Current Status of TAVR: Review of Recent Studies

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Disclosure Statement of Financial Interest

Susheel Kodali, MD

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
• Grant/Research Support	• Edwards Lifesciences
• Steering Committee	• Edwards Lifesciences, Claret Medical, Meril
• SAB (Equity)	• Thubrikar Aortic Valve, Inc

Introduction

- 5 year results from PARTNER 1
- 2 year results from CoreValve US Pivotal
- 30 day results from SAPIEN 3 trial for both high and intermediate risk patients
- 1 year results from NOTION
- 30 day results from CoreValve Evolut

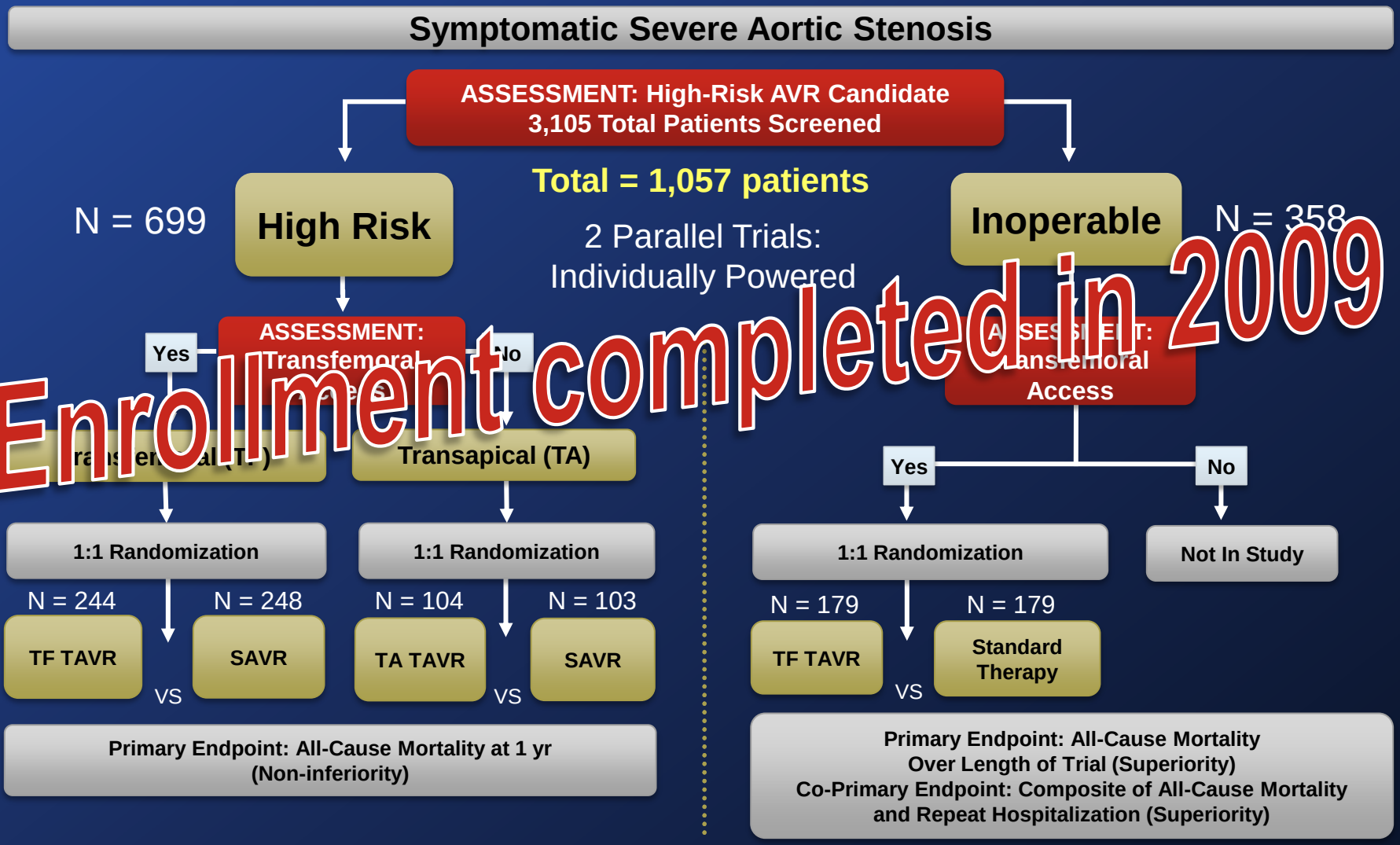
Five-Year Outcomes after Randomization to Transcatheter or Surgical Aortic Valve Replacement: Final Results of The PARTNER 1 Trial

Michael J. Mack, MD
on behalf of The PARTNER Trial Investigators

ACC 2015 | San Diego | March 15, 2015

THE PARTNER TRIAL

PARTNER Study Design



Enrollment completed in 2009

Study Devices

THE PARTNER TRIAL

Transfemoral **Transapical**

Edwards SAPIEN THV
23 and 26 mm valves

RetroFlex 1
22 and 24 F sheaths

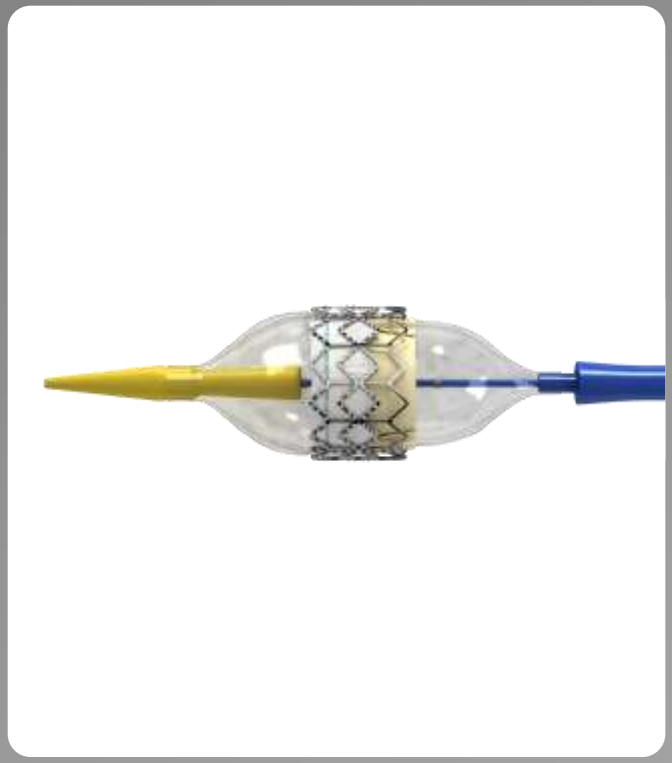
Ascendra
24 and 26 F sheaths

Study Devices

THE PARTNER TRIAL

Transfemoral | **Transapical**

Edwards SAPIEN THV
23 and 26 mm valves



RetroFlex 3
22 and 24 F sheaths

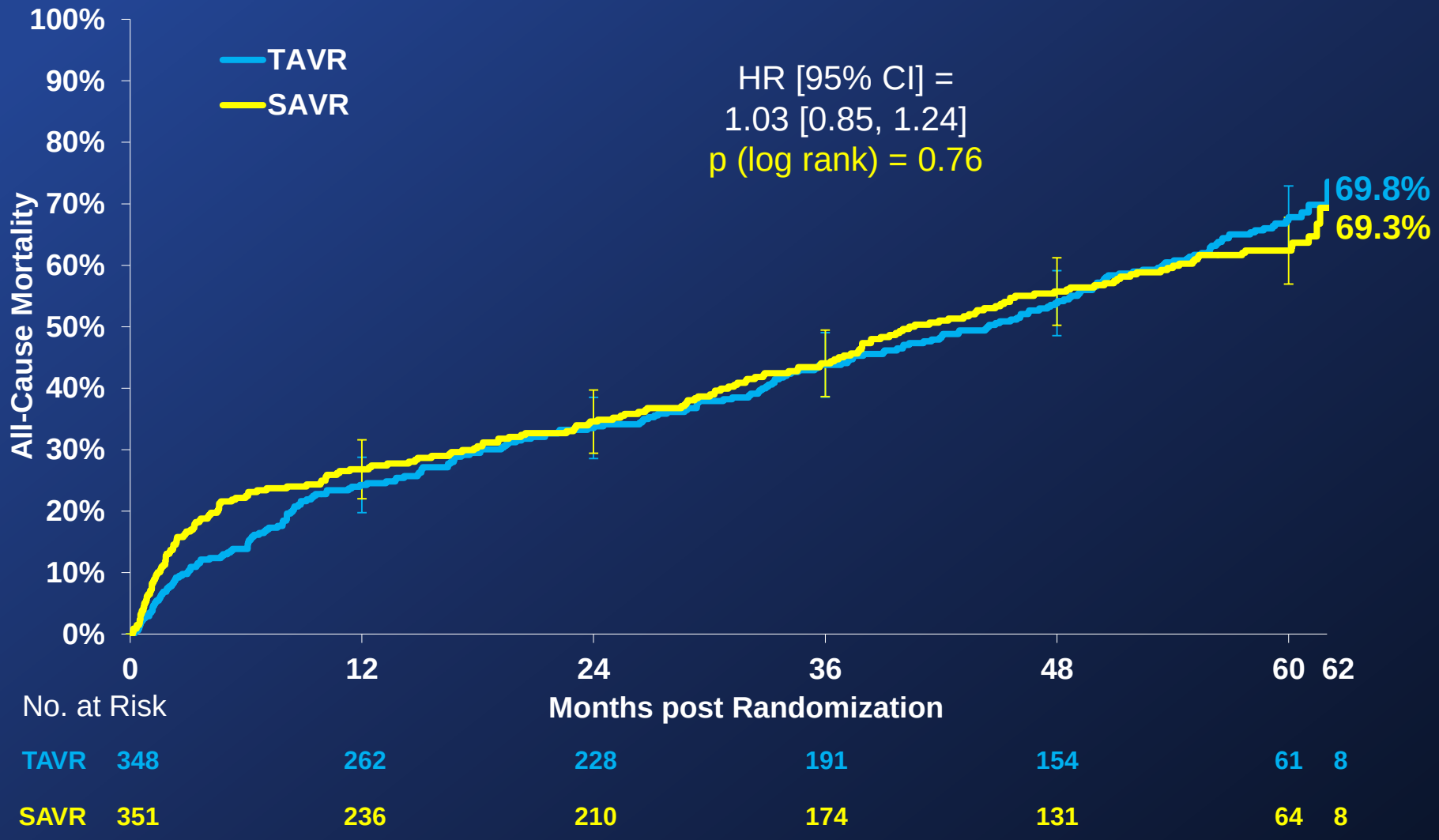
Ascendra
24 and 26 F sheaths

Baseline Patient Characteristics
Demographics

THE PARTNER TRIAL

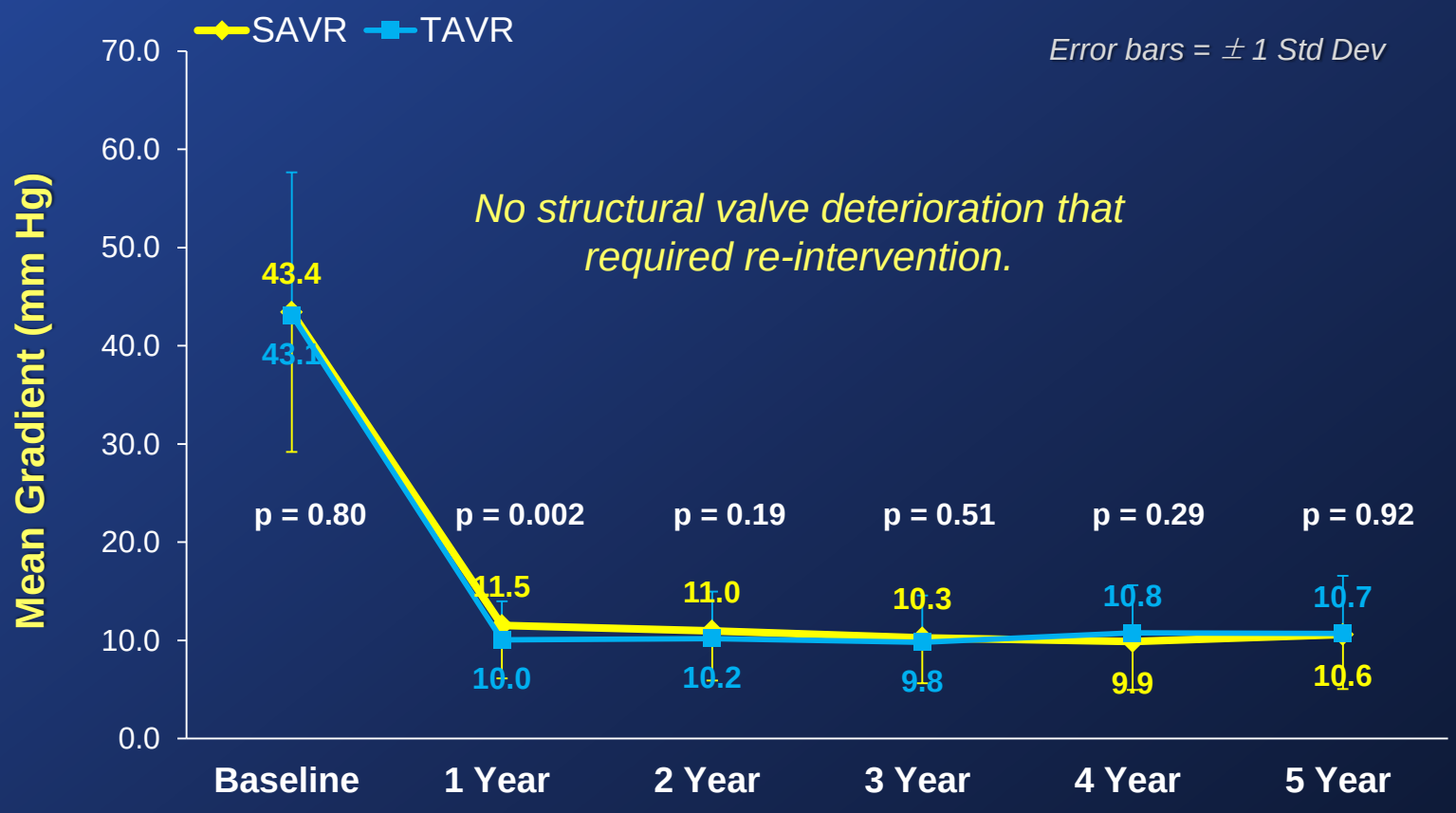
	TAVR (n=348)		SAVR (n=351)	
Characteristic	**n**		**n**	
Age – years (Mean ± SD)	348	83.6 ± 6.8	349	84.5 ± 6.4
Male	201	57.8%	198	56.7%
NYHA Class III or IV	328	94.3%	328	94.0%
Previous CABG	148	42.5%	152	43.6%
Cerebrovascular disease	96	29.4%	87	26.8%
Peripheral vascular disease	149	43.2%	142	41.6%
STS Score (Mean ± SD)	347	11.8 ± 3.3	349	11.7 ± 3.5

All-Cause Mortality (ITT)
Pooled Approaches



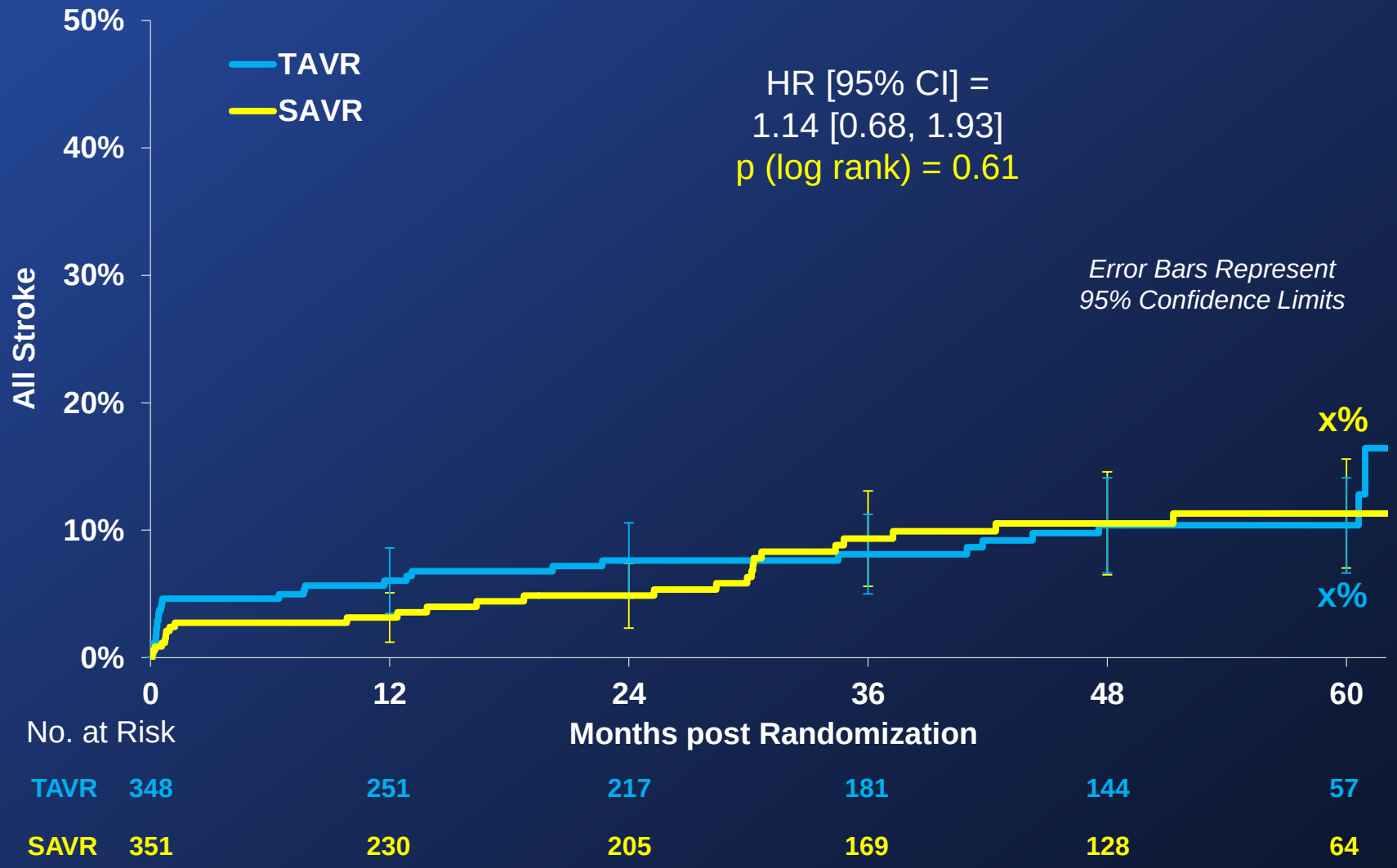
All-Cause Mortality (ITT)
Landmark Analysis

Aortic Valve Mean Gradient



	Baseline	1 Year	2 Year	3 Year	4 Year	5 Year
TAVR	310	219	156	106	79	56
SAVR	299	158	123	86	61	48

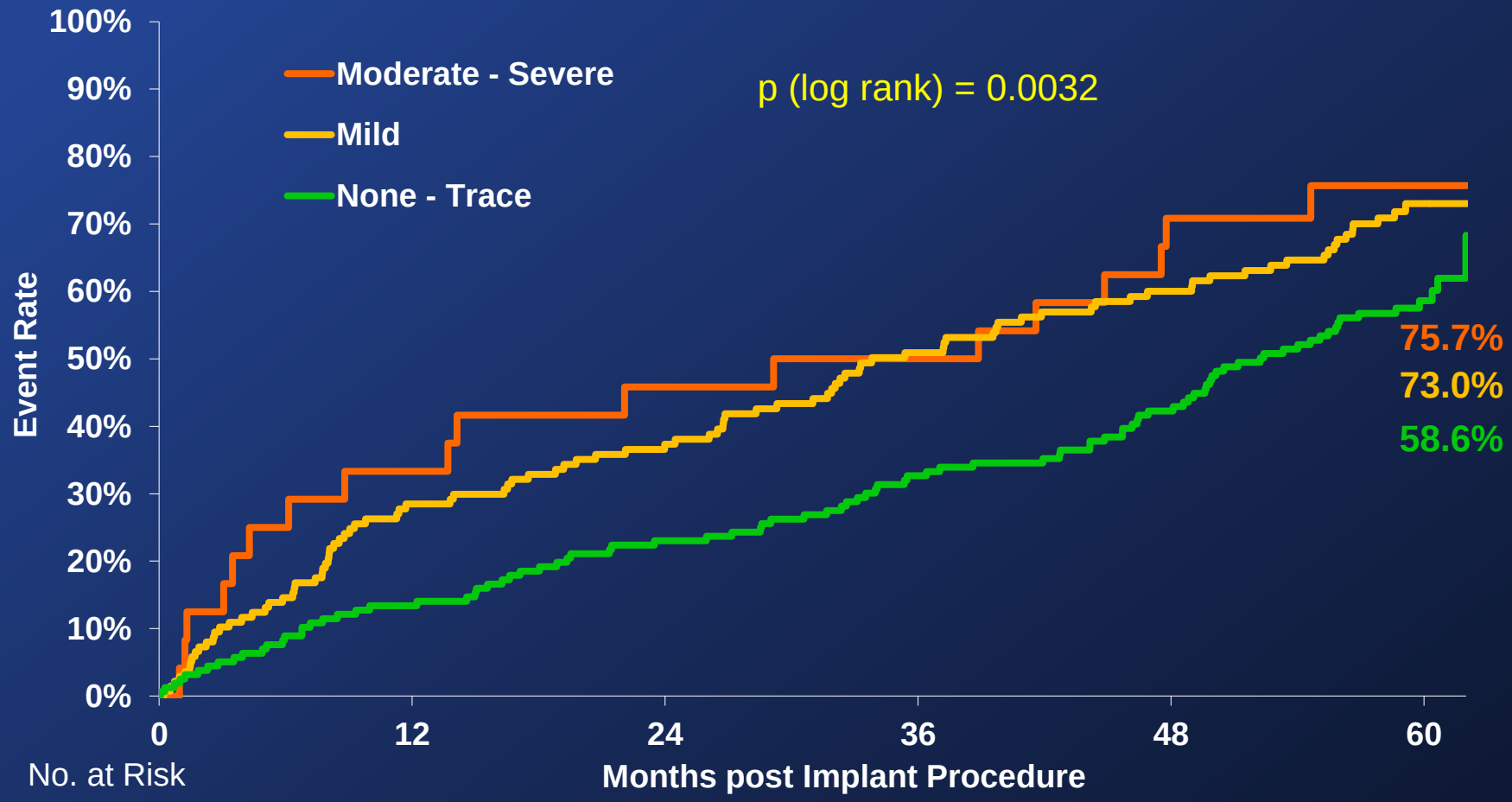
Strokes - All (ITT)
All Patients



No. at Risk

TAVR	348	251	217	181	144	57
SAVR	351	230	205	169	128	64

Mortality and Post Procedural PVL
TAVR Patients



No. at Risk

M-S	24	16	13	12	7	2
Mild	137	98	84	65	52	11
N-T	158	135	120	105	88	34

CoreValve US Pivotal Trial

A Randomized Comparison of Self-expanding Transcatheter and Surgical Aortic Valve Replacement in Patients with Severe Aortic Stenosis Deemed at Increased Risk for Surgery
2-Year Outcomes

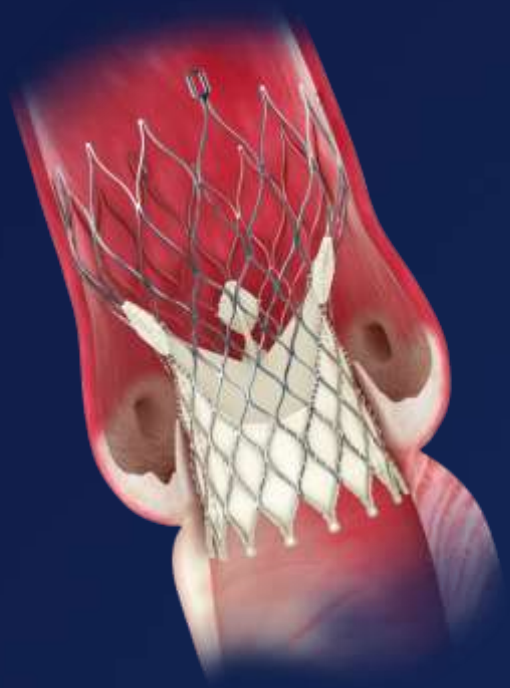
Michael J Reardon, MD, FACC
On Behalf of the CoreValve US Investigators

Pivotal Trial Design

Enrollment completed in 2012

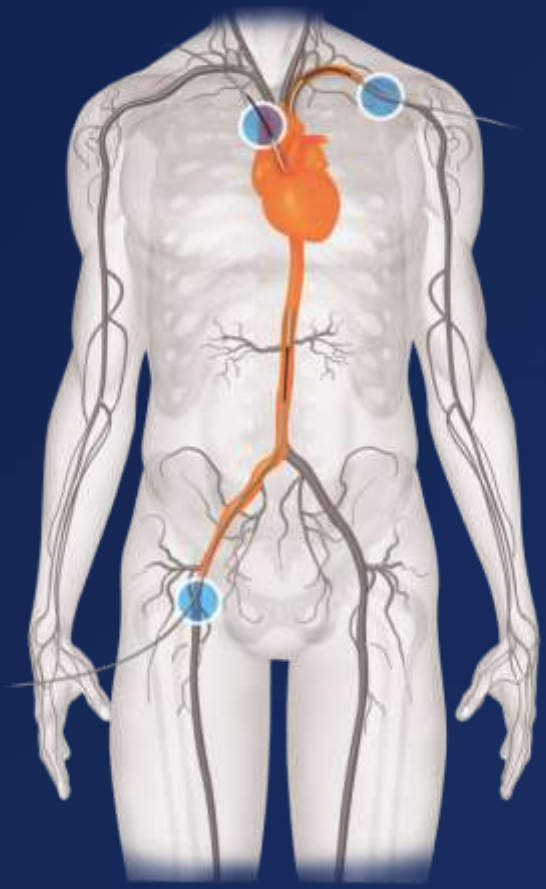
* Randomization stratified by intended access site

Study Device and Access Routes



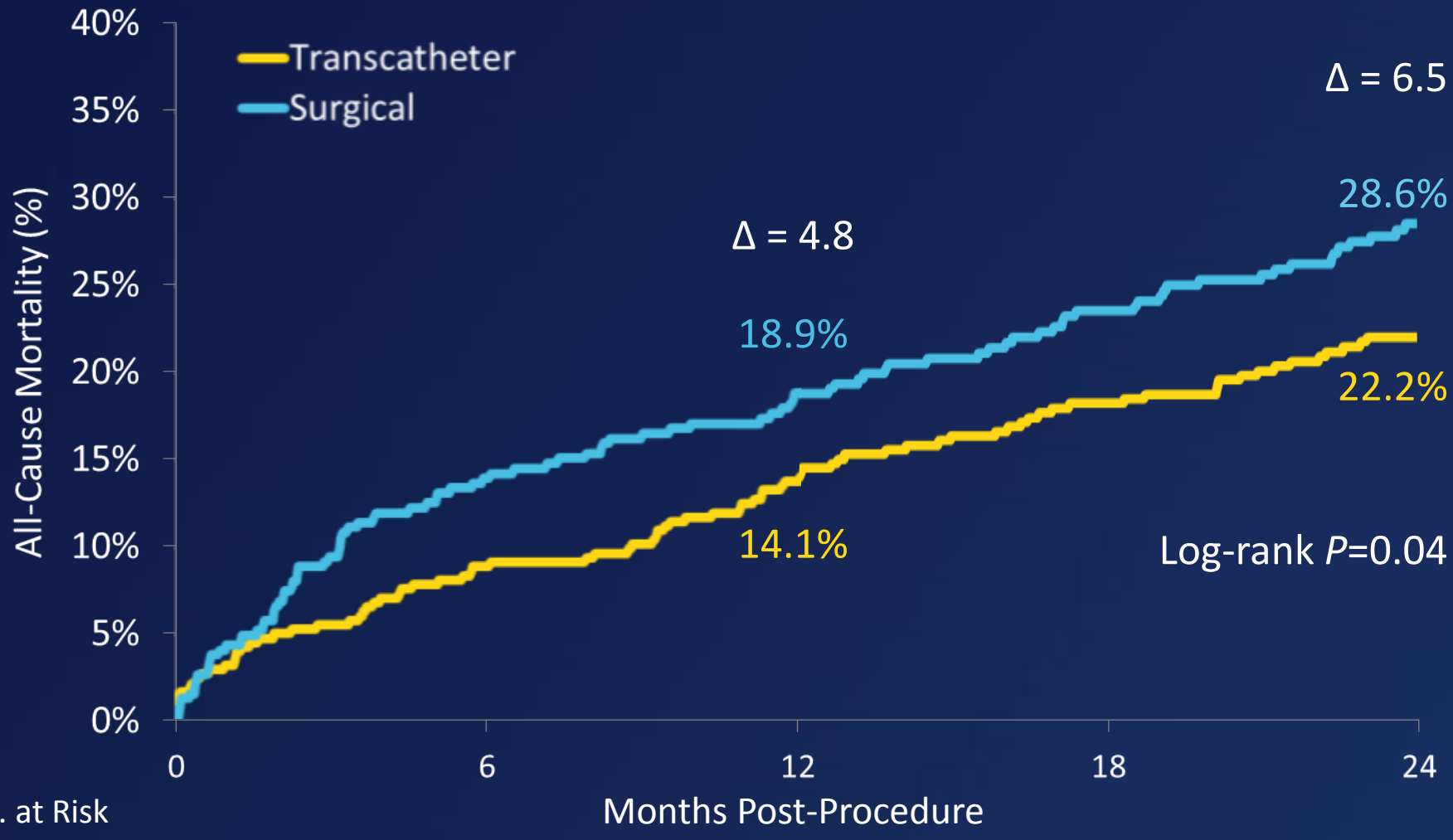
4 Valve Sizes (23, 26, 29, 31 mm)
(18-29 mm Annular Range)

18F Delivery System



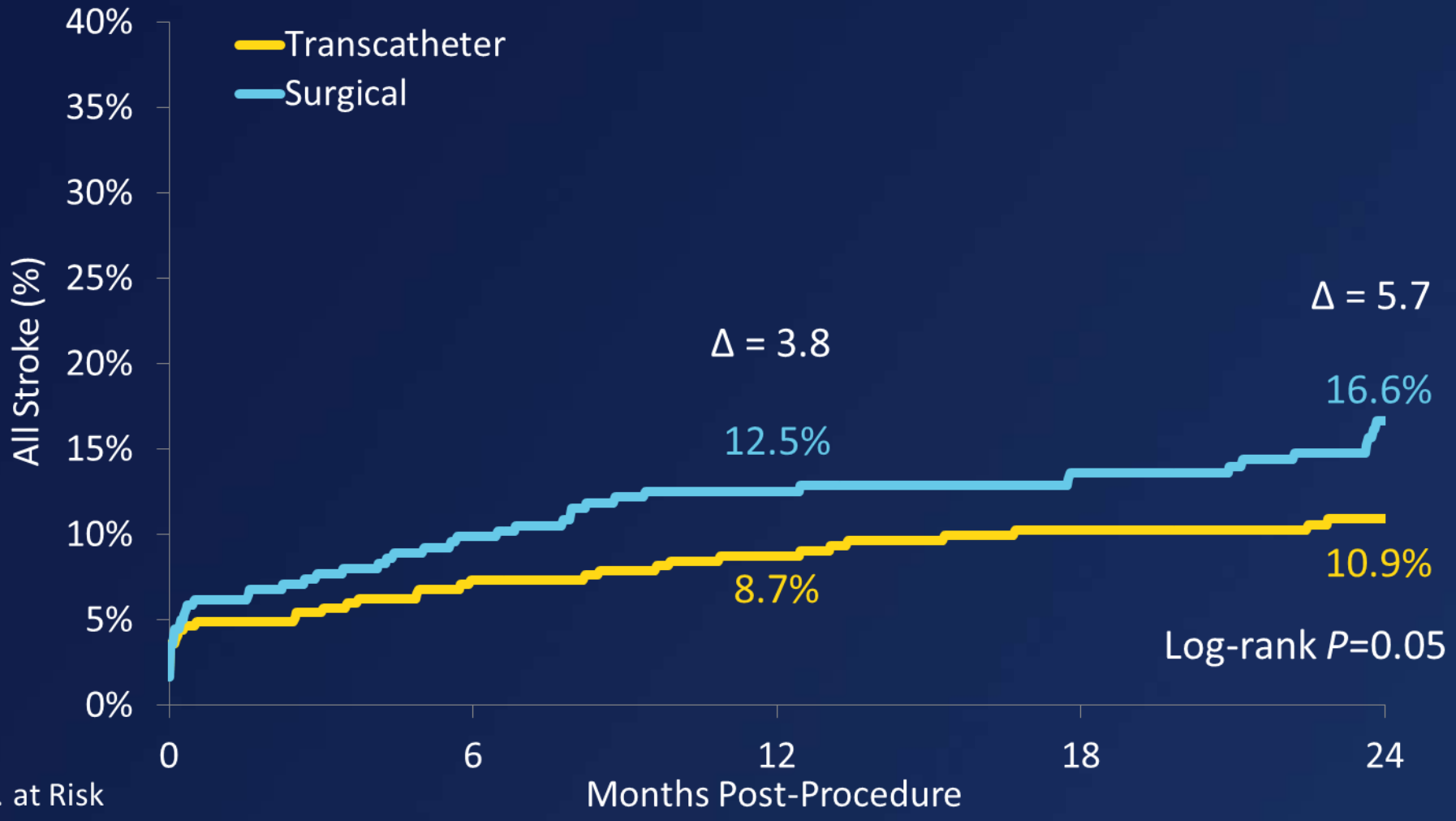
Transfemoral
Subclavian
Direct Aortic

All-Cause Mortality



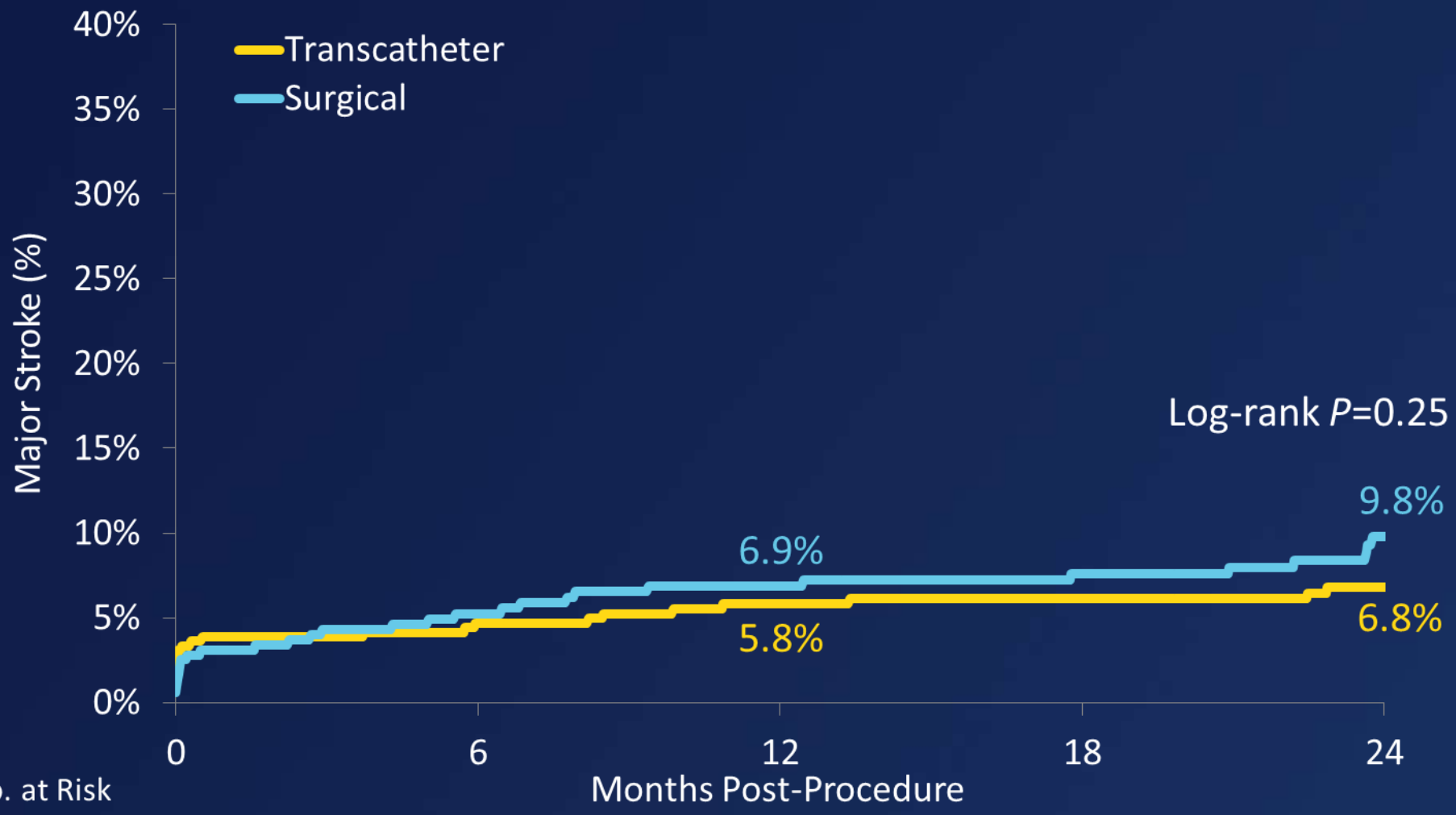
No. at Risk					
Transcatheter	391	378	354	334	219
Surgical	359	343	304	282	191

All Stroke



No. at Risk					
Transcatheter	391	364	335	318	205
Surgical	359	324	281	256	169

Major Stroke



Other Clinical Endpoints

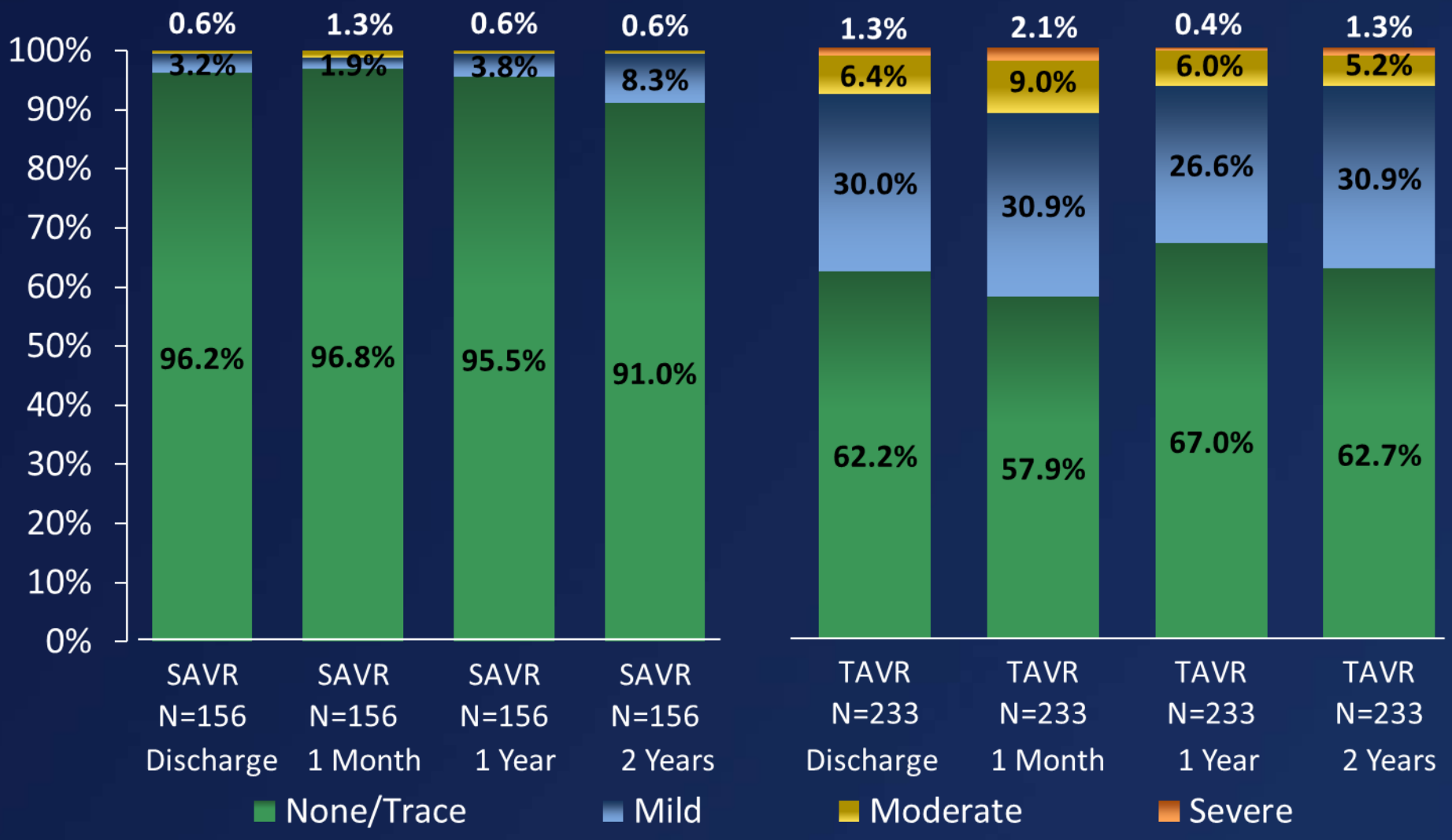
Events*	1 Month			1 Year			2 Years		
	TAVR	SAVR	*P*	TAVR	SAVR	*P*	TAVR	SAVR	*P*
Vascular complications (major)	6.2	1.7	0.002	6.4	2.0	0.003	7.1	2.0	0.001
Pacemaker implant	20.0	7.1	<0.001	22.5	11.6	<0.001	25.8	12.8	<0.001
Bleeding (life threatening or disabling)	13.6	35.1	<0.001	16.5	38.4	<0.001	18.1	39.6	<0.001
New onset or worsening atrial fibrillation	11.7	31.0	<0.001	16.4	33.2	<0.001	19.5	34.9	<0.001
Acute kidney injury	6.2	15.1	<0.001	6.2	15.1	<0.001	6.2	15.1	<0.001

* Percentages reported are Kaplan-Meier estimates and log-rank *P* values

Echocardiographic Findings

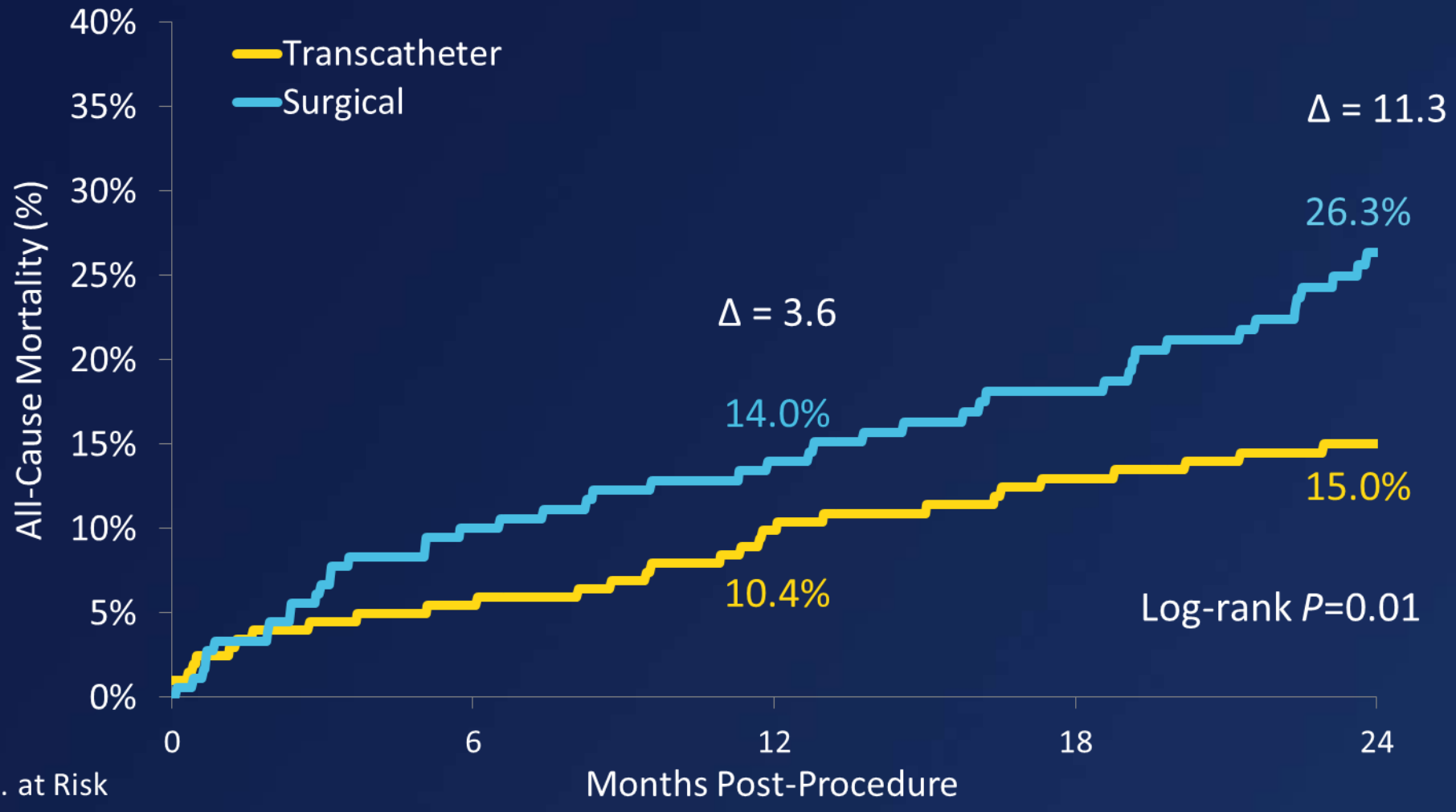
TAVR had significantly better valve performance over SAVR at all follow-up visits (*P*<0.001)

Paravalvular Regurgitation (Paired)



There was significantly lower PVL with SAVR over TAVR at each time point ($P<0.001$)

All-Cause Mortality STS ≤7%



Clinical and Echocardiographic Outcomes at 30 Days with the SAPIEN 3 TAVR System in Inoperable, High-Risk and Intermediate-Risk AS Patients

Susheel Kodali, MD
on behalf of The PARTNER Trial Investigators

ACC 2015 | San Diego | March 15, 2015

THE PARTNER II TRIAL

Evolution of the Edwards Balloon-Expandable Transcatheter Valves

THE PARTNER II TRIAL

Cribier-Edwards

2002

SAPIEN

2006

SAPIEN XT

2009

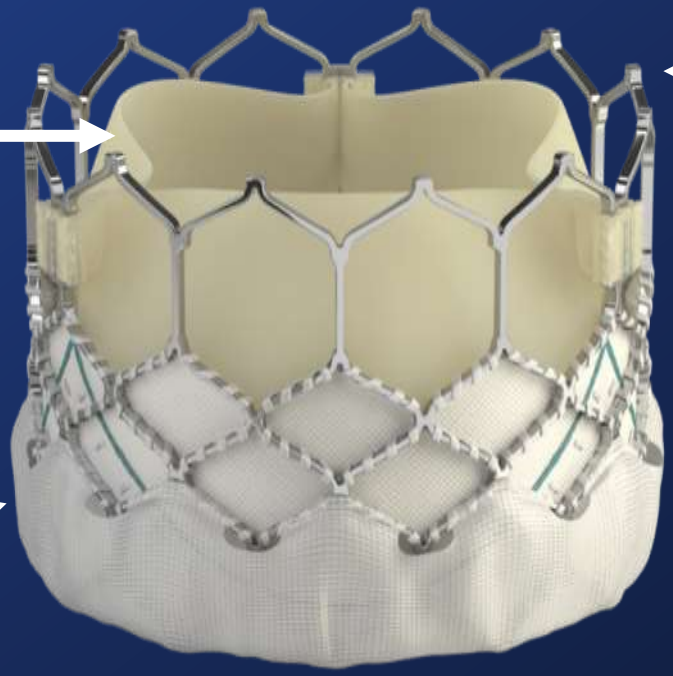
SAPIEN 3

2013

SAPIEN 3 Transcatheter Heart Valve

Distinguishing Features

THE PARTNER II TRIAL



Bovine pericardial valve

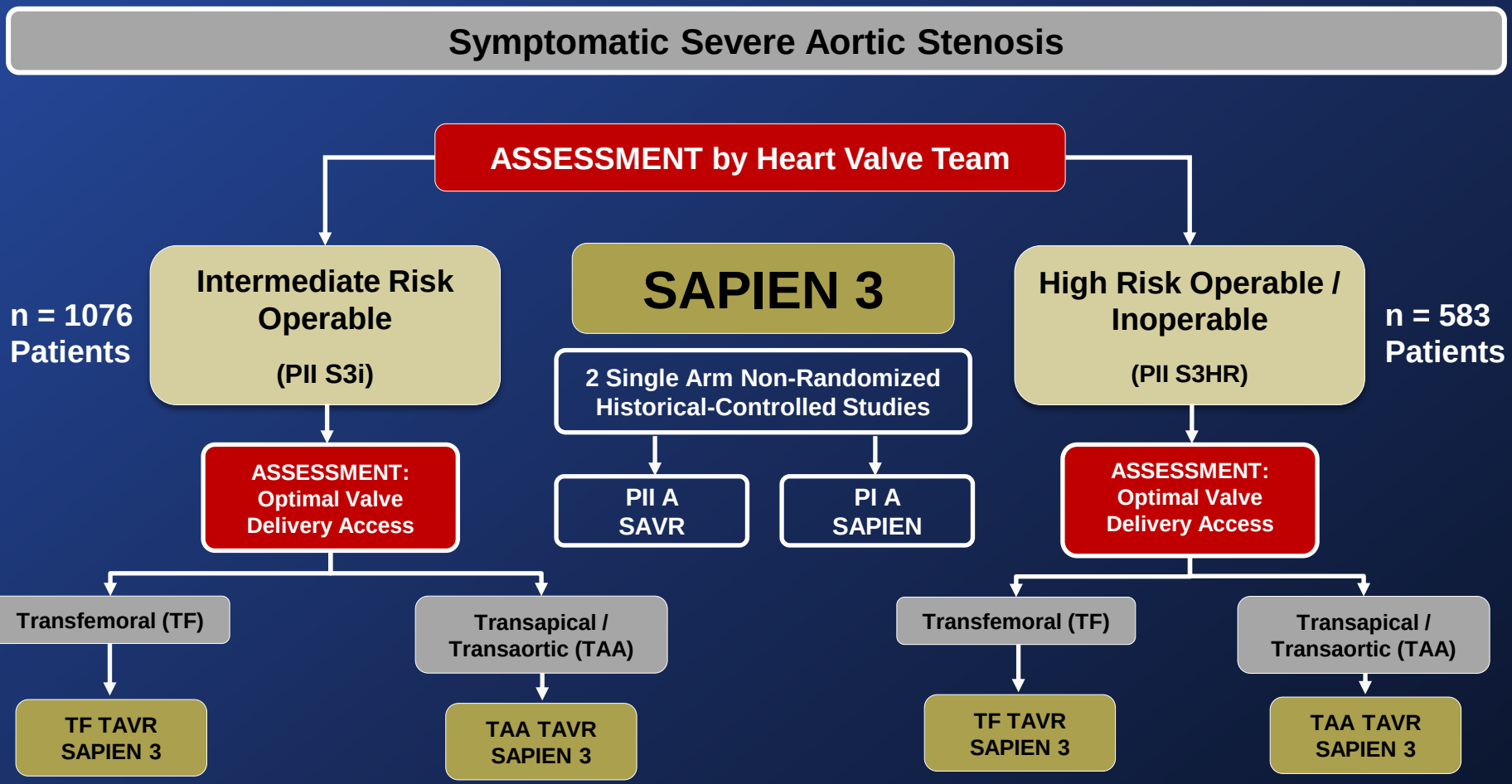
Modified frame geometry

Overall lower profile design

External skirt (to reduce PVL)

The PARTNER II S3 Trial

Study Design



Baseline Patient Characteristics

S3HR Patients

THE PARTNER II TRIAL

Average STS =

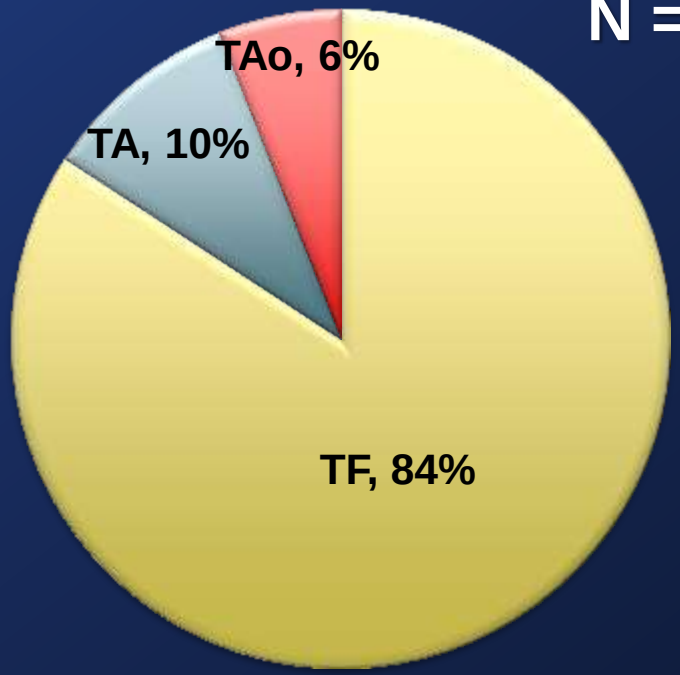
8.6%

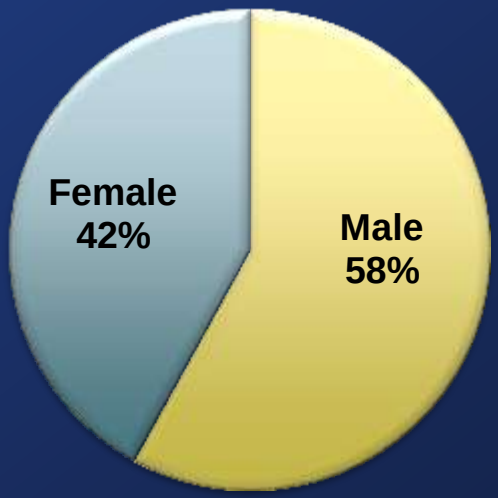
(Median 8.4%)

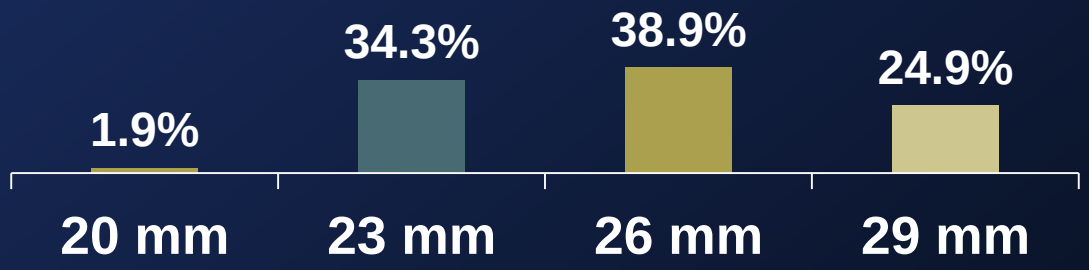
Average Age =

82.8yrs

N = 583







Baseline Patient Characteristics
S3i Patients

THE PARTNER II TRIAL

Average STS =

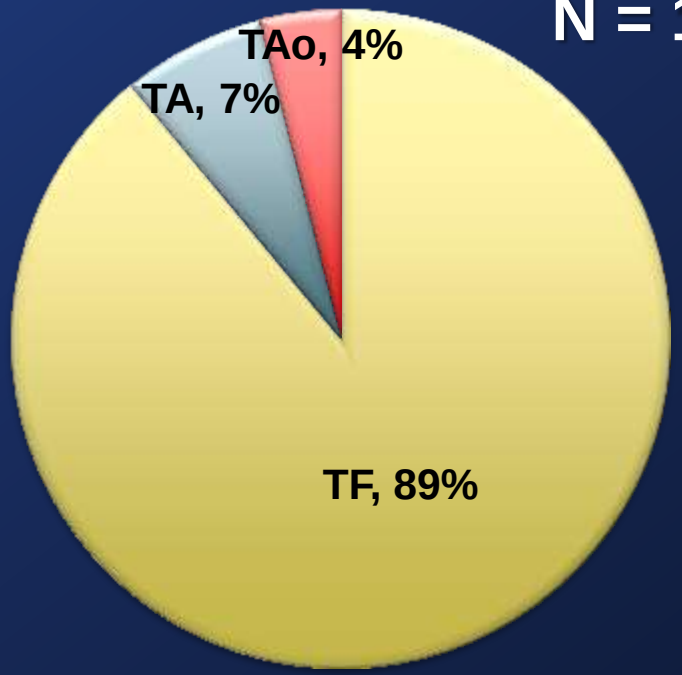
5.3%

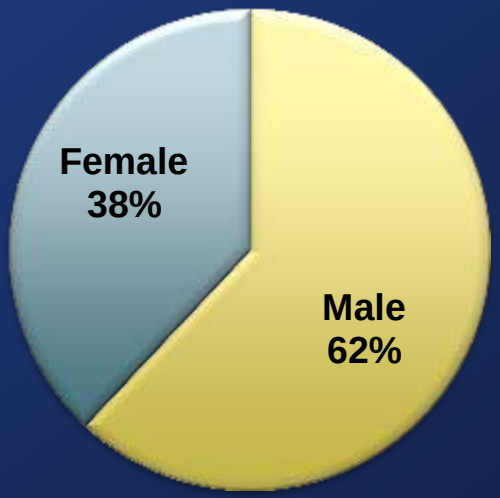
(Median 5.2%)

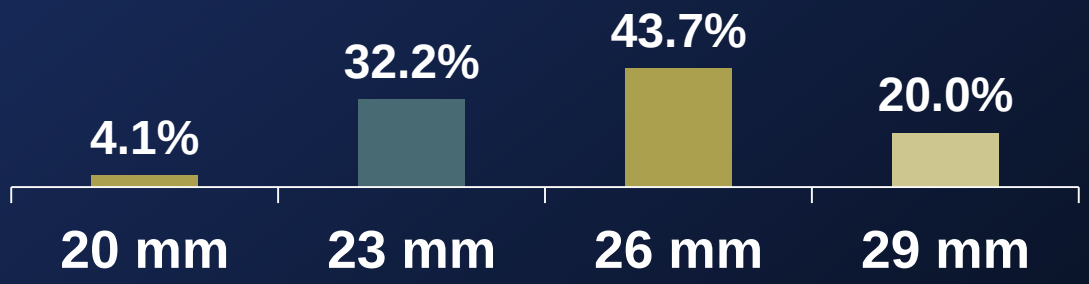
Average Age =

81.9yrs

N = 1076



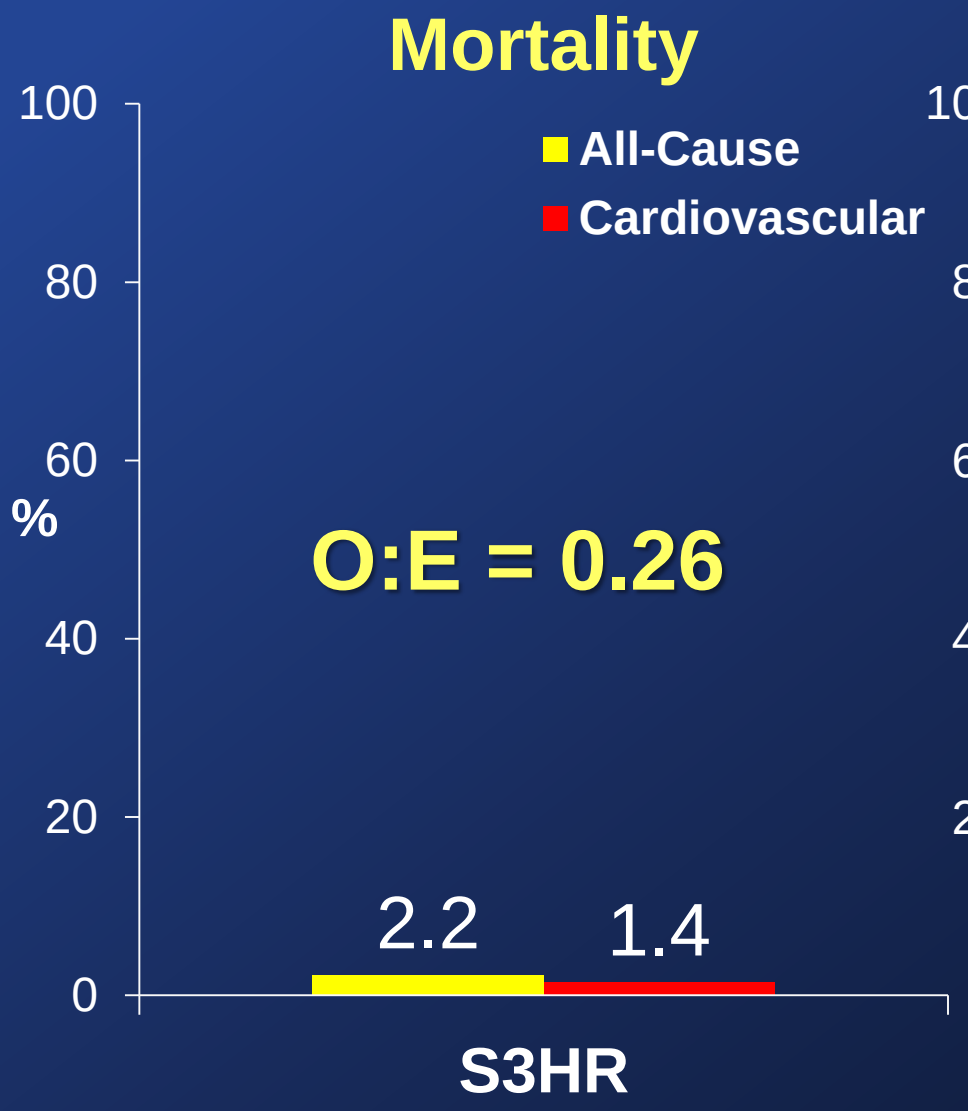


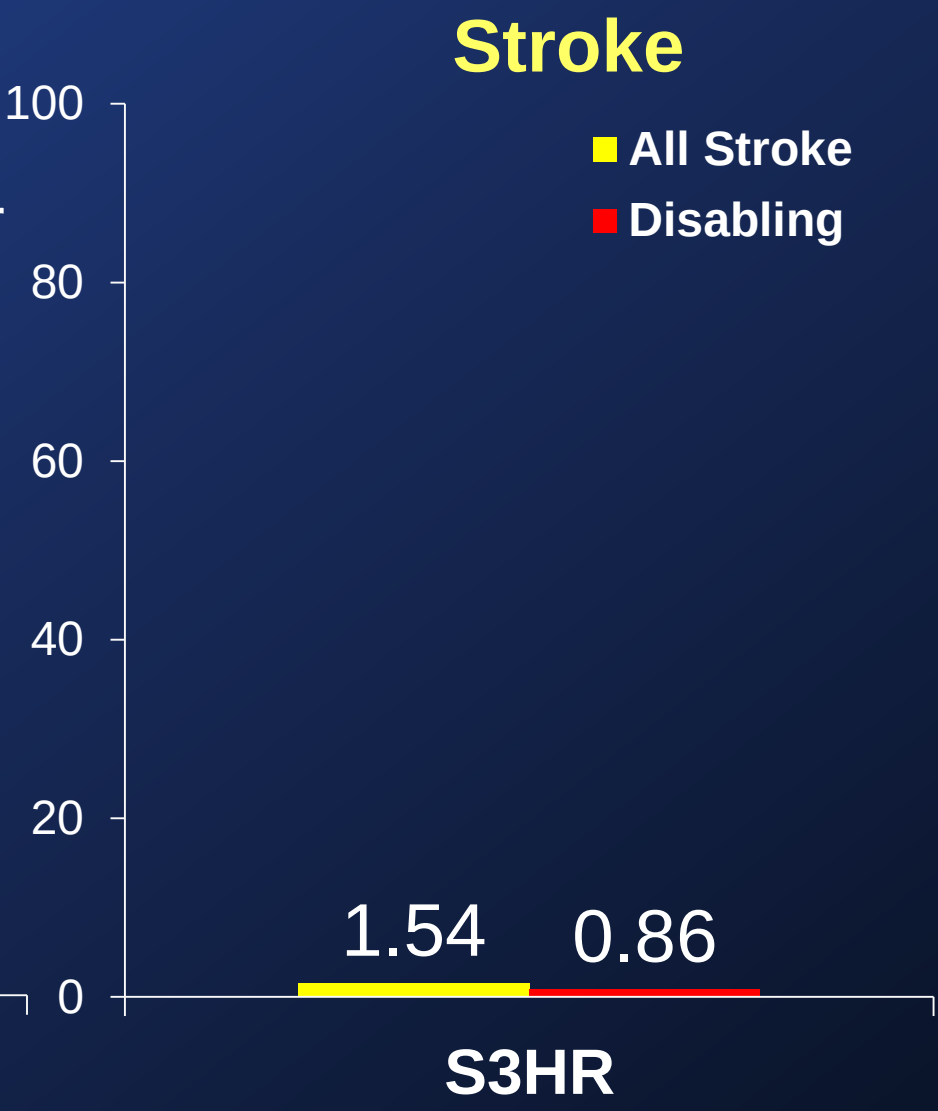


Mortality and Stroke (S3HR)

At 30 Days (As Treated Patients)

THE PARTNER II TRIAL

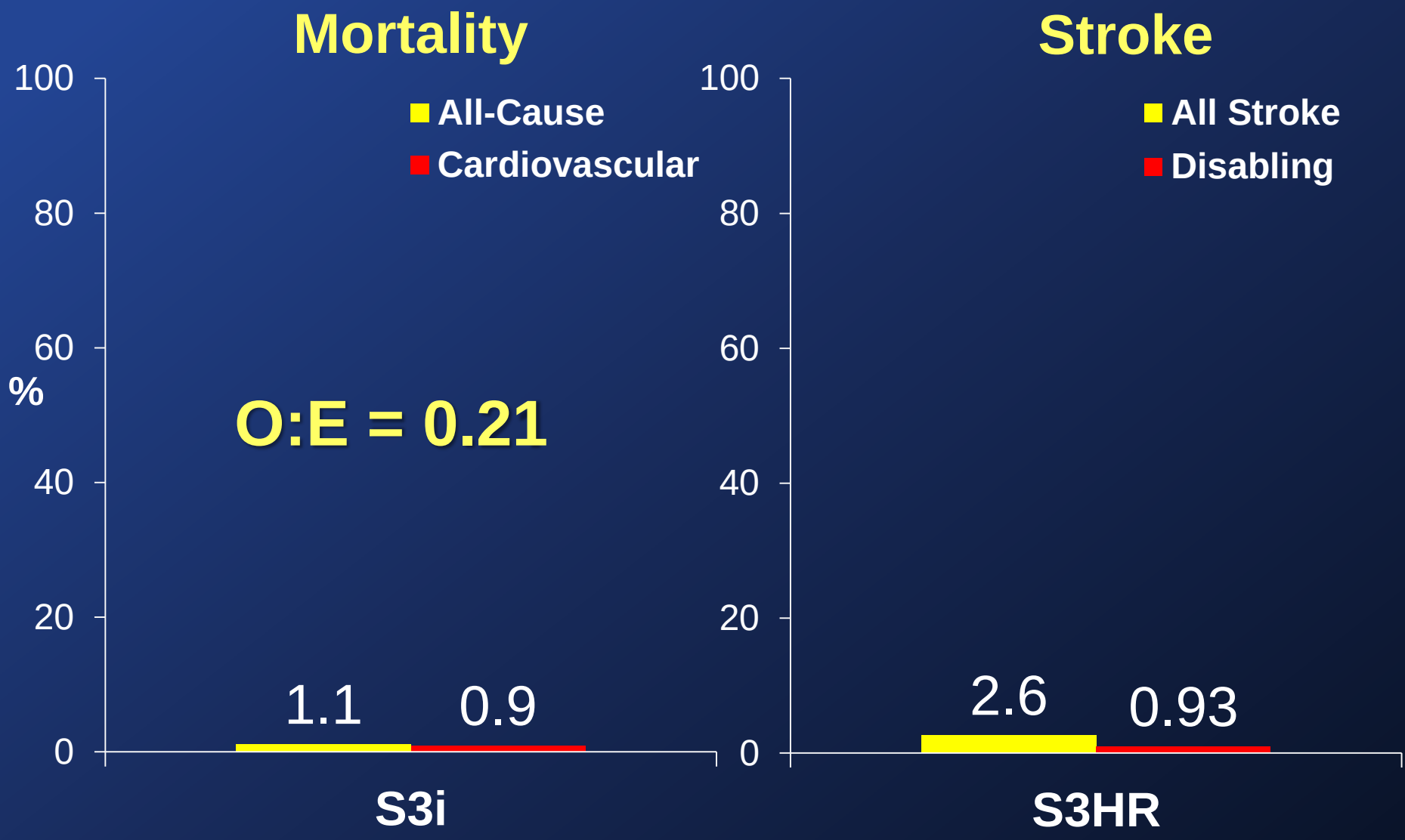




Mortality and Stroke (S3i)

At 30 Days (As Treated Patients)

THE PARTNER II TRIAL



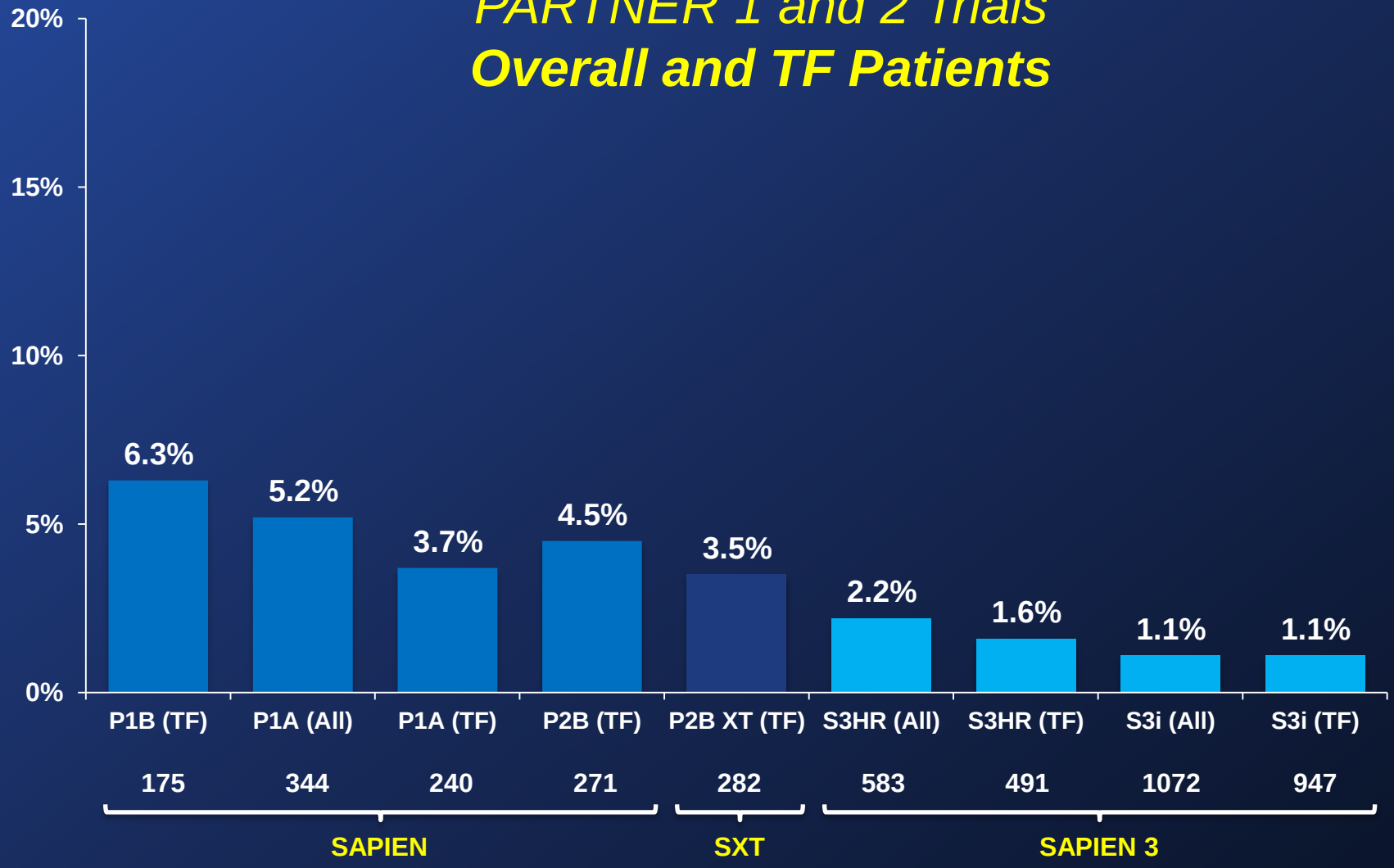
All-Cause Mortality at 30 Days

Edwards SAPIEN Valves (As Treated Patients)

THE PARTNER II TRIAL

PARTNER 1 and 2 Trials

Overall and TF Patients



Strokes
At 30 Days (As Treated Patients)

THE PARTNER II TRIAL

Events (%)	S3HR All (n=583)	S3HR TF (n=491)	S3HR TA/TAo (n=92)	S3i All (n=1076)	S3i TF (n=951)	S3i TA/TAo (n=125)
All	1.54	1.63	1.09	2.60	2.42	4.00
Disabling*	0.86	1.02	0	0.93	0.84	1.60
Non-Disabling	0.69	0.61	1.09	1.67	1.58	2.40
TIA	0.69	0.61	1.09	0.37	0.42	0

**CEC adjudicated or Modified Rankin Score ≥ 2 at 30 days*

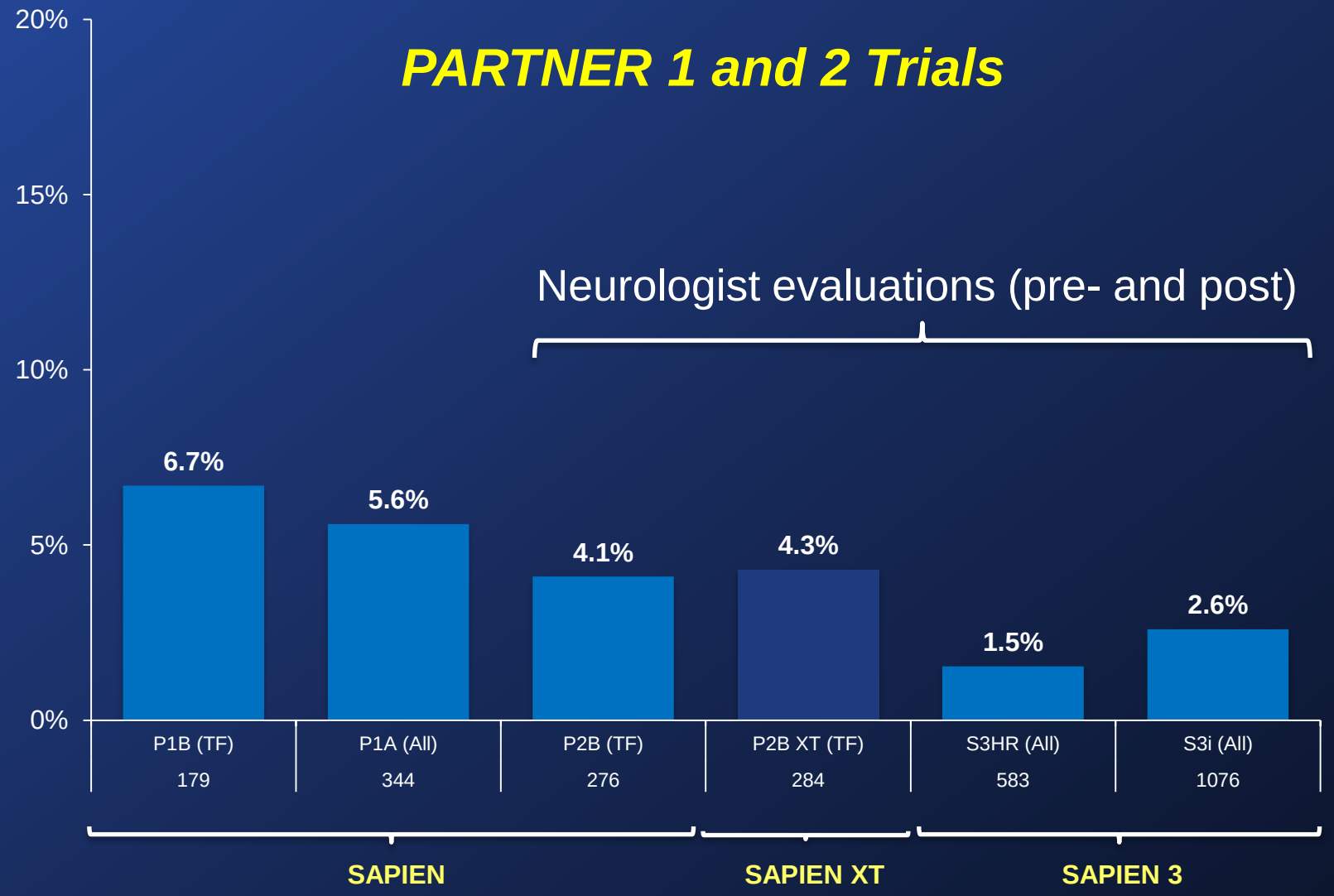
For comparison, the surgical stroke rate at 30 days is 3.5% in a STS PROM > 8% group reported by Thourani et al.

Thourani, V. H. et al. Contemporary Real-World Outcomes of Surgical Aortic Valve Replacement in 141,905 Low-Risk, Intermediate-Risk, and High-Risk Patients. Ann Thorac Surg. 2015; 99: 55-61.

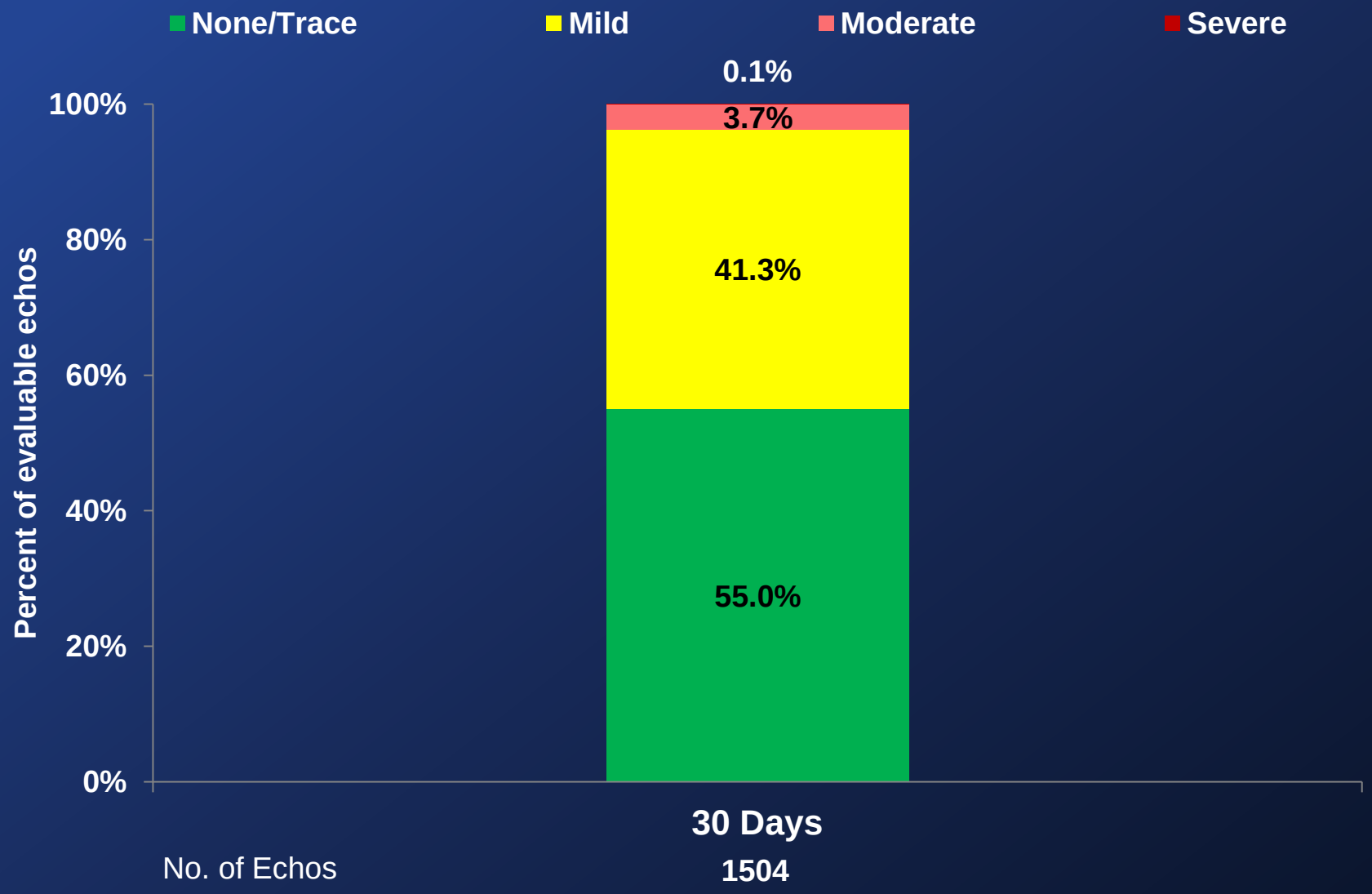
Strokes (All) at 30 Days

Edwards SAPIEN Valves

THE PARTNER II TRIAL



Paravalvular Leak: S3HR & S3i
(Valve Implant Patients)



ACC.15

TCT@ACC-i2 | innovation in intervention

64th Annual Scientific Session & Expo

An All-comers Randomized Clinical Trial Comparing Transcatheter with Surgical Aortic Valve Replacement in Patients with Aortic Valve Stenosis

On behalf of NOTION investigators:

Hans Gustav Hørsted Thyregod, MD

Dep. of Cardiothoracic Surgery

Copenhagen University Hospital, Denmark

MARCH 14 – 16, 2015

SAN DIEGO

CALIFORNIA

Nordic Aortic Valve Intervention (NOTION) Trial

Objective:	Compare TAVR vs. SAVR in patients ≥ 70 years eligible for surgery (all-comers population)
Primary outcome:	Composite rate of death from any cause, stroke or myocardial infarction at 1 year (VARC II-defined)
Secondary outcomes:	Safety and efficacy (NYHA), echocardiographic outcomes (VARC II-defined)
Design:	Prospective, multicenter, non-blinded, randomized trial
Enrollment period:	December 2009 - April 2013

Sample Size Determination

Alternative hypothesis: TAVR is superior to SAVR regarding the composite rate of death from any cause, stroke or myocardial infarction after 1 year

Sample Size Determination:

1:1 treatment allocation
Two-sided alpha = 0.05
Power = 80%

Expected rate$_{SAVR}$ = 15%
Expected rate$_{TAVR}$ = 5%

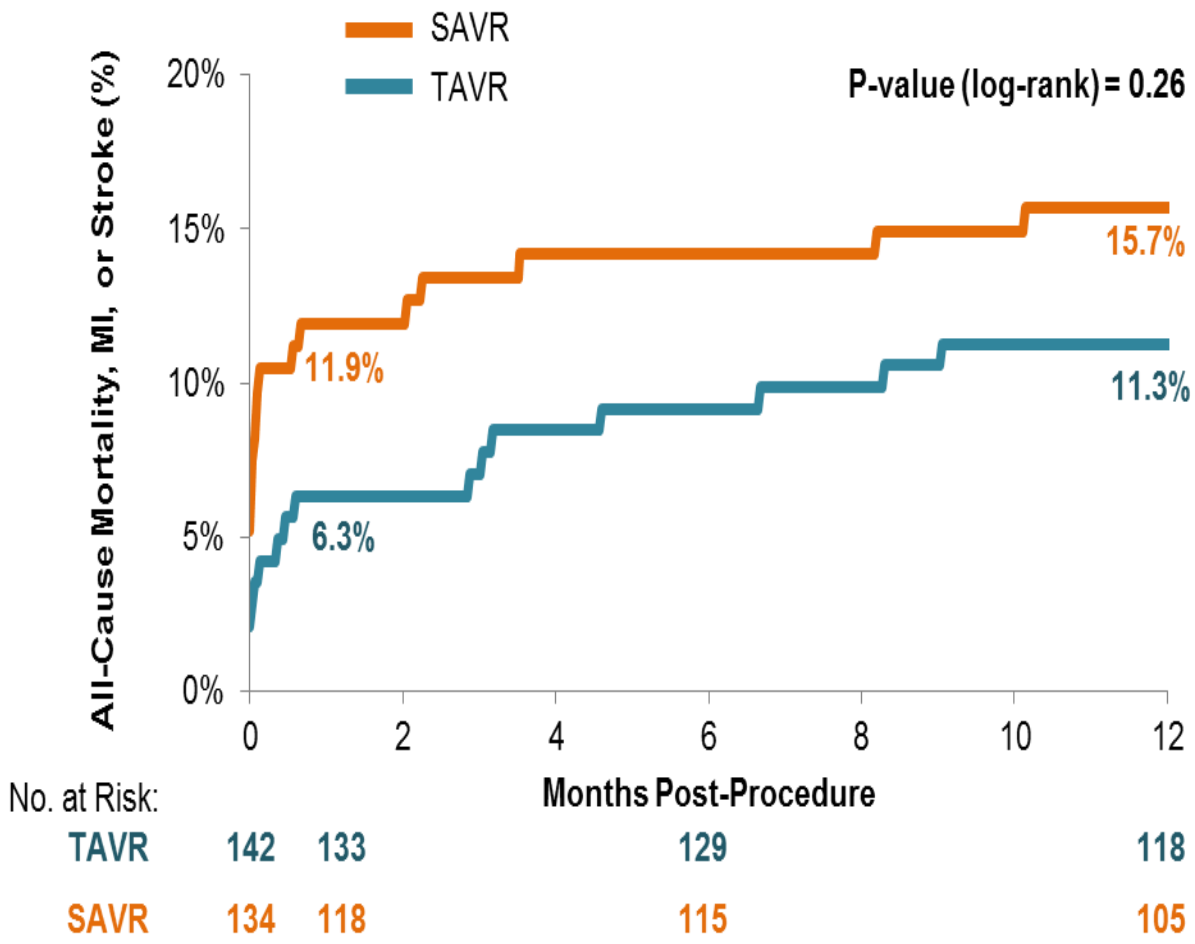
Trial Size: 280 patients

Self-expanding
bio-prosthesis
4 valve sizes
(annulus diameter
18-29 mm)

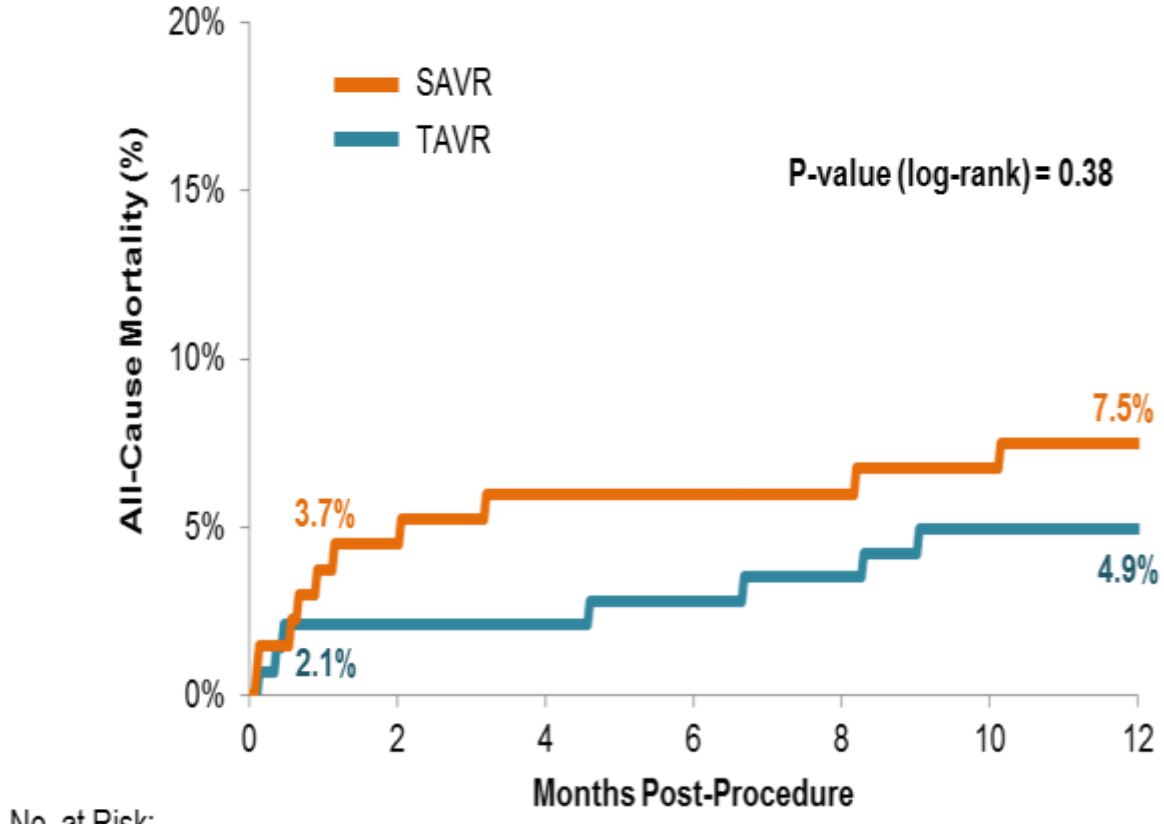
Baseline Characteristics

Characteristic, % or mean ± SD	TAVR n=145	SAVR n=135	p-value
Age (yrs)	79.2 ± 4.9	79.0 ± 4.7	0.71
Male	53.8	52.6	0.84
Society of Thoracic Surgeons (STS) Score	2.9 ± 1.6	3.1 ± 1.7	0.30
STS Score < 4%	83.4	80.0	0.46
Logistic EuroSCORE I	8.4 ± 4.0	8.9 ± 5.5	0.38
NYHA class III or IV	48.6	45.5	0.61

Death from Any Cause, Stroke or Myocardial Infarction at 1 Year in As-Treated Population



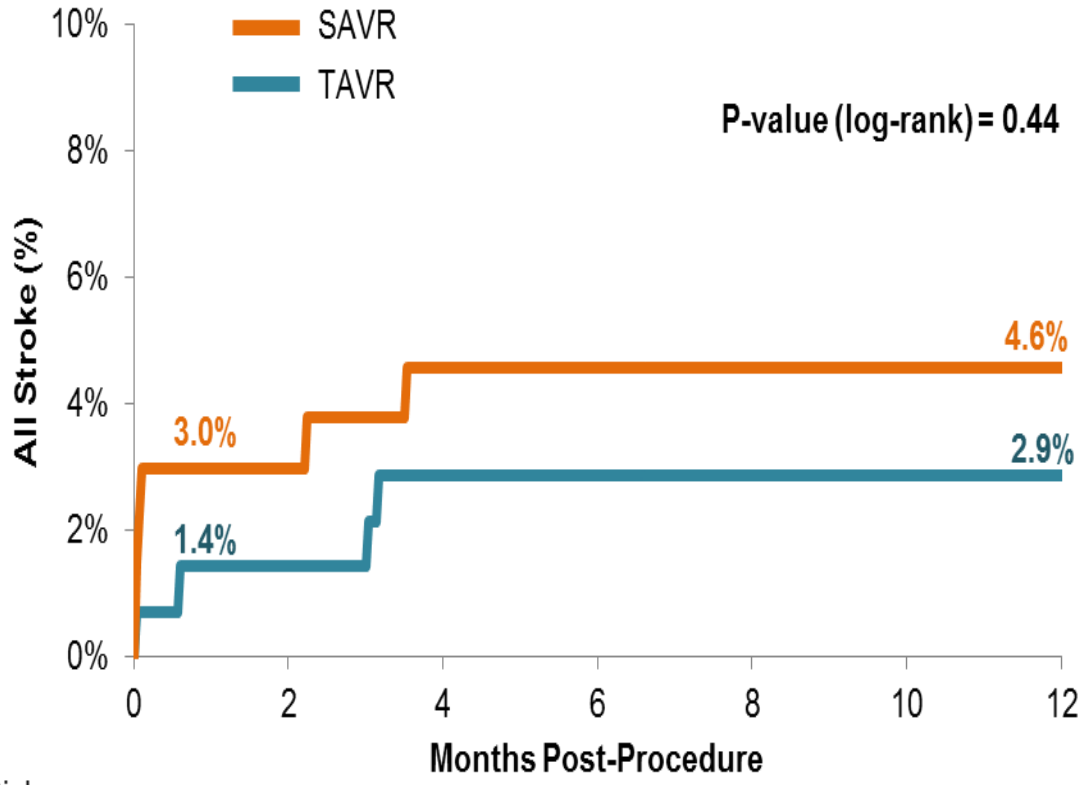
Death from Any Cause at 1 Year



No. at Risk:

TAVR	142	139	137	126
SAVR	134	128	125	115

All Stroke at 1 Year



No. at Risk:

TAVR	142	137	134	123
SAVR	134	124	120	110

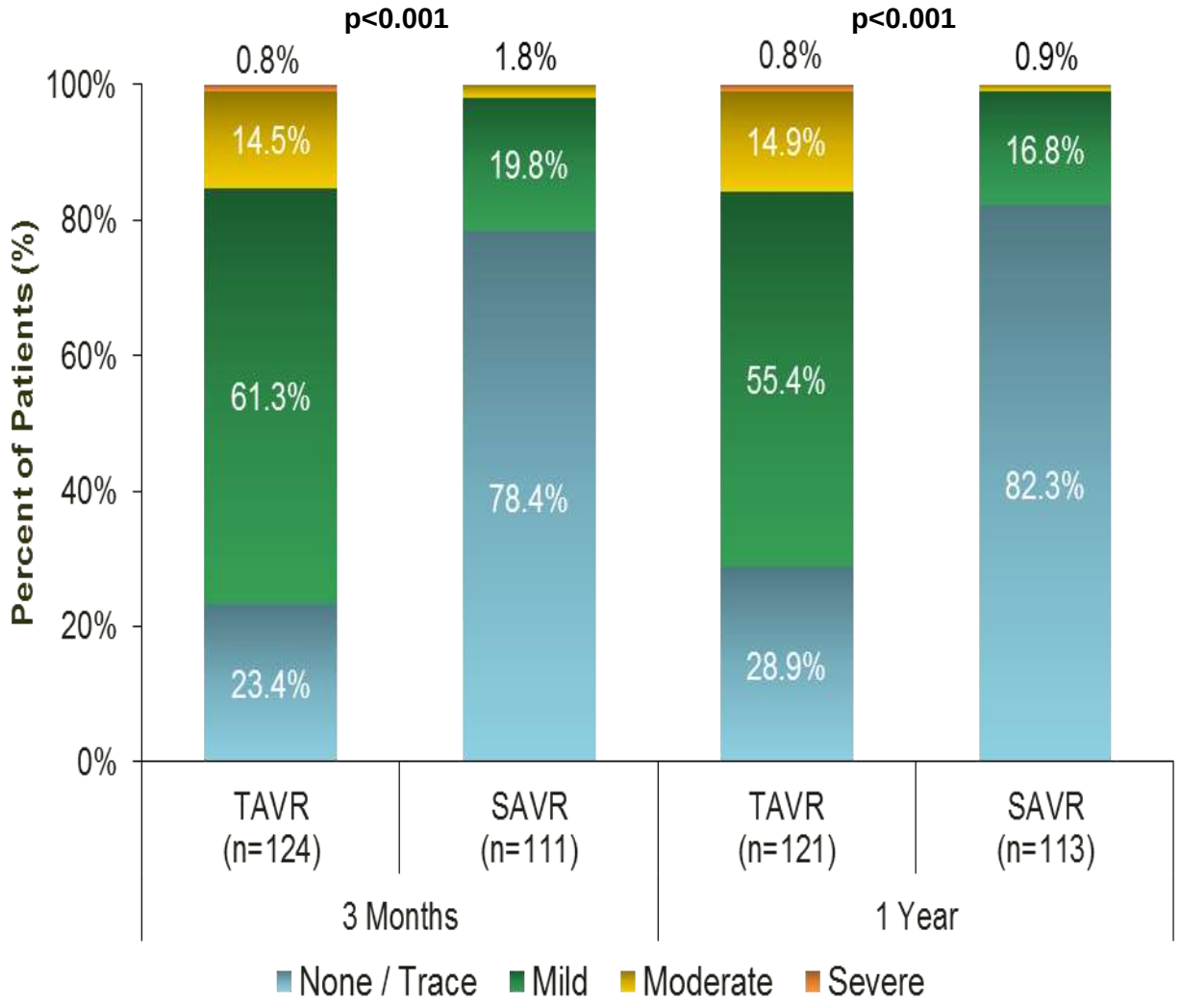
Secondary Outcomes at 30 Days

Outcome, %	TAVR n=142	SAVR n=134	p-value
Death, any cause	2.1	3.7	0.43
Death, cardiovascular	2.1	3.7	0.43
Bleeding, life-threatening+major	11.3	20.9	0.03
Cardiogenic shock	4.2	10.4	0.05
Vascular lesion, major	5.6	1.5	0.10
Acute kidney injury (stage II+III)	0.7	6.7	0.01
Stroke	1.4	3.0	0.37
TIA	1.4	0	0.17
Myocardial infarction	2.8	6.0	0.20
Atrial fibrillation	16.9	57.8	<0.001
Pacemaker	34.1	1.6	<0.001

Secondary Outcomes at 1 Year

Outcome, %	TAVR n=142	SAVR n=134	p-value
Death, any cause	4.9	7.5	0.38
Death, cardiovascular	4.3	7.5	0.25
Stroke	2.9	4.6	0.44
TIA	2.1	1.6	0.71
Myocardial infarction	3.5	6.0	0.33
Atrial fibrillation	21.2	59.4	<0.001
Pacemaker	38.0	2.4	<0.001
Aortic valve re-intervention	0.0	0.0	na

Aortic Valve Regurgitation



CoreValve Evolut System

EnVeo R w/
InLine Sheath

18 Fr
OD

14 F Equivalent

Procedural Result

Event, %	N=60
Absence of procedural mortality	100.0 (60/60)
Correct positioning of 1 valve in proper location	98.3 (59/60)
Mean gradient < 20 mm Hg or peak velocity < 3m/sec	98.3 (59/60)
Absence of moderate or severe regurgitation	93.3 (56/60)
Absence of patient prosthesis mismatch*	83.6 (46/55)
Absence of moderate or severe PVL	96.6
VARC-2 device success	78.6 (44/56)

30-Day Event, %

Event, %	N=60
All-cause mortality	0.0
All stroke	0.0
Absence of moderate or severe PVL	96.6
Permanent pacemaker implantation	11.7

Final Thoughts

- 5 year data from PARTNER demonstrates mid-term durability of TAVR
- 2 year data from CoreValve demonstrates continued superiority of TAVR over SAVR
- The Sapien 3 data demonstrates continued improvement in outcomes in high risk and intermediate risk patients with next gen devices
- All-comers trial is challenging but current data supports movement of TAVR into lower risk patients