FDA Panel on Drug-eluting Stent Safety
December 7 and 8th, 2006

Boston Scientific Presentation: Part II
Real-world use of the TAXUS® Drug-eluting Stent System

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Real-World Taxus® Stent Use Confirms Favorable Outcome Profile

- The Taxus stent has demonstrated favorable risk-benefit outcomes compared to BMS in the somewhat *"simpler" clinical trial patients*

- But how can we best evaluate TAXUS performance in the *more complex "real-world" patients* who comprise > 50% of current use?

- The *ARRIVE Registries* include > 7,000 Taxus-treated patients
  - "Simple" lesions (Taxus IV-like) have similar outcomes to RCTs
  - "Complex" lesions have expected *slightly* more adverse events

- Those outcomes are comparable to meta-analysis of other real-world data, and to of complex PCI or CABG revascularization results

- Pending results of randomization of even more complex patients in Horizons (AMI) and SYNTAX (LM and 3VD), there is no reason to believe that current clinical use exposes complex patients to excess risk compared to other available alternative revascularization therapy

Agenda

- ➢ ARRIVE Registry
- ➢ TAXUS v. ARRIVE Analysis (Simple lesions)
- ➢ ARRIVE Analysis (Complex lesions)
- ➢ Multivariate Predictor Analysis
- ➢ Summary and Conclusions

Registry Data Regarding Taxus® Stent in Complex Lesions

Background

ARRIVE 1   FDA Mandated Safety Surveillance Program

Feb 04 – May 04   N=2487

ARRIVE 2   Company-Initiated Program Expansion

Oct 04 – Oct 05   N=4906

Design

Consecutive "All-Comers" Design   Data review to improve accuracy

• Less selection bias   • All patients with cardiac events

• Community hospitals   • Random 10-20% sample

• Range of volumes   • Independent Adjudication of events

Primary endpoint: Rate of TAXUS related cardiac events at 1 year
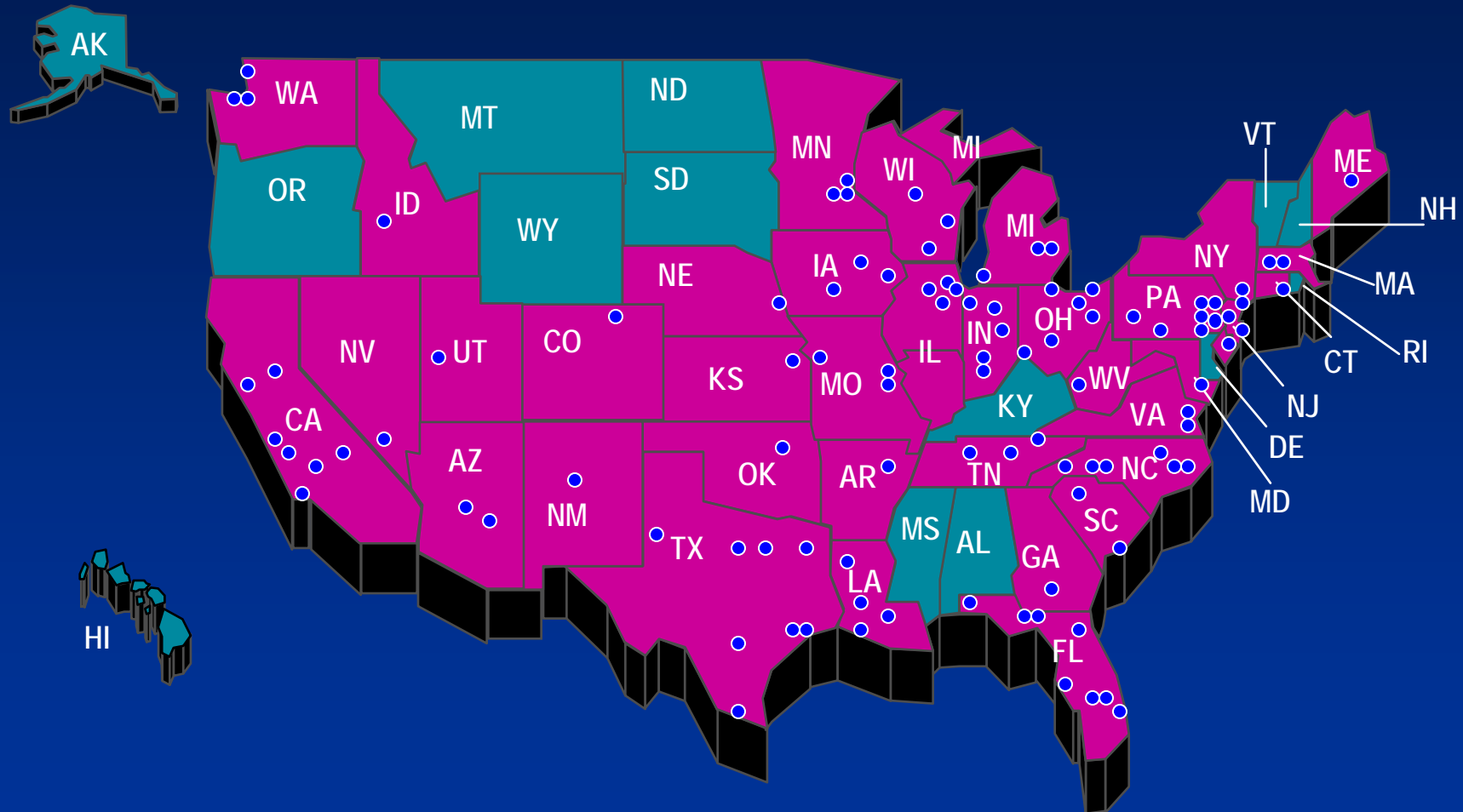
ADVANTAGES

• Very large (7,000) patient set

• Far more complex patient set than in Taxus trials

• Excellent adjudication and clinical event capture

LIMITATIONS

• Only 1-2 year follow-up

• No internal comparators (to BMS or CABG)

• Be careful with direct comparison of complex DES to older BMS data in simpler lesions
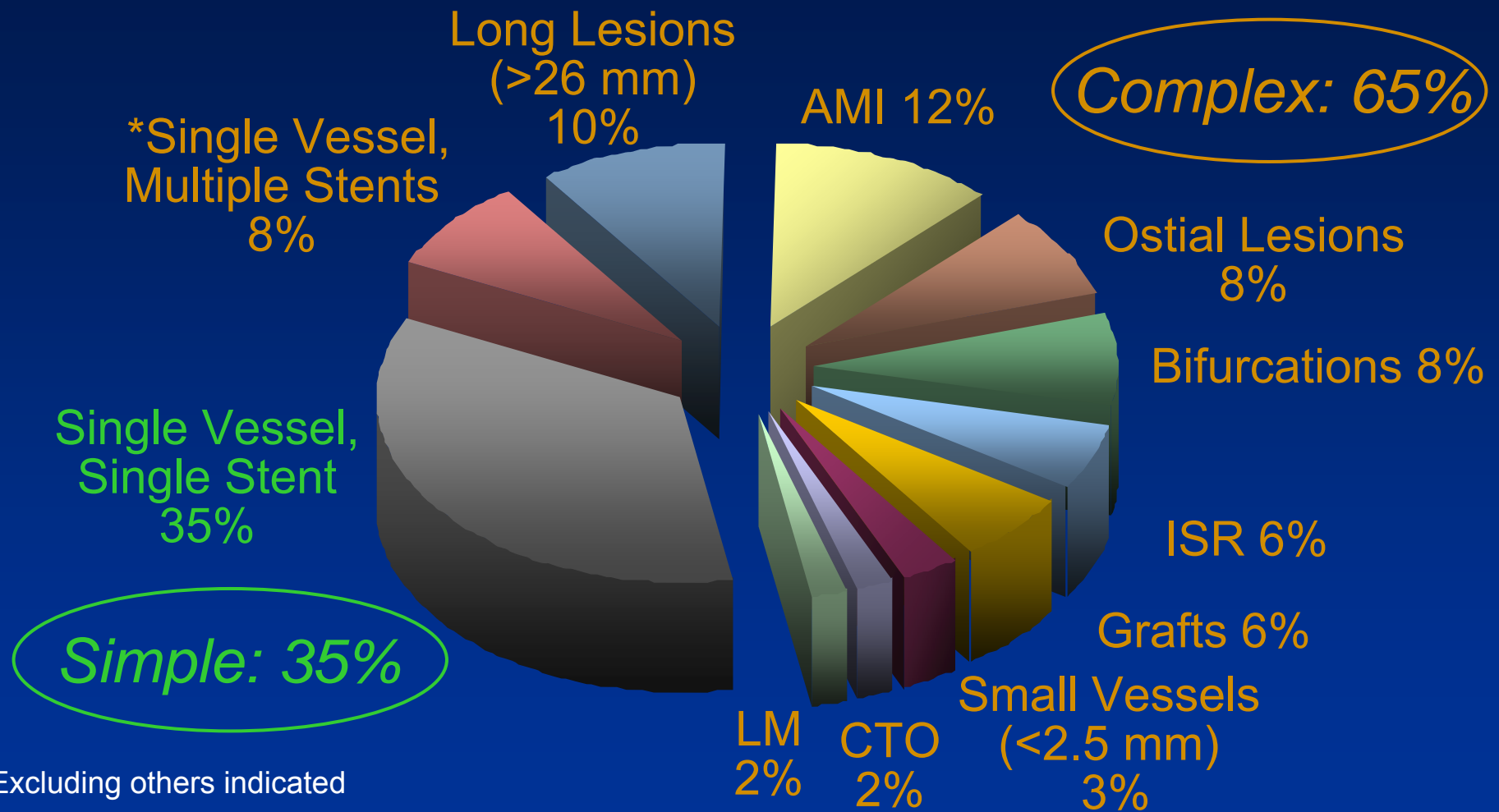
Expanded Use in the Real World
ARRIVE 1 + ARRIVE 2 Combined

Long Lesions (>26 mm) 10%

*Single Vessel, Multiple Stents 8%

AMI 12%

Complex: 65%

Ostial Lesions 8%

Bifurcations 8%

Single Vessel, Single Stent 35%

ISR 6%

Grafts 6%

Small Vessels (<2.5 mm) 3%

Simple: 35%

LM 2%

CTO 2%

*Excluding others indicated

Predominance of complex procedures

6

TAXUS® Stent-Related Cardiac Events
ARRIVE 1 at 12 Months (per patient)

N = 2,410 patients (12M)

Cardiac Event Incidence (%)

- Cardiac Death: 1.1% n=27
- MI: 1.8% n=44
- Q-MI: 0.6% n=15
- TVR: 5.6% n=136
- Overall: 7.2% n=173
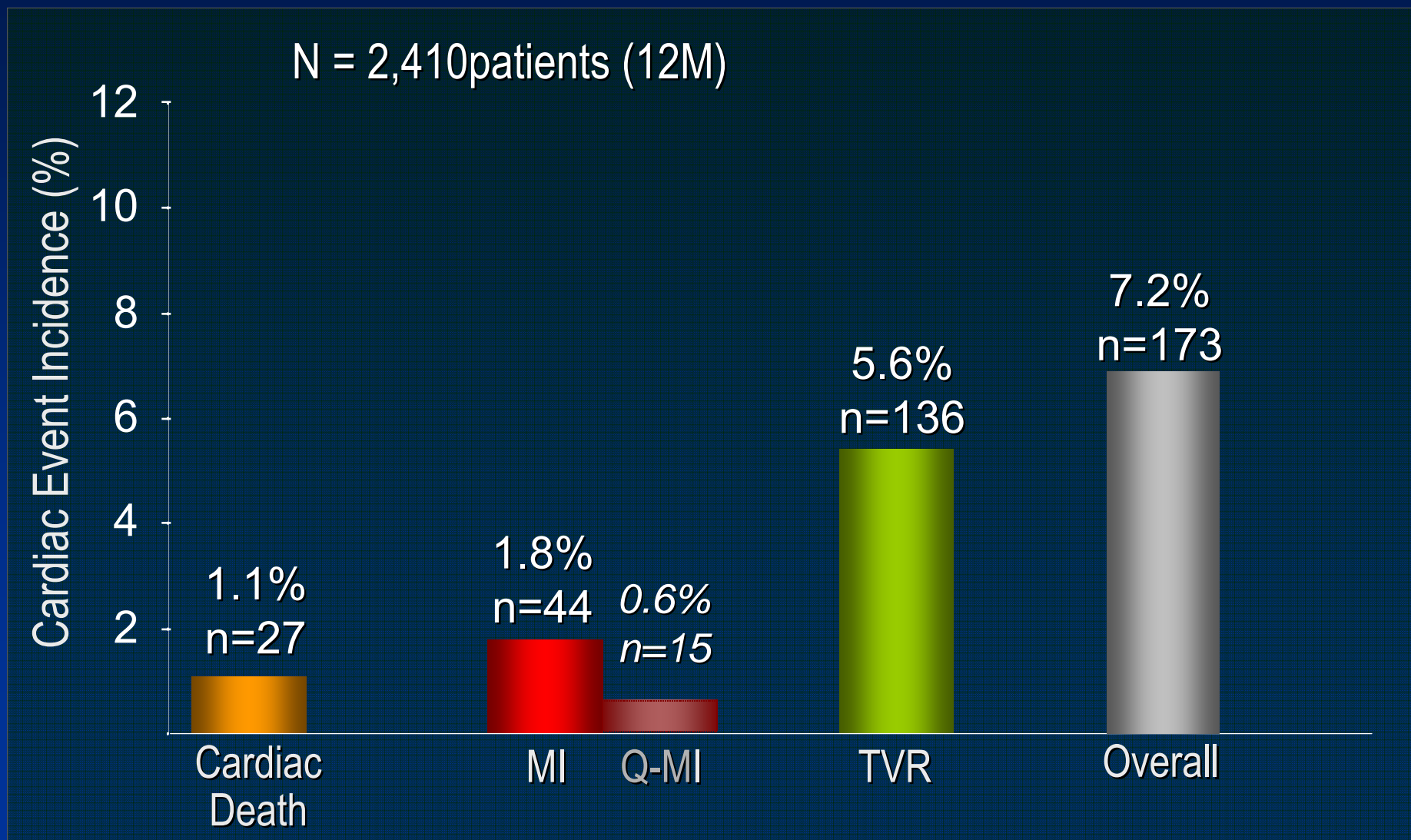
TAXUS® Stent-Related Cardiac Events
ARRIVE 1 at 24 Months (per patient)

Agenda

➢ ARRIVE Registry

➢ TAXUS v. ARRIVE Analysis (Simple lesions)

➢ ARRIVE Analysis (Complex lesions)

➢ Multivariate Predictor Analysis

➢ Summary and Conclusions

Simple Lesion Observations

- Outcomes for simple lesions in ARRIVE look very similar to the Taxus trial data (good ascertainment)
    - Significantly fewer total MI's
        - No or less routine blood sampling, weak non-Q MI detection
        - But very good matching for Q-MI
    - Significantly fewer TVR's
        - No routine angiographic subset, and hence no oculo-stenotic reflex
        - Closer to real-world outcomes
    - Similar Late ST (year 1-2) and death to Taxus
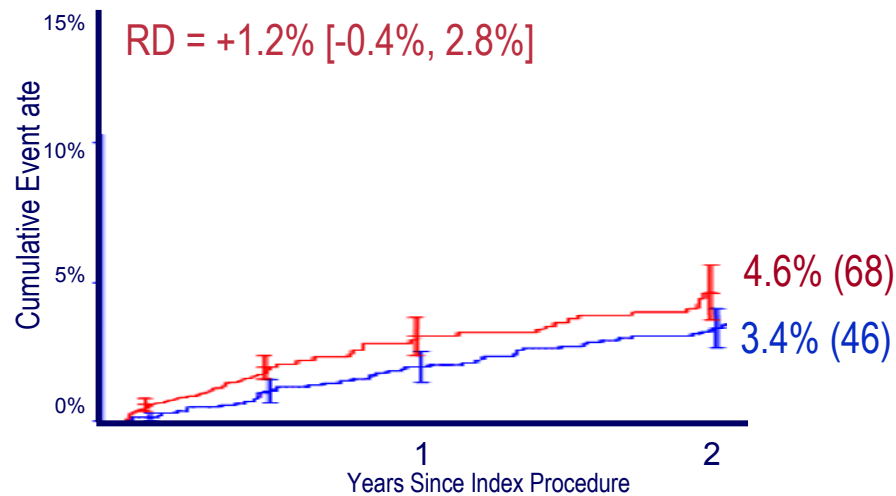   - Indicates excellent event capture in ARRIVE

Agenda

- ➢ ARRIVE Registry

- ➢ TAXUS v. ARRIVE Analysis (Simple lesions)

- ➢ ARRIVE Analysis (Complex lesions)

- ➢ Multivariate Predictor Analysis
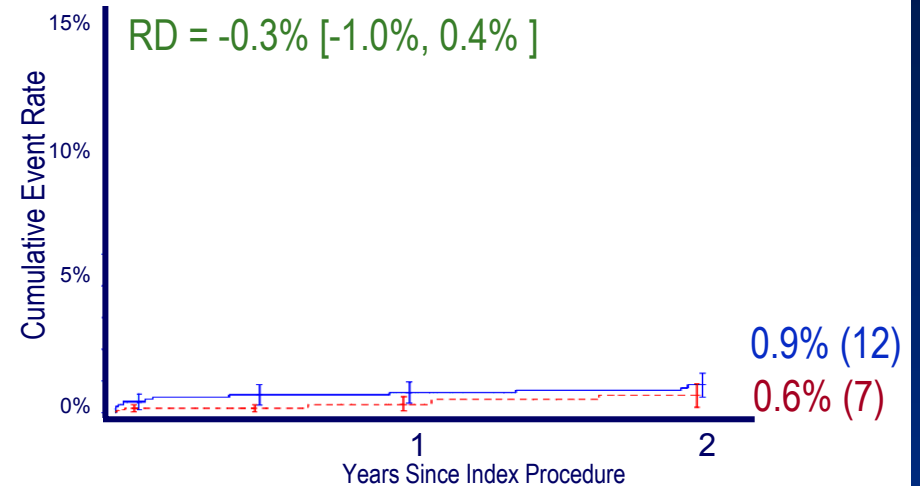
- ➢ Summary and Conclusions

ARRIVE Complex v. Simple
N = 7,393

All Death

RD = +1.9% [0.2%, 3.6%]
p = 0.08

Cumulative Event Rate

6.5% (166)
4.6% (68)

Years Since Index Procedure

Q Wave MI

RD= +0.6% [-0.1%, 1.3%]
p = 0.02

Cumulative Event Rate

1.2% (35)
0.6% (7)

Years Since Index Procedure

ARC Primary ST Definite/Probable

RD = +1.6% [0.6%, 2.6%]
p < 0.0001

After 1 Year
9 v. 4 ST
ΔRD = +0.2% p=0.81

Cumulative Event Rate

Δ0.7%
2.3%
3.0% (99)
1.4% (18)
0.9%   Δ0.5%

Years Since Index Procedure

TVR

RD= +4.3% [2.1%, 6.5%]
p <0.0001

Cumulative Event Rate

11.5% (307)
7.2% (98)

Years Since Index Procedure
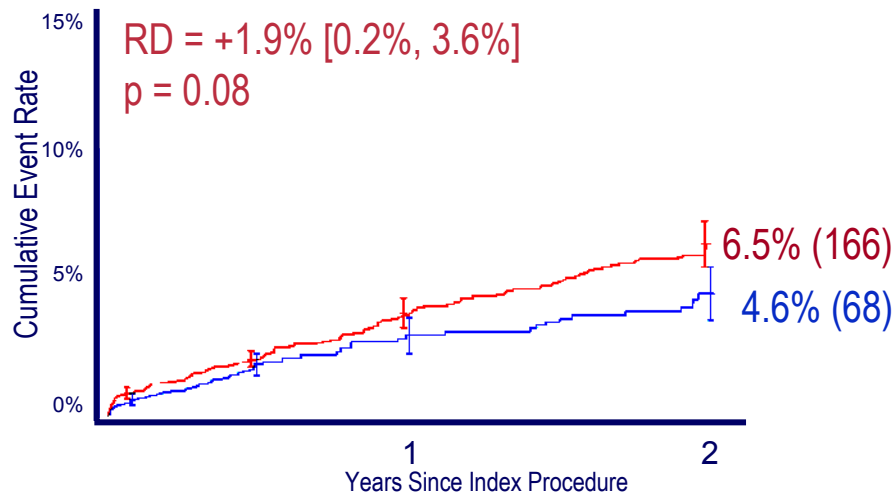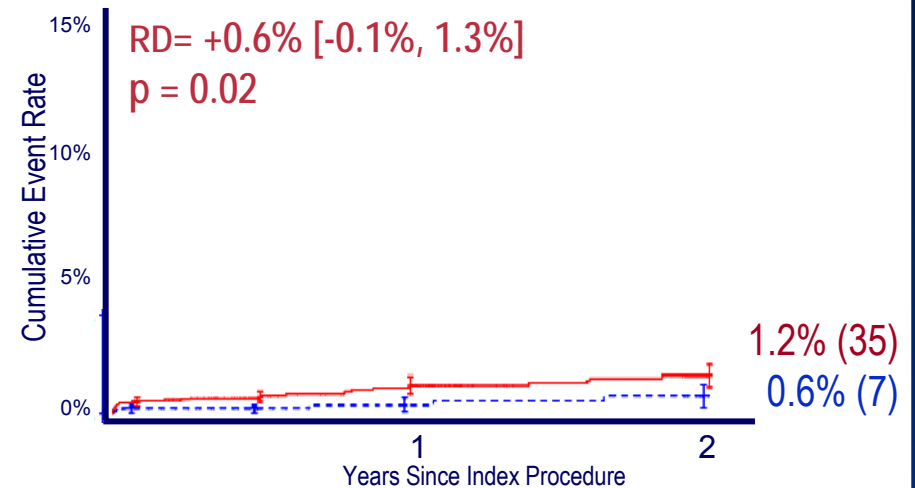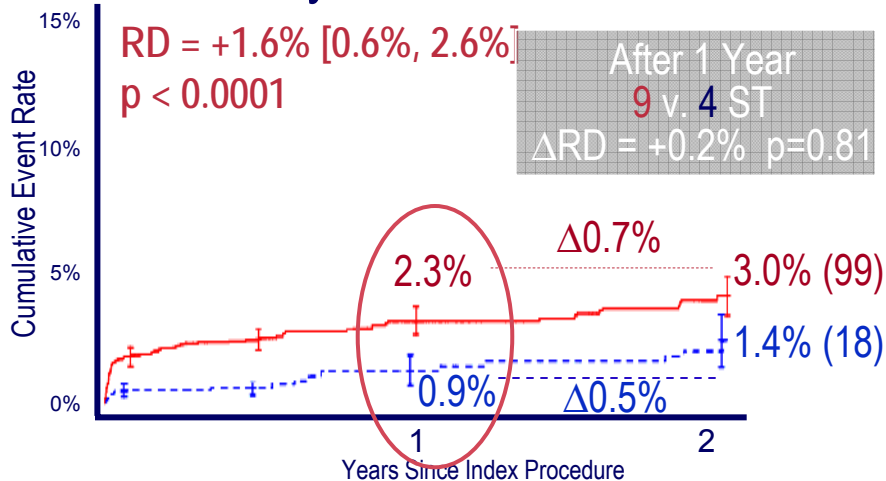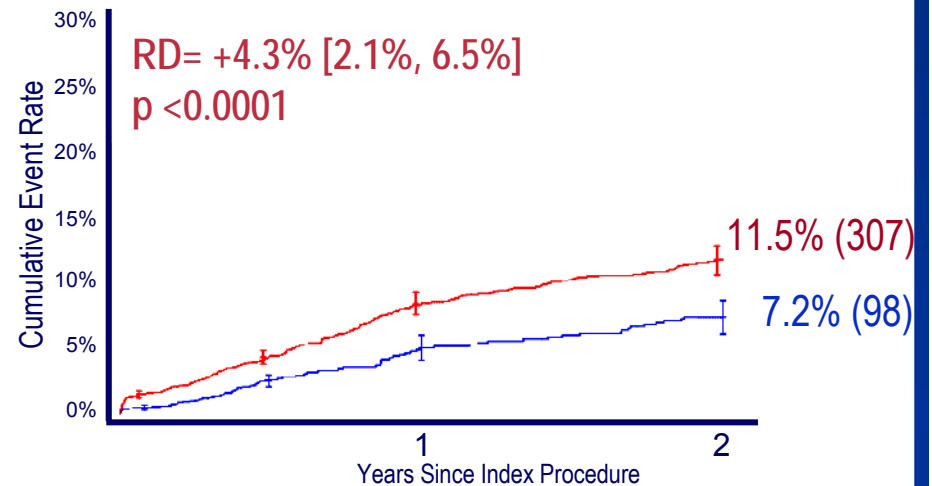
Event Rates in Prior Studies: TAXUS alone
Overall Patients (N = 7,585)

DES Cover (n=2636); SORT-OUT II (n=1033); TSEARCH/RESEARCH (n=576); REAL (n=684): MILAN (n=281); TAXI=100; SIRTAX=509; TC WYRE (n=816): REALITY (n=669)

All Death

Study name	Event rate	Lower limit	Upper limit
DESCover	0.028	0.022	0.035
SORT-OUT II	0.019	0.012	0.029
TSEARCH/ RESEARCH	0.053	0.037	0.075
REAL	0.027	0.017	0.042
MILAN	0.025	0.012	0.051
TAXI	0.010	0.001	0.068
REALITY	0.013	0.007	0.025
SIRTAX	0.027	0.016	0.045
	0.026	0.019	0.035

2.6% [1.9% 3.5%]

All MI

Study name	Event rate	Lower limit	Upper limit
DESCover	0.026	0.021	0.033
SORT-OUT II	0.020	0.013	0.031
REAL	0.042	0.029	0.060
MILAN	0.025	0.012	0.051
TC WYRE	0.029	0.019	0.043
TAXI	0.050	0.021	0.115
REALITY	0.060	0.044	0.081
SIRTAX	0.039	0.025	0.060
	0.034	0.025	0.045

3.4% [2.5%, 4.5%]

ST

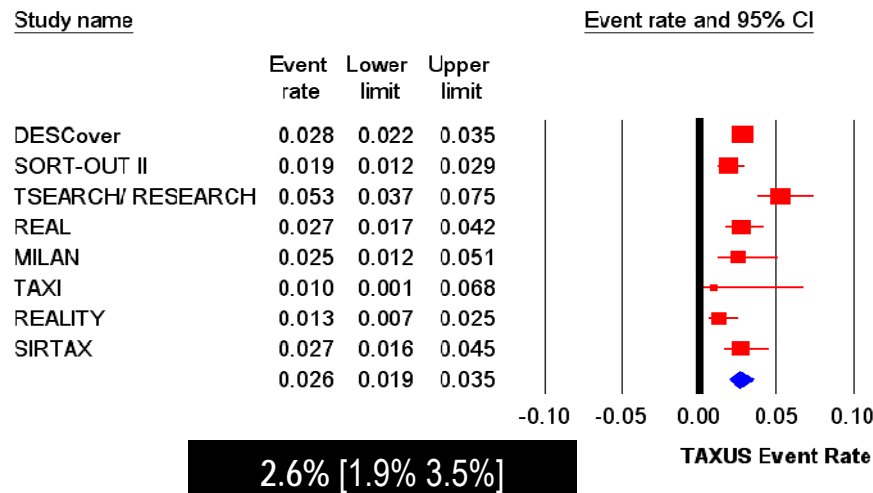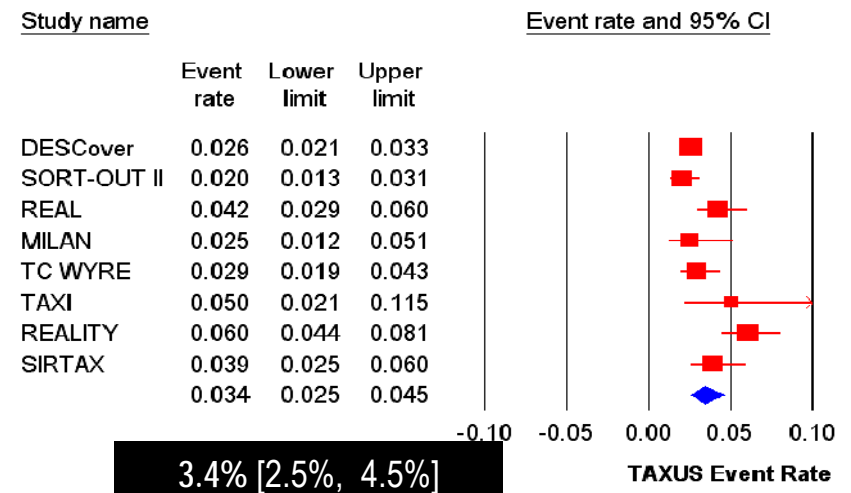| Study name	Event rate	Lower limit	Upper limit
DESCover	0.008	0.005	0.012
REAL	0.007	0.003	0.017
MILAN	0.014	0.005	0.037
TC WYRE	0.009	0.004	0.018
TAXI	0.005	0.000	0.074
REALITY	0.019	0.011	0.033
SIRTAX	0.018	0.009	0.034
	0.012	0.008	0.016

1.2% [0.8%, 1.6%]

TVR

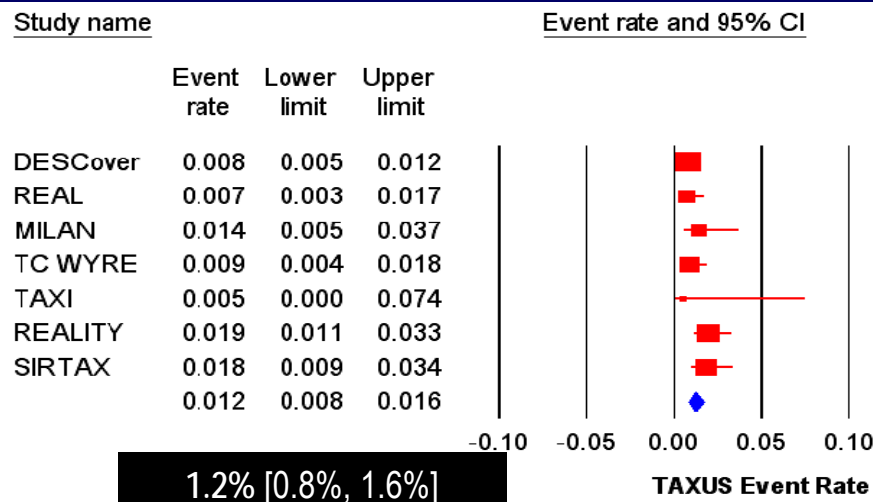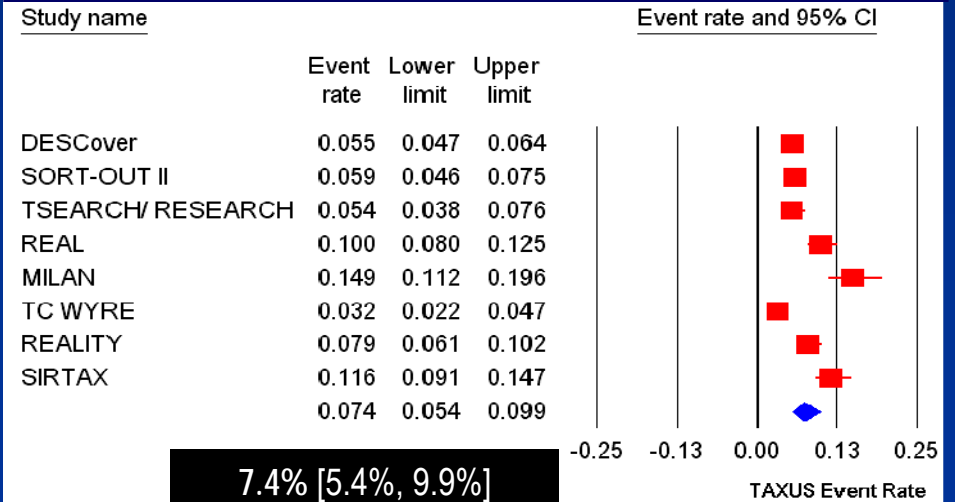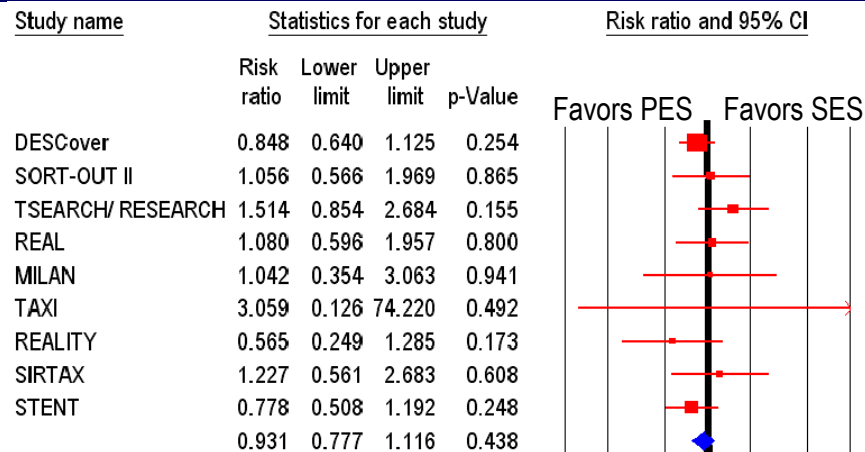| Study name	Event rate	Lower limit	Upper limit
DESCover	0.055	0.047	0.064
SORT-OUT II	0.059	0.046	0.075
TSEARCH/ RESEARCH	0.054	0.038	0.076
REAL	0.100	0.080	0.125
MILAN	0.149	0.112	0.196
TC WYRE	0.032	0.022	0.047
REALITY	0.079	0.061	0.102
SIRTAX	0.116	0.091	0.147
	0.074	0.054	0.099

7.4% [5.4%, 9.9%]

Event Rates in Prior Studies: TAXUS vs. Cypher
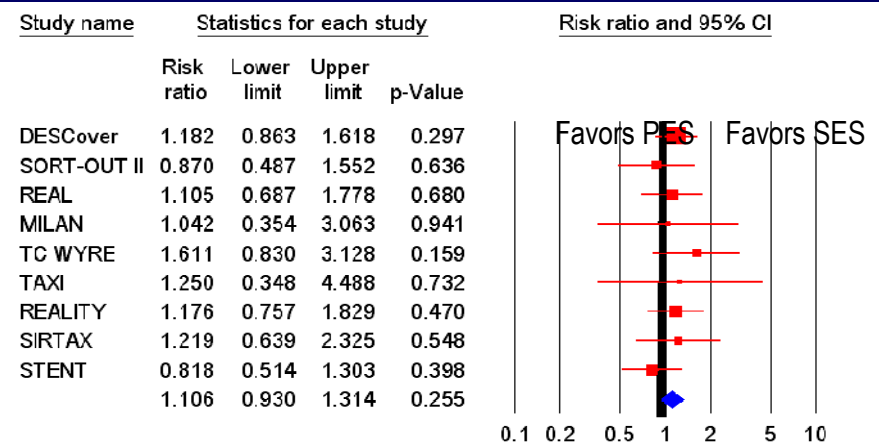## *Overall Patients (TOTAL N= 19,779)*

DESCover (n=6509); SORT-OUT II (n=2098); TSEARCH/RESEARCH (n=1084); REAL (n=1676); MILAN (n=529); TAXI (n=202); REALITY (n=1353); SIRTAX (n=1012); STENT (n=3758); TC WYRE (n=1558)
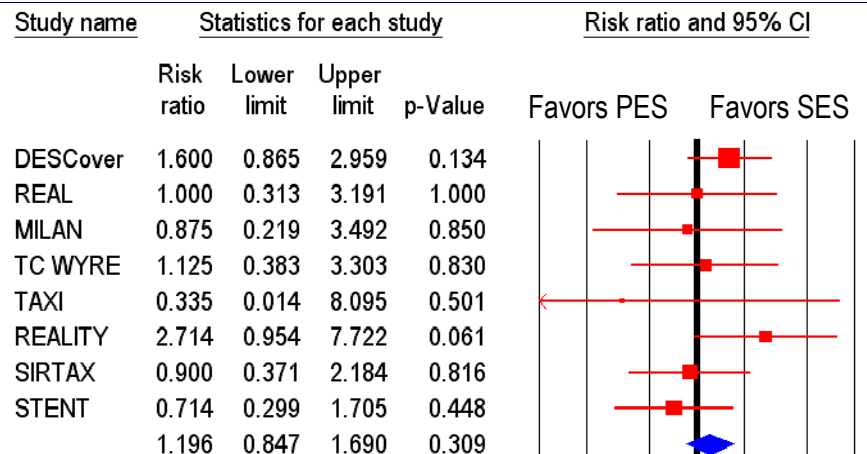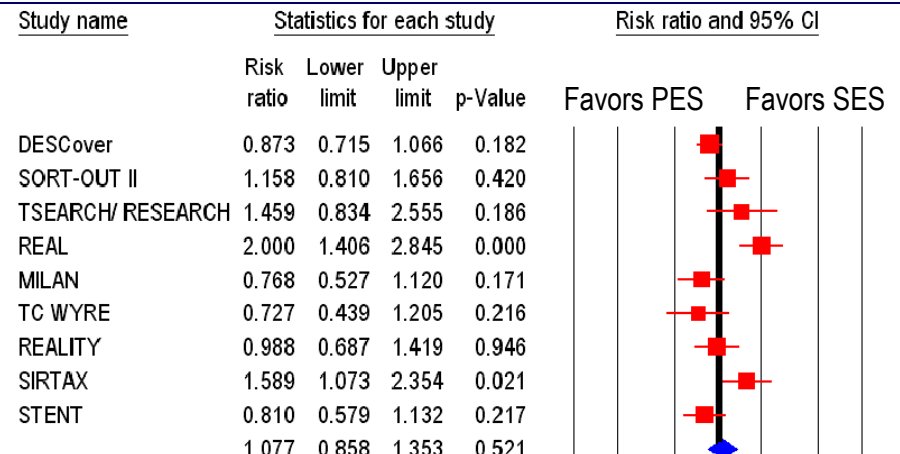
All Death

Study name	Risk ratio	Lower limit	Upper limit	p-Value
DESCover	0.848	0.640	1.125	0.254
SORT-OUT II	1.056	0.566	1.969	0.865
TSEARCH/ RESEARCH	1.514	0.854	2.684	0.155
REAL	1.080	0.596	1.957	0.800
MILAN	1.042	0.354	3.063	0.941
TAXI	3.059	0.126	74.220	0.492
REALITY	0.565	0.249	1.285	0.173
SIRTAX	1.227	0.561	2.683	0.608
STENT	0.778	0.508	1.192	0.248
	0.931	0.777	1.116	0.438

Risk Ratio: 0.93 [0.77, 1.12]

All MI

Study name	Risk ratio	Lower limit	Upper limit	p-Value
DESCover	1.182	0.863	1.618	0.297
SORT-OUT II	0.870	0.487	1.552	0.636
REAL	1.105	0.687	1.778	0.680
MILAN	1.042	0.354	3.063	0.941
TC WYRE	1.611	0.830	3.128	0.159
TAXI	1.250	0.348	4.488	0.732
REALITY	1.176	0.757	1.829	0.470
SIRTAX	1.219	0.639	2.325	0.548
STENT	0.818	0.514	1.303	0.398
	1.106	0.930	1.314	0.255

Risk Ratio: 1.1 [0.93, 1.31]

ST

Study name	Risk ratio	Lower limit	Upper limit	p-Value
DESCover	1.600	0.865	2.959	0.134
REAL	1.000	0.313	3.191	1.000
MILAN	0.875	0.219	3.492	0.850
TC WYRE	1.125	0.383	3.303	0.830
TAXI	0.335	0.014	8.095	0.501
REALITY	2.714	0.954	7.722	0.061
SIRTAX	0.900	0.371	2.184	0.816
STENT	0.714	0.299	1.705	0.448
	1.196	0.847	1.690	0.309

Risk Ratio: 1.2 [0.85, 1.7]

TVR

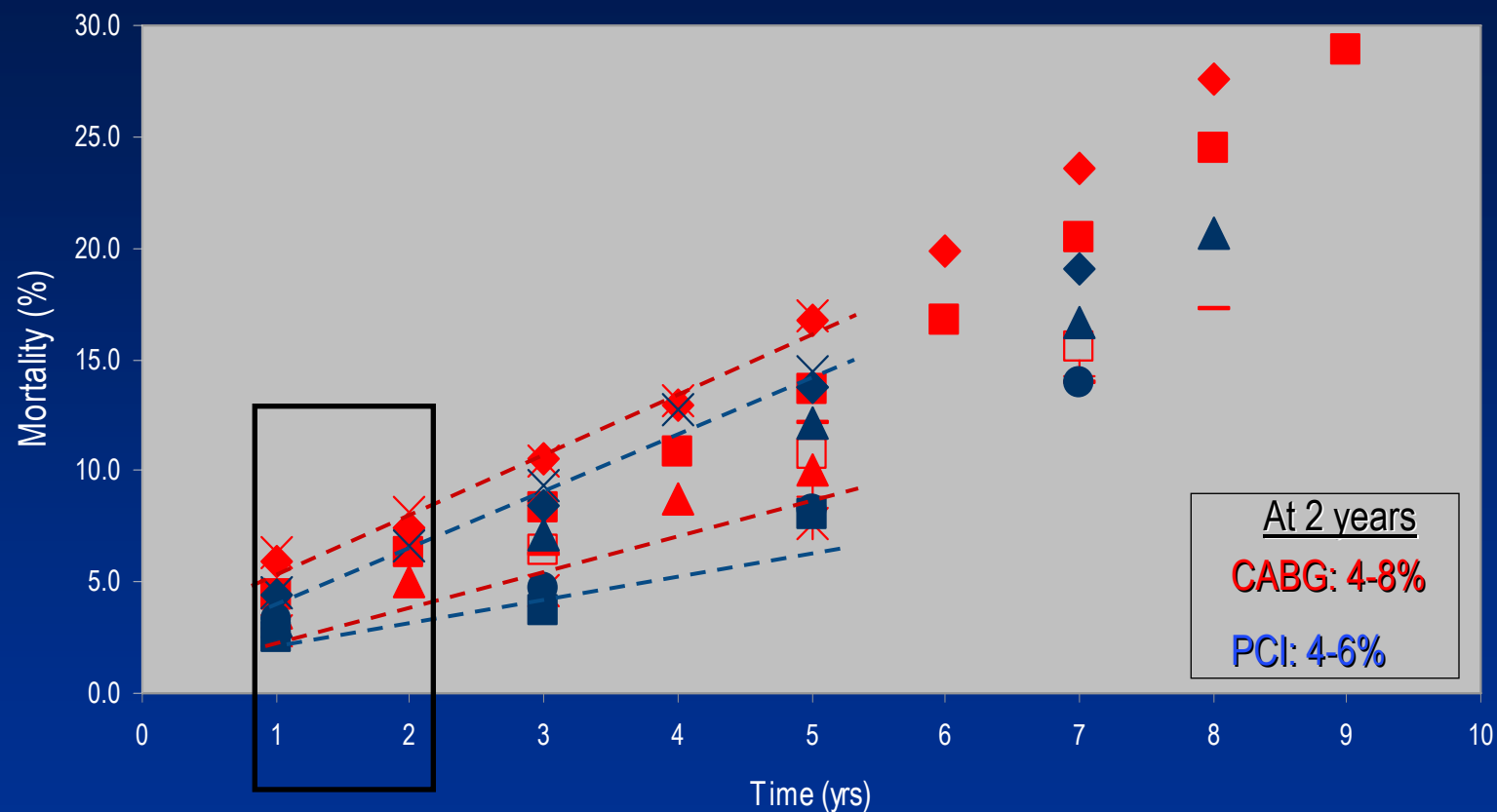| Study name	Risk ratio	Lower limit	Upper limit	p-Value
DESCover	0.873	0.715	1.066	0.182
SORT-OUT II	1.158	0.810	1.656	0.420
TSEARCH/ RESEARCH	1.459	0.834	2.555	0.186
REAL	2.000	1.406	2.845	0.000
MILAN	0.768	0.527	1.120	0.171
TC WYRE	0.727	0.439	1.205	0.216
REALITY	0.988	0.687	1.419	0.946
SIRTAX	1.589	1.073	2.354	0.021
STENT	0.810	0.579	1.132	0.217
	1.077	0.858	1.353	0.521

Risk Ratio: 1.08 [0.86,1.35]

Historical Outcomes Rates (absent an internal comparator)
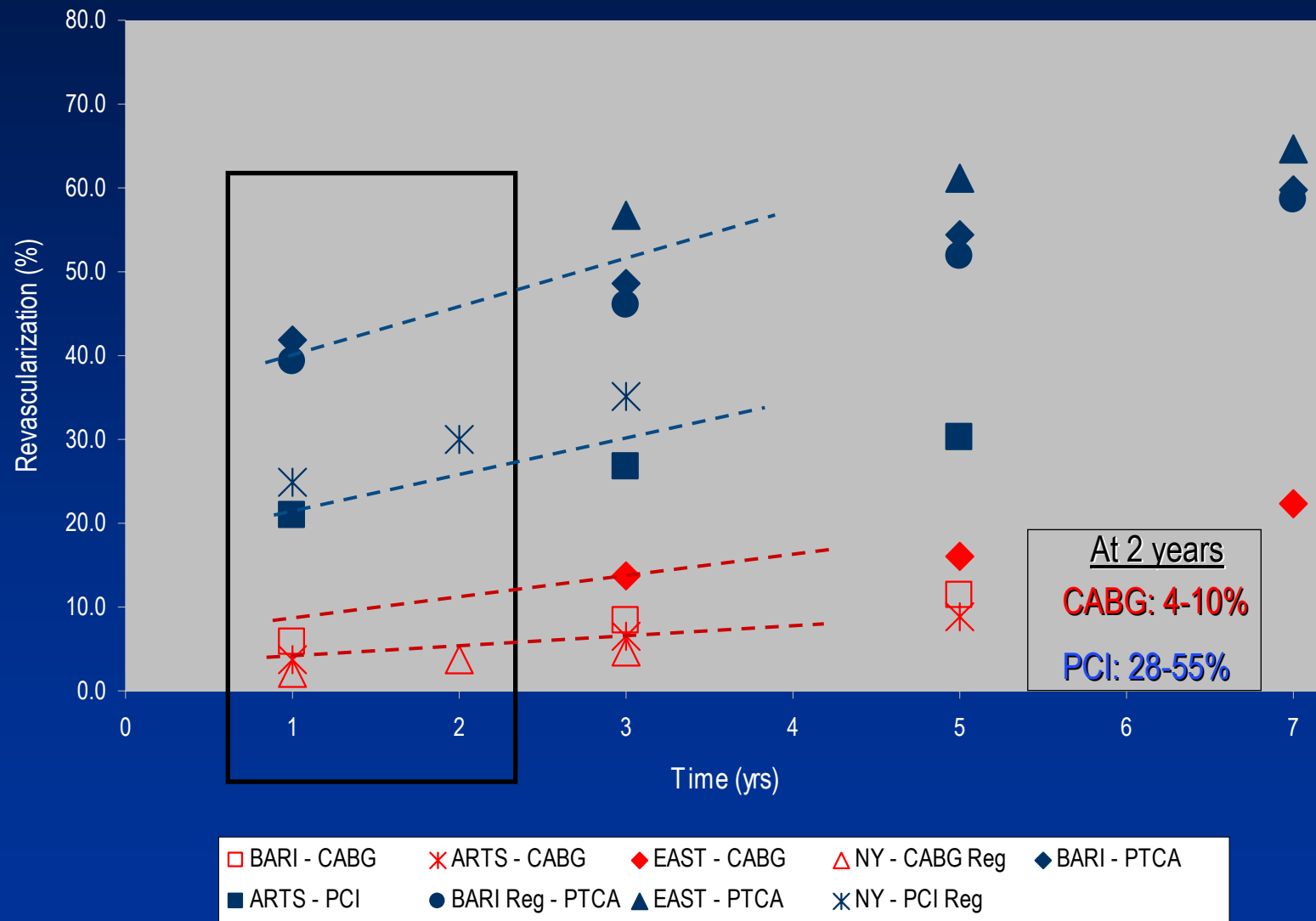## *Death in Complex PCI or CABG Cases (N = 60,078)*

Mortality (%) vs Time (yrs)

At 2 years
CABG: 4-8%
PCI: 4-6%

Legend:
- □ BARI - CABG
- + BARI Reg - CABG
- ✳ ARTS - CABG
- — EAST - CABG
- ✕ Duke - CABG
- ◆ NNECDSG - CABG
- ■ Emory - CABG
- ▲ Sweden - CABG (Univ Hosp)
- ◆ BARI - PTCA
- ● BARI Reg - PTCA
- ■ ARTS - PCI
- ▲ EAST - PTCA
- ✕ Duke - PTCA

Historical Outcomes Rates (absent an internal comparator)
MI in Complex PCI or CABG Cases (N = 13,403)

At 2 years
CABG: 4-6%
PCI: 7%

ARTS - PCI ✳ ARTS - CABG ▪ Emory - CABG
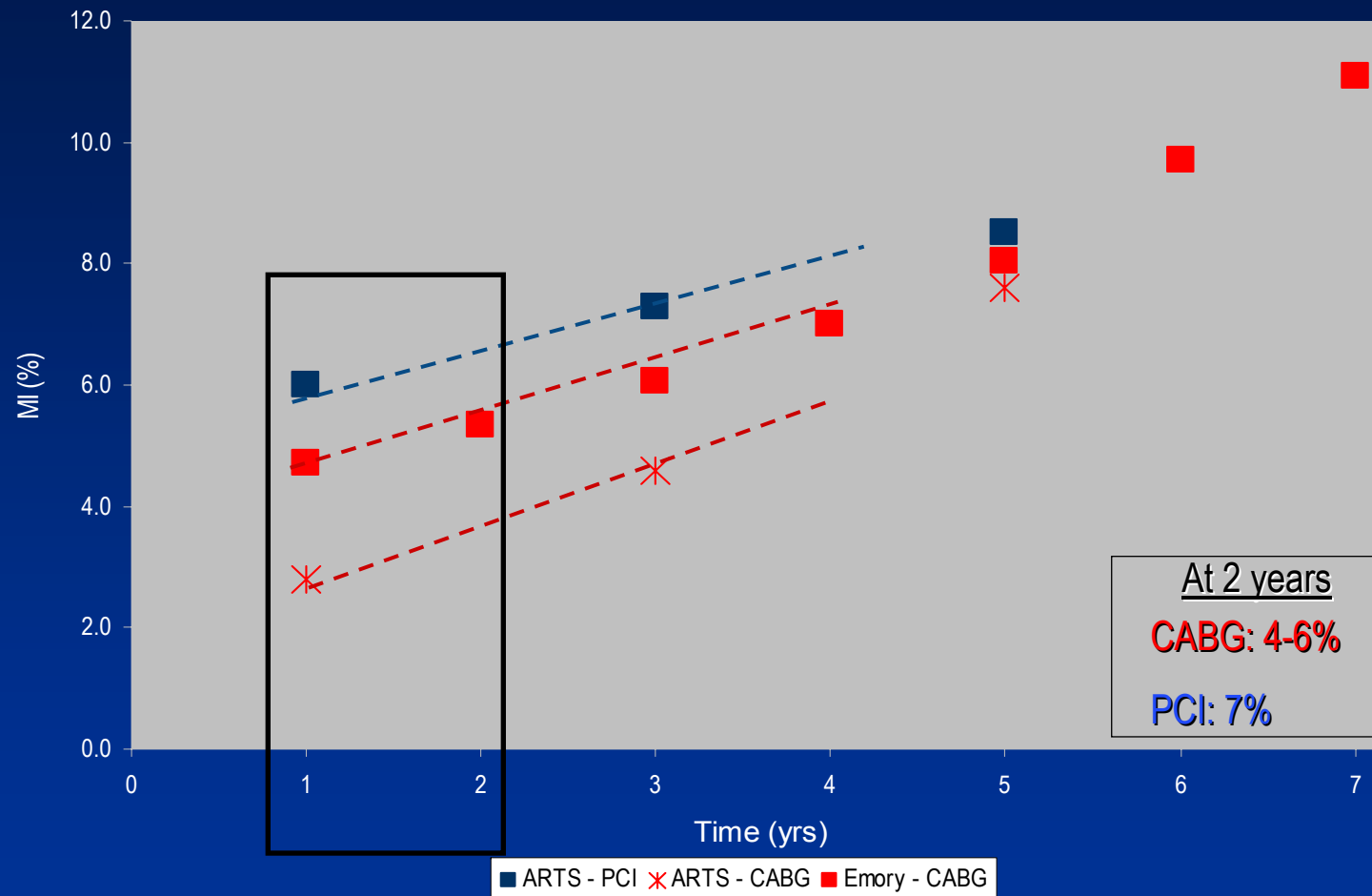
Historical Outcomes Rates (absent an internal comparator)
Revascularization in Complex PCI or CABG Cases (N = 63,929)

At 2 years
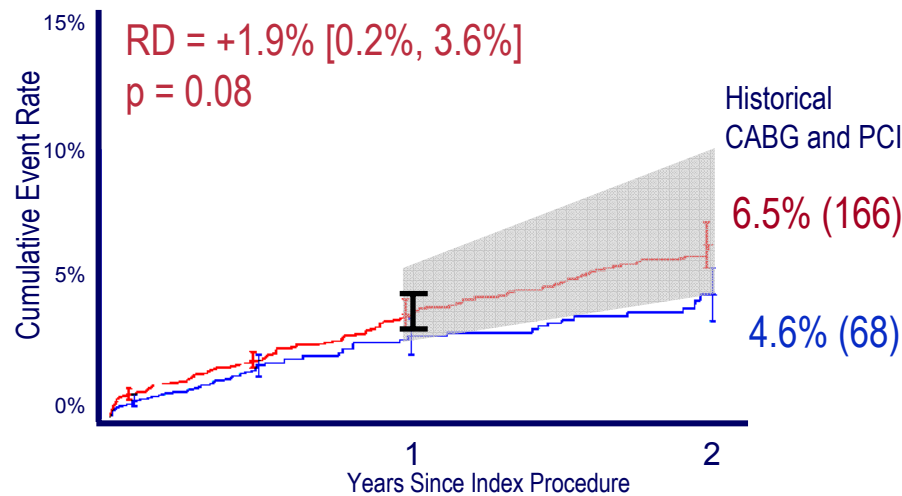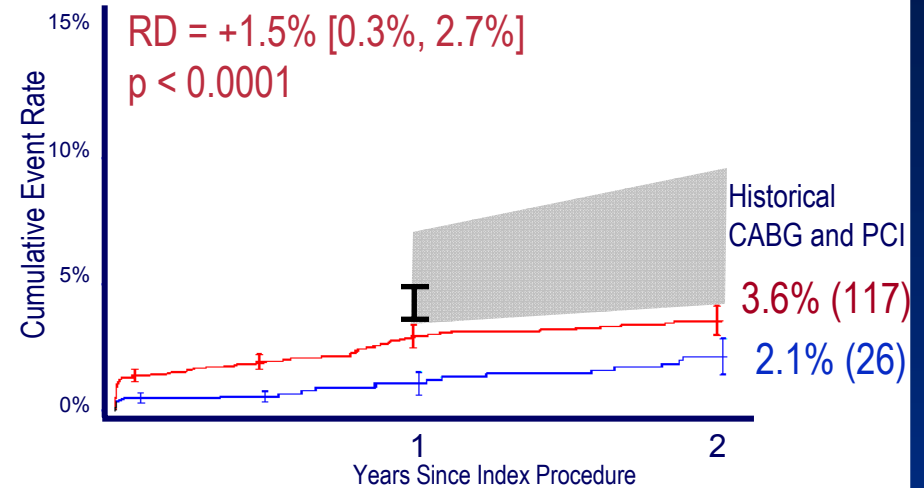CABG: 4-10%
PCI: 28-55%

Revascularization (%)

Time (yrs)

Legend:
- □ BARI - CABG
- ✳ ARTS - CABG
- ◆ EAST - CABG
- △ NY - CABG Reg
- ◆ BARI - PTCA
- ■ ARTS - PCI
- ● BARI Reg - PTCA
- ▲ EAST - PTCA
- ✳ NY - PCI Reg

ARRIVE Complex v. Simple
N = 7,393

Simple (N=2564) Complex (N=4829)
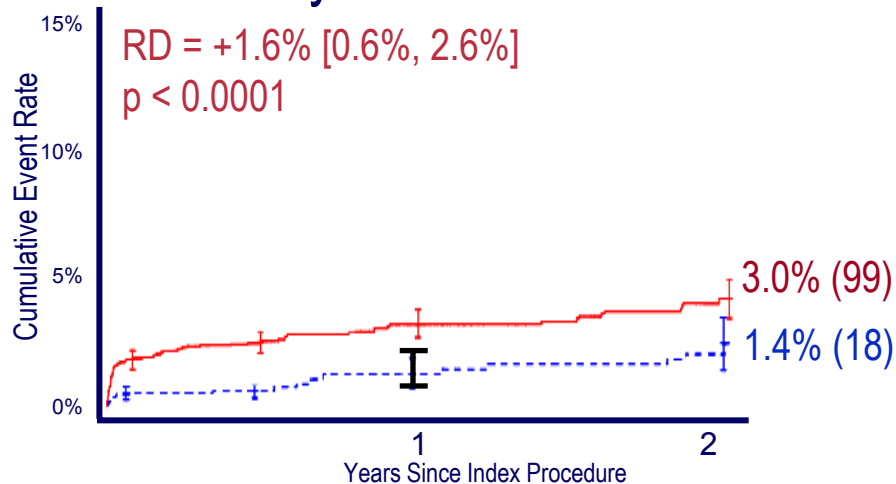RD = Rate Difference = Complex — Simple
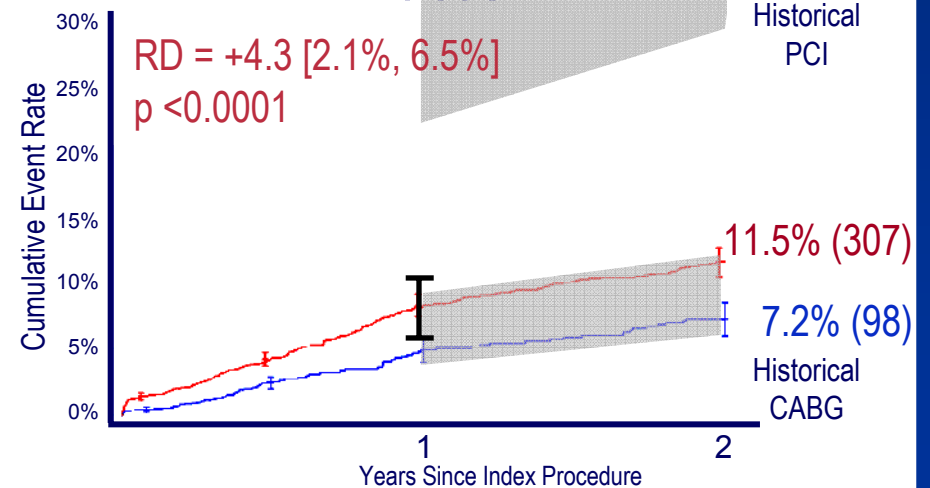No increase   Increase

All Death
RD = +1.9% [0.2%, 3.6%]
p = 0.08
Historical CABG and PCI
6.5% (166)
4.6% (68)

All MI
RD = +1.5% [0.3%, 2.7%]
p < 0.0001
Historical CABG and PCI
3.6% (117)
2.1% (26)

ARC Primary ST Definite/Probable
RD = +1.6% [0.6%, 2.6%]
p < 0.0001
3.0% (99)
1.4% (18)

TVR
RD = +4.3 [2.1%, 6.5%]
p <0.0001
Historical PCI
11.5% (307)
7.2% (98)
Historical CABG
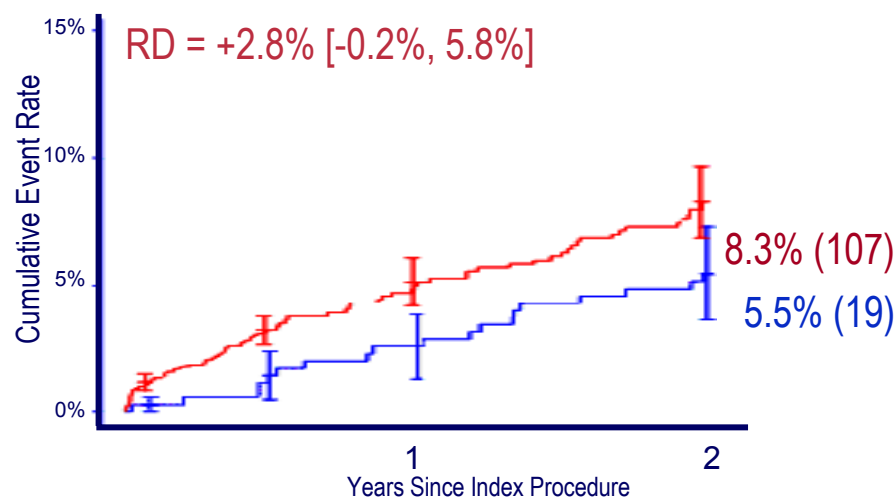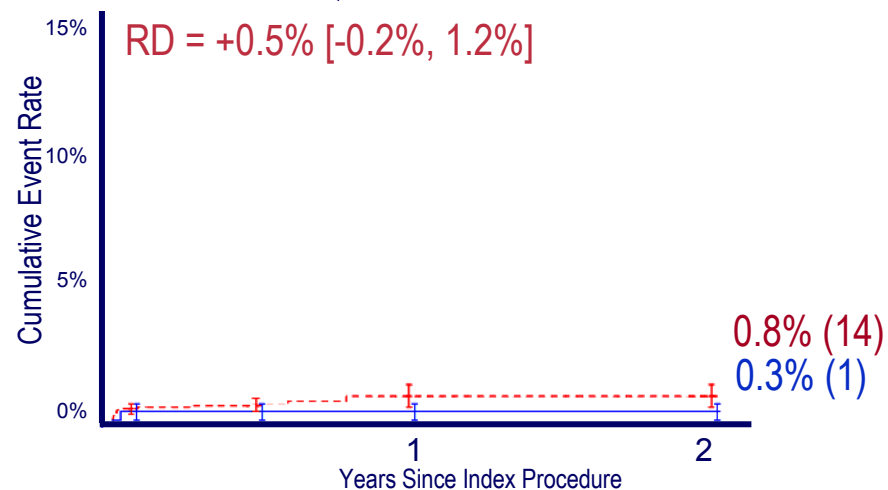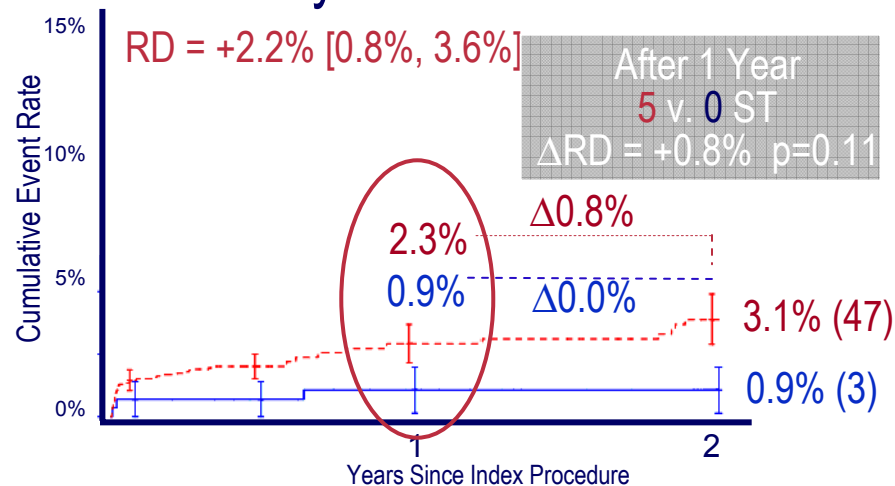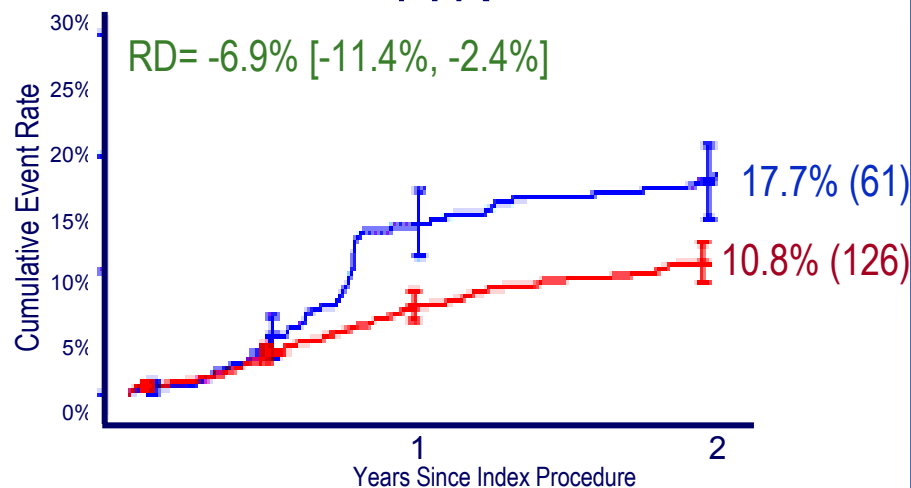
Event Rates in Prior Studies: TAXUS alone
Diabetic Patients (N=1,141)

All Death

Study name	Event rate	Lower limit	Upper limit	Event rate and 95% CI
SOLACI	0.040	0.023	0.068	
TSEARCH/ RESEARCH	0.072	0.040	0.126	
MILAN/Colombo	0.035	0.016	0.076	
Prairie Heart	0.032	0.015	0.067	
	0.044	0.031	0.063	

-0.15 -0.08 0.00 0.08 0.15

TAXUS Event Rate

4.4% [3.1%, 6.3%]

All MI

Study name	Event rate	Lower limit	Upper limit	Event rate and 95% CI
SOLACI	0.012	0.00	0.03	
MILAN/Colombo	0.041	0.02	0.08	
Prairie Heart	0.028	0.01	0.06	
	0.026	0.01	0.05	

-0.15 -0.08 0.00 0.08 0.15

TAXUS Event Rate

2.6% [1.0%, 5.0%]

ST

Study name	Event rate	Lower limit	Upper limit	Event rate and 95% CI
TSEARCH/ RESEARCH	0.020	0.01	0.06	
MILAN/Colombo	0.018	0.01	0.05	
	0.019	0.01	0.04	

-0.50 -0.25 0.00 0.25 0.50

TAXUS Event Rate

1.9% [1.0%, 4.0%]

TVR

Study name	Event rate	Lower limit	Upper limit	Event rate and 95% CI
SOLACI	0.041	0.02	0.07	
TC-WYRE	0.028	0.01	0.05	
TSEARCH/ RESEARCH	0.070	0.04	0.12	
MILAN/Colombo	0.263	0.20	0.33	
Prairie Heart	0.069	0.04	0.11	
	0.071	0.03	0.17	

-0.50 -0.25 0.00 0.25 0.50

TAXUS Event Rate

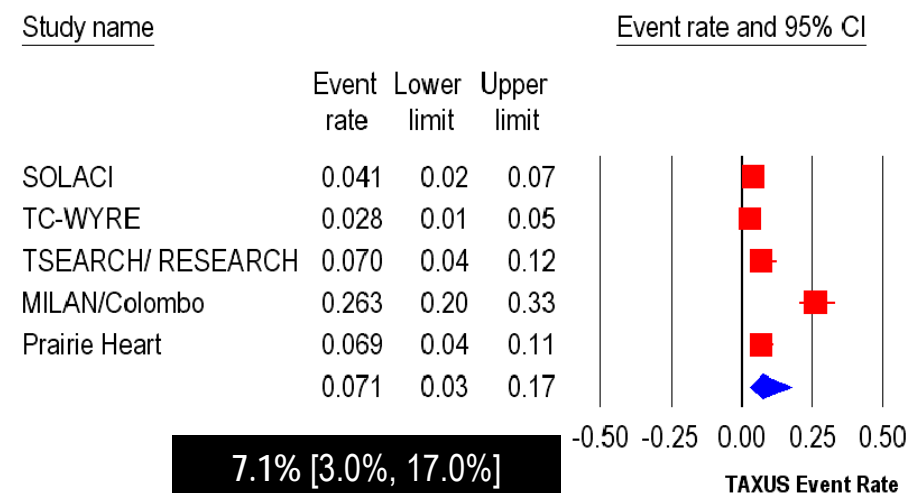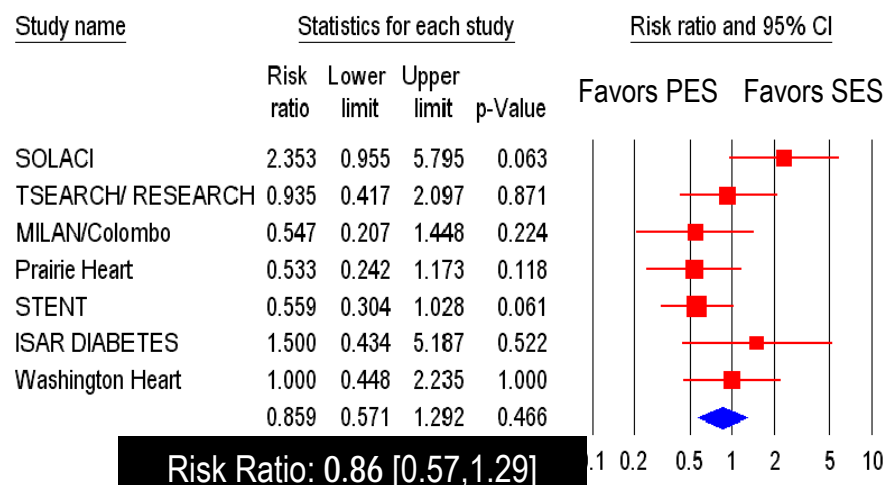**7.1% [3.0%, 17.0%]**

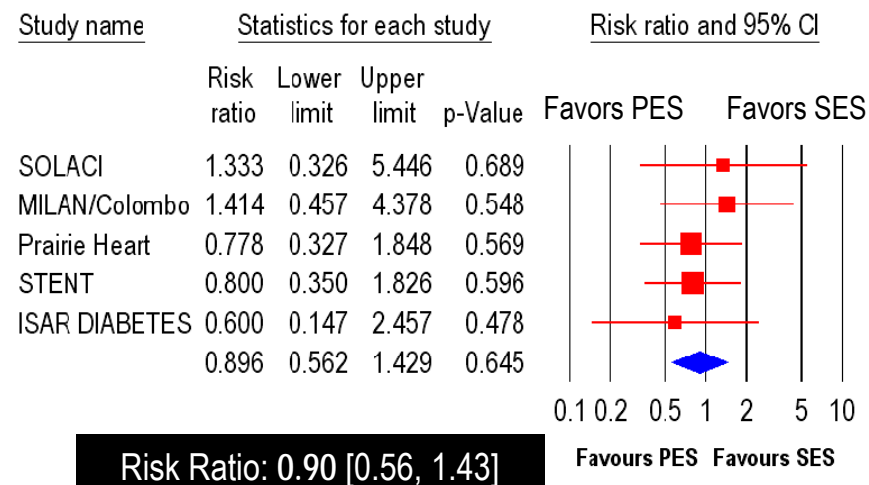# Event Rates in Prior Studies: TAXUS vs. Cypher
Diabetic Patients (N=5,423)

SOLACI (n= 745); TSEARCH/RESEARCH (n=293); MILAN/COLOMBO (n=342); Prairie Heart (n=1162); STENT (n=1680); ISAR DIABETES (n=250); Washington Heart (n=415); TC-WYRE (n=536)
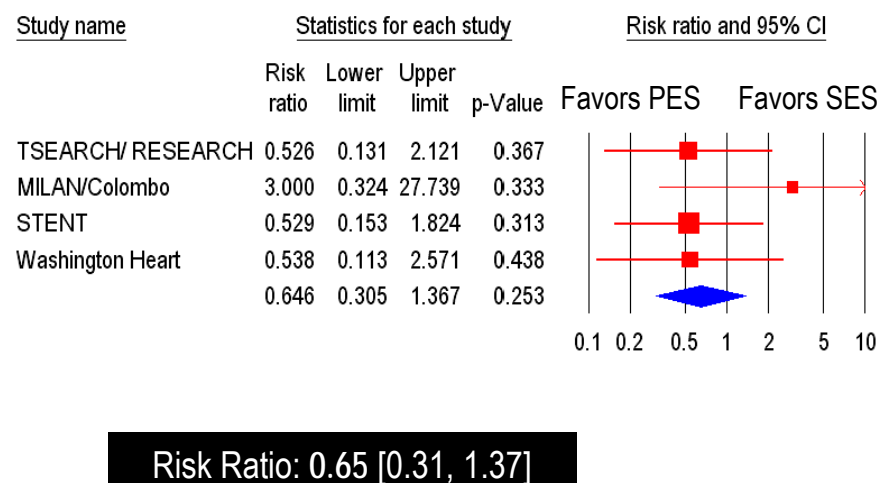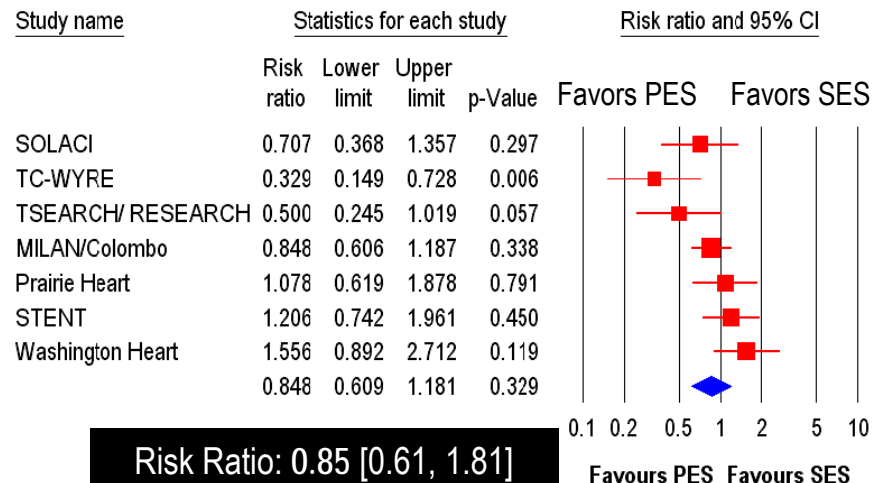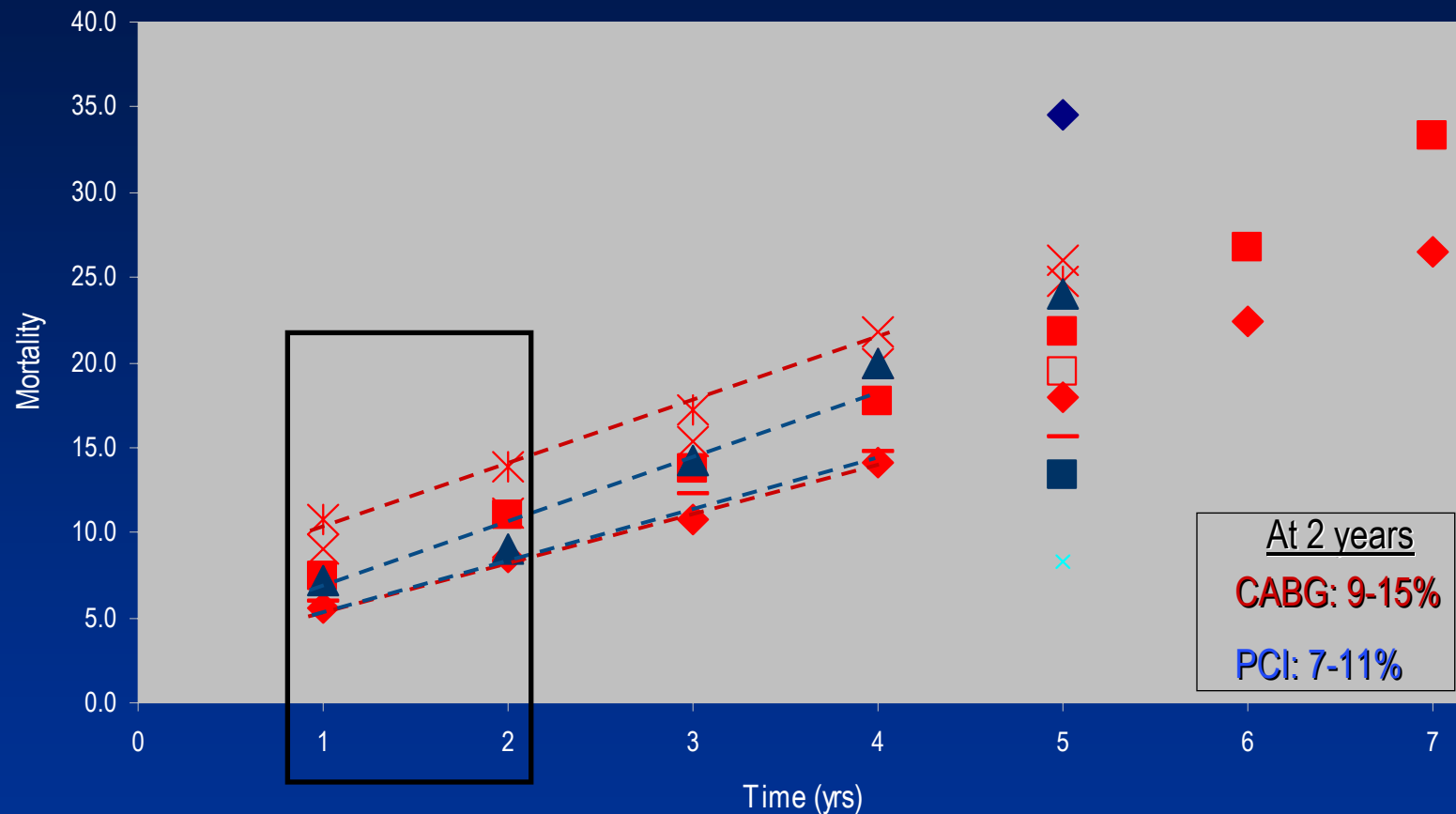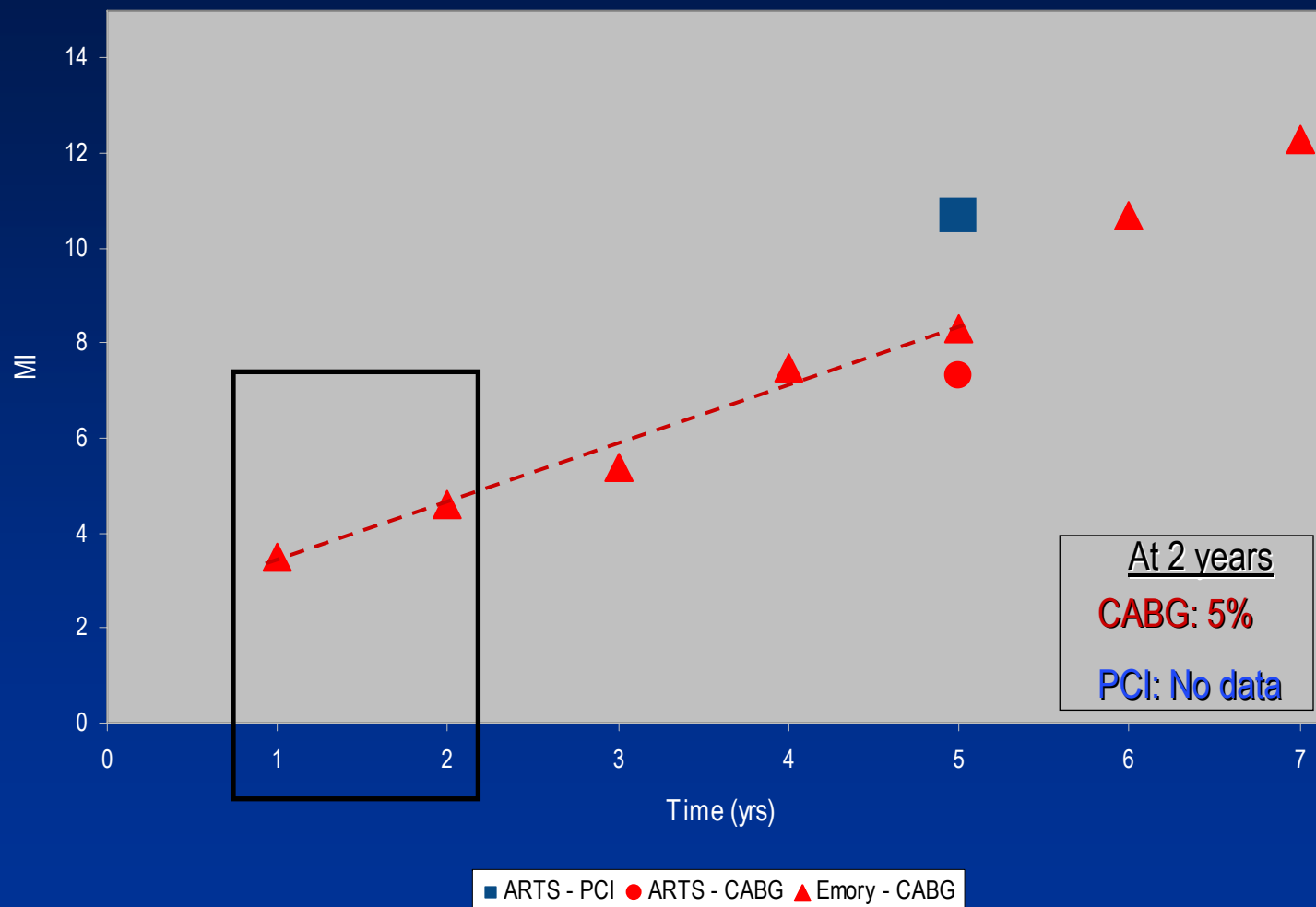
All Death

Study name	Risk ratio	Lower limit	Upper limit	p-Value
SOLACI	2.353	0.955	5.795	0.063
TSEARCH/ RESEARCH	0.935	0.417	2.097	0.871
MILAN/Colombo	0.547	0.207	1.448	0.224
Prairie Heart	0.533	0.242	1.173	0.118
STENT	0.559	0.304	1.028	0.061
ISAR DIABETES	1.500	0.434	5.187	0.522
Washington Heart	1.000	0.448	2.235	1.000
	0.859	0.571	1.292	0.466

Risk Ratio: 0.86 [0.57, 1.29]

All MI

Study name	Risk ratio	Lower limit	Upper limit	p-Value
SOLACI	1.333	0.326	5.446	0.689
MILAN/Colombo	1.414	0.457	4.378	0.548
Prairie Heart	0.778	0.327	1.848	0.569
STENT	0.800	0.350	1.826	0.596
ISAR DIABETES	0.600	0.147	2.457	0.478
	0.896	0.562	1.429	0.645

Risk Ratio: 0.90 [0.56, 1.43]

ST

Study name	Risk ratio	Lower limit	Upper limit	p-Value
TSEARCH/ RESEARCH	0.526	0.131	2.121	0.367
MILAN/Colombo	3.000	0.324	27.739	0.333
STENT	0.529	0.153	1.824	0.313
Washington Heart	0.538	0.113	2.571	0.438
	0.646	0.305	1.367	0.253

Risk Ratio: 0.65 [0.31, 1.37]

TVR

Study name	Risk ratio	Lower limit	Upper limit	p-Value
SOLACI	0.707	0.368	1.357	0.297
TC-WYRE	0.329	0.149	0.728	0.006
TSEARCH/ RESEARCH	0.500	0.245	1.019	0.057
MILAN/Colombo	0.848	0.606	1.187	0.338
Prairie Heart	1.078	0.619	1.878	0.791
STENT	1.206	0.742	1.961	0.450
Washington Heart	1.556	0.892	2.712	0.119
	0.848	0.609	1.181	0.329

Risk Ratio: 0.85 [0.61, 1.81]

Historical Outcomes Rates
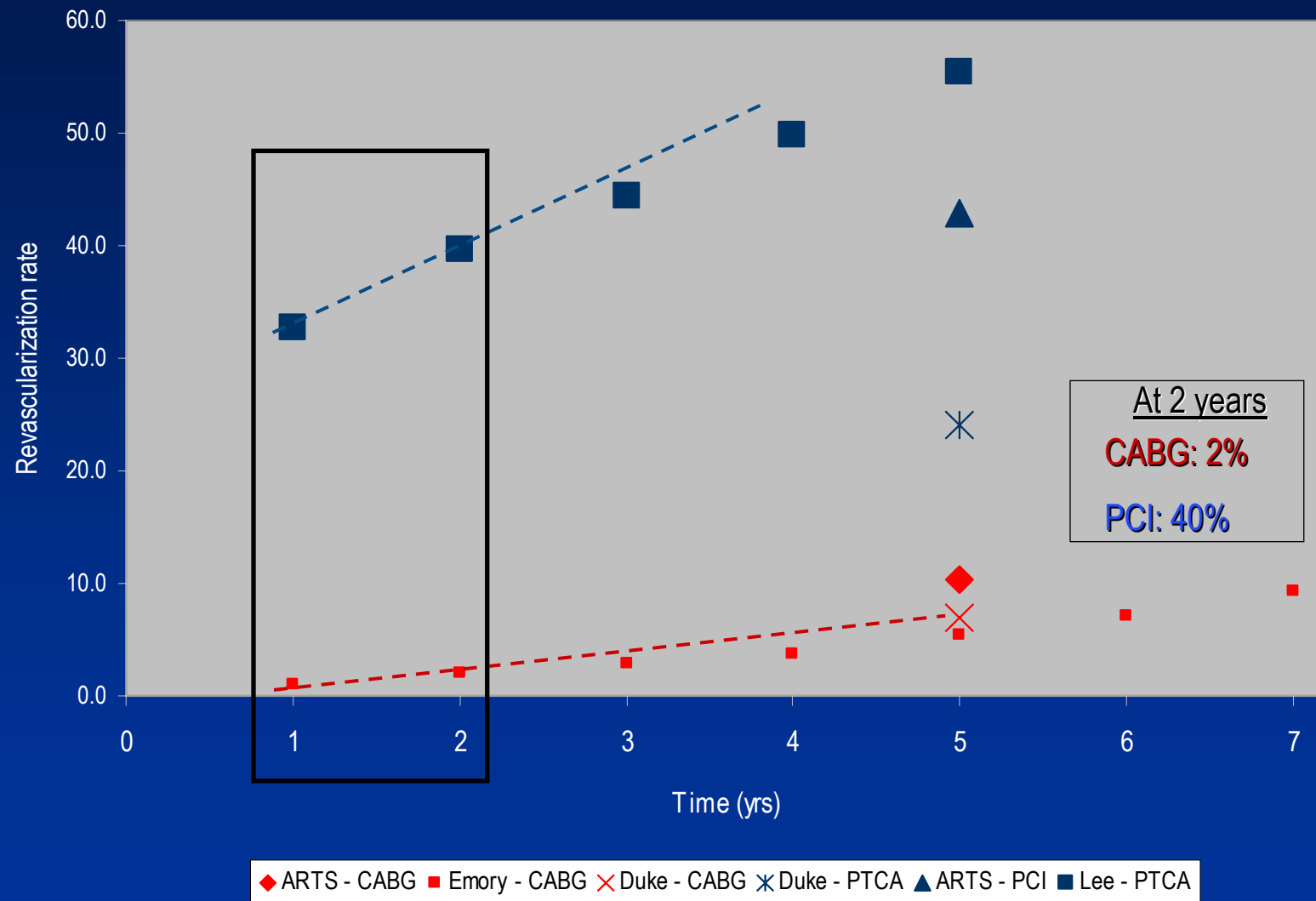## *Death in <u>Diabetics</u> undergoing Complex PCI or CABG (N = 15,269)*

At 2 years
CABG: 9-15%
PCI: 7-11%

Legend:
- □ BARI - CABG
- ✕ ARTS - CABG
- ✕ Duke - CABG
- ◆ NNECDSG - CABG
- ■ Emory - CABG
- ─ Sweden - CABG (Univ Hosp)
- ✳ WestSweden-CABG
- ◆ BARI - PTCA
- ■ ARTS - PCI
- ▲ Duke - PTCA

Historical Outcomes Rates
MI in Diabetics (N = 2,174)

At 2 years
CABG: 5%
PCI: No data

ARTS - PCI   ● ARTS - CABG   ▲ Emory - CABG

Historical Outcomes Rates
Revascularization in Diabetics (N = 3,449)

At 2 years
CABG: 2%
PCI: 40%

Revascularization rate

Time (yrs)

◆ ARTS - CABG ■ Emory - CABG ✕ Duke - CABG ✳ Duke - PTCA ▲ ARTS - PCI ■ Lee - PTCA

25

ARRIVE v. TAXUS Diabetics
N = 2,689

All Death

RD = +2.8% [-0.2%, 5.8%]

Historical CABG and PCI rates

8.3% (107)
5.5% (19)

Cumulative Event Rate
15%
10%
5%
0%

Years Since Index Procedure
1   2

All MI

RD = -1.1% [-3.6%, 1.4%]

Historical PCI rates

4.6% (16)
3.5% (53)

Cumulative Event Rate
15%
10%
5%
0%

Years Since Index Procedure
1   2

ARC Primary ST Definite/Probable

RD = +2.2% [0.8%, 3.6%]

3.1% (47)
0.9% (3)

Cumulative Event Rate
15%
10%
5%
0%

Years Since Index Procedure
1   2

TVR

RD= -6.9% [-11.4%, -2.4%]

Historical PCI –40%

17.7% (61)
10.8% (126)

Historical CABG

Cumulative Event Rate
30%
25%
20%
15%
10%
5%
0%

Years Since Index Procedure
1   2
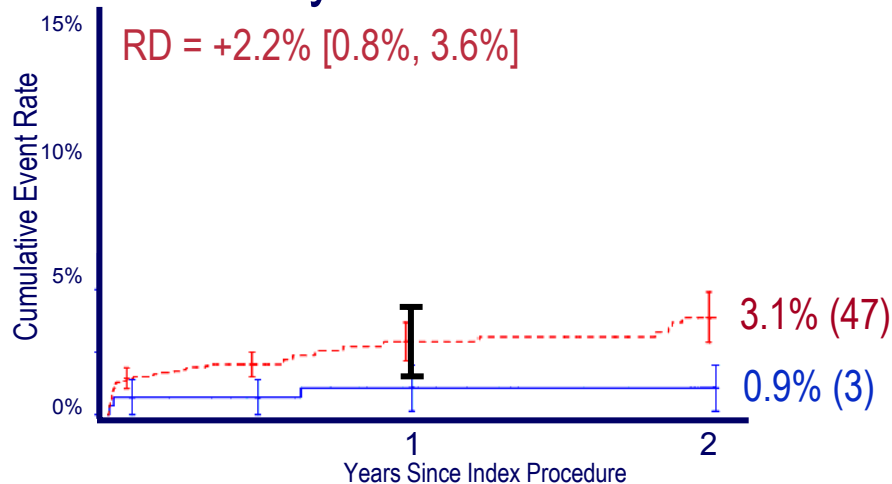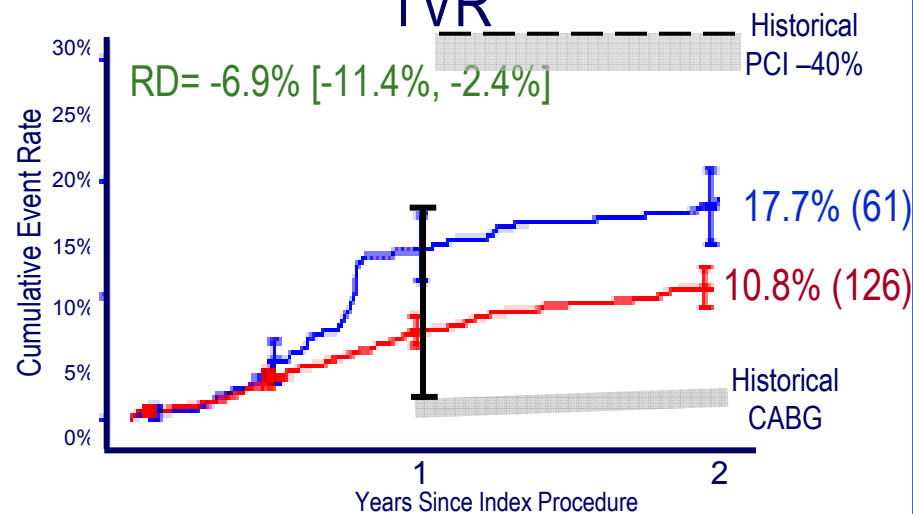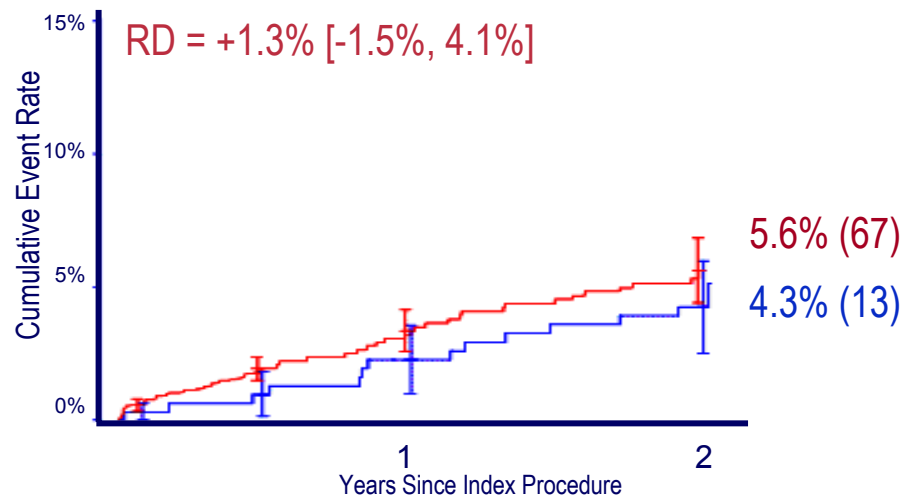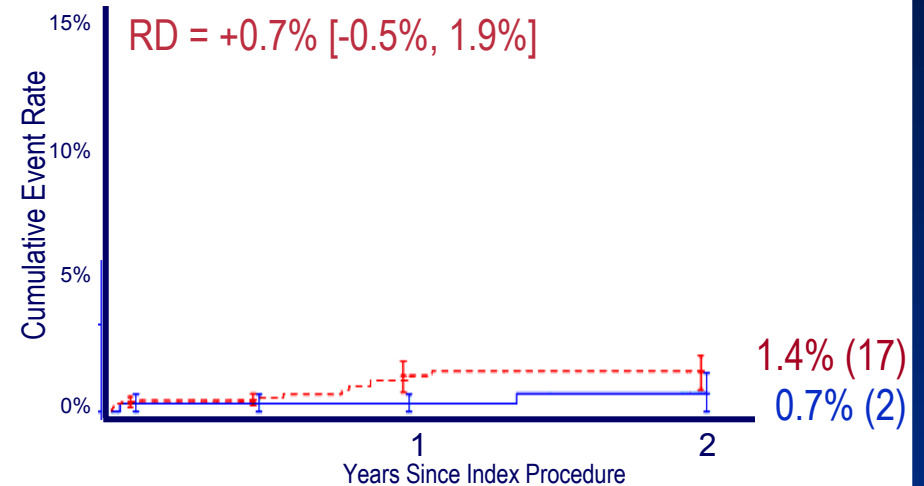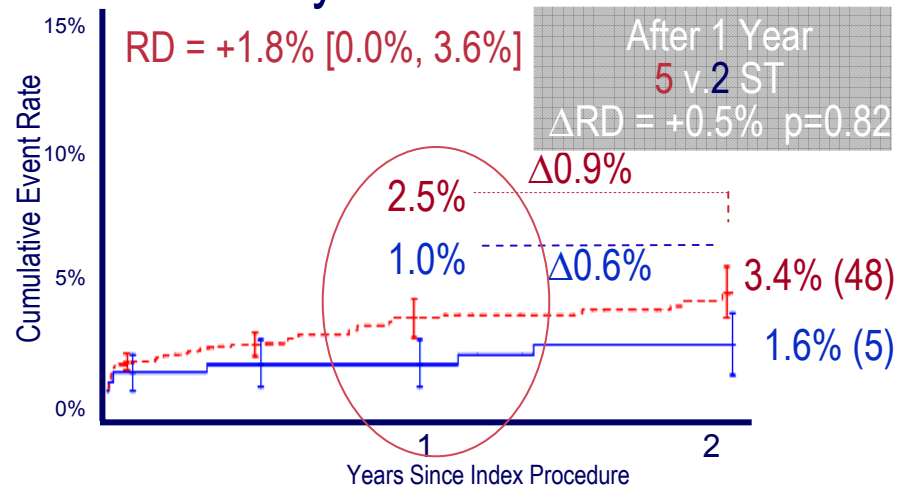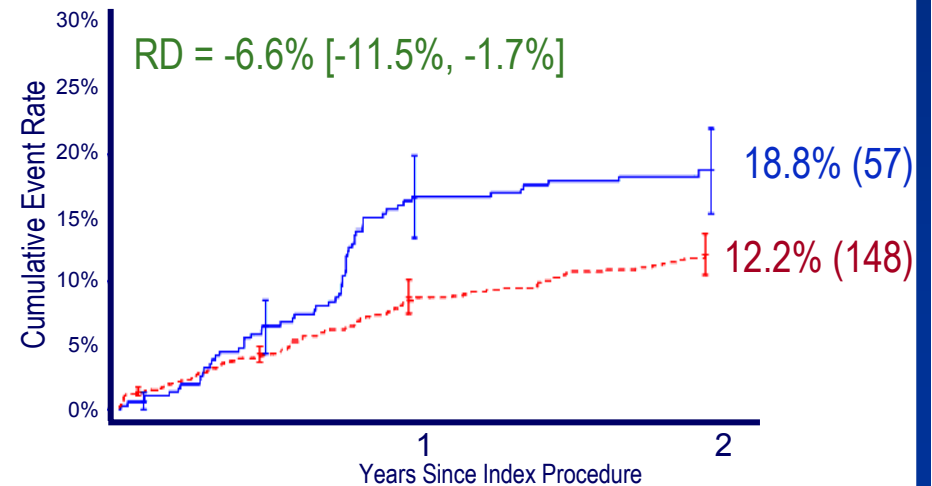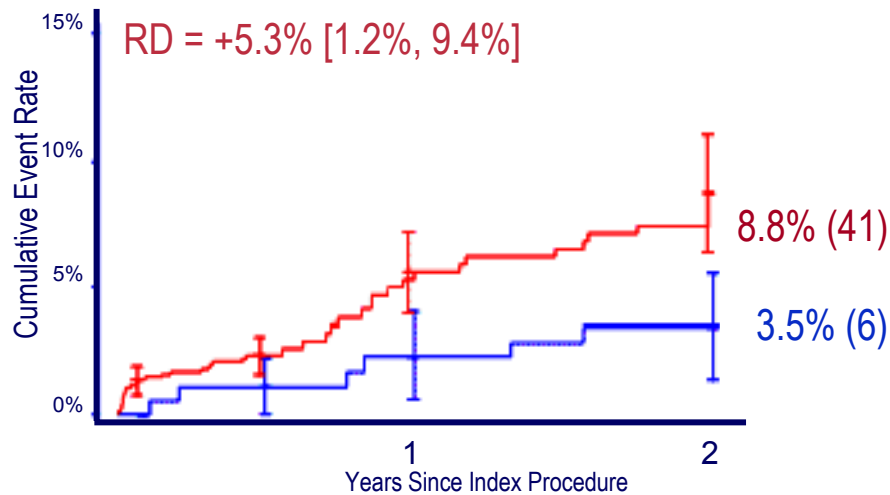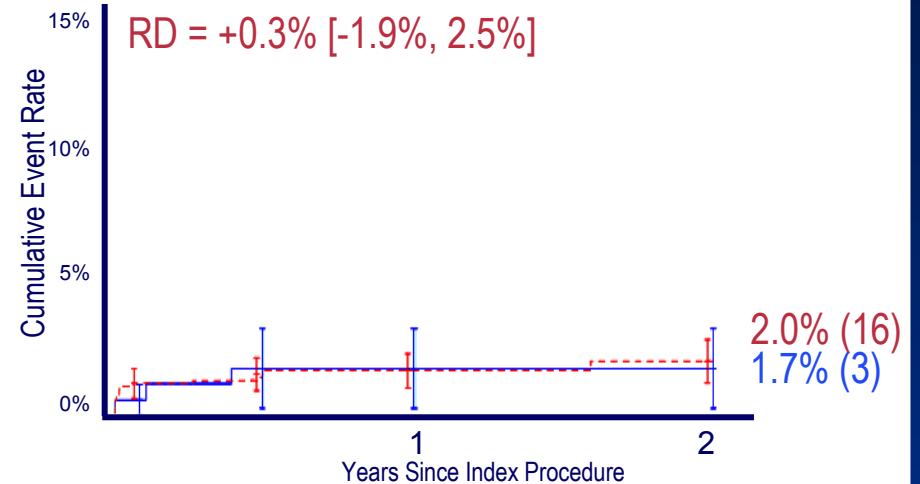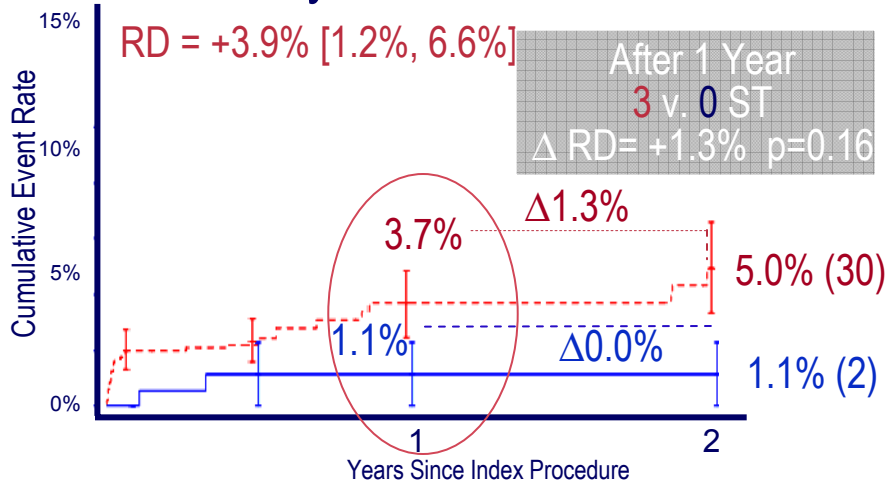
ARRIVE v. TAXUS Multiple Stents in Single Vessels (N = 2,524)

TAXUS (N=255)   ARRIVE (N=2269)

RD = Rate Difference = ARRIVE — TAXUS

No increase   Increase

All Death

RD = +3.9% [1.6%, 6.2%]

5.9% (74)

2.0% (5)

Q Wave MI

RD = +0.9% [-0.4%, 2.2%]

1.7% (27)

0.8% (2)

ARC Primary ST Definite/Probable

RD = +2.5% [0.6%, 4.4%]

After 1 Year
5 v. 0 ST
Δ RD= +0.8% p=0.17

Δ0.8%

3.3%

4.1% (63)

1.6% (4)

1.6%

Δ0.0%

TVR

RD = -4.9% [-10.2%, 0.4%]

18.4% (46)

13.5% (172)

Years Since Index Procedure

Cumulative Event Rate

29
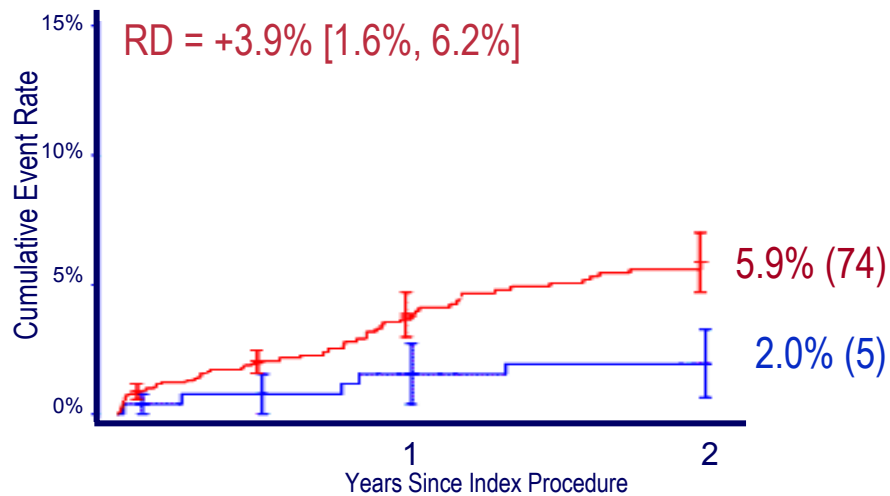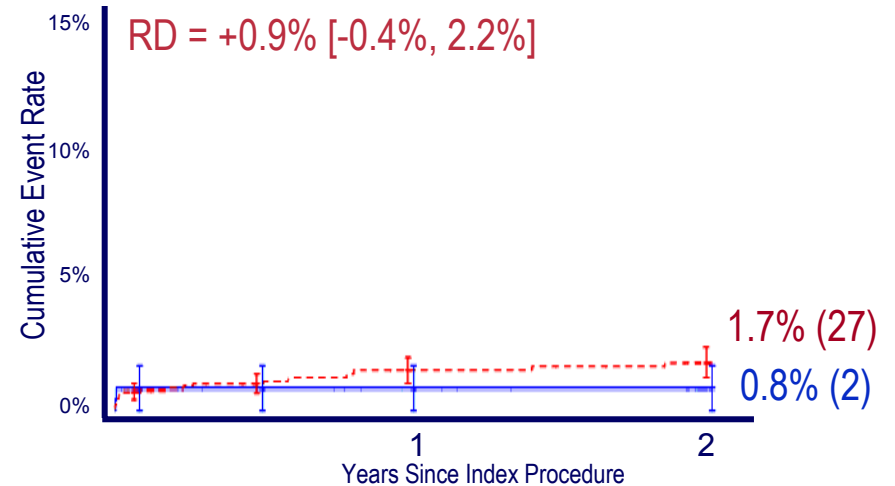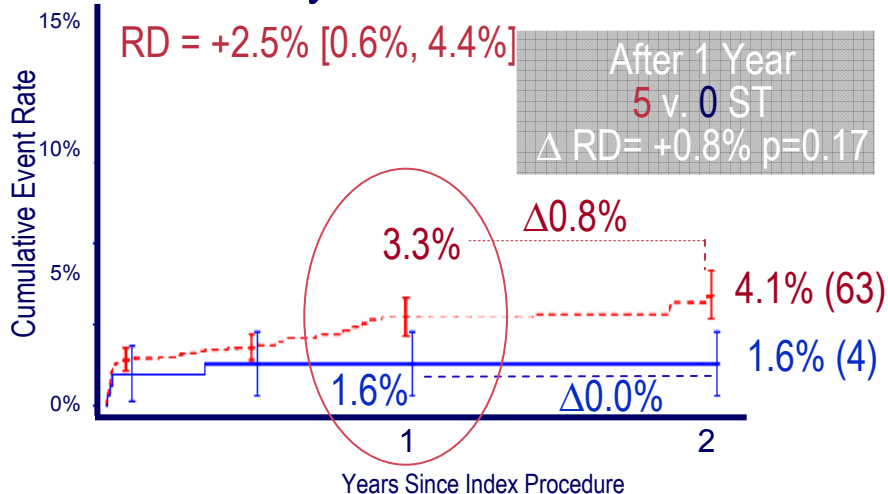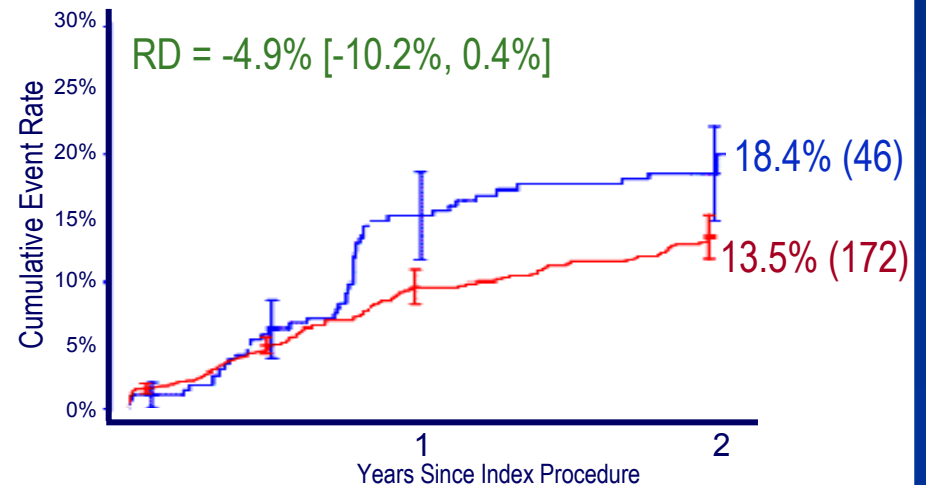
ARRIVE Multi v. Single Vessel
N = 1,153 Multi-vessel cases

Single (N=6240)   Multi (N=1153)

RD = Rate Difference = Multi — Single
No increase   Increase

All Death

RD = -0.1% [-2.3%, 2.1%]
p = 0.45

5.8% (42)
5.9% (192)

Cumulative Event Rate

15%
10%
5%
0%

1   2
Years Since Index Procedure

Q Wave MI

RD = +0.3% [-0.4%, 1.0%]
p = 0.008

1.2% (13)
0.9% (29)

Cumulative Event Rate

15%
10%
5%
0%

1   2
Years Since Index Procedure

ARC Primary ST Definite/Probable

RD = +1.5% [-0.2%, 3.2%]
p = 0.004

After 1 Year
4 v. 9 ST
Δ RD= +0.8% p=0.19

2.4%   Δ0.8%
3.7% (30)
2.2% (87)
1.7%   Δ0.5%

Cumulative Event Rate

15%
10%
5%
0%

1   2
Years Since Index Procedure

TVR

RD = +5.2% [1.9%, 8.5%]
p <0.0001

14.4% (93)
9.2% (312)

Cumulative Event Rate

30%
25%
20%
15%
10%
5%
0%

1   2
Years Since Index Procedure
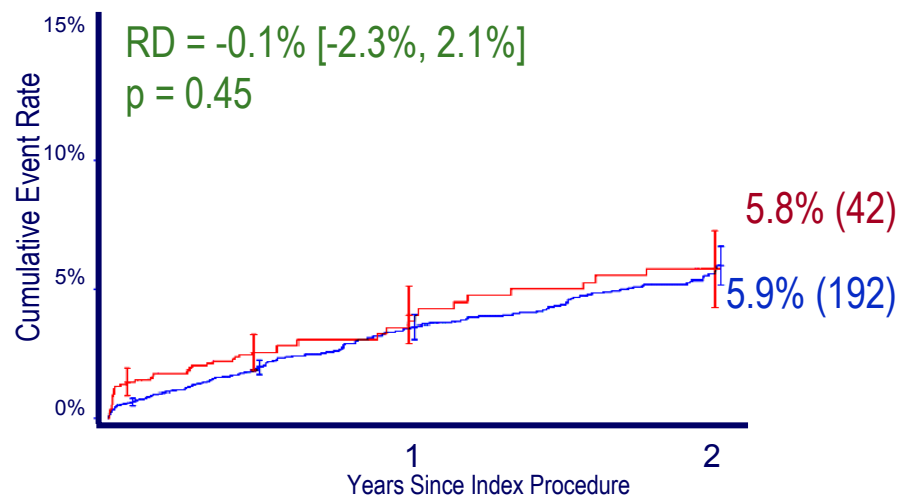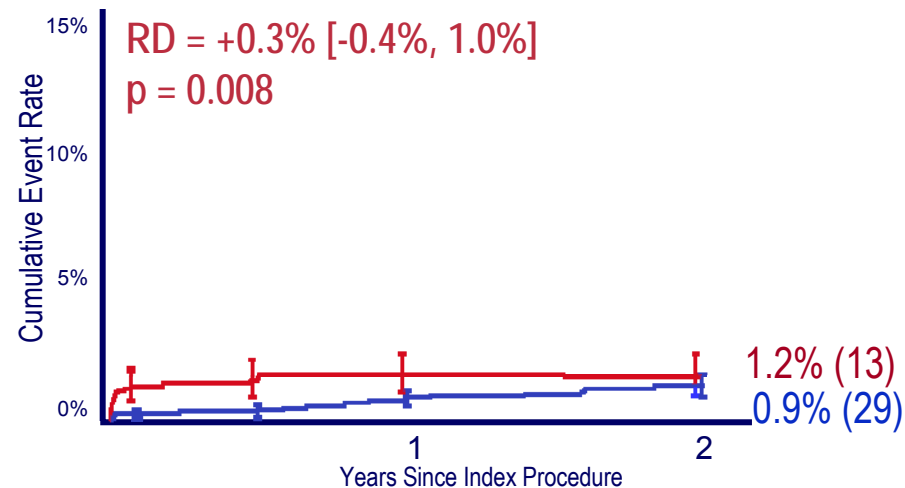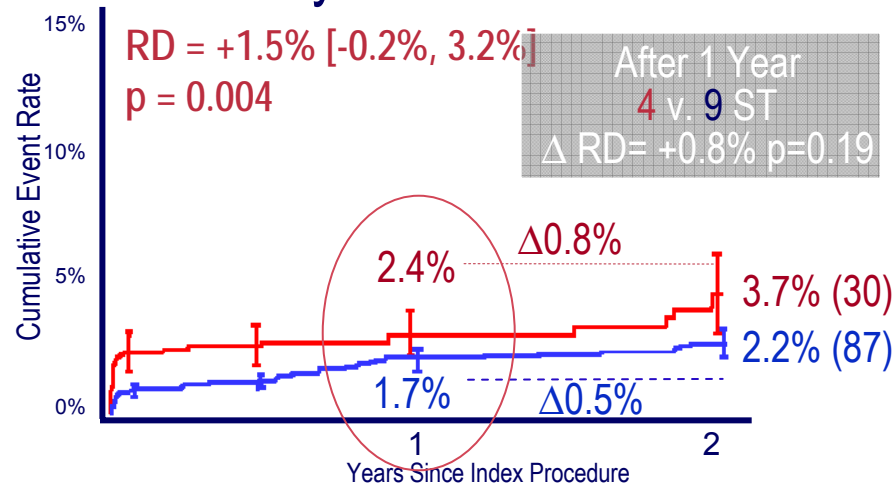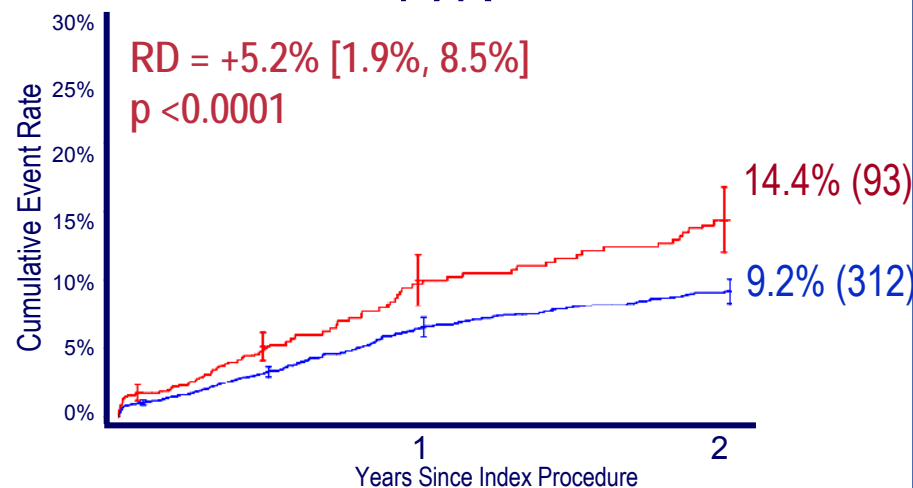
ARRIVE AMI v. non-AMI
N = 927 AMI cases

Non-AMI (N=6466)   AMI (N=927)

RD = Rate Difference = AMI — Non-AMI
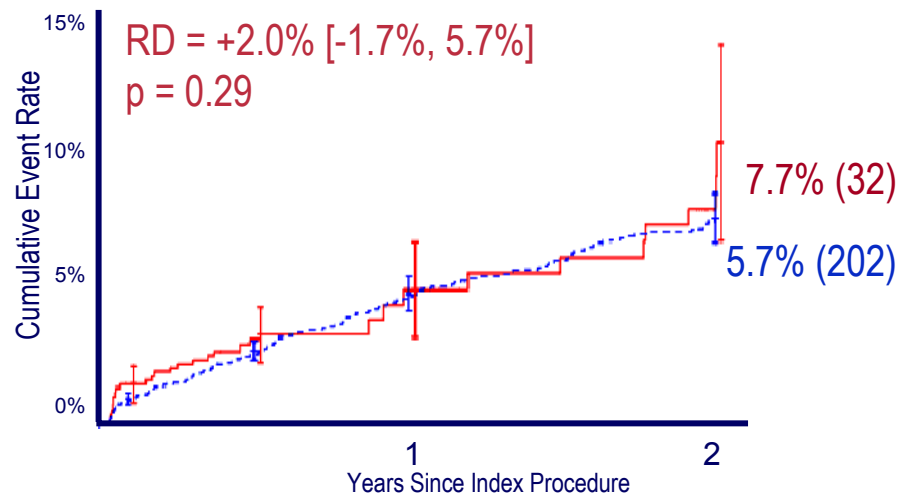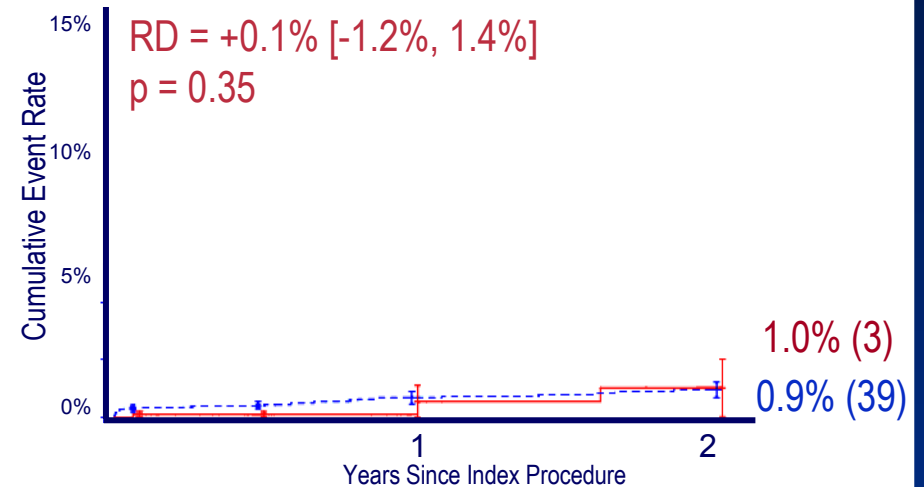
No increase   Increase

All Death

RD = +2.0% [-1.7%, 5.7%]
p = 0.29

Cumulative Event Rate

7.7% (32)

5.7% (202)

Years Since Index Procedure

Q Wave MI

RD = +0.1% [-1.2%, 1.4%]
p = 0.35

Cumulative Event Rate

1.0% (3)

0.9% (39)

Years Since Index Procedure

ARC Primary ST Definite/Probable

RD = +1.5% [-0.5%, 3.5%]
p=0.02

After 1 Year
2 v. 11 ST
Δ RD= +0.4% p=0.49

Cumulative Event Rate

2.8% Δ1.0%

3.8% (22)

2.3% (95)

1.7% Δ0.6%

Years Since Index Procedure

TVR

RD = -2.2% [-5.6%, 1.2%]
p = 0.38

Cumulative Event Rate

10.3% (364)

8.1% (41)

Years Since Index Procedure
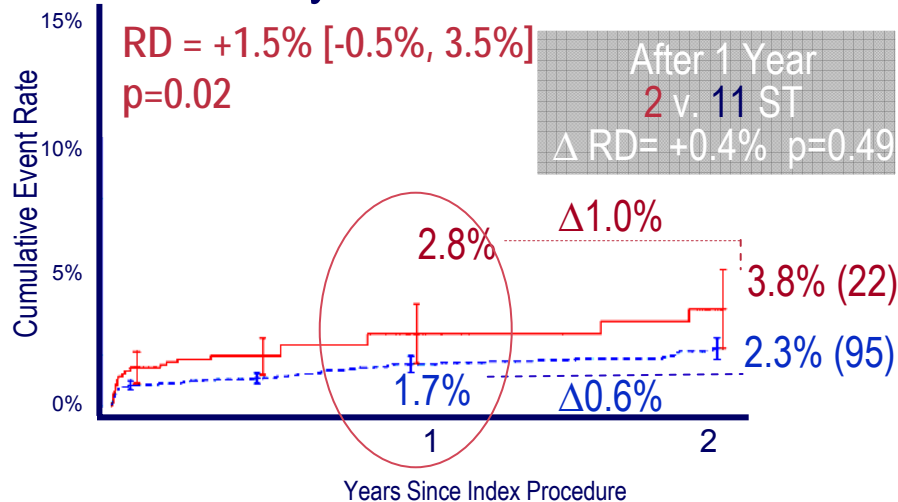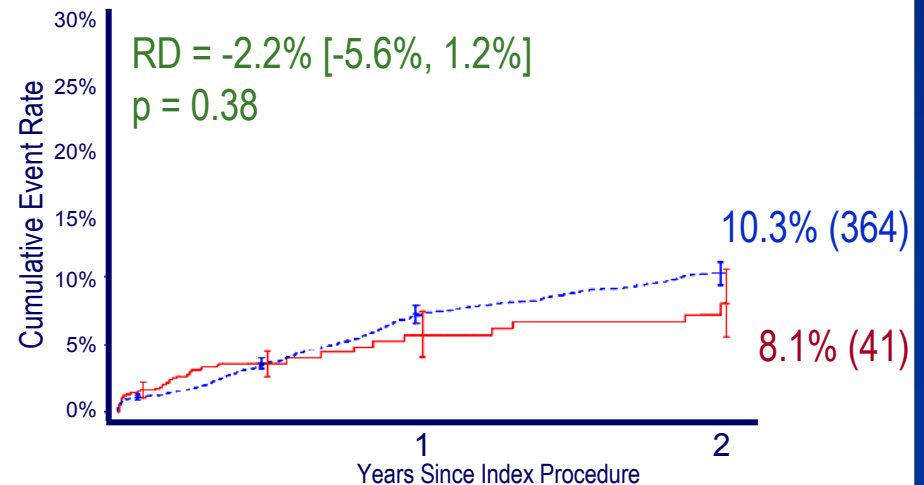
Agenda

- ➢ ARRIVE Registry

- ➢ TAXUS v. ARRIVE Analysis (Simple lesions)

- ➢ ARRIVE Analysis (Complex lesions)

- ➢ Multivariate Predictor Analysis

- ➢ Summary and Conclusions

Long-Term-Thienopyridine Intake in ARRIVE Real World Registries
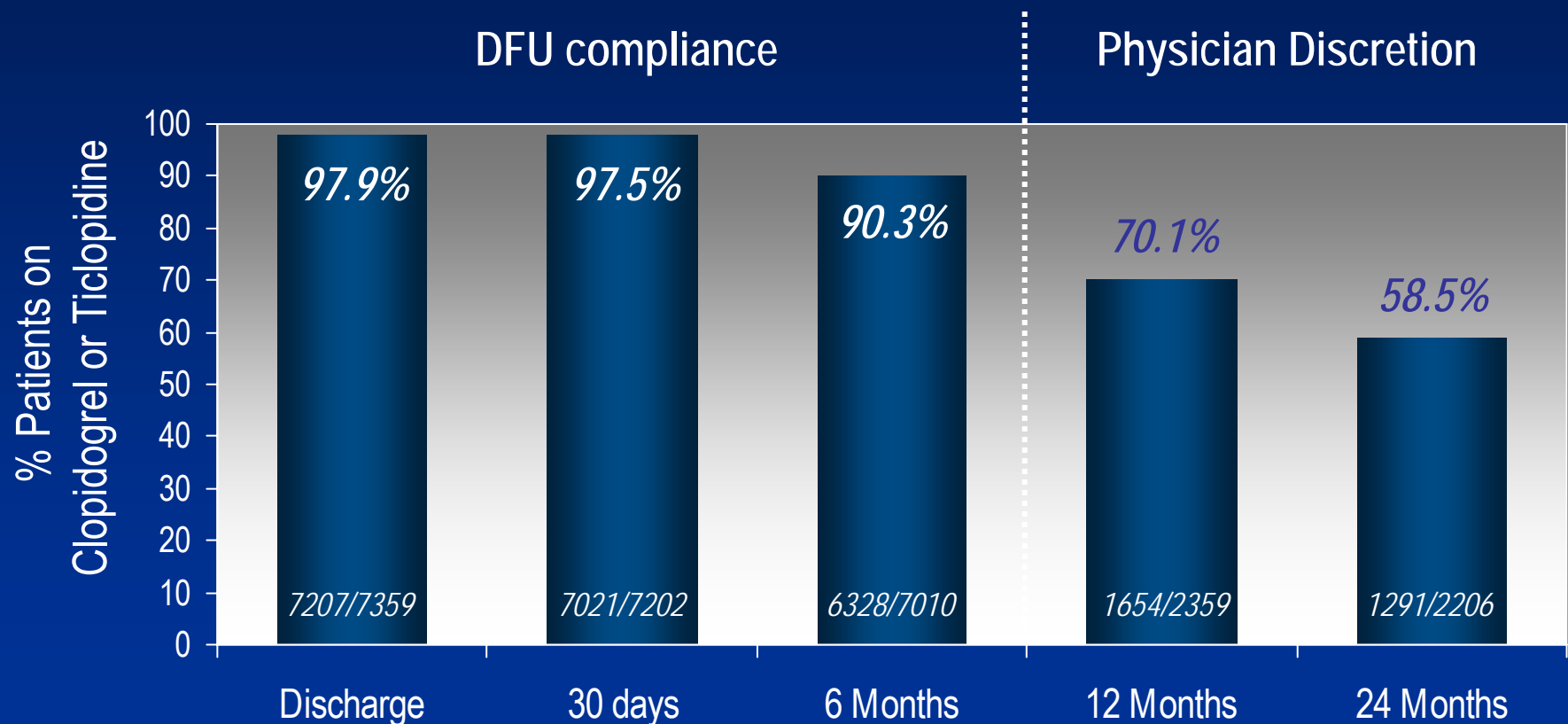
DFU compliance | Physician Discretion

% Patients on Clopidogrel or Ticlopidine

- Discharge: 97.9% (7207/7359)
- 30 days: 97.5% (7021/7202)
- 6 Months: 90.3% (6328/7010)
- 12 Months: 70.1% (1654/2359)
- 24 Months: 58.5% (1291/2206)

Plavix and Ticlid are trademarks of Sanofi-Aventis

Multivariate Predictors of Adverse Events in ARRIVE 1 (N=2,487)
Follow-up to 2 years

Multivariate Predictors of Death

Variable	Hazard Ratio (95% CI)	p-Value
Discontinued Plavix/Ticlid usage before 6 months	8.58 (6.08, 12.09)	<0.0001
Age	1.06 (1.05, 1.08)	<0.0001
Renal Disease	4.88 (3.09, 7.72)	<0.0001
Congestive Heart Failure	2.26 (1.52, 3.36)	0.0001
Diabetes	1.85 (1.31, 2.61)	0.0005
Previous Stroke	1.82 (1.13, 2.94)	0.0142
Lesion type B2 or C	1.57 (1.08, 2.26)	0.0171

Multivariate Predictors of MI

Variable	Hazard Ratio (95% CI)	p-Value
Current Smoker	2.13 (1.35, 3.35)	0.0012
Patient Minimum RVD	0.44 (0.26, 0.75)	0.0021
Prior MI	1.83 (1.17, 2.87)	0.0078
Patient Lesion Length	1.01 (1.00, 1.02)	0.0201
Discontinued Plavix/Ticlid usage before 6 months	1.82 (1.02, 3.24)	0.0429

Multivariate Predictors of ST Protocol (ST = 67)

Variable	Hazard Ratio (95% CI)	p-Value
Discontinued Plavix/Ticlid usage before 6 months	5.32 (3.24, 8.75)	<0.0001
Patient Lesion Length	1.02 (1.01, 1.03)	<0.0001
Patient Minimum RVD	0.37 (0.21, 0.66)	0.0009
Age	0.97 (0.95, 0.99)	0.0129

Multivariate Predictors of TVR

Variable	Hazard Ratio (95% CI)	p-Value
Age	0.97 (0.96, 0.98)	<0.0001
Previous PCI	1.67 (1.29, 2.17)	0.0001
Multiple Stenting	1.62 (1.25, 2.09)	0.0003
Gender(Male)	0.67 (0.51, 0.87)	0.0029
Lesion Calcification	1.37 (1.05, 1.78)	0.0202
Previous CABG	1.39 (1.02, 1.89)	0.0366

Multivariate Predictors of Adverse Events in ARRIVE 1 (N=2,487)
Follow-up to 2 years

Multivariate Predictors of ST Protocol ≤ 1y (ST = 53)

Variable	Hazard Ratio (95% CI)	p-Value
Discontinued Plavix/Ticlid usage before 6 months	5.40 (3.11, 9.39)	<0.0001
Patient Lesion Length	1.02 (1.01, 1.03)	0.0001
Patient Minimum RVD	0.37 (0.20, 0.69)	0.0017
Smoking	1.85 (1.05, 3.25)	0.0323
Left Main Stenting	2.88 (1.03, 8.07)	0.0435

Multivariate Predictors of ARC ST Primary ≤ 1y Def/Prob (ST = 53)

Variable	Hazard Ratio (95% CI)	p-Value
Discontinued Plavix/Ticlid usage before 6 months	5.47 (3.15, 9.51)	<0.0001
Multiple Stenting per patient	3.32 (1.81, 6.07)	0.0001
Patient Minimum RVD	0.42 (0.22, 0.83)	0.0122
Smoking	2.27 (1.30, 3.96)	0.0038
CHF	2.15 (1.07, 4.30)	0.0311

Multivariate Predictors of ST Protocol > 1y (ST = 14)

Variable	Hazard Ratio (95% CI)	p-Value
Prior Brachytherapy	19.98 (2.5, 159.31	0.0047
Age	0.94 (0.90, 0.99)	0.0215
Discontinued Plavix/Ticlid usage before 6 months	3.98 (1.22, 12.93)	0.0218
Prior MI	3.83 (1.19, 12.28)	0.0241
CTO Stenting	4.89 (1.05, 22.75)	0.0429
Patient Lesion Length	1.02 (1.00, 1.04)	0.0445

Multivariate Predictors of ARC ST Primary > 1y Def/Prob (ST = 13)

Variable	Hazard Ratio (95% CI)	p-Value
Discontinued Plavix/Ticlid usage before 6 months	9.26 (3.24, 26.44)	<0.0001
CTO Stenting	5.91 (1.30, 26.75)	0.0212
Prior MI	3.02 (1.00, 9.10)	0.0496
Age	0.95 (0.91, 1.00)	0.0372

Overall ARRIVE Registry

Overall, the ARRIVE Registry results show

- Significantly fewer TVR's
  - no routine angiographic subset, hence no oculo-stenotic reflex
- Significantly fewer overall MIs
  - no routine blood sampling, thus poor non-Q MI detection
  - good Q-MI ascertainment
- *Slightly* higher rates of death and of stent thrombosis in complex lesions than the Taxus trials or the simple lesion ARRIVE subset
  - expected with greater lesion length, small vessels, comorbidities, etc.
- Without an internal comparator it is difficult to determine the implication of these results *(be wary of studies using old BMS data)*
- But use of the historical PCI and CABG reference points *does* help show results consistent with real world TAXUS use, and typical for patients undergoing complex revascularization by these means

ARRIVE Complex v. Simple
N = 7,393

Simple (N=2564)   Complex (N=4829)

RD = Rate Difference = Complex — Simple

No increase   Increase

All Death

RD = +1.9% [0.2%, 3.6%]
p = 0.08

Cumulative Event Rate

Historical CABG and PCI

6.5% (166)

4.6% (68)

15%
10%
5%
0%

1   2

Years Since Index Procedure

All MI

RD = +1.5% [0.3%, 2.7%]
p < 0.0001

Cumulative Event Rate

Historical CABG and PCI

3.6% (117)

2.1% (26)

15%
10%
5%
0%

1   2

Years Since Index Procedure

ARC Primary ST Definite/Probable

RD = +1.6% [0.6%, 2.6%]
p < 0.0001

Cumulative Event Rate

3.0% (99)

1.4% (18)

15%
10%
5%
0%

1   2

Years Since Index Procedure

TVR

RD = +4.3 [2.1%, 6.5%]
p <0.0001

Cumulative Event Rate

Historical PCI

11.5% (307)

7.2% (98)

Historical CABG

30%
25%
20%
15%
10%
5%
0%

1   2

Years Since Index Procedure
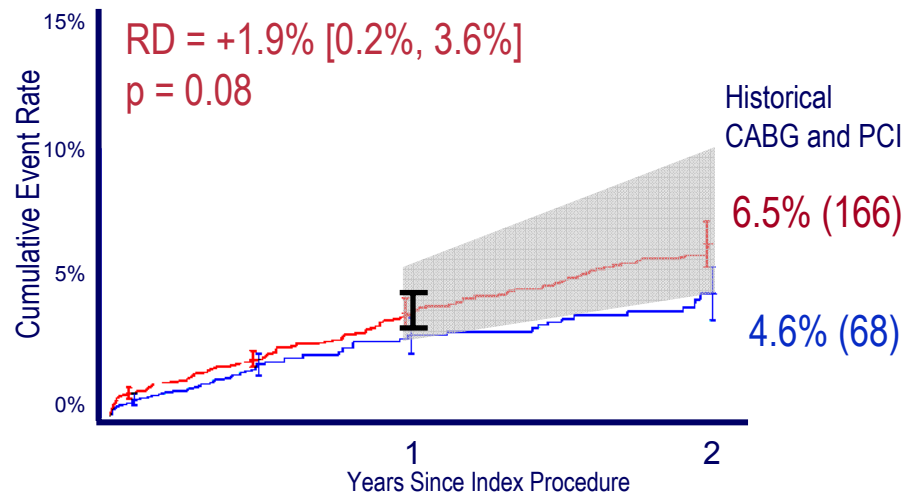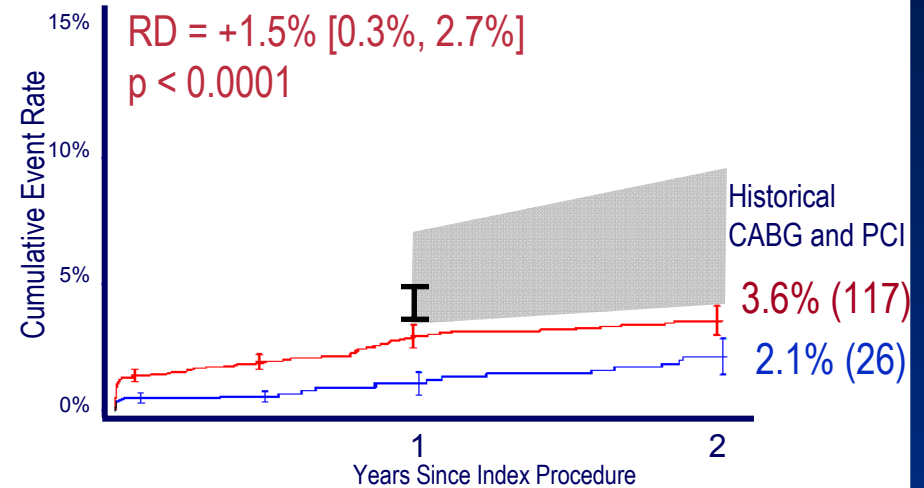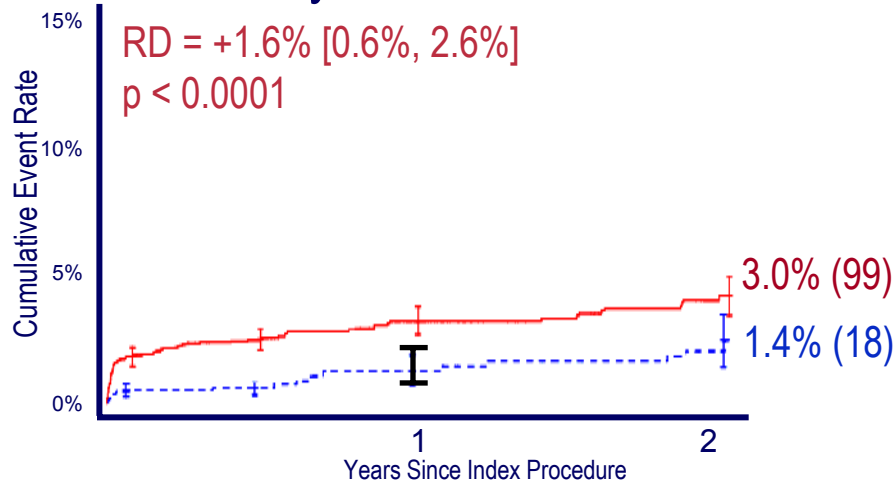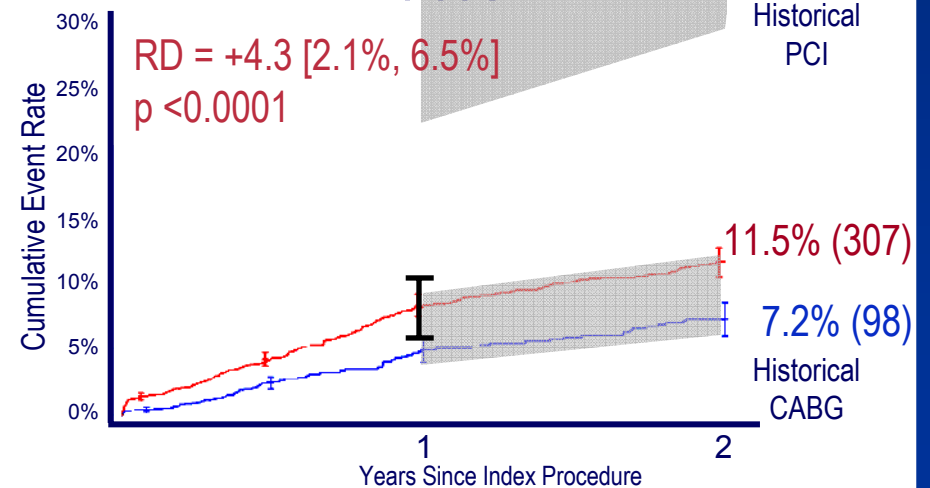
Study in Progress
HORIZON (TAXUS in AMI)
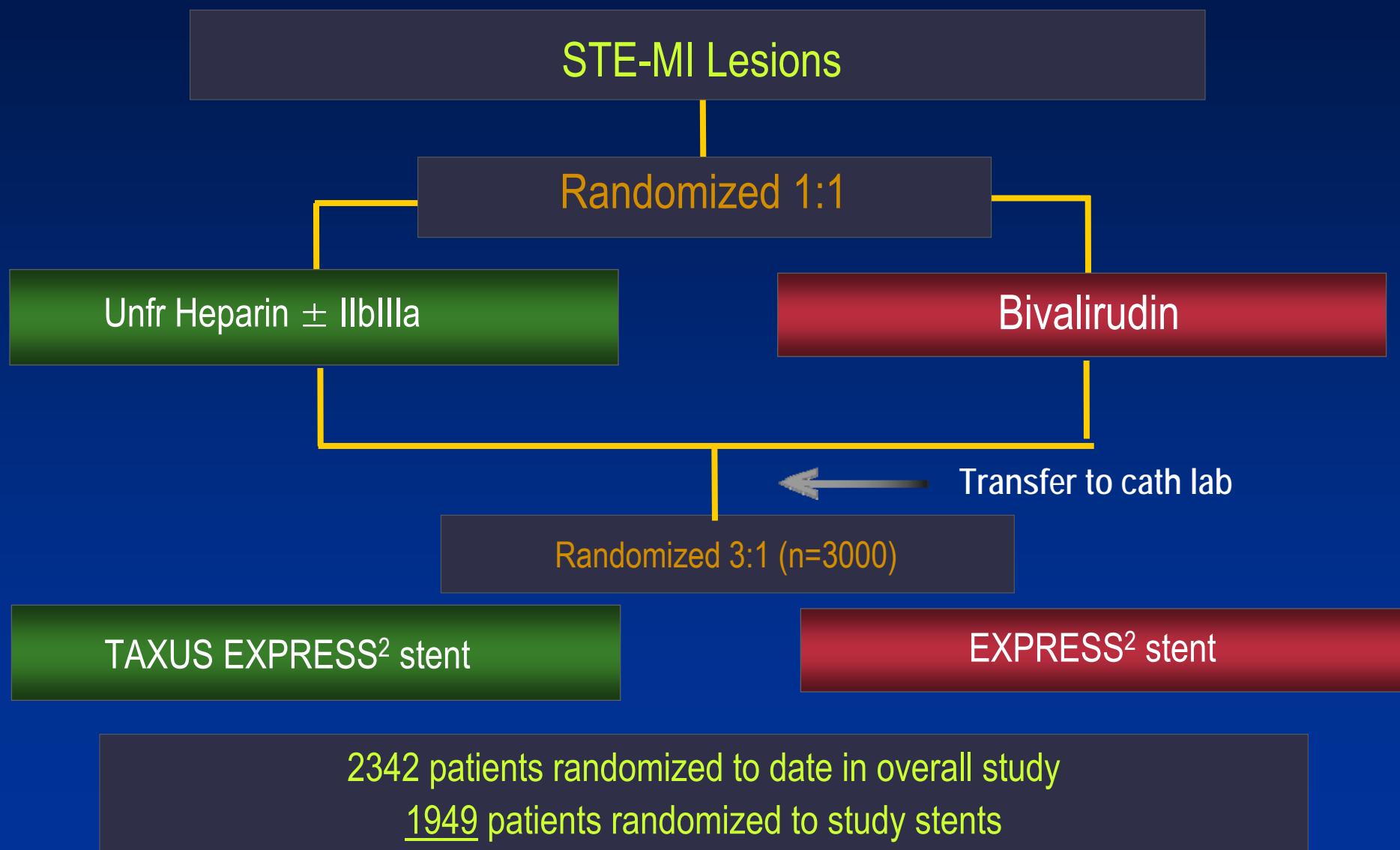
STE-MI Lesions

Randomized 1:1

Unfr Heparin $\pm$ IIbIIIa

Bivalirudin

Transfer to cath lab

Randomized 3:1 (n=3000)

TAXUS EXPRESS^2 stent

EXPRESS^2 stent

2342 patients randomized to date in overall study
1949 patients randomized to study stents

Agenda

> ➢ ARRIVE Registry

> ➢ TAXUS v. ARRIVE Analysis (Simple lesions)

> ➢ ARRIVE Analysis (Complex lesions)

> ➢ Multivariate Predictor Analysis

> ➢ Summary and Conclusions

Real-World Taxus® Stent Use Confirms Favorable Outcome Profile

- The Taxus stent has demonstrated favorable risk-benefit outcomes compared to BMS in the somewhat *"simpler" clinical trial patients*

- But how can we best evaluate TAXUS performance in the *more complex "real-world" patients* who comprise > 50% of current use?

- The *ARRIVE Registries* include > 7,000 Taxus-treated patients
  - "Simple" lesions (Taxus IV-like) have similar outcomes to RCTs
  - "Complex" lesions have expected *slightly* more adverse events

- Those outcomes are comparable to meta-analysis of other real-world data, and to of complex PCI or CABG revascularization results

- Pending results of randomization of even more complex patients in Horizons (AMI) and SYNTAX (LM and 3VD), there is no reason to believe that current clinical use exposes complex patients to excess risk compared to other available alternative revascularization therapy

Thank you

BACK-UP SLIDES

ARRIVE Overall v. TAXUS Overall
N = 8,793

All Death

RD = +2.5% [1.2%, 3.8%]

15%
10%
5%
0%

5.9% (234)
3.4% (46)

Cumulative Event Rate

1   2
Years Since Index Procedure

Q Wave MI

RD = 0.0% [-0.6%, 0.6%]

15%
10%
5%
0%

0.9% (42)
0.9% (12)

Cumulative Event Rate

1   2
Years Since Index Procedure

ARC Primary ST Definite/Probable

RD = +1.2% [0.4%, 2.0%]

After 1 Year
13 v. 5 ST
ΔRD = +0.3% p=0.34

15%
10%
5%
0%

Δ0.6%
1.8%
0.9%   Δ0.3%
2.4% (117)
1.2% (17)

Cumulative Event Rate

1   2
Years Since Index Procedure

TVR

RD = -3.3% [-5.4%, -1.2%]

30%
25%
20%
15%
10%
5%
0%

13.4% (183)
10.1% (405)

Cumulative Event Rate

1   2
Years Since Index Procedure
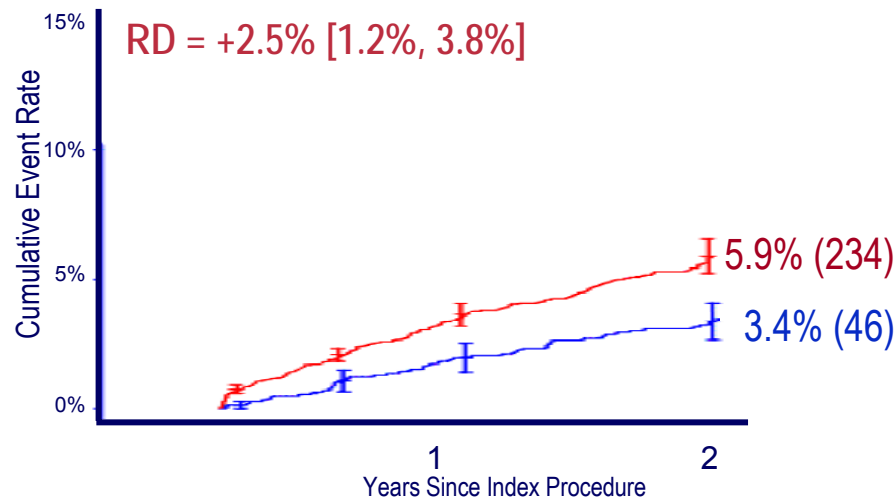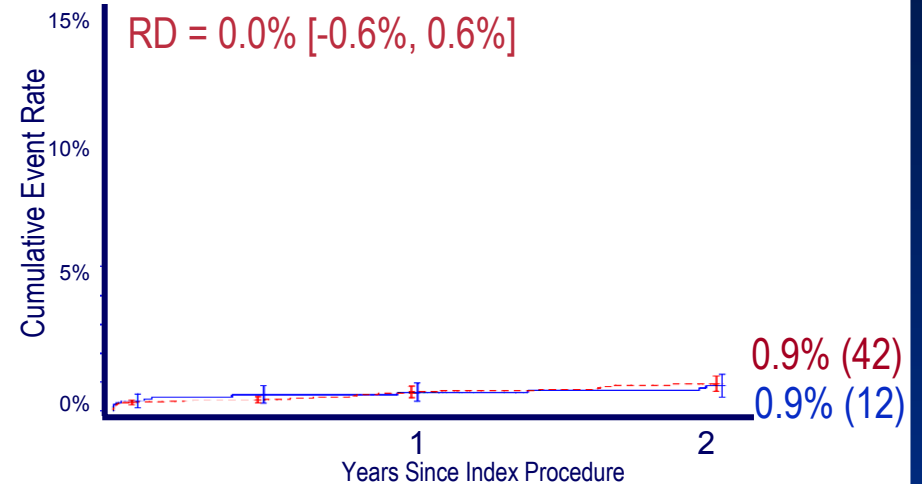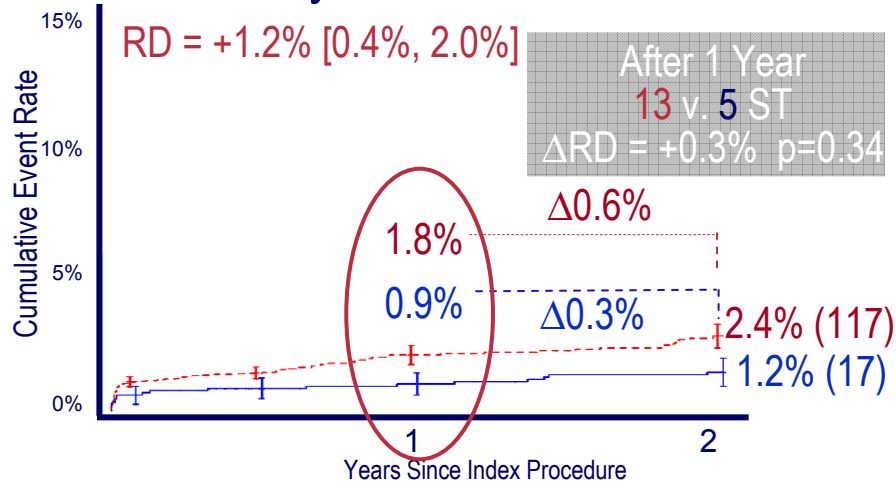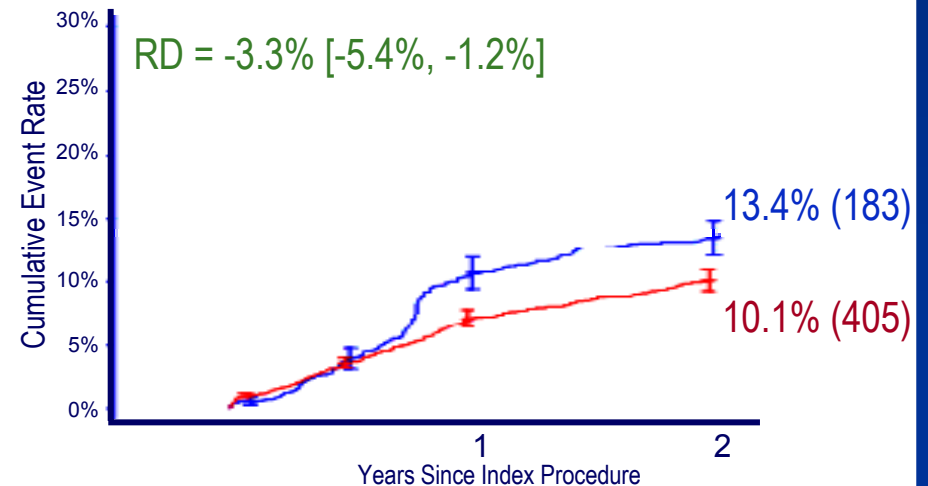
ARRIVE Diabetics (n= 2,333) v. Non Diabetics (n = 5,060)
ANNUAL HAZARD RATES

Δ = Rate Difference = DM — Non DM
No increase   Increase

Event	0-1 Year (% / patient-year)				1-2 Years (% / patient-year)				2-year Cumulative Rates (K-M estimate [%])			
	DM	Non DM	Rate Difference Δ	p	DM	Non DM	Rate Difference Δ	p	DM	Non DM	Rate Difference Δ	p
All Death	6.02	3.06	+2.96	<0.0001	3.19	1.86	+1.33	0.06	8.29	4.82	3.47	<0.0001
Cardiac Death	4.22	1.79	+2.43	<0.0001	1.28	0.80	+0.48	0.30	4.64	2.43	2.20	<0.0001
All MI	3.23	2.50	+0.73	0.19	1.13	0.80	+0.32	0.47	3.49	2.87	0.62	0.11
QWMI	0.97	0.68	+0.29	0.31	0.00	0.40	-0.40	0.11	0.81	1.00	-0.18	0.74
ST Protocol	2.87	2.03	+0.84	0.10	0.80	0.67	+0.13	0.74	2.96	2.34	0.63	0.08
Total ARC ST All	4.61	2.62	+2.00	0.0006	1.76	1.13	0.63	0.25	5.54	3.54	1.99	0.0003
TVR	7.31	7.62	-0.31	0.72	4.92	3.38	+1.54	0.10	10.8	9.76	1.04	0.87
TVR-CABG	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

p-value from Log rank test of no difference in the Kaplan-Meier curves between the groups

ARRIVE v. TAXUS Insulin-Requiring Diabetics (*N = 860*)

TAXUS (N=107)   ARRIVE (N=753)

RD = Rate Difference = ARRIVE — TAXUS
No increase   Increase

All Death

RD = +0.6% [-5.6%, 6.8%]

Cumulative Event Rate

8.4% (34)
7.8% (8)

Years Since Index Procedure

Q Wave MI

RD =+0.2% [-1.9%, 2.3%]

Cumulative Event Rate

1.1% (6)
0.9% (1)

Years Since Index Procedure

ARC Primary ST Definite/Probable

RD = +3.8% [0.1%, 7.5%]

After 1 Year
3 v. 0 ST
ΔRD = +1.4% p=0.23

Cumulative Event Rate

Δ1.4%
4.3%
5.7% (25)
1.9% (2)
1.9%
Δ0.0%

Years Since Index Procedure

TVR

RD = -6.3% [-15.4%, 2.8%]

Cumulative Event Rate

21.3% (22)
15.0% (50)

Years Since Index Procedure
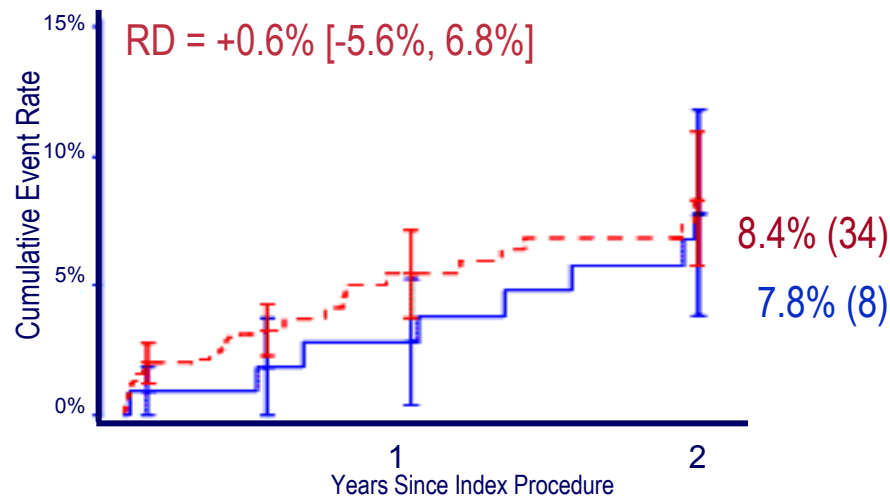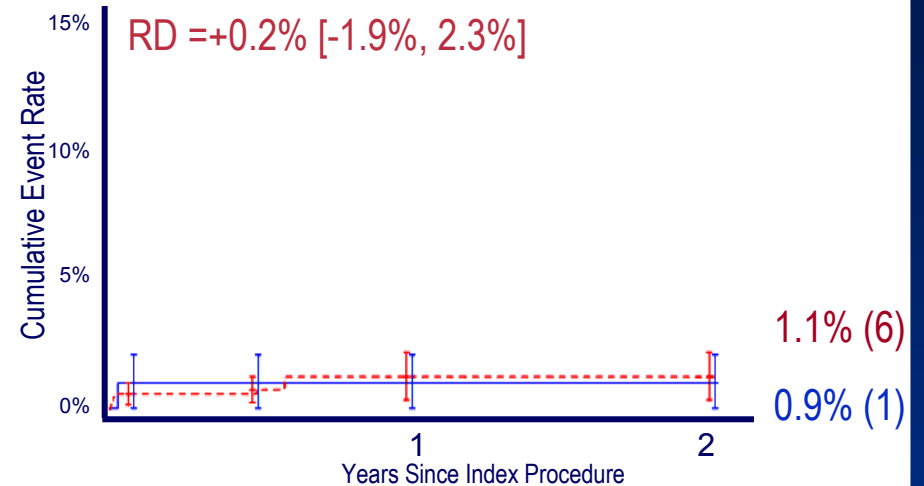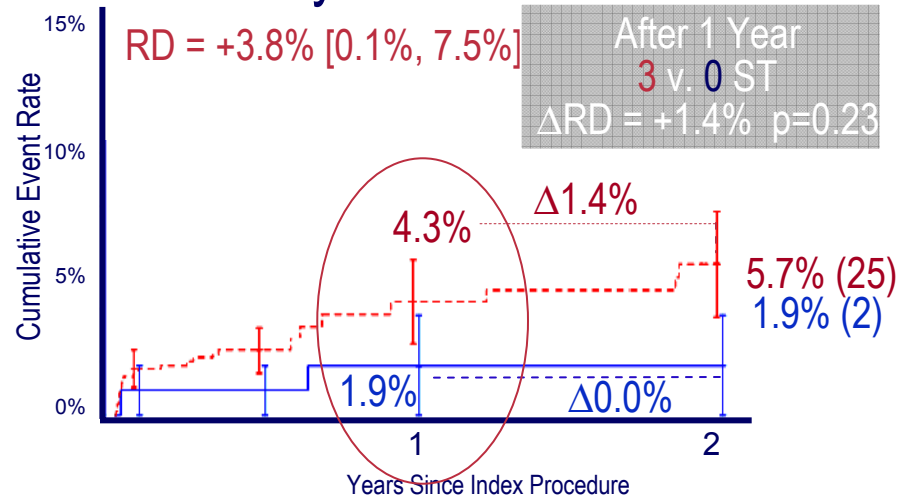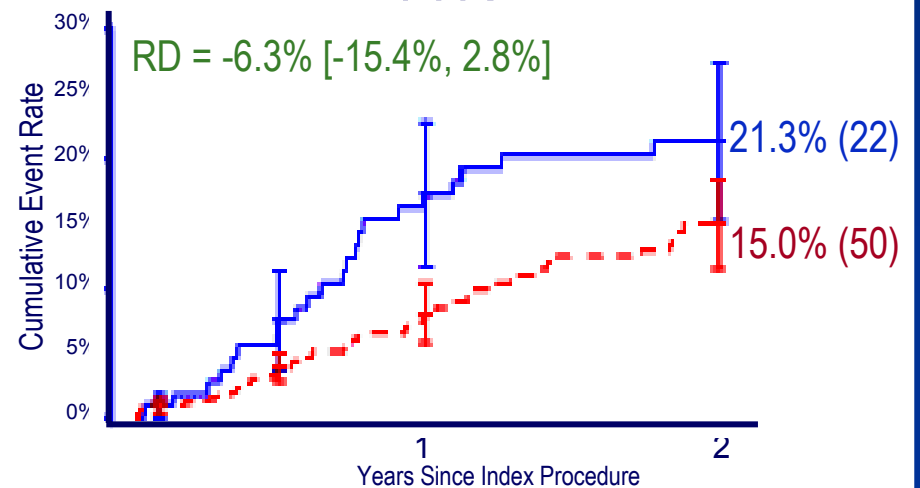
ARRIVE Vessels RVD ≤ 2.5 mm (N = 2272) v. > 2.5 mm (N = 5121) Visual (N = 7,393)
ANNUAL HAZARD RATES

Δ = Rate Difference = ≤2.5mm — >2.5mm
No increase   Increase

Event	0-1 Year (% / patient-year)				1-2 Years (% / patient-year)				2-year Cumulative Rates (K-M Estimate [%])			
	≤2.5 mm	>2.5 mm	Rate Difference		≤2.5 mm	>2.5 mm	Rate Difference		≤2.5 mm	>2.5 mm	Rate Difference	
			Δ	p			Δ	p			Δ	p
All Death	3.72	4.09	-0.36	0.56	2.23	2.27	-0.04	0.94	5.65	5.99	-0.34	0.58
Cardiac Death	2.39	2.61	-0.22	0.64	0.95	0.93	+0.02	0.97	2.92	3.20	-0.28	0.68
All MI	3.79	2.27	+1.52	0.005	0.80	0.94	-0.14	0.76	3.95	2.67	1.28	0.008
QWMI	1.13	0.62	+0.51	0.07	0.16	0.33	-0.17	0.49	1.38	0.76	0.61	0.15
ST Protocol	3.06	1.95	+1.11	0.03	0.80	0.67	+0.13	0.76	3.49	2.11	1.39	0.02
Total ARC ST All	4.12	2.84	+1.28	0.03	1.43	1.27	+0.17	0.77	4.96	3.80	1.16	0.03
TVR	9.52	6.66	+2.87	0.001	4.22	3.67	+0.55	0.55	12.7	8.92	3.77	0.001
TVR-CABG	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

p-value from Log rank test of no difference in the Kaplan-Meier curves between the groups

ARRIVE Lesions >28 mm (N = 953) v. <28 mm (N = 6440) Visual (N = 7393)
ANNUAL HAZARD RATES

Δ = Rate Difference = >28mm — <28mm
No increase   Increase

Event	0-1 Year (% / patient-year)				1-2 Years (% / patient-year)				2-year Cumulative Rates (K-M Estimate [%])			
	>28 mm	<28 mm	Rate Difference Δ	p	>28 mm	<28 mm	Rate Difference Δ	p	>28 mm	<28 mm	Rate Difference Δ	p
All Death	5.39	3.76	+1.63	0.06	2.72	2.18	+0.54	0.56	8.75	5.43	3.33	0.05
Cardiac Death	3.92	2.34	+1.58	0.02	1.02	0.93	+0.09	0.88	4.85	2.83	2.01	0.03
All MI	6.23	2.21	+4.02	<0.0001	0.68	0.93	-0.25	0.68	5.33	2.72	2.61	<0.0001
QWMI	2.48	0.52	+1.96	<0.0001	0.34	0.27	+0.07	0.84	1.96	0.80	1.16	<0.0001
ST Protocol	4.49	1.96	+2.54	0.0001	1.71	0.55	+1.16	0.03	5.23	2.12	3.11	<0.0001
Total ARC ST All	5.65	2.87	+2.78	0.0004	2.04	1.20	+0.84	0.24	7.60	3.61	3.99	0.0002
TVR	12.37	6.81	+5.56	<0.0001	6.67	3.38	+3.29	0.009	15.2	9.26	5.97	<0.0001
TVR-CABG	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

p-value from Log rank test of no difference in the Kaplan-Meier curves between the groups

48

ARRIVE Multiple (N = 2269) v. Single (N = 5124) Stents in Single Vessels (N = 7,393)
ANNUAL HAZARD RATES

	Δ = Rate Difference = Multi — Single
	No increase Increase

Event	0-1 Year (% / patient-year)				1-2 Years (% / patient-year)				2-year Cumulative Rates (K-M Estimate [%])			
	Multi	Single	Rate Difference		Multi	Single	Rate Difference		Multi	Single	Rate Difference	
			Δ	p			Δ	p			Δ	p
All Death	4.13	3.91	+0.22	0.71	2.04	2.36	-0.32	0.64	5.89	5.89	0.00	0.91
Cardiac Death	2.89	2.39	+0.50	0.30	0.87	0.97	-0.10	0.82	3.30	3.03	0.27	0.39
All MI	4.64	1.88	+2.76	<0.0001	0.58	1.05	-0.46	0.29	4.13	2.59	1.54	<0.0001
QWMI	1.73	0.34	+1.39	<0.0001	0.29	0.28	+0.01	0.96	1.67	0.62	1.05	<0.0001
ST Protocol	4.20	1.43	+2.76	<0.0001	0.87	0.63	+0.25	0.53	4.24	1.74	2.50	<0.0001
Total ARC ST All	5.03	2.43	+2.60	<0.0001	1.31	1.32	-0.01	0.98	5.61	3.49	2.12	<0.0001
TVR	10.5	6.22	+4.26	<0.0001	4.76	3.39	+1.36	0.14	13.5	8.45	5.05	<0.0001
TVR-CABG	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

ARRIVE Multi (N = 1153) v. Single (N = 6240) Vessels (N = 7,393)
Annual Event Rates

Δ = Rate Difference = Multivessel — Single
No increase   Increase

| Event | 0-1 Year (% / patient-year) | | | | 1-2 Years (% / patient-year) | | | | 2-year Cumulative Rates (K-M Estimate [%]) | | | |
| | Multi | Single | Rate Difference | | Multi | Single | Rate Difference | | Multi | Single | Rate Difference | |
			Δ	p			Δ	p			Δ	p
All Death	4.69	3.84	+0.85	0.27	1.94	2.32	-0.38	0.65	5.79	5.93	-0.14	0.45
Cardiac Death	3.22	2.42	+0.80	0.19	1.38	0.85	+0.53	0.34	3.87	2.97	0.90	0.12
All MI	4.39	2.42	+1.97	0.003	0.83	0.91	-0.08	0.89	3.78	2.94	0.84	0.005
QWMI	1.76	0.59	+1.17	0.0009	0.00	0.34	-0.34	0.27	1.16	0.92	0.24	0.008
ST Protocol	3.53	2.05	+1.49	0.01	0.83	0.68	+0.15	0.77	3.43	2.36	1.07	0.01
Total ARC ST All	4.35	3.02	+1.32	0.06	2.22	1.13	1.08	0.10	5.58	3.88	1.70	0.02
TVR	10.75	6.92	+3.83	0.0006	5.69	3.46	+2.23	0.05	14.4	9.19	5.19	<0.0001
TVR-CABG	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

p-value from Log rank test of no difference in the Kaplan-Meier curves between the groups

ARRIVE AMI (N = 927) v. non-AMI (N = 6466)
N = 7393

Δ = Rate Difference = AMI — Non-AMI
No increase | Increase

Event	0-1 Year (% / patient-year)				1-2 Years (% / patient-year)				2-year Cumulative Rates (K-M Estimate [%])			
	Non-AMI	AMI	Rate Difference		Non-AM	AMI	Rate Difference		Non-AM	AMI	Rate Difference	
			Δ	p			Δ	p			Δ	p
All Death	3.90	4.53	0.63	0.53	2.13	3.39	1.26	0.25	5.67	7.75	2.08	0.29
Cardiac Death	2.45	3.26	0.82	0.30	0.88	1.45	0.57	0.42	3.01	3.99	0.98	0.21
All MI	2.62	3.51	0.88	0.30	0.94	0.49	-0.46	0.51	2.93	4.20	1.27	0.41
QWMI	0.83	0.36	-0.46	0.23	0.26	0.49	0.23	0.56	0.95	1.03	0.08	0.35
ST Protocol	2.12	3.49	1.37	0.07	0.73	0.49	-0.24	0.69	2.47	2.88	0.41	0.10
Total ARC ST All	3.03	4.78	1.76	0.04	1.25	1.94	0.69	0.41	3.96	5.68	1.72	0.03
TVR	7.60	6.94	-0.67	0.58	4.04	1.95	-2.08	0.15	10.3	8.08	-2.19	0.38
TVR-CABG	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

p-value from Log rank test of no difference in the Kaplan-Meier curves between the groups

Multivariate Predictor Analysis
Methodology

Cox model is used to identify the predictors of Death, MI, TVR and Stent Thrombosis. The key baseline patient and lesion characteristics included in the analyses are listed in Table 1. Stepwise regression is used; the threshold to enter the model is set at 0.10 and exit the model is set at 0.05.

Gender
Age
Current Smoker
Hypercholesterolemia
Hypertension
Diabetes Mellitus
Prior MI
Previous Stroke
Renal Disease
Known Multi-vessel disease
   Previous CABG
   Previous PCI
Cardiogenic Shock
Congestive Heart Failure
Known Left Main Disease
Acute MI
Left Main Stenting
Chronic Total Occlusion
In-stent Restenosis
Failed Brachytherapy
Bifurcated Lesion
Ostial Lesion

Ostial Lesion
Multivessel Stenting
Multiple Stenting per patient
Total Stent Length per Patient
Lesion Calcification
Lesion Type B2/C
Pre-procedure TIMI=0
Total Lesion Length
Minimum RVD
Vessel Location LAD
Continued Plavix/Ticlid usage through 6 month

Multivariate Predictors
Patient Characteristics

	Death	MI	TVR	ST		ST ≤ 1 year		ST > 1 year	
				Protocol	ARC Primary	Protocol	ARC Primary	Protocol	ARC Primary
Patient History									
Previous CABG			1.4 [1.0, 1.9]						
Previous PCI			1.7 [1.3, 2.2]						
Prior MI	1.8 [1.2, 2.9]							3.8 [1.2, 12.3]	3.0 [1.0, 9.1]
Previous stroke	1.8 [1.1, 2.9]								
General Disease State									
CHF	2.3 [1.5, 3.4]				1.9 [1.0, 3.6]		2.1 [1.1, 4.3]		
Renal disease	4.9 [3.1, 7.7]								
Diabetes	1.8 [1.3, 2.6]				1.7 [1.1, 2.8]				

Multivariate Predictors
Lesion and Procedure Characteristics

	Death	MI	TVR	ST		ST ≤ 1 year		ST > 1 year	
				Protocol	Primary	Protocol	Primary	Protocol	Primary
Lesion/Vessel									
Minimum RVD		0.44 [0.26, 0.75]		0.37 [0.21, 0.66]	0.49 [0.28, 0.87]	0.35 [0.18, 0.68]	0.42 [0.22, 0.83]		
Lesion length		1.0 [1.01, 1.02)		1.0 [1.02, 1.03]	1.02 [1.01, 1.03]	1.02 [1.01, 1.03]		1.02 [1.00, 1.04]	
Lesion B2 or C	1.6 [1.1, 2.3]								
Calcification			1.4 [1.1, 1.8]						
Procedure/Therapy									
Failed brachy.								20.0 [2.5, 159.3]	
Plav/tic thru 6m	0.12 [0.08,0.16]	0.55 [0.31, 0.98]		0.20 [0.12, 0.32]	6.2 [3.8, 10.1]	0.19 [0.11, 0.34]	5.5 [3.1, 9.5]	0.25 [0.08, 0.83]	9.3 [3.2, 26.4]
CTO stenting								4.9 [1.1, 22.8]	5.9 [1.3, 26.7]
Left main stent						3.1 [1.1, 8.7]			
Multiple stenting			1.6 [1.3, 2.1]				5.5 [3.1, 9.5]		

Multivariate Predictors
Predictors of Stent Thrombosis in TAXUS I, II-SR, IV, V

	ST		ST ≤ 1 year		ST > 1 year	
	Protocol	Primary	Protocol	Primary	Protocol	Primary
TAXUS Stent[a]	1.59 [0.72, 3.50]	1.66 [0.83, 3.32]	1.14 [0.46, 2.81]	1.23 [0.53, 2.85]	6.11 [0.74, 50.69]	3.03 [0.82, 11.19]
Plav/Ticlid use at 6m	0.17 [0.08, 0.37]	0.25 [0.12, 0.51]	0.09 [0.04, 0.22]	0.14 [0.06, 0.34]		
Male	9.50 [1.29, 70.10]					
RVD					4.38 [1.14, 16.84]	

Cox model is used to identify the predictors stent thrombosis events through 4 years in TAXUS I, II-SR, IV, V

Candidate predictors entered into analysis: TAXUS stent , male, current smoking, unstable angina, age, diabetes, GPIIb/IIIa inhibitor use during procedure, clopidogrel/ticlopidine use at 4/ 6 Month (for ST ≤ 1Y) or 12 Month (for ST > 1Y), hyperlipidemia, hypertension, LAD, previous MI, unstable angina, Type C lesion, total stent length, multiple stents, lesion length (QCA), RVD (QCA), pre-procedure MLD, post-procedure in-segment %DS and MLD

a. TAXUS Stent was forced into the model regardless of its signficance.