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School of Medicine

The Safety of Second Generation DES Is it better now?

Hyeon-Cheol Gwon

Cardiac&Vascular Center, Samsung Medical Center

Sunkyunkwan University School of Medicine

Firestorm from WCC 2006

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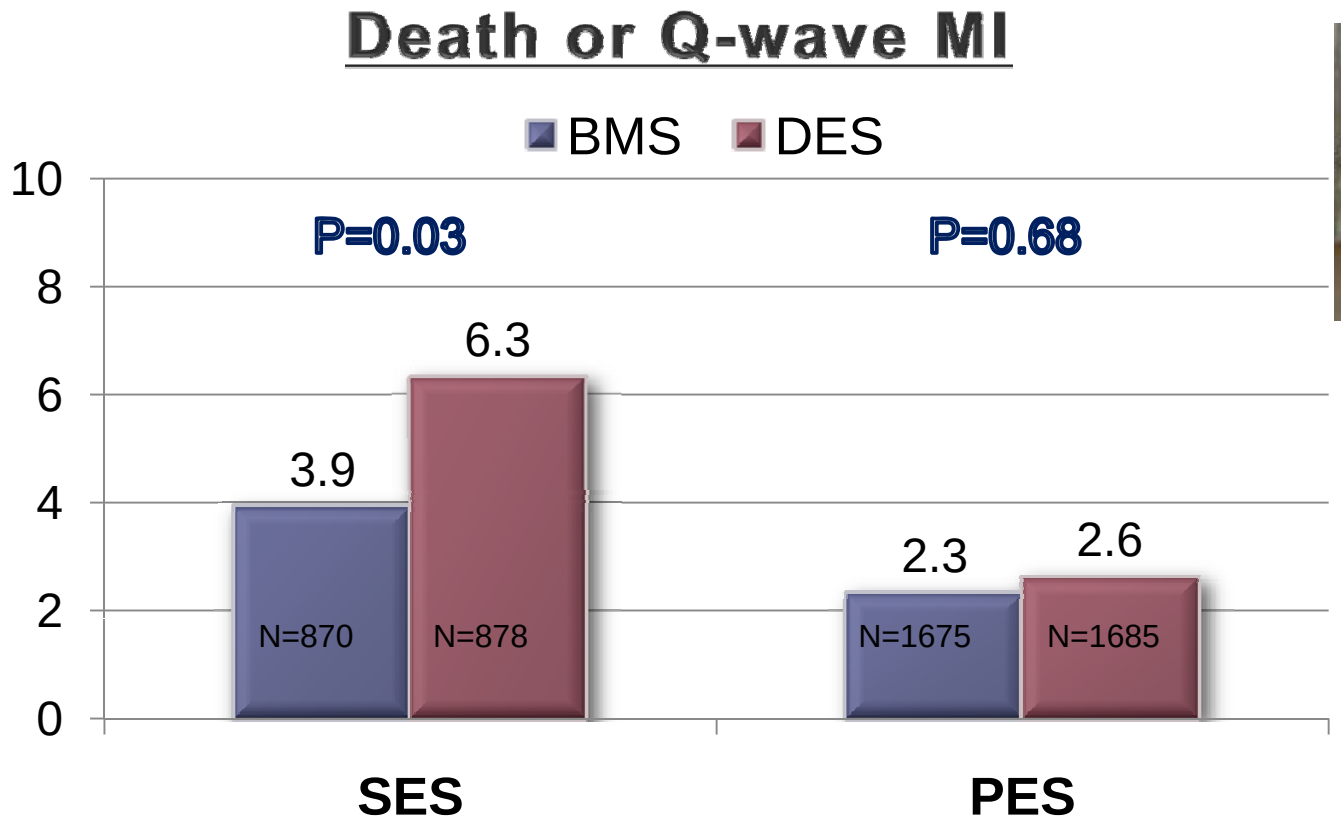
- Meta-analysis by pooling published or presented data



Camenzind E, WCC 2006

Meta-analysis of 14 trials of SES vs. BMS

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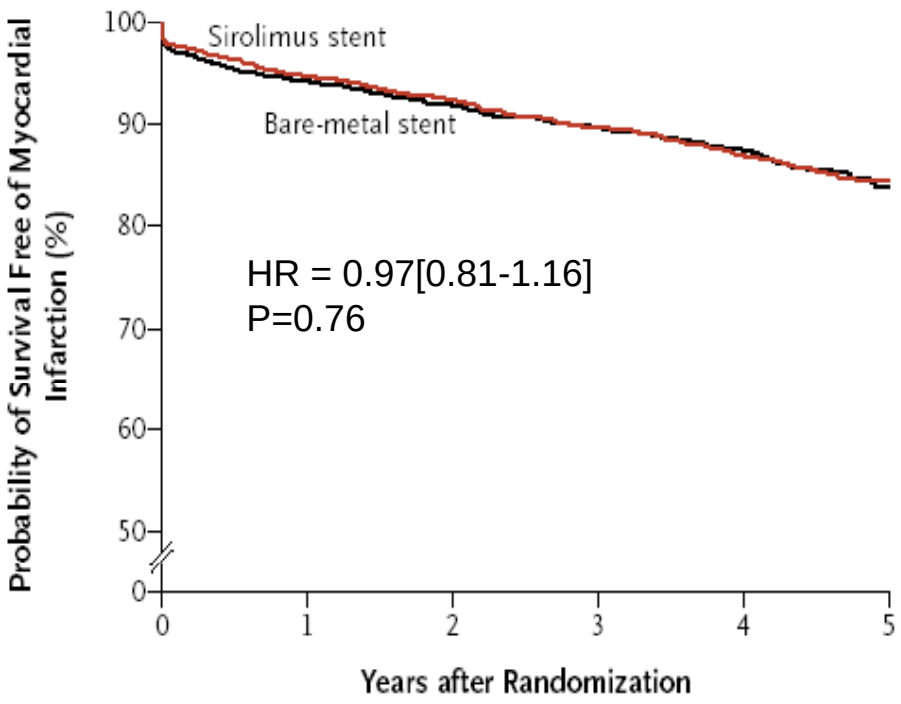
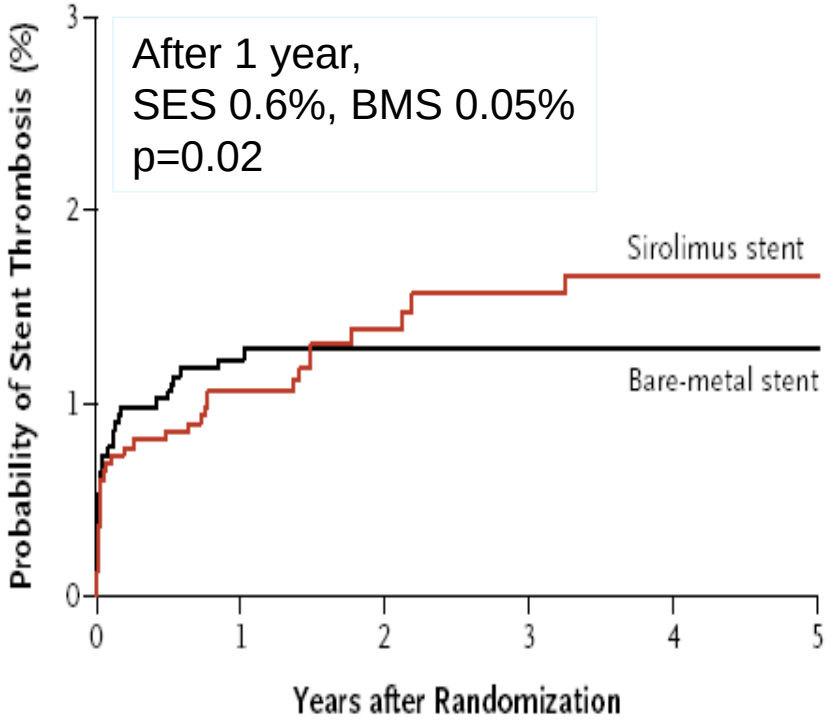
Death or MI



Stent Thrombus



Kastrati A, N Engl J Med 2007

DES is more thrombogenic than BMS

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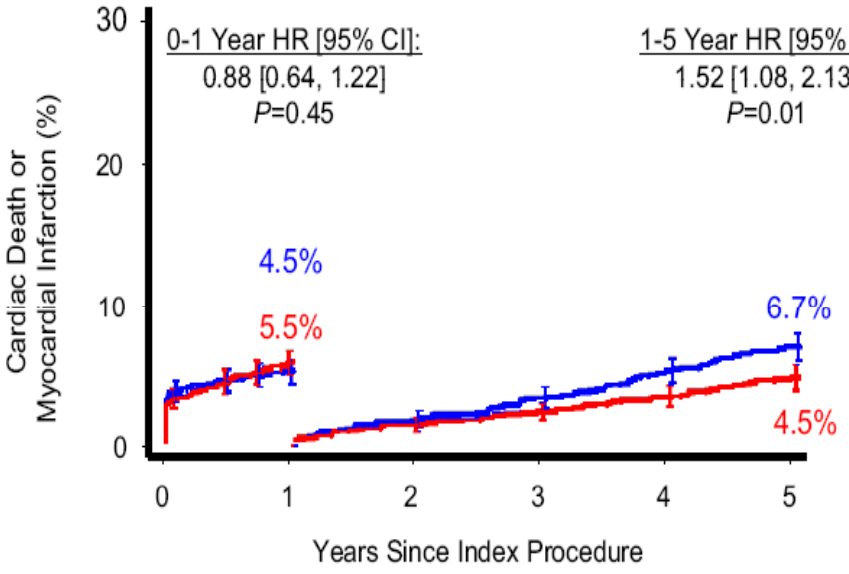
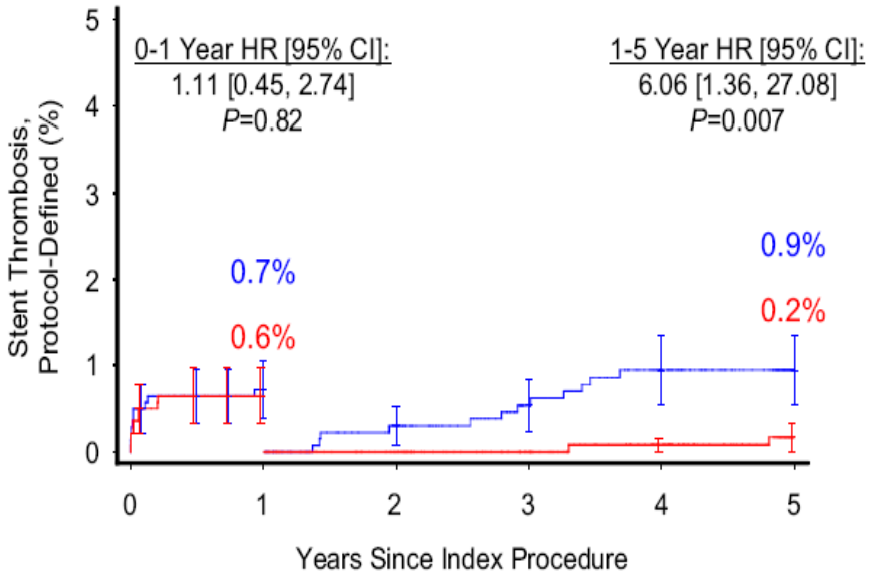
Pooled analysis of TAXUS I, II, IV, V

Cardiac death or MI



Stent thrombosis



BMS (N=1397) PES (N=1400)

Stone GW, JACC CV Int 2011;4:530

Mechanism of Late ST

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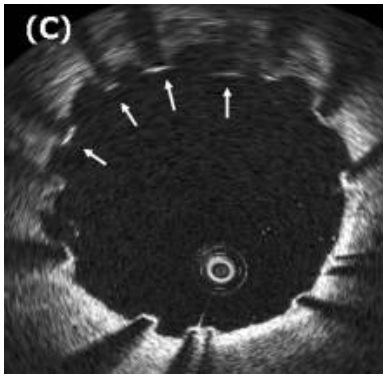
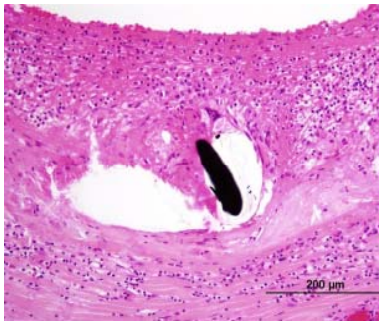
- Poor endothelial coverage of the stent
  - Non-specific antiproliferative
  - Thick strut thickness
- Localized hypersensitivity to polymer





→ Thin strut thickness
Biocompatible polymer

Nakazawa G, J Am Coll Cardiol 2011;57:390

Second Generation DES

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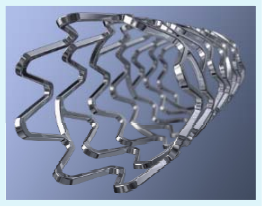
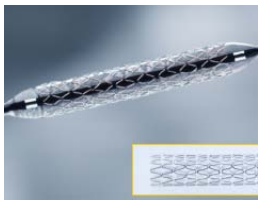
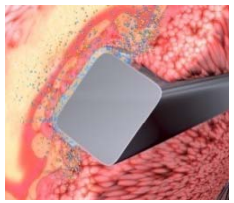
	Promus Element	Xience Prime	Endeavor Resolute	Biomatrix
Company	Boston Sci	Abbott	Metronic	Biosensors
Drug	Everolimus	Everolimus	Zotarolimus	Biolimus A9
Polymer	Fluorinated	Fluorinated	BioLinx	Bioabsorbable
Strut material	PtCr	CoCr	CoNi	316L
Strut thickness	81 um	81 um	91 um	119 um
Stent design	Element	Multilink 8^2	Driver	S-stent



EES vs. PES: Stent Thrombosis

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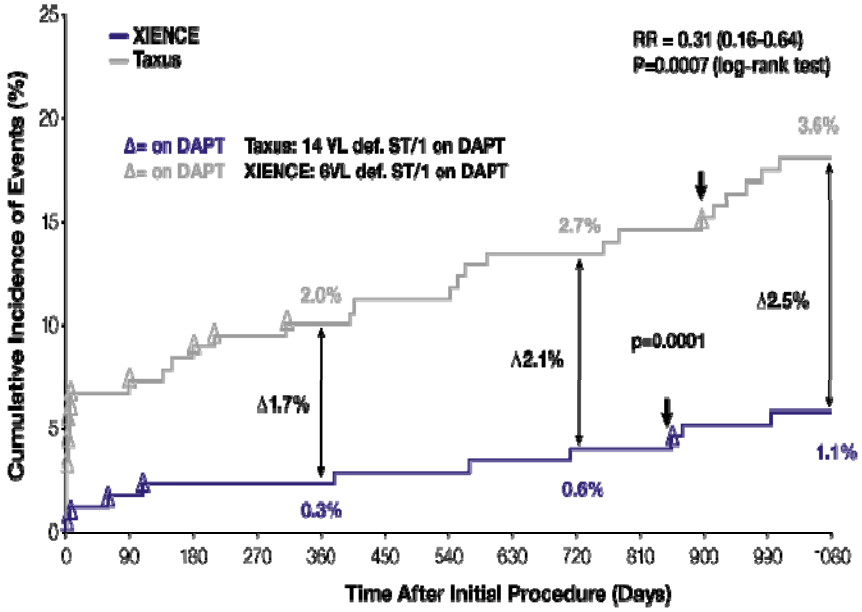
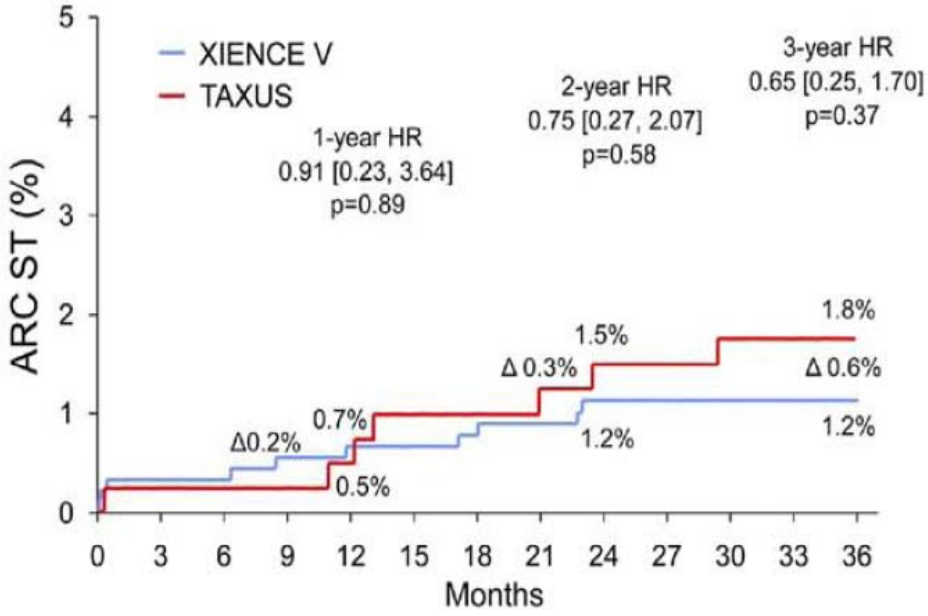
COMPARE Trial 3Y FU
N=1,800



SPIRIT II/III Pooled Analysis
N=1,302



Smits P, TCT 2011, Caixeta, JACC CV Int 2010

EES vs. SES: Stent Thrombosis

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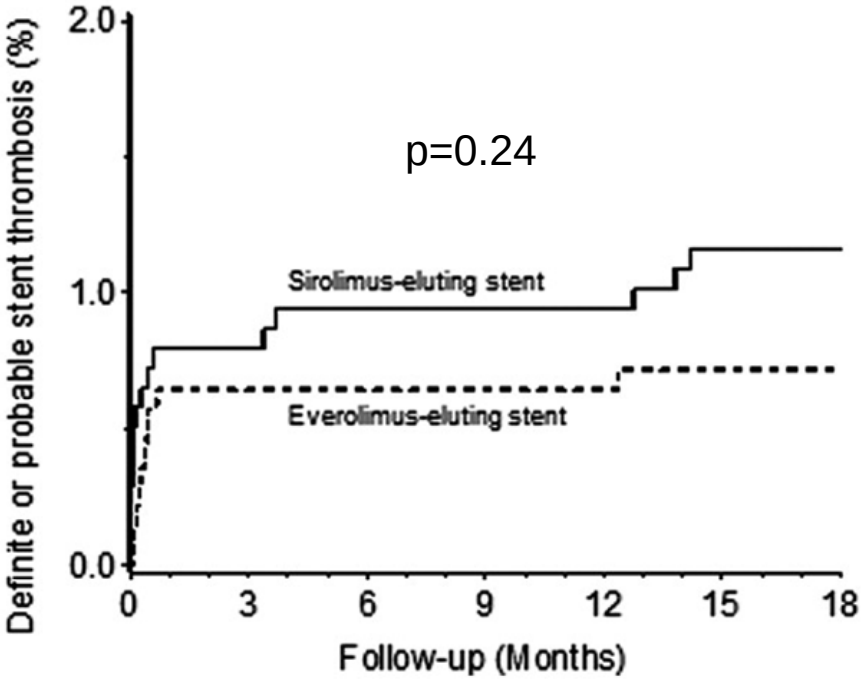
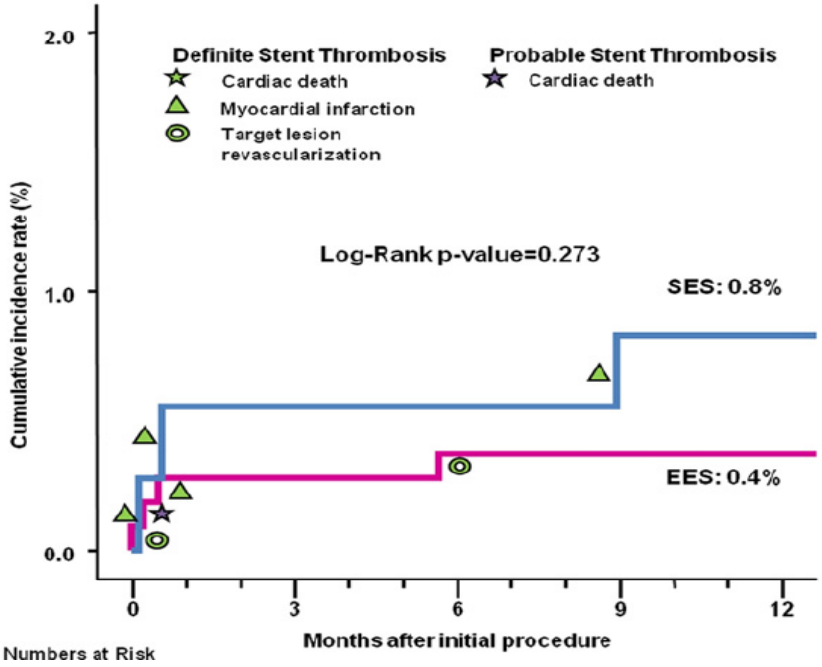
SORT OUT IV Trial
N=2,774



EXCELLENT Trial
N=1,443



* Definite or probable stent thrombosis

Lower ST Risk in New DES
SCAAR Registry

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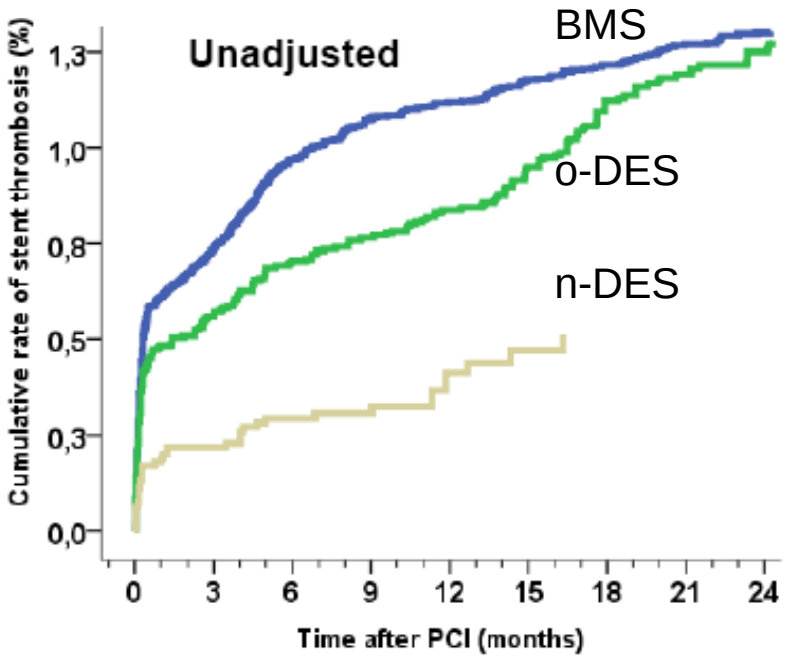
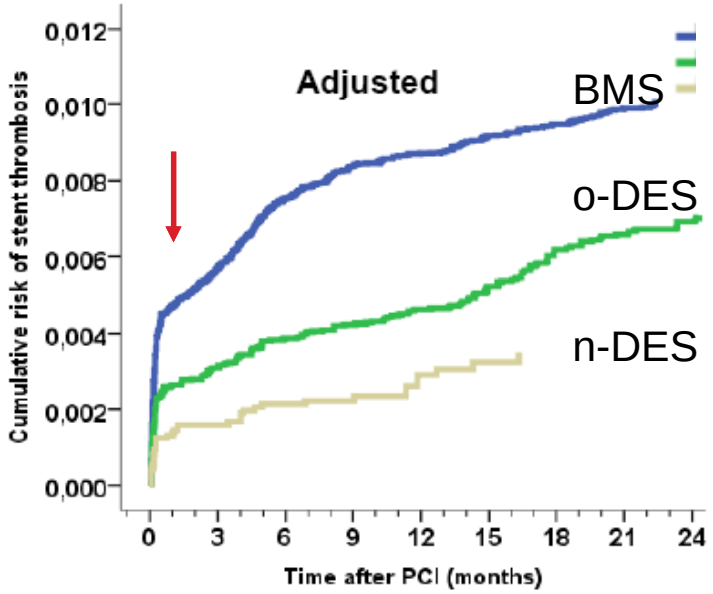
- Bare meta stent (**BMS**, N=64,631)
- Old DES (**o-DES**, N=19,202): Cypher, Taxus, and Endeavor
- New DES (**n-DES**, N=10,551): Resolute, Xience, Promus Element



n-DES vs o-DES: adjusted HR: 0.50; 95% CI: 0.35-0.71
n-DES vs BMS: adjusted HR: 0.33; 95% CI: 0.23-0.47
o-DES vs BMS: adjusted HR: 0.65; 95% CI: 0.54-0.46



Stent thrombosis: an angiographic occlusion of a previously implanted stent with an acute clinical presentation

Sarno G, European Society of Cardiology 2011

Lower ST Risk in New DES
Bern-Rotterdam Cohort Study

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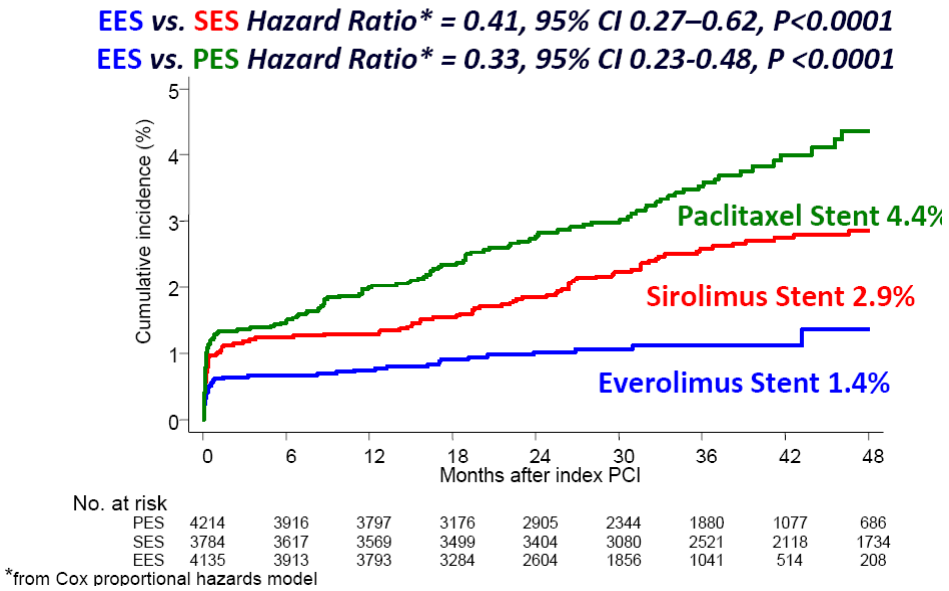
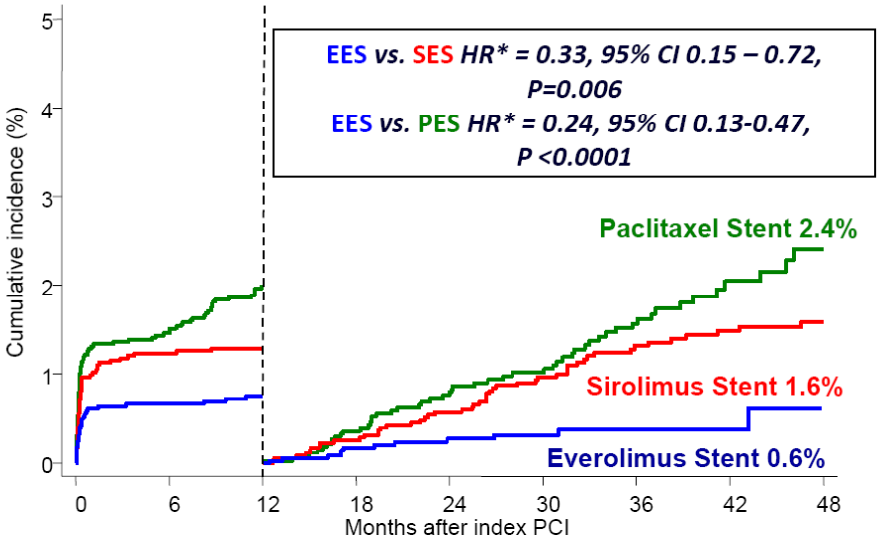
- Observation study in all consecutive patients
  - EES (n=4,212), SES (n=3,819), PES (n=4,308)

ARC Definite ST @ 4 Years



*from Cox proportional hazards model

Very Late ST (1-4 yrs)



*from Cox proportional hazards model

Network Meta-analysis

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Stent Thrombosis Network Meta-Analysis Protocol

2602 potentially relevant articles

2441 excluded
- 2117 not a comparison between DES
- 324 post-hoc, subgroup, follow-up or pooled analyses of included trials

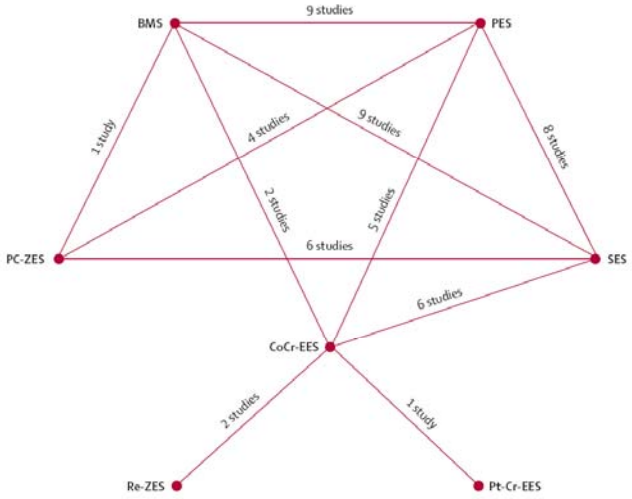
161 articles needing full review

112 excluded
- 84 not an RCT
- 13 DES not FDA approved
- 11 no ARC definition
- 4 DES pooled

49 articles meeting criteria → **49 RCTs 50,844 Patients**

FDA Approved Stents

(BMS, Cypher, Taxus, Endeavor, Endeavor Resolute, Promus Element, XIENCE)



Palmerini T, Stone G, Lancet 2012;379:1393–402

Network Meta-analysis

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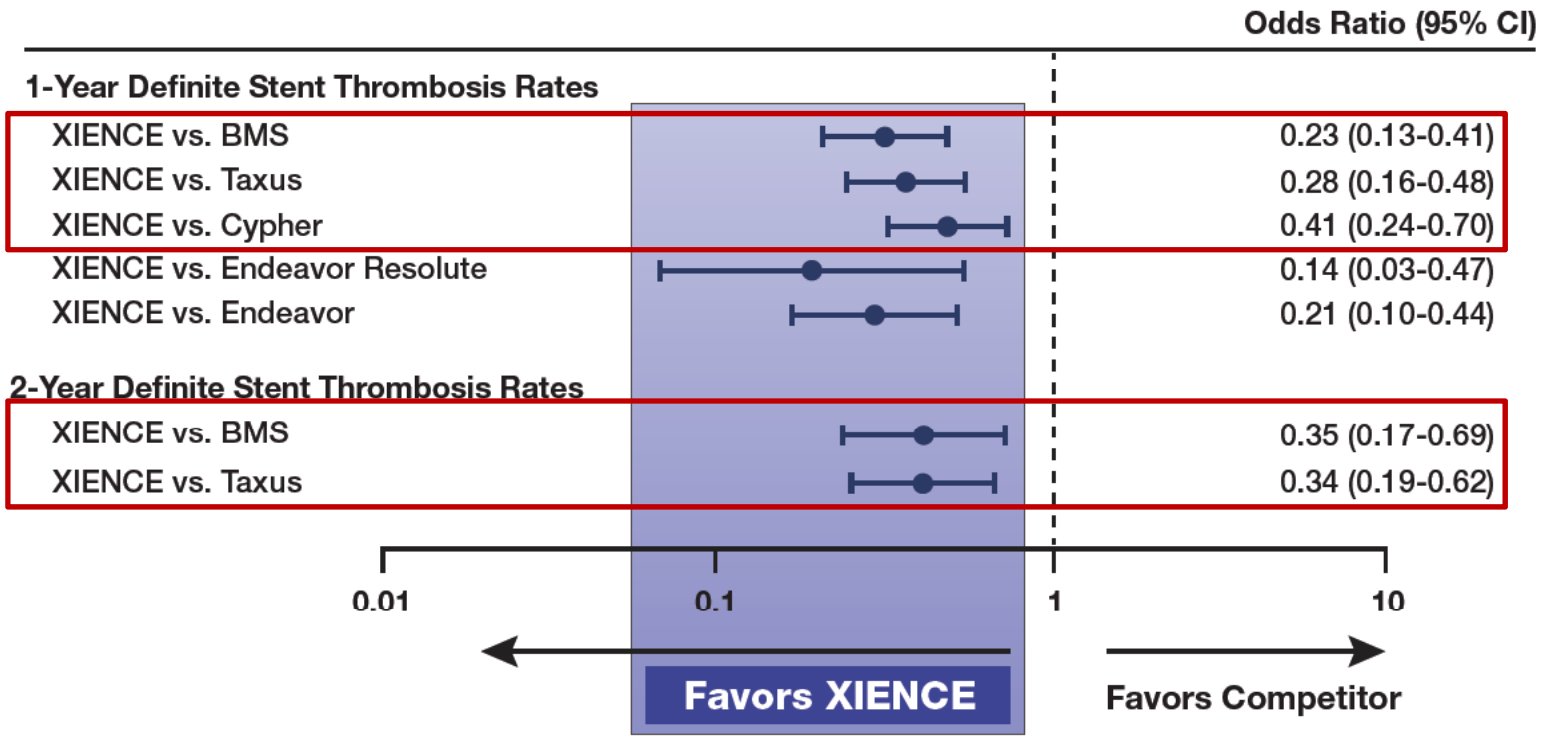
- N=50,844, from 49 RCTs



Palmerini T, Stone G, Lancet 2012;379:1393–402

EES is less thrombogenic than BMS?

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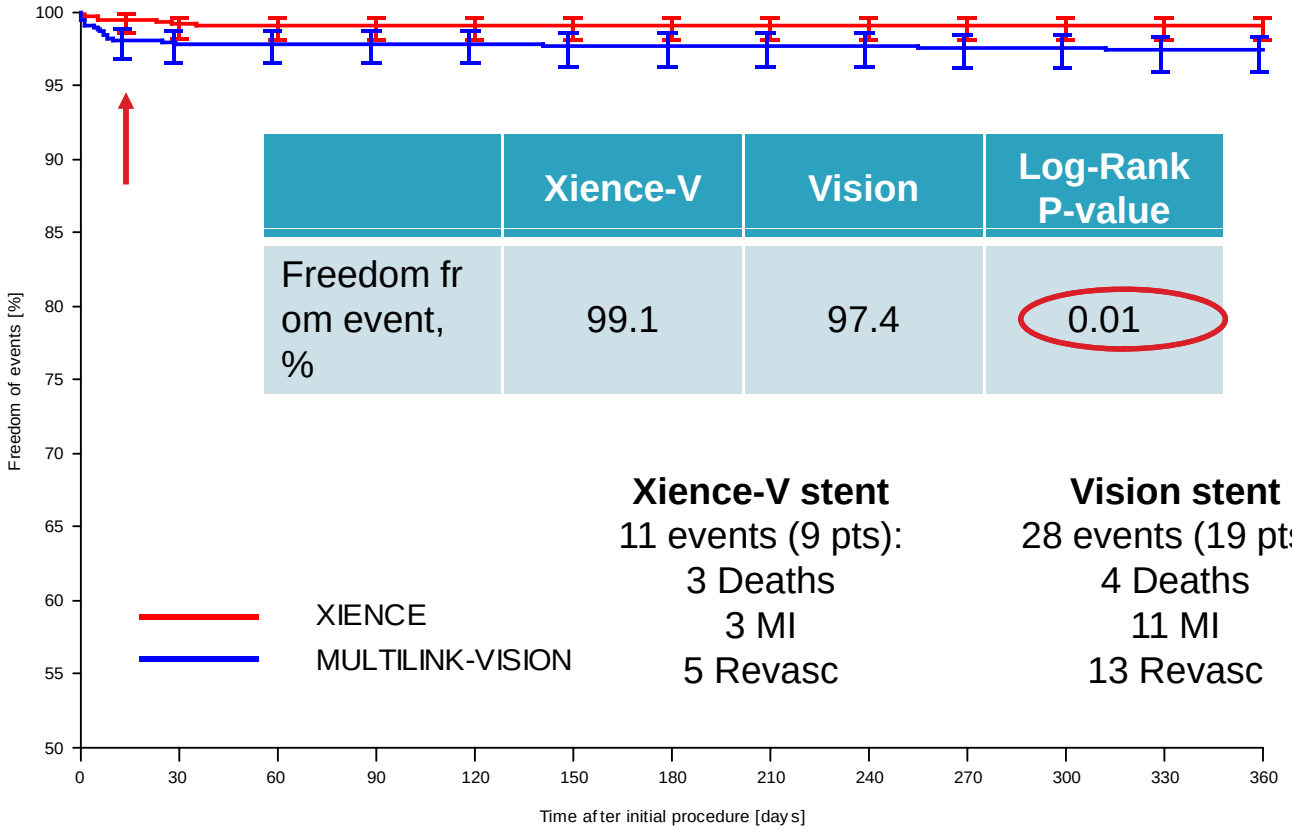
EXAMINATION Trial (N=1,504, within 48 hours of STEMI)
Definite/Probable Stent Thrombosis



	Xience-V	Vision	Log-Rank P-value
Freedom from event, %	99.1	97.4	0.01

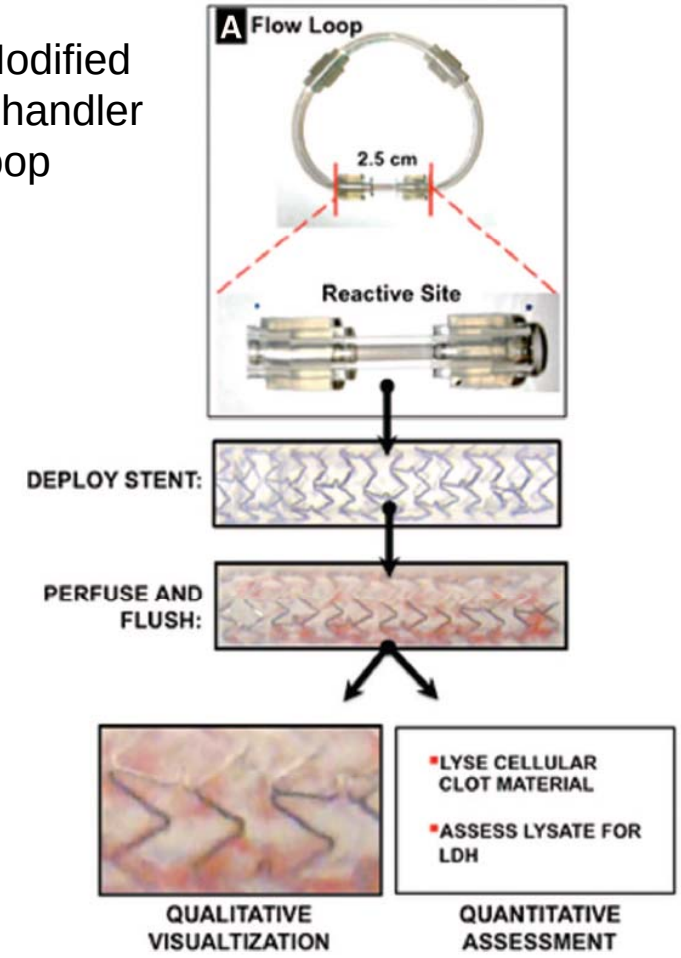
Xience-V stent
11 events (9 pts):
3 Deaths
3 MI
5 Revasc

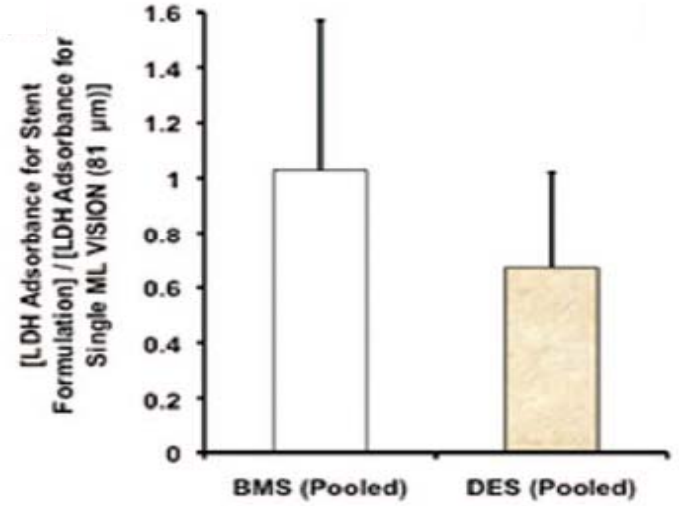
Vision stent
28 events (19 pts):
4 Deaths
11 MI
13 Revasc

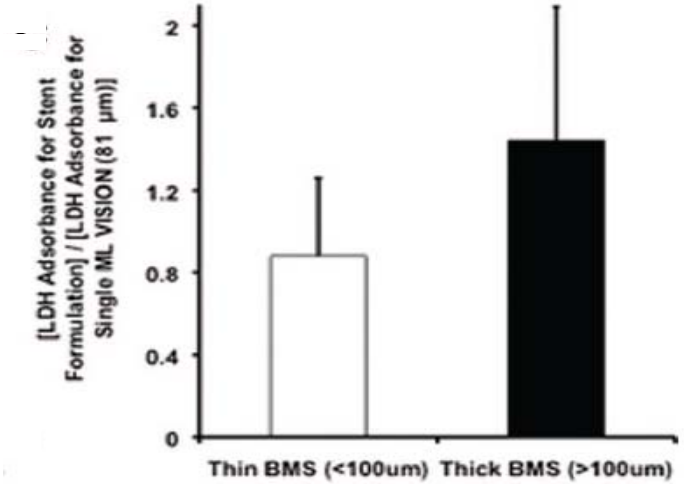
Sabate M, TCT 2011

Polymer Reduced Stent Thrombogenicity

Modified Chandler loop







Kolandaivelu K, Circulation 2011

Network Meta-analysis

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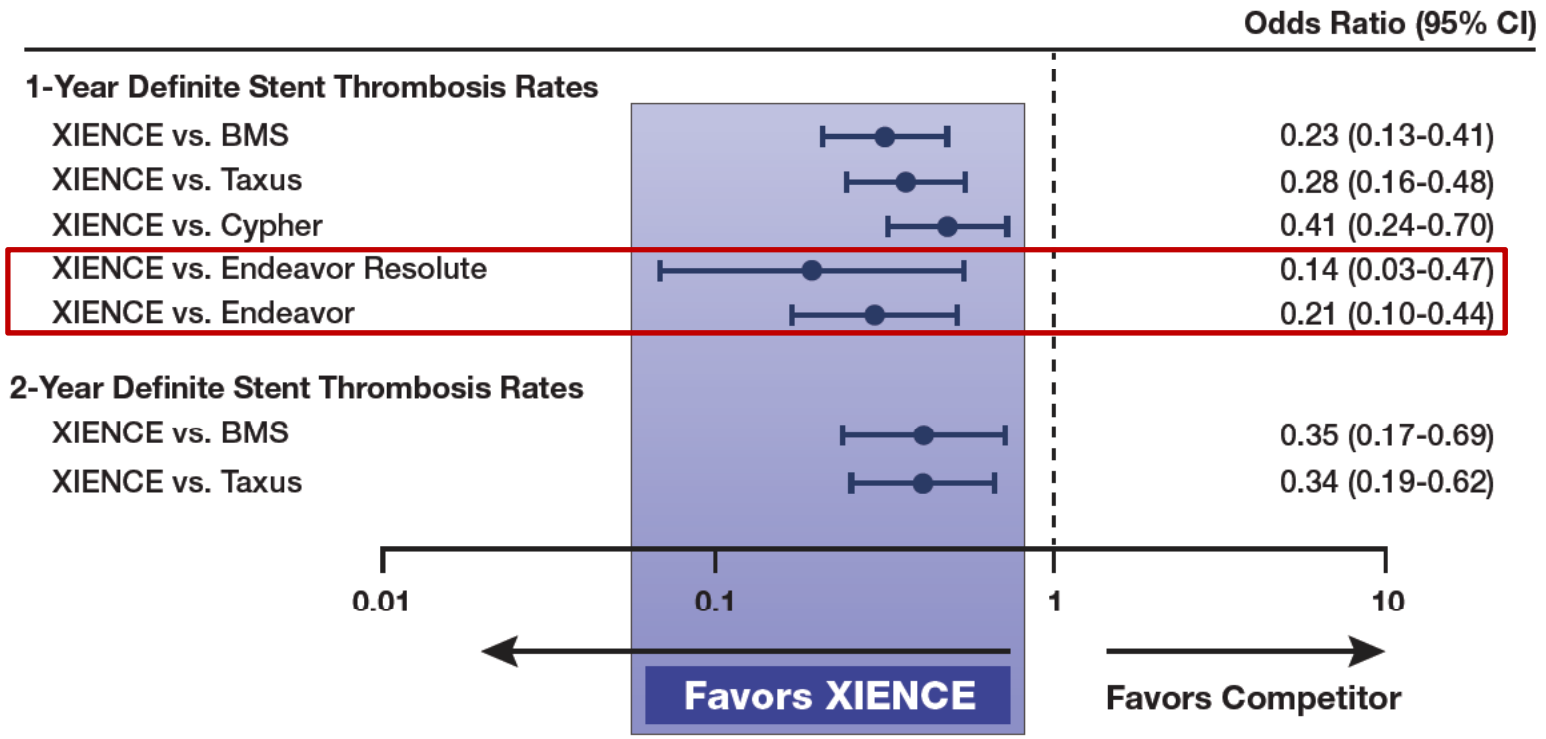
- N=50,844, from 49 RCTs



Palmerini T, Stone G, Lancet 2012;379:1393–402

Xience-V showed Lower Definite ST Rates against Endeavor Resolute

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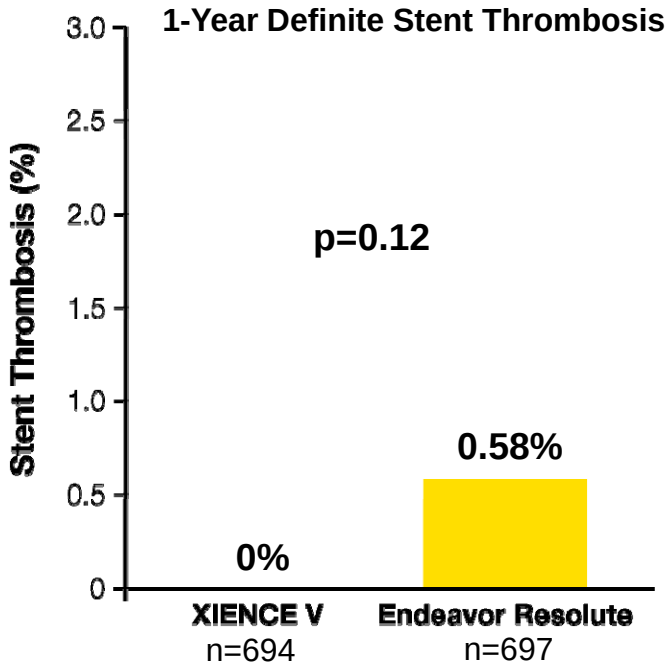
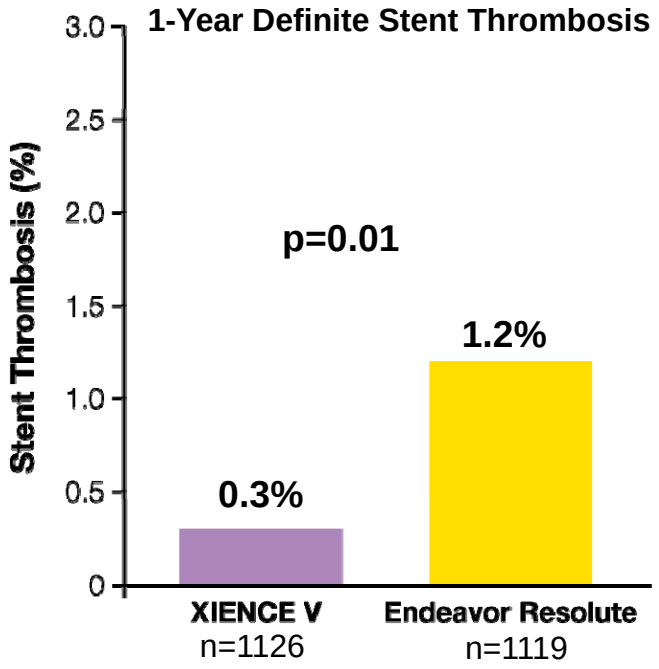
TWENTE



- Single-Center
- Investigator-sponsored
- 1,391 patients from the Netherlands
- STEMI patients excluded

RESOLUTE All Comers



- Multi-Center
- Sponsored by Medtronic
- 2,292 patients from throughout Europe
- No exclusion criteria

Von Birgelen C. TCT 2011, Serruys P, NEJM 2010

Endothelial Coverage of Stent Strut

Atherosclerotic Rabbit Iliac Model

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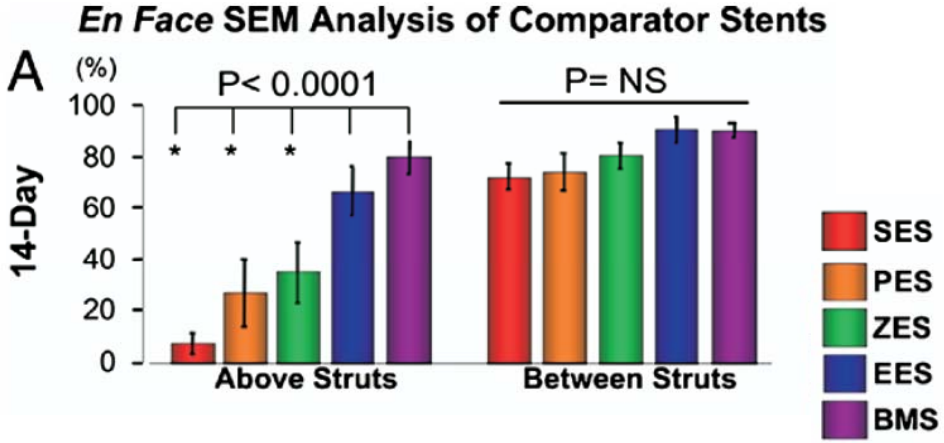
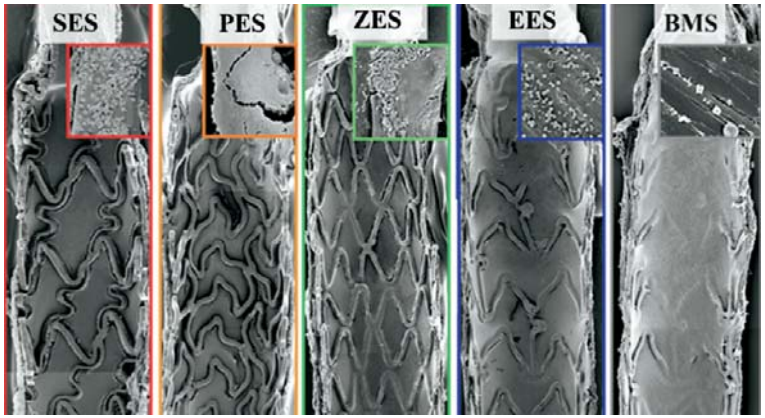
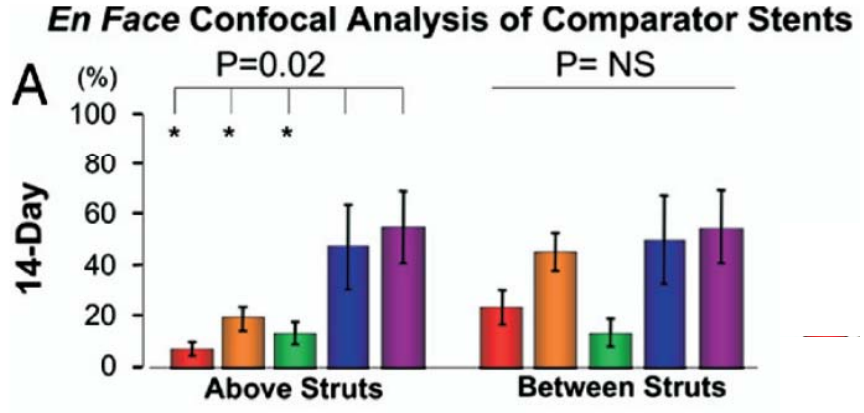
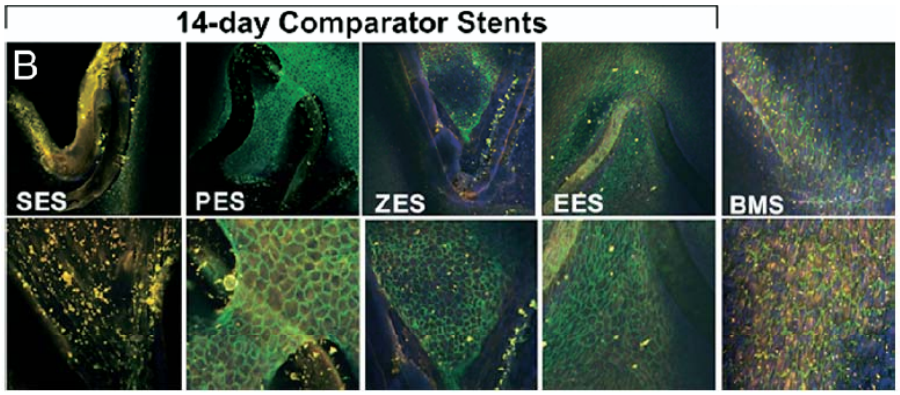
There is less endothelial cell surface coverage in other DESs compared with EES and BMS.









Joner M, Virmani R, JACC 2008

Why is EES better than other DESs?
Strut Thickness?

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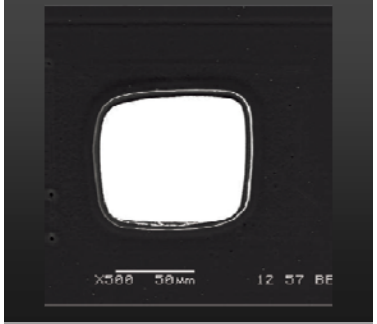
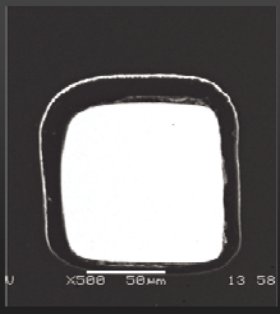
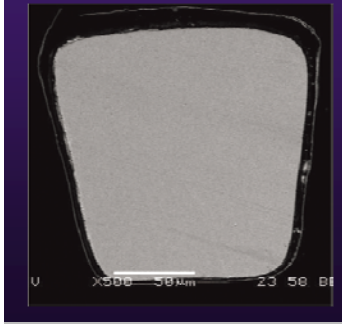
XIENCE PRIME	ENDEAVOR RESOLUTE	TAXUS Liberte	CYPHER
			
Strut Thickness:	Strut Thickness:	Strut Thickness:	Strut Thickness:
81 µm	91 µm	97 µm	140 µm
Alloy:	Alloy:	Alloy:	Alloy:
Cobalt Chromium	Cobalt Nickel	316L Stainless Steel	316L Stainless Steel
Polymer Thickness:	Polymer Thickness:	Polymer Thickness:	Polymer Thickness:
7.8 µm	6.2 µm	17.8 µm	12.6 µm

3.0 mm diameter stents, 500x magnification. Photos taken by and data on file at Abbott Vascular.

Why is EES better than other DESs?
Fluorinated Copolymer?

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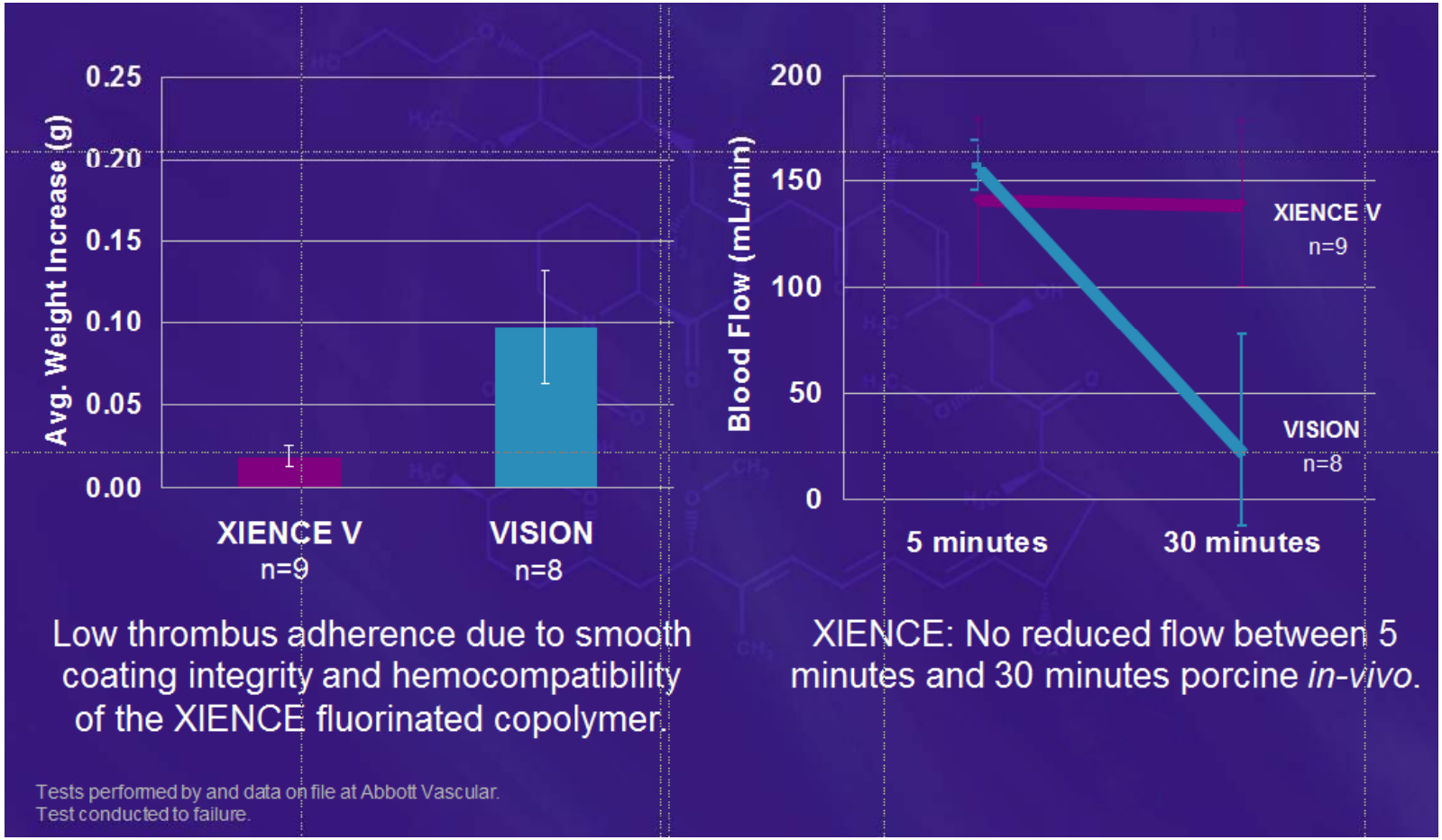
Unheparinized *Ex-Vivo* Shunt Study



Low thrombus adherence due to smooth coating integrity and hemocompatibility of the XIENCE fluorinated copolymer.

XIENCE: No reduced flow between 5 minutes and 30 minutes porcine *in-vivo*.

Tests performed by and data on file at Abbott Vascular.
Test conducted to failure.

Data from Abbott Vascular

Why is EES better than other DESs?
Fluorinated Copolymer?

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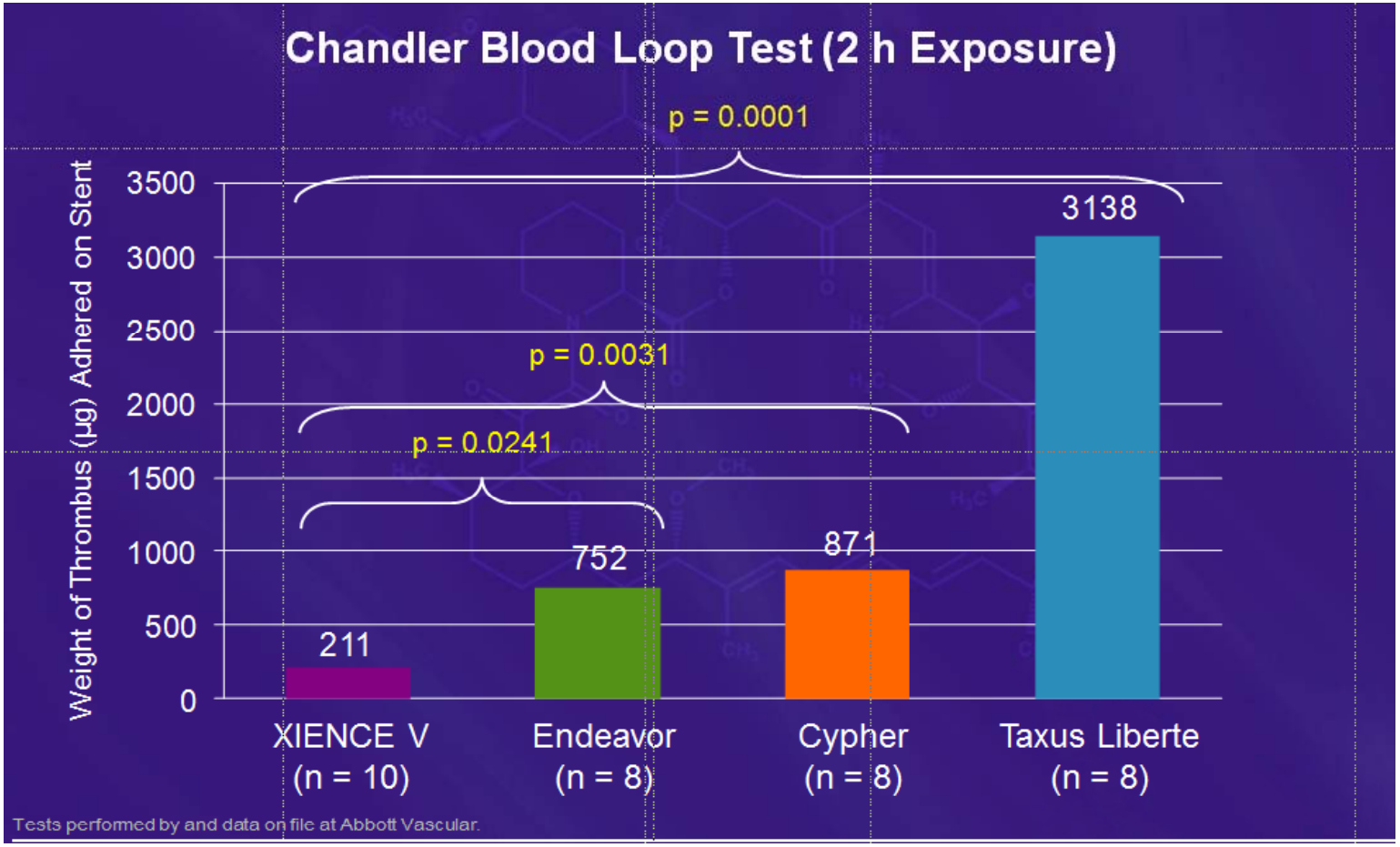
Unheparinized *Ex-Vivo* Shunt Study



Data from Abbott Vascular

Promus Element vs. Xience–V

Same drug, polymer, and strut thickness

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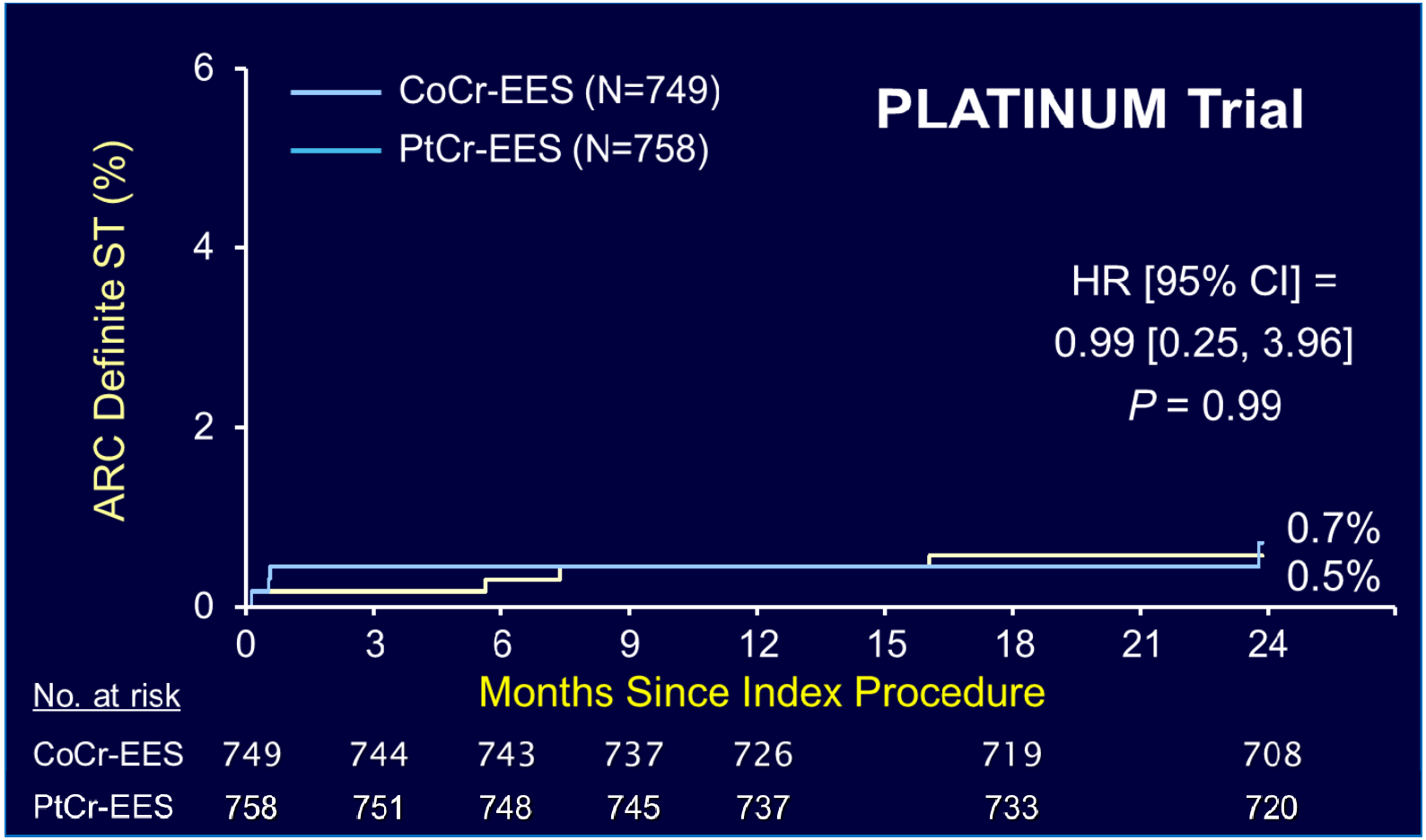
Stent Thrombosis - ARC Definite



Stone GW, ACC 2012

Next Generation DESs
How Can They Prove Better Safety?

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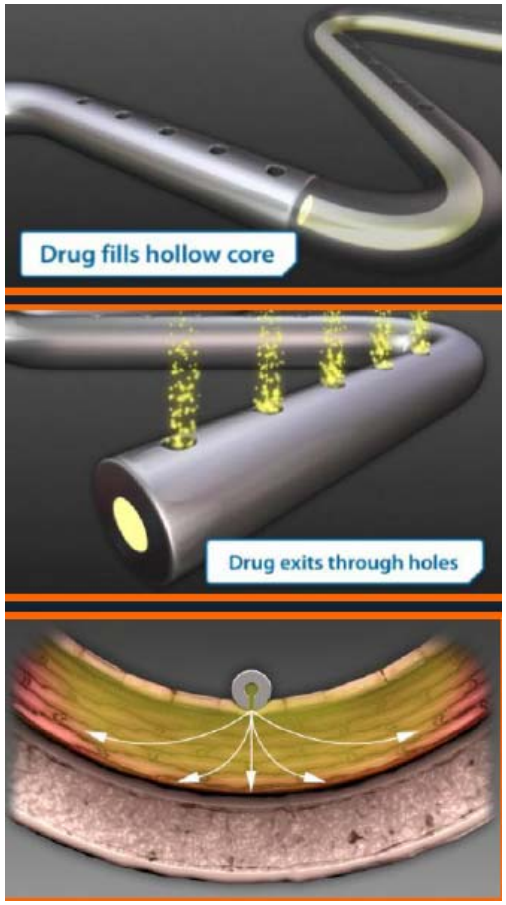

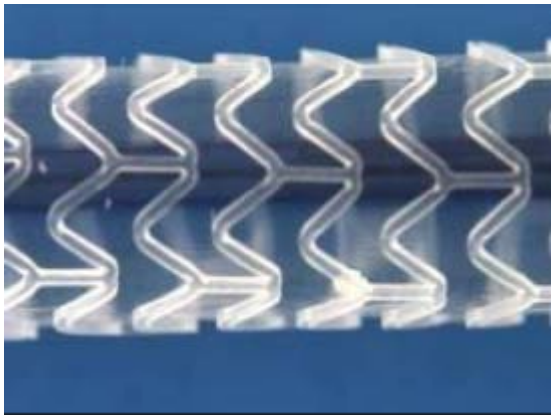

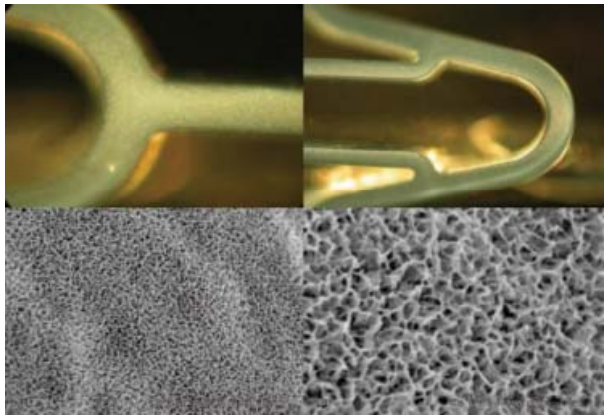

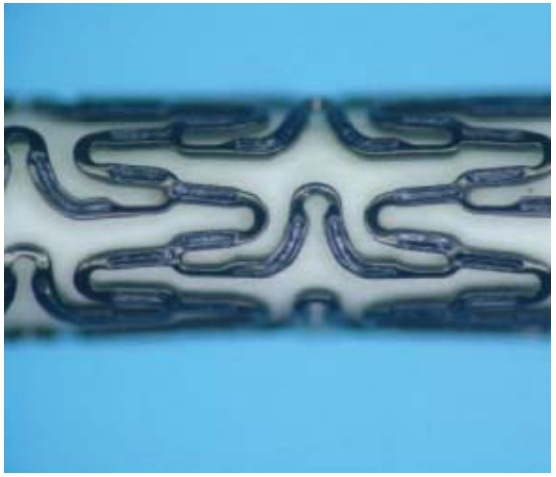

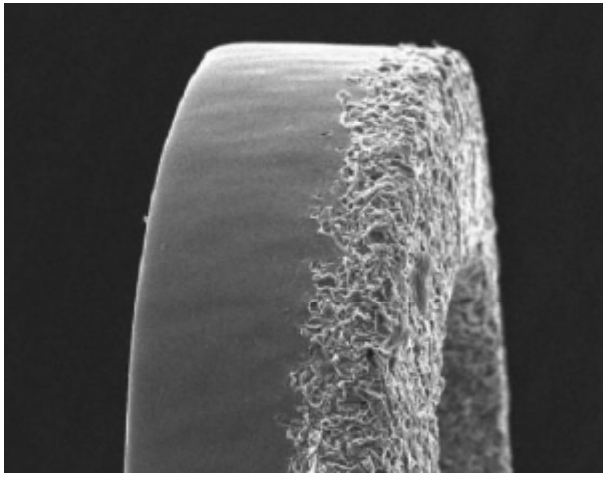

EXCELLENT Trial

1° EP: Target Vessel Failure (TVF)

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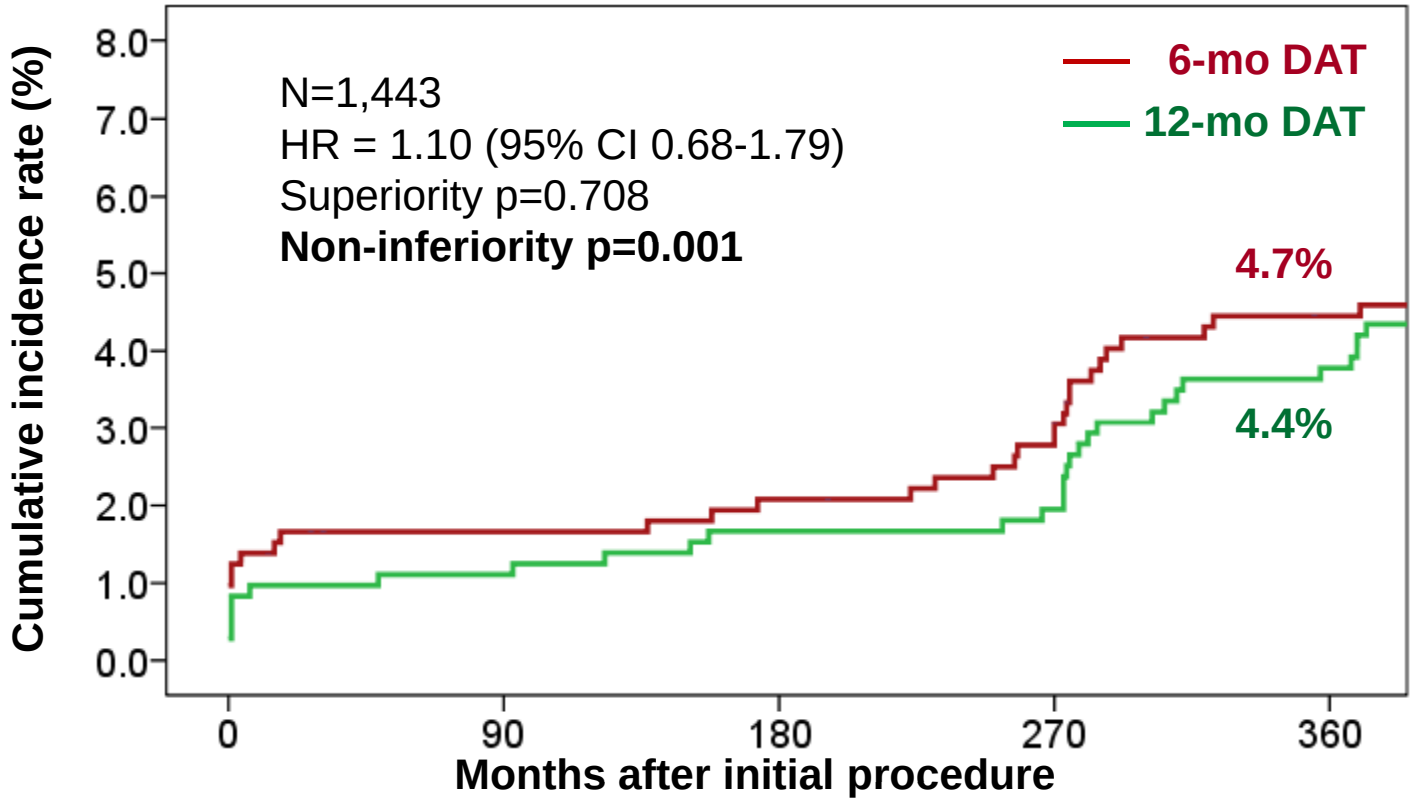

Patient Number at Risks

6-month	722	707	704	698	682
12-month	721	710	703	698	682

* DAT = dual antiplatelet therapy

EXCELLENT Trial

TVF in Stent Subgroups

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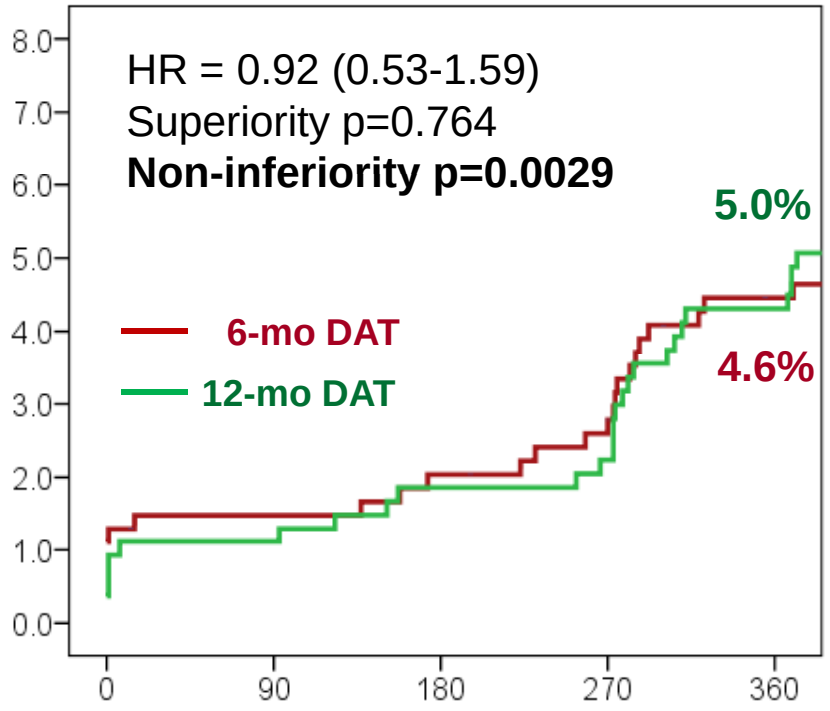
(Randomized to EES vs. SES in 3:1 fashion)

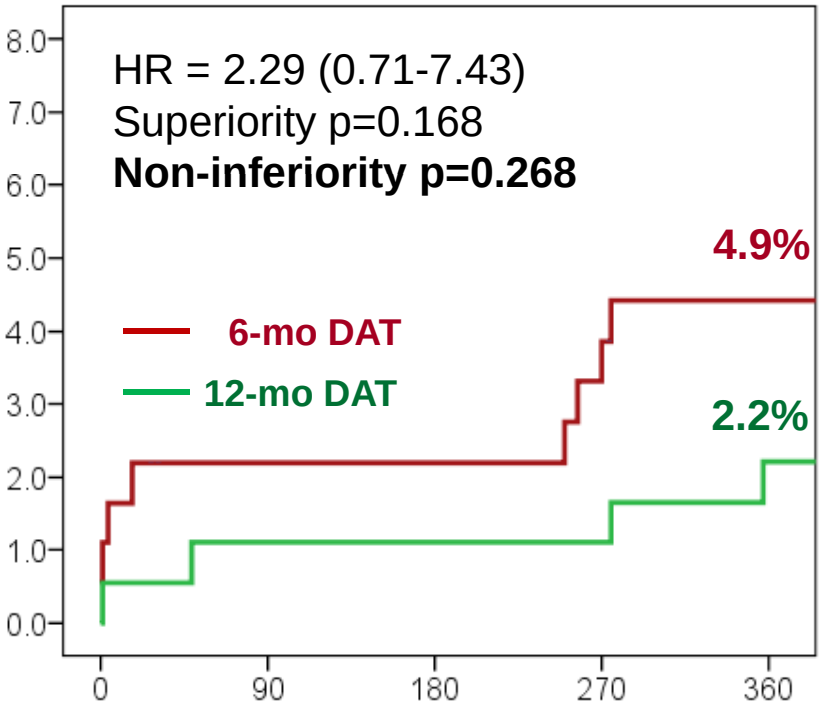
Everolimus-Eluting Stent



Patient Number at Risks

6-mo	540	531	528	524	511
12-mo	539	531	524	521	505

Sirolimus-Eluting Stent



Patient Number at Risks

182	176	176	174	171	
182	179	179	178	176	

Gwon HC, Circulation 2012

RESET Trial

E-ZES with 3 mo DAPT vs. Other DES with 12 mo DAPT

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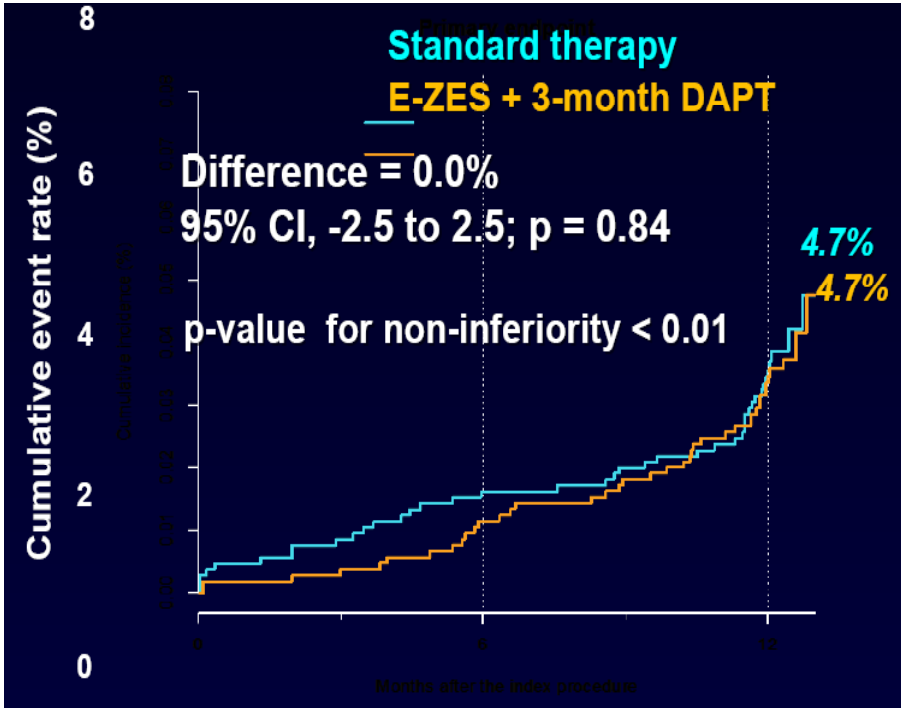
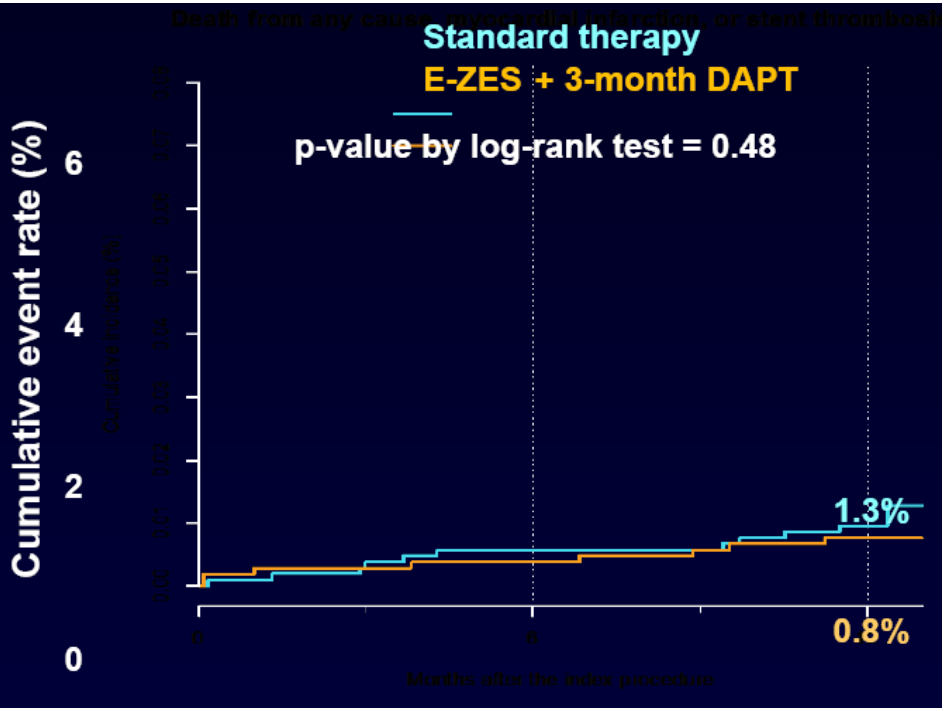
- N=2,117
- E-ZES+3-mo DAPT: 93±28 days (median 93 days)
- Standard therapy: 364±31 days (median 363 days)

1° EP: CV death, MI, ST, TVR, bleeding 1Y



Death, MI, Stent Thrombosis 1Y



Hong MK, ACC 2012

Summary and Conclusions

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- Second generation DESs seem to be safer than first generation DESs.
- Current evidences suggest that EES have the lowest rate of stent thrombosis compared to BMS as well as other DESs, which needs to be confirmed by a larger RCT data.
- EES should be regarded as the standard against which future design improvements are compared.
- I hope future DES development will focus on the shorter duration of DAPT after the procedure.