TAXUS Real-World Experience from ARRIVE Registry

Alan C. Yeung, MD
Li Ka Shing Professor of Medicine,
Stanford University, USA

Controlled Trials vs. Registries
Distinct differences

	Trial	Registry
Overall Purpose	Definitive proof of principle	Safety surveillance of broad, unstudied population
Design	Controlled or comparison	Observation of real-world usage patterns
Population	Minimize heterogeneity; limited size & subgroups	Evaluate heterogeneity; large size; subgroup analyses
Endpoint	Strict criteria	Minimal criteria
Monitoring	Complete; high data quality	Low & variable; reduced data quality
Data Capture	Freedom from event	Presence of event

→ *Registries provide data for hypothesis generation & expanded use*

ARRIVE Peri/Post-Approval Registry Program

- ARRIVE 1 & 2: US registries; successive enrollment periods
- Capture TAXUS outcomes in everyday practice
- US Safety Surveillance Program
  - Frequent FDA oversight on individual patient-level data
- Consecutive “All Comers” Design
  - Minimizes bias on patient selection
  - Only TAXUS used by physician during enrollment
  - Enroll all consented patients who are candidates for DES
- Capture Experience at Community Based Hospitals
  - Equal distribution of low, medium, & high volume operators

TAXUS ARRIVE Hybrid Registry Approach:
Integrated controlled trial process; improved data quality

- Web-based data entry with rigorous data review
  - Detailed: ~20 CRF pages per patient
  - Built-in queries to improve accuracy
- Independent Clinical Events Committee
  - Reviews & adjudicates reported cardiac events
  - Ensures harmonized classification
  - Adds previously unreported cardiac events
- Monitoring
  - Review all patients with reported cardiac events
  - Review random 10-20% sample of patients for reported accuracy

→ *Increased confidence in reported clinical outcomes*

TAXUS ARRIVE 1 and 2 Registries
Primary & secondary endpoints

Primary endpoint

- Rate of TAXUS stent related cardiac events at 1 yr

Secondary endpoints

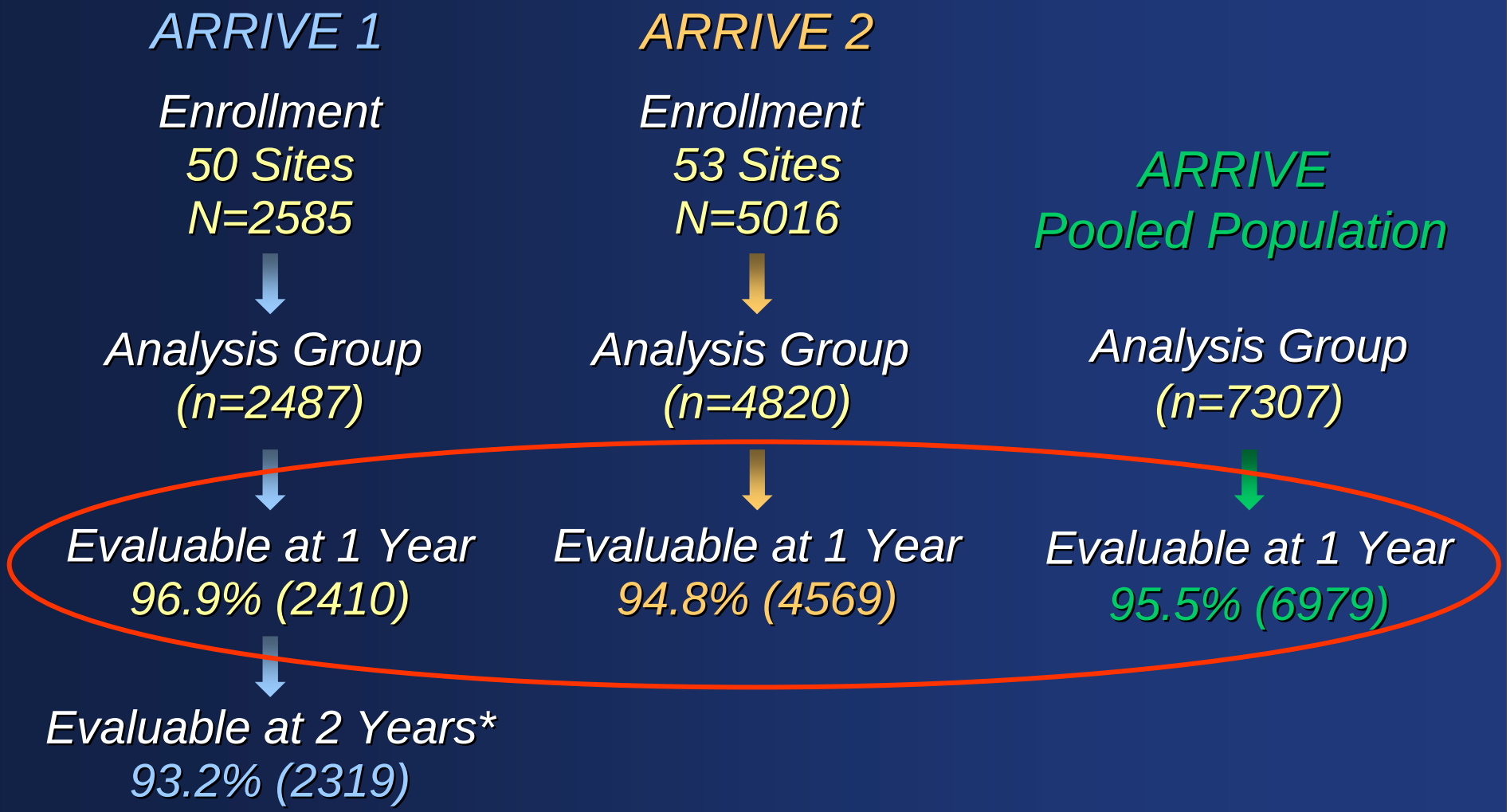
- 30-day, 6-mo, 2-yr rates
  - TAXUS stent related cardiac events
- 30-day, 6-mo, 1-yr, 2-yr rates
  - Target vessel related cardiac events (all time points)
  - Other TAXUS related events (all time points)
- Characterization of target vessel restenosis
- Clinical procedural & technical success

ARRIVE Population Characteristics

	ARRIVE 1 N=2487	*ARRIVE 2 N=4820*
Age in years (mean±SD)	63.7±11.5	64.6±11.8
Male Gender (%)	68	67
Diabetes (%)	30	32
Insulin (%)	10	10
Multivessel Disease (%)	39	36
Prior MI (%)	37	36
Prior PCI (%)	36	37
Prior CABG (%)	21	20

ARRIVE Patient Flow

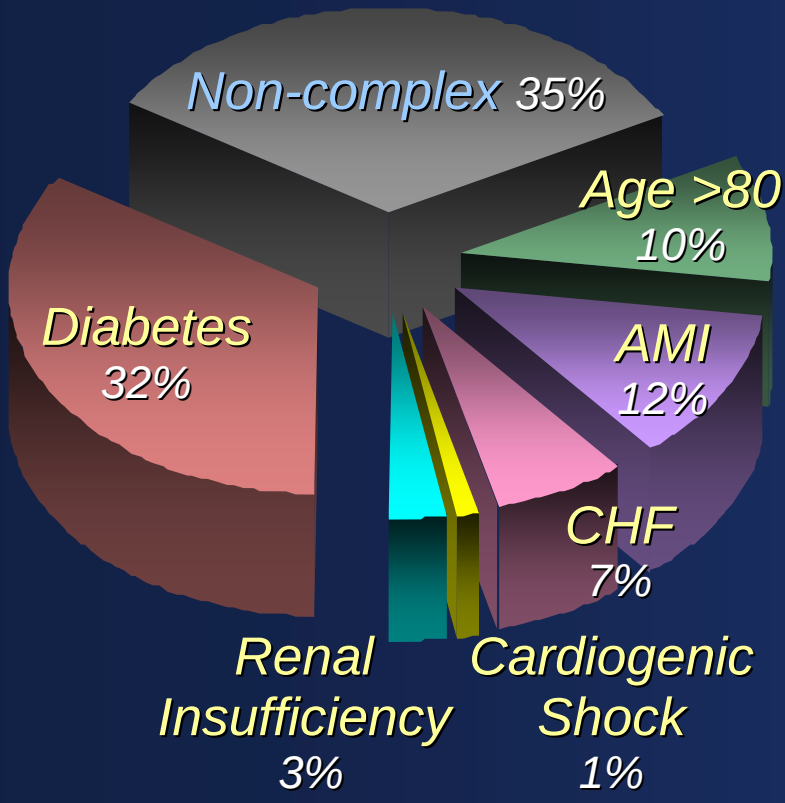
Pooled evaluable patients at 1 year = 95.5%



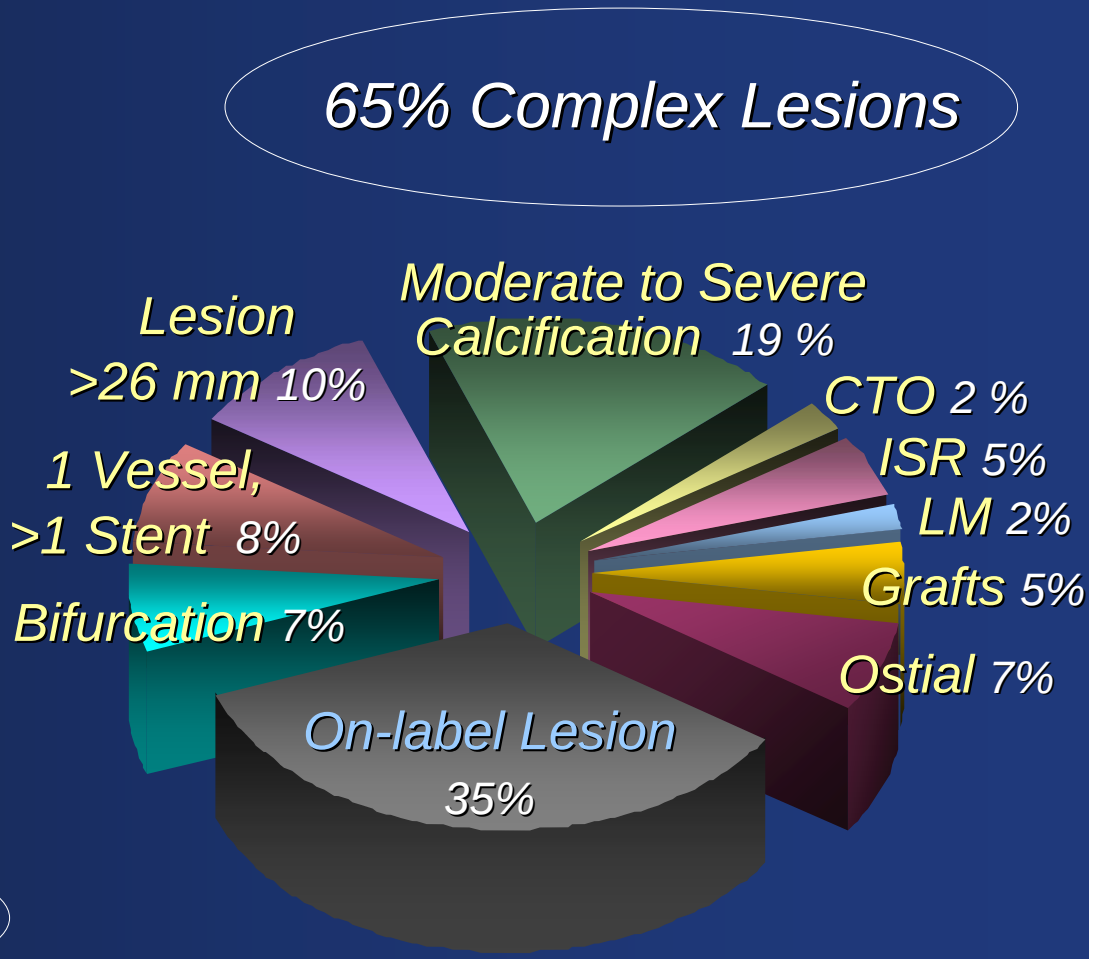
* Patients with reintervention >365 days post index procedure (n=63) will be evaluated 1 year post reintervention.

Expanded Use in Daily Practice: >7000 Patients

Complex patients/lesions predominate in ARRIVE



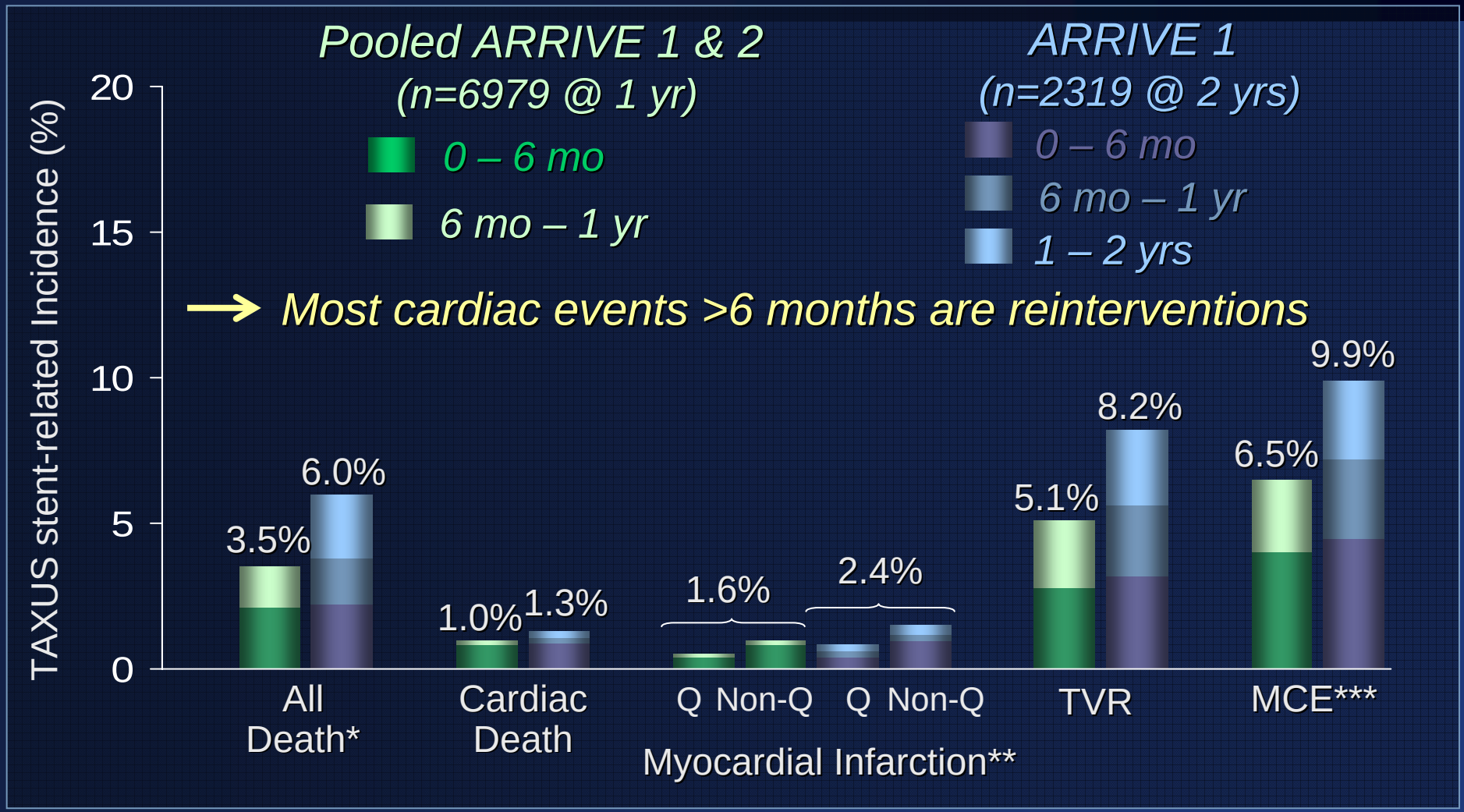
65% Complex Patients



n=7307 patients in pooled ARRIVE analysis group

Cardiac Events

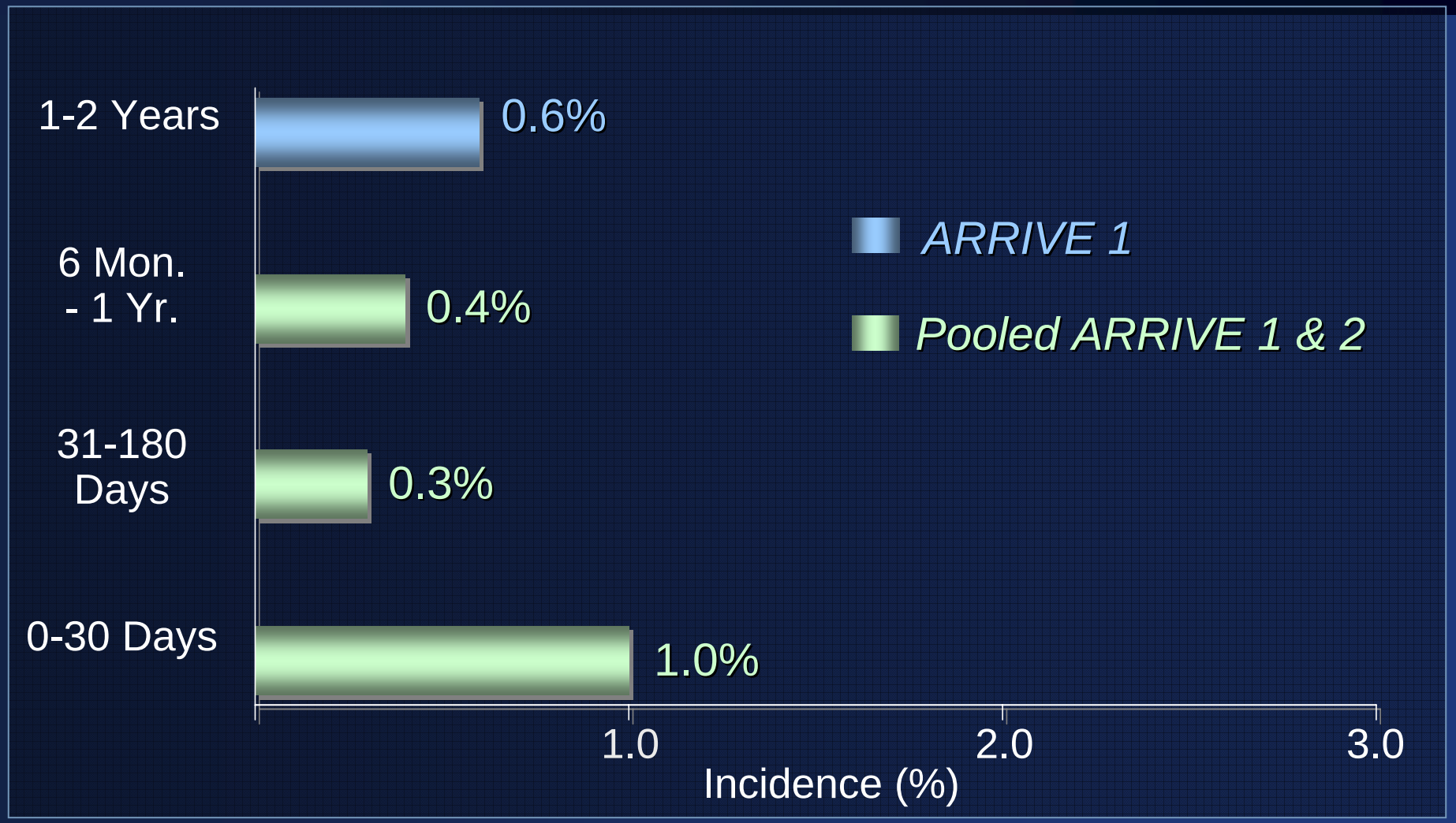
Durability in a real-world setting



*Includes non-stent-related deaths
**1 additional patient in each registry had Q- & non-Q MI at 1 year; another patient had both at 2 years
***Major cardiac events (MCE) = cardiac death, myocardial infarction (MI), and target vessel re-intervention (TVR); binary proportion

Stent Thrombosis (Presumed & Confirmed)

Rates aligned with population characteristics



Per protocol

Confirmed=angiographically documented with or without MI; Presumed=sudden death ≤30d or MI in vessel region

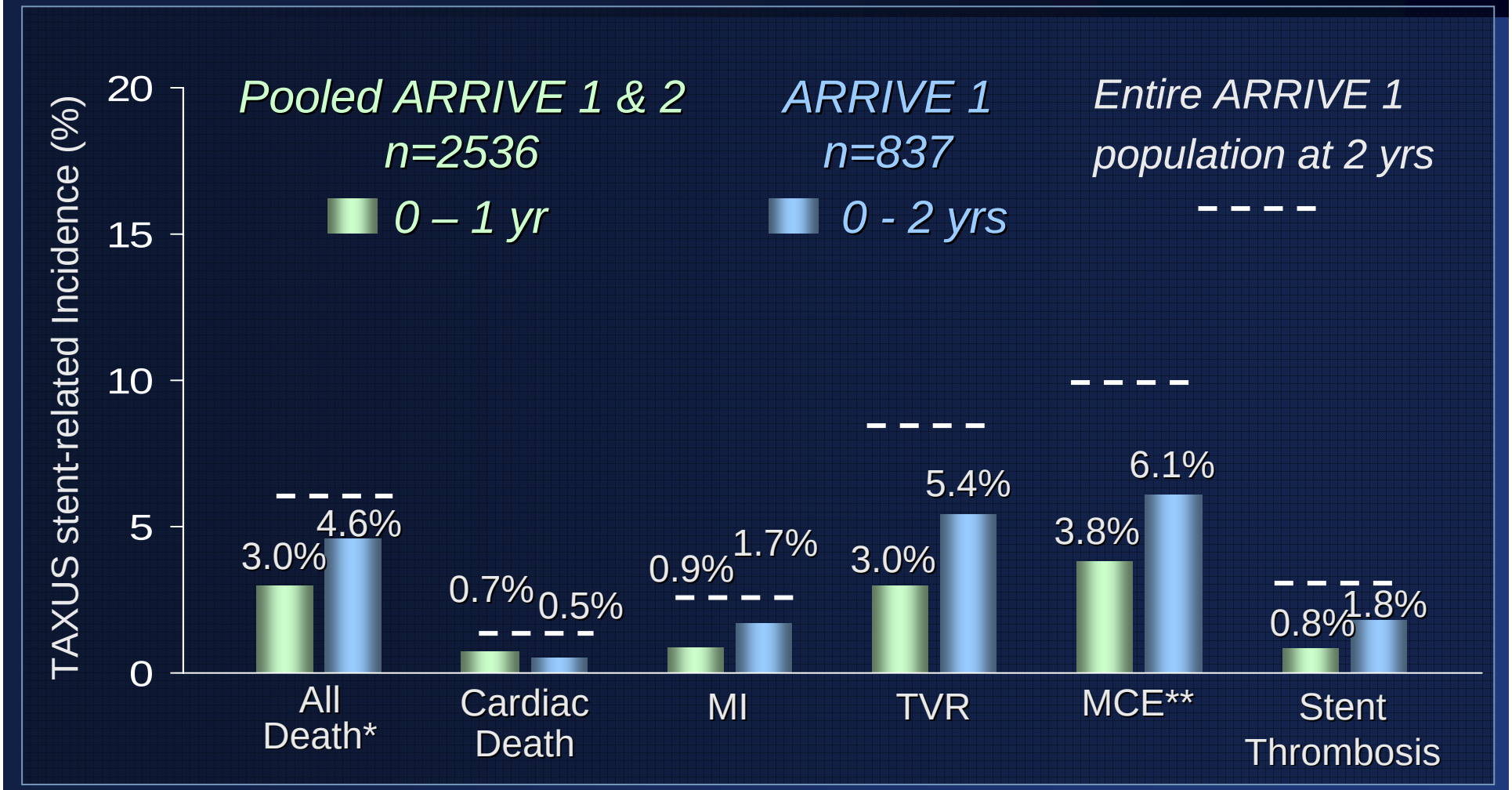
Dual Antiplatelet Therapy in ARRIVE 1
Significant predictor of cardiac death

Therapy Time Point	*Event Time Interval*	*Cardiac Death Rate*		*P value*
		Dual Therapy	*No Dual Therapy*	
Discharge	*Dis. – 1 Yr*	1.7% (39/2281)	2.9% (6/206)	0.27
30 Days	*30 D – 1 Yr*	1.3% (28/2238)	4.3% (8/188)	0.0051
6 Months	*6 M – 1 Yr*	0.7% (14/2074)	1.9% (6/313)	0.0377
Discharge	*Dis. – 2 Yr*	2.5% (56/2281)	4.4% (9/206)	0.11
30 Days	*30 D – 2 Yr*	2.0% (44/2238)	6.4% (12/188)	0.0009
6 Months	*6 M – 2 Yr*	1.4% (29/2074)	3.5% (11/313)	0.0146

Dual antiplatelet therapy = aspirin plus clopidogrel/ticlopidine

On-label Use

Low TAXUS-related event rates



*Includes non-stent-related deaths
**Major cardiac events (MCE) = cardiac death, myocardial infarction (MI), and target vessel re-intervention (TVR)
n=baseline count; binary proportion analysis; per protocol, ST = confirmed (angiographically documented with or without MI) and presumed (sudden death ≤30d or MI in vessel region).

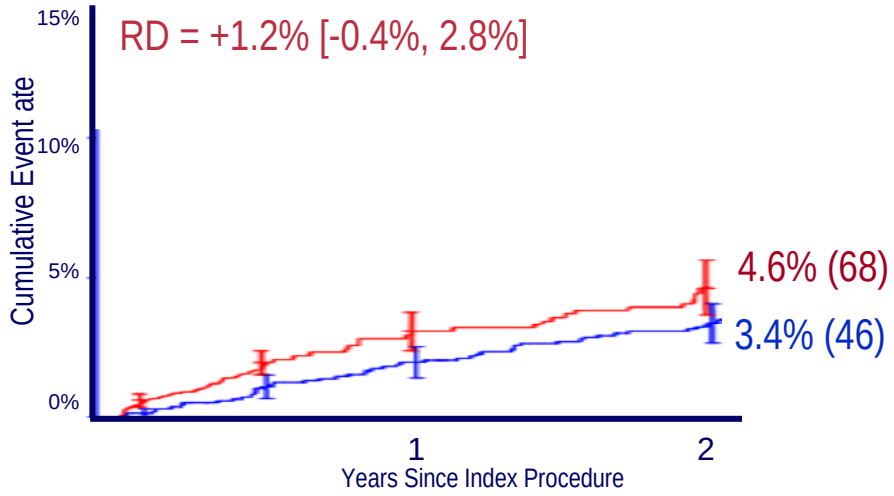
ARRIVE Simple v. TAXUS Overall
N = 3,964

TAXUS (N=1400) — ARRIVE (N=2564)

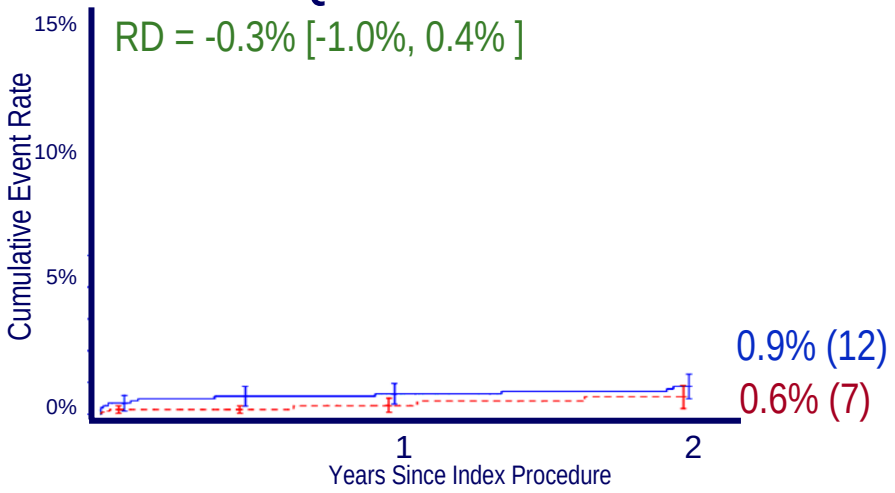
RD = Rate Difference = ARRIVE — TAXUS

No increase — Increase

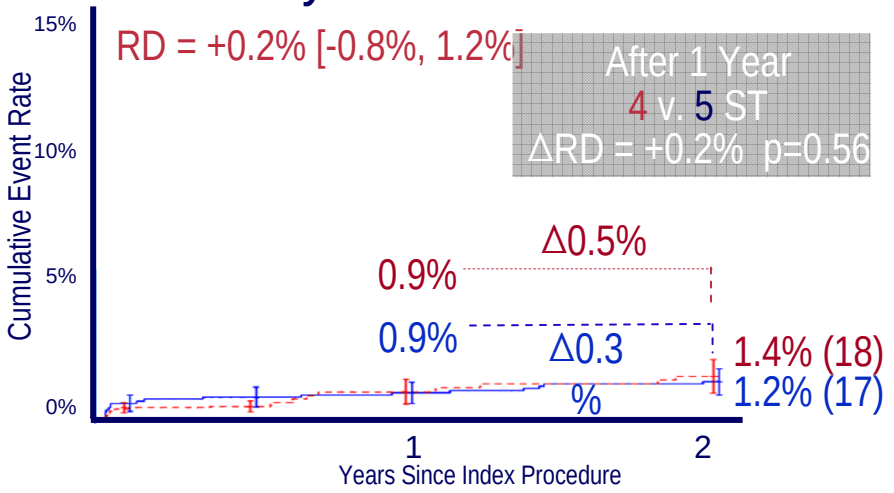
All Death



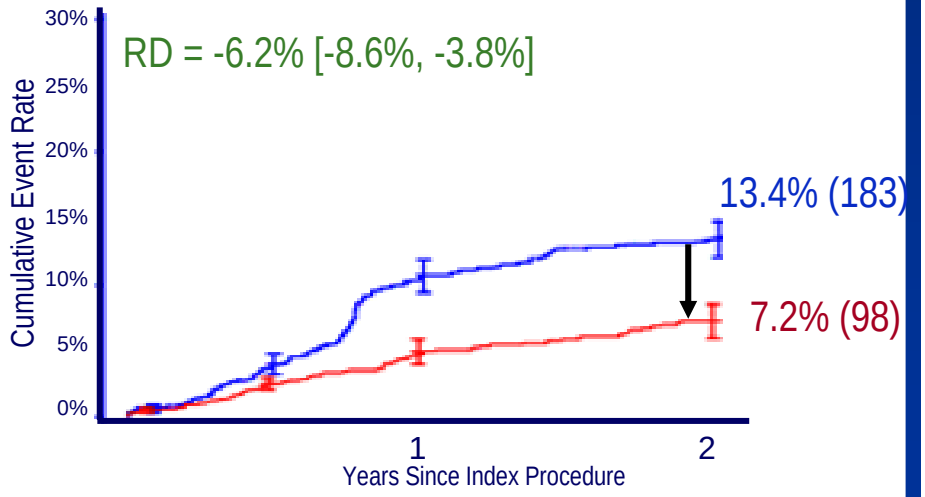
Q Wave MI



ARC Primary ST Definite/Probable



TVR



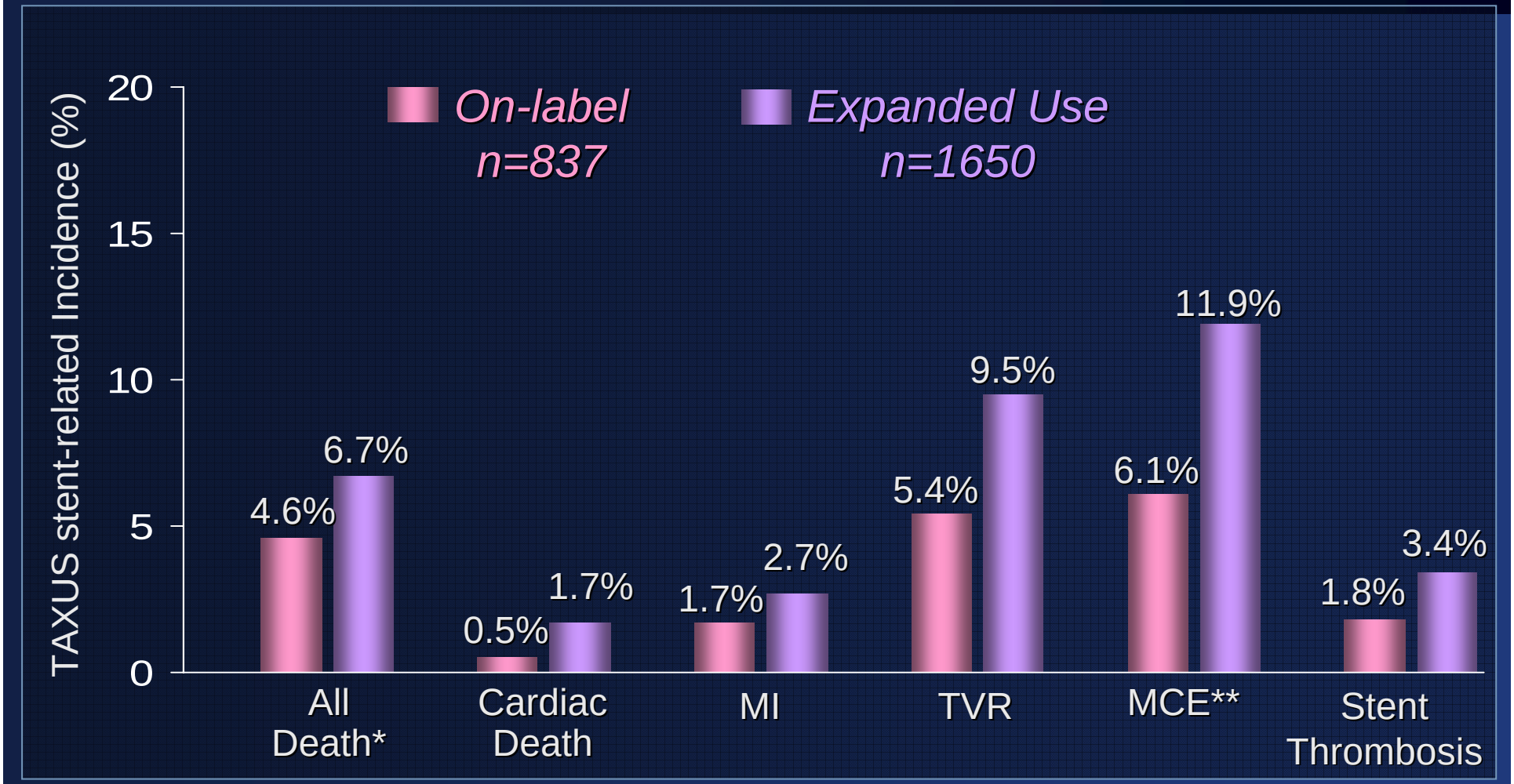
Simple Lesion Observations

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

On-label & Expanded Use in ARRIVE 1 at 2 Yrs

Expected differences in rates



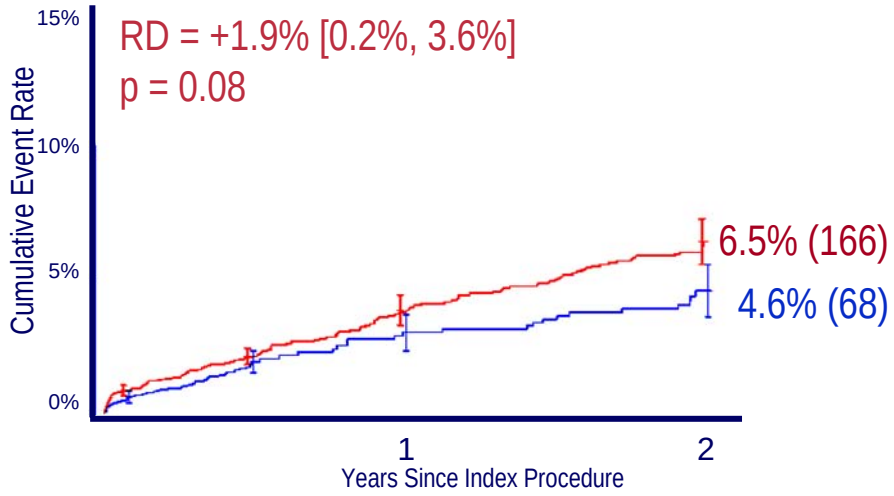
*Includes non-stent-related deaths
**Major cardiac events (MCE) = cardiac death, myocardial infarction (MI), and target vessel re-intervention (TVR)
n=baseline count; binary proportion analysis; per protocol, ST = confirmed (angiographically documented with or without MI) and presumed (sudden death ≤30d or MI in vessel region).

ARRIVE Complex v. Simple
N = 7,393

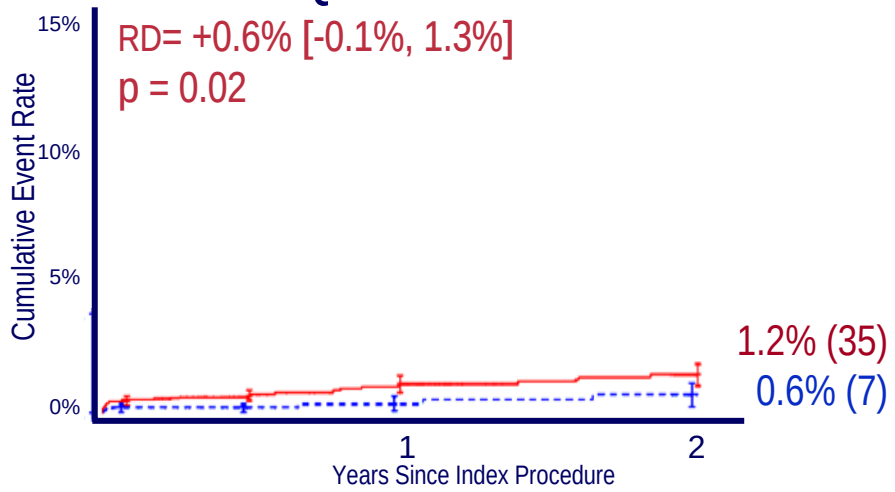
Simple (N=2564) — Complex (N=4829)

RD = Rate Difference = Complex − Simple
No increase — Increase

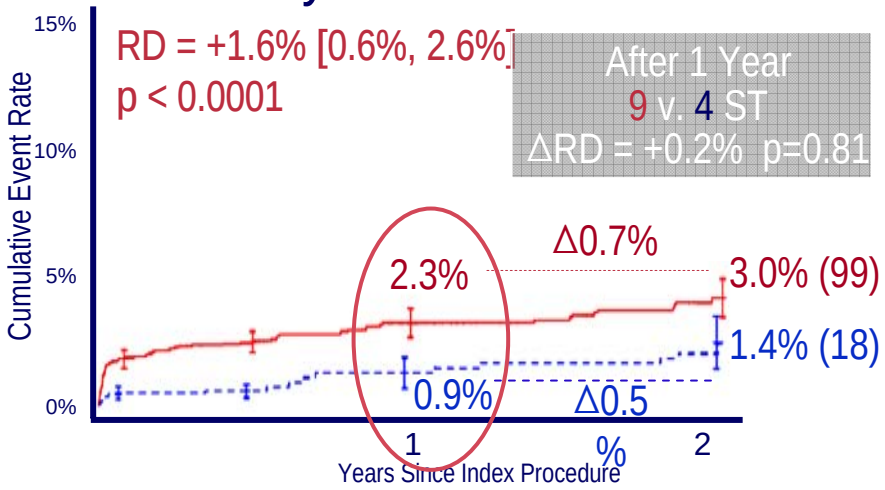
All Death



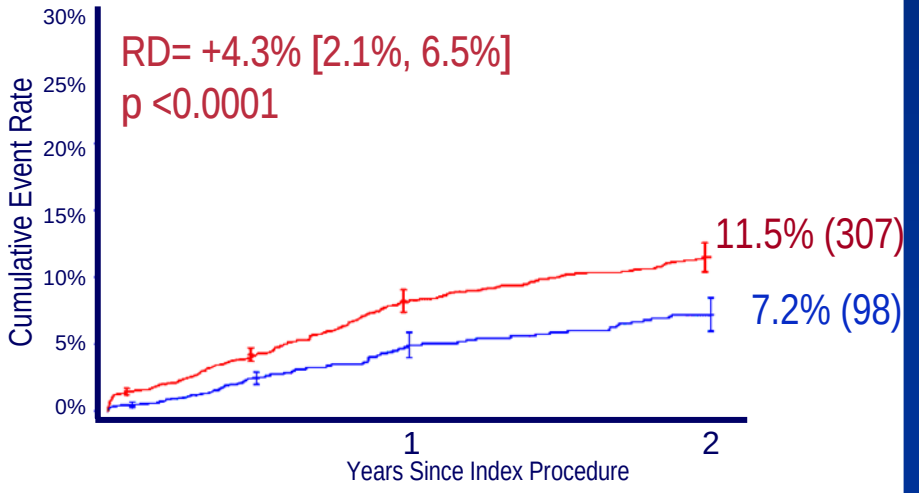
Q Wave MI



ARC Primary ST Definite/Probable



TVR

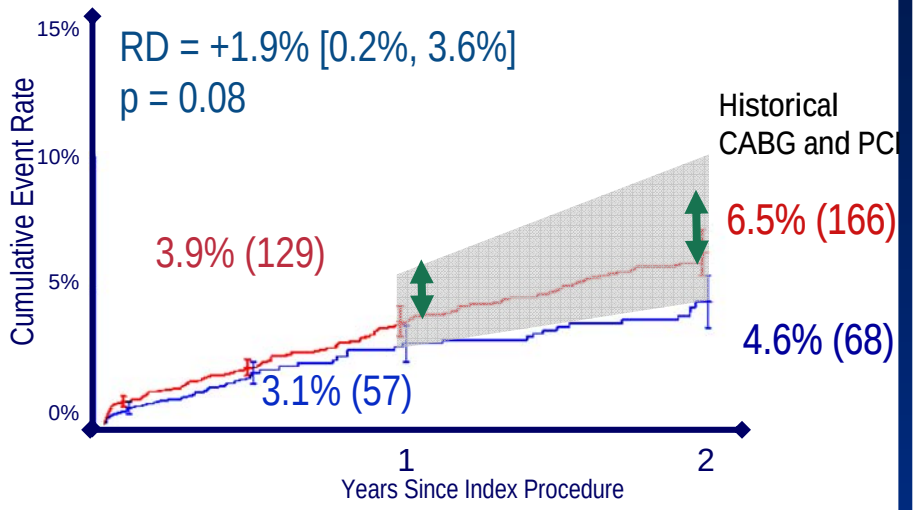


ARRIVE (n=7,393) Complex v. Simple

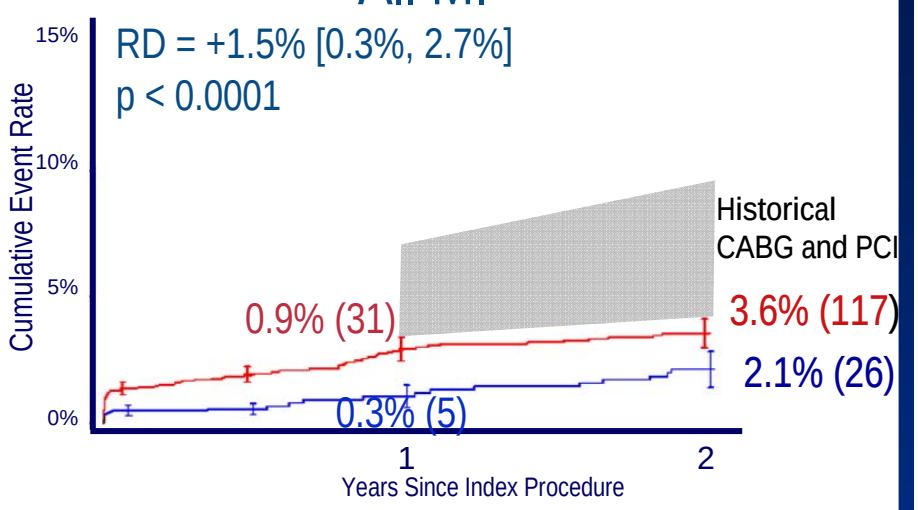
Simple (N=2564) Complex (N=4829)

RD = Rate Difference = Complex – Simple
No increase Increase

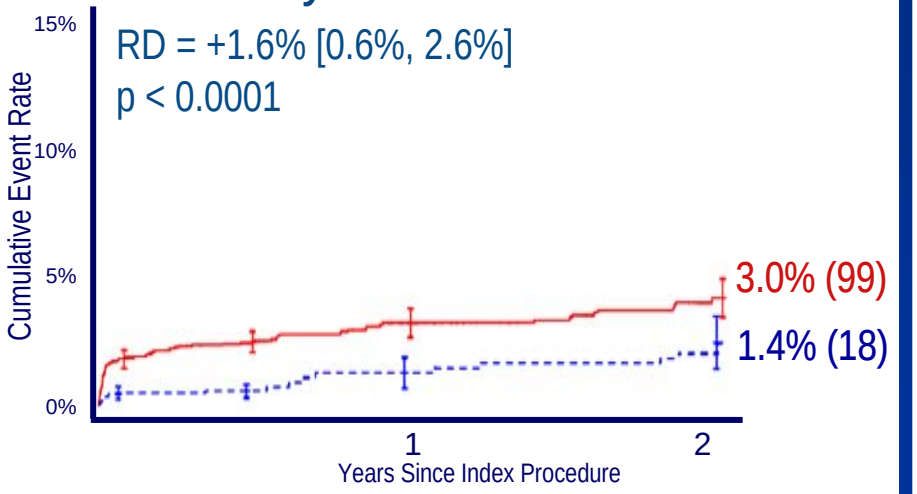
All Death



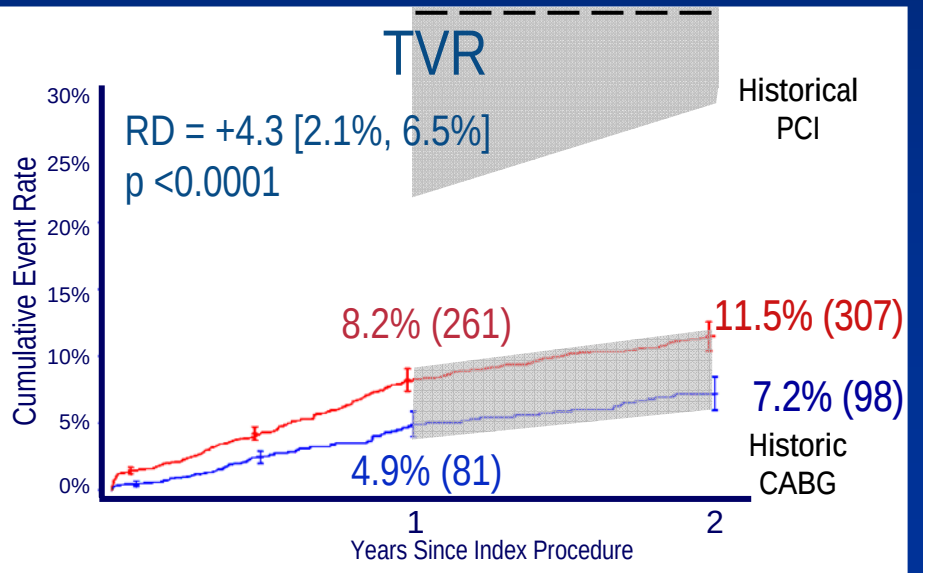
All MI



ARC Primary ST Definite/Probable

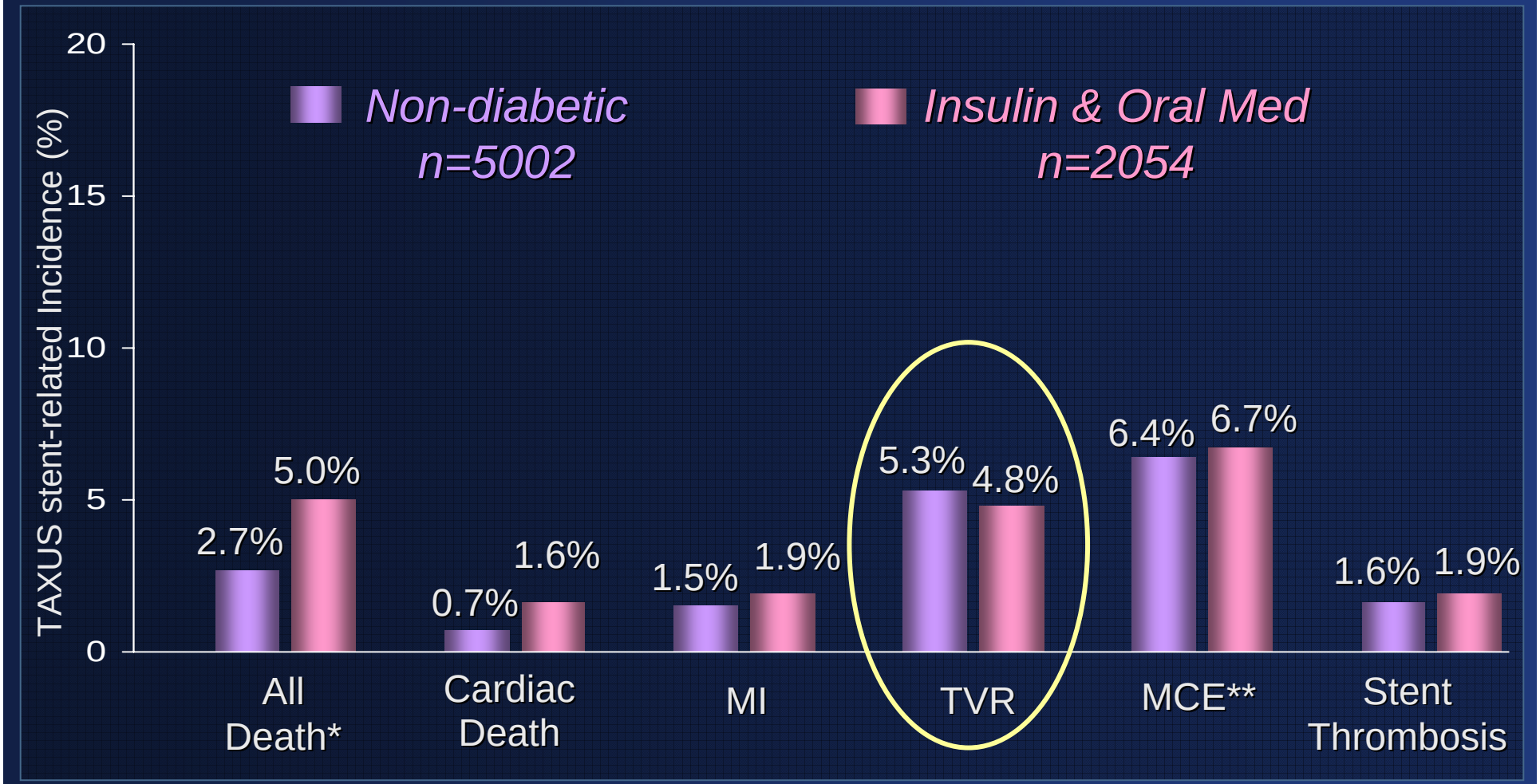


TVR



Diabetic Patients in Pooled ARRIVE Population

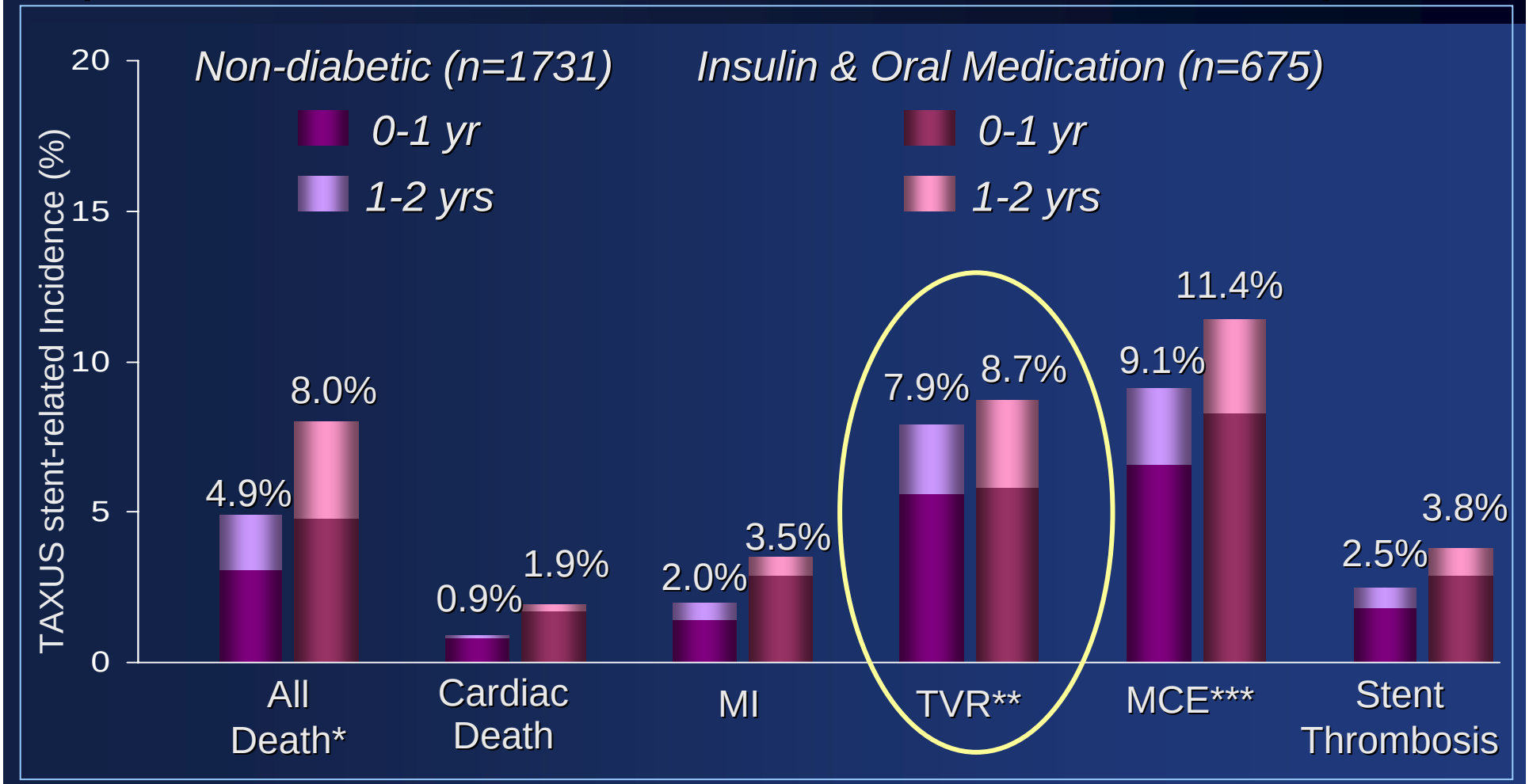
Comparable re-intervention rates at 1 year



*Includes non-stent-related deaths
**Major cardiac events (MCE) = cardiac death, myocardial infarction (MI), and target vessel re-intervention (TVR)
n=baseline count; binary proportion analysis; per protocol, ST = confirmed (angiographically documented with or without MI) and presumed (sudden death ≤30d or MI in vessel region).

Diabetic Patients in ARRIVE 1 at 2 Years

Equivalent re-intervention rates with non-diabetic patients



*Includes non-stent-related deaths
** *P* = NS by chi square test
***Major cardiac events (MCE) = cardiac death, myocardial infarction (MI), and target vessel re-intervention (TVR)
n=baseline count; binary proportion analysis; per protocol, ST = confirmed (angiographically documented with or without MI) and presumed (sudden death ≤30d or MI in vessel region).

ARRIVE subgroup outcomes (0-1 years)

* TAXUS is not approved for AMI, multivessel disease, lesions > 28 mm, vessels < 2.5 mm, or diabetics	"TAXUS IV-like" N=2564	ARRIVE overall N=7393	AMI* N=927	Multivessel* N=1153	Long (>28 mm)* N=953	Small (<2.5 mm)(N=2272	Diabetics* N=2333
Efficacy							
TVR	3.2% (81/2564)	4.6% (342/7393)	4.0% (37/927)	6.7% (77/1153)	7.6% (72/953)	5.8% (131/2272)	4.4% (103/2333)
Safety							
All death	2.2% (57/2564)	2.5% (186/7393)	2.7% (25/927)	3.0% (35/1153)	3.5% (33/953)	2.3% (53/2272)	3.7% (87/2333)
Cardiac death	1.2% (30/2564)	1.6% (119/7393)	1.9% (18/927)	2.1% (24/1153)	2.5% (24/953)	1.5% (34/2272)	2.6% (61/2333)
MI	0.7% (18/2564)	1.7% (126/7393)	2.0% (19/927)	2.8% (32/1153)	3.9% (37/953)	2.3% (53/2272)	2.0% (46/2333)
Q-wave	0.2% (5/2564)	0.5% (36/7393)	0.2% (2/927)	1.1% (13/1153)	1.6% (15/953)	0.7% (16/2272)	0.6% (14/2333)
Stent thrombosis (Per Protocol)	0.5% (14/2564)	1.4% (106/7393)	2.0% (19/927)	2.3% (26/1153)	2.8% (27/953)	1.9% (43/2272)	1.8% (41/2333)
Stent thrombosis (ARC primary definite/probable)	0.5% (14/2564)	1.4% (104/7393)	2.2% (20/927)	2.3% (26/1153)	2.8% (27/953)	1.9% (43/2272)	1.8% (42/2333)

ARRIVE subgroup outcomes (1-2 years)

* TAXUS is not approved for AMI, multivessel disease, lesions > 28 mm, vessels < 2.5 mm, or diabetics	"TAXUS IV-like" N=2564	ARRIVE overall N=7393	AMI* N=927	Multivessel* N=1153	Long (>=28 mm)* N=953	Small vessels (<2.5 mm) N=2272	Diabetics* N=2333
Efficacy							
TVR	1.4% (17/1180)	1.9% (63/3380)	1.1% (4/366)	3.1% (16/521)	2.9% (13/452)	2.0% (21/1026)	2.3% (23/1013)
Safety							
All death	0.9% (11/1180)	1.4% (48/3380)	1.9% (7/366)	1.3% (7/521)	1.8% (8/452)	1.4% (14/1026)	2.0% (20/1013)
Cardiac death	0.2% (2/1180)	0.6% (20/3380)	0.8% (3/366)	1.0% (5/521)	0.7% (3/452)	0.6% (6/1026)	0.8% (8/1013)
MI	0.7% (8/1180)	0.5% (17/3380)	0.3% (1/366)	0.6% (3/521)	0.2% (1/452)	0.5% (5/1026)	0.7% (7/1013)
Q-wave	0.2% (2/1180)	0.2% (6/3380)	0.3% (1/366)	0.0% (0/521)	0.2% (1/452)	0.1% (1/1026)	0.0% (0/1013)
Stent thrombosis (Per Protocol)	0.4% (5/1180)	0.4% (14/3380)	0.3% (1/366)	0.6% (3/521)	1.1% (5/452)	0.5% (5/1026)	0.5% (5/1013)
Stent thrombosis (ARC primary definite and probable)	0.3% (4/1180)	0.4% (13/3380)	0.5% (2/366)	0.8% (4/521)	0.7% (3/452)	0.5% (5/1026)	0.5% (5/1013)

TAXUS ARRIVE Summary
Real-world look at US interventional practice

- All-comers registries with large breadth of TAXUS stent applications
  - Cohort >7,000 includes complex patients, lesions, and procedures
- Consistent outcomes up to 2 years are observed
  - In high & low risk patient groups; broad spectrum of procedural complexity
- Acceptable TAXUS-related incidence rates observed at 1 & 2 years given the complexity studied
  - Across entire population; across 5 high-risk subgroups
- Lower rates in second year; predominant risk is reintervention
- Real-world registry ARRIVE reveals expectedly higher stent thrombosis rates in complex patients
- Absence of dual antiplatelet therapy at 30 days & 6 months is a significant predictor of cardiac death at 1 & 2 years

ARRIVE Registry Conclusions

- Safety of the TAXUS stent is confirmed at 1 year in approximately 7000 “real-world” patients, including a substantial proportion of high-risk patients and lesions
- Second year rates show 2-4% incremental increase in all death, TVR, and MCE
- TAXUS risk/benefit balance observed in clinical trials is extended to and maintained in the entire spectrum of patients and lesion types in the US