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**

Effects of cobalt-chromium everolimus eluting or bare metal stent on fatal and non-fatal cardiovascular events.

A collaborative patient-level meta-analysis, including 4,896 individuals with a median 2-year follow-up duration

Manel Sabaté, Christoph Kaiser, Salvatore Brugaletta, Jose Maria de la Torre Hernandez, Soeren Galatius, Angel Cequier, Franz Eberli, Adam de Belder, Patrick W. Serruys, Giuseppe Ferrante,

Presenter: Marco Valgimigli, MD PhD, FESC
Erasmus MC, Thoraxcenter
Rotterdam
The Netherlands

Background

- Some second-generation DES, including cobalt-chromium everolimus eluting (Co-Cr EES), have been shown to improve safety while maintaining efficacy when contrasted with first generation DES.
- However, the comparative safety and efficacy of second-generation DES as compared to BMS on fatal and non-fatal cardiovascular outcomes remains largely unknown.

This reflects the common practice in the last years to compare 2 gen DES to 1 gen DES but only rarely to BMS

Methods

- Of the 346 citations screened, 5 randomized trials were selected:

1: *J Am Coll Cardiol* 2013; Nov 21-**XIMA:**
2: Circulation. 2012;**125**(16):2015-26-**PRODIGY**
3: *N Engl J Med* 2010; **363**(24): 2310-9-**BASKET PROVE;**
4: *EuroIntervention* 2007; **3**(2): 206-12-**SPIRIT First:**
5: *Lancet* 2012; **380**(9852): 1482-90-**EXAMINATION**

Independent adjudication of events by CEC members in all 5 studies

- The principal investigators were invited provide the following data for individual patients:

Clinical data

Age
sex
body mass index
diabetes
smoking
hypertension
hypercholesterolemia
Presenting syndrome:
Stable CAD
Unstable Angina
NSTEACS
STEMI

Angiographic data

Diseased vessels
Treated lesions
No of implanted stents
Overlapping stents
Total stent length
Average stent diameter

Use of anti-thrombotics

Duration of clopidogrel therapy,
use of glycoprotein IIb/IIIa inhibitors

Outcome data

Death
Cardiac death
Myocardial infarction
Stent thrombosis
Repeat revascularization
Last follow-up contact

Methods ii

Endpoints

The primary outcome was cardiac mortality at the longest available follow-up. Cardiac mortality and not all-cause mortality was selected as primary outcome measure to minimize the confounding effect of non-cardiac events on stent performance in the context of a relatively old and unselected patient population followed-up through 2-years. Importantly, cardiac mortality was homogenously classified across the five included studies according to the ARC criteria.

Statistical Analyses

The impact of stent type (Co-Cr EES vs BMS) on outcomes was assessed by Cox regression model stratified by trial, with random-effects.

A multivariable Cox regression model was also performed after entering the following prespecified covariates: i.e. female sex, duration of DAPT > 1 year, clinical syndrome (acute coronary syndrome vs stable syndrome), use of glycoprotein IIb/IIIa inhibitors and history of diabetes mellitus.

euro PCR 2014

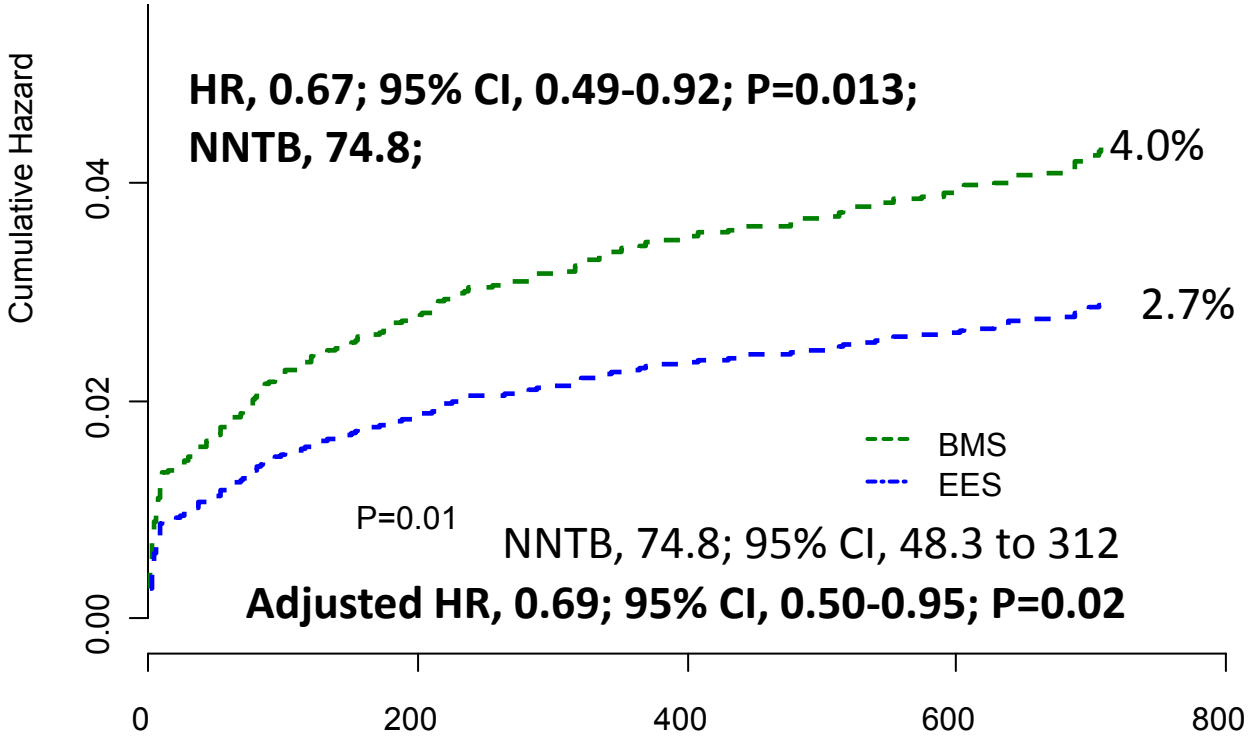
Baseline Features

Patients Characteristics	Overall N=4,896	PRODIGY N=1,003	EXAMINATION N=1,498	BASKET PROVE N=1,539	SPIRIT First N=56	XIMA N=800
Age mean±SD	67±13	69±11	61±12	64±11	63±9	83±3
Female (%)	25	25	17	24	27	40
Diabetes (%)	19	22	17	15	11	25
Prior MI (%)	15	26	5	12	0	26
Target population	…	All comer PCI	All comer STEMI	All comer PCI	Low risk population	All comer octogenarians
STEMI (%)	44	34	100	15	0	7*
NSTEACS (%)	44	20	0	80	0	68*
Stent control arm	Mixture of BMS	Mixture of BMS	Vision	Vision	Vision	Vision
Recommended DAPT duration						
Experimental arm	…	6 or 24 months	12 months	12 months	≥3 months	12 months
Control arm	…	up to 6 or 24 months	12 months	12 months	≥3 months	3 months
Follow-up (years)		2	2	2	5	1

All baseline clinical and angiographic characteristics were well matched between groups with the only exception for hypertension and hyperlipidemia being slightly more prevalent in the BMS group whereas Clopidogrel use beyond one year was slightly higher in the CoCr-EES group 15.3 vs 13.6, p=0.09

Cardiac death

At 2 years, the risk of cardiac death was significantly reduced in the Co-Cr EES group at 2.7% as compared to 4.0% in the BMS arm. At multivariable regression, cardiac mortality remained significantly lower in the in the Co-Cr EES group

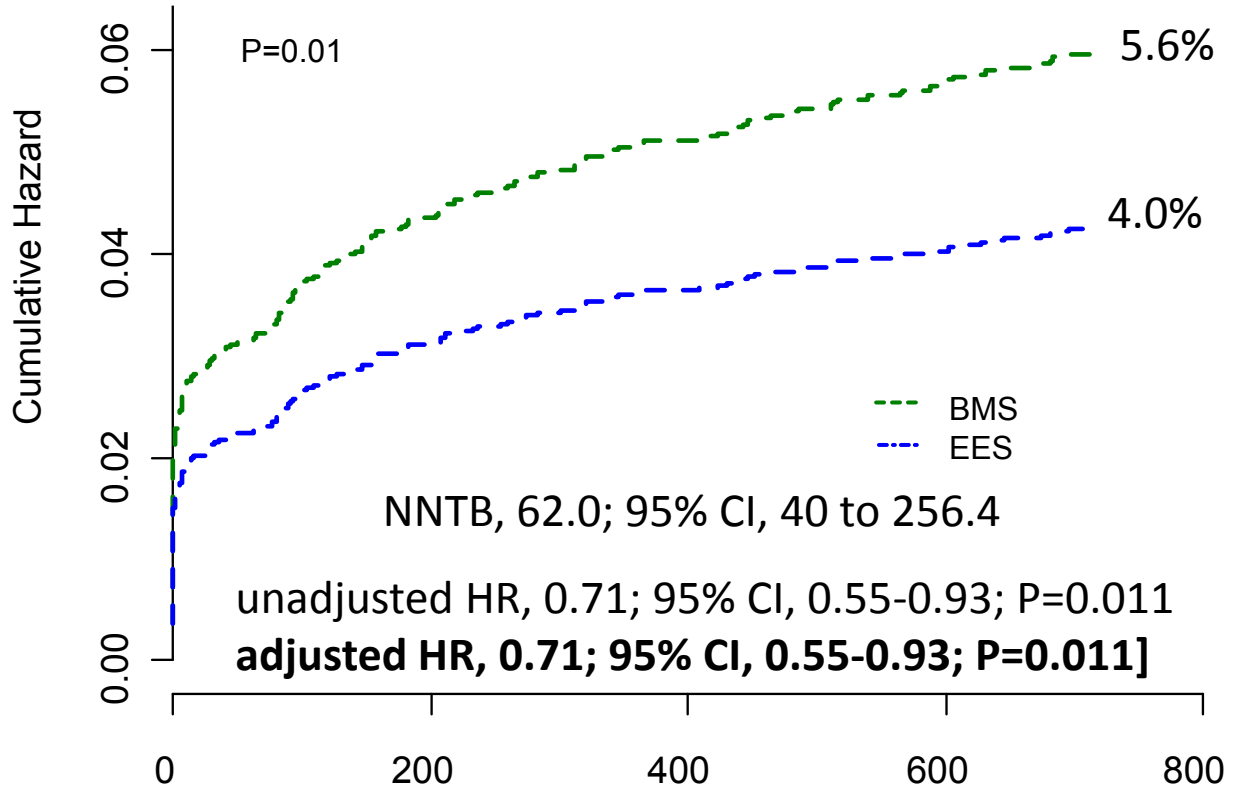


Number of patients

BMS	2444	2349	1939	1927	0
EES	2452	2376	1975	1958	0

Myocardial infarction

The risk of fatal and non-fatal MI was significantly lower in the in the Co-Cr EES group [4.0% vs 5.6% in the BMS group]

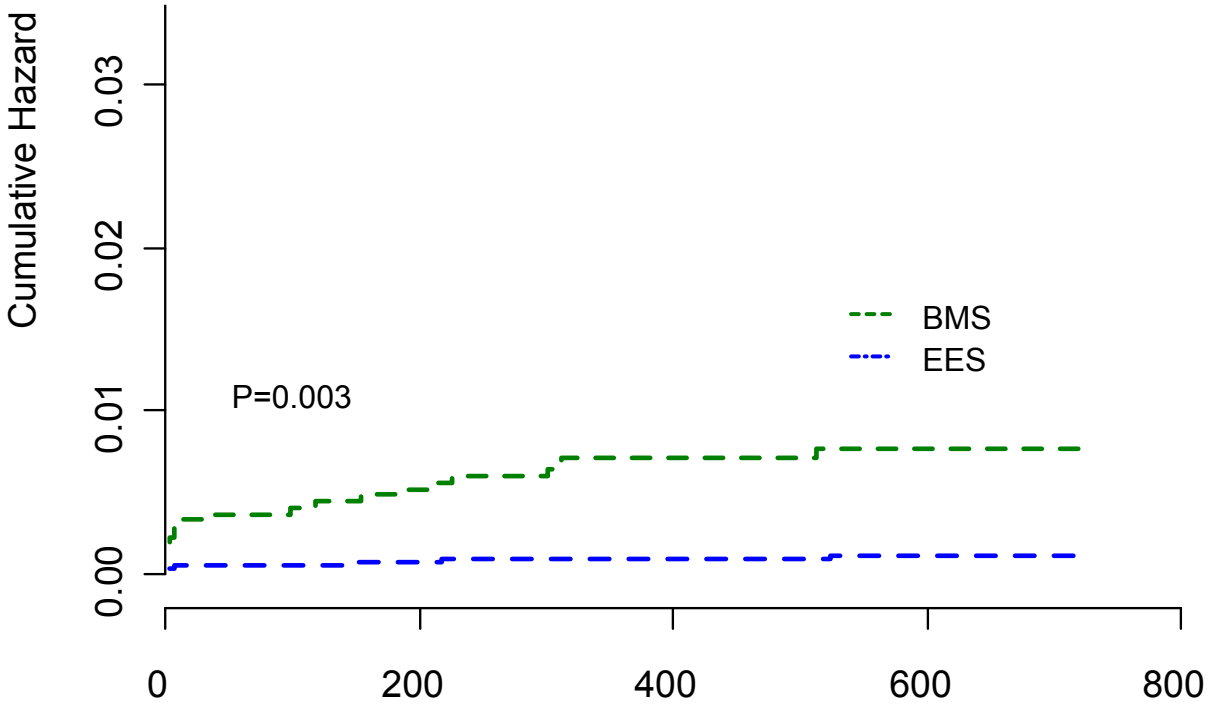


Number of patients

BMS	2444	2262	1986	1849	0
EES	2452	2311	1918	1894	0

Fatal myocardial infarction

Fatal MI was more than 80% lower in the Co-Cr EES group [0.08% vs. 0.8% in the BMS group; unadjusted HR, 0.11; 95% CI, 0.03-0.48, P=0.003; NNTB **142.2**; 95% CI, 129.8 to 243.9; **adjusted HR, 0.11; 95% CI, 0.03-0.49, P=0.004**].

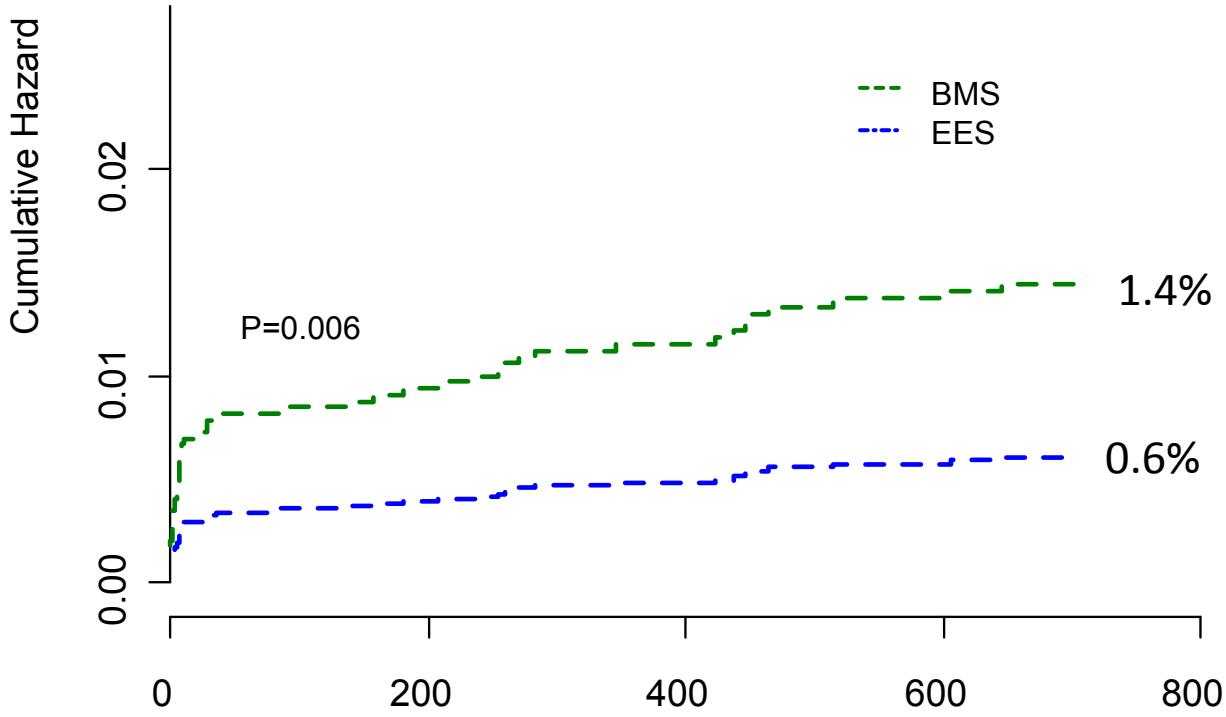


Number of patients

BMS	2444	2349	1940	1928	0
EES	2452	2377	1975	1958	0

Definite stent thrombosis

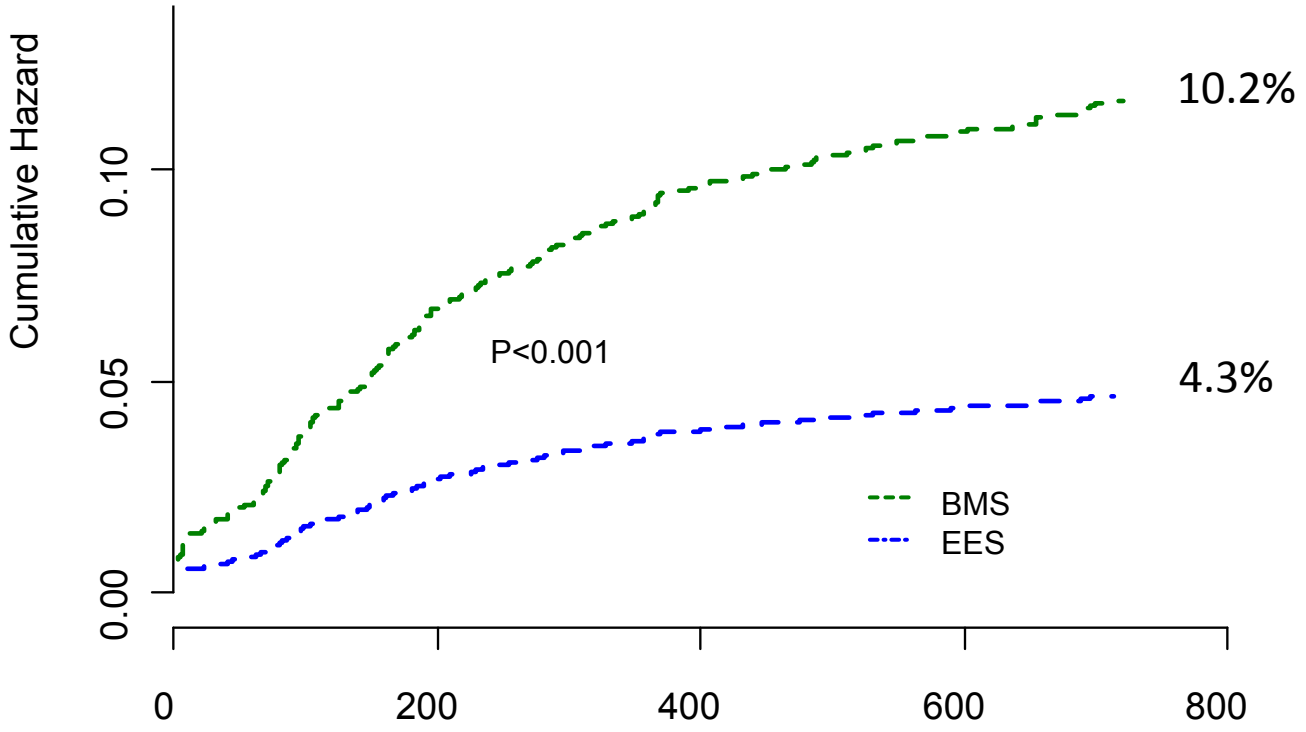
Adjusted HR, 0.41; 95% CI, 0.22-0.76; P=0.005; NNTB, **127.7;** 95% CI, 95.2 to 333.3].



Number of patients					
BMS	2444	2328	1914	1901	0
EES	2452	2369	1968	1946	0

Target vessel revascularization

the need for reintervention in the previously instrumented vessel [4.3% vs. 10.2%; adjusted **HR, 0.39;** 95% CI 0.29-0.51; P<0.001; **NNTB, 16.1;** 95% CI, 14.0 to 20.1] **was reduced by 61% in the Co-Cr EES**

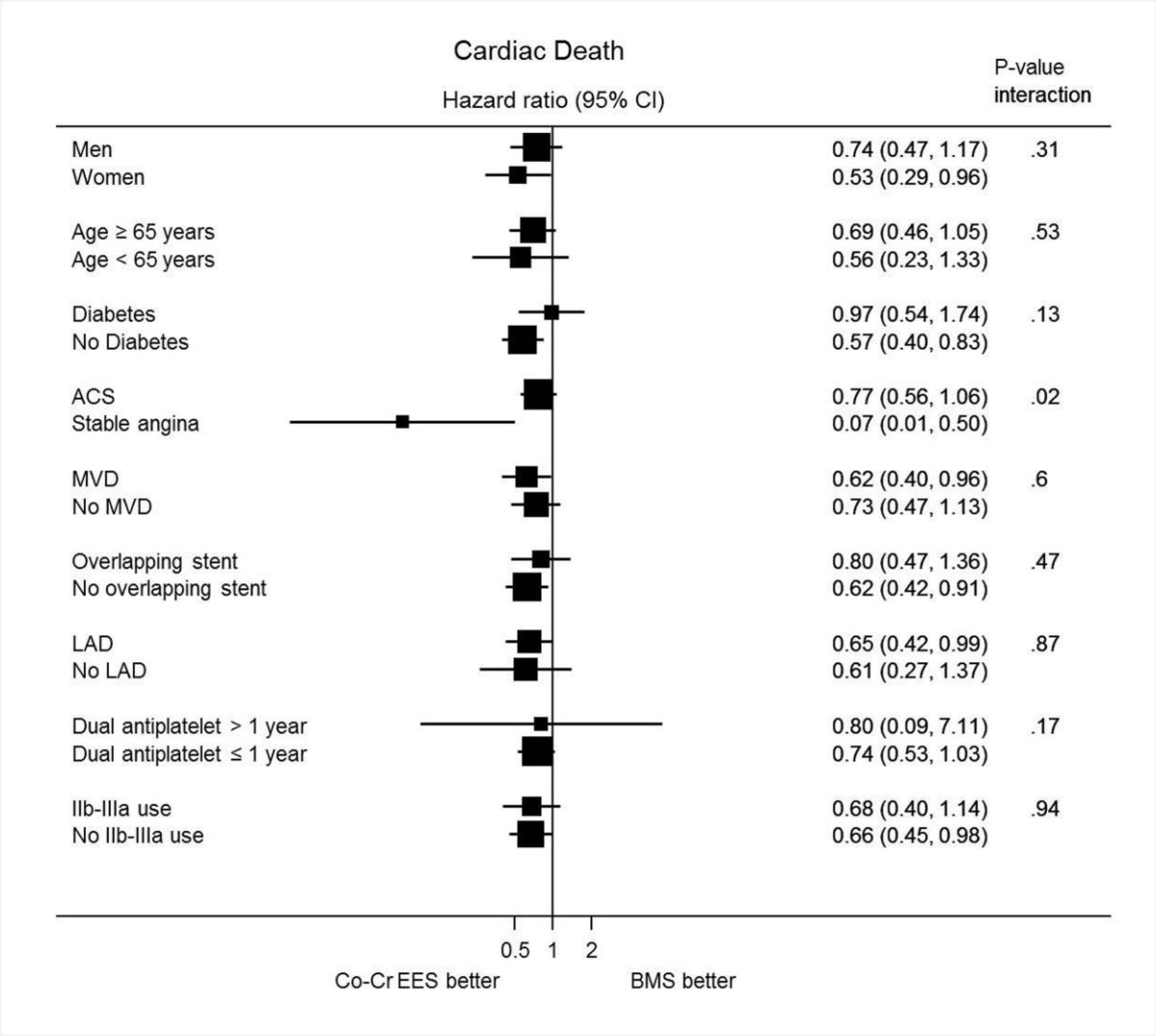


Number of patients

BMS	2444	2196	1761	1727	0
EES	2452	2328	1899	1869	0

Results

As shown in the Figure, the benefit of treatment with Co-Cr EES re cardiac death was consistent across all analysed subgroups with a qualitative positive interaction testing for stable coronary artery disease:



Conclusions

- Our collaborative individual patient-data meta-analysis of 5 studies, including 4,896 largely ACS patients shows a consistent reduction of several fatal and non-fatal ischemic endpoints in favor of Co-Cr EES as compared to BMS, including, cardiac mortality, ST (both definite and definite or probable), MI throughout 2-year follow-up.
- Our observation supports a major paradigm shift in current understanding about the safety and efficacy of coronary devices.
- This is the first observation that a specific DES implantation leads to a cardiac mortality benefit as compared to BMS