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DES or maybe BMS ?

Prof. Dr. Helmut Schühlen, FESC, FACC

**Vivantes Auguste-Viktoria-Klinikum
Berlin, Germany**



Conflict of Interest Statement

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Research support, speaker's or consulting honoraria from:

Astra Zeneca

Bayer

Boehringer Ingelheim

Correvio

Lilly

Abbott

Biotronik

Bristol Myers-Squibb

Daiichi-Sankyo

Novartis

The 1996 Grüntzig Lecture

Stents: a mechanical solution for a biological problem?

U. Sigwart

Royal Brompton Hospital, London, U.K.

'Heavier-than-air flying machines are impossible' (Lord Kelvin, President, Royal Society, 1895)

The question mark in the title of this paper may look outdated and even artificial in view of the recent exponential increase in the use of stents. This almost frightening upswing occurred after a little less than one decade following their introduction into clinical medicine^[1]. It was, however, only a few years ago that the role of stents in cardiology was in serious doubt^[2]. In what follows, I shall try to review the story of stenting in the light of my personal experience against the background of diverse currents in the catheter treatment of human vascular disease.

History

The concept of placing a scaffold into injured blood vessels, or other conduits, is so simple that it comes as no surprise to find traces of such thinking long ago. It is generally believed that Alexis Carrel (Fig. 1), who first tried to place glass tubes into the arteries of dogs in the hope of treating traumatic injury to blood vessels, also performed surgical anastomoses^[3]. Carrel was a tireless inventor and his close friend

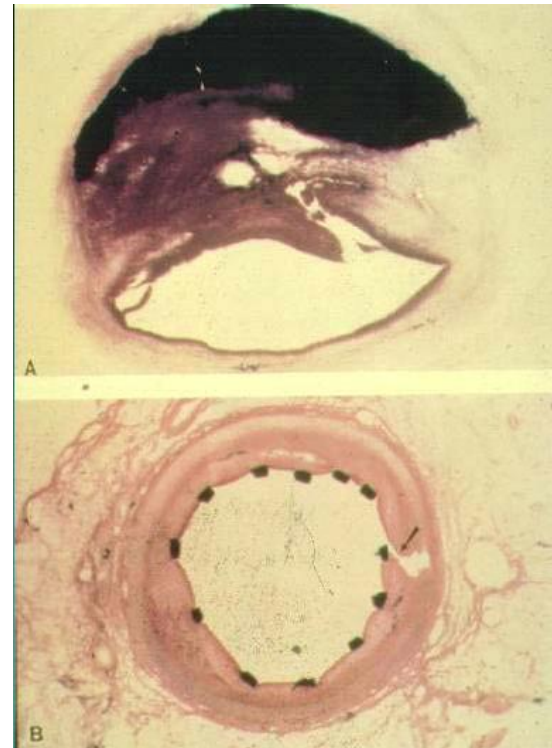


Figure 1 Alexis Carrel.

Rationale for Stents

Which Problems Did We Want to Solve With Stents ?

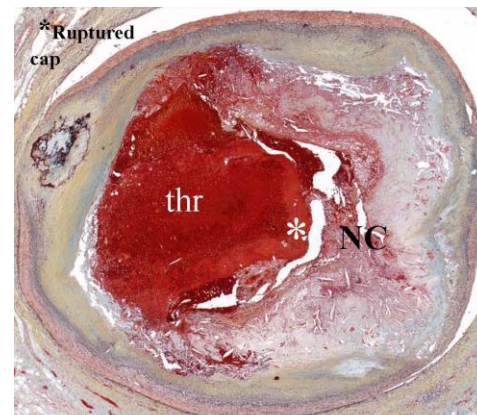
- mechanically scaffold the artery
- (re)create a larger circular lumen
- prevent abrupt vessel closure
- prevent late restenosis



Abrupt Vessel Closure

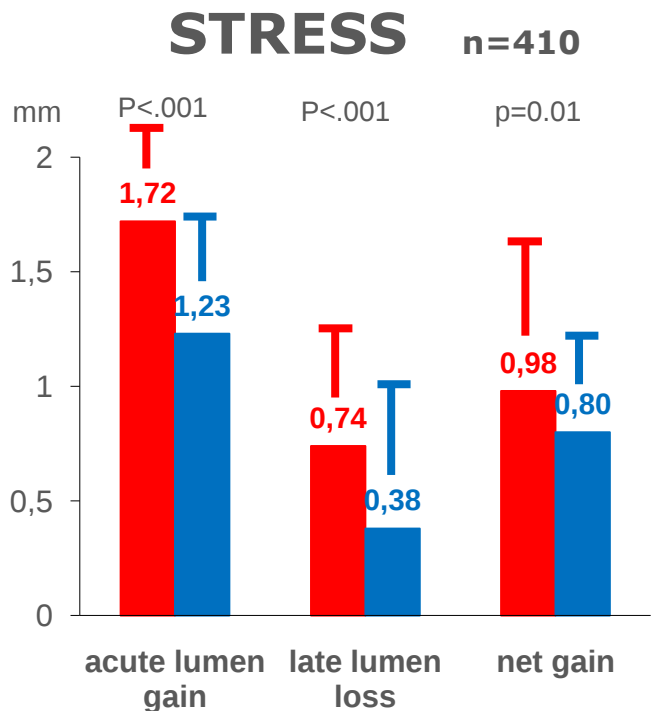
Early Data with POBA:

- frequency 5-10%
- consequences:
 - MI ~35%
 - mortality ~8-20%
 - emergency CABG ~30%
- stents for abrupt closure as bridge to bypass surgery
- stents as definite treatment for abrupt vessel closure
- routine surgical back-up became obsolete

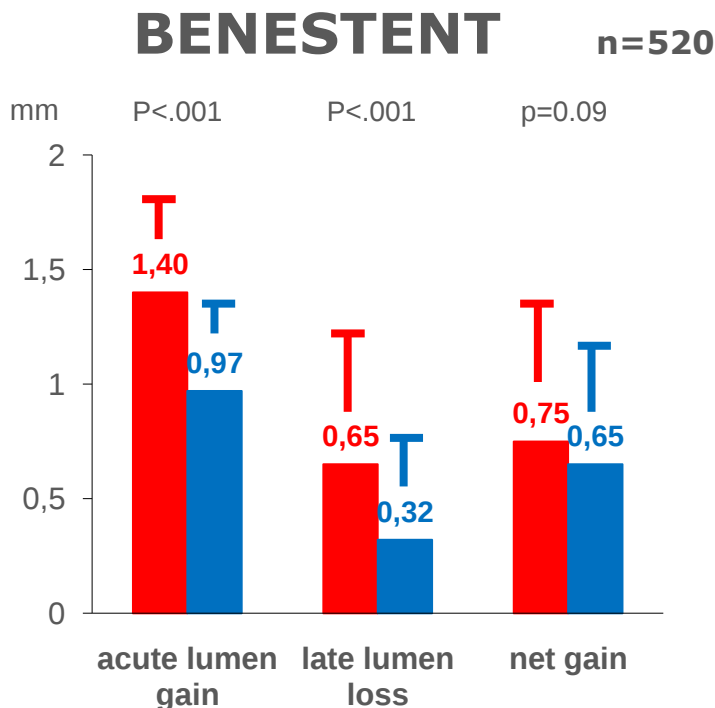


Quantitative Coronary Analysis of Stents versus POBA

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DL Fishman et al., *N Engl J Med* 1994

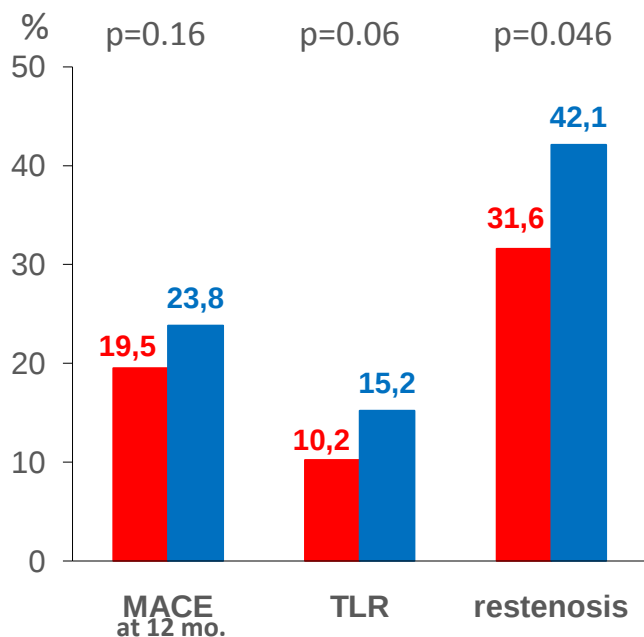


P Serruys et al., *N Engl J Med* 1994

Clinical Results & Longterm Outcome Stents versus POBA

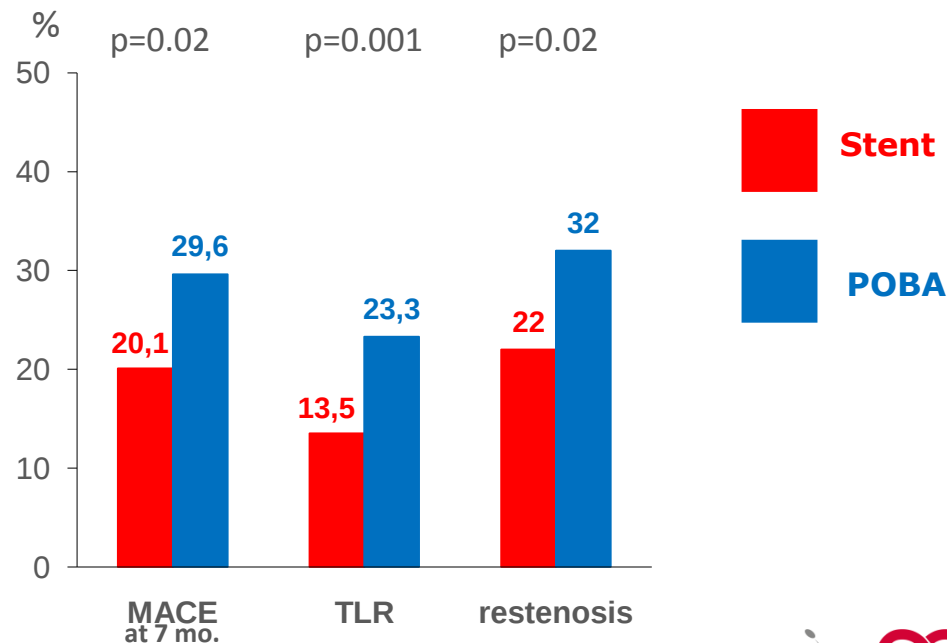
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STRESS n=410



DL Fishman et al., *N Engl J Med* 1994

BENESTENT n=520



P Serruys et al., *N Engl J Med* 1994

Randomized Trials Stent versus POBA

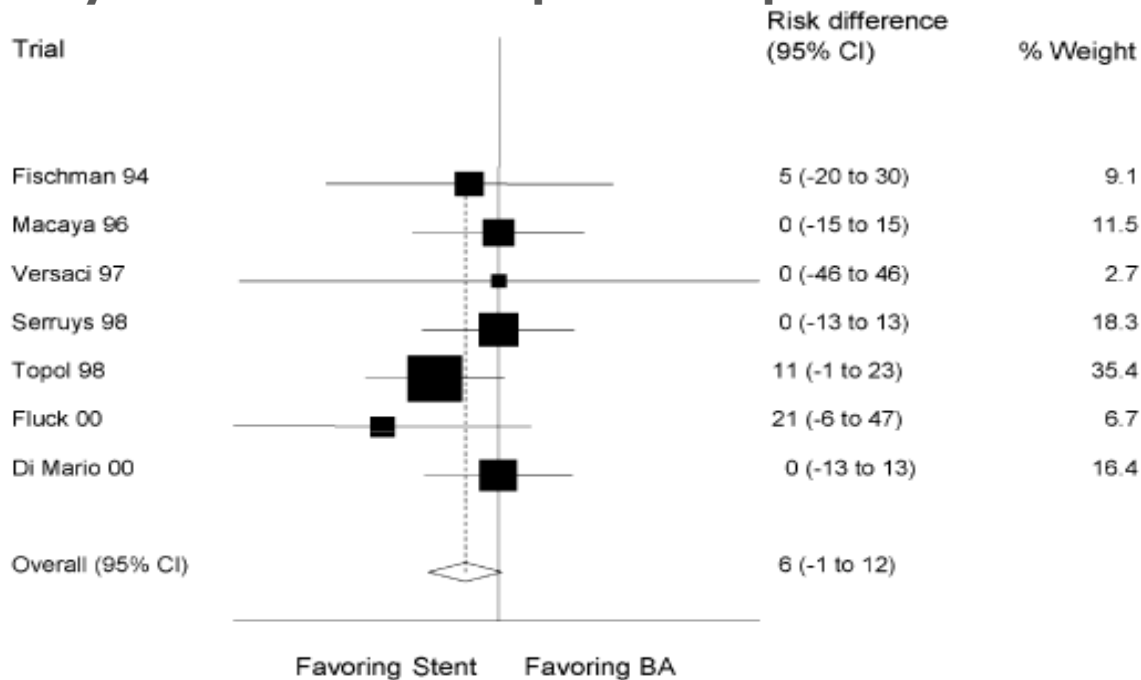
Analysis of 12 randomized trials with 6300 patients

Study, y	Follow-up, mo	No., Stent/ Angioplasty	Angiographic Restenosis, %			Target Vessel Revascularization (TVR), %		
			Stent	Angioplasty	P Value	Stent	Angioplasty	P Value
STRESS, ² 1994	6	205/202	31.6	42.1	.046	10.2	15.4	.06
Benestent, ^{3,14} 1994	7/60†	259/257	22	32	.02	13.5/17.3‡	23.3/27.6	<.05/.006
TASC I, ¹⁰ 1995§	6	270 (Overall)	31	46	.01	...	...	...
Versaci et al, ¹⁵ 1997	12	60/60	19	40	.02	6.6	22	...
STRESS II, ¹² 1998	12	100/89	...	...	...	10	20	...
Benestent II, ¹³ 1998	6	413/410	16	31	<.001	8‡	13.7	.02
OCBAS, ¹⁶ 1998	7	57/59	18.8	16.6	...	17.5	9.2	...
WIN, ¹⁷ 1998§	6	299/287	38	37	...	39	39	...
BOSS, ¹⁸ 1998§	8	40/40	...	...	...	21.4	23.5	...
EPISTENT, ^{19,20} 1998¶	6	1603/796	...	...	...	8.7	15.4	<.001
START, ¹¹ 1999	6/48#	229/223	22	37	<.002	12	24.6	<.002
OPUS, ²¹ 1999§	6	480 (Overall)	...	...	...	4.0	10.7	≤.05

J Al Suwaidi et al., JAMA 2000

Metaanalysis of Stent versus POBA Trials

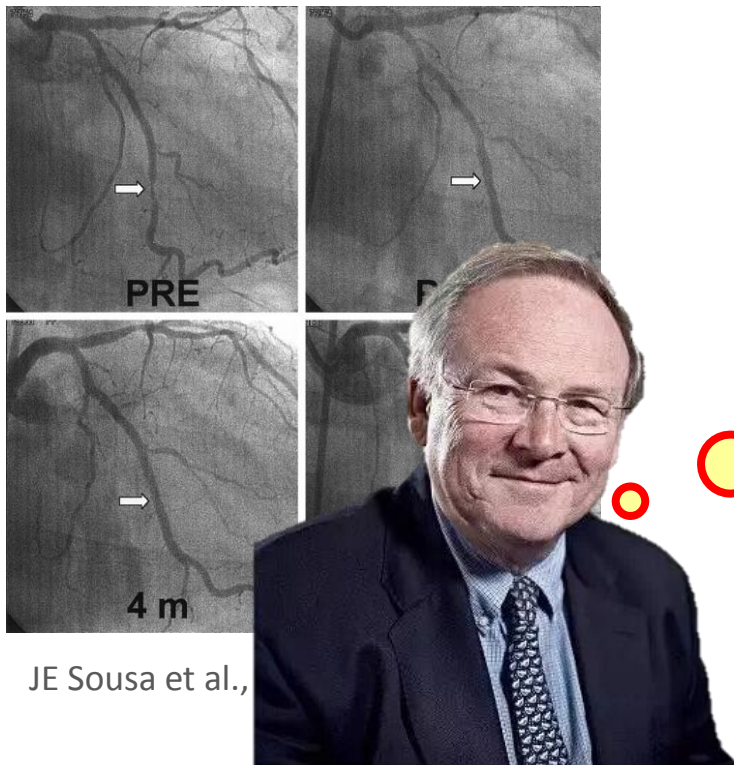
19 randomized trials with 8004 patients
- Analysis of lives saved per 1000 patients at 12 mo. -



AJ Nordmann et al.,
Eur Heart J 2004

Initial Experience with DES

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JE Sousa et al.,

The real target is
not BMS vs. DES,
it's surgery.

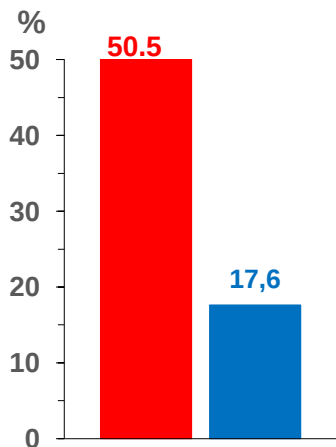
Interview at ACC 2003, www.theheart.org

Early Data for DES & BMS in Subgroups

Angiographic restenosis at 6 mo.

SIRIUS

diabetes subgroup

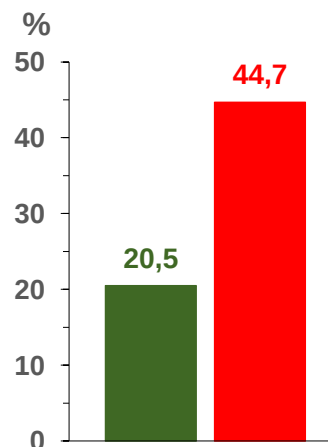


Velocity **Cypher**

J Moses, ACC 2003

ISAR-STEREO-2

diabetes subgroup



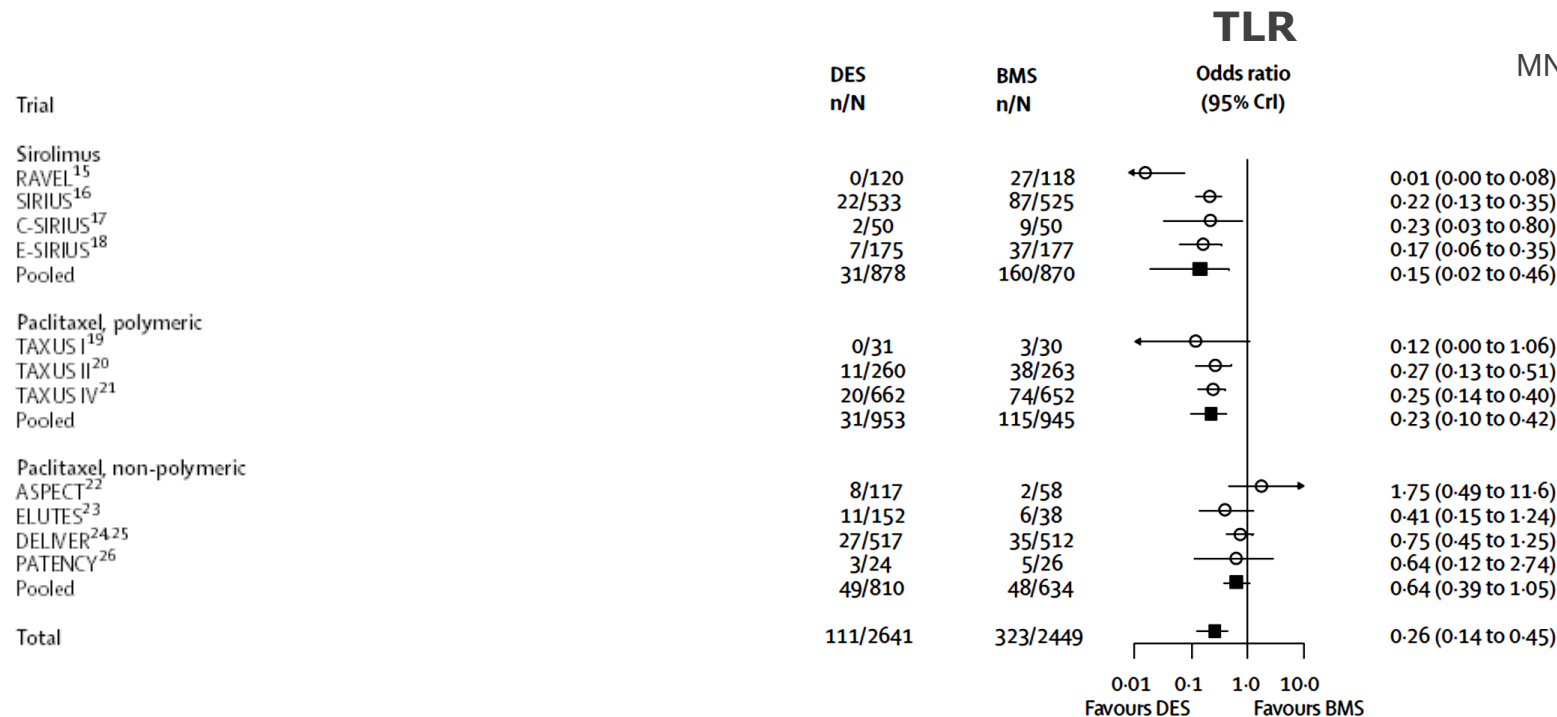
MULTI-LINK **Velocity**

J Pache et al., J Am Coll Cardiol 2003

Metaanalysis of Trials with DES versus BMS

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11 trials with 5103 patients



MN Babapulle et al.,
Lancet 2004

The Debate at ESC 2006

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TUESDAY

ESC Congress News

World Congress of Cardiology 2006
The unique meeting of the European Society of Cardiology Congress 2006 and the World Heart Federation's XVth World Congress of Cardiology

Do drug-eluting stents increase deaths?

TWO SEPARATE, independent meta-analyses, presented in Hot Line session I, suggest drug-eluting stents (DES) may increase death, Q-wave myocardial infarction (clinical surrogates of in-stent thrombosis) and cancer deaths, bringing the long-term safety of DES firmly into the spotlight. Discussant Salim Yusuf (McMaster University, Canada) hailed the data as one of the most important presentations to come out of this year's meeting.

"Six million people in the world have been implanted with DES, yet their long-term safety and efficacy is unknown," said Yusuf. "I've a feeling the data we're seeing today is only the tip of the iceberg. We need to encourage more public access to the data."



obtain this data from the manufacturer," said Nordmann. He speculated that the increase in cancer might be due to a rapid impairment of the immune system.

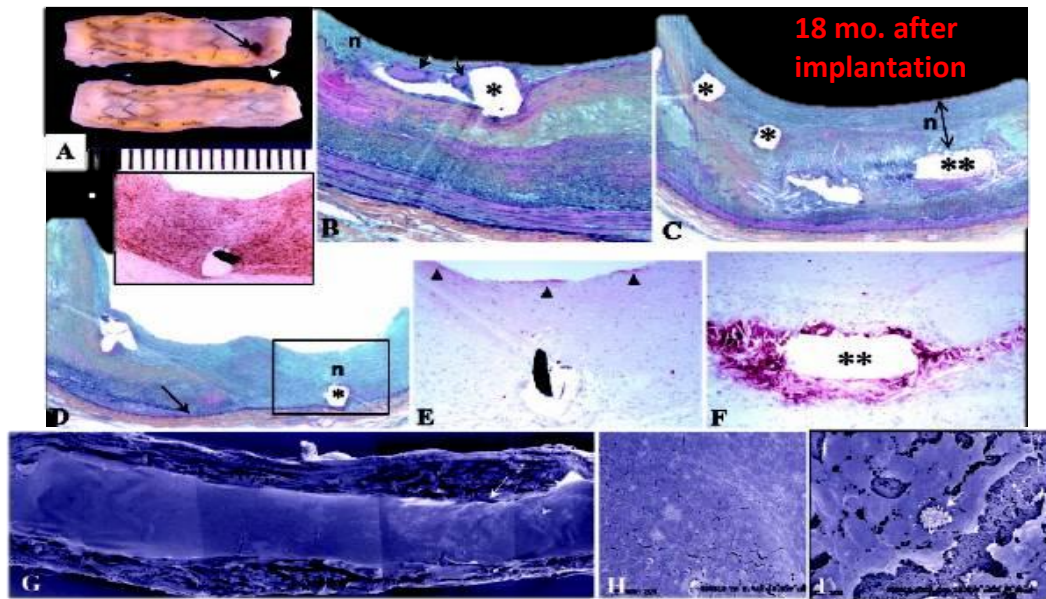
Yusuf widened the debate to include percutaneous coronary intervention (PCI). "The overuse of PCI is an insidious change in the culture of cardiology that needs to be reversed," he said. The use of PCI was established in MI, high-risk unstable angina and cardiogenic shock. However, its use in stable disease was a totally different question.

"There's no beneficial influence on mortality – PCI does nothing to prevent heart attack. All we are doing is providing short-term relief of chest pain. It's not re-stenosis that kills but the

Mechanistic Insights into the Excess Risk of Late Stent Thrombosis After 1G DES

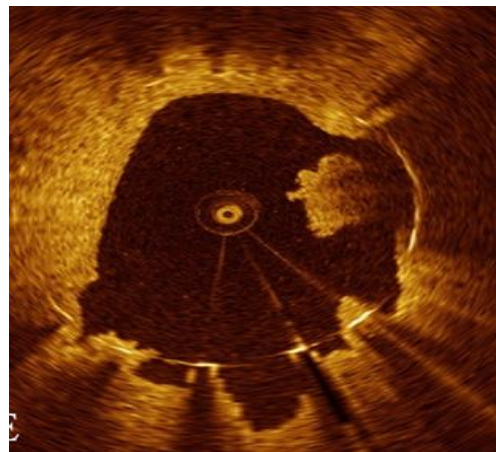
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Incomplete Endothelialization and Chronic Inflammation



Guagliumi et al, *Circulation* 2003

Acquired Malapposition



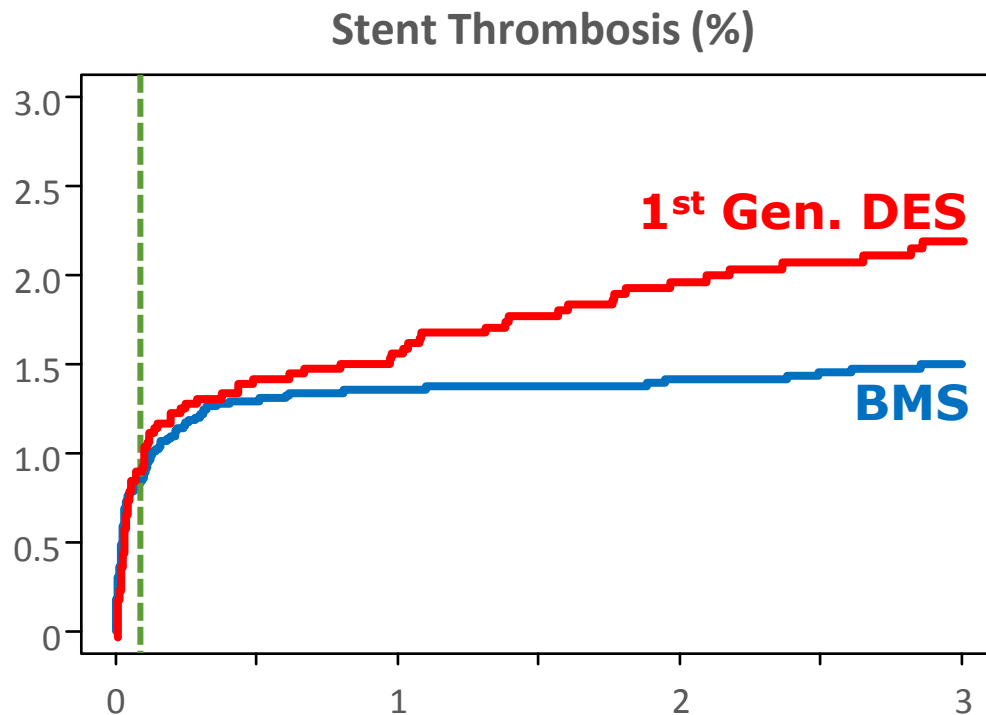
Guagliumi et al., *JACC Interv* 2012

Continuous Risk for Stent Thrombosis with 1st Gen. DES

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Registry of
18,334 pts
with BMS or DES

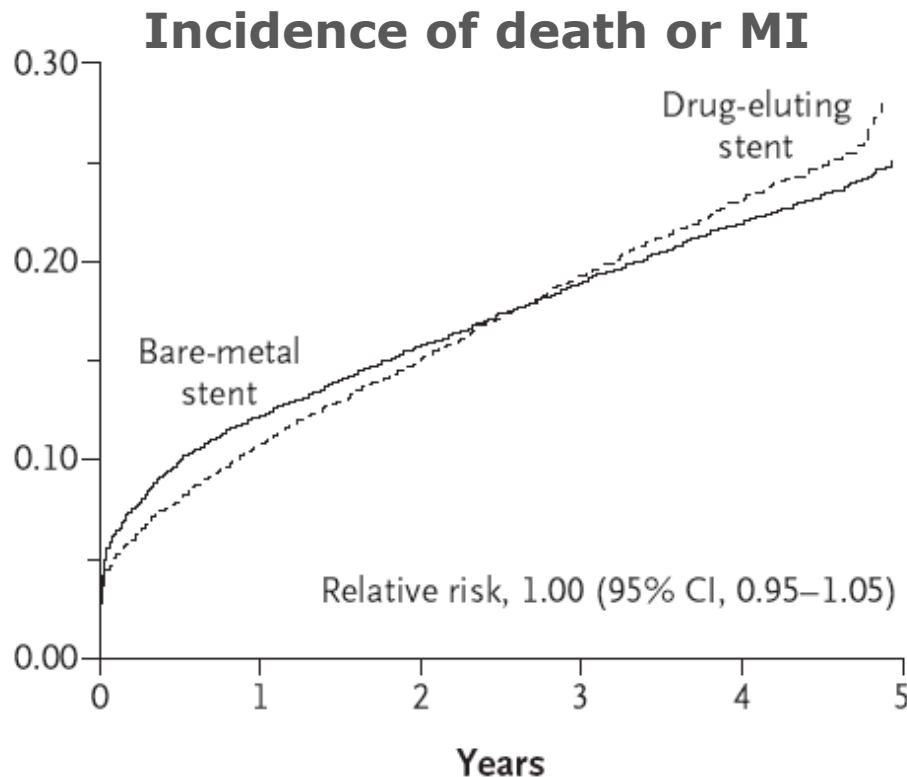
246 definite SAT



T Tada et al.,
JACC Intv 2013

Longterm Outcome with 1st-gen. DES vs. BMS

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SCAAR Registry
47967 pts.

BMS n=18659
DES n=10294

ACS ~80%
STEMI ~30%

SK James et al.,
N Engl J Med 2009

DAPT Duration in Pivotal Trials of 1G-DES

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Cypher®

sirolimus-eluting,
permanent polymer

RAVEL
SIRIUS
E- & C-SIRIUS

8 wks.
3 mo.
2 mo.

Taxus®

paclitaxel-eluting,
permanent polymer

TAXUS I, II, IV-VI

6 mo.

ESC Guidelines on DAPT after PCI in stable CAD 2005 - 2014



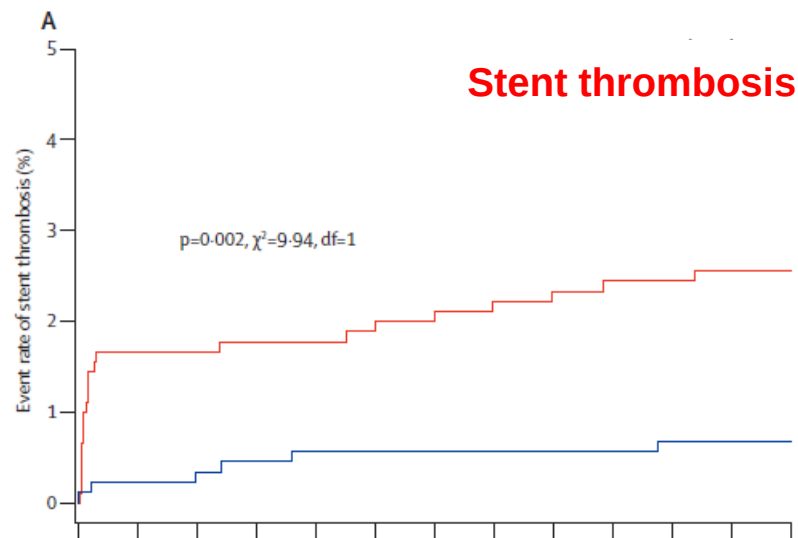
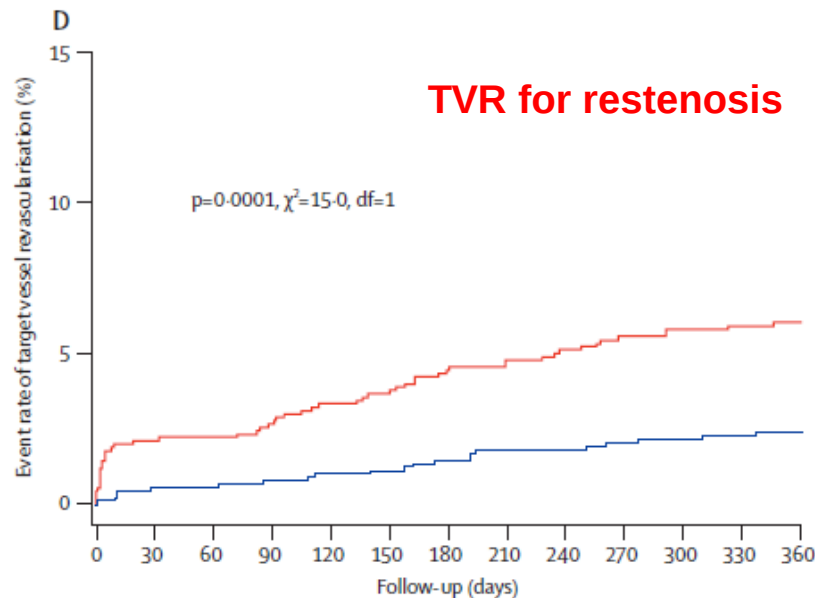
DAPT is indicated for at least 1 month after BMS implantation.	I	A
DAPT is indicated for 6 months after DES implantation.	I	B

More Favorable Results with 2nd-Gen. DES

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COMPARE Trial: 1800 patients, 60% with ACS

Taxus
Xience



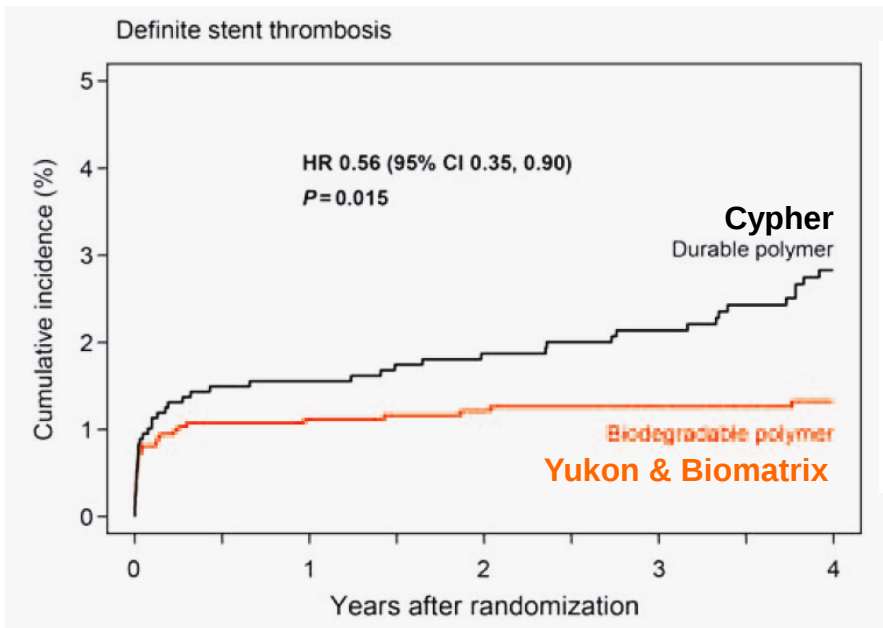
E Kedhi et al., *Lancet* 2010

Is Late Stent Thrombosis Still a Relevant Issue After 2nd-Gen. DES ?

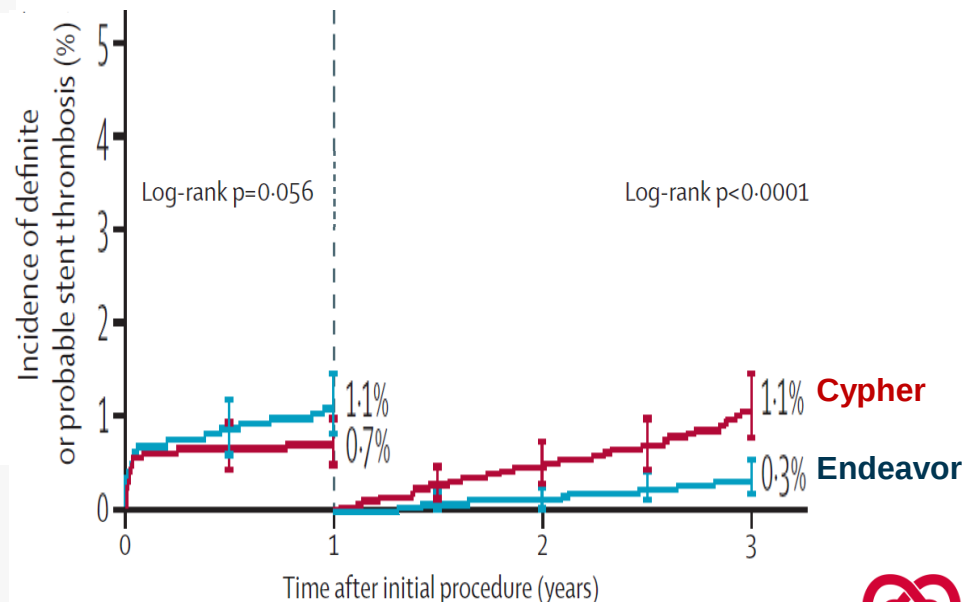
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Metaanalysis of ISAR-TEST 3 + 4 & LEADERS
4062 pts. randomized to Yukon, Biomatrix or Cypher

PROTECT trial
8709 pts. randomized to Cypher or Endeavor



GG Stefanini et al., *Eur Heart J* 2012



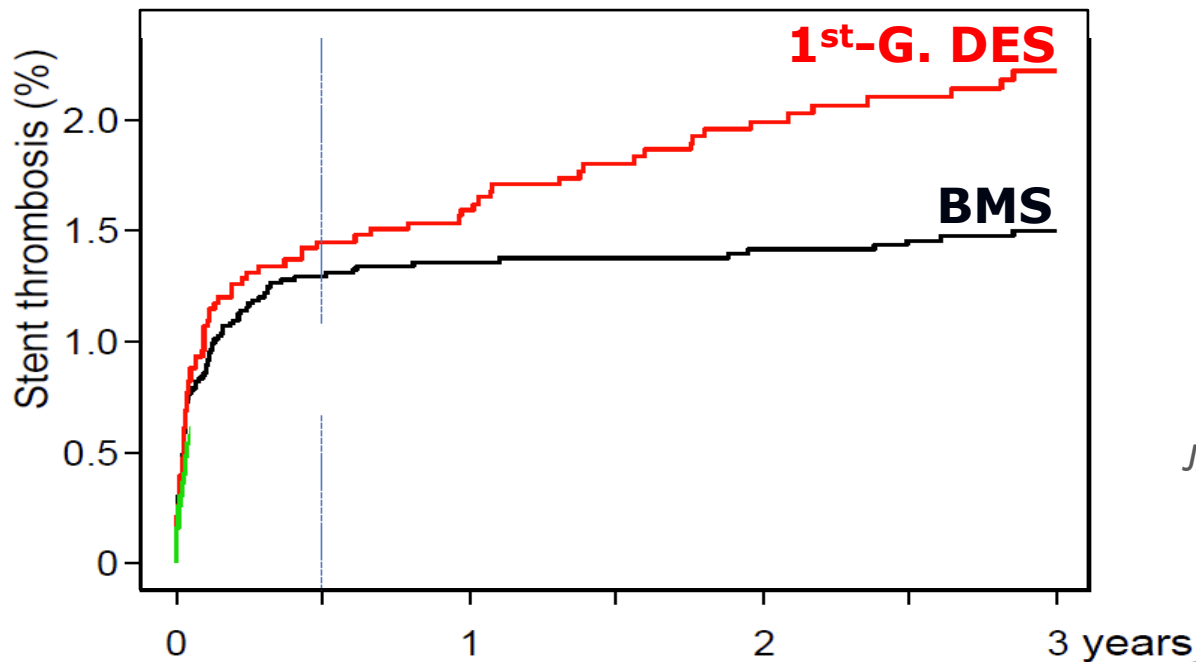
E Camenzind et al., *Lancet* 2012

Late Stent Thrombosis with BMS, 1st-Gen. & 2nd-Gen. DES

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Registry of
18,334 pts
with BMS or DES

246 definite SAT



T Tada et al.,
JACC Interv 2013

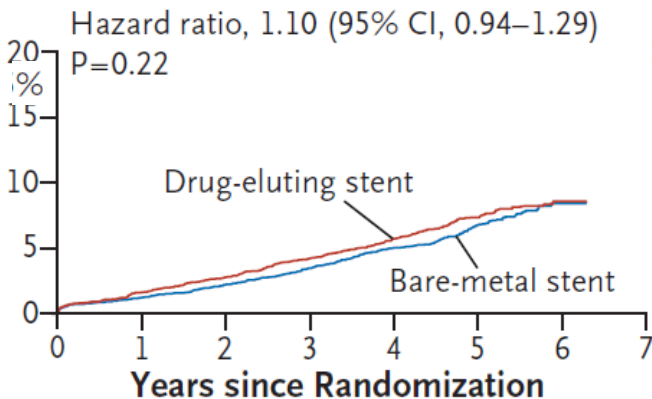
2nd-Gen. DES vs. BMS - The NORSTENT Trial

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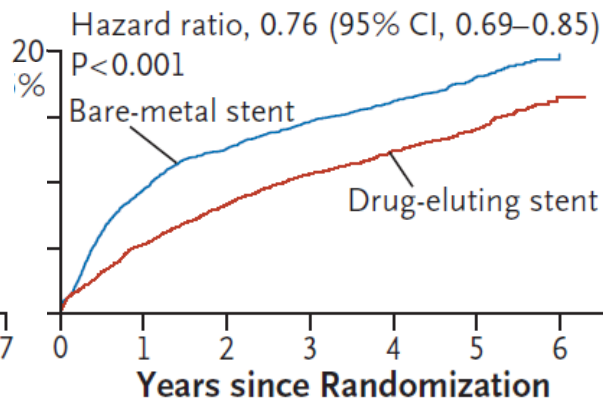
9013 patients randomized to BMS or DES; both >9 mo. DAPT; ~60% ACS

(DES group: Promus/Xience 82.3%, Endeavor 11.9%, Cypher/Taxus 5.1%)

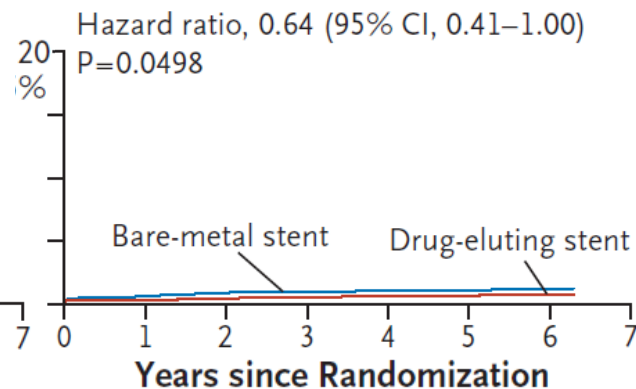
All-Cause Mortality



Revascularization (PCI or CABG)



Stent Thrombosis (definite)



KH Bønaa et al., *N Engl J Med* 2016

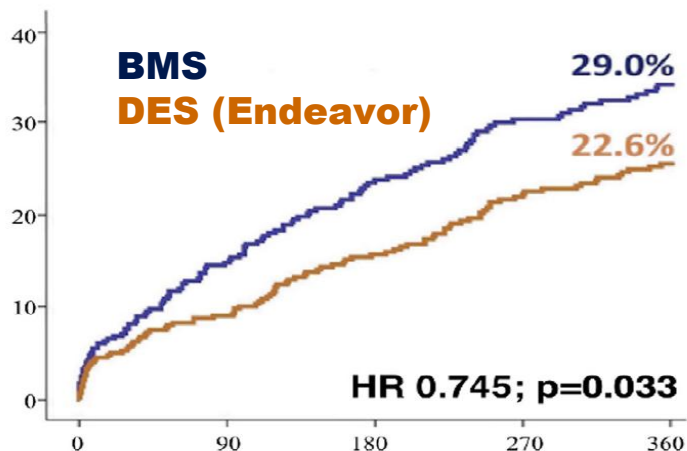
DES vs. BMS in Patients with DAPT for 1 Mo.

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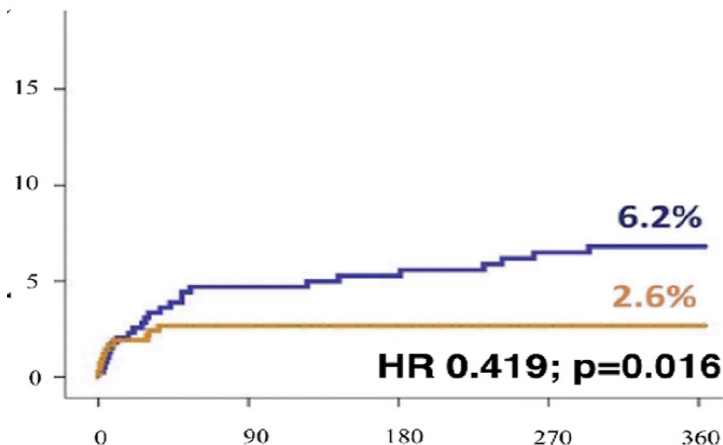


828 patients randomized to BMS or Endeavor

Death, MI or TVR



Stent Thrombosis definite or probable



S Ariotti et al.,
JACC Interv 2016

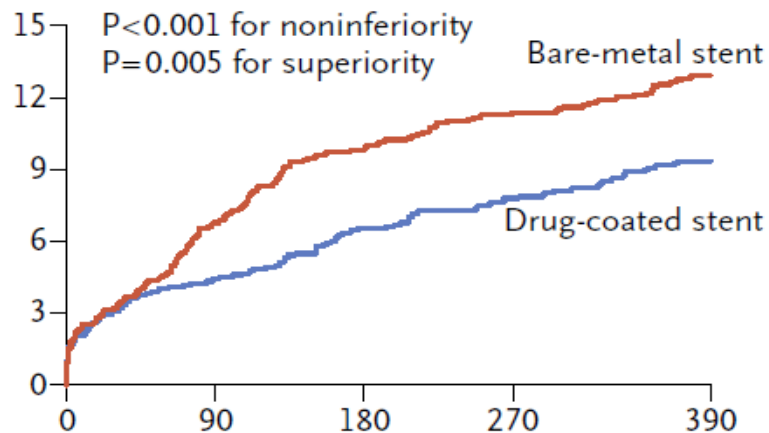
DES vs. BMS in Patients with DAPT for 1 Mo.

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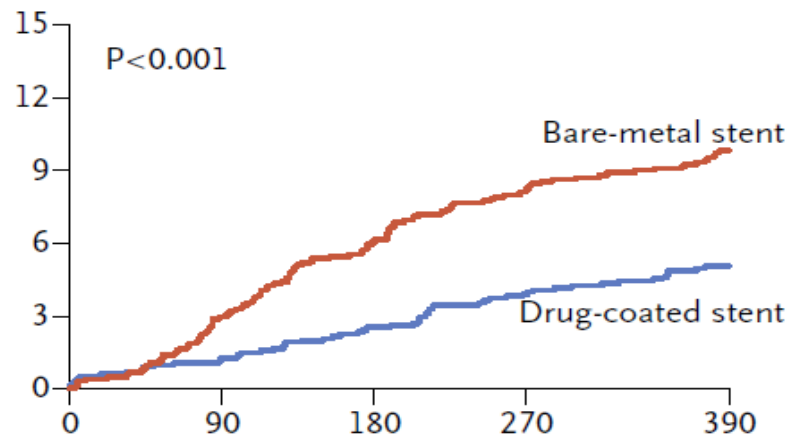
LEADERSFREE

2466 patients randomized to BMS or BioFreedom

Cardiac Death, MI or Stent Thrombosis



TLR



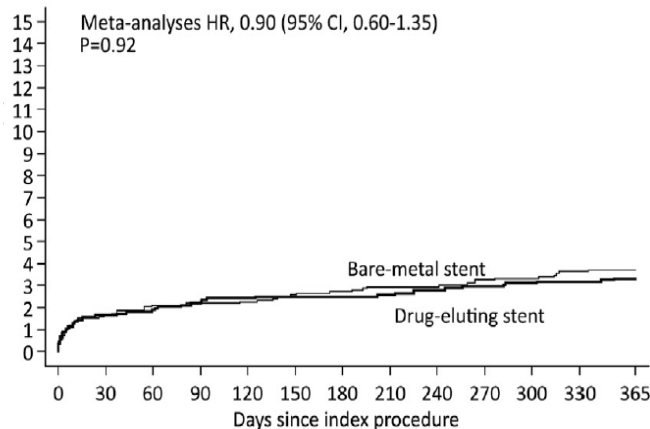
P Urban et al., *N Engl J Med* 2015

Metaanalysis 2nd-gen. DES vs. BMS in STEMI

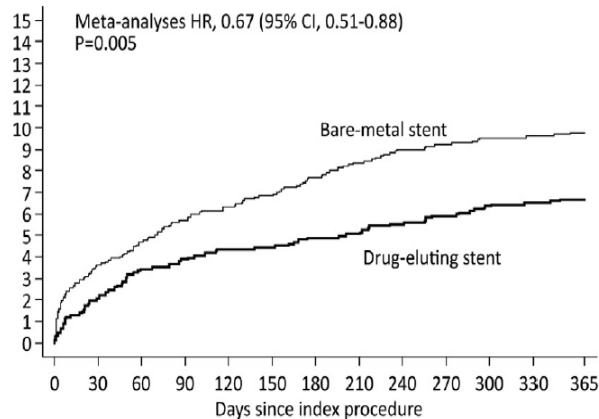
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EXAMINATION & COMFORTABLE-AMI with 2665 pts.
(Xience or Biomatrix versus BMS)

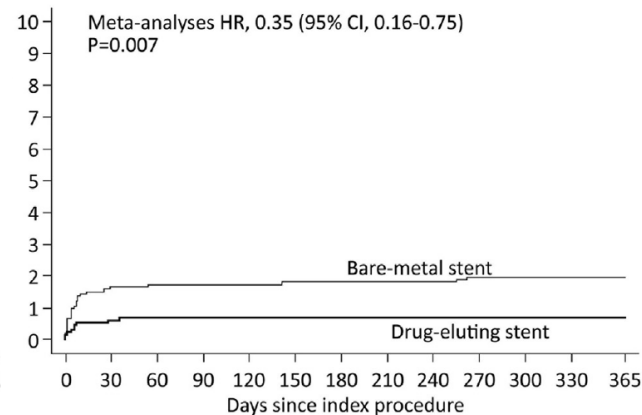
All-Cause Death



Revascularization



Stent Thrombosis (definite)



M Sabaté et al., *JACC Interv* 2014

Network Metaanalysis DES vs. BMS in STEMI

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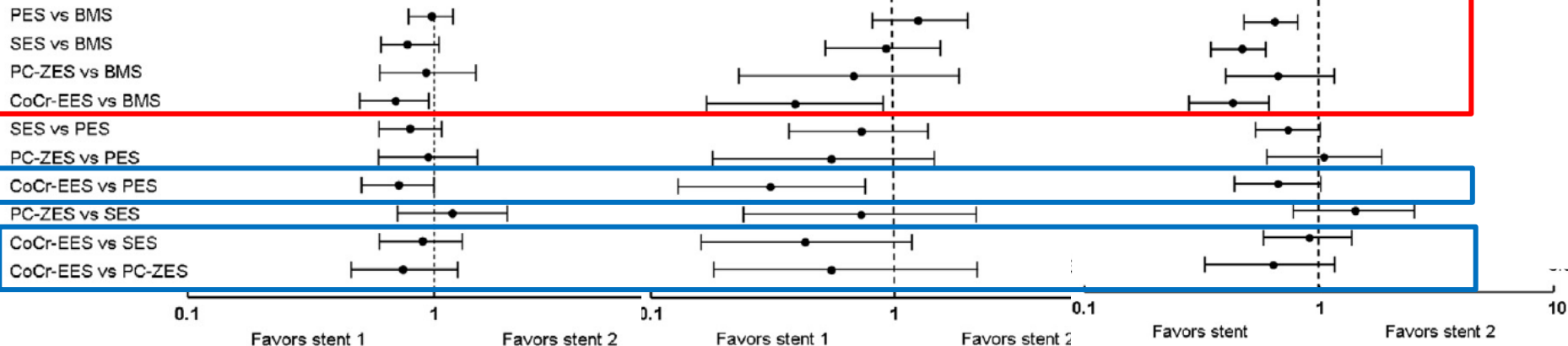
22 trials with 12453 patients

Cardiac Death or MI
per 100 patient-yrs.

Stent Thrombosis
per 100 patient-yrs. (definite)

TVR
per 100 patient-yrs.

Stent 1/Stent 2



T Palmerini et al., JACC 2013

Summary

- **Mortality is better perceived as the target for the mandatory & well-established longterm medical therapy.**
- **Stents have revolutionized & simplified PCI.**
- **Stents (BMS) increase the proliferative response to PTCA.**
- **1st-gen. DES diminished this proliferative response at the cost of deficient healing & a continuous thrombotic risk.**
- **“3rd” gen. DES are safer than BMS, even with 1 mo. DAPT.**

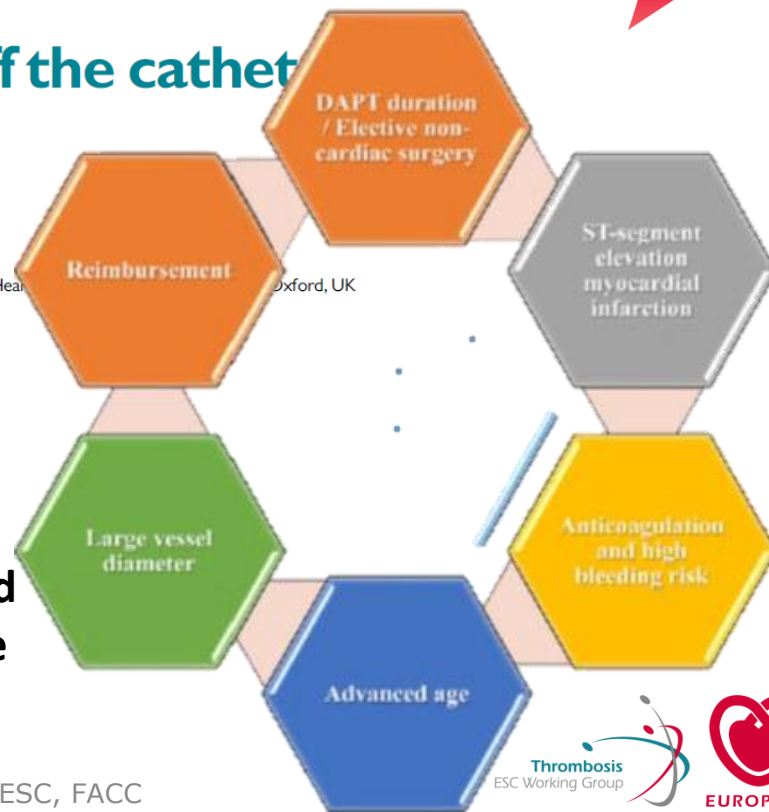
Is it time to take bare metal stents off the catheter laboratory shelf?

George Kassimis^{1*} and Adrian P. Banning²

¹Cardiology Department, NHS Gloucestershire Hospitals, Cheltenham General Hospital, Cheltenham GL53 7AN, UK; and ²Oxford Heart Centre, Oxford, UK

Our opinion of these data is that there is a clear benefit from DES... and that this benefit is independent of the clinical indication. ...

In 2016 implantation of BMS is no longer justified. We suggest that BMS should be honourably retired and added to the history books that document the evolution of interventional therapies.



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Thank you !