

***Prairie “Real World”
Drug Eluting Stent Database
Springfield, Illinois***

***FDA Circulatory System Devices
Advisory Panel December 7-8, 2006***

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Prairie Cardiovascular
The Doctors of Prairie



DISCLOSURES

Registry funding:

Boston Scientific, Cordis/J&J,
Medicine's Company

Dr. Mishkel:

Honoraria from Guidant/Abbott, Boston Scientific,
Medtronic

Ms. Moore:

No disclosures



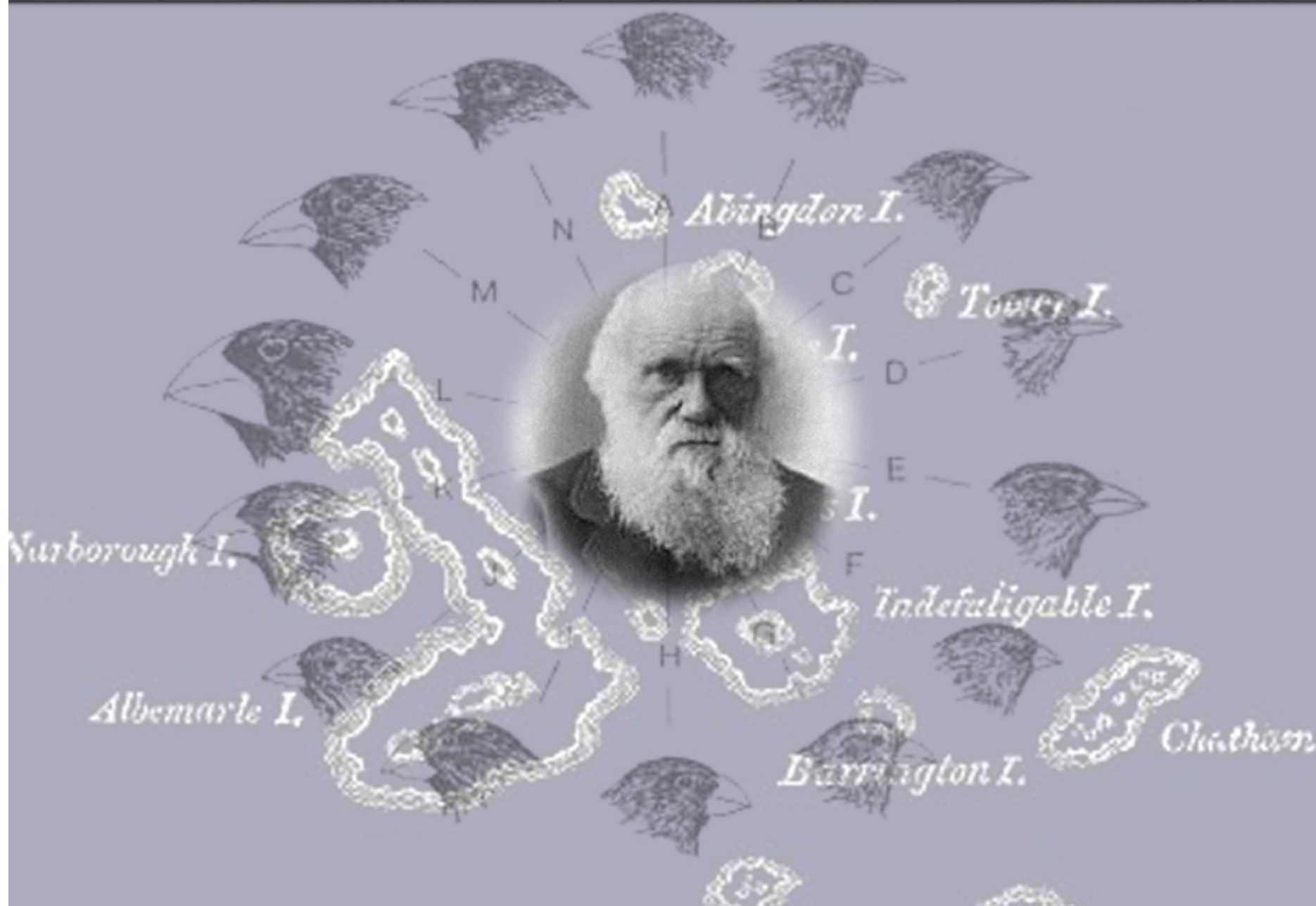
Springfield, IL: Home of the Simpsons?





Prairie Cardiovascular
The Doctors of Prairie

Prairie "Real World" Drug Eluting Stent Database





Prairie Cardiovascular
The Doctors of Prairie

Prairie "Real World" Drug Eluting Stent Database



Prairie
Heart Institute
Main Campus

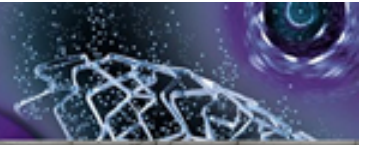


Prairie Network
Cardiovascular
Programs



Competing
Cardiovascular
Programs





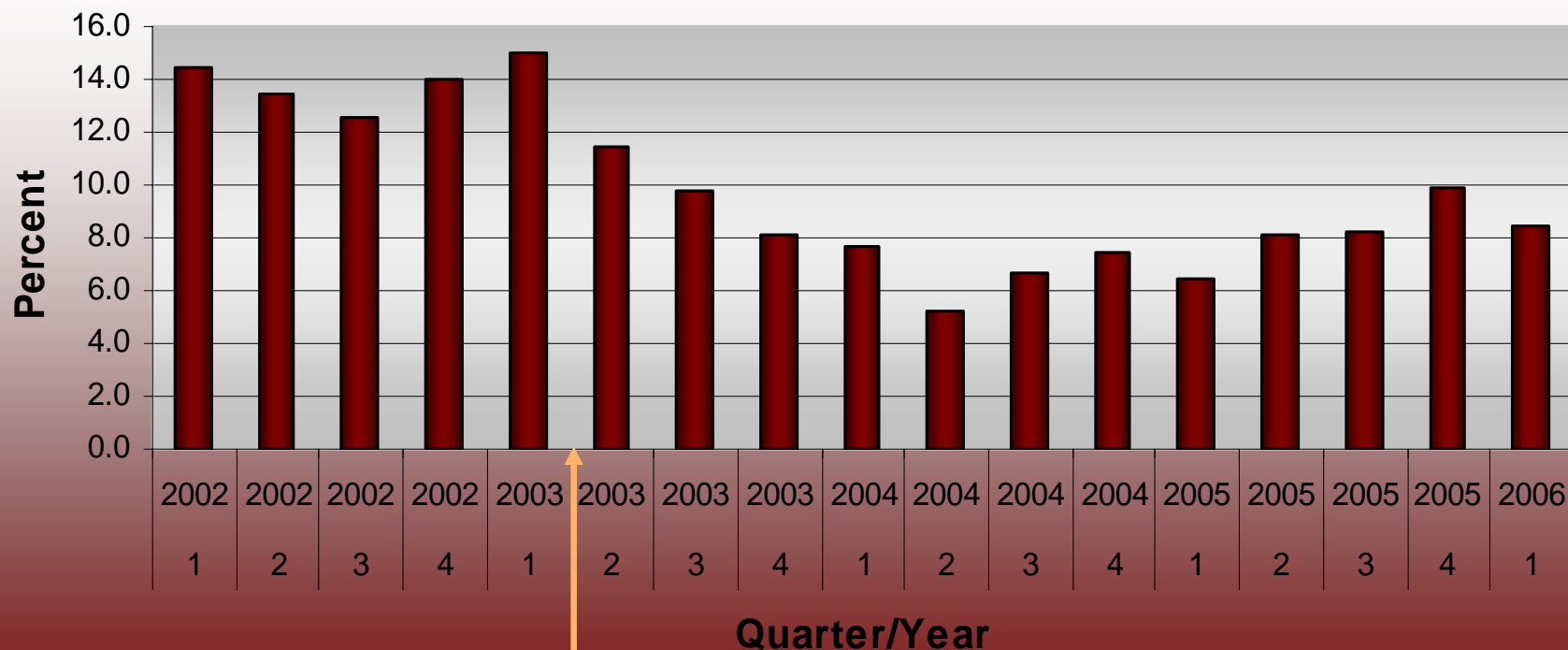
BMS Restenosis in the Pre-DES Era

- Between 7/1/01 – 5/1/03, 420 patients had repeat intervention for restenosis of a BMS
- Benign phenomenon?
 - 32 (7.6%) STEMI
 - 12 (2.9 %) died prior to hospital discharge.



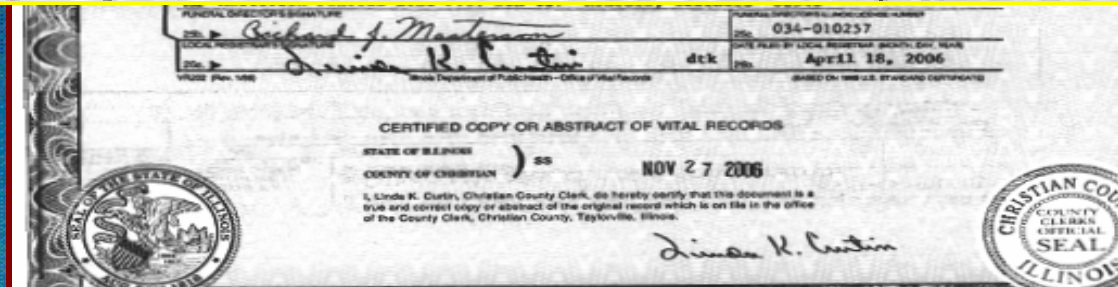
GOOD NEWS: Falling Rates of ISR

**Percentage of PCI's With Clinical Indication
of In-Stent Restenosis**



**Commercial
introduction of DES**

REPRESENTATION





Prairie "Real World" DES Registry

- The follow up database contains **5280** DES patients from 5/1/2003 – 5/31/2006.
 - >75% would have had one or more exclusion criteria from the major RCT's
- Clinical follow up obtained via:
 - Telephone calls to patient and primary MD, Springfield cardiologist, mailed surveys, electronic chart review, hospital readmissions, & death certificate review.
 - All deaths were independently adjudicated.



Percentages of completed follow up:

Patients due for:

6 month follow up = 5280 (5/1/03 – 5/31/06)

complete = 5028 (95%)

1 year follow up = 4336 (5/1/03 – 10/31/05)

complete = 3966 (91%)

2 year follow up = 2596 (5/1/03 – 10/31/04)

complete = 2337 (90%)

3 year follow up = 792 (5/1/03 – 10/31/03)

complete = 705 (89%)

Mean days to f/u = 549 ± 309



Baseline Characteristics

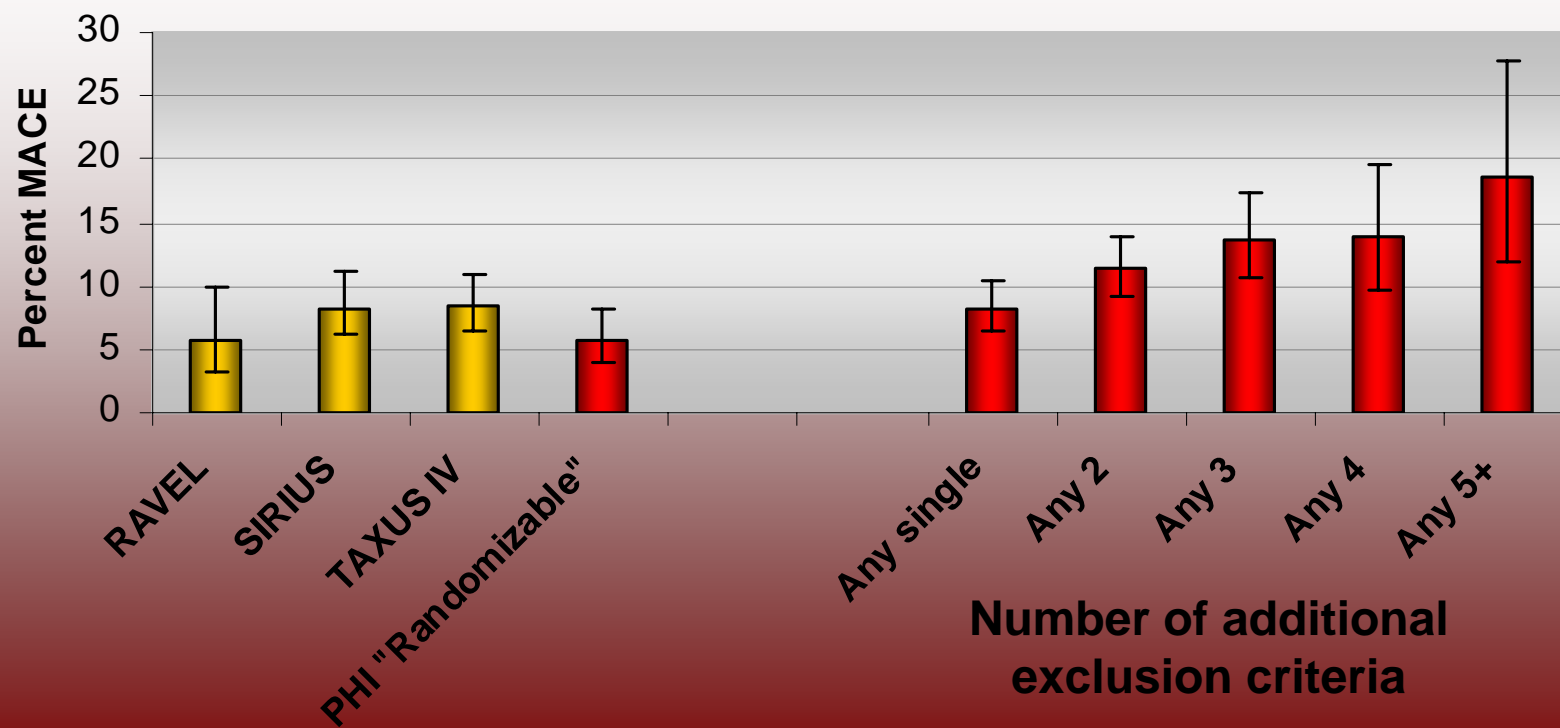
Baseline characteristics	Paclitaxel (n=911)	Sirolimus (n=4338)	p value
DES / procedure (mean \pm SD)	1.8 \pm 1.1	1.7 \pm 1.0	0.009
Age in years (mean \pm SD)	66.8 \pm 12.2	66.8 \pm 12.3	ns
Male gender	574 (63.0)	2750 (63.4)	ns
Diabetic	265 (29.1)	1259 (29.0)	ns
Insulin dependent DM	85 (9.3)	399 (9.2)	ns
Unstable angina	260 (28.5)	1464 (33.7)	0.002
STEMI	81 (8.9)	411 (9.5)	ns
Renal insufficiency (GFR <60 ml/min)	227 (25.1)	1043 (24.1)	ns
Hx Congestive heart failure	64 (7.0)	345 (8.0)	ns
Current/former smoker	585 (64.2)	2772 (63.9)	ns
LVEF (mean \pm SD)	51.4 \pm 12.4	51.6 \pm 12.0	ns
Prior MI	195 (21.4)	1076 (24.8)	0.030
Prior PCI	239 (26.2)	1289 (29.7)	0.037
Prior CABG	227 (24.9)	1035 (23.9)	ns
IIb/IIIa use	367 (40.3)	2853 (65.8)	<0.001



Comparison of "Real World" with RCT

1 year MACE rates

**Praire Real World Cohort in Comparison with
Randomized Controlled Trial Cohorts**





Total # of deaths recorded in follow up:

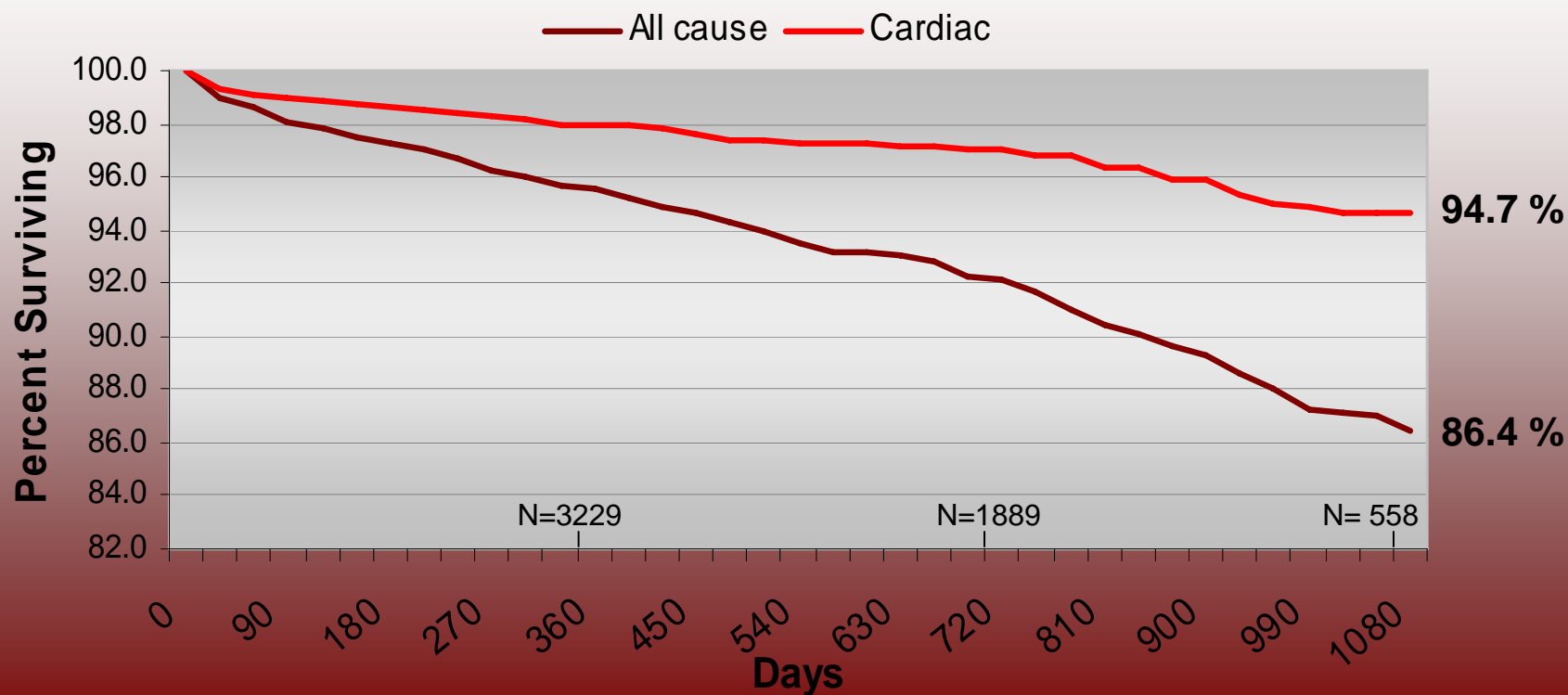
Total # of deaths	=	349 / 5280 (6.6%)
Cardiac	=	141 / 349 (40.4%)
MI	=	53
Cardiogenic shk	=	7
CAD	=	32
Cardio/resp/pulm	=	4
CHF	=	23
Atherosclerosis	=	2
Arrhythmia	=	6
Cardiomyopathy	=	11
Valvular	=	3
Non-cardiac	=	180 / 349 (51.6%)
Unknown	=	28 / 349 (8.0%)



Overall Survival

All Cause vs Cardiac

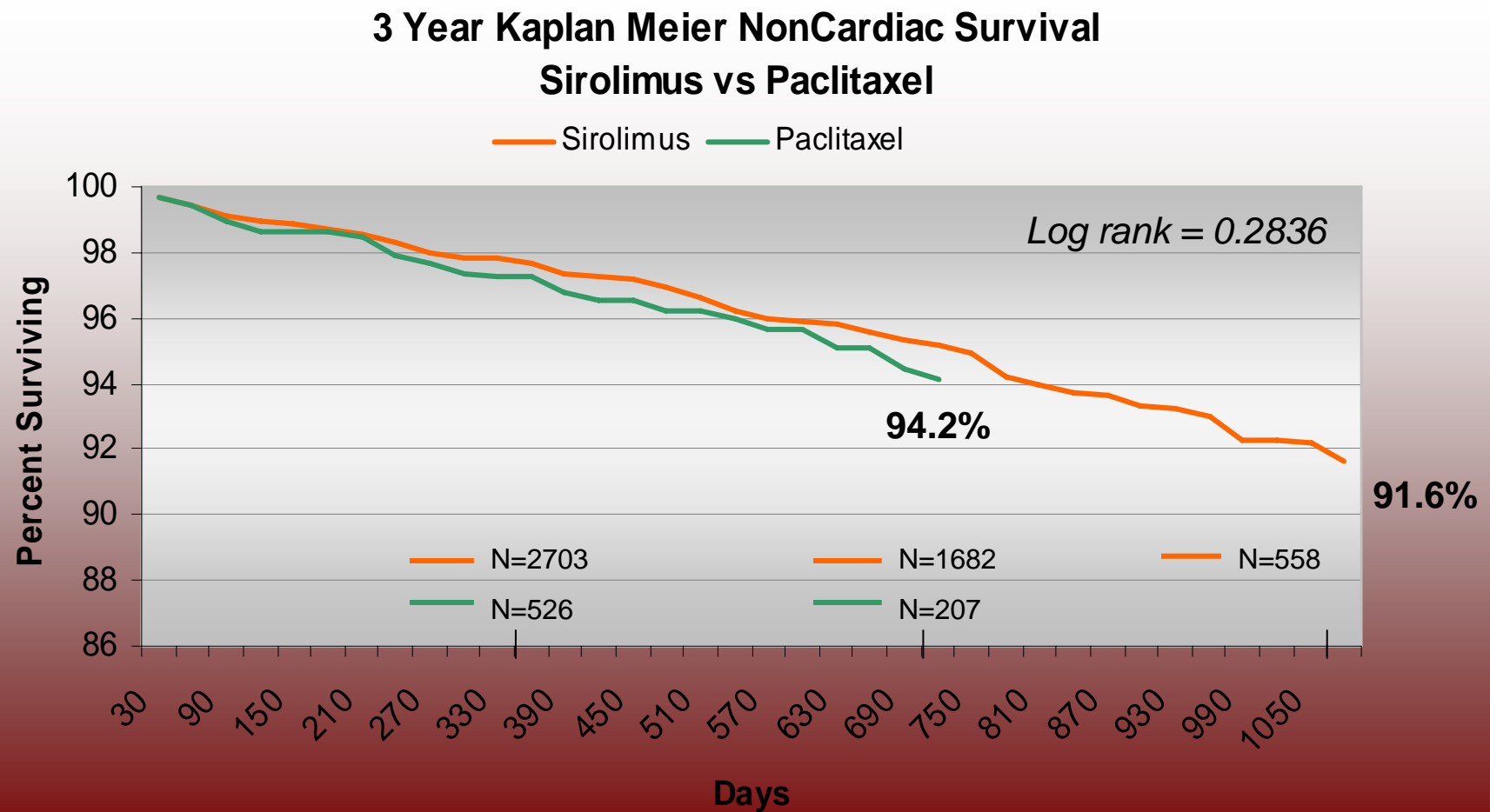
**3 Year Kaplan-Meier Survival
All-Cause vs Cardiac Mortality
DES procedures between 5/1/03-5/31/06**





Overall NonCardiac Survival

Sirolimus vs Paclitaxel

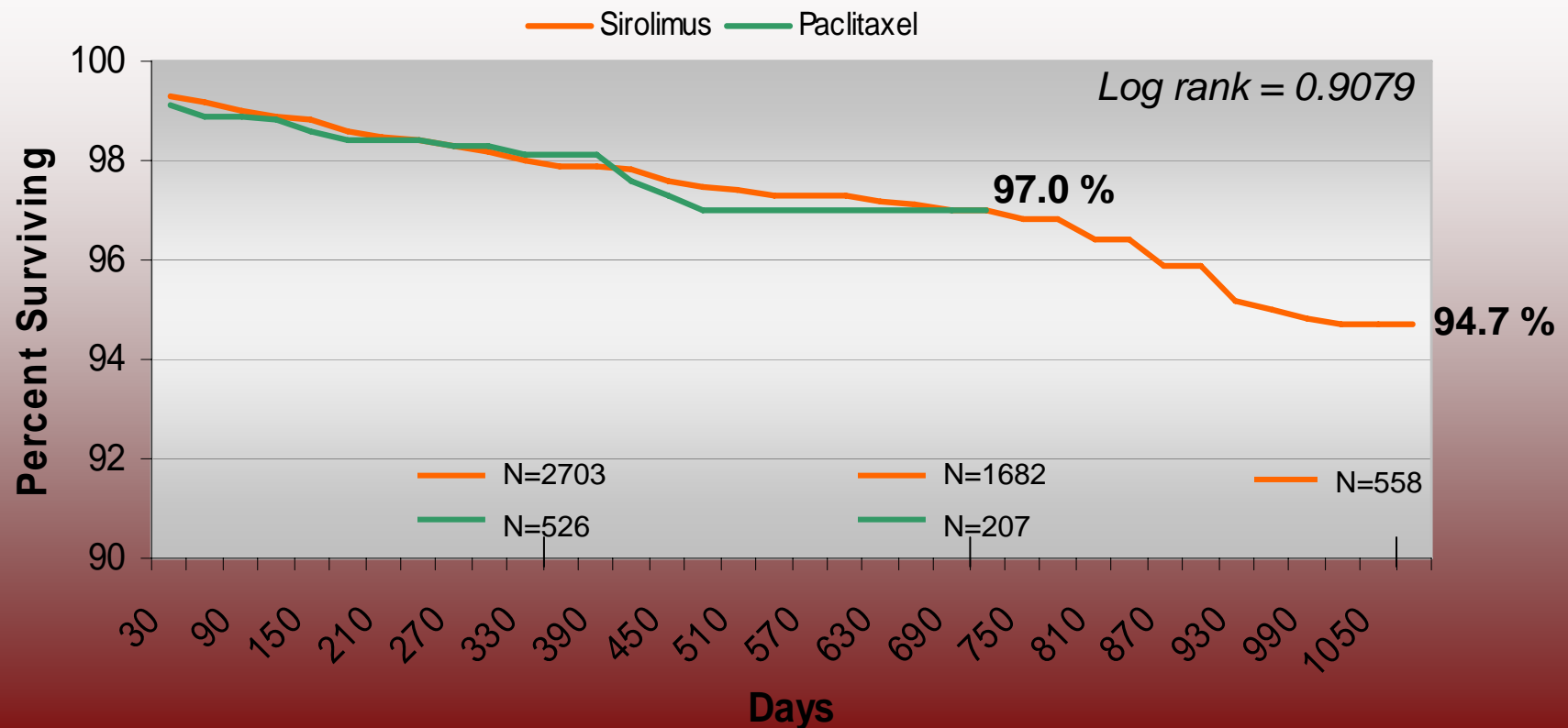




Overall Cardiac Survival

Sirolimus vs Paclitaxel

**3 Year Kaplan-Meier Cardiac Survival
Sirolimus vs Paclitaxel**





Baseline Characteristics- Diabetics only

Paclitaxel vs Sirolimus

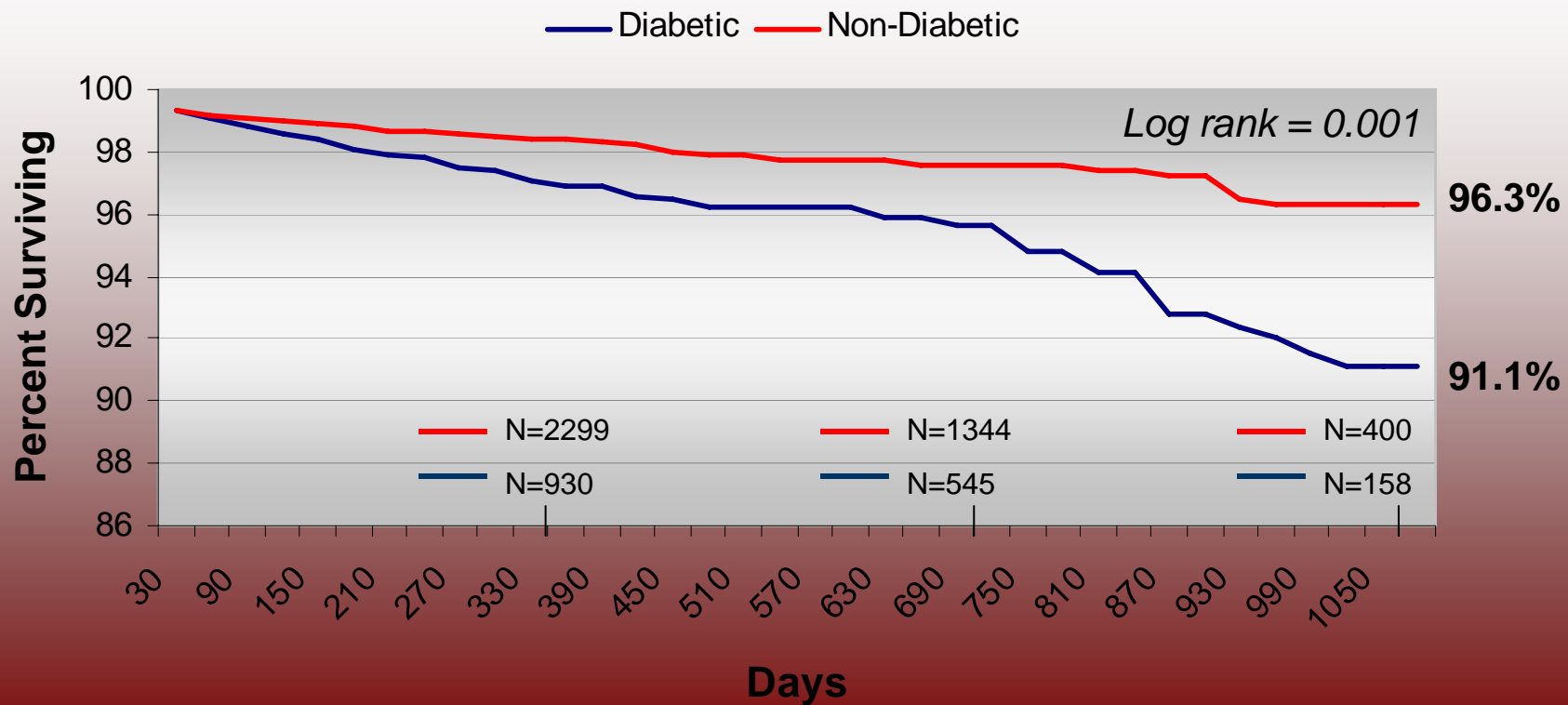
Baseline characteristics	Paclitaxel (n=265)	Sirolimus (n=1259)	p value
Male gender	158 (59.6)	748 (59.4)	ns
Age	66.8 ± 11.0	67.1 ± 11.2	ns
LVEF<30	14 (5.4)	58 (4.9)	ns
Obese (BMI >30)	150 (56.6)	739 (58.7)	ns
IDDM	85 (32.1)	399 (31.7)	ns
Unstable angina	66 (24.9)	471 (37.4)	<0.001
N-STEMI	48 (18.1)	200 (15.9)	ns
STEMI	11 (4.2)	60 (4.8)	ns
Renal Insufficiency (GFR < 60)	65 (24.7)	283 (22.6)	ns
DES in SVG	33 (12.5)	128 (10.2)	ns
Hx Congestive heart failure	29 (10.9)	161 (12.8)	ns
Current smoker	50 (18.9)	209 (16.6)	ns
Prior MI	66 (24.9)	357 (28.4)	ns
Prior PCI	73 (27.5)	425 (33.8)	0.052
IIbIIIa use	100 (37.7)	816 (64.8)	<0.001



Cardiac Survival

Diabetic vs NonDiabetic

**3 Year Kaplan-Meier Cardiac Survival
Diabetic vs Non-Diabetic**





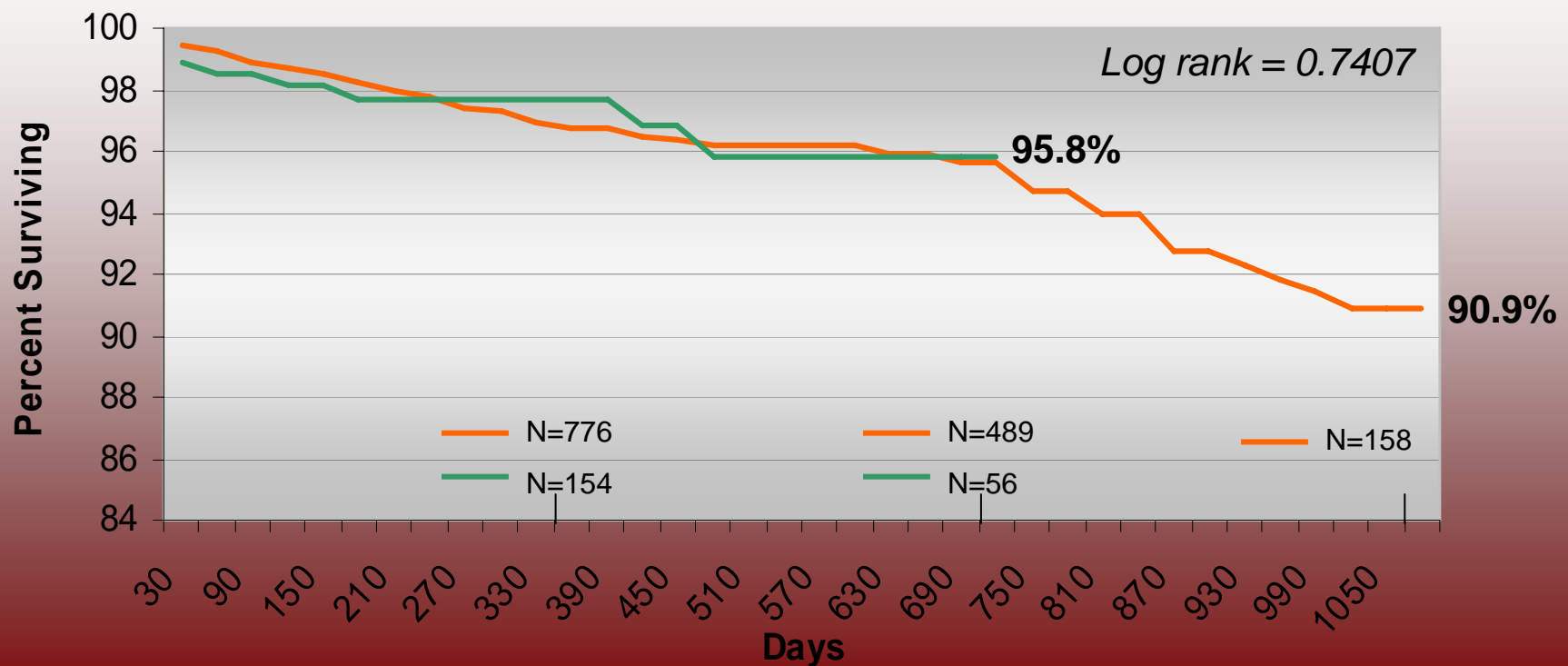
Cardiac Survival

Diabetic Subgroup

3 Year Kaplan-Meier Diabetic Cardiac Survival

Sirolimus vs Paclitaxel

— Sirolimus — Paclitaxel



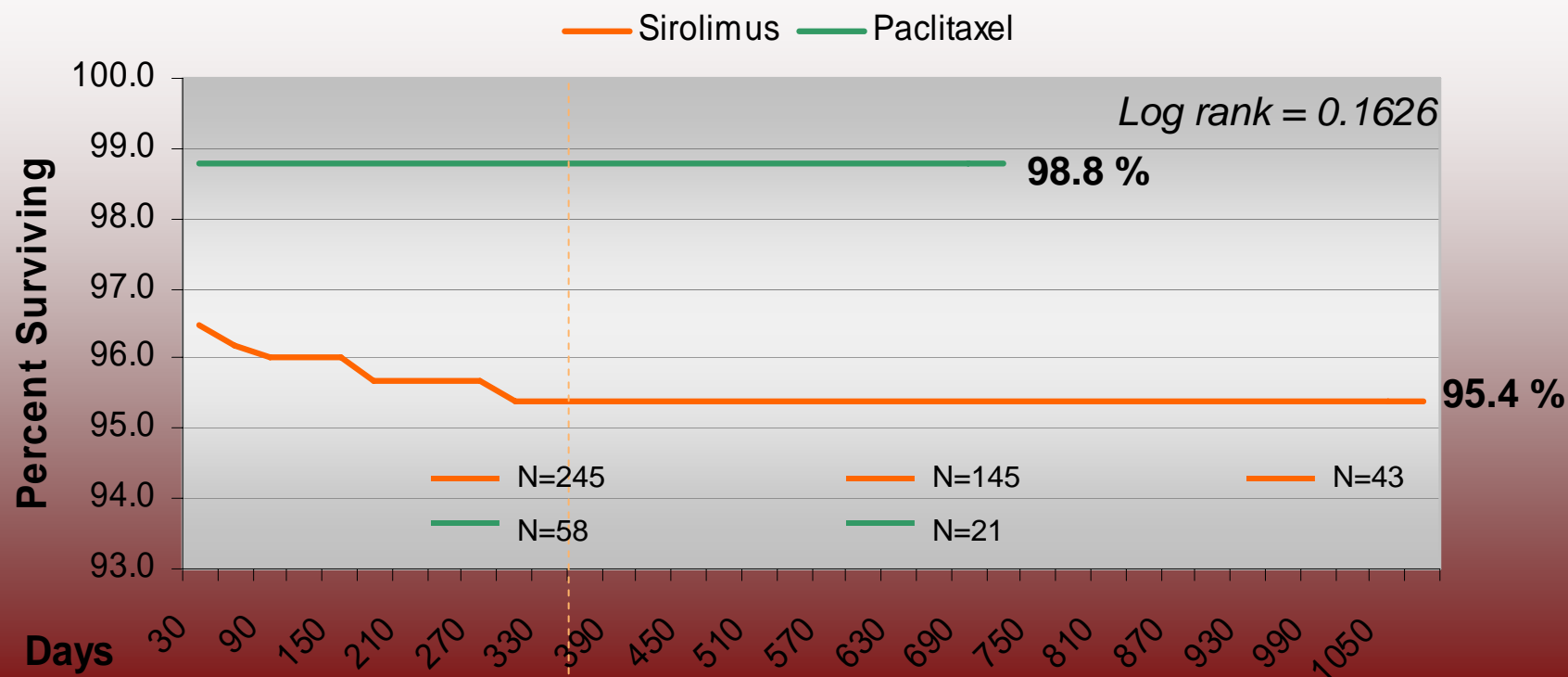


Cardiac Survival

STEMI subgroup

3 Year Kaplan-Meier STEMI Cardiac Survival

Sirolimus vs Paclitaxel



1 year cardiac survival PASSION: PES=96.1%

1 year cardiac survival TYPHOON: SES=98.0%

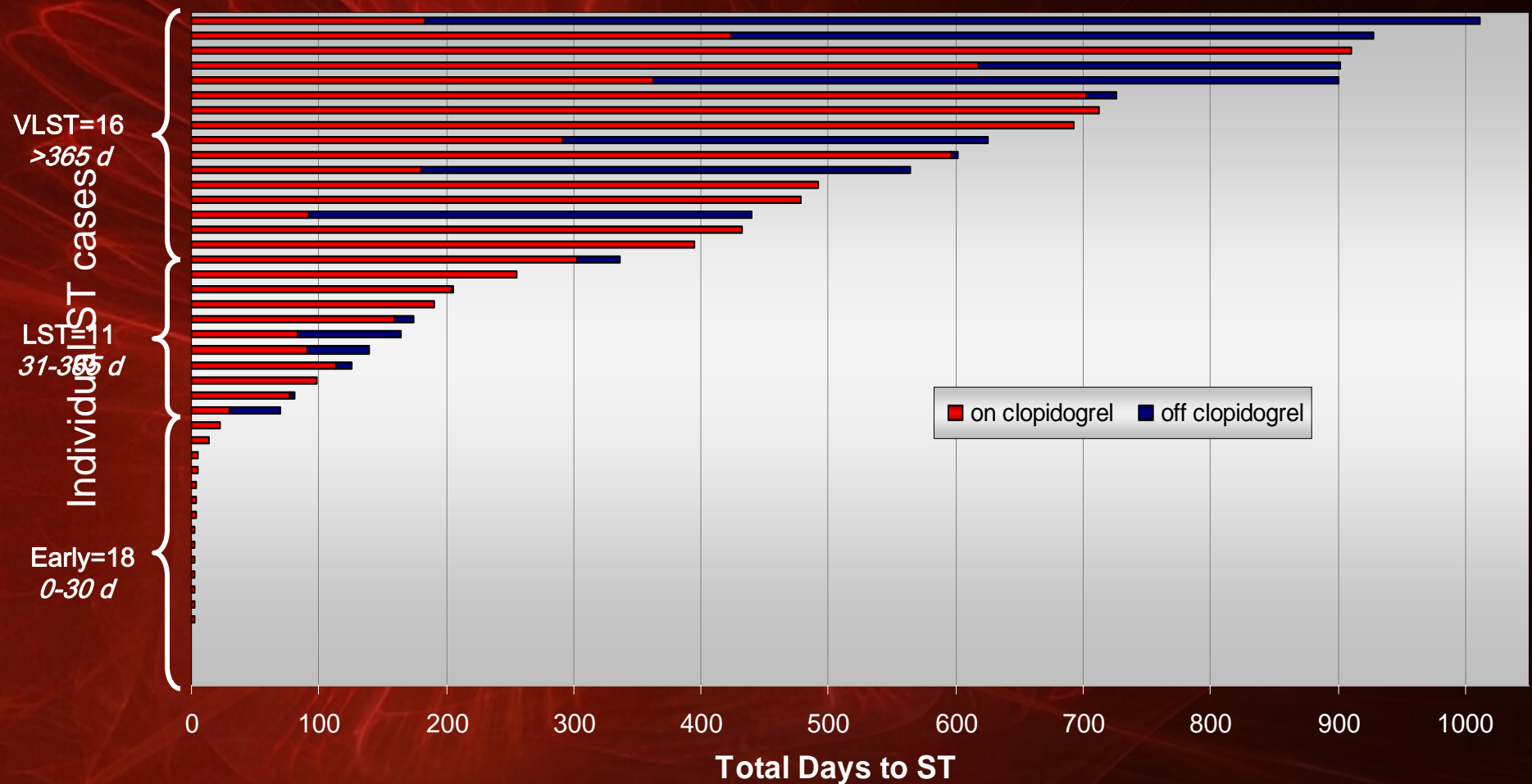


We identified 45 patients (0.85%) with "DEFINITE" ST.

Baseline characteristics of 44 definite ST	Early ST (n=18)	Late ST (n=11)	Very Late ST (n=16)
STEMI presentation at time of ST	10 (55.6)	8 (72.7)	11 (68.8)
Discontinued anti-platelet meds	0	8 (72.7)	8 (50.0)
Male gender	10 (55.6)	7 (63.6)	14 (87.5)
Current/former smoker	12 (66.7)	9 (81.8)	16 (100.0)
Diabetic	6 (33.3)	4 (36.4)	2 (12.5)
Renal insufficiency (GFR <60)*	4 (23.5)	2 (20.0)	4 (26.7)
Bifurcation lesion	5 (27.8)	2 (18.2)	3 (18.8)
Lesion in graft	2 (11.1)	0	0
ACC high risk lesion	14 (77.8)	6 (54.5)	8 (50.0)
Final balloon size	2.9 ± 0.4	2.9 ± 0.2	2.9 ± 0.4
Sirolimus ST	12 (66.7)	6 (54.5)	14 (87.5)
Paclitaxel ST	6 (33.3)	5 (45.5)	2 (12.5)
Overlapping stents	10 (55.6)	5 (45.5)	5 (31.3)
30 day mortality	3 (16.7)	3 (27.3)	2 (12.5)

*GFR data not available for 2 pts

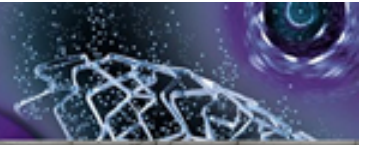
Days to Definite Stent Thrombosis





More info on Definite ST group

- Two of the Definite ST's were found by autopsy report.
- Exclusions from the Definite ST group:
 - Three pts had Definite ST in BMS (not included in analysis).
 - 2 early, 1 very late
 - Three patients had angiographically confirmed thrombus present in a previously placed DES, but no accompanying ACS.
- Several examples of multiple DES ST in same patient
 - Same vessel (n=4) – case study to follow
 - Different treated vessel (n=2)



Probable and Possible ST

- We identified 11 (0.21%) patients with "*PROBABLE*" ST from the follow up database.
- We identified 45 (0.85%) patients with "*POSSIBLE*" ST from the follow up database.
 - Simple review of death certificates would have classified 77 patients (1.4%) as a "*POSSIBLE*" ST.
 - Subsequent independent adjudication of these deaths eliminated 32 as possibles.



Logistic Regression Analysis

Definite/Probable ST

Variables considered for LRA:

Gender

Age *

DES type *

Diabetes/IDDM

Renal insufficiency

Prior MI / PCI / CABG

Obesity

Current smoker *

ACS type

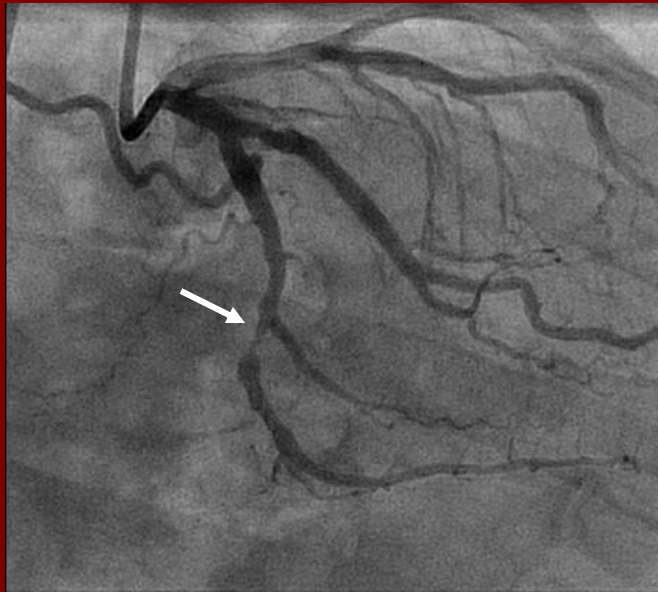
LVEF <30% *

Single DES placement

Variable	OR	95% CI	p value
Age (per yearly increment)	0.963	0.943-0.983	0.0004
Paclitaxel DES	1.897	1.053-3.416	0.0330
LVEF < 30%	3.318	1.477-7.452	0.0037

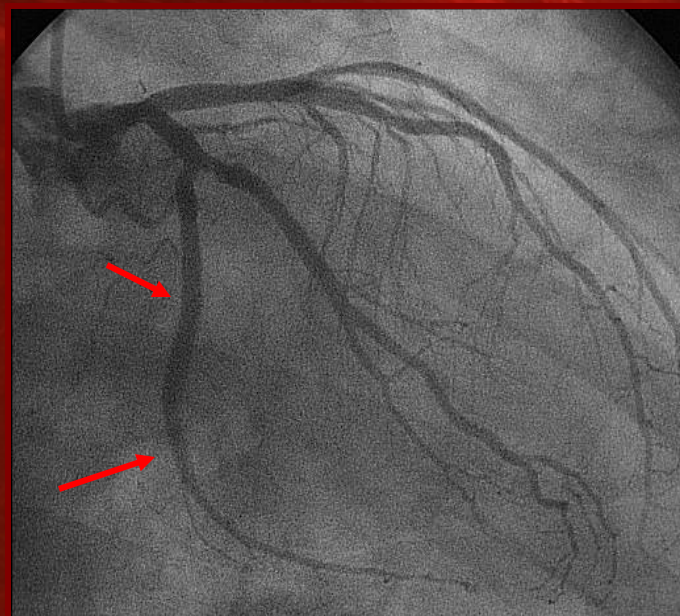
c statistic = 0.649

* significant in univariate analysis



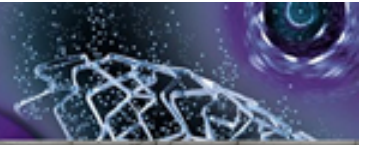
Case Study: Recurrent ST (same vessel)

- Jan 7, 2005
- Recent history of PE on coumadin therapy
 - Hypercoag w/u -ve
- 2 vessel DES to RCA and LCX
 - **3.0 mm TAXUS**



Early ST #1 (same vessel)

- Jan 9, 2005 STEMI
 - ST at 2 days post
 - Compliant with ASA/Plavix qd/coumadin
 - INR = 1.5
- Proximal placement of **3.5 mm TAXUS** and distal placement of **2.75 mm TAXUS**



Late ST #2 (same vessel)

- March 19, 2005 STEMI
 - ST at 2 months post
 - Compliant with:
 - ASA/Plavix bid/coumadin
 - Lovenox for 2 weeks after early ST #1
 - Placement of distal **2.75 mm Cypher**





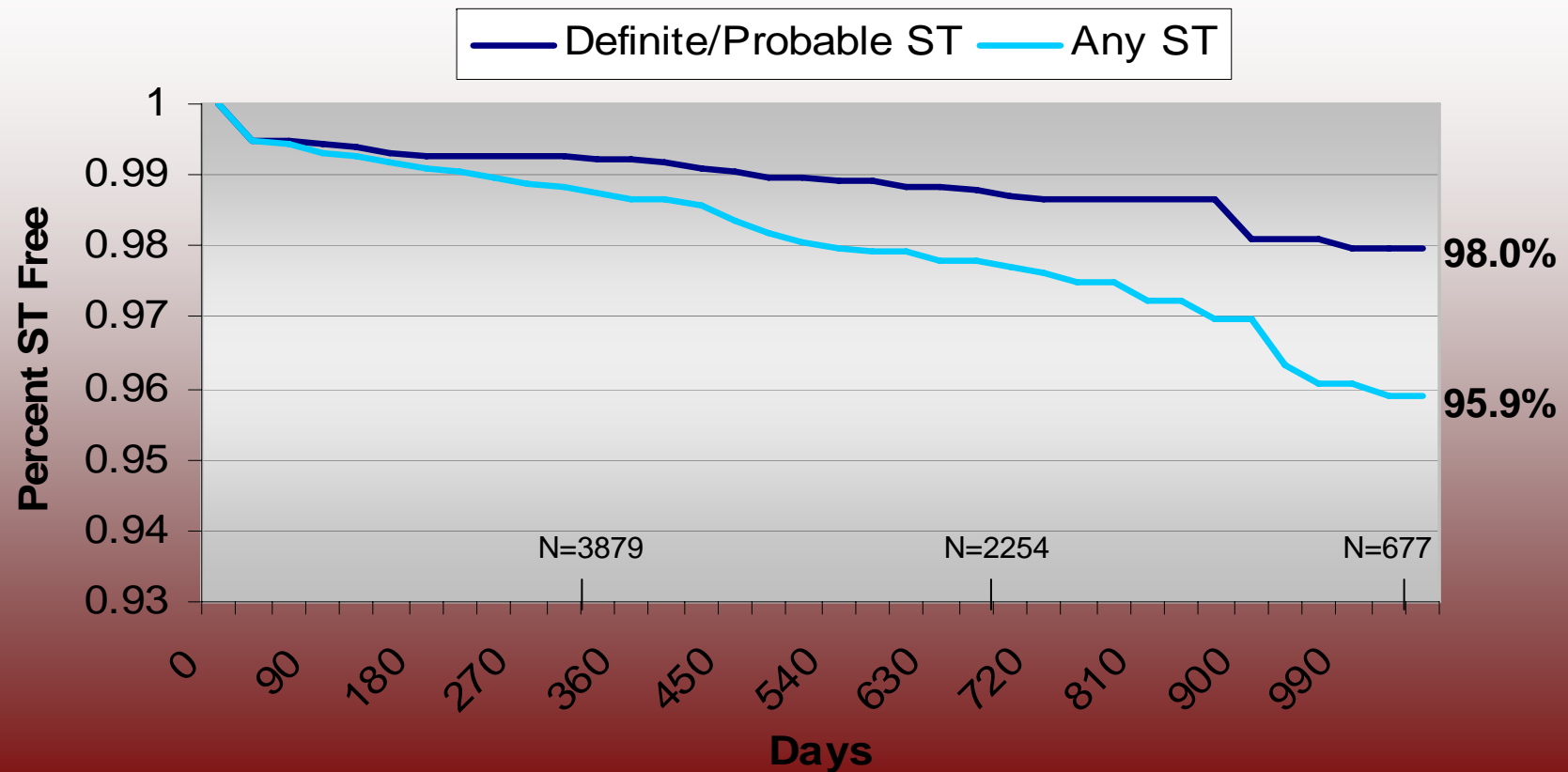
Very Late ST #3 (same vessel)

- May 30 2006 NSTEMI
 - Very late ST at 14 months
 - Discontinued Plavix 8 days prior to ST for oral surgery
 - Medical therapy



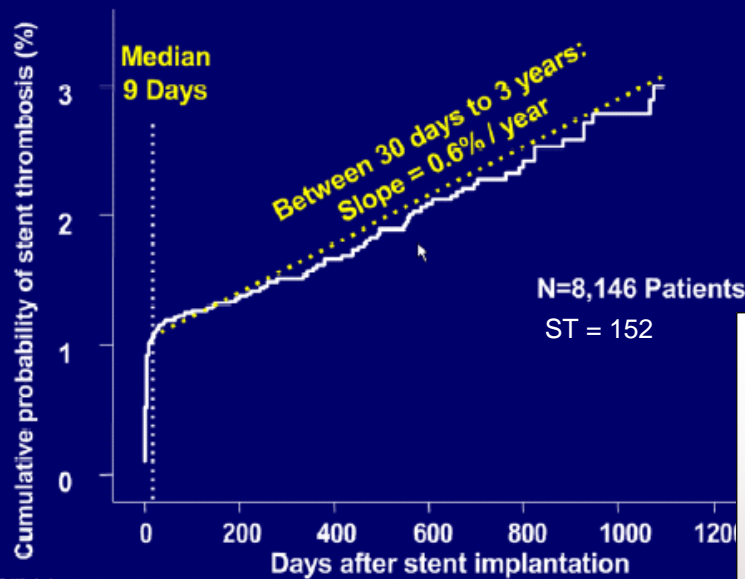
Freedom from Stent Thrombosis

Freedom from ARC Stent Thrombosis





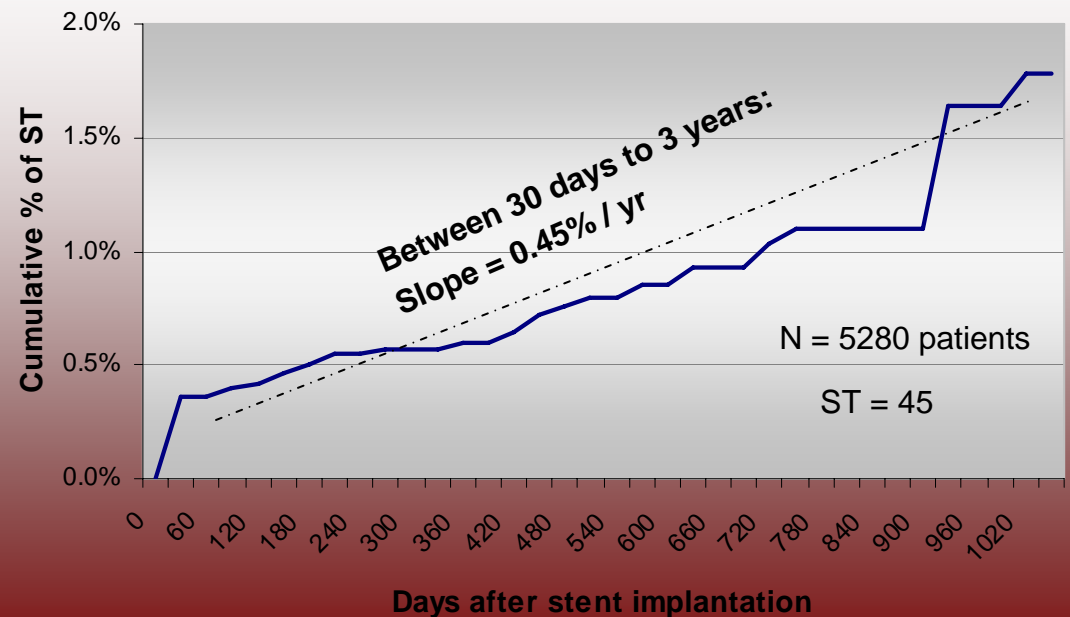
Angiographic DES Stent Thrombosis Bern - Rotterdam Cohort Study



Courtesy of Dr. S. Windecker

Cumulative Definite ST Rate

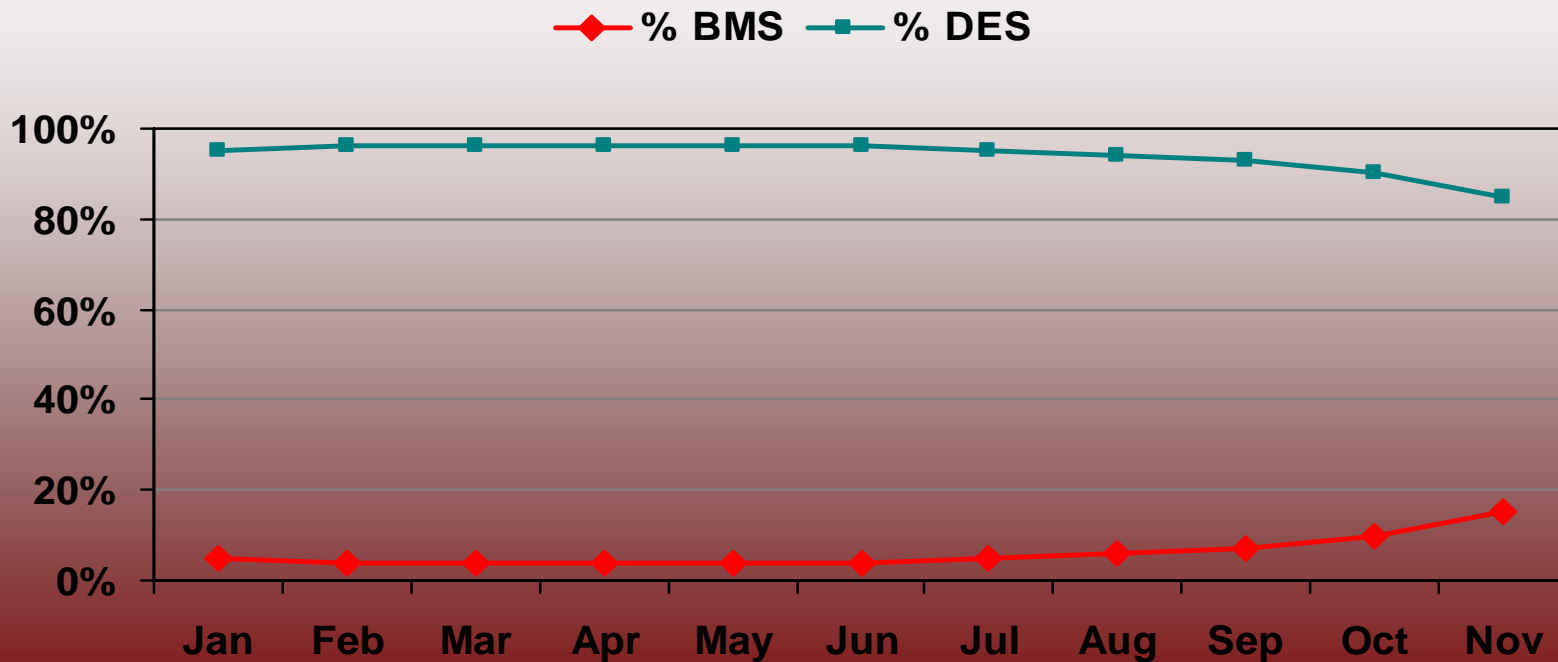
Angiographic DES Stent Thrombosis Prairie Registry





Decreasing penetration of DES subsequent to these findings

2006 Stent Utilization





Conclusions

- The total unadjusted rate of ST for the Prairie Registry over 3 years is 1.9%.
- The unadjusted rate of definite/probable ST over 3 years is 1.1%.
- Cumulative definite ST event rate is 0.45 % / year after the 1st 30 days.
- Possible ST is an overly sensitive and non-specific indicator of ST.
- Late and very late ST could not entirely be attributed to discontinuation of antiplatelet therapy.
 - Recurrent ST suggests other etiologies (ie, polymer, late remodeling)
- Any decision regarding DES implantation must weigh net clinical benefit of preventing ISR (associated morbidity/mortality) vs ST.