# 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

# 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.

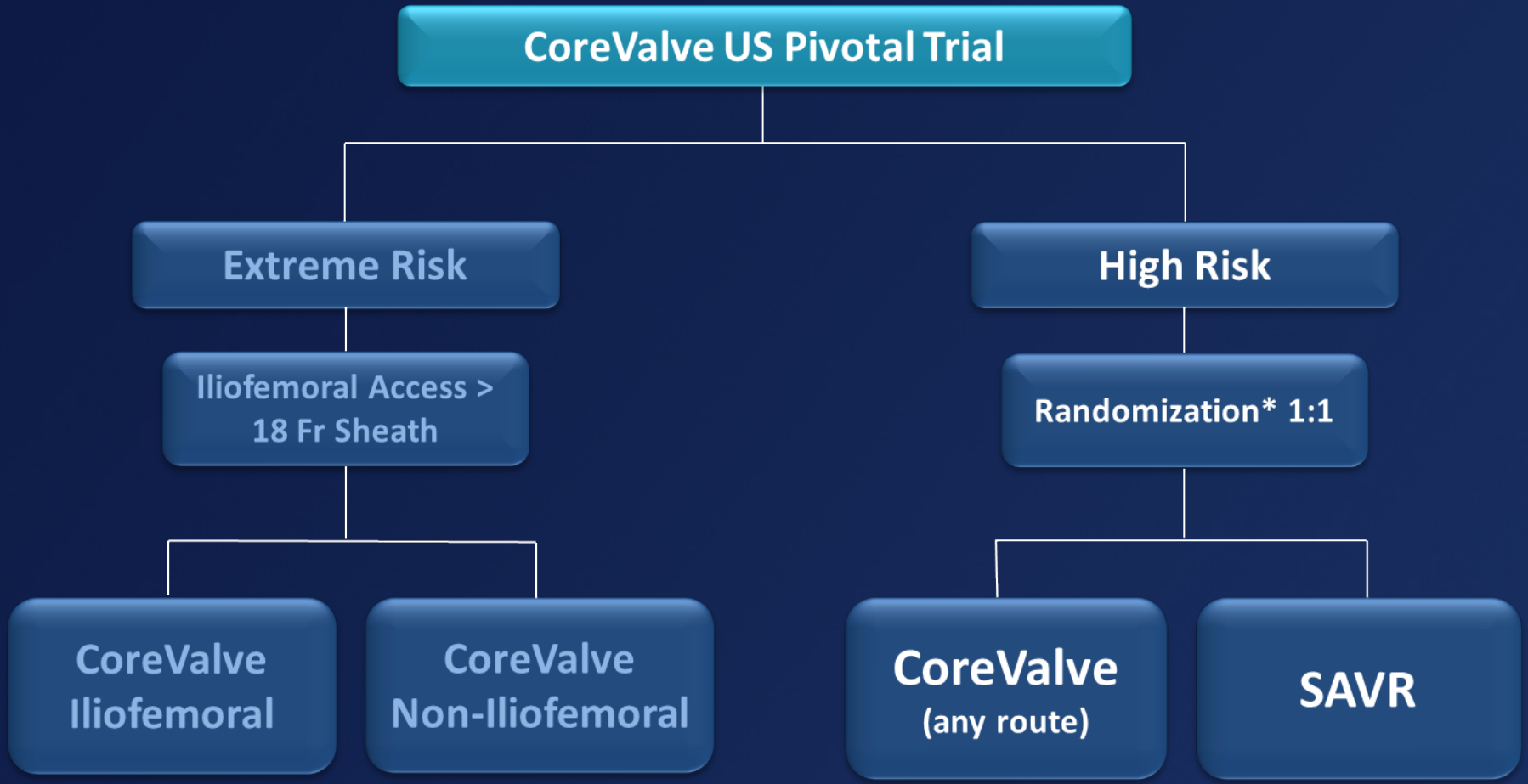
# Background

- 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.

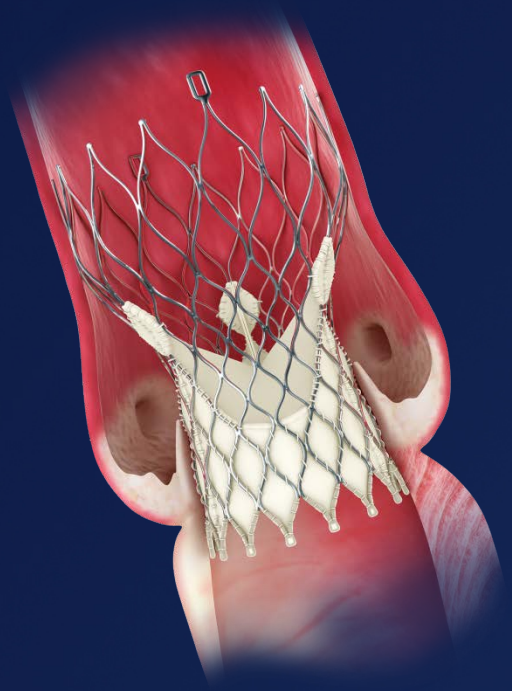
Adams DH, Popma JJ, Reardon, MJ, et al. New Engl J Med. 2014; 370: 1790-8.

# Pivotal Trial Design



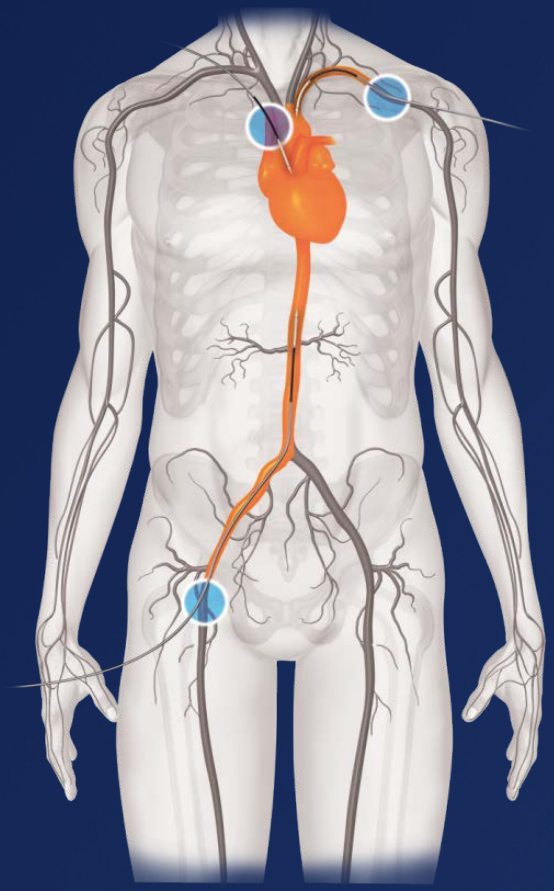

* Randomization stratified by intended access site

# 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 ≤0.8 $cm^2$ or AVAI ≤0.5 $cm^2/m^2$ AND mean gradient >40 mm Hg or peak velocity >4 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 (≤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

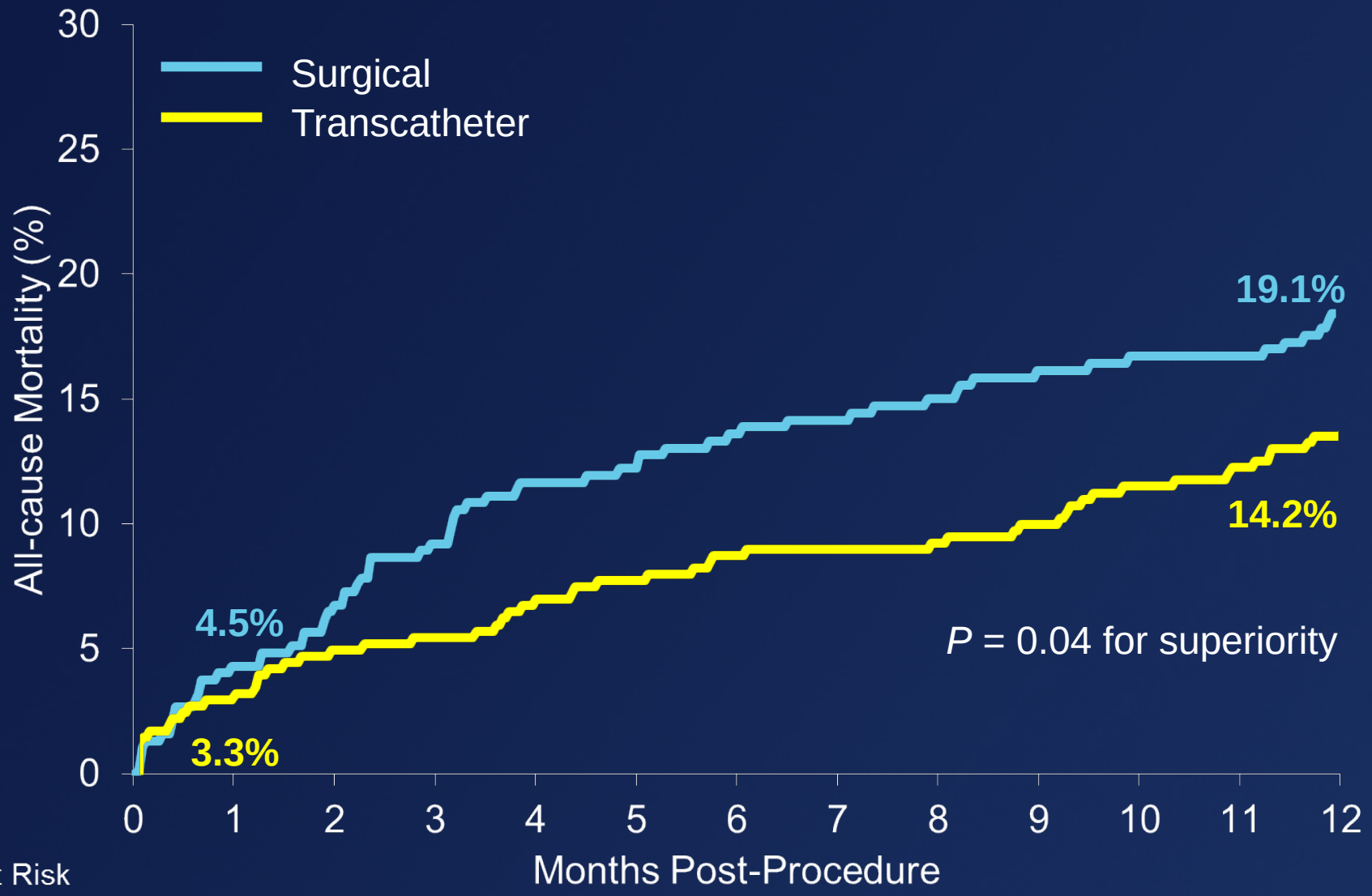
# Primary Endpoint

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



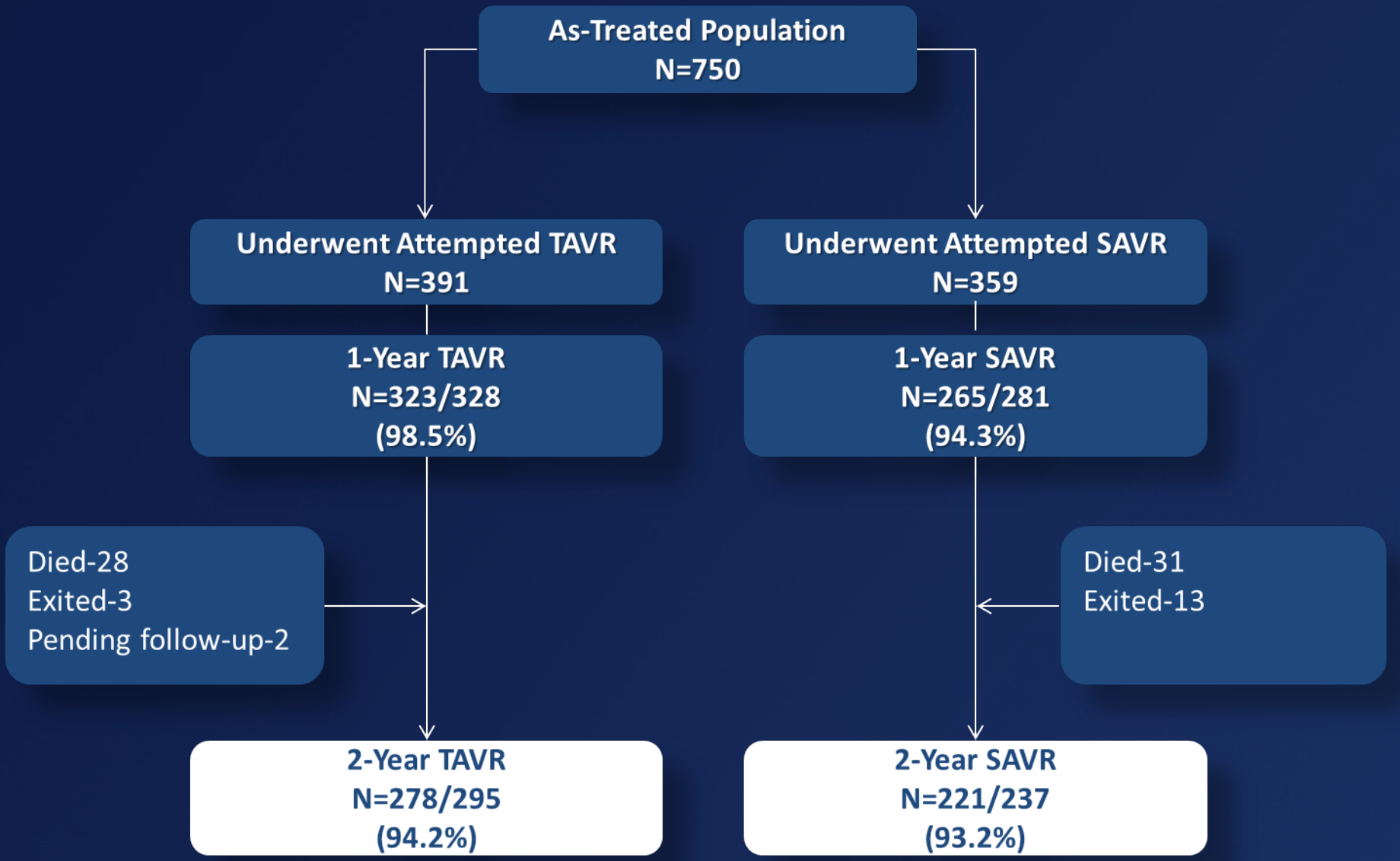

| No. at Risk | | | | | |
|---|---|---|---|---|---|
| Surgical | 357 | 341 | 297 | 274 |
| Transcatheter | 390 | 377 | 353 | 329 |

# 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

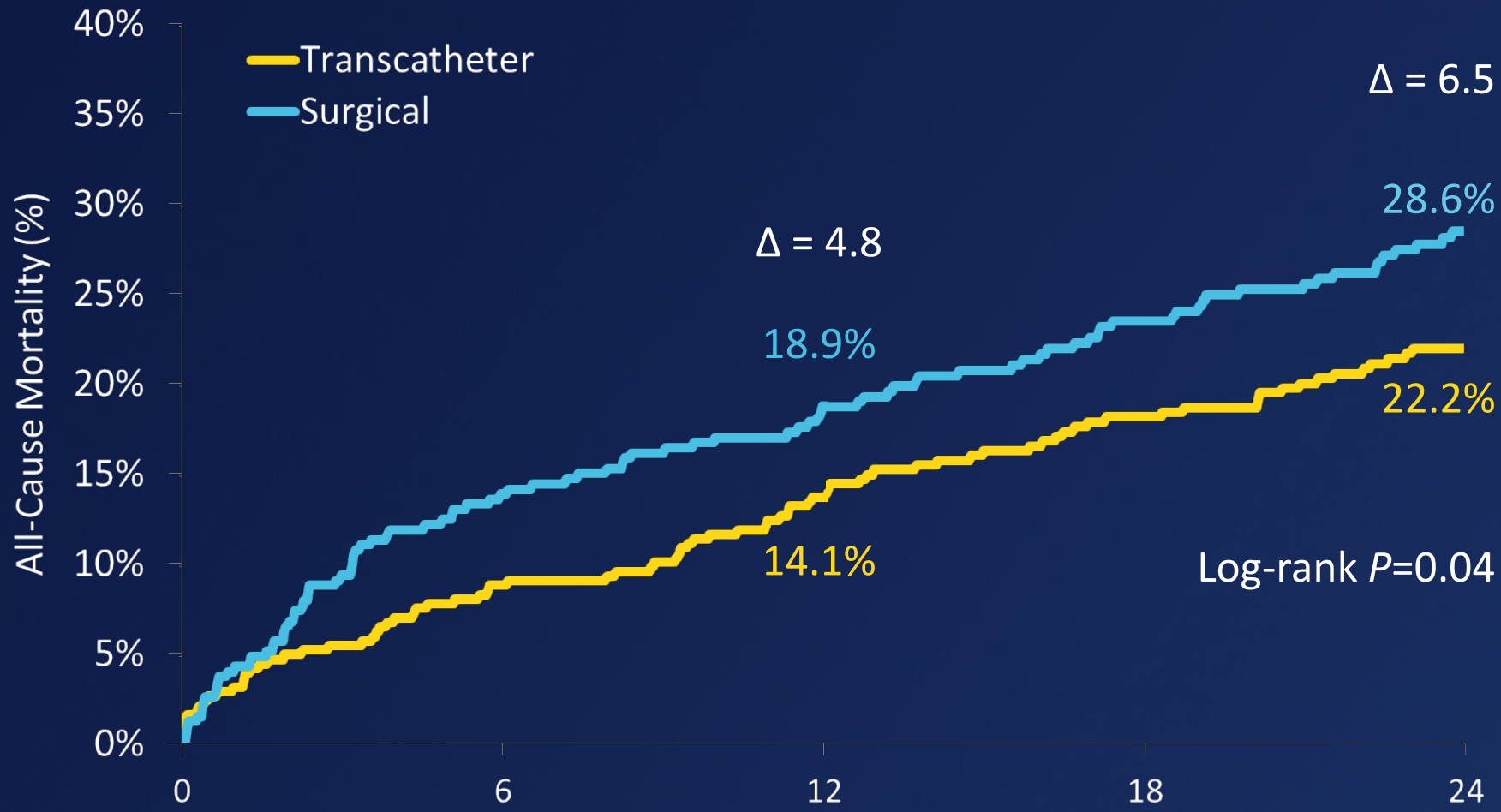
# Patient Flow



# Key Endpoints

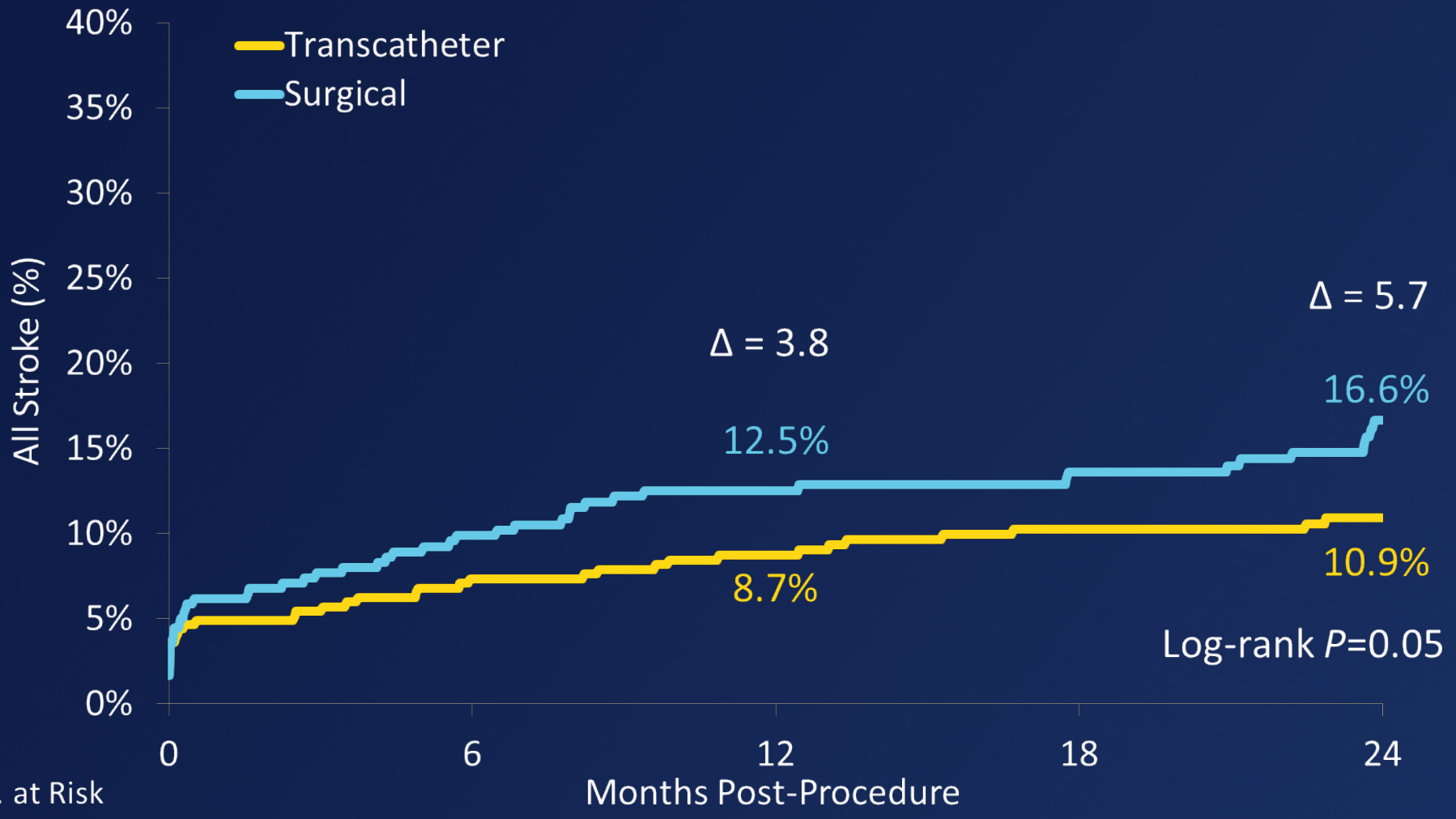
- 2-year mortality
- Neurological events
- MACCE
- Echocardiographic outcomes
- Also looked at;
  - Other clinical endpoints
  - Other adverse events

# All-Cause Mortality



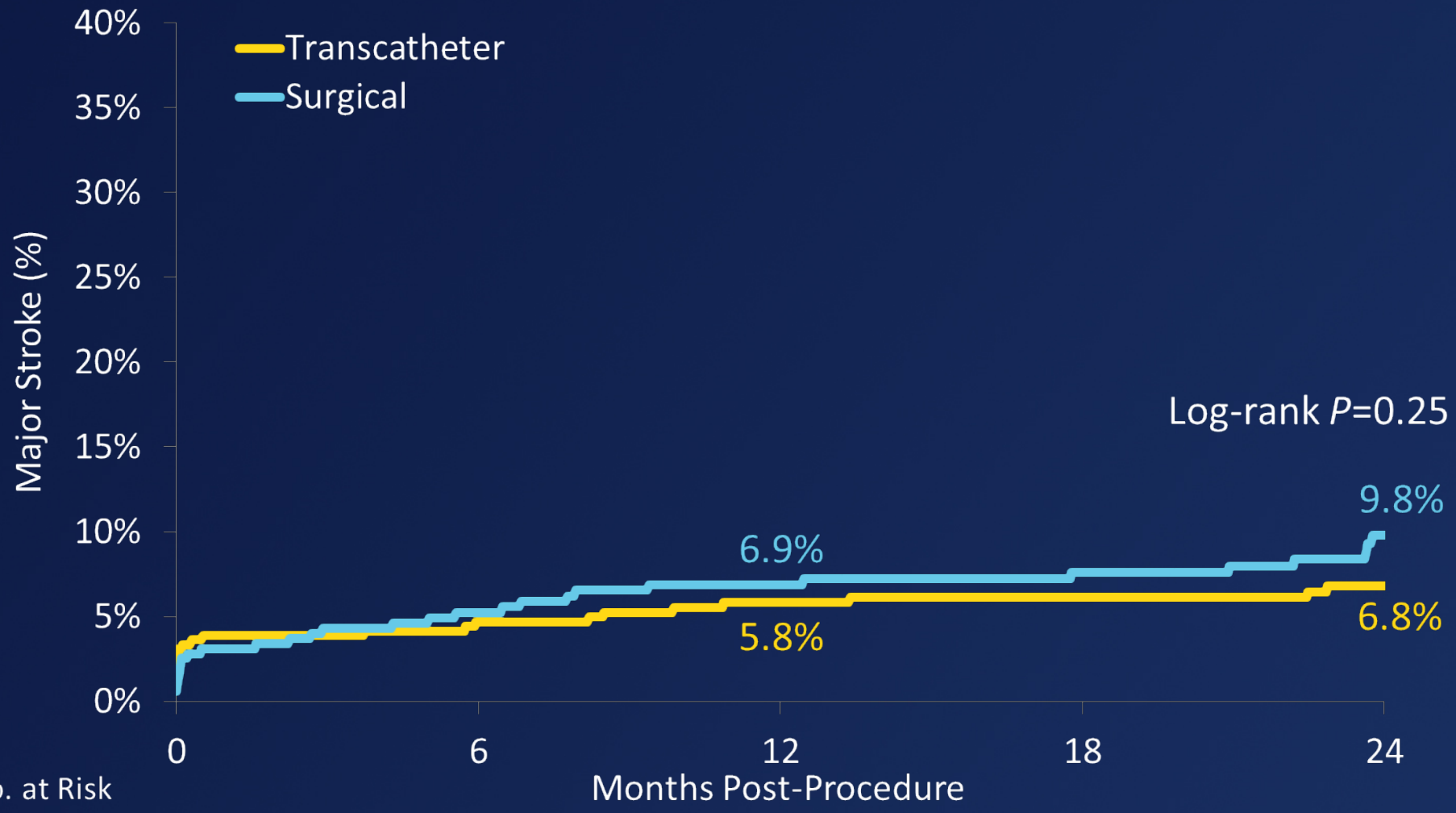

| No. at Risk | | | | | |
|---|---|---|---|---|---|
| Transcatheter | 391 | 378 | 354 | 334 | 219 |
| Surgical | 359 | 343 | 304 | 282 | 191 |

# All Stroke

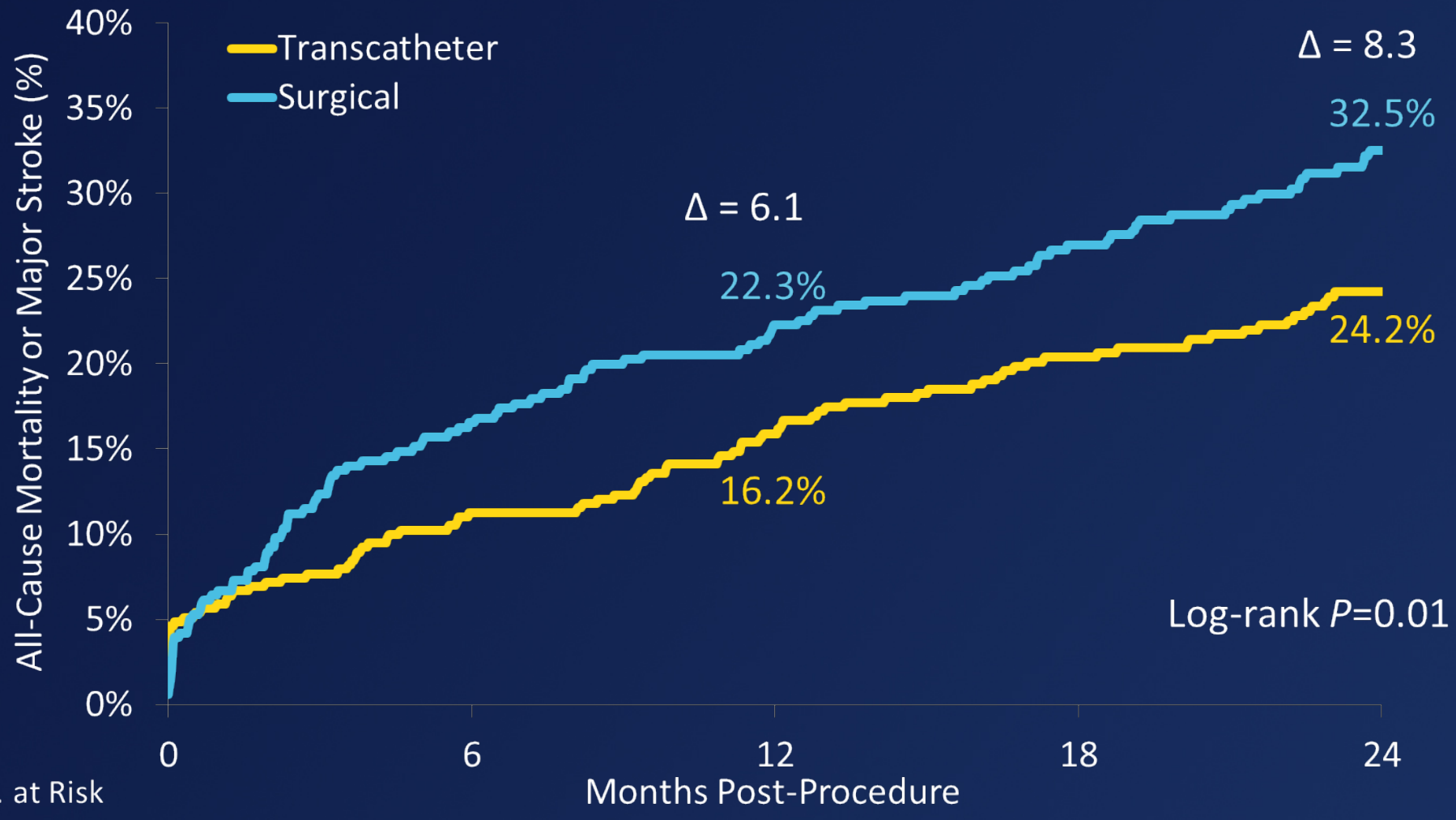



| No. at Risk | | | | | |
|---|---|---|---|---|---|
| Transcatheter | 391 | 364 | 335 | 318 | 205 |
| Surgical | 359 | 324 | 281 | 256 | 169 |

# Major Stroke

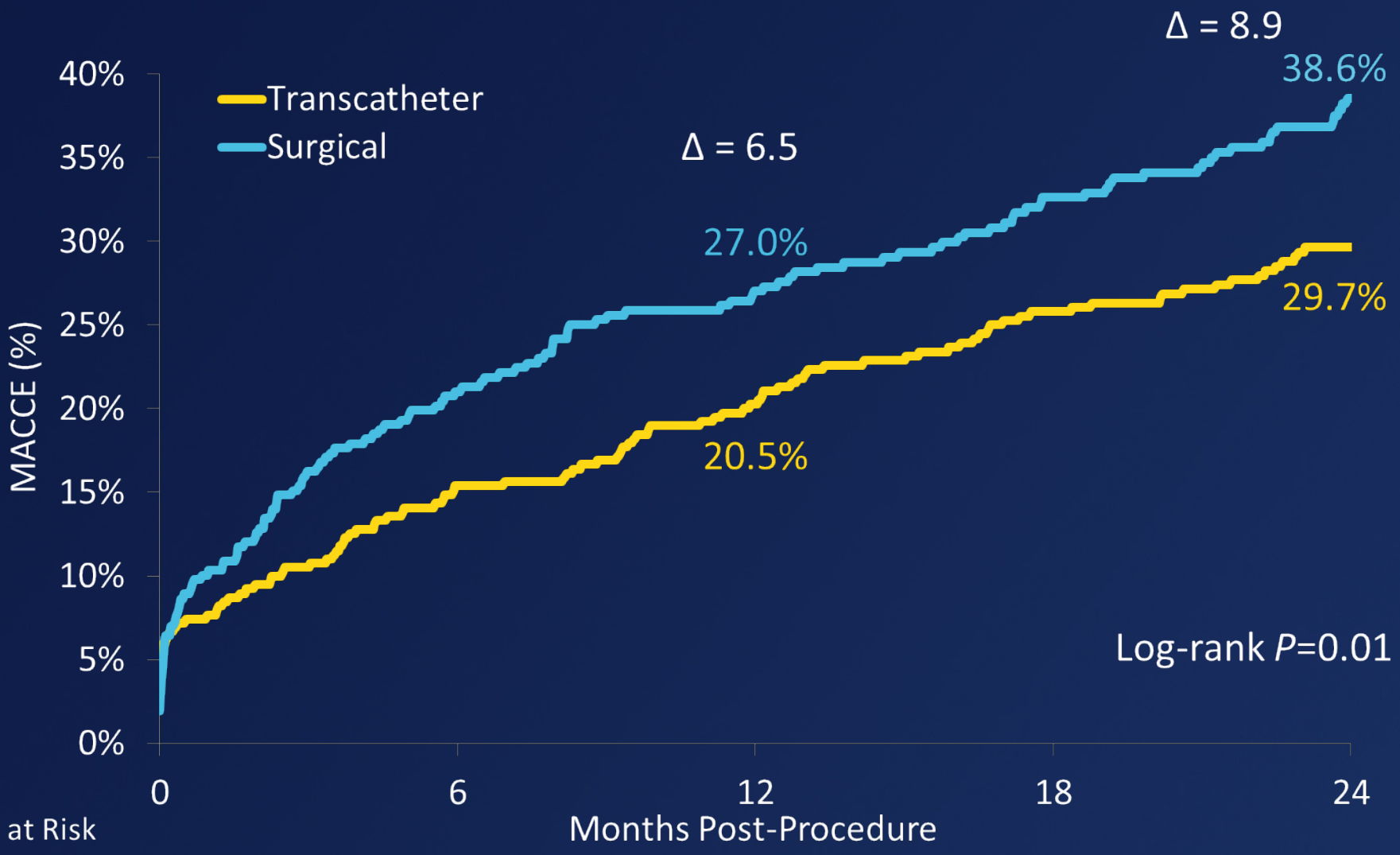


# All-Cause Mortality or Major Stroke




| No. at Risk | | | | | |
|---|---|---|---|---|---|
| Transcatheter | 391 | 368 | 345 | 326 | 214 |
| Surgical | 359 | 335 | 296 | 271 | 184 |

# MACCE




| No. at Risk | | | | | |
|---|---|---|---|---|---|
| Transcatheter | 391 | 361 | 329 | 309 | 197 |
| Surgical | 359 | 322 | 280 | 254 | 166 |

# 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 |

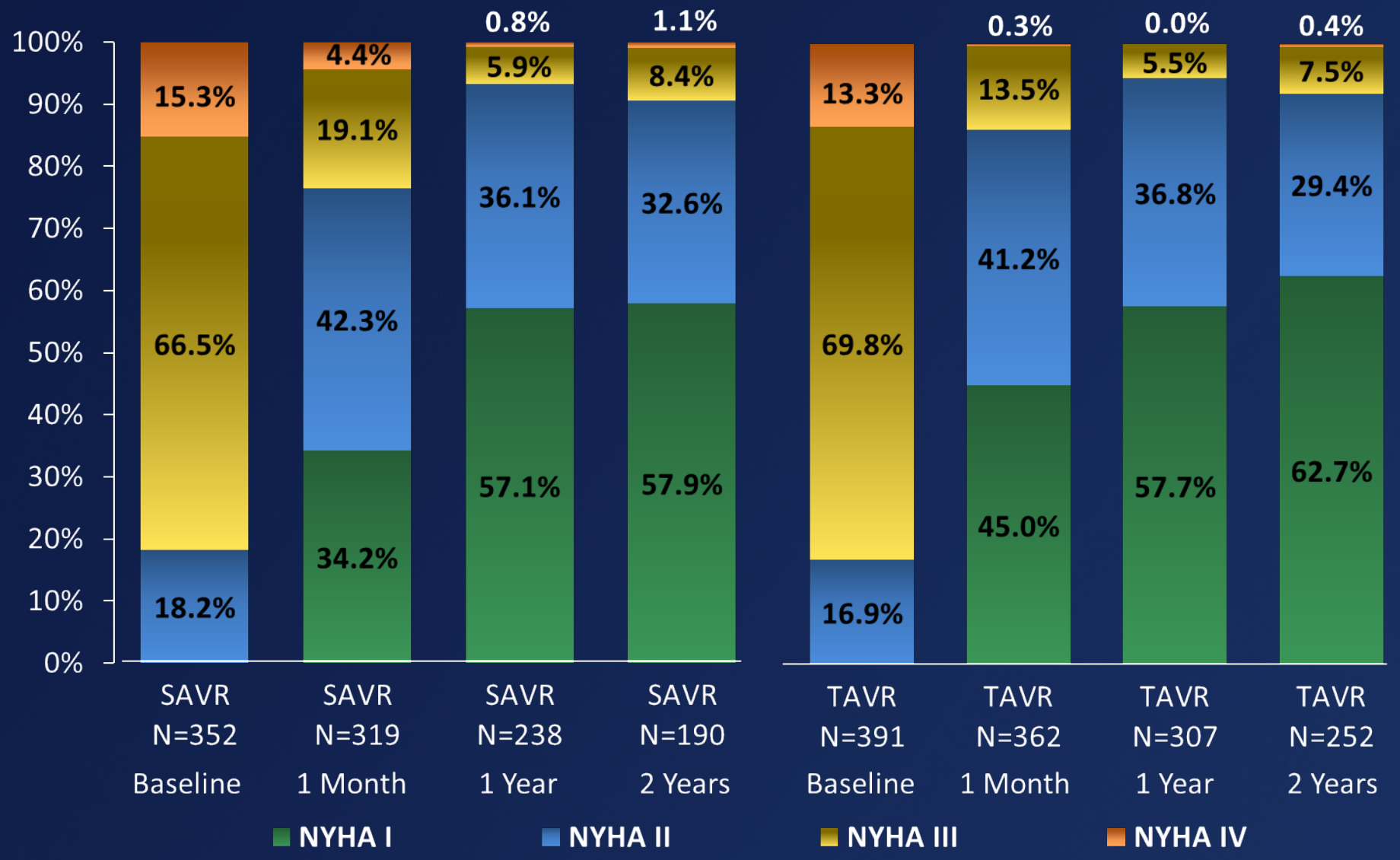
* Percentages reported are Kaplan-Meier estimates and log-rank *P* values

# Additional Adverse Events

| Events* | 1 Month | | | 1 Year | | | 2 Years | | |
|---|---|---|---|---|---|---|---|---|---|
| | TAVR | SAVR | *P* | TAVR | SAVR | *P* | TAVR | SAVR | *P* |
| 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

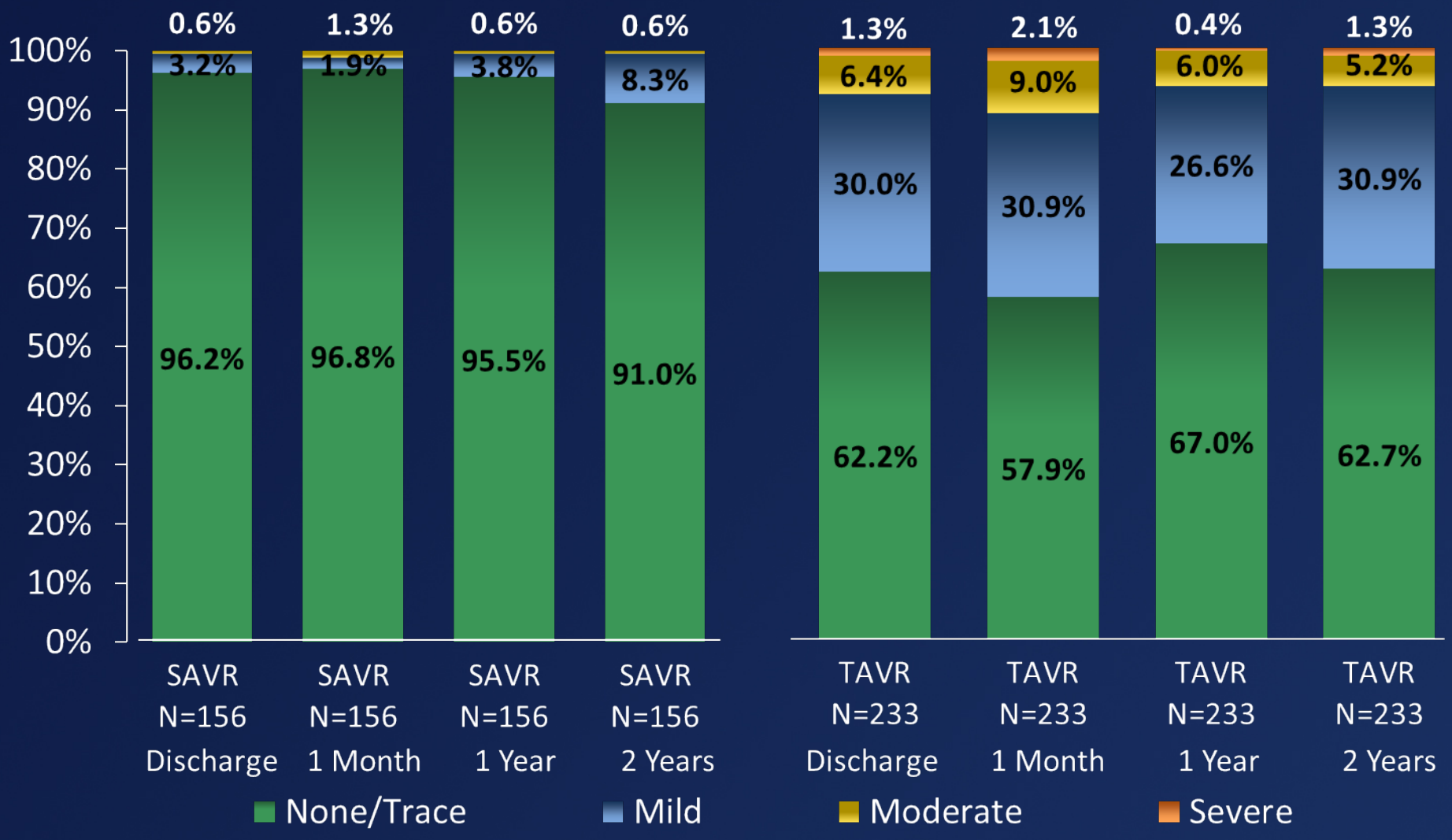
# NYHA Class


100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
15.3%
66.5%
18.2%
4.4%
19.1%
42.3%
34.2%
0.8%
5.9%
36.1%
57.1%
1.1%
8.4%
32.6%
57.9%
13.3%
69.8%
16.9%
0.3%
13.5%
41.2%
45.0%
0.0%
5.5%
36.8%
57.7%
0.4%
7.5%
29.4%
62.7%
SAVR N=352 Baseline
SAVR N=319 1 Month
SAVR N=238 1 Year
SAVR N=190 2 Years
TAVR N=391 Baseline
TAVR N=362 1 Month
TAVR N=307 1 Year
TAVR N=252 2 Years
NYHA I
NYHA II
NYHA III
NYHA IV

# Echocardiographic Findings

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

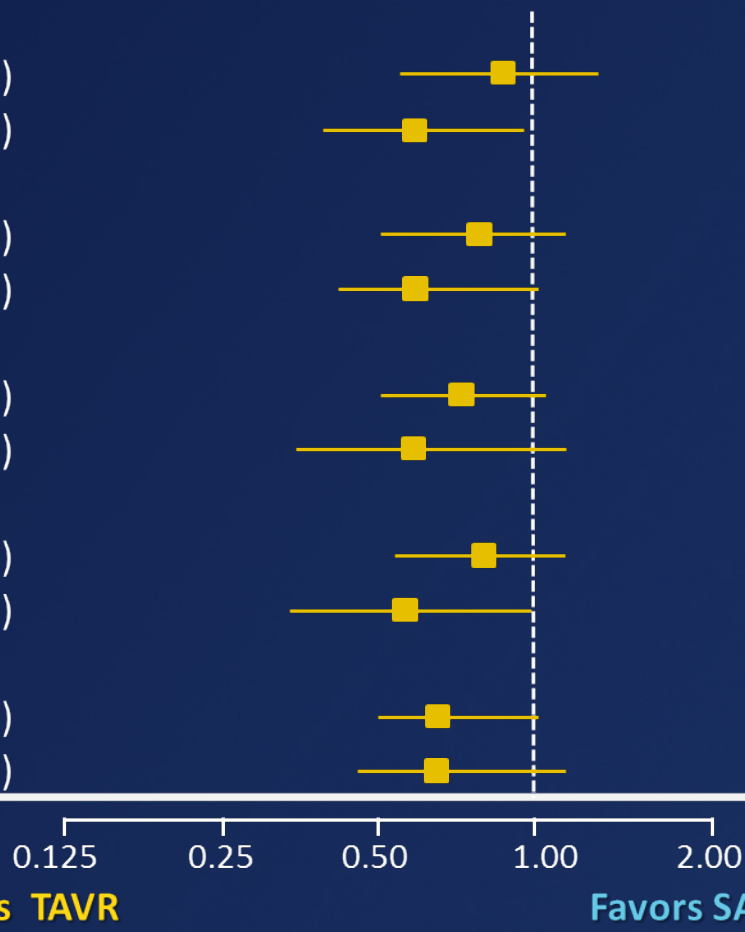
# Paravalvular Regurgitation (Paired)




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

# Subgroup Analysis for 2-Year Mortality

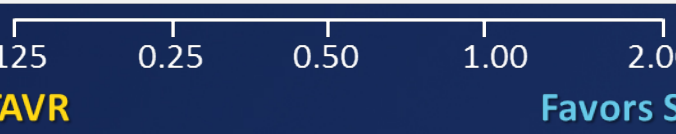
| Subgroup | All-Cause Death at 2 Years KM Rates | | Hazard Ratios (95% CI) | *P* Value* |
|---|---|---|---|---|
| | TAVR | SAVR | | |
| Age | | | | 0.26 |
| >85 | 27.0 | 29.7 | 0.87 (0.58, 1.29) | |
| ≤85 | 17.8 | 27.7 | 0.62 (0.40, 0.95) | |
| Gender | | | | 0.47 |
| Male | 24.0 | 28.9 | 0.82 (0.55, 1.21) | |
| Female | 20.1 | 28.3 | 0.66 (0.43, 1.02) | |
| BMI | | | | 0.71 |
| ≤30 | 24.2 | 30.2 | 0.75 (0.54, 1.05) | |
| >30 | 17.0 | 25.1 | 0.66 (0.37, 1.21) | |
| LVEF | | | | 0.26 |
| ≤60 | 23.9 | 26.9 | 0.85 (0.59, 1.21) | |
| >60 | 19.4 | 31.7 | 0.60 (0.36, 0.98) | |
| Diabetes | | | | 0.97 |
| No | 23.9 | 31.1 | 0.72 (0.50, 1.03) | |
| Yes | 18.9 | 25.6 | 0.71 (0.43, 1.18) | |




*For interaction

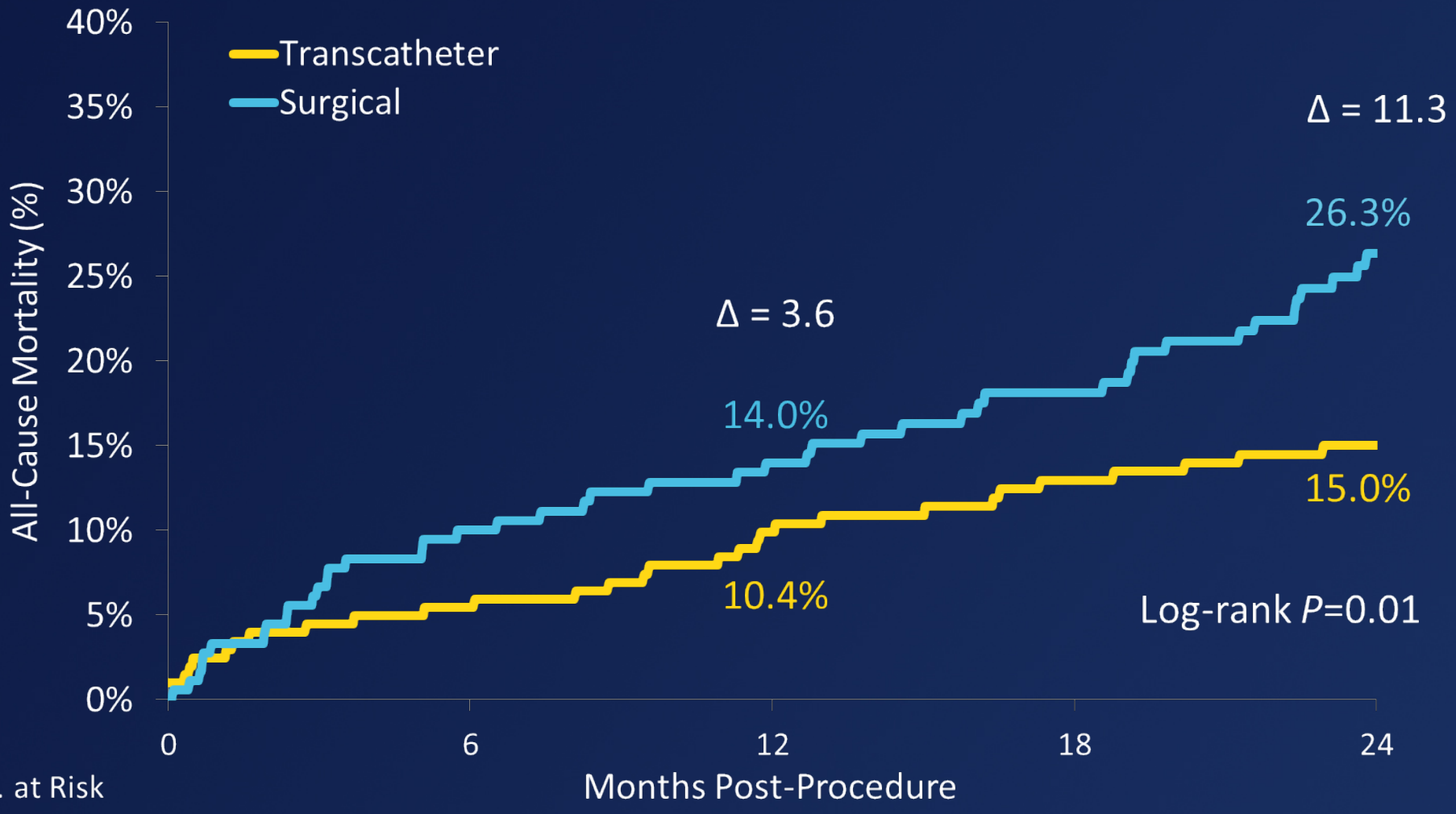
# Subgroup Analysis for 2-Year Mortality

| Subgroup | All-Cause Death at 2 Years KM Rates | | Hazard Ratios (95% CI) | *P* Value* |
|---|---|---|---|---|
| | TAVR | SAVR | | |
| Prior CABG | | | | 0.67 |
| No | 24.1 | 30.6 | 0.77 (0.55, 1.07) | |
| Yes | 17.6 | 24.5 | 0.66 (0.37, 1.18) | |
| PVD | | | | 0.82 |
| No | 22.2 | 28.1 | 0.75 (0.51, 1.10) | |
| Yes | 21.2 | 29.1 | 0.70 (0.44, 1.11) | |
| Hypertension | | | | 0.11 |
| No | 21.1 | 59.8 | 0.29 (0.09, 0.95) | |
| Yes | 22.2 | 27.4 | 0.78 (0.58, 1.05) | |
| STS Score | | | | 0.11 |
| ≤7% | 15.0 | 26.3 | 0.56 (0.35, 0.89) | |
| >7% | 29.9 | 31.1 | 0.91 (0.63, 1.33) | |




*For interaction

# All-Cause Mortality STS ≤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, Otta 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