Current Evidence:
TAVR Balloon Expandable System

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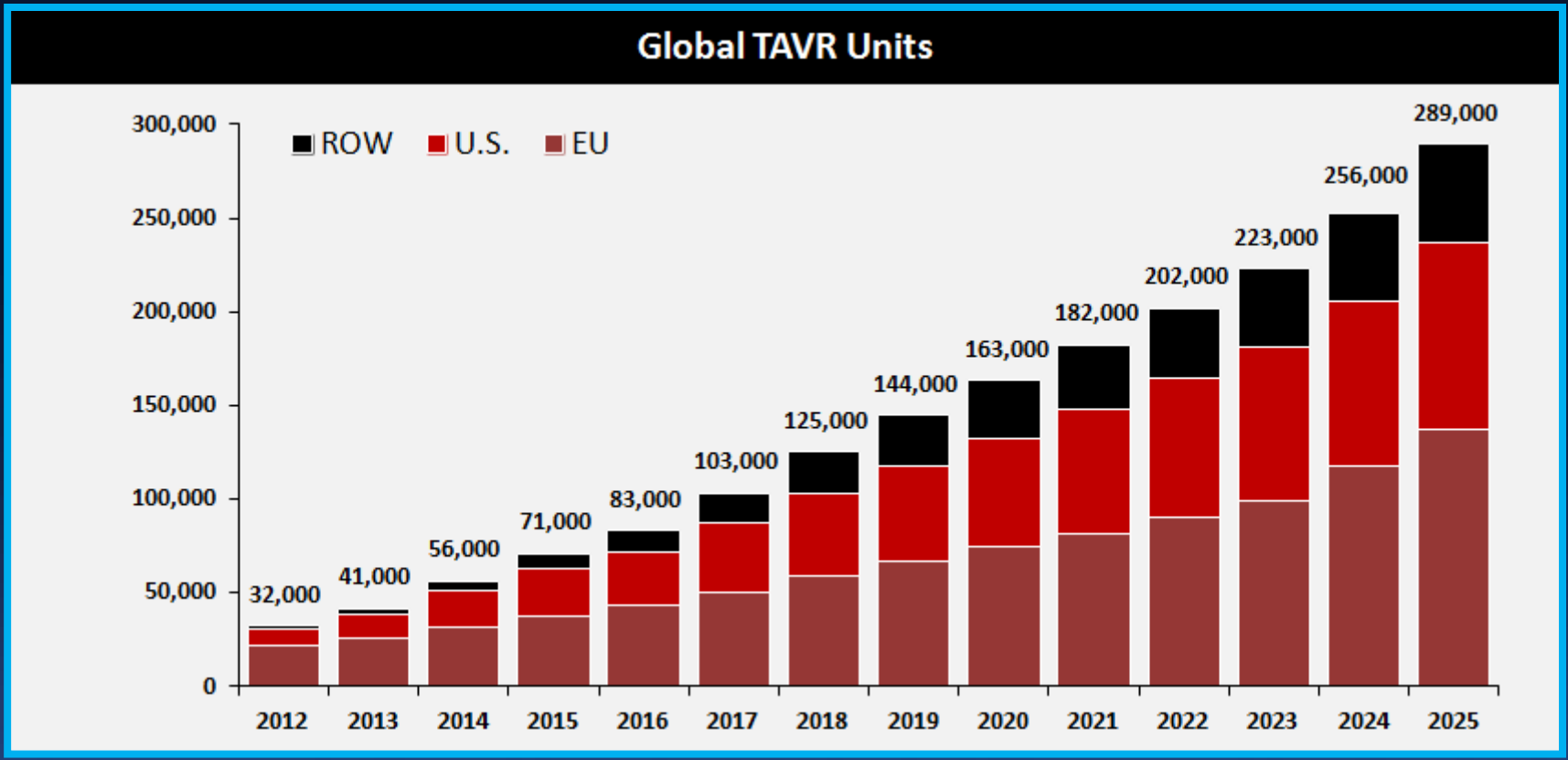
Disclosure Statement of Financial Interest

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

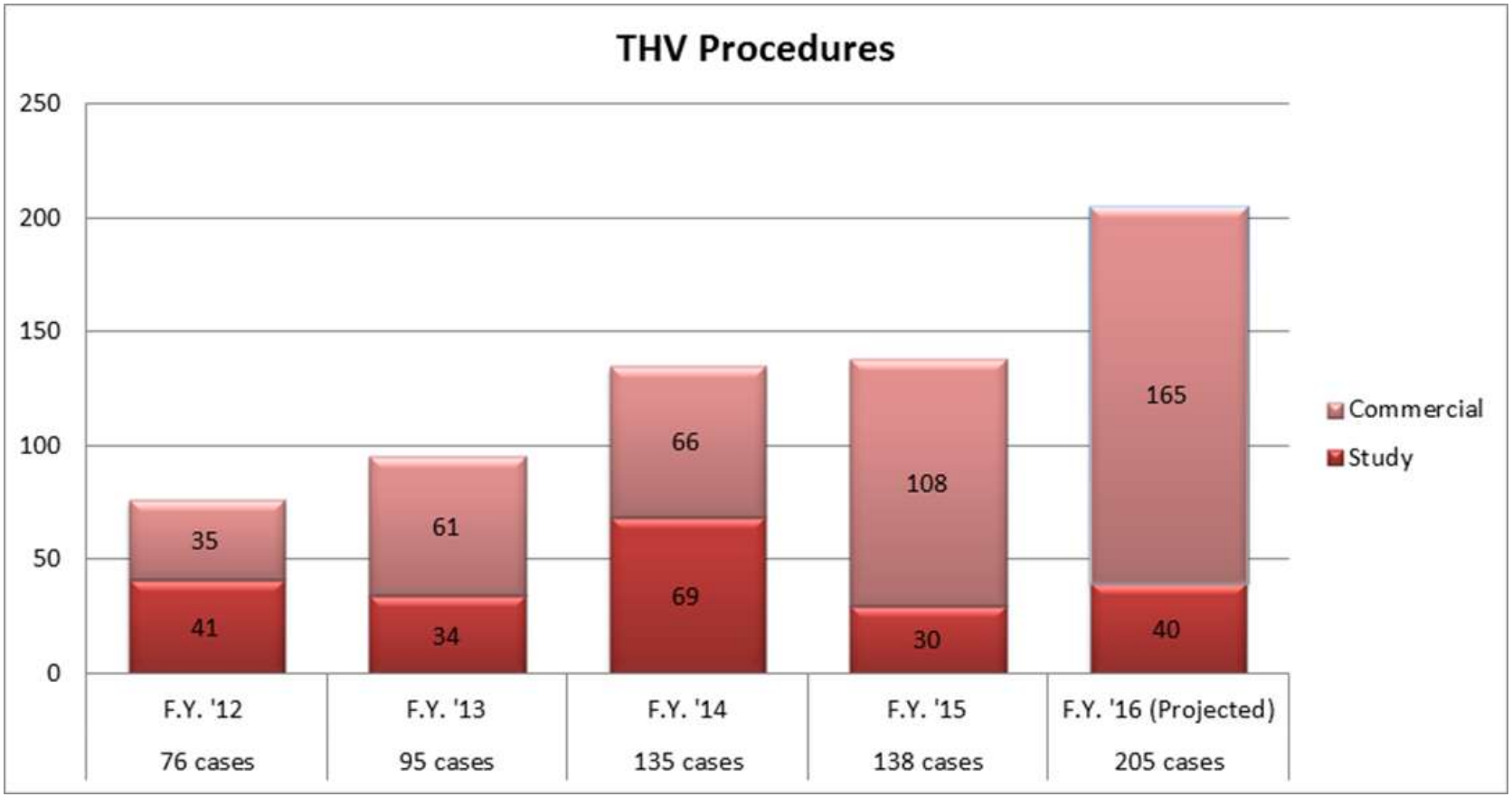
Affiliation/Financial Relationship	Company
• Grant/Research Support	• Edwards Lifesciences
• Grant/Scientific Advisory Board	• Medtronic
• Executive Physician Council	• Boston Scientific Corp

Estimated Global TAVR Growth



SOURCE: Credit Suisse TAVI Comment –January 8, 2015. ASP assumption for 2024 and 2025 based on analyst model. Revenue split assumption in 2025 is 45% U.S., 35% EU, 10% Japan, 10% ROW

In the next 10 years, TAVR growth will increase X4!


THV Procedures
250
200
150
100
50
0
35
41
61
34
66
69
108
30
165
40
Commercial
Study
F.Y. '12
76 cases
F.Y. '13
95 cases
F.Y. '14
135 cases
F.Y. '15
138 cases
F.Y. '16 (Projected)
205 cases

PARTNER SAPIEN Platforms
Device Evolution

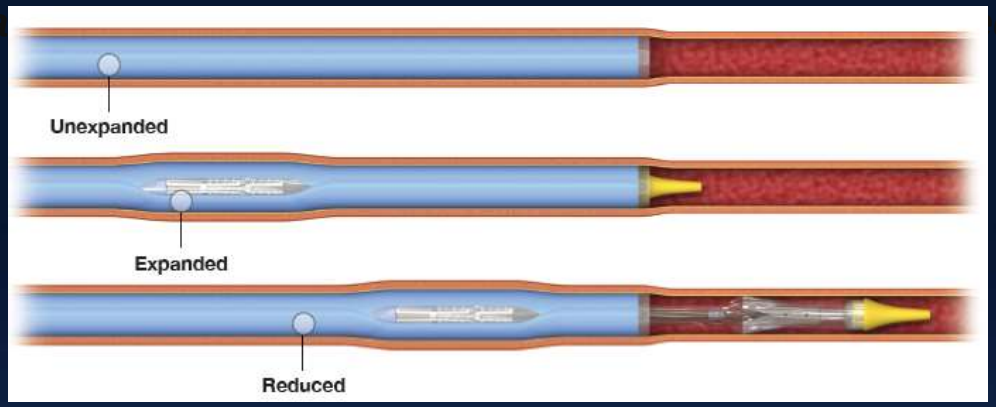
THE PARTNER II TRIAL

	SAPIEN	SAPIEN XT	SAPIEN 3
Valve Technology			
Sheath Compatibility			
Available Valve Sizes	23 mm, 26 mm	23mm, 26mm, 29mm*	20 mm, 23 mm, 26 mm, 29 mm

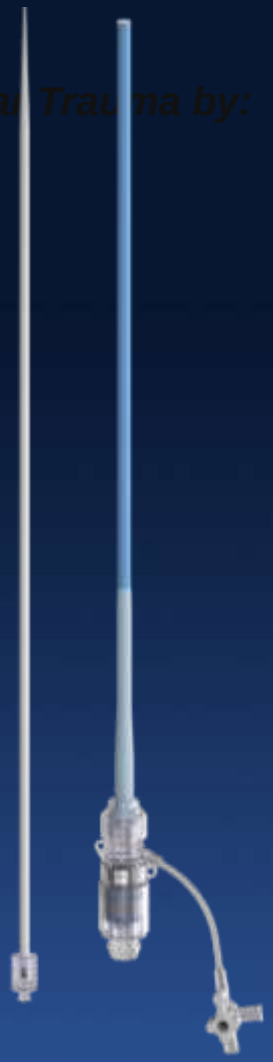
*First Implant Oct 30, 2012

Edwards Expandable Introducer Sheath

The Dyna duce Vascular Trau na by:

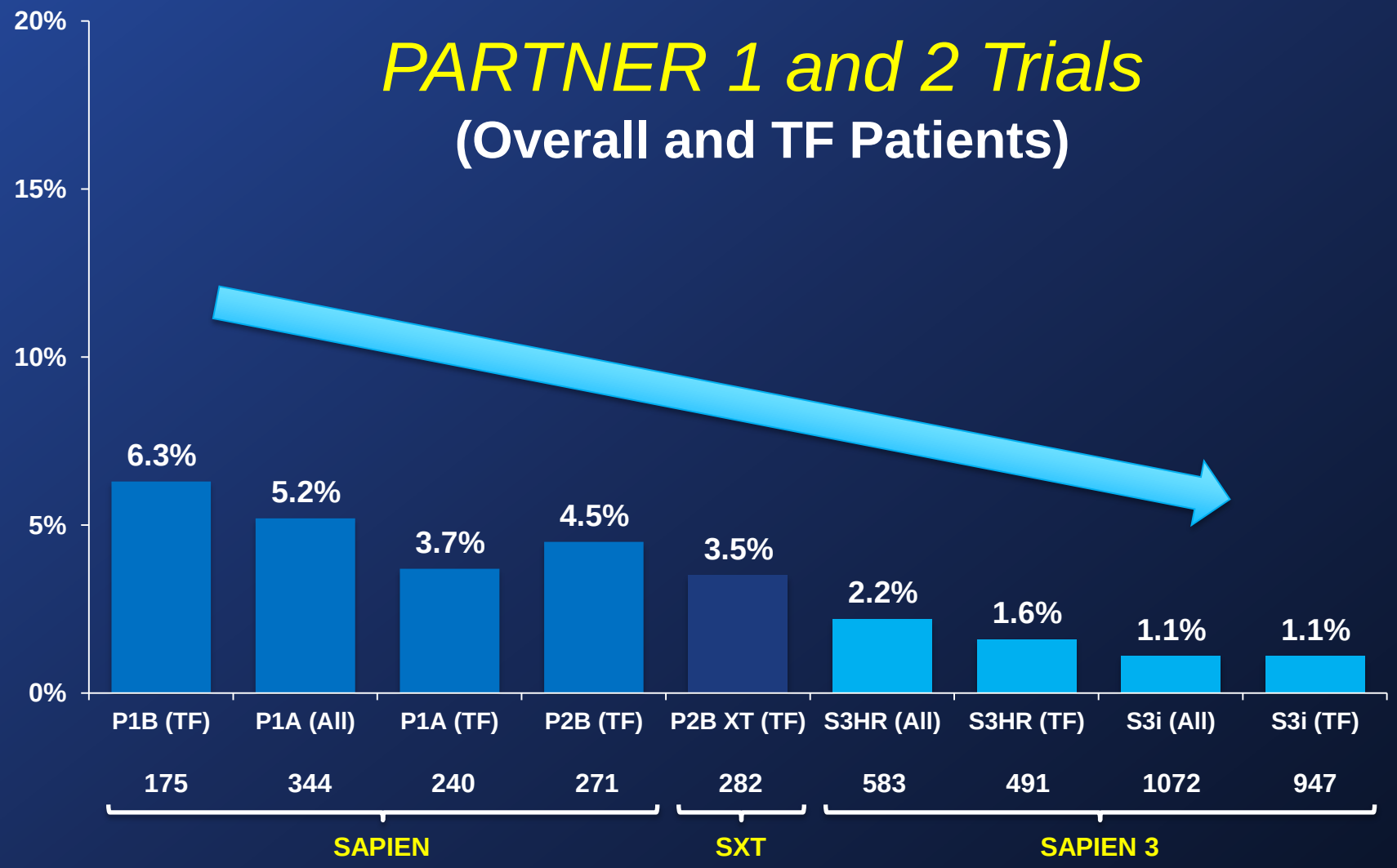


THV	eSheath I.D. (unexpanded)	eSheath OD (unexpanded)	Minimum Vessel Diameter*
23 mm SAPIEN 3	**14F (4.6 mm)**	**6.0 mm**	**5.5 mm**
26 mm SAPIEN 3	**14F (4.6 mm)**	**6.0 mm**	**5.5 mm**
29 mm SAPIEN 3	**16F (5.3 mm)**	**6.7 mm**	**6.0 mm**
23 mm SAPIEN XT	16F (5.3 mm)	6.7 mm	6.0 mm
26 mm SAPIEN XT	18F (5.9 mm)	7.2 mm	6.5 mm
29 mm SAPIEN XT	20F (6.6 mm)	8.0 mm	7.0 mm



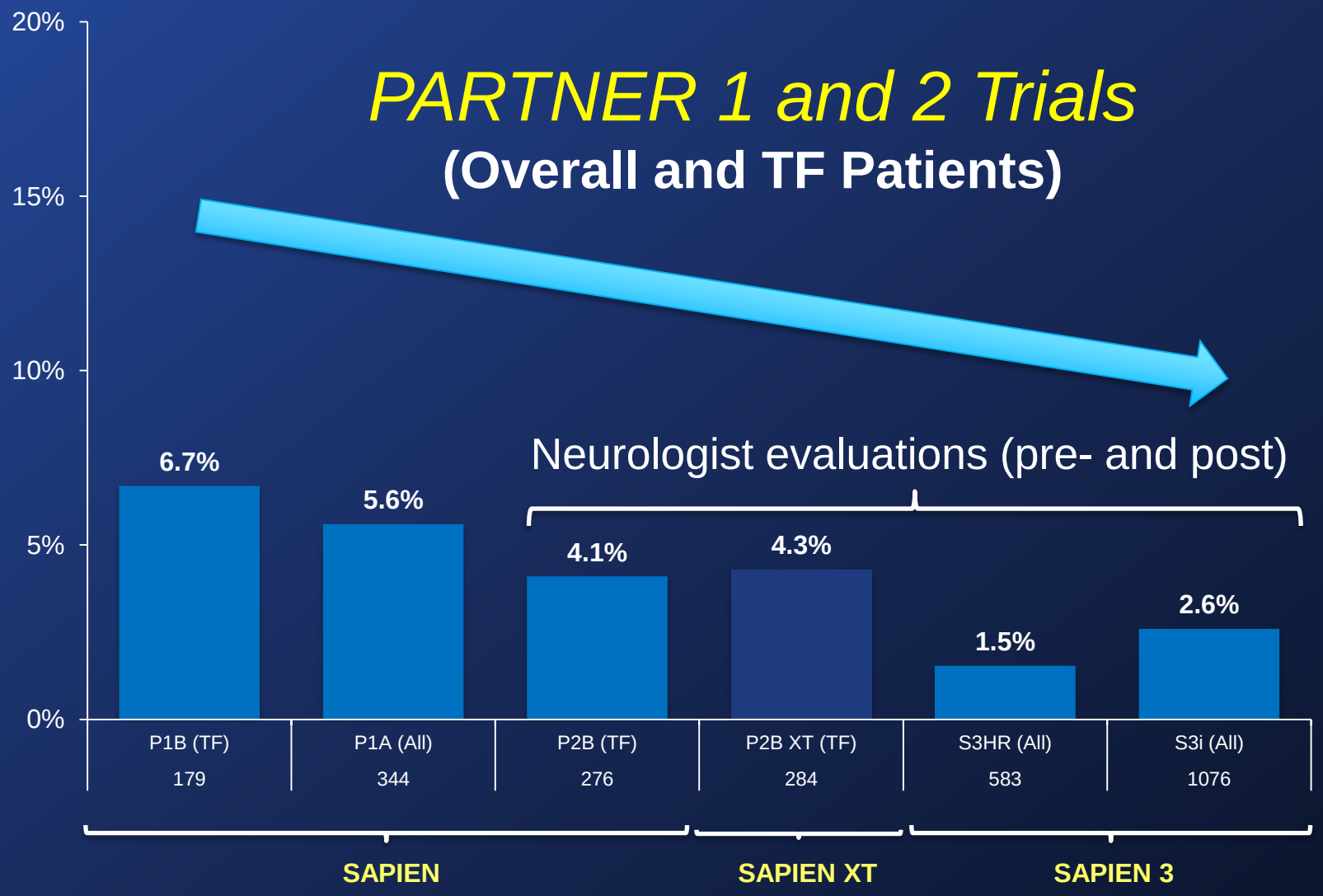
All-Cause Mortality at 30 Days

Edwards SAPIEN Valves (As Treated)



Strokes (All) at 30 Days

Edwards SAPIEN Valves



TAVR Categories
(risk is a continuum)

THE PARTNER II TRIAL

Operable AS patients

Low Risk	Moderate Risk	High Risk	Extr Risk*	Too Sick

TAVR in 2015

irresponsible, reckless	"equipoise"	OK	preferred	No

** Extreme (prohibitive) risk = "inoperable"*

Transcatheter or Surgical Aortic Valve Replacement in Intermediate Risk Patients with Aortic Stenosis:

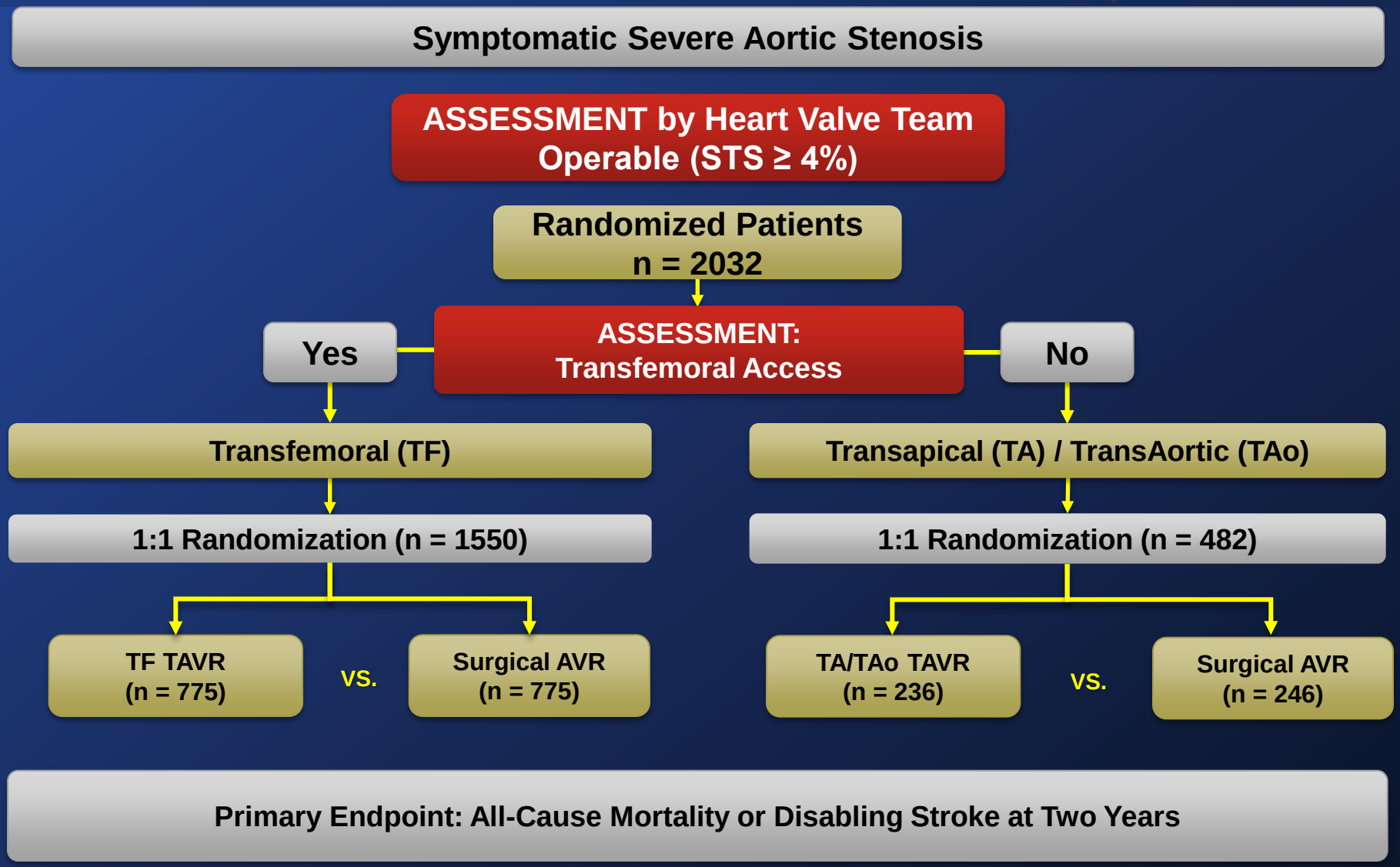
Final Results from the PARTNER 2A Trial

Craig R. Smith, MD
on behalf of the PARTNER Trial Investigators

ACC 2016 | Chicago | April 2, 2016

THE PARTNER II TRIAL

The PARTNER 2A Trial
Study Design



The PARTNER 2A Trial
Top Enrolling Sites

THE PARTNER II TRIAL

Columbia University	New York, NY Susheel Kodali & Mathew Williams	**206**
Cedars-Sinai Medical Center	Los Angeles, CA Raj Makkar & Alfredo Trento	**205**
Emory University	Atlanta, GA Vinod Thourani & Vasilis Babaliaros	**149**
University of Pennsylvania	Philadelphia, PA Howard Herrmann & Joseph Bavaria	**82**
Medical City Dallas	Dallas, TX Bruce Bowers & Todd Dewey	**75**
Barnes Jewish / Washington University	St. Louis, MO Alan Zajarias & Hersh Maniar	**68**
Washington Hospital Center	Washington, DC Augusto Pichard & Paul Corso	**57**
Stanford University	Palo Alto, CA Craig Miller & Alan Yeung	**53**
Mayo Clinic	Rochester, MN Verghese Mathew & Kevin Greason	**53**
Baylor Heart Hospital	Plano, TX William Brinkman & David Brown	**52**
Providence Heart & Vascular Institute	Portland, OR Robert Hodson & Jeffrey Swanson	**52**
The Christ Hospital	Cincinnati, OH Dean Kereiakes & Thomas Ivey	**49**
Intermountain Medical Ctr.	Murray, UT Brian Whisenant & Kent Jones	**49**
University of Virginia	Charlottesville, VA Irving Kron & Scott Lim	**48**
Scripps Green Hospital	La Jolla, CA Paul Teirstein & Scot Brewster	**42**
Brigham Women's Hospital	Boston, MA Ralph Bolman, III & Frederick G. Welt	**41**

Study Populations
ITT to AT Patient Dropouts

THE PARTNER II TRIAL

Randomized
n = 2032

TAVR (ITT) n = 1011		Surgery (ITT) n = 1021
0.6% (6)	Died before treatment - % (no.)	0.5% (5)
0	Ineligible post-randomization - % (no.)	0.4% (4)
1.1% (11)	Withdrawal - % (no.)	6.7% (68)
1.7% (17)	Total - % (no.)	7.5% (77)

Procedure Initiated (AT)
n = 994

Procedure Initiated (AT)
n = 944

Baseline Patient Characteristics
Demographics and Vascular Disease

THE PARTNER II TRIAL

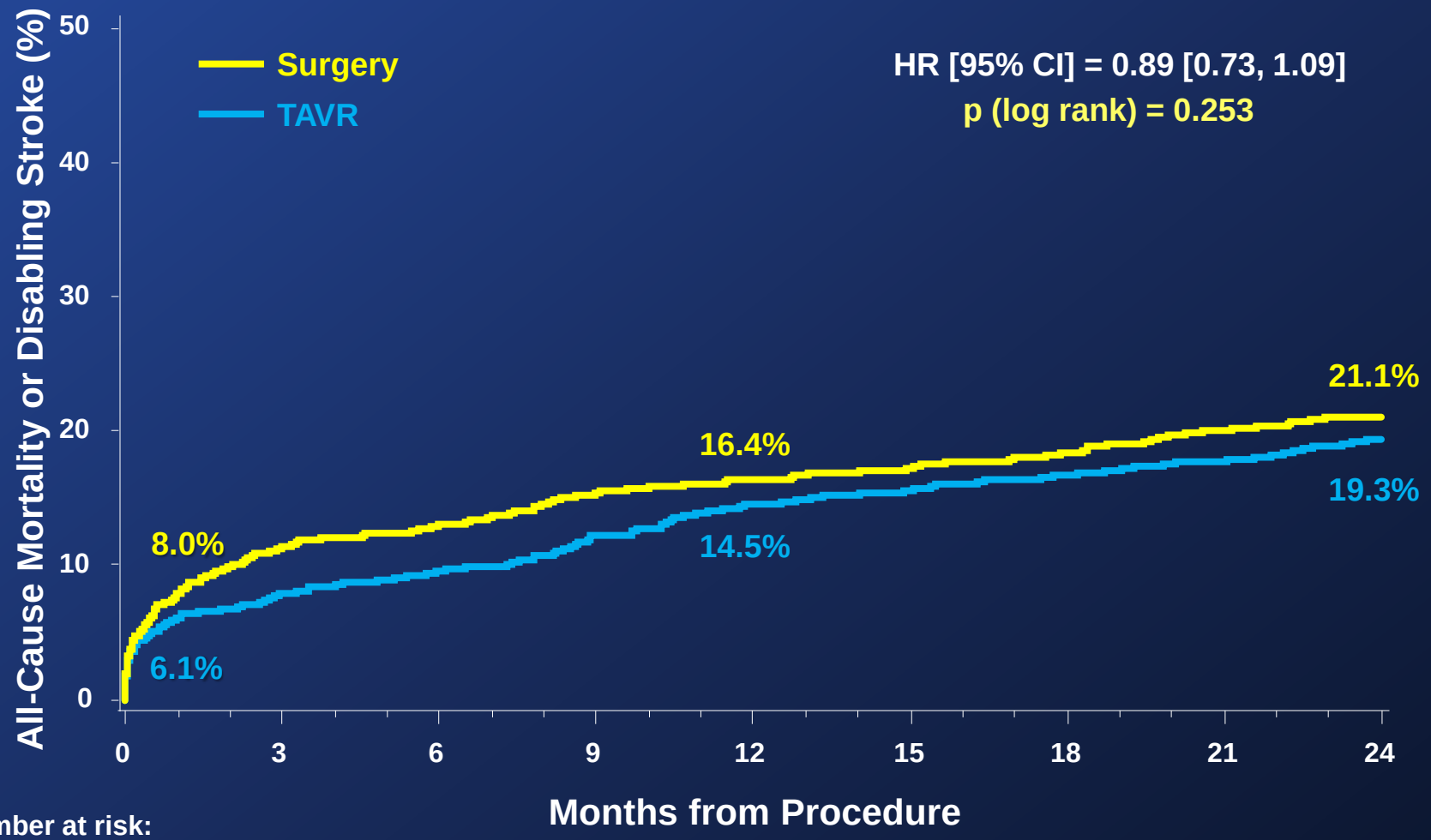
Characteristic	TAVR (n = 1011)	Surgery (n = 1021)	p-value
Age - yrs	81.5 ± 6.7	81.7 ± 6.7	0.63
Male - %	54.2	54.8	0.79
STS Score - %	5.8 ± 2.1	5.8 ± 1.9	0.29
NYHA Class III or IV - %	77.3	76.1	0.53
CAD - %	69.2	66.5	0.20
Prior CABG - %	23.6	25.6	0.33
Cerebrovascular Disease - %	32.1	31.0	0.60
PVD - %	27.9	32.9	0.02

Baseline Patient Characteristics
Other Co-morbidities

THE PARTNER II TRIAL

Characteristic (%)	TAVR (n = 1011)	Surgery (n = 1021)	p-value
Diabetes	37.7	34.2	0.11
COPD - Any	31.8	30.0	0.48
O_2 dependent	3.4	3.1	0.64
Creatinine > 2 mg/dL	5.0	5.2	0.92
Atrial Fibrillation	31.0	35.2	0.05
Permanent Pacemaker	11.7	12.0	0.84
Frailty (15 ft walk > 7 s)	44.4	46.4	0.43
Liver Disease	1.9	2.5	0.37

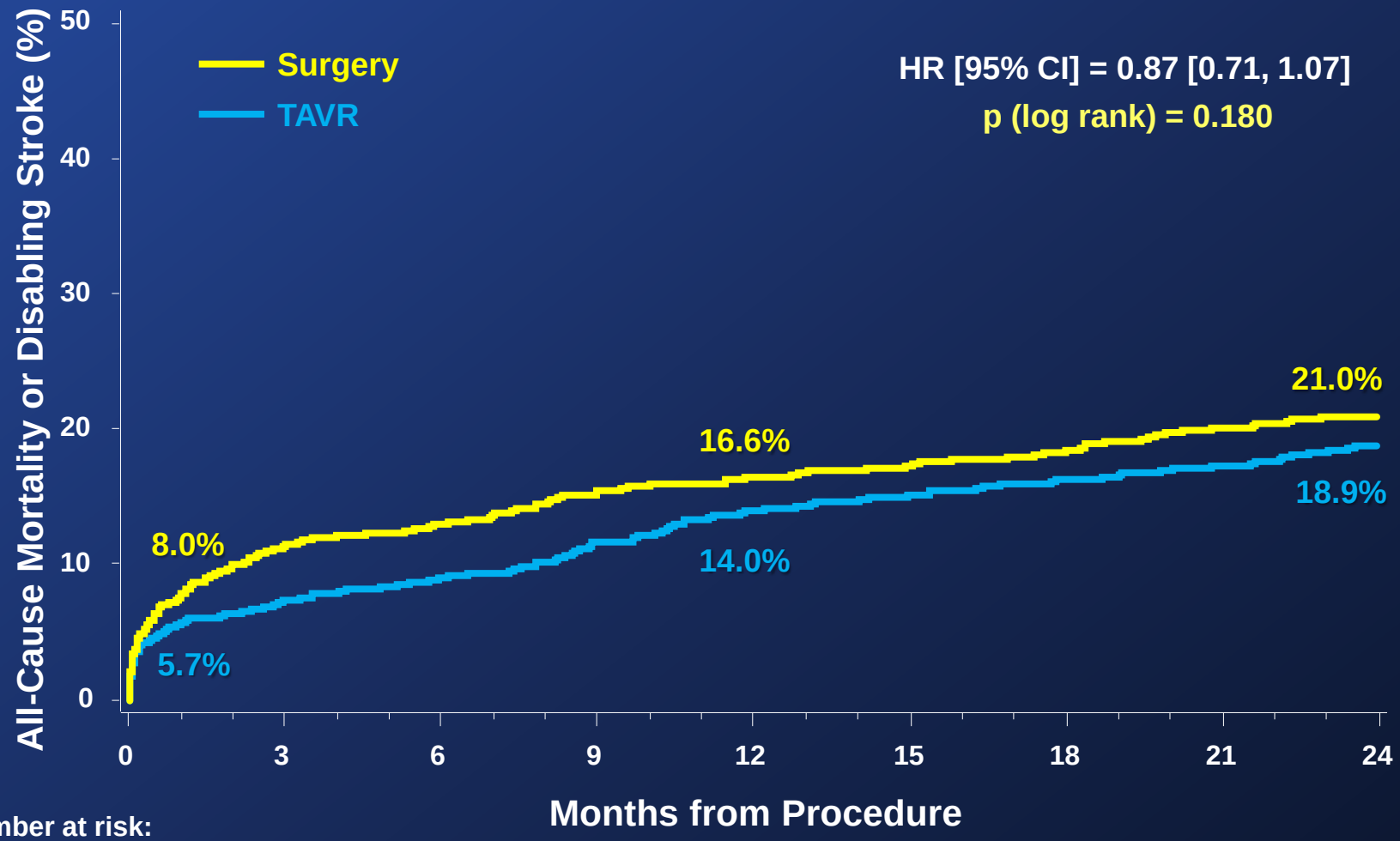
Primary Endpoint (ITT)
All-Cause Mortality or Disabling Stroke



Number at risk:

Surgery	1021	838	812	783	770	747	735	717	695
TAVR	1011	918	901	870	842	825	811	801	774

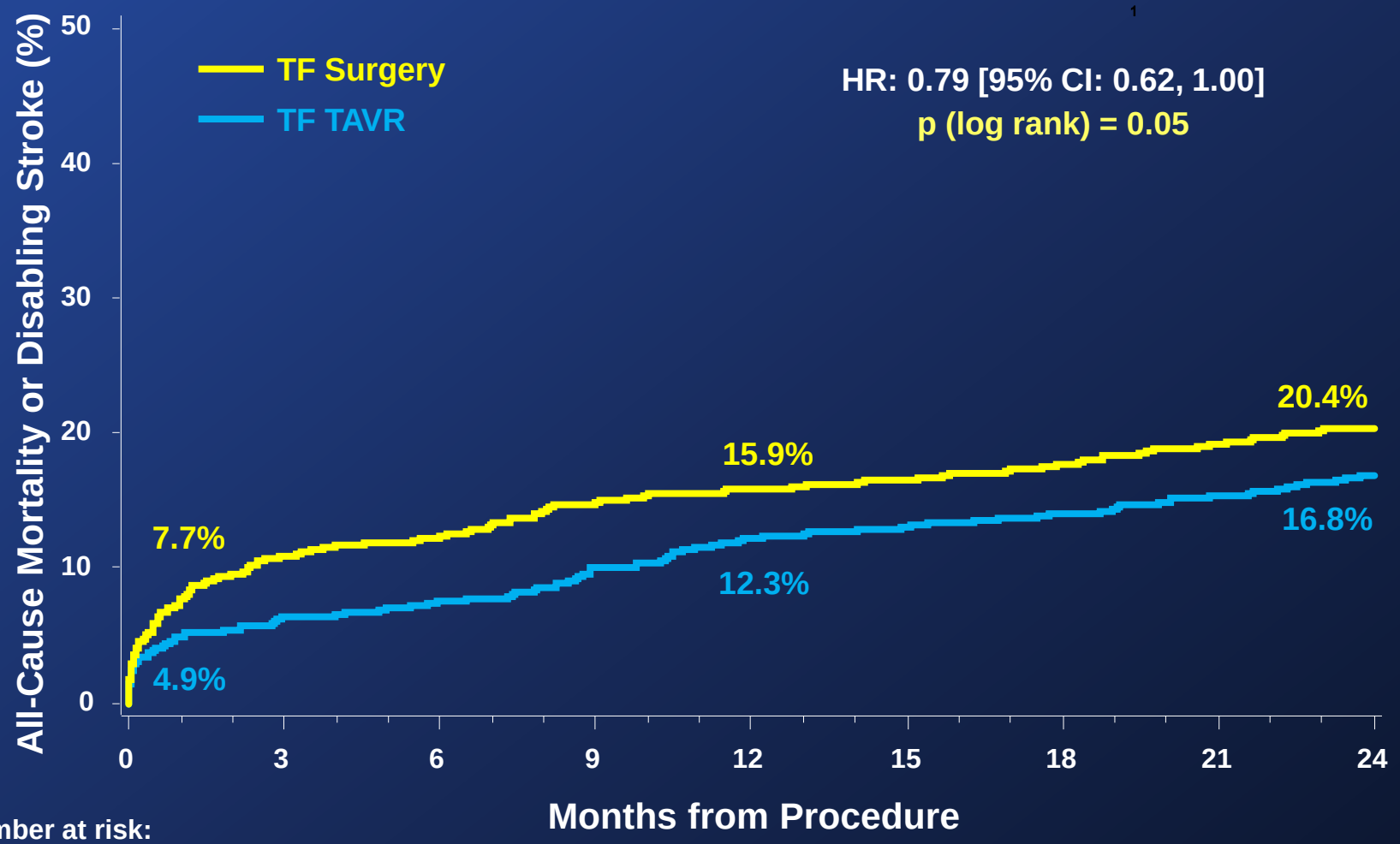
Primary Endpoint (AT)
All-Cause Mortality or Disabling Stroke



Number at risk:

Surgery	944	826	807	779	766	743	731	715	694
TAVR	994	917	900	870	842	825	811	801	774

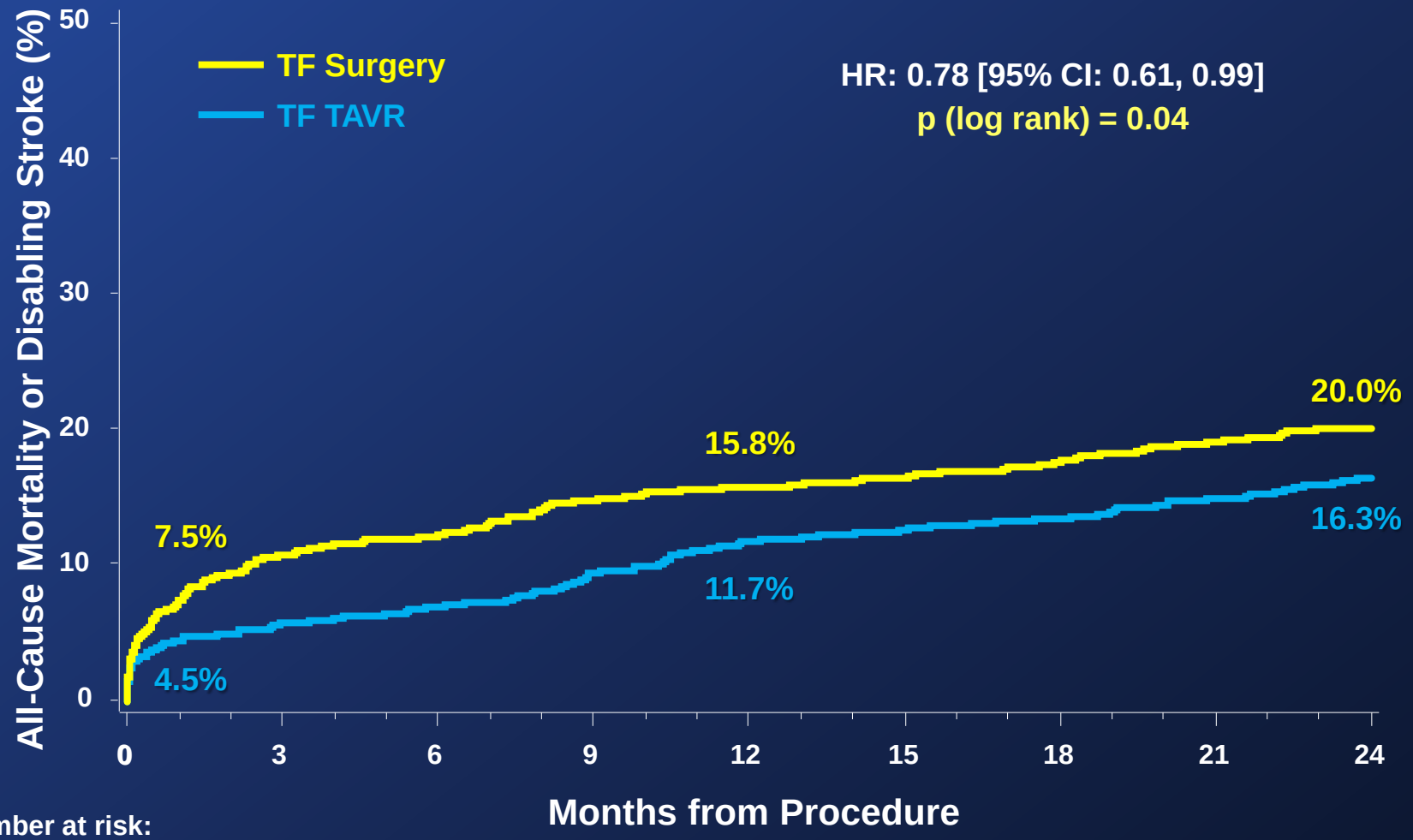
TF Primary Endpoint (ITT)
All-cause Mortality or Disabling Stroke



Number at risk:

TF Surgery	775	643	628	604	595	577	569	557	538
TF TAVR	775	718	709	685	663	652	644	634	612

TF Primary Endpoint (AT)
All-Cause Mortality or Disabling Stroke



Number at risk:

TF Surgery	722	636	624	600	591	573	565	555	537
TF TAVR	762	717	708	685	663	652	644	634	612

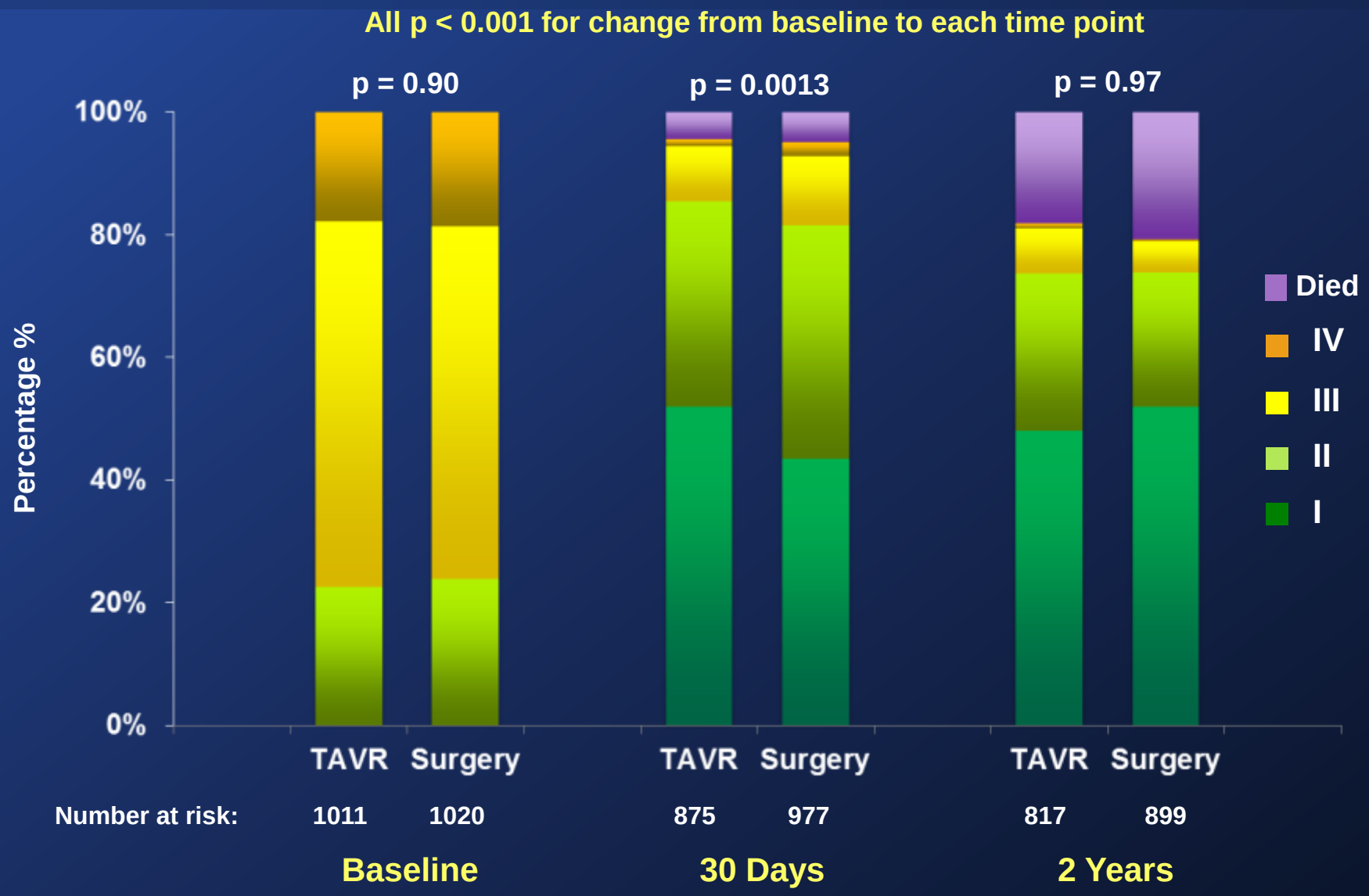
Other Clinical Endpoints (ITT)
At 30 Days and 2 Years

THE PARTNER II TRIAL

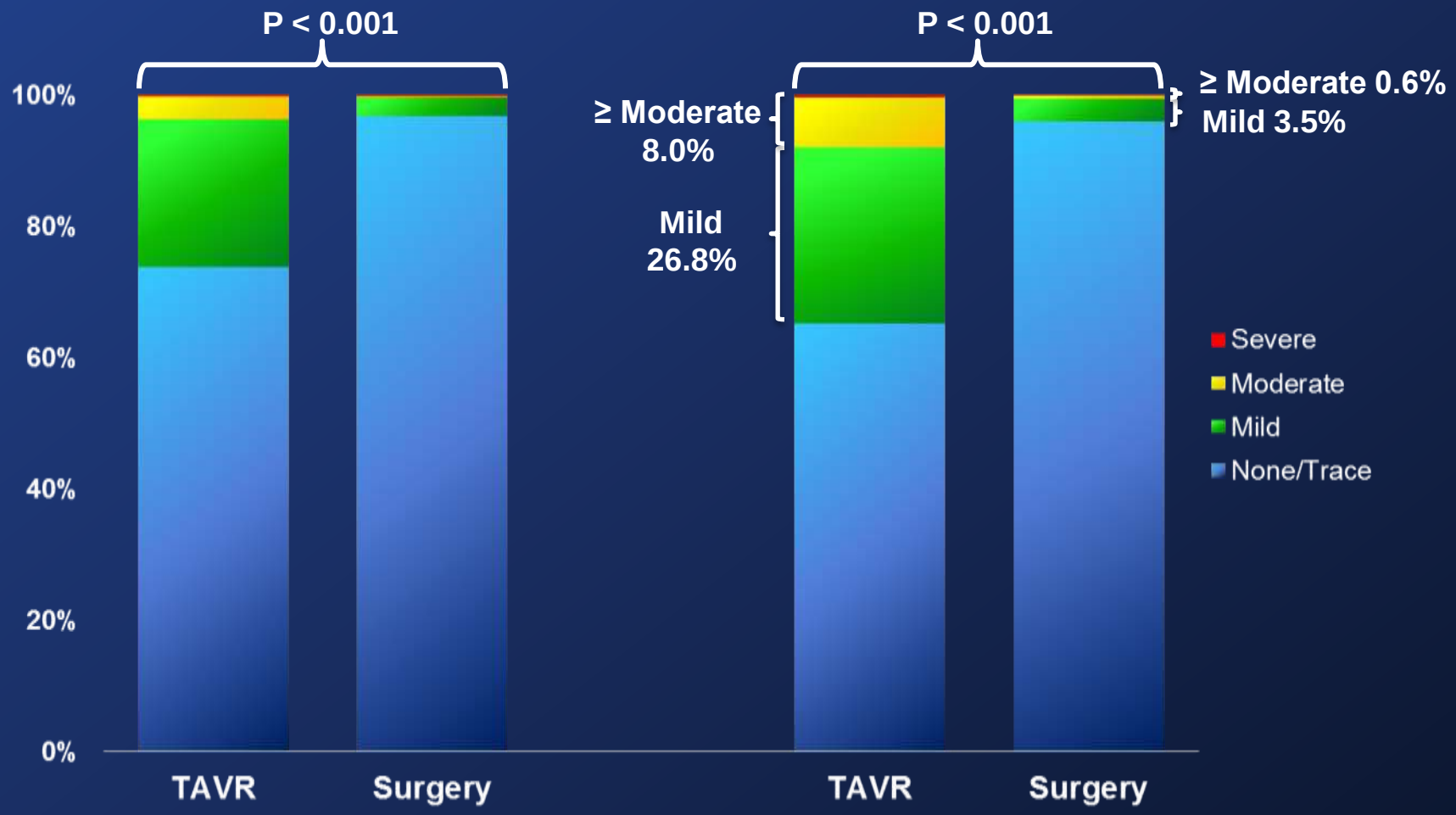
Events (%)	30 Days			2 Years		
	TAVR (n = 1011)	Surgery (n = 1021)	p-value*	TAVR (n = 1011)	Surgery (n = 1021)	p-value*
Rehospitalization	6.5	6.5	0.99	19.6	17.3	0.22
MI	1.2	1.9	0.22	3.6	4.1	0.56
Major Vascular Complications	7.9	5.0	0.008	8.6	5.5	0.006
Life-Threatening / Disabling Bleeding	10.4	43.4	<0.001	17.3	47.0	<0.001
AKI (Stage III)	1.3	3.1	0.006	3.8	6.2	0.02
New Atrial Fibrillation	9.1	26.4	<0.001	11.3	29.3	<0.001
New Permanent Pacemaker	8.5	6.9	0.17	11.8	10.3	0.29
Re-intervention	0.4	0.0	0.05	1.4	0.6	0.09
Endocarditis	0.0	0.0	NA	1.2	0.7	0.22

*Event rates are KM estimates, p-values are point in time

NYHA Class (ITT)
All Patients

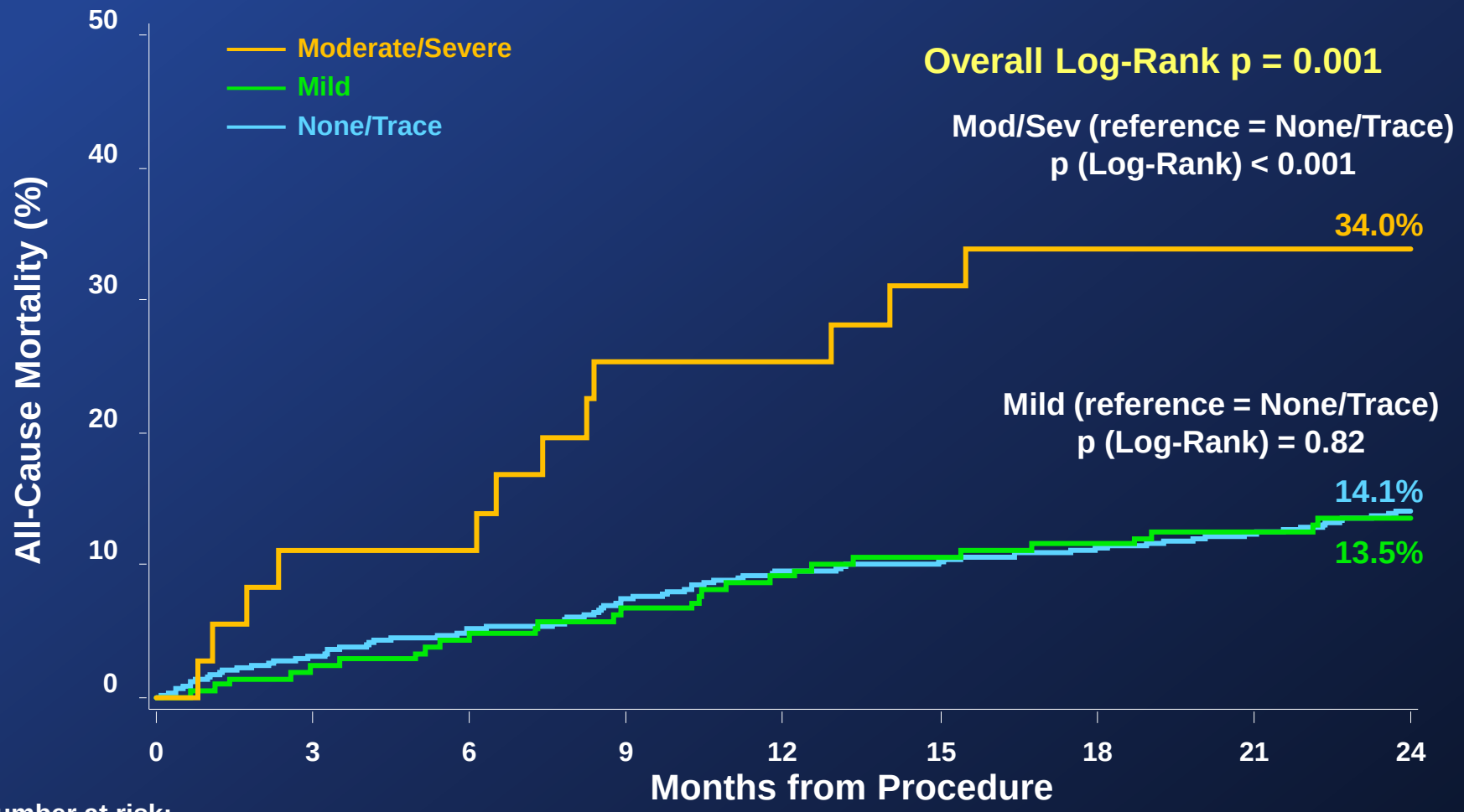


Paravalvular Regurgitation (VI)
3-Class Grading Scheme



No. of echos	30 Days	2 Years
TAVR	872	600
Surgery	757	514

Severity of PVR at 30 Days and All-cause Mortality at 2 Years (VI)



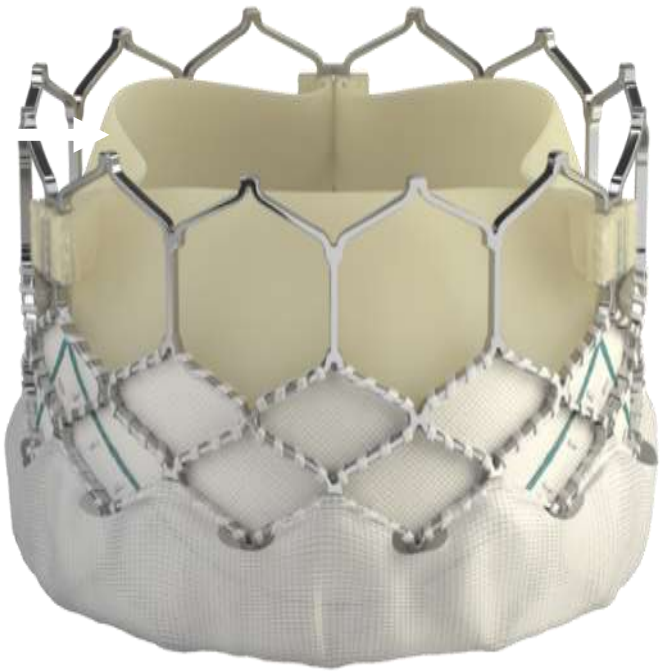
Number at risk:

Moderate/Sev	36	32	32	26	26	24	22	22	21
Mild	210	204	199	194	188	184	182	180	175
None/Trace	701	678	664	647	628	621	612	605	585

SAPIEN 3 Transcatheter Heart Valve

Distinguishing Features

Bovine pericardial valve

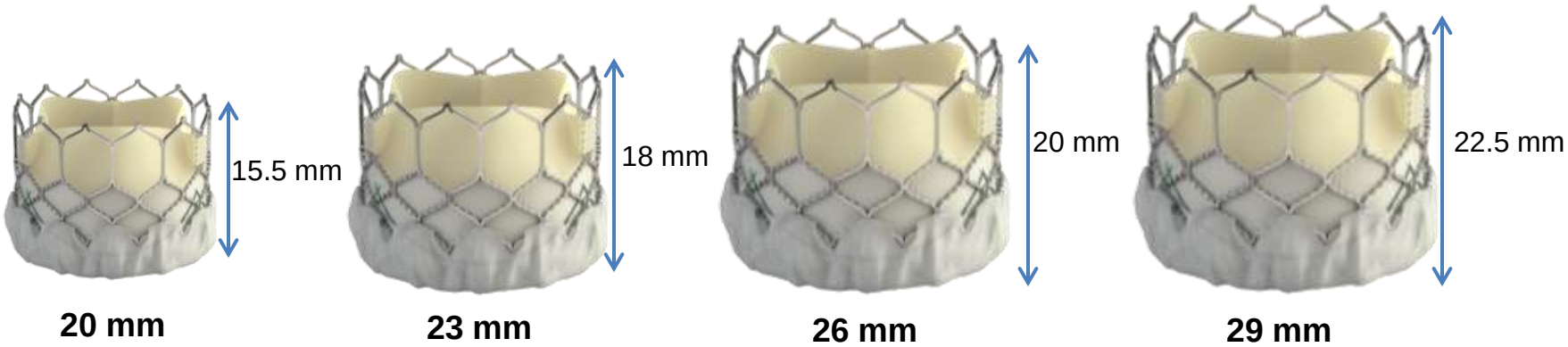


Modified frame geometry

Overall lower profile design

External skirt (to reduce PVL)

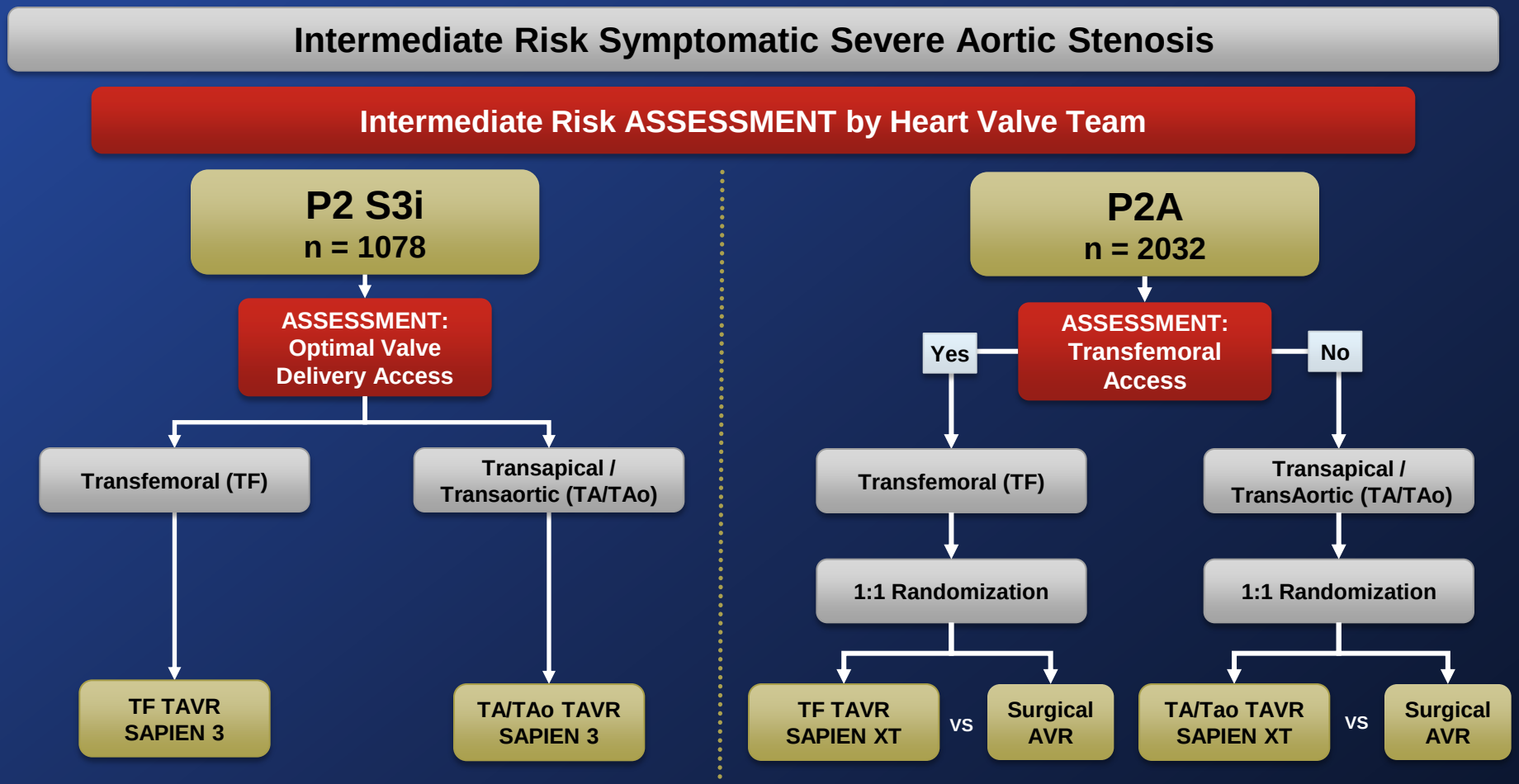
Sapien 3 foreshortens more than XT



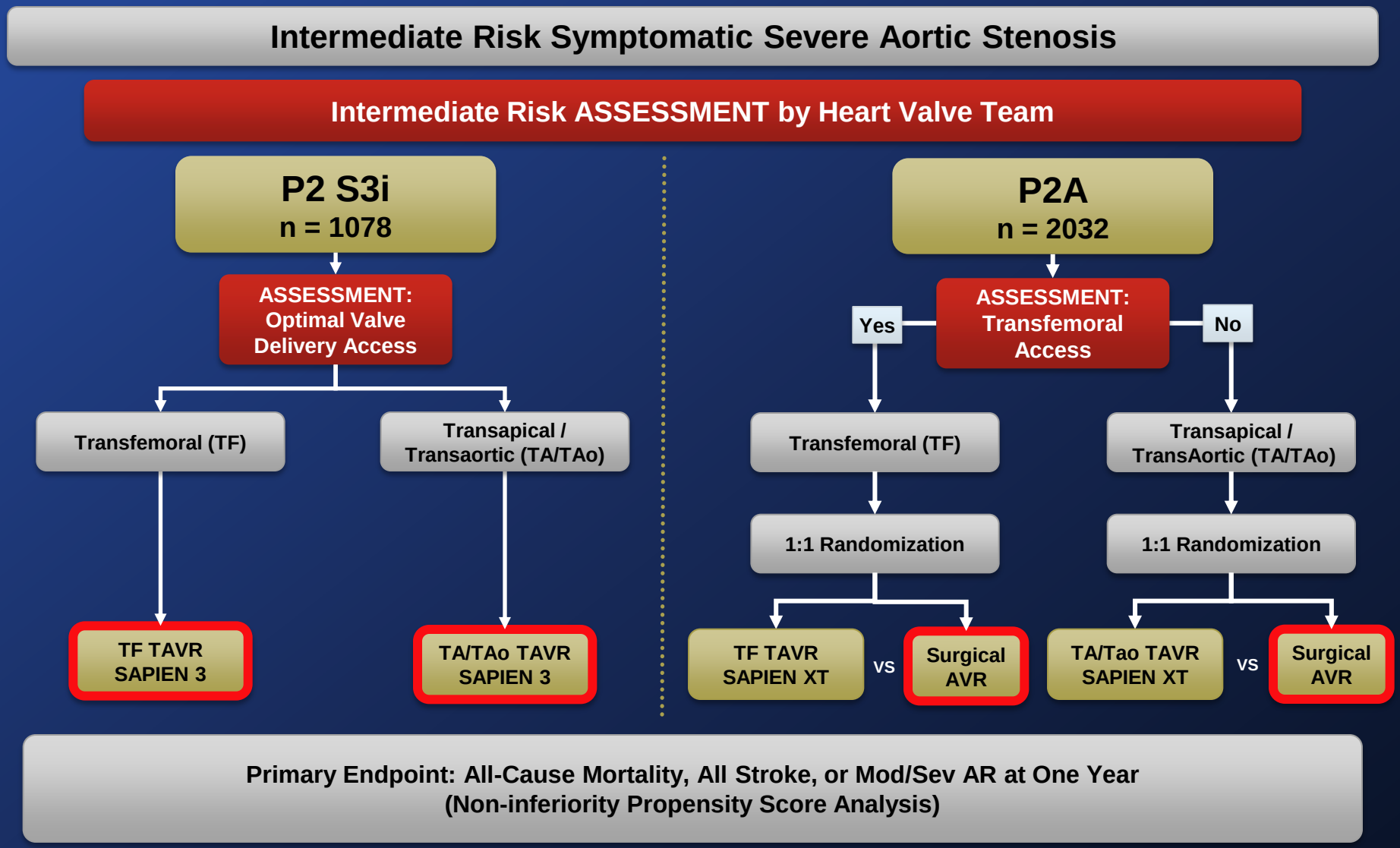
SAPIEN 3 Valve size	20 mm	23 mm	26 mm	29 mm
Crimped Height	21 mm	24.5 mm	27 mm	31 mm
Expanded Height	15.5 mm	18 mm	20 mm	22.5 mm
Foreshortening	5.5 mm	6.5 mm	7 mm	8.5 mm

Foreshortening occurs primarily from the ventricular side

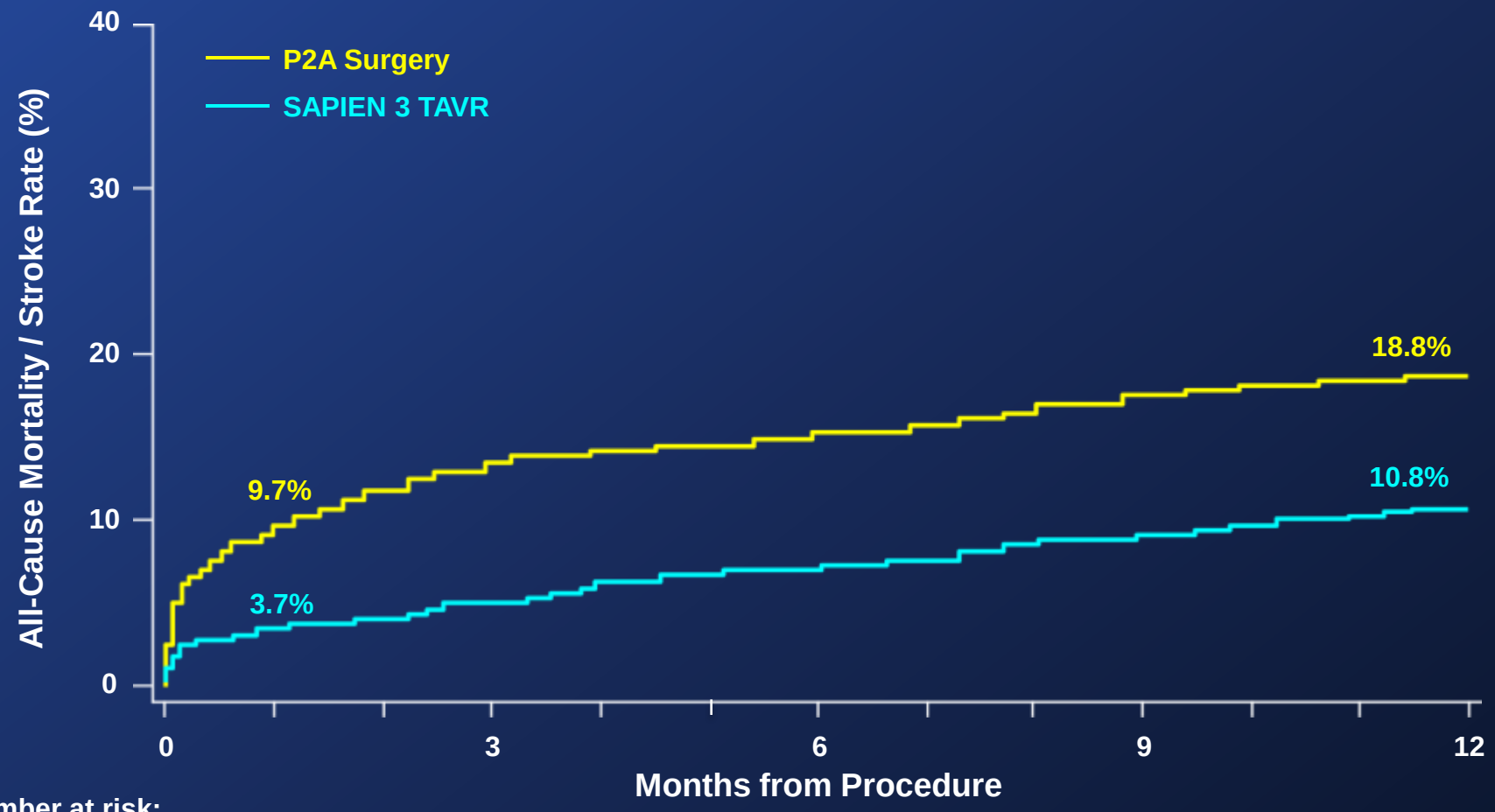
The PARTNER 2A and S3i Trials
Study Design



The PARTNER 2A and S3i Trials
Study Design



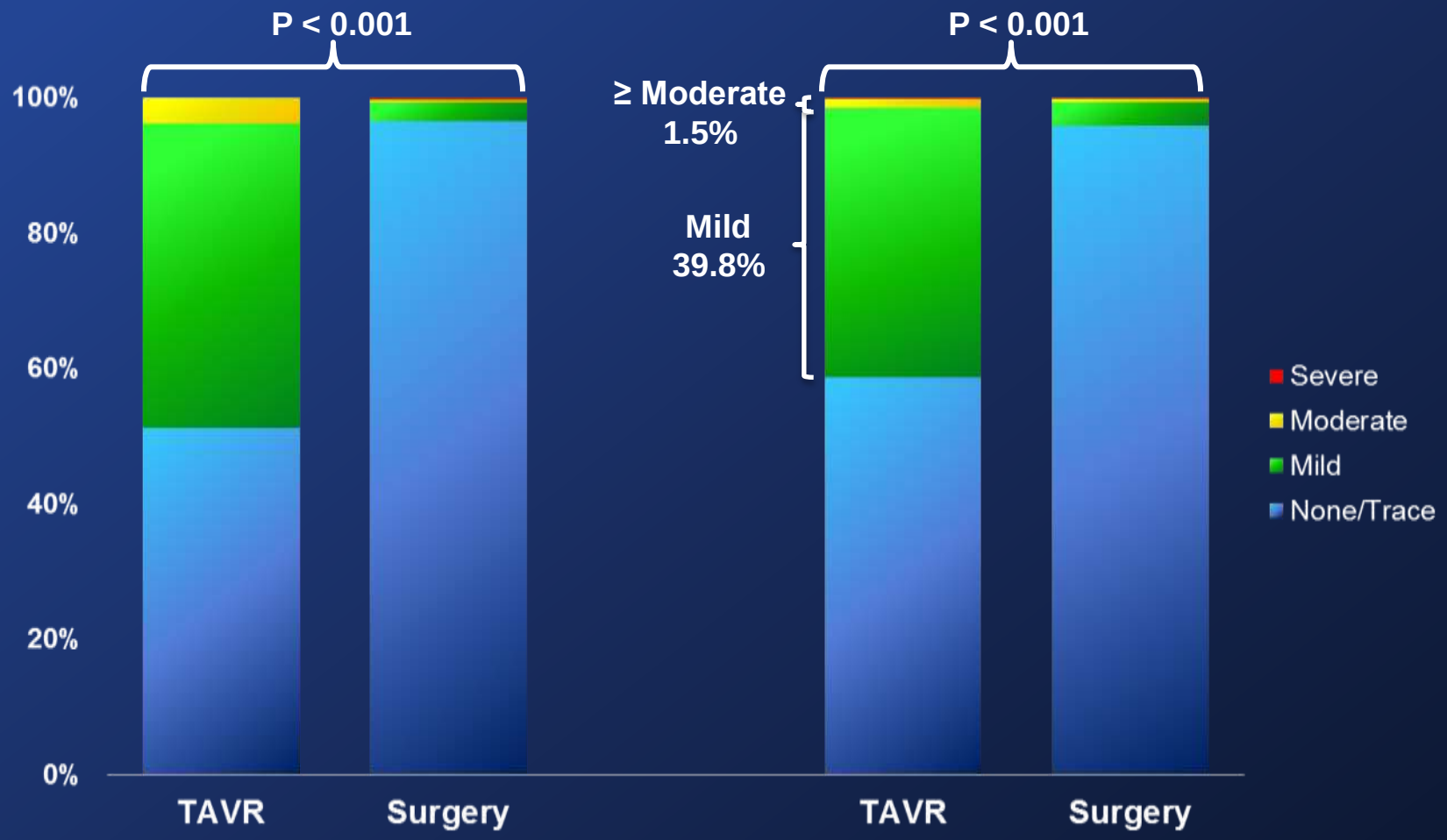
Unadjusted Time-to-Event Analysis
All-Cause Mortality and All Stroke (AT)



Number at risk:

P2A Surgery	944	805	786	757	743
S3 TAVR	1077	1012	987	962	930

Paravalvular Regurgitation
3-Class Grading Scheme (VI)



No. of echos	30 Days	1 Year
P2A Surgery	755	610
S3i TAVR	992	875

EDITORIAL

Will TAVR Become the Predominant Method for Treating Severe Aortic Stenosis?

Neil E. Moat, M.B., B.S.

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Comment

All over for valve surgery for intermediate-risk patients?

Based on the findings of three randomised trials[1-3] transcatheter aortic valve replacement (TAVR) is now first-line therapy in patients with severe aortic stenosis us with sufficient information to rule out surgery in intermediate-risk patients? No. Why?

Although the analysis was prespecified and the two

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S0140-6736(16)30122-2

Intermediate Risk Patients

THE PARTNER II TRIAL

- Intermediate risk does not mean average risk of AS patient to be intervene on
- Non-inferiority of XT is ascertained; XT TF trends superiority
- Superiority of S3 is based on non-randomized data; 90% S3 TF
- Long-term outcome of paravalvular leak needs F/U
- TAVR in small annulus worth further study
- All intermediate risk are not the same
  - Treatment of bicuspid valve in younger patients
  - Concomittent CAD treatment strategy/multi-valve

TAVR Categories
(risk is a continuum)

THE PARTNER II TRIAL

Operable AS patients

Low Risk	Moderate Risk	High Risk	Extr Risk*	Too Sick

Sapien TAVR in 2016

Onward…RCT	***= or >***	***preferred***	***No***

** Extreme (prohibitive) risk = "inoperable"*

PARTNER III: Low Risk TAVR Trial

- 1200+ patients
- 50 sites vs SAVR
- Age $\geq$ 65 years
- 4% STS or less
- TF only