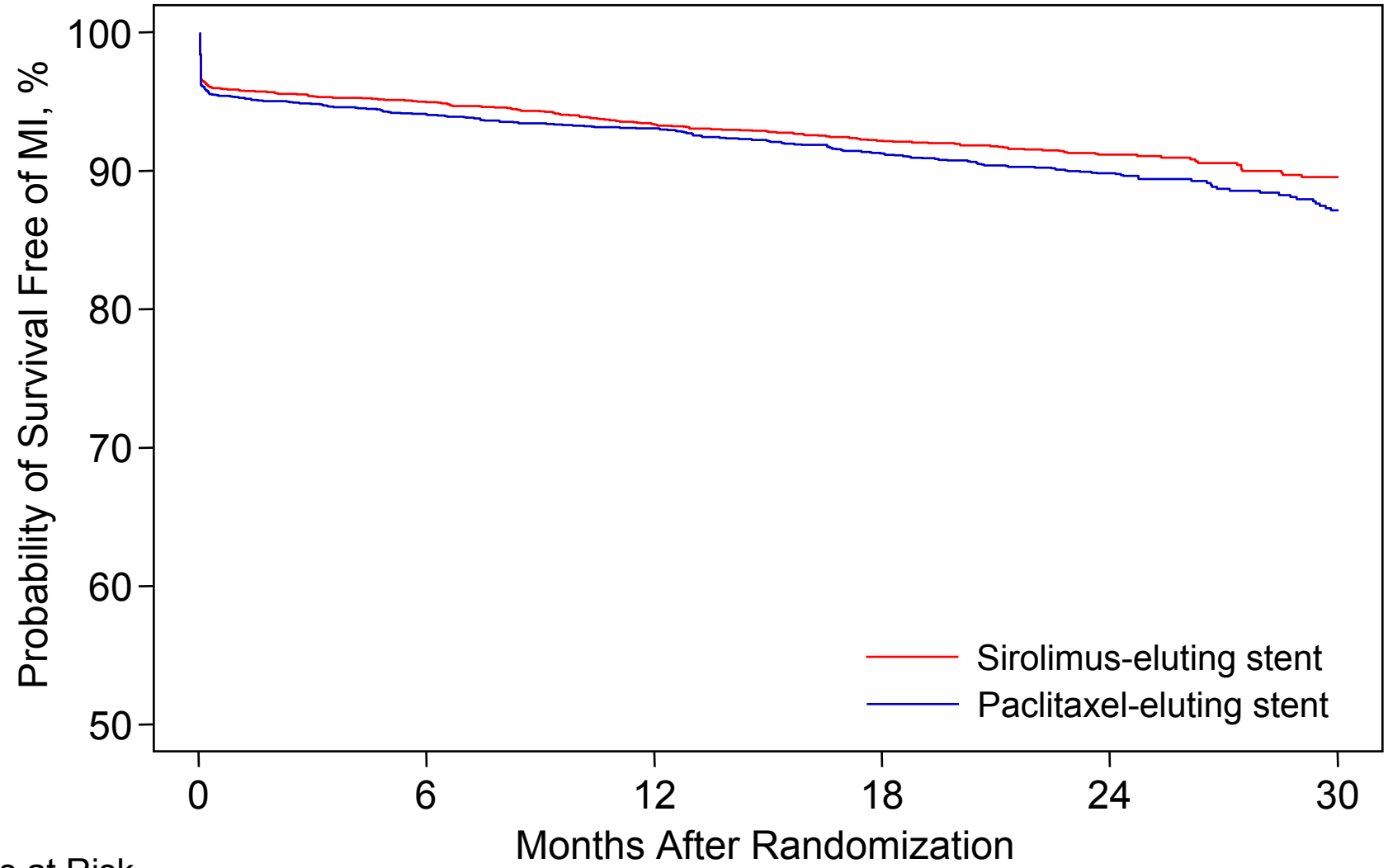
Trial	No. of events / Total No. of patients: SES group	PES group
BASKET	23/264	29/281
CORPAL	33/331	37/321
ISAR-DESIRE	11/100	10/100
ISAR-DIABETES	26/125	26/125
ISAR-SMART 3	19/180	19/180
LONG-DES II	22/250	27/250
REALITY	54/684	69/669
SIRTAX	41/503	46/509
TAXI	11/102	10/100
Overall	240/2539	273/2535



Test for Heterogeneity: *Cochran Q*=1.2 (*d.f.*=8) *P*=.99

Test for Inconsistency: I^2 =0.0%

Kaplan-Meier Curves of Survival Free of MI
-All Patients-

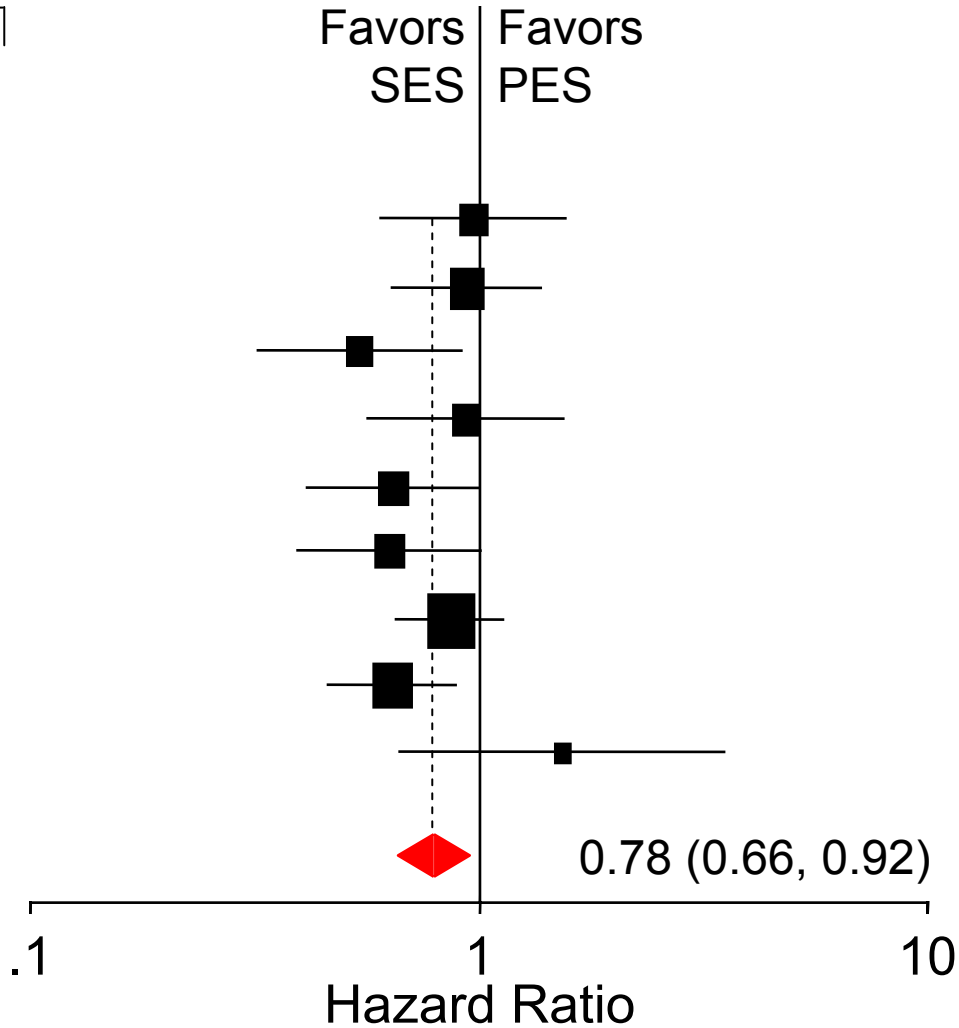


Patients at Risk

SES	2539	2401	2236	2080	1596	581
PES	2535	2361	2230	2043	1545	529

Hazard Ratios for MACE
-All Patients-

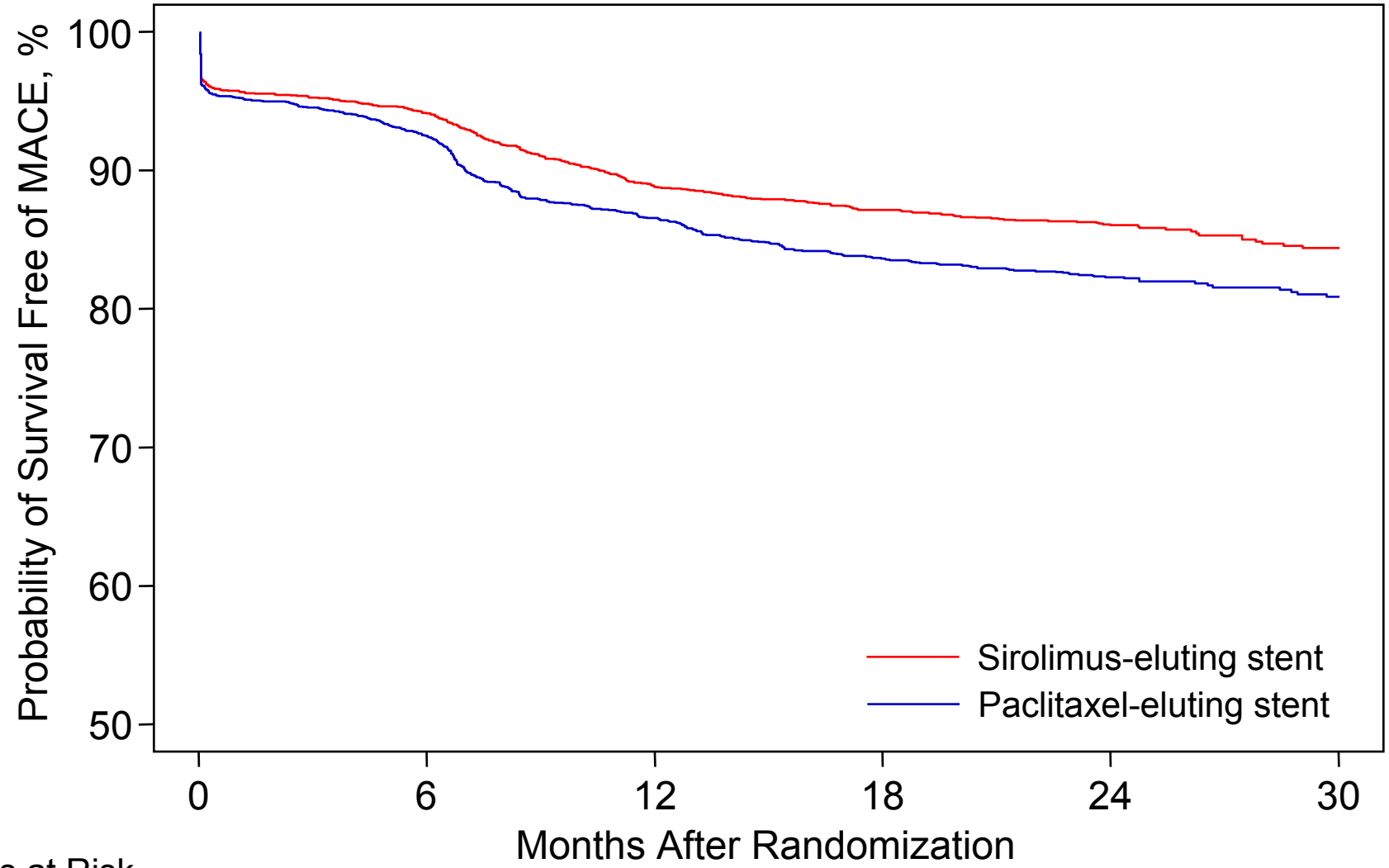
Trial	No. of events / Total No. of patients: SES group	PES group
BASKET	32/264	35/281
CORPAL	51/331	52/321
ISAR-DESIRE	23/100	37/100
ISAR-DIABETES	30/125	30/125
ISAR-SMART 3	34/180	47/180
LONG-DES II	27/250	42/250
REALITY	93/684	104/669
SIRTAX	57/503	87/509
TAXI	14/102	9/100
Overall	361/2539	443/2535



Test for Heterogeneity: *Cochran Q*=9.9 (*d.f.*=8) *P*=.27

Test for Inconsistency: I^2 =19.6%

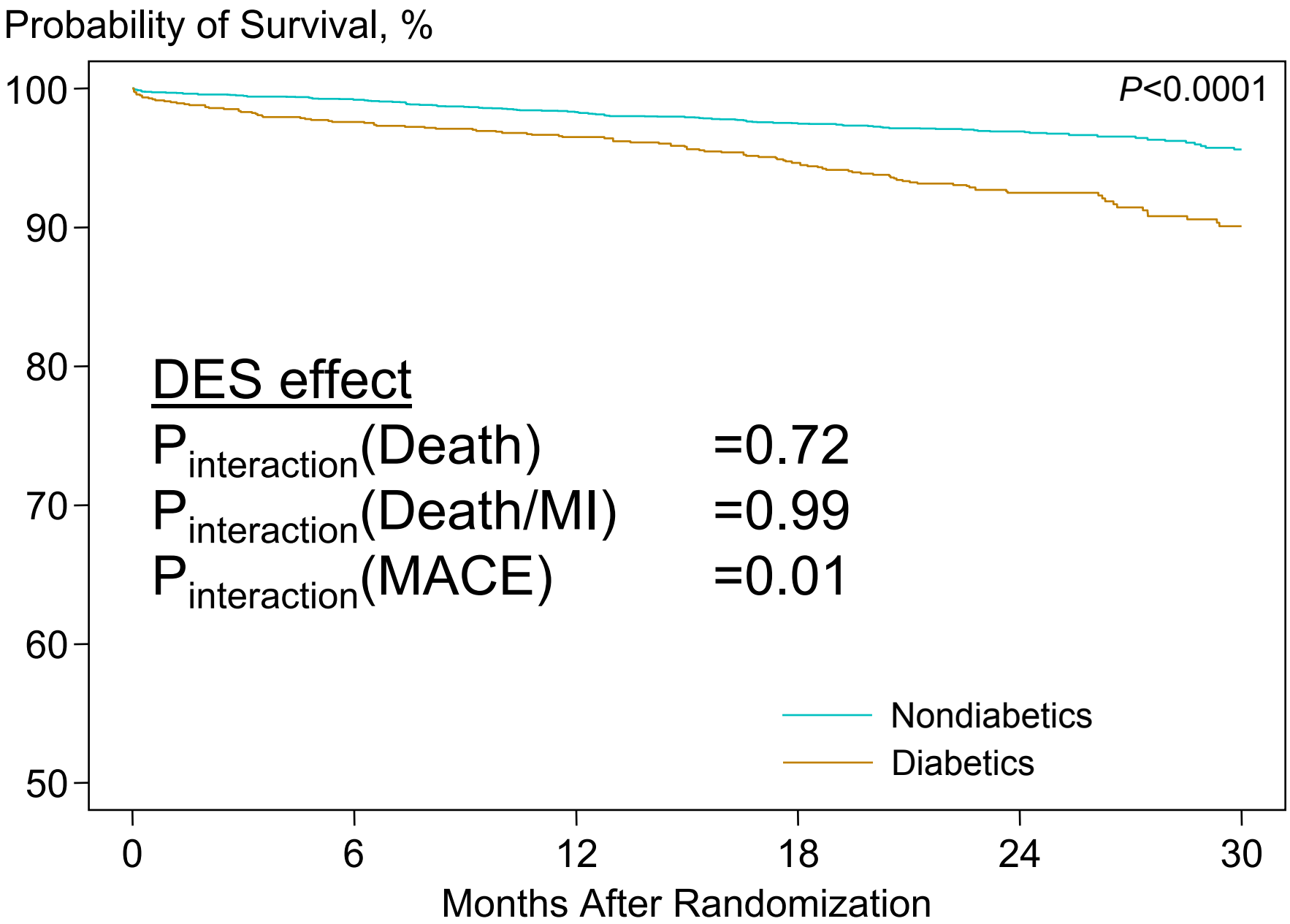
Kaplan-Meier Curves of Survival Free of MACE
-All Patients-



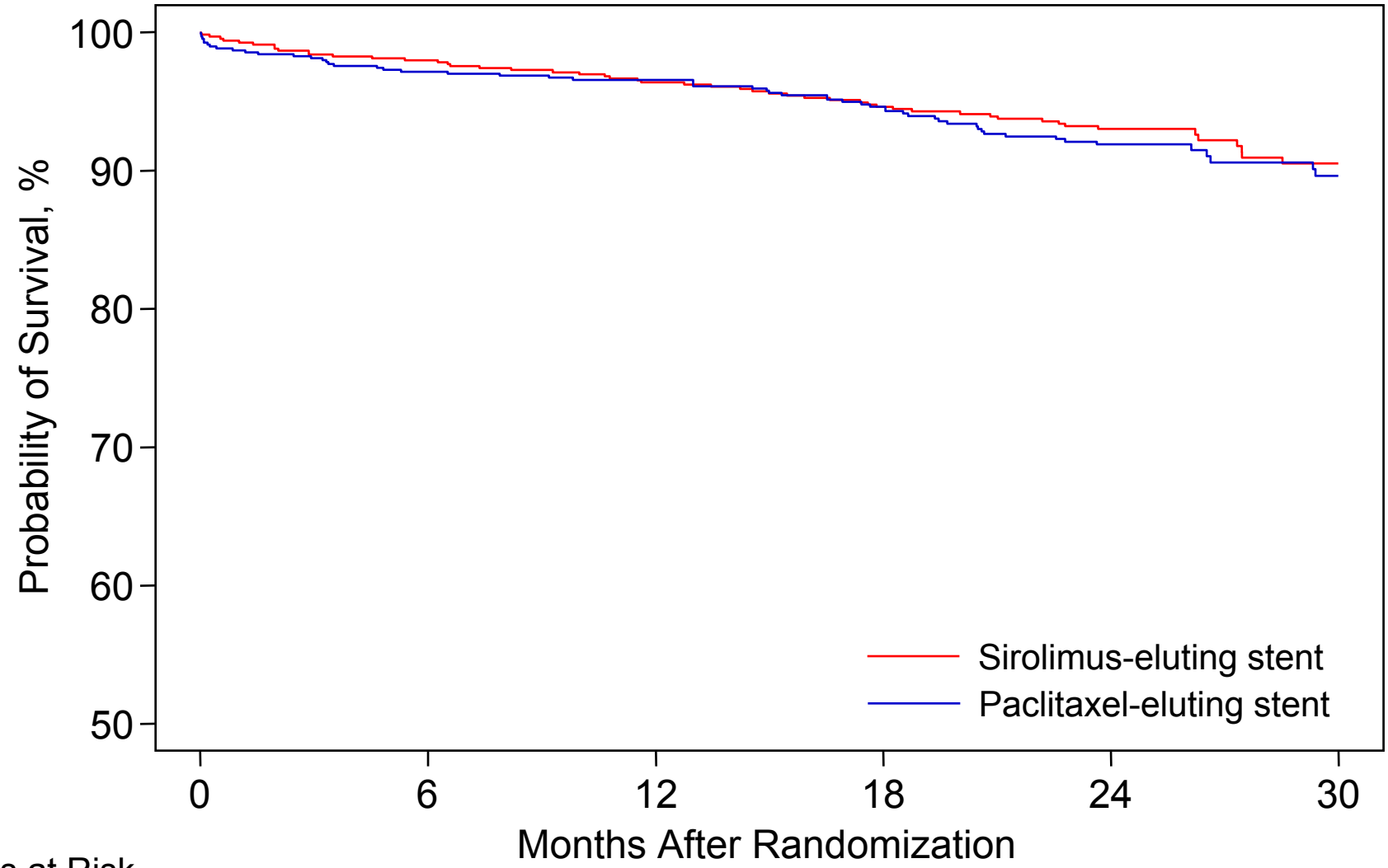
Patients at Risk

SES	2539	2374	2114	1941	1468	527
PES	2535	2313	2061	1855	1371	467

Diabetes: An Adverse Prognostic Factor in the in the SES vs. PES Trials



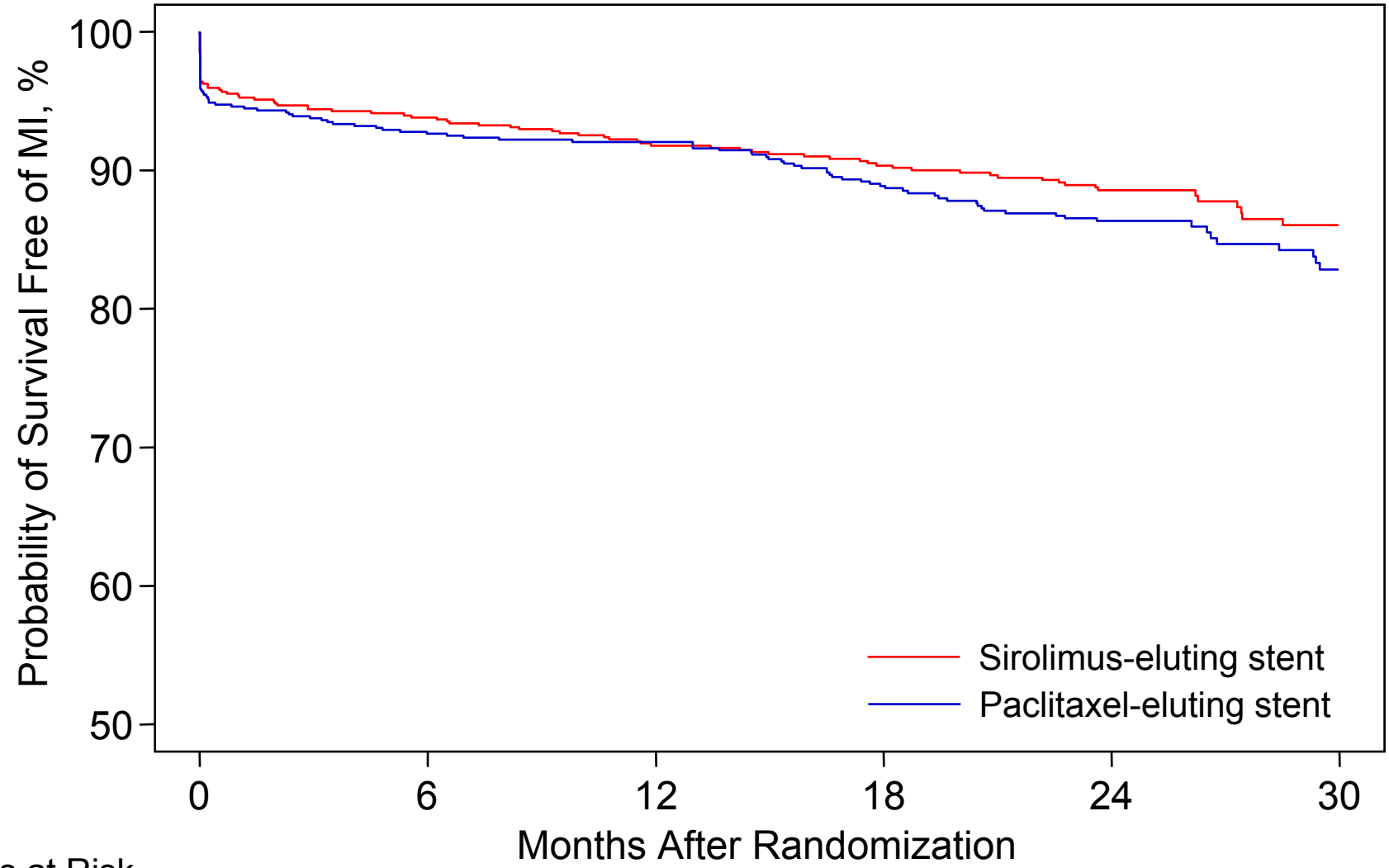
Kaplan-Meier Curves of Survival
-Diabetic Patients-



Patients at Risk

SES	704	687	641	577	475	207
PES	714	686	634	572	439	186

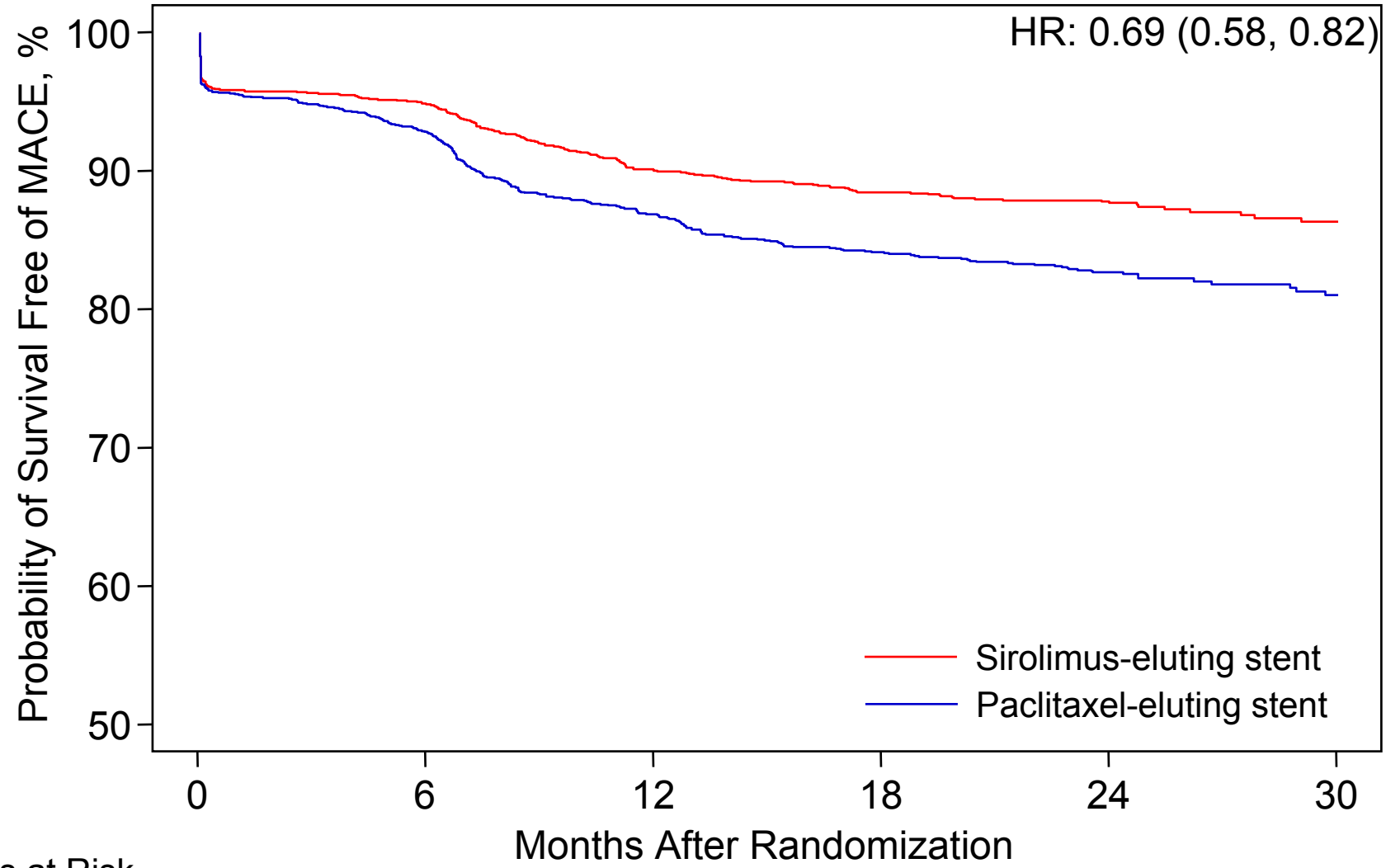
Kaplan-Meier Curves of Survival Free of MI
-Diabetic Patients-



Patients at Risk

SES	704	658	611	553	455	195
PES	714	654	610	544	421	179

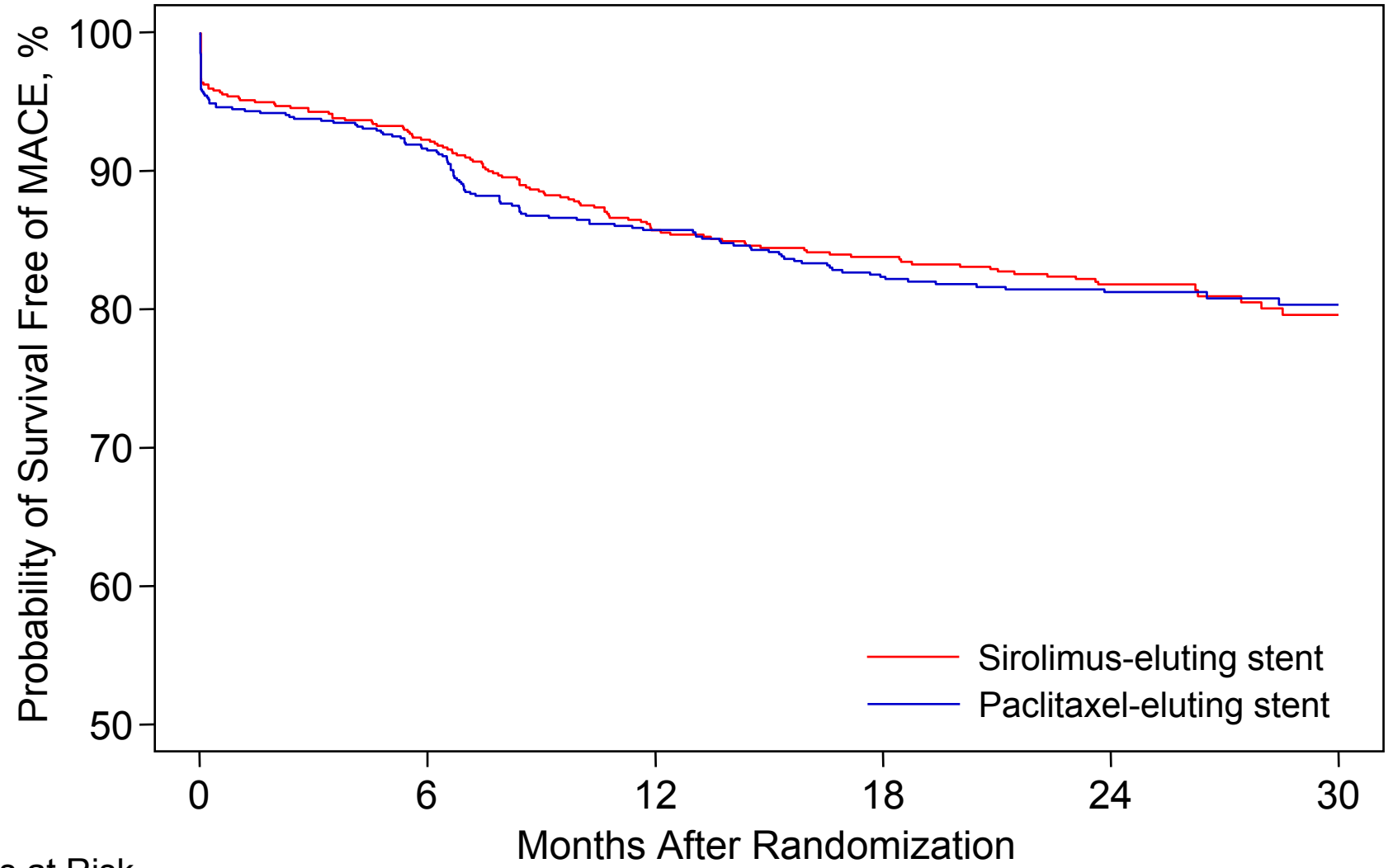
Kaplan-Meier Curves of Survival Free of MACE
-Nondiabetic Patients-



Patients at Risk

SES	1835	1728	1549	1439	1058	353
PES	1821	1670	1497	1359	992	296

Kaplan-Meier Curves of Survival Free of MACE
-Diabetic Patients-



Patients at Risk

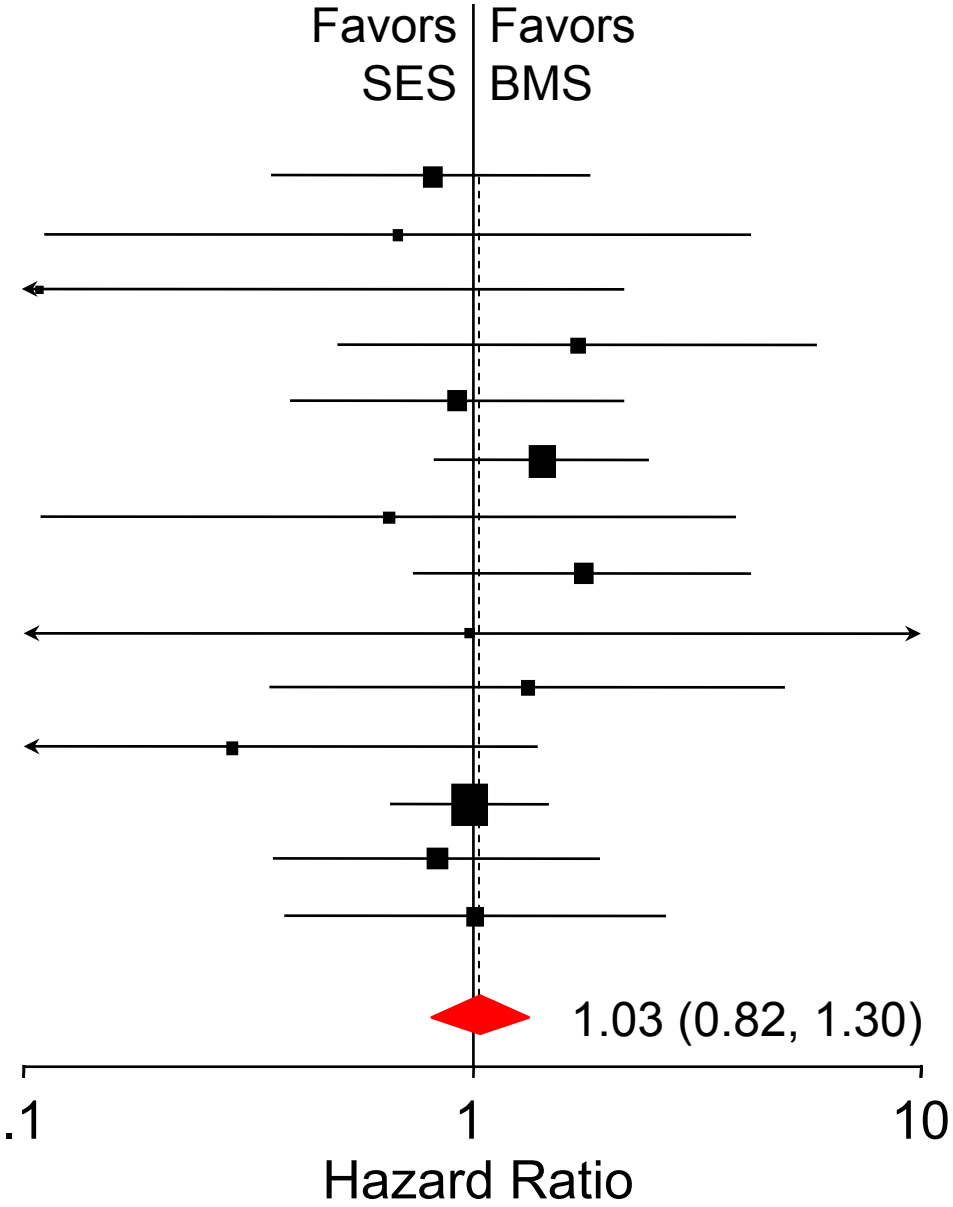
SES	704	646	565	502	410	174
PES	714	643	564	496	379	171

Main Characteristics of the SES vs. BMS Trials

Trial	Total No. of patients	Total No. of diabetic patients	Mean Clinical FU in months	Special notes
BASKET, 2005	545	101	18.3	
C-SIRIUS, 2004	100	24	48.5	
DECODE, 2005	83	83	12.7	Diabetic patients
DIABETES, 2005	160	160	25.3	Diabetic patients
E-SIRIUS, 2003	352	81	49.4	
Pache et al., 2005	500	154	46.1	
PRISON II, 2006	200	27	24.6	Totally occluded arteries
RAVEL, 2002	238	44	58.1	
SCANDSTENT, 2006	322	58	12.2	
SCORPIUS, 2004	193	193	12.7	Diabetic patients
SESAMI, 2006	320	65	12.3	Acute myocardial infarction
SIRIUS, 2003	1058	279	58.9	
STRATEGY, 2005	175	26	24.2	Acute myocardial infarction
TYPHOON, 2006	712	116	12.1	Acute myocardial infarction
Overall	4958	1411	32.7	

Hazard Ratios for Death
-All Patients-

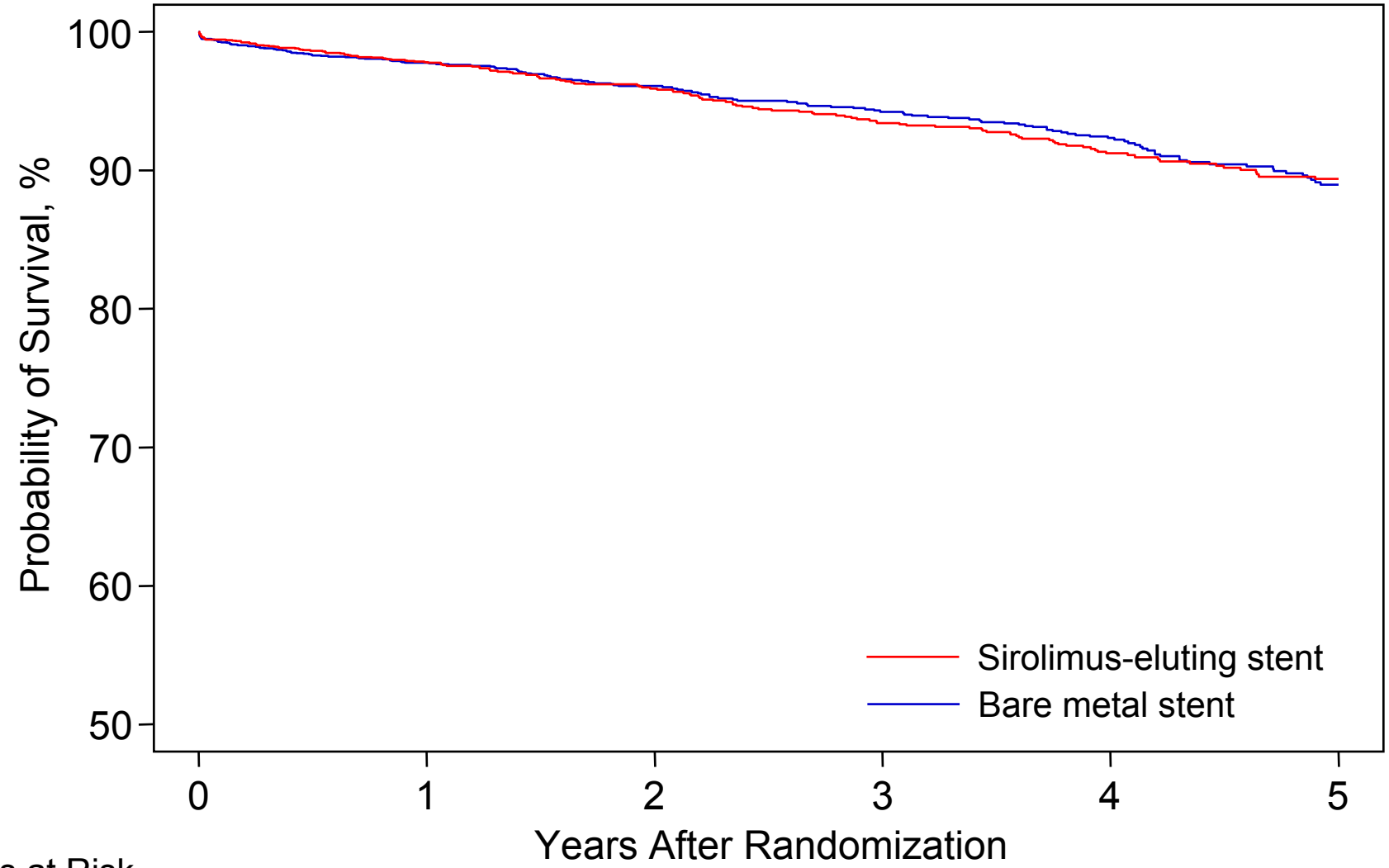
Trial	No. of events / Total No. of patients: SES group	BMS group
BASKET	10/264	13/281
CSIRIUS	2/50	3/50
DECODE	0/54	2/29
DIABETES	7/80	5/80
ESIRIUS	10/175	11/177
PACHE	29/250	24/250
PRISON II	2/100	3/100
RAVEL	14/120	8/118
SCANDSTENT	1/163	1/159
SCORPIUS	5/95	4/98
SESAMI	3/160	7/160
SIRIUS	45/533	46/525
STRATEGY	10/87	12/88
TYPHOON	8/355	8/357
Overall	146/2486	147/2472



Test for Heterogeneity: *Cochran Q*=9.3 (*d.f.*=13) *P*=.75

Test for Inconsistency: I^2 =0.0%

Kaplan-Meier Curves of Survival
-All Patients-

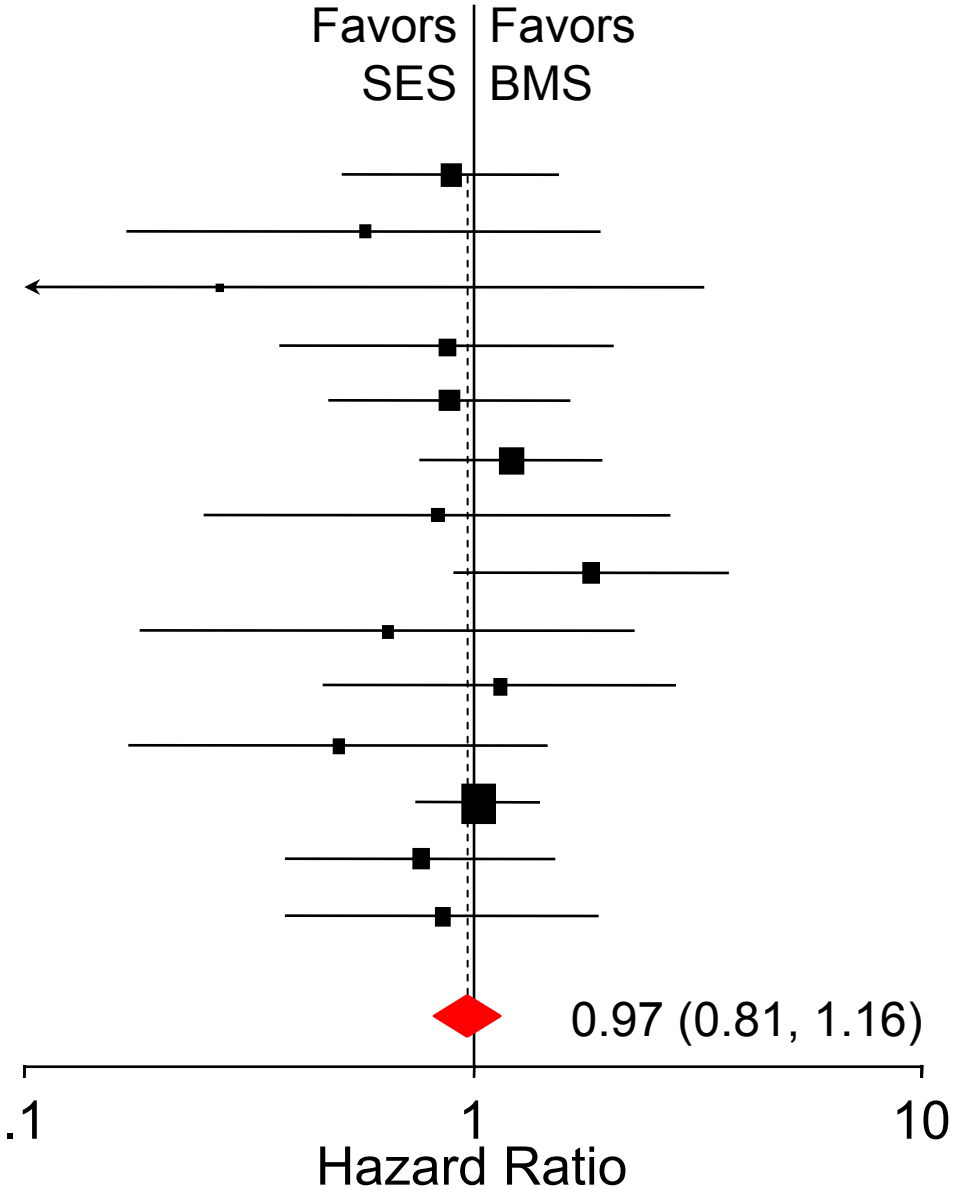


Patients at Risk

SES	2486	2056	1218	1028	765	548
BMS	2472	2063	1207	1044	842	530

Hazard Ratios for Death or MI
-All Patients-

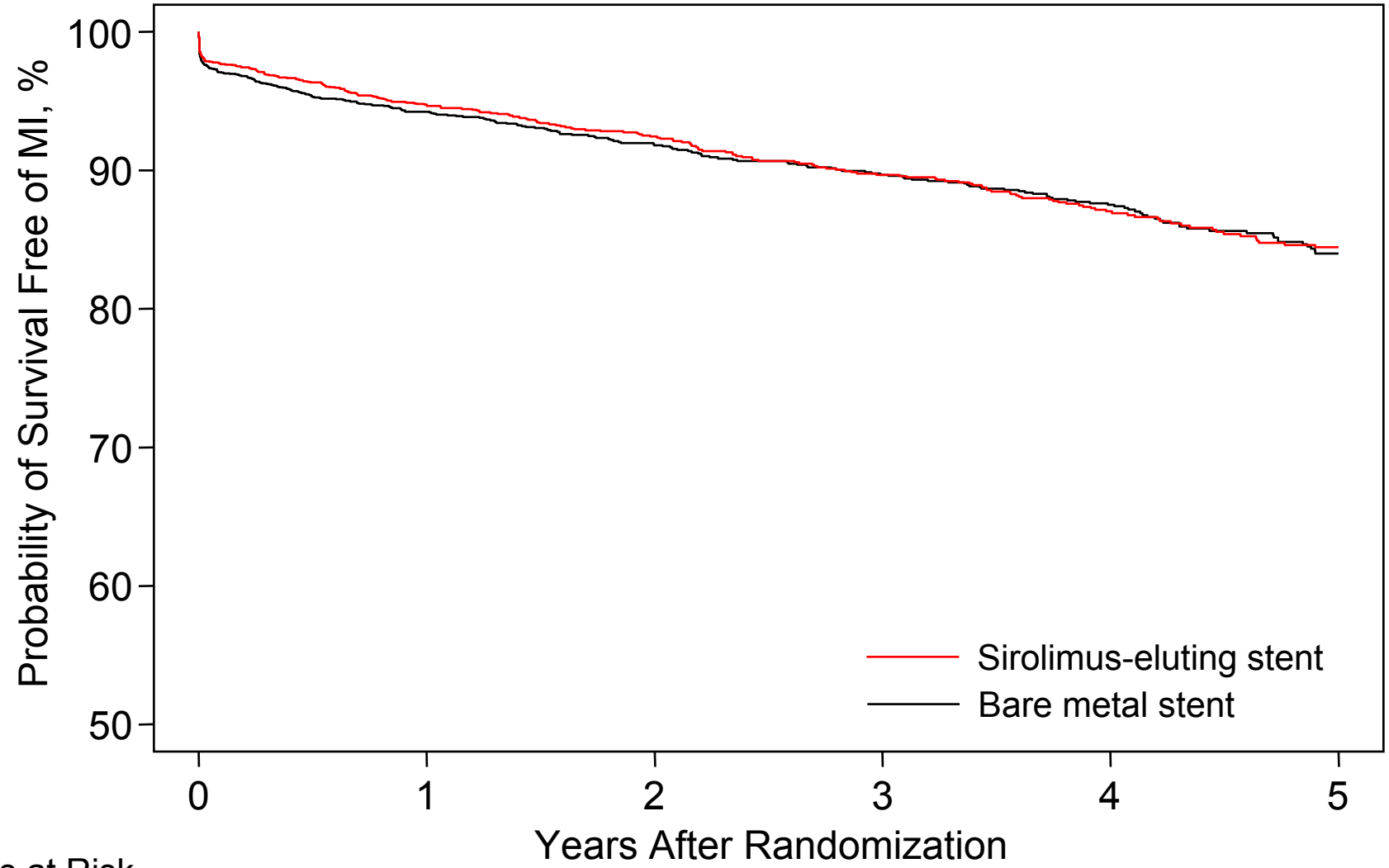
Trial	No. of events / Total No. of patients: SES group	BMS group
BASKET	23/264	27/281
CSIRIUS	4/50	7/50
DECODE	1/54	2/29
DIABETES	10/80	12/80
ESIRIUS	19/175	22/177
PACHE	38/250	35/250
PRISON II	5/100	6/100
RAVEL	22/120	12/118
SCANDSTENT	4/163	7/159
SCORPIUS	10/95	9/98
SESAMI	6/160	10/160
SIRIUS	74/533	72/525
STRATEGY	14/87	18/88
TYPHOON	11/355	13/357
Overall	241/2486	252/2472



Test for Heterogeneity: *Cochran Q*=8.7 (*d.f.*=13) *P*=.79

Test for Inconsistency: I^2 =0.0%

Kaplan-Meier Curves of Survival Free of MI
-All Patients-

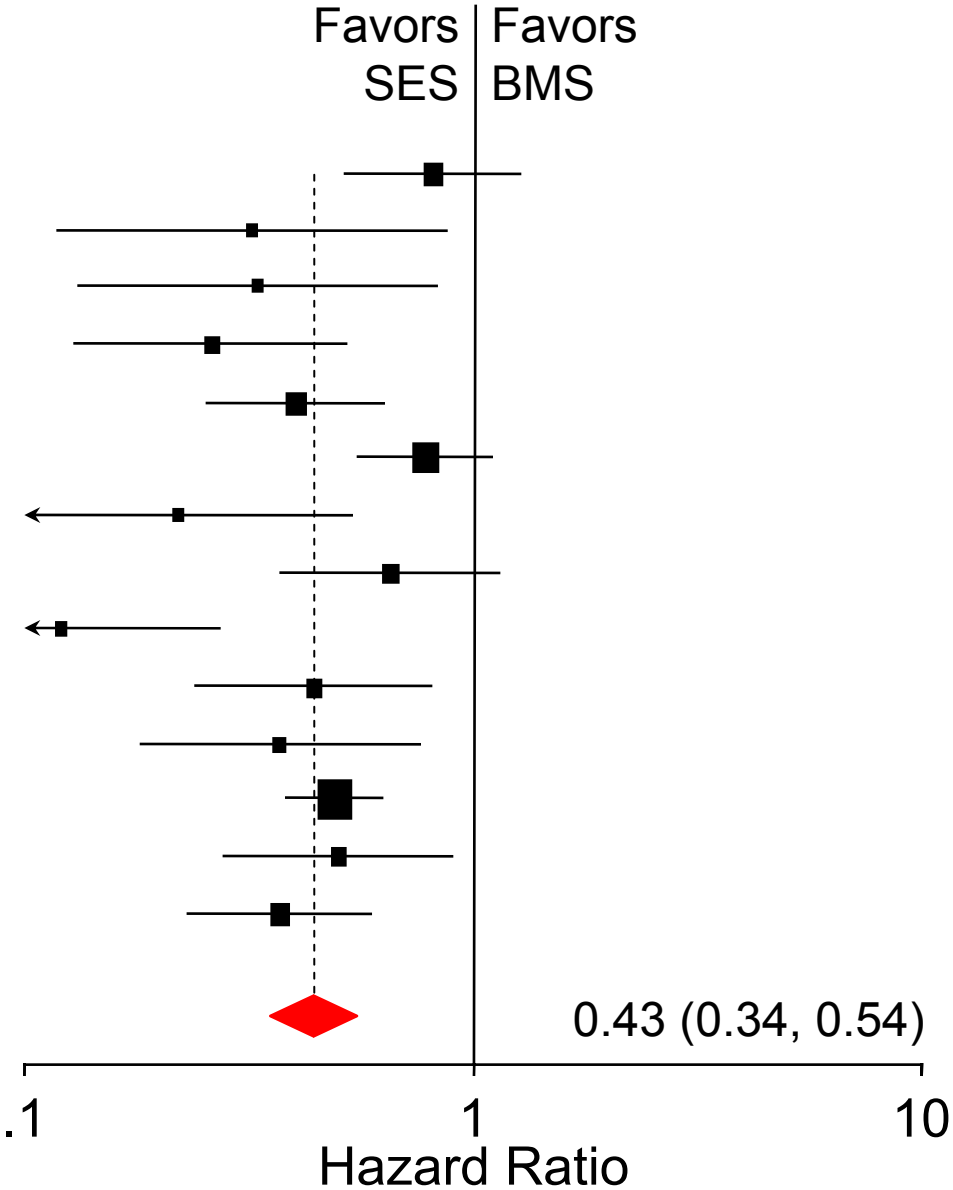


Patients at Risk

SES	2486	1985	1168	983	728	516
BMS	2472	1983	1148	992	798	505

Hazard Ratios for MACE
-All Patients-

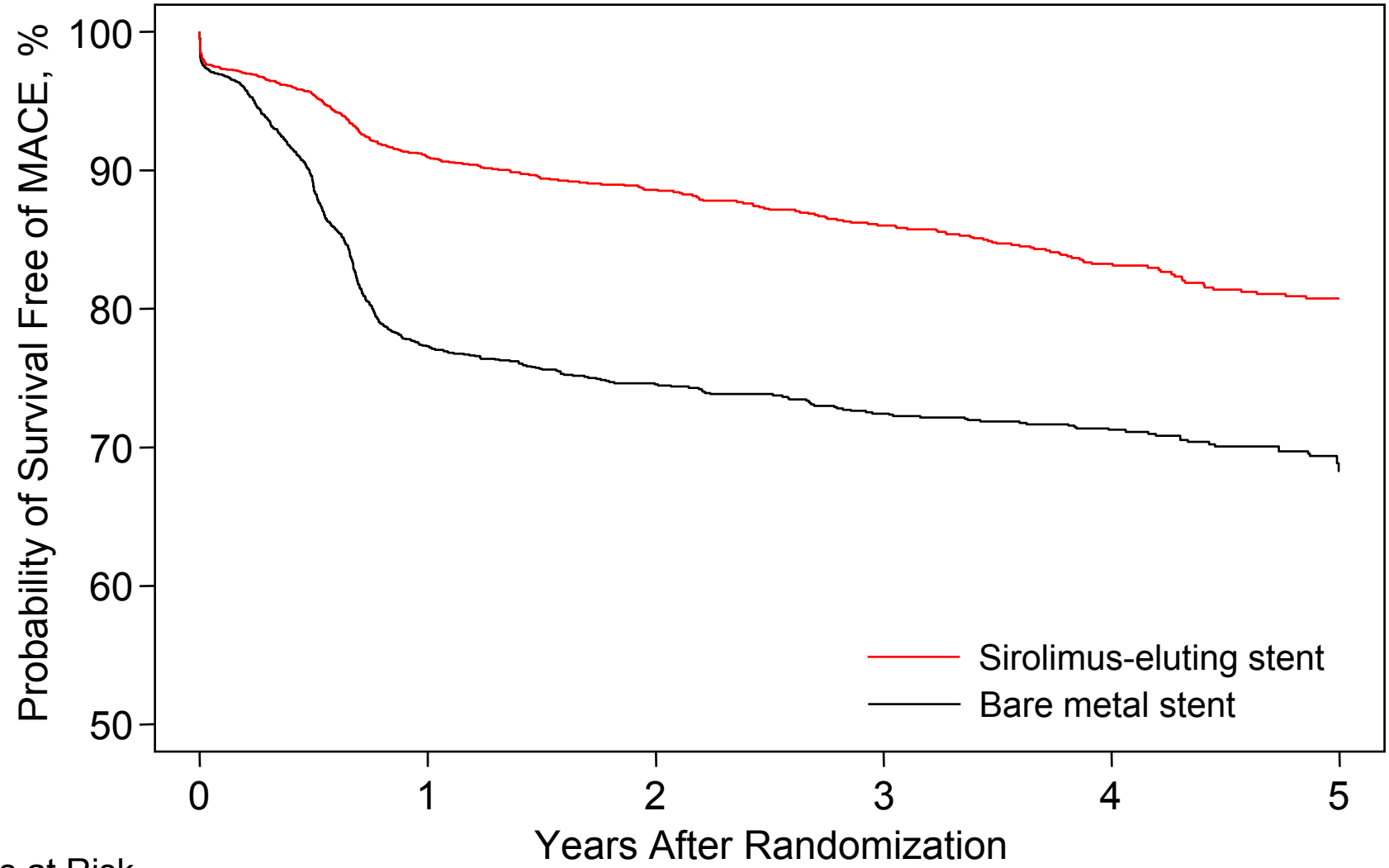
Trial	No. of events / Total No. of patients: SES group	BMS group
BASKET	32/264	41/281
CSIRIUS	5/50	14/50
DECODE	8/54	11/29
DIABETES	10/80	33/80
ESIRIUS	26/175	58/177
PACHE	59/250	73/250
PRISON II	6/100	25/100
RAVEL	20/120	28/118
SCANDSTENT	7/163	51/159
SCORPIUS	15/95	32/98
SESAMI	11/160	26/160
SIRIUS	91/533	164/525
STRATEGY	17/87	31/88
TYPHOON	24/355	62/357
Overall	331/2486	649/2472



Test for Heterogeneity: *Cochran Q*=33.9 (*d.f.*=13) *P*=.001

Test for Inconsistency: I^2 =61.7%

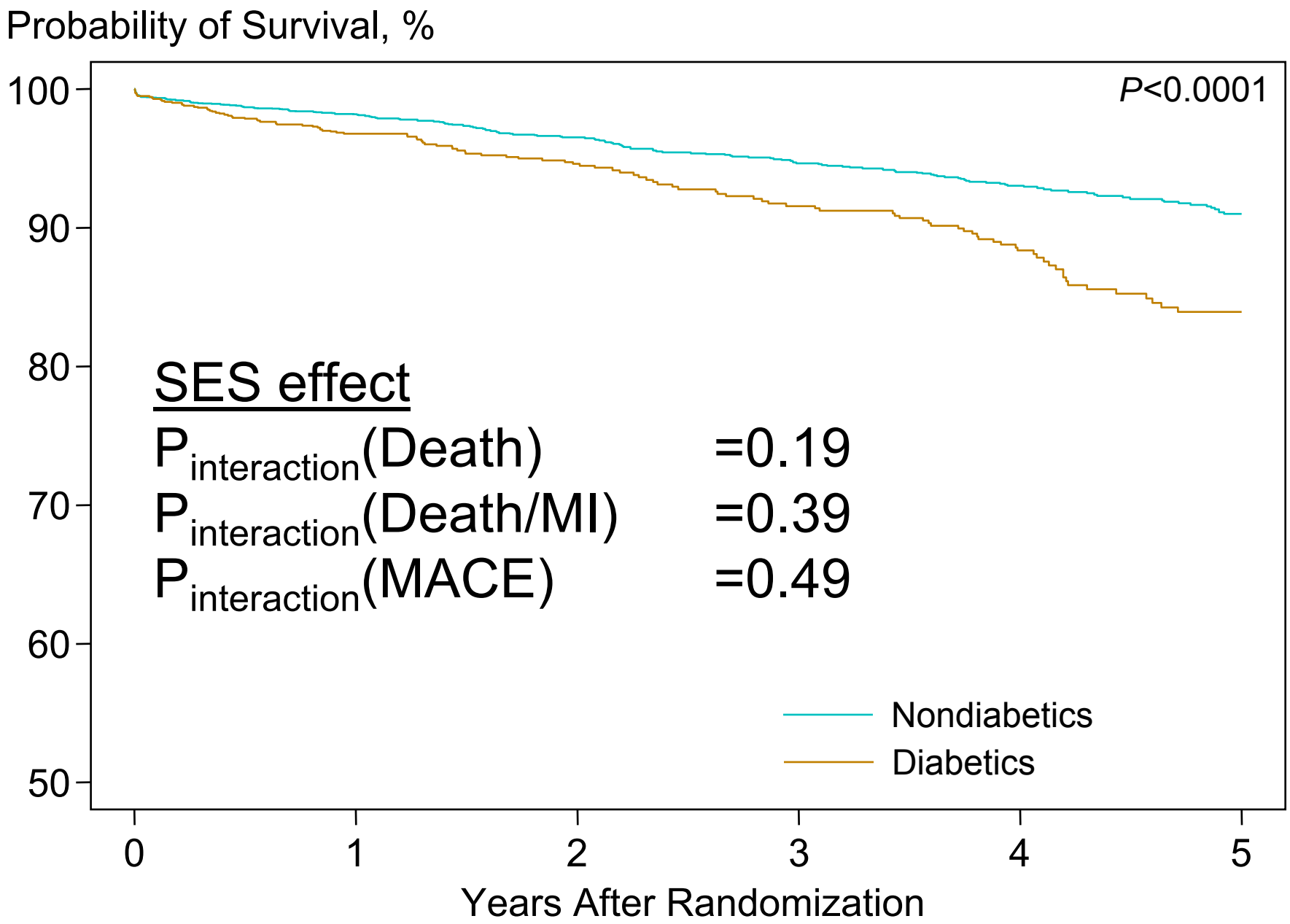
Kaplan-Meier Curves of Survival Free of MACE
-All Patients-



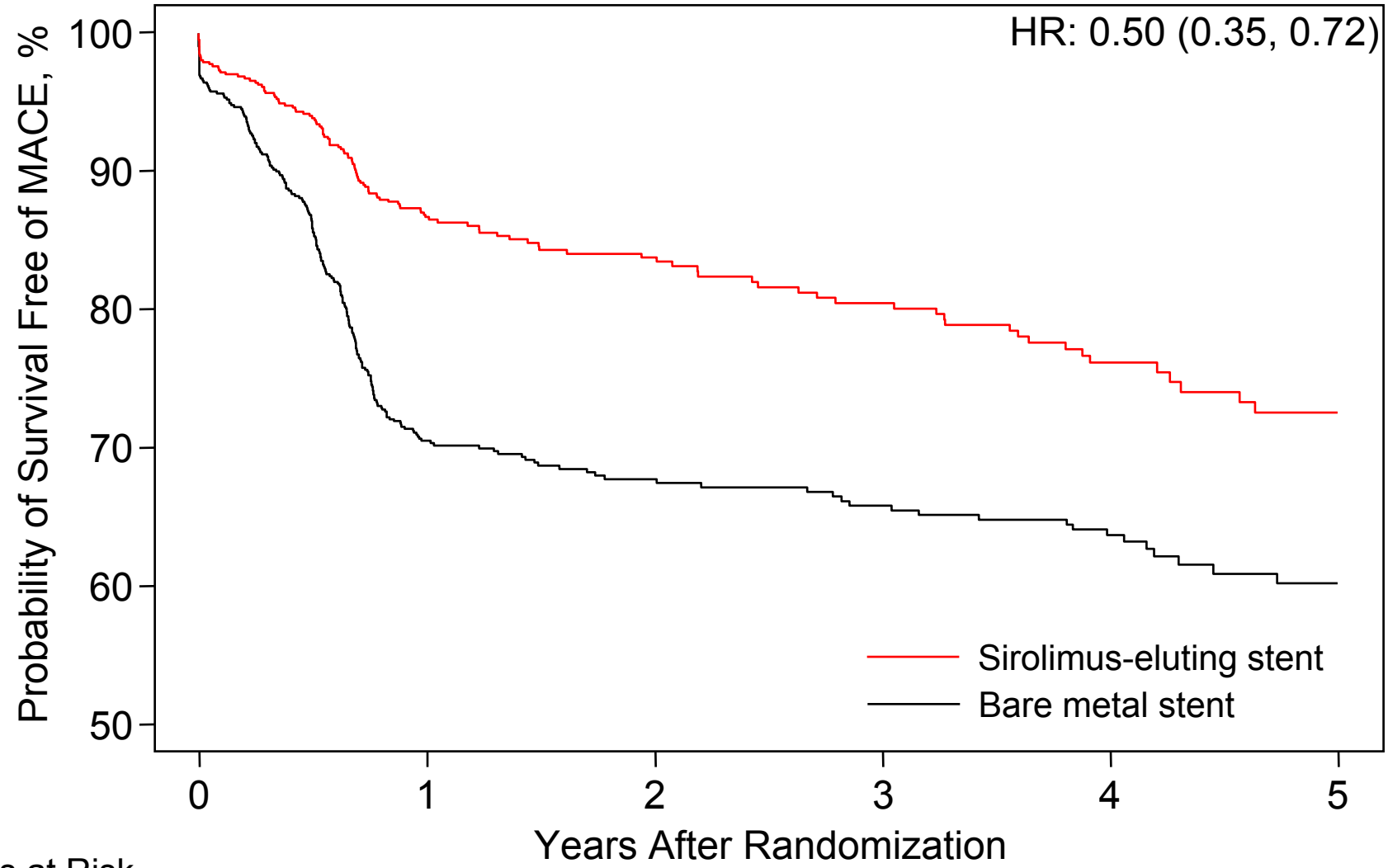
Patients at Risk

SES	2486	1891	1099	921	682	491
BMS	2472	1639	902	773	621	395

Diabetes: An Adverse Prognostic Factor In SES vs. BMS Trials



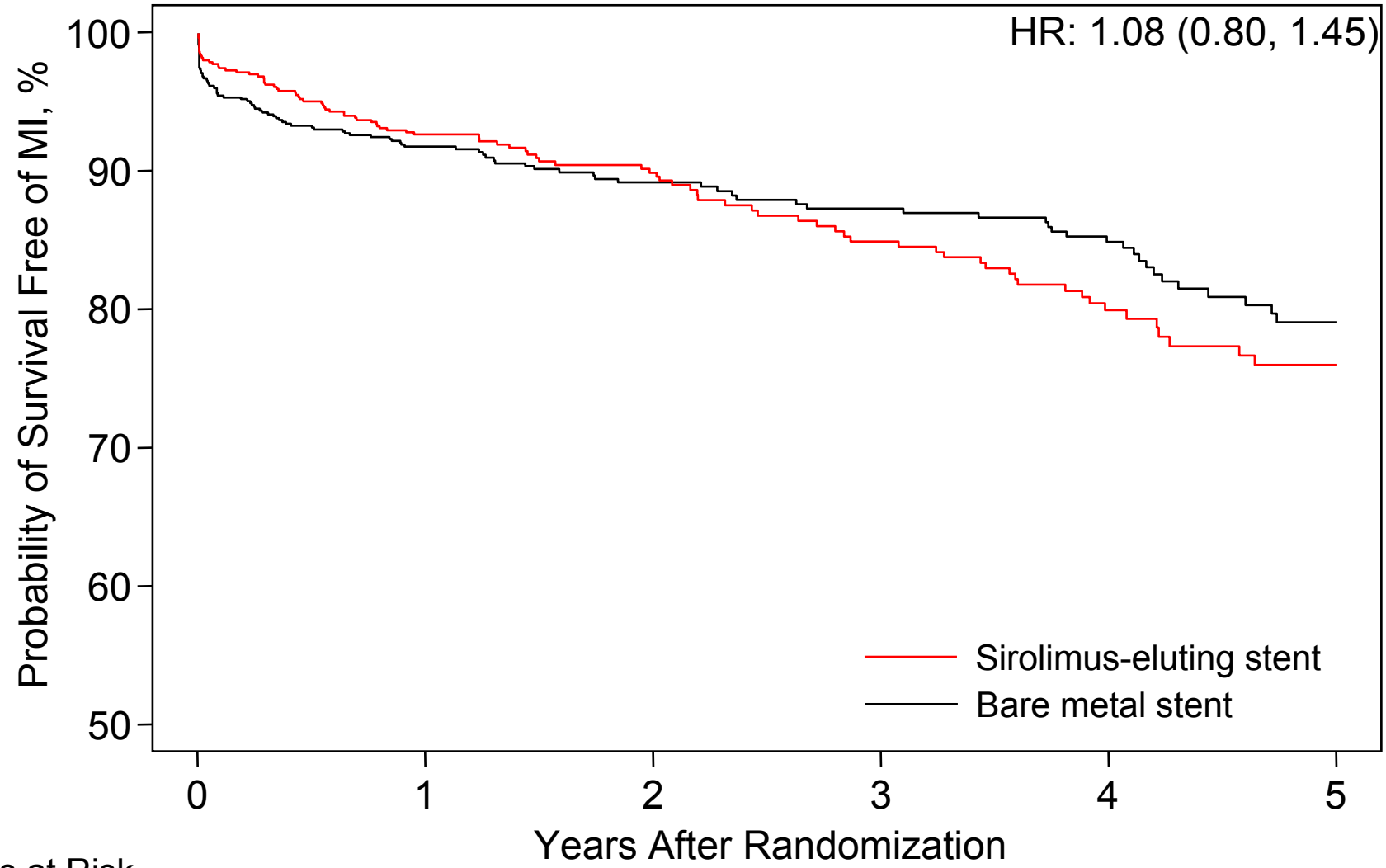
Kaplan-Meier Curves of Survival Free of MACE
-Diabetic Patients-



Patients at Risk

SES	675	492	294	207	144	100
BMS	736	449	260	198	157	88

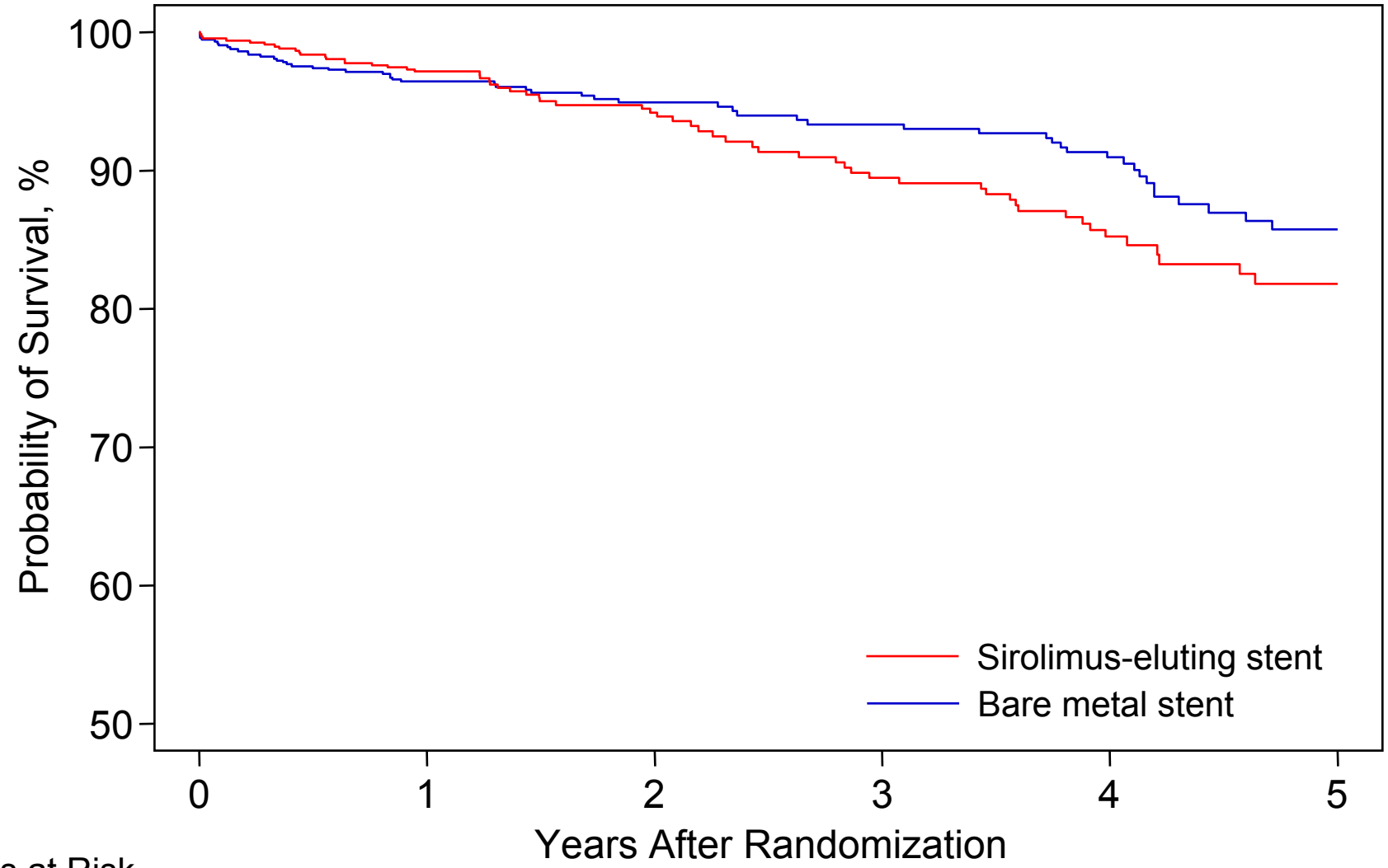
Kaplan-Meier Curves of Survival Free of MI
-Diabetic Patients-



Patients at Risk

SES	675	536	321	226	160	112
BMS	736	582	360	273	218	130

Kaplan-Meier Curves of Survival
-Diabetic Patients-

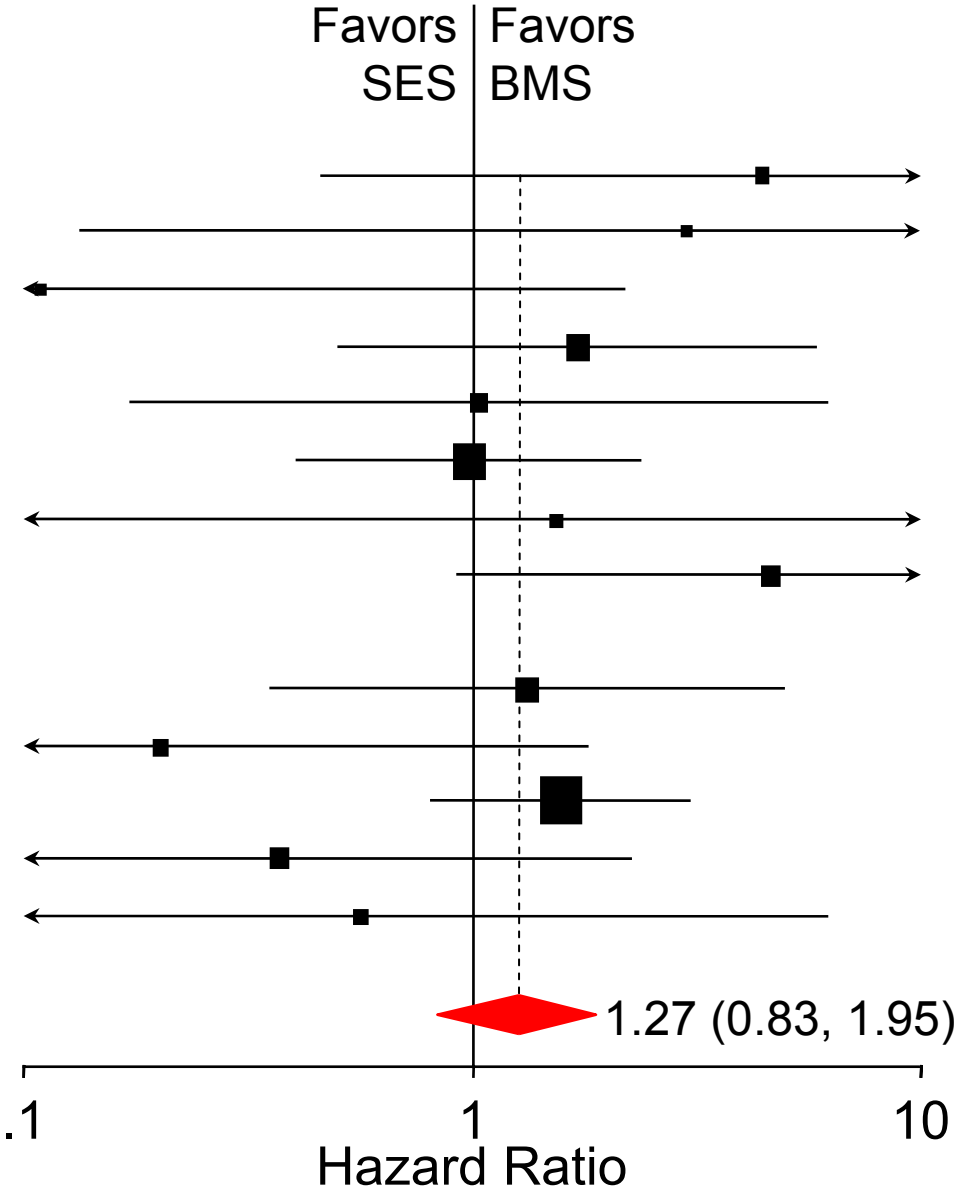


Patients at Risk

SES	675	564	335	236	167	117
BMS	736	614	386	292	235	141

Hazard Ratios for Death
-Diabetic Patients-

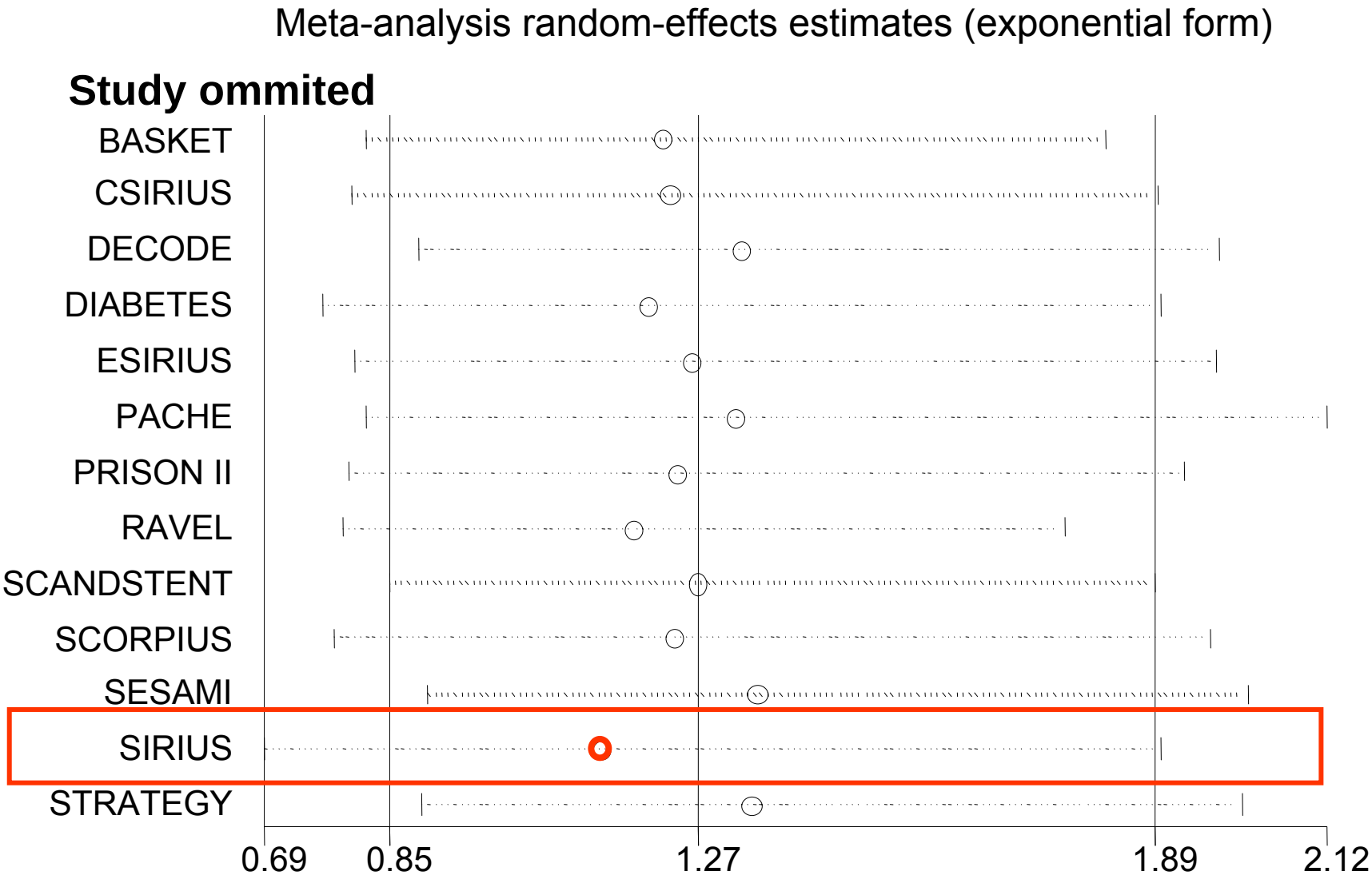
Trial	No. of events / Total No. of patients: SES group	BMS group
BASKET	3/41	1/60
CSIRIUS	1/12	0/12
DECODE	0/54	2/29
DIABETES	7/80	5/80
ESIRIUS	2/33	3/48
PACHE	9/72	12/82
PRISON II	1/11	1/16
RAVEL	6/19	2/25
SCANDSTENT	0/29	0/29
SCORPIUS	5/95	4/98
SESAMI	2/28	6/37
SIRIUS	20/131	15/148
STRATEGY	2/15	3/11
TYPHOON	1/55	2/61
Overall	59/675	56/736



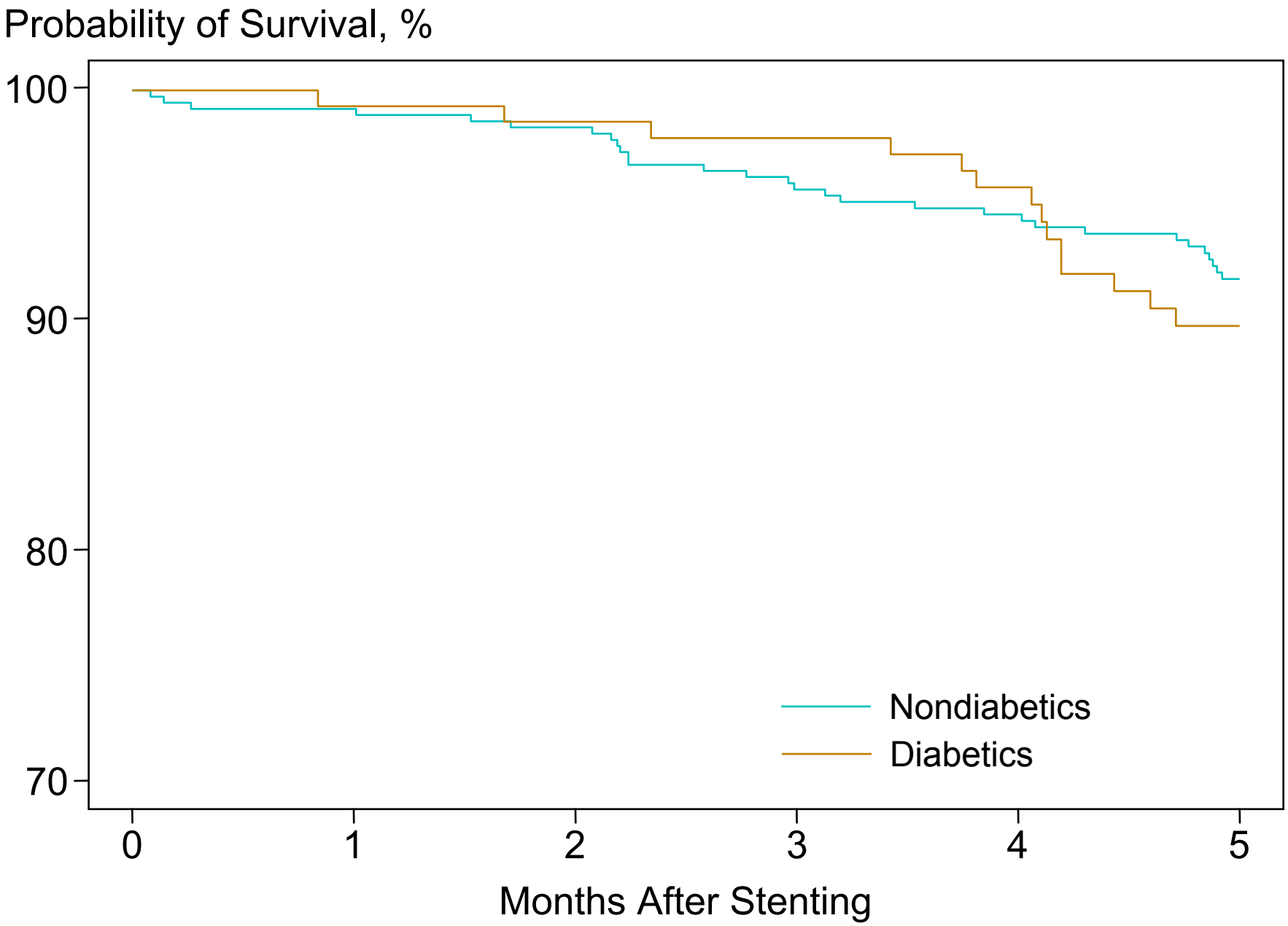
Test for Heterogeneity: *Cochran Q*=12.9 (*d.f.*=12) *P*=.38

Test for Inconsistency: I^2 =0.0%

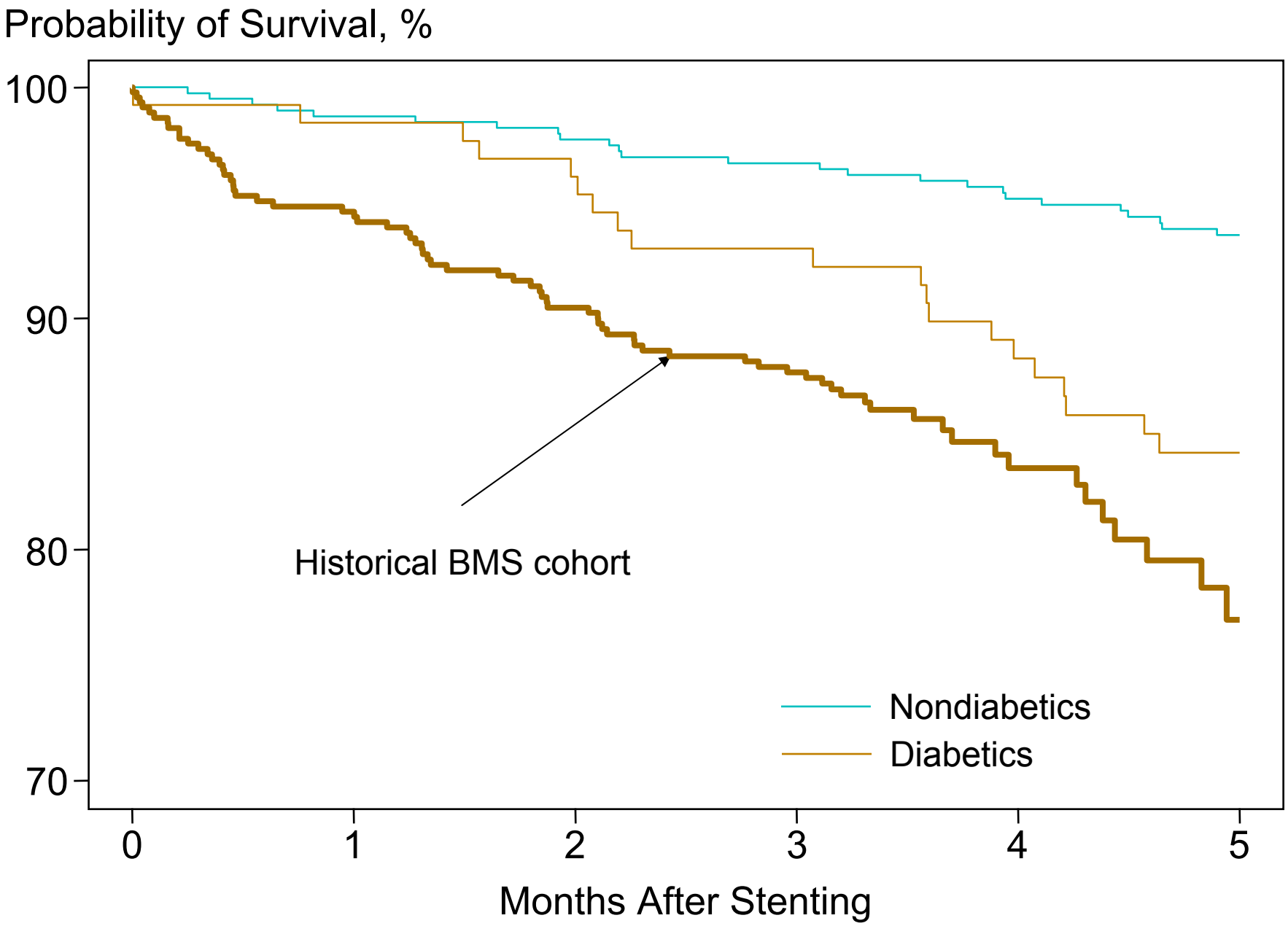
Hazard Ratios for Death in Diabetic patients
-Role of Individual Studies-



SIRIUS Trial
- Role of Diabetes in the BMS Arm-



SIRIUS Trial
- Role of Diabetes in the SES Arm-



Conclusions, I

- These individual patient data based analyses do not show any difference in long-term mortality and MI between SES and BMS as well as SES and PES.
- SES retains its superiority over BMS and PES in terms of overall reduction of MACE at long-term.

Conclusions, II

- Diabetes remains an adverse prognostic factor after the use of both drug-eluting stents, SES and PES. The lack of the expected negative impact of diabetes in the BMS arm of the SIRIUS trial needs to be clarified
- With regard to mortality and MI, there was no significant interaction between presence of diabetes and type of stent implanted.