

HORIZONSAMI

HORIZONS-AMI: Implications for Pharmaco-Adjunctive Therapy and DES Use

Gregg W. Stone MD

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

Disclosures

Gregg W. Stone MD

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Harmonizing Outcomes with Revascularization and Stents in AMI

3602 pts with STEMI with symptom onset ≤ 12 hours

Aspirin, thienopyridine

R
1:1

UFH + GP IIb/IIIa inhibitor
(abciximab or eptifibatide)

Bivalirudin monotherapy
(\pm provisional GP IIb/IIIa)

Emergent angiography, followed by triage to...

CABG – Primary PCI – Medical Rx

3006 pts eligible for stent randomization

R
3:1

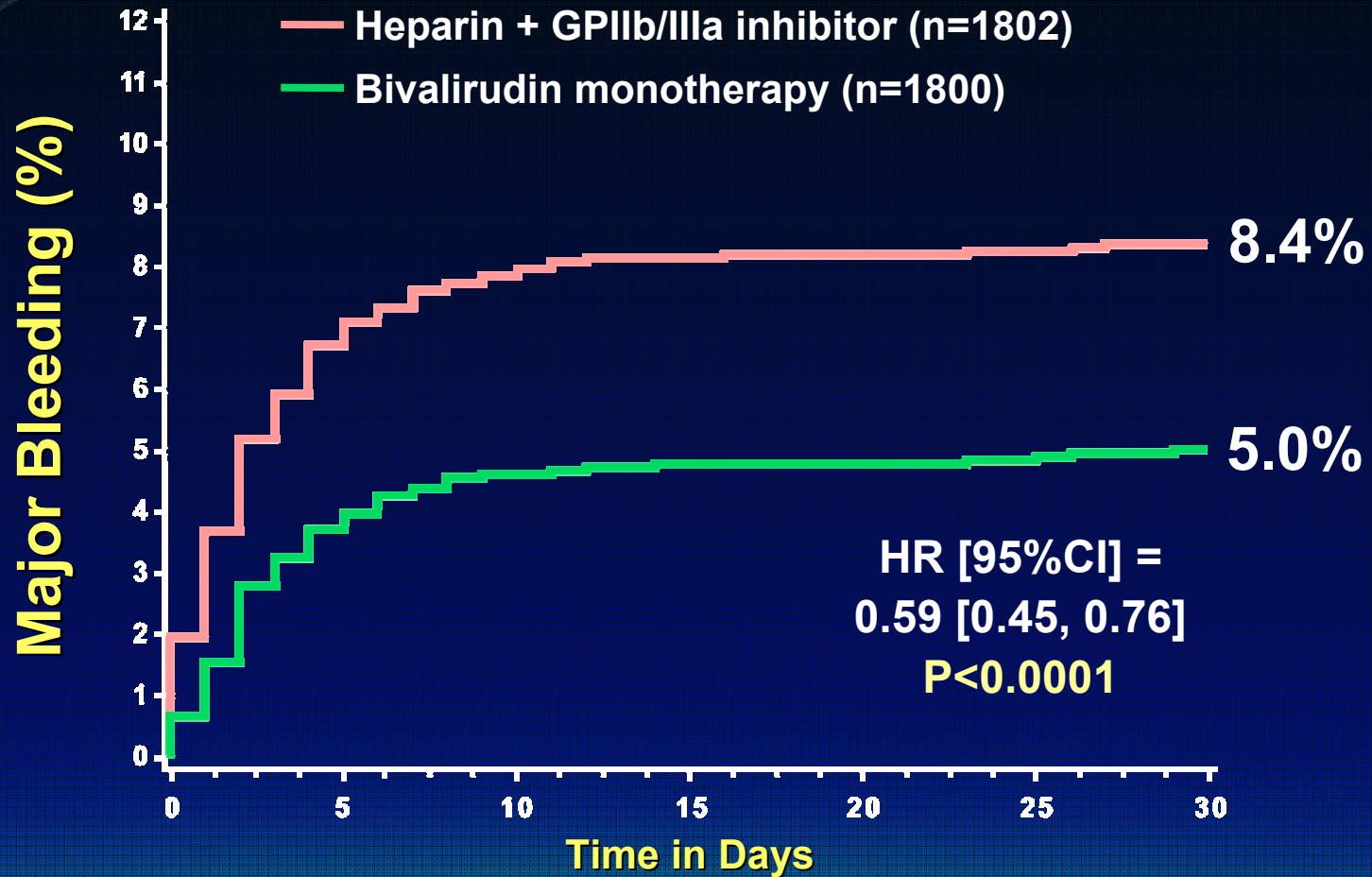
Paclitaxel-eluting TAXUS stent

Bare metal EXPRESS stent

Clinical FU at 30 days, 6 months, 1 year, and then
yearly through 5 years; angio FU at 13 months

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30 Day Major Bleeding (non-CABG)



Number at risk

Bivalirudin	1800	1697	1675	1668	1664	1653	1590
Heparin + GPIIb/IIIa	1802	1651	1617	1606	1598	1581	1511

30 Day Bleeding Endpoints*

	UFH + GP IIb/IIIa (N=1802)	Bivalirudin (N=1800)	P Value
Protocol Major, non CABG**	8.3%	4.9%	<0.0001
Protocol Major, All	10.8%	6.8%	<0.0001
Protocol Minor	15.4%	8.6%	<0.0001
Blood transfusion	3.5%	2.1%	0.009
TIMI Major	5.0%	3.1%	0.002
TIMI Minor	4.6%	2.8%	0.006
TIMI Major or Minor	9.6%	5.9%	<0.0001
GUSTO LT*** or Severe	0.6%	0.4%	0.49
GUSTO Moderate	5.0%	3.1%	0.002
GUSTO LT or Sev or Mod	5.6%	3.5%	0.002

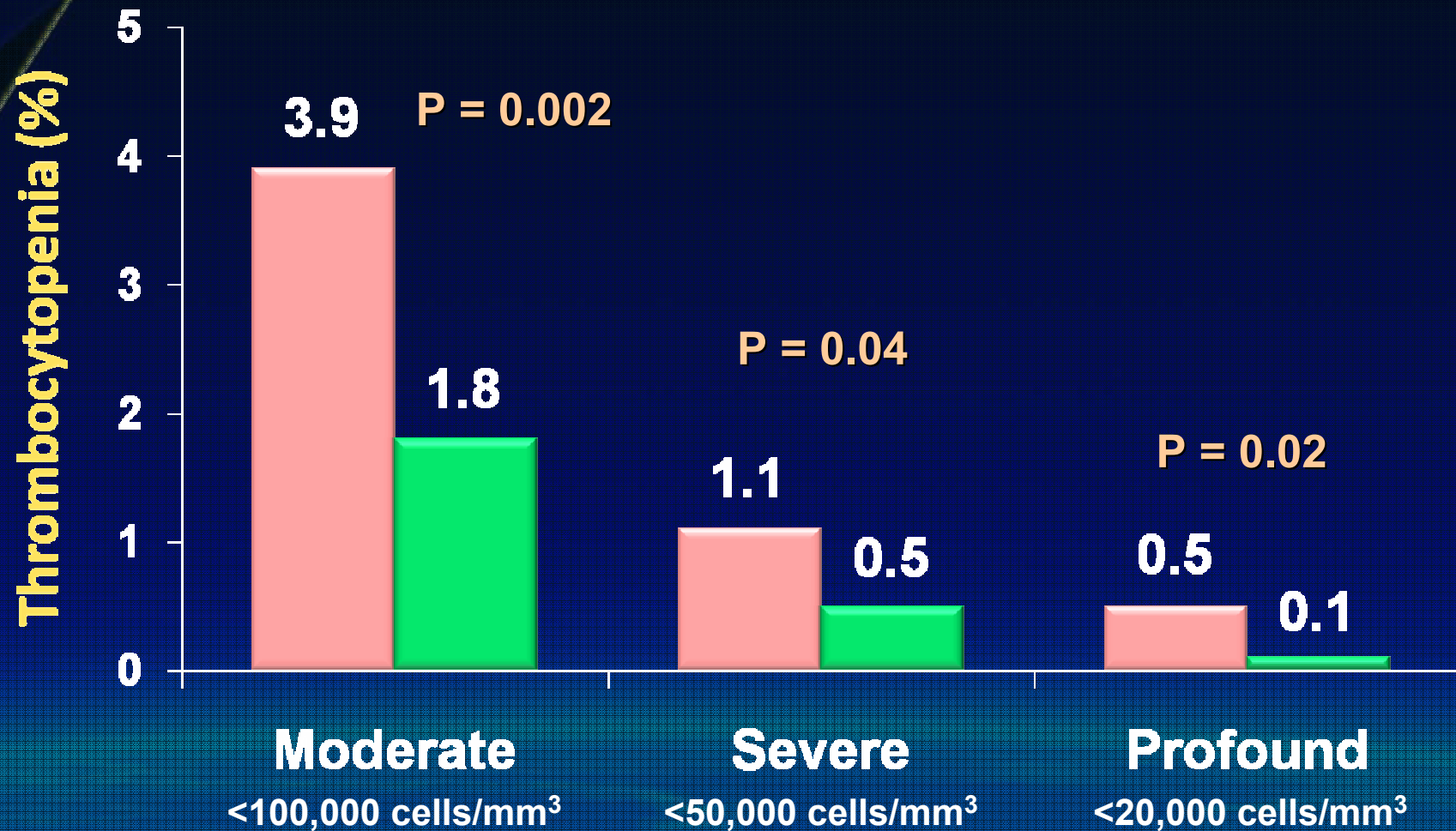
*CEC adjudicated, except protocol minor;

Primary endpoint; *Life threatening

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Thrombocytopenia

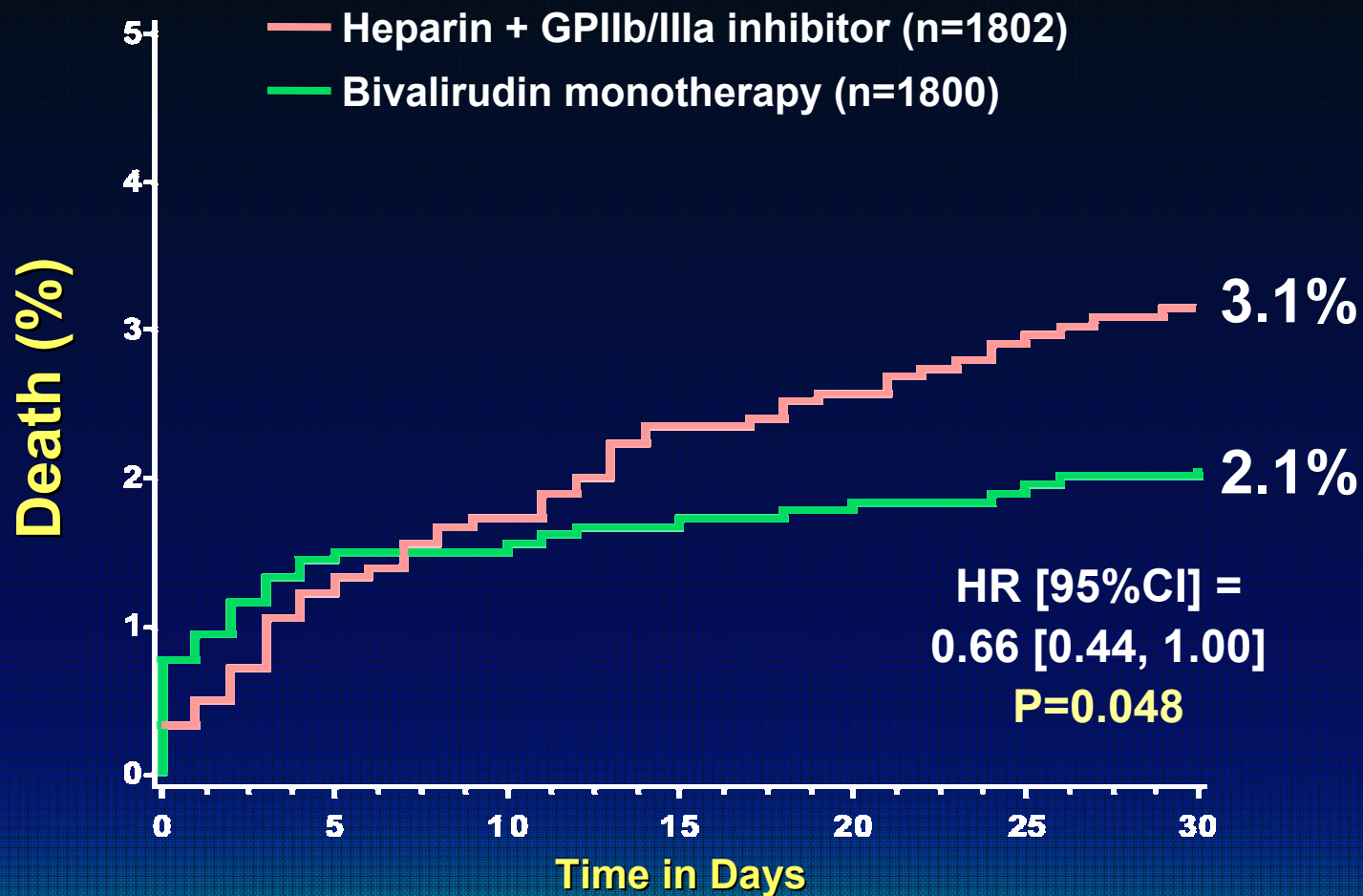
■ Heparin + GPIIb/IIIa inhibitor (n=1802) ■ Bivalirudin monotherapy (n=1800)



Stone GW et al. NEJM 2008;358:2218-30

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30 Day Mortality



Number at risk

Bivalirudin	1800	1758	1751	1746	1742	1729	1666
Heparin + GPIIb/IIIa	1802	1764	1748	1736	1728	1707	1630

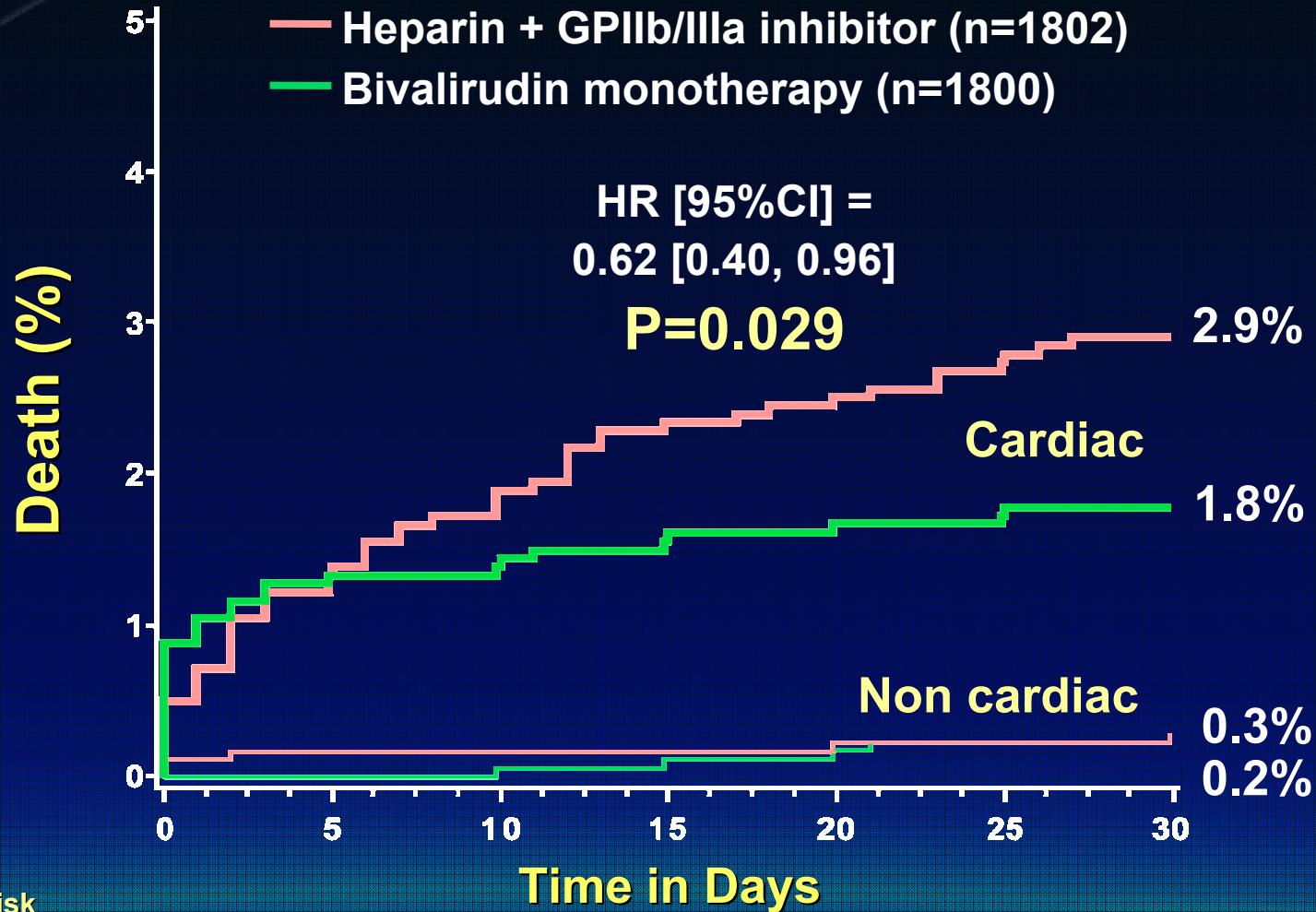
30 Day Stent Thrombosis (N=3,124)

	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

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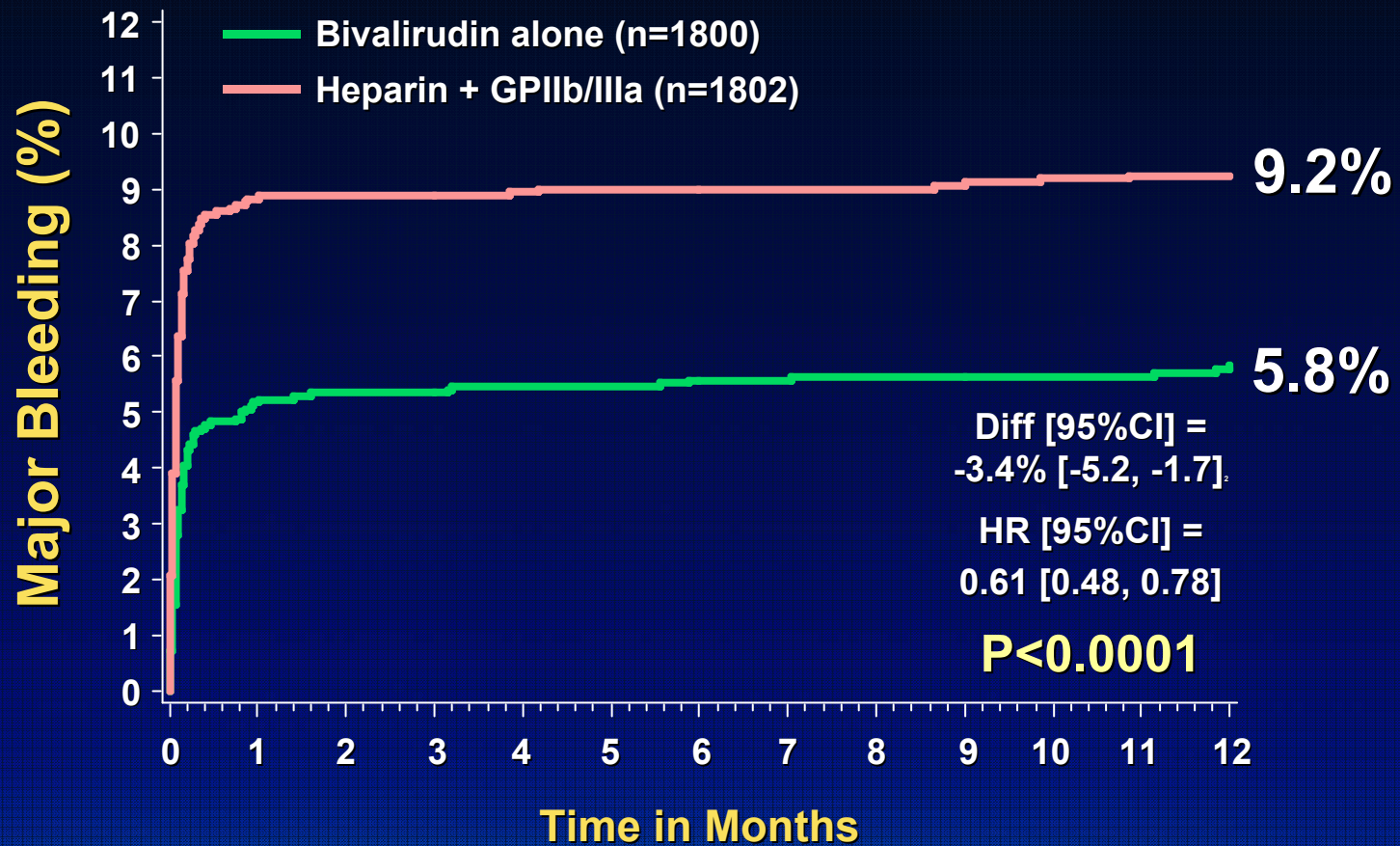
30 Day Mortality: Cardiac and Non Cardiac



Number at risk

Bivalirudin	1800	1758	1751	1746	1742	1729	1666
Heparin + GPIIb/IIIa	1802	1764	1748	1736	1728	1707	1630

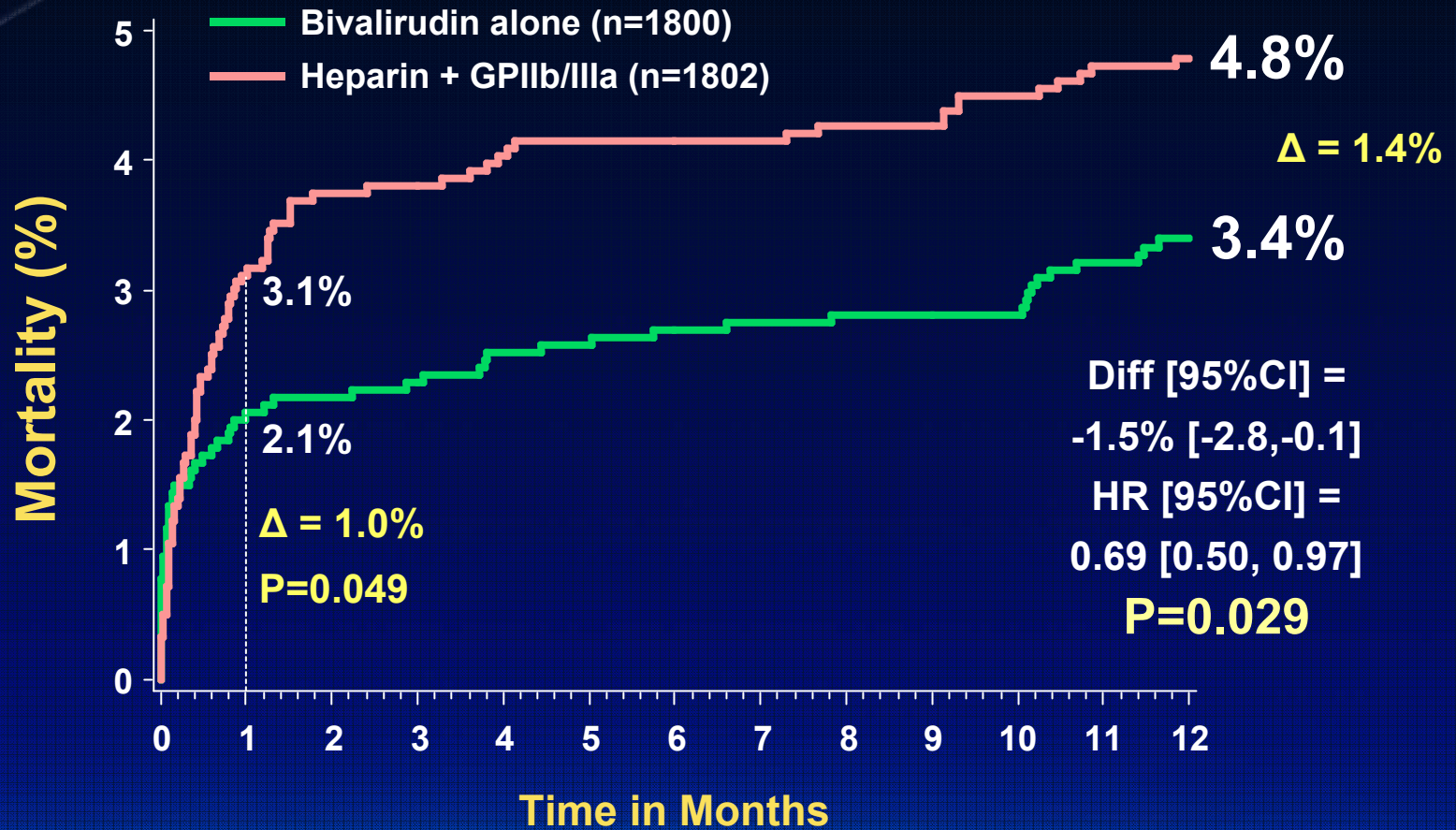
1-Year Major Bleeding (non-CABG)



Number at risk

	0	1	2	3	4	5	6	7	8	9	10	11	12
Bivalirudin alone	1800	1621	1601	1586	1586	1586	1586	1586	1586	1586	1586	1586	1448
Heparin+GPIIb/IIIa	1802	1544	1532	1515	1515	1515	1515	1515	1515	1515	1515	1515	1368

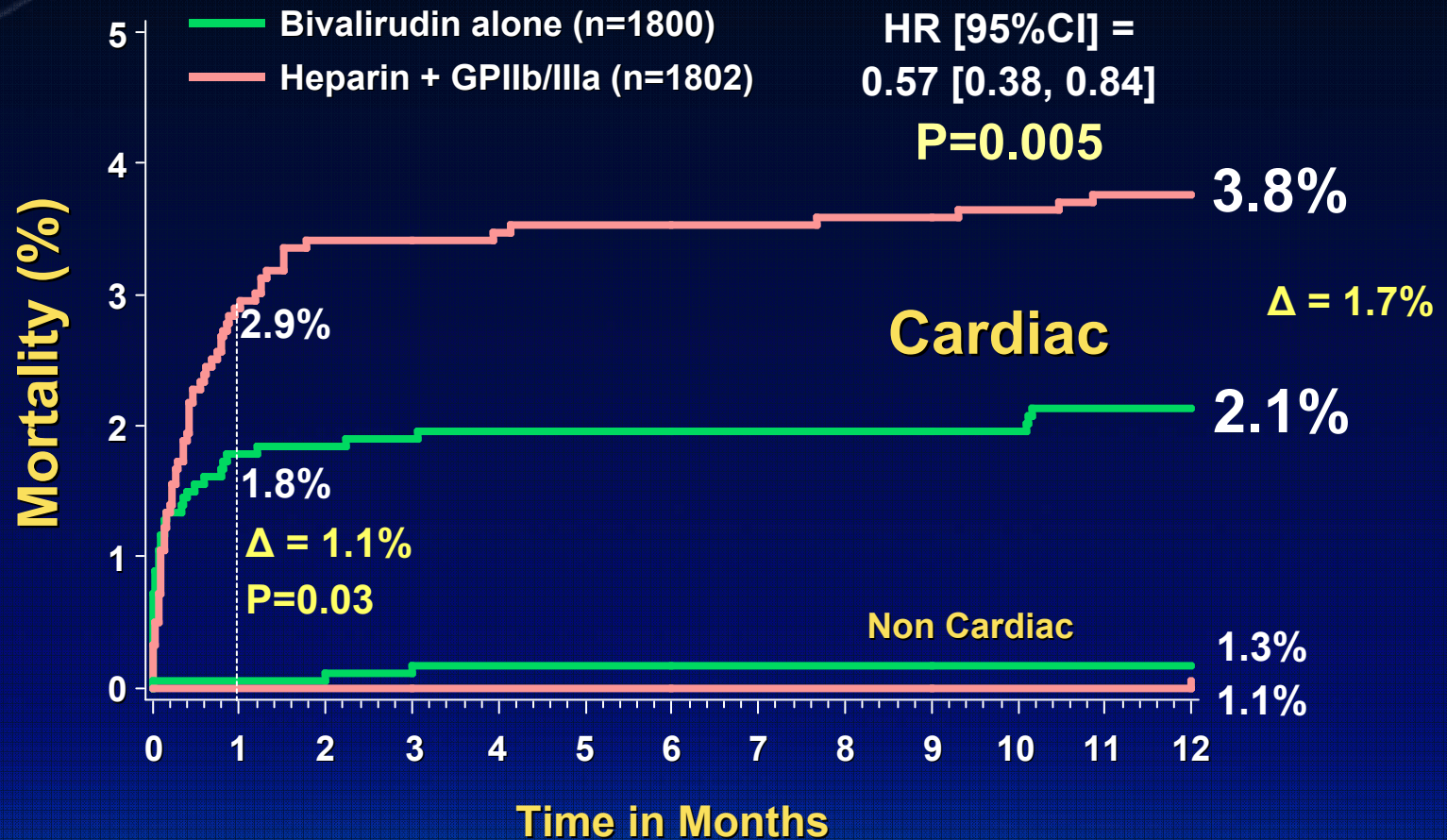
1-Year All-Cause Mortality



Number at risk

Bivalirudin alone	1800	1705	1684	1669	1520
Heparin+GPIIb/IIIa	1802	1678	1663	1646	1486

1-Year Mortality: Cardiac and Non Cardiac



Number at risk

Bivalirudin alone	1800	1705	1684	1669	1520
Heparin+GPIIb/IIIa	1802	1678	1663	1646	1486

1-Year MACE Components*

	UFH + GPI (N=1802)	Bivalirudin (N=1800)	HR [95%CI]	P Value
Death	4.8%	3.4%	0.69 [0.50,0.97]	0.029
- Cardiac	3.8%	2.1%	0.57 [0.38,0.84]	0.005
- Non cardiac	1.1%	1.3%	1.14 [0.62,2.11]	0.67
Reinfarction	4.4%	3.6%	0.81 [0.58,1.14]	0.22
- Q-wave	2.1%	2.2%	1.06 [0.67,1.67]	0.81
- Non Q-wave	2.7%	1.4%	0.53 [0.32,0.86]	0.01
Death or reinfarction	8.5%	6.6%	0.77 [0.61,0.98]	0.04
Ischemic TVR	5.9%	7.2%	1.23 [0.94,1.60]	0.12
- Ischemic TLR	4.5%	6.0%	1.34 [1.00,1.80]	0.051
- Ischemic remote TVR	2.0%	2.3%	1.13 [0.71,1.79]	0.60
Stroke	1.2%	1.1%	1.00 [0.54,1.85]	0.99

*All Kaplan-Meier estimates, CEC adjudicated

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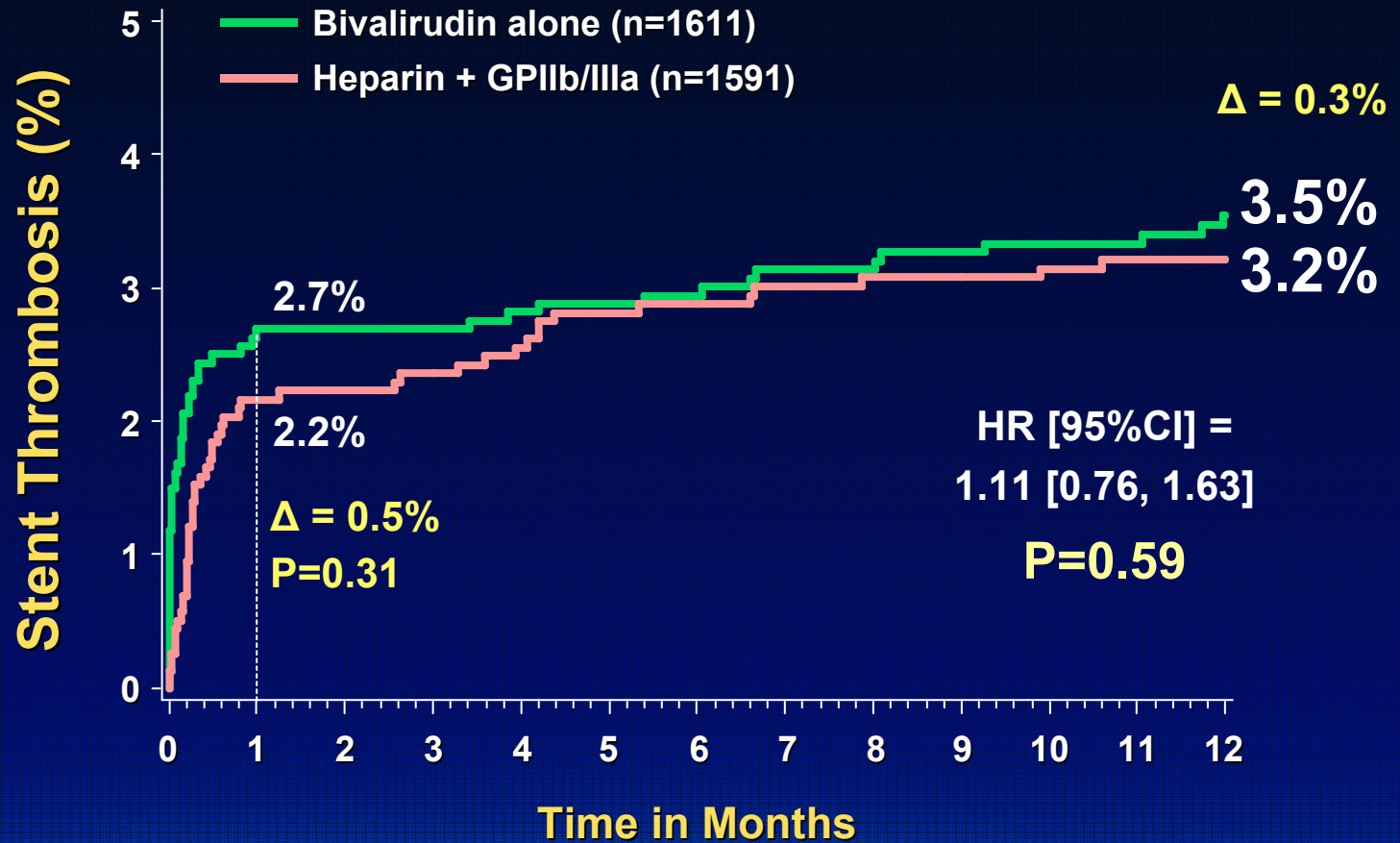
Adverse Events Between 30 Days and 1-Year

	UFH + GPI (N=1802)	Bivalirudin (N=1800)	P Value
Death	1.8%	1.4%	0.31
- Cardiac	0.9%	0.4%	0.046
- Non cardiac	0.9%	1.0%	0.75
Reinfarction	2.8%	1.7%	0.04
Death or reinfarction	4.4%	3.0%	0.02
Ischemic TVR	4.3%	4.7%	0.57
Stroke	0.5%	0.4%	0.77
MACE	7.3%	6.8%	0.52
Major bleeding (non CABG)	0.7%	0.8%	0.71
NACE	7.8%	7.3%	0.52

*Kaplan-Meier estimates, landmark analysis, CEC adjudicated

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1-Year Stent Thrombosis (ARC Definite/Probable)

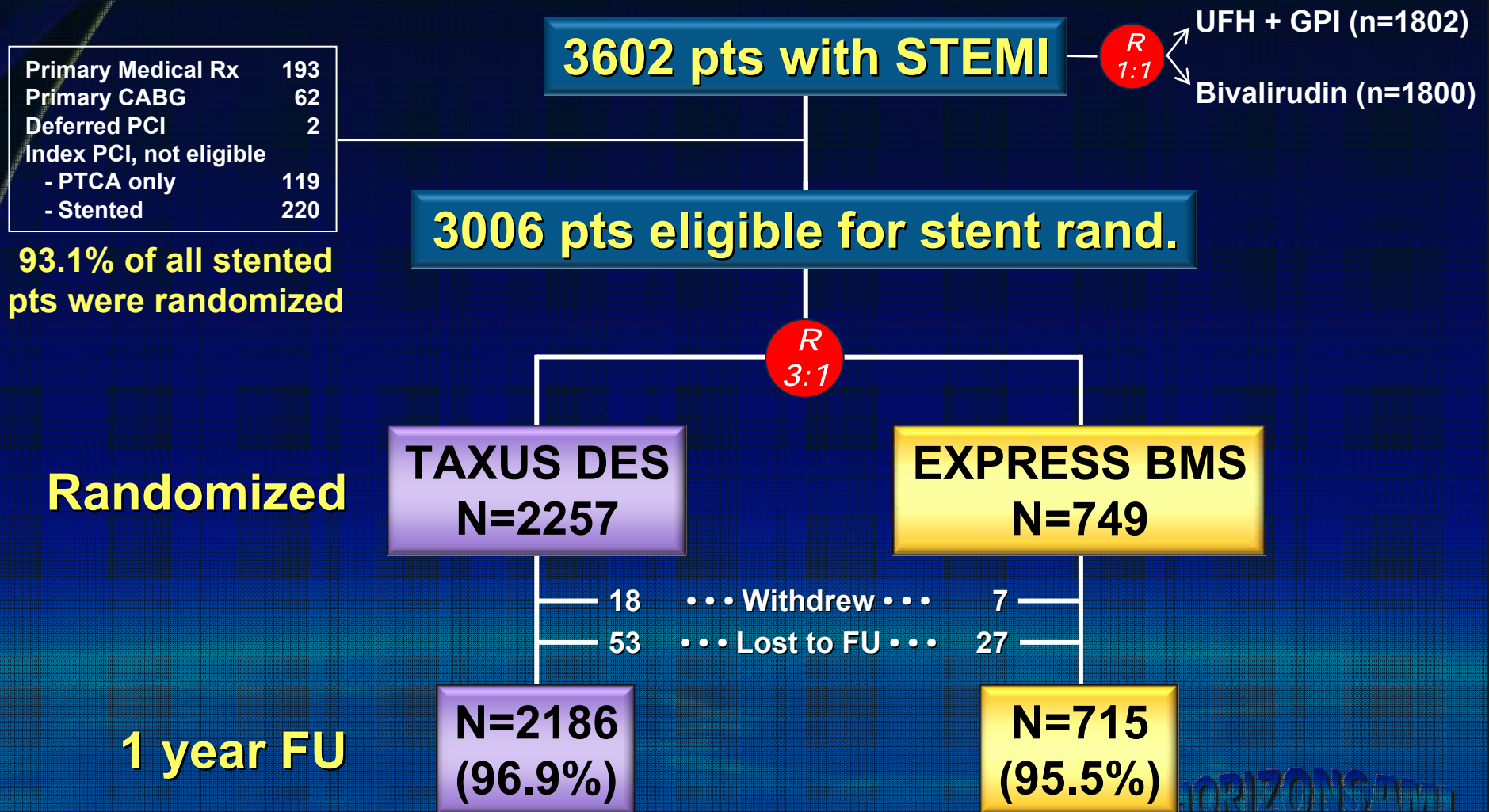


Number at risk

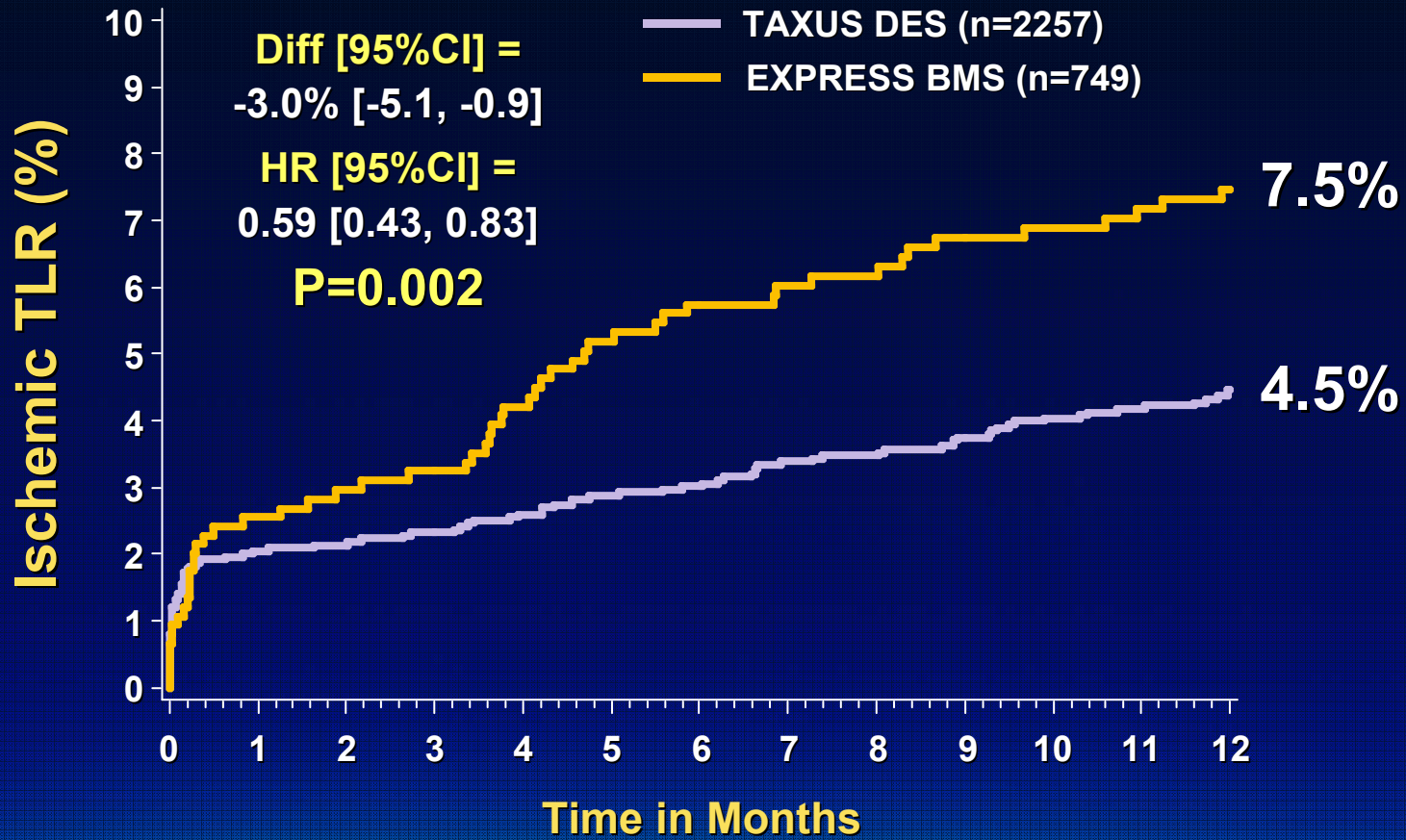
Bivalirudin alone	1611	1525	1504	1486	1356
Heparin+GPIIb/IIIa	1591	1495	1475	1457	1315

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Harmonizing Outcomes with Revascularization and Stents in AMI



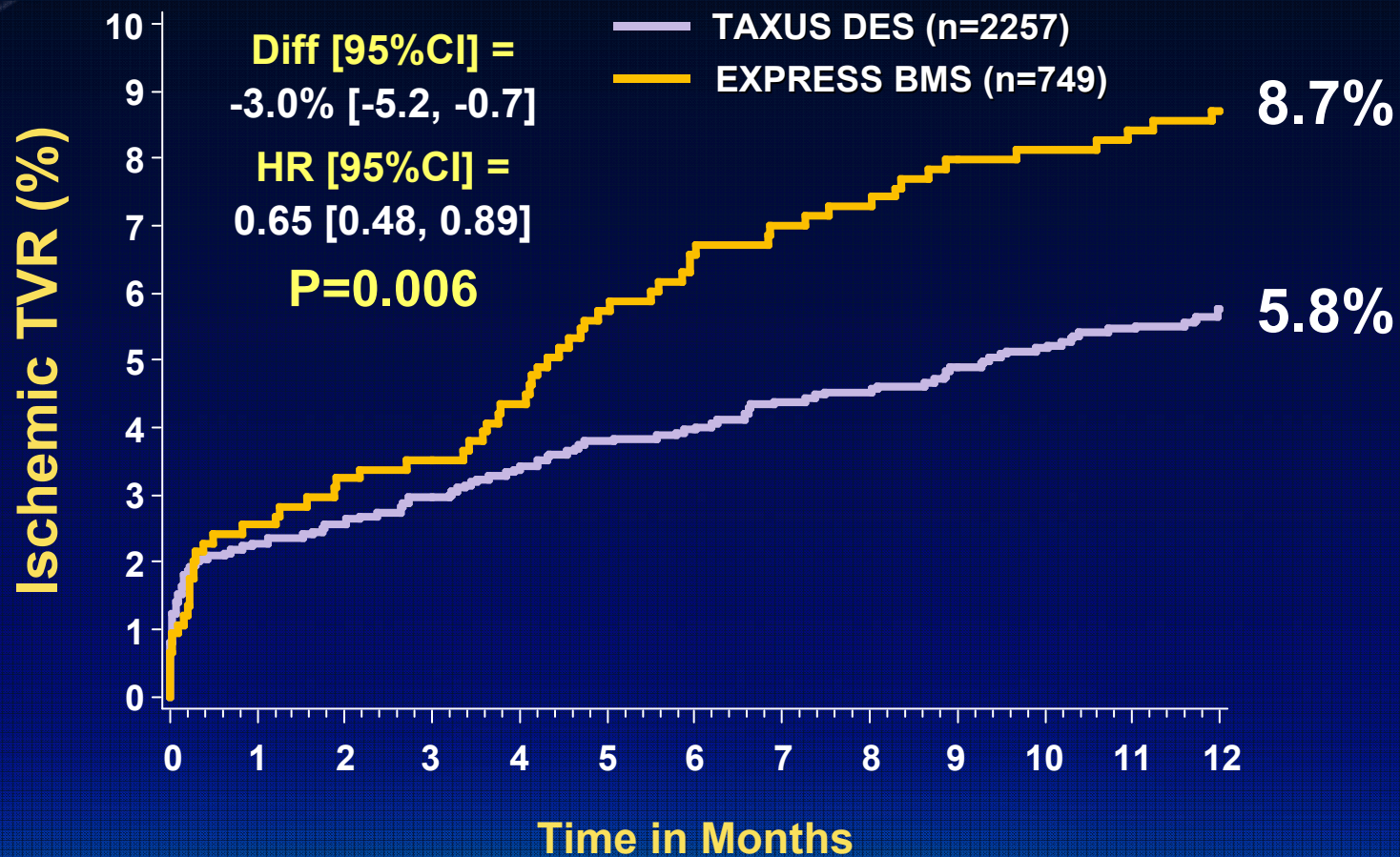
Primary Efficacy Endpoint: Ischemic TLR



Number at risk

TAXUS DES	2257	2132	2098	2069	1868
EXPRESS BMS	749	697	675	658	603

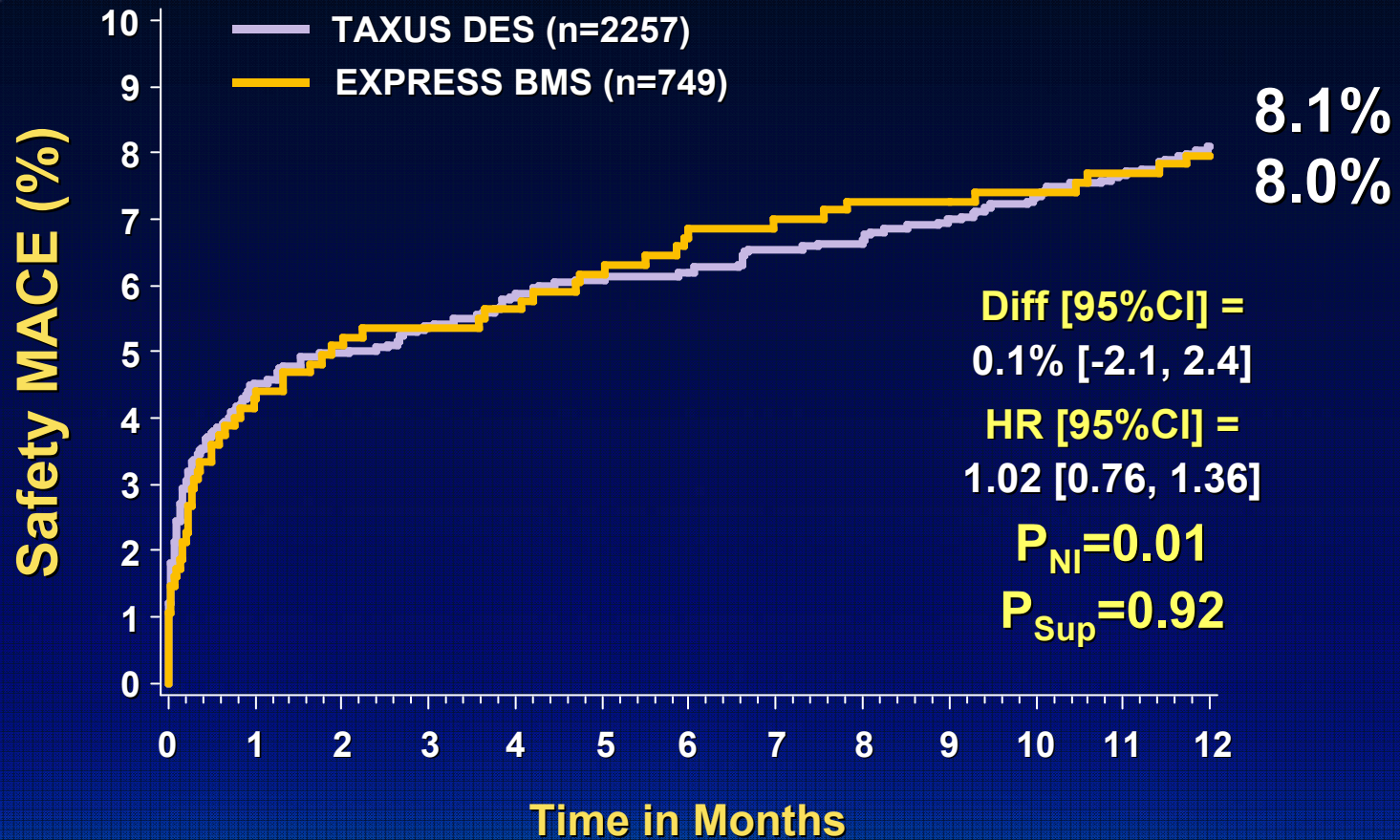
Secondary Efficacy Endpoint: **Ischemic TVR**



Number at risk

TAXUS DES	2257	2119	2078	2045	1848
EXPRESS BMS	749	695	669	650	598

Primary Safety Endpoint: **Safety MACE***



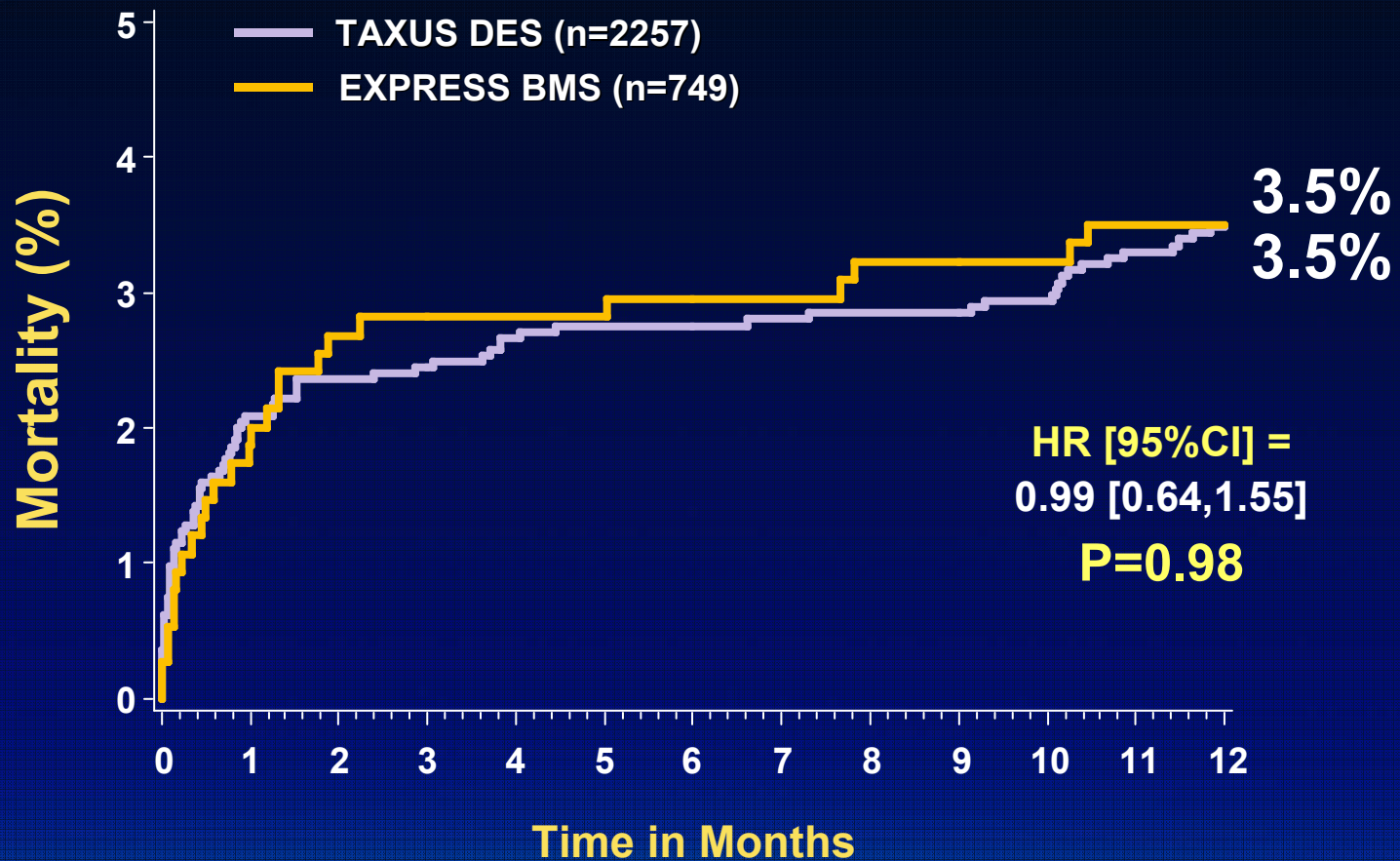
Number at risk

TAXUS DES	2257	2115	2086	2057	1856
EXPRESS BMS	749	697	683	672	619

* Safety MACE = death, reinfarction, stroke, or stent thrombosis

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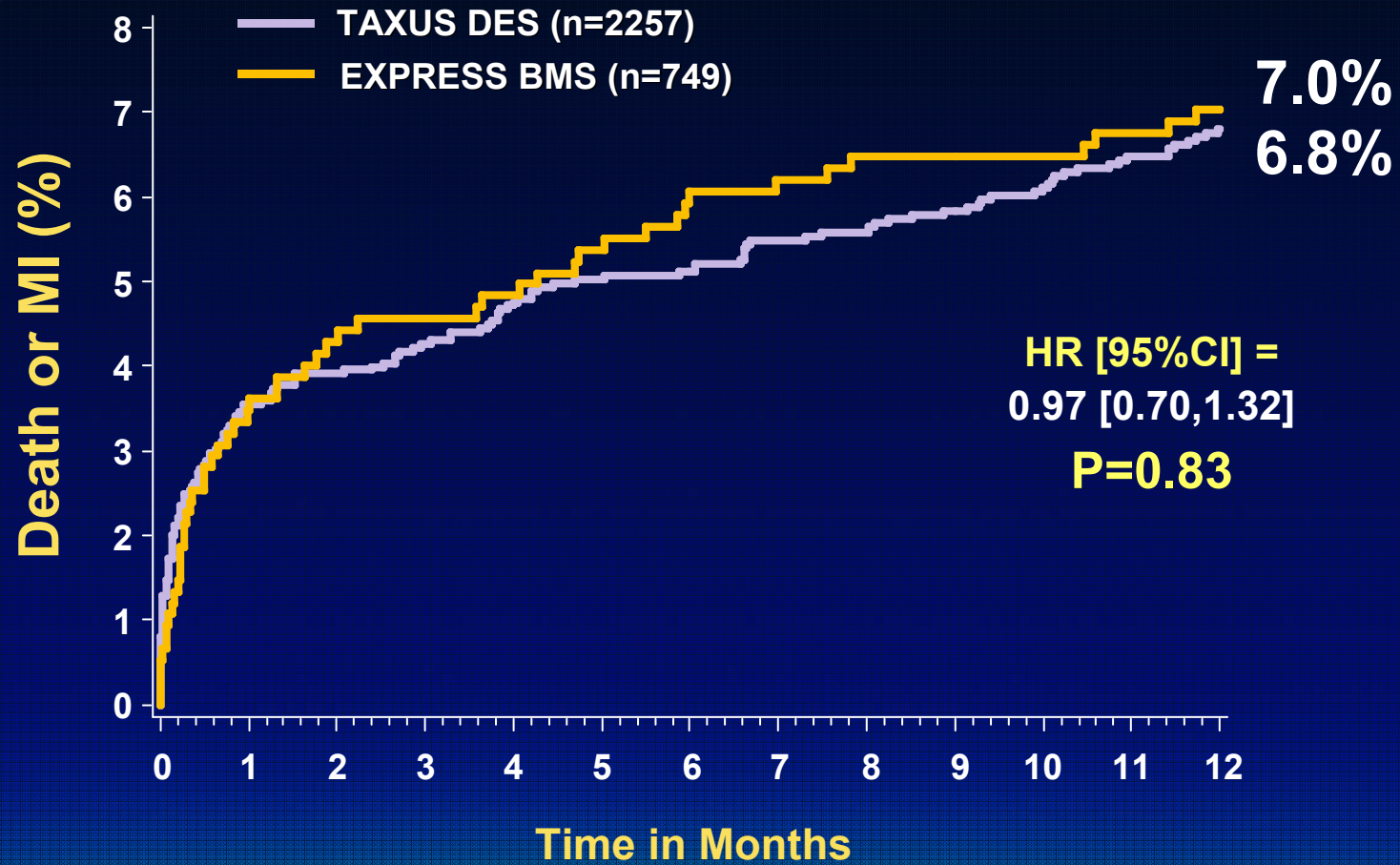
One-Year All-Cause Mortality



Number at risk

TAXUS DES	2257	2180	2161	2147	1949
EXPRESS BMS	749	716	712	702	648

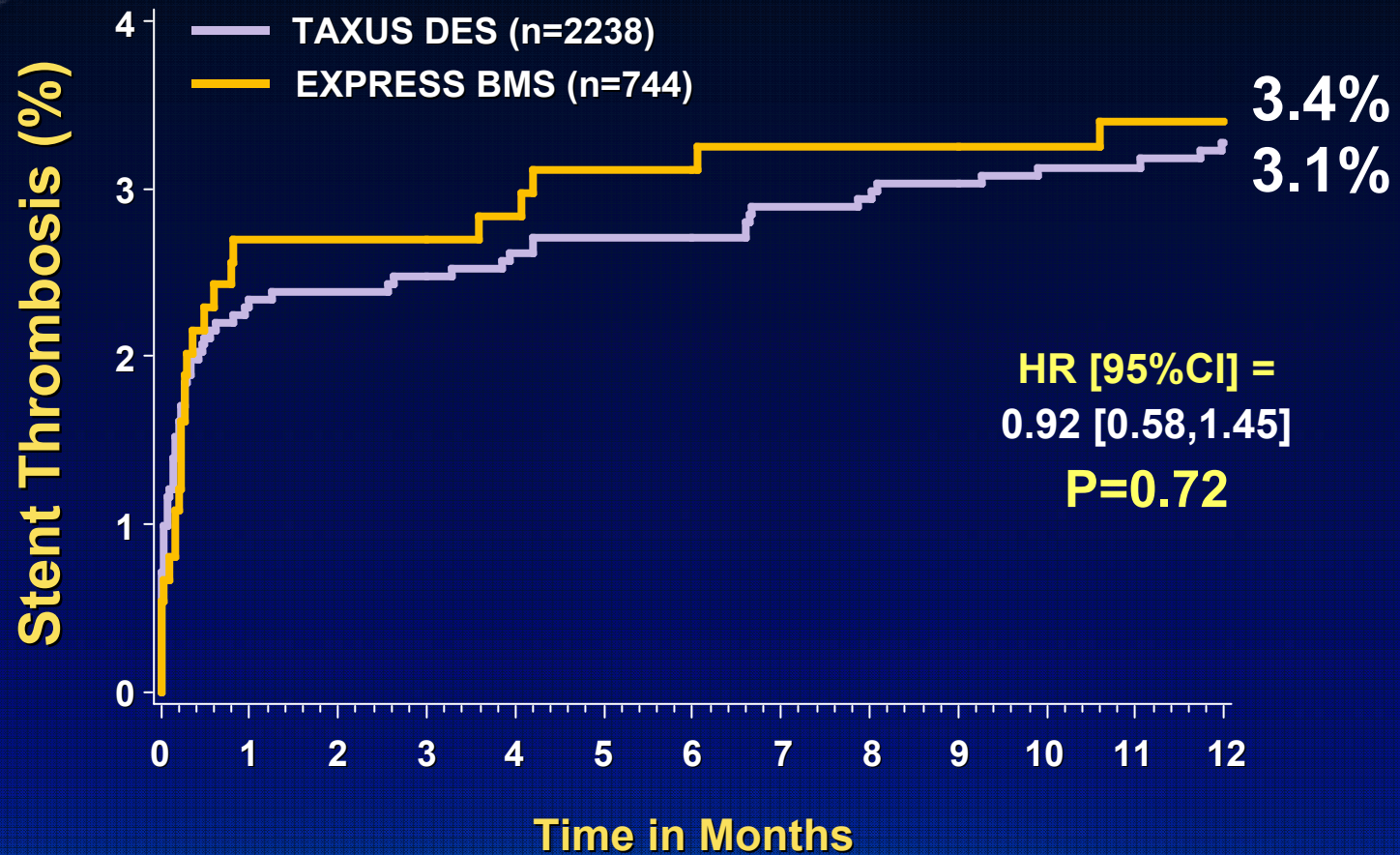
One-Year Death or Reinfarction



Number at risk

TAXUS DES	2257	2140	2110	2083	1882
EXPRESS BMS	749	703	689	678	625

Stent Thrombosis (ARC Definite or Probable)



Number at risk

TAXUS DES	2238	2122	2098	2078	1884
EXPRESS BMS	744	701	694	683	629

Stent Thrombosis Rates*

	TAXUS (N=2238)	EXPRESS (N=744)	Hazard ratio [95%CI]	P Value
Stent thrombosis, ≤30 days	2.3%	2.7%	0.87 [0.52,1.46]	0.60
- ARC definite	1.9%	2.3%	0.83 [0.47,1.45]	0.51
- ARC probable	0.5%	0.4%	1.11 [0.31,4.05]	0.87
Stent thrombosis, >30d – 1y	1.0%	0.7%	1.39 [0.52,3.68]	0.51
- ARC definite	0.9%	0.7%	1.25 [0.47,3.35]	0.65
- ARC probable	0.1%	0%	-	0.42
Stent thrombosis, ≤1 year	3.1%	3.4%	0.92 [0.58,1.45]	0.72
- ARC definite	2.6%	3.0%	0.86 [0.53,1.41]	0.55
- ARC probable	0.5%	0.4%	1.33 [0.38,4.73]	0.65

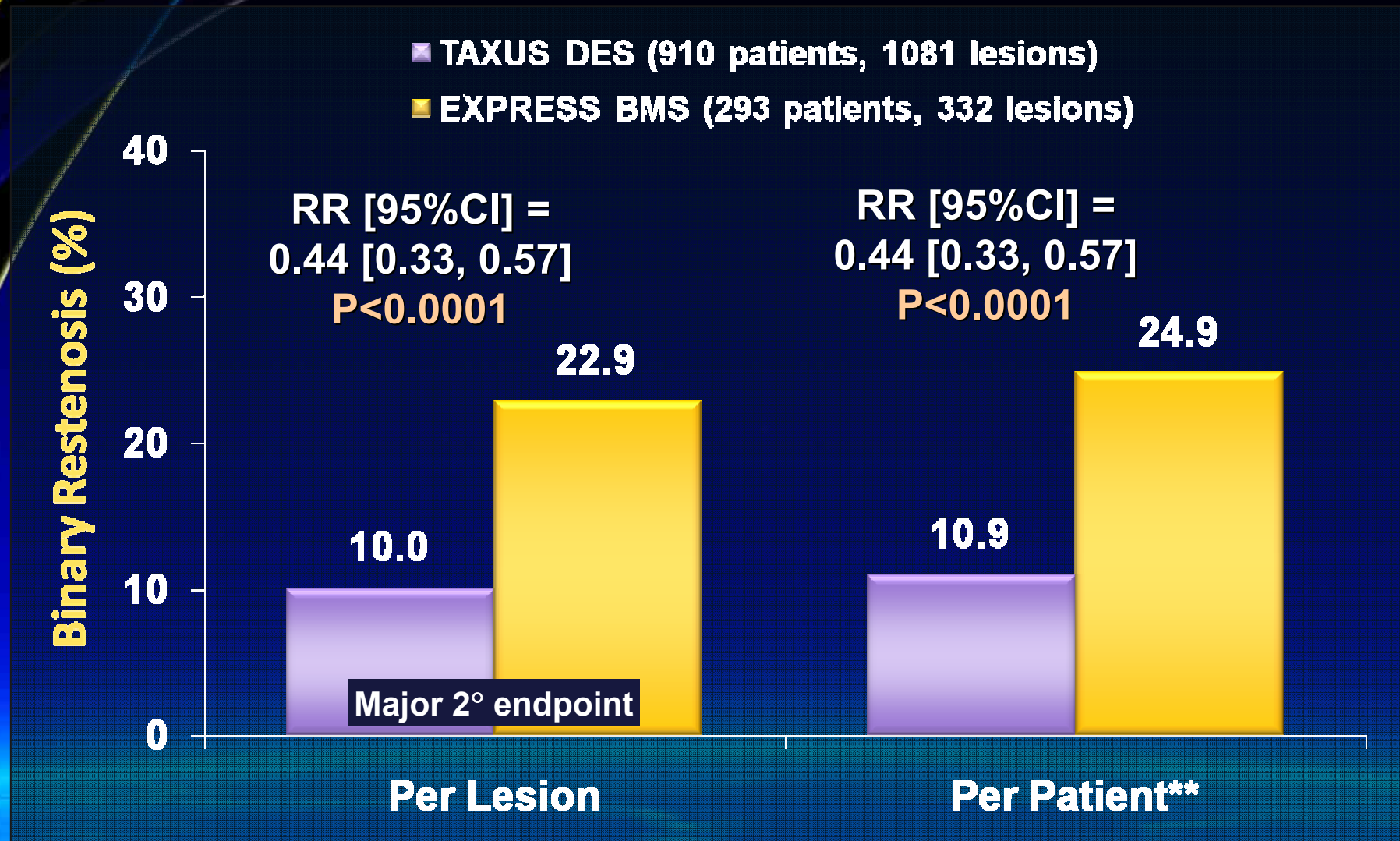
*Kaplan-Meier estimates

Stone GW. TCT 2008

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Binary Analysis Segment Restenosis at 13 Months

Patient and Lesion Level Analysis*

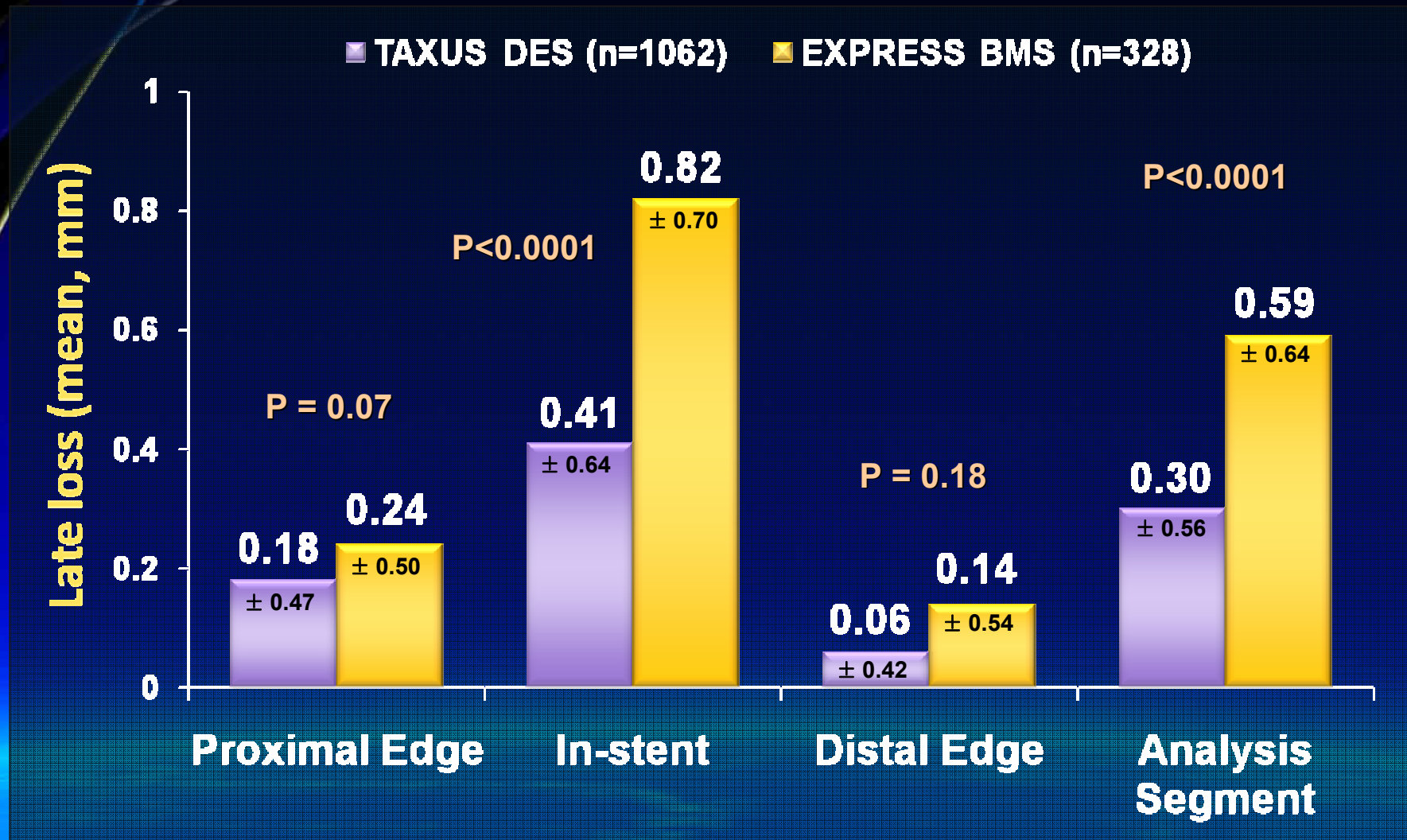


* ITT: Includes all stent randomized lesions, whether or not a stent was implanted, and whether or not non study stents were placed

** Any lesion with restenosis \Rightarrow per pt restenosis

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Angiographic Late Loss at 13 Month Lesions with Stents Implanted



Clinical Implications

- ▬ **HORIZONS-AMI has demonstrated that the prevention of hemorrhagic complications after primary PCI in STEMI results in improved early and late survival, and that paclitaxel-eluting stents safely reduce restenosis at 1 year**
 - **Optimal drug and stent selection are essential to enhance outcomes for pts undergoing interventional therapies**