

# **Drug-Eluting vs. Bare Metal Stents: Results from a Practice-Based Registry**

**Eric L. Eisenstein, DBA; Kevin J. Anstrom, PhD; David F. Kong, MD, AM;  
Linda K. Shaw, MS; Robert H. Tuttle, MSPH; Daniel B. Mark, MD, MPH;  
Judith M. Kramer, MD, MS; Robert A. Harrington, MD;  
David B. Matchar, MD; David E. Kandzari, MD;  
Eric D. Peterson, MD, MPH; Kevin A. Schulman, MD; Robert M. Califf, MD**

**From the Division of Cardiology, Department of Medicine, Duke University  
Medical Center, Duke Clinical Research Institute, Duke Translational Medicine  
Institute, Duke DECIDE Network, and the Duke Center for Clinical Health Policy  
Research, Durham, NC**

**Supported by the Agency for Healthcare Research & Quality  
Contract No. 290-05-0032**

**Duke University Medical Center Institutional Review Board Approval  
Registry Number 8223-06-2R0ER**

# Disclosures

- **DCRI Faculty Disclosures available at:**

**<http://www.dcri.org/research/coi.jsp>**

- **The authors are responsible for content. Statements should not be construed as endorsement by the Agency for Healthcare Research and Quality or the US Department of Health and Human Services.**

# Background and Objectives

- Extrapolating drug eluting stent (DES) clinical trial results onto clinical practice may be unreliable.
- Current antiplatelet regimens may not be sufficient to prevent late adverse events.
- This analysis examined outcomes for:
  - ◆ DES and bare metal stent (BMS), and
  - ◆ Clopidogrel use beyond 6 months.

# Study Population

- **Duke Databank for Cardiovascular Disease**
- **Patients receiving:**
  - ◆ **BMS, January 2000 - July 2005**
  - ◆ **DES, April 2003 - July 2005**
- **Exclusion criteria**
  - ◆ **Congenital heart disease**
  - ◆ **Valvular heart disease**
  - ◆ **Prior CABG or PCI**
  - ◆ **Left main coronary disease**

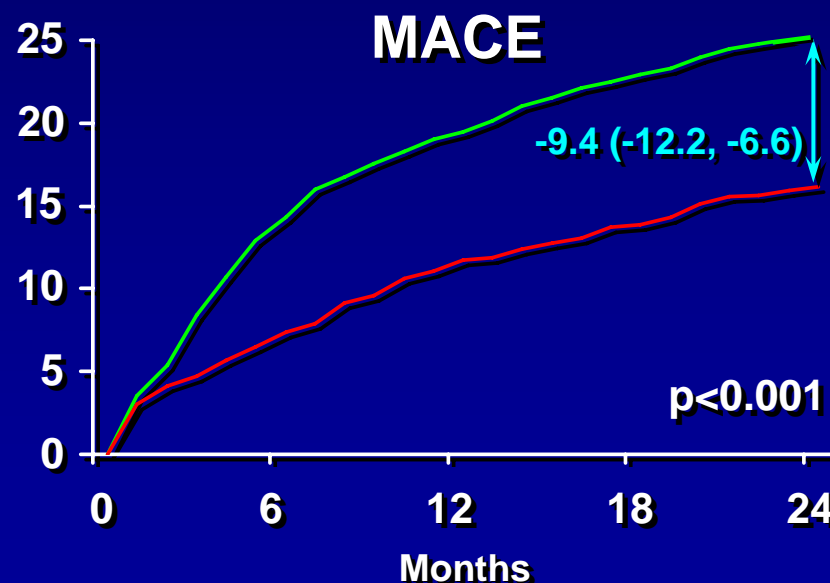
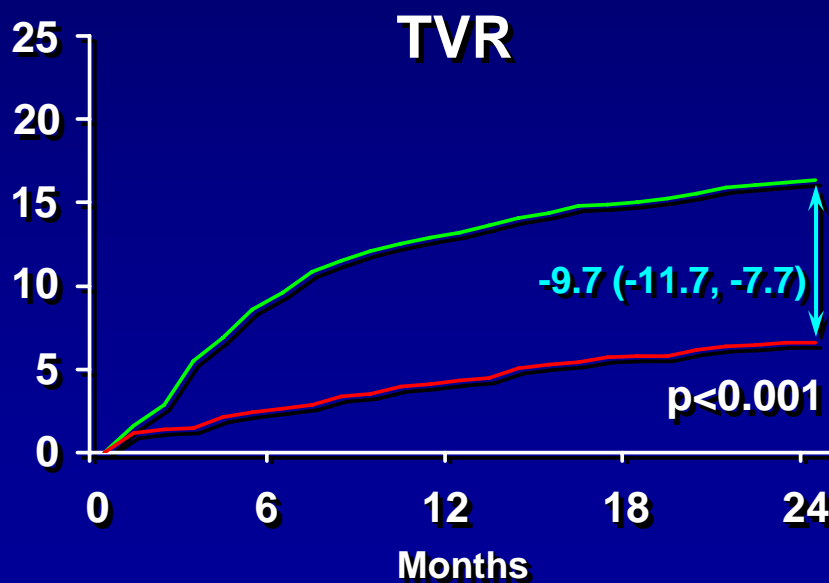
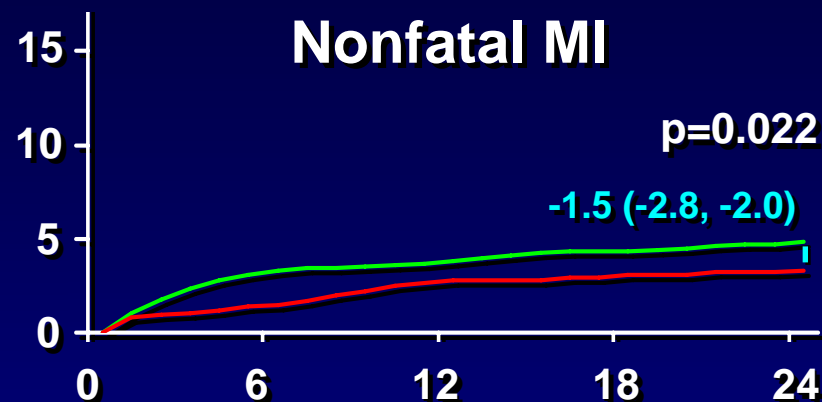
# Data Collection

- Initial: Demographic, medical history, physical examination and catheterization data
- Follow-up (at 6 months, 1 year, and then annually)
  - ◆ Medication use (Clopidogrel, aspirin)
  - ◆ Events up to 24 months (through September 7, 2006)
  - ◆ Censored at time of last contact
  - ◆ 98% follow-up completion rate
  - ◆ Median follow-up 3.1 years

# Baseline Patient Characteristics

	BMS	DES	P- value
Number of Patients	3165	1501	
Age Median (Q1,Q3)	60 (52, 70)	61 (53, 70)	0.42
White Race (%)	70	69	0.37
Male Gender (%)	63	63	0.85
Diabetes (%)	25	28	0.045
CHF (%)	11	12	0.47
Previous MI (%)	48	42	<0.001
Number of Diseased Vessels (%)			<0.001
1	64	57	
2	28	31	
3	8	12	
Stent Diameter mm			<0.001
Median (Q1,Q3)	3.0 (2.8, 3.3)	2.8 (2.5, 3.0)	

# Cumulative Incidence Rates



DES BMS  
DES-BMS (95% CI)

# Landmark Analysis

- A form of survival analysis
- The cohort consists of patients without death, MI, or revascularization at a specific time after initial stent placement (the “landmark” time point)
- Outcomes evaluated from this landmark time point forward



# Landmark Analysis

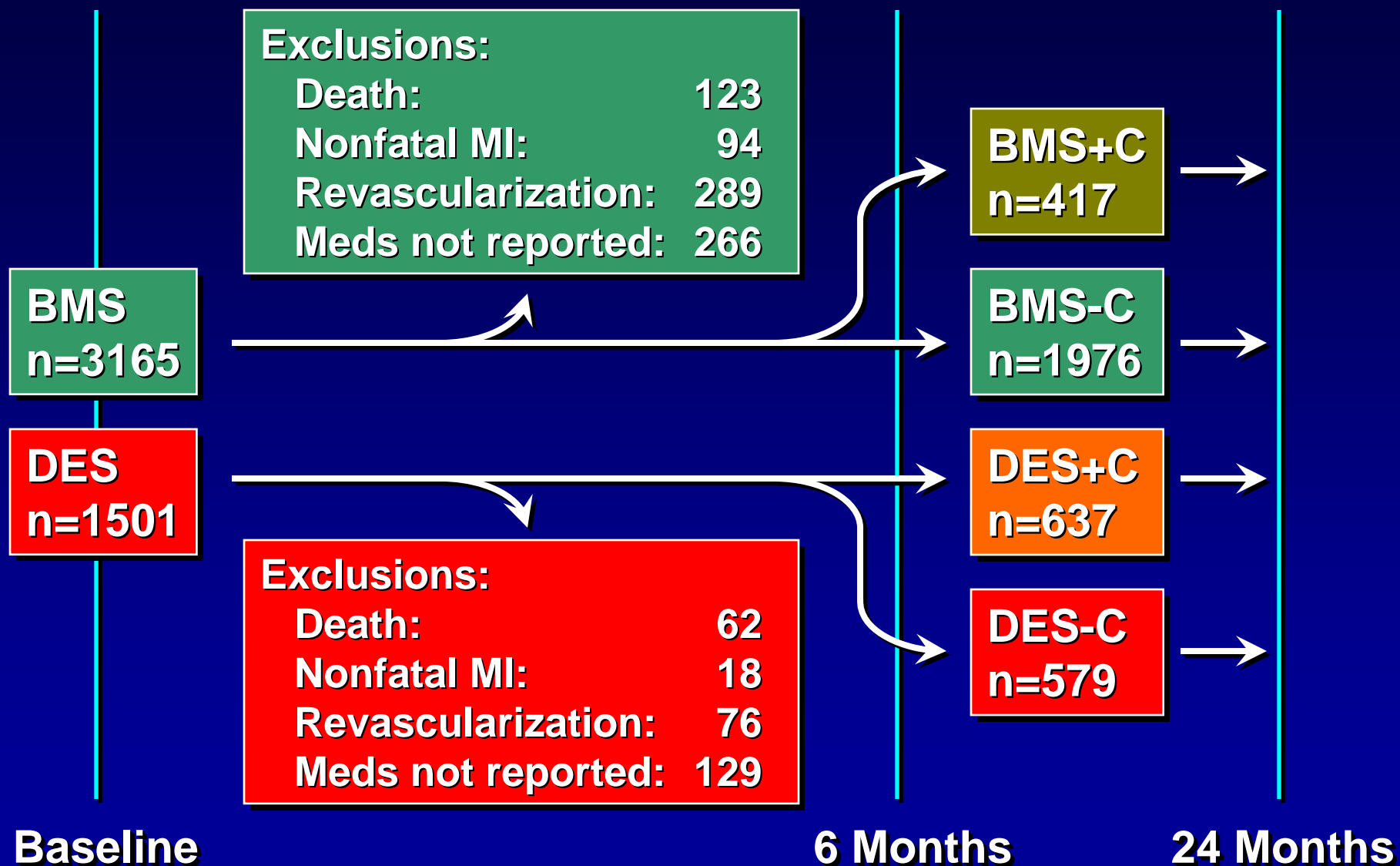
- Patients categorized into one of 4 groups:

- ◆ DES with clopidogrel (DES+C)
- ◆ DES without clopidogrel (DES-C)
- ◆ BMS with clopidogrel (BMS+C)
- ◆ BMS without clopidogrel (BMS-C)

- Two landmark analyses:

- ◆ From 6 months forward
- ◆ From 12 months forward

# 6-Month Landmark View



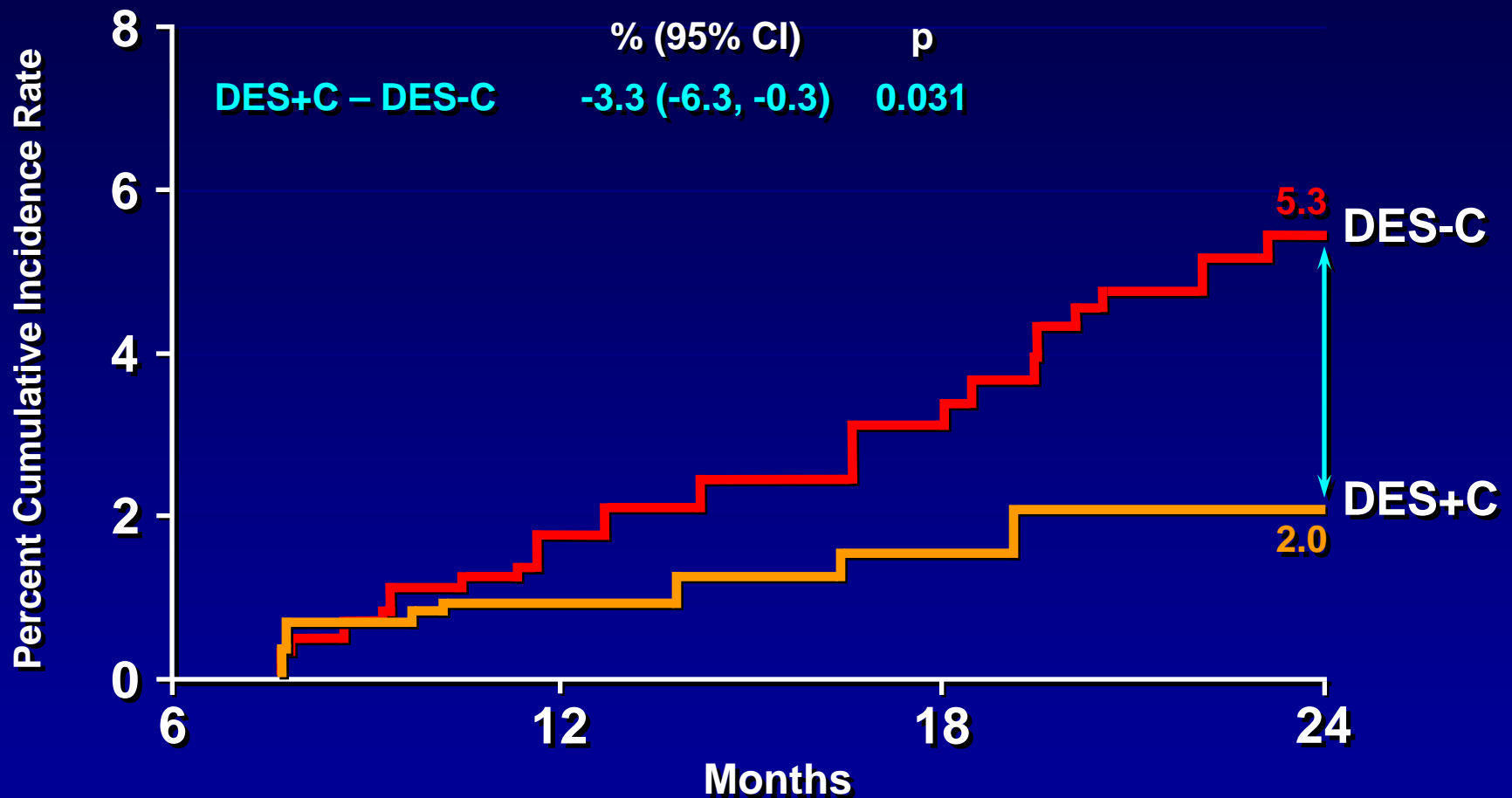
# 6-Month Landmark Patient Characteristics

	DES+C (n=637)	DES-C (n=579)	BMS+C (n=417)	BMS-C (n=1976)	p-value
Age, years	61 (53, 71)	60 (53, 70)	61 (53, 70)	61 (52, 71)	0.73
Black race (%)	19	24	20	20	0.18
Male (%)	63	64	64	63	0.93
Hx Diabetes (%)	27	30	29	23	0.001
Hx CHF (%)	10	15	9	11	0.026
Hx MI (%)	39	38	51	46	<0.001
Number of diseased vessels (%)					<0.001
1	58	62	66	67	
2	29	31	26	27	
3	13	8	8	6	

# 6-Month Landmark Medication Use

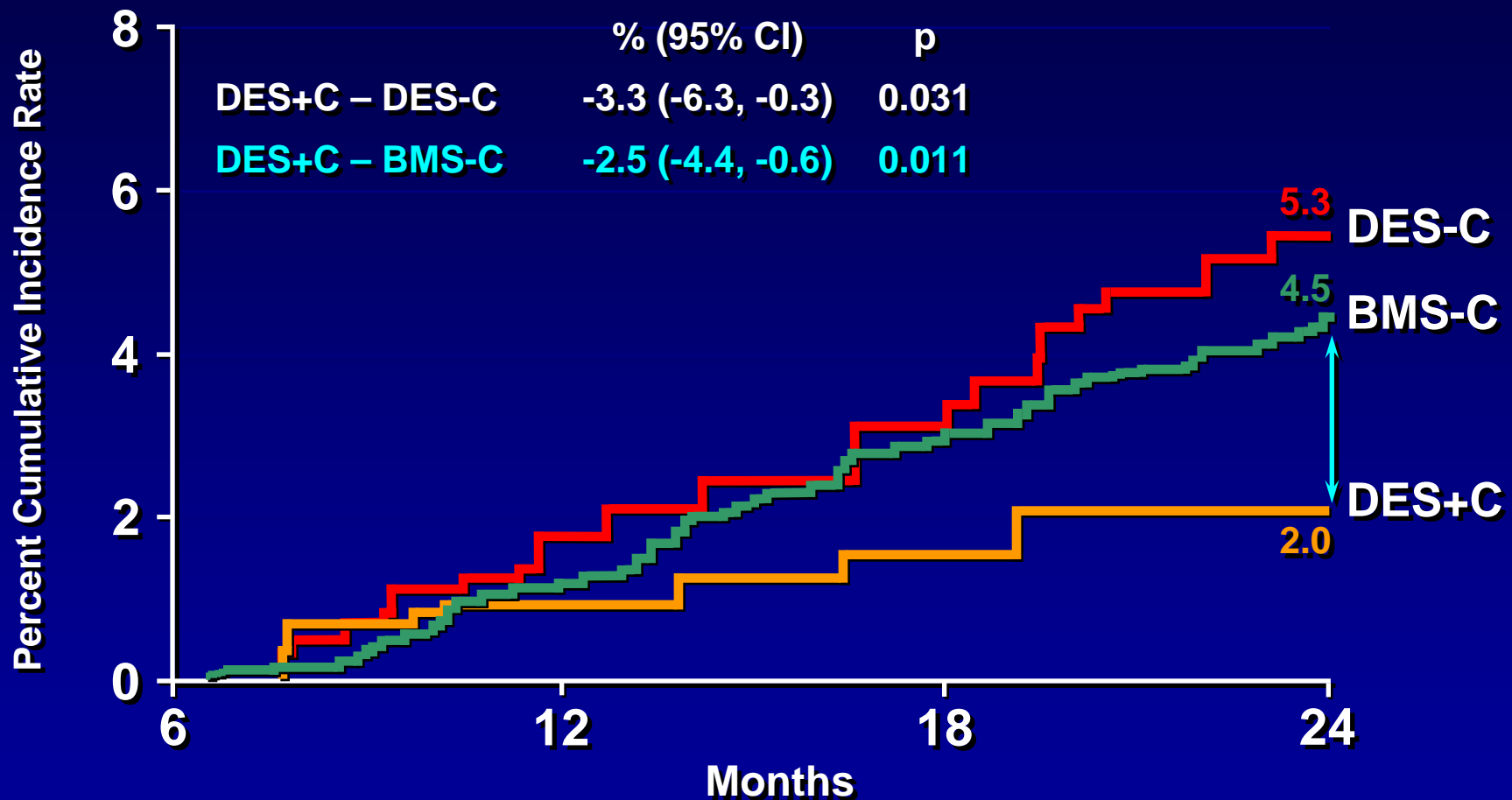
	DES+C (n=637)	DES-C (n=579)	BMS+C (n=417)	BMS-C (n=1976)	p-value
<b>Clopidogrel use at:</b>					
6 Months (%)	100	0	100	0	<0.001
12 Months (%)	73	15	77	5	<0.001
24 Months (%)	55	15	62	8	<0.001
<b>Aspirin use at:</b>					
6 Months (%)	94	74	86	80	<0.001
12 Months (%)	91	86	84	85	0.003
24 Months (%)	93	86	82	87	0.003

# 6-Month Landmark Analysis Adjusted Cumulative Mortality Rates

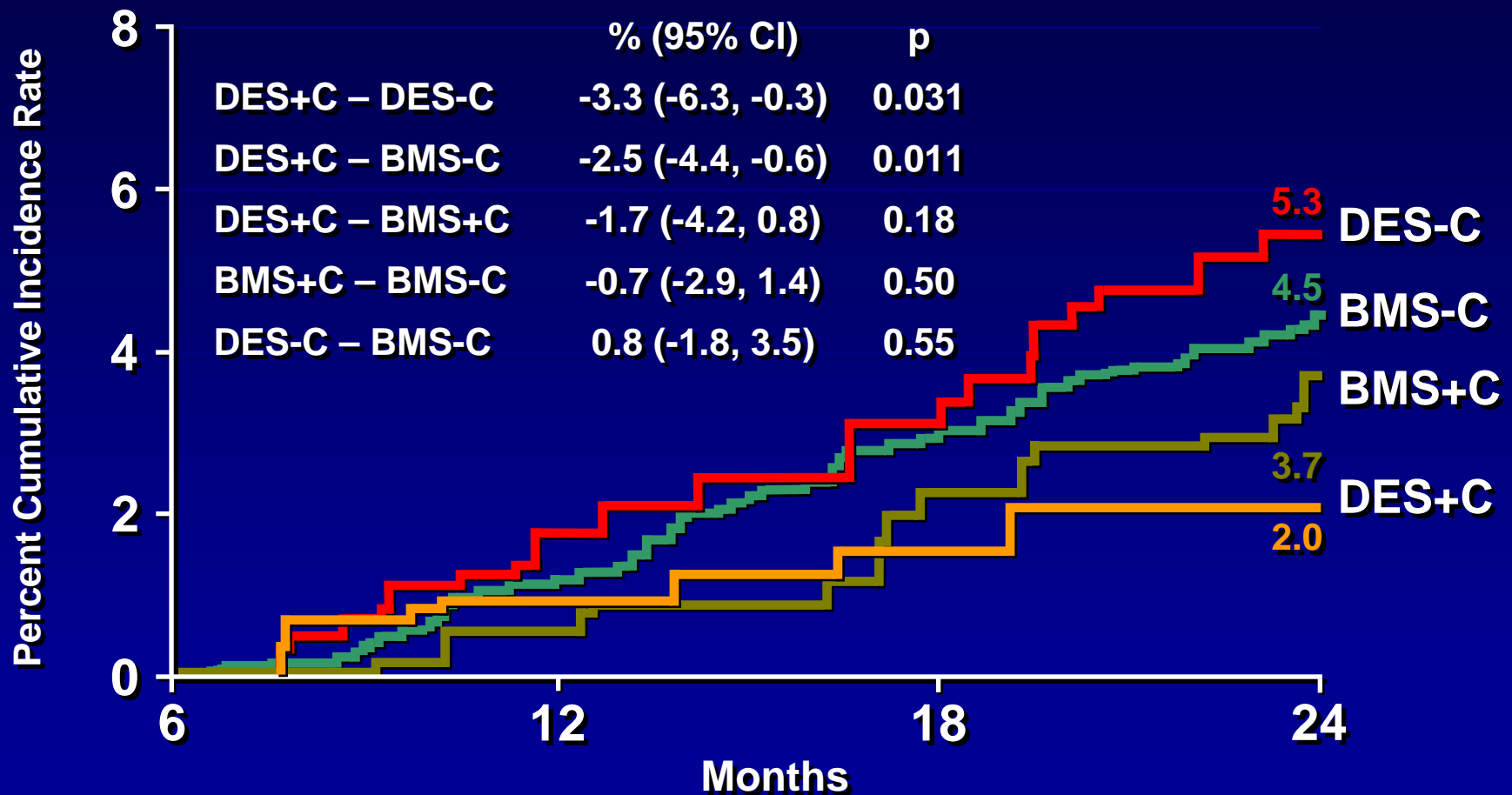


# 6-Month Landmark Analysis

## Adjusted Cumulative Mortality Rates

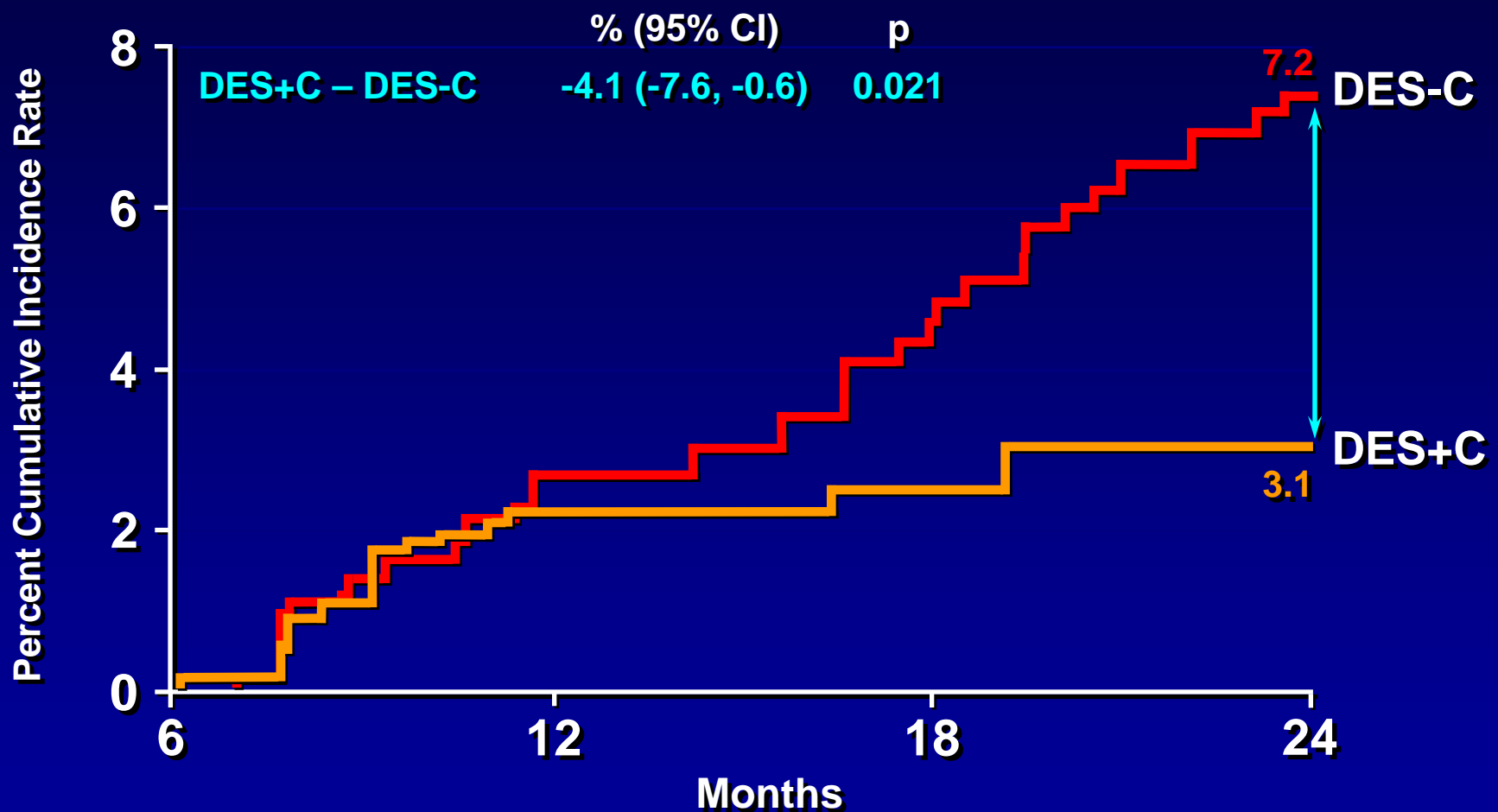


# 6-Month Landmark Analysis Adjusted Cumulative Mortality Rates



# 6-Month Landmark Analysis

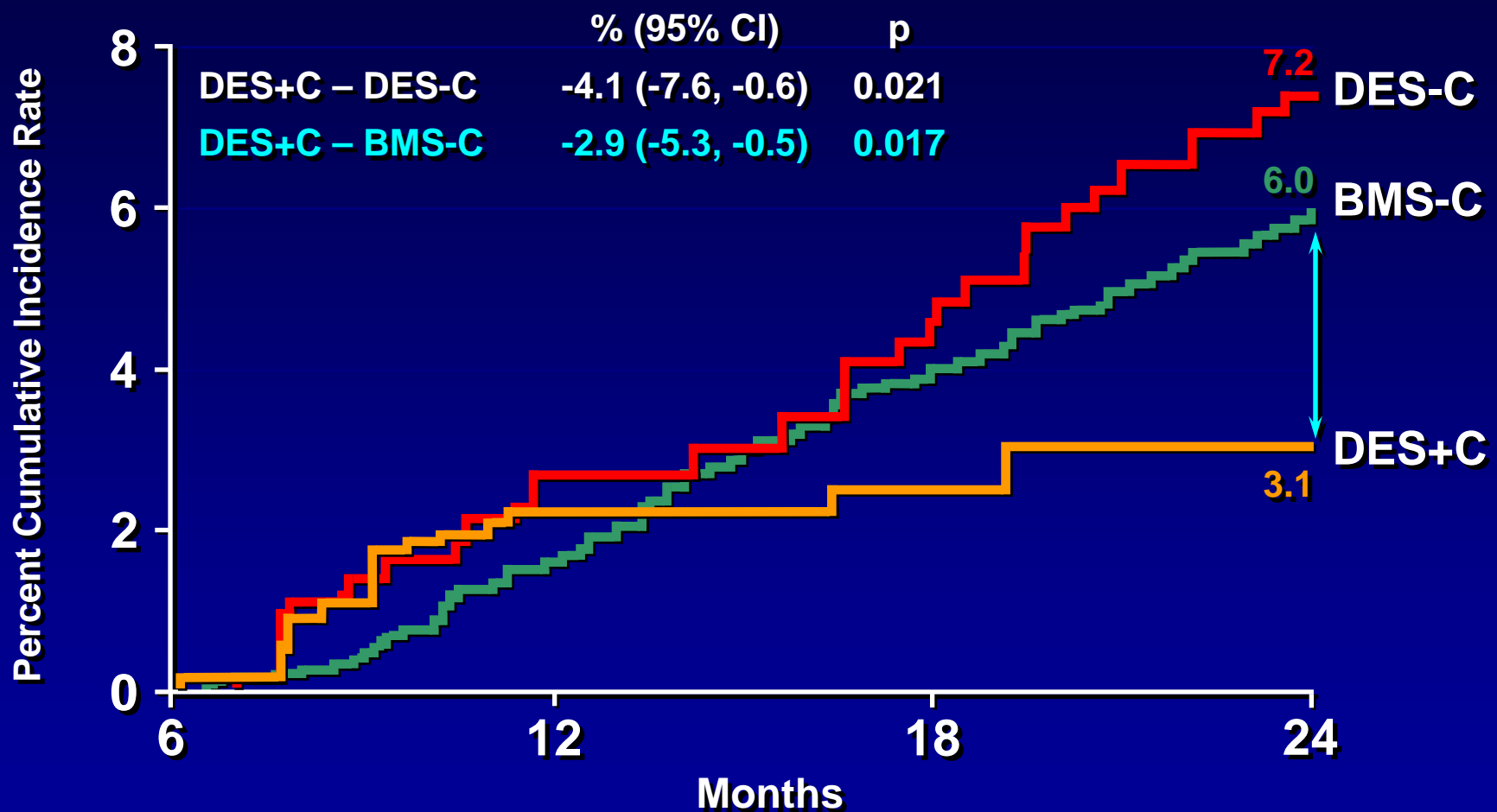
## Adjusted Cumulative Rates of Death or Nonfatal MI





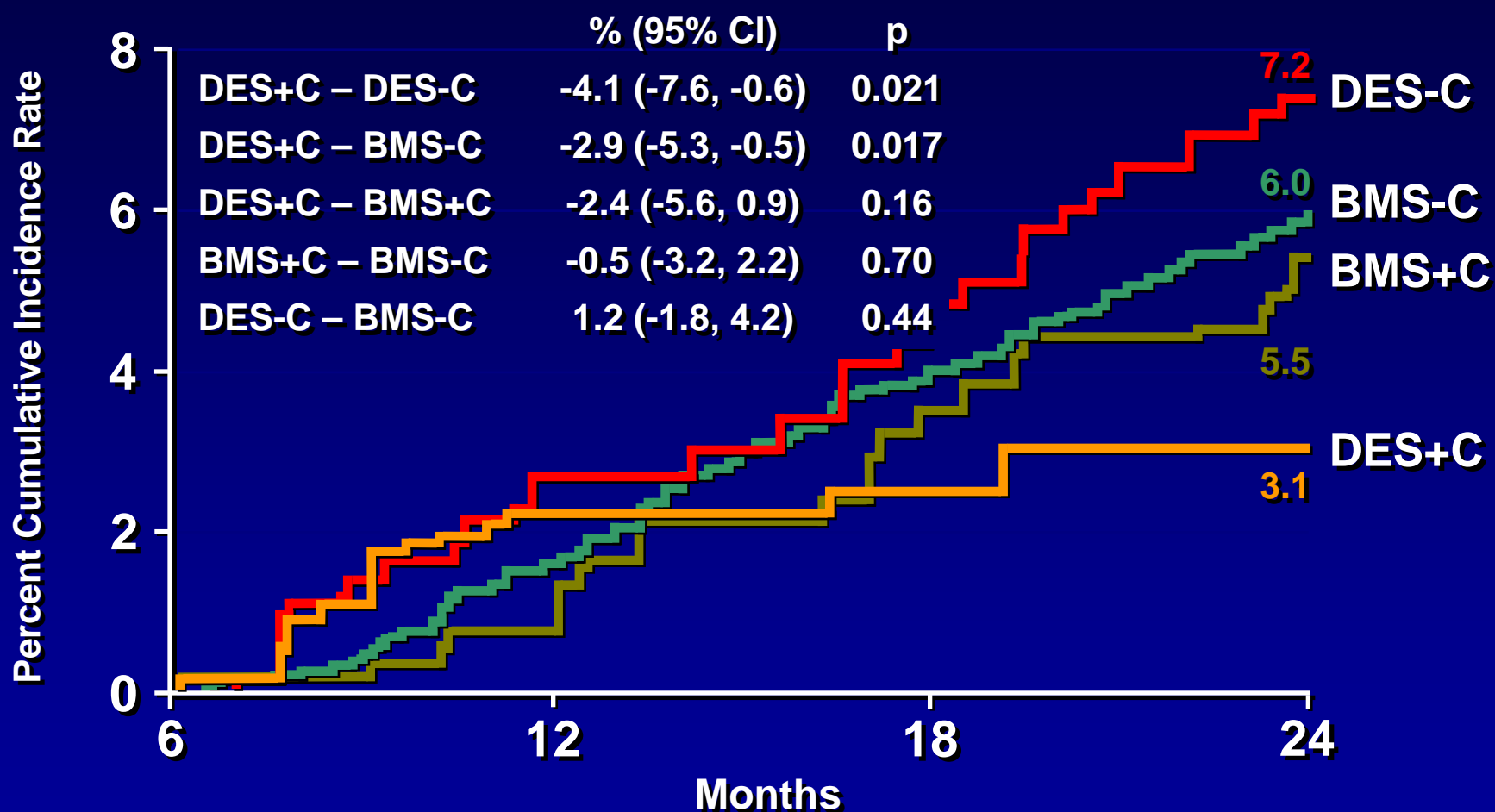
# 6-Month Landmark Analysis

## Adjusted Cumulative Rates of Death or Nonfatal MI

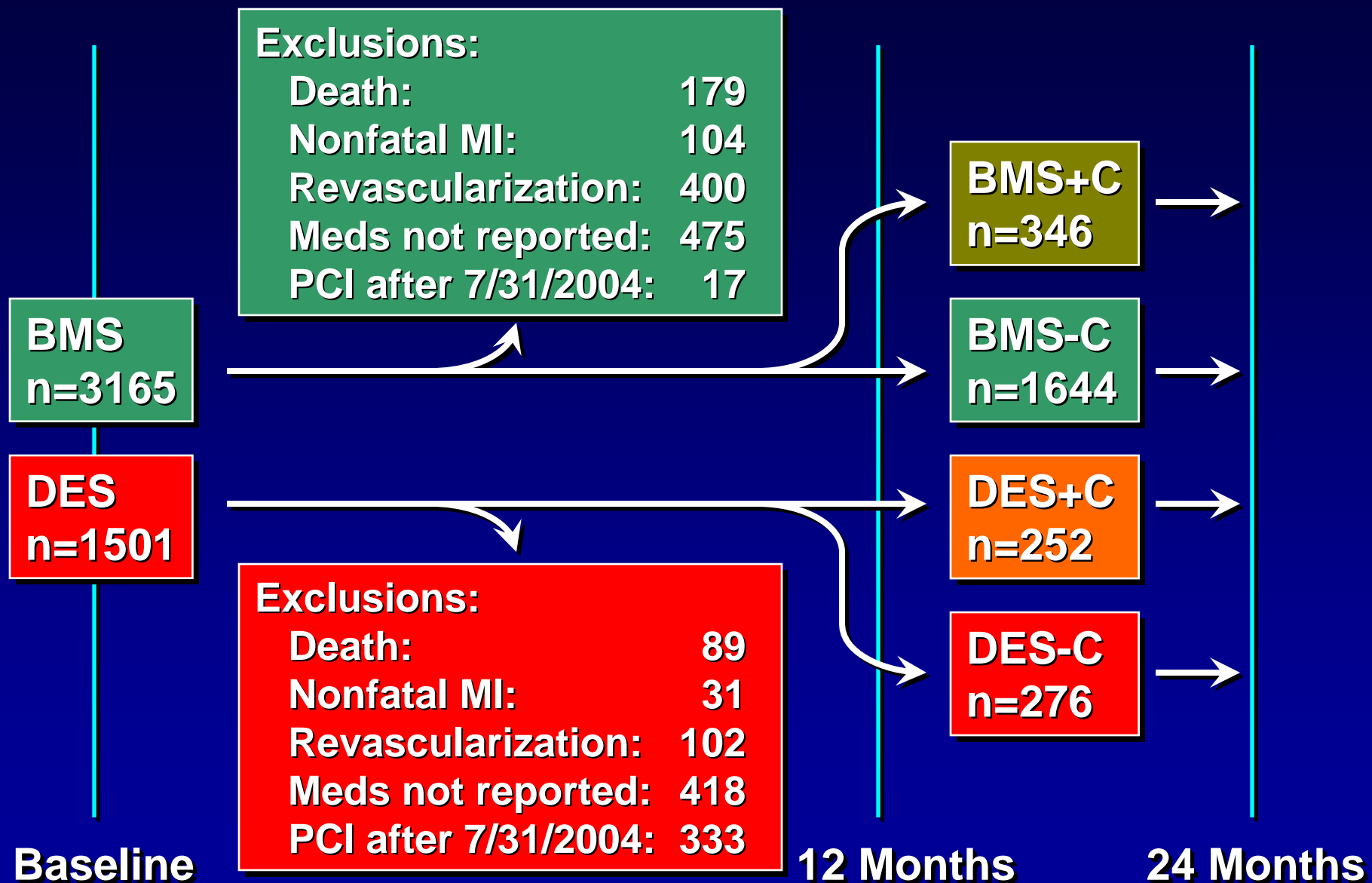


# 6-Month Landmark Analysis

## Adjusted Cumulative Rates of Death or Nonfatal MI



# 12-Month Landmark View



# Limitations

- Clopidogrel and DES use not randomized
- Unmeasured prognostic factors
- Clopidogrel use identified by patient self-report
- 90-day window used to determine follow-up contact and medication use

# Conclusions

- Compared to BMS, DES is associated with reduced rates of TVR
- Death and MI higher for DES patients stopping clopidogrel therapy at 6 months
- Results consistent with CREDO, BASKET-LATE, and PREMIER
- Need rigorous clinical trials to assess optimal duration of clopidogrel therapy



<http://jama.ama-assn.org/>

# Baseline Patient Characteristics

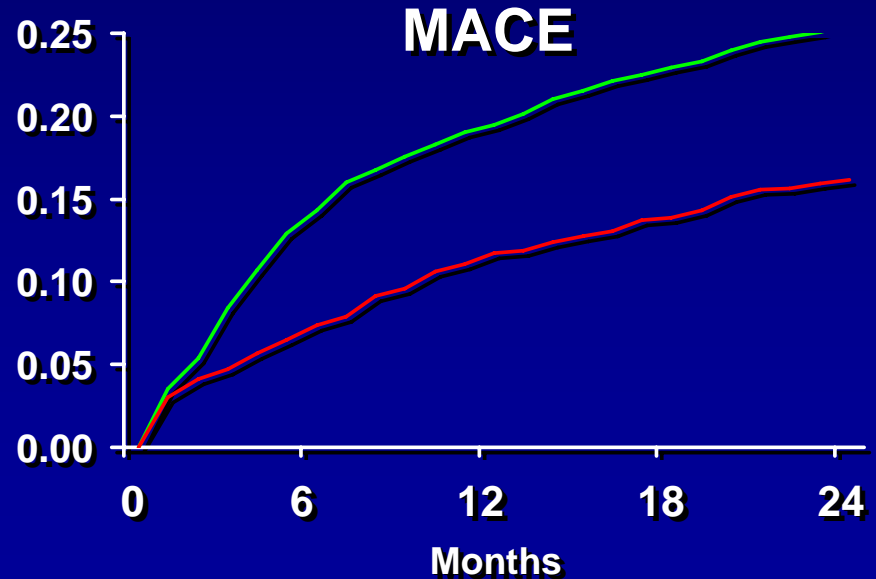
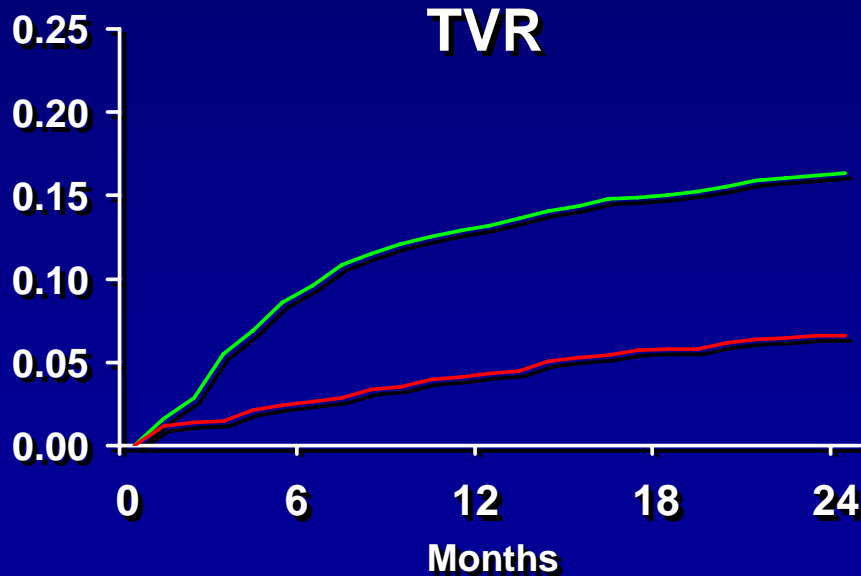
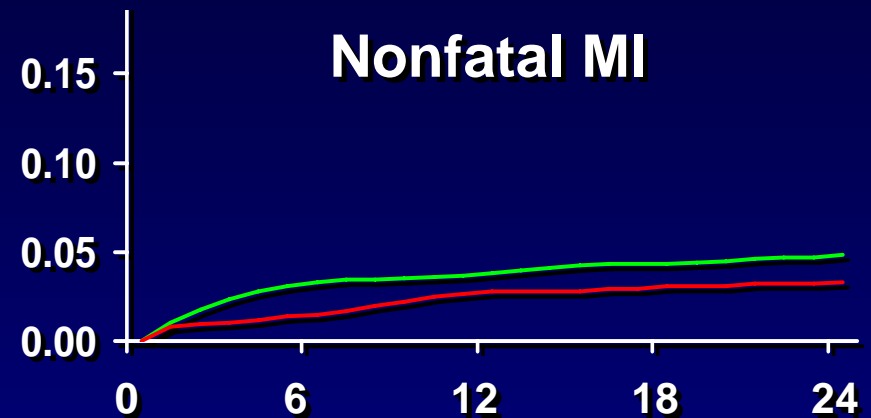
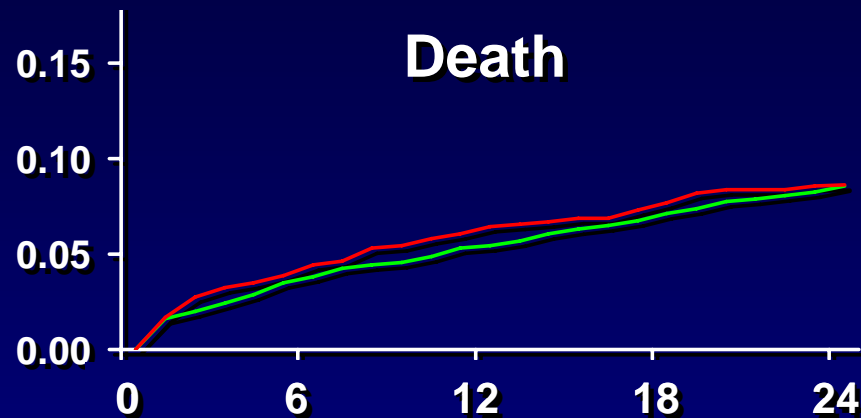
	BMS	DES	P- value
Number of Patients	3165	1501	
Age Median (Q1,Q3)	60 (52, 70)	61 (53, 70)	0.416
White Race (%)	70.3	69.0	0.374
Male Gender (%)	62.9	63.2	0.852
Diabetes (%)	25.0	27.7	0.045
CHF (%)	11.2	12.0	0.474
Previous MI (%)	48.3	42.2	<0.001
Number of Diseased Vessels (%)			<0.001
1	63.9	56.9	
2	28.4	31.4	
3	7.8	11.7	
Stent Diameter mm			<0.001
Median (Q1,Q3)	3.0 (2.8, 3.3)	2.8 (2.5, 3.0)	

# Adjusted Clinical Outcomes

	N	Death	Non-Fatal MI	TVR	Death/ MI/ TVR
<b>6 Months</b>					
BMS	3042	3.8	3.3	9.6	14.3
DES	1414	4.4	1.5	2.6	7.4
DES-BMS		0.6	-1.8	-6.9	-7.0
95% CI		(-0.7, 2.0)	(-2.7, -0.9)	(-8.3, -5.6)	(-8.9, -5.0)
P-value		0.37	<0.001	<0.001	<0.001
<b>12 Months</b>					
BMS	2983	5.4	3.8	13.2	19.5
DES	1315	6.4	2.8	4.4	11.7
DES-BMS		1.0	-1.0	-8.7	-7.7
95% CI		(-0.6, 2.6)	(-2.2, 0.2)	(-10.4, -7.1)	(-10.0, -5.4)
P-value		0.23	0.11	<0.001	<0.001
<b>24 Months</b>					
BMS	2817	8.6	4.8	16.3	25.6
DES	604	8.6	3.3	6.6	16.2
DES-BMS		0.1	-1.5	-9.7	-9.4
95% CI		(-2.0, 2.1)	(-2.8, -0.2)	(-11.7, -7.7)	(-12.2, -6.6)
P-value		0.94	0.022	<0.001	<0.001

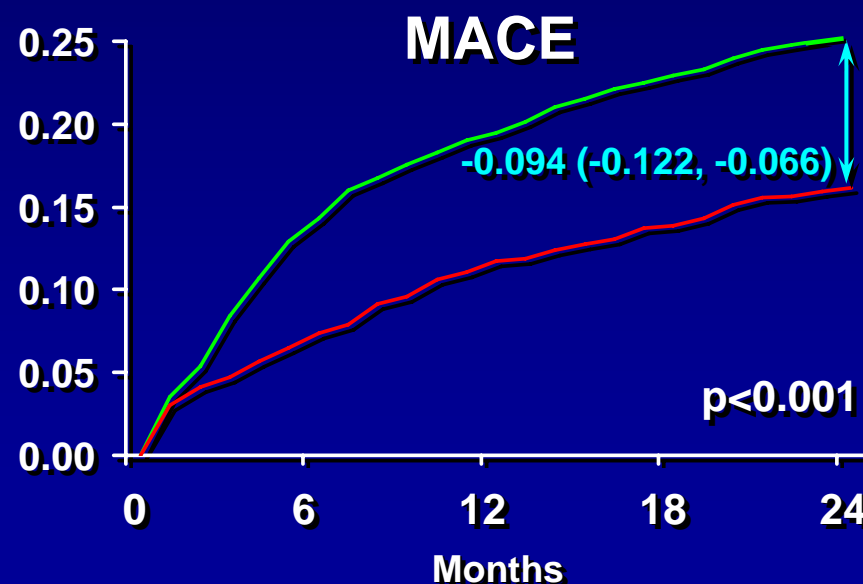
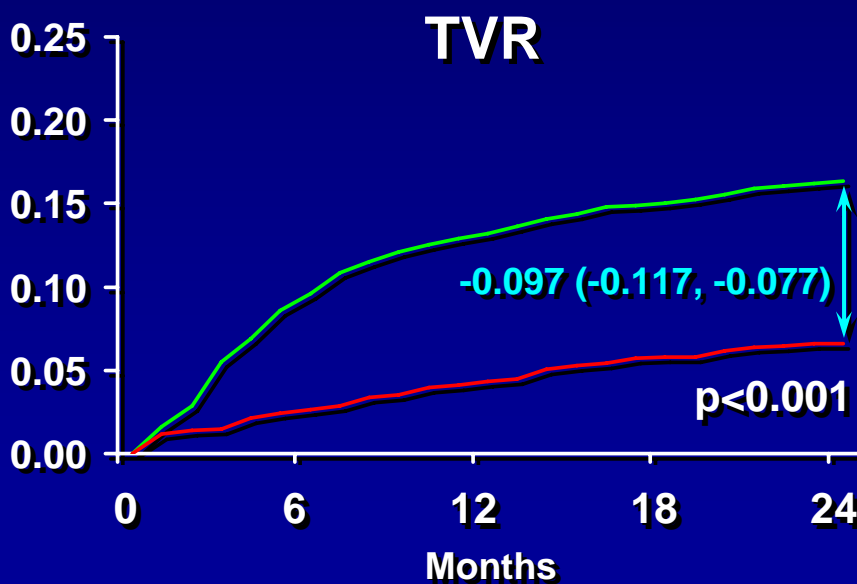
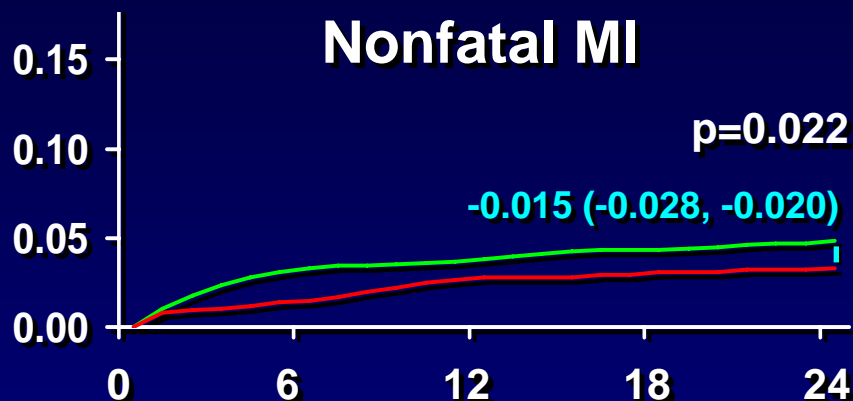


# Cumulative Incidence Rates



— DES — BMS

# Cumulative Incidence Rates



DES BMS  
DES-BMS (95% CI)

# Statistical Analyses

- Pearson Chi-square test for binary variables.
- Wilcoxon rank sum tests for continuous and ordinal categorical variables.
- Adjusted and unadjusted cumulative incidence rates were calculated using inverse probability weighted (IPW) estimators, based on partitioning data into monthly intervals.
  - ◆ Unadjusted estimates are based on weights that were a function of Kaplan-Meier estimates for treatment-specific censoring distributions.
  - ◆ Adjusted estimates were based on estimated propensity scores and Cox proportional hazards estimates of the treatment-specific censoring distributions.
- SAS PROC GENMOD with robust standard errors estimated treatment effects, 95% confidence intervals, and p-values.
- Weighted Cox proportional hazards models and adjusted cumulative incidence curves were constructed using IPW.

# 6-Month Landmark Patient Characteristics

	DES+C (n=637)	DES-C (n=579)	BMS+C (n=417)	BMS-C (n=1976)	p-value
Age, years	61 (53, 71)	60 (53, 70)	61 (53, 70)	61 (52, 71)	0.73
Black race	121 (19.0)	137 (23.7)	82 (19.7)	395 (20.0)	0.18
Male	398 (62.5)	368 (63.6)	266 (63.8)	1233 (62.4)	0.93
History of diabetes	171 (26.8)	171 (29.5)	121 (29.0)	449 (22.7)	0.001
History of CHF	60 (9.6)	82 (14.5)	38 (9.3)	208 (11.0)	0.026
History of MI	247 (38.8)	221 (38.2)	213 (51.1)	913 (46.2)	<0.001
Number of diseased vessels					<0.001
1	370 (58.1)	356 (61.5)	275 (65.9)	1331 (67.4)	
2	186 (29.2)	178 (30.7)	109 (26.1)	531 (26.9)	
3	81 (12.7)	45 (7.8)	33 (7.9)	114 (5.8)	

# 6-Month Landmark Medication Use

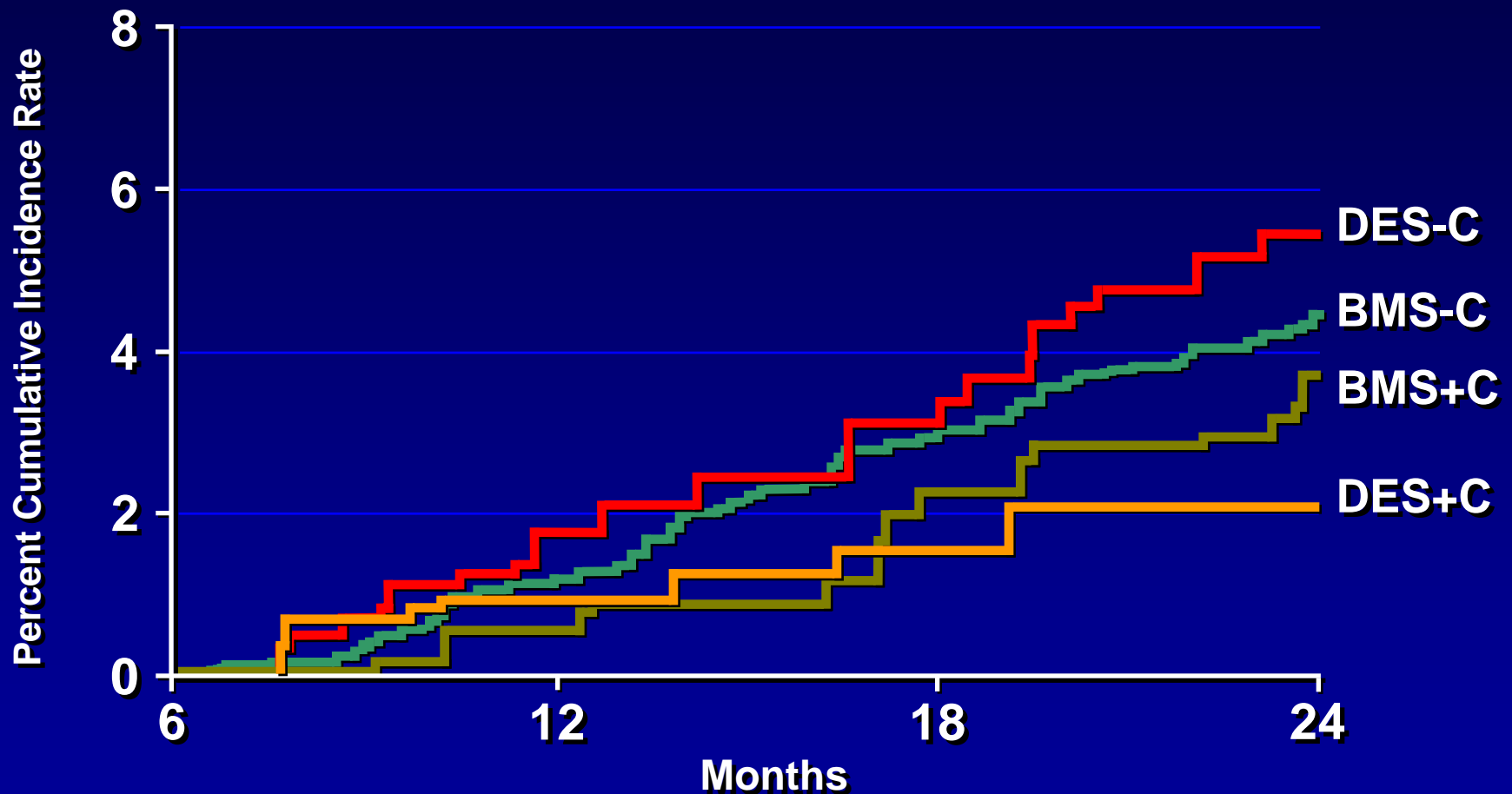
	DES+C (n=637)	DES-C (n=579)	BMS+C (n=417)	BMS-C (n=1976)	p-value
<b>Clopidogrel use at:</b>					
6 Months	637 (100)	0 (0)	417 (100)	0 (0)	<0.001
12 Months	382 (72.9)	64 (14.9)	309 (77.4)	93 (5.0)	<0.001
24 Months	106 (55.2)	25 (14.5)	230 (62.2)	143 (8.1)	<0.001
<b>Aspirin use at:</b>					
6 Months	600 (94.2)	430 (74.3)	360 (86.3)	1583 (80.1)	<0.001
12 Months	478 (91.2)	371 (86.3)	335 (84.0)	1569 (85.0)	0.003
24 Months	179 (93.2)	148 (85.6)	304 (82.2)	1541 (87.1)	0.003

# 6-Month Landmark Patient Characteristics

	DES+C (n=637)	DES-C (n=579)	BMS+C (n=417)	BMS-C (n=1976)	p-value
Income per household (\$1000)	36.5 (29.2, 41.7)	35.4 (29.3, 41.3)	35.1 (29.3, 40.6)	33.1 (29.3, 39.8)	<0.001
Average house value (\$1000)	82.9 (59.5, 120.4)	82.6 (59.5, 105.7)	80.4 (61.5, 108.5)	75.7 (62.2, 96.0)	0.006

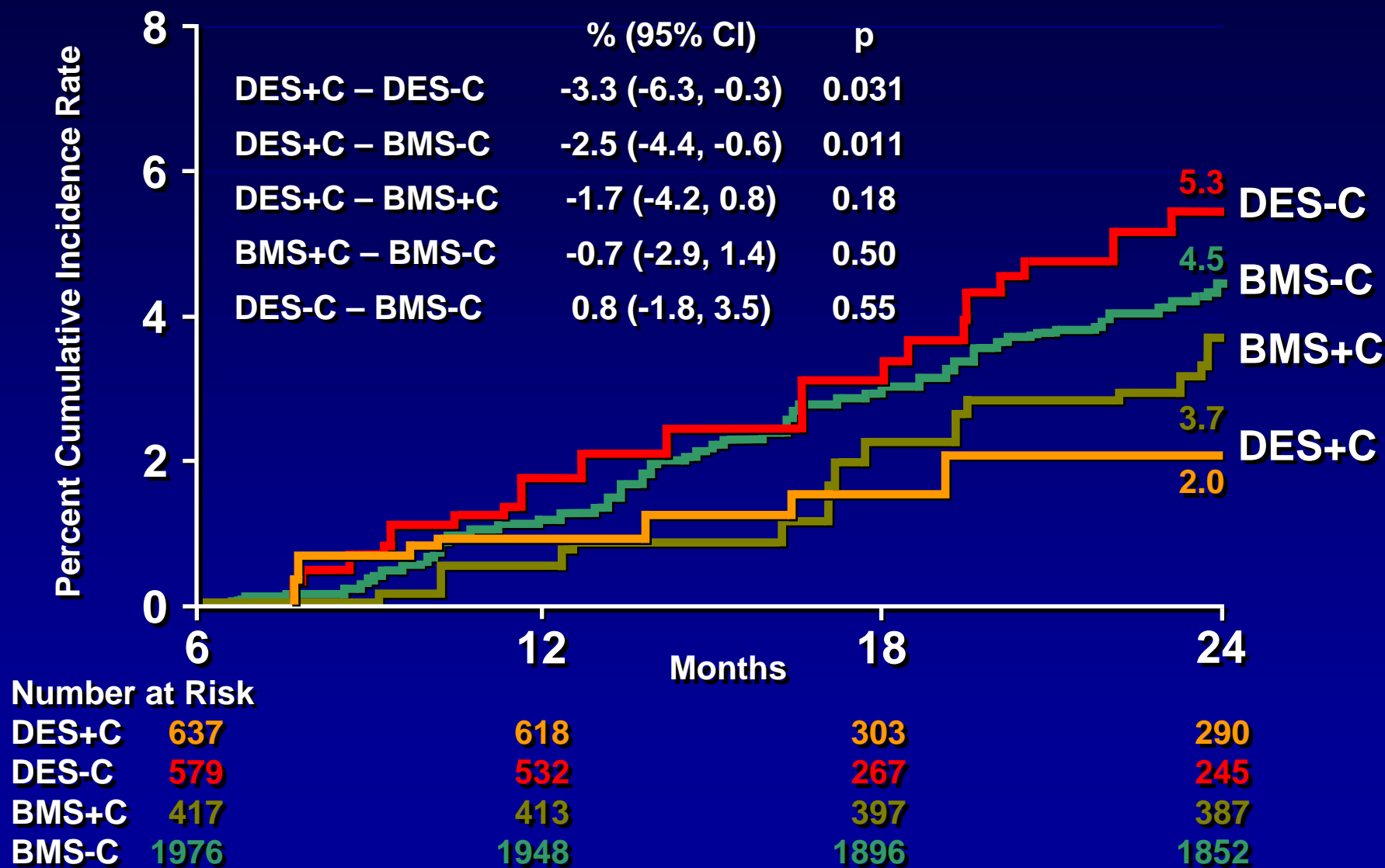
# 6-Month Landmark Analysis

## Adjusted Cumulative Mortality Rates



# 6-Month Landmark Analysis

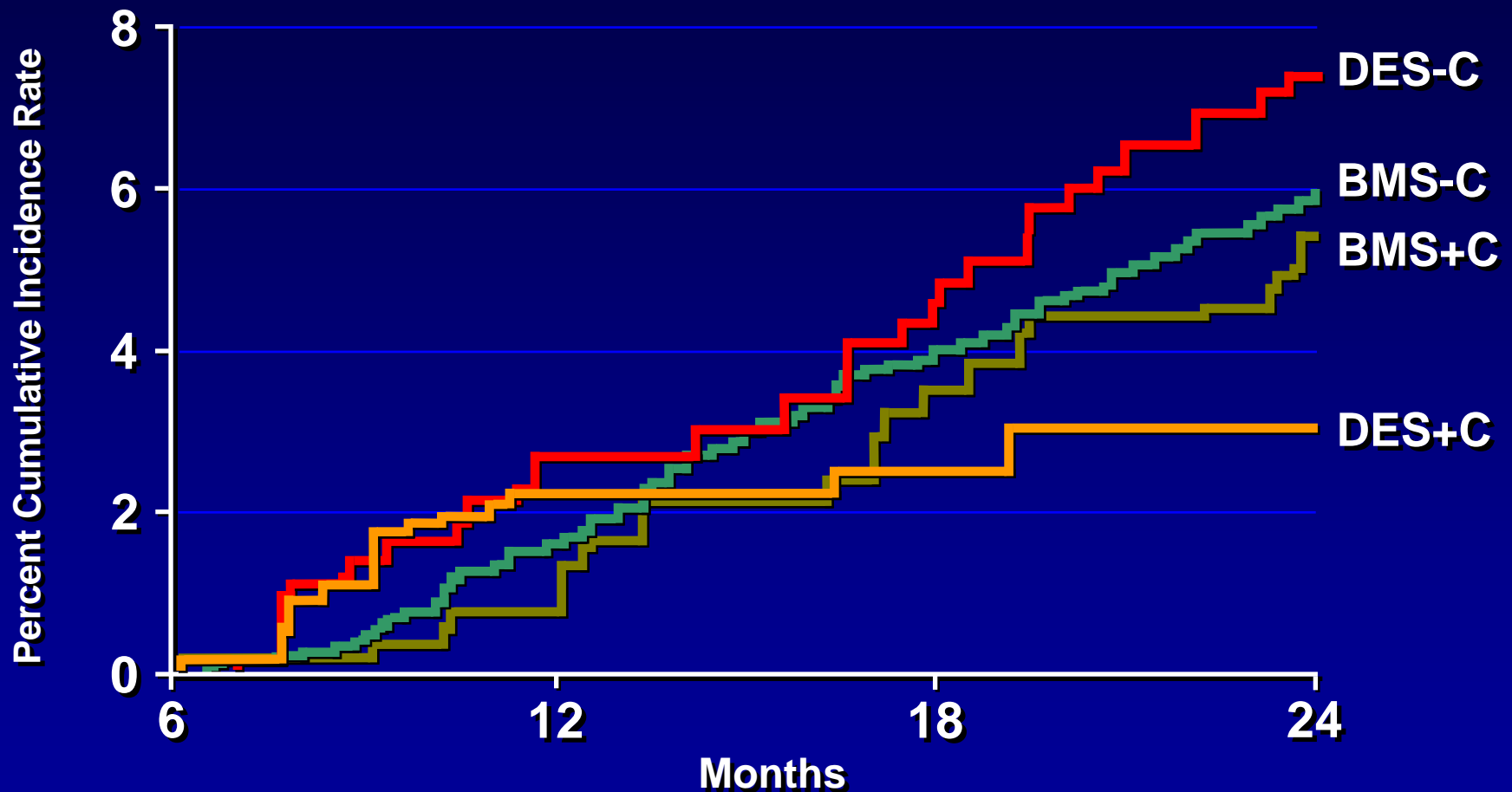
## Adjusted Cumulative Mortality Rates





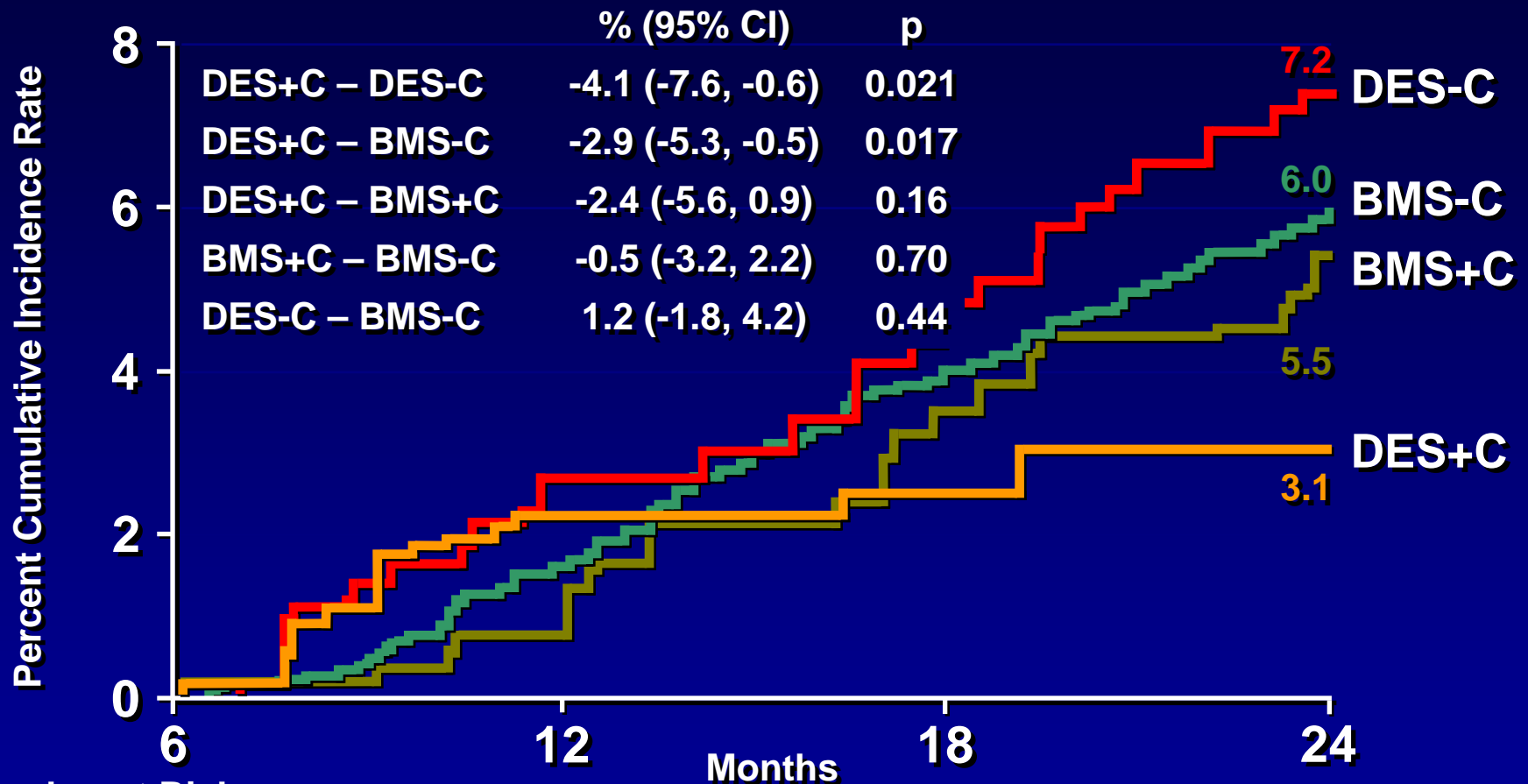
# 6-Month Landmark Analysis

## Adjusted Cumulative Rates of Death or Nonfatal MI



# 6-Month Landmark Analysis

## Adjusted Cumulative Rates of Death or Nonfatal MI



### Number at Risk

DES+C	637	613	300	287
DES-C	579	526	262	238
BMS+C	417	412	394	382
BMS-C	1976	1941	1879	1825

# 6-Month Landmark Outcomes

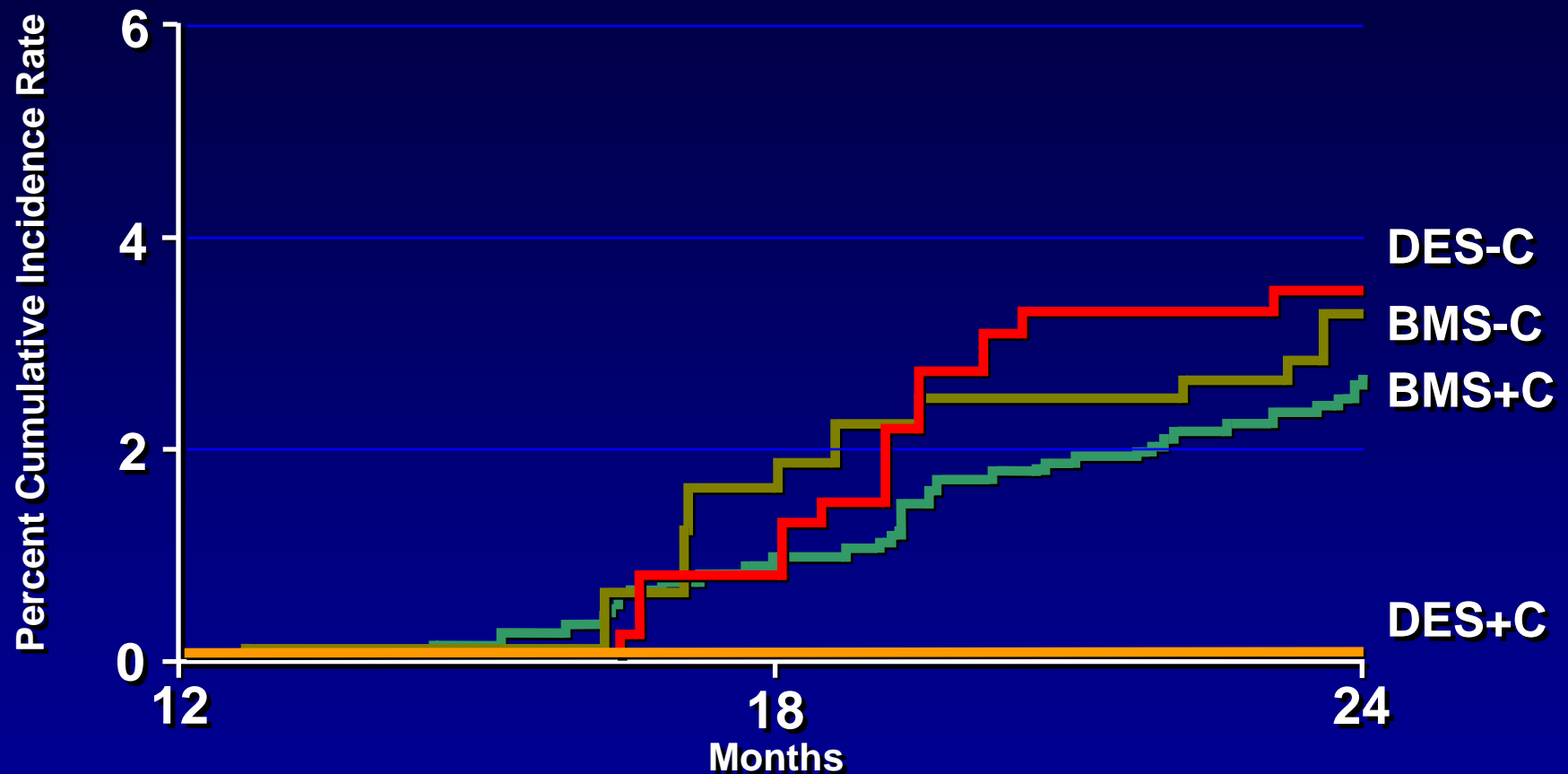
	Unadjusted Outcomes			Adjusted Outcomes		
	Death	MI	Death/ MI	Death	MI	Death/ MI
DES+C (%)	1.6	0.8	2.1	2.0	1.3	3.1
DES-C (%)	5.8	3.3	8.4	5.3	2.6	7.2
BMS+C (%)	3.9	1.2	5.1	3.7	1.7	5.5
BMS-C (%)	4.5	1.4	5.9	4.5	1.6	6.0
P-value (3df)	0.002	0.088	<0.001	0.054	0.63	0.065
Interaction P-value (1df)	0.043	0.054	0.007	0.18	0.31	0.12

## 24 Month Outcomes Based on 6 Month Patient-Reported Clopidogrel Use

	Unadjusted Outcomes			Adjusted Outcomes		
	Death	MI	Death/ MI	Death	MI	Death/ MI
DES+C – DES-C (%)	-4.2	-2.5	-6.3	-3.3	-1.3	-4.1
(95% CI)	(-7.1, -1.4)	(-4.5, -0.5)	(-9.6, -3.1)	(-6.3, -0.3)	(-3.4, 0.8)	(-7.6, -0.6)
P-value (1df)	0.004	0.015	<0.001	0.031	0.24	0.021
BMS+C - BMS-C (%)	-0.6	-0.2	-0.7	-0.7	0.2	-0.5
(95% CI)	(-2.7, 1.5)	(-1.4, 1.0)	(-3.1, 1.7)	(-2.9, 1.4)	(-1.6, 1.9)	(-3.2, 2.2)
P-value (1df)	0.60	0.74	0.55	0.50	0.86	0.70
DES+C - BMS+C (%)	-2.3	-0.4	-3.1	-1.7	-0.4	-2.4
(95% CI)	(-4.6, -0.1)	(-1.7, 0.9)	(-5.6, -0.6)	(-4.2, 0.8)	(-2.6, 1.8)	(-5.6, 0.9)
P-value (1df)	0.044	0.52	0.017	0.18	0.72	0.16
DES-C - BMS-C (%)	1.3	1.9	2.5	0.8	1.0	1.2
(95% CI)	(-1.4, 4.0)	(-0.1, 3.8)	(-0.7, 5.7)	(-1.8, 3.5)	(-0.6, 2.7)	(-1.8, 4.2)
P-value (1df)	0.34	0.061	0.12	0.55	0.22	0.44
DES+C - BMS-C (%)	-2.9	-0.6	-3.8	-2.5	-0.3	-2.9
(95% CI)	(-4.4, -1.4)	(-1.5, 0.2)	(-5.4, -2.1)	(-4.4, -0.6)	(-1.8, 1.3)	(-5.3, -0.5)
P-value (1df)	<0.001	0.16	<0.001	0.011	0.76	0.017

# 12-Month Landmark Analysis

## Adjusted Cumulative Mortality Rates

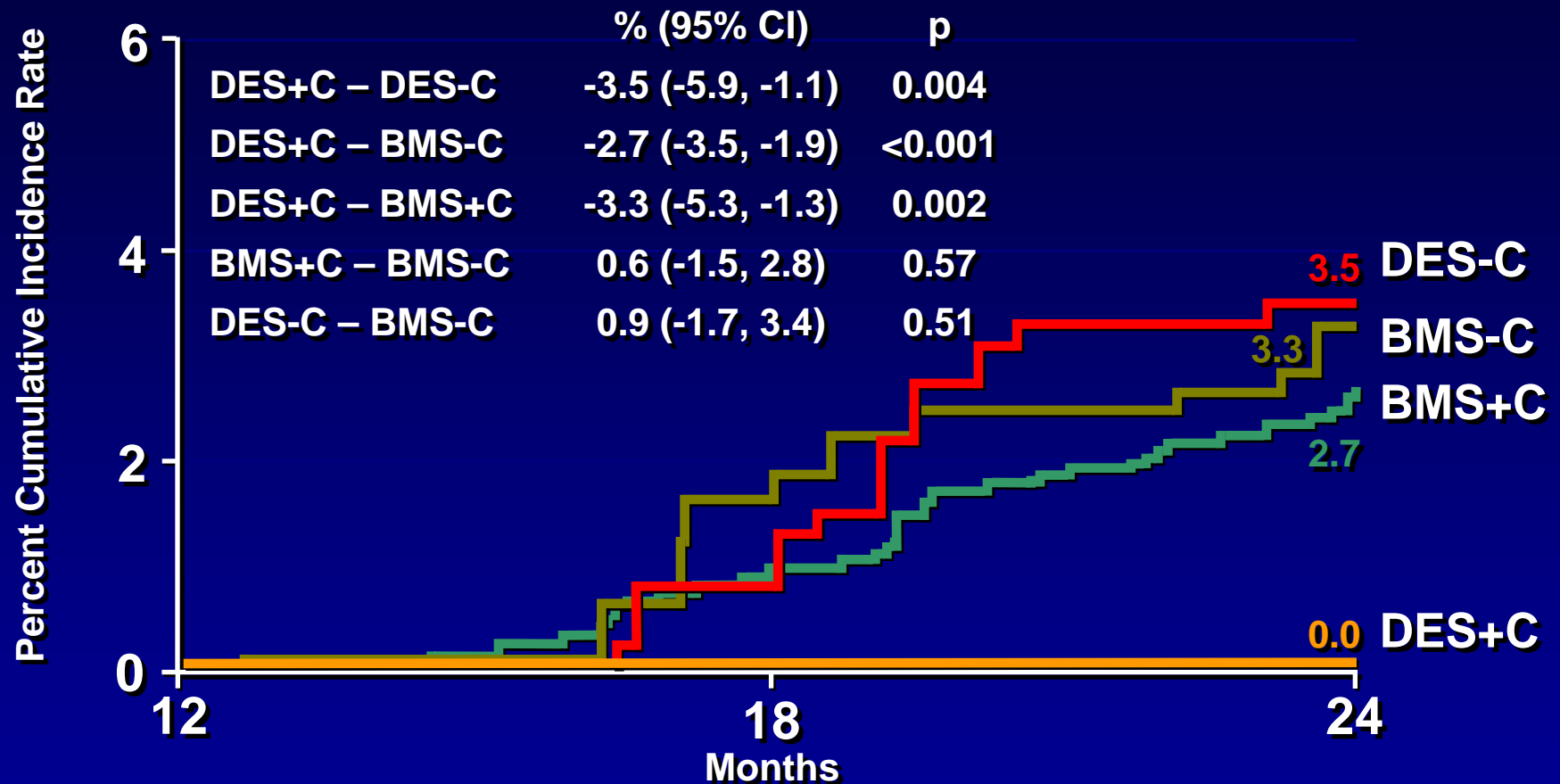


### Number at Risk

DES+C	252	237	230
DES-C	276	258	244
BMS+C	346	339	331
BMS-C	1644	1627	1596

# 12-Month Landmark Analysis

## Adjusted Cumulative Mortality Rates

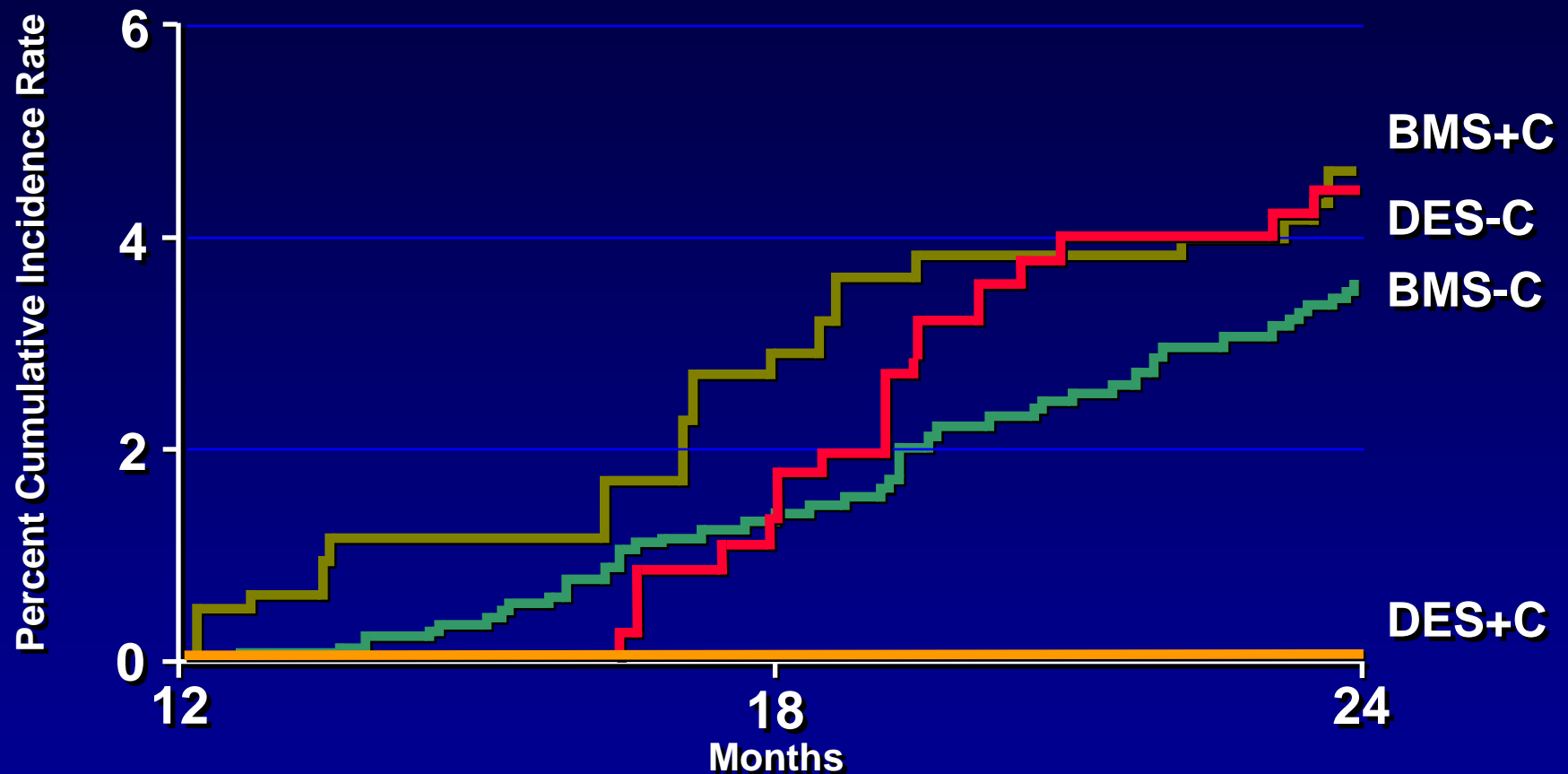


### Number at Risk

DES+C	252	237	230
DES-C	276	258	244
BMS+C	346	339	331
BMS-C	1644	1627	1596

# 12-Month Landmark Analysis

## Adjusted Cumulative Rates of Death or Nonfatal MI

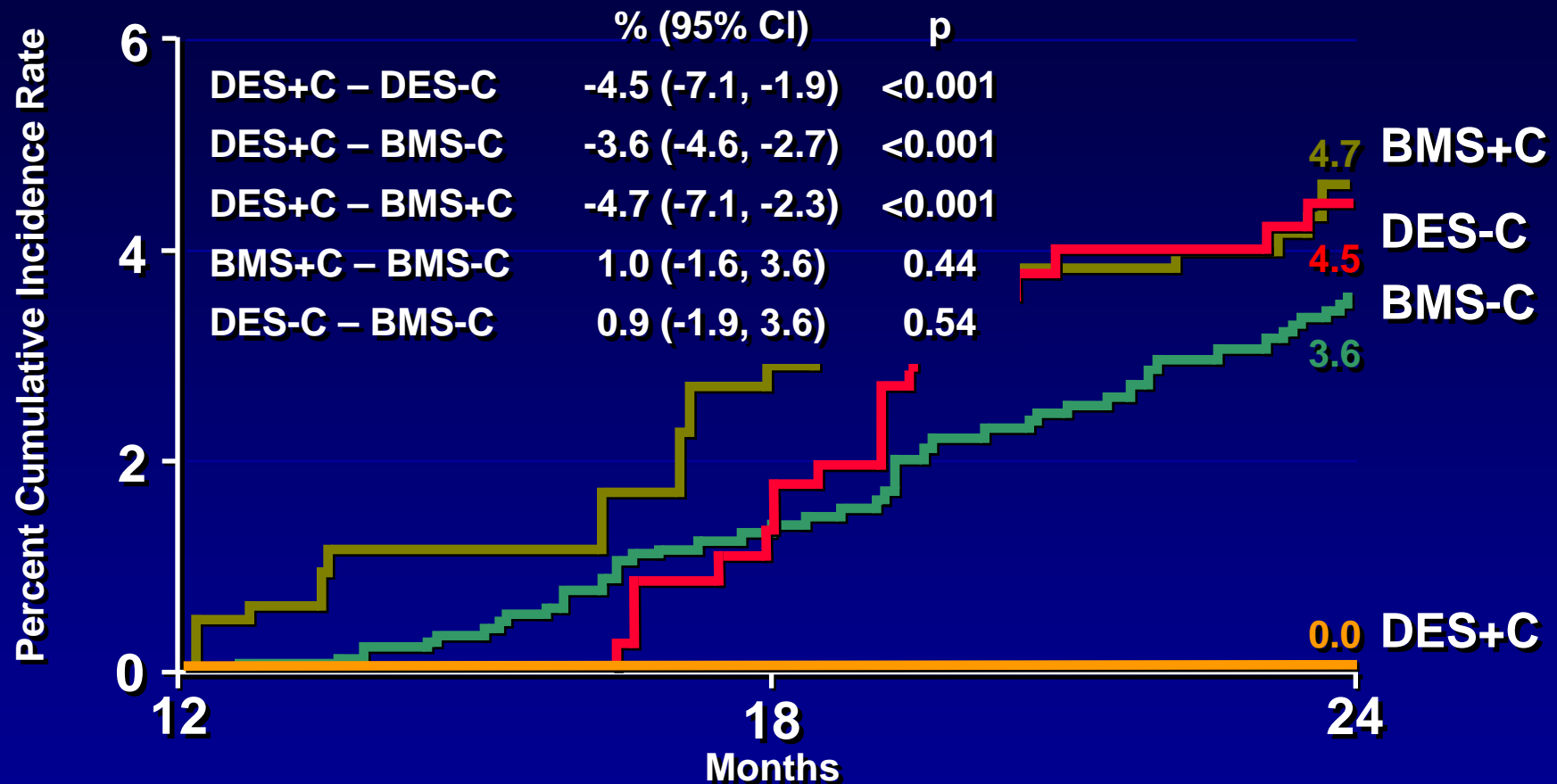


### Number at Risk

DES+C	252	237	230
DES-C	276	256	240
BMS+C	346	336	327
BMS-C	1644	1621	1582

# 12-Month Landmark Analysis

## Adjusted Cumulative Rates of Death or Nonfatal MI



### Number at Risk

DES+C	252	237	230
DES-C	276	256	240
BMS+C	346	336	327
BMS-C	1644	1621	1582