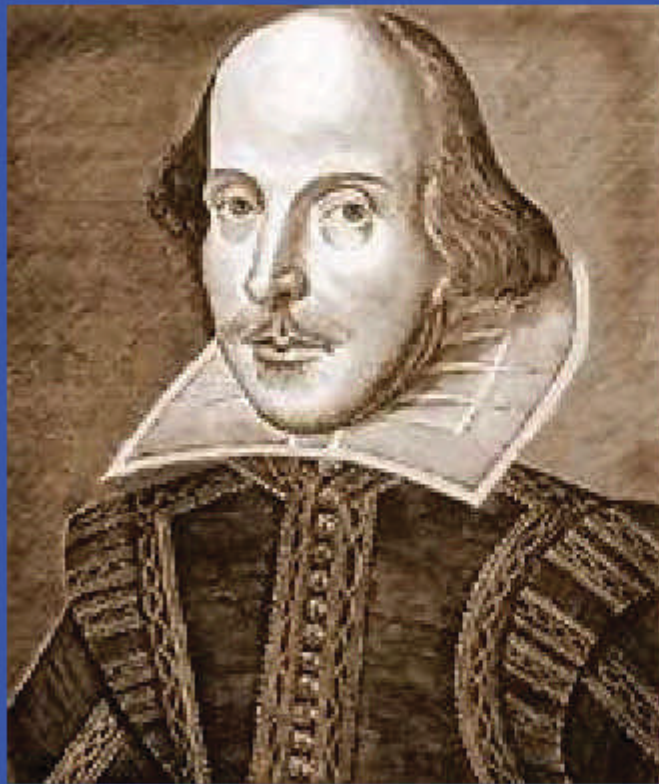


**All patients should receive
a drug eluting stent**

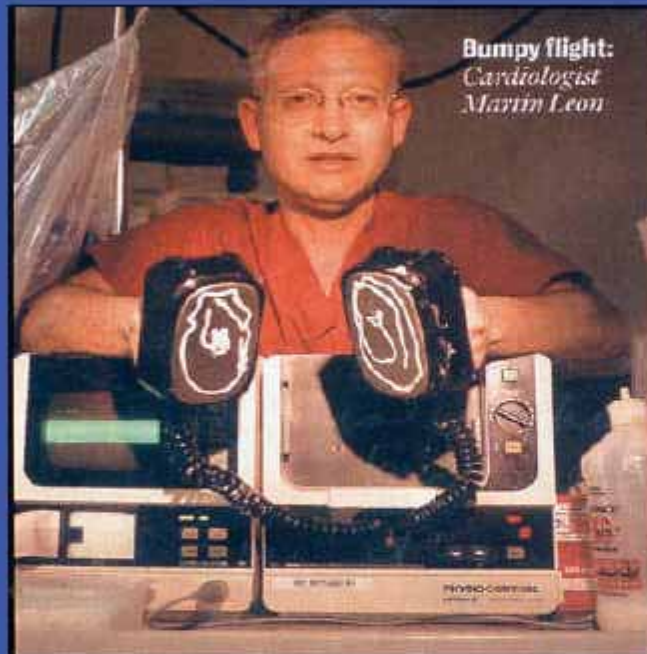
Leon

What do Shakespeare and Leon have in common?



Much Ado About Nothing

Much Ado About Nothing



Bumpy flight:
*Cardiologist
Martin Leon*

HEALTH
Midair Attacks
What airlines do when passengers
need help with medical emergencies



97 pages
966 items

**All patients should receive
a drug eluting stent**

Leon

ICBYST

What does a Class 3 Indication mean?

- It means that you should at least try to restrain yourself
- SVBG disease
- In-stent restenosis, diffuse
- Unprotected left main lesions
- Brought to you by O'Neill and LEON
June 24, 2003



100% Patients/Lesions

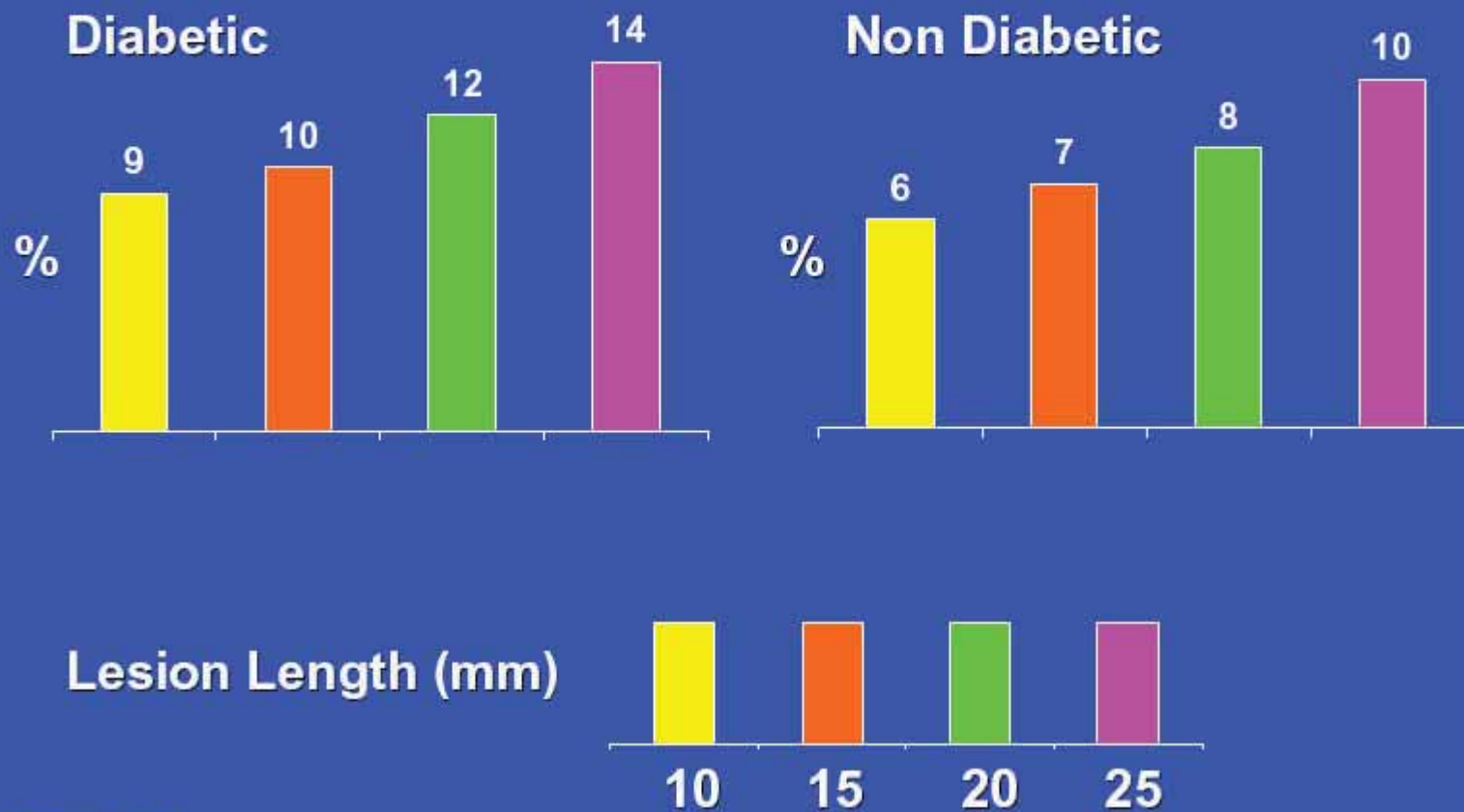


It ain't 100%

- Vessels > 4.0 mm
- Vessels ≤ 2.3 mm
- In-stent restenosis
- Vein graft disease
- Bifurcation disease
- Stenotic aneurysmal disease
- ? Thrombotic lesions
- Can't deliver the stent
- Patients/countries on limited budgets
- 3 or 4 separate vessels to be treated

Predicted Angiographic Restenosis Rates

4.0 mm In-stent MLD



Cypher Stents Available

2.5 x 23 RX = 2

2.5 x 28 RX = 2

3.0 x 23 RX = 1

3.0 x 33 RX = 2

3.5 x 18 RX = 3

3.5 x 23 RX = 3

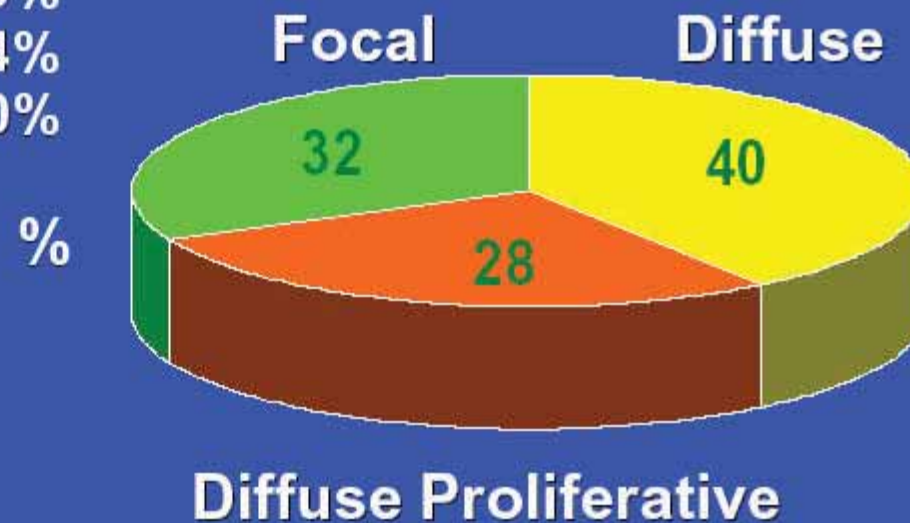
3.5 x 18 OTW = 6



SIROLIMUS for In-Stent Restenosis

- Single Center
14 co-authors, 25 patients
- Treatment with Cypher Stent

Mean Age	56 yrs
Male	80%
DM	24%
ReISR	20%



Sousa Circ 107:24-27, 2003

Sirolimus for In-Stent Restenosis

QCA

	Pre		12 Month
RD	2.78	RD	2.8
MLD	1.05	MLD	
DS	62	IS	2.35
		IL	2.18
LL	13.6	LL	
		IS	.36
Recurrent IS Restenosis 4%		LL	.16

Sousa Circ 107:24-27, 2003

Sirolimus-Eluting Bx-Velocity Stent for ISR

- N = 41 patients with ISR
- Vessel size: 2.5–3.5mm
- Open-label safety study
- 1 or 2 18mm Cypher™ stent
- All patients received
 - Aspirin (325 mg)
 - Clopidogrel (75 mg, 60 days)

1-year Clinical Events

	Brazil N=25	Rotterdam N=16	Pooled N=41
Death	0 (0%)	2 (12.5%)	2 (4.9%)
MI	0 (0%)	1 (6.3%)	1 (2.4%)
TLR	0 (0%)	2 (12.5%)	2 (4.9%)
Restenosis	1 (4%)	2 (12.5%)	3 (7.3%)

What does Edward Scissorhands have to do with Interventional Cardiology?





SISR

400 Patients with In-Stent Restenosis

Cypher Stent

Vascular Brachytherapy

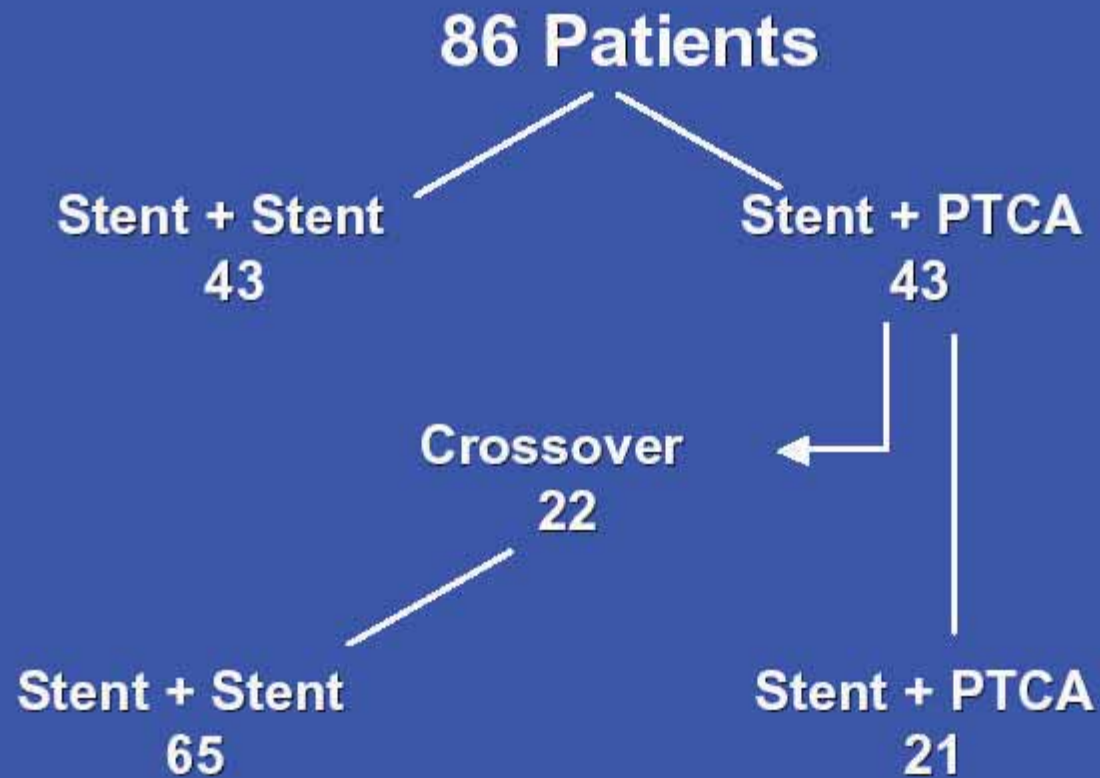
2:1 Ratio

1° Endpoint: Target vessel failure at 9 months

2° Endpoint: Binary restenosis, TLR, TVR



A Fork in the Road



Colombo 2002

A Fork in the Road In Hospital MACE

	Stent/Stent 65	Stent/PTCA 21
N %		
Death	0	0
Non QMI	6 (9.2%)	2 (9.5%)
QMI	1 (1.5%)	1 (4.7%)
CABG	0	0
Re-PTCA TLR	1 (1.5%)	1 (4.7%)
Total	8 (12.2%)	3 (14.3%)

Colombo 2002

A Fork in the Road

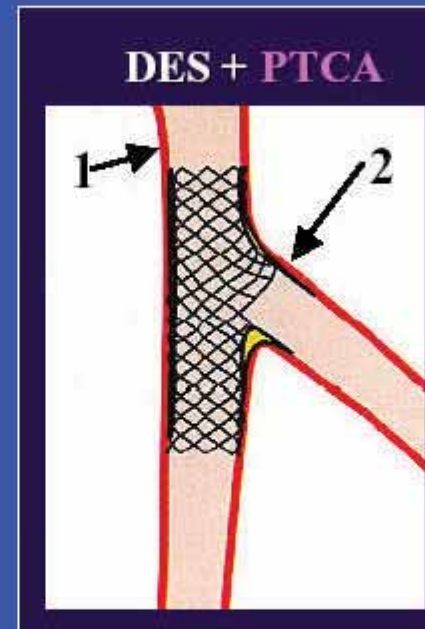
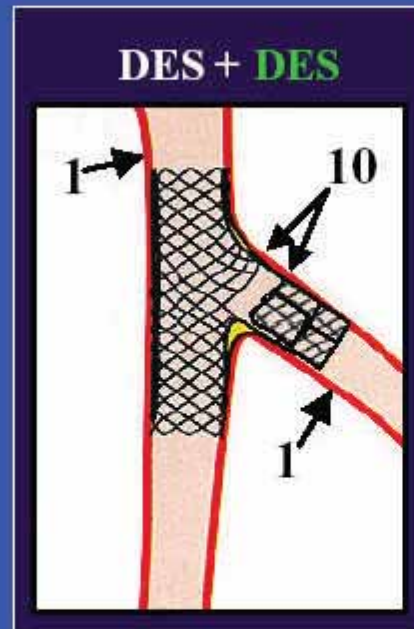
6 month MACE

	Stent/Stent 65	Stent/PTCA 21
N (%)		
Death	1 (1.5%)	0
Non QMI	7 (10.7%)	2 (9.5%)
QMI	2 (3.1%)	0
CABG	1 (1.5%)	0
TLR	9 (13.8%)	2 (9.5%)
TVR	4 (6.2%)	0
Total	24 (36.7%)	4 (19.0%)

RR 24%

Colombo 2002

Location of Restenosis

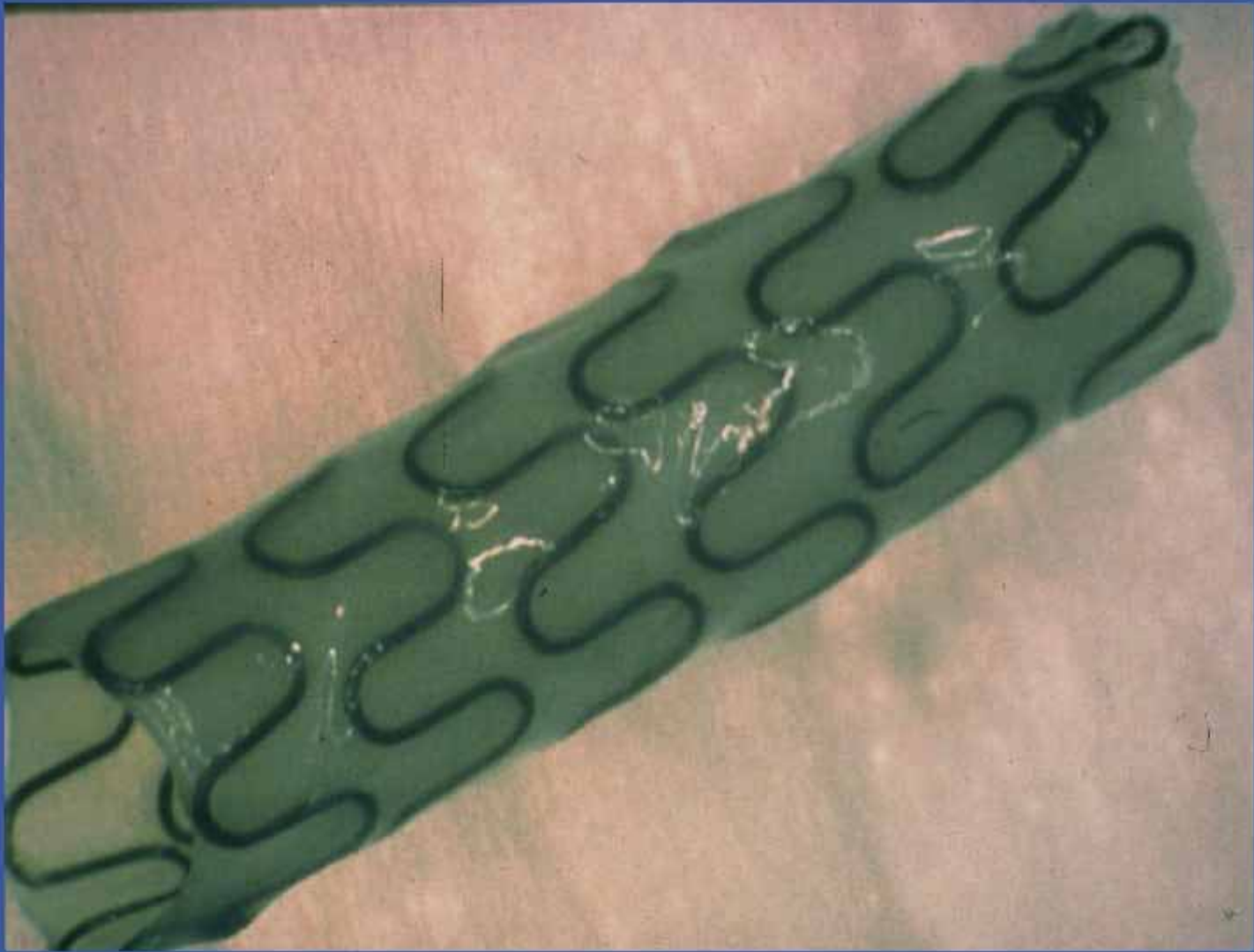


- 0% in-stent restenosis in the main
- 15.9% in-stent restenosis in the side branch
- 12 of 13 restenoses occurred in ostium of side branch



What does a Class 3 Indication mean?

- It means that you should at least try to restrain yourself
- SVBG disease
- In-stent restenosis, diffuse
- Unprotected left main lesions
- Brought to you by O'Neill and LEON
June 24, 2003



SYMBIOT II

Clinical Trial MACE to 30 Days

	Symbiot™ (%)	Wallstent ™ (%)	p-value
MACE	5.2	13.5	<0.0001
Death	0	1.7	
MI			
Q-wave	0	2.8	
Non Q-wave	3.9	8.3	
CABG	0	n/a	
TVR	2.6	3.1	

CAUTION: Investigational device. Limited by federal law to investigational use. Not available for sale in U.S.

SYMBIOT II

Clinical Trial MACE to 210 Days

	Symbiot™ (%)
MACE	14
Death	2.6*
MI	
Q-wave	0
Non Q-wave	5.3
CABG	0
TVR	9.2

CAUTION: Investigational device. Limited by federal law to investigational use.
Not available for sale in U.S.

SECURE Registry

N = 19

Age	65.22 +/- 11.79 (19)
CCS Class: III/IV	84.2% (16/19)
Smoker	78.9% (15/19)
Diabetes	26.3% (5/19)
History of CVA	0.0% (0/19)
Single Vessel Disease	100.0% (19/19)

SECURE Registry

N = 19

Events	30-Day F/U	6-Month F/U	8-Month F/U
TLR	0.0% (0/19)	25.0% (2/8)	100.0% (2/2)
PTCA	0.0% (0/19)	12.5% (1/8)	50.0% (1/2)
CABG	0.0% (0/19)	12.5% (1/8)	50.0% (1/2)
TVR	0.0% (0/19)	25.0% (2/8)	100.0% (2/2)
PTCA	0.0% (0/19)	12.5% (1/8)	50.0% (1/2)
CABG	0.0% (0/19)	12.5% (1/8)	50.0% (1/2)
Total Occlusion	0.0% (0/19)	12.5% (1/8)	50.0% (1/2)

No death or MI up to 8 months

Much ado about nothing

- Much ado about nothing, maybe means it is something.

June 19, 2003

David Holmes, MD
Mayo Clinic
St. Mary's Hospital
Division of Cardiology
1216 Second Street, SW
Rochester, MN 55902

Dear Dr. Holmes:

We are aware of a discussion circulating since the release of the CYPHER™ Stent in the U.S. that there is a subacute thrombosis problem with the CYPHER Stent.

Cordis

a Johnson & Johnson company

7 Powder Horn Drive
Warren, NJ 07059
Phone (908) 755-8300

Mailing Address:
P.O. Box 4817
Warren, NJ 07059

Cordis Corporation Issues a Health Care Professional Letter Regarding the CYPHER Stent



U.S. Food and Drug Administration



[FDA Home Page](#) | [Search FDA Site](#) | [A-Z Index](#) | [Contact FDA](#)

FDA News

FOR IMMEDIATE RELEASE

P03-50

July 8, 2003

Media Inquiries: 301-827-8242

Consumer Inquiries: 888-INFO-FDA

Cordis Corporation Issues a Health Care Professional Letter Regarding the CYPHER Stent

Cordis Corporation (Cordis) has issued the attached [letter](#) to health care professionals to inform them of the rare but potential risk of thrombosis associated with the use of its product the CYPHER Sirolimus-Eluting Coronary Stent (CYPHER stent). This letter also provides clarification on the safe use of the product in accordance with the scientific evidence that led to product approval.

- **Selection of the appropriate stent size.** The stent size should match the diameter of the vessel as closely as possible.
- **Selection of appropriate patients for implantation.** The stent is indicated for improving coronary luminal diameter in previously untreated vessels and is not indicated for the treatment of restenosis (reoclogging of a previously stented vessel).
- **Use of an adequate antiplatelet regimen.** Doctors are reminded to give adequate doses of medication that reduce the risk of clot formation.
- **Use of the proper technique for stent deployment.** The stent should be fully deployed and in contact with the vessel wall. Poor stent deployment is a factor that can increase the thrombosis risk.

Intra Procedural Stent Thrombosis

- Registry report
- Patients undergoing elective stent placement
- 1036 patients
64% Bare stents
36% DES
- Acute stent thrombosis seen in 4 patients
- All 4 patients had received DES
- No acute stent thrombosis with Bare stent

European Data

What's Wrong With This Picture?

Cordis
a Johnson & Johnson company

101 10250-1

CYPHER™ Sirolimus-eluting Coronary Stent

**For Instructions for Use
please visit**

WWW.CYPHERUSA.COM

or

call 1-800-781-0282

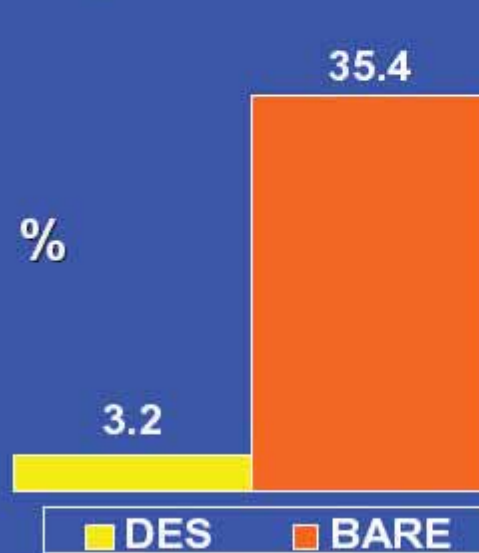
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SIRIUS Trial

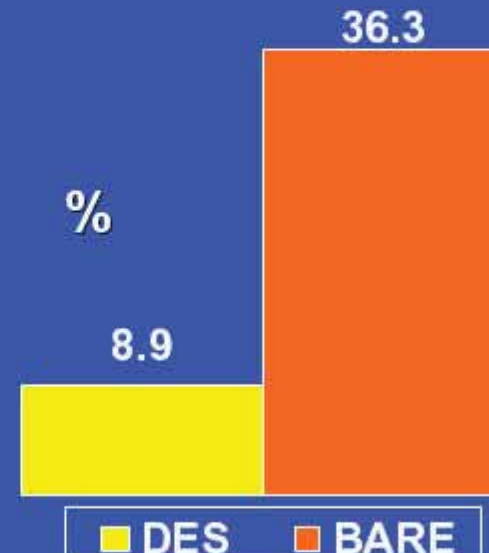
What we did

- 1.4 stents per target site
- Stent length 21.4 mm

What did we find



In-stent restenosis



In segment restenosis

Sirolimus Eluting Stents

Why is there any restenosis?

- Inadequate drug concentration
- Device damage at implant
- Device manufacture irregularities
- Are there other mechanisms of restenosis?
- Edge effect - ? stimulatory

Multi Vessel Disease

How Will It Perform?

43 - year-old

LAD	80 ⇒ 0	33 mm stent
Distal circ	70 ⇒ 0	18 mm stent
OM 1	80 ⇒ 10	23 mm stent
RCA	90 ⇒ 0	33 mm stent

Multivessel Disease

Questions

Will in segment restenosis rates be additive?

1 segment	8.9%
2 segments	17.8%
3 segments	26.7%
4 segments	35.6%



Euro PCR

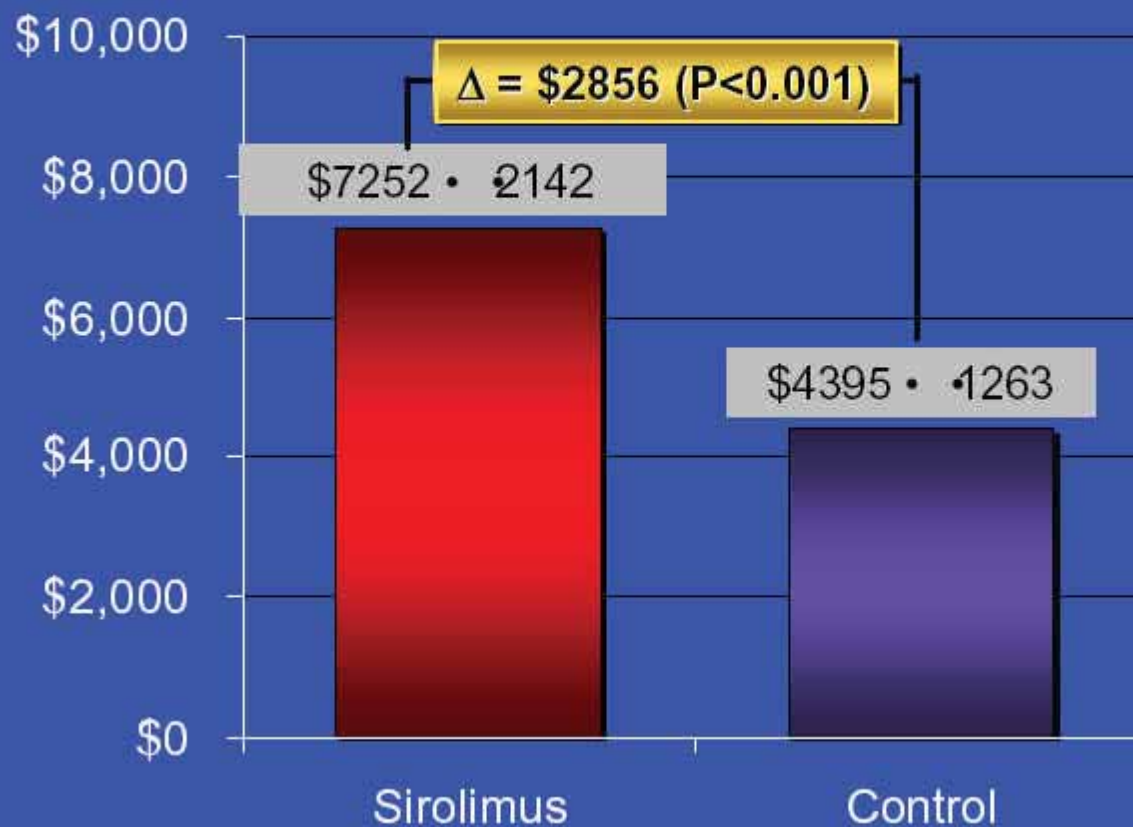
DES Market Penetration

- JJIS - 60%, BSC 40%
- Penetration only 12-13%

Industry Sources

Initial Procedural Costs

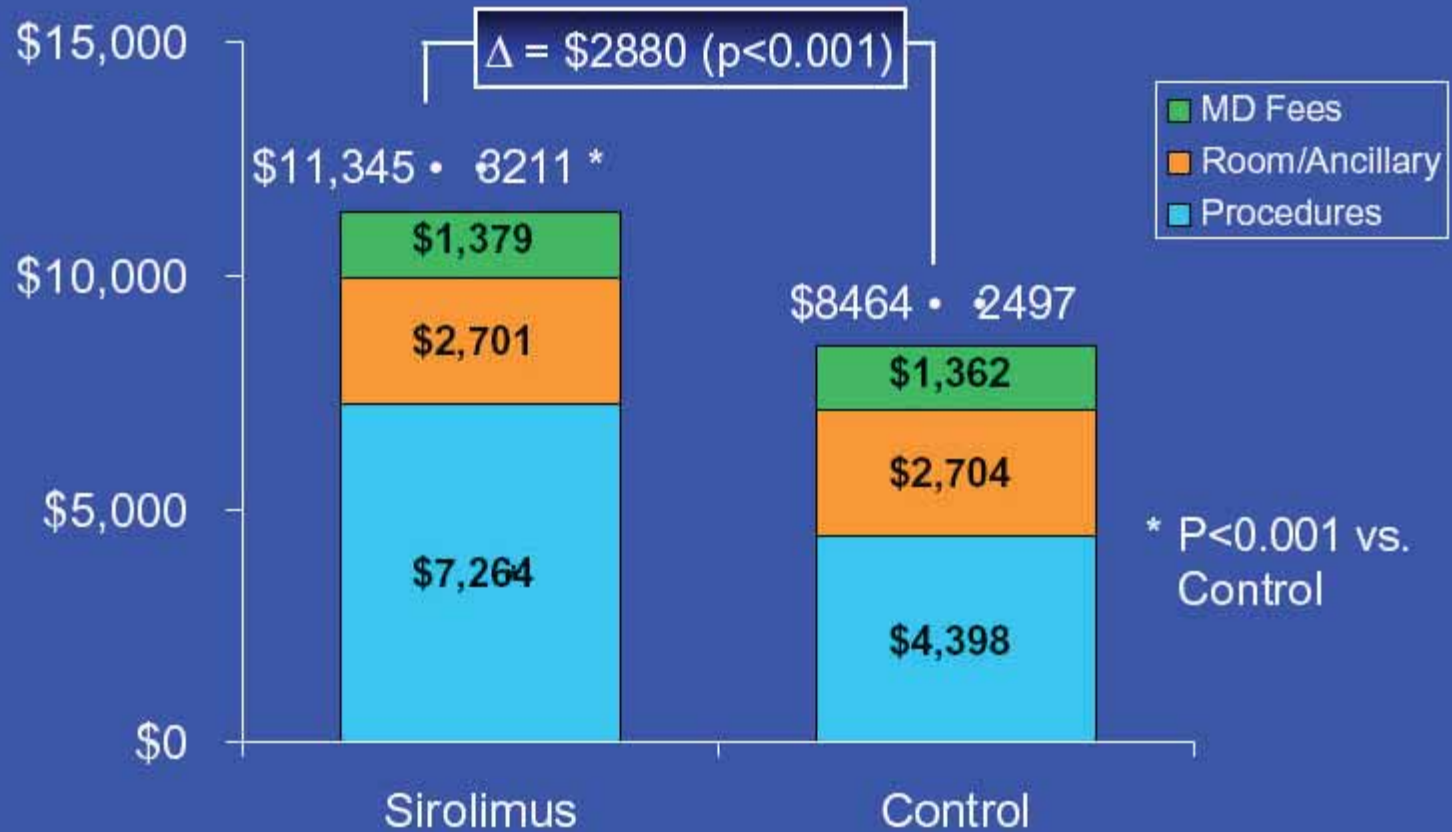
SIRIUS



Cohen, ACC 2003

Initial Hospital Costs

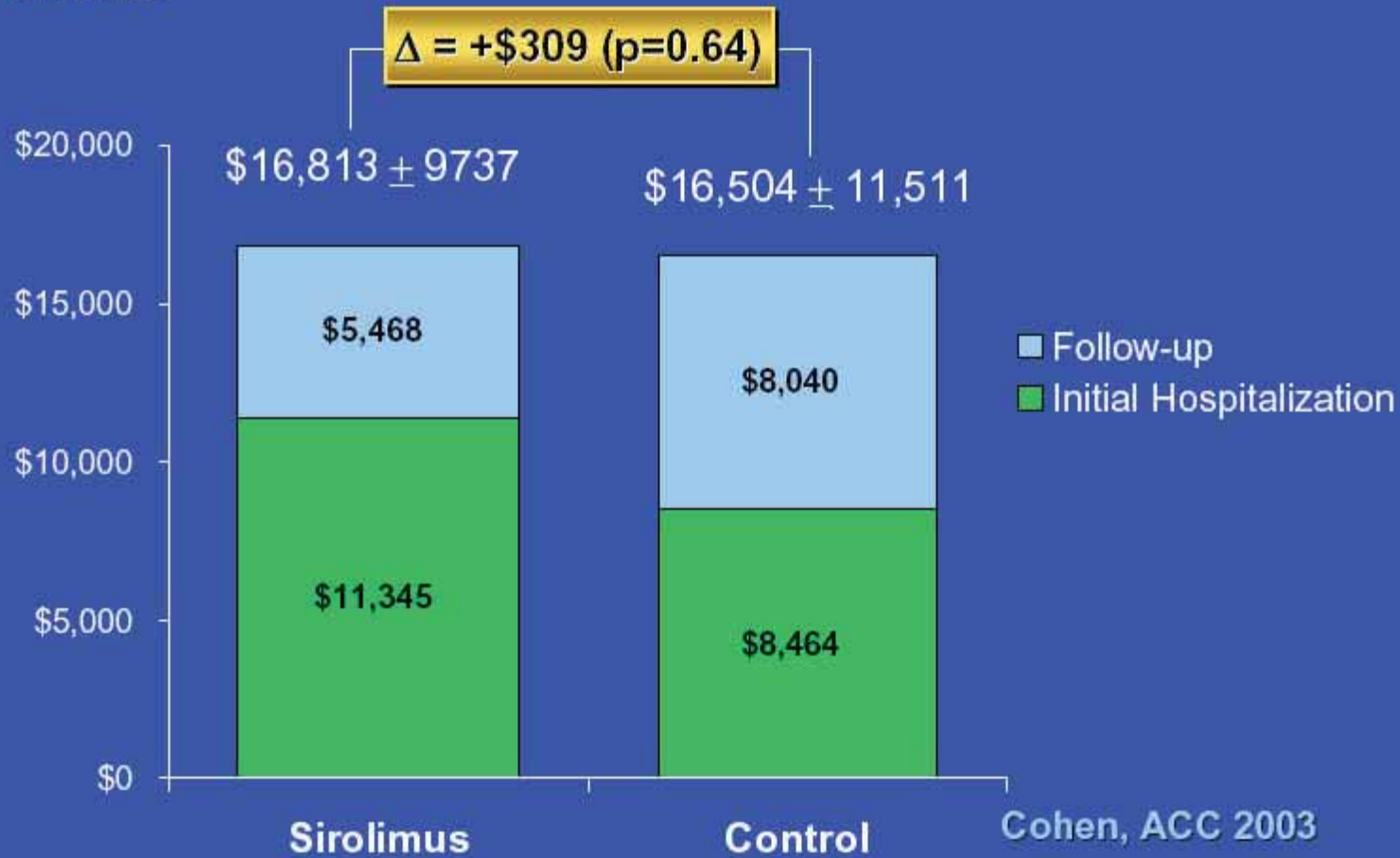
SIRIUS



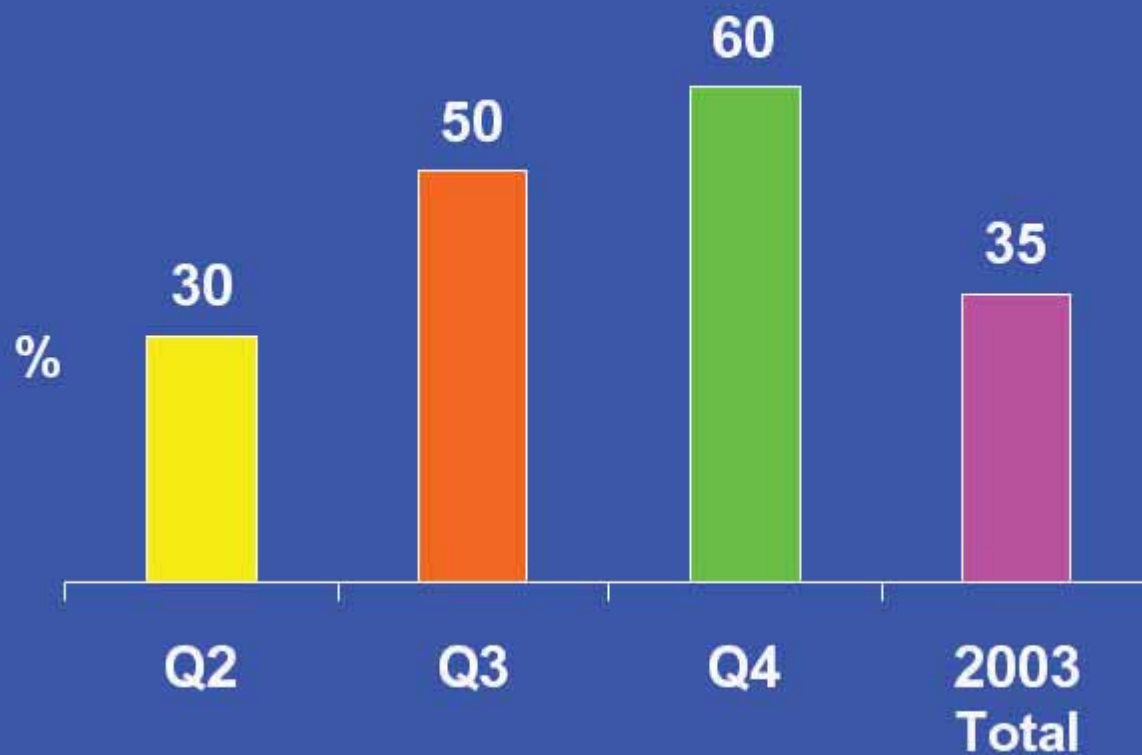
Cohen, ACC 2003

1-Year Medical Care Costs

SIRIUS



Penetration DES 2003



Drug Eluting Stents



Your Loved One Approach

Advantages

- You don't have to think
- Patient/family expectations
- Probably works
- Prevent not treat restenosis

Disadvantages

- ? Break the bank
- Longer stents
- Don't have to think

Evidence Based Approach

Advantages

- Evidence based
- More cost efficient

Disadvantages

- Hard to predict
- Have to think
- Patient/family expectations
- Legal ramifications
- May be harder to treat restenosis than prevent it

Patient Selection

Known

SIRIUS

Lesions

Probable

Ostial

Bifurcation

CTO

Unknown

Vein graft disease

Acute infarction

Small vessels

Large vessels (≥ 4.0)

Diffuse disease

SVBPG Disease

Much Ado About Nothing

What does a Class 3 indication mean?

- SVBG disease
- In- stent retenosis; diffuse
- Unprotected LMCA

Brought to you by O'Neill and LEON

- SVBG disease
- In- stent retenosis; diffuse
- Unprotected LMCA

