

**2007 Guidelines Update for DES**  
**An Evidence Based Medicine**  
**Critical Analysis: Part 1**

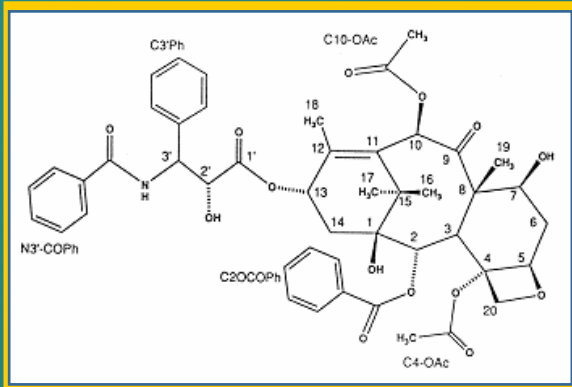
***Gregg W. Stone, MD***

***Columbia University Medical Center***  
***Cardiovascular Research Foundation***



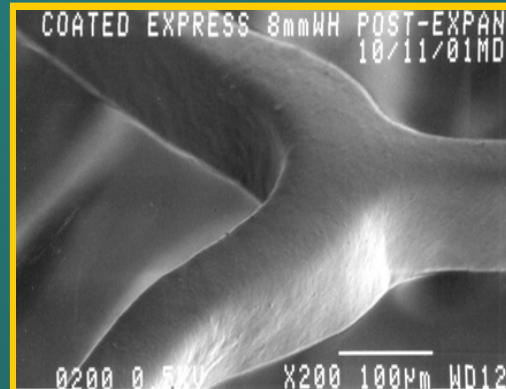
# Drug-eluting Stents in 2007

TAXUS



Paclitaxel

Drug



Polyolefin  
derivative

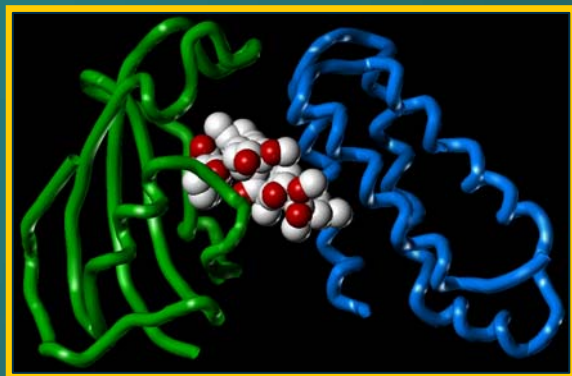
Polymer



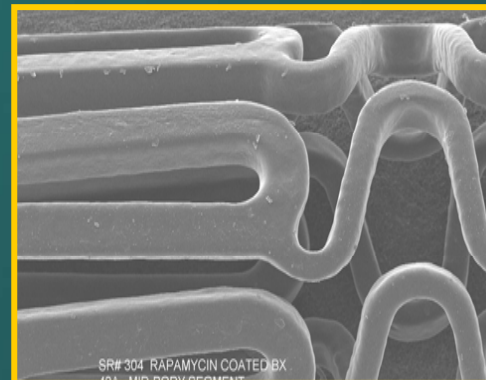
Express<sup>2</sup>

Stent

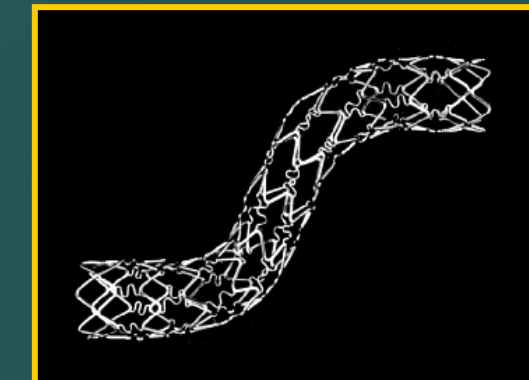
Cypher



Sirolimus



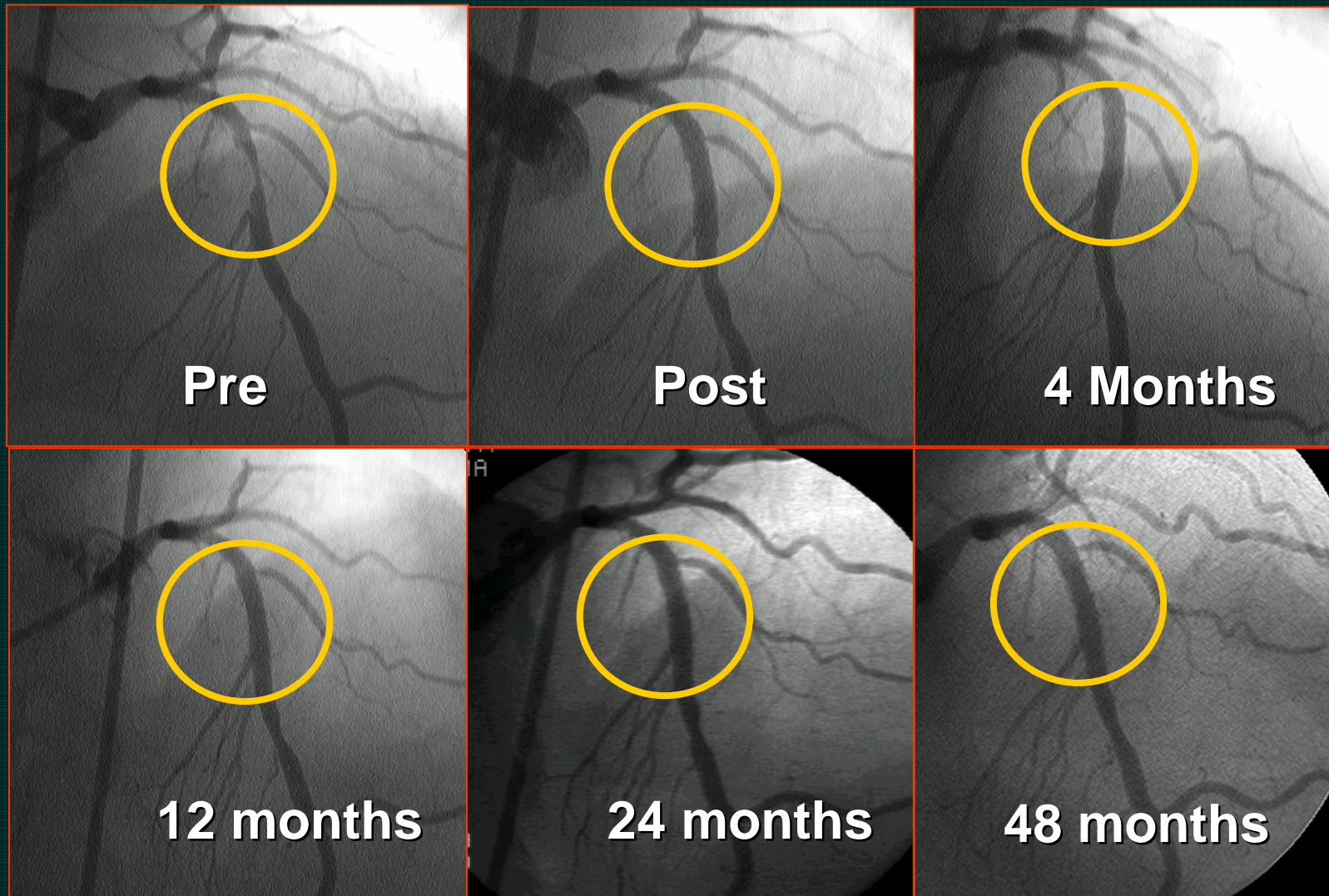
PEVA + PBMA  
blend



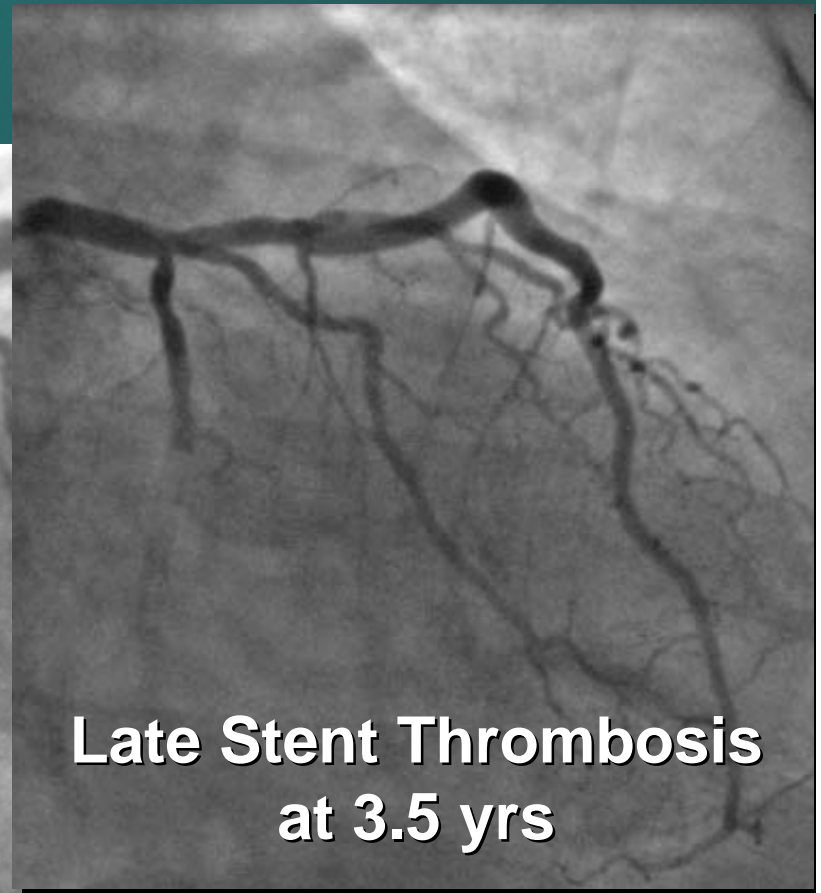
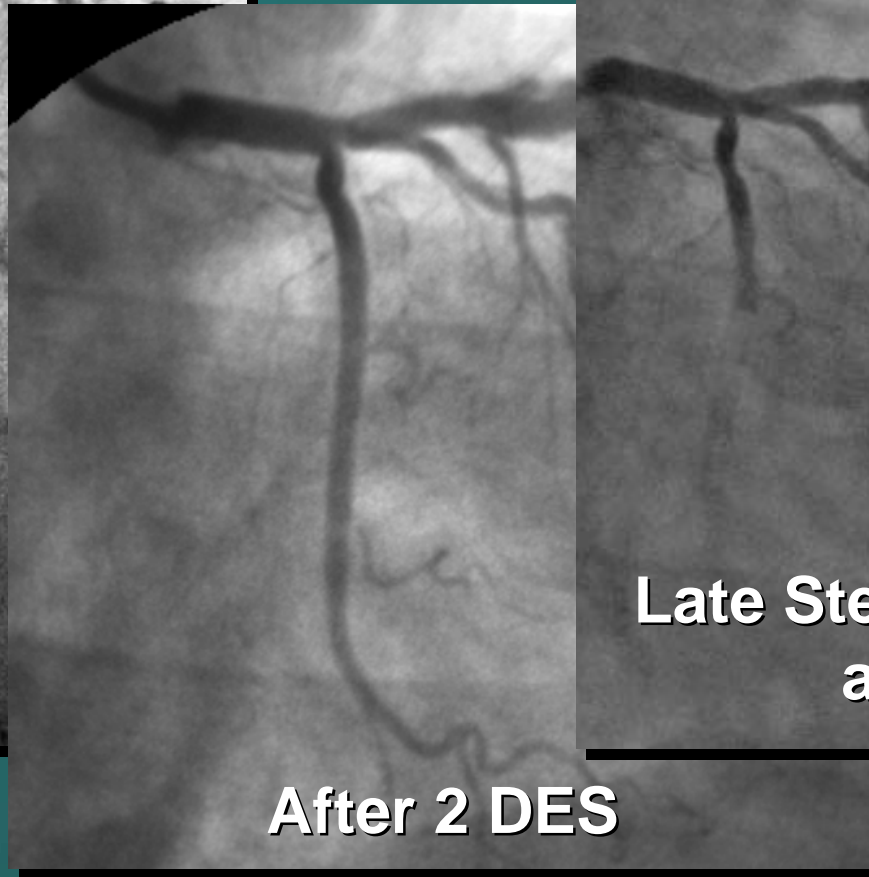
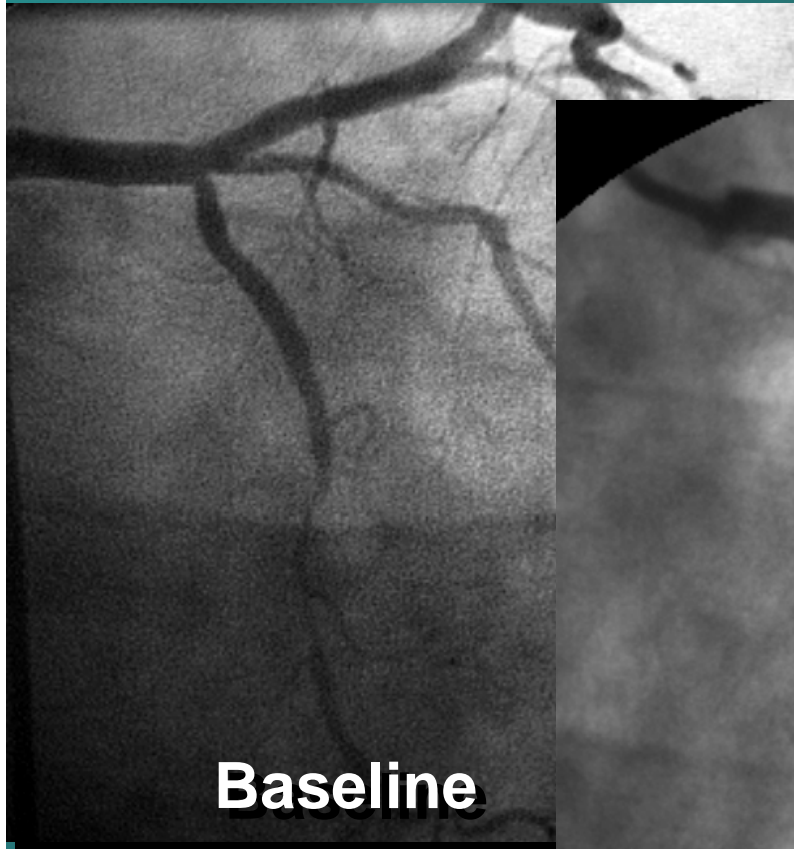
BX Velocity



# DES: A Transforming Technology



# **LaST** – Late DES Stent Thrombosis After 3 Years



# Pathology Findings - Sirolimus-Eluting Stents from Different Coronary Arteries in the Same Patient (delayed healing)



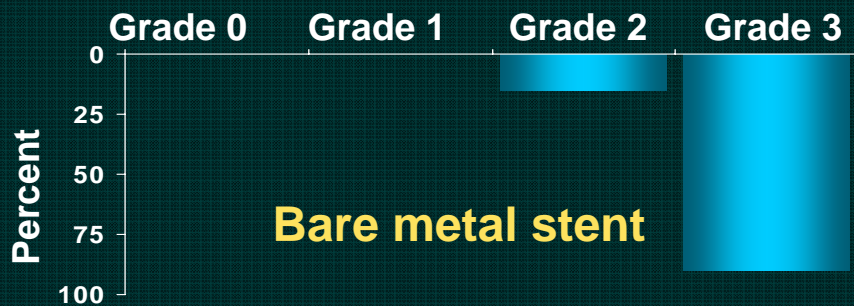
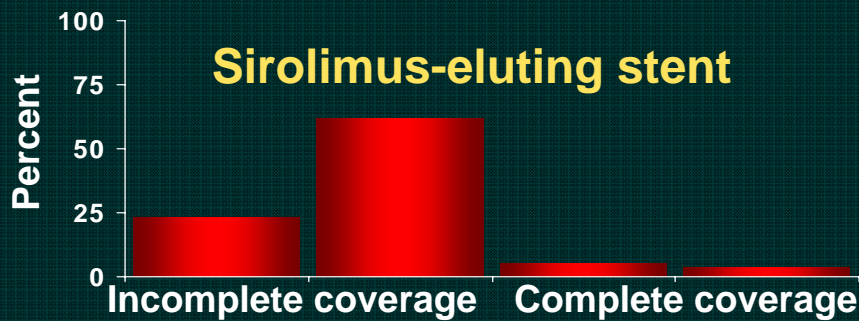
BMS 24 Months after  
Deployment



Cypher 16 Months after  
Deployment

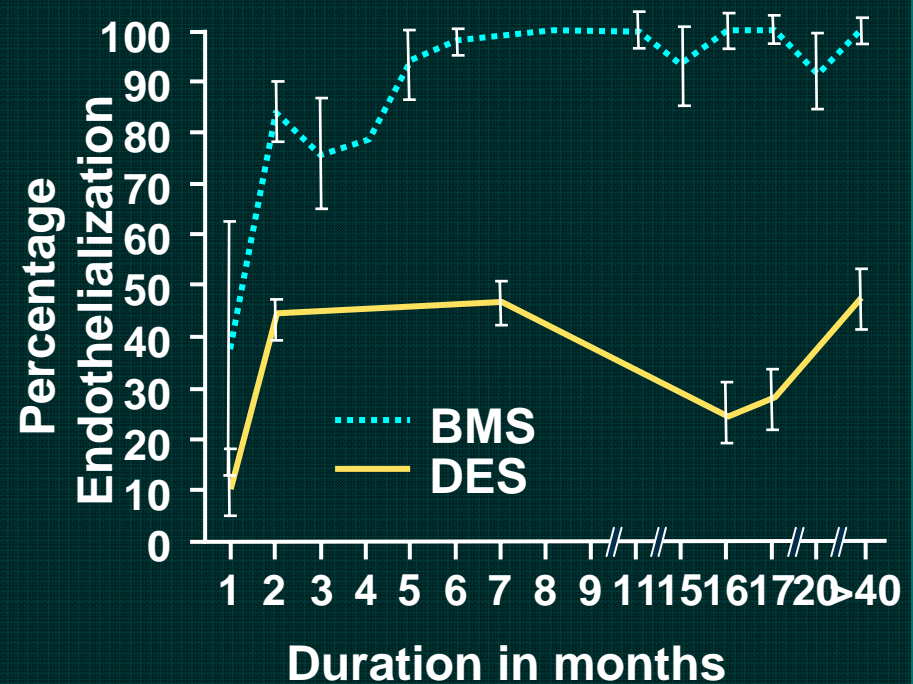


# Incomplete Strut Endothelialization With DES?



**Angioscopy at 8 months post SES implantation**

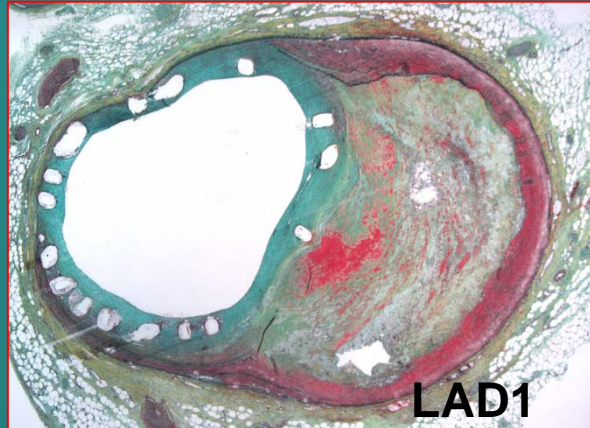
Kotani J et al. *JACC*. 2006;47:2108



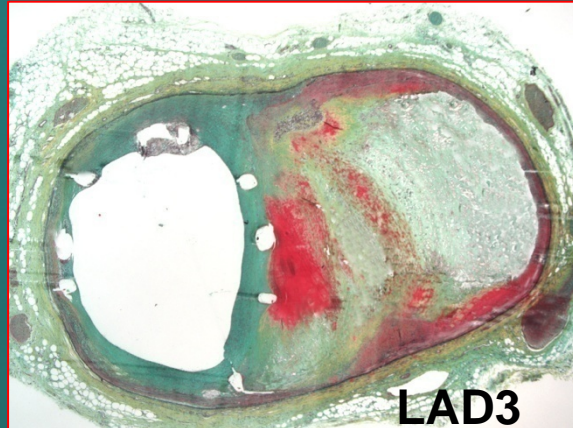
**Virmani autopsy data**

Joner M et al. *JACC*. 2006;48:193.

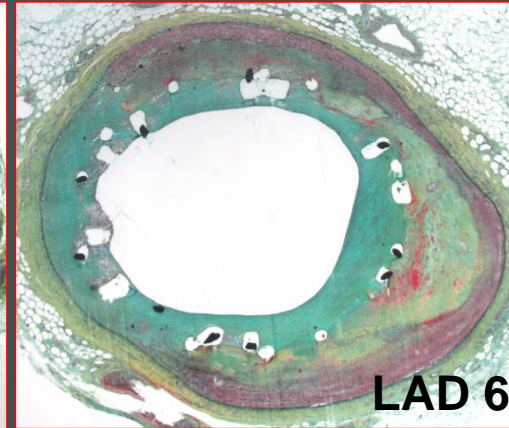
# 59 Year Old Female with TAXUS Stent in the LAD for 130 Days



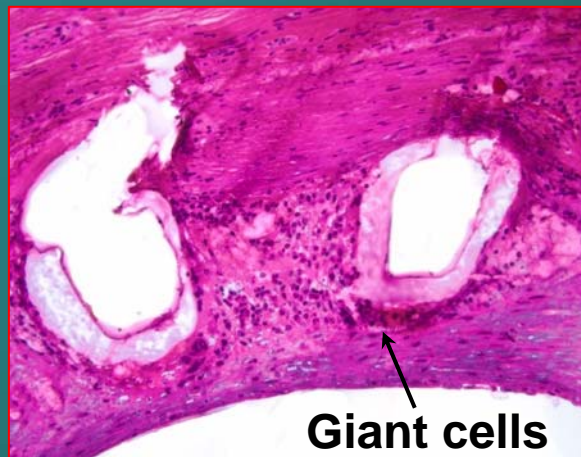
LAD1



LAD3



LAD 6



Giant cells



Eosinophils



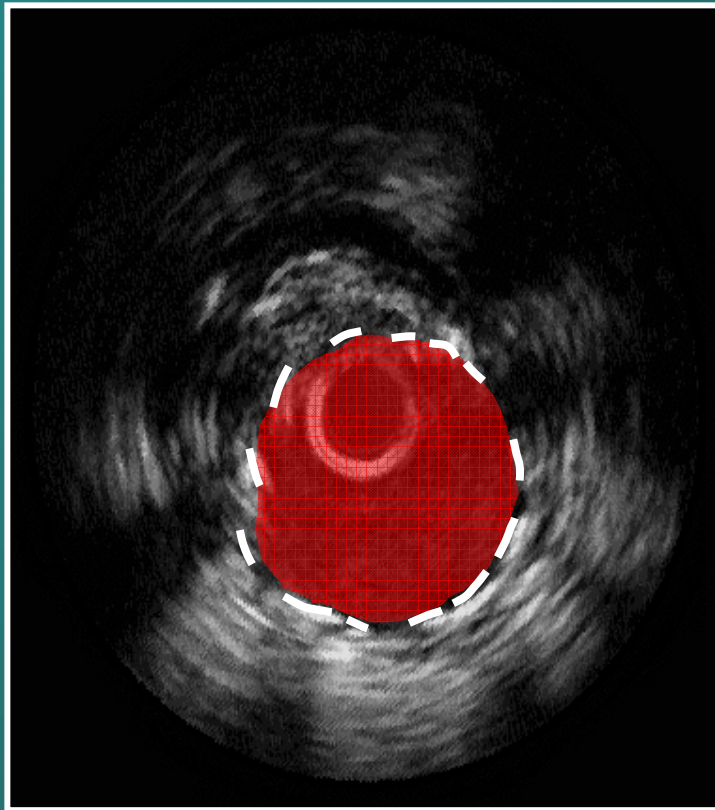
Fibrin

**80% surface endothelialized**

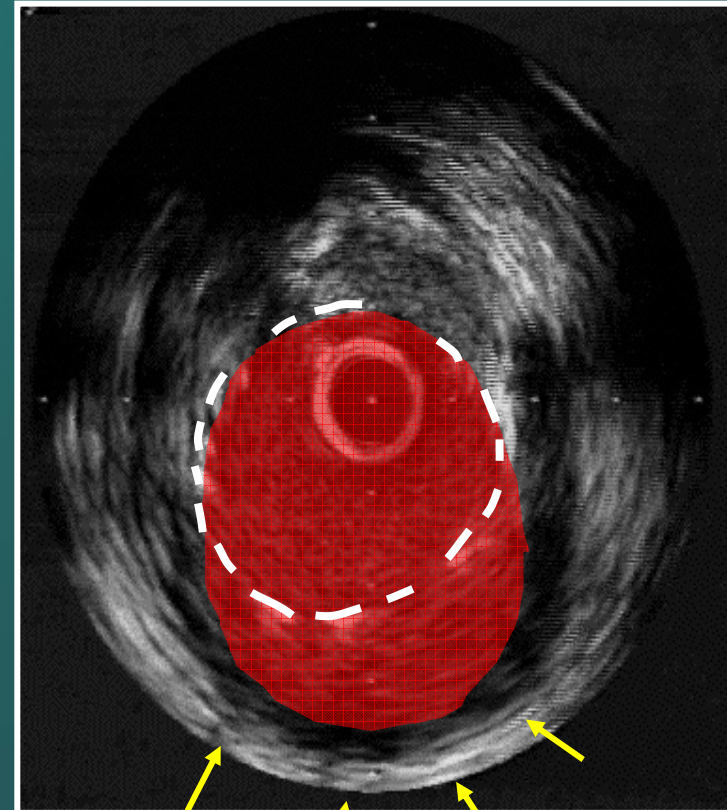


# Late Incomplete Apposition

Drug-eluting stent group



Baseline



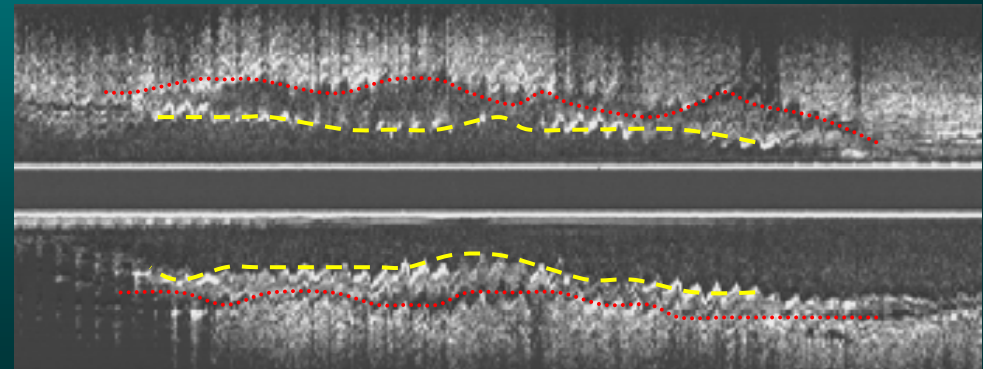
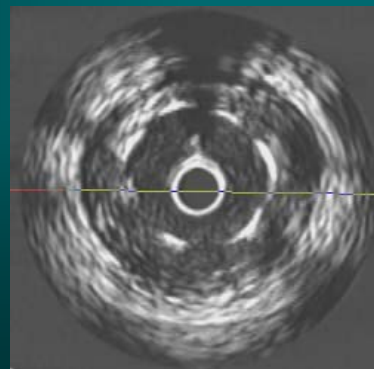
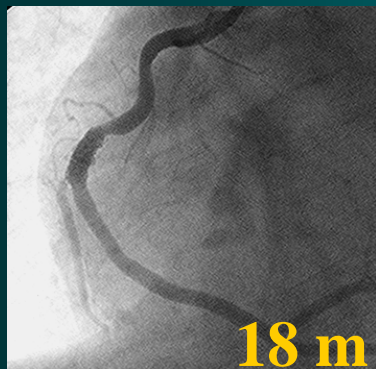
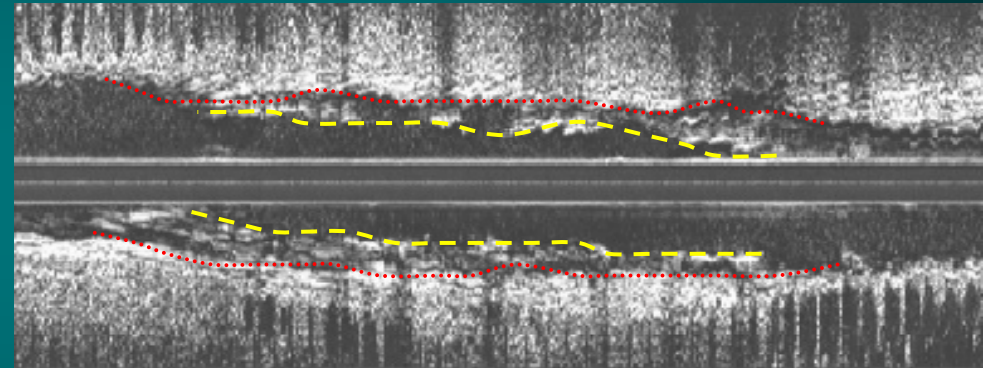
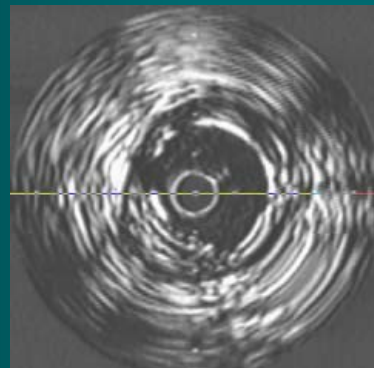
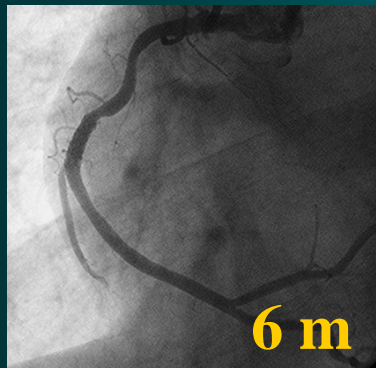
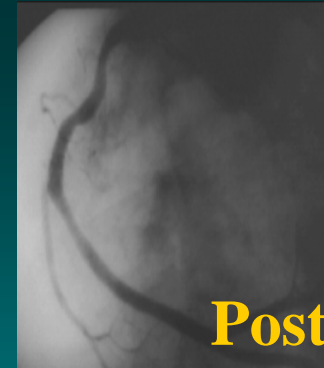
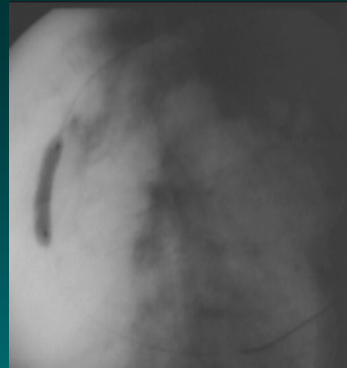
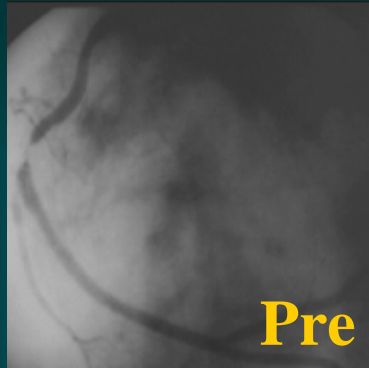
Follow-up

... vulnerable struts at the time when antiplatelets may not be taken

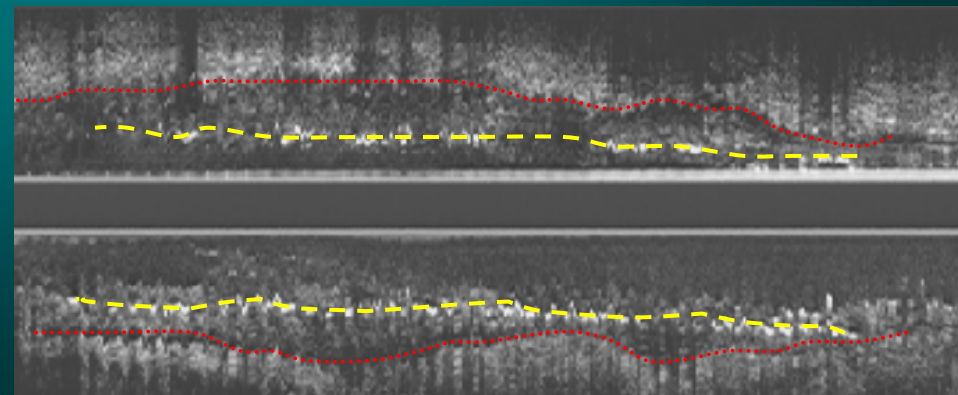
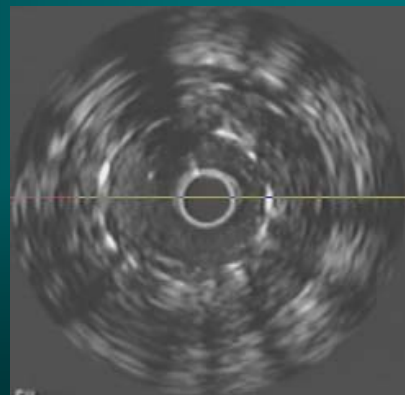
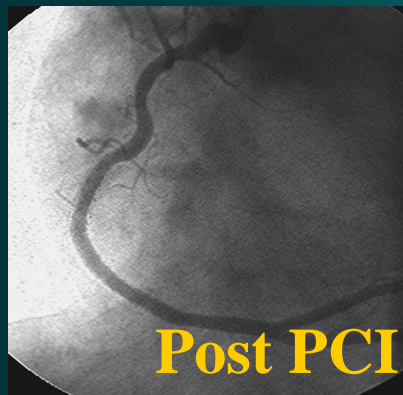
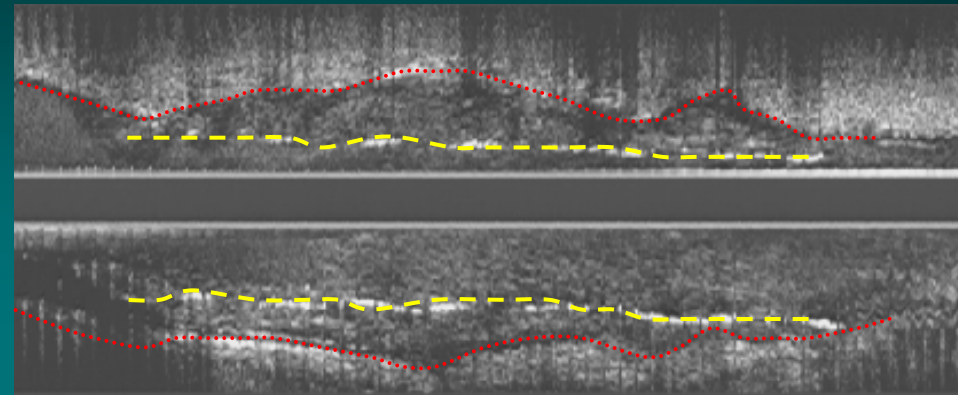
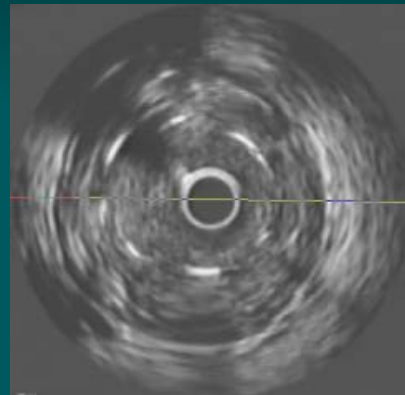
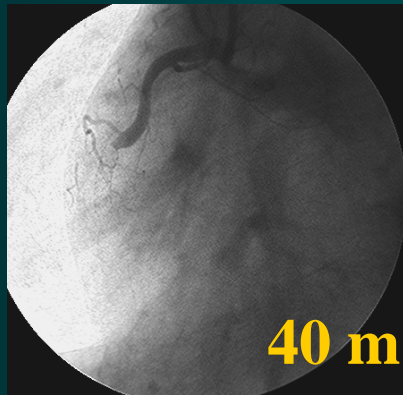




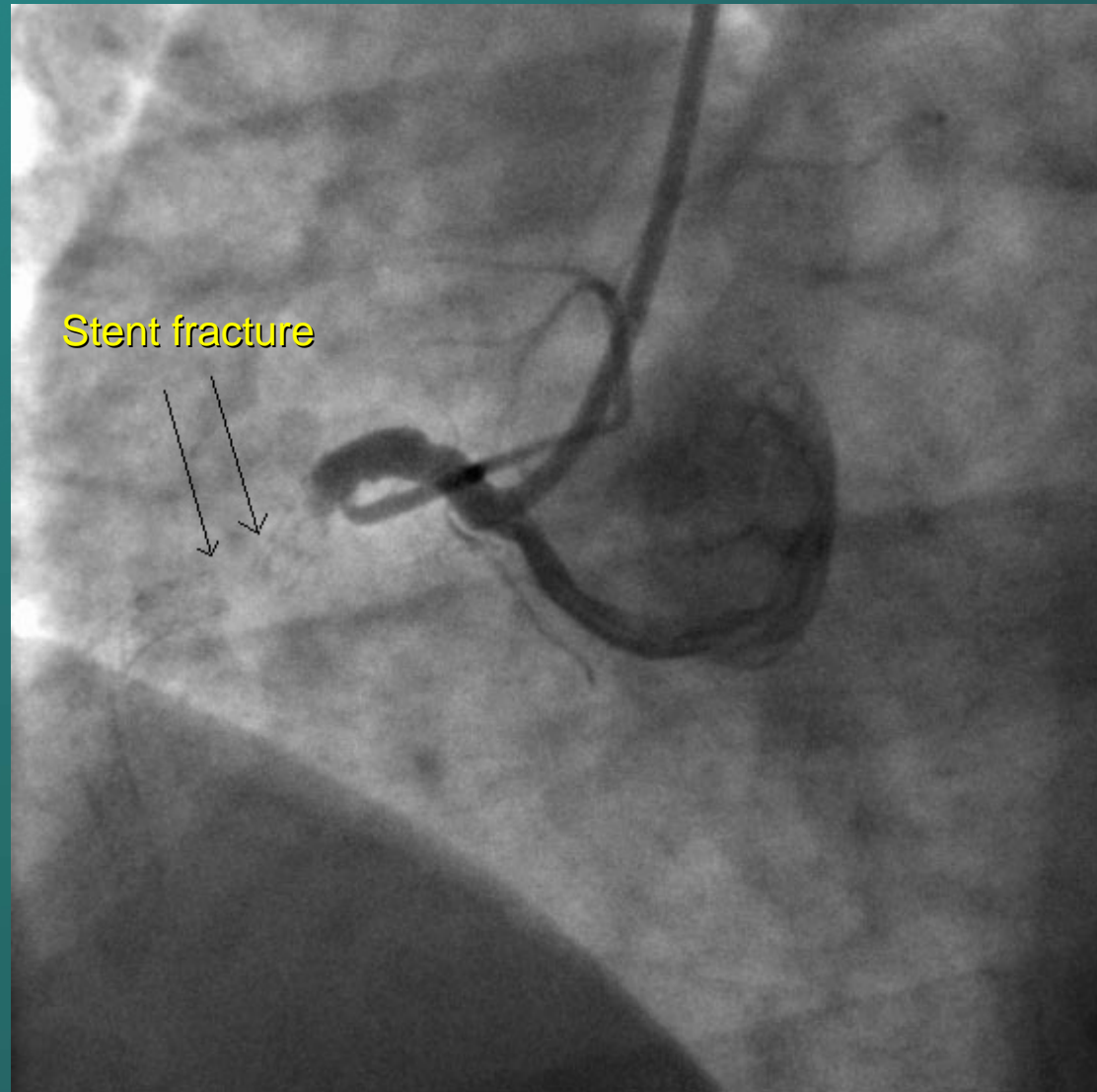
# Late incomplete apposition and Cypher® stent thrombosis



# Late incomplete apposition and Cypher® stent thrombosis



# Stent thrombosis 20 months after sirolimus-eluting stent implantation: **Strut fracture**



# When should TAXUS or CYPHER be used (rather than BMS)?

- “On-label” use
  - **Single *de novo* lesion in a native coronary artery in patients with stable CAD**
  - **Cypher: 2.5-3.5 mm RVD,  $\leq 30$  mm long**
  - **Taxus: 2.5-3.75 mm RVD,  $\leq 28$  mm long**
- “Off-label” use
  - **Everything else – multiple lesions and multiple vessels, bifurcation lesions, left main disease, thrombus and AMI, SVGs, CTOs, etc.**



# Analysis of All Patients RAVEL, SIRIUS, E-SIRIUS, C-SIRIUS

**All Patients**  
**(n=1,748)**  
**RVD 2.5 – 3.5 mm**  
**Length ≤30 mm**

**Control**  
**(n=870)**

Morice MC et al. NEJM 2002;346:1773-80  
Moses JW et al. NEJM 2003;349:1315-23

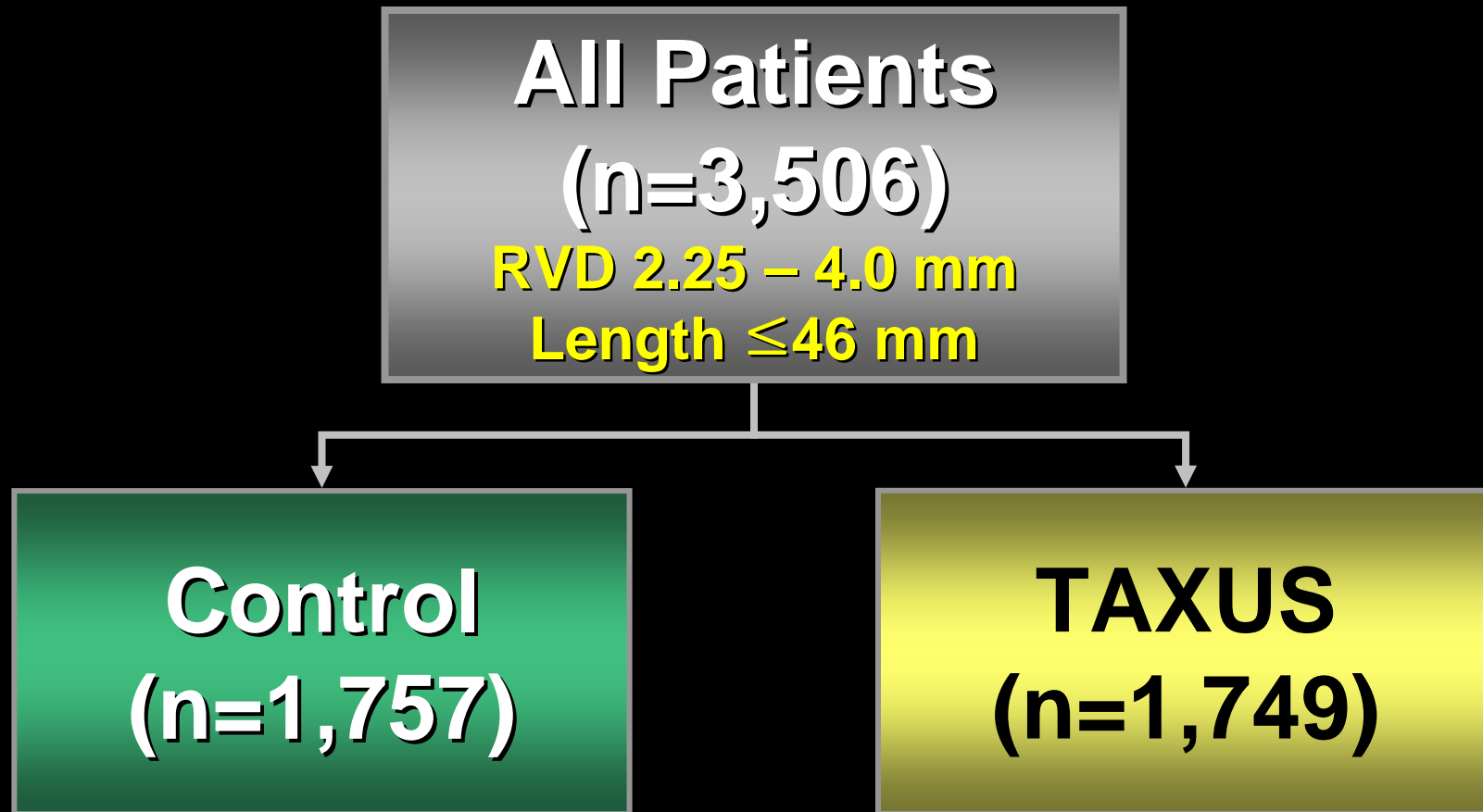
**CYPHER**  
**(n=878)**

Schofer J et al. Lancet 2003  
Schampaert E et al. JACC 2004;43:1110-5





# Analysis of All Patients TAXUS I, II, IV, V, VI

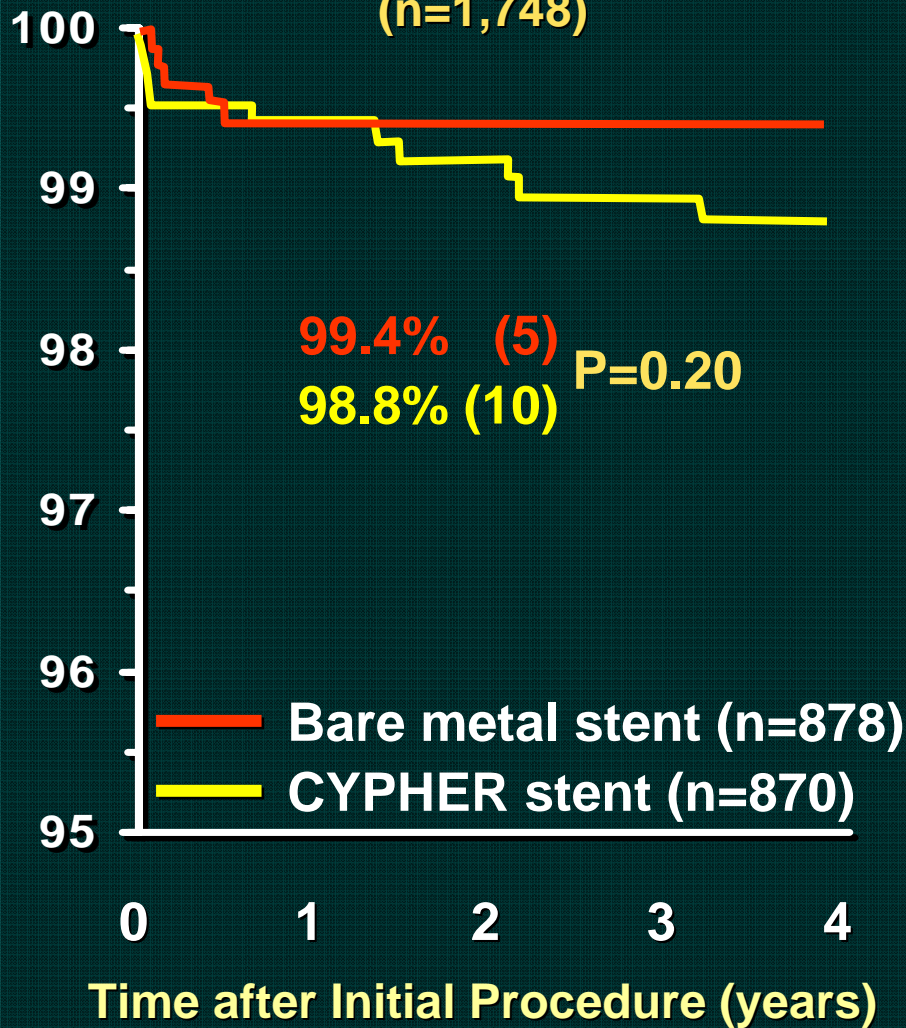


Grube E et al. Circulation 2003;107:38-42  
Colombo A et al. Circulation 2003;108:788-794  
Stone GW et al. NEJM 2004;350:221-31

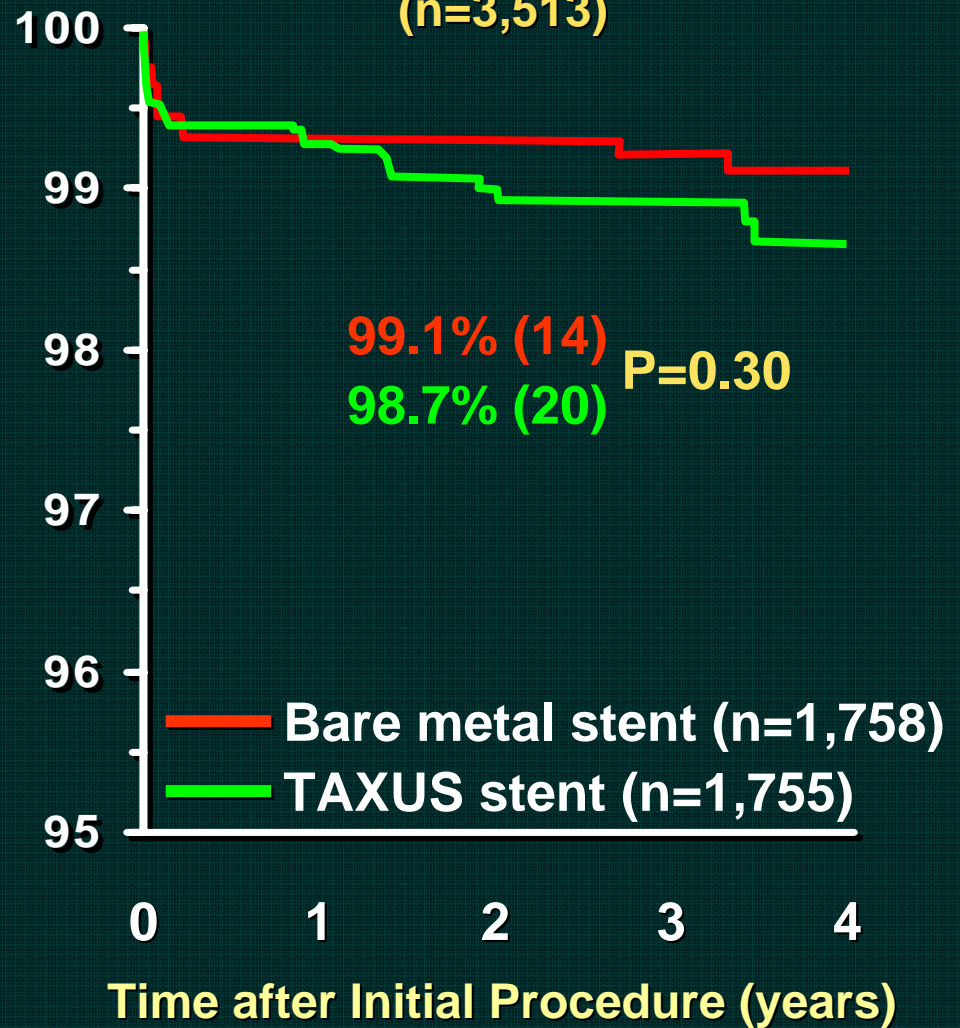
Stone GW et al. JAMA 2005;294:1215-23  
Dawkins KD et al. Circulation 2005;112:3306-3313

# 9 Prospective, Double-Blind, Randomized Trials Freedom From (Protocol) Stent Thrombosis

**RAVEL, SIRIUS, E-SIRIUS, and C-SIRIUS**  
(n=1,748)

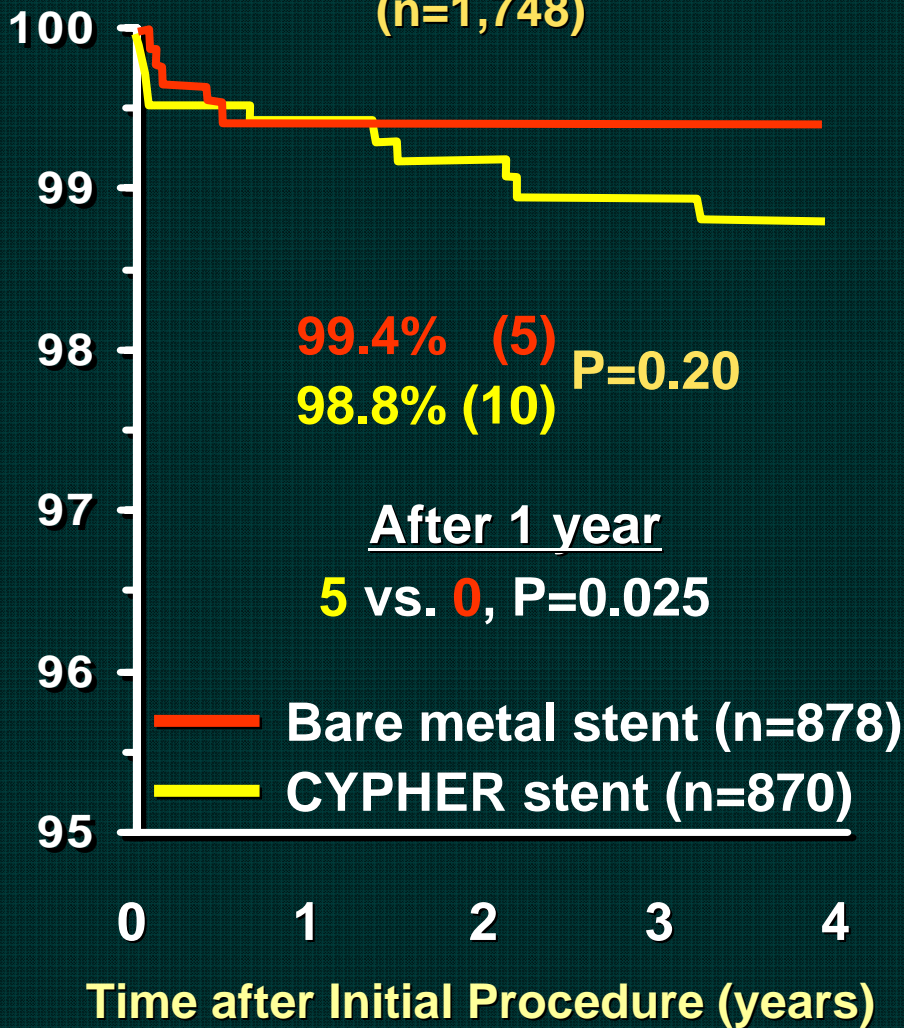


**TAXUS I, II, IV, V, VI**  
(n=3,513)

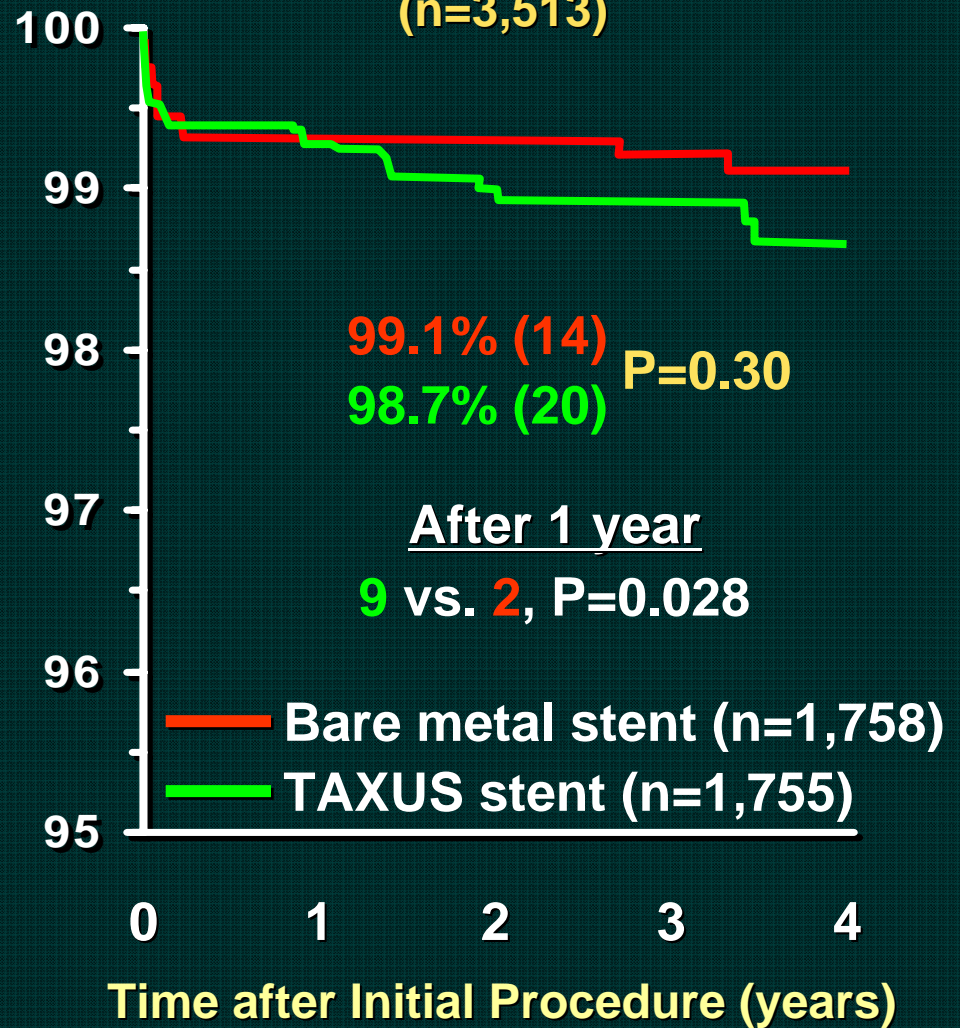


# 9 Prospective, Double-Blind, Randomized Trials Freedom From (Protocol) Stent Thrombosis

**RAVEL, SIRIUS, E-SIRIUS, and C-SIRIUS**  
(n=1,748)



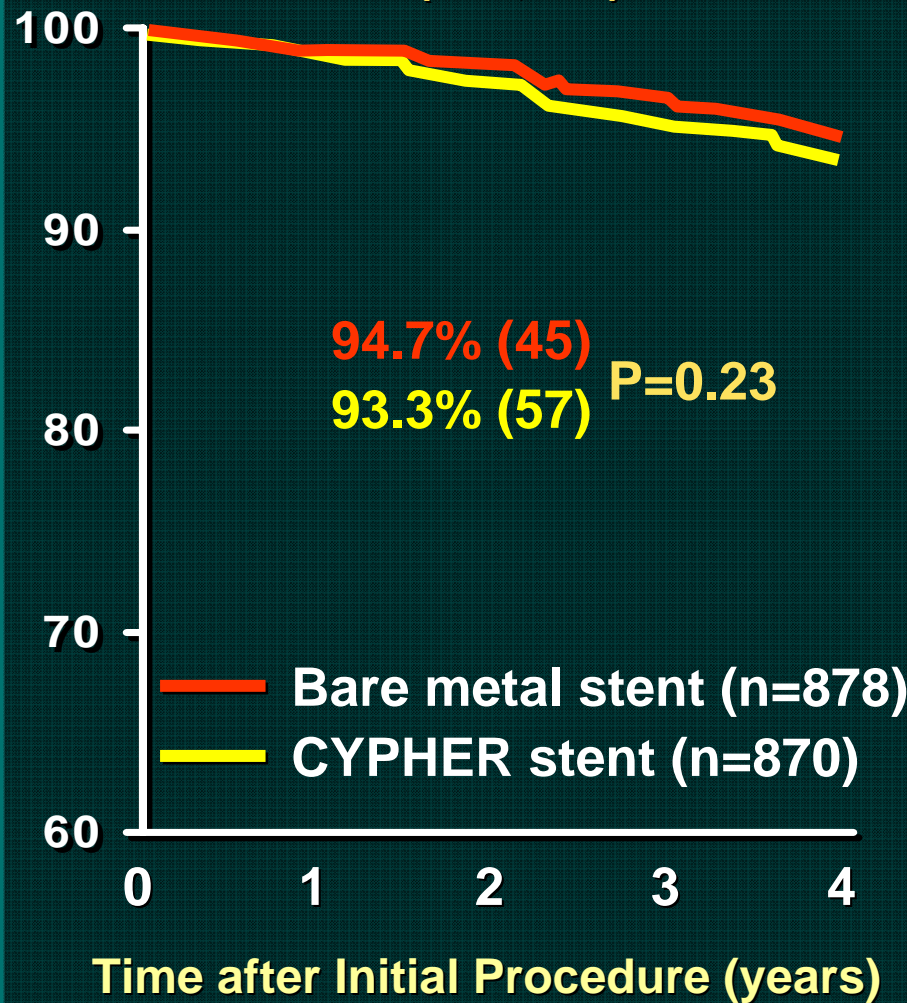
**TAXUS I, II, IV, V, VI**  
(n=3,513)



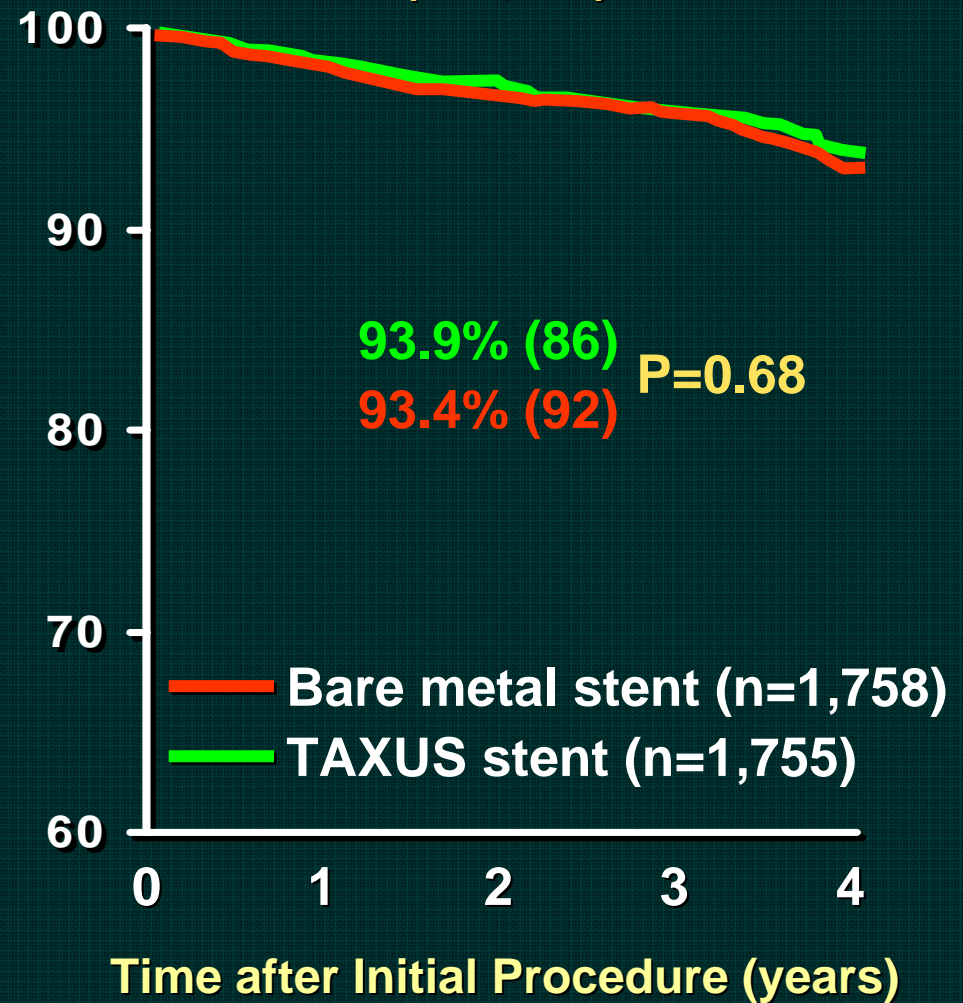


# 9 Prospective, Double-Blind, Randomized Trials Freedom From All Cause Death

**RAVEL, SIRIUS, E-SIRIUS, C-SIRIUS**  
(n=1,748)

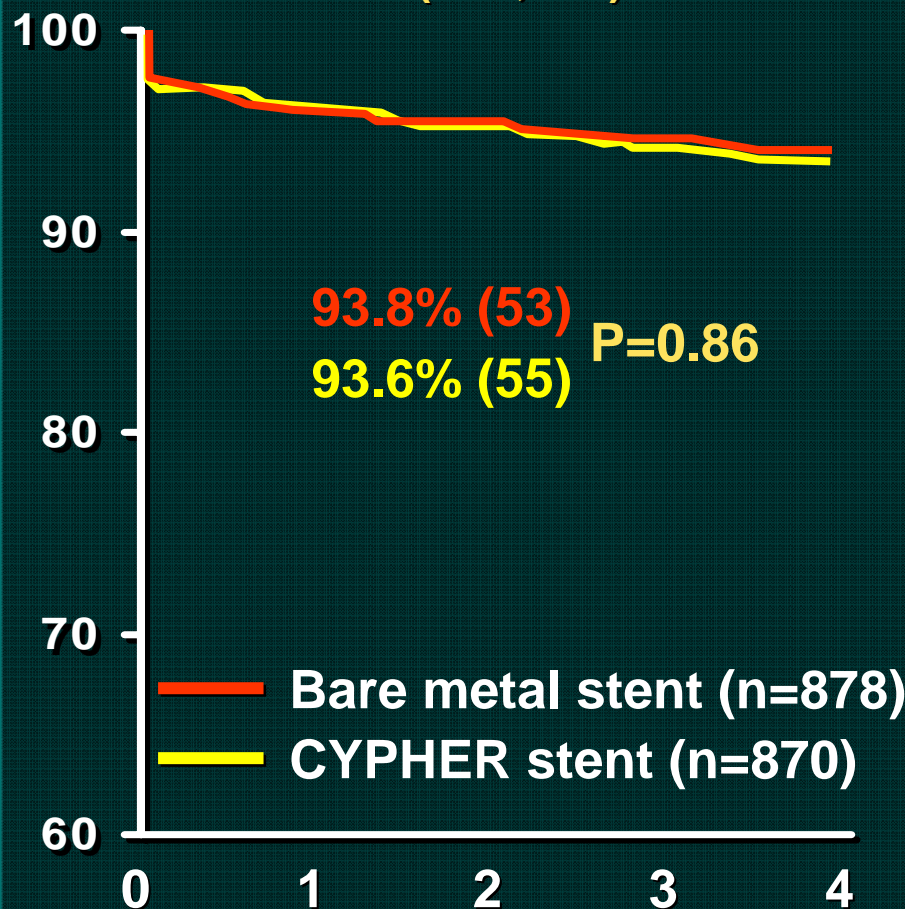


**TAXUS I, II, IV, V, VI**  
(n=3,513)



# 9 Prospective, Double-Blind, Randomized Trials Freedom From Myocardial Infarction

**RAVEL, SIRIUS, E-SIRIUS, C-SIRIUS**  
(n=1,748)

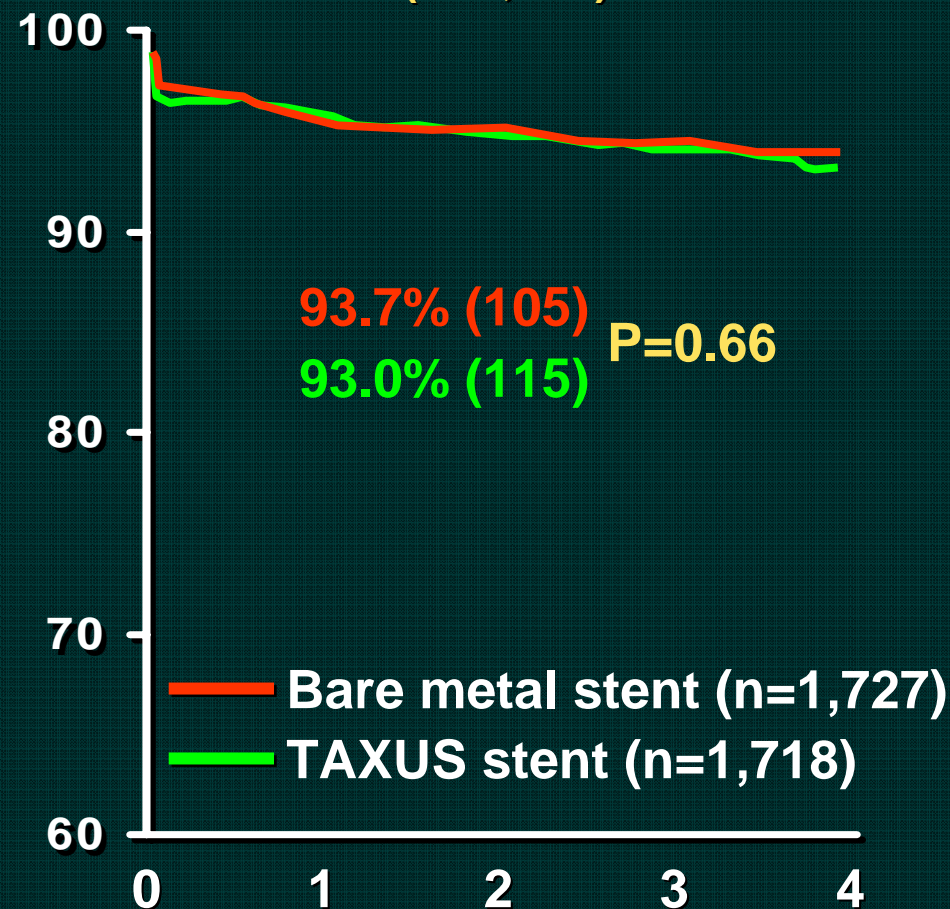


93.8% (53)  
93.6% (55) P=0.86

— Bare metal stent (n=878)  
— CYPHER stent (n=870)

Time after Initial Procedure (years)

**TAXUS I, II, IV, V, VI**  
(n=3,513)



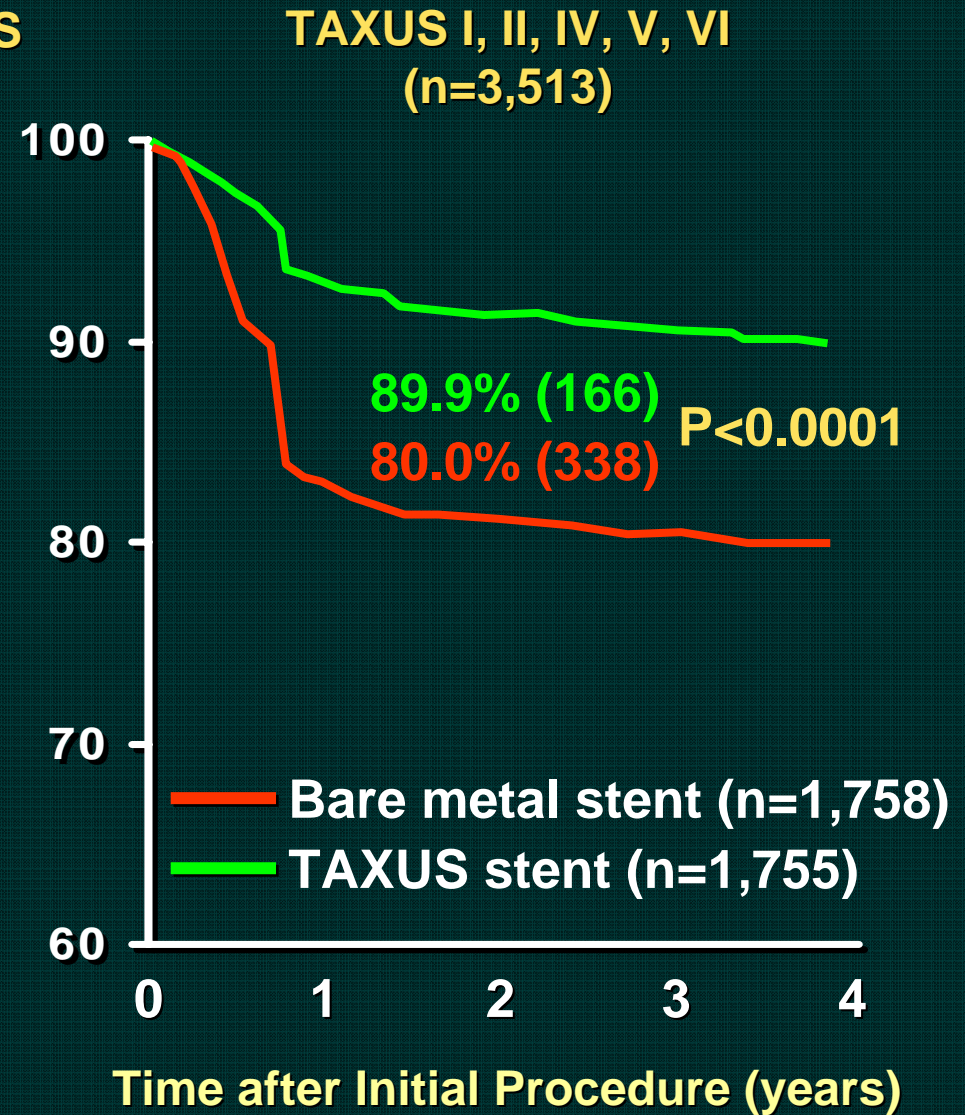
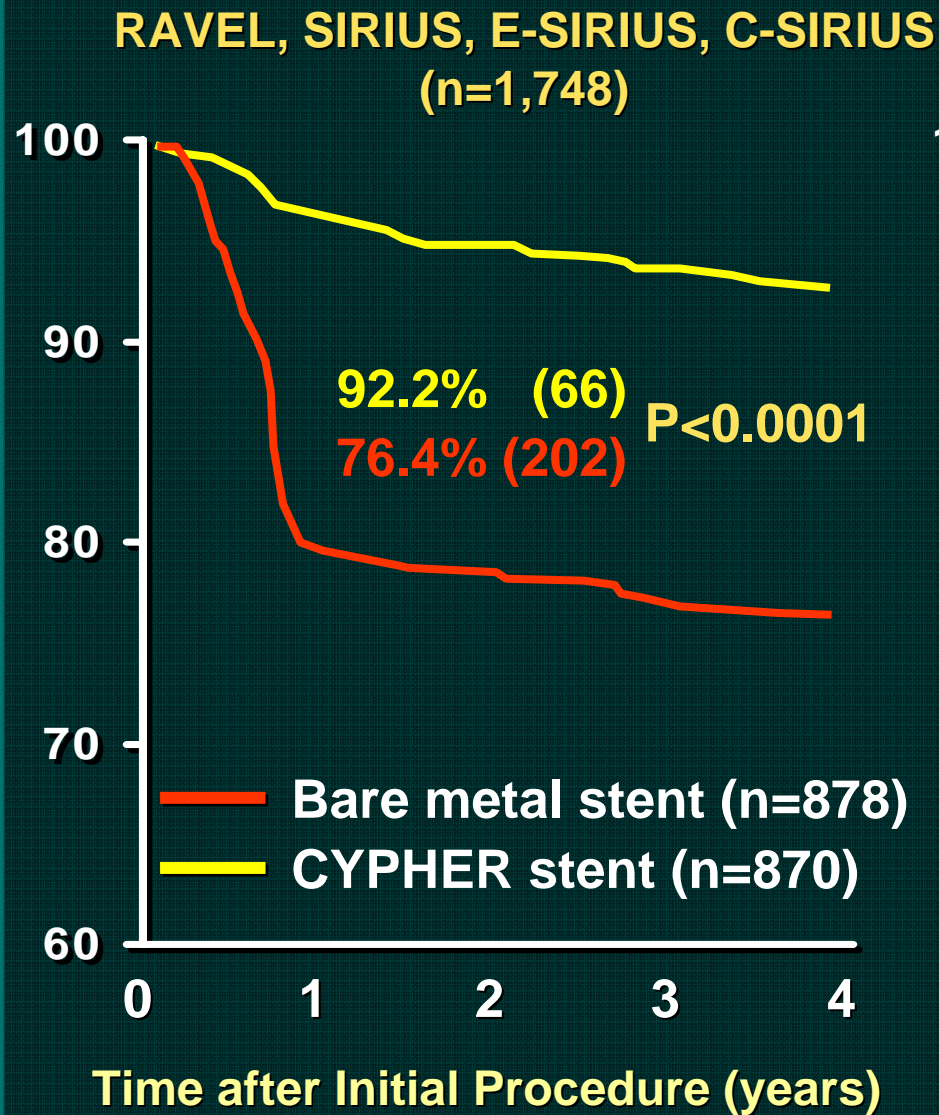
93.7% (105)  
93.0% (115) P=0.66

— Bare metal stent (n=1,727)  
— TAXUS stent (n=1,718)

Time after Initial Procedure (years)

# 9 Prospective, Double-Blind, Randomized Trials

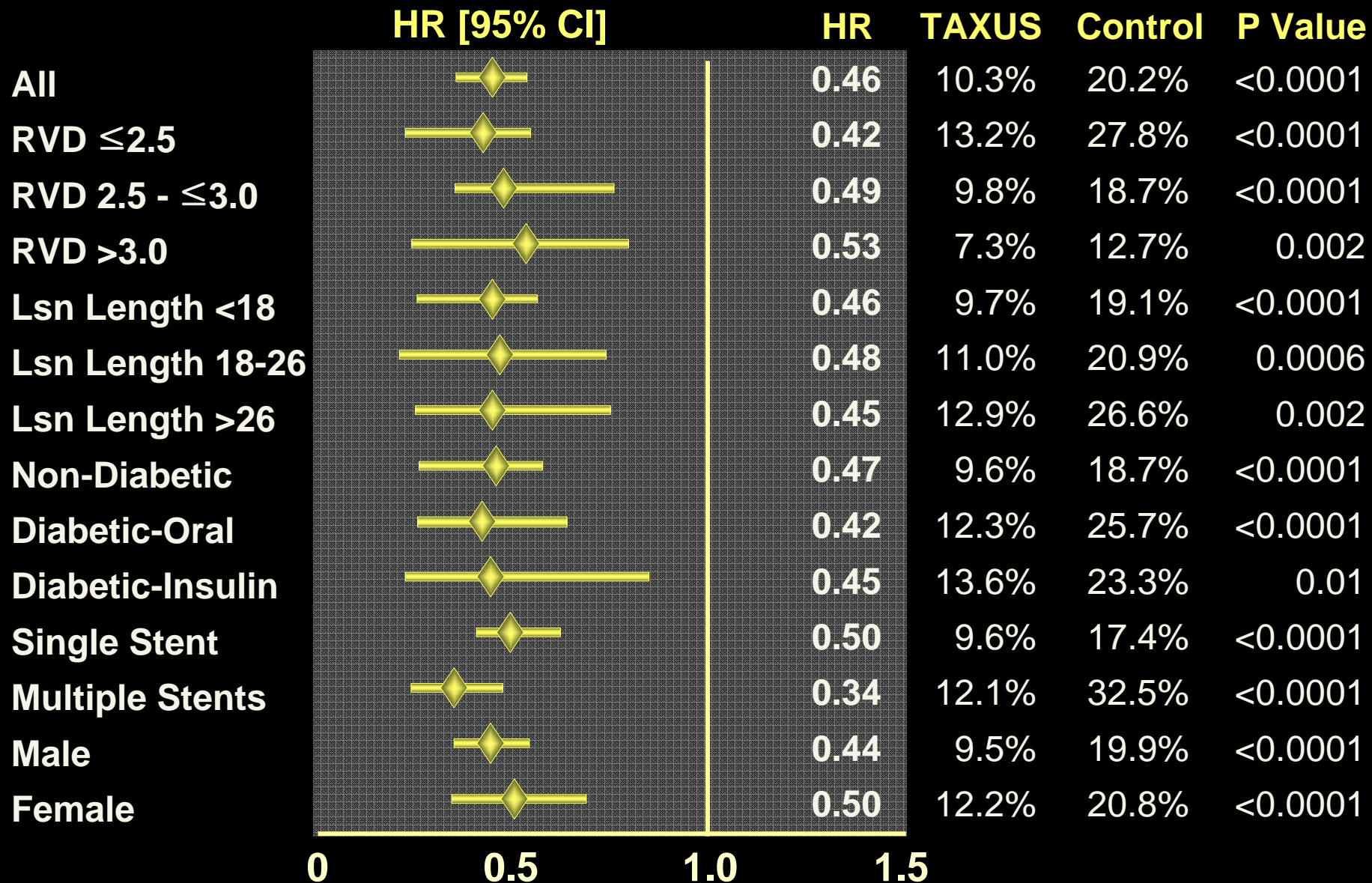
## Freedom From Ischemic TLR





# TLR up to 4 Years: Subgroup Summary

## TAXUS II, IV, V, VI Meta-analysis





# TAXUS II, IV, V, VI: Death and MI Within 7 Days of TLR and Stent Thrombosis

Total intent-to-treat population: 3445 patients

Control 1727

TAXUS 1718

Stent thrombosis  
14 pts

Ischemia-driven TLR  
290 pts

Ischemia-driven TLR  
135 pts

Stent thrombosis  
20 pts

12 patients with death or MI

11 patients with death or MI

4 patients with death or MI

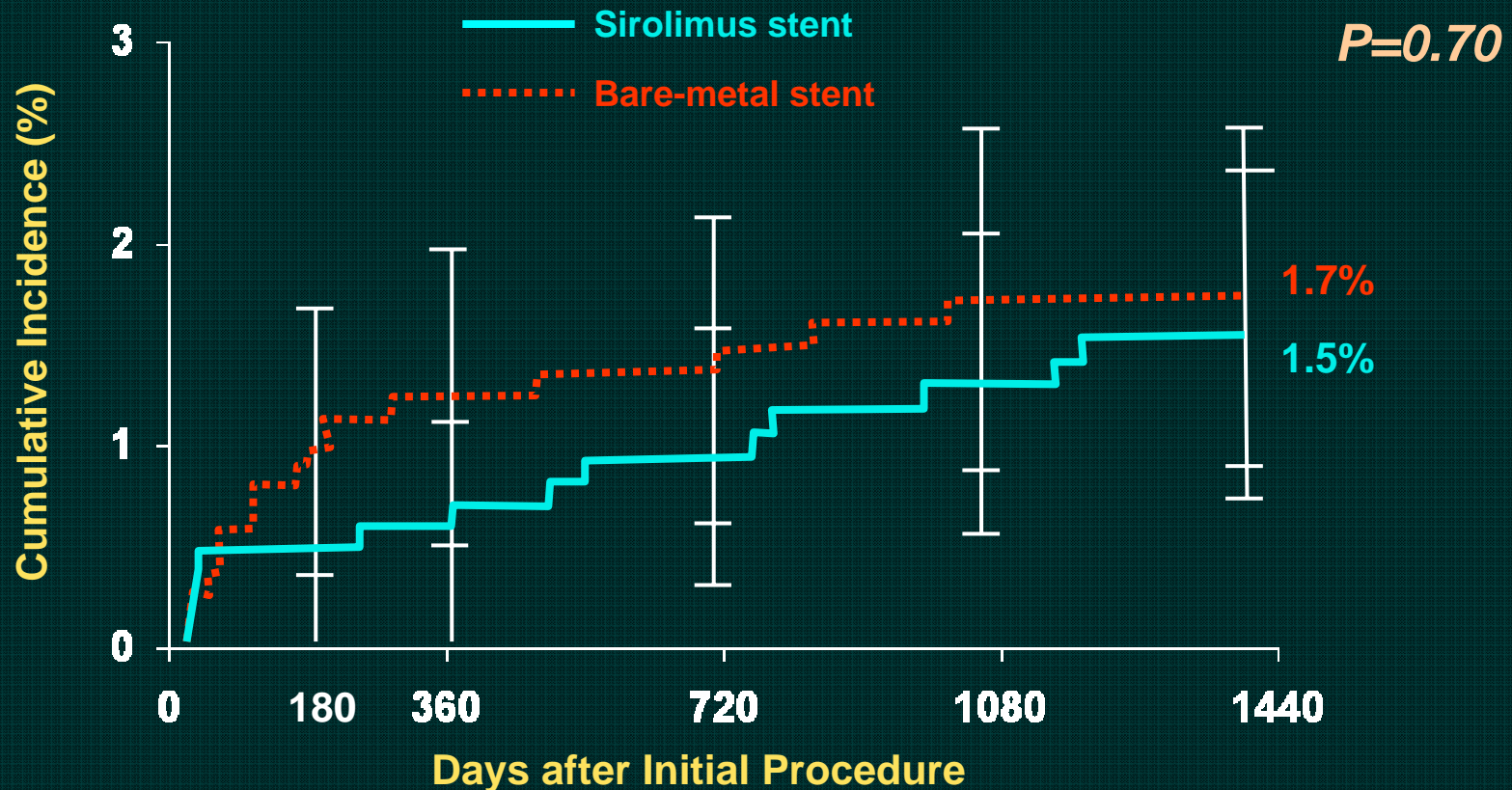
19 patients with death or MI

$\Sigma$ : 23 Pts with Death or MI  
(4 Deaths + 21 MIs)

$\Sigma$ : 23 Pts with Death or MI  
(3 Deaths + 23 MIs)

# Cumulative Incidence of Stent Thrombosis at 4 Years

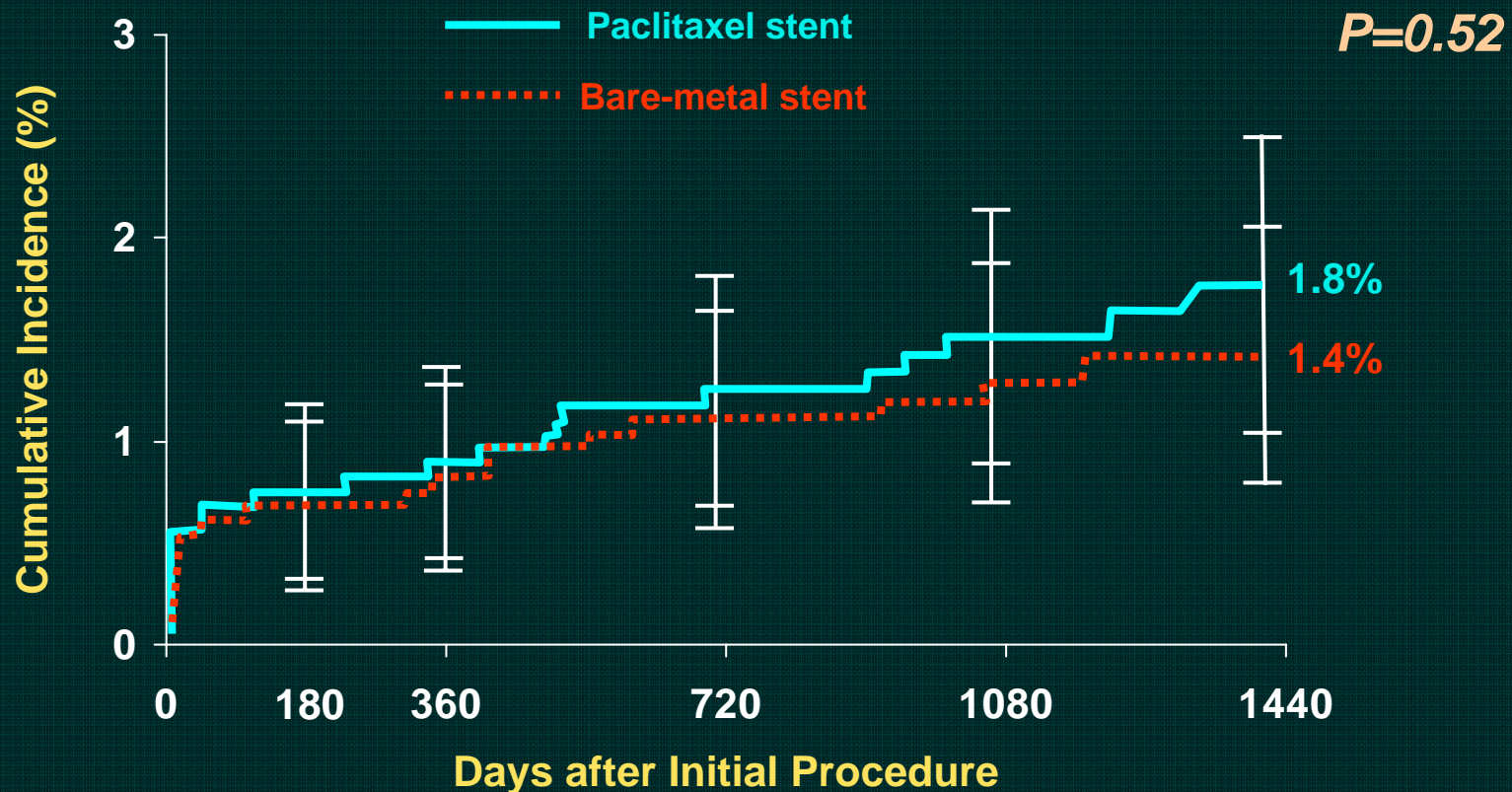
## Cypher (ARC Definite or Probable, 1° + 2°)



No. at Risk					
Sirolimus stent	878	863	848	823	788
BMS	870	853	842	825	789

# Cumulative Incidence of Stent Thrombosis at 4 Years

**TAXUS (ARC Definite or Probable, 1° + 2°)**



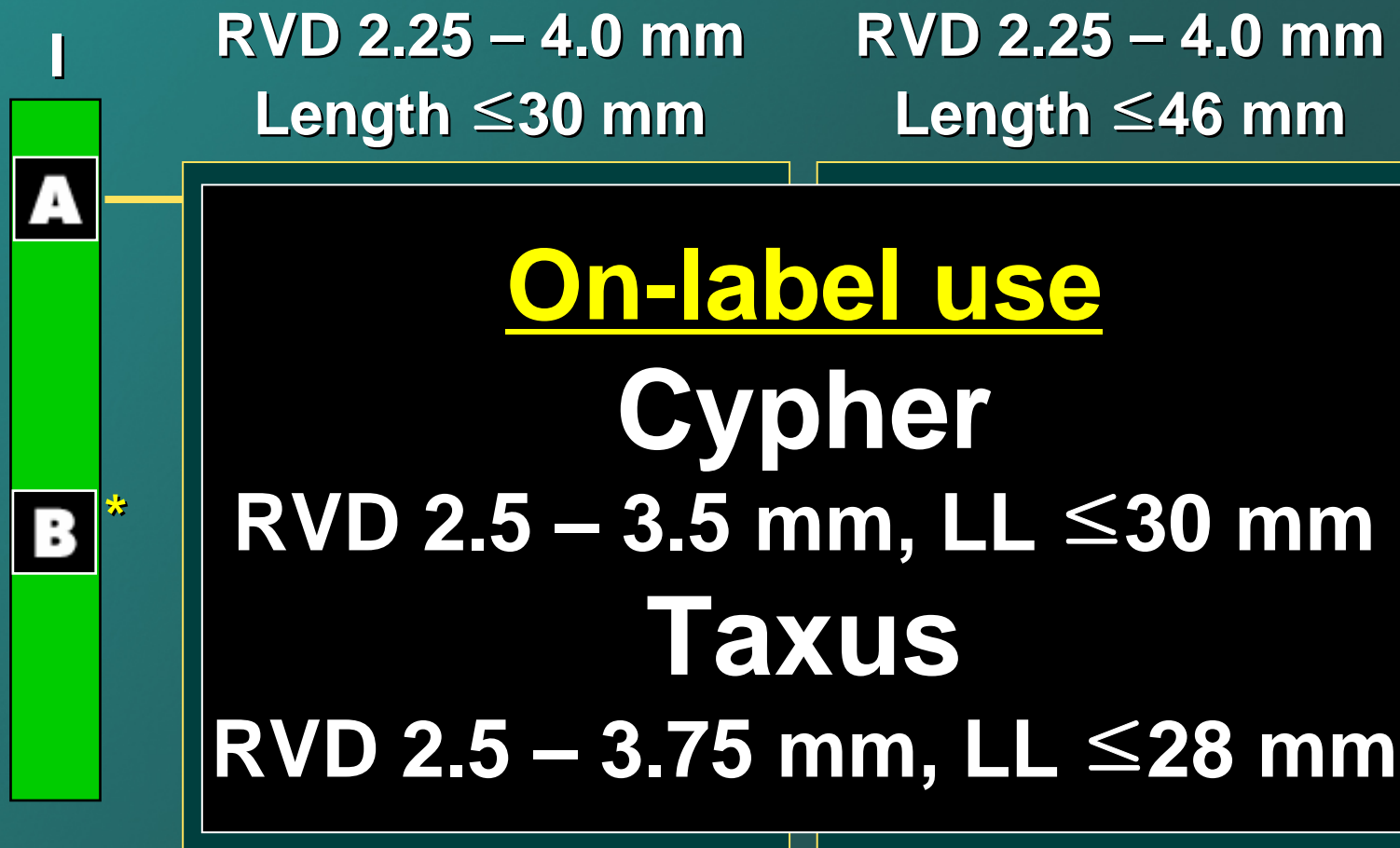
No. at Risk

Paclitaxel stent	1400	1351	1300	1117	715
BMS	1397	1353	1302	1123	743



# CRF DES Evidence-based Medicine Guidelines Summary 2007

## De Novo Lesions



\*2.25 & 4.0 mm randomized subgroups of TAXUS-V; SIRIUS registries



# DES: Off-label use

- **More complex and unapproved indications**
  - **Very small vessels and very long lesions**
  - **Chronic total occlusions**
  - **Bifurcations**
  - **Left main disease**
  - **In-stent restenosis**
  - **Multivessel disease**
  - **Saphenous vein grafts**
  - **Acute myocardial infarction**

# DES: Off-label use

- **More complex and unapproved indications**

➤ **Part II of my talk!**

