Jornada Unimed Rio

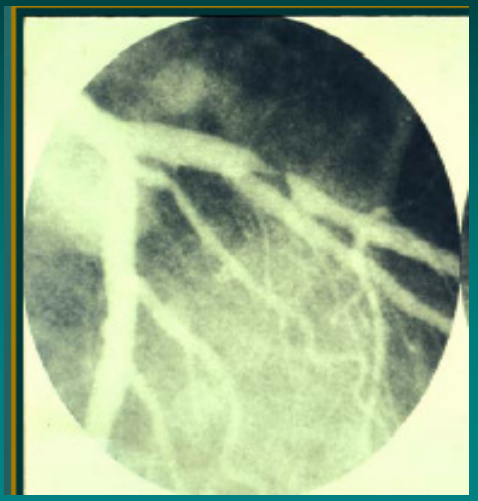
Doença coronária e o emprego racional de endopróteses (stents)

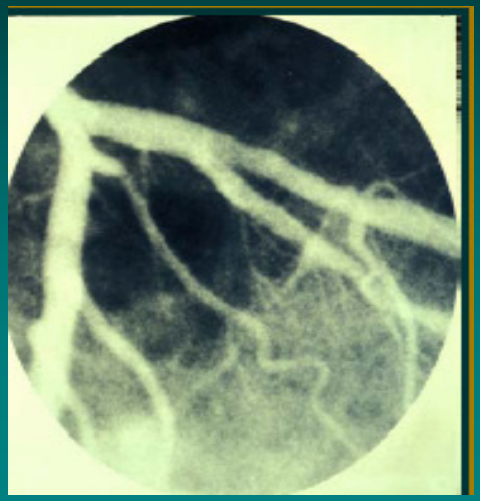
As evidências científicas que respaldam a prática clínica

Luiz Antonio Carvalho

04-08-2012

Angioplastia Coronária por Cateter Balão





1ª angioplastia

Limitações

- **Reestenose**
- **Oclusão aguda**

REESTENOSE CORONÁRIA

- **Recuo elástico**
- **Remodelamento negativo**

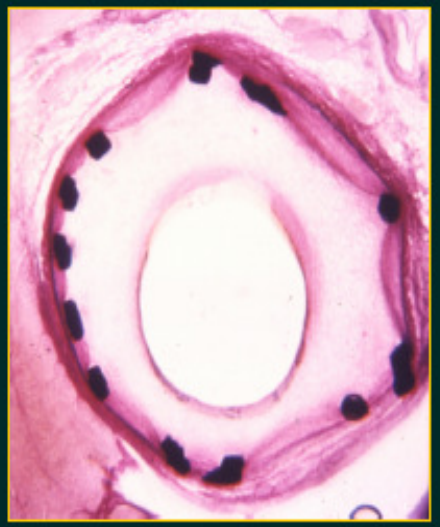
- **Proliferação neo-intimal**

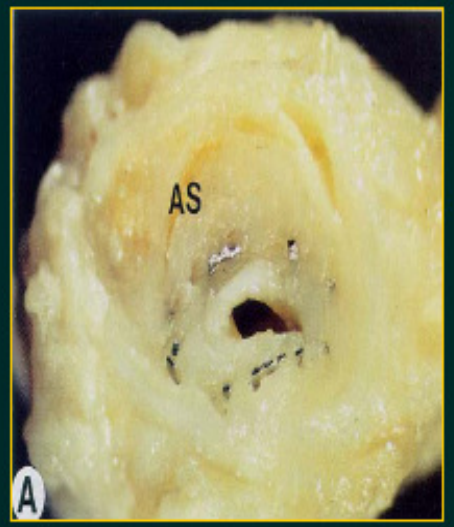
Stent convencional

<u>Situações críticas:</u>
Vaso de fino calibre
Lesões longas
Óstios
Bifurcações
Reestenose
DM
I. renal

Limitações dos Stents Convencionais

- Reestenose por Hiperplasia Neointimal

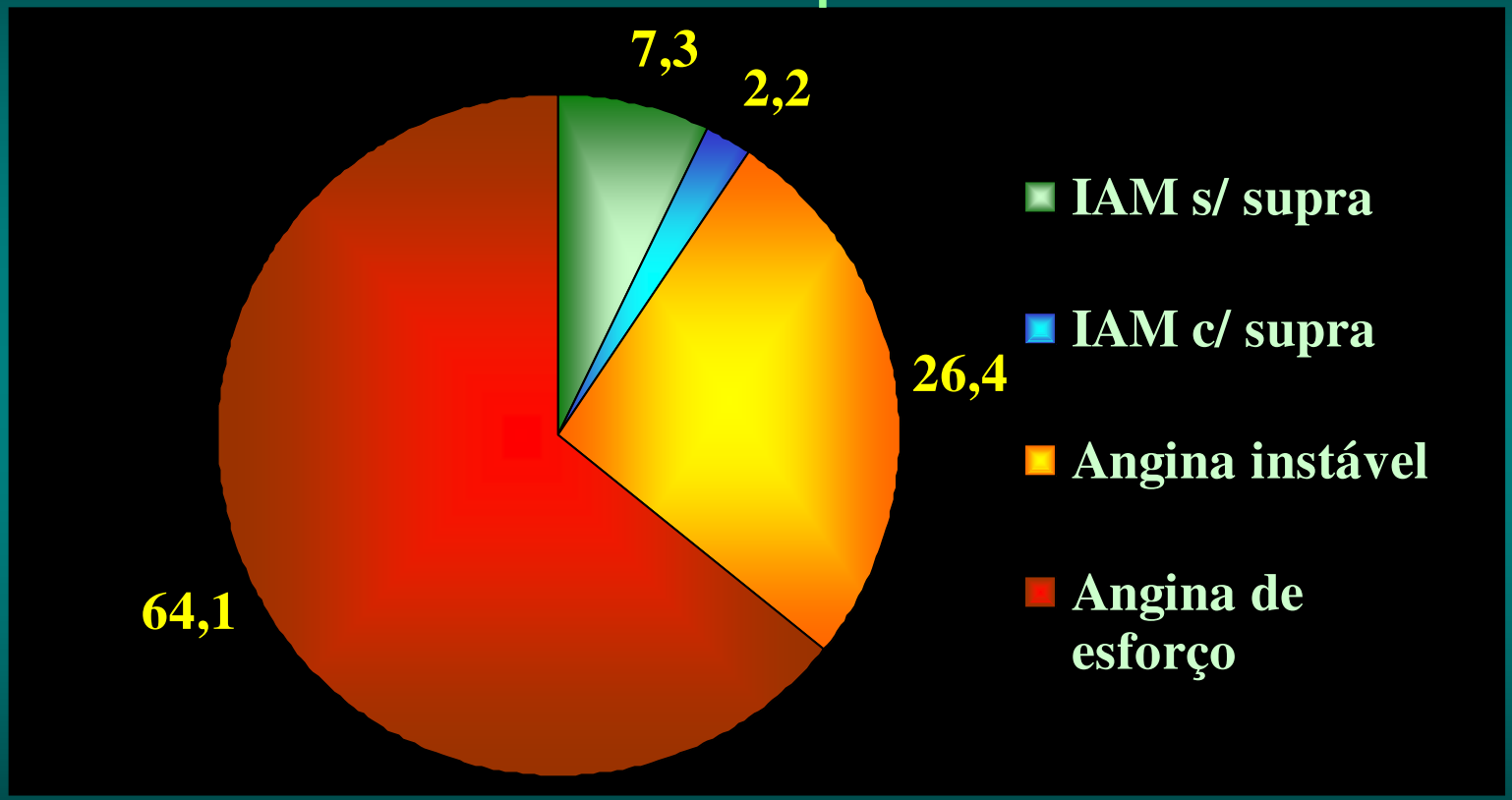




A Reestenose de Stent Convencional é Benigna?

Apresentação Clínica - Cleveland Clinic (1999 - 2003)

1186 casos - 984 pacientes



- 35,9% dos pacientes com reestenose intra-stent apresentaram-se com síndrome coronariana aguda
- 9,5% com quadro de IAM (2,2% com supra de ST)

Chen e cols, Am. Heat J, - Junho 2006

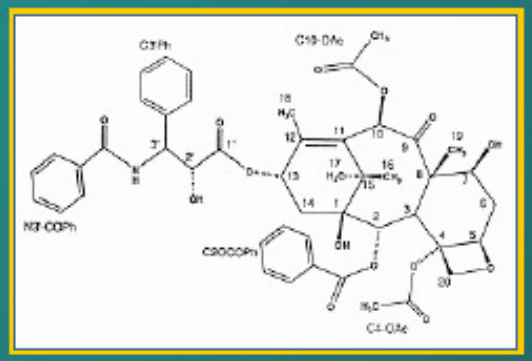
Stents Farmacológicos

OBJETIVOS

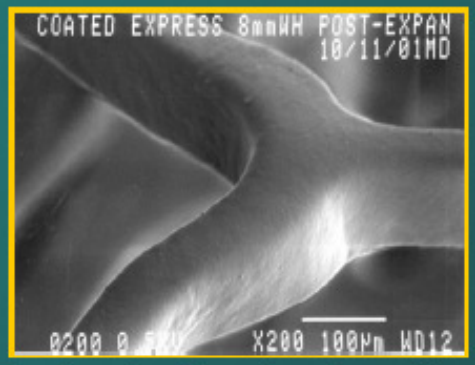
Oferecer soluções mecânicas e biológicas à reestenose

Stents Farmacológicos

TAXUS



Paclitaxel

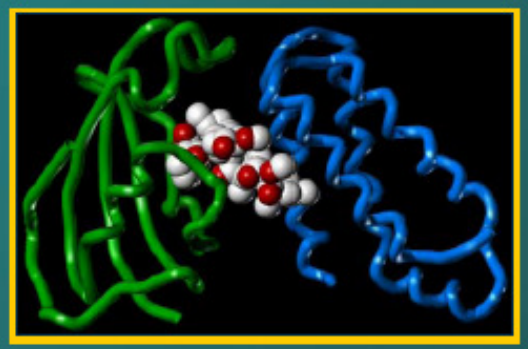


Polyolefin derivative

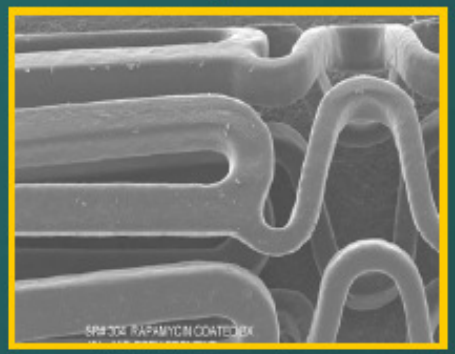
Express²

Drug **Polymer** **Stent**

Cypher



Sirolimus

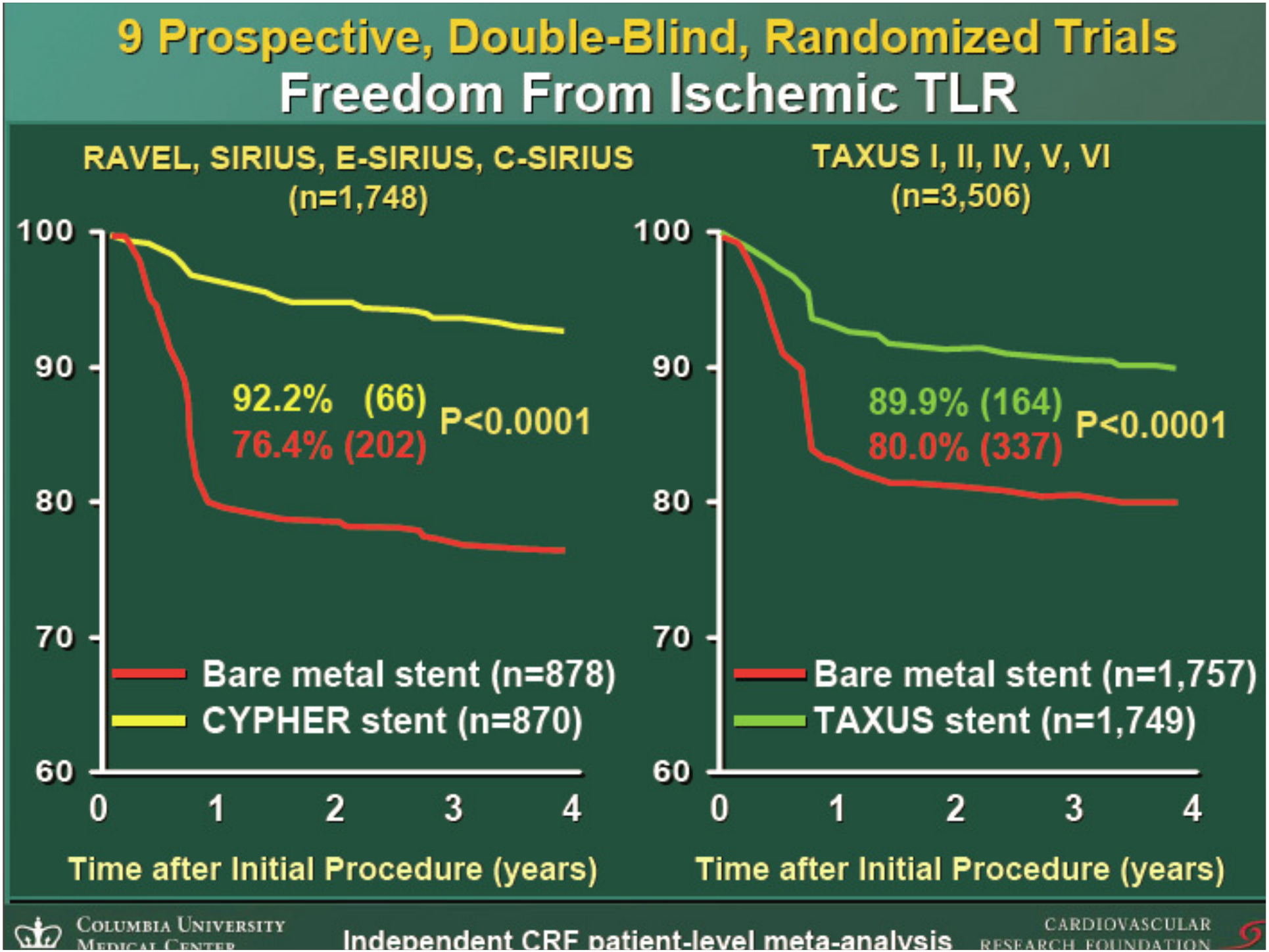


PEVA + PBMA blend

BX Velocity

9 Prospective, Double-Blind, Randomized Trials

Freedom From Ischemic TLR



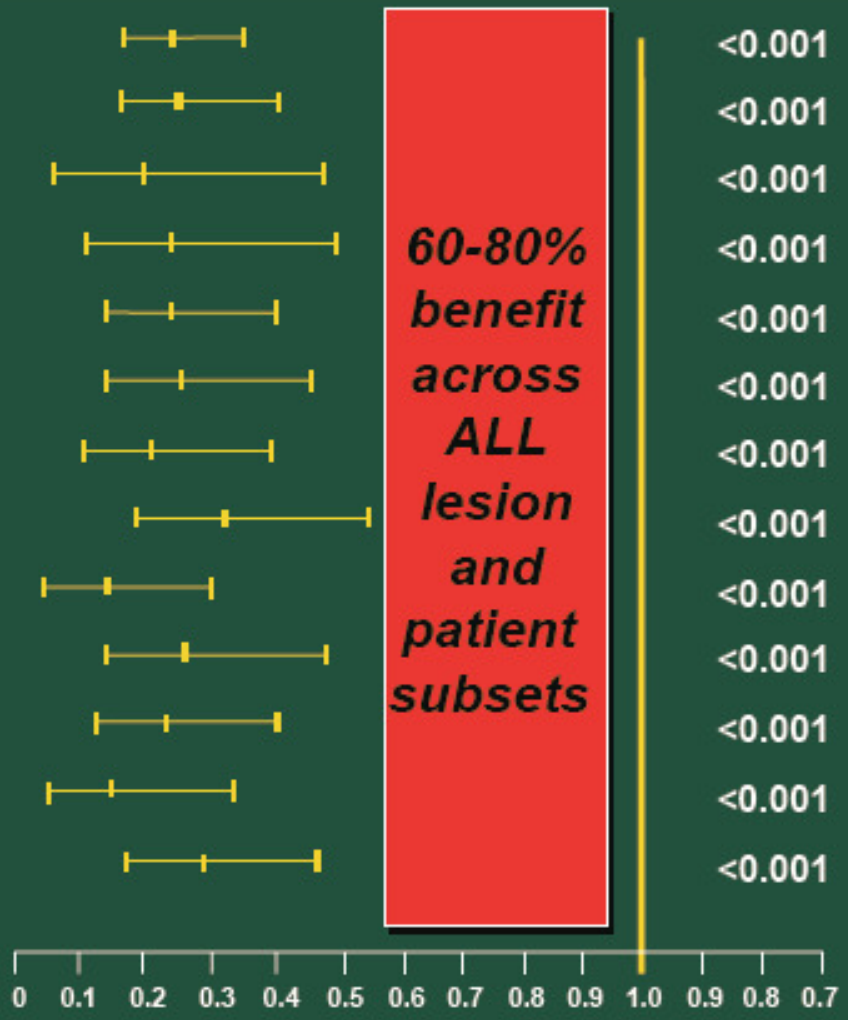
Columbia University Medical Center

Independent CRF patient-level meta-analysis

Cardiovascular Research Foundation

SIRIUS - TLR Events @ 4 Years

	Sirolimus	Control	P-value	# events prevented per 1,000 patients
Overall	7.9	23.9	<0.001	160
Male	8.5	24.7	<0.001	162
Female	6.2	22.2	<0.001	160
Diabetes	12.2	32.4	<0.001	202
No Diabetes	6.5	20.5	<0.001	140
LAD	9.8	27.9	<0.001	181
Non-LAD	6.4	21.1	<0.001	147
Small Vessel (<2.75)	11.0	26.0	<0.001	150
Large Vessel	4.9	21.9	<0.001	170
Short Lesion	7.5	21.8	<0.001	143
Long Lesion (>13.5)	8.5	26.0	<0.001	175
Overlap	10.4	29.4	<0.001	190
No Overlap	6.7	21.3	<0.001	146



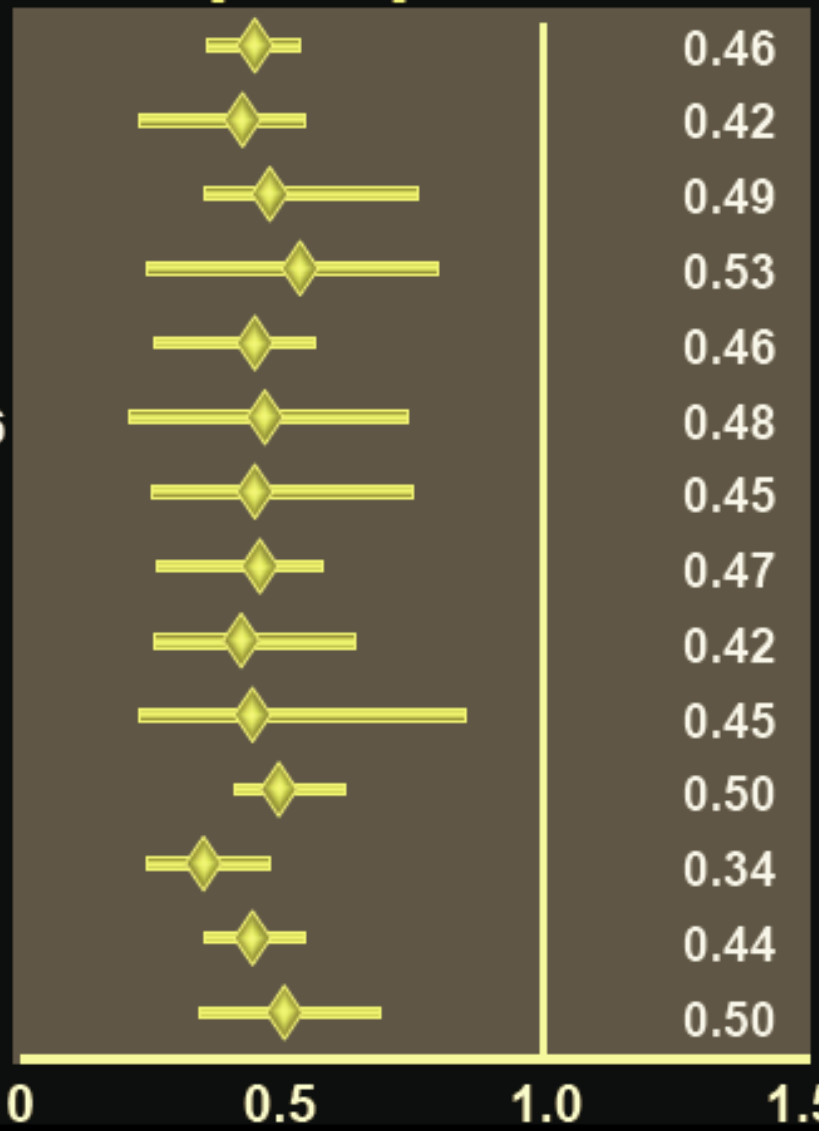
Columbia University Medical Center

Sirolimus better

Cardiovascular Research Foundation

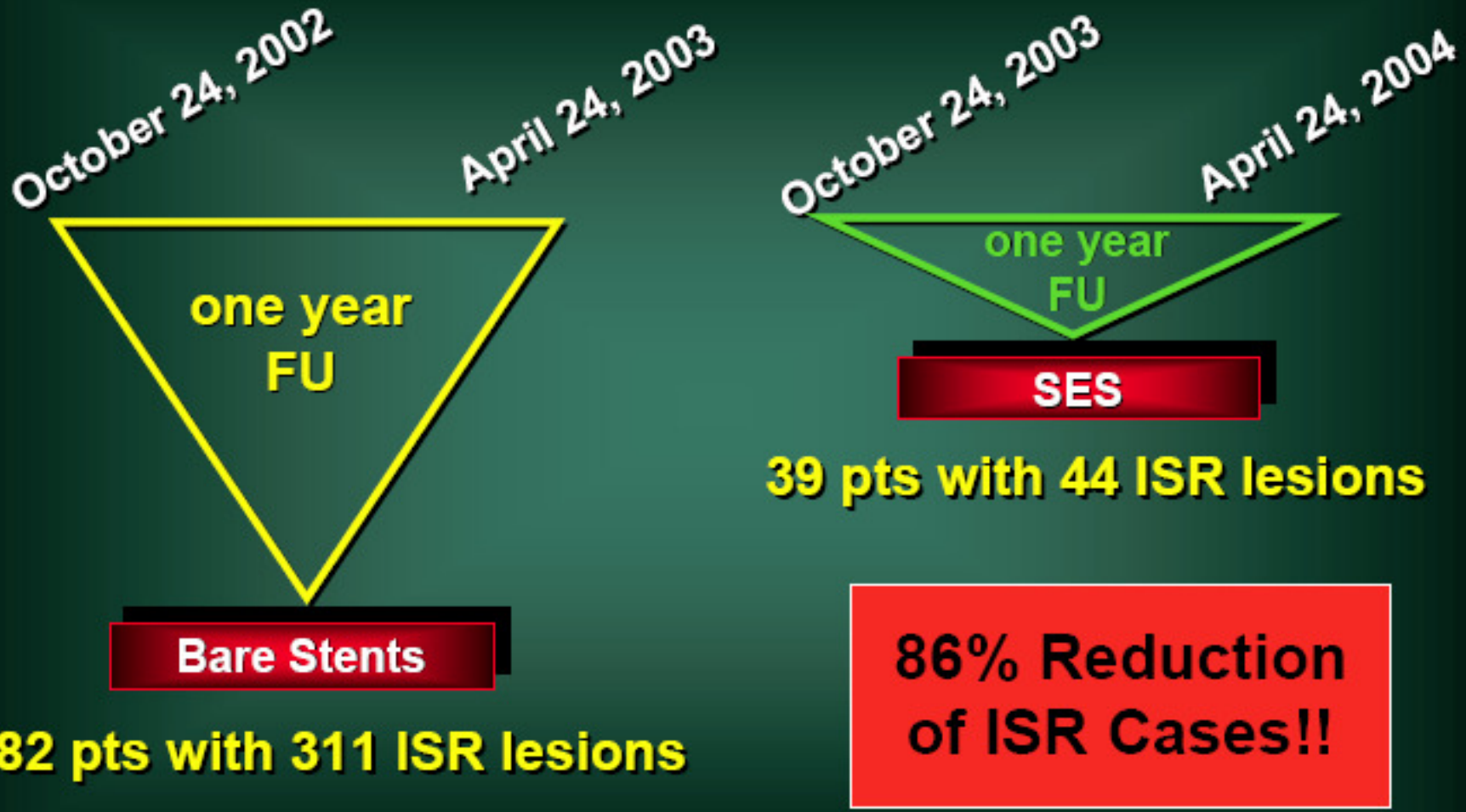
TLR up to 4 Years: Subgroup Summary

TAXUS II, IV, V, VI Meta-analysis



	HR	TAXUS	Control	P Value
All	0.46	10.3%	20.2%	<0.0001
RVD ≤2.5	0.42	13.2%	27.8%	<0.0001
RVD 2.5 - ≤3.0	0.49	9.8%	18.7%	<0.0001
RVD >3.0	0.53	7.3%	12.7%	0.002
Lsn Length <18	0.46	9.7%	19.1%	<0.0001
Lsn Length 18-26	0.48	11.0%	20.9%	0.0006
Lsn Length >26	0.45	12.9%	26.6%	0.002
Non-Diabetic	0.47	9.6%	18.7%	<0.0001
Diabetic-Oral	0.42	12.3%	25.7%	<0.0001
Diabetic-Insulin	0.45	13.6%	23.3%	0.01
Single Stent	0.50	9.6%	17.4%	<0.0001
Multiple Stents	0.34	12.1%	32.5%	<0.0001
Male	0.44	9.5%	19.9%	<0.0001
Female	0.50	12.2%	20.8%	<0.0001

Changing Patterns of ISR - CRF



Emprego racional das evidências científicas

Como entender e utilizar as diretrizes?

- as diretrizes não criam evidências.
- as diretrizes são constituídas a partir da compilação, análise, classificação e julgamento das evidências por um painel de especialistas, gerando recomendações.
- as diretrizes são excelentes ferramentas auxiliares no processo de tomada de decisão. Porém, não substituem o julgamento clínico.

Hierarquia das evidências e graus de recomendações

Graus de recomendações

CLASSE I - ***consenso de utilidade e eficácia***

CLASSE IIa – ***opinião favorece a utilização***

CLASSE IIb – ***opinião não favorece claramente a utilização***

CLASSE III – ***consenso de não utilidade, podendo gerar risco***

Níveis de evidência

NÍVEL A - ***estudos randomizados ou metanálises***

NÍVEL B - ***1 estudo randomizado ou vários não randomizados***

NÍVEL C - ***séries de casos ou opiniões de especialistas***

Tomada de decisão no paciente coronariopata

1- ESTRATÉGIA TERAPÊUTICA

TTTO CLÍNICO X REVASCULARIZAÇÃO MIOCÁRDICA

2- ESTRATÉGIA DE REVASCULARIZAÇÃO

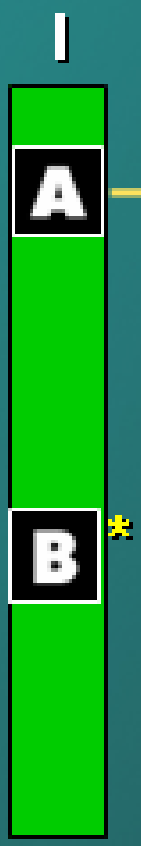
CIRÚRGICA X PERCUTÂNEA

3- TIPO DE STENT

CONVENCIONAL X FARMACOLÓGICO

CRF DES Evidence-based Medicine Guidelines Summary 2006

De Novo Lesions



RVD 2.25 – 4.0 mm Length ≤30 mm	RVD 2.25 – 4.0 mm Length ≤46 mm
Polymer-based Sirolimus-eluting Cypher™ stents	Polymer-based Paclitaxel-eluting TAXUS™ stents
RAVEL, SIRIUS	TAXUS-I
E- & C-SIRIUS	TAXUS-II
SES-SMART	TAXUS-IV
DIABETES	TAXUS-V*
2.25 & 4.0 Sirius*	TAXUS-VI

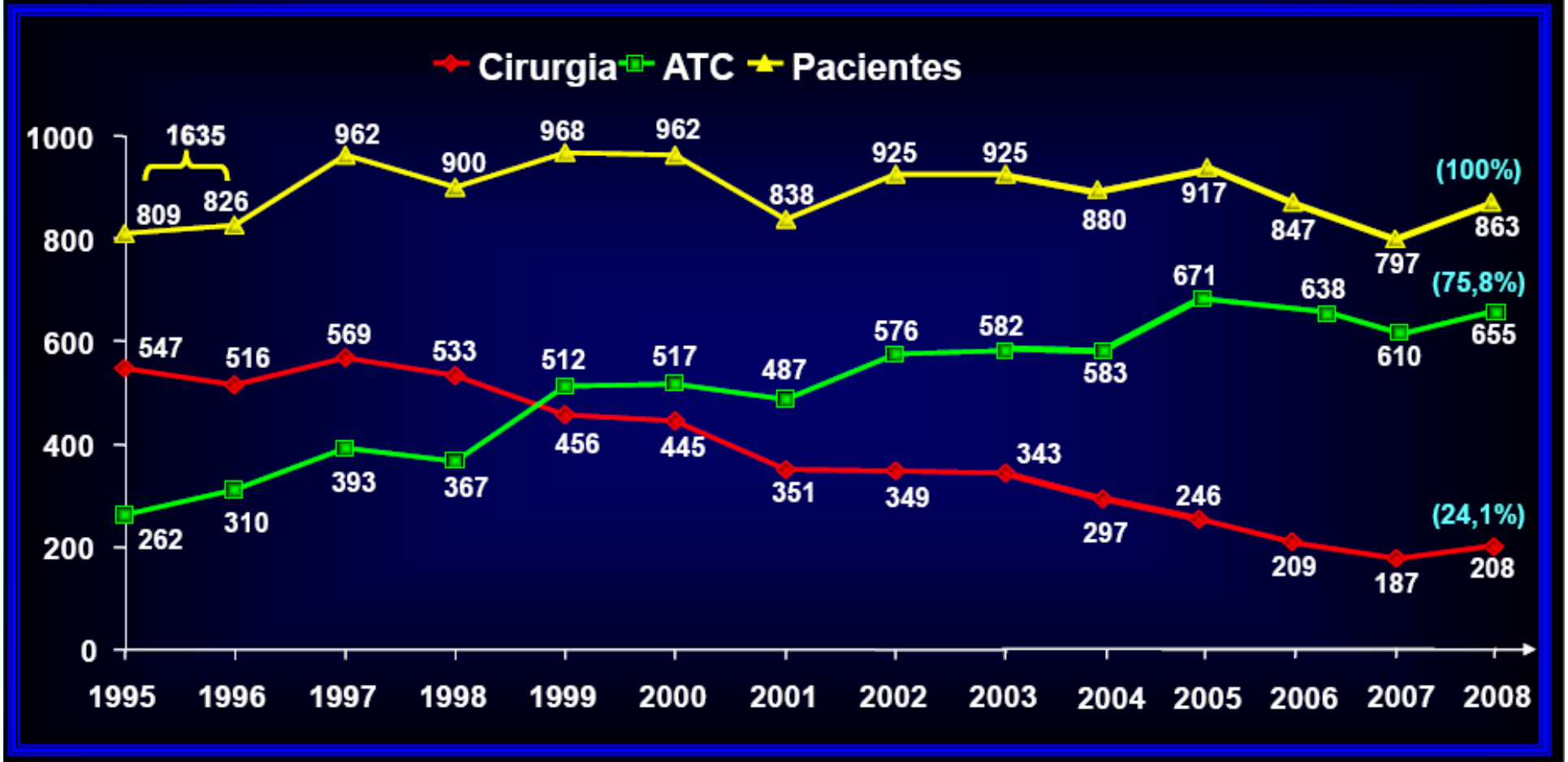
*2.25 & 4.0mm rand. subgroups of TAXUS-V; SIRIUS registries

PCI Gains Ground for Left Main and Multivessel Disease in New ESC Revascularization Guidelines

CAD subset	CABG favored	PCI favored
1- or 2-vessel disease, nonproximal LAD	IIb C	**I C**
1- or 2-vessel disease, proximal LAD	I A	**IIa B**
3-vessel disease, simple lesions, full revascularization achievable with PCI, SYNTAX score <22	I A	**IIa B**
3-vessel disease, complex lesions, incomplete revascularization achievable with PCI, SYNTAX score >22	I A	III A
Left main (isolated or 1-vessel disease ostium/shaft)	I A	**IIa B**
Left main (isolated or 1-vessel disease distal bifurcation)	I A	**IIb B**
Left main plus 2- or 3-vessel disease, SYNTAX score <32	I A	**IIb B**
Left main plus 2- or 3-vessel disease, SYNTAX score >33	I A	III B

Wijns W. Kolh P. - ESC 2010 Congress

Hospital do Coração da Associação do Sanatório Sírio
Revascularização Miocárdica: 1995-2008

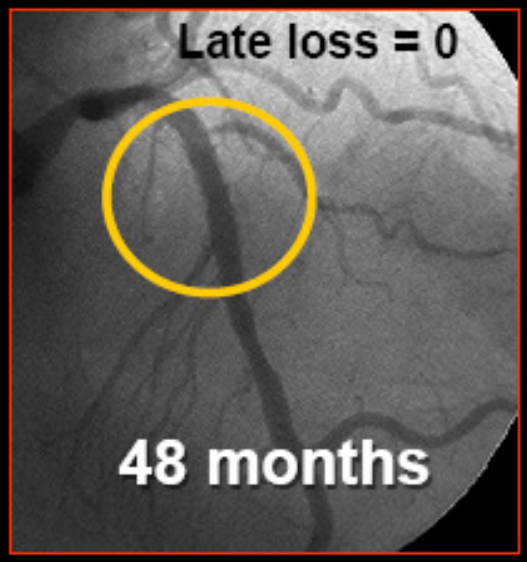


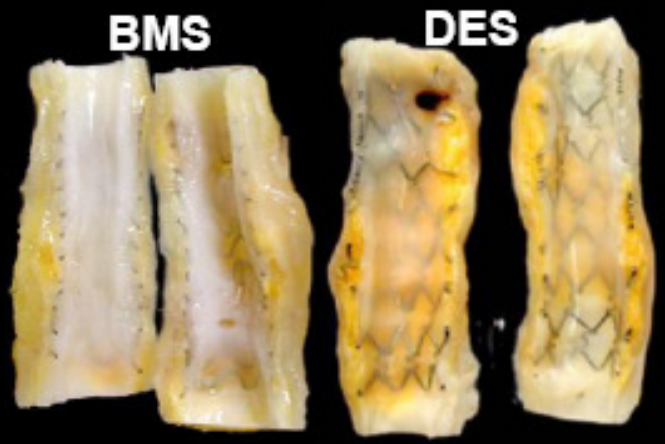
Sousa A. SOLACI 2009

Stent farmacológico

Eficácia X Segurança

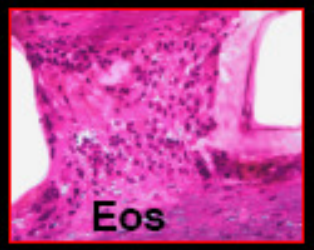
DES….the good, the bad, and the ugly!



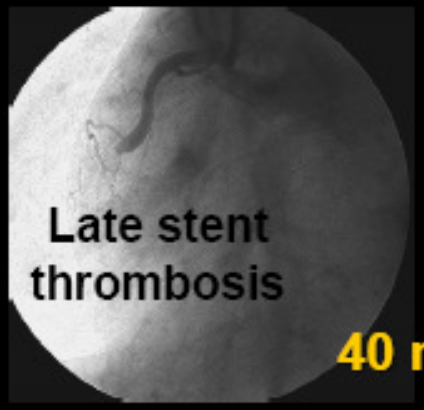


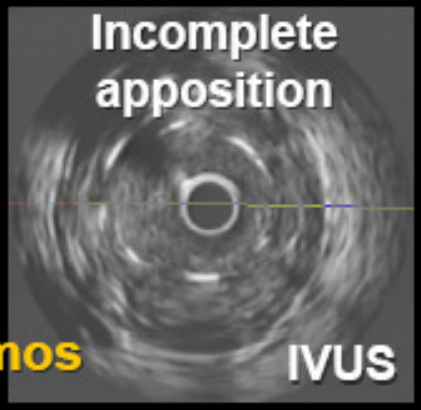
Delayed Healing!

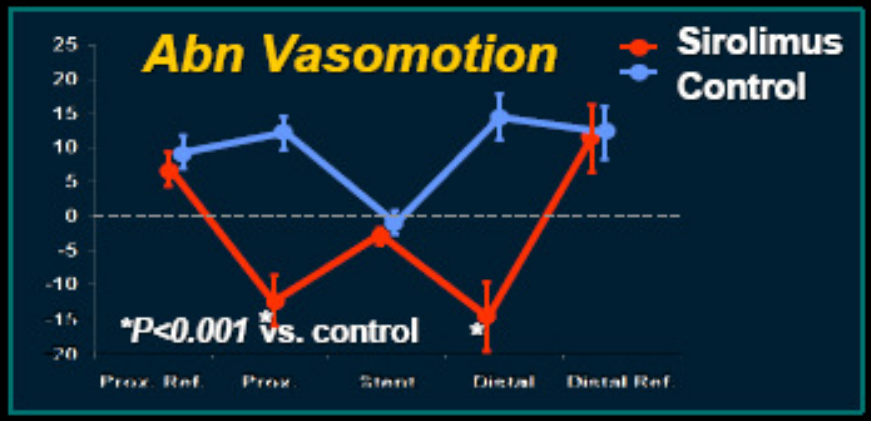
Angioscopy



Inflammation







Eventos e consequências clínicas

Stents Farmacológicos

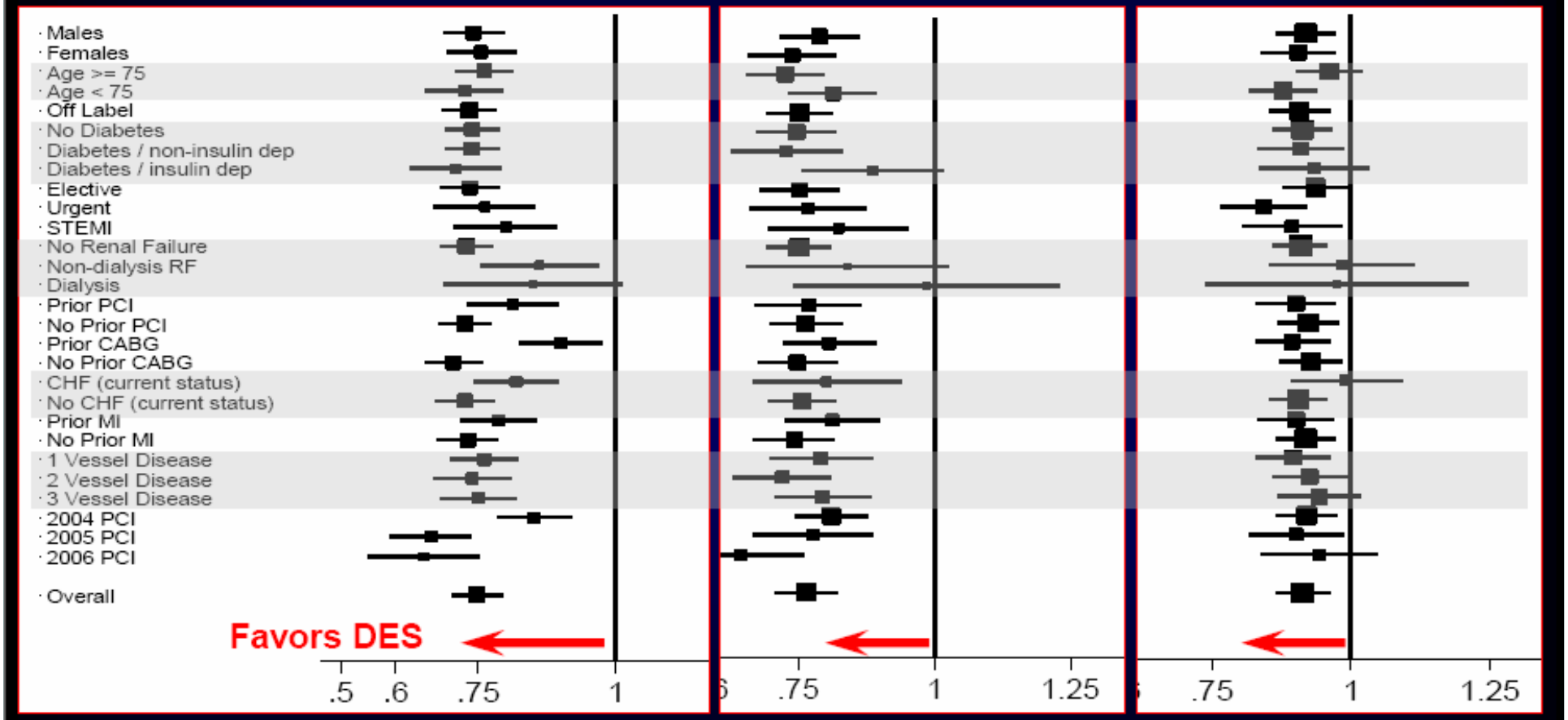
REESTENOSE

TROMBOSE DE STENT

Revascularização da lesão alvo

Morte ou IAM

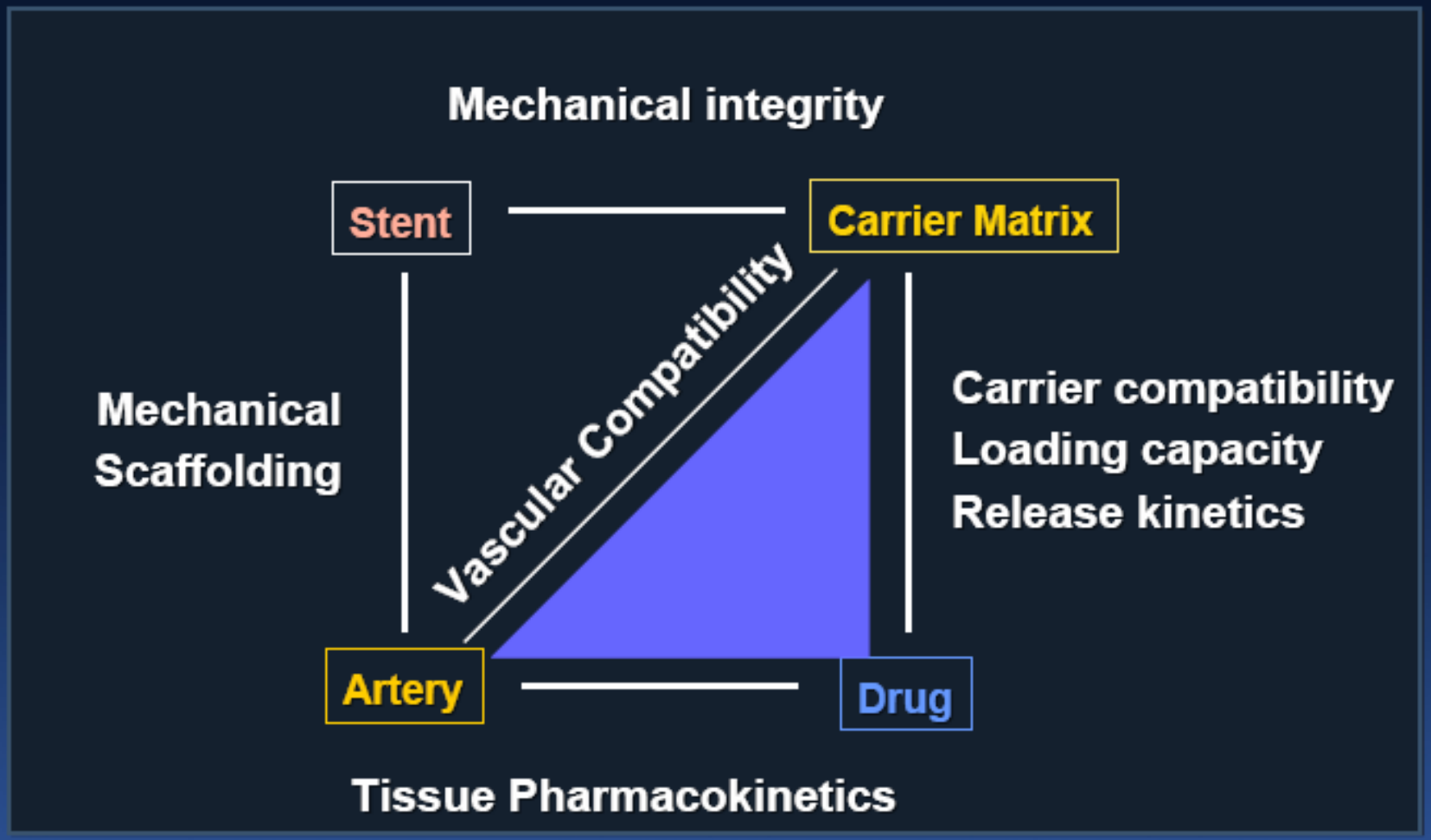
Subgroup Analyses



Douglas P. JACC 2009;53

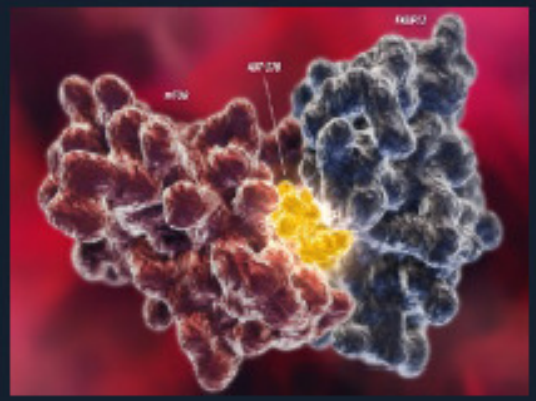
Not All DES are Created Equal

There is NO Class Effect!

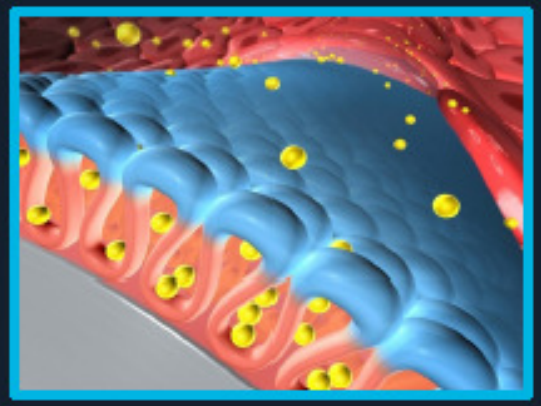


Current Generation DES

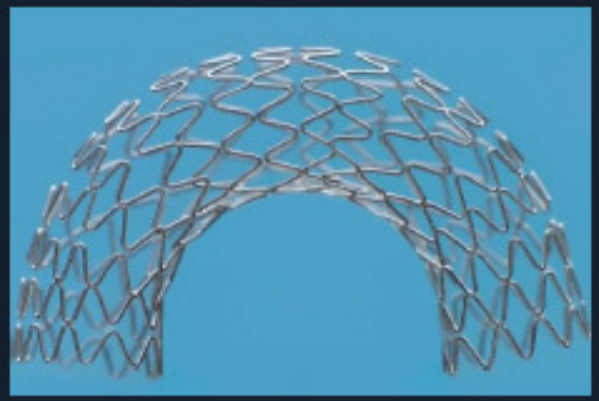
Resolute



Zotarolimus



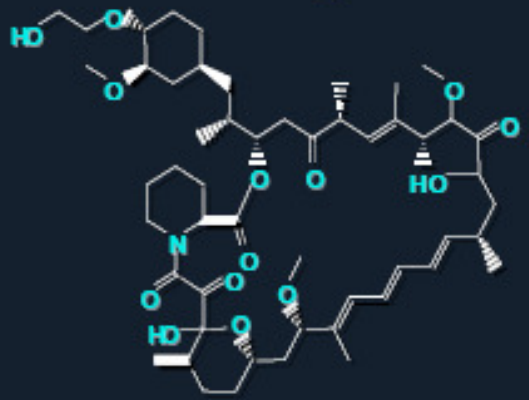
BioLinx copolymer



Driver

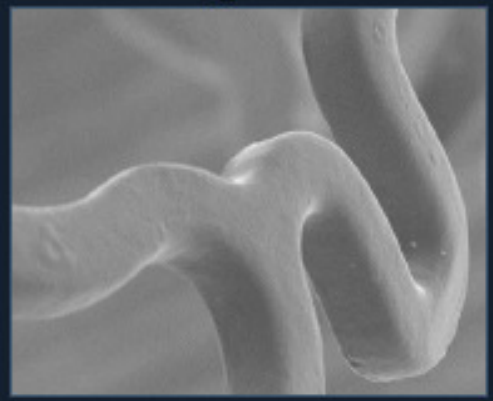
Xience V*

Drug



Everolimus

Polymer



VDF + HFP copolymer

Stent

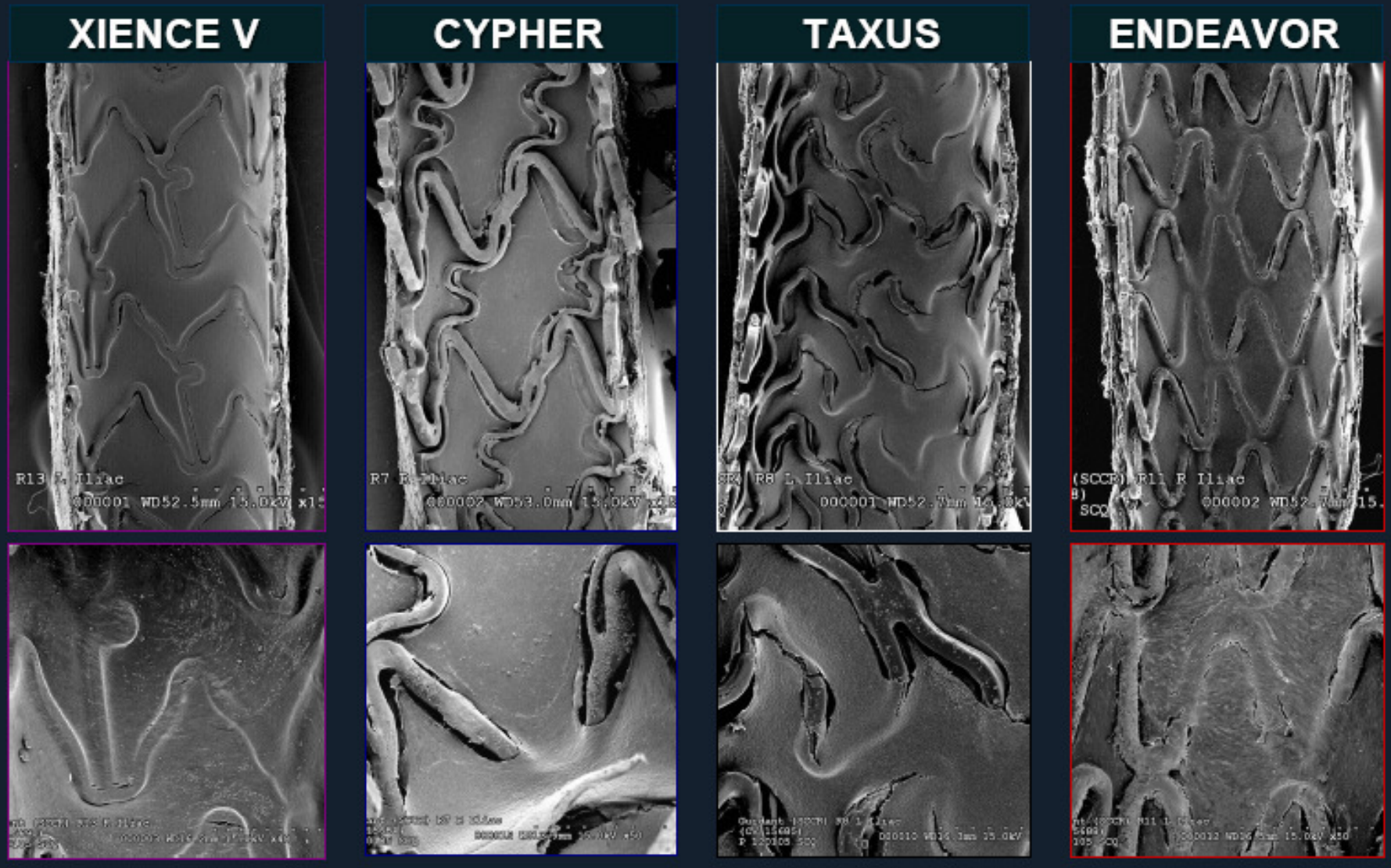
Vision

*AKA Promus

CARDIOVASCULAR RESEARCH FOUNDATION
A Passion for Innovation

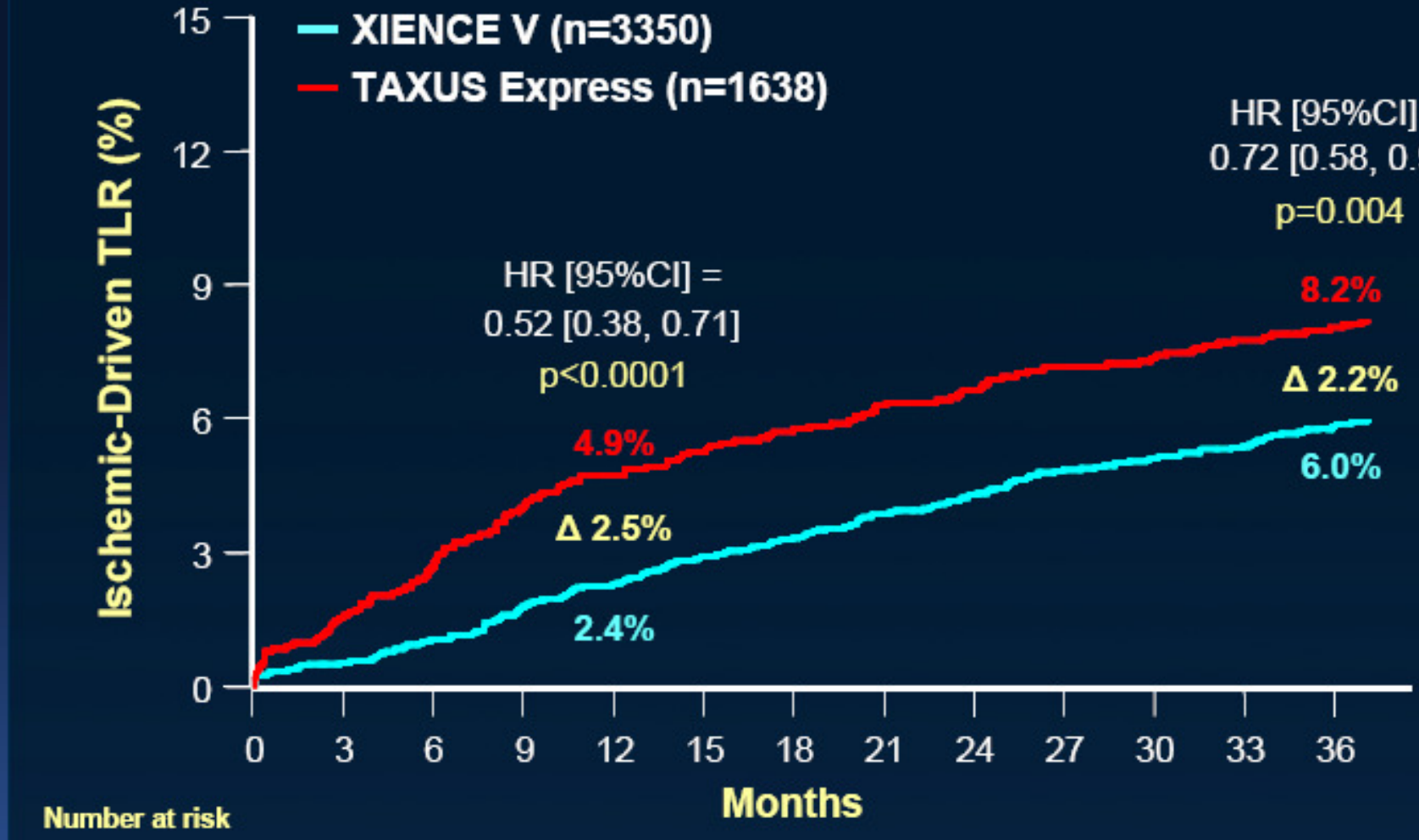
COLUMBIA UNIVERSITY MEDICAL CENTER
NewYork-Presbyterian

14 Day Endothelialization: Rabbit Iliac Model



Joner M et al. JACC 2008;52:333-42

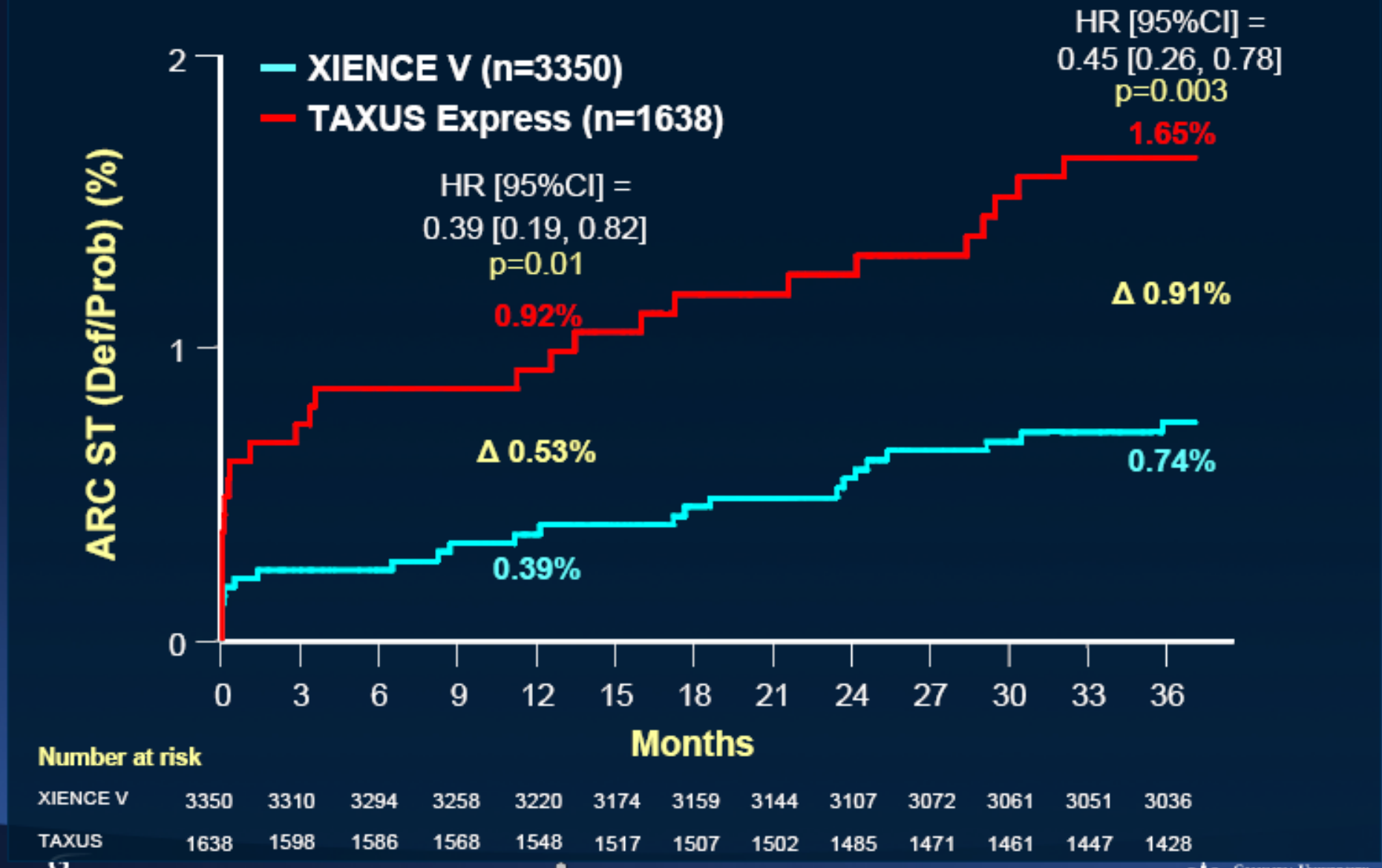
Ischemia-Driven TLR Through 3 Years



Number at risk

XIENCE V	3350	3300	3266	3207	3154	3091	3064	3034	2985	2939	2920	2898	2874
TAXUS	1638	1584	1552	1514	1485	1448	1434	1422	1399	1381	1370	1353	1331

Stent Thrombosis (ARC Def or Prob)



THE LANCET

Articles

Stent thrombosis with drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis

Tullio Palmerini, Giuseppe Biondi-Zoccai, Diego Della Riva, Christoph Stettler, Diego Sangiorgi, Fabrizio D'Ascenzo, Takeshi Kimura, Carlo Briguori, Manel Sabatè, Hyo-Soo Kim, Antoinette De Waha, Elvin Kedhi, Pieter C Smits, Christoph Kaiser, Gennaro Sardella, Antonino Marullo, Ajay J Kirtane, Martin B Leon, Gregg W Stone

Palmerini T et al. *Lancet* 2012:On-line

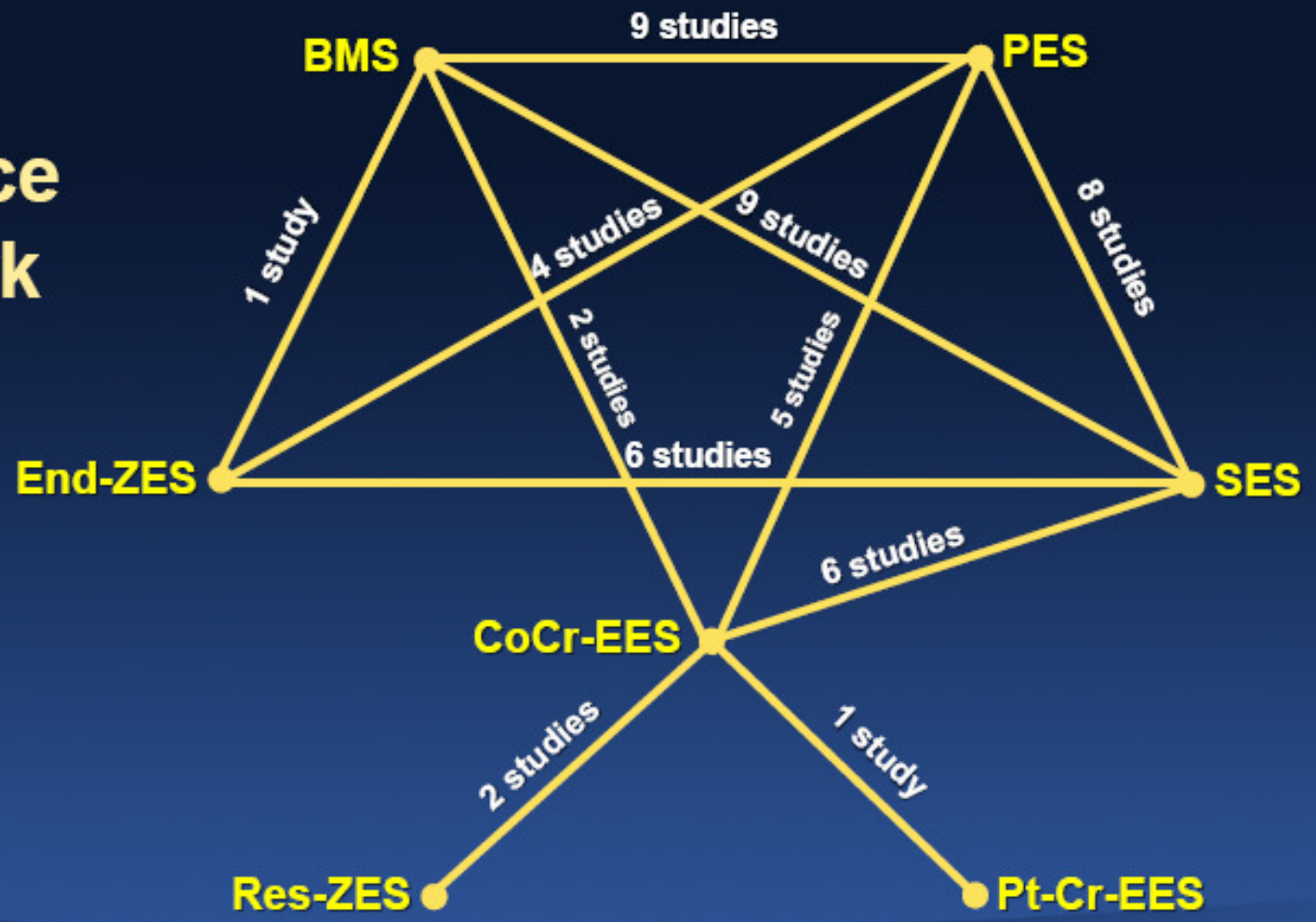
DOI:10.1016/S0140-6736(12)60324-9

Stent Thrombosis Network Meta-analysis

Primary EP: ARC Definite ST (FU through 2 years)

49 RCTs, 50,844 pts

Evidence network



Palmerini T et al. *Lancet* 2012:On-line

Stent Thrombosis Network Meta-analysis

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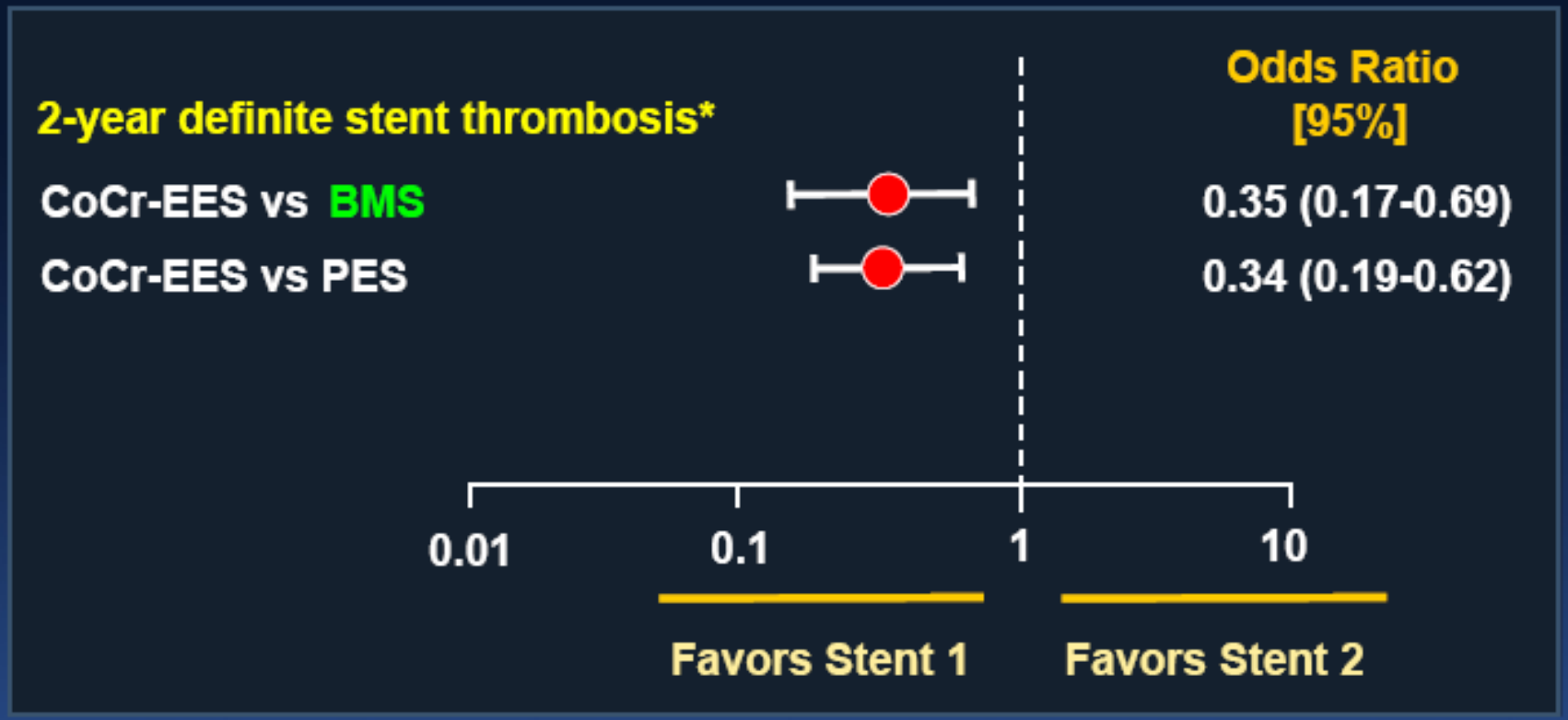


*Only statistically significant results are shown

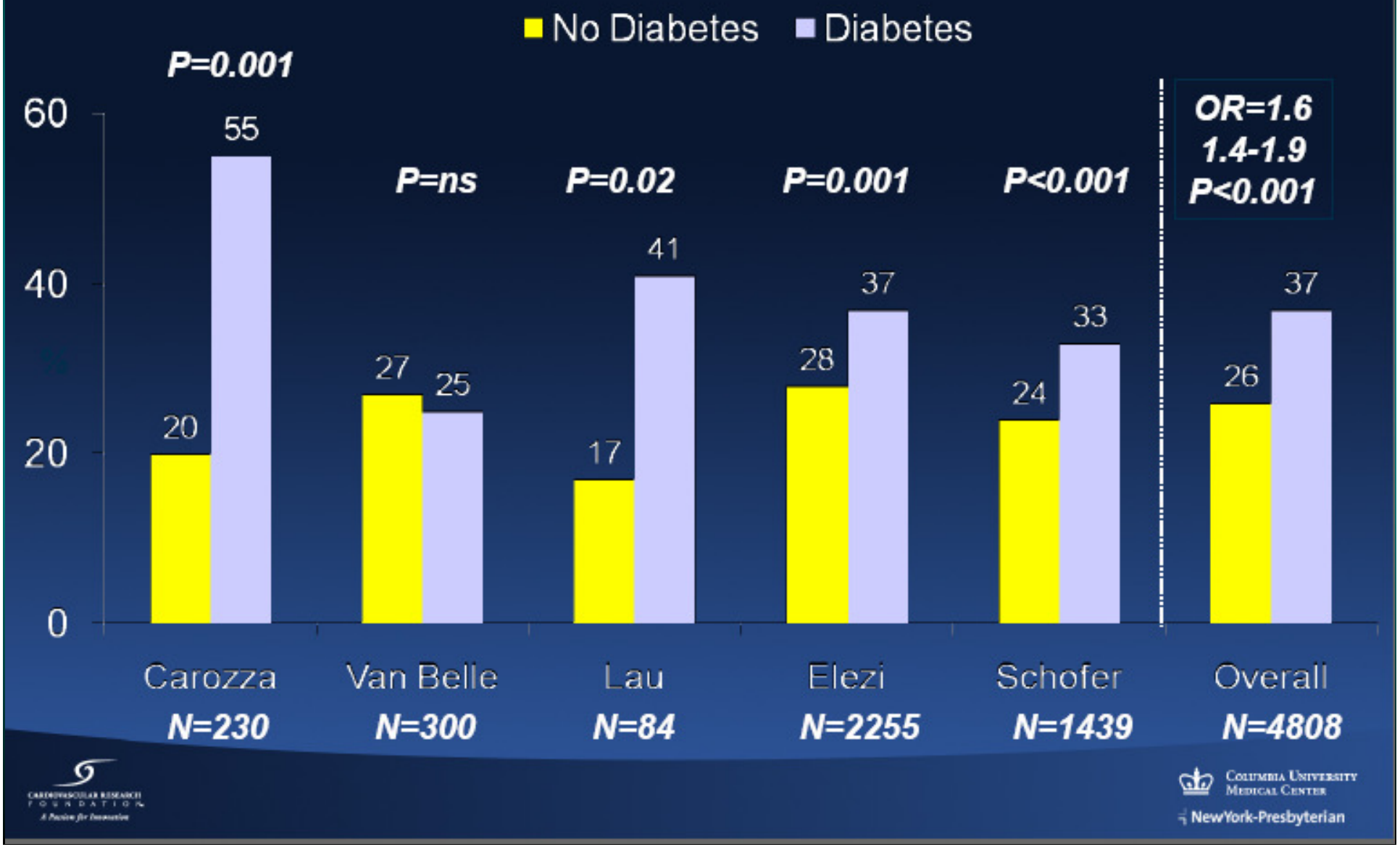
Palmerini T et al. *Lancet* 2012:On-line

Stent Selection – 2012
Patient Factors

- Diabetes – esp. IDDM
- ACS – esp. STEMI
- DAPT – related issues
  - *Compliance concerns*
  - *Risk of bleeding (e.g. coumadin, elderly)*
  - *Elective surgery*

Risk of Restenosis in the BMS Era

Diabetic vs Nondiabetic Patients

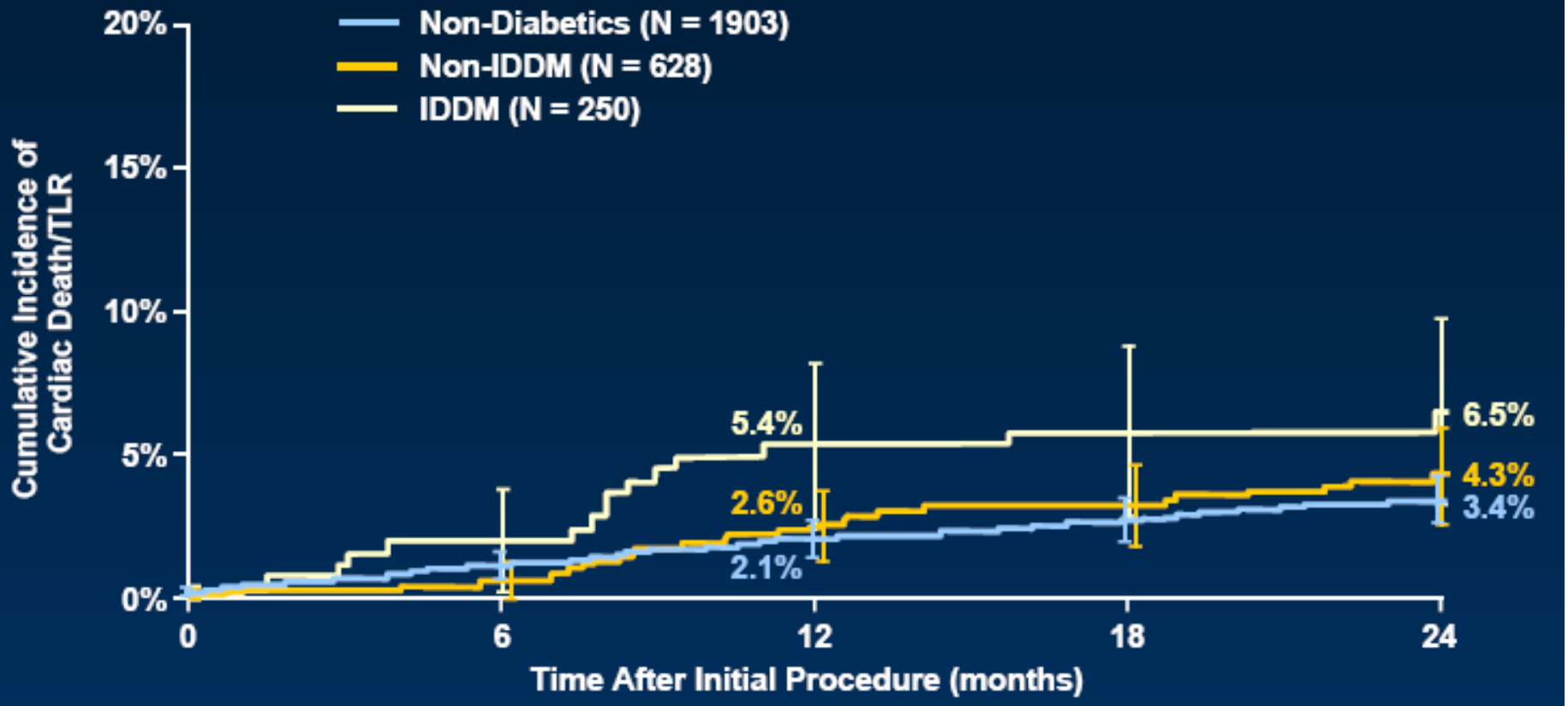


Cardiovascular Research Foundation
A Passion for Innovation

Columbia University Medical Center
NewYork-Presbyterian

RESOLUTE Pooled Diabetic Analysis

Standard Risk Pts – Target Lesion Revascularization to 2 Years



No. at risk					
Non-Diabetics	1903	1900	1859	1809	1763
Non-IDDM	628	627	614	589	579
IDDM	250	250	236	222	216

Error bars indicate a point-wise two-sided 95% confidence interval (±1.96*SE). Standard Error based on the Greenwood Formula.

Use of Drug-Eluting Stents in Acute Myocardial Infarction

A Systematic Review and Meta-Analysis

Somjot S. Brar, MD, Martin B. Leon, MD, Gregg W. Stone, MD, Roxana Mehran, MD, Jeffrey W. Moses, MD, Simerjeet K. Brar, BS, George Dangas, MD, PhD

New York, New York

Objectives The primary aim of the analysis was to compare outcomes by stent type for death, myocardial infarction (MI), target vessel revascularization (TVR), and stent thrombosis in randomized trials of ST-segment elevation myocardial infarction (STEMI). A secondary analysis was performed among registry studies.

Background It is not known whether there are differences in outcomes between drug-eluting stents (DES) and bare-metal stents (BMS) for STEMI.

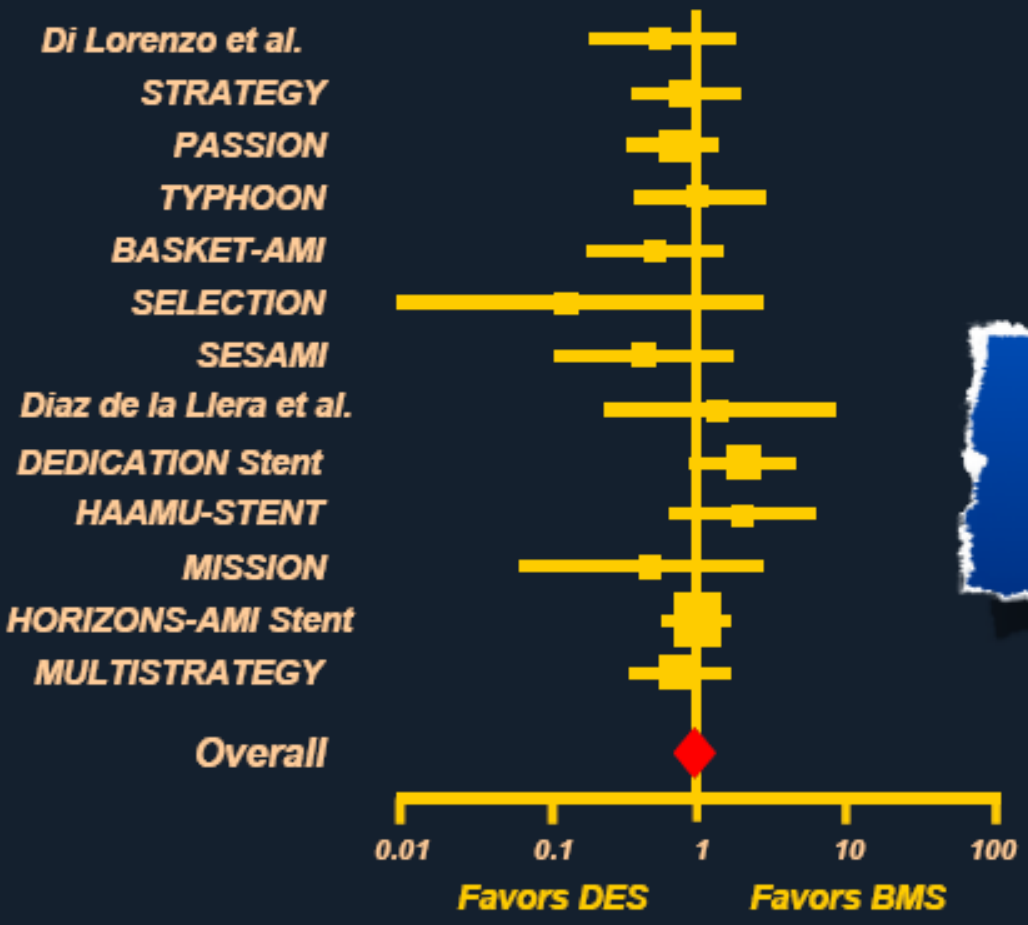
Methods We searched MEDLINE, EMBASE, the Cochrane Library, and Internet sources for articles comparing outcomes between DES and BMS among patients with STEMI between January 2000 and October 2008. Randomized controlled trials and registries including patients 18 years of age and older receiving a DES or BMS were included. We extracted variables related to the study design, setting, participants, and clinical end points.

Results Thirteen randomized trials were identified (N = 7,352). Compared with BMS, DES significantly reduced TVR (relative risk [RR]: 0.44; 95% confidence interval [CI]: 0.35 to 0.55), without increasing death (RR: 0.89; 95% CI: 0.70 to 1.14), MI (RR: 0.82; 95% CI: 0.64 to 1.05), or stent thrombosis (RR: 0.97; 95% CI: 0.73 to 1.28). These observations were durable over 2 years. Among 18 registries (N = 26,521), DES significantly reduced TVR (RR: 0.54; 95% CI: 0.40 to 0.74) without an increase in MI (RR: 0.87, 95% CI: 0.62 to 1.23). Death was significantly lower in the DES group within 1 year of the index percutaneous coronary intervention, but there were no differences within 2 years ($p = 0.45$).

Conclusions The use of DES appears safe and efficacious in randomized trials and registries of patients with STEMI. The DES significantly reduce TVR compared with BMS, without an increase in death, MI, or stent thrombosis within 2 years of the index procedure. (J Am Coll Cardiol 2009;53:1677–89)

DES in AMI Meta-Analysis

Mortality (RCTs)



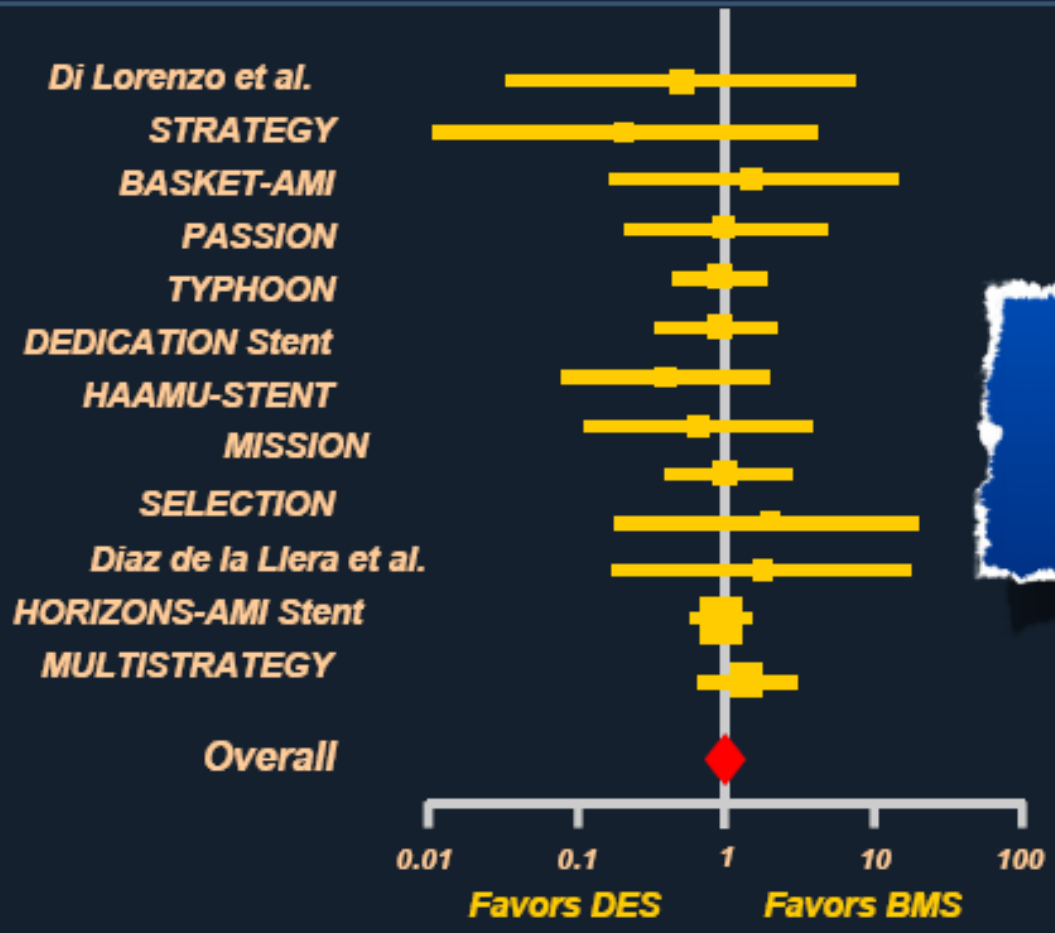
Relative Risk (95% CI)
0.89
(0.70 - 1.14)

$I^2 = 0\%$

Brar et al. JACC 2009; 53(18)

DES in AMI Meta-Analysis

Stent Thrombosis (RCTs)



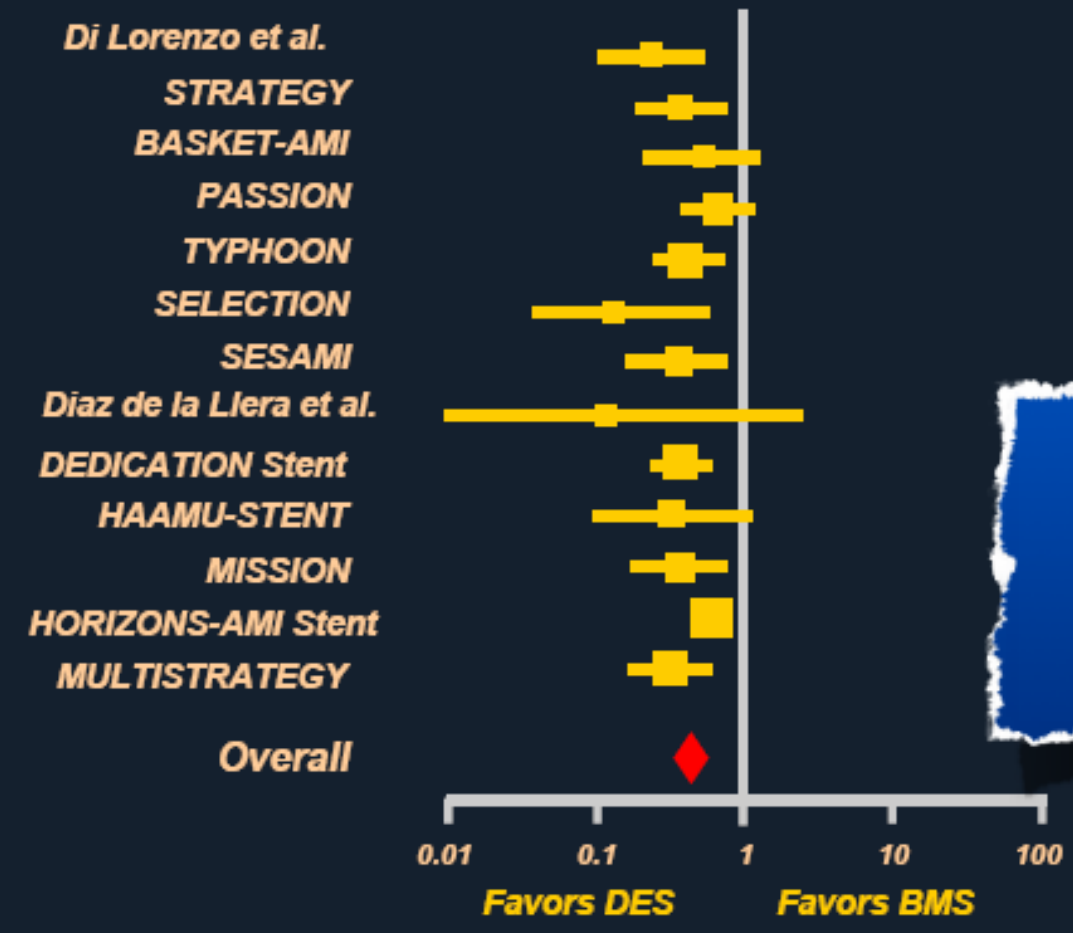
Relative Risk (95% CI)
0.97
(0.73 - 1.28)

$I^2 = 0\%$

Brar et al. JACC 2009; 53(18)

DES in AMI Meta-Analysis

Target Vessel Revascularization (RCTs)



REDUCTION

56%

Relative Risk (95% CI)
0.44
(0.35 - 0.55)
$p < 0.001$

$I^2 = 26\%$

Brar et al. JACC 2009; 53(18)

Cardiovascular Research Foundation
A Passion for Innovation

Columbia University Medical Center
NewYork-Presbyterian

Multivariable predictors of 12-month ischemic TLR among patients randomized to bare metal stents

Variable	HR [95% CI]	P	Weighted score
Total lesion length ≥30 mm	5.28 [1.73,16.15]	0.004	2
Baseline RVD ≤3.0 mm	3.27 [1.63, 6.55]	0.0008	1
Insulin-treated diabetes	3.00 [1.17, 7.66]	0.02	1

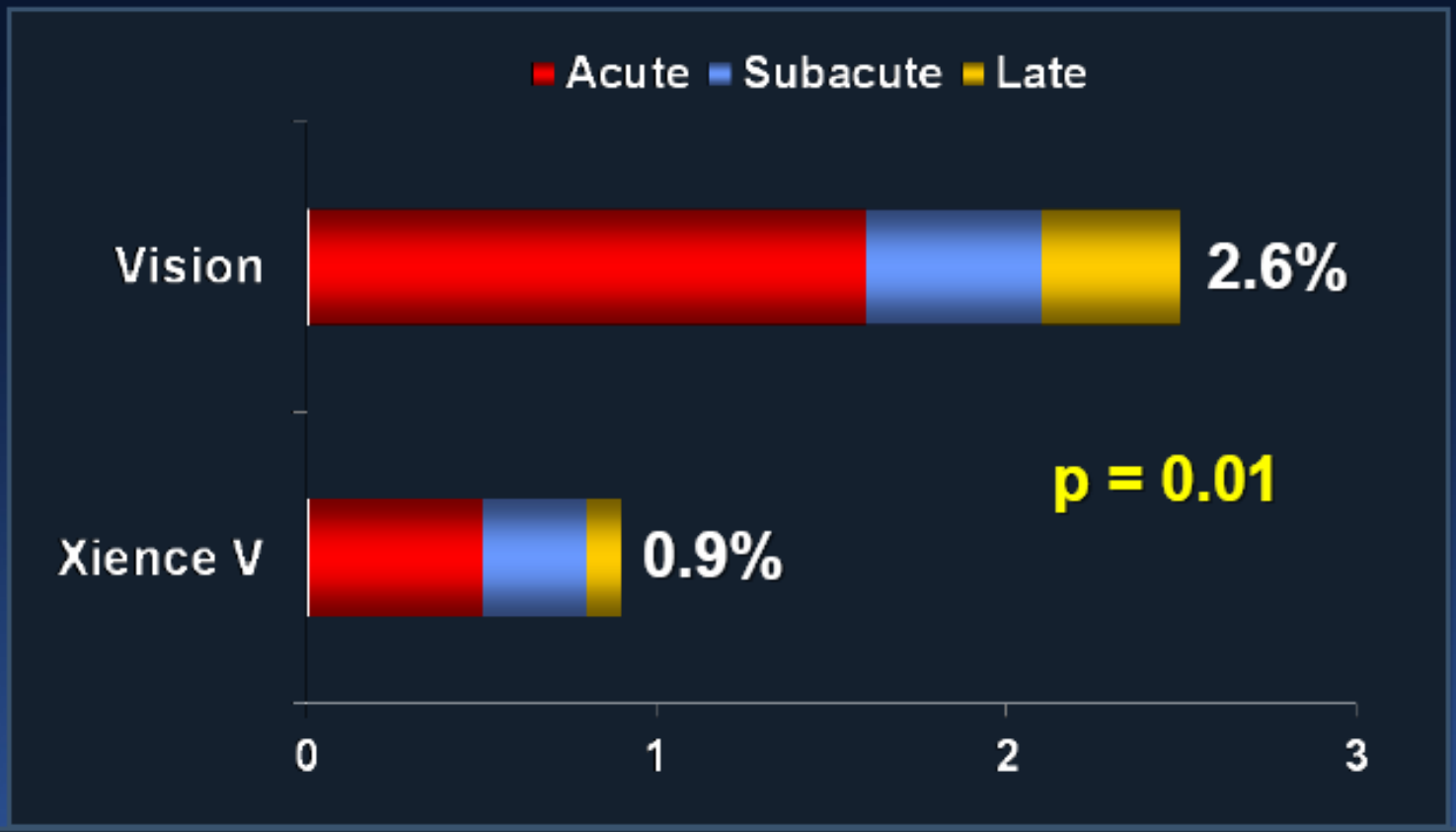
Stone GW et al. J Am CollCardiol. 2010 Nov 2;56(19):1597-604

HORIZONS AMI

EXAMINATION Trial

1504 pts with STEMI undergoing PCI within 48 ° (85% primary PCI within 12°) were randomized to Xience V EES vs. Vision BMS

Stent thrombosis (Def/prob) within 1 year



Definite ST was reduced with Xience V from 1.9% to 0.5%, p=0.01

Sabate M. ESC 2011

European Heart Journal
doi:10.1093/eurheartj/ehq277

ESC/EACTS GUIDELINES

Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Relative Contraindications to DES Use

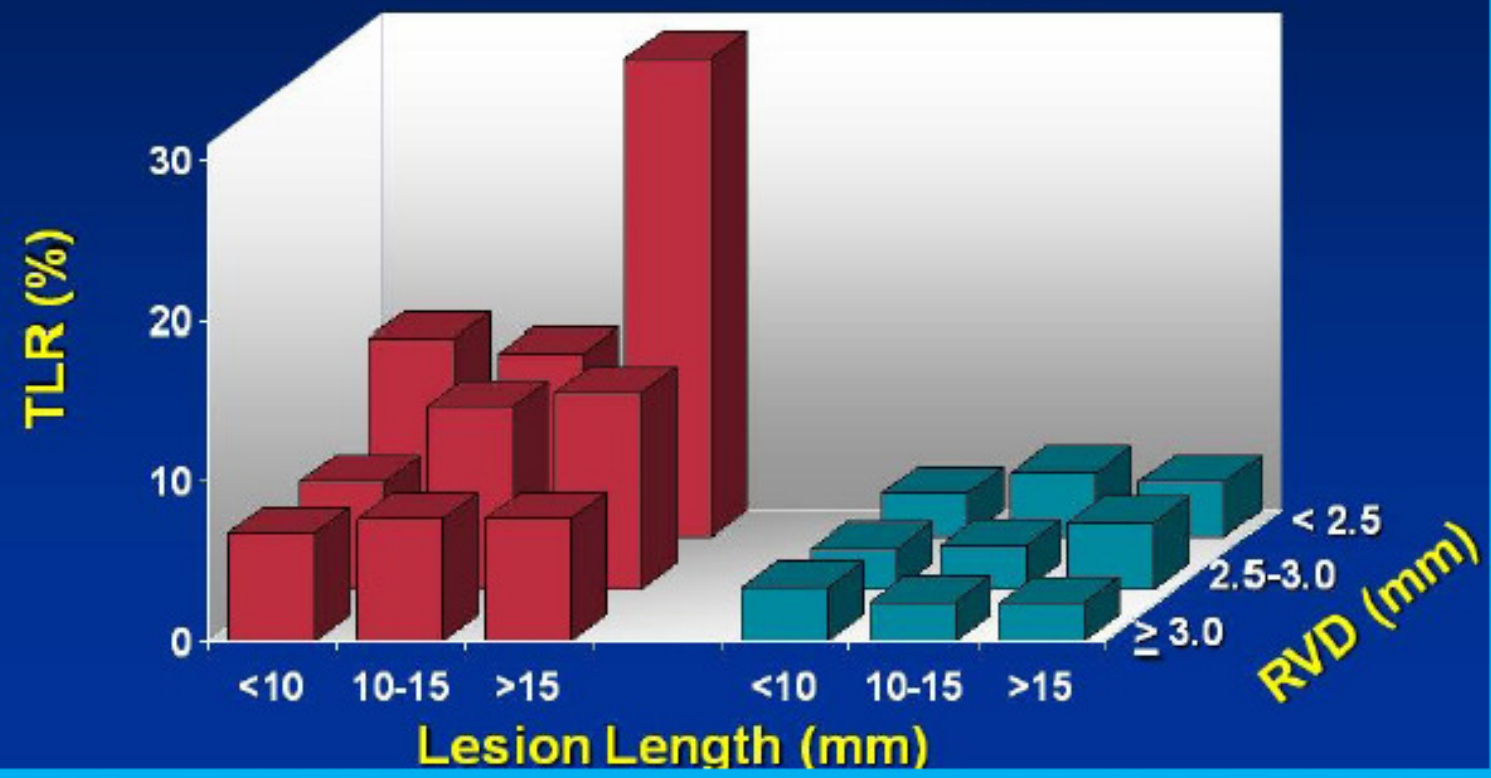
- Clinical history difficult to obtain
- Expected poor compliance with DAPT
- Non-elective surgery required
- Increased risk of bleeding
- Allergy to ASA or clopidogrel/prasugrel/ticagrelor
- Indication for long-term anticoagulation

Stent Selection - 2012

TAXUS IV study Impact of Vessel Size and Lesion Length

TLR (9 month)

Tertile analysis



Stent Selection – 2012
Lesion Factors

- **High Restenosis Risk**
  - Long lesions (diffuse disease, incl. CTOs)
  - Small vessels (< 2.5, 3.0 mm RVD)
  - Ostial lesions
  - Bifurcations
  - ISR – diffuse
  - SVGs (esp. long and < 4mm RVD)

Stent Selection – 2012
Lesion Factors

- **High Restenosis Consequences**
  - **LM disease**
  - **LAD proximal**
  - **Sole remaining vessel**

Stent Selection – 2012
*Selection Algorithm**

- **Step 1 - Patient Factors**
  - Diabetes – universal DES, esp. if IDDM
  - ACS (STEMI) – selective DES based upon patient/lesion factors
  - Prolonged DAPT safety concerns – favor BMS

** Cost insensitive*

Stent Selection – 2012
*Selection Algorithm**

- **Step 2 - Lesion Factors**
  - High restenosis risk (esp. long lesions in small vessels) – universal DES
  - Low restenosis risk (e.g. short lesions in large vessels) – selective DES
  - High restenosis consequences (e.g. LM) – universal DES

Stent Selection – 2012
Selection Algorithm

- **Step 3 – Caveats to consider**
  - Combo effects – in a given pt, multiple patient and lesion factors apply favoring either BMS or more likely DES; solution = clinical judgment
  - Stent designs – anatomic factors will direct specific stent selections (e.g. deliverability in tortuous vessels, ostial location, sidebranch access, stent thru stent, size-length matrix, edge dissections, etc.)
  - Acute stent thrombosis is a special circumstance favoring BMS use (as needed)

Stent Selection – 2012
Selection Algorithm

- **Step 3 – Caveats to consider**
  - ¡ ***Cost sensitivity – major driver favoring BMS in most regions!***

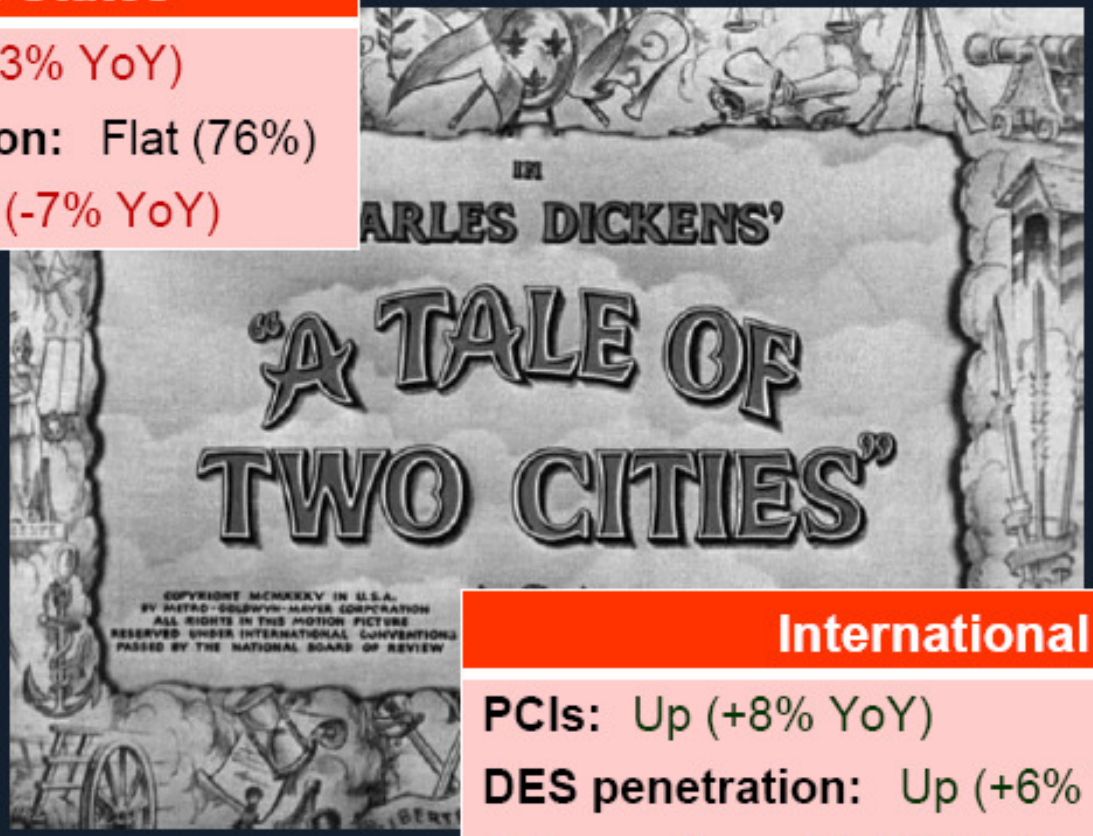
PCI - DES Penetration 2012

United States

PCIs: Down (-3% YoY)

DES penetration: Flat (76%)

Prices: Down (-7% YoY)



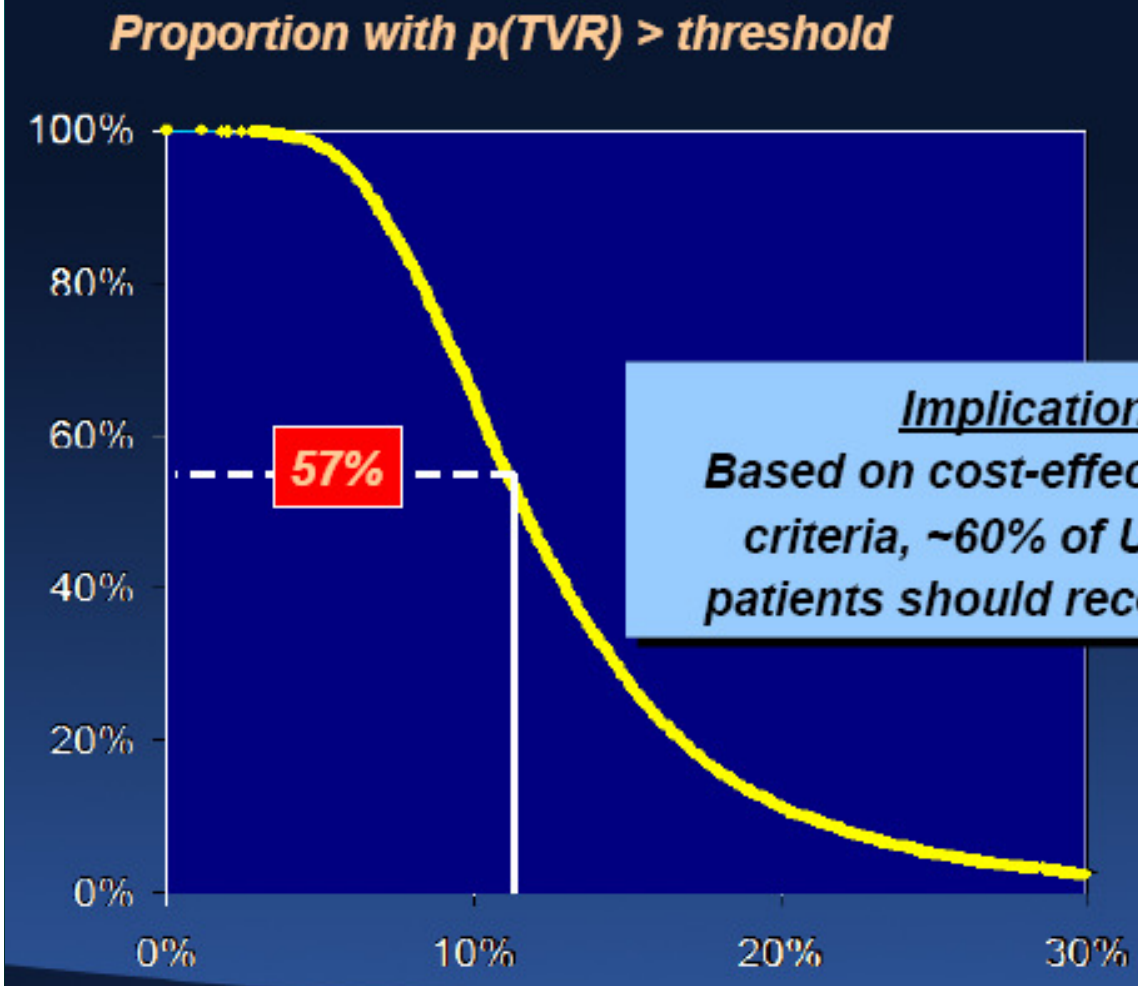
International

PCIs: Up (+8% YoY)

DES penetration: Up (+6% YoY, to 66%)

Prices: Down (-6-8% YoY)

Distribution of Predicted TVR Rates with BMS



Implication

Based on cost-effectiveness criteria, ~60% of U.S. PCI patients should receive DES

EVENT Waves 1-3

- *7447 patients/10,425 lesions*
- *Predicted TVR rate with DES and BMS based on regression*
  - *ious PCI*
  - *rence diameter*
  - *Lesion length*
  - *SVG lesion*
  - *LM lesion*

Stolker JM et al. Circ Cardiovasc Interv 2010;3:327-34

CARDIOVASCULAR RESEARCH FOUNDATION

55% RRR

COLUMBIA UNIVERSITY MEDICAL CENTER

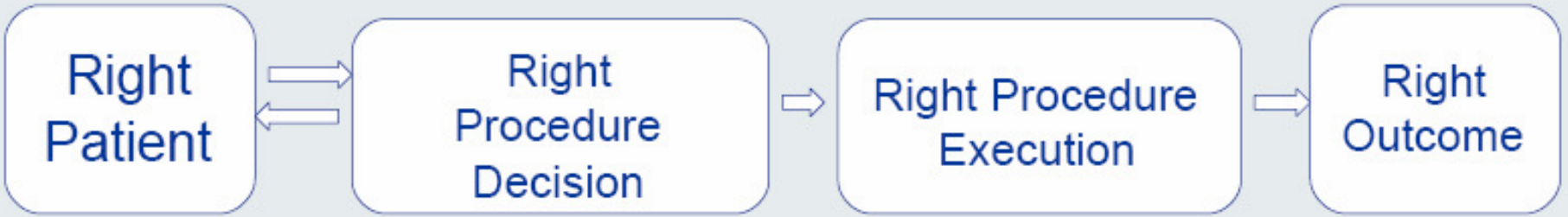
NewYork-Presbyterian

Stent Selection – 2012

Final Thoughts

- Optimal stent selection (BMS vs. DES) varies widely around the world (<40% - >90% DES use) determined largely by socio-economic factors and regional perceptions re: duration/importance of DAPT
- Beyond the cost/safety (DAPT) factors, both patient and lesion factors affecting restenosis risk should favor more aggressive DES use
- Among DES (DES vs. DES):
  - Strongly favor current generation DES
  - Future DES (absorbable polymers, polymer-free, or fully bioabsorbable stents) will likely add value
  - Impact of DCB in certain lesion subsets?

High Quality Cardiovascular Procedures



OBRIGADO !