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Comparing zotarolimus-eluting and bare-metal stent efficacy in selected high bleeding risk patients treated with a short dual antiplatelet therapy duration.

A pre-specified analysis from the The Zotarolimus-eluting Endeavor sprint stent in Uncertain DES candidates (ZEUS) study.

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ZEUS

Potential conflicts of interest

Speaker's name: Marco Valgimigli

☑ **I have the following potential conflicts of interest to report:**

Consultant:	**Abbott, CID (Carbostent & Implantable Devices), Daiichi Sankyo, Eli Lilly, Medtronic, The Medicines Company**
Speaker's bureaus:	**Abbott, Accumetrics, AstraZeneca, Daiichi Sankyo, Eli Lilly, Iroko Pharmaceuticals, Terumo**
Institutional grant/ research support:	**Iroko Pharmaceuticals, Medtronic, Terumo, The Medicines Company**

Background

- DES, instead of BMS use, remains controversial in patients at high bleeding risk (HBR) in whom long-term DAPT poses safety concerns.

- The zotarolimus-eluting Endeavor Sprint stent (E-ZES) is a hydrophilic polymer-based second-generation device with a unique drug fast-release profile.

Study Design

Am Heart J. 2013 Nov;166(5):831-8

Urgent or emergent coronary stenting in pts fulfilling ≥1 of the below:

High Bleeding Risk
- Need for OACs
- Previous Relevant Bleeding
- Age > 80 y/o
- Bleeding diathesis
- Known Anemia (Hb<10 gr/dl)
- Need for CCS or NSAID

High Thrombotic Risk
- Intolerance to ASA
- Intolerance to any $P2Y_{12}$
- Planned surgery w/in 1 year
- Cancer-life expectancy >1 Y
- Pro-thrombotic diathesis

Low Restenosis Risk
- Planned stent ≥3.0 mm, apart from LMCA and SVG intervention or for ISR lesions

Rx: 1:1, ***Sx: inclusion criteria***

1,606 pts, 20 sites in *Italy*, *Switzerland*, *Portugal* and Hungary from June 2011 to September 2012

Endeavor Sprint Zotarolimus-eluting Stent

Thin-strut Bare Metal Stent

***Personalised DAPT duration*, i.e. modelled according to the patient clinical risk profile and not by stent type**

ZEUS

ZEUS Study Design

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High Bleeding Risk
- Need for OACs
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- Bleeding diathesis
- Known Anemia (Hb<10 gr/dl)
- Need for CCS or NSAID

DAPT:
30 days

High Thrombotic Risk
- Intolerance to ASA
- Intolerance to any $P2Y_{12}$
- Planned surgery w/in 1 year
- Cancer-life expectancy >1 Y
- Pro-thrombotic diathesis

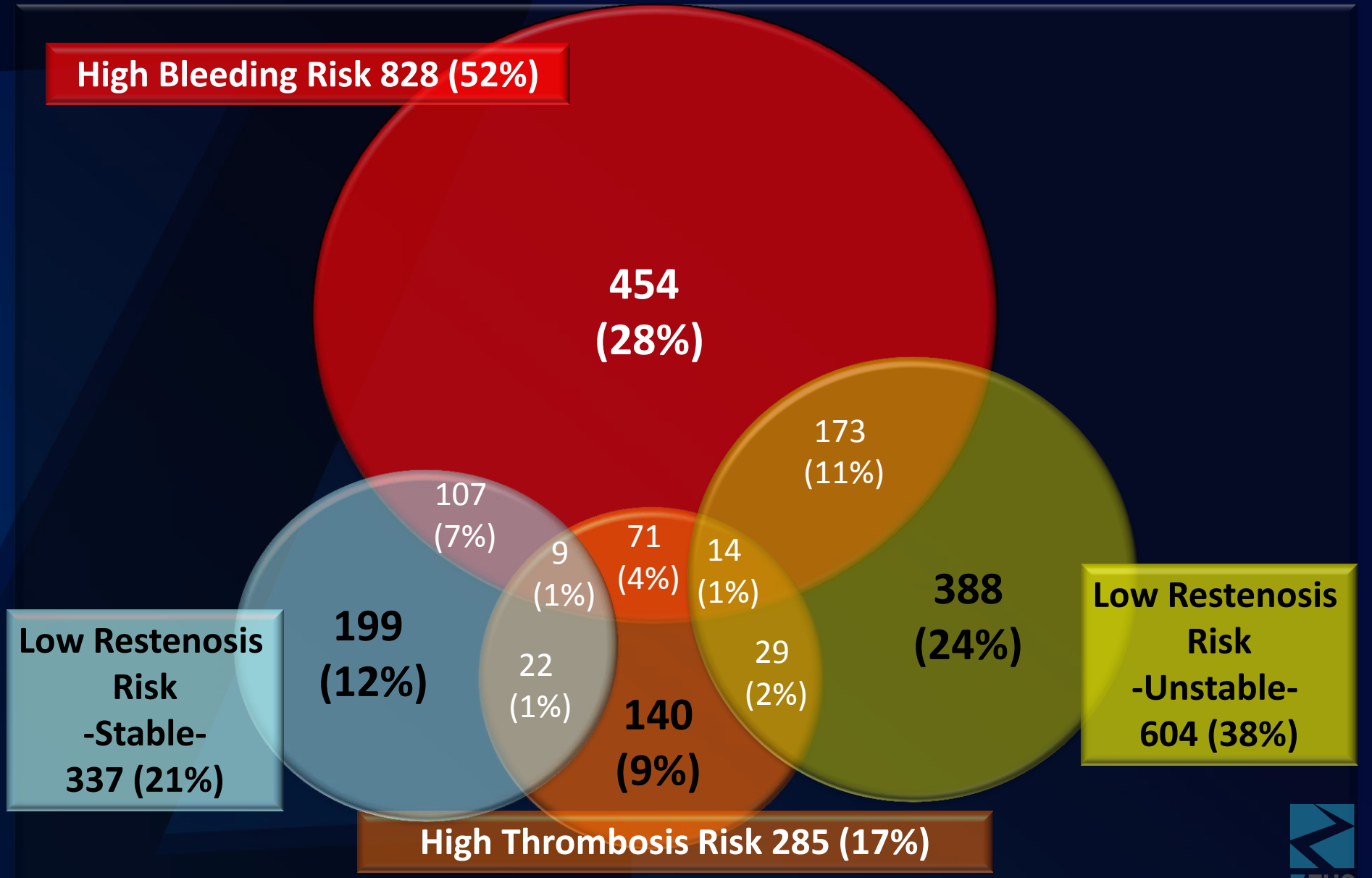
DAPT:
None if **ASA/$P2Y_{12}$i intol.**
Up to surgery **if planned**
≥ 6 mos **in others**

Low Restenosis Risk
- Planned stent ≥3.0 mm, apart from LMCA and SVG intervention or for ISR lesions

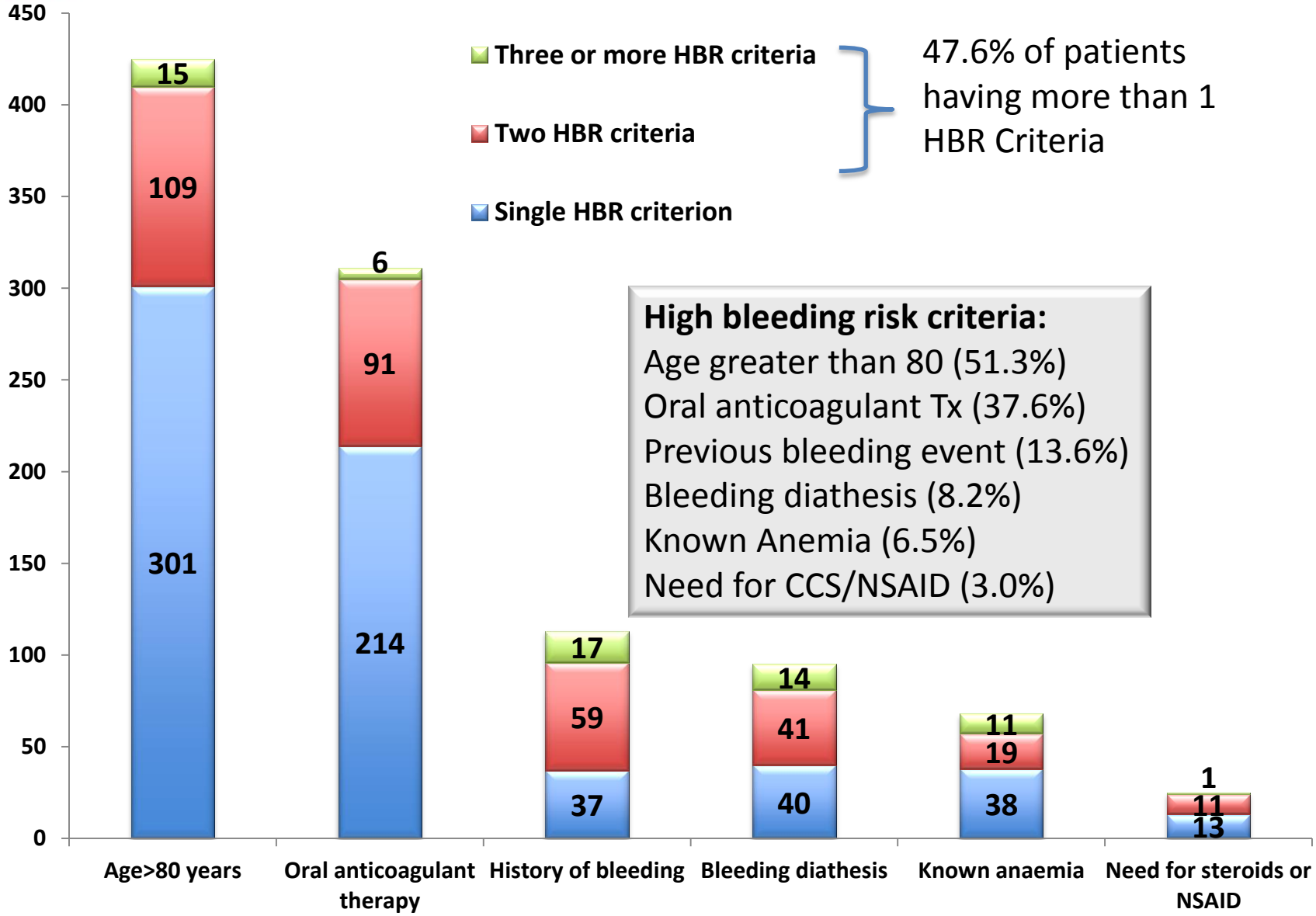
DAPT:
Stable CAD *30 days*
ACS ≥ *6 mos*

ZEUS

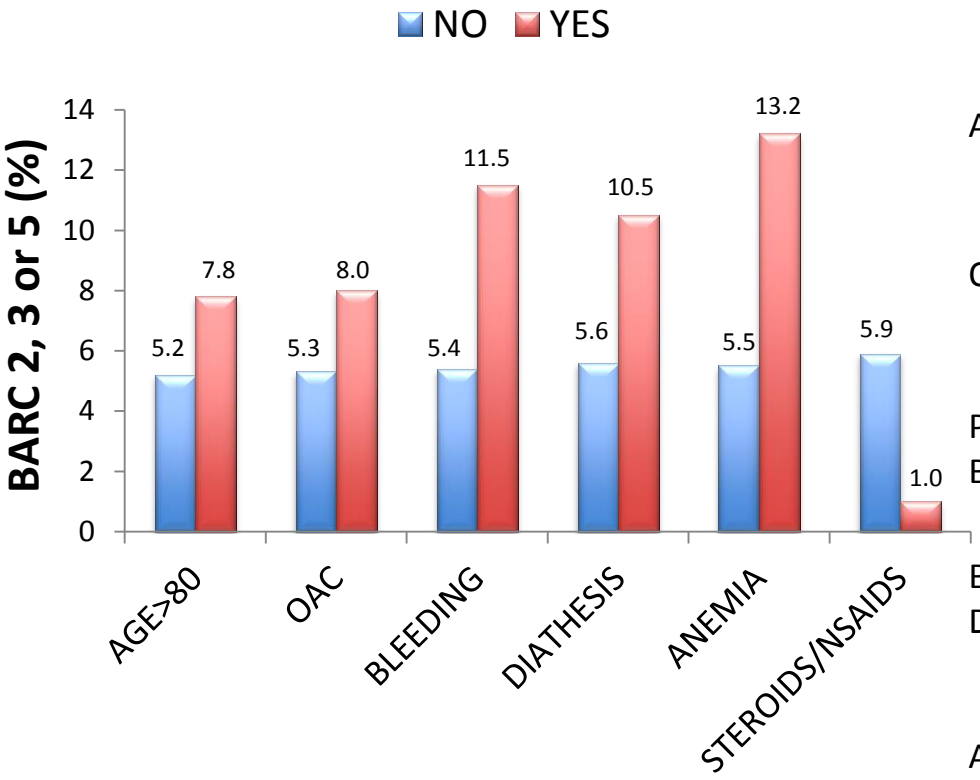
Study Population

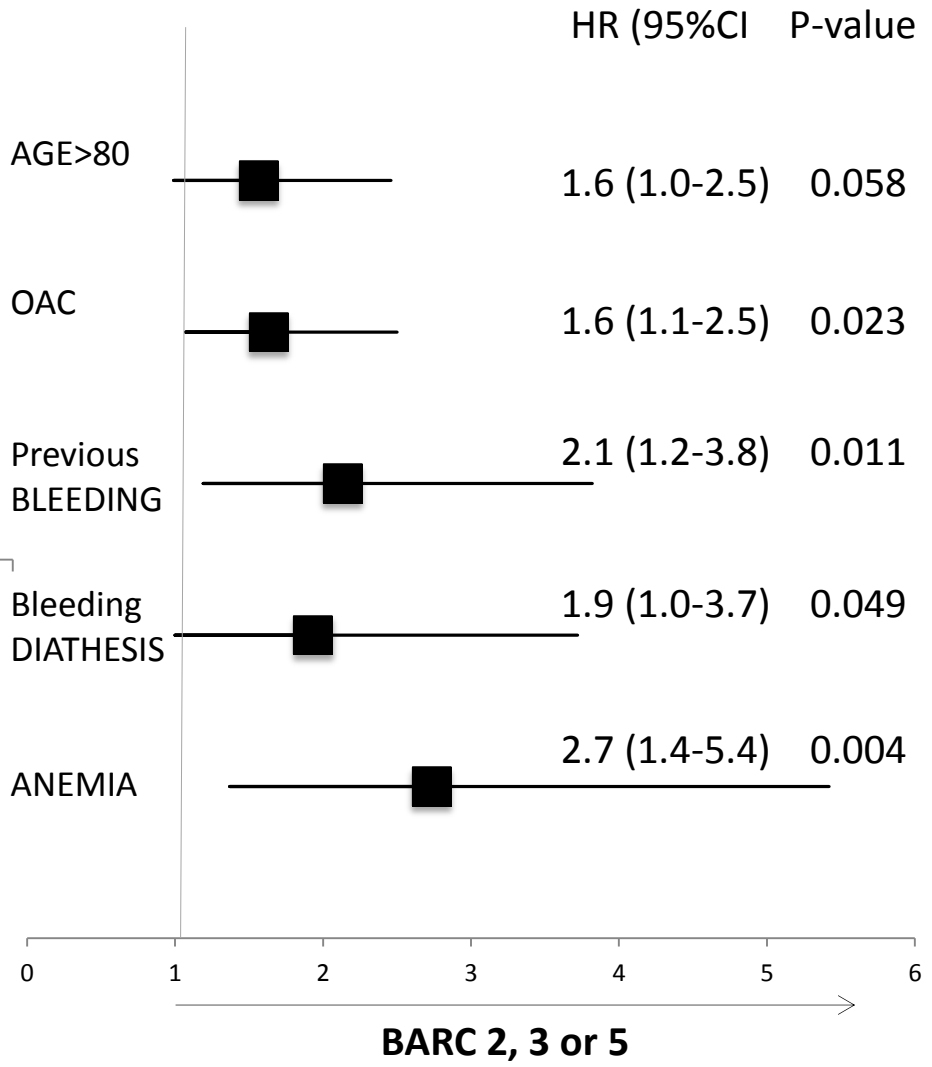


High Bleeding Risk Criteria



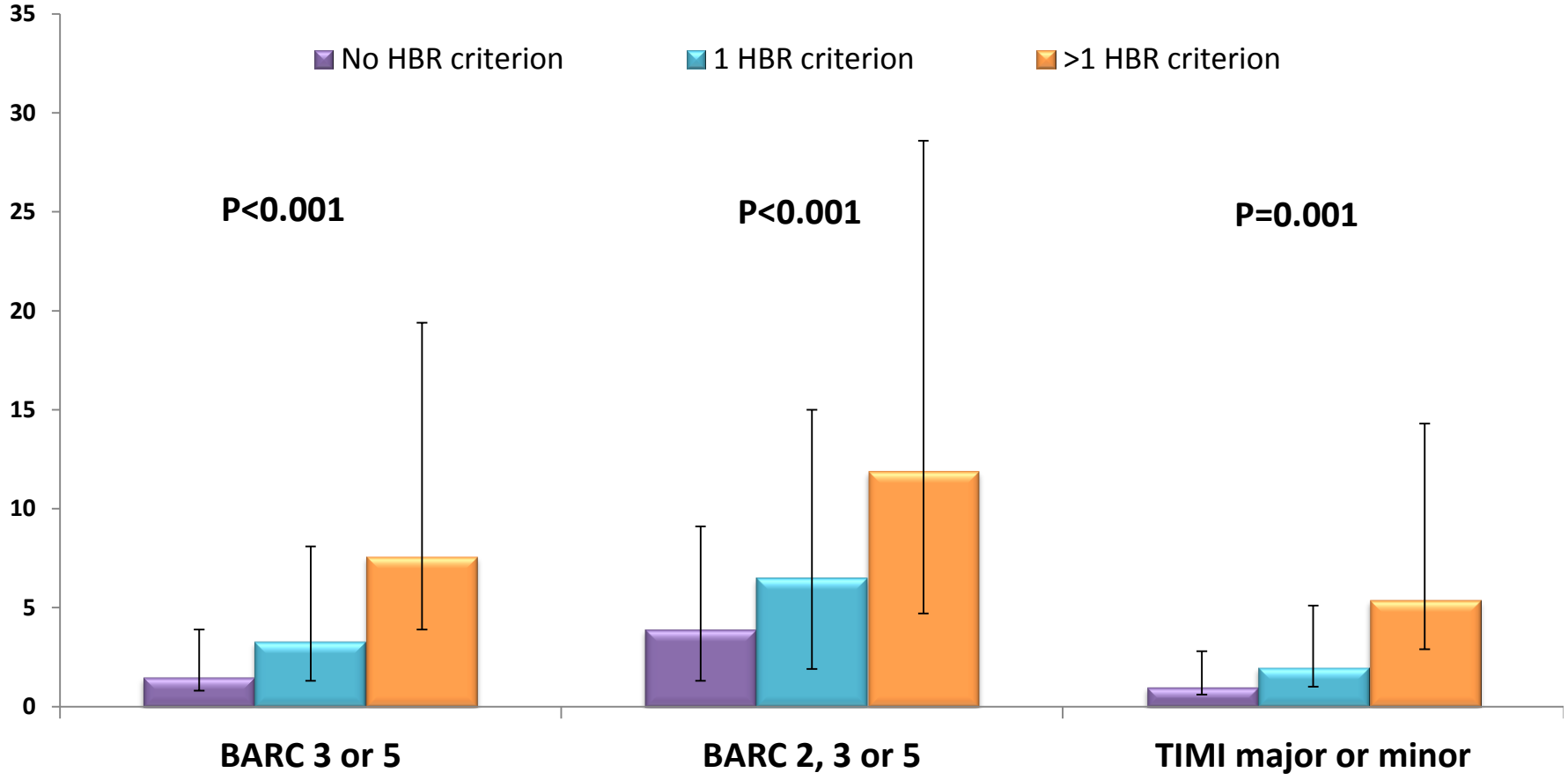
Bleeding events rate according to the presence of each HBR criterion





Bleeding events rate according to the presence of high bleeding risk criteria

Additive effect on bleeding outcomes with respect to the presence of only one or more than 1 HBR feature(s)



Baseline features according to high bleeding risk status

	High bleeding risk (N=828)	Others (N=778)
Age (yr.)	80.4 (72.4-84.2)	66.8 (58.8-74.1)*
Diabetes (%)	30.7	21.3*
Hypertension (%)	82.1	69.0*
Hyperlipidaemia (%)	50.9	46.4
Glomerular Filtration Rate <30 ml/min (%)	12.9	3.6*
Left ventricular ejection fraction (%)	48 (40-55)	50 (45-60)*
Multivessel Disease (%)	67.8	51.4*
At least one complex (type B2 or C) lesion (%)	76.2	69.9**

*P<0.001

**P<0.05

Ischemic events rate according to the presence of high bleeding risk

Endpoints	HBR patients (N = 828)	No HBR patients (N = 778)	p-value
Death, MI or TVR	213 (25.7%)	105 (13.5%)	<0.001
Death	137 (16.5%)	44 (5.7%)	<0.001
Myocardial Infarction	57 (6.9%)	31 (4.0%)	0.006
Definite or Probable ST	36 (4.3%)	13 (1.7%)	0.002

After adjustment mortality risk remaind greater in HBR patients
(adjusted-HR 1.56; 95% CI 1.06-2.28; p=0.024)

Baseline characteristics in HBR patients according to stent type

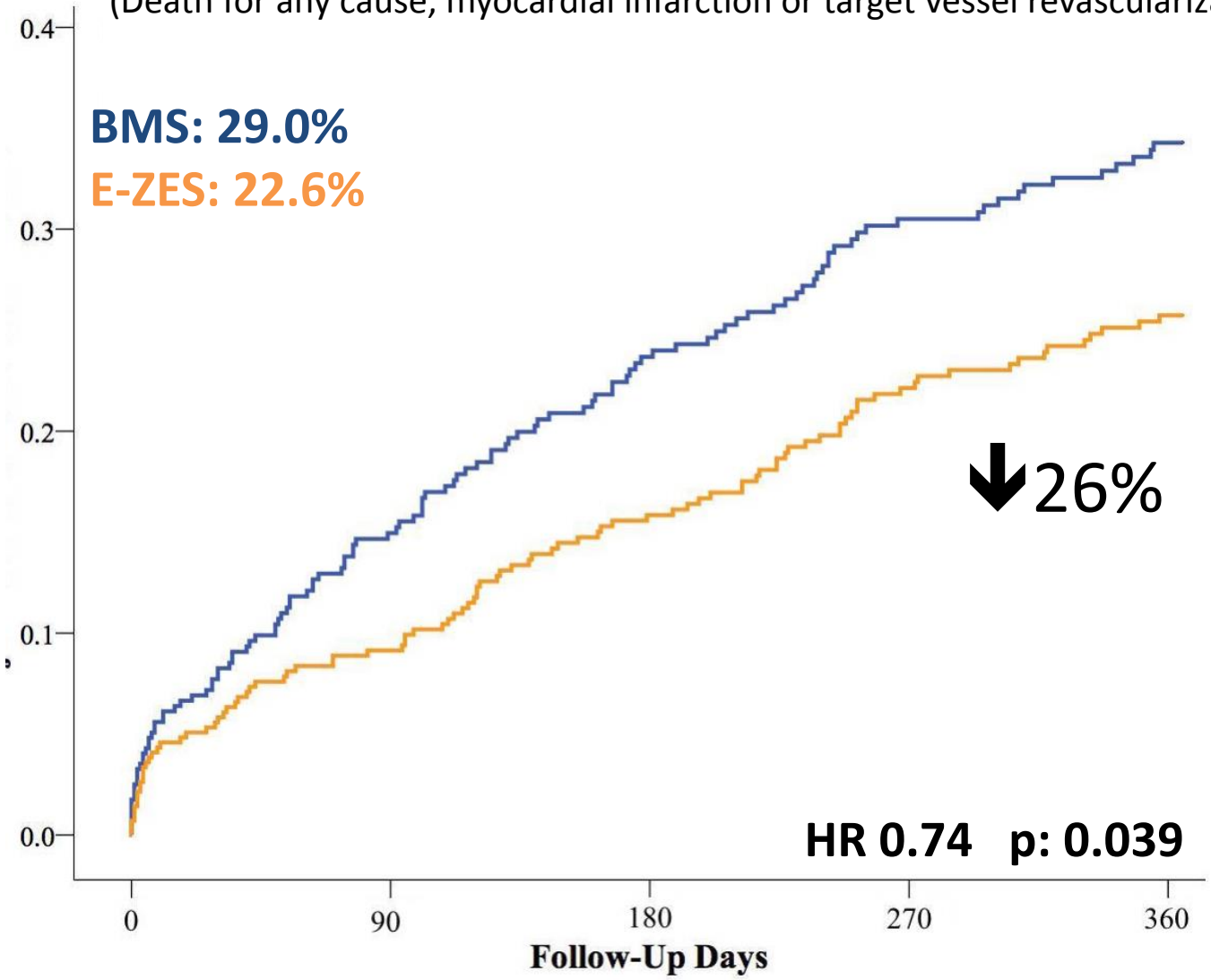
	BMS Group (N=404)	E-ZES Group (N=424)
Age (yr.)	80.5 (72.3-84.4)	80.4 (72.8-84.9)
Diabetes (%)	29.0	32.3
Glomerular Filtration Rate <30 ml/min (%)	12.9	12.8
Left Ventricle Ejection Fraction	49 (40-55)	48 (40-55)
Multivessel Disease (%)	68.3	67.2
Number of Treated Lesions	1 (1-2)	1 (1-2)
Number of Stent Implanted	1 (1-2)	1 (1-2)
Total Stent Length (mm)	28 (18-46)	30 (18-44)
Dual Antiplatelet Therapy Duration (days)	**31 (30-177)**	**30 (30-53)**

Reasons for prolonging DAPT beyond 30 days included planned or unplanned procedures in de novo lesions —which were evenly distributed between stent groups— or need for reintervention in previously instrumented coronary segments, which explained the longer DAPT duration in the BMS group.

Primary Endpoint

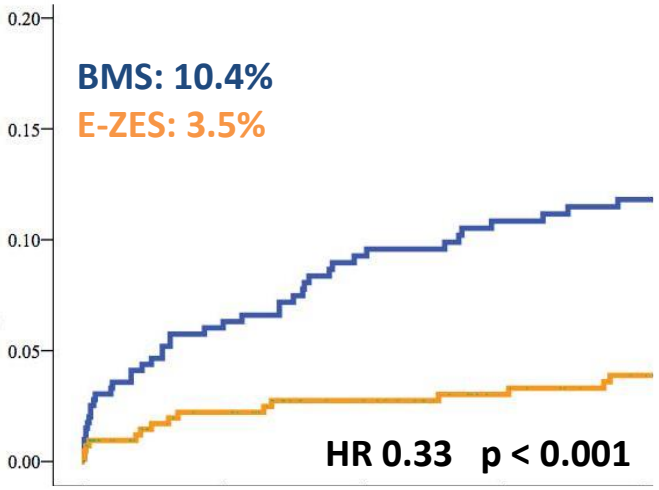
Major Adverse Cardiovascular Events

(Death for any cause, myocardial infarction or target vessel revascularization)

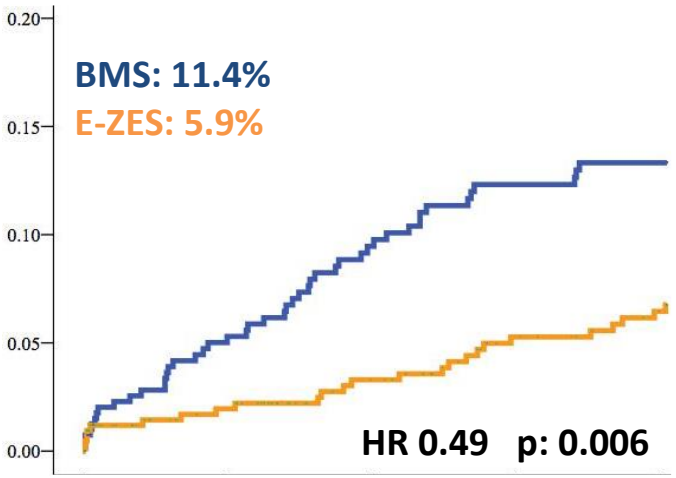


Secondary Endpoints

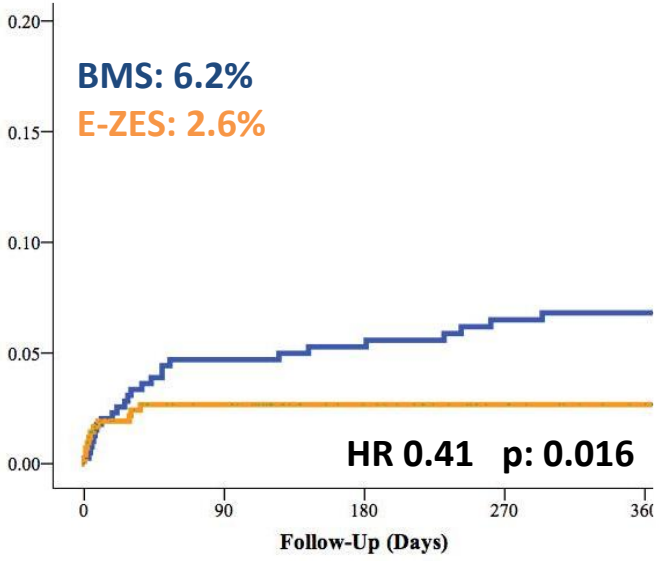
Myocardial Infarction



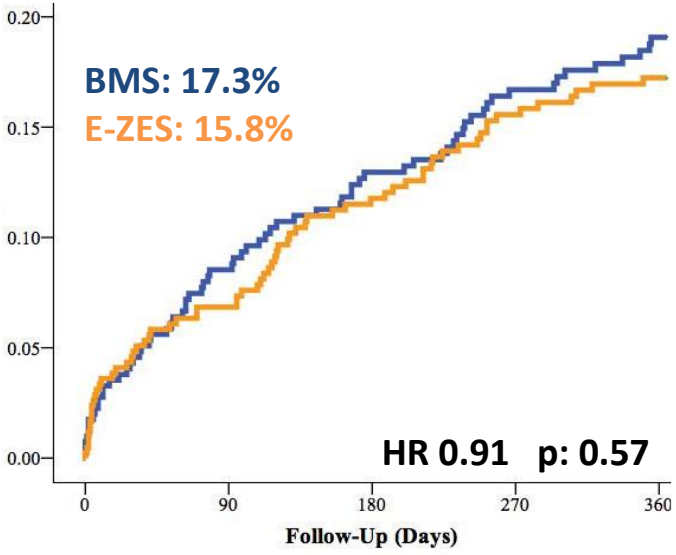
Target Vessel Revascularization



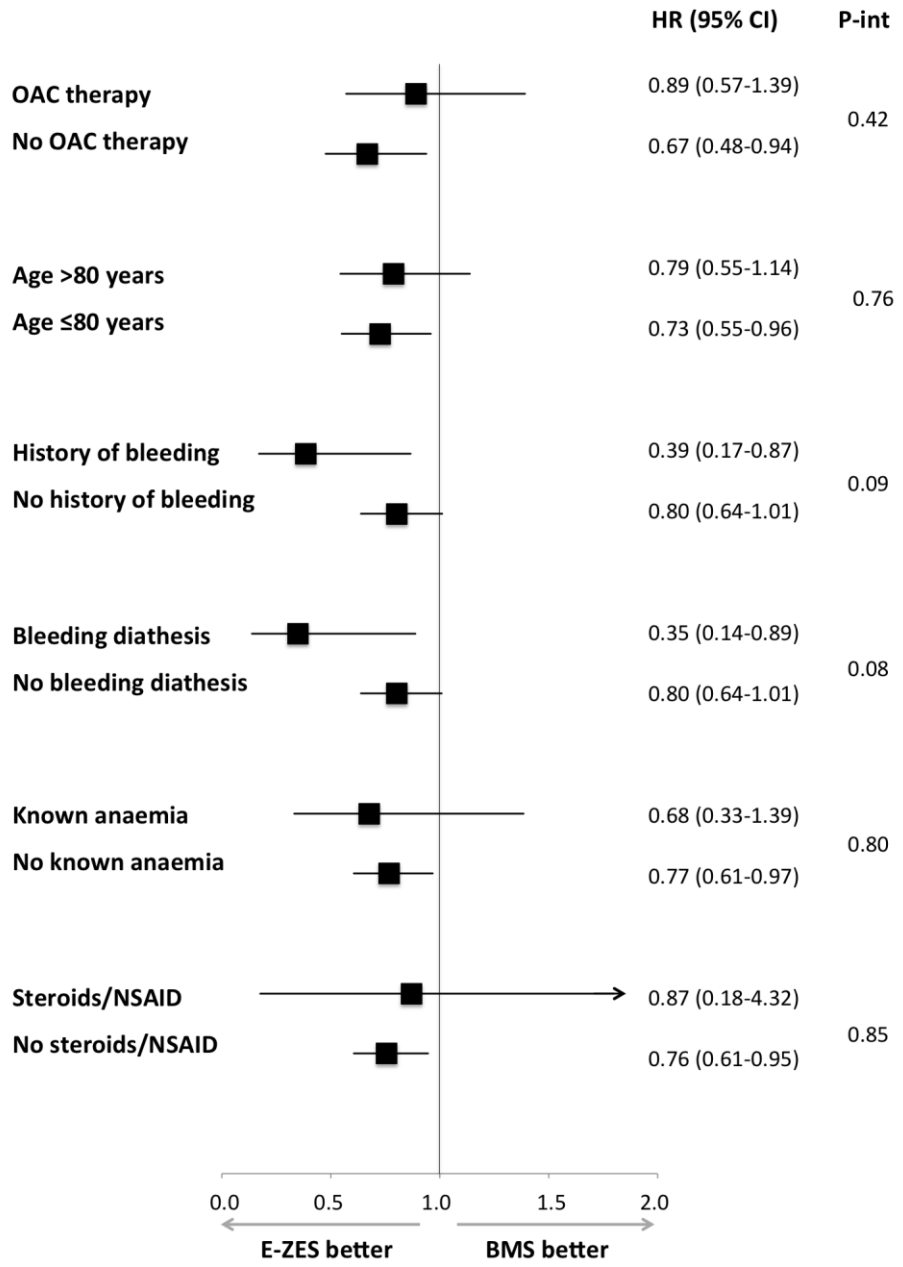
Definite or Probable Stent Thrombosis



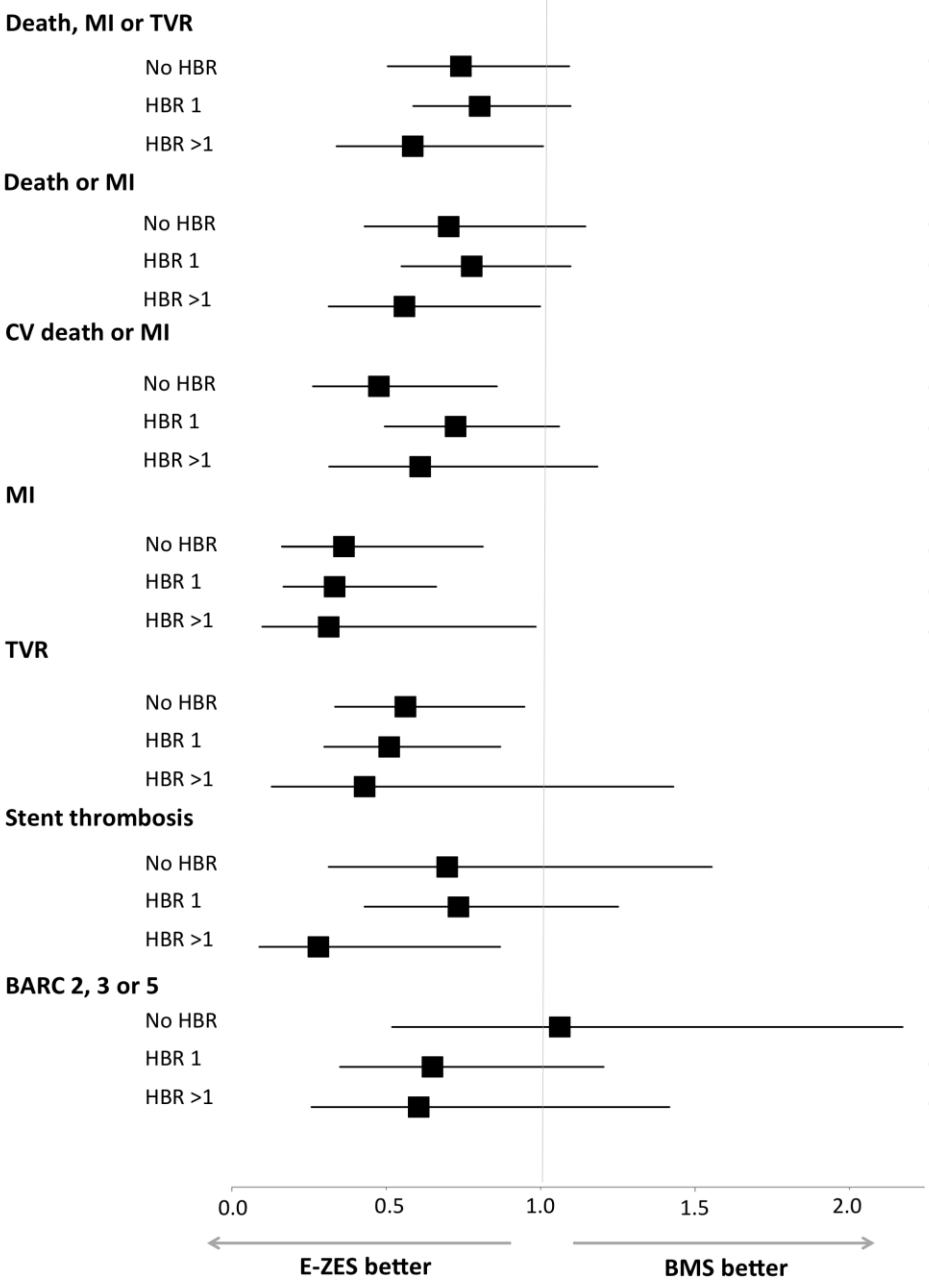
Death for all causes



Primary end-point in Zotarolimus-eluting versus Bare-Metal Stents according to presence of the single high bleeding risk criteria

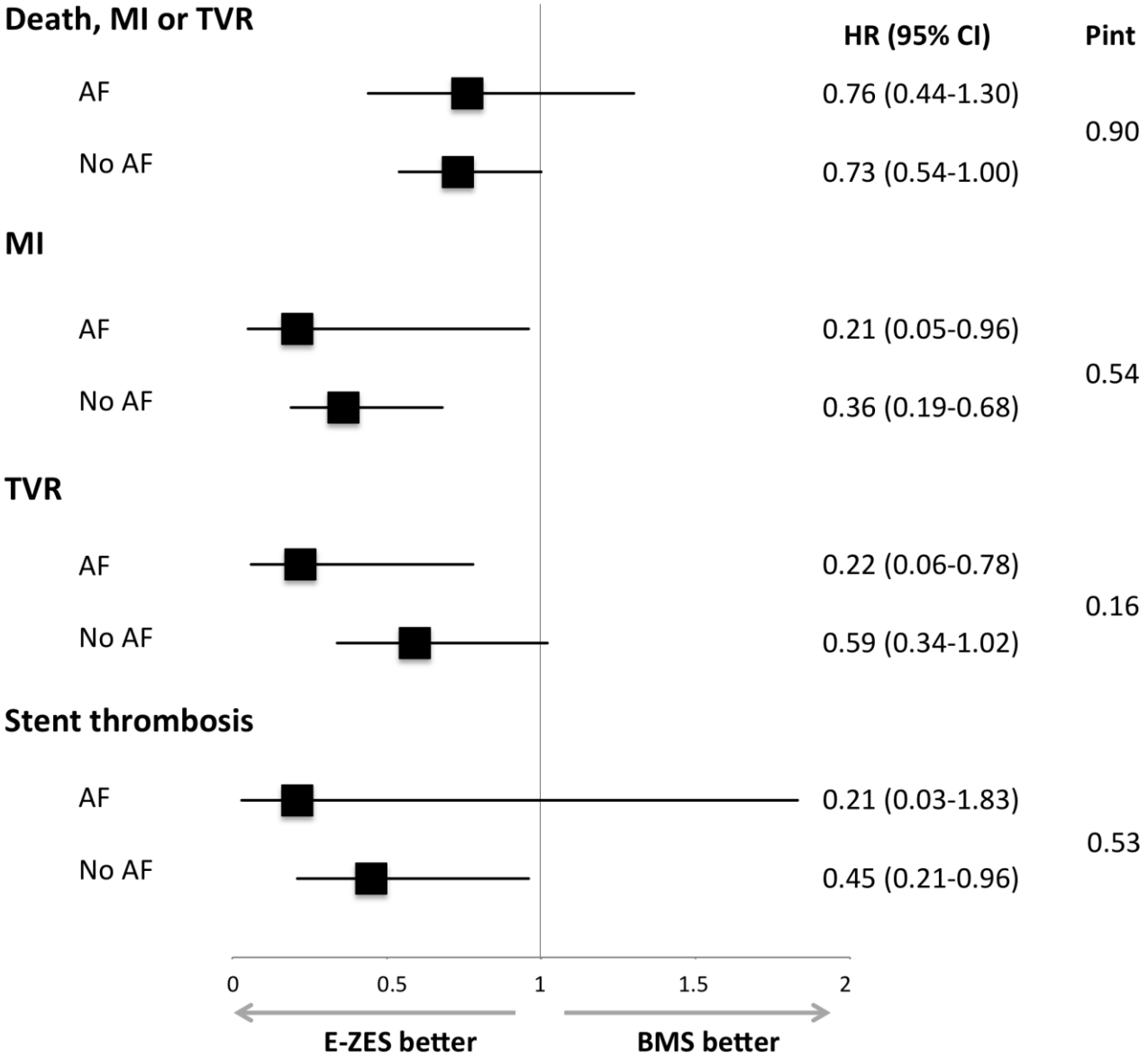


Clinical outcomes in Zotarolimus-eluting versus Bare-Metal Stents according to the absence or presence of a single or multiple HBR feature(s)



	HR (95% CI)	P-value	P-int
Death, MI or TVR			
No HBR	0.742 (0.503-1.093)	0.131	
HBR 1	0.803 (0.588-1.097)	0.168	0.61
HBR >1	0.586 (0.340-1.008)	0.053	
Death or MI			
No HBR	0.703 (0.431-1.145)	0.156	
HBR 1	0.777 (0.550-1.097)	0.152	0.66
HBR >1	0.560 (0.314-0.999)	0.049	
CV death or MI			
No HBR	0.476 (0.263-0.859)	0.014	
HBR 1	0.725 (0.495-1.060)	0.097	0.46
HBR >1	0.610 (0.315-1.184)	0.144	
MI			
No HBR	0.364 (0.163-0.813)	0.014	
HBR 1	0.333 (0.167-0.662)	0.002	0.97
HBR >1	0.314 (0.100-0.985)	0.047	
TVR			
No HBR	0.563 (0.335-0.948)	0.031	
HBR 1	0.510 (0.300-0.870)	0.013	0.93
HBR >1	0.430 (0.130-1.430)	0.169	
Stent thrombosis			
No HBR	0.698 (0.314-1.554)	0.379	
HBR 1	0.734 (0.431-1,251)	0.256	0.35
HBR >1	0.280 (0.09-0.869)	0.028	
BARC 2, 3 or 5			
No HBR	1.062 (0.519-2.172)	0.870	
HBR 1	0.650 (0.351-1.204)	0.171	0.53
HBR >1	0.606 (0.259-1.417)	0.248	

Ischemic end-points in Zotarolimus-eluting versus Bare-Metal Stents according to the presence of atrial fibrillation in high bleeding risk patients



Conclusion

Zotarolimus-eluting Endeavor Sprint stent as compared with bare metal stent **reduces**:

- major adverse cardiovascular events
- myocardial infarction
- target vessel revascularisation
- stent thrombosis

At 12-month follow-up in patients deemed at high bleeding risk and treated with an intended *30-day short dual antiplatelet therapy regimen*.