

# 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

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On Behalf of the CoreValve US Investigators

# Presenter Disclosure Information

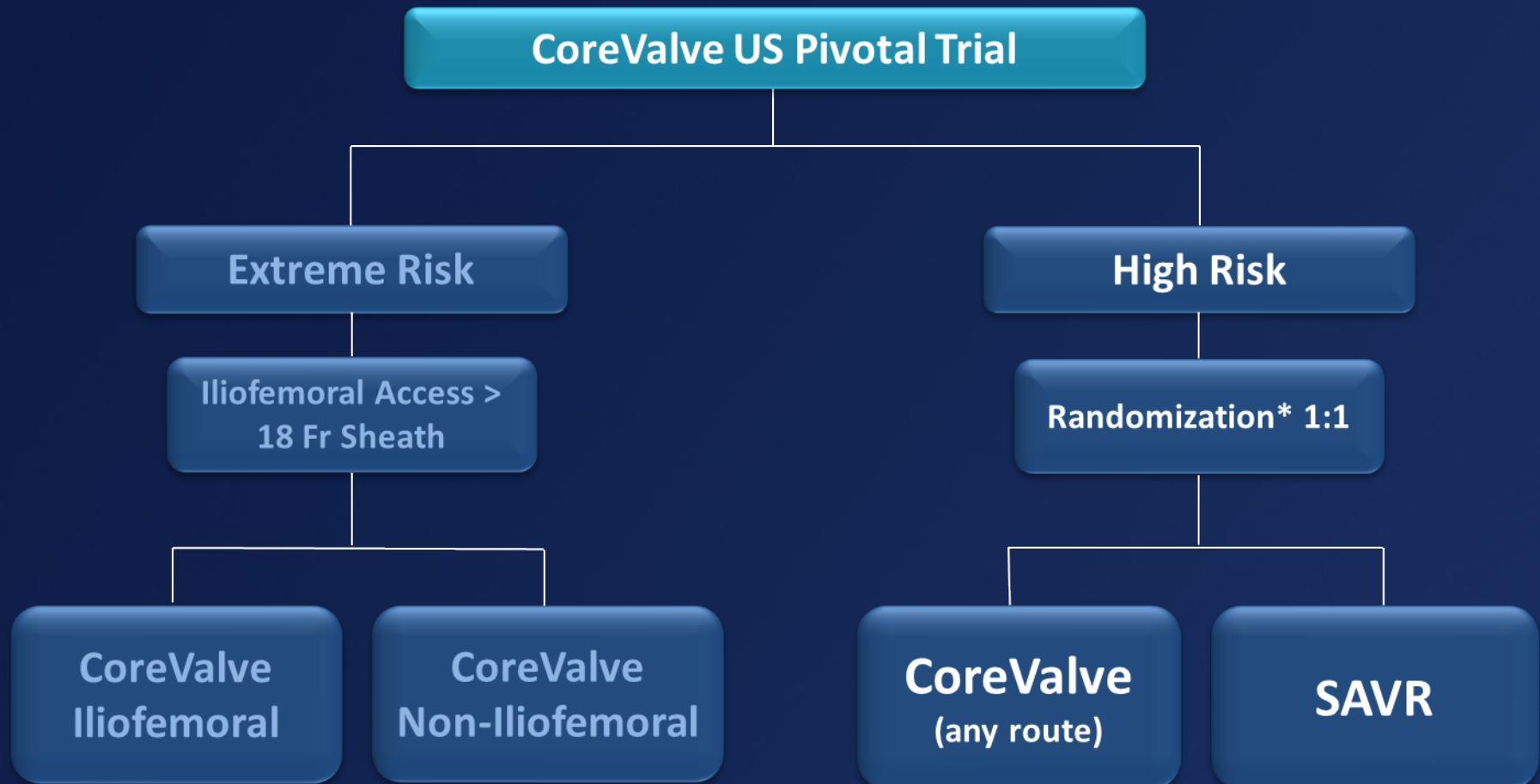
I serve on a Medical Advisory Board for Medtronic, Inc.

Medtronic personnel performed all statistical analyses and verified the accuracy of the data, and assisted in the graphical display of the data presented.

# Background

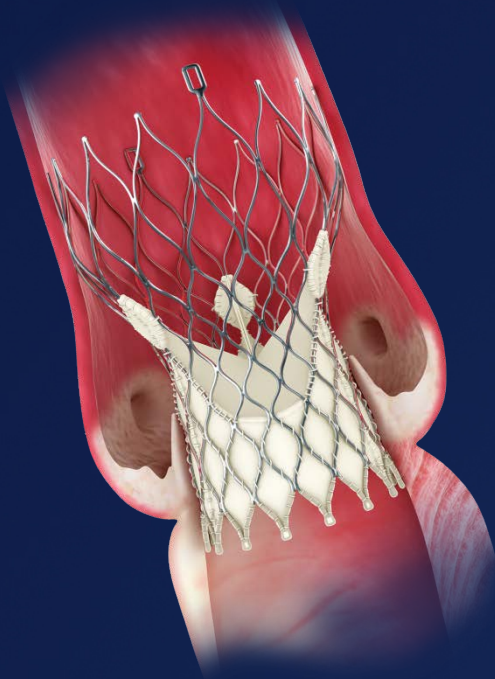
- The randomized CoreValve trial demonstrated that transcatheter aortic valve replacement (TAVR) resulted in significantly lower mortality compared with surgical AVR at 1 year in patients who were at increased risk for surgery.
- Longer-term outcomes following TAVR with the self-expanding CoreValve are necessary to further validate this survival advantage.

# Pivotal Trial Design



\* Randomization stratified by intended access site

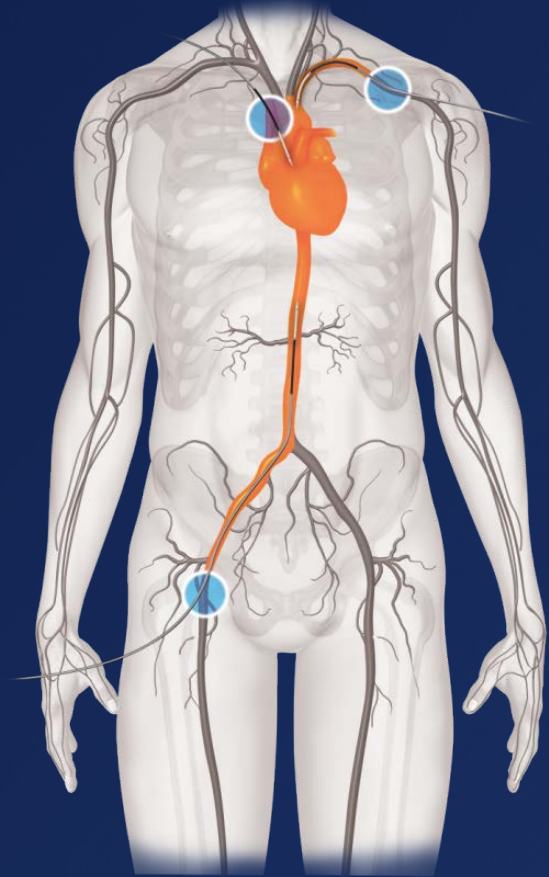
# Study Device and Access Routes



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



18F Delivery System



Transfemoral  
Subclavian  
Direct Aortic

# Inclusion Criteria

- NYHA functional class II or greater
- Severe aortic stenosis:  $AVA \leq 0.8 \text{ cm}^2$  or  $AVAI \leq 0.5 \text{ cm}^2/\text{m}^2$  AND mean gradient  $>40 \text{ mm Hg}$  or peak velocity  $>4 \text{ m/sec}$  at rest or with dobutamine stress echocardiogram
- At increased surgical risk



# Exclusion Criteria

## Clinical and Anatomic Exclusion Criteria Were:

- Recent active GI bleed (<3 months), stroke (<6 months), or MI ( $\leq$ 30 days)
- Any interventional procedure with bare metal stents (<30 days) and drug-eluting stents (<6 months)
- Creatinine clearance <20 mL/min
- Significant untreated coronary artery disease
- LVEF <20%
- Life expectancy <1 year due to comorbidities
- Annulus <18 mm or >29 mm

# Primary Endpoint

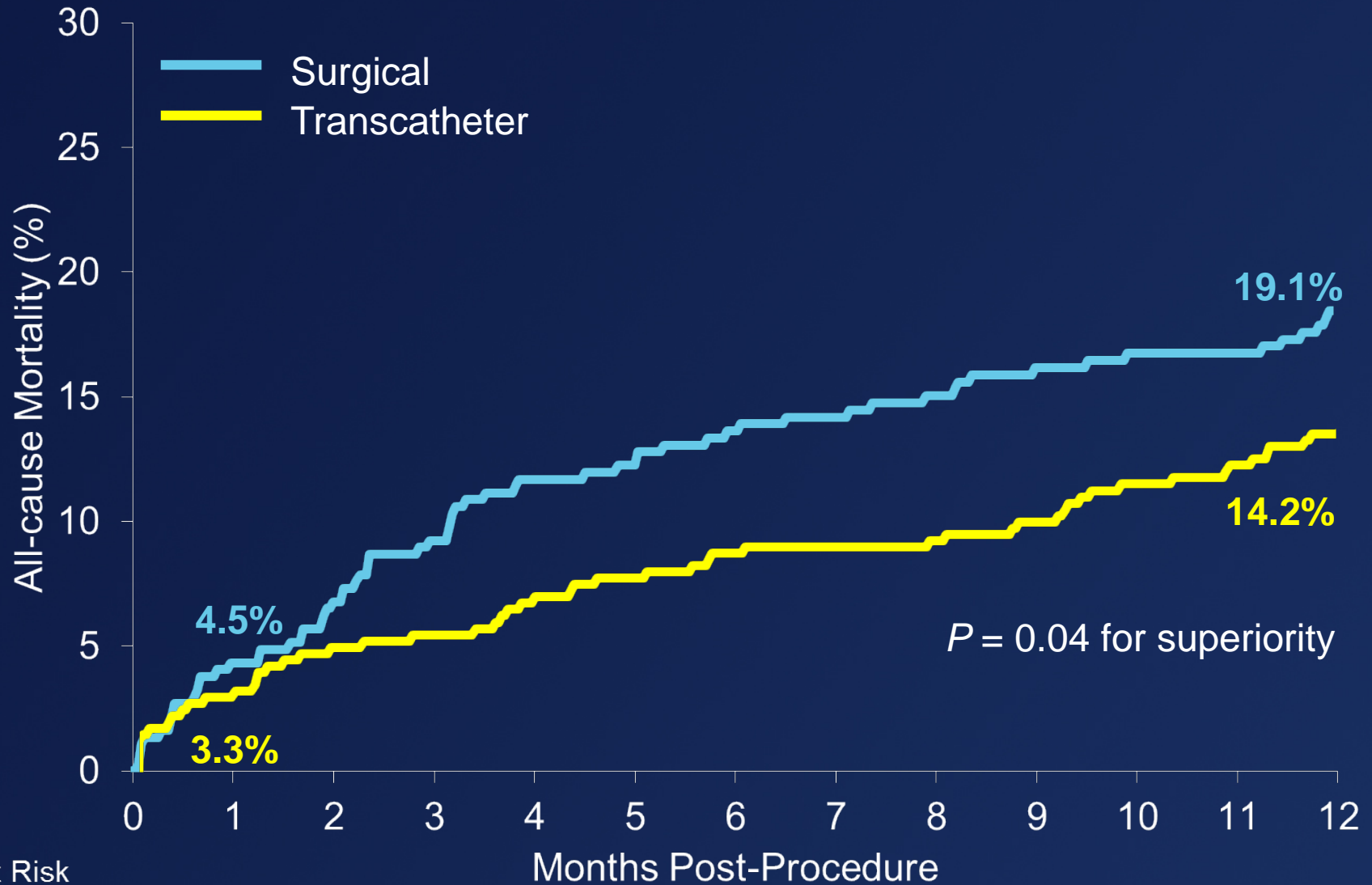
**Primary Endpoint:** All-cause mortality at 1 year

**Non-inferiority Testing:** TAVR with the CoreValve bioprosthesis was non-inferior to SAVR for 1 year all-cause mortality with a 7.5% non-inferiority margin

**Superiority Testing:** If the primary endpoint was met at the 1-sided 0.05 level, a subsequent test for superiority was performed at the 1-sided 0.05 level



# Primary Endpoint: 1 Year All-Cause Mortality



No. at Risk

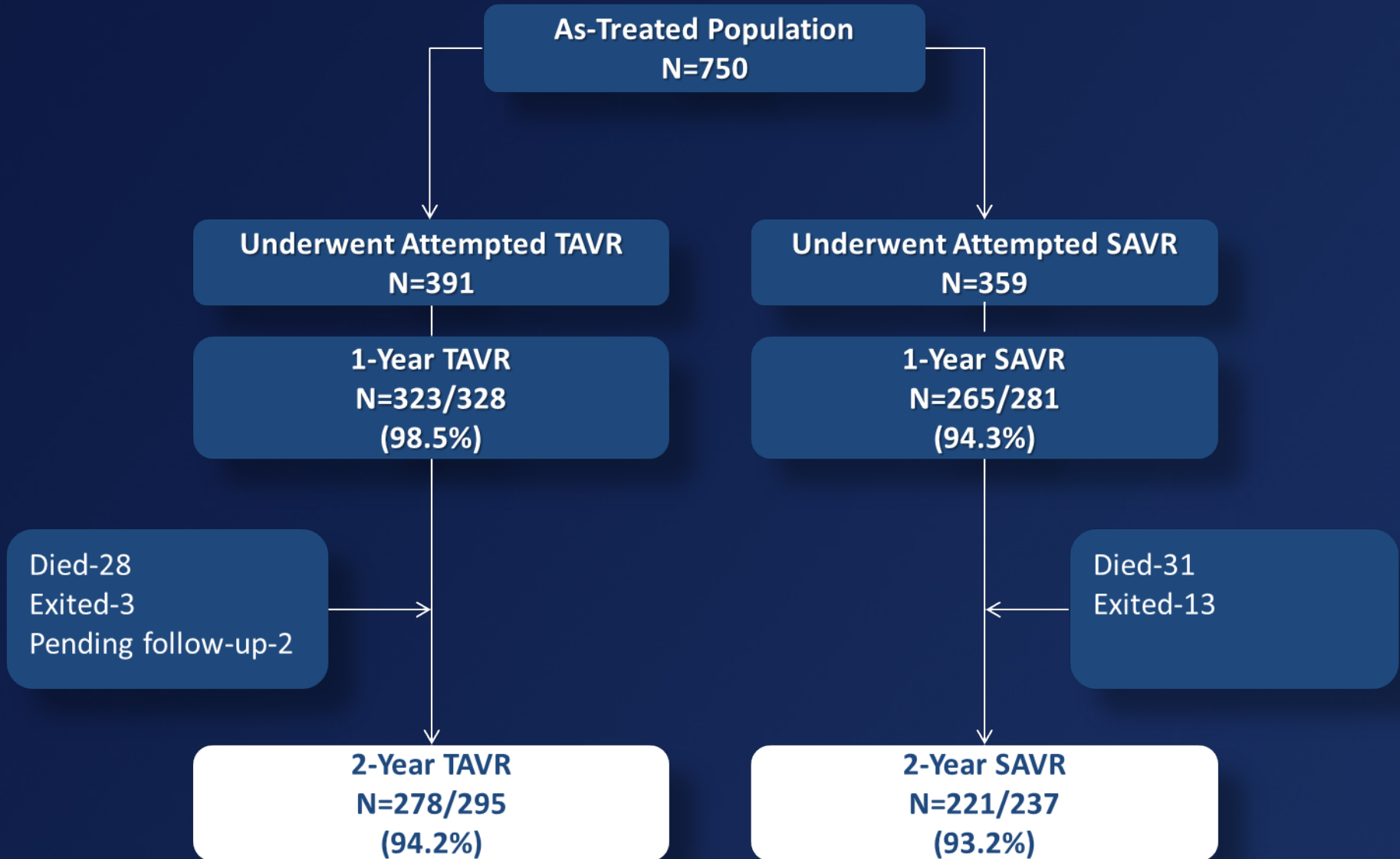
Surgical	357	341	297	274
Transcatheter	390	377	353	329

# Study Methodology

- Median patient follow-up of 24 [TAVR, 24.4; SAVR, 24.2] months
- The as-treated cohort was used as the primary analysis population
- Event rates are presented as Kaplan-Meier estimates and comparisons based on two-tailed log-rank test
- All patient had NIHSS assessment at baseline, post-procedure, discharge, at each follow up and within 24h of an aortic reintervention
- All echoes evaluated by an independent echocardiographic core laboratory

# CoreValve US Pivotal Trial High Risk 2-Year Results

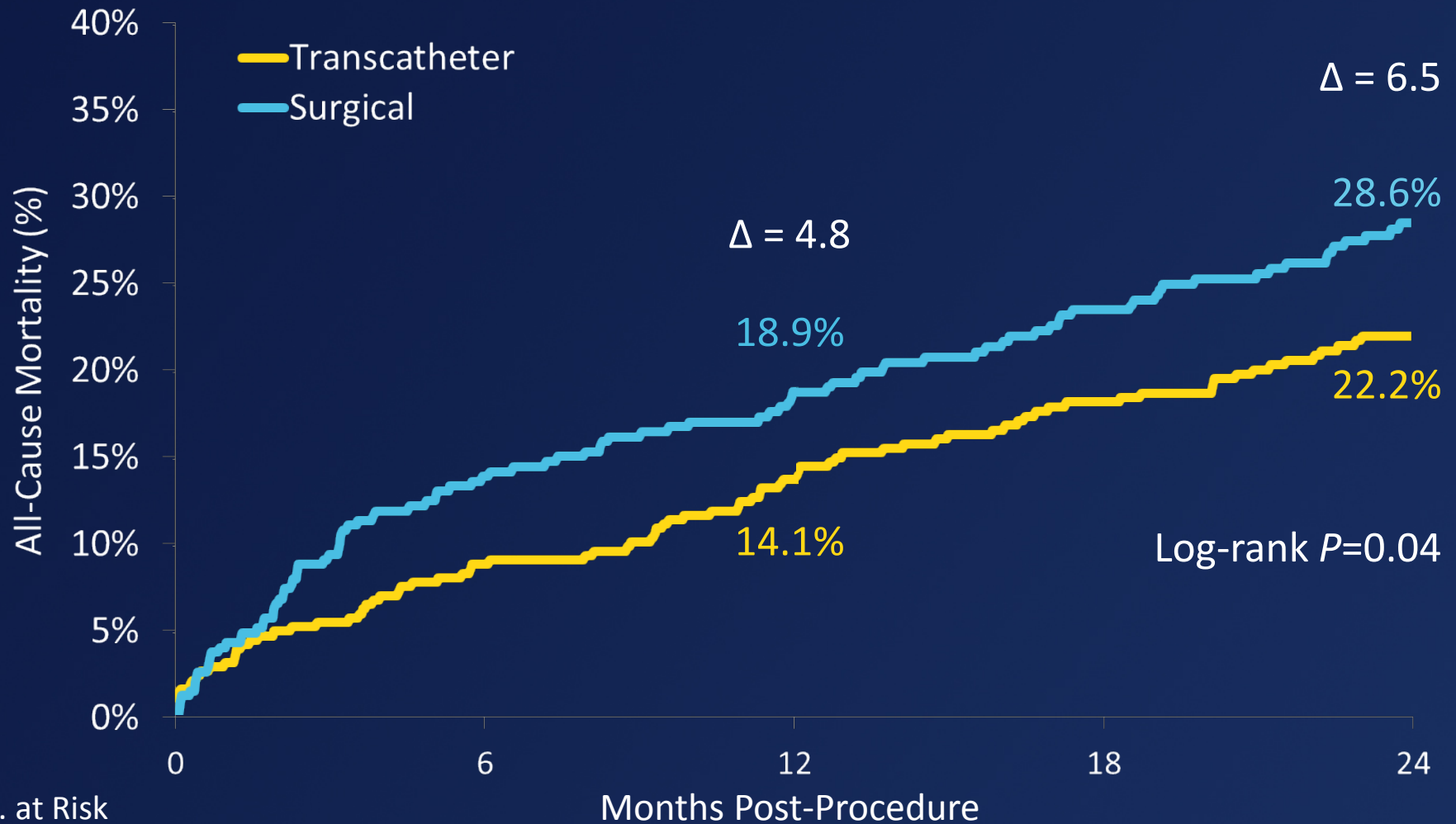
# Patient Flow



# Key Endpoints

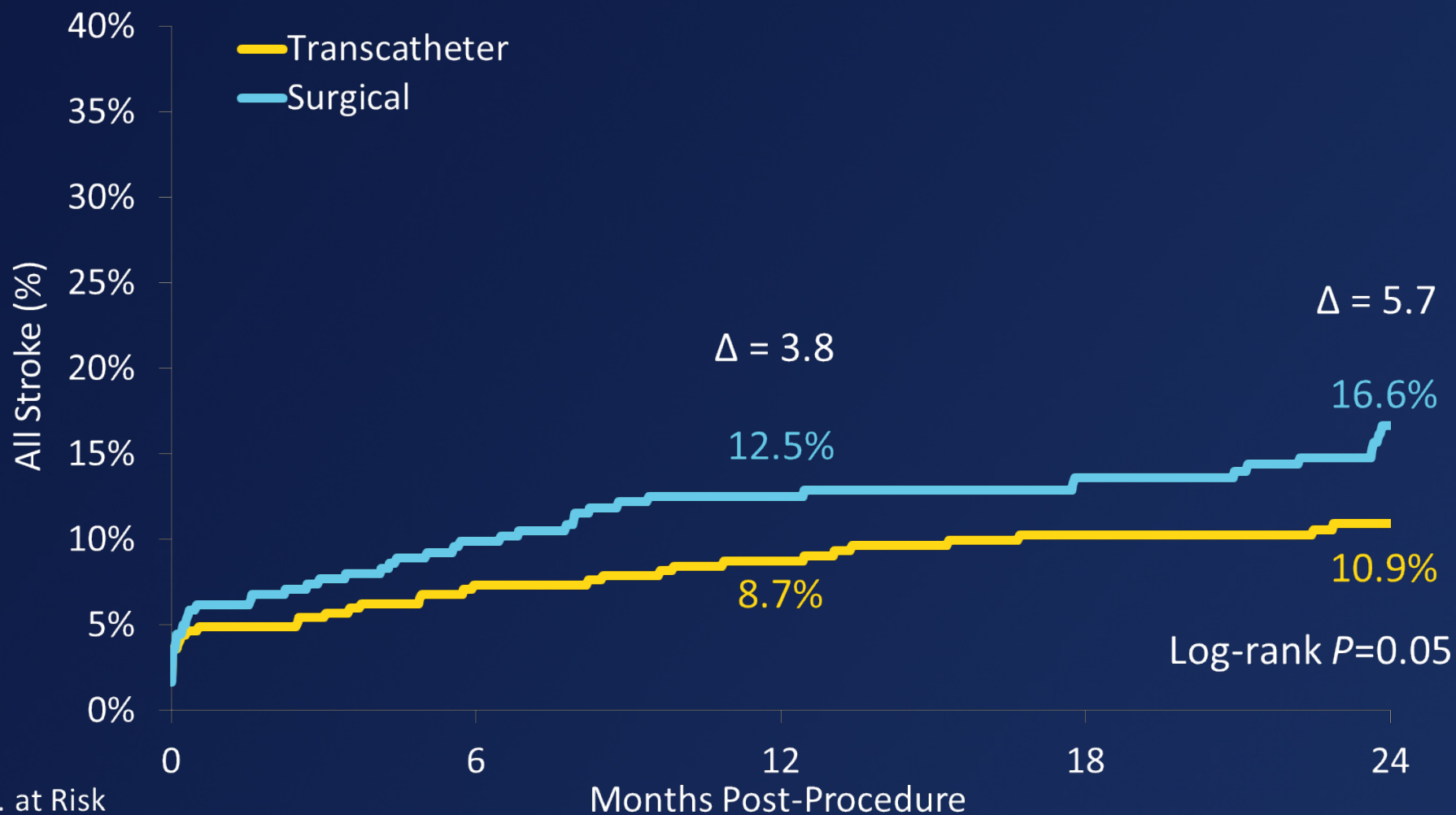
- 2-year mortality
- Neurological events
- MACCE
- Echocardiographic outcomes
- Also looked at;
  - Other clinical endpoints
  - Other adverse events

# All-Cause Mortality





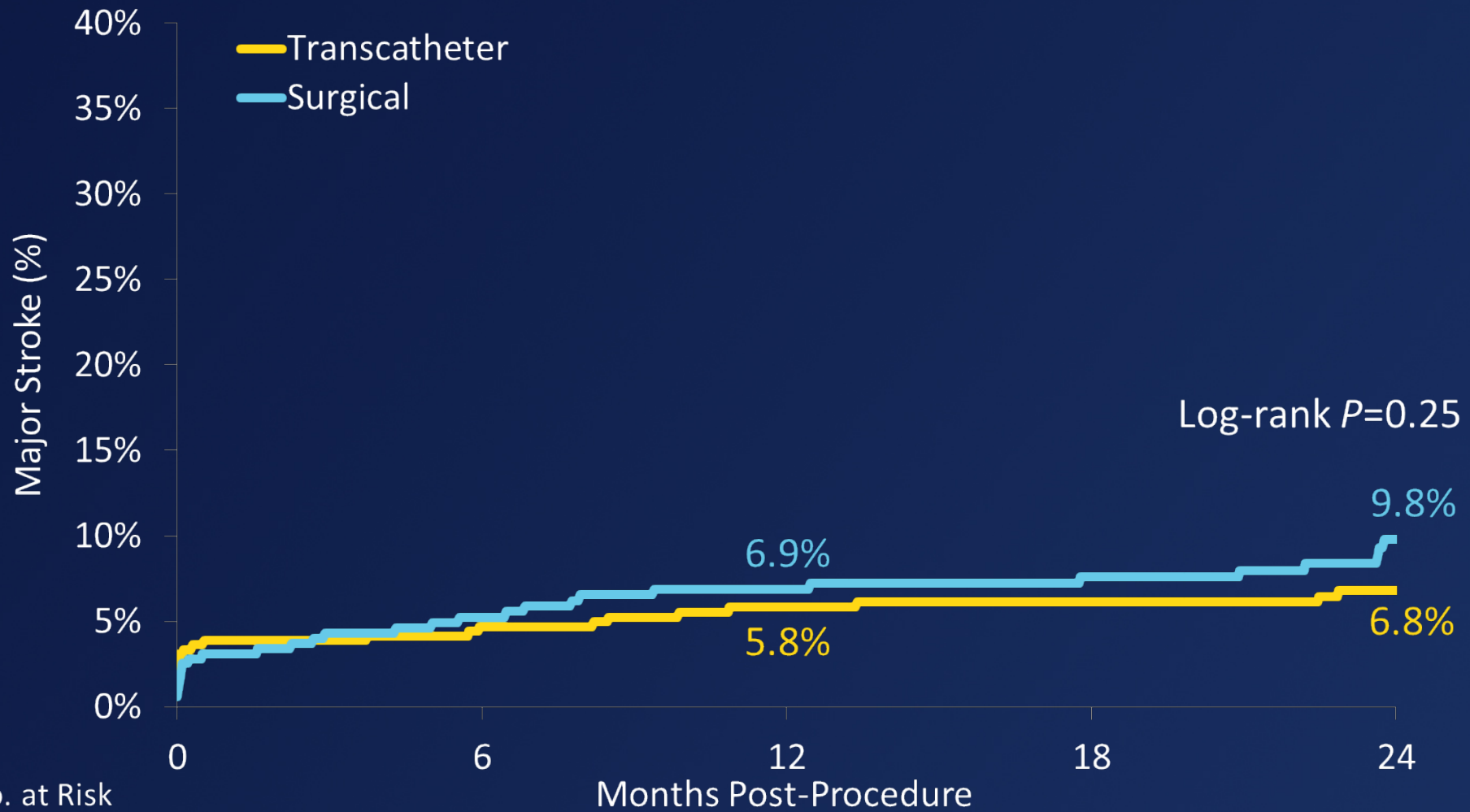
# All Stroke



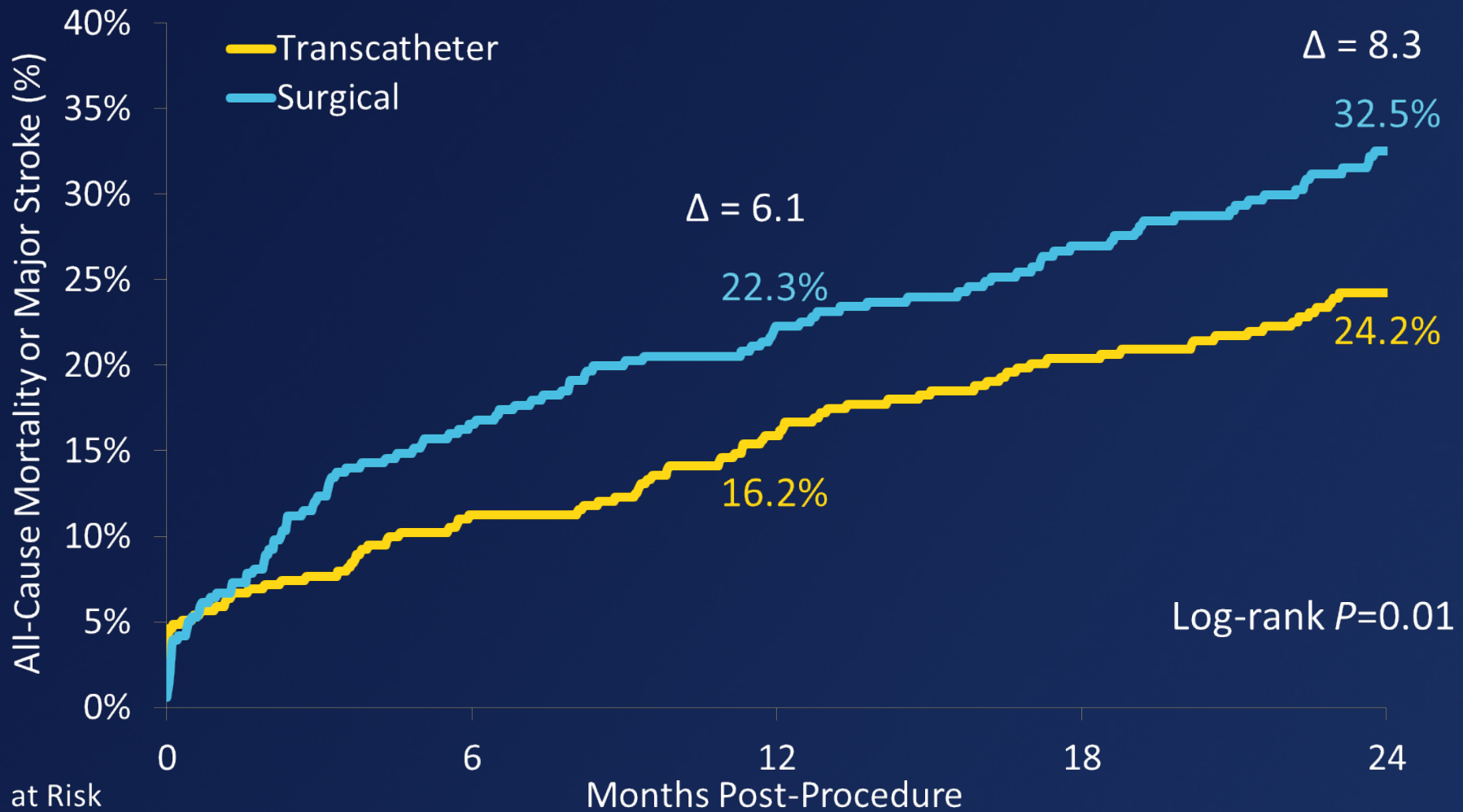
No. at Risk

Transcatheter	391	364	335	318	205
Surgical	359	324	281	256	169

# Major Stroke



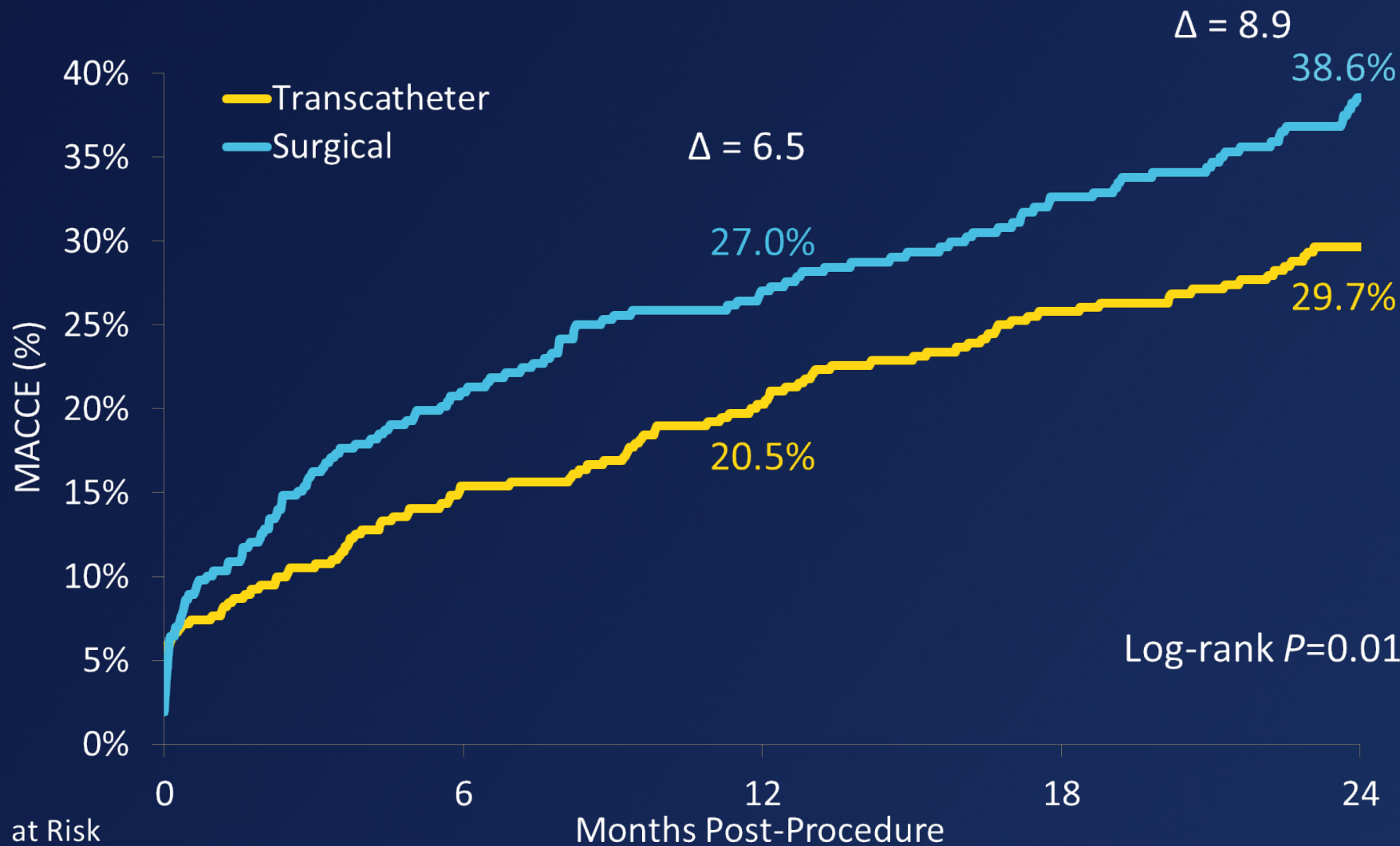
# All-Cause Mortality or Major Stroke



No. at Risk

Transcatheter	391	368	345	326	214
Surgical	359	335	296	271	184

# MACCE



# Other Clinical Endpoints

Events*	1 Month			1 Year			2 Years		
	TAVR	SAVR	<i>P</i>	TAVR	SAVR	<i>P</i>	TAVR	SAVR	<i>P</i>
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



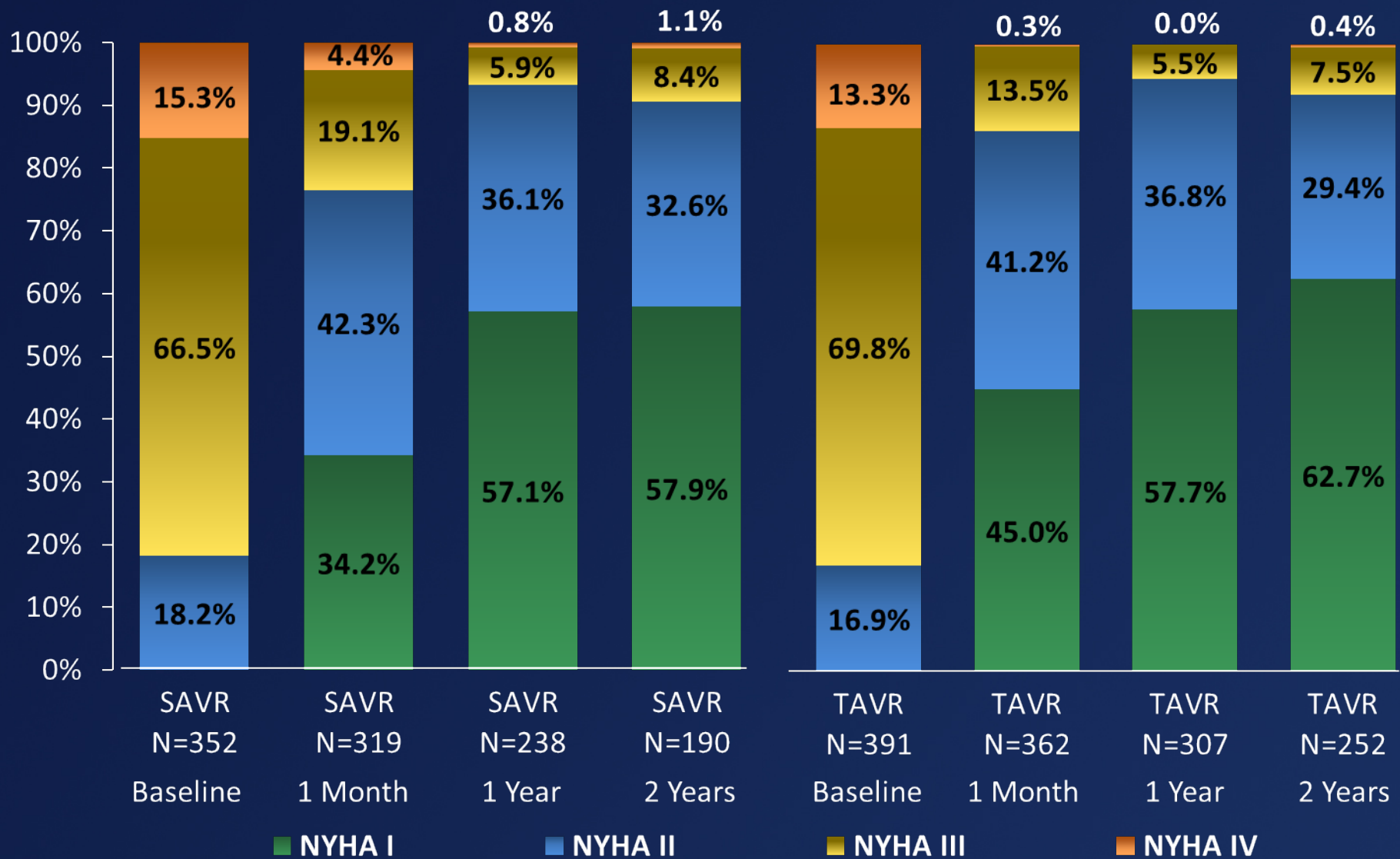
# Additional Adverse Events

Events*	1 Month			1 Year			2 Years		
	TAVR	SAVR	<i>P</i>	TAVR	SAVR	<i>P</i>	TAVR	SAVR	<i>P</i>
Reintervention	0.8	0.0	0.10	2.2	0.0	0.008	2.5	0.4	0.02
Surgical	0.5	0.0	0.18	0.8	0.0	0.10	0.8	0.4	0.38
Percutaneous	0.3	0.0	0.34	1.4	0.0	0.04	1.7	0.0	0.02
Valve endocarditis	0.0	0.0	---	0.6	1.3	0.31	0.9	1.7	0.35
Valve thrombosis	0.0	0.0	---	0.0	0.0	---	0.0	0.0	---
Embolization	0.0	0.0	---	0.0	0.0	---	0.0	0.0	---

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



# NYHA Class

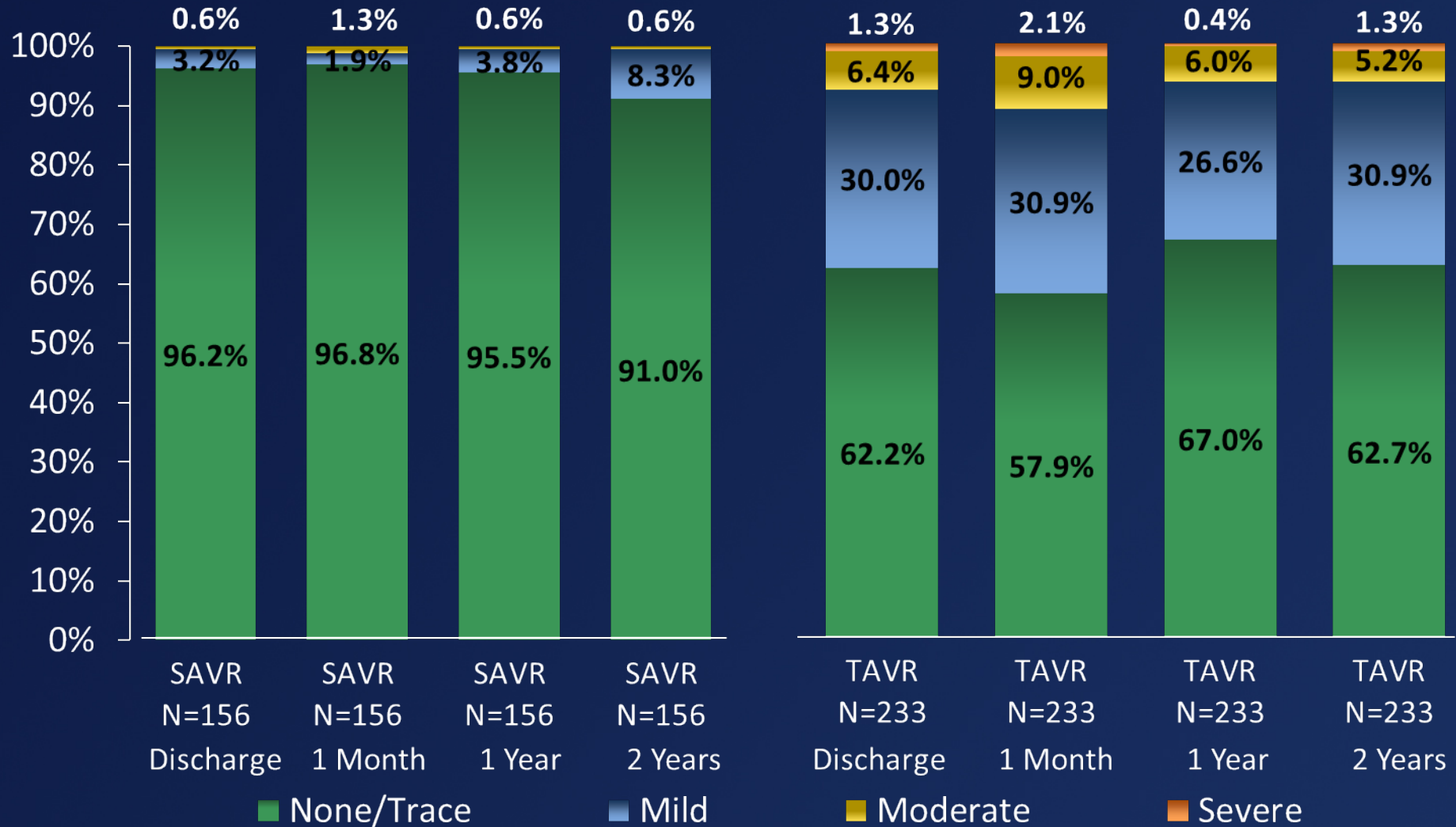


# Echocardiographic Findings

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

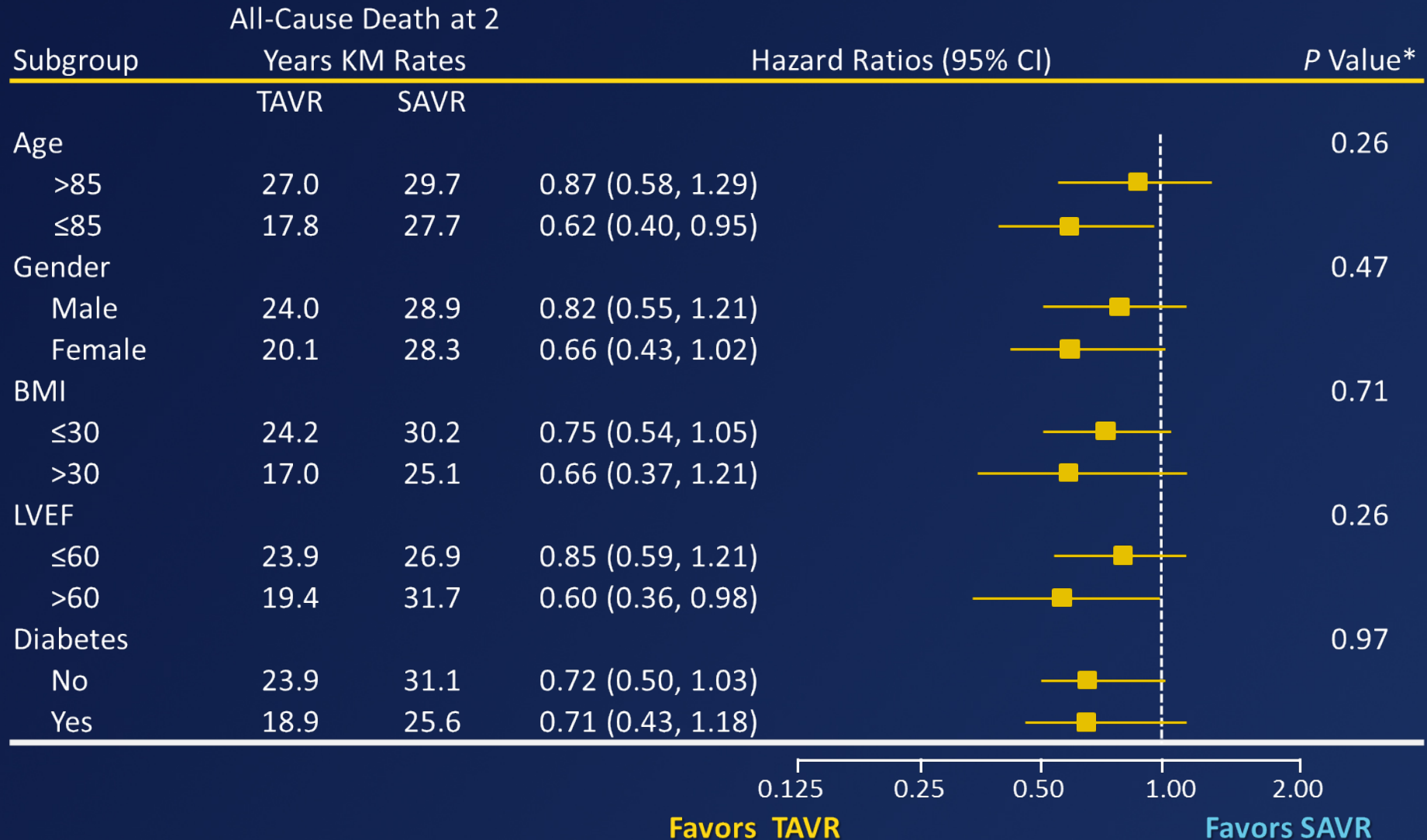


# Paravalvular Regurgitation (Paired)



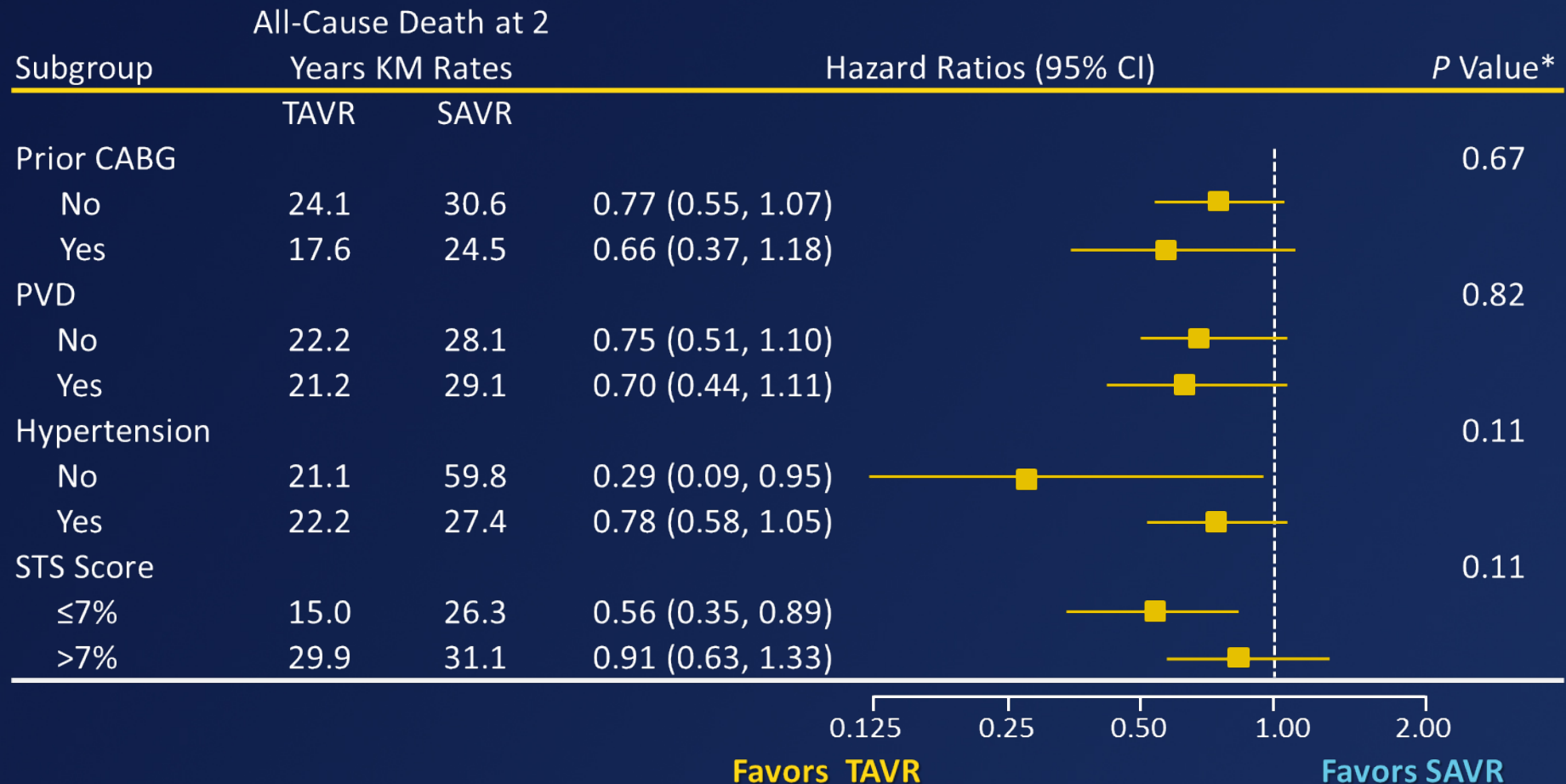
There was significantly lower PVL with SAVR over TAVR at each time point ( $P < 0.001$ )

# Subgroup Analysis for 2-Year Mortality



\*For interaction

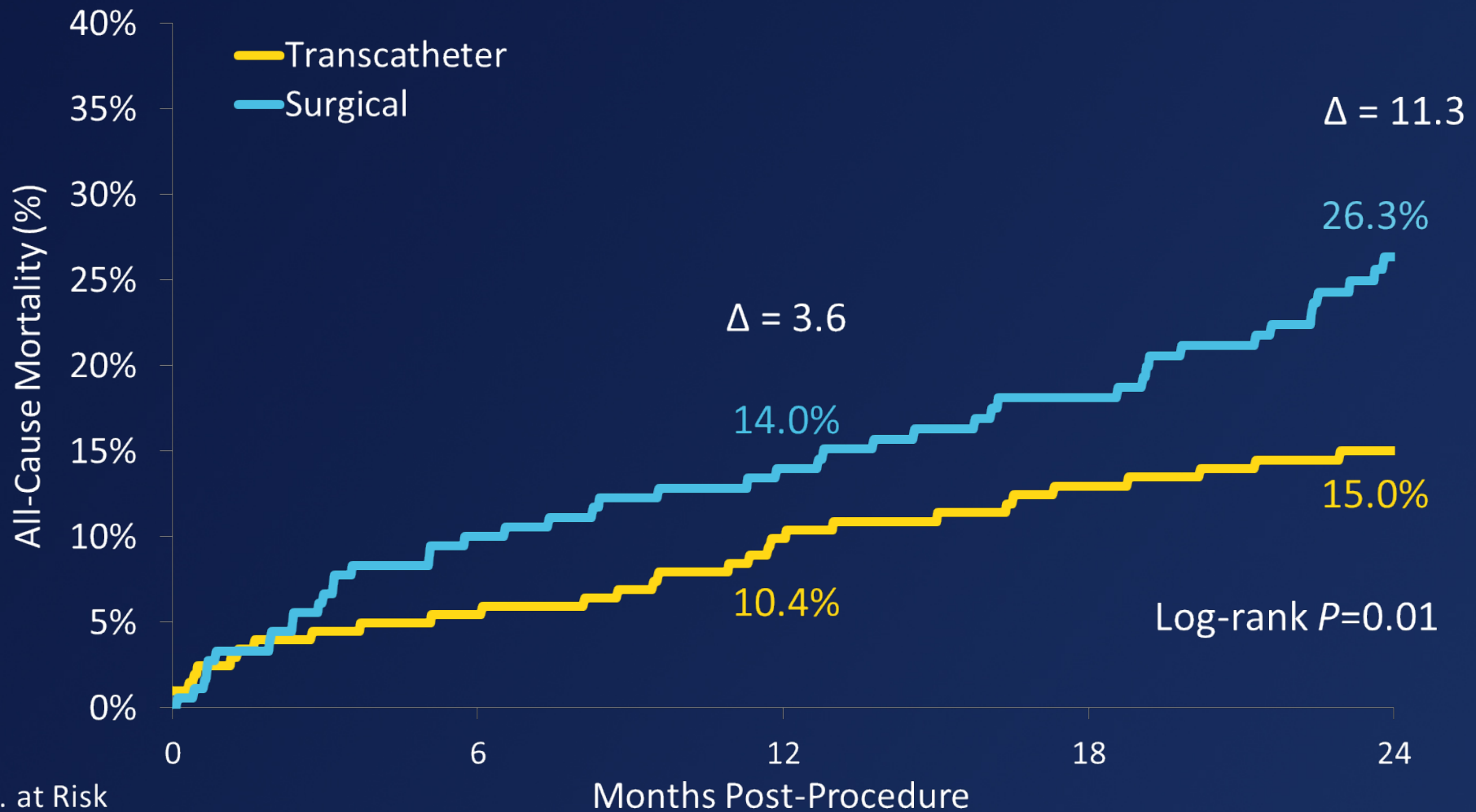
# Subgroup Analysis for 2-Year Mortality



\*For interaction



# All-Cause Mortality STS $\leq 7\%$



No. at Risk

Transcatheter	202	197	191	182	128
Surgical	181	174	161	151	93



# Conclusions

At 2 years for patients with symptomatic severe AS at increased risk of surgery;

- The superior survival seen at 1 year for TAVR over SAVR is maintained
- All stroke was less with TAVR over SAVR but major stroke showed no difference
- MACCE was significantly less with TAVR over SAVR
- Hemodynamics were superior for TAVR over SAVR at all time points without any structural valve failure
- Post-procedural AR showed a decrease in the TAVR group between 30 days and 1 year and this low level of moderate or severe PVL was maintained at 2 years
- TAVR was favored in every subgroup analysis

# Implications

Recommendations	COR	LOE
Surgical AVR is recommended in patients who meet an indication for AVR (Section 3.2.3) with low or intermediate surgical risk	I	A
For patients in whom TAVR or high-risk surgical AVR is being considered, members of a Heart Valve Team should collaborate to provide optimal patient care	I	C
TAVR is recommended in patients who meet an indication for AVR for AS who have a prohibitive surgical risk and a predicted post-TAVR survival >12 mo	I	B
TAVR is a reasonable alternative to surgical AVR in patients who meet an indication for AVR (Section 3.2.3) and who have high surgical risk (Section 2.5)	IIa	B
Percutaneous aortic balloon dilation may be considered as a bridge to surgical or transcatheter AVR in severely symptomatic patients with severe AS	IIb	C
TAVR is not recommended in patients in whom existing comorbidities would preclude the expected benefit from correction of AS	III: No Benefit	B

Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease. J Am Coll Cardiol. 2014;63:e57-185.

# Implications

These data suggest that:

TAVR with the self-expanding valve should be considered the preferred treatment in patients with symptomatic severe AS at increased risk for surgery

**Thank You**

On Behalf of the CoreValve US Investigators