Metallic DES: Tomorrow's Technology

From Proof of Concept to Clinical Evidence, Bioabsorbable Polymer Technology is Preferred to Durable Polymer

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tct2014 In Partnership with the ACC

CARDIOVASCULAR RESEARCH FOUNDATION

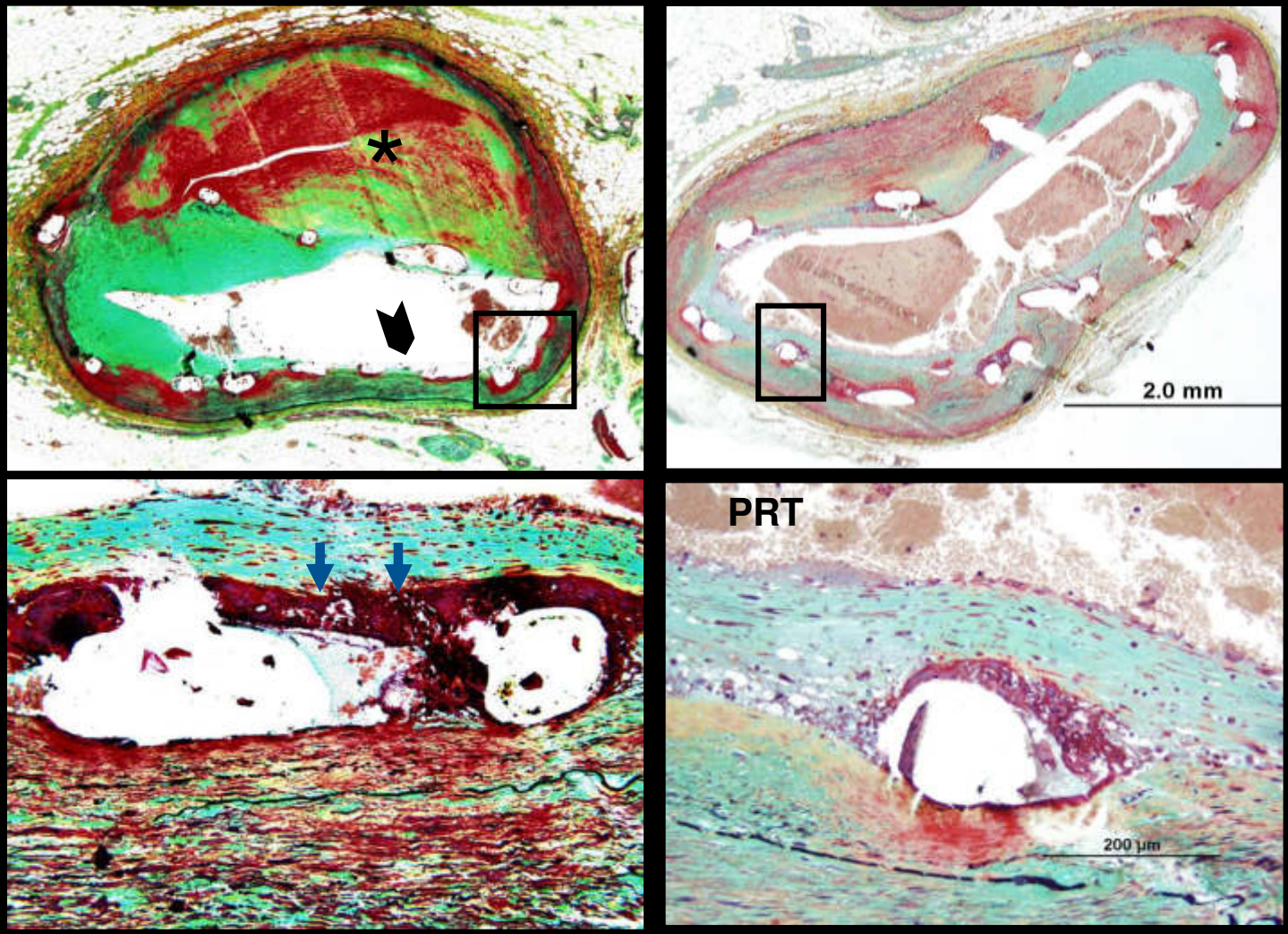
Disclosure Statement of Financial Interest

Robert A. Byrne, MB BCh PhD

Speakers fees:

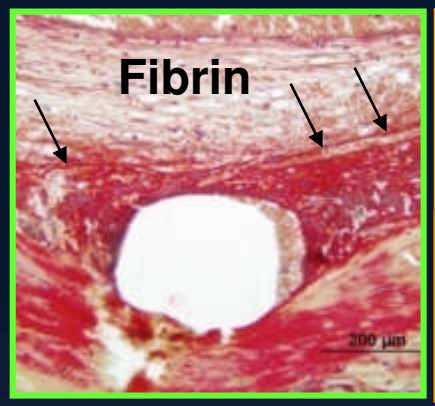
Biotronik, B. Braun Melsungen AG

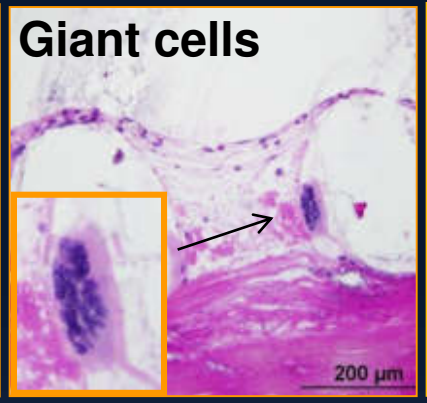
Delayed Arterial Healing After G1 DES

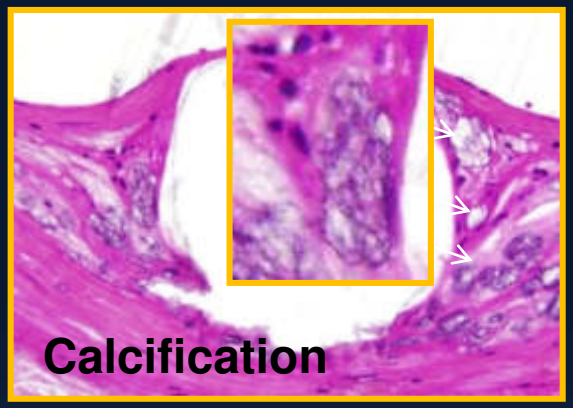


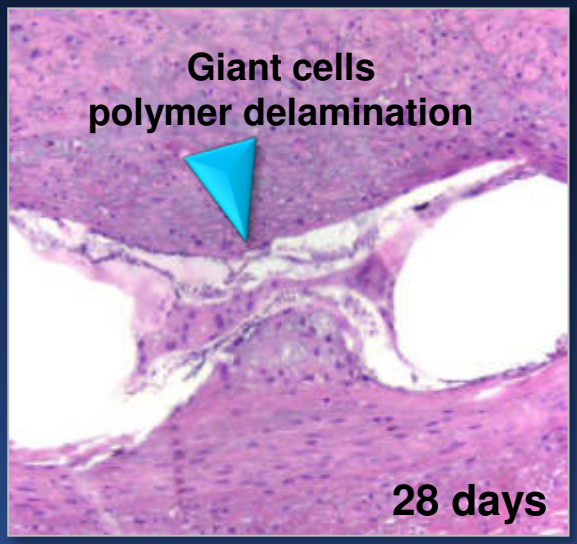
Byrne, Joner, Kastrati *Minerva Cardiol* 2009

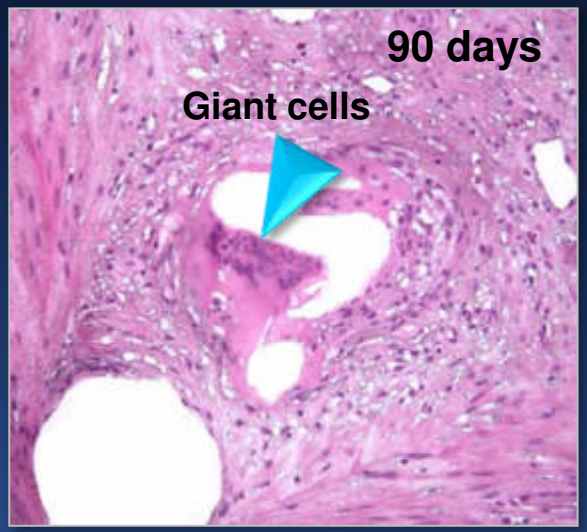
Durable Polymer Associated Inflammation

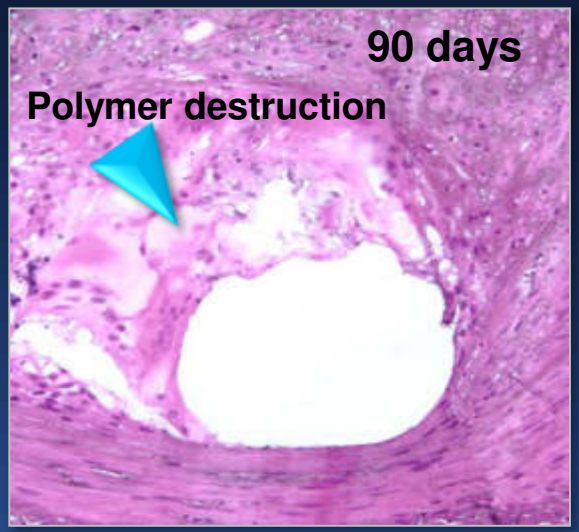










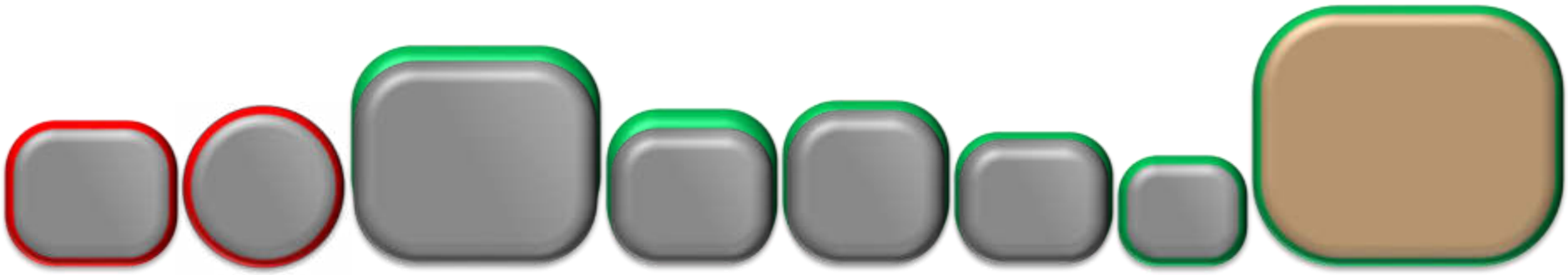


Inflammatory response to durable polymer coatings plays a central role in DAH

Overview of current stent designs

Strut and coating thickness in perspective

New Generation Durable Polymer Coated Stent		Bioabsorbable Polymer Coated Stent					Bioabsorbable Scaffold
Abbott/Boston	Medtronic	BIOSENSORS	Terumo	Translumina	Boston	BIOTRONIK	Abbott
Xience/Promus	**Resolute**	**BioMatrix**	**Ultimaster**	**Yukon Choice PC**	**Synergy**	**Orsiro**	**Absorb**
CoCr/PtCr-EES	CoNi-ZES	316L-BES	CoCr-SES	316L-SES	PtCr-EES	CoCr-SES	PLLA-EES



Strut thickness

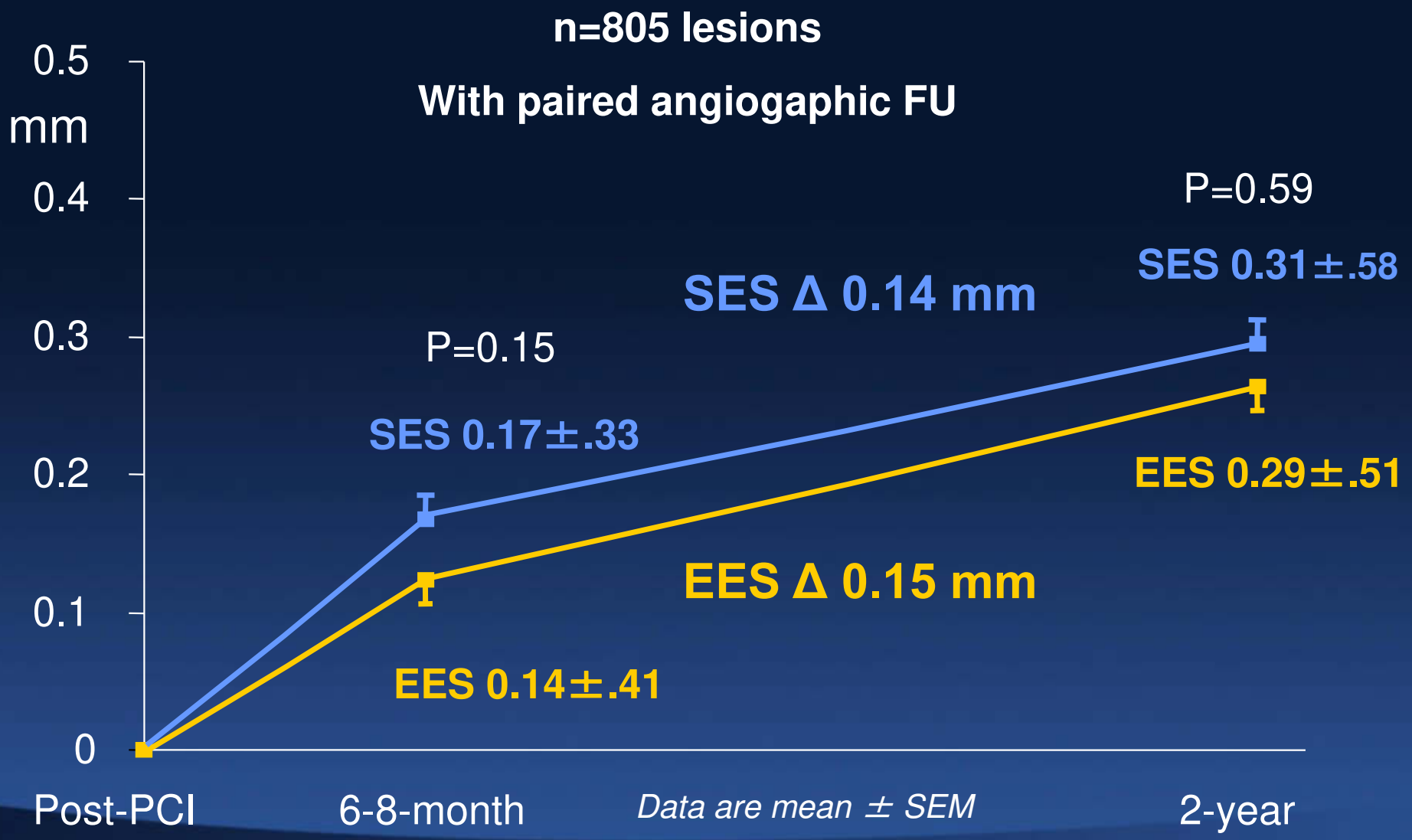
81 µm	91 µm	120 µm	80 µm	87 µm	74 µm	60 µm	150 µm

Polymer coating

Circumferential 7-8 µm/side	Circumferential 6 µm/side	Abluminal 10 µm	Abluminal 15 µm	Abluminal 5 µm	Abluminal 4 µm	Circumferential 4-7 µm/side	Circumferential 3 µm/side

Sources: 1: GG Stefanini, M Taniwaki, S Windecker, Coronary stents: novel development, Heart 2013; 2: IT Meredith, Scientific symposium, TCT 2013

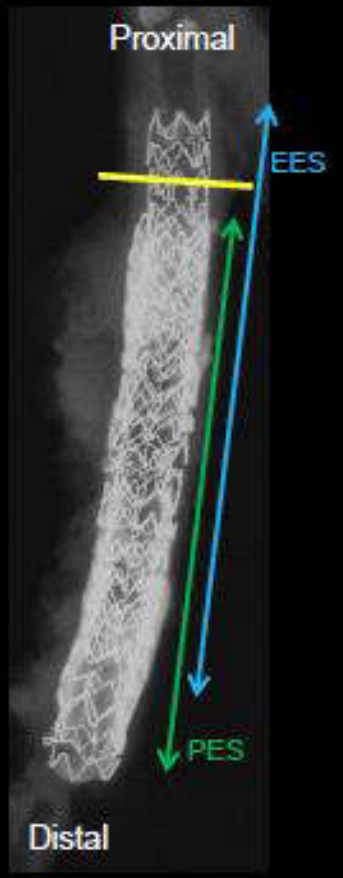
ISAR-TEST 4: Late Lumen Loss to 2 Years

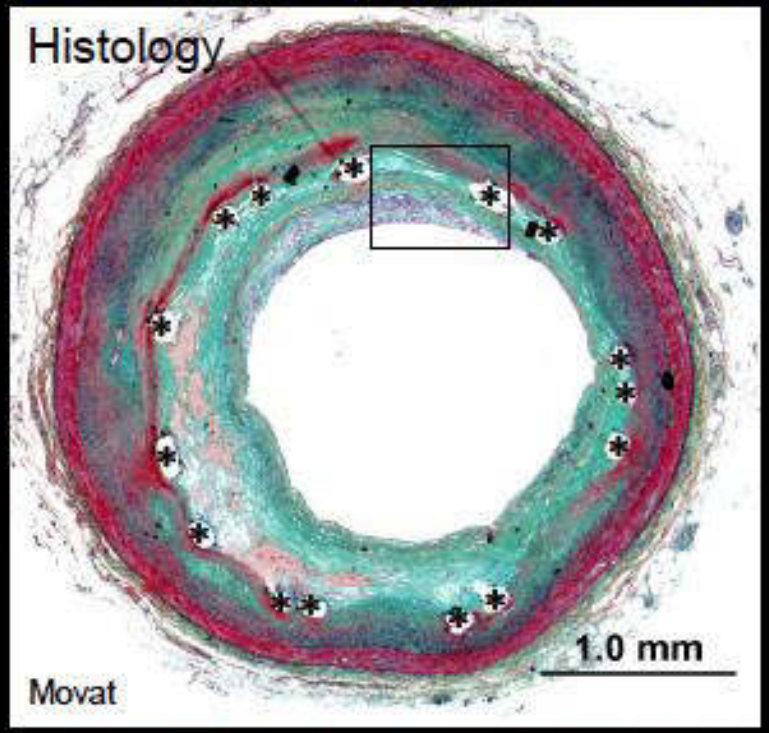


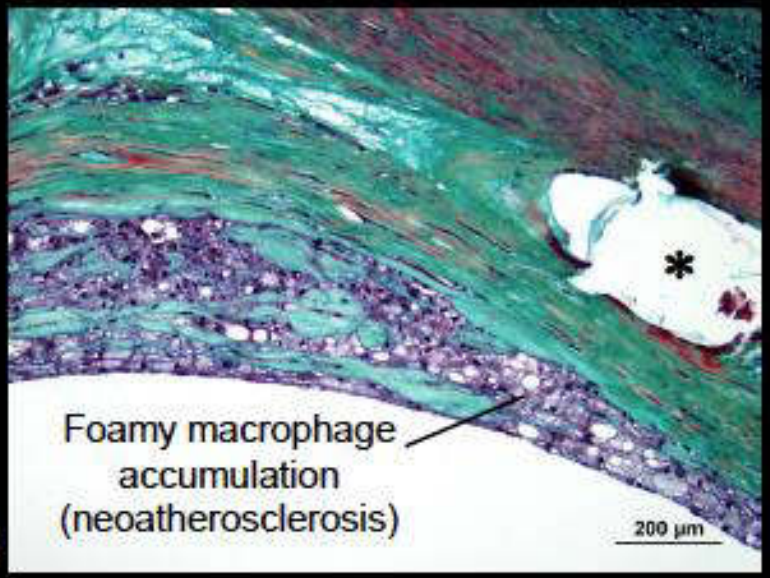
Byrne et al. *JACC* 2011

Neoatherosclerosis within the EES

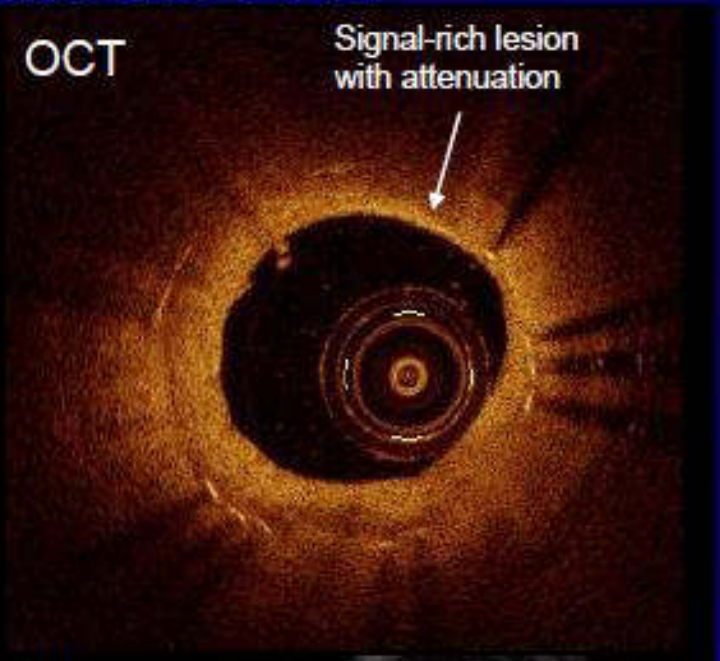
49M, EES within the PES in mid LAD

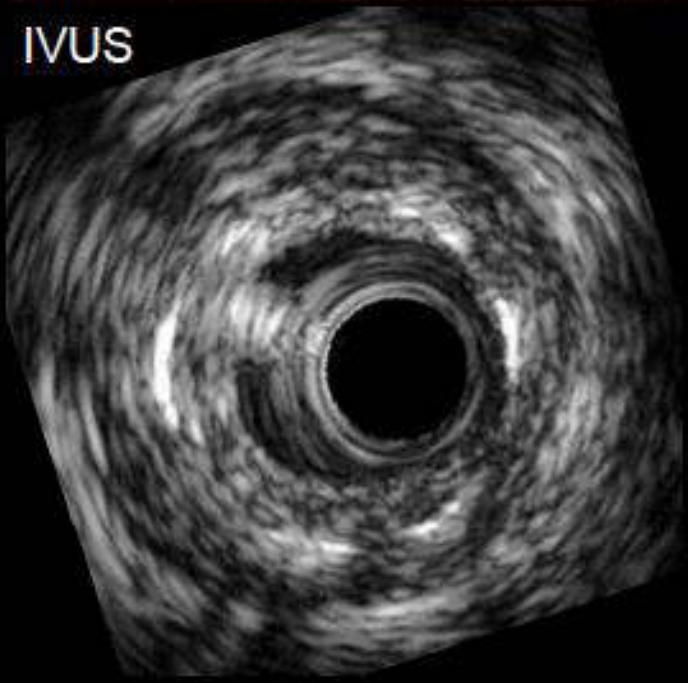






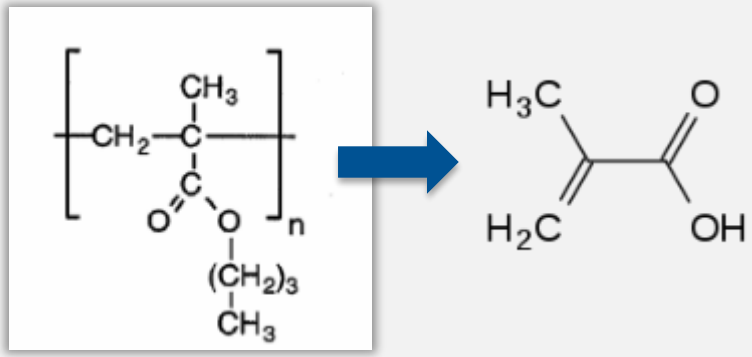
* Stent strut



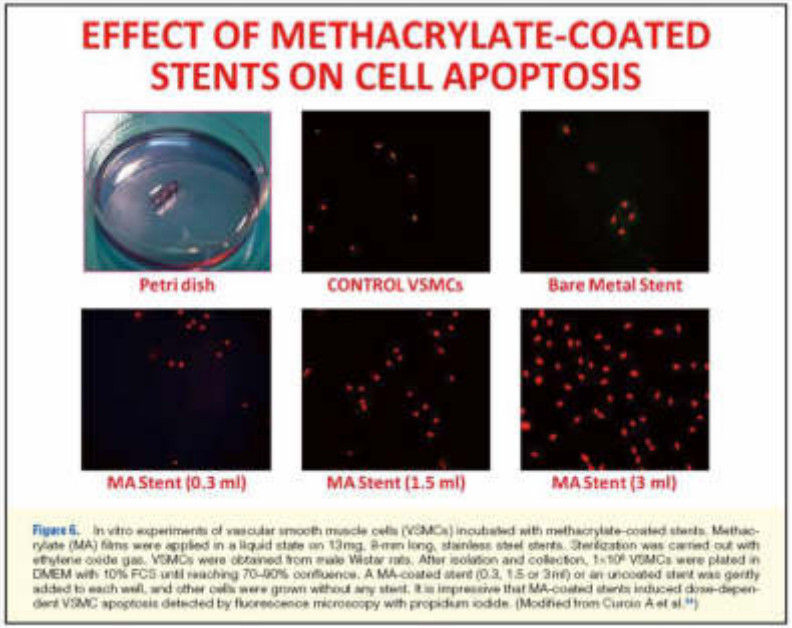


Polymer Coatings and Arterial Healing

- **Most clinically effective durable polymer DES coatings contain methacrylate polymer e.g. PBMA (Cypher SES, Xience EES, Resolute ZES)***



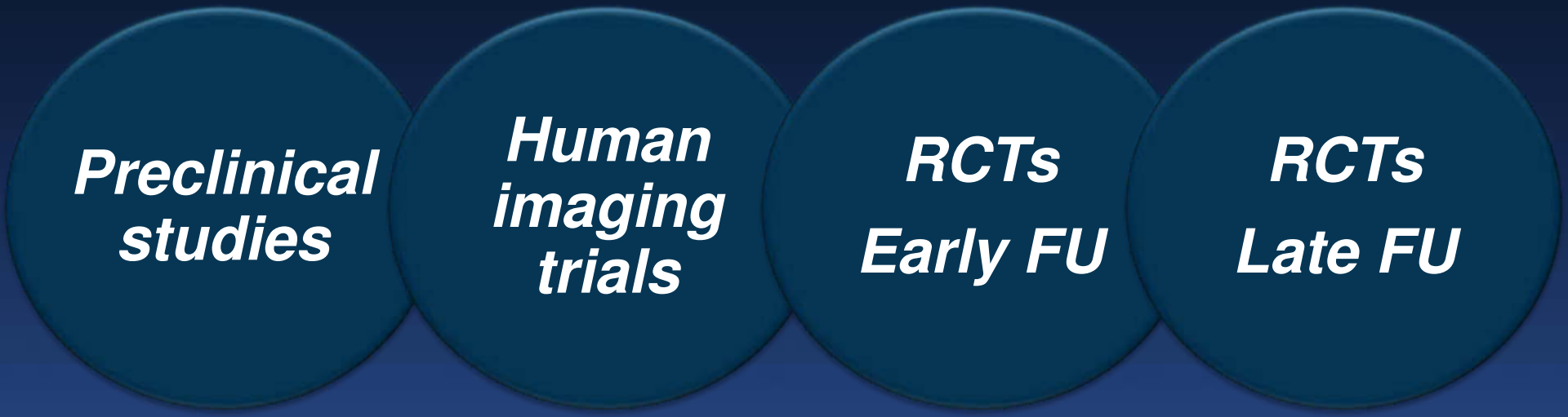
- **PBMA degrades to the monomer methacrylic acid which has proven cellular toxic effects#**



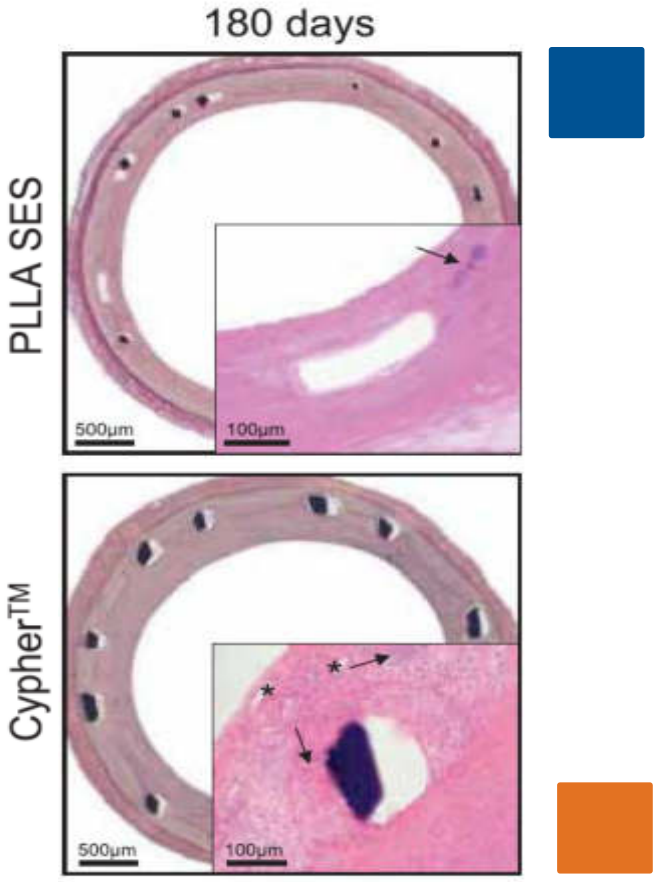
*Cypher, Xience, Resolute Product information; # Curcio et al. *Circulation Journal* 2011

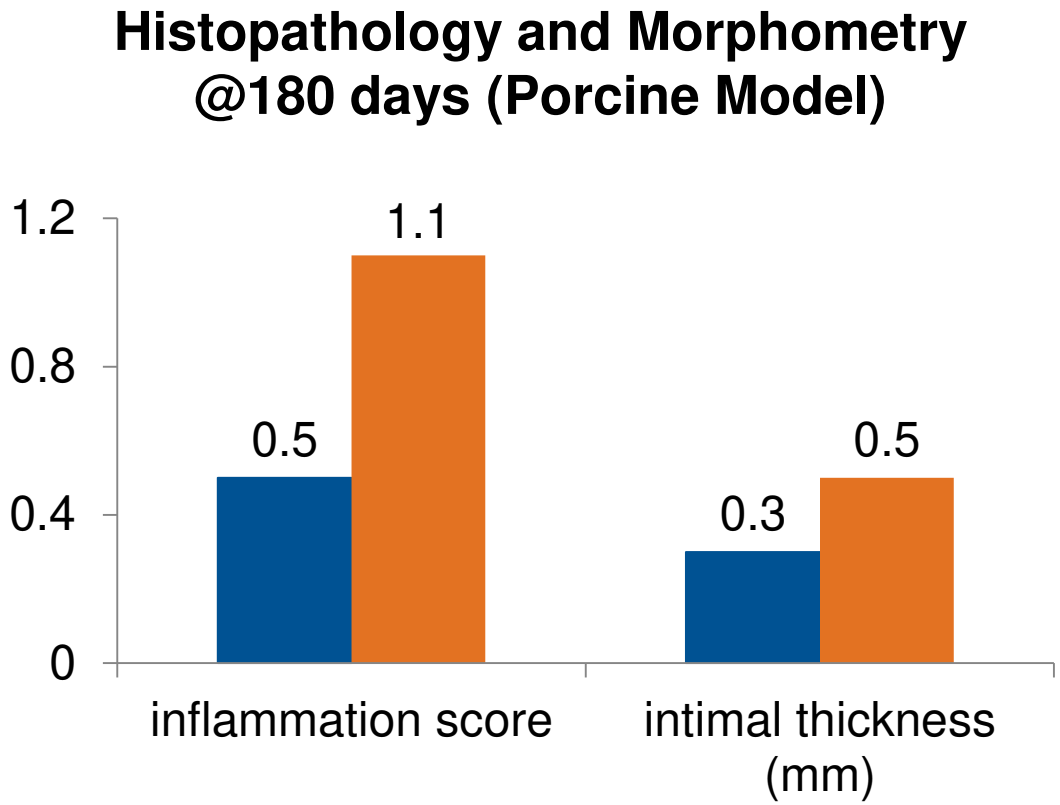
Bioabsorbable polymer DES

Proof-of-concept chain of investigation



Reuced inflammatory reaction with permanent polymers in porcine model





Koppara et al, Thromb Haemost 2012

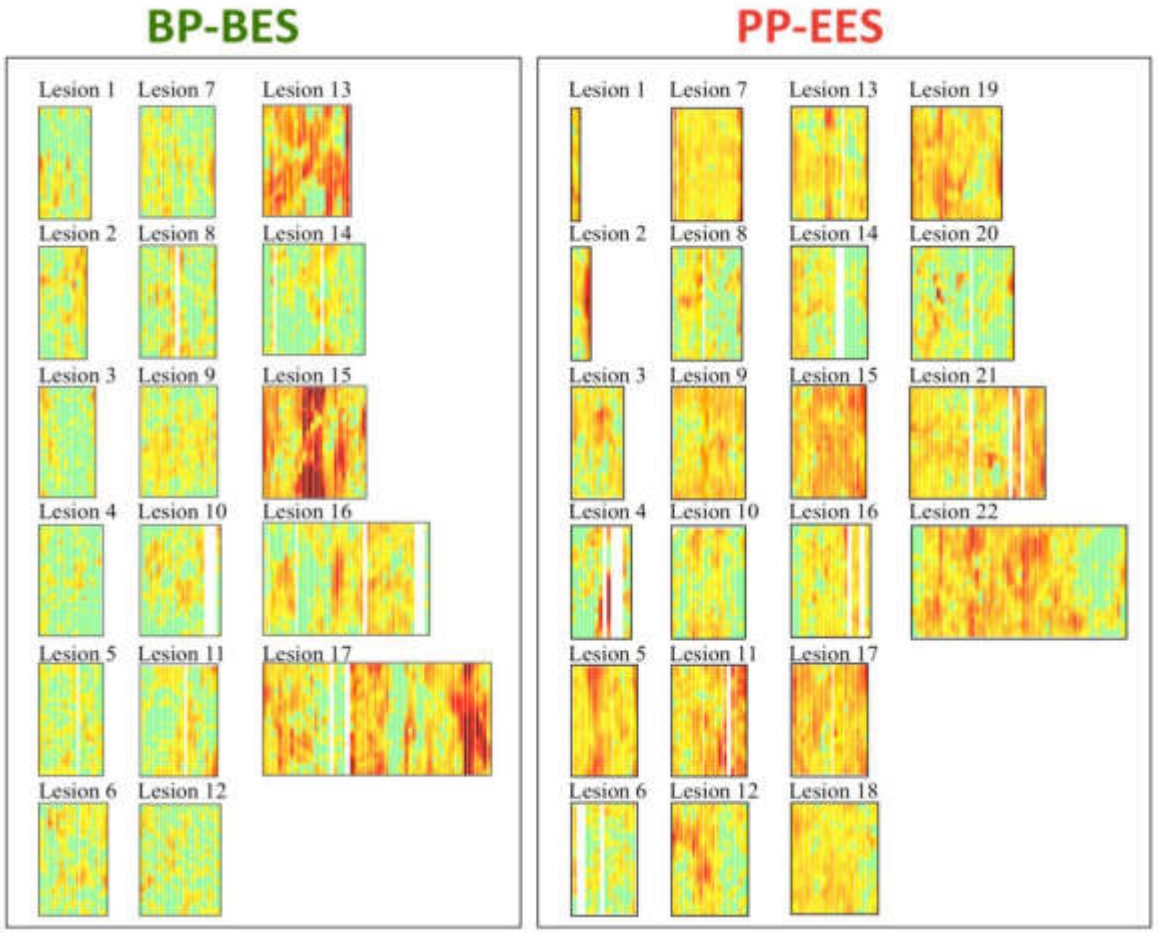
Bioabsorbable polymer DES

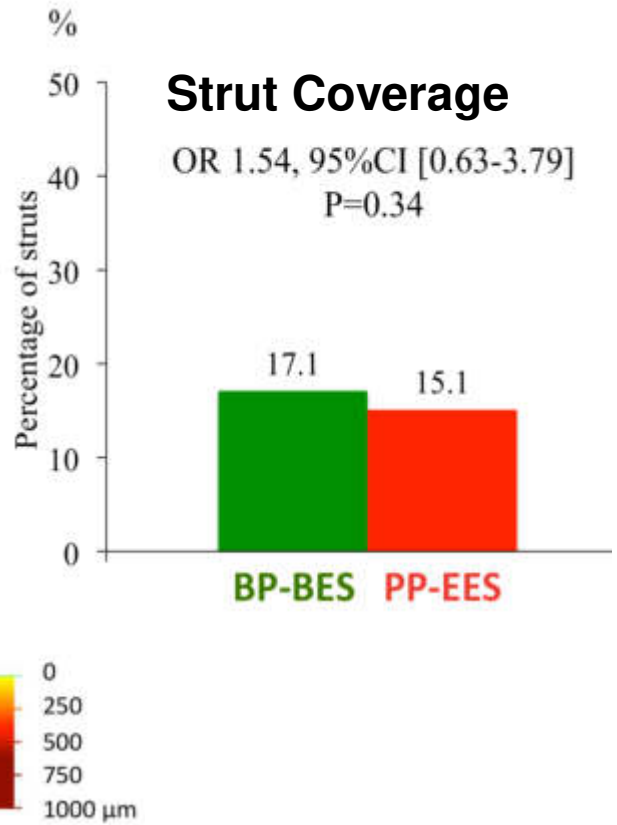
Proof-of-concept chain of investigation

ISAR-TEST 6 OCT

Nobori BES vs. **Xience EES**

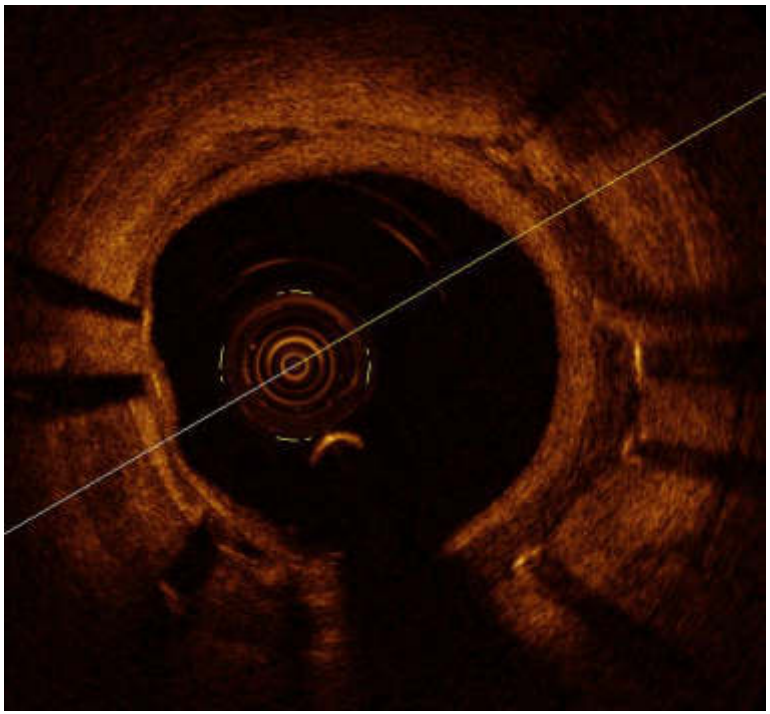
OCT at 6-8 m; n = 39

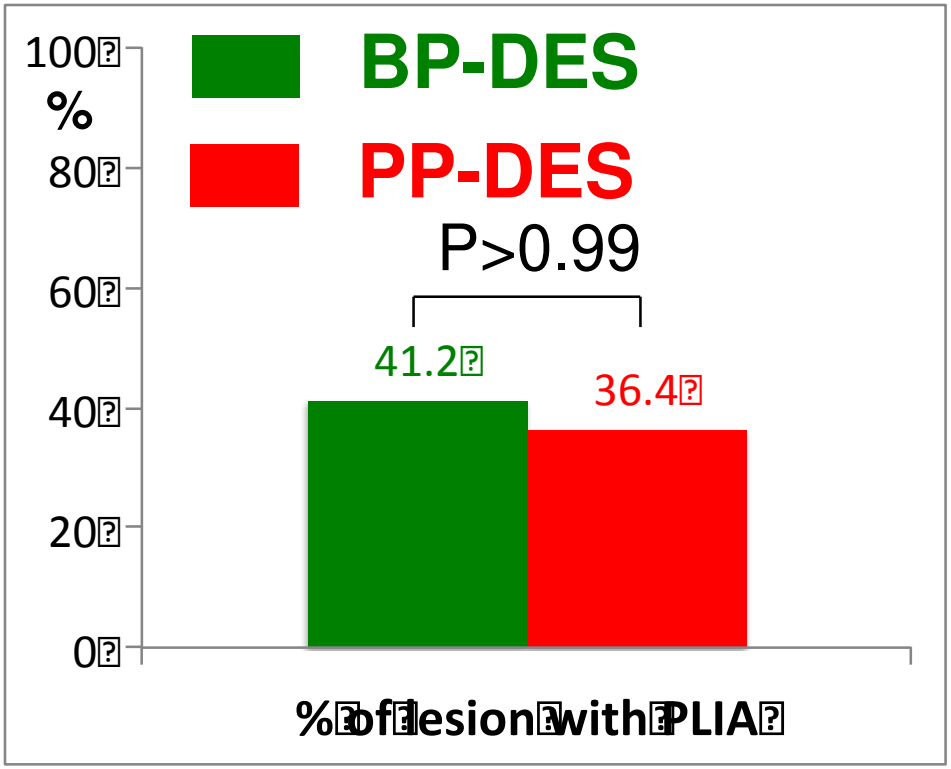




Tada et al. *Int J Cardiovasc Imaging* 2014

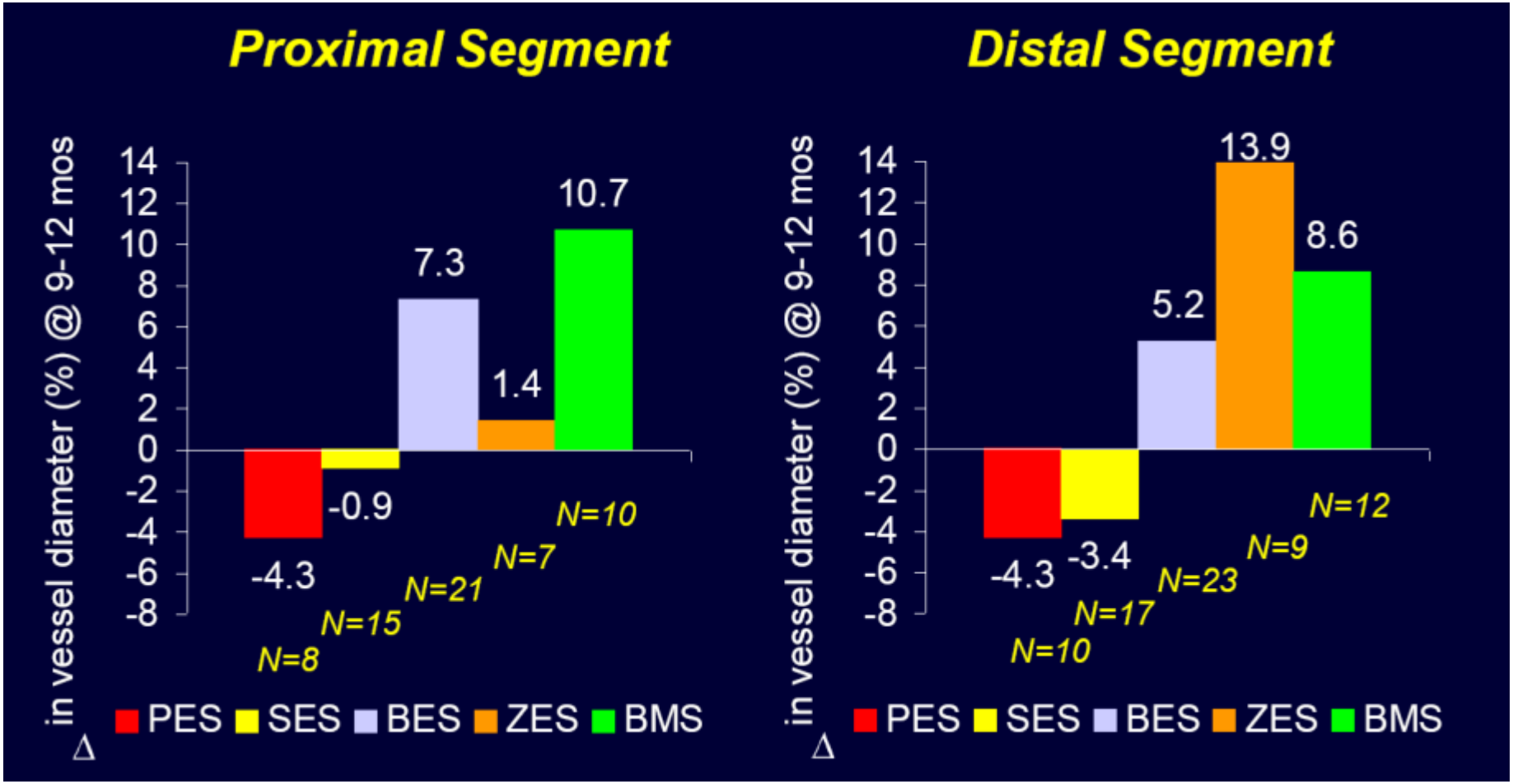
ISAR-TEST 6 OCT: Peri-stent Low Intensity Area (PLIA)





Tada et al. *Int J Cardiovasc Imaging* 2014

Improved Vasomotor Function with BP DES



Hamilos et al. *Circ Cardiovasc Interv* 2008

Bioabsorbable polymer DES

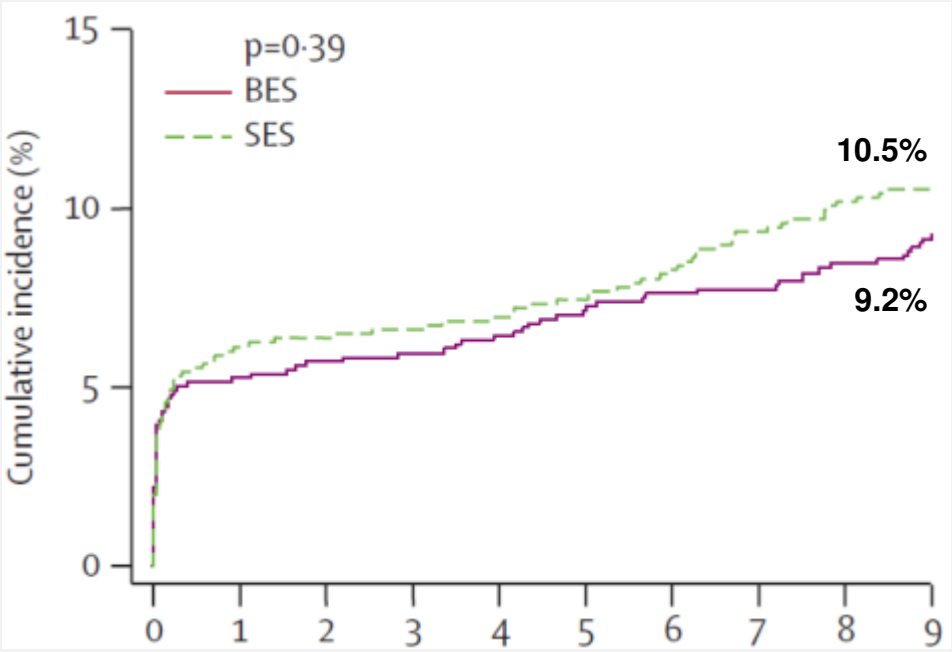
Proof-of-concept chain of investigation

LEADERS

1707 pts

- **BioMatrix (BP Biolimus)**
- **Cypher (PP Sirolimus)**

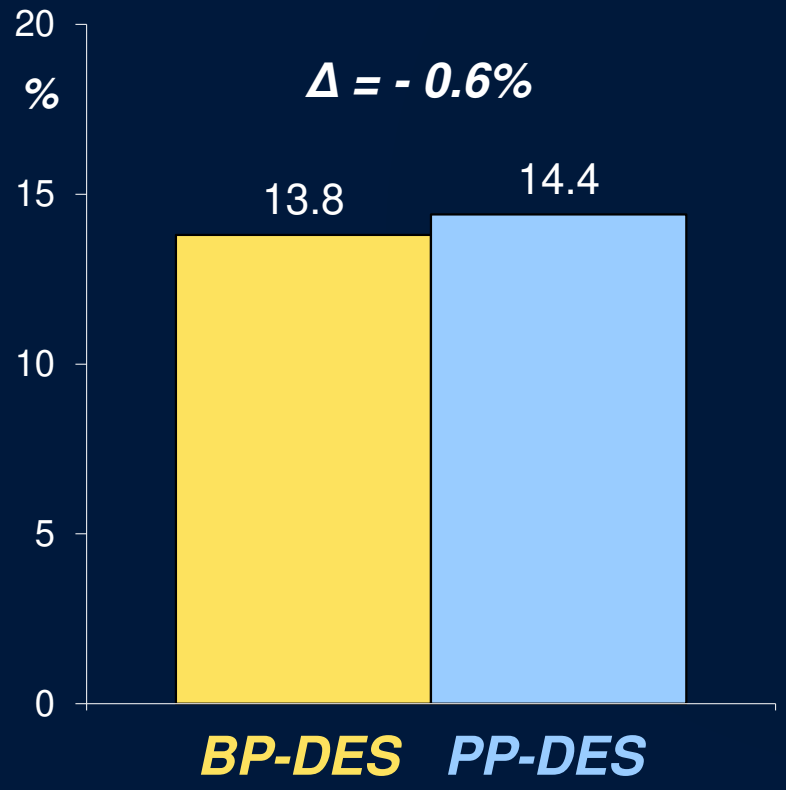
Cardiac death, MI, Reintervention

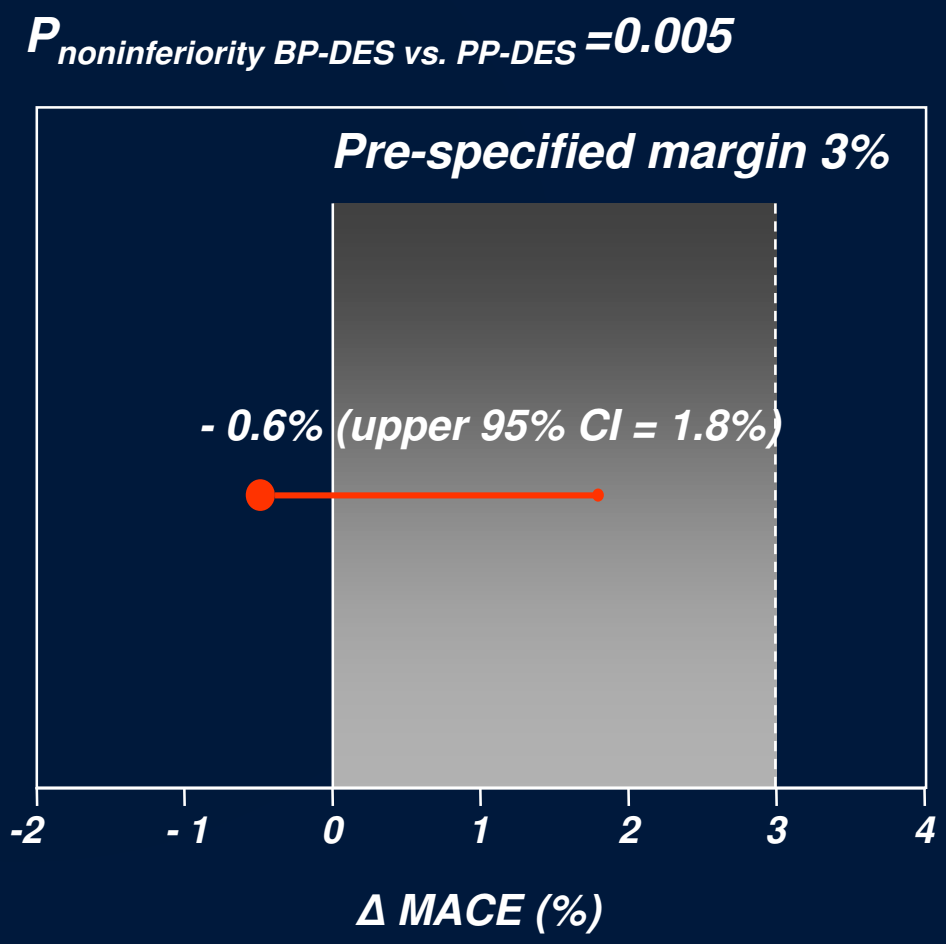


Windecker et al., Lancet 2008

ISAR-TEST 4: Primary Endpoint at 1 Year

Cardiac death or TV-related MI or TLR -





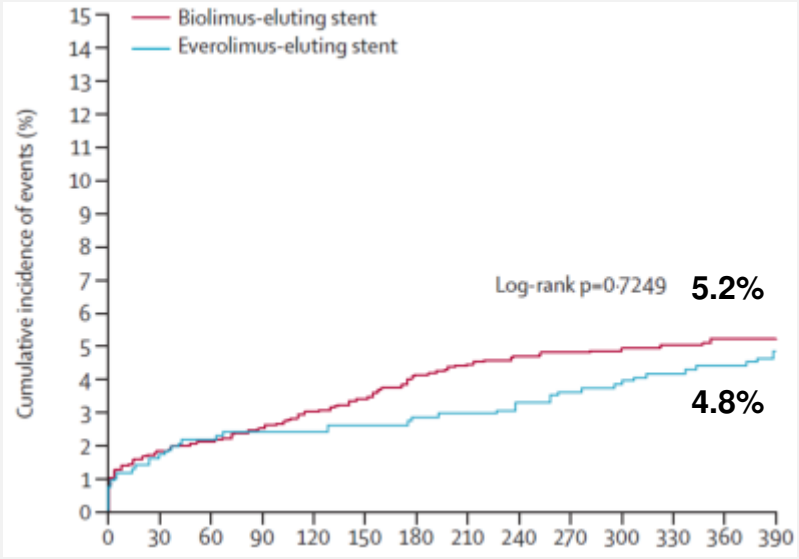
Byrne et al. *Eur Heart J* 2009

COMPARE II and NEXT

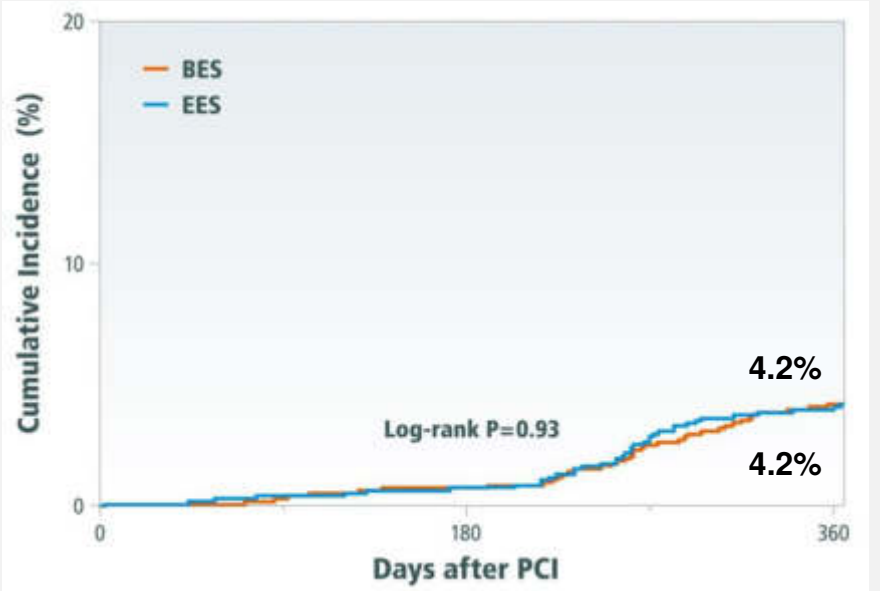
Nobori (BP Biolimus)

Xience (PP Everolimus)

Cardiac death, MI, Reintervention



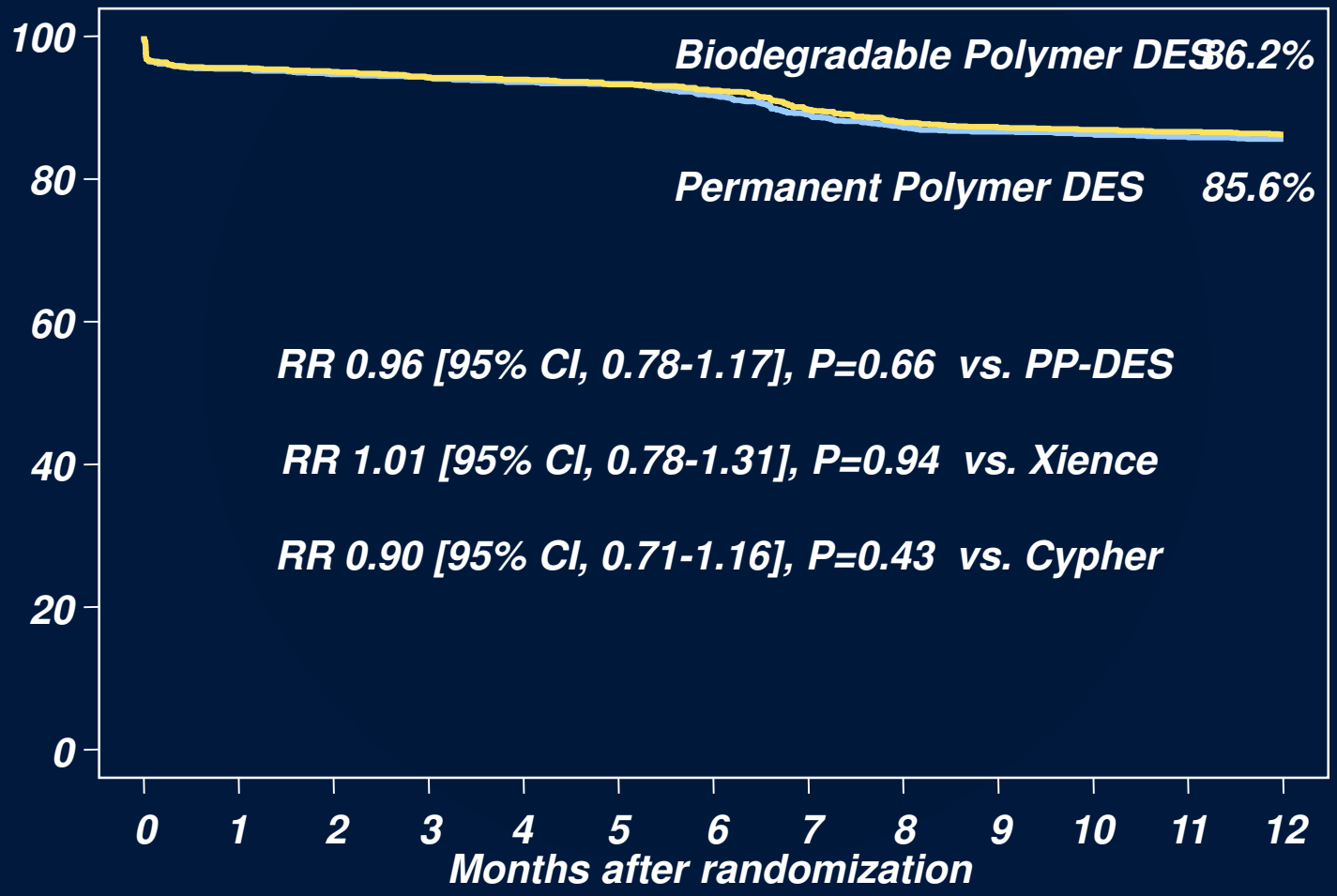
Reintervention (TLR)



Smits et al., Lancet 2013; Natsuaki et al., JACC 2013

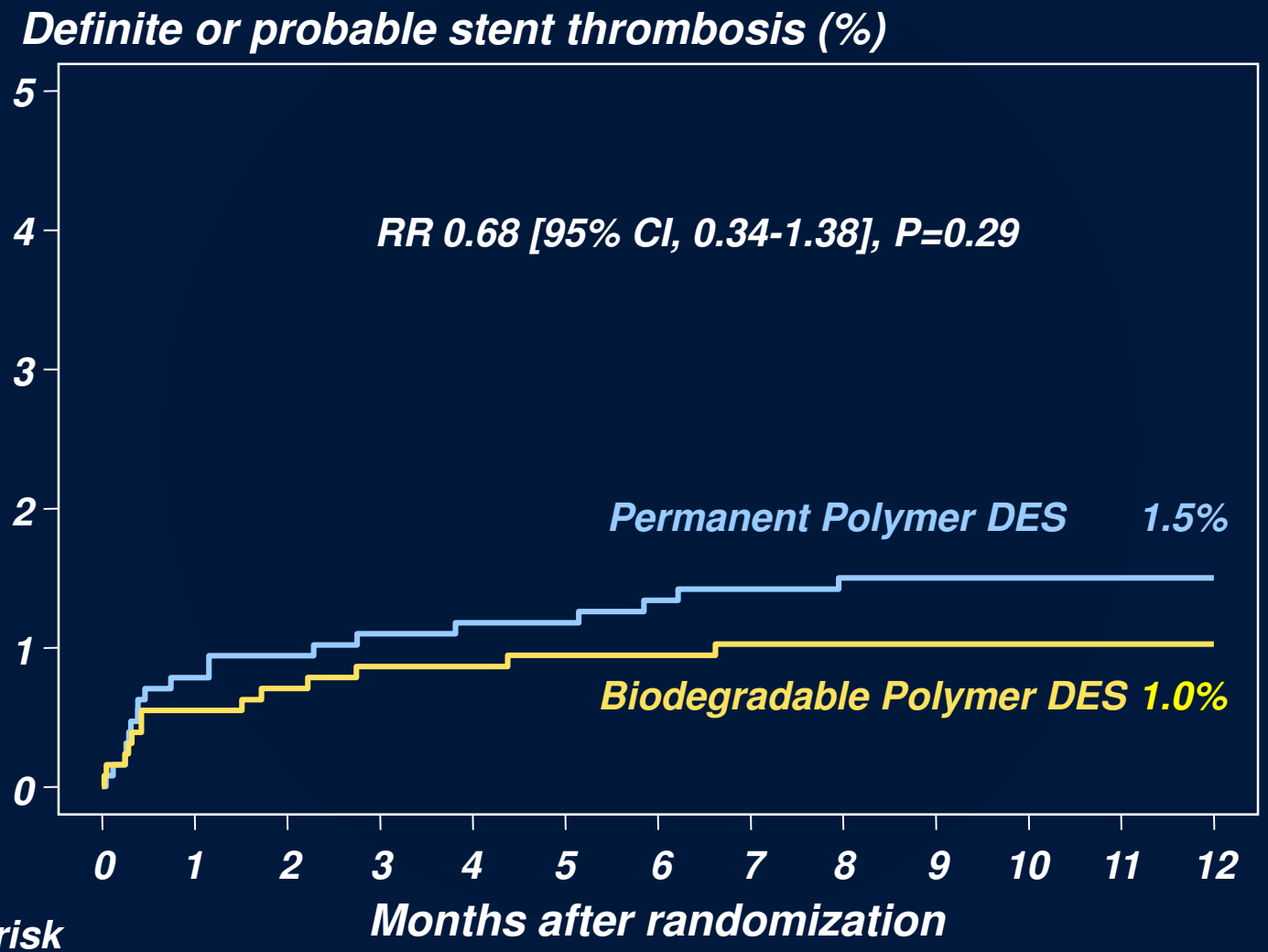
ISAR-TEST 4: Primary Endpoint at 1 Year

Survival free of cardiac death, MI related to target vessel or TLR (%)



Byrne et al. *Eur Heart J* 2009

ISAR-TEST 4: Stent thrombosis at 1 Year

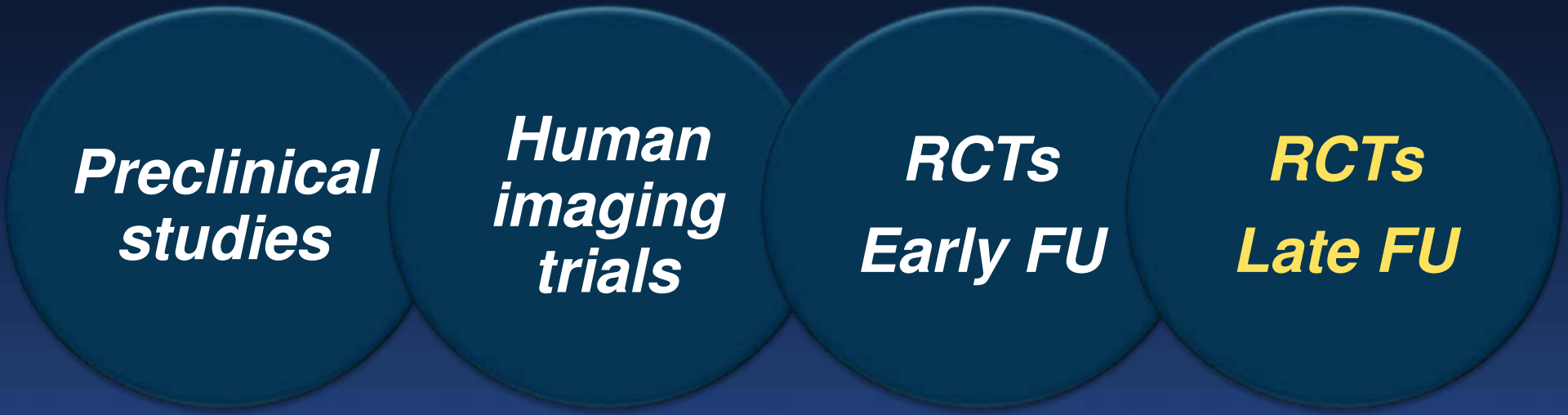


Patients at risk

BP-DES	1299	1256	1243	1236	1221	1213	1199
PP-DES	1304	1254	1240	1225	1204	1193	1189

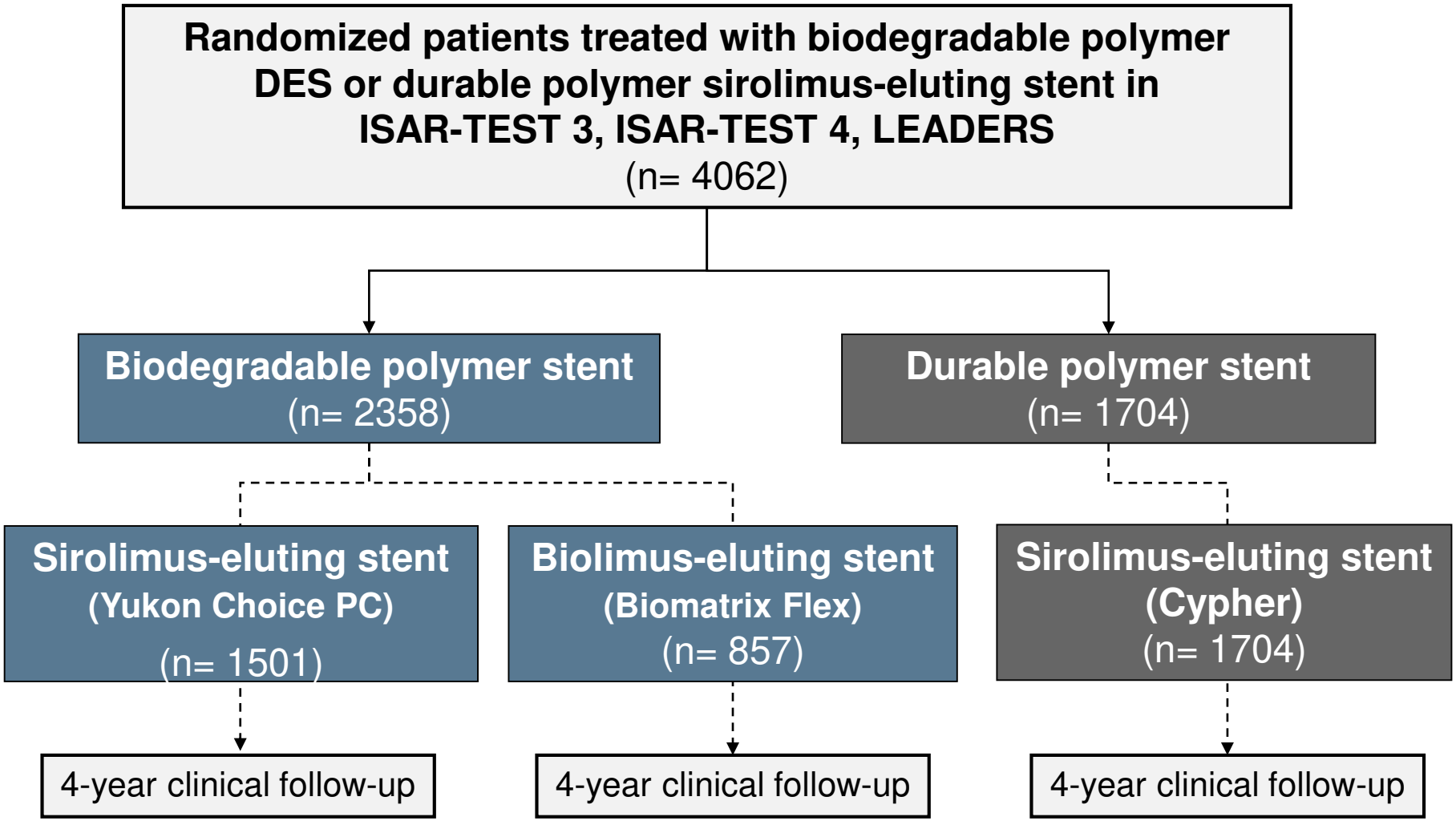
Bioabsorbable polymer DES

Proof-of-concept chain of investigation



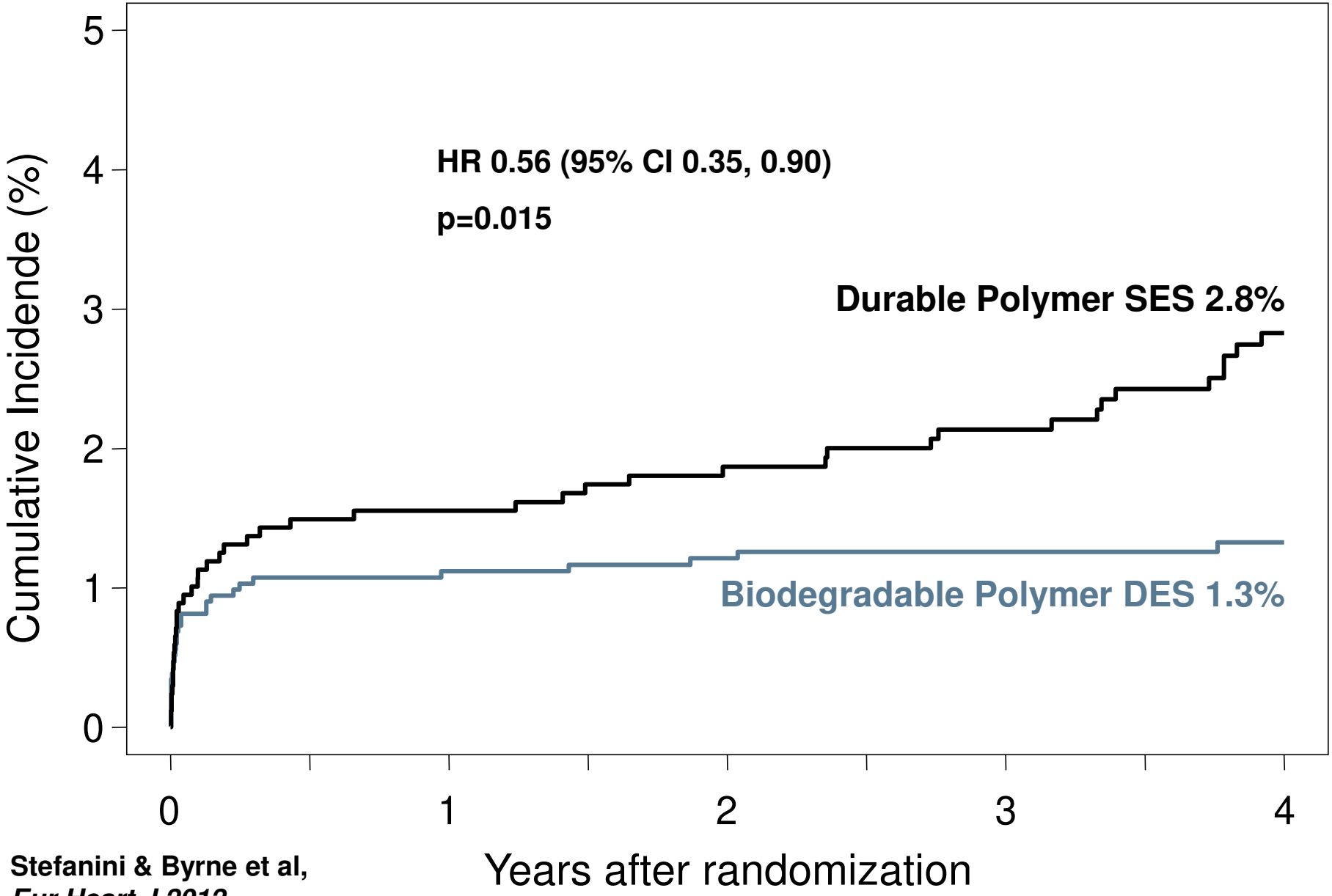
ACC Featured Clinical Study 2012

Technische Universität München



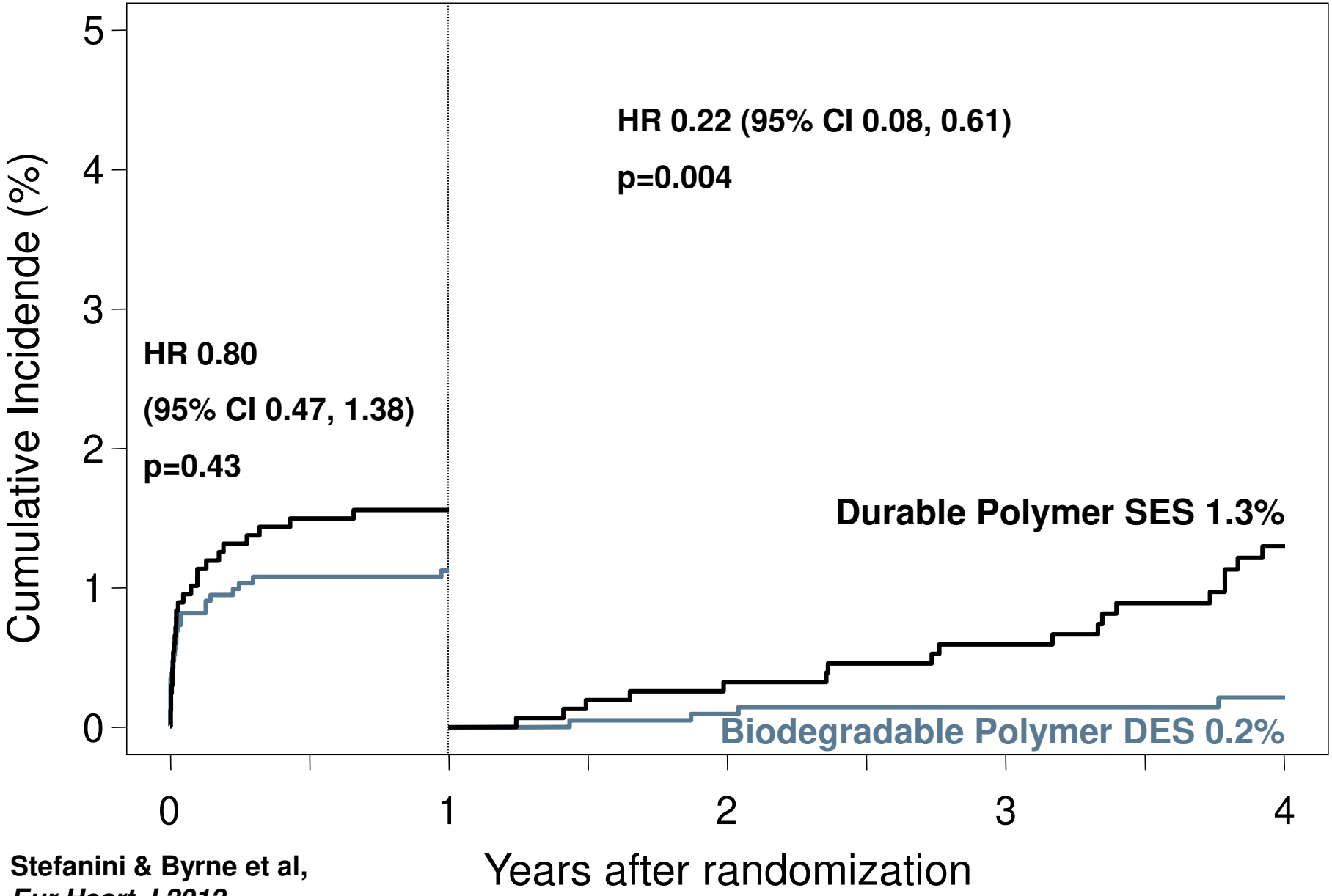
Stefanini, Byrne et al. Eur Heart J 2012

Definite Stent Thrombosis



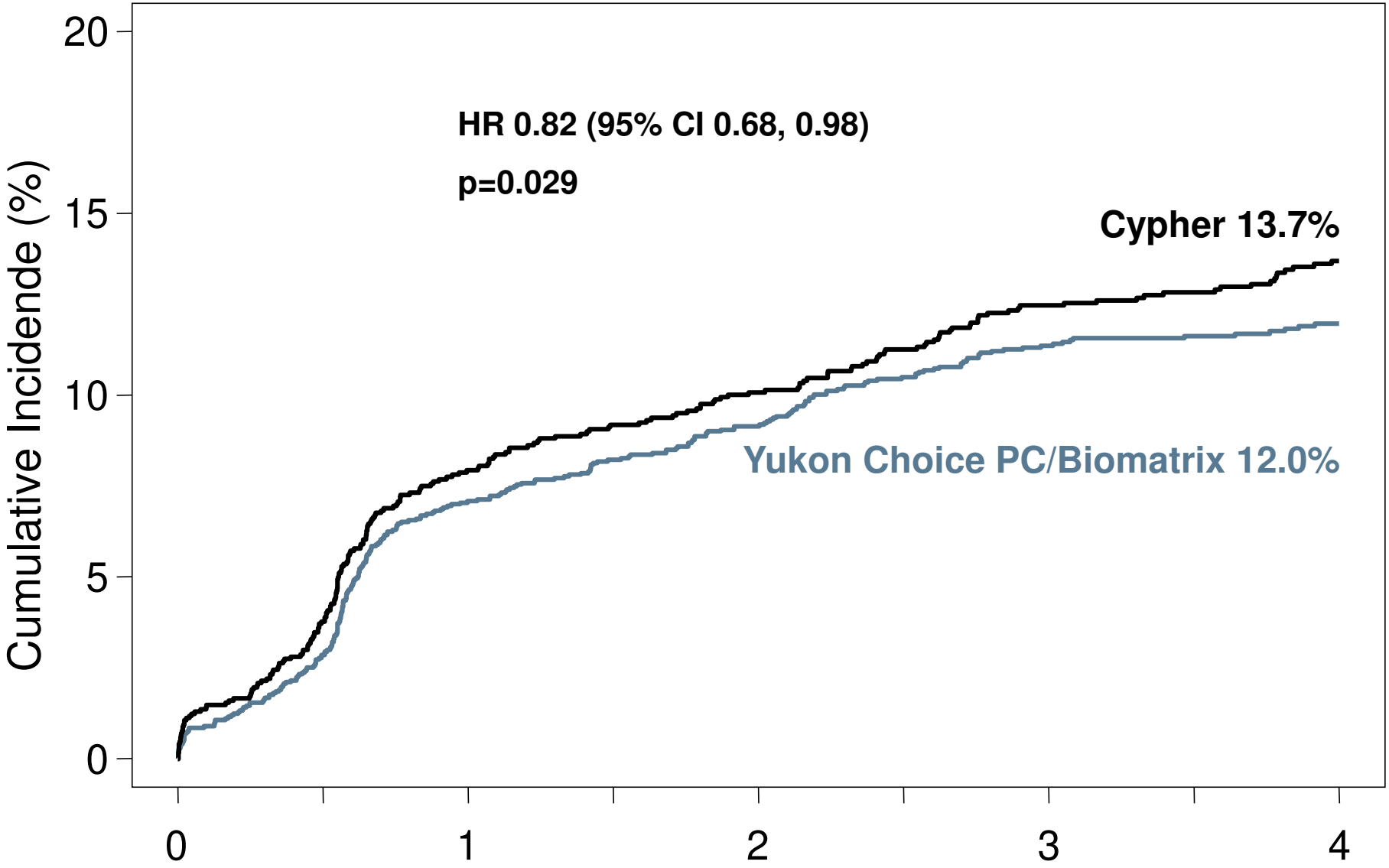
Stefanini & Byrne et al,
Eur Heart J 2012

Definite Stent Thrombosis



Stefanini & Byrne et al,
Eur Heart J 2012

Target Lesion Revascularization



Stefanini & Byrne et al,
***Eur Heart J* 2012**

Limitations of data

…cause for concern?

Bioabsorbable Polymer vs. Durable Polymer DES

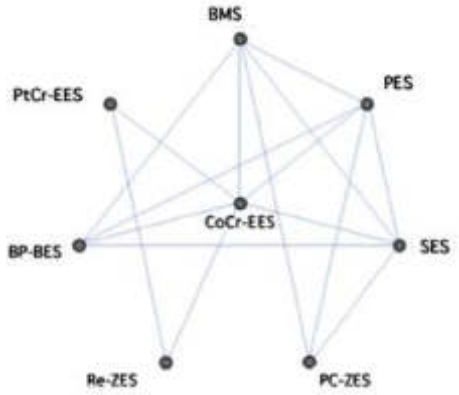
CLINICAL RESEARCH — Interventional Cardiology

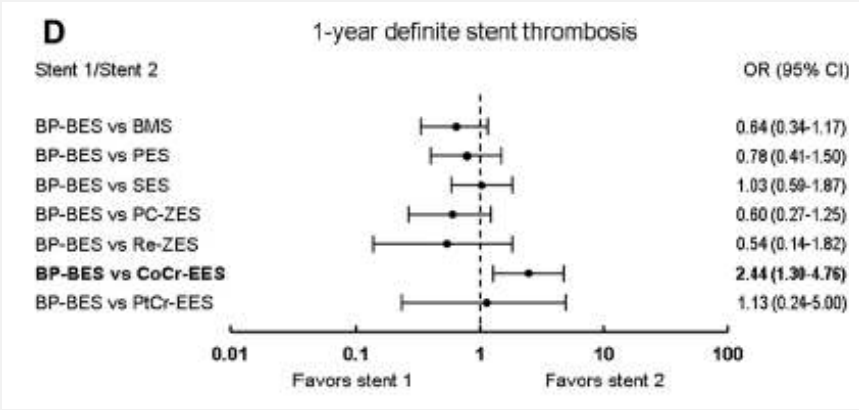
Clinical Outcomes With Bioabsorbable Polymer- Versus Durable Polymer-Based Drug-Eluting and Bare-Metal Stents

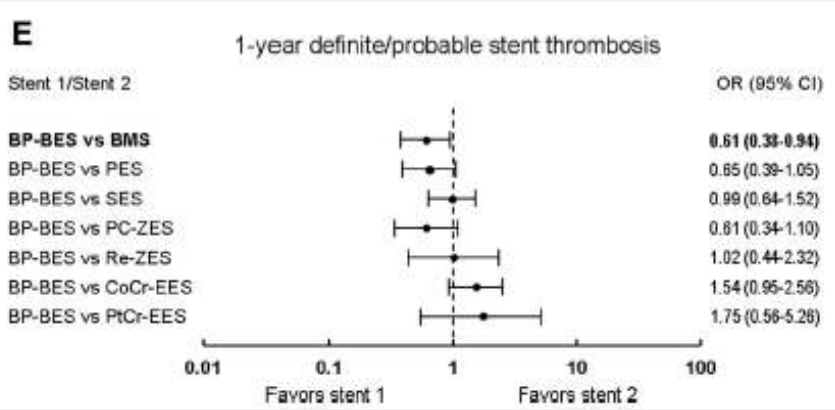
Evidence From a Comprehensive Network Meta-Analysis

Tullio Palmerini, MD,* Giuseppe Biondi-Zoccai, MD,† Diego Della Riva, MD,* Andrea Mariani, MD,* Manel Sabaté, MD,‡ Pieter C. Smits, MD,§ Christoph Kaiser, MD,‖ Fabrizio D'Ascenzo, MD,¶ Giacomo Frati, MD,†# Massimo Mancone, MD,† Philippe Genereux, MD,**†† Gregg W. Stone, MD**

Bologna, Latina, Turin, and Pozzilli, Italy; Barcelona, Spain; Rotterdam, the Netherlands; Basel, Switzerland; New York, New York; and Montreal, Quebec, Canada

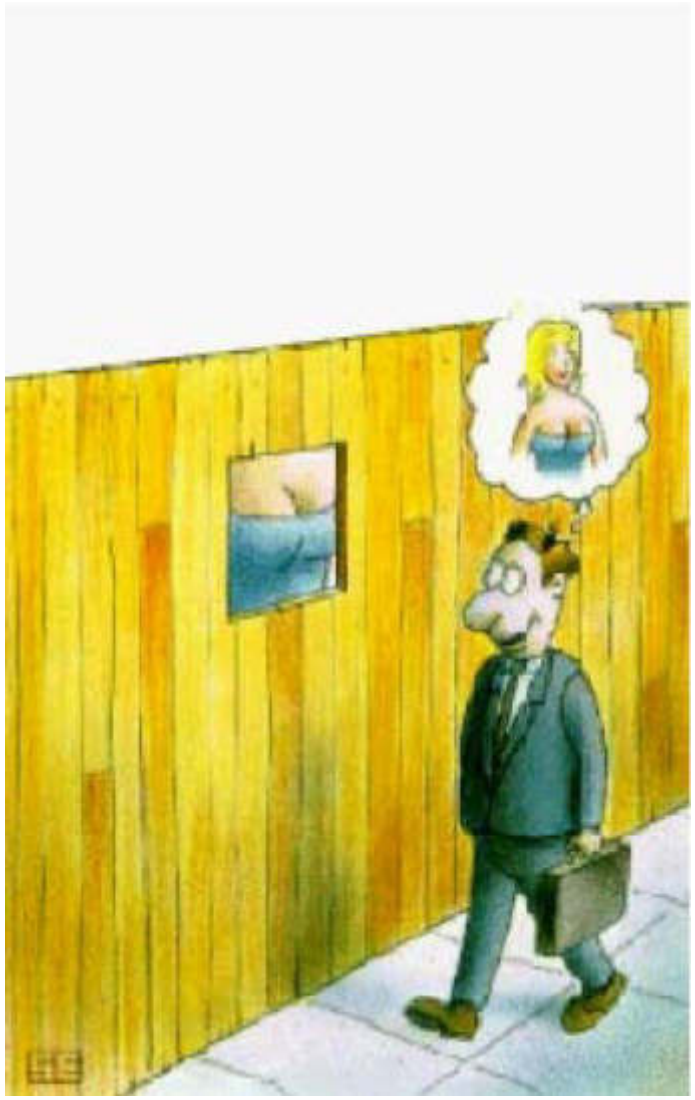






Network Meta-Analysis…

Fun to look at…



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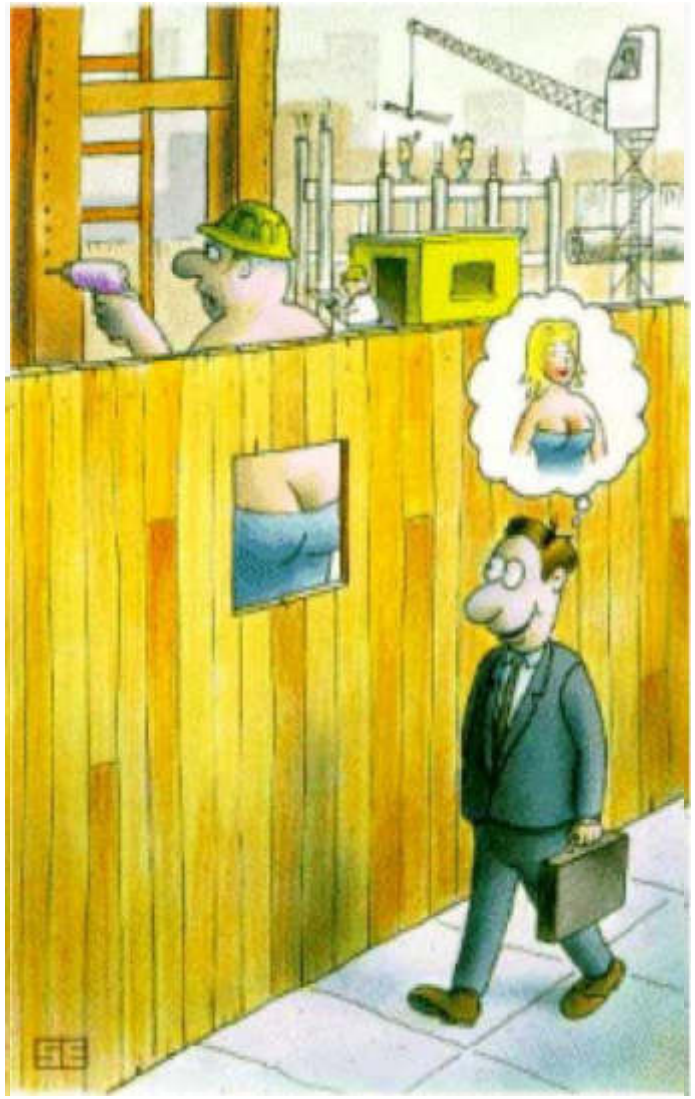
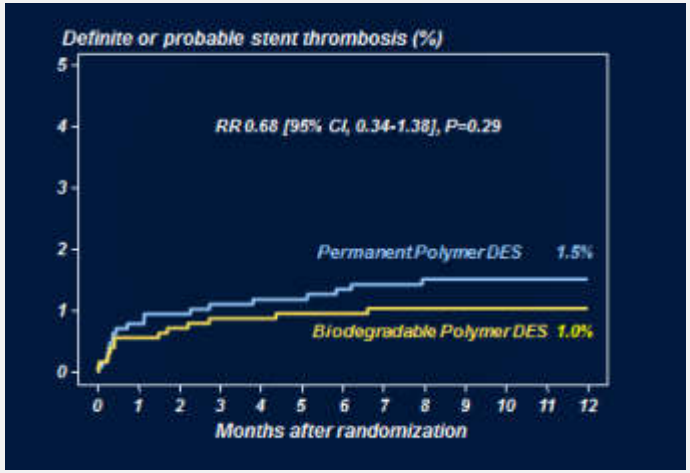


…but interpret with caution!

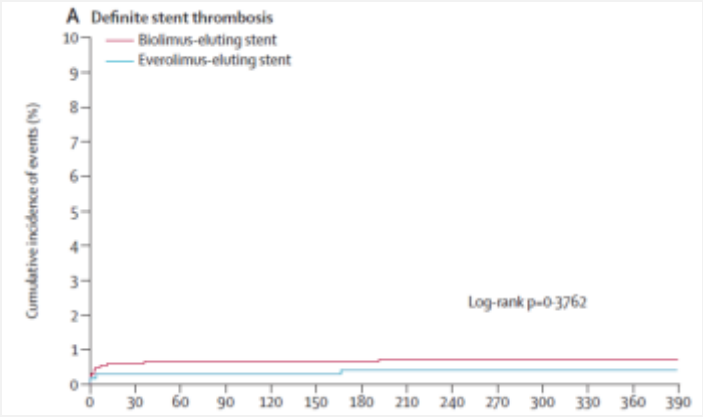
Bioabsorbable Polymer vs. Durable Polymer DES

Stent Thrombosis: Trials with direct comparison vs. EES

ISAR-TEST 4



COMPARE II



NEXT

Definite stent thrombosis				
All patients	5 (0.31)	3 (0.19)	1.67 (0.41-8.14)	.48
Acute (0-1 d)	0	1 (0.06)		
Subacute (2-30 d)	2 (0.12)	0		
Late (31-365 d)	2 (0.12)	0		
Very late (>365 d)	1 (0.07)	2 (0.13)		
Stent thrombosis				
Possible	22 (1.4)	18 (1.1)	1.22 (0.66-2.31)	.53
Definite or probable	5 (0.31)	3 (0.19)	1.67 (0.41-8.14)	.48
Definite, probable, or possible	27 (1.7)	21 (1.3)	1.29 (0.73-2.30)	.38

Bioabsorbable Polymer vs. Durable Polymer DES

CLINICAL RESEARCH — Interventional Cardiology

Clinical Outcomes With Bioabsorbable Polymer- Versus Durable Polymer-Based Drug-Eluting and Bare-Metal Stents

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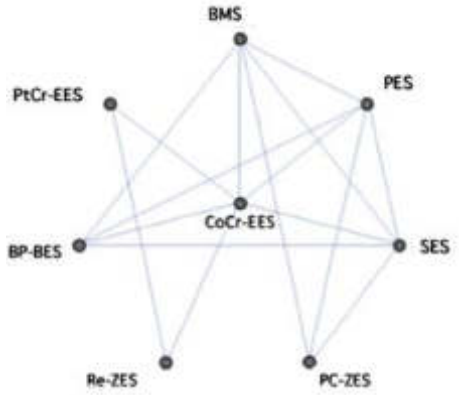
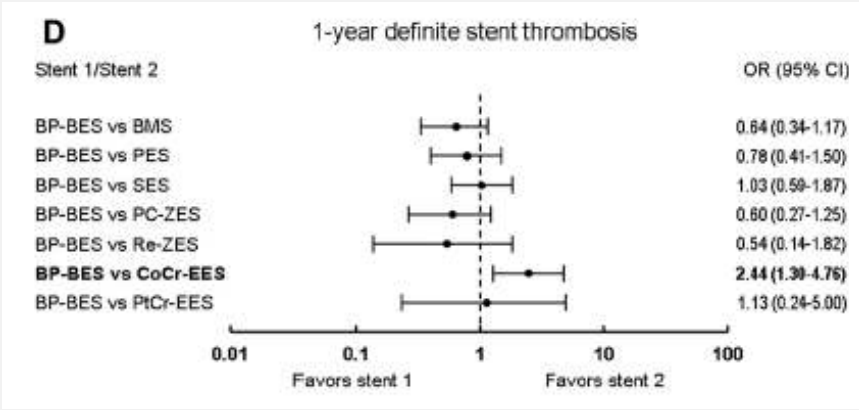
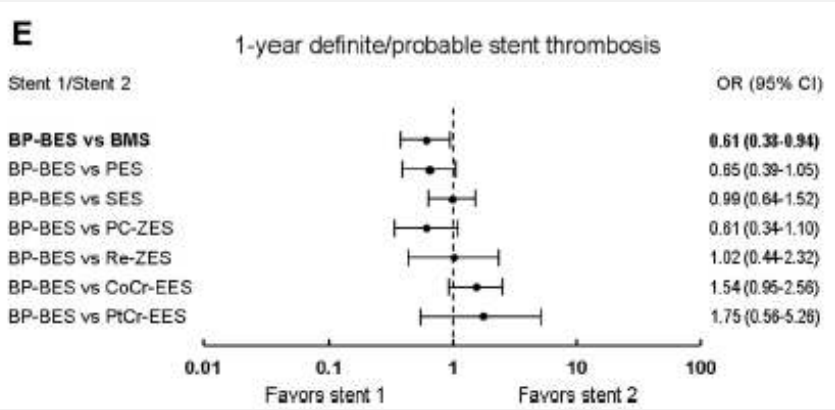






Limitations of data

…not all BP-DES are equal

Stent Design & Thrombogenicity

Kolandaivelu et al Circulation 2011

DES

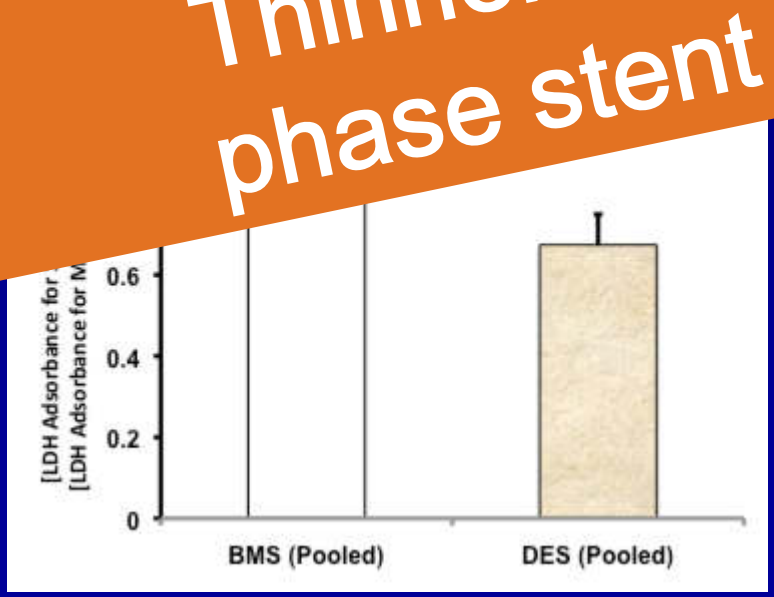
BMS

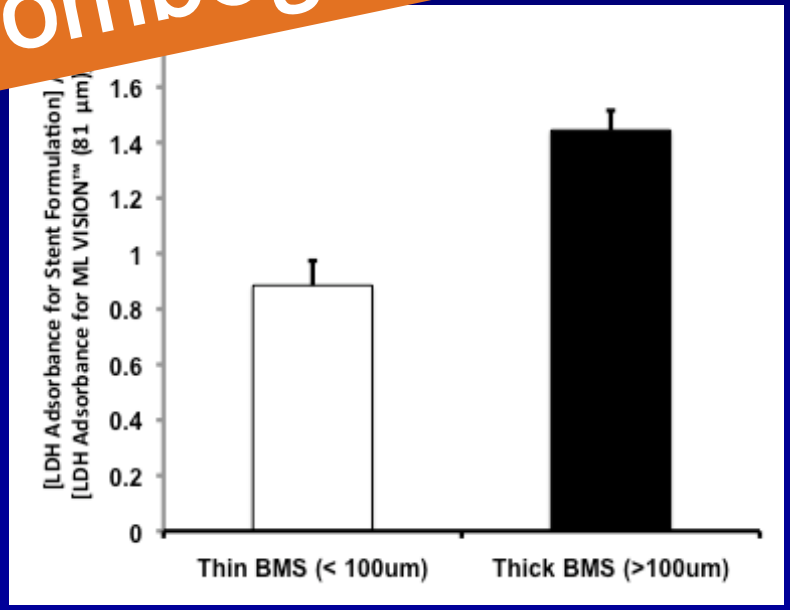
STRUT CROSS-SECTIONS

Thinner struts reduce acute phase stent thrombogenicity

POOLED

THICKNESS

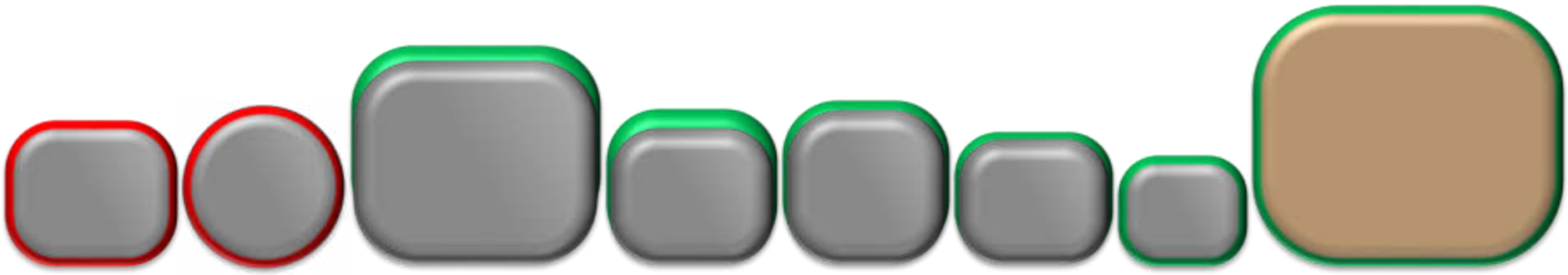




Overview of current stent designs

Strut and coating thickness in perspective

New Generation Durable Polymer Coated Stent		Bioabsorbable Polymer Coated Stent					Bioabsorbable Scaffold
Abbott/Boston	Medtronic	BIOSENSORS	Terumo	Translumina	Boston	BIOTRONIK	Abbott
Xience/Promus	**Resolute**	**BioMatrix**	**Ultimaster**	**Yukon Choice PC**	**Synergy**	**Orsiro**	**Absorb**
CoCr/PtCr-EES	CoNi-ZES	316L-BES	CoCr-SES	316L-SES	PtCr-EES	CoCr-SES	PLLA-EES



Strut thickness

81 µm	91 µm	120 µm	80 µm	87 µm	74 µm	60 µm	150 µm

Polymer coating

Circumferential 7-8 µm/side	Circumferential 6 µm/side	Abluminal 10 µm	Abluminal 15 µm	Abluminal 5 µm	Abluminal 4 µm	Circumferential 4-7 µm/side	Circumferential 3 µm/side

Sources: 1: GG Stefanini, M Taniwaki, S Windecker, Coronary stents: novel development, Heart 2013; 2: IT Meredith, Scientific symposium, TCT 2013

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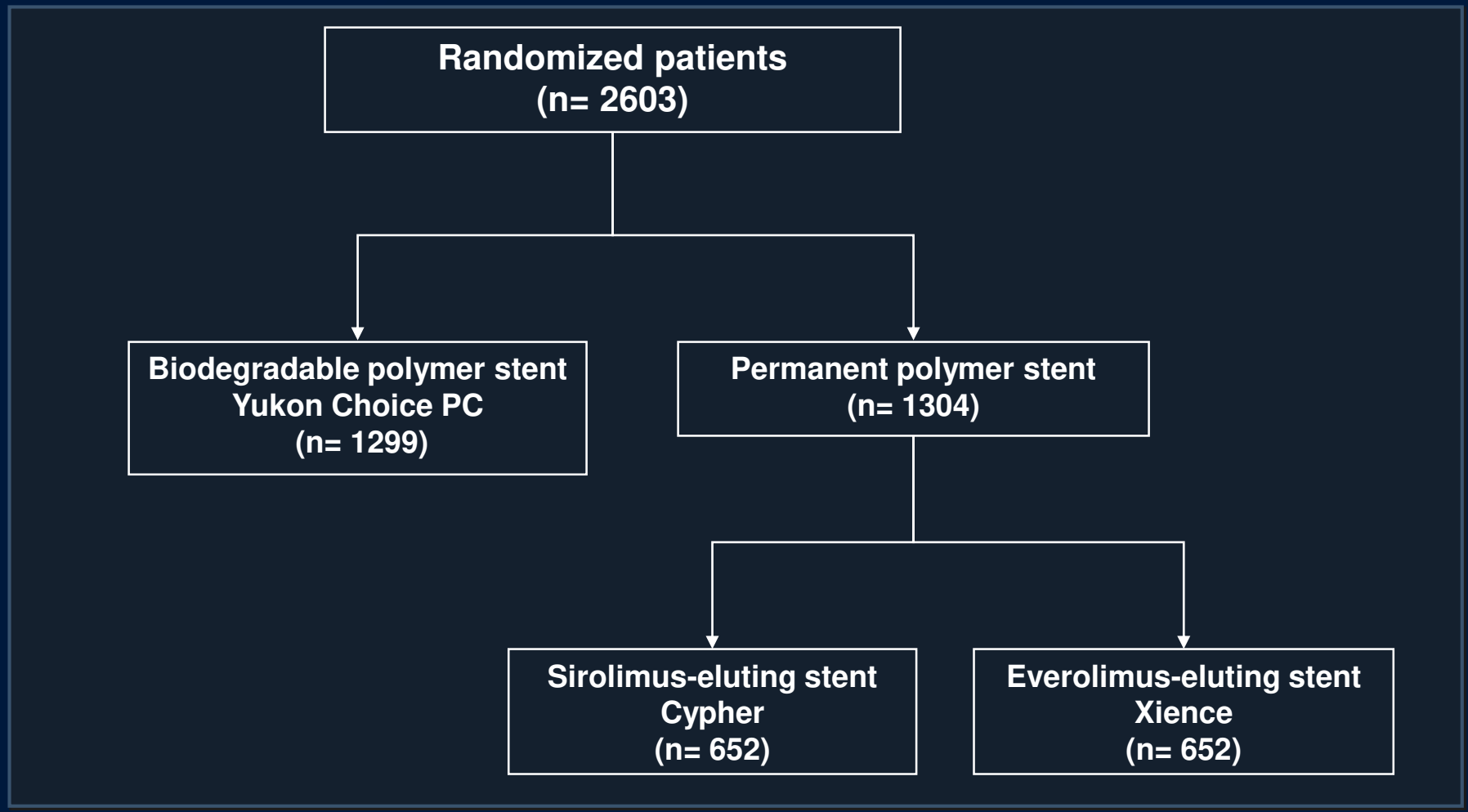
ISAR-TEST 4: Final 5-Year Data

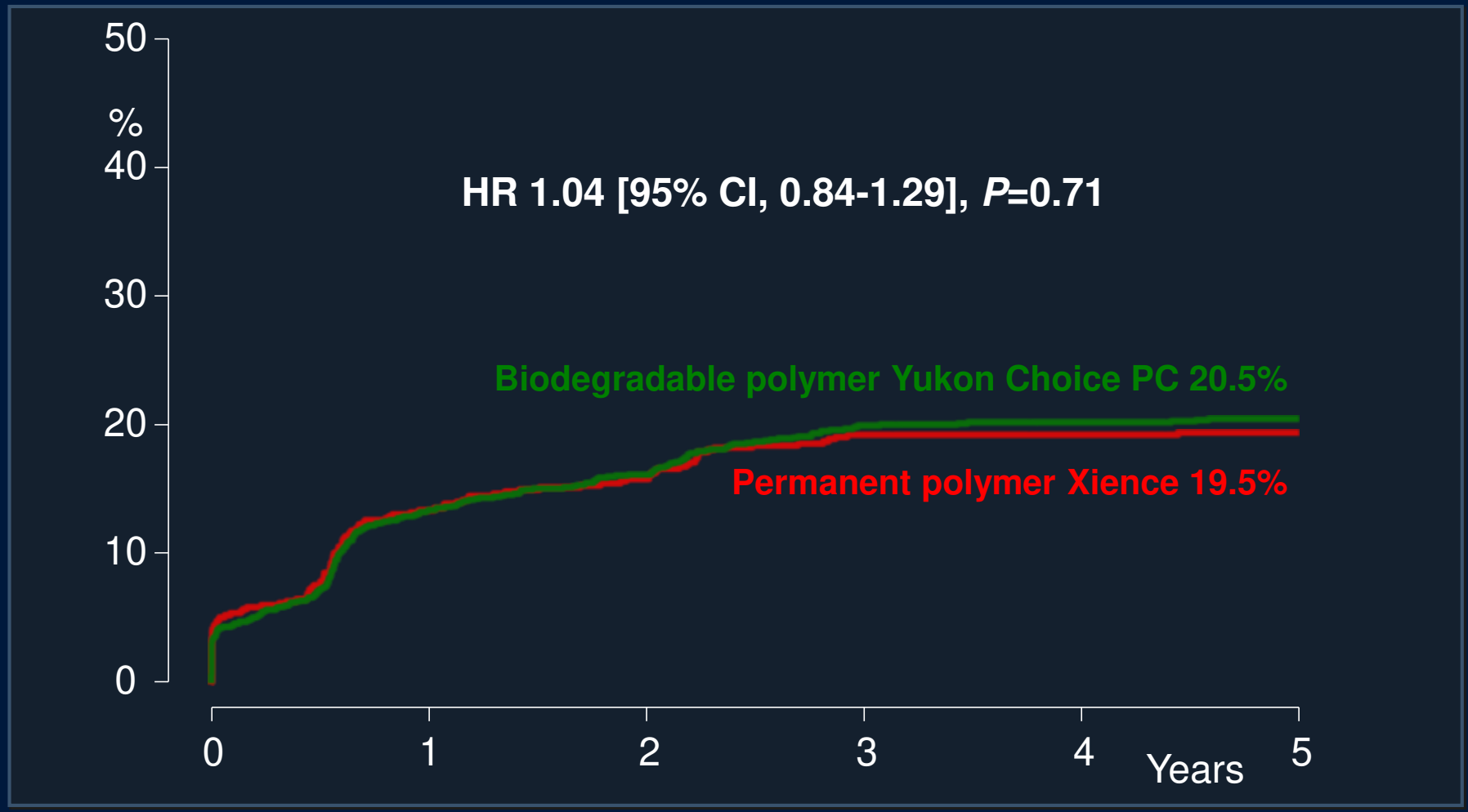
Study Design



Kufner et al. EuroIntervention in press

ISAR-TEST 4: Final 5-Year Data

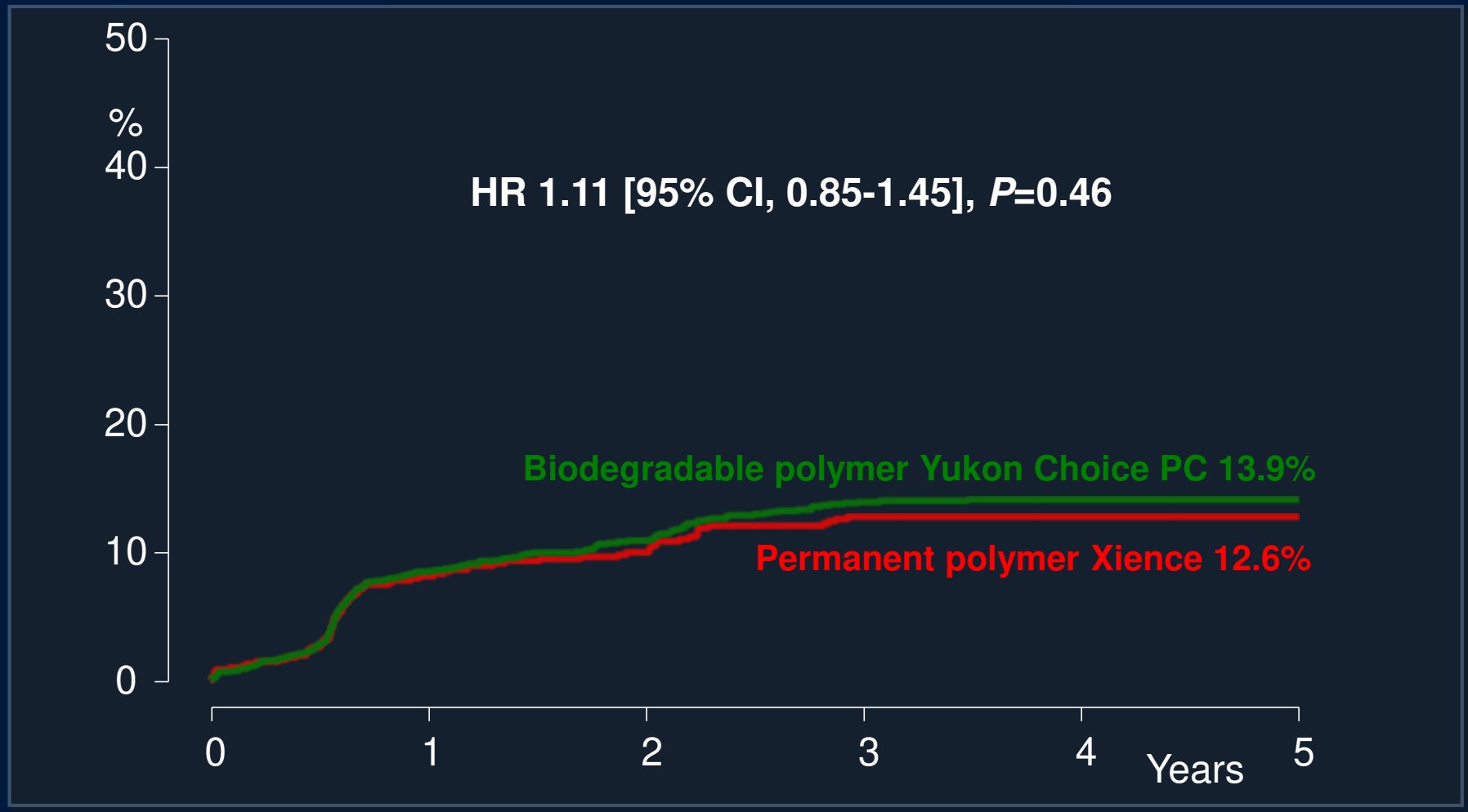
Cardiac death/target vessel MI/TLR



Kufner et al. EuroIntervention in press

ISAR-TEST 4: Final 5-Year Data

Target lesion revascularization



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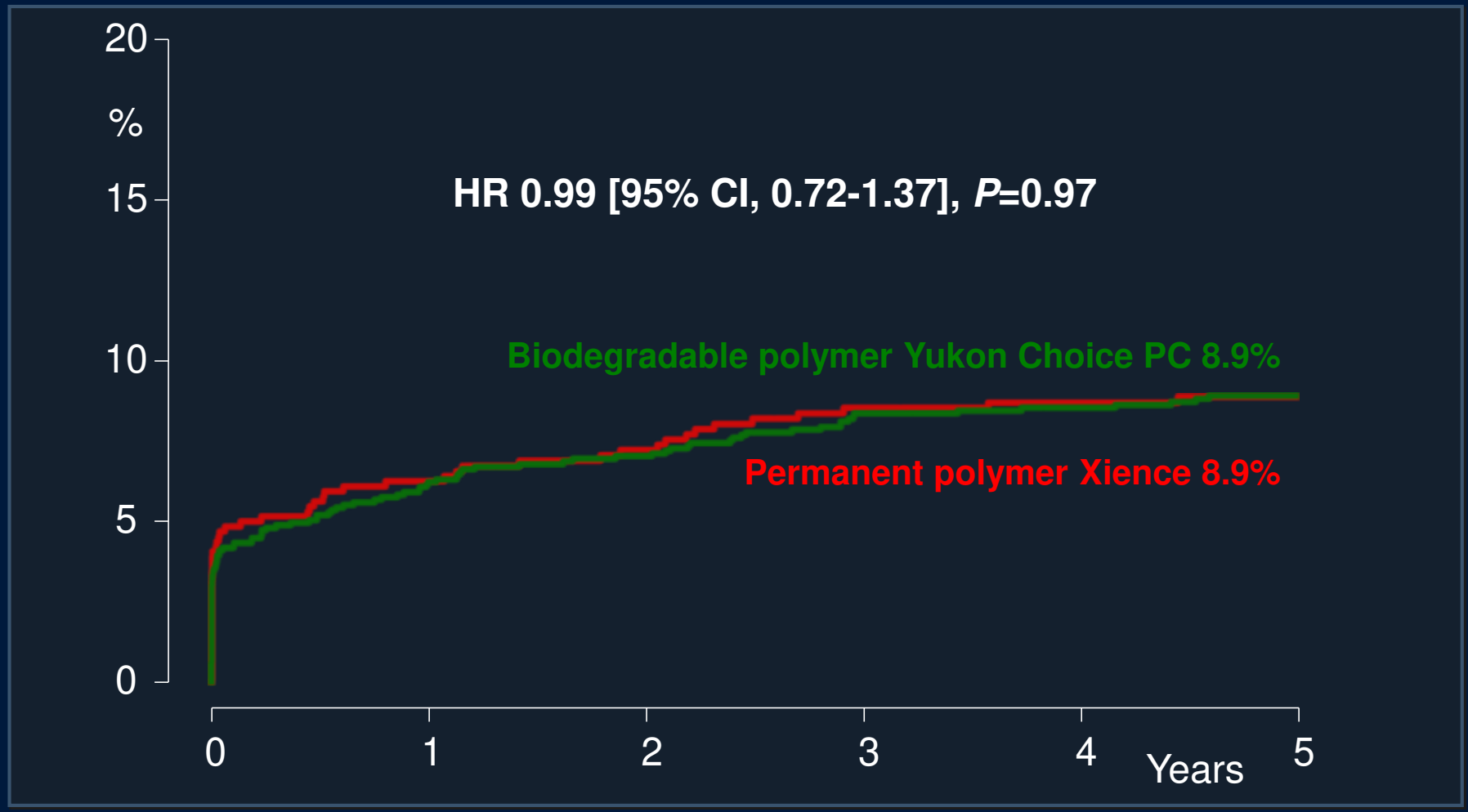
ISAR-TEST 4: Final 5-Year Data

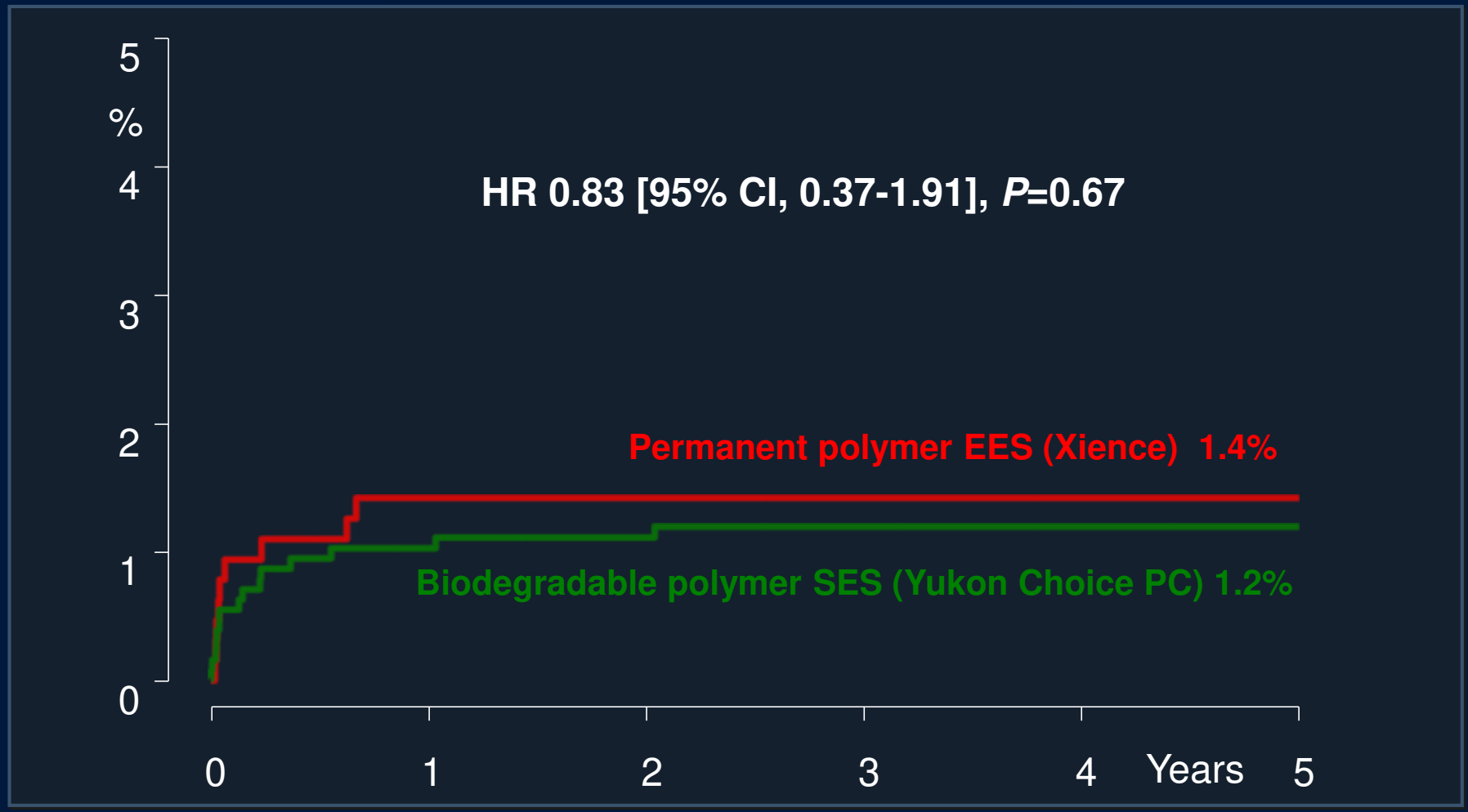
Cardiac death/target vessel MI



Kufner et al. EuroIntervention in press

ISAR-TEST 4: Final 5-Year Data

Definite/probable stent thrombosis



Kufner et al. EuroIntervention in press

Perspective

…outcomes beyond 5-years remain unclear but all other things being equal I would prefer a stent without polymer!

Metallic DES: Tomorrow's Technology

From Proof of Concept to Clinical Evidence, Bioabsorbable Polymer Technology is Preferred to Durable Polymers

Washington DC, Mon. 15th Sept. 2014

Robert A. Byrne, MB BCh PhD

Deutsches Herzzentrum, Technische Universität, Munich, Germany

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