Duration of Dual Antiplatelet Therapy : Less than 6~12months

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ESC Congress News

EUROPEAN SOCIETY OF CARDIOLOGY

WORLD HEART FEDERATION

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

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

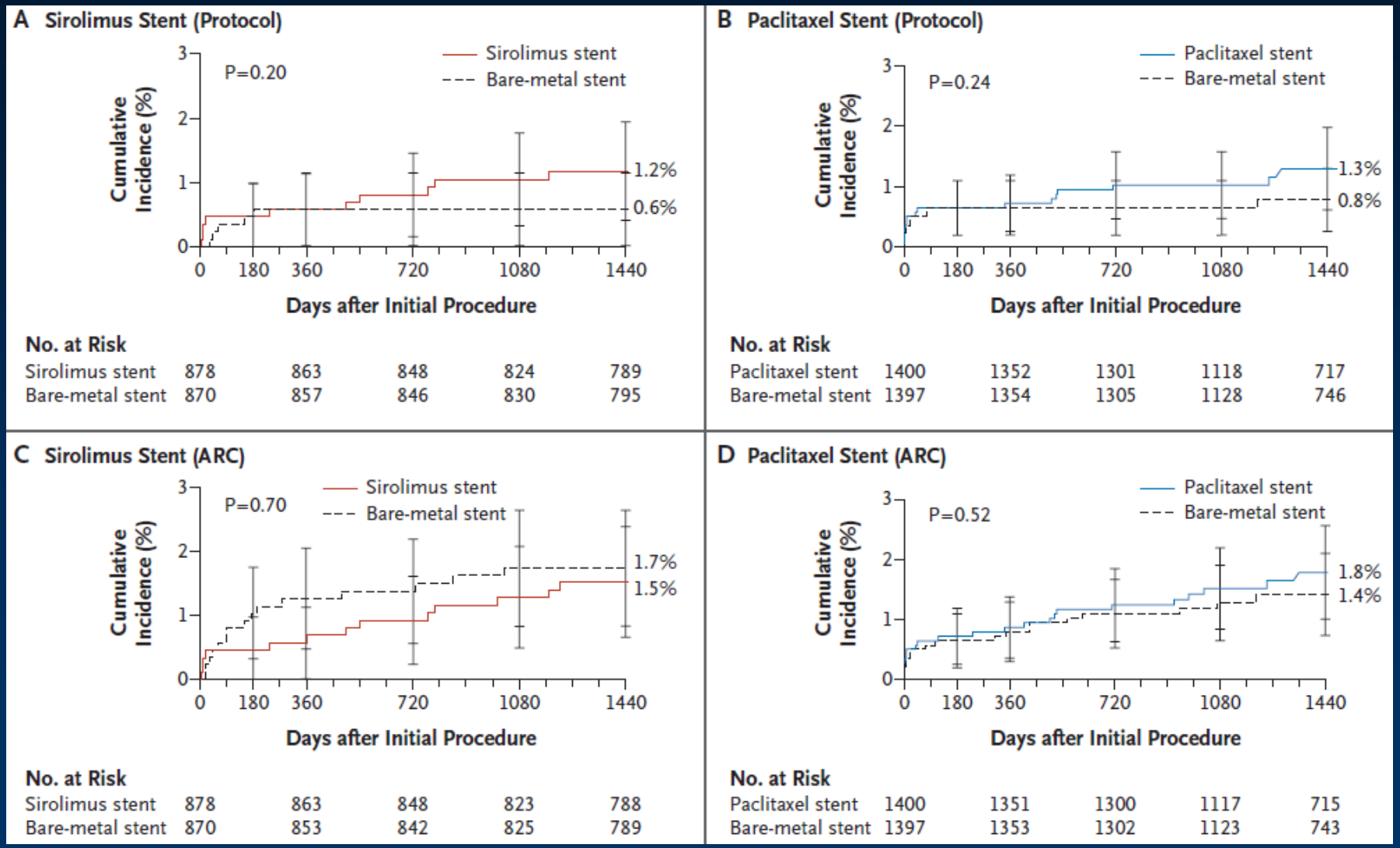
Safety of DES Highlighted at ESC 2006

‘Mandatory DAPT for 1yr’ strategy

- It was not based on prospective RCTs.
- It did not reflect the results of newer-generation DES with thinner struts and more biocompatible polymer.
- Definitions of stent thrombosis that have been used in clinical trials of drug-eluting stents have been restrictive and have not been used in a uniform manner.

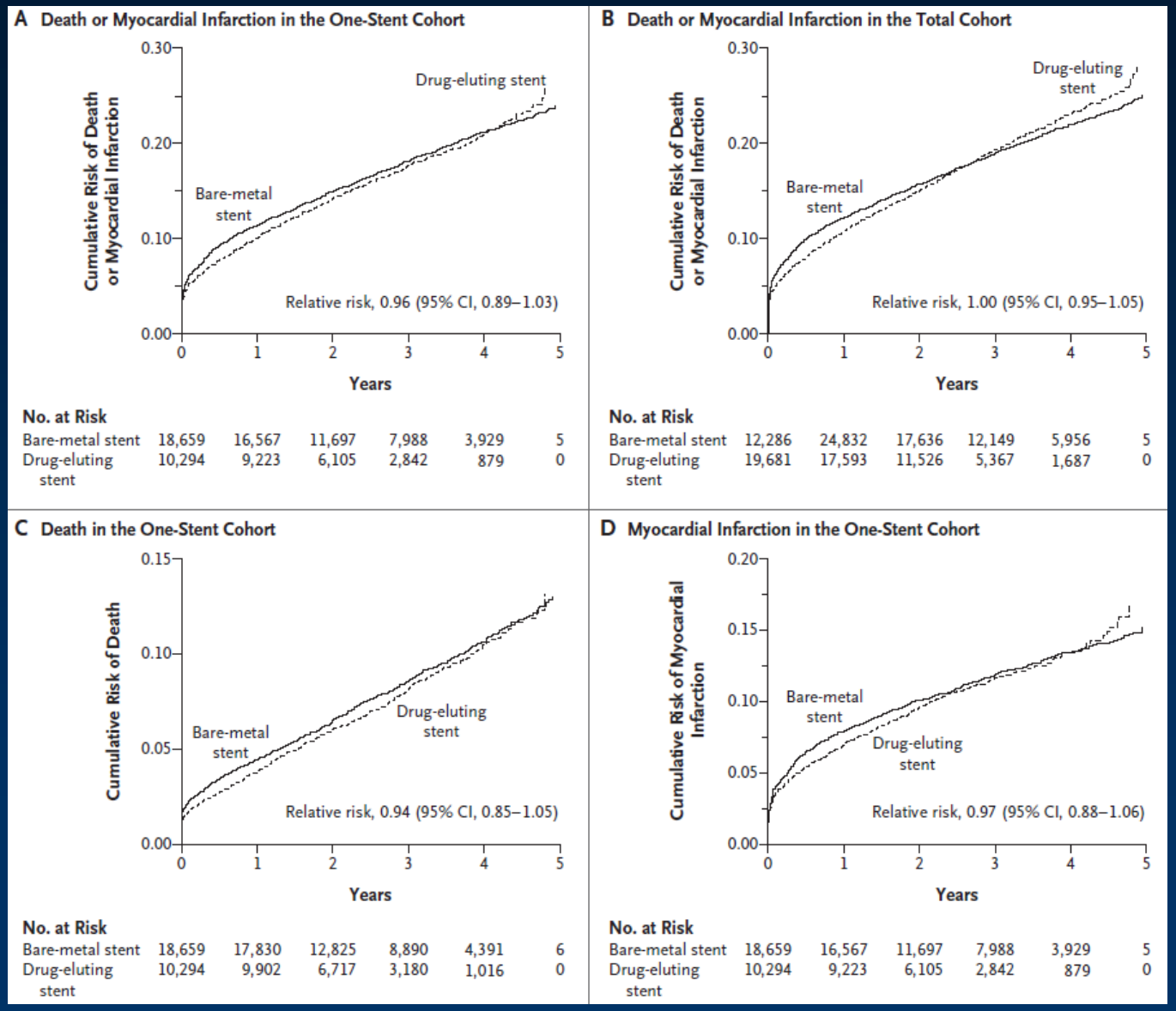
DESs, are they really vulnerable to stent thrombosis compared to BMS?

ST set by ARC definition were not different between DES vs. BMS



Mauri L, et al. N Eng J Med 2007

Long-term safety and efficacy of DES vs. BMS in Sweden



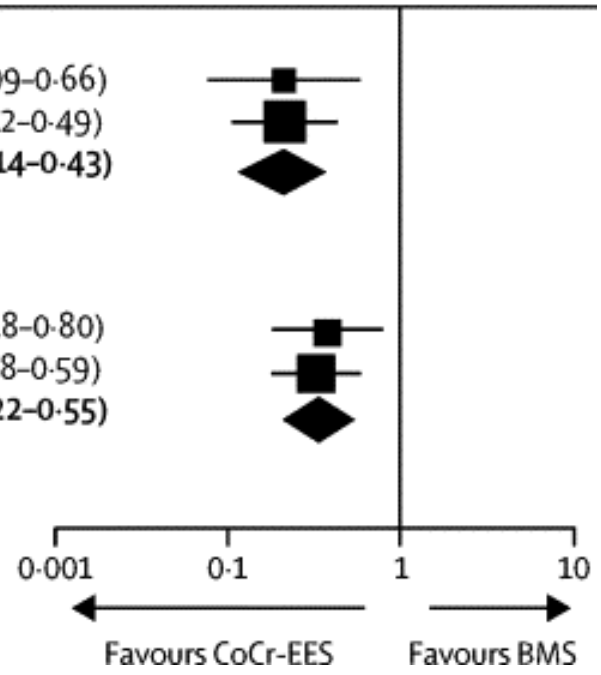
***Included stents :**

Cypher, TAXUS, Endeavor

James SK, et al. N Eng J Med 2009

CoCr-EES vs. BMS

	log (odds ratio)	SE	Weight	Odds ratio IV, random, 95% CI
(A) Definite 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)				
(B) 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 (0·18–0·59)
Total (95% CI)			**100·00%**	**0·35 (0·22–0·55)**
Test for overall effect Z=4·48 (p<0·00001)				

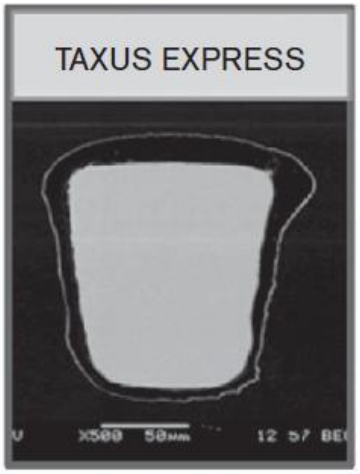


Palmerini T, et al. Lancet. 2012

1st generation vs. newer DESs

Comparison between 1st generation vs. newer DESs

Strut thickness: 140 µm
Coating thickness: 12.6 µm

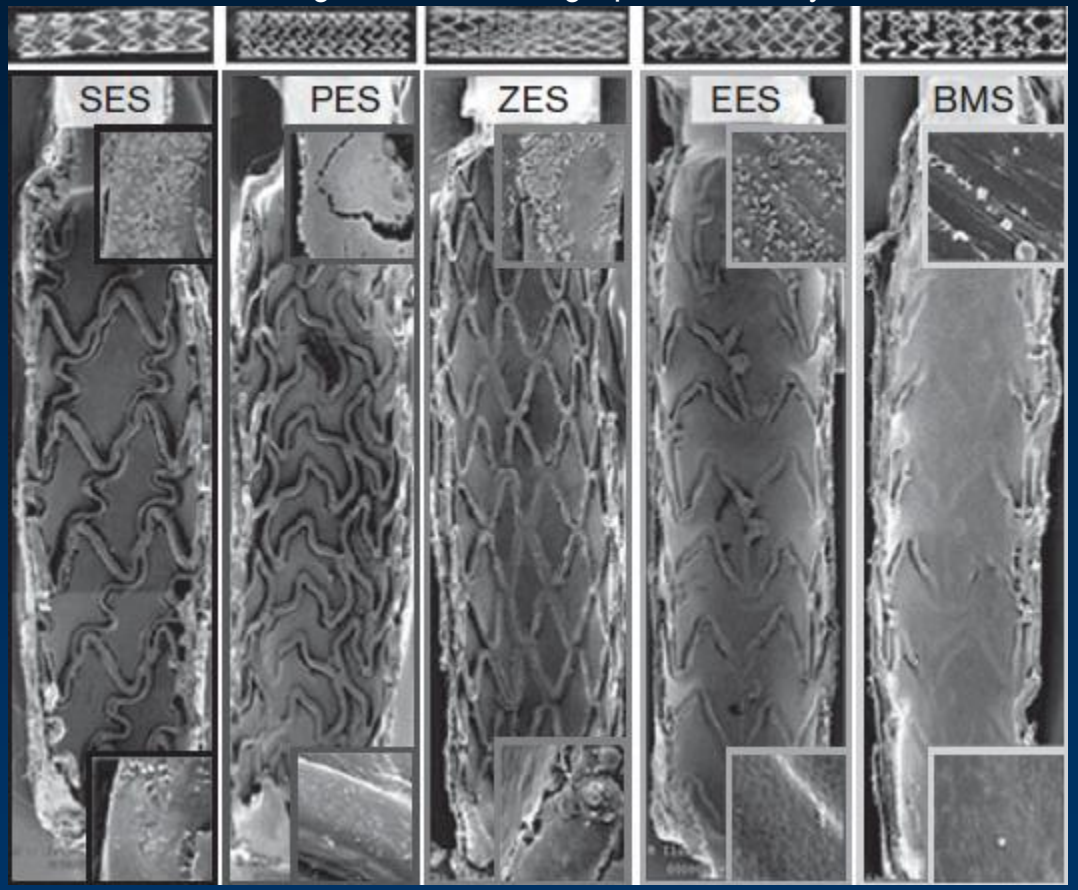


Strut thickness: 132 µm
Coating thickness: 19.6 µm

Strut thickness: 91 µm
Coating thickness: 4.8 µm

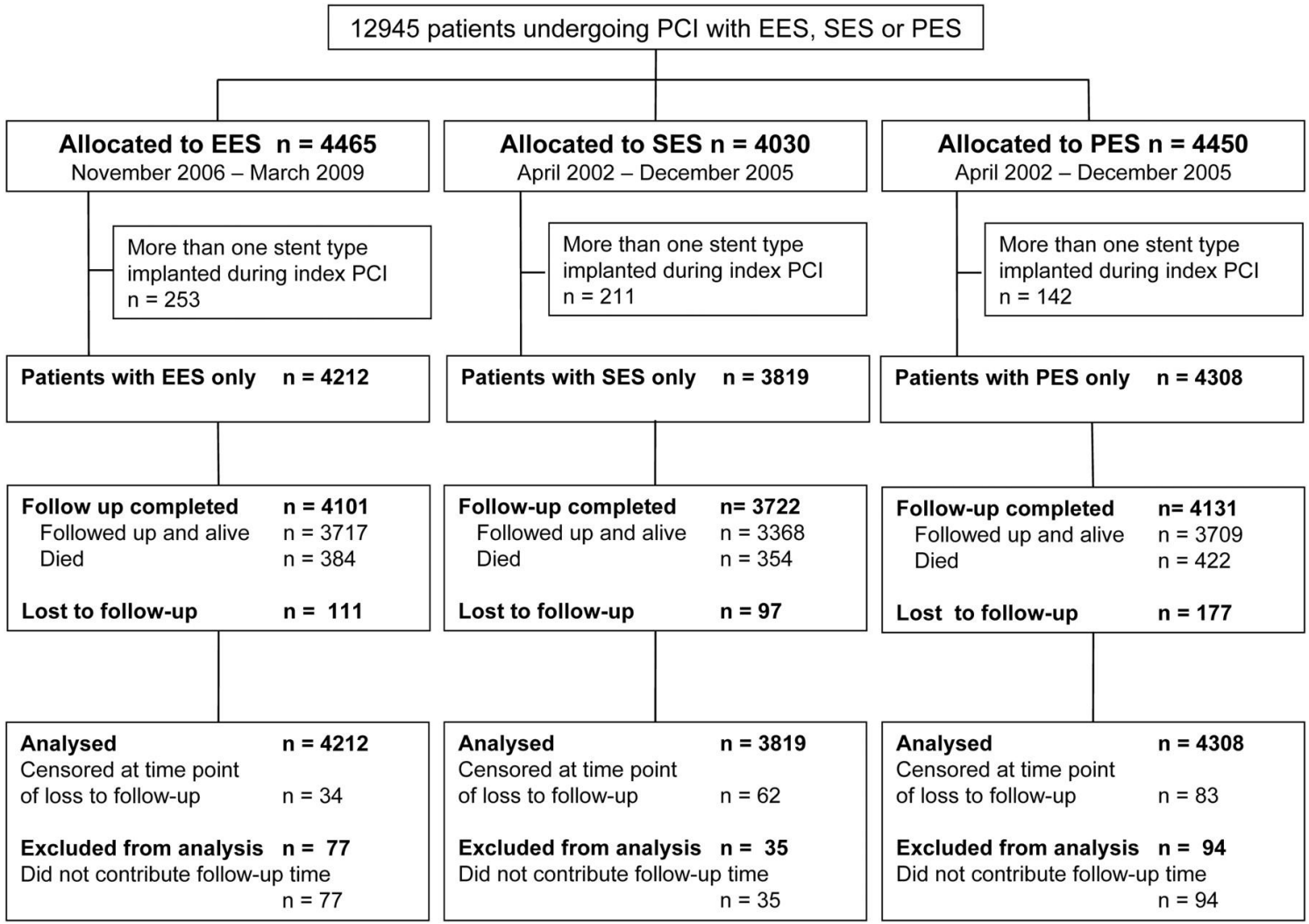
Strut thickness: 81 µm
Coating thickness: 7.8 µm

Scanning Electron Micrographs of 14-day



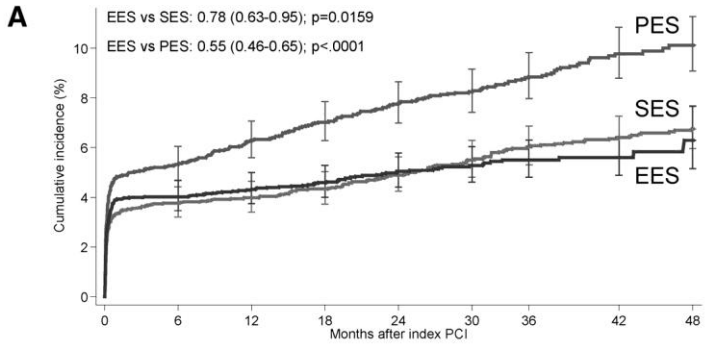
Joner M, et al. J Am Coll Cardiol. 2008

Very late ST of EES compared with 1st gen. DESs: Meta-analysis

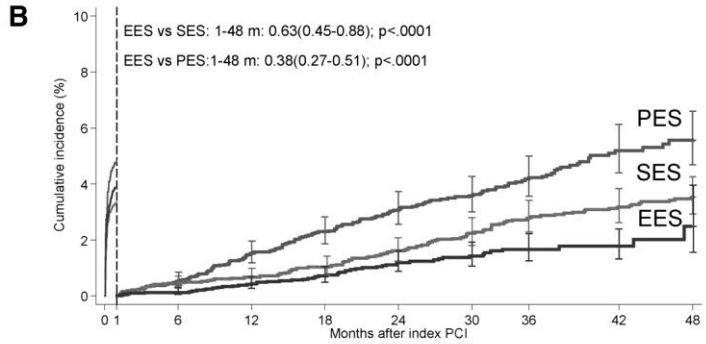


Raber L, et al. Circulation. 2012

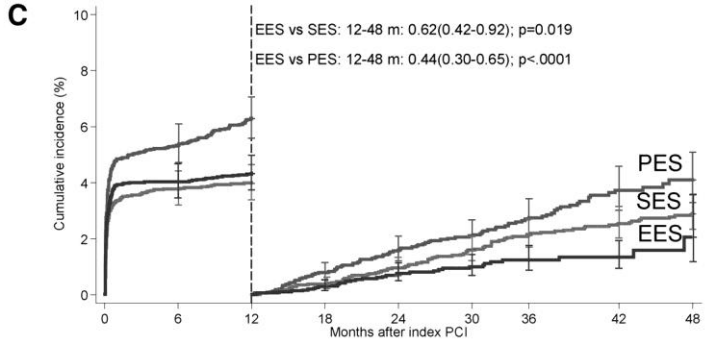
Definite or probable ST



Cumulative incidence of definite ST up to 4 years



Landmark analysis at 30 days



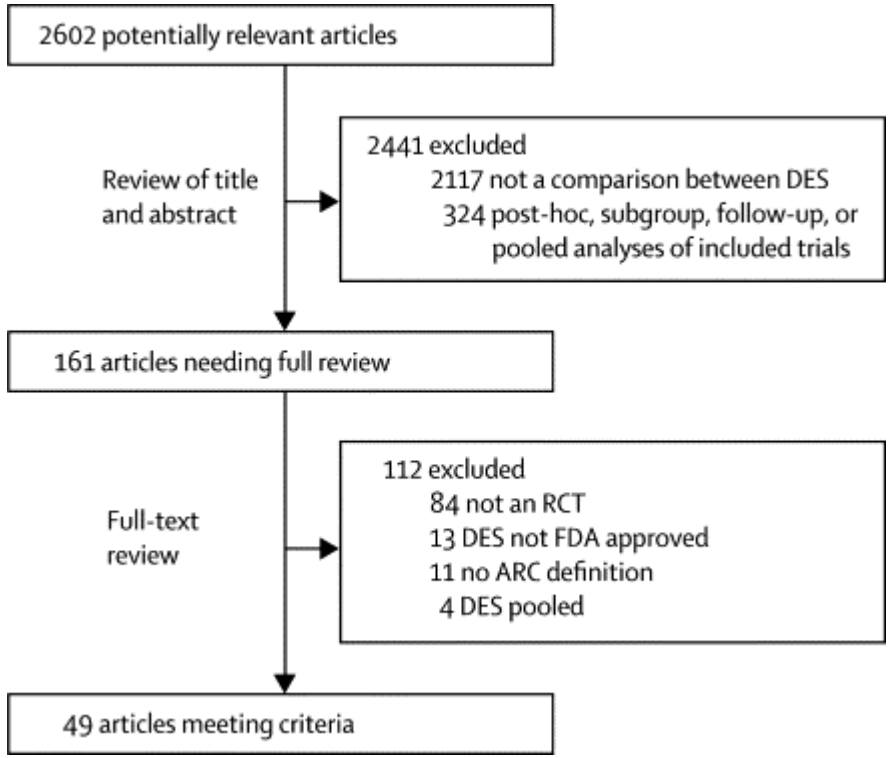
No. at risk									
PES	4214	3873	3739	3118	2843	2286	1831	1042	666
SES	3784	3587	3535	3463	3361	3031	2473	2075	1695
EES	4135	3896	3768	3254	2572	1835	1029	506	204

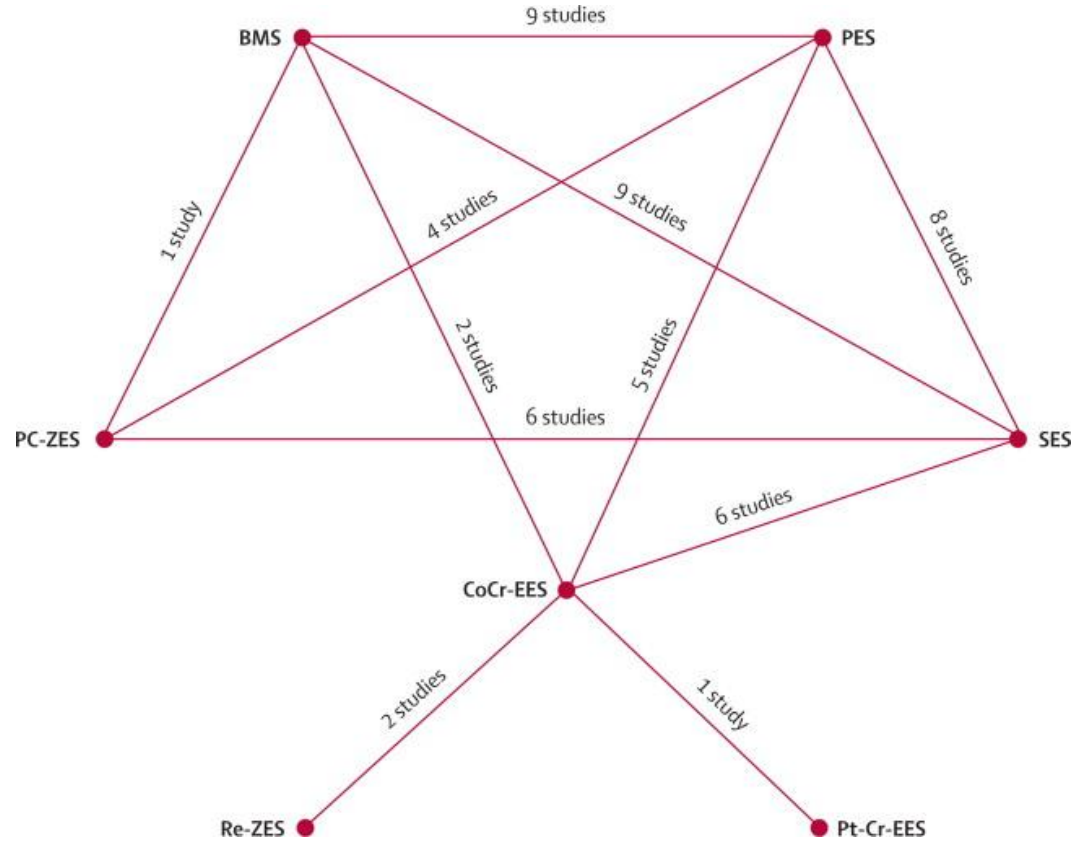
Landmark analysis at 1 year

Raber L, et al. Circulation. 2012

Stent thrombosis with DES and BMS

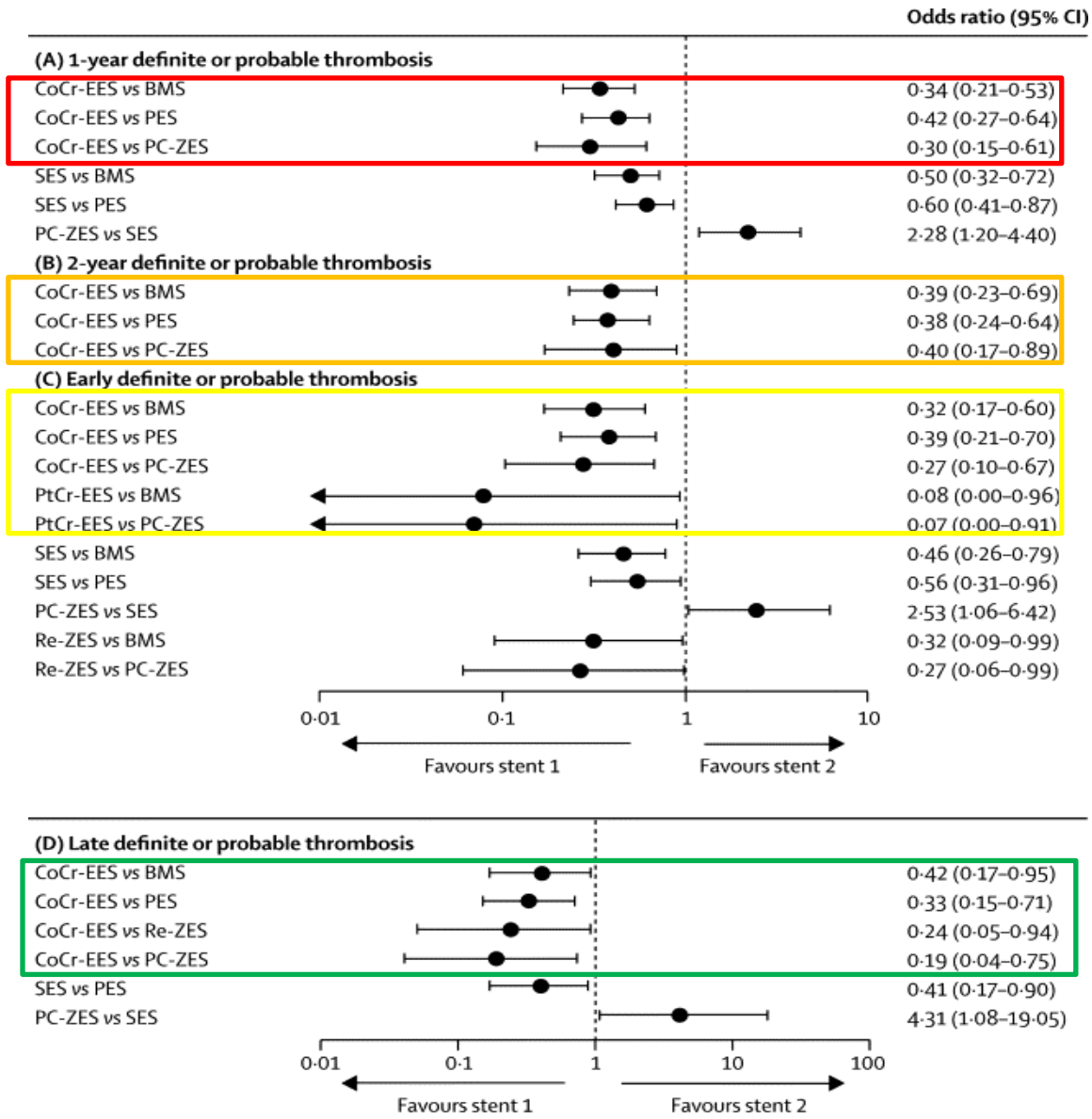
: Evidence from a comprehensive network meta-analysis





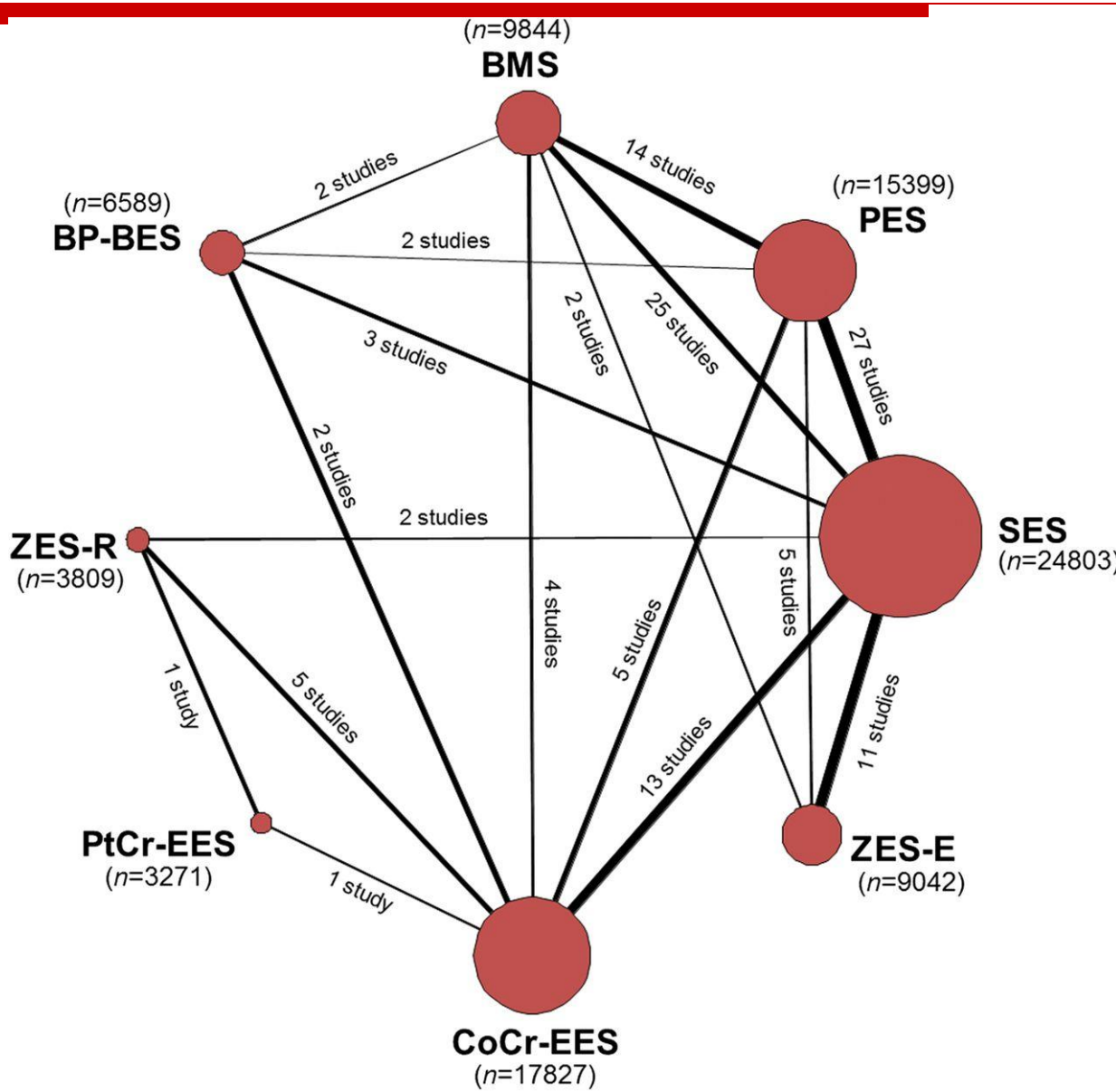
Palmerini T, et al. Lancet. 2012

Definite or probable ST



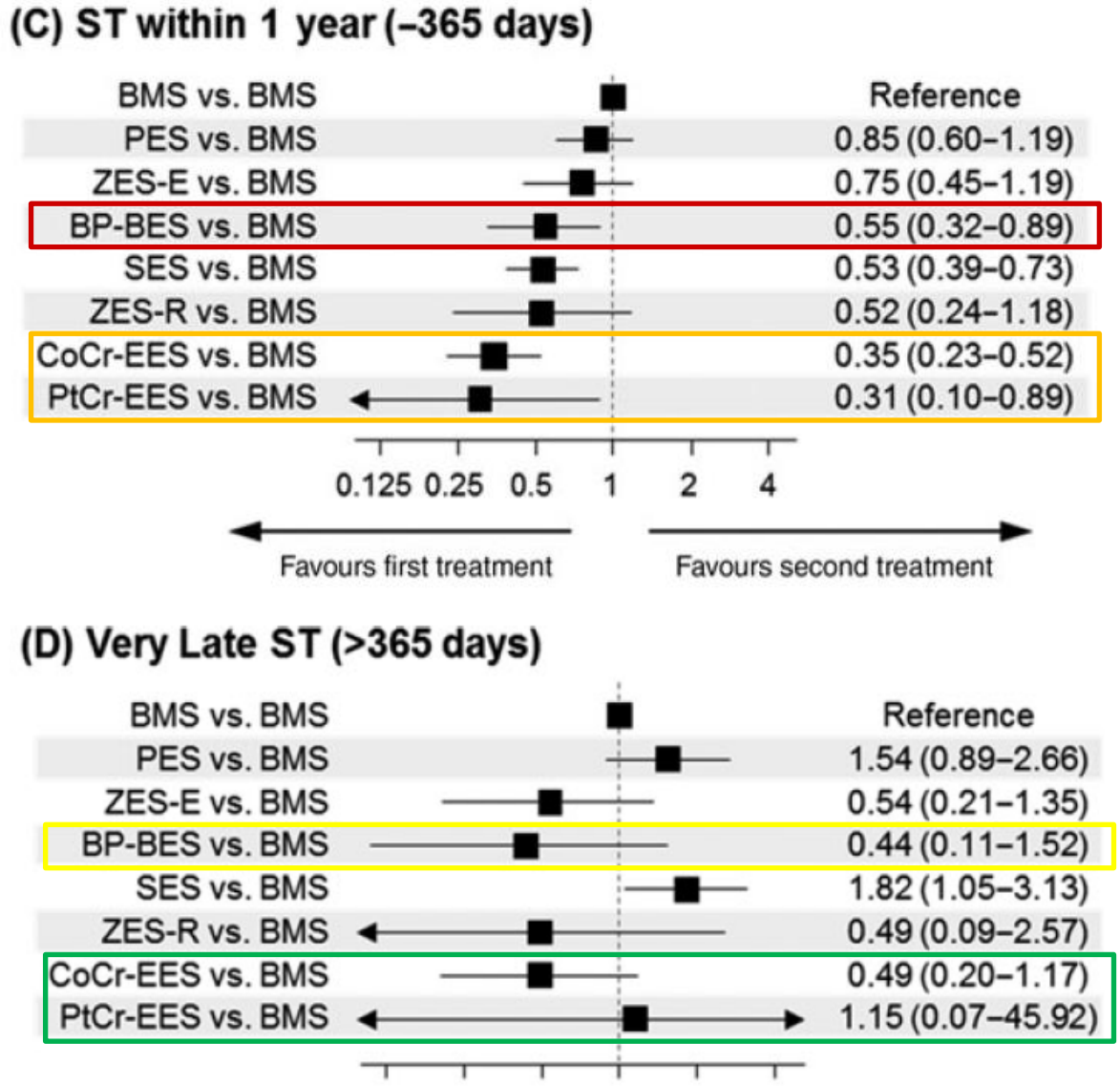
Palmerini T, et al. Lancet. 2012

Biodegradable-polymer DES vs. BMS vs. durable-polymer DES : network meta-analysis



Kang SH, et al. Eur Heart J. 2014

Definite or probable ST with reference to BMS

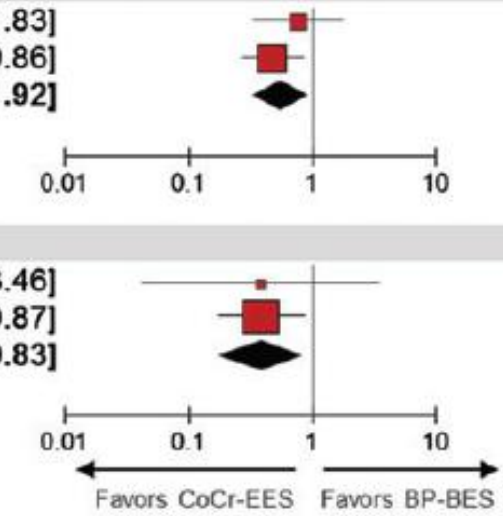


Kang SH, et al. Eur Heart J. 2014

Comparison b/w CoCr-EES vs. BP-BES

B **CoCr-EES vs. BP-BES**

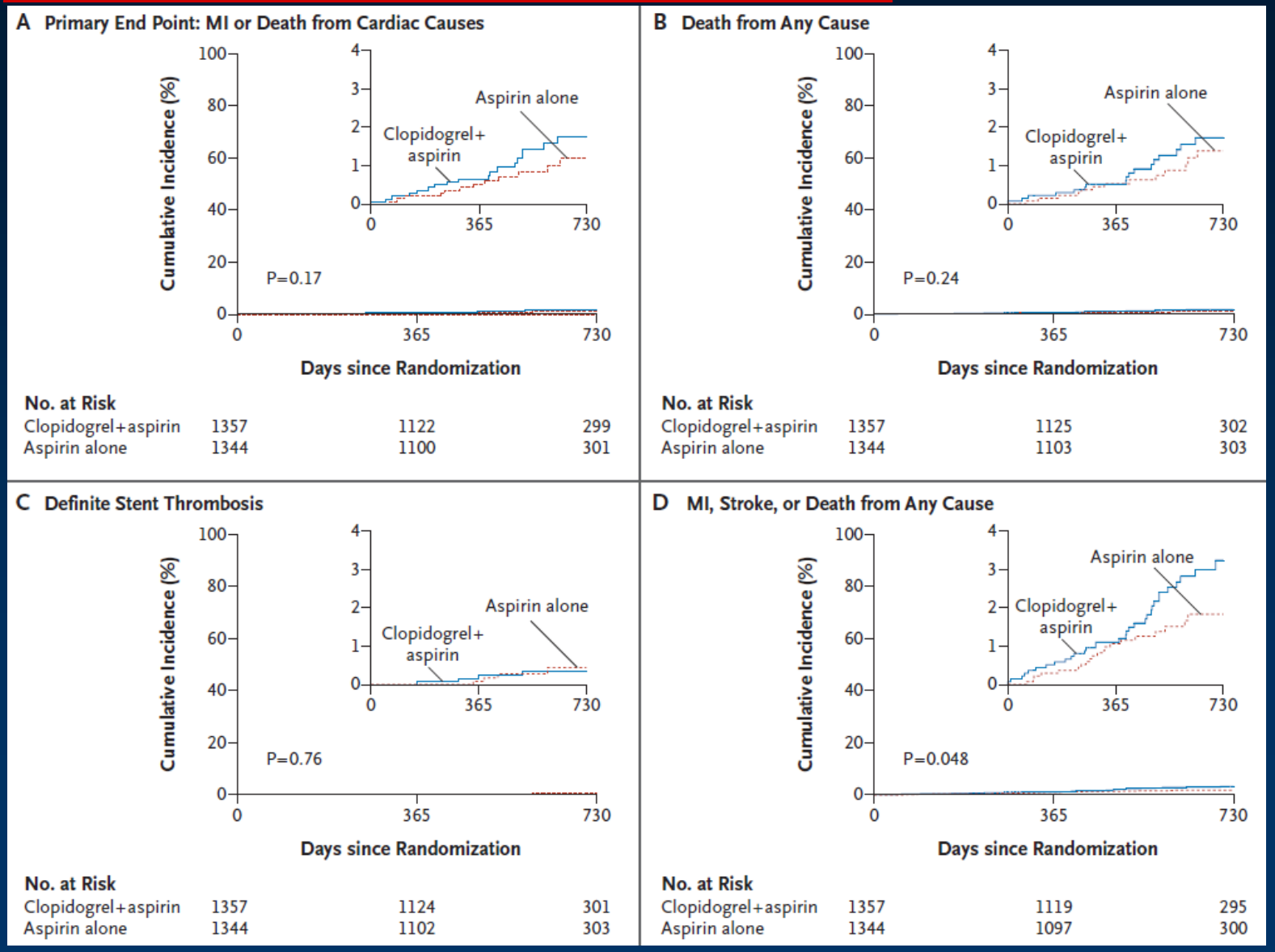
	Log (OR)	SE	Weight	OR with 95% CI Random Effects Model
Definite or Probable ST				
Direct estimate	-0.237	0.429	32.6%	0.79 [0.34, 1.83]
Indirect estimate	-0.735	0.298	67.4%	0.48 [0.27, 0.86]
Total			**100.0%**	**0.74 [0.29, 1.92]**
Heterogeneity P=0.34; I^2=0%				
Test for overall effect: Z = 2.34 (P = 0.02)				
Definite ST				
Direct estimate	-0.963	1.125	12.0%	0.38 [0.04, 3.46]
Indirect estimate	-0.951	0.415	88.0%	0.39 [0.17, 0.87]
Total			**100.0%**	**0.39 [0.18, 0.83]**
Heterogeneity P=0.99; I^2=0%				
Test for overall effect: Z = 2.44 (P = 0.01)				



Kang SH, et al. Eur Heart J. 2014

Do we really have to maintain long-term DAPT in patients with DES?

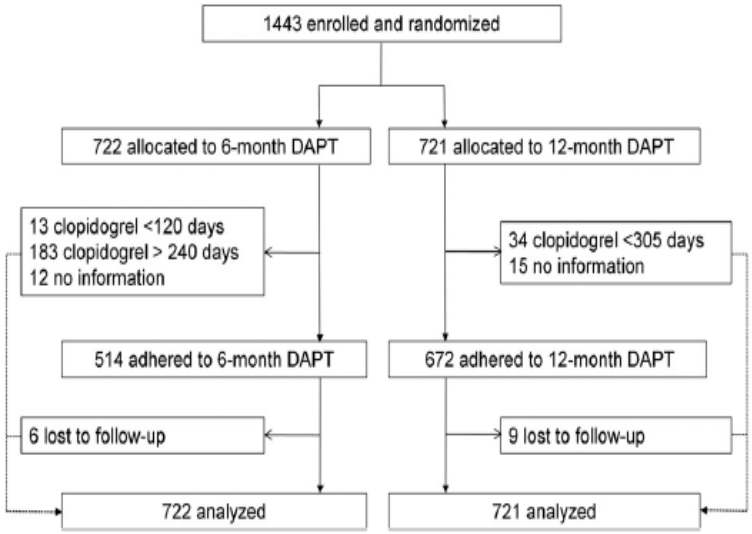
ZEST-LATE & REAL-LATE

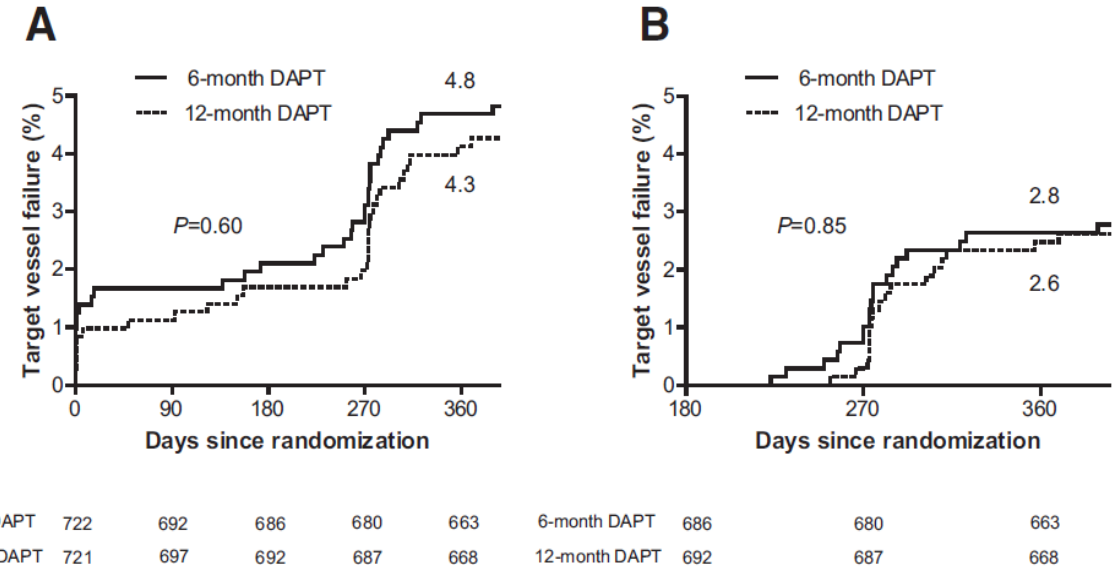


* Park SJ, et al.
N Eng J Med 2010

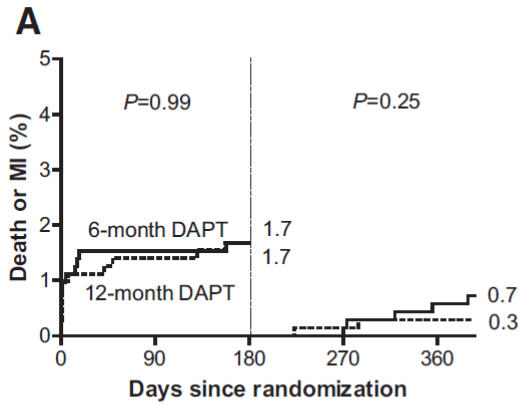
* Included Stents
: SES/ PES/ ZES

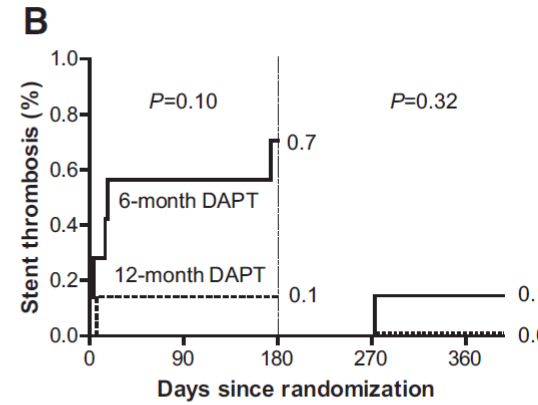
EXCELLENT





6-month DAPT	722	692	686	680	663	6-month DAPT	686	680	663
12-month DAPT	721	697	692	687	668	12-month DAPT	692	687	668





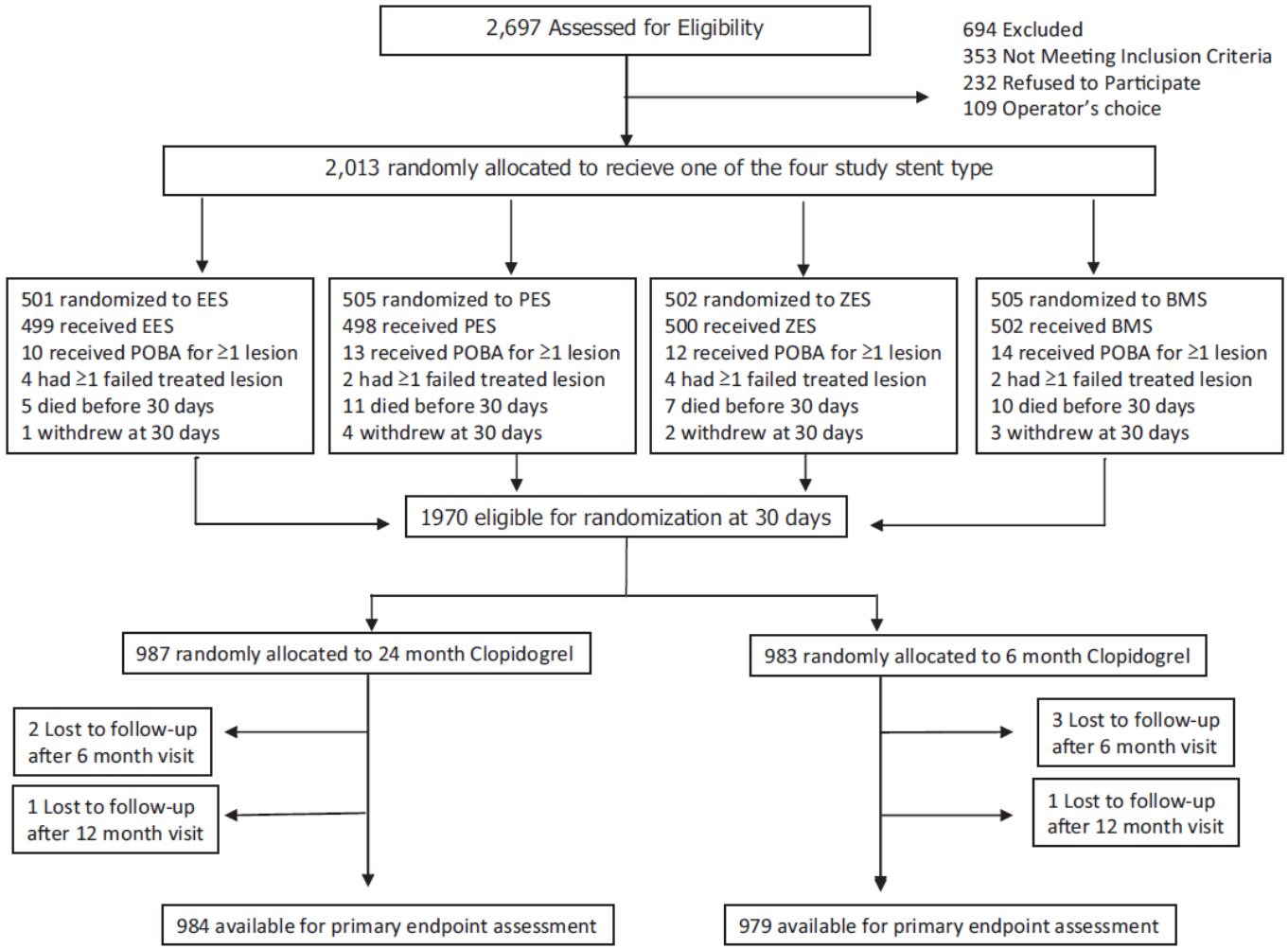
6-month DAPT	722	693	689	688	681
12-month DAPT	721	696	694	691	686

6-month DAPT	722	699	695	694	688
12-month DAPT	721	703	701	698	694

EES: SES (2:1)

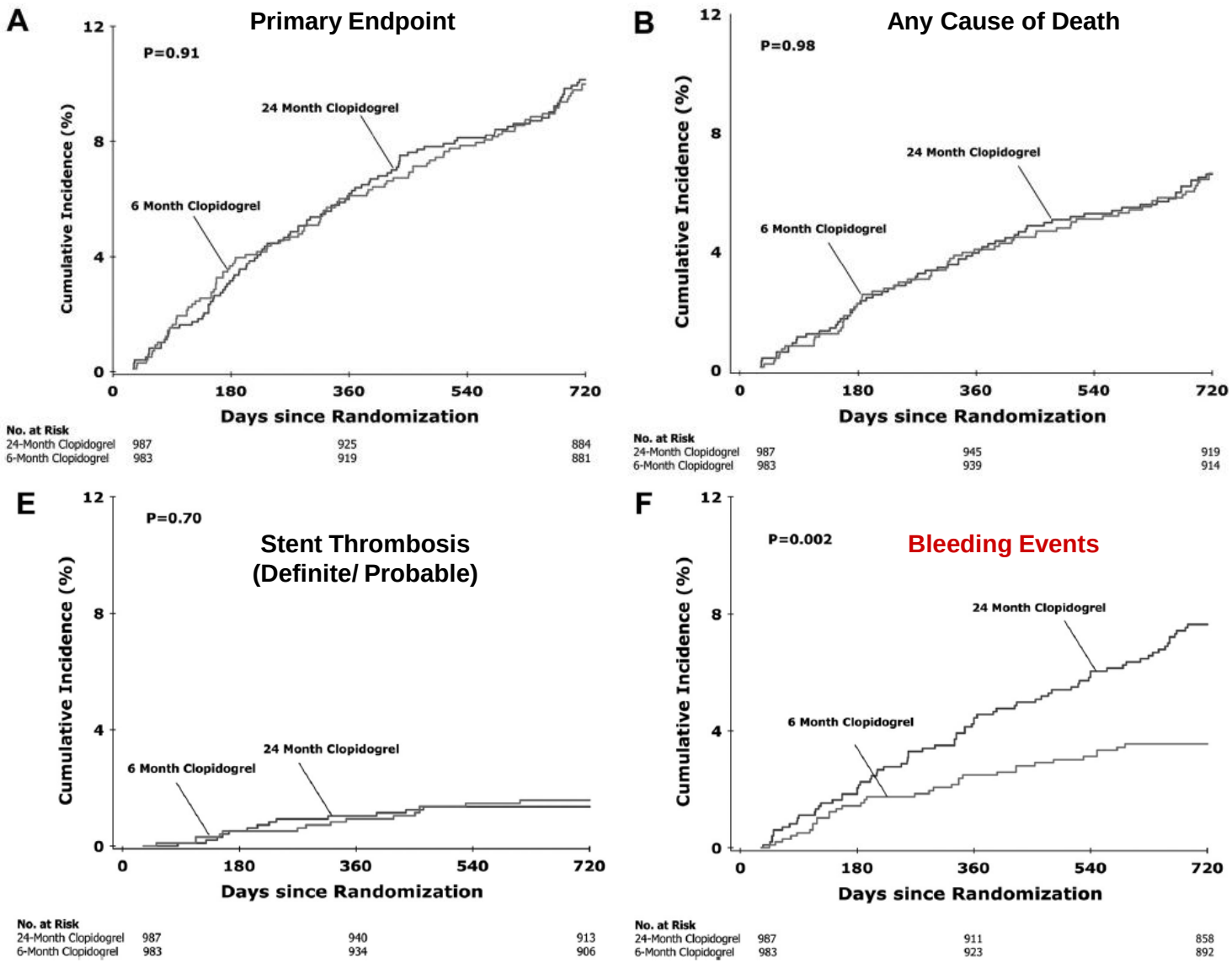
Gwon HC, et al. Circulation 2012

PRODIGY: Study flow



Valgimigli M, et al. Circulation. 2012;125:2015-26

PRODIGY



Valgimigli M, et al. Circulation.2012

Meta-analysis :
EXCELLENT,PROGIDY,REAL/ZEST-LATE & RESET

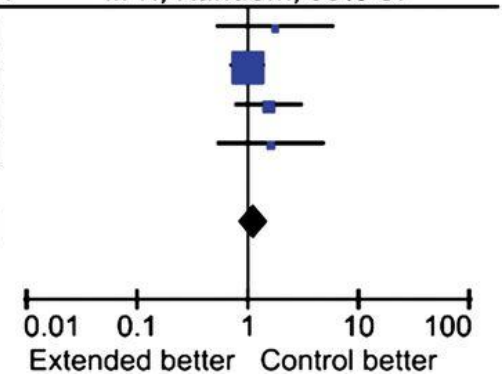
- Extended (16.8 mo) vs. Control (6.2 mo) DAPT groups
- Endpoints
  - Primary : all-cause death
  - Secondary : MI, ST, CVA, TIMI major bleedings

Death

	Extended DAPT		Control DAPT			Odds Ratio	Odds Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**	**M-H, Random, 95% CI**
EXCELLENT	7	712	4	715	5.8%	1.76 [0.51, 6.06]	
PRODIGY	65	984	65	979	69.4%	0.99 [0.70, 1.42]	
REAL/ZEST-LATE	20	1348	13	1334	17.8%	1.53 [0.76, 3.09]	
RESET	8	1042	5	1044	7.0%	1.61 [0.52, 4.93]	
Total (95% CI)		**4086**		**4072**	**100.0%**	**1.15 [0.85, 1.54]**	
Total events	100		87				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.08$, df = 3 (P = 0.56); $I^2 = 0\%$

Test for overall effect: Z = 0.91 (P = 0.36)



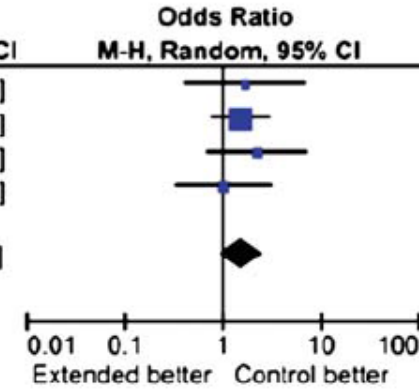
S. Cassese et al., Eur Heart J. 2012

Meta-analysis :
EXCELLENT,PROGIDY,REAL/ZEST-LATE & RESET

C **Cerebrovascular accidents**

Study or Subgroup	Extended DAPT Events	Total	Control DAPT Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
EXCELLENT	5	712	3	715	11.8%	1.68 [0.40, 7.05]
PRODIGY	21	984	14	979	52.1%	1.50 [0.76, 2.97]
REAL/ZEST-LATE	9	1348	4	1334	17.4%	2.23 [0.69, 7.27]
RESET	6	1042	6	1044	18.8%	1.00 [0.32, 3.12]
Total (95% CI)		**4086**		**4072**	**100.0%**	**1.51 [0.92, 2.47]**
Total events	41		27			

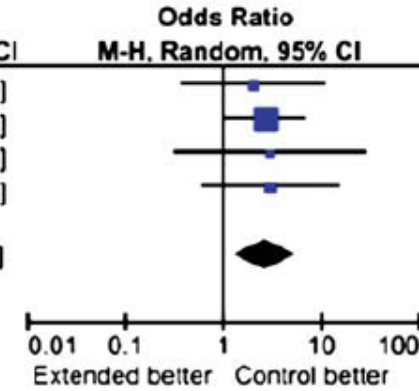
Heterogeneity: Tau² = 0.00; Chi² = 0.95, df = 3 (P = 0.81); I² = 0%
Test for overall effect: Z = 1.65 (P = 0.10)



D **TIMI Major bleeding**

Study or Subgroup	Extended DAPT Events	Total	Control DAPT Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
EXCELLENT	4	712	2	715	16.8%	2.01 [0.37, 11.03]
PRODIGY	16	984	6	979	54.8%	2.68 [1.04, 6.88]
REAL/ZEST-LATE	3	1348	1	1334	9.5%	2.97 [0.31, 28.62]
RESET	6	1042	2	1044	18.9%	3.02 [0.61, 14.98]
Total (95% CI)		**4086**		**4072**	**100.0%**	**2.64 [1.31, 5.30]**
Total events	29		11			

Heterogeneity: Tau² = 0.00; Chi² = 0.14, df = 3 (P = 0.99); I² = 0%
Test for overall effect: Z = 2.73 (P = 0.006)

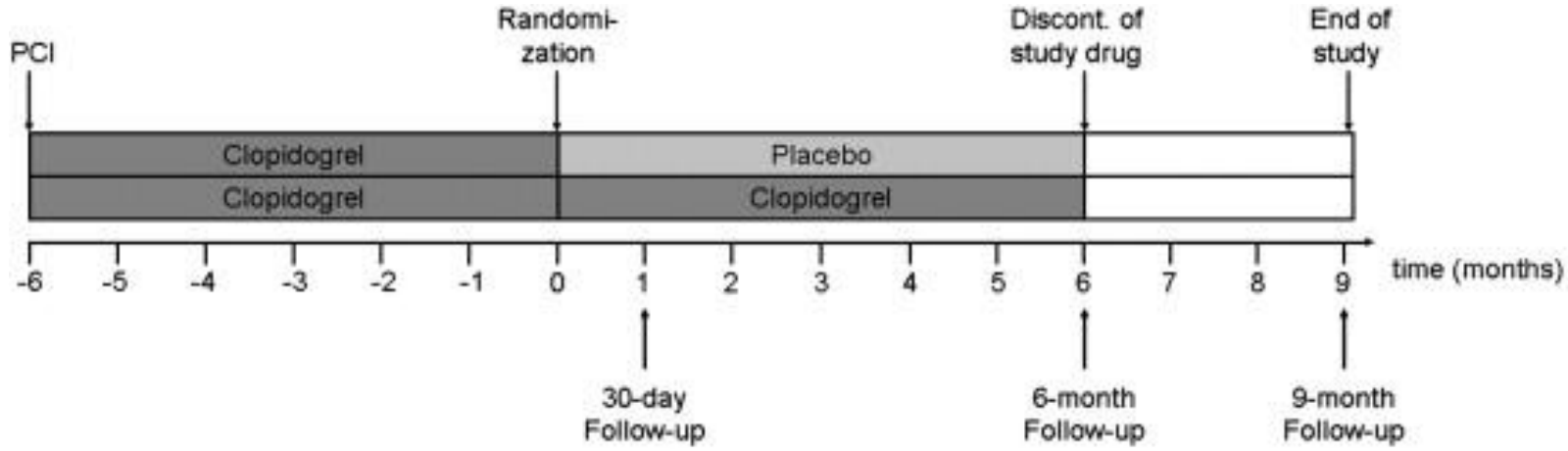


S. Cassese et al., Eur Heart J. 2012

ISAR-SAFE

- Previous trials were not powered for ischemic endpoints, were open-label and the time from stenting to randomization varied.

- Study design of ISAR-SAFE (n=6,000)



- Primary endpoint : composite of death, MI, ST, stroke, or major bleeding

ISAR-SAFE : Results (AHA 2014)

- Terminated early due to a lower than-expected event rate.
  - 12 mo. (n=2007) vs. 6 mo. (n=1997)
  - The results met the prespecified criteria for non-inferiority (p<0.001)

Table 1. Outcomes at 9 Months Postrandomization by DAPT Duration

	6 Months	12 Months	*P* Value
Primary Endpoint	1.5%	1.6%	.70
Death, MI, Definite/Probable Stent Thrombosis, Stroke	1.3%	1.5%	.59
Definite Stent Thrombosis	0.3%	0.2%	.49
MI	0.7%	0.7%	.85
TIMI Major or Minor Bleeding	0.3%	0.7%	.12

  - The results are aligned with those of several prior studies, and DAPT interruption at 6 mo may be possible.

2014 ESC/EACTS Guidelines on myocardial revascularization

- SCAD
  - DAPT for 6mo after DES → asprin (IB)
  - DAPT for 1mo after BMS → aspirin (IA)
  - Shorter DAPT duration (<6mo) may be considered after DES in patients with high risk bleeding risk (IIbA)
- NSTE-ACS
  - DAPT (ticagrelor, prasugrel > clopidogrel) over 12mo unless there are contraindications such as excessive bleeding (IA)
- STEMI
  - DAPT (ticagrelor, prasugrel > clopidogrel) over 12mo unless there are contraindications such as excessive bleeding (IA)
  - Reference : PCI-CURE, TRITON-TIMI38, PLATO

Problems of '>12mo DAPT' recommendation in ACS

- PCI-CURE did not reflect contemporary PCI.
- TRITON & PLATO trial
  - >12months use : no enough data yet
- Clinical predictors of ischemic and bleeding complications are largely overlapped.
  - Women, CKD, old age, leukocytosis, anemia, Killip class etc..
  - Bleeding complications are not negligible and they have long-term adverse effects on patient's prognosis.

Conclusion

- ≤ 6 months DAPT is reasonable in SCAD patients with newer-generation DESs, especially CoCr-EES.

- Routine 12 months' DAPT strategy in ACS patients should be confirmed.

- Weighing balance b/w ischemia vs. bleeding is required.