Bare Metal Stents vs. Drug-Eluting Stents for STEMI: Is it Settled?

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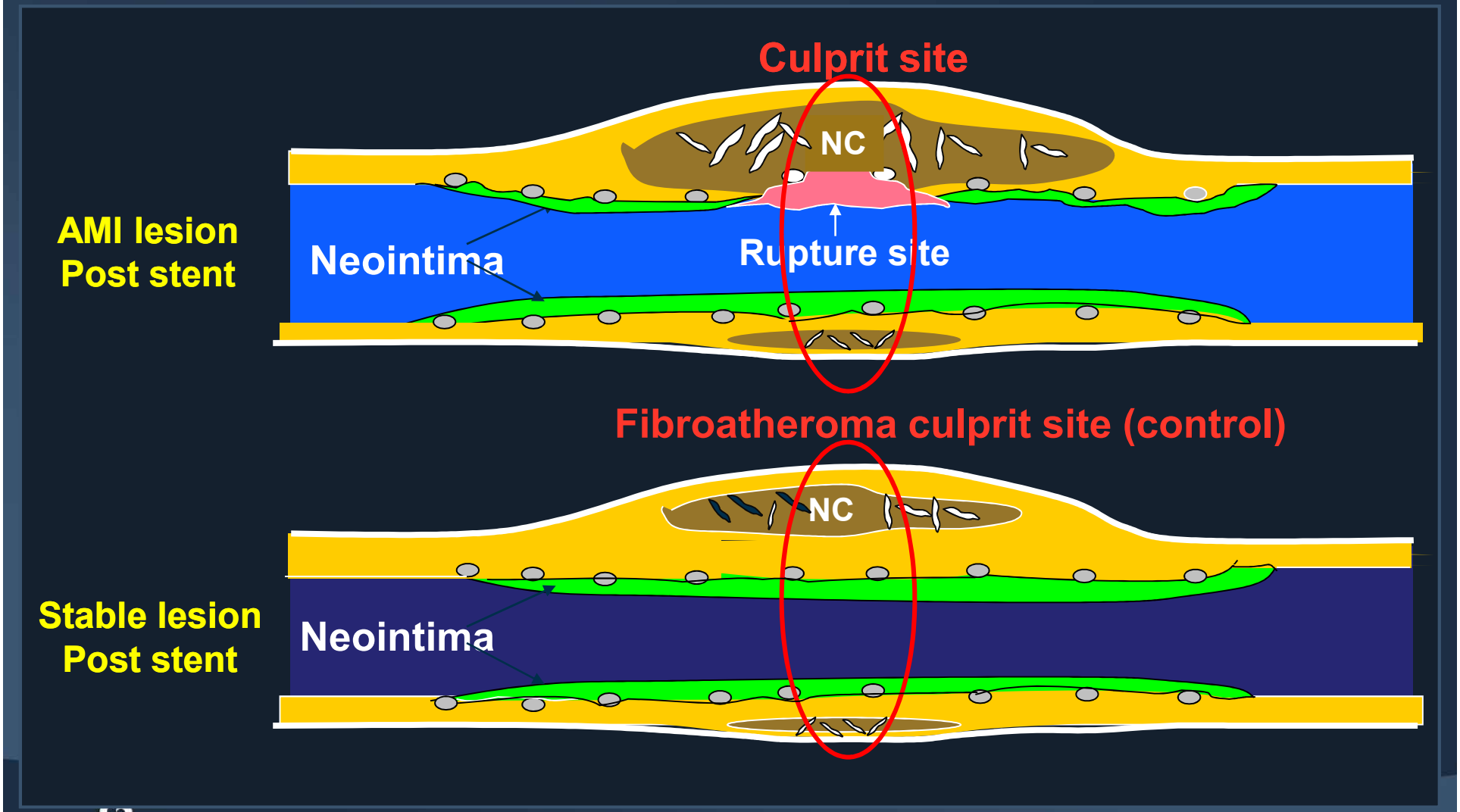
Conflict of Interest Disclosure

- Ajay J. Kirtane
  - In the last 12 months, I have received honoraria/consultancy fees from Abbott Vascular, Boston Scientific, and Medtronic CardioVascular
  - Off-label use will be discussed

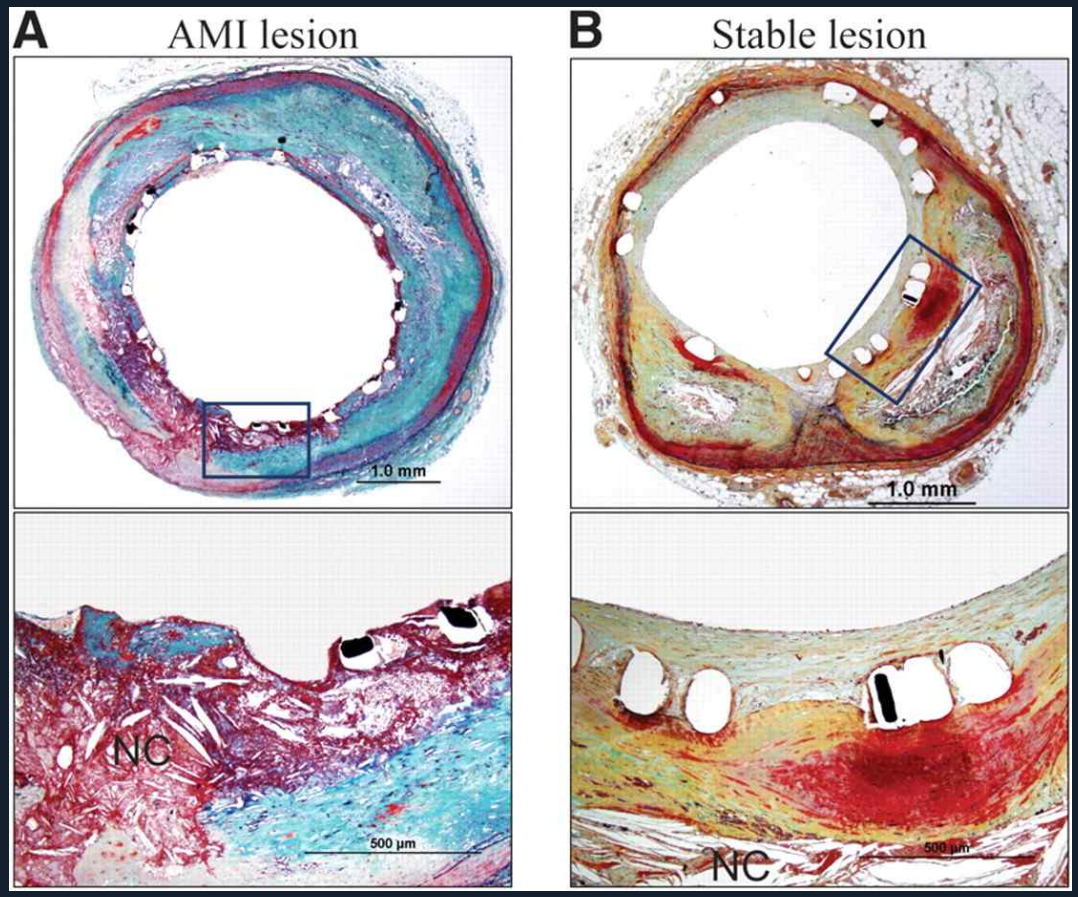
DES vs. BMS in STEMI: Why the Debate?

- **STEMI patients have the highest thrombotic risk (potential for worse safety)**
  - Worsened healing response after stenting?
  - Greater potential for malapposition and/or underexpansion
  - Highest ST rates, meeting patient "under the gun"
- **STEMI lesions have lower restenosis rates (potential for less DES efficacy)**
  - Less plaque, ISR less manifest

Distinction between AMI and Non-AMI Lesions



Delayed Arterial Healing with DES in AMI



Persistent fibrin deposition and uncovered struts in AMI compared to stable lesions treated with DES

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Nakazawa and Virmani et al. Circulation 2008

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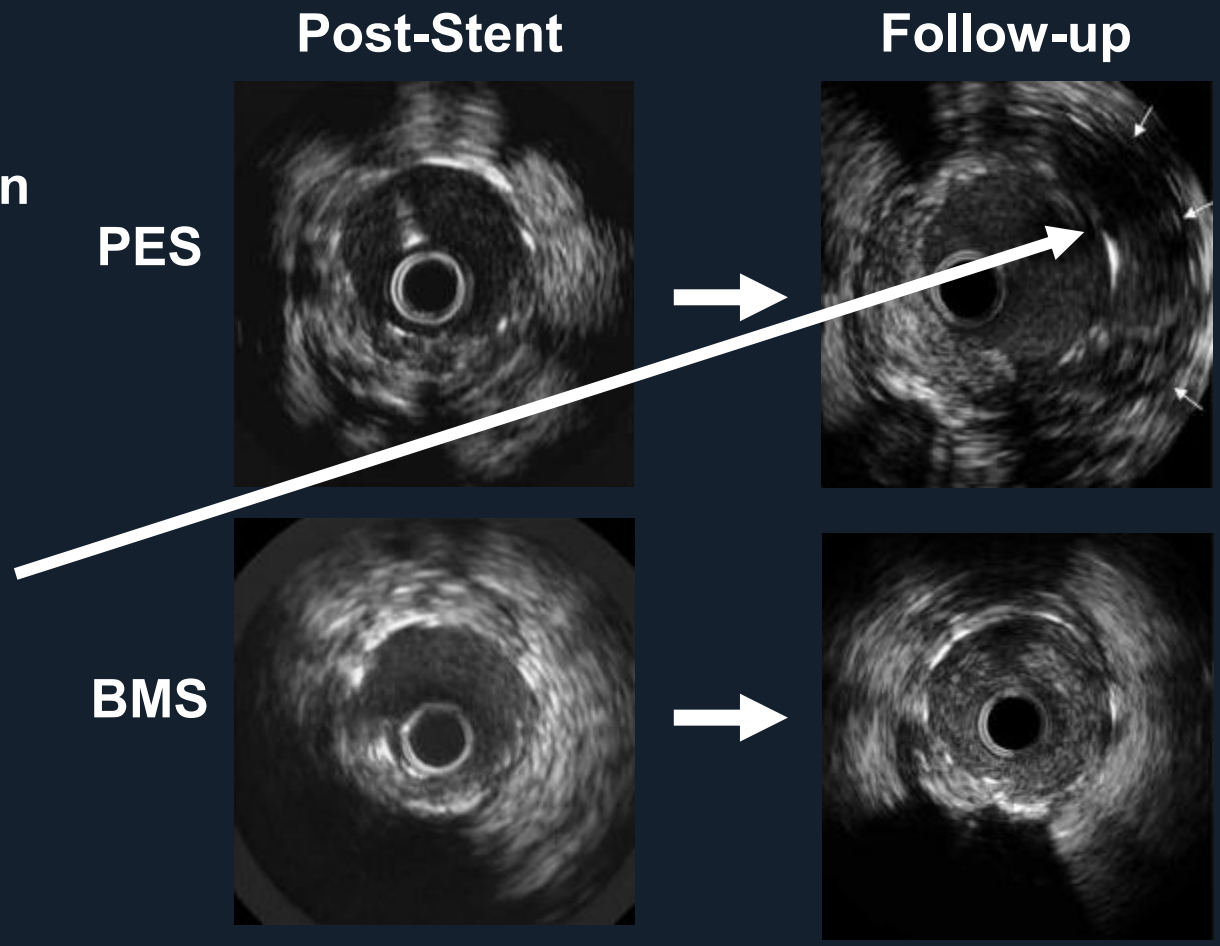
Pathologic Assessment at Culprit Site (AMI vs. Stable patients)

	AMI with rupture (n=17)	Stable with FA (n=18)	p value AMI vs. Stable
Neointimal thickness, mm	0.04 (0.02, 0.09)	0.11 (0.07, 0.21)	0.008
Strut with fibrin deposition, %	63 ± 28	36 ± 27	0.008
Strut with inflammation, %	35 (27, 49)	17 (7, 25)	0.003
Uncovered strut, %	49 (16, 96)	9 (0, 39)	0.01

HORIZONS-AMI IVUS Substudy

402 patients, 446 lesions with serial IVUS data

- PES reduced net volume obstruction compared to BMS
- PES was associated with more late malapposition compared to BMS (29.6% vs. 7.9%, p<0.001)



Maehara A et al, Circulation 2009

Stent Thrombosis
Patient, Procedure, Device

Patient Factors

- Higher Risk (Syndrome, Comorbidities)
- Adjunctive therapies
- AP Adherence and/or Responsiveness

Stent Thrombosis

Procedure

- Lesion pre/post
- Stent Expansion
- Flow/Runoff

Device

- Polymer
- Drug
- Surface

The Spanish ESTROFA Registry

23,500 pts treated w/DES at 20 Spanish hospitals from 2002–06; 63% PES, 37% SES. Dual antiplatelet Rx for 8 ± 3 months.
1.3% ST rate at median FU 22 (11, 32) mos ; 2.0% ST at 3 yrs

Multivariate Predictors of Stent Thrombosis (n=14,120)

	HR (95% CI)	P value
Late		
STEMI	5.5 (3.5–7.6)	<0.0001
LAD	3.0 (2.0–4.4)	<0.0001
Stent length (per mm↑)	1.07 (1.05–1.09)	<0.0001

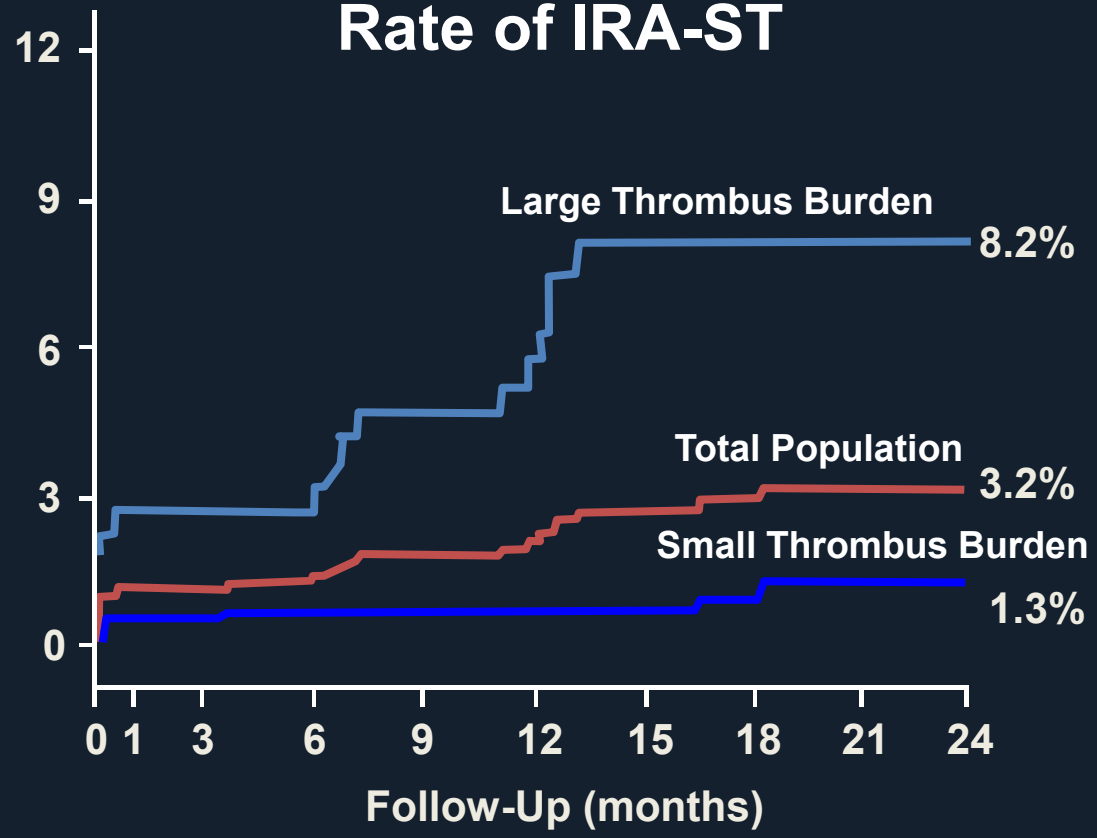
de la Torre Hernandez JM et al. *JACC* 2008;51:986-90

Impact of Thrombus Burden with DES in AMI

792 STEMI Patients with DES

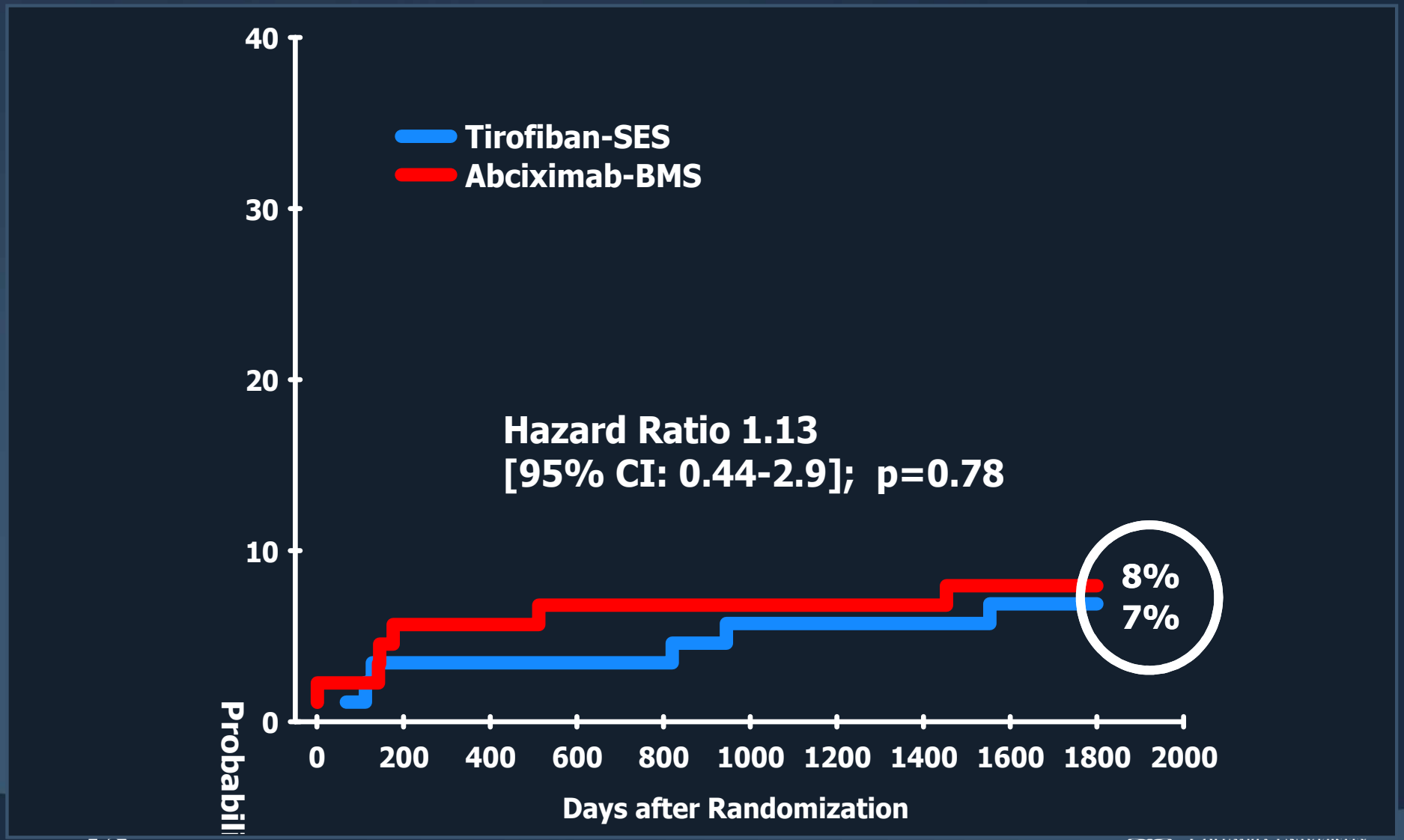
	Small	Large
Final TIMI 3	94.9%	83.6%*
TMPG-3	53.2%	35.4%*
No-reflow	0.5%	4.0%*
Distal Embol.	3.5%	17.3%*

*P<0.001



Stent Thrombosis at 5 years

ARC definite, probable, possible



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J Am Coll Cardiol in press

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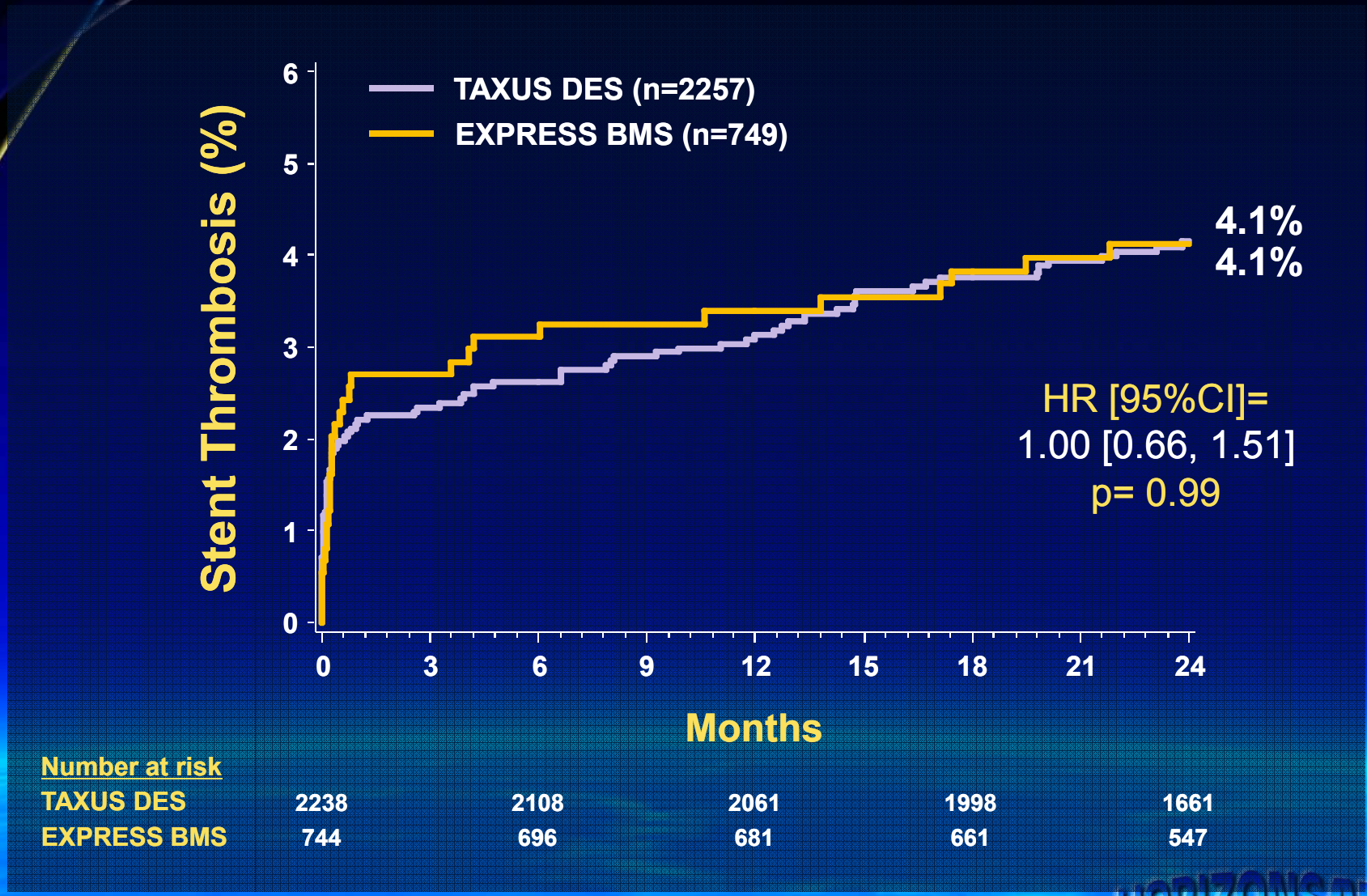
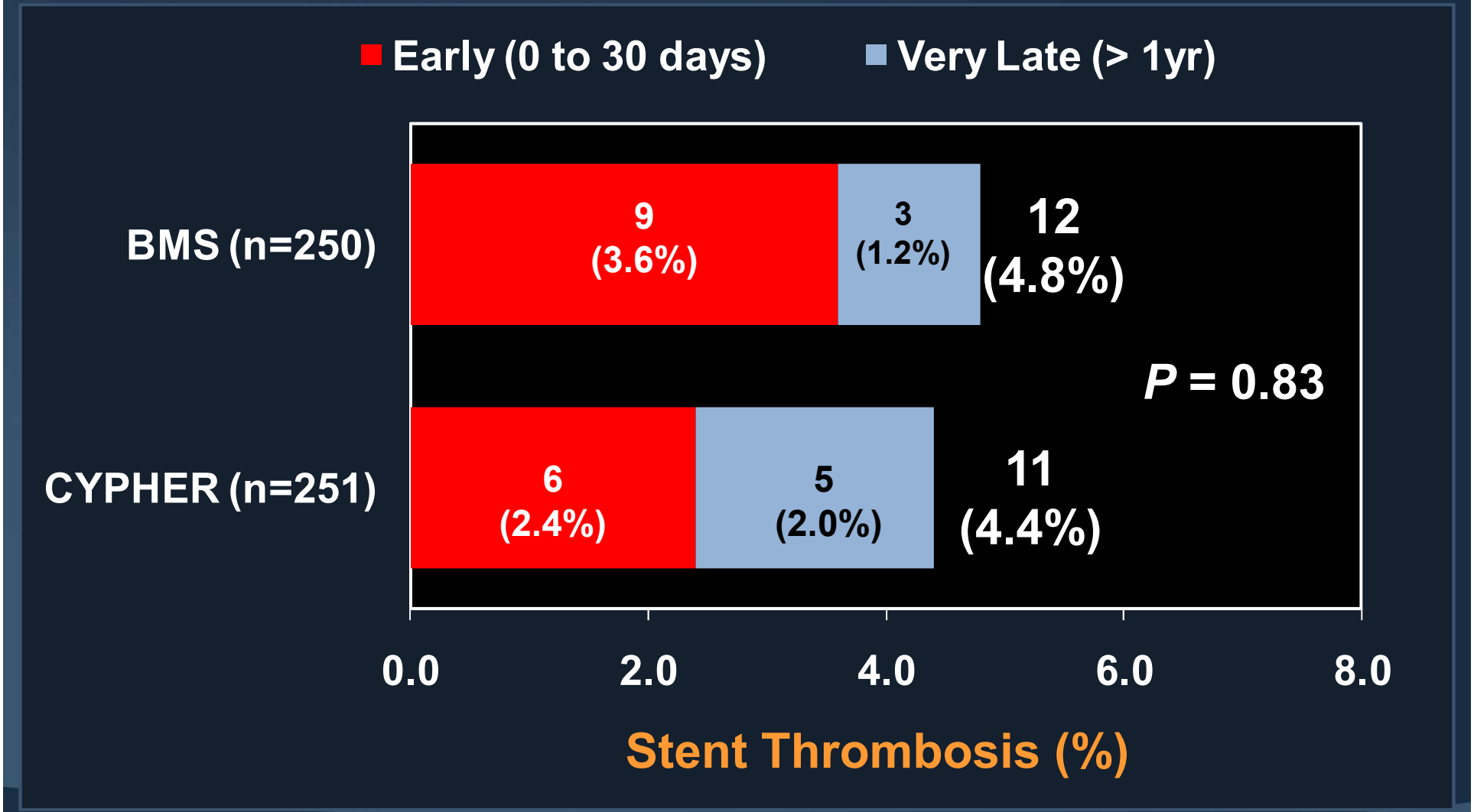
Two-Year Stent Thrombosis
(ARC Definite or Probable)



HORIZONS-AMI

TYPHOON: ARC Definite/Probable Stent Thrombosis at 4 Years



PASSION

5-Year LST and VLST

	PES N=310	BMS N=309	HR (95% CI)	*P*
Definite ST				
30 days – 1 year	1 (0.3%)	0 (0.0%)		
1 year – 5 years	7 (2.5%)	2 (0.7%)		
Total	8 (2.9%)	2 (0.8%)	3.95 (0.81 – 18.61)	0.06
Definite or Probable ST				
30 days – 1 year	2 (0.7%)	0 (0.0%)		
1 year – 5 years	7 (2.5%)	3 (1.1%)		
Total	9 (3.2%)	3 (1.1%)	2.97 (0.80 – 12.97)	0.09

Incidences were estimated from the Kaplan-Meier curves

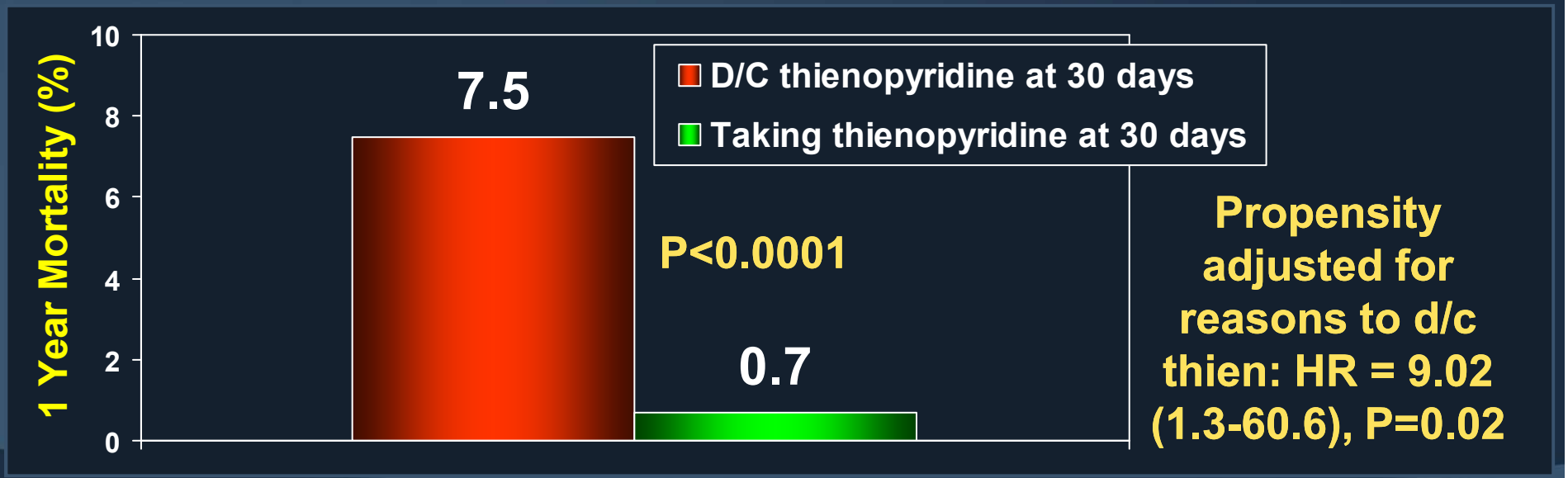
Vink, ACC/I2 2010

olvg

Impact of premature thienopyridine discontinuation: The PREMIER registry

500 pts with AMI undergoing primary PCI with DES at 19 U.S. medical centers, alive and well at 30 days

68 (13.6%) were no longer taking prescribed thienopyridines at 30 days



Propensity adjusted for reasons to d/c thien: HR = 9.02 (1.3-60.6), P=0.02

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Spertus JA et al. Circulation 2006;113:2803-9.

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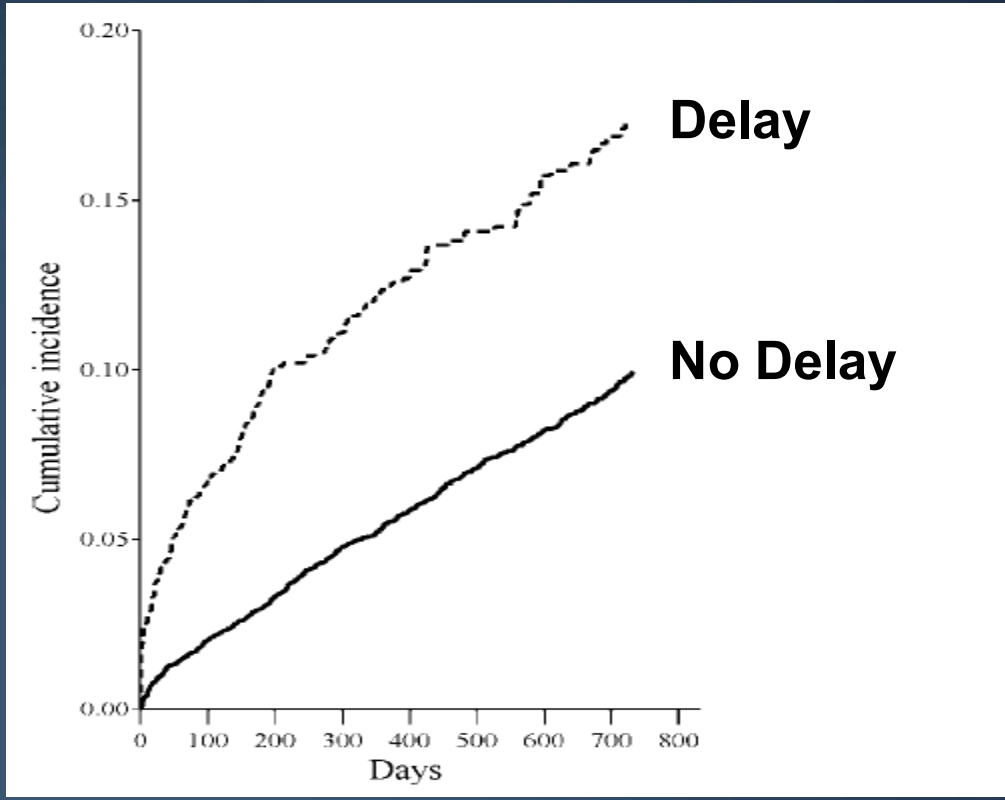
Death/MI Related to Delays in Filling Clopidogrel Prescription after DES

Of 7,402 patients, 16% did not fill a clopidogrel prescription on day of discharge (median delay of 3 days)



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Ho et al, Circ Cardiovasc Qual Outcomes 2010

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DES in AMI Meta-Analysis

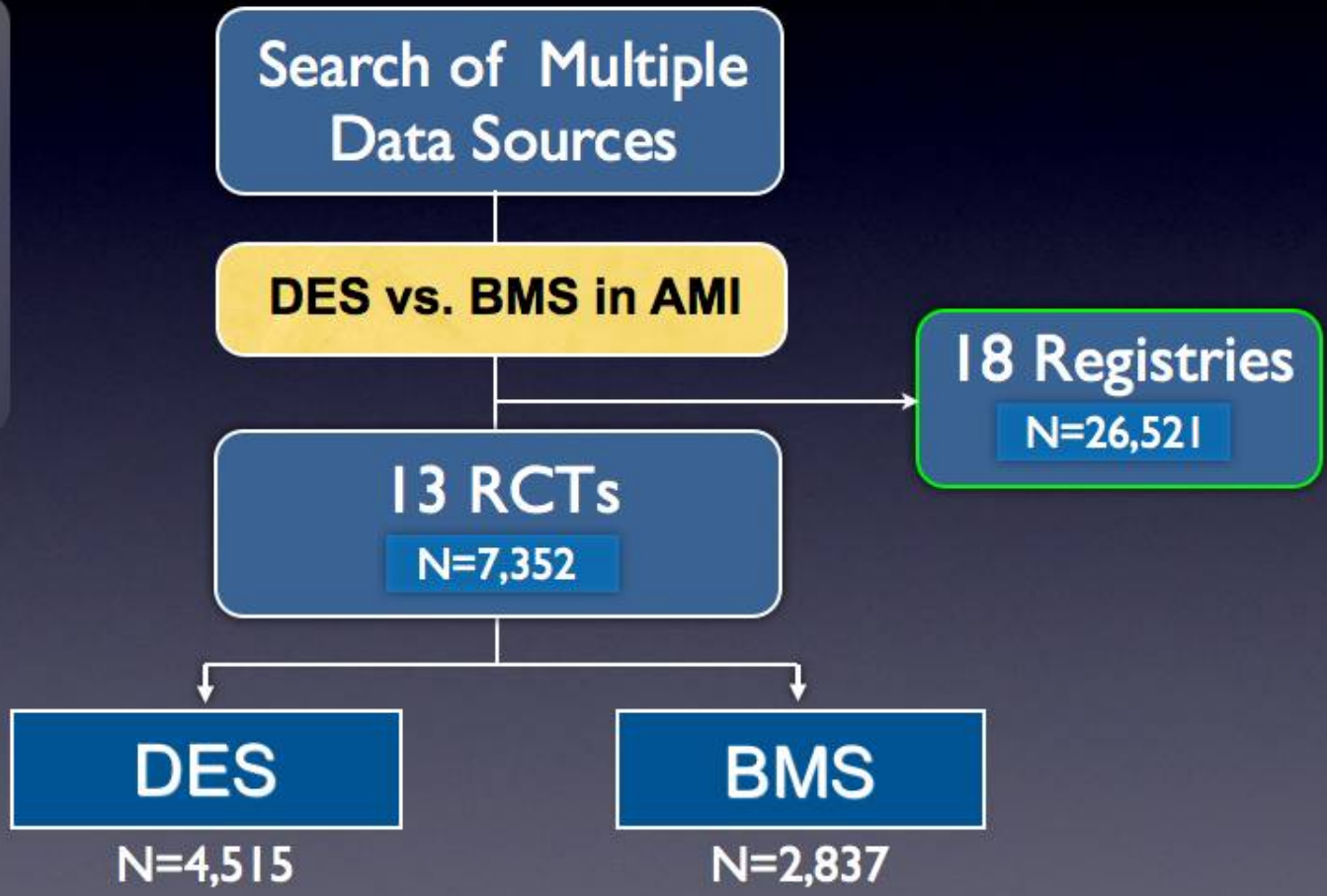
Study Flow

Dates: 2000 to 2008

FDA approved DES

Number of patients:

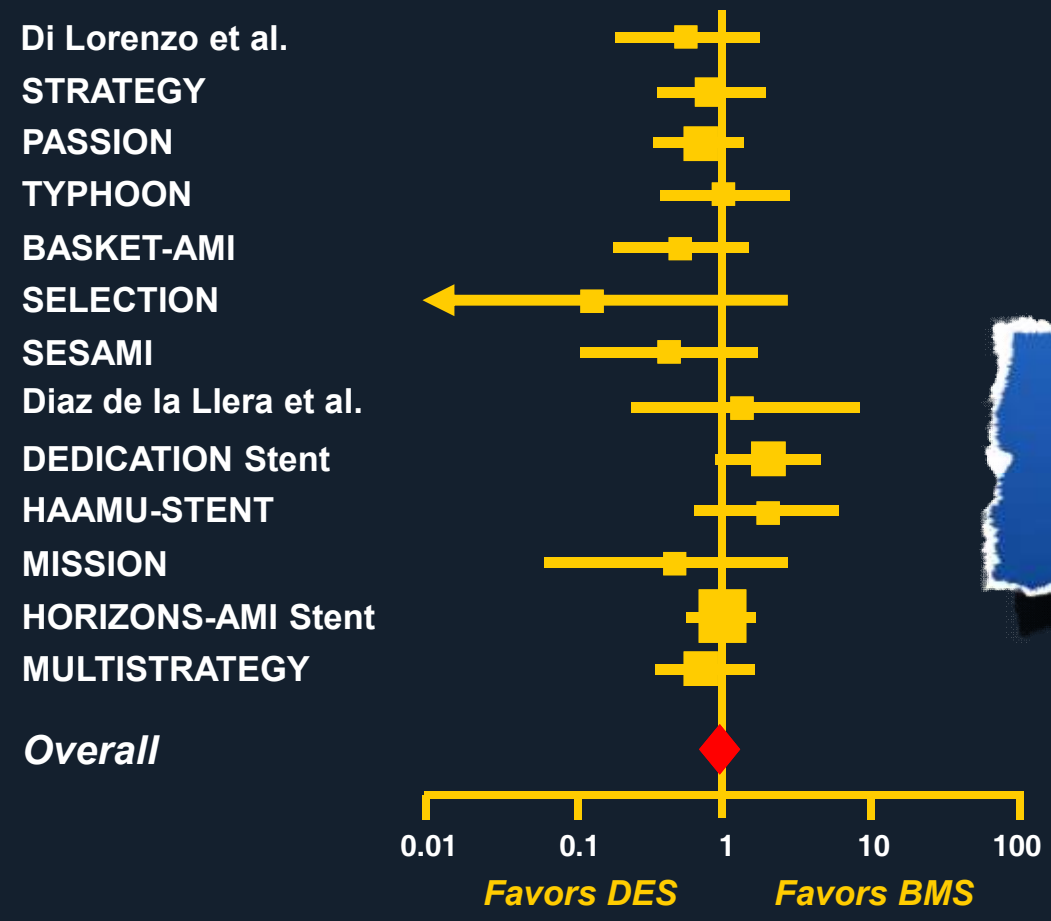
33,873



Brar et al. JACC 2009 ; 53(18)

DES in AMI Meta-Analysis

Mortality (RCTs)



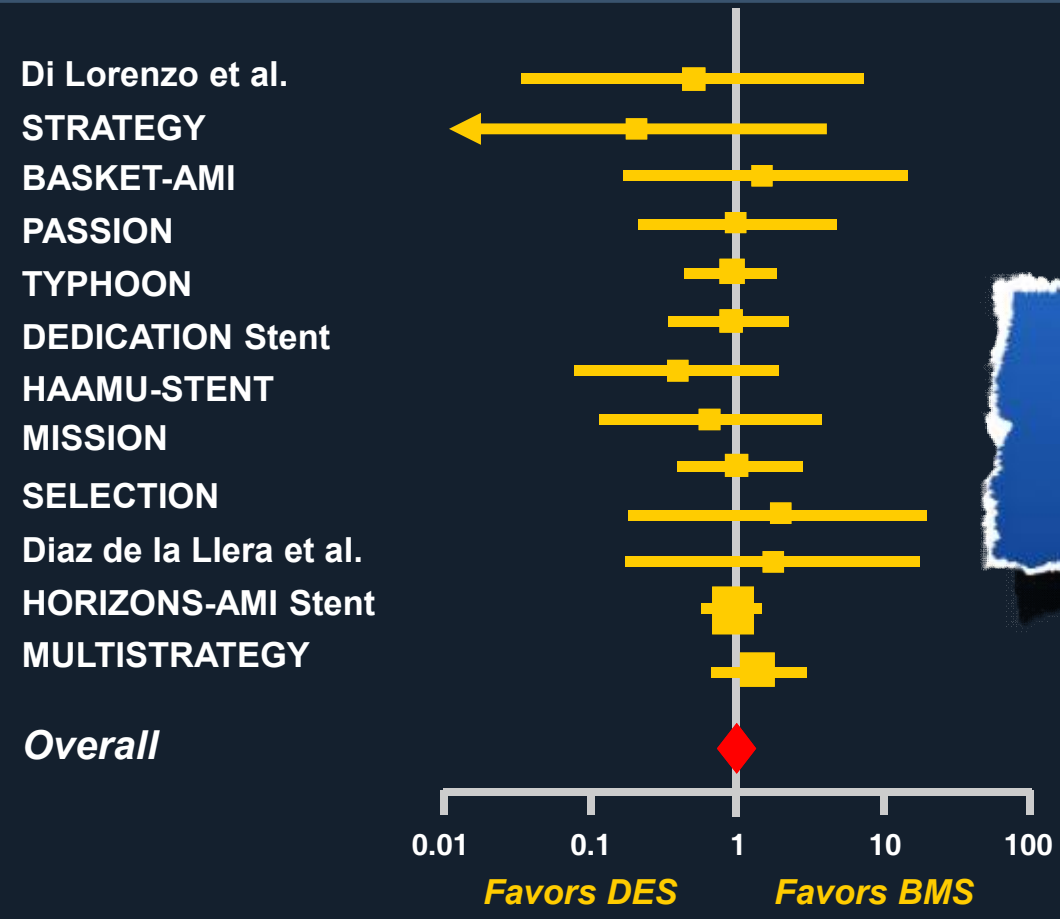
Relative Risk (95% CI)
0.89
(0.70 - 1.14)

$I^2 = 0\%$

Brar et al. *JACC* 2009; 53(18)

DES in AMI Meta-Analysis

Stent Thrombosis (RCTs)



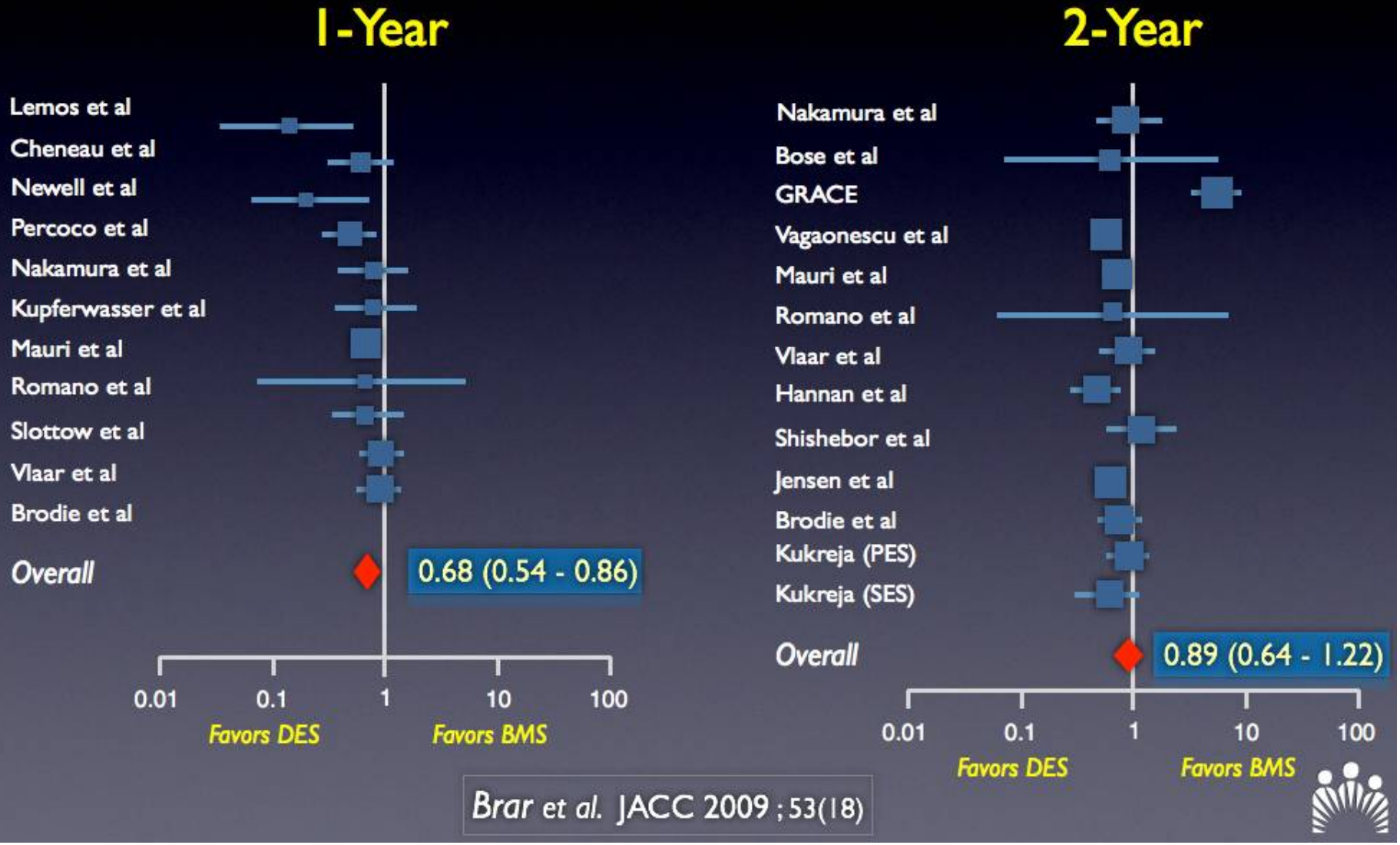
Relative Risk (95% CI)
0.97
(0.73 - 1.28)

$I^2 = 0\%$

Brar et al. *JACC* 2009; 53(18)

DES in AMI Meta-Analysis

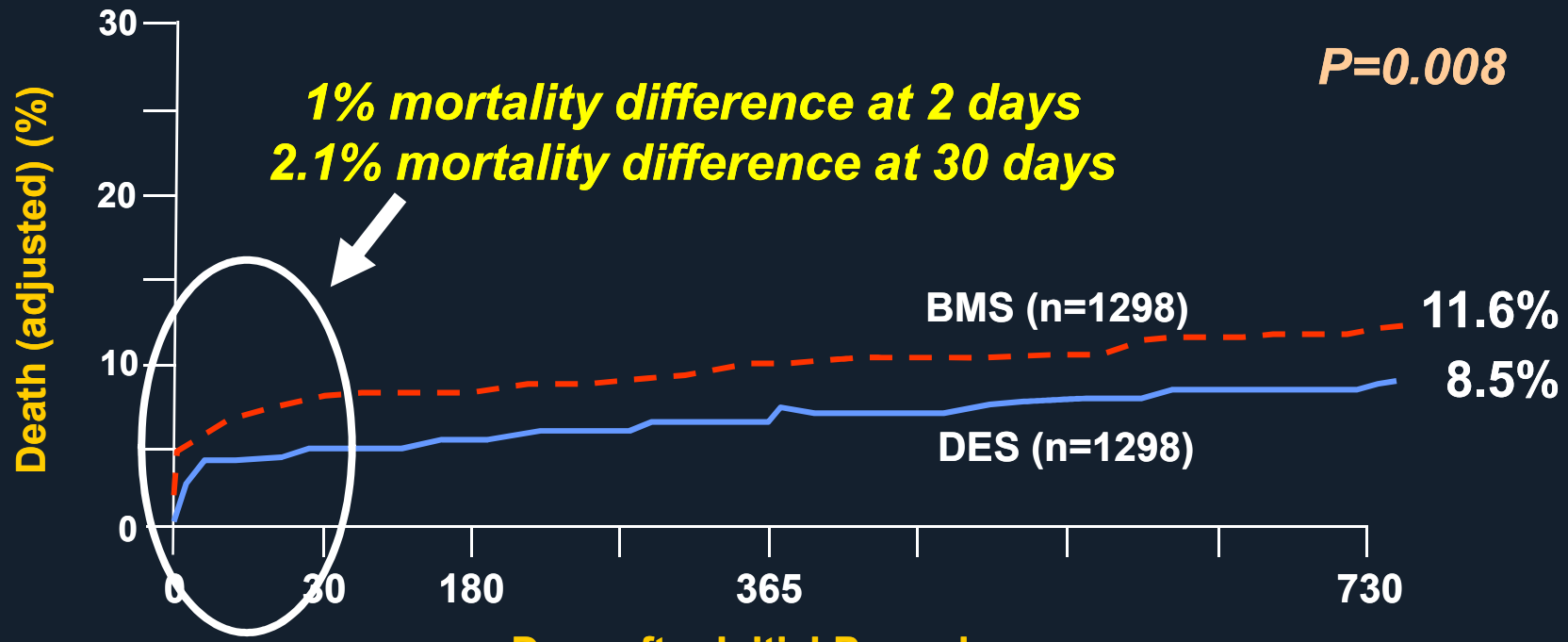
Mortality (Registries)



Brar et al. JACC 2009 ; 53(18)

Massachusetts State Registry

2-year mortality (propensity adjusted) in 1298 matched pairs (2596 pts) with STEMI at 21 hospitals between 4/03–9/04



Drug-Eluting Stent					
No. at risk	1298	1289	1250	1227	1213
Cum. incidence (%)	0.7	3.7	5.5	6.5	8.5
Bare-Metal Stent					
No. at risk	1298	1292	1223	1194	1173
Cum. incidence (%)	0.5	5.8	8.0	9.6	11.6

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Mauri L et al. *NEJM* 2008;359:1330-42

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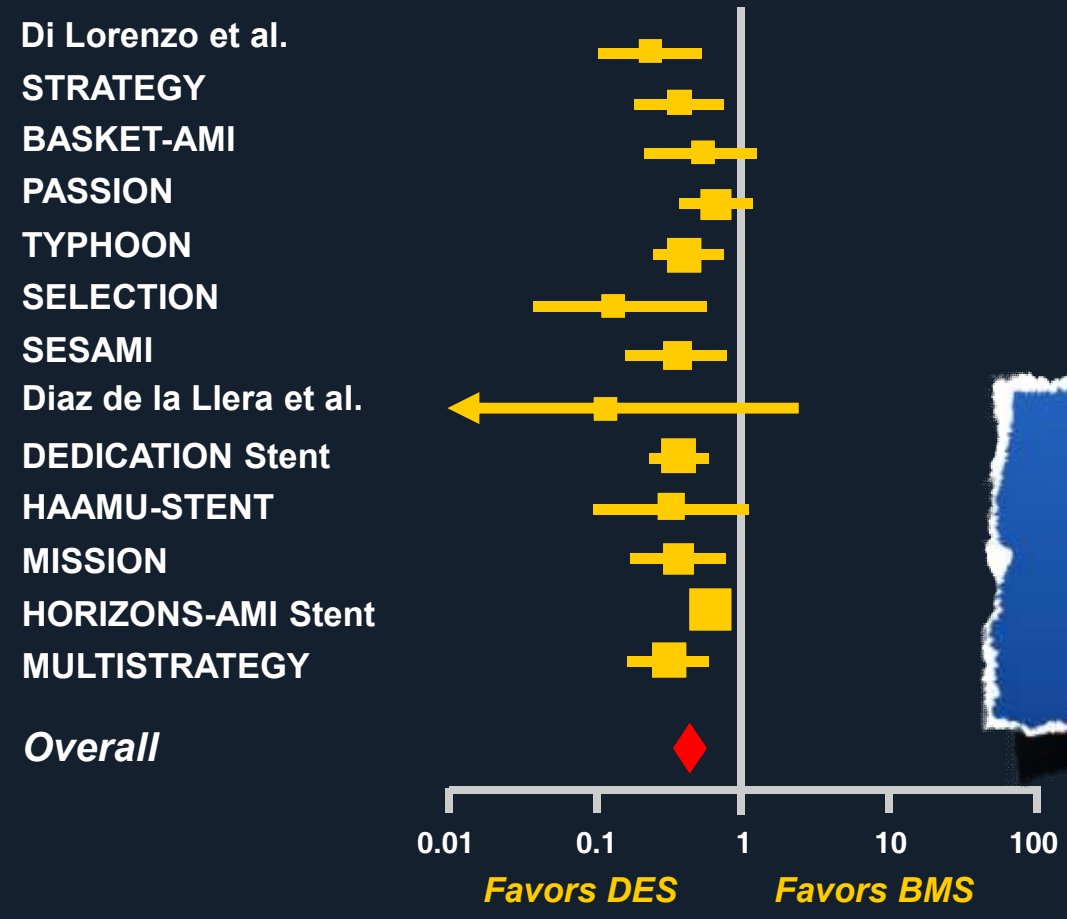
DES vs. BMS in STEMI: Case Closed?

- Despite higher theoretical risks of delayed healing, malapposition, and other potential risks…
  - Overall rates of ST and other clinical safety outcomes have been similar for BMS and DES
- So what about efficacy?

DES in AMI Meta-Analysis

Target Vessel Revascularization (RCTs)



REDUCTION

56%

Relative Risk (95% CI)

0.44

(0.35 - 0.55)

p < 0.001

I^2 = 26%

Brar et al. *JACC* 2009; 53(18)

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TYPHOON

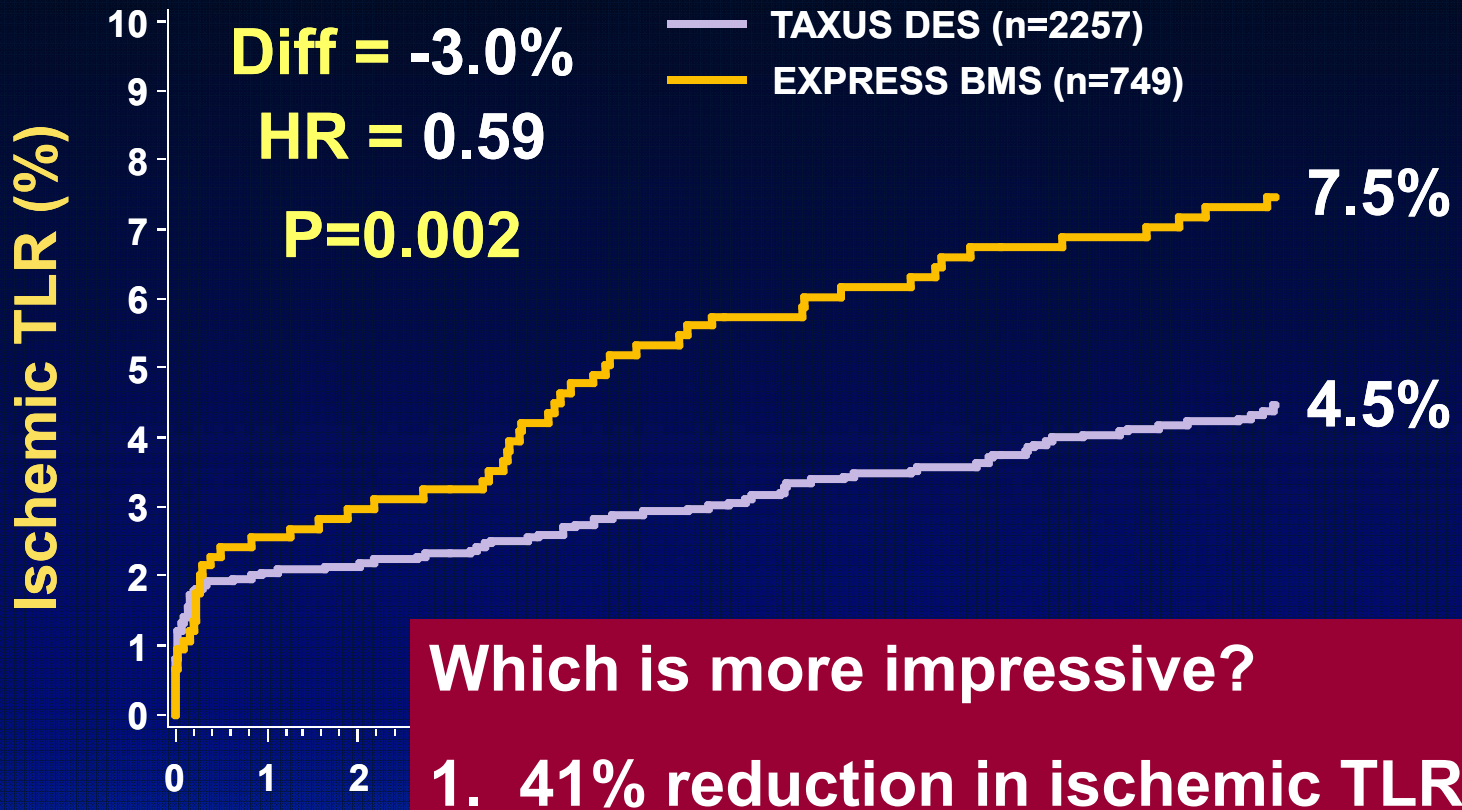
4-Year Follow-Up of SES vs. BMS for AMI

4-Year Outcomes	Cypher n = 251	BMS n = 250	*P* Value
TLR (%)	7.2	15.2	0.005
MI (%)	4.8	4.0	0.83
Death (%)	4.0	6.4	0.23

Conclusion: At 4 years, SES still maintain their initial advantage in terms of revascularization rates over BMS.

Spaulding C. Presented at: EuroPCR 2009. May 19-22, 2009.

Primary Efficacy Endpoint: Ischemic TLR



Number at risk

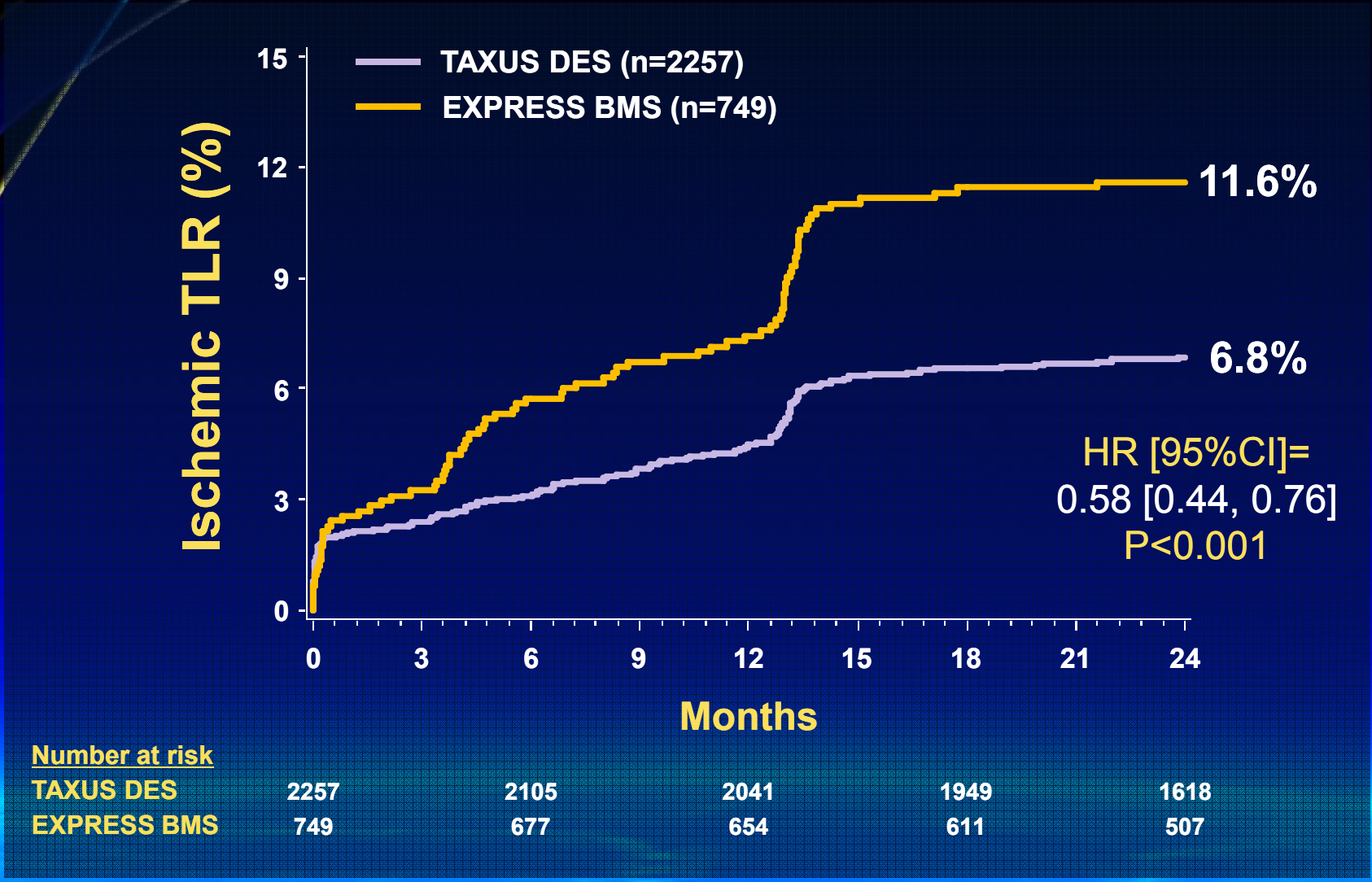
TAXUS DES	2257
EXPRESS BMS	749

Which is more impressive?

1. 41% reduction in ischemic TLR
2. Need to treat 33 patients with DES vs. BMS to prevent one TLR event

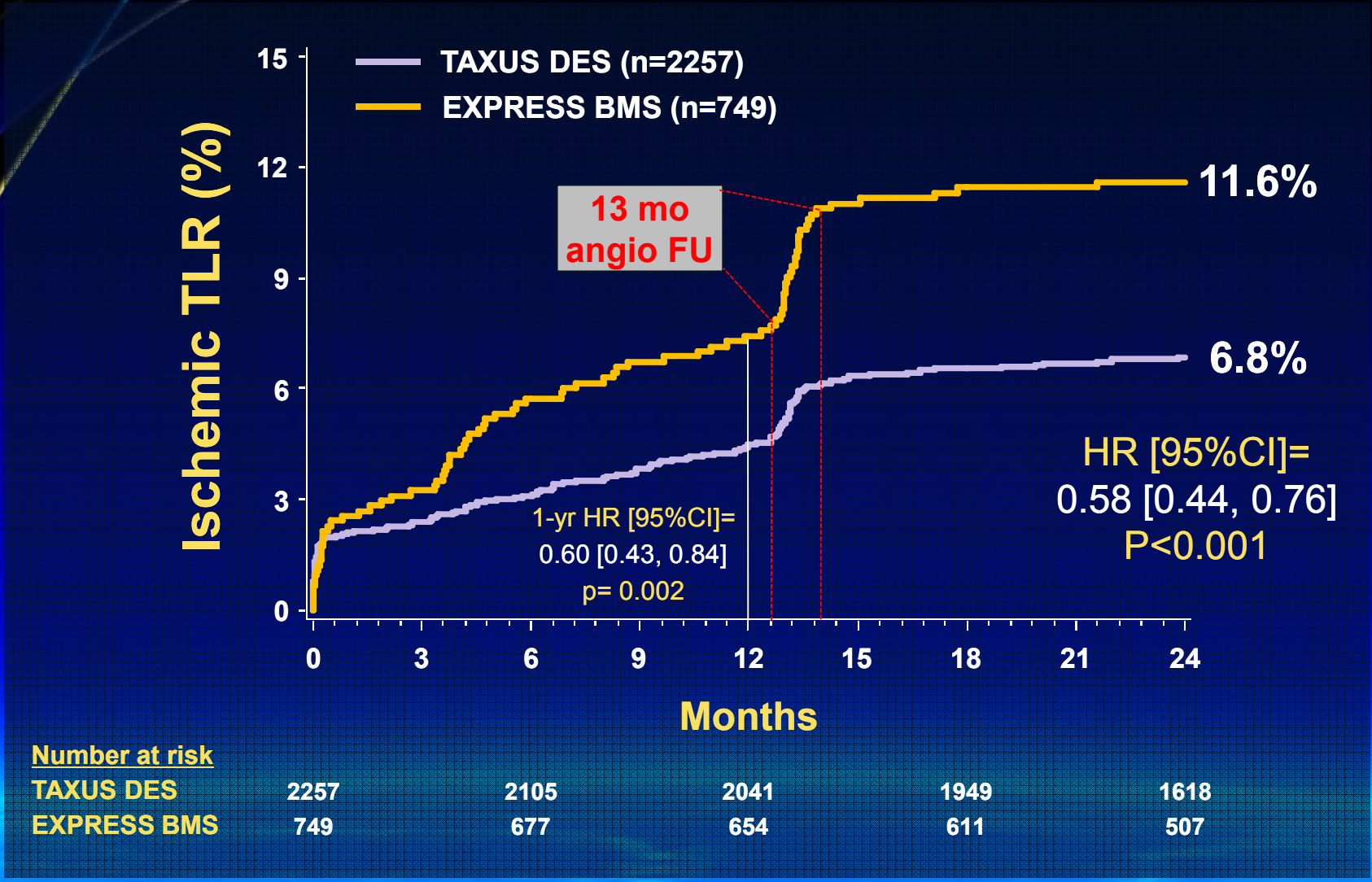
HORIZONSAMI

Primary Efficacy Endpoint: Ischemic TLR



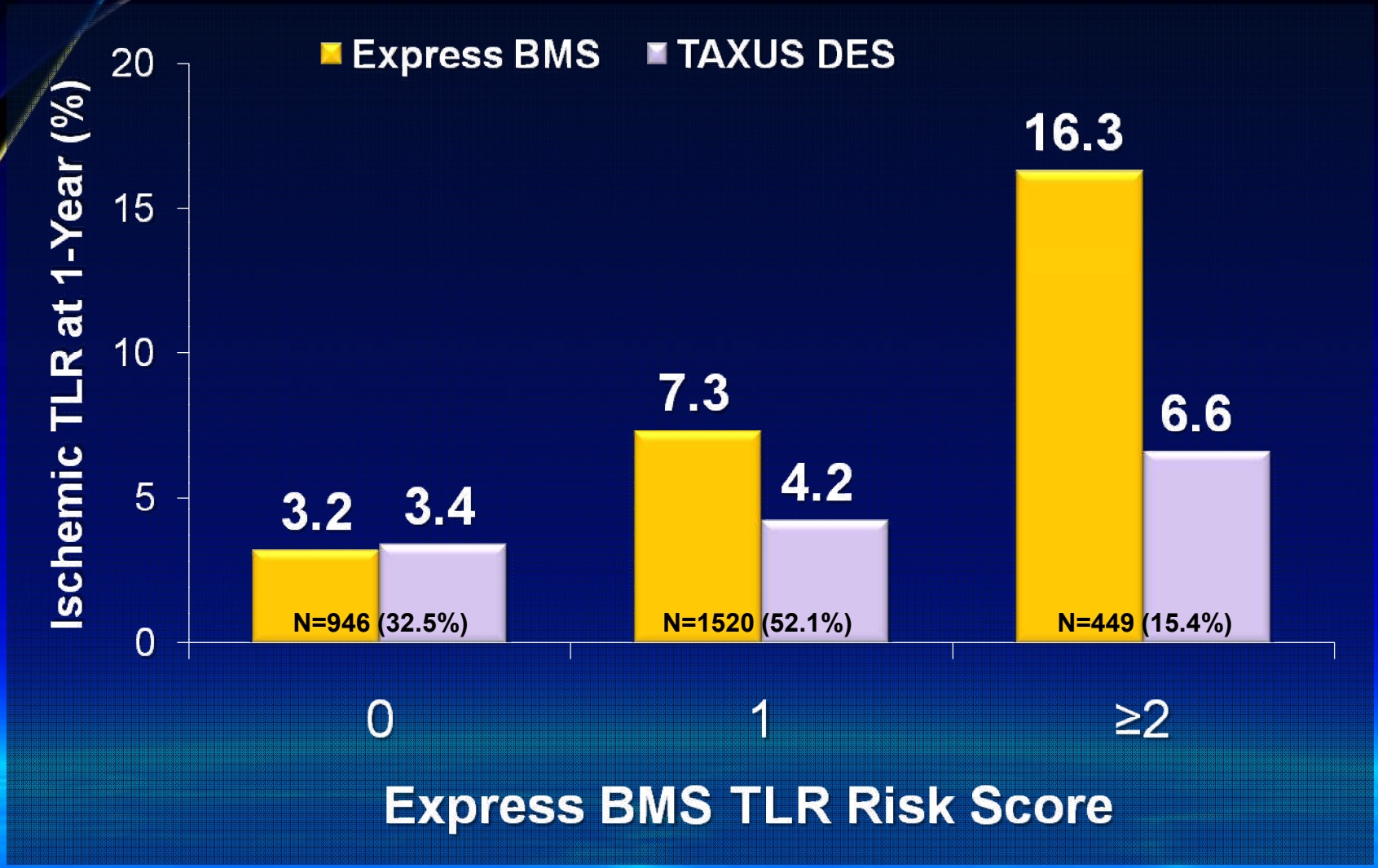
HORIZONSAMI

Primary Efficacy Endpoint: Ischemic TLR



HORIZONS AMI

1-Year TLR According to BMS Risk Score (N=2915)



HORIZONS AMI

Safety of DES vs. BMS in STEMI: Case Closed?

- Despite higher theoretical risks of delayed healing, malapposition, and other potential safety risks…
  - Overall ST and other safety outcomes (mortality, MI) have been similar for BMS and DES
  - Continued long-term FU and investigation of newer DES systems is needed
  - Issues of DAPT adherence are critical in the clinical setting

Efficacy of DES vs. BMS in STEMI: Case Closed?

- Because of lower absolute event rates of TLR, careful attention to absolute risk reductions (and number needed to treat) rather than relative risk reductions is needed
  - An estimation of baseline restenotic risk should be performed in order to determine the potential benefit of DES in an individual patient!!