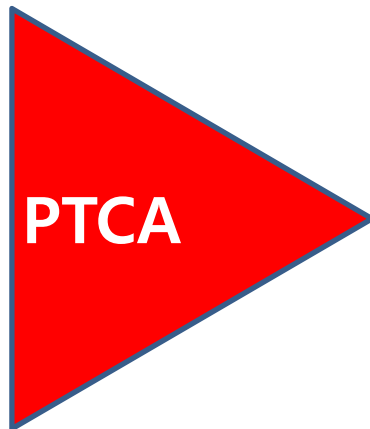


# **The Duration of Dual Anti-PLT Therapy after DES**

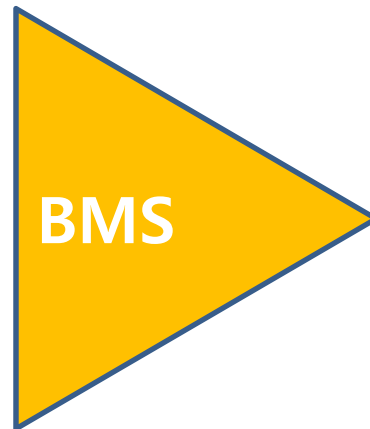
**INJE University Medical College  
Sanggye Paik Hospital, Cardiovascular Center**

**Byoung Kwon Lee**

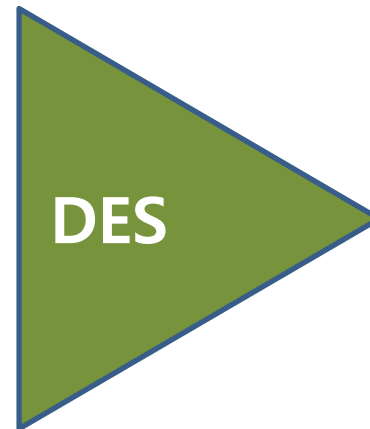
# Angioplasty has been marching through with adjunctive medical therapy



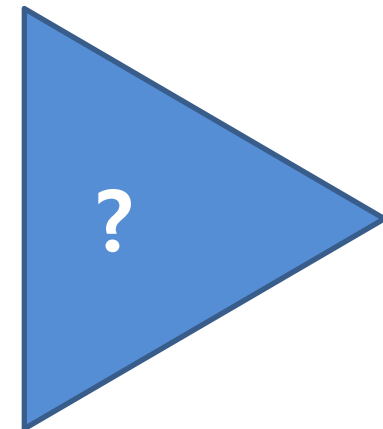
Aspirin  
Heparin



Aspirin  
Heparin  
Dextran  
Dipyridamole  
Coumadine  
Thienopyridine



**Aspirin**  
**Clopidogrel**  
**Cilostazol**  
**GP IIb/IIIa inhibitor**



# Stent thrombosis

- **Most commonly occurs in the 1<sup>st</sup> month after stent implantation, ; “subacute stent thrombosis.”**
- **“Late” stent thrombosis, particularly in DES,**
  - occurring months or even years after stenting
- Resulting in **life-threatening complications.**
  - **Death or MI** associated with angiographically documented stent thrombosis; **64.4%**
  - **Mortality rates** due to presumed or documented stent thrombosis; **20% to 45%**

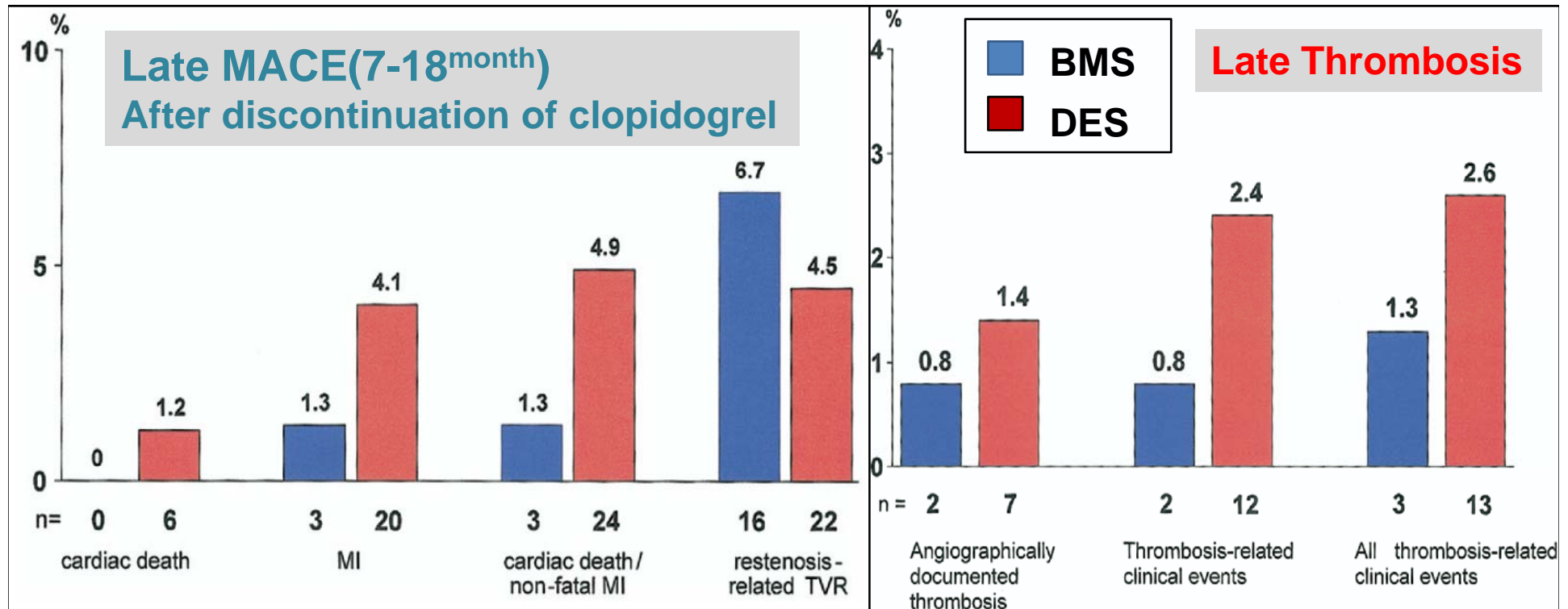
# Late Stent Thrombosis

## In the current era of DAT

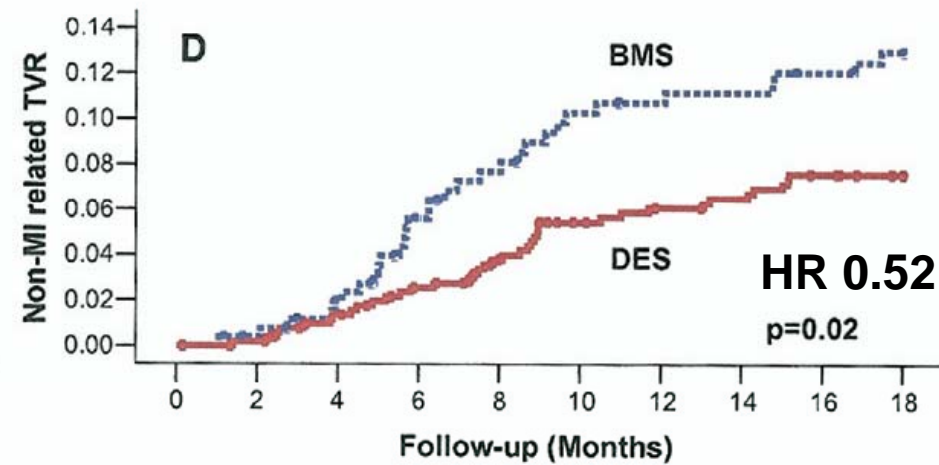
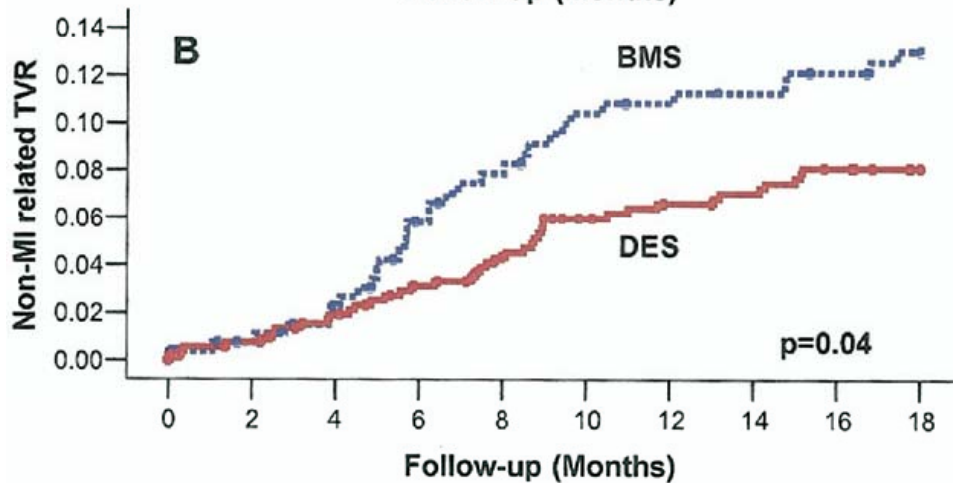
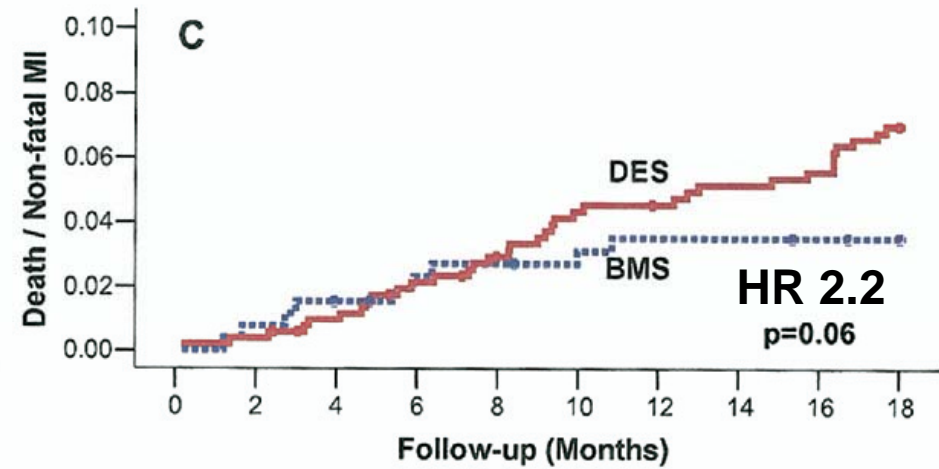
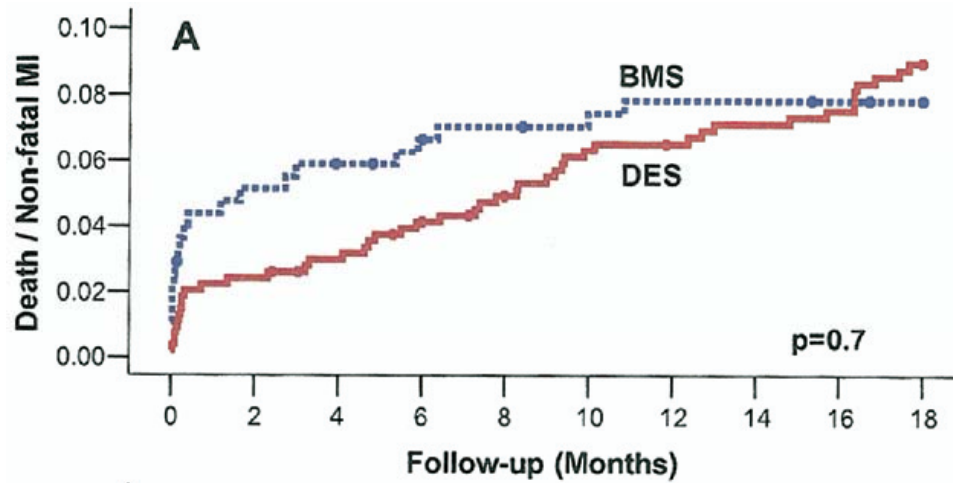
- Overall occurrence of SAST: 1%
- Late (1 to 12 months) stent thrombosis
  - not apparent with BMS
  - **0.19% of patients in a large DES registry (BASKET-LATE)**
- Many Case reports
- BASKET-LATE (*JACC 2006;48:2548*)
- SCAAR (*NEJM 2007;356:1009*)
- Denmark Registry (*JACC2007;50:463*)

# BASKET-LATE

- Observational Study for ST after D/C of DAT
- 746 patients, 1,333 stented lesion
- 6<sup>month</sup> event-free / 1yr F/U

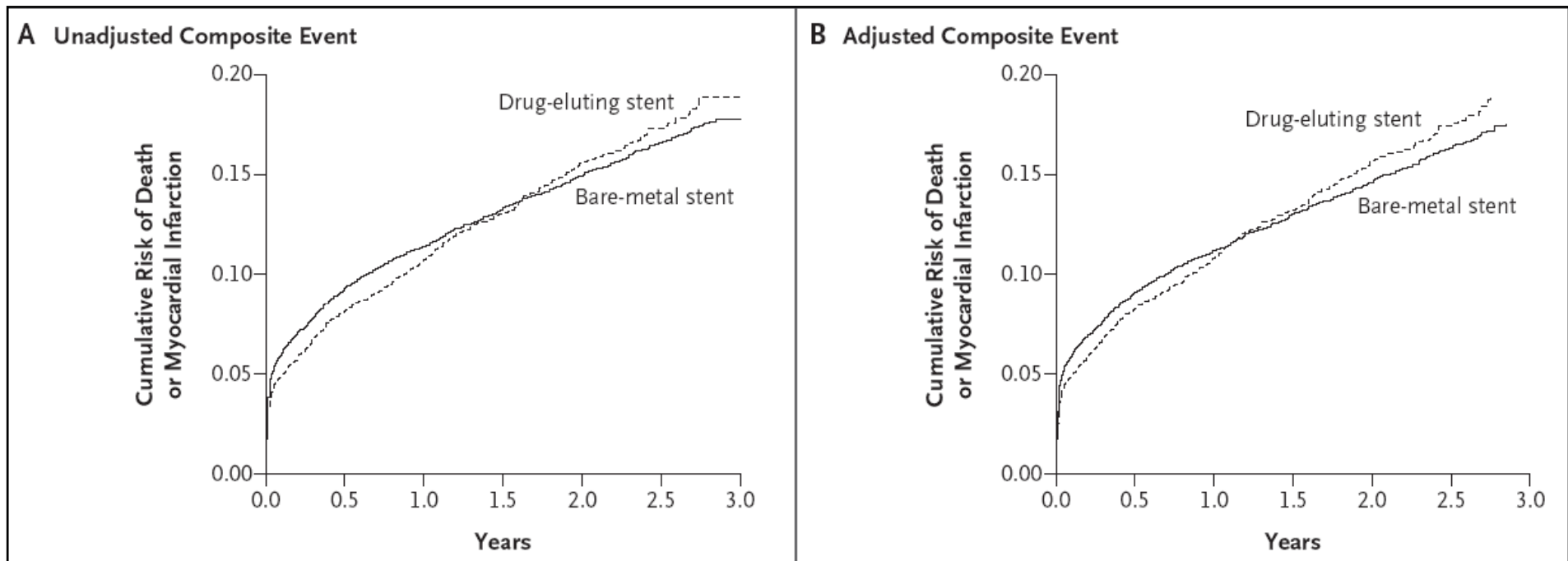


# BASKET-LATE



# SCAAR

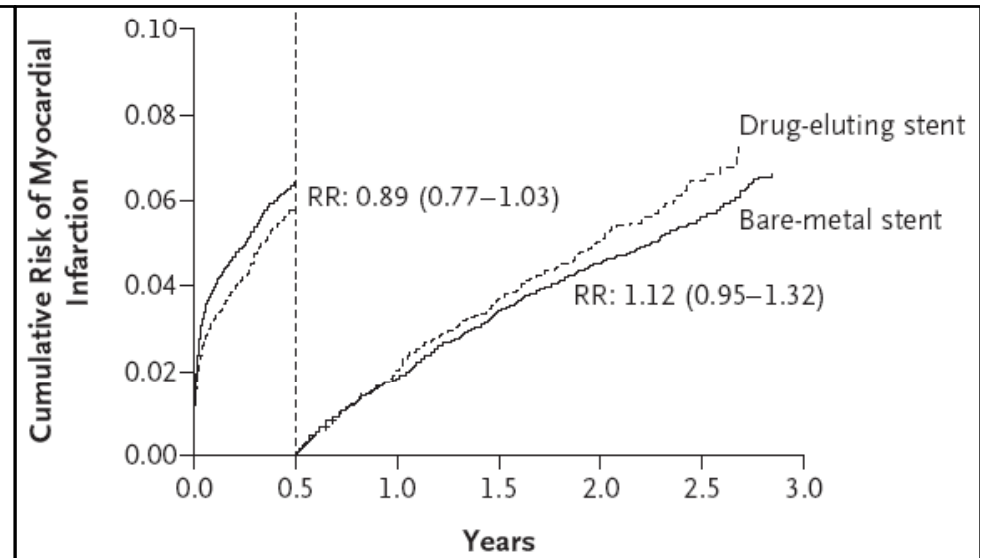
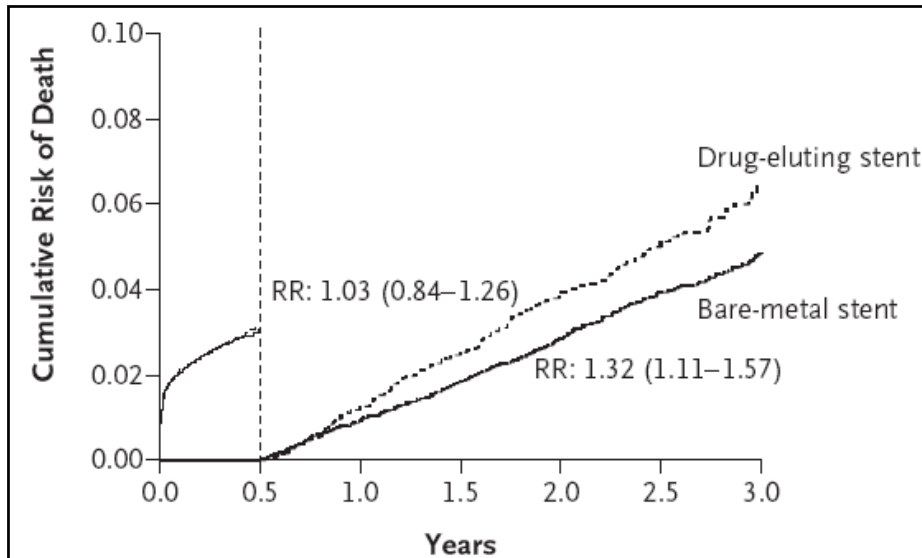
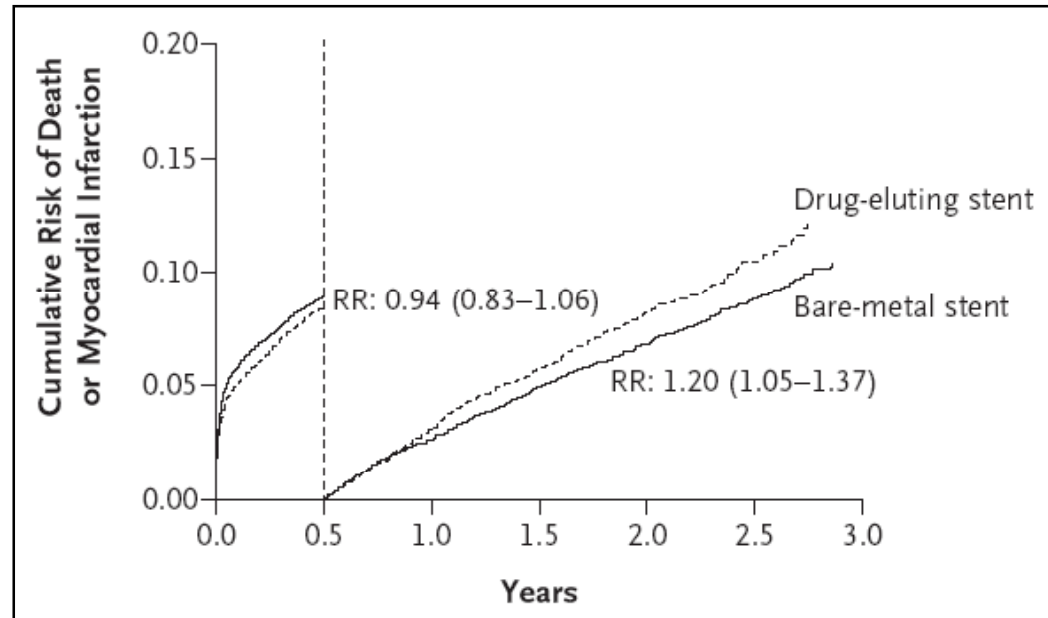
- Swedish Coronary Angioplasty Registry
- Unselected, consecutive cohort
- 6,033 with DES, and 13,738 with BMS
- DAT: 6<sup>month</sup> in DES, 1-3<sup>month</sup> in BMS



# SCAAR

## 6<sup>month</sup> landmark analysis

1. Most Swedish guideline:  
6<sup>month</sup> use of clopidogrel
2. Event rate:  
merged at 6month



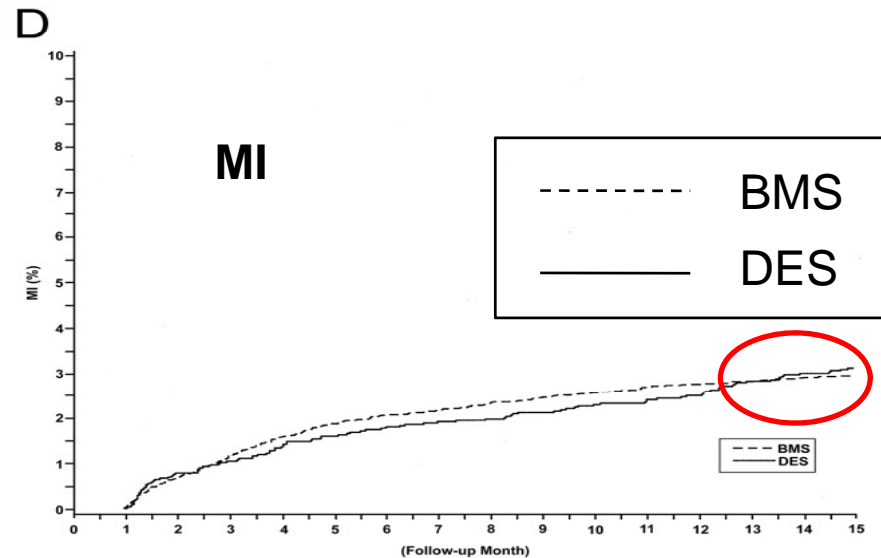
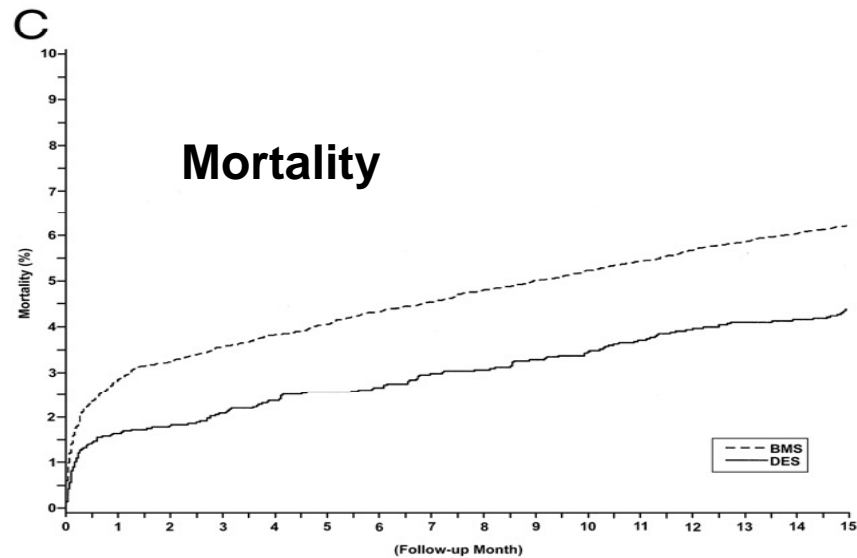
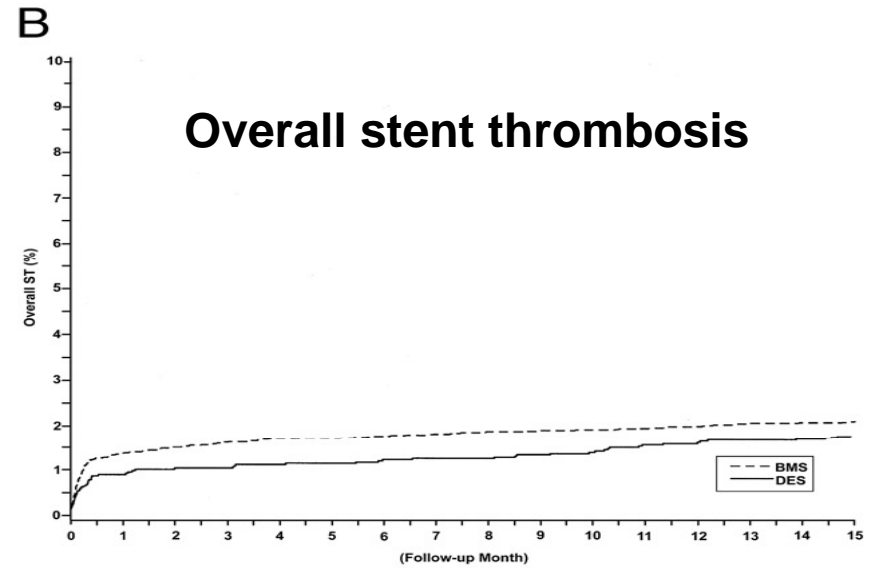
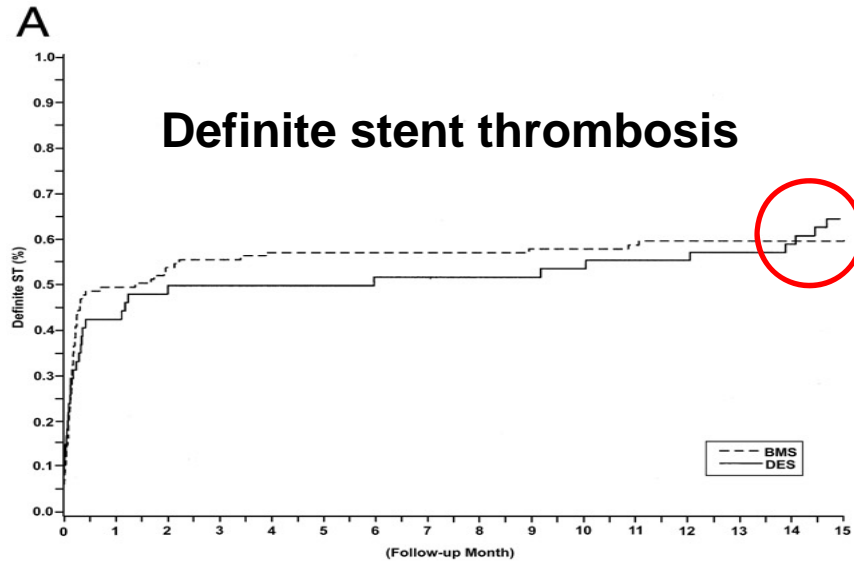
# Denmark Heart Registry

- **Prospective Registry in the Western Denmark.**
- **12,395 consecutive patients (17,152 lesions)**
- **DES: 3,548 Pt. (5,422) vs. BMS: in 8,847 Pt. (11,730)**
- **F/U for 15 months.**
- **Clopidogrel treatment duration: 3 ~ 12 months**

## Risk of Definite Stent Thrombosis in Lesions Treated With BMS, or DES

	BMS		DES		Hazard Ratio* (95% Confidence Interval)	p Value
	No. of Events	No./100 Person-Yrs	No. of Events	No./100 Person-Yrs		
All	71	0.5	35	0.5	0.93 (0.60-1.46)	0.76
Acute (24 h)	12	37.5	8	54.1	0.94 (0.33-2.67)	0.90
1 day to <30 days	46	4.9	15	3.4	0.69 (0.38-1.27)	0.23
30 days to 12 months	12	0.1	7	0.2	0.93 (0.35-2.89)	1.00
≥12 months	1	0.04	5	0.4	10.93 (1.27-93.76)	0.029

# Denmark Heart Registry



# More Prevalent in

## Clinical

- Advanced Age
- Acute coronary syndrome
- Diabetes
- Low ejection fraction
- Prior brachytherapy
- Renal failure

## Angiographic

- Long stents
- Multiple lesions
- Overlapping stents
- Ostial / bifurcation lesions
- Small vessels
- Suboptimal stent results

**Premature Withdrawal of Clopidogrel**

# Vulnerability of ST in DES

- Reduced neointima formation
- Delayed endothelialization
- More inflammation
- Hypersensitivity
- Thrombus formation
- Outward remodelling

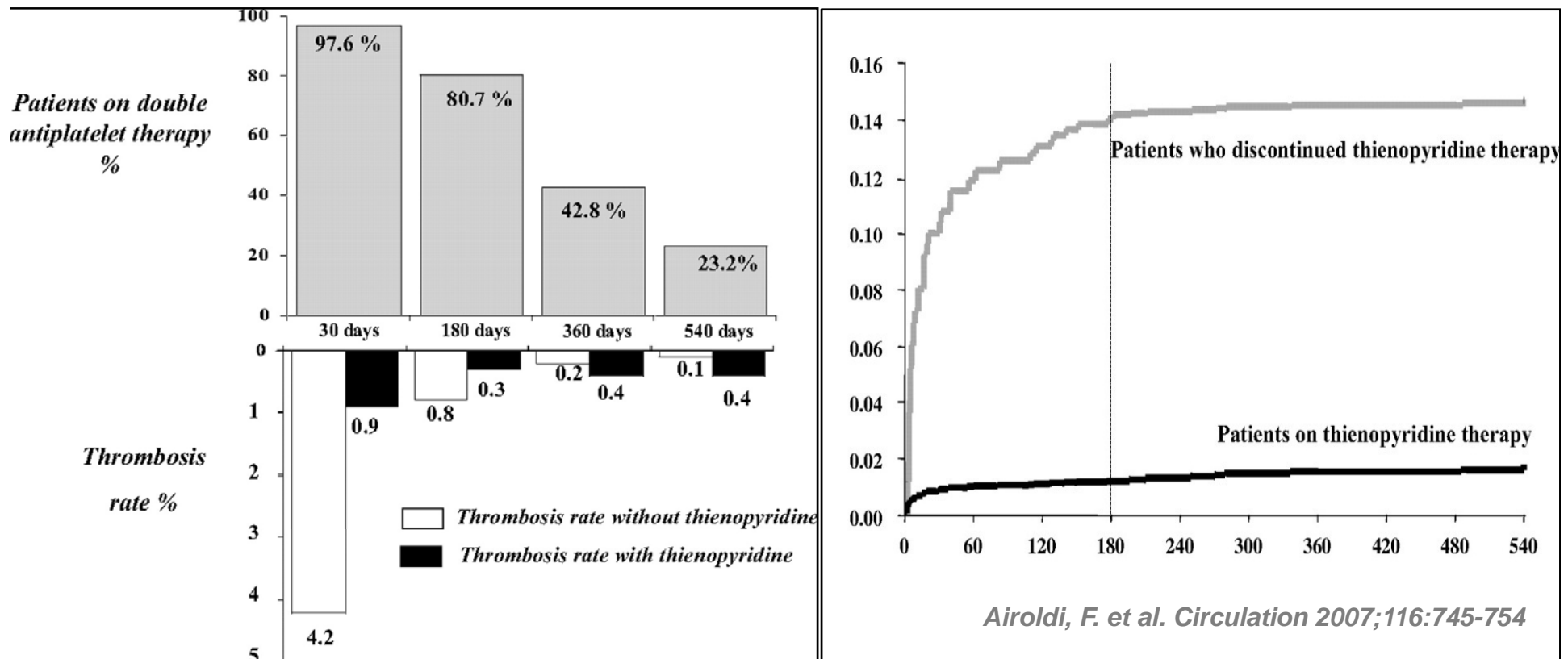
# Premature discontinuation of DAT

- **ST occurred in 29%** (*Iakovou I et al. JAMA 2005;293:2126*)
  - hazard ratio of 161(C.I: 26- 998) for SAST
  - hazard ratio of 57 (C.I: 15 - 220) for LAST.
- **In a single-site study with SES** (*Jeremias A et al. Circulation 2004;109:1930*)
  - 30-fold greater risk of stent thrombosis
  - 25% ST; discontinued DAT within the 1<sup>st</sup> month
- **Park et al.** (*Am J Cardiol 2006;98:352– 6*)
  - 7.8% ST in premature interruption of DAT
- **PREMIER registry** (*Circulation 2006;113:2803*)
  - 500 patients with acute MI treated with DES.
  - Mortality over 11 months: (stopped DAT: 7.5% vs. not stopped; 0.7%)
- **BASKET-LATE** (*J Am Coll Cardiol 2006;48:2584*)
  - 746 patients (1133 lesions) to DES vs. BMS
  - All patients; DAT for 6 months + ASA continued.

Death/MI	DES	BMS
At 30 <sup>d</sup>	2.0%	4.69%
After 6 <sup>m</sup> (LAST)	4.9% (2.6%)	1.3% (1.3%)

# ST after Clopidogrel Withdrawal

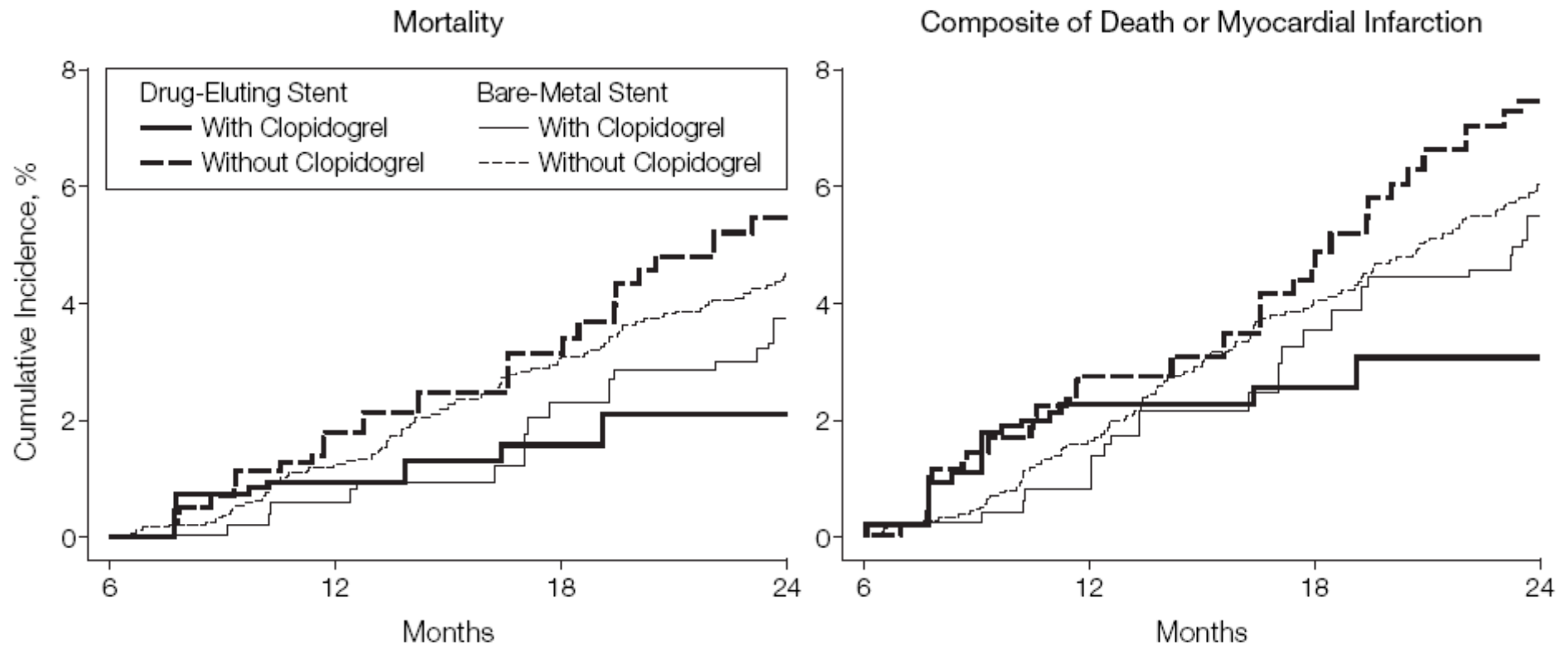
- Prospective observational cohort in Europe
- 3,021 patients, 5,389 lesions with DES
- **Within / After 6<sup>mon</sup> of Stenting; 13<sup>days</sup> / 90<sup>days</sup>**



# Duke Hospital

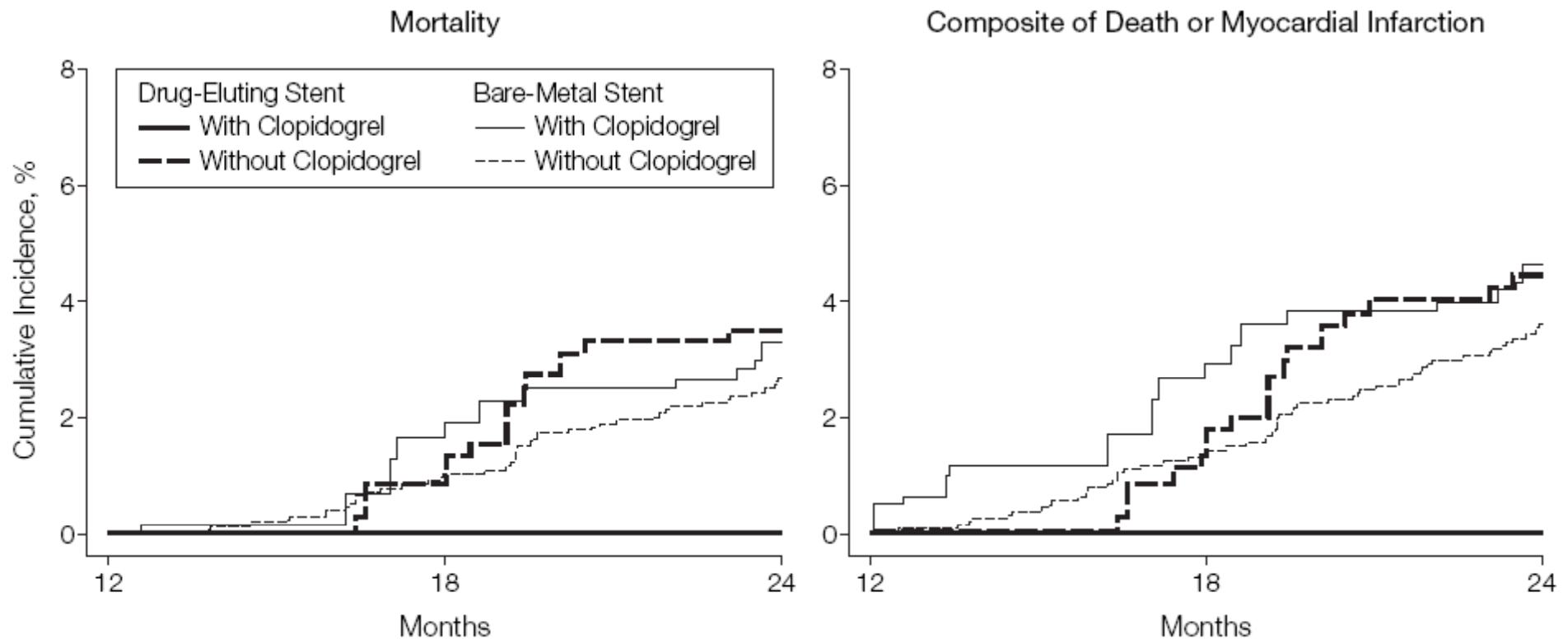
- An observational study.
- 4,666 patients; BMS (n=3,165) or DES (n=1,501).
- Landmark analyses were performed among **patients who were event free at 6/12<sup>month</sup> F/U**
- **4 groups : DES with/without clopidogrel  
BMS with/without clopidogrel**

# Mortality and Composite of Death or MI Using the 6-Month Landmark Analysis



*Einstein et al. JAMA. 2007;297:159-168*

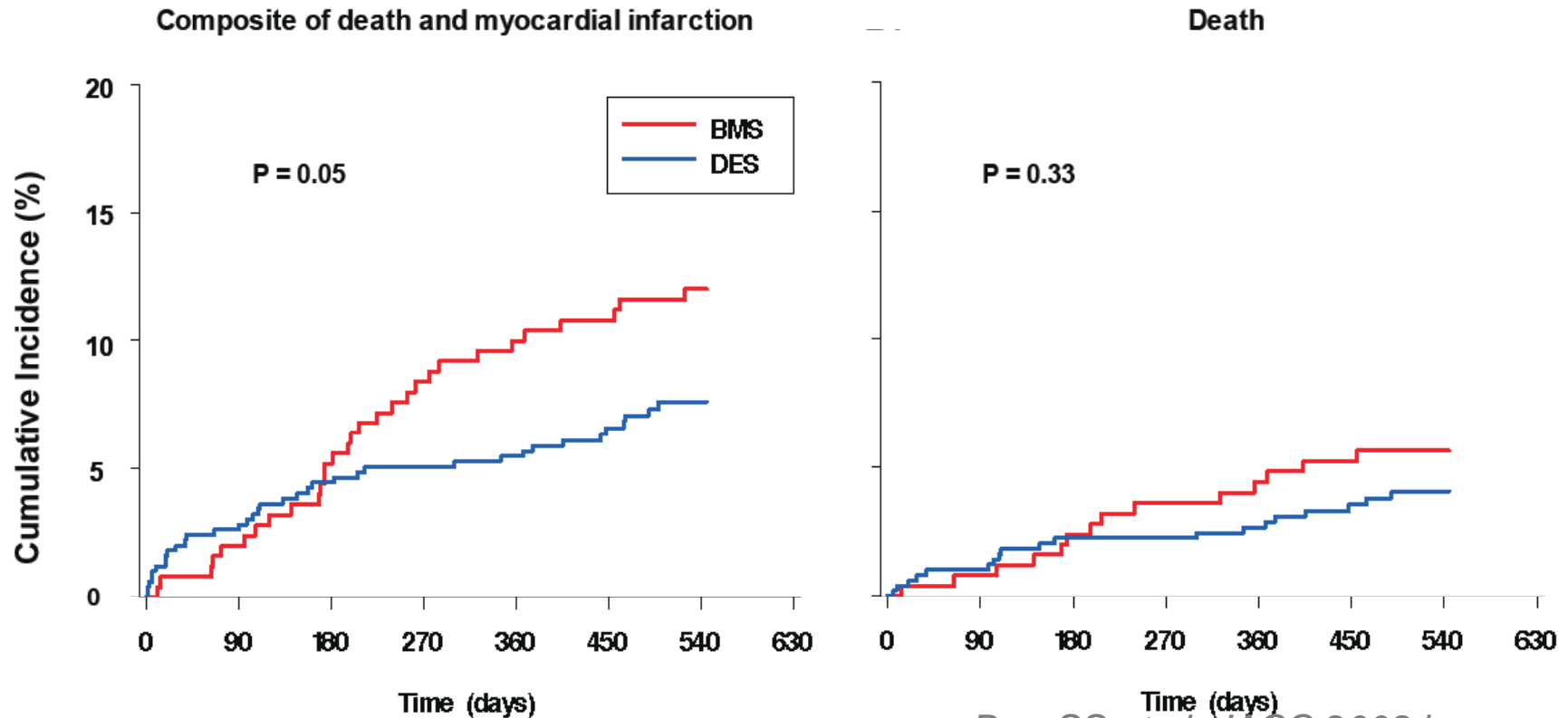
# Mortality and Composite of Death or MI Using the **12-Month** Landmark Analysis



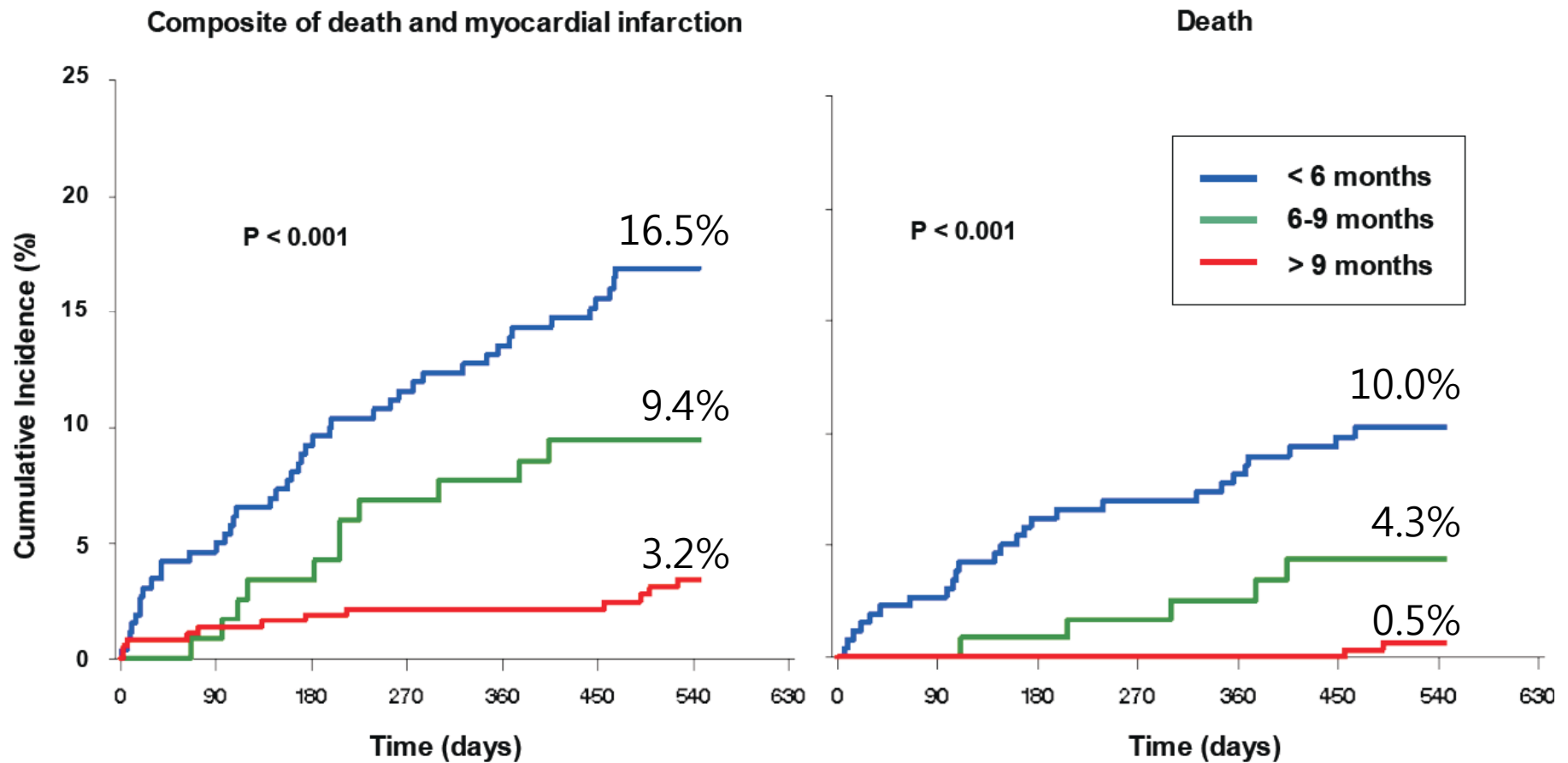
*Einstein et al. JAMA. 2007;297:159-168*

# Long-term Outcomes by Clopidogrel Duration and Stent Type in Diabetes

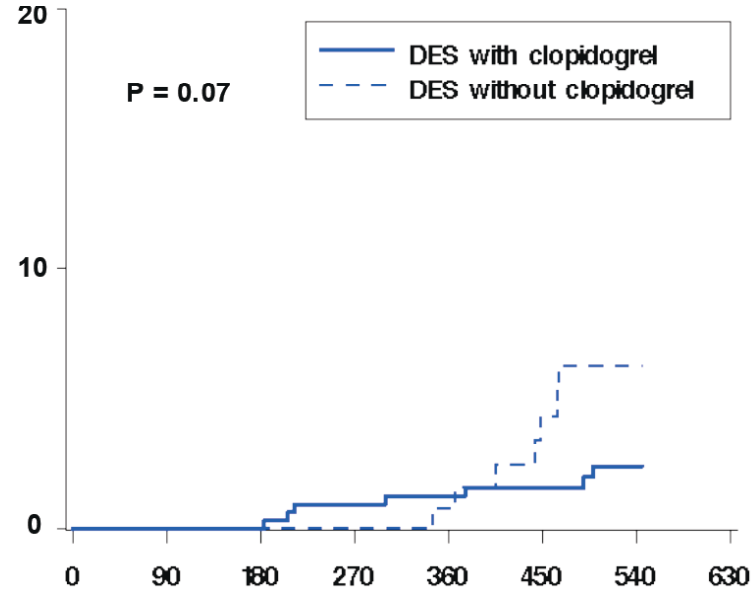
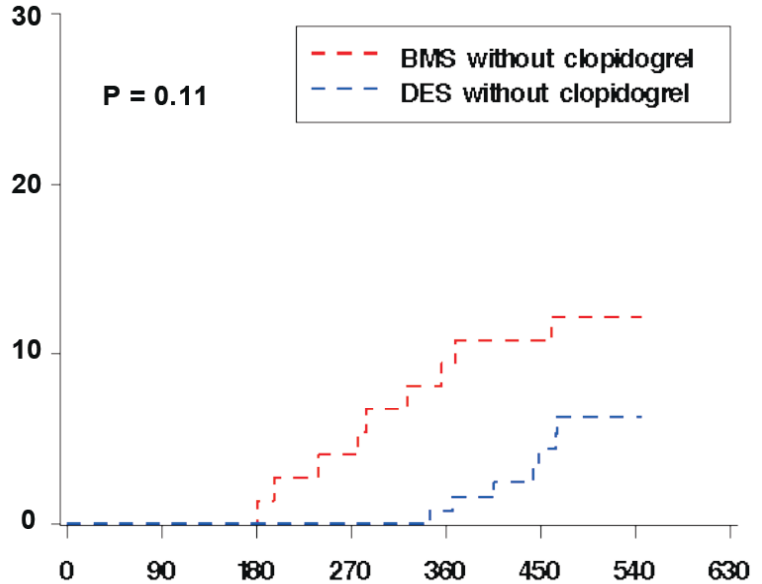
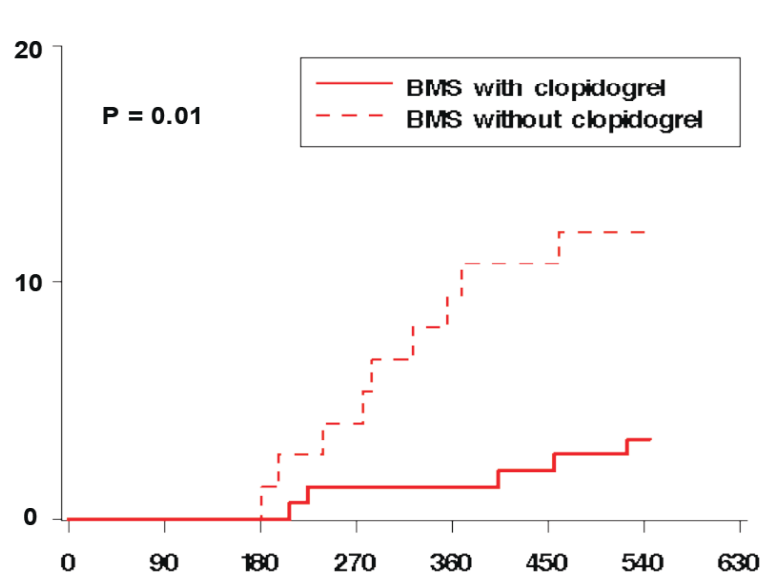
- Observational study, Los Angeles and Pasadena (UCLA)
- 749 patients with DM; BMS (n=251) vs. DES (n=498)
- Grouped by Clopidogrel; users > 180<sup>days</sup> non-users < 180<sup>days</sup>



# Composite End point and Mortality according as Clopidogrel Duration



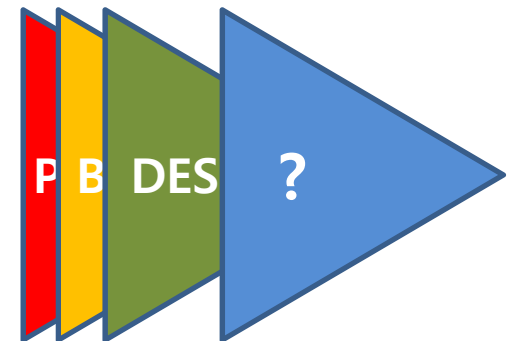
# Landmark analysis for Death and MI According as Stent type and Clopidogrel user



Hazard ratio (95% C.I)	Clopidogrel	
	Non-User	User
<b>BMS</b>	<b>Ref.</b>	<b>0.25</b> (0.08-0.81, p=0.02)
<b>DES</b>	<b>0.39</b> (0.13-0.1.13, p=0.08)	<b>0.22</b> (0.08-0.62, p=0.005)

# Evolution of DES

- **On-label USE of DES in real world?**
  - Previously untreated CAD, except ACS
  - Lesion length: <30mm
  - Ref. diameter: 2.5~3.75mm
- **New generation of DES?**
  - Sirolimus ES; Cypher<sup>®</sup>
  - Paclitaxel ES; TAXUS<sup>®</sup>, PICO elite<sup>®</sup>
  - Zotarolimus ES; Endeavor<sup>®</sup>
  - Everolimus ES; Xience<sup>®</sup>
  - Biodegradable Stent



# ACC/AHA Guideline (Clopidogrel duration in DES)

- **Class I**
  - At least 12 months, when not high risk of bleeding
- **Class IIa**
- **Class IIb**
  - Continuation of clopidogrel beyond 1<sup>yr</sup> in DES

**How long will you prescribe?**

**Consensus: at least, 1<sup>yr</sup>**

**Then, Lifelong?**