Updated meta-analysis for bioresorbable scaffolds: sum up many, many meta for BVS

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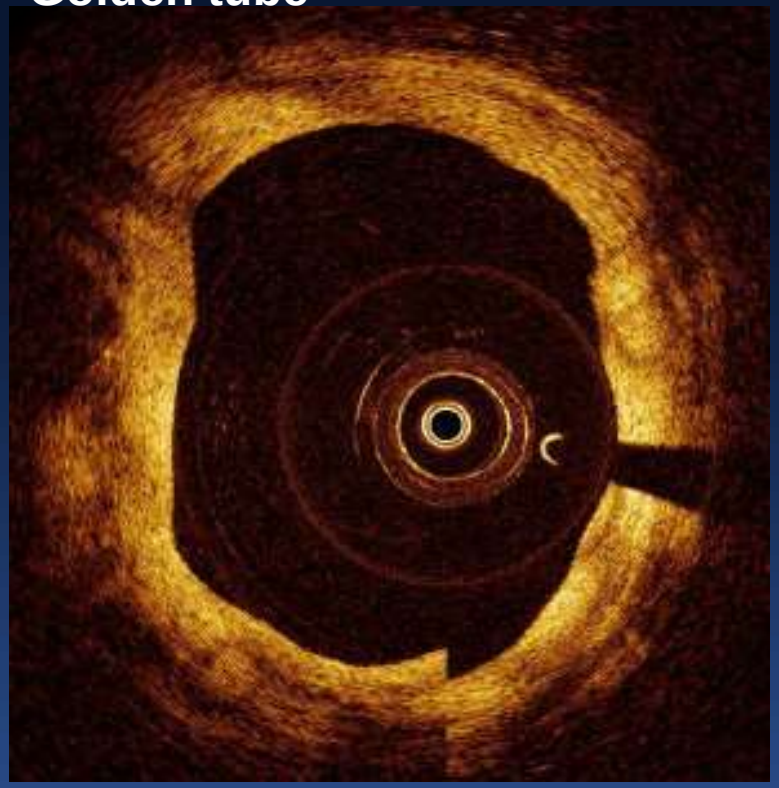
Conflict of interest

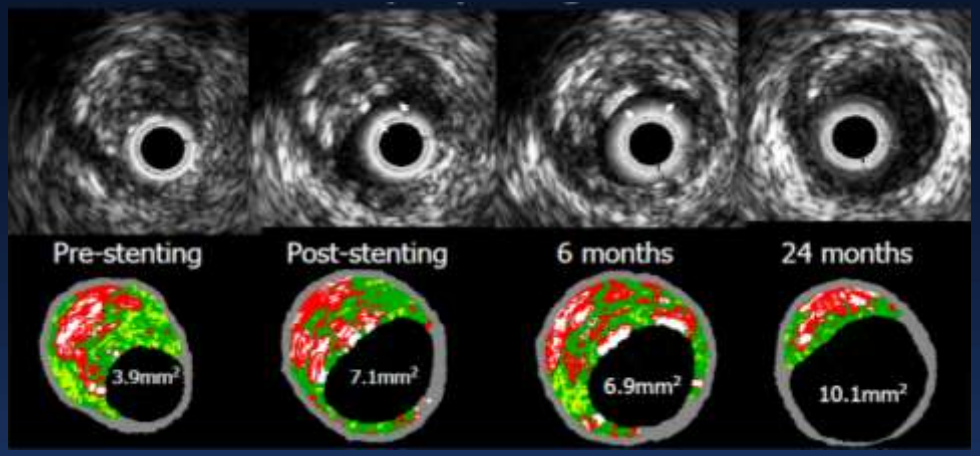
- Leture fees from Abbott

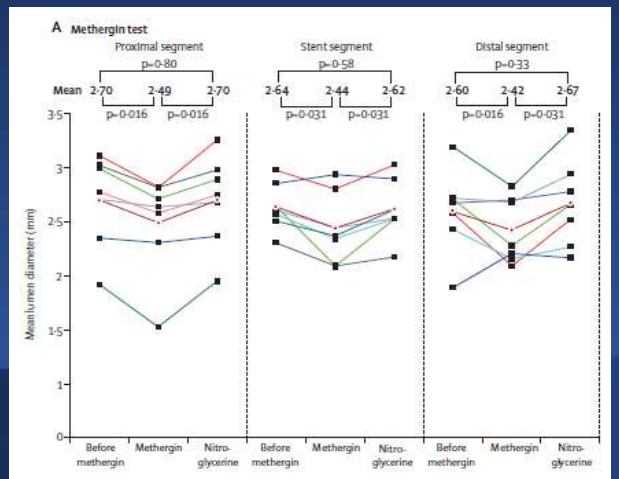
BVS: the promise of a golden tube and plaque regression

Golden tube



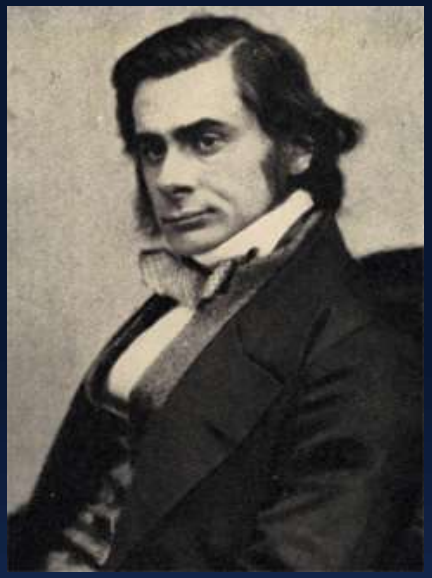
Plaque regression





Restoration of vasoreactivity

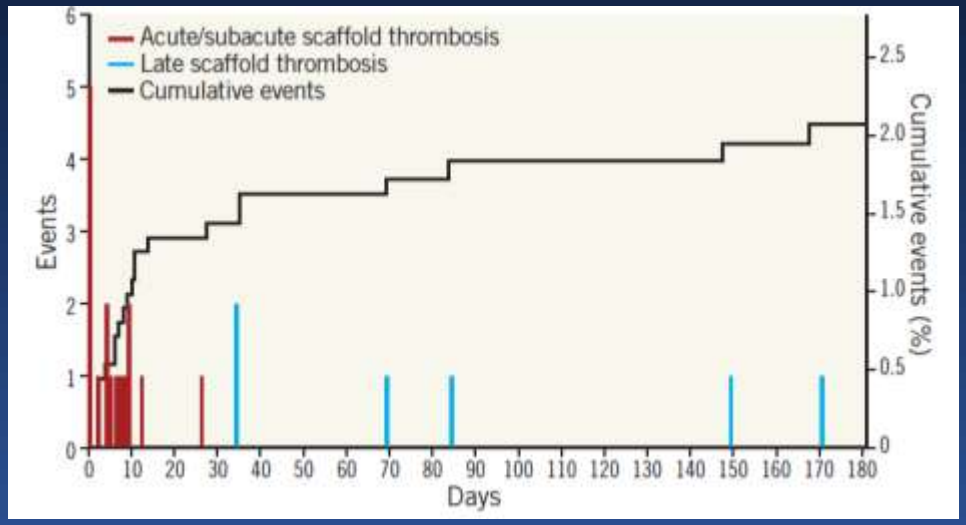
The great tragedy of science - the slaying of a beautiful hypothesis by an ugly fact.

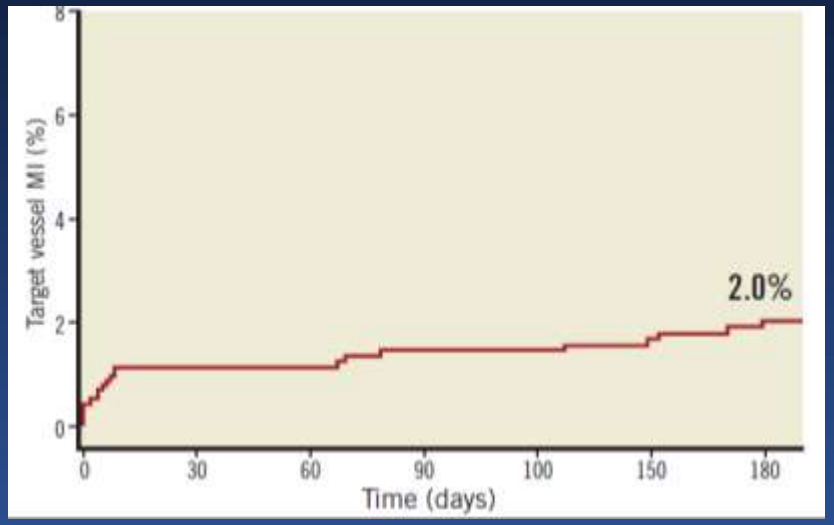


Thomas Huxley

Percutaneous coronary intervention with everolimus-eluting bioresorbable vascular scaffolds in routine clinical practice: early and midterm outcomes from the European multicentre GHOST-EU registry

Davide Capodanno[1], MD, PhD; Tommaso Gori[2], MD, PhD; Holger Nef[3], MD; Azeem Latib[4], MD; Julinda Mehilli[5], MD; Maciej Lesiak[6], MD; Giuseppe Caramanno[7], MD; Christoph Naber[8], MD; Carlo Di Mario[9], MD; Antonio Colombo[4], MD; Piera Capranzano[1], MD; Jens Wiebe[3], MD; Aleksander Araszkiewicz[6], MD; Salvatore Geraci[7], MD; Stelios Pyxaras[8], MD; Alessio Mattesini[9], MD; Toru Naganuma[4], MD; Thomas Münzel[2], MD; Corrado Tamburino[1], MD, PhD





Seven trials with BVS including 5,583 patients

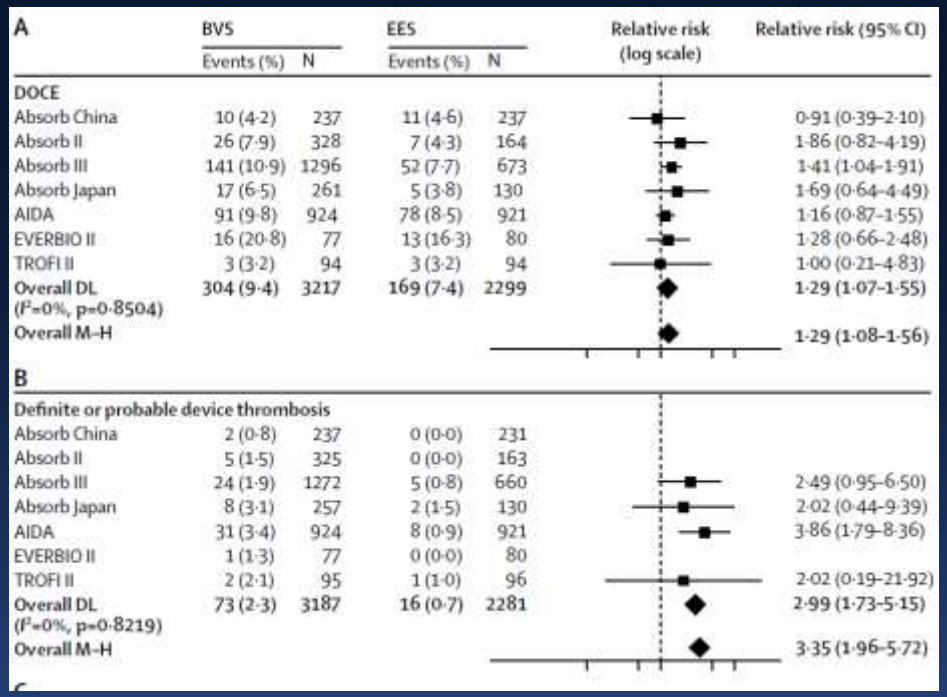
Study	Year	N of pts	Device used	Latest fup	ACS	Primary endpoint
ABSORB China	2016	480	BVS vs CoCr-EES	3 years	65 %	1-year LLL
ABSORB II	2016	501	BVS vs CoCr-EES	4 years	21%	3-year vasomotion
ABSORB III	2017	2008	BVS vs CoCr-EES	3 years	25%	1-year TLF
ABSORB JAPAN	2016	400	BVS vs CoCr-EES	3 years	13%	1-year TLF
AIDA	2017	1845	BVS vs CoCr-EES	2 years	54%	2-year TVF
EVERBIO II	2016	158	BVS vs PtCr-EES vs BES	2 years	40%	9-month LLL
TROFI II	2016	191	BVS vs CoCr-EES	2 years	100% (STEMI)	6-month healing score

Author 14 meta-analysis	Year	N of trials	Type of analyses	Mean fup	ER
Cassese S.	2016	6 RCT	Aggregate data	12 mo	OR
Lipinski M.J.	2016	2 RCT + 23 registry	Aggregate data	6.4 ± 5.1 mo	OR
Zhang X.	2016	6 RCT + 38 registry	Aggregate data	10.5 months	OR
Stone G.W.	2016	4 RCT	IPD	12 months	RR
Ziad A Ali	*2017*	7 RCT	Aggregate data + IPD	24 months	RR
Montone R. A.	2017	7 RCT	Aggregate data	24 months	HR
Nairooz R.	2017	3 RCT 2 registry	Aggregate data	24 months	OR
Polimeni A.	2017	5 RCT	Aggregate data	24 months	OR
Sorrentino S.	2017	7 RCT	Aggregate data	24 months	RR
Zhang X.	2017	7 RCT + 38 registry	Aggregate data	25 months	OR
Toyota T.	2017	3 RCT + 4 registry	Aggregate data	24 months	OR
Mahmoud A.N.	2017	6 RCT	Aggregate data	25 months	RR
Ziad A. Ali	2018	4 RCT	IPD	36 months	RR
Kang Si H	2018	91 RCT	Network, aggregate data	42 months	OR

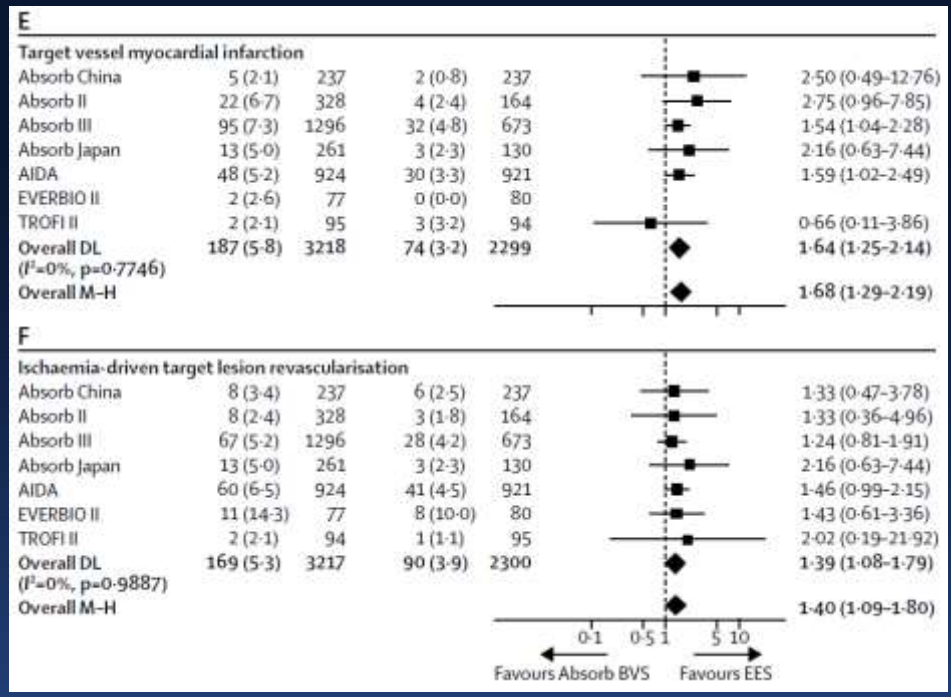
Summing up meta-analyses

- No significant difference in mortality.
- Increased rates of stent thrombosis with BVS.
- Increased rates of MI with BVS (driven by higher rates of target vessel-related MI).
- Higher rates of TLF and ischemia driven TLR in some, but not all meta-analyses (depending on fup duration).
- Greater in-device late lumen loss.

BVS vs metallic DES: 2-year outcomes



A	BVS Events (%)	BVS N	EES Events (%)	EES N	Relative risk (log scale)	Relative risk (95% CI)
DOCE						
Absorb China	10 (4·2)	237	11 (4·6)	237		0·91 (0·39–2·10)
Absorb II	26 (7·9)	328	7 (4·3)	164		1·86 (0·82–4·19)
Absorb III	141 (10·9)	1296	52 (7·7)	673		1·41 (1·04–1·91)
Absorb Japan	17 (6·5)	261	5 (3·8)	130		1·69 (0·64–4·49)
AIDA	91 (9·8)	924	78 (8·5)	921		1·16 (0·87–1·55)
EVERBIO II	16 (20·8)	77	13 (16·3)	80		1·28 (0·66–2·48)
TROFI II	3 (3·2)	94	3 (3·2)	94		1·00 (0·21–4·83)
Overall DL (I^2=0%, p=0·8504)	304 (9·4)	3217	169 (7·4)	2299		1·29 (1·07–1·55)
Overall M–H						1·29 (1·08–1·56)
B						
Definite or probable device thrombosis						
Absorb China	2 (0·8)	237	0 (0·0)	231		
Absorb II	5 (1·5)	325	0 (0·0)	163		
Absorb III	24 (1·9)	1272	5 (0·8)	660		2·49 (0·95–6·50)
Absorb Japan	8 (3·1)	257	2 (1·5)	130		2·02 (0·44–9·39)
AIDA	31 (3·4)	924	8 (0·9)	921		3·86 (1·79–8·36)
EVERBIO II	1 (1·3)	77	0 (0·0)	80		
TROFI II	2 (2·1)	95	1 (1·0)	96		2·02 (0·19–21·92)
Overall DL (I^2=0%, p=0·8219)	73 (2·3)	3187	16 (0·7)	2281		2·99 (1·73–5·15)
Overall M–H						3·35 (1·96–5·72)



E						
Target vessel myocardial infarction						
Absorb China	5 (2·1)	237	2 (0·8)	237		2·50 (0·49–12·76)
Absorb II	22 (6·7)	328	4 (2·4)	164		2·75 (0·96–7·85)
Absorb III	95 (7·3)	1296	32 (4·8)	673		1·54 (1·04–2·28)
Absorb Japan	13 (5·0)	261	3 (2·3)	130		2·16 (0·63–7·44)
AIDA	48 (5·2)	924	30 (3·3)	921		1·59 (1·02–2·49)
EVERBIO II	2 (2·6)	77	0 (0·0)	80		
TROFI II	2 (2·1)	95	3 (3·2)	94		0·66 (0·11–3·86)
Overall DL (I^2=0%, p=0·7746)	187 (5·8)	3218	74 (3·2)	2299		1·64 (1·25–2·14)
Overall M–H						1·68 (1·29–2·19)
F						
Ischaemia-driven target lesion revascularisation						
Absorb China	8 (3·4)	237	6 (2·5)	237		1·33 (0·47–3·78)
Absorb II	8 (2·4)	328	3 (1·8)	164		1·33 (0·36–4·96)
Absorb III	67 (5·2)	1296	28 (4·2)	673		1·24 (0·81–1·91)
Absorb Japan	13 (5·0)	261	3 (2·3)	130		2·16 (0·63–7·44)
AIDA	60 (6·5)	924	41 (4·5)	921		1·46 (0·99–2·15)
EVERBIO II	11 (14·3)	77	8 (10·0)	80		1·43 (0·61–3·36)
TROFI II	2 (2·1)	94	1 (1·1)	95		2·02 (0·19–21·92)
Overall DL (I^2=0%, p=0·9887)	169 (5·3)	3217	90 (3·9)	2300		1·39 (1·08–1·79)
Overall M–H						1·40 (1·09–1·80)

0·1 0·5 1 5 10

Favours Absorb BVS Favours EES

Ali et al; Lancet 2016

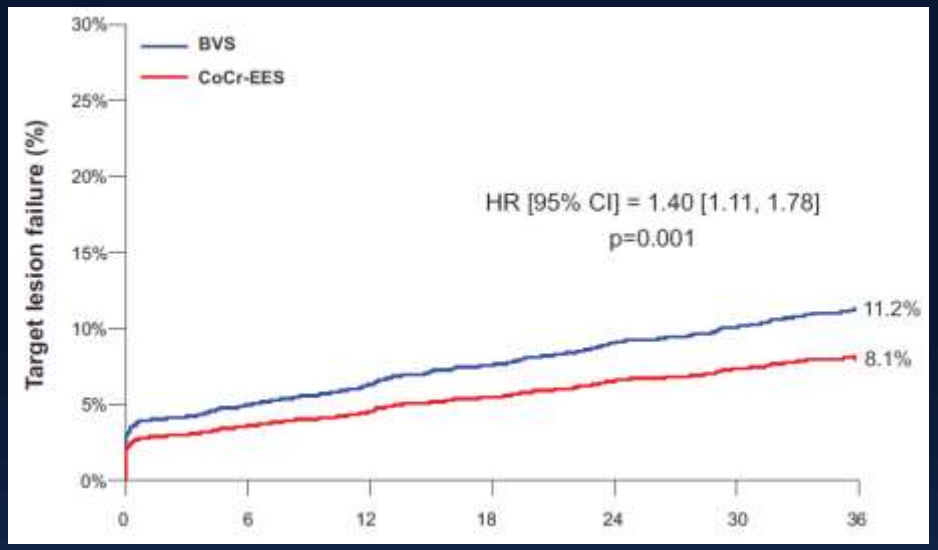
Three-Year Outcomes With the Absorb Bioresorbable Scaffold

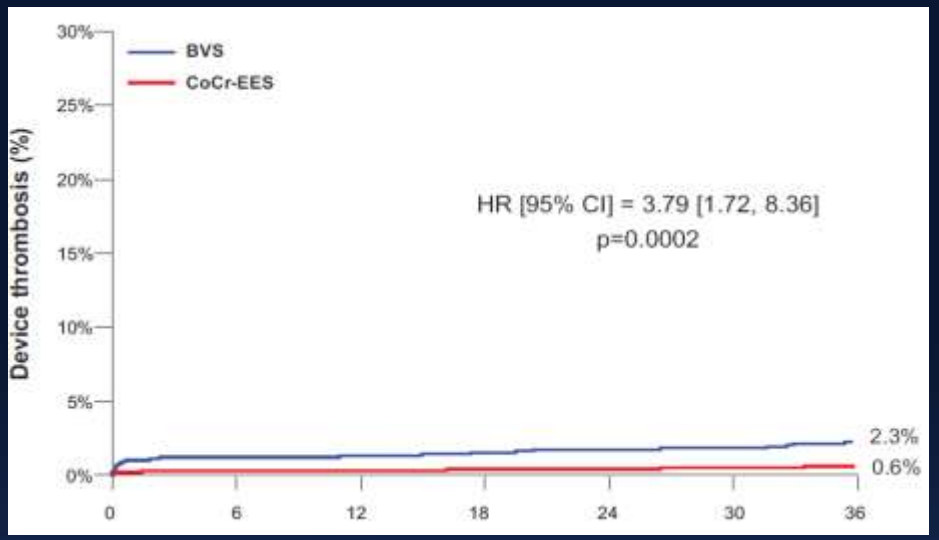
Individual-Patient-Data Meta-Analysis From the ABSORB Randomized Trials

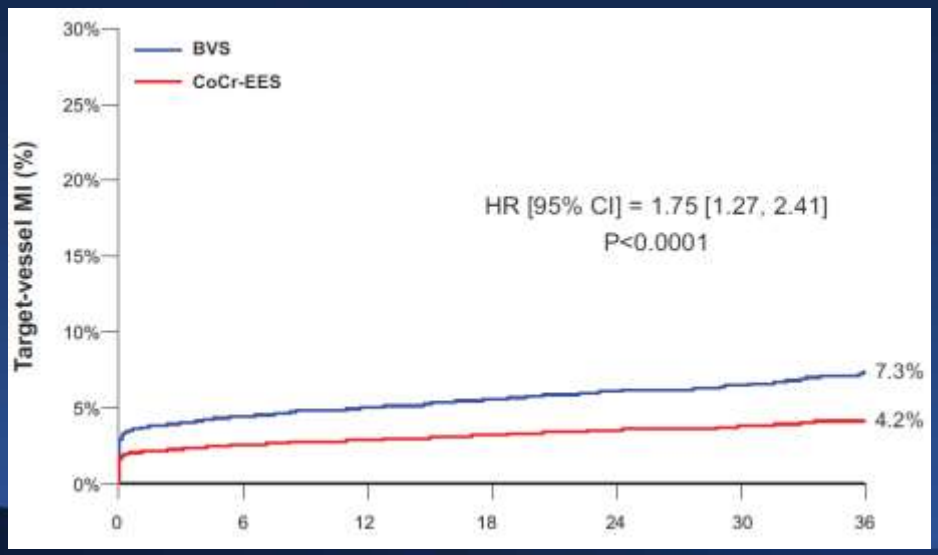
- **Time to event curves to elucidate the temporal sequence of events.**
- **Multivariable analyses to identify independent predictors of outcomes.**
- **Consistency of treatment effect across subgroups of patients**

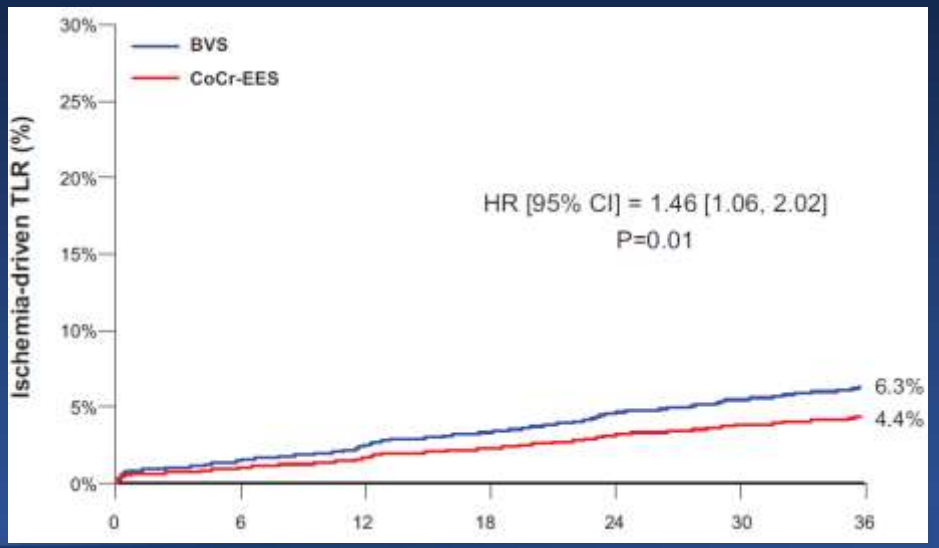
Ali et al; Circulation 2018

IPD from 4 ABSORB trials and 3,389 pts

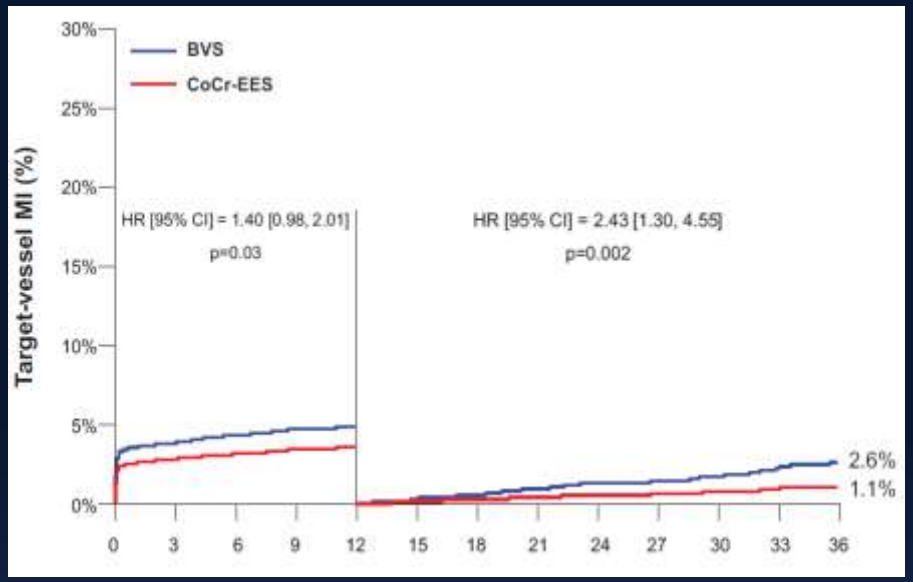


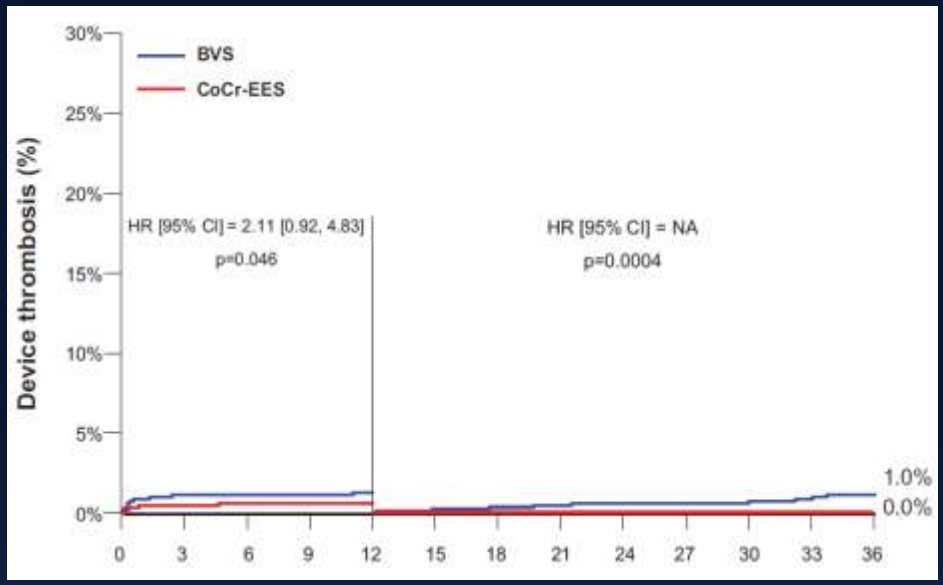


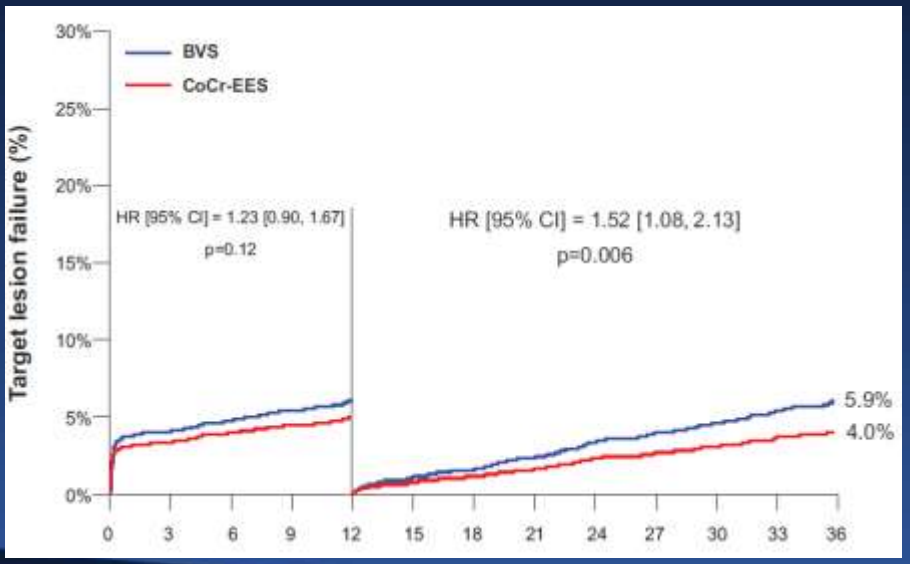


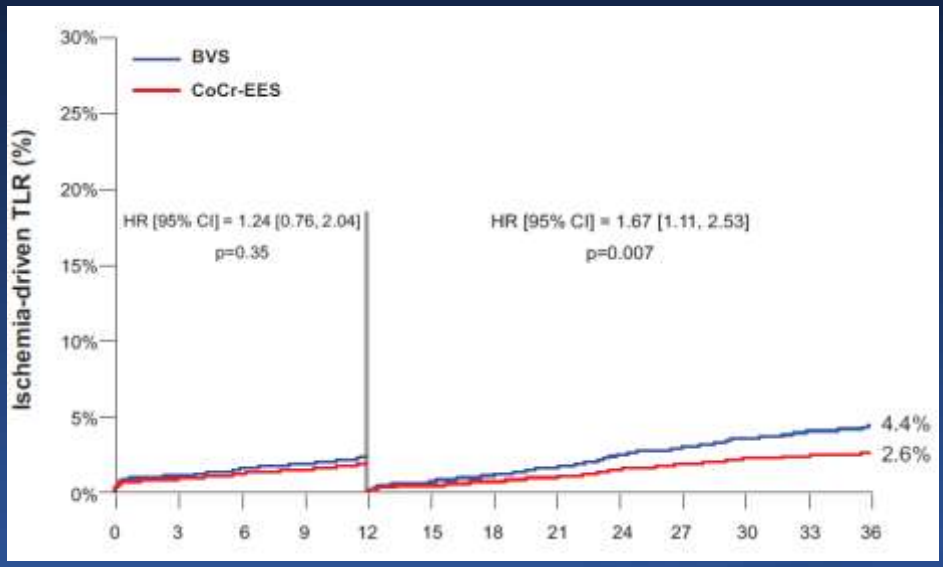


Ali et al; Circulation 2018



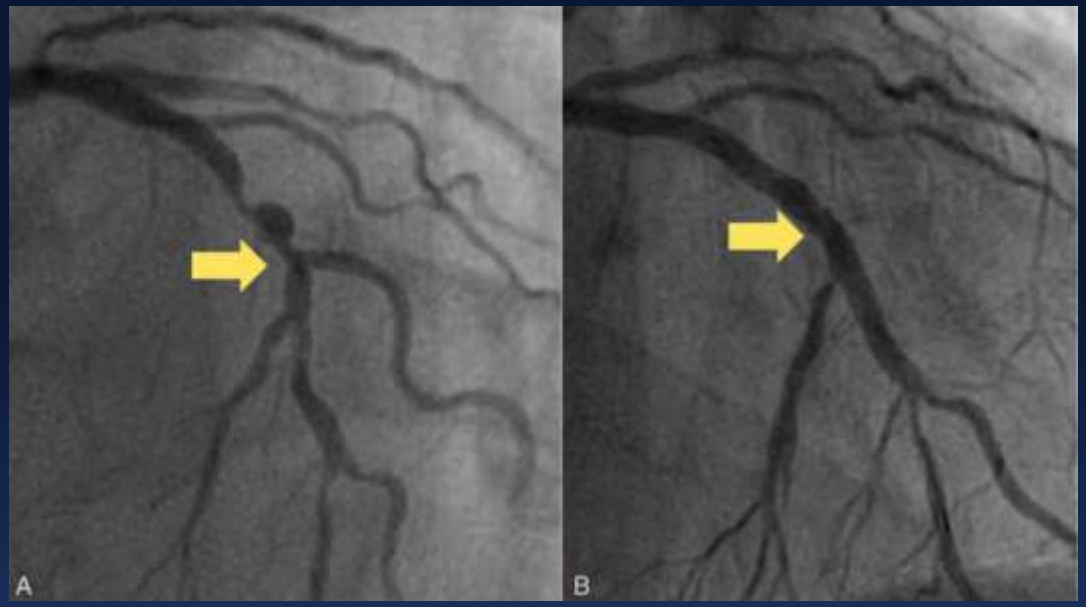






Ali et al; Circulation 2018

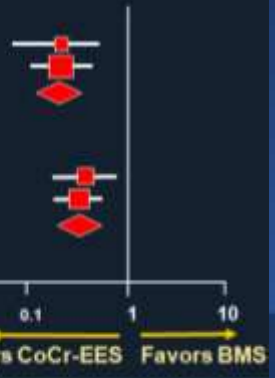
Increased 1-year rates of thrombosis and MI



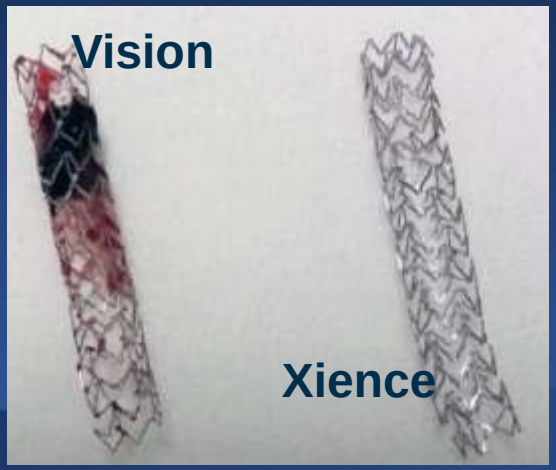
Consistency between direct and indirect estimates of 1-year stent thrombosis for CoCr-EES vs. BMS

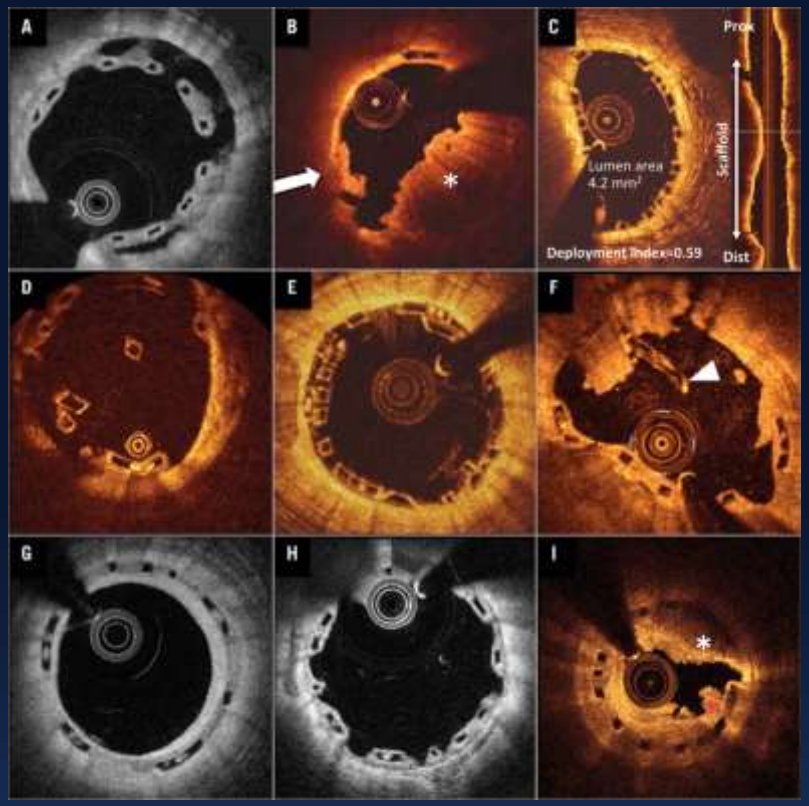
	Log (odds ratio)	SE	Weight	Odds Ratio IV Random, 95% CI
Definite stent thrombosis				
Direct estimate	-1.427	0.519	32.4%	0.24 (0.09-0.66)
Indirect estimate	-1.421	0.359	67.6%	0.24 (0.12-0.49)
Total (95% CI)			100.00%	0.24 (0.14-0.43)
Test for overall effect Z=4.82 (p<0.00001)				
Definite or probable thrombosis				
Direct estimate	-0.968	0.377	39.4%	0.38 (0.18-0.80)
Indirect estimate	-1.122	0.304	60.6%	0.33 (0.18-0.53)
Total (95% CI)			100.00%	0.35 (0.22-0.55)
Test for overall effect Z=4.48 (p<0.00001)				

IV = inverse variance
SE = standard error



Palmerini T et al. *Lancet* 2012

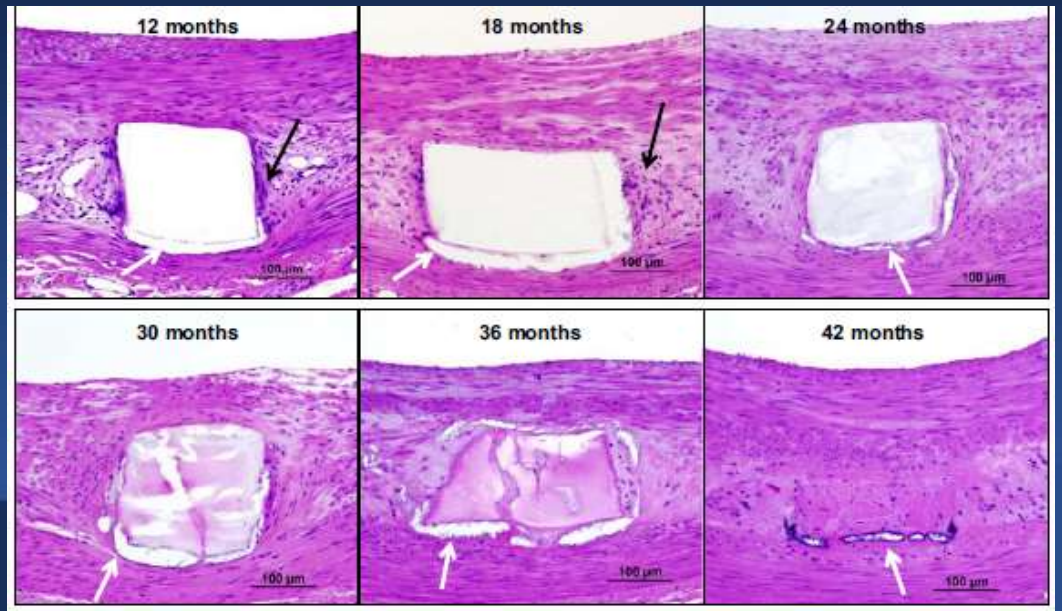




Late strut discontinuity
Endovascular dislocation

Sotomi et al; EuroInt 2017

Persistent inflammation up to 36 months

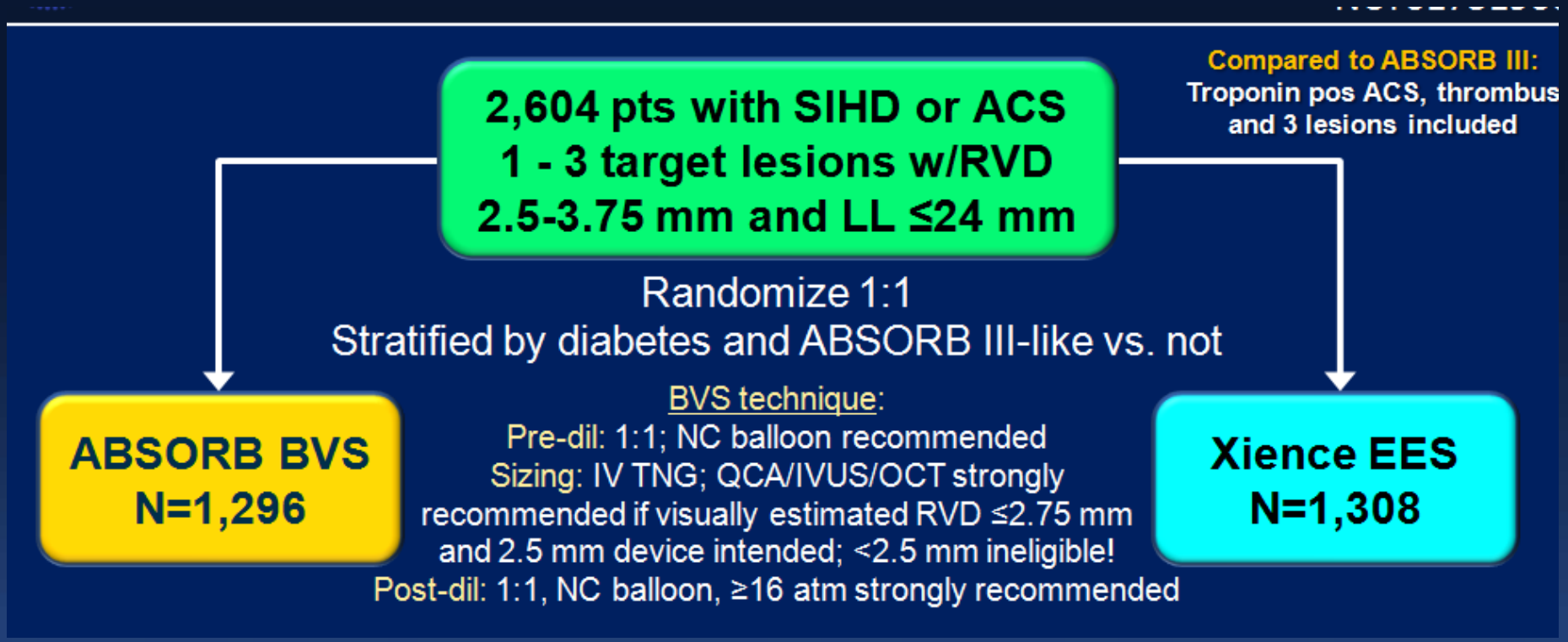


Otsuaka et al; Circ Cv Int 2016

Independent predictors of TLF and device thromboisis

	Relative risk [95%CI]	P value
3-year cumulative		
Target lesion failure		
Pre-procedure RVD (<2.25 mm vs. ≥2.25 mm)*	1.44 [1.14, 1.81]	0.003
Diabetes present	1.41 [1.15, 1.73]	0.001
Prior coronary interventions	1.41 [1.15, 1.73]	0.001
BVS (vs. CoCr-EES)	1.37 [1.09, 1.72]	0.005
Number of target lesions (2 vs. 1)	1.33 [1.03, 1.71]	0.04
Current tobacco use	1.25 [1.00, 1.57]	0.04
ABSORB China vs ABSORB III	0.50 [0.33, 0.76]	0.04
Device thrombosis		
BVS (vs. CoCr-EES)	3.95 [1.80, 8.67]	0.0006
Diabetes present	2.71 [1.62, 4.54]	0.0002
Pre-procedure RVD (<2.25 mm vs. ≥2.25 mm)*	1.90 [1.09, 3.32]	0.03

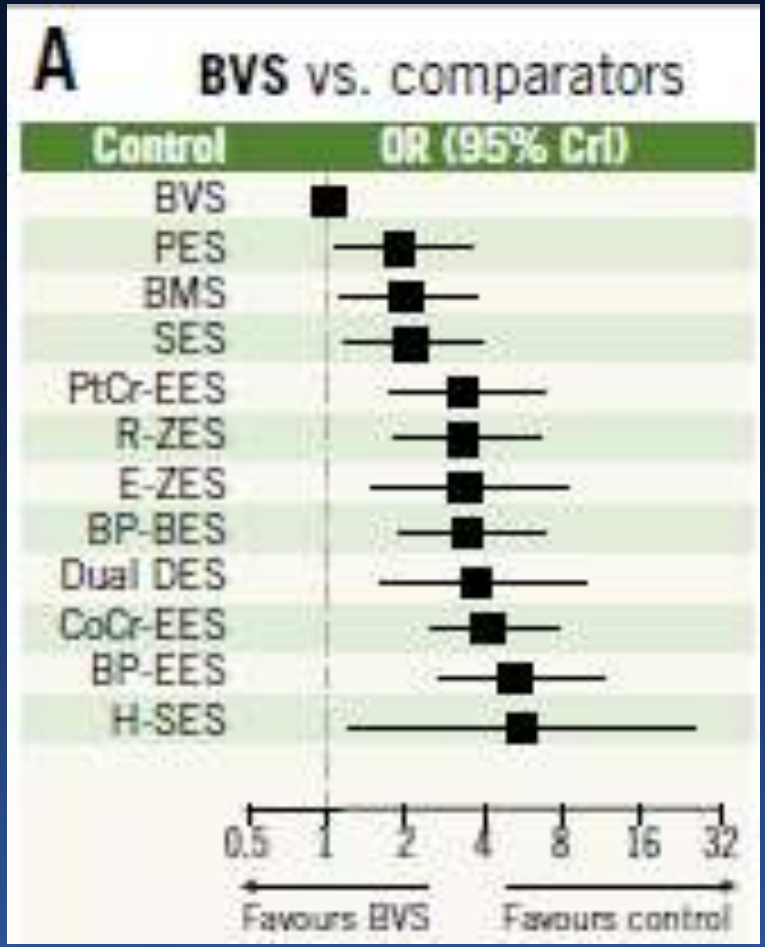
ABSORB IV design



Subgroup analysis for TLF

Subgroup		% (n/N)	Absorb BVS (N=2164)	XIENCE (N=1225)	Relative Risk [95% CI]*	P value Interaction*
Pre-procedural variables						
Age	< median (63 yrs)	47.6% (1610/3384)	11.1% (107/968)	7.9% (45/571)	1.29 [0.93, 1.80]	0.63
	≥ median	52.4% (1774/3384)	12.4% (136/1101)	8.4% (50/596)	1.45 [1.06, 1.97]	
Sex	Female	27.5% (932/3384)	11.1% (63/570)	8.8% (28/318)	1.18 [0.77, 1.80]	0.44
	Male	72.5% (2452/3384)	12.0% (180/1499)	7.9% (67/849)	1.46 [1.12, 1.91]	
Current smoking	Yes	23.1% (781/3384)	14.3% (66/463)	7.6% (21/278)	1.81 [1.13, 2.89]	0.24
	No	76.9% (2603/3384)	11.0% (177/1606)	8.3% (74/889)	1.26 [0.97, 1.63]	
Hypertension	Yes	74.6% (2524/3384)	12.1% (187/1546)	9.6% (82/856)	1.20 [0.94, 1.53]	0.04
	No	25.4% (860/3384)	10.7% (56/523)	4.2% (13/311)	2.56 [1.42, 4.62]	
Hyperlipidemia	Yes	70.6% (2390/3384)	12.4% (183/1470)	8.5% (69/811)	1.42 [1.10, 1.85]	0.57
	No	29.4% (994/3384)	10.0% (60/599)	7.3% (26/356)	1.24 [0.80, 1.94]	
Diabetes	Yes	30.2% (1020/3382)	13.9% (87/626)	12.6% (44/348)	1.06 [0.75, 1.48]	0.08
	No	69.8% (2362/3382)	10.6% (155/1462)	6.1% (51/835)	1.66 [1.22, 2.25]	
Prior MI	Yes	21.6% (727/3361)	13.7% (59/430)	12.1% (30/247)	1.05 [0.70, 1.58]	0.20
	No	78.4% (2634/3361)	11.2% (181/1623)	7.1% (65/915)	1.49 [1.14, 1.96]	
Prior intervention	Yes	33.7% (1141/3382)	14.5% (103/712)	12.4% (45/362)	1.14 [0.82, 1.58]	0.17
	No	66.3% (2241/3382)	10.3% (140/1357)	6.1% (49/803)	1.61 [1.17, 2.20]	
Presentation	ACS	32.5% (1100/3383)	11.2% (71/632)	7.7% (31/405)	1.27 [0.85, 1.91]	0.69
	Stable CAD	67.5% (2283/3383)	12.0% (172/1436)	8.4% (64/762)	1.42 [1.08, 1.87]	
No of target lesions	1	94.8% (3207/3383)	11.6% (226/1956)	8.2% (91/1108)	1.35 [1.07, 1.70]	0.44
	2	5.2% (176/3383)	15.0% (17/113)	6.8% (4/59)	1.97 [0.69, 5.61]	
P2Y12 loading	Clopidogrel/ticlopidine	77.0% (2560/3323)	11.2% (173/1549)	7.9% (72/906)	1.33 [1.02, 1.73]	0.41
	Prasugrel/ticagrelor	23.0% (763/3323)	13.6% (67/492)	8.1% (19/234)	1.66 [1.02, 2.70]	
RVD	< median (2.65 mm)	50.9% (1716/3372)	12.9% (139/1077)	11.3% (65/573)	1.12 [0.85, 1.47]	0.03
	≥ median	49.1% (1656/3372)	10.5% (104/988)	5.1% (30/589)	1.96 [1.32, 2.90]	

Long-term safety of bioresorbable scaffolds: insights from a network meta-analysis including 91 trials



Kang et al; EuroInt 2017

Stent Thrombosis Network Meta-analysis

Primary EP: ARC Definite ST (FU through 2 years)

49 RCTs, 50,844 pts

Consistency between direct and indirect estimates of 1-year stent thrombosis for CoCr-EES vs. BMS

	Log (odds ratio)	SE	Weight	Odds Ratio IV Random, 95% CI
Definite stent thrombosis				
Direct estimate	-1.427	0.519	32.4%	0.24 (0.09-0.66)
Indirect estimate	-1.421	0.359	67.6%	0.24 (0.12-0.49)
Total (95% CI)			100.00%	0.24 (0.14-0.43)
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Definite or probable thrombosis				
Direct estimate	-0.968	0.377	39.4%	0.38 (0.18-0.80)
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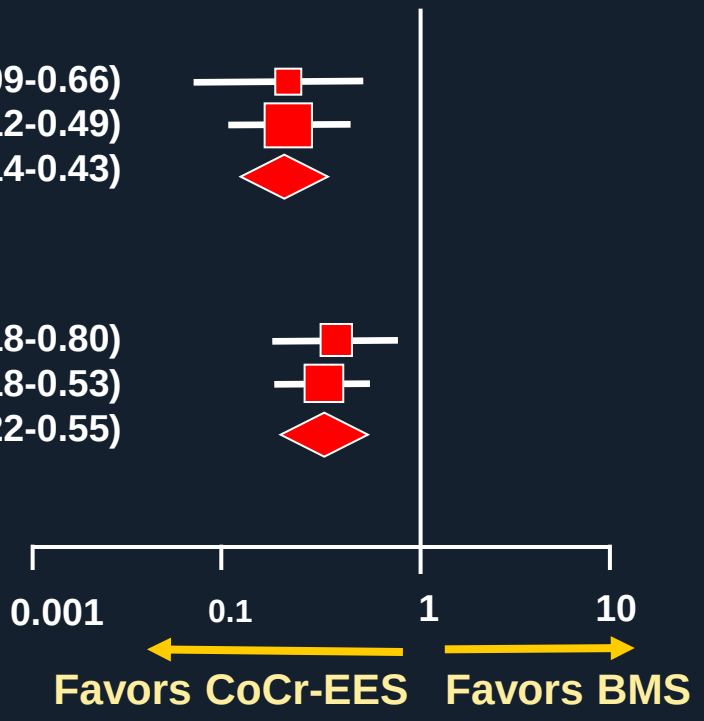
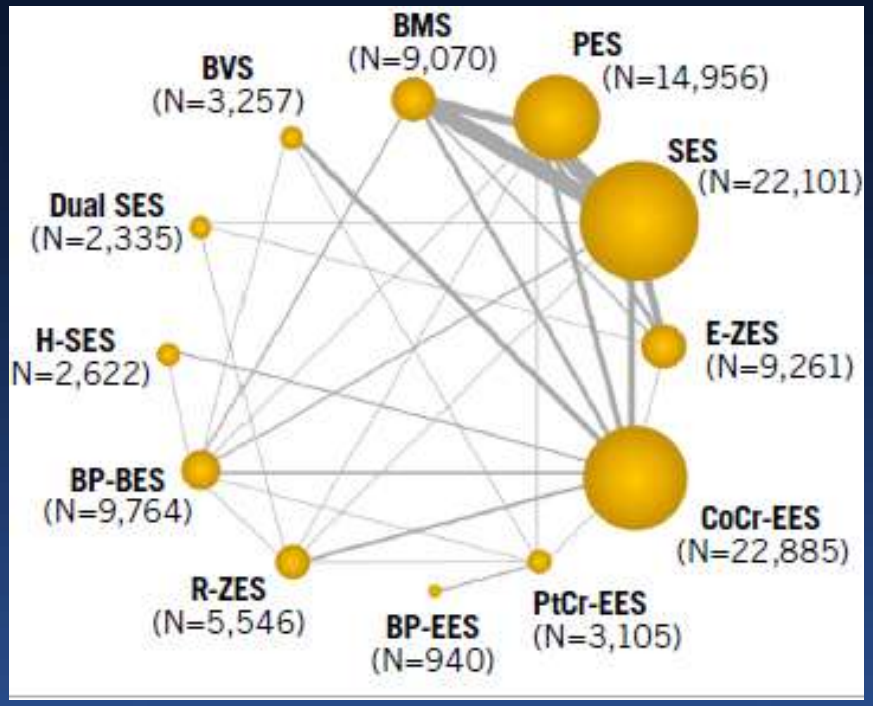


IV = inverse variance
SE = standard error

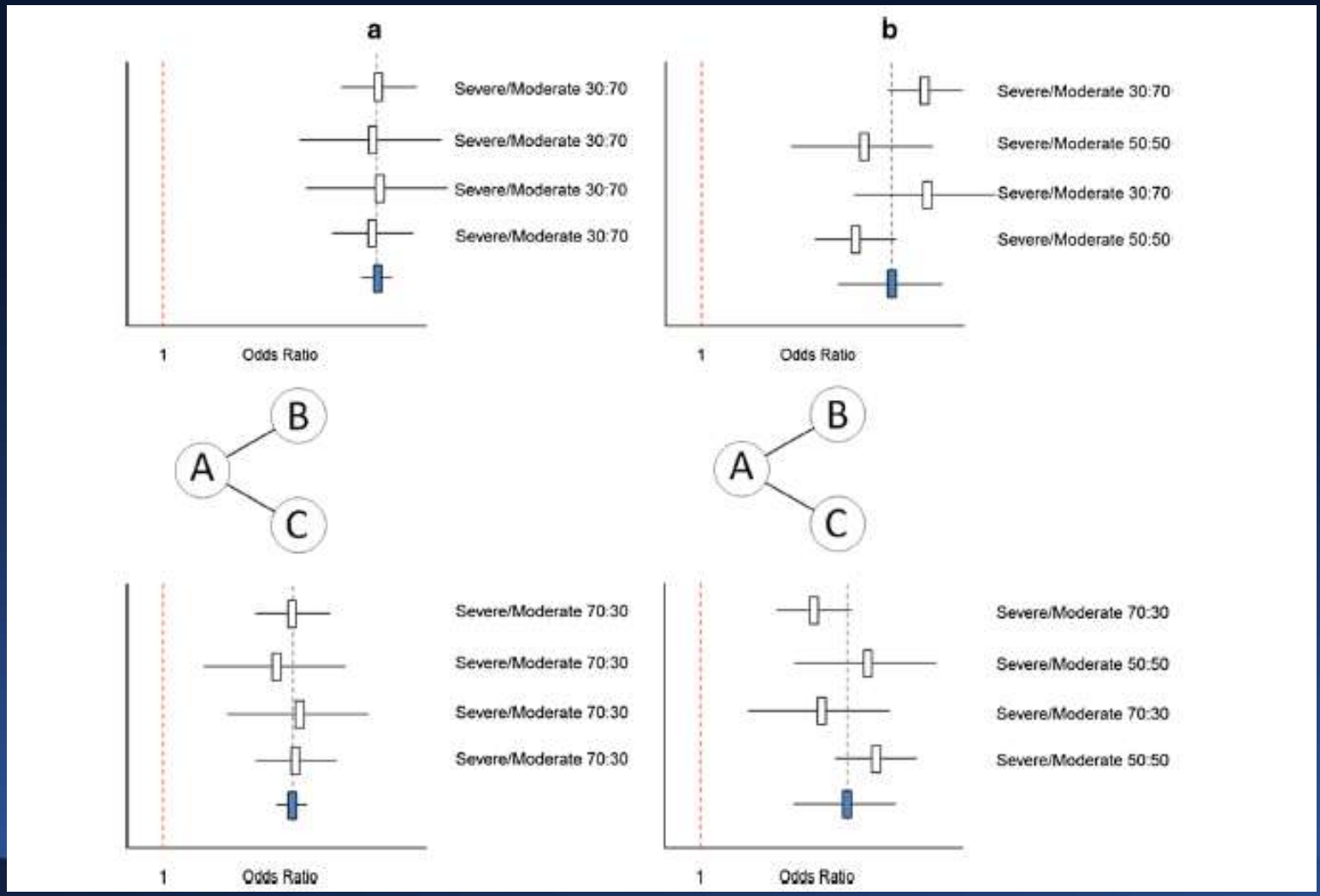
Palmerini T et al. *Lancet* 2012

Long-term safety of bioresorbable scaffolds: insights from a network meta-analysis including 91 trials



Kang et al; EuroInt 2017

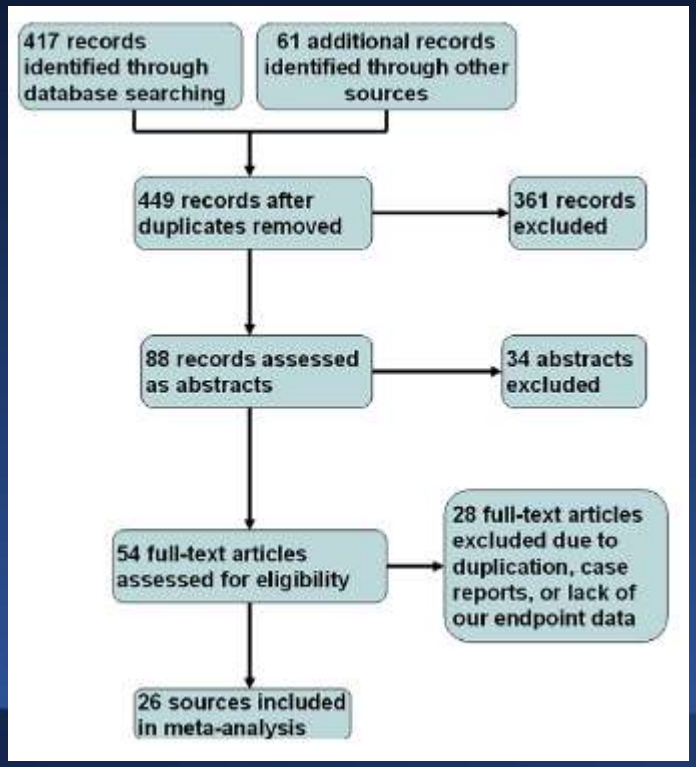
Between comparison variation in effect modifiers



Scaffold Thrombosis After Percutaneous Coronary Intervention With ABSORB Bioresorbable Vascular Scaffold

A Systematic Review and Meta-Analysis

Michael J. Lipinski, MD, PhD, Ricardo O. Escarcega, MD, Nevin C. Baker, DO, Hadiya A. Benn, Michael A. Gaglia, Jr, MD, MSc, Rebecca Torguson, MPH, Ron Waksman, MD

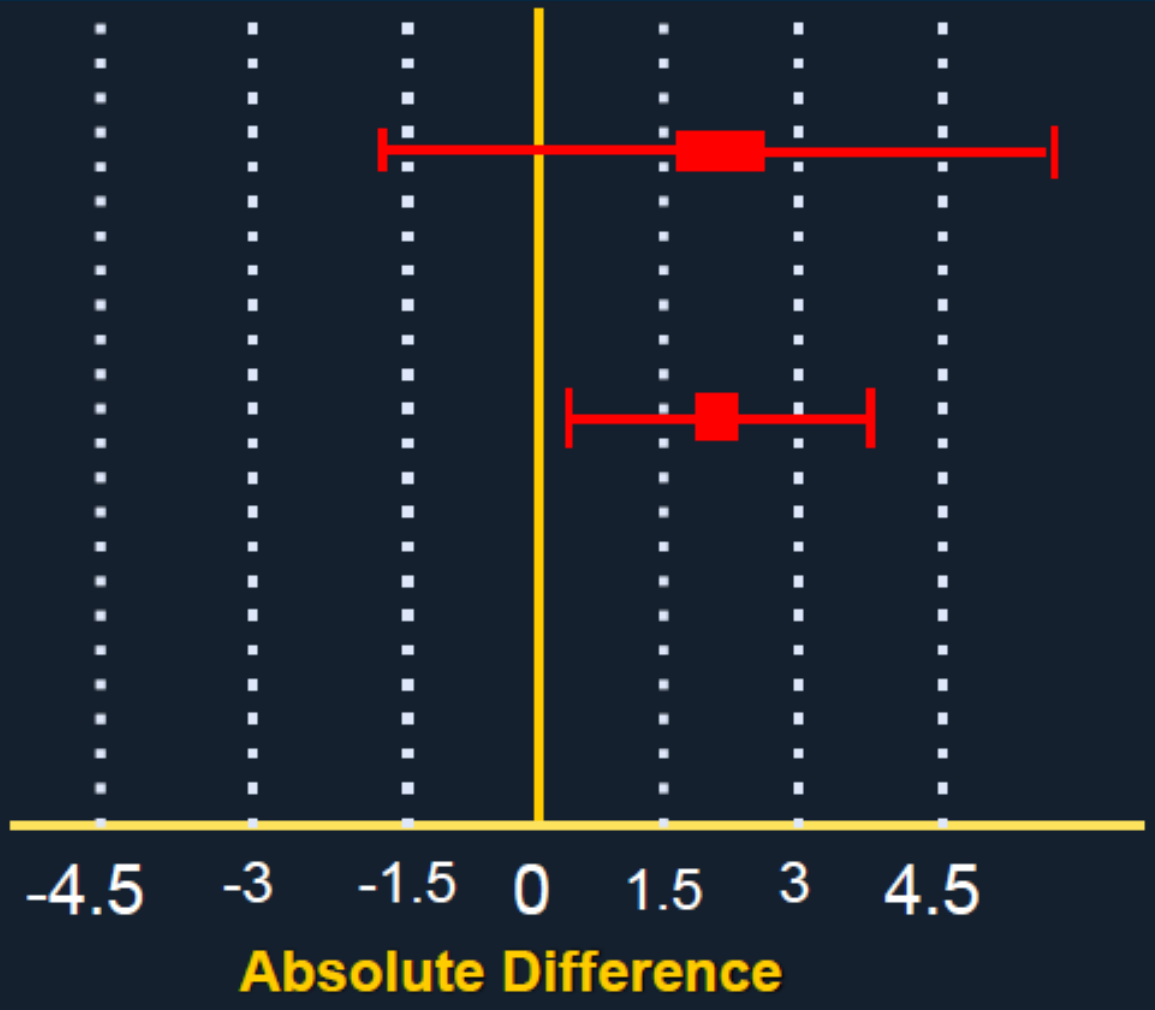


Potential problem

Individual Small Trial

Meta-analysis of several such trials

If all the trials have the same systemic bias, all we have done is to tighten the confidence intervals!



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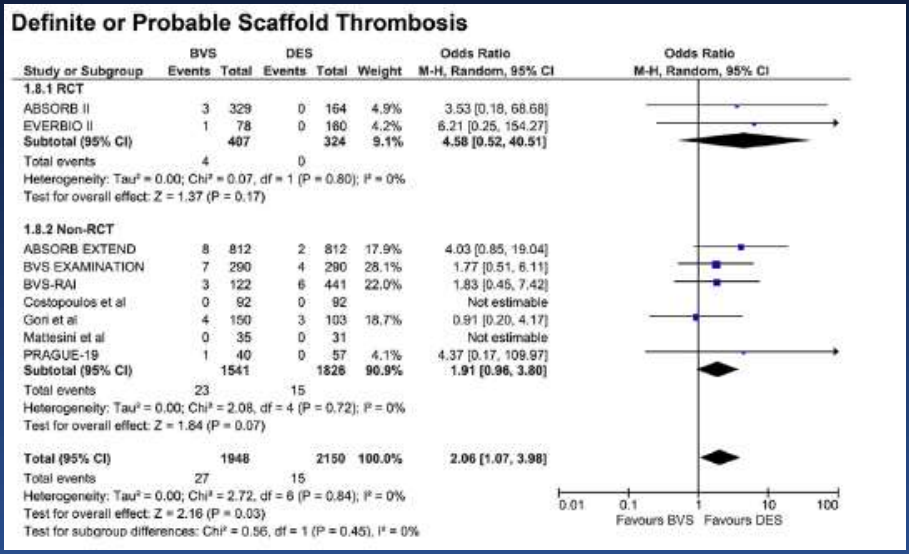
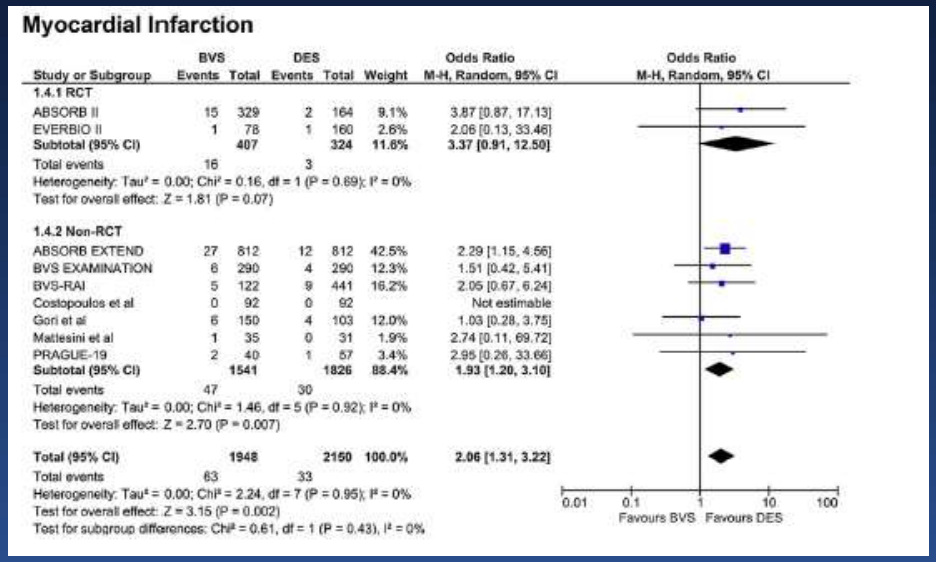
Definite or Probable Scaffold Thrombosis



Myocardial Infarction



Conclusions

- There are 7 RCTs and at least 15-meta-analyses comparing BVS versus metallic DES (CoCr-EES or PtCR-EES).
- Meta-analyses differ for design (IPD vs aggregate data), number of studies included (4-7), summary statistics, lenght of fup (2-4 years).
- Notwithstanding the limited number of studies and the potential of duplicate results, meta-analyses have provided complimentary information that have enriched our knowledge on the relative safety and efficacy of BVS vs. metallic DES.
- Summary evidence suggest no difference in mortality between the two devices, but higher rates of ST and TV-related MI and TLR with BVS compared with metallic DES.