Can Different DES Make a Different Outcome?

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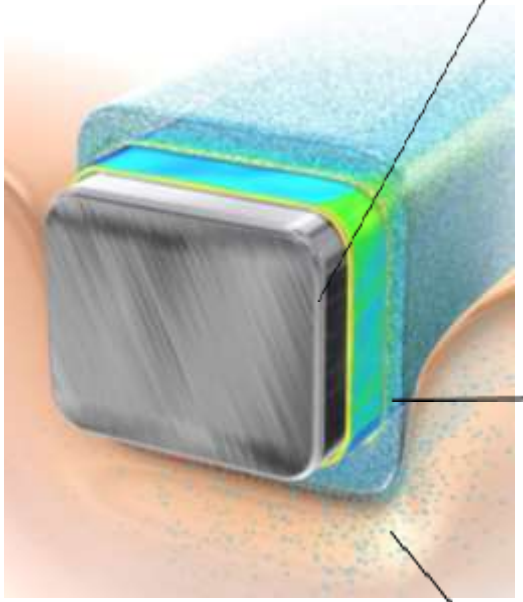
Metallic DES Evolution



Polymer modification

- *Non-biodegradable*
  - *PBMA/PEVA*
  - *SIBS*
  - *PC*
  - *BioLinks*
  - ***PVDF-HFP***
- *Biodegradable*
  - ***PDLLA***
  - *PLGA*
  - *PLEC*
- *No polymer*

Design modification

- *Cobalt Cromium* → ***Thin strut***
- *Stainless steel* → *Thick-strut*

Drug selection

- *Paclitaxel*
- *Sirolimus*

→
- *Sirolimus*
- *Everolimus*
- *Zotarolimus*
- *Biolimus*
- *Picrolimus*
- *Myolimus...*

Evolution of DES Technology

First Gen

Durable Polymer Stents

	Cypher	TAXUS Express	TAXUS Liberte
Strut Thickness	140 µm	132 µm	96 µm
Coat Thickness	7µm / side	16µm/side	14µm/side

Bioabsorbable Polymer Stents

	Biomatrix	Nobori
Strut Thickness	120 µm	125 µm
Coat Thickness	10 µm	20 µm

Second Gen

	Resolute Integrity	Xience Xpedition	Promus PREMIER
Strut Thickness	89 µm	81 µm	81 µm
Coat Thickness	6µm / side	8µm / side	8µm / side

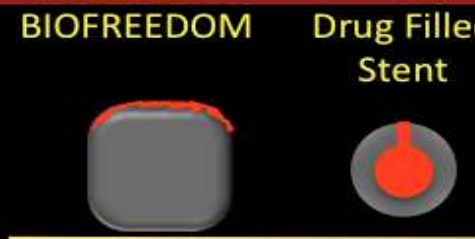
	Firehawk	Synergy	Ultimaster
Strut Thickness	86µm	74µm	80µm
Coat Thickness	10 µm	4 µm	14 µm

First Generation Future Technologies

Fully Bioresorbable Stents

	BVS	ELIXIR DESolve	DREAMS II
Strut Thickness	150 µm	150 µm	150 µm
Coat Thickness	3 µm / side	<3 µm / side	8 µm / side

Polymer Free Stents



	BIOFREEDOM	Drug Filled Stent
Strut Thickness	112	86
Coat Thickness	NA	NA

Different Metallic Property; Stent Expansion Chart

DES Designs Overexpansion

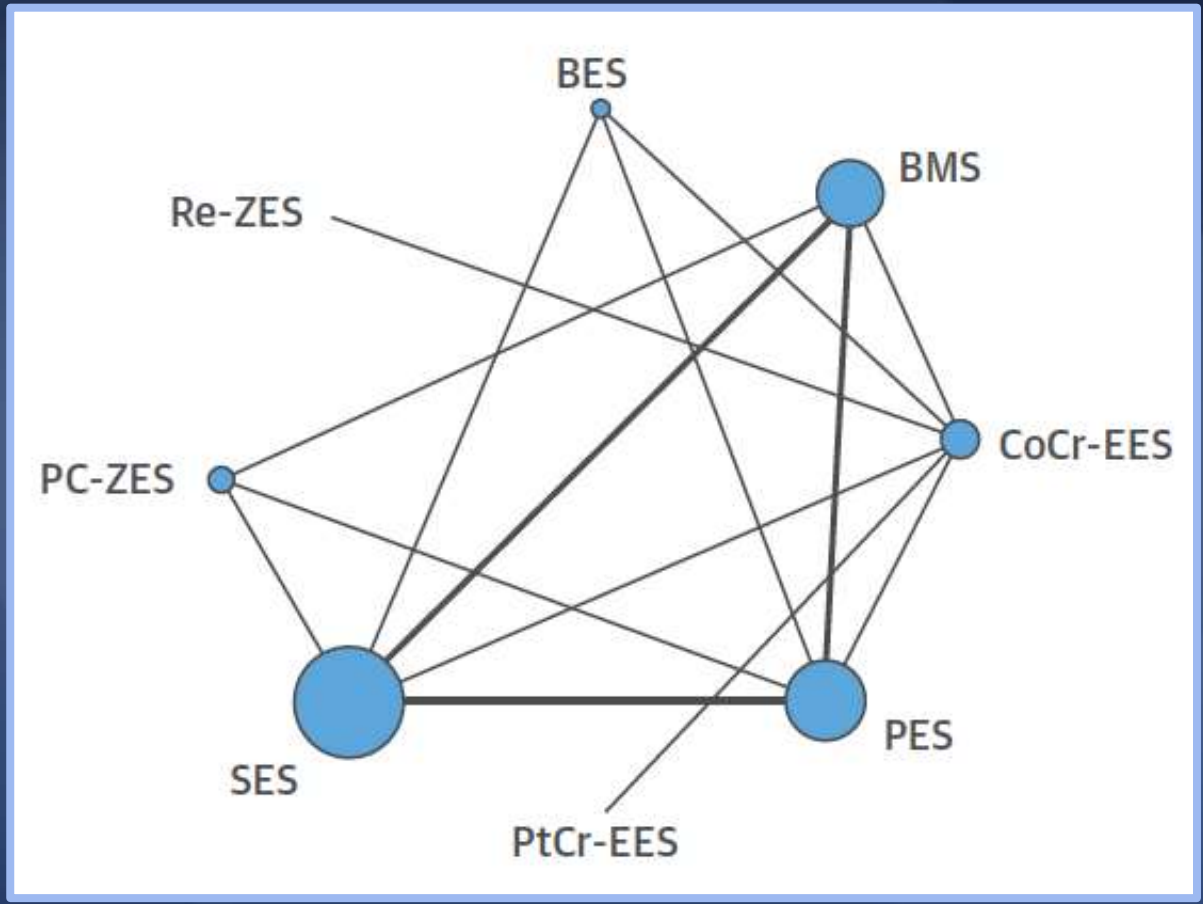
Balloon Max Size		Synergy	Xpedition	Res. Onyx	Ultimaster	BioMatrix A	Orsiro
4.0	2.25	Small vessel (8 crowns, 2-4 connectors) *Expansion: 3.6mm*	Small vessel (6 crowns, 3 connectors) *Expansion: 4.1mm*	Small vessel workhorse (6.5 crowns, 2 connectors) *Expan: 3.3mm*	Small vessel (8 crowns, 2 connectors) *Expansion: 4.3mm*	Small vessel (6 crowns, 2 connectors) *Expansion: 4.1mm*	Small vessel (6 crowns, 3 connectors) *Expansion: 4.0mm*
	2.50						
5.0	2.75			Medium vessel workhorse (8.5 crowns, 2 connectors) *Expansion: 4.4mm*			
	3.00	Workhorse (8 crowns, 2-4 connectors) *Expansion: 4.2mm*					
	3.50		Large vessel (9 crowns, 3 connectors) *Expansion: 5.6mm*	Large vessel (9.5 crowns, 2.5 connectors) *Expansion: 5.6mm*	Large vessel (8 crowns, 2 connectors) *Expansion: 5.8mm*	Large vessel (9 crowns, 3 connectors) *Expansion: 5.9mm*	Large vessel (6 crowns, 3 connectors) *Expansion: 5.3mm*
6.0	4.00	Large vessel (10 crowns, 2-5 connectors) *Exp: 5.7mm*					
	4.50			Extra-Large vessel (10.5 crowns, 2.5 connectors) *Expansion: 6.0mm*			
	5.00						

- *Expansion : inner stent MLD excluding struts*
- *Max balloon size : Maverick 6.0mm at 14 ATM*

JACC Interventions 2016:1861-78

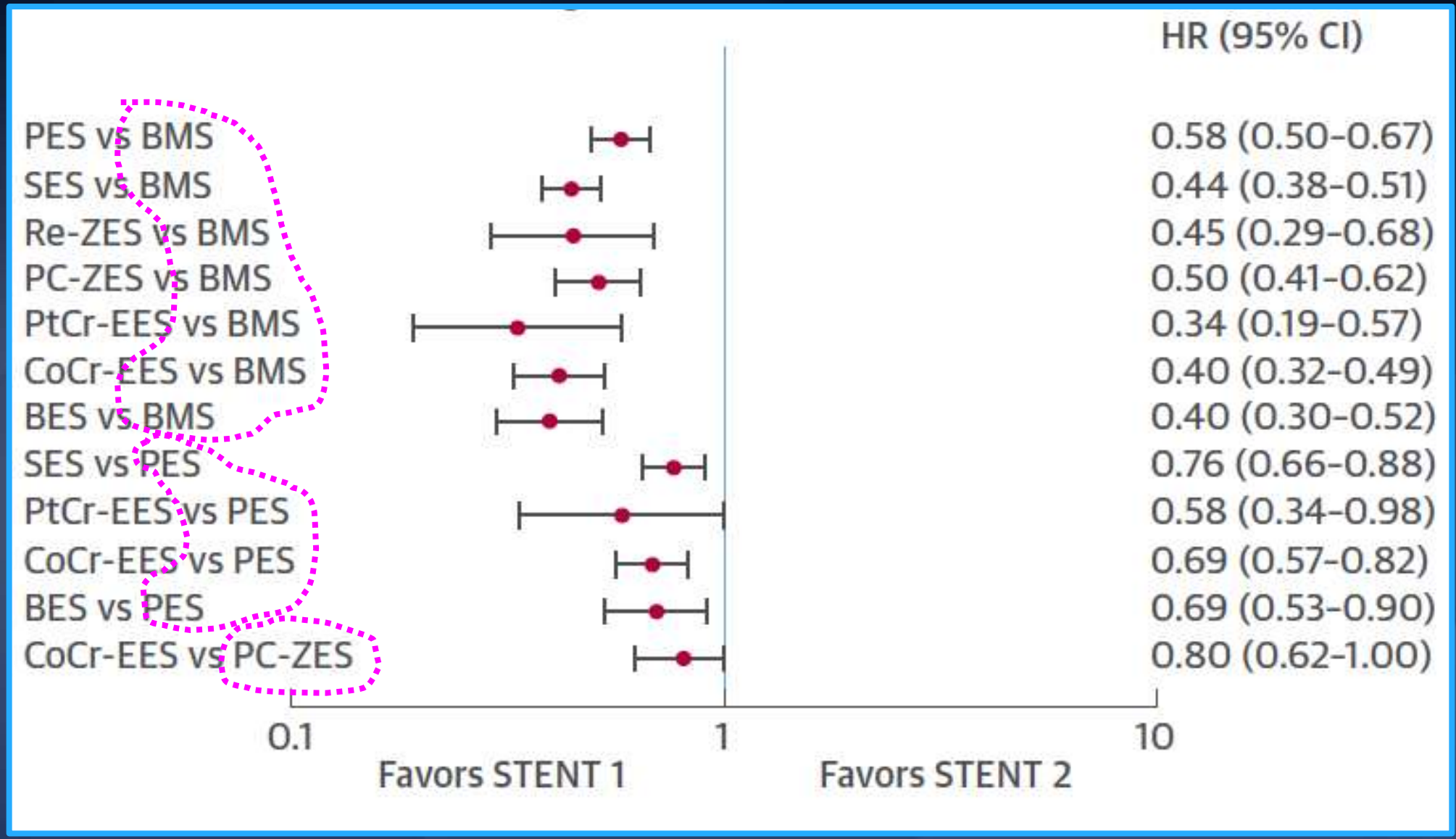
Updated Network Meta-Analysis including RCT with at least 3 year FU

51 RCTs; 52,158 patients (median 3.8 yr FU)



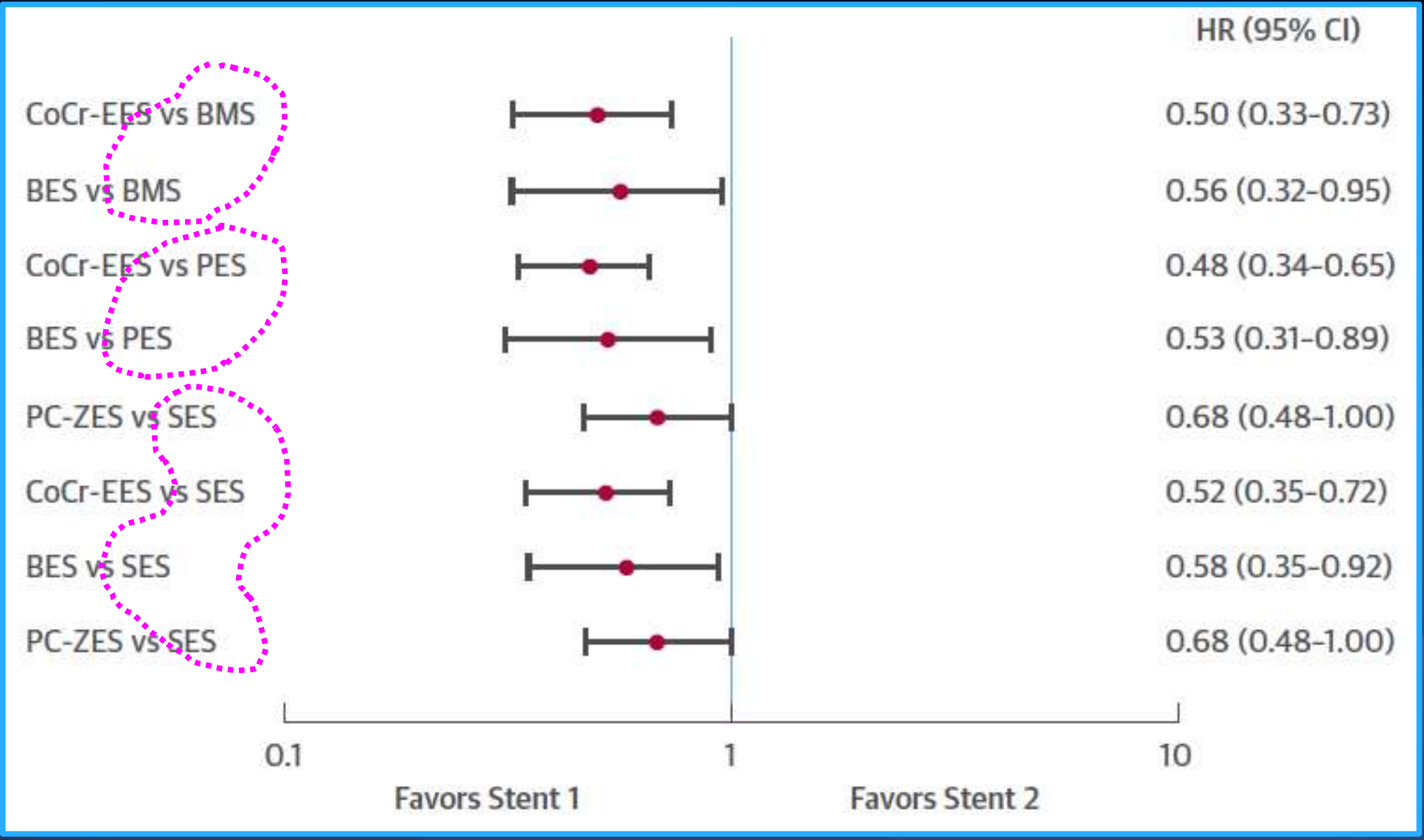
Palmerini et al. J AmColl Cardiol 2015;65:2496–507

Efficacy; TVR



Palmerini et al. J AmColl Cardiol 2015;65:2496–507

Safety; Definite or Probable ST



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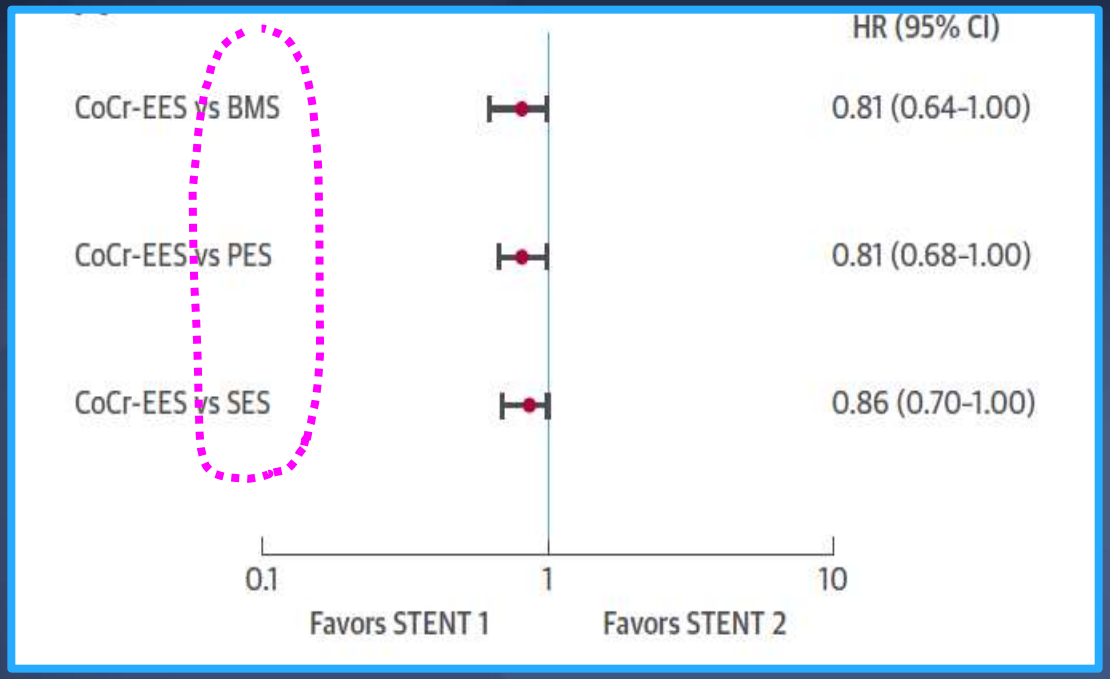
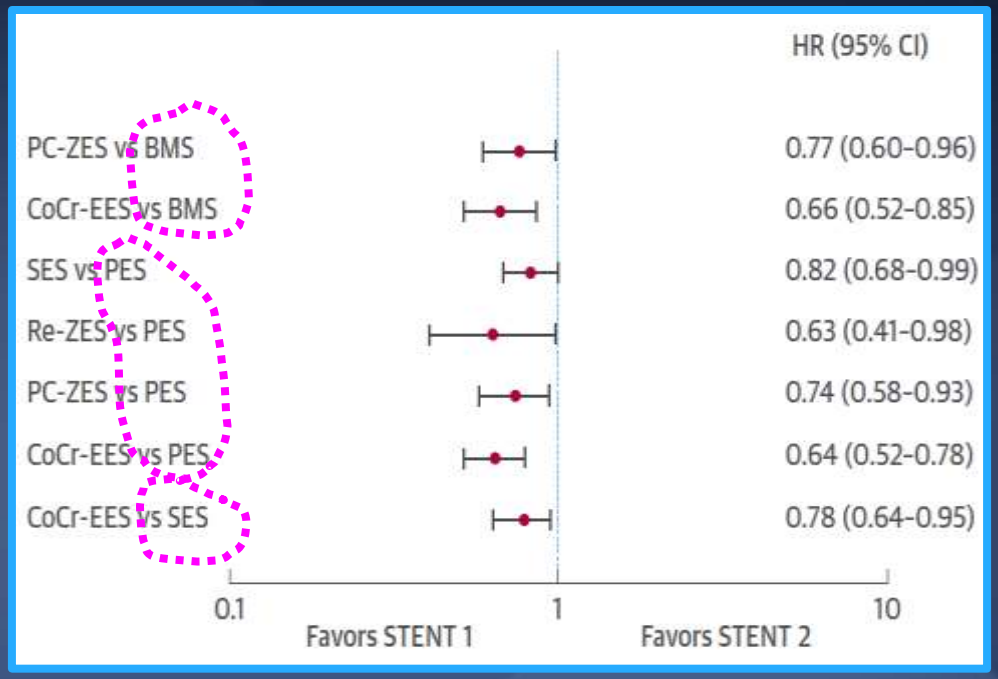
Hard Clinical Endpoints

Death



MI



Palmerini et al. J AmColl Cardiol 2015;65:2496–507

Contemporary DES; Enhanced Safety and Efficacy than BMS and 1st DES

- By a meta-analysis of 51 comparative trials, second-generation DES showed better efficacy outcomes than either BMS or 1st DES during median 4-year FU.

- Second-generation DES showed better safety outcomes (ST, death, or MI) than first-generation DES or BMS during long-term FU.

Are There Any MAJOR Differences in Mechanical Performance or Outcomes Between the Most Widely Used Contemporary Metallic DES?

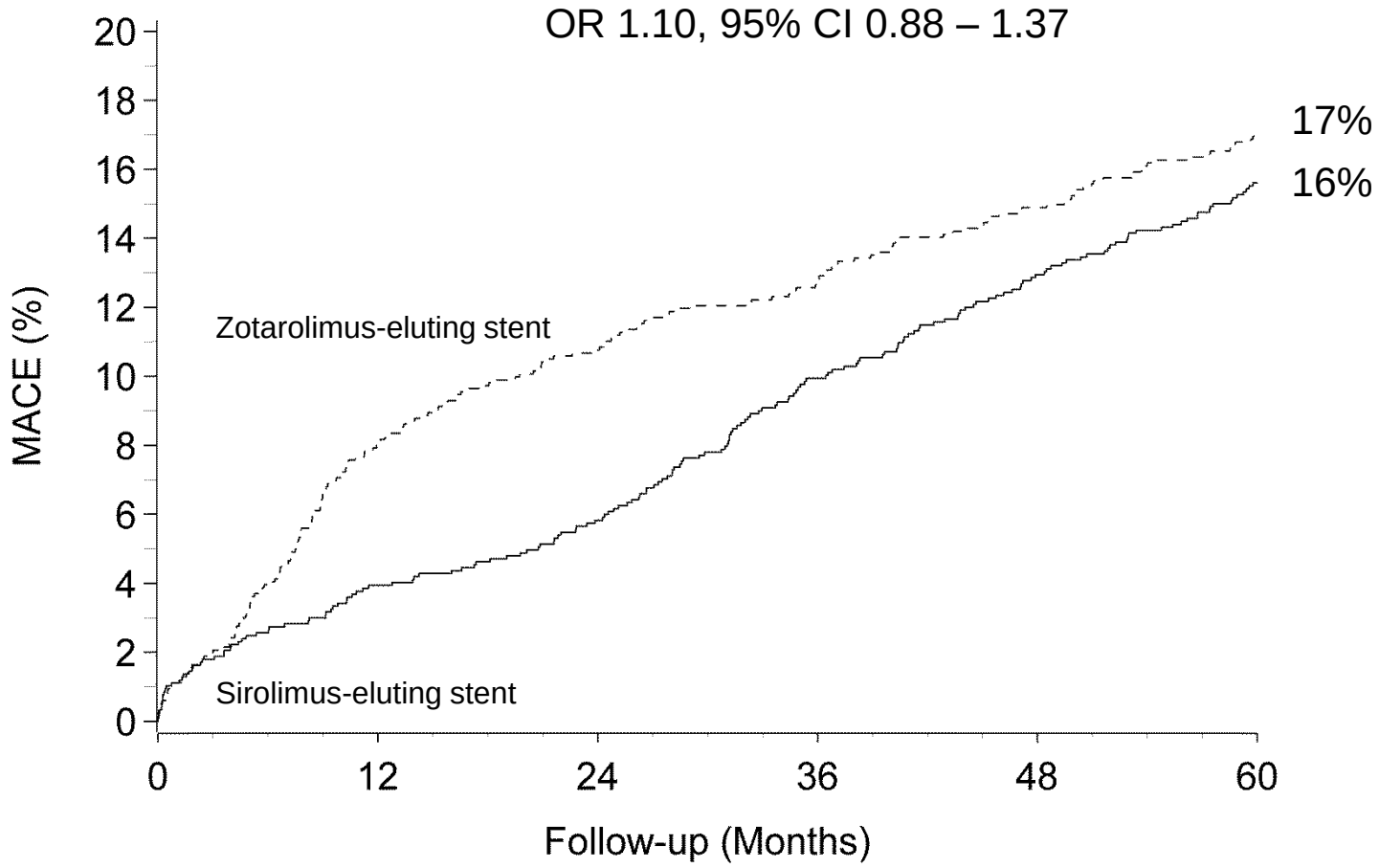
Do you feel any difference?

YES or NO

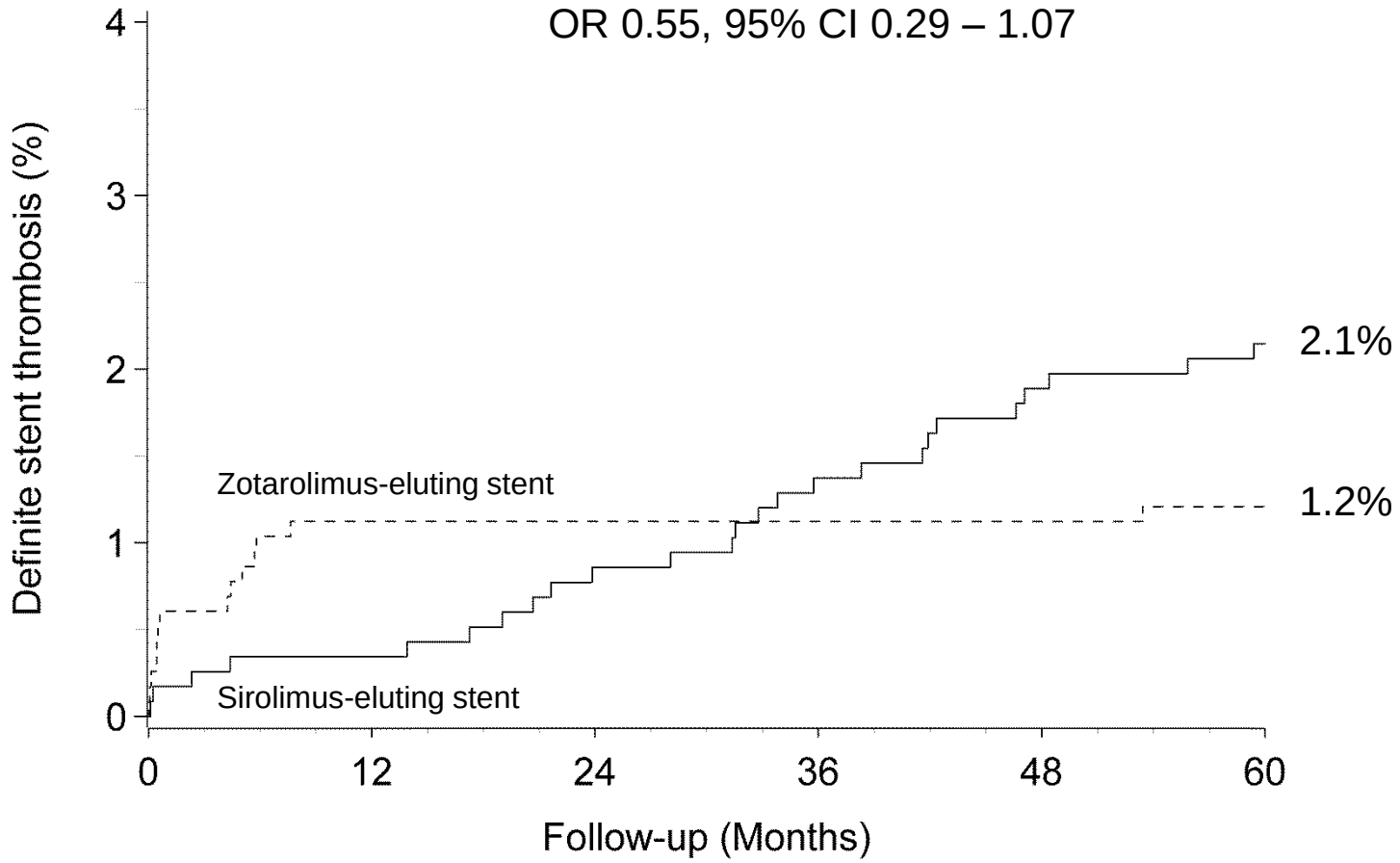
SORT-OUT RCT Program

SORT OUT	STENTS	Results (primary endpoint)	Published
SORT OUT	BxSonic, Express, Flexmaster	No difference	EuroIntervention 2005
SORT OUT II	Cypher vs. Taxus	No difference	JAMA 2008
SORT OUT III	Cypher vs. Endeavor	SES superior to ZES	Lancet 2010
SORT OUT IV	Cypher vs. Xience	EES non-inferior to SES	Circulation 2012
SORT OUT V	Cypher vs. Nobori	BES not non-inferior to SES	Lancet 2013
SORT OUT VI	Resolute vs. Biomatrix	ZES non-inferior to BES	Lancet 2015
SORT OUT VII	Orsiro vs. Nobori	SES non-inferior to BES	Circulation Cintv 2016
SORT OUT VIII	Synergy vs. Biomatrix	Enrolment completed	Not yet
SORT OUT IX	BioFreedom vs. Orsiro	Ongoing	Not yet

SO III; 5-Yr MACE

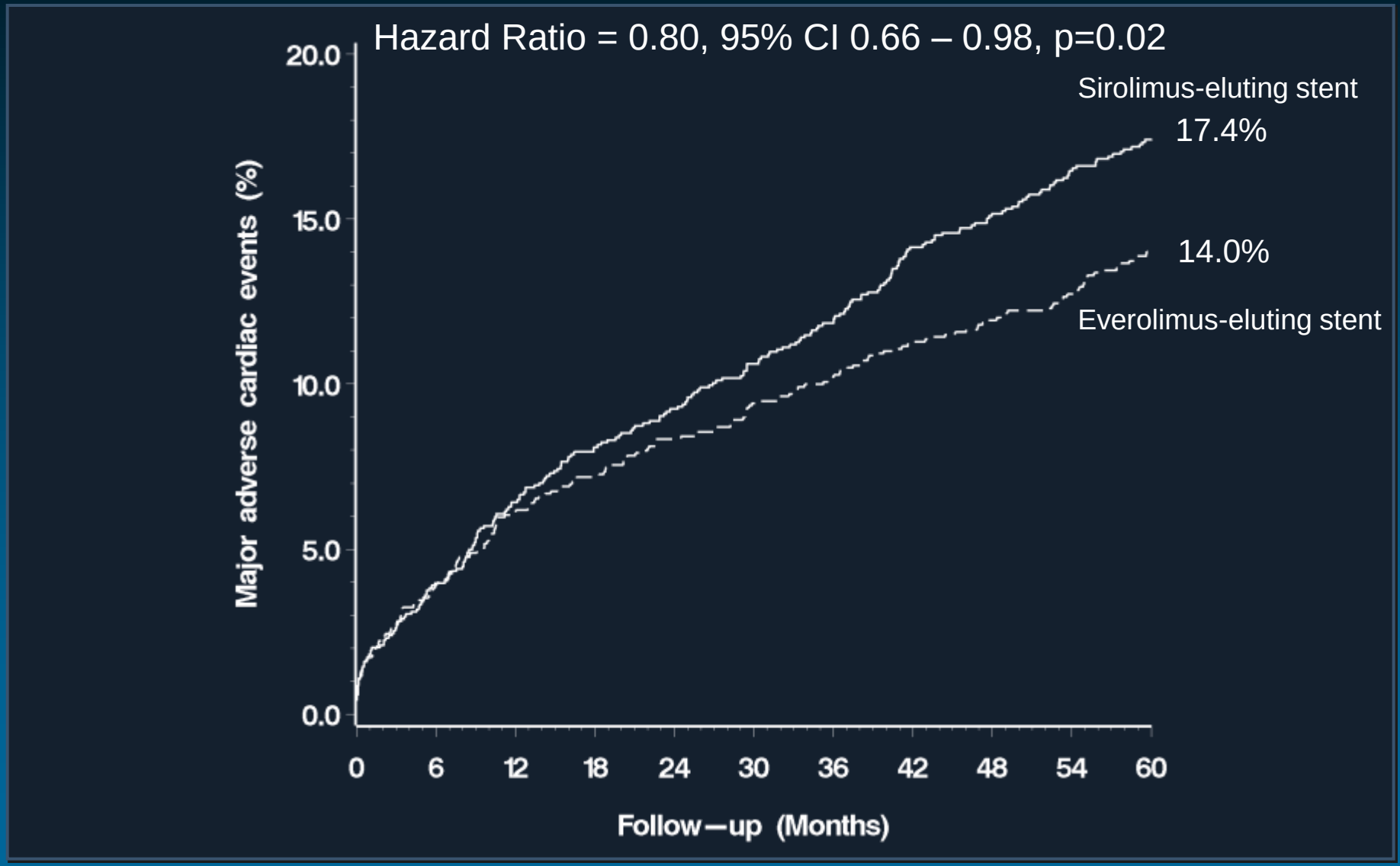


SO III – 5Yr Stent Thrombosis



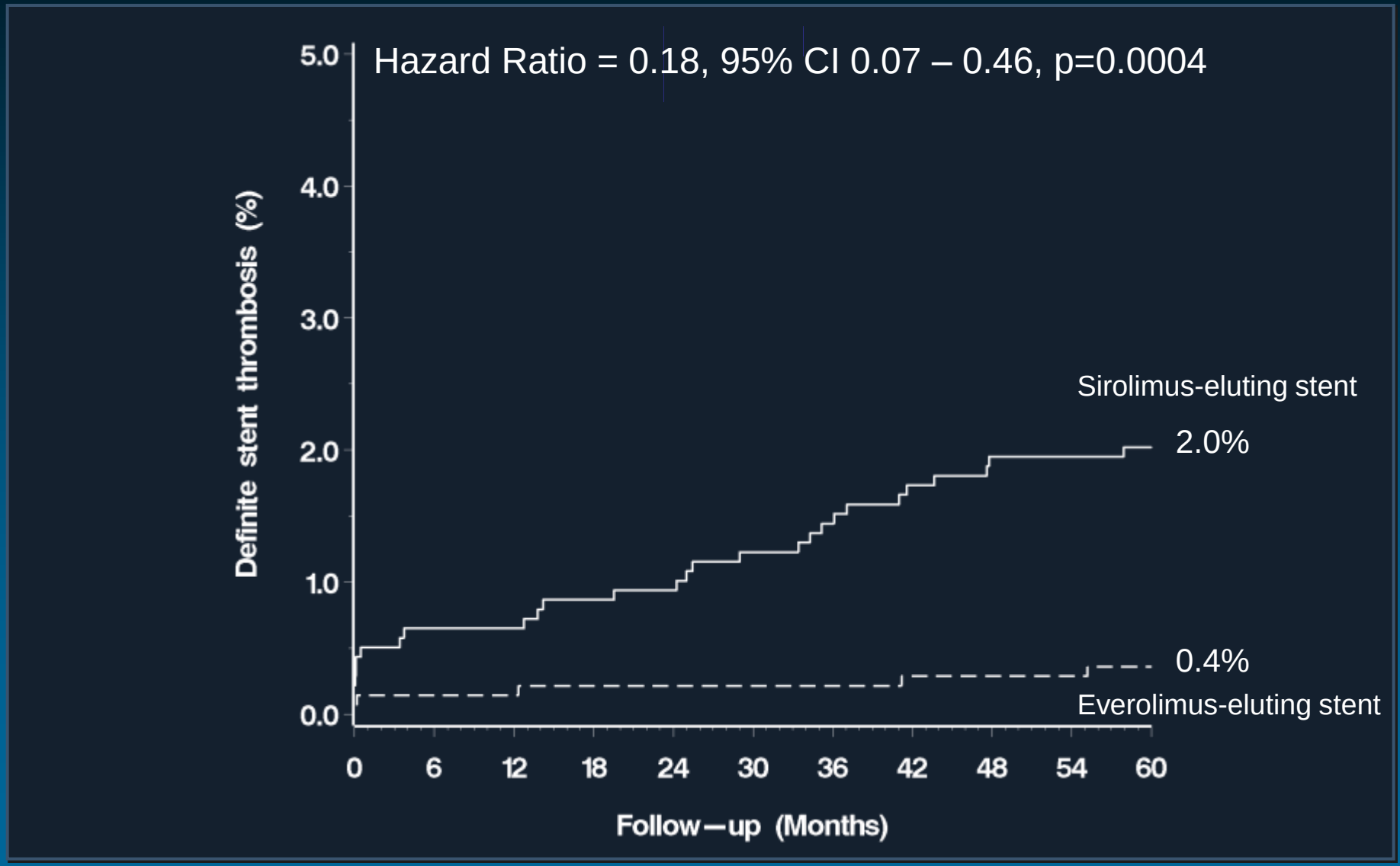
SO IV: MACE

(Cardiac death, myocardial infarction, definite stent thrombosis, target vessel revascularization)



Jensen LO J Am Coll Cardiol. 2016;67:751-62

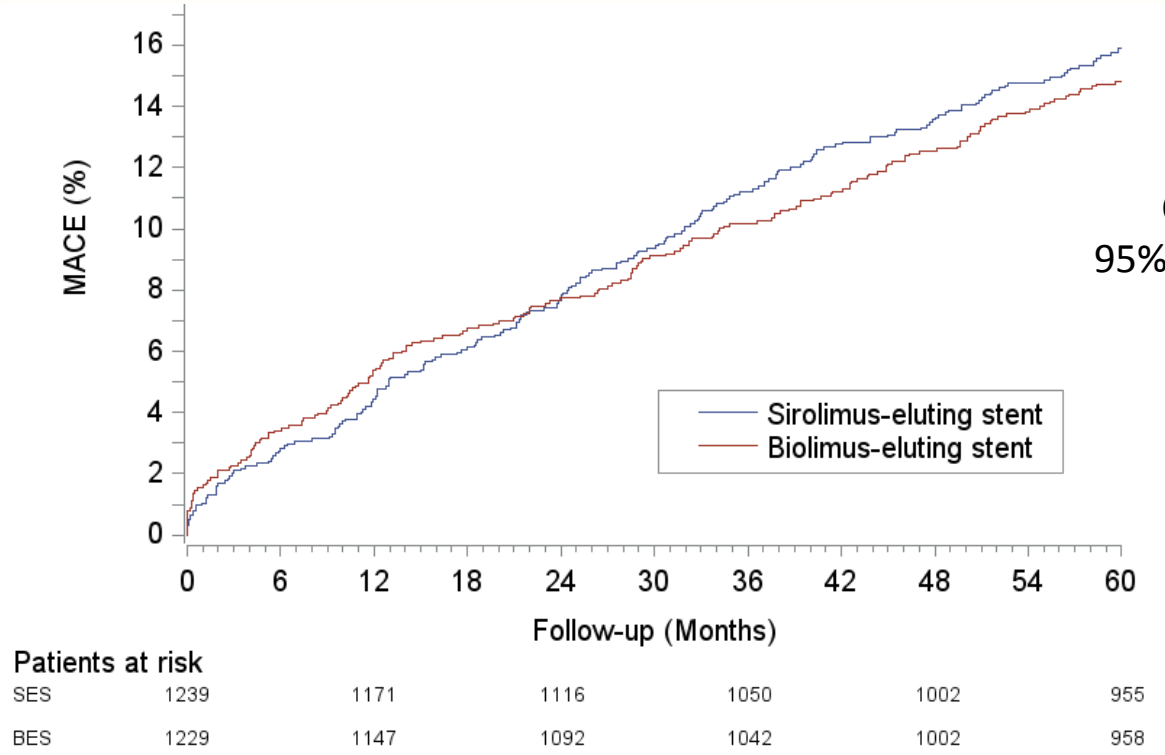
SO IV Stent Thrombosis



Jensen LO J Am Coll Cardiol. 2016;67:751-62

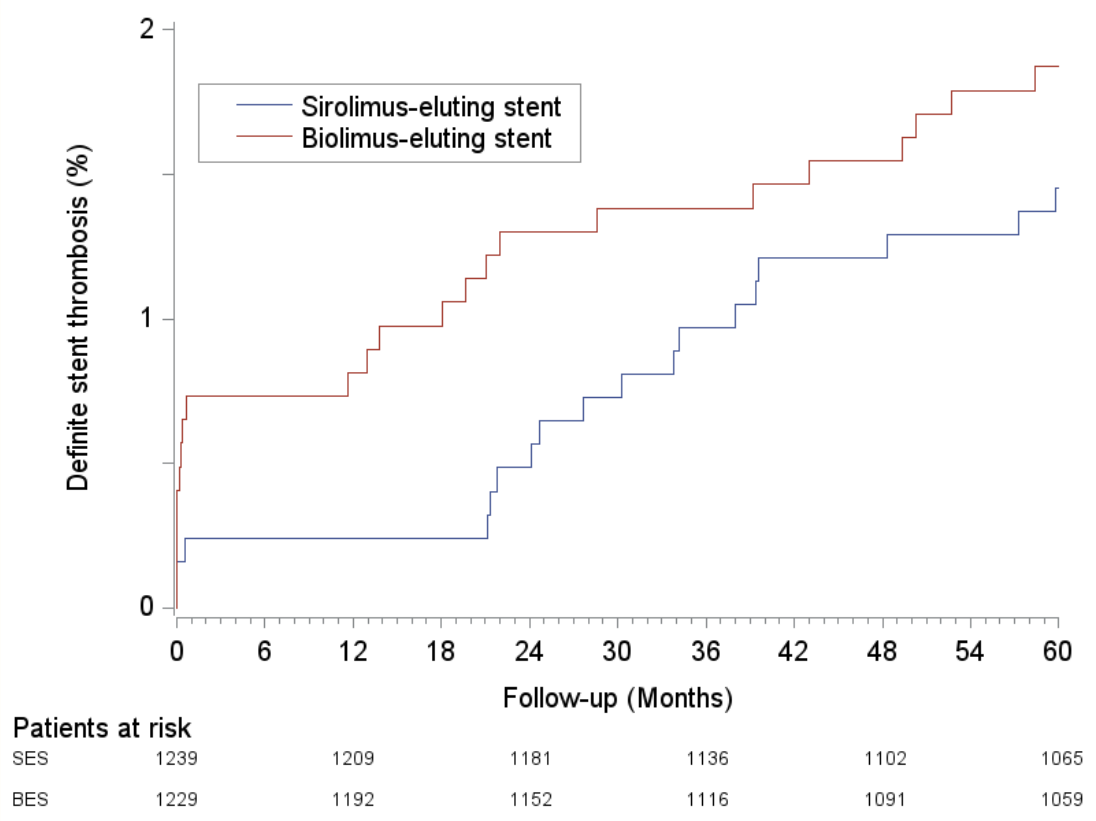
SO V; 5-Yr MACE

(Cardiac death, myocardial infarction, definite stent thrombosis, target vessel revascularization)



OR=0.93
95%CI:0.75-1.16
P=0.53

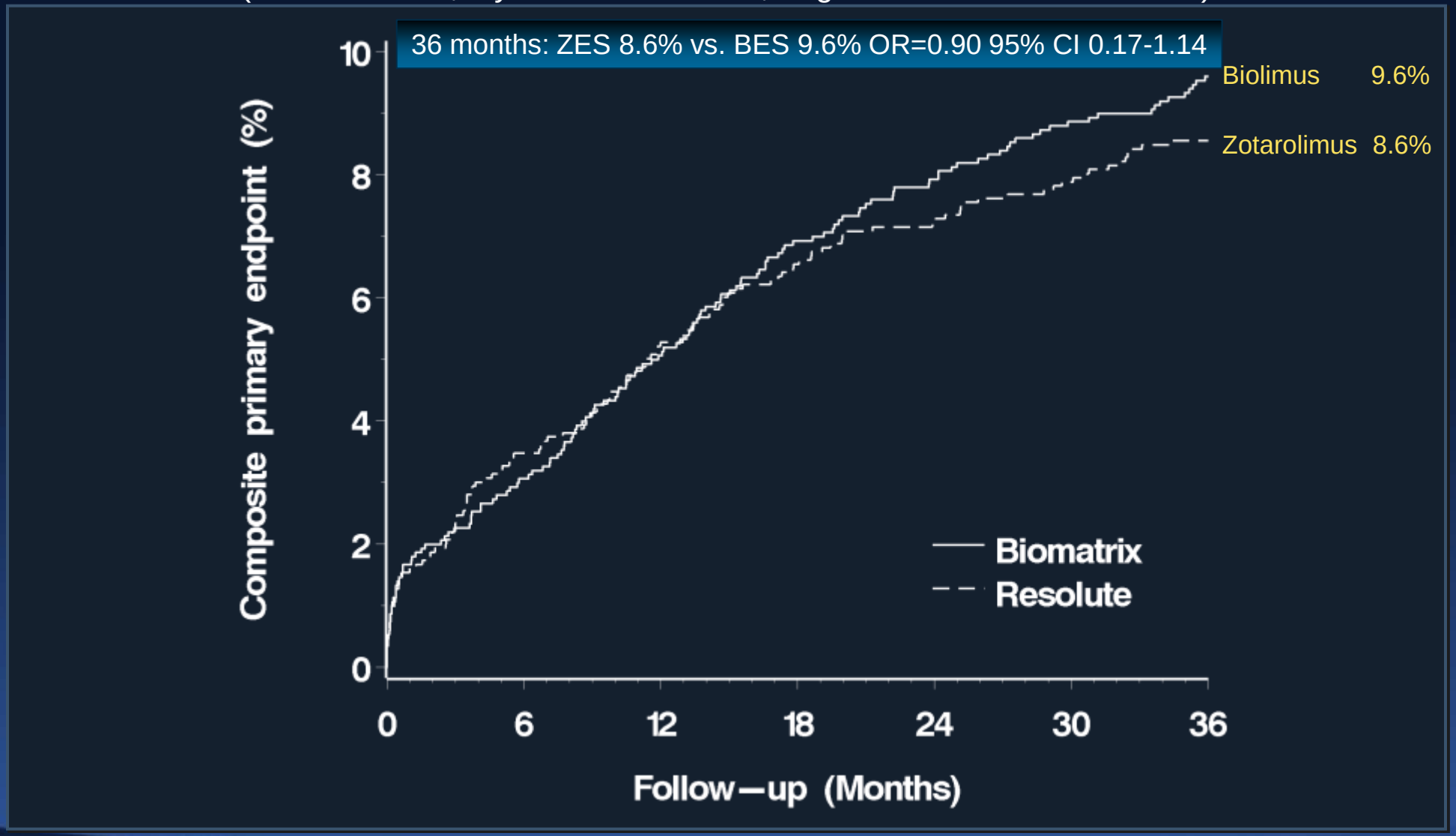
SO V; 5Y Definite Stent thrombosis



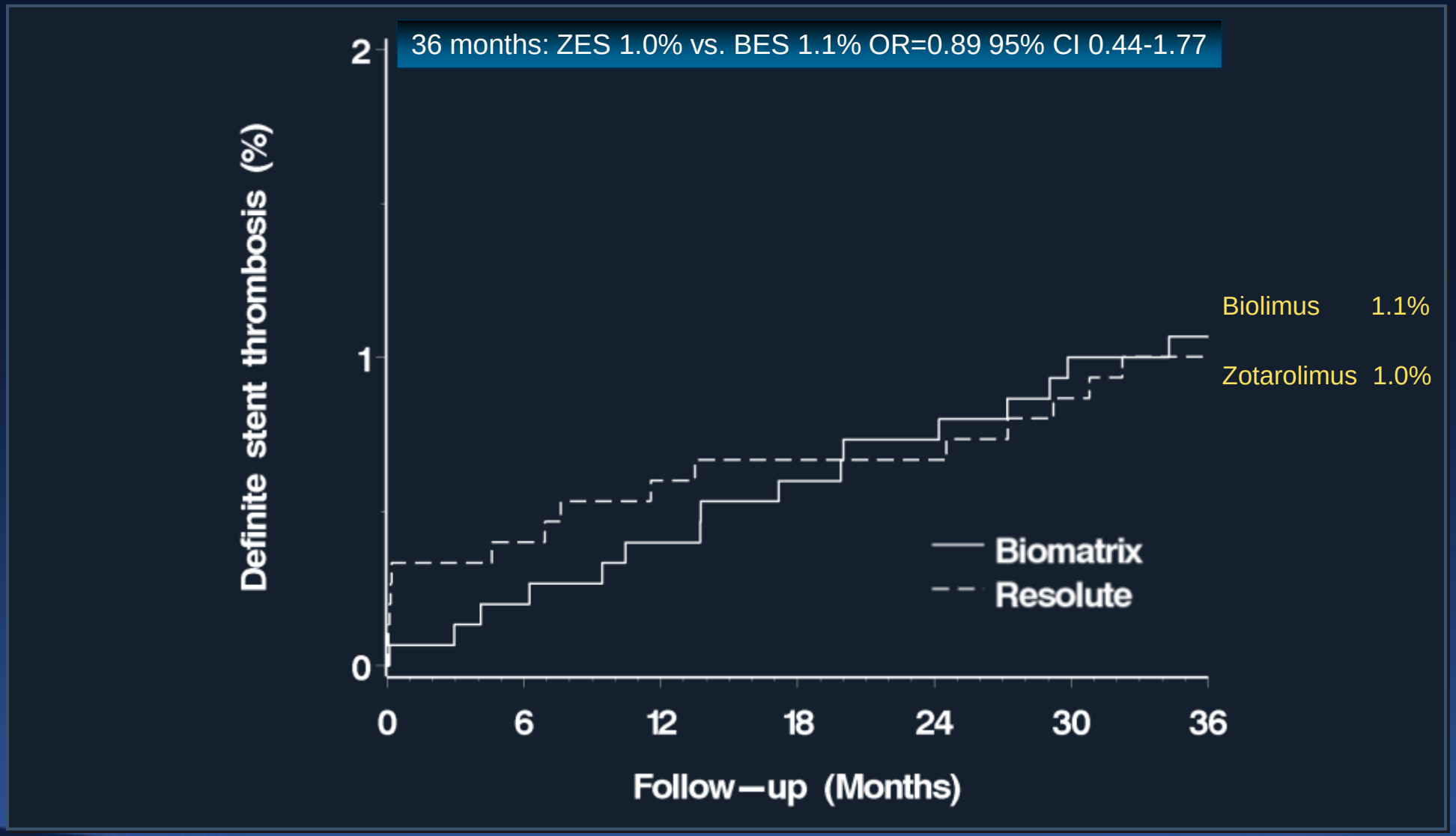
OR=1.31
95%CI:0.70-2.47
P=0.40

SO VI: MACE

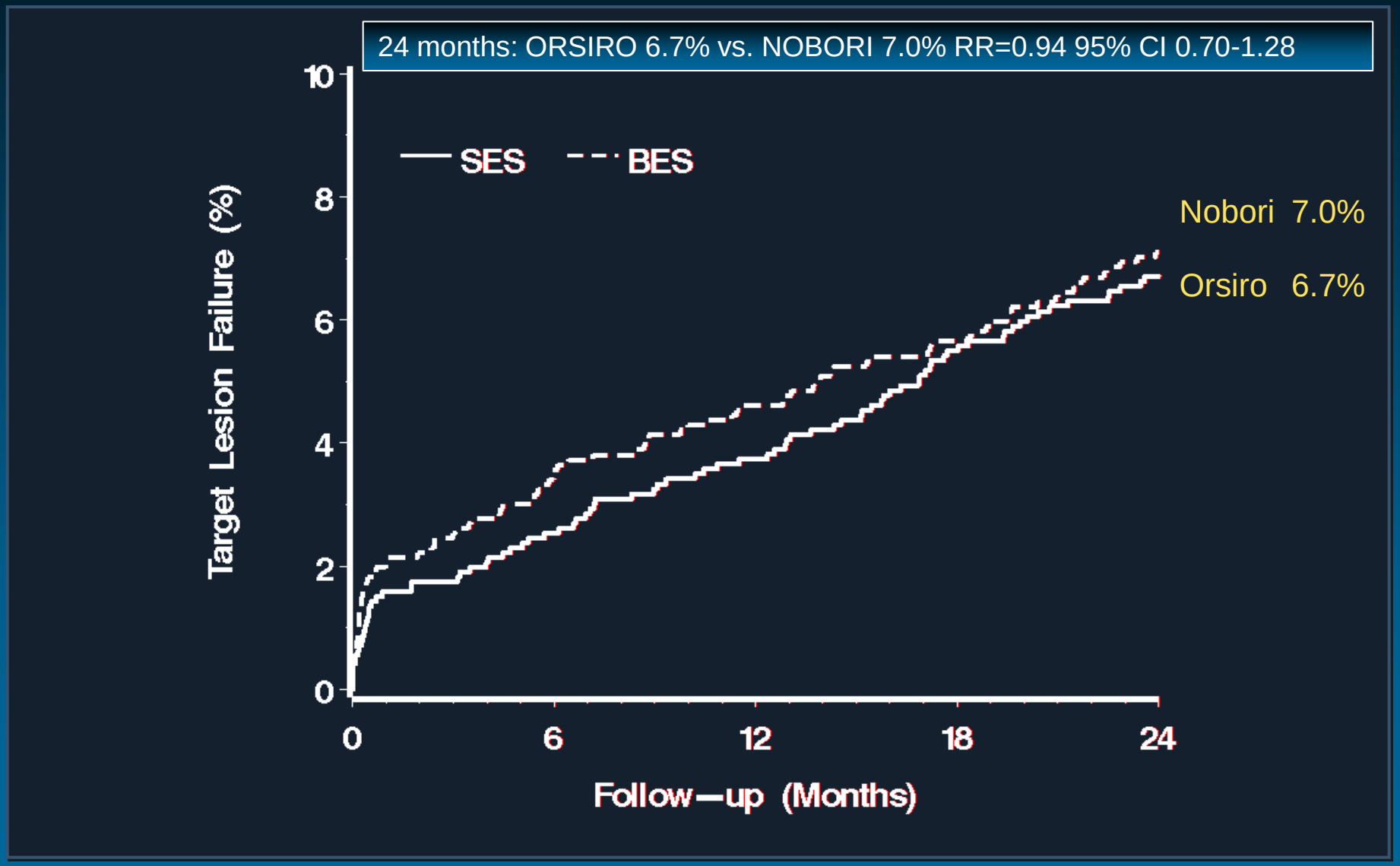
(Cardiac death, myocardial infarction, target lesion revascularization)



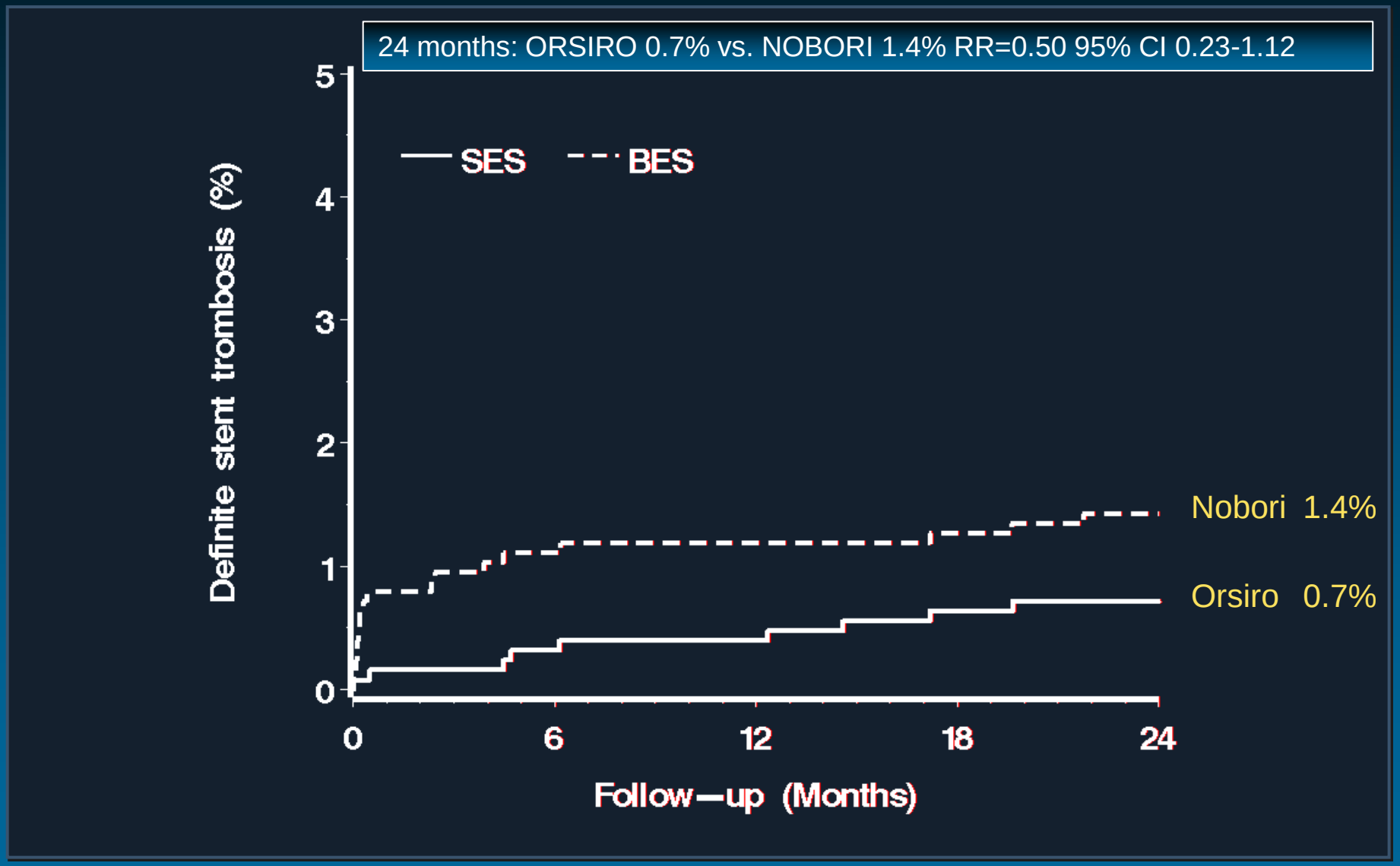
SO VI Stent Thrombosis



SO VII: Target Lesion Failure



SO VII: Definite Stent Thrombosis

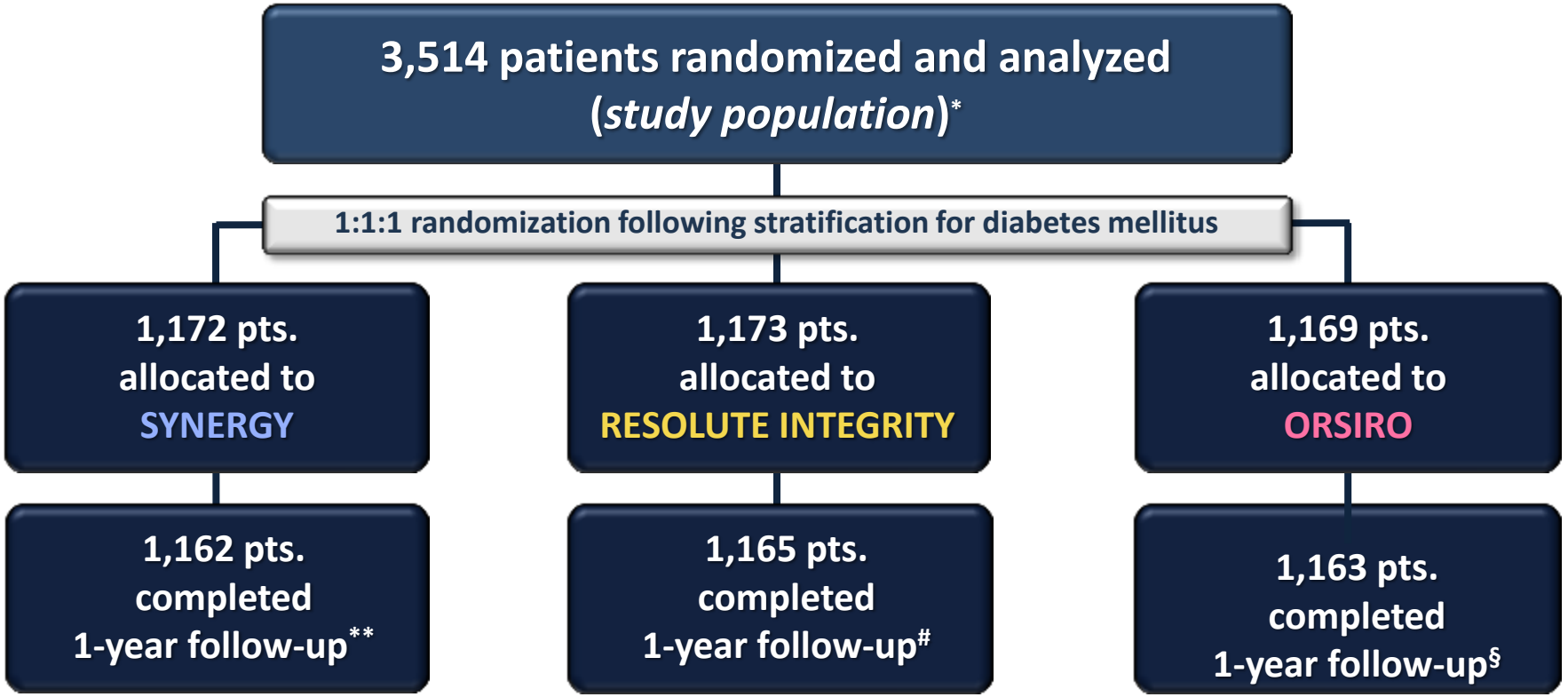


Conclusion SORT OUT Series

- Compared to SES, the last generation of EES, ZES, or BES may have the potential to reduce the rate of stent thrombosis to a very low rate. ***(SORT OUT III, IV, V)***

- There was no between-group difference of polymer-durable and –free (any drug) DES with respect to efficacy and safety outcome. ***(SORT OUT VI, VII)***

BIO-RESORT (TWENTE III)

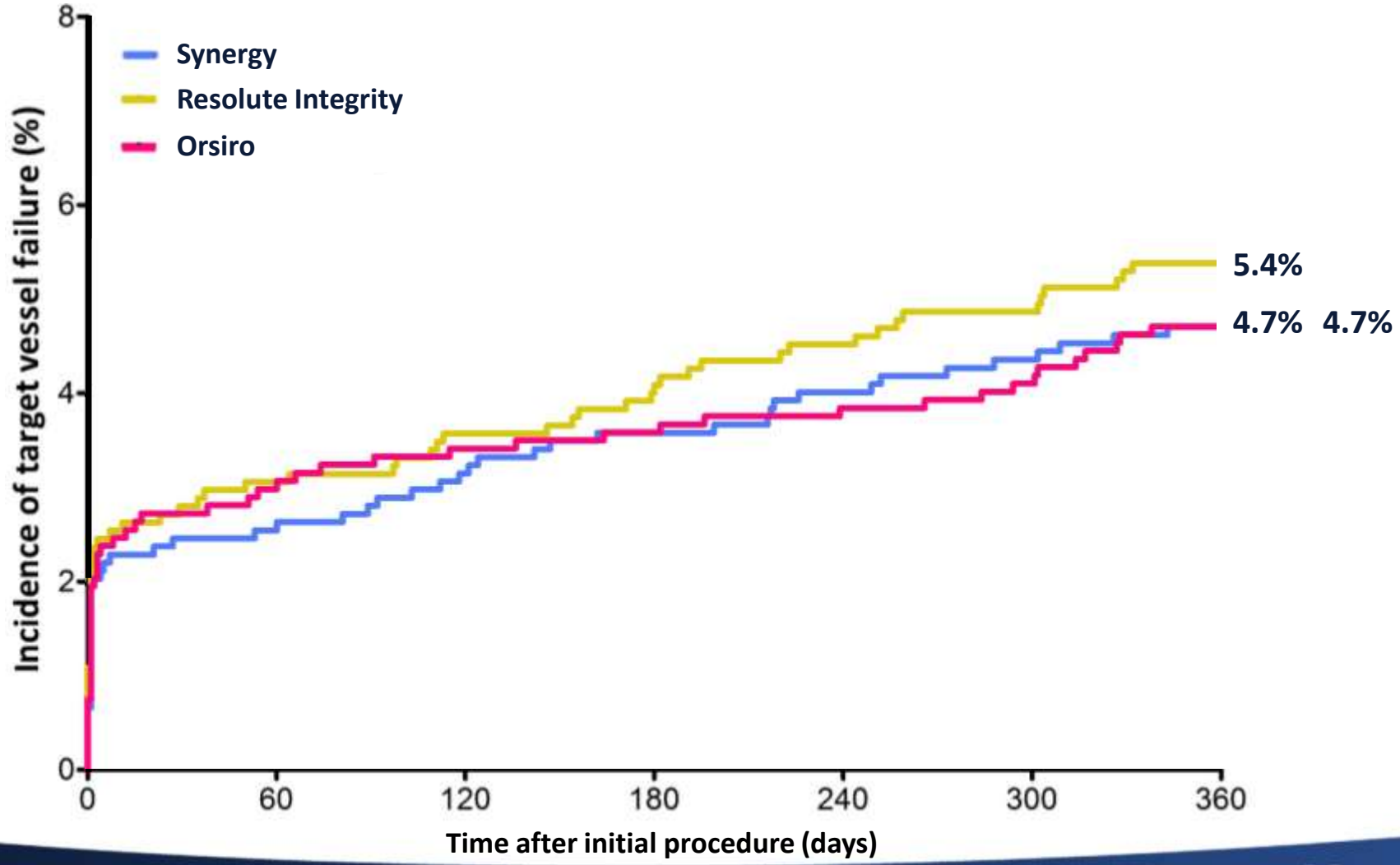


- 1-year follow-up data were obtained from 99.3% of the study population, which represents 99.9% of the patients who still participated in the trial or had died.
- During the first year of follow-up, 21 patients (0.6%) withdrew consent, while only 3 / 3,514 patients (< 1 ‰) were actually "lost" (i.e., could not be contacted).

* During active study enrollment, 7,928 patients were treated with DES (no data on the number of eligible patients are available). 3,545 pts. were initially randomized; 31 pts. were excluded; 3,514 pts. were analyzed and represent the study population.
** 2 patients lost to follow-up, 8 patients withdrew consent; # 1 patient lost to follow-up, 7 patients withdrew consent;
§ 6 patients withdrew consent. Monitoring and an independent clinical event adjudication (CEC) by CRO Diagram, Zwolle. Analyses were based on intention to treat.

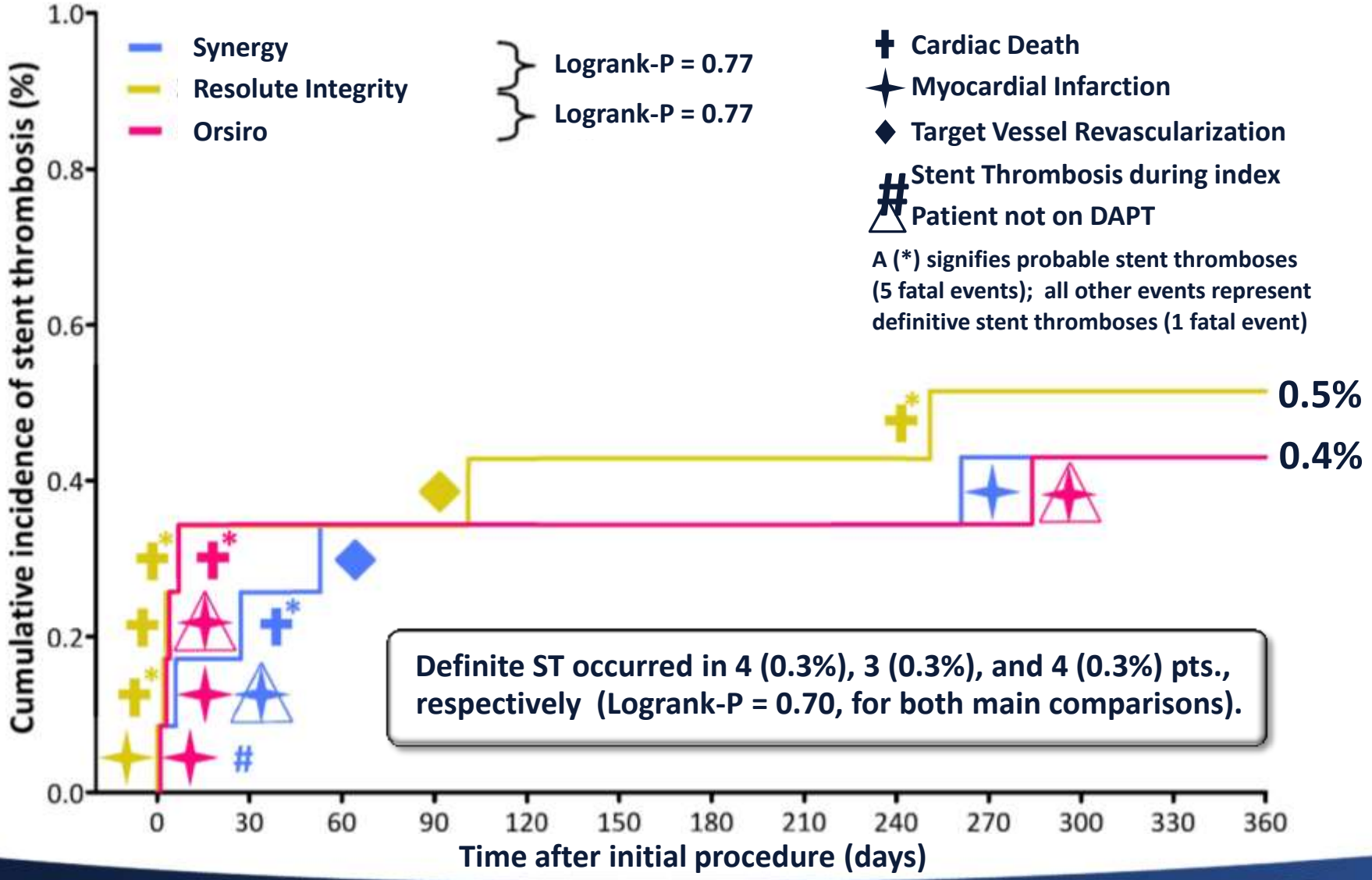
Primary Endpoint

Target Vessel Failure at 1-Year Follow-Up



Target Vessel Failure is a composite of cardiac death, target vessel-related MI, or clinically driven target vessel revascularization.
Events displayed in the graph were calculated by Kaplan-Meier methods and compared with the log-rank test.

Definite or Probable Stent Thrombosis

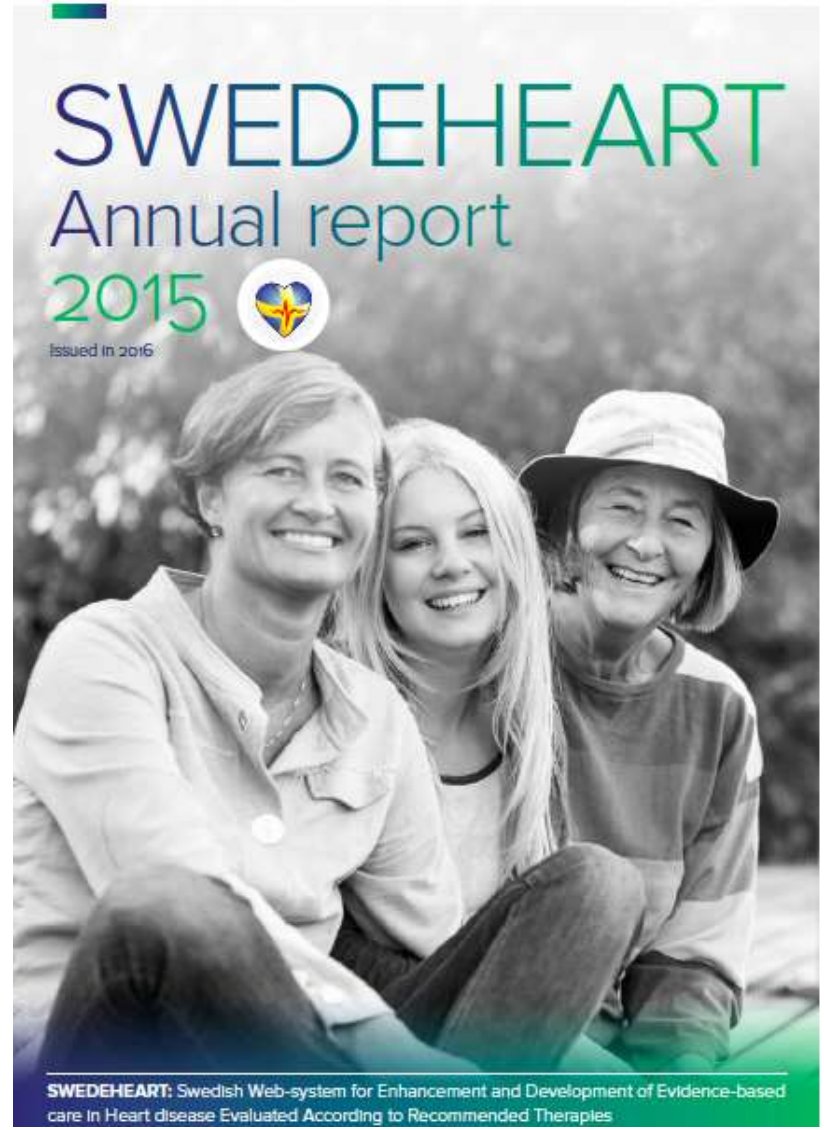


Stent thrombosis (ST) was defined according to the Academic Research Consortium (ARC). DAPT = dual antiplatelet therapy.

SWEDE HEART

Number of cases annually: 80 000

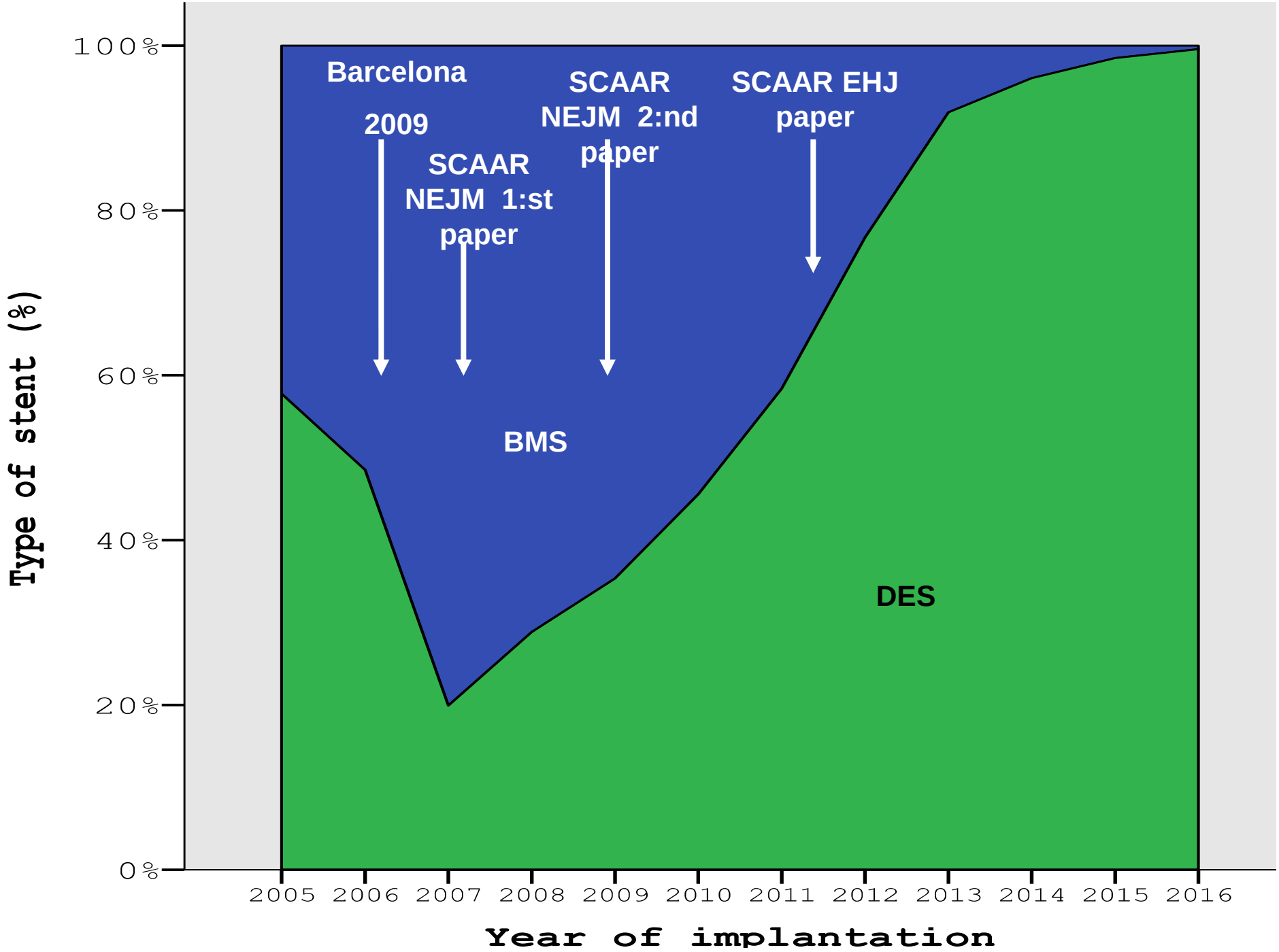
RIKS-HIA	**73 CCU hospitals, 100%**
SCAAR	**30 PCI hospitals, 100%**
Percutaneous valves	**7 hospitals, 100%**
Heart surgery	**7 hospitals, 100%**
Secondary prevention	**65 hospitals, 85%**
Cardiogenetic registry	**New**

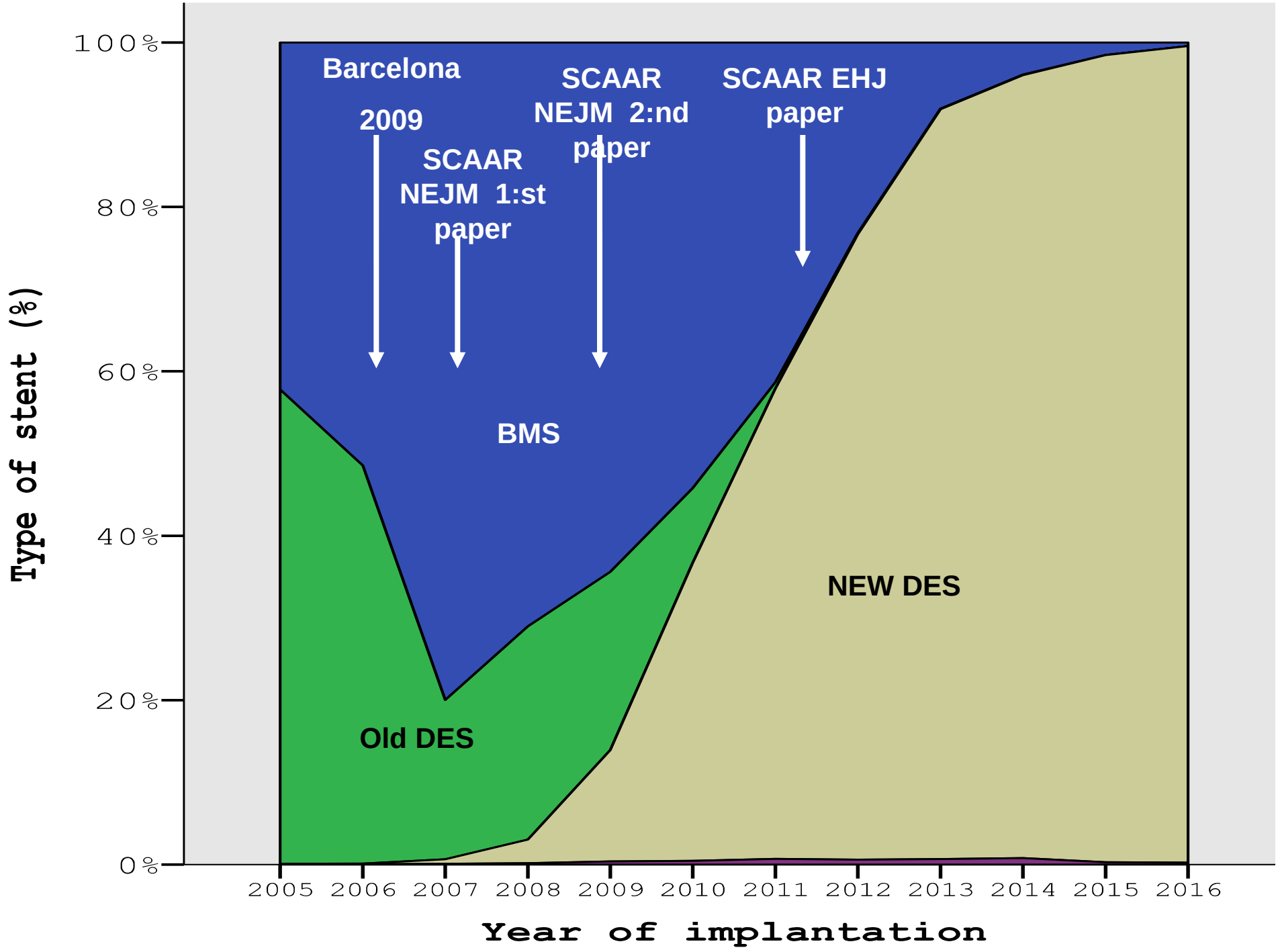


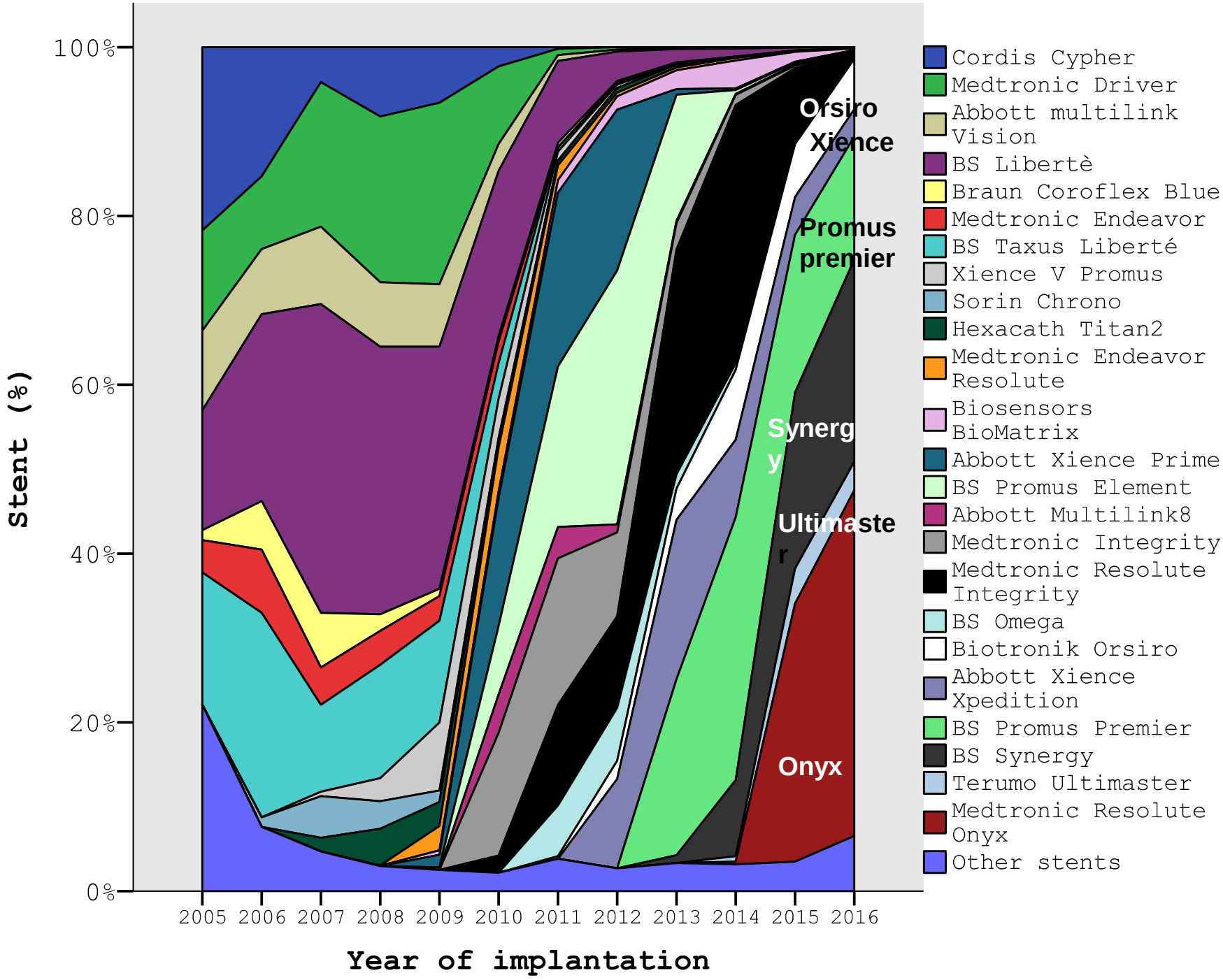
>300 variables (Baseline data, procedural and outcome measures)

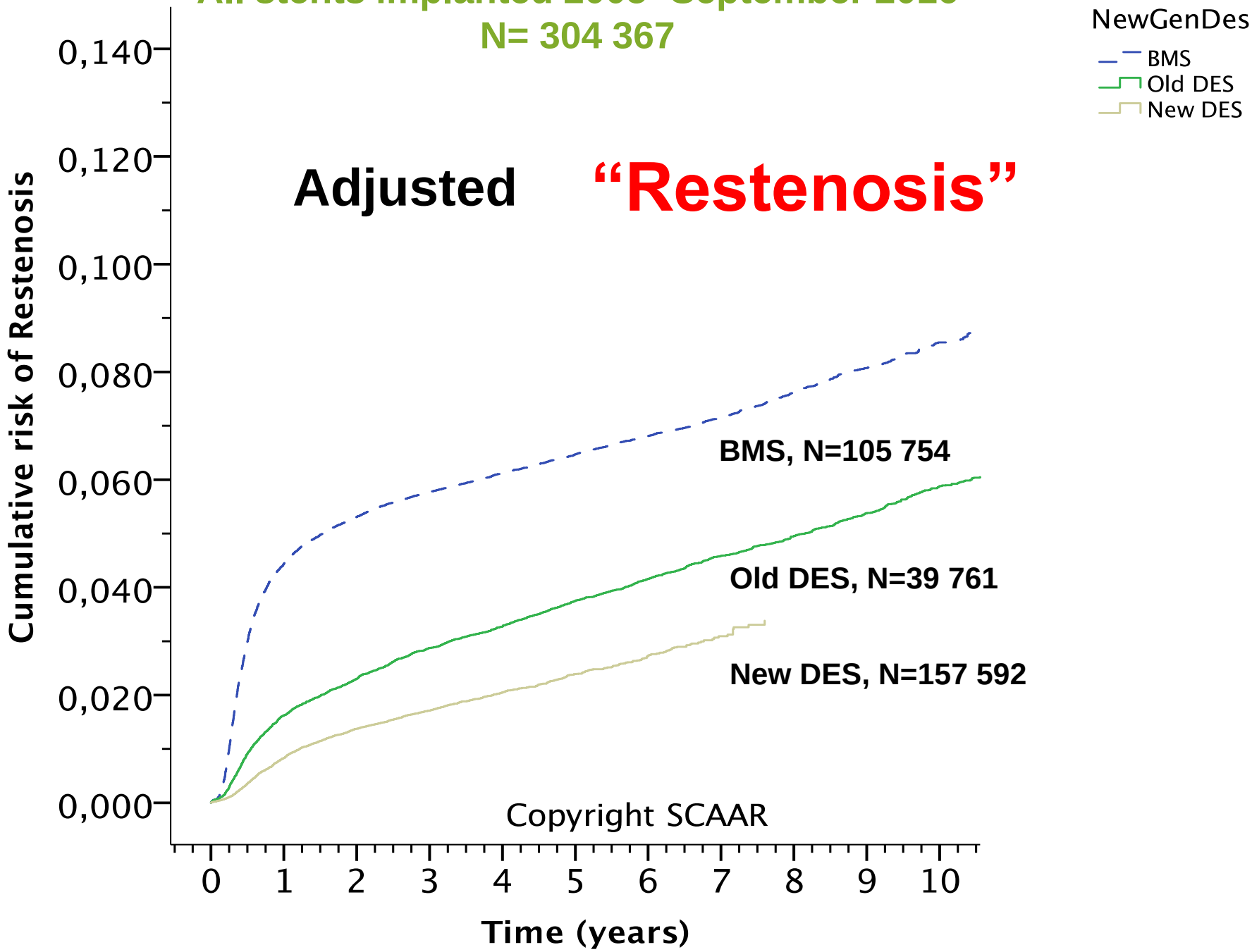
At monitoring: 95-96% agreement between files and registry.

UCR

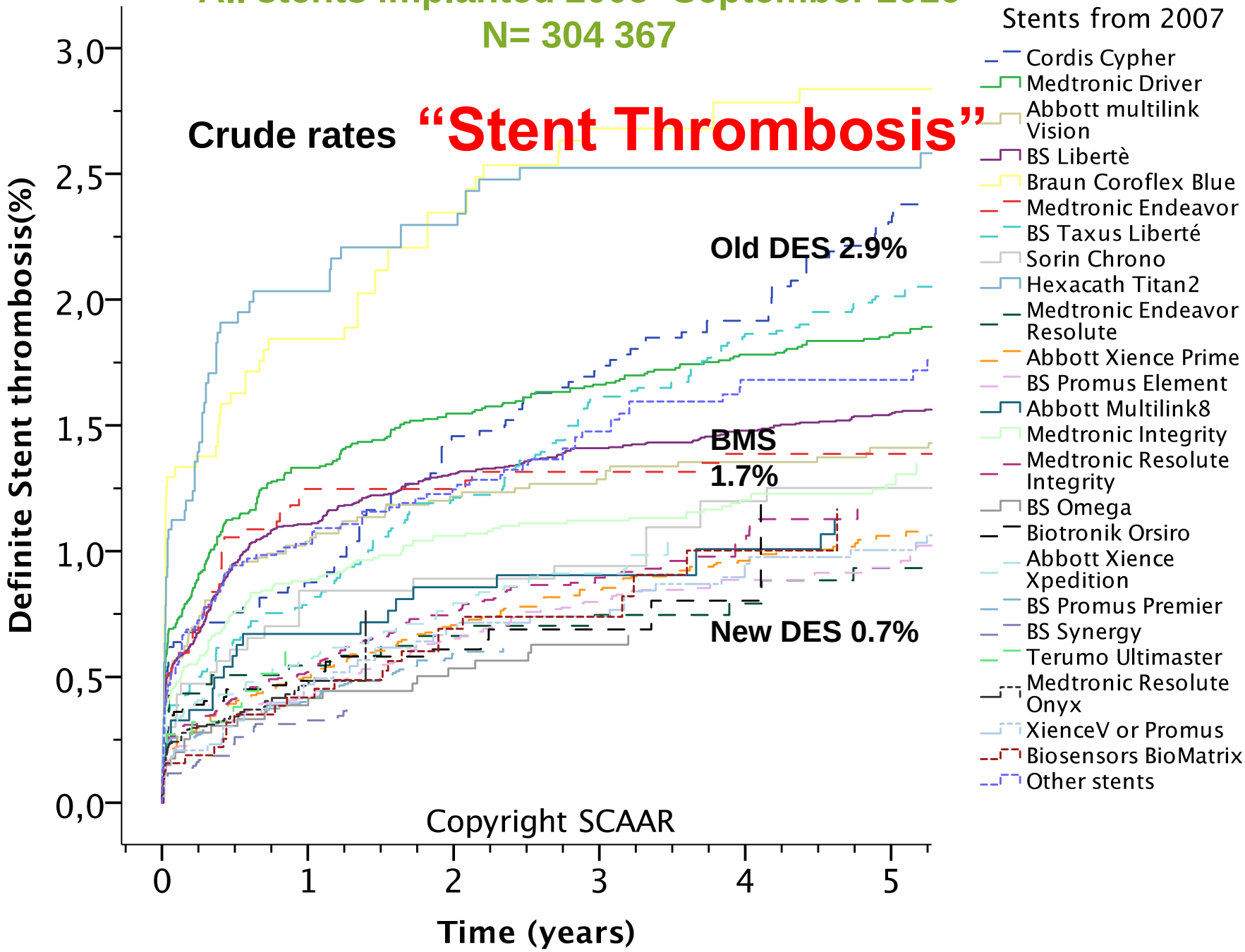

100%
80%
60%
40%
20%
0%
Type of stent (%)
Barcelona
2009
SCAAR
NEJM 1:st
paper
SCAAR
NEJM 2:nd
paper
SCAAR EHJ
paper
BMS
DES
2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016
Year of implantation

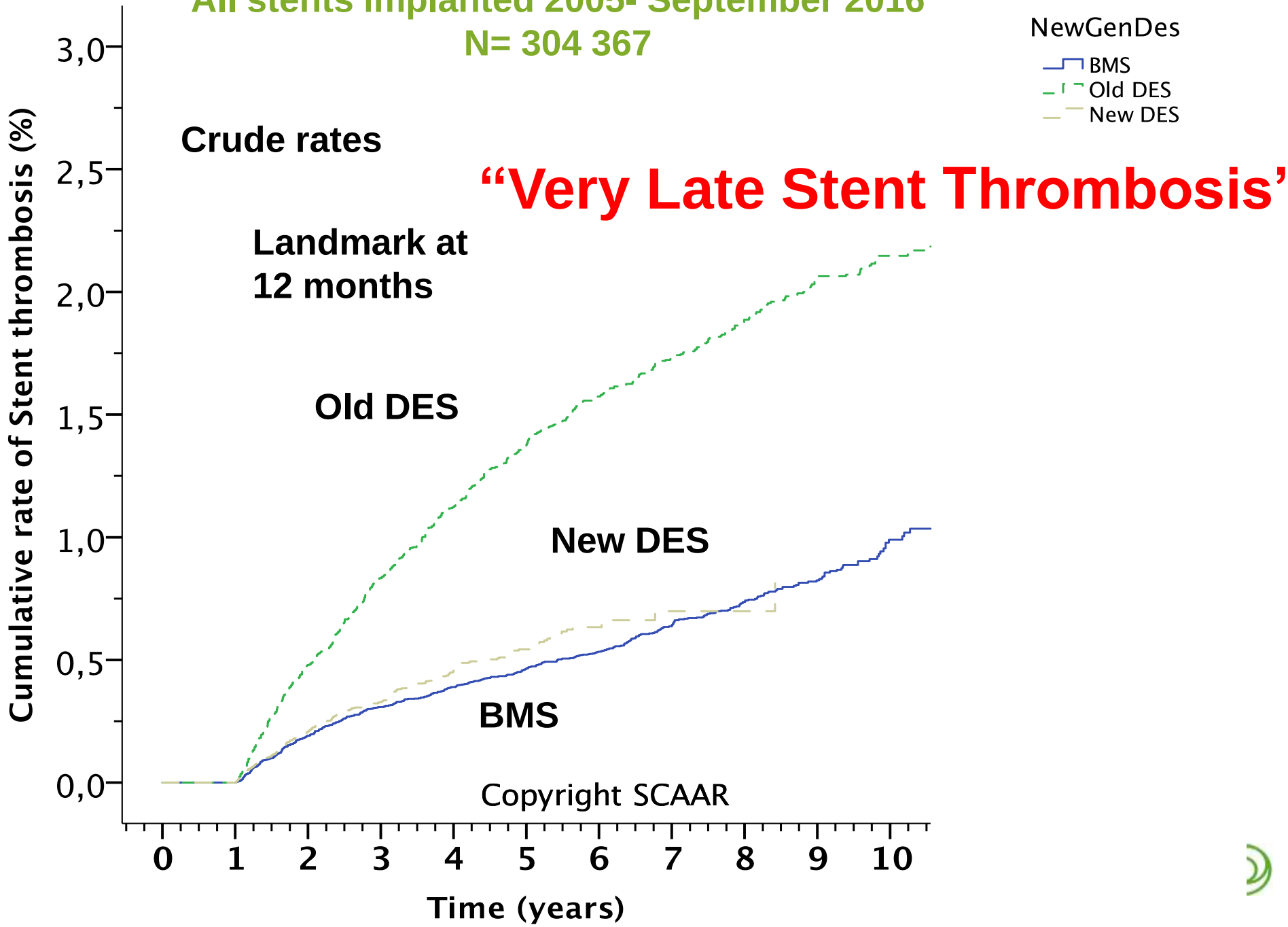

100%
80%
60%
40%
20%
0%
Type of stent (%)
Barcelona
2009
SCAAR
NEJM 1:st
paper
SCAAR
NEJM 2:nd
paper
SCAAR EHJ
paper
BMS
Old DES
NEW DES
2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016
Year of implantation


100%
80%
60%
40%
20%
0%
Stent (%)
2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016
Year of implantation
Orsiro
Xience
Promus
premier
Synerg
y
Ultimaste
r
Onyx
Cordis Cypher
Medtronic Driver
Abbott multilink Vision
BS Libertè
Braun Coroflex Blue
Medtronic Endeavor
BS Taxus Liberté
Xience V Promus
Sorin Chrono
Hexacath Titan2
Medtronic Endeavor Resolute
Biosensors BioMatrix
Abbott Xience Prime
BS Promus Element
Abbott Multilink8
Medtronic Integrity
Medtronic Resolute Integrity
BS Omega
Biotronik Orsiro
Abbott Xience Xpedition
BS Promus Premier
BS Synergy
Terumo Ultimaster
Medtronic Resolute Onyx
Other stents

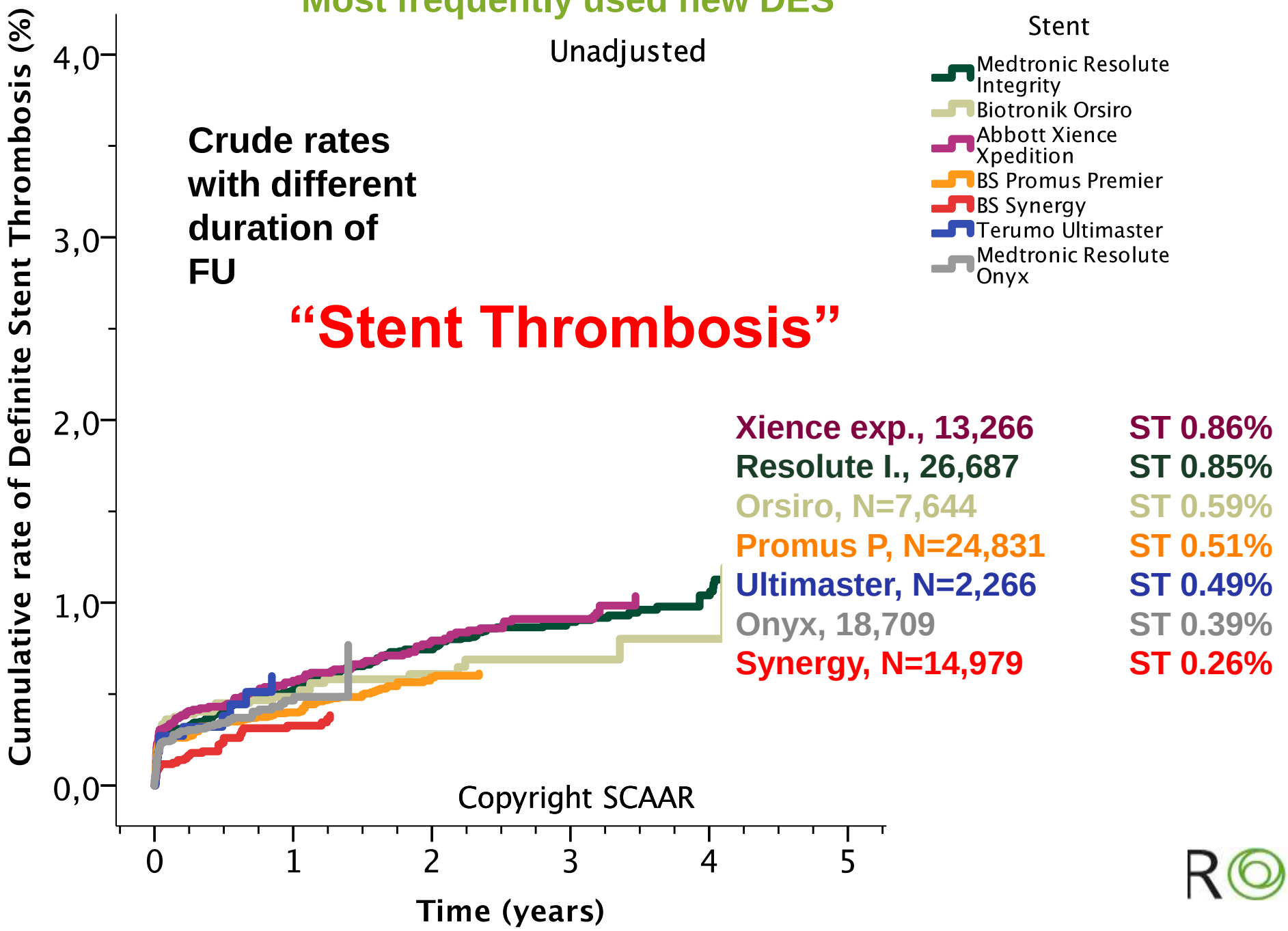

All stents implanted 2005- September 2016
N= 304 367
NewGenDes
BMS
Old DES
New DES
Adjusted
"Restenosis"
Cumulative risk of Restenosis
0,140
0,120
0,100
0,080
0,060
0,040
0,020
0,000
BMS, N=105 754
Old DES, N=39 761
New DES, N=157 592
Copyright SCAAR
0
1
2
3
4
5
6
7
8
9
10
Time (years)

All stents implanted 2005- September 2016
N= 304 367




All stents implanted 2005- September 2016
N= 304 367
NewGenDes
BMS
Old DES
New DES
Crude rates
"Very Late Stent Thrombosis"
Landmark at
12 months
Old DES
New DES
BMS
Copyright SCAAR
Cumulative rate of Stent thrombosis (%)
3,0
2,5
2,0
1,5
1,0
0,5
0,0
0
1
2
3
4
5
6
7
8
9
10
Time (years)

Most frequently used new DES



IRIS-DES Registry

Design

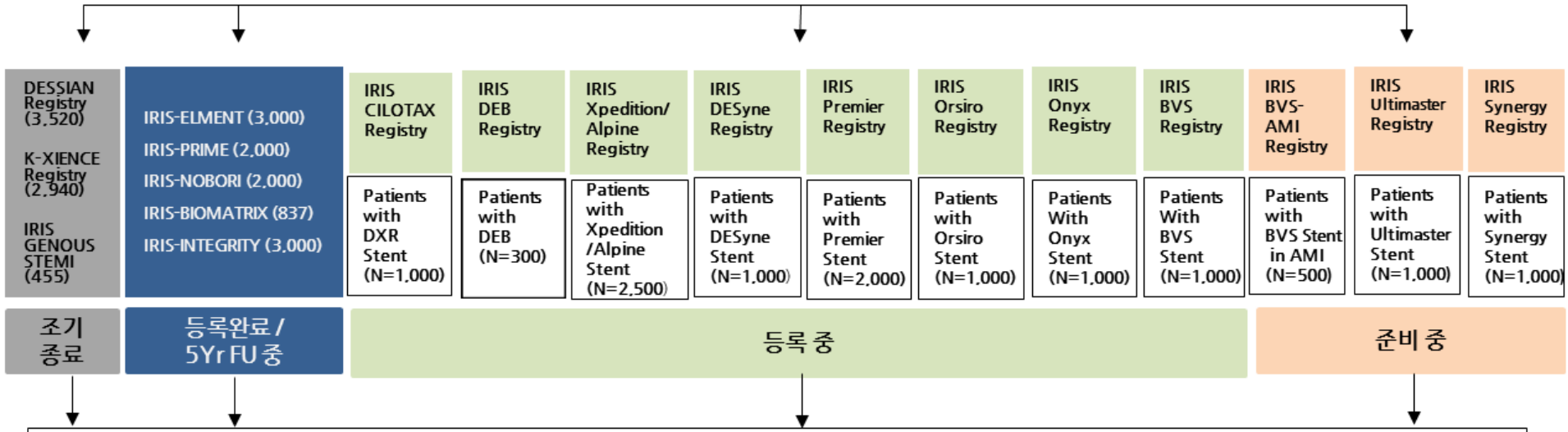
- DESIGN: An unrestricted, multicenter, prospective cohort
- OBJECTIVE: To compare the safety and efficacy of the second- or newer-generation DES and the first-generation DES in everyday clinical practice,
- PRINCIPAL INVESTIGATOR
  Seung-Jung Park, MD, PhD, Asan Medical Center, Seoul, Korea

Evaluation of Effectiveness and Safety of the First, Second, and New Drug-Eluting Stents in Routine Clinical Practice;

IRIS-DES Registry

Consecutive PCI patients receiving New DES without a mixture of other DES

Prospective Enrollment



Clinical follow-up at 1-, 6-, and 12-months, and annually up to 5 years

***Primary end point: Composite of Death, MI, and TVR at 12-months**

Outcomes After Unrestricted Use of Everolimus-Eluting and Sirolimus-Eluting Stents in Routine Clinical Practice

A Multicenter, Prospective Cohort Study

Duk-Woo Park, MD; Young-Hak Kim, MD; Hae-Geun Song, MD; Jung-Min Ahn, MD; Won-Jang Kim, MD; Jong-Young Lee, MD; Soo-Jin Kang, MD; Seung-Whan Lee, MD; Cheol Whan Lee, MD; Seong-Wook Park, MD; Sung-Cheol Yun, PhD; Sung Ho Her, MD; Seung Ho Hur, MD; Jin Sik Park, MD; Myeong-Kon Kim, MD; Yun Seok Choi, MD; Hyun Sook Kim, MD; Jang-Hyun Cho, MD; Sang Gon Lee, MD; Yong Whi Park, MD; Myung-Ho Jeong, MD; Bong Ki Lee, MD; Nae-Hee Lee, MD; Do-Sun Lim, MD; Junghan Yoon, MD; Ki Bae Seung, MD; Won-Yong Shin, MD; Seung-Woon Rha, MD; Kee-Sik Kim, MD; Seung-Jea Tahk, MD; Byoung Eun Park, MD; Taehoon Ahn, MD; Joo-Young Yang, MD; Yong Seok Jeong, MD; Jay-Hyun Rhew, MD; Seung-Jung Park, MD; for the IRIS-DES Investigators*

Background—It remains unclear whether there are differences in the safety and efficacy outcomes between everolimus-eluting stents (EES) and sirolimus-eluting stents (SES) in contemporary practice.

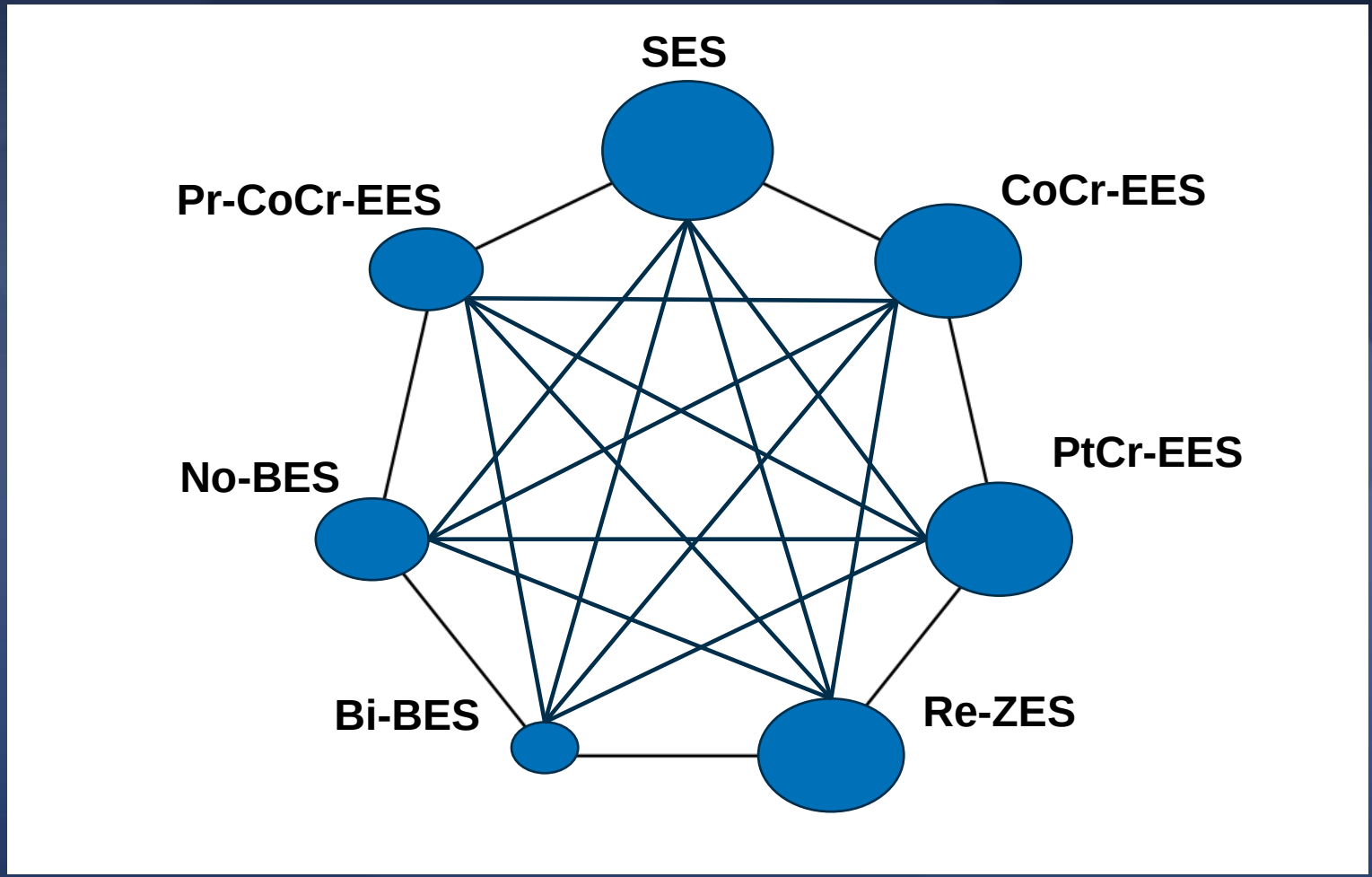
Methods and Results—We prospectively enrolled 6166 consecutive patients who received EES (3081 patients) and SES (3085 patients) between April 2008, and June 2010, using data from the Interventional Cardiology Research In-Cooperation Society-Drug-Eluting Stents Registry. The primary end point was a composite of death, nonfatal myocardial infarction (MI), or target-vessel revascularization (TVR). At 2 years of follow-up, the 2 study groups did not differ significantly in crude risk of the primary end point (12.1% for EES versus 12.4% for SES; HR, 0.97; 95% CI, 0.84–1.12, P=0.66). After adjustment for differences in baseline risk factors, the adjusted risk for the primary end point remained similar for the 2 stent types (HR, 0.96; 95% CI, 0.82–1.12, P=0.60). There were also no differences between the stent groups in the adjusted risks of the individual component of death (HR, 0.93; 95% CI, 0.67–1.30, P=0.68), MI (HR, 0.97; 95% CI, 0.79–1.18, P=0.74), and TVR (HR, 1.10; 95% CI, 0.82–1.49, P=0.51). The adjusted risk of stent thrombosis also was similar (HR, 1.16; 95% CI, 0.47–2.84, P=0.75).

Conclusions—In contemporary practice of percutaneous coronary intervention procedures, the unrestricted use of EES and SES showed similar rates of safety and efficacy outcomes with regard to death, MI, sent thrombosis, and TVR. Future longer-term follow-up is needed to better define the relative benefits of these drug-eluting stents.

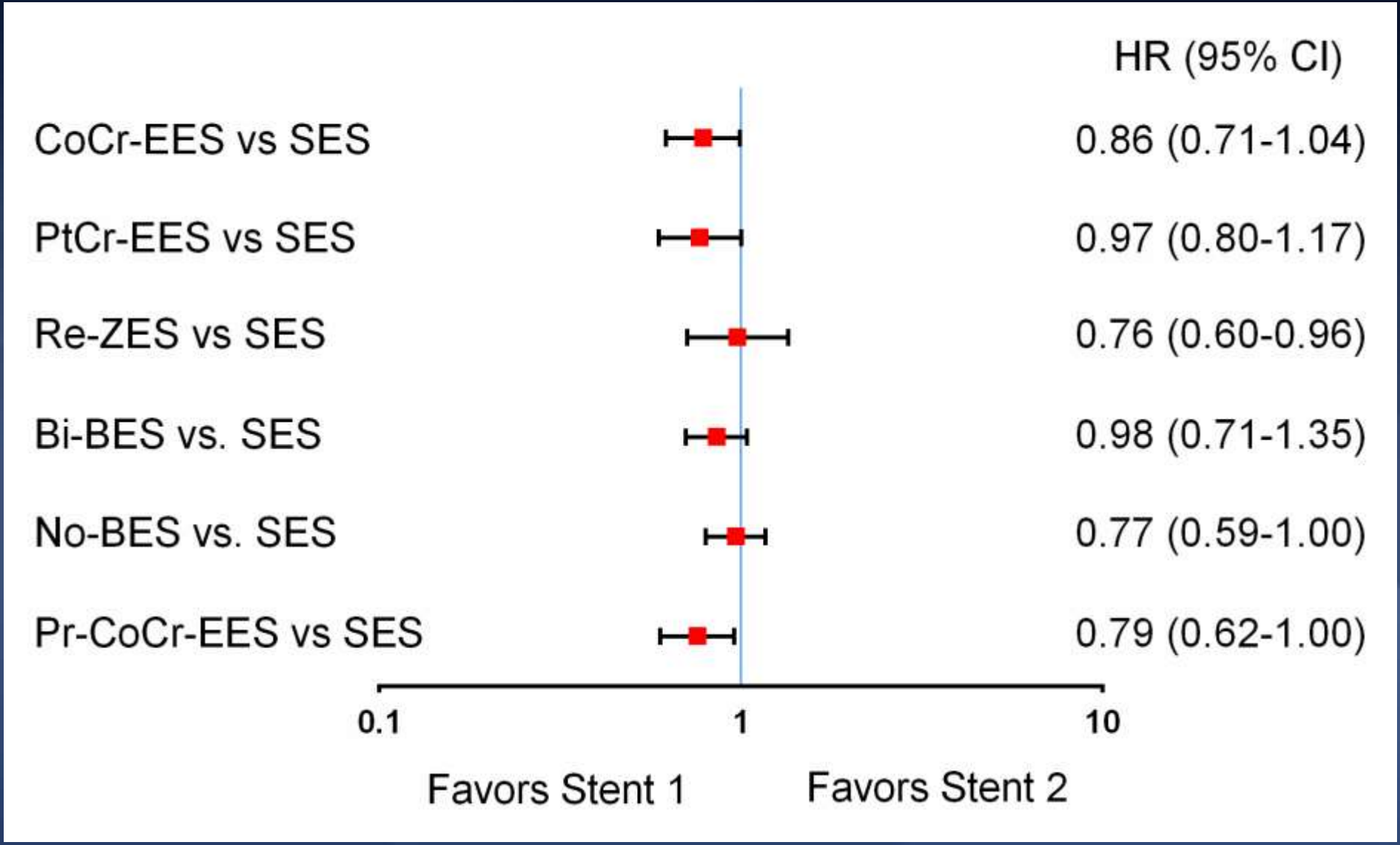
Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT01070420. ***(Circ Cardiovasc Interv*. 2012;5:365-371.)**

Updated Analysis of IRIS-DES Registry

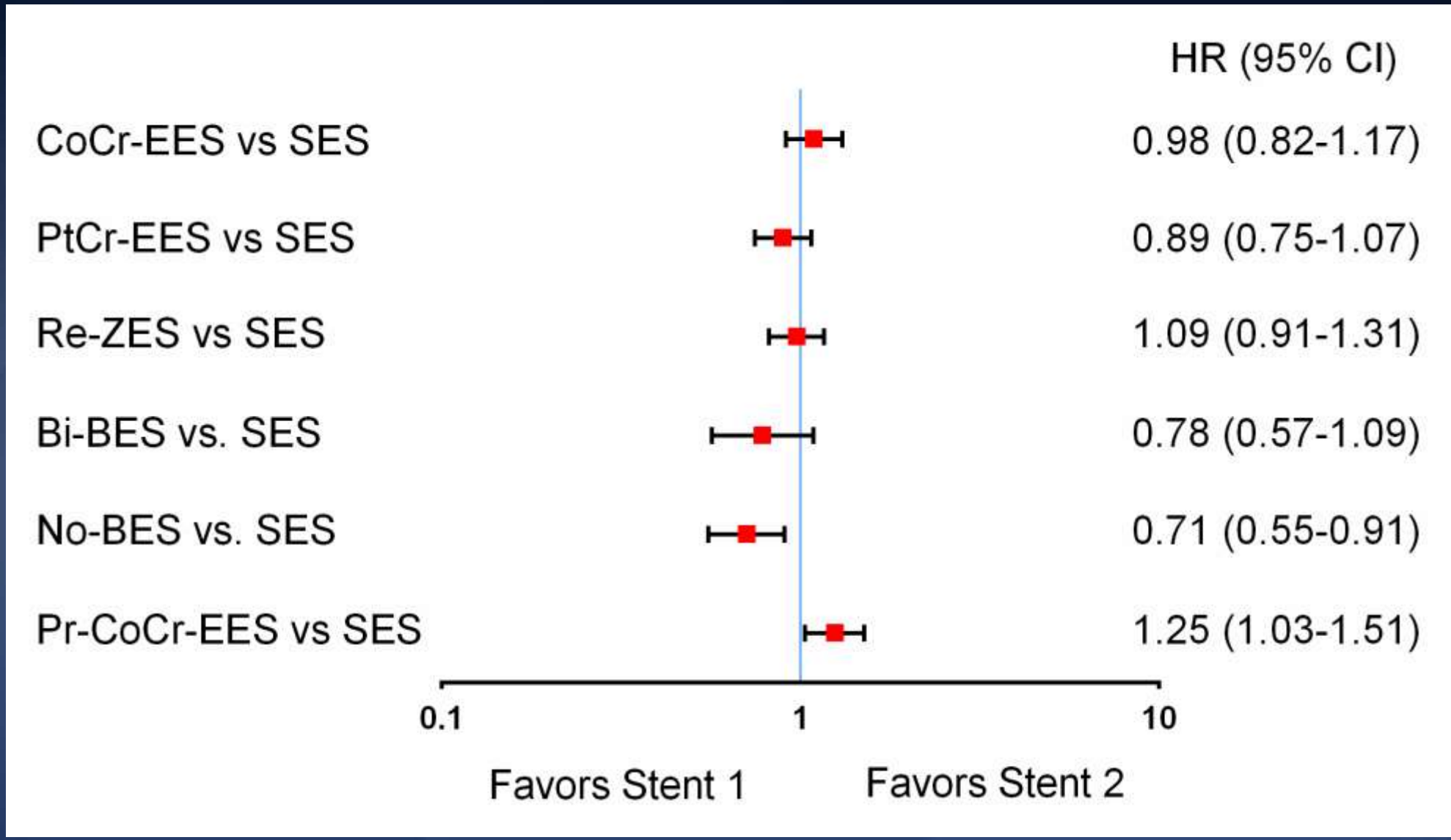
7 registry; 17,196 patients, median 3.3 years



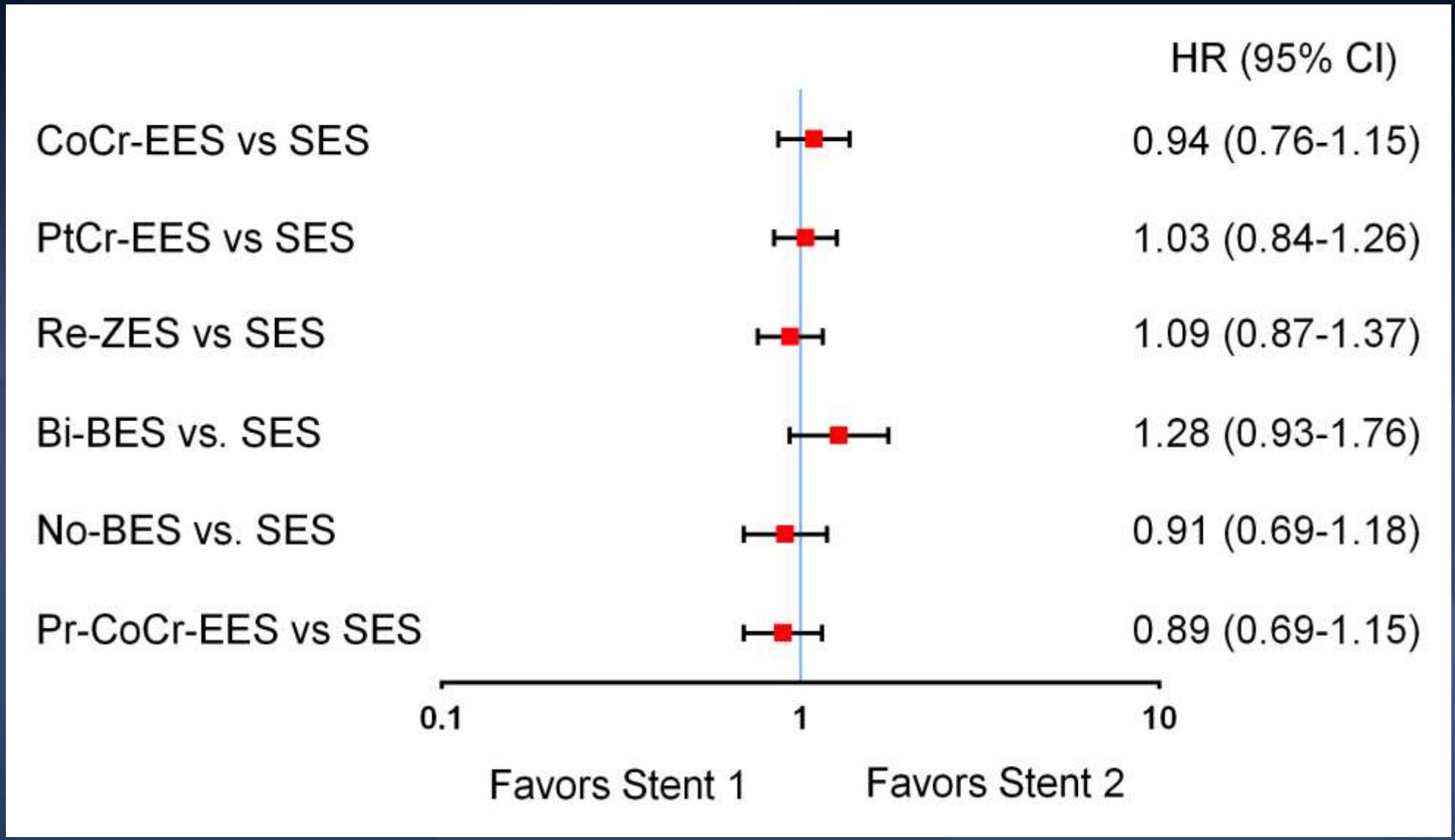
All-cause death



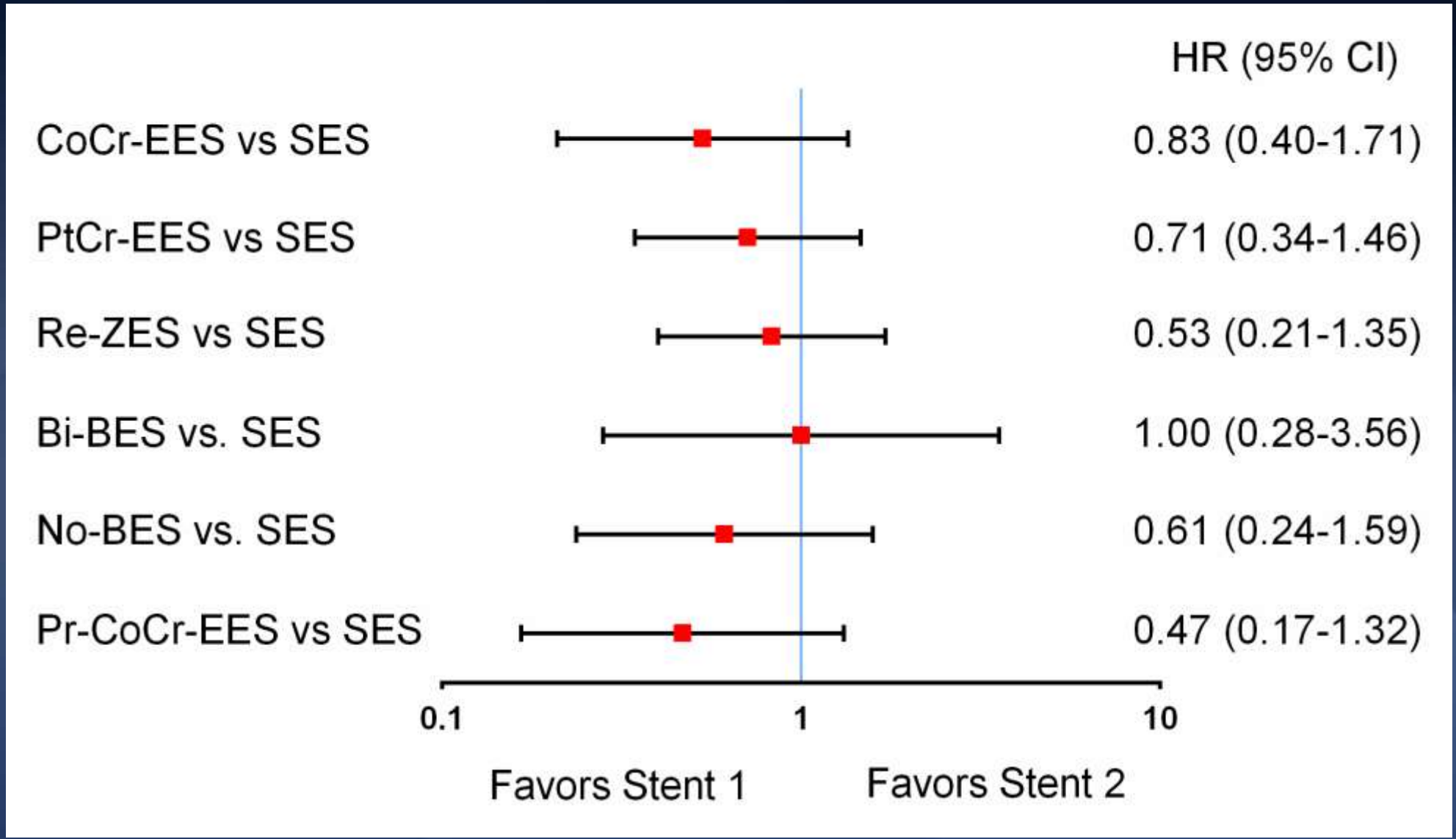
MI


HR (95% CI)
CoCr-EES vs SES
0.98 (0.82-1.17)
PtCr-EES vs SES
0.89 (0.75-1.07)
Re-ZES vs SES
1.09 (0.91-1.31)
Bi-BES vs. SES
0.78 (0.57-1.09)
No-BES vs. SES
0.71 (0.55-0.91)
Pr-CoCr-EES vs SES
1.25 (1.03-1.51)
0.1
1
10
Favors Stent 1
Favors Stent 2

TVR

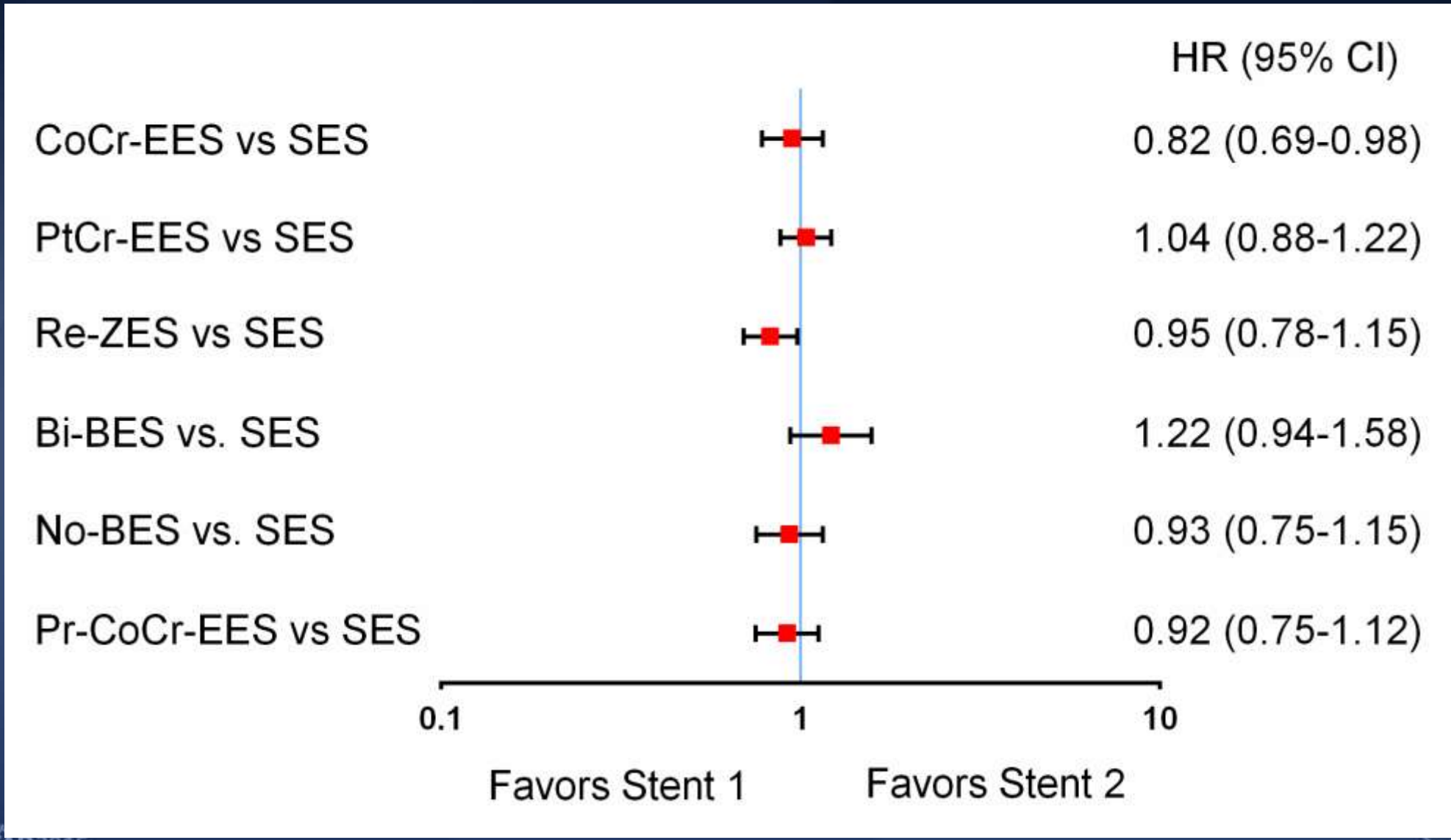

HR (95% CI)
CoCr-EES vs SES
0.94 (0.76-1.15)
PtCr-EES vs SES
1.03 (0.84-1.26)
Re-ZES vs SES
1.09 (0.87-1.37)
Bi-BES vs. SES
1.28 (0.93-1.76)
No-BES vs. SES
0.91 (0.69-1.18)
Pr-CoCr-EES vs SES
0.89 (0.69-1.15)
0.1
1
10
Favors Stent 1
Favors Stent 2

Definite or Probable ST



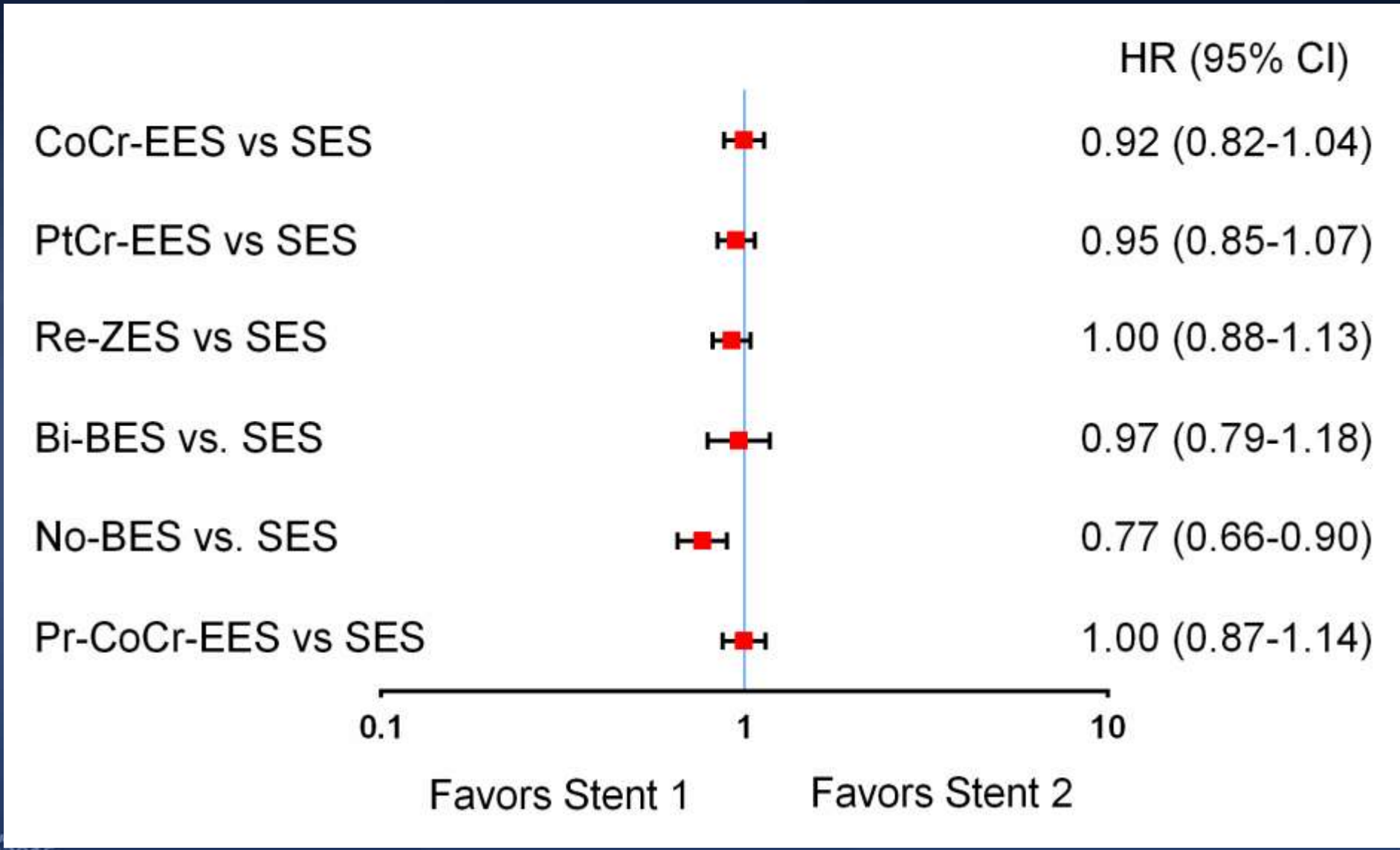
Target-vessel failure (TVF)

; CV death, target MI, or clinically indicated TVR



MACE

; Any death, any MI, or any TVR



Contemporary PCI with Second-Generation DES

- In contemporary DES era, there was no remarkable between-stent difference with respect to clinically relevant efficacy and safety outcomes
- We can choose any contemporary DES on the basis of clinical and lesion subsets and combined with the physician's preference.

Contemporary PCI with Second-Generation DES

- We now have reached a matured milestone in PCI with contemporary DES.
- However, “When technology stops continued innovation”, “The Knowledge will also stops”
  - Further effort for better device outcomes should not be stopped.