The interventional Trials of the Year: 2007-2008 (TCT, AHA, and ACC)

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Associate Professor of Medicine
Joint Chief Scientific Officer

Columbia University Medical Center
Cardiovascular Research Foundation

TCT 2007
TRANSCATHETER CARDIOVASCULAR THERAPEUTICS

CARDIOVASCULAR RESEARCH FOUNDATION

Disclosures

- **Roxana Mehran**
  - **Research support: Boston Scientific, Abbott Vascular and The Medicines Company**
  - **Consultant: Abbott Vascular, Medtronic, The Medicines Company**

Trial of the Year: Topics to Cover

1. "Real world" DES v. BMS use
2. Next generation stents in the U.S.
   - Endeavor and Xience V
3. Balance of Bleeding vs. ischemic complications post PCI
4. Left Main and Bifurcation lesions

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4. **Left Main and Bifurcation lesions**

Swedish Coronary Angiography and Angioplasty Registry

Outcome of Drug eluting compared to Bare metal stents in Sweden- "On" versus "off label" indications

Jörg Carlsson, Stefan James, Johan Lindbäck, Tage Nilsson, Ulf Stenestrand, Lars Wallentin and Bo Lagerqvist for the SCAAR study group

Presented by Stefan James, MD, PhD

Uppsala Clinical Research center

Uppsala University hospital, Sweden

Non of the authors have any conflicts of interest in relation to the presentation and the SCAAR registry is not industry sponsored

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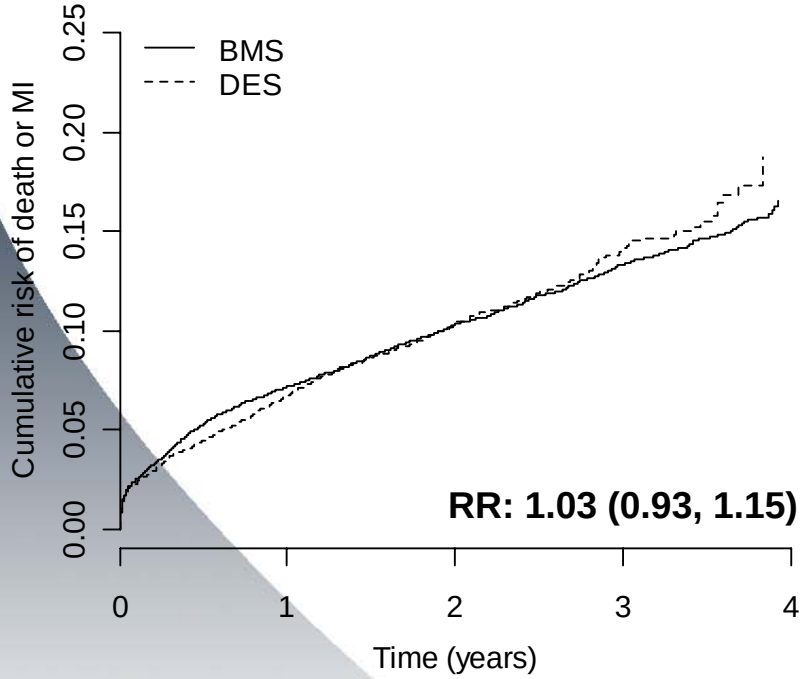
SCAAR

Adjusted Death /MI
Total cohort

On label use

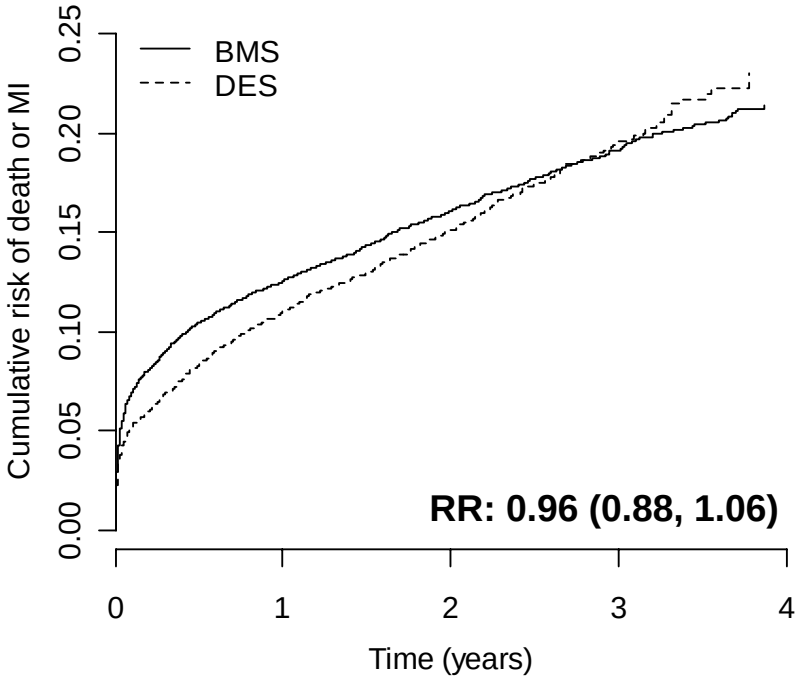
N=17 664



BMS	10049	9529	9343	8112	6742	5265	3486	1892	5
DES	6523	6222	6069	4428	2947	1868	908	322	0

Off label use

N=16 866



BMS	9434	8424	8223	6896	5431	4012	2433	1285	2
DES	6165	5673	5512	3792	2508	1525	780	287	0

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SCAAR

Two-Year Clinical Outcome After Implantation of Drug Eluting or Bare Metal Coronary Stents in Western Denmark

Lisette Okkels Jensen[1], Anne Kaltoft[2], Michael Maeng[2], Per Thayssen[1], Hans Henrik Tilsted Hansen[3], Morten Bottcher[2], Jens Flensted Lassen[2], Lars Romer Krusell[2], Klaus Rasmussen[3], Knud Noerregaard Hansen[1], Knud Erik Pedersen[1], Henrik Toft Soerensen[4], Lars Pedersen[4], Soeren Paaske Johnsen[4], Leif Thuesen[2]

[1]Odense University Hospital, [2]Skejby Hospital, [3]Aalborg Hospital, [4]Department of Clinical Epidemiology, University of Aarhus, Denmark

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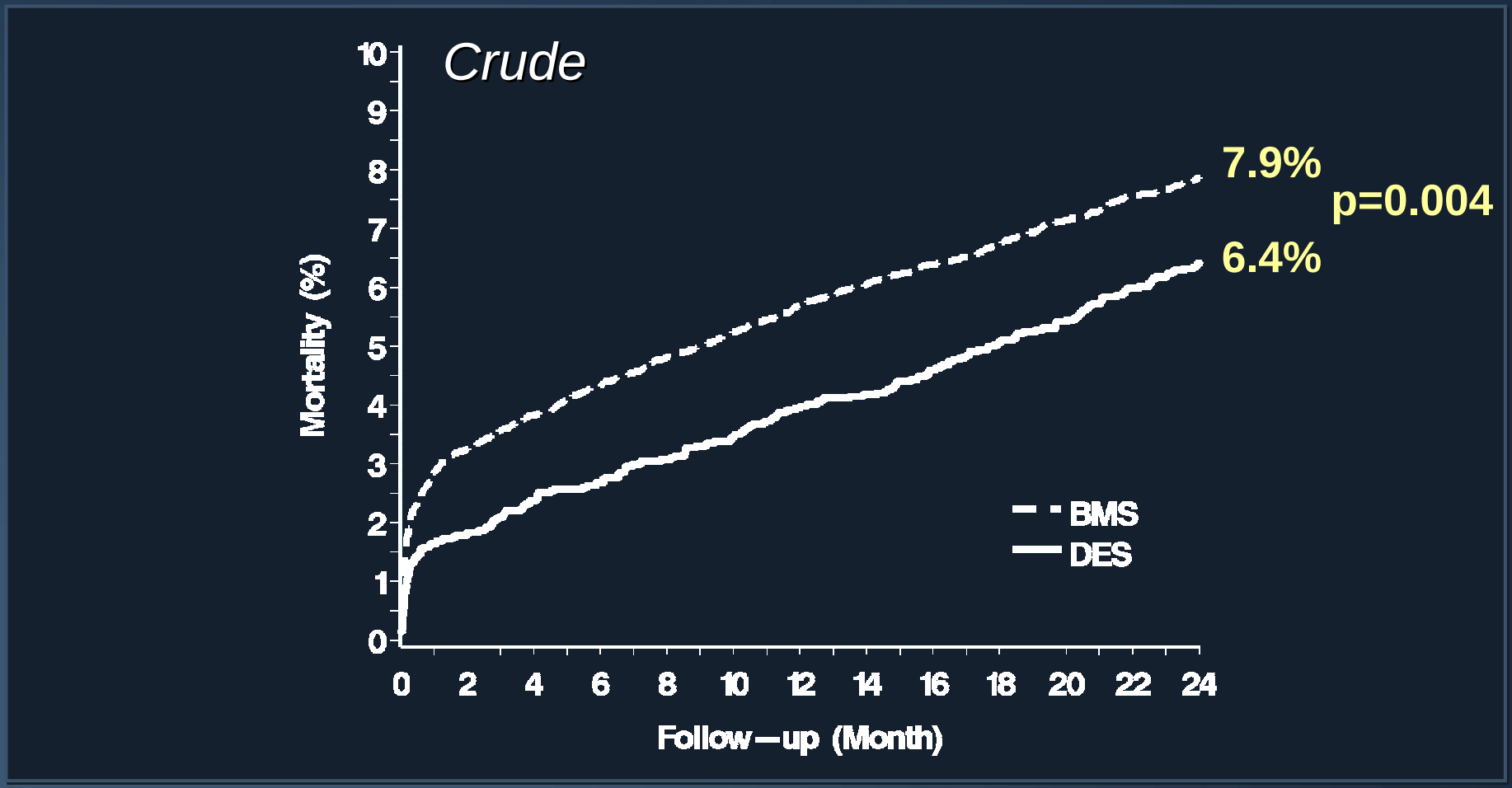
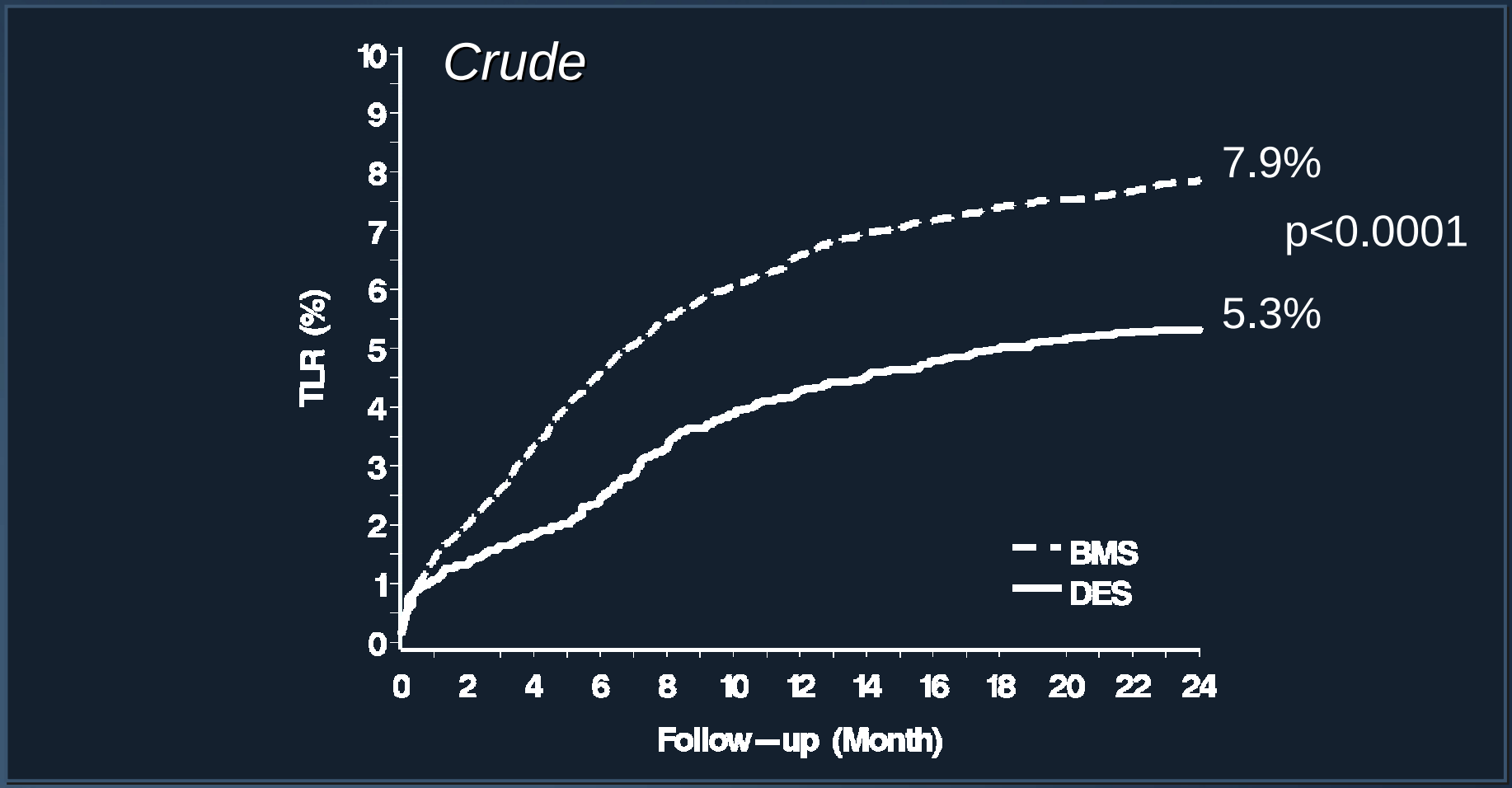
All Cause Mortality

BMS n= 8,847, DES n=3,548



Target Lesion Revascularization

BMS n= 8,847, DES n=3,548

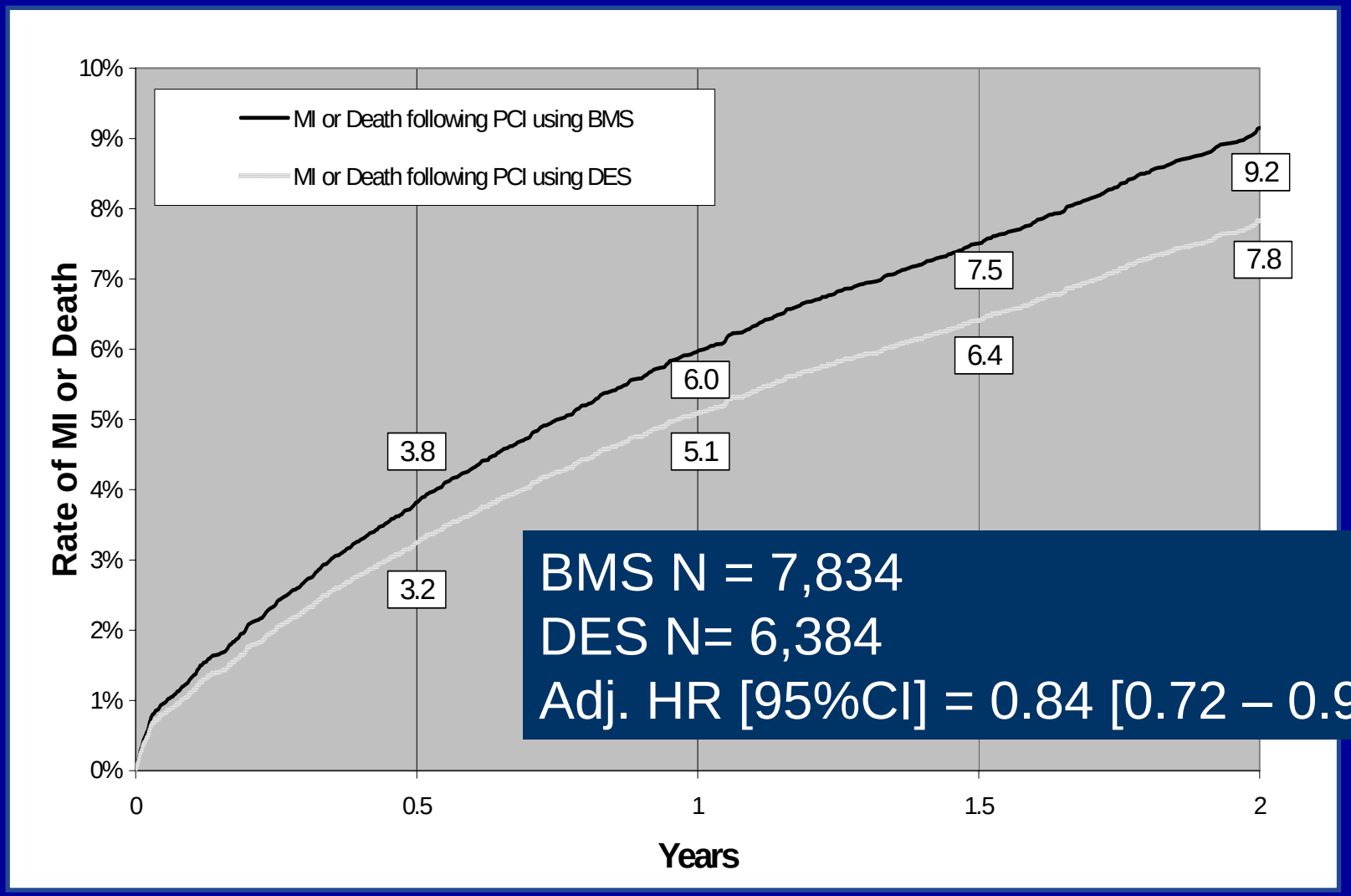


Outcomes of Drug-Eluting vs. Bare-Metal Stents in New York

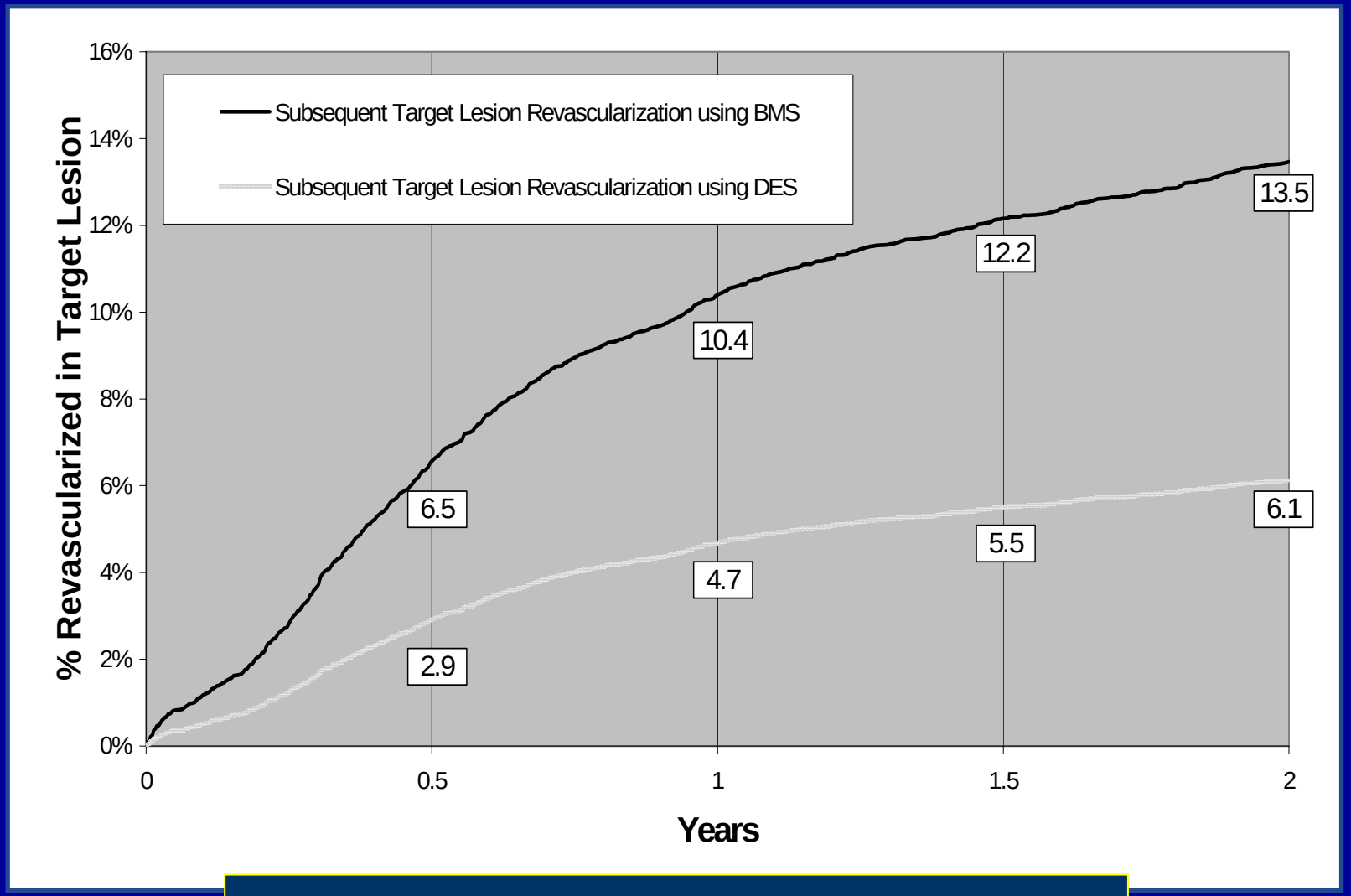
Edward L. Hannan, PhD, MS, MS, FACC

Michael Racz, MA, PhD

Two Year Adjusted Outcome (MI or Death) following PCI: Bare Metal Stent(BMS) vs. Drug Eluting Stent (DES)



Adjusted Rates of Subsequent Revascularization in Target Lesion: Bare Metal Stent(BMS) vs. Drug Eluting Stent(DES)



Adj. HR [95%CI] = 0.43 [0.39 – 0.49]

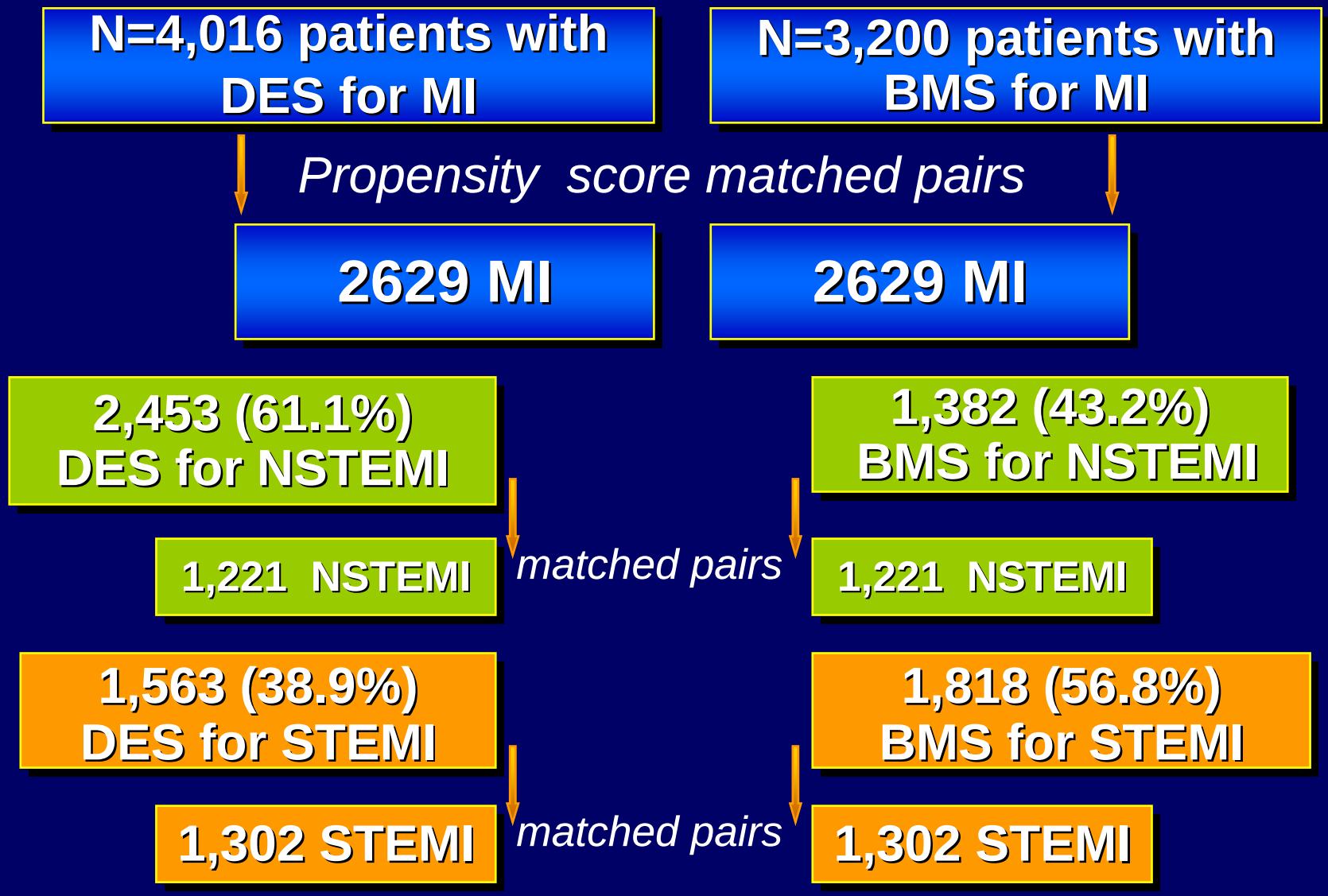
Drug-Eluting and Bare Metal Stenting for Acute Myocardial Infarction in Massachusetts

Laura Mauri, Treacy S. Silbaugh, Robert E. Wolf, Katya Zelevinsky, Ann Lovett, Manu Varma, and Sharon-Lise T. Normand

Brigham and Women's Hospital, Harvard Medical School, Harvard School of Public Health all in Boston, Massachusetts

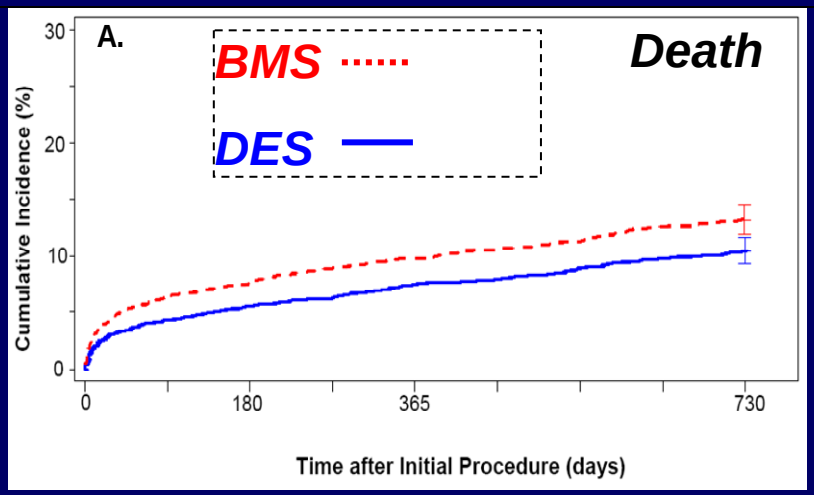
March 30, 2008
American College of Cardiology, Chicago

Drug-Eluting and Bare Metal Stenting for Acute Myocardial Infarction

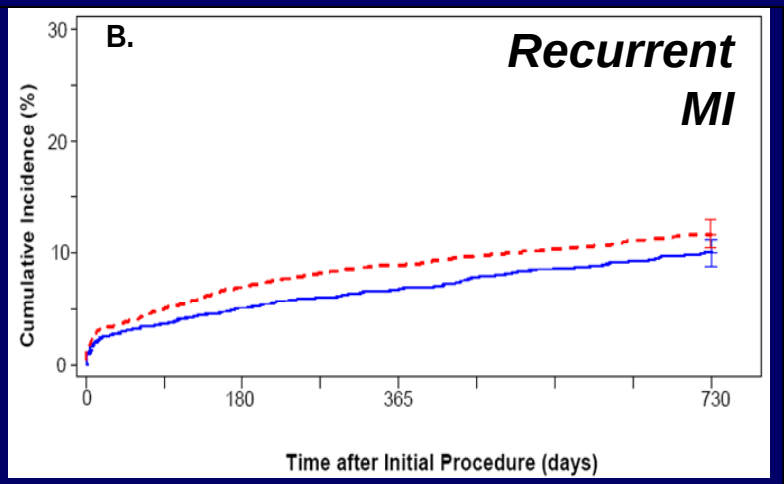


Drug-Eluting & Bare Metal Stenting in Massachusetts

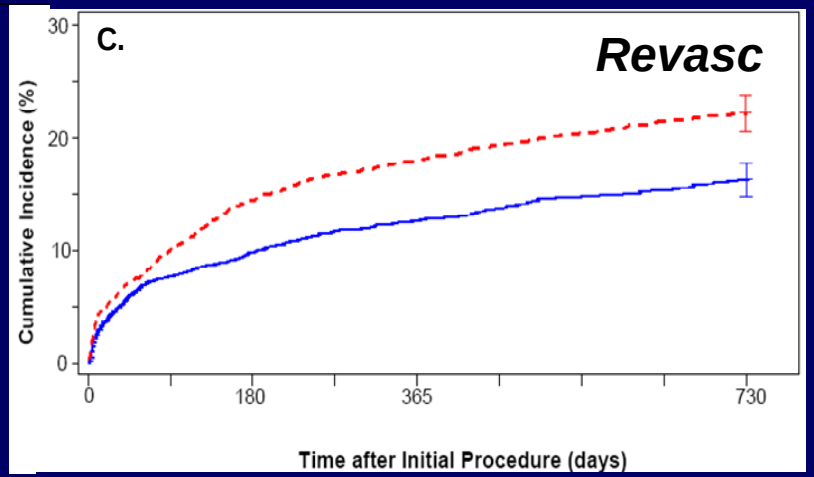
2-Year Outcome in Matched MI Patients



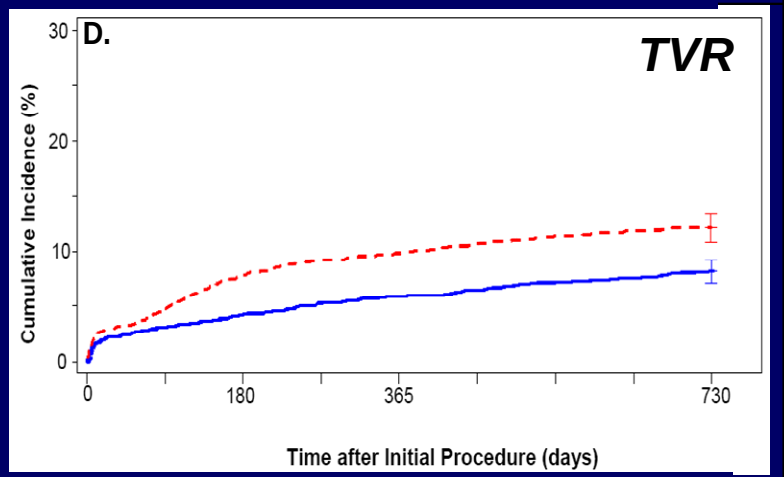
No. at Risk	0	30	180	365	730
DES	2629	2618	2550	2484	2433
BMS	2629	2614	2512	2431	2373



No. at Risk	0	30	180	365	730
DES	2629	2604	2483	2368	2283
BMS	2629	2592	2430	2285	2192



No. at Risk	0	30	180	365	730
DES	2629	2624	2427	2243	2127
BMS	2629	2618	2372	2091	1957



No. at Risk	0	30	180	365	730
DES	2629	2624	2492	2380	2291
BMS	2629	2618	2443	2250	2148

Trial of the Year: Topics to Cover

1. **"Real world" DES v. BMS use**
2. *Next generation stents in the U.S.*
   - *Endeavor and Xience V*
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4. **Left Main and Bifurcation lesions**

Endeavor 4: A Randomized Comparison of a Zotarolimus-Eluting Stent and a Paclitaxel-Eluting Stent in Patients with Coronary Artery Disease

Martin B. Leon, MD

Columbia University Medical Center
Cardiovascular Research Foundation
New York City

TCT 2007
TRANSCATHETER CARDIOVASCULAR THERAPEUTICS

Monday, October 22, 2007

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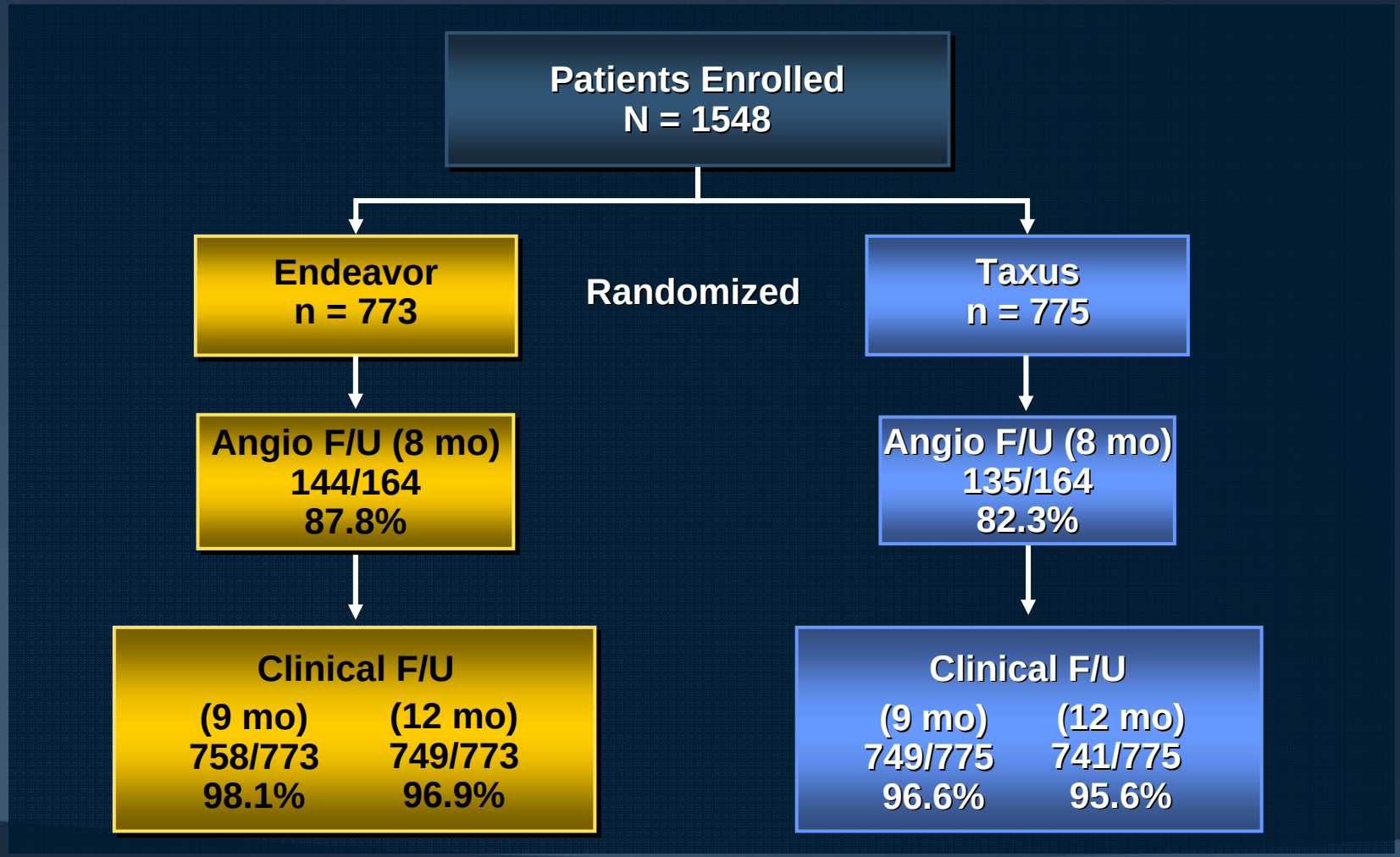
Endeavor IV
Patient Flowchart



18.6% with angio FU

Endeavor IV
Restenosis at 8 Months (QCA)

	Endeavor (144 pts)	Taxus (135 pts)	*P value*
Binary Restenosis - % (#)			
In-stent	13.3 (19)	6.7 (9)	0.075
Proximal edge	3.6 (5)	3.8 (5)	1.000
Distal edge	0.7 (1)	0.7 (1)	1.000
In-segment	15.3 (22)	10.4 (14)	0.284

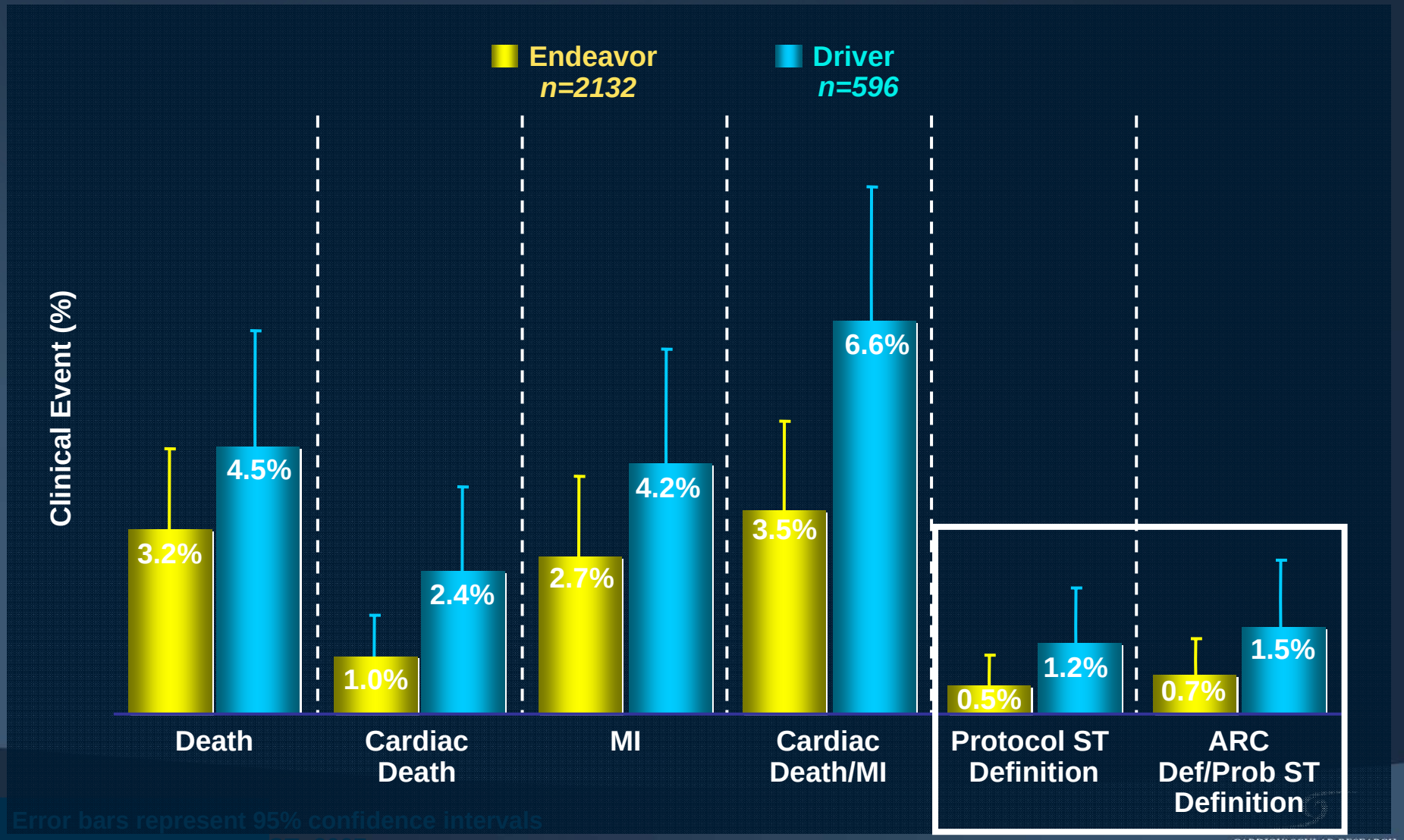
Endeavor IV
Clinical Events at 9 months

	Endeavor n=758	Taxus n=749	*P-Value*
Death (all) – % (#)	0.7 (5)	0.8 (6)	0.772
Cardiac	0.4 (3)	0.3 (2)	1.000
MI (all) – % (#)	1.5 (11)	2.4 (18)	0.194
Q Wave	0.3 (2)	0.1 (1)	1.000
Non Q wave	1.2 (9)	2.3 (17)	0.117
Death (cardiac) + MI (all) – % (#)	1.8 (14)	2.7 (20)	0.303
Stent Thrombosis (all) – % (#)	0.8 (6)	0.1 (1)	0.124
0-30 days	0.4 (3)	0.1 (1)	0.625
31-270days	0.4* (3)	0	0.250
TLR – % (#)	4.1 (31)	2.7 (20)	0.154
TVR (non-TL) – % (#)	2.0 (15)	2.8 (21)	0.316
TVR – % (#)	5.4 (41)	4.9 (37)	0.728
MACE – % (#)	5.5 (42)	5.6 (42)	1.000
TVF – % (#)	6.6 (50)	7.2 (54)	0.685

*Day 83, 145, 171

Endeavor Safety Analysis

Cumulative Incidence of Safety Endpoints to 1080 Days

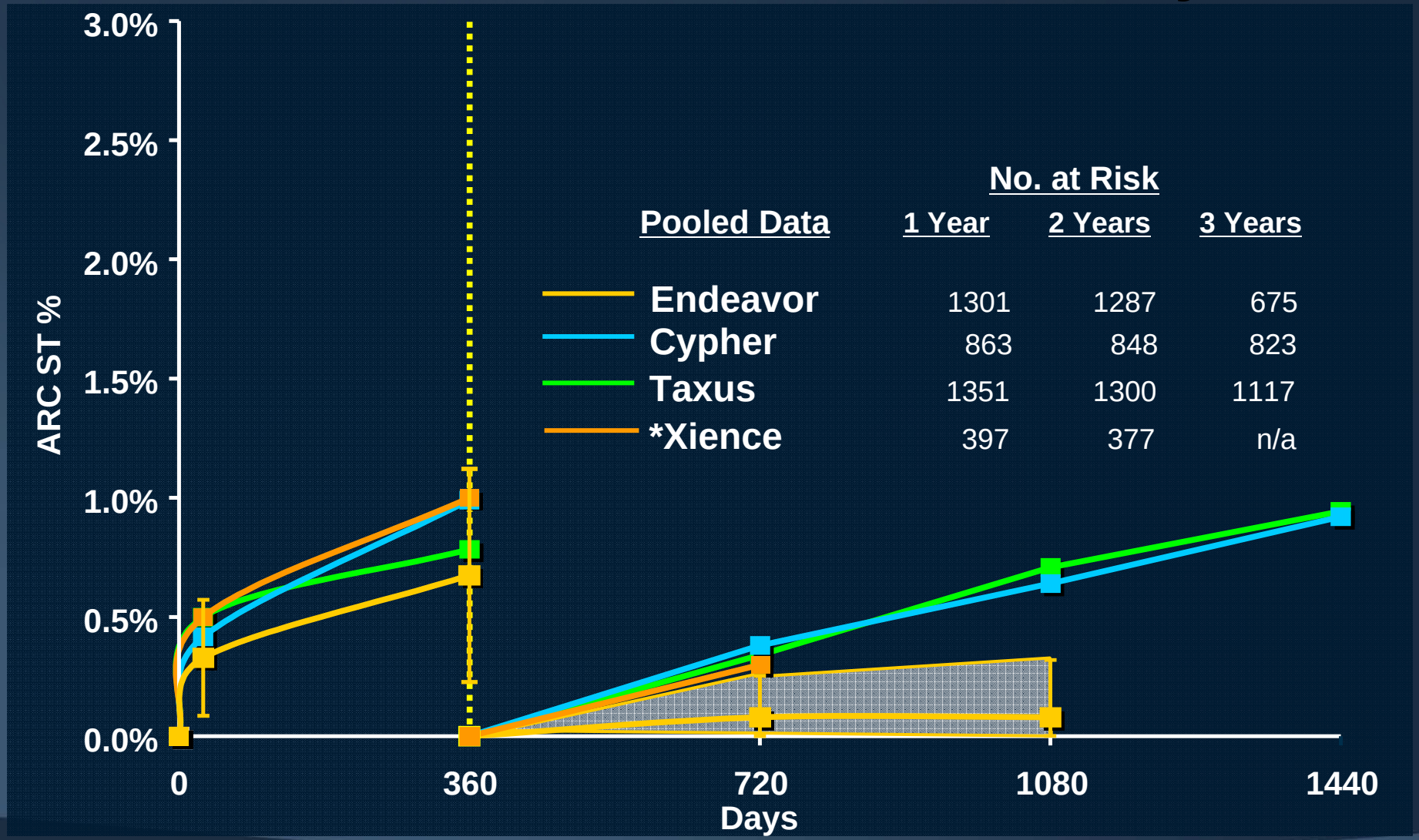


Error bars represent 95% confidence intervals

CT. 2007

DES Comparison

ARC Definite and Probable ST to 3 years



Pooled Data	No. at Risk 1 Year	2 Years	3 Years
Endeavor	1301	1287	675
Cypher	863	848	823
Taxus	1351	1300	1117
*Xience	397	377	n/a

Mauri et al. N Engl J Med 2007;356:1020-9.
Endeavor: Mauri et al. TCT. 2007
Xience: FDA Panel Meeting Nov. 29, 2007
*Represents “SPIRIT II and III 2-year Complete Analysis” from FDA Panel

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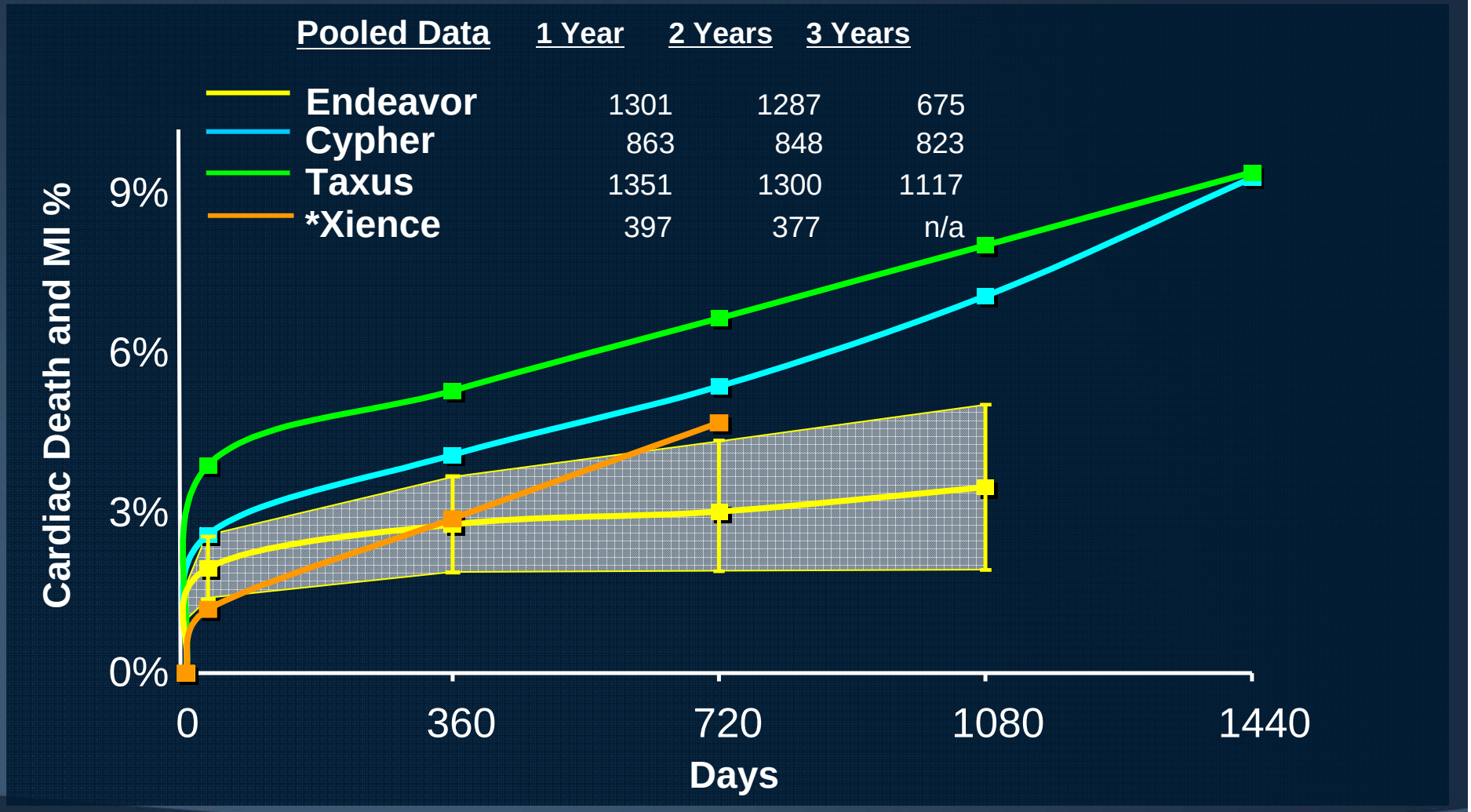
Mauri et al. N Engl J Med 2007;356:1020-9.
Endeavor: Mauri et al. TCT. 2007
Xience: FDA Panel Meeting Nov. 29, 2007

DES Comparison

Cardiac Death and MI to 3 years



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SPIRIT III: Study Algorithm

1002 pts enrolled at 65 U.S sites

RVD ≥2.5 mm - ≤3.75 mm; Lesion length ≤28 mm

Max. 2 lesions each in a different epicardial vessel

Pre-rand: ASA ≥ 300 mg, clopidogrel ≥300 mg load unless on chronic Rx

Randomized 2:1 XIENCE V:TAXUS

Stratified by diabetes and intent for 1 vs. 2 lesion treatment

Pre-dilatation mandatory

Everolimus-eluting

XIENCE V

Paclitaxel-eluting

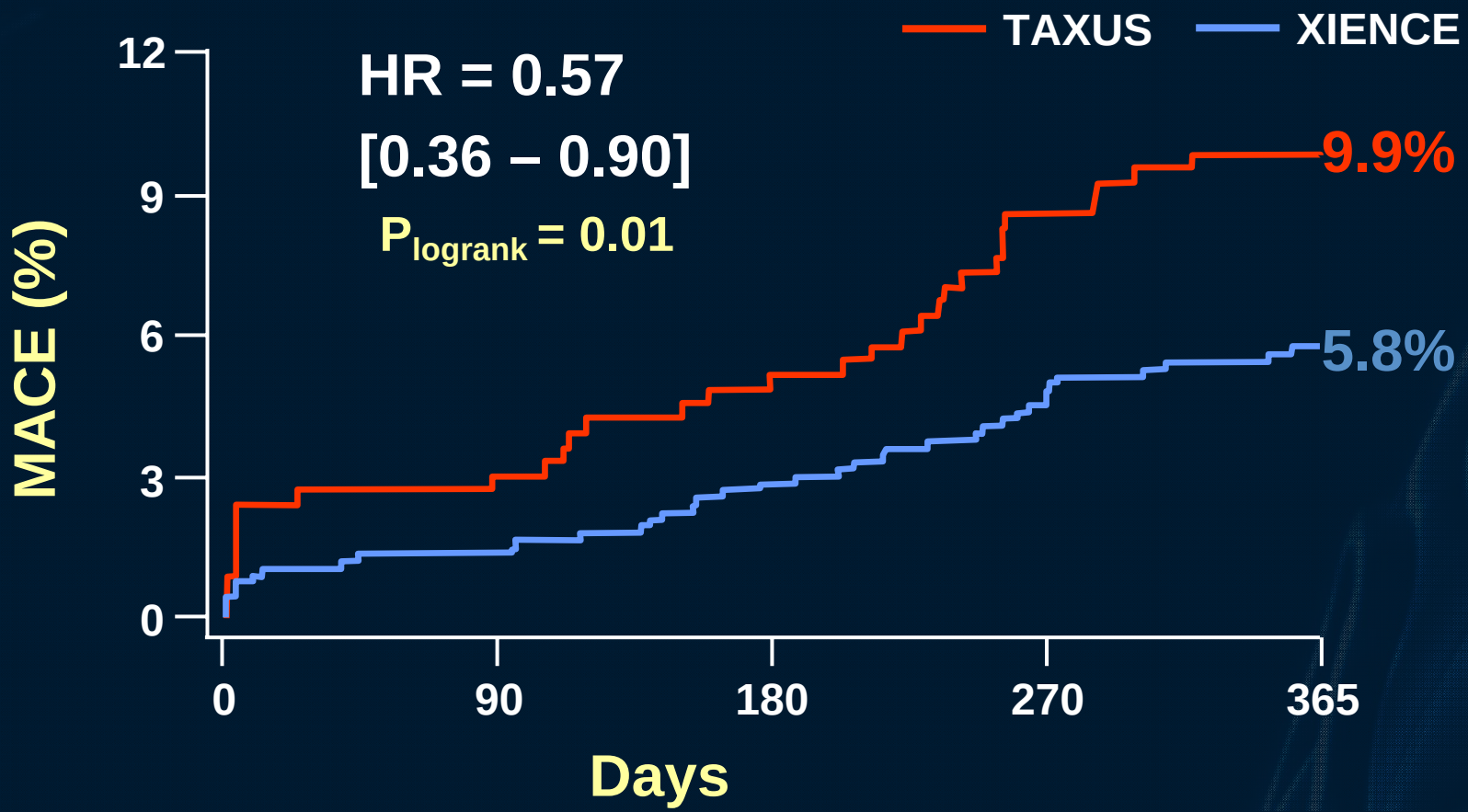
TAXUS

Aspirin ≥ 80 mg QD for 5 years; Clopidogrel 75mg QD for ≥6 months

Clinical f/u: 1, 6, 9 months and yearly for 1-5 years

Angio f/u (N=564) @ 8 mos; IVUS f/u (N=240) @ 8 mos

MACE Through 365 Days



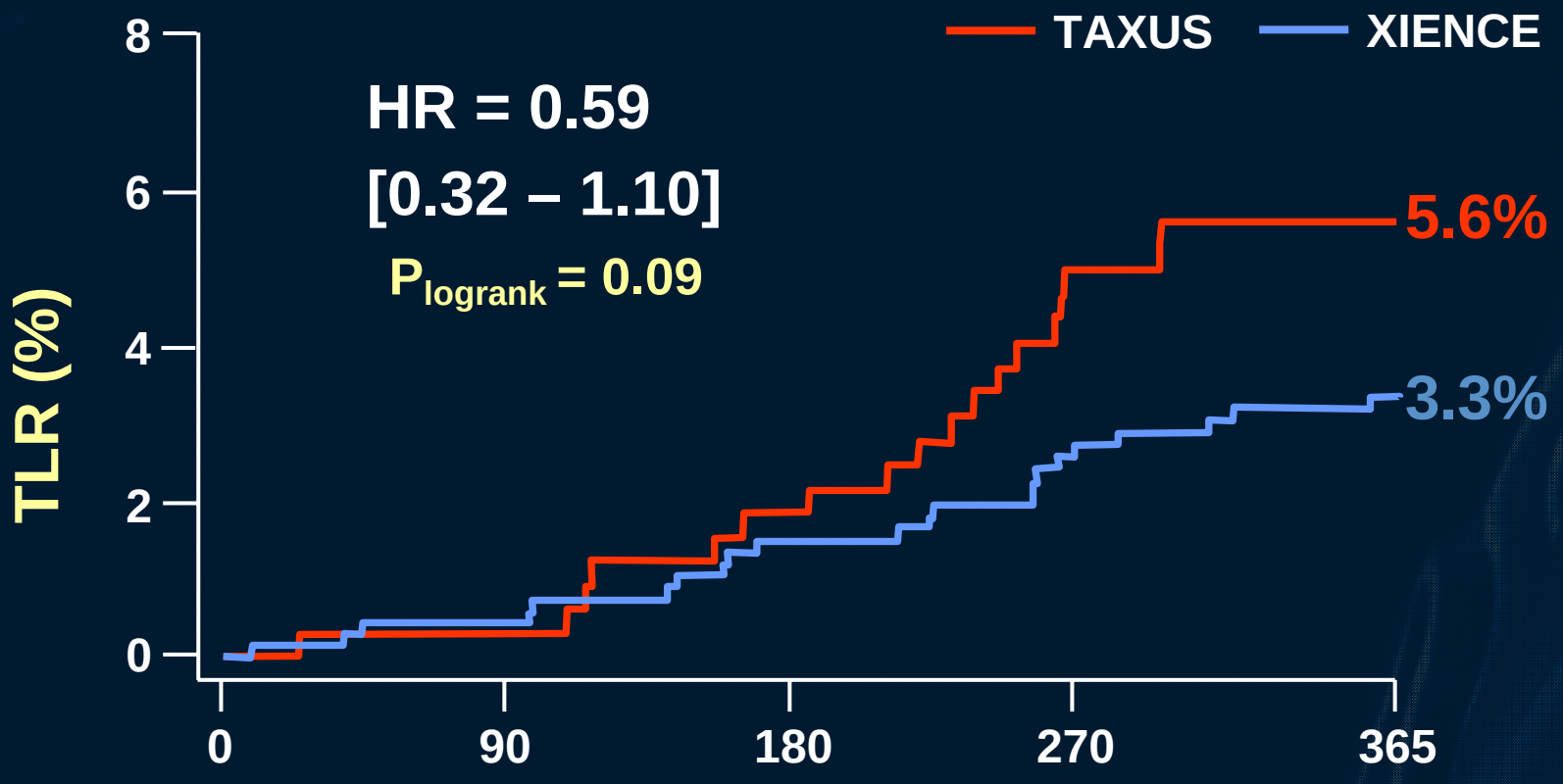
Number at risk

XIENCE	669	651	642	626	614
TAXUS	332	312	309	292	287

MACE = cardiac death, MI, or ischemia-driven TLR

Spirit III

Ischemia-driven TLR Through 365 Days



Number at risk

XIENCE	669	658	650	635	625
TAXUS	332	321	318	302	297

Spirit III

The SPIRIT II Study - A Clinical Evaluation of the XIENCE™ V Everolimus Eluting Coronary Stent System in the Treatment of Patients With *De Novo* Native Coronary Artery Lesions

Clinical, Angiographic and IVUS 2 year results

Patrick W. Serruys, MD, PhD

Thoraxcenter, Erasmus Medical Center, Rotterdam, the Netherlands

SCAI-ACCi2 Late-Breaking Clinical Trials III: DES

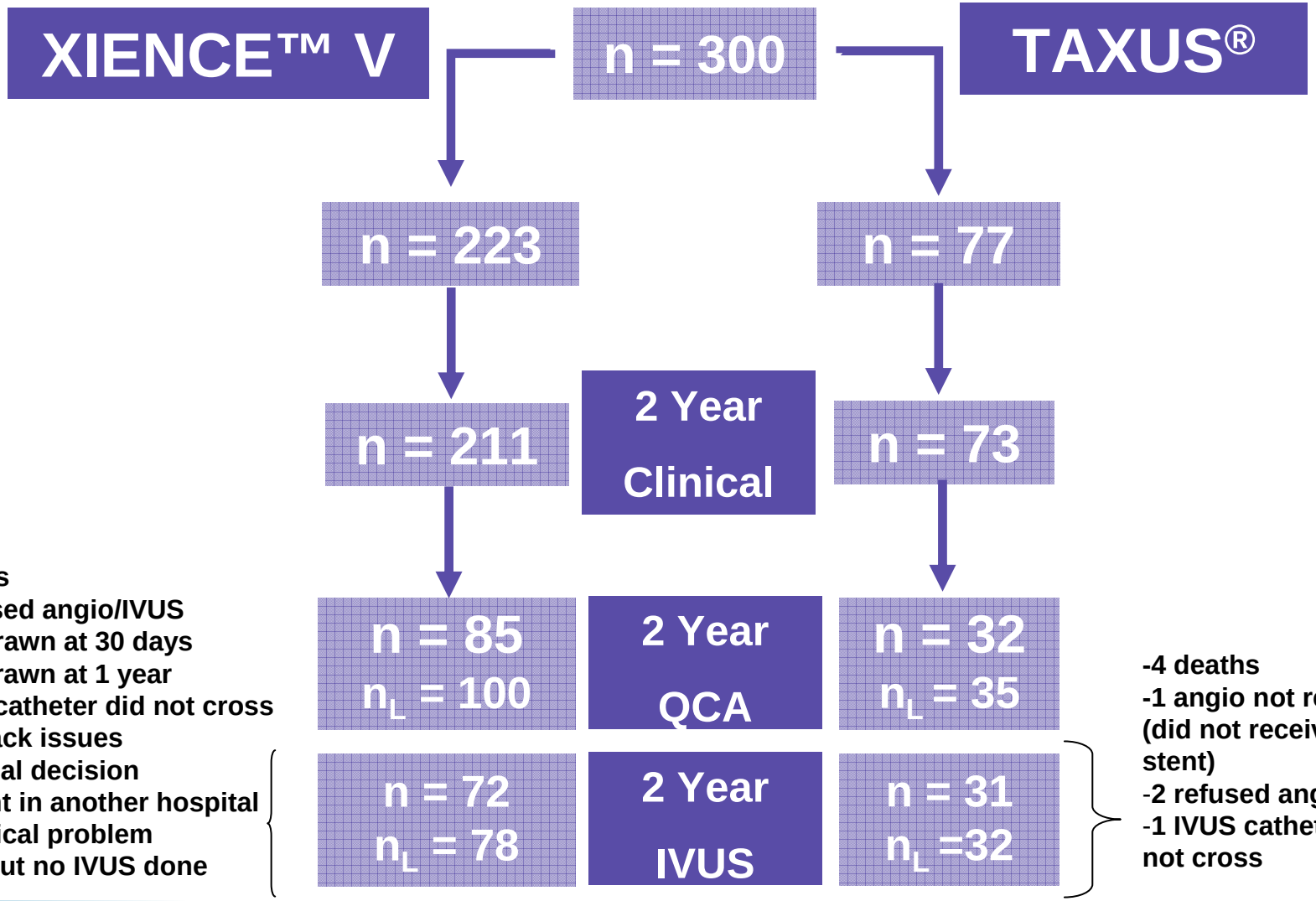
Monday March 31st, 2008 **8.45 am**

Professor Serruys has no conflict of interest related to this presentation

SE2926406 REV A

Clinical Study Population

Spirit II



*Total angiographic and IVUS subgroup: 152 patients (113 XIENCE™ V, 39 TAXUS®)

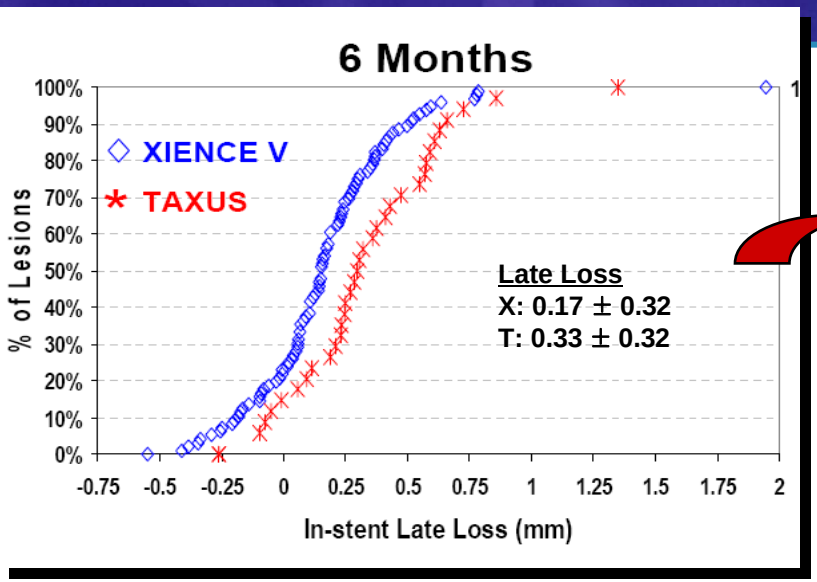
n_L: number of lesions

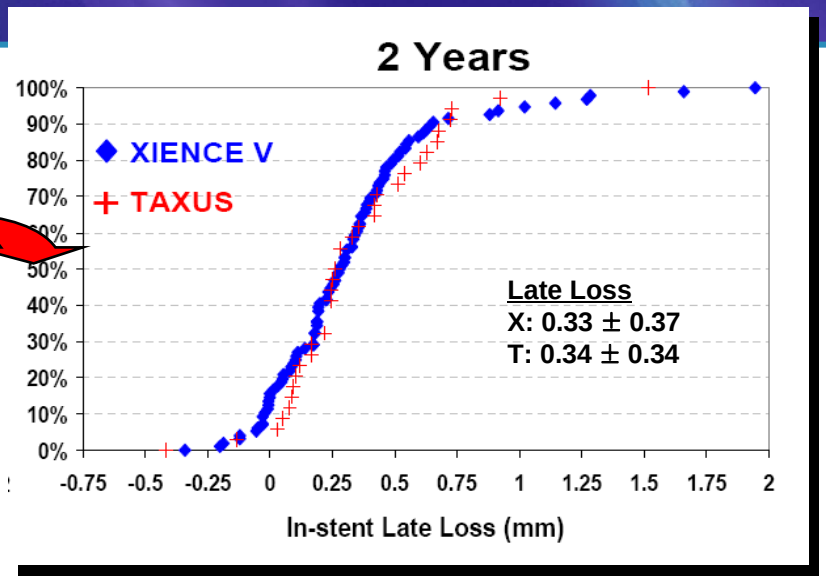
Angiographic follow-up at 2-year follow-up: XIENCE™ V: 75%; TAXUS®: 82% IVUS follow-up at 2-year follow-up: XIENCE™ V: 64%; TAXUS®: 79%

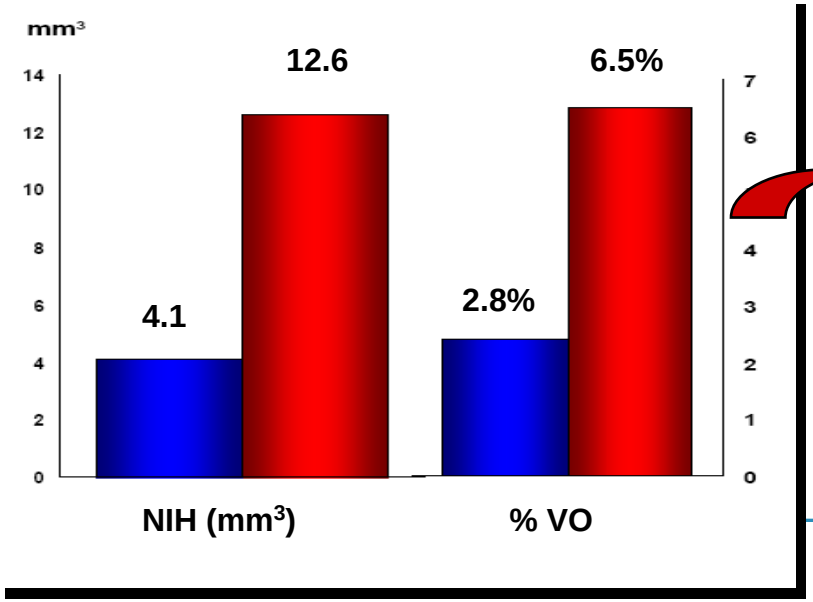
CAUTION: XIENCE™ V is an Investigational device. Limited by Federal (U.S.) law to investigational use only.

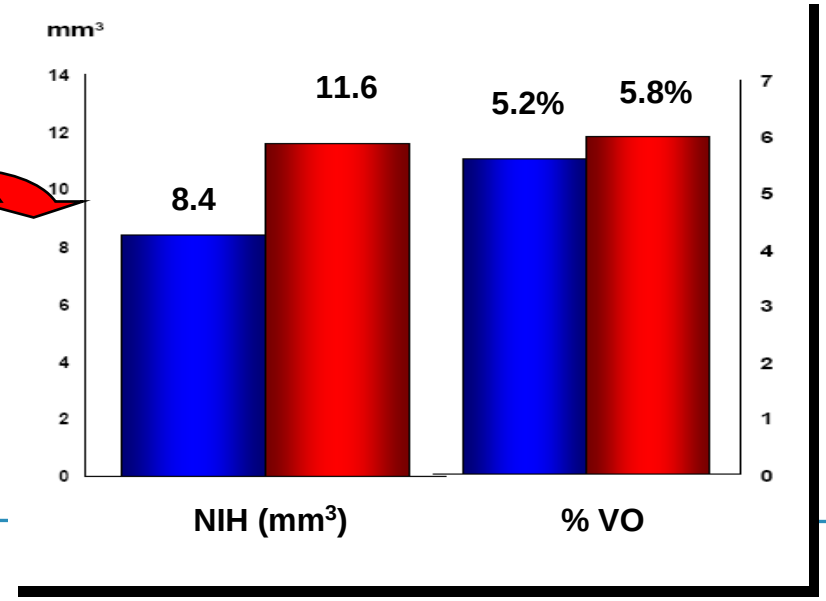
Xience-V: ↑Late Neointimal Growth

Spirit II



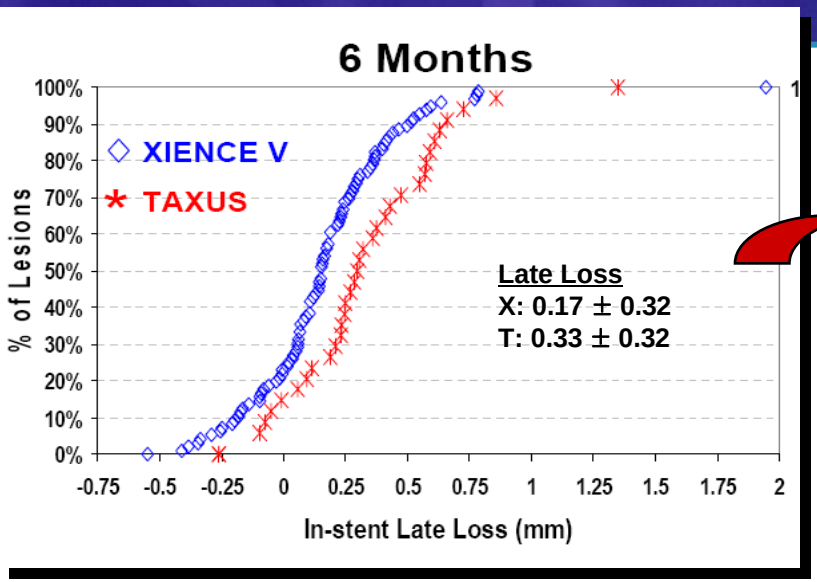


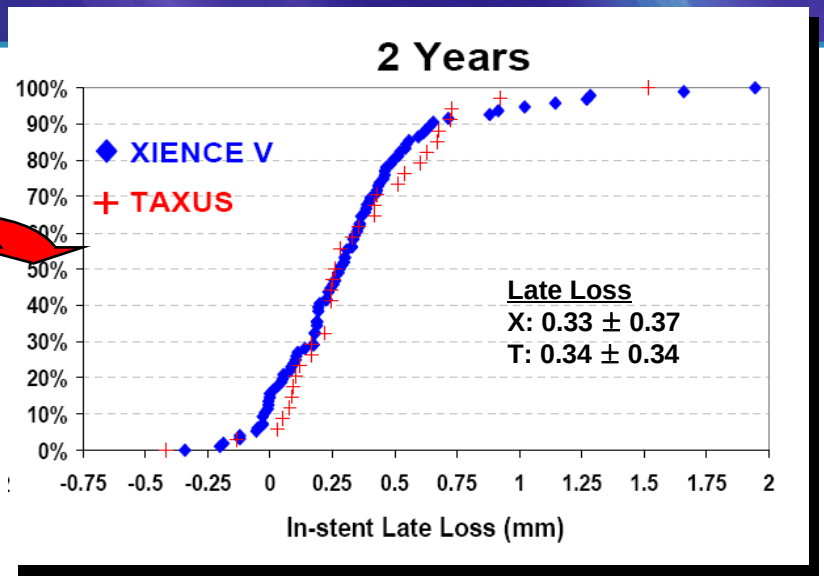


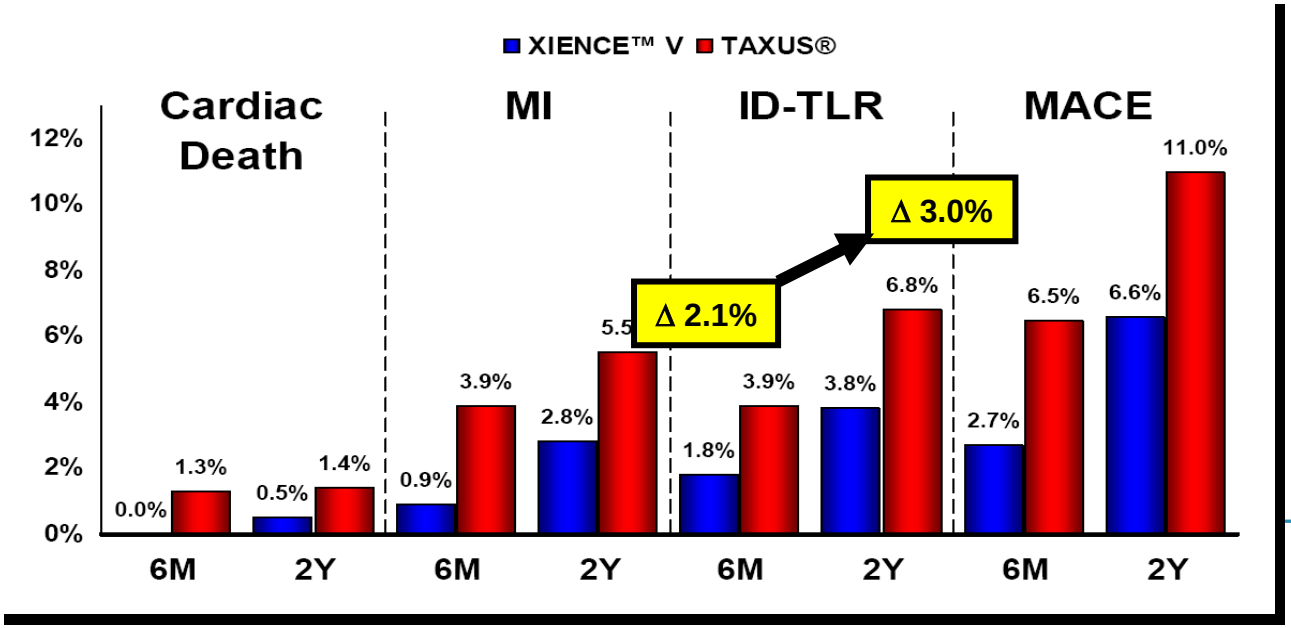


Angiographic-Clinical Dissociation?

Spirit II







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HORIZONS AMI

A Prospective, Randomized Comparison of Bivalirudin vs. Heparin Plus Glycoprotein IIb/IIIa Inhibitors During Primary Angioplasty in Acute Myocardial Infarction

– 30 Day Results –

Gregg W. Stone MD
For the HORIZONS AMI Investigators

HORIZONS AMI

Harmonizing **O**utcomes with **R**evascularization and **S**tents in AMI

3,602 pts with STEMI with symptom onset ≤12 hours

Aspirin, thienopyridine

R 1:1

- **UFH + GP IIb/IIIa inhibitor (abciximab or eptifibatide)**
- **Bivalirudin monotherapy (± provisional GP IIb/IIIa)**

Emergent angiography, followed by triage to…

CABG – Primary PCI – Medical Rx

3000 pts eligible for stent randomization

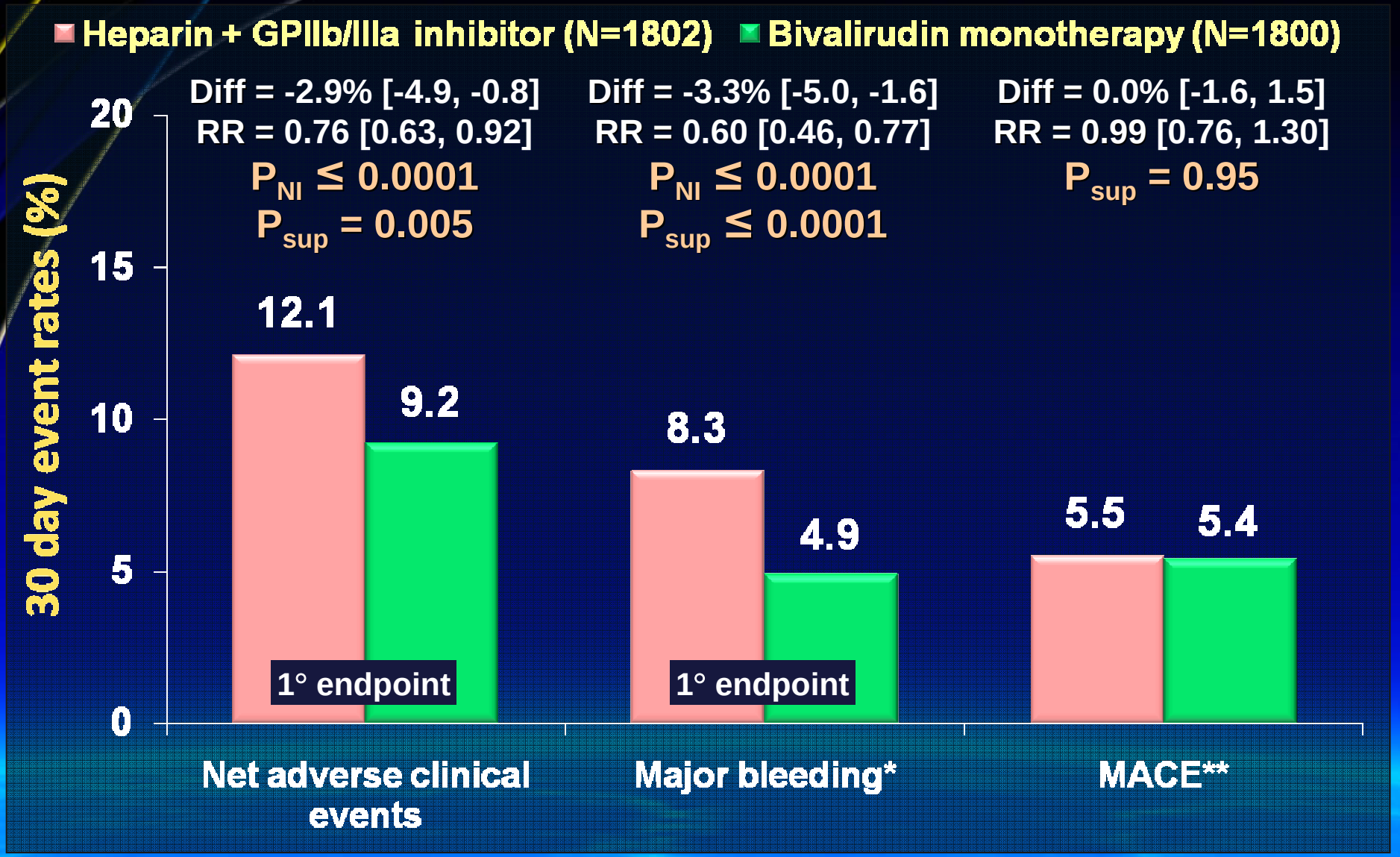
R 1:3

- **Bare metal stent**
- **TAXUS paclitaxel-eluting stent**

Clinical FU at 30 days, 6 months, 1 year, and then yearly through 5 years

HORIZONS AMI

Primary Outcome Measures (ITT)

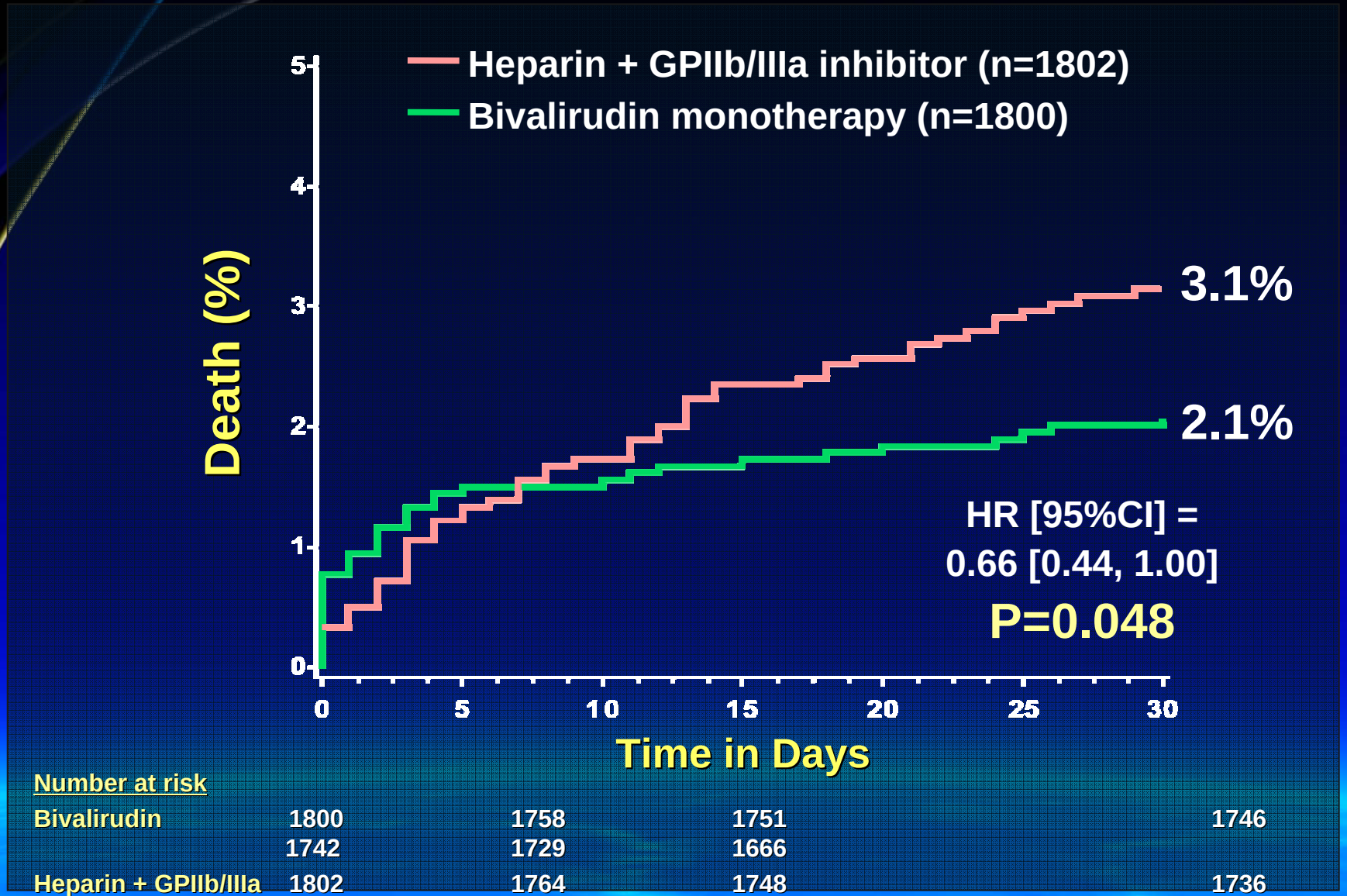


*Not related to CABG

**MACE = All cause death, reinfarction, ischemic TVR or stroke

HORIZONS-AMI

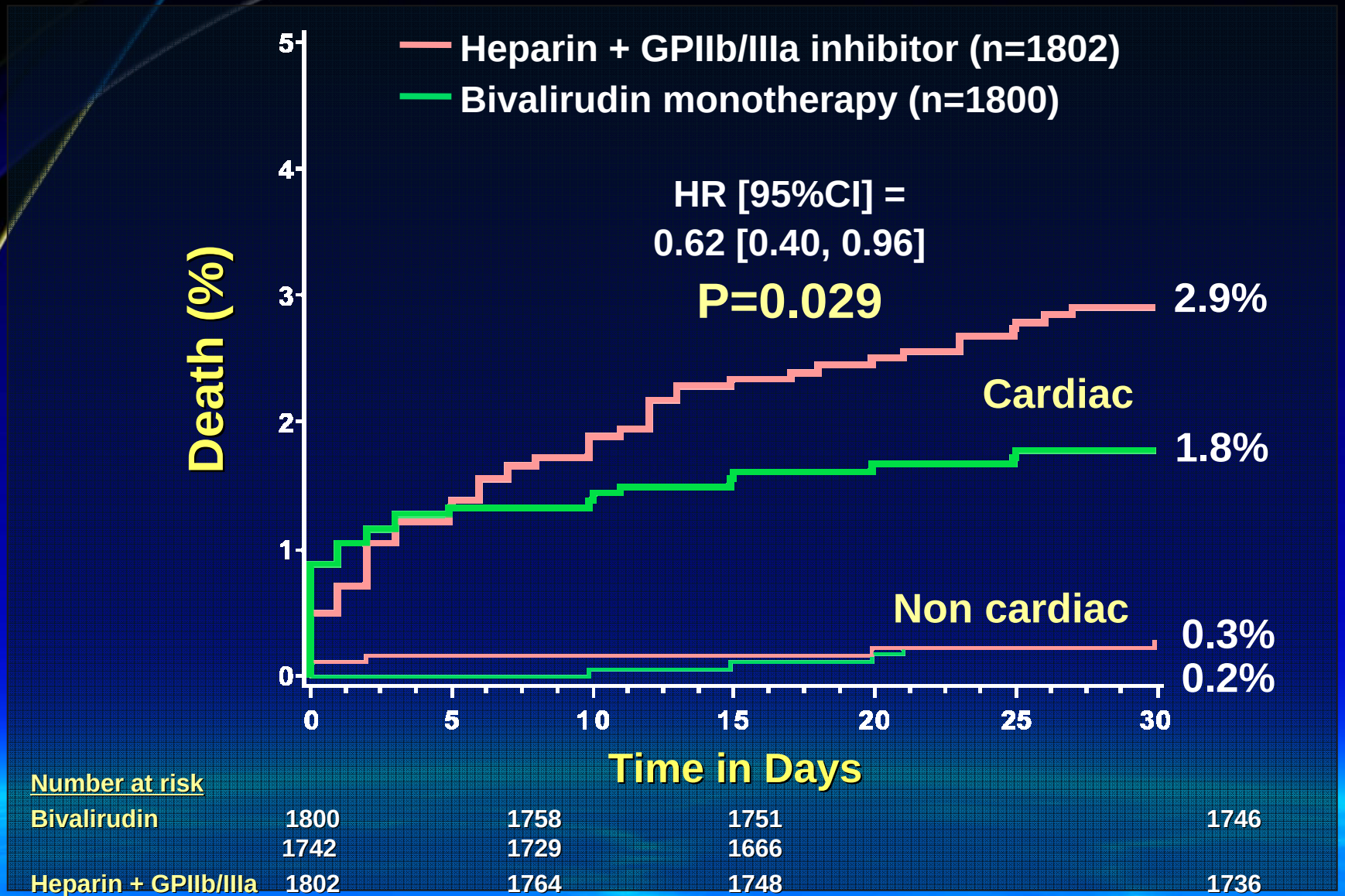
30 Day Mortality



Stone GW et al. In press.

HORIZONS-AMI

30 Day Mortality: Cardiac and Non Cardiac



Stone GW et al. In press.

HORIZONS AMI

30 Day Stent Thrombosis
(N=3,124 successfully stented pts)

	UFH + GP IIb/IIIa (N=1553)	Bivalirudin (N=1571)	P Value
ARC 30d definite or probable stent thrombosis*	**1.9%**	**2.5%**	**0.30**
- definite	1.4%	2.2%	0.09
- probable	0.5%	0.3%	0.24
- acute (≤24 hrs)	0.3%	1.3%	0.0007
- subacute (>24 hrs – 30d)	1.7%	1.2%	0.28

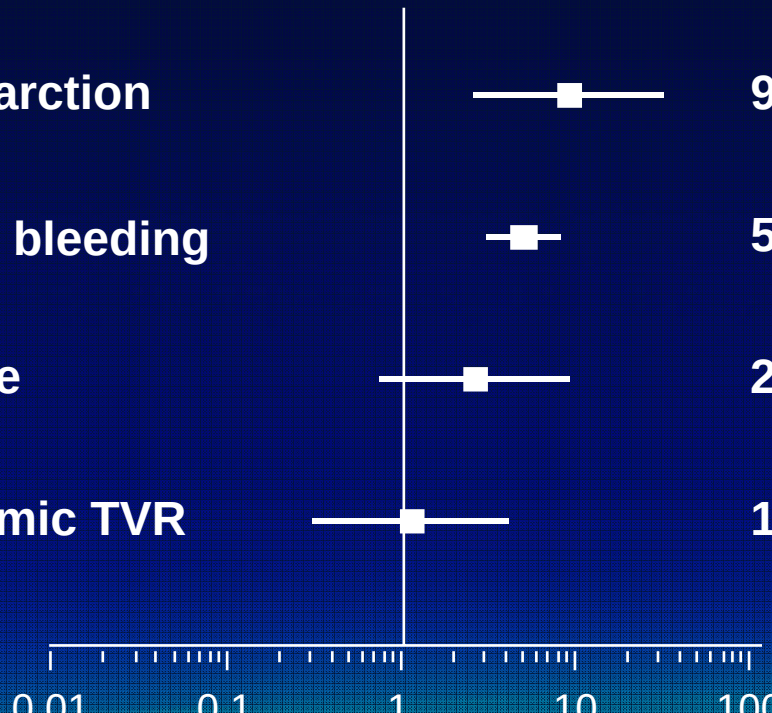
*Protocol definition of stent thrombosis, CEC adjudicated

HORIZONS-AMI

Time-updated covariate adjusted Cox model relating 30-day events to 30-day mortality

- Complete model with MACE components and major bleeding -

Risk Factor	HR [95% CI]	P-value	Attributable Deaths
Reinfarction	9.13 [2.62,31.85]	<0.001	8.9*
Major bleeding	5.08 [3.10, 8.35]	<0.001	20.9**
Stroke	2.65 [0.74, 9.43]	0.13	1.9
Ischemic TVR	1.15 [0.31, 4.20]	0.83	1.2



*9.6% of 93 total deaths

**22.5% of 93 total deaths

C-statistic = 0.87. Attributable deaths = N deaths among pts with the time updated event (attribute) X (adj. HR – 1)/adj. HR

HORIZONS-AMI

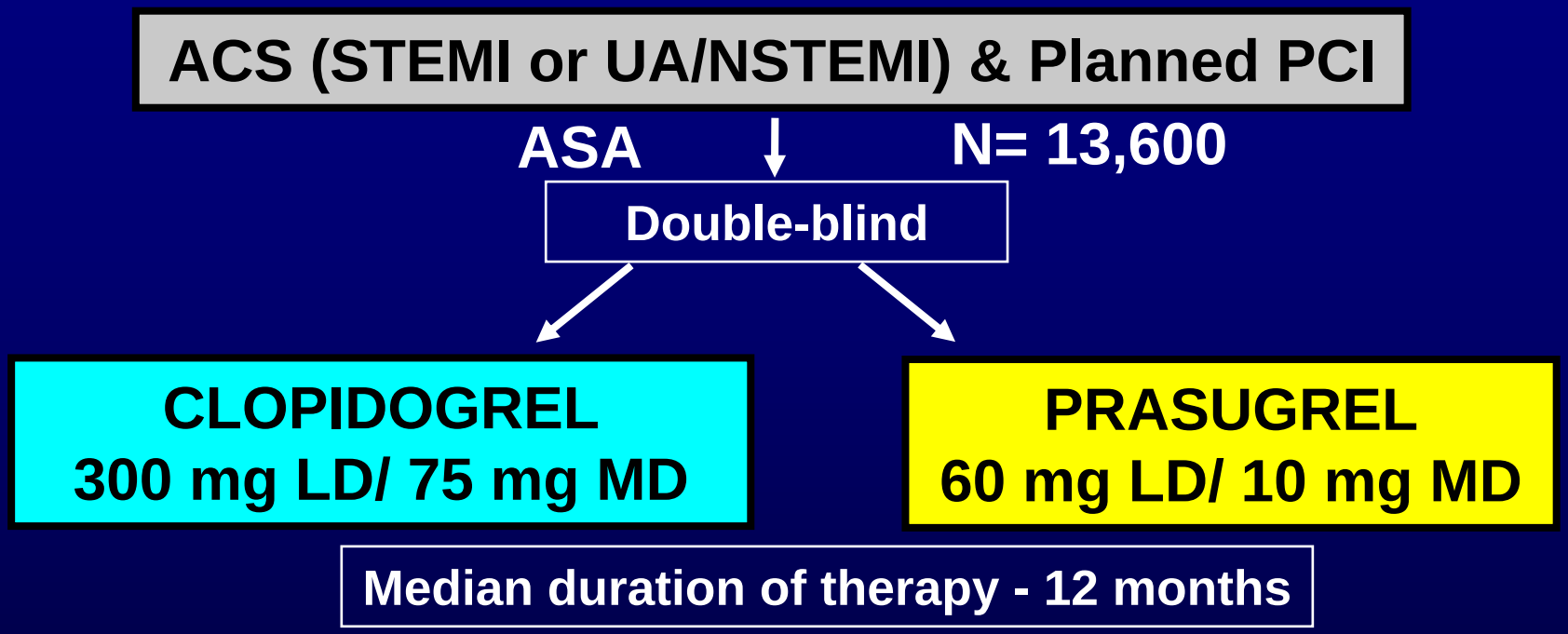
TRial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet InhibitioN with Prasugrel

TRITON-TIMI 38
AHA 2007
Orlando, Florida

***Disclosure Statement*:**
The TRITON-TIMI 38 trial was supported by a research grant to the Brigham and Women's Hospital from Daiichi Sankyo Co. Ltd and Eli Lilly & Co.

TRITON TIMI-38

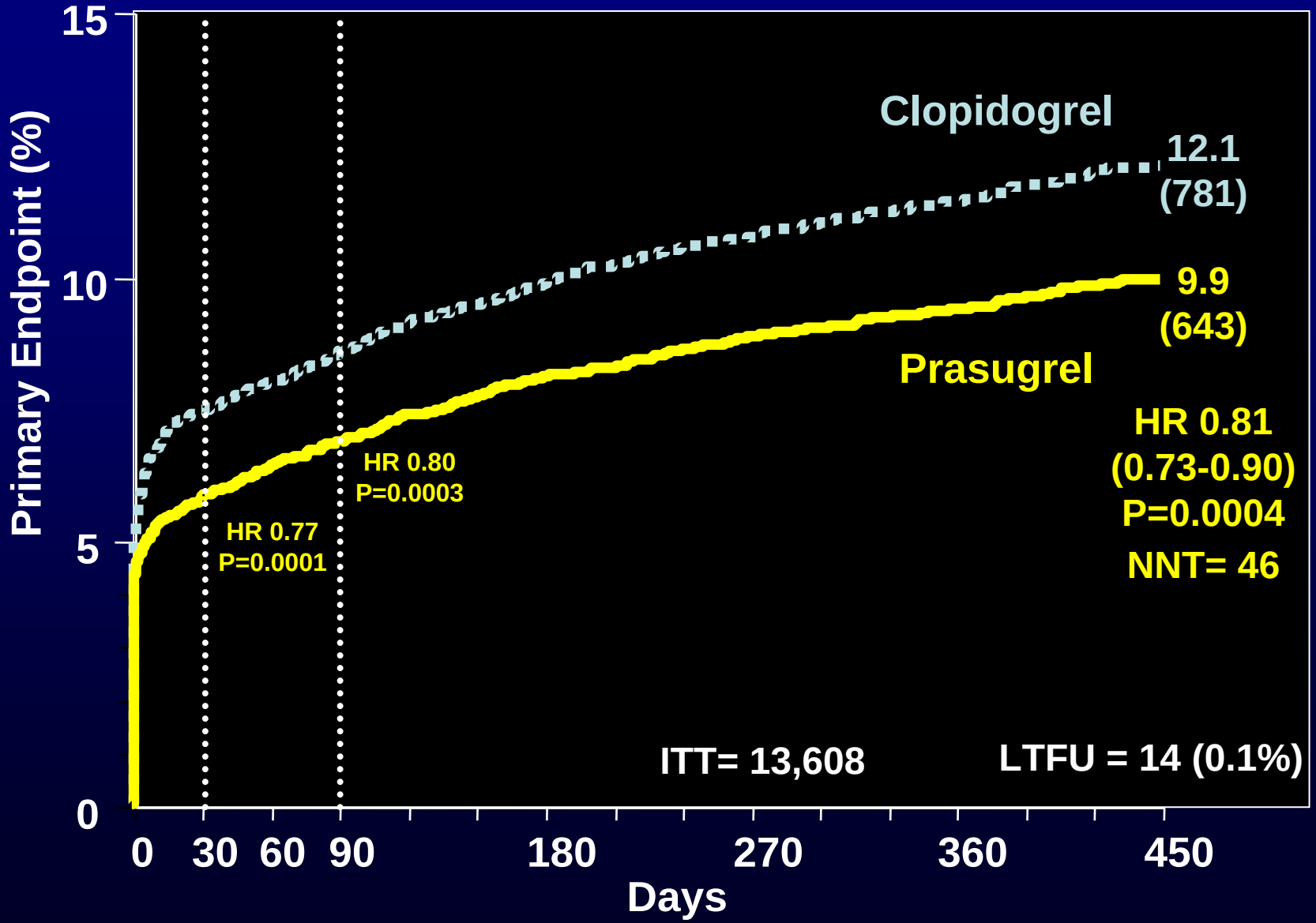
Study Design



1º endpoint:	CV death, MI, Stroke
2º endpoints:	CV death, MI, Stroke, Rehosp-Rec Isch
	CV death, MI, UTVR
	Stent Thrombosis (ARC definite/prob.)
Safety endpoints:	TIMI major bleeds, Life-threatening bleeds
Key Substudies:	Pharmacokinetic, Genomic

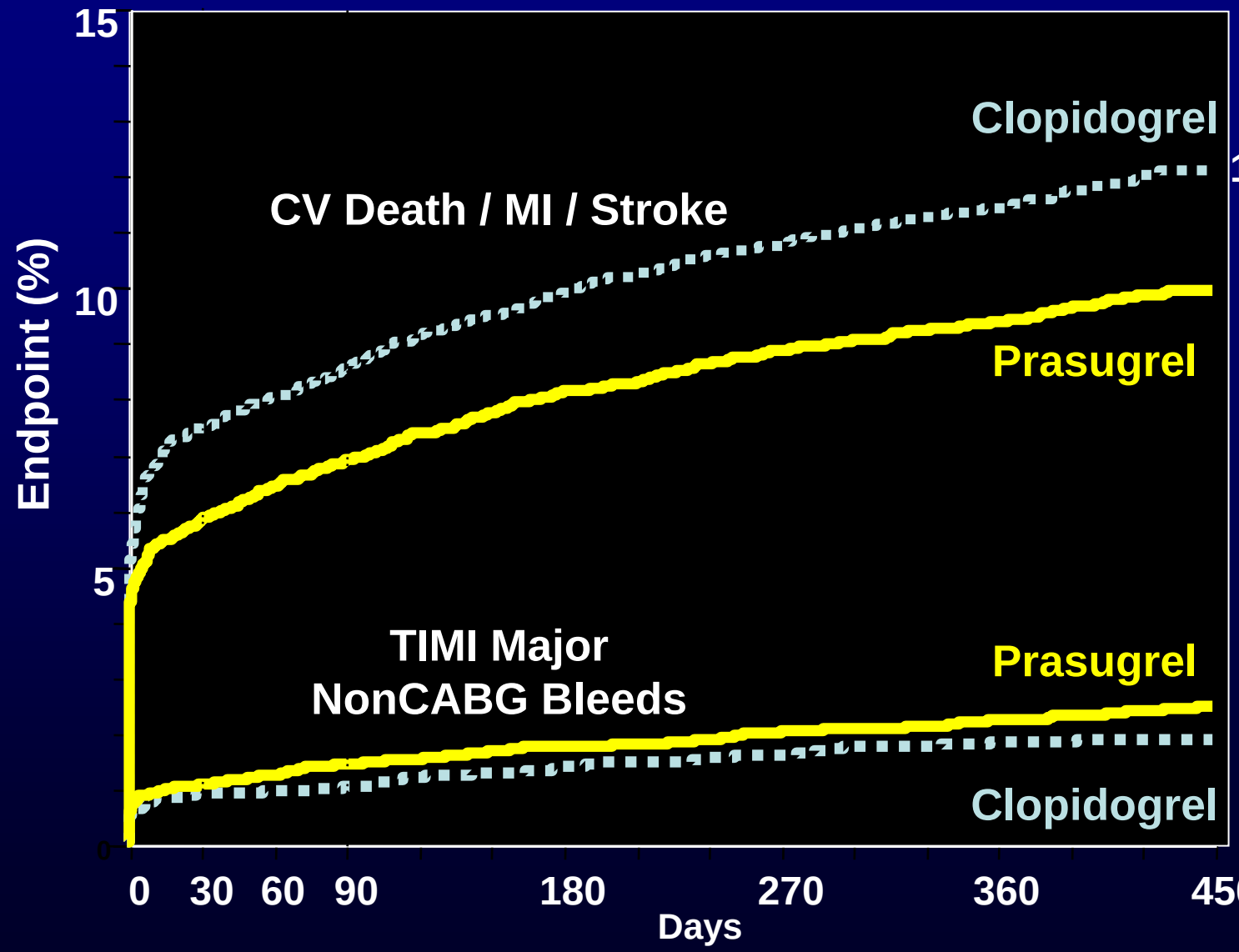
TRITON TIMI-38

Primary Endpoint
CV Death,MI,Stroke



TRITON TIMI-38

Balance of Efficacy and Safety



↓ 138 events

HR 0.81
(0.73-0.90)
P=0.0004

NNT = 46

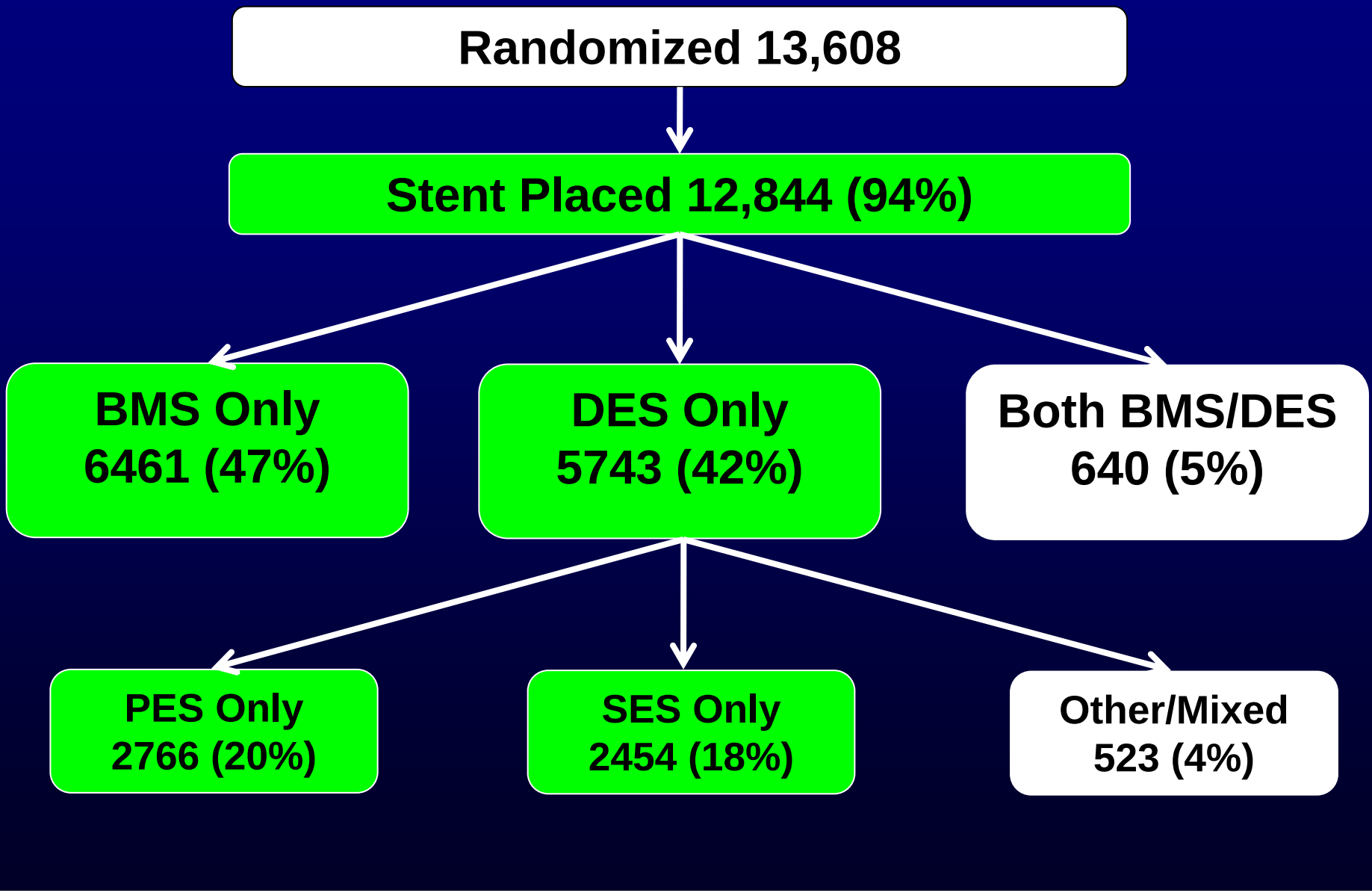
↑ 35 events

HR 1.32
(1.03-1.68)
P=0.03

NNH = 167

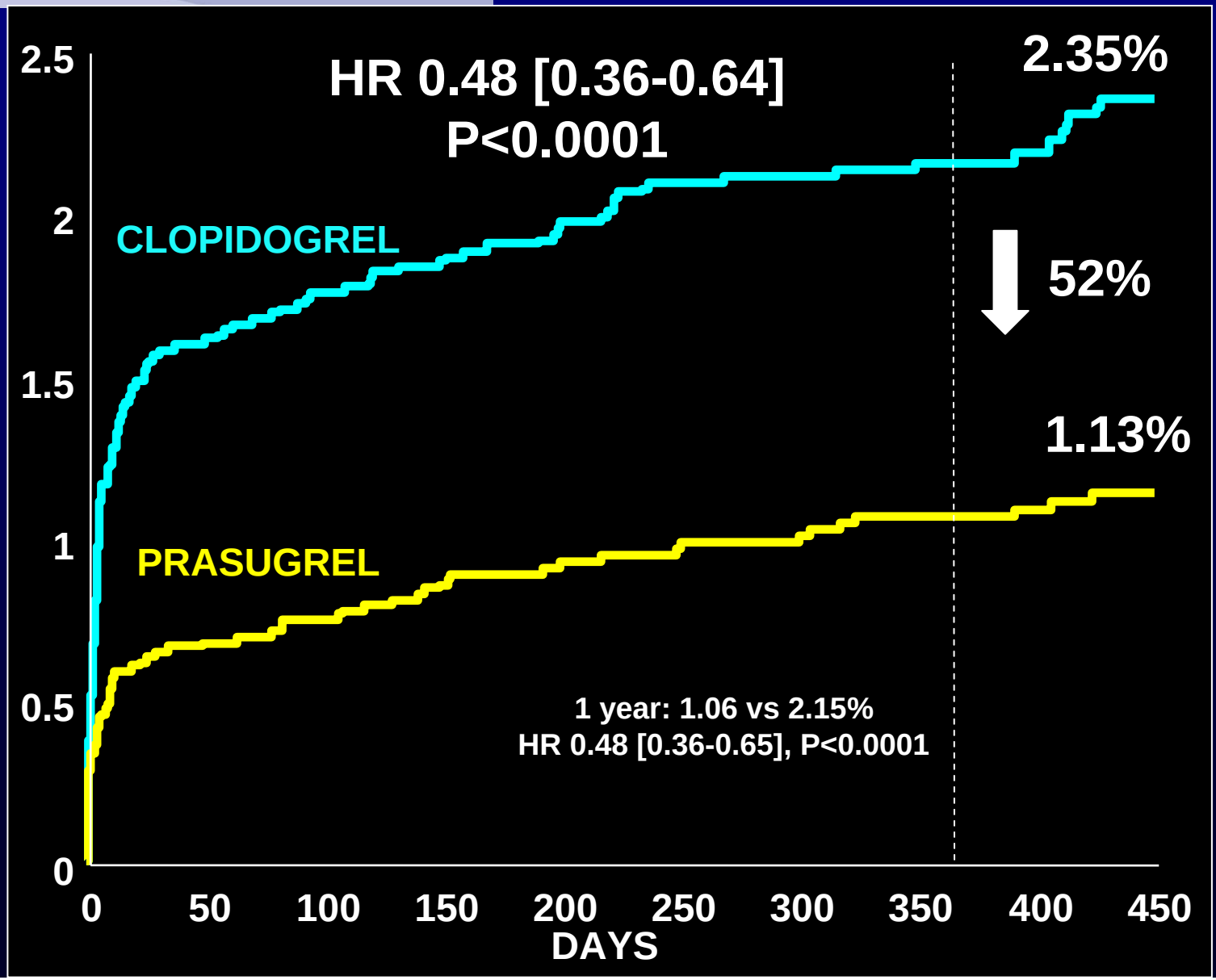
TRÎTON TIMI-38
STENT ANALYSIS

Patient Population



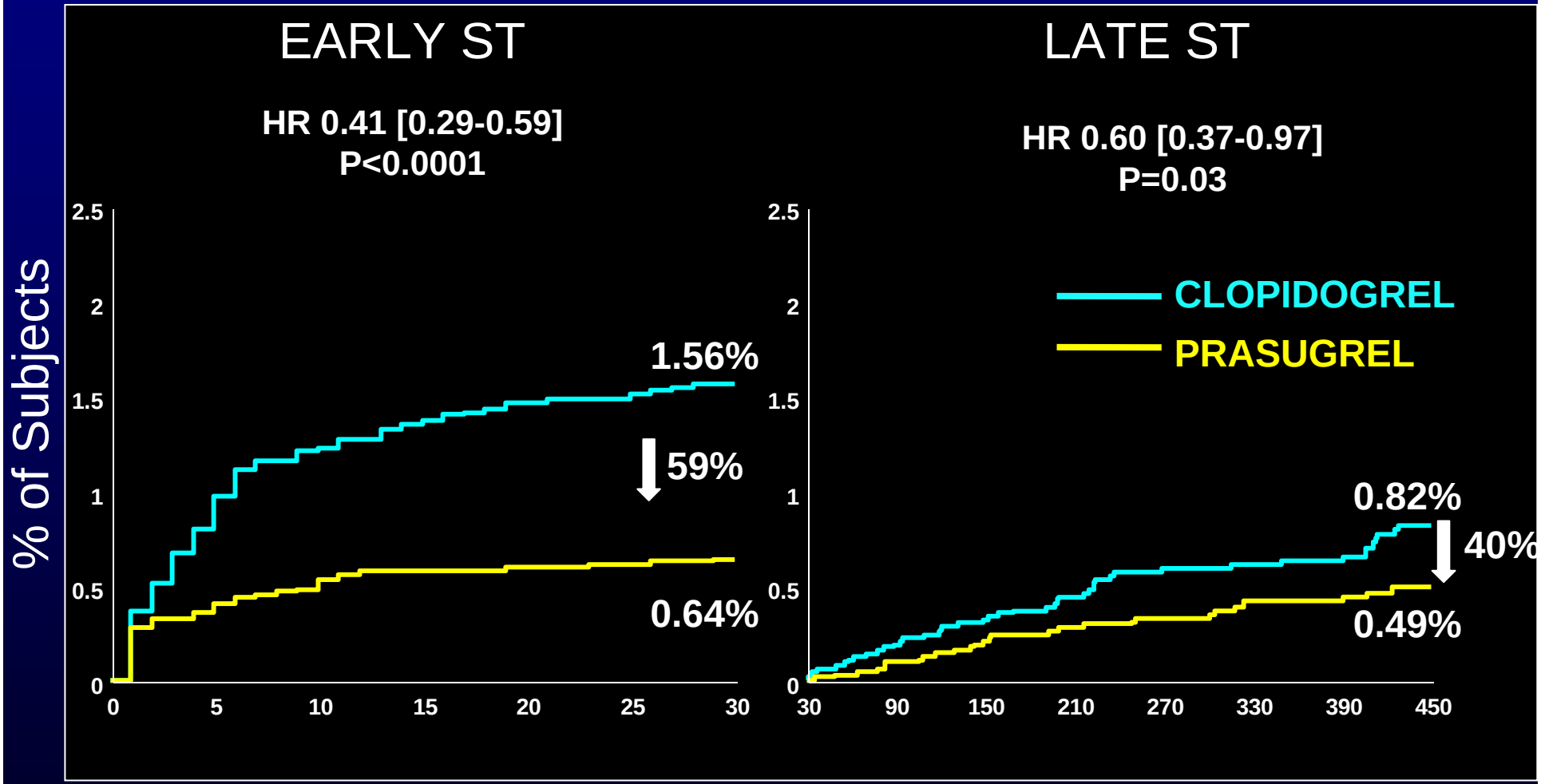
TRITON TIMI-38
STENT ANALYSIS

Definite/Probable ST: Any Stent (N=12844)



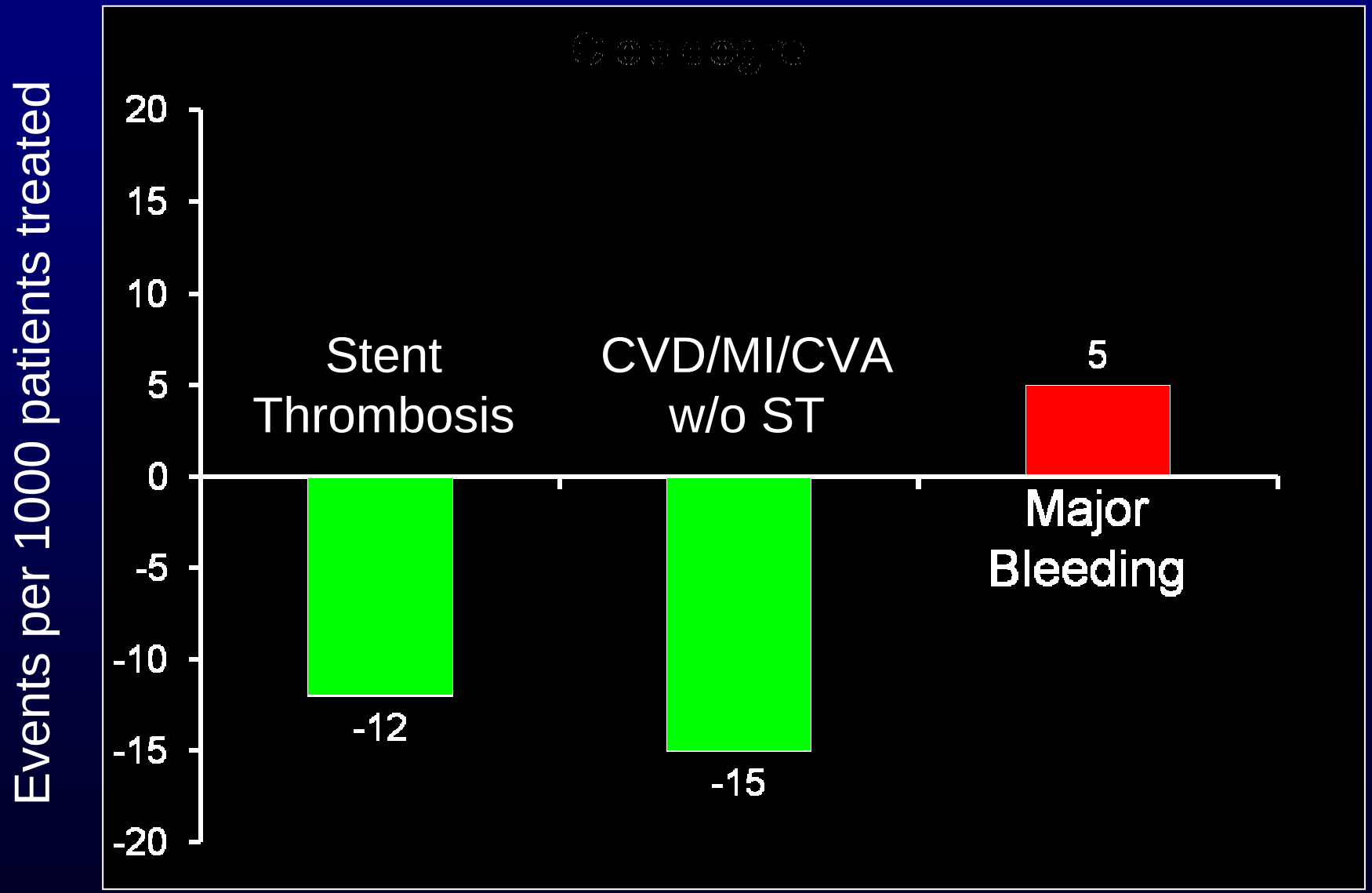
TRITON TIMI-38
STENT ANALYSIS

Definite/Probable ST: Any Stent (N=12844)



TRÎTON TIMI·38
STENT ANALYSIS

Balance of Efficacy and Safety (Stented Population)



ClinicalTrials.gov Identifier NCT00262054

Bivalirudin Versus Unfractionated Heparin in Biomarker Negative Patients With Stable and Unstable Angina Undergoing PCI

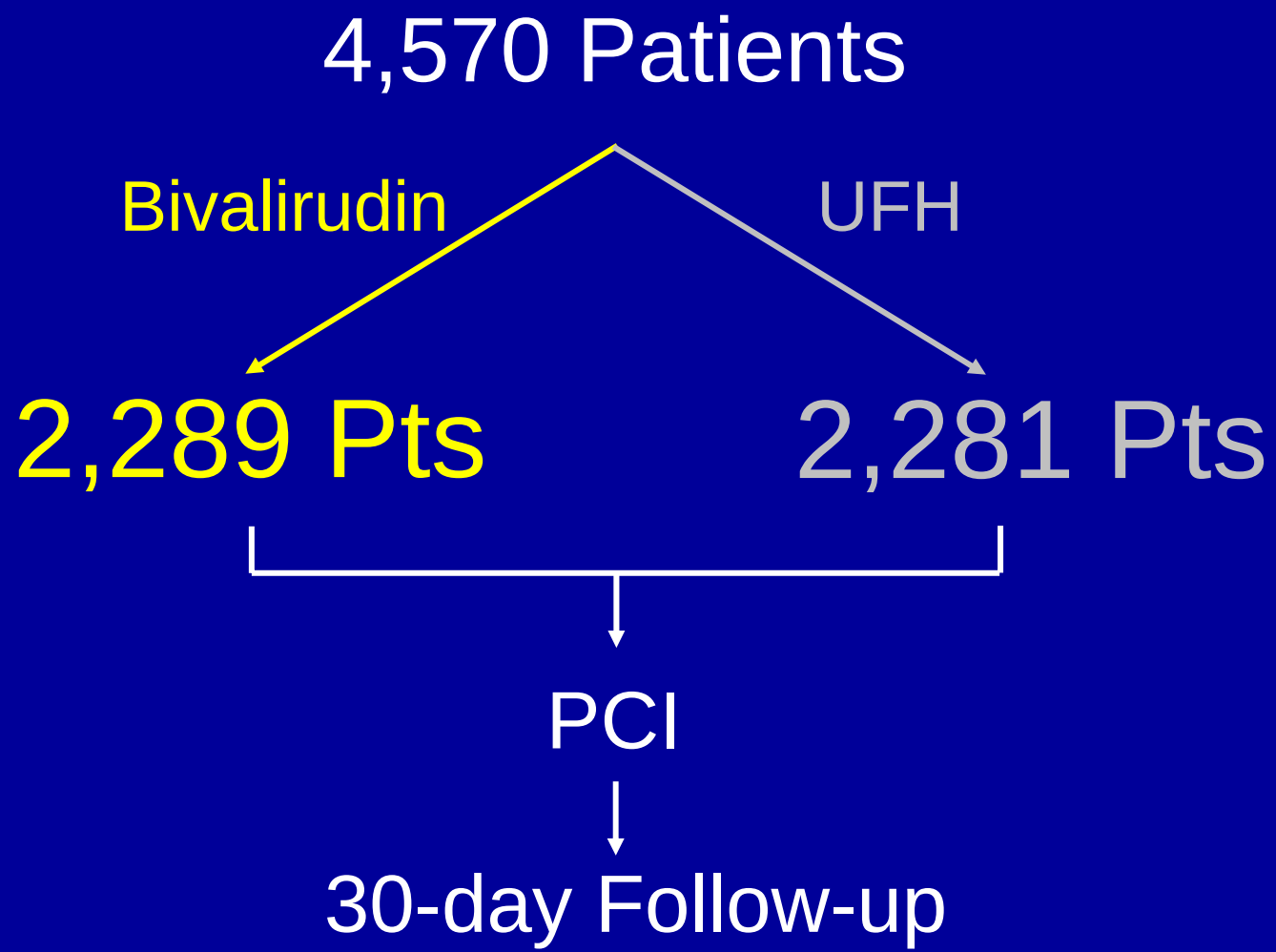
ISAR-REACT 3

(Intracoronary Stenting and Antithrombotic Regimen-Rapid Early Action for Coronary Treatment 3)

A. Kastrati, F.-J. Neumann, J. Mehilli, S. Schulz, G. Richardt, R. Iijima, R.A. Byrne, P.B. Berger, A. Schömig

ACC.08

Study Population



Treatment Regimens

Clopidogrel 600 mg at least 2 hours before PCI
Aspirin ≥325 mg orally or intravenously

Double-blind randomization; double-dummy administration

Bivalirudin group

- Bolus of 0.75 mg/kg
- Infusion of 1.75 mg/kg/hr

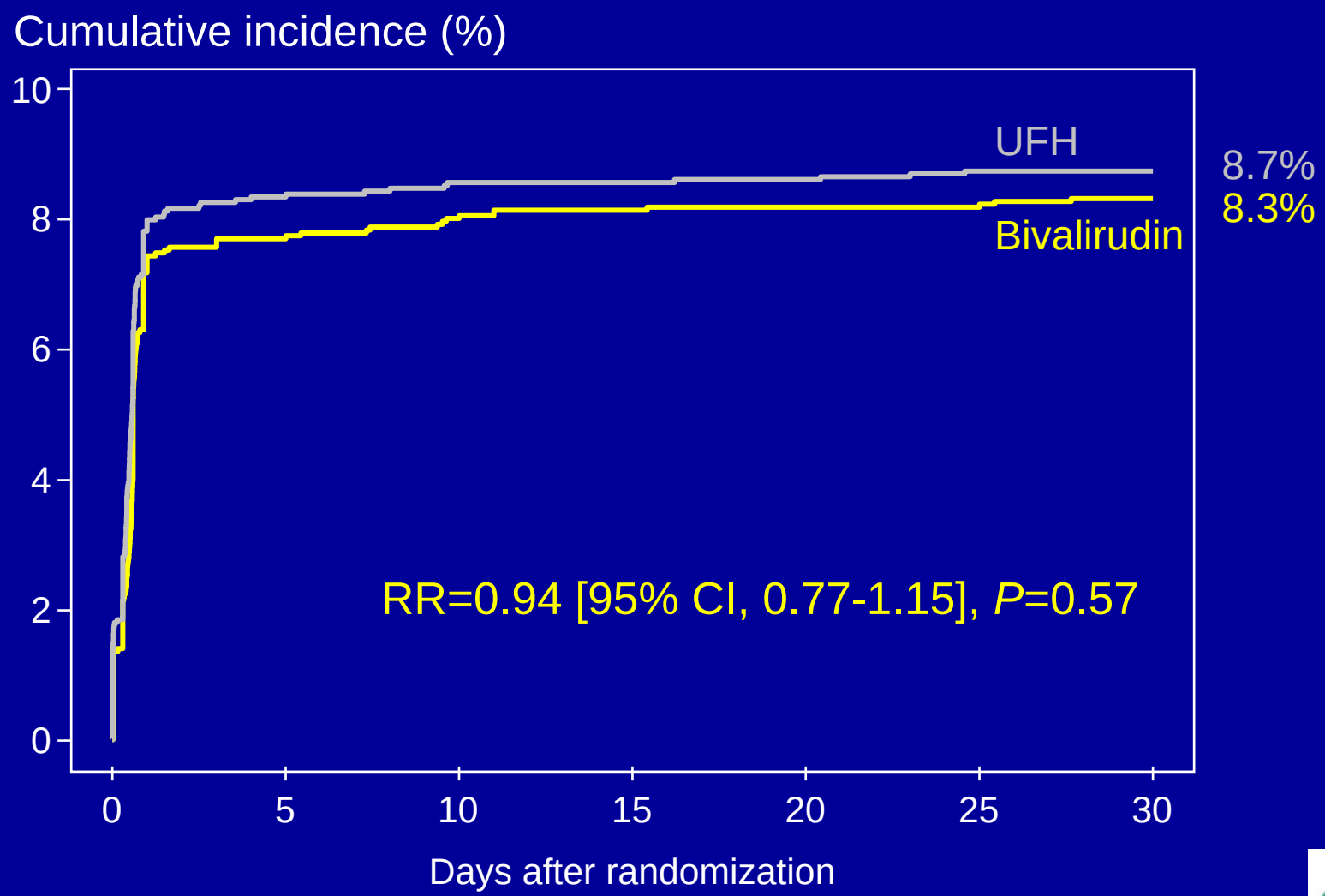
UFH group

- Bolus of 140 U/kg
- Placebo Infusion

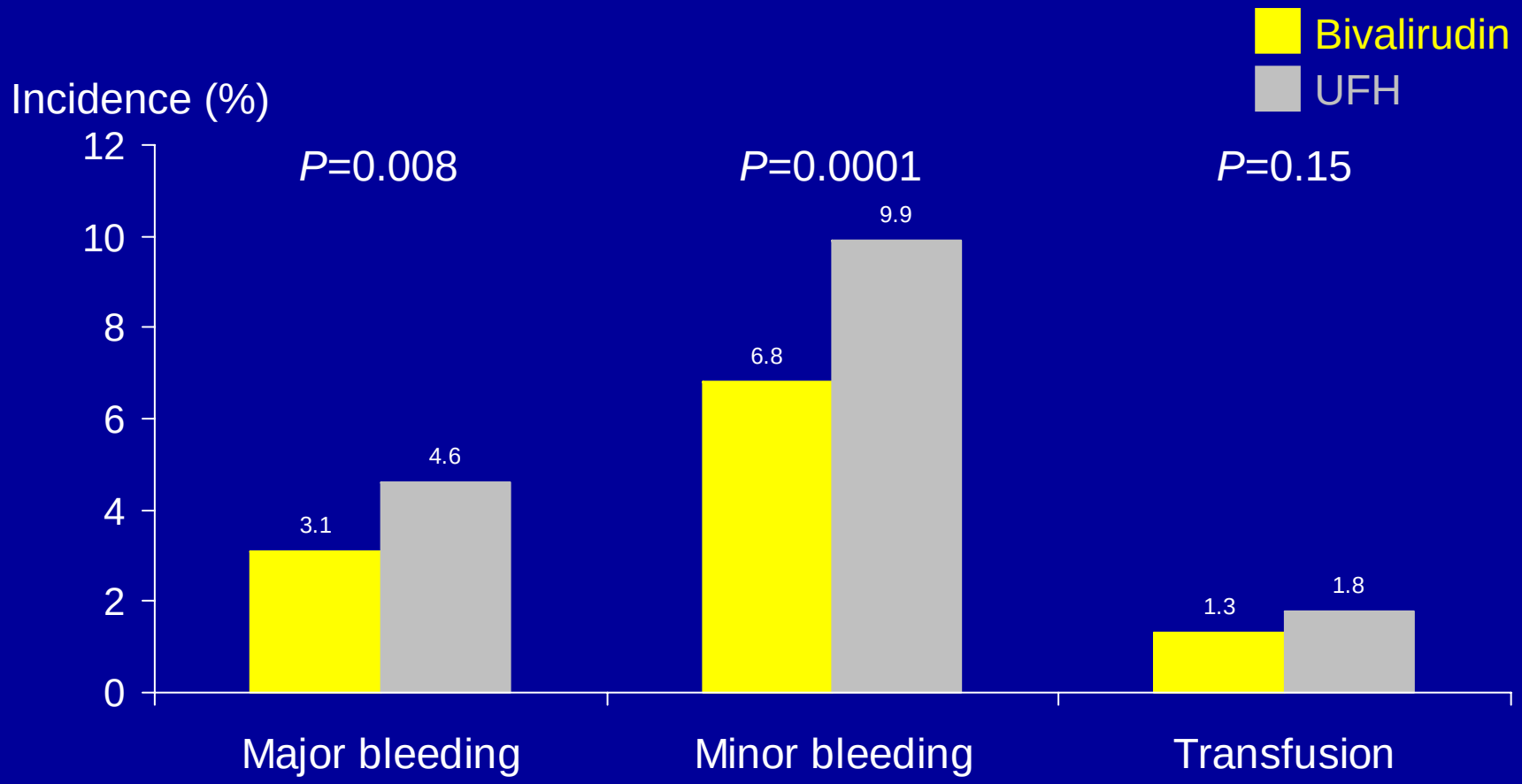
Clopidogrel 75-150 mg/day until discharge (≤3 days)
75 mg/day for at least 6 months

Aspirin 80-325 mg/day indefinitely

Primary (Quadruple) Endpoint
Death, MI, UTVR, Major Bleeding



Bleeding Events



Trial of the Year: Topics to Cover

1. **"Real world" DES v. BMS use**
2. **Next generation stents in the U.S.**
   - **Endeavor and Xience V**
3. **Balance of Bleeding vs. ischemic complications post PCI**
4. *Left Main and Bifurcation lesions*

Nordic Bifurcation Study II

The Nordic Stent Technique Study:

A Randomized Study of Crush vs. Culotte Stent Techniques with Sirolimus Eluting Stents in Bifurcation Lesions

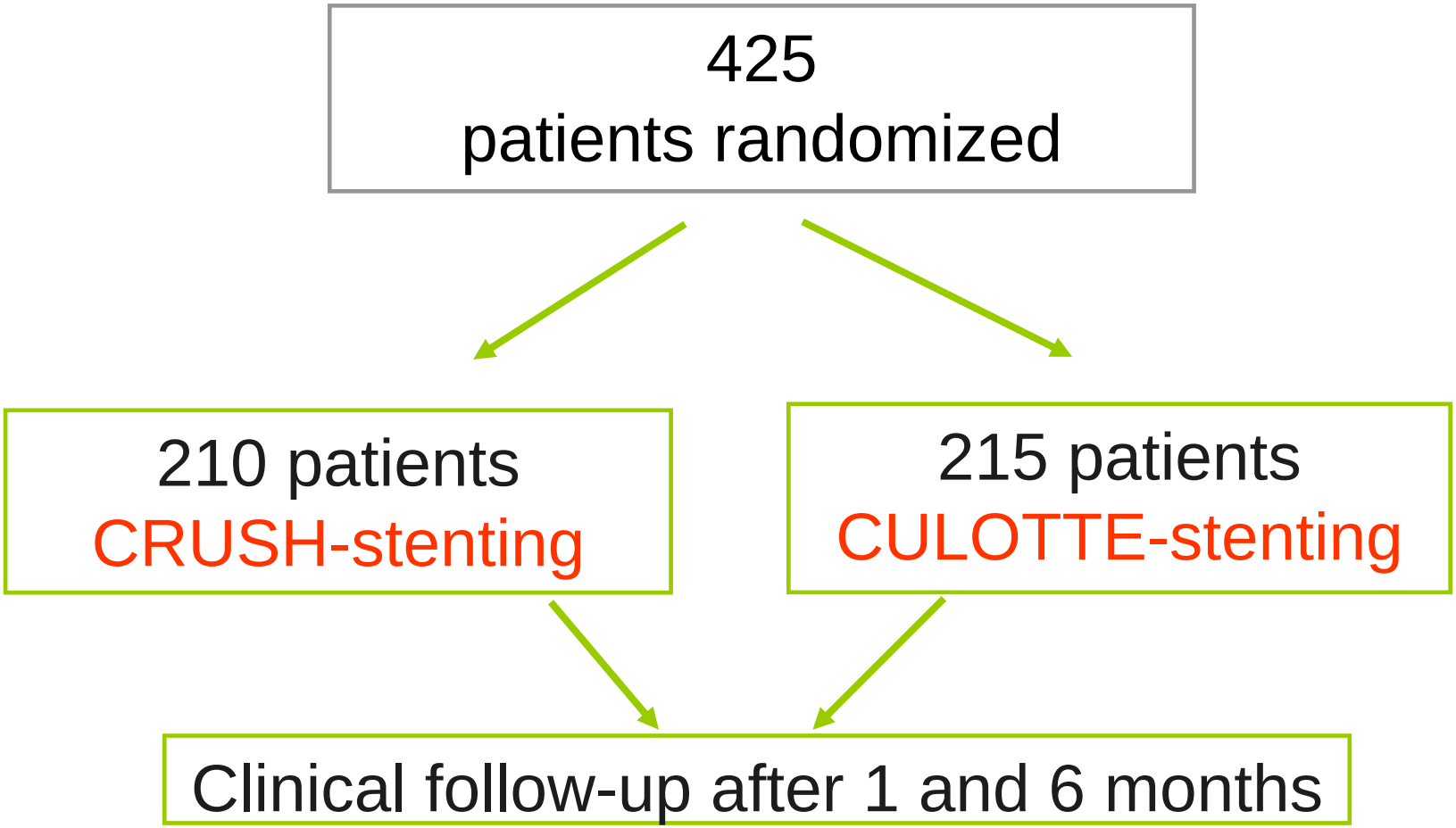
Matti Niemela, Kari Kervinen, Andrejs Erglis, Jens F Lassen, Paul Gunnes, Terje Steigen, Jan Ravkilde, Timo Makikallio, Kari Ylitalo, Indulis Kumsars, Inga Narbute, Evald Christensen, Lars Krusell, Sindre Stavnes, Jan Skov Jensen, Ulrik Abildgaard, Anders Galløe, Jan Mannsverk, Tor Trovik, Per Thayssen, Steffen Helqvist, Saila Vikman, Rune Wiseth, Jens Aarøe, Leif Thuesen

On behalf of the Nordic PCI Study Group

TCT2007
TRANSCATHETER CARDIOVASCULAR THERAPEUTICS

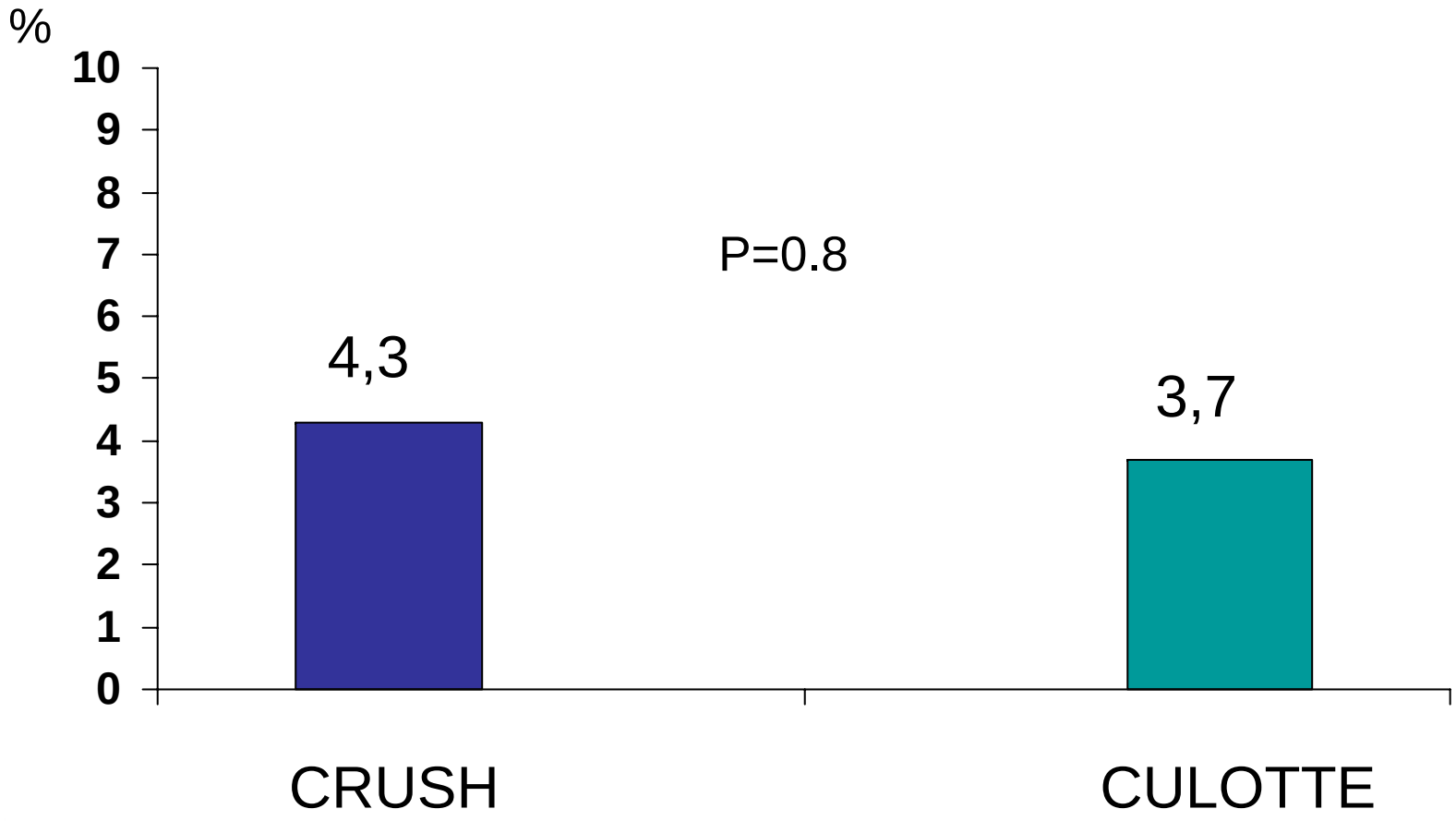
CARDIOVASCULAR RESEARCH FOUNDATION

Randomization



Primary endpoint

Cardiac death, myocardial infarction, TVR and stent thrombosis after 6 months



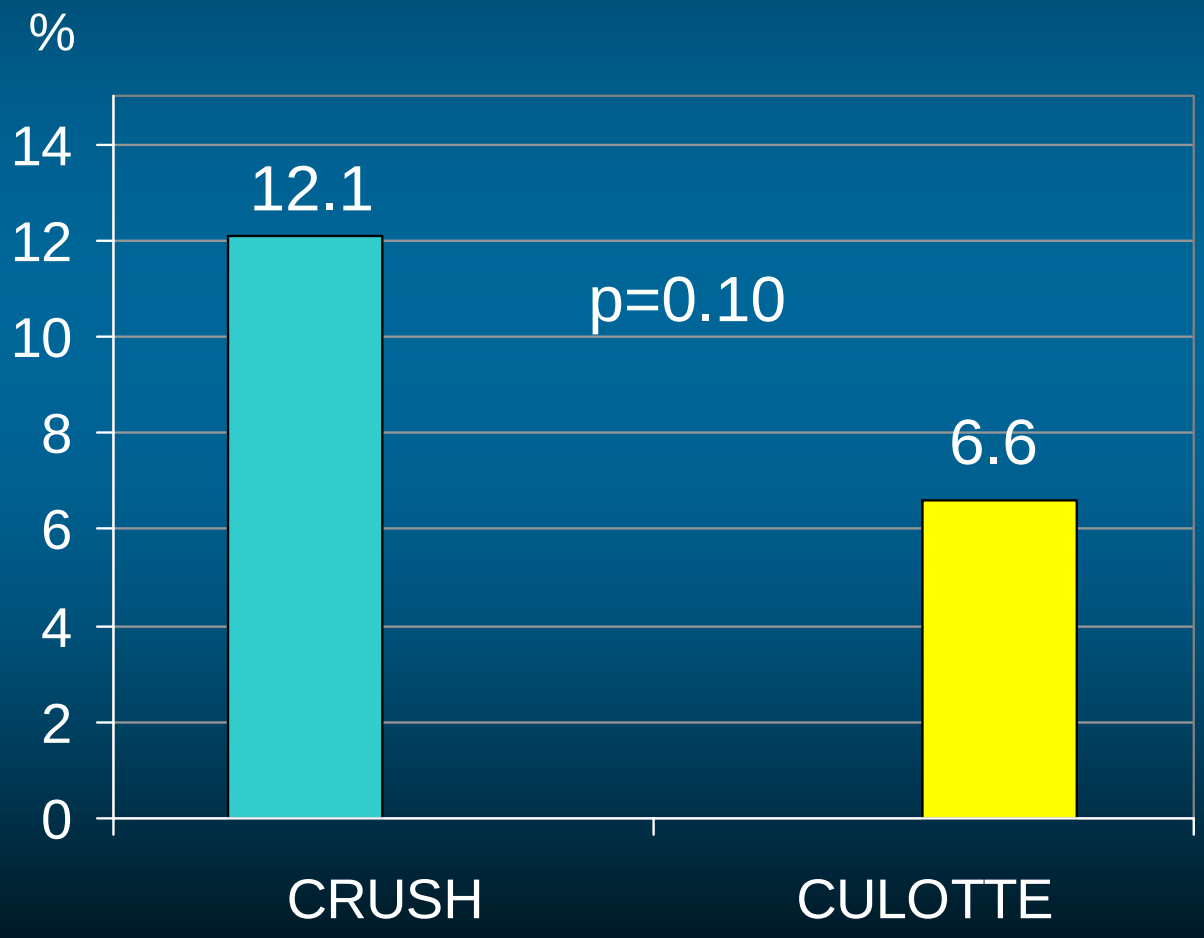
Eight Months Angiographic Follow-up in Patients Randomized to Crush or Culotte Stenting of Coronary Artery Bifurcation Lesions

The Nordic Bifurcation Stent Technique Study

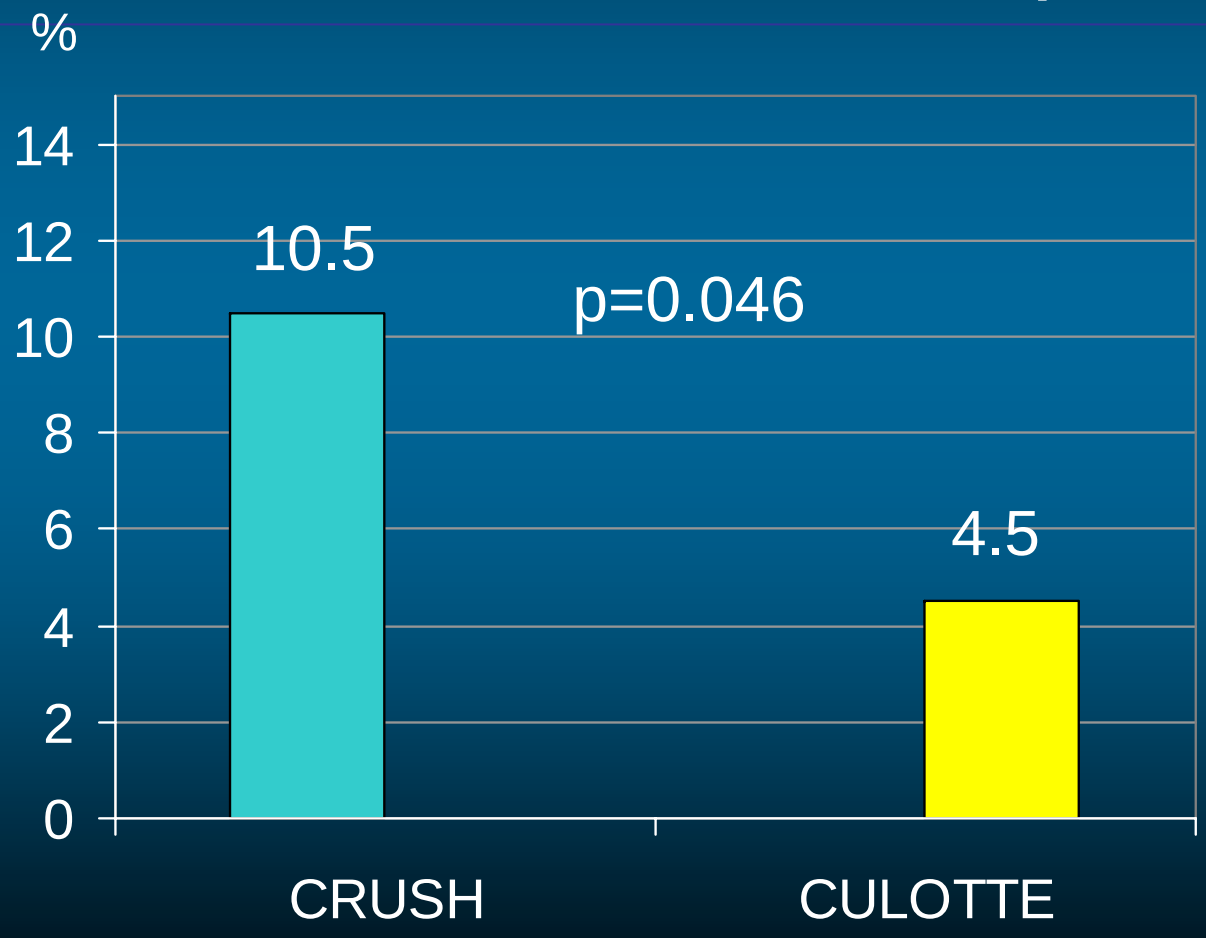
Pål Gunnes, Matti Niemela, Kari Kervinen, Andrejs Erglis, Indulis Kumsars, Jens F Lassen, Michael Mæng, Jan Skov Jensen, Anders Galløe, Terje Steigen, Jan Ravkilde, Timo Makikallio, Kari Ylitalo, Inga Narbute, Evald Christiansen, Lars Krusell, Sindre Stavnes, Ulrik Abildgaard, Peter Riis Hansen, Jan Mannsverk, Thor Trovik, Per Thayssen, Steffen Helqvist, Saila Vikman, Rune Wiseth, Jens Aarøe, Leif Thuesen

For the Nordic-Baltic PCI Study Group

Rate of main vessel and/or side branch in-lesion diameter stenosis >50% at 8 months follow-up



Rate of main vessel and/or side branch in-stent diameter stenosis >50% at 8 months follow-up



Long-Term Outcomes of Coronary Stent Implantation versus Bypass Surgery for the Treatment of Unprotected Left Main Coronary Artery Disease

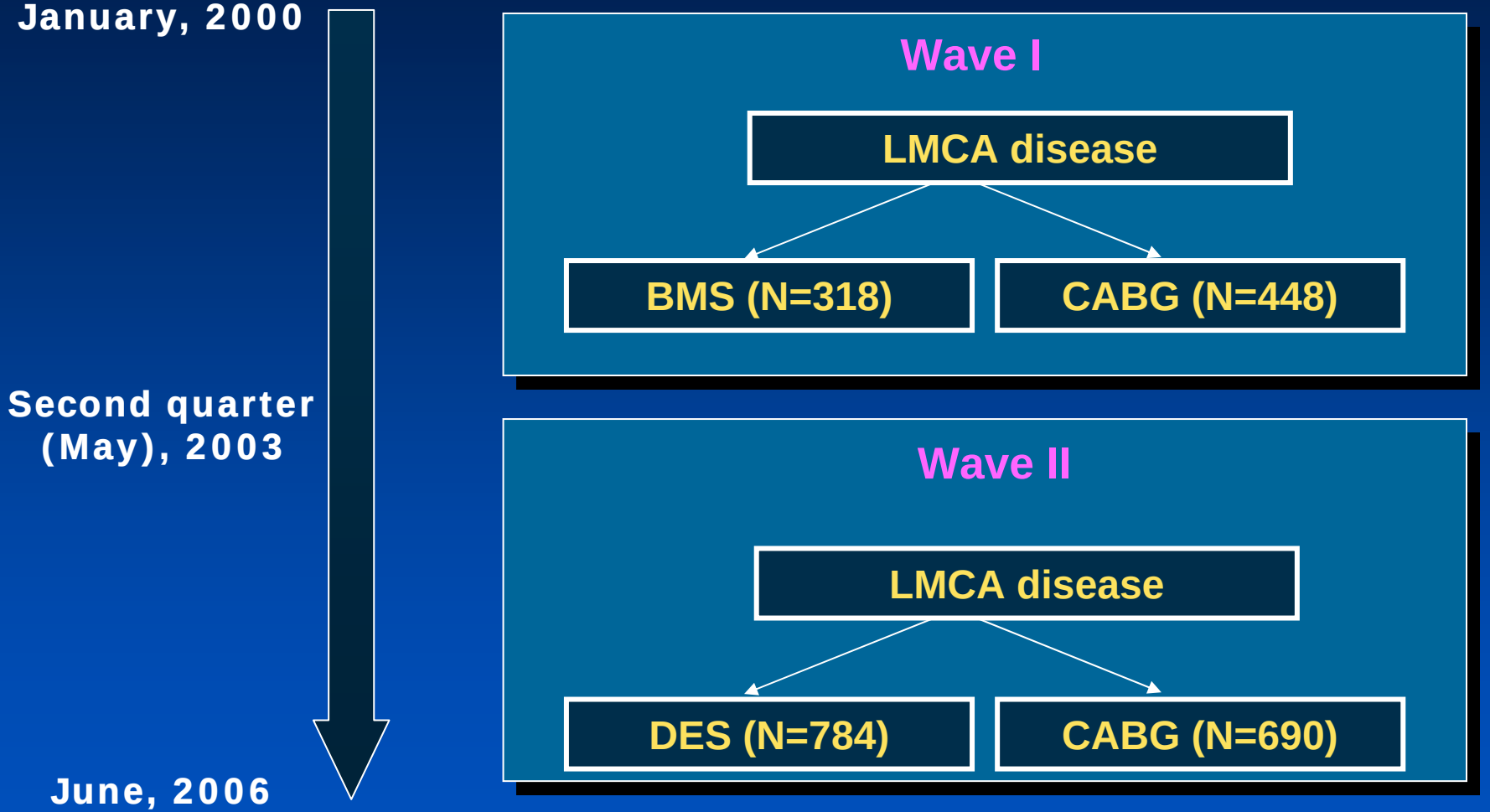
Revascularization for Unprotected Left *MAIN* Coronary Artery Stenosis: *COM*parison of *P*ercutaneous Coronary *A*ngioplasty versus Surgical *RE*vascularization from Multi-Center Registry:

The MAIN-COMPARE Study

Seung-Jung Park, MD, PhD and Ki-Bae Seung, MD, PhD,
on behalf of the MAIN-COMPARE Study Group

MAIN-COMPARE Study

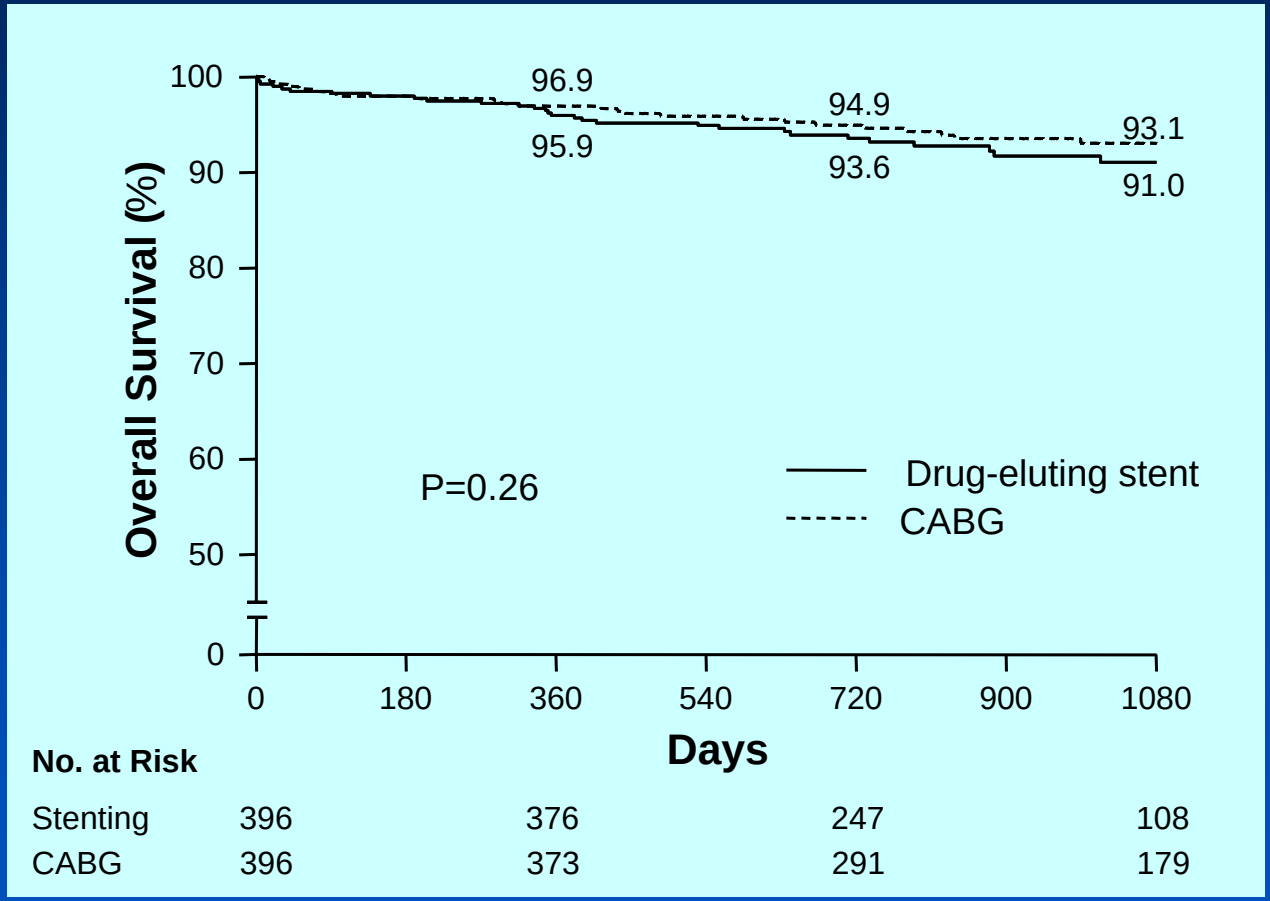
Stenting (BMS or DES) vs. CABG



Total (N=2240) | **PCI (N=1102)** | **CABG(N=1138)**

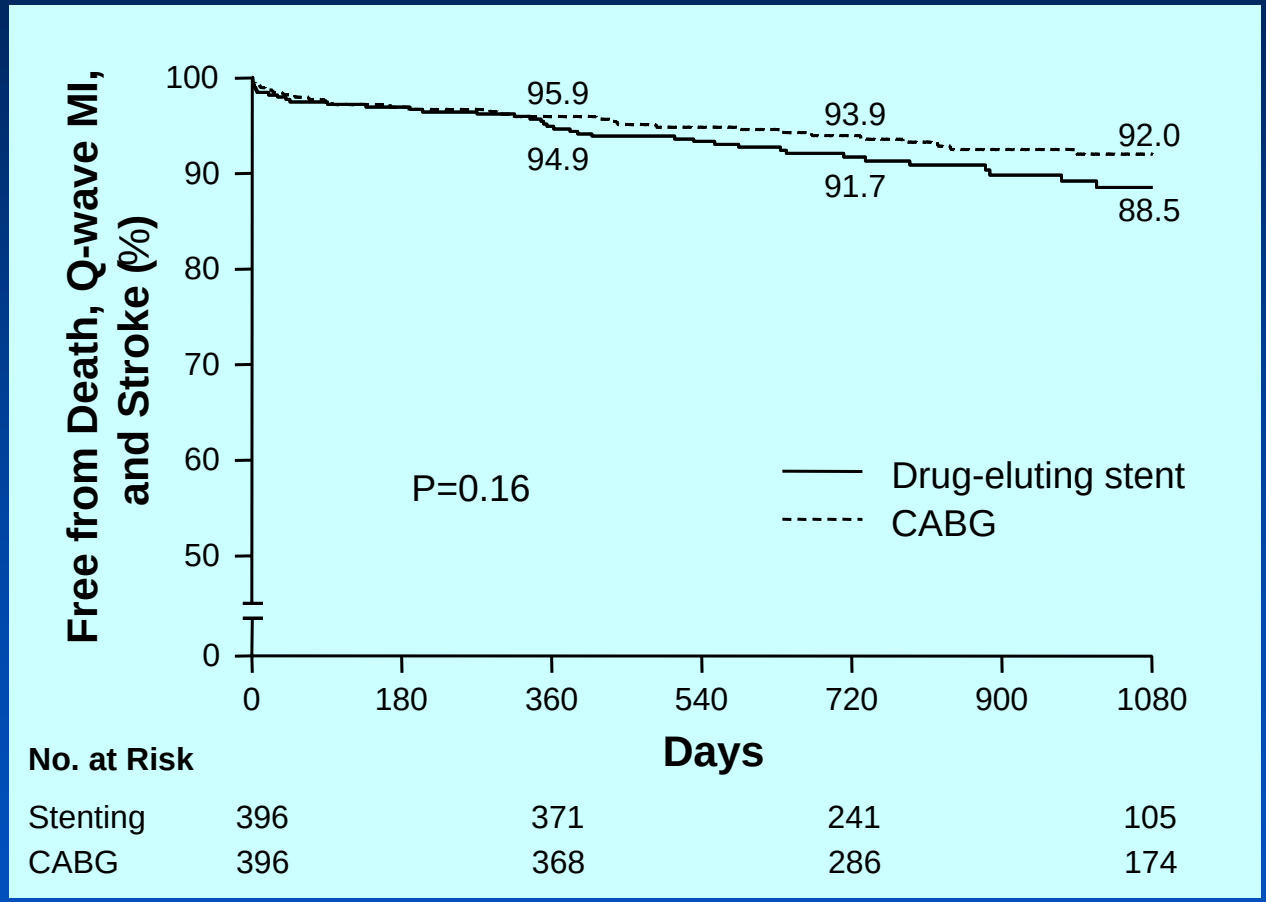
Death

(DES and contemporary CABG matched cohort: 396 pairs)



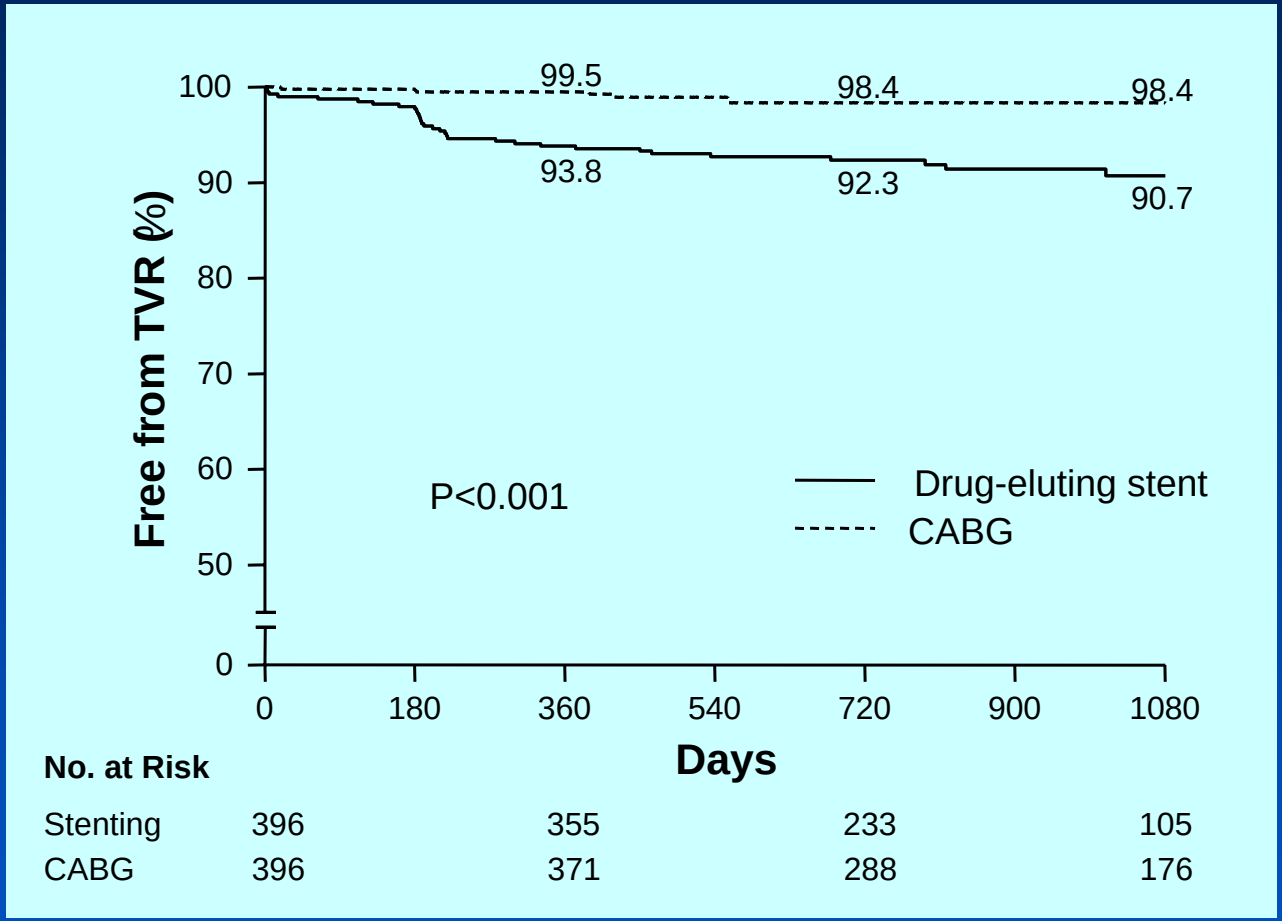
Death, Q-MI, or Stroke

(DES and contemporary CABG matched cohort: 396 pairs)



Target-vessel revascularization

(DES and contemporary CABG matched cohort: 396 pairs)



Trials of the Year: Lessons Learned

1. "Real world" DES v. BMS use-

   DES is No Less Safe than BMS!

2. Next generation stents in the U.S.

   Are Here To Stay..

3. Balance of Bleeding vs. ischemic complications post PCI

   Bleeding is an hazardous and common event and should be considered in PCI studies

4. Left Main and Bifurcation lesions

   Left Main stenting with DES is comparable to CABG; Awaiting SYNTAX…..

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