

A Prospective “All Comers” Single Arm Study in Complex Patients: The MATRIX Trial

IDE: G030229/S003

Cypher™ Sirolimus-Eluting Coronary Stent

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Disclosures

Company Name	Affiliation/Interest
Cordis	Lecture fees, research grant (CRF)
Conor MEDsystems	Research Grant (CRF)
Boston Scientific	Lecture fees, research grant (CRF)
The Medicines Company	Lecture fees, research grant (CRF)
DEVAX	Research grant (CRF)



MATRIX: Goals and Design

- Prospective single arm study initiated in 2004 as a 3,500 patient trial under a physician driven IDE (1st submitted in October 2003)
- Designed to evaluate the outcomes of SES in consecutive “real world” population undergoing PCI with SES
- Both on- and off-label SES use
- Clinical follow-up at 1 month, 6 months, 1 year and 2 years, and yearly
- Angiographic follow-up at 6 months in sub group of patients undergoing PCI for CTO and Acute MI



Study Organization

- **Principal Investigator: George Dangas, MD, PhD**
- **Data management: Cardiovascular Research Foundation**
- **Independent CEC**
- **100% monitoring of all data fields of the first 1,000 pts**
- **Independent QCA lab for the first 800 lesions treated**



MATRIX Registry: Sub-Studies

- **Bifurcation lesions**
- **CTO**
- **Acute MI**
- **Diabetic patients**
- **Multivessel disease**
- **SVGs**
- **>three stents**



Medication Regimen

Pre-procedure :

- Aspirin 325 mg
- Clopidogrel loading dose of 300 to 600 mg within 24 hours followed by 75 mg once daily or Ticlopidine loading dose of 500 mg within 24 hours, followed by 250 mg twice a day.

During procedure:

- Angiomax or Heparin \pm GP IIb/IIIa inhibitors

Post-procedure and after discharge:

- Aspirin 325 mg for 1 months, thereafter ASA 81 mg indefinitely
- Clopidogrel 75 mg once daily for at least three months but recommend up to 1 year to all patients

Matrix Registry

Inclusion Criteria

All consecutive patients treated with Cypher stent (Cordis, J&J)

No exclusions- except refusal to consent



Follow-Up

N=1,521 patients

**Eligible for
F/U**

30 days

1521

6 months

1372

1 year

1003

2 years

642

Baseline Clinical Characteristics

N = 1,521 patients

Age, mean \pm SD (years) **64.8 \pm 11.2**

Male gender **74.7%**

Race

Caucasian **61.4%**

African American **6.3%**

Hispanic **10.0%**

Asian-Pacific **1.1%**

Others/non-disclosed **21.1%**

History of PCI **44.6%**

History of CABG **21.0%**

Baseline Clinical Characteristics

N = 1,521	
Diabetes mellitus	33.8%
Hyperlipidemia	84.8%
Hypertension	82.5%
History of CVA/TIA	8.0%
Prior myocardial infarction	33.4%
Smoking within 30 days	11.0%
Unstable angina	46.3%
History of peripheral vessel ds	7.3%
History of renal impairment	11.0%
Menopausal women	20.4%



Baseline Angiographic Characteristics (1)

N = 2,608 lesions

Target vessel

Unprotected LM	1.5%
LAD	37.2%
LCX	29.4%
RCA	27.5%
SVG	4.5%

Arterial conduit	0.6%
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Target lesion location

Ostial	7.3%
Proximal	43.7%
Chronic total occlusion	4.3%
Bifurcation stenting	12.4%
De novo lesion	90.7%
Restenotic lesion	9.3%



Procedural Characteristics

N = 1,521 patients

No. of stents per procedure	2.0±1.1
No. of stents per lesion	1.2±0.5
Unfractionated heparin	16.0%
Bivalirudin used	84.9%
IIb/IIIa inhibitors administered	8.0%
Procedure success	96.0%
Device success (N=2536 Lesions)	98.5%

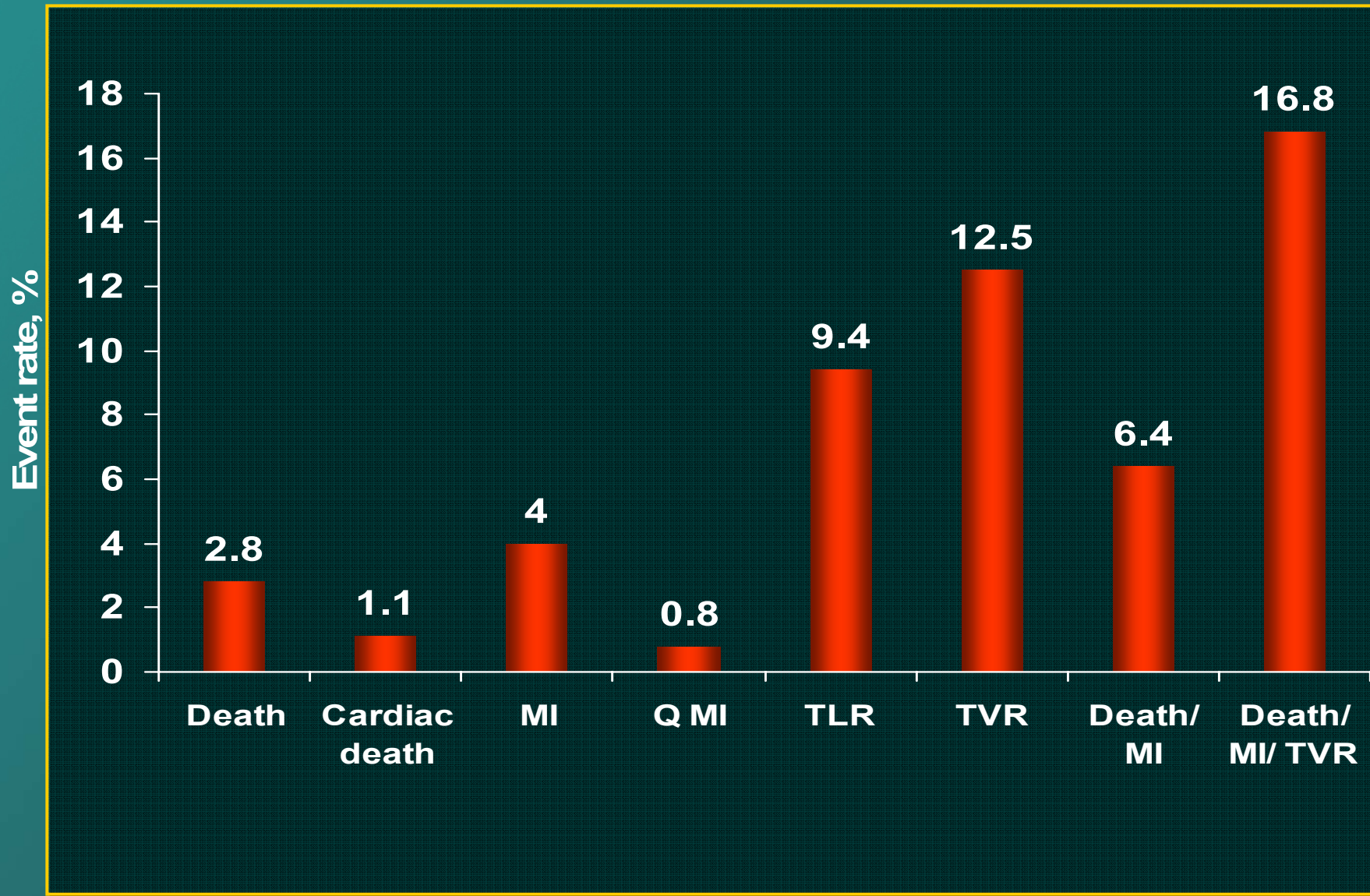
Outcomes up to 2 Years (K-M)

N=1,521 patients	
Death	2.8% (27)
Cardiac death	1.1% (13)
Non-cardiac death	1.5% (11)
Unknown death	0.2% (3)
Myocardial infarction	4.0% (50)
Q wave	0.8% (8)
Non-Q wave	3.2% (42)
TLR	9.4% (92)
TVR	12.5% (125)
Death/ MI	6.4% (72)
Death/ MI/ TVR	16.8% (179)

Follow-up (median, IQR), 397 days (196 to 746)



Outcomes up to 2 Years



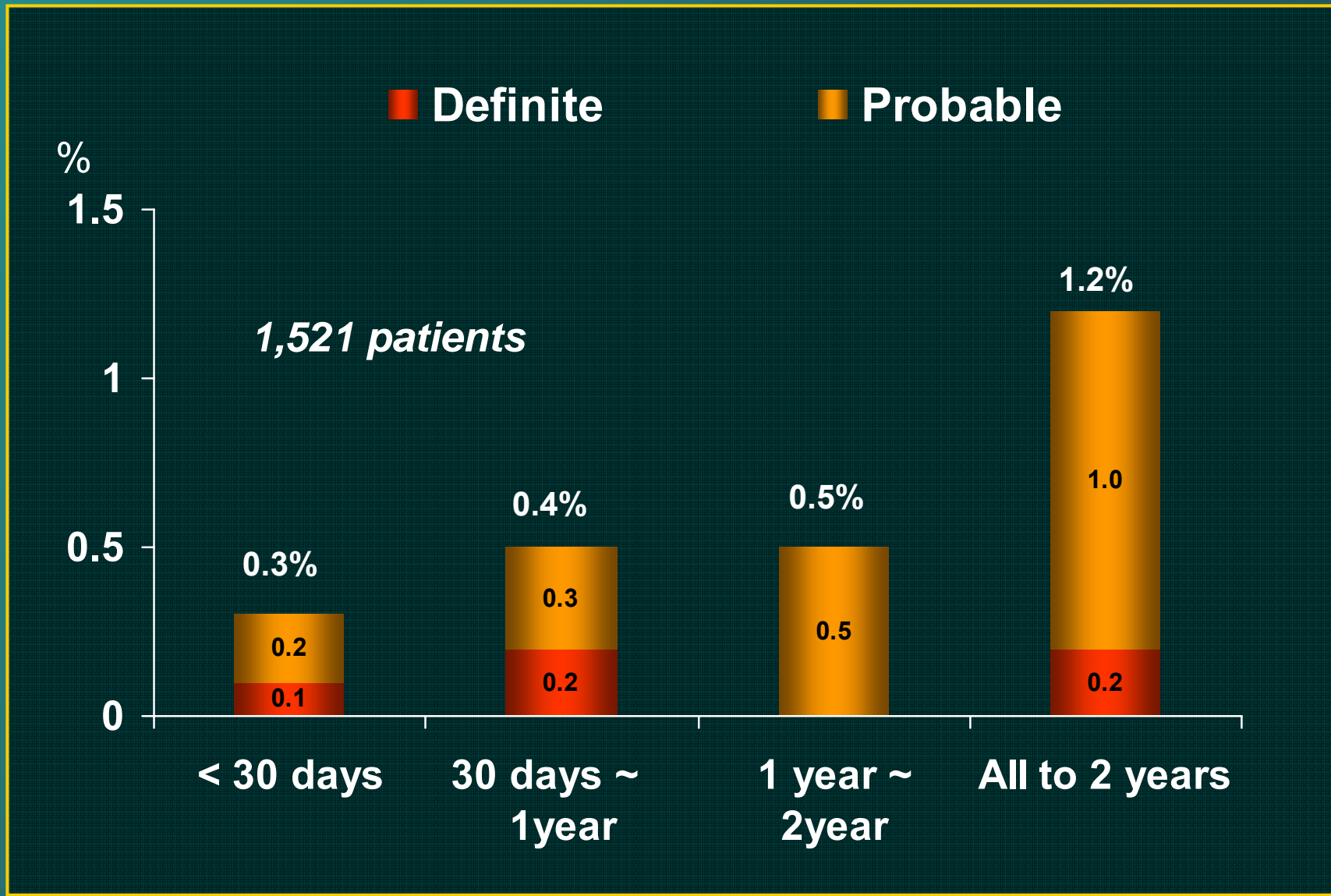
Stent Thrombosis (K-M)

N=1,521 patients

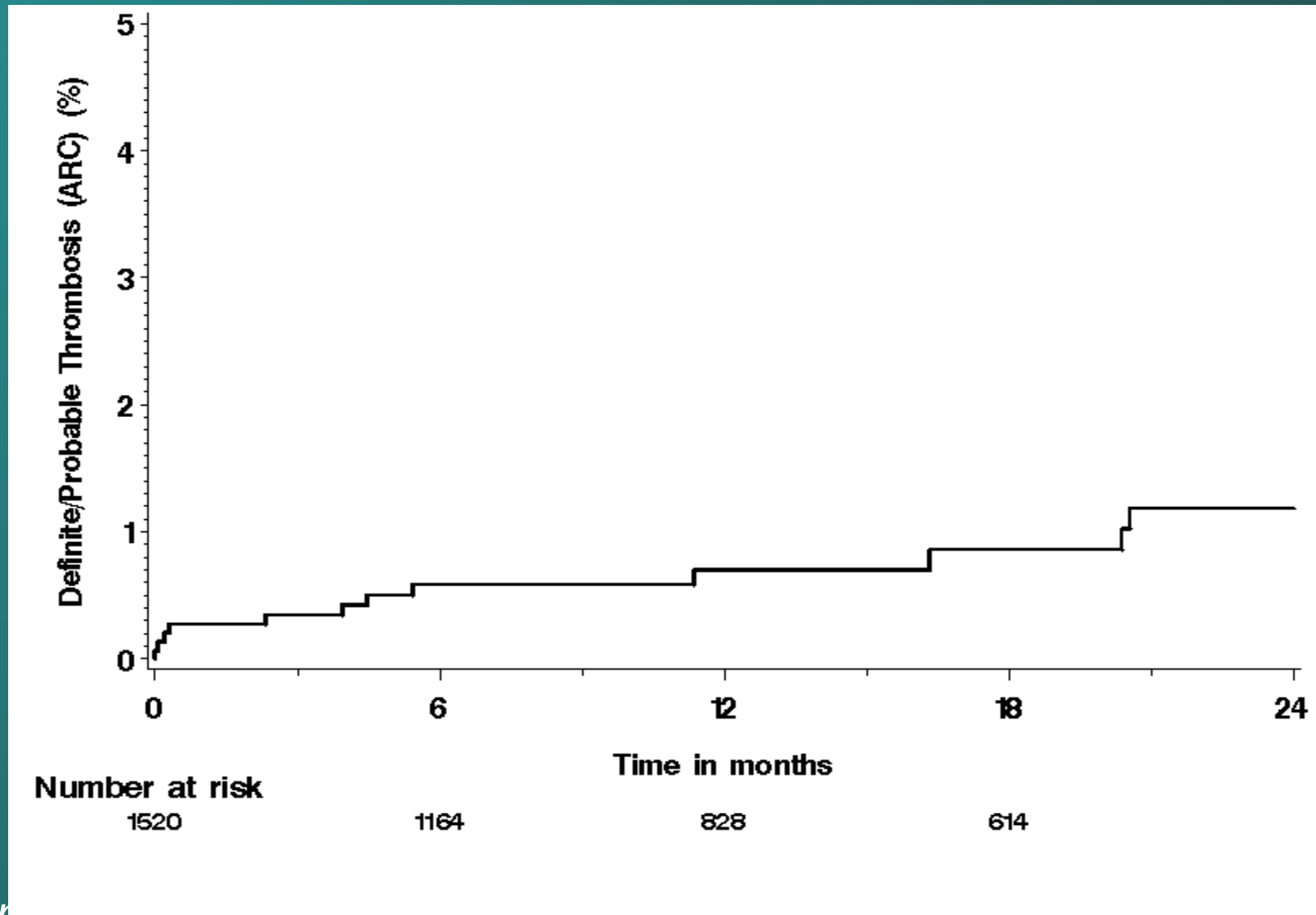
	Definite	Probable	Total
Acute and Subacute (≤ 30 days)	0.1% (1)	0.2% (3)	0.3% (4)
Late (> 30 days and ≤ 1 year)	0.2% (2)	0.3% (3)	0.4% (5)
Very late (> 1 year and ≤ 2 years)	0% (0)	0.5% (3)	0.5% (3)
Total (to 2 years)	0.2% (3)	1.0% (9)	1.2% (12)



Stent Thrombosis



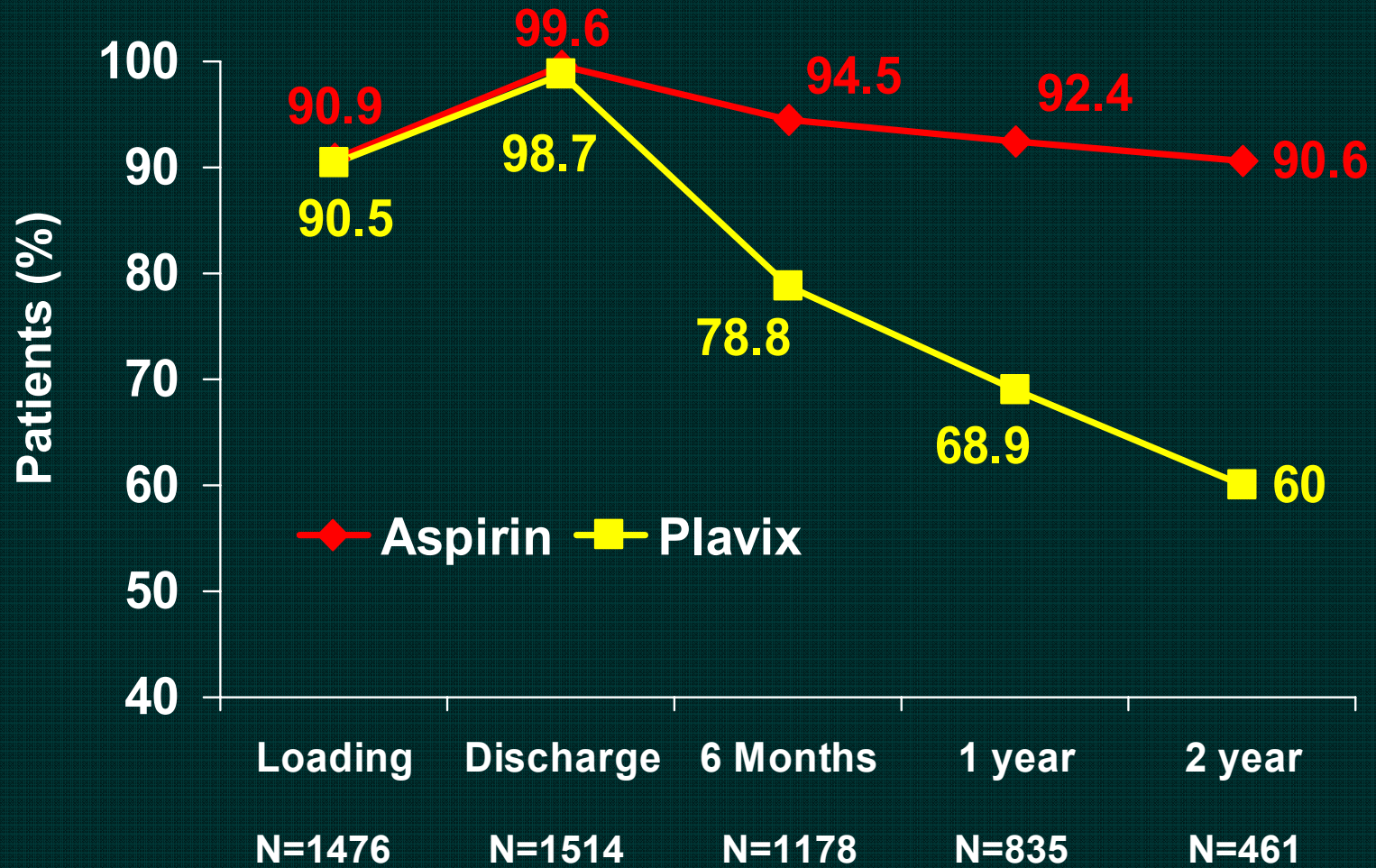
K-M Curve of Stent Thrombosis



Definite and probable ST-Ts with ARC definition were included.



Antiplatelet Adherence



Outcomes for Patients Without Clopidogrel at 30 Days

2 Year events	Off clopidogrel (N=61)	On clopidogrel (N=1355)	HR (95% CI)
Death	3.3% (2)	1.9% (14)	2.06 (0.47 – 9.12)
MI	5.3% (3)	1.2% (8)	5.25 (1.38 – 19.96)
Death/ MI	6.8% (4)	2.9% (21)	2.73 (0.93 – 7.98)
Definite/ Probable ST	1.7% (1)	0.9% (7)	2.13 (0.26 – 17.46)

Outcomes for Patients Without Clopidogrel at 1 Year

2 Year events	Off clopidogrel (N=61)	On clopidogrel (N=1355)	HR (95% CI)
Death	2.2% (5)	0.5% (2)	4.96 (0.96 – 25.6)
MI	1.5% (3)	0.7% (3)	1.94 (0.39 – 9.60)
Death/ MI	3.6% (8)	1.0% (4)	3.94 (1.18 – 13.07)
Definite/ Probable ST	0% (0)	0.7% (3)	N/A

Outcomes up to 2 Years (K-M)

	DM (N=511)	Non-DM (N=1001)	p
Days (median, IQR)	394 (194,744)	397 (196,746)	
Death	5.1% (17)	1.6% (10)	0.001
Myocardial infarction	5.7% (23)	3.1% (26)	0.048
Q wave	1.2% (4)	0.6% (4)	0.327
Non-Q wave	4.5% (19)	2.5% (22)	0.085
TLR	13.6% (44)	7.2% (47)	0.002
TVR	17.7% (58)	9.8% (66)	0.001
Death/ MI	10.1% (37)	4.4% (34)	<0.001
Death/ MI/ TVR	23.2% (82)	13.4% (95)	<0.001
Definite/ Probable ST	1.6% (6)	1.0% (6)	0.231



Outcomes up to 2 Years (K-M)

	CKD (N=148)	No-CKD (N=1250)	p
Days (median, IQR)	370 (200,726)	399 (200,747)	
Death	7.5% (8)	2.2% (16)	<0.001
Myocardial infarction	9.8% (10)	3.7% (38)	0.015
TLR	17.6% (15)	8.6% (69)	0.017
TVR	19.5% (17)	11.6% (95)	0.072
Death/ MI	15.6% (16)	5.4% (51)	<0.001
Death/ MI/ TVR	29.2% (30)	15.3% (132)	<0.001
Definite/ Probable ST	0.7% (1)	1.3% (11)	0.836



Outcomes up to 2 Years (K-M)

	Multivessel (N=473)	Single Vessel (N=1040)	p
Days (median, IQR)	455 (208,750)	375 (185,735)	
Death	1.7% (6)	3.4% (21)	0.211
Myocardial infarction	4.7% (20)	3.8% (30)	0.233
TLR	10.6% (35)	9.0% (57)	0.319
TVR	13.6% (47)	12.2% (78)	0.253
Death/ MI	5.8% (24)	6.9% (48)	0.876
Death/ MI/ TVR	17.6% (64)	16.8% (115)	0.336
Definite/ Probable ST	1.8% (5)	0.8% (7))	0.545



Outcomes up to 2 Years (K-M)

	3+ stents (N=391)	<3 stents (N=1058)	p
Days (median, IQR)	462 (206,749)	388 (200,746)	
Death	1.6% (4)	3.3% (22)	0.134
Myocardial infarction	6.0% (22)	3.2% (24)	0.002
TLR	13.1% (35)	8.0% (55)	0.023
TVR	15.7% (43)	11.3% (79)	0.080
Death/ MI	7.6% (26)	5.9% (42)	0.047
Death/ MI/ TVR	20.4% (61)	15.4% (111)	0.015
Definite/ Probable ST	1.7% (5)	0.9% (6)	0.214



Outcomes up to 2 Years (K-M)

	Bifurcations (N=289)
Days (median, IQR)	412 (190, 748)
Death	4.4% (7)
Myocardial infarction	3.7% (10)
TLR	6.9% (14)
TVR	9.1% (18)
Death/ MI	7.6% (16)
Death/ MI/ TVR	15.2% (32)
Definite/ Probable ST	1.3% (3)



MATRIX - Conclusions (1)

In this preliminary interim analysis of the first 1,521 patients from the MATRIX registry which included patients with complex coronary artery disease treated with the sirolimus-eluting Bx VELOCITY™ stent (Cypher stent)

- The frequency of early and late adverse events was low, and similar to those previously reported with simple low-risk lesions



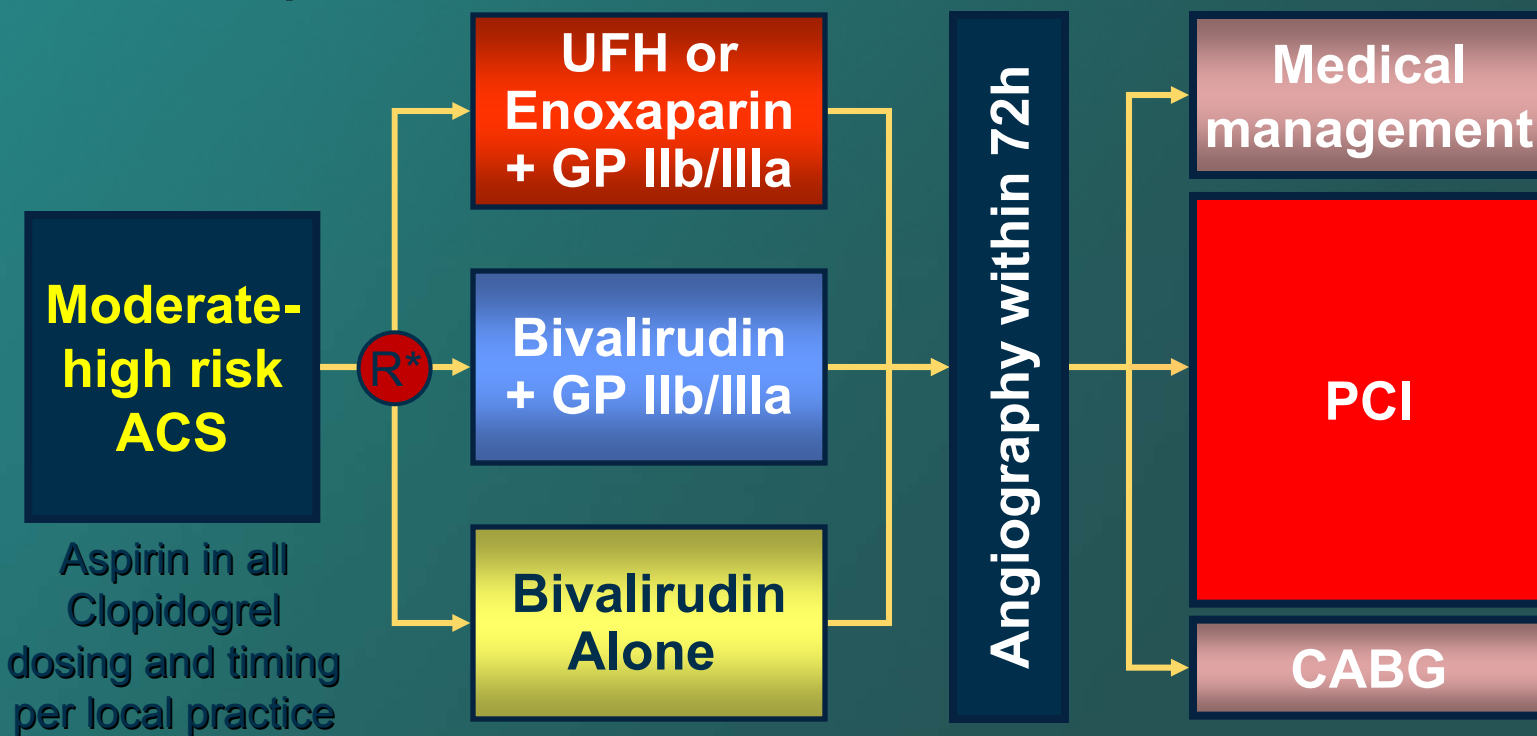
MATRIX – Conclusions (2)

- Overall incidence of stent thrombosis assessed with an expanded definition was 1.2%, if include possible-2.0%.
- Late SAT after two years is rare but is observed
- Patients with DM, CKD, >3 stents had higher rates of death, MI, TLR but not probable/definite stent thrombosis compared to non-diabetics.
- Long-term outcomes of Cypher implantation for multi-vessel stenting, multiple stenting (≥ 3), CTO, Acute MI, and SVG lesions are being evaluated on a yearly basis under this IDE, with evaluation of antiplatelet regimen status of patients.



ACUITY Study Design

- Moderate-high risk unstable angina or NSTEMI undergoing an invasive strategy (N = 13,819)



Stone et al. NEJM 2006

*Stratified by pre-angiography thienopyridine use or administration



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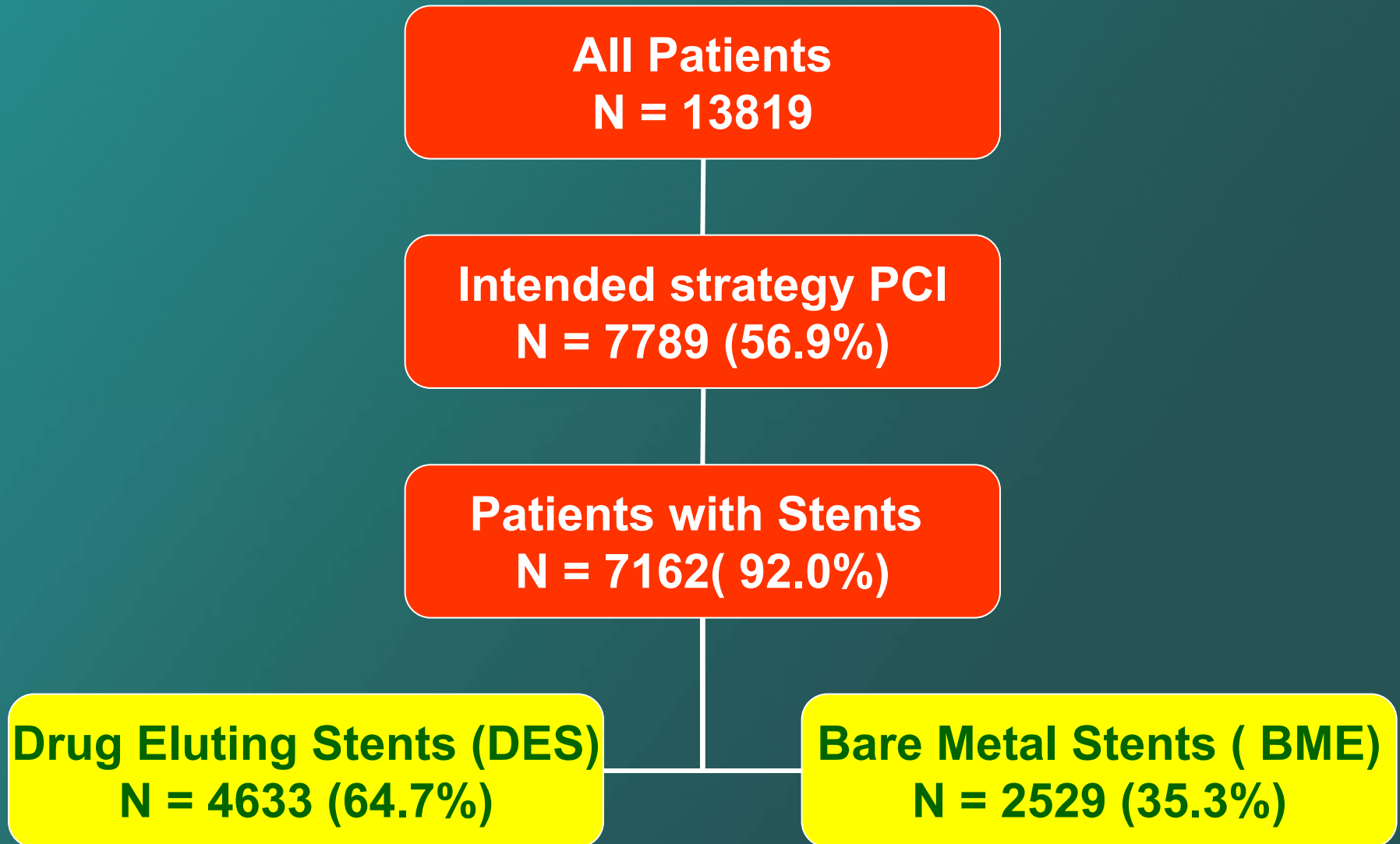
MEDICAL CENTER

Stone GW et al. AHJ 2004;148:764-75

CARDIOVASCULAR
RESEARCH FOUNDATION



Patient Flow Chart



Baseline Characteristics: DES vs. BMS

	DES (N=4633)	BMS (N=2529)	P-value
Age (median [range], yrs)	61.0 [21, 95]	65.0 [31, 92]	<0.0001
Female (%)	27.8	24.2	0.0008
Weight (median [IQR], kg)	85.0 [75.0- 98.0]	82.0 [73.0, 92.0]	<0.0001
Diabetes(%)	29.2	22.5	<0.0001
Hypertension (%)	65.7	61.6	0.0004
Hyperlipidemia (%)	58.5	46.6	<0.0001
Current smoker (%)	31.1	29.9	0.319
Prior MI (%)	31.2	24.6	<0.0001
Prior PCI (%)	42.8	26.0	<0.0001
Prior CABG (%)	18.6	13.9	<0.0001
Thienopyridine exposure	65.8	71.8	<0.0001
Renal insufficiency* (%)	17.1	20.2	0.0017
High Risk* (%)	71.4	86.9	<0.0001



Procedural Characteristics – PCI pts

	DES (N=4633)	BMS (N=2529)	P-value
Attempted lesions per pt			
- 1	63.8	63.3	0.6376
- 2	25.3	26.4	0.2582
- ≥3	10.8	10.3	0.6701
Attempted vessels per pt			
- ≥2	19.9	12.9	<0.0001
Target Vessel			
- Left main	1.7	1.6	0.8301
- LAD	41.9	44.5	0.1408
- LCX	34.8	34.9	0.7217
- RCA	38.5	36.6	0.1344
- Bypass graft conduit	6.8	7.4	0.7280

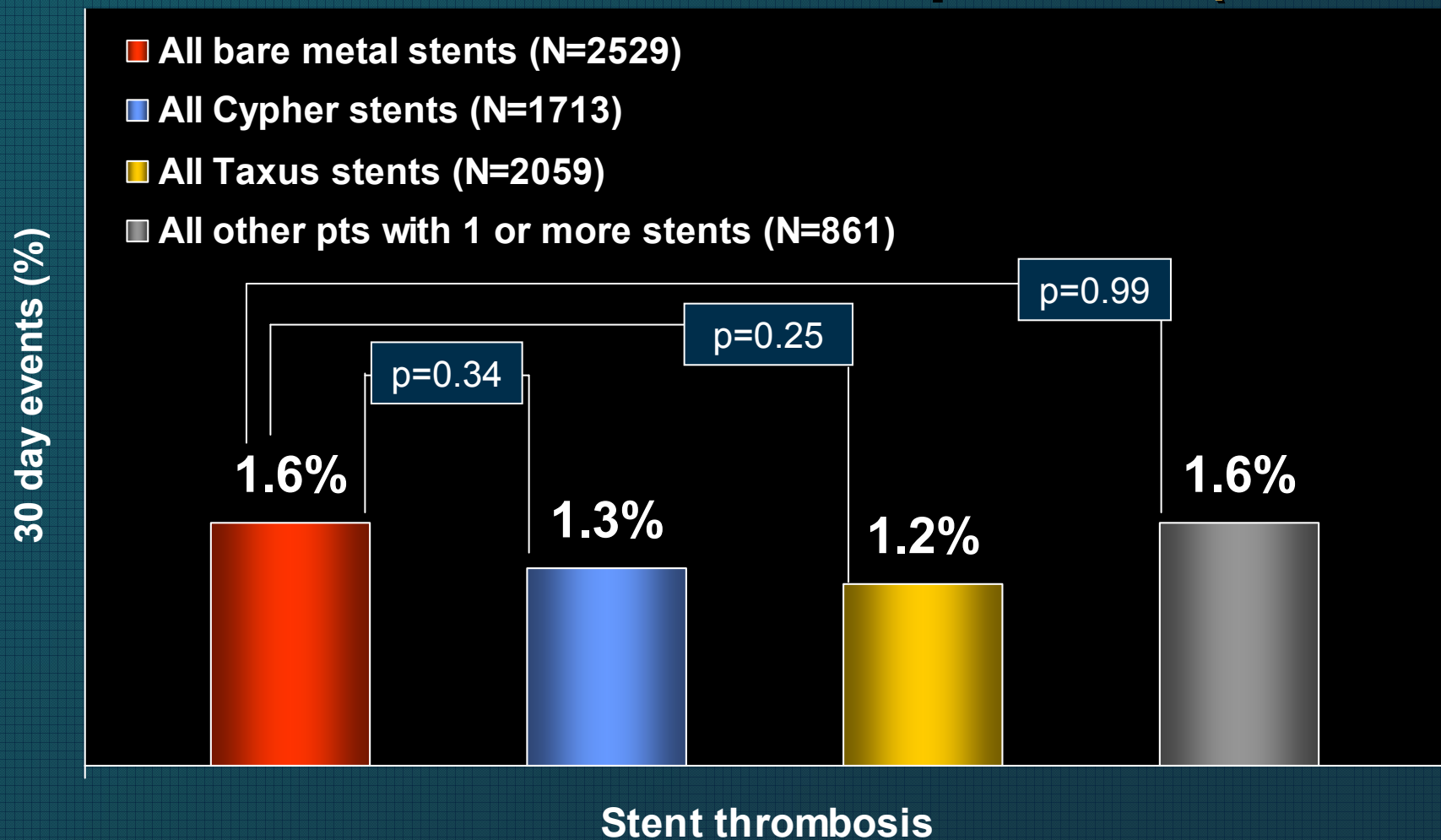
Stent Thrombosis Adjudication

- **Total Stent Thrombosis = 107**
 - **Definite Thrombosis = 59**
(angio confirmed)
 - **Probable Thrombosis = 48**



Adjudicated Stent Thrombosis

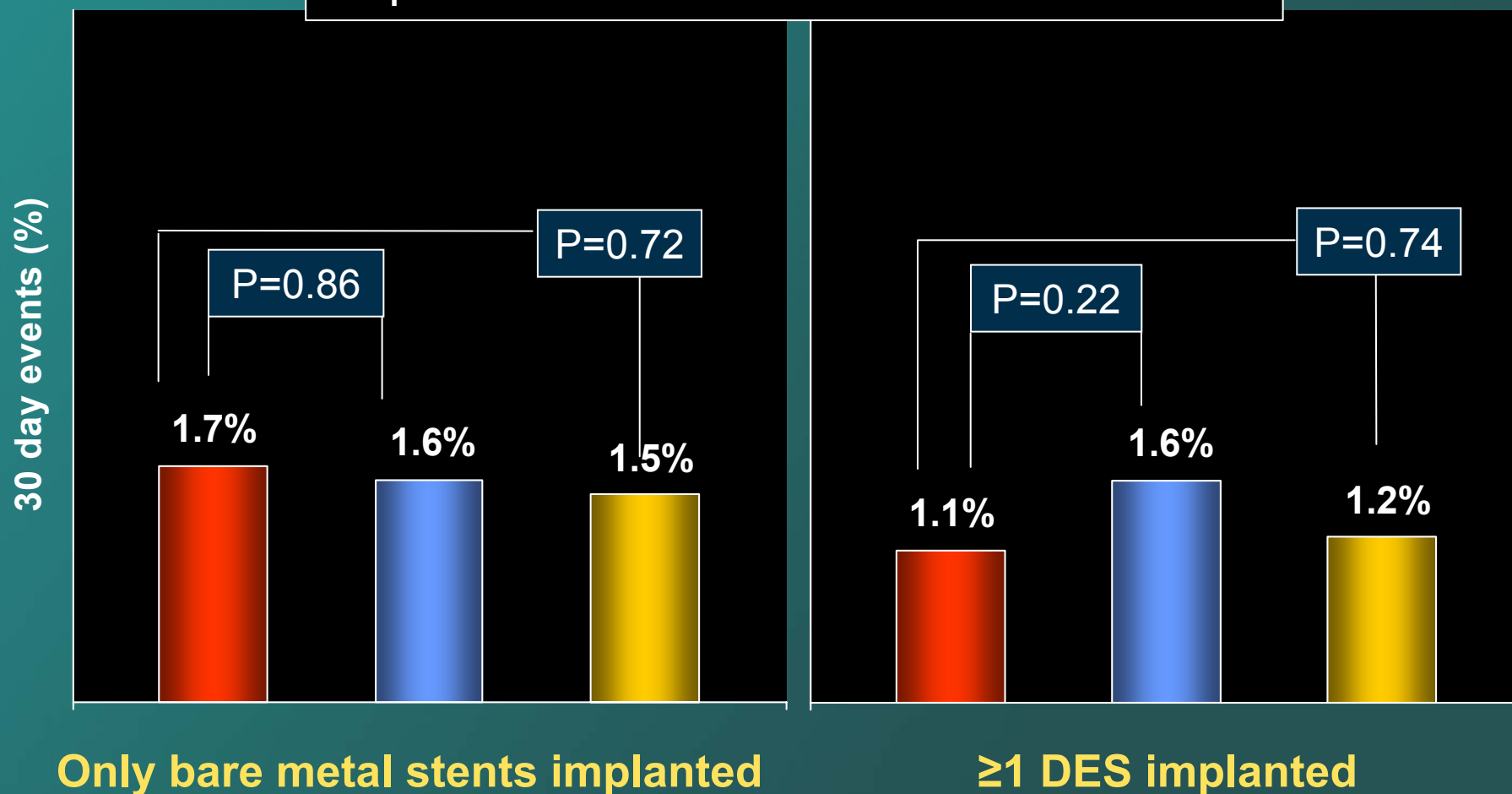
PCI Patients With ≥ 1 Stent Implanted (N=7,162)



Adjudicated Stent Thrombosis

PCI Patients With ≥ 1 Stent Implanted (N=7,162)

■ Heparin+IIb/IIIa ■ Bivalirudin+IIb/IIIa ■ Bivalirudin alone



Summary

- **Early Stent thrombosis in consecutive series of patients presenting with ACS undergoing PCI is higher than observed in controlled clinical trials of DES/BMS**
- **The rate is no different between DES and BMS**
- **One year follow-up is complete and adjudication for LATE SAT is ongoing using ARC definitions for presentation at ACC 2007 in March.**

