Reconciling Angiographic and Clinical Results After Stent Treatment: A Critical Appraisal

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The concept was 12 years in the making . . ..

Our Preoccupation With Coronary Luminology

The Dissociation Between Clinical and Angiographic Findings in Ischemic Heart Disease

Eric J. Topol, MD; Steven E. Nissen, MD

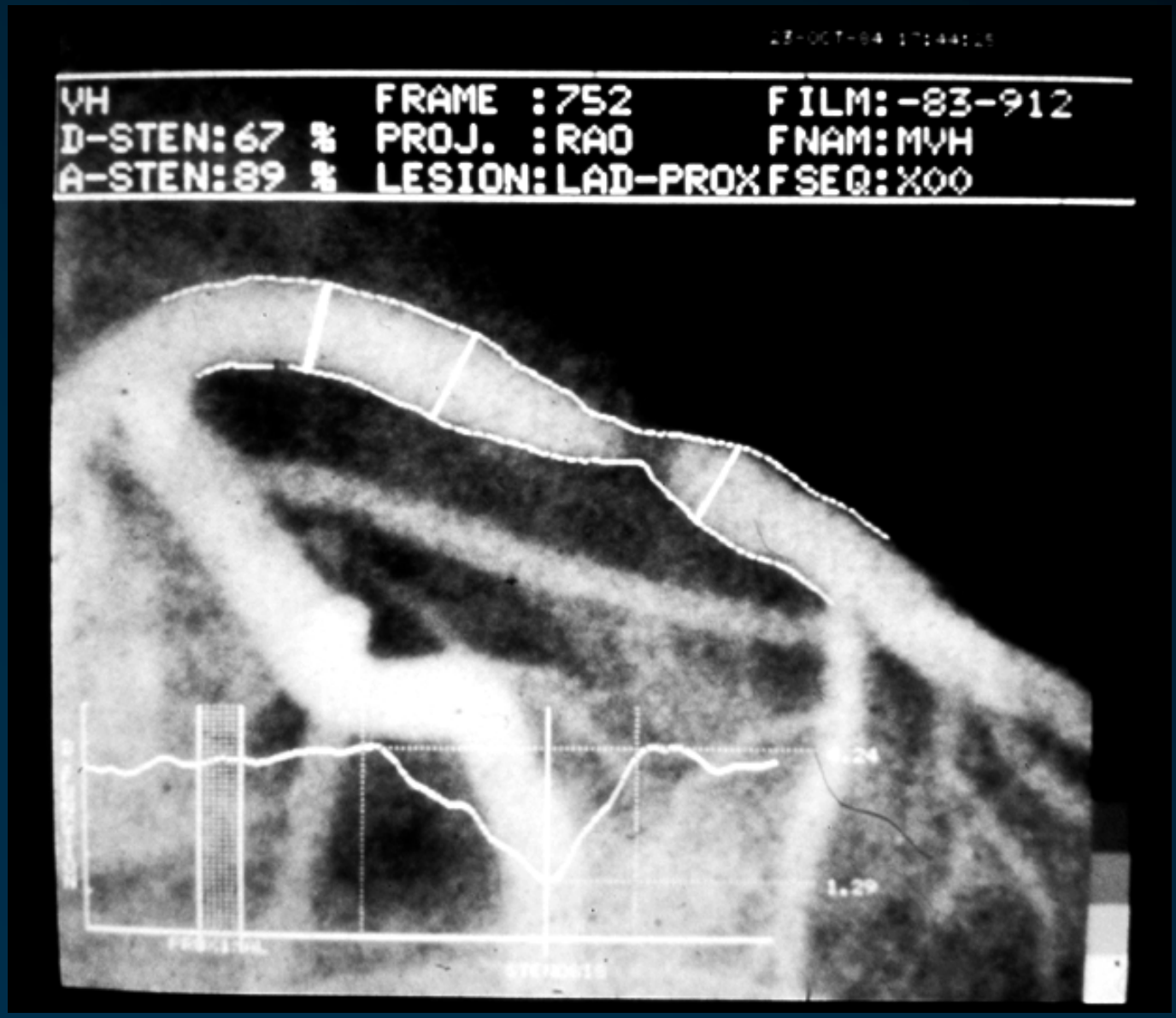
Abstract Nearly 40 years after its invention, the angiogram is still considered by most physicians to be the "gold standard" for defining coronary anatomy. Careful investigations have revealed many deficiencies inherent in this app... purpose of this article is to outline the eviden... current preoccupation with coronary "luminolog... misguided and to propose a rational paradigm... practice and investigation. Angiography depicts co... omy from a planar two-dimensional silhouette of... Angiography is limited in resolution to four or fi... per millimeter. Confounding factors include vessel tortuosity, overlap of structures, and the effects of lumen shape. After intervention, a hazy, broadened silhouette may overestimate the actual gain in lumen size. Studies show marked disparity between the apparent severity of lesions and their physiological effects. After myocardial infarction, cardiologists too often do not make an attempt to demonstrate the physiological significance of the stenosis before performing percutaneous coronary revascularization. Similarly, the allure of a better, more grati... ...rs to be ...rdiolo... angio... ...gnized ...clinical ...view of ...ng the ...logy to achieving the desired clinical end point: promoting survival and long-term freedom from myocardial infarction and the disabling symptoms of coronary heart disease. (***Circulation.*** **1995; 92:2333-2342.)**

Key Words • angiography • myocardial infarction • atherosclerosis • revascularization • angioplasty

Original source
"Oculostenotic reflex"

Topol et al Circulation 1995;92:2342

QCA was initially very primitive, and maybe inaccurate



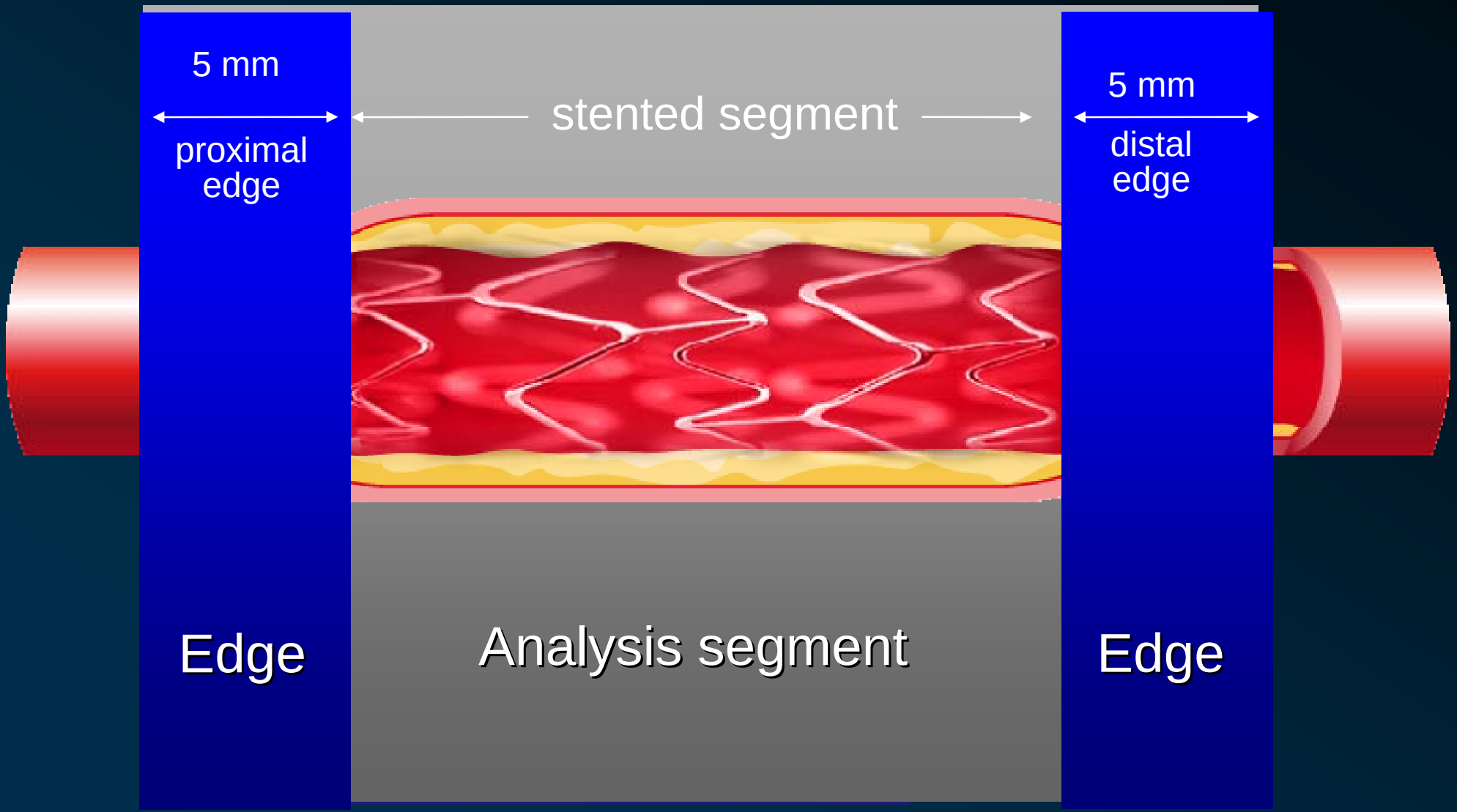
Clinical Events After PCI

Death	Total Plaque Burden, LVEF
Myocardial Infarction	Plaque stability

Target Lesion Ischemia CABG Re PTCA	Relative Lumen Dimensions QCA, IVUS CFR

Ca: 1994

DES Angiographic Analysis

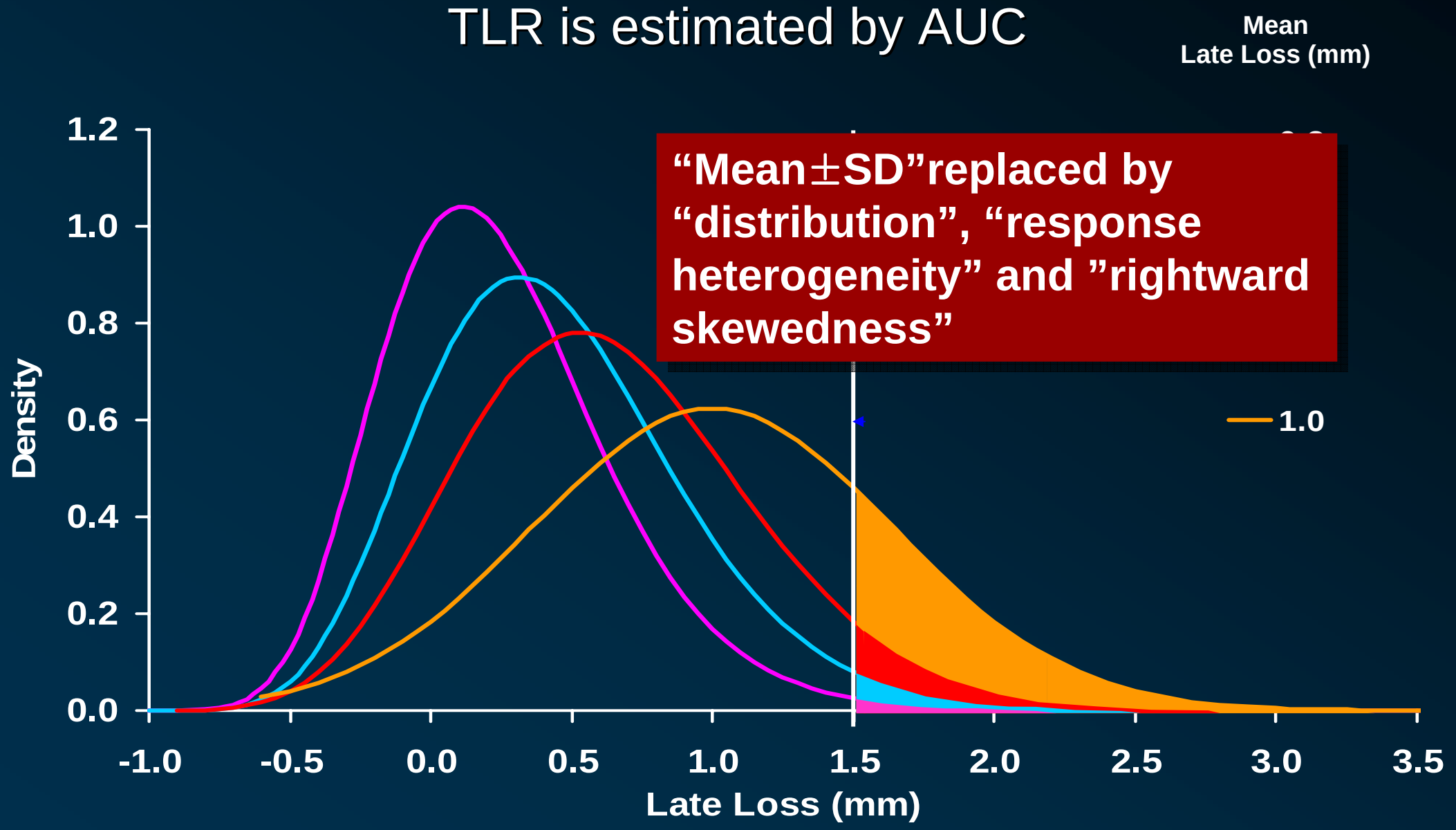


The fundamental concepts of “acute gain” and “late loss” were developed simply to explain why devices work

There terms “In-stent” and “in-segment” “late loss” were catchy, simple, and provide at way to measure the amount of tissue growth within a stent

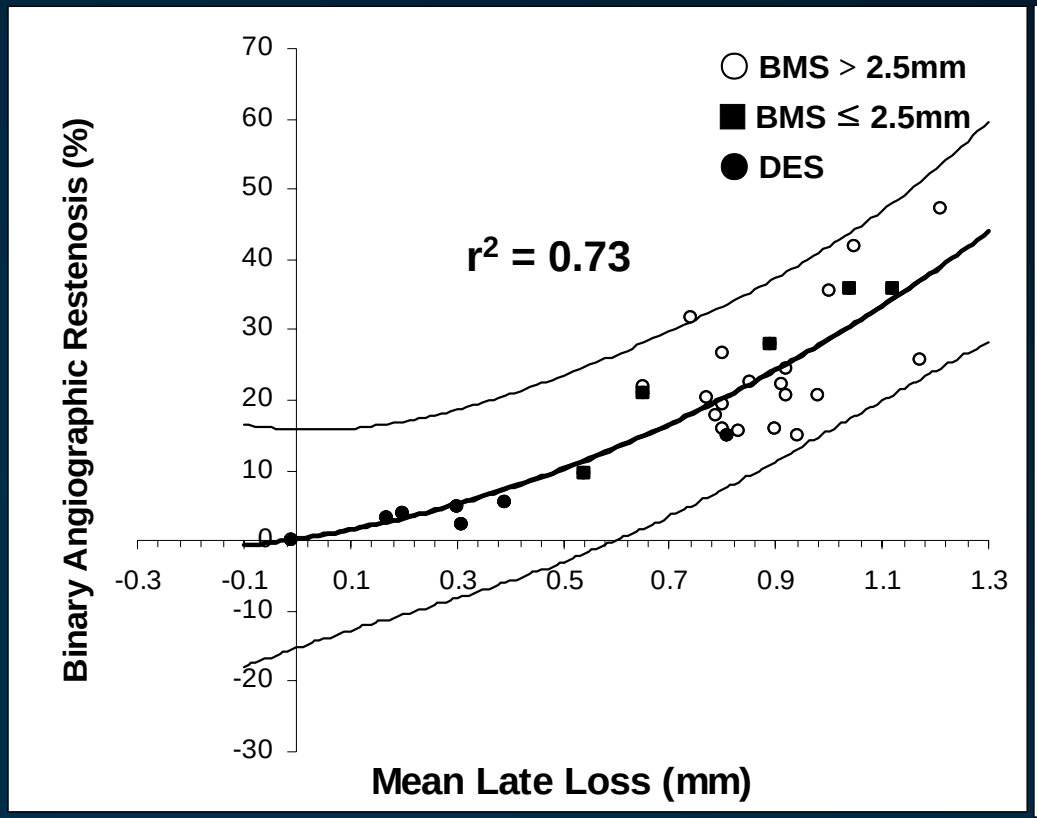
Late Loss Predicts Clinical Restenosis Rate

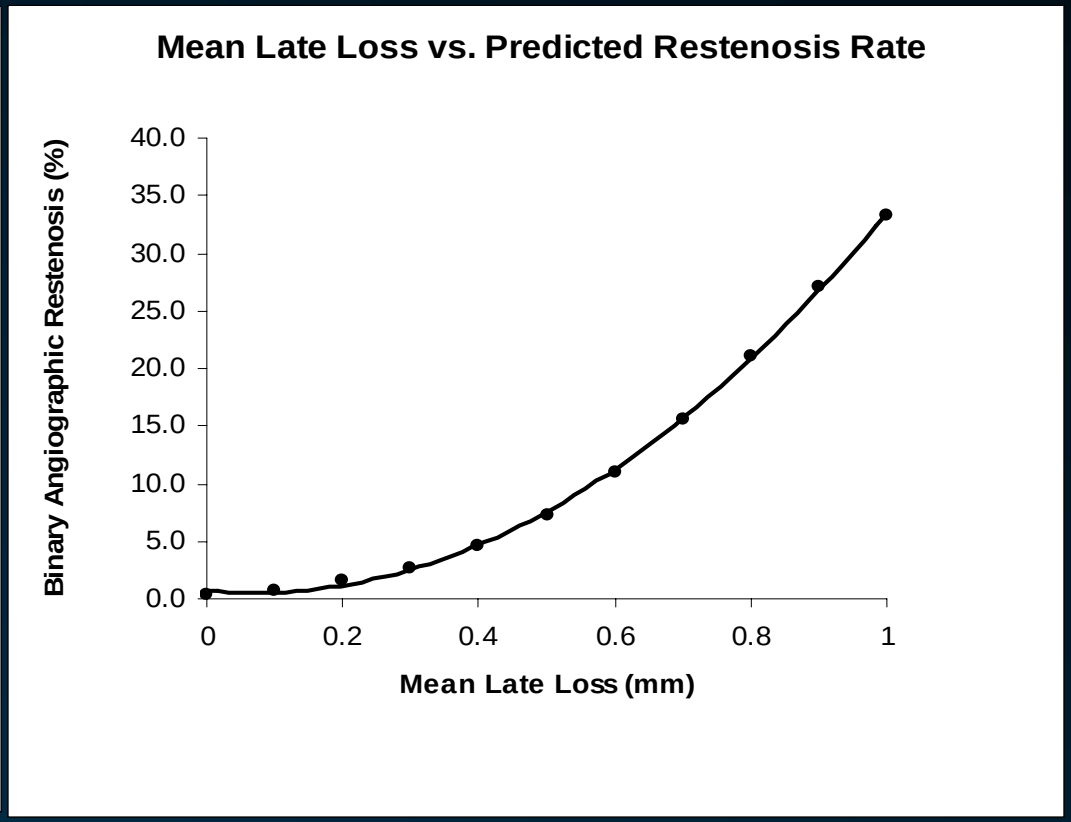
TLR is estimated by AUC



“Mean±SD”replaced by “distribution”, “response heterogeneity” and ”rightward skewedness”

Late Loss Predicts Restenosis Rate





Monotonic relationship means that higher late loss translates to more restenosis

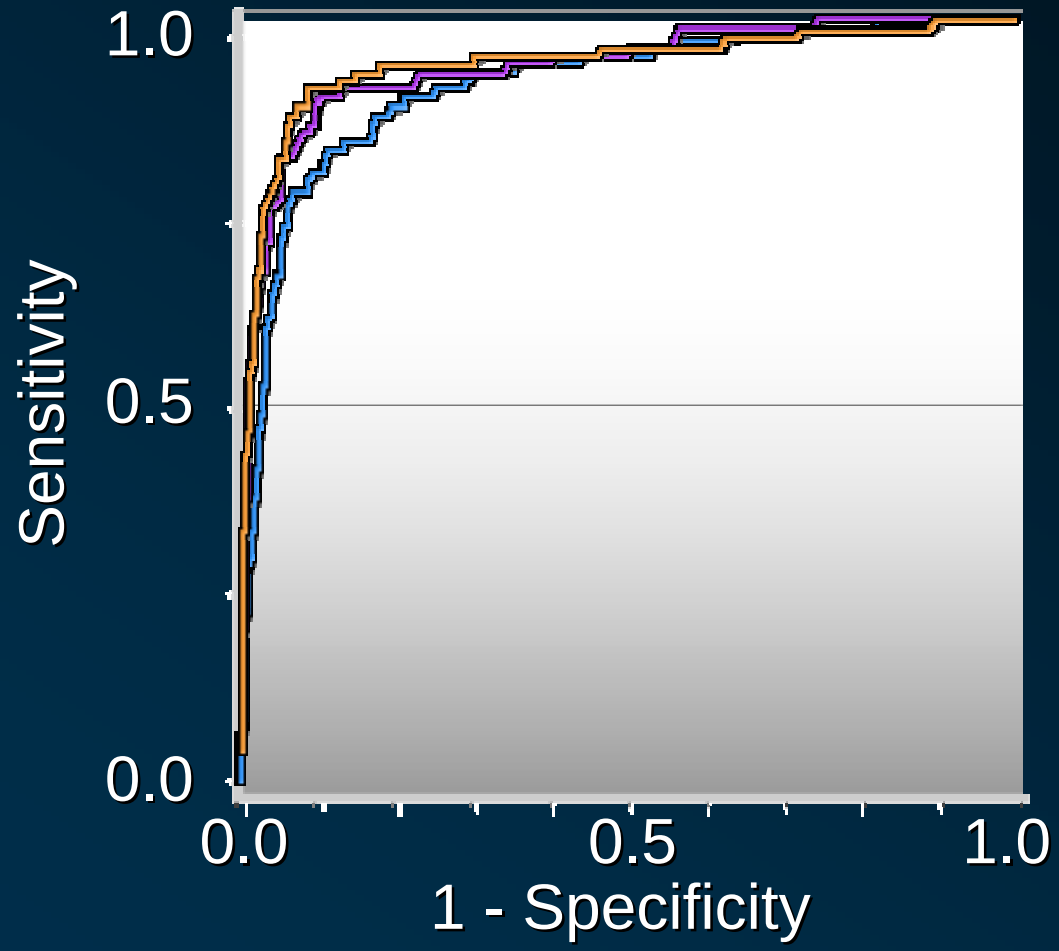
Mauri et al. Circulation. 2005:111:3435-3442.

So What Went Wrong with LLL

	In-Stent LLL	TLR
SIRIUS	0.17 mm	4%
TAXUS	0.39 mm	3%

Angiographic predictors of TLR

ROC Analysis combining all patients



Late Loss
AUC = 0.918

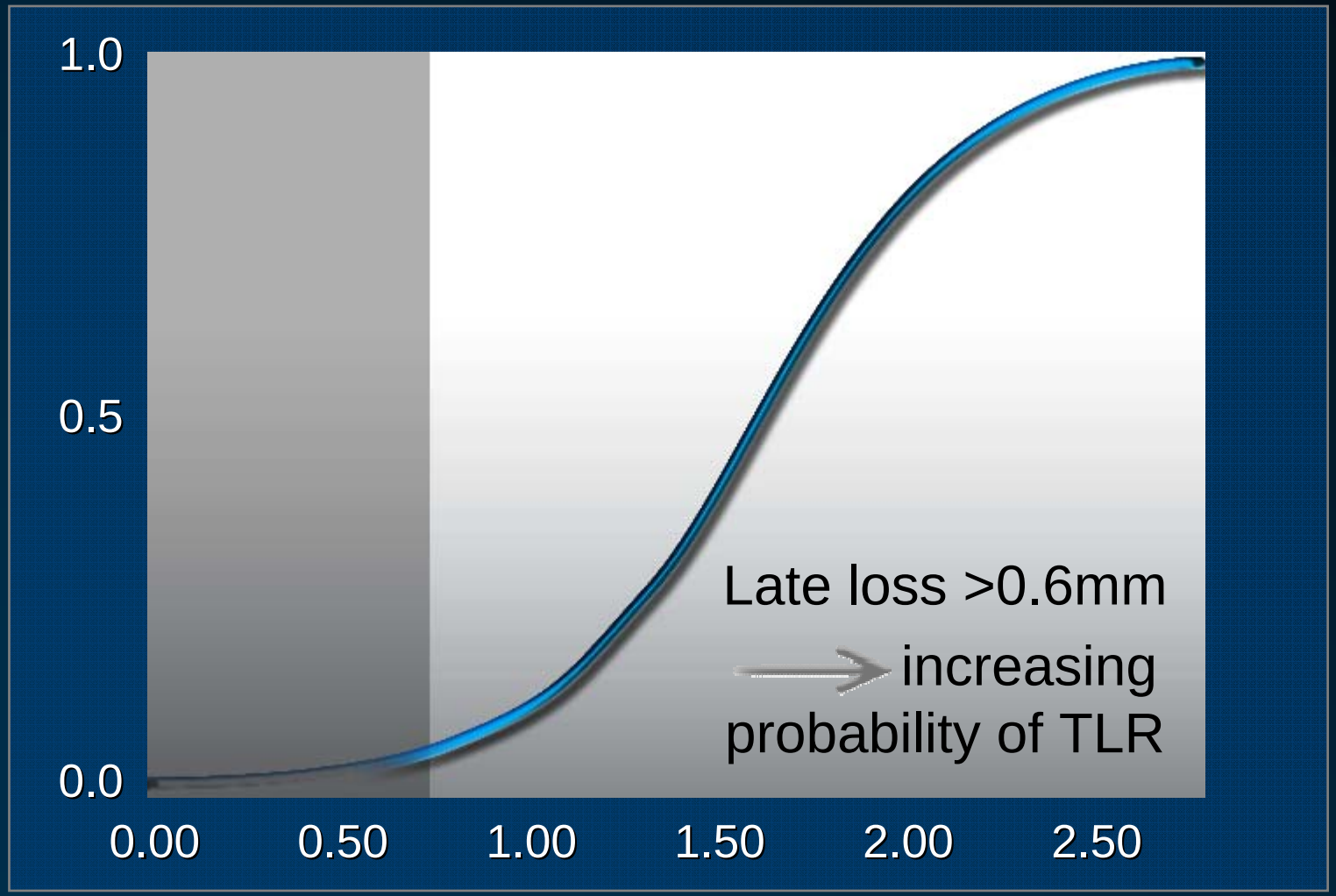
MLD
AUC = 0.940

Diameter Stenosis
AUC = 0.944

→ Late loss as the weakest angiographic predictor

Taxus IV Late loss as a predictor of TLR

Logistic regression combining all patients

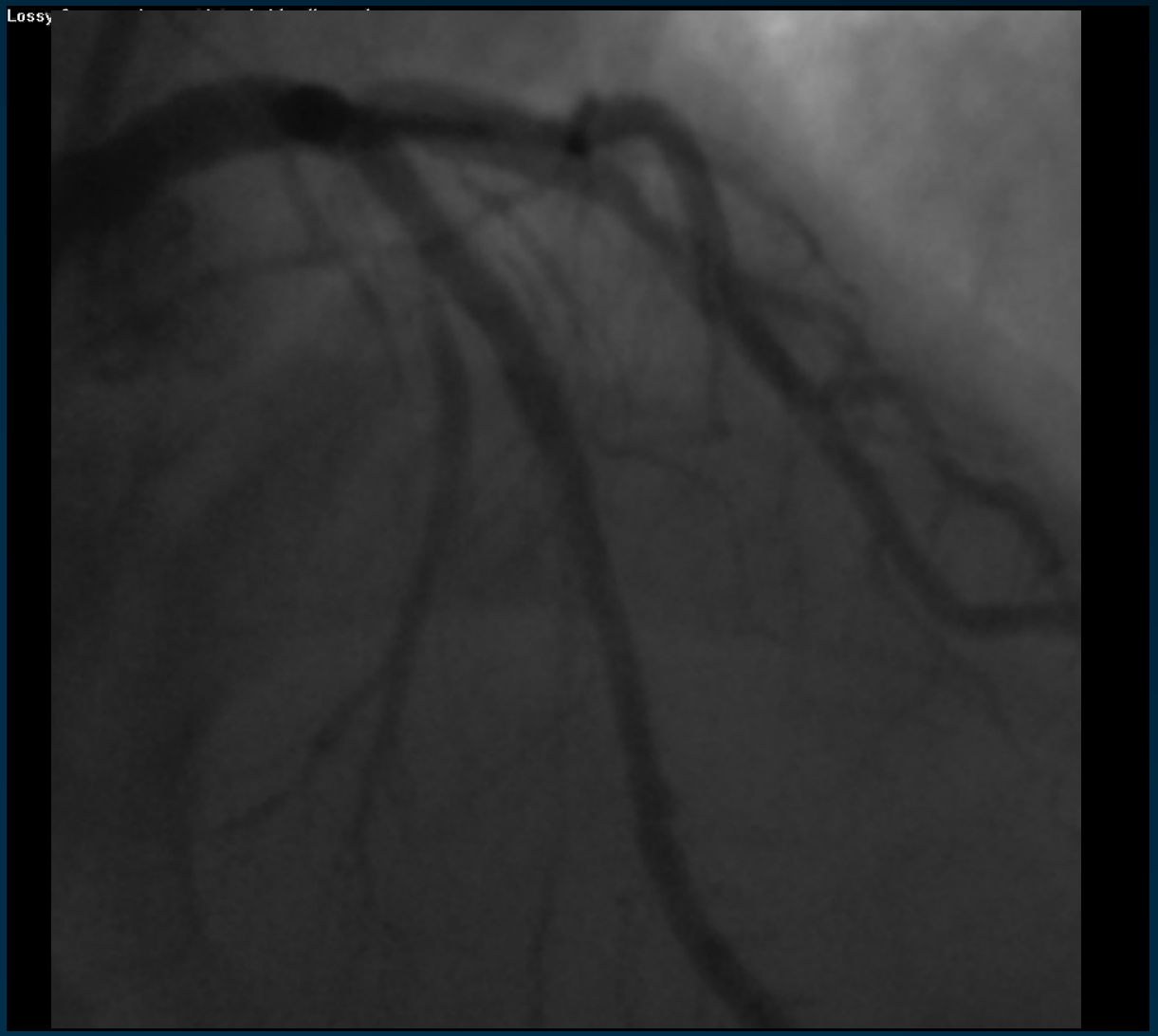


The Endeavor I: Day of QCA Reckoning

	4 Months	12 Months
RVD, mm	2.97±0.46	2.91±0.44
In-Stent		
MLD	2.50±0.45	2.24±0.50
% Stenosis	15.2±13.7	22.3±15.8
Late Lumen Loss	0.36±0.39	0.61±0.45
Angio % Obstruction	4.9±18.7	15.4±21.7
IVUS % Obstruction	4.6 ± 8.5	9.6 ± 8.5
In-Lesion		
MLD	2.28±0.46	2.09±0.47
% Stenosis	22.8±11.8	27.7±13.3
Late Lumen Loss	0.22±0.41	0.42±0.45

ENDEAVOR I: 12 Month Results

Grade 0 Intimal Hyperplasia (N=22)



RVD = 2.85

Stent MLD = 2.57

Stent % Stenosis = 9.3

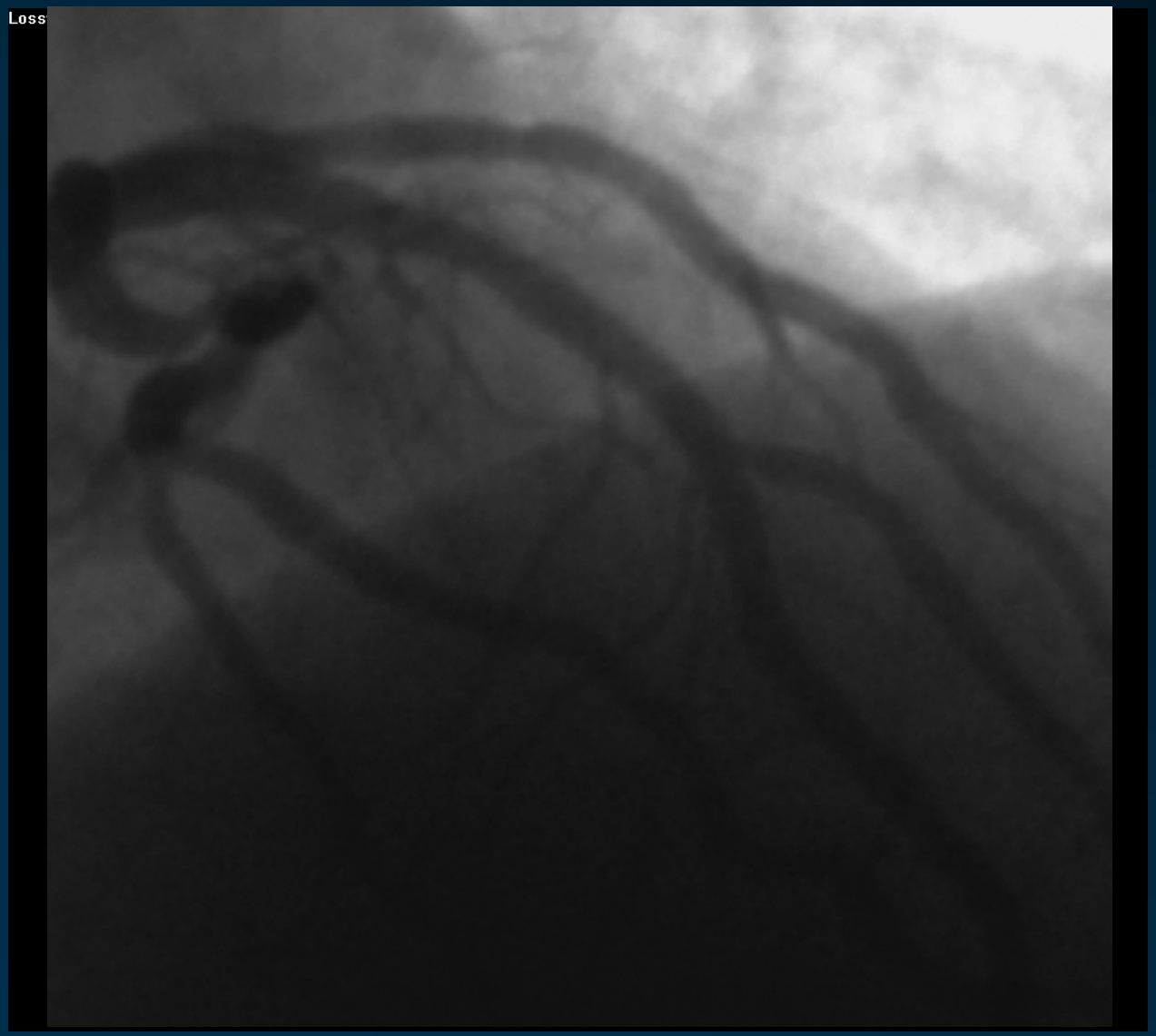
% CSN = 16.9

Stent LLL = 0.19

% Volume Obst = 1.6%

ENDEAVOR I: 12 Month Results

Grade 1 Intimal Hyperplasia (N=32)



RVD = 3.00

Stent MLD = 2.48

Stent % Stenosis = 17.7

% CSN = 30.5

Stent LLL = 0.50

% Volume Obst = 9.6%

ENDEAVOR I: 12 Month Results

Grade 3 Intimal Hyperplasia (N=14)

RVD = 2.82

Stent MLD = 1.92

Stent % Stenosis = 32

% CSN = 53.3

Stent LLL = 0.82

% Volume Obst = 28.6%

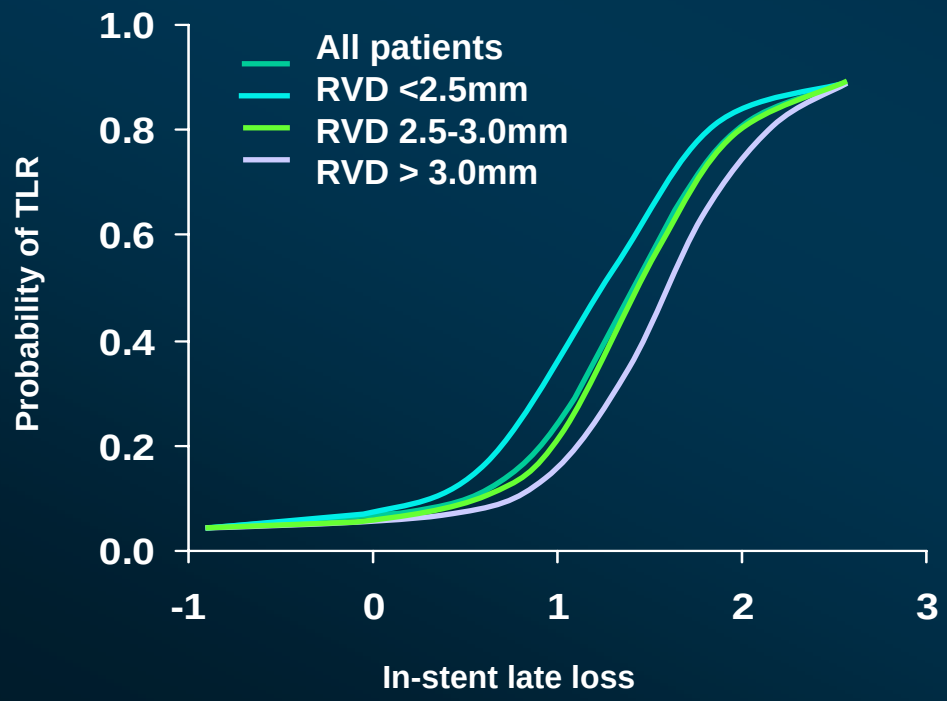
ENDEAVOR I: 12 Month Results

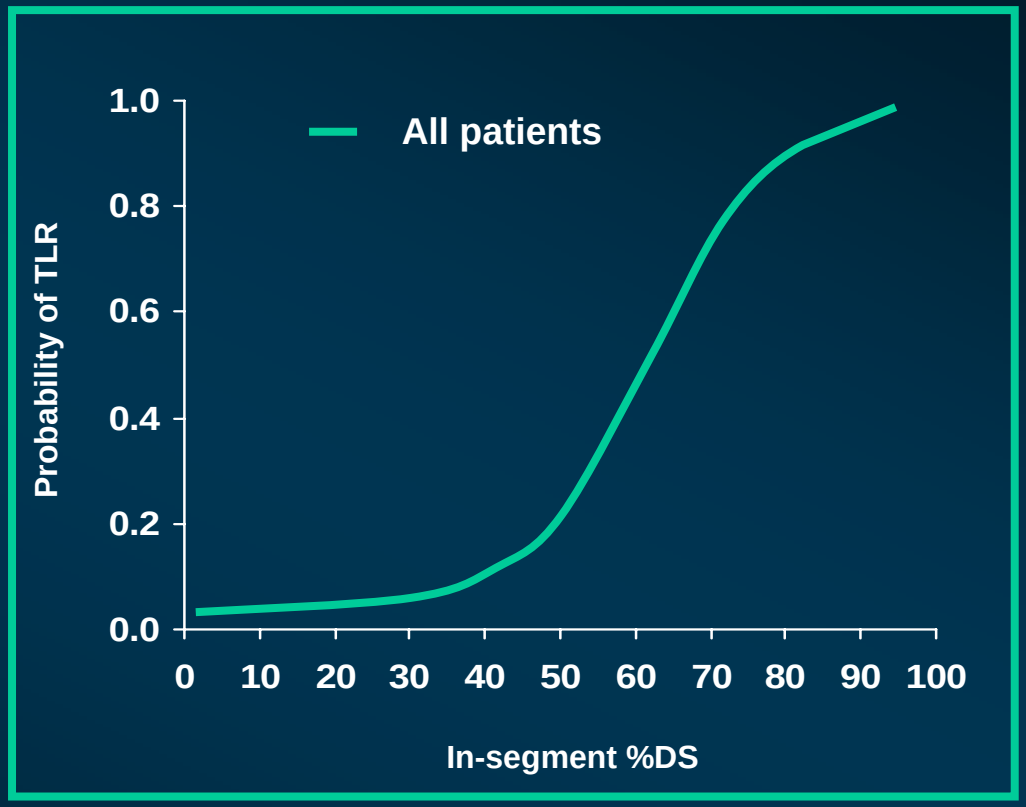
Grade 5 Intimal Hyperplasia (N=5)

RVD = 2.99
Stent MLD = 1.12
Stent % Stenosis = 61.3
% CSN = 88.9
Stent LLL = 1.72
% Volume Obst = 46.5%

11 RCTs with Cypher, Taxus, Endeavor, and BMS (5381 pts)

LL and % DS vs. TLR - A curvilinear relationship





Pocock S. et al., JACC 2008

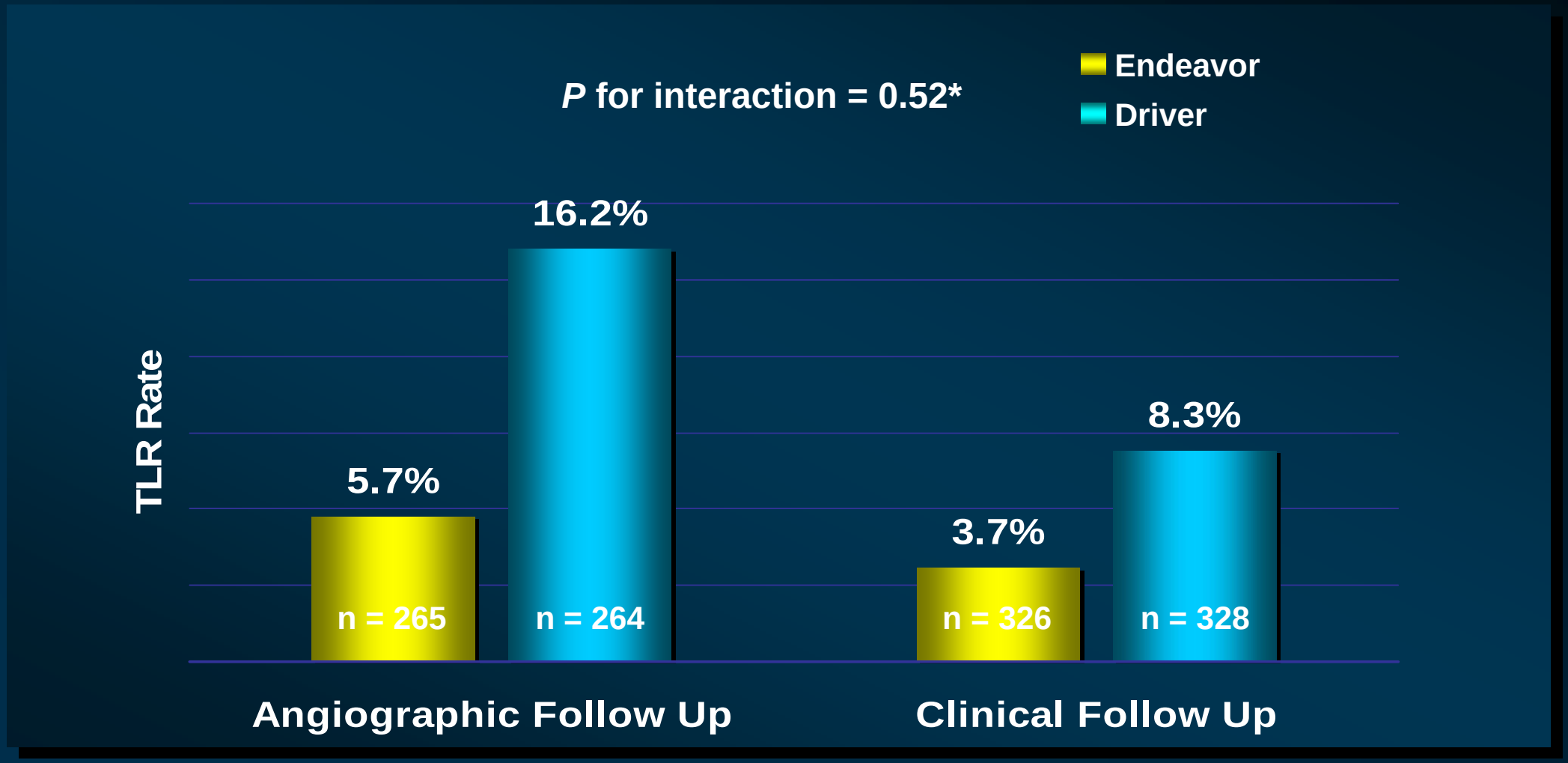
A Summary Statement on LL-TLR

The relationship between late lumen loss and TLR is “monotonic”, “curvilinear”, and the Endeavor stent operates on the “flatter portion” of the LLL-TLR curve – providing comparable clinical effects to other DES programs at these levels of LLL in non complex (“workhorse”) lesion subsets

Scheduled surveillance follow-up angiography has a profound effect on the occurrence of “ischemia-driven” TLR

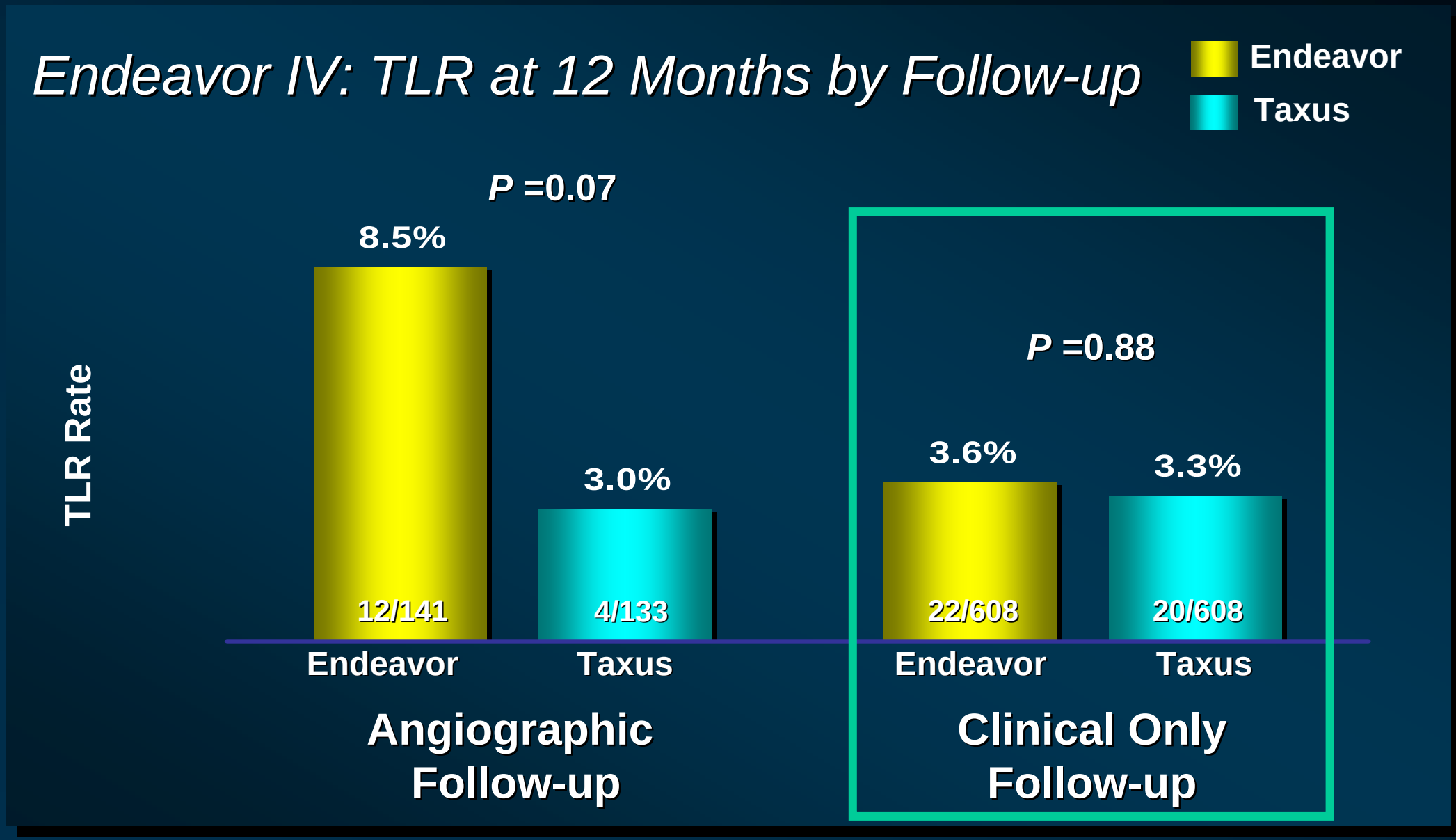
ENDEAVOR II

TLR at 9 Months by Treatment Assignment

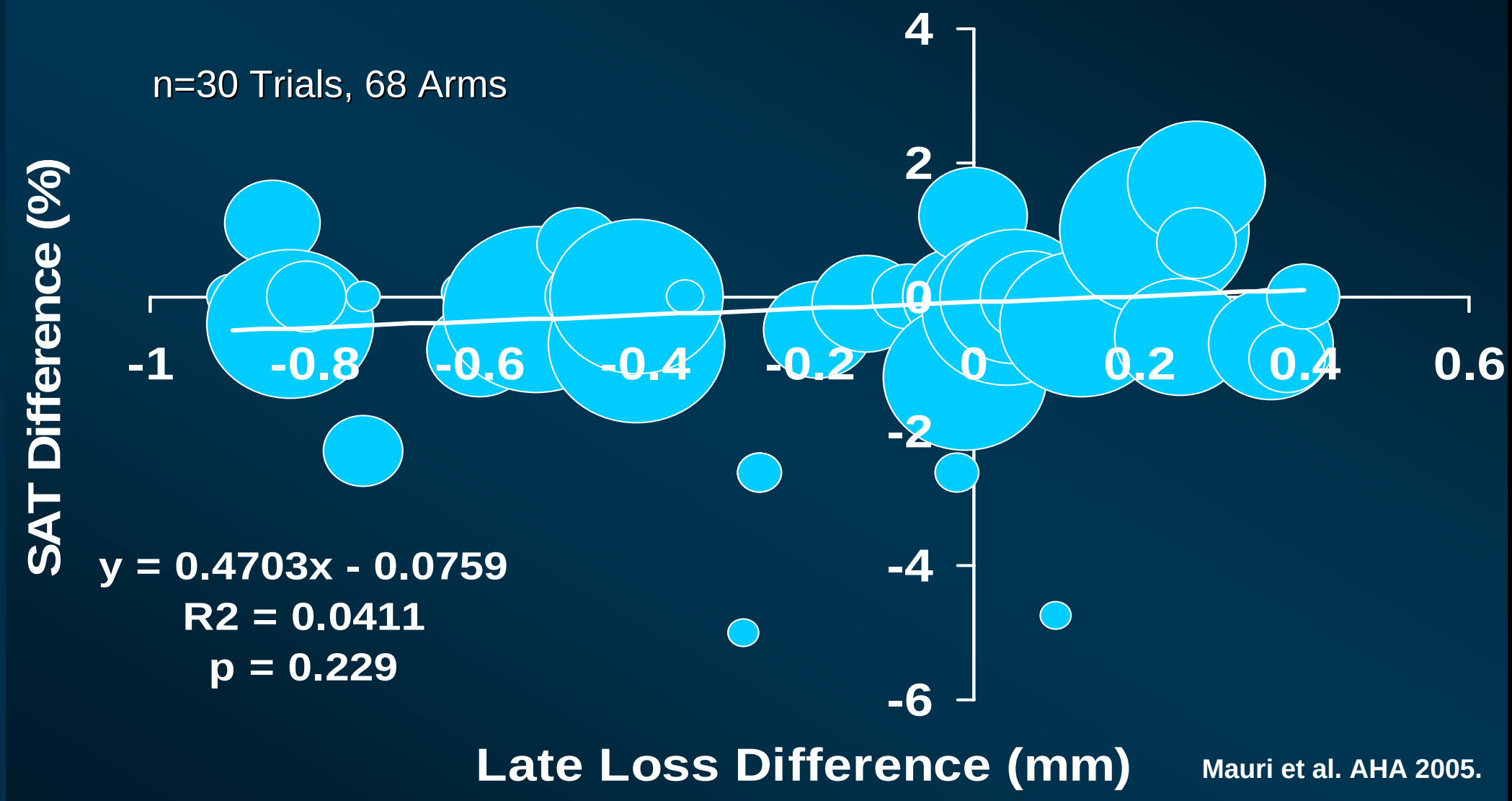


*Non-significant interaction P-value demonstrates uniform treatment effect across angio and clinical follow up patients.

What Can be Said about TLR Rates?



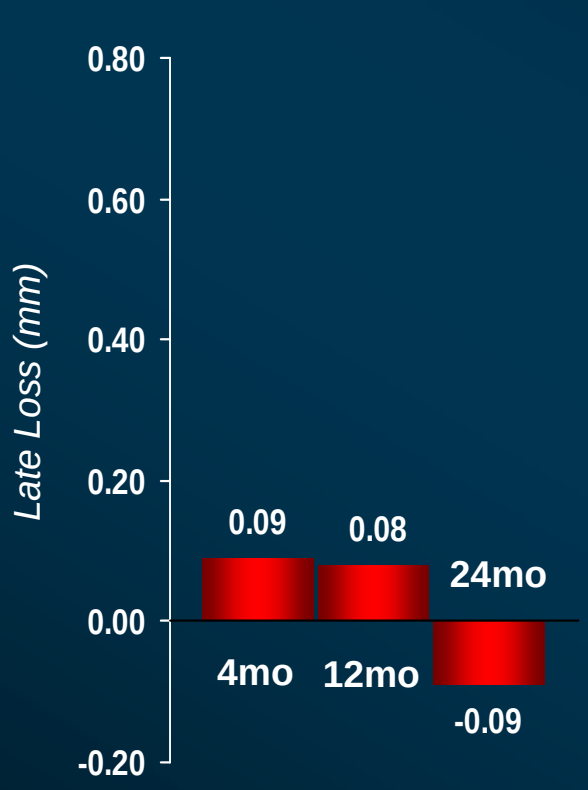
Can Late Loss predict Stent Thrombosis?

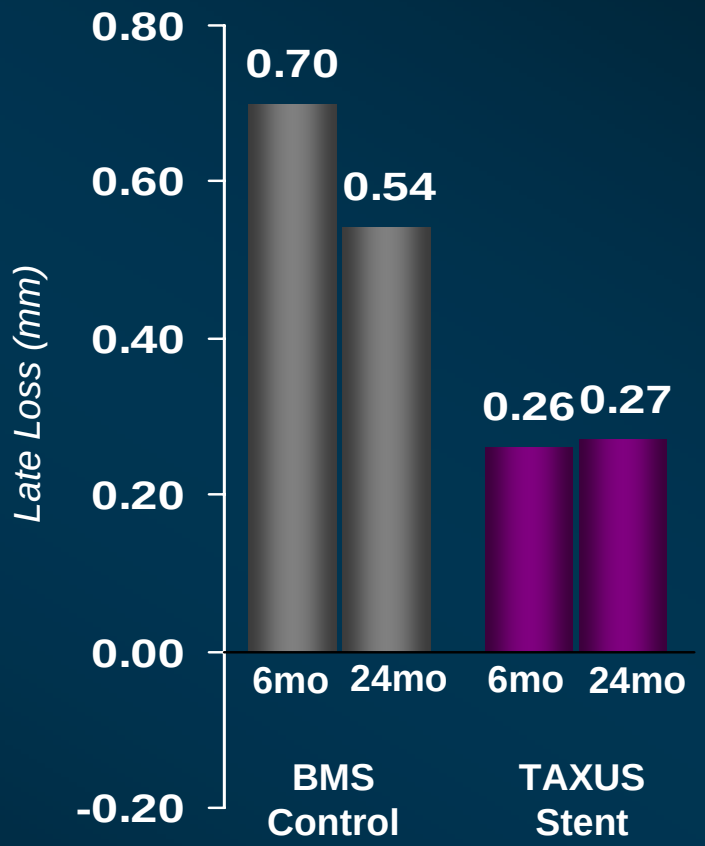


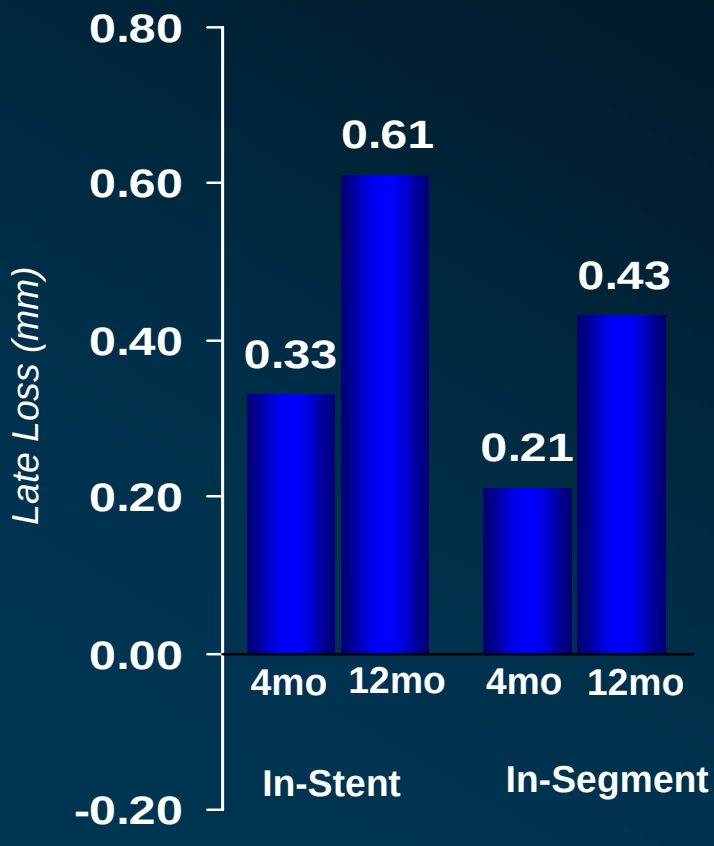
Mauri et al. AHA 2005.

When should late lumen loss be measured?

Serial QCA Historical References







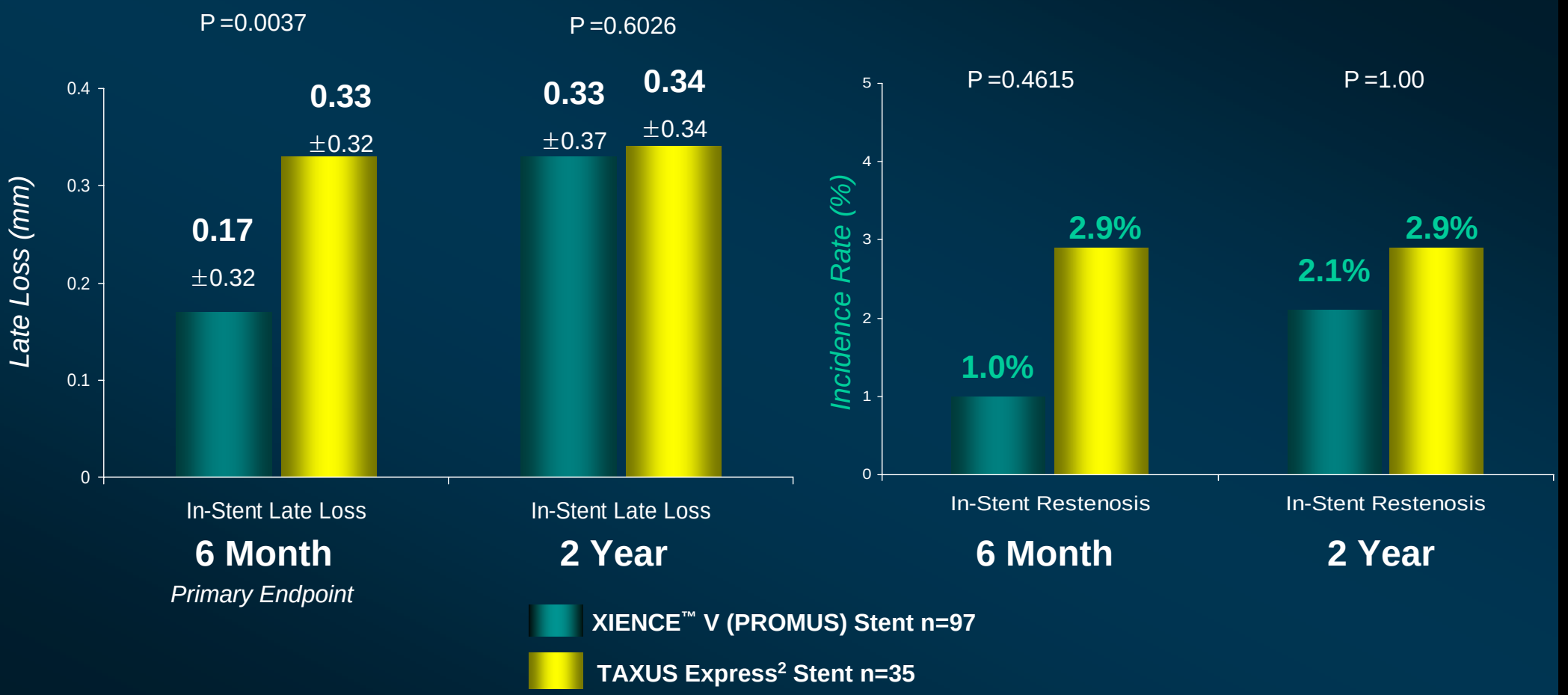
Cypher FIM
N=45

TAXUS II SR
N=54 TAXUS Stent
N=104 BMS Control

ENDEAVOR I
N=100

SPIRIT II Study

6-month and 2-year Angiographic Results

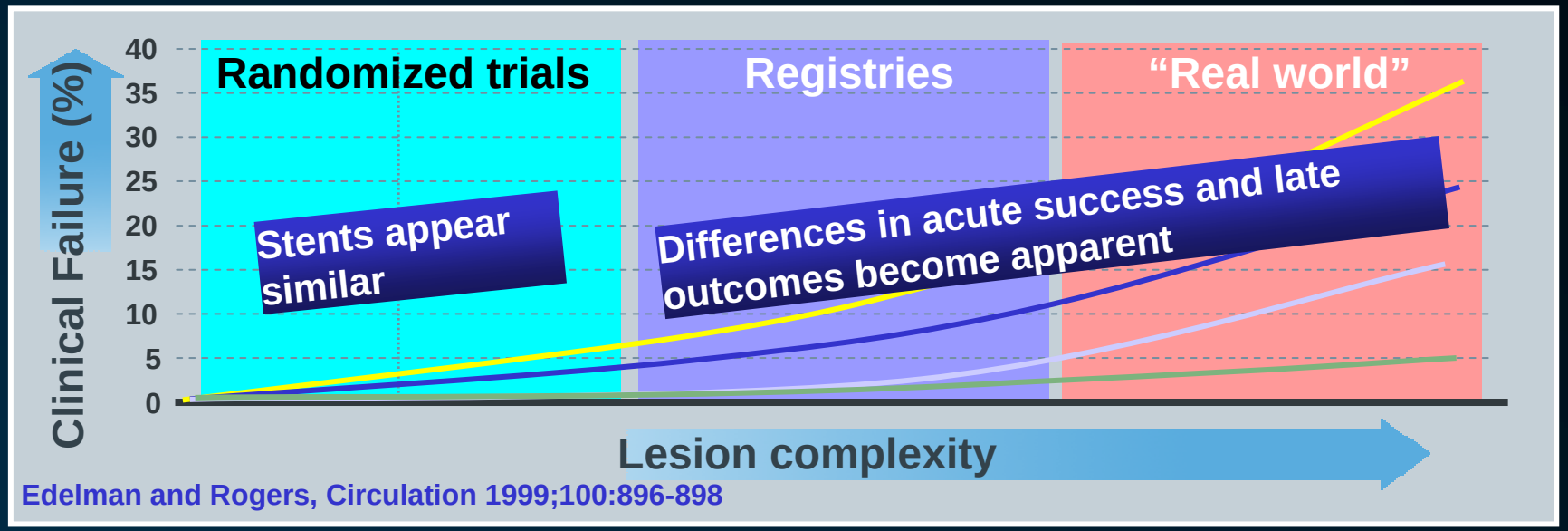


SPIRIT II Presentation, ACC 2008; Presented by Dr. Patrick Serruys

Will the concept of “headroom” prove to be the differentiating factor – proving LLL as a useful surrogate marker?

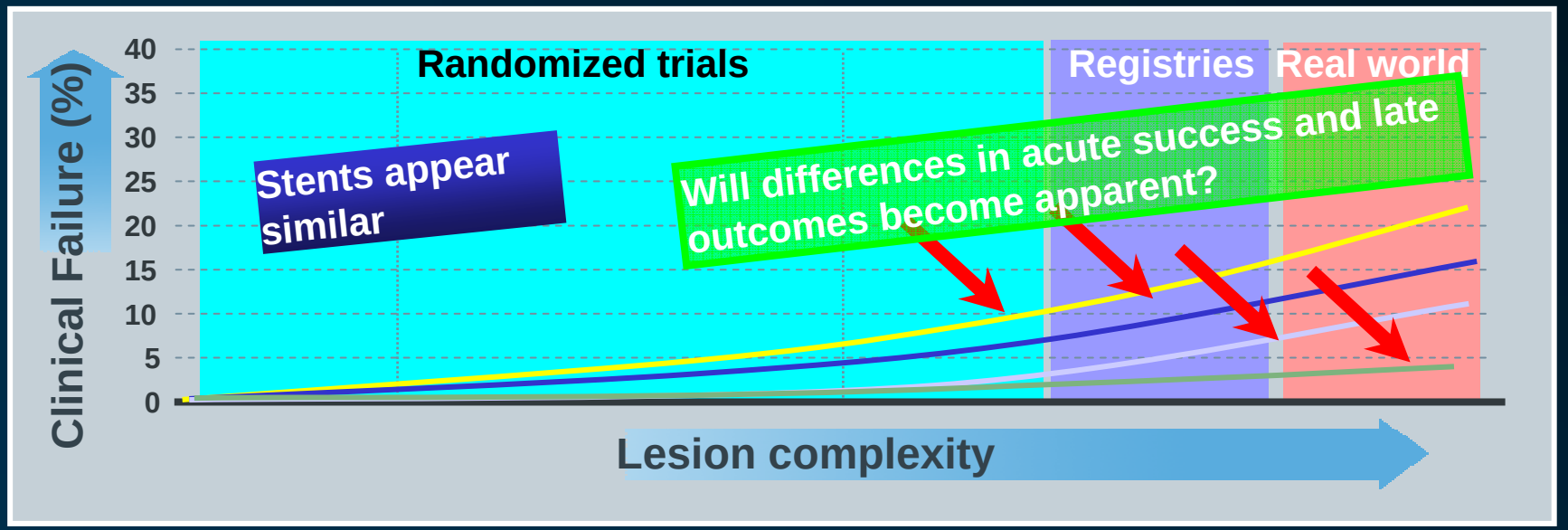
Lesion complexity vs. Stent Performance

BMS era



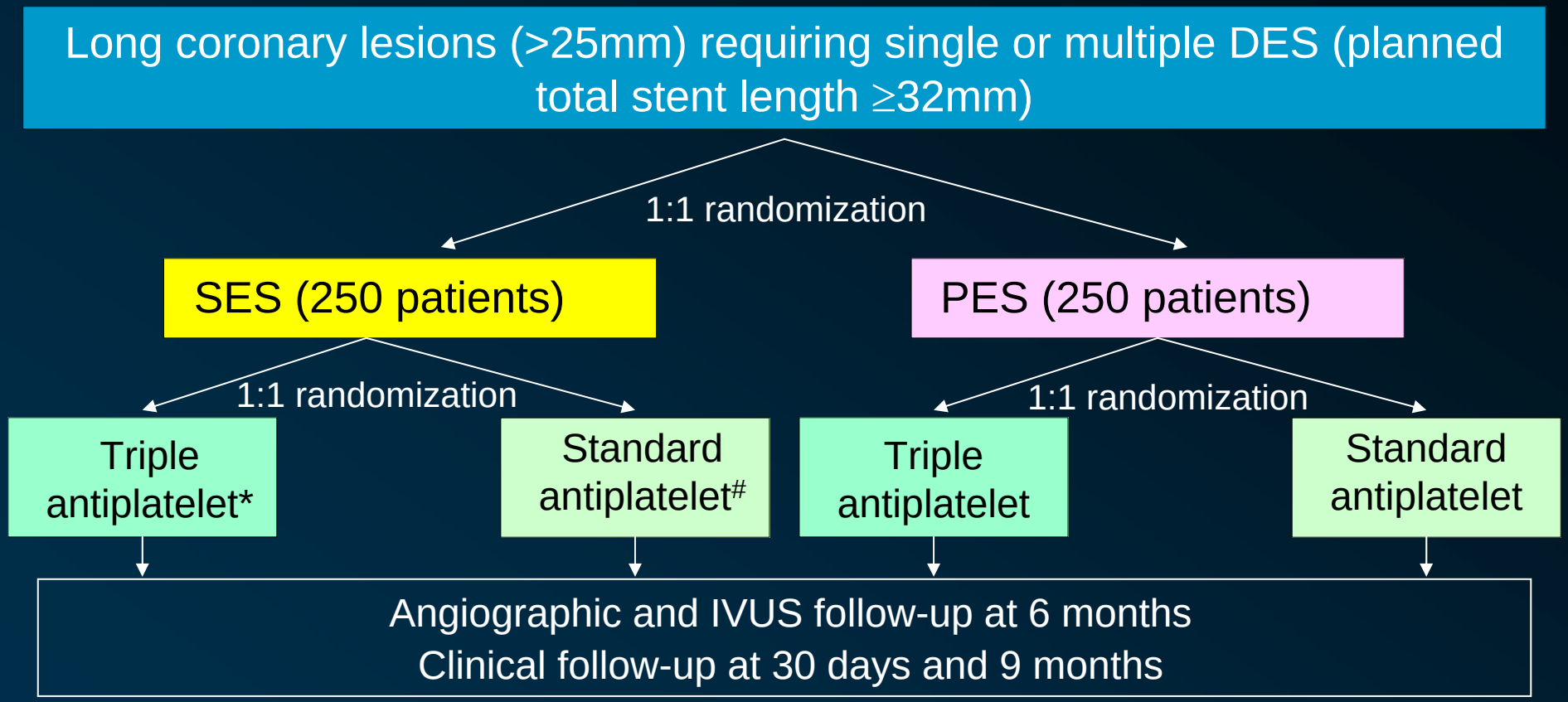
Edelman and Rogers, Circulation 1999;100:896-898

DES era



Courtesy of Campbell Rogers, MD

Park Long Lesion-II Study Design



* Triple antiplatelet : aspirin plus clopidogrel plus cilostazol for 6 months

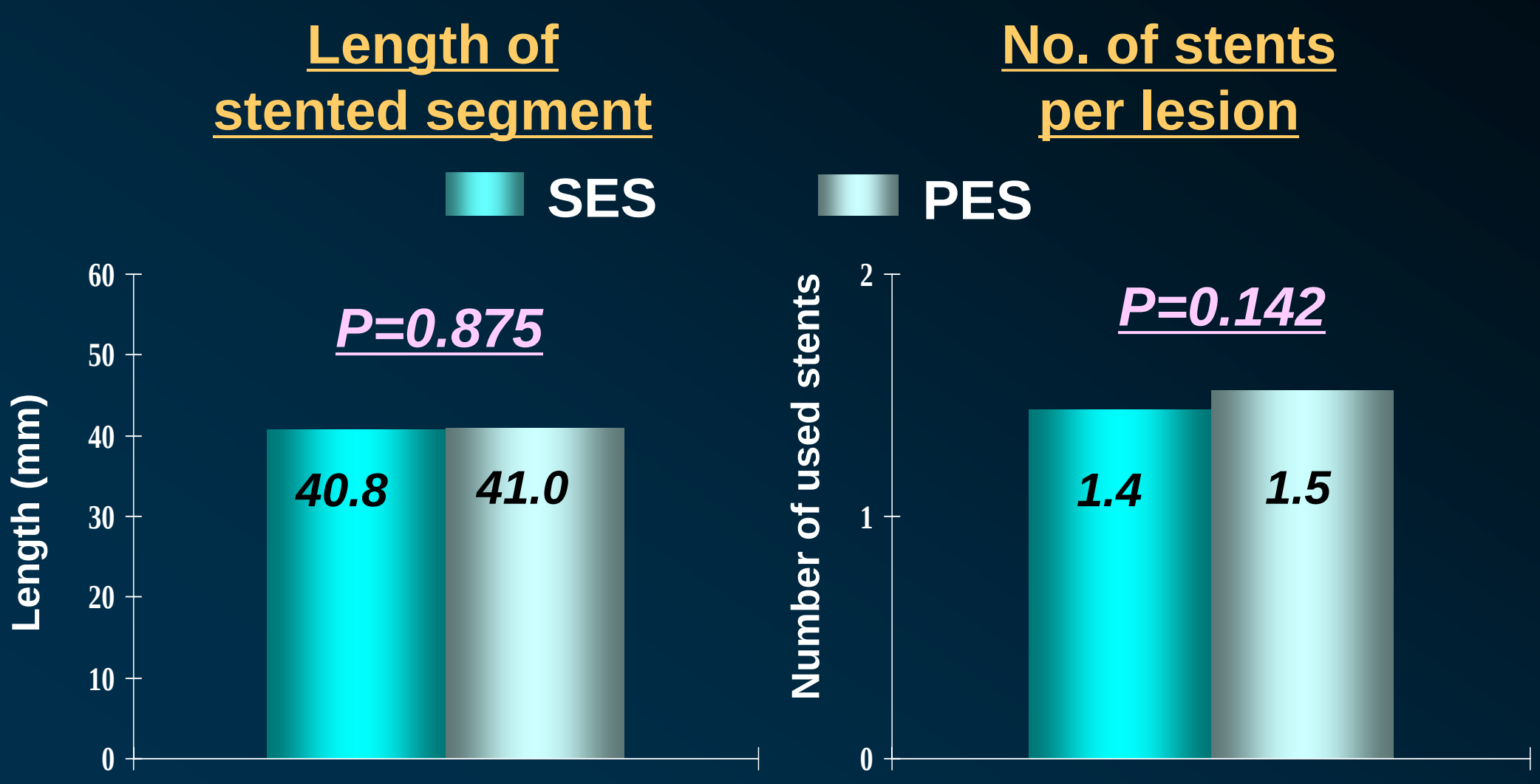
Standard antiplatelet : aspirin plus clopidogrel for 6 months

Primary endpoint:

1. Comparison of SES or PES: binary in-segment restenosis at 6 months
2. Comparison of triple and standard antiplatelet: in-stent late loss at 6 months

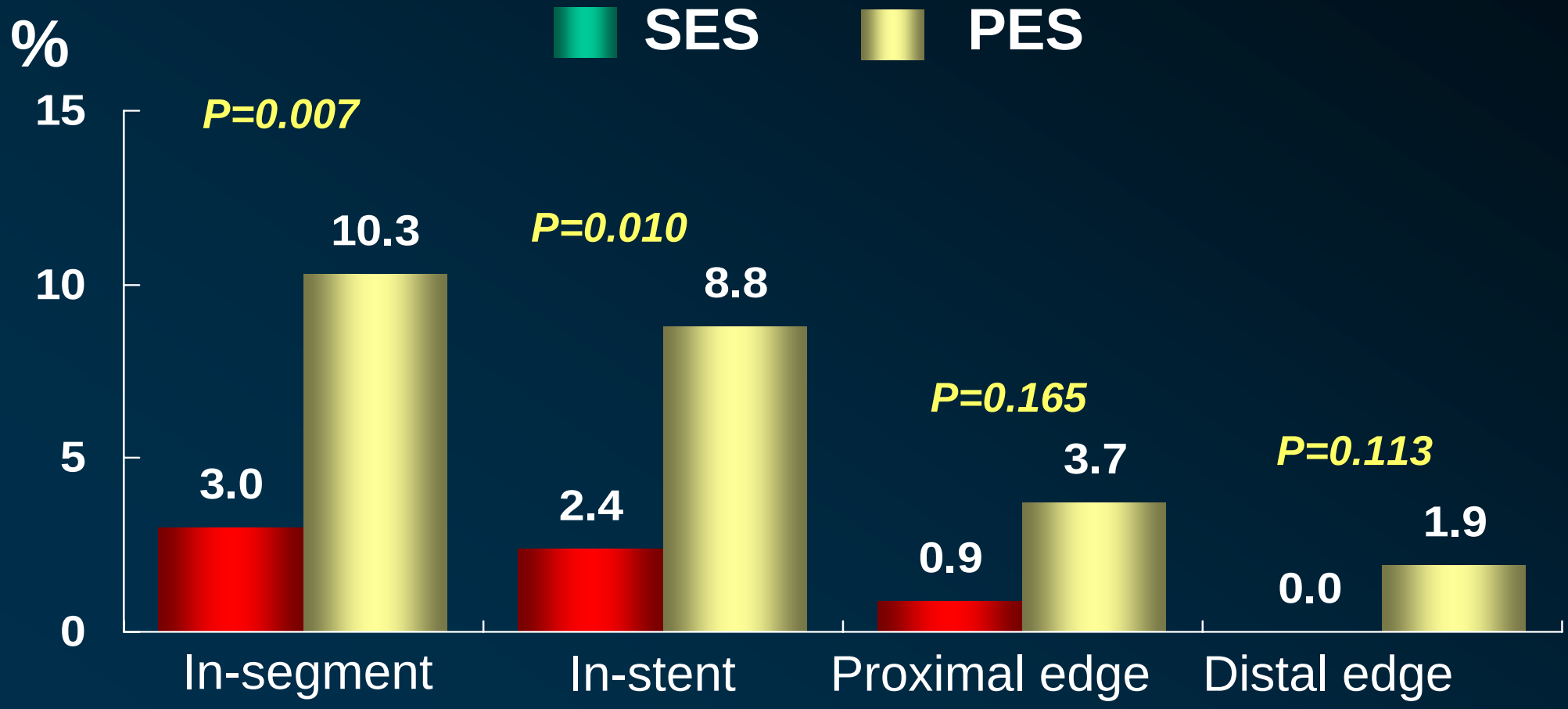
Park SJ et al ACC2006

Length and No. of Used DESs



Park SJ et al ACC2006

Angiographic Restenosis



Park SJ et al ACC2006

Clinical Outcomes at 9 Months

	SES	PES	P
Patients	200	206	
Death	1 (1.0%)	0	0.493
Cardiac	1 (1.0%)	0	
Non-cardiac	0	0	
MI	2 (1.0%) *	0	0.242
Stent thrombosis	2 (1.0%)	0	0.242
Acute	0	0	
Subacute	1	0	
Late	1**	0	
TLR	5 (2.5%)	16 (7.8%)	0.014
MACE	6 (3.0%)	16 (7.8%)	0.027

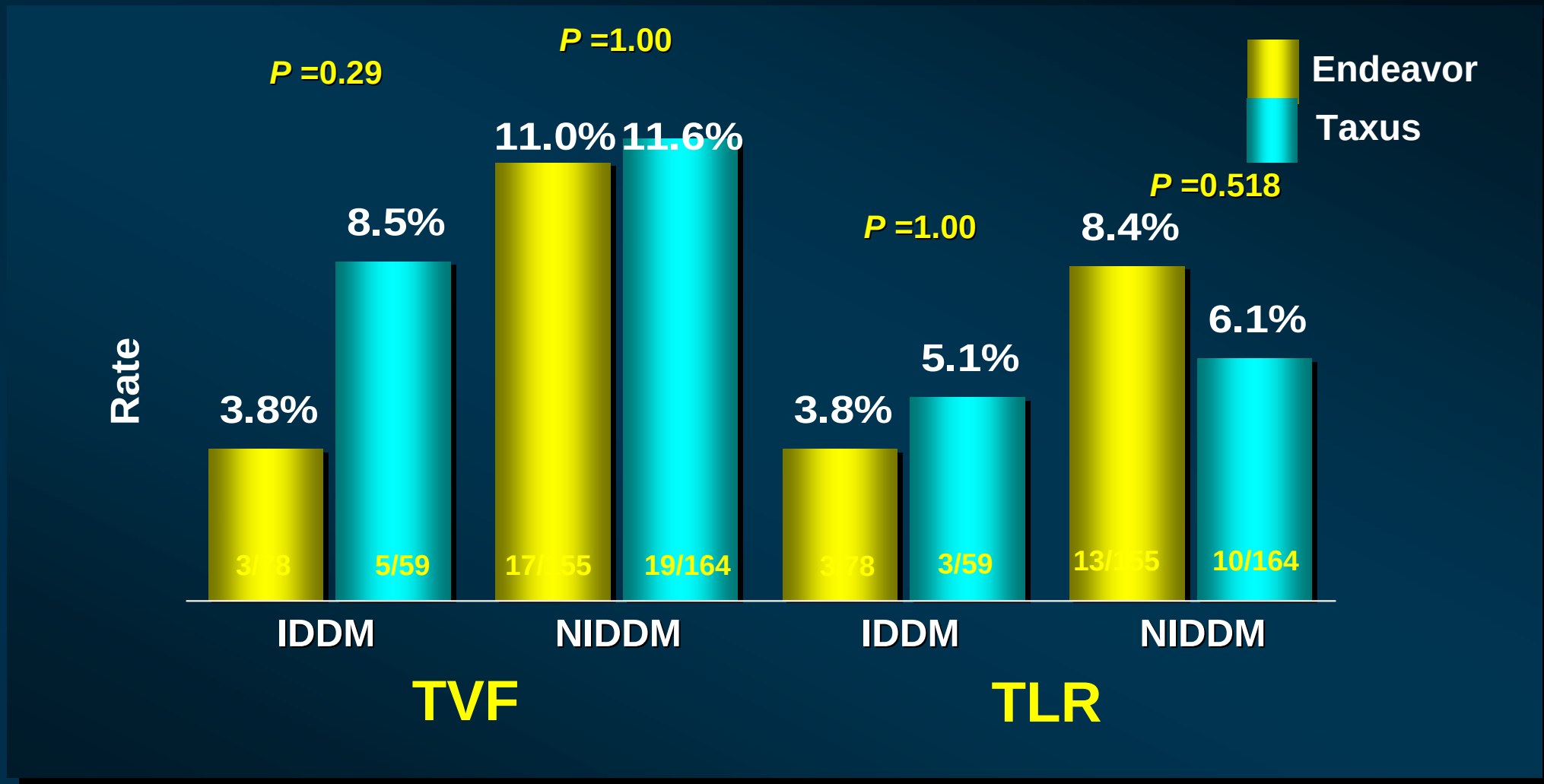
Park SJ et al ACC2006

What Argues Against The Concept of “Headroom”?

ENDEAVOR IV: IRDM

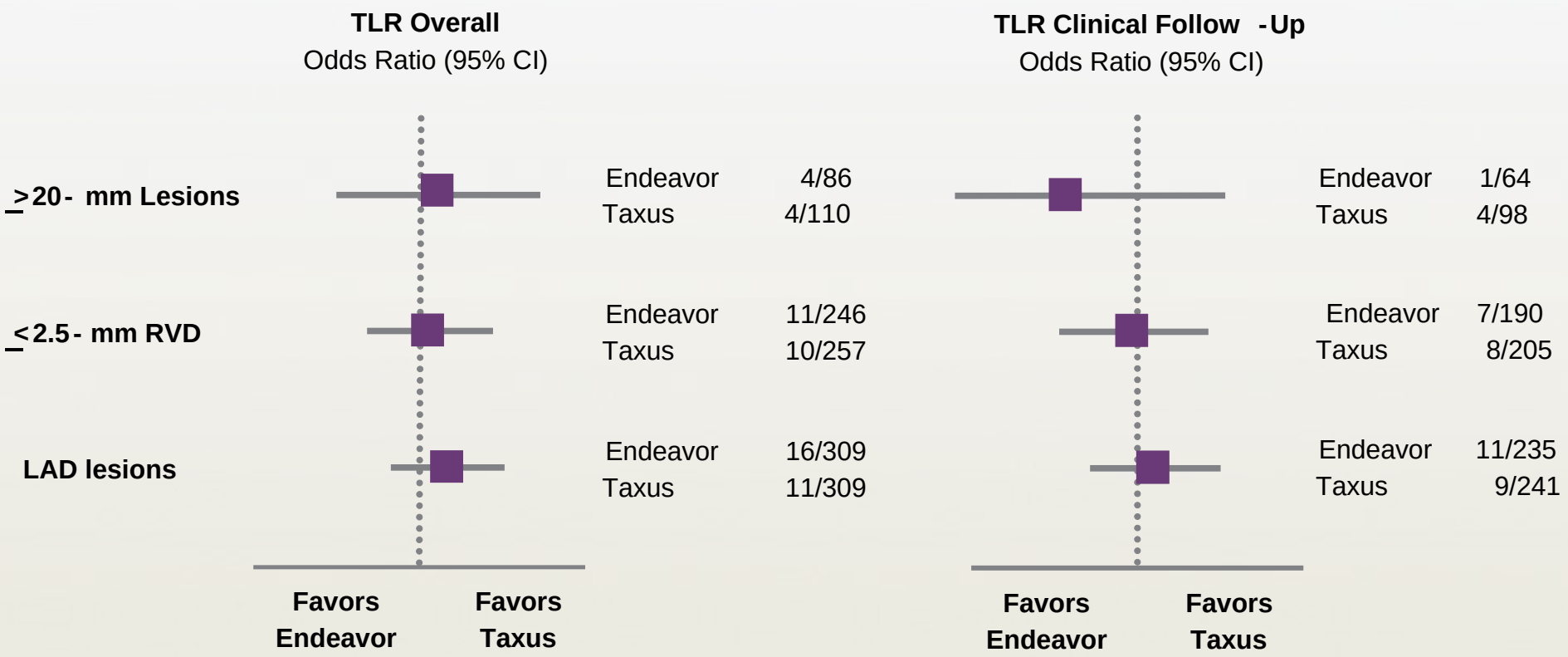
TVF and TLR at 12 months

144 IDDM (30.2% of E IV Diabetic patients)



Endeavor IV: Consistent TLR Reduction Across Subsets

Comparable efficacy to Taxus across subsets including small vessels, long lesions and LAD lesions



Disrepancies - Summary

It is not really a “discordance” between angiographic and clinical results

Instead, it is a description of a biologic change within the stent, and its clinical import on the patients symptoms

We need more RCT data in complex lesions subsets with clinical (not angiographically driven) endpoints