Cypher vs TAXUS
TAXUS vs Cypher

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Drug Eluting Stent

- Drug
- Polymer
- Stent design

Drug Eluting Stent

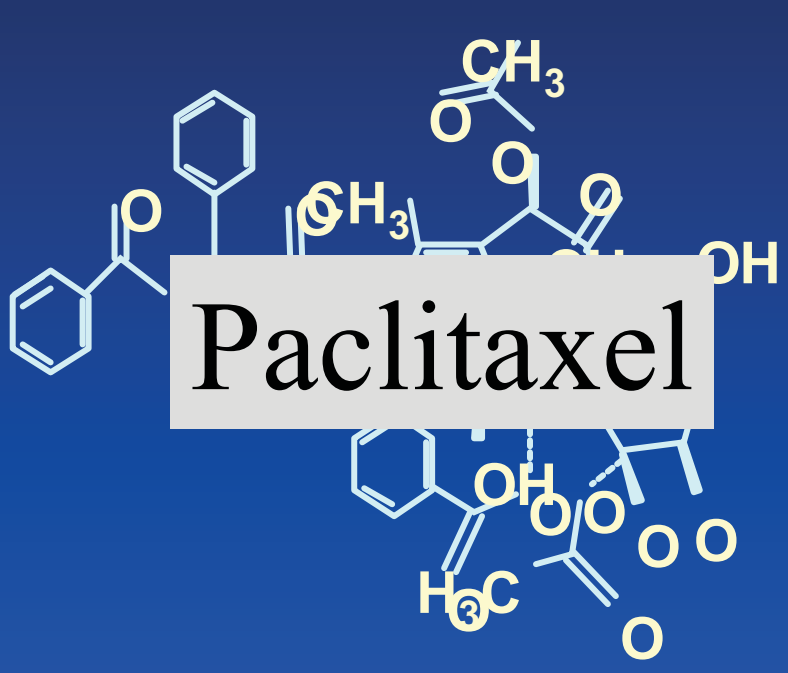
- Drug

Ideal Drug ?

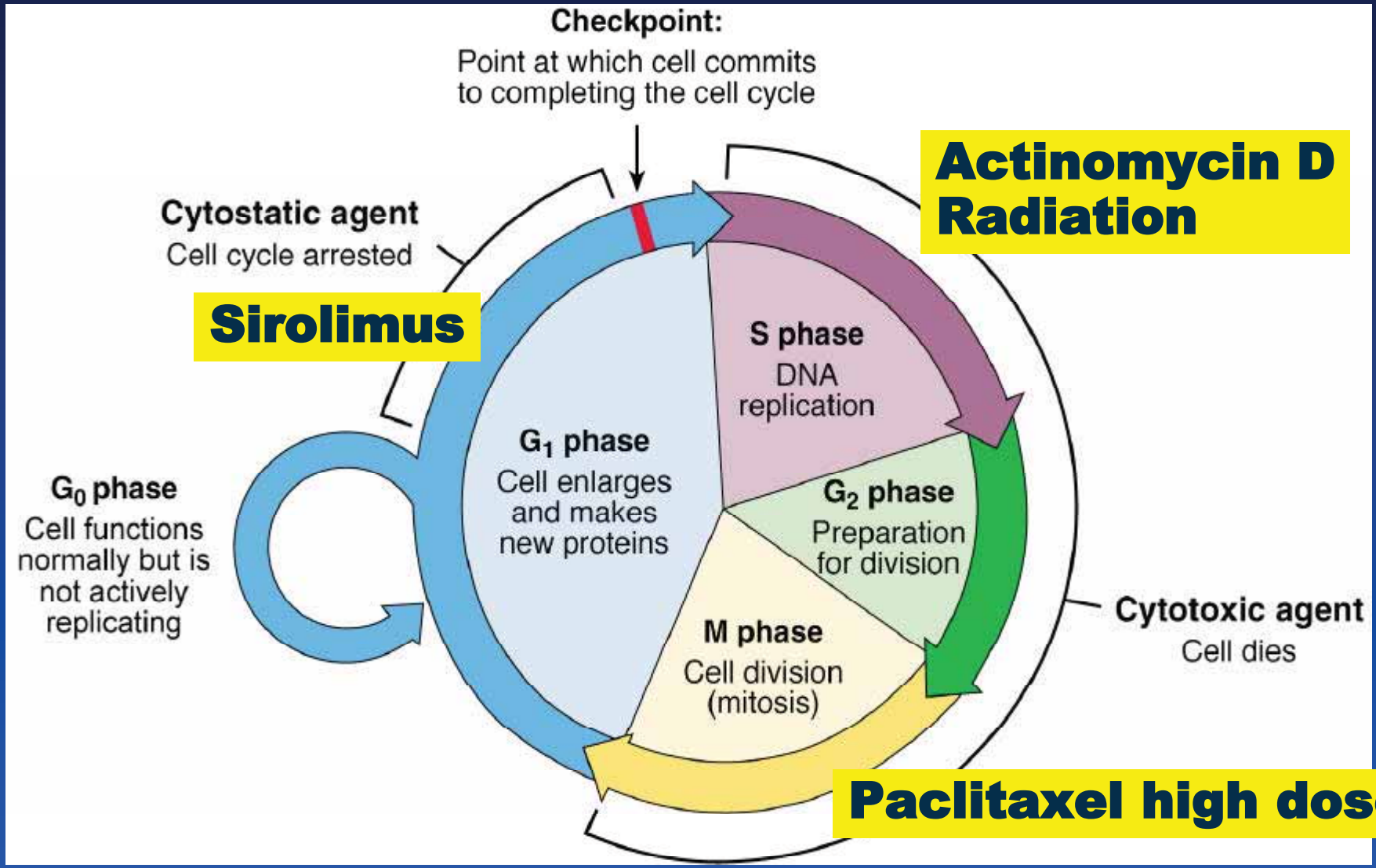
- Wide therapeutic dose range for least toxicity in local administration
- Ability to inhibit smooth muscle proliferation
- Allow normal endothelization of stent
- Low inflammatory response
- Controlled release

TAXUS vs Cypher

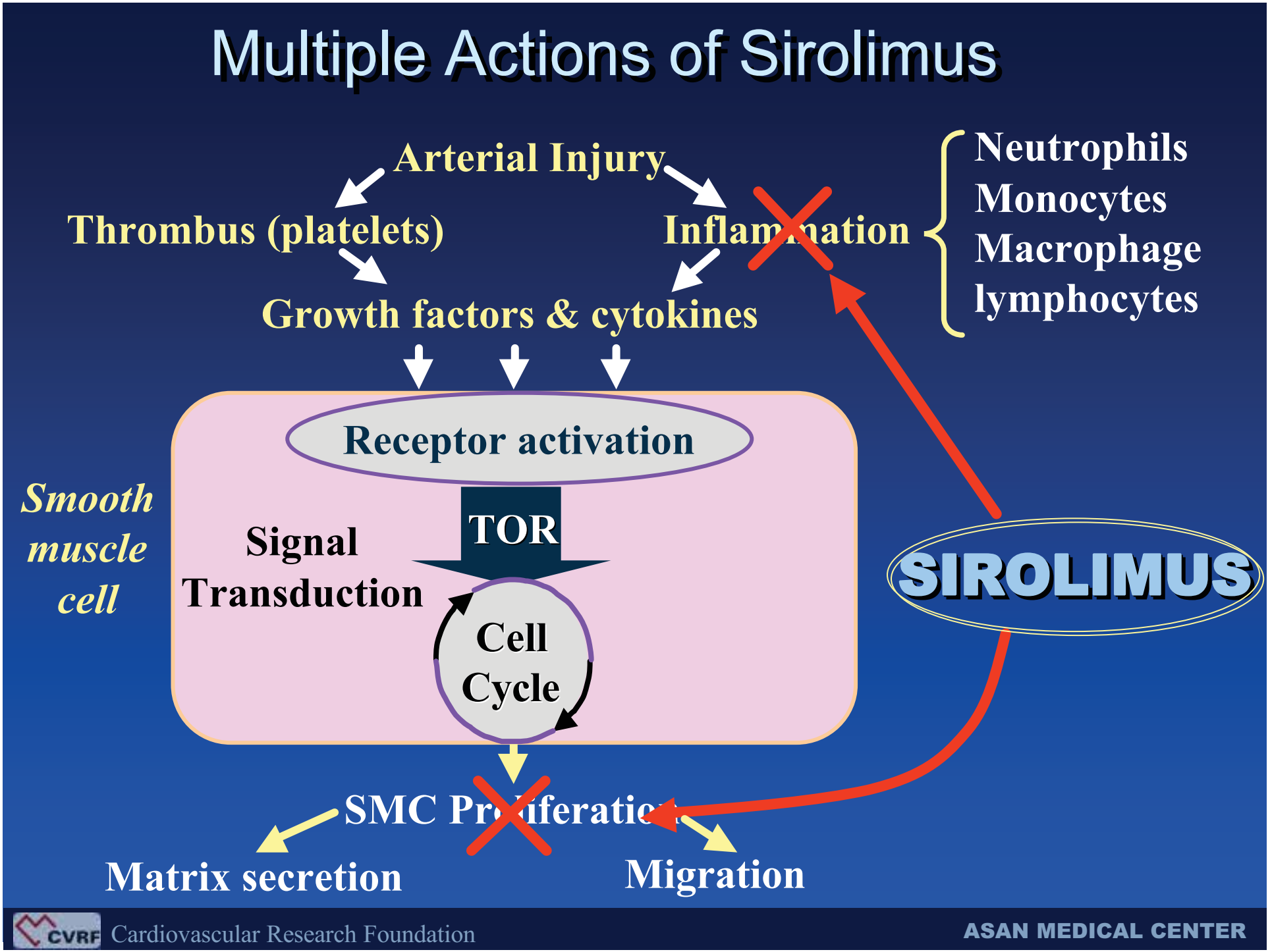
Drug

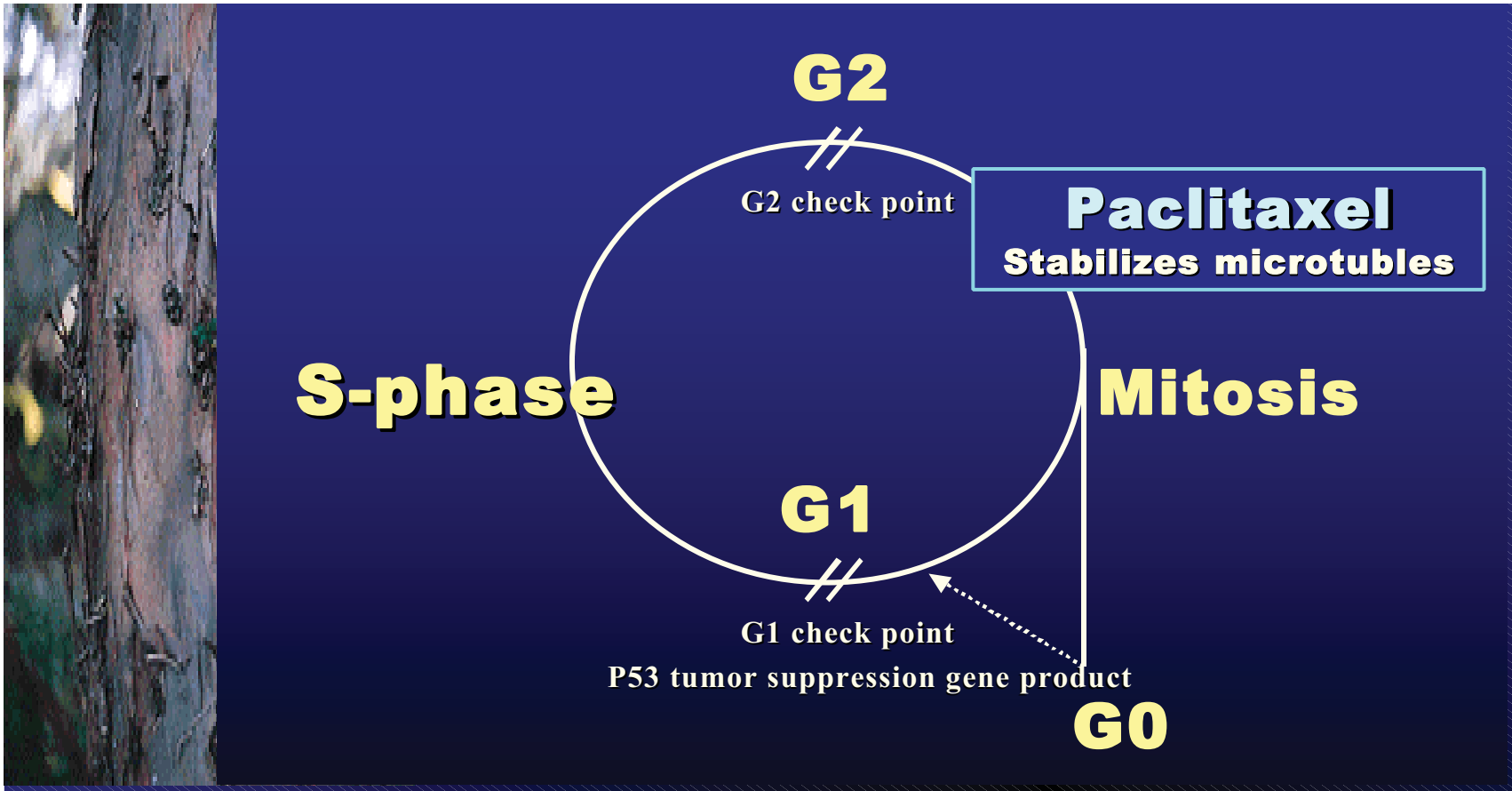


Cytostatic ? Cytotoxic ?



Multiple Actions of Sirolimus





Paclitaxel inhibits cell processes dependent on microtubule turnover including mitosis, cell proliferation and cell migration while the cells remain viable.

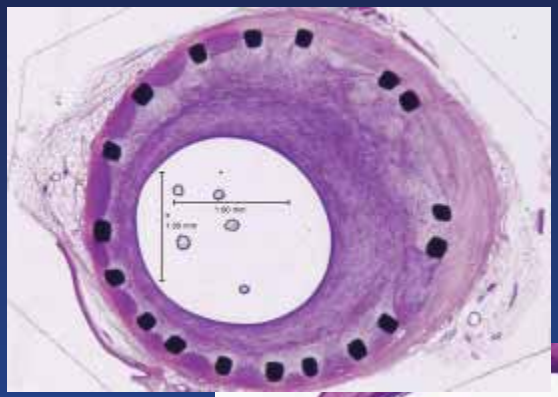
Dose Comparison

	Concentration*	Ther. Window
Guidant - Act D	2.5, 10	2.5 - 60
BSC - Taxol	50	15 - 90
Cook - Taxol	15, 30, 60, 90	15 - 90
Cordis - Sirolimus	180	35 - >430

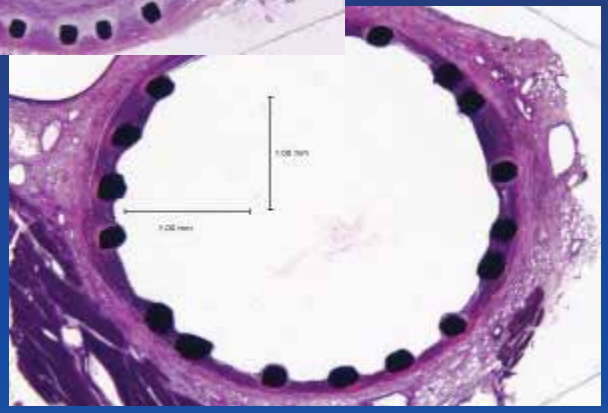
Concentration* ug/stent

* Used in clinical trials. Average dose for 15 - 18 mm length stent.

In vivo Vascular compatibility
TAVUS vs Cypher



Paclitaxel



Sirolimus

Complete healing, re-endothelization, minimal inflammation…

Cypher vs TAXUS

Sirolimus

- Immunosuppressive
- Interrupts TOR pathway and prevent down regulation of p27
- Reduce proliferating SMC
- Reduce inflammatory cell activities

Paclitaxel

- Antiproliferative
- Microtubular stabilization
- Reduce proliferation and migration of SMC
- Reduce secretion of extracelluar matrix

Comparison of Two Drugs

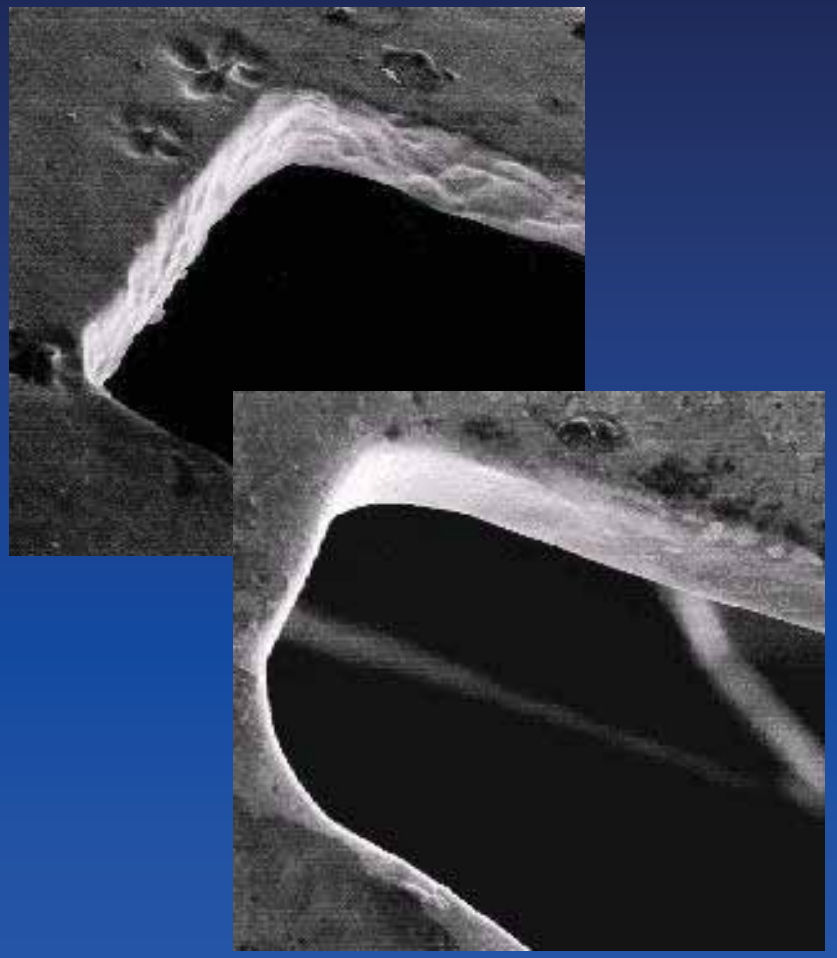
- Experimental data showed that both drugs have similar effectiveness for preventing intimal growth with preservation of re-endothelization in appropriate therapeutic dose.
- In current doses of drug eluting stents, both drugs have cytostatic activity rather than cytotoxic.

Drug Eluting Stent

- Drug
- Polymer

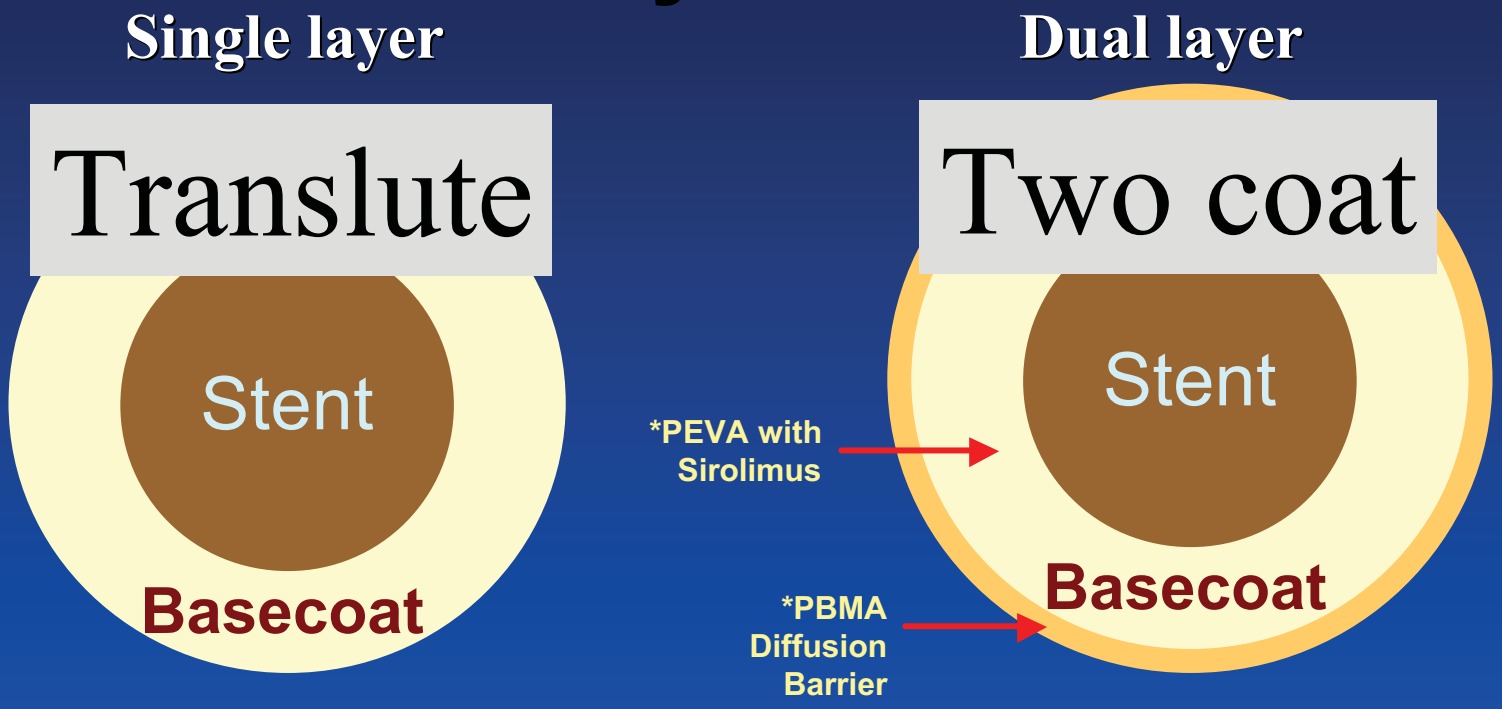
Why Polymer coating?

1. Consistent dosing
2. Controlled release kinetics
3. Structural integrity



TAXUS vs Cypher

Polymer



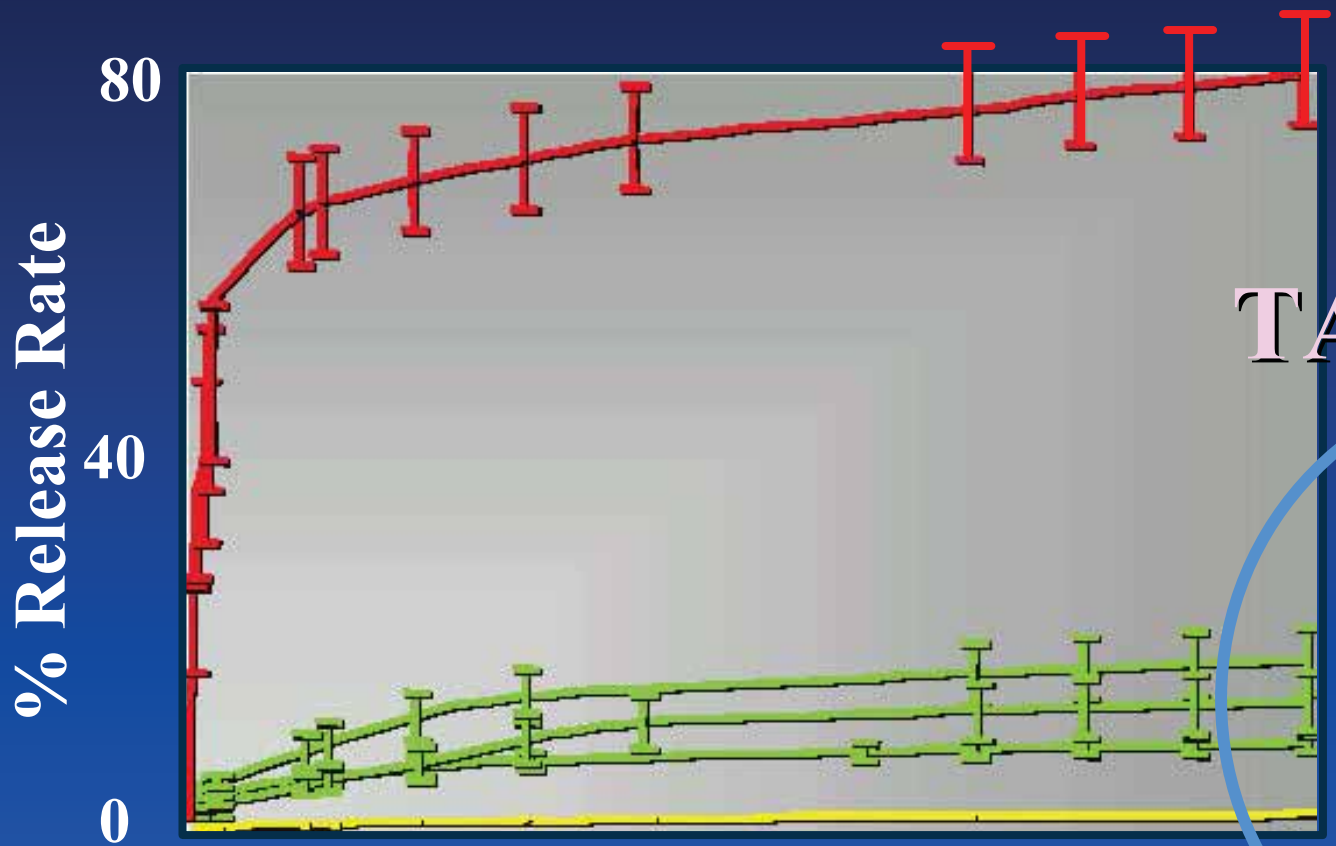
polymer + drug

Basecoat = polymer + drug
Topcoat = diffusion barrior

TAXUS

Controlled Moderate or Slow Release

In vivo Paclitaxel Elution



Fast release

- 1 ug/mm^2 (108ug)

TAXUS trial

Moderate release

-4 ug/mm^2 (432ug)

-2 ug/mm^2 (216ug)

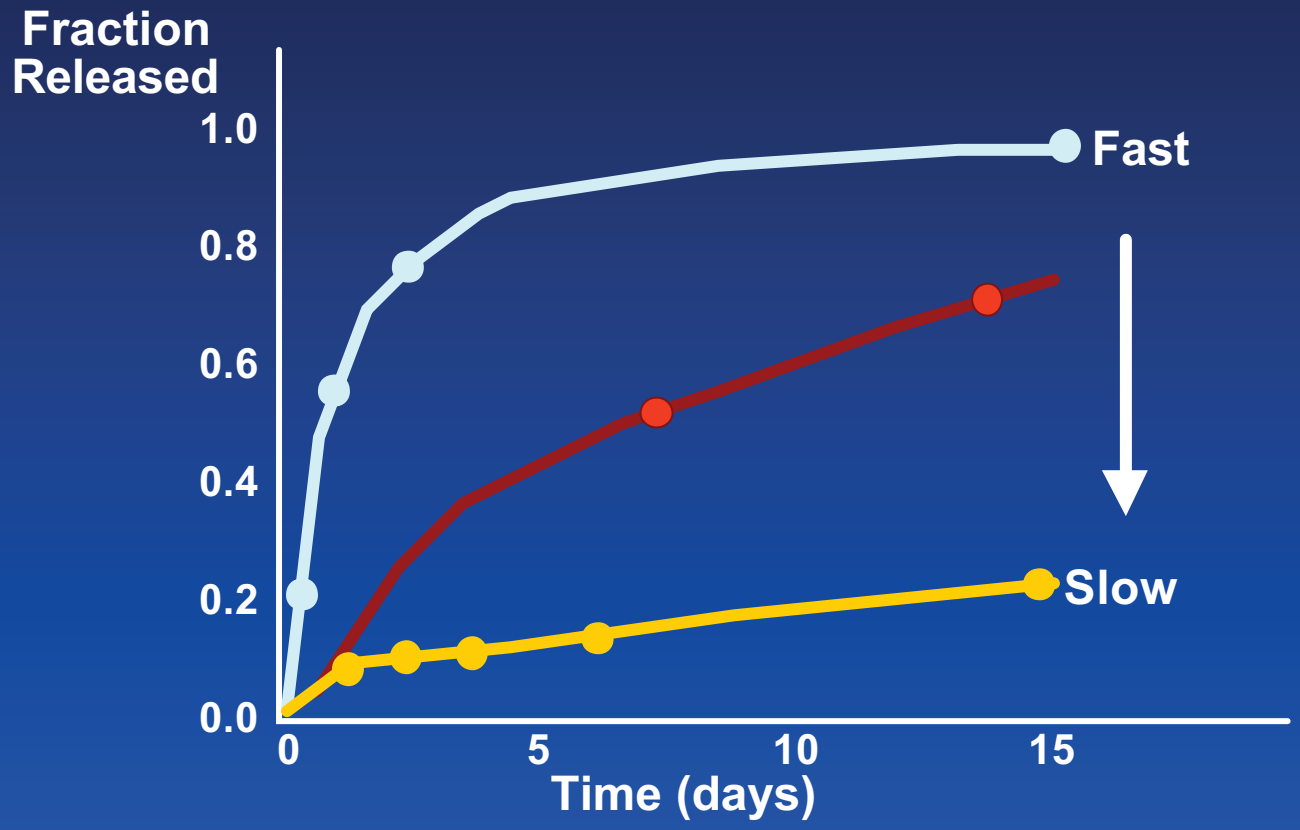
-1ug/mm^2 (108ug)

Slow release

- 1 ug/mm^2 (108ug)

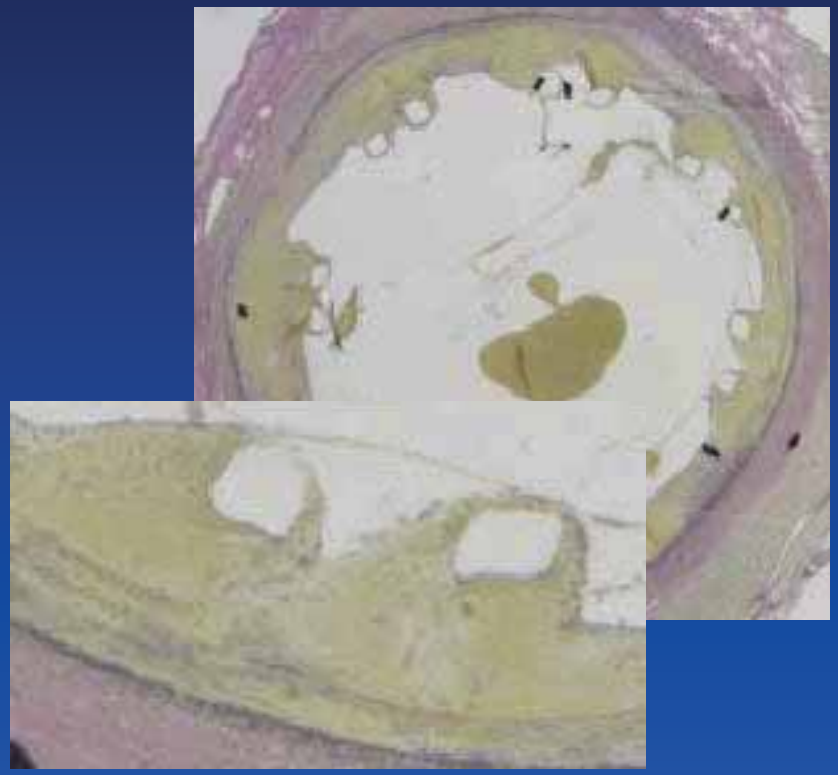
Cypher
Controlled Drug Release in Porcine Study

In Vivo Release Kinetics

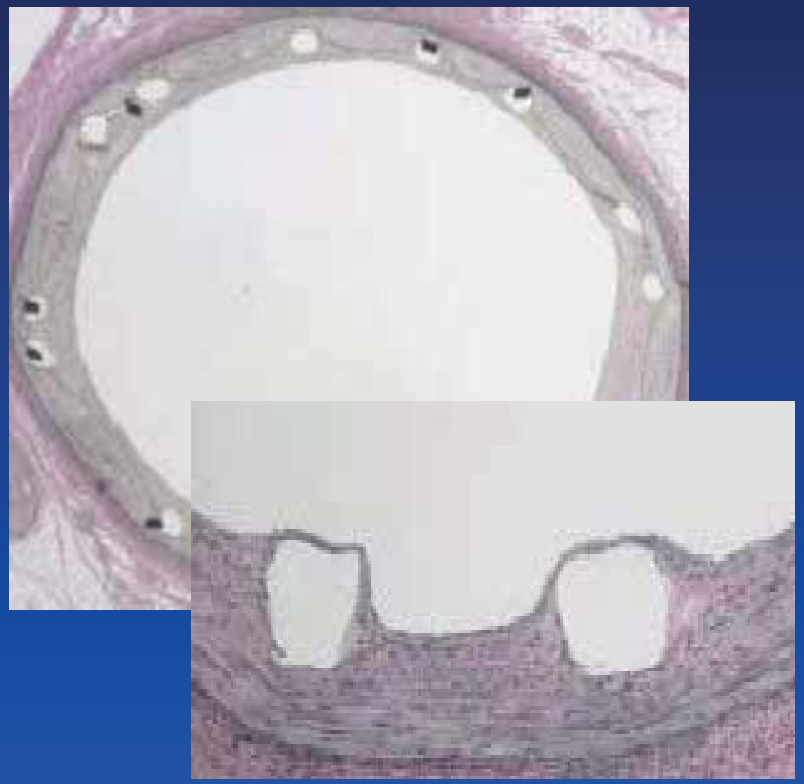


Vascular Inflammation

Fast release vs. Slow release



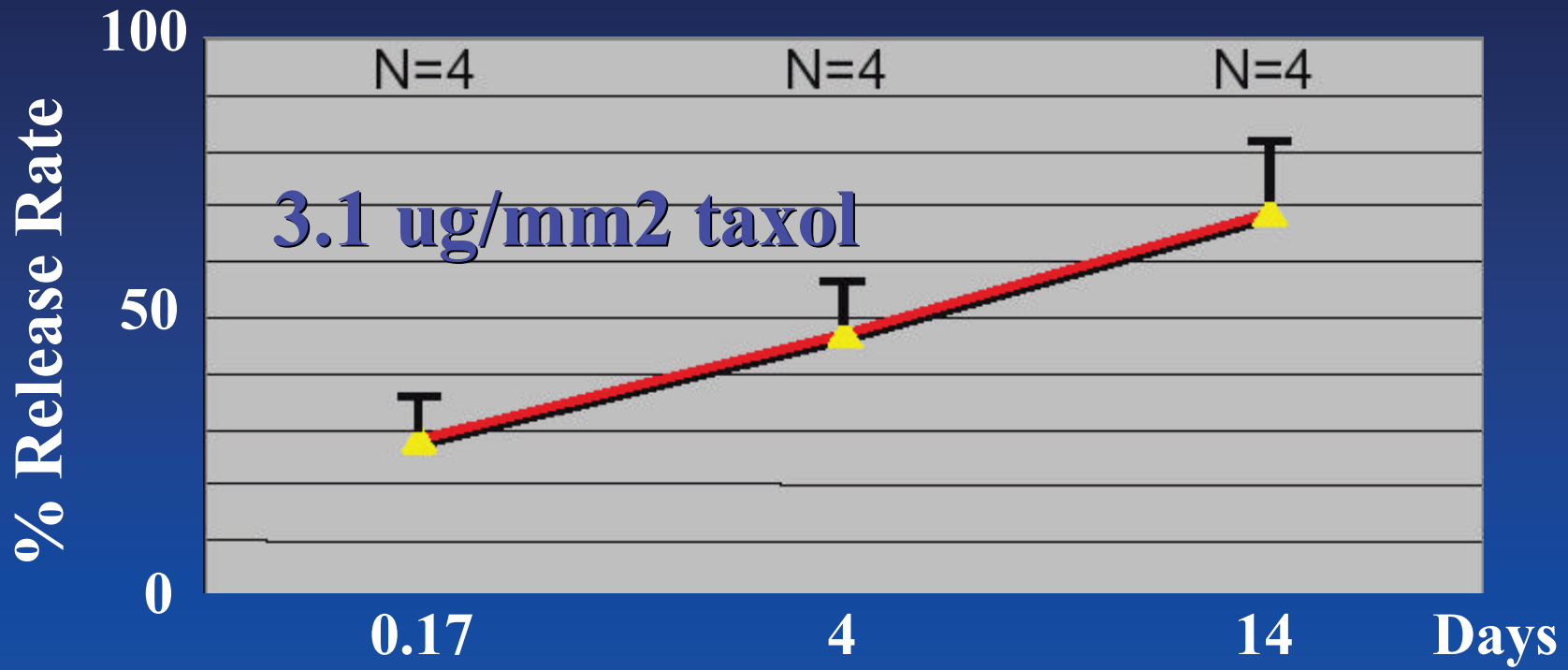
Fast release



Slow release

Non-Polymer SUPRA G stent (Cook)

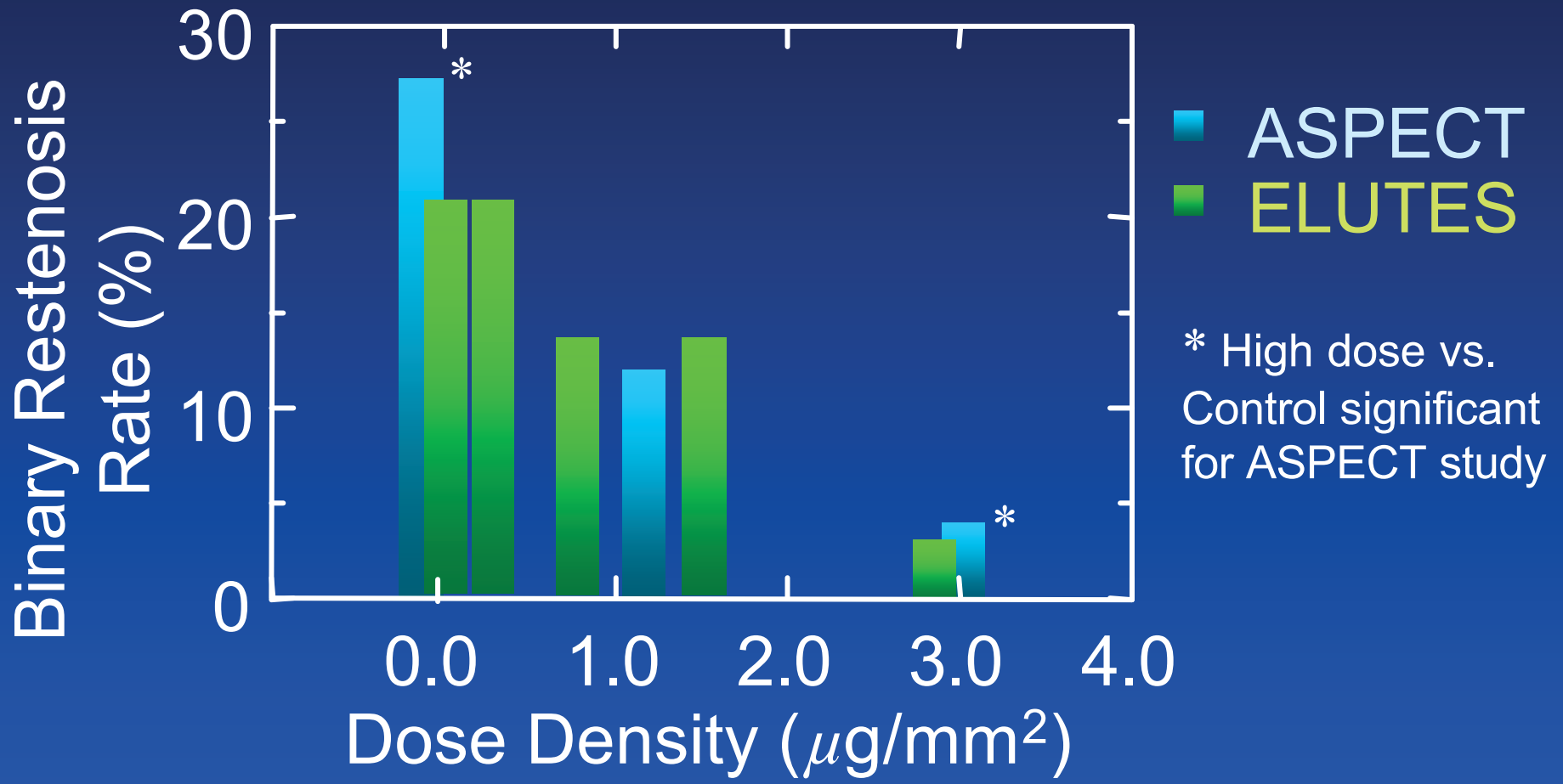
In vivo Paclitaxel Elution



Faster Release ?

Binary Restenosis -Dose response

6-Month QCA Results:



* High dose vs. Control significant for ASPECT study

Why could they not demonstrate the same efficacy of the Non-polymer Paclitaxel eluting stents in DELIVER ?

By chance or inevitable ?

Comparison of Two Polymers

- Both DES system use different polymers for effective drug delivery.
- Preclinical data showed that both DES systems achieved safe, effective, controlled, and slow drug diffusion into surrounding tissue without initiating tissue-polymer reaction.

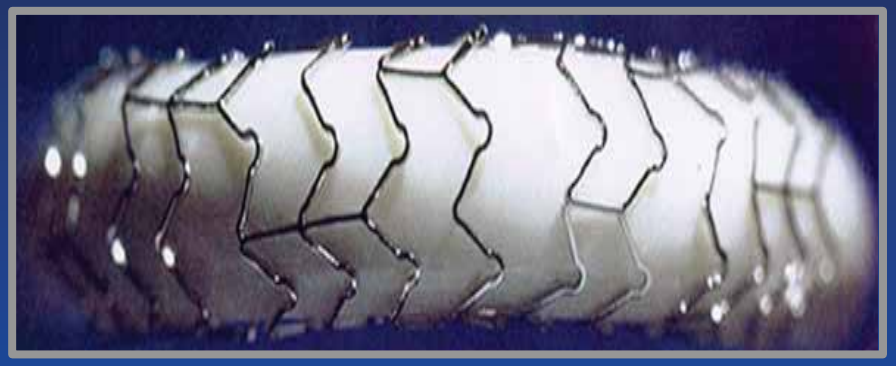
Drug Eluting Stent

- Drug
- Polymer
- Stent design

NIR

TAXUS I
TAXUS II
TAXUS III

Express



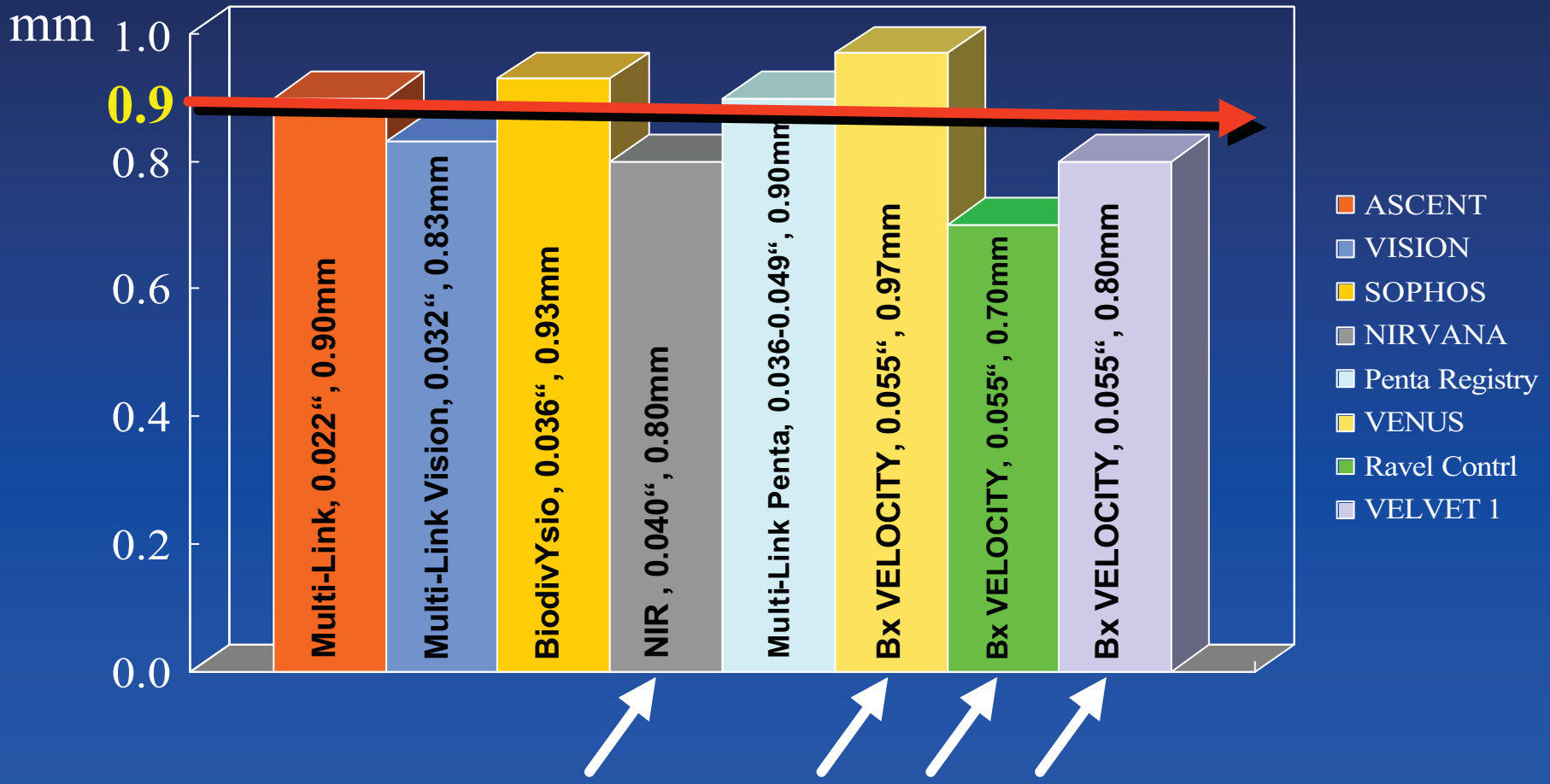
TAXUS IV
TAXUS V
TAXUS VI

Bx Velocity

RAVEL
SIRIUS

Late Loss
By Stent Design of Bare Metal Stent

No significant diference in terms of stent design and thickness

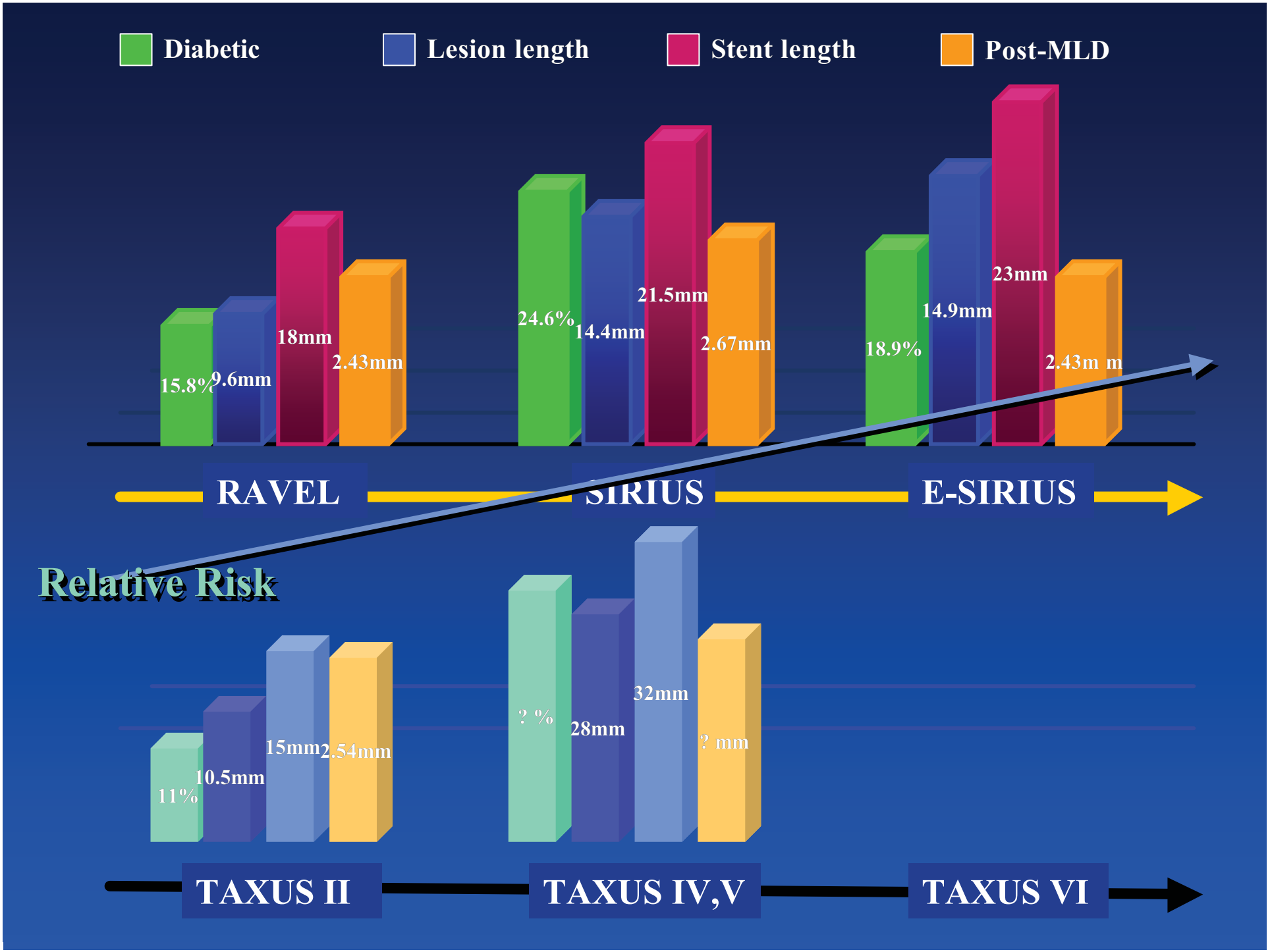


Comparison of Two Stents

Theoretically both stents might be good stent platforms for even drug delivery to arterial wall.

Cypher vs TAXUS
TAXUS vs Cypher

Comparison of Clinical Data


Diabetic
Lesion length
Stent length
Post-MLD
15.8%
9.6mm
18mm
2.43mm
24.6%
14.4mm
21.5mm
2.67mm
18.9%
14.9mm
23mm
2.43m m
RAVEL
SIRIUS
E-SIRIUS
Relative Risk
11%
10.5mm
15mm
2.54mm
? %
28mm
32mm
? mm
TAXUS II
TAXUS IV,V
TAXUS VI

Different Study Patients

%	TAXUS II SR	TAXUS II MR	RAVEL	SIRIUS
Number	131	135	120	1,100
Age (yr)	61.5	59.3	60	62
Male	70	76	81	73
Risk factors				
Diabetes	11	17	21	25
Hypertension	63	60	61	68
PMI	35	39	34	28
Hyperchol	NA	NA	43	73
Smoking	21	24	33	18
Unstable Angina	35	30	48	NA
Multi-vessel	NA	NA	75	42
IIb/IIIa use	NA	NA	11	60

Different Study Design

	TAXUS II SR	TAXUS II MR	RAVEL	SIRIUS
Sponsor	Boston	Boston	Cordis	Cordis
Drug	Paclitaxel	Paclitaxel	Sirolimus	Sirolimus
Dose	1.0 ug/mm^2	1.0 ug/mm^2	185ug	185ug
Polymer	Translute	Translute	2 coat	2 coat
Release	Slow	Moderate	Slow	Slow
Stent platform	NIRx	NIRx	Bx Velocity	Bx Velocity
length (mm)	15	15	18	18
Dia (mm)	3.0 & 3.5	3.0 & 3.5	2.5,3.0,3.5	2.5,3.0,3.5
Lesion length	≤ 12mm	≤ 12mm	≤ 18	≤ 30
Dia. (mm)	≥ 3.0, ≤3.5	≥3.0, ≤3.5	≥2.5, ≤3.5	≥2.5, ≤3.5

Different Study Design

%	TAXUS II SR	TAXUS II MR	RAVEL	SIRIUS
Number	131	135	120	1,100
Location				
LAD	40	42	49	45
LCX	38	33	27	25
RCA	22	25	24	30
Lesion characteristics				
Type A	32	NA	8	7
Type B1	39	NA	39	34
Type B2	29	NA	54	33
Type C	0	0	0	26
Multiple stent	5	4	3	35

Reasonable Comparison Would be …

TAXUS II vs RAVEL
TAXUS IV,V vs SIRIUS

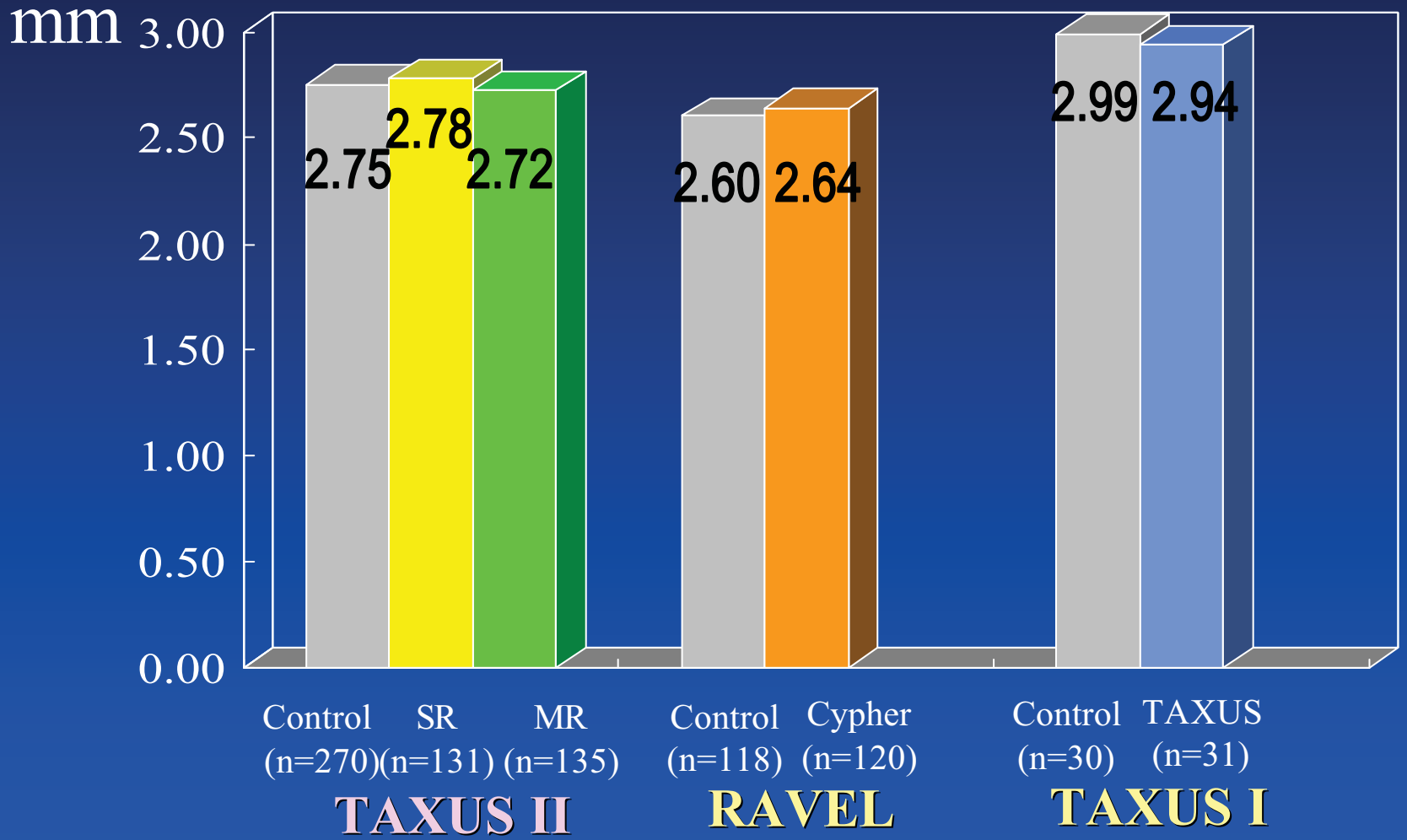
TAXUS I

De novo, 3.0 and 3.5 mm
61 pts at 3 sites
1:1 Randomization (31 coated, 30 bare)

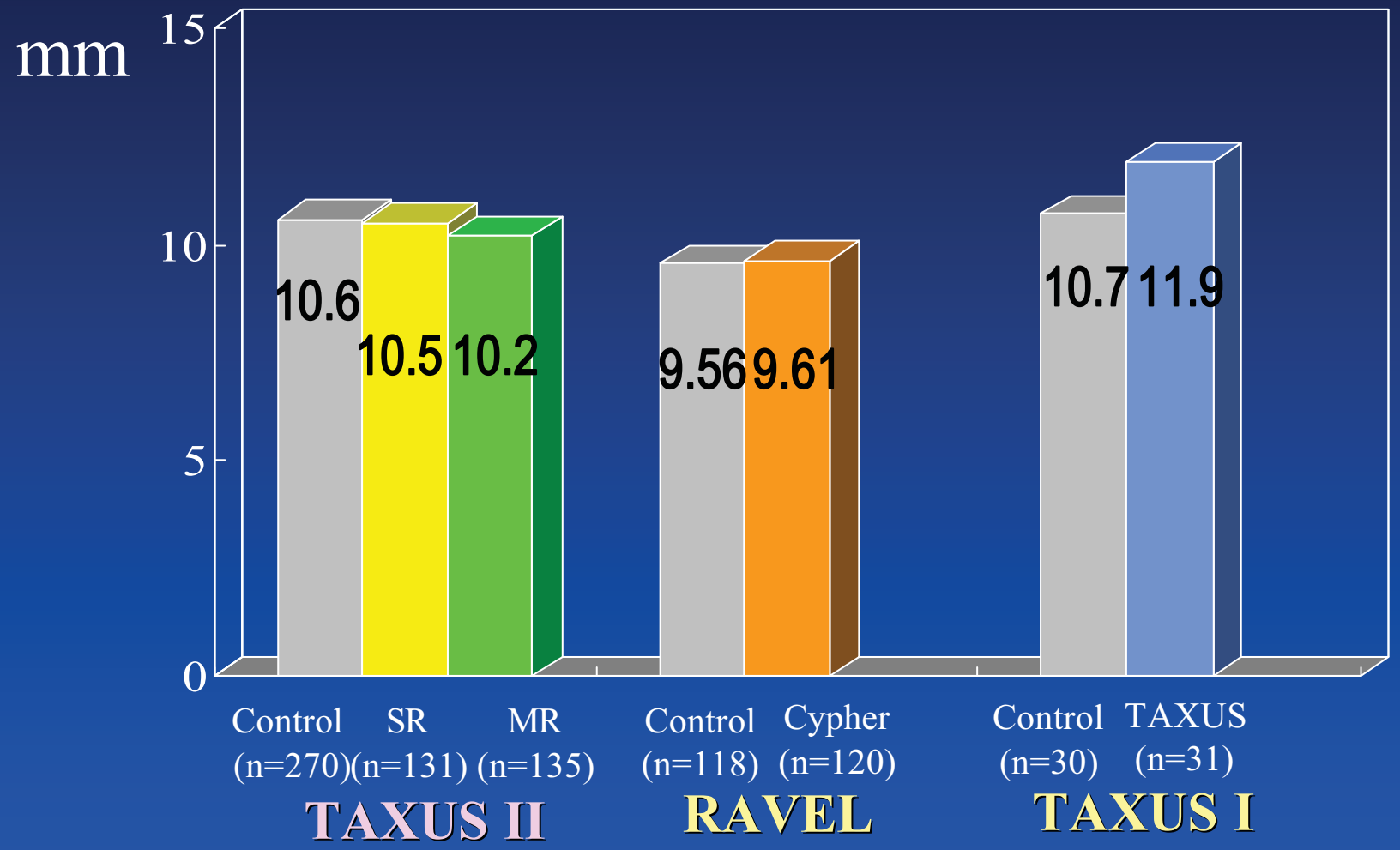
	TAXUS NIR	Bare
30 day MACE	0 %	0 %
Restenosis Rate	0 %	10 %
6-month MACE	0 %	7 %

Reference Size

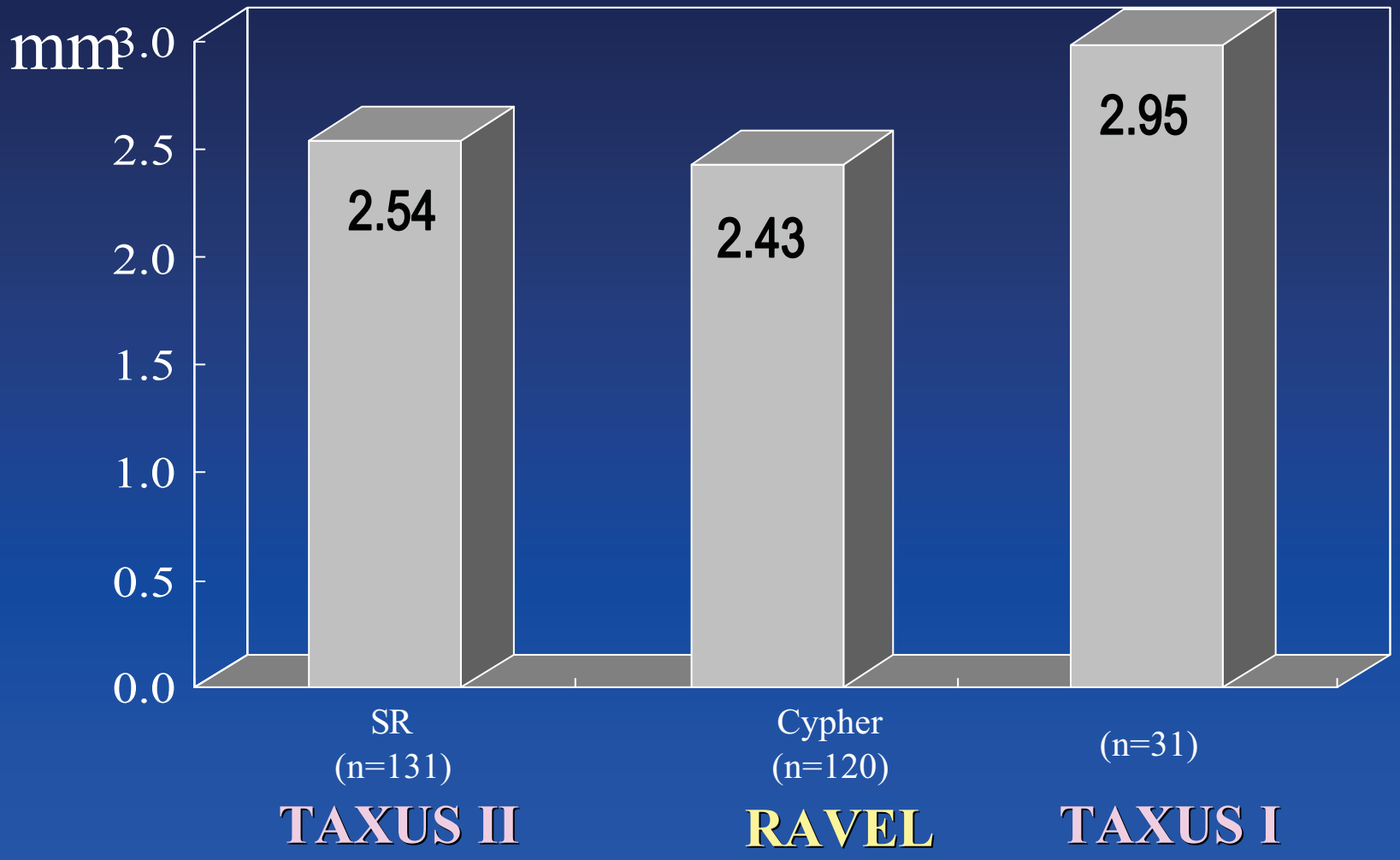
Slightly larger in TAXUS II than in RAVEL



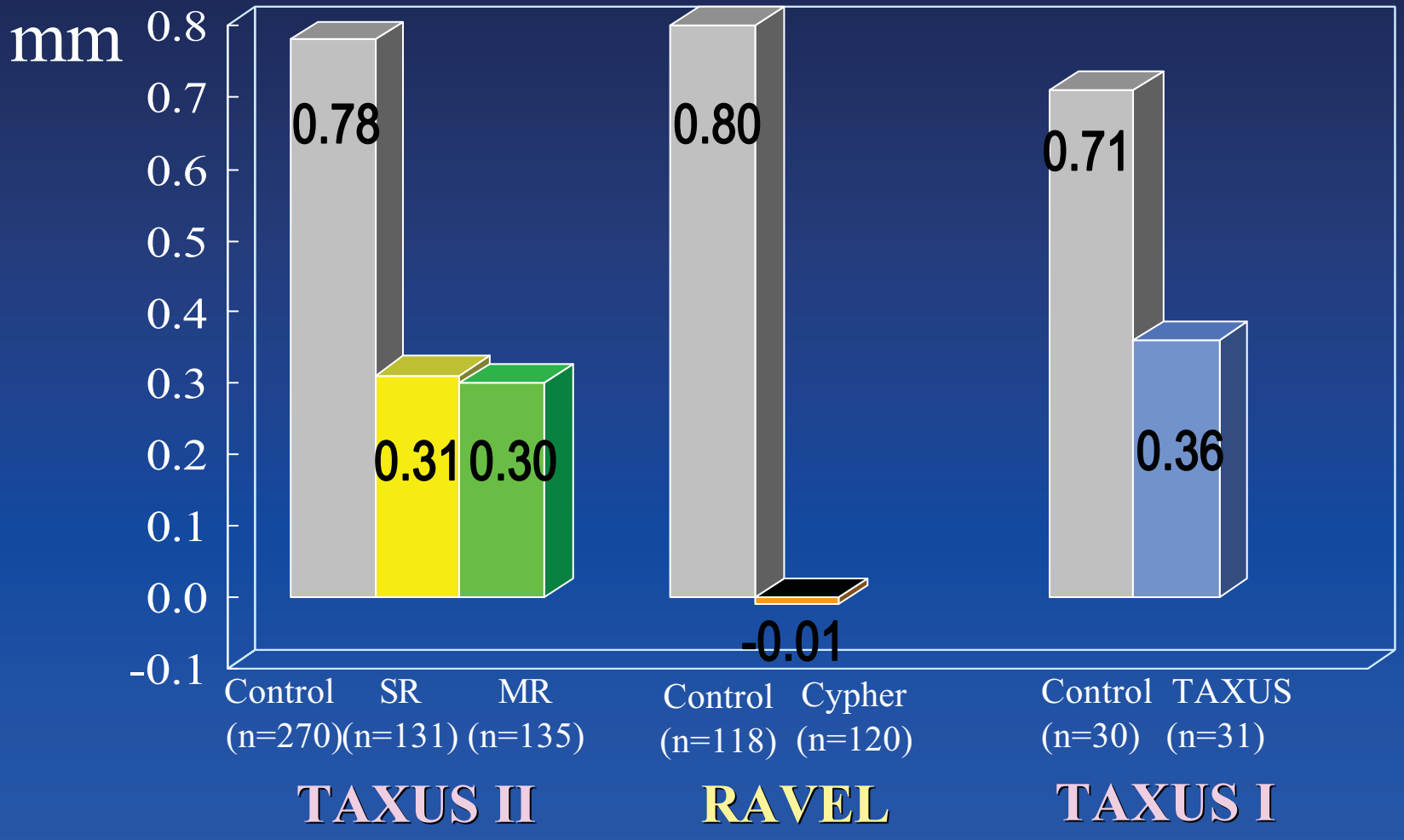
Lesion Length



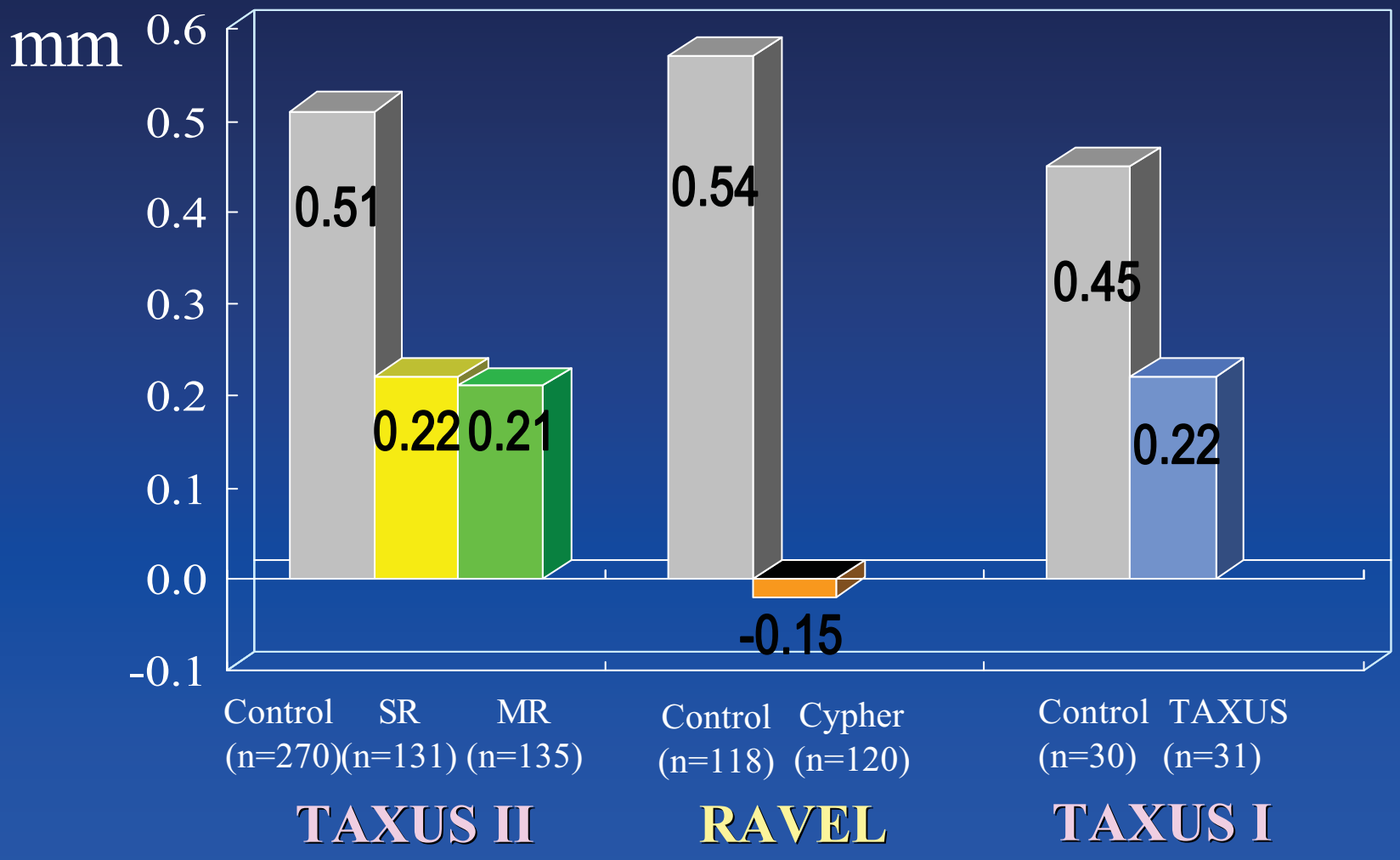
Post MLD


mm
3.0
2.5
2.0
1.5
1.0
0.5
0.0
2.54
2.43
2.95
SR
(n=131)
TAXUS II
Cypher
(n=120)
RAVEL
(n=31)
TAXUS I

Late Loss

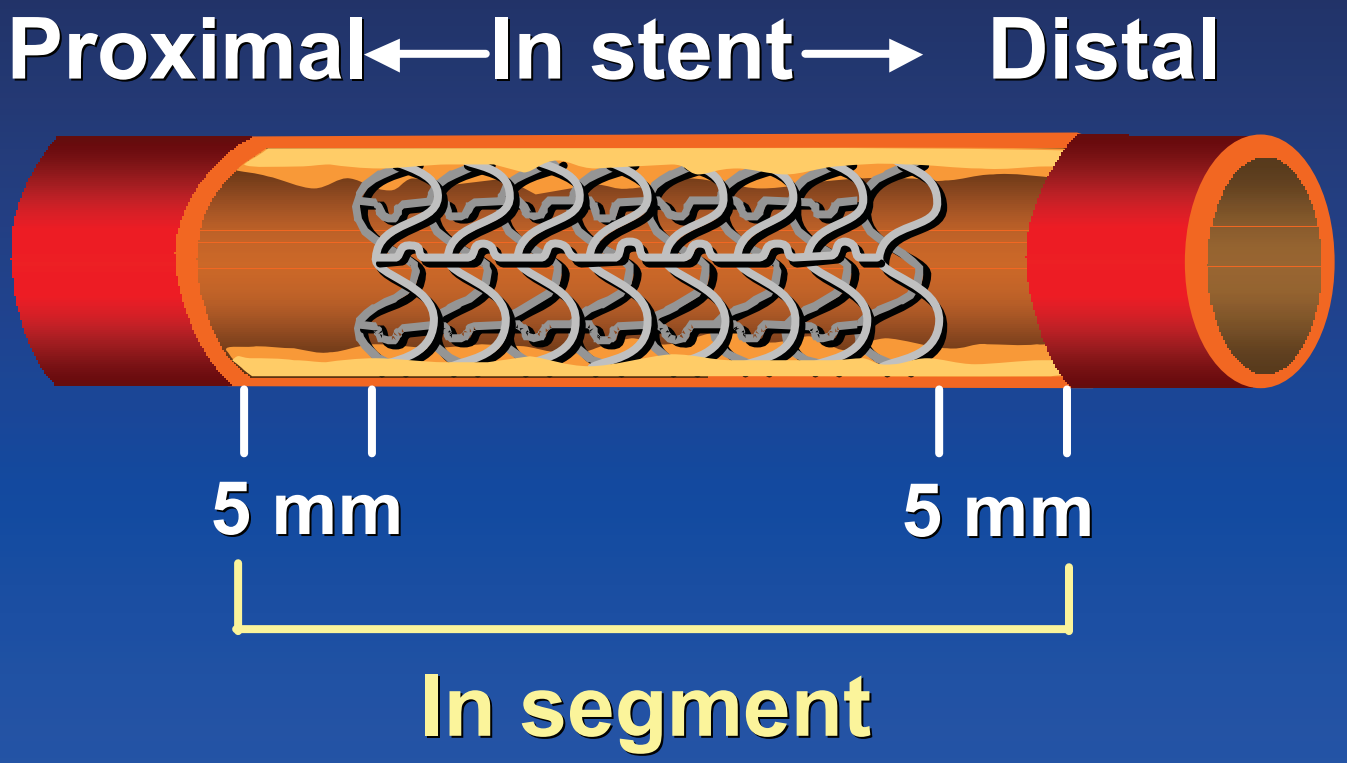

mm
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
-0.1
0.78
0.31
0.30
0.80
-0.01
0.71
0.36
Control
SR
MR
(n=270)
(n=131)
(n=135)
Control
Cypher
(n=118)
(n=120)
Control
TAXUS
(n=30)
(n=31)
TAXUS II
RAVEL
TAXUS I

Loss Index

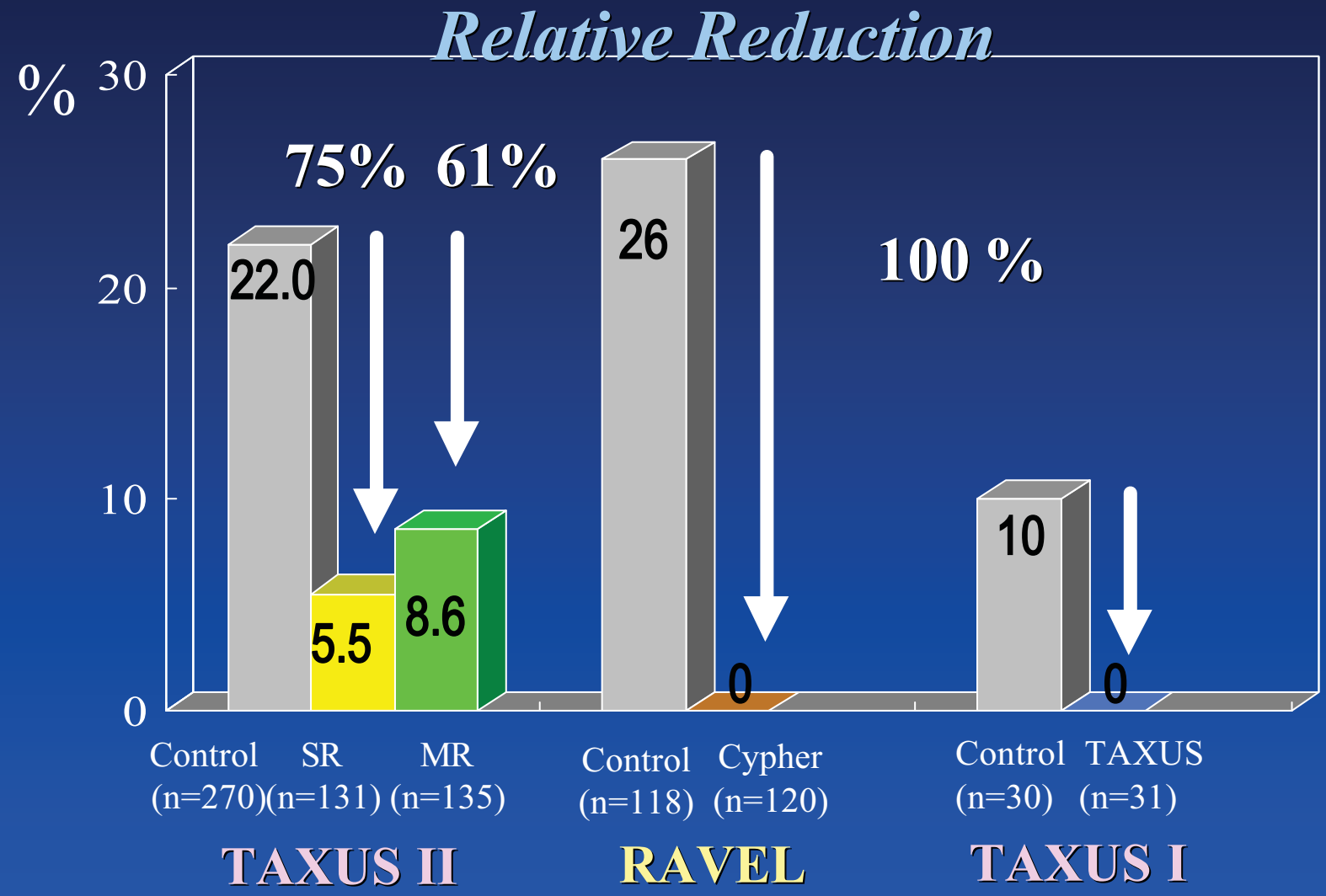

mm
0.6
0.5
0.4
0.3
0.2
0.1
0.0
-0.1
0.51
0.22
0.21
0.54
-0.15
0.45
0.22
Control (n=270)
SR (n=131)
MR (n=135)
Control (n=118)
Cypher (n=120)
Control (n=30)
TAXUS (n=31)
TAXUS II
RAVEL
TAXUS I

Definition of Restenosis

Angiographic follow-up

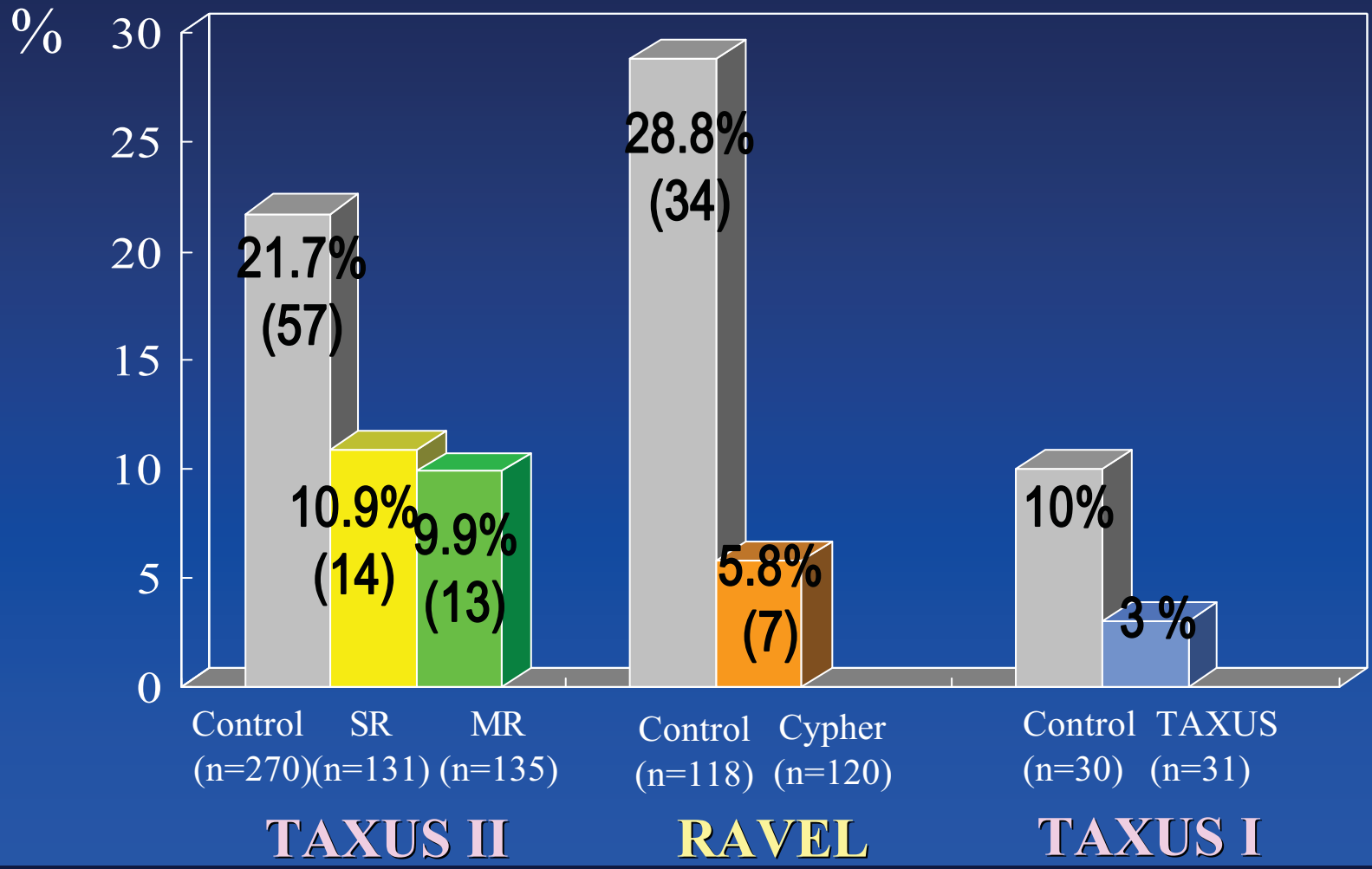


In-Segment Restenosis



Long-Term Result

12 months MACE



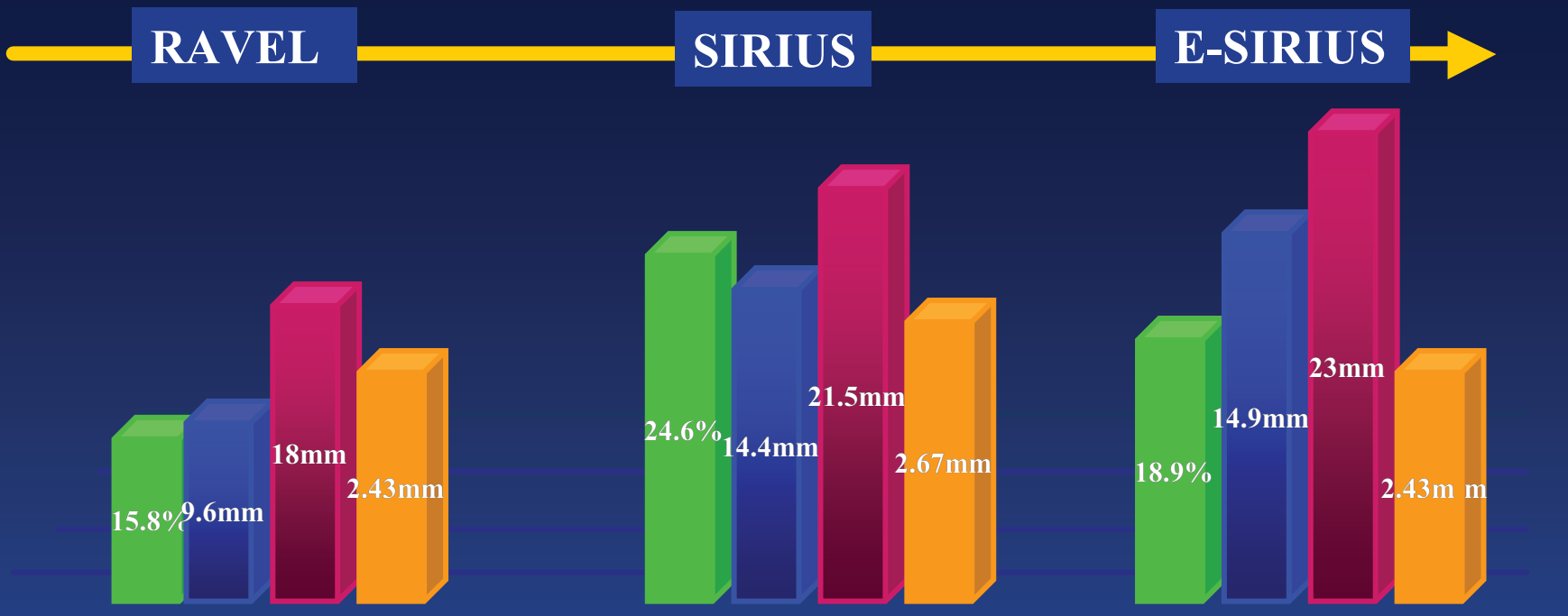
TAXUS II & RAVEL have comparable risk factors

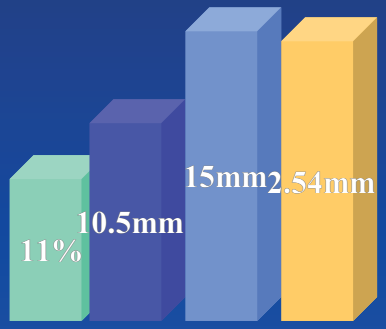
RAVEL		TAXUS II-SR
15.8 %	Diabetic	10.7 %
9.6 mm	Lesion length	10.5 mm
18 mm	Stent length	15 mm
2.43 mm	Post MLD	2.54 mm

Efficacy

Relative Reduction		
-0.01	Late Loss	0.31 mm
0%	Restenosis Rate	5.5%
100 %	Restenosis Rate	75 %
80 %	MACE	49 %
0%	SAT(<360days)	1.6%

TAXUS II versus SIRIUS



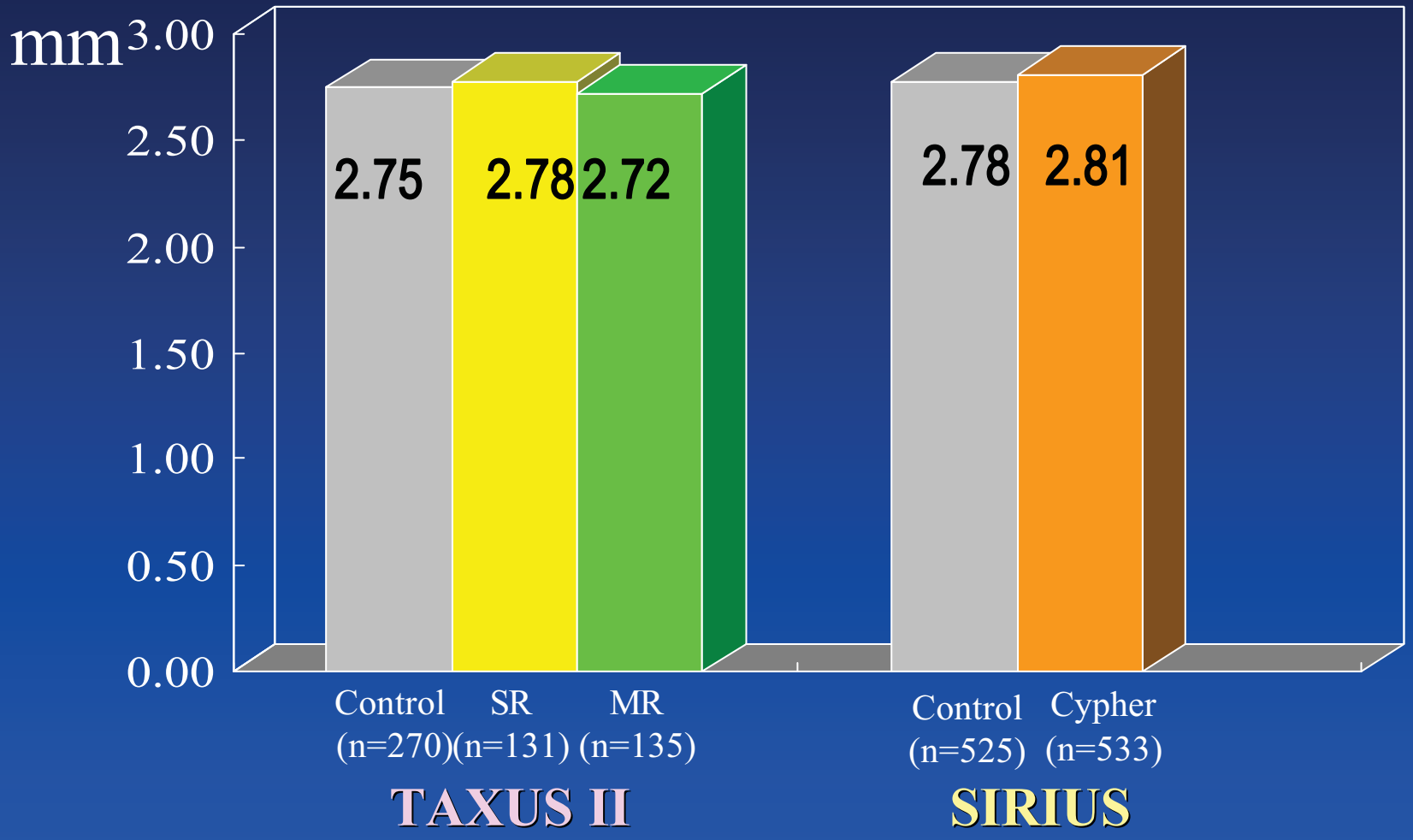


Stent-overlapping (29%), multiple stent (35%) were permitted and more complex lesions (type C 26%) and longer lesion (14mm) in SIRIUS trial.

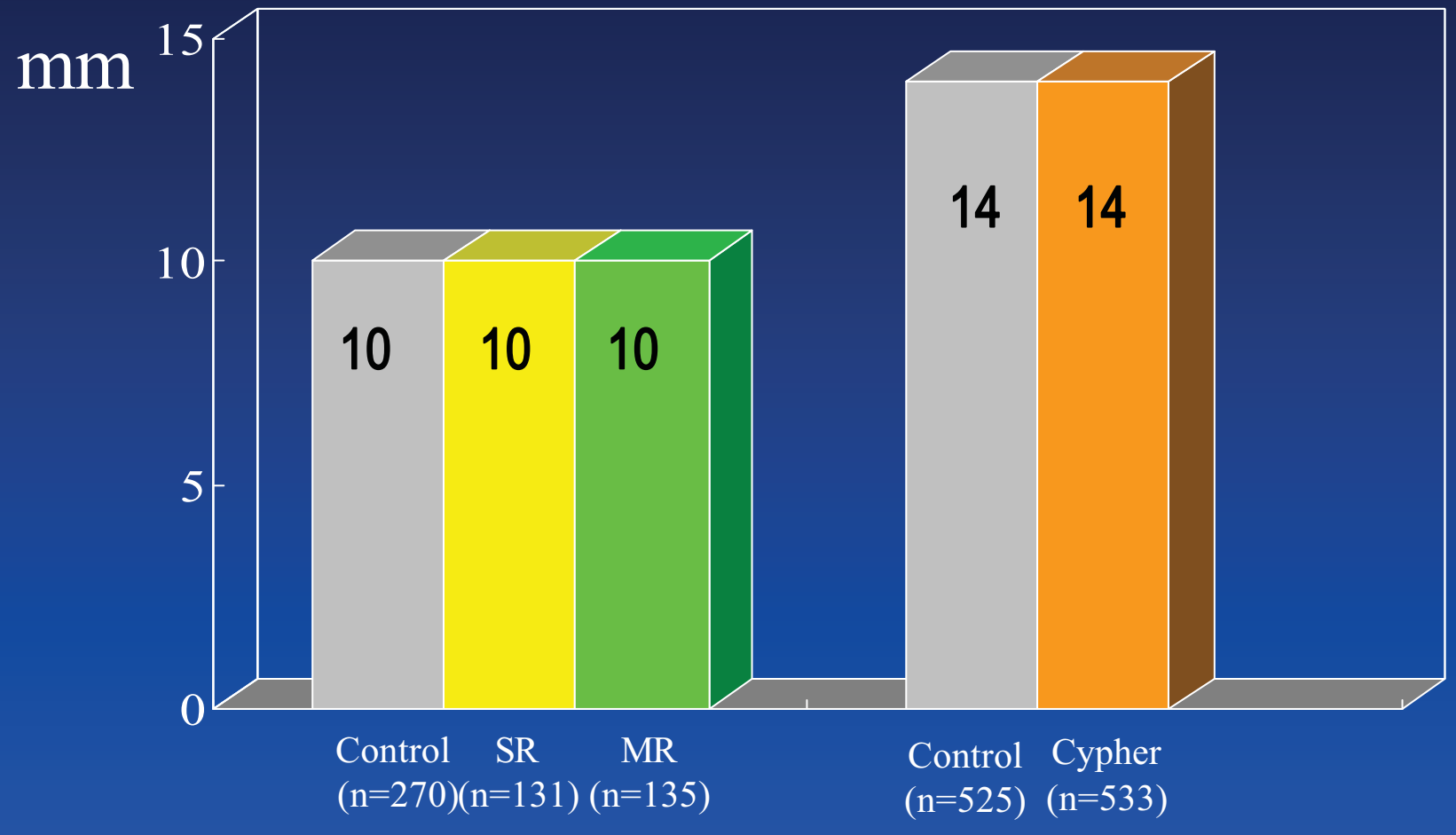
TAXUS II — TAXUS IV,V — TAXUS VI

Diabetic | Lesion length | Stent length | Post-MLD

Reference Size



Lesion Length



Different Study Subjects

%	TAXUS II SR	TAXUS II MR	RAVEL	SIRIUS
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RCA	22	25	24	30
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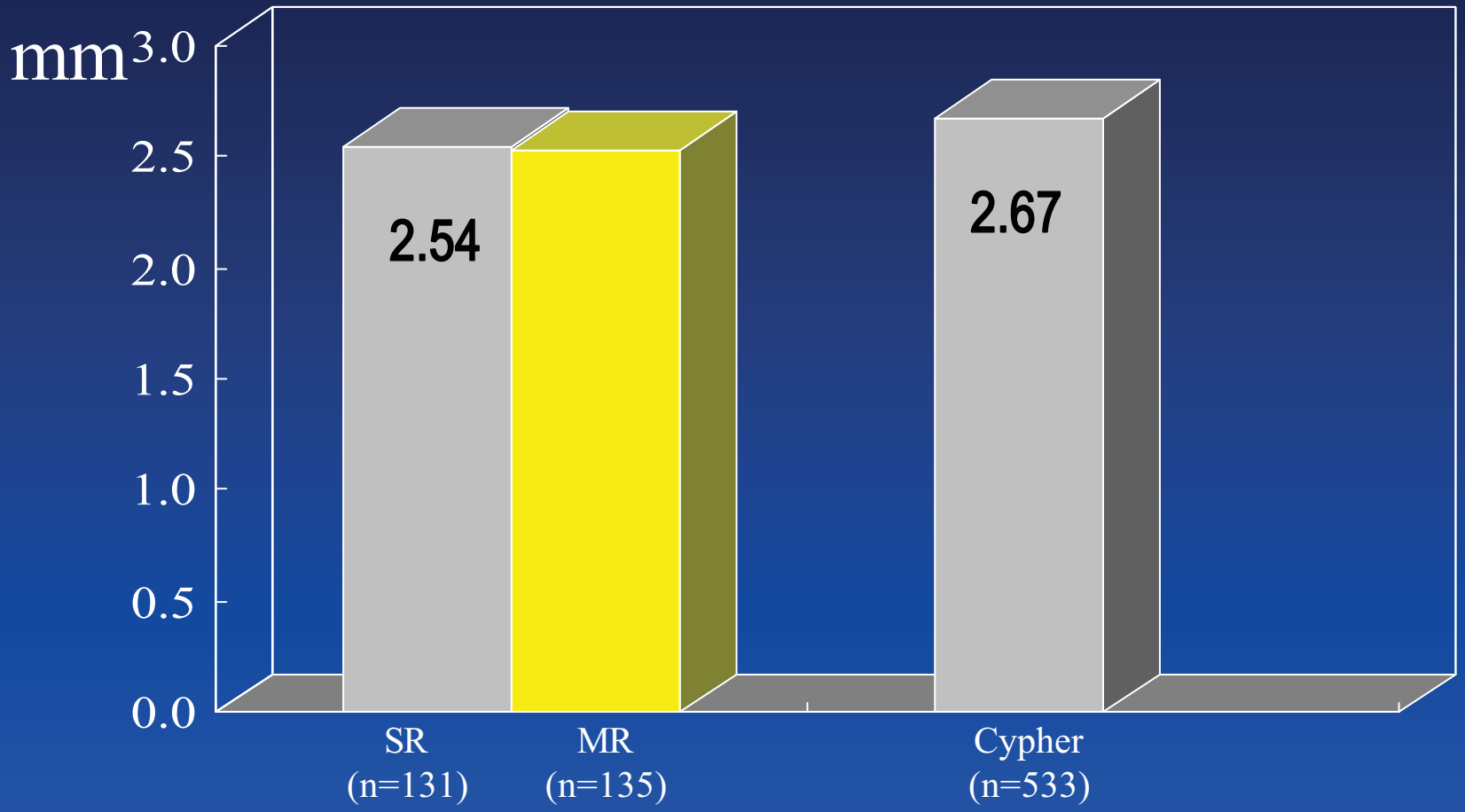
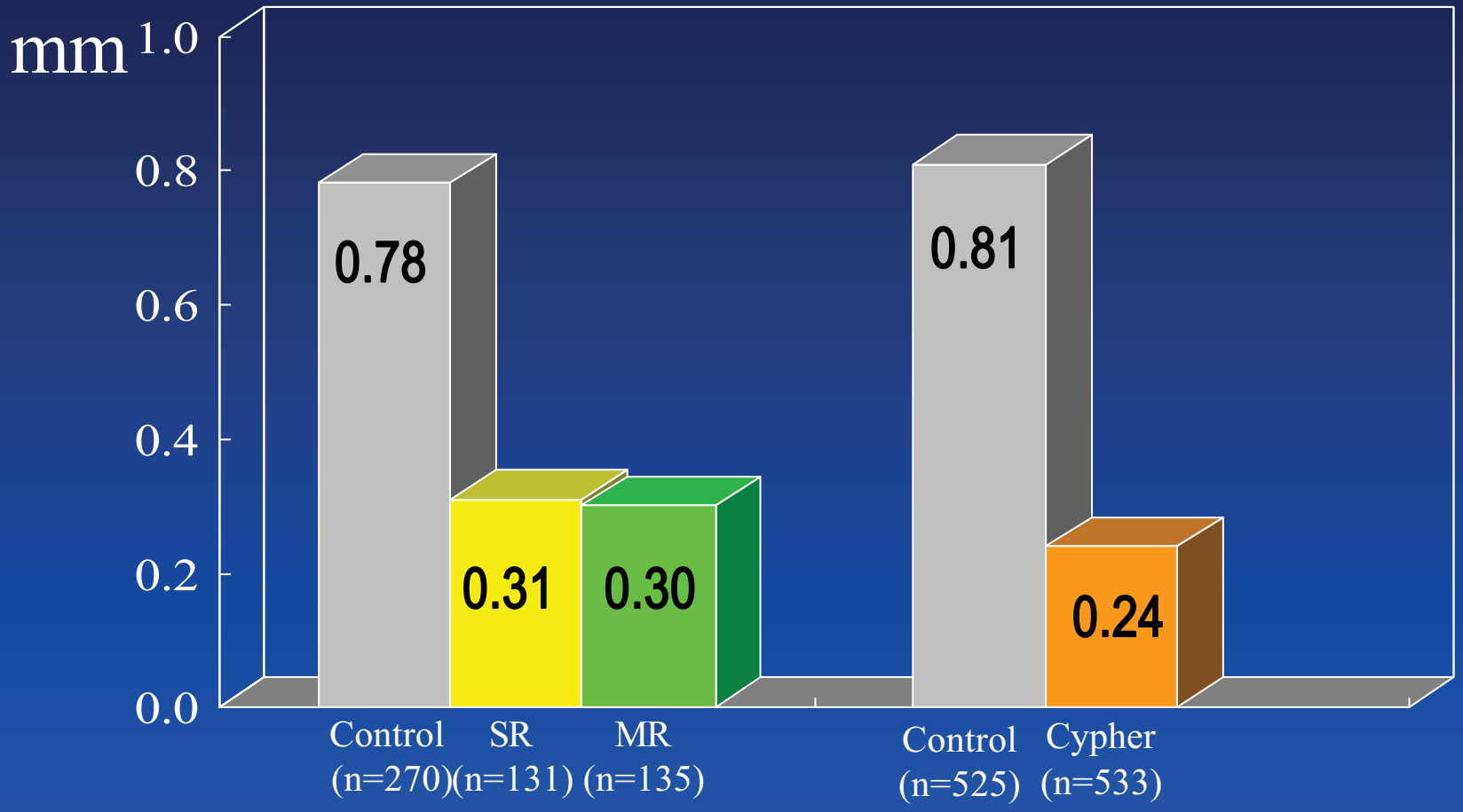
Type B1	39	NA	39	34
Type B2	29	NA	54	33
Type C	0	0	0	26
Multiple stent	5	4	3	35

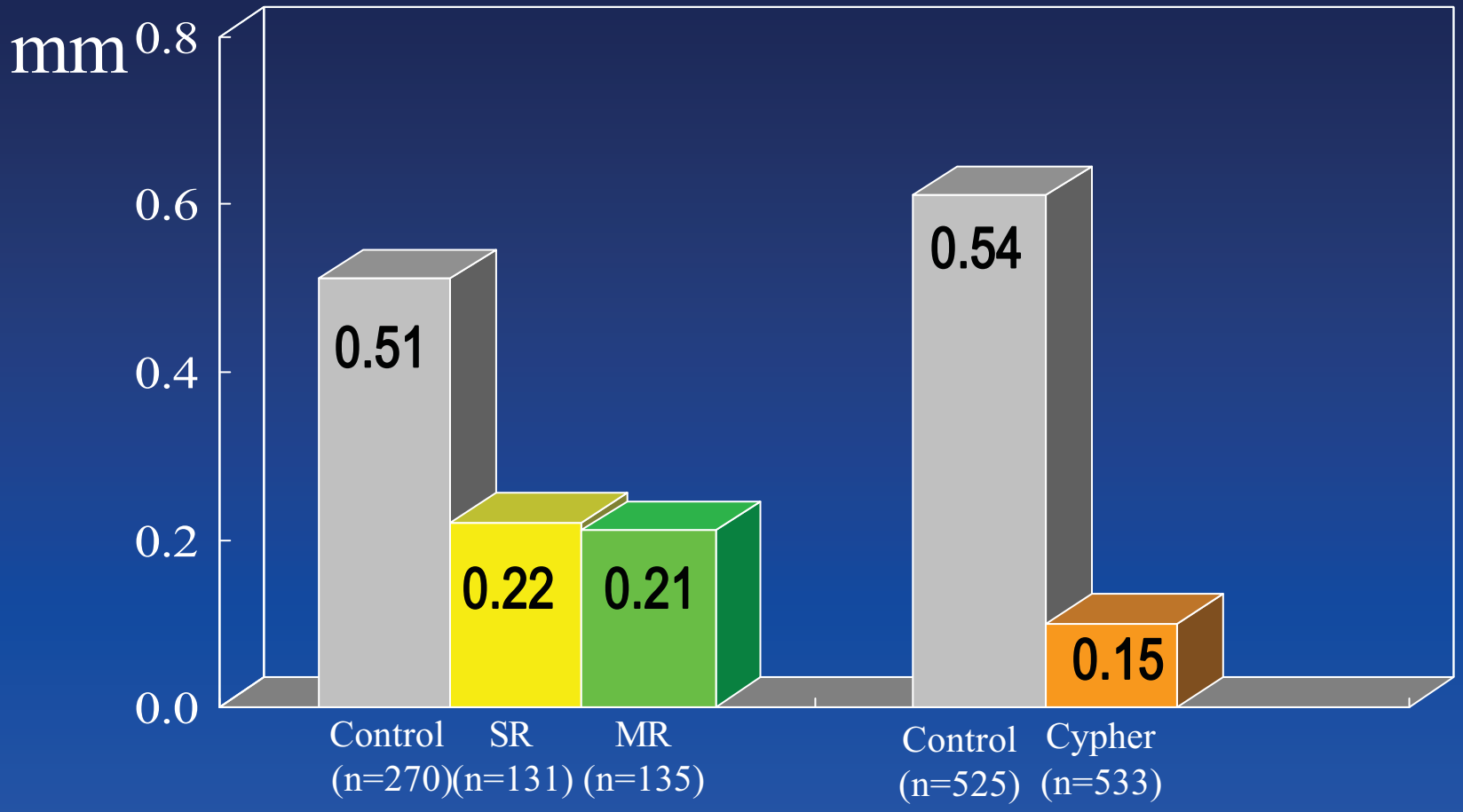
Post MLD


mm
3.0
2.5
2.0
1.5
1.0
0.5
0.0
2.54
2.67
SR
(n=131)
MR
(n=135)
Cypher
(n=533)
TAXUS II
SIRIUS

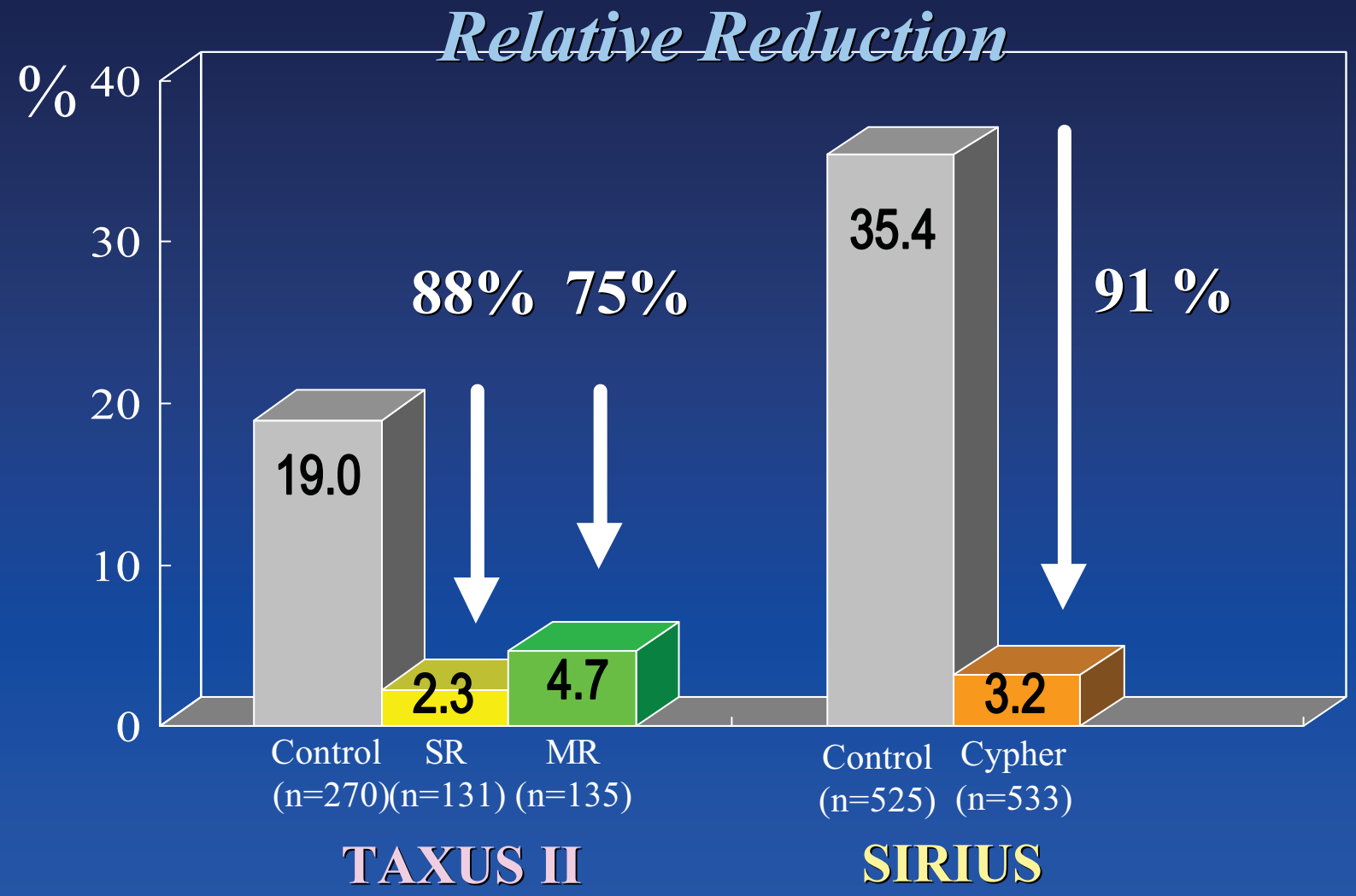
Late Loss


mm
1.0
0.8
0.6
0.4
0.2
0.0
0.78
0.31
0.30
0.81
0.24
Control (n=270)
SR (n=131)
MR (n=135)
Control (n=525)
Cypher (n=533)
TAXUS II
SIRIUS

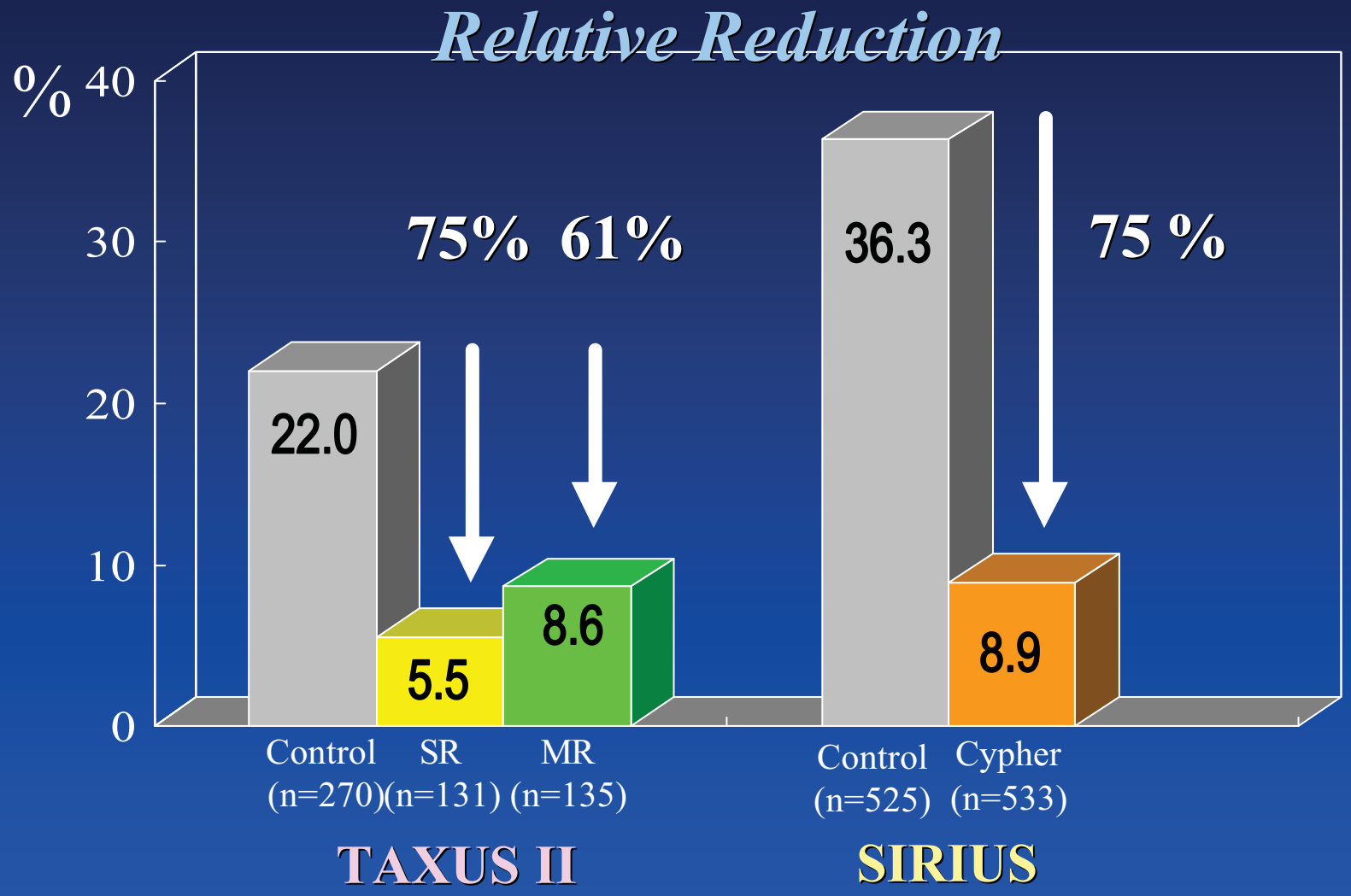
Loss Index


mm
0.8
0.6
0.4
0.2
0.0
0.51
0.22
0.21
0.54
0.15
Control (n=270)
SR (n=131)
MR (n=135)
Control (n=525)
Cypher (n=533)
TAXUS II
SIRIUS

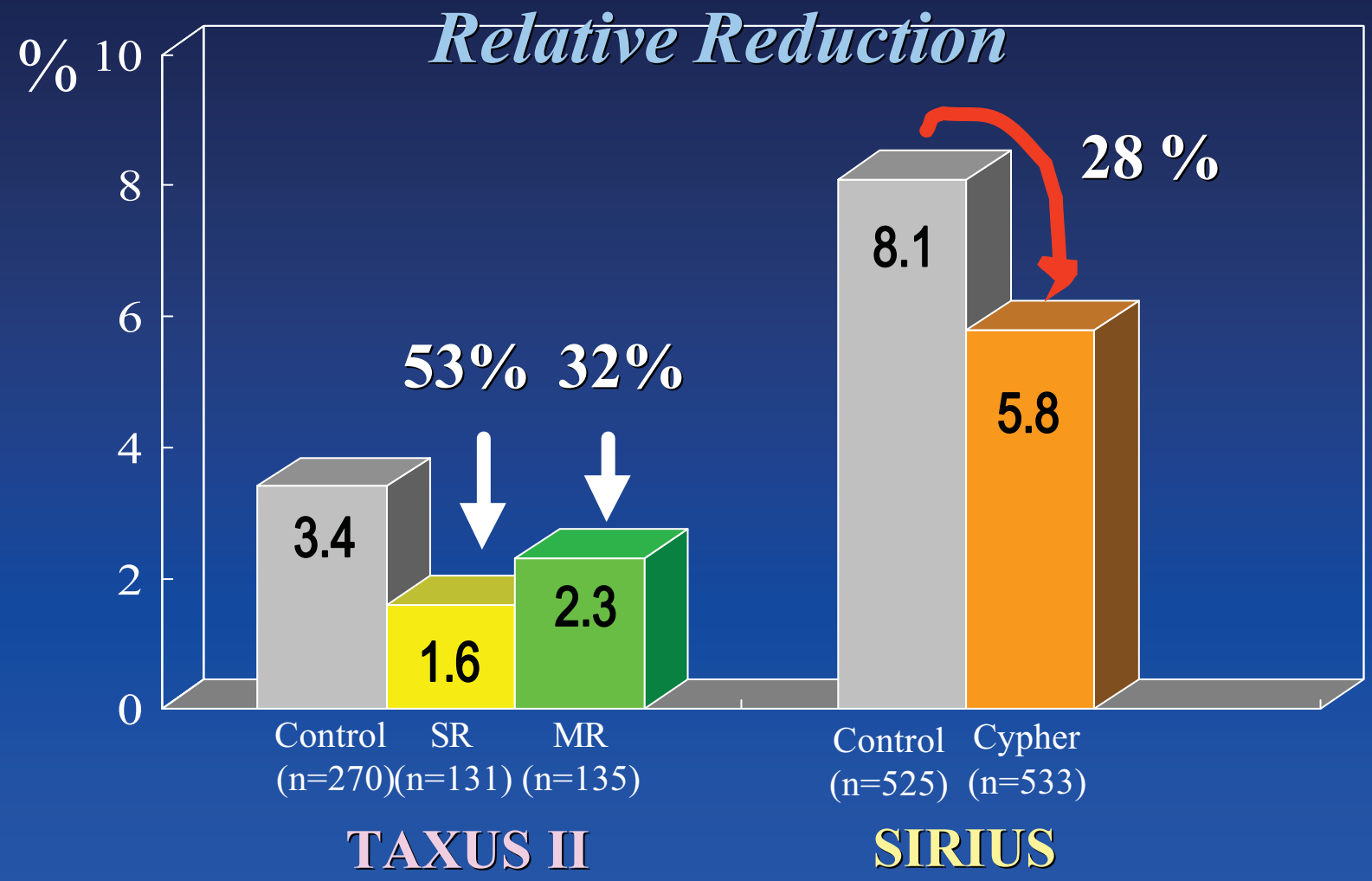
In-Stent Restenosis



In-Segment Restenosis

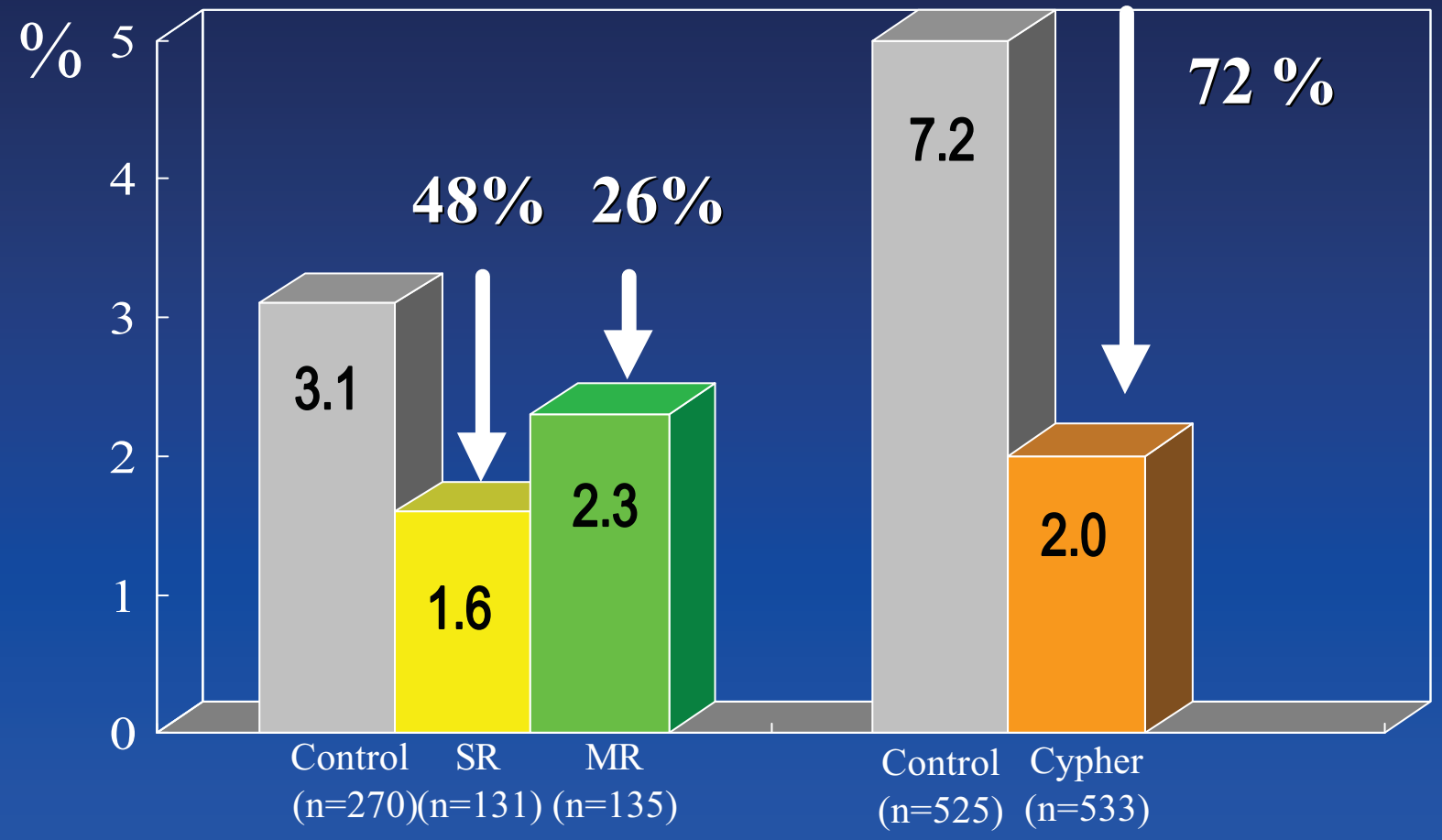


Proximal Edge Restenosis

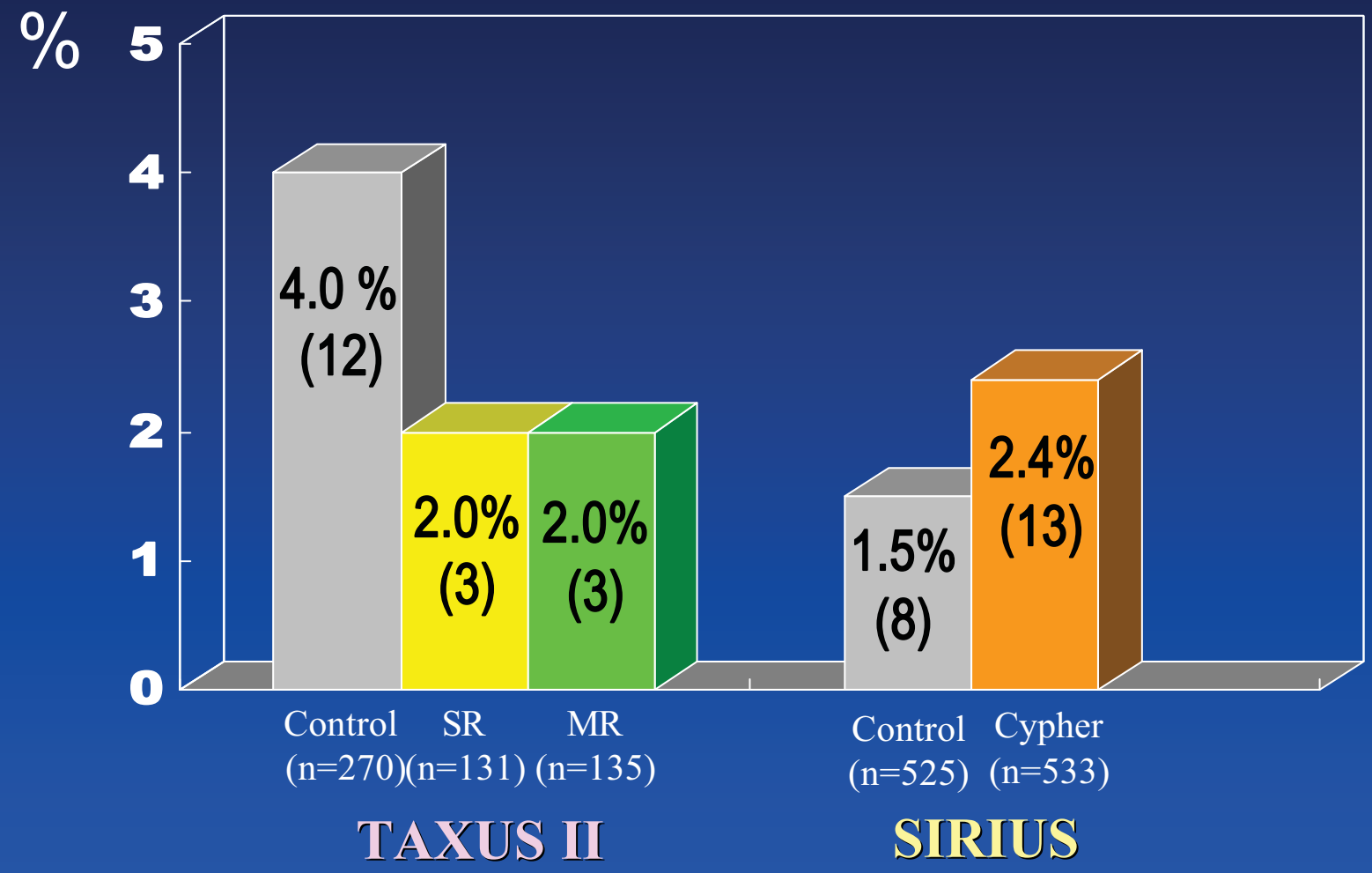


Distal Edge Restenosis

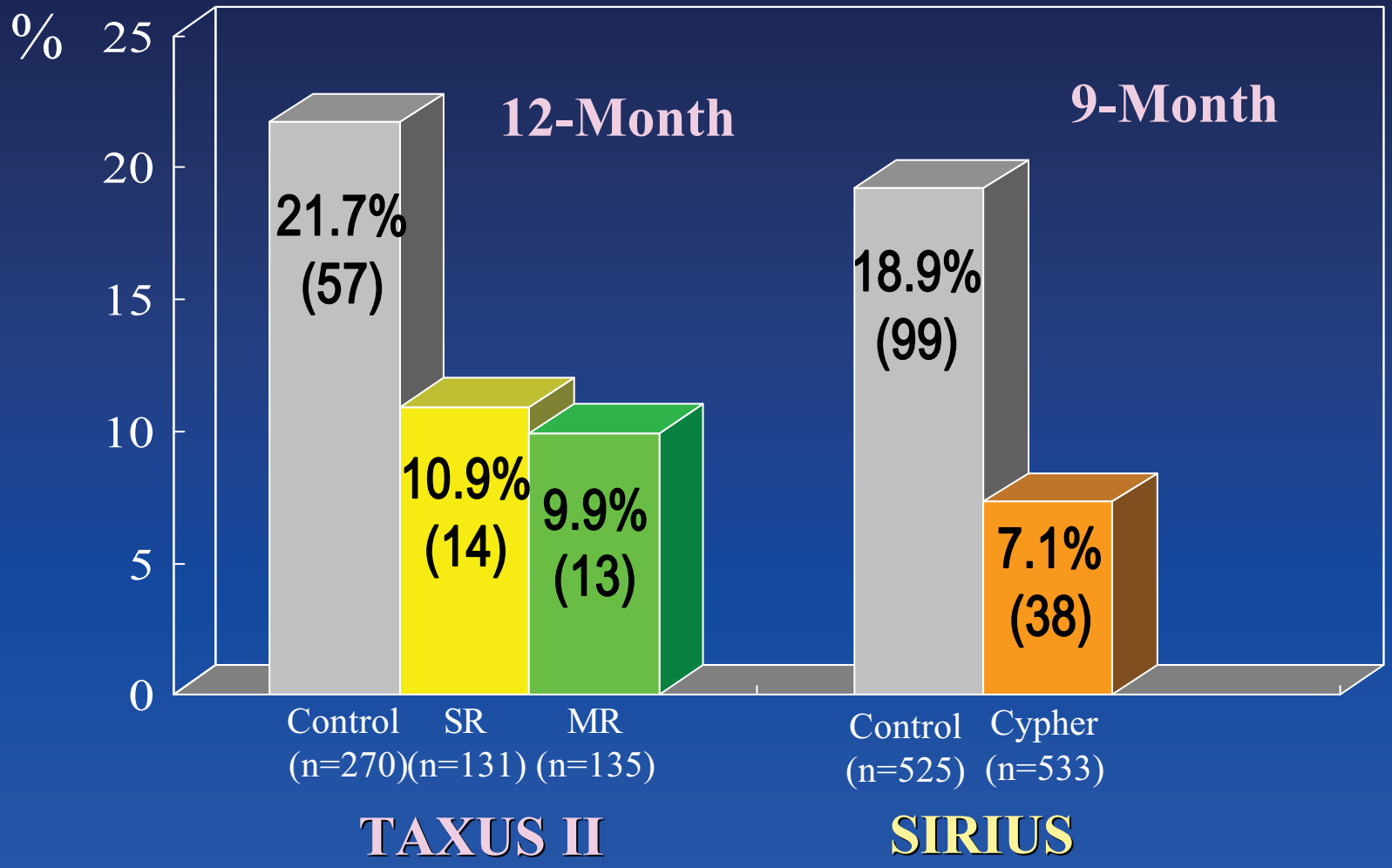
Relative Reduction



In-Hospital MACE



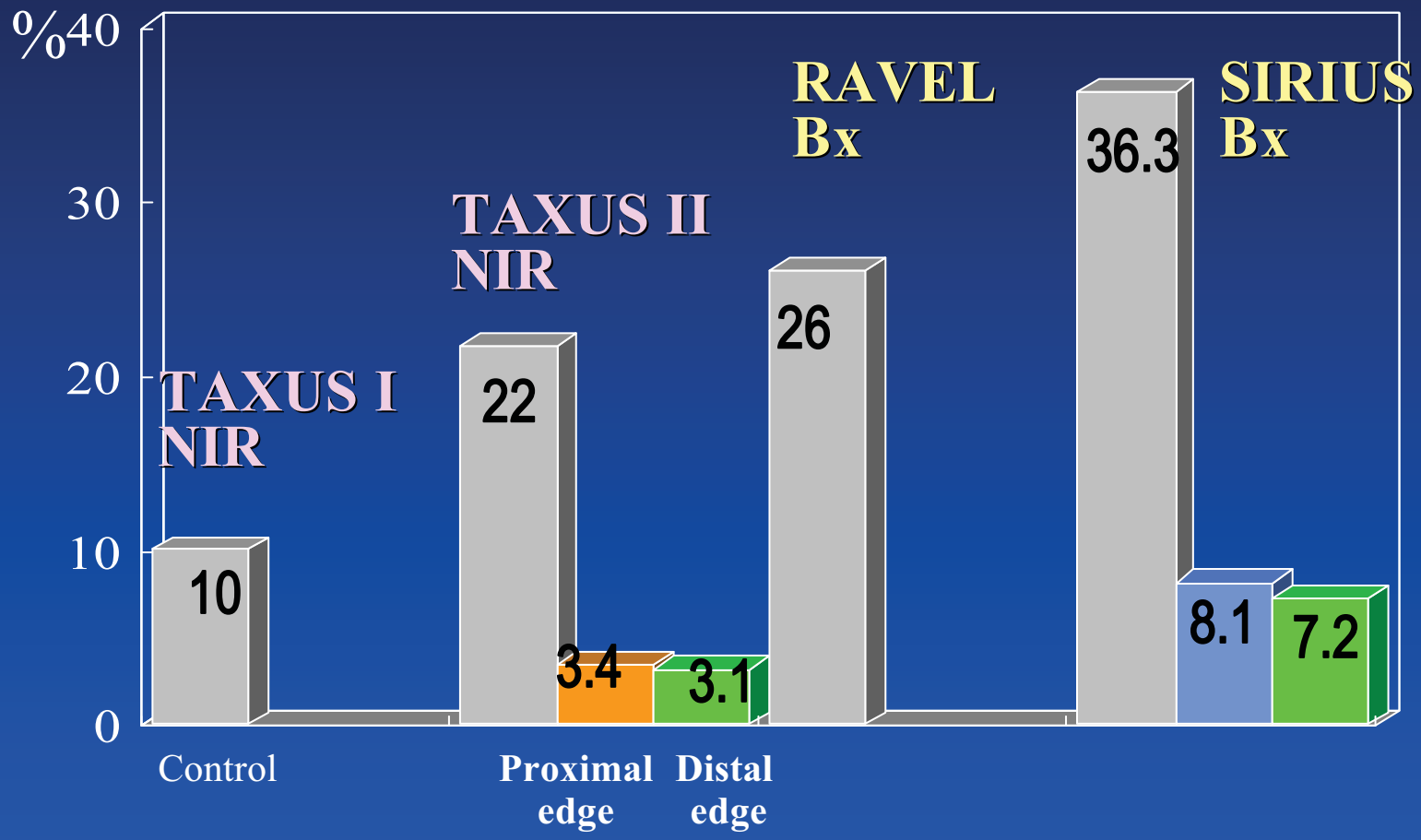
12 months MACE



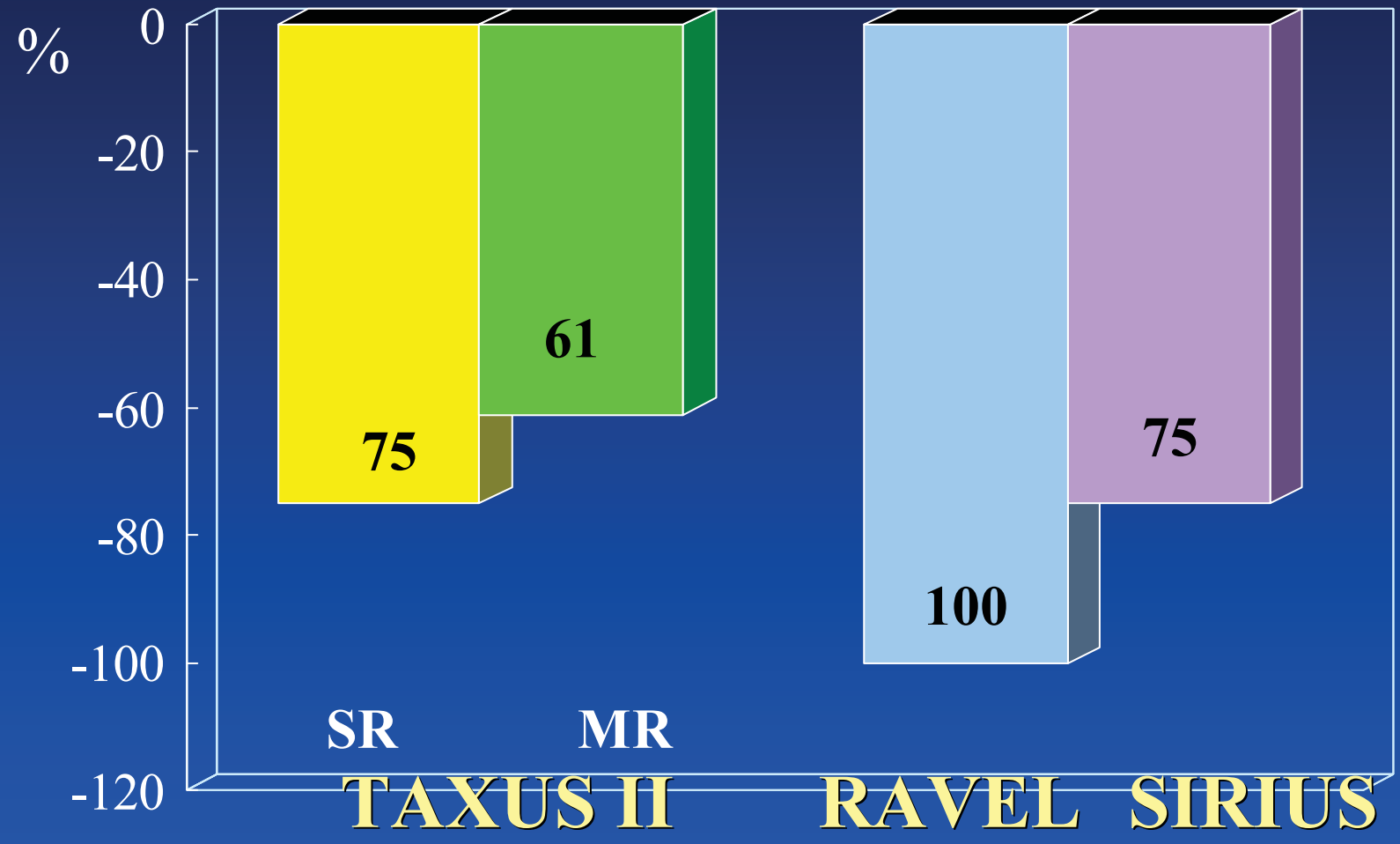
TAXUS II versus SIRIUS

Let's see Relative Reduction…

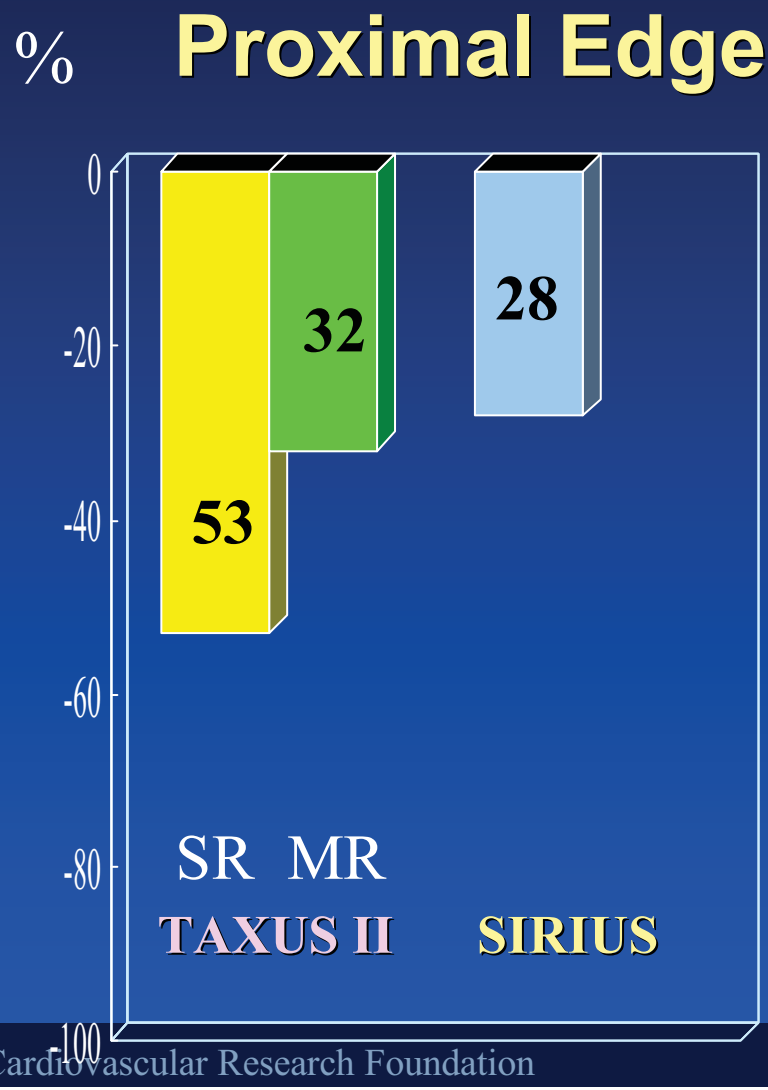
Restenosis Rate of bare metal NIR stent may be better than that of Bx Velocity ?

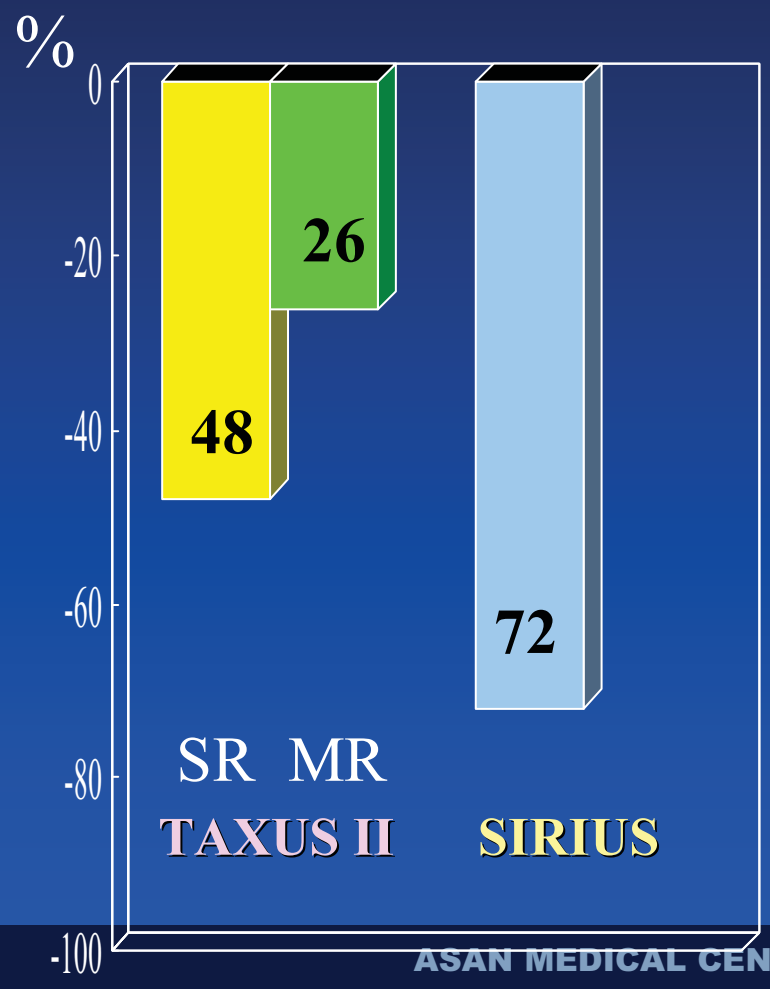


Relative Reduction of In-segment Restenosis Rate

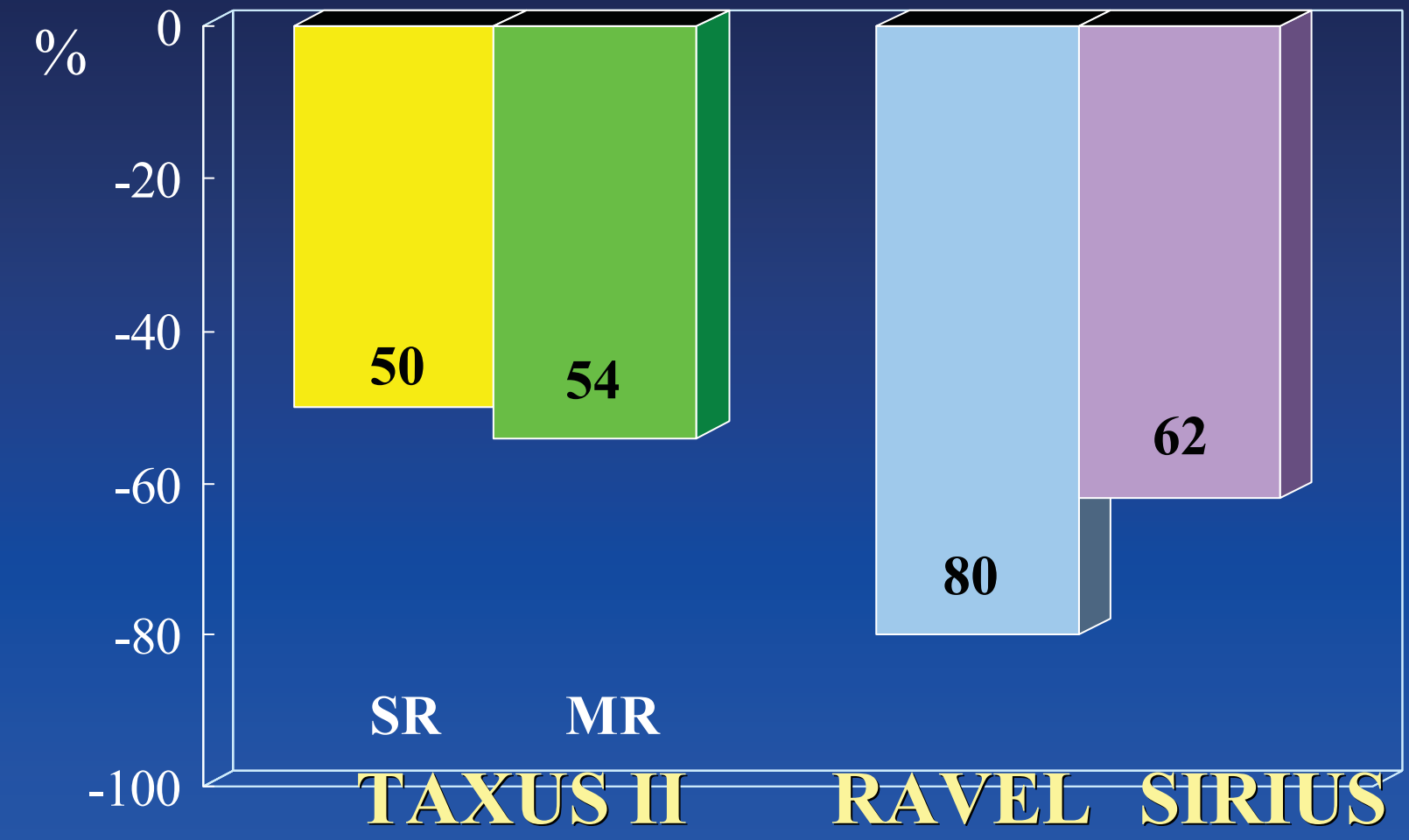


Relative Reduction of Restenosis Rate in the Proximal and Distal edge

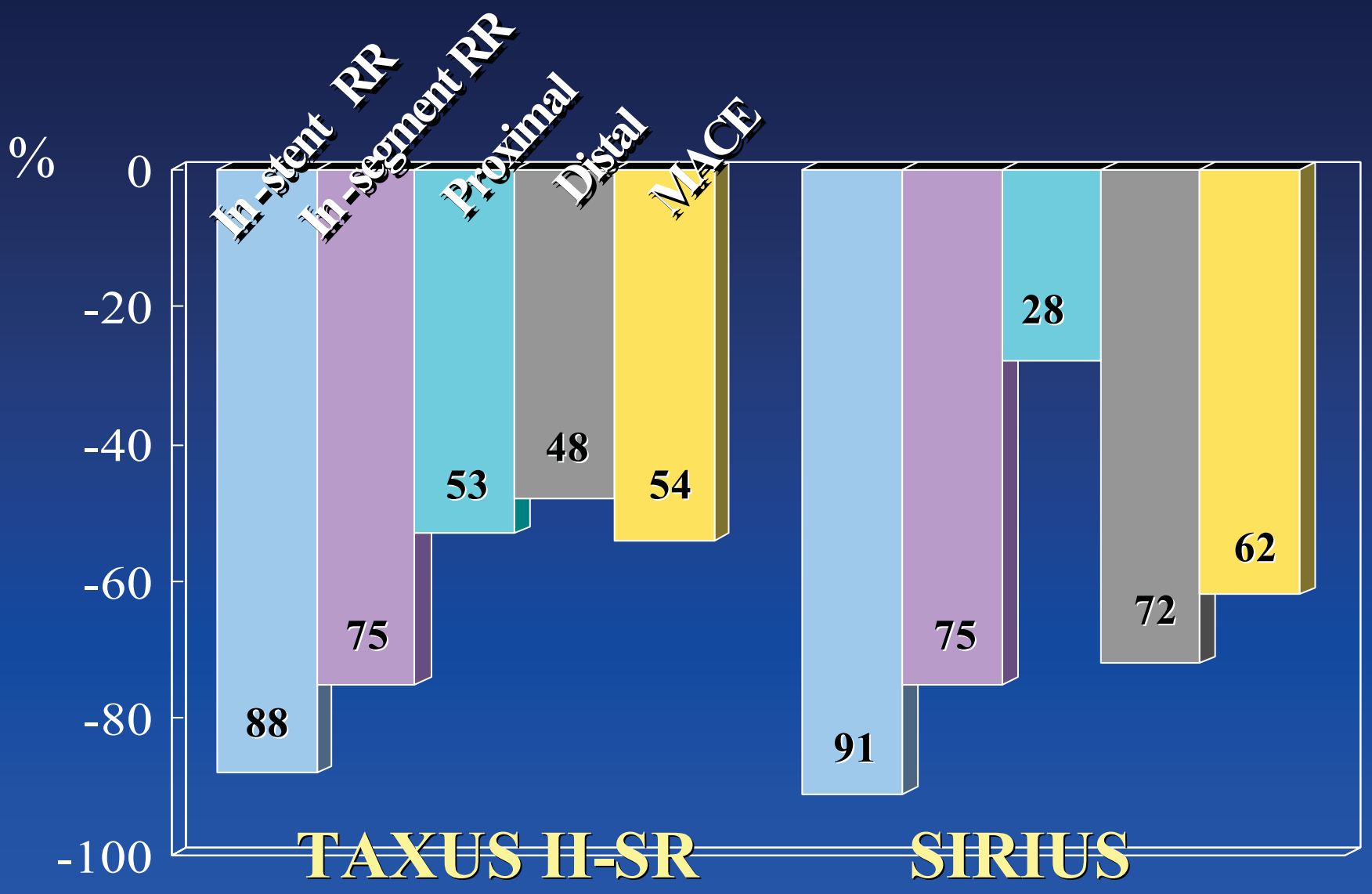




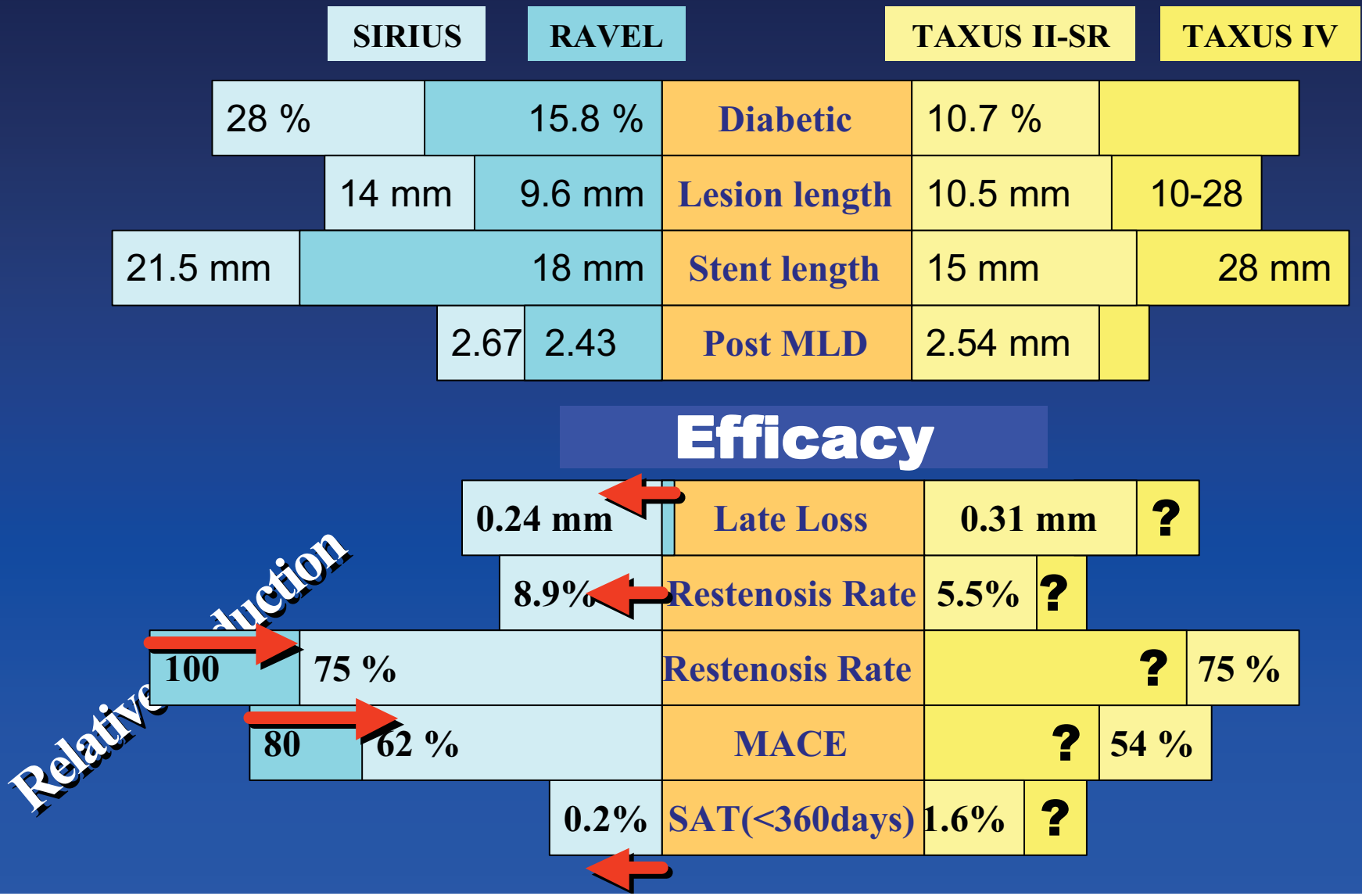
Relative Reduction of 12 months MACE



Relative Reduction



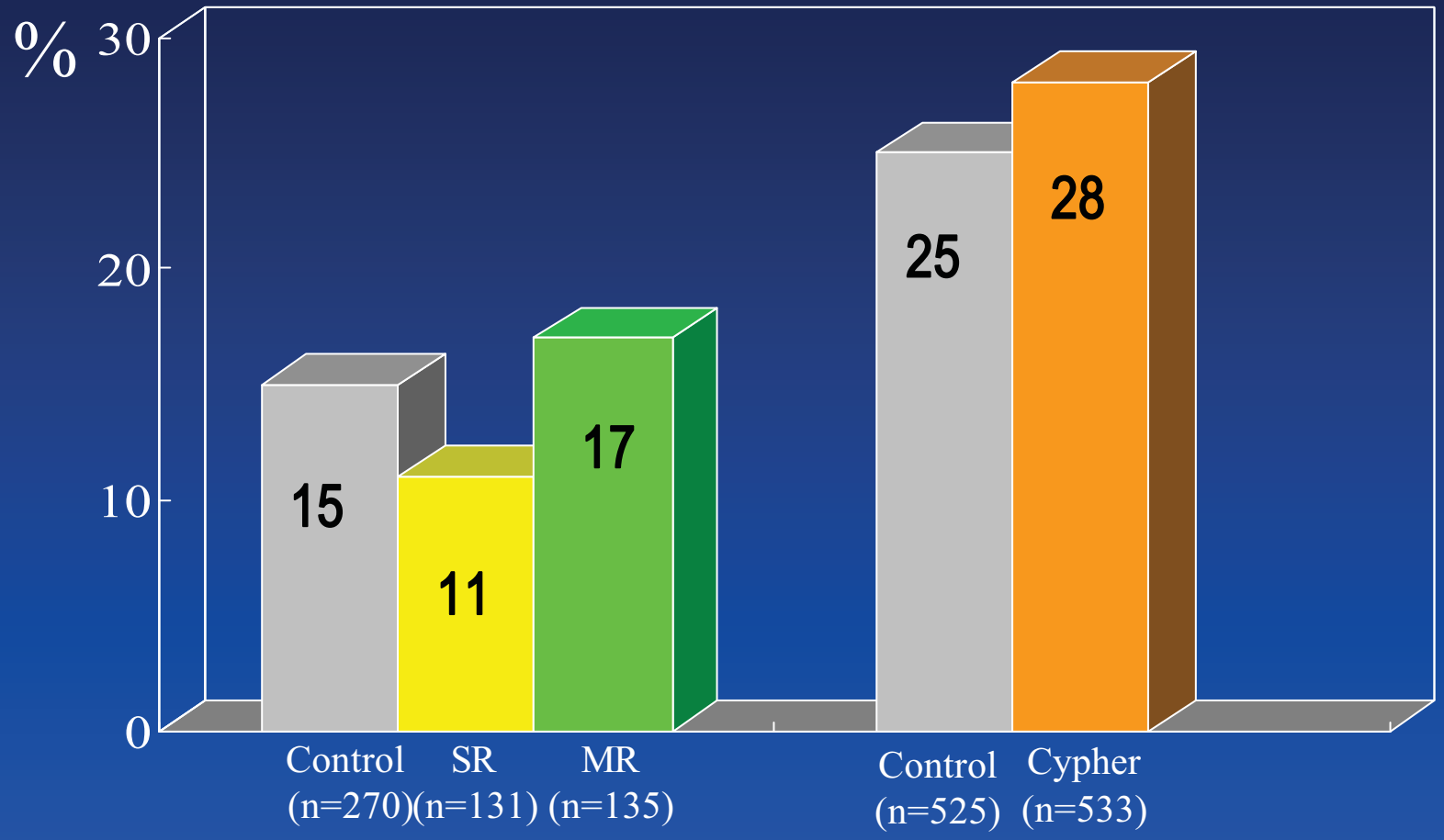
TAXUS II & SIRIUS have different study patients. We are waiting the long-term data about the TAXUS IV, V, and VI



TAXUS II versus SIRIUS

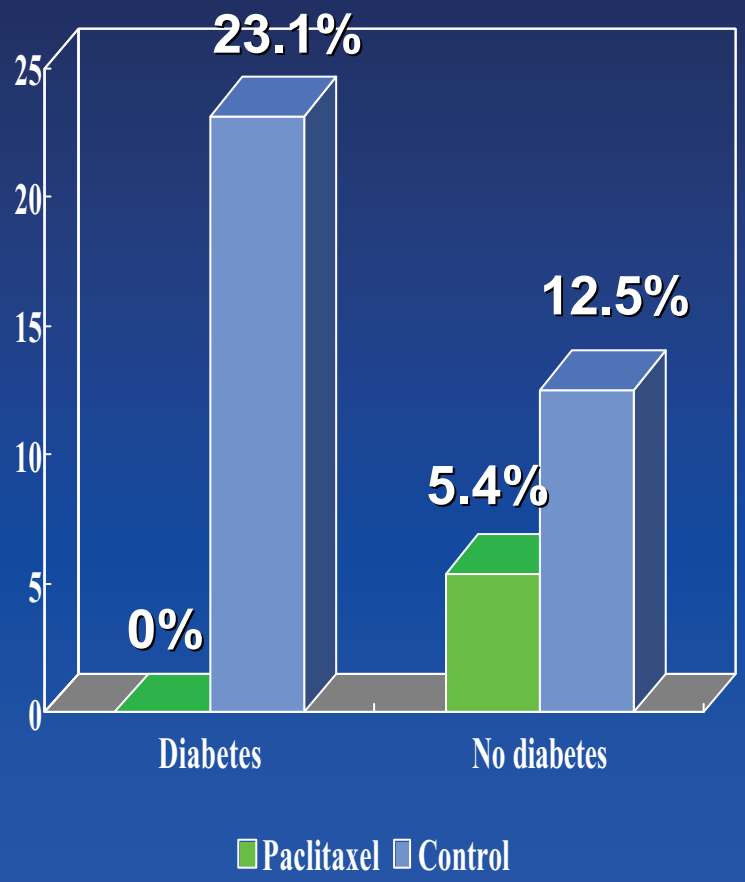
Subgroup Analysis

Enrollment of Diabetes

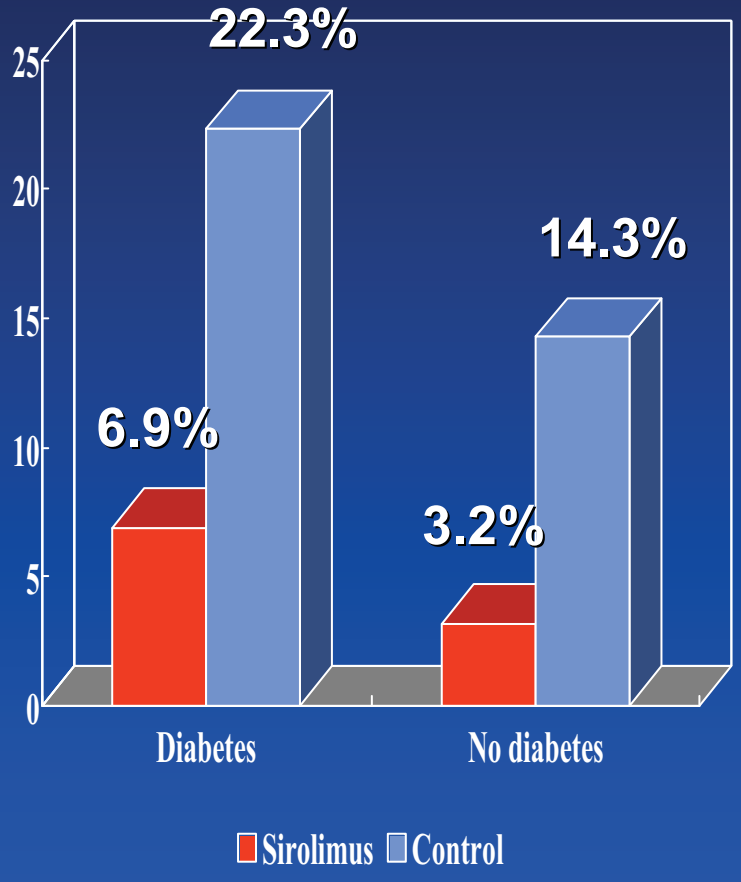


TLR in Diabetics

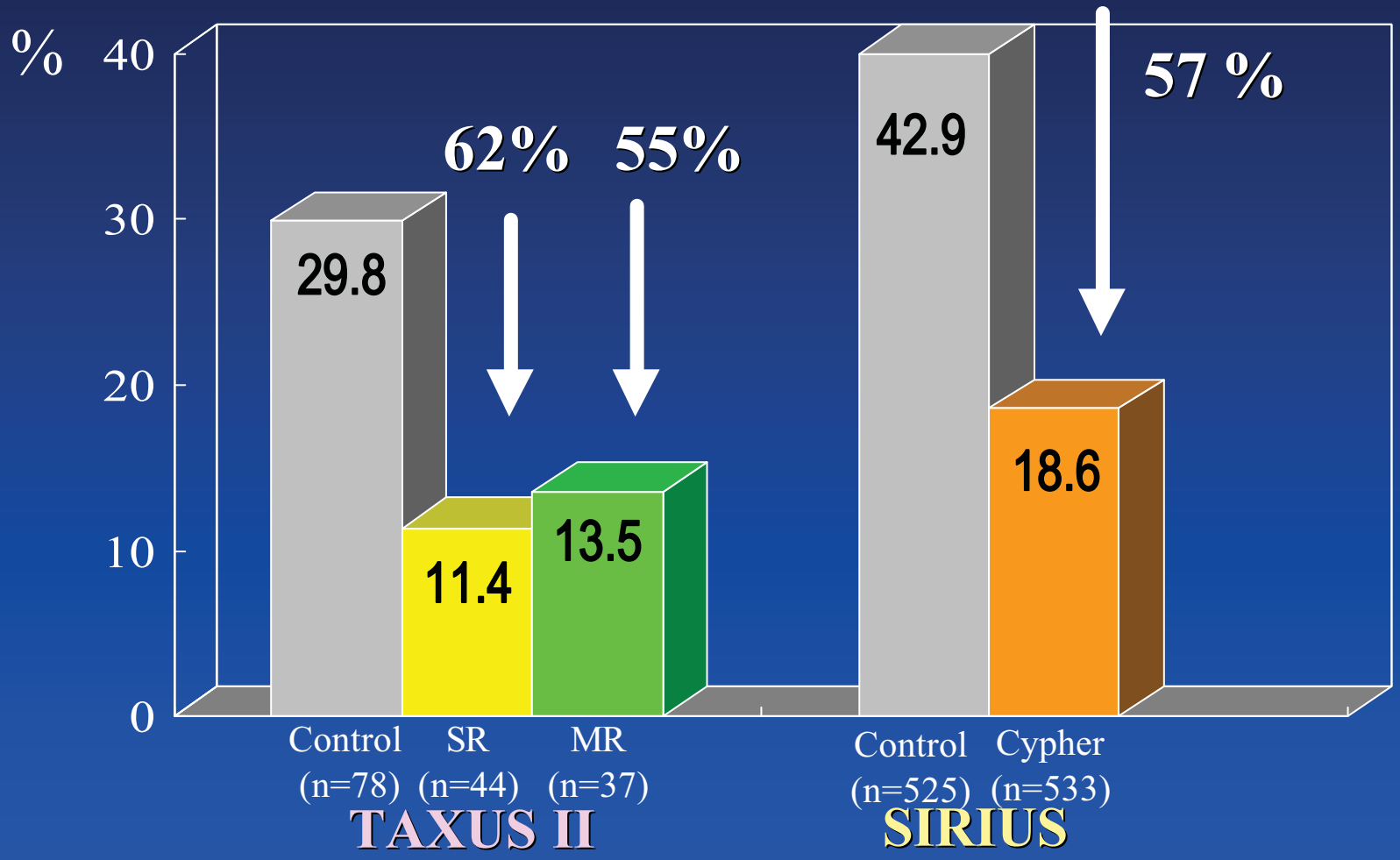
TAXUS II 6 months



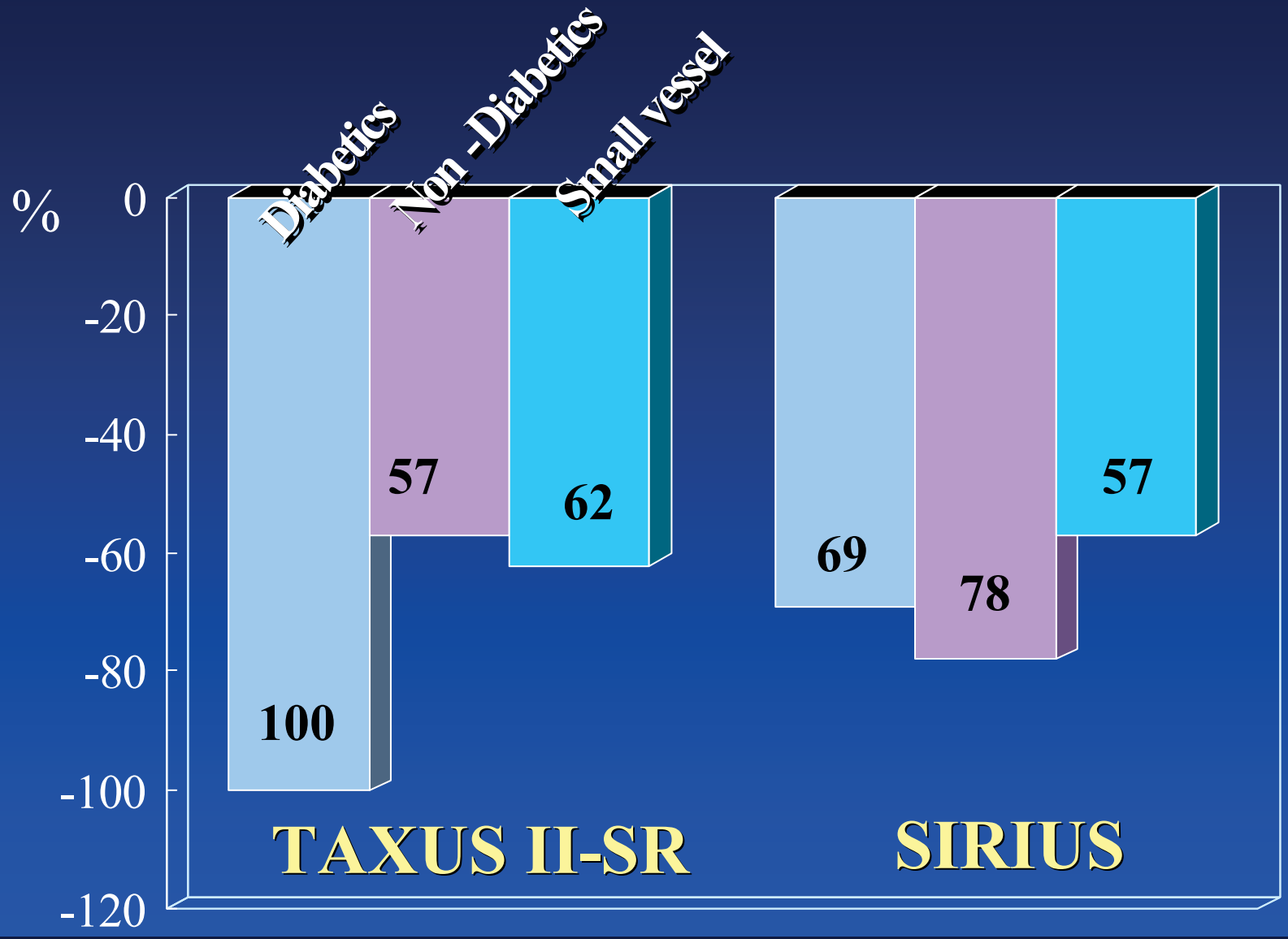
SIRIUS 9 months



In-segment Restenosi in Small Vessels (≤ 2.5mm)



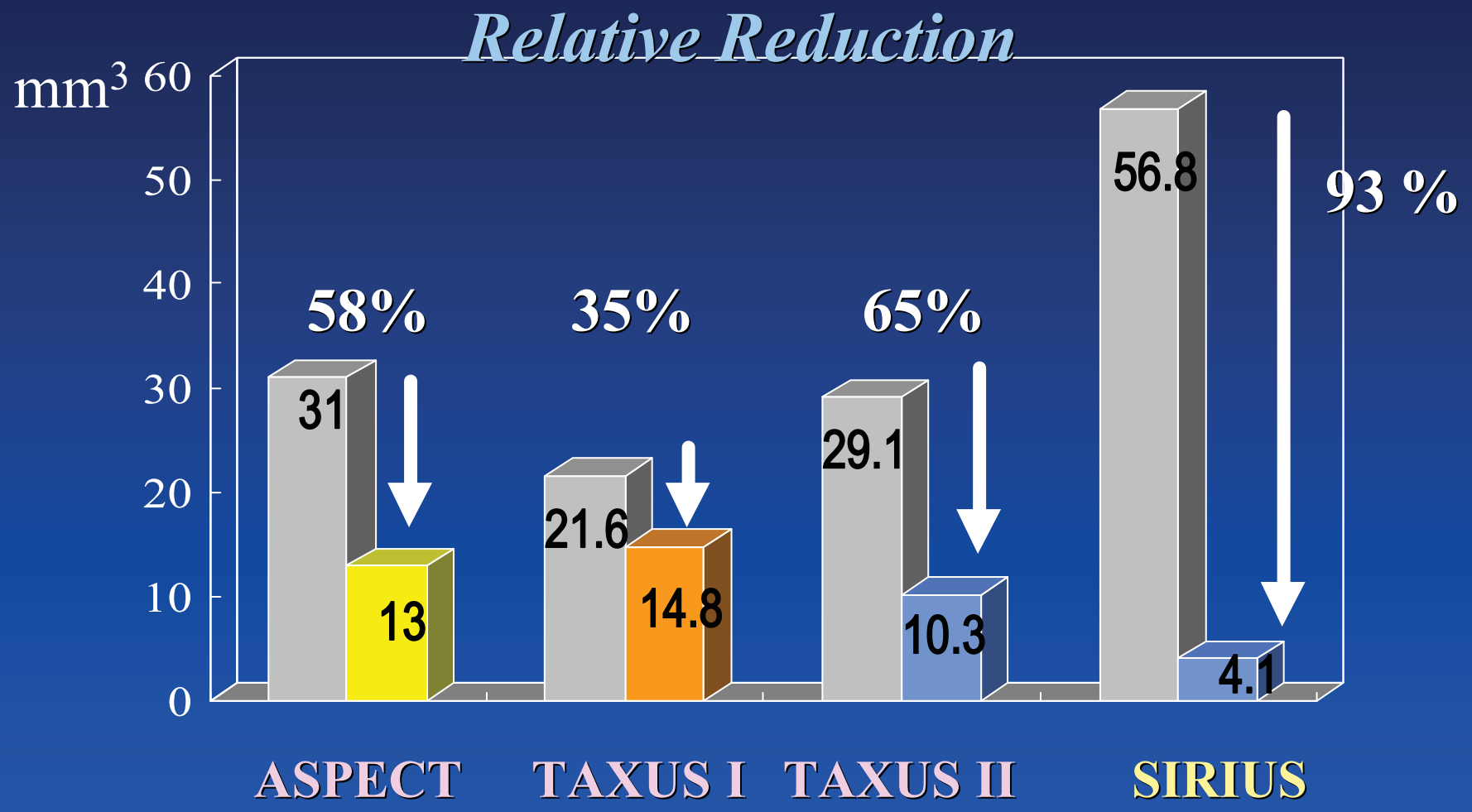
Relative Reduction



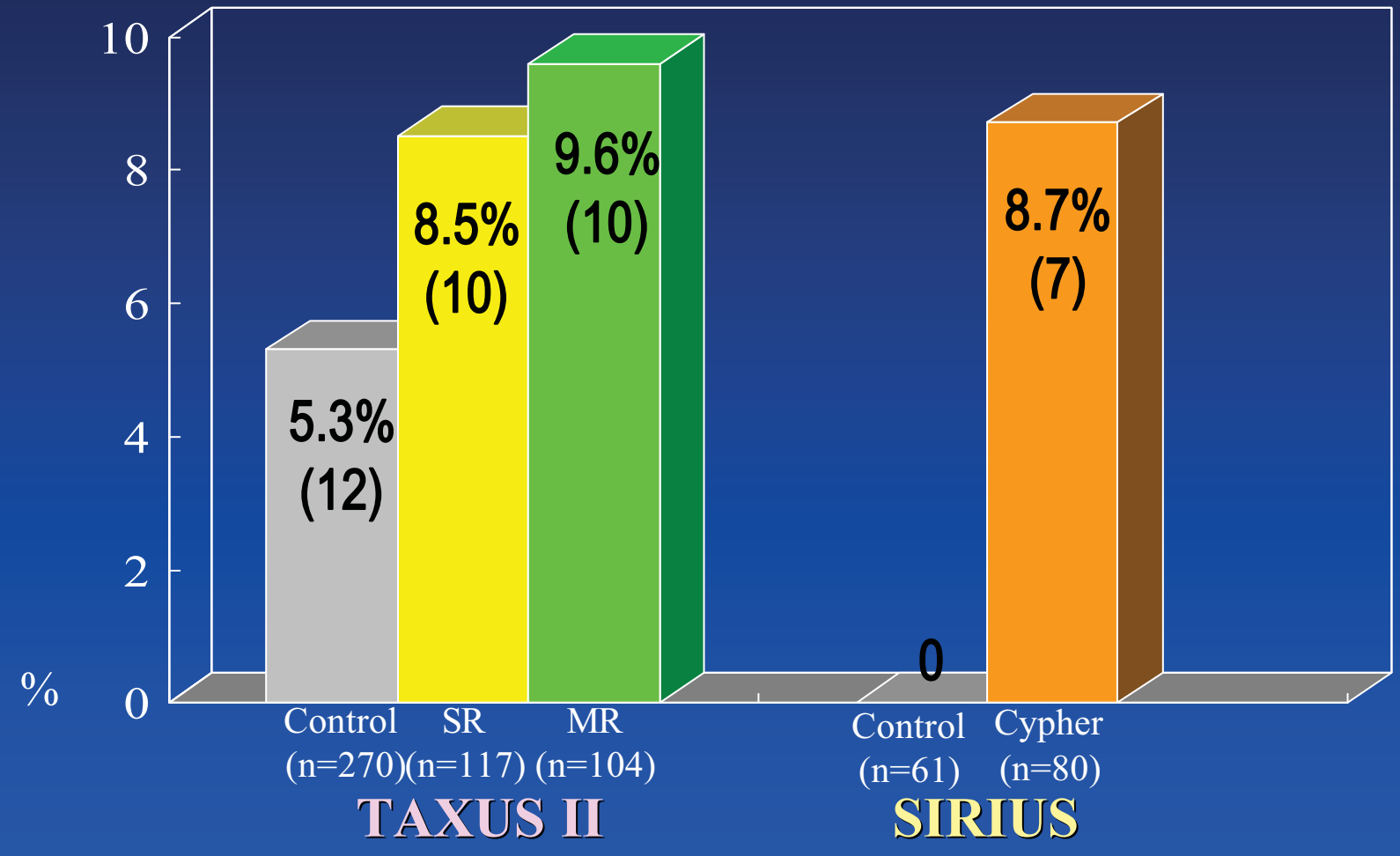
TAXUS II versus SIRIUS

IVUS Analysis

Neoinitimal Hyperplasia Volume inhibition may be better in Cypher …



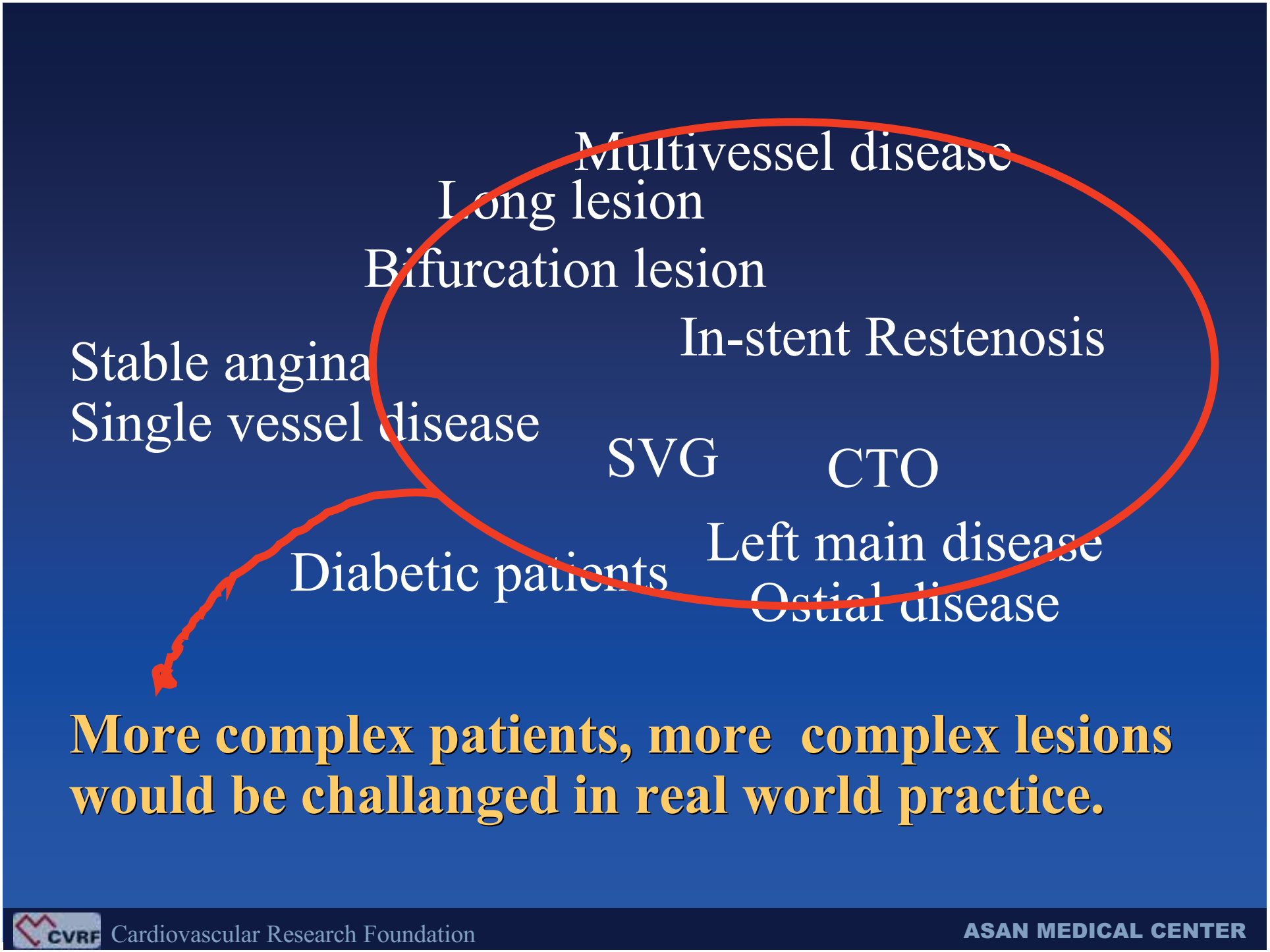
The incidence of the **Late Stent Inapposition** was similar between both trials, which did not cause serious cardiac events.



DES for ISR

	TAXUS III	Brazil	Rotterdam
No (pts)	28	25	16
Lesion length (mm)	13.6		18.4
Restenosis Rate (%)	16	4	20
TVR	21	0	12.5
MACE	29	0	
Death	0	0	12.5
SAT	0	0	

K Tanabe, Circulation 2003;107
Degertkin M.JACC 2003;41:184


Multivessel disease
Long lesion
Bifurcation lesion
In-stent Restenosis
Stable angina
Single vessel disease
SVG
CTO
Left main disease
Diabetic patients
Ostial disease
More complex patients, more complex lesions would be challanged in real world practice.

Different Stent, Different Design…

Bx velocity

Express

Cypher vs TAXUS
TAXUS vs Cypher

- Two stents would be good enough in the simple lesion subsets based on the current studies.
- We need more data about real world lesion subsets and patients subsets. (TAXUS Express IV,V,VI)
- Economic factors will play an important role in strategic case-based decision-making.