Evolution of BVS, Unique Benefits, and Clinical Perspectives of Angina

Gregg W. Stone MD

Columbia University Medical Center

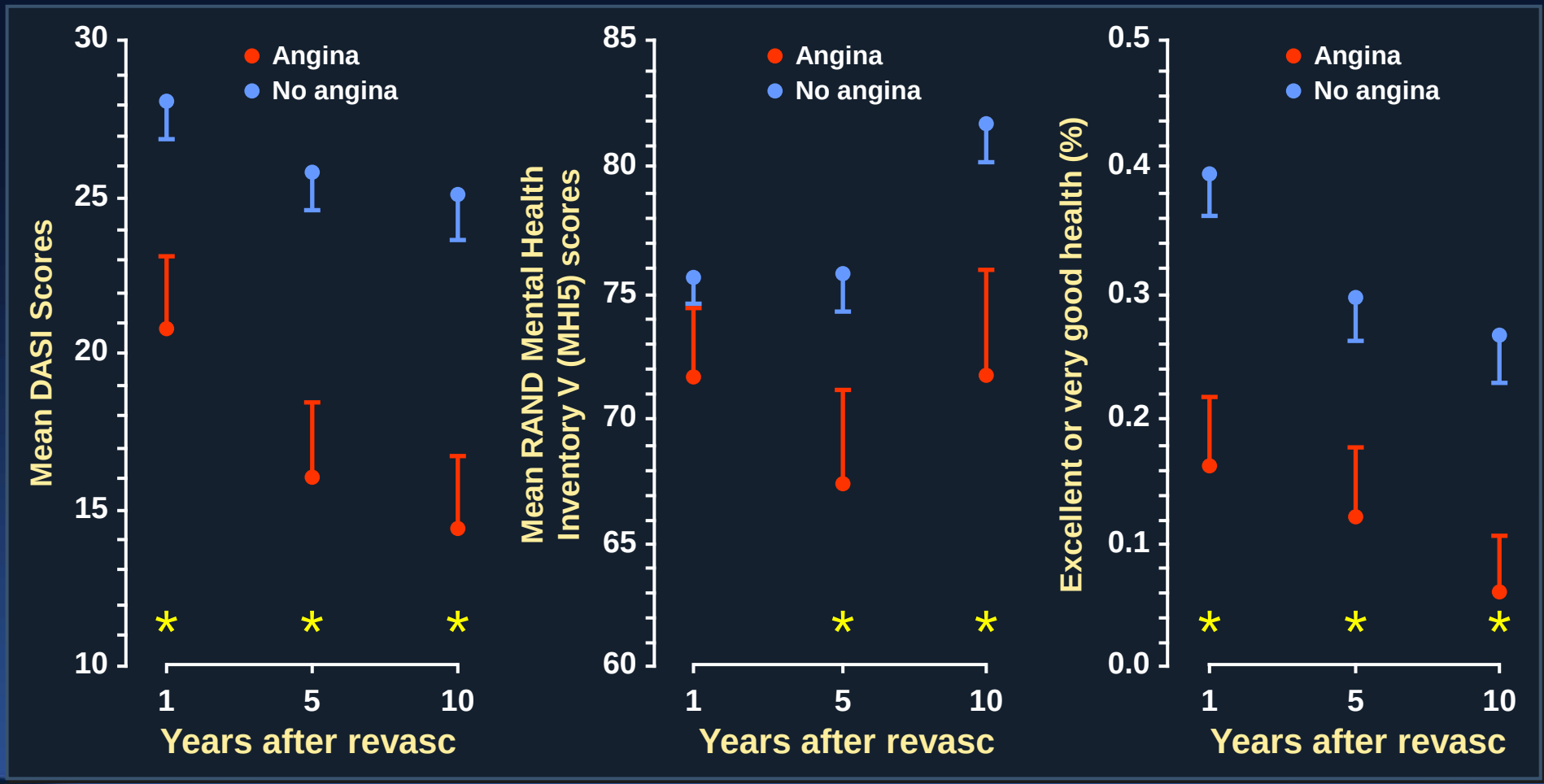
The Cardiovascular Research Foundation

Disclosures

- Consultant to Reva

BARI: Recurrent Angina After Revascularization Affects QOL

10-year FU after randomization to PCI vs CABG (n=934)



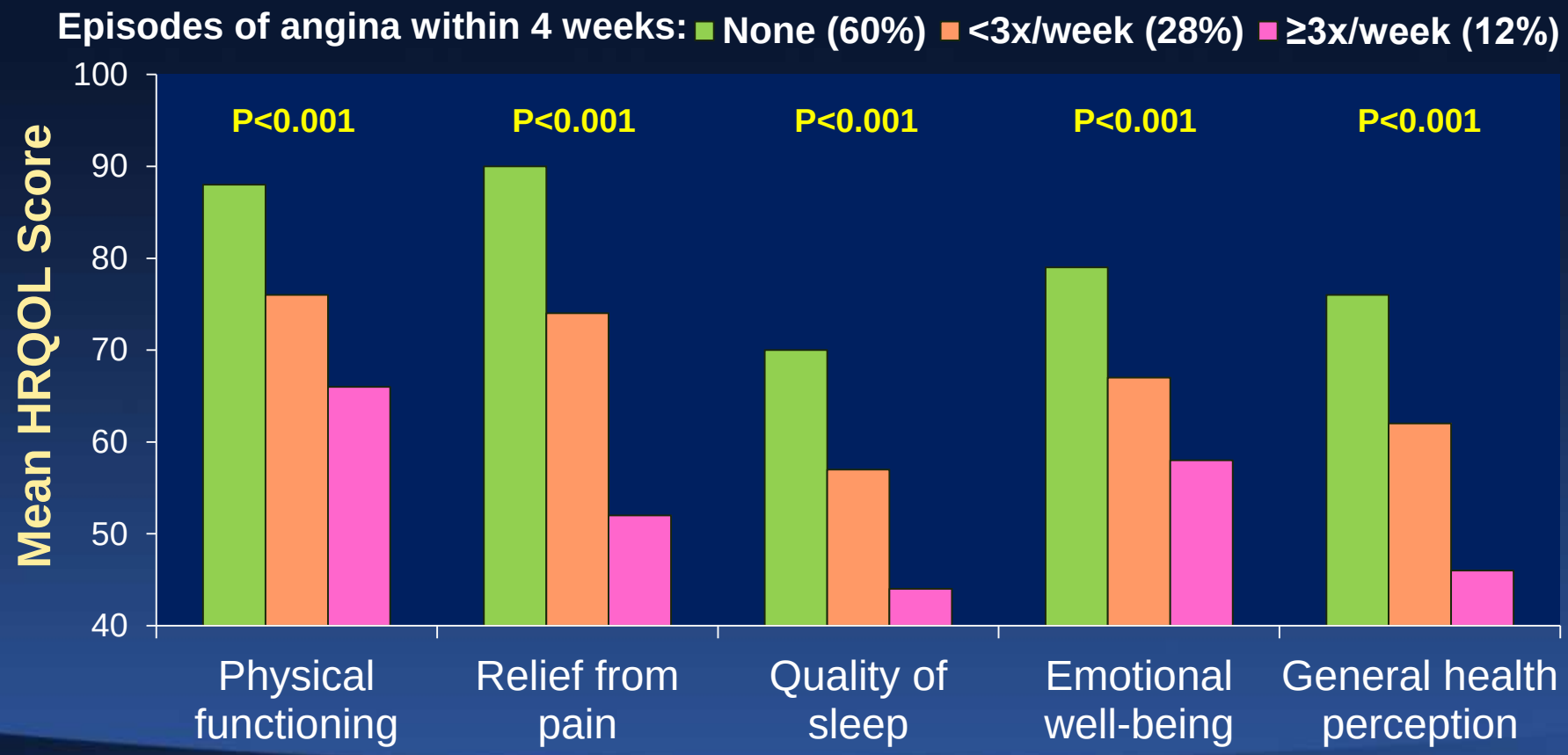
* *P*<0.001

Hlatky MA et al. *Circulation*. 2004;110:1960-6

Implications of Chronic Stable Angina Before and After Revascularization

827 pts aged 55–79 yrs in Sweden with CSA who underwent PCI or CABG in 1994 or 1995 and completed a baseline and 4-year HRQOL survey

Status 4 years after revascularization



Brorsson B et al. Heart 2002;87:140–5

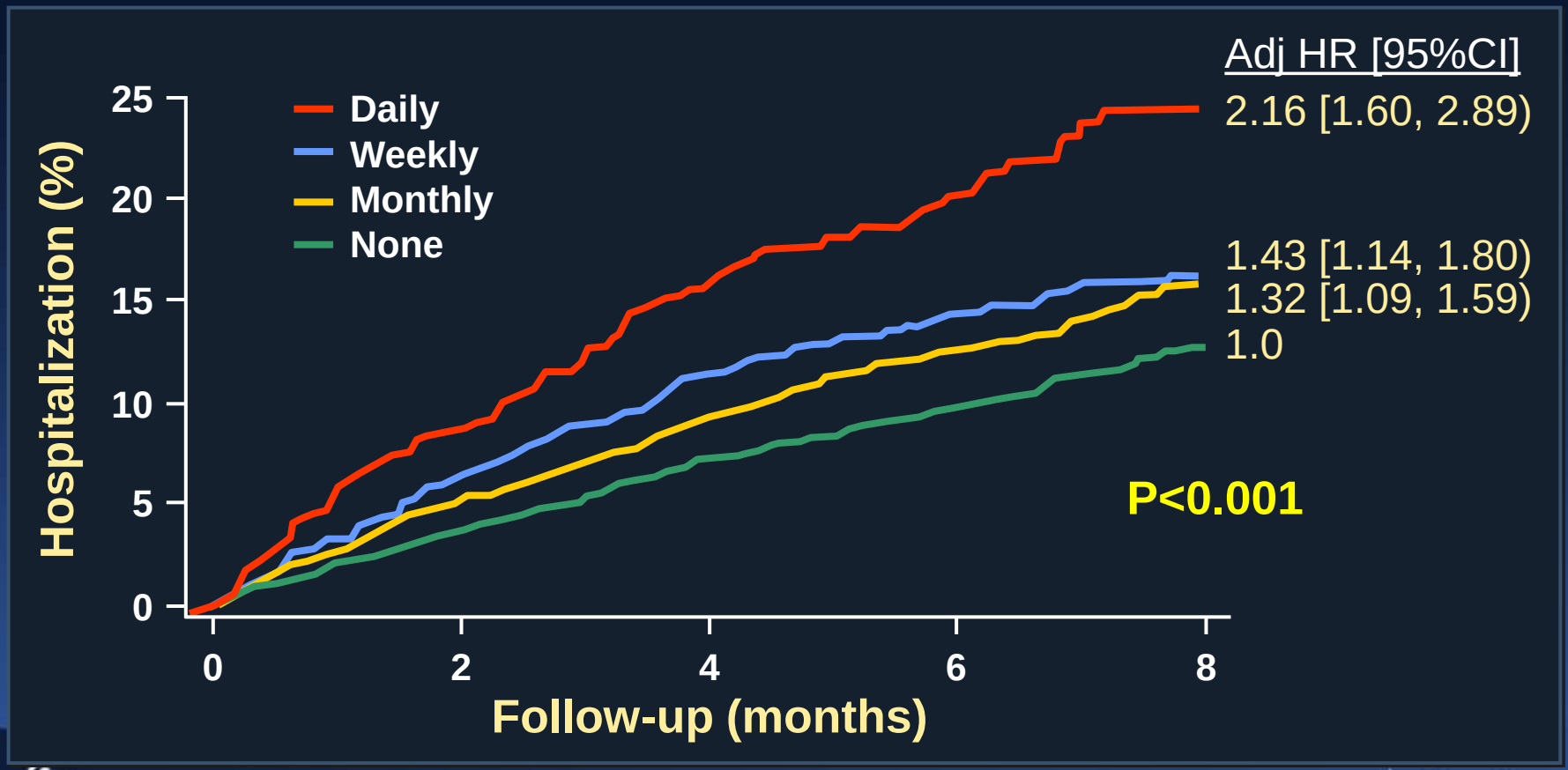
Impact of Angina: Rehospitalizations

SAQ performed in 5,460 stable pts 4 months after treatment for ACS in MERLIN, who were then followed for 8 more months

49.8% of pts reported angina at 4 months

(35.1% who had earlier revasc vs. 58.3% who did not)

8 mo CV hospitalization rates according to angina status at 4 mos



Arnold SV et al. *Circ CV Qual Outcomes* 2009;2:344-53

Readmission within 30 Days after PCI

893 (9.8%) of 9081 pts at 2 Mass. Hospitals

Top 10 causes for readmission

Chest pain or symptoms c/w angina	341 (38.1%)
Staged PCI without new symptoms	59 (6.6%)
Congestive heart failure	53 (5.9%)
Vascular/bleeding complication of PCI	39 (4.4%)
Gastrointestinal hemorrhage	28 (3.1%)
Stent thrombosis	22 (2.5%)
Syncope or presyncope	22 (2.5%)
Elective PV procedure unrelated to PCI	20 (2.2%)
Elective CABG	19 (2.1%)
Cholecystitis, colitis/enteritis, pancreatitis, cholangitis, or abdominal pain	18 (2.0%)

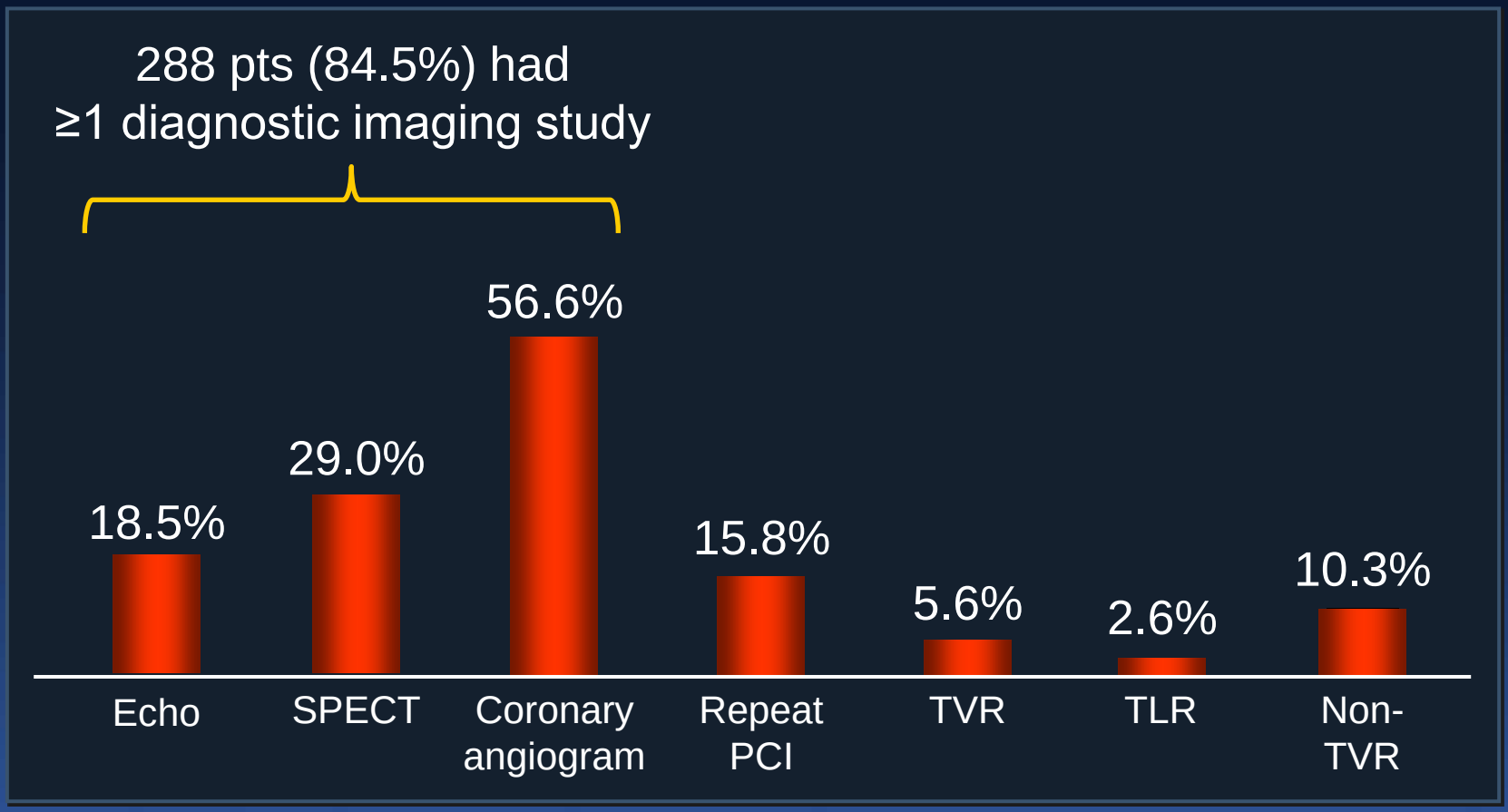
21 (6.2%) met criteria for MI

Wasfy JH et al. *Circ Cardiovasc Interv*. 2014:on-line

Readmission within 30 Days after PCI

893 (9.8%) of 9081 pts at 2 Mass. Hospitals

Resource use in 341 pts readmitted for chest pain/angina



Wasfy JH et al. *Circ Cardiovasc Interv*. 2014:on-line

Economic Impact of Angina

SAQ performed in 5,460 stable pts 4 months after treatment for ACS in MERLIN, who were then followed for 8 more months

49.8% of pts reported angina at 4 months

(35.1% who had earlier revasc vs. 58.3% who did not)

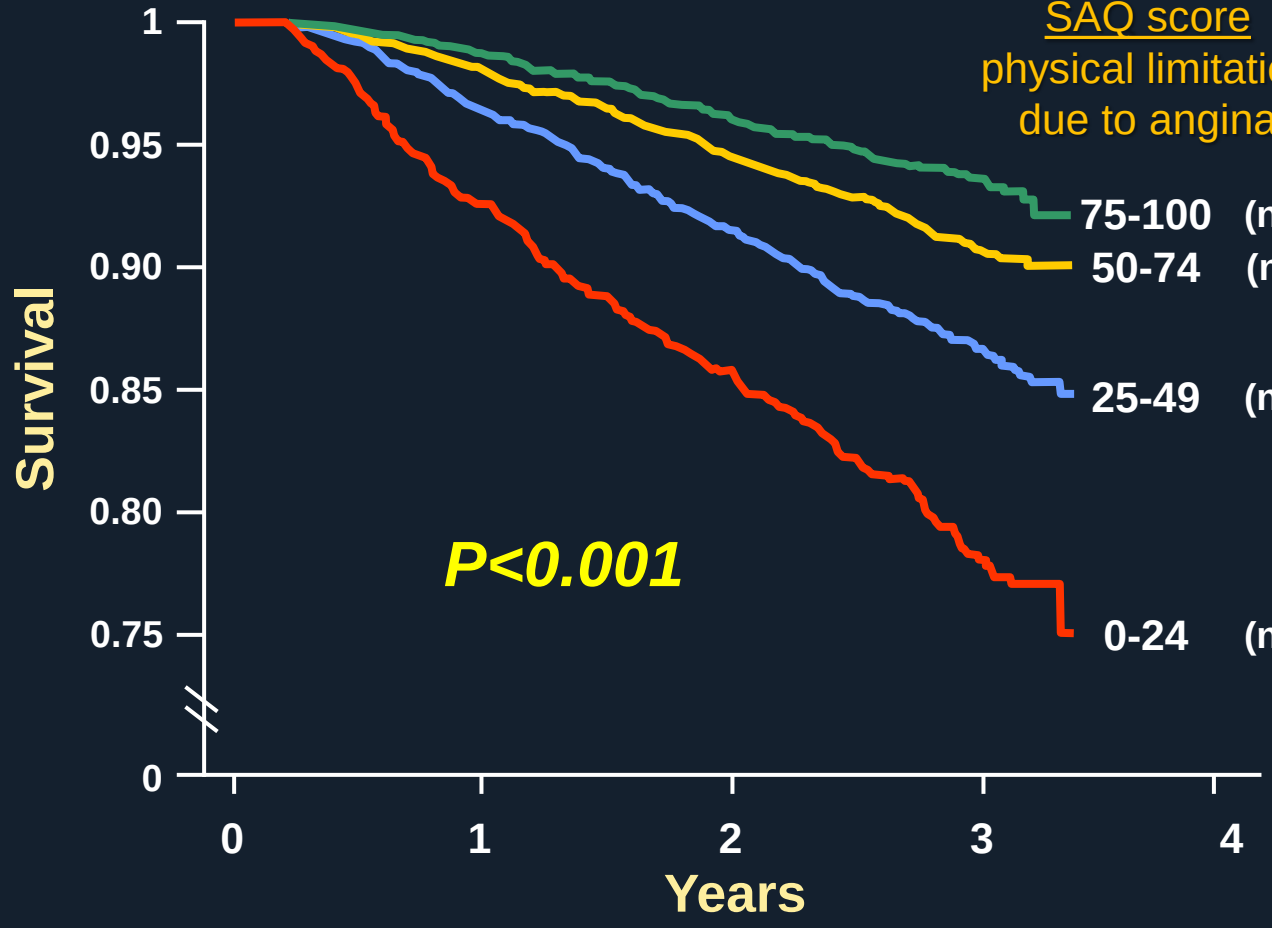
8 mo subsequent healthcare costs in pts with prior revasc according to SAQ at 4 mos

Angina frequency:	**None (n=1290)**	**Monthly (n=473)**	**Weekly (n=182)**	**Daily (n=42)**	***P***
Inpatient utilization, $					
Coronary angiogram ± PCI	578 ± 2684	1469 ± 4338	1778 ± 4239	3174 ± 6134	<0.001
Bypass graft surgeries	153 ± 2077	797 ± 4999	331 ± 3148	1993 ± 7284	<0.001
MI or angina	52 ± 550	133 ± 854	202 ± 1037	216 ± 674	0.008
Other cardiovascular diagnosis	152 ± 1725	204 ± 1937	123 ± 848	713 ± 2598	0.21
Physician fees	284 ± 1147	789 ± 2176	774 ± 1654	1889 ± 2775	<0.001
Total inpatient costs, $	1219 ± 5115	3393 ± 9574	3208 ± 7084	7985 ± 12201	<0.001
Total outpatient costs, $	311 ± 448	402 ± 558	497 ± 697	617 ± 755	<0.001
Medication cost, $	1428 ± 823	1562 ± 846	1634 ± 899	1636 ± 946	<0.001
Total costs, $	2958 ± 5362	5357 ± 9822	5339 ± 7431	10238 ± 12503	<0.001

Differences in costs were attributable primarily to higher rates of ACS hospitalization and coronary revascularization among pts with more severe angina

Angina Predicts Mortality

SAQ administered to 8,908 out-pts with CAD at 7 VA hospitals, followed for mean 2 yrs (896 deaths)



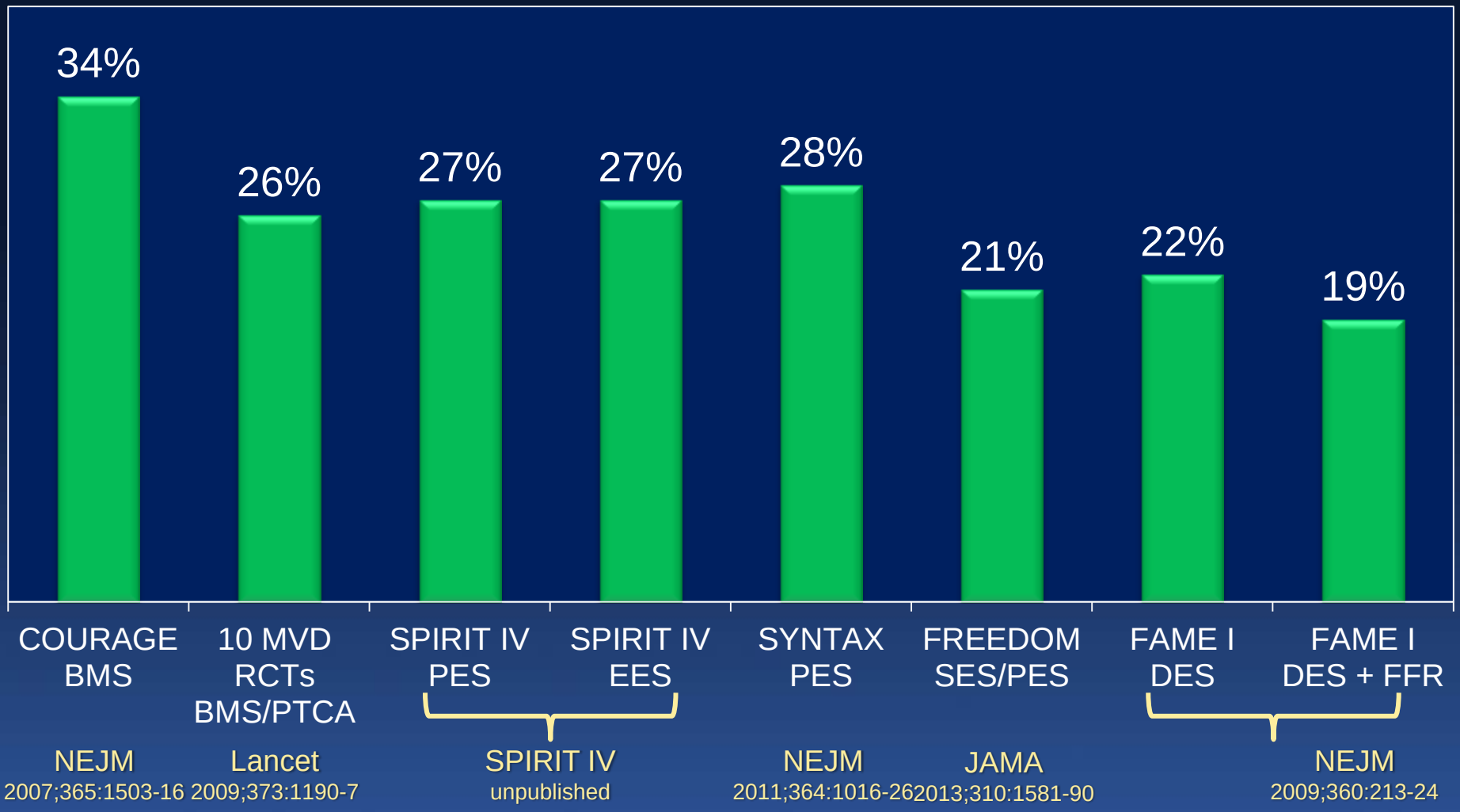
SAQ score
physical limitation
due to angina

		Adj HR [95%CI]
75-100	(n=2,073)	1.0
50-74	(n=2,462)	1.35 [1.06, 1.72)
25-49	(n=3,073)	2.08 [1.67, 2.59)
0-24	(n=1,300)	3.65 [2.91, 4.96)

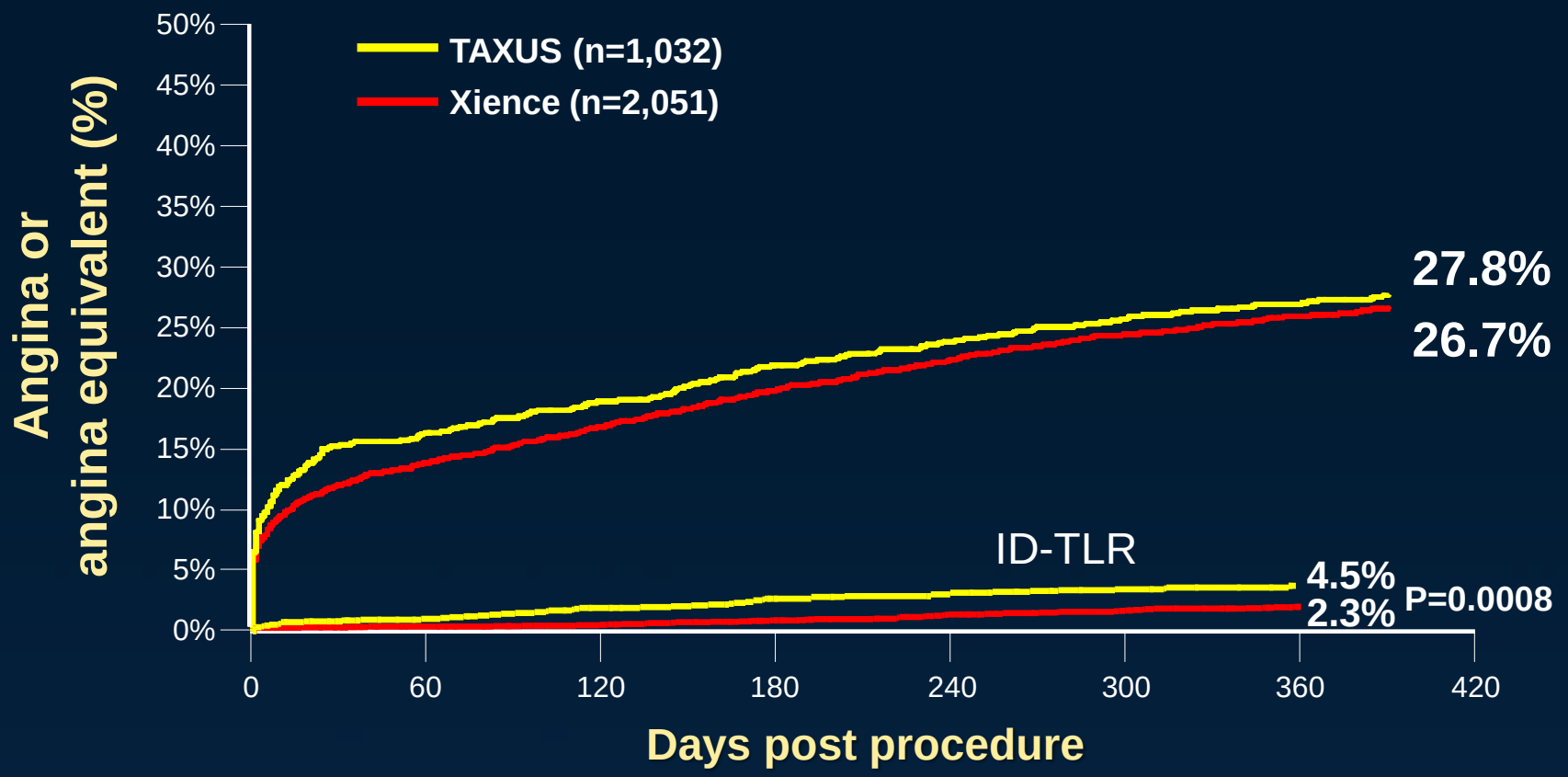
All *P<0.001* compared to score 75-100

Mozaffarian D et al. *Am Heart J* 2003;146:101-22

Angina at 1 Year After PCI



SPIRIT IV
Recurrent angina

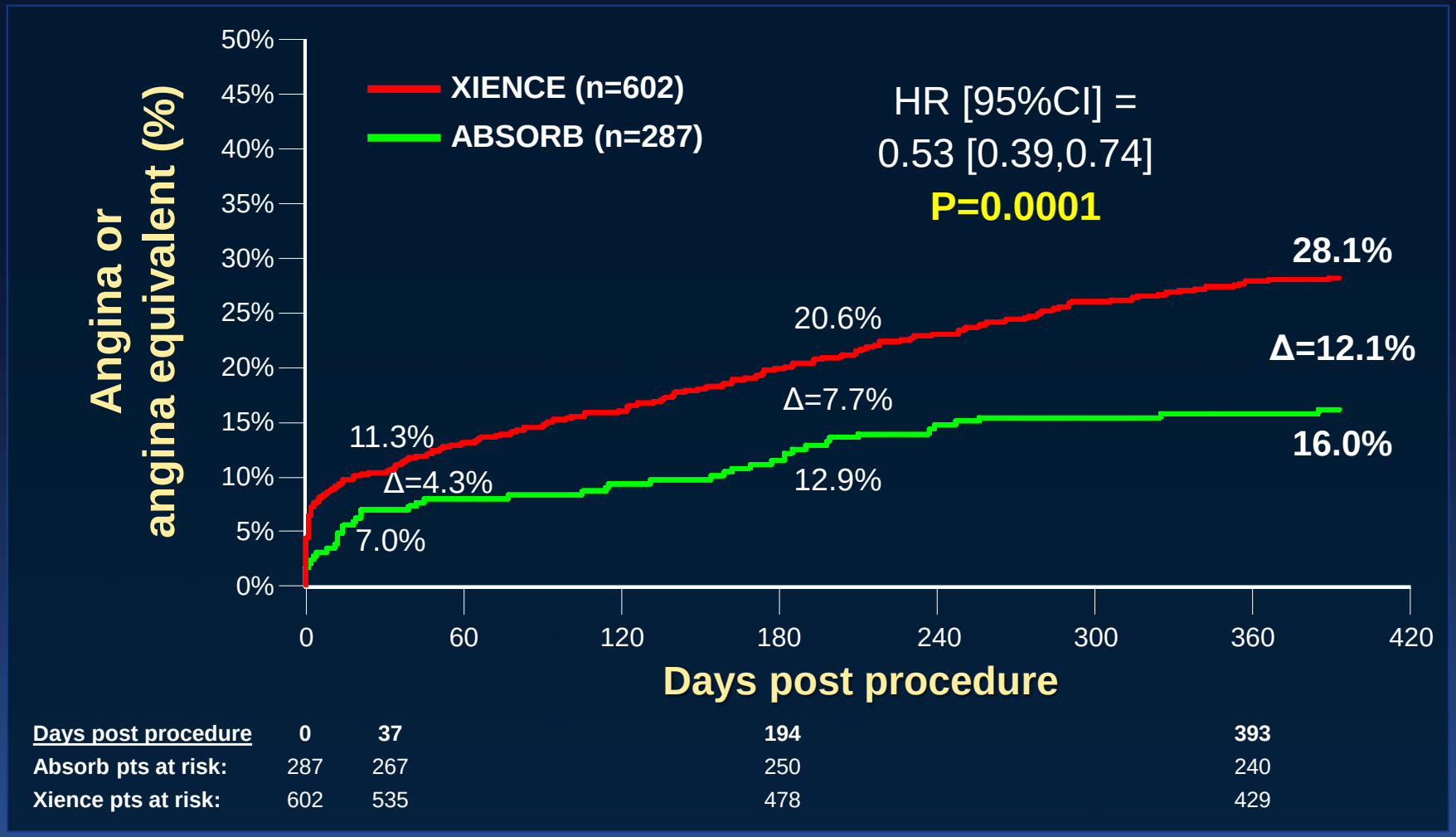


Days post procedure	0	37	194	393
Taxus pts at risk:	1032	859	782	711
Xience pts at risk:	2051	1784	1600	1438

Stone GW. TCT 2013

Angina Status: EXTEND* vs. SPIRIT IV**

Propensity matched cohorts



Days post procedure	0	37	194	393
Absorb pts at risk:	287	267	250	240
Xience pts at risk:	602	535	478	429

*Excludes non-Japanese Asian pts because of low event reporting rates; **Excludes complex pts and lesions (3 vessel PCI; PCI of 2 lesions per vessel; RCA aorto-ostial lesions; bifurcation lesions)

Data on file, Abbott Vascular

ABSORB II Randomized Trial

Prospective, single blind, randomized 2:1 Absorb BVS vs EES

501 subjects at 46 European, Israeli, and New Zealand sites

Treatment of up to 2 *de novo* lesions in separate epicardial vessels

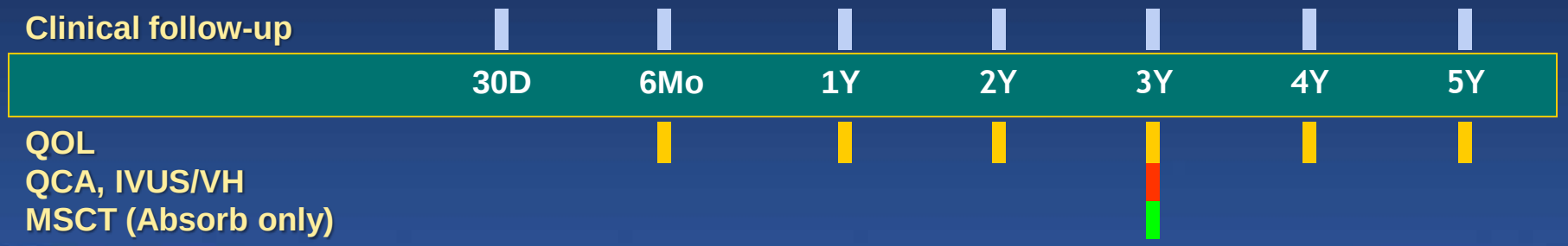
Lesion length ≤48 mm; Dmax 2.25 mm – 3.8 mm

Scaffold / stent diameters: 2.5, 3.0, 3.5 mm

Scaffold / stent lengths: 12 (3.5 mm dia), 18, 28 mm

Co-Primary Endpoints

1) Nitro-induced vasomotion at 2 years by QCA (superiority)
2) Late loss at 2 years by QCA (non-inferiority to superiority)

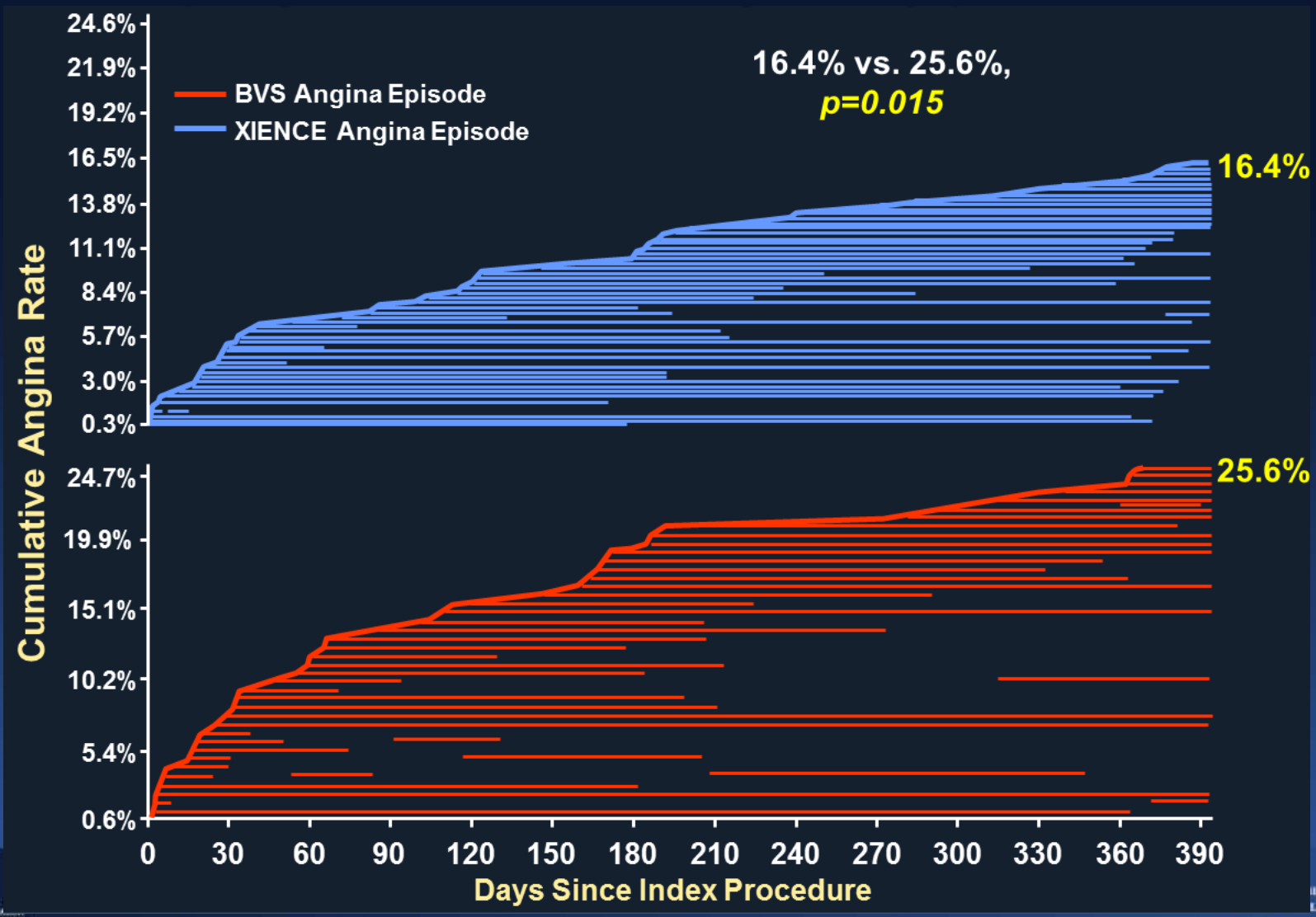


PI: Patrick W. Serruys

Co-PI: Bernard Chevalier

ABSORB II: Time to the first occurrence of angina and its duration according to AE reporting

(excluding first 7 days post randomization)



ABSORB II: Medication and Exercise Testing

	6 months			12 months		
	Absorb 335 pts	Xience 166 pts	*P*	Absorb 335 pts	Xience 166 pts	*P*
Anti-angina medications, %						
- Beta-blockers	71.0	67.9	0.48	70.5	65.9	0.29
- Calcium channel blockers	20.8	21.2	0.92	23.7	23.2	0.89
- Nitrates	17.8	26.7	0.02	19.5	26.2	0.09
- Dual antiplatelet therapy	97.3	97.0	1.00	82.8	83.1	0.93
Exercise test performed, %	91.9	94.6	0.28	86.0	85.5	0.9
- Maximal HR (beats/min)	132	132	0.93	133	135	0.38
- Maximal workload (METS)	9.02	9.05	0.95	9.32	9.41	0.83
- Exercise duration (mins)	8.10	8.53	0.22	8.55	8.99	0.26
- ≥0.1 mV ST depression or chest pain, %	18.2	20.4	0.57	15.0	15.5	0.9
Terminated due to >0.2 mV ST depression, %	4.3	17.2	0.05	4.9	5.9	1.0

Serruys PW et al. *Lancet* 2014

Possible Mechanisms for Reduced Angina with Absorb vs. Xience

- **Reduced ischemia**
  - Reduced fixed (re)stenosis
  - Reduced dynamic (re)stenosis
  - Improved vasomotor responses
  - Improved microcirculatory function
- **Neurogenic mechanism**
- **Psychogenic** (active placebo ± Hawthorne effect)

Restoration of contractile phenotype of SMC after implantation of BRS

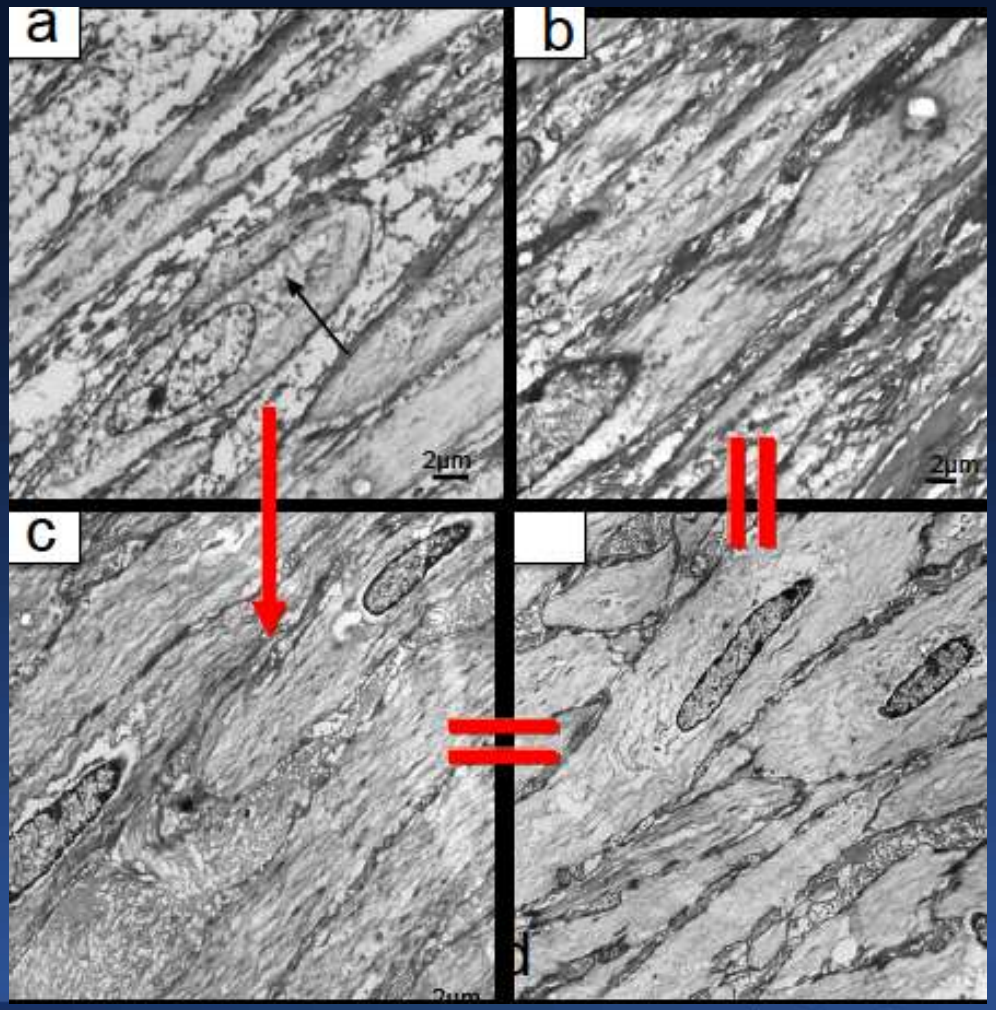
Transmission electron microscopy of neointima and media

1 month

6 months

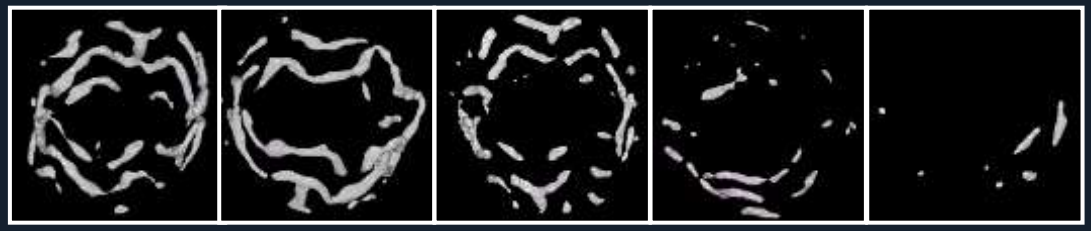
Neointima

Media



Data on file, Abbott Vascular

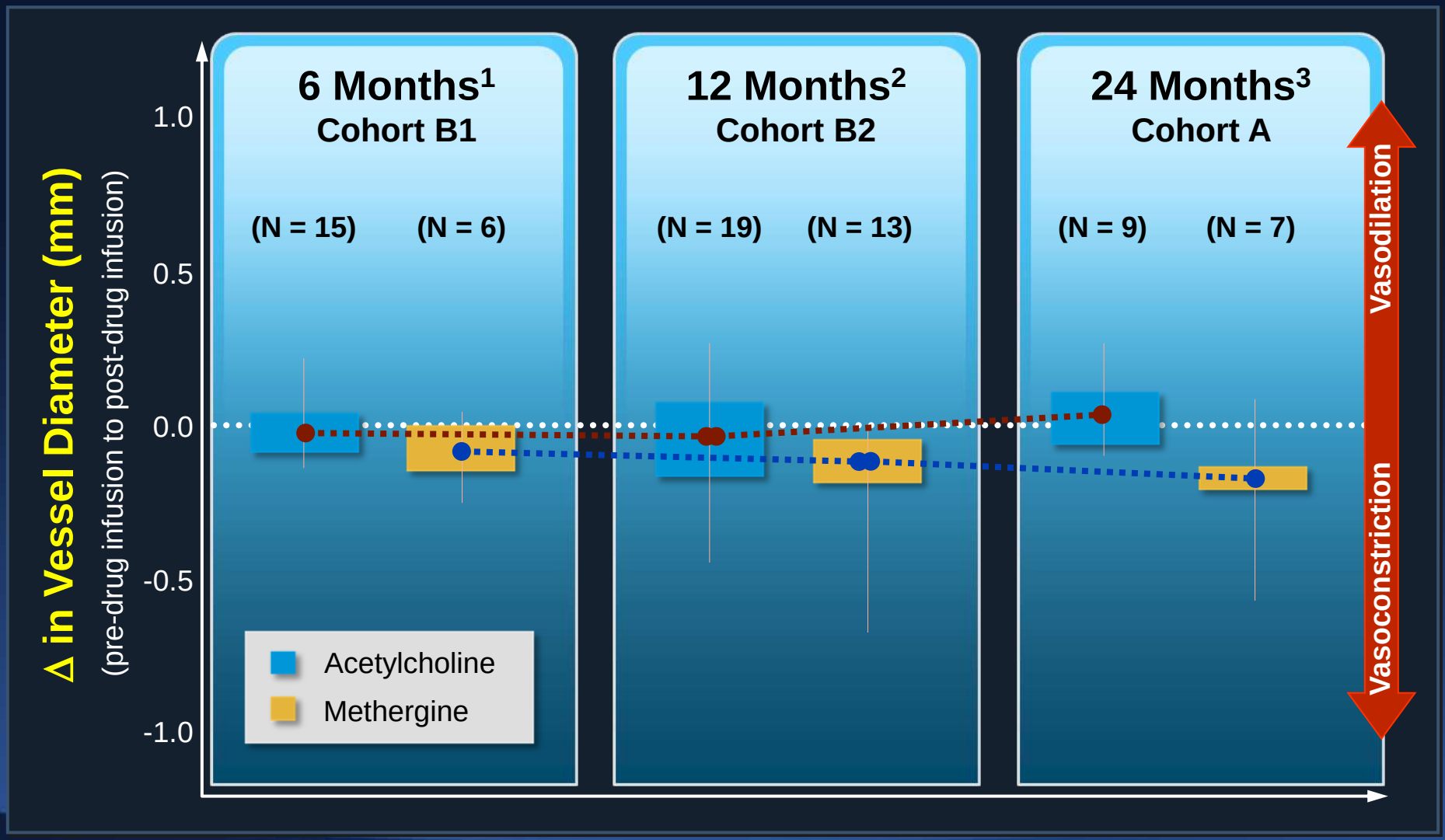
BVS: Restoration of Pulsatility in the Porcine Coronary Model



Data on file, Abbott Vascular

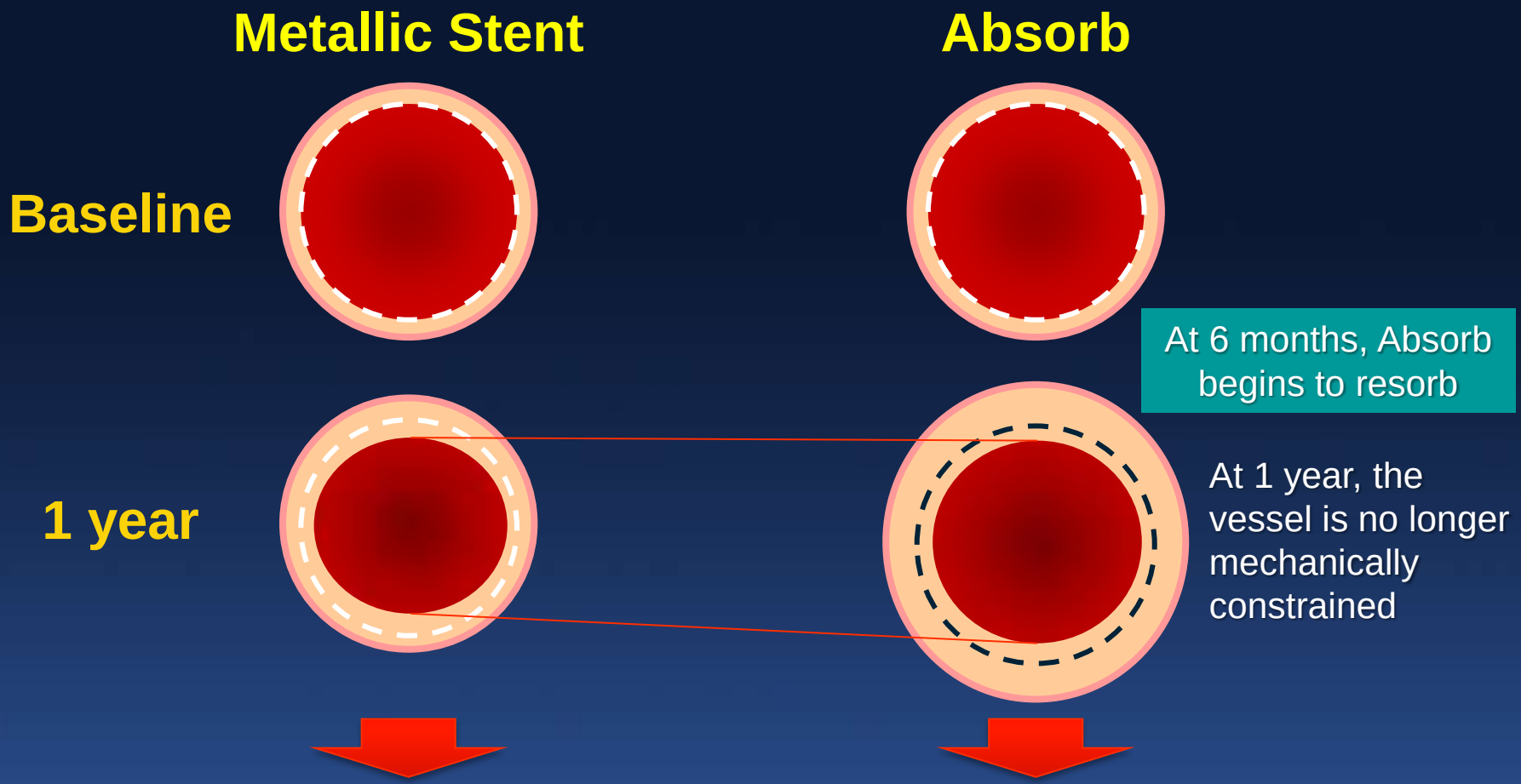
ABSORB: Vasomotion Restoration

Restoring Natural Vessel Function

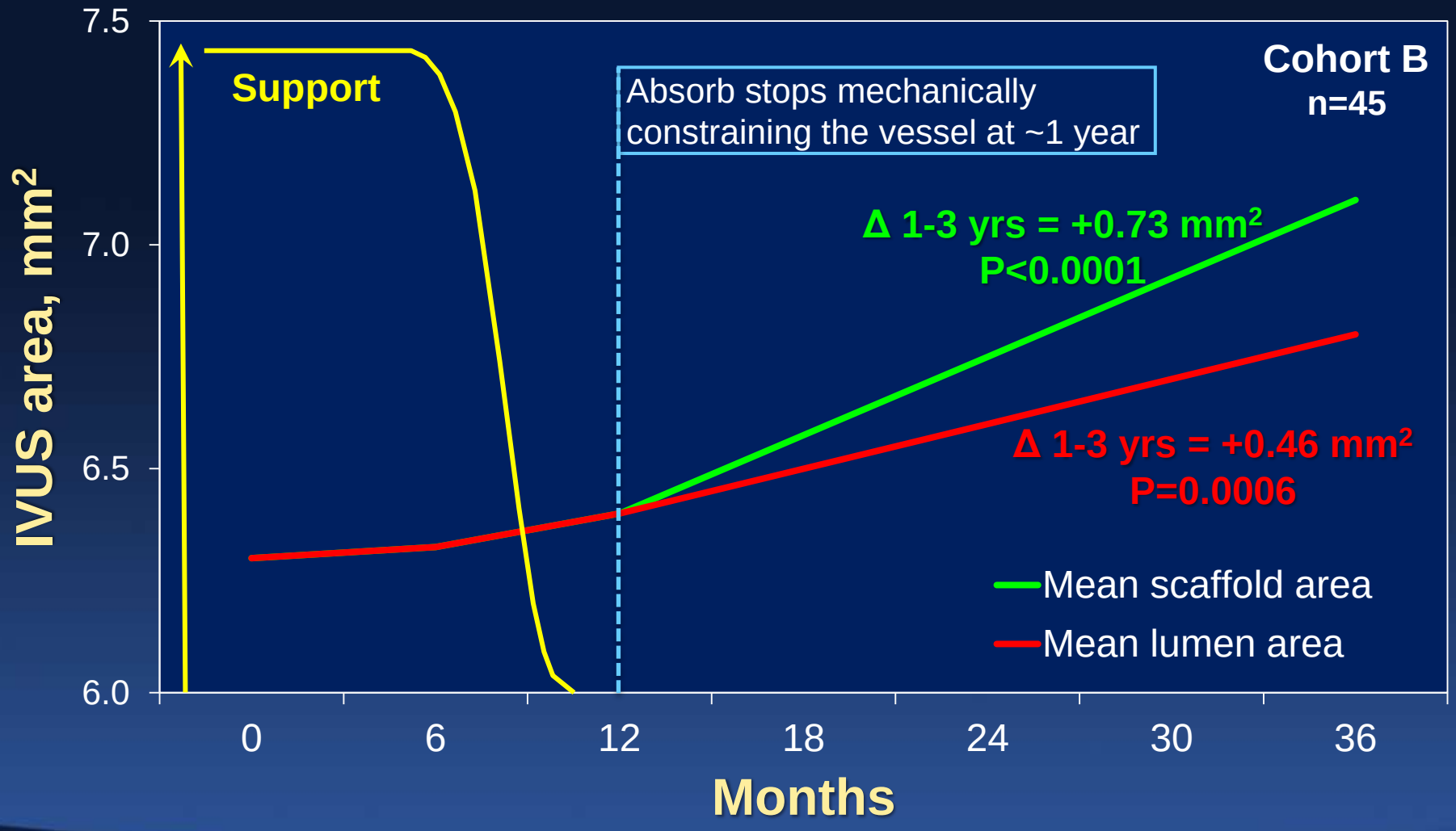


[1,2]Serruys PW. ACC 2011; [3]Serruys PW et al. *Lancet* 2009;373:897-910

Potential Causes for Less Angina and Ischemia with Absorb Compared to Metallic Stents



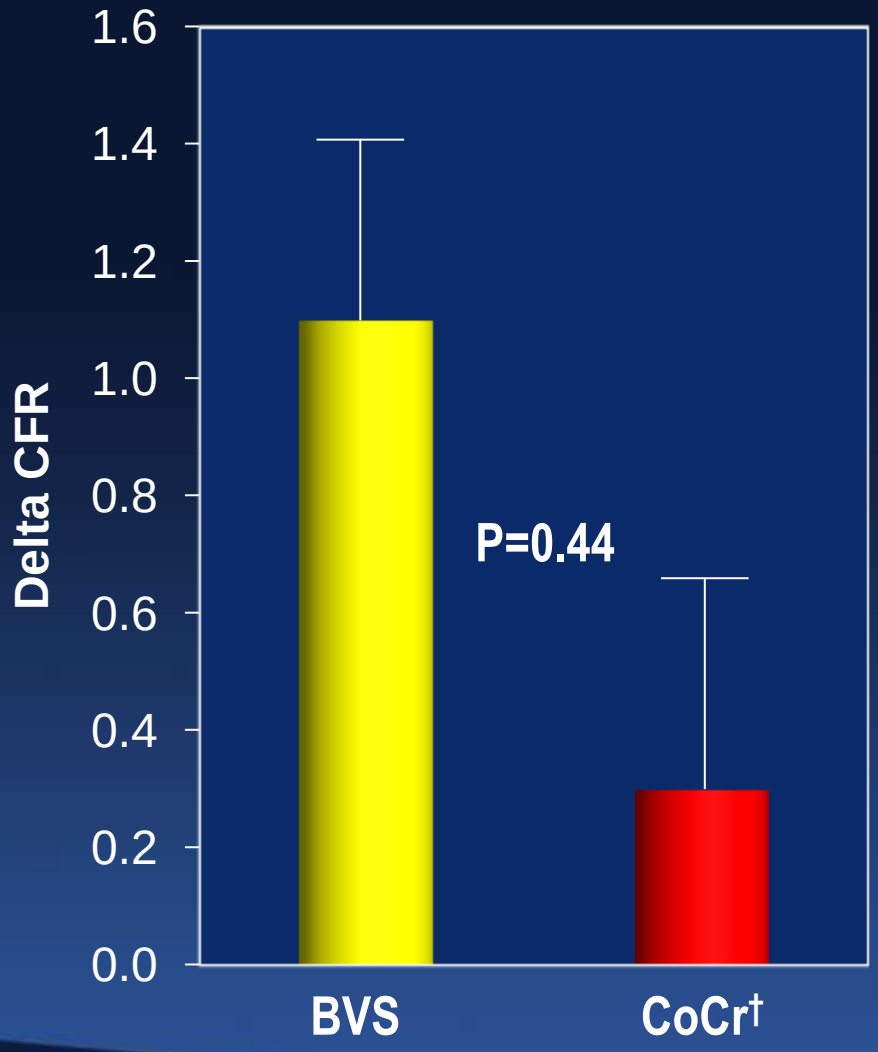
Potential Paradigm Shift: Late Lumen Gain Offers the Potential for Late Post PCI Angina Reduction

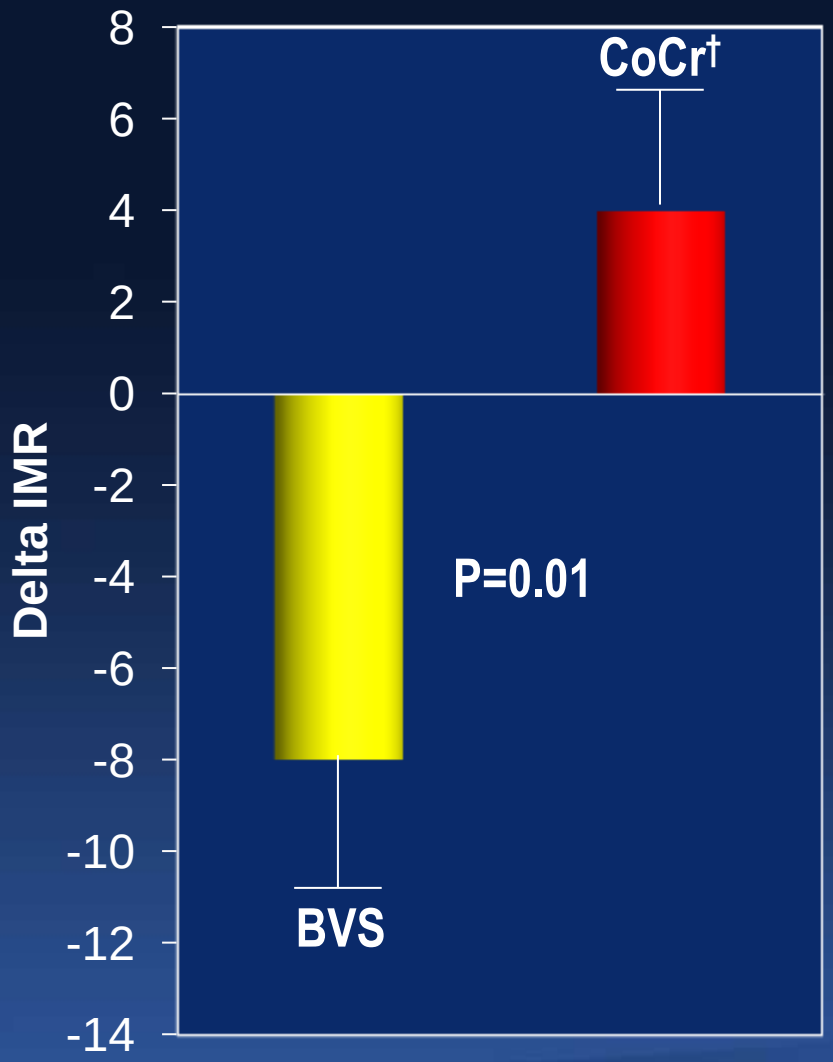


Serruys PW. EuroIntervention 2014

Change in CFR and IMR

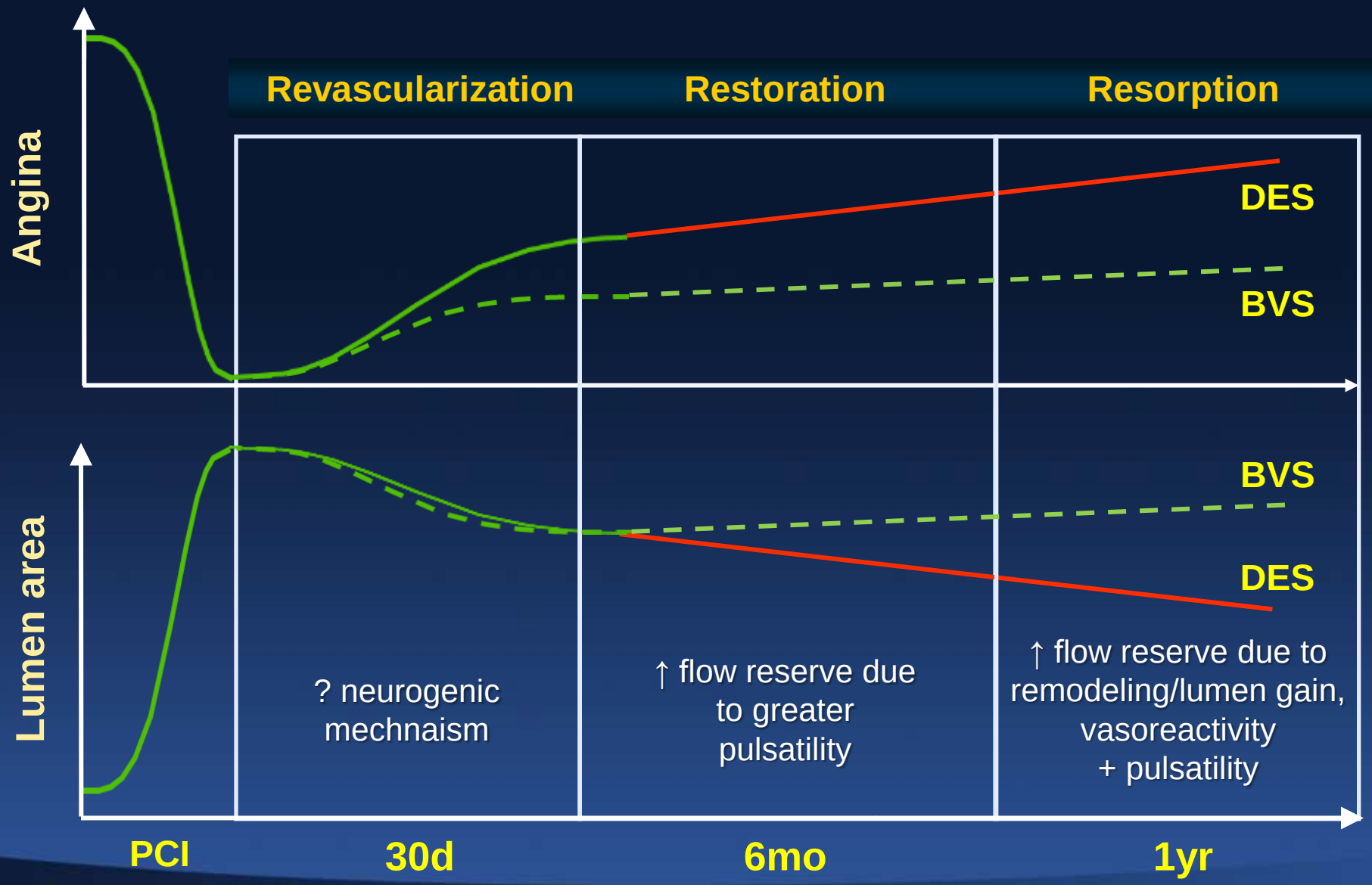
† size matched to BVS cohort (n=9)





Hoole, West , et al. EuroPCR 2014

Hypothesis on Angina vs. Lumen Size



ABSORB III + IV Randomized Trials

~5,000 pts with up to 3 de novo lesions in different epicardial vessels randomized to ABSORB v XIENCE, with FU for at least 5 years, at up to 130 sites

Primary ABSORB IV endpoints (superiority):

1. Angina at 1 year (n=3,000 from ABSORB IV)
2. TLF between 1 and 5 yrs (n=5,000, landmark analysis)

Absorb IV PRO (baseline, 1, 3, 6, 9 months, 1, 2 and 3 years)

Detailed angina CRF, + validated instruments: Seattle Angina Questionnaire (SAQ), Rose Dyspnea Scale (RDS), EuroQoL 5D (EQ5D)

Detailed assessment of hospitalizations, revascularizations, MACE

Detailed resource utilization and cost data through 5 years

Ischemia substudy (RESOLVE): CTA, CT perfusion, CT_{FFR} and SPECT at multiple time points

CARDIOVASCULAR RESEARCH FOUNDATION
A Passion for Innovation

PI: GW Stone
Co-PIs: SG Ellis, DJ Kereiakes

COLUMBIA UNIVERSITY MEDICAL CENTER
NewYork-Presbyterian

Assessment of Angina in ABSORB IV
Unique aspects

- Inclusion criteria
  - Symptomatic angina (stable or ACS) or if silent ischemia, history of typical angina within prior 1 year
  - Evidence of ischemia if DS <70% (e.g. +FFR)
- Detailed 5 page eCRF to ask about anginal symptoms at 1, 3, 6, 9, 12 months, and then yearly through 5 years
- Detailed collection of anti-ischemic meds at each FU time
- Angina Primary Endpoint: Angina or angina equivalent symptoms within 1 yr (excluding symptoms through hosp discharge or 7 days, whichever occurs first) as adjudicated by a blinded clinical events committee (CEC) from the eCRF and source docs
- QCA assessment of incomplete revascularization and its relationship to angina

Assessment of Angina in ABSORB IV
Maintaining the blind

- Single-blind trial
- Study site personnel will be trained not to disclose the treatment assignment to the subject
- Headphones playing music during the procedure will be worn by the patient to reduce the possibility of unblinding
- Blinded follow-up site personnel, not present at the index procedure, will be assigned to conduct the clinical follow-up using a standard follow-up interview script in order to reduce bias

Assessment of Angina in ABSORB IV

Perception analysis

- Pts may develop a belief as to which device they received, even if the blind is maintained, which may affect PRO
- A perception assessment questionnaire will be administered by the research coordinator post-procedure (≥4 hours to ≤7 days after the procedure, during the angina “blanking” period), and at 1 year
- Angina outcomes will be analyzed according to perception of treatment received

Assessment of Angina in ABSORB IV

ABSORB-RESOLVe Ischemia Substudy

- 370 pts successfully treated with the assigned study device will undergo:
  - Immediate post-PCI (<7d) CTA, CT perfusion, and FFR_{CT}
  - 1 year exercise SPECT
  - 5 year CTA, CT perfusion, and FFR_{CT}
- Blinded SPECT and CT core lab analysis
- Endpoints:
  - Target lesion/vessel and global ischemia
    - Between group and within person (serial CT)
      - Exercise and pharmacologic stress
      - At different life-cycles of the scaffold
  - Morphologic lesion changes at 5 years (CTA)

ABSORB III + IV

Status Update

1) ABSORB III: 2,008 patients were enrolled as of April 3rd, 2013

1-year results will be reported in Fall of 2015

2) ABSORB IV: Enrollment is ongoing at ~130 US and Canadian sites