TAVR in Intermediate Risk Patients: Update on the Outcomes

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TCT Meeting
Washington DC
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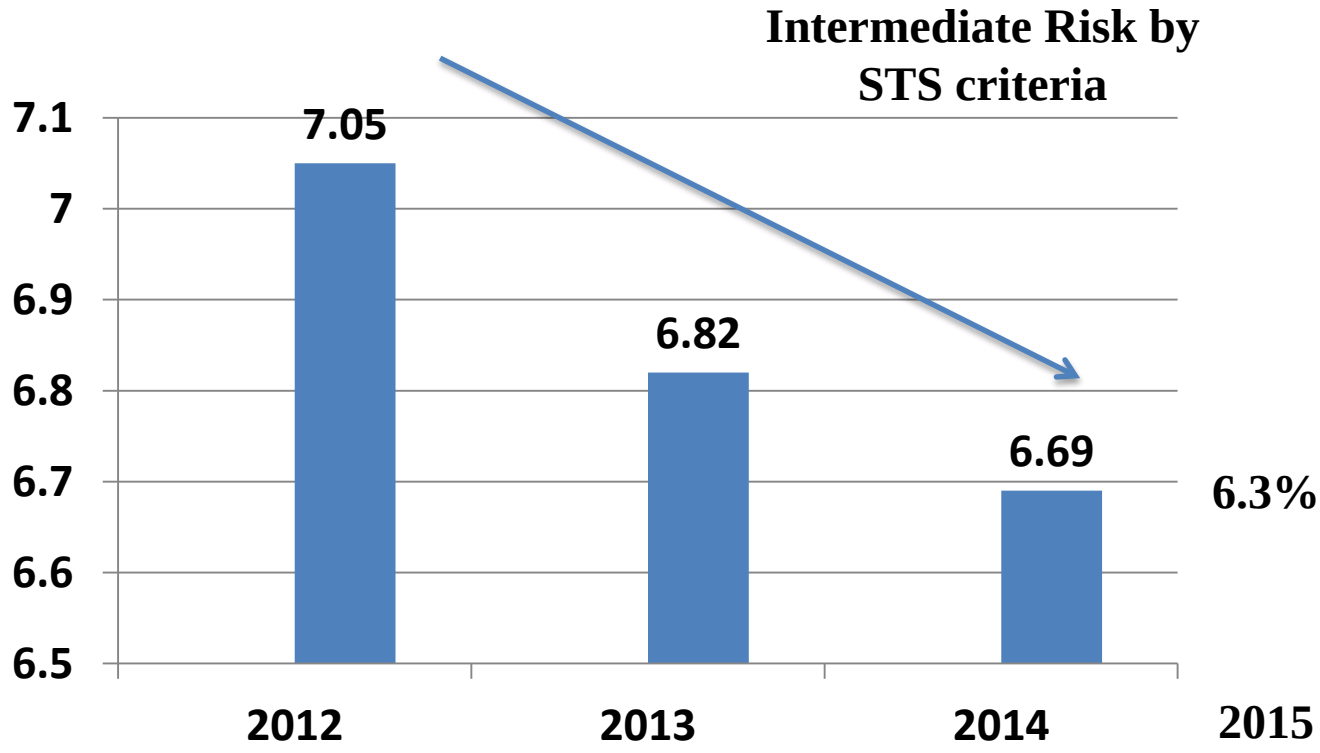
Disclosures

- **Abbott Medical**
  - **Emory Co-PI: Coapt Trial**
  - **Consultant**
- **Boston Scientific**
  - **Emory PI: REPRISE Trial**
- **Edwards Lifesciences**
  - **National Co-PI: PARTNER 2 (SAPIEN 3 Trial)**
  - **Steering Committee: PARTNER 3**
  - **Emory PI: Cardiaq Trial**
  - **Consultant**
- **Jenavalve**
  - **National Co-PI**
- **Medtronic**
  - **Emory PI: SURTAVI Trial**
- **St. Jude Medical**
  - **Emory PI: Portico Trial (Steering Committee)**

Introduction

- EU and US guidelines have stated that TAVR is the preferred or an alternative treatment to surgery in extreme risk ("inoperable") and high risk patients with AS
- The penetrance of TAVR in these patient populations has increased steadily over the last several years
- In recent years, TAVR has moved into intermediate and lower risk patients … *Is there data to support this?*

Median STS Risk Score for all TAVR Procedures

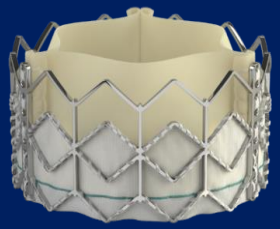
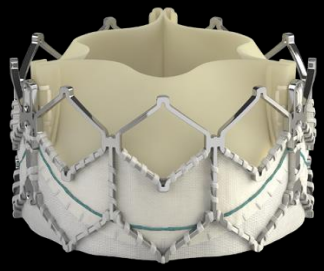
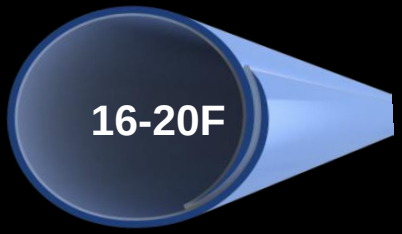


STS National Database™
Using data to drive quality

NCDR®
NATIONAL CARDIOVASCULAR DATA REGISTRY

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

The PARTNER 2A Trial

THE PARTNER II TRIAL

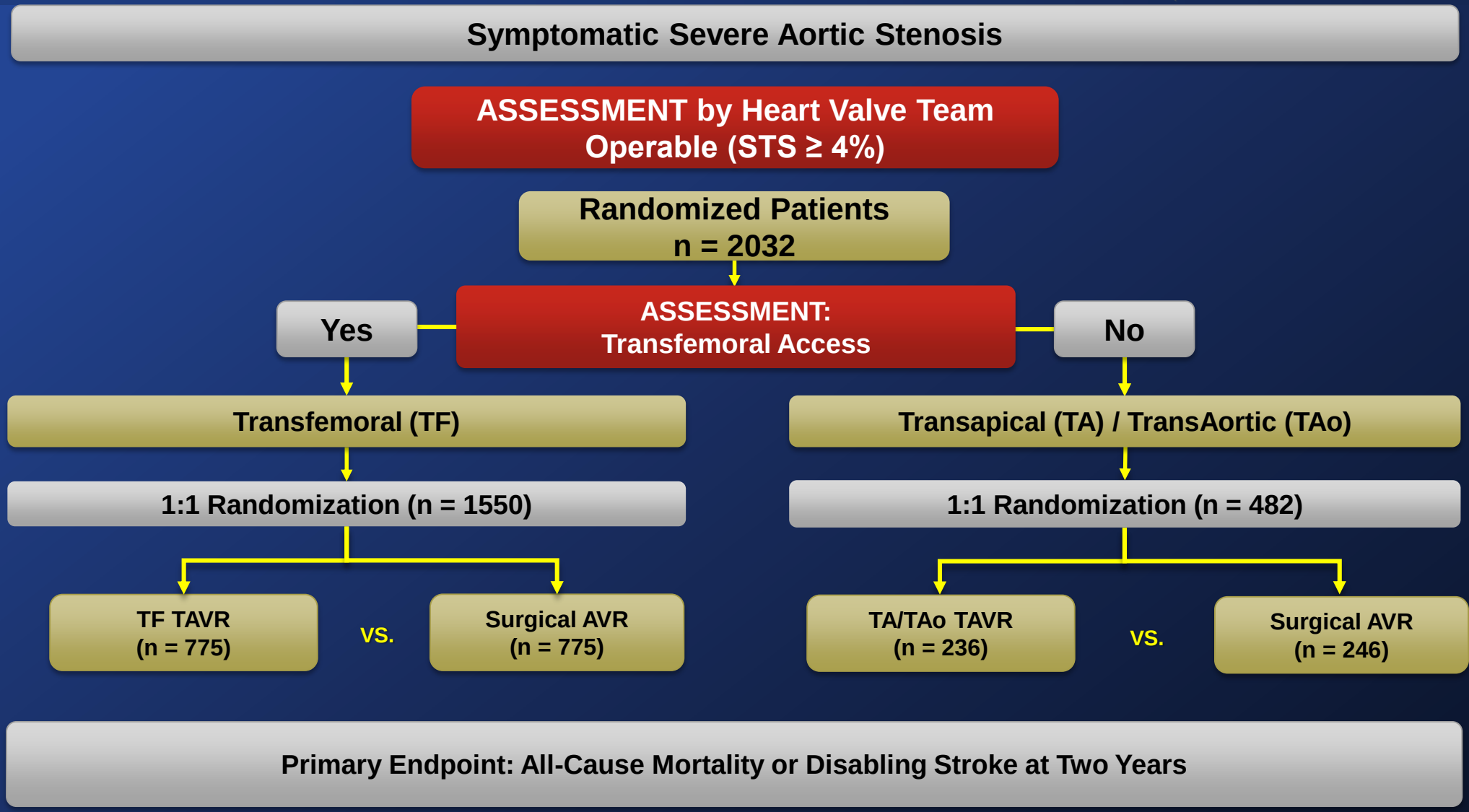
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients

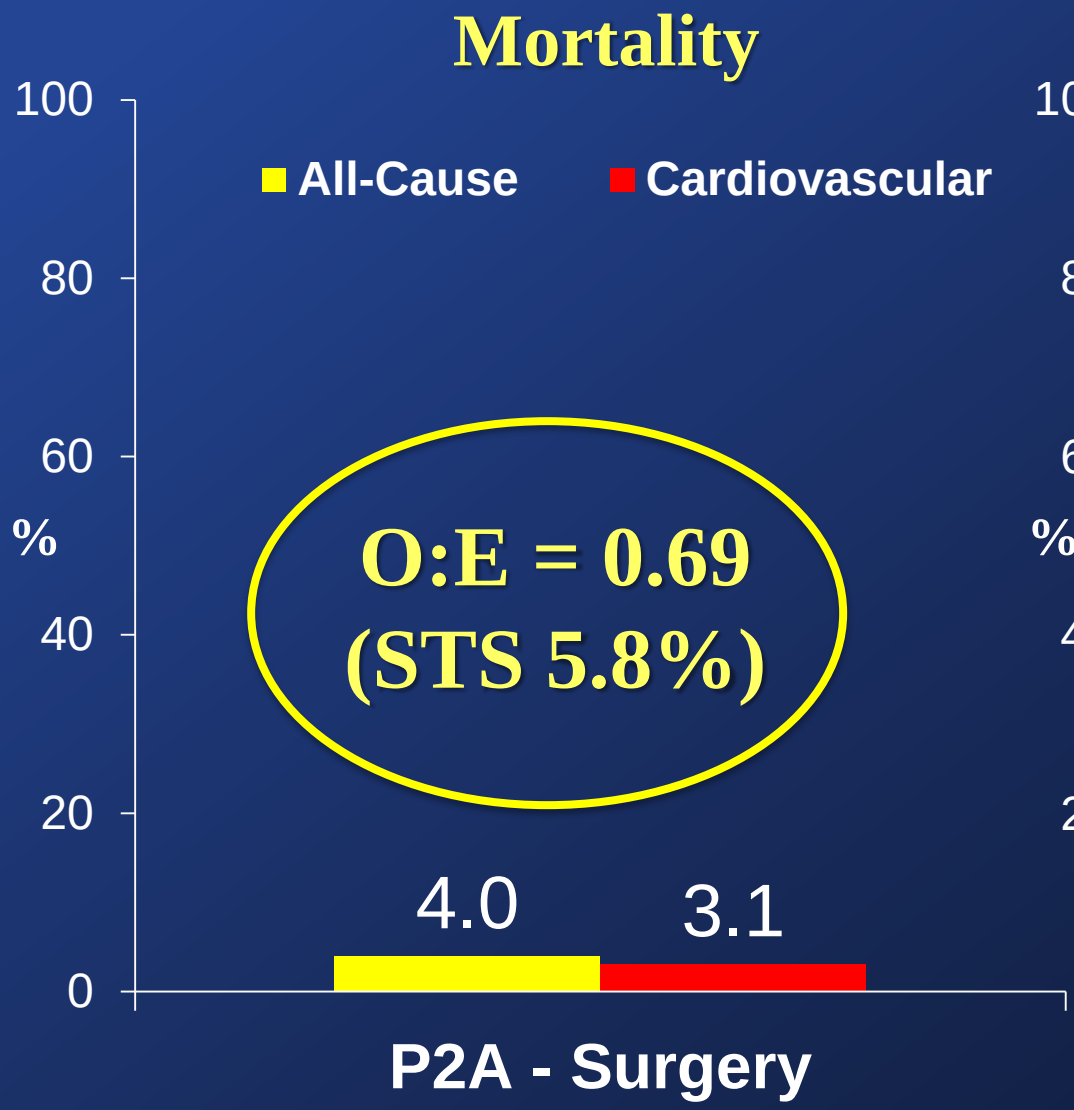
Martin B. Leon, M.D., Craig R. Smith, M.D., Michael J. Mack, M.D., Raj R. Makkar, M.D., Lars G. Svensson, M.D., Ph.D., Susheel K. Kodali, M.D., Vinod H. Thourani, M.D., E. Murat Tuzcu, M.D., D. Craig Miller, M.D., Howard C. Herrmann, M.D., Darshan Doshi, M.D., David J. Cohen, M.D., Augusto D. Pichard, M.D., Samir Kapadia, M.D., Todd Dewey, M.D., Vasilis Babaliaros, M.D., Wilson Y. Szeto, M.D., Mathew R. Williams, M.D., Dean Kereiakes, M.D., Alan Zajarias, M.D., Kevin L. Greason, M.D., Brian K. Whisenant, M.D., Robert W. Hodson, M.D., Jeffrey W. Moses, M.D., Alfredo Trento, M.D., David L. Brown, M.D., William F. Fearon, M.D., Philippe Pibarot, D.V.M., Ph.D., Rebecca T. Hahn, M.D., Wael A. Jaber, M.D., William N. Anderson, Ph.D., Maria C. Alu, M.M., and John G. Webb, M.D., for the PARTNER 2 Investigators*

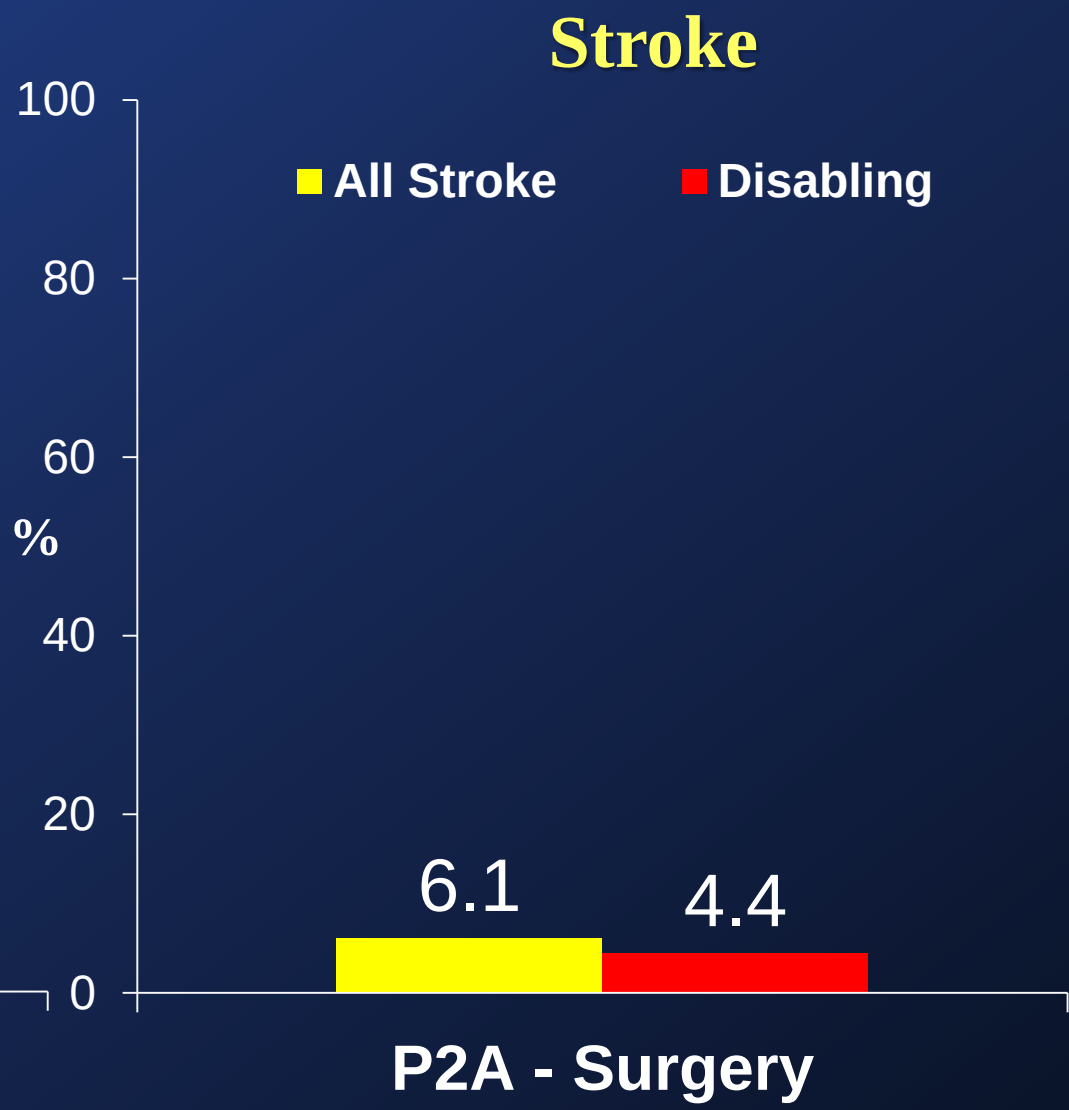
The PARTNER 2A Trial
Study Design



Mortality and Stroke:
P2A Surgery At 30 Days (AT)

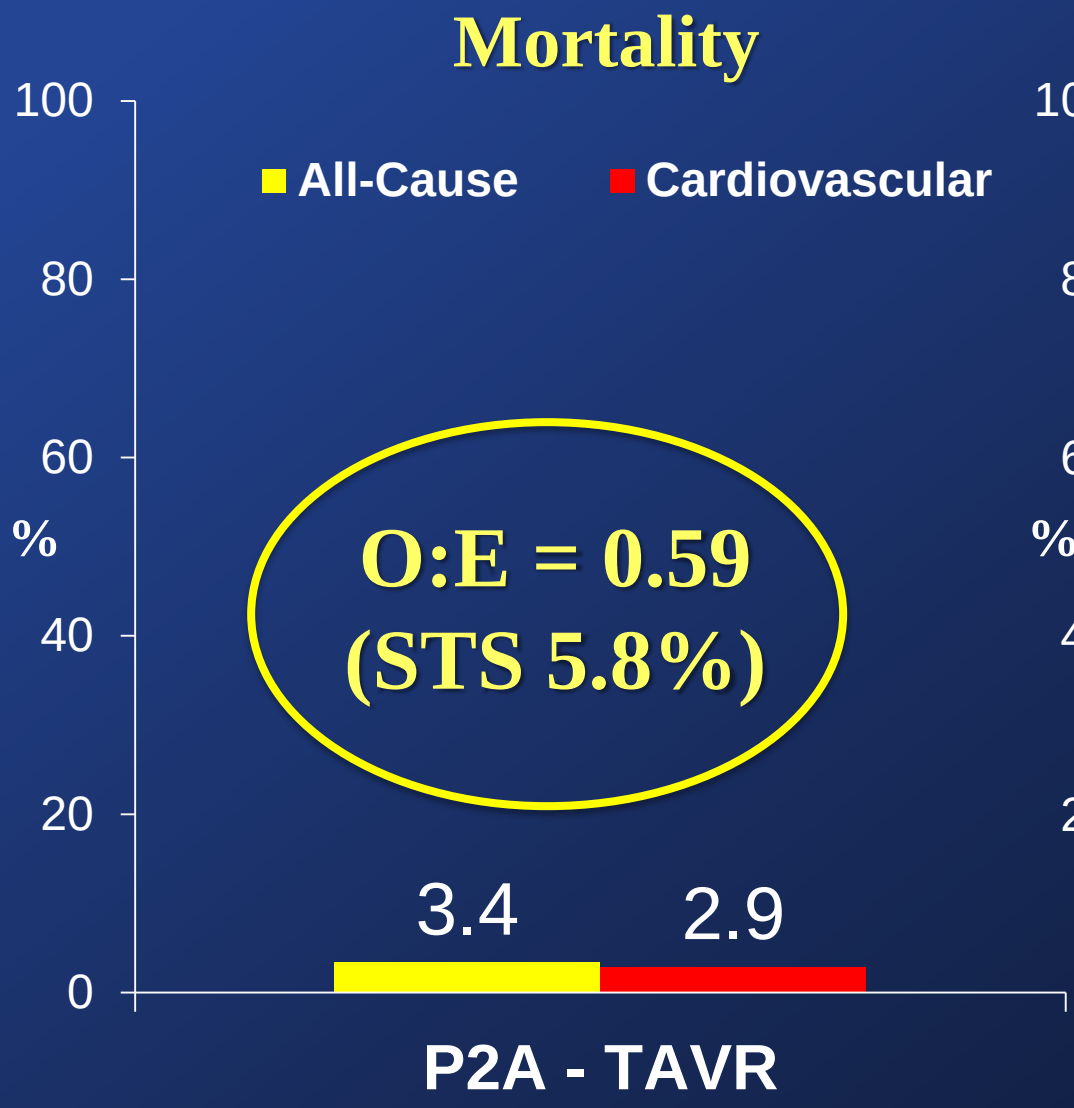
THE PARTNER II TRIAL

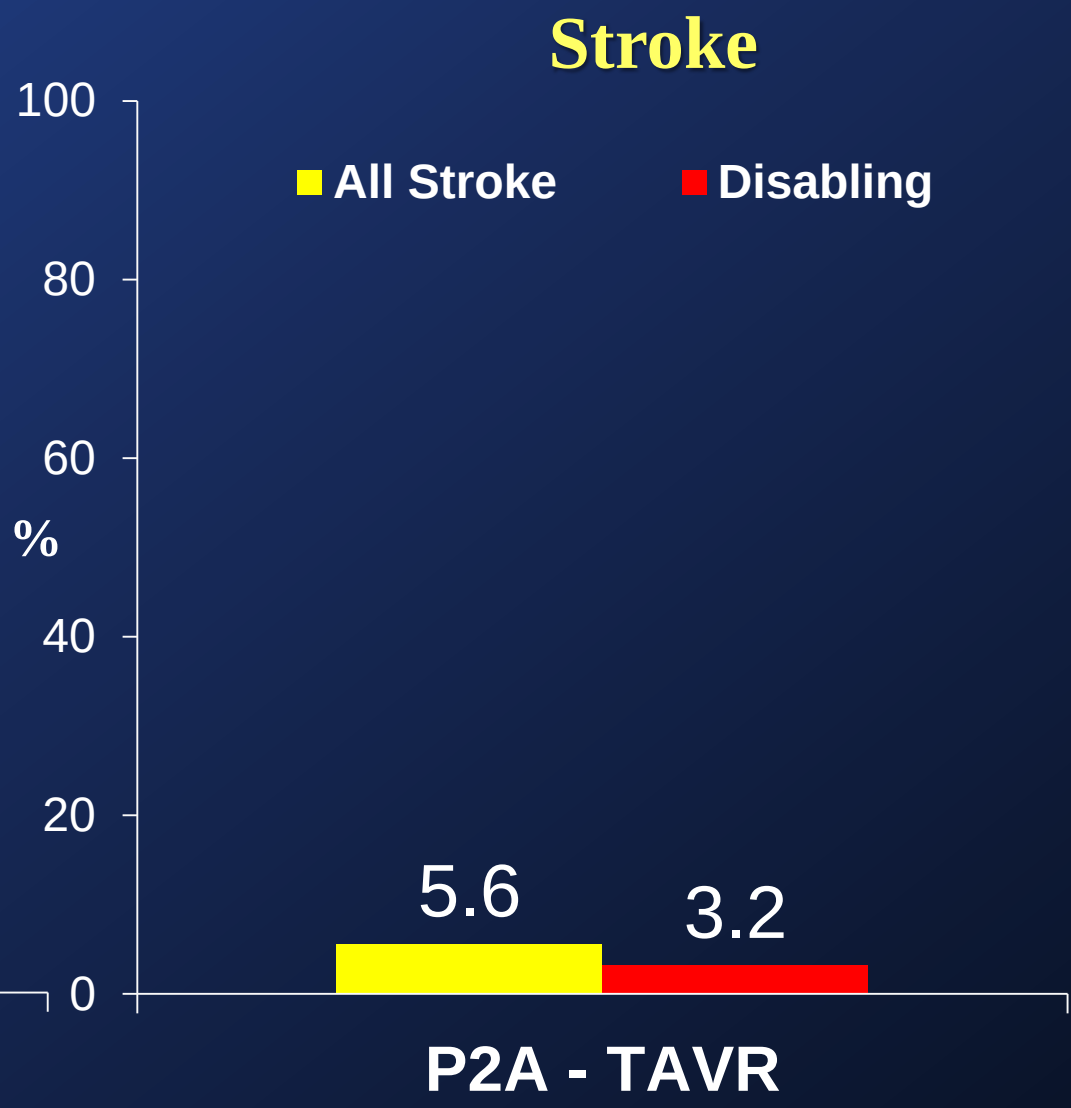




Mortality and Stroke:
P2A SAPIEN XT At 30 Days (AT)

THE PARTNER II TRIAL





Procedural Characteristics (AT)

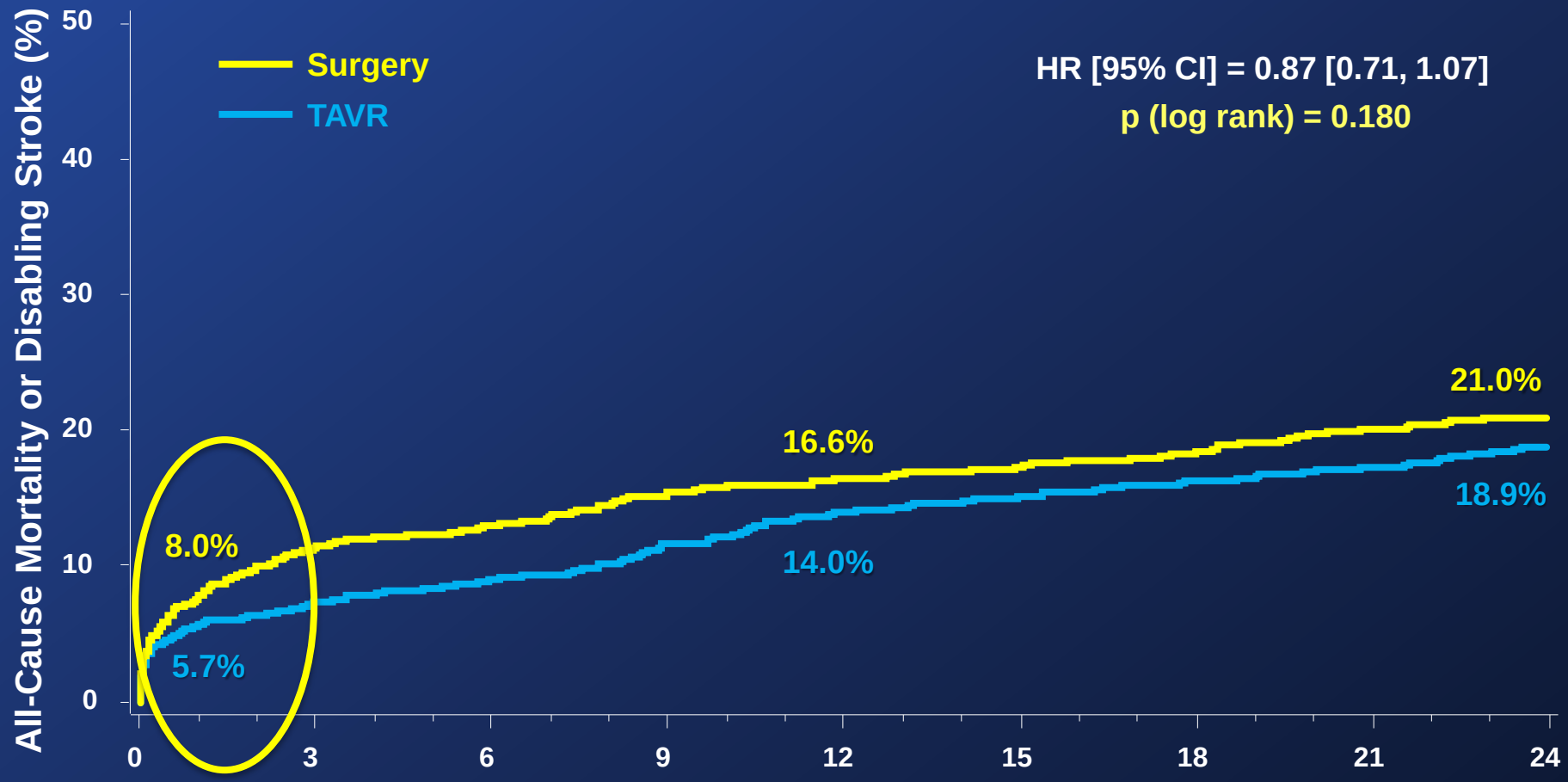
THE PARTNER II TRIAL

Characteristic	TAVR (n = 994)	Surgery (n = 944)	p-value
Anesthesia Time (min)	207	333	< 0.001
Procedure Time (min)	103	237	< 0.001
Fluoroscopy Time (min)	20	NA	NA
Aortic Cross-clamp Time (min)	NA	75	NA
Total CPB Time (min)	NA	104	NA
Median ICU Stay (days)	2.0 [2, 4]	4.0 [3, 6]	< 0.001
Median Total Length of Stay (days)	6.0 [4, 9]	9.0 [8, 14]	< 0.001

Median [IQR]

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

THE PARTNER II TRIAL

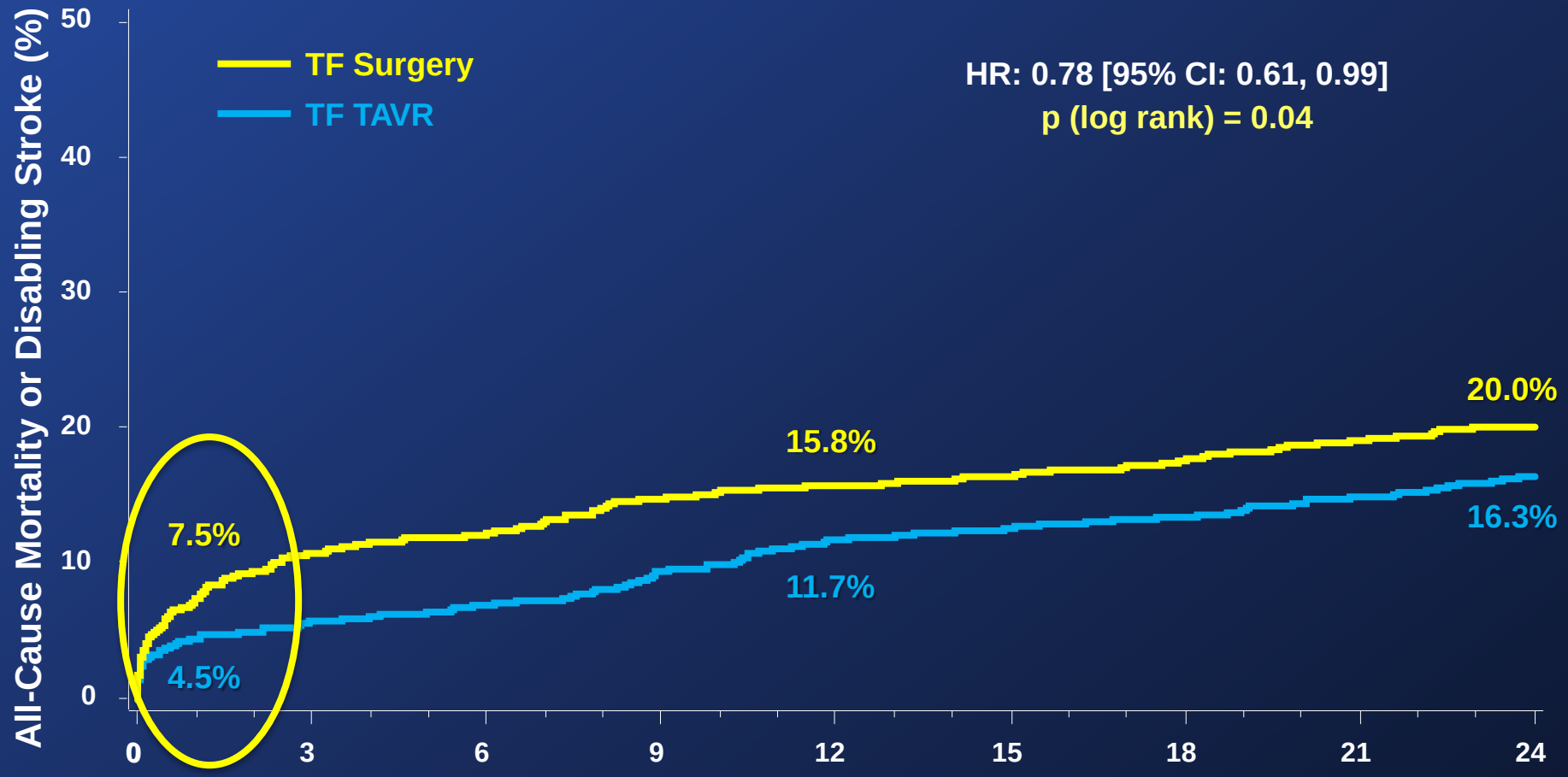


Number at risk:

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

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

THE PARTNER II TRIAL



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

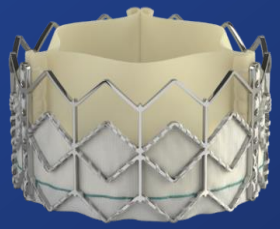
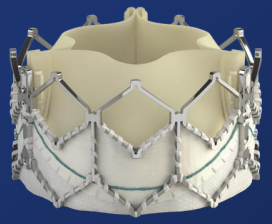
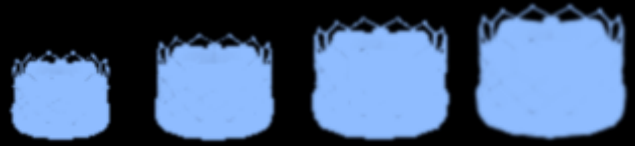
THE PARTNER II TRIAL

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	27.3	<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

SAPIEN Platforms in PARTNER
Device Evolution

THE PARTNER II TRIAL

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

The PARTNER 2A and S3i Trials
Study Design

THE PARTNER II TRIAL

Intermediate Risk Symptomatic Severe Aortic Stenosis

Intermediate Risk ASSESSMENT by Heart Valve Team

P2 S3i
n = 1078

ASSESSMENT: Optimal Valve Delivery Access

- **Transfemoral (TF)** → **TF TAVR SAPIEN 3**
- **Transapical / Transaortic (TA/TAo)** → **TA/TAo TAVR SAPIEN 3**

P2A
n = 2032

ASSESSMENT: Transfemoral Access

- **Yes** → **Transfemoral (TF)** → **1:1 Randomization** → **TF TAVR SAPIEN XT** vs **Surgical AVR**
- **No** → **Transapical / TransAortic (TA/TAo)** → **1:1 Randomization** → **TA/Tao TAVR SAPIEN 3** vs **Surgical AVR**

Primary Endpoint: All-Cause Mortality, All Stroke, or Mod/Sev AR at One Year
(Non-inferiority Propensity Score Analysis)

Baseline Patient Characteristics

S3i Patients

THE PARTNER II TRIAL

N = 1,076

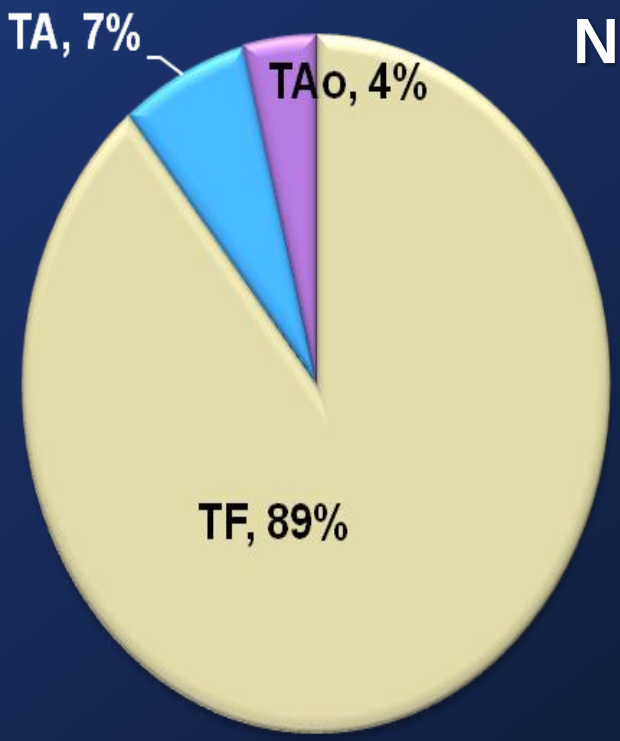
Average STS =

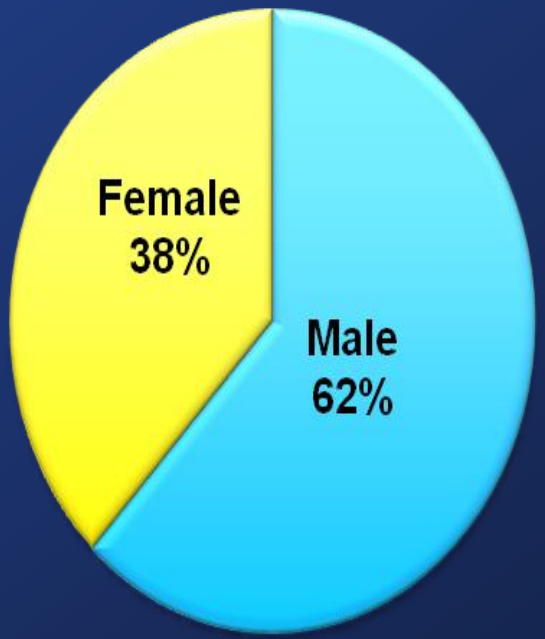
5.3%

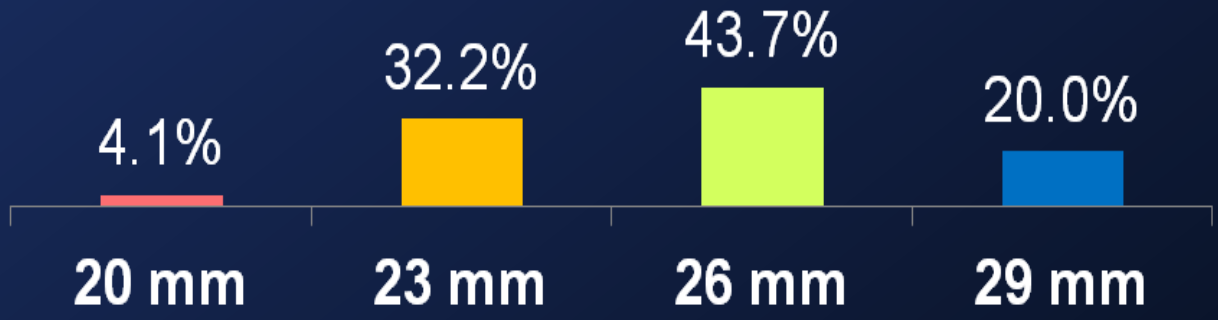
(Median 5.2%)

Average Age =

81.9yrs





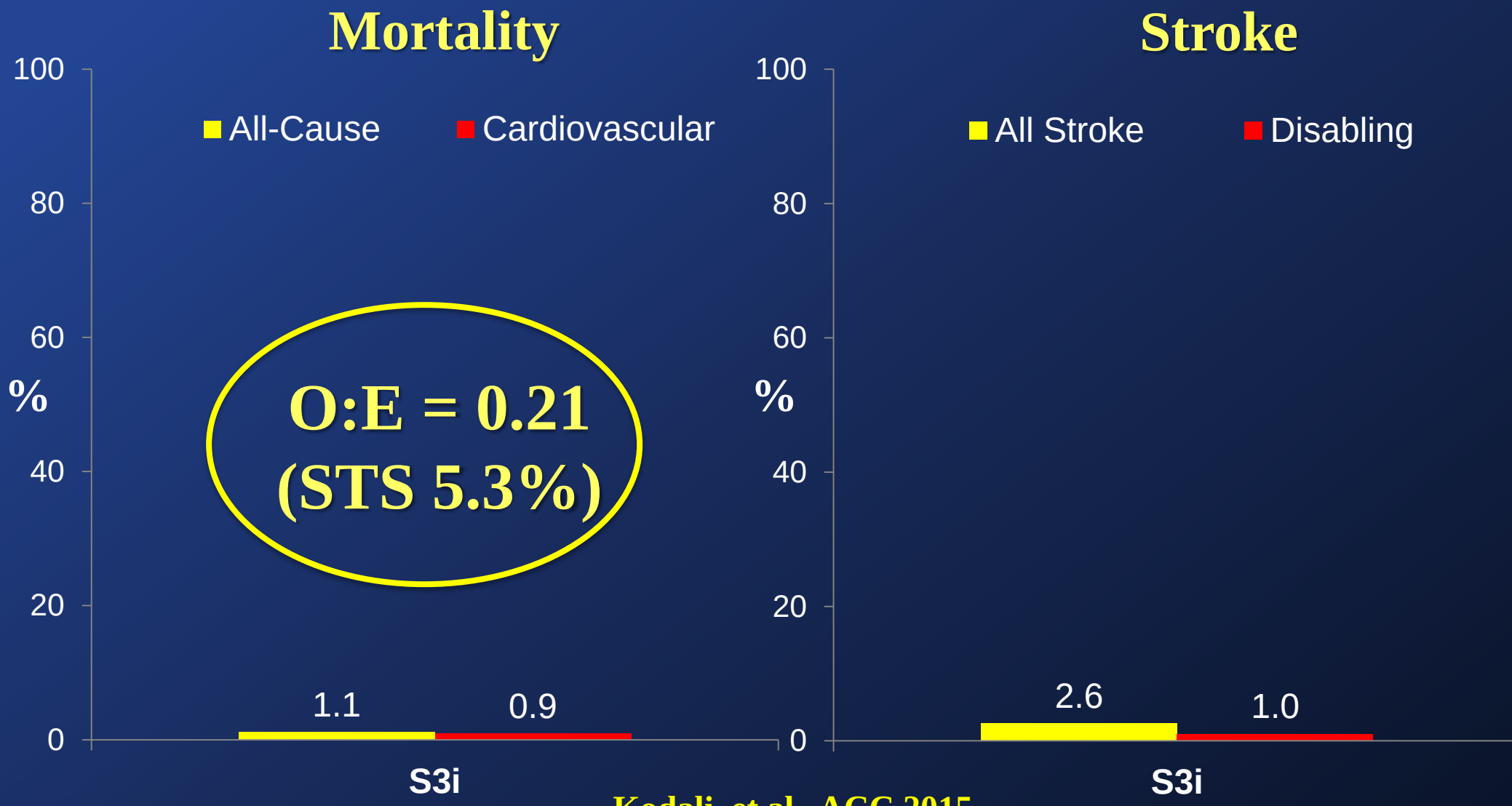


Kodali, et al. EHJ 2016

Mortality and Stroke: S3i

At 30 Days (As Treated Patients)

THE PARTNER II TRIAL



Kodali, et al. ACC 2015

The PARTNER 2 - S3i Trial
The Lancet On-line

THE PARTNER II TRIAL

Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis

Vinod H Thourani, Susheel Kodali, Raj R Makkar, Howard C Herrmann, Mathew Williams, Vasilis Babaliaros, Richard Smalling, Scott Lim, S Chris Malaisrie, Samir Kapadia, Wilson Y Szeto, Kevin L Greason, Dean Kereiakes, Gorav Ailawadi, Brian K Whisenant, Chandan Devireddy, Jonathon Leipsic, Rebecca T Hahn, Philippe Pibarot, Neil J Weissman, Wael A Jaber, David J Cohen, Rakesh Suri, E Murat Tuzcu, Lars G Svensson, John G Webb, Jeffrey W Moses, Michael J Mack, D Craig Miller, Craig R Smith, Maria C Alu, Rupa Parvataneni, Ralph B D'Agostino Jr, Martin B Leon

Lancet 2016

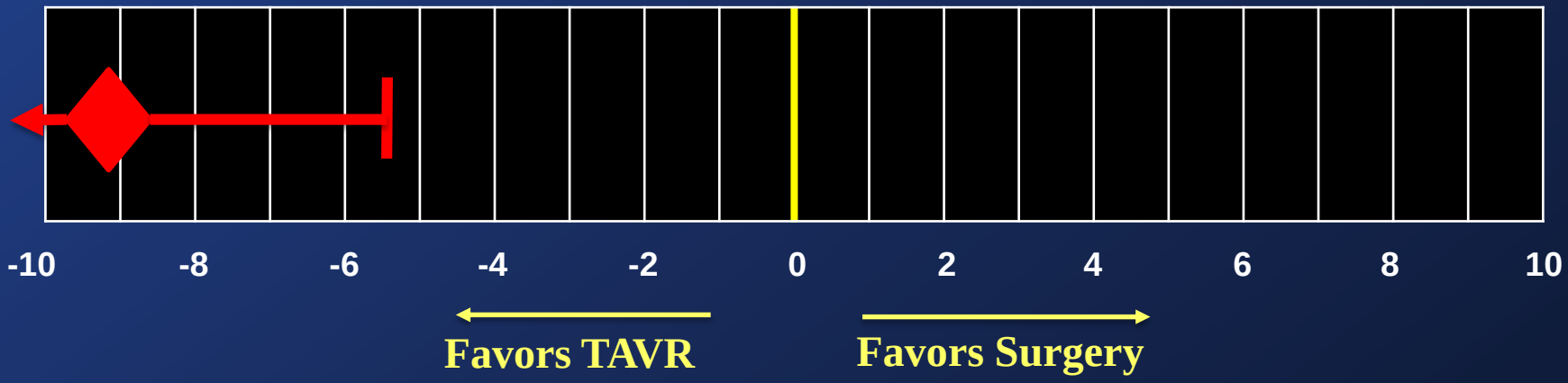
Primary Endpoint - Superiority

Death, Stroke, or AR ≥ Mod at 1 Year (VI)

THE PARTNER II TRIAL

Weighted Difference	-9.2%
Upper 2-sided 95.0% CI	-5.4%

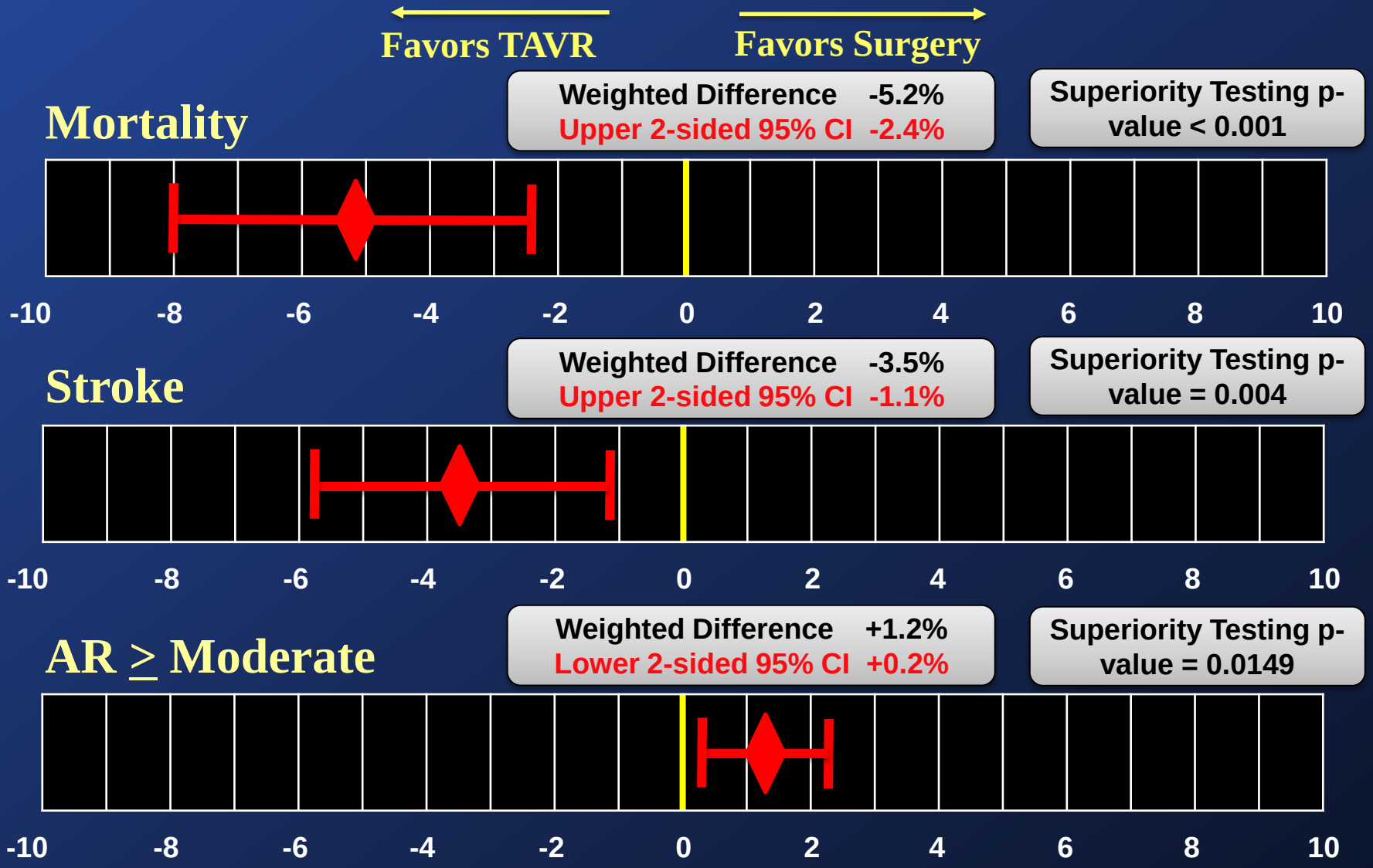
Superiority Testing p-value < 0.001



Superiority Achieved

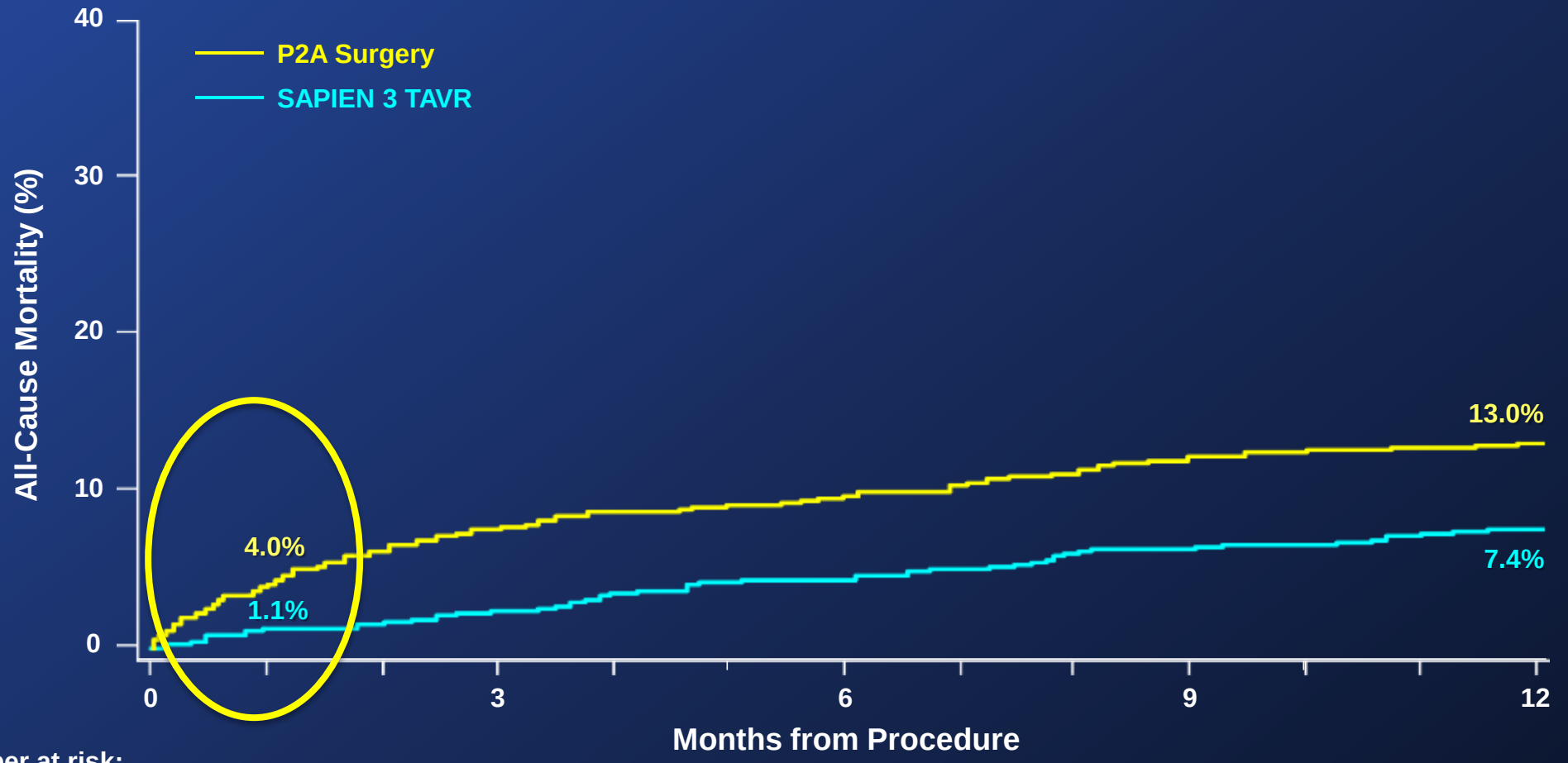
Superiority Analysis
Components of Primary Endpoint (VI)

THE PARTNER II TRIAL



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

THE PARTNER II TRIAL

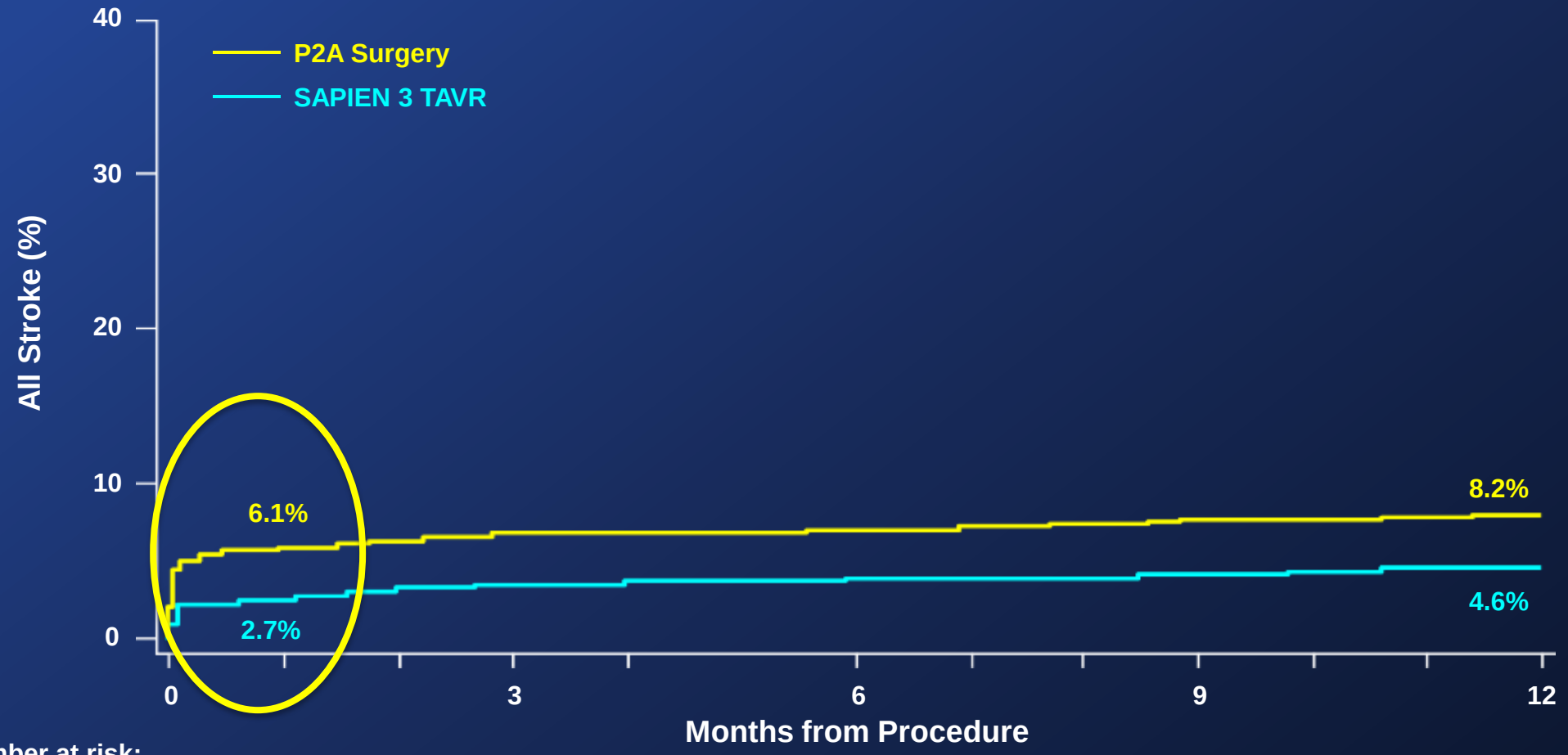


Number at risk:

P2A Surgery	944	859	836	808	795
S3 TAVR	1077	1043	1017	991	963

Unadjusted Time-to-Event Analysis
All Stroke (AT)

THE PARTNER II TRIAL



Number at risk:

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

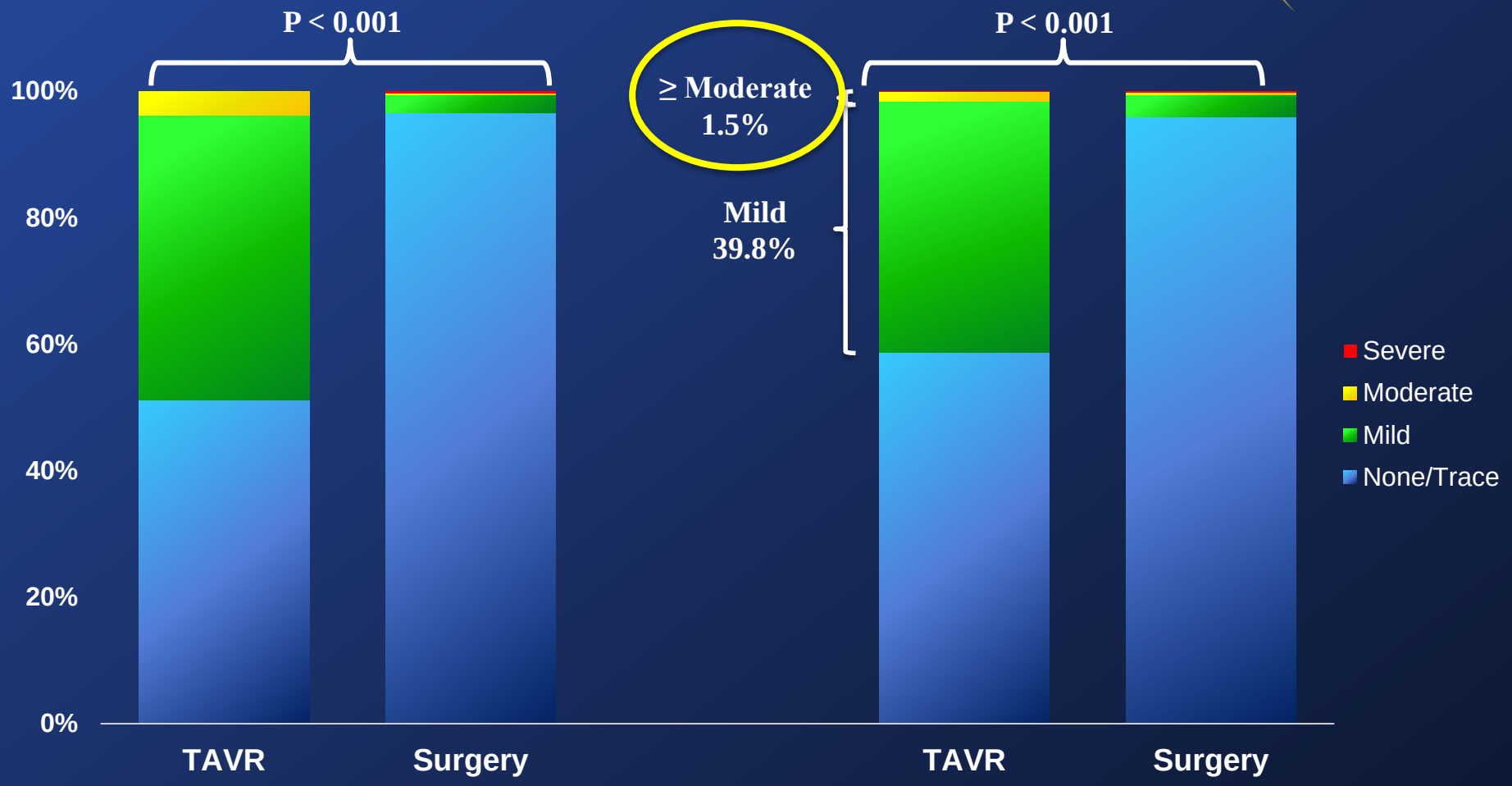
Other Unadjusted Clinical Outcomes
At 30 Days and 1 Year (AT)

THE PARTNER II TRIAL

Events (%)	30 Days		1 Year	
	TAVR (n = 1077)	Surgery (n = 944)	TAVR (n = 1077)	Surgery (n = 944)
Re-hospitalization	4.6	6.8	11.4	15.1
MI	0.3	1.9	1.8	3.1
Major Vascular Complication	6.1	5.4	---	---
AKI (Stage III)	0.5	3.3	---	---
Life-Threatening/Disabling Bleeding	4.6	46.7	---	---
New Atrial Fibrillation	5.0	28.3	5.9	29.2
New Permanent Pacemaker	10.2	7.3	12.4	9.4
Re-intervention	0.1	0.0	0.6	0.5
Endocarditis	0.2	0.0	0.8	0.7

Paravalvular Regurgitation
3-Class Grading Scheme (VI)

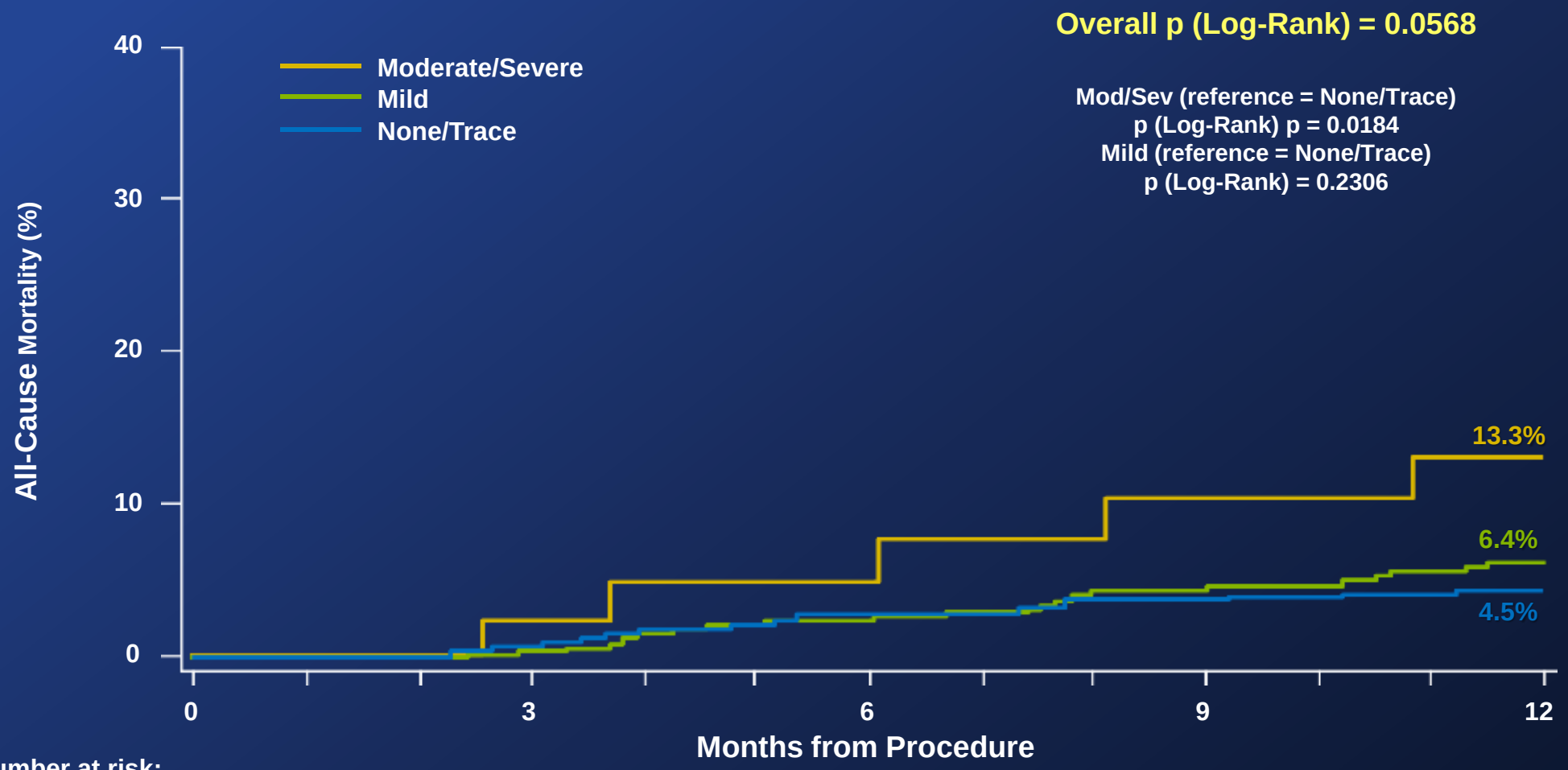
THE PARTNER II TRIAL



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

Mortality by PVR Severity
S3i (VI)

THE PARTNER II TRIAL

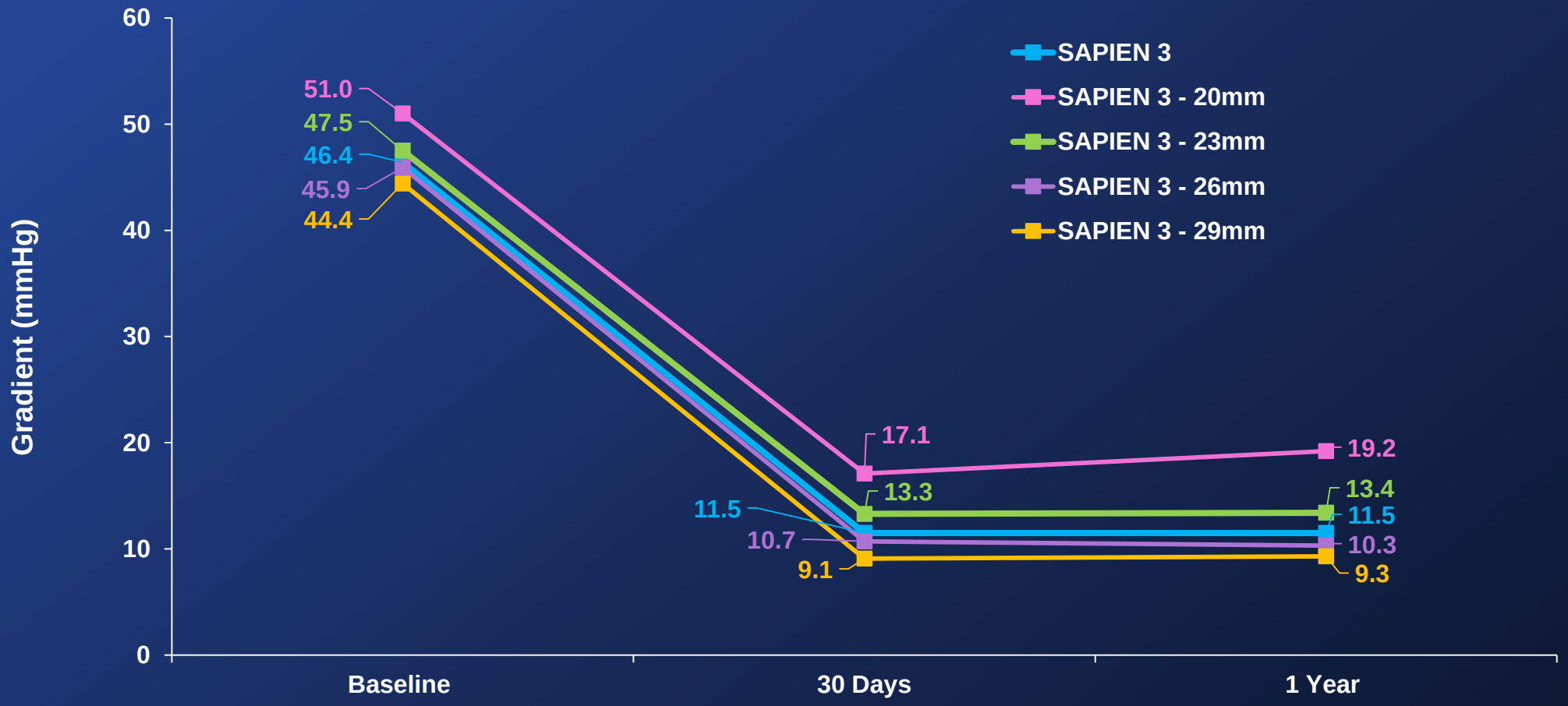


Number at risk:

Mod/Sev	38	37	36	33	31
Mild	446	440	430	419	406
None/Trace	508	503	492	484	474

Echocardiographic Findings:
Mean Gradients (VI)

THE PARTNER II TRIAL



No. of Echos				
SAPIEN 3	SAPIEN 3 - 20mm	SAPIEN 3 - 23mm	SAPIEN 3 - 26mm	SAPIEN 3 - 29mm
840	35	276	372	157

The PARTNER 2A and S3i Trials
Clinical Implications

THE PARTNER II TRIAL

The conclusions from the PARTNER 2A randomized trial and the S3i propensity score analysis (~3,000 pts) provide strong evidence that in intermediate-risk patients with severe AS, SAPIEN 3 TAVR when compared with surgery improves clinical outcomes and may be the preferred therapy

Thanks

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