Comparative Effectiveness and Safety of New-versus Early-Generation Drug-Eluting Stents according to the Complexity of Coronary Artery Disease : A Patient-Level Pooled Analysis of 6,081 Patients

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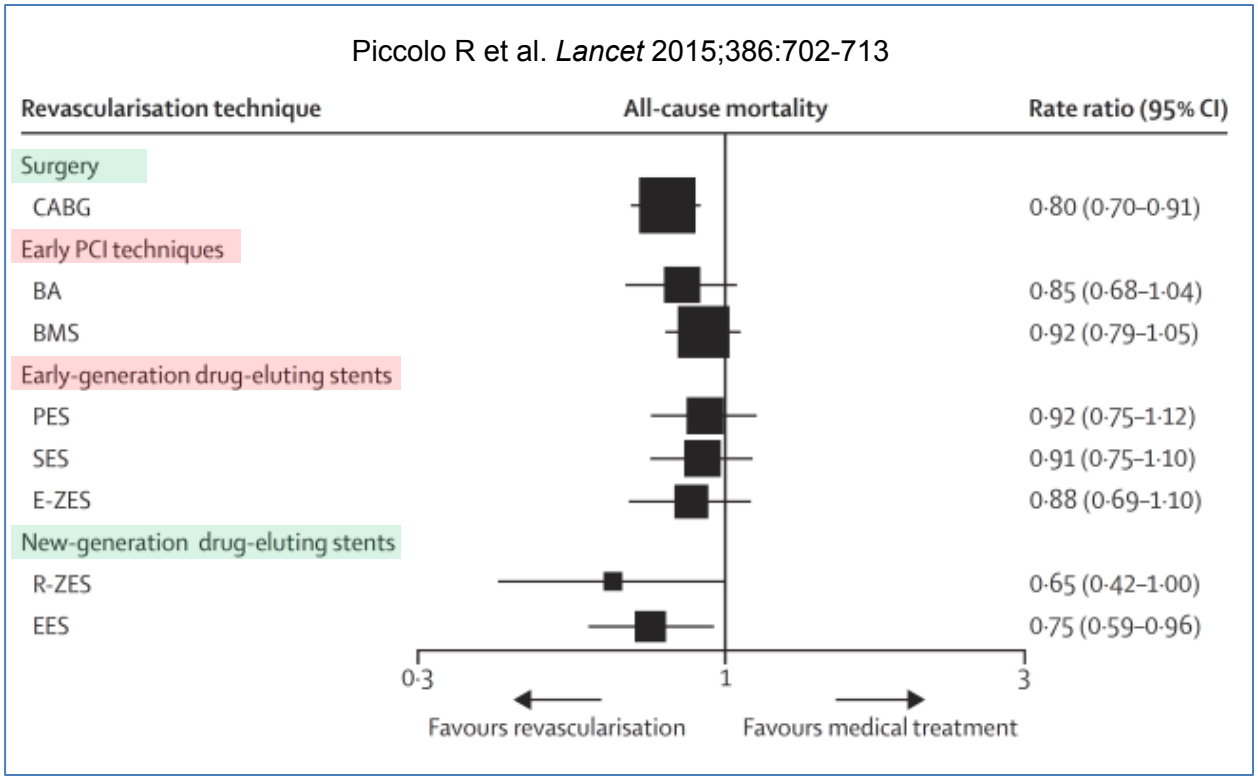
DECLARATION OF INTEREST

- I have nothing to declare

Progress with Metallic Drug-Eluting Stents

Piccolo R et al. *Lancet* 2015;386:702-713

STUDY OBJECTIVE



New-generation DES improved the safety and efficacy compared with Early-generation DES

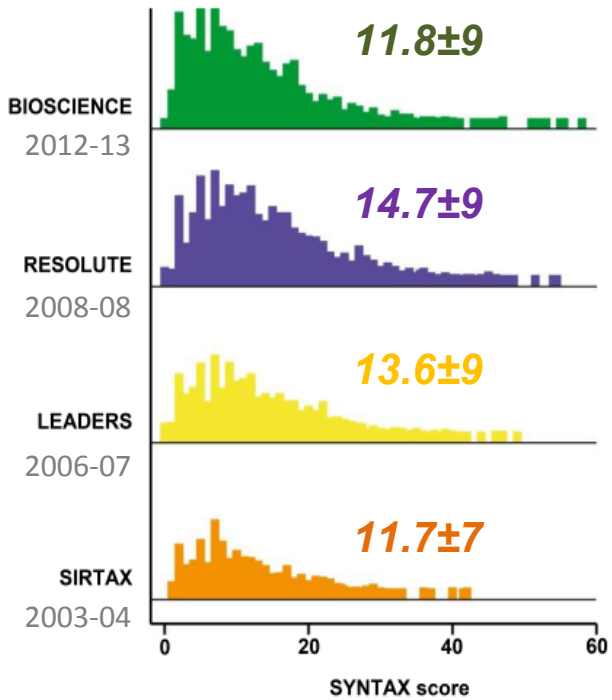
It is not well established whether the anatomic complexity of CAD influences the clinical benefits of New-generation DES

AIM: To investigate the safety and effectiveness of New-DES vs Early-DES in relation to anatomic CAD Complexity as assessed by the SYNTAX score

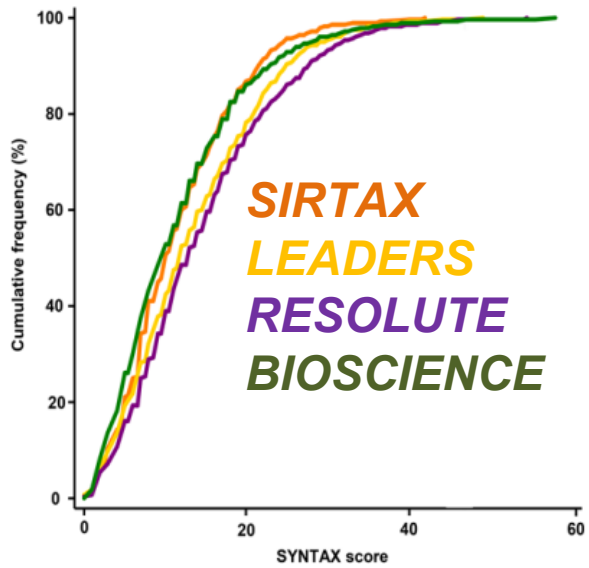
METHODS

4 All-comers RCTs (n=6,081)

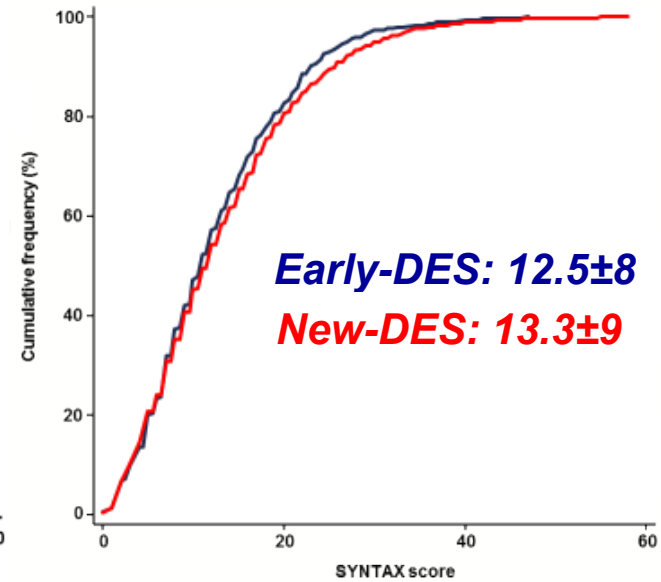
SYNTAX Score Distribution



Pooled trials



New- vs. Early-DES



- *Primary device-oriented endpoint: the composite of cardiac death, MI, or ischemia-driven TLR*
- *Principal effectiveness and safety endpoints: TLR and definite stent thrombosis (ST)*

- *Early-DES: SES and PES (SIRTAX and LEADERS)*
- *New-DES: EES, Resolute ZES, BP-BES, and BP-SES (LEADERS, RESOLUTE, BIOSCIENCE)*

Baseline Clinical Characteristics

	New-DES (n =4,554)	Early-DES (n =1,527)	p-value
Age — years	64.5±11.2	62.7±11.1	<0.001
Female gender	1,117 (24.5%)	380 (24.9%)	0.78
Diabetes	1,012 (22.2%)	298 (19.5%)	0.03
Insulin-requiring	330 (7.2%)	101 (6.6%)	0.42
Hypertension	3,160 (69.4%)	998 (65.4%)	0.003
Hypercholesterolemia	2,915 (64.0%)	934 (61.2%)	0.05
Renal Failure	625 (14.3%)	172 (13.3%)	0.39
Current smoker	1,317 (28.9%)	512 (34.3%)	<0.001
Family history of CAD	1,347 (31.8%)	606 (39.7%)	<0.001
Previous MI	1,043 (23.1%)	432 (28.3%)	<0.001
Previous PCI	1,297 (28.5%)	387 (25.3%)	0.02

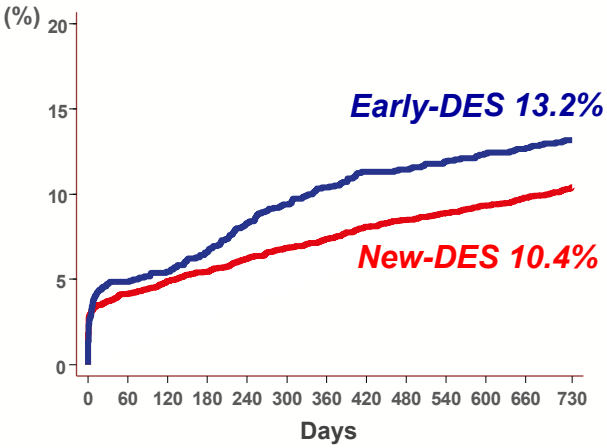
Angiographic and Procedural Characteristics

	New-DES (n =4,554)	Early-DES (n =1,527)	p-value
No. of treated lesions per patient	**1.48±0.75**	**1.41±0.66**	0.043
Multivessel treatment per patient	**1,076 (23.6%)**	**277 (18.1%)**	<0.001
Target-vessel location			<0.001
Right coronary artery	**2,169 (32.2%)**	**724 (33.6%)**	
Left main artery	**75 (1.1%)**	**12 (0.6%)**	
Left anterior descending artery	**2,885 (42.8%)**	**975 (45.3%)**	
Left circumflex artery	**1,610 (23.9%)**	**441 (20.5%)**	
Bypass graft	**4 (0.1%)**	**0 (0.0%)**	
De novo lesion per lesion	**6,289 (93.8%)**	**2,061 (95.9%)**	0.001
Occlusion per lesion	**640 (9.6%)**	**148 (6.9%)**	<0.001
Number of stents per lesion	**1.32±0.67**	**1.20±0.56**	<0.001

New-Generation vs. Early-Generation DES: 2-Year Follow-Up

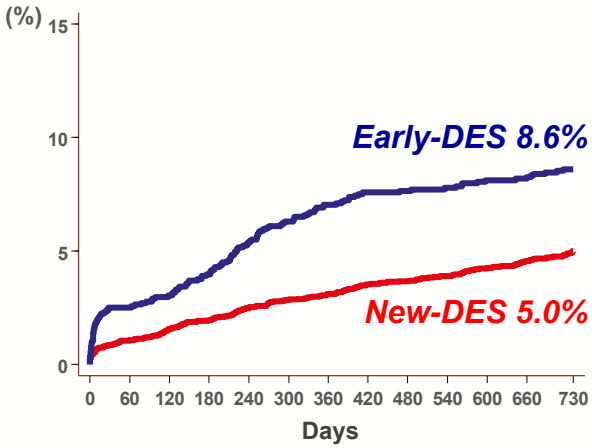
Cdeath, MI, TLR

Adjusted HR 0.75 (0.63-0.89), P=0.001



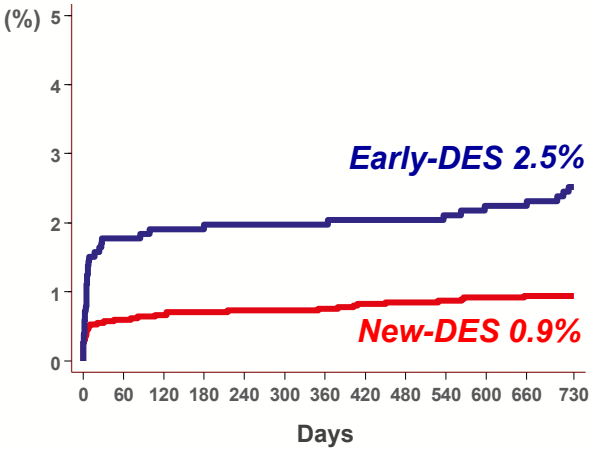
Target-Lesion Revasc

Adjusted HR 0.56 (0.44-0.70), P<0.001



Definite ST

Adjusted HR 0.40 (0.25-0.65), P<0.001

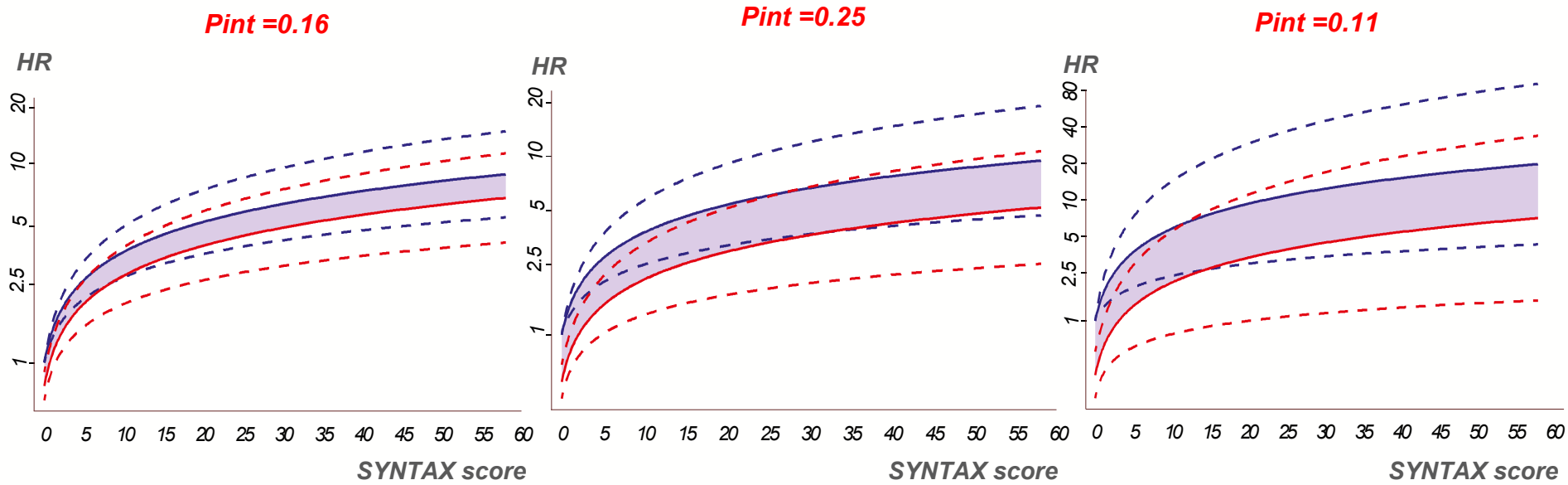


New-DES (n =4,554), Early-DES (n =1,527). Follow-up available in 97.2% of patients at 2-year

HR (95% CI) and p-values are from Cox Regressions. Adjusted HR (95% CI) and p-values are from Multiple Imputation estimated Cox Regressions (20 data-sets using Rubin's rule to combine estimates), adjusting for baseline variables associated with the primary outcome: age, diabetes, renal failure, previous myocardial infarction

Clinical Outcomes According to The SYNTAX Score

Cdeath, MI, TLR | **Target-Lesion Revasc** | **Definite ST**



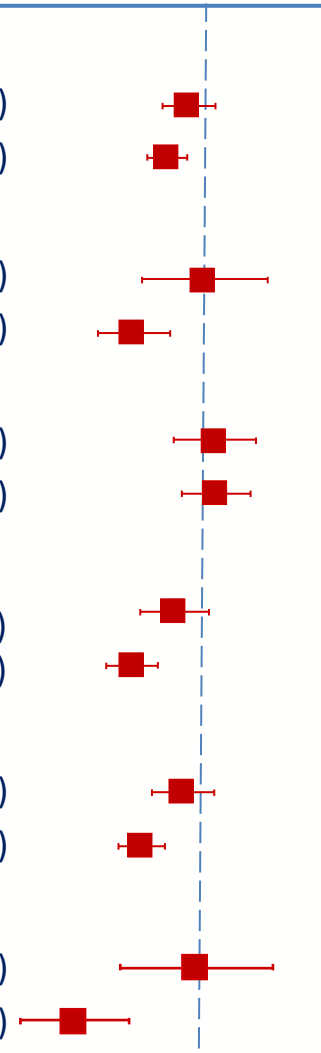
Early-DES | New-DES | Benefit of New-DES vs. Early-DES

No significant interaction between the type of DES and the SYNTAX score

The interaction between the type of DES (new-generation vs. early-generation DES) and the SYNTAX score (after logarithm transformation) was tested in the Cox-regression analyses and graphically represented the results with spline curves by using a flexible STATA model (xblc command)

Stratified Analysis of Clinical Endpoints

	New-DES	Early-DES	Adj HR (95% CI)	p	$p_{interaction}$
Primary Endpoint					**0.22**
SYNTAX score ≤11	**175 (8.0%)**	**71 (8.9%)**	0.86 (0.64-1.16)	0.32	
SYNTAX score >11	**287 (12.7%)**	**129 (17.8%)**	0.68 (0.54-0.85)	0.001	
Cardiac death					**0.042**
SYNTAX score ≤11	**39 (1.8%)**	**10 (1.3%)**	1.03 (0.51-2.09)	0.93	
SYNTAX score >11	**67 (3.0%)**	**40 (5.5%)**	0.46 (0.31-0.70)	<0.001	
Any MI					**0.87**
SYNTAX score ≤11	**87 (4.0%)**	**28 (3.5%)**	1.16 (0.73-1.84)	0.54	
SYNTAX score >11	**141 (6.2%)**	**41 (5.7%)**	1.18 (0.80-1.73)	0.41	
ID-TLR					**0.059**
SYNTAX score ≤11	**88 (4.1%)**	**45 (5.7%)**	0.74 (0.50-1.08)	0.12	
SYNTAX score >11	**129 (5.9%)**	**84 (11.9%)**	0.46 (0.34-0.61)	<0.001	
ID-TVR					**0.039**
SYNTAX score ≤11	**110 (5.1%)**	**52 (6.6%)**	0.81 (0.57-1.15)	0.23	
SYNTAX score >11	**167 (7.6%)**	**100 (14.1%)**	0.51 (0.39-0.66)	<0.001	
Definite ST					**0.013**
SYNTAX score ≤11	**20 (0.9%)**	**10 (1.3%)**	0.94 (0.40-2.23)	0.89	
SYNTAX score >11	**22 (1.0%)**	**28 (3.9%)**	0.24 (0.13-0.44)	<0.001	



Favours New-DES *Favours Early-DES*

CONCLUSIONS

- New-generation DES provide greater safety and effectiveness compared with early-generation DES in the overall population by reducing the risk of the primary device-oriented endpoint, ischemia-driven TLR, and definite ST
- The anatomic complexity of CAD does not impact on the benefits of new-generation DES
- The safety and the effectiveness of new-generation DES is greater in patients with SYNTAX score >11
- Additional benefits conferred by new-generation DES can be expected in patients with high SYNTAX scores, which may have important implications in the comparative effectiveness of PCI versus coronary artery bypass grafting